UC Irvine
UC Irvine Electronic Theses and Dissertations

Title
An Enantiospecific Formal Synthesis of (+)-7,20-Diisocyanoadociane

Permalink
https://escholarship.org/uc/item/3w69n33q

Author
Roosen, Philipp Christopher

Publication Date
2016

Peer reviewed|Thesis/dissertation

eScholarship.org Powered by the California Digital Library
University of California

UNIVERSITY OF CALIFORNIA,
IRVINE

An Enantiospecific Formal Synthesis of (+)-7,20-Diisocyanoadociane

DISSERTATION

submitted in partial satisfaction of the requirements for the degree of

DOCTOR OF PHILOSOPHY

In Chemistry

By

Philipp Christopher Roosen

Dissertation Committee:
Professor Christopher D. Vanderwal, Chair
Professor Larry E. Overman
Professor Sergey V. Pronin

2016

Portions of Chapter 3 are adapted, according to the ACS AuthorChoice agreement, from: Roosen, P. C.; Vanderwal, C. D. *Org. Lett.* **2014**, *16*, 4368 © American Chemical Society

Portions of Chapter 5 are adapted from: Roosen, P. C.; Vanderwal, C. D. *Angew. Chem. Int. Ed*. **2016**, *55*, 7180–718355; *Angew. Chem.* **2016**, 128, 7296–7299.

© 2016 Philipp Christopher Roosen

DEDICATION

To My Loving Wife Michelle Coscia-Roosen

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

LIST OF SCHEMES

LIST OF ACROYNMS AND ABBREVIATIONS

Å	Ångstrom
°C	degrees Celsius
$[\alpha]_D^T$	specific rotation at wavelength of sodium D line at temperature T
Ac	acetate
acac	acetoacetate
AIBN	2,2'-azobisisobutyronitrile
aq.	aqueous
Ar	aryl
Bn	benzyl
bp	boiling point
bs	broad singlet
Bu	butyl
Bz	benzoyl
C_6H_6	benzene
cat.	catalytic
CCDC	Cambridge Crystallographic Data Centre
cm^{-1}	wavenumber(s)
d	doublet
DABCO	1,4-diazabicyclo[2.2.2]octane
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
1,2-DCB	1,2-dichlorobenzene
DCE	1,2-dichloroethane
DIBAl	diisobutylaluminum hydride
DICA	7,20-diisocyanoadociane
DMAP	4-dimethylaminopyridine
DME	1,2-dimethoxyethane
DMF	dimethylformamide
3,5-DMP	3,5-dimethylpyrazole
DMP	Dess–Martin periodinane
DMPU	N,N'-dimethylpropylene urea
DMSO	dimethylsulfoxide
dr	diastereomeric ratio
EC_{50}	half maximal effective concentration
EDA	1,2-ethylenediamine
EDTA	ethylenendiaminetetraacetic acid
ee	enantiomeric excess
ESI	electrospray ionization
Et	ethyl
g	grams
HMDS	hexamethyldisilazide
HMPA	hexamethylphosphoramide
HPLC	high-performance liquid chromatography
HRMS	high-resolution mass spectrometry
HWE	Horner–Wadsworth–Emmons

Hz	hertz
i-Pr	iso-propyl
IBX	2-iodoxybenzoic acid
IC_{50}	half maximal inhibitory concentration
ICT	isocyanoterpene
IR	infrared (spectroscopy)
J	coupling constant
Karstedt	platinum(0)-1,3-divinyl-1,1,3,3-tetramethyldisiloxane complex
LA	Lewis acid
LDA	lithium diisopropylamide
lit.	literature
mCPBA	meta-chloroperoxybenzoic acid
Me	methyl
mg	milligrams
MHz	megahertz
mL	milliliters
mmHg	millimeters of mercury
mmol	millimole
mp	melting point
Ms	methansulfonyl
MS	molecular sieves
MVK	methyl vinyl ketone
n-	normal
NBS	N-bromosuccinimide
NMO	N-methylmorpholine N-oxide
NMR	nuclear magnetic resonance
noe	nuclear Overhauser effect
NR	no reaction
PCC	pyridinium chlorochromate
PDC	pyridinium dichromate
Ph	phenyl
Phen	1,10-phenanthroline
Piv	pivaloyl
PPA	polyphosphoric acid
ppm	parts per million
PPTS	pyridinium para-toluenesulfonate
Pr	propyl
psi	pounds per square inch
q	quartet
Red-Al	sodium bis(2-methoxyethoxy)aluminum hydride
RSM	recovered starting material
RT	room temperature
s	singlet
Si	silicon-based protecting group
SI	selectivity index
SM	starting material

Stryker's	(triphenylphosphine)copper hydride hexamer
t	triplet
t-Bu	tert-butyl
TBAF	tetrabutylammonium fluoride
TBAI	tetrabutylammonium iodide
TBD	1,5,7-triazabicyclo[4.4.0]dec-5-ene
TBS	tert-butyldimethylsilyl
TEMPO	2,2,6,6-tetramethyl-1-piperidinyloxy
TES	triethylsilyl
Tf	trifluorosulfonyl
TFA	trifluoroacetic acid
TFAA	trifluoroacetic anhydride
TFDO	methyl(trifluoromethyl)dioxirane
THF	tetrahydrofuran
TIPS	triisopropylsilyl
TLC	thin layer chromatography
TMEDA	N,N,N',N'-tetramethylethane-1,2-diamine
TMS	trimethylsilyl
TPAP	tetrapropylammonium perruthenate
Trt	triphenylmethyl
Ts	para-toluenesulfonyl
UHP	urea hydrogen peroxide

ACKNOWLEDGMENTS

I would like to thank my graduate advisor Prof. Chris Vanderwal for inviting me to join the lab and providing the right environment to explore chemistry for five years. Your dedication to total synthesis has been infectious. I appreciate the independence you offered in the whole of my experience, from the chemistry to investigate, the route selection and the decision to stop and pivot approaches. In addition to chemistry, I thank you for the flexibility during the growth of my family. The support and time off for the birth of my two daughters is not necessarily provided by every advisor, but it's something I will take with me.

Thank you Prof. Larry Overman for being both on my second year oral committee and my dissertation committee. The scholarship, curiosity, attention to detail and professionalism with which you approach chemical problems has been more than inspiring. I would like to also thank Prof. Sergey Pronin for being on my dissertation committee. Seeing first hand how dedicated you are to starting a lab has been eye opening. I look forward to the many successes to come out of your and your student's efforts. As a side note, knowing you were working on DICA was very intimidating but I was then very happy when you stopped and joined UCI.

The Vanderwal lab has been an amazing place to work. I thoroughly enjoyed our powerhouse bay (ex. circus bay) of Jon, Won-jin, Alex and Sharon. So many people came through the fifth floor bays that it's difficult to acknowledge everyone. Special thanks however should be given to Carl for being my first bay mate and Peter for the many late night discussions and chemistry fun. The ongoing projects are all exciting and I thank you group for tolerating my (typically unsolicited) advice. The group is an amazing place for friendships and I am thrilled to continue them after departing.

The whole UCI chemistry community is wonderfully integrated. I appreciate the friendship of people in many groups, whose interaction during colloquium organization, admissions work and just simple fun will stay with me.

My interest in chemistry did not arise out of thin air. My guidance and mentoring started with Profs. Vanessa McCaffrey, Cliff Harris and Andrew French at Albion College. This small college can boast of three fantastic organic professors, which all three opened me up to chemistry. My graduate advisor Prof. Mitch Smith cemented my concentration in chemistry. I appreciate his knowledge and ability to drive projects further than I had ever witnessed before and he was a fantastic mentor. Although our time together was short, without his mentorship I would not have the opportunities before me today and thank him for his continued relationship.

My family means the world to me. I couldn't thank you enough mom and dad for the foundation, support and persistence you instilled in me. This appreciation has only deepened as I now have children of my own. The hours of sacrifice to place education first have paid off in the most unexpected of ways. I look forward to many years of visits and enjoyment together.

After meeting each other at Albion, I could never have foreseen a decade like the one we experienced together, Coscia. An initial stint in the middle of Michigan and shuttling between Albion, Mason and East Lansing seemed too long ago. Thank you for being brave with me and

taking a leap out to California. Getting married and raising two beautiful girls has been most fulfilling. I admire you for a huge number of things, but most recently your dedication to our girls and the love you commit to our family. A special thank you also needs to be offered to the Coscia family for the continued support and love. We are going to have a fantastic life together. :o)

I would like to acknowledge *J. Am. Chem. Soc.* **1976**, *98*, 4010 for reprint of the crystal structure of 7,20-diisocyanoadociane and *J. Chem. Soc. Perkin Trans 1* **1988**, 1003 for reprint of the crystal structure of a p-bromobenzoate derivative of 7,20-diisocyanoadociane.

CURRICULUM VITAE

PHILIPP CHRISTOPHER ROOSEN

1102 Natural Sciences II • University of California • Irvine, CA 92697-2025
Email: philipp.roosen@gmail.com

Education

University of California, Irvine, CA 2016
Doctor of Philosophy in Organic Chemistry
Thesis: "An Enantiospecific Formal Synthesis of (+)-7,20-Diisocyanoadociane"

Michigan State University, East Lansing, MI 2011
Master of Science in Organic Chemistry
Thesis: "A Hydrogen Bonding ortho-Directing Effect for the Iridium-Catalyzed Borylation of NH(t-Boc) Aromatics"

Albion College, **Albion, MI** 2008
Bachelor of Arts in Biology, minor in Chemistry, Cum Laude

Research Experience

University of California, Department of Chemistry, Irvine, CA 2011 – 2016
Advisor: Prof. Christopher Vanderwal

- Developed an enantiospecific formal synthesis of the antiplasmodial, marine isocyanoterpene (+)-7,20-diisocyanoadociane
- Initiated a synthesis of the antivirals wickerols A and B

Michigan State University, Department of Chemistry, East Lansing, MI 2008 – 2011
Advisor: Prof. Milton Smith, III in collaboration with Prof. Robert Maleczka, Jr.

- Discovered and elucidated the mechanism of the hydrogen bonding *ortho*-directing effect of iridium catalyzed C–H borylation of N-(*tert*-butoxycarbonyl) anilines
- Married the *ortho*-directed borylation of N-(*tert*-butoxycarbonyl) anlines with subsequent coupling reactions to access 3,4-dihydroquinolin-2-one and N-Boc-indole heterocycles
- Initiated the systematic evaluation of iridium C–H borylation catalyst systems and reaction conditions to establish reaction parameters

Research Experience (continued)

Albion College, Department of Chemistry, **Albion, MI** 2007 – 2008

Advisor: Prof. Andrew French

› Designed and synthesized novel chiral hypervalent iodine (III) reagents for oxidative transformations

Henry Ford Hospital, Department of Neurology, Detroit, MI summer 2007

Advisor: Dr. Michael Chopp

› Assisted in studying the enzyme ADAM17/TACE's influence on glioblastoma tumor angiogenesis

Publications

- Roosen, P. C.; Vanderwal, C. D. "A Formal Enantiospecific Synthesis of 7,20-Diisocyanoadociane" *Angew. Chem. Int. Ed*. **2016**, *55*, 7180–718355; *Angew. Chem.* **2016**, 128, 7296–7299.
- Roosen, P. C.; Vanderwal, C. D. "Investigations into an Anionic Oxy-Cope/Transannular Conjugate Addition Approach to 7,20-Diisocyanoadociane" *Org. Lett.* **2014**, *16*, 4368–4371.
- Roosen, P. C.; Kallepalli, V. A.; Chattopadhyay, B.; Singleton, D. A.; Maleczka, R. E., Jr.; Smith, M. R., III "Outer-Sphere Direction in Iridium C–H Borylation" *J. Am. Chem. Soc.* **2012**, *134*, 11350–11353.
- Vanchura, B. V., II; Preshlock, S. M.; Roosen, P. C.; Kallepalli, V. A.; Staples, R. J.; Maleczka, R. E., Jr.; Singleton, D. A.; Smith, M. R., III "Electronic Effects in Iridium C–H Borylations: Insights from Unencumbered Substrates and Variation of Boryl Ligand Substituents" *Chem. Commun.* **2010**, *46*, 7724–7726.

Research Presentations

- Roosen, P. C.; Vanderwal, C. D. "Progress Towards the Synthesis of 7,20-Diisocyanoadociane" American Chemical Society Annual Meeting (Denver, CO) March 2015.
- Roosen, P. C.; Kallepalli, V. A.; Smith, M. R., III "*ortho*-Directed Iridium Mediate C–H Activation/Borylation of N-(*tert*-butoxycarbonyl)-Anilines" Boron in the Americas XII Conference (East Lansing, MI) June 2010.
- Roosen, P. C.; Logan, M. M.; French, A. N. "Modifications of Chiral Iodoarenes *Ortho*: Progress on the Synthesis and Examination of Select Target Molecules" Elkin R. Isaac Student Research Symposium (Albion, MI) April 2008.

Honors and Awards

- University of California Regents' Dissertation Fellowship (2016)
- UCI Graduate Award for Departmental Service (2015)
- UCI Department of Chemistry Safety Award (2015)
- UCI School of Physical Sciences travel award (2015)
- Associated Graduate Students travel grant (2015)
- Sigma Xi (2008)
- Beta Beta Beta (2007)
- Foundation for Undergraduate Research Scholarship and Creative Activity (FURSCA) grant (2007 – 2008)

Professional Organizations

- American Chemical Society member (2007 – present)

ABSTRACT OF THE DISSERTATION

An Enantiospecific Formal Synthesis of (+)-7,20-Diisocyanoadociane

By

Philipp Christopher Roosen

Doctor of Philosophy in Chemistry

University of California, Irvine, 2016

Professor Christopher D. Vanderwal, Chair

Described in this dissertation work are the paths, dead-ends and detours involved in eventually securing an enantiospecific formal synthesis of (+)-7,20-diisocyanoadociane (DICA) via Corey's dione, a project spanning early 2012 to early 2016. Highlighted is the isolation and biological background to DICA and isocyanoterpenes in general, in addition to the prior synthetic art for the preparation of cycloamphilectane and isocycloamphilectanes. Initial attempts at an entry into the DICA framework included a polyene cyclization, Diels–Alder/aldol condensation and reductive enone coupling strategy. Although these routes were unsuccessful they served as essential evolutionary precursors to the eventual completion of Corey's dione. Efforts to utilize Swaminathans oxy-Cope/transannular Michael cascade to construct the perhydropyrene scaffold of DICA led to a structural reassignment. Further mechanistic investigations into this reaction elucidated that the transannular Michael reaction was in fact under kinetic control. A phenanthrenone reduction route led to an unexpected stereochemical outcome that could be useful for predictive control of either cis or trans outcomes. An enantiospecific formal synthesis of DICA was eventually secured through a dihydronaphthalene reduction. A general approach to multiple C7-isocyano(iso)cycloamphilectanes is also discussed.

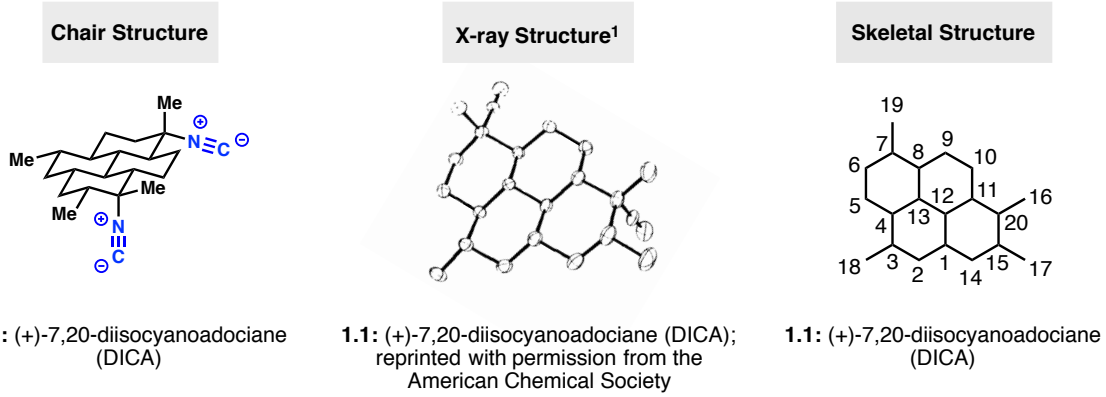
CHAPTER 1:

BACKGROUND TO (+)-7,20-DIISOCYANOADOCIANE

1.1 Introduction

(+)-7,20-Diisocyanoadociane[1] (**1.1**, DICA) is a polycyclic marine isocyanoterpene (ICT) with potent antiplasmodial activity that has attracted synthetic interest for over 30 years. Its *trans*-fused perhydropyrene ring system and salient isonitriles are marked challenges that have yet to be both addressed by the same synthetic design. In addition to a synthetic allure, the biology of DICA and ICTs more generally has further elevated interest in this family.

Figure 1.1 The structure of (+)-DICA.



1.1: (+)-7,20-diisocyanoadociane (DICA)

1.1: (+)-7,20-diisocyanoadociane (DICA); reprinted with permission from the American Chemical Society

1.1: (+)-7,20-diisocyanoadociane (DICA)

1.2 Isolation and Structure Determination

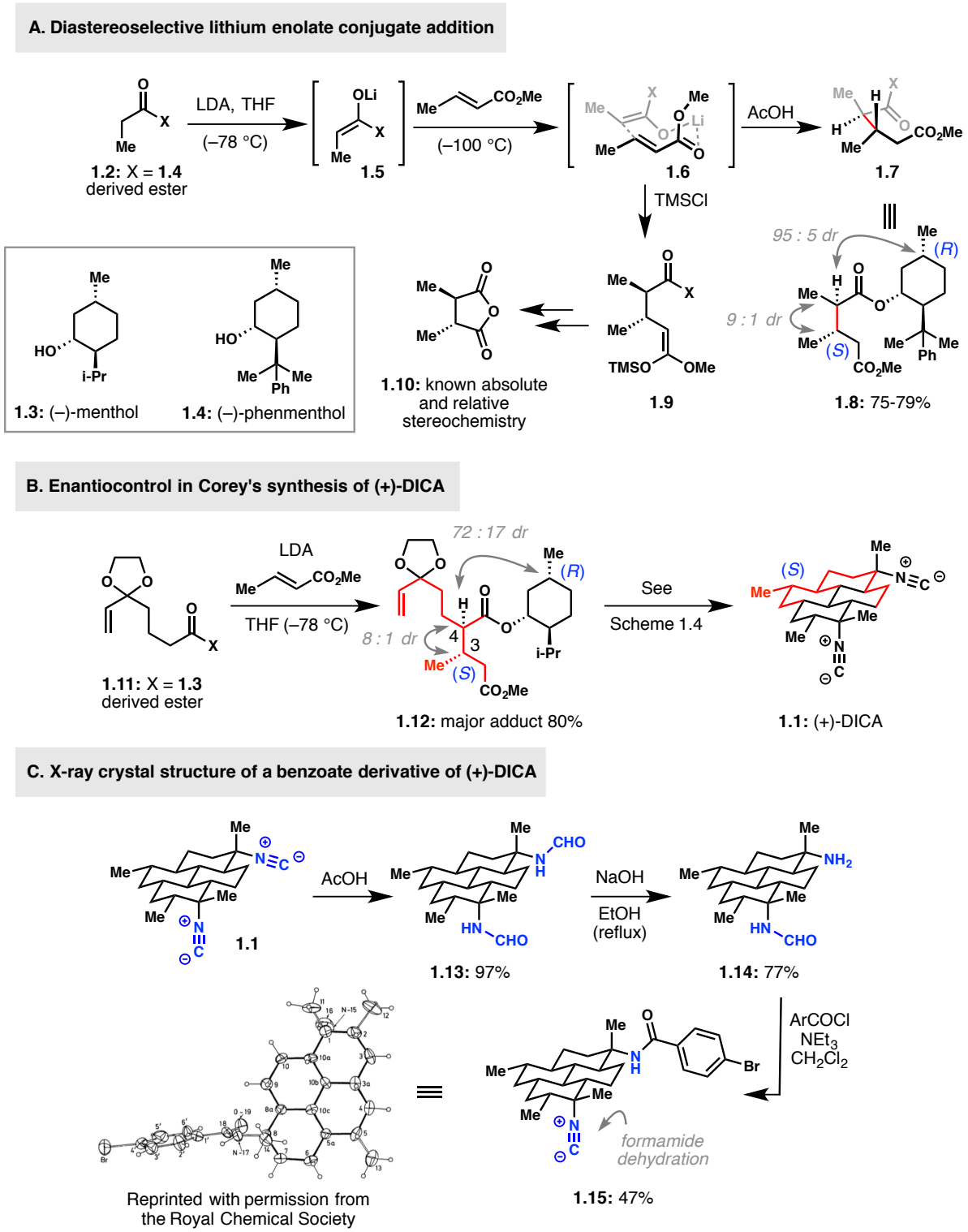
The marine sponges *Cymbastella hooperi* (ex. *Adocia* sp.) and *Amphimedon terpenensis* are native to the Great Barrier Reef, Australia and are identified by their cupped morphology and by their secondary metabolites.[2] Controversy surrounds whether these isolated sponges are identical species or two similar organisms that are both miscategorized.[3] DICA was isolated in the early 1970s from a collection of *Adocia* sp., now identified as *C. hooperi*,[2] in 2% yield by

cold petroleum ether extraction of the milled freeze-dried sponge.[1] Its optical rotation was measured at $[\alpha]^{22}_{D}$ +47.4° (*c* 0.7, CH_2Cl_2). High-resolution mass spectrometry obtained e/z = 324.2565, suggesting the molecular formula of $C_{22}H_{32}N_2$. The IR spectrum showed peaks at 2130 and 2140 cm^{-1} (s), indicating the presence of isonitrile functionalities. A 100-MHz ^1H NMR spectrum revealed two methyl signals at δ 1.37 and 1.29 and two methyl doublets at δ 1.06 (*J* = 6 Hz) and 0.88 (*J* = 6 Hz), with no other resonances identifiable. Full high field ^1H, ^{13}C and 2D NMR analysis was published two decades later.[4] The presence of two isonitriles was further confirmed by hydrolysis with mild acid to generate a structure with molecular formula $C_{22}H_{36}N_2O_2$, bearing appropriate ^1H NMR data for a bis-secondary formamide molecule. Double recrystallization of the original isolate from hexane afforded crystals in the orthorhombic space group, $P2_12_12_1$ with a = 7.086 ± 0.004 Å, b = 21.630 ± 0.011 Å, c = 13.104 ± 0.007 Å, Z = 4, d_c = d_m = 1.079 g/cm^3 and solved as structure **1.1** (Figure 1.1).

The absolute stereochemistry of DICA was assigned first by synthesis (see Scheme 1.1).[5] Corey's use of chiral-auxiliary-based Michael addition onto methyl crotonate was used to set the C3–C4 bond in a relative and absolute sense (Scheme 1.1B).[6,7] Although diastereocontrol in the simple propionate **1.2** case is excellent, it erodes for the substrate required for synthesis. Improved diastereocontrol on **1.11** is observed for the (–)-phenmenthol auxiliary at –100 °C over the (–)-menthol based auxiliary at –78 °C; however, for the purposes of synthesis, the menthol auxiliary was chosen for cost effectiveness. Even with a 60% ee, this preparation of DICA enabled the absolute stereochemical assignment as dextrorotatory.

Shortly after Corey's assignment of (+)-DICA, a crystal structure of benzoate derivative **1.15** was reported and was in agreement with the absolute stereochemistry established by synthesis.[8]

Scheme 1.1 Assignment of the absolute stereochemistry of (+)-DICA.



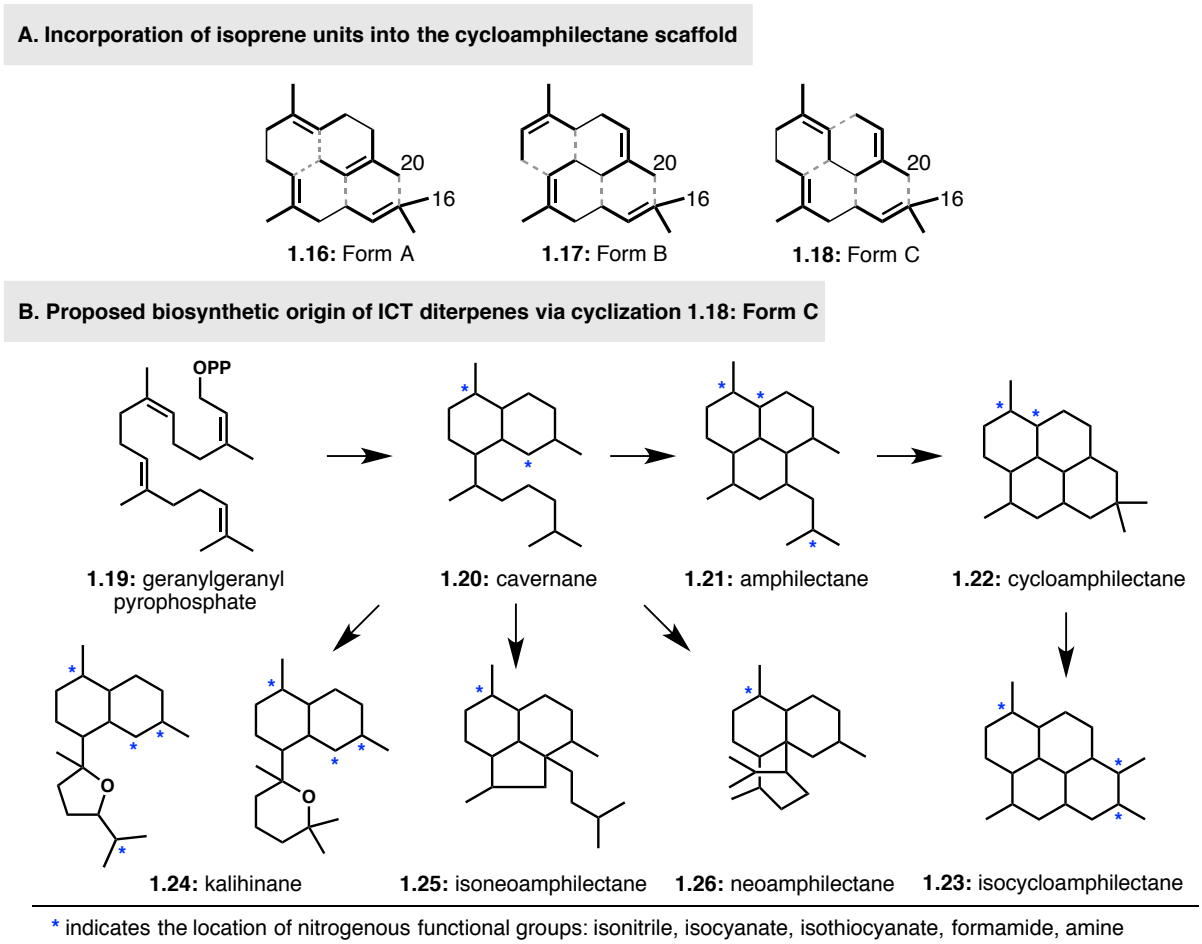
1.3 Biosynthesis

The complex relationship between sponges and the flora and fauna in their environment greatly challenges the delineation of the biosynthesis of their isolated secondary metabolites. Nonetheless, the origin and synthesis of DICA's carbon skeleton and isonitrile units has gathered significant attention.

DICA is comprised of a C20 skeleton and hence classified as a diterpene. There are several options for housing four isoprene units in the methylated pyrene structure, recognizing a single C16-methyl shift (Figure 1.2A).[1,9] Garson has elegantly confirmed DICA is associated with the sponge and not a symbiotic or closely associated organism, for example cyanobacteria.[10] The difficulty comes in determining the source of the C20 fragment, since it was shown that sodium [2-^{14}C]acetate is not a carbon-source for DICA.[11] Typical terpene precursors like acetate, mevalonate, glucose and leucine are generally not incorporated into sponge terpenes as determined by feeding studies.[8,11,12] This result indicates that either the marine sponges *de novo* terpene synthesis requires other building blocks or more elaborated hydrocarbon fragments are obtained from external sources. Incorporation of [2-^{14}C]acetate into carotenoids known to arise from blue-green algae symbiosis during feeding studies of other sponges supports the latter proposal.[13] Still, by examining the isolated natural products of *C. hooperi* a biosynthetic relationship between ICT diterpenes has been proposed (Figure 1.2B).[14] The cyclization of geranylgeranyl pyrophosphate **1.19** affords the cavernane scaffold **1.20**, a main branching point to ICT diterpenes. Further cyclization of **1.20** via amphilectane **1.21** and cycloamphilectane **1.22** sets up a methyl shift to the isocycloamphilectane **1.23** scaffold. Based on the proposed biosynthetic relationship between ICT sub-classes, the four isoprene units required to generate DICA are most likely arranged as depicted in **1.18**, Form C. The exact source of carbon, the

location in the sponge where cyclization is performed and the manner in which folding occurs remains unconfirmed for DICA, and ICTs more broadly.

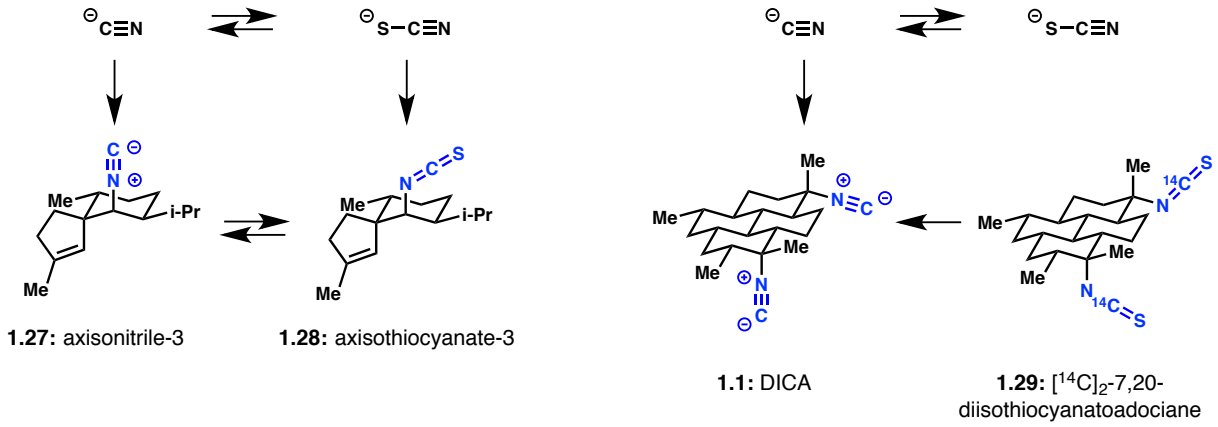
Figure 1.2 Isoprene units of the cycloamphilectane skeleton and C16 to C20 methyl shift to access the isocycloamphilectane skeleton.



Arguably more interesting than terpene biosynthesis is the inclusion of cyanide into marine ICTs. Radiolabelling studies feeding Na[^{14}C]N to *A. terpenensis* followed by isolation of DICA showed incorporation of ^{14}C.[11] Radiolabelling was retained upon hydrolysis of DICA to the bis-formamide. Upon cleavage of one formamide to the amine, 49% radioactivity remained and upon double deformylation only trace background activity was observed. This sequence

shows that the carbon of exogenous cyanide is incorporated into the isonitriles of DICA. A variety of other marine ICT natural products also show integration of radiolabeled cyanide during feeding studies.[14] Additionally, feeding of doubly labeled cyanide, Na[^{13}C][^{15}N], confirmed that both carbon and nitrogen of free cyanide are incorporated into the isonitrile goup of the related ICT 9-isocyanoneopupukeanane.[15] Although the doubly labeled cyanide feeding study has not been performed for DICA to date, the example of 9-isocyanoneopupukeanane is likely representative for all ICTs.

Scheme 1.2 Established biosynthetic relationship between cyanide, thiocyanate and their respective terpene derivatives.



Studies were undertaken to detect the origin of inorganic cyanide available to the organism and the manifold by which the isocyanate, isothiocyanate, formamide and amine functionalities are born out. By observations and labeling studies of cyanide and axisonitrile-3 **1.27**, it was found that cyanide and thiocyanate are interconverted at an inorganic level (Scheme 1.2).[16] Additionally, isonitrile **1.27** and isothiocyanate **1.28** are each interconverted, and importantly, without expulsion of either isonitrile or isothiocyanate. These experiments were also performed in part on DICA and showed that radiolabelled isothiocyanate is also biosynthetically

introduced into DICA via cyanide and that the organism is capable of desulfurizing the non-natural product [^{14}C]$_2$-7,20-diisothiocyanatoadociane **1.29**.[17] Inclusion of cyanide into ICTs and the interconversion of isocyano- and isothiocyanatoterpenes have both been shown to be enzyme-mediated processes.[14,15] The occurrence of isocyanate, formamide and free amine derivatives has not been deeply studied but could be reasonably explained from hydrolysis of the isothiocyanate and isonitrile natural products.

Further investigation into the origin of the carbon and nitrogen in cyanide used by marine sponges is warranted. As determined by the significant production of ICTs, these sponges require significant quantities of the otherwise toxic cyanide. The seawater ecosystem home to ICT-producing sponges most likely contains minimal if any free cyanide, suggesting that cyanide is produced biosynthetically.[14] Labeling studies have indicated that the cyanide used to produce DICA is not of amino acid origin.[8] Although not experimentally determined, the biosynthetic origin of cyanide may involve microbial symbionts, as documented for other secondary metabolites.[14]

1.4 Function and Ecology

The abundance of ICTs in sponges of marine origin begs the question of their function and ecology. A wide variety of proposals exist for the various sesqui- and diterpenes, including structural, defense and symbiotic.[14] For the purposes of this dissertation, only information relevant to DICA will be presented.

Marine sponges generate DICA in significant quantities; it is obtained in 2% of the dry weight of collected sponge.[1] The production of DICA does not vary significantly with season or geography.[13] Upon dissection of *A. terpenensis*, DICA is found in both superficial ectosome and

deeper choanosome sponge tissue.[10] Higher concentrations of DICA relative to sterols were observed in larger nucleolated cells compared to small non-nucleated cells; the concentration of sterols in larger nucleolated cells was negligible. Further study revealed DICA to be associated with the sponge cell membrane; however, in vitro analysis using conventional phospholipids showed that DICA was not integral.[18] *Amphimedon* sp. phospholipids are unconventional by virtue of their significant quantities of unusual, brominated fatty acids.[19,20] Studies examining DICA in this lipid system have not been disclosed. The location and quantities of DICA available to the sponge suggest a structural role.[18] Further study on the precise roles of DICA and other ICTs are warranted.

1.5 Biological Activity

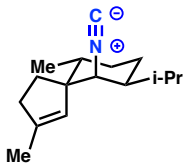
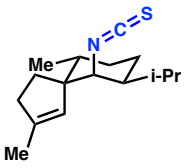
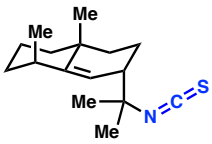
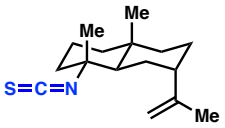
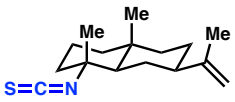
1.5.1 Introduction

A distinctive characteristic of ICTs is not only their structural diversity, but also their biological profile. This class of molecules, which encompasses both sesqui- and diterpenes, has a vast array of biological activity that for the purposes of this dissertation will focus on DICA.

DICA was first shown to exhibit in vitro antimicrobial activity against gram-positive bacteria although no precise detail was provided.[21] DICA was also shown to have vasodilative properties on isolated guinea pig hearts (EC_{50} = 22 μg/heart), although no follow-up studies have been disclosed.[22] Significant interest in ICTs came out of an early evaluation of antiplasmodial activity. In collaborative work between the Angerhofer and König groups, ICTs **1.27**, **1.28** and **1.30**–**1.32** were screened against chloroquine-sensitive D6 and chloroquine-resistant W2 strains of *Plasmodium falciparum*, a malaria-causing parasite (Table 1.1).[23] The isonitrile **1.27** was markedly more potent than the isothiocyanates screened. These preliminary results led to a larger

screening program, in which DICA was also involved.[24,25]

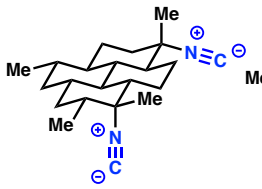
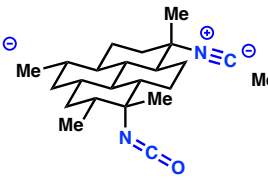
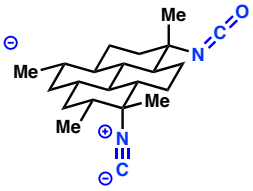
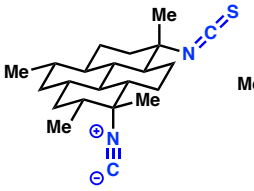
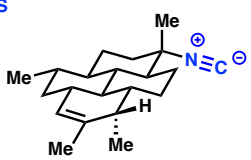
Table 1.1 Initial evaluation of antiplasmodial activity and cytotoxicity of ICTs.

	1.27: axisonitrile-3	**1.28:** axisothiocyanate-3	**1.30**	**1.31**	**1.32**
D6[a]	610	47,000	8,500	15,000	>38,000
W2[a]	71	12,000	2,300	2,100	>38,000

[a] IC_{50} values in nM; all ICT IC_{50} values of human KB cell cytotoxicity were >75,000 nM

Table 1.2 Evaluation of isocycloamphilectane ICTs against *P. falciparum*.

	1.1: (+)-DICA	**1.33**	**1.34**	**1.35**	**1.36**
D6[a]	14	9	220	126	210
W2[a]	13	7	265	80	66
KB Cells[b]	14,483	12,628	5,874	4,487	61,179

[a] IC_{50} values in nM [b] IC_{50} values of human KB cells cytotoxicity in nM

DICA exhibited significant in vitro activity against both D6 and W2 strains of *P. falciparum*, while also maintaining high selectivity for the parasite over human cells (Table 1.2). DICA derivatives **1.33**–**1.36**, bearing isothiocyanate or cyanate functionality and also isolated from *C. hooperi* show dramatic differences in activity. The position of the isocyanate is critically linked to biological activity as shown in **1.33** and **1.34**. C7 isothiocyanate **1.34** and isocyanate **1.35** show a 10–20 fold drop in activity, while a C20 isocyanate increases potency. Isocycloamphilectane **1.36**, containing only a single isonitrile, also showed a significant drop in

activity compared to DICA. The scope is too small to deduce structure-activity relationships, although the isonitriles are clearly critical for antiplasmodial activity.

The strong antiplasmodial activity inspired more biological evaluation of ICTs. Wright and coworkers approached with this opportunity, screened DICA and other ICTs against various targets.[26] The experiments were performed with 50 μg disk^{-1} and the inhibition was measured in millimeters from the edge of the disk. DICA was examined for antibacterial activity against Gram-negative *Escherichia coli* (1 mm) and *Vibrio harveyi* (IC_{50} of 2,500 nM) and Gram-positive *Bacillus megaterium* (3 mm), with success. Antifungal activity was found against *Eurotium repens* (3 mm) and *Mycotypha microspore* (4 mm) but none against *Fusarium oxysporum*. Antialgal activity was assessed also by using 50 μg disk^{-1} against *Chlorella fusca* (2 mm). Photosynthesis could be reduced by DICA by 36.9% at a test concentration of 0.2 mg mL^{-1}. DICAs antitubercular activity against *Mycobacterium tuberculosis* had an IC_{50} value of 8,000 nM. Although DICA has a broad-ranging biological profile, the most potent and arguably most interesting phenotype is its antiplasmodial activity.

1.5.2 Studies on Antiplasmodial Activity

Malaria afflicts millions of people and causes approximately 1 million deaths annually, mostly in developing countries.[27] The current frontline treatment of artemisinin combination therapies has revolutionized the management of this illness; however, malaria-causing parasites are continuously evolving and have already begun showing signs of artemisinin resistance.[28] This is an early warning that new antimalarial medicines are needed, especially those containing novel pharmacophores or mechanisms of action. The current pipeline offers only more of the same medicinal derivatives, making a major conceptual leap in antimalarial therapeutics greatly

desired.[29] ICTs precisely fill this requirement as a potential lead since the isonitrile functional group constitutes a new warhead for exploration. DICA's potent activity against drug-resistant *P. falciparum* has elevated the molecule to further detailed study.

During erythrocyte infection, the parasite actively feeds on hemoglobin, thereby releasing toxic heme and hydrogen peroxide.[30] These molecules require neutralizing to avoid parasite self-destruction. This process is performed by the biocrystallization of heme into hemozoin and by various peroxidative pathways.[31] Interruption of these processes is proposed to be a major antiplasmodial mechanism of action for current antimalarial medicines and is a logical starting point for studying ICT-parasite interaction.[32] Wright and coworkers have performed initial studies, but the mechanism of action for DICA's potent biological activity is yet to be elucidated.[24,33]

A dual computational and experimental approach evaluated DICAs coordination to heme and subsequent inhibition of hemozoin formation as an explanation for antiplasmodial activity. The combination of 3D-QSAR and receptor modeling methodologies determined that the parasite target requires a hydrophobic pocket and is capable of forming electrostatic interactions.[33] There is a positive correlation between the structural homology of other ICTs and DICA to their antiplasmodial activity. This correlation was also observed experimentally as DICA showed strong coordination to heme by UV-vis, while less active ICTs showed subdued coordination. Experimental observations that DICA inhibited peroxidase-like activity of heme, oxidative heme decomposition and glutathione-dependent heme decomposition were also noted. Further studies revealed DICA inhibited the in vitro formation of β-hematin (the synthetic equivalent to hemazoin) from free heme.[34] These computational and experimental data were interpreted as key evidence that antiplasmodial activity is integrally related to interrupting

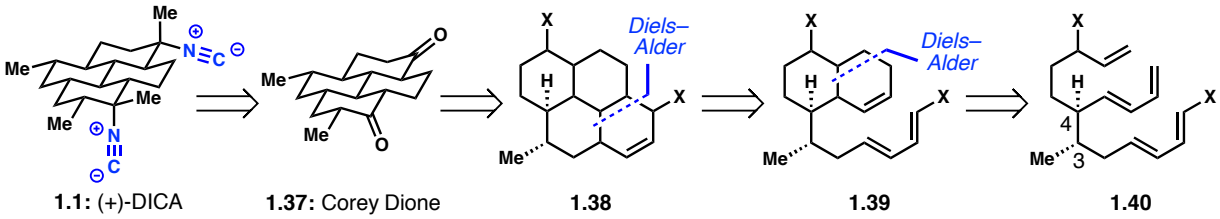
detoxification processes. These exciting results justify a continued pursuit in explaining DICAs strong potency.

1.6 Previous Syntheses of Cycloamphiletanes and Isocycloamphilectanes

1.6.1 Corey's Synthesis of (+)-7,20-Diisocyanoadociane (1987)

Corey and Magriotis reported the first synthesis of an isocycloamphilectane ICT by completing the synthesis of (+)-DICA.[5] Motivation for this synthetic effort was the unusual perhydropyrene structure, unprecedented biosynthesis and unknown absolute configuration. The Corey group disconnected DICA at the isonitrile carbons back to dione intermediate **1.37** (Corey's dione). Two elegant Diels–Alder disconnections take **1.37** back to the hypothetical molecule **1.40**. Of beauty is how one Diels–Alder sets up for the next, thereby generating five stereodefined centers of the perhydropyrene scaffold from the initially set C3–C4 connection.

Scheme 1.3 Corey's retrosynthetic analysis of (+)-DICA via double Diels–Alder reaction.



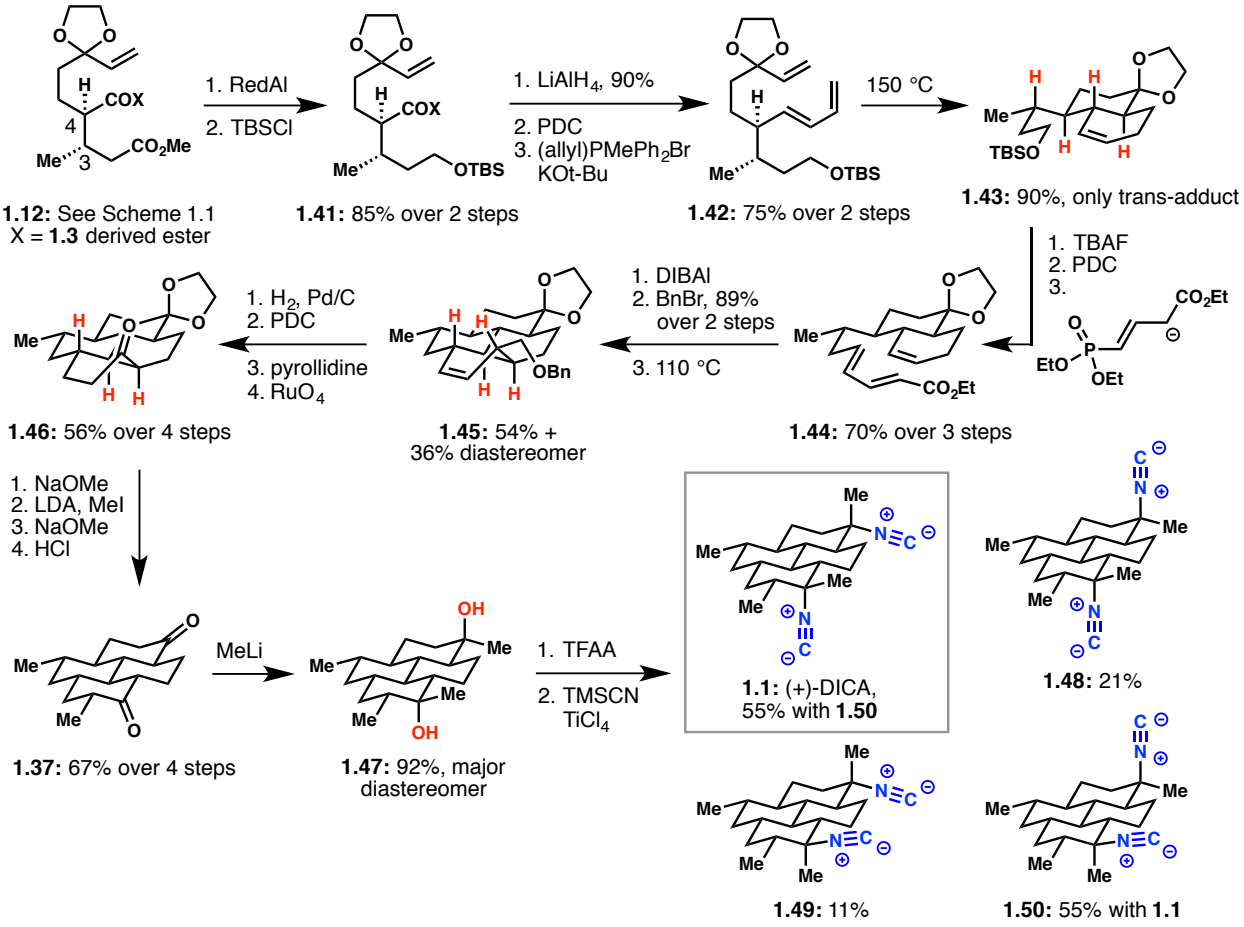
1.1: (+)-DICA **1.37:** Corey Dione **1.38** **1.39** **1.40**

The synthesis began with establishing the C3–C4 stereochemical relationship via Corey's auxiliary-controlled asymmetric enolate conjugate addition (see Scheme 1.1).[6] Functional group interconversions led to Diels–Alder precursor **1.42**. Thermal cycloaddition afforded **1.43** in 90% yield as a single *trans*-decalin. Revealing the masked C1 aldehyde by TBAF deprotection and PDC oxidation enabled installation of the remaining skeletal carbons at the alkene oxidation states of **1.44**. Cycloaddition of ester **1.44** was unable to provide the correct stereochemistry;

reduction, benzyl protection and thermal cycloaddition generated **1.45**, which bore the correct C1–C12 *trans*-relationship. Oxidative removal of the superfluous carbon was accomplished by RuO_4 cleavage of the corresponding exocyclic enamine to afford **1.46**. After C17 methyl installation, the stereochemistry needed to be adjusted to the all-*trans* **1.37**. Double methyllithium addition afforded **1.47** as the diaxial diol. Trifluoroacetylation and ionization of the bistrifluoroacetates with $TiCl_4$ and capture with TMSCN generated (+)-DICA and three more diastereomers. Purification by silica gel chromatography afforded a mixture of (+)-DICA and **1.50** in 55% yield. (+)-DICA was isolated upon further purification by HPLC; however, the final yield remained unreported.

This first synthetic preparation of (+)-DICA confirmed the absolute stereochemistry of the natural product. The double Diels–Alder approach is an elegant solution to the construction of a perhydropyrene scaffold in which one Diels–Alder sets up for the next. Although the natural product synthesis was successful, certain elements could still be improved. First, while beautiful in design, the synthesis relies on several redox and protecting group manipulations to generate DICA in a total of 31 steps and a longest linear of 29 steps from commercial material. A concise, efficient and stereoselective synthesis of (+)-DICA or dione precursor **1.37** would be a worthwhile contribution. Second, stereocontrol of the second Diels–Alder to generate the perhydropyrene scaffold was sufficient for completion of the synthesis, but the 1.5:1 reaction selectivity could still be improved. When examining this synthesis, still the most pressing issue is the nonselective isonitrile installation. Ionization of the trifluoroacetates creates competitive axial and equatorial attack of TMSCN. One solution to this problem uses $Sc(OTf)_3$ as described by Shenvi, which promotes a mostly stereoinvertive-isonitrile displacement.[35,36] Additional efforts in the realm of direct isonitrile installations are however still warranted.

Scheme 1.4 Corey's synthesis of (+)-DICA.

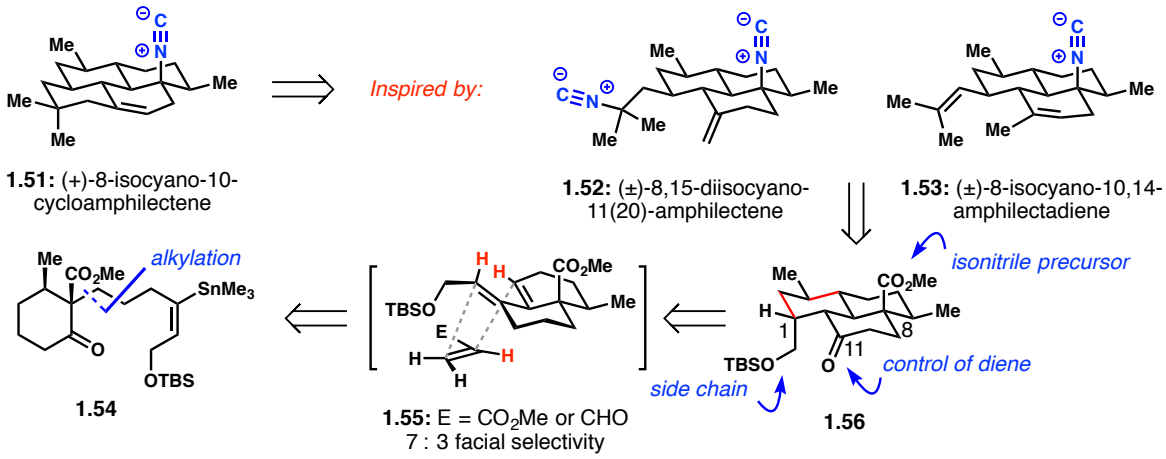


1.6.2 Piers's Synthesis of (+)-8-Isocyano-10-Cycloamphilectene (1998)

The only reported preparation of a cycloamphilectane ICT was completed by Piers and Schindeler and published only in a thesis.[9] The Piers lab's interest in methodology-inspired natural product synthesis drove the ICT syntheses of **1.52** and **1.53**.[37–39] The synthesis of **1.51** was initiated to further highlight the versatility of **1.56**, an intermediate scaffold obtained by an intramolecular Piers–Stille annulation and Diels–Alder reaction, and to determine the absolute configuration of **1.51** (Scheme 1.5). The synthetic branching point **1.56** contains three key functionalities: (1) a C8 ester as an isonitrile precursor, (2) a C11 ketone to control the alkene

functionality or ring closure to the cycloamphilectane target and (3) a C1 silyloxymethyl unit for diversification of the side chain.[7]

Scheme 1.5 Piers's retrosynthetic analysis of (+)-8-isocyano-10-cycloamphilectene based on a Piers–Stille annulation and previous amphilectane syntheses.

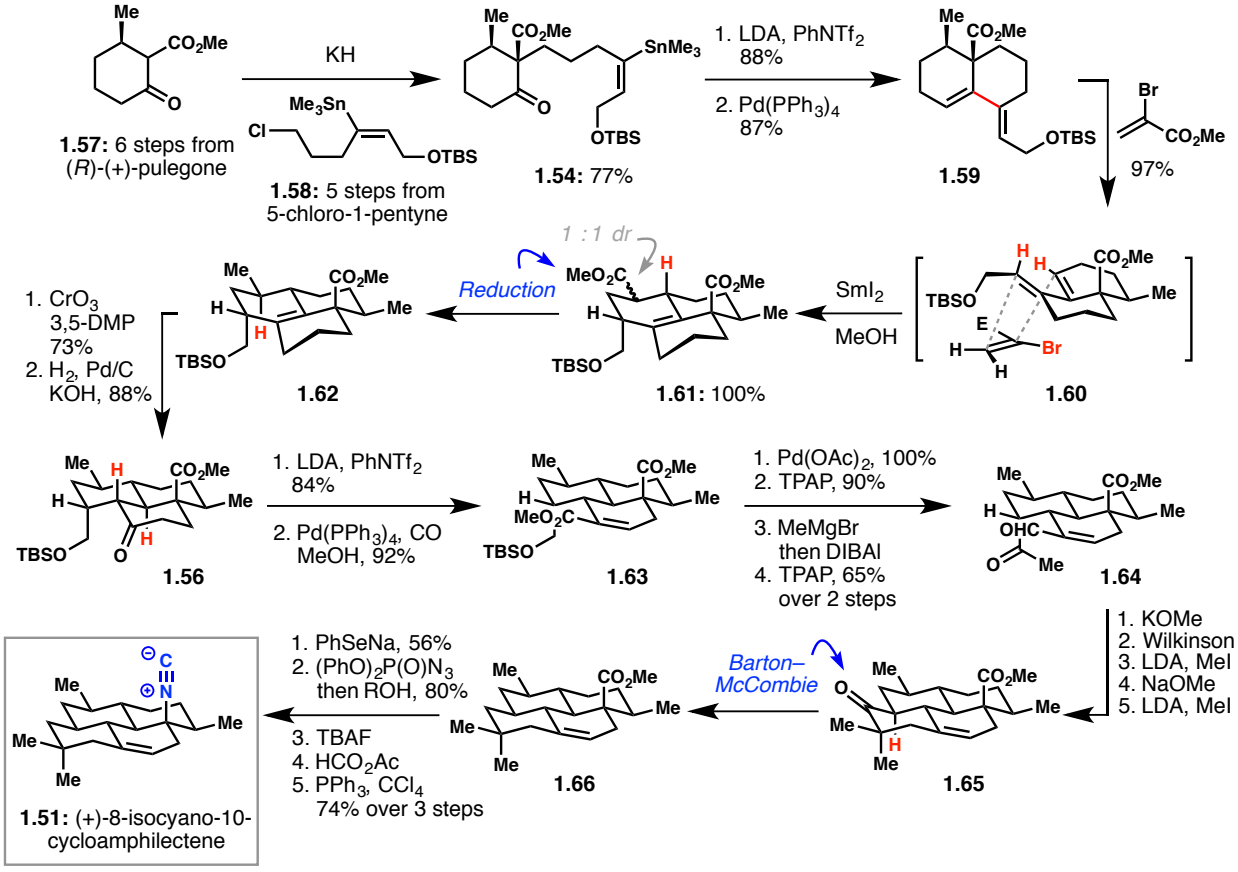


The first objective for a synthesis of **1.51** was improving the preparation of **1.56** for three reasons: (1) the earlier amphilectane syntheses were racemic, (2) the Diels–Alder reaction provided low facial selectivity and (3) an enone reduction to set the internal stereocenter of **1.56** was capricious. Piers and Schindeler addressed the first problem by starting from chiral pool material (*R*)-(+)-pulegone. The absolute stereochemistry of several amphilectanes and DICA was established with uniformity at the time of Piers and Schindeler's synthetic work, therefore it is unclear why the use of (*R*)-(+)-pulegone was chosen as it would generate the unnatural enantiomer. (*S*)-(–)-pulegone is significantly more expensive, but still readily prepared from (*S*)-(–)-citronellal. Upon alkylation of **1.57** with **1.58** and palladium-mediate cross coupling, the Diels–Alder reaction of **1.59** with methyl 1-bromoacrylate proceeded with complete facial selectivity. Sequential protodehalogenation and methyl ester reduction generated **1.62**, which was oxidized to the enone with CrO_3•3,5-dimethylpyrazole and then reduced selectively via

hydrogenation in a strongly basic medium to afford the branching intermediate **1.56** in significantly optimized form as a single enantiomer.

Annulation of the fourth ring became the next challenge. The C11 ketone was derivatized to an unsaturated aldehyde and the C1 silyloxymethyl to a methyl ketone which upon exposure to base, cyclized to a dienone. Selective reduction of the disubstituted alkene followed by gem-dimethyl installation generated structure **1.65**. A Barton–McCombie radical deoxygenation was chosen to remove the C14 ketone, leaving only conversion of the ester into the C8 isonitrile to finish the synthesis of **1.51**.

Scheme 1.6 Piers's synthesis of (+)-8-isocyano-10-cycloamphilectene.

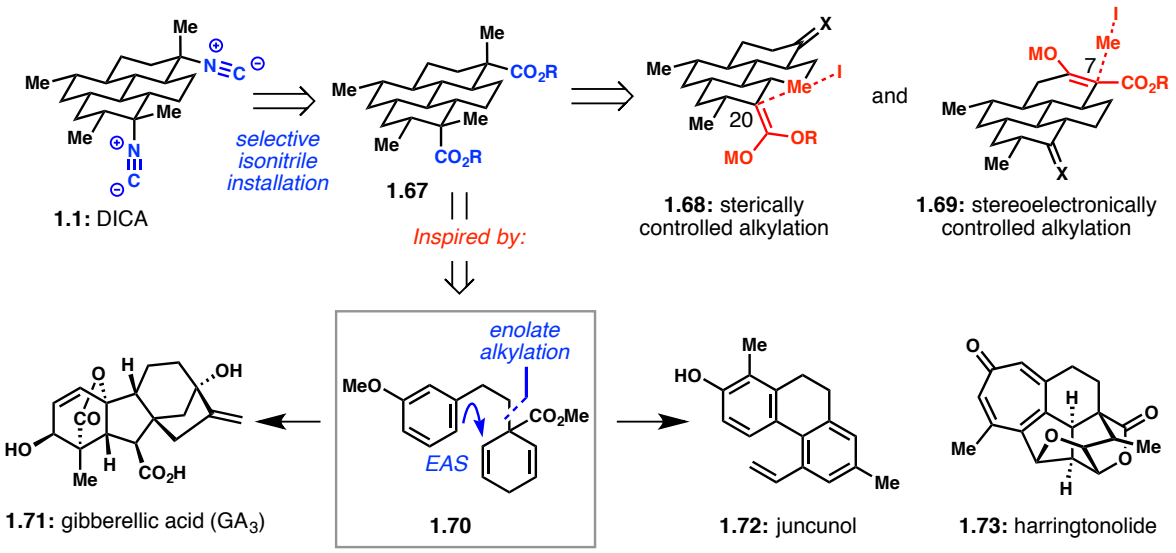


The Piers and Schindeler synthesis of **1.51** is an extension of earlier work from the Piers laboratory. A Piers–Stille annulation/Diels–Alder strategy enabled access to not only tricyclic amphilectane ICTs but also tetracyclic congeners. This synthesis addressed some of the shortcomings of earlier amphilectane syntheses, most notably the enantiospecific entry into ICTs by using chiral pool starting material, fashioning a highly facially selective Diels–Alder reaction, and optimizing for a robust enone reduction with excellent stereocontrol. To date, it is the only reported synthesis of a cycloamphilectane. The main drawback of this design is the step count, with a total of 46 steps and a longest linear of 36 steps from commercial material.

1.6.3 Mander's Formal Synthesis of (±)-7,20-Diisocyanoadociane (2006)

The selective installation of tertiary isonitriles has been a formidable challenge in the context of ICT syntheses.[40] At the outset of Mander's interest in DICA, which started in the 1980's,[41] the most substantive solution was the Curtius rearrangement, formylation and dehydration first applied to ICTs by Piers.[9,37–39] With this method at hand, the most logical synthesis of the ester precursors is by stereoselective alkylation (Scheme 1.7). Alkylation under steric control was proposed to install the equatorial methyl at C20, while stereoelectronic control using a β-ketoester would provide axial methyl approach at C7.[42] The Curtius rearrangement's stereoretentive nature ensures that the configuration of the ester is relayed to the amine. Inspiration for construction of the perhydropyrene skeleton came from Mander's strong interest in using polyaromatics in natural product synthesis (Scheme 1.7).[43,44]

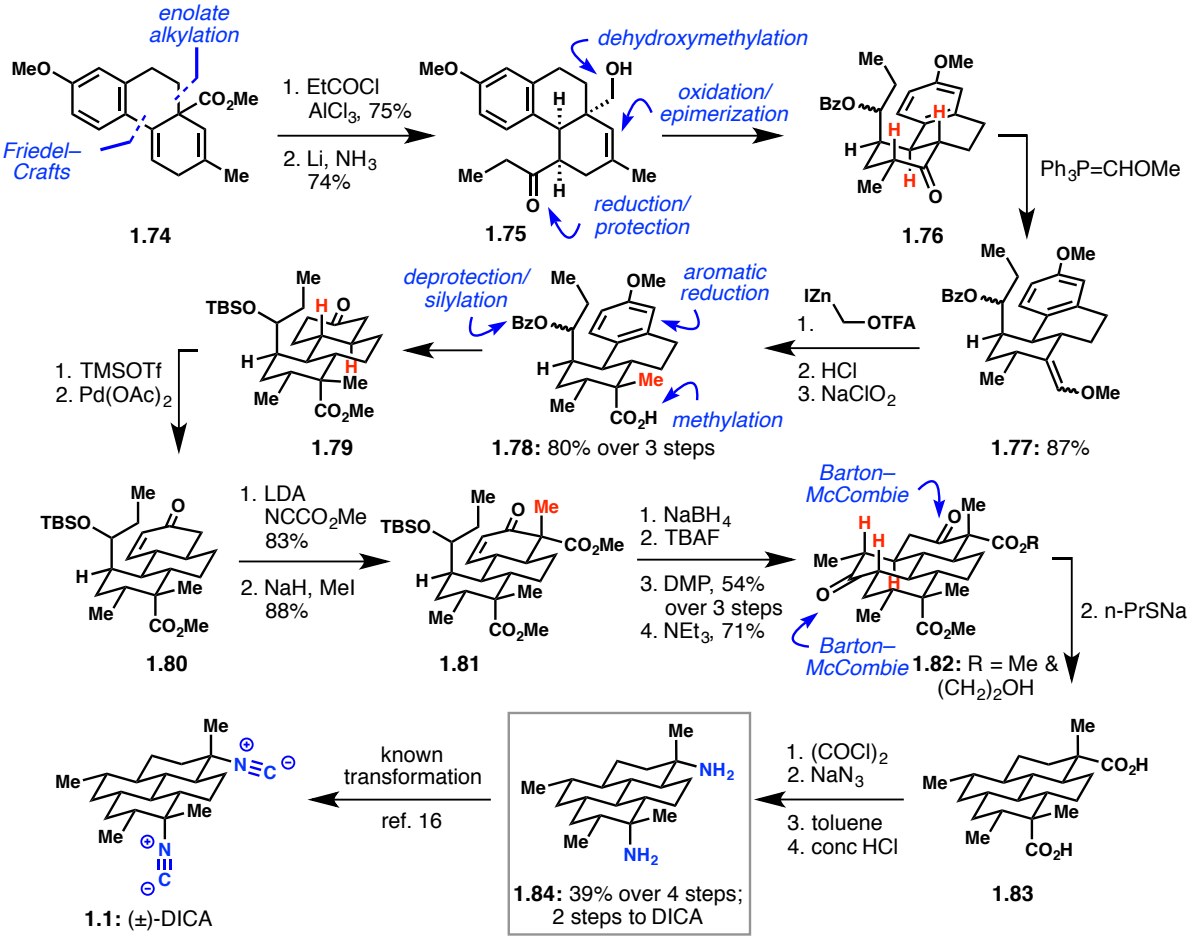
Scheme 1.7 Mander's impetus and inspiration for the synthesis of DICA.



Phenanthrene **1.74**, generated by precedented Birch reduction/Friedel–Crafts condensation, became the unsaturated building block for Mander's stereoselective synthesis of DICA. An asymmetric manifold is only alluded to as potentially possible from diastereoselective Birch alkylation using a chiral benzamide.[45] From **1.74**, acylation and enone reduction with Li/NH_3 afforded **1.75**. Curiously the stereochemistry of reduction is *cis* (see Chapter 4 for discussion of similar reactivity). Further functional group manipulation and stereochemical correction sets the stage for the first methyl installation at C20. Although direct alkylation failed, cyclopropanation and acid-mediated ring opening afforded carboxylic acid **1.78**. Reduction of the aromatic and significant functional group manipulations generated **1.80**, ready for C7 alkylation. Deprotonation and alkylation of the corresponding β-ketoester produced axially methylated product **1.81**. The final ring was closed by intramolecular Michael addition of the revealed ethyl ketone and fused cyclohexenone. Barton–McCombie deoxygenation of **1.82** and functional group manipulation afforded diacid **1.83**. In a sequence analogous to the work by Piers, the diacid **1.83** was converted into free diamine **1.84**, a target readily transformed to DICA

via known means.[16]

Scheme 1.8 Mander's formal synthesis of (±)-DICA.

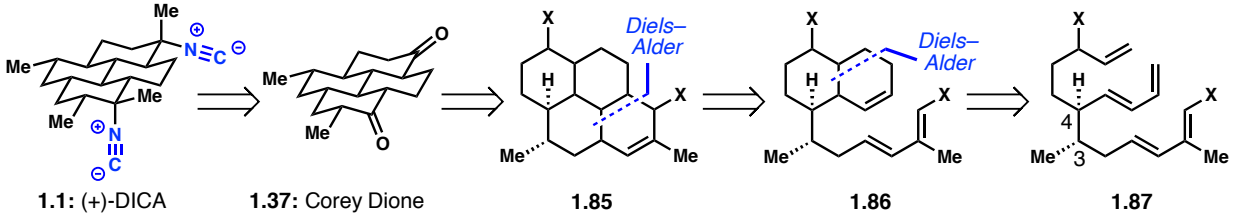


Mander's synthesis of DICA is the first and only synthesis with stereocontrol of the isonitrile moieties. It is designed around well-established enolate alkylation methods to control for equatorial and axial methylation. The obtained diester is transformed to the diamine via stereoretentive Curtius rearrangement, thereby completing a formal synthesis. The approach generates all stereocenters with excellent diastereocontrol and the diamine is completed in 48 total steps and 42 steps longest linear from commercial materials; an additional two steps are required to complete DICA.

1.6.4 Miyaoka's Formal Synthesis of (+)-7,20-Diisocyanoadociane (2011)

Miyaoka's formal synthesis of (+)-DICA follows almost the identical path as Corey's, 24 years prior (see Section 1.6.1).[5,46] The key C–C forming strategy also involved two Diels–Alder reactions to generate all stereocenters except C3 and C4 (Scheme 1.9). Distinct from Corey, Miyaoka sets the C3 and C4 stereocenters by alkylation of chiral lactone (*S*)-(–)-**1.88** (Scheme 1.10).

Scheme 1.9 Miyaoka's double Diels–Alder strategy to Corey's dione.

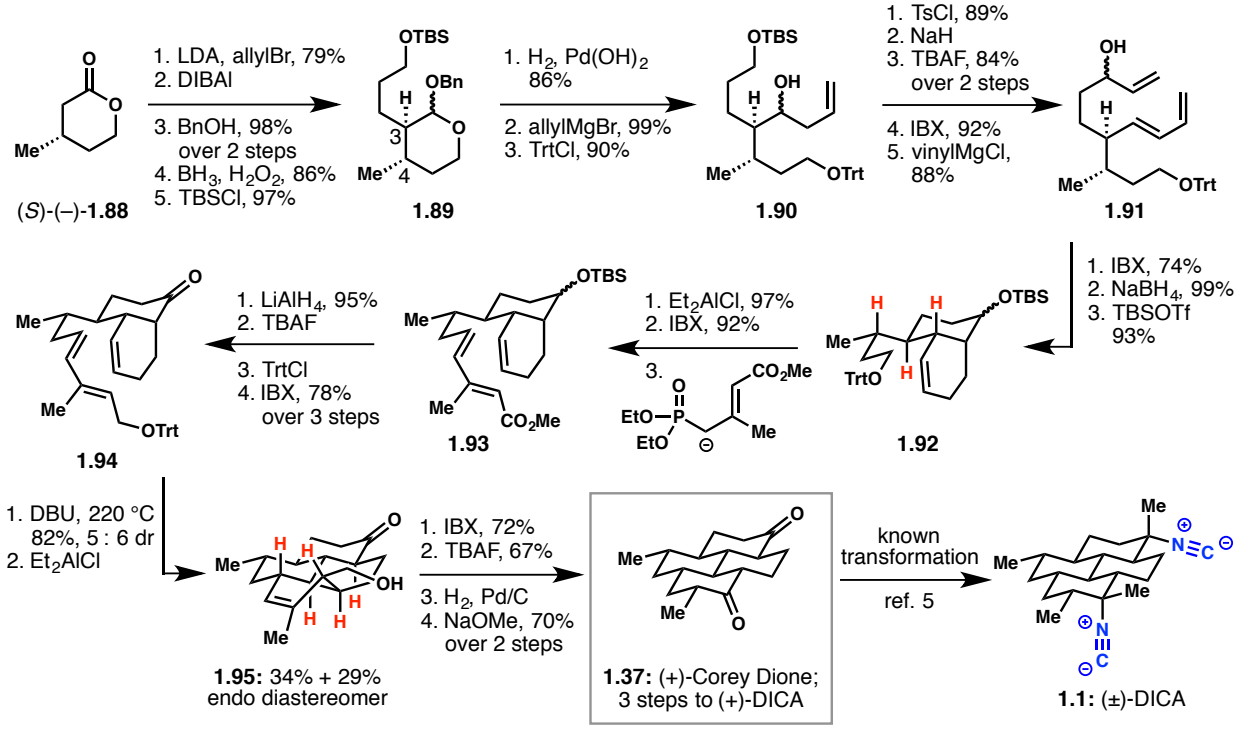


1.1: (+)-DICA **1.37:** Corey Dione **1.85** **1.86** **1.87**

Miyaoka's synthesis began with a known synthesis of (*S*)-(–)-**1.88**, via an esterase catalyzed desymmetrization.[47] Ester enolate allylation secured the *trans* relationship between C3 and C4, a vital control element for the subsequent Diels–Alder reactions (Scheme 1.10). Redox and protecting group manipulations afforded homoallylic alcohol **1.90**. Tosylation and elimination generated the diene, while silyl deprotection, oxidation and vinyl Grignard addition set up the alkenes for an oxidation triggered Diels–Alder (an observation also made by Corey in the context of DICA).[5] The remaining carbons were introduced via Horner–Wadsworth–Emmons (HWE) reaction of the corresponding **1.92** C1 aldehyde. Conversion of the unsaturated ester to the protected alcohol and oxidation of the C7 alcohol to the ketone afforded triene **1.94**. The next cycloaddition was performed with added DBU to ensure epimerization of the *cis*-decalin. Treatment of **1.94** at high temperatures afforded cycloaddition in 5 : 6 dr favoring an undesired endo diastereomer. Deprotection of the trityl group ensured clean isolation of the

desired diastereomer **1.95**. Oxidation to the skipped enal and unusual TBAF mediated oxidative deformylation[48] followed by hydrogenation and epimerization provided Corey's dione **1.37** in enantioenriched form to claim a formal synthesis of (+)-DICA.

Scheme 1.10 Miyaoka's formal synthesis of (+)-DICA.



The purpose of Miyaoka's DICA synthesis is unclear as the main double Diels–Alder strategy is identical to Corey's (see Section 1.6.1).[5] Speculatively, Miyaoka's DICA synthesis was to fit with a broader approach to ICTs since an amphilectane[49] and several kalihinanes[50–52] were prepared by a similar Diels–Alder cycloaddition. There are only small differences compared to Corey's previously published work. First, the C3–C4 stereochemical relationship in Diels–Alder triene precursor **1.91** arises from substrate-controlled alkylation of lactone (*S*)-(–)-**1.88** instead of auxiliary controlled Michael addition. Second, the C17 methyl is incorporated into the HWE reagent instead of later installation via alkylation. And lastly, oxidative

demethylation of the extraneous carbon in **1.95** was accomplished via unique TBAF method[53] instead of oxidative cleavage of an enamine. Miyaoka's preparation of Corey's dione takes a total of 39 steps and 35 steps longest linear from commercial material, and requires another three steps to DICA.[54]

1.7 Goals for the Synthesis of (+)-Diisocyanoadociane

ICTs, and specifically DICA, have attracted synthetic chemists with their unique structures and rich biological activity.[55] The widespread affliction of malaria and its negative impact on societies, especially for developing nations, requires continuous and persistent effort in building new methods of combat. In addition, the fundamental science revolving around antiplasmodial agents and the biology of this parasitic disease continues to be of interest. In this vein, the Vanderwal group initiated a research program to prepare and study ICTs. Synthetic studies towards (+)-DICA have been a cornerstone in this program since early 2012.

As DICA has already been prepared on multiple occasions, scaling the mountain of synthesis to this molecule again needs strong justification. First, DICA remains a structural terrain that has yet to succumb to concise synthesis and the construction of the all-*trans* perhydropyrene scaffold could still benefit from strategic chemical exercise. Second, the selective installation of the two isonitriles has been accomplished only by a single effort via a rather long sequence. Alternatives to the Curtius rearrangement have yet to be explored in the context of DICA. The need to install both an axial and equatorial isonitrile for DICA elevates this challenge. Overall, the structural, chemical and biological potential of DICA make it an attractive target.

1.8 References and Notes

(1) Baker, J. T.; Wells, J. R.; Oberhänsli, W. E.; Hawes, G. B. *J. Am. Chem. Soc.* **1976**, *98*, 4010.

(2) van Soest, W. M.; Desqueyroux-Faúdez, R.; Wright, A. D.; König, G. M. *Bull. Ins. R. Sci. Nat. Belg. Biol.* **1996**, *66*, 103.

(3) König, G. M.; Wright, A. D. *Mem. Queensl. Museum* **1999**, *44*, 281.

(4) Konig, G. M.; Wright, A. D. *Magn. Reson. Chem.* **1995**, *33*, 694.

(5) Corey, E. J.; Magriotis, P. A. *J. Am. Chem. Soc.* **1987**, *109*, 287.

(6) Corey, E. J.; Peterson, R. T. *Tetrahedron Lett.* **1985**, *26*, 5025.

(7) Numbering matches the adociane scaffold, i.e. 7, 20-Diisocyanoadociane.

(8) Fookes, C. J. R.; Garson, M. J.; MacLeod, J. K.; Skelton, B. W.; White, A. H. *J. Chem. Soc. Perkin Trans. 1* **1988**, 1003.

(9) Schindeler, T. W. Ph.D. Dissertation, University of British Columbia, 1998.

(10) Garson, M. J.; Thompson, J. E.; Larsen, R. M.; Battershill, C. N.; Murphy, P. T.; Bergquist, P. R. *Lipids* **1992**, *27*, 378.

(11) Garson, M. J. *J. Chem. Soc. Chem. Commun.* **1986**, 35.

(12) De Roa, M.; Minale, L.; Sodano, G. *Comp. Biochem. Physiol.* **1973**, *45B*, 883.

(13) Garson, M. J. *Nat. Prod. Rep.* **1989**, *6*, 143.

(14) Garson, M. J.; Simpson, J. S. *Nat. Prod. Rep.* **2004**, *21*, 164.

(15) Karuso, P.; Scheuer, P. J. *J. Org. Chem.* **1989**, *54*, 2092.

(16) Simpson, J. S.; Garson, M. J. *Org. Biomol. Chem.* **2004**, *2*, 939.

(17) Simpson, J. S.; Garson, M. J. *Tetrahedron Lett.* **1999**, *40*, 3909.

(18) Garson, M. J. *Chem. Rev.* **1993**, *93*, 1699.

(19) Garson, M. J.; Zimmermann, M. P.; Battershill, C. N.; Holden, J. L.; Murphy, P. T. *Lipids* **1994**, *29*, 509.

(20) Garson, M. J.; Zimmermann, M. P.; Hoberg, M.; Larsen, R. M.; Battershill, C. N.; Murphy, P. T. *Lipids* **1993**, *28*, 1011.

(21) Kazlauskas, R.; Murphy, P. T.; Wells, R. J.; Blount, J. F. *Tetrahedron Lett.* **1980**, *21*, 315.

(22) Morita, M.; Endo, M. *J. Pharmacobio-Dyn.* **1985**, *8*, s74.

(23) Angerhofer, C. K.; Pezzuto, J. M.; König, G. M.; Wright, A. D.; Sticher, O. *J. Nat. Prod.* **1992**, *55*, 1787.

(24) Wright, A. D.; König, G. M.; Angerhofer, C. K.; Greenidge, P.; Linden, A.; Desqueyroux-Faúndez, R. *J. Nat. Prod.* **1996**, *59*, 710.

(25) König, G. M.; Wright, A. D.; Angerhofer, C. K. *J. Org. Chem.* **1996**, *61* (10), 3259.

(26) Wright, A. D.; McCluskey, A.; Robertson, M. J.; MacGregor, K. A.; Gordon, C. P.; Guenther, J. *Org. Biomol. Chem.* **2011**, *9*, 400.

(27) Gelb, M. H. *Curr. Opin. Chem. Biol.* **2007**, *11*, 440.

(28) Dondorp, A. M.; Nosten, F.; Poravuth, Y.; Das, D.; Phyo, A. P.; Tarning, J.; Lwin, K. M.; Ariey, F.; Hanpithakpong, W.; Lee, S. J.; Ringwald, P.; Silamut, K.; Imwong, M.; Chotivanich, K.; Lim, P.; Herdman, T.; An, S. S.; Yeung, S.; Singhasivanon, P.; Day, N. J. *N. Eng. J. Med.* **2009**, *361*, 455.

(29) Flannery, E. L.; Chatterjee, A. K.; Winzeler, E. A. *Nat. Rev. Microbiol.* **2013**, *11*, 849.

(30) Miller, L. H.; Ackerman, H. C.; Su, X.-z.; Wellems, T. E. *Nat. Med.* **2013**, *19*, 156.

(31) Weissbuch, I.; Leiserowitz, L. *Chem. Rev.* **2008**, *108*, 4899.

(32) Wang, J.; Zhang, C.-J.; Chia, W. N.; Loh, C. C. Y.; Li, Z.; Lee, Y. M.; He, Y.; Yuan, L.-X.; Lim, T. K.; Liu, M.; Liew, C. X.; Lee, Y. Q.; Zhang, J.; Lu, N.; Lim, C. T.; Hua, Z.-

C.; Liu, B.; Shen, H.-M.; Tan, K. S. W.; Lin, Q. *Nat. Commun.* **2015**, *6*, 10111.

(33) Wright, A. D.; Wang, H.; Gurrath, M.; König, G. M.; Kocak, G.; Neumann, G.; Loria, P.; Foley, M.; Tilley, L. *J. Med. Chem.* **2001**, *44*, 873.

(34) Young, R. M.; Adendorff, M. R.; Wright, A. D.; Davies-Coleman, M. T. *Eur. J. Med. Chem.* **2015**, *93*, 373.

(35) Pronin, S. V.; Shenvi, R. A. *J. Am. Chem. Soc.* **2012**, *134*, 19604.

(36) Pronin, S. V.; Reiher, C. A.; Shenvi, R. A. *Nature* **2013**, *501*, 195.

(37) Piers, E.; Llinas-Brunet, M. *J. Org. Chem.* **1989**, *54*, 1483.

(38) Piers, E.; Llinas-Brunet, M.; Oballa, R. M. *Can. J. Chem.* **1993**, *71*, 1484.

(39) Piers, E.; Romero, M. A. *Tetrahedron* **1993**, *49*, 5791.

(40) Schnermann, M. J.; Shenvi, R. A. *Nat. Prod. Rep.* **2015**, *32*, 543.

(41) Crabtree, S. R. Ph.D. Dissertation, Australia National University, 1990.

(42) Evans, D. A. "Stereoselective Alkylation Reactions of Chiral Metal Enolates" In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, 1984; p 2.

(43) Cossey, A. L.; Gunter, M. J.; Mander, L. N. *Tetrahedron Lett.* **1980**, *21*, 3309.

(44) Mander, L. N. *Synlett* **1991**, 134.

(45) Schultz, A. G.; Macielag, M.; Podhorez, D. E.; Suhadolnik, J. C.; Kullnig, R. K. *J. Org. Chem.* **1988**, *53*, 2456.

(46) Miyaoka, H.; Okubo, Y.; Muroi, M.; Mitome, H.; Kawashima, E. *Chem. Lett.* **2011**, *40*, 246.

(47) Francis, C. J.; Jones, J. B. *J. Chem. Soc. Chem. Commun.* **1984**, 579.

(48) Kuroda, C.; Murase, A.; Suzuki, H.; Endo, S.; Anzai, S. *Bull. Chem. Soc. Jpn.* **1998**, *71*, 1639.

(49) Miyaoka, H.; Okubo, Y. *Synlett* **2011**, 547.

(50) Miyaoka, H.; Abe, Y.; Sekiya, N.; Mitome, H.; Kawashima, E. *Chem. Commun.* **2012**, *48*, 901.

(51) Miyaoka, H.; Shida, H.; Yamada, N.; Mitome, H.; Yamada, Y. *Tetrahedron Lett.* **2002**, *43*, 2227.

(52) Miyaoka, H.; Abe, Y.; Kawashima, E. *Chem. Pharm. Bull.* **2012**, *60*, 1224.

(53) Kuroda, C.; Murase, A.; Suzuki, H.; Endo, T.; Anzai, S. *Bull. Chem. Soc. Jpn.* **1998**, *71*, 1639.

(54) The preparation of **1.88** is counted as taking three steps from commercial 3-methylglutaric acid.

(55) During the preparation of this dissertation a synthesis of DICA and preliminary antiplasmodial activity during the liver stage was published: Lu, H.-H.; Pronin, S. V.; Antonova-Koch, Y.; Meister, S.; Winzeler, E. A.; Shenvi, R. A. *J. Am. Chem. Soc.* **2016**, DOI: 10.1021/jacs.6b03899.

CHAPTER 2:

INITIAL EFFORTS TOWARDS 7,20-DIISOCYANOADOCIANE

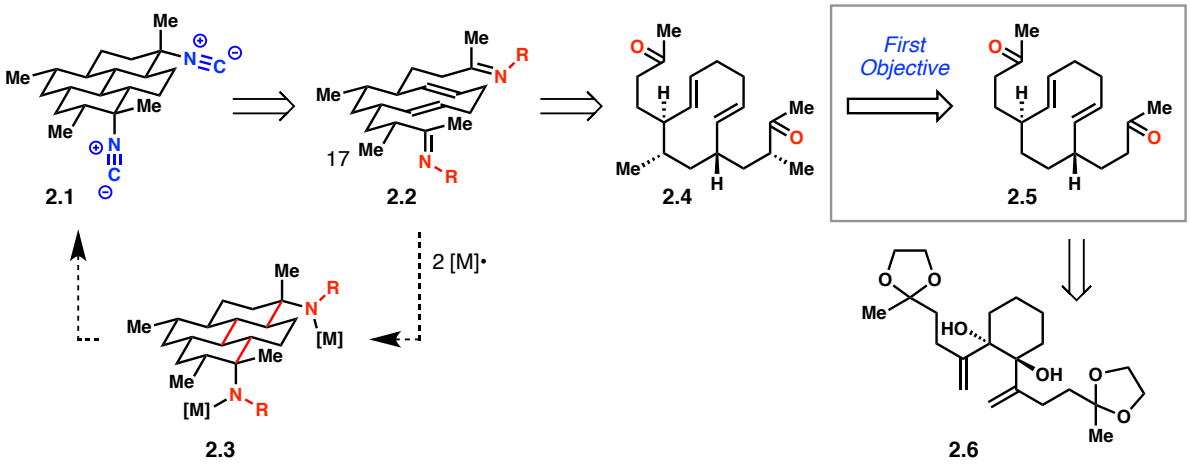
2.1 Introduction

7,20-Diisocyanoadociane (**2.1**, DICA) was chosen as a synthetic target for its complex tetracyclic structure, unusual incorporation of isonitriles and because so far it has not succumbed to a concise and efficient synthesis.[1–3] This synthetic program was not initiated because of a specific methodology or targeted post-synthetic study and thereby provided a freedom in ideas and execution. This autonomy offered both a great opportunity to explore reactivity and designs, but also at times became a challenge when prioritizing multiple avenues. Described here are the initial pursuits to DICA.

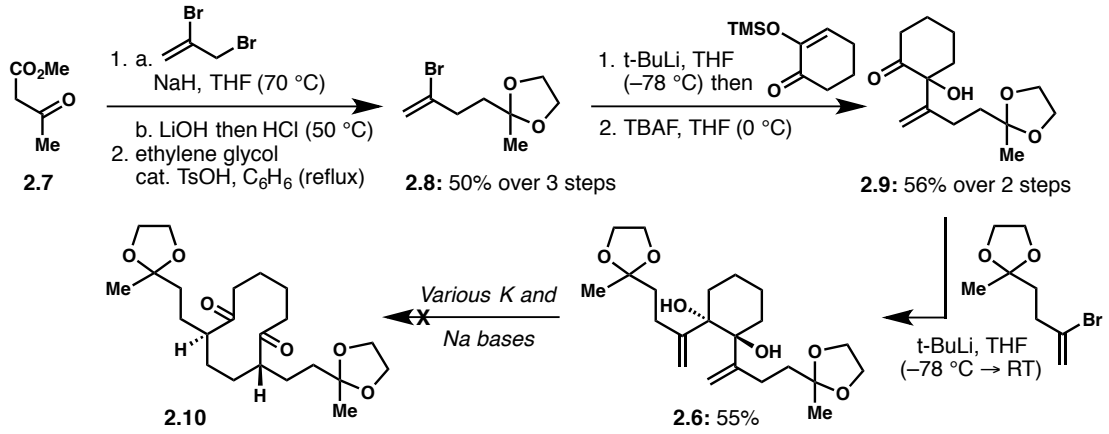
2.2 A Polyene Imino–Pinacol Coupling Approach

The first synthetic idea for tackling DICA was a proposed radical polyene cyclization.[4] The framework of DICA would be constructed by single electron reduction of an imine in **2.2** to the radical anion, two six-endo cyclizations and a six-exo termination onto the second imine followed by final reduction with a second equivalent of reductant (Scheme 2.1). The resulting bis-amine could be elaborated into DICA. Overall, the desired transformation can be classified as a polyene imino–pinacol coupling,[5] a currently unknown transformation. The stereochemical outcome of this reaction was not considered, but the C17 methyl group could potentially induce some stereocontrol. Synthetically, the first objective was to prepare **2.5**, a desmethyl analog to diketone **2.4**. Among the various ideas proposed, a bis-anionic oxy-Cope reaction was attractive for its use of symmetry.

Scheme 2.1 An initial polyene imino–pinacol coupling idea.



Scheme 2.2 An attempted bis-oxy-Cope rearrangement.



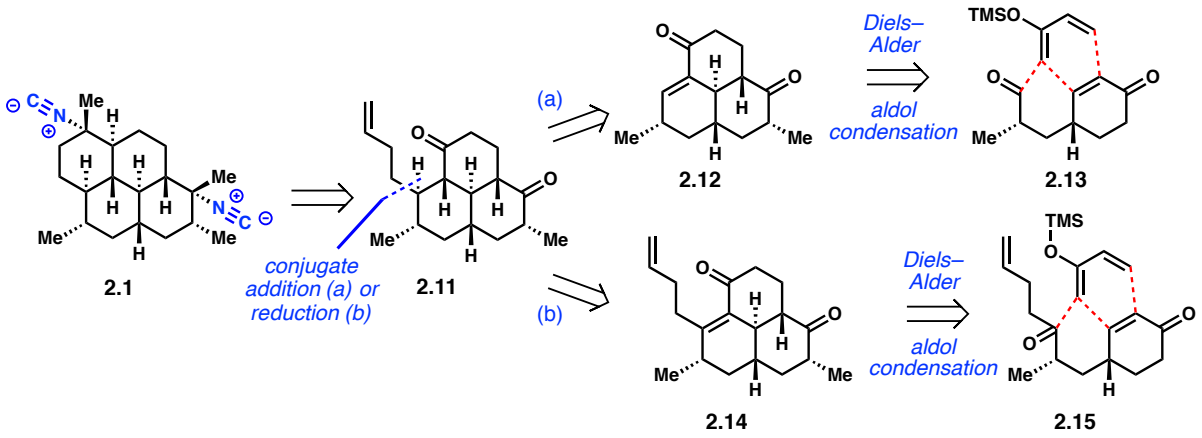
The approach was initiated by the preparation of vinyl bromide **2.8** via β-ketoester alkylation, decarboxylation and ketal protection. Lithium/halogen exchange with t-BuLi and addition to 2-(trimethylsiloxy)cyclohex-2-enone afforded **2.9** following TBAF desilylation. A second vinyllithium addition afforded *trans*-diol **2.6**. Unfortunately using KHMDS, KOt-Bu, K_2CO_3, or NaH in THF up to reflux and in the microwave in DMF and DCB, no product suggestive of **2.10** was observed. Literature precedent indicates that after a bis-oxy-Cope reaction, the substrates are well established to undergo transannular aldol reactions.[6–8] This

reactivity could also be imagined complicating the outcome of the attempted bis-oxy-Cope rearrangements of **2.6**.

2.3 A Diels–Alder/Aldol Condensation Pursuit

The polyene cyclization idea was set aside in favor of an anionic oxy-Cope/Michael approach inspired by a literature reaction (see Chapter 3). Upon recognizing and explaining the unexpected stereochemical complexities,[9] the targeted intermediate **2.11** was still attractive for another attempt (Scheme 2.3). Two ideas were conceived: (1) a conjugate addition to **2.12**, and (2) a conjugate reduction of **2.14**. The synthesis of both enones **2.12** and **2.14** was disconnected via a Diels–Alder/aldol condensation cascade. The construction of aldehyde **2.13** was considered easier and therefore pursued first.

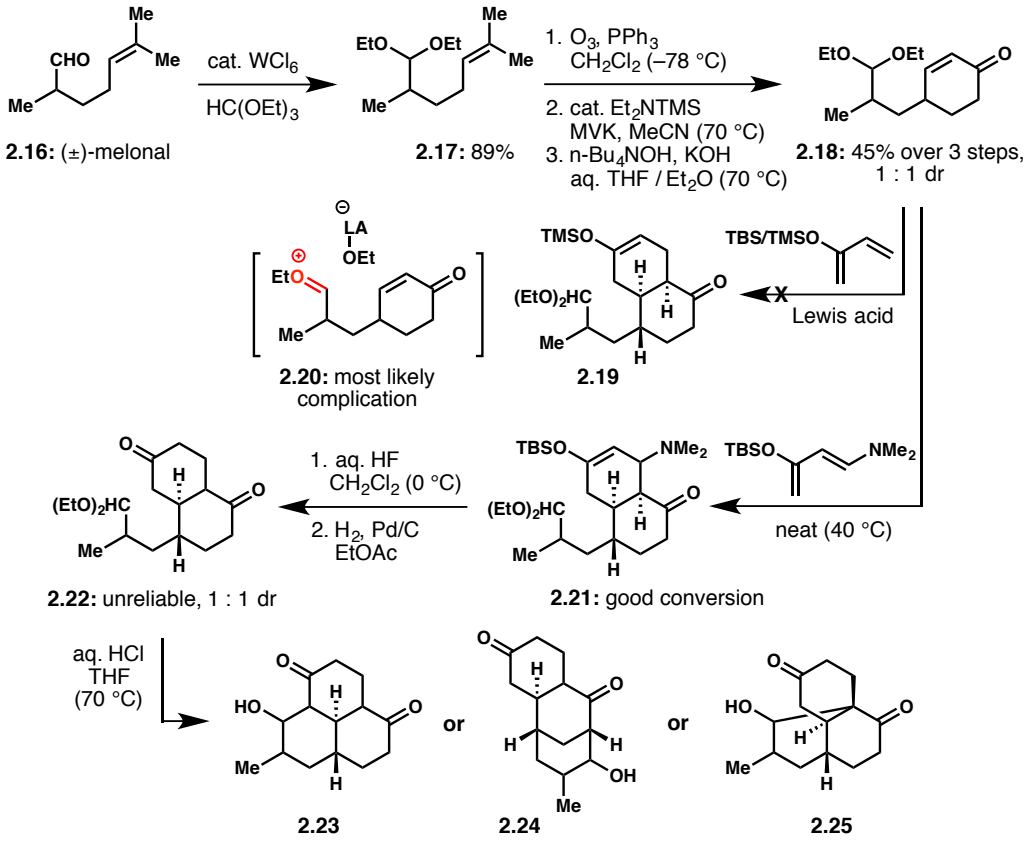
Scheme 2.3 A Diels–Alder/aldol condensation proposal to DICA.



The route began with a ketal protection of melonal **2.16**,[10] followed by an ozonolysis and Robinson annulation to generate **2.18** (Scheme 2.4). A ketal-protecting group was chosen because a one step deprotection and aldol condensation was envisioned to forge the third ring. Unfortunately, the ketal caused significant problems during the Diels–Alder reaction. Lewis acid

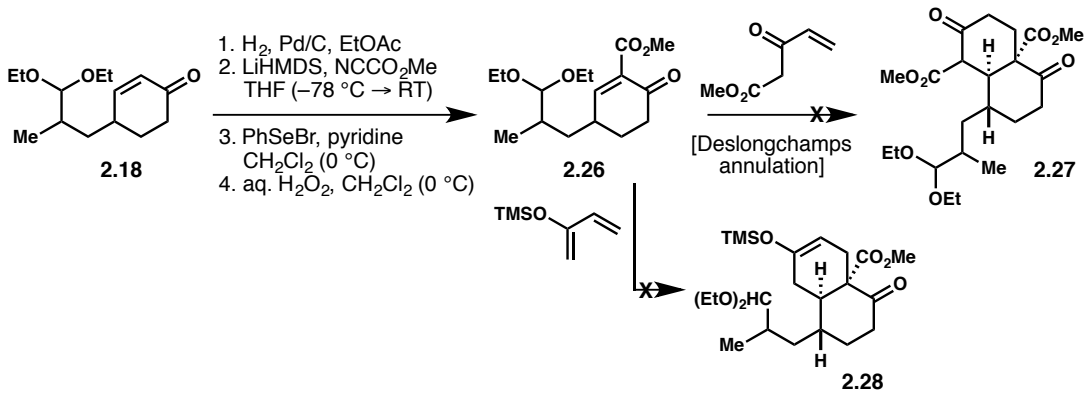
mediated cyclization did not provide cycloadduct **2.19**, most likely because of competitive ionization of the ketal (**2.20**). Heating a neat mixture of 2-(trimethylsiloxy)butadiene[11] and **2.18** was also unsuccessful. Good reactivity was found when neat Rawal's diene[12] and **2.18** were heated at slightly elevated temperature. Disappointingly, the deprotection and installation of the enone was not successful. In retrospect, running the reaction in an HF soluble solvent such as MeCN would have been a wiser decision than CH_2Cl_2 and could have led to success. Still, small quantities of **2.22** were obtained, which when heated in the presence of aqueous HCl generated a single diastereomer of an alcohol-bearing aldol product. Unfortunately, the structure was not determined, but is likely to be **2.23**, **2.24** or **2.25**. To better understand this reactivity, a more reliable route to **2.22** was sought.

Scheme 2.4 Initial success of the Diels–Alder/aldol condensation idea.



To improve the material throughput to **2.22**, a dienophile-activating group was introduced (Scheme 2.5). The ester unit on **2.26** was installed using Mander's reagent followed by selenylation and selenoxide elimination. Deslongchamps annulation[13,14] using Nazarov reagent[15] **2.26** under acidic, basic or neutral conditions in numerous solvents did not afford **2.27**. The Deslongchamps annulation has been used extensively in total synthesis, but a unifying feature is that all examples feature a β-substituted Nazarov reagent. A control reaction using such a β-substituted Nazarov reagent was not attempted, but would give good indication on whether **2.26** is a competent coupling partner. Thermal conditions using 2-(trimethylsilyloxy)butadiene only returned starting material.[16] In the wake of semi-success at the Diels–Alder/aldol condensation idea, elimination of the problematic ketal in **2.18** was pursued.

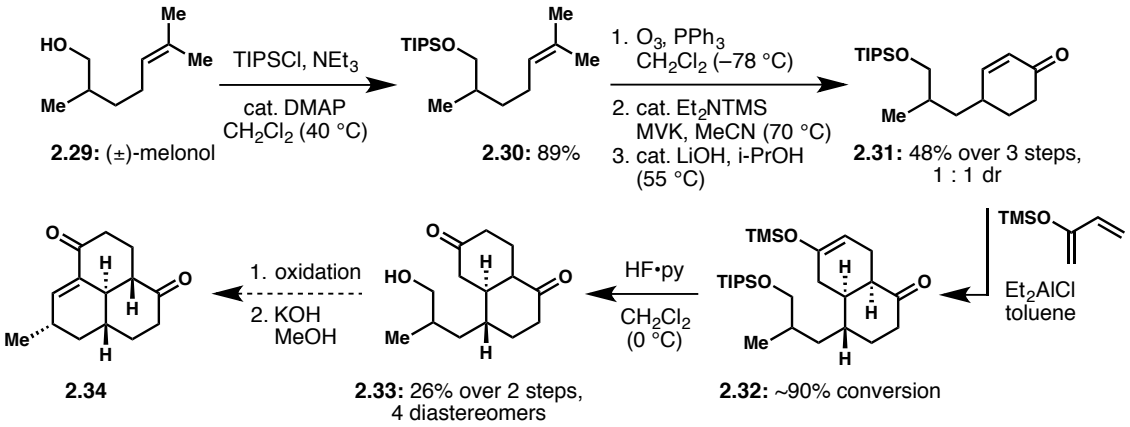
Scheme 2.5 Attempted Diels–Alder reaction via dienophile activation.



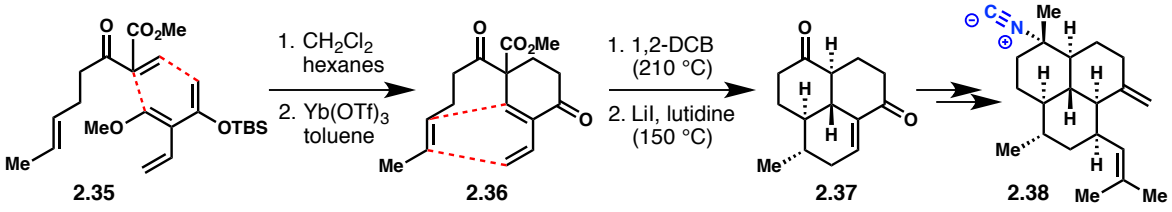
Instead of using a ketal as the masked aldehyde, which complicated Lewis acid activation of the dienophile for Diels–Alder reactivity, **2.29** could be converted into TIPS protected alcohol **2.30** (Scheme 2.6). Oxidative cleavage of the alkene then set up for another Robinson annulation. Standard diethylaminotrimethylsilane-catalyzed conjugate addition conditions were retained, but homogenous LiOH-mediated aldol condensation conditions[17] were implemented to furnish **2.31** instead, as biphasic conditions were unsuccessful in generating **2.18**. Diels–Alder with 2-

(trimethylsiloxy)butadiene in the presence of two equivalents of Et_2AlCl led to good conversion to **2.32**. The last aldol condensation was not attempted on this system because at this point the general approach was considered too close to an ICT synthesis reported concurrently by Shenvi (Scheme 2.7).[18]

Scheme 2.6 Incomplete efforts towards a Diels–Alder/aldol condensation sequence.



Scheme 2.7 An ICT synthesis by Shenvi.



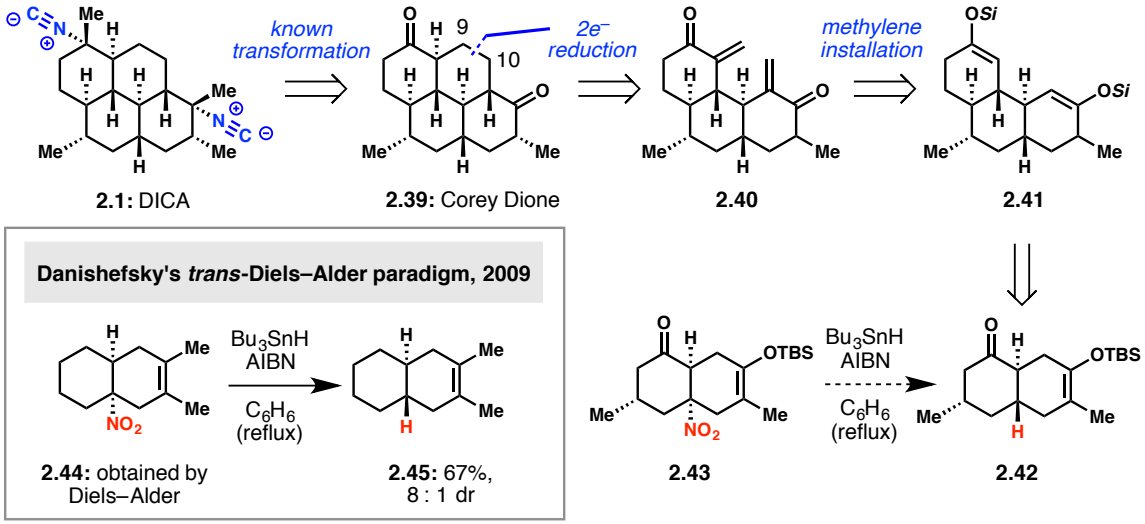
2.4 The Methylenation/Reductive Ring Closure Approach

2.4.1 Application of Danishefsky's trans-Diels–Alder Paradigm

The next set of ideas revolved around a complete redesign of a synthesis of DICA (Scheme 2.8). Corey's dione **2.39** was disconnected between C9–C10 back to bis-enone **2.40**. The last ring closure would occur by a two-electron reductive coupling of bis-enone **2.40**.[19] The

pseudo-symmetric **2.40** was further disconnected to bis-enoxysilane **2.41**. Danishefsky's *trans*-Diels–Alder reaction was considered advantageous for gaining entry into the required *trans*-stereochemistry of decalin **2.42**.[20]

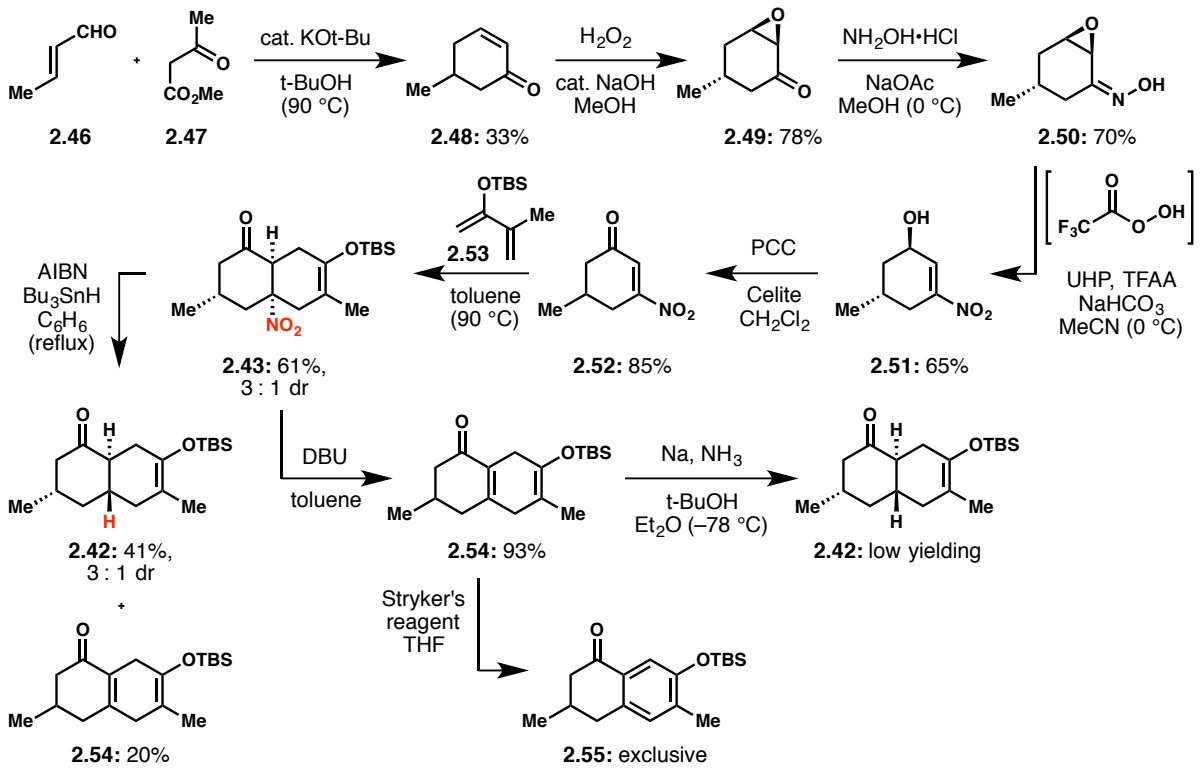
Scheme 2.8 General proposal for a final reductive ring closure.



The synthesis of **2.43** was performed in an analogous manner to a Corey procedure (Scheme 2.9).[21] Cyclohexenone **2.48** was smoothly epoxidized under basic conditions and then treated with hydroxylamine to generate oxime **2.50**. Trifluoroperoxyacetic acid oxidized the oxime to a nitro functional group, which triggered opening of the epoxide. After oxidation of the alcohol, the doubly activated alkene **2.52** was subjected to Diels–Alder reaction with dienoxysilane **2.53** to generate **2.43** in 3 : 1 dr. The stereochemistry depicted was assigned based on an analogous literature reaction.[22] Tributyltin hydride radical denitration successfully afforded **2.42**, although significant elimination product **2.54** was also observed. Alternatively, the nitro could be eliminated with DBU to afford **2.54**. Conjugate reduction with Stryker's reagent afforded only tetralone **2.55**. Birch reduction of **2.54** generated **2.42**, however in low yields.

After a more critical examination of this route, the undesired alkene-orientation of **2.42** and the fairly involved sequence of steps made a different approach more appealing.

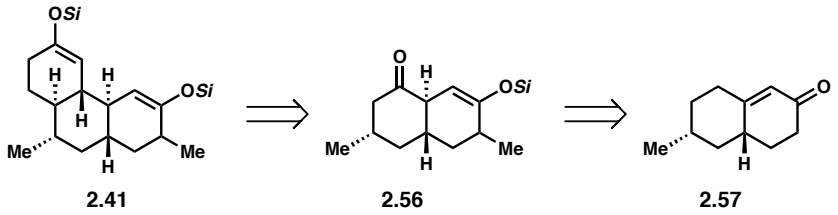
Scheme 2.9. Diels–Alder reactivity of an activated nitroalkene.



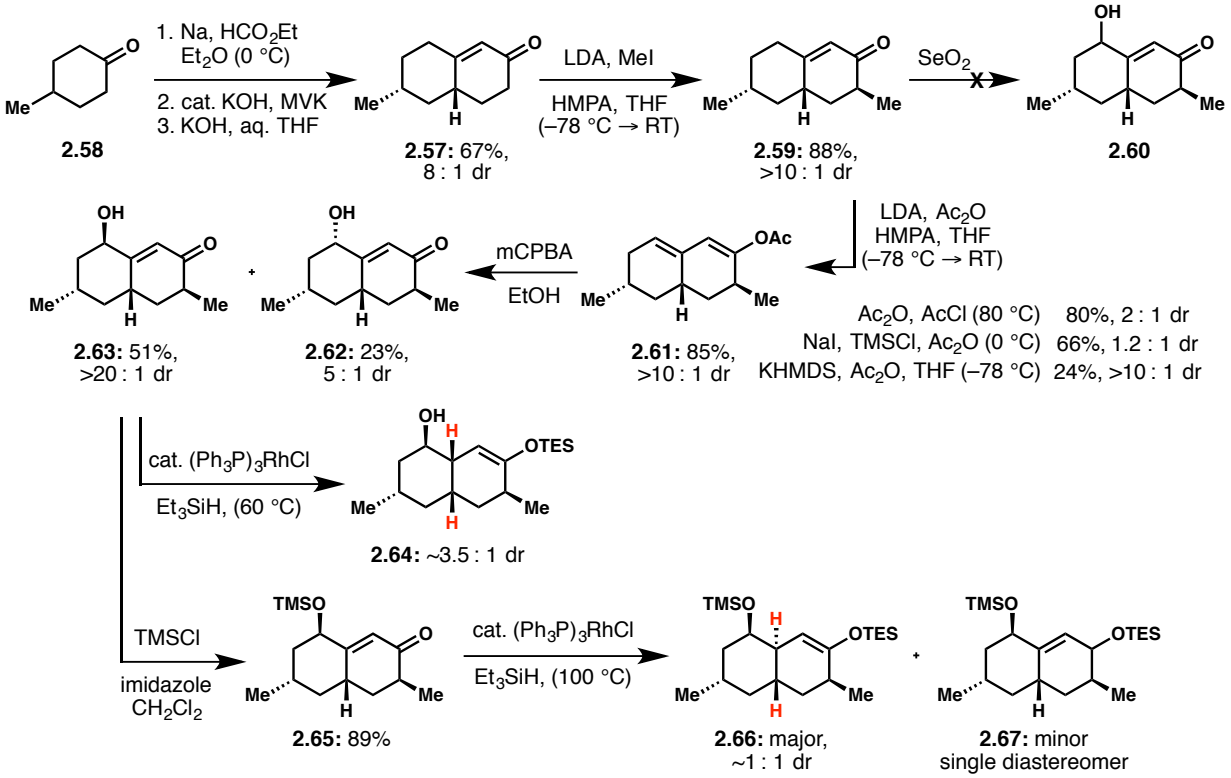
2.4.2 Efforts Towards a trans-Selective Conjugate Hydrosilylation Approach

The previous approach was changed because of perceived complications in having the enoxysilane enolized in the incorrect direction (Scheme 2.10). The basic idea of a reductive enone coupling idea was still exciting, but correct orientation of the C20 enoxysilane in **2.41** was considered important. In a second-generation approach, **2.41** was disconnected back to enone **2.57**.

Scheme 2.10 Tracing tricyclic bis-enoxysilane **2.41** back to a simple octalone starting material.



Scheme 2.11 Initial success of a *trans*-selective conjugate hydrosilylation.

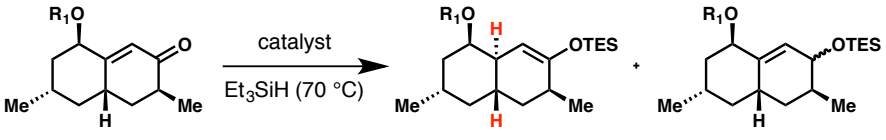


The octalone **2.57** was constructed by Robinson annulation onto 4-methylcyclohexenone **2.58** (Scheme 2.11). Alkylation of the cross-conjugated dienolate with MeI installed the C17 methyl group in excellent diastereoselectivity. A direct allylic oxidation with selenium dioxide did not afford any **2.60** and therefore a two-step protocol was implemented instead. Generation of the conjugated dienoxy acetate was accomplished under a variety of conditions; however, epimerization of the C17 methyl group was consistently observed. The use of LDA with HMPA

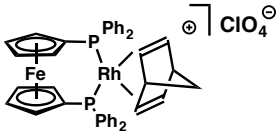
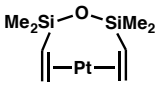
and Ac_2O was eventually successful in affording **2.61** as a single diastereomer. Oxidation of **2.61** with in situ generated DMDO was successful in generating **2.62** and **2.63**; however, low yields and a messy reaction profile were reason to switch to mCPBA. Conjugate reduction of **2.63** with Li/NH_3 only caused elimination of the gamma-hydroxide. Conjugate hydrosilylation was accomplished with Wilkinson's catalyst in triethylsilane at elevated temperatures to afford **2.64** bearing a *cis*-ring fusion. Installing a bulky trimethylsilyl group on the alcohol was designed to block the *cis*-face of the enone and direct to a more *trans*-selective hydrosilylation. Delightfully, this design was successful! The reduction of **2.65** with Wilkinson's catalyst afforded a 1 : 1 mixture of *cis*- and *trans*-ring fusions. Unfortunately, 1,2-reduction of the enone was also observed. The next step was to improve the 1 : 1 dr by using larger alcohol protecting groups and evaluating different catalysts.

Several combinations of alcohol protecting group and catalyst were examined (Table 2.1). A general reactivity screen narrowed the catalysts to those providing clean conjugate reduction. Pivaloyl protecting the alcohol of **2.63** enhanced the selectivity from *cis*-conjugate silylation to an approximately 1 : 1 mixture. Karstedt's catalyst was determined to be the most reliable in affording 1,4 over 1,2-reductions (entry 6). Other platinum sources such as $Pt(PPh_3)_4$ and PtO_2 provided similar diastereoselectivity, but were much less active than Karstedt's catalyst or competitively conducted 1,2-reduction (entries 8, 9).

Table 2.1 Consolidation of conjugate hydrosilylation reactions.

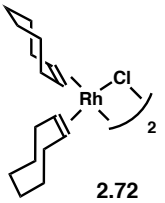


2.68 **2.69** **2.70**

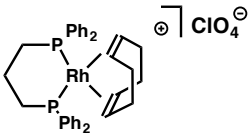
Entry	Catalyst[b]	R_1	Yield	2.69 trans / cis[a]	2.70
1	$Rh_2(OAc)_4$	TMS		**1 : 4**	
2		TMS		**1 : 4**	
3		Bz		**1 : 9**	
4		Piv		**1 : 1.4**	
5		Bz		**1 : 3.5**	
6	Karstedt's Catalyst	Piv	**80%**	**1.1 : 1**	
7	Grubbs I, II Stewart–Grubbs	Piv			**exclusive**
8	$Pt(PPh_3)_4$	Piv		**1.3 : 1**	
9	PtO_2	Piv		**1.2 : 1**	**major**
10	Pt/C	Piv			**major**

[a] Ratio by ^1H NMR of crude reaction mixture without an internal standard
[b] Catalysts with unsuccessful conversions or messy reaction outcomes:

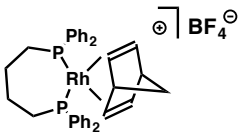
$Rh_2(TFA)_4$ **2.71**



2.72



2.73

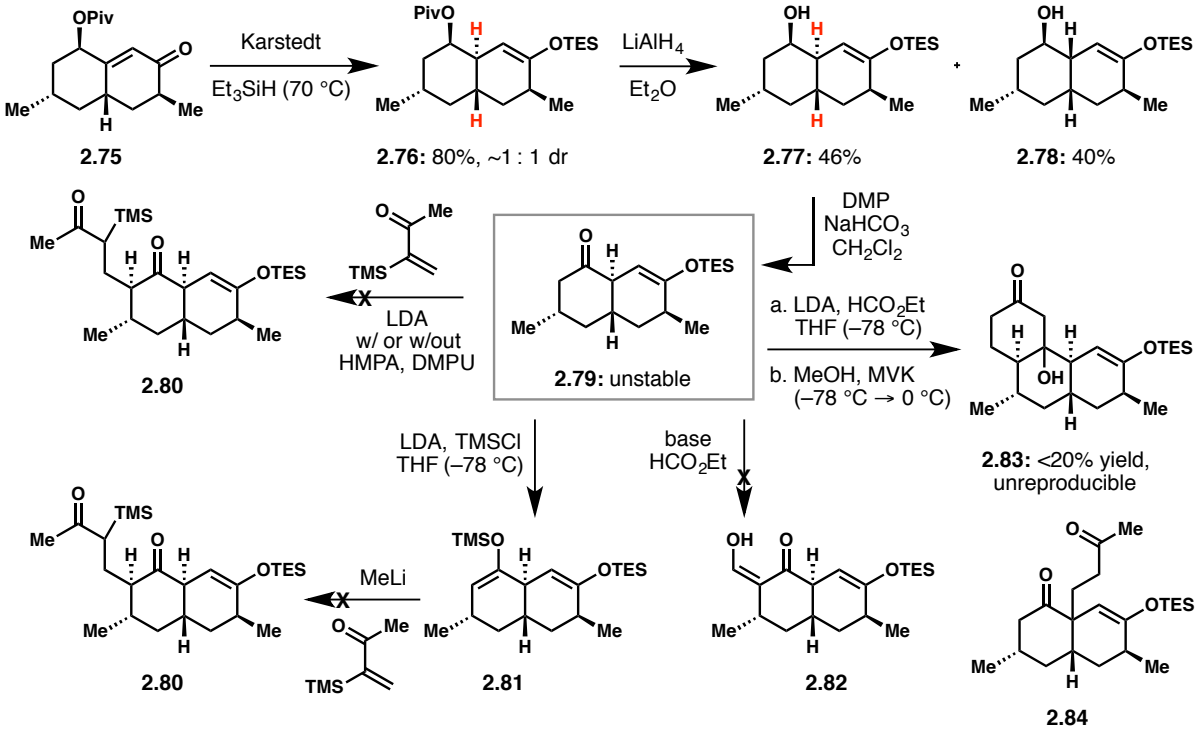


2.74

With a relatively acceptable 1.1 : 1 *trans*-selective hydrosilylation established, the route was continued (Scheme 2.12). Deprotection of the pivaloyl group with $LiAlH_4$ generated separable alcohols **2.77** and **2.78**, both of which were readily handled, stable to silica gel and storable at room temperature. Upon oxidation of **2.77** to ketone **2.79**, the material became much more unstable and needed to be used without purification within an hour. The first attempted Robinson annulation used the Stork–Ganem reagent.[23] However, enolizing **2.79** with LDA and attempting conjugate addition did not furnish any product reminiscent of **2.80**. The

enoxytrimethylsilane **2.81** could be generated cleanly by action of LDA, indicating that enolization occurs as expected. Attempts to reveal the enolate with MeLi were unsuccessful, leading to only decomposition, even upon simple aqueous quench. Standard Claisen condensation conditions of treating **2.79** with base, such as KOt-Bu, NaH or LDA and ethyl formate did not provide any **2.82**. The only conditions successful at generating the desired C–C bond involved treating **2.79** with LDA and ethyl formate, followed by quenching with methanol and excess methyl vinyl ketone. An additional compound, proposed to be **2.84** was also isolated. The low yield and unreliable preparation of **2.83** led to a reevaluation of strategy.

Scheme 2.12 Exploring a Robinson annulation onto **2.79**.

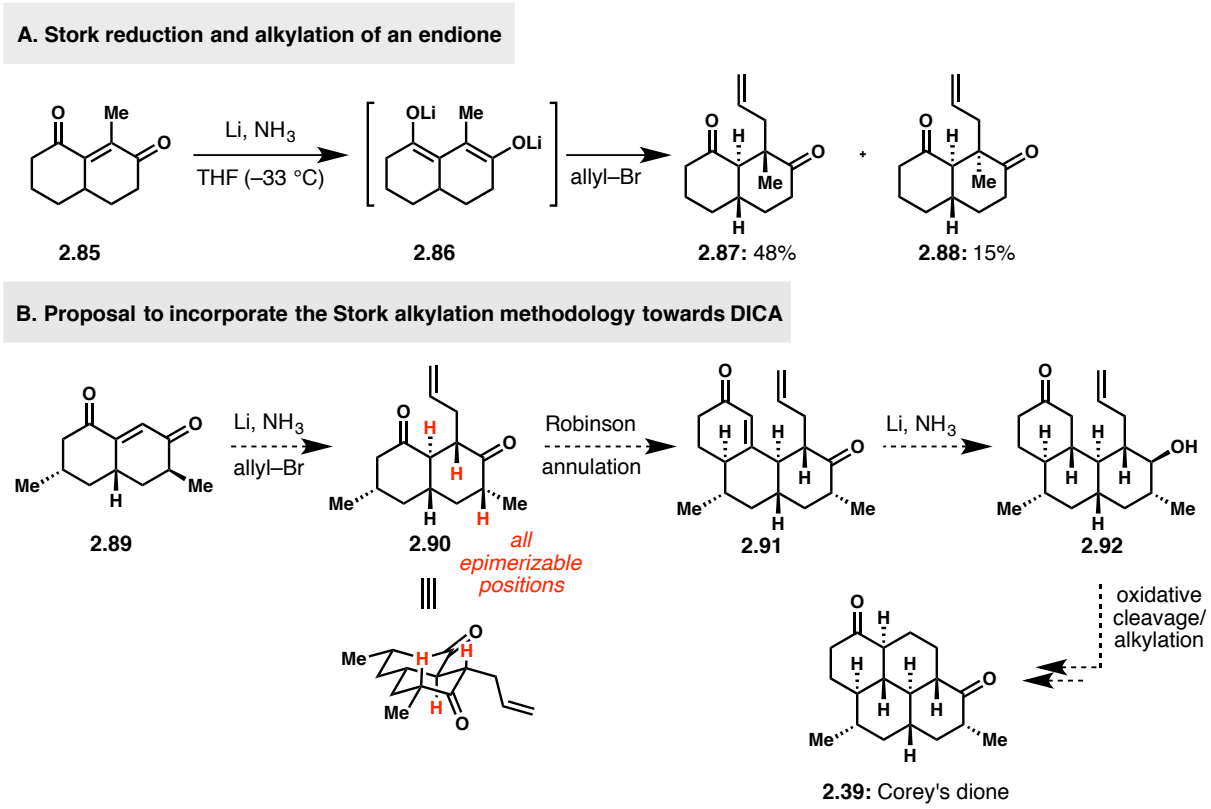


2.4.3 A Reductive Stork Alkylation

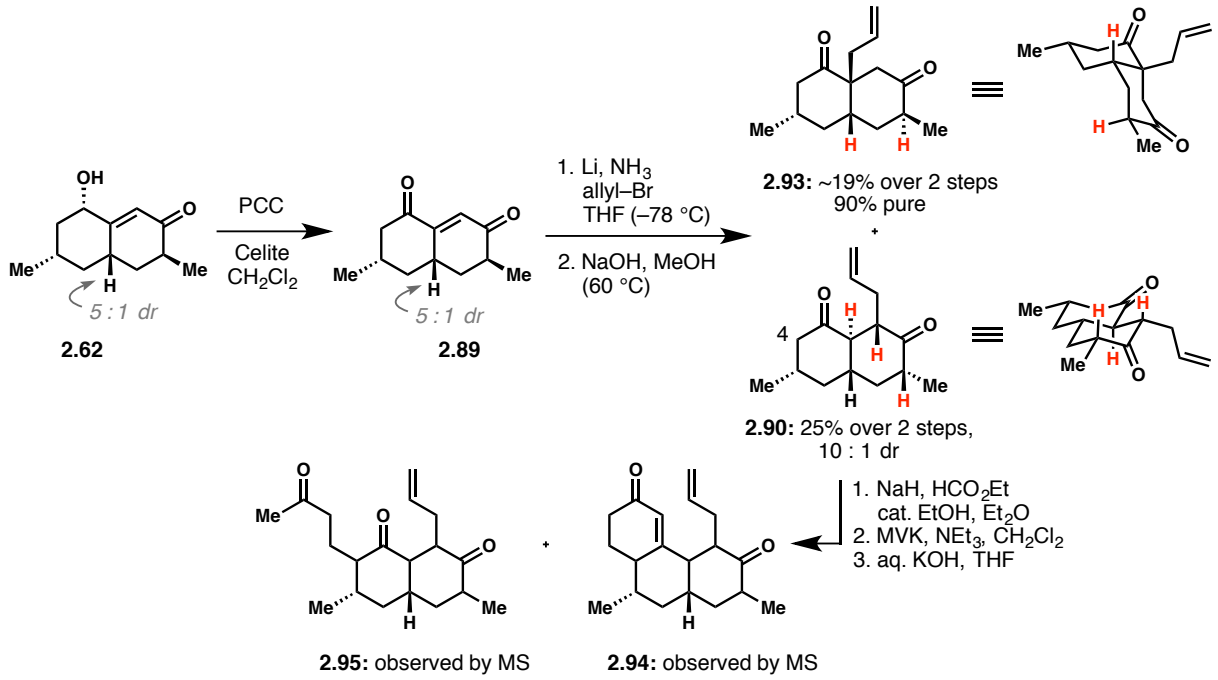
A more robust approach was attempted owing to the difficulty in executing a Robinson

annulation onto **2.79**. An inspiration for the next attempt was Stork's reduction of enedione **2.85** to the dienolate **2.86** and subsequent alkylation (Scheme 2.13A).[24] This procedure has found extensive utility in steroid chemistry[25–28] and other total syntheses,[29,30] making it reliable enough to commit towards DICA. Reductive alkylation of **2.89** would generate **2.90** after epimerization of the three enolizable positions (Scheme 2.13B). A Robinson annulation onto **2.90** via activation through the keto-aldehyde would ensure selective enolization. A final ring closure would then prepare Corey's dione **2.39**.

Scheme 2.13 Allylation and subsequent ring closures based on a reductive Stork alkylation.



Scheme 2.14 A reductive Stork alkylation towards DICA.



The undesired minor diastereomer from the hydrosilylation approach, **2.62** was oxidized to enedione **2.89** (Scheme 2.14). Addition of **2.89** to a solution of Li/NH_3 and quenching with allyl bromide generated a mixture of compounds that could be converged to two mono-allylated products **2.93** and **2.90** upon equilibration with base. Di-allylated products were also observed, but not quantified or characterized. The undesired mono-allyl product **2.93** arose from alkylation at the ring fusion. The *cis*-alkylation was assigned because equilibrating conditions after alkylation did not change the ^{1}H NMR spectrum and this could only be possible if the β-methyl group is already in an equatorial orientation as in **2.93**. The desired allylation product was equilibrated to the all-equatorially oriented **2.90** and then subjected to Robinson annulation. Activation of the C4 position as the keto-aldehyde set up for a selective Michael addition and ring closure. This procedure produced a mixture of compounds, but by mass spectrometry both **2.95** and the fully condensed **2.94** were observed, indicating feasibility of the original plan. The route however, fell out of favor owing to the irreproducibility and low yield of the enolate

alkylation and conception of a more robust entry to molecules similar to **2.94** (Chapter 4). In retrospect, the complications experienced during the reductive alkylation are most likely due to the inexperience in handling dissolving metal reductions.

2.5 Conclusions

The project of synthesizing 7,20-diisocyanoadociane was initiated with the goal of contributing a short and selective synthesis. The synthetic journey started with a bold radical cascade idea. Although it was never attempted, a ketyl or amine radical anion polyene cyclization could still be an interesting methodology to investigate. This early work was essential in probing possible avenues for a synthetic program. Retrospectively, these early explorations had fatal flaws, were discontinued due to inexperience or were simply supplanted by "better" ideas. A continuous evolution in ideas and change in strategy continuously sharpened the trajectory towards a synthesis of DICA and were directly continued in Chapter 4.

2.6 Experimental Procedures

Purifications –

Solvents: Dry tetrahydrofuran (THF), diethyl ether (Et_2O), dichloromethane (CH_2Cl_2), toluene, benzene (C_6H_6), dimethylformamide (DMF), acetonitrile (MeCN), methanol (MeOH) were obtained by passing commercially available formulations through activated alumina columns. tert-Butyl alcohol (t-BuOH) was purified by distillation from CaH_2.

Amines: Triethylamine (NEt_3), N,N'-dimethylpropylene urea (DMPU) hexamethylphosphoramide (HMPA), pyridine (py) was purified by distillation from CaH_2.

Halides: Trimethylsilyl chloride was purified by distillation from CaH_2.

Miscellaneous: Tributyltin hydride was purified by distillation. Melonal was obtained from Sigma-Aldrich and purified by column chromatography (100:1 hexanes/EtOAc). Methyl vinyl ketone (MVK) was purified by distillation. Acetic anhydride was purified by fractional distillation. Allyl bromide was purified by distillation and stored over copper beads at –20 °C. Trifluoroacetic anhydride was purified by distillation from CaH_2.

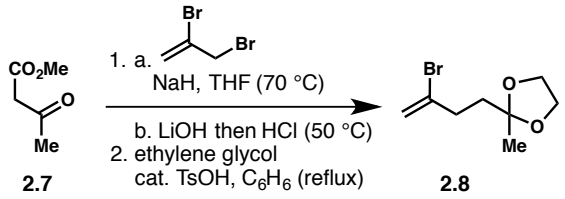
Titrations – Alkyllithium reagents were titrated using 2,6-di-(tert-butyl)-4-methylphenol (BHT) as the sacrificial proton source and fluorene as an indicator in THF or using diphenylacetic acid in THF. Grignard reagents were titrated using salicylaldehyde phenylhydrazone in THF.[31]

Reaction Setup – All reactions were carried out under an argon atmosphere with dry solvents under anhydrous conditions, unless otherwise noted. Argon balloons were the sole inert

atmosphere used. Reactions run at an ambient temperature of 20–25 °C are designated as room temperature. Microwave reactions were performed in an Anton Paar Microwave. Yields refer to chromatographically and spectroscopically homogeneous materials, unless otherwise stated.

Analysis – Thin layer chromatography was performed on 0.25 mm EMD glass-backed TLC plates impregnated with a fluorescent dye and visualized with UV light and $KMnO_4$ in K_2CO_3/NaOH/water or *p*-anisaldehyde in ethanol/aqueous H_2SO_4/AcOH and heat as a developing agent. Forced flow (flash) chromatography was performed on EMD Silica 60, mesh 0.04-0.063 silica gel. NMR spectra were recorded on Bruker 500 MHz instrument, obtained at 298 K unless otherwise noted and calibrated to residual undeuterated solvent as an internal reference. Chemical shifts are reported in ppm with the following abbreviations to explain multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, quin = quintuplet, sext = setet, sep = septet, bs = broad signal, m = multiplet. All coupling constants are apparent *J* values measured at the indicated field strengths. FT-IR spectra were recorded on a Perkin-Elmer spectrum RX1 spectrometer. High-resolution mass spectra (HRMS) were recorded on a H2Os LCT Premier spectrometer using ESI-TOF (electrospray ionization-time of flight). Melting points were measured on a MEL-TEMP II capillary apparatus and stand uncorrected.

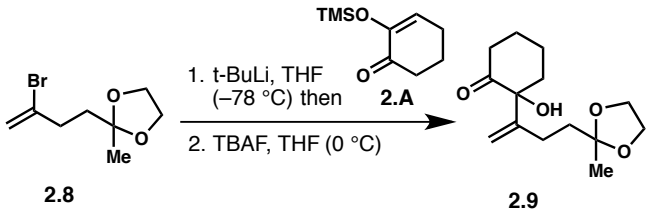
Vinyl Bromide 2.8



2.7 **2.8**

To a stirring suspension of 1.1 g (27 mmol) NaH (60% in mineral oil) in 30 mL THF cooled in an ice bath, was added 3.2 mL (30 mmol) **2.7** before the addition of 2.1 mL (22 mmol) 2,3-dibromopropene.[32] The reaction was warmed to room temperature, fitted with a reflux condenser and heated at 70 °C for 1 hour. After cooling the reaction to room temperature, 60 mL water, an additional 30 mL THF and 2.52 g (60 mmol) $LiOH•H_2O$ were added and the reaction heated at 50 °C. After 23 hours the reaction was cooled to room temperature and 6 M aq. HCl was added until bubbling subsided. The solution was extracted thrice with EtOAc. All organic layers were collected, washed thrice with sat. aq. $NaHCO_3$ and brine before being dried over $MgSO_4$ and stripped of all volatiles. The oil was dissolved in 60 mL C_6H_6 and refluxed under a Dean-Stark apparatus with 50 mg (0.26 mmol) *p*-$TsOH•H_2O$ and 1.7 mL (30 mmol) ethylene glycol. After cooling to room temperature, the organic layer was washed thrice with sat. aq. $NaHCO_3$, then water and brine before being dried over $MgSO_4$ and all volatiles removed in vacuo. The material was purified by column chromatography (30:1 hexanes/EtOAc) to afford 2.41 g (50% over 3 steps) **2.8** as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 5.59 (d, J = 1.4, 1H), 5.39 (d, J = 1.7, 1H), 3.99-3.92 (m, 4H), 2.56-2.53 (m, 2H), 1.95-1.92 (m, 2H), 1.35 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 134.3, 116.3, 109.2, 64.8, 37.7, 36.2, 24.0; IR (thin film) 2982, 2881, 1630, 1055 cm^{-1}; HRMS (ESI) calculated for $C_8H_{13}O_2Br$ $[M+Na]^+$ 221.0177 found 221.0181.

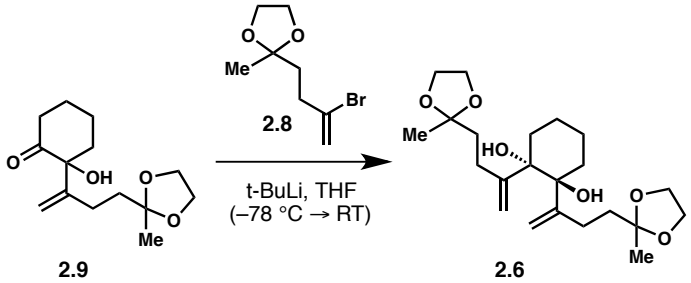
Hydroxyketone 2.9



2.8 2.9

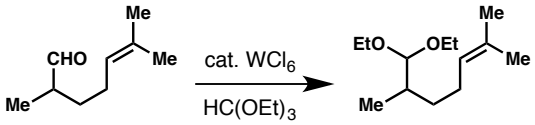
A solution of 0.82 g (7.3 mmol) 1,2-cyclohexanedione, 1.9 mL (15.0 mmol) TMSCl and 20 mL CH_2Cl_2 was treated with 3 mL (21.5 mmol) NEt_3 at room temperature. After 5 minutes, the solution was filtered and all volatiles removed in vacuo. The remaining solid was filtered through a fine frit with hexanes and all volatiles removed in vacuo to afford **2.A**. A solution of 1.95 g (8.8 mmol) **2.8** in 20 mL THF was cooled to –78 °C then treated with 13 mL t-BuLi (19.5 mmol, 1.5 M in pentane). After 10 minutes **2.A** in 6 mL THF was slowly added with a 2 mL THF wash. After 2 hours at –78 °C, the reaction was quenched with sat. aq. NH_4Cl, warmed to room temperature and extracted thrice with EtOAc. The organic layer was dried over $MgSO_4$ and all volatiles removed in vacuo. The crude oil was dissolved in 20 mL THF, cooled in an ice bath and diluted with 15 mL TBAF (15 mmol, 1 M in THF). The reaction was warmed to room temperature over 20 minutes, diluted with water and extracted thrice with EtOAc. The organic layer was dried over $MgSO_4$, all volatiles removed in vacuo and the crude oil purified by column chromatography (5:1→4:1 hexanes/EtOAc) to afford 1.04 g (56%) **2.9** as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 5.14 (t, J = 1.6, 1H), 5.12 (s, 1H), 4.19 (s, 1H), 3.97-3.91 (m, 4H), 2.64 (dq, J = 13.9, 3.0, 1H), 2.59-2.52 (m, 2H), 2.18-2.06 (m, 2H), 2.01-1.94 (m, 1H), 1.87-1.77 (m, 3H), 1.73 (dt, J = 12.9, 3.2, 1H), 1.70-1.56 (m, 2H), 1.33 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 213.4, 147.7, 113.0, 109.6, 81.2, 64.6, 39.0, 38.5, 37.6, 28.2, 25.2, 23.9, 23.0; IR (thin film) 3457, 2938, 2870, 1711, 1641, 1055 cm^{-1}; HRMS (ESI) calculated for $C_{14}H_{22}O_4$ $[M+Na]^+$ 277.1416 found 277.1410.

Diol 2.6



A solution of 495 mg (2.24 mmol) **2.8** in 20 mL THF was cooled to –78 °C then treated with 3.3 mL t-BuLi (4.95 mmol, 1.5 M in pentane). The reaction was stirred for 10 minutes then 150 mg (0.59 mmol) **2.9** in 1 mL THF with 0.4 mL THF wash was slowly added. The reaction was warmed to room temperature over 17 hours. Sat. aq. NH_4Cl was added and the reaction extracted thrice with EtOAc. The organic layers were collected, dried over $MgSO_4$, all volatiles removed in vacuo and the crude oil purified by column chromatography (10:1→4:1 hexanes/EtOAc) to afford 130 mg (55%) **2.6** as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 5.01 (s, 2H), 4.96 (s, 2H), 3.97-3.88 (m, 8H), 2.36 (s, 2H), 2.30-2.20 (m, 4H), 2.08-2.01 (m, 2H), 1.85 (td, J = 12.5, 4.5, 2H), 1.73-1.70 (m, 4H), 1.52-1.50 (m, 2H), 1.45 (d, J = 12.7, 2H), 1.34 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 154.6, 110.6, 110.0, 77.2, 64.6, 38.6, 33.5, 27.8, 23.7, 20.6; IR (thin film) 3475, 3092, 2980, 2930, 2881, 1630, 1058 cm^{-1}; HRMS (ESI) calculated for $C_{22}H_{36}O_6$ $[M+Na]^+$ 419.2410 found 419.2403.

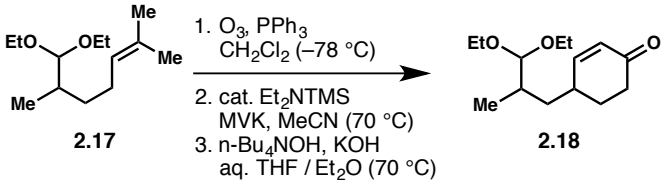
Ketal 2.17 [Adapted from the literature.][33]



2.16: (±)-melonal **2.17**

In a glove box, 101 mg (0.25 mmol) WCl_6 was weighed into a round bottom flask, the flask sealed with a rubber septum and moved into a fume hood. To this flask was added 3.60 g (25.7 mmol) **2.16** and 10.7 mL (64.2 mmol) ethyl orthoformate. The reaction was stirred for 3 hours after which 15 mL 1M NaOH was added and the contents extracted twice with CH_2Cl_2. The organic layers were combined, washed with water, then brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. Distillation (90 °C/3.5 mmHg) afforded 3.4 g (61%) **2.17** as a colorless liquid. ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 5.17 (tdt, J = 7.1, 2.7, 1.4, 1H), 4.23 (d, J = 6.4, 1H), 3.72 (ddq, J = 11.2, 9.4, 7.0, 2H), 3.55 (dqd, J = 9.3, 7.1, 2.3, 2H), 2.15-2.08 (m, 1H), 2.04-1.96 (m, 1H), 1.82-1.77 (m, 1H), 1.74 (d, J = 1.1, 3H), 1.67 (s, 3H), 1.65-1.58 (m, 1H), 1.27 (td, J = 7.1, 1.7, 6H), 1.24-1.16 (m, 1H), 0.977 (d, J = 6.8, 3H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 131.3, 124.7, 106.9, 62.0, 36.0, 32.0, 25.7, 25.4, 17.6, 15.3, 14.4.

Cyclohexenone 2.18

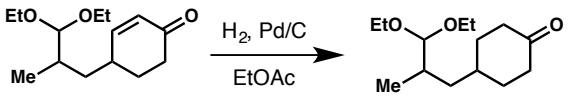


2.17 **2.18**

A solution of 2.30 g (10.7 mmol) **2.17** in 90 mL CH_2Cl_2 was ozonoloyzed at –78 °C. After excess ozone was purged from the solution, 5.60 g (21.4 mmol) triphenylphosphine was added and the reaction warmed to room temperature. After stirring for 2 hours all volatiles were

removed in vacuo. The solid was stirred with 30 mL pentane at 0 °C, filtered and all volatiles removed in vacuo. The crude material was heated at 70 °C with 0.5 mL (2.7 mmol) Et_2NTMS and 1.3 mL (16.2 mmol) MVK in 60 mL MeCN. After 38 hours all volatiles were removed in vacuo. The crude material was heated at 70 °C with 300 mg (5.35 mmol) KOH, 0.8 mL 40% aq. n-Bu_4NOH in 63 mL THF/Et_2O/H_2O (1:4:4) mixture. After 5 hours the layers were separated. The aqueous layer was extracted twice with Et_2O. All organic layers were combined, washed twice with brine, dried over $MgSO_4$, filtered and purified by column chromatograph (10:1→8:1 hexanes/EtOAc) to afford 1.40 g (54%, 1:1 dr) **2.18** as colorless liquid. ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 6.90-6.87 (m, 0.5H), 6.84-6.82 (m, 0.5H), 5.98 (dt, *J* = 10.1, 1.8 Hz, 1H), 4.20 (d, *J* = 5.7 Hz, 0.5H), 4.19 (d, *J* = 5.7 Hz, 0.5H), 3.72-3.65 (m, 2H), 3.54-3.47 (m, 2H), 2.55-2.48 (m, 2H), 2.41-2.32 (m, 1H), 2.15-2.07 (m, 1H), 1.93-1.85 (m, 1H), 1.72 (ddd, *J* = 13.5, 9.2, 4.4 Hz, 1H), 1.67-1.59 (m, 1H), 1.34 (ddd, *J* = 14.0, 9.6, 4.7 Hz, 0.5H), 1.25-1.20 (m, 6.5H), 0.99 (d, *J* = 6.9 Hz, 1.5H), 0.97 (d, *J* = 6.9 Hz, 1.5H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 200.0, 199.9, 156.0, 154.5, 128.9, 128.8, 107.0, 63.0, 62.7, 62.4, 37.0, 36.7, 36.6, 36.3, 34.1, 33.9, 33.6, 33.4, 29.8, 28.0, 15.34, 15.32, 15.2, 14.6; IR (thin film) 2973, 2874, 1680, 1450, 1114, 1059 cm^{-1}; HRMS (ESI) calculated for $C_{14}H_{24}O_3$ $[M+NH_4]^+$ 258.2069 found 258.2076.

Cyclohexanone 2.B

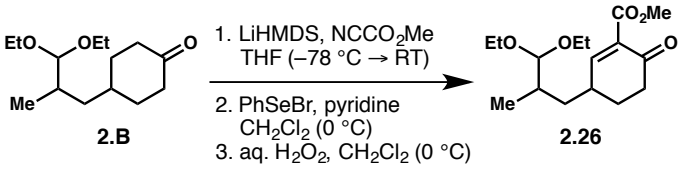


2.18 **2.B**

A solution of 305 mg (1.27 mmol) **2.18** in 5 mL EtOAc was stirred over 13 mg (0.4 mol% Pd) 10% Pd/C (55% wetted) under a hydrogen balloon at room temperature. After 7 hours celite was added and the reaction filtered through a pad of celite to afford 302 mg (98%) ketone as a

colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 4.17 (d, *J* = 5.9 Hz, 1H), 3.67 (dqd, *J* = 9.4, 7.0, 4.5 Hz, 2H), 3.53-3.46 (m, 2H), 2.40-2.28 (m, 4H), 2.09-1.99 (m, 2H), 1.86-1.80 (m, 2H), 1.48 (dtd, *J* = 14.9, 10.5, 4.5 Hz, 2H), 1.32 (qd, *J* = 12.0, 4.7 Hz, 1H), 1.21 (td, *J* = 7.0, 2.7 Hz, 6H), 1.15 (ddd, *J* = 13.9, 9.6, 4.5 Hz, 1H), 0.95 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 212.4, 107.2, 62.5, 62.4, 40.9, 40.7, 37.4, 34.1, 34.0, 33.2, 31.7, 15.3, 14.9; IR (thin film) 2923, 1716, 1113, 1060 cm^{-1}; HRMS (ESI) calculated for $C_{14}H_{26}O_3$ $[M+NH_4]^+$ 260.2226 found 260.2237.

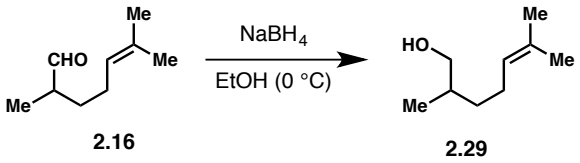
Cyclohexenone 2.26



To 0.5 mL (0.5 mmol) LiHMDS (1.0 M in THF) cooled to –78 °C was added 50 mg (0.21 mmol) **2.B** in 0.3 mL THF and washed with 0.2 + 0.2 mL THF. After 30 minutes, 23 mg (0.27 mmol) methyl cyanoformate in 0.3 mL THF was added. The reaction was stirred for 10 minutes, the cold bath removed and stirring continued. After 2 hours, sat. aq. NaCl was added and the aqueous layer extracted twice with EtOAc. The organic layers were collected dried over $MgSO_4$, filtered, all volatiles removed in vacuo and the crude material taken on to the next step. To an ice cold solution of 55 mg (0.23 mmol) PhSeBr in 0.3 mL CH_2Cl_2 was added 0.1 mL (0.25 mmol, 2.5 M in CH_2Cl_2) pyridine. After 5 minutes, crude β-ketoester was added with 0.6 mL CH_2Cl_2. The reaction was stirred at 0 °C for 30 minutes then room temperature for 1.5 hours. The organic layer was washed with sat. aq. NH_4Cl, sat. aq. $NaHCO_3$ and brine, then dried over MgSO4, filtered and all volatiles removed in vacuo. This material was dissolved in 1 mL CH_2Cl_2, cooled

to 0 °C and treated with aq. H_2O_2 until complete conversion by TLC. The organic layer was washed with sat. $NaHCO_3$, sat. $Na_2S_2O_3$ and brine then dried over $MgSO_4$, filtered and all volatiles removed in vacuo to afford 57 mg (90% over 3 steps) of crude **2.26** with good purity (>90%). The obtained material was found to be incompatible with silica gel, even when treated with 2% NEt_3 and Florisil. ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 194.7, 165.33, 165.25, 161.6, 160.3, 131.8, 131.7, 106.93, 106.87, 63.4, 63.0, 62.5, 52.2, 37.8, 37.5, 36.3, 36.0, 34.4, 34.2, 34.1, 34.0, 29.0, 27.4, 15.4, 15.35, 15.33, 14.7; IR (thin film) 2973, 1745, 1691, 1721, 1113, 1060 cm^{-1}.

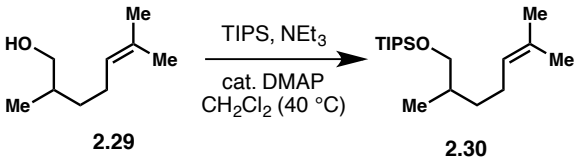
Melonol 2.29 [Adapted from the literature.][34]



2.16 **2.29**

To 30 mL EtOH were added 580 mg (15.3 mmol) $NaBH_4$ at 0 °C. After 15 minutes, 2.14 g (15.3 mmol) **2.16** was added dropwise. The reaction was stirred for 10 minutes at 0 °C before being diluted with EtOAc and quenched slowly with sat. aq. NH_4Cl. After warming up to room temperature and ensuring all solids were dissolved by the addition of water, the layers were separated and the aqueous layer extracted thrice with EtOAc. All organic layers were collected, solid NaCl was added, the layers separated. The organic layer was dried over $MgSO_4$, filtered, filtered and all volatiles removed in vacuo. The crude material was purified by column chromatography (10:1→7:1 hexanes/EtOAc) to provide 2.01 g (93%) **2.29** as a colorless liquid. The spectral data matched the literature.[34]

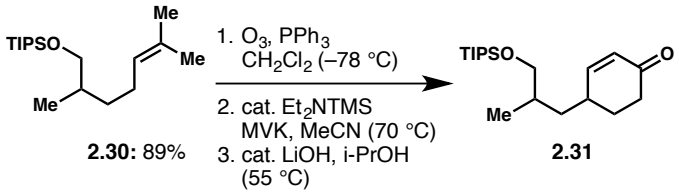
Silylether 2.30



2.29 **2.30**

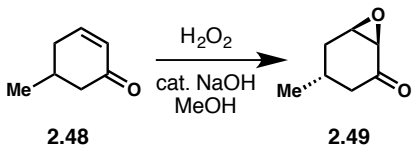
A solution of 2.00 g (14.1 mmol) **2.18**, 4.4 mL (21.1 mmol) TIPSCl, 3.3 mL (23.9 mmol) and 171 mg (1.4 mmol) DMAP in 30 mL CH_2Cl_2 was heated at 40 °C for 20 hours. After the allotted time, 10 mL sat. aq. NH_4Cl and 40 mL EtOAc were added and transferred to a seperatory funnel. The flask was rinsed with 20 mL (1:1 sat. aq. NH4Cl/EtOAc), 10 mL EtOAc and 10 mL water. The layers were separated and the organic layer washed once with sat. aq. NH_4Cl, water and brine, then dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The material was purified by column chromatography (hexanes) to afford 3.72 g (89%) **2.30** as a colorless liquid. ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 5.12 (t, *J* = 7.0 Hz, 1H), 3.55 (dd, *J* = 9.5, 5.7 Hz, 1H), 3.47 (dd, *J* = 9.5, 6.4 Hz, 1H), 2.07-1.93 (m, 2H), 1.69 (s, 3H), 1.65-1.59 (m, 1H), 1.61 (s, 3H), 1.50-1.43 (m, 1H), 1.16-1.01 (m, 22H), 0.91 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 131.1, 125.0, 68.5, 35.6, 33.3, 25.7, 25.6, 18.1, 17.6, 16.8, 12.0; IR (thin film) 2942, 2865, 1653 cm^{-1}; HRMS (ESI) calculated for $C_{18}H_{38}OSi$ $[M+H]^+$ 299.2770 found 299.2775.

Enone 2.31



A solution of 3.70 g (12.4 mmol) **2.30** in 60 mL CH_2Cl_2 was ozonolyzed at –78 °C. After the excess ozone was purged from the solution, 7.25 g (27.6 mmol) triphenylphosphine were added and the reaction warmed to room temperature. After stirring for 2 hours all volatiles were removed in vacuo. The solid was stirred with 30 mL hexanes at 0 °C, filtered, washed in 3 portions with 40 mL ice cold hexanes and all volatiles removed in vacuo. The crude material was heated at 70 °C with 0.6 mL (3.1 mmol) Et_2NTMS and 1.5 mL (18.6 mmol) MVK in 30 mL MeCN. After 15 hours all volatiles were removed in vacuo. The crude material was heated at 55 °C with 50 mg (1.2 mmol) LiOH in 30 mL i-PrOH. After 3 hours all volatiles were removed in vacuo and the crude oil separated between EtOAc and sat. aq. NH_4Cl. The layers were separated and the organic layer then washed once with NH_4Cl, twice with sat. $NaHCO_3$, brine, dried over $MgSO_4$, filtered and purified by column chromatography (20:1 hexanes/EtOAc) to afford 1.9 g (48%, 1:1 dr) **2.31** as a colorless liquid. ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 6.90-6.85 (m, 1H), 5.99 (d, J = 2.1 Hz, 0.5H), 5.97 (d, J = 2.2 Hz, 0.5H), 3.59-3.48 (m, 2H), 2.56-2.48 (m, 2H), 2.41-2.32 (m, 1H), 2.17-2.11 (m, 1H), 1.83-1.77 (m, 1H), 1.74-1.56 (m, 2H), 1.33-1.26 (m, 1H), 1.23-1.18 (m, 1H), 1.14-1.01 (m, 20H), 0.97 (d, J = 6.7 Hz, 1.5H), 0.95 (d, J = 6.7 Hz, 1.5H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 200.04, 199.97, 155.9, 155.1, 128.82, 128.78, 68.7, 68.4, 38.6, 38.3, 36.9, 36.7, 33.7, 33.6, 33.3, 29.5, 28.5, 18.0, 17.7, 17.3, 16.6, 12.0; IR (thin film) 2942, 2865, 1685, 1462, 1101 cm^{-1}; HRMS (ESI) calculated for $C_{18}H_{36}O_2Si$ $[M+Na]^+$ 347.2382 found 347.2381.

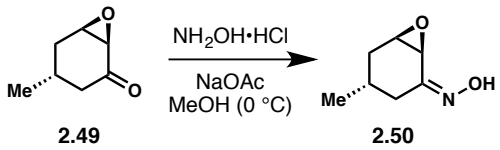
Epoxide 2.49



2.48 **2.49**

To a solution of 2.86 g (26.0 mmol) **2.48** in 25 mL MeOH cooled in an ice bath, was added 7.8 mL (77.9 mmol) 30% aq. H_2O_2. The reaction was initiated with 0.1 mL (0.5 mmol) 5 M aq. NaOH. The internal temperature rose to 10 °C and kept at 10-15 °C with the dropwise addition of an additional 0.1 mL (0.5 mmol) 5 M aq. NaOH. The reaction was stirred for a total time of 30 minutes then poured into 60 mL brine and 40 g ice. The aqueous solution was extracted with 60 mL CH_2Cl_2 then 4 times with 30 mL CH_2Cl_2. The organic layers were combined and washed with 40 mL 1:1 sat. $Na_2S_2O_3/H_2O$ solution, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude material was purified by distillation (98 °C/25 mmHg) to afford 2.54 g (78%) **2.49** as a colorless liquid. ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 3.56 (dd, J = 4.6, 1.9 Hz, 1H), 3.22 (d, J = 3.8 Hz, 1H), 2.54 (dd, J = 18.0, 4.8 Hz, 1H), 2.36-2.31 (m, 1H), 2.26-2.16 (m, 1H), 1.77 (dd, J = 18.0, 11.2 Hz, 1H), 1.60 (ddd, J = 14.8, 10.7, 1.0 Hz, 1H), 0.96 (d, J = 6.8 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 205.5, 54.9, 54.3, 44.8, 31.4, 22.6, 21.1; IR (thin film) 2958, 1711 cm^{-1}; HRMS (ESI) calculated for $C_7H_{10}O_2$ $[M+NH_4]^+$ 144.1024 found 144.1017.

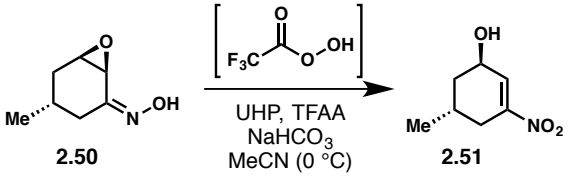
Oxime 2.50



2.49 2.50

To a solution of 2.53 g (20.0 mmol) **2.49** in 15 mL MeOH was added 3.59 g (43.8 mmol) NaOAc and 1.52 g (21.9 mmol) NH_2OH•HCl sequentially at 0°C. After 1.5 hours at 0 °C the reaction was poured into 60 mL brine and 40 g ice. The aqueous solution was extracted with 60 mL CH_2Cl_2 then 4 times 30 mL CH_2Cl_2. The organic layers were combined and washed with 50 mL brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude material was purified by column chromatography (2:1 hexanes/EtOAc) and recrystallized from Et_2O/hexanes to afford 1.78 g (62%) **2.50** as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) mixture of oxime diastereomers δ 8.32-8.29 (m), 8.15-8.06 (m), 4.11 (d, *J* = 3.8 Hz), 3.52 (dd, *J* = 8.6, 3.5 Hz), 3.44 (t, *J* = 1.8 Hz), 2.83-2.78 (m), 2.36 (dd, *J* = 14.9, 2.3 Hz), 2.27 (dt, *J* = 15.0, 2.1 Hz), 1.84-1.80 (m), 1.72 (dd, *J* = 14.9, 11.6 Hz), 1.65 (d, *J* = 12.3 H), 1.47 (ddd, *J* = 14.9, 10.2, 1.6 Hz), 0.97 (d, *J* = 6.7 Hz); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) major δ 154.6, 53.0, 44.1, 35.0, 32.8, 23.6, 21.2, minor 155.3, 53.2, 51.7, 32.2, 30.0, 21.3, 20.9; IR (thin film) 3246, 2954, 1654, 1457, 971 cm^{-1}; HRMS (ESI) calculated for $C_7H_{10}NO_2$ $[M-H]^-$ 140.0712 found 140.0715.

Nitroalkene 2.51

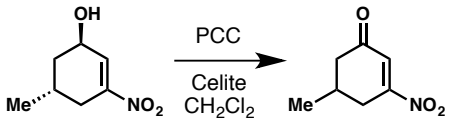


2.50 2.51

Trifluoroperoxyacetic acid was prepared by the dropwise addition of 5.7 mL (40.3 mmol) trifluoroacetic anhydride in 10 mL MeCN to 4.57 g (48.5 mmol) urea hydrogen peroxide in 50

mL MeCN at 0 °C. This solution was added dropwise via teflon canula to a stirring mixture of 1.96 g (13.9 mmol) **2.50** and 7.09 g (84.4 mmol) $NaHCO_3$ in 30 mL MeCN at 0 °C. After a total time of 2 hours at 0 °C, the reaction was carefully quenched with 25 mL sat. $Na_2S_2O_3$ and 25 mL water then 80 mL of volatiles removed in vacuo. The aqueous phase was diluted with 20 mL water and extracted 7 times with 50 mL EtOAc (until no oxime was observed by TLC, 2:1 hexanes/EtOAc, R_f = 0.36). The organic layers were combined, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude material was purified by column chromatography (2:1 hexanes/EtOAc) to afford 1.42 g (65%) **2.51** as yellow sheets. ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 7.21-7.20 (m, 1H), 4.57 (d, *J* = 2.1 Hz, 1H), 2.83 (q, *J* = 11.1 Hz, 1H), 2.09 (t, *J* = 10.9 Hz, 2H), 1.84 (t, *J* = 16.3 Hz, 2H), 1.51-1.45 (m, 1H), 1.11 (d, *J* = 5.9 Hz, 4H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 151.8, 131.0, 63.8, 38.0, 32.1, 24.1, 20.7; IR (thin film) 3368, 2956, 1521, 1337 cm^{-1}; HRMS (ESI) calculated for $C_7H_{10}NO_3$ $[M-H]^-$ 156.0661 found 156.0667.

Nitroenone 2.52

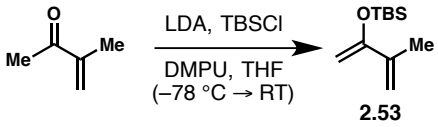


2.51 **2.52**

A flask was charged with 1.41 g (8.97 mmol) **2.51**, 52 mL CH_2Cl_2 and 9.7 g Celite. To the reaction was added 4.83 g (22.4 mmol) PCC portionwise and the contents stirred for 4 hours. The reaction was concentrated to 25% volume, filtered through silica gel with 500 mL Et_2O and all volatiles removed in vacuo. The crude material was purified by column chromatography (4:1 hexanes/EtOAc) to afford 1.19 g (85%) **2.52** as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 6.94 (s, 1H), 3.07 (dd, *J* = 18.8, 4.6 Hz, 1H), 2.62 (dd, *J* = 16.4, 3.4 Hz, 1H), 2.57-2.51 (m, 1H), 2.41-2.35 (m, 1H), 2.21 (dd, *J* = 16.3, 12.2 Hz, 1H), 1.21 (d, *J* = 6.6 Hz, 3H); IR (thin

film) 2960, 1694, 1531, 1343, 1324, 754, 714 cm^{-1}; HRMS (ESI) calculated for $C_7H_8NO_3$ $[M-H]^-$ 154.0504 found 154.0502.

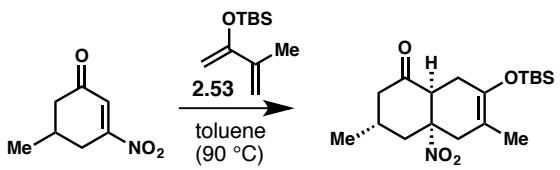
Diene 2.53 [Adapted from the literature.][35]



2.53

To a solution of LDA, prepared from 5.5 mL (14.3 mmol, 2.60 M / hexanes) n-BuLi and 2.1 mL (15.0 mmol) diisopropylamine in 15 mL THF was added 1.10 g (13.0 mmol) methyl isopropenyl ketone in 1 mL THF at –78 °C. After 10 minutes, 3.5 mL (28.9 mmol) DMPU was added neat. The reaction was stirred at –78 °C for 10 minutes then treated with 1.95 g (13.0 mmol) TBSCl in 1 mL THF and stirred for 10 minutes before the cold bath was removed. After 50 minutes the reaction was quenched with the addition of 60 mL half sat. $NaHCO_3$ at 0 °C. The solution was extracted with 75 mL hexanes and the organic phase washed with 40 mL water, 20 mL brine, then dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The residue was purified by column chromatrography (200:1 hexanes/NEt_3) to afford 1.50 g (58%) **2.53** as a colorless liquid. The spectral data was identical to the literature.[35]

Cycloadduct 2.43

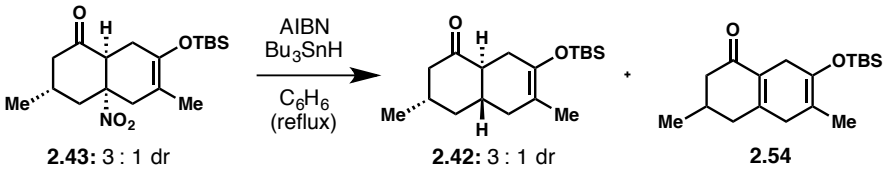


2.52 **2.43:** 3 : 1 dr

A microwave vial was charged with 107 mg (0.69 mmol) **2.52** and 255 mg (1.28 mmol) **2.53**, placed under argon and set into an oil bath at 90 °C. After 7 hours the reaction was cooled and

purified by column chromatography (10:1 hexanes/EtOAc) to afford 145 mg (59%, 3:1 dr) **2.43** as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) major δ 204.8, 140.4, 105.9, 91.2, 50.7, 48.0, 44.2, 34.0, 29.8, 25.8, 25.7, 25.3, 21.9, 16.1, 3.9, 4.2; IR (thin film) 2923, 1722, 1542, 1257, 1194 cm^{-1}; HRMS (ESI) calculated for $C_{18}H_{31}NO_4Si$ $[M+Na]^+$ 376.1920 found 376.1918.

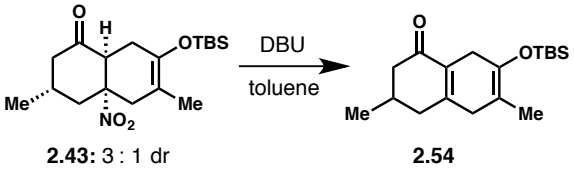
Decalin 2.42



2.43: 3 : 1 dr **2.42:** 3 : 1 dr **2.54**

A 10 mL round bottom flask was charged with 50 mg (0.14 mmol) 2.43, 0.13 mL (0.47 mmol) Bu_3SnH and 0.5 mL C_6H_6 then the reaction was heated to 80 °C. AIBN was added portionwise until complete conversion by TLC. The mixture was concentrated in vacuo and purified by column chromatography (20:1 hexanes/EtOAc) to afford 18 mg (41%) **2.42** and 9 mg (20%) **2.54**. **2.42**: ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 2.41-1.87 (m, 10H), 1.66-1.53 (m, 5H), 1.21-0.93 (m, 14H), 0.24-0.07 (m, 6H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 211.3, 141.9, 110.0, 50.5, 49.8, 40.9, 39.2, 38.4, 33.5, 29.4, 26.0, 25.8, 22.4, 16.0, –3.7, –3.9; IR (thin film) 2927, 2853, 1712, 1686, 1176 cm^{-1}; HRMS (ESI) calculated for $C_{18}H_{32}O_2Si$ $[M+Na]^+$ 331.2069 found 331.2060. **2.54**: ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 2.86 (s, 4H), 2.51-2.47 (m, 1H), 2.28-2.00 (m, 5H), 1.61 (m, 1H), 1.06 (d, J = 6.4 Hz, 3H), 0.97 (s, 10H), 0.15 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 198.6, 153.0, 141.5, 129.3, 106.3, 45.7, 39.5, 38.4, 29.7, 28.6, 25.8, 21.3, 15.1, –3.7; IR (thin film) 2954, 1670 cm^{-1}; HRMS (ESI) calculated for $C_{18}H_{30}O_2Si$ $[M+Na]^+$ 329.1913 found 329.1912.

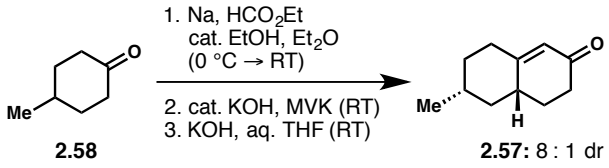
Cyclohexadiene 2.54



2.43: 3 : 1 dr **2.54**

To a solution of 53 mg (0.15 mmol) **2.43** in 0.4 mL toluene was added 27 mg (0.18 mmol) DBU in 0.3 mL toluene at room temperature. After 30 minutes the solution was loaded onto a column and eluted (10:1 hexanes/EtOAc) to provide 42 mg (93%) **2.54** as a white solid.

Enone 2.57

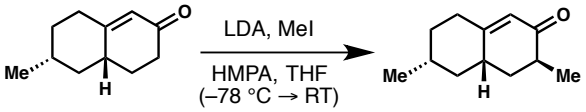


2.58 **2.57:** 8 : 1 dr

To 100 mL ice cold Et_2O, under a purging argon atmosphere was added 1.2 g (52.2 mmol) Na metal cut and flattened then concomitantly 5.00 g (44.6 mmol) **2.58** and 5.3 mL (66.2 mmol) ethyl formate via syringe. The reaction was initiated with 0.3 mL EtOH and stirred for 1 hour at 0 °C during which the reaction precipitated a thick orange solid. The ice bath was removed and stirring continued for 9 hours. A single portion of 50 mL water was added slowly, the layers separated and the aqueous phase washed twice with 50 mL Et_2O. The aqueous layer was acidified with 20 mL 6M HCl and extracted twice with 50 mL Et_2O. The organic layers were combined, washed with 10 mL brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. To crude β-ketoaldehyde and 8.5 mL (102 mmol) methyl vinyl ketone was added 200 mg (3.56 mmol) powdered KOH in 50 mg portion at room temperature until the reaction produced an exotherm. After 45 min, the contents were diluted with 50 mL EtOAc and 50 mL sat. NH_4Cl, the contents transferred to a seperatory funnel and the flask rinsed twice with 25 mL EtOAc and

10 mL water. The layers were separated, then the organic layer washed with 20 mL water, 20 mL brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. To crude tricarbonyl dissolved in 150 mL THF and cooled in an ice bath was added dropwise an ice cold solution of 11.2 g (200 mmol) KOH in 150 mL water. After the addition over 0.5 hour, the ice bath was removed and the reaction stirred for an additional 16.5 hours before 120 mL volatiles were removed in vacuo. The remaining solution was extracted with 100 mL and two times 50 mL EtOAc, then the organic layers were combined, washed with 20 mL water, 20 mL brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The residue was purified by column chromatography (8:1 hexanes/EtOAc) to afford 4.72 g (67% over 3 steps, 8:1 dr) 2.57 as a colorless liquid. ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) major δ 5.82 (s, 1H), 2.46-2.23 (m, 5H), 2.08 (dq, J = 13.7, 4.7 Hz, 1H), 1.92-1.83 (m, 2H), 1.72-1.57 (m, 3H), 1.14-1.05 (m, 1H), 0.95 (d, J = 6.6 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 200.1, 166.9, 124.3, 42.9, 37.5, 36.6, 35.3, 35.0, 31.9, 29.2, 21.9; IR (thin film) 2923, 2865, 1668, 1620, 1455 cm^{-1}; HRMS (ESI) calculated for $C_{11}H_{16}O$ $[M+NH_4]^+$ 182.1545 found 182.1552.

Enone 2.59

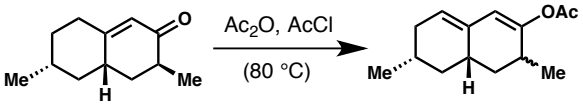


2.57: 8 : 1 dr **2.59**

To a solution of LDA, prepared from 12.7 mL (35.8 mmol) 2.61 M n-BuLi/hexanes and 5.5 mL (39.2 mmol) diisopropylamine in 30 mL THF at 0 °C, was added at –78 °C, 4.90 g (29.8 mmol) **2.57** with 30 mL THF. After 30 minutes, 6.3 mL (36.2 mmol) HMPA was added neat. The reaction was kept at –78 °C for 10 minutes, then treated with 5.6 mL (90.0 mmol) methyl iodide neat and stirred for 10 minutes before the cold bath was removed. After 50 minutes the reaction

was quenched with the addition of 150 mL half sat. NH_4Cl at 0 °C and 40 mL of volatiles were removed in vacuo. The mixture was poured into a seperatory funnel and the flask rinsed with 150 mL EtOAc. The layers were separated and the organic phase washed with 50 mL water and 30 mL brine. All aqueous layers were collected and extracted with 50 mL EtOAc. This organic layer was washed with 10 mL brine, combined with the previous organic phase, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The residue was purified by column chromatography (12:1 hexanes/EtOAc) to afford 4.71 g (88%) **2.59** as a light yellow liquid. ^1H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 5.74 (s, 1H), 2.43-2.37 (m, 3H), 2.23 (td, J = 13.6, 4.5 Hz, 1H), 1.91-185 (m, 3H), 1.78-1.67 (m, 2H), 1.11 (t, J = 6.2 Hz, 3H), 1.14-1.02 (m, 2H), 0.94 (d, J = 6.6 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 203.1, 166.2, 122.4, 42.6, 38.6, 35.9, 35.9, 35.5, 35.4, 32.3, 21.8, 15.8; HRMS (ESI) calculated for $C_{12}H_{18}O$ $[M+H]^+$ 179.1442 found 179.1436.

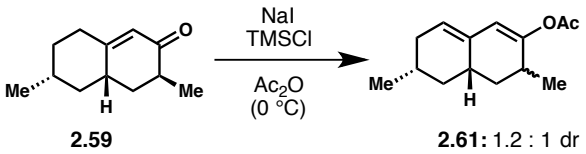
Dienol Acetate 2.61



2.59 **2.61:** 2 : 1 dr

A solution of 50 mg (0.28 mmol) **2.59** in 3.7 mL Ac_2O/AcCl (2.6:1) was heated at 80 °C for 1 hour. The reaction was cooled and all volatiles removed in vacuo then taken up in 20 mL EtOAc and washed thrice with $NaHCO_3$, brine and dried over $MgSO_4$, filtered. All volatiles were removed and the crude material purified by column chromatography (20:1 hexanes/EtOAc) to afford 49 mg (80%, 2:1 dr) **2.61** acetate as a colorless oil.

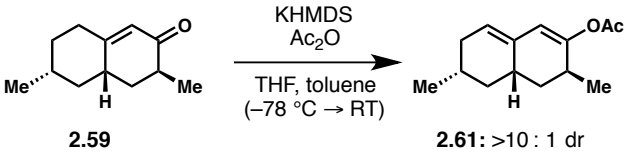
Dienol acetate 2.61



2.59 **2.61:** 1.2 : 1 dr

To a solution of 50 mg (0.28 mmol) **2.59** in 1.4 mL Ac_2O was added sequentially 128 mg (0.86 mmol) NaI then 0.11 mL (0.86 mmol) TMSCl at 0 °C. After 2 hours in the ice bath, 0.5 mL NEt_3 and 10 mL sat. aq. $NaHCO_3$ were added. The reaction was further diluted with 20 mL EtOAc and the layers separated. The organic layer was washed with 10 mL 1 M NaOH, 10 mL brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. Purification of the crude material by column chromatography (30:1 hexanes/EtOAc) provided 41 mg (66%, 1.2:1 dr) **2.61** as a colorless oil.

Dienol Acetate 2.61

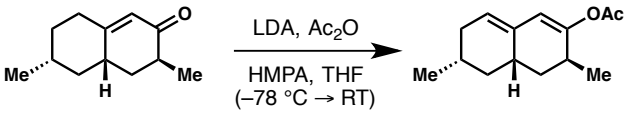


2.59 **2.61:** >10 : 1 dr

A solution of 14.5 mL (7.25 mmol) 0.5 M KHMDS/toluene in 10 mL THF was treated with 1.00 g (5.60 mmol) enone dissolved in 20 mL THF at –78 °C. After 20 minutes the solution was canula transferred to a stirring mixture of 1.6 mL (7.0 mmol) Ac_2O in 20 mL THF cooled to –78 °C. The cold bath was removed and stirring continued for 1 h as the reaction warmed to room temperature. The reaction was quenched with 100 mL water, volatiles removed in vacuo and the remaining liquid extracted with 60 mL EtOAc. The organic layer was washed with 50 mL water, 20 mL brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. Purification of the

residue by column chromatrography (100:1 hexanes/EtOAc) provided 298 mg (24%) dienol acetate as a colorless oil.

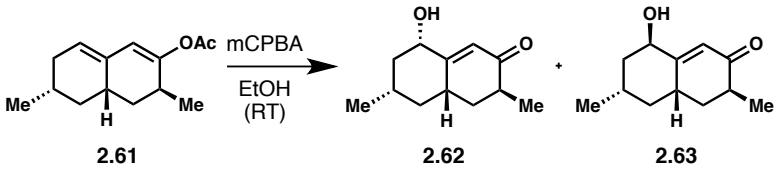
Dienol acetate 2.61



2.59 **2.61:** >10 : 1 dr

LDA was prepared from 4.8 mL (34.2 mmol) i-Pr_2NH, 12.0 mL (31.3 mmol) 2.61 M n-BuLi/hexanes in 40 mL THF at 0 °C was cooled to –78 °C and treated with 12.0 mL (69.0 mmol) HMPA. After 20 minutes, 4.65 g (26.1 mmol) **2.59** was added with 30 mL THF. After 20 minutes the solution was canula transferred into a solution of 7.4 mL (78.4 mmol) Ac_2O in 50 mL THF stirring at –78 °C. Cooling was continued for 10 minutes before the bath was removed. After an additional 50 minutes, 100 mL sat. $NaHCO_3$ was added, approximatly 80 mL volatiles removed in vacuo and the remaining liquid partioned between an additional 100 mL water and 150 mL EtOAc. The layers were separated and the organic layer washed with 100 mL water, 50 mL water and 30 mL brine, then dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude material was purified by column chromatrography (30:1 hexanes/EtOAc) to provide 4.92 g (85%) **2.61** as a light yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 5.77 (s, 1H), 5.47 (t, *J* = 2.4 Hz, 1H), 2.45 (t, *J* = 6.7 Hz, 1H), 2.37-2.34 (m, 1H), 2.20-2.17 (m, 1H), 1.78-1.57 (m, 6H), 1.12 (d, *J* = 7.2 Hz, 3H), 0.98 (d, *J* = 6.4 Hz, 3H), 1.02-0.92 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 169.4, 152.3, 134.8, 124.4, 117.1, 38.7, 36.7, 34.7, 31.8, 30.1, 29.2, 22.4, 21.2, 18.4; IR (thin film) 2926, 2871, 1742 cm^{-1}; HRMS (ESI) calculated for $C_{14}H_{20}O_2$ $[M+H]^+$ 221.1542 found 221.1534.

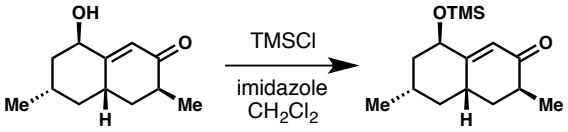
Alcohols 2.62 and 2.63



To 8.55 g (38.1 mmol, 77% purity) mCPBA in 80 mL EtOH cooled to 0 °C was added 4.92 g (22.3 mmol) **2.61** in 40 mL EtOH. The ice bath was removed and stirred for 1 hour before slowly quenching with 150 mL equal parts sat. $Na_2S_2O_3$/sat. $NaHCO_3$/water at 0 °C. Approximately 100 mL volatiles were removed in vacuo and the mixture extracted with 150 mL EtOAc. The organic phase was washed with 60 mL equal parts sat. $Na_2S_2O_3$/sat. $NaHCO_3$/water, 60 mL water and 30 mL brine. All aqueous washings were combined and extracted thrice with 50 mL EtOAc. These organic layers were combined, washed with 30 mL brine and combined with the previous organic solution. After drying over $MgSO_4$, the solution was filtered and all volatiles removed in vacuo. The residue was purified by column chromatograph (6:1 hexanes/EtOAc) to provide 2.25 g (51%, >20:1 dr) **2.63** as a white solid, recyrstallization from EtOAc/hexanes afforded colorless prisms (mp = 51–53 °C). The column was flushed with EtOAc and the remainder purified by column chromatrography (2:1 hexanes/EtOAc) to afford 1.04 g (23%, 5:1 dr) **2.62** as a light yellow oil. **2.62**: ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 6.10 (s, 1H), 4.24 (dd, *J* = 5.9, 5.6 Hz, 1H), 2.50-2.44 (m, 1H), 2.35 (dq, *J* = 12.6, 4.6 Hz, 1H), 2.25-2.20 (m, 1H), 1.98-1.77 (m, 5H), 1.18-1.10 (m, 2H), 1.12 (d, *J* = 6.9 Hz, 3H), 1.00 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 202.7, 167.1, 118.5, 71.3, 45.4, 41.8, 38.1, 35.6, 30.9, 30.3, 21.3, 15.4; IR (thin film) 3412, 2953, 2925, 2869, 1664, 1457, 1065 cm^{-1}; HRMS (ESI) calculated for $C_{12}H_{18}O_2$ $[M+NH_4]^+$ 212.1651 found 212.1650. **2.63**: ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 5.82 (d, *J* = 1.1 Hz, 1H), 4.40 (s, 1H), 2.90 (dq, *J* = 11.5, 5.6 Hz, 1H), 2.49-2.42 (m, 1H), 2.21-2.16 (m,

1H), 2.04 (dq, *J* = 14.4, 2.8 Hz, 1H), 1.95-1.85 (m, 3H), 1.79 (dt, *J* = 13.8, 5.3 Hz, 1H), 1.28 (td, *J* = 13.2, 2.3 Hz, 1H), 1.12 (d, *J* = 7.0 Hz, 3H), 1.16-1.08 (m, 1H), 0.95 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 203.5, 165.1, 122.7, 72.2, 42.6, 42.1, 38.3, 35.5, 30.9, 26.0, 21.5, 25.4; IR (thin film) 3412, 2951, 2923, 2870, 1667 cm^{-1}; HRMS (ESI) calculated for $C_{12}H_{18}O_2$ $[M+Na]^+$ 217.1205 found 217.1204.

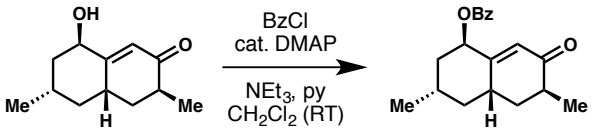
Silyl Ether 2.65



2.63 **2.65**

A solution of 37 mg (0.19 mmol) **2.63** and 45 mg (0.66 mmol) imidazole in 2 mL CH_2Cl_2 was added 0.040 mL (0.32 mmol) TMSCl at 0 °C. The ice bath was removed and the reaction stirred for 7 hours. After being recooled to 0 °C, the reaction was quenched with 10 mL half sat. $NaHCO_3$ and partioned with 10 mL EtOAc. The layers were separated and the organic layer washed with 3 mL brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The residue was purified by column chromatrography (40:2:1 hexanes/EtOAc/NEt_3) to afford 45 mg (89%) **2.65** as a colorless liquid. ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 5.77 (s, 1H), 4.31 (d, *J* = 2.4 Hz, 1H), 2.85 (dd, *J* = 12.5, 4.7 Hz, 1H), 2.46-2.41 (m, 1H), 2.20 (td, *J* = 6.4, 2.9 Hz, 1H), 1.92-1.75 (m, 4H), 1.26-1.15 (m, 2H), 1.11 (d, *J* = 6.9 Hz, 3H), 0.91 (d, *J* = 6.7 Hz, 3H), 0.09 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 203.2, 166.4, 121.6, 72.7, 44.3, 42.0, 37.8, 35.9, 31.4, 26.0, 21.5, 15.2, 0.1; IR (thin film) 2954, 2924, 2872, 1680 cm^{-1}; HRMS (ESI) calculated for $C_{15}H_{26}O_2Si$ $[M+Na]^+$ 289.1600 found 289.1597.

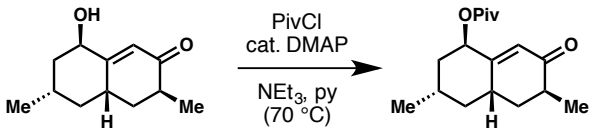
Benzoate 2.C



2.63 2.C

A vial containing 20 mg (0.104 mmol) **2.63**, 1.2 mg (0.010 mmol) DMAP, 0.05 mL (0.36 mmol) NEt3, 0.2 mL (2.48 mmol) pyridine and 0.02 mL (0.17 mmol) benzoyl chloride in 1 mL CH_2Cl_2 was stirred at room temperature for 16 hours. The reaction was partitioned between sat. $NaHCO_3$ and EtOAc. The layers were separated and the organic phase washed with brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude material was purified by column chromatography (8:1 hexanes/EtOAc) to afford 27 mg (86%) **2.68Bz** as a white solid (mp = 93–95 °C). ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 8.04 (dd, *J* = 8.3, 1.2 Hz, 2H), 7.59 (t, J = 7.4 Hz, 1H), 7.46 (t, J = 7.7 Hz, 2H), 6.04 (s, 1H), 5.65 (s, 1H), 2.85 (dd, J = 12.0, 5.3 Hz, 1H), 2.51-2.44 (m, 1H), 2.27-2.20 (m, 2H), 1.97 (ddd, J = 13.8, 10.2, 5.6 Hz, 2H), 1.83 (dt, J = 13.9, 4.9 Hz, 1H), 1.44-1.38 (m, 1H), 1.32-1.24 (m, 1H), 1.11 (d, J = 6.9 Hz, 3H), 1.00 (d, J = 6.5 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 202.5, 165.3, 159.7, 133.2, 130.2, 129.6, 128.5, 124.9, 74.6, 41.7, 40.6, 38.1, 35.4, 32.3, 27.2, 21.5, 15.2; IR (thin film) 2954, 2924, 1719, 1679, 1268 cm^{-1}; HRMS (ESI) calculated for $C_{19}H_{22}O_3$ $[M+Na]^+$ 321.1467 found 321.1462.

Pivalate 2.75

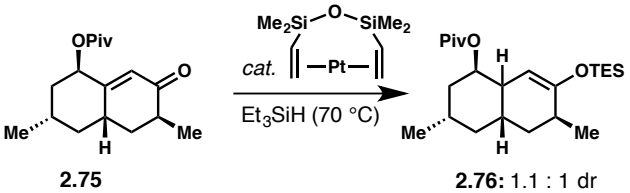


2.63 2.75

A flask was charged with 2.10 g (10.8 mmol) **2.63**, 40 mL pyridine, 3.0 mL (21.5 mmol) NEt_3, 130 mg (1.06 mmol) DMAP and 5.3 mL (43.1 mmol) trimethylacetyl chloride then stirred at 70

°C. After 18 hours the reaction was cooled, volatiles removed in vacuo and the contents partitioned between 150 mL EtOAc and 150 mL water. The layers were separated and the organic phase washed twice with 100 mL 3M HCl and 50 mL water. The aqueous phases were combined and extracted with 50 mL EtOAc. This organic layer was washed with 20 mL water and combined with the previous organic layer, then washed with 50 mL sat. $NaHCO_3$, 50 mL brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The residue was purified by column chromatography (8:1 hexanes/EtOAc) to afford 2.33 g (77%) **2.75** as a light yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 5.94 (s, 1H), 5.37 (s, 1H), 2.70 (dq, *J* = 11.7, 5.7 Hz, 1H), 2.49-2.42 (m, 1H), 2.06 (dd, *J* = 11.7, 2.6 Hz, 2H), 1.97-1.88 (m, 2H), 1.80 (dt, *J* = 13.8, 5.2 Hz, 1H), 1.33-1.25 (m, 1H), 1.20 (s, 9H), 1.20-1.15 (m, 1H), 1.12 (t, *J* = 12.9 Hz, 3H), 0.97 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 202.7, 177.1, 159.6, 124.7, 73.6, 41.8, 40.3, 38.9, 38.3, 35.3, 31.8, 27.1, 26.9, 21.5, 15.3; IR (thin film) 2957, 2927,2871, 1730, 1681, 1150 cm^{-1}; HRMS (ESI) calculated for $C_{17}H_{26}O_3$ $[M+Na]^+$ 301.1780 found 301.1783.

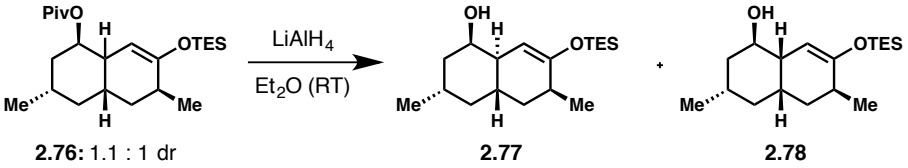
Enoxysilane 2.76



A flask was charged with 206 mg (0.74 mmol) **2.75**, 36 mg (~2% Pt in xylenes, 0.0037 mmol) Karstedt's Complex and 1.0 mL (6.3 mmol) Et_3SiH, then heated at 70 °C for 4 hours. The reaction was cooled, all volatiles removed in vacuo and the remaining crude material purified by column chromatography (50:1:1 hexanes/EtOAc/NEt_3) to afford 251 mg (86%, 1.2:1 dr) enoxysilane as a colorless oil. Mixture of diastereomers: ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27

ppm) mixture of diastereomers δ 5.04 (s), 4.83 (s), 4.48 (s), 4.40 (s), 2.49 (s), 2.21-2.18 (m), 2.13 (t, *J* = 6.7 Hz), 2.01-1.98 (m), 1.91 (d, *J* = 10.5 Hz), 1.86-1.73 (m), 1.62 (d, *J* = 12.7 Hz), 1.53 (td, *J* = 12.7, 6.2 Hz), 1.42 (d, *J* = 12.8 Hz), 1.39-1.32 (m), 1.21 (s), 1.19 (s), 1.12-1.03 (m), 1.02-0.92 (m), 0.88 (dd, *J* = 19.6, 6.5 Hz), 0.74-0.60 (m); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 178.1, 177.8, 155.7, 154.5, 103.0, 102.1, 74.2, 71.9, 44.8, 41.3, 39.0, 38.9, 38.8, 37.8, 37.3, 34.2, 34.0, 33.8, 30.5, 30.1, 28.6, 27.7, 27.3, 27.2, 26.1, 22.5, 22.3, 19.7, 18.6, 6.8, 6.7, 5.1, 4.9; IR (thin film) 2955, 2912, 2876, 1727, 1656, 1164 cm^{-1}; HRMS (ESI) calculated for $C_{23}H_{42}O_3Si$ $[M+H]^+$ 395.2982 found 395.2984.

***Trans*-Decalin 2.77 and *Cis*-Decalin 2.78**

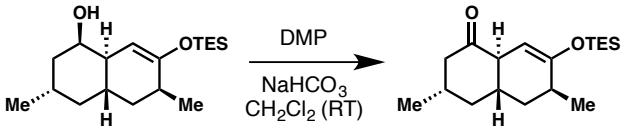


2.76: 1.1 : 1 dr **2.77** **2.78**

To a slurry of 49 mg (1.29 mmol) $LiAlH_4$ in 3.5 mL Et_2O was added 123 mg (0.312 mmol) **2.76** in 1.5 mL Et_2O at 0 °C. The ice bath was removed and the reaction stirred for 30 minutes. Quenching was performed at 0 °C by sequential addition of 0.1 mL EtOAc, 0.05 mL water, 0.05 mL 5M NaOH and 0.15 mL water, then stirring rapidly for 30 minutes at room temperature. After the addition of Na_2SO_4, the mixture was filtered over Celite, washed through with Et_2O and all volatiles removed in vacuo. The crude material was purified by column chromatography (50:5:1 hexanes/EtOAc/NEt_3) to afford 41 mg (42%) **2.77** as a colorless oil and 35 mg (36%) **2.78** as a white solid, recrystallization from EtOAc afford a white solid (mp = 68–70 °C). **2.77**: ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 4.57 (s, 1H), 3.86 (s, 1H), 2.16 (t, *J* = 6.8 Hz, 1H), 1.89 (dt, *J* = 23.4, 9.3 Hz, 3H), 1.69 (d, *J* = 13.9 Hz, 1H), 1.59-1.50 (m, 2H), 1.41 (d, *J* = 11.8

Hz, 2H), 1.13-1.03 (m, 2H), 1.12 (d, *J* = 7.1 Hz, 3H), 1.03 (s, 9H), 0.90 (d, *J* = 6.5 Hz, 3H), 0.68 (q, J = 8.0 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 158.2, 103.7, 70.1, 46.3, 41.3, 40.6, 37.1, 34.0, 27.6, 27.0, 22.3, 19.6, 6.7, 5.1; IR (thin film) 3449, 2953, 2911, 2875, 1656, 1200, 1172 cm^{-1}; HRMS (ESI) calculated for $C_{17}H_{34}O_2Si$ $[M+Na]^+$ 333.2226 found 333.2224. **2.78**: ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 4.38 (s, 1H), 3.83 (s, 1H), 2.47 (s, 1H), 2.21-2.18 (m, 1H), 2.06 (td, *J* = 8.1, 4.1 Hz, 1H), 1.86-1.80 (m, 1H), 1.75 (ddd, *J* = 13.4, 6.0, 3.3 Hz, 1H), 1.60-1.58 (m, 2H), 1.41 (s, 1H), 1.38-1.26 (m, 2H), 1.17-1.07 (m, 2H), 1.05 (d, *J* = 6.9 Hz, 3H), 0.99 (t, *J* = 8.0 Hz, 9H), 0.87 (d, *J* = 6.6 Hz, 3H), 0.68 (q, *J* = 7.9 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 154.1, 103.3, 72.3, 42.0, 37.9, 37.0, 34.4, 30.7, 29.4, 25.2, 22.5, 18.6, 6.8, 5.1; IR (thin film) 3344, 2952, 2912, 2875, 1655, 1196 cm^{-1}; HRMS (ESI) calculated for $C_{18}H_{34}O_2Si$ $[M+H]^+$ 311.2406 found 311.2403.

Ketone 2.79

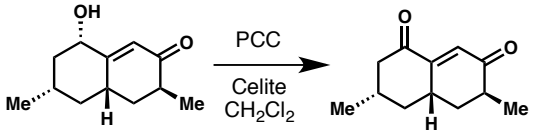


2.77 **2.79**

To a solution of 39 m g (0.126 mmol) **2.77** in 0.6 mL CH_2Cl_2 was added 32 mg (0.381 mmol) $NaHCO_3$ and 75 mg (0.177) Dess-Martin Periodinane at 0 °C. The ice bath was immediately removed and the contents stirred for 30 minute2s. The reaction was poured into 3 mL stirring hexanes, filtered through a cotton filter with hexanes, then washed with 10 mL 1:1 sat. $NaHCO_3$/sat. $Na_2S_2O_3$, 5 mL half sat. $NaHCO_3$, 5 mL brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo to afford **2.79** as a colorless oil that decomposed upon purification by chromatography. ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 5.09 (s, 1H), 2.75 (d, *J* = 11.2 Hz,

1H), 2.36 (d, *J* = 11.4 Hz, 1H), 2.19 (t, *J* = 6.7 Hz, 1H), 2.06-1.98 (m, 2H), 1.80-1.71 (m, 1H), 1.64-1.56 (m, 2H), 1.09 (t, *J* = 7.5 Hz, 3H), 1.04 (d, *J* = 6.1 Hz, 3H), 1.10-0.91 (m, 2H), 1.00-0.93 (m, 9H), 0.70 (q, *J* = 7.8 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 209.8, 155.4, 98.6, 52.9, 49.2, 40.7, 37.8, 35.7, 34.3, 34.0, 22.4, 19.5, 6.8, 5.0; IR (thin film) 2954, 2913, 2874, 1714, 1657, 1195 cm^{-1}; HRMS (ESI) calculated for $C_{18}H_{32}O_2Si$ $[M+Na]^+$ 331.2069 found 331.2064.

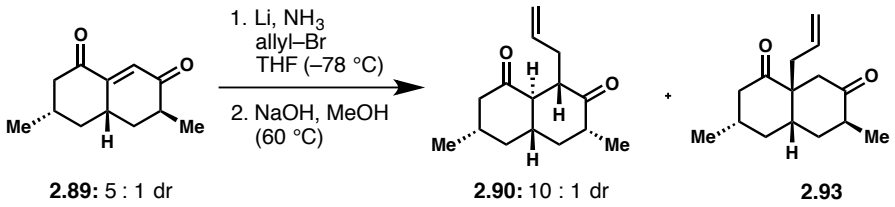
Enedione 2.89



2.62: 5 : 1 dr **2.89:** 5 : 1 dr

A 50 mL round bottom flask was charged with 840 mg (4.32 mmol) **2.62**, 20 mL CH_2Cl_2 and 4 g Celite. To the reaction was added 1.55 g (7.2 mmol) PCC and the contents stirred for 2 hours. After the addition of another 0.50 g (2.3 mmol) PCC and 3 hours of stirring, the reaction was diluted with 20 mL Et_2O, filtered through silica gel with 350 mL Et_2O and all volatiles removed in vacuo. The crude material was purified by column chromatography (3:1 hexanes/EtOAc) to afford 740 mg (89%) **2.89** as a yellow wax. ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 6.40 (d, *J* = 2.6 Hz, 1H), 2.86-2.79 (m, 1H), 2.73 (dd, *J* = 12.8, 2.4 Hz, 1H), 2.63-2.57 (m, 1H), 2.09 (m, 1H), 2.00-1.96 (m, 2H), 1.24 (t, *J* = 12.3 Hz, 1H), 1.17 (d, *J* = 7.5 Hz, 3H), 1.16 (m, 2H), 1.09 (d, *J* = 6.0 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 203.3, 200.7, 153.4, 126.6, 49.1, 40.3, 39.5, 36.7, 33.1, 30.0, 22.0, 15.7.

Allyl Diketone 2.90 and 2.93



2.89: 5 : 1 dr **2.90:** 10 : 1 dr **2.93**

A 25 mL round bottom flask was charged with 9 mg (1.2 mmol) lithium metal and ammonia at –78 °C. To the stirring blue solution was slowly added 60 mg (0.31 mmol) **2.89**. After complete addition isoprene and 0.05 mL (0.58 mmol) allyl bromide were added. The reaction was stirred 10 minutes before solid NH4Cl was added and the mixture warmed to room temperature. The mixture was partitioned between water and EtOAc. The organic layers were combined, washed with sat. aq. brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude oil was dissolved in 3 mL methanol and 0.3 mL 1 M NaOH/methanol. The reaction was heated to 60 °C for 3 hours then cooled, partitioned between aq. NH_4Cl and EtOAc. The organic layers were combined, washed with sat. aq. brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude oil was purified by column chromatography (10:1 hexanes/EtOAc) to afford 18 mg (25%) **2.90** and 14 mg (19%) **2.93**. **2.90**: ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 5.81-5.73 (m, 1H), 4.96 (dd, J = 21.5, 12.6 Hz, 2H), 2.74 (t, J = 8.9 Hz, 1H), 2.44-2.26 (m, 5H), 2.09-1.88 (m, 5H), 1.34-1.16 (m, 2H), 1.06 (d, J = 6.1 Hz, 3H), 1.02 (d, J = 6.5 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 212.4, 209.5, 136.9, 116.4, 58.4, 49.9, 47.6, 44.1, 43.1, 42.5, 41.1, 35.3, 30.9, 22.3, 14.4; **2.93:** ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 5.59 (dtd, J = 15.9, 10.5, 5.3 Hz, 1H), 5.00 (dd, J = 16.5, 8.2 Hz, 2H), 2.75 (dd, J = 13.9, 4.5 Hz, 2H), 2.64 (t, J = 6.5 Hz, 1H), 2.38-2.35 (m, 1H), 2.29-2.23 (m, 2H), 2.11 (d, J = 4.8 Hz, 1H), 2.01-1.77 (m, 5H), 1.10-1.01 (m, 7H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 210.0, 209.8, 133.6, 117.9, 55.4, 46.1, 45.7, 40.4, 37.2, 37.0, 36.5, 36.1, 32.0, 22.3, 14.3**.**

2.7 References and Notes

(1) Corey, E. J.; Magriotis, P. A. *J. Am. Chem. Soc.* **1987**, *109*, 287.

(2) Miyaoka, H.; Okubo, Y.; Muroi, M.; Mitome, H.; Kawashima, E. *Chem. Lett.* **2011**, *40*, 246.

(3) Fairweather, K. A.; Mander, L. N. *Org. Lett.* **2006**, *8*, 3395.

(4) Yoder, R. A.; Johnston, J. N. *Chem. Rev.* **2005**, *105*, 4730.

(5) Faugeroux, V.; Génisson, Y. *Curr. Org. Chem.* **2008**, *12*, 751.

(6) Fallis, A. . *Tetrahedron Lett.* **1969**, *10*, 1337.

(7) Clausen, C.; Wartchow, R.; Butenschön, H. *European J. Org. Chem.* **2001**, 93.

(8) Cossy, J.; BouzBouz, S.; Laghgar, M.; Tabyaoui, B. *Tetrahedron Lett.* **2002**, *43*, 823.

(9) Roosen, P. C.; Vanderwal, C. D. *Org. Lett.* **2014**, *16*, 4368.

(10) Firouzabadi, H.; Iranpoor, N.; Karimi, B. *Synth. Commun.* **1999**, *29*, 2255.

(11) Jung, M. E.; McCombs, C. A. *Org. Synth.* **1978**, *58*, 163.

(12) Kozmin, S. A.; Rawal, V. H. *J. Org. Chem.* **1997**, *62*, 5252.

(13) Tricotet, T.; Brückner, R. *European J. Org. Chem.* **2007**, 1069.

(14) Lavallée, J.–F.; Spino, C.; Ruel, R.; Hogan, K. T.; Deslongchamps, P. *Can. J. Chem.* **1992**, *70*, 1406.

(15) Audran, G.; Brémond, P.; Feuerstein, M.; Marque, S. R. A.; Santelli, M. *Tetrahedron* **2013**, *69*, 8325.

(16) Liu, H.–J.; Ngooi, T. K.; Browne, E. N. C. *Can. J. Chem.* **1988**, *66*, 3143.

(17) Chen, K.; Baran, P. S. *Nature* **2009**, *459*, 824.

(18) Pronin, S. V.; Shenvi, R. A. *J. Am. Chem. Soc.* **2012**, *134*, 19604.

(19) Streuff, J. *Synthesis* **2013**, 281.

(20) Kim, W. H.; Lee, J. H.; Danishefsky, S. J. *J. Am. Chem. Soc.* **2009**, *131*, 12576.

(21) Corey, E. J.; Estreicher, H. *Tetrahedron Lett.* **1981**, *22*, 603.

(22) Cheng, X.; Waters, S. P. *Org. Lett.* **2010**, *12*, 205.

(23) Stork, G.; Ganem, B. *J. Am. Chem. Soc.* **1973**, *95*, 6152.

(24) Stork, G.; Logusch, E. W. *J. Am. Chem. Soc.* **1980**, *102*, 1218.

(25) Stork, G.; Logusch, E. W. *J. Am. Chem. Soc.* **1980**, *102*, 1219.

(26) Stork, G.; Winkler, J. D.; Shiner, C. S. *J. Am. Chem. Soc.* **1982**, *104*, 3767.

(27) Nemoto, H.; Matsuhashi, N.; Imaizumi, M.; Nagai, M.; Fukumoto, K. *J. Org. Chem.* **1990**, *55*, 5625.

(28) Jung, M. E.; Yoo, D. *Org. Lett.* **2011**, *13*, 2698.

(29) Ushakov, D. B.; Maier, M. E. *Synlett* **2013**, 705.

(30) Orru, R. V. A.; Wijnberg, J. B. P. A.; de Groot, A. *J. Org. Chem.* **1995**, *60*, 4233.

(31) Love, B. E.; Jones, E. G. *J. Org. Chem.* **1999**, *64*, 3755.

(32) Lespieau, R.; Bourguel, M. *Org. Synth.* **1925**, *5*, 49.

(33) Firouzabadi, H.; Iranpoor, N.; Karimi, B. *Synth. Commun.* **1999**, *29*, 2255.

(34) Lee. J.; Ryu, T.; Park, S.; Lee, P. H. *J. Org. Chem.* **2012**, *77*, 4821.

(35) Ireland, R. E.; Thompson, W. J. *J. Org. Chem.* **1979**, *44*, 3041.

CHAPTER 3:

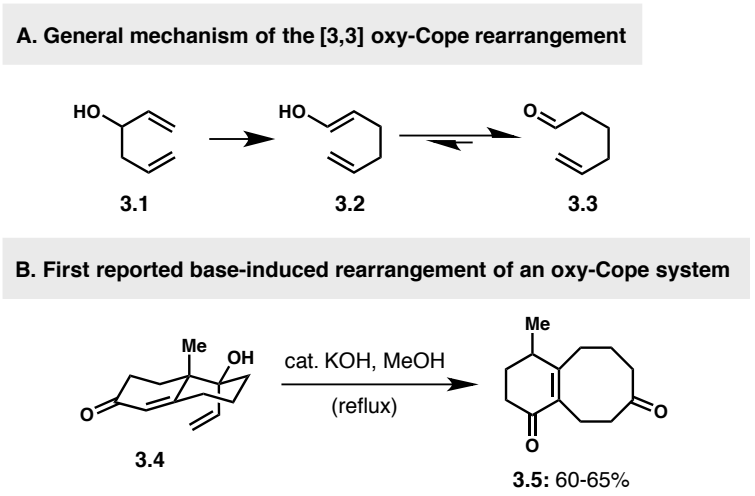
AN OXY-COPE/TRANSANNULAR MICHAEL APPROACH TOWARDS 7,20-DIISOCYANOADOCIANE

3.1 Background on the Electronic Reorganization of 3-Oxy-1,5-Hexadiene Systems (the oxy-Cope Rearrangement)

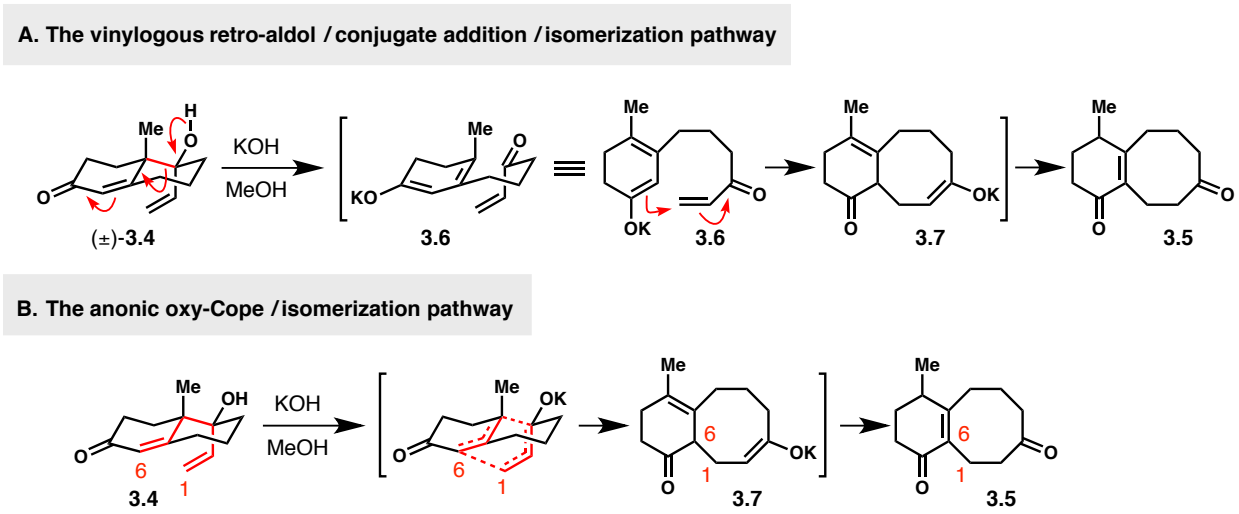
Pericyclic reactions have enabled the construction of a myriad of complex structures because of their ability to perform difficult C–C bond forming transformations and the facility of their coupling in tandem with a host of other reactions.[1] Among these, the oxy-Cope rearrangement (Scheme 3.1A) has been widely adopted for its mild conditions, predictable outcome and ease of starting material synthesis.[2–4]

One of the earliest investigators of oxy-Cope systems was Swaminathan with the groundwork laid by rearrangement of 1,5-hexadiene **3.4** to **3.5** in the presence of catalytic amounts of KOH (Scheme 3.1B).[5] This first report of a base-catalyzed reorganization of an oxy-Cope system was reported[6] before the term "oxy-Cope" was coined[7] and over a decade prior to the classic disclosure of significant rate increase using potassium alkoxide by Evans and Golob.[8] Several mechanistic pathways have been proposed for the transformation (Scheme 3.2). The original report suggests the product arises via a vinylogous retro-aldol/conjugate addition/isomerization cascade (Scheme 3.2A); however, after description of the oxy-Cope reaction,[7] an alternative oxy-Cope reaction/isomerization was also suggested (Scheme 3.2B).[9]

Scheme 3.1 Rearrangement of the 3-oxy-1,5-hexadiene system.



Scheme 3.2 The two proposed mechanisms to explain the conversion of **3.4** to **3.5**.

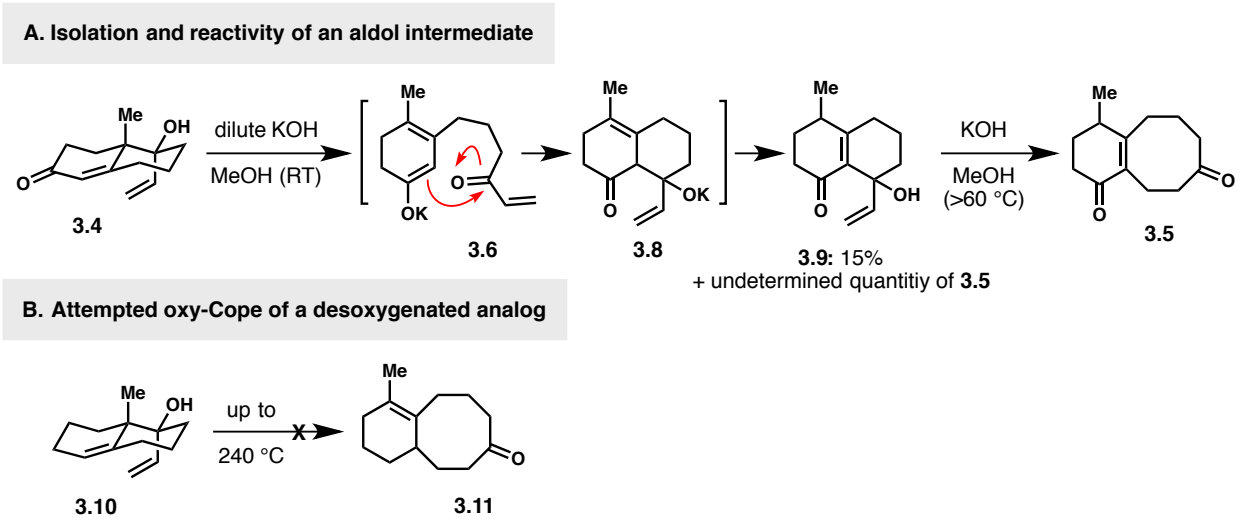


Significant effort was put into probing whether the mechanism of this transformation proceeded via Scheme 3.2A or 3.2B.[5] Three initial results attest to favoring the retro-aldol mechanism (Scheme 3.3). First, the alcohol epimer of **3.4** in basic methanol still affords **3.5**. Second, running the reaction more dilute at a lower temperature with less base enabled the isolation of **3.9**, which arises from the vinylogous retro-aldol/aldol addition/isomerization reaction of **3.4**. Upon heating to >60 °C **3.9** cleanly converted to **3.5**. Finally, **3.10**, which has the

enone replaced with an electron neutral alkene is thermally stable up to 240 °C in the absence of base. Contrarily, enone **3.4** provides **3.5** when refluxed in ethylene glycol.[9,10]

Although these experiments may imply the relevance of the vinylogous retro-aldol mechanism, they are not completely conclusive. First, the equatorial vinyl-subsituted **3.4** may operate under a different mechanism than the axial vinyl-substituted **3.4**. Second, under the more mild reaction conditions in which **3.9** was isolated, there is no mention of the quantities of **3.5** obtained. This lack of information severely undermines the formation of **3.9** as mechanistic evidence since intermediate **3.9** does not afford **3.5** until heated to 60 °C. Thus, it is not clear how **3.5** is originally formed. Third, no experiments on exposing **3.10** to the standard conditions of base at elevated temperatures were reported. The absence of this experiment makes it difficult to gauge the influence of anionic rate acceleration.

Scheme 3.3 Initial mechanistic implications for a vinylogous retro-aldol mechanism.



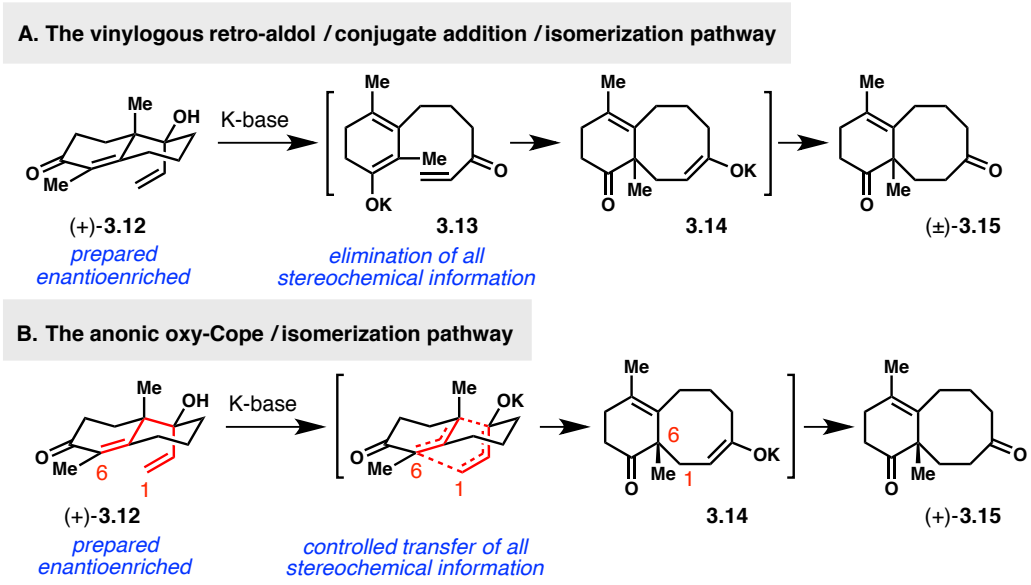
Not until 22 years after the initial disclosure was more light shed on the mechanism in an elegantly designed set of experiments.[11] To distinguish between the two mechanisms, the retention (or erosion) of enantioenrichment in **3.12** was evaluated (Scheme 3.4). If the retro-aldol

mechanism were operable, any enantioenrichment of **3.12** would be erased as the intermediate dienolate **3.13** is achiral. If, however, the oxy-Cope mechanism were operable, then the enantiopurity of the starting material would be transferred to the ring-expanded product. The last enone isomerization step needs to be eliminated to unequivocally use optical purity as a mechanistic probe. This was accomplished by using the tetra-substituted enone **3.12**.

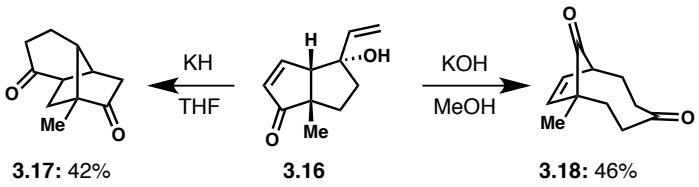
When (+)-**3.12** was exposed to basic methanol, the isolated product **3.15** had no optical rotation. This result implies the reaction operates via a vinylogous retro-aldol fragmentation. Interestingly, when (+)-**3.12** was reacted with KH in THF at room temperature, product **3.15** did have significant optical rotation, implying a concerted oxy-Cope mechanism![12] These results suggest that the mechanism is dependent upon the reaction conditions. Disappointingly, a control experiment ensuring that (+)-**3.15** does not racemize under standard methoxide conditions was not mentioned. To the best of the presented evidence the rearrangement of **3.4** with basic methanol follows a fragmentation/recombination pathway.

Swaminathan and coworkers are not the only group to have observed a difference in reaction progression between aprotic and protic rearrangement conditions of oxy-Cope systems. Heathcock[13] observed an interesting divergence of reactivity when bicycle **3.26** was treated with either KH or KOH in methanol (Scheme 3.5).

Scheme 3.4 Determining the mechanism for the rearrangement of **3.4** with the optically active tetrasubstituted alkene surrogate (+)-**3.12**.



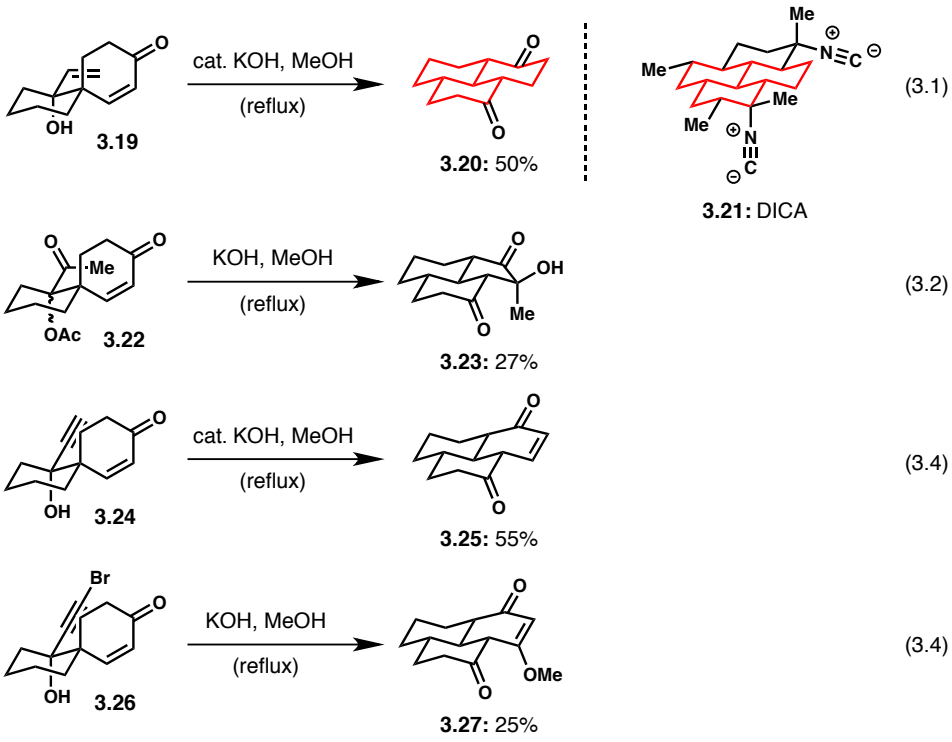
Scheme 3.5 Heathcock's alternative reaction mechanisms depending on reaction conditions.



3.2 Literature Precedent of an oxy-Cope Rearrangement with Relevance To 7,20-Diisocyanoadociane

Among the explored base-induced rearrangements related to **3.4** to **3.5**, one directly addresses our interest in synthetic work towards the marine isocyanoterpene 7,20-diisocyanoadociane (DICA, **3.21**). In the presence of base, spirocycle **3.19** was reported to yield the perhydropyrene scaffold **3.20** (Equation 3.1).[14] The proposed all-*trans* stereochemistry and location of functional groups map directly onto the core structure of DICA.

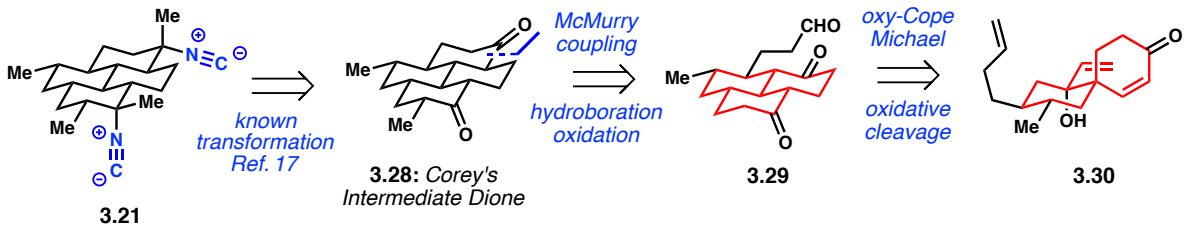
This transformation was proposed to operate by a retro-vinylogous aldol/double Michael addition, as this fragmentation pathway appears to be related to mechanistic study on the system **3.4**. No experimental evidence for either mechanism was reported. The rearrangement of several other similar spirocyclic structures have also been disclosed (Equations 3.2-3.4).[14–16] The reaction of acetate **3.22** with base most reasonably caused deprotection followed by a retro-vinylogous aldol and recombination to **3.23**. Consistent with the conversion of **3.19** to **3.20**, alkyne **3.24** rearranges to enone **3.25**. Bromoalkyne **3.26** also proceeds similarily to **3.24**, but undergoes halogen displacement with methoxide to provide vinylogous ester **3.27**.



With this inspiration, a synthetic approach to DICA was devised (Scheme 3.6); a summary of the work presented in this chapter was published.[17] Corey's intermediate dione **3.28** was initially targeted.[18] The last ring would be annulated via a McMurry coupling and a hydroboration/oxidation sequence, leading back to the oxy-Cope rearrangement product, perhydrophenalene **3.29**. The spirocyclic substrate **3.30** bears an additional methyl and butenyl

chain required for further elaboration. Spirocycle **3.30** could be constructed in a similar fashion to the literature precedent from Swaminathan.[14,19,20]

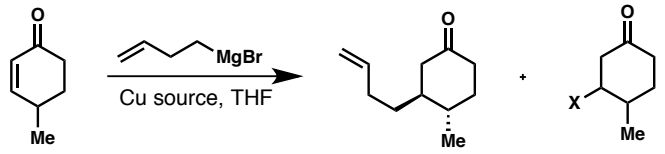
Scheme 3.6 Retrosynthetic analysis of DICA back to a spiro-fused oxy-Cope system.



3.3 Synthetic Efforts to Realize the oxy-Cope/Michael Cascade Towards 7,20-Diisocyanoadociane

Application of the oxy-Cope/Michael reaction towards DICA was initiated because its application would contribute a vastly lower step count than previous syntheses and would provide an interesting and strategically different disconnection. Syntheses of polycyclic molecules, and the previous approaches to DICA specifically,[18,21,22] typically progress via the sequential annulation of rings. The oxy-Cope/Michael cascade generates three rings in a single reaction from a spirocycle without conservation of any original rings: a unique and unusual feature in synthetic planning.

Table 3.1 Evaluation of copper mediated conjugate additions into **3.31**.



3.31 **3.32** **3.33**

Entry	*Conditions*		*Observations* *Yield*	*dr*[a]	*X = Ligand Addition*
1	CuI, CuCN or CuBr•DMS w/ & w/out TMSCl orHMPA in THF or Et_2O	Various temperatures (–78 °C, –60 °C, 0 °C, RT)	competitive 1,2 addition, low conversions		
2	cat. CuBr•DMS, BF_3•OEt_2	(78 °C → RT)	67%	6 : 1	
3	$(butenyl)_2CuMgBr$, BF_3•OEt_2	(–78 °C)	–	7 : 1	
4	(butenyl)Cu, BF_3•OEt_2	(–78 °C)	–	5 : 1	
5	(COD)CuBr•(butenylMgBr)	(–78 °C)	–	12 : 1	
	CuBr•DMS, X–Li[b] then butenylMgBr[c]	(–78 °C)			
6	PhO–Cu•(butenylMgBr)		65%	>20 : 1	
7	t-BuO–Cu•(butenylMgBr)		–	19 : 1	
8	t-Bu–Cu•(butenylMgBr)		–	19 : 1	3 : 1
9	TMSM–Cu•(butenylMgBr)		–	>20 1	>20 : 1
10	Mes–Cu•(butenylMgBr)		–	>20 : 1	2 : 1
11	$(butenyl)_2CuMgBr$	(–78 °C)	–	19 : 1	

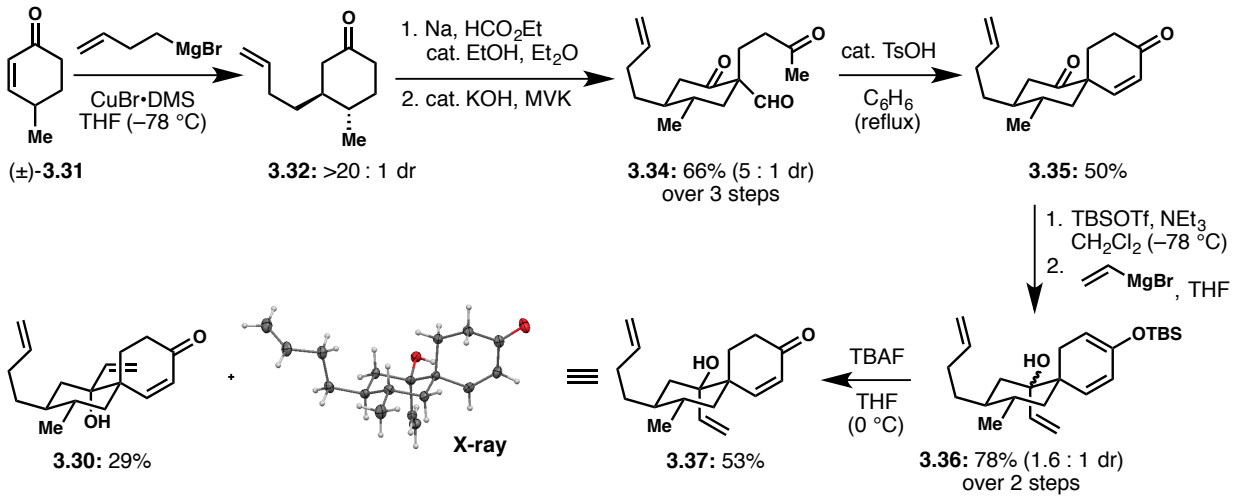
[a] dr was determined by NMR or GC-FID [b] at 0 °C [c] at –78 °C

The synthesis of spirocycle **3.30** commenced with a conjugate addition to enone **3.31**. Although the reaction should have been a straightforward transformation to **3.32**, optimization to avoid 1,2-addition and to improve *trans* diastereoselectivity was required (Table 3.1). Of the copper salts screened, CuBr•DMS enabled the cleanest formation of alkylcopper reagents, as determined by homogeneity of the reaction mixture. Lewis acids, such as TMSCl and BF_3•OEt_2 did not have a beneficial effect and led to relatively low diastereoselectivity (entries 1-4). The copper source (COD)CuBr[23,24] was evaluated for being a stable copper source that requires only one equivalent of nucleophile. While it afforded an improved 12:1 dr, the stoichiometric COD made this copper source unappealing. Mixed cuprates,[25] such as Posner's heteroatom cuprates,[26,27] Bertz's TMSM-cuprate[28] and Saegusa's Mes-cuprate[29] afforded excellent *trans* diastereoselectivity. In situ-generated copper phenoxide afforded >20:1 dr; however, isolation

was complicated by the difficult separation of stoichiometric phenol (entry 6). All mixed cuprates required the pregeneration of an active copper species, an inconvenience in reaction setup. Additionally, t-Bu and Mes transferred competitively with the desired butenyl group (entries 8, 10). Although the TMSM-cuprate was found to provide superior diastereoselectivity and reactivity, its expense mitigated further implementation (entry 9). Ultimately the most user-friendly and reliable conditions were using the basic Gilman cuprate, generated from two equivalents of butenylmagnesium bromide, one equivalent CuBr•DMS and without Lewis acid. These simple conditions afforded excellent diastereoselectivity, as well as selectivity for conjugate addition over 1,2-carbonyl addition, and provided material of sufficient quality to continue without purification.

With practical conjugate addition conditions available, the spirocyclic Robinson annulation was performed to afford **3.35** as a single diastereomer (Scheme 3.7). Silylation of enone **3.35** ensured vinylmagnesium bromide addition occurred solely into the ketone, affording **3.36** as a 1.6 : 1 mixture of equatorial and axial alcohols. Desilylation of **3.36** with TBAF generated the separable enones **3.37** and **3.30**. Structure determination was accomplished by X-ray analysis of **3.37**.

Scheme 3.7 Generation of spirocyclic hydroxyenones **3.30** and **3.37**.



The desired anionic oxy-Cope/Michael reactivity was explored using both diastereomeric enones **3.30** and **3.37** (Scheme 3.8). To our surprise and disappointment, exposing either alcohol diastereomer to the standard conditions of KOH in methanol afforded an intractable mixture of compounds. Further evaluation via kaliation did not lead to any success (Scheme 3.8A). Metal-mediated reactions using Pd(II)[30] or Hg(II) also proved unsuccessful (Scheme 3.8B).[31,32]

Although the anionic version of the oxy-Cope is the standard rearrangement of 3-oxy-1,5-hexadiene systems, a neutral variant is also available. In contrast to the experiments under basic conditions, simply heating diene **3.30** in an inert solvent led to a clean reaction; however, instead of isolating the expected oxy-Cope product [7.3.1]-bicycle **3.40**, tricycle **3.41** was the only observed product (Scheme 3.8C). Although **3.41** is not the desired compound, this experiment validated that the oxy-Cope rearrangement of **3.30** can occur! Not unsurprisingly, upon oxy-Cope and enol tautomerization, the cyclodecenone **3.40** is well positioned to undergo a transannular carbonyl-ene reaction to afford **3.41** as a single diastereomer.

Scheme 3.8 Attempting an oxy-Cope/Michael cascade.

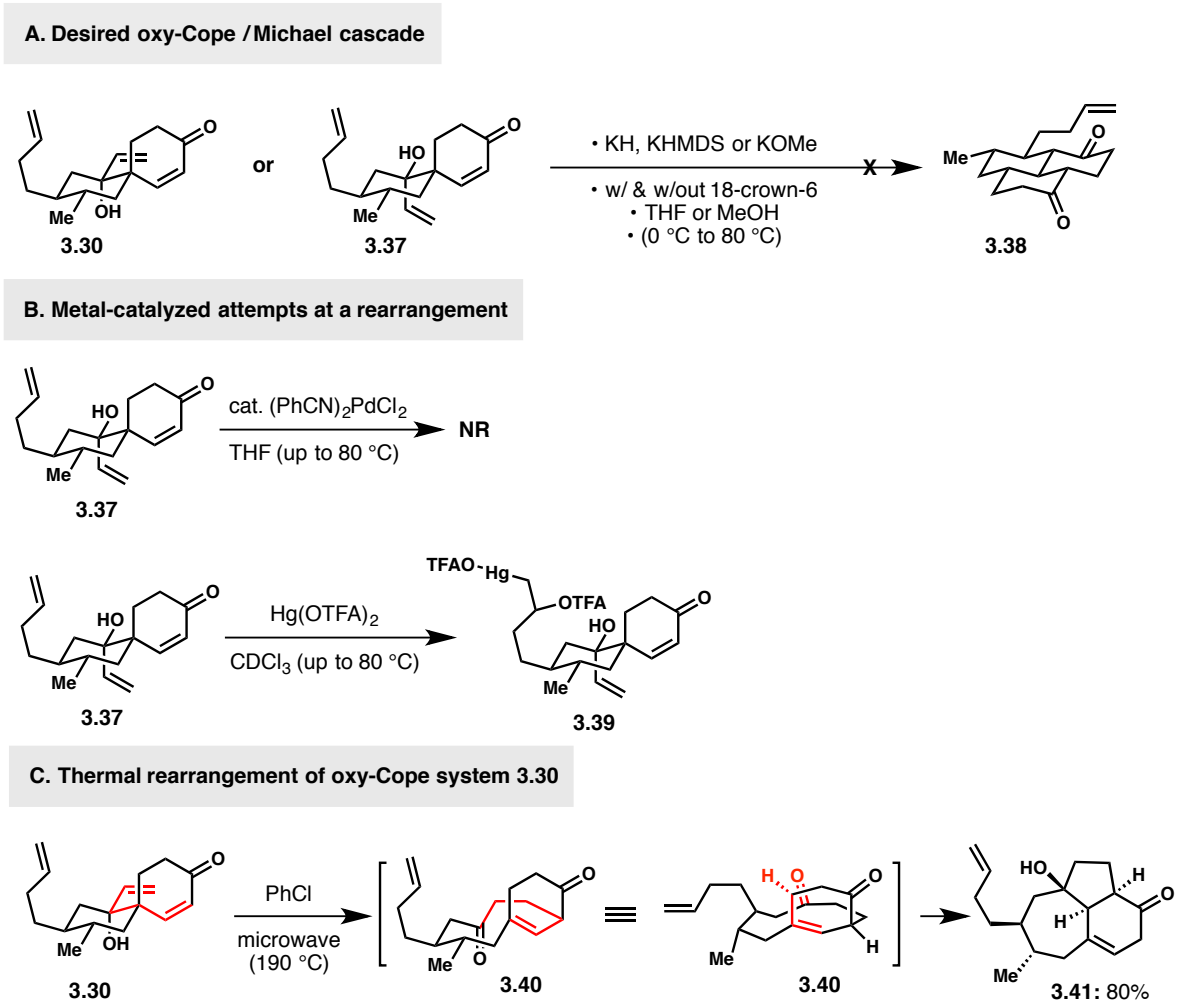
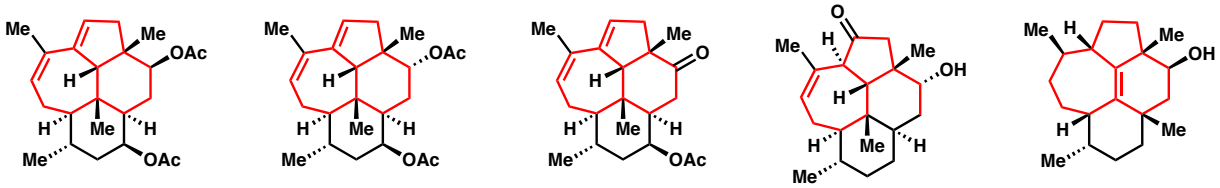


Figure 3.1 Kempane and rippertane structures.



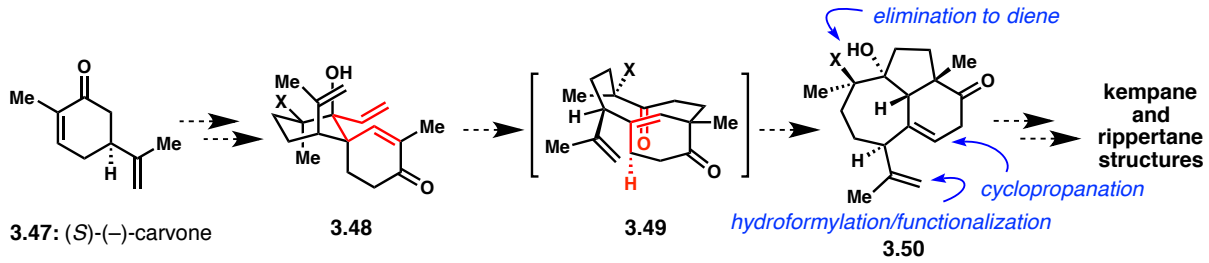
3.42: (+)-kempene 1 **3.43:** (+)-3-epi-kempene 1 **3.44:** (+)-kempene 2 **3.45:** (?)-3β-hydroxy-7β-kemp-8(9)-en-6-one **3.46:** (?)-rippertol

The tricyclic ring system of **3.41** is reminiscent of the kempane and rippertane core (Figure 3.1) and an approach using this tandem thermal reaction could be imagined.[33,34]

Currently no efforts using an oxy-Cope/carbonyl-ene reaction towards these molecules have been reported, though other natural products have been prepared using this tandem methodology.[35,36] The synthesis of these natural products still holds exciting challenges.

Starting from (*S*)-(–)-carvone, **3.47**, Li/NH_3 reduction of the enone and capture of the resultant enolate with a group capable of reforming the alkene (SPh, SePh, etc.) followed by spirocyclic Robinson annulation—MVK would arrive *trans* to the isopropenyl—could generate the ketone precursor to **3.48**. The sequence of enone silylation, Grignard reagent addition and deprotection would generate decorated spirocyclic enone **3.48**. Exposing this substrate to thermal conditions could trigger the desired oxy-Cope/carbonyl-ene rearrangement to the core kempane structure (Scheme 3.9). The 1,5-diene of **3.48** highlighted in red would selectively undergo oxy-Cope rearrangement and upon carbonyl-ene, generate a tertiary alcohol for elimination. The isopropenyl substituent could be elaborated via hydroformylation to address annulation of the southern ring and a cyclopropanation/fragmentation to introduce the remaining methyl group.

Scheme 3.9 An envisioned oxy-Cope/carbonyl-ene approach to kempane natural products.

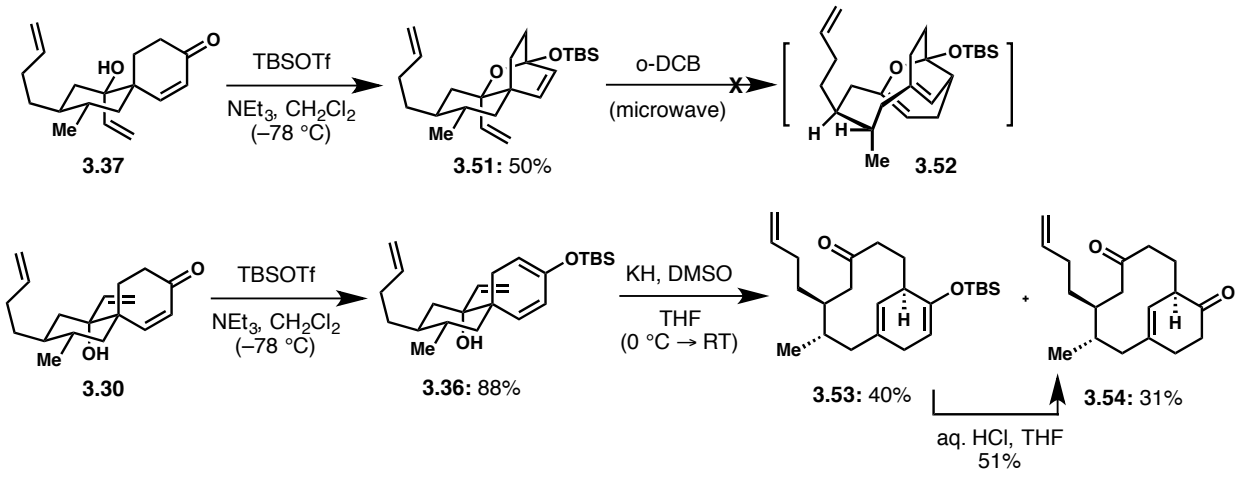


Although the anionic oxy-Cope transformation of enones **3.30** and **3.37** had failed, the success of a thermal oxy-Cope encouraged a sustained effort. In this vein, masking the enone functionality was evaluated next (Scheme 3.10). Attempted enoxysilane formation of **3.37** with TBSOTf led to [2.2.2]-oxabicycle **3.49**. Oxy-Cope rearrangement of this molecule was

unsuccessful, most likely because of the strain and frailty of **3.50** generated upon [3,3]-rearrangement, so silylation of the other allylic acohol diastereomer was pursued.

Treating enone **3.30** with TBSOTf smoothly afforded siloxydiene **3.36**. Deprotonating the alcohol with KH and DMSO at 0 °C and warming the reaction to room temperature led to formation of a single product by TLC analysis. Upon quenching with ethanol the two products **3.53** and **3.54** were isolated. Both compounds were generated via [3,3]-rearrangement, and could be funneled to the skipped enone **3.54** upon deprotecting enoxysilane **3.53** with acid.

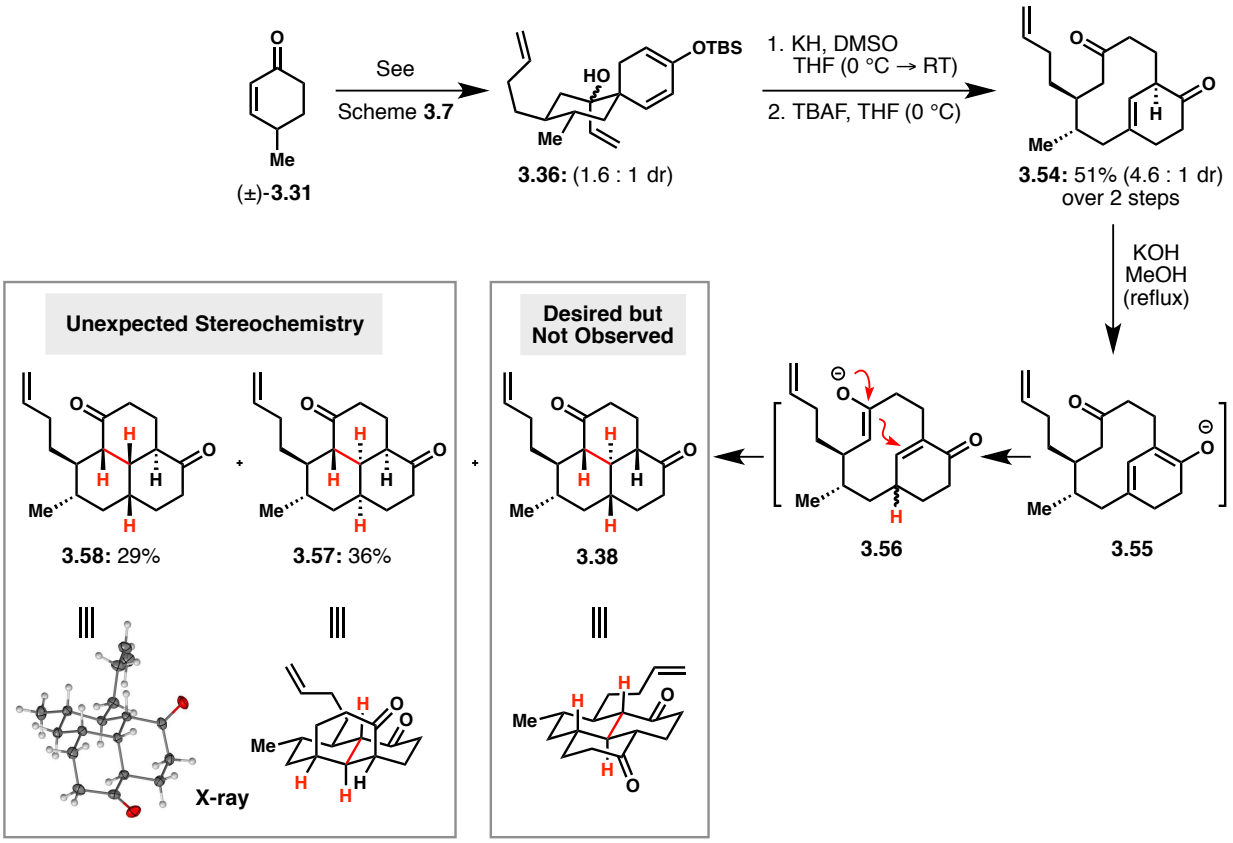
Scheme 3.10 Silylation of spirocyclic enones in efforts towards an oxy-Cope rearrangement.



With a basic synthetic outline to obtain oxy-Cope product **3.54** established, a more streamlined preparation was sought. As the synthesis outlined in Scheme 3.7 and 3.10 proceeds through enoxysilane **3.36** as a mixture of alcohol diastereomers, the anionic oxy-Cope could be attempted at this stage. Two outcomes were envisioned: 1. only the axial-alcohol diastereomer undergoes rearrangement or 2. both diastereomers could rearrange leading to better material throughput. Gratifyingly, when **3.36** was deprotonated with KH and warmed to room temperature, a single compound was obtained; both diastereomers of **3.36** cleanly underwent ring

expansion (Scheme 3.11). Treating the crude cyclohexadiene with cold TBAF afforded **3.54**. Although the sigmatropic rearrangement is high yielding, the relatively low isolated yield of **3.54** is due to decomposition during desilylation. Still, this consolidated approach allows for a rapid build up of material when compared to the previous sequence.

Scheme 3.11 Improved synthesis of [7.3.1]-bicycle **3.54** via an anionic oxy-Cope rearrangement and subsequent transannular Michael reaction.



With the oxy-Cope ring expansion reaction completed, transannular cyclization of bicycle **3.54** was examined. Treating **3.54** with hot, basic methanol afforded two products. The desired pathway would isomerize the skipped enone into conjugation to **3.55**, and be followed by *trans*-selective cyclization to **3.38** as precedented by Swaminathan (Equation 3.1).[14] Instead, the two products formed arose from indiscriminant protonation of the extended enolate **3.55** at the

gamma position, followed by a *cis*-selective cyclization to generate **3.57** and **3.58**. No desired *trans* ring-closure was observed. This disappointing result brought into question the original literature report.

3.4 A Literature Reevaluation of the Transannular Michael Stereochemistry

The original Swaminathan report of the oxy-Cope/Michael cascade of **3.19** reported the product perhydrophenalene to be in the all-*trans* configuration (Equation 3.1, Figure 3.2).[14] When this reaction sequence was adapted towards DICA, the transannular Michael reaction provided two products via a *cis*-selective ring closure (Scheme 3.11). These two contradicting results and the lack of rigorous stereochemical determination originally performed by Swaminathan (Figure 3.2), made a reinvestigation prudent.

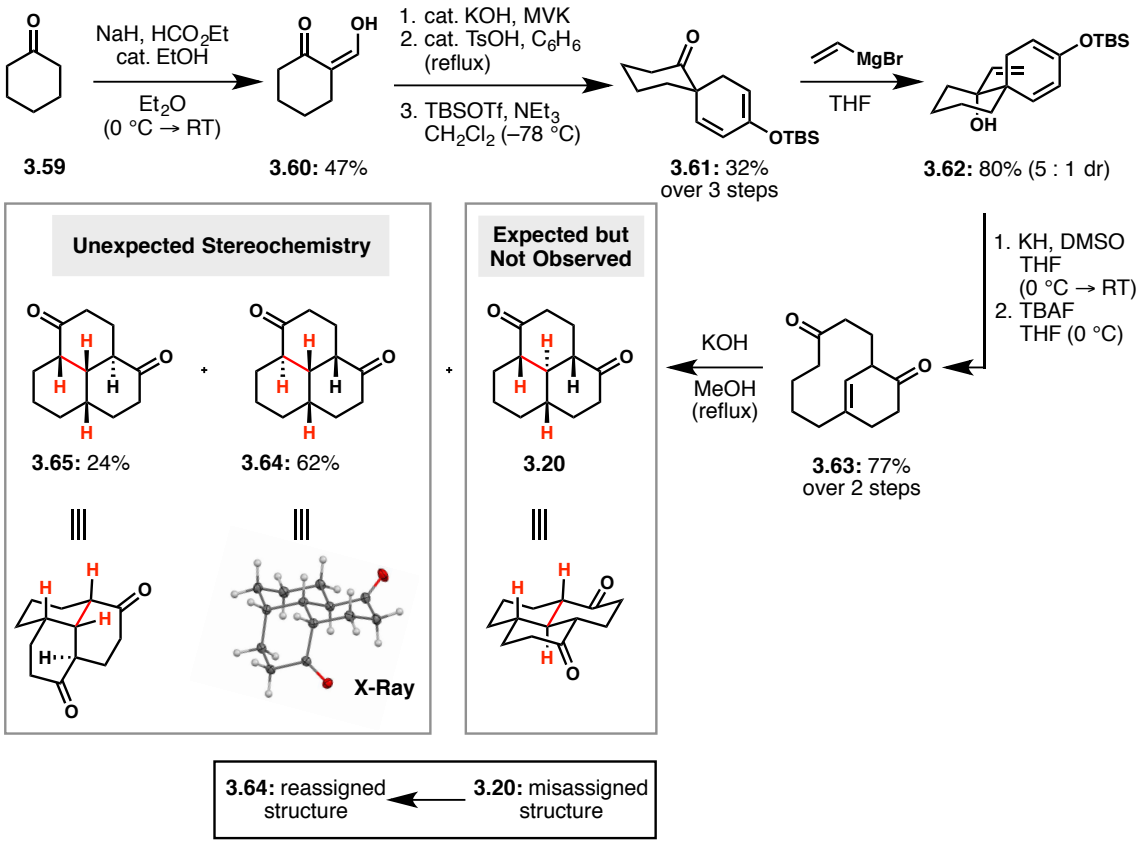
Figure 3.2 Stereochemical determination of oxy-Cope/Michael reaction product by Swaminathan. "Dione 6" refers to structure **3.20**.[14]

> Since the rearrangement is being carried out under equilibrating conditions, the dione **6** may be expected to take up the most stable conformation *viz.* the all *trans* conformation **6a**.

A synthetic sequence similar to the approach for DICA was initiated for the simple unsubstituted literature system (Scheme 3.12). Spirocyclic Robinson annulation on cyclohexanone **3.59** and silylation afforded silyloxydiene **3.61**. Vinylmagnesium bromide addition followed by deprotonation with KH and deprotection with TBAF generated the ring expanded **3.63**. Treatment of **3.63** with potassium hydroxide in methanol triggered the transannular Michael addition and afforded a major compound with identical ^{1}H and ^{13}C NMR

data as reported by Swaminathan[14] who assigned structure **3.20**. X-Ray crystallography was chosen as the most rigorous means of structural determination. Instead of the expected all-*trans* **3.20**, analysis revealed the stereochemistry was **3.64**. The structure reported by Swaminathan was thus misassigned and was thereby corrected to **3.64**, a compound obtained from a *cis*-selective Michael addition (the bond highlight in red). A second compound (**3.65**) was isolated as a minor component and clearly arises via epimerization of the α-carbons. The structural reassignment of **3.20** to **3.64** requires that caution be exercised with the other reported structures obtained via such cascades (Equations 3.2-3.4).[14–16]

Scheme 3.12 Reevaluation of the original oxy-Cope/Michael cascade.



3.5 Evaluating the Reversibility of the Transannular Michael Reaction

Swaminathan's assertion that the oxy-Cope/Michael reaction of **3.19** should provide a perhydrophenalendione in an all-*trans* relationship because of the equilibrating conditions, even though incorrect, is still interesting (Figure 3.2). The reaction of **3.63** with basic methanol to afford **3.64** and **3.65** could simply be the outcome of a kinetic conjugate addition. Under thermodynamic control, the ring closure would be reversible and therefore could still equilibrate to the more stable all-*trans* **3.20** (Scheme 3.13). Computations have already established the all-*trans*, all-chair conformation of unsubstituted perhydrophenalene **3.69** to be most thermodynamically stable (Scheme 3.13).[37] The known reversibility of Michael reactions lends credence to the possible equilibration of **3.64** to **3.20**.[38,39] Disappointingly, exposing **3.64** to higher temperatures in methanol or basic ethylene glycol did not lead to any change in product distributions. Also, if the retro-Michael were to have occured, at elevated temperatures, a carbonyl-ene product similar to **3.41** could also be imagined; however, such a product was never observed.

Scheme 3.13 Proposed pathway for the equilibration of a perhydrophenalenedione system via a retro-Michael/transannular Michael sequence and calculations of perhydrophenalene stability.[37]

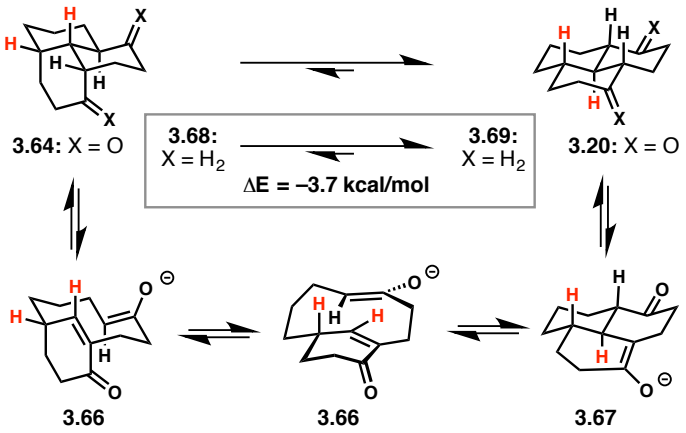
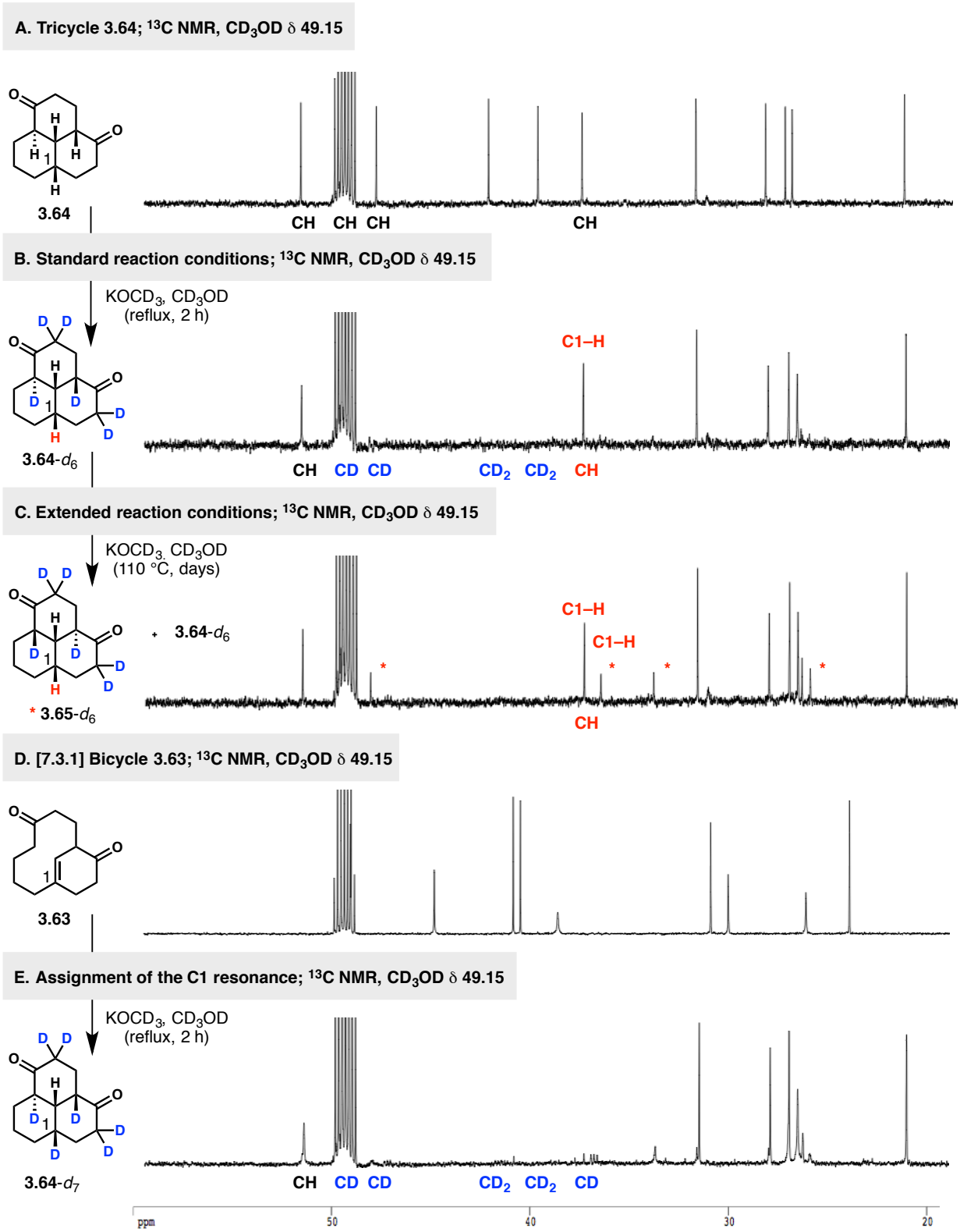


Figure 3.3 NMR study in CD_3OD to determine the reversibility of the Michael reaction.



Because the equilibration of **3.64** to **3.20** relies on a retro-Michael reaction, a detailed investigation into the feasibility of the retro-transannular Michael reaction was initiated to better understand the failed equilibration. Two possibilities exist for the observed lack of equilibration: 1. the retro-Michael reaction may not be occurring under the experimental conditions or 2. the retro-Michael may be facile, but the transannular ring closure is only *cis*-selective. Deuterium labeling studies were devised to distinguish between the two possibilities.

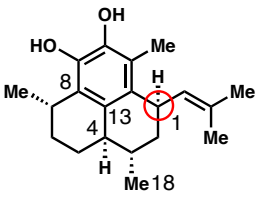
Tracking the incorporation of deuterium provided insight into the reversibility of the transannular Michael reaction (Figure 3.3). Treating **3.64** with $KOCD_3/CD_3OD$ under typical cyclization conditions incorporated deuterium at all enolizable positions to afford **3.64**-d_6 (Figure 3.3A-B). No deuterium incorporation was observed at the gamma-position, C1.[40] Extended heating of **3.64**-d_6 afforded only a mixture of **3.64**-d_6 and **3.65**-d_6; still, no incorporation of deuterium at C1 was observed (Figure 3.3B-C). To assign the residual methine carbons δ 51.4 and 37.1, the cyclodecenone **3.63** was closed in CD_3OD (Figure 3.3D-E). The C1 position was deuterated upon enone isomerization to enable the cyclization to **3.64**-d_7. The peak at δ 37.1 was assigned to C1 as δ 51.4 remained protiated. Based on these reactivity studies, the transannular Michael reaction, which is necessary for conversion of **3.64** to **3.20** is irreversible in basic methanol (Scheme 3.13).

3.6 Outlook for the oxy-Cope/Michael Reaction in Natural Product Synthesis

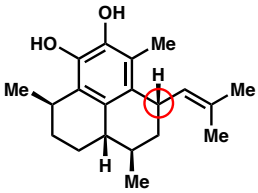
Swaminathan's oxy-Cope/Michael cascade proceeded smoothly to construct the perhydrophenalene C–C bonds; however, in the context of DICA, not with the desired stereochemical outcome. The ease of starting material synthesis and rapid construction of molecular complexity makes the oxy-Cope/Michael reaction a powerful method of polycyclic

assembly. The attempted implementation of this strategy towards DICA supported this point, but because of a stereochemical misassignment, DICA ended up as the wrong target for this reaction.

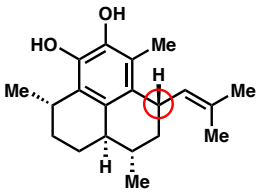
Figure 3.4 Pseudopterosin aglycones.



(–)-**3.70:** pseudopterosin A-F, Z aglycone



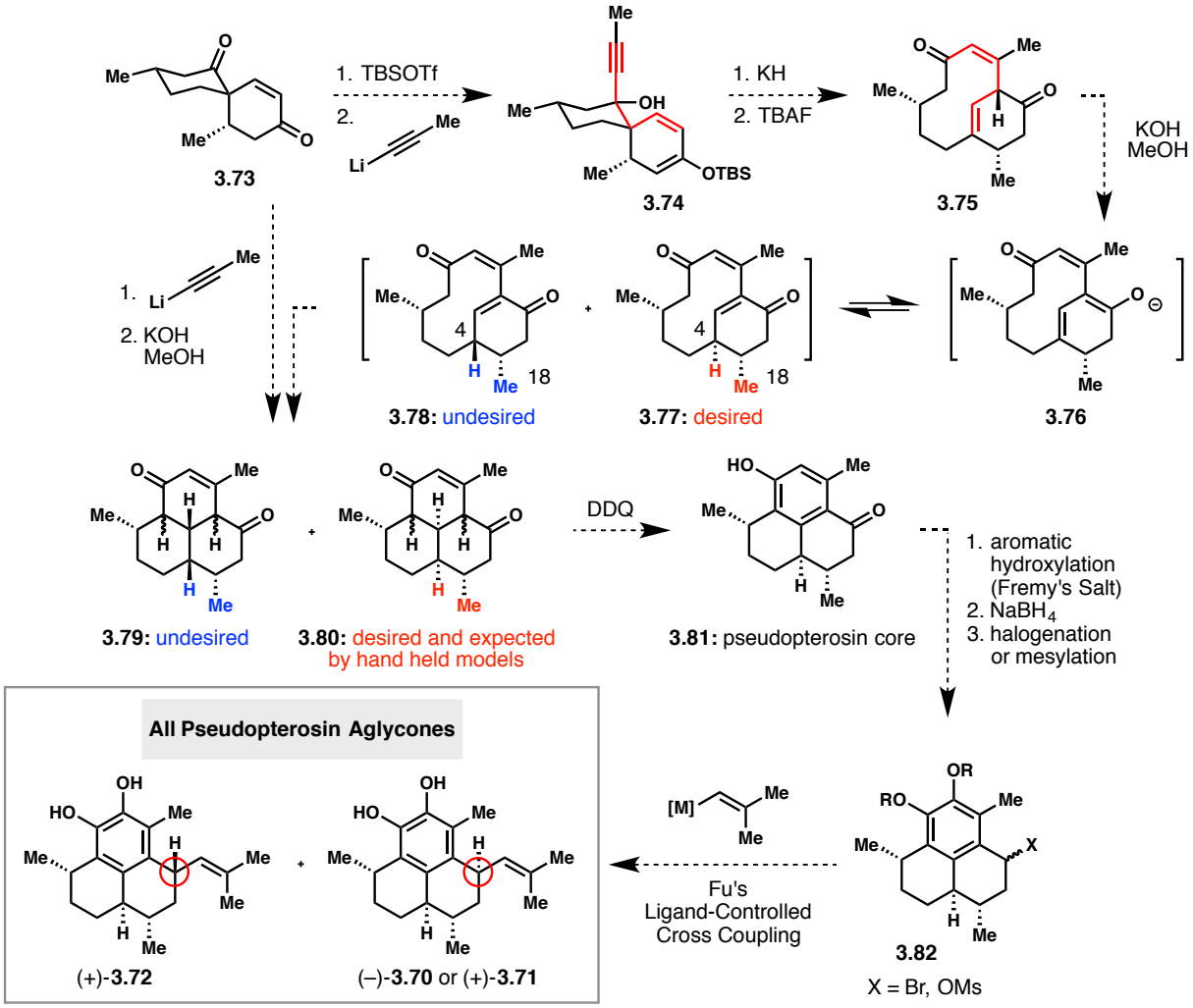
(+)-**3.71:** pseudopterosin K-L aglycone



(+)-**3.72:** pseudopterosin G-J, M-Y aglycone

Although disappointing that the designed strategy towards DICA did not bear fruit, Swaminathan's transformation to the perhydrophenalene scaffold could still be useful for natural product synthesis. Of the phenalene containing natural products, the pseudopterosins may be most readily accessed (Figure 3.4).[41–43] This class of molecules consists of numerous members with variation in glycosylation pattern of a substituted phenalene core. The cores can be divided into one set of enantiomers, (–)-**3.70** and (+)-**3.71**, and into the side chain epimer, (+)-**3.72**. The pseudopterosin aglycones have been prepared synthetically on 15 occasions, with the latest by Sherburn in 2015.[44,45]

Scheme 3.14 Proposed approach to all pseudopterosine aglycones.



An approach using the oxy-Cope/Michael rearrangement could start from simple spirocycle **3.73** (Scheme 3.14). In an optimized sense, taking **3.73** to **3.80** could mirror Swaminathan's two-step alkyne addition and basic rearrangement; however, based on previous successes, a stepwise transformation through siloxydiene **3.74** may be initially more successful. Isomerizing the skipped enone **3.75** into conjugation would set the single stereocenter of interest at C4. Although this isomerization may be unselective, molecular models indicate that the transannular Michael would arise only from the desired epimer **3.77** and not the undesired **3.78**. The overlap between enolate and enone of **3.78** places the C18 methyl inside the ten-membered

ring, directly into the seven-carbon tether. The stereocenters generated at C8, C12 and C13[46] are inconsequential, as the cyclohexenone ring would be immediately oxidized to phenol **3.79**, an intermediate prepared previously.[43,47–49] The remaining functionalizations include an aromatic hydroxylation, followed by the installation of the side chain. Implementation of Fu's enantioselective cross-coupling technology[50,51] could enable the selective synthesis of all pseudopterosin aglycones (–)-**3.70**, (+)-**3.71** and (+)-**3.72**, *a feat not achieved by any of the 15 currently published total synthesis strategies*.[45]

Use of the oxy-Cope/Michael rearrangement towards the pseudopterosins would contribute an entirely new synthetic design for a popular target. All approaches, except for the recent Sherburn synthesis, rely either on a terpene or aromatic starting material as a scaffold to construct subsequent rings: termed "structure-goal strategy."[44] An oxy-Cope/Michael strategy originating from a spirocycle starting material would be the only synthesis to construct all three rings simultaneously and also deviates from the previously relied on "structure-goal strategy". It would also reprise a strategy that was unsuccessful in the context of DICA to another natural product system.

3.7 Conclusions

The oxy-Cope/transannular Michael cascade of spirocyclic enones was uncovered in the literature and evaluated in the interest of a synthesis of DICA. The course of the reaction generated the desired carbocyclic framework required for the proposed synthesis, but upon examining the products in detail, an undesired *cis* ring-fusion was observed. This turned our attention to reevaluating the literature report's proposed claims. A structural misassignment of the literature compound was uncovered by X-ray analysis. As previously noticed in an

application towards DICA, the transannular Michael undergoes only a *cis*-selective addition. Further deuterium studies confirmed a suspicion that the conjugate addition is irreversible in refluxing basic methanol, counter to Swaminathan's assertions. Although the oxy-Cope/Michael reaction strategy towards DICA was unsuccessful, the reaction could still have a bright future in natural product synthesis; accessing the pseudopterosins is one example.

3.8 Experimental Procedures

Purifications –

Solvents: Dry tetrahydrofuran (THF), diethyl ether (Et_2O), dichloromethane (CH_2Cl_2), toluene, benzene (C_6H_6), dimethylformamide (DMF), methanol (MeOH) were obtained by passing commercially available formulations through activated alumina columns

Amines: Triethylamine (NEt_3) was purified by distillation from CaH_2.

Triflates: *tert*-Butyldimethylsilyl trifluoromethanesulfonate (TBSOTf) was purified by distillation over CaH_2.

Metals: Copper(I) iodide (CuI) was purified by Soxhlet extraction with THF followed by drying of the solid under high vacuum. (COD)CuBr was prepared according to the literature.[24]

Miscellaneous: Methyl vinyl ketone (MVK) was purified by distillation. BF_3•OEt_2 was purified by distillation from CaH_2. $KOCD_3$ was prepared by addition of CD_3OD to a suspention of KH in toluene, removing all volatiles in vacuo and washing the remaining solid with pentane.

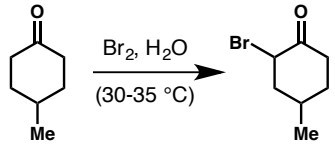
Titrations – Alkyllithium reagents were titrated using 2,6-di-(tert-butyl)-4-methylphenol (BHT) as the sacrificial proton source and fluorene as an indicator in THF or using diphenylacetic acid in THF. Grignard reagents were titrated using salicylaldehyde phenylhydrazone in THF.[52]

Reaction Setup – All reactions were carried out under an argon atmosphere with dry solvents under anhydrous conditions, unless otherwise noted. Argon balloons were the sole inert atmosphere used. Reactions run at an ambient temperature of 20–25 °C are designated as room

temperature. Microwave reactions were performed in an Anton Paar Microwave. Yields refer to chromatographically and spectroscopically homogeneous materials, unless otherwise stated.

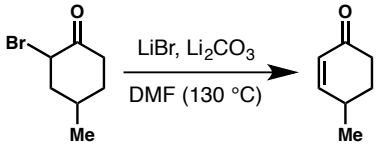
Analysis – Thin layer chromatography was performed on 0.25 mm EMD glass-backed TLC plates impregnated with a fluorescent dye and visualized with UV light and $KMnO_4$ in K_2CO_3/NaOH/water or *p*-anisaldehyde in ethanol/aqueous H_2SO_4/AcOH and heat as a developing agent. Forced flow (flash) chromatography was performed on EMD Silica 60, mesh 0.04-0.063 silica gel. NMR spectra were recorded on Bruker 500 MHz instrument, obtained at 298 K unless otherwise noted and calibrated to residual undeuterated solvent as an internal reference. Chemical shifts are reported in ppm with the following abbreviations to explain multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, quin = quintuplet, sext = setet, sep = septet, bs = broad signal, m = multiplet. All coupling constants are apparent *J* values measured at the indicated field strengths. FT-IR spectra were recorded on a Perkin-Elmer spectrum RX1 spectrometer. High-resolution mass spectra (HRMS) were recorded on a H2Os LCT Premier spectrometer using ESI-TOF (electrospray ionization-time of flight). Melting points were measured on a MEL-TEMP II capillary apparatus and stand uncorrected.

2-Bromo-4-methyl cyclohexanone [Adapted from the literature][53]



A 250 mL round bottom flask was charged with 20.0 g (0.178 mol) 4-methylcyclohexanone and 60 mL water and placed in an empty crystallizing dish. The rapidly stirring solution was treated dropwise with 8.4 mL (0.164 mol) bromine over the course of 30 minutes, keeping an internal reaction temperature between 30-35 °C by adding ice to the crystallizing dish. After stirring for an additional 1.5 hours the reaction turned colorless, then diluted with 20 mL sat. $Na_2S_2O_3$ and 40 mL water, partioned with 200 mL EtOAc and the layers separated. The organic phase was washed twice with 50 mL sat. $NaHCO_3$ and 50 mL brine. All aqueous layers were collected and back extracted with 50 mL EtOAc. This organic layer was washed twice with 20 mL sat. $NaHCO_3$, 20 mL brine and combined with the previously obtained organic phase, dried over $MgSO_4$, filtered, all volatiles removed in vacuo and the crude material distilled (60-73 °C/0.6 mmHg) to afford 24.2 g (77%, 2:1 dr) 2-bromo-4-methyl cyclohexanone as a colorless liquid. The spectral data was identical to the literature.[54]

4-Methylcyclohex-2-en-1-one 3.31 [Adapted from the literature][55]

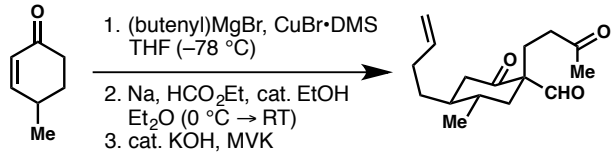


3.31

A three neck 1 L flask was fitted with a mechanical stirrer, a rubber septum and a reflux condenser, and flushed with argon. The flask was charged with 24.1 g (0.127 mol) 2-bromo-4-methyl cyclohexanone, 250 mL DMF, 23.5 g (0.318 mol) Li_2CO_3 and 27.8 g (0.320 mol) LiBr,

the septum replaced with a glass stopper and the reaction placed in an oil bath set to 130 °C. After 3 hours the reaction was cooled to room temperature, diluted with 250 mL EtOAc and filtered through Celite. The filter cake was washed four times with 250 mL EtOAc portions. Five seperatory funnels were set up in tandem, the first loaded with the filtrate solution and the other four with 250 mL fresh EtOAc each. To the first funnel was added 1 L water and after vigorous shaking, the aqueous layer drained and poured into the second funnel. After vigorous shaking, the aqueous layer was drained and poured into the third funnel, shaken and continued with the fourth and fifth seperatory funnel. This process was repeated three additional times with 750 and twice with 500 mL water portions. The first seperatory funnel was washed with 150 mL brine, the other four with 50 mL brine, then all organic layers collected, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude material was distilled (48-52 °C/4.5 mmHg) to afford 8.62 g (62%, ~3% DMF contamination) **3.31** as a colorless liquid. The spectral data was identical to the literature.[54]

Michael Adduct 3.34



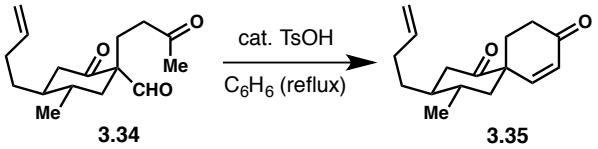
3.32 **3.34**

A 250 mL round bottom flask was charged with 70 mL (25.6 mmol) freshly prepared 0.37 M butenylmagnesium bromide/THF. The reaction was cooled to –78 °C then treated with 2.67 g (13.0 mmol) CuBr•DMS. The cuprate was aged 45 minutes before 1.19 g (10.8 mmol) **3.32** in 15 mL THF was added over the course of 15 minutes. After stirring at –78 °C for a total of 3 hours, the reaction was quenched with 10 mL sat. NH_4Cl and filtered through Celite with the assistance

of 150 mL EtOAc. All volatiles were removed, the residue dissolved in 150 mL EtOAc, washed thrice with 50 mL portions 2:1 1 M NaOH/sat. NH_4Cl then 30 mL brine. The organic layer was dried over $MgSO_4$, filtered and all volatiles removed in vacuo. Crude ketone (>20:1 dr) was of sufficient purity to move forward. To an ice cooled 50 mL round bottom flask containing 20 mL Et_2O was added 300 mg (13 mol) Na metal cut and flattened, then crude ketone from above in 5 mL Et_2O and 1.3 mL (16.1 mmol) ethyl formate were added. The reaction was initiated with 0.1 mL EtOH and the ice bath allowed to melt over the course of 5 hours. The contents were stirred for 10 minutes after the addition of 6 mL 0.5 M NaOH, diluted with 24 mL 0.5 M NaOH and the layers seperated. The aqueous layer was washed twice with 20 mL Et_2O. All organic layers were combined and back extracted twice with 20 mL 0.5 M NaOH. The aqueous phases were collected, acidified with 20 mL 6 M HCl then extracted with 40 mL and thrice with 20 mL Et_2O. These organic layers were combined, washed with 10 mL water, 10 mL half sat. $NaHCO_3$, 10 mL brine, then dried over $MgSO_4$ and all volatiles removed in vacuo to afford a ketoaldehyde of sufficient purity to proceed. A 50 mL round bottom flask was charged with crude ketoaldehyde, 1.3 mL (16.1 mmol) methyl vinyl ketone and 33 mg (0.59 mmol) powdered KOH at room temperature (exotherm). After stirring for 30 minutes, the contents were diluted with 60 mL Et_2O and washed twice with 10 mL water then 10 mL brine. The organic layer was dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The residue was purified by column chromatography (5:1 hexanes/EtOAc) to afford 1.92 g (66% over 3 steps, 5.2:1 dr) **3.34** as a light yellow oil. ^1H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) major δ 9.61 (s, 1H), 9.41 (s, 1H), 5.76 (dddd, J = 16.1, 11.9, 8.6, 4.1, 1H), 5.03 (d, J = 17.1, 1H), 4.99 (d, J = 12.2, 1H), 2.62-2.38 (m, 2H), 2.28-2.12 (m, 3H), 2.10 (s, 3H), 2.06-1.85 (m, 3H), 1.76-1.69 (m, 2H), 1.62 (dd, J = 13.8, 3.5, 1H), 1.53-1.45 (m, 1H), 1.43-1.24 (m, 1H), 1.03 (d, J = 6.4, 3H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm)

major δ 212.3, 207.3, 200.9, 137.9, 115.1, 62.3, 43.7, 43.5, 39.5, 38.1, 32.5, 30.9, 30.0, 29.9, 25.1, 18.8; IR (thin film) 2926, 2854, 2740, 1718, 1639 cm^{-1}; HRMS (ESI) calculated for $C_{16}H_{24}O_3$ $[M+Na]^+$ 287.1623 found 287.1621.

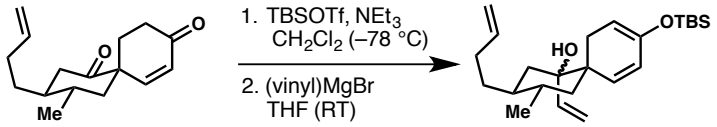
Spiro Enone 3.35



3.34 3.35

An azeotropically dried solution of 70 mg (0.37 mmol) p-TsOH•H_2O in 40 mL benzene was added to 1.90 g (7.19 mmol) **3.34** in a 100 mL round bottom flask and refluxed over a Hickman still. After 2 hours the reaction was cooled to room temperature, diluted with 50 mL Et_2O, washed twice with 10 mL sat. $NaHCO_3$, 10 mL water, 10 mL brine then dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude material was purified by column chromatography (9:1 hexanes/EtOAc) then recrystallized from Et_2O/hexanes to afford 902 mg (50%) **3.35** as fluffy white needles (mp = 42-44 °C). ^1H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 6.77 (d, J = 10.3, 1H), 6.06 (d, J = 10.3, 1H), 5.79 (ddt, J = 16.9, 10.2, 6.7, 1H), 5.05 (d, J = 17.1, 1H), 4.99 (d, J = 10.2, 1H), 2.52-2.45 (m, 2H), 2.37-2.12 (m, 5H), 2.01-1.94 (m, 2H), 1.88-1.81 (m, 1H), 1.76 (ddt, J = 13.3, 6.7, 3.3, 1H), 1.55 (t, J = 13.1, 1H), 1.52-1.46 (m, 1H), 1.34 (dtd, J = 13.7, 9.1, 4.8, 1H), 1.04 (d, J = 6.4, 3H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 211.5, 198.3, 152.5, 138.0, 129.5, 115.1, 50.9, 44.3, 44.2, 42.7, 33.3, 32.7, 31.5, 30.4, 29.9, 18.8; IR (thin film) 2919, 1702, 1684, 1450, 1227 cm^{-1}; HRMS (ESI) calculated for $C_{16}H_{22}O_2$ $[M+Na]^+$ 269.1518 found 269.1518.

Siloxydienes 3.36

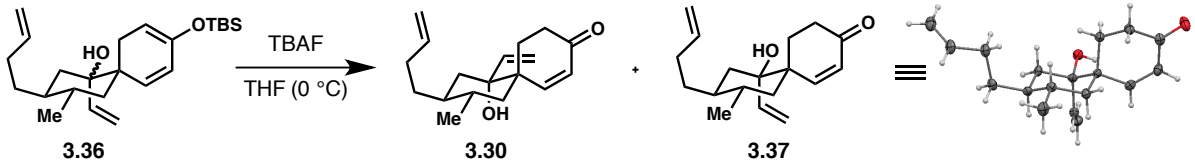


3.35 **3.36**

To a solution of 303 mg (1.23 mmol) **3.35** in 13 mL CH_2Cl_2 was added 0.60 mL (4.3 mmol) NEt_3 and 0.32 mL (1.4 mmol) TBSOTf at –78 °C. After 3 hours of stirring at –78 °C the reaction was diluted with 10 mL hexanes and poured into a separatory funnel containing 10 mL sat. $NaHCO_3$. The flask was rinsed twice with 10 mL pentane, the organic layer washed with 10 mL sat. $NaHCO_3$, 10 mL water, 5 mL brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo to afford a compound of sufficient purity to proceed. The crude material from the previous step in 7 mL THF was treated with 7.0 mL (5.0 mmol) 0.71 M vinylmagnesium bromide/THF at 0 °C. The ice bath was removed and stirring continued for 8 hours. The reaction was quenched at 0 °C with 20 mL half sat. NH_4Cl, diluted with 30 mL EtOAc and the phases separated. The organic layer was washed with 10 mL sat. $NaHCO_3$, 5 mL water and 10 mL brine, then dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude oil was purified by column chromatography (160:4:1 hexanes/EtOAc/NEt_3) to afford 373 mg (78% over two steps, 1:1.6 dr) **3.36** as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) major δ 6.39 (dd, J = 17.0, 10.9, 1H), 5.86-5.75 (m, 2H), 5.71 (dd, J = 10.2, 2.2, 1H), 5.44 (d, J = 10.2, 1H), 5.42 (dd, J = 17.0, 1.8, 1H), 4.83 (dt, J = 4.7, 2.2, 1H), 2.86 (dd, J = 17.6, 4.5, 1H), 1.78 (s, 1H), 1.74 (dd, J = 14.0, 4.0, 1H), 1.49 (t, J = 12.7, 1H), minor δ 6.06 (dd, J = 17.4, 10.9, 1H), 5.86-5.75 (m, 1H), 5.65 (dd, J = 10.2, 2.1, 1H), 4.67-4.65 (m, 1H) (mixed) 5.20-5.08 (m, 3H), 5.04-4.92 (m, 4H), 2.36-2.22 (m, 3H), 2.18-2.08 (m, 2H), 2.00-1.89 (m, 2H), 1.69-1.56 (m, 6H), 1.43-1.33 (m, 4H), 1.22-1.13 (m, 4H), 0.95-0.90 (m, 24H), 0.13 (s, 6H), 0.13 (s, 3H), 0.12 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) combined δ 147.2, 146.7, 143.9, 141.3, 139.2, 138.9, 134.7, 134.1, 127.0,

125.6, 114.3, 114.2, 113.9, 112.7, 101.9, 100.4, 77.9, 76.1, 42.2, 42.1, 41.7, 39.9, 39.8, 39.0, 37.7, 37.6, 32.8, 32.3, 30.9, 30.52, 30.47, 29.1, 27.6, 25.7, 25.7, 19.6, 19.5, 18.0, 18.0, –4.4, –4.45, –4.48; IR (thin film) 2928, 1654, 1252, 1201 cm^{-1}; HRMS (ESI) calculated for $C_{24}H_{40}O_2Si$ $[M+Na]^+$ 411.2695 found 411.2693.

Spirocyclic Enones 3.30 and 3.37

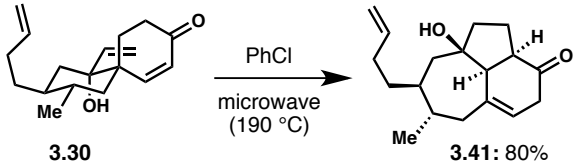


3.36 **3.30** **3.37**

To a solution of 0.99 g (2.54 mmol) **3.36** in 10 mL THF was added 4 mL TBAF (1 M in THF) at 0 °C. After 2 minutes at 0 °C, the reaction was diluted with sat. aq. $NaHCO_3$ and poured into EtOAc. The layers were separated and the organic layer washed twice with sat. aq. $NaHCO_3$, brine, dried over $MgSO_4$ and all volatiles removed in vacuo. The crude material was purified by column chromatography (10:1 hexanes/EtOAc) to afford 201 mg (28%) 3.30 as a colorless oil and 394 mg (56%) **3.37** as a white solid. **3.30**: ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 7.21 (dd, J = 10.4, 1.8, 1H), 5.95 (d, J = 17.4, 1H), 5.93 (dd, J = 17.4, 10.7, 1H), 5.82 (ddt, J = 17.0, 10.3, 6.7, 1H), 5.25 (dd, J = 17.4, 0.9, 1H), 5.16 (d, J = 10.9, 1H), 5.03 (dd, J = 17.1, 1.6, 1H), 4.98-4.95 (m, 1H), 2.49-2.41 (m, 1H), 2.35 (dt, J = 17.4, 4.5, 1H), 2.20-2.12 (m, 1H), 2.08-1.88 (m, 3H), 1.75-1.64 (m, 4H), 1.58-1.43 (m, 3H), 1.38 (s, 1H), 1.28-1.21 (m, 1H), 0.97 (d, J = 6.1, 3H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 199.4, 156.1, 142.6, 138.9, 128.7, 114.7, 114.4, 75.1, 43.3, 37.47, 37.46, 37.2, 33.6, 32.2, 31.7, 30.5, 27.0, 19.6; IR (thin film) 3435, 2924, 1664 cm^{-1}; HRMS (ESI) calculated for $C_{18}H_{26}O_2$ $[M+Na]^+$ 297.1830 found 297.1830. **3.37**: ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 6.68 (d, J = 10.4, 1H), 6.50 (dd, J = 17.1, 10.9, 1H), 5.97 (d, J

= 10.4, 1H), 5.78 (ddt, J = 17.0, 10.3, 6.7, 1H), 5.40 (dd, J = 17.1, 1.2, 1H), 5.28 (dd, J = 10.9, 1.1, 1H), 5.00 (dq, J = 17.1, 1.6, 1H), 4.95 (dt, J = 10.2, 0.8, 1H), 2.68 (ddd, J = 17.2, 7.1, 5.3, 1H), 2.54 (ddd, J = 14.1, 9.4, 4.9, 1H), 2.41 (ddd, J = 17.2, 9.7, 5.4, 1H), 2.17-2.10 (m, 1H), 2.01-1.92 (m, 2H), 1.72-1.63 (m, 3H), 1.59 (dd, J = 13.6, 3.6, 1H), 1.54 (s, 1H), 1.53-1.45 (m, 1H), 1.41 (t, J = 12.9, 1H), 1.31-1.26 (m, 1H), 1.19 (dtd, J = 13.7, 9.1, 4.7, 1H), 0.97 (d, J = 6.2, 3H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 200.0, 155.3, 141.0, 138.6, 130.0, 114.63, 114.58, 77.3, 43.4, 41.7, 41.1, 40.0, 34.4, 32.7, 31.6, 30.4, 26.5, 19.5; IR (thin film) 3433, 2920, 1663, 1450 cm^{-1}; HRMS (ESI) calculated for $C_{18}H_{26}O_2$ $[M+Na]^+$ 297.1830 found 297.1829. X-Ray quality crystals were grown from pentane / CH_2Cl_2 (mp = 123-125 °C).

Tricycle 3.41

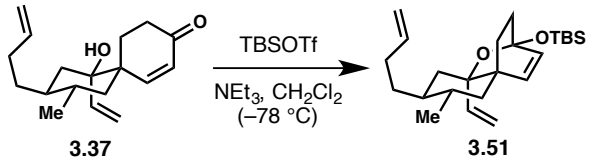


3.30 **3.41:** 80%

A microwave vial was charged with 18.8 mg (0.0685 mmol) **3.30** and 1 mL chlorobenzene, sealed and heated at 190 °C in a microwave for 4 hours + 4 hours. All volatiles were removed in vacuo and the crude material purified by column chromatography (6:1 hexanes/EtOAc) to afford 15.0 mg (80%) **3.41** as a white solid, which partially isomerized upon attempted recrystallization. ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 5.81-5.73 (m, 1H), 5.64 (s, 1H), 5.00 (d, *J* = 17.2, 1H), 4.94 (d, *J* = 10.0, 1H), 2.97 (d, *J* = 21.0, 1H), 2.82-2.90 (m, 2H), 2.56-2.50 (m, 1H), 2.37 (d, *J* = 14.0, 1H), 2.15-2.05 (m, 2H), 2.02-1.44 (m, 12H), 1.04 (d, *J* = 6.4, 3H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 209.4, 138.8, 136.7, 121.5, 114.5, 82.2, 57.3,

48.6, 43.7, 41.8, 40.4, 39.7, 39.2, 39.0, 34.6, 31.8, 22.9, 21.6; IR (thin film) 3467, 2917, 2850, 1708, 1459 cm^{-1}; HRMS (ESI) calculated for $C_{18}H_{26}O_2$ $[M+Na]^+$ 297.1830 found 297.1834.

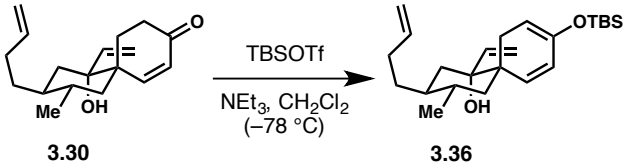
[2.2.2] Bicycle 3.51



3.37 **3.51**

To a solution of 10 mg (0.036 mmol) **42** in 0.5 mL CH_2Cl_2 was added 0.2 mL (1.4 mmol) NEt_3 and 50μL (0.22 mmol) TBSOTf in –78 °C. After 1 hours of stirring at –78 °C the reaction was diluted with CH_2Cl_2 and poured into a separatory funnel containing sat. aq. $NaHCO_3$. The flask was rinsed twice with CH_2Cl_2 and the organic layer washed with sat. aq. $NaHCO_3$, brine, dried over $MgSO_4$ and all volatiles removed in vacuo. The crude material was purified by column chromatography to afford 7 mg (50%) **44** as a colorless oil. ^1H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 6.12-6.06 (m, 2H), 5.86 (d, J = 8.3, 1H), 5.80 (ddt, J = 17.0, 10.3, 6.7, 1H), 5.16 (dd, J = 17.0, 2.3, 1H), 5.04-4.99 (m, 2H), 4.94 (d, J = 10.1, 1H), 2.29 (ddd, J = 12.6, 9.8, 2.8, 1H), 2.19-2.12 (m, 1H), 1.95 (dq, J = 14.7, 7.4, 1H), 1.90-1.85 (m, 2H), 1.70-1.63 (m, 2H), 1.61-1.46 (m, 4H), 1.23-1.15 (m, 2H), 1.04 (td, J = 12.5, 4.8, 1H), 0.94 (d, J = 5.6, 3H), 0.91 (s, 9H), 0.19 (s, 3H), 0.15 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 141.7, 139.1, 137.0, 136.1, 115.1, 114.3, 97.6, 79.8, 40.11, 39.9, 39.62, 39.56, 34.6, 33.1, 31.6, 30.6, 25.9, 25.7, 20.0, 17.9, –2.4, –2.7; IR (thin film) 2928, 1684, 1640, 1212 cm^{-1}; HRMS (ESI) calculated for $C_{24}H_{40}O_2Si$ $[M+Na]^+$ 411.2695 found 411.2667

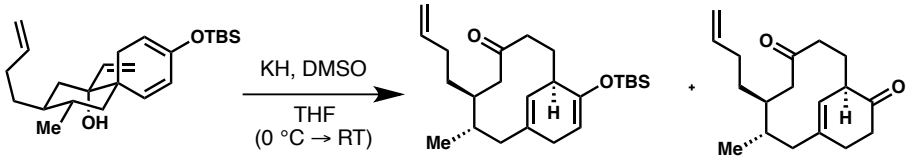
Dienoxysilane 3.36



3.30 **3.36**

To a solution of 52 mg (0.19 mmol) **3.30** in 4 mL CH_2Cl_2 was added 0.4 mL (2.9 mmol) NEt_3 and 0.1 mL (0.44 mmol) TBSOTf at –78 °C. After 1 hours of stirring at –78 °C the reaction was diluted with CH_2Cl_2 and poured into a separatory funnel containing sat. aq. $NaHCO_3$. The flask was rinsed twice with CH_2Cl_2 and the organic layer washed with brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude material was purified by column chromatography (hexanes→20:1 hexanes/EtOAc) to afford 62 mg (85%) **3.36** as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 6.06 (dd, J = 17.4, 10.9, 1H), 5.83-5.75 (m, 1H), 5.81 (d, J = 10.1, 1H), 5.65 (dd, J = 10.2, 2.1, 1H), 5.17 (dd, J = 17.4, 1.3, 1H), 5.10 (dd, J = 10.9, 1.3, 1H), 5.02 (dq, J = 17.1, 1.8, 1H), 4.96 (ddt, J = 10.2, 2.3, 1.1, 1H), 4.67-4.65 (m, 1H), 2.35 (dd, J = 17.2, 3.9, 1H), 2.25 (dd, J = 17.3, 5.5, 1H), 2.17-2.11 (m, 1H), 2.00-1.93 (m, 1H), 1.72-1.64 (m, 2H), 1.58 (dd, J = 13.6, 3.4, 1H), 1.49 (t, J = 12.7, 2H), 1.44-1.37 (m, 3H), 1.24-1.18 (m, 1H), 0.94-0.90 (m, 12H), 0.13 (s, 3H), 0.12 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 147.2, 143.9, 139.2, 134.7, 125.6, 114.2, 112.7, 100.4, 76.1, 41.7, 39.0, 37.7, 37.6, 32.3, 30.54, 30.52, 29.1, 25.7, 19.7, 18.0, –4.4, –4.5; IR (thin film) 3435, 2928, 2856, 1652 cm^{-1}; HRMS (ESI) calculated for $C_{24}H_{40}O_2Si$ $[M+Na]^+$ 411.2695 found 411.2693.

Enoxysilane 3.53 and Skipped Enone 3.54

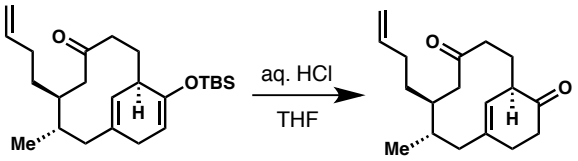


3.36 3.53 3.54

To a stirring solution of oil free KH in 0.5 mL THF was added 20 mg (0.26 mmol) DMSO in 0.5 mL THF at room temperature, followed by 50 mg (0.13 mmol) **3.36** in 0.6 mL THF with 0.4 mL and 0.5 mL THF rinses at 0 °C. The ice bath was removed after 10 minutes and the reaction stirred for 35 minutes. The reaction was quenched with 10 drops EtOH, then sat. aq. $NaHCO_3$. The aqueous phase was extracted twice with EtOAc. The organic phases were combined, washd with brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude material was purified by column chromatography (hexanes→40:1 hexanes/EtOAc) to afford 20 mg (40%) **3.53** as a waxy solid and 11 mg (31%) **3.54** as a waxy solid. **3.53**: ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 5.83 (ddt, J = 17.0, 10.3, 6.6, 1H), 5.03-4.92 (m, 4H), 3.05-3.00 (m, 1H), 2.79 (s, 1H), 2.69-2.60 (m, 2H), 2.43 (td, J = 13.2, 1.6, 1H), 2.27-2.20 (m, 1H), 2.12-1.99 (m, 4H), 1.97-1.90 (m, 4H), 1.68-1.62 (m, 1H), 1.54-1.48 (m, 1H), 1.40-1.33 (m, 1H), 0.93 (s, 12H), 0.17 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 212.4, 149.1, 139.1, 134.4, 129.0, 114.1, 101.5, 50.4, 48.0, 40.3, 37.9, 37.8, 34.8, 34.3, 31.6, 29.7, 25.7, 21.4, 18.1, –4.4, –4.5; IR (thin film) 2854, 2927, 2856, 1705, 1658, 1203 cm^{-1}; HRMS (ESI) calculated for $C_{24}H_{40}O_2Si$ $[M+Na]^+$ 411.2695 found 411.2687. **3.54**: ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ (major) 5.80 (ddt, J = 16.9, 10.2, 6.7, 1H), 5.21 (s, 1H), 5.00 (d, J = 17.2, 1H), 4.93 (d, J = 10.1, 1H), 2.93 (s, 1H), 2.69-2.47 (m, 5H), 2.38-2.33 (m, 1H), 2.25-1.87 (m, 9H), 1.63-1.55 (m, 1H), 1.53-1.47 (m, 1H), 1.42-1.34 (m, 1H), 0.95 (d, J = 6.7 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ (major) 212.0, 211.1, 138.8, 138.5, 130.1, 114.3, 51.0, 48.9, 47.6, 39.4, 39.3, 37.8, 35.0, 34.2, 30.22,

29.4, 28.7, 21.6; IR (thin film) 2955, 2924, 2914, 1706, 1436 cm^{-1}; HRMS (ESI) calculated for $C_{18}H_{26}O_2$ $[M+Na]^+$ 297.1830 found 297.1831.

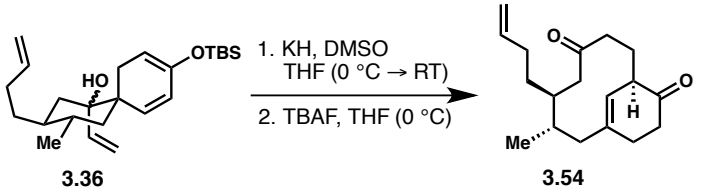
Skipped Enone 3.54



3.53 **3.54**

A solution of 18 mg (0.046 mmol) **3.53** in 0.8 mL THF was treated with 1.6 mL 1M aq. HCl. After stirring overnight, 6M aq. HCl was added until most starting material had disappeared and new polar spots appeared. After 14 h the reaction was quenched with sat. aq. $NaHCO_3$ and extracted with EtOAc. The organic layer was washed with brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude material was purified by column chromatography (hexanes→30:1→8:1→1:1 hexanes/EtOAc) to afford 3 mg (17%) recovered **3.53**, 6.5 mg (51%) **3.54** as a waxy solid and 2 mg of two unknown compounds. ^1H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) major δ 5.80 (ddt, J = 16.9, 10.2, 6.7, 1H), 5.21 (s, 1H), 5.00 (d, J = 17.2, 1H), 4.93 (d, J = 10.1, 1H), 2.93 (s, 1H), 2.69-2.47 (m, 5H), 2.38-2.33 (m, 1H), 2.25-1.87 (m, 9H), 1.63-1.55 (m, 1H), 1.53-1.47 (m, 1H), 1.42-1.34 (m, 1H), 0.95 (d, J = 6.7 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) major δ 212.0, 211.1, 138.8, 138.5, 130.1, 114.3, 51.0, 48.9, 47.6, 39.4, 39.3, 37.8, 35.0, 34.2, 30.22, 29.4, 28.7, 21.6; IR (thin film) 2955, 2924, 2914, 1706, 1436 cm^{-1}; HRMS (ESI) calculated for $C_{18}H_{26}O_2$ $[M+Na]^+$ 297.1830 found 297.1831.

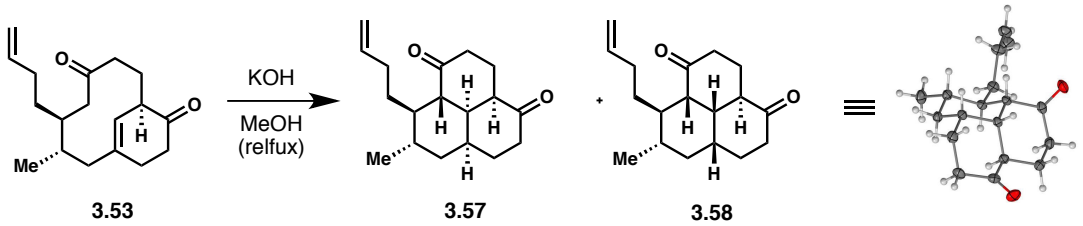
Skipped Enone 3.54



3.36 **3.54**

To a slurry of 152 mg (3.79 mmol) oil free potassium hydride in 7 mL THF was added 0.13 mL (1.8 mmol) DMSO at 0 °C. After stirring for 10 minutes, 363 mg (0.933 mmol) **3.36** in 3 mL THF was added at 0 °C. The ice bath was removed and stirring continued for 1 hour before being cooled back to 0 °C and quenched with 0.25 mL AcOH. The reaction was partioned between 45 mL third sat. $NaHCO_3$ and 50 mL EtOAc. The organic layer was washed twice with 10 mL water, then 10 mL brine, dried over $MgSO_4$, filtered and all volatiles removed to afford a crude residue. The crude material was dissolved in 8.5 mL THF, cooled to 0 °C and treated with 2.3 mL (2.3 mmol) 1 M TBAF/THF. After 10 minutes, 30 mL half sat. NH_4Cl and 40 mL EtOAc was added and the layers separated. The organic layer was washed with 10 mL water, 5 mL brine, dried over $MgSO_4$, filtered and volatiles removed in vacuo. The crude material was purified by column chromatography (4:1 hexanes/EtOAc) to afford 130 mg (51% over 2 steps, 4.6:1 dr) **3.54** as a white wax. ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) major δ 5.80 (ddt, J = 16.9, 10.2, 6.7, 1H), 5.21 (s, 1H), 5.00 (d, J = 17.2, 1H), 4.93 (d, J = 10.1, 1H), 2.93 (s, 1H), 2.69-2.47 (m, 5H), 2.38-2.33 (m, 1H), 2.25-1.87 (m, 9H), 1.63-1.55 (m, 1H), 1.53-1.47 (m, 1H), 1.42-1.34 (m, 1H), 0.95 (d, J = 6.7 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) major δ 212.0, 211.1, 138.8, 138.5, 130.1, 114.3, 51.0, 48.9, 47.6, 39.4, 39.3, 37.8, 35.0, 34.2, 30.22, 29.4, 28.7, 21.6; IR (thin film) 2955, 2924, 2914, 1706, 1436 cm^{-1}; HRMS (ESI) calculated for $C_{18}H_{26}O_2$ $[M+Na]^+$ 297.1830 found 297.1831.

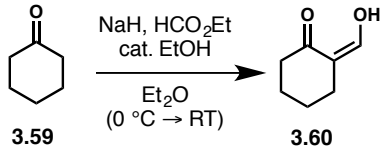
Perhydrophenalenediones 3.57 and 3.58



A 10 mL round bottom flask was charged with 42.0 mg (0.153 mmol) **3.53**, 2.0 mL (0.11 mmol) 0.054 M KOH/MeOH, fitted with a reflux condenser and heated at 75 °C under rigorous exclusion of oxygen. The reaction was cooled to room temperature after 3 hours, all volatiles removed in vacuo and the residue dissolved in 5 mL CH_2Cl_2. The organic layer was washed with 5 mL water, 4 mL half sat. NH_4Cl, 3 mL brine, then dried over $MgSO_4$, filtered and all volatiles removed in vacuo to afford a mixture of **3.57** and **3.58** in >80% crude yield. The crude oil purified by column chromatography (100:1→40:1 C_6H_6/EtOAc) to afford 12.1 mg (29%) **3.58** as a white solid which was recrystalized from CH_2Cl_2/pentane to afford colorless needles (mp = 111-113°C) and 15.1 mg (36%) **3.57** as a colorless oil. **3.57**: ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 5.74 (ddt, J = 16.9, 10.2, 6.6, 1H), 4.96 (d, J = 17.1, 1H), 4.89 (d, J = 10.2, 1H), 2.71-2.65 (m, 2H), 2.57 (dd, J = 13.3, 6.1, 1H), 2.51-2.46 (m, 2H), 2.40-2.30 (m, 3H), 2.21 (dd, J = 11.9, 4.7, 1H), 2.16-2.05 (m, 2H), 1.91-1.83 (m, 2H), 1.62-1.52 (m, 4H), 1.47-1.38 (m, 2H), 1.32 (td, J = 12.7, 3.6, 1H), 0.91 (d, J = 6.2, 3H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 213.6, 211.2, 139.3, 113.9, 51.6, 50.4, 48.7, 41.01, 41.00, 40.1, 39.0, 36.1, 30.1, 30.0, 28.5, 27.3, 27.0, 20.2; IR (thin film) 2927, 1710, 1443 cm^{-1}; HRMS (ESI) calculated for $C_{18}H_{26}O_2$ $[M+Na]^+$ 297.1830 found 297.1840. **3.58**: ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 5.75 (ddt, J = 16.9, 10.2, 6.7, 1H), 5.01 (d, J = 17.1, 1H), 4.93 (d, J = 10.1, 1H), 2.95 (t, J = 12.3, 1H), 2.56-2.40 (m, 3H), 2.34-2.27 (m, 3H), 2.17-2.08 (m, 2H), 1.94-1.85 (m, 3H), 1.77 (q, J = 12.4, 1H), 1.70-1.59 (m, 3H), 1.55-1.50 (m, 1H), 1.26-1.18 (m, 3H), 1.06 (d, J = 6.3, 3H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77

ppm) δ 212.9, 211.4, 138.7, 114.6, 56.7, 47.9, 43.8, 39.3, 37.7, 37.4, 34.9, 34.8, 34.7, 32.0, 28.1, 27.9, 26.2, 19.9; IR (thin film) 2921, 1709 cm^{-1}; HRMS (ESI) calculated for $C_{18}H_{26}O_2$ $[M+Na]^+$ 297.1830 found 297.1838.

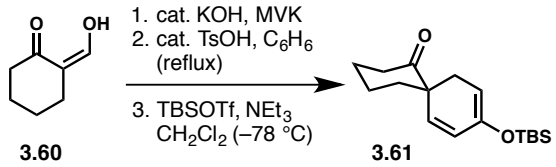
2-Hydroxymethylenecyclohexanone 3.60 [Adapted from the literature][56]



3.59 **3.60**

To an ice cooled solution of 1.11 g (48.3 mmol) Na metal cut and flattened in 100 mL Et_2O was added 4.6 mL (44.4 mmol) cyclohexanone, 5.3 mL (65.6 mmol) ethyl formate, and 0.2 mL EtOH. The ice bath was allowed to melt over the course of 2 hours, during which time the reaction turned into a thick orange mass. The contents were stirred for an additional 2 hours, quenched with 50 mL water, the phases seperated and the aqueous phase washed twice with 50 mL Et_2O. The aqueous layer was acidified with 10 mL 6 M HCl and extracted twice with 50 mL Et_2O. These organic layers were combined, washed with 10 mL water, 10 mL half sat. $NaHCO_3$, 10 mL brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The yellow oil was distilled (63-65 °C/3.5 mmHg) to afford 2.64 g (47%) **3.60** as a colorless liquid. The spectral data was identical to the literature.[57]

Silyloxydiene 3.61

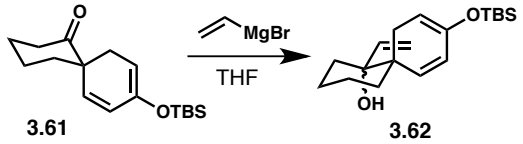


3.60 3.61

A flask was charged with 2.63 g (20.9 mmol) **3.60**, 4.3 mL (52.1 mmol) methyl vinyl ketone and 75 mg (1.3 mmol) powdered KOH at room temperature (exotherm). After stirring for 9 hours the contents were diluted with EtOAc, washed twice with sat. $NaHCO_3$, once with sat. NH_4Cl then brine. The organic layer was dried over $MgSO_4$, filtered and all volatiles removed in vacuo to afford a yellow oil. The crude oil was dissolved in 100 mL benzene and refluxed over Dean-Stark with 200 mg (1.0 mmol) p-TsOH•H_2O. After 3 hours the reaction was cooled to room temperature and washed thrice with sat. $NaHCO_3$, then brine. The organic layer was dried over $MgSO_4$ and all volatiles removed in vacuo. The dark oil was purified by column chromatography (6:1→4:1 hexanes/EtOAc) to afford 1.73 g of an impure product. To 1.65 g impure enone in 50 mL CH_2Cl_2 cooled to –78 °C was added 5.2 mL (37 mmol) NEt_3 and 2.1 mL (9.26 mmol) TBSOTf sequentially. After 3 hours the flask was removed from the cold bath, diluted with 25 mL pentane and poured into stirring sat. $NaHCO_3$. The flask was rinsed with an additional 50 mL pentane. The layers were separated and the organic layer washed once with sat. $NaHCO_3$, water and brine, then dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The yellow oil was purified by column (50:1→20:1 hexanes/EtOAc) to afford 1.96 g (32% over 3 steps) **3.61** as a colorless wax. ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 5.90 (d, J = 10.1, 1H), 5.73 (dd, J = 10.0, 2.1, 1H), 4.78-4.76 (m, 1H), 2.67 (dd, J = 17.0, 4.0, 1H), 2.51 (ddd, J = 14.0, 8.7, 5.4, 1H), 2.33 (ddd, J = 13.5, 7.8, 5.4, 1H), 2.19 (dd, J = 17.0, 5.4, 1H), 1.89-1.65 (m, 6H), 0.90 (s, 9H), 0.11 (s, 3H), 0.10 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 212.3, 144.9, 130.8, 126.6,

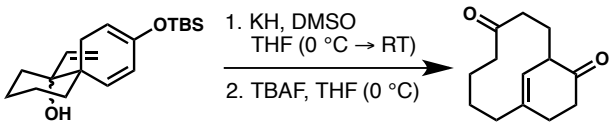
100.5, 49.8, 38.4, 36.8, 29.9, 27.8, 25.6, 20.8, 18.0, –4.58, –4.63; IR (thin film) 3046, 2931, 2894, 2857, 1708, 1653, 1254, 1225, 1212, 1182, 1127 cm^{-1}; HRMS (ESI) calculated for $C_{17}H_{28}O_2Si$ $[M+Na]^+$ 315.1756 found 315.1751.

Allylic Alcohols 3.62



To a solution of 1.92 g (6.56 mmol) **3.61** in 30 mL THF was added 27 mL (27 mmol) 1.0 M vinylmagnesium bromide/THF at 0 °C. After 10 minutes the cold bath was removed and the contents stirred for 6 hours. The reaction was quenched at 0 °C with 1 mL sat. NH_4Cl and 5 mL sat. $NaHCO_3$, then passed through a pad of Celite with 300 mL Et_2O. The organic layer was washed once with sat. $NaHCO_3$, water, brine then dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The oil was purified by column chromatography (20:1→10:1 hexanes/EtOAc) to afford 1.69 g (80%, 5.4:1 dr) **3.62** as a colorless oil. ^1H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) major δ 6.07 (dd, *J* = 17.2, 10.9, 1H), 5.81 (d, *J* = 10.3, 1H), 5.67 (dd, *J* = 10.3, 2.2, 1H), 5.26 (dd, *J* = 17.2, 1.5, 1H), 5.11 (dd, *J* = 10.9, 1.4, 1H), 4.75 (dt, *J* = 5.9, 2.9, 1H), 2.60 (dd, *J* = 17.2, 3.3, 1H), 1.96 (dd, *J* = 17.2, 6.1, 1H), 1.92-1.81 (m, 2H), 1.70-1.61 (m, 2H), 1.58-1.44 (m, 4H), 1.41 (s, 1H), 0.92 (s, 9H), 0.13 (m, 6H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) major δ 146.3, 144.3, 133.8, 126.0, 112.3, 101.4, 76.4, 41.1, 34.5, 32.6, 29.9, 25.7, 21.5, 21.1, 18.0, –4.49, –4.51; IR (thin film) 3482, 2931, 2858, 1654, 1252, 1223, 1190 cm^{-1}; HRMS (ESI) calculated for $C_{19}H_{32}O_2Si$ $[M+H]^+$ 321.2250 found 321.2239.

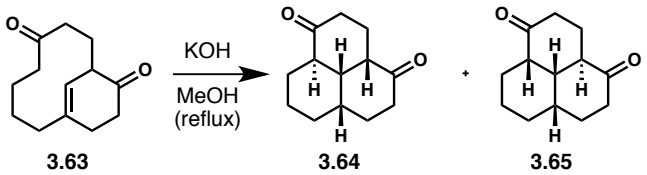
Skipped Enone 3.63



3.62 **3.63**

To slurry of 87 mg (2.2 mmol) oil free potassium hydride in 3 mL THF was added 0.09 mL (1.27 mmol) DMSO at 0 °C. After stirring for 10 minutes, 205 mg (0.639 mmol) **3.62** in 1.5 mL THF was added at 0 °C. The ice bath was removed and stirring continued for 1 hour before being cooled back to 0 °C and quenched with 0.15 mL AcOH. The reaction was partioned between 20 mL half sat. $NaHCO_3$ and 20 mL EtOAc. The layers were separated and the organic phase washed with 5 mL sat. $NaHCO_3$, 5 mL water, 5 mL brine, dried over $MgSO_4$, filtered and all volatiles removed. The crude material was dissolved in 6 mL THF, cooled to 0 °C and treated with 1.9 mL (1.9 mmol) 1 M TBAF/THF. After 10 minutes, 30 mL half sat. NH_4Cl and 20 mL EtOAc was added, the layers separated and the aqueous phase washed with 10 mL EtOAc. The organic layers were combined, washed with 10 mL water, 5 mL brine, dried over $MgSO_4$, filtered and volatiles removed in vacuo. The crude material was purified by column chromatography (5:1 hexanes/EtOAc) to afford 102 mg (77% over 2 steps) **3.63** as a white solid, which was recrystallized from Et_2O/hexanes to afford white needles (mp = 50-51°C). ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 5.25 (s, 1H), 2.94 (bs, 1H), 2.63-2.46 (m, 4H), 2.42-2.20 (m, 5H), 2.10-1.98 (m, 4H), 1.78-1.72 (m, 1H), 1.62-1.56 (m, 1H), 1.52-1.45 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 212.2, 212.1, 138.5, 127.8, 47.5, 43.8, 39.8, 39.3, 37.1, 29.5, 28.8, 24.7, 22.4; IR (thin film) 2926, 1704, 1437 cm^{-1}; HRMS (ESI) calculated for $C_{13}H_{18}O_2$ $[M+Na]^+$ 229.1205 found 229.1206.

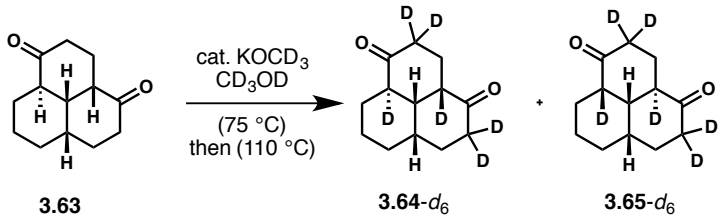
Tricycles 3.64 & 3.65



3.63 3.64 3.65

A 10 mL round bottom flask was charged with 41.6 mg (0.202 mmol) **3.63** and 2 mL (0.14 mmol) 0.07 M KOH/MeOH before being fitted with a reflux condenser and heated at 75 °C under rigorous exclusion of oxygen. The reaction was cooled to room temperature after 2 hours, partitioned between 5 mL EtOAc and 5 mL half sat. NH_4Cl. The aqueous layer was extracted twice with 3 mL EtOAc. The organic layers were combined, washed with 2 mL brine, dried over $MgSO_4$, filtered, the volatiles removed in vacuo and the crude oil purified by column chromatography (8:1→3:2 hexanes/EtOAc) to afford 25.6 mg (62%) **3.64** as a white solid, which was recrystallized from CH_2Cl_2/pentane to afford a single colorless prism (mp = 91-93 °C) and 10.2 mg (24%) **3.65** as a colorless oil. **3.64**: ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 2.70-2.63 (m, 2H), 2.545-2.47 (m, 3H), 2.42-2.39 (m, 1H), 2.34-2.31 (m, 1H), 2.26-2.15 (m, 3H), 1.93 (d, J = 13.8, 1H), 1.84-1.80 (m, 1H), 1.65-1.52 (m, 4H), 1.46-1.36 (m, 1H), 1.28-1.20 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 212.6, 211.2, 49.7, 48.1, 46.3, 41.0, 38.4, 35.8, 30.1, 26.7, 25.4, 25.3, 19.7; IR (thin film) 2917, 2848, 1709 cm^{-1}; HRMS (ESI) calculated for $C_{13}H_{18}O_2$ $[M+Na]^+$ 229.1205 found 229.1206. **3.65**: ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 2.93 (t, J = 12.3, 1H), 2.57-2.42 (m, 3H), 2.35-2.27 (m, 3H), 2.17 (dt, J = 12.7, 4.0, 1H), 2.01 (dt, J = 13.2, 2.9, 1H), 1.96-1.86 (m, 3H), 1.79 (dt, J = 12.8, 3.2, 1H), 1.70-1.57 (m, 4H), 1.51-1.42 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 213.0, 211.6, 52.8, 46.2, 43.1, 37.4, 36.9, 34.6, 32.4, 25.4, 25.2, 25.0, 24.6; IR (thin film) 2927, 2860, 1706 cm^{-1}; HRMS (ESI) calculated for $C_{13}H_{18}O_2$ $[M+Na]^+$ 229.1205 found 229.1206.

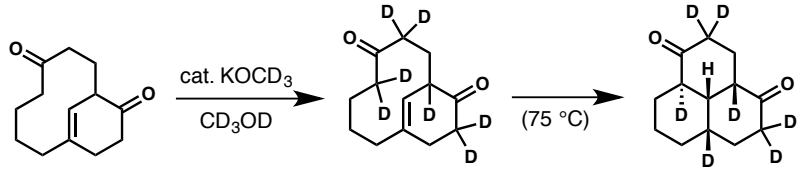
Deuteration Experiments on 3.64



3.63 **3.64**-d_6 **3.65**-d_6

A J-Young tube was charged with a solution of 6.0 mg (0.029 mmol) **3.64** in 0.6 mL CD_3OD and analyzed by ^1H, ^{13}C and DEPT-Q NMR. Then 0.05 mL (0.02 mmol) 0.4 M $KOCD_3/DOCD_3$ (prepared from potassium hydride and CD_3OD in toluene, followed by removal of all volatiles and washing with pentane) was added and placed in an oil bath preheated to 75 °C and reacted for 2 hours. Analysis was performed by ^1H and ^{13}C NMR; **3.64**-d_6 was observed. After 4 days at 110 °C a ~2:1 mixture **3.64**-d_6 and **3.65**-d_6 was observed by ^{13}C NMR.

Deuteration Experiments on 3.63



3.63 **3.63**-d_7 **3.64**-d_7

A J-Young tube was charged with a solution of 17.0 mg (0.0824 mmol) **3.63** in 0.6 mL CD_3OD and analyzed by ^1H, ^{13}C and DEPT-Q NMR. Then 0.05 mL (0.055 mmol) 1.1 M $KOCD_3/DOCD_3$ (prepared from potassium hydride and CD_3OD in toluene, followed by removal of all volatiles and washing with pentane) was added and sonicated for a half hour and analyzed by ^1H and ^{13}C NMR; **3.63**-d_7 was observed. The reaction was quenched with 0.1 mL CD_3CO_2D, diluted with 3 mL water and extracted thrice with 3 mL Et_2O. The organic layers were combined, washed with 1 mL water, 1 mL brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The residue was taken up in 0.6 mL CD_3OD and treated with with 0.05 mL (0.055 mmol)

$KOCD_3/DOCD_3$ and the NMR tube placed in an oil bath preheated to 75 °C and reacted for 2 hours. Analysis was performed by ^1H and ^{13}C NMR; **3.64**-d_7 was observed.

3.9 References and Notes

(1) Flemming, I. *Pericyclic Reactions*, 1st ed.; Oxford University Press, 1998.

(2) Paquette, L. A. *Synlett* **1990**, 67.

(3) Wilson, S. R. *Org. React.* **1993**, *43*, 93.

(4) Paquette, L. A. *Tetrahedron* **1997**, *53*, 13971.

(5) Swaminathan, S. *J. Indian Chem. Soc.* **1984**, *61*, 99.

(6) Swaminathan, S.; John, J. P.; Ramachandran, S. *Tetrahedron Lett.* **1962**, *3*, 729.

(7) Berson, J. A.; Jones, M. *J. Am. Chem. Soc.* **1964**, *86*, 5019.

(8) Evans, D. A.; Golob, A. M. *J. Am. Chem. Soc.* **1975**, *97*, 4765.

(9) Swaminathan, S.; Srinivasan, K. G.; Vankataramani, P. S. *Tetrahedron* **1970**, *26*, 1453.

(10) Chanddrasekaren, S.; Vankataramani, P. S.; Srinivasen, K. G. . S. S. *Tetrahedron Lett.* **1973**, *14*, 991.

(11) Uma, R.; Swaminathan, S.; Rajagopalan, K. *Tetrahedron Lett.* **1984**, *25*, 5825.

(12) An additional compound was isolated. Its structure was not conclusively assigned, but the proposed structure would have arisen via a [1, 3] rearrangement. .

(13) Tice, C. M.; Heathcock, C. H. *J. Org. Chem.* **1981**, *46*, 9.

(14) Rao, C. S. S.; Kumar, G.; Rajagopalan, K.; Swaminathan, S. *Tetrahedron* **1982**, *38*, 2195.

(15) Shanmugam, P.; Devan, B.; Srinivasan, R.; Rajagopalan, K. *Tetrahedron* **1997**, *53*, 12637.

(16) Ravikumar, V. T.; Rajagopalan, K.; Swaminathan, S. *Tetrahedron Lett.* **1985**, *26*, 6137.

(17) Roosen, P. C.; Vanderwal, C. D. *Org. Lett.* **2014**, *16*, 4368.

(18) Corey, E. J.; Magriotis, P. A. *J. Am. Chem. Soc.* **1987**, *109*, 287.

(19) Dave, V.; Whitehurst, J. S. *J. Chem. Soc. Perkin I* **1973**, 393.

(20) Eaton, P. E.; Jobe, P. G. *Synthesis* **1983**, 796.

(21) Fairweather, K. A.; Mander, L. N. *Org. Lett.* **2006**, *8*, 3395.

(22) Miyaoka, H.; Okubo, Y.; Muroi, M.; Mitome, H.; Kawashima, E. *Chem. Lett.* **2011**, *40*, 246.

(23) Leyendecker, F.; Jesser, F. *Tetrahedron Lett.* **1980**, *21*, 1311.

(24) Cook, B. W.; Miller, R. G. J.; Todd, P. F. *J. Organomet. Chem.* **1969**, *19*, 421.

(25) Woodward, S. *Chem. Soc. Rev.* **2000**, *29*, 393.

(26) Posner, G. H.; Whitten, C. E. *Tetrahedron Lett.* **1973**, *14*, 1815.

(27) Posner, G. H.; Whitten, C. E.; Sterling, J. J. *J. Am. Chem. Soc.* **1973**, *95*, 7788.

(28) Bertz, S. H.; Eriksson, M.; Miao, G.; Snyder, J. P. *J. Am. Chem. Soc.* **1996**, *118*, 10906.

(29) Tsuda, T.; Yazawa, T.; Watanabe, K.; Fujii, T.; Saegusa, T. *J. Org. Chem.* **1981**, *46*, 192.

(30) Bluthe, N.; Malacria, M.; Gore, J. *Tetrahedron Lett.* **1983**, *24*, 1157.

(31) Bluthe, N.; Malacria, M.; Gore, J. *Tetrahedron* **1984**, *40*, 3277.

(32) Bluthe, N.; Malacria, M.; Gore, J. *Tetrahedron Lett.* **1982**, *23*, 4263.

(33) Prestwich, G. D.; Solheim, B. A.; Clardy, J.; Pilkiewicz, F. G.; Miura, L.; Tanis, S. P.; Nakanishi, K. *J. Am. Chem. Soc.* **1977**, *99*, 8082.

(34) Schubert, M.; Metz, P. *Angew. Chemie Int. Ed.* **2011**, *50*, 2954.

(35) Anagnostaki, E. E.; Zografos, A. L. *Org. Lett.* **2013**, *15*, 152.

(36) Barriault, L.; Deon, D. H. *Org. Lett.* **2001**, *3*, 1925.

(37) Dillen, J. L. M. *J. Org. Chem.* **1984**, *49*, 3800.

(38) Julia, S. A.; Eschenmoser, A.; Heusser, H.; Tarköy, N. *Helv. Chim. Acta* **1953**, *36*, 1885.

(39) Kuo, F.; Fuchs, P. L. *Synth. Commun.* **1986**, *16*, 1745.

(40) Numbering matches the isocycloamphilectane scaffold, i.e. 7, 20-diisocyanoadociane.

(41) Berrue, F.; Kerr, R. G. *Nat. Prod. Rep.* **2009**, *26*, 681.

(42) Heckrodt, T. J.; Mulzer, J. *Top. Curr. Chem.* **2005**, *244*, 1.

(43) Newton, C. G.; Sherburn, M. S. *Nat. Prod. Rep.* **2015**, *32*, 865.

(44) Newton, C. G.; Drew, S. L.; Lawrence, A. L.; Willis, A. C.; Paddon-Row, M. N.; Sherburn, M. S. *Nat. Chem.* **2015**, *7*, 82.

(45) During the preparation of this dissertation a report on the synthesis of various amphilectane and serrulatane diterpenoids described the synthetic divergence to pseudopterosins aglycons of type **3.70**, **3.71** and **3.72** based on an unselective cyclization to both C1 epimers: Yu, X.; Su, F.; Liu, C.; Yuan, H.; Zhao, S.; Zhou, Z.; Quan, T.; Luo, T. *J. Am. Chem. Soc.* **2016**, *138*, 6261.

(46) Numbering matches pseudopterosin structures.

(47) Yadav, J. S.; Bhasker, E. V.; Srihari, P. *Tetrahedron* **2010**, *66*, 1997.

(48) Corey, E. J.; Carpino, P. *J. Am. Chem. Soc.* **1989**, *111*, 5472.

(49) Kocienski, P. J.; Pontiroli, A.; Qun, L. *J. Chem. Soc. Perkin Trans. 1* **2001**, 2356.

(50) Arp, F. O.; Fu, G. C. *J. Am. Chem. Soc.* **2005**, *127*, 10482.

(51) Do, H.-Q.; Chandrashekar, E. R. R.; Fu, G. C. *J. Am. Chem. Soc.* **2013**, *135*, 16288.

(52) Love, B. E.; Jones, E. G. *J. Org. Chem.* **1999**, *64*, 3755.

(53) Draper, A. L.; Heilman, W. J.; Schaefer, W. E.; Shine, H. J.; Shoolery, J. N. *J. Org. Chem.* **1962**, *27*, 2727.

(54) Hoke, M. E.; Brescia, M.-R.; Bogaczyk, S.; DeShong, P.; King, B. W.; Crimmins, M. T. *J. Org. Chem.* **2002**, *67*, 327.

(55) Beckwith, A. L. J.; Phillipou, G. *Aust. J. Chem.* **1976**, *29*, 1277.

(56) Ainsworth, C. *Org. Synth.* **1959**, *39*, 27.

(57) Wu, Z.; Li, Y.; Cai, Y.; Yuan, J.; Yuan, C. *Bioorg. Med. Chem. Lett.* **2013**, *23*, 4903.

CHAPTER 4:

EXPLORING A PHENANTHRENONE REDUCTION APPROACH TO 7,20-DIISOCYANOADOCIANE

4.1 Introduction

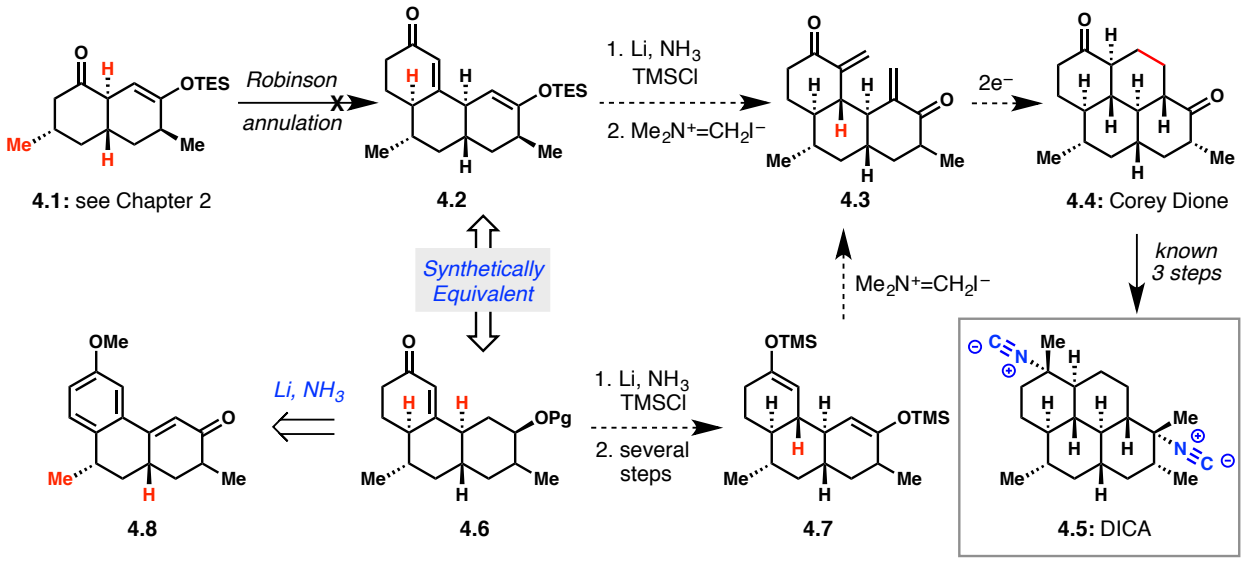
The goal of efficient access to 7,20-diisocyanoadociane (**4.5**, DICA) continued to drive the project. An allylic oxidation/hydrosilylation/Robinson annulation design, which intended to establish all the functionality for succinct ring closure, was not successfully executed (Scheme 4.1, see Chapter 2 for more detail), but became the foundation for a new idea. Several rounds of evolution were realized during the following phenanthrenone-based Birch reduction approach towards DICA. A study on the Birch reduction of phenanthrenone substrates, with particular attention paid to stereochemistry is described.

4.2 Entry into a Phenanthrenone Reduction Route

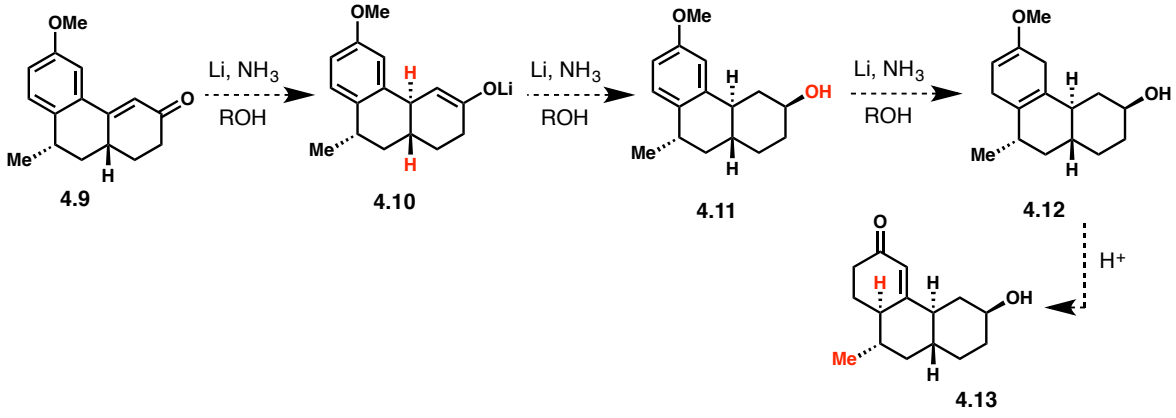
Robinson annulation onto decalone **4.1** into tricyclic enone **4.2** was intended to lead to bis-enone **4.3**. This bis-enone, upon two electron reduction,[1] would create Corey's dione **4.4**, a direct precursor to DICA.[2] Problems executing the Robinson annulation led to a reevaluation of strategy. Tricyclic enone of the type **4.3** was still considered an attractive target, but the fragile triethylenoxysilane moiety needed replacing. Thus, the synthetically equivalent molecule **4.6**, bearing instead a protected alcohol, was considered. The same reductive coupling of bis-enone **4.3** to **4.4** was still intended as a final ring closure. Although the proposed elaboration of protected alcohol **4.6** to enoxysilane **4.7** would most likely require more steps than directly having the enoxysilane, as in **4.2**, this substrate opened up a highly attractive Birch reduction

approach from phenanthrenone **4.8**.

Scheme 4.1 Origin of the phenanthrenone reduction idea.



Scheme 4.2 Proposed reaction course for the Birch reduction of a phenanthrenone system relevant to DICA.

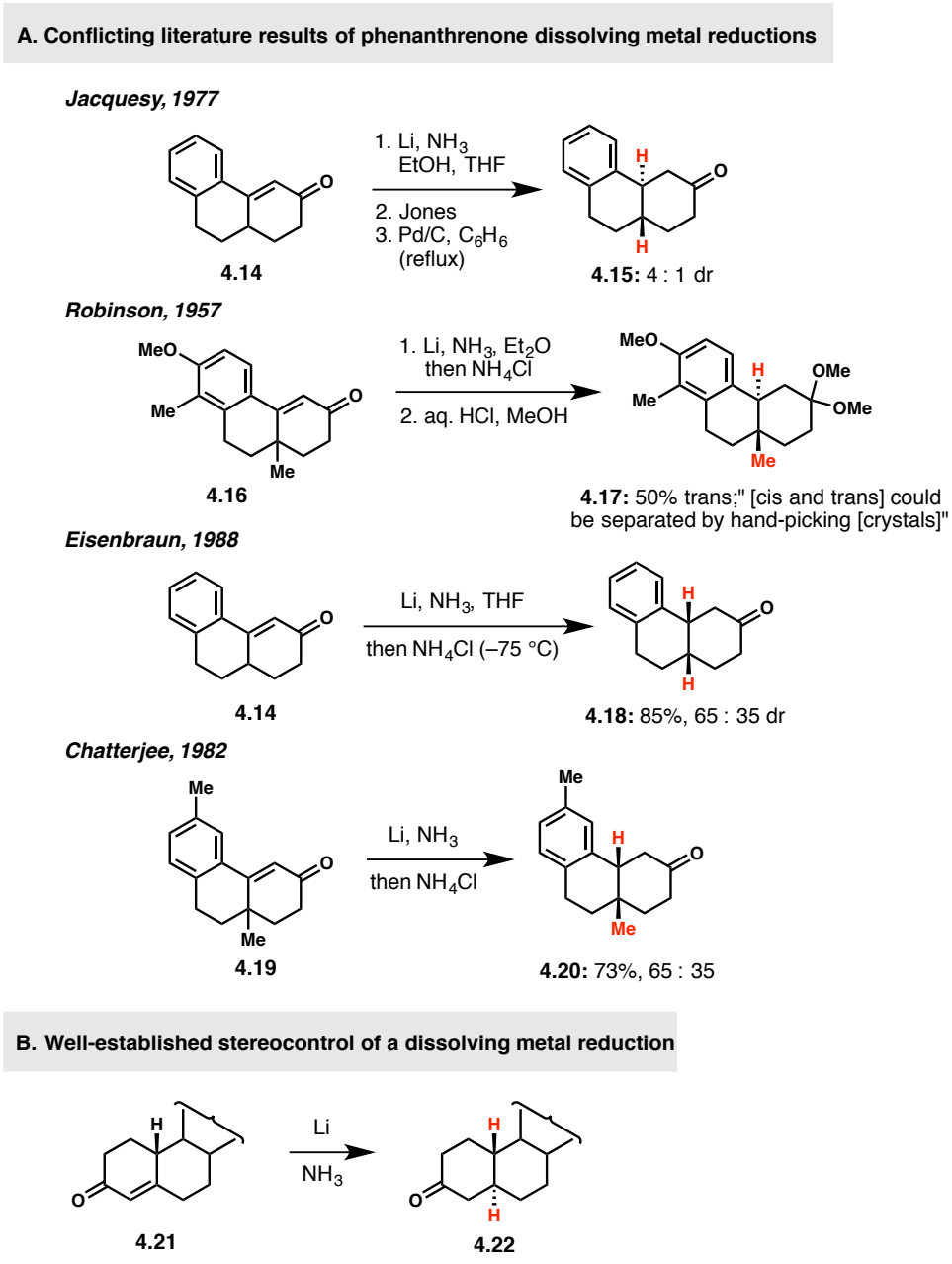


A first approach to the system **4.13** was designed around a dissolving metal reduction of phenanthrenone **4.9** (Scheme 4.2). Conjugated phenanthrenones such as **4.9** are readily prepared from a tetralone and an alkyl vinyl ketone via Robinson annulation. The phenanthrenone **4.9** has

within it, an enone and aromatic functionality, both of which can be reduced under dissolving metal conditions. With excess metal in ammonia and alcohol, the enone is predicted to reduce to enolate **4.10**.[3,4] Subsequent protonation and ketone reduction affords equatorial alcohol **4.11**.[5] The anisole moiety is then cleaved and isomerized to enone **4.13** in classic Birch reduction fashion.[6,7]

With the general course of the reaction rationalized, the issue of stereochemistry needed to be addressed. The literature revealed four conflicting reports on the stereochemical outcomes of conjugated phenanthrenone reductions with dissolving metals. Two reports of a phenanthrenone enone-reduction claim *trans*-selectivity,[8,9] while the other two claim a *cis*-selective reduction (Scheme 4.3A).[10,11] Either small differences in Li/NH_3 reduction conditions change the selectivity between *cis* and *trans*, or two groups are correct in their stereochemical assignment, while the other two are not. Interestingly, both Jacquesy[10] and Eisenbraun[8] reduce the identical, unsubstituted phenanthrenone **4.14** and reported different results under essentially identical conditions; one group claims to have performed a *trans*-reduction, the other group claims a *cis*-reduction. Support for the groups claiming a *trans*-reduction can be found in the reduction of octalone **4.21** to **4.22** or well precedented steroid A/B ring reductions both of which give excellent *trans*-selectivity (Scheme 4.3B).[3,12] Faced with these literature discrepancies, the best course forward was to evaluate the desired system on route to DICA and determine the stereochemistry independently.

Scheme 4.3 The stereochemical course of phenanthrenone Birch reductions.



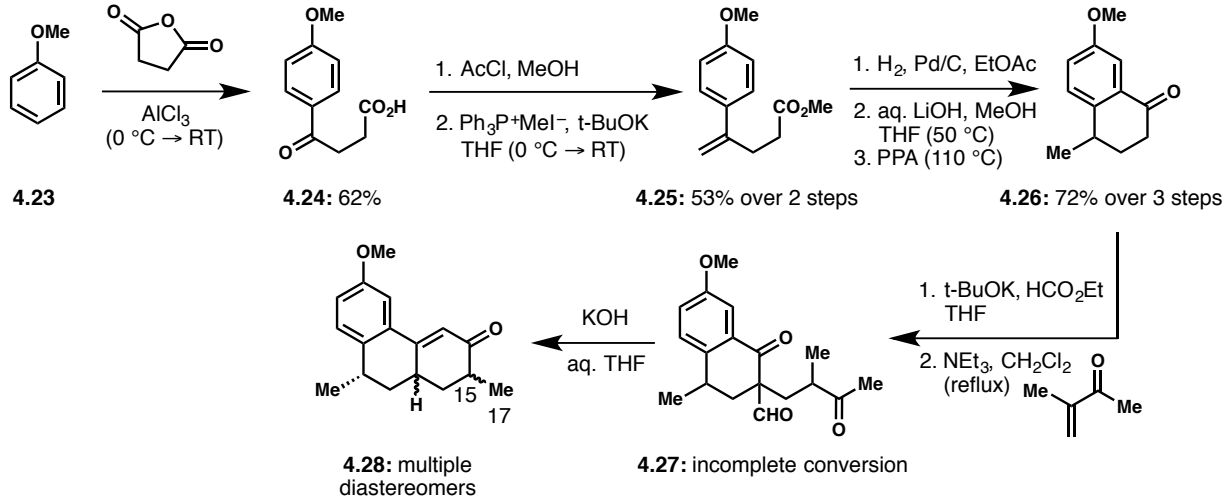
4.3 Results from a Phenanthrenone Reduction Approach

4.3.1 Phenanthrenone Synthesis and Confirmation of Basic Birch Reactivity

Phenanthrenones are typically accessed from a tetralone precursor, and the preparation of **4.28** was no different. Although shorter and more elegant syntheses of tetralone **4.26** could be

imagined, a literature report sufficed for exploratory chemistry.[13] Starting from anisole, a six-step sequence was completed to afford multi-gram quantities of tetralone **4.26** on a first pass (Scheme 4.4). A Robinson annulation of **4.26** with methyl isopropenyl ketone was implemented to generate the desired phenanthrenone bearing the required C17 methyl group.[14] Experimentally, the corresponding β-ketoaldehyde of **4.26** performed poorly in a conjugate addition with methyl isopropenyl ketone. Although incomplete conversion was observed, the crude product was treated with aqueous base to trigger the subsequent cyclization. Disappointingly, the obtained phenanthrenone **4.28** was isolated as a mixture of diastereomers, both at the ring fusion and at the C15 methyl-bearing stereogenic center. To better understand this system the C17 des-methyl analog of **4.28**, **4.29** was targeted (Scheme 4.5).

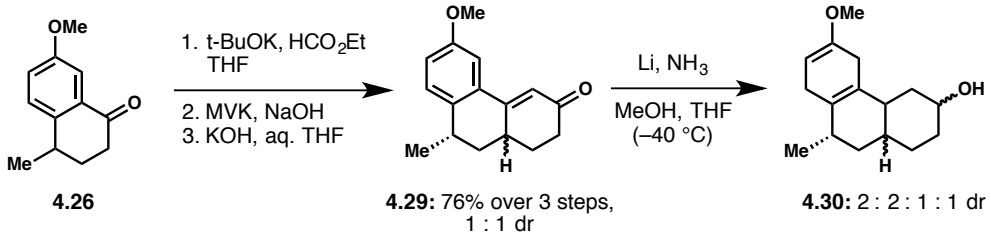
Scheme 4.4 A tetralone synthesis and first phenanthrenone derivative.



The Robinson annulation of **4.26** with methyl vinyl ketone performed better than with methyl isopropenyl ketone and generated phenanthrenone **4.29** in good yield; however, it too lacked stereocontrol (Scheme 4.5). Regardless, it was anticipated that the correct diastereomer could be separated at a later stage. Treating **4.29** with excess Li/NH_3 accomplished the desired reduction

to **4.30**. Therefore the proposed one-pot enone and aromatic reduction was successful! Although the desired reduction was accomplished, stereocontrol was problematic. The original 1 : 1 dr in **4.29** was further aggravated to a 2 : 2 : 1 : 1 mixture. This route could have been pursued further, but an approach more strongly emphasizing stereocontrol was prioritized.

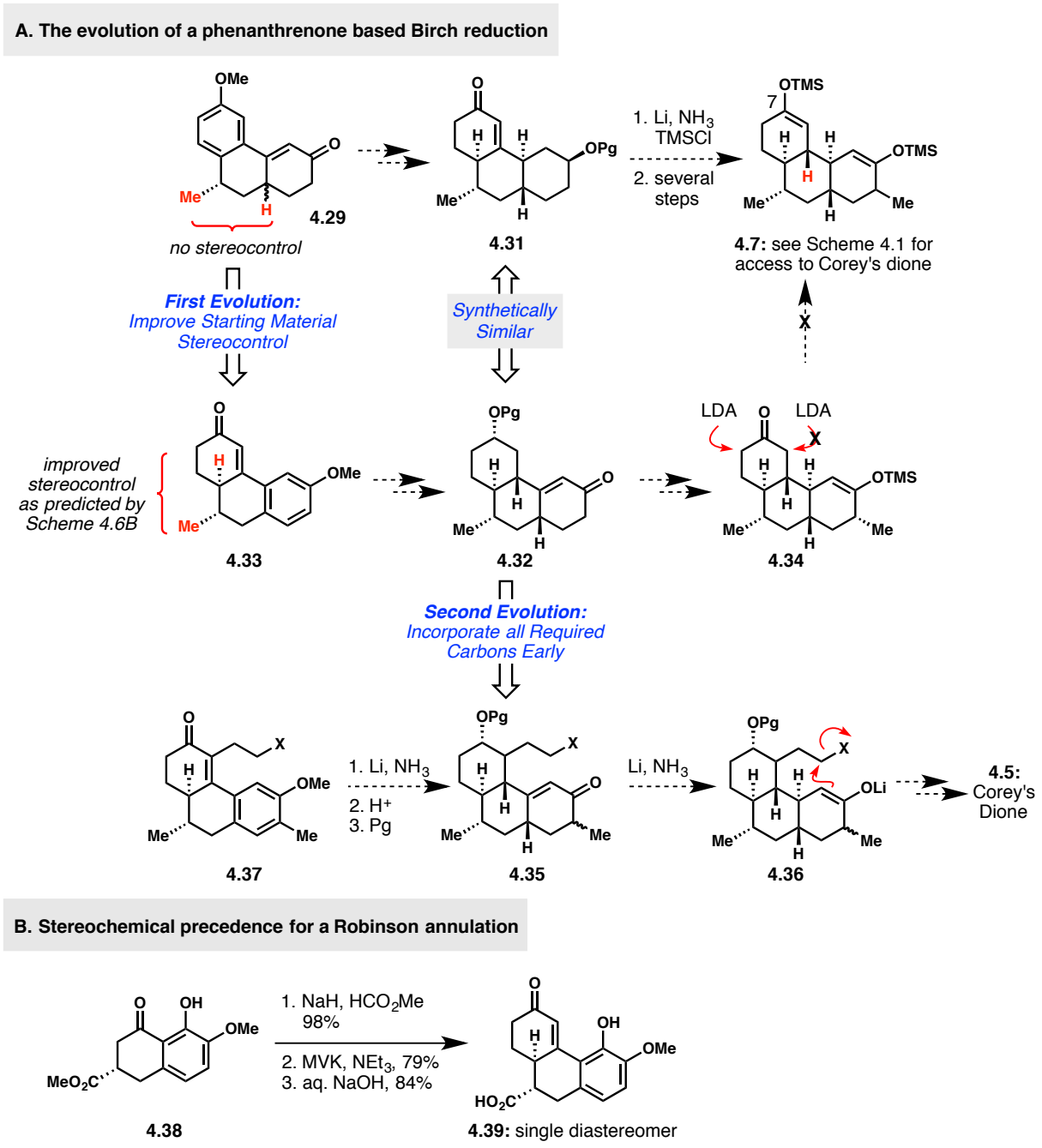
Scheme 4.5 A successful phenanthrenone Birch reduction.



4.26 **4.29:** 76% over 3 steps, 1 : 1 dr **4.30:** 2 : 2 : 1 : 1 dr

While stereocontrol in the synthesis of **4.30** was lacking, its reactivity to produce a structure of type **4.31** was not in doubt (Scheme 4.6A), but the poor diasterocontrol obtained by Robinson annulation and from the Birch reduction triggered reevaluation. Better control in the Robinson annulation was imagined if the two stereocenters were vicinal, as in **4.33**. Literature precedent supported this proposal as **4.39** could be prepared as a single diastereomer (Scheme 4.6B).[15] Subsequent Birch reduction of **4.33** would lead to intermediate **4.32**, a synthetically similar molecule to the originally targeted **4.31**. In a forward sense, however, cyclohexenone **4.34** was expected to be problematic. At a stage in which the C7 enoxysilane[14] would be installed, such as on **4.34**, correct regiochemical enolization would be unfavored, barring chiral base deprotonation.[16] This problem of selectivity could be addressed by changing the fourth ring closure to an alkylation proceeding through enolate **4.36**. This second evolution meant an elaborated vinyl ketone would be needed to generate **4.37** by Robinson annulation.

Scheme 4.6. A redesigned phenanthrenone Birch reduction route.

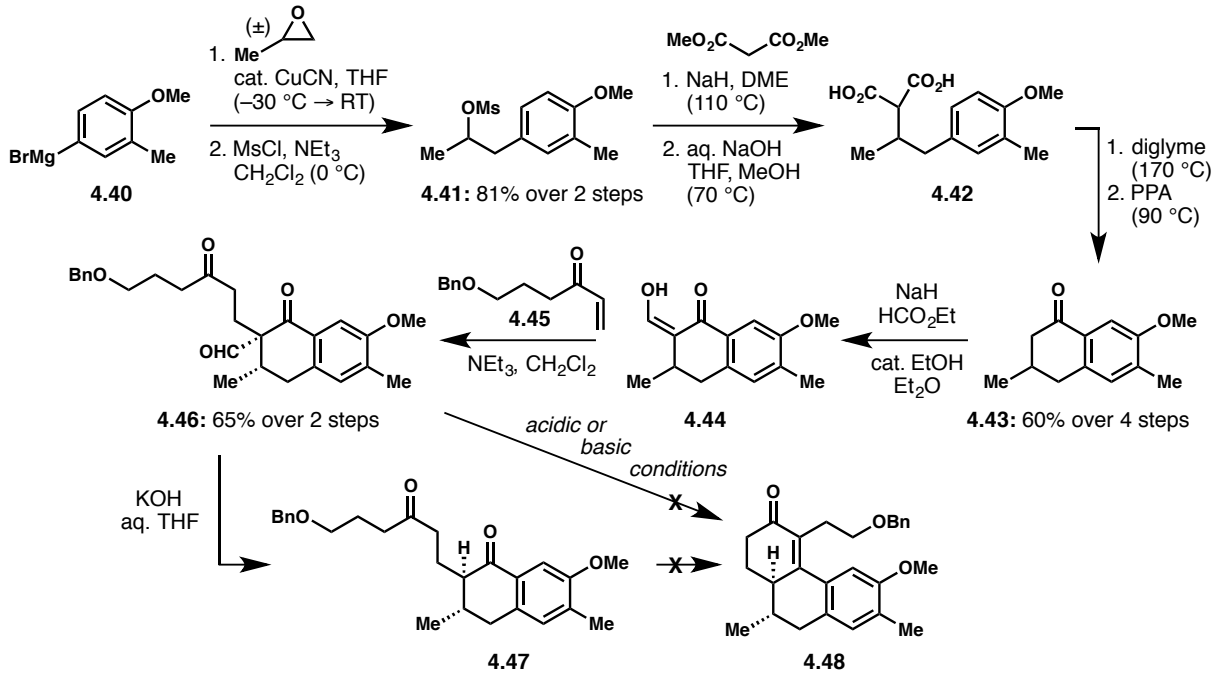


4.3.2 A Reworked Phenanthrenone Approach Emphasizing Stereocontrol

The synthesis of a phenanthrenone of the type **4.37** and evaluation of the subsequent Birch reduction became the next objective. A synthesis of its tetralone precursor was conceived

of de novo, and started by opening of propene oxide with aromatic Grignard reagent **4.40**, followed by mesylation (Scheme 4.7). A malonic ester synthesis and carboxylic acid cyclization of **4.42** to **4.30** required optimization, but eventually led to significant quantities of tetralone **4.43**. An asymmetric synthesis of tetralone **4.43** would simply require enantioenriched propylene oxide.[17] Formylation of **4.43** was complicated by aromatization if not monitored. Michael addition of **4.44** with **4.45** proceeded smoothly. Disappointingly the ring closing aldol condensation was problematic and cyclization was not observed. The only products were those of deformylation under basic conditions and recovered starting material.

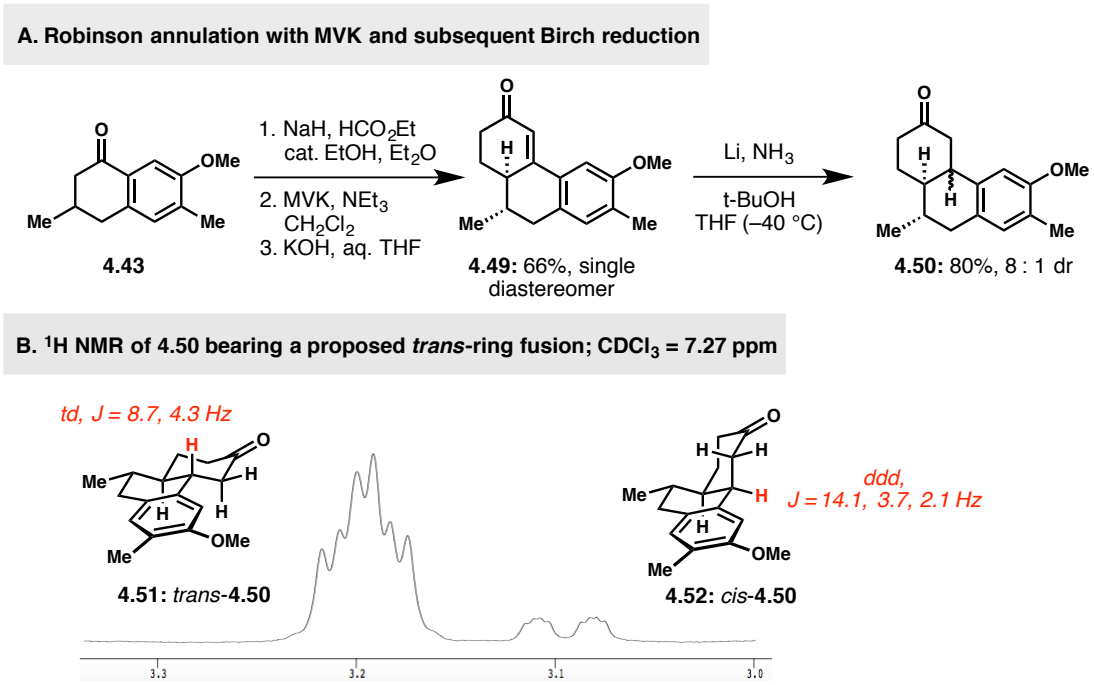
Scheme 4.7 First pass at the new phenanthrenone-based synthesis of DICA.



Although it was attractive to bring all carbons in early with vinyl ketone **4.45**, the problem of phenanthrenone reduction stereochemistry and reactivity still needed addressing. At this point, the elaborated **4.45** was replaced with methyl vinyl ketone, the product of which underwent the Robinson annulation efficiently to afford **4.49** (Scheme 4.8A). Birch reduction of

4.49 with Li/NH_3 in the presence of excess t-BuOH provided only reduction of the enone to ketone **4.50**; a curiosity when compared to the earlier reduction successes of **4.29** (Scheme 4.5). The advantage at this point was that the relative stereochemistry of enone reduction could be obtained. Analysis of the ^{1}H NMR determined that the major species in an 8 : 1 mixture of **4.50** bore the *trans*-ring junction (Scheme 4.8B).

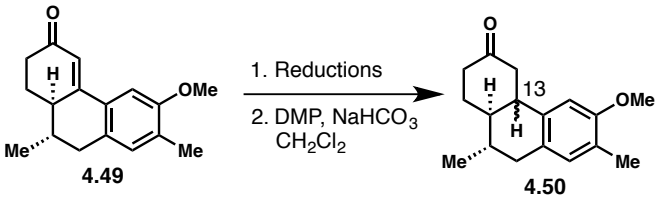
Scheme 4.8 A selective phenanthrenone reduction with Li/NH_3.



In stark contrast to the previously run Birch reduction (Scheme 4.5), several attempts at reducing the aromatic **4.49** were not successful. Even under the influence of a large excess of Li and t-BuOH, neither the ketone nor the aromatic was reduced. In addition to t-BuOH, isopropanol and ethanol were also screened as proton sources for attempted aromatic cleavage. Both ethanol and isopropanol reduced the ketone, but still did not reduce the aromatic. Phenanthrenone **4.49**'s limited solubility in THF, insolubility in diethyl ether and insolubility in ammonia made evaluating this reaction difficult. The lack of solubility may have also

contributed to the absence of reactivity. A further screen of Mg in methanol and hydrogenation were screened to possibly improve setting the C13 stereocenter, and unsurprisingly did not reduce the aromatic ring. The lack of aromatic reduction in **4.49** is difficult to explain because the literature contains many examples of Birch reductions of 1,2,4,5-tetrasubstituted anisoles; select examples are provided in equations 4.1-4.3.[18–20] The issue of difficult aromatic reductions has been addressed before, most notably by the procedures of Benkeser using alkylamine solvent.[21] These conditions have the added advantage of being performed above the boiling point of ammonia at –33 °C.[22]

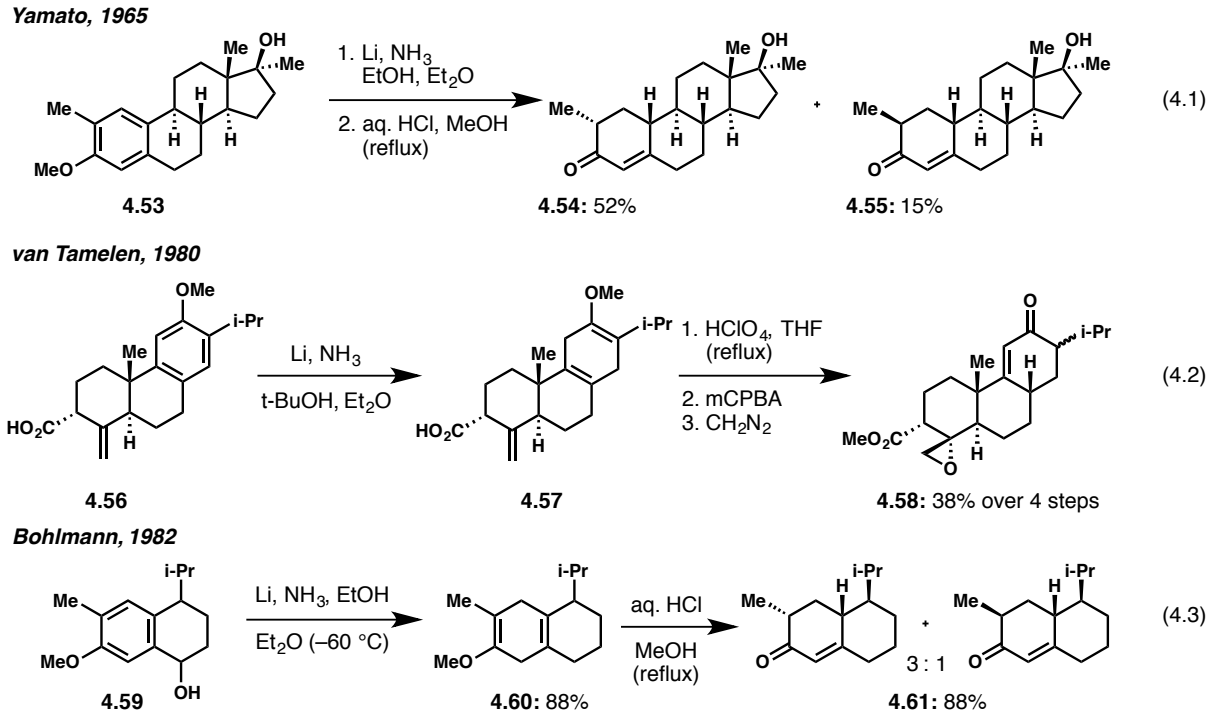
Table 4.1 Small screen of reduction conditions in attempting to fully reduce **4.49**.



4.49 **4.50**

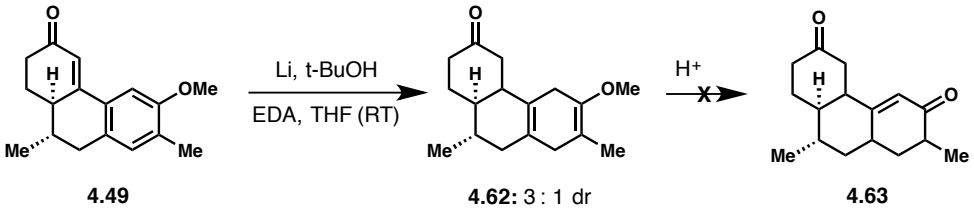
Entry	Reductions	4:51 *trans*[a]		4.52: *cis*[a]
1	Li, NH_3 with EtOH, i-PrOH or t-BuOH THF (–40 °C)	**variable**		
2	Mg, cat. $HgCl_2$, MeOH	**1.1**	:	**1**
3	H_2, Pd/C, EtOAc	**1**	:	**3**
4	H_2, PtO_2, EtOAc	**1**	:	**1.7**

[a] as proposed initally by NMR data (see Table 4.3 for more information)



Stronger and higher temperature reducing agents were evaluated for the recalcitrant reduction of **4.49**. Classic Benkeser reductions in methylamine and ethylamine were not pursued because these controlled substances are inconvenient to obtain. Alternative Benkeser reductions were tried instead. Using Ca in ethylene diamine, propylamine, and THF provided only starting material.[23] Li or Na in neat HMPA caused decomposition of material.[24] Modified ethylenediamine based conditions eventually were successful in reducing the aromatic ring (Scheme 4.9). Several literature reports include propylamine as a solvent; however, it was found not necessary for effective reduction.[25,26] Although the aromatic moiety was reduced, the ketone was not! Presumably, ethylenediamine condensed either onto the enone or the transiently generated ketone, thereby masking the carbonyl reduction.

Scheme 4.9 Successful ethylene diamine based reduction of phenanthrenone **4.49**.



4.49 **4.62:** 3 : 1 dr **4.63**

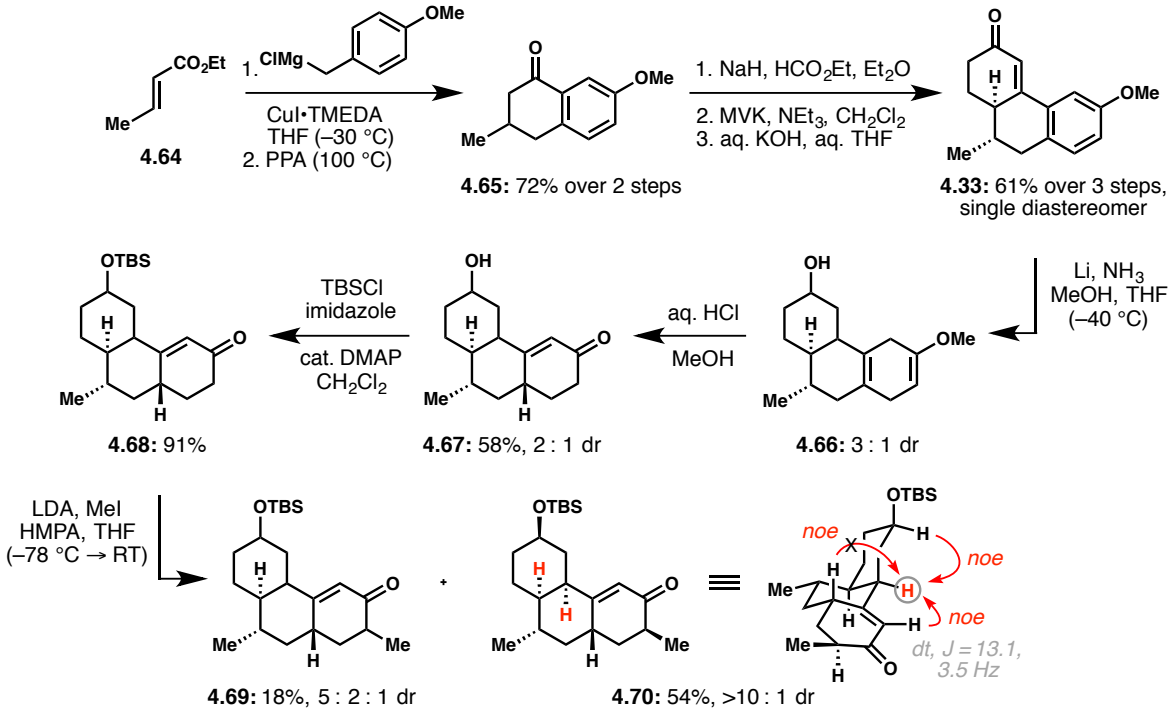
Having successfully reduced the aromatic, the next step was hydrolysis and isomerization to the conjugated enone **4.63** (Scheme 4.9). Standard conditions of aqueous HCl in methanol failed. Hydrolysis of the vinyl ether to the corresponding ketone was achieved with mild acid, but attempts at isomerizing the skipped enone into conjugation under acid or basic conditions were once again unsuccessful. Complexity in the lack of reduction of the aromatic under standard Birch conditions, problems with low mass recovery in the ethylene diamine-based reductions, and difficulties in enone isomerization were all attributed to the C17 methyl group.[14] An approach that installs this methyl later was therefore pursued.

4.3.3 Identifying a Conflicting Stereochemical Outcome

To examine whether the singular C17 methyl group may inhibit aromatic reduction, the des-methyl analog of **4.49** was prepared (Scheme 4.10). The TMEDA-ligated p-methoxybenzylcopper reagent was added to ethyl crotonate and the corresponding ester treated with polyphosphoric acid to generate tetralone **4.65** via a slightly modified literature procedure.[27] Robinson annulation with methyl vinyl ketone generated **4.33**, and in analogy to **4.49**, also as a single diastereomer. Treatment of this phenanthrenone with excess Li/NH_3, in the presence of excess methanol in THF, cleanly reduced the system down to alcohol **4.66**. Although the hydrolysis and enone isomerization to **4.67** was difficult, it could be accomplished with aqueous acid while carefully monitoring by TLC. The obtained 2 : 1 mixture of diastereomers was

silylated and then methylated via the cross-conjugated dienolate. Two sets of fractions were separated, one consisted of a mixture of diastereomers and assigned as structure **4.69** and one was highly enriched in the major diastereomer. As judged by NMR analysis, the major diastereomer was consistent with structure **4.70**, bearing a *cis*-ring fusion. This ring fusion came from reduction of phenanthrenone **4.33** using Li/NH_3 and is in direct contradiction to the previously proposed stereochemistry of reduction (Scheme 4.8)! It is impossible for the assignment of both **4.51** and **4.70** to be correct. This discrepancy required further clarification.

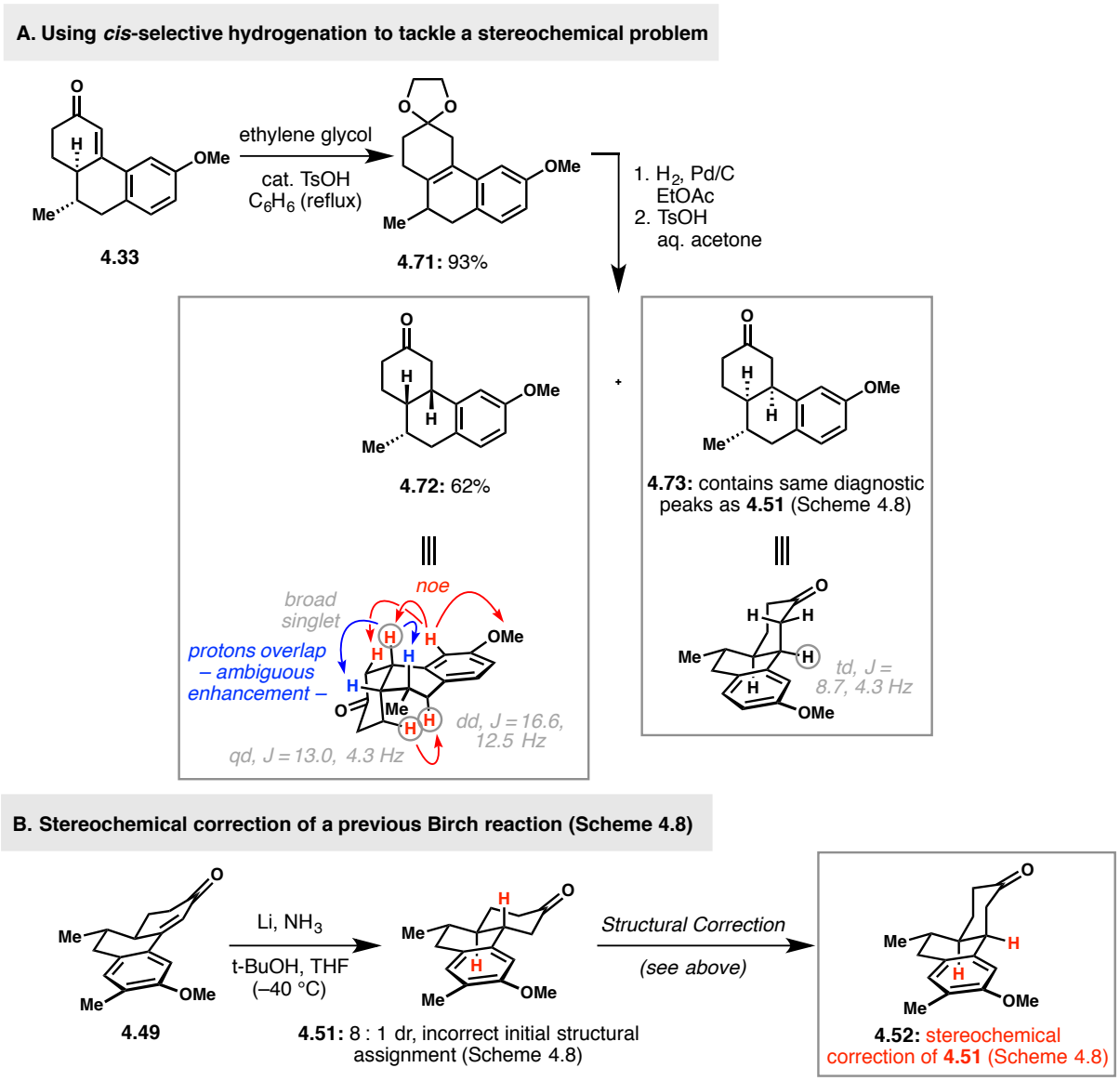
Scheme 4.10 A des-methyl phenanthrenone undergoes successful Birch reduction.



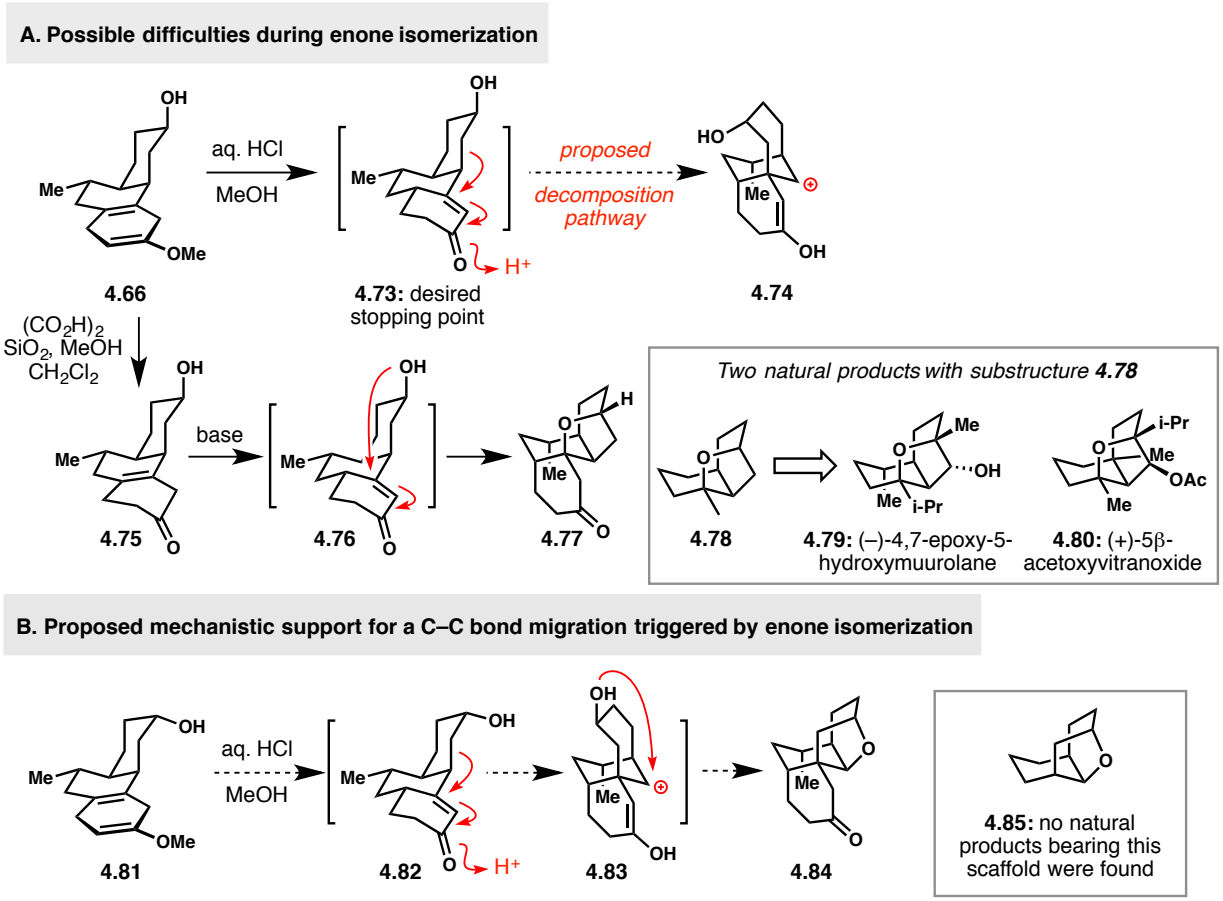
4.3.4 Settling the Phenanthrenone Birch Reduction Stereochemical Conundrum

An empirically guided approach to determining the stereochemical course of phenanthrenone Birch reductions was sought. Phenanthrenone **4.33** was chosen as the substrate to evaluate since large quantities were available at the time and **4.49** was not. The C17 methyl[14] group was considered too distal to be considered relevant to the herein described experiments. Ketalization of **4.33** migrated the double bond out of its original position to afford **4.71** (Scheme 4.11A). Hydrogenation of alkene **4.71** over Pd/C provided a 4 : 1 mixture of diastereomers. Since surface catalysts strongly enforce *cis*-reduction, the two diastereomers obtained arose from hydrogen delivery to the face opposite of the methyl and to the same face as the methyl. Acidic ketal deprotection yielded two separable ketones. The major constituent was identified as structure **4.72**. The minor isomer was therefore structure **4.73**. This material had an almost identical ^{1}H NMR spectrum to the major product obtained from Birch reduction of **4.49** (Scheme 4.5). The major isomer upon reduction of **4.49** was thus corrected to **4.52** (Scheme 4.11B).

Scheme 4.11 Alkene hydrogenation to determine the stereochemical course of the Birch reduction in conjugated phenanthrenones.



Scheme 4.12 Proposed difficulties isomerizing a skipped enone into conjugation.



The stereochemical correction of **4.51** to **4.52** allows for a reflection on the conflicting literature reports (Scheme 4.3A). Based on the results described, the stereochemistry of all four reports is highly likely *cis*. Caution should be applied when using the Jacquesy[8] and Robinson[9] examples as precedent since their stereochemical assignment is questionable. In addition, the observed *cis* stereochemistry explains the difficulty experienced in isomerizing enones **4.62** and **4.66** into conjugation (Scheme 4.9 and 4.10). For representative example **4.66**, under acidic conditions, carbonyl protononation may cause C–C bond migration to cation **4.74**, an intermediate with the ability to decompose further (Scheme 4.12A). The migrating bond has good overlap with the enone, and could explain why careful monitoring of the isomerization was essential. A probe for this decomposition pathway could shed light onto its existence. If

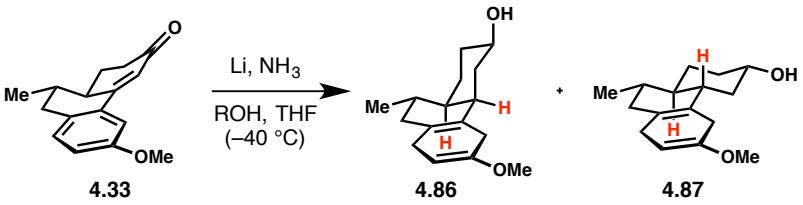
migration of the C–C bond is occurring, then the alcohol epimer **4.81** may possibly trap the formed cation and generate tetrahydrofuran **4.84** (Scheme 4.12B). Basic isomerization attempts of **4.75**, which was generated with mild acid from **4.66**, afforded among other compounds, a ketone containing product. Isolation and full characterization was not performed, but NMR of the crude reaction mixture and TLC analysis suggests **4.77** as a possibility. If this tetrahydrofuran formation is occurring, then an oxy-Michael reaction could be envisioned for preparing natural products **4.79**[28] and **4.80**.[29]

4.4 Phenanthrenone Birch Reduction Optimization Attempts

Since the relative stereochemistry of phenanthrenone Birch reductions has now been established as *cis*, altering the selectivity was attempted. An inspiration for this possibility was that the reduction of **4.49** with Li/NH_3 and t-BuOH provided **4.50** in 8 : 1 dr, while the literature examples using EtOH provided 2-3 : 1 *cis*/*trans* selectivity.

Using phenanthrenone **4.33**, a small screen of alcoholic additives displayed a clear trend between alcohol sterics and *cis*/*trans* selectivity upon reduction. While methanol provided a 3 : 1 mixture of *cis*/*trans*, the selectivity for *cis*-reduction increased in correlation with alcohol bulk up to 8 : 1 *cis*/*trans* with t-BuOH (Table 4.2 and 4.3). This trend can be rationalized by comparing both the *cis*- and *trans*-protonation states (Figure 4.1). Although *trans*-reduction of enones is electronically favored for dissolving metal reductions,[3,4] it is likely that the allylic strain present in *trans*-protonation state **4.88** actually switches inherent favorability to the *cis*-protonation state **4.89** (Figure 4.1A). An additional contribution is that the *cis*-face of the enone is sterically more available (Figure 4.1B). Bulky alcohols push an already *cis*-selective reduction further to **4.91** because of a steric preference to approach from the more open enone face.

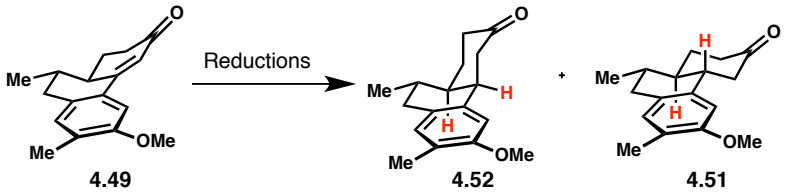
Table 4.2 Impact of alcohol additive on stereochemistry.



Entry	ROH	4.86: cis[a]	:	4.87: trans[a]
1	MeOH	**3**	:	**1**
2	EtOH	**4**	:	**1**
3	i-PrOH[b]	**5**	:	**1**

[a] ratios obtained by crude ^{1}H NMR [b] MeOH quench

Table 4.3 Correcting the stereochemical outcome described in Table 4.1.



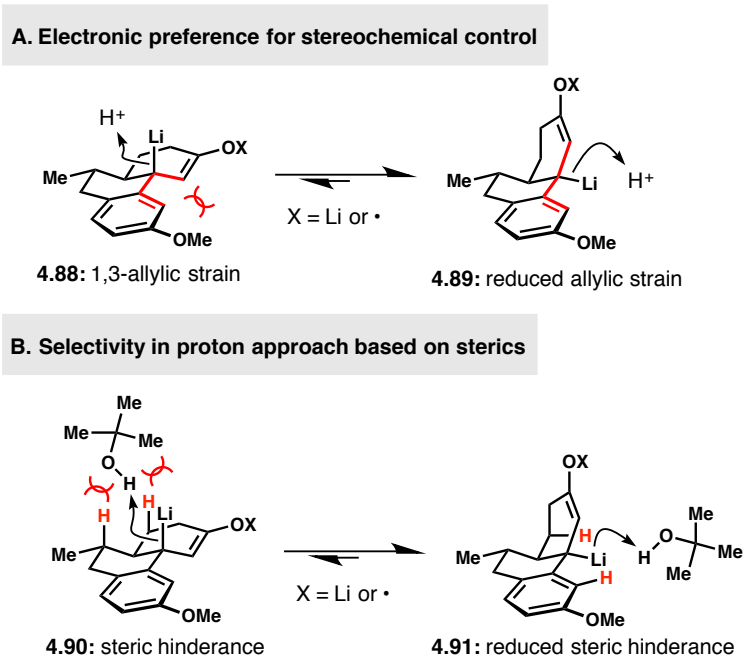
Entry	Reductions	4.52: cis[a]	:	4.51: trans[a]
1	Li, NH_3, t-BuOH, THF (–40 °C) (see Scheme 4.8)	**8**	:	**1**
2	Mg, cat. $HgCl_2$, MeOH[b]	**1.1**	:	**1**
3	H_2, Pd/C, EtOAc[b]	**1**	:	**3**
4	H_2, PtO_2, EtOAc[b]	**1**	:	**1.7**

[a] ratios obtained by crude ^{1}H NMR [b] 2. DMP, $NaHCO_3$, CH_2Cl_2

Because of the correction in stereochemical assignment (Scheme 4.3.4), the reduction attempts on **4.49**, initially presented in Table 4.1, also require correcting (Table 4.3). Curiously, Mg in methanol provided the best *trans*-selectivity via a single electron reduction pathway providing an almost 1 : 1 *cis*/*trans* ratio. Hydrogenation catalysts afford the *trans*-isomer as the major product. These hydrogenation conditions were not pursued further towards DICA because of the relatively low selectivity in both enone reduction and subsequent ketone reduction and requirement for an additional aromatic reduction. The ideal of reducing an aromatic substrate in

a single step was still a main objective.

Figure 4.1 Rationalizing the phenanthrenone reduction stereochemistry.



Although it was discouraging that changing alcohol additives in these Birch reductions did not afford the *trans* isomer as the major product, this screen holds interesting insight in a broader sense. The literature on dissolving metal reductions of enones suggest each substrate has an innate selectivity that is solely dependent on its structure and not reaction conditions.[3] *The experiments just presented fully contradict these claims*.[30] Further collaborative investigation using experimental and computational methods could elucidate this curious trend in stereoselectivity, and perhaps lead to greater selectivity in one direction or another. Obvious evaluation of reaction conditions such as metal, temperature, cosolvents and additives were not performed, but are expected, as already shown with Mg in methanol, to have significant impact on diastereoselectivity. Overall, this inquiry would be interesting from a fundamental reactivity standpoint and expand on 50 years of dissolving metal *trans*-reduction dogma.

4.5 Conclusions

A rationally derived phenanthrenone Birch reduction was conceived to address problems of the all-*trans* stereochemistry required for a synthetic preparation of DICA. With the literature split on the outcome of such a reduction, an independent evaluation was important not only as a direct entry into perhydrophenanthrene systems, but also as a contribution to clear up ambiguity in the literature. An initial *trans* stereochemical assignment inspired continued efforts in this area. After a successful evolution in approaches addressing the lack of aromatic reduction, the major observed product was found to have a *cis*-ring fusion! Stereochemical assignment obtained by hydrogenation was found to support a *cis*-ring fusion, thereby correcting the previously assigned *trans* stereochemistry and indicating which literature precedent is correct in their assignment. In attempts to switch the stereochemical reduction to *trans*, a positive correlation between alcohol size and improved *cis*-selectivity were observed. The phenanthrenone reduction approach could still be continued using a mostly *trans*-selective hydrogenation, but was replaced by a better approach to DICA (see Chapter 5).

4.6 Experimental Procedures

Purifications –

Solvents: Dry tetrahydrofuran (THF), diethyl ether (Et_2O), dichloromethane (CH_2Cl_2), toluene, benzene (C_6H_6) and methanol (MeOH) were obtained by passing commercially available formulations through activated alumina columns. tert-Butyl alcohol (t-BuOH) was purified by distillation over CaH_2.

Amines: Diisopropylamine (i-Pr_2NH), triethylamine (NEt_3), N,N'-dimethylpropylene urea (DMPU), propylamine (n-$PrNH_2$), N,N,N',N'-tetramethylethylene-1,2-diamine (TMEDA) and hexamethylphosphoramide (HMPA) were purified by distillation from CaH_2. Ethylenediamine (EDA) was purified by distillation from sodium metal.

Chlorides: Acetyl chloride (AcCl) was purified by distillation from phosphorus pentachloride.

Metals: Copper(I) cyanide (CuCN) was purified by refluxing in degassed water, filtering, washing with ethanol, diethyl ether and drying under high vacuum. Copper(I) iodide (CuI) was purified by Soxlet extractor with THF then drying the solid under high vacuum.

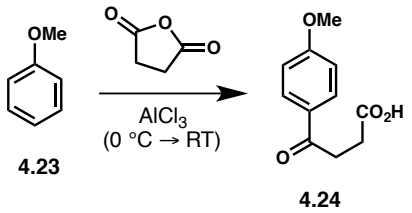
Miscellaneous: Methyl vinyl ketone (MVK) and (±)-propylene oxide were purified by distillation.

Titrations – Alkyllithium reagents were titrated using 2,6-di-(tert-butyl)-4-methylphenol (BHT) as the sacrificial proton source and fluorene as an indicator in THF or using diphenylacetic acid in THF. Grignard reagents were titrated using salicylaldehyde phenylhydrazone in THF.[31]

Reaction Setup – All reactions were carried out under an argon atmosphere with dry solvents under anhydrous conditions, unless otherwise noted. Argon balloons were the sole inert atmosphere used. Reactions run at an ambient temperature of 20–25 °C are designated as room temperature. Yields refer to chromatographically and spectroscopically homogeneous materials, unless otherwise stated.

Analysis – Thin layer chromatography was performed on 0.25 mm EMD glass-backed TLC plates impregnated with a fluorescent dye and visualized with UV light and $KMnO_4$ in K_2CO_3/NaOH/water or *p*-anisaldehyde in ethanol/aqueous H_2SO_4/AcOH and heat as a developing agent. Forced flow (flash) chromatography was performed on EMD Silica 60, mesh 0.04-0.063 silica gel. NMR spectra were recorded on Bruker 500 MHz instrument, obtained at 298 K unless otherwise noted and calibrated to residual undeuterated solvent as an internal reference. Chemical shifts are reported in ppm with the following abbreviations to explain multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, quin = quintuplet, sext = setet, sep = septet, bs = broad signal, m = multiplet. All coupling constants are apparent *J* values measured at the indicated field strengths. FT-IR spectra were recorded on a Perkin-Elmer spectrum RX1 spectrometer. High-resolution mass spectra (HRMS) were recorded on a H2Os LCT Premier spectrometer using ESI-TOF (electrospray ionization-time of flight). Melting points were measured on a MEL-TEMP II capillary apparatus and stand uncorrected.

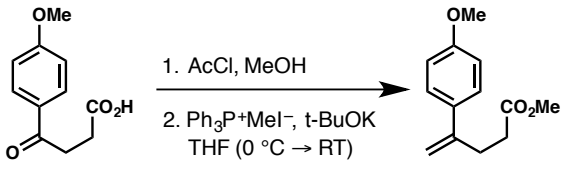
Carboxylic Acid 4.24 [Adapted from the literature][32]



4.23 **4.24**

A 500 mL 3-neck round bottom flask, fitted with an overhead stirrer, a septum and a pressure release tube submerged in an aqueous NaOH trap, was charged with 75 mL (0.690 mmol) **4.23**, 10.2 g (0.102 mmol) succinic anhydride and cooled in an ice bath. In one portion 27.0 g (0.202 mmol) $AlCl_3$ was added. The reaction was stirred at 0 °C for 2 hours then the bath was removed. After 2 hours the contents were poured into 250 mL conc. HCl cooled to 0 °C under overhead stirring. The pink solution was stirred at room temperature for 1 hour, filtered over a fritted funnel and the contents washed with 200 mL water and thrice with 100 mL water. The solid was azeotropically dried with toluene then crystallized from 300 mL toluene and recrystallized from 100 mL toluene to afford 13.4 g (62%) **4.24**. The spectral data was identical to the literature.[33]

Ester 4.25 [Adapted from the literature][13]

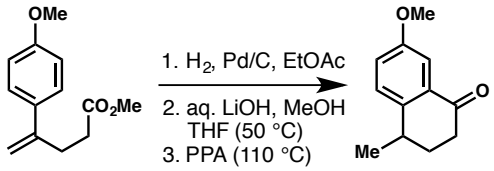


4.24 **4.25**

A 250 mL round bottom flask was charged with 13.13 g (63.1 mmol) **4.24**, 150 mL MeOH and 5.0 mL (70.3 mmol) acetyl chloride. After stirring for 18 hours at room temperature, 80 mL sat. $NaHCO_3$ was added and 60 mL volatiles removed in vacuo. The solution was diluted with 80 mL water and extracted with 200 mL Et_2O. The organic phase was washed with 50 mL water. All aqueous phases were combined and extracted with 50 mL Et_2O. The organic phase was washed

with 20 mL water and combined with the previous organic phase. This process was repeated a total of four times. The combined organic layer was washed with 25 mL brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. A 1 L round bottom flask containing crude keto-ester, 33 g (81 mmol) methyltriphenylphosphonium iodide and 150 mL THF was cooled in an ice bath and fitted with an addition funnel. A solution of 8.5 g (76 mmol) t-BuOK in 60 mL THF was added dropwise over the course of 15 minutes, the addition funnel washed with 50 mL THF and the reaction stirred for 30 minutes at 0 °C, then 30 minutes after removing the cold bath. After the addition of 100 mL water, 200 mL volatiles were removed and the solution extracted with 200 mL Et_2O, then thrice with 50 mL Et_2O. All organic layers were combined, washed with 30 mL third sat. $Na_2S_2O_3$, 30 mL water, 25 mL brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude solid was triturated with 50 mL portions of hexanes and filtered over celite for a total of ~800 mL hexanes. All washings were combined and the volatiles removed in vacuo. The crude oil was purified by column chromatograph (8:1 hexanes/EtOAc) to afford 7.39 g (53% over 2 steps) **4.25** as a yellow wax.

Tetralone 4.26 [Adapted from the literature][13]

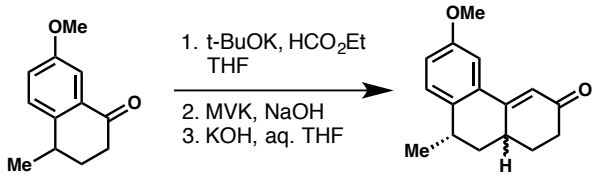


4.25 **4.26**

A 500 mL round bottom flask was charged with 7.39 g (33.5 mmol) **4.25**, 100 mL EtOAc, 1.04 g 10% Pd/C and stirred under a hydrogen balloon. After 15 hours, 5 g Celite was added and the contents filtered over a celite plug with the assistance of fresh EtOAc. All volatiles were removed in vacuo. A 500 mL round bottom flask containing crude ester was stirred with 100 mL

THF/MeOH/water (2:1:1) and 2.58 g (61.5 mmol) $LiOH•H_2O$ at 50 °C. After 1 hour the reaction was quenched with 40 mL 3M HCl, and extracted with 100 mL, then thrice with 50 mL Et_2O. The organic layers were combined, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. Polyphosphoric acid (70 g P_2O_5 and 60 g H_3PO_4, 100 °C, 9 h) was added to crude acid and heated at 110 °C for 2 hours in a 500 mL round bottom flask. The reaction was partially cooled and 300 g ice added slowly. The solution was extracted 8 times with 50 mL portions CH_2Cl_2. The organic layers were combined and washed with 100 mL brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The black residue was purified by column chromatography (10:1→9:1 hexanes/EtOAc) to afford 4.62 g (70% over 3 steps) **4.26** as a yellow oil. The spectral data was identical to the literature.[13]

Phenanthrenone 4.29

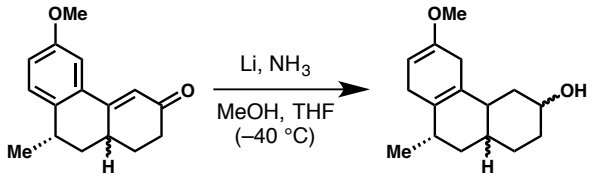


4.26 **4.29:** 1 : 1 dr

A 25 mL round bottom flask containing 201 mg (1.06 mmol) **4.26** and 0.15 mL (1.86 mmol) ethyl formate in 5 mL THF was cooled in an ice bath and treated with 1.3 mL (1.3 mmol) 1 M t-BuOK/THF. The ice bath was removed upon complete addition and stirring continued for 1 hour. The reaction was treated with 2 mL 6 M HCl and 8 mL water, then extracted 3 times with 5 mL CH_2Cl_2. The organic layers were combined, washed with 10 mL half sat. brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude mixture in a 10 mL round bottom flask was stirred with 0.30 mL (3.60 mmol) MVK and 7 mg (0.18 mmol) powdered NaOH (exotherm). After 20 minutes the reaction was diluted with 5 mL sat. NH_4Cl and extracted twice

with 5 mL CH_2Cl_2. The organic layers were combined, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. A 25 mL round bottom flask containing the crude material in 4 mL THF was treated with 210 mg (5.25 mmol) NaOH in 4 mL water at 0 °C. The ice bath was immediately removed and stirring continued for 36 hours. The reaction was quenched with 10 mL half sat. NH_4Cl and extracted twice with 10 mL CH_2Cl_2. The organic layers were combined, washed with 5 mL brine, dried over $MgSO_4$, filtered and all volatiles were removed. The residue was purified by column chromatography (5:1 hexanes/EtOAc) to afford 195 mg (74% over 3 steps, 1:1 dr) **4.29** as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 7.33 (d, J = 8.7 Hz, 1H), 7.25 (d, J = 2.6 Hz, 1H), 7.21 (d, J = 2.6 Hz, 1H), 7.13 (d, J = 8.5 Hz, 1H), 6.98 (dd, J = 8.7, 2.7 Hz, 1H), 6.95 (dd, J = 8.5, 2.6 Hz, 1H), 6.61 (s, 2H), 3.82 (s, 3H), 3.81 (s, 3H), 3.09 (qt, J = 7.2, 3.6 Hz, 1H), 2.97 (dquintet, J = 12.0, 6.0 Hz, 1H), 2.92-2.85 (m, 1H), 2.73-2.66 (m, 1H), 2.62-2.54 (m, 2H), 2.53-2.42 (m, 2H), 2.23-2.12 (m, 3H), 2.04 (dt, J = 12.9, 4.2 Hz, 1H), 1.84-1.75 (m, 4H), 1.40-1.38 (m, 2H), 1.37 (d, J = 6.8 Hz, 3H), 1.32 (d, J = 7.2 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 200.4, 200.3, 159.1, 158.3, 158.0, 157.9, 137.4, 137.0, 132.1, 131.3, 130.5, 128.1, 120.6, 120.3, 118.5, 118.2, 108.7, 108.3, 55.3 (2 C), 40.2, 37.5, 37.2, 36.9, 36.8, 32.4, 32.1, 31.0, 30.4, 30.1, 22.7, 21.1; IR (thin film) 2927, 2856, 1660, 1611, 1589, 1493 cm^{-1}; HRMS (ESI) calculated for $C_{16}H_{18}O_2$ $[M+Na]^+$ 265.1205 found 265.1210.

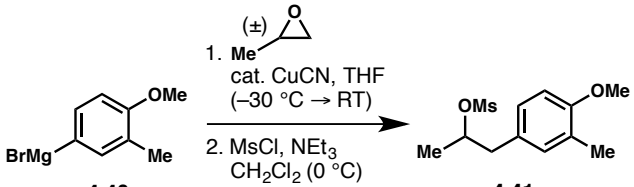
Birch Reduction to 4.30



4.29: 1 : 1 dr **4.30**

A 25 mL round bottom flask was charged with 8 mL ammonia, 34 mg (0.14 mmol) **4.29** in 1.4 mL THF and 0.25 mL (6.2 mmol) MeOH. Slow, portionwise addition of 43 mg (6.2 mmol) lithium metal was conducted at –40 °C. After complete addition of metal, 450 mg (8.5 mmol) NH_4Cl was added, the ammonia evaporated, water and EtOAc added. The organic layer was washed with brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo to afford **4.30** as a mixture of diastereomers (2:2:1:1 dr).

Mesylate 4.41

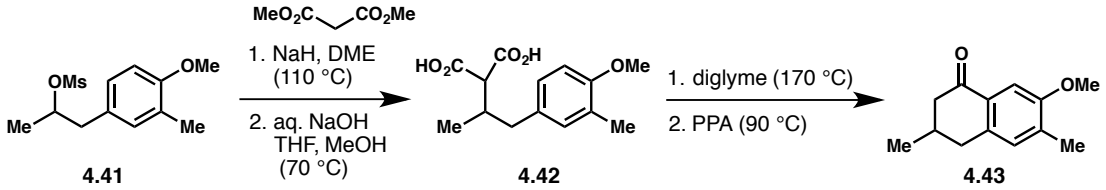


4.40 **4.41**

A 100 mL round bottom flask containing 720 mg (29.6 mmol) magnesium metal was flame-dried, layered with 5 mL THF (rigorously degassed solvent was used during this procedure), treated with a couple drops of dibromoethane and heated to 70 °C. A solution of 5.00 g (24.9 mmol) 4-bromo-2-methylanisole in 25 mL THF was added dropwise as to maintain a gentle reflux. After complete addition the reaction was stirred at 70 °C another hour then cooled to –30 °C. After the addition of 70 mg (0.80 mmol) CuCN and 2.0 mL (28.6 mmol) (rac)-propylene oxide the reaction was stirred for 1 hour with gradual warming to 0 °C, then stirred an additional half hour at room temperature. The reaction was quenched with 100 mL half sat. NH_4Cl and

extracted with 100 mL EtOAc. The aqueous layer was separated and back extracted with 20 mL EtOAc. Both organic layers were combined, washed with 50 mL sat. NH_4Cl, 30 mL third sat. NH_4Cl, 20 mL brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The residue was used for the next without purification. To a 250 mL round bottom flask containing crude alcohol, was added 80 mL CH_2Cl_2 and 15 mL (108 mmol) NEt_3. After the dropwise addition of 3.0 mL (38.8 mmol) methanesulfonyl chloride at 0 °C, the reaction was stirred at 0 °C for 2 hours. To the stirring mixture was added 150 mL sat. $NaHCO_3$ and vigorous stirring continued without external cooling for 20 minutes. Layers were separated and the aqueous layer washed with 20 mL CH_2Cl_2. The organic layers were combined, washed with 40 mL brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The residue was purified by column chromatography (5:1 hexanes/EtOAc) then recrystallized from Et_2O/pentane to afford 5.24 g (81% over 2 steps) **4.41** as white crystals (mp = 60–62 °C). ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 7.03-6.98 (m, 2H), 6.77 (d, *J* = 8.1 Hz, 1H), 4.85 (ttd, *J* = 6.6, 6.4, 6.2 Hz, 1H), 3.82 (s, 3H), 2.91 (dd, *J* = 14.1, 8.0 Hz, 1H), 2.81 (dd, *J* = 14.0, 5.4 Hz, 1H), 2.54-2.52 (m, 3H), 2.18-2.16 (m, 3H), 1.46 (d, *J* = 6.2 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 156.8, 131.8, 128.3, 127.7, 126.8, 109.9, 81.8, 55.3, 42.1, 37.8, 21.4, 16.2; IR (thin film) 2935, 2836, 1612, 1505, 1346, 1253, 1172 cm^{-1}; HRMS (ESI) calculated for $C_{12}H_{18}O_4S$ $[M+Na]^+$ 281.0833 found 281.0823.

Tetralone 4.43

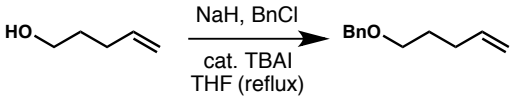


4.41 **4.42** **4.43**

A 100 mL round bottom flask containing 24 mL DME and 0.970 g (24.3 mmol) NaH 60% in mineral oil was cooled in an ice bath and 2.7 mL (23.6 mmol) dimethylmalonate added dropwise. After the reaction was warmed to room temperature 3.00 g (11.6 mmol) **4.41** was added in one portion, the flask fitted with a good reflux condenser and the reaction placed in a 110 °C oil bath. After 20 hours, the reaction was cooled, the volatiles stripped in vacuo and the solid mass dissolved in 60 mL two-thirds sat. NH_4Cl and 60 mL EtOAc. The aqueous layer was washed with an additional 20 mL EtOAc. The combined organic phases were washed with 20 mL brine, dried over $MgSO_4$, filtered all volatiles removed in vacuo. The crude material was taken forward. The crude diester was placed into a 250 mL round bottom flask, diluted with 60 mL 1:1:1 THF/MeOH/water and treated with 4.64 g (116 mmol) powdered NaOH. The flask was placed into a 70 °C oil bath. After 1.5 hours, the reaction was cooled, the volatiles stripped in vacuo and crude material taken up in 120 mL water. The aqueous solution was washed with two portions of 20 mL Et_2O, then 40 mL conc. HCl added and the aqueous phase extracted twice with 60 mL Et_2O. The organic layers were combined, washed with 20 mL brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The solid was subjected to the next reaction crude. Crude diacid in a 100 mL round bottom flask was dissolved in 35 mL diglyme and placed in a 170 °C oil bath for 1 hour. The reaction was cooled and all volatiles were removed in vacuo. The obtained oil was treated to the next reaction crude. Crude acid in a 100 mL round bottom flask was treated with 38 g polyphosphoric acid (prepared from 25 g H_3PO_4 and 15 g P_2O_5) and

heated at 90 °C for 3 hours. External heating was removed and the reaction treated slowly with 150 g ice, then 20 mL 5 M NaOH and the resulting aqueous solution extracted with two portions of 60 mL CH_2Cl_2. The organic layers were collected, washed with 20 mL brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude solid was dissolved in 20 mL hexanes, filtered over Celite, concentrated to approximately half volume and crystallized in a freezer overnight. The solvent was removed via cannula, the crystals washed twice with 2 mL portions of hexanes then the remaining solvent removed in vacuo to afford 1.44 g (60% over 4 steps) **4.43** as a white solid (mp = 68–69 °C). ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 7.44 (s, 1H), 7.01 (s, 1H), 3.87 (s, 3H), 2.88 (dd, *J* = 15.9, 3.6 Hz, 1H), 2.70 (dd, *J* = 13.1, 1.5 Hz, 1H), 2.59 (dd, *J* = 15.9, 10.3 Hz, 1H), 2.33-2.26 (m, 2H), 2.26-2.24 (m, 3H), 1.13 (d, *J* = 6.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 198.5, 156.6, 136.4, 133.9, 130.9, 130.9, 106.6, 55.5, 46.9, 37.2, 30.9, 21.4, 16.6; IR (thin film) 2951, 1678, 1510, 1496, 1302, 1210 cm^{-1}; HRMS (ESI) calculated for $C_{13}H_{16}O_2$ $[M+H]^+$ 205.1228 found 205.1221.

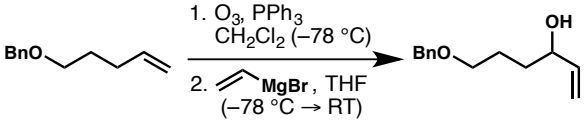
1-Benzyloxy-4-pentene [Adapted from the literature][34]



A 250 mL round bottom flask was charged with 70 mL THF and 5.2 mL (50.4 mmol) 4-penten-1-ol and treated portionwise with 2.1 g (52.5 mmol) 60% NaH in mineral oil at 0 °C. The reaction was warmed to room temperature and 6.4 mL (55.6 mmol) benzyl chloride and 185 mg (0.5 mmol) tetrabutylammonium iodide were added. The reaction was heated to 80 °C in an oil bath for 18 hours. After cooling to room temperature, 50 mL 1 M HCl were added, most volatiles removed in vacuo and the contents partitioned with 100 mL Et_2O. The aqueous phase was

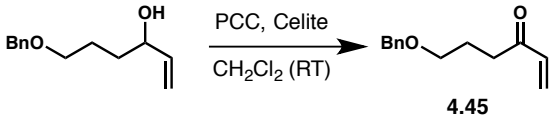
removed and back extracted with 25 mL Et_2O. Both organic layers were combined, washed twice with 25 mL water, 25 mL brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo to afford a liquid that was distilled (75-78 °C/0.5 mmHg) to afford 7.10 g (80%) 1-benzyloxy-4-pentene as a colorless liquid. Spectral data was identical to the literature.[34]

6-Benzyloxyhex-1-en-3-ol



A 50 mL round bottom flask containing 563 mg (3.19 mmol) 1-benzyloxy-4-pentene in 20 mL CH_2Cl_2 cooled to –78 °C was bubbled a stream of ozone until a blue color persisted. The contents were treated with 1.10 g (4.19 mmol) PPh_3 and the reaction warmed to room temperature. After all ozonide was quenched the reaction was dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude aldehyde in a 100 mL round bottom flask was diluted with 15 mL THF, cooled to –78 °C and 4.5 mL (4.5 mmol) 1.0 M vinylmagnesium bromide/THF was added dropwise. After 15 minutes the cold bath was removed. After 8 hours of stirring 10 mL 3 M HCl and 25 mL EtOAc was added. The layers were separated and the organic layer washed twice with 10 mL 3 M HCl. The aqueous washings were collected, back extracted twice with 10 mL EtOAc. The organic layers were combined, washed with 5 mL water, 10 mL sat. $NaHCO_3$, 5 mL brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The residue was purified by column chromatography (4:1 hexanes/EtOAc) to afford 285 mg (43% over 2 steps) 6-benzyloxyhex-1-en-3-ol as a colorless oil and 131 mg (23% over 2 steps) 4-benzyloxy-1-butanol.[35] The spectral data was identical to the literature.[36]

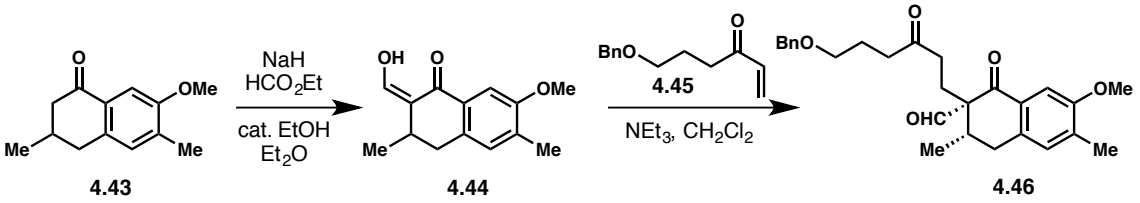
6-(Benzyloxy)hex-1-en-3-one 4.45



4.45

A 20 mL scintillation vial was charged with 270 mg (1.31 mmol) 6-benzyloxyhex-1-en-3-ol, 5 mL CH_2Cl_2, 1.2 g celite and 588 mg (2.73 mmol) PCC. After 2 hours the reaction was diluted with Et_2O and filtered over Et_2O to afford 128 mg (48%) **4.45** as a colorless liquid. The spectral data was identical to the literature.[37]

Michael Adduct 4.46

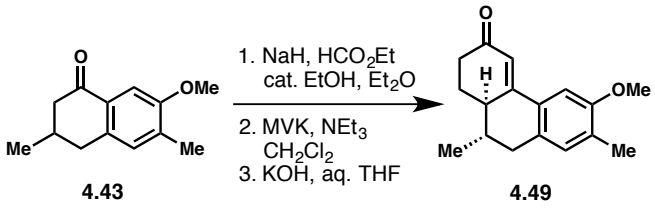


4.43 4.44 4.46

A 1 dram vial containing 14 mg (0.35 mmol) NaH (60% in mineral oil) in 0.7 mL Et_2O was cooled in an ice bath and treated sequentially with 0.05 mL (0.62 mmol) ethyl formate, 30 mg (0.145 mmol) **4.43** and 1 drop ethanol. Stirring was continued at 0 °C for 20 minutes before the bath was removed. After an additional hour and 40 minutes 1 M NaOH was added and the solution extracted thrice with Et2O. The aqueous layer was back extracted with 1 M NaOH. The aqueous layer was acidified with 6 M HCl and extracted trice with Et_2O. The organic layers were combined, washed with brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude vinylogous acid in a 1 dram vial was dissolved in 0.3 mL CH_2Cl_2 and 0.2 mL (1.43 mmol) NEt_3 at room temperature and treated with 45 mg (0.22 mmol) enone. After 30 hours the reaction wash treated with 1 M HCl, extracted with EtOAc, dried over MgSO4 and all volatiles were removed in vacuo. The crude material was purified by column chromatography (5:1

hexanes/EtOAc) to afford 41 mg (65% over 2 steps, single diastereomer) **4.46** as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 9.98 (s, 1H), 7.38 (s, 1H), 7.30-7.22 (m, 5H), 6.95 (s, 1H), 4.41 (s, 2H), 3.82 (s, 3H), 3.40 (t, *J* = 6.1 Hz, 2H), 3.14 (dd, *J* = 17.1, 4.7 Hz, 1H), 2.68 (dd, *J* = 17.1, 5.6 Hz, 1H), 2.50-2.34 (m, 4H), 2.32-2.26 (m, 2H), 2.22 (s, 3H), 2.12-2.05 (m, 1H), 1.81 (quintet, *J* = 6.6 Hz, 2H), 1.07 (d, *J* = 7.0 Hz, 3H).; ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 209.1, 203.6, 197.1, 156.8, 138.3, 135.2, 133.6, 131.3, 129.6, 128.3, 127.6, 127.5, 106.8, 72.8, 69.2, 62.4, 55.4, 39.4, 37.0, 35.3, 32.7, 24.7, 23.8, 16.7, 16.1.

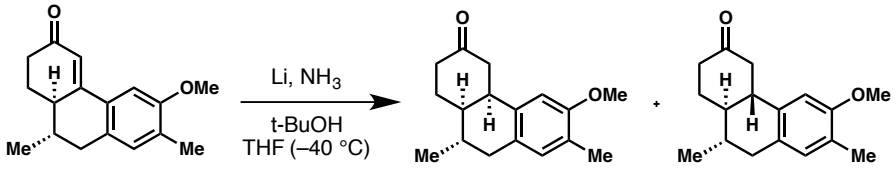
Phenanthrenone 4.49



A 50 mL round bottom flask containing 304 mg (7.60 mmol) NaH (60% in mineral oil) in 15 mL Et_2O was cooled in an ice bath and treated sequentially with 0.95 mL (11.8 mmol) ethyl formate, 602 mg (2.95 mmol) **4.43** and 0.05 mL (0.86 mmol) ethanol. Stirring was continued at 0 °C for 20 minutes before the bath was removed. After an additional hour and 40 minutes 40 mL 0.25 M NaOH was added, the layers separated and the aqueous phase extracted twice with 10 mL Et_2O. The aqueous layer was acidified with 10 mL 6 M HCl and extracted with 40 mL and 10 mL Et_2O. The organic layers were combined, washed with 10 mL brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude vinylogous acid in a 100 mL round bottom flask was dissolved in 3 mL CH_2Cl_2 and 3 mL (21.5 mmol) NEt_3 at room temperature and treated with 0.75 mL (9.00 mmol) MVK. All volatiles were removed in vacuo after 13 hours at room temperature. The crude solid was dissolved in 8 mL THF, cooled ot 0°C and treated by the

dropwise addition of 980 mg (17.5 mmol) KOH in 8 mL water. After complete addition the cold bath was removed and the reaction stirred for 5 days. Volatiles were removed in vacuo and the remaining solution partitioned between 10 mL sat. NH_4Cl and 30 mL EtOAc and the layers separated. The aqueous layer was extracted with 10 mL EtOAc. The combined organic layers were washed with 10 mL brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude material was resubjected to the same conditions as described above for an additional 4 days. Work up consisted of the above procedure. Crystallization from CH_2Cl_2/hexanes afford 501 mg (66%, single diastereomer) **4.49** (mp = 188–190 °C) as an off-white crystalline solid. ^1H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 7.15 (s, 1H), 6.94 (s, 1H), 6.64 (s, 1H), 3.83 (s, 3H), 2.79 (dd, *J* = 16.3, 4.1 Hz, 1H), 2.63-2.54 (m, 2H), 2.45-2.37 (m, 2H), 2.28-2.25 (m, 1H), 2.22 (s, 3H), 1.74-1.61 (m, 2H), 1.16 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 200.3, 158.8, 156.4, 132.4, 131.2, 130.9, 129.5, 119.8, 105.1, 55.3, 43.3, 38.3, 37.2, 35.3, 27.0, 19.5, 16.2; IR (thin film) 2949, 2913, 1654, 1205 cm^{-1}; HRMS (ESI) calculated for $C_{17}H_{20}O_2$ $[M+H]^+$ 257.1541 found 257.1529.

Anisole 4.50

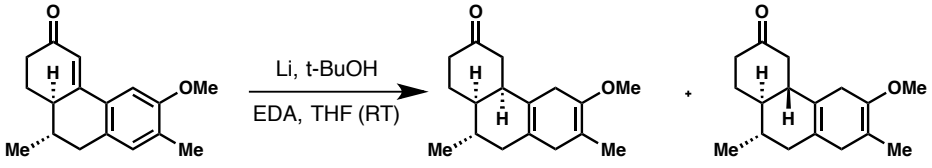


4.49 **4.50:** 8 : 1 dr

A 10 mL round bottom flask was charged with excess lithium metal and ammomia at –40 °C, then 10 mg (0.039 mmol) **4.49** and 58 mg (0.78 mmol) t-BuOH in 0.5 mL THF was added dropwise. After 30 min another portion of 58 mg (0.78 mmol) t-BuOH in 0.2 mL THF was addd. The reaction was quenched with solid NH_4Cl, warmed to room temperature, diluted with water

and extracted with EtOAc. The organic layer was dried over $MgSO_4$, filtered and all volatiles removed. The crude solid was puriifed by column chromatography (8:1 hexanes/EtOAc) to afford 8.0 mg (80%, 8:1 dr) **4.50** as a white wax. ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) major δ 6.87 (s, 1H), 6.50 (s, 1H), 3.79 (s, 3H), 3.20 (td, *J* = 8.6, 4.3 Hz, 1H), 3.09 (ddd, *J* = 14.1, 3.7, 2.1 Hz, 3H), 2.86 (dd, *J* = 16.3, 5.1 Hz, 1H), 2.57-2.55 (m, 2H), 2.47-2.19 (m, 5H), 2.19 (s, 3H), 1.86 (ddq, *J* = 14.1, 9.2, 4.6 Hz, 2H), 1.14 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) major δ 211.5, 156.0, 137.5, 130.9, 127.0, 125.0, 109.0, 55.3, 47.6, 42.4, 39.0, 37.3, 29.7, 27.3, 26.3, 19.2, 15.8; IR (thin film) 2919, 2853, 1710 cm^{-1}; HRMS (ESI) calculated for $C_{17}H_{22}O_2$ $[M+NH_4]^+$ 276.1964 found 276.1967.

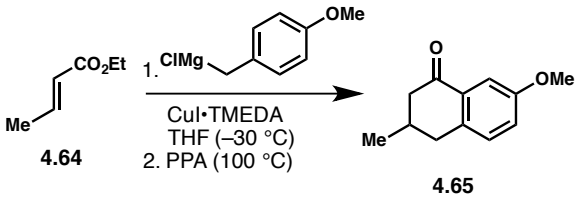
Cyclohexadiene 4.62



4.49 **4.62:** 3 : 1 dr

To a 25 mL round bottom flask was added 20 mg (0.080 mmol) **4.49**, 0.38 mL (4.0 mmol) t-BuOH, 0.8 mL ethylenediamine, 0.8 mL THF and a vigorously stirring glass stir bar. At room temperature 25 mg (3.6 mmol) lithium metal was added over the course of 2 hours. After stirring overnight the mixture was diluted with 5 mL THF and cannula transferred into a stirring mixture of 10 mL water and 15 mL Et_2O. The layers were separated and the aqueous solution extracted with Et_2O. The organic layers were combined, washed with brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo to afford **4.62** (3:1 dr).

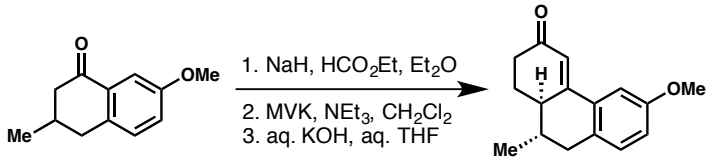
PCR <u>3.225-227</u> [Adapted from the literature][27]



A 50 mL 2 neck round bottom flask filled with 2.29 g (94.4 mmol) magnesium metal was flame-dried under vacuum, allowed to cool, flushed with argon, fitted with a thermometer and an addition funnel, then layered with 9 mL THF. To the vigorously stirring mixture was added 0.05 mL 1,2-dibromoethane, then 3.2 mL (23.6 mmol) p-methoxybenzyl chloride in 6 mL THF was added from the addition funnel to maintain an internal temperature of 60-65 °C. After complete addition the solution was stirred for an additional 2 hours. A 250 mL round bottom flask was charged with 3.62 g (19.0 mmol) CuI, 80 mL THF and 3.1 mL (21.4 mmol) TMEDA at room temperature and stirred until a homogeneous solution was obtained. The flask was fitted with an addition funnel and cooled to –78 °C. The freshly prepared Grignard reagent was loaded to the addition funnel and added dropwise. After stirring for 30 minutes at –78 °C a new addition funnel was fitted and loaded with 1.9 mL (15.3 mmol) ethyl trans-2-butenoate, 4.9 mL (38.6 mmol) TMSCl and 20 mL THF. After dropwise addition of this mixture, the reaction was warmed to –30 °C. After 18 hours stirring at –30 °C, the reaction was poured into 125 mL sat. NH_4Cl/75 mL sat. NH_4OH and partitioned with 100 mL Et_2O. The layers were separated, the aqueous layer extracted with 25 mL Et_2O and all organic layers combined. The ethereal phase was washed twice with 50 mL water, 20 mL brine, dried over $MgSO_4$, filtered all volatiles removed in vacuo. The crude mixture was swirled with 40 mL hexanes, filtered and washed with thrice with 10 mL hexanes. The hexanes washes were concentrated and the crude material carried on to the next step. The crude ester was treated with 30 g PPA and heated at 100 °C for

1.5 hour. The heating source was removed and 100 g ice water was added. The aqueous solution was extracted twice with 40 mL EtOAc. All organic layers were combined, washed with 30 mL sat. $NaHCO_3$, 20 mL brine, dried over $MgSO_4$, stirred vigorously with 6 g charcoal overnight, filtered and all volatiles removed in vacuo. The crude material was purified by crystallization from hexanes to afford 1.47 g (51%) **4.65** as small, off-white needles (mp = 43–44 °C). The spectral data was identical to the literature.[27]

Phenanthrenone 4.33

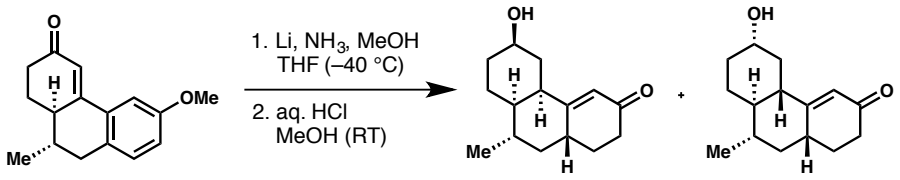


4.65 **4.33**

A 100 mL round bottom flask containing 750 mg (18.8 mmol) NaH (60% in mineral oil) in 50 mL Et_2O was cooled in an ice bath. Sequentially, 2.4 mL (30 mmol) ethyl formate, 1.42 g (7.46 mmol) **4.65** and 0.1 mL (1.7 mmol) ethanol was added. Stirring was continued at 0 °C for 20 minutes before the bath was removed. After 6 hours stirring, 30 mL water was added, the layers separated and the aqueous phase extracted twice with 10 mL Et_2O. The ethereal layers were washed twice with 10 mL 1 M NaOH. The aqueous layers were combined, acidified with 10 mL 6 M HCl and extracted with 30 mL and 10 mL Et_2O. The organic layers were combined, washed with 10 mL brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude vinylogous acid in a 200 mL round bottom flask was dissolved in 10 mL CH_2Cl_2 and 5.2 mL (37 mmol) NEt_3 at room temperature and treated with 1.9 mL (23 mmol) MVK. All volatiles were removed in vacuo after 25 hours at room temperature. The crude solid was dissolved in 35 mL THF, cooled ot 0°C and treated by the dropwise addition of 2.1 g (37 mmol) KOH in 35 mL

water. After complete addition the cold bath was removed and the reaction stirred for 2 days. All volatiles were removed in vacuo and the remaining solution partitioned between 20 mL sat. NH_4Cl and 40 mL EtOAc and the layers separated. The aqueous layer was extracted with 10 mL EtOAc. The combined organic layers were washed with 10 mL brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. Crystallization from EtOAc afforded 1.12 g (61%) **4.33** (mp = 143–145 °C) as an off-white crystalline solid. ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 7.25 (d, *J* = 2.4 Hz, 1H), 7.09 (d, *J* = 8.4 Hz, 1H), 6.93 (dd, *J* = 8.4, 2.5 Hz, 1H), 6.65 (d, *J* = 1.8 Hz, 1H), 3.82 (s, 3H), 2.84 (dd, *J* = 16.3, 4.1 Hz, 1H), 2.64-2.57 (m, 2H), 2.46-2.37 (m, 2H), 2.30-2.24 (m, 1H), 1.75-1.63 (m, 2H), 1.17 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 200.3, 158.3, 158.1, 132.5, 132.1, 130.2, 120.8, 118.2, 108.3, 55.4, 43.3, 38.4, 37.2, 35.2, 27.0, 19.5; IR (thin film) 2946, 2907, 1655, 1498 cm^{-1}; HRMS (ESI) calculated for $C_{16}H_{18}O_2$ $[M+H]^+$ 243.1385 found 243.1376.

Enone 4.67

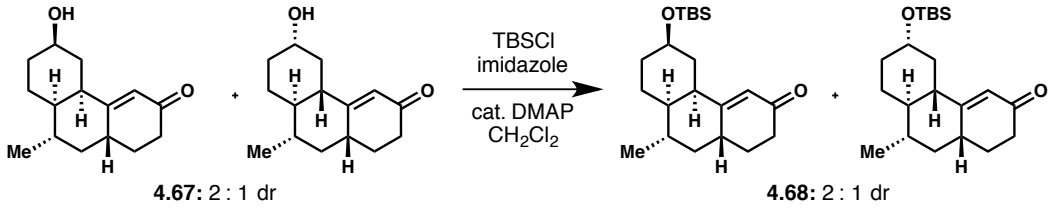


4.33 **4.67:** 2 : 1 dr

A 250 mL round bottom flask was charged with 50 mL ammonia, 25 mL THF, 5 mL MeOH and 500 mg (2.06 mmol) **4.33**. Slow, portionwise addition of 470 mg (68 mmol) lithium metal was conducted at –40 °C. After complete addition of metal, 1 g NH_4Cl was added, the ammonia evaporated, 30 mL water and 50 mL EtOAc added. The organic layer was washed with 10 mL brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude oil in a 25 mL round bottom flask was dissolved in 15 mL MeOH, treated with 1.5 mL 6 M HCl. After 24 hours

th reaction was poured into 40 mL sat. $NaHCO_3$ and 40 mL EtOAc. The organic layer was washed with 20 mL brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude material was purifed by column chromatography (1:1→1:2 hexanes/EtOAc) to afford 280 mg (58%, 2:1 dr) **4.67** as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) combined δ 5.83 (s, 0.7H), 5.81 (s, 0.3H), 3.71-3.64 (m, 1H), 2.57-2.52 (m, 1H), 2.47 (dt, *J* = 11.3, 5.2 Hz, 1H), 2.42-2.25 (m, 2H), 2.16-1.73 (m, 6H), 1.74-1.52 (m, 2H), 1.47-1.30 (m, 2H), 1.27-1.00 (m, 2H), 0.98-0.86 (m, 4H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) major δ 200.5, 170.3, 124.1, 70.6, 45.9, 43.4, 42.0, 38.1, 36.7, 34.4, 29.4, 29.3, 27.1, 25.3, 19.0, minor δ 200.3, 168.6, 121.0, 70.5, 48.9, 45.2, 43.4, 38.0, 37.4, 36.8, 35.5, 34.9, 29.3, 28.4, 19.2; IR (thin film) 3405, 2927, 2859, 1665, 1451 cm^{-1}; HRMS (ESI) calculated for $C_{15}H_{22}O_2$ $[M+H]^+$ 235.1698 found 235.1688.

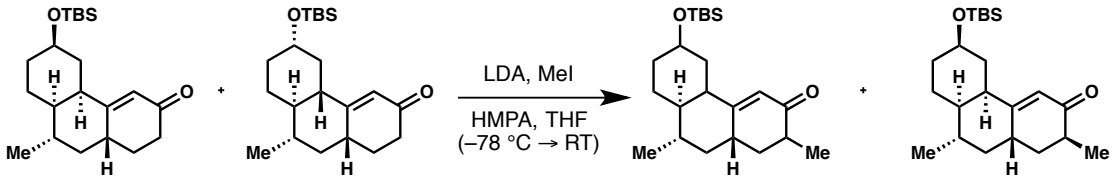
Silyl Ether 4.68



To a 25 mL round bottom flask was added 268 mg (1.14 mmol, 2:1 dr) **4.67**, 10 mL CH_2Cl_2, 150 mg (2.20 mmol) imidazole, 9 mg (0.07 mmol) DMAP and 220 mg (1.46 mmol) TBSCl at room temperature. After 36 hours, 30 mL EtOAc was added and the solution washed with 20 mL water and 10 mL sat. $NaHCO_3$. The aqueous layers were combined and extracted with 10 mL EtOAc. Both organic layers were combined, washed with 10 mL brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude residue was purified by column (10:1 hexanes/EtOAc) to afford 370 mg (91%, 2:1 dr) **4.68** as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) mixture δ 5.83 (s, 1H), 3.62 (qt, *J* = 8.1, 4.0 Hz, 1H), 2.59-2.53 (m, 1H), 2.46-2.26 (m, 3H),

2.16-1.82 (m, 4H), 1.72-1.53 (m, 3H), 1.41-1.09 (m, 3H), 1.05-0.74 (m, 14H), 0.07 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) major δ 200.5, 170.6, 124.0, 71.5, 46.1, 43.5, 42.1, 38.7, 36.8, 34.5, 30.0, 29.4, 27.1, 25.9, 25.6, 25.5, 18.9, 4.65, minor δ 200.3, 168.8, 121.1, 71.3, 48.9, 45.3, 43.5, 38.1, 37.7, 36.8, 35.6, 35.4, 29.4, 28.5, 25.9, 19.2, 18.2, 4.6; IR (thin film) 2930, 2856, 1676, 1618, 1253, 1089 cm^{-1}; HRMS (ESI) calculated for $C_{21}H_{36}O_2Si$ $[M+H]^+$ 349.2563 found major diastereomer 349.2558, minor diastereomer 349.2574.

Alkylated 4.69 and 4.70

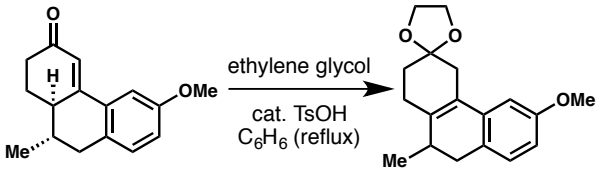


4.68: 2 : 1 dr **4.69:** 5 : 2 : 1 dr **4.70:** >10 : 1 dr

LDA was prepared in a 25 mL round bottom flask by addition of 0.45 mL (1.2 mmol) 2.7 M n-BuLi/hexanes to 0.20 mL (1.4 mmol) diisopropylamine in 4 mL THF at 0 °C. To the stirring LDA solution at –78 °C was added 346 mg (0.99 mmol) **4.68** with the assistance of 2 mL THF. After 10 minutes, 0.22 mL (1.3 mmol) HMPA was added neat followed by 0.18 mL (2.9 mmol) methyl iodide. The cold bath was removed after an additional 10 minutes and the reaction stirred for 1 hour before 10 mL half sat. NH_4Cl and 20 mL EtOAc was added. The organic layer was separated, washed with 5 mL brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude mixture was purified by column chromatography (40:1→30:1 hexanes/EtOAc) to afford 28 mg (26%, 5:2:1 dr) **4.69** and 194 mg (54%, >10:1 dr) **4.70** as a colorless oil. **4.70:** ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 5.75 (s, 1H), 3.63 (tt, *J* = 10.0, 4.9 Hz, 1H), 2.67-2.63 (m, 1H), 2.43 (dt, *J* = 12.4, 6.1 Hz, 2H), 2.07-2.01 (m, 1H), 1.95 (d, *J* = 12.1 Hz, 1H), 1.89-1.82 (m, 2H), 1.75-1.64 (m, 3H), 1.57 (d, *J* = 12.5 Hz, 1H), 1.39-1.26 (m, 3H), 1.11 (d, *J* = 7.2 Hz,

3H), 1.01 (s, 1H), 0.92-0.88 (m, 3H), 0.88 (s, 9H), 0.06 (d, J = 2.5 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 203.7, 169.3, 122.1, 71.5, 46.2, 43.2, 42.7, 39.1, 37.9, 35.7, 31.2, 30.1, 27.6, 25.9, 25.6, 19.0, 18.2, 16.1, 4.6; IR (thin film) 2929, 2856, 1675, 1622, 1460, 1255, 1090 cm^{-1}; HRMS (ESI) calculated for $C_{22}H_{38}O_2Si$ $[M+H]^+$ 363.2719 found 363.2728.

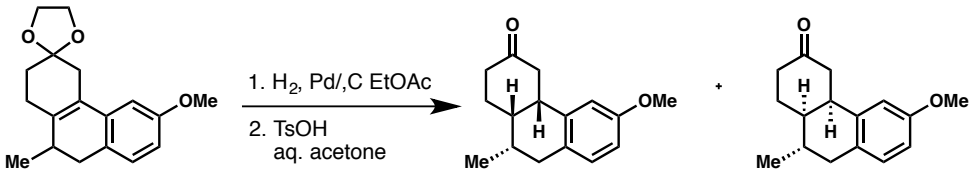
Ketal 4.71



4.33 **4.71**

A 10 mL round bottom flask containing 0.05 mL (0.9 mmol) ethylene glycol and 8 mg (0.04 mmol) TsOH•H_2O in 5 mL benzene was refluxed under a Hickman still for 20 minutes. The solution was cooled, 100 mg (0.413 mmol) **4.33** added and the reaction refluxed under a Hickman still. After 2 hours the reaction was cooled, diluted with 10 mL EtOAc, washed with 3 mL sat. $NaHCO_3$, 2 mL brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude material was purfied by column chromatography (10:1 hexanes/EtOAc) to afford 110 mg (93%) **4.71** as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 7.02 (d, J = 8.1 Hz, 1H), 6.70-6.66 (m, 2H), 4.08-4.02 (m, 4H), 3.80 (s, 3H), 2.96 (dd, J = 15.1, 6.5 Hz, 1H), 2.73 (d, J = 16.6 Hz, 1H), 2.52 (d, J = 17.9 Hz, 1H), 2.50-2.44 (m, 3H), 2.30-2.23 (m, 1H), 1.91-1.80 (m, 2H), 0.94 (d, J = 7.2 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 158.2, 138.3, 136.3, 128.5, 125.8, 123.4, 110.5, 108.5, 107.7, 64.4, 55.2, 35.7, 34.7, 32.7, 31.2, 28.0, 16.9; IR (thin film) 2953, 2883, 2830, 1605, 1574, 1493, 1210, 1039 cm^{-1}; HRMS (ESI) calculated for $C_{18}H_{22}O_3$ $[M+H]^+$ 287.1647 found 287.1640.

Ketone 4.72 and 4.73



To a 10 mL round bottom flask was added 31 mg (0.11 mmol) 4.71, 1.2 mL EtOAc, 5 mg 10% Pd/C. The reaction was stirred under a hydrogen balloon for 20 hours at room temperature. Celite was added and th reaction was filtered over Celite, washing with EtOAc to afford ~95% conversion to a 4:1 mixture of diastereomers. The crude mixture was dissolved in 1 mL 5:1 acetone/water then catalytic TsOH•H_2O added. After 4 days at room temperature 3 mL water and 2 mL sat. $NaHCO_3$ was added and the solution extracted with 5 mL EtOAc. The organic layer was washed with 2 mL brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude was purified by column chromatography (8:1 hexanes/EtOAc) to afford 6 mg **4.73** as an impure oil and 16 mg (62%) **4.72** as a white solid that was recrystallized from Et_2O to provide white fluffy needles (mp = 140–142 °C). The minor diastereomer 1H NMR spectrum significantly matched that of **4.50**. **4.72**: ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 6.98 (d, *J* = 8.4 Hz, 1H), 6.86 (s, 1H), 6.70 (d, *J* = 8.3 Hz, 1H), 3.78 (s, 3H), 3.48 (s, 1H), 3.10 (d, *J* = 14.7 Hz, 1H), 2.77-2.73 (m, 2H), 2.44 (t, *J* = 14.6 Hz, 1H), 2.34 (dd, *J* = 13.6, 6.2 Hz, 1H), 2.30-2.27 (m, 1H), 2.20 (t, *J* = 12.1 Hz, 2H), 1.93-1.91 (m, 1H), 1.51 (dd, *J* = 13.0, 4.9 Hz, 1H), 1.12 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 210.9, 158.0, 136.9, 130.0, 128.1, 112.3, 112.1, 55.3, 44.6, 42.4, 40.5, 40.2, 33.4, 32.3, 20.2, 19.7; IR (thin film) 2952, 1701, 1495, 1239, 1040 cm^{-1}; HRMS (ESI) calculated for $C_{16}H_{20}O_2$ $[M+Na]^+$ 267.1361 found 267.1357.

4.7 References and Notes

(1) Streuff, J. *Synthesis* **2013**, 281.

(2) Corey, E. J.; Magriotis, P. A. *J. Am. Chem. Soc.* **1987**, *109*, 287.

(3) Caine, D. *Org. React.* **1976**, *23*, 1.

(4) Keinan, E.; Greenspoon, N. "Reduction of α,β-unsaturated carbonyl compounds" In *The Chemistry of Enones*; Patai, S.; Rappoport, Z., Ed.; John Wiley & Sons, Ltd, 1989; pp 923–1022.

(5) Huffman, J. W. "Reduction of C=X to CHXH by Dissolving Metals and Related Methods" In *Comprehensive Organic Synthesis*; Trost, B. M.; Fleming, I., Ed.; Elsevier Science Ltd., 1991; pp 107–127.

(6) Hook, J. M.; Mander, L. N. *Nat. Prod. Rep.* **1986**, *3*, 35.

(7) Rabideau, P. W.; Marcinow, Z. *Org. React.* **1992**, *42*, 1.

(8) Gesson, J.-P.; Jacquesy, J.-C.; Jacquesy, R. *Nouv. J. Chim.* **1977**, *1*, 511.

(9) Robinson, M. J. T. *Tetrahedron* **1957**, *1*, 49.

(10) Bansal, R. C.; Browne, C. E.; Eisenbraun, E. J.; Thomson, J. S. *J. Org. Chem.* **1988**, *53*, 452.

(11) Chatterjee, A.; Chaudhuri, S. R. R.; Chatterjee, S. K. *J. Chem. Soc., Chem. Commun.* **1982**, 24.

(12) Barton, D. H. R.; Robinson, C. H. *J. Chem. Soc.* **1954**, 3045.

(13) Nadeau, E.; Ventura, D. L.; Brekan, J. A.; Davies, H. M. *J. Org. Chem.* **2010**, *75*, 1927.

(14) Numbering matches the isocycloamphilectane scaffold, i.e. 7,20-diisocyanoadociane.

(15) White, J. D.; Hrnciar, P.; Stappenbeck, F. *J. Org. Chem.* **1999**, *64*, 7871.

(16) Sobukawa, M.; Nakajima, M.; Koga, K. *Tetrahedron: Asymmetry* **1990**, *1*, 295.

(17) Taguri, T.; Yamamoto, M.; Fujii, T.; Muraki, Y.; Ando, T. *European J. Org. Chem.* **2013**, 6924.

(18) van Tamelen, E. E.; Taylor, E. G. *J. Am. Chem. Soc.* **1980**, *102*, 1202.

(19) Yamato, Y.; Kaneko, H. *Tetrahedron* **1965**, *21*, 2501.

(20) Bohlmann, F.; Giencke, W. *Tetrahedron* **1983**, *39*, 443.

(21) Benkeser, R. A.; Sgihotri, R. K.; Burbous, M. L.; Kaiser, E. M.; Mallan, J. M.; Ryan, P. W. *J. Org. Chem.* **1964**, *29*, 1313.

(22) Kaiser, E. M. *Synthesis* **1972**, 391.

(23) Benkeser, R. A.; Laugal, J.; Rappa, A. *Tetrahedron Lett.* **1984**, *25*, 2089.

(24) Kotlarek, W. *Pol. J. Chem.* **1983**, *57*, 809.

(25) Kwart, H.; Conley, R. A. *J. Org. Chem.* **1973**, *38*, 2011.

(26) Garst, M. E.; Dolby, L. J.; Esfandiari, S.; Fedoruk, N. A.; Chamberlain, N. C.; Avey, A. A. *J. Org. Chem.* **2000**, *65*, 7098.

(27) Scopton, A.; Kelly, T. R. *J. Org. Chem.* **2005**, *70*, 10004.

(28) Brown, G. D. *Phytochemistry* **1994**, *35*, 425.

(29) Shu, Y.-F.; Wei, H.-C.; Wu, C.-L. *Phytochemistry* **1994**, *37*, 773.

(30) Granger, R.; Chapat, J. P.; Crassous, J.; Simon, F. *Bull. Chim. Soc. Fr.* **1968**, 4265.

(31) Love, B. E.; Jones, E. G. *J. Org. Chem.* **1999**, *64*, 3755.

(32) Seed, A. J.; Sonpatki, V.; Herbert, M. R. *Org. Synth.* **2002**, *79*, 204.

(33) Rassadin, V. A.; Six, Y. *Tetrahedron* **2014**, *70*, 787.

(34) Lowik, D. W. P. M.; Liskamp, R. M. *European J. Org. Chem.* **2000**, 1219.

(35) Kiddle, J. J.; Green, D. L. C.; Thompson, C. M. *Tetrahedron* **1995**, *51*, 2851.

(36) Kyne, R. E.; Ryan, M. C.; Kliman, L. T.; Morken, J. P. *Org. Lett.* **2010**, *12*, 3796.

(37) Iyengar, R.; Schildknegt, K.; Morton, M.; Aubé, J. *J. Org. Chem.* **2005**, *70*, 10645.

CHAPTER 5:

A FORMAL SYNTHESIS OF (+)-7,20-DIISOCYANOADOCIANE

5.1 Introduction

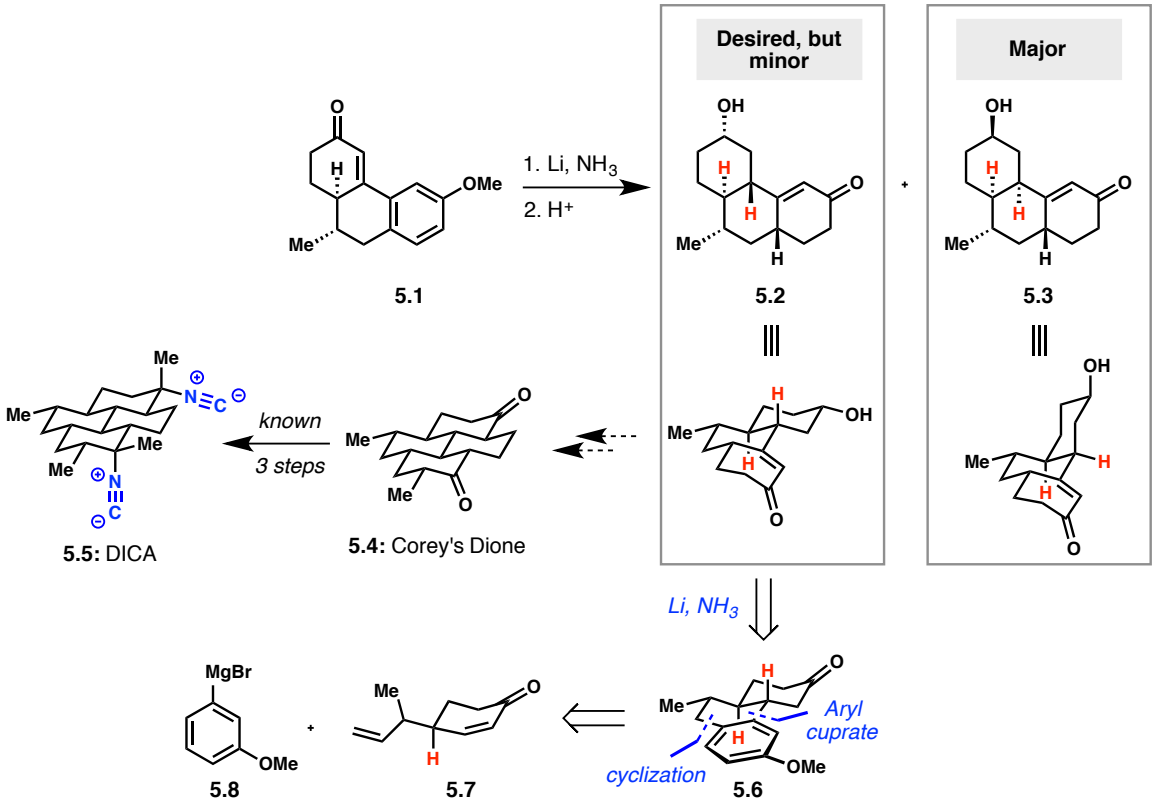
A synthesis of 7,20-diisocyanoadociane (**5.5**, DICA) via reduction of an unsaturated polycyclic intermediate was considered highly attractive both because unsaturated molecules can be rapidly constructed and can provide multiple options in controlling stereochemistry. Previously, Birch reduction of a phenanthrenone substrate successfully generated a tricyclic scaffold relevant to DICA in short order, but failed due to an undesired stereochemical outcome (see Chapter 4). Described here is a revised approach that successfully secured an enantiospecific formal synthesis of (+)-DICA and could serve as a platform to access more 7-isocyano(iso)cycloamphilectanes.

5.2 A New Design to Control the All-*trans* Stereochemistry

Initial studies concerning the reduction of phenanthrenones towards DICA showed an undesirable tendency for *cis*-reduction (Scheme 5.1). Attempts at switching selectivity to the *trans*-ring fusion using hydrogenation were modestly promising, but a synthetic redesign to substantially improve stereocontrol was preferred. The minor diastereomer obtained by phenanthrenone reduction, **5.2**, was still a desirable target and considered a key intermediate. If a synthesis of **5.2** could be secured in an elegant manner, then a single ring closure to Corey's dione **5.4** would be the only operation remaining.[1] Rapidly generating phenanthrenone **5.1** highlights the advantage aromatic starting materials may have in synthetic design;[2,3] therefore the enone of **5.2** was still retrosynthetically traced back to an anisole, such as **5.6**. Based on previous

experience, the challenge of setting the *trans*-ring fusion was to be tackled directly by a robust and stereochemically assured method. A cuprate conjugate addition would be suited to the task.

Scheme 5.1 A previous attempt and a revision in using a Birch reduction approach to DICA.



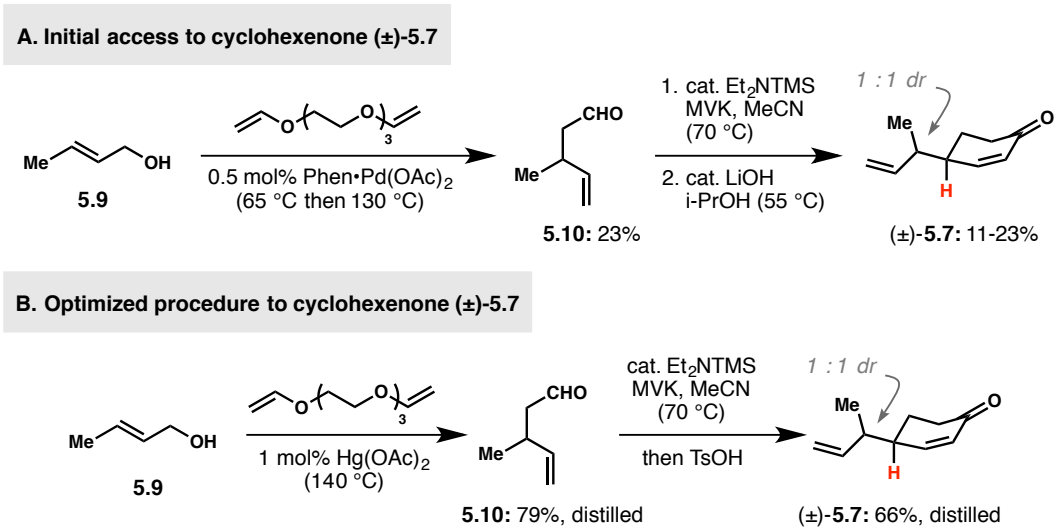
5.3 The C8–C9 Ring Closing Strategy

5.3.1 Successes in Generating trans-Ring Fusions

A Robinson annulation to generate **5.7** was devised, surmising that application of a chiral organocatalyst to the Michael addition step would render the route highly enantioselective.[4–6] The synthesis began with a Claisen rearrangement of crotyl alcohol (**5.9**) by intermediacy of the vinyl enol ether (Scheme 5.2). Palladium-mediated conditions were originally used, but suffered from incomplete conversion and difficulty in purification.[7] Diethyltrimethylsilylamine facilitated

a Michael addition to methyl vinyl ketone to provide the adduct in excellent yield; however, aldol ring closure under literature[8] conditions, previously successful in a slightly different context (see Chapter 2), afforded **5.7** in low yield. Although this three-step sequence of generating **5.7** was sufficient for the exploratory stage, optimization quickly became a priority. Returning to classic $Hg(OAc)_2$ catalyzed Claisen rearrangement afforded **5.10** in a reliable and scalable manner.[9] No change was made to the Michael addition; however, a screen of various reactions was performed to improve the aldol condensation. The most effective conditions were TsOH in acetonitrile, meaning that TsOH could simply be added upon complete Michael addition to afford **5.7**. This three-step/two-pot process prepared enough **5.7** to fuel studies.

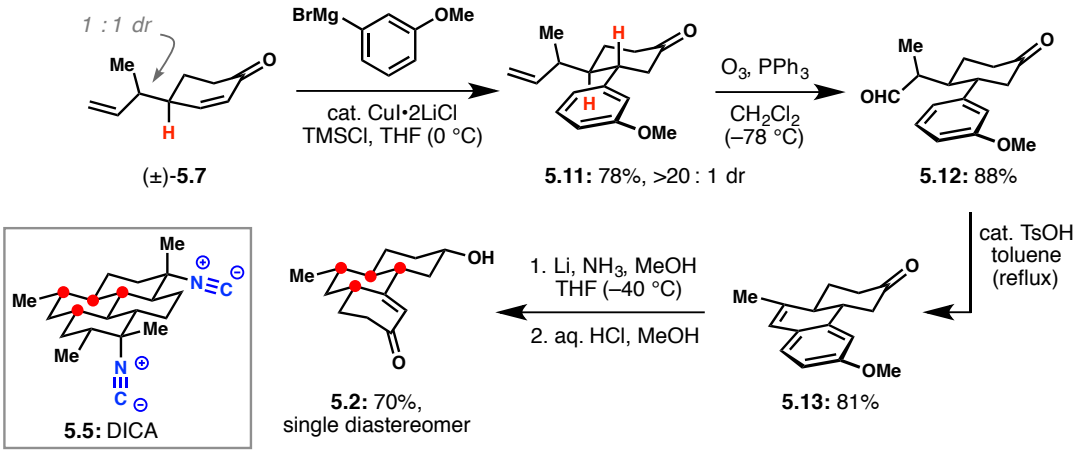
Scheme 5.2 A Robinson annulation entry towards dihydronaphthalene studies of DICA.



The dihydronaphthalene Birch reduction idea was continued via cuprate addition to **5.7** (Scheme 5.3). Initial stoichiometric cuprate conditions with CuI afforded **5.11** in ~50% yield with tedious workup. Employing catalytic quantities of the soluble Reetz CuI•2LiCl not only improved the yield, but also the ease of reaction setup and workup.[10] Ozonolysis and Friedel–Crafts cyclodehydration afforded dihydronaphthalene **5.13**. Treating **5.13** with Li/NH_3 and

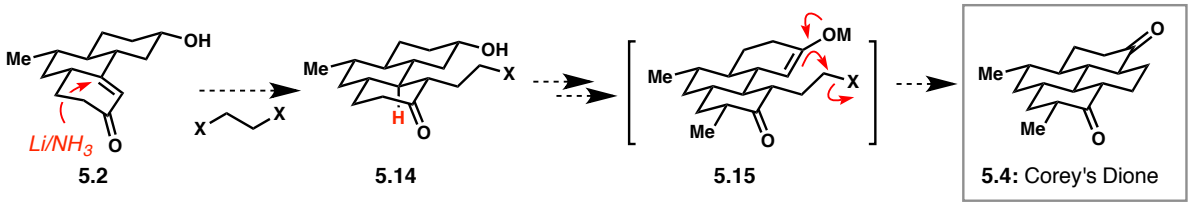
excess methanol followed by aqueous HCl furnished **5.2** without issue as a single diastereomer on the first attempt. The synthesis of a scaffold bearing four desired stereocenters reminiscent of DICA in an all *trans*-arrangement was finally successful.

Scheme 5.3 Efficient preparation of **5.2** by dihydrophthalene reduction.

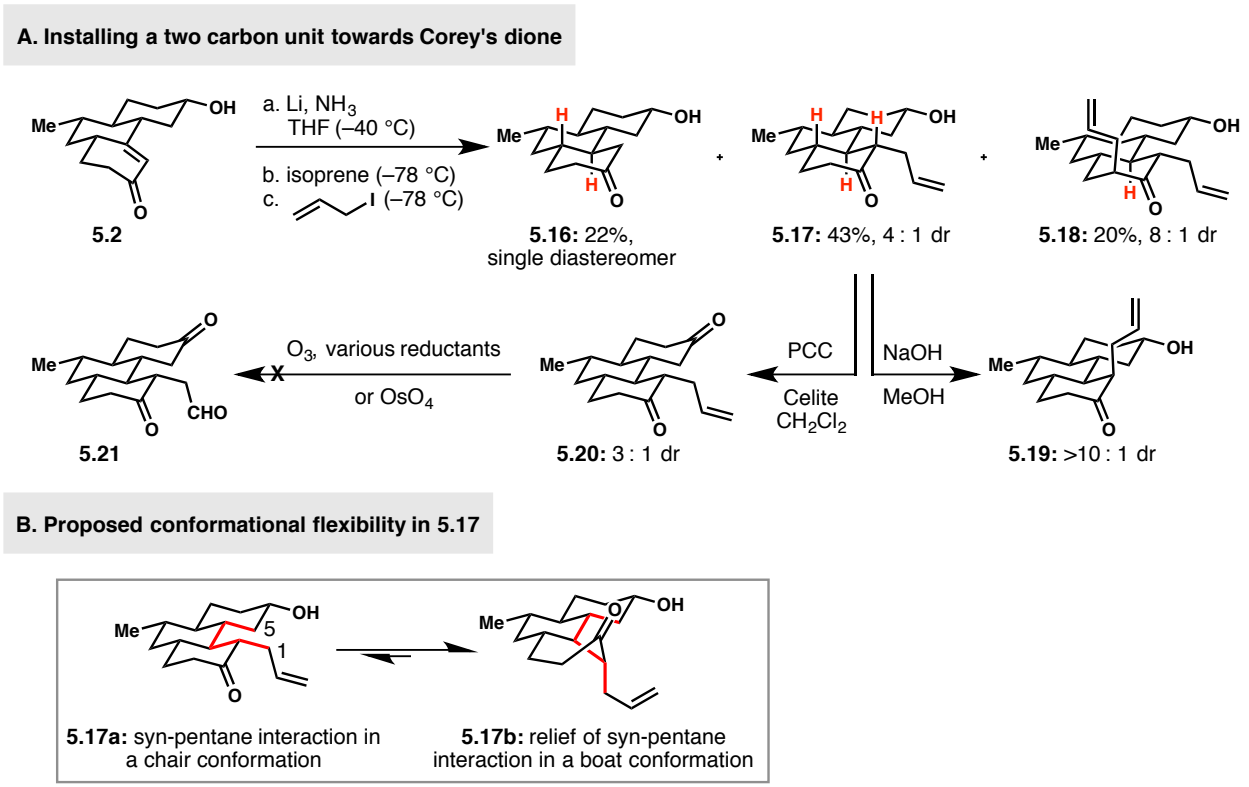


Tricycle **5.2** needs to be stitched together with an appropriate two-carbon unit to intercept Corey's dione (Scheme 5.4). The first step requires introducing a proton at the beta carbon of enone **5.2** in an axial orientation by well precedented Li/NH_3 reduction.[11,12] The hereby-generated enolate could then be alkylated with a 1,2-difunctionalized ethane to provide **5.14**. The last C–C bond could then be formed by enolate alkylation to generate Corey's dione **5.4**.

Scheme 5.4 Proposed path forward to Corey's dione.



Scheme 5.5 Early developments installing the two-carbon bridge.



As a first pass, the free C7 alcohol[13] of **5.2** was not protected and submitted directly to Li/NH_3 (Scheme 5.5A). Upon reduction, the enolate was allylated to afford the three products **5.16**, **5.17** and **5.18**. The des-allyl **5.16** was isolated as a single diastereomer, indicating that the β-position had exclusively protonated axially. The desired compound **5.17** was purified as a 3 : 1 mixture of diastereomers at the allyl position. The diastereoselectivity could not be improved in the desired direction by epimerization, because the thermodynamic preference of the allyl is not the expected equatorial orientation, but is axial instead. Syn-pentane interactions in the chair conformation are believed to cause this discrepency (Scheme 5.5B). The bis-allylated **5.18** was also separated and arose from allylation of the enolate of **5.17**, which was generated by deprotonation with lithium amide. Next, the alkene of **5.17** needed to be dehomologated and converted into a leaving group. Disappointingly, cleavage by ozonolysis or OsO_4 led to heavy

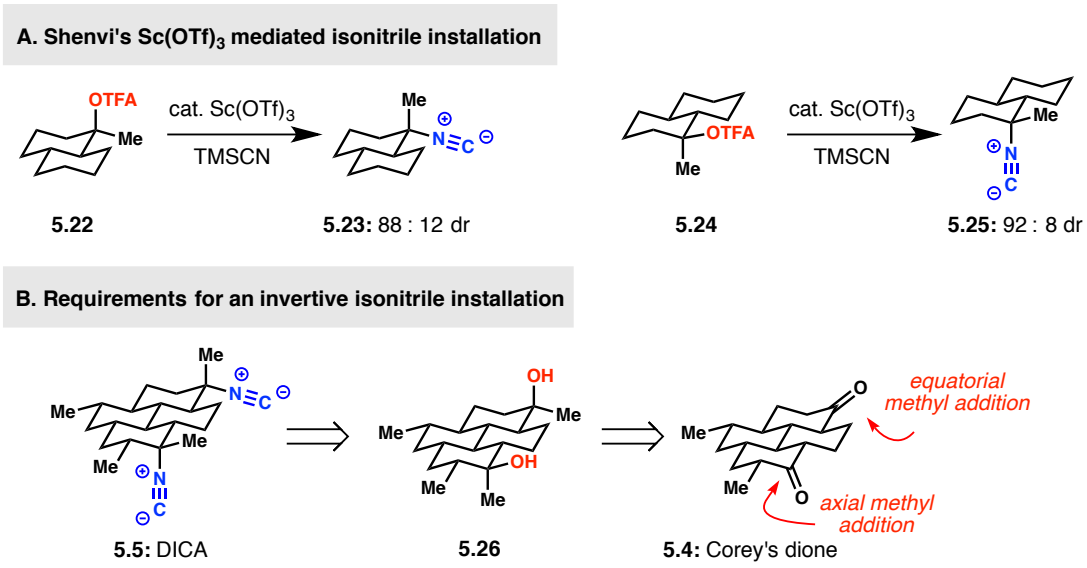
mixtures of compounds that were unable to be carried forward, even in crude form through the aldol condensation.

5.3.2 Considering a $Sc(OTf)_3$-Mediated Isonitrile Installation to 7,20-Diisocyanoadociane

Concurrent with the success in generating all-*trans* ring fusions (Scheme 5.5), the endgame isonitrile installation began to be considered. At the outset of this project, a path through Corey's dione was sought; however, during the course of these studies, Shenvi[14,15] disclosed an invertive displacement of tertiary trifluoroacetates with TMSCN using $Sc(OTf)_3$ as an elegant and selective advancement to the originally used $TiCl_4$[1,16] (Scheme 5.6A). This methodology was applied to the synthesis of 7-isocyano-11(20),14-epiamphilectadiene by Shenvi,[15] and its implementation to DICA quickly became a goal. The selective synthesis of **5.26**, bearing both an axial and an equatorial alcohol is required for this approach (Scheme 5.6B). This challenge could be addressed either by derivatizing Corey's dione **5.4** to **5.26**, or by controlling the axial or equatorial configuration of the tertiary alcohols independently.

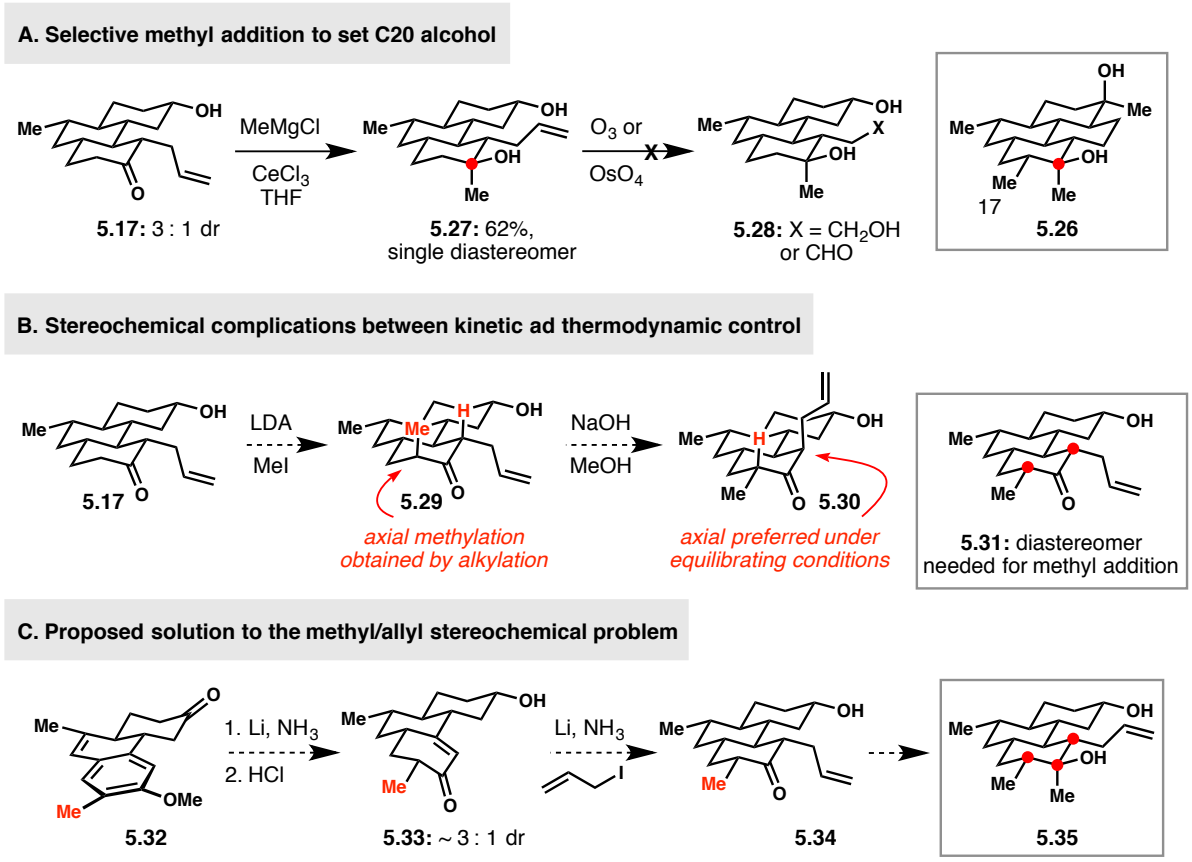
For the current approach, intermediate **5.17** would be appropriate to begin derivatization to diol **5.26** as the C7 and C20 positions are already differentiated (Scheme 5.7). After a screen of MAD,[17] $AlMe_3$,[18] organomanganese reagents,[19] methylmagnesium halide and methyllithium, a clean methyl addition to **5.17** to afford **5.27** was found with methylmagnesium chloride/$CeCl_3$ complex. The unusual axial selectivity presumably arose from the equilibrium between **5.17a** and **5.17b** favoring the boat conformation and thereby presenting only a "convex" face for nucleophile addition (Scheme 5.5B).

Scheme 5.6 Use of an invertive isonitrile synthesis towards DICA.



Although this nucleophilic methyl addition conveniently generates the desired C20 tertiary alcohol, the C17 methyl group in **5.27** is absent and still needs to be installed. Overall, correctly placing this equatorial methyl group is complicated (Scheme 5.7). Alkylation of **5.17** could install the methyl group; however, it would be introduced axial. While equilibrating conditions would reasonably epimerize the methyl group to the equatorial orientation, these same conditions would also epimerize the allyl group axial to form **5.30** (Scheme 5.7B). The stereochemical arrangement of **5.30** precludes methyl addition to the ketone, as there is no manner of correcting the allyl moiety. A proposed solution to this problem could be the incorporation of the C17 methyl group earlier. Although at equilibrium the methyl enone is predicted to arrive at ~2 : 1 dr, the mixture could be advanced through the reductive allylation and methyl addition to generate the stereotriad of **5.35** (Scheme 5.7C). Even though the reduction of 1,2,4,5-tetrasubstituted anisoles was previously problematic (Chapter 4), this idea was still pursued.

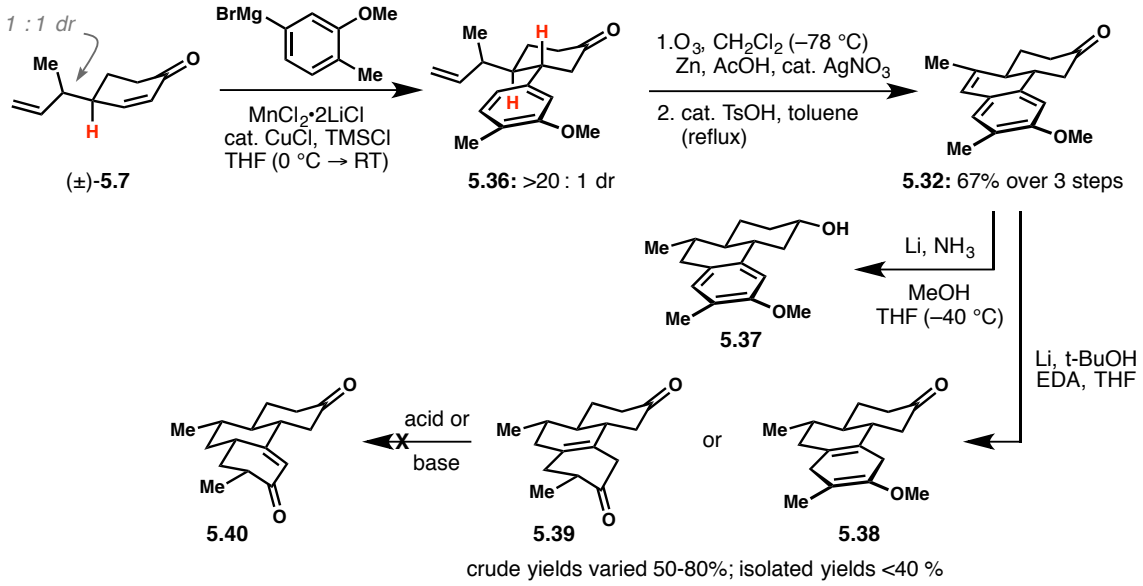
Scheme 5.7 Exploring options for a selective diol synthesis.



Cuprate addition into enone **5.7** using Cahiez organomanganate[19] conditions afforded cleaner conversion to **5.36** than previously under Reetz[10] conditions and was advantageous in carrying **5.36** forward without purification (Scheme 5.8). Ozonolysis and quench by zinc reduction also facilitated in moving the aldehyde through the Friedel–Crafts cyclodehydration in crude form. Dihydronaphthalene **5.32** was thus generated in 67% yield over three steps with a single purification, an advantage over the three purifications previously required. At this point, dissolving metal reduction using Li/NH_3 and methanol once again failed to reduce the aromatic moiety as had been previously observed with the *cis*-diastereomer of **5.32** (see Chapter 4). The ethylene diamine conditions[20] adapted in Chapter 4 performed just as expected and reduced the dihydronaphthalene successfully, but not the ketone of **5.32**. Depending on the workup

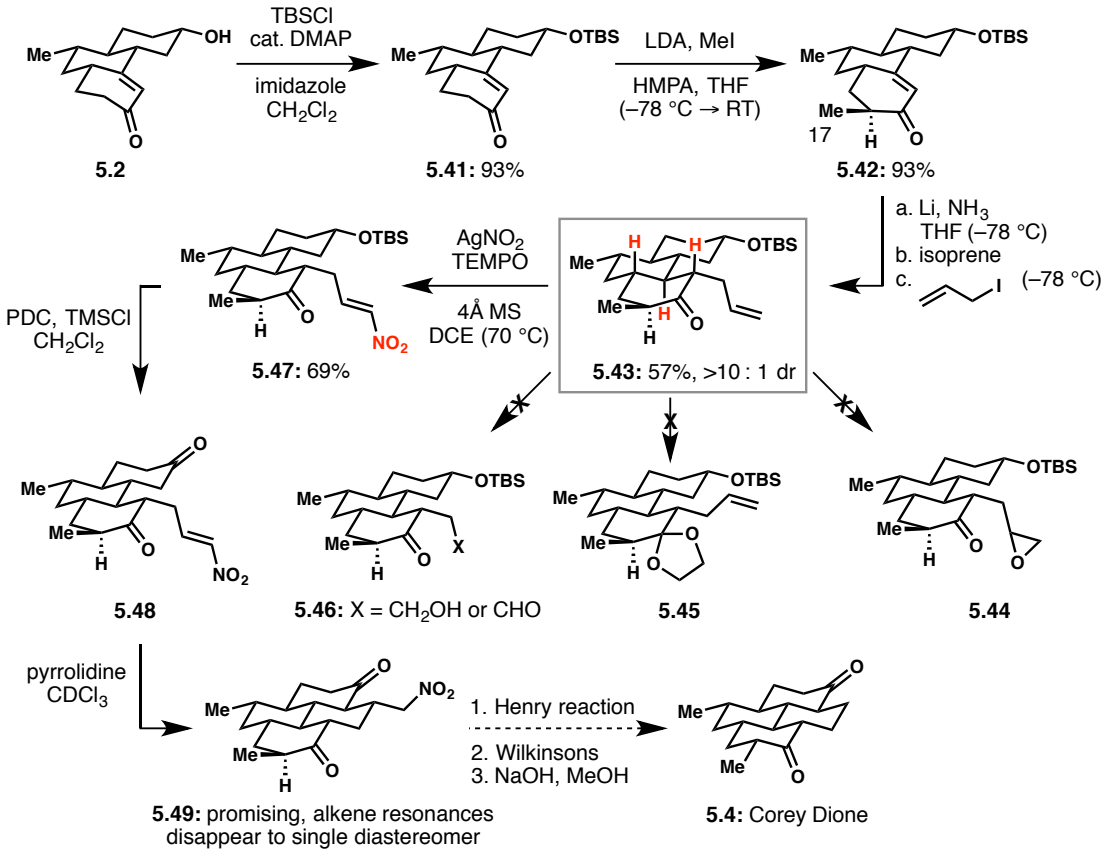
conditions, either the cyclohexadiene **5.38** (using aqueous NH_4Cl) or the skipped enone **5.39** (using aqueous HCl) could be isolated, although both in relatively low yields. A short screen of acidic and basic conditions did not effectively provide the desired conjugated enone and therefore attention was turned to methyl group installation by enone alkylation.

Scheme 5.8 Efforts to install the C17 methyl group from the aromatic Grignard reagent.



The alcohol of **5.2** was protected and the methyl group was installed by action of LDA and methyl iodide (Scheme 5.9). At this point, no effort was made in addressing the strategy of targeting diol **5.26** for the $Sc(OTf)_3$ mediated TMSCN displacement methodology (Scheme 5.7C); instead, the C20 ketone was maintained for another charge to Corey's dione **5.4**. Enone reduction with carefully measured equivalents of Li followed by allylation afforded **5.43** with excellent diastereocontrol.

Scheme 5.9 C17 Methyl installation by alkylation and subsequent ring closure strategies.



Tricycle **5.43** became the platform for numerous ring closure attempts. Epoxidation with mCPBA, DMDO or trifluoroperoxyacetic acid led only to multiple unidentifiable products. Under standard ketal protection conditions (TsOH in refluxing benzene), **5.43** was recovered unchanged, while toluene at reflux afforded several unidentified compounds. Similarly to the previous attempts on **5.20**, ozonolysis or dihydroxylation and diol cleavage of **5.43** also formed multiple unidentified products.

A reaction that functioned surprisingly well in this context was radical alkene nitration. Several conditions[21–24] were tried but the most successful procedure[25] involved heating a sealed vial without rigorous exclusion of air or moisture, containing substrate, excess $AgNO_2$, excess TEMPO, molecular sieves and DCE at 70 °C for 30 hours. At this point deprotection of the tert-

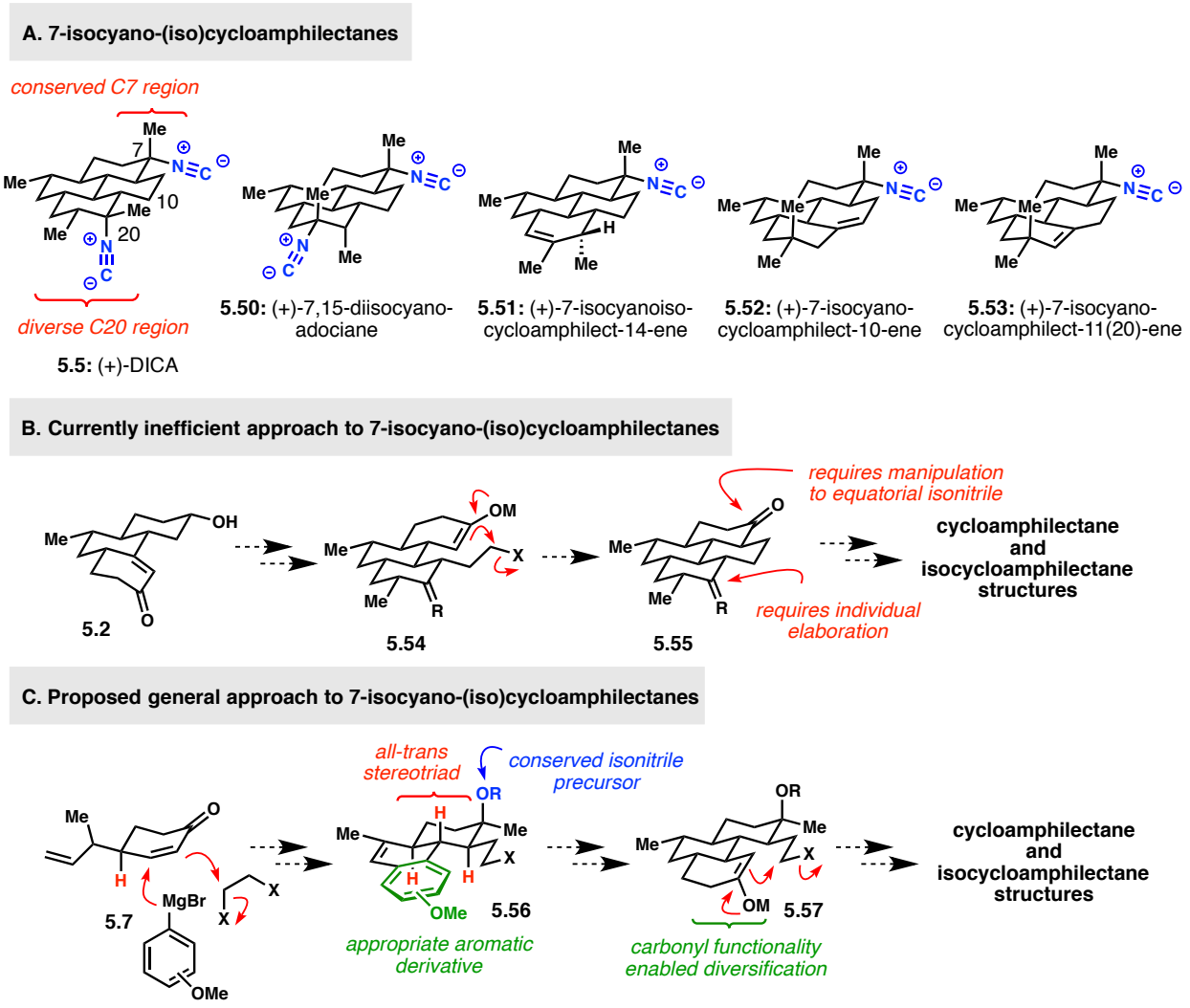
butyldimethylsilyl group failed using TBAF, aqueous HCl, TsOH or HF. The sensitive nitroalkene most likely complicated this operation. Luckily, in situ generated trimethylsilyl chlorochromate[26] was successful in direct deprotection and oxidation to **5.47**. Only one conjugate addition was attempted with the small quantities of material obtained. Addition of pyrrolidine to **5.48** in $CDCl_3$ led to almost immediate disappearance of the alkene resonances by ^1H NMR to afford a single diastereomer of an enamine-containing compound of unknown structure. Although this result was likely a first success in forging the tetracyclic scaffold of DICA, at this point a broader analysis of the ICT family[27] was performed and a slightly modified, more global approach was given attention.

5.4 A Global Approach to 7,20-Diisocyanoadociane and Other (Iso)Cycloamphilectanes

5.4.1 The Evolution to a C10–C11 Ring Closing Strategy

The close structural similarity in ICT natural products provides an opportunity not just to synthesize a single member, but instead to develop a more general approach. A number of cycloamphilectanes and isocycloamphilectanes exhibit a conserved C7 region and a diversified C20 region (Scheme 5.10A). A general approach would rest on a common advanced intermediate, from which **5.5**, **5.50**–**5.53** are accessed. The current C8–C9 ring closing approach to DICA requires a late stage manipulation of both the C7 and C20 regions to access (iso)cycloamphilectanes since a ketone at C7 is essential for ring closure (Scheme 5.10B). Ideally, an advanced common intermediate should contain a conserved C7 isonitrile precursor and appropriate functionality to diversify the C20 region (Scheme 5.10C). A C7 axial tertiary alcohol would be ideal as an isonitrile precursor since $Sc(OTf)_3$ and TMSCN could readily install the equatorial isonitrile.[14,15] A possible structure that meets these requirements is **5.56**.

Scheme 5.10 Cycloamphilectane and isocycloamphilectanes with a conserved C7 and diverse C20 region.

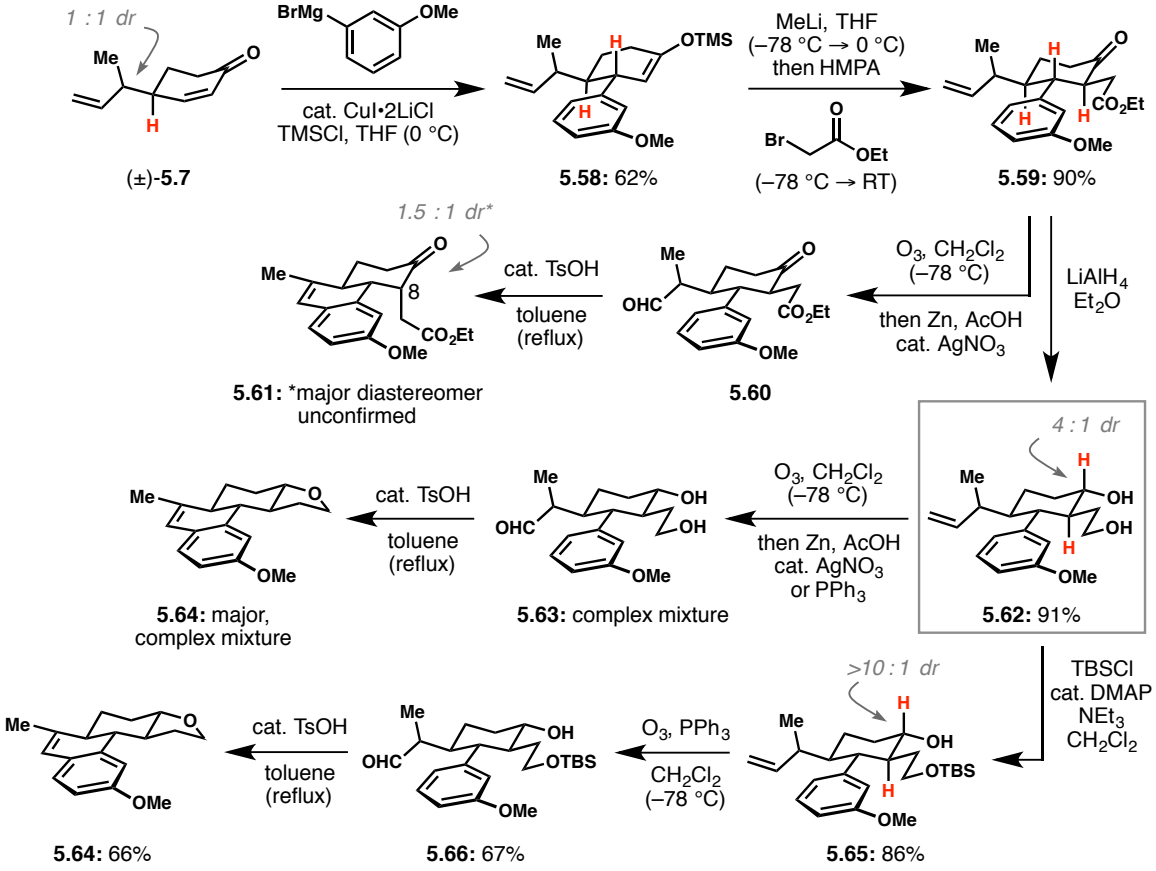


Using a tertiary alcohol at C7 has several advantages (Scheme 5.10C). First, this idea requires revising the ring closing location to the C10–C11 bond, suggesting the key dihydronaphthalene intermediate **5.56** could be obtained via a vicinal difunctionalization of **5.7**. Also, the C7 tertiary alcohol locks the all-*trans* stereotriad generated by vicinal difunctionalization and enables selective manipulation of the C20 region to **5.5**, **5.50**–**5.53**. A first proof-of-principle synthesis to determine the feasibility of this approach would be access to Corey's dione **5.4**.

5.4.2 A Proof-of-Principle Preparation of a Perhydropyrene Relevant to 7,20-Diisocyanoadociane

A unified approach to (iso)cycloamphilectane was initiated by examining the vicinal difunctionalization of **5.7** (Scheme 5.11). The enoxysilane generated upon cuprate addition could be retained with careful workup and purification using Florisil® silica gel column chromatography. Revealing the free enolate of **5.58** was accomplished with MeLi and alkylation with ethyl bromoacetate accessed **5.59** in >20:1 selectivity for the all-*trans* stereotriad. Ozonolysis and acid-mediated cyclodehydration generated the required carbon skeleton of **5.61**, but in 1.5 : 1 dr. The acidic conditions caused epimerization of the C8 position[13] to avoid negative steric interaction between the aromatic and ester side chain. This epimerization issue was resolved by reducing **5.59** to diol **5.62**. Ozonolysis of **5.62** led to a complex mixture of products that could be taken on in crude form to the Friedel–Crafts cyclodehydration. However, instead of obtaining the expected dihydronaphthalene bearing a diol, **5.64** was isolated; the diol had condensed to a THF ring. Trying to avoid this acid mediated cyclization, the primary alcohol of **5.62** was TBS protected. Mono-TBS ether **5.65** was taken through the sequence, but was also found to cyclize to THF **5.64**. Although other protecting group schemes could be devised, the diol's propensity to cyclize indicated a path forward.

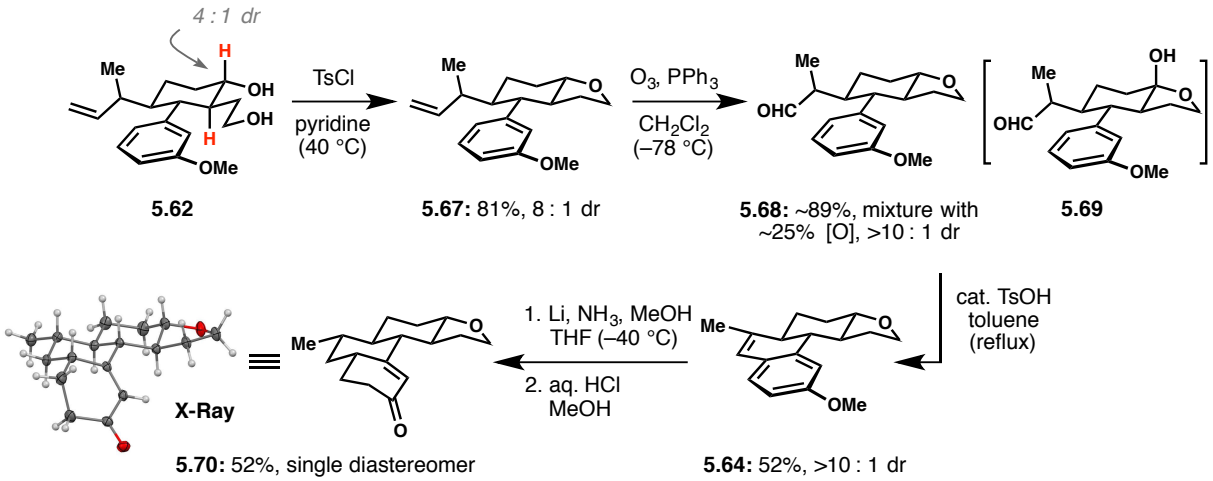
Scheme 5.11 Exploring the reactivity after a vicinal difunctionalization.



Capitalizing on the inherent reactivity of the molecule, the diol was intentionally condensed into a THF ring. This diol masking strategy enabled a smooth transformation through the Birch reduction phase (Scheme 5.12). Tosylation of the primary alcohol and intramolecular displacement generated the *trans*-perhydrobenzofuran **5.67**. Ozonolysis of this compound provided the desired aldehyde **5.68**, but contaminated with an unknown oxidation product. Retrospectively, this could be the C–H oxidized **5.69** (see Section 5.4.3 for more details). Cyclodehydration of **5.68** in the usual way generated dihydronaphthalene **5.64** that was subjected to Birch reduction and isomerization to readily afford **5.70** in excellent diastereocontrol. X-ray crystallographic analysis confirmed the structure of **5.70**. With the general reactivity established, but seeking to avoid the tedious intermediacy of enoxysilane **5.58**, the procedure was optimized

(Scheme 5.13).

Scheme 5.12 An initial procedure through a successful Birch reduction.



5.62

5.67: 81%, 8 : 1 dr

5.68: ~89%, mixture with ~25% [O], >10 : 1 dr

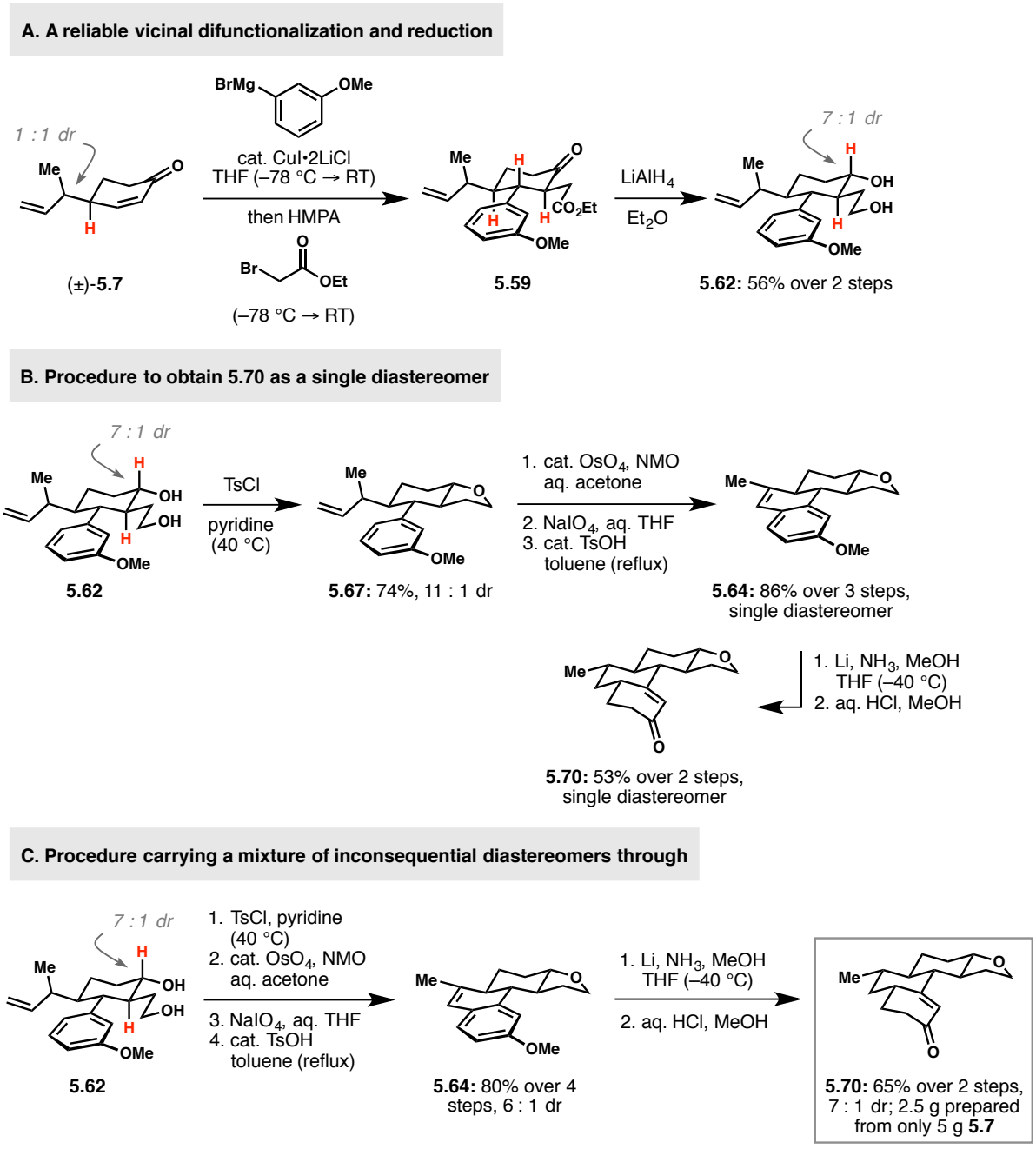
5.69

5.70: 52%, single diastereomer

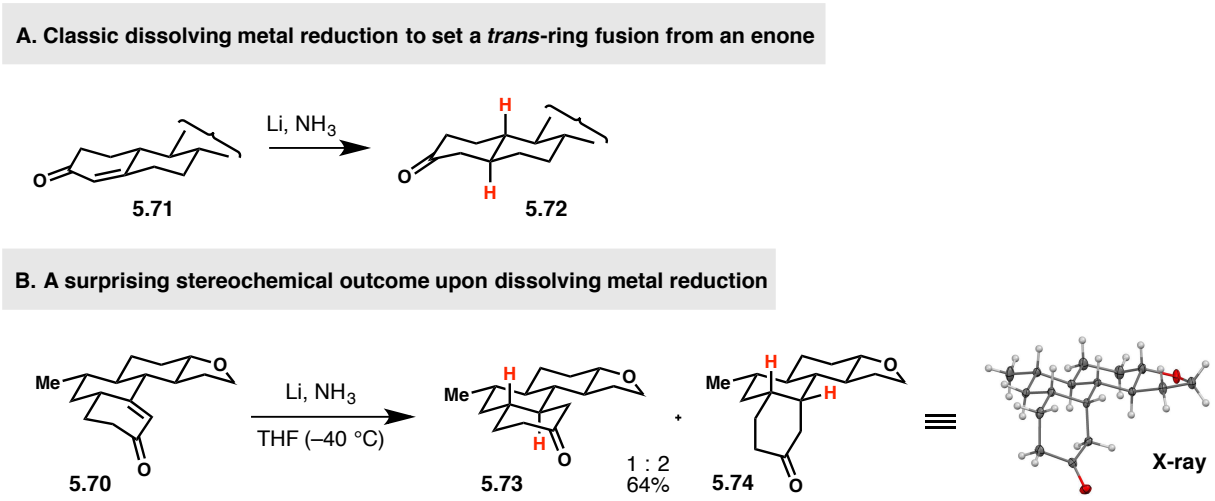
5.64: 52%, >10 : 1 dr

Conjugate addition of 3-methoxymagnesium bromide operated effectively without added TMSCl (Scheme 5.13A). The obtained enolate was alkylated with ethyl bromoacetate, but required 30 hours at room temperature for satisfactory conversion. Reduction of the crude reaction product with $LiAlH_4$ provided diol **5.62** in an improved 7 : 1 dr, most likely because of the residual HMPA. At this point two options exist for generating **5.70**. The first involved enriching the major diastereomer over the course of multiple steps to eventually arrive at **5.70** as a single diastereomer (Scheme 5.13B). Since for this first foray of targeting Corey's dione **5.4** the C7 alcohol[13] epimer is inconsequential, both diastereomers can also be carried through to **5.70** (Scheme 5.13C).

Scheme 5.13 An optimized vicinal difunctionalization and subsequent synthetic elaboration.



Scheme 5.14 Another unexpected stereochemical outcome from a dissolving metal reduction.

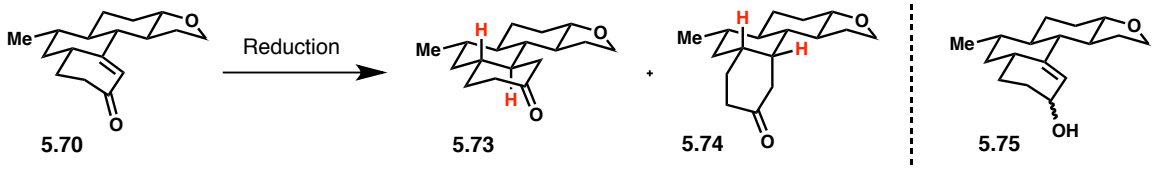


The next step of reducing enone **5.70** was expected to be accomplished with Li/NH_3, as it is widely used to generate *trans*-decalin ring junctions (Scheme 5.14A).[11,12,28] Surprisingly, treating **5.70** with Li/NH_3 afforded a 2 : 1 mixture of ketones, favoring the *cis*-ring junction **5.74** (Scheme 5.14B). Further exploring the reducing metal did not change the selectivity dramatically (Table 5.1, entries 1–2), while adding a bulky proton source simply improved *cis*-selectivity (entry 3). Selecting for the *trans*-ring fusion proved challenging in this case, most likely due to the *syn*-pentane interaction present in the key reduction intermediate (Figure 5.1). Homogeneous hydride reagents such as Karstedt's catalyst[29] and t-BuCu/DIBAl enhanced the *cis*-selectivity, even though the latter is exceptional in providing *trans*-selectivity in other decalin systems[30] and the Hajos–Parrish ketone[31] (entries 5–6). Fortunately, heterogeneous reducing agents provided mixtures significantly enriched in the *trans* product **5.73** (entries 7–9). A small screen of hydrogenation catalysts led to the discovery that reductions with Rh/C were highly *trans*-selective (15 : 1 dr). High-pressure reductions with Pt/C and Ru/C fared poorly, giving trace reaction or the allylic alcohol **5.75**.

Since the *trans*-reduction of **5.70** using Rh/C provided high selectivity, only two more

transformations are required: (1) THF ring opening and alkylation and (2) installation of the C17 methyl group by alkylation (Scheme 5.15).

Table 5.1 Optimizing for a *trans*-reduction of enone **5.70**.

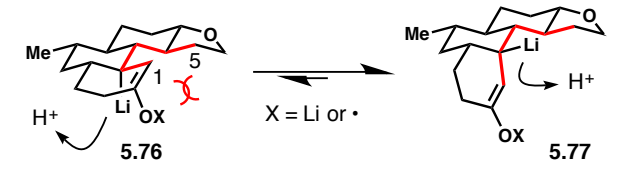


5.70 5.73 5.74 5.75

Entry	Reduction	Yield[a]	5.73: *trans*		5.74: *cis*
1	Na, NH_3, THF (–78 °C)	**85%**	**1**	**:**	**1**
2	K, NH_3, THF (–78 °C)	**82%**	**1**	**:**	**1**
3	K, t-BuOH, NH_3, THF (–78 °C)	**80%**	**1**	**:**	**3**
4	Mg, MeOH	**decomposition**			
5	1. cat. Karstedt, Et_3SiH (70 °C) 2. TBAF, THF	**92%**	**1**	**:**	**5**
6	t-BuCu, DIBAlH, HMPA, THF (–50 °C)	**86%**	**1**	**:**	**>20**
7	H_2 balloon, Pd/C, EtOAc	**94%**	**6**	**:**	**1**
8	400 psi H_2, Rh/alumina, EtOAc[b]	**93%**	**8**	**:**	**1**
9	500 psi H_2, Rh/C, EtOAc[b]	**93%**	**15**	**:**	**1**
10	1300 psi H_2, Pt/C, EtOAc	**trace**			
11	1300 psi H_2, Ru/C, EtOAc	**5.75 as major**	**~10**	**:**	**1**

[a] Yield of purified material after column chromatography [b] 2. PCC, Celite, CH_2Cl_2

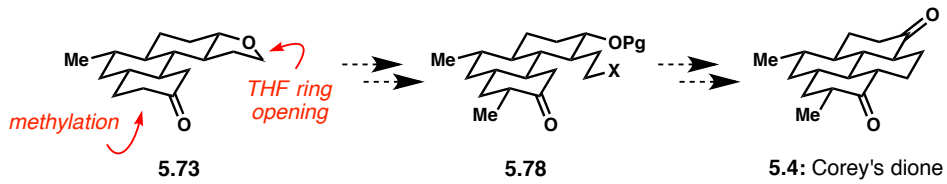
Figure 5.1 Comparison of protonation events to explain the preference for *cis*-reduction.



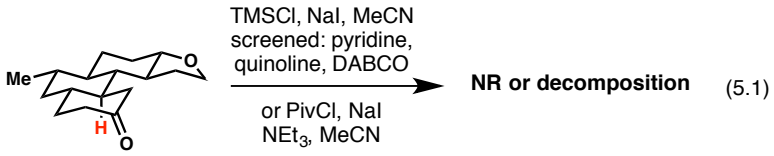
5.76 5.77

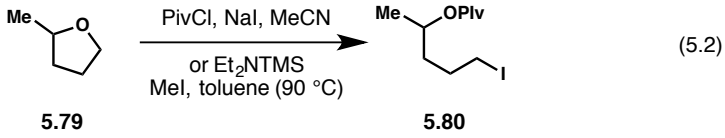
towards *trans*-protonation towards *cis*-protonation

Scheme 5.15 Remaining requirements to complete Corey's dione.



The planned THF ring opening was to be facilitated by a Lewis acid/nucleophile combination.[32–41] Only a couple conditions were screened, and were unsuccessful in opening the THF ring of **5.73** (Equation 5.1). Evaluating select conditions on 2-methyltetrahydrofuran (**5.79**) showed success only at concentrations of 1 Molar and on greater than 0.5 mmol scale (Equation 5.2). At the time, large quantities of **5.73** were not available and the material on hand was considered too precious to commit. A nucleophilic ring opening, a C–H oxidation and reductive ring opening advancement was pursued instead.



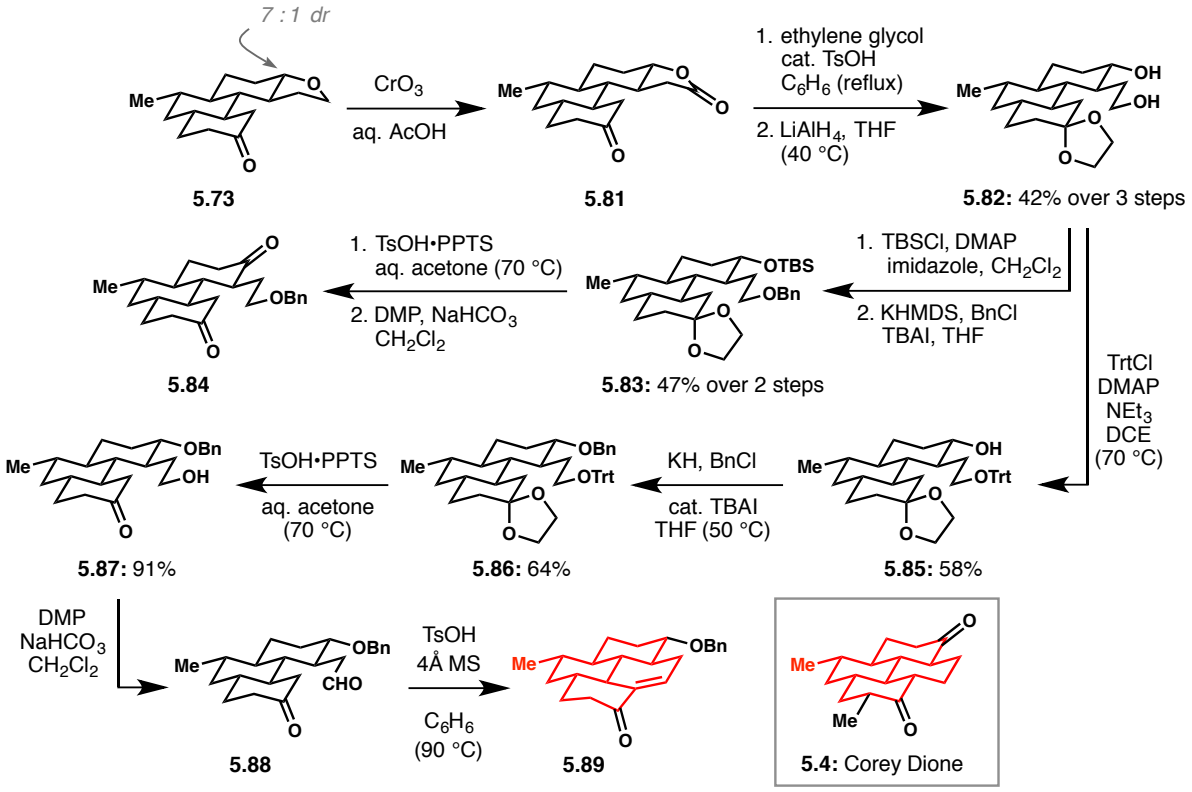


One of the first C–H oxidation reactions transforming **5.73** to lactone **5.81** was successful (Scheme 5.16). Stirring **5.73** in the presence of a slight excess of CrO_3 in aqueous acetic acid (Fieser's reagent) afforded **5.81**.[42] The C20 ketone[13] was protected and the lactone opened with $LiAlH_4$ to generate diol **5.82**. At this point the secondary diol needed to be protected. A scheme involving double protection followed by deprotection of the primary alcohol was envisioned. Silylation of the primary alcohol followed by benzyl protection smoothly generated **5.83**. It was discovered after continuing with the sequence that the TBS group migrated to the secondary

alcohol during benzyl protection. Deprotection of **5.83** with buffered acid and oxidation afforded a ketone and not an aldehyde carbonyl.

The successful sequence started with a trityl protection of **5.82**, followed by benzyl protection. Then, acidic conditions deprotected both the trityl and ketal groups to afford **5.87**. The fourth ring was cyclized by alcohol oxidation and then aldol condensation between the C20 ketone and C10 aldehyde to afford enone **5.89** in sub-milligram quantities.[13] This marks the preparation of all four rings of DICA in the all-*trans* relationship by means of a dihydronaphthalene reduction route.

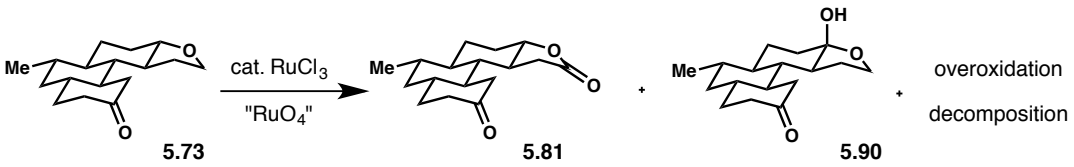
Scheme 5.16 A successful fourth ring closure.



5.4.3 Improving the THF C–H Oxidation to a Butyrolactone

The C–H oxidation to lactone **5.81** was a low yielding reaction with CrO_3 and required improvement.[43] A standard method of THF to lactone oxidation is the use of RuO_4.[44,45] A number of different conditions were tried, but unfortunately none was more effective than Fieser's reagent (Table 5.2). Although all reactions supposedly generate RuO_4, each set of conditions provided a different product profile. In addition to lactone **5.81**, competitive oxidation provided lactol **5.90** and three other oxidation products in variable quantities. A general trend showed that more polar organic reaction media favored formation of **5.90**, while the less polar CCl_4 generated parity between **5.81** and **5.90** without preference. Inexplicably, co-oxidant H_5IO_6 led to complete formation of lactone **5.81**; however, heavy side oxidation was problematic (entry 6). Overall, the choice of co-oxidant impacted not only product distribution but also side product formation. These results are a curious anomaly since all reagent combinations should form the same "RuO_4" and would be predicted to react identically.

Table 5.2 Screening RuO_4 mediated THF C–H Oxidations.



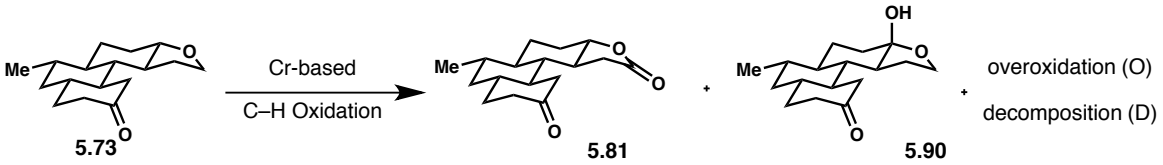
5.73 5.81 5.90

Entry	Conditions	SM[a]	5.81	5.90	5.81 : 5.90	Unidentified Products A, B & C		
	EtOAc, MeCN aq. Na_2EDTA							
1	$NaHCO_3$, oxone	20%	15%	50%	1 : 3.3			15%
2	$NaHCO_3$, $NaIO_4$	8%	21%	71%	1 : 3.4			trace
	CCl_4, aq. MeCN							
3	$NaHCO_3$, oxone	45%	13%	32%	1 : 2.5			10%
4	$NaHCO_3$, $NaIO_4$	10%	33%	33%	1 : 1			24%
5	$NaHCO_3$, NaOCl		33%	67%	1 : 2			trace
6	H_5IO_6		16%		>20 : 1	26%	57%	
7	$NaHCO_3$, $NaIO_4$ aq. acetone	59%	7%	34%	1 : 4.9			
8	$Pb(OAc)_4$, aq. AcOH	46%				18%	36%	

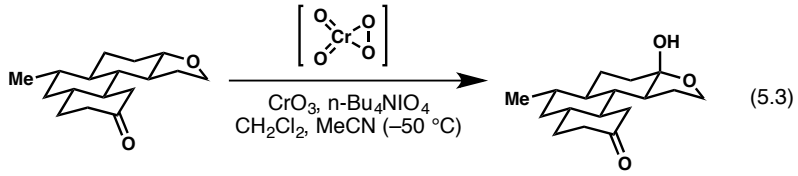
[a] Percentages were obtained by ^1H NMR integration without internal standard

Early successes with Fieser's reagent guided the exploration of more Cr-based C–H oxidation conditions.[46] Lactone **5.81** was frequently observed during these studies (Table 5.3), but disappointingly, these reactions were also contaminated with unidentified overoxidation products and general decomposition. From this compilation of oxidations three interesting results are of further note. Jones reagent (CrO_3 in aqueous sulfuric acid) was highly selective in providing only **5.81** without side oxidations. Unfortunately, the reaction was plagued by low conversions and low mass recovery. Only trace reactivity was observed in the absence of sulfuric acid. The Fuchs reagent (chromyl peroxide "CrO_4") selectively and cleanly provided only lactol **5.91** with recovered starting material (Equation 5.3).[47] No other oxidation products or decomposition was observed. Alternatively, concentrated Fieser's reagent dissolved in $MeNO_2$ improved the yield of **5.81** to 38% (Equation 5.4). The increased yield is most likely to due to the ease with which $MeNO_2$ is worked up rather than improvement in the course of the oxidation.

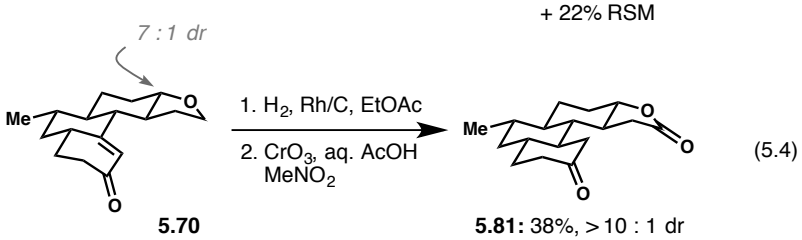
Table 5.3 A Cr-based screen for C–H oxidation.



Entry	Conditions	Results	Corresponding Literature
1	CrO_3, aq. AcOH in MeCN, acetone, DMF, C_6H_6, CH_2Cl_2 or $MeNO_2$	**5.81**, O, D	among others: Wettstein, A.; Mischer, K. *Helv. Chim. Acta* **1942**, *25*, 718
2	CrO_3, aq. H_2SO_4 in AcOH, MeCN, acetone, Et_2O, CH_2Cl_2, C_6H_6 or $MeNO_2$	**5.81**, D	among others: (1) Brown, H. C.; Garg, C. P.; Liu, K.-T. *J. Org. Chem.* **1971**, *36*, 387 (2) Kropp, P. J.; Worsham, P. R.; Davidson, R. I; Jones, T. H. *J. Am. Chem. Soc.* **1982**, *104*, 3972
3	CrO_3, Ac_2O, C_6H_6 (up to reflux)	D	Frauenrath, H.; Philipps, T. *Liebigs Ann. Chem.* **1985**, 1951
4	CrO_3, $TMSONO_2$, MeCN, CH_2Cl_2	**5.81**, O, D	Shahi, S. P.; Gupta, A.; Pitre, S. V.; Reddy, M. V. R.; Kumareswaran, S.; Vankar, Y. D. *J. Org. Chem.* **1999**, *64*, 4509
5	CrO_3, pyridine, DCE (up to 50 °C)	NR	Okabe, M.; Abe, M.; Tada, M. *J. Org. Chem.* **1982**, *47*, 1775
6	CrO_3, 3,5-DMP, CH_2Cl_2 (–20 °C up to RT)	**5.81**, O, D	Salmond, W. G.; Barta, M. A.; Havens, J. L. *J. Org. Chem.* **1978**, *43*, 2057
7	PCC, H_5IO_6, MeCN	**5.81**, O, D	Piccialli, V.; Zaccaria, S.; Oliviero, G.; D'Errico, S.; D'Atri, V.; Borbone, N. *Eur. J. Org. Chem.* **2012,** 4293
8	PCC, Celite, C_6H_6 (reflux)	NR	
9	PDC, t-BuO_2H, C_6H_6	**5.81**, O, D	Chidambaram, N.; Chandrasekaran, S. *J. Org. Chem.* **1987**, *52*, 5048
10	CrO_3, n-Bu_4NIO_4, CH_2Cl_2, MeCN (–50 °C)	**5.90**	Lee, S.; Fuchs, P. L. *Org. Lett.* **2004**, *6*, 1437

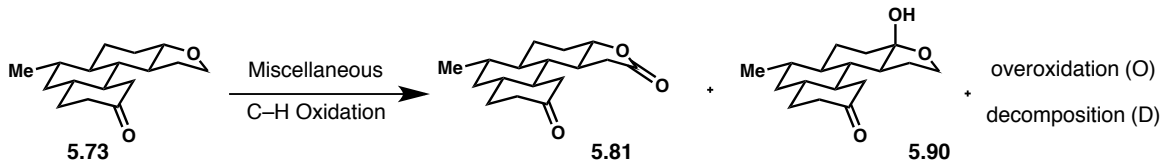


(5.3)



(5.4)

Table 5.4 Miscellaneous C–H oxidation attempts to install a lactone functionality.



5.73 **5.81** **5.90**

Entry	Conditions	Results	Corresponding Literature
1	$Pb(OAc)_4$, C_6H_6 (reflux)	NR	
2	$KMnO_4/CuSO_4 \cdot 5H_2O$ w/ and w/out alumina CH_2Cl_2, DCE, neat (up to reflux)	1 : 2 to 1 : 1 **5.81** / **5.90** O, D	among others: Zhao, D.; Lee, D. G. *Synthesis* **1994**, 910
3	O_3, SiO_2	**5.81**, O, D	Cohen, Z.; Keinan, E.; Mazur, Y.; Varkony, T. H. *J. Org. Chem.* **1975**, *40*, 2141
4	$CoCl_2$ or $Co(acac)_3$, O_2 DME (reflux)	NR	Reetz, M. T.; Töllner, K. *Tetrahedron Lett.* **1995**, *36,* 9461
5	$PhI(OAc)_2$, t-BuO_2H, $MeNO_2$	D	Zhao, Y.; Ang, J. Q. L.; Ng, A. W. T.; Yeung, Y.-Y. *RSC Adv.* **2013**, *3*, 19765
6	$Ca(OCl)_2$ AcOH, MeCN	D	Nwaukwa, S. O. ; Keehn, P. M. *Tetrahedron Lett.* **1982**, *23*, 35
7	$KBrO_3$, $NaHSO_4$ aq. CH_2Cl_2	NR	Metsger, L.; Bittner, S. *Tetrahedron* **2000**, *56*, 1905
8	TFDO, aq. MeCN (0 °C)	**5.90**, D	Curci, R.; D'Accolti, L.; Fiorentino, M.; Fusco, C.; Adam, W.; González-Nuñez, M. E.; Mello, R. *Tetrahedron Lett.* **1992**, *33*, 4225

A variety of conditions that are not Ru or Cr-based are also known to provide THF oxidation (Table 5.4). A handful of these were screened in the context of **5.73**. Strong oxidants like $KMnO_4$ once again competitively underwent 3° C–H oxidation to lactol **5.91** (Entry 2). In situ generated TFDO oxidized **5.73** to only **5.91**, although not as cleanly as with CrO_4 (Equation 5.3). After having spent effort evaluating a wide variety of C–H oxidation reactions, CrO_3 in acetic acid and $MeNO_2$ could be considered as the currently optimal conditions.

5.4.4 Finishing the Synthesis of Corey's Dione

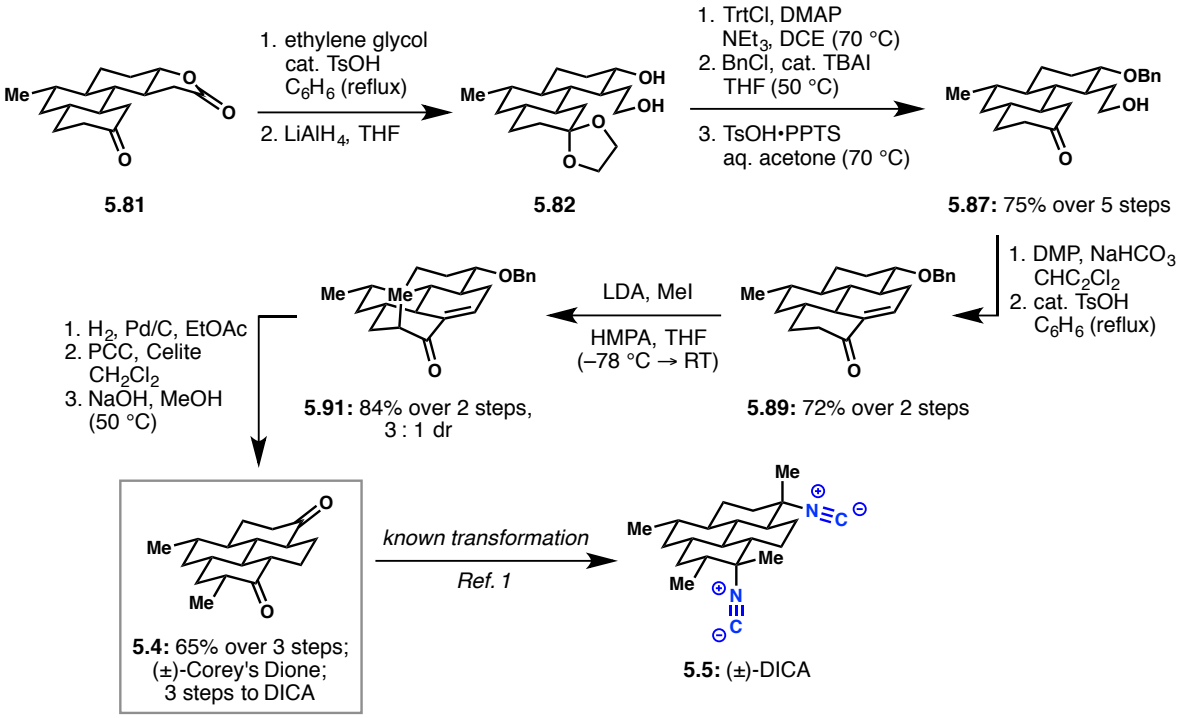
An improved preparation of **5.89** and completion of Corey's intermediate was pursued next (Scheme 5.17). The first improvement was the conversion of **5.81** to **5.87** without intermediate purification. The alcohol oxidation and acid-mediated aldol condensation afforded

enone **5.89** efficiently. The cross-conjugated dienolate derived from enone **5.89** was methylated with a moderate axial preference; after enone hydrogenation/benzyl ether hydrogenolysis and oxidation of the C7 alcohol, base-mediated equilibration afforded Corey's dione **5.4**. Access to this target, completed a formal synthesis of racemic DICA.

Corey's intermediate was prepared in a total of 24 steps and a longest linear sequence of 24 steps from commercially available crotyl alcohol and tri(ethyleneglycol) divinyl ether. Highlights of this synthesis include the telescoping of several steps and the high degree of stereocontrol. Corey's dione **5.4** was prepared using only two distillations and eight chromatographic purifications. Excellent relative stereochemical control at all eight centers of the perhydropyrene scaffold was obtained; all stereocenters were introduced with >20 : 1 dr, except C12 which was installed in 15 : 1 dr. The 1.7% overall yield from commercial material is unoptimized. To date this report is the shortest and most selective synthesis of DICA. Introduction of the isonitriles has not been attempted, but was described by Corey.[1] This synthesis affirms that the general design in Scheme 5.10C is useful in preparing the isocycloamphilectane scaffold.

This proof-of-principle synthesis opens several directions for future effort. A top priority was rendering the synthesis enantioselective. Additionally, accessing Corey's dione currently does not selectively generate DICA since the isonitrile installation is not stereorcontrolled. A second-generation synthesis needs to address selective installation of these salient isonitriles. During the next charge, the redox and protecting group steps of the current iteration will need to be reworked. And lastly, the dihydronaphthalene Birch reduction design needs to be applied to other isocycloamphilectanes and cycloamphilectanes.

Scheme 5.17 End game to Corey's Dione.

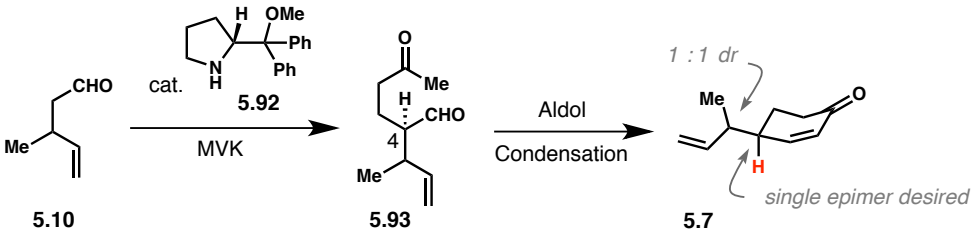


5.5 An Asymmetric Formal Synthesis of (+)-7,20-Diisocyanoadociane

5.5.1 The Asymmetric Robinson Annulation Reaction

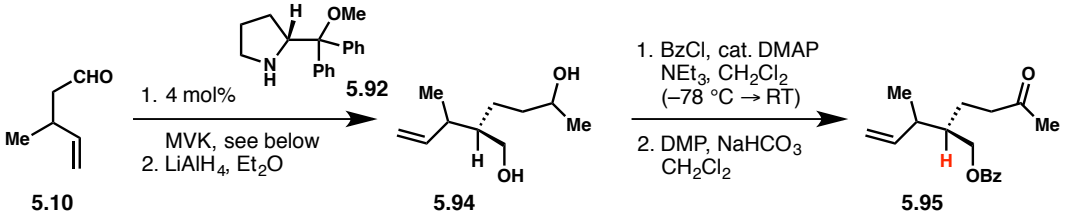
From the outset, the synthesis of DICA was intended to be asymmetric. The attractiveness of generating cyclohexenone **5.7** via Robinson annulation was that its preparation could be rapidly adapted asymmetric via chiral catalysis.[4,8,48–51] Starting from racemic **5.10**, an asymmetric conjugate addition using Gellman's catalyst[4] would set the C4 stereocenter (Scheme 5.18). The complicated part of the annulation is retaining the aldehyde stereocenter while enolizing the methyl ketone for aldol condensation. Several reports indicate that this is a surmountable challenge.[6,8,48,49]

Scheme 5.18 General approach to enantioenriched **5.7**.



A goal for beginning this synthesis was the scalability and operational ease for at least the early steps. This was accomplished for the racemic synthesis of cyclohexenone **5.7** and consisted of two straightforward distillations. The prolinol catalyzed conjugate addition of aldehydes onto vinyl ketones requires significant quantities of catechol additives under the literature conditions. This additional reagent requires removal by column chromatography and was therefore avoided. With this intended divergence from literature conditions, the enantioselectivity of the conjugate addition needed evaluating (Table 5.5).

Table 5.5 Screening the asymmetric conjugate addition reaction.



Entry	Solvent [a]	Conditions [a]	Yield of 5.94	dr (d1 : d2)[b]	Diastereomer 1 (%ee)[b]	Diastereomer 2 (%ee)[b]
1	neat	RT	7%	[c]	[c]	[c]
2	Et_2O	RT	7%	52 : 48	81	84
3	MeOH	RT	24%	[c]	[c]	[c]
4	neat	40 °C	40%	51 : 49	88	89
5	MeOH	40 °C	77%	49 : 51	81	80

[a] MeCN, toluene, EtOAc (RT) gave < 3% yield
[b] Analyzed by chiral HPLC
[c] Chiral HPLC analysis was inconclusive

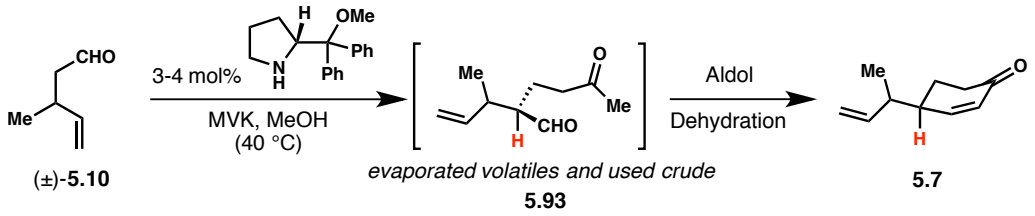
Since removing the catechol significantly suppressed reactivity (Table 5.5, entry 1), a solvent and temperature screen was performed. A spectrum of solvents ranging from non-polar

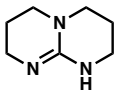
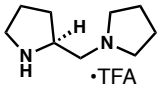
(toluene), medium polarity (Et_2O, EtOAc) to polar (MeCN) and polar protic (methanol) was evaluated. Methanol provided the best reactivity, affording diol **5.94** in 77% yield over 2 steps after immediate $LiAlH_4$ reduction (entry 5). Derivatization to the primary benzoylated product **5.95** and chiral HPLC analysis showed both diastereomers to have ~80% ee. Although the enantiomeric excess was not ideal, a fluorinated version of prolinol catalyst **5.92** has been shown to catalyze conjugate additions to methyl vinyl ketone in 95% ee without catechol additive and could be used instead.[51] At the time, this prolinol catalyst was simply not considered worth the effort to prepare.

With an enantioselective conjugate addition available, the next consideration became retention of the newly forged stereocenter during the intramolecular aldol addition. A number of conditions were tried (Table 5.6). Literature precedent of using catalytic LiOH in isopropanol[8] or phase-transfer conditions of Bu_4NOH in aqueous THF/Et_2O[49] afforded <15% yields and mostly decomposition. Literature conditions of using DBU provided almost complete racemization (entries 1–2).[48] The more basic and nucleophilic TBD slightly improved retention of stereochemistry, but still only provided maximum 46% ee (entries 4–8). The McQuade catalyst was most successful since a good yield of **5.7** was obtained (entry 9), but a 66% ee and an enantiospecificity of 83% was still not satisfactory. The best conservation of stereochemical information was obtained with LDA, but the low yield precluded its further implementation (entry 10).

Although the asymmetric Robinson annulation did not render the synthesis highly enantioselective, this reaction still provided material that was moderately enantioenriched. A more effective asymmetric entry to DICA and thereby the general family of 7-isocyano(iso)cycloamphilectane was still desired.

Table 5.6 Conditions to effect the aldol condensation of enantioenriched Michael adduct **5.93**.



Entry	Aldol	Dehydration	Yield[a]	Diastereomer 1 (% ee / % es)[b]	Diastereomer 2 (% ee / % es)[b]
1	DBU, CH_2Cl_2	then MsCl	59%	4 / 5	6 / 8
2	"wet" DBU, CH_2Cl_2	MsCl, cat. DMAP, NEt_3, CH_2Cl_2	54%	4 / 5	6 / 8
3	TsOH, MeCN		62%	34 / 43	32 / 40
	cat. 				
4	THF	then MsCl, cat. DMAP,NEt_3	59%	32 / 40	34 / 43
5	THF	then Ac_2O, cat. DMAP, NEt_3	66%	32 / 40	32 / 40
6	MeCN	then TsOH	68%	34 / 43	36 / 45
7	CH_2Cl_2	then MsCl, cat. DMAP, NEt_3	56%	34 / 43	36 / 45
8	MeOH	MsCl, cat. DMAP, NEt_3, CH_2Cl_2	55%	46 / 58	46 / 58
9	cat.  •TFA hexanes (RT, 24 h)		62%	66 / 83	66 / 83
10	LDA, THF (–78 °C)	MsCl, cat. DMAP NEt_3, CH_2Cl_2	23%[c]	76 / 95	78 / 98
11	10 mol% t-BuOK THF (0 °C)	MsCl, cat. DMAP NEt_3, CH_2Cl_2	43%	62 / 78	56 / 70

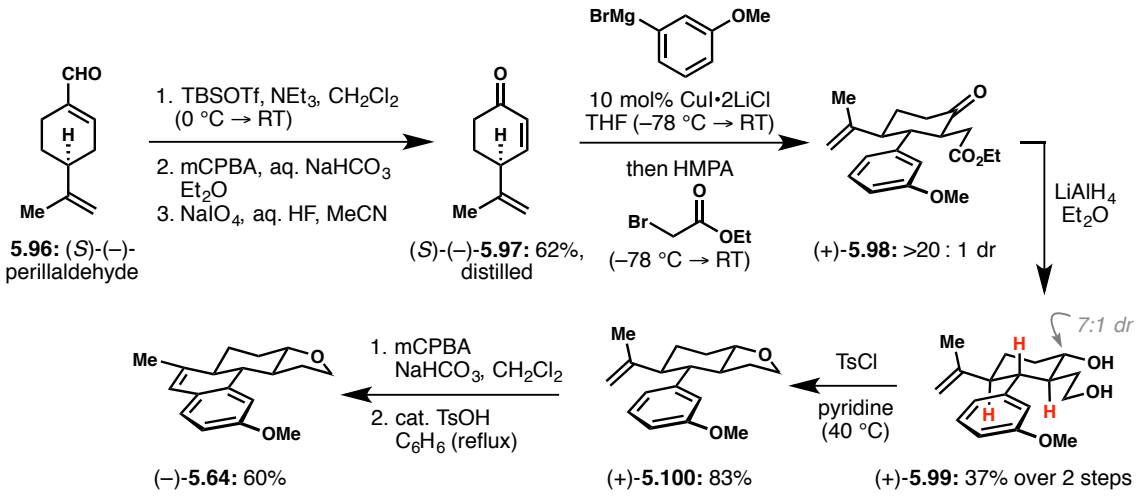
[a] Yields reflect material after silica-gel column chromatography
[b] Analyzed by chiral HPLC; es = [(%$ee_{5.7}$) / (%$ee_{5.95}$)] x 100; dr ~ 1 : 1 for all reactions
[c] 27% Michael adduct isolated

5.5.2 A Perillaldehyde-Based Formal Synthesis

After attempts at improving a less than ideal asymmetric Robinson annulation, a new enantiocontrolled entry was required. Inspiration for a new starting point came from analysis of the synthesis in hand. While the preparation of dihydronaphthalene **5.64** requires an oxidative

cleavage of the alkene, this intermediate aldehyde could instead arise from a dehomologated alkene via oxidation. This insight identified the known cyclohexenone (–)-**5.97**, available in enantiopure form,[52,53] as an attractive starting material. The inexpensive terpene (–)-perillaldehyde's conversion to cyclohexenone (–)-**5.97** on gram scale has been previously reported;[53] however, purification by distillation was preferable to improve throughput (Scheme 5.19).

Scheme 5.19 An enantiospecific formal synthesis of (+)-DICA from (–)-perillaldehyde.



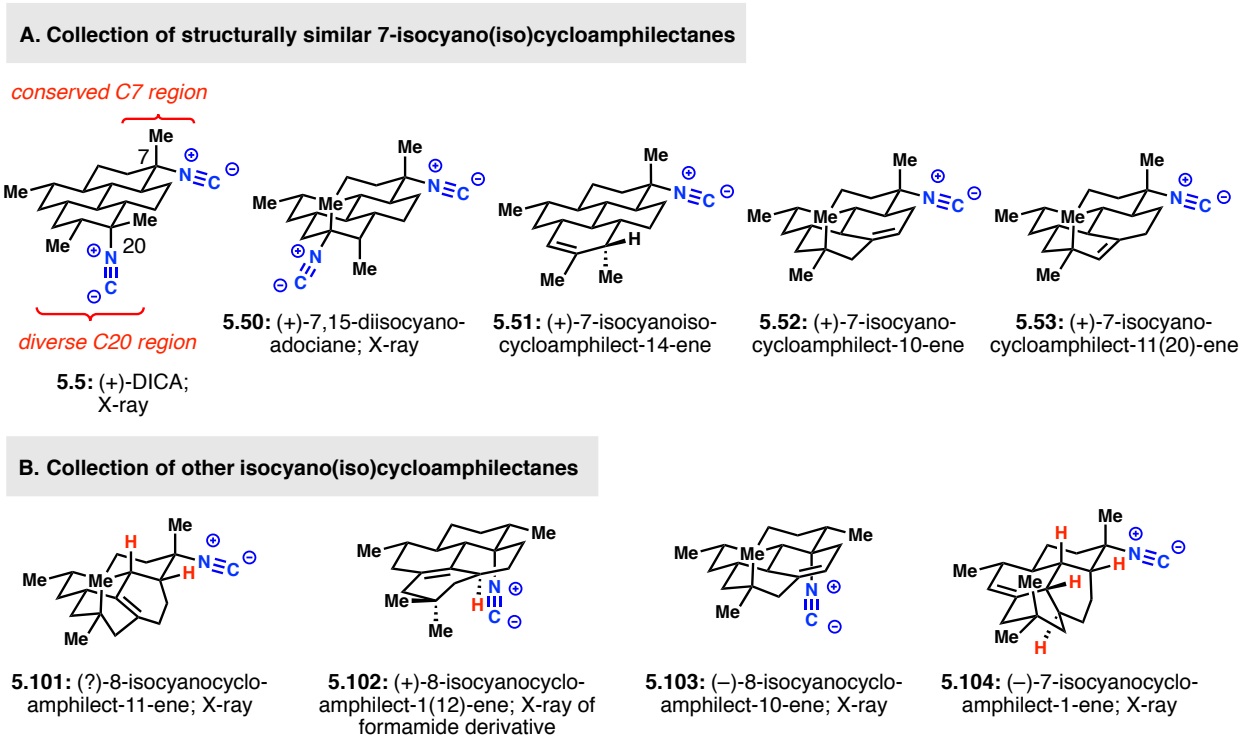
In an unoptimized sequence, conjugate addition and alkylation selectively installed the three stereogenic centers with desired diastereoselectivity as seen in (+)-**5.99**, in a similar manner previously shown to make **5.62**. Condensation of diol (+)-**5.99** via the tosylate furnished *trans*-fused THF (+)-**5.100**. Alkene epoxidation was followed by heating at reflux with acid, which presumably triggered epoxide rearrangement to the aldehyde followed by in situ cyclodehydration to dihydronaphthalene (–)-**5.64**. This sequence intersects the racemic synthesis of DICA described earlier (Section 5.4), permitting access to all later intermediates in enantiopure form. Because of the desire to improve several aspects of the overall synthesis, the

formal synthesis of DICA using this optically active material was not revisited, though it is clear that this chiral pool approach is suitable for doing so with respect both to control of absolute configuration and material throughput concerns. In its current form, this route is still 24 steps in longest linear sequence and total steps from perillaldehyde with only 10 purifications in an unoptimized form.

5.6 Outlook Towards the Synthesis of 7-Isocyano-(Iso)Cycloamphilectanes

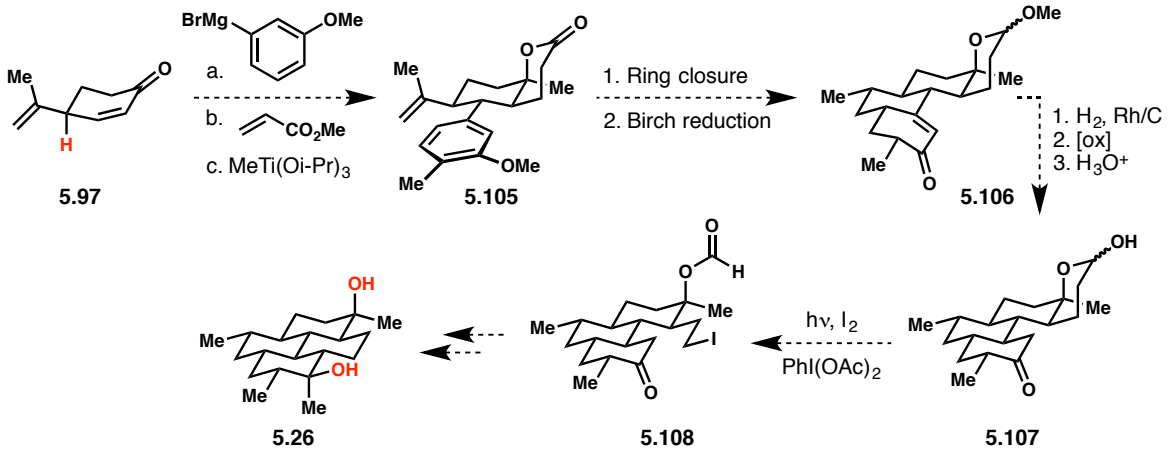
Having accomplished the formal synthesis of DICA in asymmetric form, two directions can be envisioned for this project: (1) adapt the knowledge gained about stereocontrol to a concise synthesis of DICA that includes introduction of the salient isonitriles, and (2) showcase the generality of this approach to other (iso)cycloamphilectane ICTs (Figure 5.2).[27]

Figure 5.2 A collection of (iso)cycloamphilectane natural products.



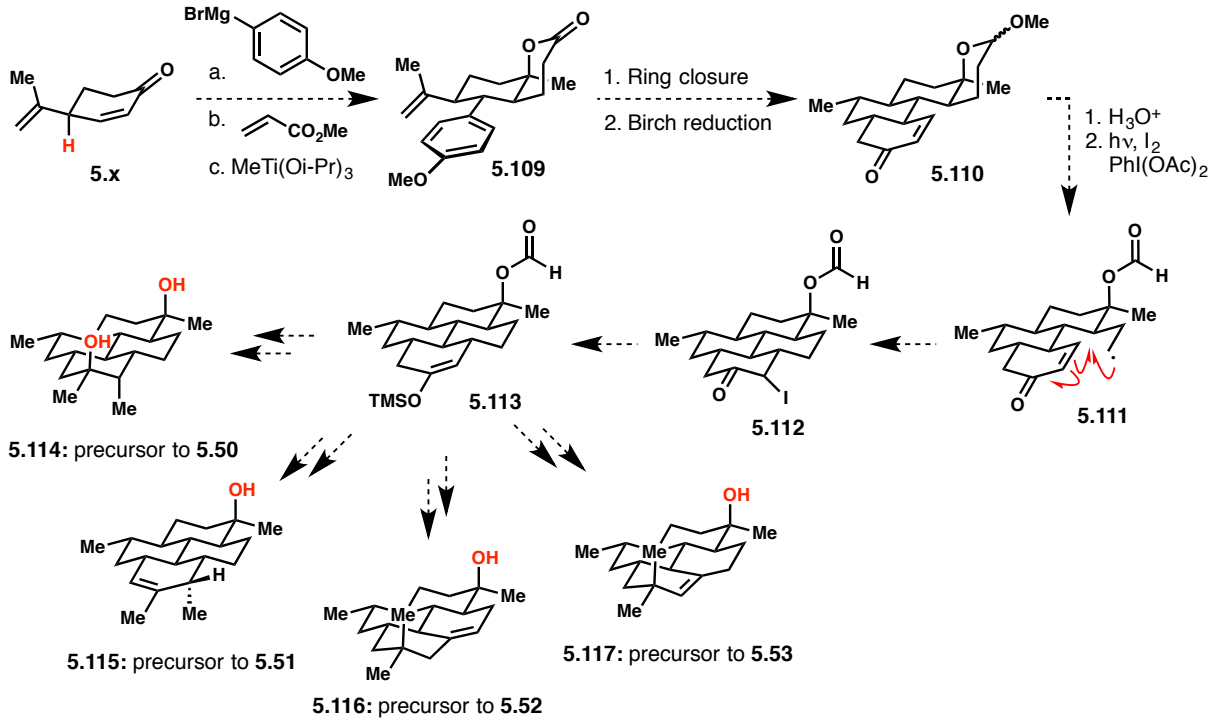
To improve the synthesis of DICA, several aspects of the current formal synthesis need to be addressed, mainly the drawback of forming the THF ring. Ideally, the functionality at C10 should be directly amenable to ring closure and not require extensive redox and protecting group manipulations. Additionally, to address selective introduction of the isonitriles, the current state-of-the-art $Sc(OTf)_3$-mediated invertive isonitrile installation would be most attractive. In a forward sense, the stereocontrol elements used in the formal synthesis would be applied to a second-generation synthesis. The synthesis could start from the same perillaldehyde derived enone **5.97** (Scheme 5.20). Several routes could be imagined, but the following idea would address several of the required improvements. A conjugate addition/Michael reaction would set the required stereocenters *trans*. Selective methyl addition into the ketone from the equatorial face would close the lactone to **5.105**.[19,54–57] Enone **5.106** would be formed by the previously used acid-induced cyclization and Birch reduction. Hydrogenation would generate the last internal stereocenter and sets up **5.107** for a photoinduced β-fragmentation of an alkoxy radical to generate alkyl iodide **5.108**.[58,59] Alkylation and methylation would generate the appropriate diol for an invertive isonitrile displacement.

Scheme 5.20 Proposed access to diol **5.26** utilizing reductive stereocontrol elements.



The formation of the perhydropyrene scaffold via alkylation and reduction previously used to access DICA could also be implemented to prepare other 7-isocyano(iso)cycloamphilectanes (Scheme 5.21). A conjugate addition of 4-methoxyphenylmagnesium bromide puts the oxidation state in a more favorable position in comparison to 3-methoxyphenylmagnesium bromide. The oxygen radical fragmentation may directly add into the C11–C20 electron deficient alkene of **5.111** or be trapped with I_2 and set up for an anionic conjugate addition. Alternatively, SmI_2 combined with the Suárez photofragmentation may allow for nucleophilic conjugate addition in the presence of the radical fragmentation. The enoxysilane **5.113** bears all the handles necessary to prepare **5.114**–**5.117**, the direct precursors to their respective ICTs (Figure 5.2).

Scheme 5.21 General approach to 7-isocyano(iso)cycloamphilectanes.



5.7 Conclusions

The formal synthesis of DICA was accomplished by a continuous evolution of ideas. The failures of previous routes led to both subtle and dramatic changes in strategies that culminated in a highly stereoselective perhydropyrene synthesis using a tandem vicinal difunctionalization, dissolving metal reduction and hydrogenation reactions. When examining the synthesis as a whole, it becomes clear how overwhelmingly important the carbonyl group was in this effort. A carbonyl was used in every productive C–C bond constructing step, using either its natural electrophilic reactivity, nucleophilic tendency in the forms of the enolate, or activating ability as an electron withdrawing group. The main takeaway from this adventure has been the development of excellent stereocontrol strategies with the power to address a variety of perhydropyrene ICT (iso)cycloamphilectanes.

5.8 Experimental Procedures

Purifications –

Solvents: Dry tetrahydrofuran (THF), diethyl ether (Et_2O), dichloromethane (CH_2Cl_2), toluene, benzene (C_6H_6), acetonitrile (MeCN), dimethylformamide (DMF) and methanol (MeOH) were obtained by passing commercially available formulations through activated alumina columns. tert-Butyl alcohol (t-BuOH) was purified by distillation over CaH_2.

Amines: Diisopropylamine (i-Pr_2NH), triethylamine (NEt_3), pyridine (py), and hexamethylphosphoramide (HMPA) were purified by distillation from CaH_2. Ethylene diamine (EDA) was purified by distillation from sodium metal.

Chlorides and Triflates: tert-Butyldimethylsilyl trifluoromethanesulfonate (TBSOTf), trimethylsilyl chloride (TMSCl), and benzyl chloride (BnCl) were purified by distillation over CaH_2.

Metals: Copper(I) iodide (CuI) was purified by Soxlet extractor with THF then drying the solid under high vacuum. Copper(I) chloride (CuCl) was purified by dissolving in conc. HCl then adding water until all material precipitated. The material was collected by filtration, washed generously with water, ethanol then ether and dried in vacuo. Manganese(II) chloride tetrahydrate was azeotropically dried with toluene under a Dean–Stark apparatus, then concentrated in vacuo.

Miscellaneous: Methyl vinyl ketone (MVK) was purified by distillation. Allyl iodide was purified by distillation and stored over copper beads at –20 °C. Ethyl bromoacetate was purified by washing thrice with 2 M Na_2CO_3, twice with brine, drying over $MgSO_4$, filtering and distillation.

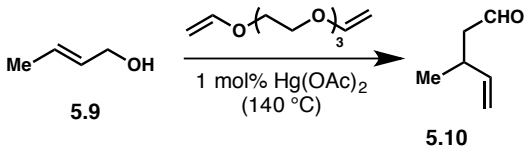
Titrations – Alkyllithium reagents were titrated using 2,6-di-(tert-butyl)-4-methylphenol (BHT) as the sacrificial proton source and fluorene as an indicator in THF or using diphenylacetic acid in THF. Grignard reagents were titrated using salicylaldehyde phenylhydrazone in THF.[60]

Reaction Setup – All reactions were carried out under an argon atmosphere with dry solvents under anhydrous conditions, unless otherwise noted. Argon balloons were the sole inert atmosphere used. Reactions run at an ambient temperature of 20–25 °C are designated as room temperature. Yields refer to chromatographically and spectroscopically homogeneous materials, unless otherwise stated.

Analysis – Thin layer chromatography was performed on 0.25 mm EMD glass-backed TLC plates impregnated with a fluorescent dye and visualized with UV light and $KMnO_4$ in K_2CO_3/NaOH/water or *p*-anisaldehyde in ethanol/aqueous H_2SO_4/AcOH and heat as a developing agent. Forced flow (flash) chromatography was performed on EMD Silica 60, mesh 0.04-0.063 silica gel. NMR spectra were recorded on Bruker 500 MHz instrument, obtained at 298 K unless otherwise noted and calibrated to residual undeuterated solvent as an internal reference. Chemical shifts are reported in ppm with the following abbreviations to explain multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, quin = quintuplet, sext = setet, sep = septet, bs = broad signal, m = multiplet. All coupling constants are apparent *J* values measured at the indicated field strengths. FT-IR spectra were recorded on a Perkin-Elmer spectrum RX1 spectrometer. High-resolution mass spectra (HRMS) were recorded on a H2Os LCT Premier spectrometer using ESI-TOF (electrospray ionization-time of flight). Melting points were measured on a MEL-TEMP II capillary apparatus and stand uncorrected. Optical rotations were

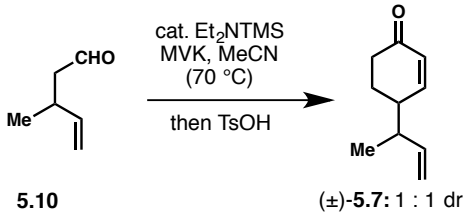
measured with a Jasco P-1010 polarimeter operating on the sodium D-line (589 nm) using a 50 mm path-length cell and are reported as: $[\alpha]^{T}_{D}$ (concentration in g/100 mL, solvent). Analytical chiral HPLC was performed with an Agilent 110 Series HPLC using a Chiralpak AS-H column (0.46 cm x 25 cm) obtained from Daicel Chemical Industries Ltd. and Chiralpak AD-H (0.46 cm x 25 cm) obtained from Daicel Chemical Industries Ltd. with visualization at the mentioned wavelength.

3-Methyl-4-pentenal 5.10 [Adapted from the literature][7,9]



A 500 mL round bottom flask was charged with a stir bar, 90 g (1.25 mol) **5.9**, 250 mL (1.25 mol) tri(ethylene glycol) divinyl ether and 2.01 g (6.35 mmol) $Hg(OAc)_2$. An excellent reflux condenser was greased[61] and fitted, then the flask immersed in a 140 °C oil bath for 8 hours. The reaction was cooled to room temperature and an additional 1.98 g (6.21 mmol) $Hg(OAc)_2$ was added before the reaction was reheated to 140 °C. After 20 hours the reaction was cooled, the reflux condenser replaced for a simple distillation head and distilled (80 °C/200 mmHg) directly into an iced receiving flask to afford 95 g (77%) **5.10** as a colorless liquid. Spectral data was identical to the literature.[7] Note: The general procedure for Wei et al.[7] palladium catalyzed *trans*-vinylation/Claisen rearrangement was inferior in our hands to the procedure described above using mercury. Although mercury is highly toxic, this procedure was more reliable in advancing material. All glassware was washed with concentrated nitric acid after use, then diluted with water.

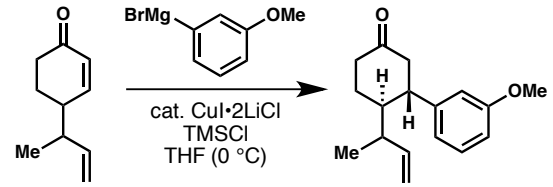
Cyclohexenone (±)-5.7



A 1 L round bottom flask was charged with 9.80 g (99.8 mmol) **5.10**, 280 mL MeCN, 10 mL (123 mmol) MVK and 3.5 mL (18.5 mmol) Et_2NTMS. The flask was fitted with a reflux

condenser and immersed into a 90 °C oil bath for 21 hours. The reaction was cooled to room temperature and 38 g (200 mmol) TsOH•H_2O added. After 8 hours the reaction was cooled in an ice bath and 120 mL 1 M NaOH added, followed by 120 mL sat. aq. $NaHCO_3$, ensuring the temperature remained below 10 °C. Approximately 280 mL of volatiles were removed in vacuo and the remaining liquid diluted with 90 mL water and 200 mL Et_2O. The phases were separated and the aqueous phase extracted twice with 100 mL Et_2O. All organic layers were combined, washed twice with 75 mL sat. aq. $NaHCO_3$ and back extracted with 30 mL Et_2O. The organic layers were combined, washed with 50 mL brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude material was purified by distillation (77-80 °C/1.0 mmHg) to afford 10.0 g (66%, 1:1 dr) **5.7** as a colorless liquid. ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 6.94 (dt, *J* = 10.3, 2.0 Hz, 0.5H), 6.91 (ddd, *J* = 10.3, 2.3, 1.6 Hz, 0.5H), 6.02 (dt, *J* = 10.3, 2.6, 0.5H), 6.02 (dt, *J* = 10.3, 2.6, 0.5H), 5.75 (m, 1H), 5.09-5.05 (m, 2H), 2.54 (t, *J* = 4.3 Hz, 0.5H), 2.50 (t, *J* = 4.3 Hz, 0.5H), 2.47-2.29 (m, 3H), 2.08-2.01 (m, 1H), 1.78 (m, 1H), 1.09 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 199.89, 199.87, 153.5, 153.4, 141.2, 141.0, 129.8, 129.7, 115.4, 114.9, 41.7, 41.2, 41.1, 40.9, 37.4, 37.2, 26.1, 26.0, 17.2, 16.4; IR (thin film) 3077, 2963, 2871, 1682 cm^{-1}; HRMS (ESI) calculated for $C_{10}H_{14}O$ $[M+Na]^+$ 173.0942 found 173.0950.

Cyclohexanone 5.11

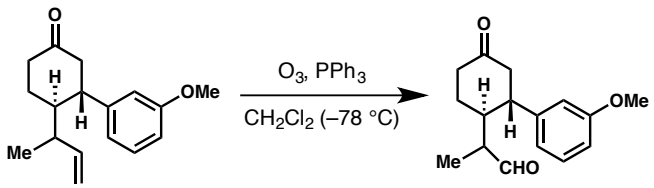


(±)-**5.7:** 1 : 1 dr **5.11**

3-Methoxyphenylmagnesium bromide was prepared by addition of 3.0 mL (23.7 mmol) 3-bromoanisole in 3.0 mL THF to 0.865 g (35.6 mmol) magnesium metal in 12 mL THF activated by dibromoethane, maintaining reflux. To a 250 mL round bottom flask charged with 2.00 g (13.3 mmol) **5.7**, 0.255 g (0.133 mmol) CuI, 0.125 g (2.95 mmol) LiCl and 1.9 mL (15.0 mmol) TMSCl in 80 mL THF, cooled to 0 °C was added 13.5 mL (16.2 mmol) 1.2 M 3-methoxyphenylmagnesium bromide dropwise over 30 minutes. The reaction was stirred for an additional hour then quenched at 0 °C by addition of 50 mL 1 M HCl and warmed to room temperature. The mixture was extracted with 50 mL and 25 mL Et_2O. The organic layer was washed with 40 mL 3 M HCl, 20 mL water, 40 mL 3:1 sat. aq. NH_4Cl/5 M NaOH, 20 mL brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude oil was purified by column chromatopraphy (10:1 hexanes/EtOAc) to afford 2.67 g (78%, 1:1 dr) **5.11** as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 7.28-7.25 (m, 2H), 6.79 (td, *J* = 15.7, 7.6 Hz, 6H), 5.81 (ddd, *J* = 17.0, 10.7, 6.1 Hz, 1H), 5.67 (dt, *J* = 17.8, 8.9 Hz, 1H), 5.00 (d, *J* = 10.5 Hz, 2H), 4.93 (d, *J* = 17.3 Hz, 1H), 4.82 (d, *J* = 17.1 Hz, 1H), 3.82 (s, 6H), 2.88 (td, *J* = 20.4, 11.3 Hz, 2H), 2.59-2.41 (m, 8H), 2.22-2.09 (m, 4H), 2.05-1.99 (m, 2H), 1.55 (quintetd, *J* = 12.9, 4.9 Hz, 2H), 1.01 (d, *J* = 7.0 Hz, 3H), 0.84 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 210.69, 210.66, 159.9, 159.8, 145.0, 144.8, 143.3, 138.8, 129.9, 129.8, 119.8, 119.5, 115.7, 113.6, 113.5, 113.4, 111.5, 111.5, 55.2, 49.7, 49.5, 48.2, 47.7, 46.4, 45.7, 41.1, 41.0, 37.2,

36.2, 25.3, 25.1, 18.9, 11.5; IR (thin film) 2959, 1714, 1600, 1487, 1263, 1046 cm^{-1}; HRMS (ESI) calculated for $C_{17}H_{22}O_2$ $[M+Na]^+$ 281.1518 found 281.1511.

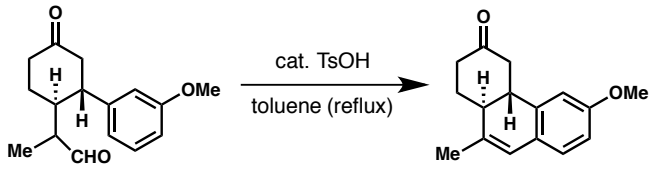
Aldehyde 5.12



5.11 **5.12**

A 250 mL round bottom flask containing 2.67 g (10.3 mmol) **5.11** in 100 mL CH_2Cl_2 was treated with ozone at –78 °C. After a persistent blue color, the color was discharged by bubbling oxygen and 3.22 g (12.2 mmol) PPh_3 added. The reaction was allowed to warm to room temperature over several hours. All volatiles were removed and the residue purified by column chromatography (3:1 hexanes/EtOAc) to afford 2.40 g (88%, 1:1 dr) **5.12** as a colorless oil. ^1H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 9.59 (s, 1H), 9.47 (s, 1H), 7.28 (q, *J* = 8.0 Hz, 2H), 6.79 (td, *J* = 17.7, 7.7 Hz, 6H), 3.79 (d, *J* = 8.0 Hz, 6H), 3.12 (q, *J* = 9.8 Hz, 1H), 2.88 (td, *J* = 11.5, 5.4 Hz, 1H), 2.73-2.67 (m, 1H), 2.64-2.46 (m, 8H), 2.41-2.36 (m, 2H), 2.25 (qd, *J* = 7.2, 2.5 Hz, 1H), 2.20-2.14 (m, 1H), 1.87-1.67 (m, 2H), 1.60 (dtd, *J* = 16.7, 11.3, 5.0 Hz, 1H), 1.11 (d, *J* = 7.0 Hz, 3H), 1.01 (d, *J* = 7.3 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 209.50, 209.47, 205.5, 203.2, 160.1, 160.0, 143.72, 143.69, 130.3, 130.1, 119.6, 119.3, 113.6, 113.3, 112.2, 112.0, 55.2, 49.4, 49.2, 47.4, 47.2, 47.0, 46.7, 44.8, 41.0, 41.1, 40.2, 27.9, 26.2, 11.2, 7.1; IR (thin film) 2943, 2719, 1716, 1600, 1488, 1263, 1046 cm^{-1}; HRMS (ESI) calculated for $C_{16}H_{20}O_3$ $[M+Na]^+$ 283.1310 found 283.1307.

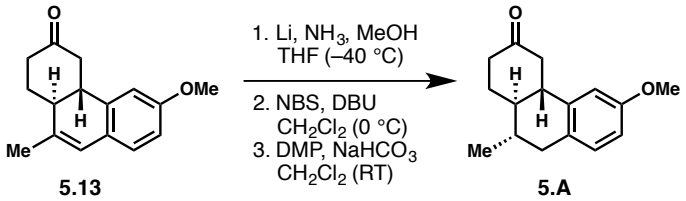
Dihydronaphthalene 5.13



5.12 **5.13**

A 100 mL round bottom flask containing 2.36 g (9.07 mmol) **5.12**, 86 mg (0.45 mmol) TsOH•H_2O and 70 mL toluene was refluxed under a Dean-Stark trap. After 2 hours the reaction was cooled, diluted with 100 mL Et_2O, washed with 20 mL sat. aq. $NaHCO_3$, 20 mL brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude material was purfied by column chromatography (6:1 hexanes/EtOAc) to afford 1.78 g (81%) **5.13** as a white solid that was crystallized from Et_2O to afford a single cubic crystal (mp = 132–134 °C). ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 6.97 (d, *J* = 7.9 Hz, 1H), 6.73 (d, *J* = 7.5 Hz, 1H), 6.72-6.67 (m, 1H), 6.29 (s, 1H), 3.80 (s, 3H), 3.04 (d, *J* = 13.6 Hz, 1H), 2.87 (t, *J* = 12.7 Hz, 1H), 2.58-2.39 (m, 5H), 1.92 (s, 3H), 1.63 (t, *J* = 11.4 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 210.5, 158.5, 138.1, 136.0, 127.7, 126.3, 124.1, 110.8, 110.1, 55.2, 43.8, 42.2, 40.9, 40.7, 28.7, 20.6; IR (thin film) 2918, 2849, 1713, 1606, 1571, 1242, 1159 cm^{-1}; HRMS (ESI) calculated for $C_{16}H_{18}O_2$ $[M+Na]^+$ 265.1205 found 265.1210.

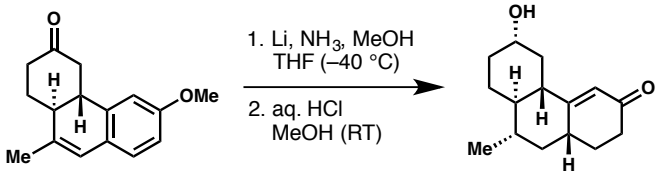
Independent Analysis of Birch Reduction Stereochemistry



To a 10 mL round bottom flask charged with a glass stir bar was condensed 2 mL ammonia followed by the addition of 12 mg (0.050 mmol) **5.13** in 0.5 mL THF and 0.2 mL MeOH. Slowly, 12 mg (1.73 mmol) lithium metal was added in small pieces at –40 °C. After complete addition, ammonia was evaporated and the residue then taken up in EtOAc and water. The organic layer was separated and washed with brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. To a 10 mL round bottom flask containing crude cyclohexadiene was added 0.5 mL CH_2Cl_2 and 0.02 mL (0.13 mmol) DBU, cooled to 0 °C and treated with 14 mg (0.079 mmol) NBS. After 20 minutes at 0 °C sat. aq. $Na_2S_2O_3$, water and EtOAc was added. The layers were separated and the organic layer was washed with water and brine. All aqueous washings were combined, back extracted with EtOAc and all organic layers combined. The EtOAc layer was dried over $MgSO_4$, filtered and all volatiles removed in vacuo. To a 10 mL round bottom flask containing crude alcohol was added 0.4 mL CH_2Cl_2, 40 mg (0.48 mmol) $NaHCO_3$ and at 0 °C 32 mg (0.075 mmol) DMP. The ice bath was removed. After overnight stirring EtOAc was added and the reaction filtered over Celite. Sat. aq. $Na_2S_2O_3$ and water were added, the layers separated and the organic phase washed with sat. aq. $NaHCO_3$. The EtOAc layer was washed with brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude material was purified by column chromatography (10:1 hexanes/EtOAc) to afford 5.0 mg (41%, single diastereomer) **5.A** as a white solid that was recrystallized from Et_2O to afford white needles (mp = 111–113 °C). ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 7.03 (d, J = 8.3 Hz, 1H), 6.73 (dd, J

= 8.3, 2.4 Hz, 1H), 6.71 (d, *J* = 2.1 Hz, 1H), 3.78 (s, 3H), 3.08 (ddd, *J* = 14.2, 4.0, 2.2 Hz, 1H), 2.85-2.81 (m, 2H), 2.57-2.51 (m, 2H), 2.43-2.32 (m, 3H), 1.74-1.64 (m, 1H), 1.51-1.40 (m, 2H), 1.11 (t, *J* = 10.8 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 211.2, 157.9, 139.4, 129.7, 128.8, 112.2, 110.4, 55.3, 46.5, 45.1, 43.8, 41.1, 38.4, 33.5, 29.4, 19.6; IR (thin film) 2950, 2920, 1709, 1606, 1501, 1239, 1038 cm^{-1}; HRMS (ESI) calculated for $C_{16}H_{20}O_2$ $[M+Na]^+$ 267.1361 found 267.1371.

Enone 5.2

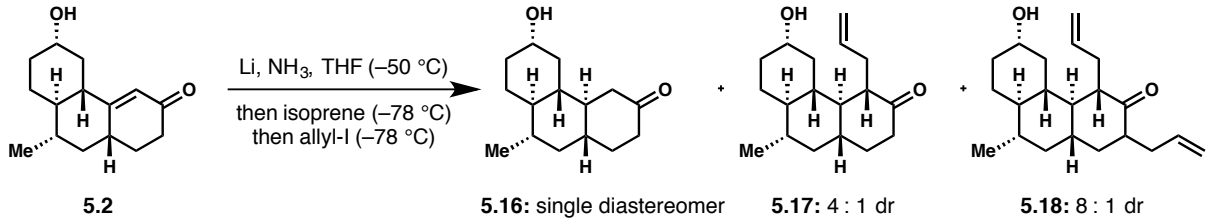


5.13 **5.2**

To a 1 L 3-neck round bottom flask fitted with a low-temperature thermometer, was charged with a glass stir bar, 1.77 g (7.30 mmol) **5.13** in 75 mL THF and 230 mL ammonia and 15 mL (370 mmol) MeOH at –60 °C. Slowly, 2.50 g (260 mmol) lithium metal was added in small pieces at –40 °C. After the blue color discharged, 20 g (374 mmol) solid NH_4Cl was added and the ammonia evaporated overnight. The white residue taken up in 50 mL water and extracted with 100 mL, 50 mL and 25 mL EtOAc. The organic layers were combined, washed with 20 mL brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. To a 300 mL flask containing crude material was added 75 mL MeOH followed by 7.5 mL 6 M HCl. After 8 hours 100 mL sat. aq. $NaHCO_3$ was added and after 1 hour of stirring ~60 mL volatiles were removed in vacuo. The remaining solution was extracted with 75 mL, 50 mL and twice with 25 mL EtOAc. All organic layers were combined, washed with 30 mL brine and back extracted with 25 mL EtOAc, then dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude

material was purified by column chromatography (1:1→1:3 hexanes/EtOAc) to afford 1.20 g (70%) **5.2** as a white solid that was recrystallized from Et_2O to afford colorless prisms (mp = 139–140 °C). ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 5.80 (s, 1H), 3.64 (tt, *J* = 10.3, 4.8 Hz, 1H), 2.40-2.24 (m, 4H), 2.15-2.02 (m, 5H), 1.89-1.85 (m, 2H), 1.66-1.58 (m, 1H), 1.38 (dddt, *J* = 12.5, 9.4, 6.3, 3.1 Hz, 1H), 1.26-1.09 (m, 4H), 1.07-0.98 (m, 1H), 0.92 (t, *J* = 9.6 Hz, 3H), 0.90-0.85 (m, 1H), 0.78 (qd, *J* = 10.9, 3.1 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 200.6, 169.0, 121.0, 70.5, 48.9, 45.2, 43.4, 38.1, 37.4, 36.8, 35.5, 34.9, 29.3, 28.5, 19.3; IR (thin film) 3392, 2926, 2857, 1658, 1057 cm^{-1}; HRMS (ESI) calculated for $C_{15}H_{22}O_2$ $[M+Na]^+$ 257.1518 found 257.1521.

Allylation to 5.16, 5.17 and 5.18



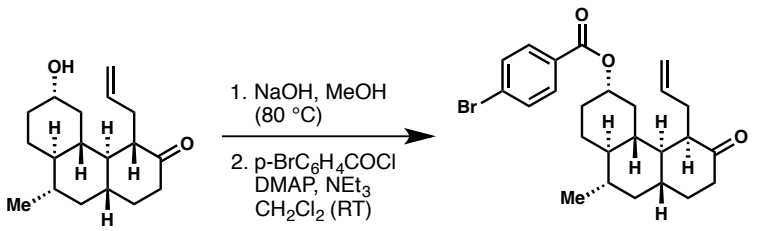
5.2 **5.16:** single diastereomer **5.17:** 4 : 1 dr **5.18:** 8 : 1 dr

To a 25 mL round bottom flask containing a glass stir bar and 7.7 mg (1.1 mmol) lithium metal was condensed 7 mL ammonia and 1.5 mL THF added. At –50 °C 76 mg (0.32 mmol) **5.2** in 1.5 mL THF was added. The reaction was cooled to –78 °C then treated with 0.1 mL isoprene and stirred until all lithium was discharged. To the white slurry was added 69 mg (0.41 mmol) allyl iodide at –78 °C. The reaction was stirred for 2.5 hours before 3 mL sat. aq. NH_4Cl was added slowly and warmed to room temperature. The mixture was partitioned between 5 mL water and 15 mL EtOAc. The organic layer was washed with 5 mL brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude material was purified by column chromatography (4:1→1:2 hexanes/EtOAc) to afford 17 mg (22%, >20:1 dr) **5.16** as a white solid which was

recrystallized from Et_2O to afford white crystals (mp = 139–140 °C), 38 mg (43%, 4:1 dr) **5.17** as a white wax and 20 mg (20%, 8:1 dr) **5.18** as a white solid which was recrystallized from Et_2O to afford a single diastereomer as white needles (mp = 118–120 °C). **5.16**: ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 3.57-3.53 (m, 1H), 2.62 (dd, *J* = 14.0, 1.8 Hz, 1H), 2.40-2.29 (m, 2H), 2.08-2.00 (m, 3H), 1.96 (ddt, *J* = 13.1, 6.2, 3.1 Hz, 1H), 1.88 (t, *J* = 13.3 Hz, 1H), 1.72 (dt, *J* = 13.1, 3.4 Hz, 1H), 1.48 (qt, *J* = 11.6, 3.1 Hz, 1H), 1.35 (qd, *J* = 12.6, 4.9 Hz, 1H), 1.25-1.15 (m, 4H), 0.92 (d, *J* = 6.5 Hz, 3H), 1.00-0.77 (m, 4H), 0.59 (qd, *J* = 10.8, 2.9 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 211.9, 70.7, 47.4, 47.3, 46.1, 45.1, 41.8, 41.3, 40.9, 38.8, 36.5, 35.3, 33.2, 28.3, 19.9; IR (thin film) 3400, 2921, 2855, 1711, 1455, 1041 cm^{-1}; HRMS (ESI) calculated for $C_{15}H_{24}O_2$ $[M+Na]^+$ 259.1674 found 259.1674. **5.17**: ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 5.71-5.60 (m, 1H), 5.12-4.97 (m, 2H), 3.54 (t, *J* = 10.4 Hz, 1H), 2.48 (td, *J* = 15.7, 8.2 Hz, 2H), 2.32-2.22 (m, 3H), 2.11 (d, *J* = 9.7 Hz, 1H), 2.02-1.96 (m, 2H), 1.75-1.59 (m, 4H), 1.32-1.11 (m, 5H), 0.99-0.75 (m, 6H), 0.61 (q, *J* = 10.4 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) major δ 216.0, 134.9, 117.2, 70,7, 53.2, 50.9, 48.0, 46.6, 42.6, 39.9, 39.8, 39.4, 37.2, 36.5, 35.5, 28.8, 28.3, 20.0, minor δ 214.4, 134.9, 116.6, 70.6, 51.3, 50.2, 47.3, 42.4, 40.8, 38.1, 38.0, 36.3, 35.4, 34.4, 34.2, 30.4, 28.4, 19.9; IR (thin film) 3388, 2923, 2858, 1702, 1444, 1051, 1023 cm^{-1}; HRMS (ESI) calculated for $C_{18}H_{28}O_2$ $[M+Na]^+$ 299.1987 found 299.1994. **5.18**: ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 5.78-5.63 (m, 2H), 5.05-4.98 (m, 4H), 3.57-3.52 (m, 1H), 2.61-2.55 (m, 1H), 2.52-2.45 (m, 2H), 2.36-2.21 (m, 2H), 2.13-1.96 (m, 4H), 1.86-1.75 (m, 1H), 1.73-1.50 (m, 2H), 1.33-1.01 (m, 5H), 1.00-0.76 (m, 7H), 0.59 (dt, *J* = 18.4, 9.2 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 216.2, 136.4, 135.0, 116.8, 116.4, 70.7, 54.1, 51.8, 47.6, 46.8, 42.50, 42.47, 40.0, 39.0, 39.4, 37.6, 36.4, 35.4, 35.3, 34.6, 28.2, 19.9; IR (thin film)

3262, 2920, 2853, 1698, 1441, 1059 cm^{-1}; HRMS (ESI) calculated for $C_{21}H_{32}O_2$ $[M+Na]^+$ 339.2300 found 339.2307.

Axial Allyl 5.19 and Benzoate 5.B

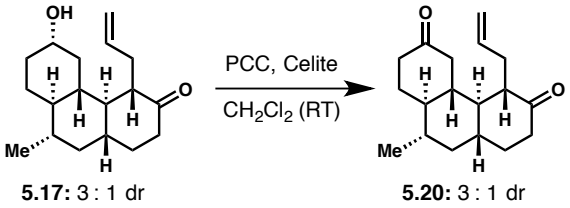


5.17 **5.B**

To 1 dram vial containing 6 mg (0.0.25 mmol, 3:1 dr) **5.17** in 0.3 mL MeOH was added 0.05 mL (0.05 mmol) 1 M NaOH/MeOH at room temperature, the flask sealed and the reaction heated to 80 °C. After 2 hours, sat. aq. NH_4Cl was added and the mixture extracted thrice with Et_2O. The organic layers were combined, washed with brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo to afford a single diastereomer. The crude material in a 1 dram vial and 4 mg (0.033 mmol) DMAP was diluted with 0.4 mL 1:1 CH_2Cl_2/NEt_3 and treated with 11 mg (0.050 mmol) p-bromobenzoyl chloride at room temperature. The reaction was was stirred for 1 hour then quenched with sat. aq. $NaHCO_3$ and extracted four times with EtOAc. The organic layers were combined, washed with 1:1 brine/$NaHCO_3$, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude material was purified by column chromatography (10:1 hexanes/EtOAc) to provide 7 mg (70%, >10:1 dr) **5.B** as a colorless oil. ^1H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 7.90-7.88 (m, 2H), 7.59-7.57 (m, 2H), 5.62 (dddd, *J* = 16.7, 10.3, 8.3, 6.1 Hz, 1H), 5.05 (dd, *J* = 17.0, 1.0 Hz, 1H), 4.99 (d, *J* = 10.1 Hz, 1H), 4.91 (tt, *J* = 11.4, 4.5 Hz, 1H), 2.60 (dt, *J* = 8.0, 3.8 Hz, 1H), 2.49 (td, *J* = 14.0, 6.4 Hz, 1H), 2.39-2.34 (m, 1H), 2.29 (dd, *J* = 12.0, 8.4 Hz, 1H), 2.24-2.09 (m, 4H), 1.98 (ddt, *J* = 13.0, 6.6, 3.1 Hz, 1H), 1.82-1.75 (m, 2H),

1.45-1.37 (m, 1H), 1.36-1.25 (m, 3H), 1.23-1.17 (m, 1H), 1.10-0.99 (m, 2H), 0.94 (d, J = 6.5 Hz, 3H), 0.80 (q, J = 12.7 Hz, 1H), 0.70-0.64 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 214.2, 165.3, 134.8, 131.6, 131.1, 129.6, 127.9, 116.7, 73.9, 51.4, 50.4, 47.4, 42.4, 40.8, 38.1, 36.2, 34.3, 34.2, 34.2, 31.5, 30.4, 28.2, 19.8; IR (thin film) 2922, 2865, 1713, 1590, 1272, 1103 cm^{-1}; HRMS (ESI) calculated for $C_{25}H_{31}BrO_3$ $[M+Na]^+$ 481.1354 found 481.1342.

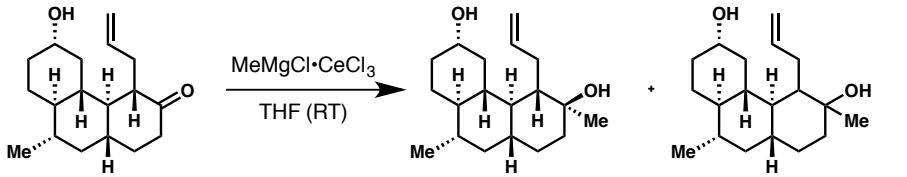
Ketone 5.20



5.17: 3 : 1 dr **5.20:** 3 : 1 dr

To 1 dram vial of 14 mg (0.051 mmol, 3:1 dr) **5.17** and 60 mg celite in 0.8 mL CH_2Cl_2 was added 30 mg (0.14 mmol) PCC at room temperature. After 16 hours the mixture was diluted with Et_2O, passed through a silica gel column and concentrated. The crude material was purified by column chromatography (4:1 hexanes/EtOAc) to provide 12 mg (85%, 3:1 dr) **5.20** as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 5.70-5.57 (m, 1H), 5.07-4.98 (m, 2H), 2.56-2.21 (m, 10H), 2.05-1.89 (m, 1H), 1.81-1.72 (m, 2H), 1.68-1.58 (m, 1H), 1.41-1.32 (m, 1H), 1.30-1.17 (m, 3H), 1.10 (q, J = 10.6 Hz, 1H), 1.03-0.82 (m, 4H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) major δ 214.7, 210.7, 134.6, 117.6, 52.7, 51.6, 48.7, 47.6, 45.5, 42.3, 41.0, 39.8, 39.7, 37.2, 36.3, 29.9, 28.6, 20.0, minor δ 213.7, 211.0, 134.3, 116.9, 51.2, 51.1, 46.9, 44.0, 43.1, 42.1, 41.0, 37.9, 36.1, 34.3, 33.9, 30.2, 30.1, 19.9; IR (thin film) 2960, 2916, 2859, 1713 cm^{-1}; HRMS (ESI) calculated for $C_{18}H_{26}O_2$ $[M+Na]^+$ 297.1830 found 297.1836.

Diol 5.27 and 5.C

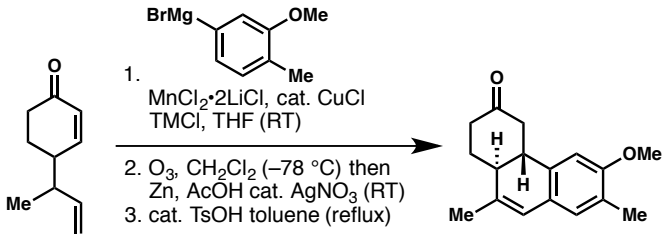


5.17: 4 : 1 dr **5.27** **5.C:** 7 (axial allyl) : 2 : 1 dr

To 1 dram vial was added 45 mg (0.18 mmol) $CeCl_3$ and dried under vacuum at 160 °C for 5 hours. The solid was cooled under argon and stirred with 0.6 mL THF for 30 minutes before being cooled in an ice bath and treated with 0.07 mL (0.19 mmol) 2.7 M MeMgCl/THF. After 30 minutes at 0 °C a solution of 10 mg (0.036 mmol) **5.17** in 0.3 mL THF was added dropwise at 0°C. The ice bath was removed after 10 minutes. After 5 hours the reaction was recooled to 0°C and quenched with 1 mL 3 M HCl, then extracted thrice with Et_2O. The organic layers were combined, washed with sat. aq. $NaHCO_3$, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude material was purified by column chromatography (3:1→1:1 hexanes/EtOAc) to provide 6.5 mg (62%, single diastereomer) **5.27** as a white solid and 2.6 mg (25%, 7 (axial allyl):2:1 dr) **5.C** as a colorless oil. **5.27**: ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 6.03-5.95 (m, 1H), 5.09-5.02 (m, 2H), 3.50-3.46 (m, 1H), 2.71-2.66 (m, 1H), 2.34-2.32 (m, 1H), 2.23-2.18 (m, 1H), 2.06-1.95 (m, 2H), 1.65 (dt, *J* = 13.2, 3.6 Hz, 1H), 1.55 (dt, *J* = 12.9, 3.3 Hz, 1H), 1.50-1.44 (m, 1H), 1.41-1.30 (m, 4H), 1.27 (t, *J* = 7.1 Hz, 1H), 1.22 (s, 3H), 1.21-1.02 (m, 6H), 0.90 (t, *J* = 5.7 Hz, 3H), 0.95-0.83 (m, 2H), 0.70 (t, *J* = 9.4 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 140.5, 115.1, 73.6, 71.6, 49.1, 48.0, 47.4, 44.2, 42.6, 42.1, 39.4, 37.4, 35.1, 34.8, 30.8, 29.3, 28.4, 20.4; IR (thin film) 3389, 3322, 2922, 1638, 1403, 1045 cm^{-1}; HRMS (ESI) calculated for $C_{19}H_{32}O_2$ $[M+NH_4]^+$ 310.2746 found 310.2743. **5.C**: ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) mixture δ 6.12-6.04 (m, 0.09H), 6.03-5.94 (m, 0.6H), 5.90-5.81 (m, 0.2H), 5.15-5.00 (m, 1.2H), 4.97-4.93 (m, 0.7H), 3.58-3.43 (m, 1H), 2.35-2.27 (m, 1H), 2.15-2.00 (m, 3H),

1.94-1.86 (m, 1H), 1.79-1.51 (m, 4H), 1.49-1.37 (m, 2H), 1.33-1.13 (m, 5H), 1.12-0.98 (m, 4H), 0.95-0.81 (m, 5H), 0.80-0.68 (m, 2H), 0.61-0.56 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) major δ 141.7, 114.2, 70.7, 48.1, 47.8, 45.8, 43.3, 41.2, 38.8, 36.3, 35.4, 34.6, 34.4, 31.7, 29.4, 28.6, 27.7, 20.0; IR (thin film) 3369, 2924, 2856, 1637, 1459, 1050 cm^{-1}; HRMS (ESI) calculated for $C_{19}H_{32}O_2$ $[M+Na]^+$ 315.2300 found 315.2308.

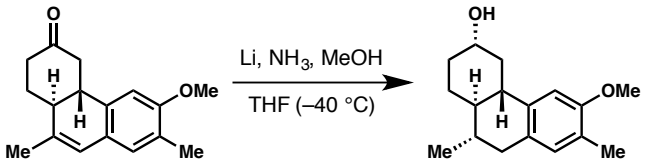
Dihydronaphthalene 5.32



3-Methoxy-4-methylphenylmagnesium bromide was prepared by addition of 1.60 g (7.96 mmol) 5-bromo-2-methylanisole in 1.0 mL THF to 0.220 g (9.0 mmol) magnesium metal in 5.0 mL THF activated by dibromoethane maintaining 40–50 °C. A 50 mL round bottom flask containing 154 mg (1.22 mmol) $MnCl_2$ and 109 mg (2.57 mmol) LiCl was dried under high vaccum in a 150 °C oil bath for 10 hours. The flask was cooled, placed under an argon balloon and 10 mL THF added to dissolve the salts. At 0 °C, 540 mg (3.60 mmol) **5.7** in 4 mL THF and 10 mg (0.010 mmol) CuCl were added. After 10 minutes 0.64 mL (5.9 mmol) TMSCl was added, followed by the dropwise addition of 3.9 mL (4.1 mmol) 1.05 M 3-methoxy-4-methylphenylmagnesium bromide over the course of 5 minutes. Stirring at 0 °C was continued for 10 minutes before the cold bath was removed. After 5 hours at room temperature, the flask was again cooled in an ice bath and 20 mL 3 M HCl added slowly. The ice bath was removed and stirred for 10 minutes. The mixture was partitioned between an additional 10 mL 3 M HCl and 30 mL Et_2O. The layers

were separated and the aqueous layer extracted with 10 mL Et_2O. The organic layers were combined, washed with 10 mL sat. aq. $NaHCO_3$, 10 mL brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude oil was carried on crude. Crude alkene in a 100 mL round bottom flask was dissolved in 30 mL CH_2Cl_2, cooled to –78 °C and ozonized. After the solution became blue, the solution was sparged with oxygen. A single portion of 3 mL AcOH, 1.2 g (18 mmol) Zn powder and 15 mg (0.088 mmol) $AgNO_3$ was added. After stirring at –78 °C for 2 hours, the bath was removed and stirring continued for 2 hours. The reduction was determined complete by TLC and the solution was filtered over Celite, washing with CH_2Cl_2 (~100 mL as determined by TLC). The filtrate was washed with 50 mL water, 50 mL sat. aq. $NaHCO_3$, 20 mL brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. A 100 mL round bottom flask containing crude aldehyde in 50 mL toluene was treated with 34 mg (0.18 mmol) $TsOH•H_2O$ and heated to 140 °C under a Dean–Stark trap. After 2 hours the reaction was cooled, diluted with 20 mL Et_2O, washed with 20 mL half sat. aq. $NaHCO_3$ and 10 mL brine. The aqueous layers were combined and back extracted with 10 mL Et_2O. All organic layers were combined, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude material was purified by trituration with hexanes to afford 628 mg (67%) **5.32** as a tan solid which was recrystallized from EtOAc to afford wispy white needles (mp = 193–194 °C). ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 6.86 (s, 1H), 6.62 (s, 1H), 6.27 (s, 1H), 3.84 (s, 4H), 3.11 (ddd, *J* = 14.1, 4.0, 2.2 Hz, 1H), 2.91 (td, *J* = 13.9, 3.8 Hz, 1H), 2.61-2.41 (m, 6H), 2.20 (s, 4H), 1.93 (s, 3H), 1.69 (qd, *J* = 12.6, 4.7 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 210.9, 156.5, 135.8, 135.1, 128.0, 127.2, 124.7, 124.2, 105.6, 55.5, 44.2, 42.2, 41.0, 40.9, 28.8, 20.6, 15.8; IR (thin film) 2923, 2852, 1714, 1611 cm^{-1}; HRMS (ESI) calculated for $C_{17}H_{20}O_2$ $[M+NH_4]^+$ 274.1807 found 274.1800.

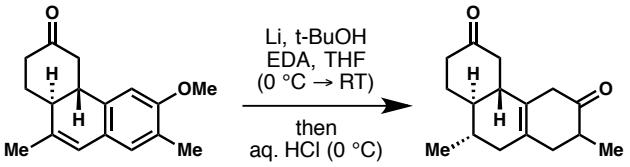
Anisole 5.37



5.32 **5.37**

To a 10 mL round bottom flask charged with a glass stir bar was condensed 3 mL ammonia followed by the addition of 24 mg (0.094 mmol) **5.32** in 1 mL THF and 0.3 mL MeOH. Slowly, 24 mg (3.46 mmol) lithium metal was added in small pieces at –40 °C. After the blue color discharged, 0.140 g (2.62 mmol) solid NH_4Cl was added and the ammonia evaporated. The white residue taken up in water and EtOAc. The organic layer was separated and washed with brine. The aqueous layers were combined and back extracted with EtOAc. The organic layers were combined, dried over $MgSO_4$, filtered and all volatiles removed in vacuo to afford a crude aromatic material assigned as **5.37**.

Skipped Enone 5.39

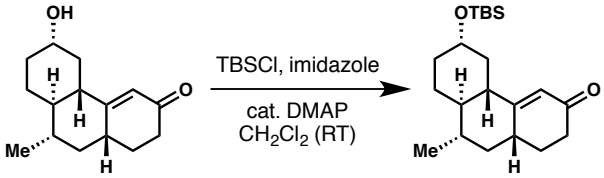


5.32 **5.39:** 1.6 : 1 dr

To a 25 mL round bottom flask charged with a glass stir bar was added 125 mg (0.488 mmol) **5.32**, 5.0 mL THF and 2.5 mL (37 mmol) ethylene diamine before being cooled in an ice bath. After the addition of 1.2 mL (12.5 mmol) t-BuOH, 80 mg (11.5 mmol) lithium metal was added in small pieces over the course of 3 hours at 0 °C. After complete consumption of lithium metal, the cold bath was removed and stirring continued for 1 hour. The flask was recooled to 0 °C and canula transferred into a vigorously stirring flask of 10 mL conc. HCl and 50 g ice. Best results

were obtained by submerging the canula into the aqueous solution. After complete transfer the reaction flask was washed twice with 1.5 mL Et_2O. The aqueous mixture was warmed to room temperature and extracted with 25 mL EtOAc, then four times with 10 mL EtOAc. The organic layers were combined, washed with 10 mL 6 M HCl then back extracted with 5 mL EtOAc and combined with the remaining organic layers. The organic phase was washed with 5 mL water, 5 mL sat. aq. $NaHCO_3$, 10 mL brine, dried over $MgSO_4$ and all volatiles removed in vacuo to afford 100 mg (83%, 1.6:1 dr) crude material of good purity. Column chromatography (4:1 hexanes/EtOAc) afforded 40 mg (33%, 1.8:1 dr) **5.39** as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 2.91 (d, *J* = 19.8 Hz, 1H), 2.81 (d, *J* = 20.5 Hz, 0.5H), 2.69 (td, *J* = 12.9, 6.7 Hz, 1H), 2.60-2.56 (m, 2H), 2.51-2.41 (m, 3H), 2.37-2.27 (m, 3H), 2.21-1.80 (m, 8H), 1.58-1.54 (m, 1H), 1.52-1.45 (m, 1H), 1.39-1.20 (m, 4H), 1.11 (d, *J* = 6.7 Hz, 1.5H), 1.07 (d, *J* = 6.5 Hz, 3H), 1.02 (d, *J* = 6.3 Hz, 1.5H), 1.01 (d, *J* = 6.5 Hz, 3H), 0.94-0.86 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) major δ 211.6, 211.0, 130.0, 126.7, 44.9, 44.8, 44.7, 41.9, 41.2, 41.1, 40.1, 39.4, 32.7, 28.7, 18.9, 13.5, minor δ 212.1, 211.1, 129.6, 126.3, 45.1, 45.0, 44.5, 42.4, 41.1, 40.4, 39.8, 39.1, 32.9, 28.9, 19.0, 14.6; IR (thin film) 2962, 2926, 2874, 1716, 1453 cm^{-1}; HRMS (ESI) calculated for $C_{16}H_{22}O_2$ $[M+Na]^+$ 269.1518 found 269.1516.

Enone 5.41

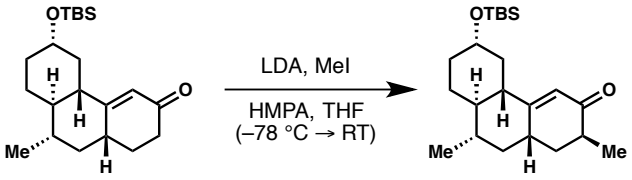


5.2 **5.41**

To 100 mL round bottom flask containing 1.20 g (5.12 mmol) **5.2**, 0.525 g (7.71) imidazole and 60 mg (0.49 mmol) DMAP in 25 mL CH_2Cl_2 was added 0.950 g (6.30 mmol) TBSCl at room

temperature. After 15 hours, 100 mL half sat. aq. $NaHCO_3$ was added and the mixture extracted with 100 mL and 50 mL EtOAc. The organic layers were combined, washed with 20 mL brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude material was purified by column chromatography (6:1 hexanes/EtOAc) to provide 1.67 g (93%) **5.41** as a white solid which was recrystallized from pentane to afford colorless prisms (mp = 110–112 °C). ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 5.84 (s, 1H), 3.61 (tt, *J* = 10.8, 4.3 Hz, 1H), 2.42-2.26 (m, 3H), 2.16-2.10 (m, 1H), 2.08-2.00 (m, 2H), 1.94-1.82 (m, 3H), 1.68-1.62 (m, 1H), 1.42-1.34 (m, 1H), 1.32-1.21 (m, 2H), 1.14 (q, *J* = 12.5 Hz, 1H), 1.01 (qd, *J* = 12.5, 3.2 Hz, 1H), 0.95 (d, *J* = 6.5 Hz, 3H), 0.89 (s, 9H), 0.78 (qd, *J* = 10.9, 3.0 Hz, 1H), 0.06 (d, *J* = 1.8 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 200.4, 168.9, 121.1, 71.3, 48.9, 45.3, 43.5, 38.1, 37.7, 36.9, 35.6, 35.4, 29.5, 28.5, 25.9, 19.2, 18.2, –4.6; IR (thin film) 2929, 2857, 1677, 1092 cm^{-1}; HRMS (ESI) calculated for $C_{21}H_{36}O_2Si$ $[M+Na]^+$ 371.2382 found 371.2388.

Enone 5.42

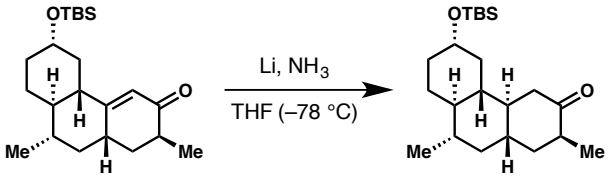


5.41 **5.42:** 13 : 1 dr

LDA was prepared in a 50 mL round bottom flask by addition of 1.90 mL (5.13 mmol) 2.7 M n-BuLi/hexanes to 0.81 mL (5.78 mmol) diisopropylamine in 17 mL THF at 0 °C. To the stirring LDA solution at –78 °C was added 1.55 g (4.45 mmol) **5.41** with the assistance of 9 mL THF. After 10 minutes, 1.0 mL (5.75 mmol) HMPA was added neat followed by 0.83 mL (13.3 mmol) methyl iodide. The cold bath was removed after an additional 10 minutes and the reaction stirred for 50 minutes before 20 mL half sat. aq. NH_4Cl was added. The solution was extracted with 50

mL and 25 mL EtOAc. The organic layers were combined, washed with 20 mL brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude mixture was purified by column chromatography (10:1 hexanes/EtOAc) to afford 1.51 g (93%, 13:1 dr) **5.42** as a white wax. ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 5.75 (s, 1H), 3.63 (tt, *J* = 10.8, 4.4 Hz, 1H), 2.47-2.40 (m, 1H), 2.35 (dq, *J* = 11.6, 5.5 Hz, 1H), 2.05 (dq, *J* = 13.3, 3.6 Hz, 1H), 2.00-1.83 (m, 5H), 1.77 (dt, *J* = 13.7, 4.7 Hz, 1H), 1.44-1.23 (m, 4H), 1.11 (d, *J* = 6.9 Hz, 3H), 1.06-0.98 (m, 1H), 0.95 (d, *J* = 6.3 Hz, 3H), 0.89 (s, 9H), 0.74 (qd, *J* = 10.6, 3.1 Hz, 1H), 0.06 (d, *J* = 1.8 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 202.9, 168.1, 119.5, 71.2, 49.9, 45.7, 42.8, 37.8, 37.6, 37.4, 37.2, 36.0, 35.5, 29.6, 25.9, 19.2, 18.2, 15.4, –4.6; IR (thin film) 2928, 2856, 1675, 1627, 1249, 1092, 863, 835, 775 cm^{-1}; HRMS (ESI) calculated for $C_{22}H_{38}O_2Si$ $[M+H]^+$ 363.2719 found 363.2715.

Ketone 5.D

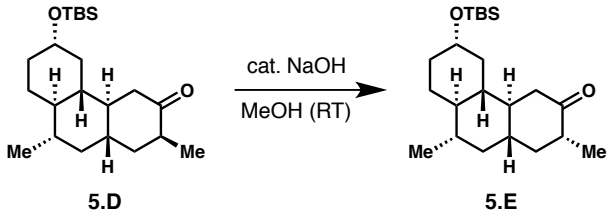


5.42: 11 : 1 dr **5.D**

To a 10 mL round bottom flask containing a glass stir bar and 5 mg (0.72 mmol) lithium metal then 3 mL ammonia was condensed and 0.4 mL THF added. At –78 °C 10 mg (0.028 mmol) **5.42** in 0.4 mL THF was added. After 2 minutes, 0.1 mL isoprene and 91 mg (1.7 mmol) solid NH_4Cl was added and the flask warmed to room temperature. The mixture was partitioned between 2 mL water and 5 mL EtOAc. The organic layer was washed with 2 mL brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude material was purified by column chromatography (20:1 hexanes/EtOAc) to afford 8.9 mg (89%, >20:1 dr) **5.D** as a

colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 3.54-3.48 (tt, *J* = 10.8, 4.4 Hz, 1H), 2.56-2.49 (m, 2H), 2.05 (dd, *J* = 14.7, 12.8 Hz, 1H), 2.01-1.93 (m, 2H), 1.91-1.86 (m, 1H), 1.68-1.54 (m, 4H), 1.27-1.12 (m, 3H), 1.20 (d, *J* = 7.3 Hz, 3H), 0.96-0.80 (m, 4H), 0.92 (d, *J* = 6.5 Hz, 3H), 0.88 (d, *J* = 9.4 Hz, 9H), 0.56 (qd, *J* = 10.8, 3.3 Hz, 1H), 0.04 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 216.0, 71.5, 47.3, 47.2, 46.2, 43.8, 42.1, 41.6, 39.5, 39.1, 36.7, 35.7, 35.3, 28.5, 20.0, 18.2, 17.7, –4.55, –4.60; IR (thin film) 2927, 2856, 1711, 1460, 1087, 860, 835, 774 cm^{-1}; HRMS (ESI) calculated for $C_{22}H_{40}O_2Si$ $[M+Na]^+$ 387.2695 found 387.2703.

Ketone 5.E

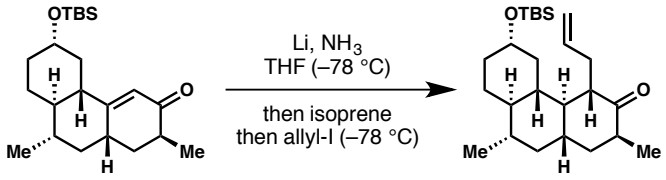


5.D 5.E

To a 1 dram vial was added 8.1 mg (0.022 mmol) **5.D** in 0.2 mL MeOH and 0.1 mL (0.013 mmol) 0.13 M NaOH/MeOH. After 2 hours at room temperature, 2 mL sat. aq. NH_4Cl and and 5 mL EtOAc were added. The organic layer was separated, washed with 2 mL brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo to afford 7.9 mg (97%, >10:1 dr) **5.E** as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 3.53-3.47 (tt, *J* = 10.8, 4.4 Hz, 1H), 2.64 (dd, *J* = 13.3, 3.9 Hz, 1H), 2.42 (dquintet, *J* = 12.9, 6.4 Hz, 1H), 2.01-1.87 (m, 5H), 1.69 (dt, *J* = 13.0, 3.5 Hz, 1H), 1.54 (qt, *J* = 10.7, 3.2, 1H), 1.26-1.07 (m, 4H), 1.02 (d, *J* = 6.5 Hz, 3H), 0.95-0.75 (m, 4H), 0.91 (s, 3H), 0.88 (s, 9H), 0.55 (qd, *J* = 10.8, 3.2 Hz, 1H), 0.06 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 213.2, 71.5, 48.4, 47.3, 46.2, 45.2, 44.7, 42.6, 41.7, 41.5, 39.3, 36.6, 35.7, 28.5, 25.9, 20.0, 18.2, 14.3, –4.54, –4.59; IR (thin film) 2927, 2856, 1713,

1460, 1250, 1090, 860, 835, 774 cm^{-1}; HRMS (ESI) calculated for $C_{22}H_{40}O_2Si$ $[M+Na]^+$ 387.2695 found 387.2687.

Allyl 5.43

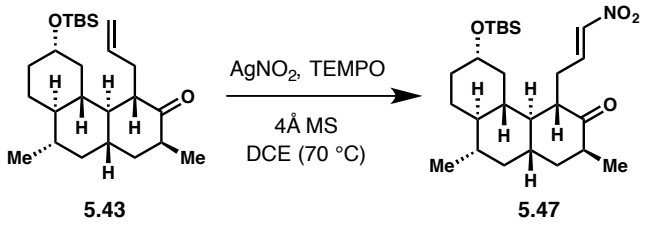


5.42 **5.43**

To a 25 mL round bottom flask containing a glass stir bar and 4.0 mg (0.58 mmol) lithium metal was condensed 7 mL ammonia and 4 mL THF added. At –78 °C 85 mg (0.23 mmol) **5.42**, 17 mg (0.23 mmol) t-BuOH in 3 mL THF was added. After stirring for 10 minutes, 0.1 mL isoprene was added and stirred until all lithium was discharged. To the white slurry was added 0.045 mL (0.50 mmol) allyl iodide at –78 °C. The reaction was stirred for 2.5 hours before 3 mL sat. aq. NH_4Cl was added slowly and warmed to room temperature. The mixture was partitioned between 5 mL water and 15 mL EtOAc. The organic layer was washed with 5 mL brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude material was purified by column chromatography (30:1 hexanes/EtOAc) to afford 54 mg (56%, >10:1 dr) **5.43** as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 5.68 (ddt, *J* = 16.9, 10.0, 7.0 Hz, 1H), 5.01 (d, *J* = 7.0 Hz, 1H), 4.99 (s, 1H), 3.49 (tt, *J* = 10.1, 4.8 Hz, 1H), 2.64 (dqd, *J* = 10.3, 6.9, 3.4 Hz, 1H), 2.44 (dt, *J* = 13.3, 6.3 Hz, 1H), 2.31-2.25 (m, 1H), 2.19 (dt, *J* = 10.1, 4.9 Hz, 1H), 2.02-1.88 (m, 4H), 1.64-1.57 (m, 2H), 1.39 (dt, *J* = 13.5, 3.3 Hz, 1H), 1.28-1.21 (m, 1H), 1.16-1.06 (m, 3H), 1.04 (d, *J* = 6.9 Hz, 3H), 0.89 (s, 9H), 0.97-0.77 (m, 6H), 0.56 (qd, *J* = 10.5, 2.5 Hz, 1H), 0.06 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 217.9, 135.1, 116.7, 71.6, 54.4, 51.9, 47.7, 47.1, 42.7, 40.1, 40.0, 38.5, 37.7, 37.5, 36.5, 35.8, 28.4, 25.9, 19.9, 18.3, 16.3, –4.48,

–4.55; IR (thin film) 2927, 2857, 1709, 1461, 1249, 1089, 835, 775 cm^{-1}; HRMS (ESI) calculated for $C_{25}H_{44}O_2$ $[M+Na]^+$ 427.3008 found 427.3014.

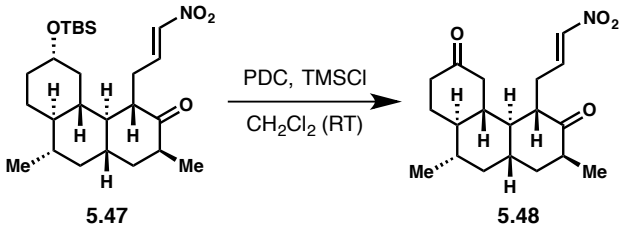
Nitroalkene 5.47



5.43 5.47

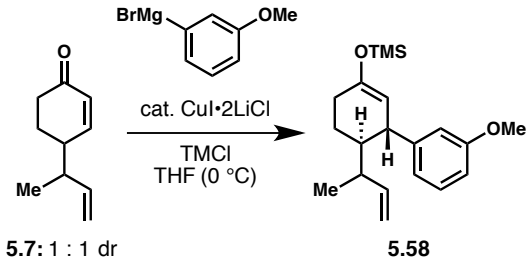
A 1 dram vial containing 30 mg (0.0741 mmol) **5.43** and 32 mg 4Å MS in 0.5 mL DCE was stirred for 15 minutes before 116 mg (0.754 mmol) $AgNO_2$ and 20 mg (0.128 mmol) TEMPO was added. The flask was sealed and heated at 70 °C for 30 hours. The flask was cooled, filtered over Celite with EtOAc, then concentrated in vacuo. The crude material was purified by column chromatography (10:1 hexanes/EtOAc) to afford 23 mg (69%, >20:1 E/Z) **5.47** as a light red oil. ^1H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 7.15 (dt, *J* = 13.5, 7.0 Hz, 1H), 6.98 (d, *J* = 13.5 Hz, 1H), 3.51 (d, *J* = 0.4 Hz, 1H), 2.65-2.60 (m, 2H), 2.48 (dt, *J* = 15.9, 8.4 Hz, 1H), 2.30-2.28 (m, 1H), 1.66 (t, *J* = 13.9 Hz, 2H), 1.52-1.43 (m, 3H), 1.09 (d, *J* = 6.5 Hz, 3H), 1.31-0.78 (m, 12H), 0.91 (s, 9H), 0.62-0.58 (m, 1H), 0.07 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 215.8, 140.1, 138.3, 71.0, 52.3, 51.5, 47.2, 46.9, 42.3, 39.9, 38.0, 37.7, 36.9, 36.2, 35.4, 33.1, 28.0, 25.6, 19.6, 17.9, 16.0, –4.7, –4.9; IR (thin film) 2928, 2857, 1706, 1527, 1461, 1349, 1089, 860, 835, 775 cm^{-1}; HRMS (ESI) calculated for $C_{25}H_{43}NO_4Si$ $[M+Na]^+$ 472.2859 found 472.2862.

Ketone 5.48



A 1 dram vial containing 5 mg (0.013 mmol) PDC, 0.1 mL CH_2Cl_2 at 0 °C was treated with 0.1 mL (0.031 mmol) 0.31 M TMSCl/CH_2Cl_2. After 10 minutes ~2 mg (0.0044 mmol) **5.47** in 0.2 mL CH_2Cl_2 was added. After 5 minutes the cold bath was removed and after 12 hours silica gel was added and the contents filtered over silica gel with EtOAc. The filtrate was concentrated and the crude material was purified by column chromatography (3:1 hexanes/EtOAc) to afford ~0.5 mg (33%) **5.48**.

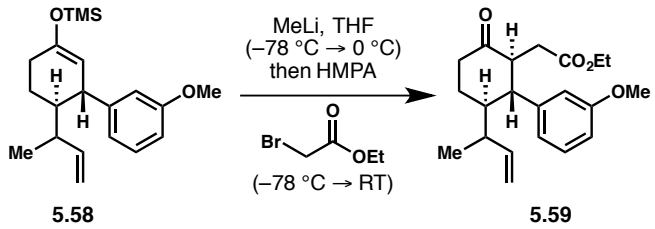
Enoxysilane 5.58



3-Methoxyphenylmagnesium bromide was prepared by addition of 1.9 mL (15.0 mmol) 3-bromoanisole in 1.9 mL THF to 440 mg (18.1 mmol) magnesium metal in 7.5 mL THF activated by dibromoethane maintaining 40–50 °C. A 50 mL round bottom flask was charged with 17 mL THF (rigorously degassed by purging with argon under sonication) then 0.80 mL (0.40 mmol) 0.50 M CuI•2LiCl/THF. At 0 °C, 602 mg (4.01 mmol) **5.7** in 6 mL THF and 0.55 mL (4.3 mmol) TMSCl was added, followed by the dropwise addition of 3.4 mL (4.8 mmol) 1.41 M 3-methoxyphenylmagnesium bromide over the course of 5 minutes. Stirring at 0 °C was continued

for 1.5 hours before 2 mL NEt_3 was added and the reaction poured into a rapidly stiring solution of 25 mL sat. aq. NH_4Cl, 25 g ice, 25 mL Et_2O and 2 mL NEt_3 cooled in an ice bath. After all salts dissolved an additional 25 mL Et_2O was added, the layers were separated and the organic layer washed with 20 mL half sat. aq. $NaHCO_3$, 15 mL brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude oil was flushed through a pad of Florisil®, pretreated with hexanes 1% NEt_3, with hexanes 1% NEt_3 to afford 830 mg (62%, >20:1 conjugate addition dr) **5.58** as a colorless oil. ^{1}H NMR (500 MHz, C_6D_6 at 7.15 ppm) δ 7.16-7.12 (m, 1H), 7.01 (dt, *J* = 6.7, 1.9 Hz, 1H), 6.93 (d, *J* = 7.6 Hz, 0.5H), 6.89 (d, *J* = 7.6 Hz, 0.5H), 6.71-6.68 (m, 1H), 5.70-5.62 (m, 1H), 5.03-4.88 (m, 3H), 3.41 (dq, *J* = 8.6, 2.6 Hz, 1H), 3.37 (s, 1.5H), 3.36 (s, 1.5 H), 2.35-2.28 (m, 1H), 2.19-2.13 (m, 2H), 1.69-1.58 (m, 2H), 1.51 (ddt, *J* = 11.4, 8.3, 3.1 Hz, 1H), 1.41-1.32 (m, 1H), 0.88 (d, *J* = 6.9 Hz, 1.5H), 0.86 (d, *J* = 6.9 Hz, 1.5H), 0.17 (s, 4.5H), 0.16 (s, 4.5H); ^{13}C NMR (126 MHz, C_6D_6 at 128 ppm) mixture δ 160.4, 151.6, 151.3, 148.50, 148.46, 141.4, 141.1, 129.6, 129.5, 121.2, 121.1, 115.0, 114.8, 114.6, 113.5, 111.8, 111.7, 108.2, 107.5, 54.7, 47.2, 46.1, 45.4, 44.7, 38.1, 37.3, 30.2, 29.6, 22.5, 21.8, 19.5, 14.2, 0.4; IR (thin film) 2958, 2873, 2835, 1665, 1251, 1184, 845 cm^{-1}; HRMS (ESI) calculated for desilylation only, $C_{17}H_{22}O_2$ $[M+Na]^+$ 281.1518 found 281.1523.

Ketoester 5.59

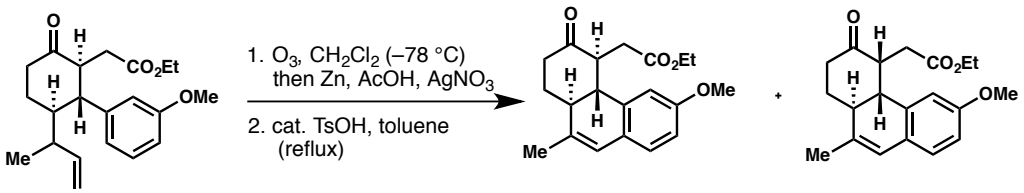


5.58 5.59

To 25 mL round bottom flask containing 819 mg (2.48 mmol) **5.58** in 10 mL THF was added 1.9 mL (2.6 mmol) 1.40 M MeLi/Et_2O at –78 °C. After 30 minutes the flask was placed into an ice bath and stirring continued for 30 minutes. The reaction was recooled to –78 °C then treated with 0.90 mL (5.2 mmol) HMPA and stirred until homogeneous. After the addition of 0.70 mL (6.3 mmol) ethyl bromoacetate the reaction was kept at –78 °C for 30 minutes. The cold bath was removed. After 1 hour the reaction was poured into 30 mL half sat. aq. NH_4Cl and extracted with 30 mL EtOAc and 10 mL EtOAc. The organic layers were combined, washed with 10 mL brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude oil was purifed by column chromatography (5:1 hexanes/EtOAc) to afford 768 mg (90%, >20:1 alkylation) **5.59** as a white wax. ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 7.28-7.24 (m, 1H), 6.80-6.72 (m, 3H), 5.78 (ddd, *J* = 17.2, 10.6, 5.8 Hz, 0.5H), 5.65 (ddd, *J* = 17.2, 10.3, 8.0 Hz, 0.5H), 5.01-4.96 (m, 1H), 4.89 (dt, *J* = 17.3, 1.6 Hz, 0.5H), 4.84-4.80 (m, 0.5H), 4.06-3.94 (m, 2H), 3.81 (s, 3H), 3.09 (dddd, *J* = 16.7, 12.5, 8.9, 3.8 Hz, 1H), 2.63 (t, *J* = 11.7 Hz, 0.5H), 2.60-2.50 (m, 2.5H), 2.43 (ddd, *J* = 16.5, 9.4, 6.9 Hz, 1H), 2.22-2.00 (m, 3H), 1.92 (ddd, *J* = 20.2, 16.7, 3.5 Hz, 1H), 1.54 (ddd, *J* = 12.6, 7.8, 5.0 Hz, 1H), 1.20-1.16 (m, 3H), 0.98 (d, *J* = 7.0 Hz, 1.5H), 0.81 (d, *J* = 6.9 Hz, 1.5H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) mixture δ 210.02, 209.97, 172.7, 172.7, 159.97, 159.85, 143.3, 143.0, 142.8, 138.5, 130.0, 129.8, 115.9, 113.5, 111.90, 111.88, 60.31, 60.29, 55.19, 55.18, 53.6, 53.0, 52.3, 52.5, 47.4, 46.7, 41.2, 41.0, 37.4, 36.4, 32.45, 32.44, 26.0, 25.7, 19.0, 14.1, 11.0; IR (thin film) 3076, 2962, 2938, 2836, 1731, 1715, 1599, 1584, 1262,

1195, 1156, 1041 cm^{-1}; HRMS (ESI) calculated for $C_{21}H_{28}O_4$ $[M+Na]^+$ 367.1885 found 367.1866.

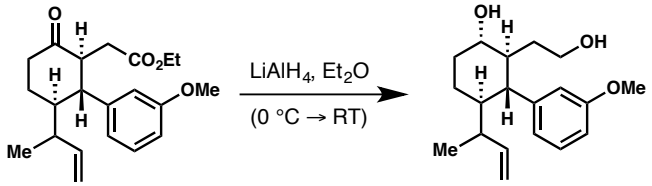
Ketoester 5.61



5.59 5.61

A 100 mL round bottom flask containing 30 mg (0.087 mmol) **5.59** dissolved in 2 mL CH_2Cl_2 was cooled to –78 °C and treated with a stream of ozone. After the solution became blue, the solution was sparged with oxygen. A single portion of 0.2 mL AcOH, 30 mg (0.46 mmol) Zn powder and 1 mg (0.0059 mmol) $AgNO_3$ was added. After stirring at –78 °C for 2 hours, the bath was removed and stirring continued for 2 hours. The reduction was determined complete by TLC and the solution was filtered over Celite, washing with CH_2Cl_2. The filtrate was washed with water, sat. aq. $NaHCO_3$, brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. A round bottom flask containing crude aldehyde in toluene was treated with $TsOH•H_2O$ and heated to 140 °C under a Dean–Stark trap. After 2 hours the reaction was cooled, diluted with Et_2O, washed with half sat. aq. $NaHCO_3$ and brine. The aqueous layers were combined and back extracted with Et_2O. All organic layers were combined, dried over $MgSO_4$, filtered and all volatiles removed in vacuo to afford a crude material assigned as **5.61** as a 1.6:1 mixture of diastereomers.

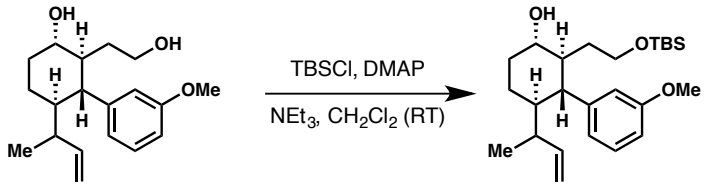
Diol 5.62



5.59 **5.62**

A 100 mL 3-neck round bottom flask fitted with a thermometer was charged with 15 mL Et_2O, cooled in an ice bath and 260 mg (6.85 mmol) $LiAlH_4$ added. After 10 minutes 768 mg (2.23 mmol) dicarbonyl was added with the assistance of 7 mL Et_2O ensuring the internal temperature remained below 4 °C over the course of 30 minutes. The ice bath was removed. After 3 hours 0.25 mL EtOAc was added at 0 °C then 0.25 mL water, 0.25 5 M NaOH, 0.75 mL water and 0.50 g Na_2SO_4. After 30 minutes of vigorous stirring the contents were filtered over Celite®; the filter cake was washed with 150 mL Et_2O. The filtrate was concentrated and the residue purified by column chromatography (1:2 hexanes/EtOAc) to afford 624 mg (91%, 4:1 dr) **5.62** as a viscous colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) mixture of diastereomers and slow rotation δ 7.22 (bs, 1H), 6.76-6.69 (m, 3H), 5.83-5.67 (m, 1H), 4.99 (dd, *J* = 10.3, 1.4 Hz, 0.5), 4.91-4.89 (m, 0.5), 4.85-4.79 (m, 1H), 3.81 (s, 3H), 3.59-3.54 (m, 1H), 3.45-3.37 (m, 1H), 3.31-3.23 (m, 1H), 2.27-2.20 (m, 1H), 2.12 (ddq, *J* = 12.6, 8.5, 4.1 Hz, 1H), 1.93-1.82 (m, 2H), 1.71-1.40 (m, 5H), 1.19 (quintett, *J* = 12.7, 2.7 Hz, 1H), 0.89 (d, *J* = 6.8 Hz, 0.2H), 0.88 (d, *J* = 7.0 Hz, 1.3H), 0.86 (d, *J* = 6.9 Hz, 0.2H), 0.80 (d, *J* = 6.9 Hz, 1.3H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) mixture or diastereomers and slow rotation δ 145.0, 144.8, 144.1, 139.6, 115.1, 112.7, 74.8, 74.6, 62.2, 62.1, 55.1, 55.1, 49.91, 49.87, 48.1, 47.4, 37.6, 36.6, 35.05, 35.00, 34.7, 34.5, 23.3, 23.2, 19.0, 11.1; IR (thin film) 3304, 3077, 2997, 2932, 2882, 1599, 1584, 1487, 1260, 1046 cm^{-1}; HRMS (ESI) calculated for $C_{19}H_{28}O_3$ $[M+Na]^+$ 327.1936 found 327.1933.

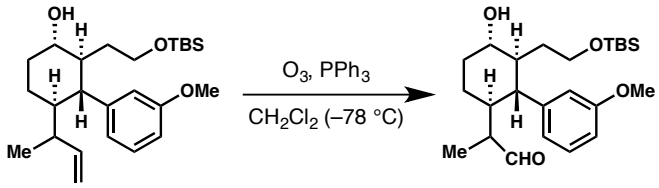
TBS ether 5.65



5.62: 7 : 1 dr **5.65:** >10 : 1 dr

To a 1 dram vial containing 15 mg (0.050 mmol) **5.62** in 1 mL CH_2Cl_2 was added 7 mg (0.057 mmol) DMAP and 0.05 mL (0.36 mmol) NEt_3. After the addition of 19 mg (0.13 mmol) TBSCl the reaction stirred for 3 days. The reaction was quenches with sat. aq. $NaHCO_3$, extraced thrice with EtOAc. The organic layers were combined and washed with brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude oil was purified by column chromatography (10:1 hexanes/EtOAc) to afford 18 mg (86%, >10:1 dr) **5.65** as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 7.21 (bs, 1H), 6.81-6.61 (m, 3H), 5.75-5.68 (m, 1H), 4.98 (dd, *J* = 10.3, 2.0 Hz, 0.5H), 4.89 (dt, *J* = 10.5, 1.6 Hz, 0.5H), 4.84-4.78 (m, 1H), 4.66 (bs, 1H), 3.80 (s, 3H), 3.60-3.54 (m, 1H), 3.34 (dtd, *J* = 14.7, 10.1, 4.4 Hz, 1H), 3.28-3.20 (m, 1H), 2.25-2.12 (m, 2H), 1.93-1.80 (m, 1H), 1.74-1.50 (m, 4H), 1.45-1.34 (m, 2H), 1.29-1.12 (m, 1H), 0.88 (d, *J* = 1.6 Hz, 10.5H), 0.80 (d, *J* = 6.9 Hz, 1.5H), 0.043 (s, 1.5H), 0.038 (s, 1.5H), 0.035 (s, 1.5H), 0.031 (s, 1.5H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 145.4, 145.1, 144.2, 139.9, 115.0, 112.6, 74.3, 74.2, 63.1, 55.12, 55.11, 50.60, 50.54, 48.3, 47.6, 37.8, 36.7, 36.6, 35.0, 34.9, 34.4, 34.3, 25.9, 23.4, 23.2, 19.0, 18.2, 11.2, –5.5, –5.6; IR (thin film) 3416, 3077, 2953, 2929, 2858, 2882, 1599, 1584, 1257, 1080, 1048, 836, 777 cm^{-1}; HRMS (ESI) calculated for $C_{25}H_{42}O_3Si$ $[M+Na]^+$ 441.2801 found 441.2784.

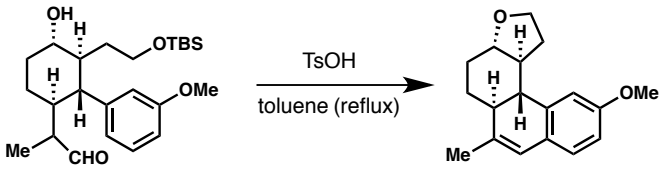
Aldehyde 5.66



5.65 **5.66**

To a 1 dram vial containing 12 mg (0.029 mmol) **5.65** in 0.5 mL CH_2Cl_2 was bubbled O_3/O_2 at –78 °C until the solution turned blue. The flask was purged with O_2 until the blue color faded, then 9 mg (0.034 mmol) PPh_3 in 0.2 mL CH_2Cl_2 was added. Stirring was continued at –78 °C for 1 hour then the bath was removed. After 2 hours the contents were diluted with EtOAc, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude oil was purified by column chromatography (5:1 hexanes/EtOAc) to afford 8 mg (67%) **5.66** as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 9.47 (s, 0.5H), 9.40 (s, 0.5H), 7.21 (bs, 1H), 6.88-6.57 (m, 3H), 4.80 (bs, 1H), 3.81 (s, 1.5H), 3.80 (s, 1.5H), 3.61-3.58 (m, 1H), 3.39 (qd, *J* = 10.1, 3.7 Hz, 1H), 3.31-3.24 (m, 1H), 2.25-2.13 (m, 2H), 1.97-1.86 (m, 2H), 1.74-1.22 (m, 5H), 1.00 (d, *J* = 7.1 Hz, 1.5H), 1.01-0.89 (m, 1H), 0.95 (d, *J* = 7.1 Hz, 1.5H), 0.89 (s, 4.5H), 0.89 (s, 4.5H), 0.05 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 205.1, 203.9, 144.2, 144.1, 73.8, 73.8, 63.0, 55.2, 48.2, 47.8, 46.5, 35.1, 34.8, 34.4, 34.0, 26.8, 25.9, 24.6, 18.2, 10.9, 6.8, –5.5, –5.6; IR (thin film) 3410, 2929, 2857, 1721, 1599, 1464, 1256, 1081, 1047, 836, 778 cm^{-1}; HRMS (ESI) calculated for $C_{24}H_{40}O_4Si$ $[M+Na]^+$ 443.2594 found 443.2595.

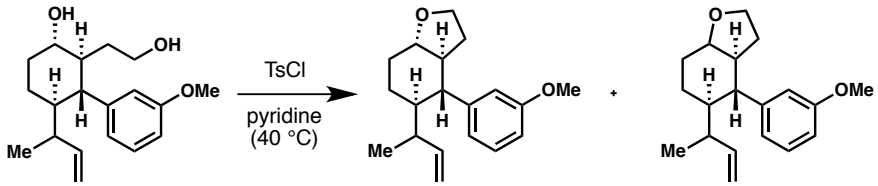
Dihydronaphthalene 5.64



5.66 **5.64**

To a 5 mL round bottom flask containing 7 mg (0.017 mmol) **5.66** was added a solution of 2 mg (0.011 mmol) TsOH•H_2O predried with 2 mL toluene over a Hickmann still. The reaction was refluxed over a Hickmann still for 2 hours. The reaction was cooled, diluted with sat. aq. $NaHCO_3$, EtOAc and the layers separated. The organic layer was washed with brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude oil was purified by column chromatography (5:1 hexanes/EtOAc) to afford 3 mg (66%, single diastereomer) **5.64** as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 7.05 (s, 1H), 6.94 (d, *J* = 8.2 Hz, 1H), 6.71 (dd, *J* = 8.3, 2.4 Hz, 1H), 6.25 (s, 1H), 4.09 (q, *J* = 8.1 Hz, 1H), 3.97 (td, *J* = 8.6, 3.5 Hz, 1H), 3.81 (s, 3H), 3.20 (ddd, *J* = 11.0, 9.7, 3.5 Hz, 1H), 2.75 (dtd, *J* = 11.1, 7.5, 3.6 Hz, 1H), 2.51 (dd, *J* = 14.0, 10.5 Hz, 1H), 2.24 (ddq, *J* = 14.0, 10.5, 3.5 Hz, 2H), 2.12 (t, *J* = 14.0 Hz, 1H), 1.91 (s, 3H), 1.88-1.74 (m, 2H), 1.55-1.39 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 157.9, 139.5, 138.4, 128.7, 125.7, 123.6, 112.4, 109.9, 83.7, 67.1, 55.2, 46.8, 46.4, 41.9, 31.8, 29.9, 27.0, 20.8; IR (thin film) 2935, 2869, 1607, 1489, 1157, 1064, 1041 cm^{-1}; HRMS (ESI) calculated for $C_{18}H_{22}O_2$ $[M+NH_4]^+$ 288.1964 found 288.1955.

Perhydrobenzofuran 5.67 and 5.F

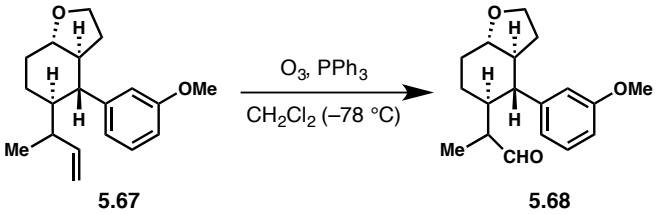


5.62: 4 : 1 dr **5.67:** 11 : 1 dr **5.F**

To a 25 mL round bottom flask containing 510 mg (1.68 mmol) **5.62** in 8 mL pyridine was added 820 mg (4.30 mmol) p-toluenesulfonyl chloride at room temperature. The flask was placed in a 40 °C oil bath. After 15 hours the reaction was cooled to room temperature and quenched with 10 mL sat. aq. $NaHCO_3$, 5 mL water and extraced with 30 mL EtOAc. The organic layer was washed thrice with 10 mL 6 M HCl then 5 mL water. The acidic aqueous washings were combined, back extraced with 10 mL EtOAc and all organic phases combined. The organic medium was washed with 10 mL sat. aq. $NaHCO_3$, 10 mL brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude oil was purified by column chromatography (10:1 hexanes/EtOAc) to afford 358 mg (74%, 11:1 dr) **5.67** as a colorless oil and 74 mg (15%, 2.7:1.8:1.7:1 dr) **5.F** as a colorless oil. **5.67:** ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) spectrum for an 8:1 mixture of diastereomers δ 7.24 (t, *J* = 7.8 Hz, 0.5H), 7.23 (t, *J* = 7.9 Hz, 0.5H), 6.79-6.72 (m, 3H), 5.80-5.70 (m, 1H), 4.99 (d, *J* = 10.5 Hz,), 4.92 (d, *J* = 10.5 Hz, 1H), 4.84 (dd, *J* = 17.2, 11.2 Hz, 1H), 3.88 (qd, *J* = 9.1, 2.6 Hz, 1H), 3.84-3.79 (m, 1H), 3.82 (s, 3H), 3.16 (ddq, *J* = 16.4, 10.6, 5.5 Hz, 1H), 2.31 (dt, *J* = 15.5, 10.9 Hz, 1H), 2.21 (ddq, *J* = 12.0, 8.2, 3.9 Hz, 1H), 2.12-2.04 (m, 1H), 1.97 (dq, *J* = 13.7, 3.5 Hz, 1H), 1.83-1.40 (m, 7H), 1.32-1.20 (m, 1H), 0.95 (d, *J* = 7.0 Hz, 1.4H), 0.91 (d, *J* = 7.0 Hz, 0.2H), 0.84 (d, *J* = 7.0 Hz, 1.4H), 0.79 (d, *J* = 6.9 Hz, 0.2H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) major δ 144.8, 144.6, 144.1, 139.8, 129.5, 129.4, 115.0, 112.7, 110.9, 82.8, 82.6, 67.1, 67.1, 55.1, 52.1, 52.0, 50.3, 49.9, 48.0, 47.4, 37.3, 36.2, 30.6, 30.5, 30.0, 30.0, 23.51, 23.45, 19.1, 11.6; IR (thin film) 3073, 2934, 2871, 1600, 1583,

1261, 1047, 911, 778, 701 cm^{-1}; HRMS could not be obtained. **5.F:** ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 7.25-7.21 (m, 1H), 6.80-6.72 (m, 3H), 5.80-5.66 (m, 1H), 5.00-4.73 (m, 2H), 4.02 (dq, *J* = 14.7, 7.6 Hz, 0.6H), 3.90-3.80 (m, 5H), 3.20-3.12 (m, 0.4H), 2.34-2.05 (m, 3H), 1.98-1.89 (m, 1H), 1.85-1.31 (m, 7H), 1.29-1.21 (m, 1H), 0.95 (d, *J* = 7.0 Hz, 0.7H), 0.91 (d, *J* = 7.0 Hz, 1.3H), 0.84 (d, *J* = 7.0 Hz, 0.4H), 0.79 (d, *J* = 6.9 Hz, 0.8H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) mixture δ 159.6, 159.5, 146.0, 145.7, 144.8, 144.6, 144.2, 144.1, 139.80, 139.76, 129.4, 129.4, 129.3, 129.1, 115.0, 114.8, 112.7, 112.6, 110.94, 110.86, 110.8, 82.8, 82.6, 77.6, 77.4, 67.1, 67.1, 65.8, 65.7, 55.13, 55.11, 52.1, 52.0, 50.3, 49.9, 48.1, 48.0, 47.7, 47.4, 46.6, 46.1, 46.0, 45.8, 37.9, 37.3, 36.8, 36.2, 30.9, 30.9, 30.6, 30.5, 30.0, 28.09, 28.06, 23.51, 23.45, 19.7, 19.6, 19.1, 18.9, 11.6, 11.2; IR (thin film) 2934, 2869, 1599, 1486, 1458, 1261, 1047, 667, 702 cm^{-1}; HRMS could not be obtained.

Aldehyde 5.68

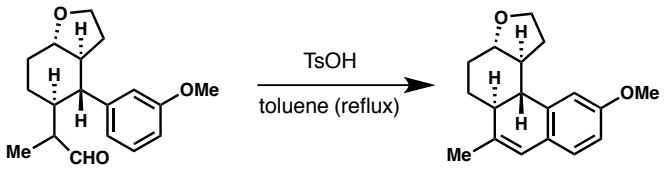


5.67 **5.68**

To a 1 dram vial containing 73 mg (0.255 mmol) **5.67** in 2.5 mL CH_2Cl_2 was bubbled O_3/O_2 at –78 °C until the solution turned blue. The flask was purged with O_2 until the blue color faded, then 80 mg (0.305 mmol) PPh_3 was added. Stirring was continued at –78 °C for 2 hours then the bath was removed. After 6 hours the reaction was dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude oil was purified by column chromatography (3:1→1:2 hexanes/EtOAc) to afford 65 mg (89%, with ~25% over oxidation) **5.68** as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) major δ 9.55 (s, 0.5H), 9.49 (s, 0.5H), 7.29-7.23 (m, 1H),

6.81-6.74 (m, 3H), 4.09 (s, 1H), 3.94-3.85 (m, 2H), 3.83 (s, 1.5H), 3.82 (s, 1.5H), 3.21 (dtd, *J* = 17.8, 10.5, 3.5 Hz, 1H), 2.56 (t, *J* = 10.9 Hz, 1H), 2.39-2.16 (m, 3H), 2.10-1.99 (m, 1H), 1.83-1.35 (m, 4H), 1.07 (d, *J* = 7.1 Hz, 1.5H), 1.00 (d, *J* = 7.1 Hz, 1.5H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 205.1, 204.1, 143.62, 143.59, 129.9, 129.84, 129.80, 111.8, 67.3, 67.2, 55.3, 55.2, 51.9, 51.7, 47.6, 47.0, 46.4, 42.2, 30.8, 30.4, 30.1, 29.9, 27.0, 24.8, 14.3, 11.3, 7.1; IR (thin film) 2936, 2879, 1720, 1600, 1485, 1262, 1158, 1045 cm^{-1}; HRMS (ESI) calculated for $C_{18}H_{24}O_3$ [M-+Na]$^+$ 311.1623 found 311.1635.

Dihydronaphthalene 5.64

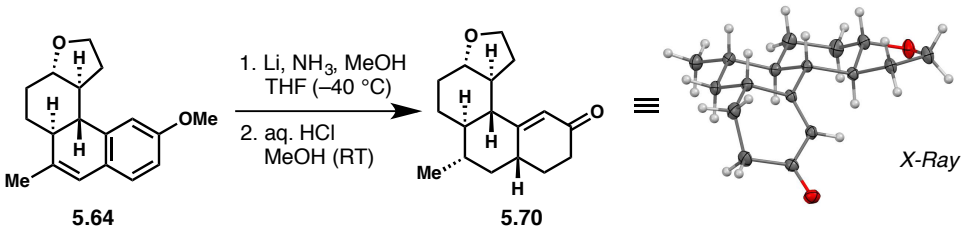


5.68 **5.64**

To a 10 mL round bottom flask containing 63 mg (0.218 mmol) **5.68** was added a solution of 2 mg (0.011 mmol) TsOH•H_2O predried with 3 mL toluene under a Hickmann still. The reaction was heated to reflux under a Hickmann still for 2 hours. The reaction was cooled, diluted with sat. aq. $NaHCO_3$, EtOAc and the layers separated. The organic layer was washed with brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude oil was purified by column chromatography (5:1 hexanes/EtOAc) to afford 31 mg (52%, single diastereomer) **5.64** as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 7.05 (s, 1H), 6.94 (d, *J* = 8.2 Hz, 1H), 6.71 (dd, *J* = 8.3, 2.4 Hz, 1H), 6.25 (s, 1H), 4.09 (q, *J* = 8.1 Hz, 1H), 3.97 (td, *J* = 8.6, 3.5 Hz, 1H), 3.81 (s, 3H), 3.20 (ddd, *J* = 11.0, 9.7, 3.5 Hz, 1H), 2.75 (dtd, *J* = 11.1, 7.5, 3.6 Hz, 1H), 2.51 (dd, *J* = 14.0, 10.5 Hz, 1H), 2.24 (ddq, *J* = 14.0, 10.5, 3.5 Hz, 2H), 2.12 (t, *J* = 14.0 Hz, 1H), 1.91 (s, 3H), 1.88-1.74 (m, 2H), 1.55-1.39 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ

157.9, 139.5, 138.4, 128.7, 125.7, 123.6, 112.4, 109.9, 83.7, 67.1, 55.2, 46.8, 46.4, 41.9, 31.8, 29.9, 27.0, 20.8; IR (thin film) 2935, 2869, 1607, 1489, 1157, 1064, 1041 cm^{-1}; HRMS (ESI) calculated for $C_{18}H_{22}O_2$ $[M+NH_4]^+$ 288.1964 found 288.1955.

Enone 5.70

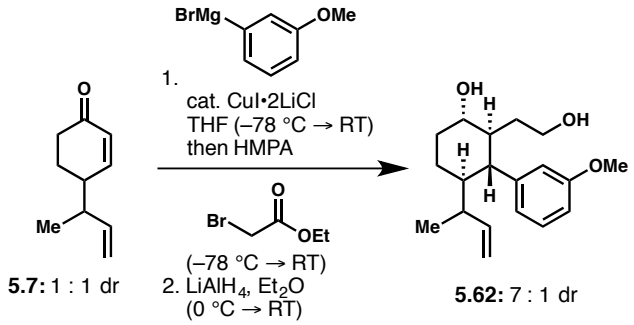


5.64 5.70

To a 10 mL round bottom flask charged with a glass stir bar was condensed 4 mL ammonia followed by the addition of 30 mg (0.11 mmol) **5.64** in 1.1 mL THF and 0.30 mL (4.9 mmol) MeOH. Slowly, 34 mg (4.9 mmol) lithium metal was added in small pieces at –40 °C. After complete addition and the blue color discharged, 275mg solid NH_4Cl was added and the ammonia evaporated. The white residue taken up in 3 mL water and 4 mL EtOAc. The organic layer was separated and washed with 1 mL brine. The aqueous layers were combined and back extracted with 2 mL EtOAc. The organic layers were combined, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude material in a 10 mL round bottom flask was dissolved in 1.1 mL MeOH and treated with 0.1 mL 6 M HCl. After 16 hours at room temperature half sat. aq. $NaHCO_3$ and EOAc were added. The layers were separated and the aqueous extracted with EtOAc. All organic layers were collected washed with brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude material was purified by column chromatography (3:1 hexanes/EtOAc) to afford 16 mg (52% over 2 steps) **5.70** as a white solid that recrystallized from benzene to afford colorless prisms (mp = 85–86 °C). ^1H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 5.85 (s, 1H), 3.97-3.88 (m, 2H), 3.15 (ddd, *J* = 11.4, 9.6, 3.4, 1H), 2.42-2.29 (m, 4H), 2.23-2.12

(m, 3H), 1.90 (dt, J = 12.7, 4.2 Hz, 1H), 1.84 (t, J = 10.5 Hz, 1H), 1.75-1.66 (m, 1H), 1.56-1.26 (m, 5H), 1.15-1.08 (m, 1H), 0.98-0.89 (m, 1H), 0.96 (d, J = 6.5 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 199.9, 168.8, 121.1, 82.9, 67.1, 51.6, 51.4, 45.1, 43.2, 38.4, 37.4, 34.1, 29.9, 29.7, 29.2, 27.4, 19.6; IR (thin film) 2927, 2868, 1667, 1622 cm^{-1}; HRMS (ESI) calculated for $C_{17}H_{24}O_2$ $[M+Na]^+$ 283.1674 found 283.1682.

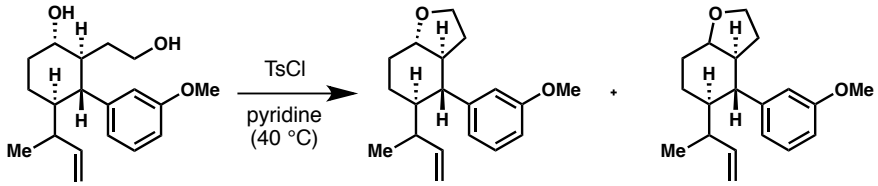
Diol 5.62



3-Methoxyphenylmagnesium bromide was prepared by addition of 7 mL (56 mmol) 3-bromoanisole in 7 mL THF to 1.77 g (73 mmol) magnesium metal in 28 mL THF activated by dibromoethane maintaining 40-50 °C. A 250 mL 3-neck round bottom flask fitted with a low temperature thermometer was charged with 110 mL THF and 31 mL (39 mmol) 1.26 M 3-methoxyphenylmagnesium bromide. At –78 °C, 9 mL (3.3 mmol) 0.37 M CuI•2LiCl/THF was added followed by 5.01 g (33.3 mmol, 1:1 dr) **5.7** in 15 mL THF while mainting at least –72 °C. Stirring at –78 °C was continued for 2 hours before the cold bath was removed. After 1 hour the reaction was recooled to –78 °C. To the solution was added 12 mL (82.8 mmol) HMPA. After 1 hour 15 mL (136 mmol) ethyl bromoacetate was added. The reaction was stirred at –78 °C for 10 minutes then the cold bath removed. After stirring for 28 hours at room temperature, the reaction was cooled in an ice bath and treated with 100 mL sat. aq. NH_4Cl, 100 mL water, extracted with

100 mL and twice with 50 mL Et_2O. The organic layers were combined, washed with 50 mL half sat. aq. NH_4Cl, 30 mL brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo to afford a crude oil. To an ice cooled 1 L 3-neck round bottom flask fitted with an overhead stirrer and thermometer, containing 300 mL Et_2O was added 5.05 g (133 mmol) $LiAlH_4$. The crude oil in 50 mL Et_2O was added via canula and washed with an additional 50 mL Et_2O, maintaining an internal temperature below 6 °C over the course of 1.5 hours. The ice bath was removed after 30 minutes. After 5 hours the flask was recooled in an ice bath and 5 mL EtOAc added over the course of 30 minutes. An oil bubbler was connected and 5 mL water, 5 mL 5 M NaOH, 15 mL water and 40 g Na_2SO_4 were added with careful temperature monitoring. After stirring the contents overnight, the solution was filtered over Celite and the filter cake washed with Et_2O (~1.2 L as determined by TLC). The filtrate was concentrated and the residue purified by column chromatography (1:2→1:1 hexanes/EtOAc) to afford 5.68 g (56% over 2 steps, 7:1 dr) **5.62** as a viscous colorless oil. ^1H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) mixture of diastereomers and slow rotation δ 7.22 (bs, 1H), 6.76-6.69 (m, 3H), 5.83-5.67 (m, 1H), 4.99 (dd, *J* = 10.3, 1.4 Hz, 0.5), 4.91-4.89 (m, 0.5), 4.85-4.79 (m, 1H), 3.81 (s, 3H), 3.59-3.54 (m, 1H), 3.45-3.37 (m, 1H), 3.31-3.23 (m, 1H), 2.27-2.20 (m, 1H), 2.12 (ddq, *J* = 12.6, 8.5, 4.1 Hz, 1H), 1.93-1.82 (m, 2H), 1.71-1.40 (m, 5H), 1.19 (quintett, *J* = 12.7, 2.7 Hz, 1H), 0.89 (d, *J* = 6.8 Hz, 0.2H), 0.88 (d, *J* = 7.0 Hz, 1.3H), 0.86 (d, *J* = 6.9 Hz, 0.2H), 0.80 (d, *J* = 6.9 Hz, 1.3H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) mixture or diastereomers and slow rotation δ 145.0, 144.8, 144.1, 139.6, 115.1, 112.7, 74.8, 74.6, 62.2, 62.1, 55.1, 55.1, 49.91, 49.87, 48.1, 47.4, 37.6, 36.6, 35.05, 35.00, 34.7, 34.5, 23.3, 23.2, 19.0, 11.1; IR (thin film) 3304, 3077, 2997, 2932, 2882, 1599, 1584, 1487, 1260, 1046 cm^{-1}; HRMS (ESI) calculated for $C_{19}H_{28}O_3$ $[M+Na]^+$ 327.1936 found 327.1933.

***Trans*-Perhydrobenzofuran 5.67 and 5.G**

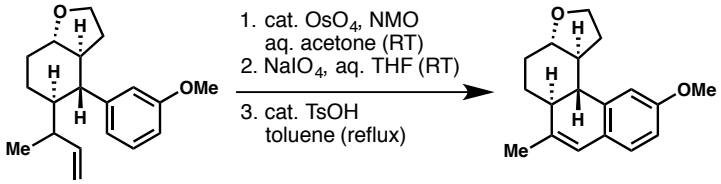


5.62: 4 : 1 dr **5.67:** 11 : 1 dr **5.G:** mixture

To a 25 mL round bottom flask containing 510 mg (1.68 mmol, 4:1 dr) **5.62** in 8 mL pyridine was added 820 mg (4.30 mmol) p-toluenesulfonyl chloride at room temperature. The flask was placed in a 40 °C oil bath. After 15 hours the reaction was cooled to room temperature and quenched with 10 mL sat. aq. $NaHCO_3$, 5 mL water and extraced with 30 mL EtOAc. The organic layer was washed thrice with 10 mL 6 M HCl then 5 mL water. The acidic aqueous washings were combined, back extraced with 10 mL EtOAc and all organic phases combined. The organic medium was washed with 10 mL sat. aq. $NaHCO_3$, 10 mL brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude oil was purified by column chromatography (10:1 hexanes/EtOAc) to afford 358 mg (74%, 11:1 dr) **5.67** as a colorless oil and 74 mg (15%, 2.7:1.8:1.7:1 dr) **5.G** as a colorless oil. **5.67:** ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) spectrum for an 8:1 mixture of diastereomers δ 7.24 (t, *J* = 7.8 Hz, 0.5H), 7.23 (t, *J* = 7.9 Hz, 0.5H), 6.79-6.72 (m, 3H), 5.80-5.70 (m, 1H), 4.99 (d, *J* = 10.5 Hz,), 4.92 (d, *J* = 10.5 Hz, 1H), 4.84 (dd, *J* = 17.2, 11.2 Hz, 1H), 3.88 (qd, *J* = 9.1, 2.6 Hz, 1H), 3.84-3.79 (m, 1H), 3.82 (s, 3H), 3.16 (ddq, *J* = 16.4, 10.6, 5.5 Hz, 1H), 2.31 (dt, *J* = 15.5, 10.9 Hz, 1H), 2.21 (ddq, *J* = 12.0, 8.2, 3.9 Hz, 1H), 2.12-2.04 (m, 1H), 1.97 (dq, *J* = 13.7, 3.5 Hz, 1H), 1.83-1.40 (m, 7H), 1.32-1.20 (m, 1H), 0.95 (d, *J* = 7.0 Hz, 1.4H), 0.91 (d, *J* = 7.0 Hz, 0.2H), 0.84 (d, *J* = 7.0 Hz, 1.4H), 0.79 (d, *J* = 6.9 Hz, 0.2H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) major δ 144.8, 144.6, 144.1, 139.8, 129.5, 129.4, 115.0, 112.7, 110.9, 82.8, 82.6, 67.1, 67.1, 55.1, 52.1, 52.0, 50.3, 49.9, 48.0, 47.4, 37.3, 36.2, 30.6, 30.5, 30.0, 30.0, 23.51, 23.45, 19.1, 11.6; IR (thin film) 3073,

2934, 2871, 1600, 1583, 1261, 1047, 911, 778, 701 cm^{-1}; HRMS could not be obtained. **5.G:** ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 7.25-7.21 (m, 1H), 6.80-6.72 (m, 3H), 5.80-5.66 (m, 1H), 5.00-4.73 (m, 2H), 4.02 (dq, *J* = 14.7, 7.6 Hz, 0.6H), 3.90-3.80 (m, 5H), 3.20-3.12 (m, 0.4H), 2.34-2.05 (m, 3H), 1.98-1.89 (m, 1H), 1.85-1.31 (m, 7H), 1.29-1.21 (m, 1H), 0.95 (d, *J* = 7.0 Hz, 0.7H), 0.91 (d, *J* = 7.0 Hz, 1.3H), 0.84 (d, *J* = 7.0 Hz, 0.4H), 0.79 (d, *J* = 6.9 Hz, 0.8H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) mixture δ 159.6, 159.5, 146.0, 145.7, 144.8, 144.6, 144.2, 144.1, 139.80, 139.76, 129.4, 129.4, 129.3, 129.1, 115.0, 114.8, 112.7, 112.6, 110.94, 110.86, 110.8, 82.8, 82.6, 77.6, 77.4, 67.1, 67.1, 65.8, 65.7, 55.13, 55.11, 52.1, 52.0, 50.3, 49.9, 48.1, 48.0, 47.7, 47.4, 46.6, 46.1, 46.0, 45.8, 37.9, 37.3, 36.8, 36.2, 30.9, 30.9, 30.6, 30.5, 30.0, 28.09, 28.06, 23.51, 23.45, 19.7, 19.6, 19.1, 18.9, 11.6, 11.2; IR (thin film) 2934, 2869, 1599, 1486, 1458, 1261, 1047, 667, 702 cm^{-1}; HRMS could not be obtained.

Dihydronaphthalene 5.64

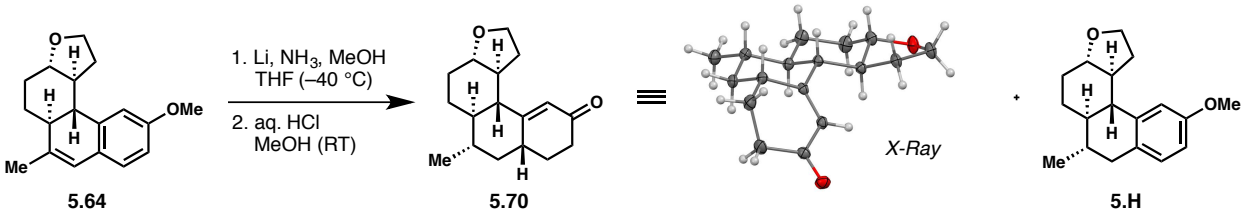


5.67: 11 : 1 dr **5.64:** single diastereomer

To a 25 mL round bottom flask containing 320 mg (1.12 mmol, 11:1 dr) **5.67** in 8 mL acetone and 2.6 mL nano-pure water was added 0.14 mL (0.022 mmol) 4 wt% OsO_4 in water then 270 mg (2.30 mmol) NMO at 0 °C open to air. The ice bath was immediately removed and after stirring 12 hours at room temperature 10 mL water and 1.20 g $NaHSO_3$ was added. After 10 minutes the solution was extracted thrice with 15 mL EtOAc. All organic layers were combined, washed with 10 mL sat. aq. $NaHCO_3$ and 10 mL brine. The aqueous layers were combined and back extracted with 5 mL EtOAc. The organic layers were combined dried over $MgSO_4$, filtered

and all volatiles removed in vacuo. The crude material was subjected to the next reaction without further purification. To a 100 mL round bottom flask containing the crude oil was added 10 mL 1:1 THF/water then 485 mg (2.27 mmol) $NaIO_4$ open to air. After 1 hour 10 mL water was added followed by 1.20 g $NaHSO_3$. The mixture was extracted thrice with 15 mL EtOAc. All organic layers were combined, washed with 10 mL sat. aq. $NaHCO_3$ and 10 mL brine. The aqueous layers were combined and back extracted with 5 mL EtOAc. The organic layers were combined dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude material was subjected to the next reaction without further purification. To a 25 mL round bottom flask containing crude aldehyde was added a solution of 12 mg (0.063 mmol) $TsOH•H_2O$ predried with 11 mL toluene over a Hickmann still. The reaction was refluxed over a Hickmann still for 2 hours. The reaction was cooled, diluted with 10 mL sat. aq. $NaHCO_3$, 20 mL EtOAc and the layers separated. The organic layer was washed with 5 mL brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude oil was purified by column chromatography (7:1→5:1 hexanes/EtOAc) to afford 262 mg (86% over 3 steps, single diastereomer) **5.64** as a white solid that was recrystallized from Et_2O to afford colorless prisms (mp =134–136 °C). ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 7.05 (s, 1H), 6.94 (d, *J* = 8.2 Hz, 1H), 6.71 (dd, *J* = 8.3, 2.4 Hz, 1H), 6.25 (s, 1H), 4.09 (q, *J* = 8.1 Hz, 1H), 3.97 (td, *J* = 8.6, 3.5 Hz, 1H), 3.81 (s, 3H), 3.20 (ddd, *J* = 11.0, 9.7, 3.5 Hz, 1H), 2.75 (dtd, *J* = 11.1, 7.5, 3.6 Hz, 1H), 2.51 (dd, *J* = 14.0, 10.5 Hz, 1H), 2.24 (ddq, *J* = 14.0, 10.5, 3.5 Hz, 2H), 2.12 (t, *J* = 14.0 Hz, 1H), 1.91 (s, 3H), 1.88-1.74 (m, 2H), 1.55-1.39 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 157.9, 139.5, 138.4, 128.7, 125.7, 123.6, 112.4, 109.9, 83.7, 67.1, 55.2, 46.8, 46.4, 41.9, 31.8, 29.9, 27.0, 20.8; IR (thin film) 2935, 2869, 1607, 1489, 1157, 1064, 1041 cm^{-1}; HRMS (ESI) calculated for $C_{18}H_{22}O_2$ $[M+NH_4]^+$ 288.1964 found 288.1955.

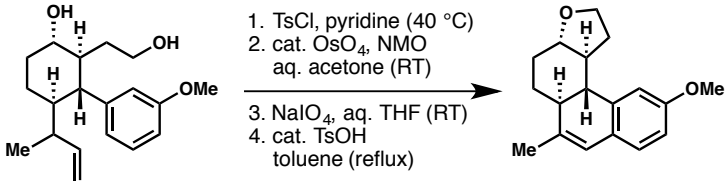
Tetracyclic Enone 5.70 and Anisole 5.H



To a 50 mL round bottom flask charged with a glass stir bar was condensed 20 mL ammonia followed by the addition of 248 mg (0.917 mmol) **12** in 4.5 mL THF and 1.9 mL (47 mmol) MeOH. Slowly, 250 mg (36 mmol) lithium metal was added in small pieces at –40 °C. The side of the flasks were washed with 0.3 mL (7.4 mmol) MeOH after 150 mg lithium metal was added. After complete addition and the blue color discharged, 2.1 g (39 mmol) solid NH_4Cl was added and the ammonia evaporated. The white residue was taken up in 5 mL water and 20 mL EtOAc. The organic layer was separated and washed with 5 mL brine. The aqueous layers were combined and back extracted with 5 mL EtOAc. The organic layers were combined, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude material in a 50 mL round bottom flask was dissolved in 10 mL MeOH and treated with 0.5 mL 6 M HCl. After 16 hours at room temperature 20 mL half sat. aq. $NaHCO_3$ and 20 mL EOAc were added. The layers were separated and the aqueous extracted with 10 mL and 5 mL EtOAc. All organic layers were collected washed with 5 mL brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude material was purified by column chromatography (4:1→2:1 hexanes/EtOAc) to afford 44 mg (18% over 2 steps) **5.G** as a white solid that was recrystallized from Et_2O to afford colorless needles (mp = 80–82 °C) and 128 mg (53% over 2 steps) **5.70** as a white solid that recrystallized from benzene to afford colorless prisms (mp = 85–86 °C). **5.H:** ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 7.04 (d, J = 8.3 Hz, 1H), 6.96 (d, J = 1.9 Hz, 1H), 6.72 (dd, J = 8.2, 2.3 Hz, 1H), 4.03-4.00 (m, 2H), 3.83 (s, 3H), 3.31 (td, J = 10.6, 3.1 Hz, 1H), 2.79 (dd, J = 15.3,

6.3 Hz, 1H), 2.61 (dq, *J* = 11.5, 5.8 Hz, 1H), 2.41 (dd, *J* = 15.3, 6.7 Hz, 1H), 2.33 (t, *J* = 10.7 Hz, 1H), 2.22 (dq, *J* = 11.5, 3.6 Hz, 1H), 2.13 (dq, *J* = 13.4, 3.5 Hz, 1H), 1.97 (ddd, J = 20.8, 11.5, 9.3 Hz, 1H), 1.75-1.64 (m, 2H), 1.45 (qd, *J* = 12.1, 3.5 Hz, 1H), 1.29-1.21 (m, 1H), 0.96-0.89 (m, 1H), 0.94 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 157.6, 141.87, 129.9, 129.2, 112.1, 110.4, 83.7, 67.1, 55.2, 48.5, 47.7, 46.1, 37.3, 33.8, 31.8, 30.5, 29.1, 21.1; IR (thin film) 2929, 2870, 1610, 1495, 1237, 1062, 1040, 805 cm^{-1}; HRMS (ESI) calculated for $C_{18}H_{24}O_2$ $[M+NH_4]^+$ 290.2120 found 290.2113. **5.70:** ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 5.85 (s, 1H), 3.97-3.88 (m, 2H), 3.15 (ddd, *J* = 11.4, 9.6, 3.4, 1H), 2.42-2.29 (m, 4H), 2.23-2.12 (m, 3H), 1.90 (dt, *J* = 12.7, 4.2 Hz, 1H), 1.84 (t, *J* = 10.5 Hz, 1H), 1.75-1.66 (m, 1H), 1.56-1.26 (m, 5H), 1.15-1.08 (m, 1H), 0.98-0.89 (m, 1H), 0.96 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 199.9, 168.8, 121.1, 82.9, 67.1, 51.6, 51.4, 45.1, 43.2, 38.4, 37.4, 34.1, 29.9, 29.7, 29.2, 27.4, 19.6; IR (thin film) 2927, 2868, 1667, 1622 cm^{-1}; HRMS (ESI) calculated for $C_{17}H_{24}O_2$ $[M+Na]^+$ 283.1674 found 283.1682.

Dihydronaphthalene 5.64



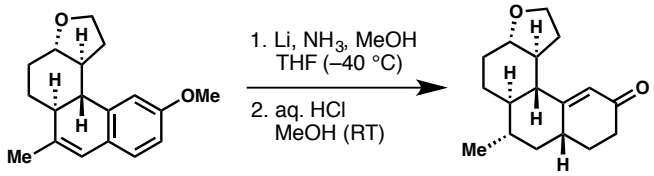
5.62: 7 : 1 dr **5.70:** 6 : 1 dr

To a 500 mL round bottom flask containing 5.68 g (18.7 mmol, 7:1 dr) **5.62** in 95 mL pyridine was added 8.91 g (47.1 mmol) p-toluenesulfonyl chloride at room temperature. The flask was placed in a 40 °C oil bath. After 15 hours the reaction was cooled to room temperature and quenched with 100 mL sat. aq. $NaHCO_3$, 50 mL water and extracted with 300 mL and 50 mL EtOAc. The organic layers were washed thrice with ice cold 100 mL 6 M HCl then 50 mL water.

The acidic aqueous washings were combined, back extracted with 100 mL and 50 mL EtOAc and all organic phases combined. The organic medium was washed with 50 mL sat. aq. $NaHCO_3$, 50 mL brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude oil was taken on to the next step. To a 500 mL round bottom flask containing crude alkene in 150 mL acetone and 50 mL nano-pure water was added 1.2 mL (0.189 mmol) 4 wt% OsO_4 in water then 4.40 g (37.6 mmol) NMO at 0 °C open to air. The ice bath was immediately removed and after stirring 20 hours at room temperature 9.5 g (75 mmol) Na_2SO_3 in 50 mL water was added. After 20 minutes, 5 g NaCl was added and the solution was extracted with 150 mL, 100 mL and 50 mL EtOAc. All organic layers were combined, washed with 50 mL sat. aq. $NaHCO_3$ and 50 mL brine. The aqueous layers were combined and back extracted with 50 mL EtOAc. The organic layers were combined, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude material was subjected to the next reaction without further purification. To a 1 L round bottom flask containing the crude oil was added 190 mL 1:1 THF/water then immersed in a room temperature water bath and 8.14 g (38.1 mmol) $NaIO_4$ added open to air. After 1 hour 18 g (150 mmol) Na_2SO_3 suspended in 150 mL water was added. The mixture was extracted with 150 mL and 100 mL EtOAc. The organic layers were combined and washed with 50 mL sat. aq. $NaHCO_3$ and 50 mL brine. The aqueous layers were combined and back extracted with 50 mL EtOAc. The organic layers were combined dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude material was subjected to the next reaction without further purification. To a 250 mL round bottom flask containing crude aldehyde was added 180 mL toluene and 180 mg (0.95 mmol) $TsOH•H_2O$. The reaction was refluxed over a Dean-Stark trap for 2 hours. The reaction was cooled, diluted with 50 mL sat. aq. $NaHCO_3$, 100 mL EtOAc and the layers separated. The organic layer was washed with 50 mL brine, dried over $MgSO_4$, filtered and all

volatiles removed in vacuo. The crude oil was purified by column chromatography (5:1 hexanes/EtOAc) to afford 4.04 g (80% over 4 steps, 6:1 dr) **5.70** as a white wax. ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) major δ 7.05 (s, 1H), 6.94 (d, *J* = 8.2 Hz, 1H), 6.71 (dd, *J* = 8.3, 2.4 Hz, 1H), 6.25 (s, 1H), 4.09 (q, *J* = 8.1 Hz, 1H), 3.97 (td, *J* = 8.6, 3.5 Hz, 1H), 3.81 (s, 3H), 3.20 (ddd, *J* = 11.0, 9.7, 3.5 Hz, 1H), 2.75 (dtd, *J* = 11.1, 7.5, 3.6 Hz, 1H), 2.51 (dd, *J* = 14.0, 10.5 Hz, 1H), 2.24 (ddq, *J* = 14.0, 10.5, 3.5 Hz, 2H), 2.12 (t, *J* = 14.0 Hz, 1H), 1.91 (s, 3H), 1.88-1.74 (m, 2H), 1.55-1.39 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) major δ 157.9, 139.5, 138.4, 128.7, 125.7, 123.6, 112.4, 109.9, 83.7, 67.1, 55.2, 46.8, 46.4, 41.9, 31.8, 29.9, 27.0, 20.8; IR (thin film) 2935, 2869, 1607, 1489, 1157, 1064, 1041 cm^{-1}; HRMS (ESI) calculated for $C_{18}H_{22}O_2$ $[M+NH_4]^+$ 288.1964 found 288.1955.

Tetracyclic Enone 5.70

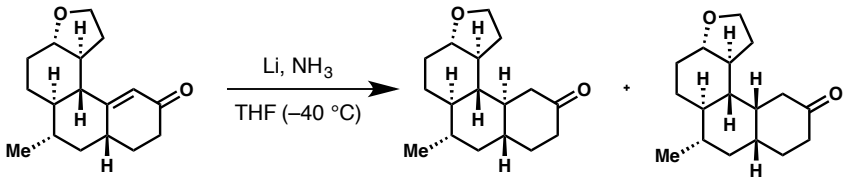


5.64: 6 : 1 dr **5.70:** 7 : 1 dr

To a 1 L 3-neck round bottom flask fitted with an overhead stirrer was added 4.04 g (14.9 mmol, 6:1 dr) **5.64** in 100 mL THF followed by 300 mL ammonia and 6 mL MeOH. At –40 °C, a total of 4.17 g (600 mmol) lithium metal was added while additional 6 mL MeOH was added after 0.93 g, 1.80 g and 2.86 g lithium. After complete addition of lithium and disappearance of a blue color, an additional 1 mL MeOH and 35 g (654 mmol) solid NH_4Cl was added and the ammonia evaporated overnight. The white residue taken up in 100 mL water and extracted with 200 mL and 100 mL EtOAc. The organic layers were combined, washed twice with 50 mL brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude material in a 1 L round

bottom flask was dissolved in 150 mL MeOH and treated with 15 mL 6 M HCl. After 10 hours at room temperature 200 mL sat. aq. $NaHCO_3$ and 100 mL water were added while controlling the temperature. The mixture was extracted with 300 mL and thrice with 100 mL EtOAc. All organic layers were collected washed with 50 mL sat. aq. $NaHCO_3$, 50 mL water and 50 mL brine. These aqueous washings were combined and back extracted with 50 mL EtOAc. The organic layers were combined, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude material was purified by column chromatography (4:1→2:1 hexanes/EtOAc) to afford 2.55 g (65% over 2 steps, 7:1 dr) **5.70** as a white wax. ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) major δ 5.85 (s, 1H), 3.97-3.88 (m, 2H), 3.15 (ddd, *J* = 11.4, 9.6, 3.4, 1H), 2.42-2.29 (m, 4H), 2.23-2.12 (m, 3H), 1.90 (dt, *J* = 12.7, 4.2 Hz, 1H), 1.84 (t, *J* = 10.5 Hz, 1H), 1.75-1.66 (m, 1H), 1.56-1.26 (m, 5H), 1.15-1.08 (m, 1H), 0.98-0.89 (m, 1H), 0.96 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) major δ 199.9, 168.8, 121.1, 82.9, 67.1, 51.6, 51.4, 45.1, 43.2, 38.4, 37.4, 34.1, 29.9, 29.7, 29.2, 27.4, 19.6; IR (thin film) 2927, 2868, 1667, 1622 cm^{-1}; HRMS (ESI) calculated for $C_{17}H_{24}O_2$ $[M+Na]^+$ 283.1674 found 283.1682.

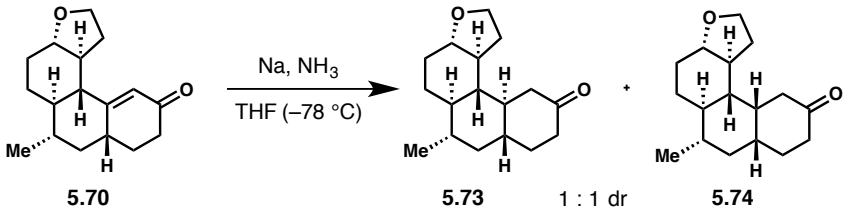
Li/NH_3 Reduction to 5.73 and 5.74



A 10 mL round bottom flask was charged with a glass stir bar and filled with 3 mL liquid ammonia. To the stirring solution was added 3 mg (0.43 mmol) lithium metal and 0.2 mL THF. At –40 °C 14 mg (0.054 mmol) **5.70** was added with the assistance of 0.5 mL THF. After 2 minutes 0.1 mL isoprene was added, followed by 75 mg solid NH_4Cl. The flask was warmed to

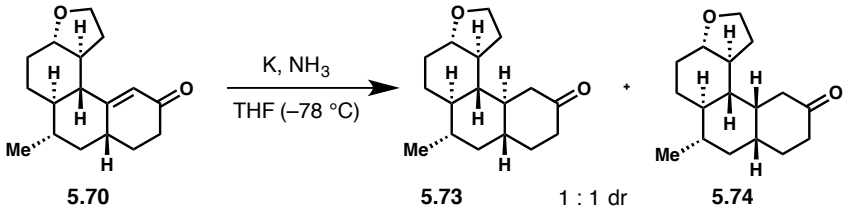
room temperature. After evaporation of the ammonia, 1 mL water and 2 mL EtOAc were added. The layers separated and the organic phase washed with 1 mL brine, dried over $MgSO_4$, filtered and all volatiles removed in vauo. The crude solid was purified by column chromatography (2:1 hexanes/EtOAc) to afford 9.0 mg (64%, 1:2 dr) **5.73**/**5.74** as a colorless oil.

Table 5.1, Entry 1: Na/NH_3 Reduction to 5.73 and 5.74



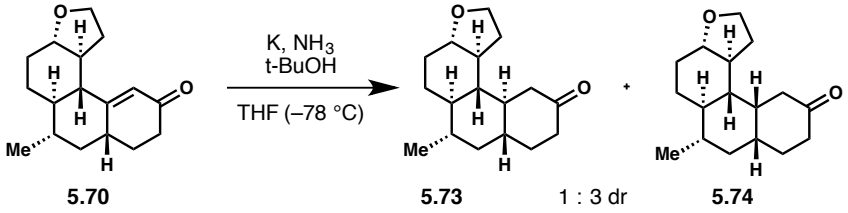
A 10 mL round bottom flask was charged with a glass stir bar and filled with 3 mL liquid ammonia. To the stirring solution was added 10 mg (0.038 mmol) **5.70** with 0.8 mL THF followed by 16 mg (0.70 mmol) sodium metal at –78 °C. After 3 minutes 0.15 mL isoprene was added, followed by 62 mg solid NH_4Cl. The flask was warmed to room temperature. After evaporation of the ammonia, 1 mL water and 2 mL EtOAc were added. The layers separated and the organic phase washed with 1 mL brine, dried over $MgSO_4$, filtered and all volatiles removed in vauo. The crude solid was purified by column chromatography (2:1 hexanes/EtOAc) to afford 8.5 mg (85%, 1:1 dr) **5.73**/**5.74** as a colorless oil.

Table 5.1, Entry 2: K/NH_3 Reduction to 5.73 and 5.74



A 10 mL round bottom flask was charged with a glass stir bar and filled with 3 mL liquid ammonia. To the stirring solution was added 10.4 mg (0.040 mmol) **5.70** with 0.8 mL THF followed by 30 mg (0.70 mmol) potassium metal at –78 °C. After 30 minutes 0.10 mL isoprene was added, followed by 71 mg solid NH_4Cl. The flask was warmed to room temperature. After evaporation of the ammonia, 2 mL water and 5 mL EtOAc were added. The layers separated and the organic phase washed with 2 mL brine, dried over $MgSO_4$, filtered and all volatiles removed in vauo. The crude solid was purified by column chromatography (3:1 hexanes/EtOAc) to afford 8.6 mg (82%, 1:1 dr) **5.73/5.74** as a colorless oil.

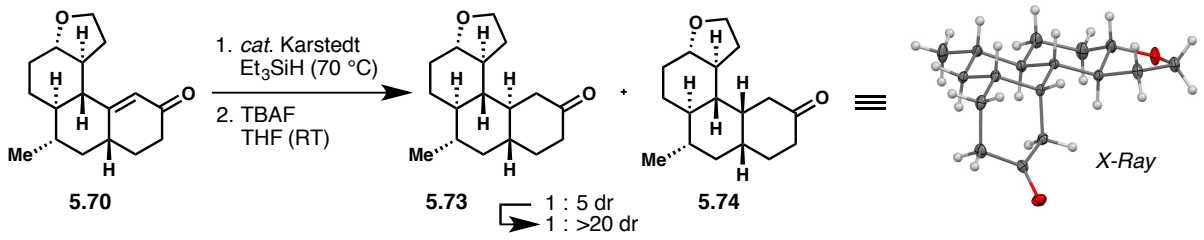
Table 5.1, Entry 3: K/NH_3/t-BuOH Reduction 5.73 and 5.74



A 10 mL round bottom flask was charged with a glass stir bar and filled with 3 mL liquid ammonia. To the stirring solution was added 10 mg (0.038 mmol) **5.70** with 0.8 mL THF and 0.18 mL (1.9 mmol) t-BuOH followed by 30 mg (0.77 mmol) potassium metal at –78 °C. After 30 minutes, 0.10 mL isoprene was added, followed by 71 mg solid NH_4Cl. The flask was warmed to room temperature. After evaporation of the ammonia, 2 mL water and 3 mL EtOAc were added. The layers separated and the organic phase washed with 2 mL brine, dried over

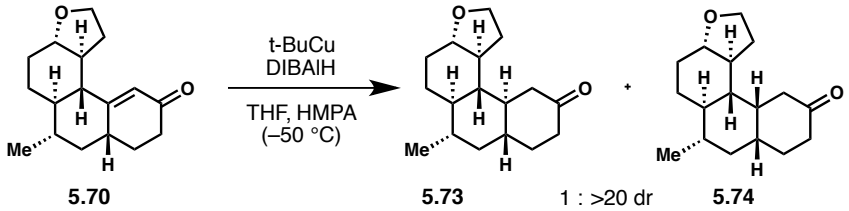
$MgSO_4$, filtered and all volatiles removed in vauo. The crude solid was purified by column chromatography (3:1 hexanes/EtOAc) to afford 8.0 mg (80%, 1:3 dr) **5.73/5.74** as a white wax.

Table 5.1, Entry 5: Karstedt/Et_3SiH Reduction to 5.73 and 5.74



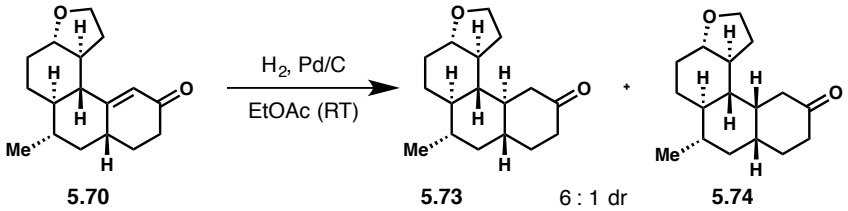
A 1 dram vial was charged with 15 mg (0.058 mmol) **5.70**, 3 mg (0.00016 mmol) Karstedt's catalyst 2 wt% in xylene and 0.4 mL triethylsilane, capped and heated to 70 °C. After 12 hours the reaction was cooled and all volatiles removed in vacuo. The crude material was dissolved in 0.4 mL THF and treated with 0.15 mL (0.15 mmol) TBAF 1 M/THF open to air. After 30 minutes 1 mL sat. aq. NH_4Cl was added and the mixture extracted twice with 2 mL EtOAc. The organic layers were combined, washed with 1 mL brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude solid was purified by column chromatography (2:1 hexanes/EtOAc) to afford 14 mg (92% over 2 steps, 1:5 dr) **5.73/5.74** as a white solid. Crystallization from pentane/EtOAc afforded **5.74** as a single diastereomer in colorless prisms (mp = 137–139 °C).

Table 5.1, Entry 6: t-BuCu/DIBAl Reduction to 5.73 and 5.74



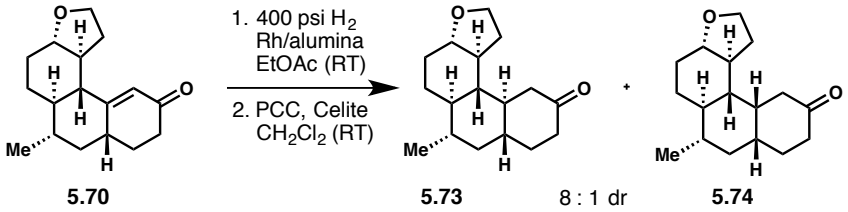
A 1 dram vial containing 7.9 mg (0.041 mmol) CuI in 0.4 mL THF was cooled to –78 °C and treated with 0.03 mL (0.042 mmol) 1.4 M t-BuLi/pentane. After stirring at –50 °C for 15 minutes the flask was recooled to –78 °C and treated with 0.10 mL (0.57 mmol) HMPA then 0.10 mL (0.1 mmol) 1.0 M DIBAlH/hexanes. After 20 minutes at –50 °C the flask was recooled to –78 °C and 11.3 mg (0.043 mmol) **5.70** in 0.4 mL THF was added slowly. The reaction was stirred at –50 °C for 8 hours, after which it was removed from the cold bath and quenched with 2 mL 2 M HCl. The flask was warmed to room temperature and partitioned with 6 mL EtOAc. The organic layer was washed with 2 mL 3:1 sat. aq. NH_4Cl/5 M NaOH twice then 2 mL brine, dried over $MgSO_4$, filtered and all volatiles removed in vauo. The crude material was purified by column chromatography (3:1 hexanes/EtOAc) to afford 9.8 mg (86%, 1:>20 dr) **5.73/5.74** as a white solid. Crystallization from pentane/EtOAc afforded colorless prisms (mp = 137–139 °C). **5.74:** ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 3.95-3.88 (m, 2H), 3.11-3.06 (m, 1H), 2.47-2.38 (m, 2H), 2.25-2.10 (m, 5H), 2.00 (dtd, *J* = 11.0, 7.4, 3.3 Hz, 1H), 1.92-1.88 (m, 3H), 1.54 (dd, *J* = 24.5, 11.9 Hz, 1H), 1.49-1.43 (m, 2H), 1.35-1.13 (m, 4H), 1.00-0.93 (m, 2H) 1.00 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 212.7, 83.2, 67.3, 47.3, 46.5, 41.1, 40.4, 38.3, 37.5, 37.2, 35.2, 34.3, 31.3, 30.5, 28.5, 28.3, 20.4; IR (thin film) 2924, 2866, 1711, 1453, 1058 cm^{-1}; HRMS (ESI) calculated for $C_{17}H_{26}O_2$ $[M+Na]^+$ 285.1830 found 285.1843.

Table 5.1, Entry 7: Pd/C Reduction to 5.73 and 5.74



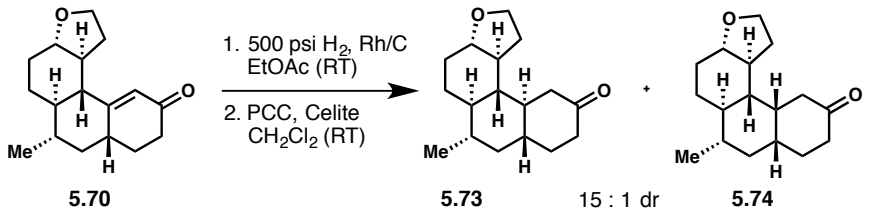
A 1 dram vial containing 5.3 mg (0.020 mmol) **5.70** and catalytic Pd/C in 0.4 mL EtOAc was stirred under a hydrogen balloon for 20 hours. The reaction was filtered over Celite, eluting with EtOAc and all volatiles removed in vauo. The crude solid was purified by column chromatography (3:1 hexanes/EtOAc) to afford 5.0 mg (94%, 6:1 dr) **5.73/5.74** as a white semi-solid.

Table 5.1, Entry 8: Rh/alumina Reduction to 5.73 and 5.74



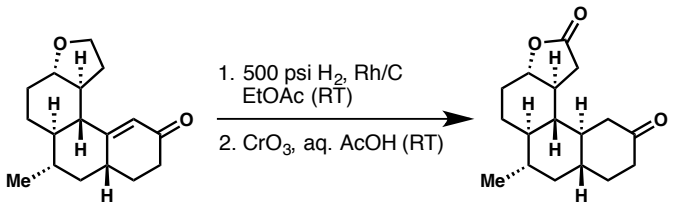
A 1 dram vial containing 5.9 mg (0.023mmol) **5.70** and catalytic Rh/alumina in 0.4 mL EtOAc was stirred under 400 psi H_2 in a bomb reactor. After 20 hours, the reaction was filtered over Celite, eluting with EtOAc and all volatiles removed in vauo to afford an alcohol as a mixture of diastereomers. The crude material was dissolved in 0.5 mL CH_2Cl_2 and 22 mg Celite added followed by 21 mg (0.097 mmol) PCC open to air. After 5 hours the reaction was diluted with Et_2O and filtered over silica gel, eluting with Et_2O. All volatiles were removed in vacuo and the crude material was purified by column chromatography (3:1 hexanes/EtOAc) to afford 5.5 mg (93% over 2 steps, 8:1 dr) **5.73/5.74** as a white semi-solid.

Table 5.1, Entry 9: Rh/C Reduction to 5.73 and 5.74



A 25 mL round bottom containing 563 mg (1.26 mmol, 7:1 dr) **5.70** and 46 mg (0.022 mmol) 5% Rh/C in 10 mL EtOAc was stirred under 500 psi H_2 in a bomb reactor. After 24 hours, the reaction was filtered over Celite, eluting with 30 mL EtOAc and all volatiles removed in vauo to afford a mixture of ketone and alcohol. The crude material in a 50 mL round bottom flask was dissolved in 10 mL CH_2Cl_2 and 550 mg Celite added followed by 470 mg (2.18 mmol) PCC open to air. After 5 hours the reaction was diluted with 20 mL Et_2O and filtered over silica gel, eluting with 120 mL Et_2O. All volatiles were removed in vacuo and the crude material was purified by column chromatography (3:1 hexanes/EtOAc) to afford 525 mg (93% over 2 steps, 15:1 dr) **5.73/5.74** as a white semi-solid. **5.73:** ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 3.88-3.85 (m, 2H), 3.07 (ddd, *J* = 11.2, 10.0, 3.7 Hz, 1H), 2.82 (ddd, *J* = 14.1, 3.9, 1.8 Hz, 1H), 2.41-2.31 (m, 2H), 2.25 (dq, *J* = 11.5, 5.8 Hz, 1H), 2.17-2.09 (m, 2H), 2.02 (t, *J* = 13.3 Hz, 1H), 1.96 (ddt, *J* = 13.2, 6.0, 3.0 Hz, 1H), 1.73 (dt, *J* = 13.1, 3.5 Hz, 1H), 1.70-1.62 (m, 1H), 1.54-1.46 (m, 1H), 1.43-1.19 (m, 5H), 1.03-0.72 (m, 4H), 0.95 (d, *J* = 6.5, 3H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 212.0 83.5, 66.9, 50.7, 49.3, 48.9, 47.9, 47.4, 42.4, 41.2, 41.1, 36.5, 33.3, 32.6, 30.5, 28.2, 20.8; IR (thin film) 2925, 2865, 1711, 1455, 1062 cm^{-1}; HRMS (ESI) calculated for $C_{17}H_{26}O_2$ $[M+NH_4]^+$ 280.2277 found 280.2279.

Lactone 5.81 using Fieser's Reagent

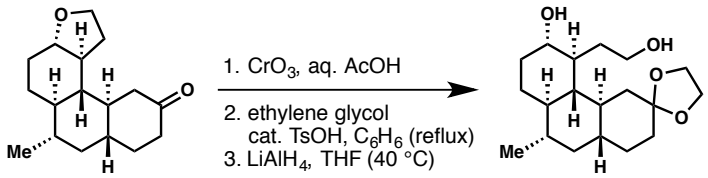


5.70: 7 : 1 dr **5.81:** >10 : 1 dr

A 25 mL round bottom flask containing dram vial containing 292 mg (1.12 mmol, 7:1 dr) **5.70** and 35 mg (0.017) 5% Rh/C in 5.5 mL EtOAc was stirred under 500 psi H_2 in a bomb reactor. After 18 hours, the reaction was filtered over Celite, eluting with EtOAc and all volatiles removed in vacuo to afford a mixture of ketone and alcohol. Only 247 mg (~81%) crude material in a 20 mL scintillation vial was dissolved in 4 mL AcOH and treated with 410 mg (4.10 mmol) CrO_3 in 6 mL 5:1 AcOH/water open to air. After 20 hours, 0.20 mL i-PrOH was added and stirring continuted for 20 minutes. After being poured into 70 mL ice cold stirring water, the solution was treated with 30 mL 5 M NaOH at 0 °C and extracted with 30 mL, 20 mL and 10 mL Et_2O. The organic layers were combined, washed with 10 mL water, 10 mL sat. aq. $NaHCO_3$ and 10 mL brine. The aqueous washings were combined and back extracted with 20 mL Et_2O. All organic layers were combined, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude material was purified by column chromatography (1:2 hexanes/Et_2O) to afford 69 mg (27% over 2 steps, >10:1 dr) **5.81** as a white semi-solid. ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 3.84 (td, *J* = 11.1, 3.5 Hz, 1H), 2.76 (dd, *J* = 16.1, 6.4 Hz, 1H), 2.57 (ddd, *J* = 13.9, 3.9, 1.8 Hz, 1H), 2.40-2.20 (m, 5H), 2.03-1.95 (m, 2H), 1.79-1.74 (m, 2H), 1.58-1.49 (m, 3H), 1.42-1.06 (m, 2H), 1.19-1.04 (m, 2H), 0.96-0.83 (m, 2H), 0.96 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 210.6, 175.9, 84.9, 50.2, 48.4, 48.2, 47.1, 46.8, 42.0, 41.0, 40.9, 37.4,

36.5, 32.9, 29.6, 27.7, 20.3; IR (thin film) 2920, 2867, 1781, 1710, 1210, 1041, 966 cm^{-1}; HRMS (ESI) calculated for $C_{17}H_{24}O_3$ $[M+Na]^+$ 299.1623 found 299.1624.

Diol 5.82

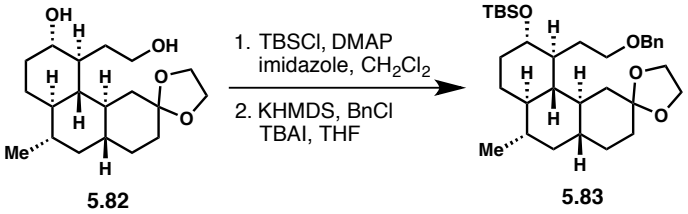


5.73 **5.82**

To a 1 dram vial containing 30 mg (0.111 mmol) **5.73** in 0.3 mL AcOH was added 51 mg (0.51 mmol) CrO_3 in 0.8 mL 9:1 AcOH/water open to air. After 23 hours, 0.10 mL i-PrOH was added and stirring continuted for 20 minutes. After being poured into 7 mL ice cold stirring water and 5 mL Et_2O, the solution was treated with 3 mL 5 M NaOH at 0 °C and extracted with 5 mL Et_2O. The organic layers were combined, washed twice with 2 mL water and 2 mL sat. aq. $NaHCO_3$. The aqueous washings were combined and back extracted with 3 mL Et_2O. All organic layers were combined, washed with 2 mL brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. A 10 mL round bottom flask containing crude C–H oxidation product in 2.5 mL C_6H_6 was refluxed with 0.03 mL (0.54 mmol) ethylene glycol and 2 mg (0.011 mmol) $TsOH•H_2O$ under a Hickman Still. After 2 hours the reaction was cooled, diluted with 5 mL EtOAc and washed with 2 mL sat. aq. $NaHCO_3$ and 2 mL brine. The organic layer was dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude lactone was added with the assistance of 01 mL THF to 16 mg (0.42 mmol) $LiAlH_4$ in 1 mL THF at 0 °C. The flask was immediately removed from the cold bath and stirred for 10 minutes before being heated to 40 °C for 1 hour. After cooling the flask to 0 °C, 0.05 mL EtOAc, 0.02 mL water, 0.02 mL 5 M NaOH, 0.06 mL water and Na_2SO_4 were carefully added sequentially. The solution was filtered over Celite and

washed with Et_2O (~40 mL as determined by TLC) and all volatiles removed in vacuo. The crude material was purified by column chromatography (EtOAc) to afford 15 mg (42% over 3 steps, >10:1 dr) **5.82** as a white semi-solid. ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 3.94 (s, 4H), 3.81-3.62 (m, 2H), 3.47-3.31 (m, 2H), 2.05-1.46 (m, 10H), 1.35-1.10 (m, 7H), 0.92-0.81 (m, 7H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 109.4, 76.2, 64.3, 64.1, 62.3, 50.1, 47.9, 47.7, 45.6, 43.3, 41.6, 40.7, 39.4, 37.6, 34.2, 32.1, 31.4, 26.0, 20.2.

Benzyl Ether 5.83

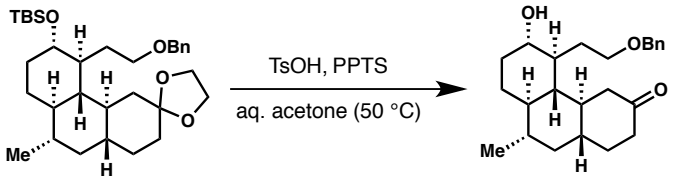


5.82 **5.83**

To a 1 dram vial containing 11 mg (0.034 mmol) **5.82** was added 5.5 (0.081 mmol) imidazole, 2.5 mg (0.020 mmol) DMAP and 0.5 mL CH_2Cl_2. At 0 °C 7.0 mg (0.046 mmol) TBSCl was added and the cooling bath removed. After 10 hours sat. aq. $NaHCO_3$ was added and the mixture extracted with EtOAc. The organic layers were combined, washed with sat. aq. brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude material and 2 mg (0.0054 mmol) TBAI in a 1 dram vial were dissolved in 0.4 mL THF and at 0 °C treated with 0.2 mL (0.10 mmol) KHMDS 0.5M/toluene and 0.02 mL (0.17 mmol) benzyl chloride. The cold bath was immediately removed. After 1 hour the reaction was recooled to 0 °C and quenched with half sat. aq. $NaHCO_3$ and extracted with EtOAc. The organic layers were combined, washed with sat. aq. brine, dried over $MgSO_4$, filtered and all volatiles removed. The crude material was purified by column chromatography (20:1 hexanes/EtOAc) to afford 8.5 mg (47%) **5.83** as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 7.34-7.26 (m, 5H), 4.53-4.41 (m, 2H), 3.93-3.87 (m,

2H), 3.81-3.76 (m, 1H), 3.75-3.64 (m, 2H), 3.55-3.48 (m, 2H), 2.11 (d, *J* = 12.0 Hz, 1H), 2.04-2.02 (m, 1H), 1.92-1.86 (m, 1H), 1.74-1.35 (m, 10H), 1.32-0.95 (m, 5H), 0.95-0.77 (m, 13H), 0.62-0.50 (m, 1H), 0.04 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 138.6, 128.3, 127.81, 127.77, 127.44, 124.41, 109.5, 73.2, 71.8, 69.3, 64.0, 63.9, 48.6, 47.3, 42.9, 42.0, 41.8, 41.7, 38.6, 38.4, 35.0, 34.8, 31.3, 26.4, 25.9, 24.2, 20.0, 17.9, –4.6, –4.7.

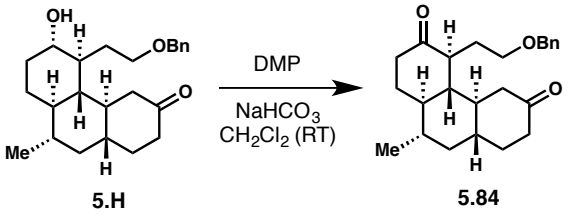
Benzyl Ether 5.H



5.83 **5.H**

A 1 dram vial containing 8.5 mg (0.016 mmol) **5.82**, 4 mg (0.016 mmol) PPTS and 3 mg (0.016 mmol) TsOH•H_2O in 0.2 mL 3:1 acetone/water was sealed and heated to 70 °C for 6 hours. The reaction was cooled, diluted with sat. aq. $NaHCO_3$ and extracted with EtOAc. The organic layers were combined, washed with sat. aq. brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude material was purified by column chromatograph (3:1 hexanes/EtOAc) to afford 3.7 mg (62%) **5.H** as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 7.37-7.29 (m, 4H), 4.57 (d, *J* = 11.8 Hz, 1H), 4.51 (d, *J* = 11.8 Hz, 1H), 3.63-3.55 (m, 2H), 3.49-3.44 (m, 2H), 2.54 (dd, *J* = 12.8, 3.1 Hz, 1H), 2.35 (m, 2H), 2.13 (t, *J* = 13.0 Hz, 1H), 2.00-1.89 (m, 3H), 1.81-1.51 (m, 6H), 1.42-1.15 (m, 6H), 0.91 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 211.7, 137.5, 128.5, 127.8, 74.6, 73.4, 69.7, 50.43, 50.39, 47.7, 46.7, 45.7, 42.6, 41.7 41.0, 37.4, 35.9, 33.7, 30.5, 25.5, 20.1.

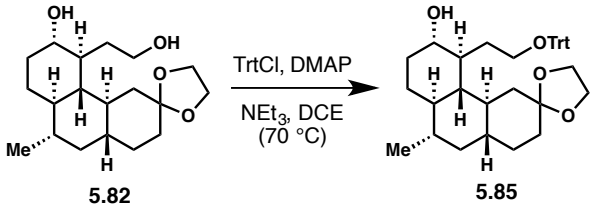
Ketone 5.84



5.H 5.84

A 1 dram vial containing **5.H**, DMP and $NaHCO_3$ in 0.2 mL CH_2Cl_2 was stirred for 30 minutes. The reaction was cooled, diluted with sat. aq. $Na_2S_2O_3$, sat. aq. $NaHCO_3$ and extracted with EtOAc. The organic layers were combined, washed with sat. aq. $NaHCO_3$, sat. aq. brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo to afford a crude material assigned as **5.84**.

Trityl Alcohol 5.85

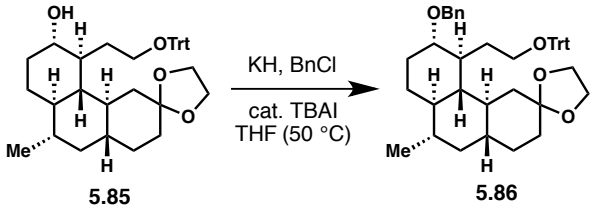


5.82 5.85

A 5 mL round bottom flask was charged with 15 mg (0.046 mmol) **5.82**, 6.8 mg (0.056 mmol) DMAP, 0.03 mL (0.22 mmol) NEt_3 and 18 mg (0.064 mmol) triphenylmethyl chloride in 1 mL DCE. After stirring the reaction at 85 °C for 3 hours the solution was cooled, diluted with sat. aq. $NaHCO_3$ and extracted with EtOAc. The organic layers were combined, washed with sat. aq. brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude material was purified by column chromatography (5:1 hexanes/EtOAc) to afford 15 mg (58%) **5.85** as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 7.44 (d, J = 7.5 Hz, 6H), 7.31 (t, J = 7.6 Hz, 6H), 7.23 (t, J = 7.3 Hz, 3H), 3.85-3.79 (m, 2H), 3.72-3.67 (m, 1H), 3.63-3.58 (m, 1H), 3.47-3.43 (m, 1H), 3.30-3.24 (m, 1H), 3.13 (dt, J = 9.1, 6.1 Hz, 1H), 1.92-1.80 (m, 4H), 1.69-1.46 (m,

7H), 1.39-0.98 (m, 9H), 0.87 (d, J = 6.4 Hz, 3H), 0.91-0.78 (m, 3H), 0.70 (t, J = 8.9 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 171.1, 143.9, 128.7, 128.6, 127.8, 127.0, 109.4, 87.4, 77.3, 77.0 76.8, 74.0, 64.2, 64.0, 63.3, 60.4, 49.5, 47.5, 45.7, 44.4, 43.0, 41.6, 40.0, 37.9, 36.0, 34.5, 31.4, 29.3, 25.1, 21.1, 20.1, 14.2.

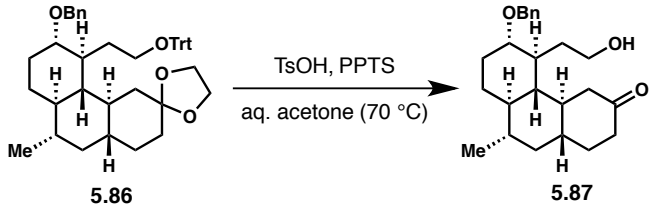
Benzyl Ether 5.86



5.85 **5.86**

A 1 dram vial was charged with 5 mg (~0.12 mmol) oil free KH and layered with 0.2 mL THF. At 0 °C a solution of 1 mg (0.0026 mmol) TBAI and 15 mg (0.026 mmol) **5.82** was added with a total of 0.5 mL THF. After the addition of 1 drop benzyl chloride the reaction was heated to 50 °C for 2 hours. The reaction was cooled, then treated with water and extracted with EtOAc. The organic layers were combined, washed with sat. aq. brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude material was purified by column chromatography (15:1 hexanes/EtOAc) to afford 11 mg (64%) **5.86** as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 7.47 (d, J = 7.4 Hz, 5H), 7.34-7.22 (m, 15H), 4.44 (d, J = 12.3 Hz, 1H), 4.40 (d, J = 12.3 Hz, 1H), 3.87-3.81 (m, 2H), 3.66-3.64 (m, 1H), 3.29 (bs, 1H), 3.10 (t, J = 6.0 Hz, 2H), 2.19 (d, J = 10.8 Hz, 1H), 1.98-1.84 (m, 3H), 1.78-1.55 (m, 7H), 1.46-1.37 (m, 2H), 1.36-1.23 (m, 6H), 1.13-1.03 (m, 2H), 0.99-0.86 (m, 3H), 0.91 (d, J = 6.3 Hz, 3H) 0.70-0.65 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 144.4, 139.4, 128.7, 128.2, 127.71, 127.68, 127.65, 127.2, 127.0, 126.8, 109.5, 78.0, 69.6, 64.3, 64.0, 62.2, 60.4, 48.4, 47.3, 42.7, 42.0, 41.5, 39.5, 38.7, 38.1, 35.1, 34.8, 31.2, 24.1, 22.7, 21.1, 19.9, 14.2.

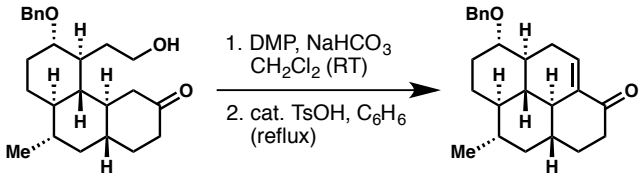
Ketoalcohol 5.87



5.86 **5.87**

A 1 dram vial containing 11 mg (0.016 mmol) **5.86**, 4.5 mg (0.018 mmol) PPTS and 6.8 mg (0.036 mmol) TsOH•H_2O dissolved in 0.6 mL 5:1 acetone/water was sealed and heated to 70 °C. After 1 hour the reaction was cooled, diluted with sat. aq. $NaHCO_3$ and extracted with EtOAc. The organic layers were combined, washed with brine, dried over $MgSO_4$ and filtered. The brine layer was back extracted with EtOAc, dried over $MgSO_4$, filtered, combined with the previously dried organic layer and all volatiles removed in vacuo. The crude material was purified by column chromatography (2:1→1:1 hexanes/EtOAc) to afford 5.7 mg (91%) **5.87** as a white semi-solid. ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 7.36-7.26 (m, 5H), 4.57 (d, *J* = 12.1 Hz, 1H), 4.46 (d, *J* = 12.1 Hz, 1H), 3.66-3.57 (m, 2H), 3.33 (q, *J* = 4.4 Hz, 1H), 2.66 (dd, *J* = 13.3, 3.1 Hz, 1H), 2.35 (dd, *J* = 10.4, 4.9 Hz, 2H), 2.08 (t, *J* = 13.6 Hz, 1H), 1.96 (ddq, *J* = 13.3, 8.6, 4.5 Hz, 2H), 1.86-1.79 (m, 1H), 1.73-1.56 (m, 4H), 1.53-1.40 (m, 2H), 1.39-1.23 (m, 4H), 1.19-1.11 (m, 1H), 1.00-0.83 (m, 3H), 0.91 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 211.9, 138.7, 128.3, 127.6, 127.5, 79.2, 69.9, 61.4, 50.4, 50.0, 46.5, 43.1, 42.2, 41.4, 41.1, 39.2, 38.3, 38.0, 33.5, 24.2, 23.8, 19.9; IR (thin film) 3418, 2921, 1711, 1065, 734 cm^{-1}; HRMS (ESI) calculated for $C_{24}H_{34}O_3$ $[M+Na]^+$ 393.2406 found 393.2389.

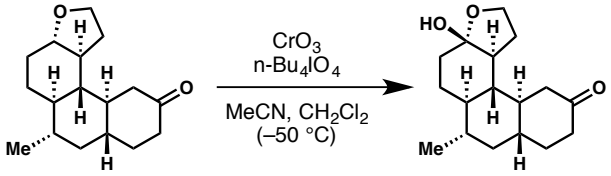
Enone 5.89



5.87 **5.89**

A 1 dram vial containing **5.87**, $NaHCO_3$ and DMP in 0.2 mL CH_2Cl_2 was stirred at room temperature. After 10 minutes the reaction was treated with $Na_2S_2O_3$, water and extracted with EtOAc. The organic layer was separated, washed with sat. aq. $NaHCO_3$, sat. aq. brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. A 1 dram vial containing crude **5.88** in 0.5 mL C_6H_6 was refluxed with $TsOH•H_2O$ and 4Å MS. After 20 minutes the reaction was cooled, treated with sat. aq. $NaHCO_3$, diluted with EtOAc and the layers separated. The organic layer was washed with brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo to afford crude **5.89**.

Lactol 5.90

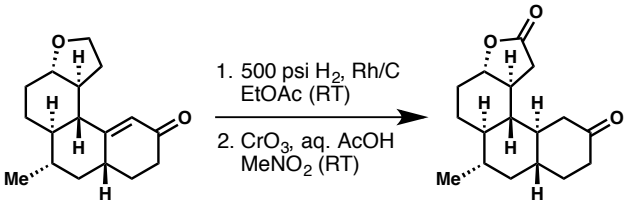


5.73: 7 : 1 dr **5.90**

A 1 dram vial containing 6.9 mg (0.069 mmol) CrO_3 dissolved in 0.4 mL MeCN was cooled to –40 °C and 4.4 mg (0.017 mmol) **5.73** added with 0.2 mL CH_2Cl_2. The reaction was cooled to –50 to –55 °C °C under vigorous stirring and treated with 30 mg (0.069 mmol) n-Bu_4NIO_4 in 0.2 mL MeCN. After 15 minutes 1 mL 1:1:2 sat. aq. $NaHCO_3$/sat. aq. $Na_2S_2O_3$/water was added, the mixture warmed to room temperature and extracted twice with 2 mL EtOAc. The organic layers were combined, washed with 1:1:2 sat. aq. $NaHCO_3$/sat. aq. $Na_2S_2O_3$/water, 1 mL brine, dried

over MgSO4, filtered and all volatiles removed in vacuo. The crude material was purified by column chromatography (1:1→1:4 hexanes/EtOAc) to afford 2.7 mg (58%) **5.90** as a colorless oil and 1.0 mg (22%) recovered starting material as a thin film. ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 4.02 (td, *J* = 8.8, 3.4 Hz, 1H), 3.90 (q, *J* = 8.1 Hz, 1H), 2.63-2.59 (m, 1H), 2.55-2.47 (m, 1H), 2.38-2.36 (m, 1H), 2.15-2.10 (m, 1H), 2.08-1.49 (m, 8H), 1.41-1.15 (m, 4H), 1.11-0.98 (m, 2H), 0.94 (d, *J* = 6.5 Hz, 3H), 0.96-0.73 (m, 3H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 211.6, 105.6, 65.8, 50.6, 49.1, 47.6, 47.4, 46.8, 42.5, 41.0, 40.9, 36.7, 35.3, 33.6, 32.7, 25.1, 20.1; IR (thin film) 3405, 2923, 2863, 1713, 1455, 1116, 1052, 1029 cm^{-1}; HRMS (ESI) calculated for $C_{17}H_{26}O_3$ $[M+Na]^+$ 301.1780 found 301.1773.

Lactone 5.81 using Fieser's Reagent in $MeNO_2$

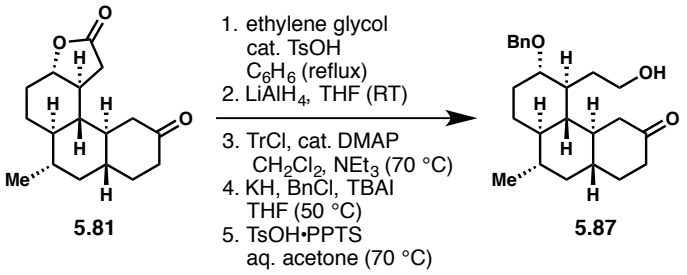


5.70: 7 : 1 dr **5.81:** >10 : 1 dr

A 10 mL round bottom flask containing 108 mg (0.414 mmol, 7:1 dr) **5.70** and 9 mg (0.0044 mmol) 5% Rh/C in 1.8 mL EtOAc was stirred under 500 psi H_2 in a bomb reactor. After 23 hours, the reaction was filtered over Celite, eluting with EtOAc and all volatiles removed in vacuo to afford a mixture of ketone and alcohol. In a 25 mL round bottom flask, crude THF tetracycle was dissolved in 4 mL $MeNO_2$, cooled to 0 °C and treated with 166 mg (1.66 mmol) CrO_3 dissolved in 0.8 mL 10:1 AcOH/water open to air. After 20 hours at room temperature, the reaction was recooled to 0°C then 5 mL half sat. aq. $Na_2S_2O_3$ and 5 mL water added. The solution was extracted with 15 mLand 5 mL EtOAc. The organic layers were combined, washed

with 3 mL sat. aq. $NaHCO_3$ and 3 mL brine. The aqueous washings were combined and backextracted with 3 mL EtOAc. All organic layers were combined, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude material was purified by column chromatography (1:2→1:4 hexanes/Et_2O) to afford 43 mg (38% over 2 steps, >10:1 dr) **5.81** as a white semi-solid. ^1H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 3.84 (td, J = 11.1, 3.5 Hz, 1H), 2.76 (dd, J = 16.1, 6.4 Hz, 1H), 2.57 (ddd, J = 13.9, 3.9, 1.8 Hz, 1H), 2.40-2.20 (m, 5H), 2.03-1.95 (m, 2H), 1.79-1.74 (m, 2H), 1.58-1.49 (m, 3H), 1.42-1.06 (m, 2H), 1.19-1.04 (m, 2H), 0.96-0.83 (m, 2H), 0.96 (d, J = 6.5 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 210.6, 175.9, 84.9, 50.2, 48.4, 48.2, 47.1, 46.8, 42.0, 41.0, 40.9, 37.4, 36.5, 32.9, 29.6, 27.7, 20.3; IR (thin film) 2920, 2867, 1781, 1710, 1210, 1041, 966 cm^{-1}; HRMS (ESI) calculated for $C_{17}H_{24}O_3$ $[M+Na]^+$ 299.1623 found 299.1624.

Hydroxyketone 17

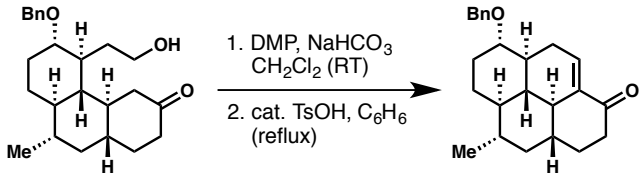


A 10 mL round bottom flask containing 67 mg (0.242 mmol >10:1 dr) **5.81** in 3.5 mL benzene was refluxed with 0.07 mL (1.25 mmol) ethylene glycol and 3 mg (0.016 mmol) $TsOH•H_2O$ over a Hickman Still. After 2 hours the reaction was cooled, diluted with 10 mL EtOAc and washed with 2 mL sat. aq. $NaHCO_3$ and 2 mL brine. The organic layer was dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude lactone was added with the assistance of 0.9 mL THF to 19 mg (0.501 mmol) $LiAlH_4$ in 1 mL THF at 0 °C. The flask was immediately

removed from the cold bath and stirred for 14 hours. After cooling the flask to 0 °C, 0.02 mL water, 0.02 mL 5 M NaOH, 0.06 mL water and Na_2SO_4 were carefully added sequentially. The solution was filtered over Celite and washed with Et_2O (~40 mL as determined by TLC) and all volatiles removed in vacuo. To a 10 mL round bottom flask containing crude diol in 2.2 mL DCE and 0.2 mL (1.43 mmol) NEt_3 was added 3 mg (0.024 mmol) DMAP and 68 mg (0.244 mmol) triphenylmethyl chloride. After heating the mixture at 70 °C for 9 hours, the reaction was cooled, treated with 2 mL sat. aq. $NaHCO_3$ and extracted with 10 mL EtOAc. The organic layer was separated, washed with 2 mL brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. A 10 mL round bottom flask containing 36 mg (0.90 mmol) KH freed from oil with three pentane washings was added 0.5 mL THF and 10 mg (0.027 mmol) TBAI at 0 °C. Crude alcohol was added with the assistance of 2 mL THF followed by 0.06 mL (0.52 mmol) benzyl chloride. The cold bath was removed and the reaction stirred for 30 minutes, after which the reaction was heated to 50 °C. After 2 hours the flask was cooled in an ice bath, treated carefully with 2 mL water and extracted with 10 mL EtOAc. The organic layer was separated, washed with 2 mL brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude material in a 10 mL round bottom flask was dissolved in 4 mL 5:1 acetone/water then treated with 21 mg (0.084 mmol) PPTS and 35 mg (0.18 mmol) $TsOH•H_2O$. A reflux condenser was fitted and the reaction immersed in a 70 °C oil bath open to air. After 2 hours the reaction was cooled, diluted with 2 mL sat. aq. $NaHCO_3$ and extracted with 10 mL and 5 mL EtOAc. The organic layers were combined, washed with 2 mL brine, dried over $MgSO_4$ and filtered. The brine layer was back extracted with 3 mL EtOAc, dried over $MgSO_4$, filtered, combined with the previously dried organic layer and all volatiles removed in vacuo. The crude material was purified by column chromatography (2:1→1:1 hexanes/EtOAc) to afford 68 mg (75% over 5 steps, >10:1 dr) **5.87** as

a white semi-solid. ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 7.36-7.26 (m, 5H), 4.57 (d, *J* = 12.1 Hz, 1H), 4.46 (d, *J* = 12.1 Hz, 1H), 3.66-3.57 (m, 2H), 3.33 (q, *J* = 4.4 Hz, 1H), 2.66 (dd, *J* = 13.3, 3.1 Hz, 1H), 2.35 (dd, *J* = 10.4, 4.9 Hz, 2H), 2.08 (t, *J* = 13.6 Hz, 1H), 1.96 (ddq, *J* = 13.3, 8.6, 4.5 Hz, 2H), 1.86-1.79 (m, 1H), 1.73-1.56 (m, 4H), 1.53-1.40 (m, 2H), 1.39-1.23 (m, 4H), 1.19-1.11 (m, 1H), 1.00-0.83 (m, 3H), 0.91 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 211.9, 138.7, 128.3, 127.6, 127.5, 79.2, 69.9, 61.4, 50.4, 50.0, 46.5, 43.1, 42.2, 41.4, 41.1, 39.2, 38.3, 38.0, 33.5, 24.2, 23.8, 19.9; IR (thin film) 3418, 2921, 1711, 1065, 734 cm^{-1}; HRMS (ESI) calculated for $C_{24}H_{34}O_3$ $[M+Na]^+$ 393.2406 found 393.2389.

Tetracyclic Enone 5.89

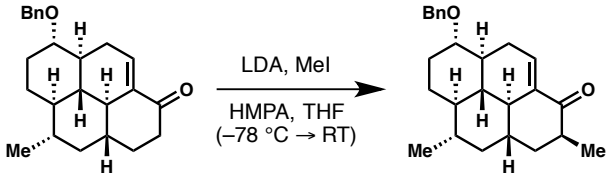


5.87: >10 : 1 dr **5.89:** 15 : 1 dr

A 10 mL round bottom flask containing 65 mg (0.175 mmol, >10:1 dr) **17** and 264 mg (3.14 mmol) $NaHCO_3$ in 2 mL CH_2Cl_2 was added 149 mg (0.351 mmol) DMP at room temperature open to air. After 20 minutes the reaction was treated carefully with 1 mL $Na_2S_2O_3$ and stirred for 20 minutes before being diluted with an additional 1 mL $Na_2S_2O_3$ and 2 mL water and extracted with 10 mL EtOAc. The organic layer was separated, washed twice with 2 mL sat. aq. $NaHCO_3$, 2 mL brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. A 10 mL round bottom flask containing crude keto-aldehyde in 3 mL benzene was refluxed with 4 mg (0.021 mmol) $TsOH•H_2O$ over a Hickman Still. After 20 minutes the reaction was cooled, treated with 2 mL sat. aq. $NaHCO_3$, diluted with 10 mL EtOAc and the layers separated. The organic layer was washed with 2 mL brine, dried over $MgSO_4$, filtered and all volatiles removed

in vacuo. The crude material was purified by column chromatography (6:1 hexanes/EtOAc) to afford 44 mg (72%, 15:1 dr) **5.89** as a light yellow semi-solid. ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 7.36-7.28 (m, 5H), 6.79 (t, *J* = 2.3 Hz, 1H), 4.69 (d, *J* = 11.6 Hz, 1H), 4.43 (d, *J* = 11.6 Hz, 1H), 3.01 (td, *J* = 10.4, 3.9 Hz, 1H), 2.80 (dtd, *J* = 20.4, 5.0, 2.6 Hz, 1H), 2.59-2.55 (m, 1H), 2.28 (tdd, *J* = 21.5, 11.5, 5.3 Hz, 2H), 2.07 (dq, *J* = 9.8, 3.4 Hz, 1H), 1.87-1.76 (m, 4H), 1.54-1.38 (m, 3H), 1.33-1.22 (m, 2H), 0.98-0.73 (m, 4H), 0.95 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 200.2, 138.8, 136.8, 135.6, 128.3, 127.7, 127.5, 82.9, 70.5, 46.9, 46.8, 45.7, 42.4, 41.4, 39.5, 39.3, 36.8, 30.7, 30.1, 29.9, 27.5, 19.7; IR (thin film) 2917, 2858, 1686, 1619, 1454, 1256 cm^{-1}; HRMS (ESI) calculated for $C_{24}H_{30}O_2$ $[M+Na]^+$ 373.2144 found 373.2159.

Methyl Enone 5.91

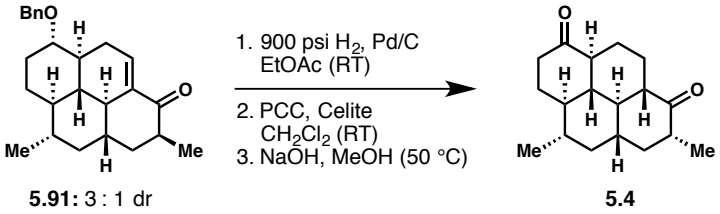


5.89 **5.91:** 3 : 1 dr

LDA was prepared in a 1 dram vial by addition of 0.3 mL (0.17 mmol) 0.57 M diisopropylamine/THF followed by 0.06 mL (0.15 mmol) 2.5 M/hexanes at 0 °C. To the stirring LDA solution at –78 °C was added 42 mg (0.12 mmol, >10:1 dr) **5.89** with the assistance of 0.5 mL THF. After 10 minutes, 0.03 mL (0.17 mmol) HMPA was added neat followed by 0.03 mL (0.48 mmol) methyl iodide. The cold bath was removed after an additional 10 minutes and the reaction stirred for 50 minutes before 2 mL half sat. aq. NH_4Cl was added. The solution was extracted with 10 mL EtOAc. The organic layer was separated, washed with 2 mL brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude mixture was purified by

column chromatography (10:1→5:1 hexanes/EtOAc) to afford 37 mg (84%, 3:1 dr, ~15% dimethylation?) **5.91** as a yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 7.36-7.29 (m, 5H), 6.79 (t, *J* = 2.3 Hz, 0.7H), 6.69 (t, *J* = 2.3 Hz, 0.2), 4.69 (d, *J* = 11.6 Hz, 1H), 4.43 (d, *J* = 11.6 Hz, 1H), 3.01 (td, *J* = 10.4, 3.9 Hz, 1H), 2.83-2.77 (m, 1H), 2.65-2.59 (m, 1H), 2.31-2.24 (m, 1H), 2.09-2.06 (m, 1H), 1.87-1.45 (m, 6H), 1.33-1.21 (m, 3H), 1.14 (d, *J* = 7.4 Hz, 3H), 0.97-0.74 (m, 4H), 0.96 (d, J = 6.5 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) major δ (major) 204.0, (mixture of diastereomers) 138.82, 136.0, 135.9, 134.5, 128.3, 127.7, 127.7, 127.5, (major) 82.9, 70.5, 46.9, 46.8, 46.7, 45.9, 42.7, 41.5, 41.3, 37.1, 36.9, 34.1, 30.9, 30.2, 27.6, 19.7, 18.6; IR (thin film) 2917, 2864, 1684, 1769, 1453, 1093, 735 cm^{-1}; HRMS (ESI) calculated for $C_{25}H_{32}O_2$ $[M+Na]^+$ 387.2300 found 387.2293.

Corey's Dione 5.4



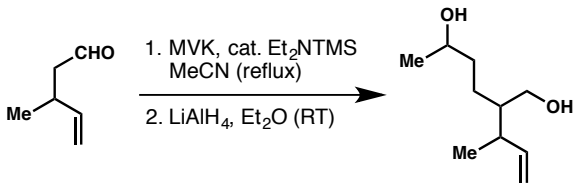
5.91: 3 : 1 dr

5.4

A 1 dram vial containing 27 mg (0.074 mmol, 3:1 dr) **5.91** and 9 mg (0.0042 mmol) 10% Pd/C (50% wetted) in 0.8 mL EtOAc was stirred under 900 psi H_2 in a bomb reactor. After 23 hours, the reaction was filtered over Celite, eluting with EtOAc (~10 mL as determined by TLC) and all volatiles removed in vauo to afford a keto-alcohol as a mixture of diastereomers. The crude material in a 1 dram vial was dissolved in 0.4 mL CH_2Cl_2 and 64 mg Celite added followed by 60 mg (0.278 mmol) PCC open to air. After 2 hours the reaction was diluted with 1 mL Et_2O and filtered over silica gel, eluting with Et_2O (~30 mL as determined by TLC) and all volatiles were removed in vacuo. The crude material in a 1 dram vial was dissolved in 0.6 mL MeOH and 0.6

mL (0.078 mmol) 0.13 M NaOH/MeOH. After 30 minutes at 50 °C the reaction was cooled, diluted with 2 mL half sat. aq. NH_4Cl and extracted with 10 mL EtOAc. The organic layer was washed with 2 mL brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude material was purified by column chromatography (5:1 hexanes/EtOAc) to afford 13 mg (65% over 3 steps, >20:1 dr) **5.4** as a white solid that was recrystallized from Et_2O to afford whispy white needles (mp = 160–161 °C, Corey's mp (no solvent specified, 60% ee) = 137–140 °C[1], Miyaoka's mp (no solvent specified, no enantiopurity mentioned) = 123–125 °C[62]). ^1H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 2.50-2.32 (m, 4H), 2.05-1.97 (m, 5H), 1.75 (dt, *J* = 13.1, 3.4 Hz, 1H), 1.67 (qt, *J* = 11.5, 3.4 Hz, 1H), 1.34-1.13 (m, 6H), 1.10-1.03 (m, 2H), 1.01 (d, *J* = 6.5 Hz, 3H), 0.99 (d, *J* = 6.5 Hz, 3H), 0.87 (q, *J* = 12.3 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 213.0, 212.0, 53.6, 52.7, 52.1, 52.1, 46.3, 44.3, 43.0, 41.2, 41.0, 40.4, 36.4, 31.0, 23.7, 23.6, 19.9, 14.4; IR (thin film) 2923, 2859, 1710, 1455, 1259, 1088, 800 cm^{-1}; HRMS (ESI) calculated for $C_{18}H_{26}O_2$ $[M]^+$ 274.1933 found 274.1944.

Diol (±)-5.94

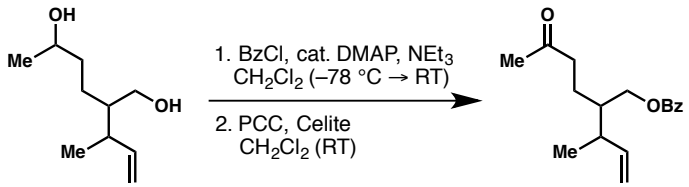


5.10 **5.94:** 1 : 1 : 1 : 1 dr

A 1 dram vial was charged with 52 mg (0.530 mmol) **5.10**, 1.5 mL MeCN, 0.05 mL (0.83 mmol) MVK and 0.02 mL (0.11 mmol) Et_2NTMS. The vial sealed and immersed into a 90 °C oil bath for 21 hours. The reaction was cooled to room temperature and all volatiles removed in vacuo. The crude Michael adduct was added to 21 mg (0.52 mmol) $LiAlH_4$ in 3 mL Et_2O at 0 °C with the assistance of 2 mL Et_2O. The ice bath was removed and stirring continued for 30 minutes

before being recooled to 0 °C and treated with 0.09 mL water, 0.02 mL 5 M NaOH and Na_2SO_4. After 30 minuted of vigorous stirring the solution was filtered over Celite, eluting with Et2O (~15 mL as determined by TLC) and all volatiles removed in vacuo. The crude material was purified by column chromatography (1:2→1:3 Hexanes/EtOAc) to afford 77 mg (85%, 1:1:1:1 dr) (±)-**5.94** as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 5.83-5.74 (m, 1H), 5.03-4.98 (m, 2H), 3.83-3.75 (m, 1H), 3.65-3.53 (m, 2H), 2.37-2.23 (m, 1H), 2.13-2.04 (m, 2H), 1.54-1.32 (m, 5H), 1.19 (d, *J* = 6.2 Hz, 3H), 1.02 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 142.97, 142.87, 142.85, 142.77, 114.0, 113.80, 113.76, 68.4, 68.0, 63.6, 63.5, 63.35, 63.25, 45.5, 45.4, 45.09, 45.06, 38.8, 38.74, 38.71, 38.7, 37.1, 36.8, 36.7, 36.4, 24.1, 24.0, 23.8, 23.6, 23.6, 23.5, 17.0, 16.9, 16.8, 16.8; IR (thin film) 3335, 2964, 2928, 2875 cm^{-1}; HRMS (ESI) calculated for $C_{10}H_{20}O_2$ $[M+Na]^+$ 195.1361 found 195.1353.

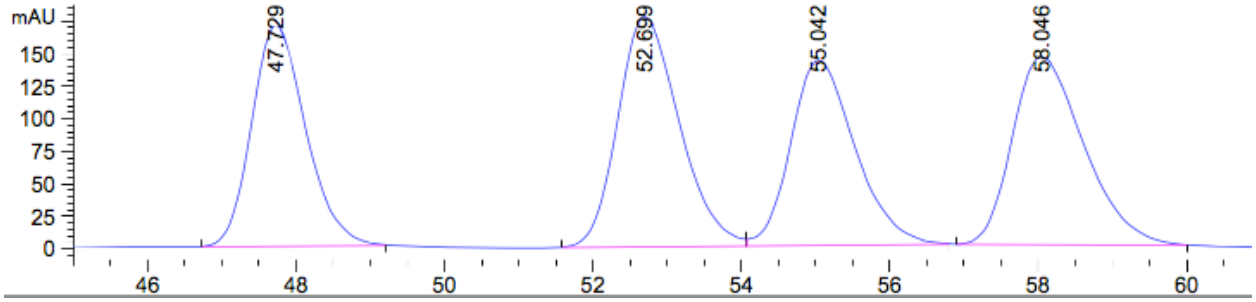
Benzoate (±)-5.95



A 1 dram vial containing 12 mg (0.070 mmol, 1:1:1:1 dr) (±)-**S94**, 1.7 mg (0.014 mmol) DMAP, 0.5 mL CH_2Cl_2 and 0.1 mL (0.72 mmol) NEt_3 was cooled to –78 °C. The reaction was treated with 0.1 mL (0.070 mmol) 0.7 M BzCl/CH_2Cl_2 and stirred for 1 hour before the cold bath was removed. After 30 minutes at room temperature the reaction was quenched with 1 mL sat. aq. $NaHCO_3$ and extracted with 5 mL EtOAc. The organic layer was separated, washed with 1 mL brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude alcohol was dissolved in 0.4 mL CH_2Cl_2 and stirred for 2 hours with 48 mg Celite and 32 mg (0.15 mmol)

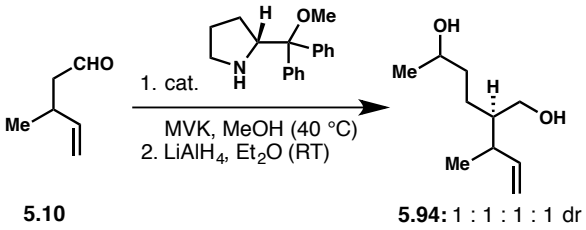
PCC open to air. The reaction was diluted with 2 mL Et_2O and filtered over silica with Et_2O (~15 mL as determined by TLC). All volatiles were removed in vacuo and purified by column chromatography to afford 8.2 mg (42%, 1:1 dr) (±)-**5.95** as colorless oil. Chiral HPLC analaysis was obtained on an AD-H column, 99:1 hexanes/IPA at 0.4 mL/min, visualization at 230 nm, 54:46 dr, 50.1:49.9 (0%ee) diastereomer 1, 51.4:48.6 (3%ee) diastereomer 2. ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) δ 8.04 (d, *J* = 8.2 Hz, 2H), 7.58 (t, *J* = 7.4 Hz, 1H), 7.46 (t, *J* = 7.4 Hz, 2H), 5.82-5.75 (m, 1H), 5.08-5.03 (m, 2H), 4.35-4.23 (m, 2H), 2.63-2.48 (m, 2H), 2.42 (dquintet, *J* = 12.8, 6.4 Hz, 1H), 2.15 (s, 3H), 1.90-1.72 (m, 2H), 1.68-1.55 (m, 1H), 1.10 (d, *J* = 6.9 Hz, 1.5H), 1.09 (d, *J* = 6.9 Hz, 1.5H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ 208.5, 166.6, 141.5, 133.0, 130.2, 129.5, 128.4, 114.8, 114.7, 65.3, 65.2, 42.0, 41.8, 41.6, 41.4, 39.0, 38.9, 30.0, 22.5, 22.5, 17.0, 16.8; IR (thin film) 2963, 2928 cm^{-1}; HRMS (ESI) calculated for $C_{17}H_{22}O_3$ $[M+Na]^+$ 297.1467 found 297.1464.

Figure 5.3. Chiral HPLC chromatogram of (±)-**5.95**.



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	47.729	BB	0.7815	8621.78125	170.04095	23.2650
2	52.699	BV	0.8397	1.02010e4	177.18556	27.5264
3	55.042	VB	0.9185	8572.58203	142.37033	23.1323
4	58.046	BB	1.0185	9663.60156	144.44186	26.0763
Totals :				3.70590e4	634.03871	

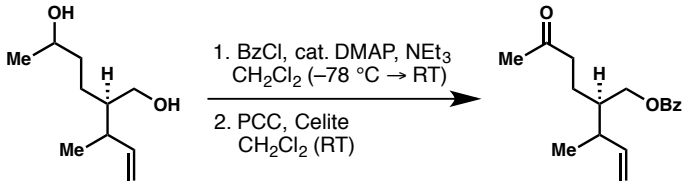
Diol 5.94



5.10 **5.94:** 1 : 1 : 1 : 1 dr

A 1 dram vial was charged with 5.7 mg (0.021 mmol) prolinol catalyst,[63] 52 mg (0.53 mmol) **5.10**, 1 mL MeOH and 0.05 mL (0.83 mmol) MVK. The vial sealed and heated at 40 °C. After 36 hours, the reaction was cooled to room temperature and all volatiles removed in vacuo. The crude Michael adduct was added to 25 mg (0.66 mmol) $LiAlH_4$ in 3 mL Et_2O at 0 °C with the assistance of 2 mL Et_2O. The ice bath was removed and stirring continued for 30 minutes before being recooled to 0 °C and treated with 0.09 mL water, 0.02 mL 5 M NaOH and Na_2SO_4. After a minimum of 30 minutes of vigorous stirring, the solution was filtered over Celite, eluting with Et_2O (~15 mL as determined by TLC) and all volatiles removed in vacuo. The crude material was purified by column chromatography (1:2→1:3 Hexanes/EtOAc) to afford 70 mg (77%) **5.94** as a colorless oil. The spectral data was identical to (±)-**5.94**.

Benzoate 5.95

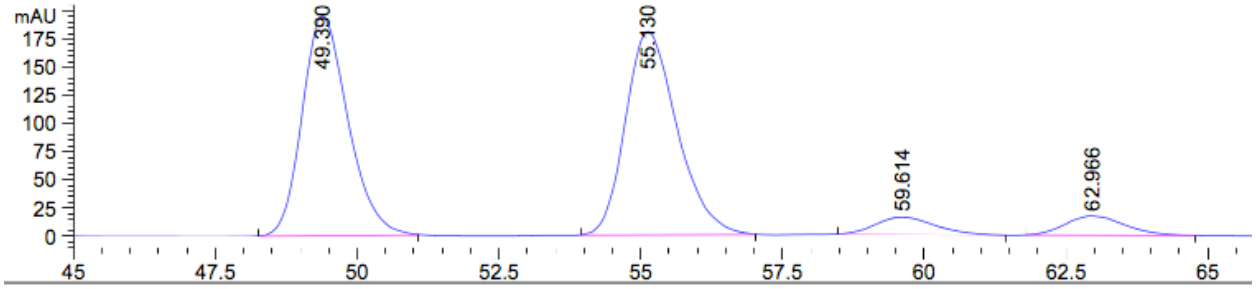


5.94: 1 : 1 : 1 : 1 dr **5.95:** 1 : 1 dr

A 1 dram vial containing 70 mg (0.41 mmol) **5.94**, 10 mg (0.82 mmol) DMAP, 3 mL CH_2Cl_2 and 0.4 mL (2.8 mmol) NEt_3 was cooled to –78 °C. The reaction was treated with 0.2 mL (0.50 mmol) 0.25 M BzCl/CH_2Cl_2 and stirred for 0.5 hour before the cold bath was removed. After 1

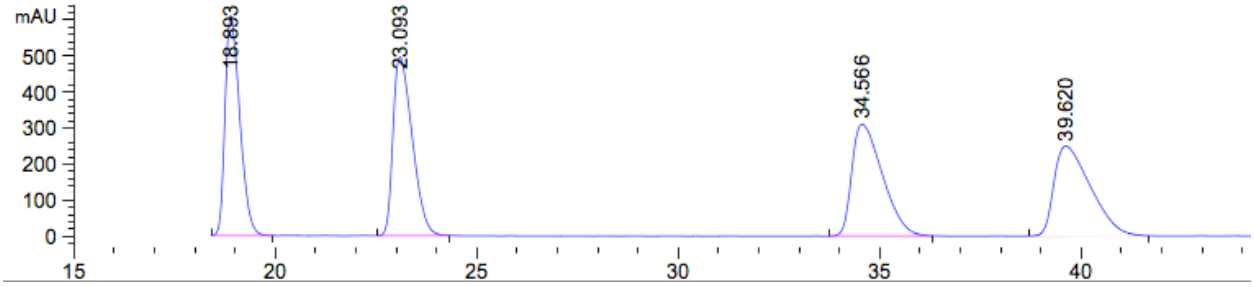
hour at room temperature the reaction was quenched with $NaHCO_3$ and extracted with EtOAc. The organic layer was separated, washed with brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude alcohol was dissolved in 4 mL CH_2Cl_2 and treated with 350 mg (4.2 mmol) $NaHCO_3$ and 257 mg (0.61 mmol) DMP, then stirred until complete open to air. The reaction was quenched with sat. aq. $Na_2S_2O_3$ and sat. aq. $NaHCO_3$, before being extracted with EtOAc. The organic layer was separated and washed with sat. aq. $NaHCO_3$, brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude material was purified by column chromatography (8:1 hexanes/EtOAc) to afford 82 mg (74%, 49:51 dr) **5.95** as a colorless oil, 90.7:9.3 (81%ee) diastereomer 1, 90.2:9.8 (80%ee) diastereomer 2. Chiral HPLC analaysis was obtained on an AD-H column, using 99:1 hexanes/IPA at 0.4 mL/min and visualized at 230 nm. The spectral data was identical to (±)-**5.95**.

Figure 5.4. Chiral HPLC chromatogram for Table 5.5, Entry5 for **5.95**

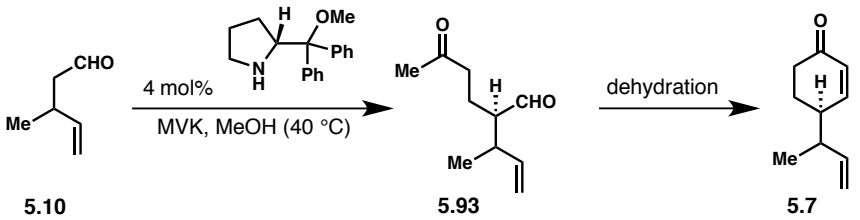


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	49.390	BB	0.8615	1.09725e4	195.29369	44.2210
2	55.130	BB	0.9783	1.14675e4	180.70807	46.2157
3	59.614	BB	1.0741	1127.78943	15.40550	4.5452
4	62.966	BB	1.0540	1245.13989	17.17105	5.0181
Totals :				2.48129e4	408.57830	

Figure 5.5. Chiral HPLC chromatogram for cyclohexenone (±)-**5.7**.



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.893	BB	0.3973	1.55348e4	609.68811	24.2550
2	23.093	BB	0.5215	1.64443e4	495.12198	25.6750
3	34.566	BB	0.8165	1.63599e4	310.61008	25.5433
4	39.620	BB	0.9747	1.57088e4	249.44130	24.5267
Totals :				6.40477e4	1664.86147	



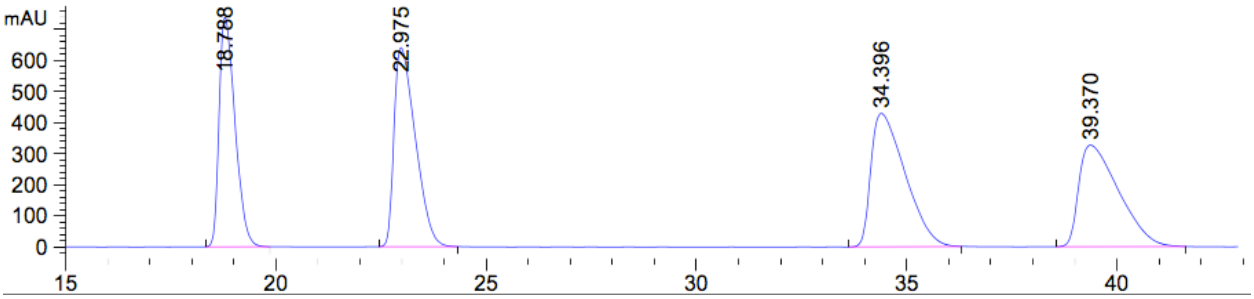
5.10 **5.93** **5.7**

A 1 dram vial was charged with 11 mg (0.042 mmol) prolinol,[63] 108 mg (1.10 mmol **5.10**, 1.1 mL MeOH and 0.13 mL (1.6 mmol) MVK. The vial was sealed and immersed in a 40 °C oil bath. After 39 hours the reaction was cooled and all volatiles removed in vacuo. Chiral HPLC analaysis was obtained on an AS-H column, using 90:10 hexanes/IPA at 0.75 mL/min and visualized at 230 nm. The crude Michael adduct **5.93** was divided evenly into three 1 dram vials.

Table 5.6, Entry 1: 1. DBU 2. MsCl:[64] The crude **5.93** was dissolved in 1.2 mL dry CH_2Cl_2, cooled to 0 °C and treated with 0.17 mL (1.1 mmol) DBU. The cold bath was immediately removed and the reaction stirred for 10 hours. The reaction was then treated with 0.05 mL (0.65 mmol) MsCl at 0 °C. The cold bath was removed. After stirring for 12 hours the reaction was

cooled to 0 °C, quenched with sat. aq. $NaHCO_3$ and extracted with EtOAc. The organic layer was washed with brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude material was purified by column chromatography (10:1→8:1 hexanes/EtOAc) to afford 33 mg (59%) enantioenriched **5.7** as a colorless oil, 53:47 dr, 52:48 (4%ee) diastereomer 1, 53:47 (6%ee) diastereomer 2.

Figure 5.6. Chiral HPLC chromatogram for Table 5.6, entry 1.

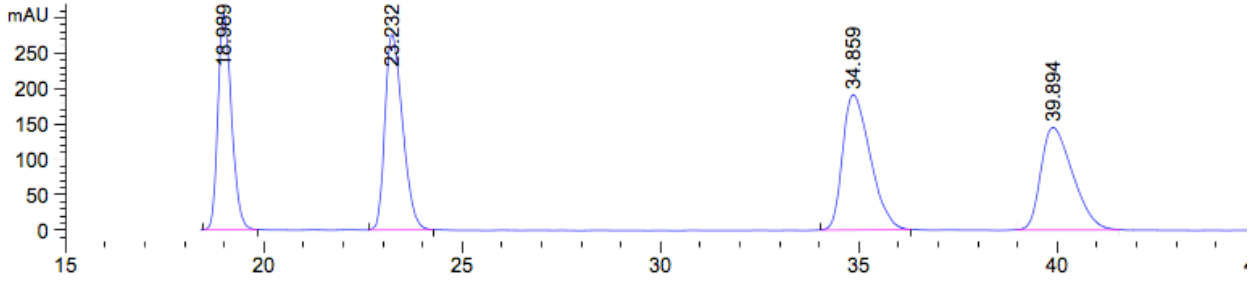


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.788	BB	0.4103	1.94112e4	739.35992	22.0992
2	22.975	BB	0.5386	2.25859e4	641.78729	25.7136
3	34.396	BB	0.8884	2.42658e4	429.96042	27.6260
4	39.370	BB	1.0293	2.15737e4	327.15155	24.5612
Totals :				8.78366e4	2138.25919	

Table 5.6, Entry 2: 1. DBU 2. MsCl:[64] The crude **5.93** was dissolved in 1.2 mL "wet" CH_2Cl_2, cooled to 0 °C and treated with 0.17 mL (1.1 mmol) DBU open to air. The cold was immediately removed and stirred for 8 hours. The reaction was quenched with brine and extracted with EtOAc. The organic phase was washed with brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude hydroxyketone was dissolved in 1 mL CH_2Cl_2 and treated with 0.27 mL (1.9 mmol) NEt_3 and 0.05 mL (0.65 mmol) MsCl at 0 °C. The cold bath was removed. After stirring for 30 hours the reaction was cooled to 0 °C, quenched with sat. aq. $NaHCO_3$ and extracted with EtOAc. The organic layer was washed with brine, dried over $MgSO_4$, filtered and

all volatiles removed in vacuo. The crude material was purified by column chromatography (10:1→8:1 hexanes/EtOAc) to afford 30 mg (54%) enantioenriched **5.7** as a colorless oil, 54:46 dr, 52:48 (4%ee) diastereomer 1, 53:47 (6%ee) diastereomer 2.

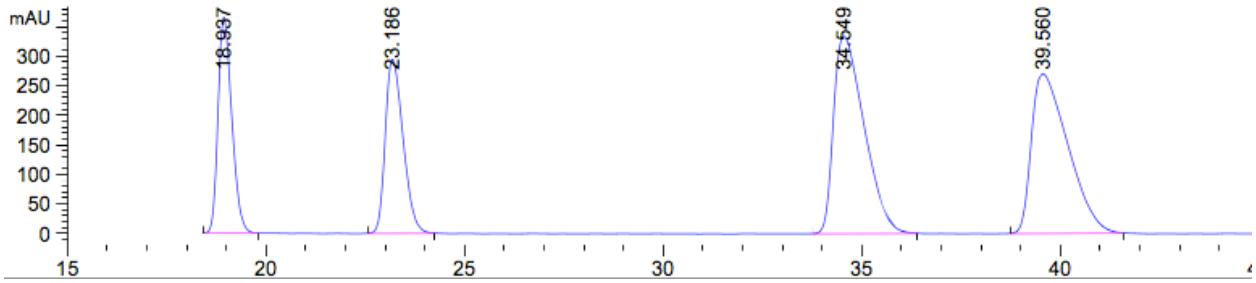
Figure 5.7. Chiral HPLC chromatogram for Table 5.6, entry 2.



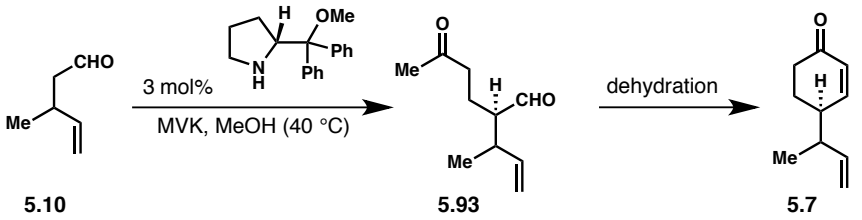
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.989	BB	0.3700	7254.34424	304.45834	21.8662
2	23.232	BB	0.4841	8535.32324	276.49997	25.7273
3	34.859	BB	0.7583	9281.19043	191.19160	27.9755
4	39.894	BB	0.8745	8105.24902	144.91580	24.4310
Totals :				3.31761e4	917.06572	

Table 5.6, Entry 3: TsOH, MeCN: The crude **5.93** was dissolved in 1 mL MeCN then 140 mg (0.74 mmol) TsOH•H_2O added open to air. After 8 hours, the reaction was cooled to 0 °C and quenched with 0.7 mL 1 M NacOH and sat. aq. $NaHCO_3$. All volatiles were removed in vacuo an the aqueous layer extracted with EtOAc. The organic layer was washed with brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude material was purified by column chromatography (10:1→8:1 hexanes/EtOAc) to afford 36 mg (62%) enantioenriched **5.7** as a colorless oil, 51:49 dr, 67:33 (34%ee) diastereomer 1, 66:34 (32%ee) diastereomer 2.

Figure 5.8. Chiral HPLC chromatogram for Table 5.6, entry 3.



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.937	BB	0.3673	8803.39941	365.06793	16.5764
2	23.186	BB	0.4860	9190.24023	294.55118	17.3048
3	34.549	BB	0.8253	1.78740e4	334.55463	33.6559
4	39.560	BB	0.9282	1.72404e4	270.27594	32.4629
Totals :				5.31080e4	1264.44968	



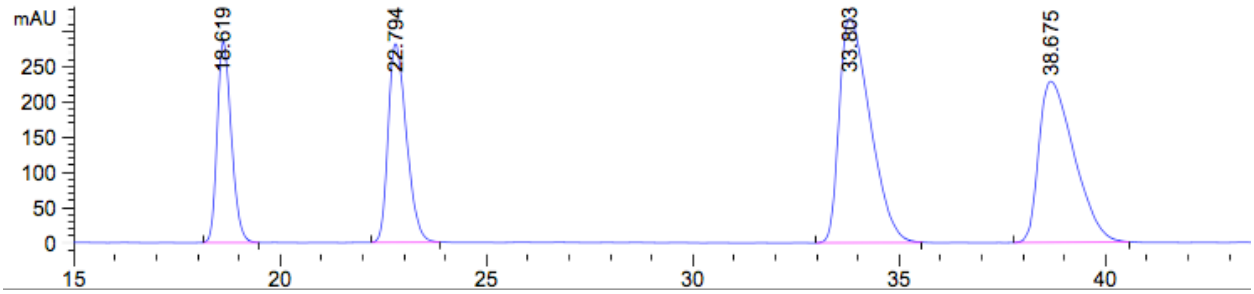
5.10 **5.93** **5.7**

A 1 dram vial was charged with 11 mg (0.043 mmol) prolinol,[63] 113 mg (1.15 mmol) **5.10**, 1.1 mL MeOH and 0.13 mL (1.6 mmol) MVK. The vial was sealed and immersed in a 40 °C oil bath. After 36 hours the reaction was cooled and all volatiles removed in vacuo. Chiral HPLC analaysis was obtained on an AS-H column, using 90:10 hexanes/IPA at 0.75 mL/min and visualized at 230 nm. The crude Michael adduct **5.93** was divided evenly into four 1 dram vials.

Table 5.6, Entry 4: TBD, THF then MsCl: The crude **5.93** was dissolved in 1 mL THF and treated with 2.6 mg (0.02 mmol) TBD. Stirring was continued for 20 minutes after which time the reaction was cooled to 0 °C and 0.16 mL (1.1 mL) NEt_3, ~2 mg DMAP and 0.03 mL (0.39 mmol) MsCl added. The cold bath was removed. After stirring for 22 hours the reaction was

cooled to 0 °C, quenched with sat. aq. $NaHCO_3$ and extracted with EtOAc. The organic layer was washed with brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude material was purified by column chromatography (10:1→8:1 hexanes/EtOAc) to afford 26 mg (59%) enantioenriched **5.7** as a colorless liquid, 55:45 dr, 66:34 (32%ee) diastereomer 1, 67:33 (34%ee) diastereomer 2.

Figure 5.9. Chiral HPLC chromatogram for Table 5.6, entry 4.

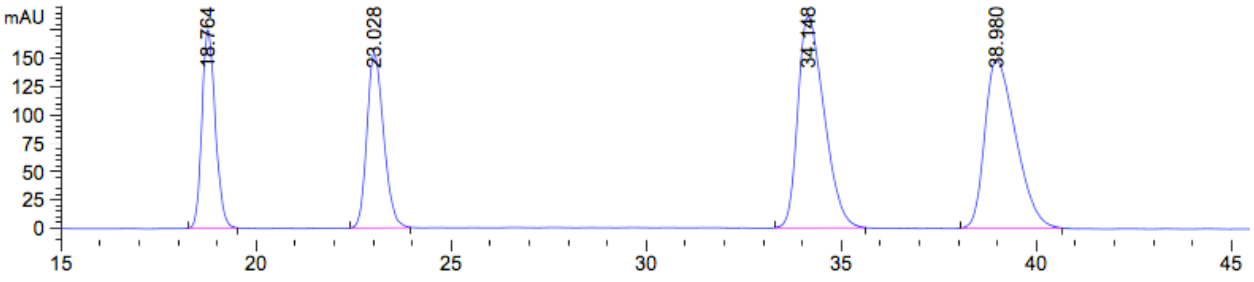


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.619	BB	0.3682	6800.22998	285.19995	14.9101
2	22.794	BB	0.4794	8667.25586	281.39078	19.0038
3	33.803	BB	0.8085	1.65248e4	318.93164	36.2323
4	38.675	BB	0.9267	1.36158e4	228.67078	29.8538
Totals :				4.56081e4	1114.19315	

Table 5.6, Entry 5: TBD, THF then Ac_2O: The crude **5.93** was dissolved in 1 mL THF and treated with 2.6 mg (0.02 mmol) TBD. Stirring was continued for 20 minutes after which time the reaction was cooled to 0 °C and 0.16 mL (1.1 mL) NEt_3, ~2 mg DMAP and 0.04 mL (0.42 mmol) Ac_2O added. The cold bath was removed. After stirring for 22 hours the reaction was cooled to 0 °C, quenched with sat. aq. $NaHCO_3$ and extracted with EtOAc. The organic layer was washed with brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude material was purified by column chromatography (10:1→8:1 hexanes/EtOAc) to afford 29 mg

(66%) enantioenriched **5.7** as a colorless liquid, 52:48 dr, 66:34 (32%ee) diastereomer 1, 66:34 (32%ee) diastereomer 2.

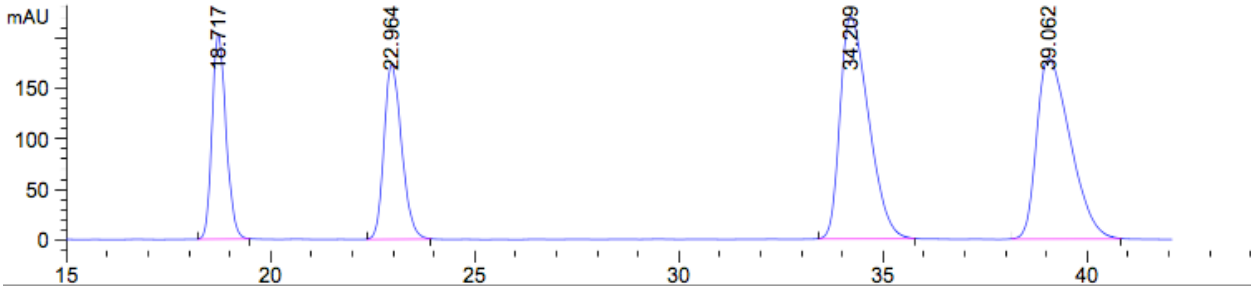
Figure 5.10. Chiral HPLC chromatogram for Table 5.6, entry 5.



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.764	BB	0.3700	4173.20020	175.11093	16.1926
2	23.028	BB	0.4626	4606.64111	154.15210	17.8744
3	34.148	BB	0.7252	8746.12207	186.47589	33.9362
4	38.980	BB	0.8508	8246.30078	148.75092	31.9968
Totals :				2.57723e4	664.48984	

Table 5.6, Entry 6: TBD, MeCN then TsOH: The crude **5.93** was dissolved in 1 mL MeCN and treated with 2.7 mg (0.02 mmol) TBD. Stirring was continued for 20 minutes after which time 54 mg (0.28 mmol) TsOH•H_2O was added. After stirring for 4 hours the reaction was cooled to 0 °C, quenched with 0.2 mL 1 M NaOH, sat. aq. $NaHCO_3$ and extracted with EtOAc. The organic layer was washed with brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude material was purified by column chromatography (10:1→8:1 hexanes/EtOAc) to afford 30 mg (68%) enantioenriched **5.7** as a colorless liquid, 51:49 dr, 67:33 (34%ee) diastereomer 1, 68:32 (36%ee) diastereomer 2.

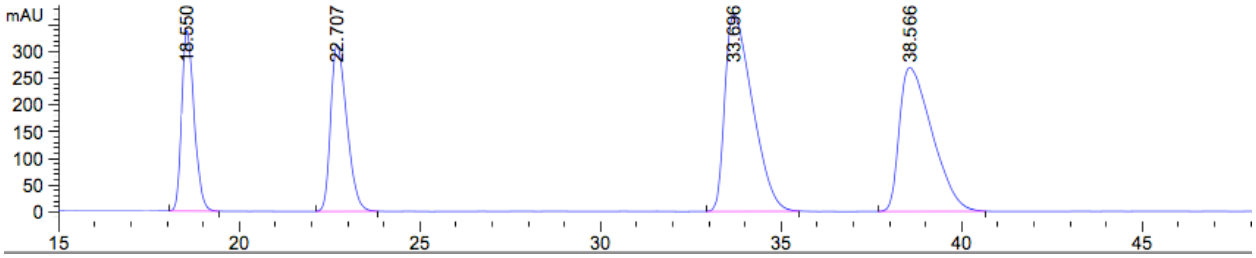
Figure 5.11. Chiral HPLC chromatogram for Table 5.6, entry 6.



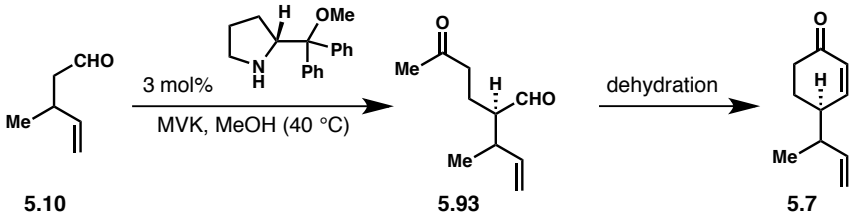
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.717	BB	0.3669	4822.41992	203.15219	15.6002
2	22.964	BB	0.4670	5209.96826	173.15804	16.8539
3	34.209	BB	0.7605	1.06787e4	219.92101	34.5447
4	39.062	BB	0.8749	1.02016e4	178.45639	33.0013
Totals :				3.09126e4	774.68762	

Table 5.6, Entry 7: TBD, CH_2Cl_2 then MsCl: The crude **5.93** was dissolved in 1 mL CH_2Cl_2 and treated with 2.8 mg (0.02 mmol) TBD. Stirring was continued for 3.5 hours after which time the reaction was cooled to 0 °C and 0.16 mL (1.1 mmmol) NEt_3, ~2 mg DMAP and 0.03 mL (0.39 mmol) MsCl added. The cold bath was removed. After stirring for 18 hours the reaction was cooled to 0 °C, quenched with sat. aq. $NaHCO_3$ and extracted with EtOAc. The organic layer was washed with brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude material was purified by column chromatography (10:1→8:1 hexanes/EtOAc) to afford 25 mg (56%) enantioenriched **5.7** as a colorless liquid, 54:46 dr, 67:33 (34%ee) diastereomer 1, 68:32 (36%ee) diastereomer 2.

Figure 5.12. Chiral HPLC chromatogram for Table 5.6, entry 7.



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.550	BB	0.3734	8078.80713	337.34940	14.8667
2	22.707	BB	0.4832	9689.58984	311.28677	17.8309
3	33.696	BB	0.8292	1.95834e4	367.78485	36.0376
4	38.566	BB	0.9827	1.69898e4	269.79337	31.2648
Totals :				5.43416e4	1286.21439	



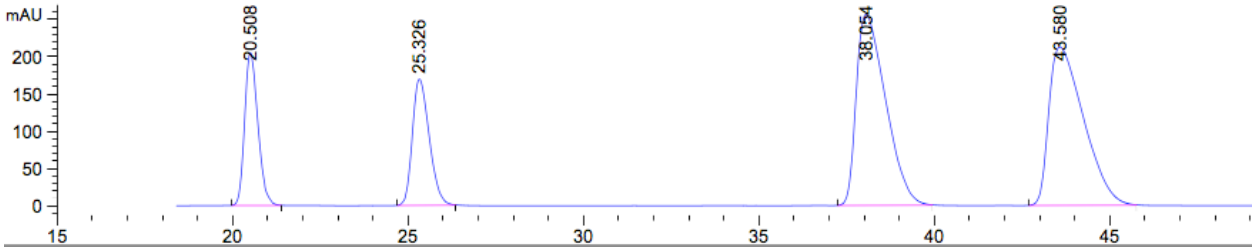
5.10 5.93 5.7

A 1 dram vial was charged with 14 mg (0.050 mmol) prolinol,[63] 166 mg (1.69 mmol) **5.10**, 1.5 mL MeOH and 0.2 mL (2.5 mmol) MVK. The vial was sealed and immersed in a 40 °C oil bath. After 36 hours the reaction was cooled and all volatiles removed in vacuo. Chiral HPLC analaysis was obtained on an AS-H column, using 90:10 hexanes/IPA at 0.75 mL/min and visualized at 230 nm. The crude Michael adduct was divided evenly into six 1 dram vials.

Table 5.6, Entry 8: 1. TBD, MeOH 2. MsCl: The crude **5.93** was dissolved in 1 mL MeOH and treated with 1.7 mg (0.012 mmol) TBD. Stirring was continued for 4 hours after which time the reaction was quenched with sat. aq. NH_4Cl and extracted with EtOAc. The organic layer was separated, washed with brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The

crude material was dissolved in 1 mL CH_2Cl_2, cooled to 0 °C and treated with 0.25 mL (1.8 mmol) NEt_3, ~3 mg DMAP and 0.03 mL (0.39 mmol) MsCl added. The cold bath was removed. After stirring for 18 hours the reaction was cooled to 0 °C, quenched with sat. aq. $NaHCO_3$ and extracted with EtOAc. The organic layer was washed with brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude material was purified by column chromatography (10:1→8:1 hexanes/EtOAc) to afford 23 mg (55%) enantioenriched **5.7** as a colorless liquid, 51:49 dr, 73:27 (46%ee) diastereomer 1, 73:27 (46%ee) diastereomer 2.

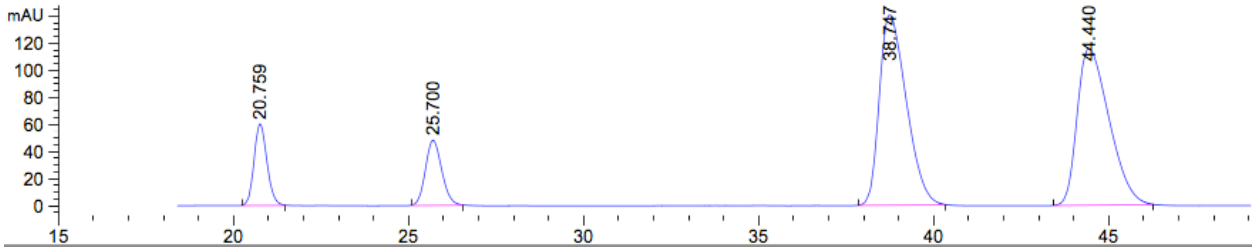
Figure 5.13. Chiral HPLC chromatogram for Table 5.6, entry 8.



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.508	BB	0.4085	5384.68018	204.93588	13.2588
2	25.326	BB	0.5222	5673.17920	169.64209	13.9692
3	38.054	BB	0.9115	1.49161e4	256.09473	36.7281
4	43.580	BB	1.0575	1.46382e4	212.55324	36.0439
Totals :				4.06122e4	843.22594	

Table 5.6, Entry 9: McQuade Diamine Catalyst:[6] The crude **5.93** was dissolved in 1 mL hexanes and treated with 22 mg (0.087 mmol) McQuade diamine catalyst. Stirring was continued for 24 hours after which time the reaction was diluted with water and extracted with EtOAc. The organic layer was washed with brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude material was purified by column chromatography (10:1→8:1 hexanes/EtOAc) to afford 26 mg (62%) enantioenriched **5.7** as a colorless liquid, 51:49 dr, 83:17 (66%ee) diastereomer 1, 83:17 (66%ee) diastereomer 2.

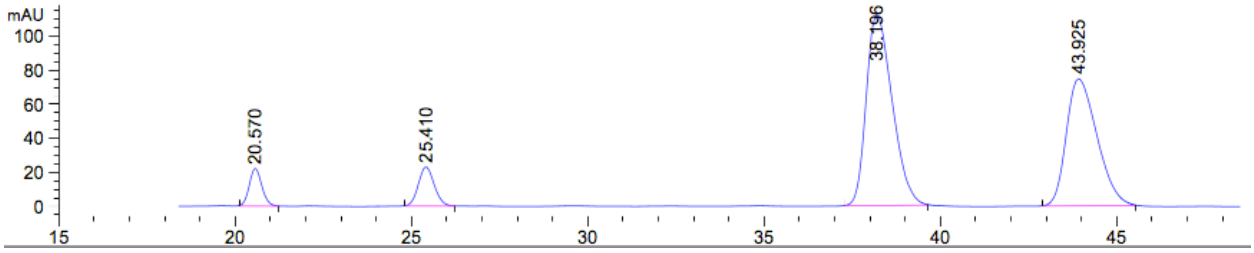
Figure 5.14. Chiral HPLC chromatogram for Table 5.6, entry 9.



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.759	BB	0.3977	1548.58093	60.28382	8.5989
2	25.700	BB	0.5025	1563.21143	48.17989	8.6801
3	38.747	BB	0.8317	7550.24658	140.78036	41.9247
4	44.440	BB	0.9838	7347.04687	115.85931	40.7963
Totals :				1.80091e4	365.10339	

Table 5.6, Entry 10: 1. LDA 2. MsCl: The crude **5.93** was dissolved in 1 mL THF and treated with 0.3 mL (0.32 mmol) 0.93 M LDA/THF slowly at –78 °C. Stirring was continued for 1 minute after which time the reaction was quenched with half sat. aq. NH_4Cl and extracted with EtOAc. The organic layer was separated, washed with brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude material was dissolved in 1 mL CH_2Cl_2, cooled to 0 °C and treated with 0.25 mL (1.8 mmol) NEt_3, ~3 mg DMAP and 0.03 mL (0.39 mmol) MsCl added. The cold bath was removed. After stirring for 18 hours the reaction was cooled to 0 °C, quenched with sat. aq. $NaHCO_3$ and extracted with EtOAc. The organic layer was washed with brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude material was purified by column chromatography (10:1→8:1 hexanes/EtOAc) to afford 10 mg (23%) enantioenriched **5.7** as a colorless liquid, 56:44 dr, 88:12 (76%ee) diastereomer 1, 89:11 (78%ee) diastereomer 2 and 13 mg (27%) Michael adduct.

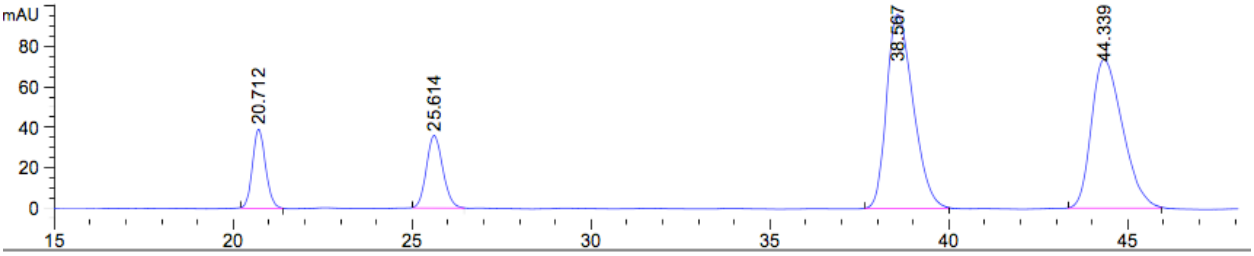
Figure 5.15. Chiral HPLC chromatogram for Table 5.6, entry 10.



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.570	BB	0.3832	547.76123	22.09510	4.7484
2	25.410	BB	0.4856	720.13940	22.98220	6.2427
3	38.196	BB	0.7967	5744.96094	112.31967	49.8016
4	43.925	BB	0.9422	4522.82471	74.71611	39.2072
Totals :				1.15357e4	232.11308	

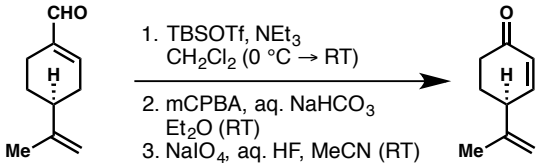
Table 5.6, Entry 11: 1. KOt-Bu 2. MsCl: A 1 dram vial was charged with 0.5 mL (0.08 mmol) 0.16 M KOt-Bu/THF and cooled to 0 °C. The crude **5.93** was added dropwise with the assistance of 1 mL THF. Stirring was continued for 1 minute after which time the reaction was quenched with half sat. aq. NH_4Cl and extracted with EtOAc. The organic layer was separated, washed with brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude material was dissolved in 1 mL CH_2Cl_2, cooled to 0 °C and treated with 0.25 mL (1.8 mmol) NEt_3, ~3 mg DMAP and 0.03 mL (0.39 mmol) MsCl added. The cold bath was removed. After stirring for 18 hours the reaction was cooled to 0 °C, quenched with sat. aq. $NaHCO_3$ and extracted with EtOAc. The organic layer was washed with brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude material was purified by column chromatography (10:1→8:1 hexanes/EtOAc) to afford 18 mg (43%) enantioenriched **5.7** as a colorless liquid, 53:47 dr, 81:19 (62%ee) diastereomer 1, 78:22 (56%ee) diastereomer 2.

Figure 5.16. Chiral HPLC chromatogram for Table 5.6, entry 11.



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.712	BB	0.3936	1001.28882	39.25832	8.6459
2	25.614	BB	0.4922	1147.34888	35.96552	9.9071
3	38.567	BB	0.8054	4966.41357	96.33973	42.8838
4	44.339	BB	0.9323	4466.03418	73.76998	38.5632
Totals :				1.15811e4	245.33355	

(S)-(–)-97 [Adapted from the literature][65]

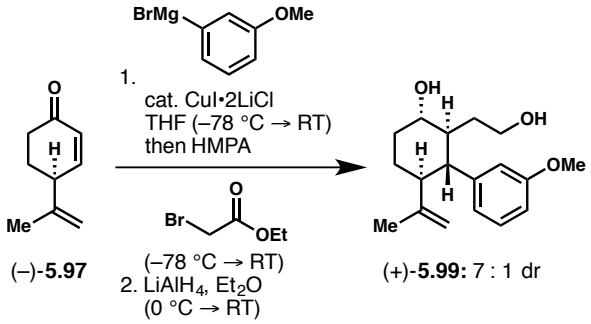


(–)-**5.96** (–)-**5.97**

A 250 mL round bottom flask was charged with 5.20 g (34.6 mmol) 90% pure (S)-(–)-perillaldehyde [(S)-(–)-**5.96**] and 130 mL CH_2Cl_2, cooled to 0 °C and sequentially treated with 10 mL (71.7 mmol) NEt_3 and 8.7 mL (37.9 mmol) TBSOTf. After 10 minutes at 0 °C, the flask was removed and stirring continued for 20 minutes. The contents were poured into 60 mL stirring sat. aq. $NaHCO_3$ and the flask was rinsed with 20 mL CH_2Cl_2. The layers were separated and the aqueous layer extracted with 20 mL CH_2Cl_2. The organic layers were combined, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude dienoxysilane in a 500 mL round bottom flask was dissolved in 130 mL Et_2O and 150 mL sat. aq. $NaHCO_3$ open to air. To the vigorously stirring mixture was added portionwise 14.7 g (59.7-63.9 mmol) 70-75% pure

mCPBA. Upon complete consumption of dienoxysilane by TLC the layers were separated and extracted with 50 mL Et_2O. The organic layers were combined, washed with 20 mL sat. aq. $NaHCO_3$, 20 mL brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. To a 500 mL round bottom flask containing crude epoxide was added 100 mL MeCN then at 0 °C, 10.3 (48.2 mmol) $NaIO_4$ and slowly 2.5 mL HF in 25 mL water open to air. The reaction was further stirred for 5 minutes then the cold bath removed. After 2 hours 250 mL water was added and the solution extracted thrice with 125 mL Et_2O. The organic layers were combined, washed with 25 mL sat. aq. $NaHCO_3$ and 25 mL brine. The last two aqueous washings were combined and back extracted with 30 mL Et_2O. All organic layers were combined, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude material was purified by distillation (68–75 °C/1.5 mmHg) to afford 2.93 g (62% over 3 steps) (S)-(–)-**5.97** as a colorless solution. Spectral data was identical to the literature.[65] Optical rotation $[\alpha]^{23}_D$ –159.1° (*c* 1.03, MeOH) and $[\alpha]^{24}_D$ –189.4° (*c* 0.0162, MeOH); lit. for (S)-4-(2-propenyl)-2-cycloexen-1-one is $[\alpha]^{26}_D$ –153.8° (*c* 1.03, MeOH),[66] for (R)-4-(2-propenyl)-2-cycloexen-1-one is $[\alpha]^{26}_D$ +192.2° (*c* 0.0162, MeOH)[65] and $[\alpha]^{22}_D$ +157.6° (*c* 1.37, $CHCl_3$).[67]

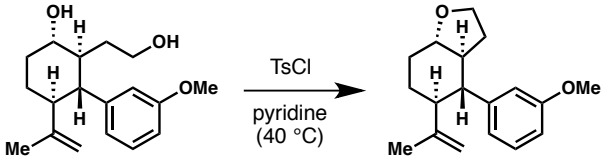
Diol (+)-5.100



3-Methoxyphenylmagnesium bromide was prepared by addition of 0.7 mL (5.6 mmol) 3-bromoanisole in 0.7 mL THF to 0.177 g (7.3 mmol) magnesium metal in 2.8 mL THF activated by dibromoethane maintaining 40–50 °C. A 10 mL round bottom flask was charged with 2 mL THF and 0.7 mL (0.90 mmol) 1.29 M 3-methoxyphenylmagnesium bromide. At –78 °C, 0.3 mL (0.075 mmol) 0.25 M CuI•2LiCl/THF was added followed by 100 mg (0.73 mmol) (S)-(–)-**5.97** in 0.6 mL THF. Stirring at –78 °C was continued for 2 hours before the cold bath was removed. After 1 hour the reaction was recooled to –78 °C. To the solution was added 0.26 mL (1.50 mmol) HMPA. After 1 hour 0.30 mL (3.62 mmol) ethyl bromoacetate was added. The reaction was stirred at –78 °C for 10 minutes then the cold bath removed. After stirring for 29 hours at room temperature, the reaction was cooled in an ice bath and treated with 1.5 mL sat. aq. NH_4Cl, 1.5 mL water, extracted with 10 mL and twice with 5 mL Et_2O. The organic layers were combined, washed with 1 mL half sat. aq. NH_4Cl, 1 mL brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo to afford a crude oil. To an ice cooled 25 mL round bottom flask containing 5 mL Et_2O was added 158 mg (4.2 mmol) $LiAlH_4$. The crude oil was transferred using 5 mL Et_2O dropwise. The ice bath was removed after 5 minutes. After 5 hours the reaction was placed into a room temperature water bath and 0.3 mL EtOAc added, then the flask was recooled in an ice bath and 0.16 mL water, 0.16 mL 5 M NaOH, 0.45 mL water and $MgSO_4$ was added. After stirring the contents for several hours, the solution was filtered over Celite and the

filter cake washed with Et_2O until no more product was detected by TLC (~75 mL Et_2O). The filtrate was concentrated and the residue purified by column chromatography (1:3→1:5 hexanes/EtOAc) to afford 79 mg (37% over 2 steps, 7:1 dr) (+)-**5.99** as a viscous colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) mixture of diastereomers and slow rotation δ 7.15 (s, 1H), 6.70-6.63 (m, 3H), 4.52 (bs, 2H), 4.46 (d, *J* = 7.6 Hz, 2H), 3.77 (s, 3H), 3.52 (dt, *J* = 10.1, 4.8 Hz, 1H), 3.44 (td, *J* = 9.6, 4.1 Hz, 1H), 3.26-3.22 (m, 1H), 2.33-2.23 (m, 2H), 2.14-2.10 (m, 1H), 2.04-1.90 (m, 1H), 1.81-1.70 (m, 1H), 1.66-1.49 (m, 2H), 1.46 (s, 3H), 1.44-1.39 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) major with some resonances missing due to slow rotation δ 147.4, 144.6, 111.5, 74.3, 61.8, 55.0, 52.1, 49.5, 34.9, 34.5, 30.1, 19.6; IR (thin film) 3320, 2930, 1600, 1488, 1258, 1047 cm^{-1}; HRMS (ESI) calculated for $C_{18}H_{26}O_3$ $[M+Na]^+$ 313.1780 found 313.1771; $[\alpha]^{22}_D$ +35.5° (*c* 0.50, $CHCl_3$).

Perhydrobenzofuran (+)-5.100

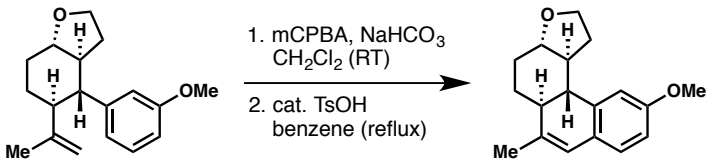


(+)-**5.99:** 7 : 1 dr (+)-**5.100:** 7 : 1 dr

To a 10 mL round bottom flask containing 73 mg (0.251 mmol, 7:1 dr) (+)-**5.99** in 1.2 mL pyridine was added 125 mg (0.66 mmol) p-toluenesulfonyl chloride at room temperature. The flask was placed in a 40 °C oil bath. After 22 hours the reaction was cooled to room temperature and quenched with 3 mL sat. aq. $NaHCO_3$, 1.5 mL water and extraced with 15 mL and 10 mL EtOAc. The organic layers were washed with 3 mL, 2 mL and 1 mL ice cold 6 M HCl then 1 mL water. The acidic aqueous washings were combined, back extracted twice with 3 mL EtOAc and all organic phases combined. The organic medium was washed with 2 mL sat. aq. $NaHCO_3$, 2

mL brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude oil was purified by column chromatography (5:1 hexanes/EtOAc) to afford 57 mg (83%, 7:1 dr) (+)-**5.100** as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$ at 7.27 ppm) major δ 7.19 (t, *J* = 7.9 Hz, 1H), 6.74-6.68 (m, 3H), 4.57 (s, 2H), 3.91 (td, *J* = 9.1, 2.7 Hz, 1H), 3.85 (q, *J* = 8.0 Hz, 1H), 3.80 (s, 3H), 3.26 (td, *J* = 10.1, 4.0 Hz, 1H), 2.45-2.35 (m, 2H), 2.24-2.21 (m, 1H), 1.92 (td, *J* = 6.6, 3.6 Hz, 1H), 1.88-1.77 (m, 1H), 1.70-1.49 (m, 4H), 1.54 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$ at 77 ppm) δ (mixture of diastereomers) 159.4, 146.8, 144.5, 129.1, 128.9, 121.2, 120.0, 114.9, 113.7, 112.0, 111.3, 110.9, 110.7 (major) 82.6, 67.1, 55.1, 51.7, 51.6, 50.4, 30.8, 30.6, 30.0, 19.9; IR (thin film) 3070, 2934, 2876, 1645, 1601, 1489, 1261, 1048, 776, 700 cm^{-1}; HRMS (ESI) calculated for $C_{18}H_{24}O_2$ $[M+Na]^+$ 295.1674 found 295.1664; $[\alpha]^{22}_D$ +17.5° (*c* 0.50, $CHCl_3$).

Dihydronaphthalene (–)-5.64



(+)-**5.100:** 7 : 1 dr (–)-**5.64:** 6 : 1 dr

To a 1 dram vial containing 5 mg (0.018 mmol, 7:1 dr) (+)-**5.100** and 19 mg (0.23 mmol) $NaHCO_3$ in 0.3 mL CH_2Cl_2 was added 9 mg (0.037 mmol) 70% mCPBA at room temperature open to air. After 13 hours 1 mL half sat. aq. $Na_2S_2O_3$ was added and the mixture extracted with 2 mL and 1 mL EtOAc. The organic layers were combined, washed with 1 mL sat. aq. $NaHCO_3$, 1 mL brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. To a 5 mL round bottom flask containing crude epoxide was added 2 mL benzene and 2 mg (0.011 mmol) $TsOH•H_2O$. The reaction was refluxed over a Hickman still for 2 hours. The reaction was

cooled, diluted with 1 mL sat. aq. $NaHCO_3$, 3 mL EtOAc and the layers separated. The organic layer was washed with 1 mL brine, dried over $MgSO_4$, filtered and all volatiles removed in vacuo. The crude oil was purified by column chromatography (6:1 hexanes/EtOAc) to afford 3 mg (60% over 2 steps, 6:1 dr) (–)-**5.64** as a white wax. Spectral data was identical to (±)-**5.64**; $[\alpha]^{22}_{D}$ –165.0° (*c* 0.50, $CHCl_3$).

5.9 References and Notes

(1) Corey, E. J.; Magriotis, P. A. *J. Am. Chem. Soc.* **1987**, *109*, 287.

(2) Mander, L. N. *Synlett* **1991**, 134.

(3) Parr, B. T.; Economou, C.; Herzon, S. B. *Nature* **2015**, *525*, 507.

(4) Chi, Y.; Gellman, S. H. *Org. Lett.* **2005**, *7*, 4253.

(5) Franzén, J.; Marigo, M.; Fielenbach, D.; Wabnitz, T. C.; Kjærsgaard, A.; Jørgensen, K. A. *J. Am. Chem. Soc.* **2005**, *127*, 18296.

(6) Houjeiry, T. I.; Poe, S. L.; Mcquade, D. T. *Org. Lett.* **2012**, *14*, 4394.

(7) Wei, X.; Lorenz, J. C.; Kapadia, S.; Saha, A.; Haddad, N.; Busacca, C. A.; Senanayake, C. H. *J. Org. Chem.* **2007**, *72*, 4250.

(8) Chen, K.; Baran, P. S. *Nature* **2009**, *459*, 824.

(9) Watanabe, W. H.; Conlon, L. E. *J. Am. Chem. Soc.* **1957**, *79*, 2828.

(10) Reetz, M. T.; Kindler, A. *J. Organomet. Chem.* **1995**, *502*, C5.

(11) Keinan, E.; Greenspoon, N. "Reduction of alpha,beta-Unsaturated Carbonyl Compounds" In *The Chemistry of Enones*; Patai, S.; Rappoport, Z., Ed.; John Wiley & Sons, Ltd, 1989; pp 923–1022.

(12) Caine, D. *Org. React.* **1976**, *23*, 1.

(13) Numbering matches the isocycloamphilectane scaffold, i.e. 7, 20-diisocyanoadociane.

(14) Pronin, S. V.; Reiher, C. A.; Shenvi, R. A. *Nature* **2013**, *501*, 195.

(15) Pronin, S. V.; Shenvi, R. A. *J. Am. Chem. Soc.* **2012**, *134*, 19604.

(16) Sasaki, T.; Nakanishi, A.; Ohno, M. *J. Org. Chem.* **1981**, *46*, 5445.

(17) Maruoka, K.; Itoh, T.; Yamamoto, H. *J. Am. Chem. Soc.* **1985**, *107*, 4573.

(18) Suzuki, T.; Kobayashi, T.; Takegami, Y.; Kawasaki, Y. *Bull. Chem. Soc. Jpn.* **1974**, *47*,

1971.

(19) Cahiez, G.; Duplais, C.; Buendia, J. *Chem. Rev.* **2009**, *109*, 1434.

(20) Garst, M. E.; Dolby, L. J.; Esfandiari, S.; Fedoruk, N. A.; Chamberlain, N. C.; Avey, A. A. *J. Org. Chem.* **2000**, *65*, 7098.

(21) Hassner, A.; Kropp, J. E.; Kent, G. J. *J. Org. Chem.* **1969**, *34*, 2628.

(22) Sy, W.-W.; By, A. W. *Tetrahedron Lett.* **1985**, *26*, 1193.

(23) Taniguchi, T.; Fujii, T.; Ishibashi, H. *J. Org. Chem.* **2010**, *75*, 8126.

(24) Maity, S.; Naveen, T.; Sharma, U.; Maiti, D. *Org. Lett.* **2013**, *15*, 3384.

(25) Maity, S.; Manna, S.; Rana, S.; Naveen, T.; Mallick, A.; Maita, D. *J. Am. Chem. Soc.* **2013**, *135*, 3355.

(26) Cossio, F. P.; Aizpurua, J. M.; Palomo, C. *Can. J. Chem.* **1986**, *64*, 225.

(27) Emsermann, J.; Kauhl, U.; Opatz, T. *Mar. Drugs* **2016**, *14*, 16.

(28) Huffman, J. W. "Reduction of C=X to CHXH by Dissolving Metals and Related Methods" In *Comprehensive Organic Synthesis*; Trost, B. M.; Fleming, I., Ed.; Elsevier Science Ltd., 1991; pp 107–127.

(29) Johnson, C. R.; Raheja, R. K. *J. Org. Chem.* **1994**, *59*, 2287.

(30) Tsuda, T.; Hayashi, T.; Satomi, H.; Kawamoto, T.; Saegusa, T. *J. Org. Chem.* **1986**, *51*, 537.

(31) Daniewski, A. R.; Kiegiel, J. *Synth. Commun.* **1988**, *18*, 115.

(32) Krüerke, U. *Chem. Ber.* **1962**, *95*, 174.

(33) Karger, M. H.; Mazur, Y. *J. Am. Chem. Soc.* **1969**, *91*, 5663.

(34) Karger, M. H.; Mazur, Y. *J. Org. Chem.* **1971**, *36*, 532.

(35) Beard, C. D.; Baum, K.; Grakauskas, V. *J. Org. Chem.* **1973**, *38*, 3673.

(36) Guindon, Y.; Therien, M.; Girard, Y.; Yoakim, C. *J. Org. Chem.* **1987**, *52*, 1680.

(37) Forbus, Jr, T. R.; Taylor, S. L.; Martin, J. C. *J. Org. Chem.* **1987**, *52*, 4156.

(38) Ohshita, J.; Iwata, A.; Kanetani, F.; Kunai, A.; Yamamoto, Y.; Matui, C. *J. Org. Chem.* **1999**, *64*, 8024.

(39) Iqbal, J.; Srivastava, R. R. *Tetrahedron* **1991**, *47*, 3155.

(40) Node, M.; Kajimoto, T.; Nishide, K.; Fujita, E.; Fuji, K. *Tetrahedron Lett.* **1984**, *25*, 219.

(41) Funk, R. L.; Mossman, C. J.; Zeller, W. E. *Tetrahedron Lett.* **1984**, *25*, 1655.

(42) Wettstein, A.; Mischer, K. *Helv. Chim. Acta* **1942**, *25*, 718.

(43) Godfrey, C. R. A. "Oxidation Adjacent to Oxygen of Ethers" In *Comprehensive Organic Synthesis*; Trost, B. M.; Fleming, I., Ed.; Elsevier Science Ltd., 1991; Vol. 7, pp 235–250.

(44) Courtney, J. L. "Ruthenium Tetroxide Oxidations" In *Organic Syntheses by Oxidation with Metal Compounds*; Mijs, W. J.; de Jonge, C. R. H. I., Ed.; Plenum Press: New York, 1986; pp 445–468.

(45) Lee, J. S.; Cao, H.; Fuchs, P. L. *J. Org. Chem.* **2007**, *72*, 5820.

(46) Freeman, F. "Oxidation by Chromium(VI) Compounds" In *Organic Syntheses by Oxidation with Metal Compounds*; Mijs, W. J.; de Jonge, C. R. H. I., Ed.; Plenum Press: New York, 1986; pp 41–118.

(47) Lee, S.; Fuchs, P. L. *Org. Lett.* **2004**, *6*, 1437.

(48) Wang, J.; Ma, A.; Ma, D. *Org. Lett.* **2008**, *10*, 5425.

(49) Nicolaou, K. C.; Sarlah, D.; Shaw, D. M. *Angew. Chemie Int. Ed.* **2007**, *46*, 4708.

(50) Daub, M. E.; Prudhomme, J.; Le Roch, K.; Vanderwal, C. D. *J. Am. Chem. Soc.* **2015**, *137*, 4912.

(51) Franzén, J.; Marigo, M.; Fielenbach, D.; Wabnitz, T. C.; Kjærsgaard, A.; Jørgensen, K. A.

J. Am. Chem. Soc. **2005**, *127*, 18296.

(52) Stevens, R. V.; Albizati, K. F. *J. Org. Chem.* **1985**, *50*, 632.

(53) Siegel, C.; Gordon, P. M.; Uliss, D. B.; Handrick, G. R.; Dalzell, H. C.; Razdan, R. K. *J. Org. Chem.* **1991**, *56*, 6865.

(54) Weidmann, B.; Seebach, D. *Angew. Chemie Int. Ed.* **1983**, *22*, 31.

(55) Reetz, M. T.; Haning, H.; Stanchev, S. *Tetrahedron Lett.* **1992**, *33*, 6963.

(56) Reetz, M. T. *Top. Curr. Chem.* **1982**, *106*, 1.

(57) Ashby, E. C.; Laemmle, J. T. *Chem. Rev.* **1975**, *75* (4), 521.

(58) Francisco, C. G.; Freire, R.; Rodríguez, M. S.; Suárez, E. *Tetrahedron Lett.* **1987**, *28*, 3397.

(59) Suginome, H.; Yamada, S. *J. Org. Chem.* **1985**, *50*, 2489.

(60) Love, B. E.; Jones, E. G. *J. Org. Chem.* **1999**, *64*, 3755.

(61) An ungreased joint led to a decreased yield of more than 20%. .

(62) Miyaoka, H.; Okubo, Y.; Muroi, M.; Mitome, H.; Kawashima, E. *Chem. Lett.* **2011**, *40*, 246.

(63) Enders, D.; Kipphardt, H.; Gerdes, P.; Breña-Valle, L. J.; Bhushan, V. *Bull. Soc. Chim. Belg.* **1988**, *97*, 693.

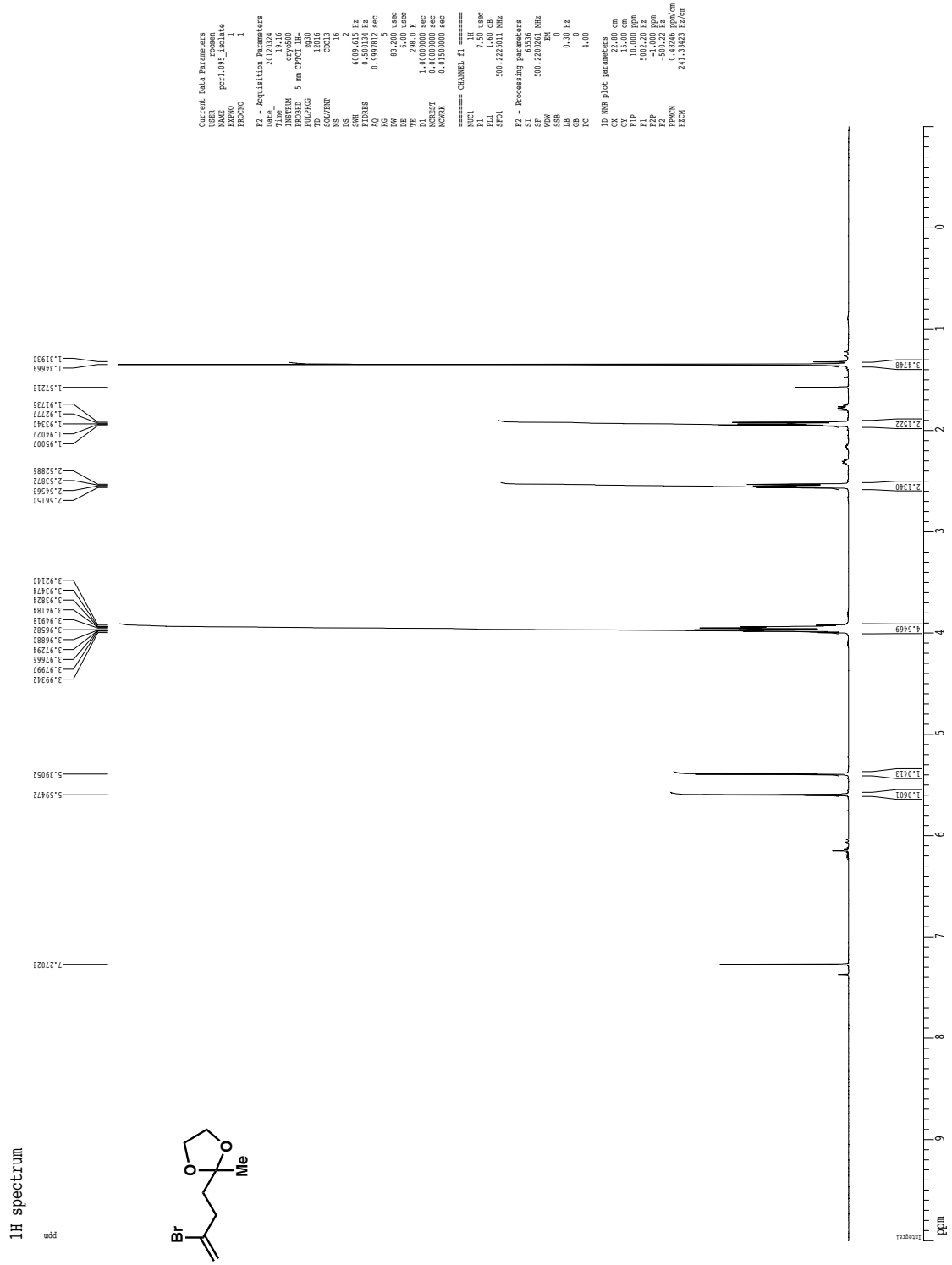
(64) Wang, J.; Ma, A.; Ma, D. *Org. Lett.* **2008**, *10*, 5425.

(65) Siegel, C.; Gordon, P. M.; Uliss, D. B.; Handrick, G. R.; Dalzell, H. C.; Razdan, R. K. *J. Org. Chem.* **1991**, *56*, 6865.

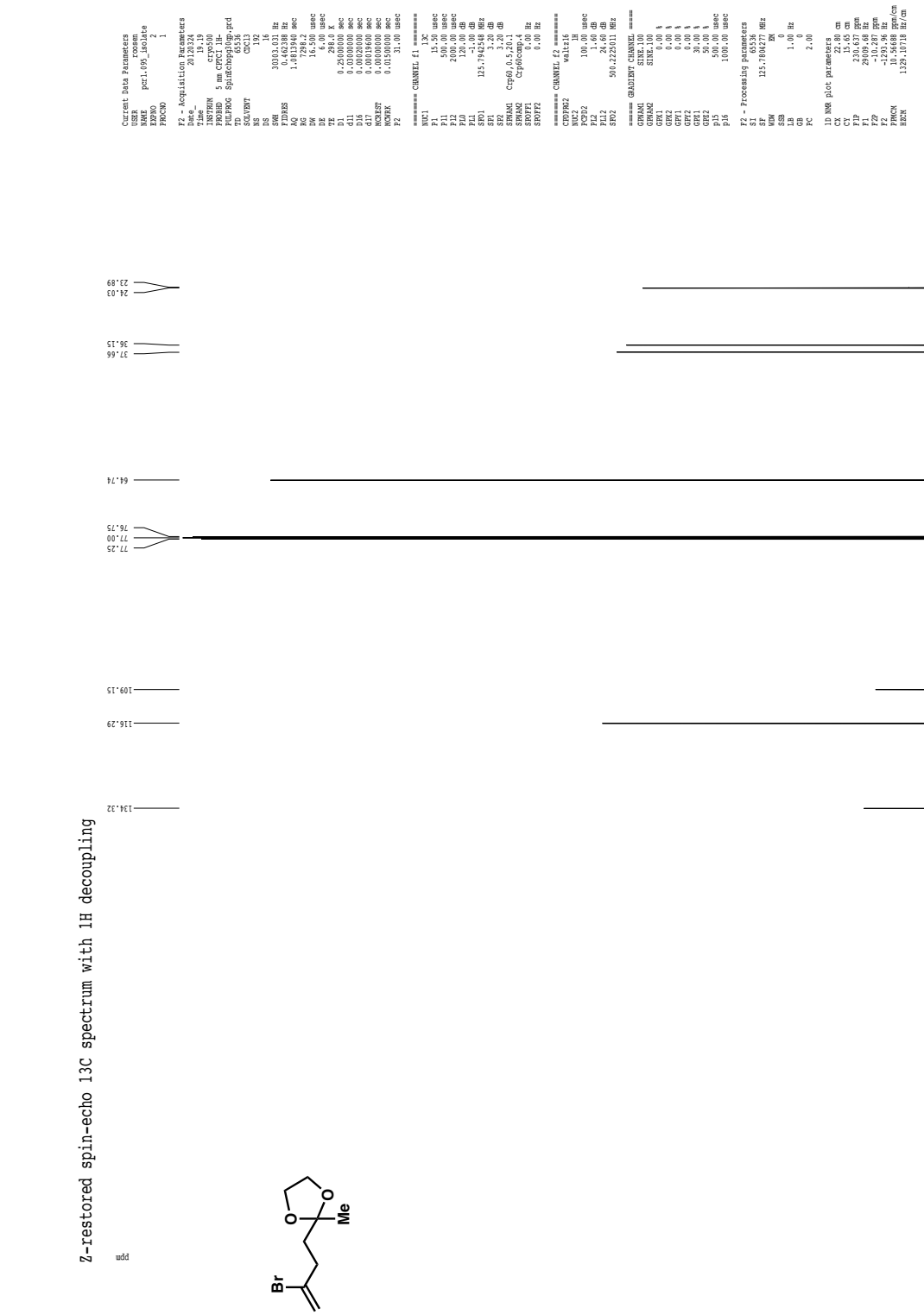
(66) Stevens, R. V; Albizati, K. F. *J. Org. Chem.* **1985**, *50*, 632.

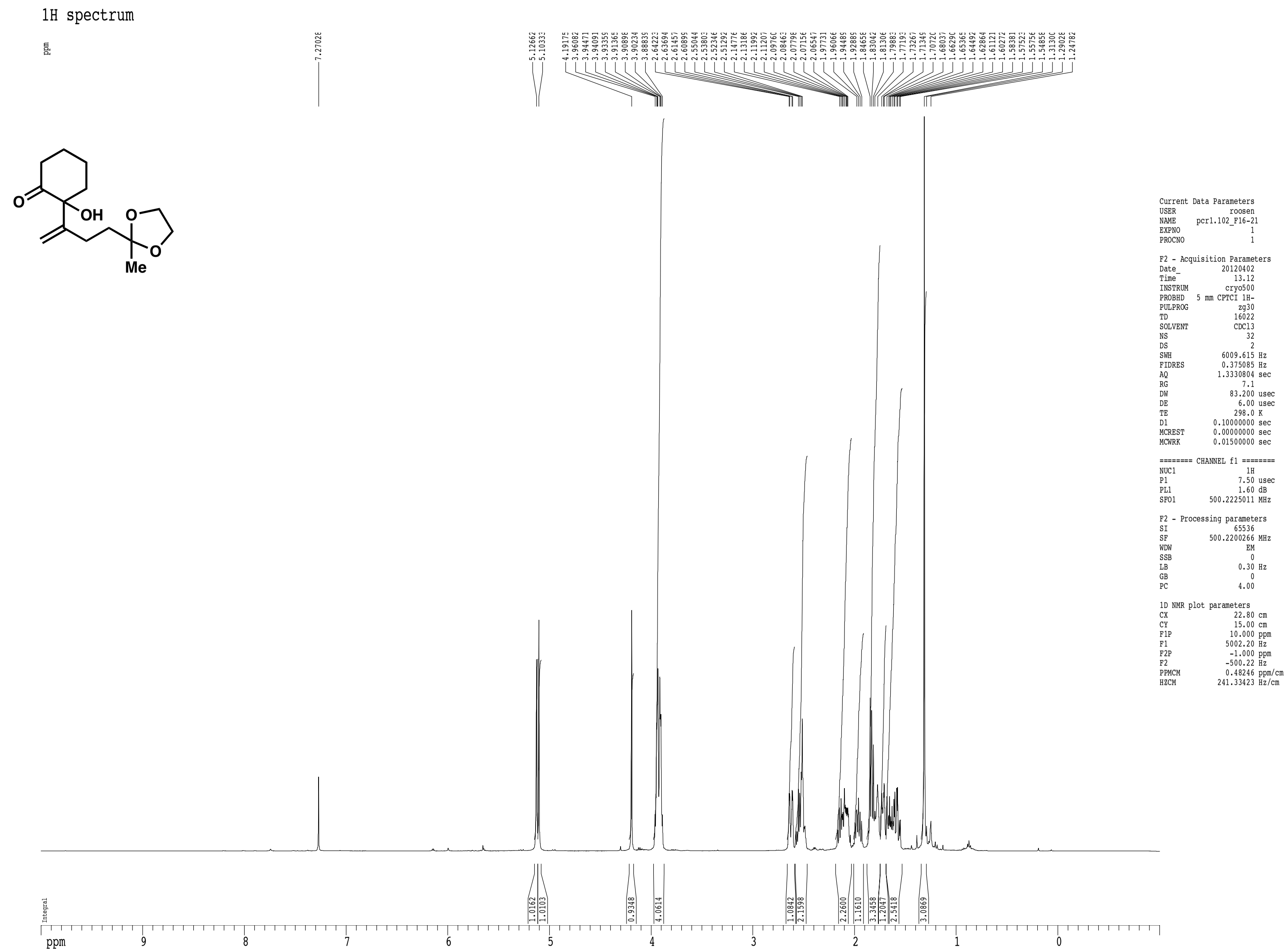
(67) Sato, T.; Gotoh, Y.; Watanabe, M.; Fujisawa, T. *Chem. Lett.* **1983**, 1533.

APPENDIX A: NMR Data

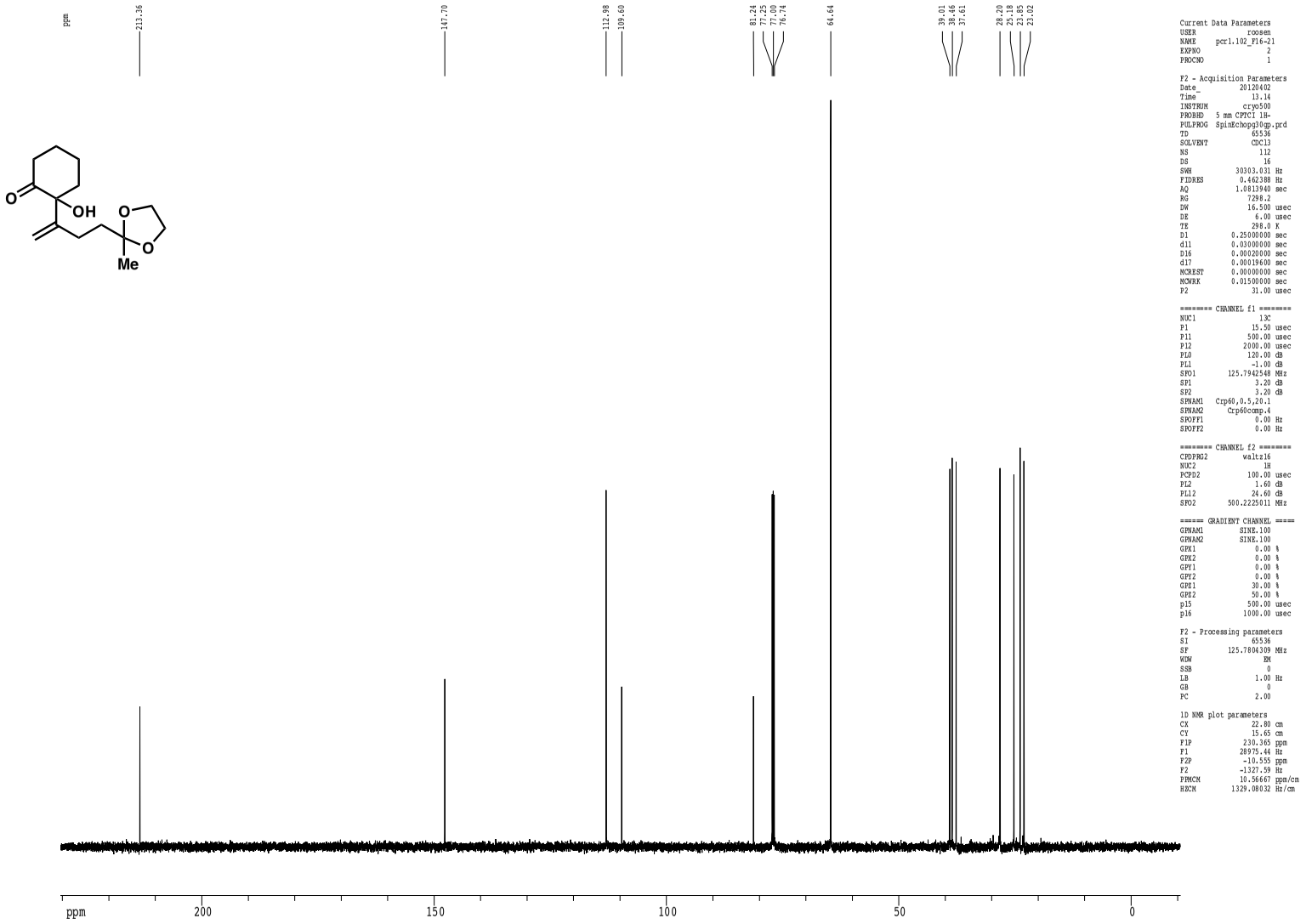


Z-restored spin-echo 13C spectrum with 1H decoupling




1H spectrum
ppm
7.2702
5.1266
5.1033
4.1917
3.9608
3.9447
3.9409
3.9335
3.9136
3.9089
3.9023
3.8883
2.6422
2.6369
2.6145
2.6089
2.5504
2.5380
2.5234
2.5129
2.1477
2.1318
2.1199
2.1120
2.0976
2.0846
2.0779
2.0715
2.0654
1.9773
1.9606
1.9448
1.9288
1.8465
1.8304
1.8130
1.7988
1.7719
1.7326
1.7134
1.7072
1.6803
1.6629
1.6536
1.6449
1.6286
1.6112
1.6027
1.5838
1.5752
1.5575
1.5485
1.3130
1.2902
1.2478
O
OH
O
O
Me
Current Data Parameters
USER roosen
NAME pcr1.102_F16-21
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20120402
Time 13.12
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 16022
SOLVENT CDCl3
NS 32
DS 2
SWH 6009.615 Hz
FIDRES 0.375085 Hz
AQ 1.3330804 sec
RG 7.1
DW 83.200 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 7.50 usec
PL1 1.60 dB
SFO1 500.2225011 MHz
F2 - Processing parameters
SI 65536
SF 500.2200266 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00
1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 10.000 ppm
F1 5002.20 Hz
F2P -1.000 ppm
F2 -500.22 Hz
PPMCM 0.48246 ppm/cm
HZCM 241.33423 Hz/cm
Integral
1.0162
1.0103
0.9348
4.0614
1.0842
2.1598
2.2600
1.1610
3.3458
1.2047
2.5418
3.0869
ppm
9
8
7
6
5
4
3
2
1
0

Z-restored spin-echo 13C spectrum with 1H decoupling



Current Data Parameters
USER roosen
NAME pcr1.102_F16-21
EXPNO 2
PROCNO 1

F2 - Acquisition Parameters
Date_ 20120402
Time 13.14
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG SpinEchopg30gp.prd
TD 65536
SOLVENT CDCl3
NS 112
DS 16
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0813940 sec
RG 7298.2
DW 16.500 usec
DE 6.00 usec
TE 298.0 K
D1 0.25000000 sec
d11 0.03000000 sec
D16 0.00020000 sec
d17 0.00019600 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
P2 31.00 usec

======= CHANNEL f1 =======
NUC1 13C
P1 15.50 usec
P11 500.00 usec
P12 2000.00 usec
PL0 120.00 dB
PL1 -1.00 dB
SFO1 125.7942548 MHz
SP1 3.20 dB
SP2 3.20 dB
SPNAM1 Crp60,0.5,20.1
SPNAM2 Crp60comp.4
SFOFF1 0.00 Hz
SFOFF2 0.00 Hz

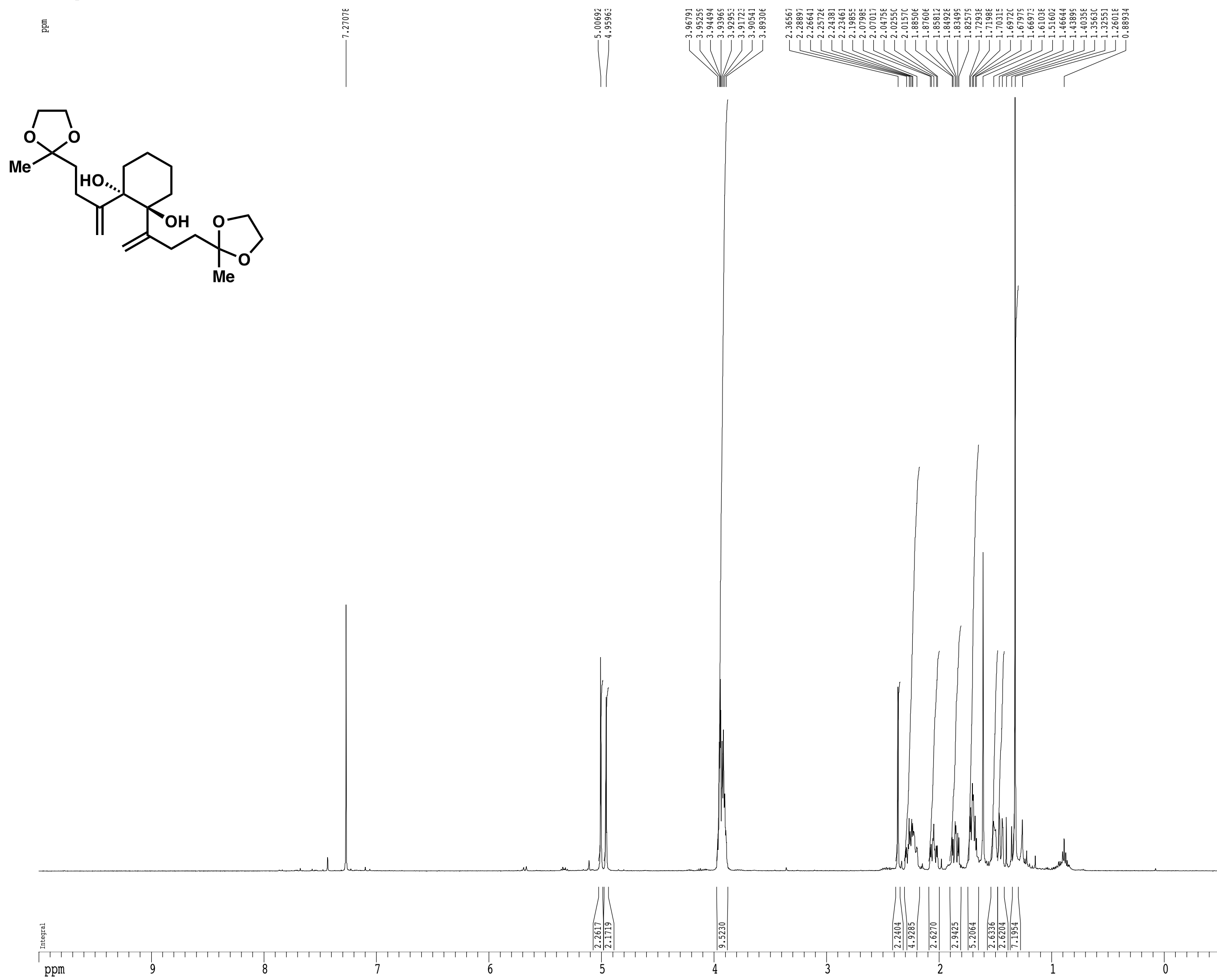
======= CHANNEL f2 =======
CPDPRG2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 1.60 dB
PL12 24.60 dB
SFO2 500.2225011 MHz

===== GRADIENT CHANNEL ====
GPNAM1 SINE.100
GPNAM2 SINE.100
GPX1 0.00 %
GPX2 0.00 %
GPY1 0.00 %
GPY2 0.00 %
GPZ1 30.00 %
GPZ2 50.00 %
p15 500.00 usec
p16 1000.00 usec

F2 - Processing parameters
SI 65536
SF 125.7804309 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00

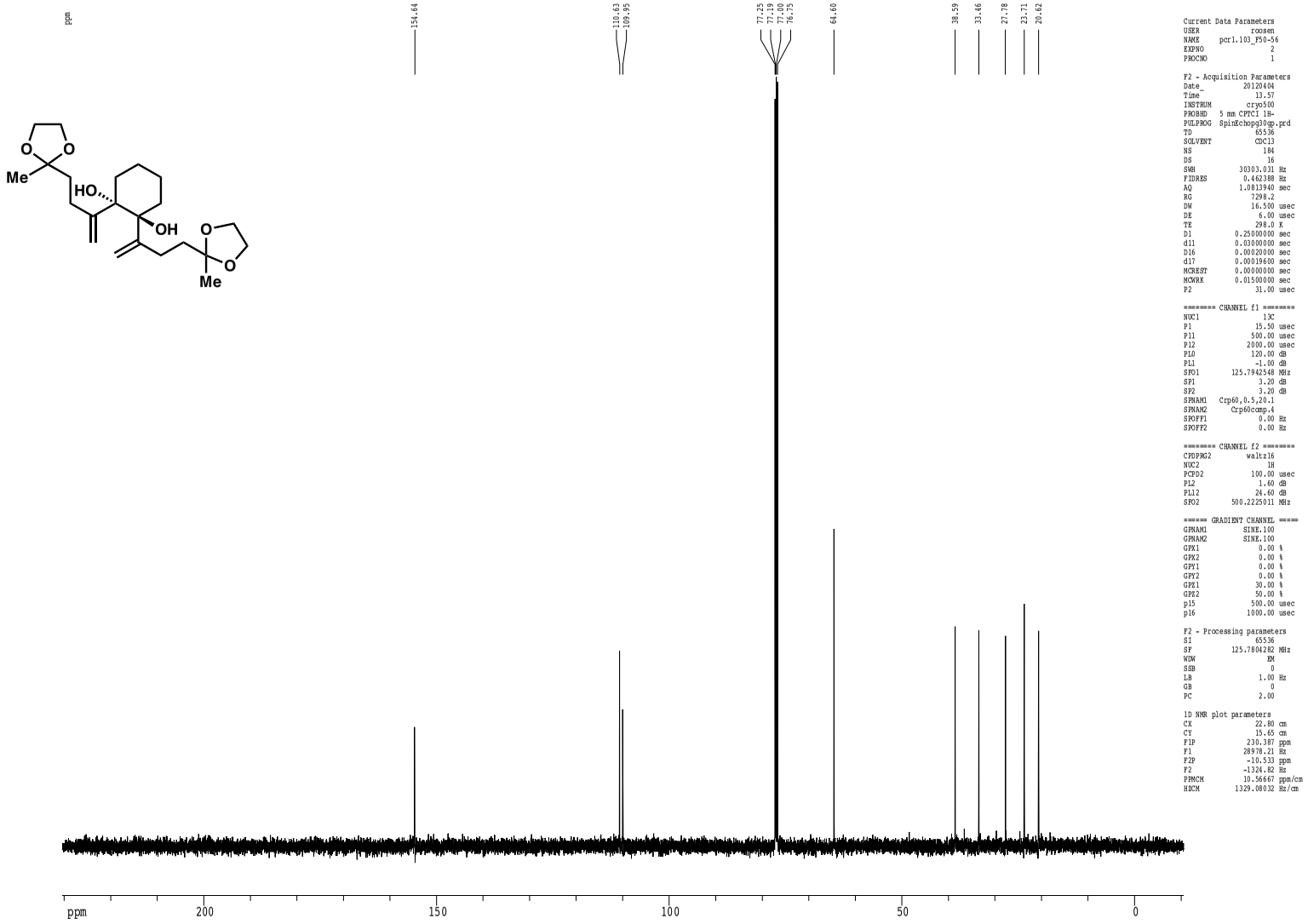
1D NMR plot parameters
CX 22.80 cm
CY 15.65 cm
F1P 230.365 ppm
F1 28975.44 Hz
F2P -10.555 ppm
F2 -1327.59 Hz
PPMCM 10.56667 ppm/cm
HZCM 1329.08032 Hz/cm

1H spectrum

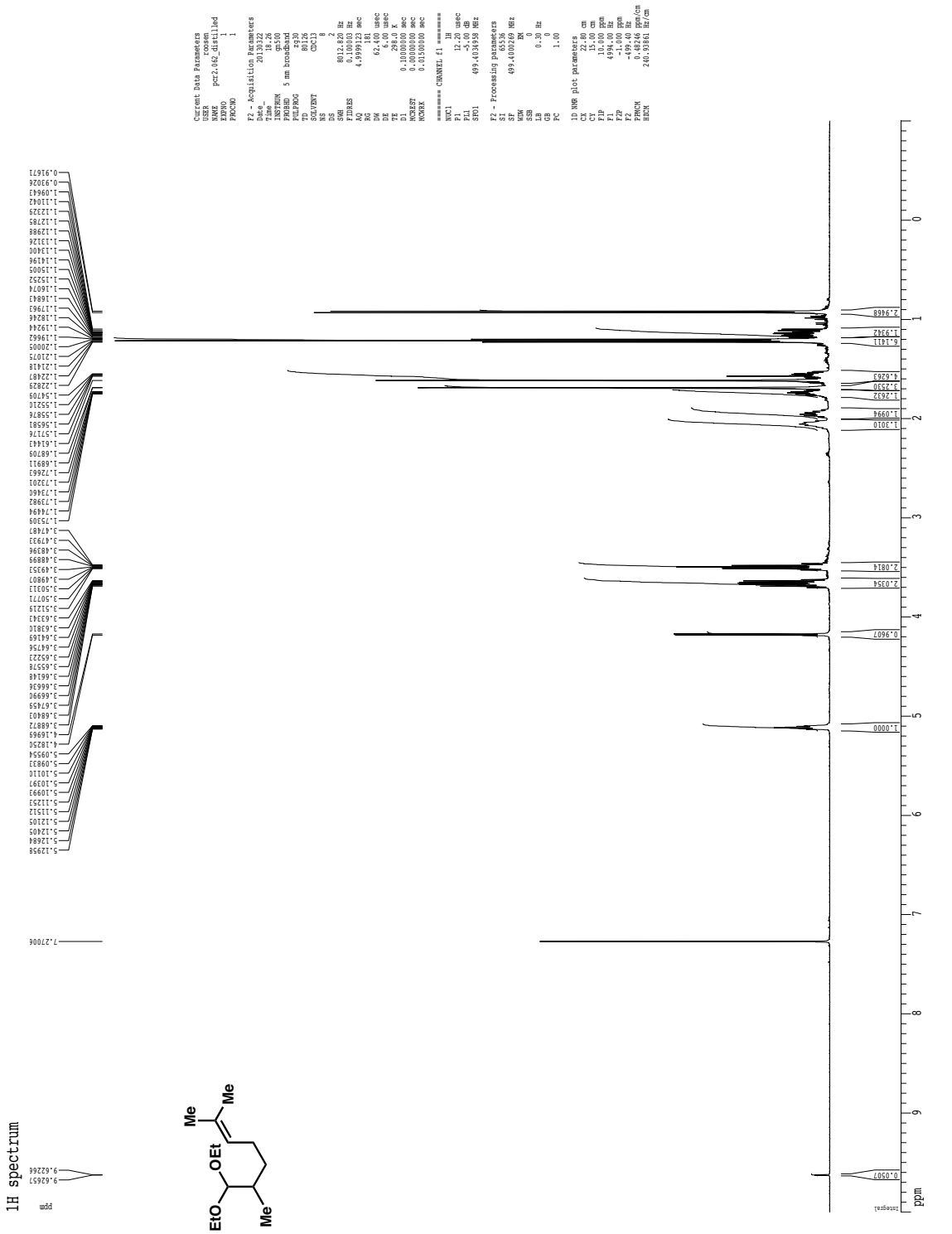


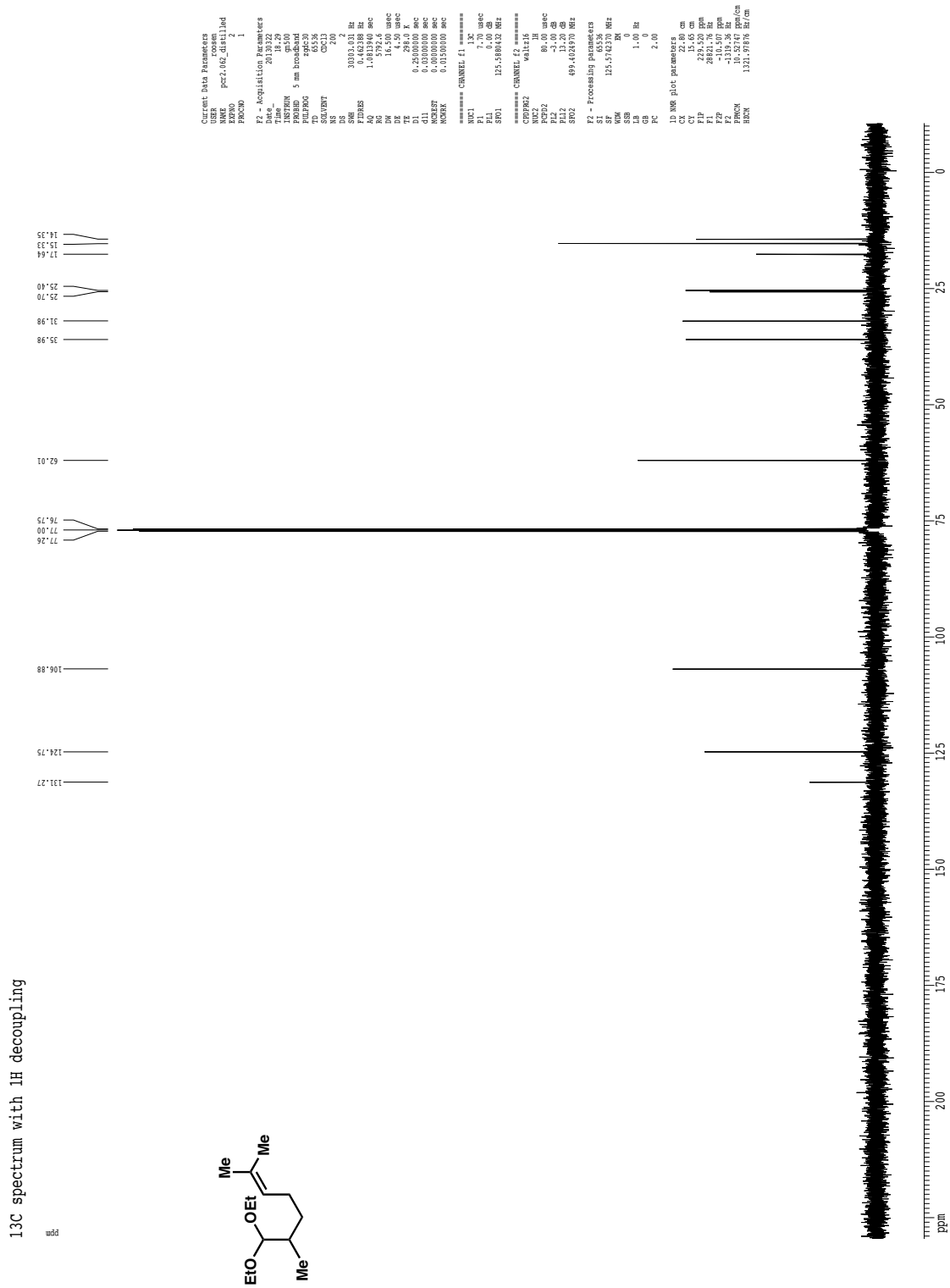

```
Current Data Parameters
USER        roosen
NAME        pcr1.103_F50-56
EXPNO       1
PROCNO      1

F2 - Acquisition Parameters
Date_       20120404
Time        13.55
INSTRUM     cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG     zg30
TD          16022
SOLVENT     CDCl3
NS          1
DS          0
SWH         6009.615 Hz
FIDRES      0.375085 Hz
AQ          1.3330804 sec
RG          71.8
DW          83.200 usec
DE          6.00 usec
TE          298.0 K
D1          0.10000000 sec
MCREST      0.00000000 sec
MCWRK       0.01500000 sec

======== CHANNEL f1 ========
NUC1        1H
P1          7.50 usec
PL1         1.60 dB
SFO1        500.2225011 MHz

F2 - Processing parameters
SI          65536
SF          500.2200267 MHz
WDW         EM
SSB         0
LB          0.30 Hz
GB          0
PC          4.00

1D NMR plot parameters
CX          22.80 cm
CY          15.00 cm
F1P         10.000 ppm
F1          5002.20 Hz
F2P         -0.500 ppm
F2          -250.11 Hz
PPMCM       0.46053 ppm/cm
HZCM        230.36450 Hz/cm
```

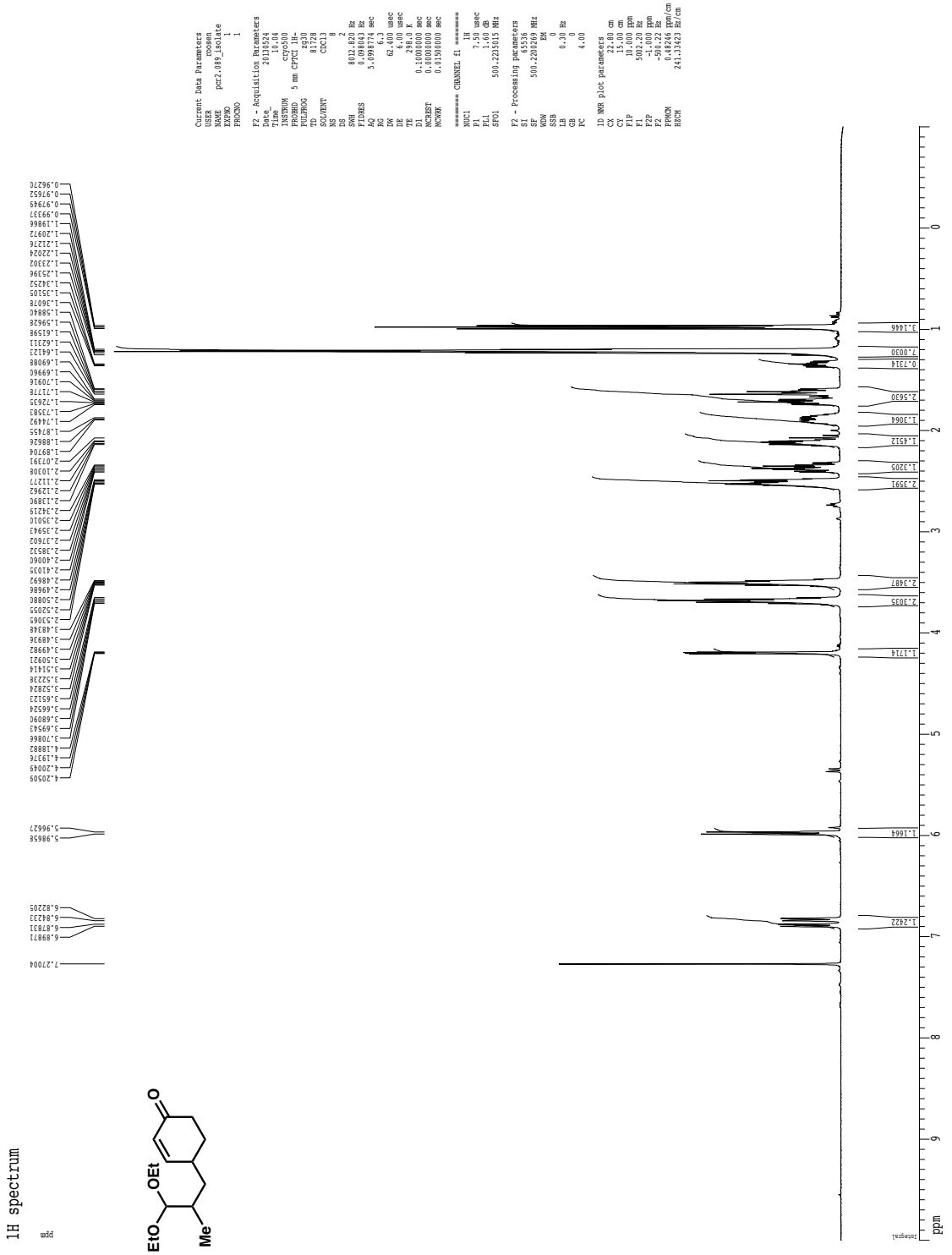
Z-restored spin-echo 13C spectrum with 1H decoupling



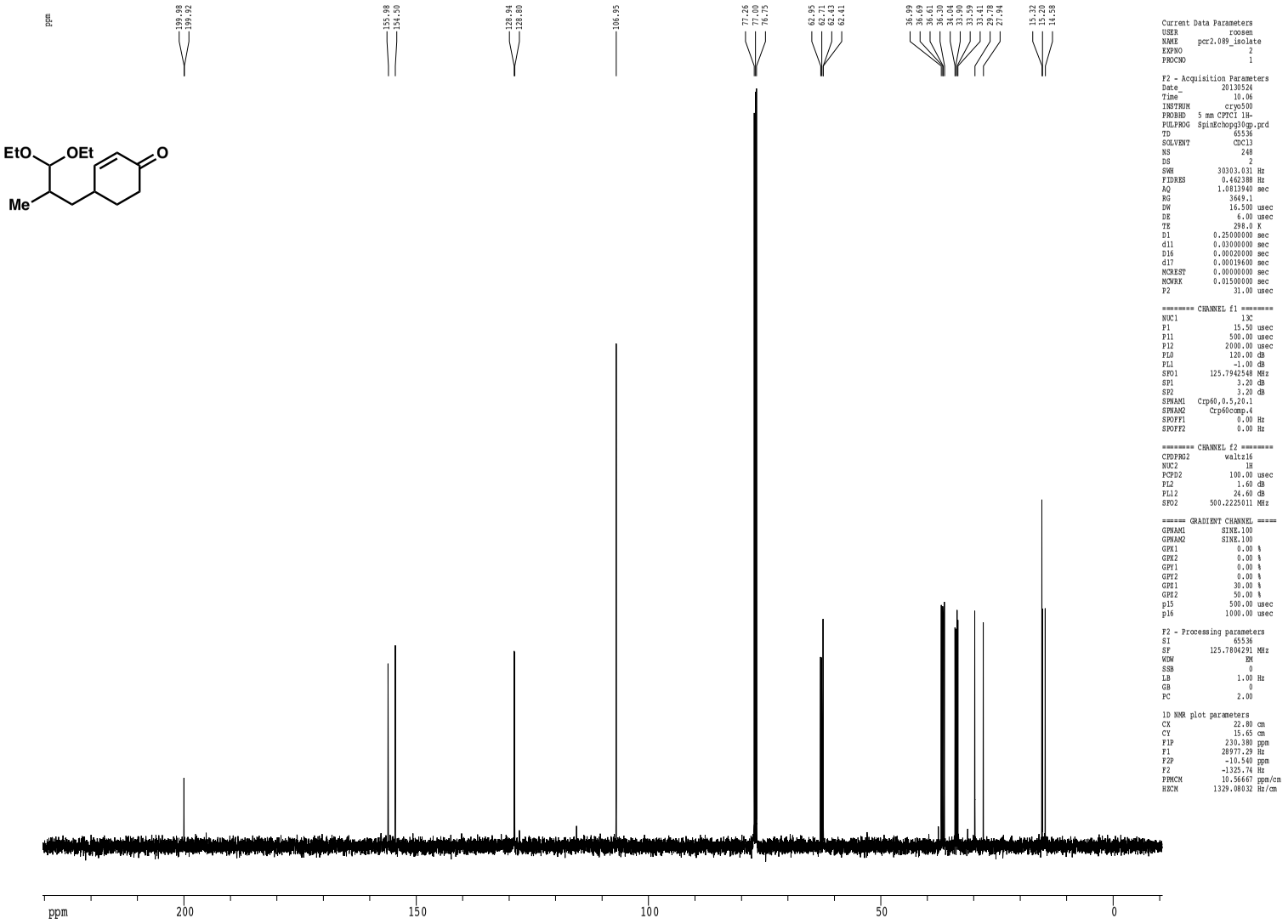

```
Current Data Parameters
USER                 roosen
NAME       pcr1.103_P50-56
EXPNO                     2
PROCNO                    1

F2 - Acquisition Parameters
Date_             20120404
Time                 13.57
INSTRUM           cryo500
PROBHD    5 mm CPTCI 1H-
PULPROG   SpinEchopg30gp.prd
TD                   65536
SOLVENT              CDCl3
NS                     184
DS                      16
SWH              30303.031 Hz
FIDRES               0.462388 Hz
AQ                1.0813940 sec
RG                   7298.2
DW                  16.500 usec
DE                   6.00 usec
TE                  298.0 K
D1              0.25000000 sec
d11             0.03000000 sec
D16             0.00020000 sec
d17             0.00019600 sec
MCREST          0.00000000 sec
MCWRK           0.01500000 sec
P2                  31.00 usec

======= CHANNEL f1 =======
NUC1                  13C
P1                  15.50 usec
P11                500.00 usec
P12               2000.00 usec
PL0                120.00 dB
PL1                 -1.00 dB
SFO1          125.7942548 MHz
SP1                 3.20 dB
SP2                 3.20 dB
SPNAM1    Crp60,0.5,20.1
SPNAM2       Crp60comp.4
SFOFF1               0.00 Hz
SFOFF2               0.00 Hz

======= CHANNEL f2 =======
CPDPRG2           waltz16
NUC2                  1H
PCPD2              100.00 usec
PL2                  1.60 dB
PL12                24.60 dB
SFO2         500.2225011 MHz

===== GRADIENT CHANNEL ====
GPNAM1           SINE.100
GPNAM2           SINE.100
GPX1                 0.00 %
GPX2                 0.00 %
GPY1                 0.00 %
GPY2                 0.00 %
GPZ1                30.00 %
GPZ2                50.00 %
p15                500.00 usec
p16               1000.00 usec

F2 - Processing parameters
SI                   65536
SF            125.7804282 MHz
WDW                    EM
SSB                     0
LB                   1.00 Hz
GB                      0
PC                   2.00

1D NMR plot parameters
CX                  22.80 cm
CY                  15.65 cm
F1P               230.387 ppm
F1                28978.21 Hz
F2P               -10.533 ppm
F2               -1324.82 Hz
PPMCM             10.56667 ppm/cm
HZCM          1329.08032 Hz/cm
```


1H spectrum
ppm
Me
Me
OEt
EtO
Me

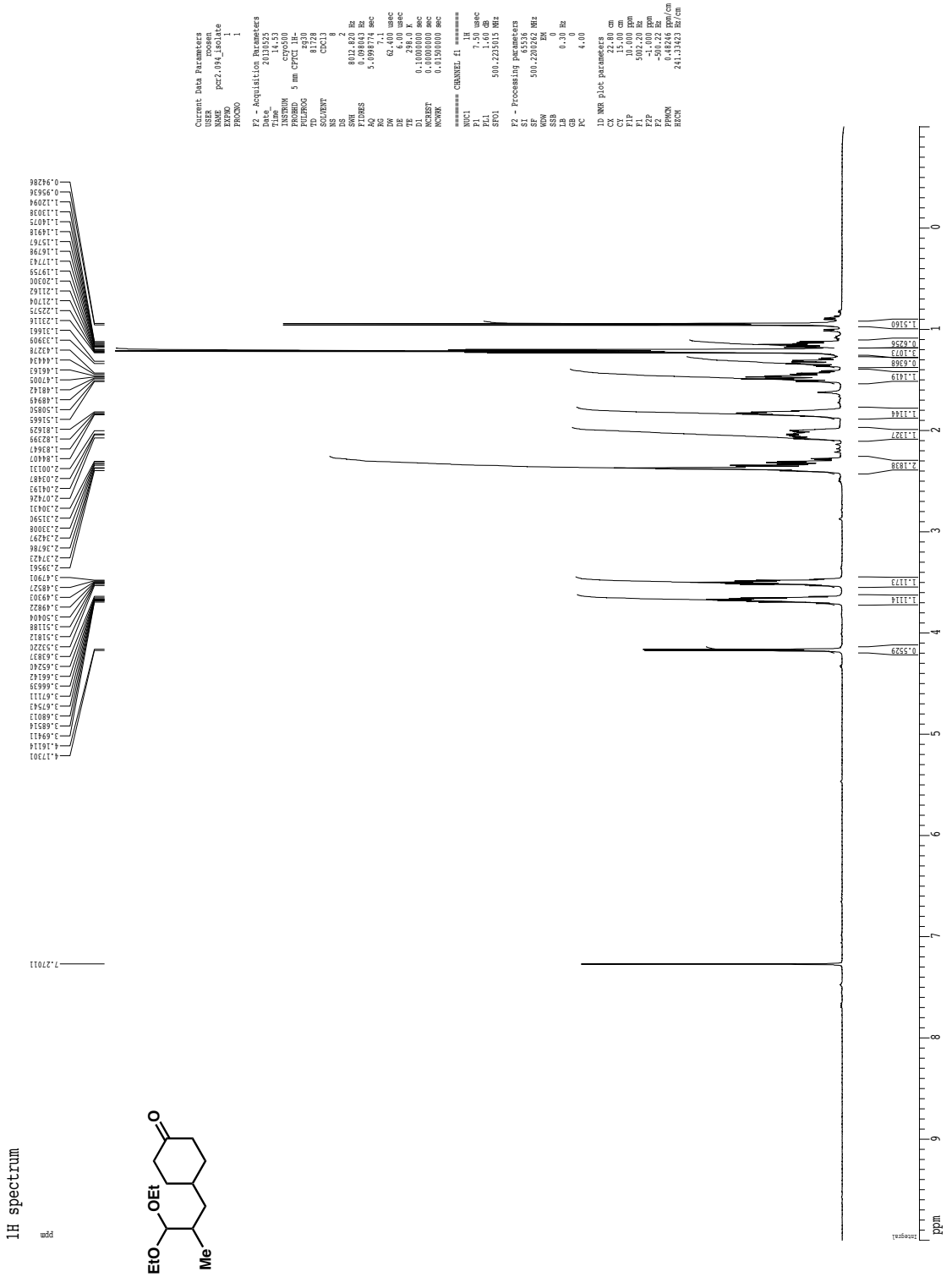

13C spectrum with 1H decoupling
ppm
Me
OEt
Me
EtO
Me
14.35
15.33
17.64
25.40
25.70
31.98
35.98
62.01
76.75
77.00
77.26
106.88
124.75
131.27
0
25
50
75
100
125
150
175
200
ppm

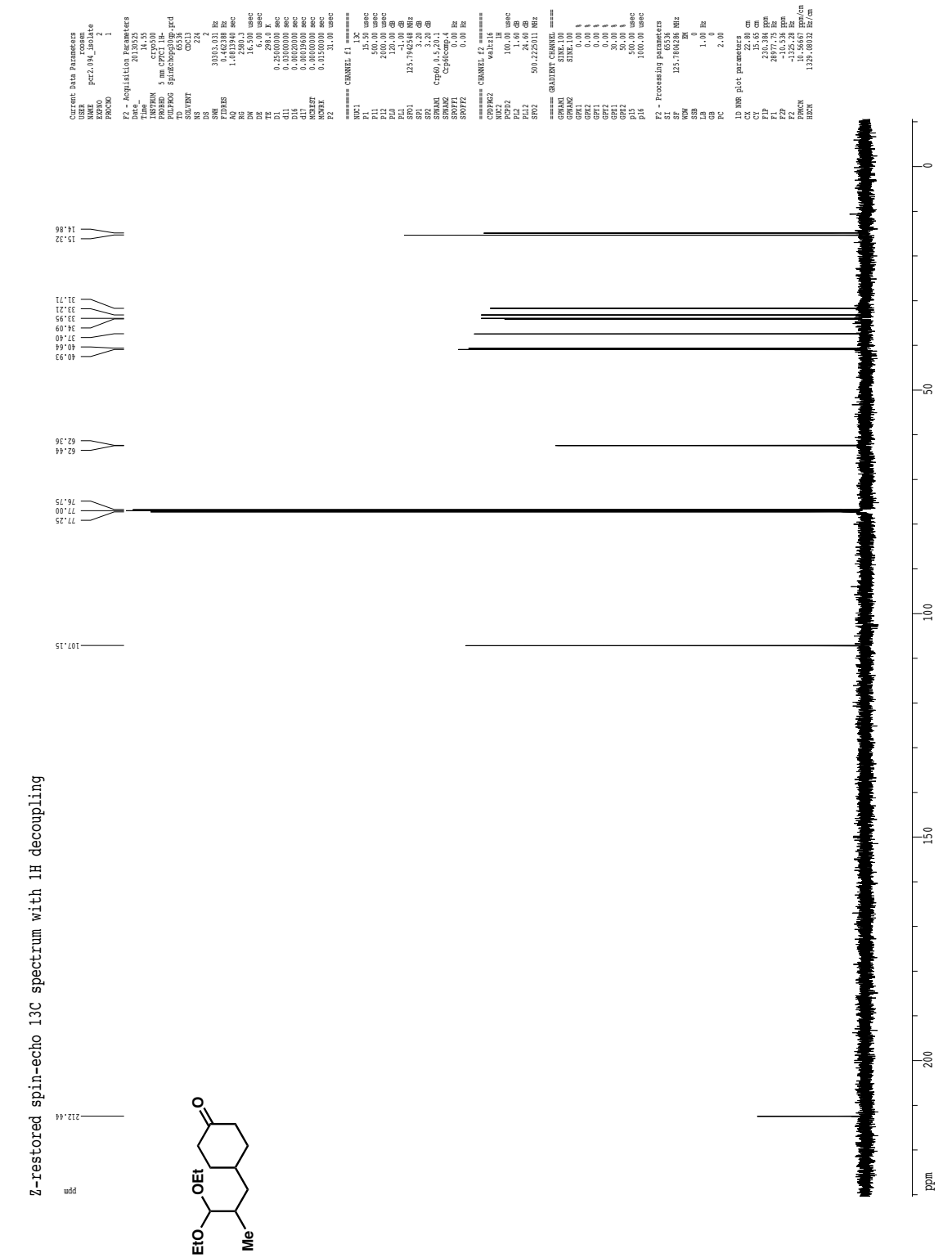

1H spectrum
ppm
EtO
OEt
Me
Current Data Parameters
F2 - Acquisition Parameters
F2 - Processing parameters
1D NMR plot parameters
======= CHANNEL f1 =======
ppm

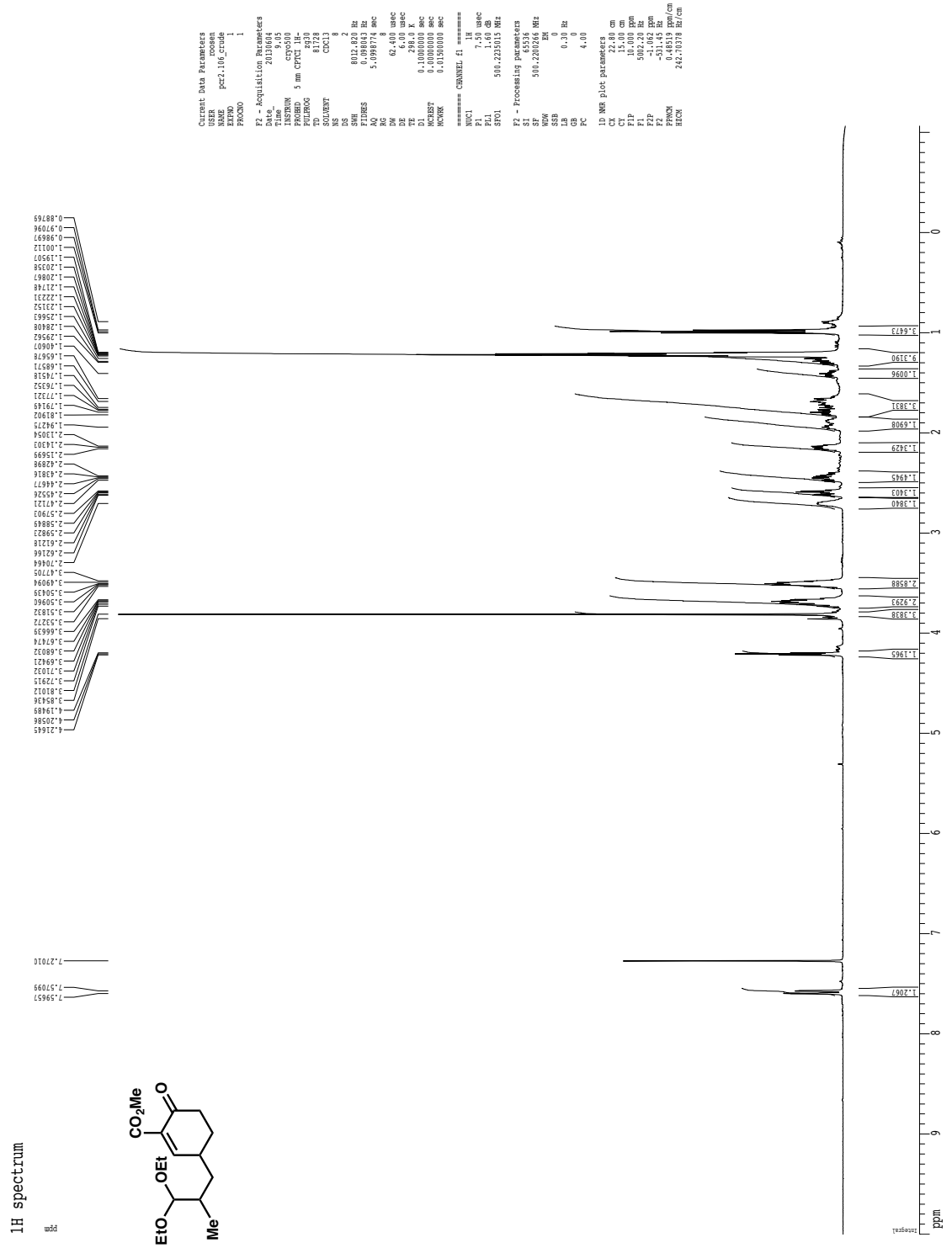
Z-restored spin-echo 13C spectrum with 1H decoupling



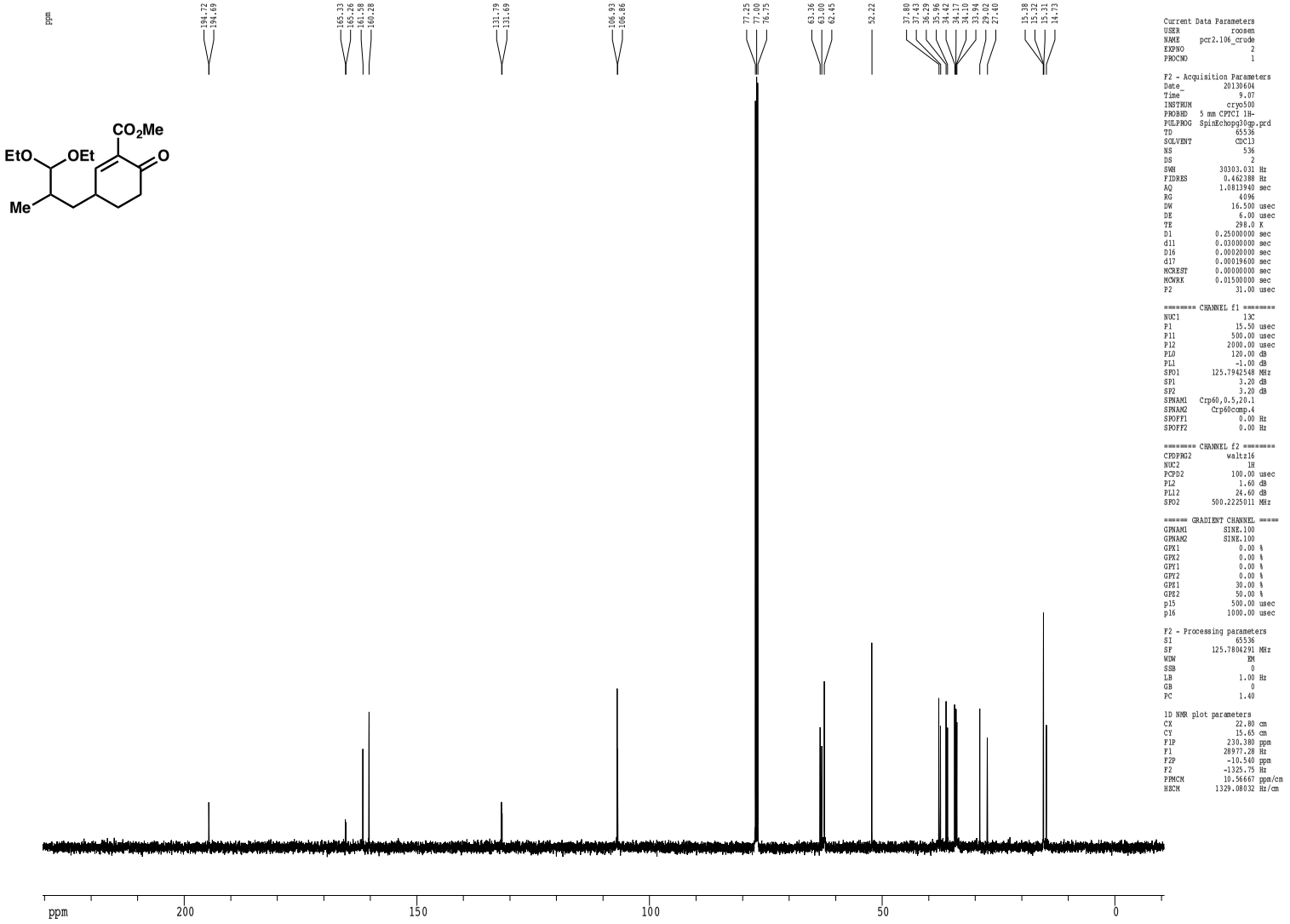

```
Current Data Parameters
USER                roosen
NAME          pcr2.089_isolate
EXPNO                    2
PROCNO                   1

F2 - Acquisition Parameters
Date_              20130524
Time                 10.06
INSTRUM            cryo500
PROBHD    5 mm CPTCI 1H-
PULPROG   SpinEchopg30gp.prd
TD                   65536
SOLVENT              CDCl3
NS                     248
DS                       2
SWH              30303.031 Hz
FIDRES           0.462388 Hz
AQ               1.0813940 sec
RG                  3649.1
DW                  16.500 usec
DE                   6.00 usec
TE                  298.0 K
D1             0.25000000 sec
d11            0.03000000 sec
D16            0.00020000 sec
d17            0.00019600 sec
MCREST         0.00000000 sec
MCWRK          0.01500000 sec
P2                  31.00 usec

======= CHANNEL f1 =======
NUC1                  13C
P1                  15.50 usec
P11                500.00 usec
P12               2000.00 usec
PL0                120.00 dB
PL1                 -1.00 dB
SFO1          125.7942548 MHz
SP1                  3.20 dB
SP2                  3.20 dB
SPNAM1    Crp60,0.5,20.1
SPNAM2       Crp60comp.4
SPOFF1               0.00 Hz
SPOFF2               0.00 Hz

======= CHANNEL f2 =======
CPDPRG2           waltz16
NUC2                   1H
PCPD2              100.00 usec
PL2                  1.60 dB
PL12                24.60 dB
SFO2         500.2225011 MHz

===== GRADIENT CHANNEL ====
GPNAM1           SINE.100
GPNAM2           SINE.100
GPX1                 0.00 %
GPX2                 0.00 %
GPY1                 0.00 %
GPY2                 0.00 %
GPZ1                30.00 %
GPZ2                50.00 %
p15                500.00 usec
p16               1000.00 usec

F2 - Processing parameters
SI                   65536
SF            125.7804291 MHz
WDW                    EM
SSB                     0
LB                   1.00 Hz
GB                      0
PC                   2.00

1D NMR plot parameters
CX                  22.80 cm
CY                  15.65 cm
F1P                230.380 ppm
F1                 28977.29 Hz
F2P                -10.540 ppm
F2                 -1325.74 Hz
PPMCM              10.56667 ppm/cm
HZCM            1329.08032 Hz/cm
```


1H spectrum
ppm
EtO
OEt
Me
O
Current Data Parameters
USER ccosen
NAME pcr2.094_isolate
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20130525
Time 14.53
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 81728
SOLVENT CDCl3
NS 8
DS 2
SWH 8012.820 Hz
FIDRES 0.098043 Hz
AQ 5.0998774 sec
RG 7.1
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======= CHANNEL f1 =======
NUC1 1H
P1 7.50 usec
PL1 1.50 dB
SFO1 500.2235913 MHz
F2 - Processing parameters
SI 65536
SF 500.2200262 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00
1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 10.000 ppm
F1 5002.23 Hz
F2P -1.000 ppm
F2 -500.22 Hz
PPMCM 0.48246 ppm/cm
HZCM 241.33423 Hz/cm
7.27011
4.17301
4.16114
3.69411
3.68014
3.67643
3.66139
3.65240
3.63837
3.52220
3.51812
3.51188
3.50404
3.49822
3.49303
3.48527
3.47901
3.39561
2.37423
2.36786
2.34297
2.31594
2.30008
2.00131
2.03487
2.04197
2.07426
2.30431
2.82399
2.81629
2.84607
2.88647
2.50850
2.48949
2.48142
2.47005
2.46163
2.44434
2.43278
2.31661
2.23909
2.22575
2.21704
2.21162
2.20306
1.97959
1.97743
1.96798
1.95767
1.94918
1.94075
1.93038
1.92094
0.95636
0.94286
1.5160
0.6256
3.1073
0.6368
1.1419
1.1144
1.1327
2.1838
1.1173
1.1114
0.5529
Internal
ppm

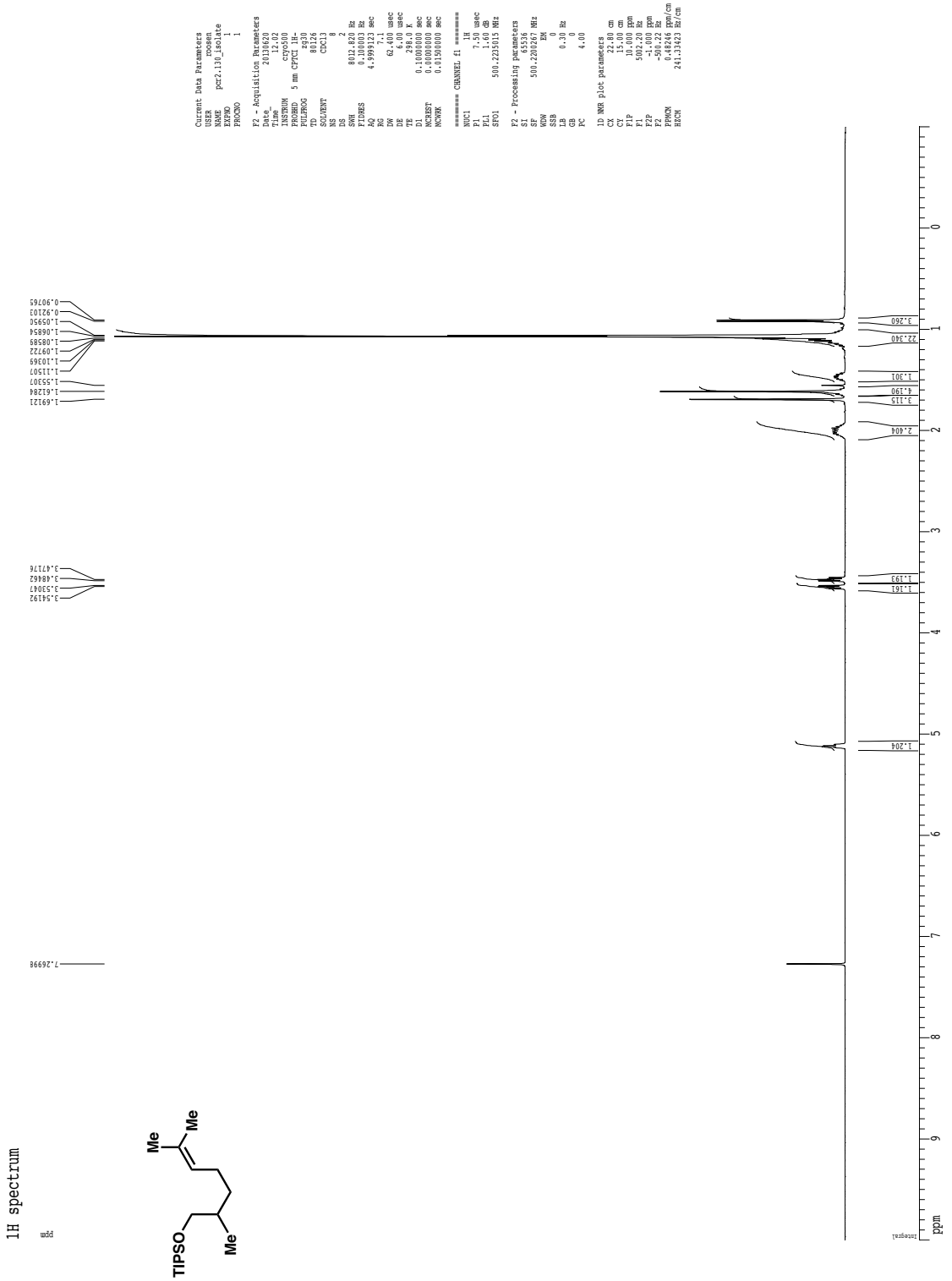

Z-restored spin-echo 13C spectrum with 1H decoupling
ppm
212.44
107.15
77.25
77.00
76.75
62.44
62.36
40.93
40.64
34.09
33.95
33.21
31.71
15.32
14.86
EtO
OEt
Me
0
50
100
150
200
ppm

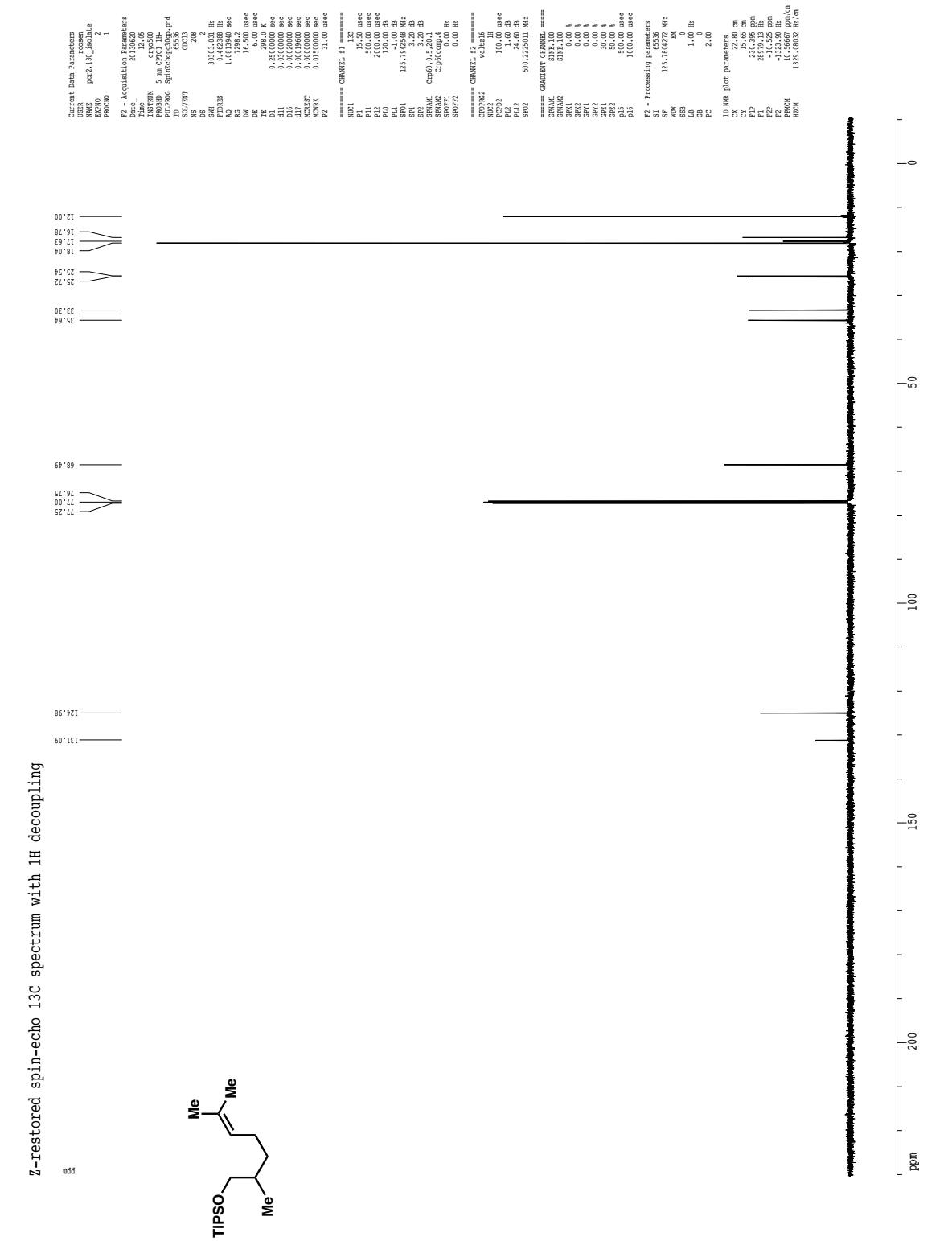

1H spectrum
ppm
CO2Me
O
OEt
EtO
Me
Current Data Parameters
USER zcosen
NAME pcr2.106_crude
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20130604
Time 9.05
INSTRUM crys500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 81728
SOLVENT CDCl3
NS 8
DS 2
SWH 8012.820 Hz
FIDRES 0.098043 Hz
AQ 5.0998774 sec
RG 64
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======= CHANNEL f1 =======
NUC1 1H
P1 7.50 usec
PL1 1.50 dB
SFO1 500.2235913 MHz
F2 - Processing parameters
SI 65536
SF 500.2200246 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00
1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 10.000 ppm
F1 5002.229 Hz
F2P -1.460 ppm
F2 -731.45 Hz
PPMCM 0.48519 ppm/cm
HZCM 242.70370 Hz/cm
7.27012
7.59957
7.57099
4.21645
4.20586
4.19489
3.85436
3.81012
3.72915
3.71032
3.69621
3.68032
3.67474
3.66639
3.52372
3.51832
3.50960
3.50439
3.49094
3.47705
2.70464
2.62166
2.61218
2.59823
2.58849
2.57903
2.47121
2.45526
2.44677
2.43816
2.42898
2.18302
2.13054
1.94275
1.81902
1.79149
1.77221
1.76352
1.74518
1.68571
1.65678
1.60607
1.59542
1.56608
1.55663
1.52152
1.52231
1.21748
1.20867
1.19507
1.00112
0.98697
0.97096
0.88769
3.64173
9.31190
1.00961
3.38311
1.69081
1.34279
1.49465
1.38603
1.38601
7.85881
7.92931
3.38381
1.19651
1.20671
ppm

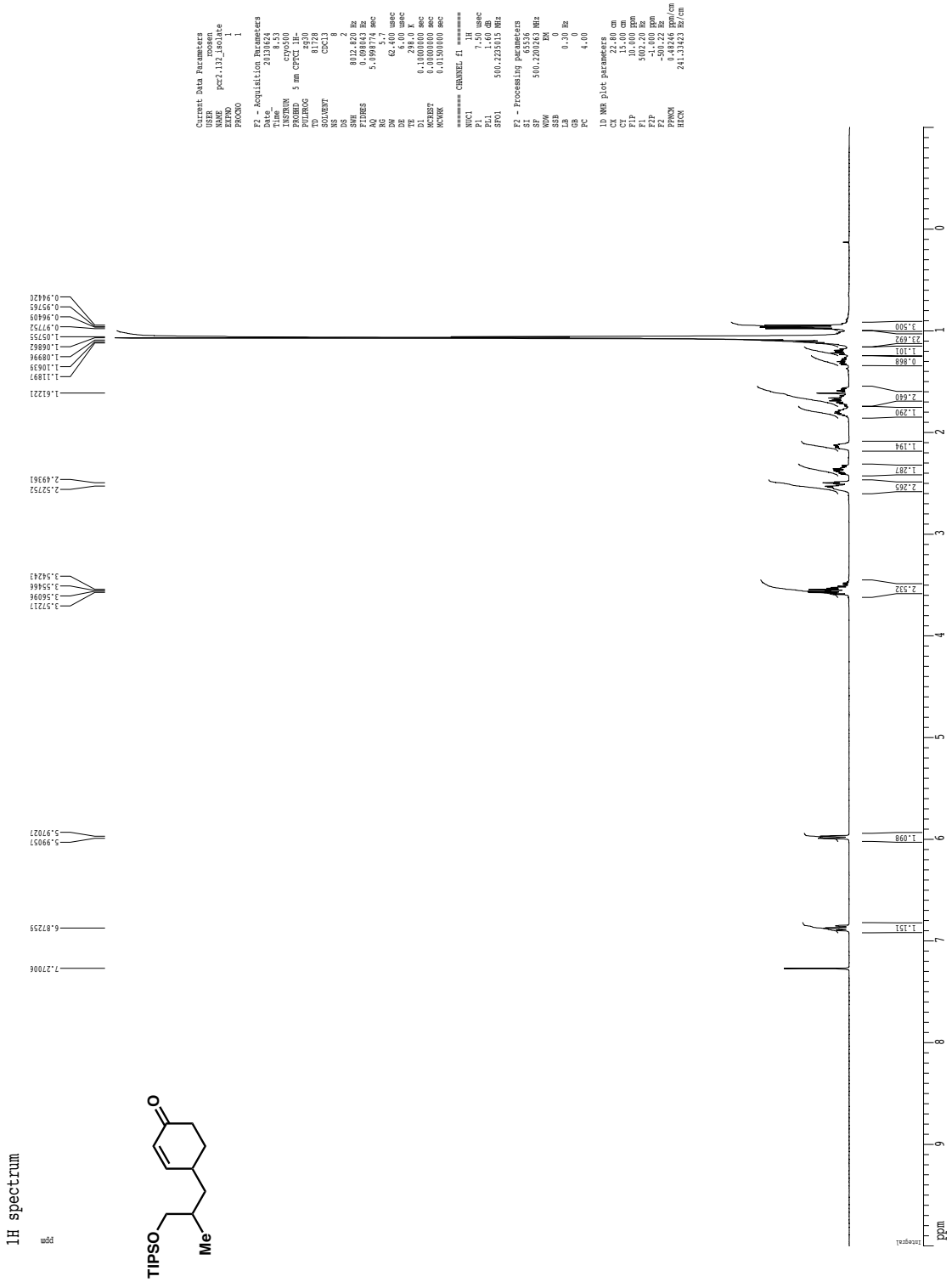
Z-restored spin-echo 13C spectrum with 1H decoupling



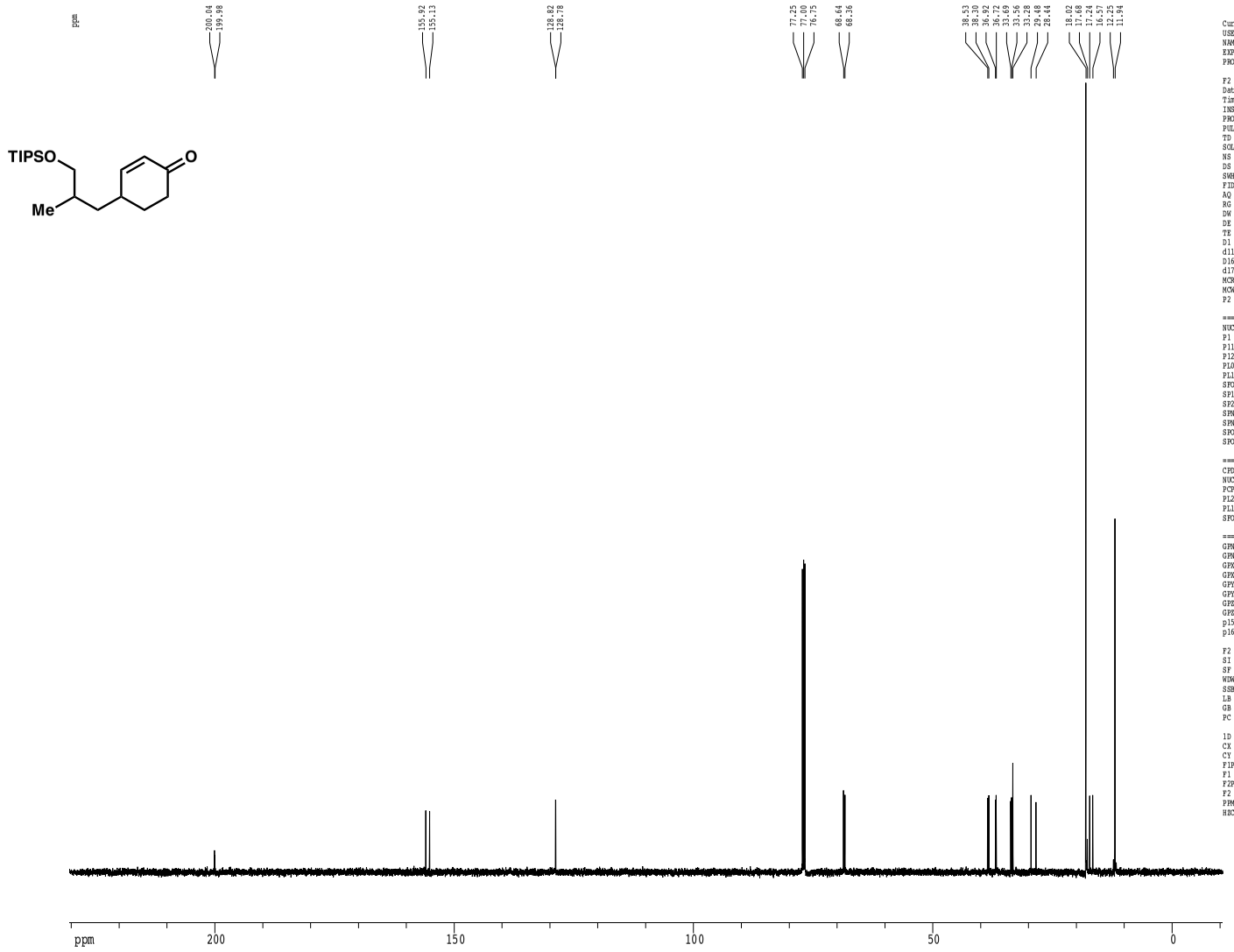

```
Current Data Parameters
USER                roosen
NAME          pcr2.106_crude
EXPNO                     2
PROCNO                    1

F2 - Acquisition Parameters
Date_              20130604
Time                   9.07
INSTRUM              cryo500
PROBHD    5 mm CPTCI 1H-
PULPROG   SpinEchopg30gp.prd
TD                    65536
SOLVENT               CDCl3
NS                      536
DS                        2
SWH               30303.031 Hz
FIDRES            0.462388 Hz
AQ                1.0813940 sec
RG                     4096
DW                  16.500 usec
DE                   6.00 usec
TE                   298.0 K
D1              0.25000000 sec
d11             0.03000000 sec
D16             0.00020000 sec
d17             0.00019600 sec
MCREST          0.00000000 sec
MCWRK           0.01500000 sec
P2                  31.00 usec

======= CHANNEL f1 =======
NUC1                   13C
P1                   15.50 usec
P11                 500.00 usec
P12                2000.00 usec
PL0                 120.00 dB
PL1                  -1.00 dB
SFO1          125.7942548 MHz
SP1                  3.20 dB
SP2                  3.20 dB
SPNAM1    Crp60,0.5,20.1
SPNAM2       Crp60comp.4
SFOFF1               0.00 Hz
SFOFF2               0.00 Hz

======= CHANNEL f2 =======
CPDPRG2           waltz16
NUC2                   1H
PCPD2               100.00 usec
PL2                  1.60 dB
PL12                24.60 dB
SFO2         500.2225011 MHz

===== GRADIENT CHANNEL ====
GPNAM1           SINE.100
GPNAM2           SINE.100
GPX1                 0.00 %
GPX2                 0.00 %
GPY1                 0.00 %
GPY2                 0.00 %
GPZ1                30.00 %
GPZ2                50.00 %
p15                500.00 usec
p16               1000.00 usec

F2 - Processing parameters
SI                    65536
SF            125.7804291 MHz
WDW                     EM
SSB                      0
LB                   1.00 Hz
GB                       0
PC                    1.40

1D NMR plot parameters
CX                   22.80 cm
CY                   15.65 cm
F1P                230.380 ppm
F1                 28977.28 Hz
F2P                -10.540 ppm
F2                 -1325.75 Hz
PPMCM             10.56667 ppm/cm
HZCM           1329.08032 Hz/cm
```


1H spectrum
ppm
TIPSO
Me
Me
Me
Current Data Parameters
USER zocosen
NAME pcr2.130_isolate
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20130620
Time 12.02
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 80126
SOLVENT CDCl3
NS 8
DS 2
SWH 8012.820 Hz
FIDRES 0.100003 Hz
AQ 4.9999123 sec
RG 7.1
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======= CHANNEL f1 =======
NUC1 1H
P1 7.50 usec
PL1 1.50 dB
SFO1 500.2235913 MHz
F2 - Processing parameters
SI 65536
SF 500.2200247 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00
1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 10.000 ppm
F1 5002.23 Hz
F2P -1.000 ppm
F2 -500.22 Hz
PPMCM 0.48246 ppm/cm
HZCM 241.33423 Hz/cm
0.90765
0.92103
1.05950
1.06854
1.08589
1.09172
1.11369
1.11507
1.55307
1.61244
1.69121
3.54192
3.53047
3.48462
3.47176
7.26998
1.204
1.161
1.193
2.464
1.301
4.190
3.115
22.340
3.260
ppm

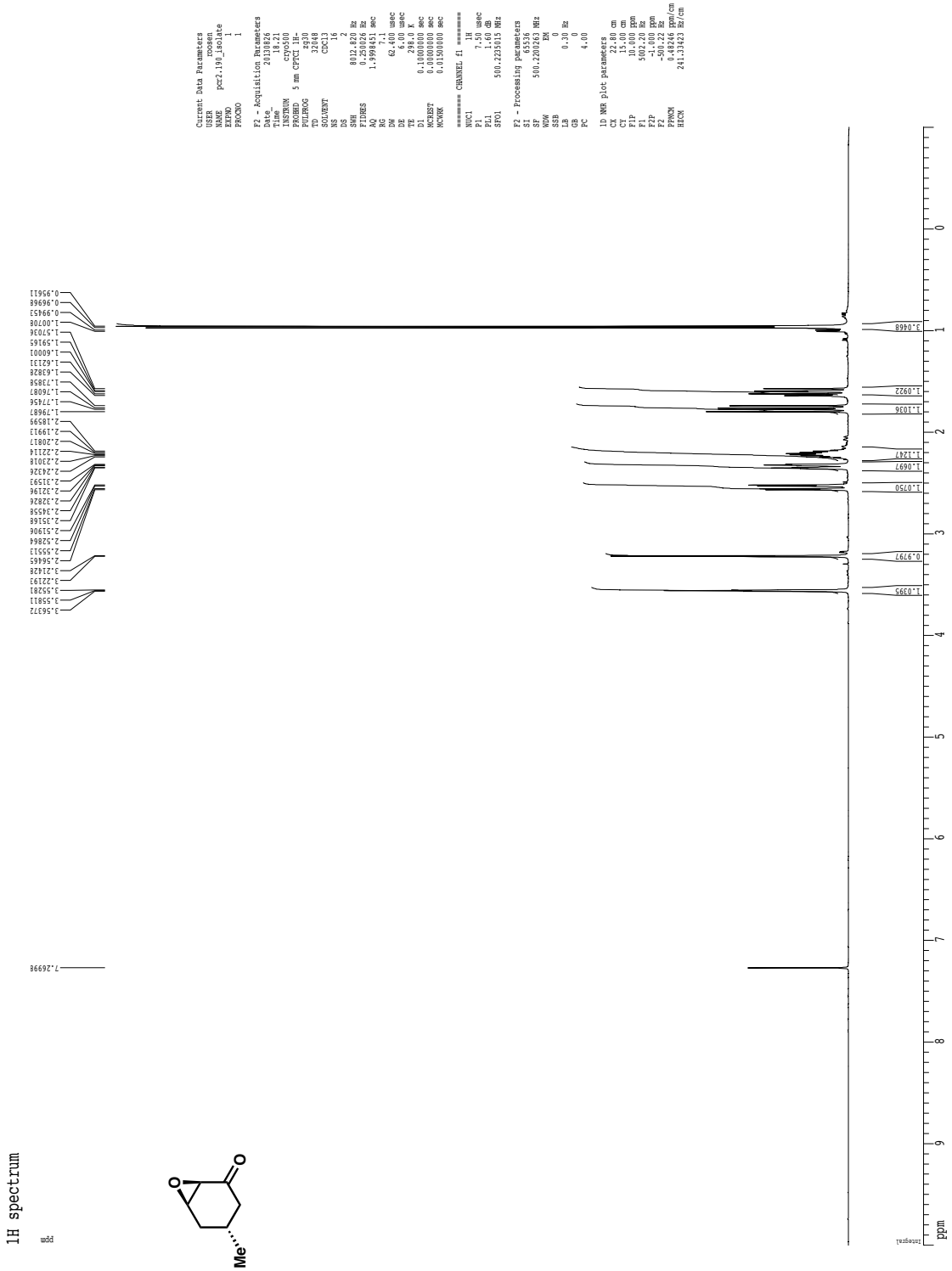

Z-restored spin-echo 13C spectrum with 1H decoupling
Me
Me
TIPSO
Me
ppm
0
50
100
150
200
131.09
124.98
77.25
77.00
76.75
68.49
35.64
33.30
25.72
25.54
18.04
17.63
16.78
12.00


1H spectrum
TIPSO
Me
Current Data Parameters
USER zcosen
NAME pcr2.132_isolate
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20130624
Time 8.53
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 81728
SOLVENT CDCl3
NS 8
DS 2
SWH 8012.820 Hz
FIDRES 0.098043 Hz
AQ 5.0998774 sec
RG 5.7
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======= CHANNEL f1 =======
NUC1 1H
P1 7.50 usec
PL1 1.50 dB
SFO1 500.2235919 MHz
F2 - Processing parameters
SI 65536
SF 500.2200262 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00
1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 10.000 ppm
F1 5002.20 Hz
F2P -1.000 ppm
F2 -500.22 Hz
PPMCM 0.48246 ppm/cm
HZCM 241.33423 Hz/cm
0.94420
0.95765
0.96409
0.97752
1.05755
1.06862
1.08996
1.10639
1.11897
1.61221
2.49361
2.52752
3.54243
3.55466
3.56096
3.57217
5.97027
5.99057
6.87259
7.27006
3.500
23.692
1.101
0.868
2.660
1.290
1.394
1.287
2.265
2.532
1.098
1.151
ppm

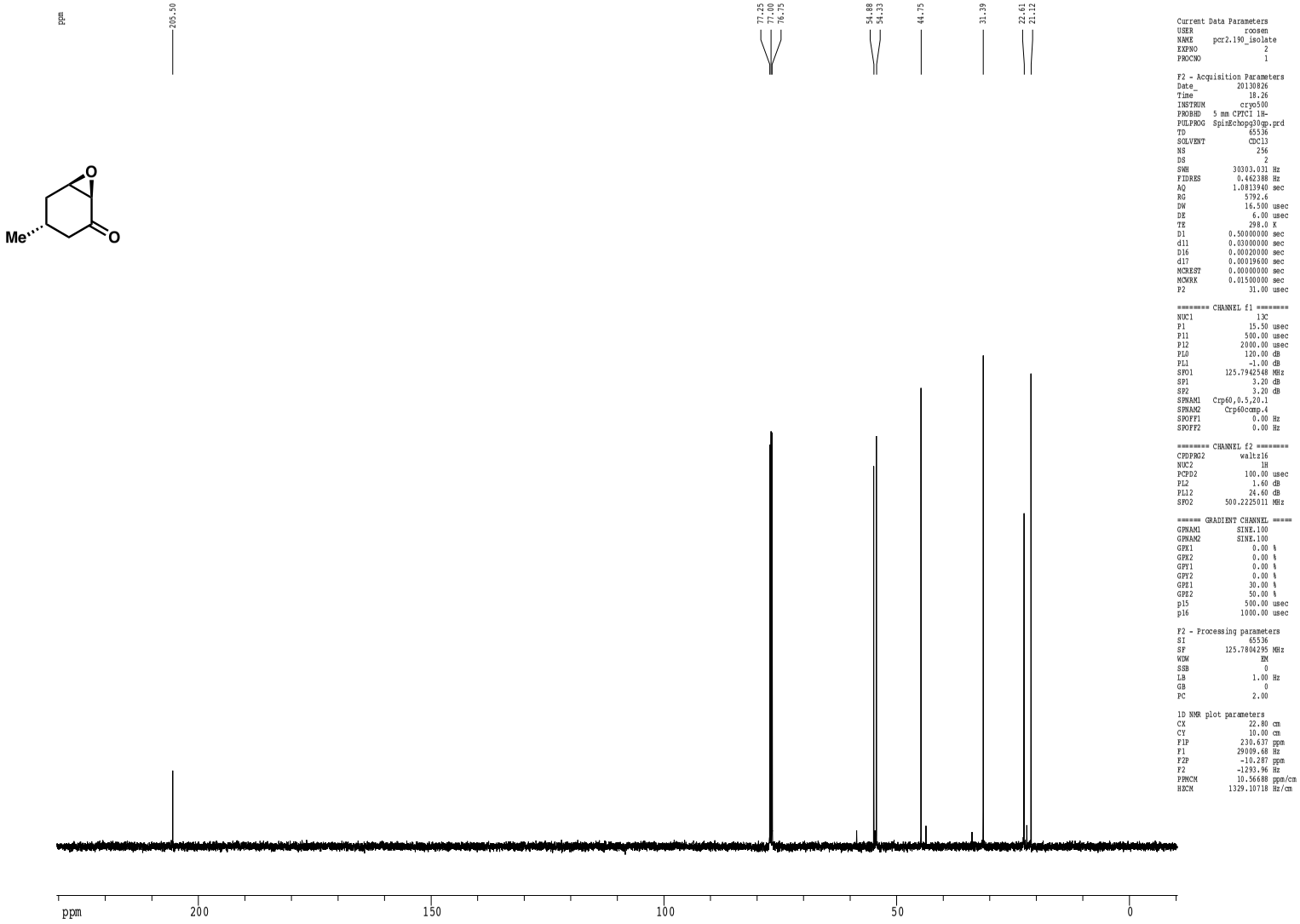
Z-restored spin-echo 13C spectrum with 1H decoupling



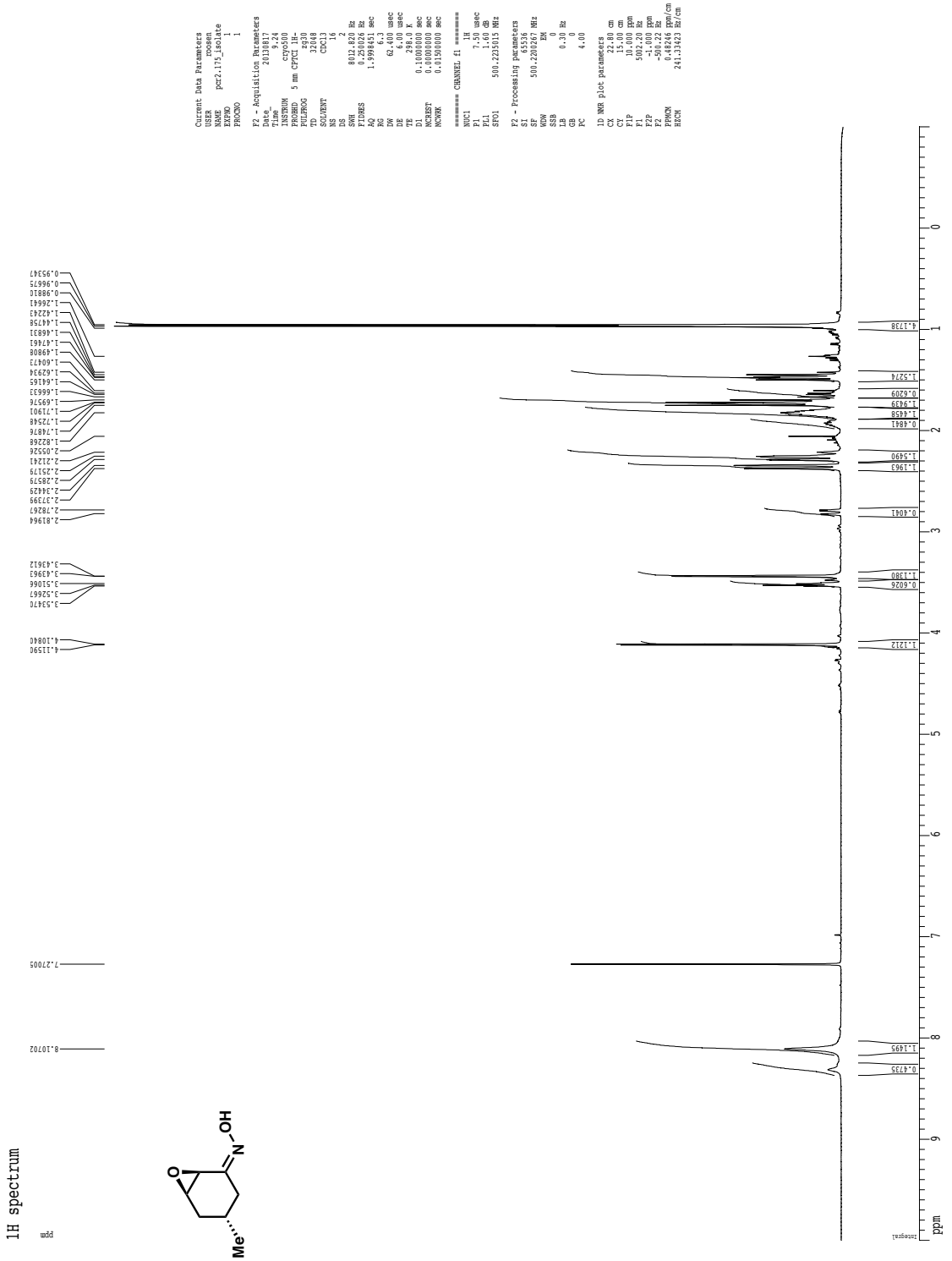

```
Current Data Parameters
USER            roosen
NAME      pcr2.132_isolate
EXPNO                 2
PROCNO                1

F2 - Acquisition Parameters
Date_          20130624
Time               8.57
INSTRUM         cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD                65536
SOLVENT           CDCl3
NS                  216
DS                    2
SWH           30303.031 Hz
FIDRES        0.462388 Hz
AQ            1.0813940 sec
RG               7298.2
DW              16.500 usec
DE               6.00 usec
TE              298.0 K
D1          0.25000000 sec
d11         0.03000000 sec
D16         0.00020000 sec
d17         0.00019600 sec
MCREST      0.00000000 sec
MCWRK       0.01500000 sec
P2              31.00 usec

======= CHANNEL f1 =======
NUC1               13C
P1              15.50 usec
P11            500.00 usec
P12           2000.00 usec
PL0            120.00 dB
PL1             -1.00 dB
SFO1       125.7942548 MHz
SP1             3.20 dB
SP2             3.20 dB
SPNAM1   Crp60,0.5,20.1
SPNAM2      Crp60comp.4
SPOFF1             0.00 Hz
SPOFF2             0.00 Hz

======= CHANNEL f2 =======
CPDPRG2         waltz16
NUC2               1H
PCPD2          100.00 usec
PL2              1.60 dB
PL12            24.60 dB
SFO2       500.2225011 MHz

===== GRADIENT CHANNEL ====
GPNAM1         SINE.100
GPNAM2         SINE.100
GPX1              0.00 %
GPX2              0.00 %
GPY1              0.00 %
GPY2              0.00 %
GPZ1             30.00 %
GPZ2             50.00 %
p15             500.00 usec
p16            1000.00 usec

F2 - Processing parameters
SI                65536
SF         125.7804281 MHz
WDW                  EM
SSB                   0
LB                1.00 Hz
GB                    0
PC                2.00

1D NMR plot parameters
CX               22.80 cm
CY               15.65 cm
F1P             230.387 ppm
F1              28978.21 Hz
F2P             -10.533 ppm
F2             -1324.82 Hz
PPMCM          10.56667 ppm/cm
HZCM        1329.08032 Hz/cm
```


1H spectrum
Me
ppm

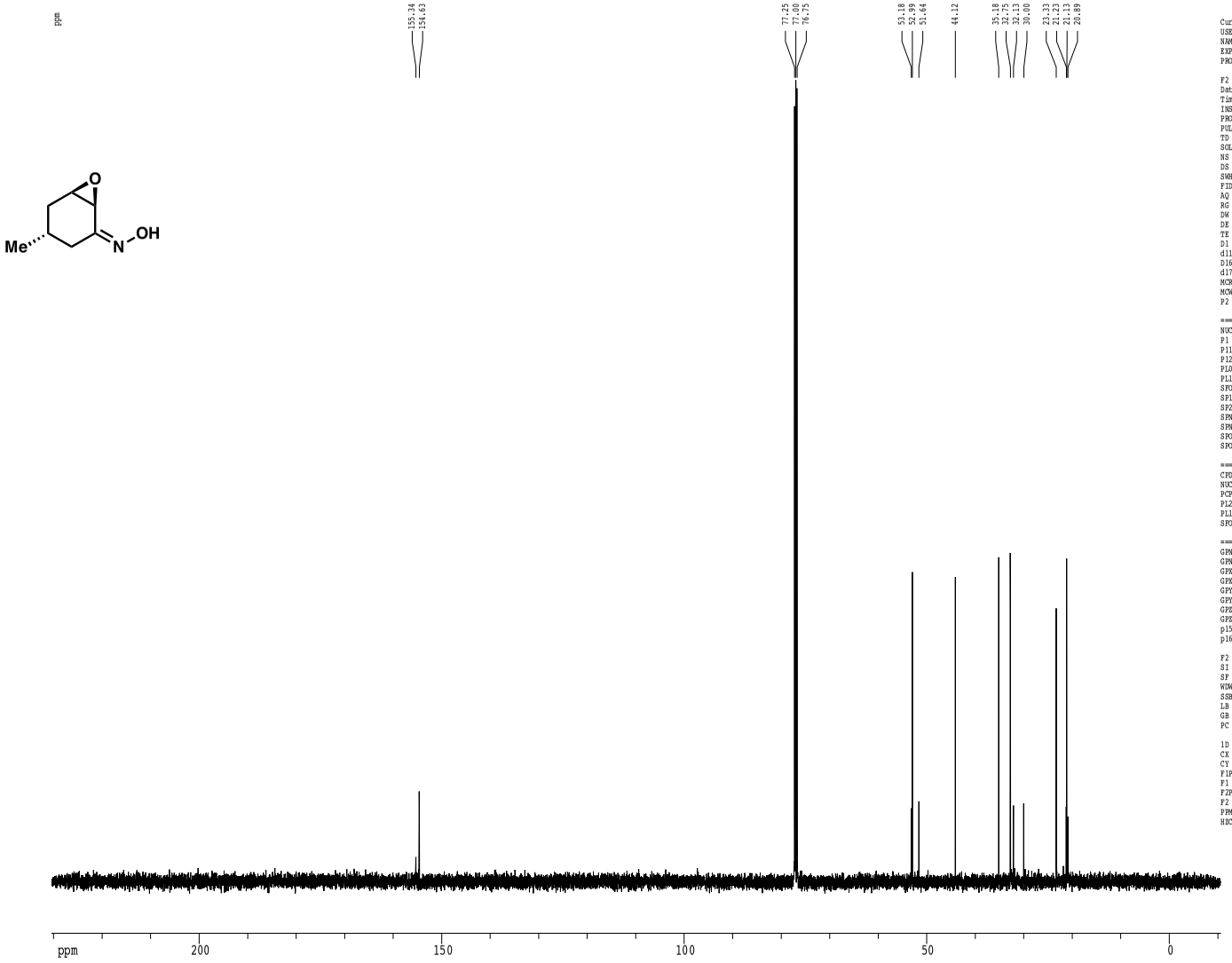
Z-restored spin-echo 13C spectrum with 1H decoupling



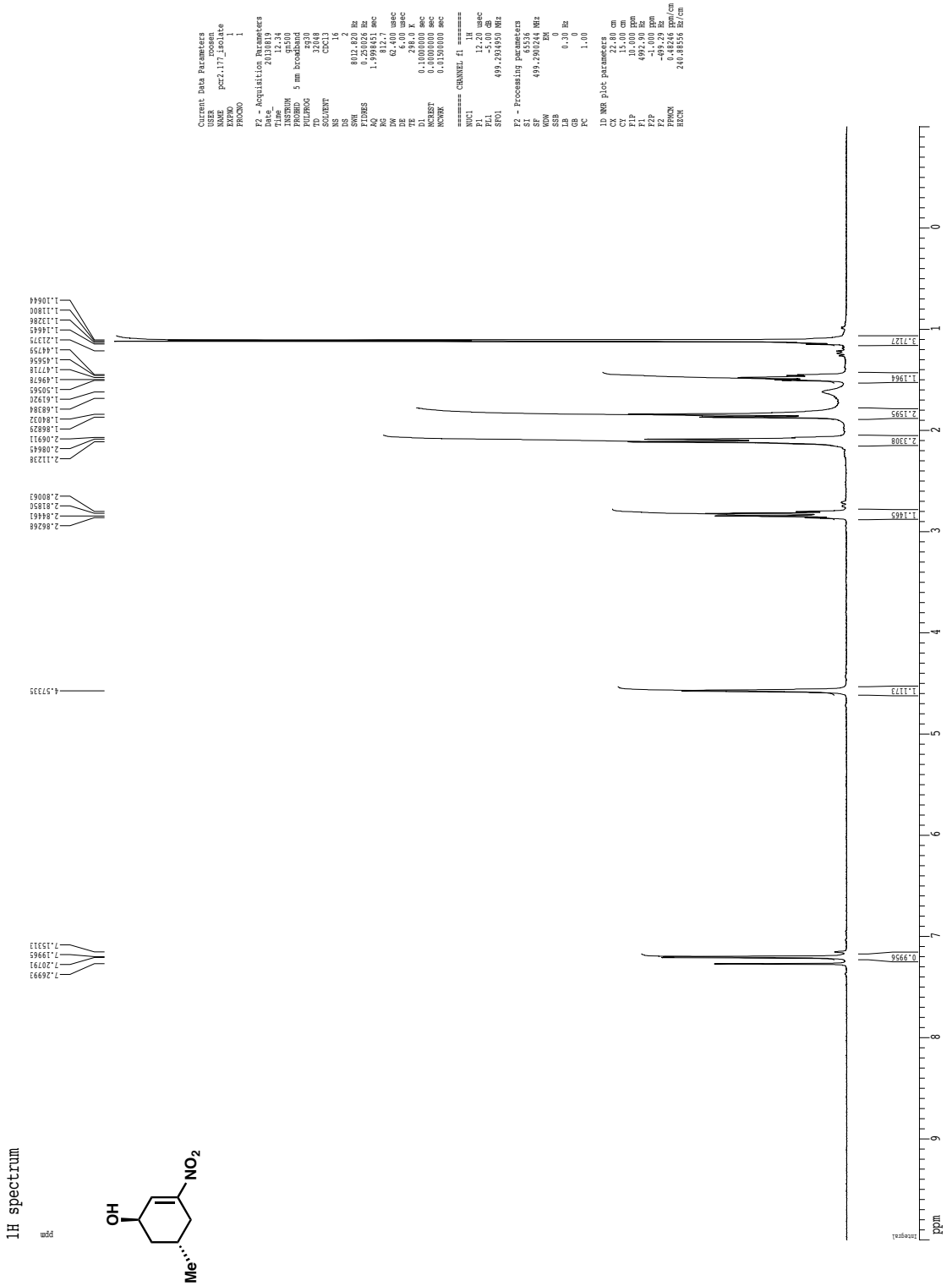

```
Current Data Parameters
USER                roosen
NAME          pcr2.190_isolate
EXPNO                    2
PROCNO                   1

F2 - Acquisition Parameters
Date_              20130826
Time                 18.26
INSTRUM            cryo500
PROBHD    5 mm CPTCI 1H-
PULPROG   SpinEchopg30gp.prd
TD                   65536
SOLVENT              CDCl3
NS                     256
DS                       2
SWH              30303.031 Hz
FIDRES           0.462388 Hz
AQ               1.0813940 sec
RG                  5792.6
DW                  16.500 usec
DE                   6.00 usec
TE                  298.0 K
D1              0.50000000 sec
d11             0.03000000 sec
D16             0.00020000 sec
d17             0.00019600 sec
MCREST          0.00000000 sec
MCWRK           0.01500000 sec
P2                  31.00 usec

======= CHANNEL f1 =======
NUC1                  13C
P1                  15.50 usec
P11                500.00 usec
P12               2000.00 usec
PL0                 120.00 dB
PL1                  -1.00 dB
SFO1          125.7942548 MHz
SP1                  3.20 dB
SP2                  3.20 dB
SPNAM1    Crp60,0.5,20.1
SPNAM2       Crp60comp.4
SFOFF1               0.00 Hz
SFOFF2               0.00 Hz

======= CHANNEL f2 =======
CPDPRG2           waltz16
NUC2                  1H
PCPD2              100.00 usec
PL2                  1.60 dB
PL12                24.60 dB
SFO2         500.2225011 MHz

===== GRADIENT CHANNEL ====
GPNAM1           SINE.100
GPNAM2           SINE.100
GPX1                 0.00 %
GPX2                 0.00 %
GPY1                 0.00 %
GPY2                 0.00 %
GPZ1                30.00 %
GPZ2                50.00 %
p15                500.00 usec
p16               1000.00 usec

F2 - Processing parameters
SI                   65536
SF            125.7804295 MHz
WDW                    EM
SSB                     0
LB                   1.00 Hz
GB                      0
PC                   2.00

1D NMR plot parameters
CX                  22.80 cm
CY                  10.00 cm
F1P                230.637 ppm
F1                 29009.68 Hz
F2P                -10.287 ppm
F2                 -1293.96 Hz
PPMCM              10.56688 ppm/cm
HZCM             1329.10718 Hz/cm
```


1H spectrum
ppm
Me
OH
N
O
Current Data Parameters
USER zcosen
NAME pcr2.175_isolate
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20130817
Time 9.24
INSTRUM crycs500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 32048
SOLVENT CDCl3
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.250026 Hz
AQ 1.9998451 sec
RG 6.3
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 7.50 usec
PL1 1.50 dB
SFO1 500.2235913 MHz
F2 - Processing parameters
SI 65536
SF 500.2200247 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00
1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 10.000 ppm
F1 5002.23 Hz
F2P -1.000 ppm
F2 -500.22 Hz
PPMCM 0.48246 ppm/cm
HZCM 241.33423 Hz/cm
4.17738
1.52744
0.62094
1.99394
1.44584
0.48414
1.54904
1.19634
0.40414
1.13804
0.60264
1.12124
1.14954
0.47354
7.27004
8.10704
4.11594
4.10844
3.53474
3.52664
3.51064
3.44634
3.43634
2.81964
2.78264
2.37394
2.34424
2.28574
2.25124
2.21244
2.05524
1.82264
1.74874
1.72584
1.71904
1.69574
1.66634
1.64164
1.62934
1.60474
1.49804
1.47464
1.46634
1.44794
1.42244
1.26664
0.99814
0.96674
0.95344
ppm

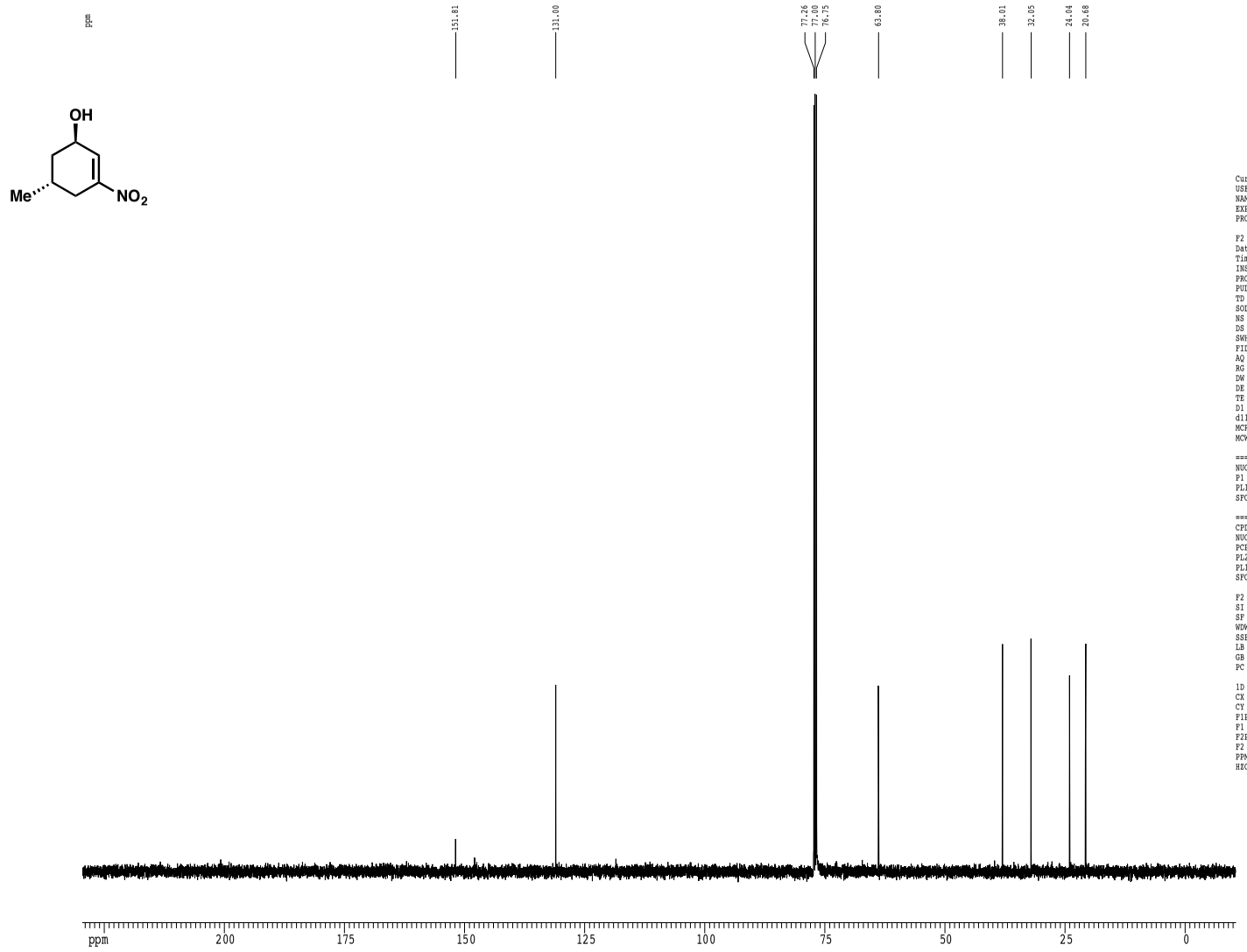
Z-restored spin-echo 13C spectrum with 1H decoupling




```
Current Data Parameters
USER            roosen
NAME      pcr2.175_isolate
EXPNO                 2
PROCNO                1

F2 - Acquisition Parameters
Date_          20130817
Time               9.27
INSTRUM         cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD                65536
SOLVENT           CDCl3
NS                  232
DS                    2
SWH           30303.031 Hz
FIDRES        0.462388 Hz
AQ            1.0813940 sec
RG               3649.1
DW               16.500 usec
DE                6.00 usec
TE                298.0 K
D1           0.25000000 sec
d11          0.03000000 sec
D16          0.00020000 sec
d17          0.00019600 sec
MCREST       0.00000000 sec
MCWRK        0.01500000 sec
P2                31.00 usec

======= CHANNEL f1 =======
NUC1                13C
P1                15.50 usec
P11              500.00 usec
P12             2000.00 usec
PL0              120.00 dB
PL1               -1.00 dB
SFO1         125.7942548 MHz
SP1               3.20 dB
SP2               3.20 dB
SPNAM1   Crp60,0.5,20.1
SPNAM2      Crp60comp.4
SPOFF1               0.00 Hz
SPOFF2               0.00 Hz

======= CHANNEL f2 =======
CPDPRG2          waltz16
NUC2                1H
PCPD2            100.00 usec
PL2                1.60 dB
PL12              24.60 dB
SFO2        500.2225011 MHz

===== GRADIENT CHANNEL ====
GPNAM1          SINE.100
GPNAM2          SINE.100
GPX1                0.00 %
GPX2                0.00 %
GPY1                0.00 %
GPY2                0.00 %
GPZ1               30.00 %
GPZ2               50.00 %
p15              500.00 usec
p16             1000.00 usec

F2 - Processing parameters
SI                 65536
SF          125.7804286 MHz
WDW                   EM
SSB                    0
LB                 1.00 Hz
GB                     0
PC                 1.30

1D NMR plot parameters
CX                22.80 cm
CY                15.65 cm
F1P              230.384 ppm
F1               28977.75 Hz
F2P              -10.536 ppm
F2              -1325.28 Hz
PPMCM            10.56667 ppm/cm
HZCM          1329.08032 Hz/cm
```


1H spectrum
ppm
OH
NO2
Me
Current Data Parameters
F2 - Acquisition Parameters
F2 - Processing parameters
1D NMR plot parameters
ppm

13C spectrum with 1H decoupling



Current Data Parameters
USER roomen
NAME pcr2.177_isolate
EXPNO 2
PROCNO 1

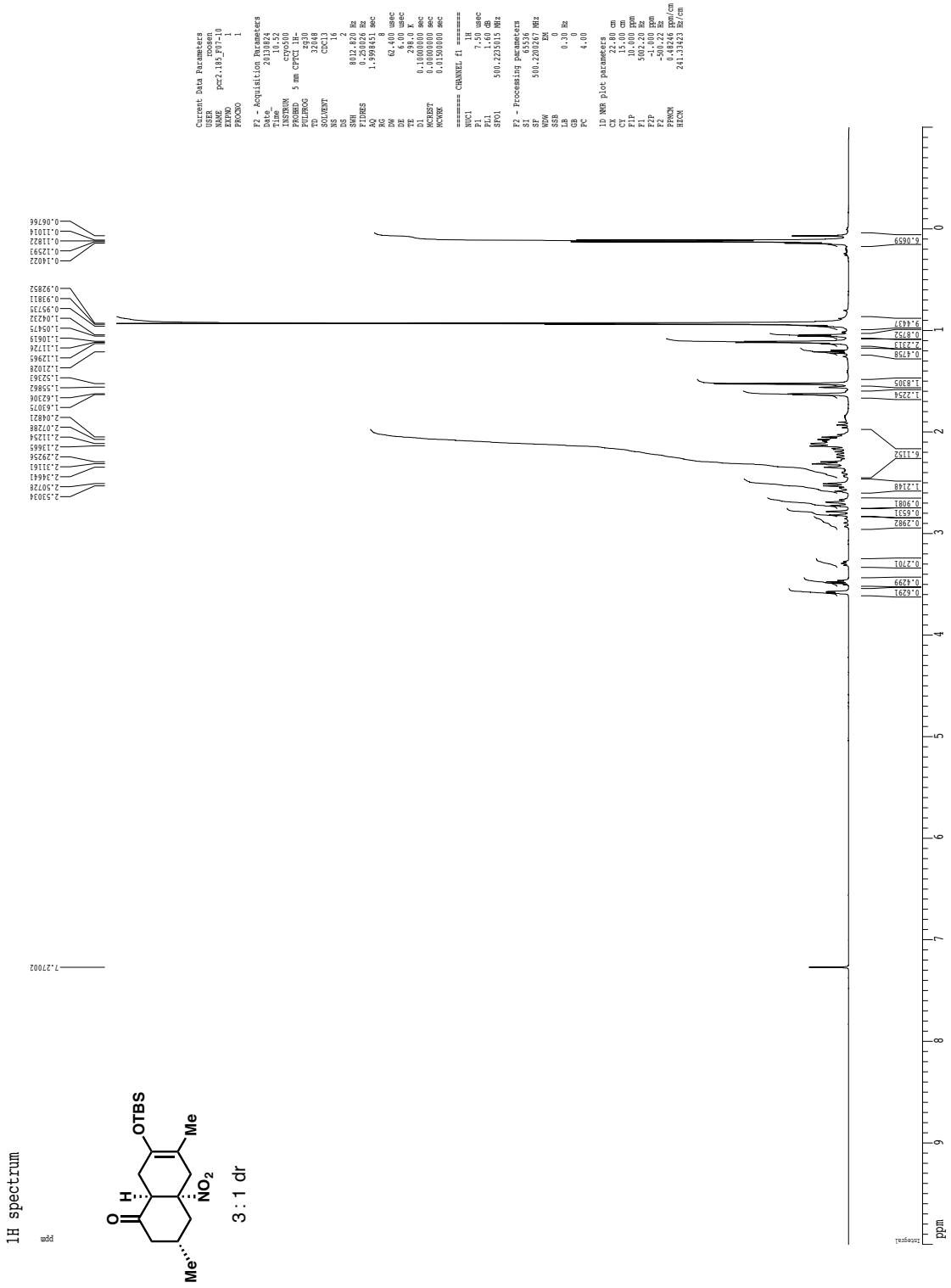
F2 - Acquisition Parameters
Date_ 20130819
Time 12.38
INSTRUM gn500
PROBHD 5 mm broadband
PULPROG zgdc30
TD 65536
SOLVENT CDCl3
NS 512
DS 2
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0813940 sec
RG 6502
DW 16.500 usec
DE 4.50 usec
TE 298.0 K
D1 0.25000000 sec
d11 0.03000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec

======== CHANNEL f1 ========
NUC1 13C
P1 7.70 usec
PL1 0.00 dB
SFO1 125.5603801 MHz

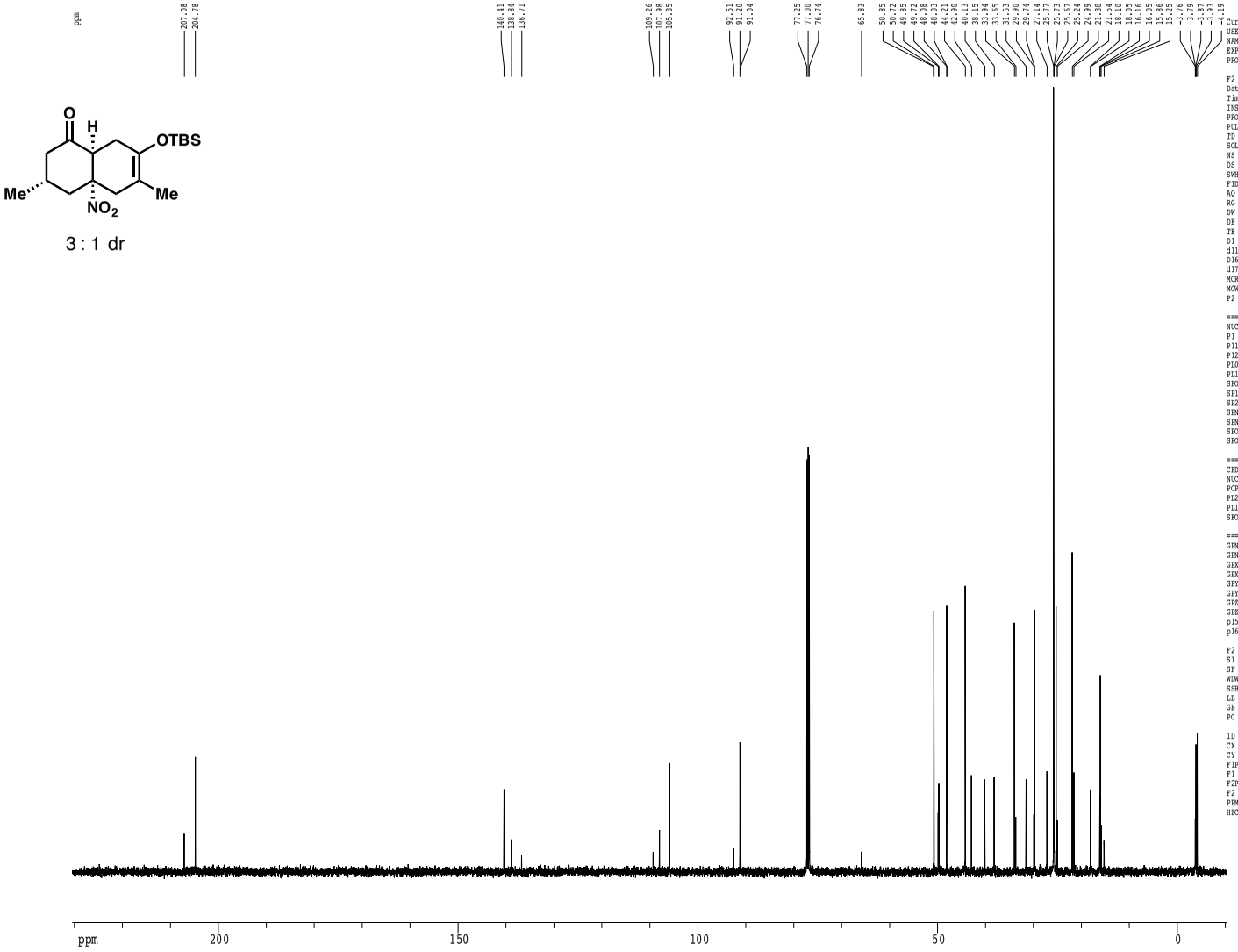
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 -3.00 dB
PL12 13.20 dB
SFO2 499.2924964 MHz

F2 - Processing parameters
SI 65536
SF 125.5465779 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00

1D NMR plot parameters
CX 22.80 cm
CY 15.65 cm
F1P 229.520 ppm
F1 28815.41 Hz
F2P -10.507 ppm
F2 -1319.07 Hz
PPMCM 10.52747 ppm/cm
HZCM 1321.68762 Hz/cm


1H spectrum
OTBS
Me
H
O
NO2
Me
3 : 1 dr
ppm

Z-restored spin-echo 13C spectrum with 1H decoupling



Current Data Parameters
USER roosen
NAME pcr2.185_F07-10
EXPNO 2
PROCNO 1

F2 - Acquisition Parameters
Date_ 20130824
Time 10.54
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG SpinEchopg30gp.prd
TD 65536
SOLVENT CDCl3
NS 264
DS 2
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0813940 sec
RG 7298.2
DW 16.500 usec
DE 6.00 usec
TE 298.0 K
D1 0.50000000 sec
d11 0.03000000 sec
D16 0.00020000 sec
d17 0.00019600 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
P2 31.00 usec

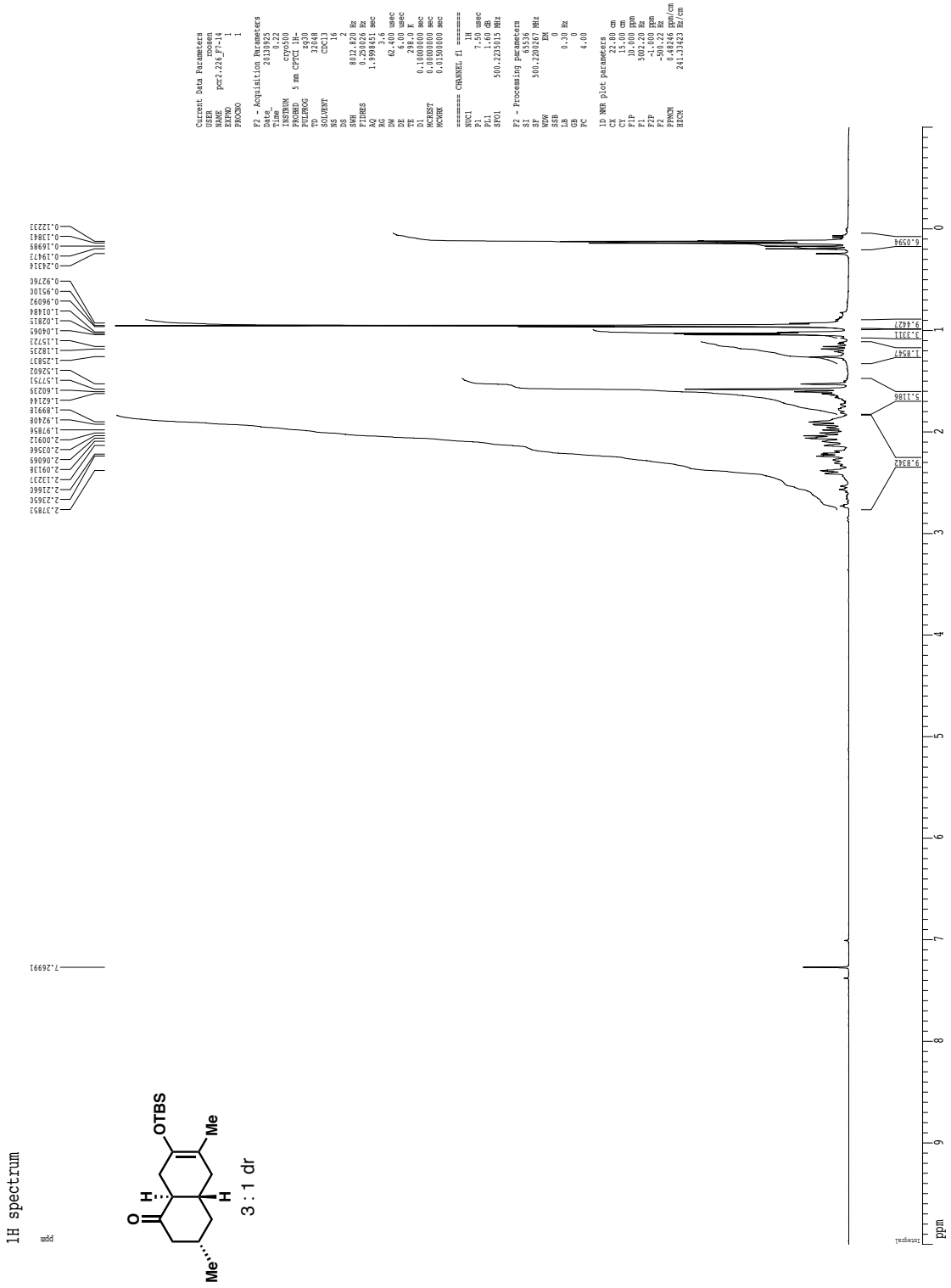
======= CHANNEL f1 =======
NUC1 13C
P1 15.50 usec
P11 500.00 usec
P12 2000.00 usec
PL0 120.00 dB
PL1 -1.00 dB
SFO1 125.7942548 MHz
SP1 3.20 dB
SP2 3.20 dB
SPNAM1 Crp60,0.5,20.1
SPNAM2 Crp60comp.4
SFOFF1 0.00 Hz
SFOFF2 0.00 Hz

======= CHANNEL f2 =======
CPDPRG2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 1.60 dB
PL12 24.60 dB
SFO2 500.2225011 MHz

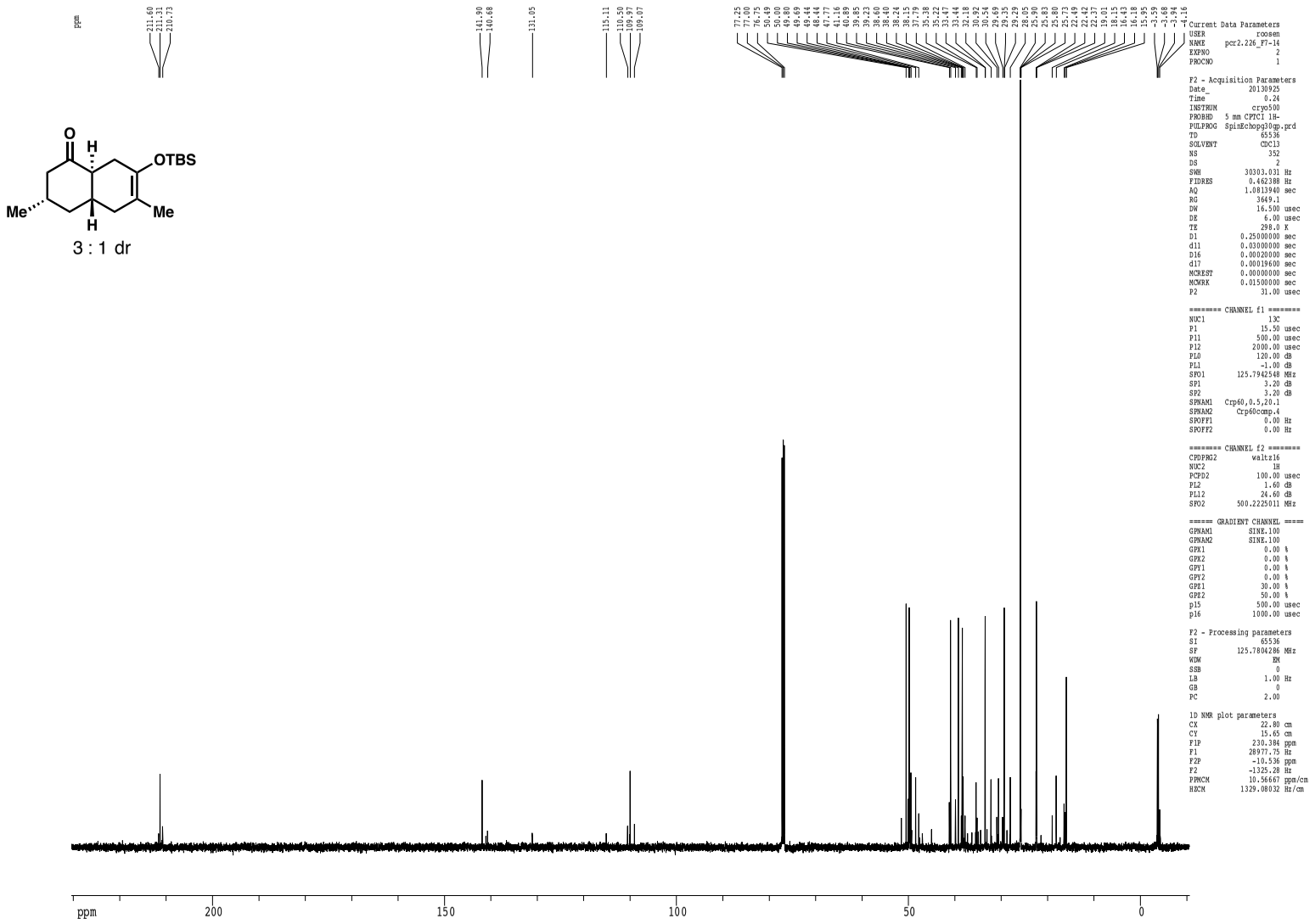
===== GRADIENT CHANNEL ====
GPNAM1 SINE.100
GPNAM2 SINE.100
GPX1 0.00 %
GPX2 0.00 %
GPY1 0.00 %
GPY2 0.00 %
GPZ1 30.00 %
GPZ2 50.00 %
p15 500.00 usec
p16 1000.00 usec

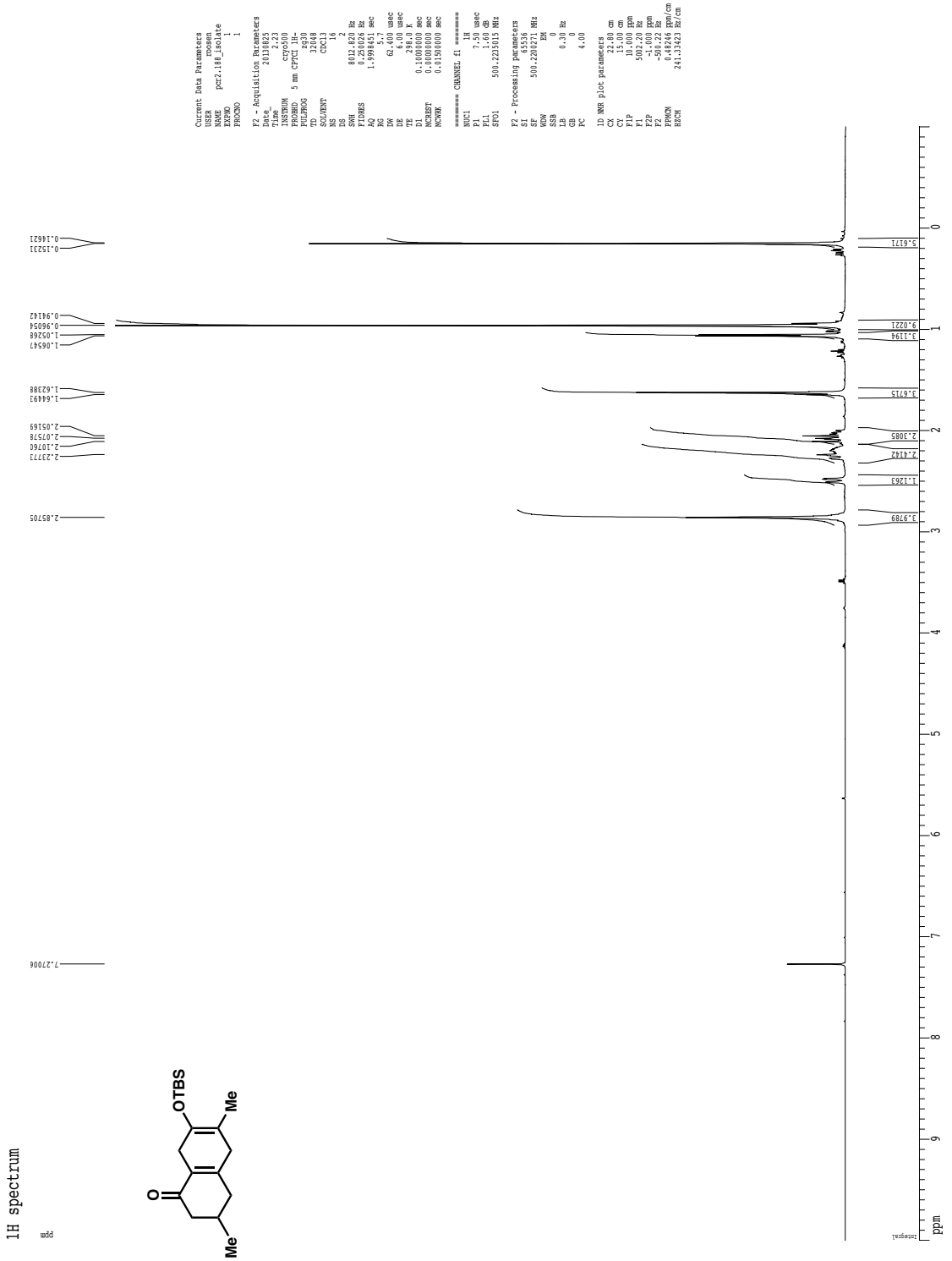
F2 - Processing parameters
SI 65536
SF 125.7804295 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.30

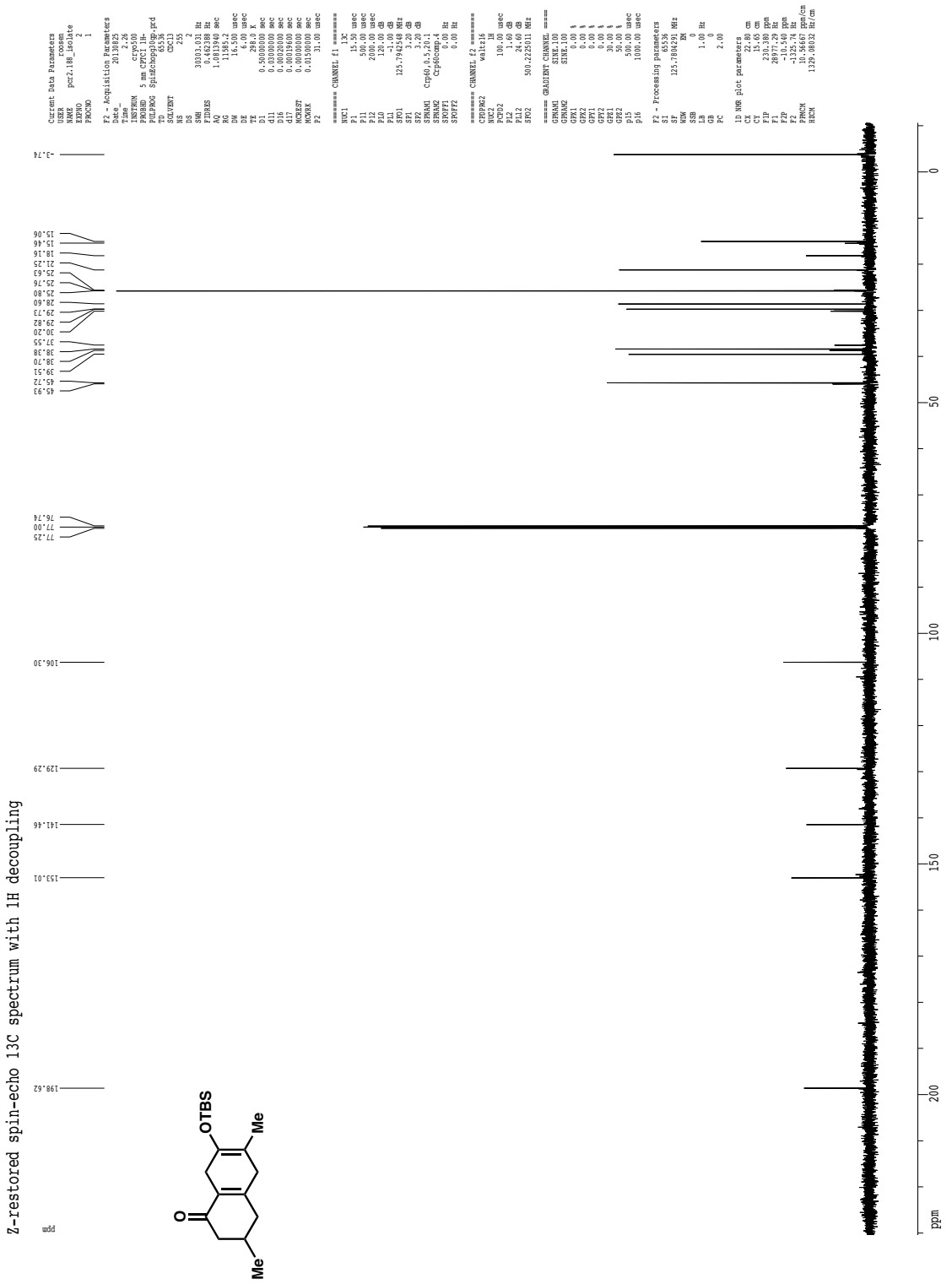
1D NMR plot parameters
CX 22.80 cm
CY 15.65 cm
F1P 230.637 ppm
F1 29009.68 Hz
F2P -10.287 ppm
F2 -1293.96 Hz
PPMCM 10.56688 ppm/cm
HZCM 1329.10718 Hz/cm

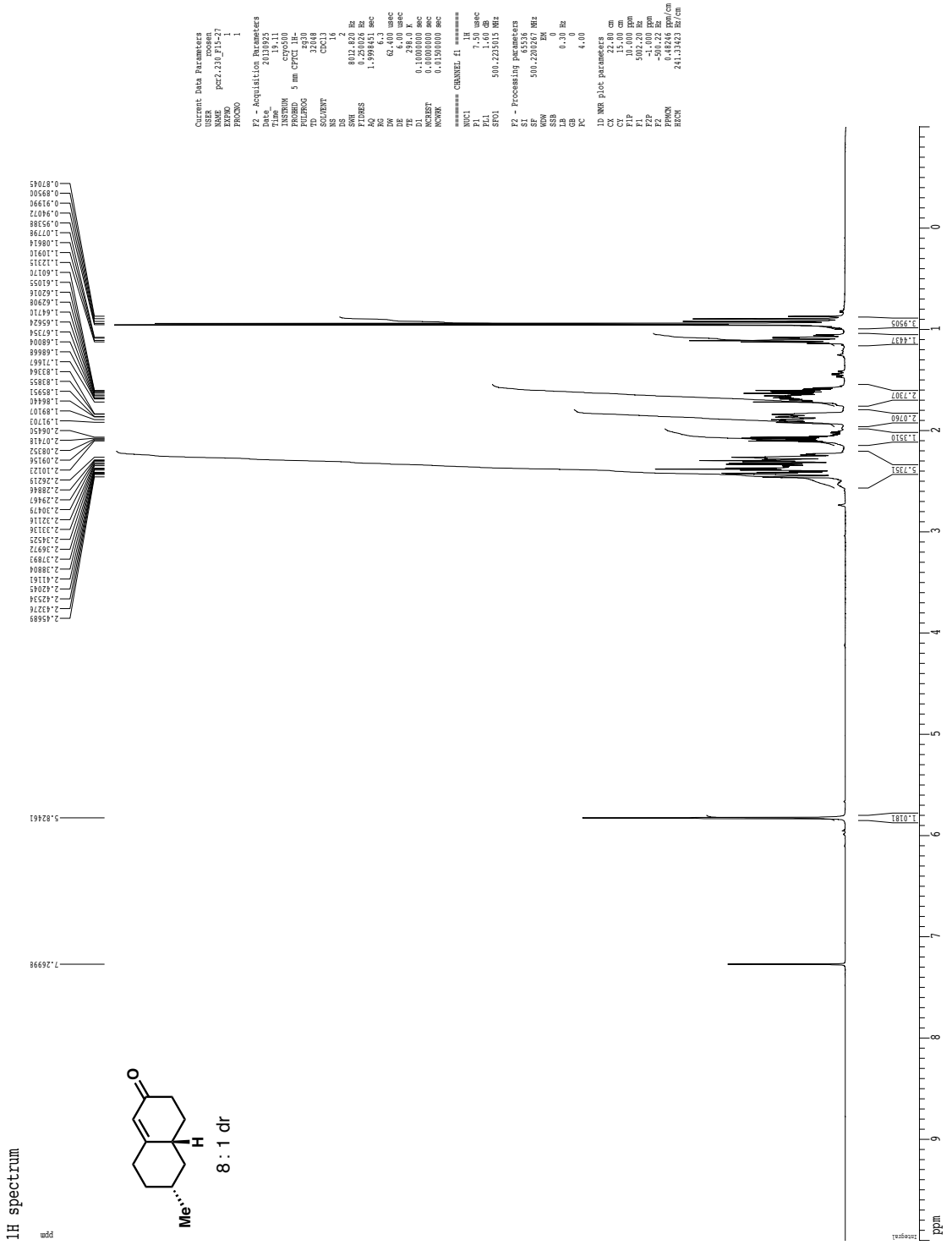

1H spectrum
OTBS
Me
H
O
H
Me
3 : 1 dr

Z-restored spin-echo 13C spectrum with 1H decoupling

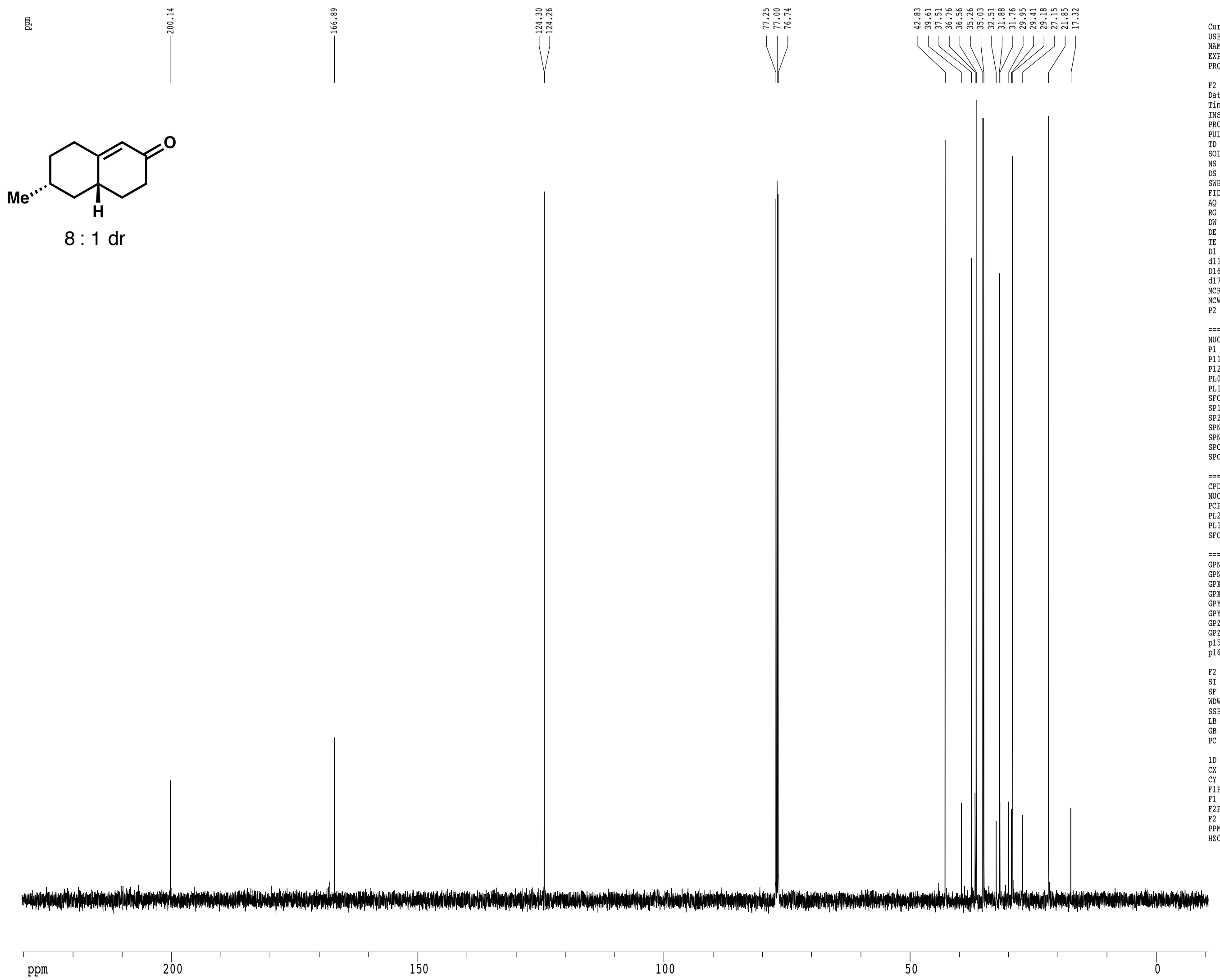



1H spectrum
ppm
OTBS
Me
Me
O
Current Data Parameters
USER rcosen
NAME pcr2.188_isolate
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20130825
Time 2.23
INSTRUM crys500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 32048
SOLVENT CDCl3
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.250026 Hz
AQ 1.9998451 sec
RG 5.7
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======= CHANNEL f1 =======
NUC1 1H
P1 7.50 usec
PL1 1.50 dB
SFO1 500.2235910 MHz
F2 - Processing parameters
SI 65536
SF 500.2200271 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00
1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 10.000 ppm
F1 5002.23 Hz
F2P -1.000 ppm
F2 -500.22 Hz
PPMCM 0.48246 ppm/cm
HZCM 241.33423 Hz/cm
0.14621
0.15231
0.94142
0.96054
1.05268
1.06547
1.62388
1.64493
2.05169
2.07578
2.10764
2.23773
2.85705
7.27006
5.6171
9.0221
3.1194
3.6715
2.3085
2.4142
1.1263
3.9789
ppm

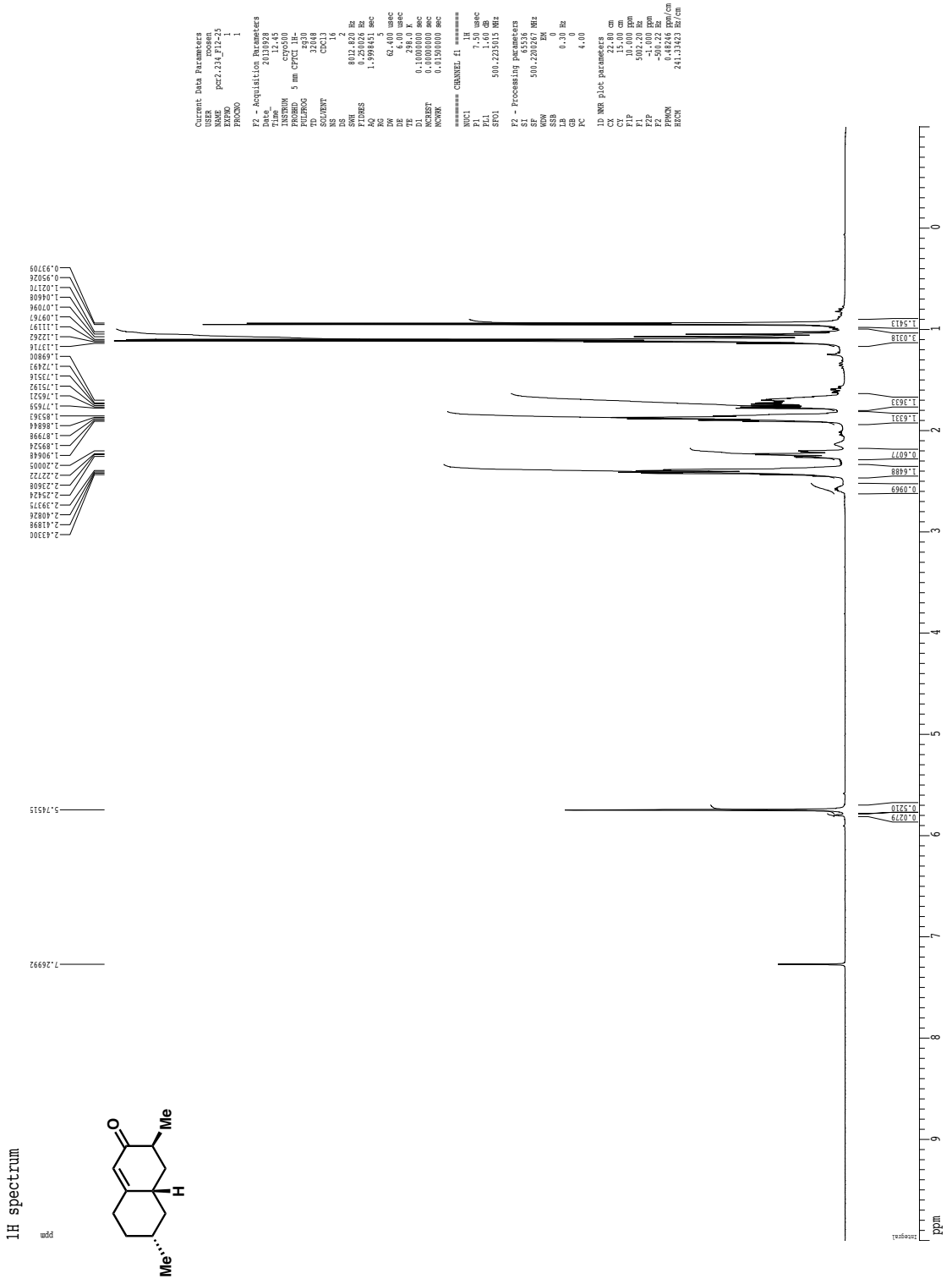

Z-restored spin-echo 13C spectrum with 1H decoupling
OTBS
Me
Me
O
ppm
198.62
153.01
141.46
129.29
106.30
77.25
77.00
76.74
45.93
45.72
39.51
38.70
38.38
37.55
30.20
29.82
29.73
28.60
25.80
25.76
25.63
21.25
18.16
15.46
15.06
-3.74
Current Data Parameters
USER coosen
NAME pcc2.10B_acetate
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20130825
Time_ 2.26
crys500
INSTRUM
PROBHD 5 mm CPTCI 1H-
PULPROG spinEchoAmp1d.pcd
TD 65536
SOLVENT CDCl3
NS 255
DS 2
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0819940 sec
RG 1185.2
DW 16.500 usec
DE 6.00 usec
TE 298.0 K
D1 0.50000000 sec
D11 0.03000000 sec
D16 0.00020000 sec
d17 0.00019600 sec
WCHEXT 0.00000000 sec
WCHPK 0.01500000 sec
P2 31.00 usec
======== CHANNEL f1 ========
NUC1 13C
P1 15.50 usec
P11 500.00 usec
P12 2000.00 usec
PL0 120.00 dB
PL1 1.00 dB
SFO1 125.7742160 MHz
SPI 3.20 dB
SP2 3.20 dB
SPNAM1 Crp60,0.5,20.1
SPOAL2 Crp60comp.4
SPOFF1 0.00 Hz
SPOFF2 0.00 Hz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 1.60 dB
PL12 24.60 dB
SFO2 500.2225011 MHz
===== GRADIENT CHANNEL =====
GPNAM1 SINE.100
GPNAM2 SINE.100
GPZ1 0.00 %
GPZ2 0.00 %
GPZ11 0.00 %
GPZ12 0.00 %
GPZ21 30.00 %
GPZ22 50.00 %
p15 500.00 usec
p16 1000.00 usec
F2 - Processing parameters
SI 65536
SF 125.7694191 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00
1D NMR plot parameters
CX 22.80 cm
CY 15.40 cm
F1P 230.980 ppm
F1 28977.29 Hz
F2P -10.540 ppm
F2 -1325.74 Hz
PPMCM 10.56667 ppm/cm
HZCM 1329.08032 Hz/cm
ppm
0
50
100
150
200

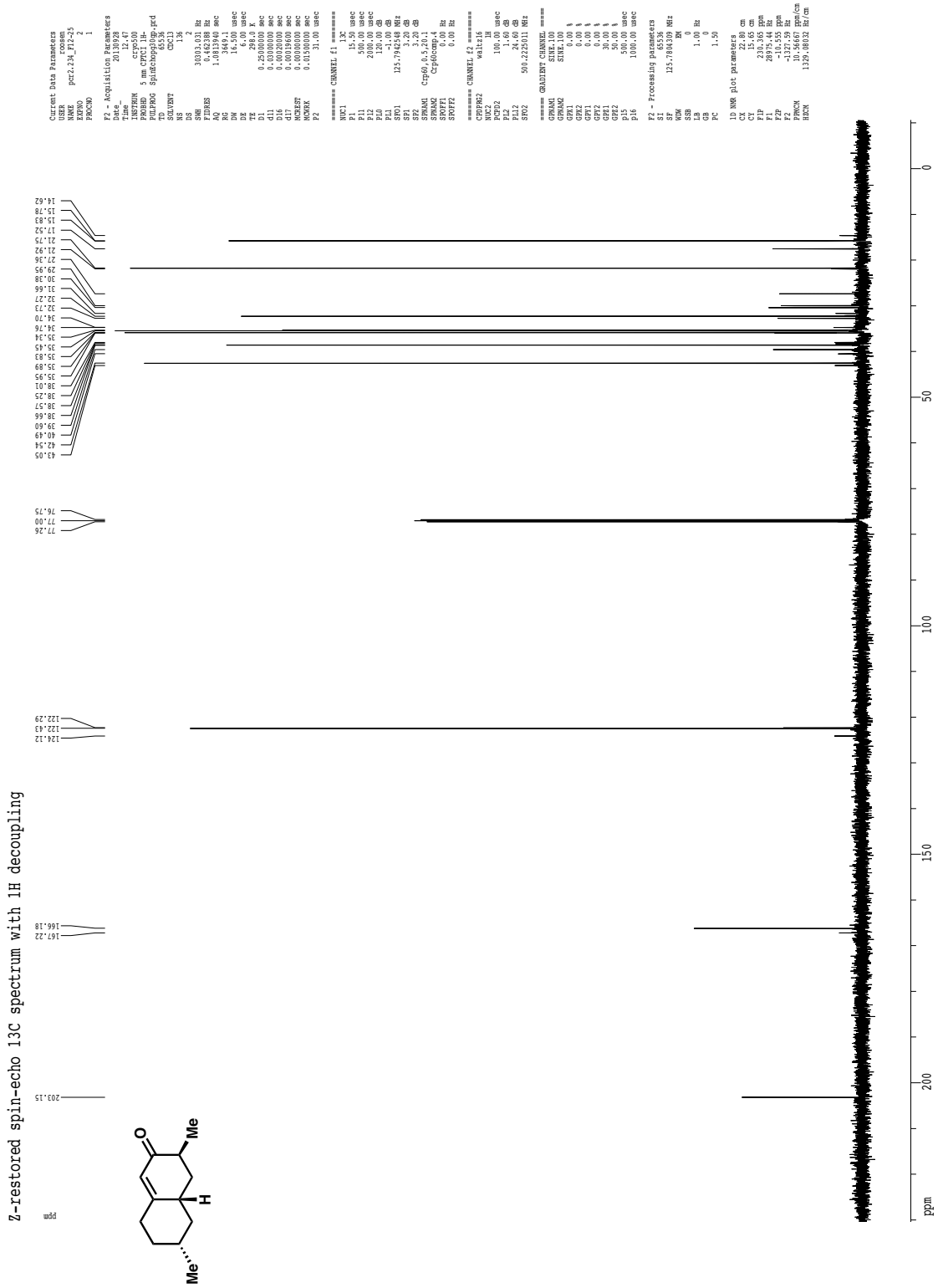

1H spectrum
8 : 1 dr
Me
H
O
Current Data Parameters
USER ccosen
NAME pcr2.230_F15-27
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20130925
Time 19.11
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 32048
SOLVENT CDCl3
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.250026 Hz
AQ 1.9998451 sec
RG 6.3
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 7.50 usec
PL1 1.50 dB
SFO1 500.2235913 MHz
F2 - Processing parameters
SI 65536
SF 500.2200247 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00
1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 10.000 ppm
F1 5002.23 Hz
F2P -1.000 ppm
F2 -500.22 Hz
PPMCM 0.48246 ppm/cm
HZCM 241.33423 Hz/cm
7.26998
5.82461
1.0181
5.7351
3.9505
1.4437
2.7307
2.0760
1.3510
ppm

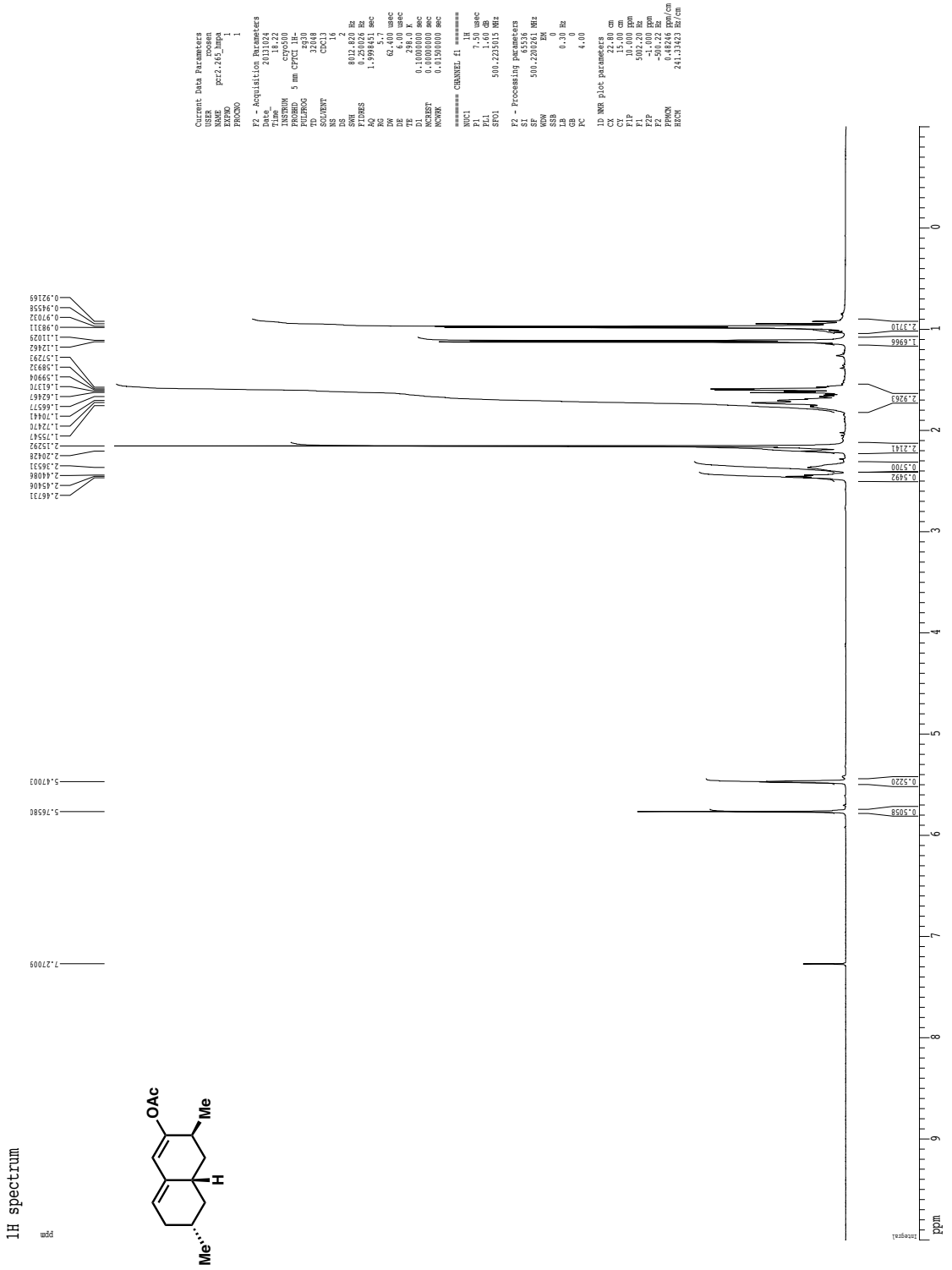
Z-restored spin-echo 13C spectrum with 1H decoupling



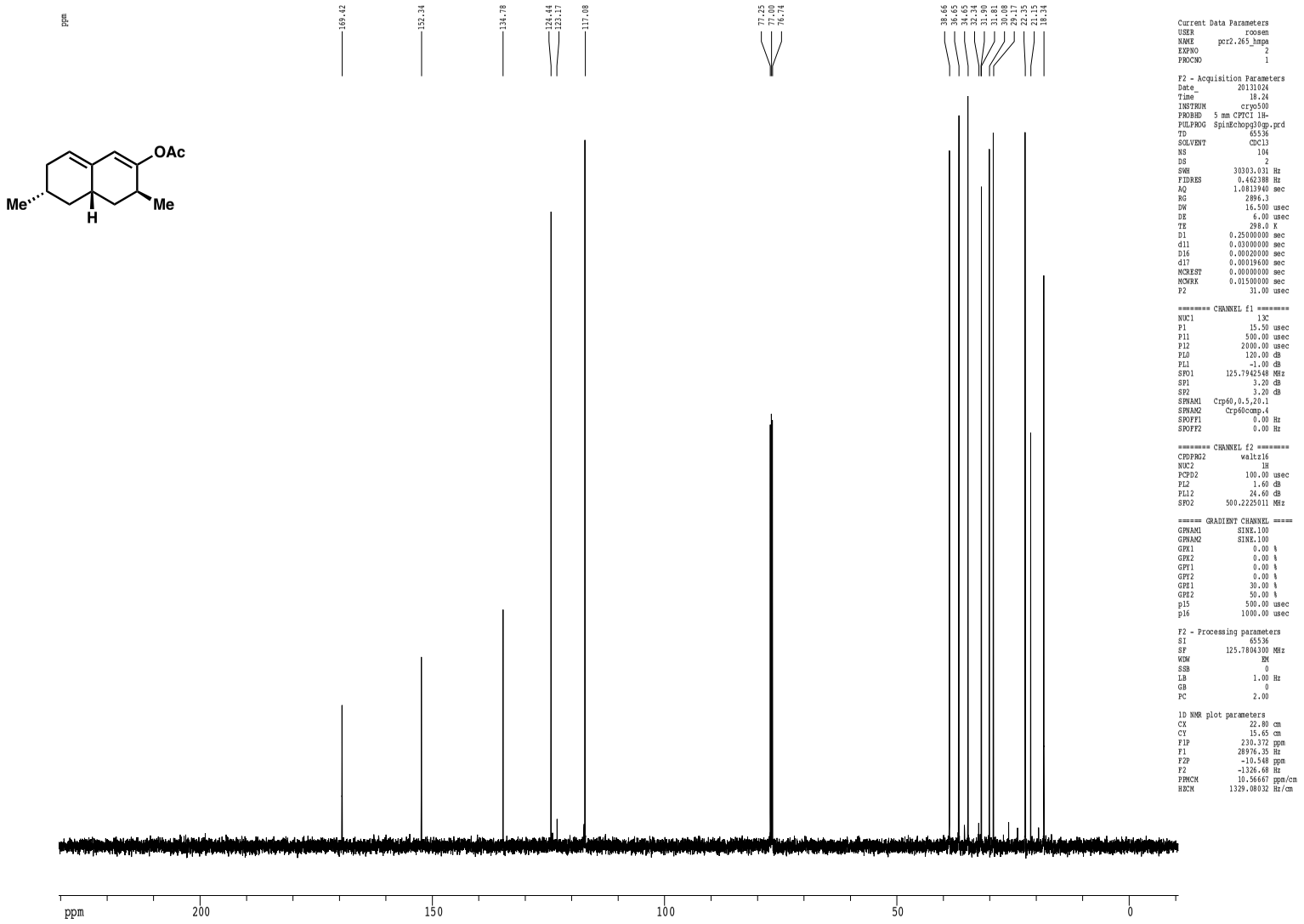

```
Current Data Parameters
USER              roosen
NAME     pcr2.230_F15-27
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20130925
Time               19.13
INSTRUM          cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD                 65536
SOLVENT            CDCl3
NS                   280
DS                     2
SWH            30303.031 Hz
FIDRES          0.462388 Hz
AQ             1.0813940 sec
RG                 13004
DW                16.500 usec
DE                  6.00 usec
TE                 298.0 K
D1            0.50000000 sec
d11           0.03000000 sec
D16           0.00020000 sec
d17           0.00019600 sec
MCREST        0.00000000 sec
MCWRK         0.01500000 sec
P2                 31.00 usec

======== CHANNEL f1 ========
NUC1                 13C
P1                 15.50 usec
P11               500.00 usec
P12              2000.00 usec
PL0               120.00 dB
PL1                -1.00 dB
SFO1         125.7942548 MHz
SP1                 3.20 dB
SP2                 3.20 dB
SPNAM1   Crp60,0.5,20.1
SPNAM2      Crp60comp.4
SPOFF1              0.00 Hz
SPOFF2              0.00 Hz

======== CHANNEL f2 ========
CPDPRG2          waltz16
NUC2                  1H
PCPD2             100.00 usec
PL2                 1.60 dB
PL12               24.60 dB
SFO2         500.2225011 MHz

====== GRADIENT CHANNEL =====
GPNAM1          SINE.100
GPNAM2          SINE.100
GPX1                0.00 %
GPX2                0.00 %
GPY1                0.00 %
GPY2                0.00 %
GPZ1               30.00 %
GPZ2               50.00 %
p15               500.00 usec
p16              1000.00 usec

F2 - Processing parameters
SI                 65536
SF           125.7804305 MHz
WDW                   EM
SSB                    0
LB                  1.00 Hz
GB                     0
PC                  2.00

1D NMR plot parameters
CX                 22.80 cm
CY                 15.65 cm
F1P              230.369 ppm
F1              28975.90 Hz
F2P              -10.551 ppm
F2              -1327.13 Hz
PPMCM           10.56667 ppm/cm
HZCM          1329.08032 Hz/cm
```


1H spectrum
ppm
Me
H
Me
Current Data Parameters
USER tcosden
NAME pcr2.234_F12-25
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20130928
Time 12.45
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 32048
SOLVENT CDCl3
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.250026 Hz
AQ 1.9998451 sec
RG 64
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======= CHANNEL f1 =======
NUC1 1H
P1 7.50 usec
PL1 1.00 dB
SFO1 500.2235913 MHz
F2 - Processing parameters
SI 65536
SF 500.2200247 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00
1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 10.000 ppm
F1 5002.23 Hz
F2P -1.000 ppm
F2 -500.22 Hz
PPMCM 0.48246 ppm/cm
HZCM 241.33423 Hz/cm
7.26992
5.74515
2.43300
2.41898
2.40826
2.39375
2.23624
2.22722
2.20005
1.90648
1.89524
1.87998
1.86844
1.85363
1.77659
1.76521
1.75192
1.73514
1.72493
1.69800
1.13716
1.12262
1.11197
1.09767
1.07096
1.04608
1.02170
0.95026
0.93709
1.5413
3.0318
1.3633
1.6331
0.6077
1.6488
0.0969
0.9210
0.0279
ppm

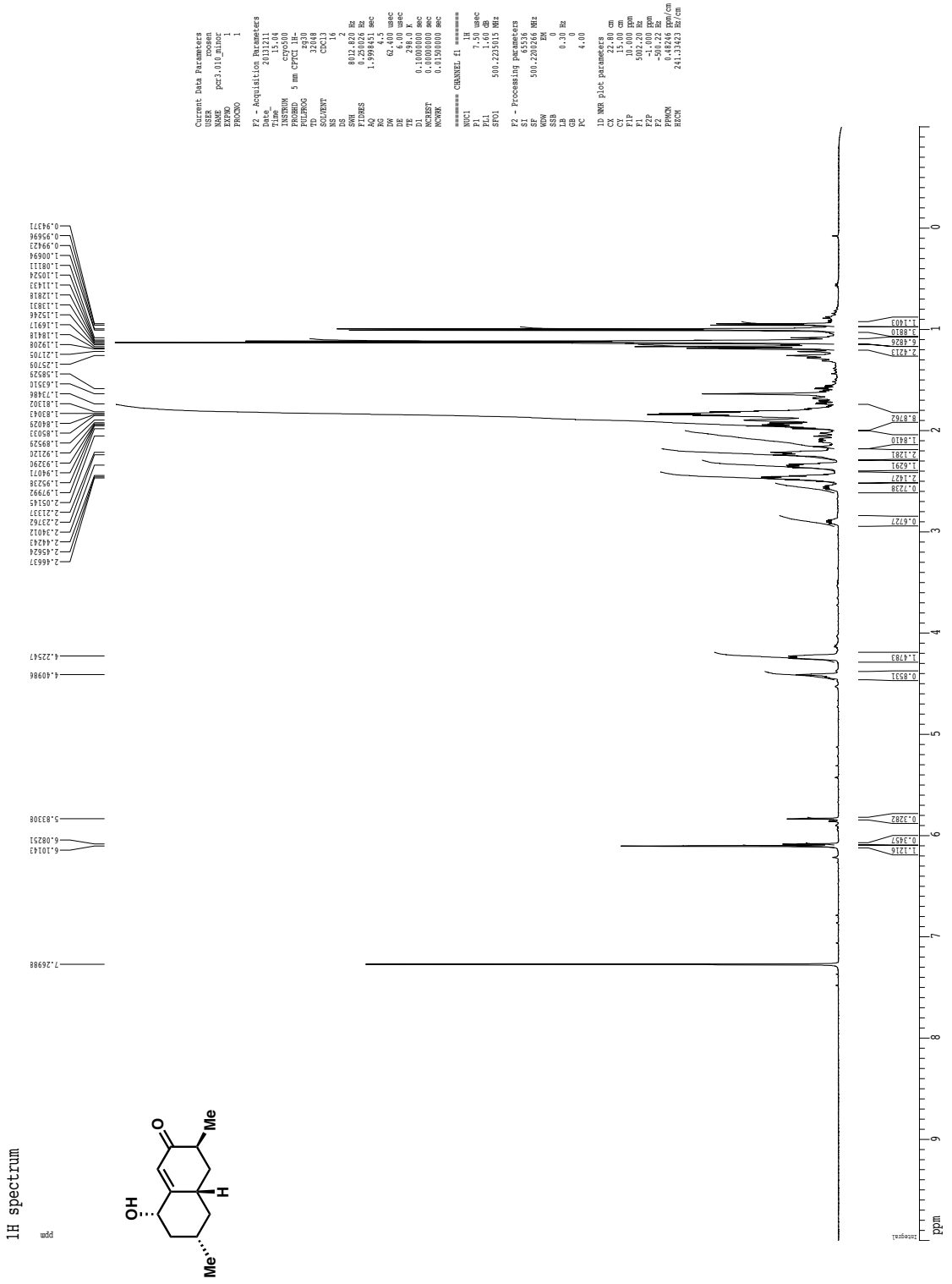

Z-restored spin-echo 13C spectrum with 1H decoupling
Current Data Parameters
Acquisition Parameters
CHANNEL f1
CHANNEL f2
GRADIENT CHANNEL
Processing parameters
1D NMR plot parameters
Me
H
Me
ppm
0
50
100
150
200
ppm

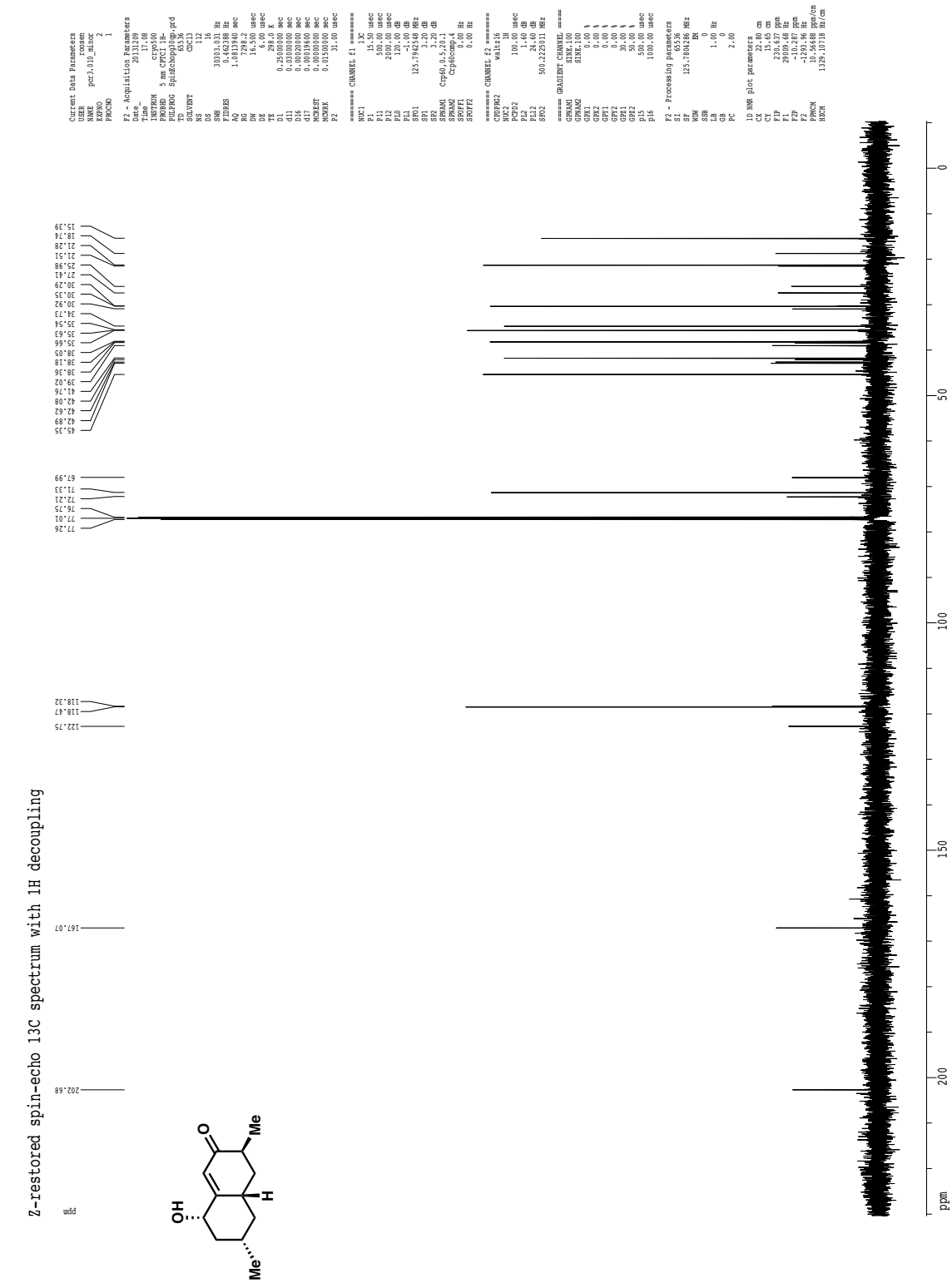

1H spectrum
OAc
Me
H
Me
ppm

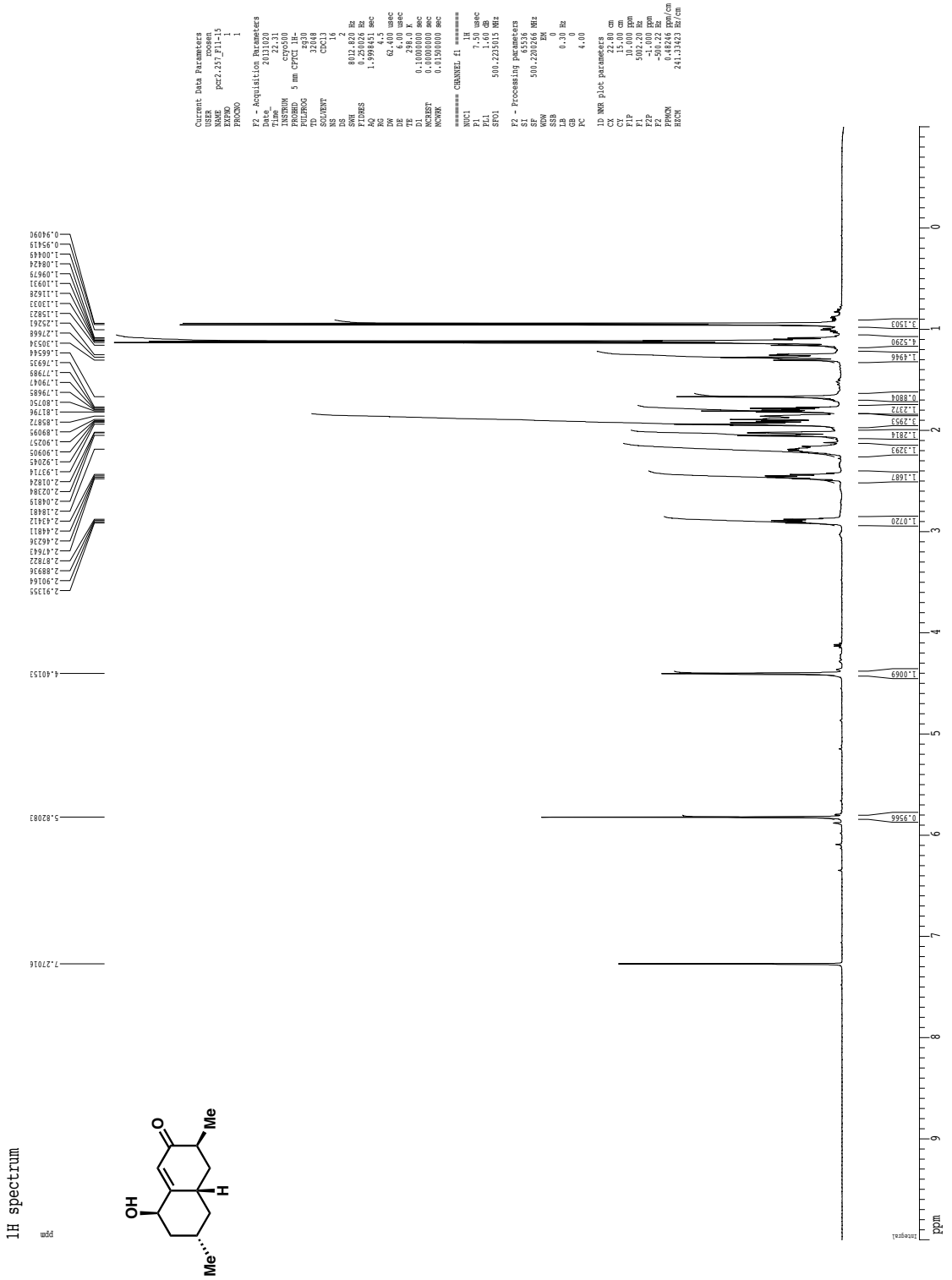
Z-restored spin-echo 13C spectrum with 1H decoupling



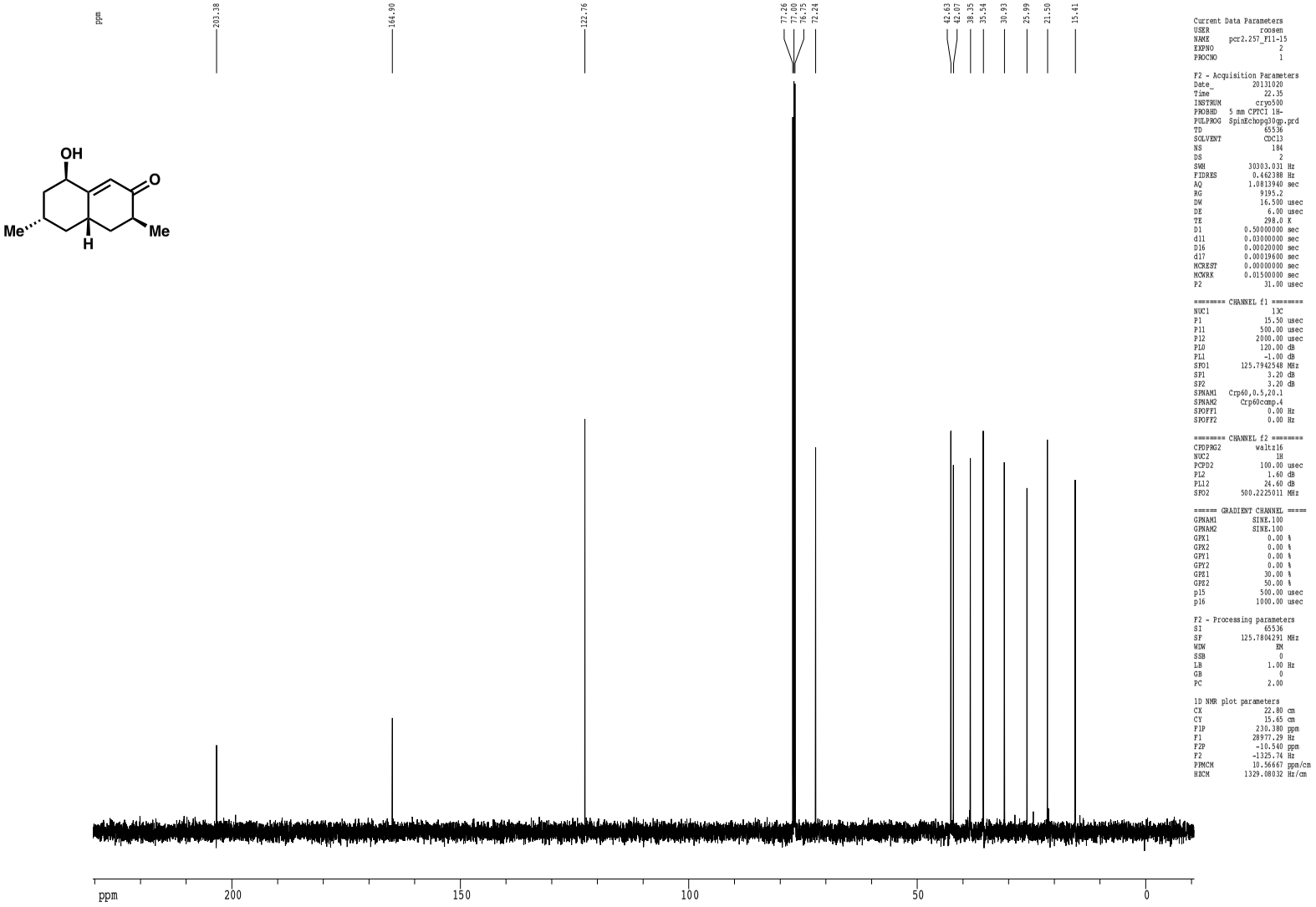

```
Current Data Parameters
USER                roosen
NAME          pcr2.265_hmpa
EXPNO                    2
PROCNO                   1

F2 - Acquisition Parameters
Date_              20131024
Time                 18.24
INSTRUM            cryo500
PROBHD    5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD                   65536
SOLVENT              CDCl3
NS                     104
DS                       2
SWH              30303.031 Hz
FIDRES           0.462388 Hz
AQ               1.0813940 sec
RG                  2896.3
DW                 16.500 usec
DE                  6.00 usec
TE                 298.0 K
D1              0.25000000 sec
d11             0.03000000 sec
D16             0.00020000 sec
d17             0.00019600 sec
MCREST          0.00000000 sec
MCWRK           0.01500000 sec
P2                 31.00 usec

======= CHANNEL f1 =======
NUC1                   13C
P1                 15.50 usec
P11               500.00 usec
P12              2000.00 usec
PL0                120.00 dB
PL1                 -1.00 dB
SFO1          125.7942548 MHz
SP1                 3.20 dB
SP2                 3.20 dB
SPNAM1    Crp60,0.5,20.1
SPNAM2       Crp60comp.4
SFOFF1               0.00 Hz
SFOFF2               0.00 Hz

======= CHANNEL f2 =======
CPDPRG2           waltz16
NUC2                   1H
PCPD2             100.00 usec
PL2                 1.60 dB
PL12               24.60 dB
SFO2         500.2225011 MHz

===== GRADIENT CHANNEL ====
GPNAM1           SINE.100
GPNAM2           SINE.100
GPX1                0.00 %
GPX2                0.00 %
GPY1                0.00 %
GPY2                0.00 %
GPZ1               30.00 %
GPZ2               50.00 %
p15               500.00 usec
p16              1000.00 usec

F2 - Processing parameters
SI                   65536
SF            125.7804300 MHz
WDW                    EM
SSB                     0
LB                  1.00 Hz
GB                      0
PC                  2.00

1D NMR plot parameters
CX                 22.80 cm
CY                 15.65 cm
F1P               230.372 ppm
F1                28976.35 Hz
F2P               -10.548 ppm
F2                -1326.68 Hz
PPMCM             10.56667 ppm/cm
HZCM          1329.08032 Hz/cm
```


1H spectrum
ppm
Me
H
OH
Me
O

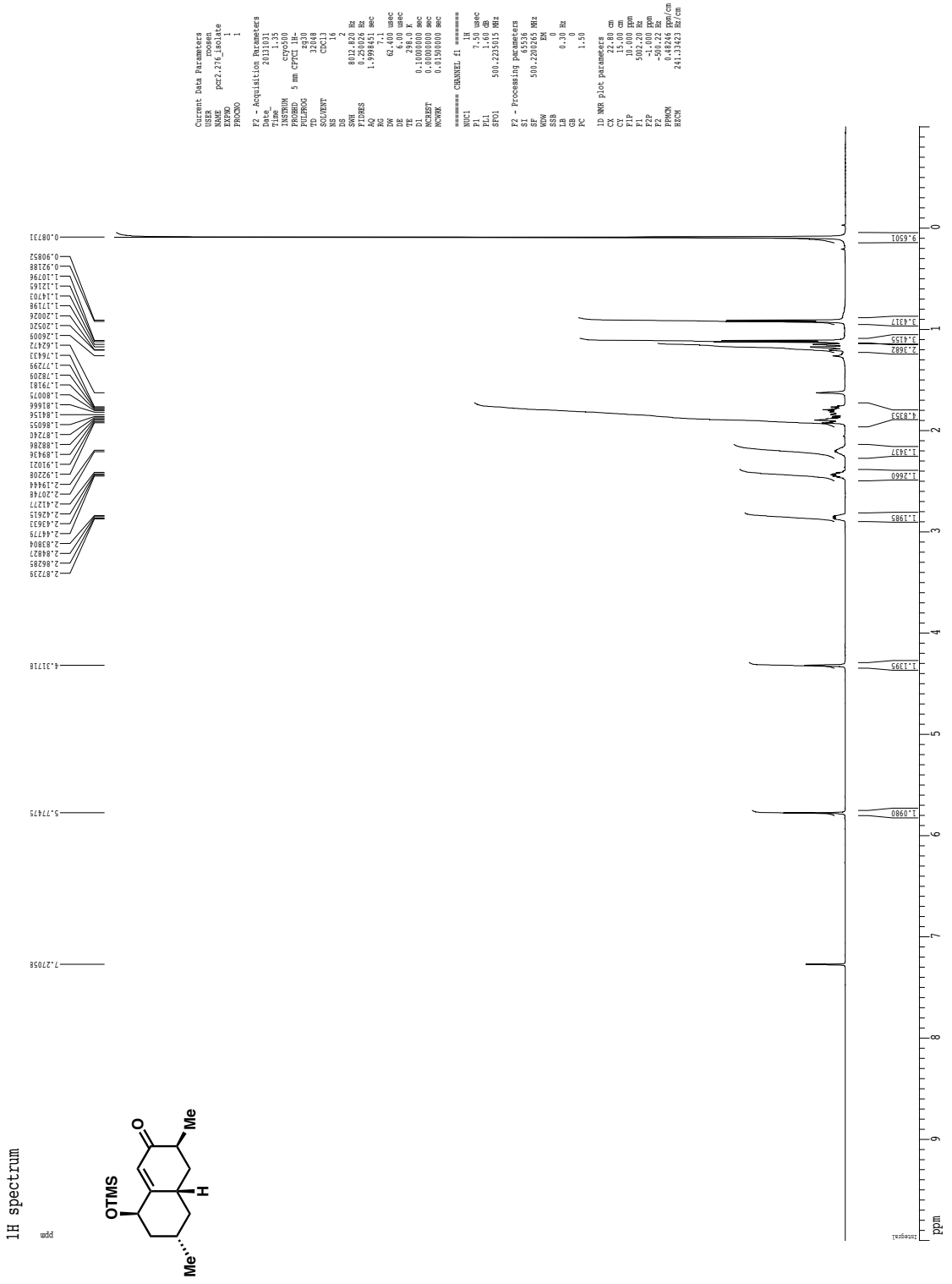

Z-restored spin-echo 13C spectrum with 1H decoupling
ppm
202.68
167.07
122.75
118.47
118.32
77.26
77.01
76.75
72.21
71.33
67.99
45.35
42.89
42.62
42.08
41.76
39.02
38.36
38.18
38.05
35.66
35.63
35.54
34.73
30.92
30.35
30.29
27.41
25.98
21.51
21.28
18.74
15.39
OH
Me
H
Me
0
50
100
150
200
pgm

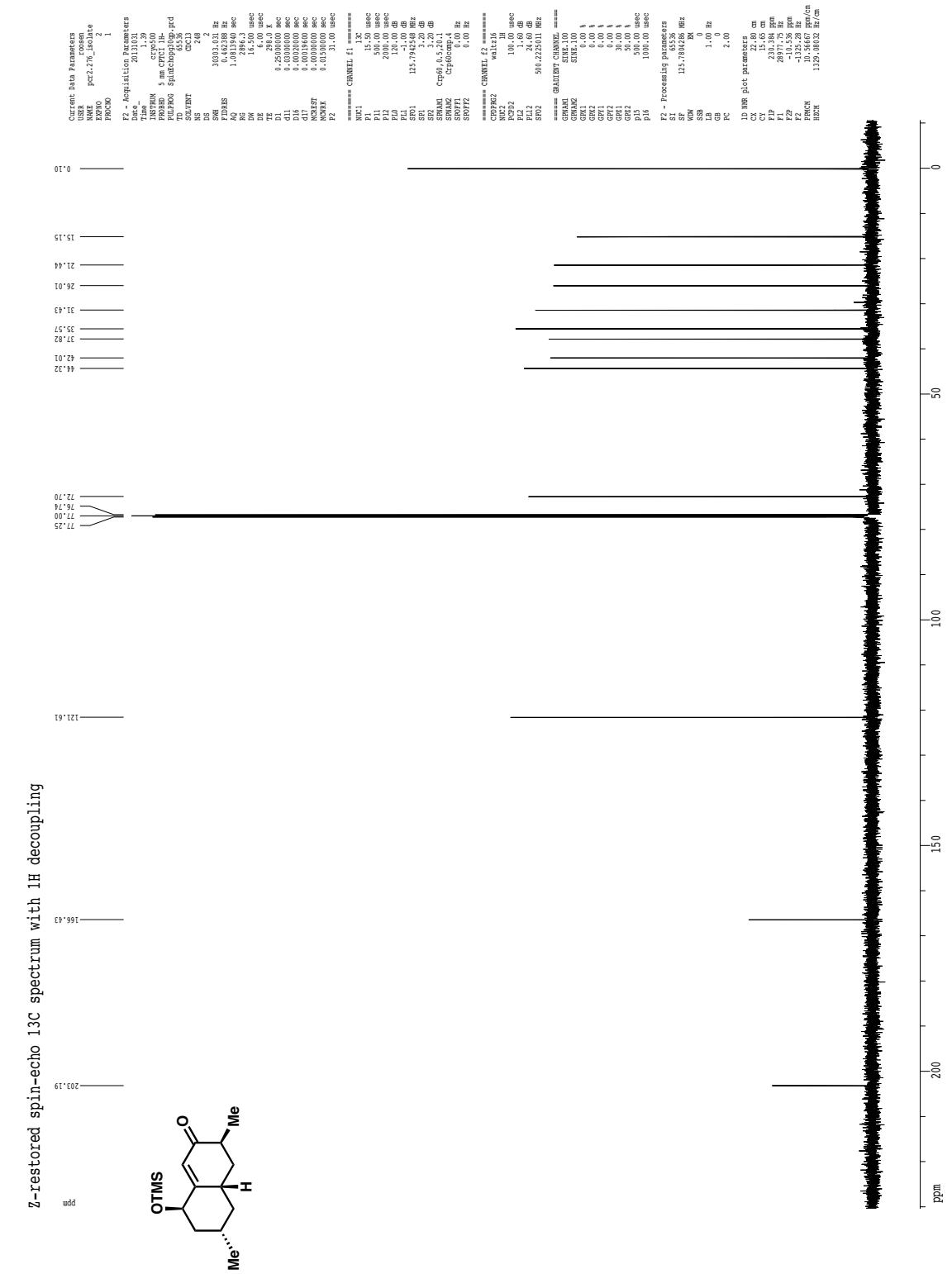

1H spectrum
ppm
Me
OH
H
Me
O

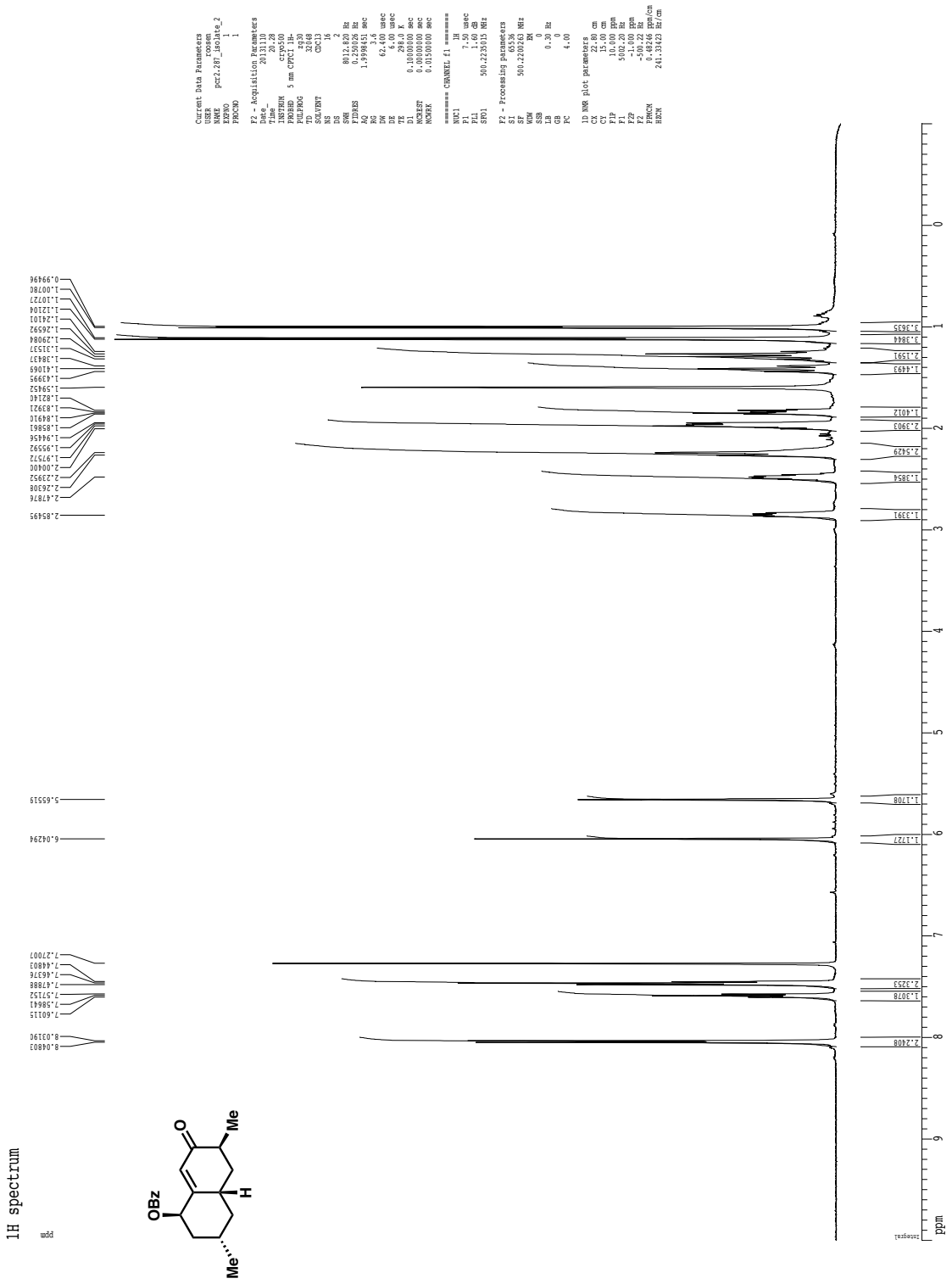
Z-restored spin-echo 13C spectrum with 1H decoupling

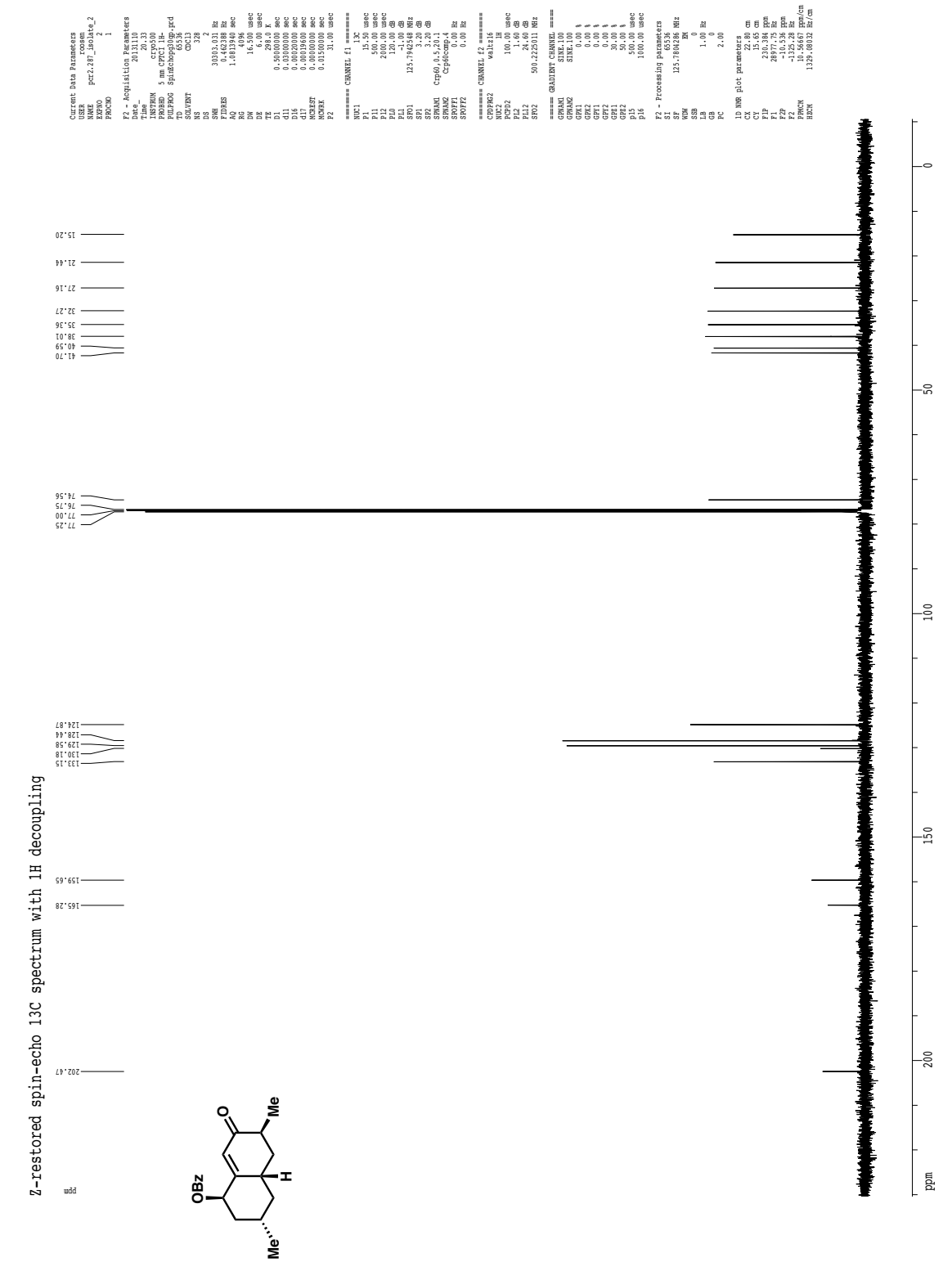


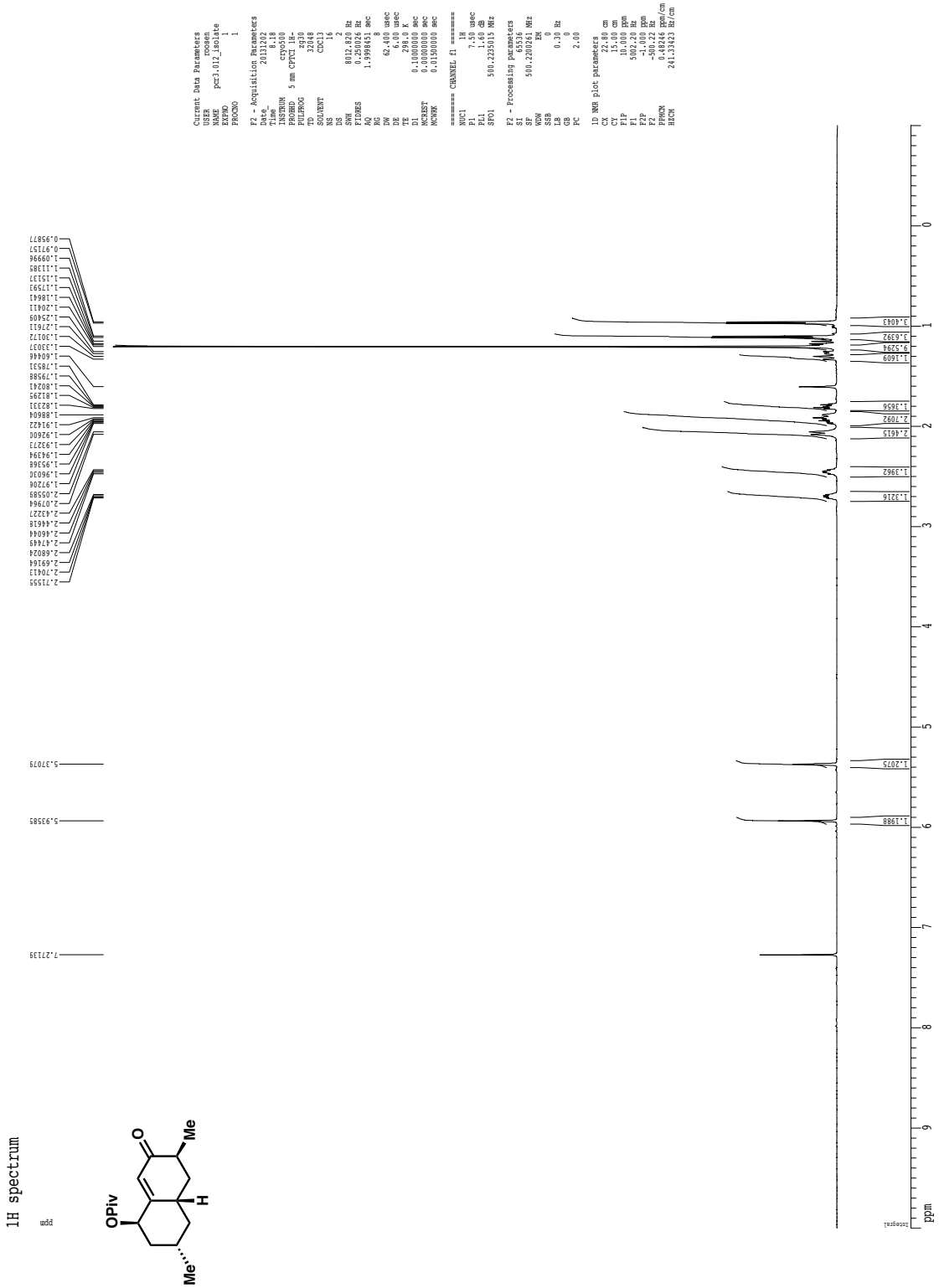

```
Current Data Parameters
USER                roosen
NAME          pcr2.257_F11-15
EXPNO                    2
PROCNO                   1

F2 - Acquisition Parameters
Date_            20131020
Time_               22.35
INSTRUM          cryo500
PROBHD    5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD                  65536
SOLVENT             CDCl3
NS                    184
DS                      2
SWH             30303.031 Hz
FIDRES          0.462388 Hz
AQ              1.0813940 sec
RG                 9195.2
DW                16.500 usec
DE                 6.00 usec
TE                298.0 K
D1             0.50000000 sec
d11            0.03000000 sec
D16            0.00020000 sec
d17            0.00019600 sec
MCREST         0.00000000 sec
MCWRK          0.01500000 sec
P2                31.00 usec

======= CHANNEL f1 =======
NUC1                 13C
P1                15.50 usec
P11              500.00 usec
P12             2000.00 usec
PL0               120.00 dB
PL1                -1.00 dB
SFO1         125.7942548 MHz
SP1                3.20 dB
SP2                3.20 dB
SPNAM1    Crp60,0.5,20.1
SPNAM2       Crp60comp.4
SPOFF1               0.00 Hz
SPOFF2               0.00 Hz

======= CHANNEL f2 =======
CPDPRG2          waltz16
NUC2                 1H
PCPD2             100.00 usec
PL2                1.60 dB
PL12              24.60 dB
SFO2         500.2225011 MHz

===== GRADIENT CHANNEL ====
GPNAM1           SINE.100
GPNAM2           SINE.100
GPX1                0.00 %
GPX2                0.00 %
GPY1                0.00 %
GPY2                0.00 %
GPZ1               30.00 %
GPZ2               50.00 %
p15               500.00 usec
p16              1000.00 usec

F2 - Processing parameters
SI                  65536
SF           125.7804291 MHz
WDW                  EM
SSB                  0
LB                 1.00 Hz
GB                   0
PC                 2.00

1D NMR plot parameters
CX                 22.80 cm
CY                 15.65 cm
F1P               230.380 ppm
F1                28977.29 Hz
F2P               -10.540 ppm
F2                -1325.74 Hz
PPMCM             10.56667 ppm/cm
HZCM          1329.08032 Hz/cm
```


1H spectrum
ppm
OTMS
Me
H
Me
Current Data Parameters
USER zocesen
NAME pcr2.276_isolate
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20131031
Time 1.35
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 32048
SOLVENT CDCl3
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.250026 Hz
AQ 1.9998451 sec
RG 7.1
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 7.50 usec
PL1 1.50 dB
SFO1 500.2235913 MHz
F2 - Processing parameters
SI 65536
SF 500.2200265 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.50
1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 10.000 ppm
F1 5002.23 Hz
F2P -1.000 ppm
F2 -500.22 Hz
PPMCM 0.48246 ppm/cm
HZCM 241.33423 Hz/cm
0.08731
0.90852
0.92188
1.10796
1.12165
1.14703
1.17198
1.20026
1.20520
1.26009
1.62472
1.76432
1.77299
1.78209
1.79181
1.80075
1.81666
1.84156
1.86055
1.87246
1.88286
1.89436
1.91021
1.92208
2.19444
2.20748
2.41277
2.42615
2.43633
2.44779
2.83804
2.88627
2.88285
2.87239
4.31718
5.77475
7.27058
9.6501
3.4317
3.4155
2.3682
4.8353
1.3437
1.2660
1.1985
1.1395
1.0980
ppm

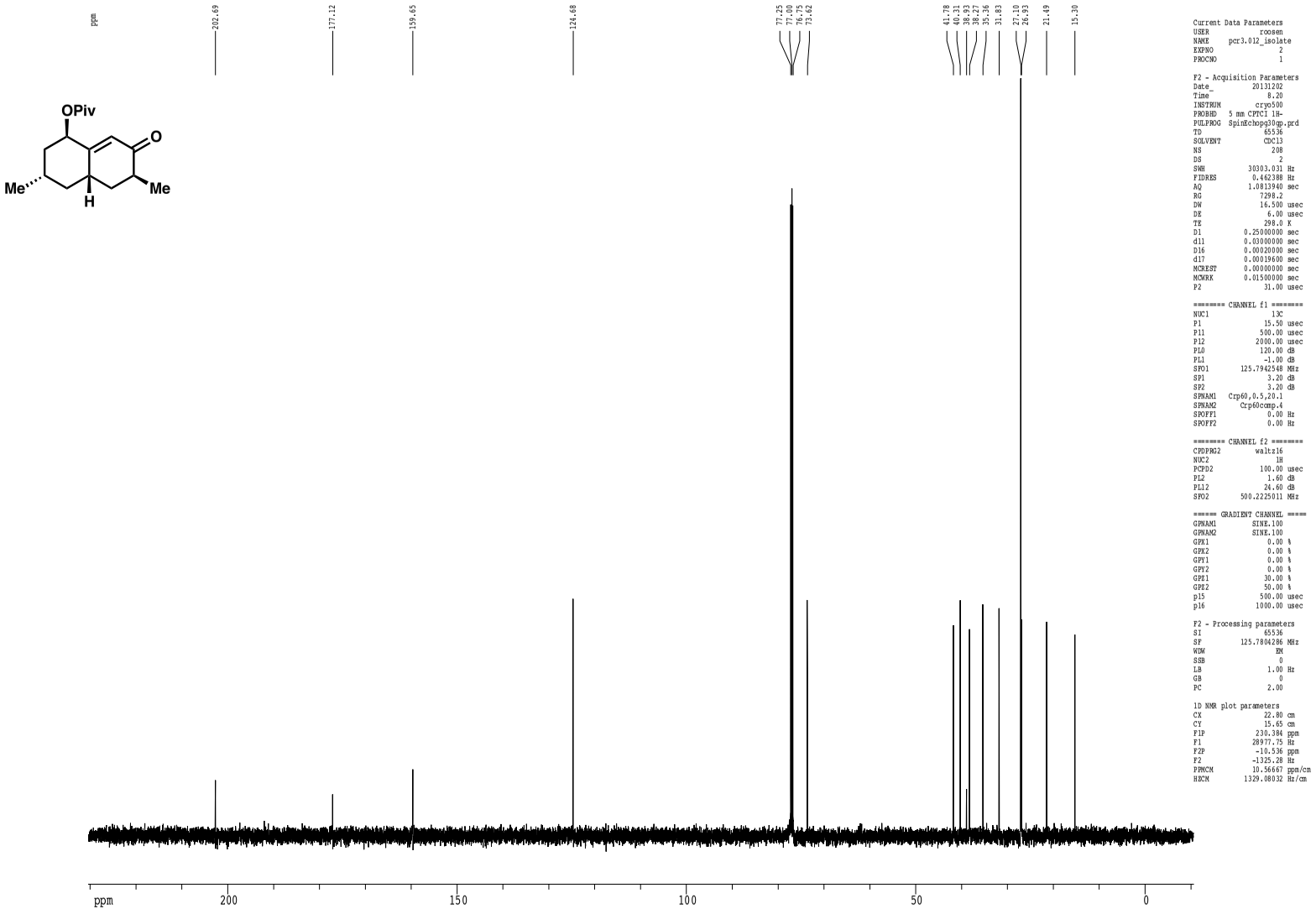

Z-restored spin-echo 13C spectrum with 1H decoupling
OTMS
Me
H
Me
ppm


1H spectrum
ppm
OBz
Me
H
Me
O

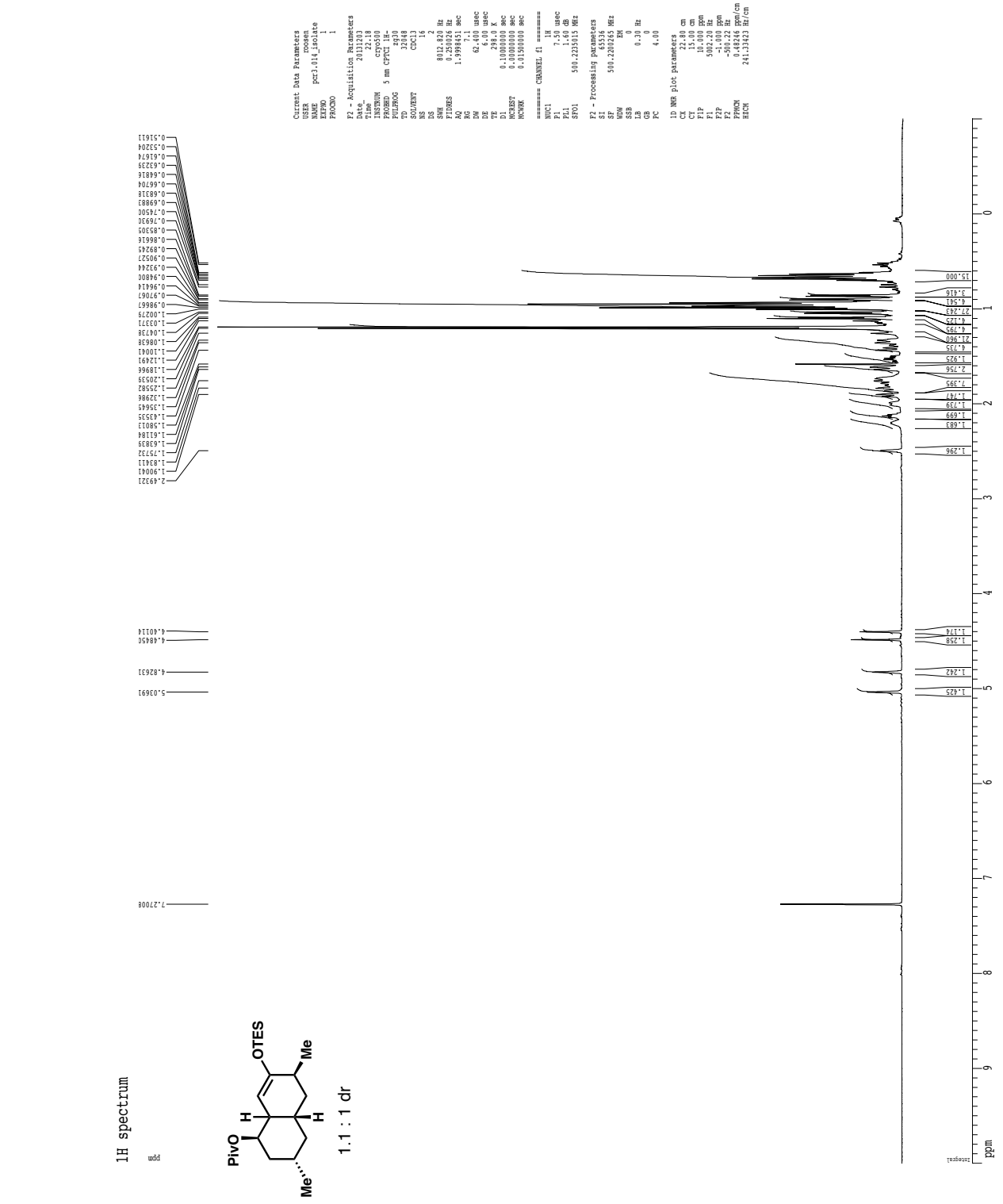

Z-restored spin-echo 13C spectrum with 1H decoupling
ppm
OBz
Me
H
Me
202.47
165.28
159.65
133.15
130.18
129.58
128.44
124.87
77.25
76.75
77.00
74.56
41.70
40.59
38.01
35.36
32.27
27.16
21.44
15.20
0
50
100
150
200
ppm


1H spectrum
ppm
OPiv
O
Me
H
Me
Current Data Parameters
USER zocosen
NAME pcr3.012_isolate
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20131202
Time 8.18
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 32048
SOLVENT CDCl3
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.250026 Hz
AQ 1.9998451 sec
RG 64
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======= CHANNEL f1 =======
NUC1 1H
P1 7.50 usec
PL1 1.50 dB
SFO1 500.2235913 MHz
F2 - Processing parameters
SI 65536
SF 500.2200241 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 2.00
1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 10.000 ppm
F1 5002.23 Hz
F2P -1.000 ppm
F2 -500.22 Hz
PPMCM 0.48246 ppm/cm
HZCM 241.33423 Hz/cm
7.27139
5.93585
5.37079
2.71555
2.70613
2.69164
2.68024
2.67449
2.66044
2.65048
2.44618
2.43227
2.07964
2.05589
1.97206
1.96030
1.95368
1.94394
1.93273
1.92600
1.91422
1.88604
1.82231
1.81295
1.80241
1.79588
1.78531
1.60446
1.33037
1.30172
1.27611
1.25609
1.20411
1.17593
1.15137
1.11385
0.99996
0.97157
0.95877
1.2075
1.1988
3.4043
3.6392
9.5294
1.1609
1.3656
2.7092
2.4615
1.3962
1.3216
ppm

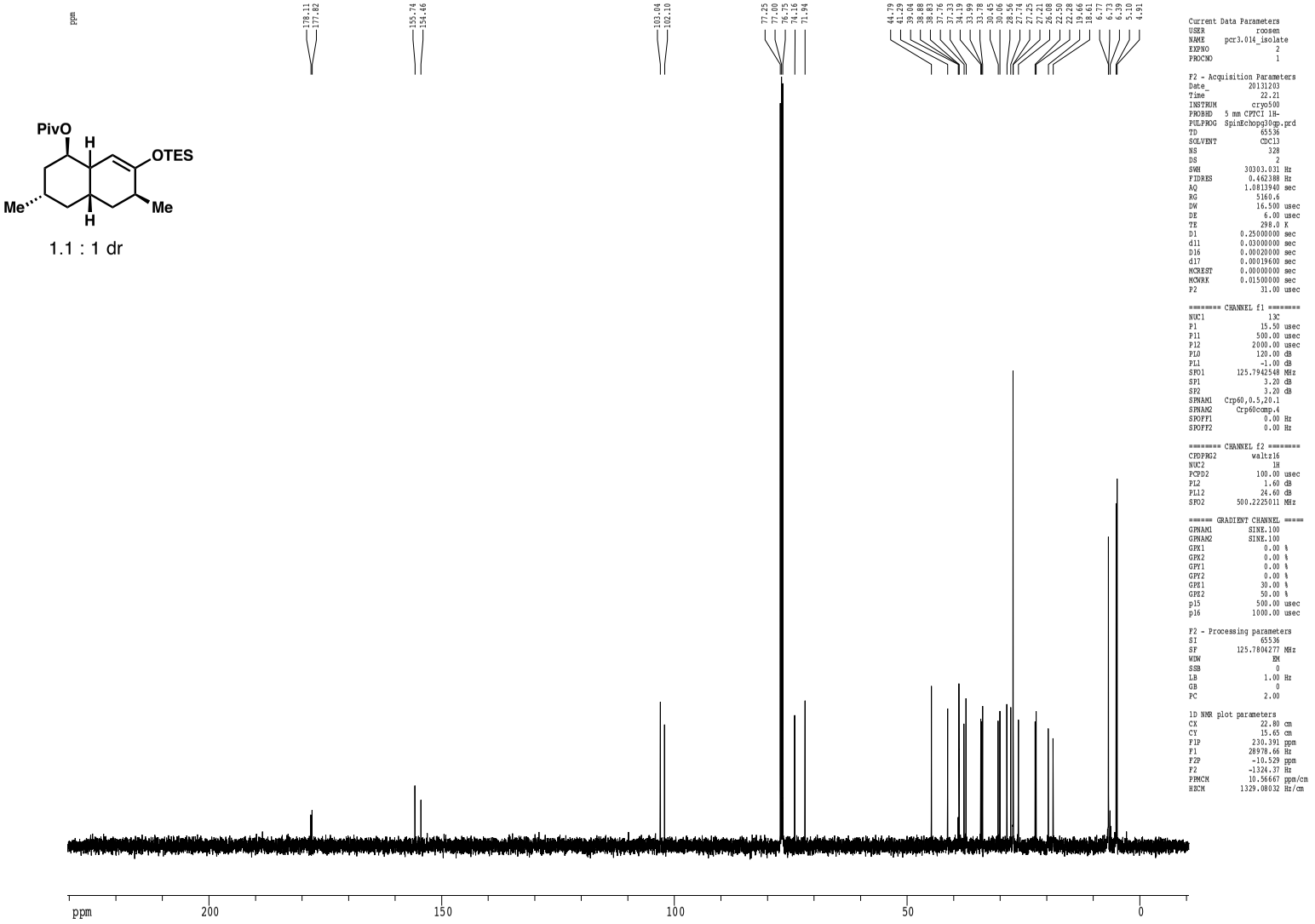
Z-restored spin-echo 13C spectrum with 1H decoupling




```
Current Data Parameters
USER                 roosen
NAME          pcr3.012_isolate
EXPNO                      2
PROCNO                     1

F2 - Acquisition Parameters
Date_              20131202
Time                   8.20
INSTRUM             cryo500
PROBHD    5 mm CPTCI 1H-
PULPROG   SpinEchopg30gp.prd
TD                     65536
SOLVENT                CDCl3
NS                       208
DS                         2
SWH                30303.031 Hz
FIDRES              0.462388 Hz
AQ                  1.0813940 sec
RG                     7298.2
DW                    16.500 usec
DE                     6.00 usec
TE                     298.0 K
D1                 0.25000000 sec
d11                0.03000000 sec
D16                0.00020000 sec
d17                0.00019600 sec
MCREST             0.00000000 sec
MCWRK              0.01500000 sec
P2                    31.00 usec

======= CHANNEL f1 =======
NUC1                      13C
P1                    15.50 usec
P11                  500.00 usec
P12                 2000.00 usec
PL0                  120.00 dB
PL1                   -1.00 dB
SFO1           125.7942548 MHz
SP1                   3.20 dB
SP2                   3.20 dB
SPNAM1    Crp60,0.5,20.1
SPNAM2       Crp60comp.4
SFOFF1                0.00 Hz
SFOFF2                0.00 Hz

======= CHANNEL f2 =======
CPDPRG2             waltz16
NUC2                      1H
PCPD2                100.00 usec
PL2                   1.60 dB
PL12                 24.60 dB
SFO2           500.2225011 MHz

===== GRADIENT CHANNEL ====
GPNAM1              SINE.100
GPNAM2              SINE.100
GPX1                  0.00 %
GPX2                  0.00 %
GPY1                  0.00 %
GPY2                  0.00 %
GPZ1                 30.00 %
GPZ2                 50.00 %
p15                 500.00 usec
p16                1000.00 usec

F2 - Processing parameters
SI                     65536
SF             125.7804286 MHz
WDW                       EM
SSB                        0
LB                    1.00 Hz
GB                         0
PC                    2.00

1D NMR plot parameters
CX                   22.80 cm
CY                   15.65 cm
F1P                 230.384 ppm
F1                  28977.75 Hz
F2P                 -10.536 ppm
F2                 -1325.28 Hz
PPMCM              10.56667 ppm/cm
HZCM             1329.08032 Hz/cm
```


1H spectrum
PivO
H
OTES
Me
H
Me
1.1 : 1 dr

Z-restored spin-echo 13C spectrum with 1H decoupling



Current Data Parameters
USER roosen
NAME pcr3.014_isolate
EXPNO 2
PROCNO 1

F2 - Acquisition Parameters
Date_ 20131203
Time 22.21
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG SpinEchopg30gp.prd
TD 65536
SOLVENT CDCl3
NS 328
DS 2
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0813940 sec
RG 5160.6
DW 16.500 usec
DE 6.00 usec
TE 298.0 K
D1 0.25000000 sec
d11 0.03000000 sec
D16 0.00020000 sec
d17 0.00019600 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
P2 31.00 usec

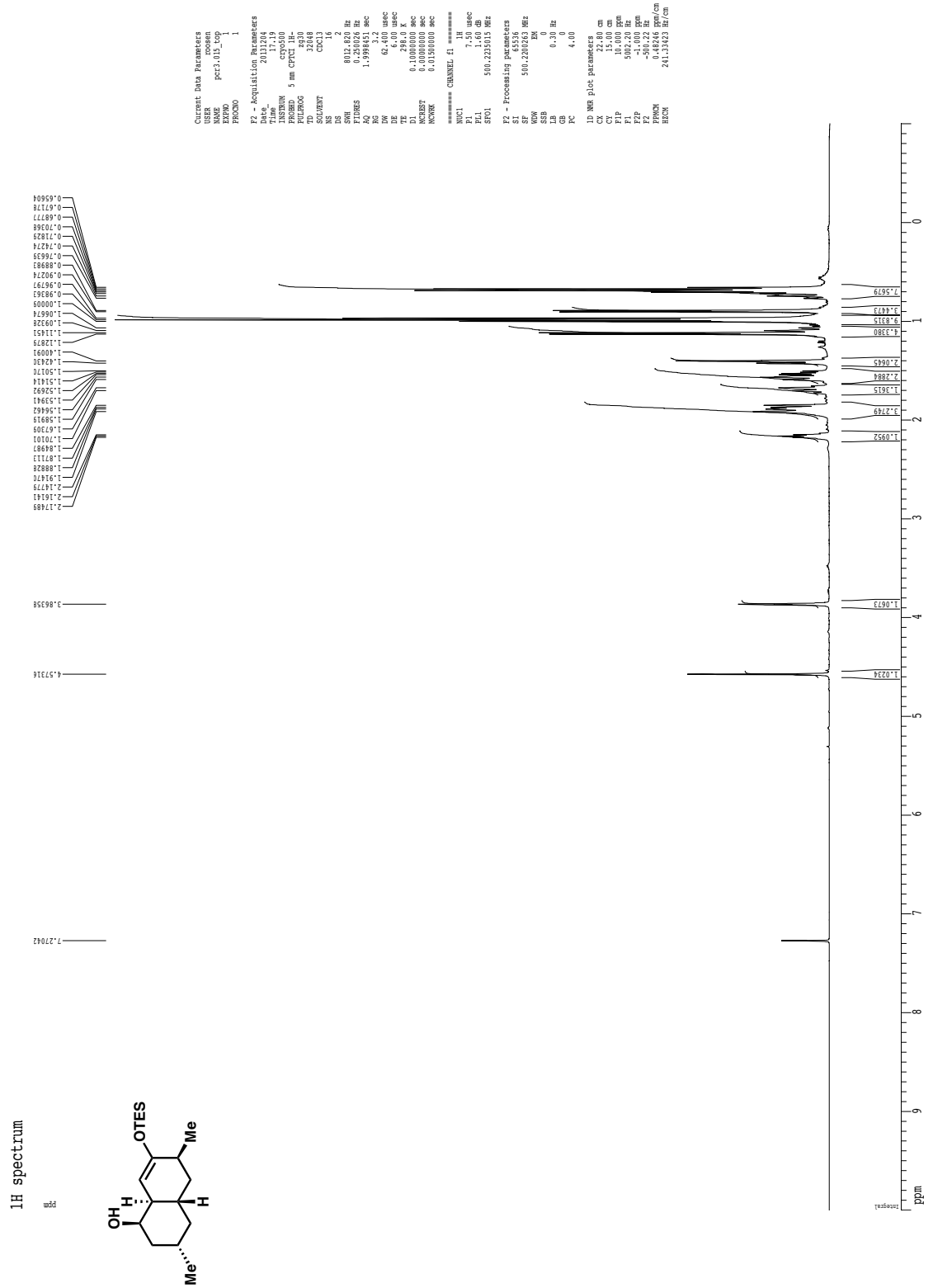
======= CHANNEL f1 =======
NUC1 13C
P1 15.50 usec
P11 500.00 usec
P12 2000.00 usec
PL0 120.00 dB
PL1 -1.00 dB
SFO1 125.7942548 MHz
SP1 3.20 dB
SP2 3.20 dB
SPNAM1 Crp60,0.5,20.1
SPNAM2 Crp60comp.4
SFOFF1 0.00 Hz
SFOFF2 0.00 Hz

======= CHANNEL f2 =======
CPDPRG2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 1.60 dB
PL12 24.60 dB
SFO2 500.2225011 MHz

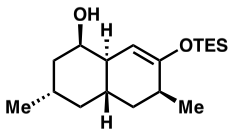
===== GRADIENT CHANNEL ====
GPNAM1 SINE.100
GPNAM2 SINE.100
GPX1 0.00 %
GPX2 0.00 %
GPY1 0.00 %
GPY2 0.00 %
GPZ1 30.00 %
GPZ2 50.00 %
p15 500.00 usec
p16 1000.00 usec

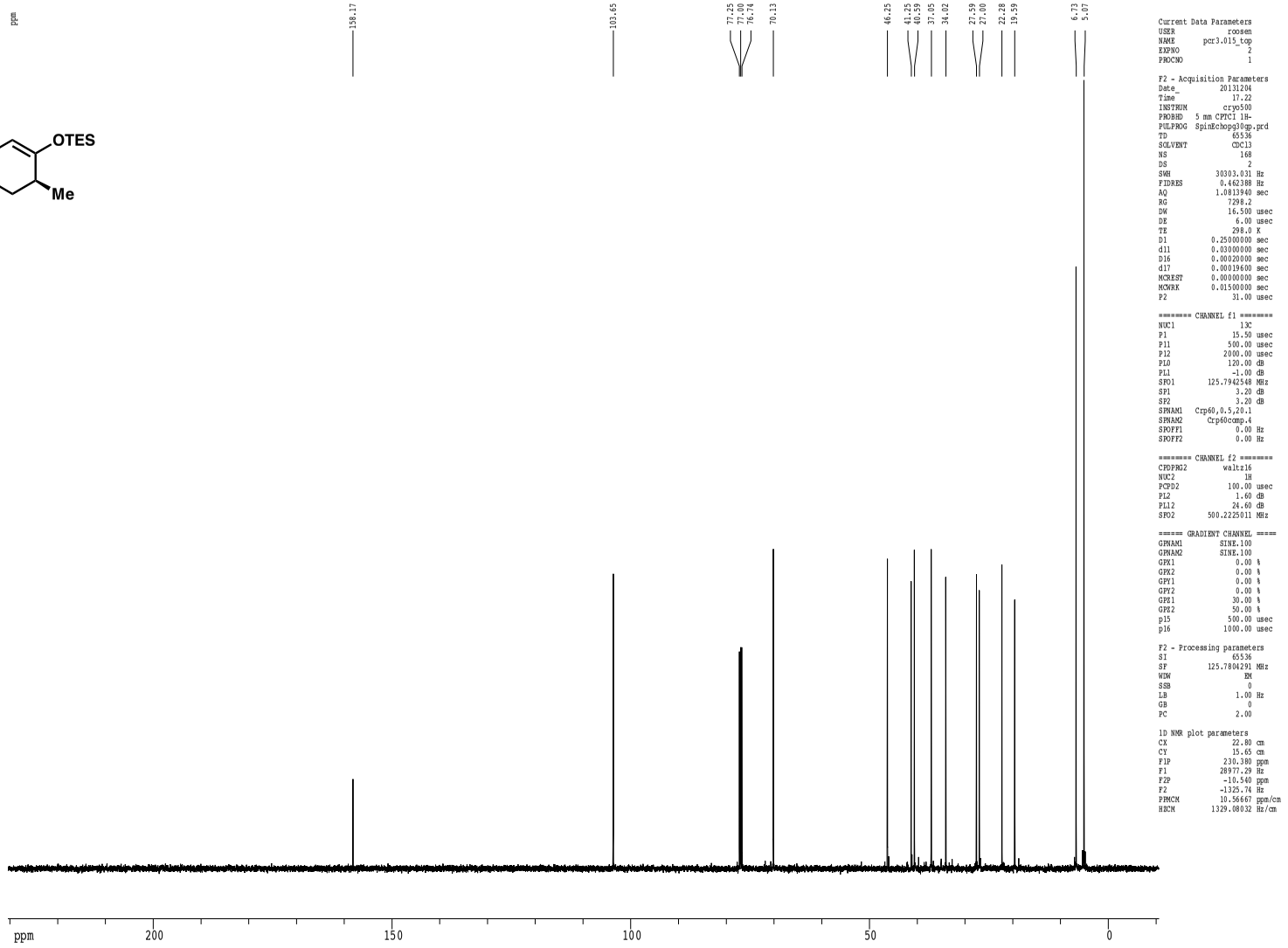
F2 - Processing parameters
SI 65536
SF 125.7804277 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00

1D NMR plot parameters
CX 22.80 cm
CY 15.65 cm
F1P 230.391 ppm
F1 28978.66 Hz
F2P -10.529 ppm
F2 -1324.37 Hz
PPMCM 10.56667 ppm/cm
HZCM 1329.08032 Hz/cm

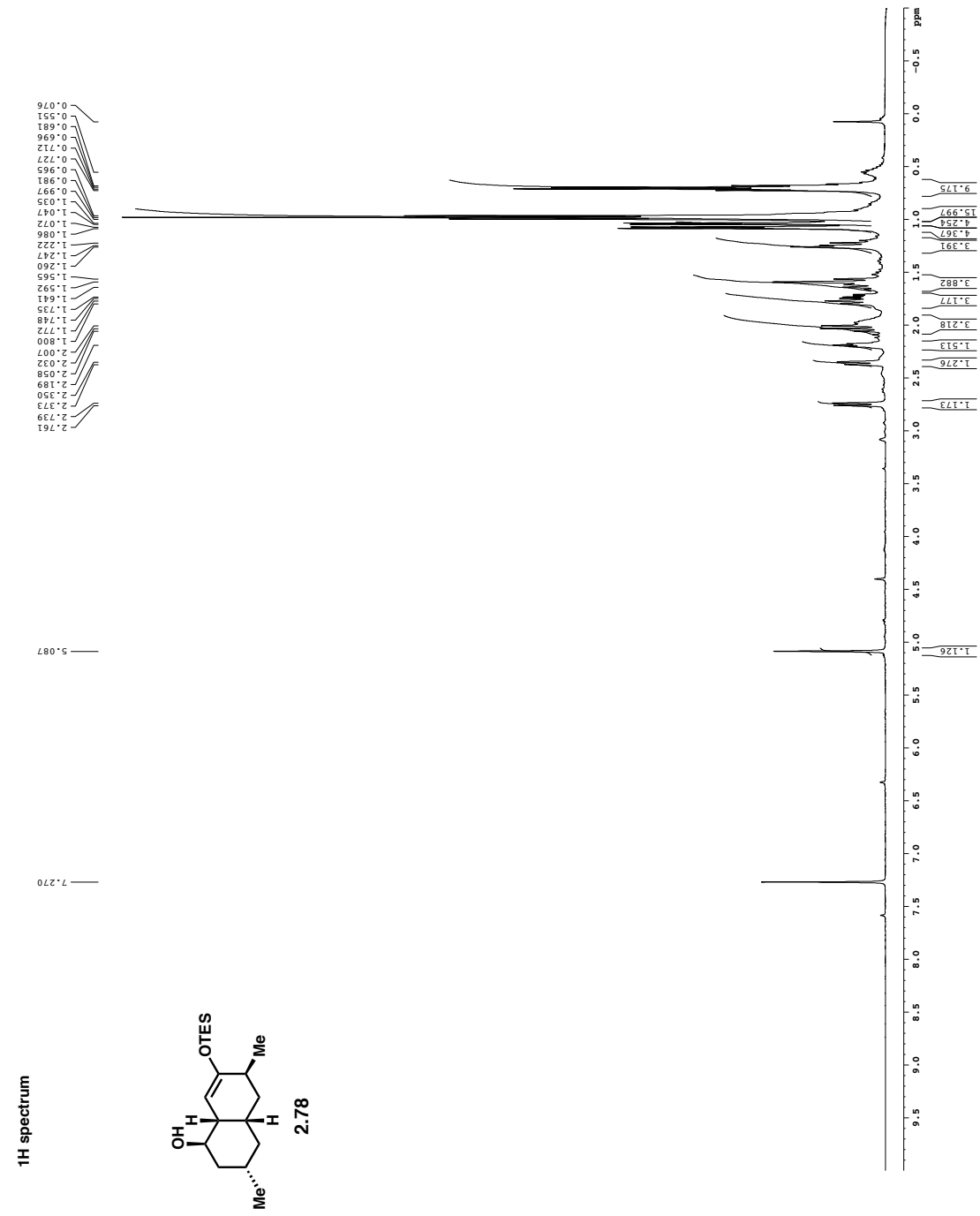

1H spectrum
ppm
OTES
Me
H
OH
H
Me
Current Data Parameters
USER zcosen
NAME pcr3.015_top
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20131204
Time 17:19
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 32048
SOLVENT CDCl3
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.250026 Hz
AQ 1.9998451 sec
RG 3.2
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======= CHANNEL f1 =======
NUC1 1H
P1 7.50 usec
PL1 1.40 dB
SFO1 500.2235913 MHz
F2 - Processing parameters
SI 65536
SF 500.2200262 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00
1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 10.000 ppm
F1 5002.23 Hz
F2P -1.000 ppm
F2 -500.22 Hz
PPMCM 0.48246 ppm/cm
HZCM 241.33423 Hz/cm
7.27042
4.57316
3.86358
2.17489
2.16141
2.14779
1.91470
1.88828
1.87113
1.85987
1.70101
1.67309
1.58919
1.56462
1.53961
1.52692
1.51414
1.50170
1.42430
1.40091
1.13879
1.11451
1.09328
1.06674
1.00009
0.98363
0.96797
0.88983
0.90274
0.76639
0.74274
0.71829
0.70368
0.68977
0.67178
0.65604
7.5679
5.4473
4.8315
4.3380
2.0645
2.2884
1.3615
3.2749
1.0952
1.0673
1.0234
ppm

Z-restored spin-echo 13C spectrum with 1H decoupling





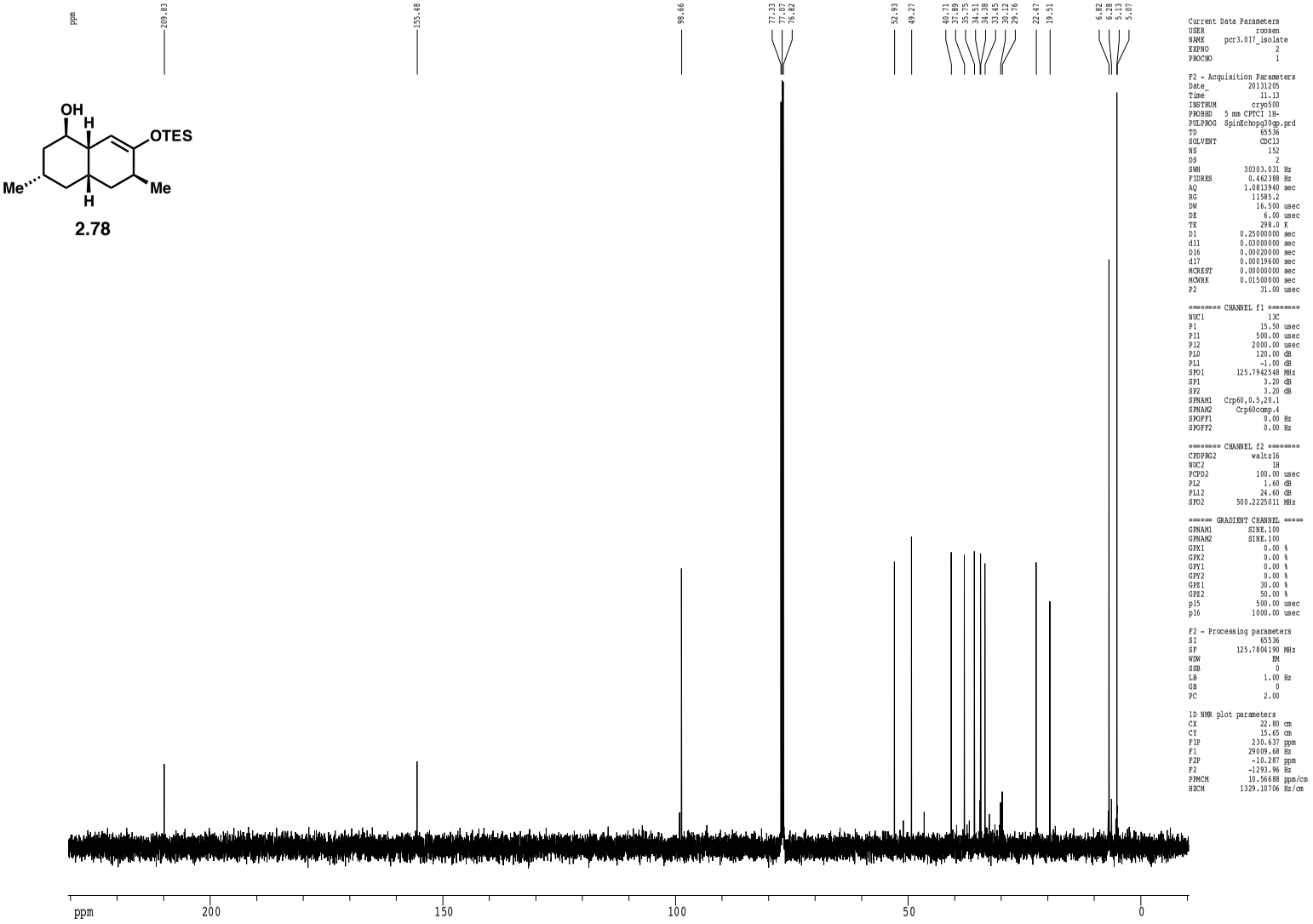

```
Current Data Parameters
USER              roosen
NAME        pcr3.015_top
EXPNO                   2
PROCNO                  1

F2 - Acquisition Parameters
Date_          20131204
Time               17.22
INSTRUM          cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD                 65536
SOLVENT            CDCl3
NS                   168
DS                     2
SWH            30303.031 Hz
FIDRES         0.462388 Hz
AQ             1.0813940 sec
RG                7298.2
DW                16.500 usec
DE                 6.00 usec
TE                298.0 K
D1           0.25000000 sec
d11          0.03000000 sec
D16          0.00020000 sec
d17          0.00019600 sec
MCREST       0.00000000 sec
MCWRK        0.01500000 sec
P2                31.00 usec

======= CHANNEL f1 =======
NUC1                13C
P1                15.50 usec
P11              500.00 usec
P12             2000.00 usec
PL0              120.00 dB
PL1               -1.00 dB
SFO1         125.7942548 MHz
SP1               3.20 dB
SP2               3.20 dB
SPNAM1   Crp60,0.5,20.1
SPNAM2      Crp60comp.4
SPOFF1               0.00 Hz
SPOFF2               0.00 Hz

======= CHANNEL f2 =======
CPDPRG2          waltz16
NUC2                1H
PCPD2            100.00 usec
PL2                1.60 dB
PL12              24.60 dB
SFO2        500.2225011 MHz

===== GRADIENT CHANNEL ====
GPNAM1          SINE.100
GPNAM2          SINE.100
GPX1                0.00 %
GPX2                0.00 %
GPY1                0.00 %
GPY2                0.00 %
GPZ1               30.00 %
GPZ2               50.00 %
p15              500.00 usec
p16             1000.00 usec

F2 - Processing parameters
SI                 65536
SF          125.7804291 MHz
WDW                   EM
SSB                    0
LB                  1.00 Hz
GB                     0
PC                  2.00

1D NMR plot parameters
CX                 22.80 cm
CY                 15.65 cm
F1P               230.380 ppm
F1                28977.29 Hz
F2P               -10.540 ppm
F2                -1325.74 Hz
PPMCM             10.56667 ppm/cm
HZCM          1329.08032 Hz/cm
```



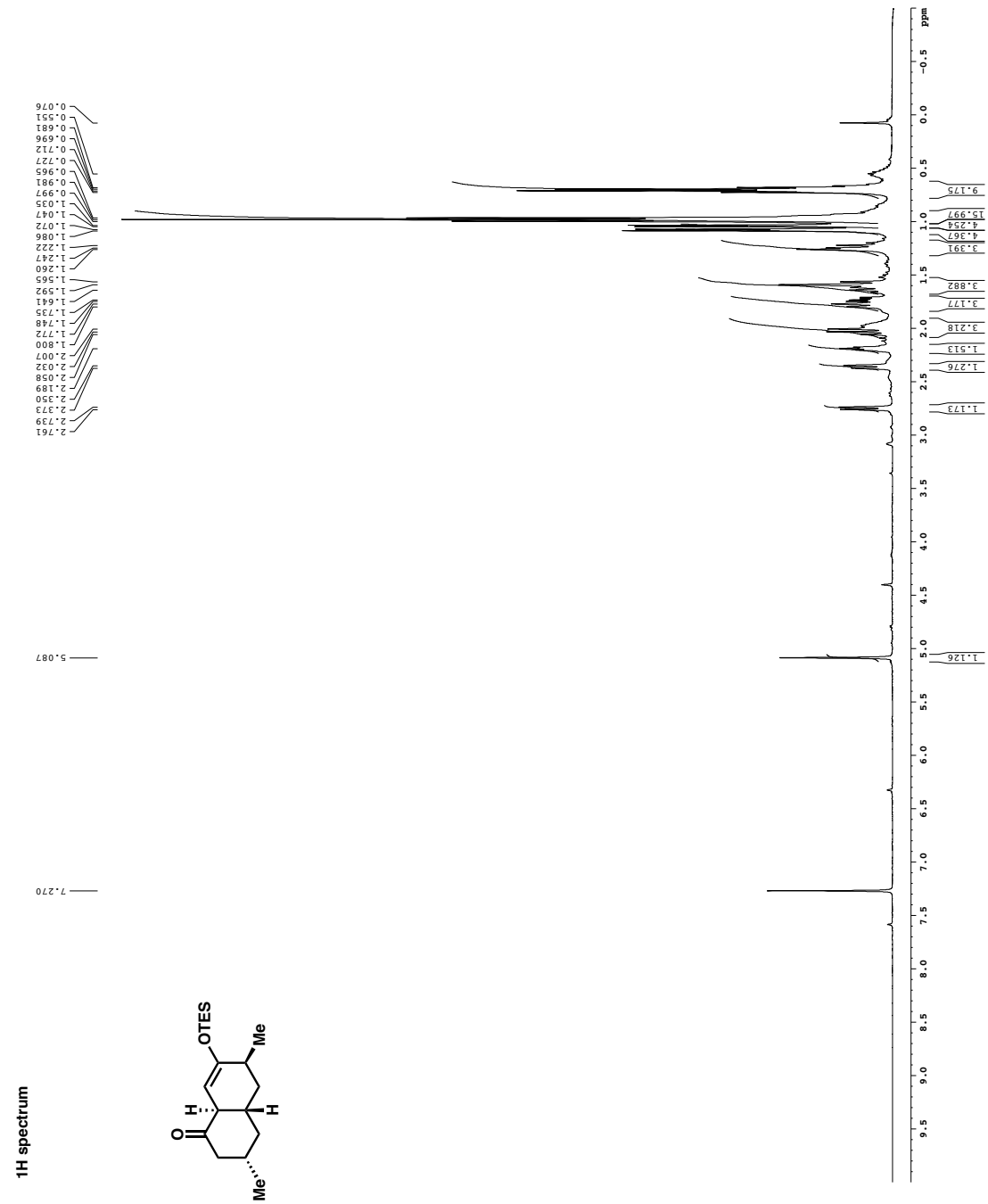
1H spectrum

2.78

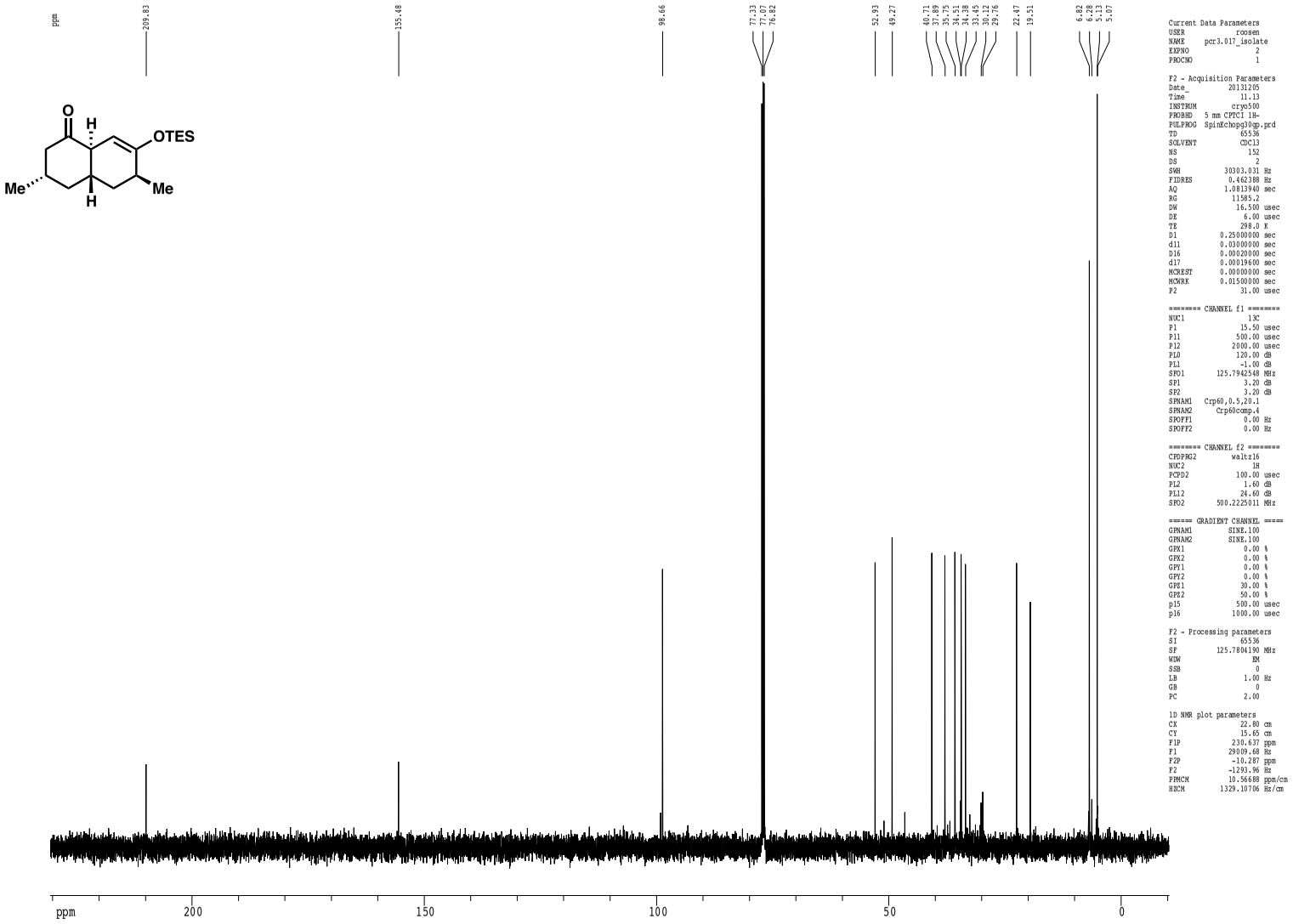
Z-restored spin-echo 13C spectrum with 1H decoupling



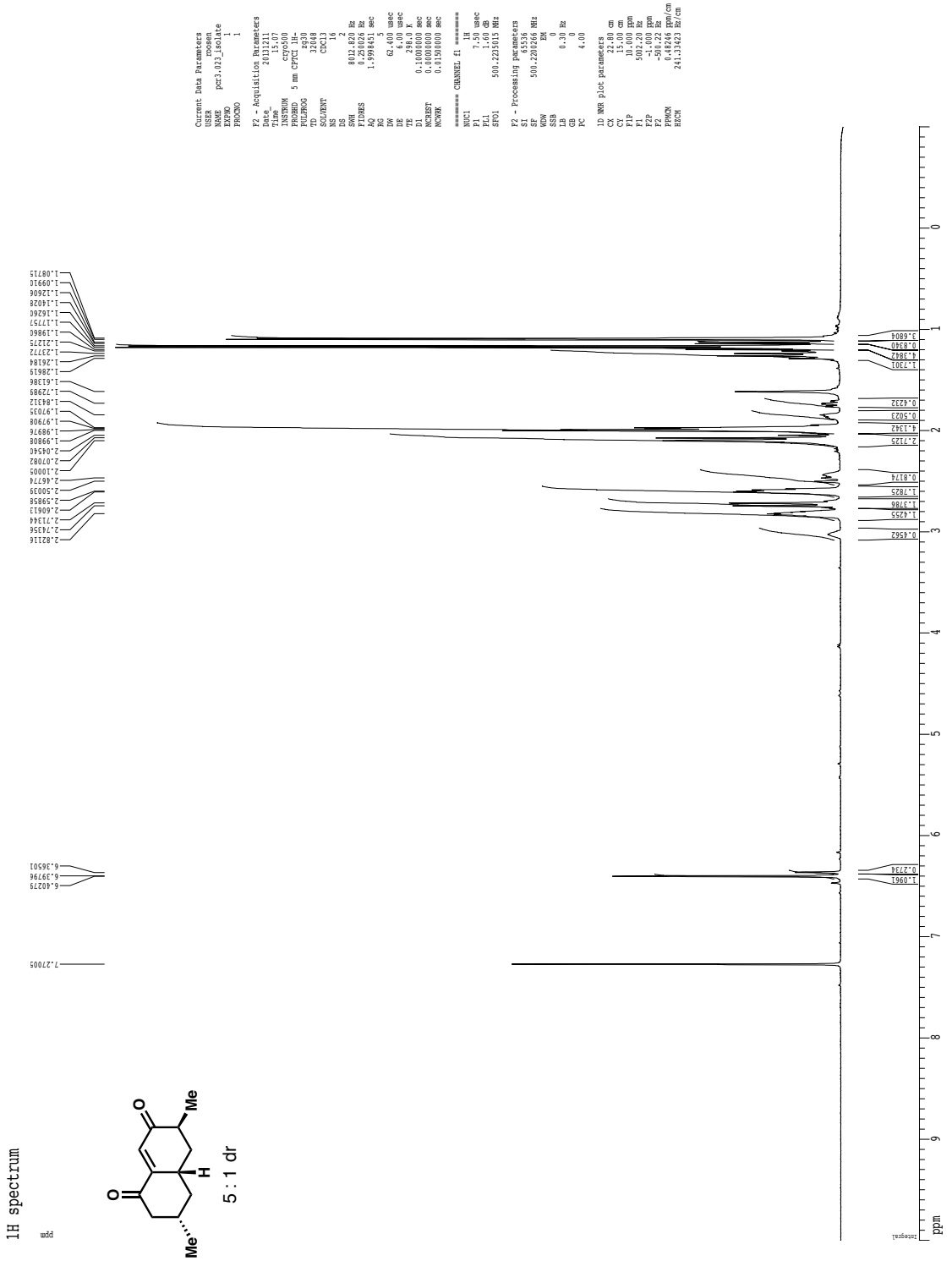

```
Current Data Parameters
USER                roosen
NAME          pcr3.017_isolate
EXPNO                    2
PROCNO                   1

F2 - Acquisition Parameters
Date_              20131205
Time                 11.13
INSTRUM            cryo500
PROBHD    5 mm CPTCI 1H-
PULPROG   SpinEchopg30gp.prd
TD                   65536
SOLVENT              CDCl3
NS                     152
DS                       2
SWH              30303.031 Hz
FIDRES           0.462388 Hz
AQ               1.0813940 sec
RG                 11585.2
DW                 16.500 usec
DE                  6.00 usec
TE                 298.0 K
D1            0.25000000 sec
d11           0.03000000 sec
D16           0.00020000 sec
d17           0.00019600 sec
MCREST        0.00000000 sec
MCWRK         0.01500000 sec
P2                 31.00 usec

======= CHANNEL f1 =======
NUC1                 13C
P1                 15.50 usec
P11               500.00 usec
P12              2000.00 usec
PL0               120.00 dB
PL1                -1.00 dB
SFO1         125.7942548 MHz
SP1                3.20 dB
SP2                3.20 dB
SPNAM1    Crp60,0.5,20.1
SPNAM2       Crp60comp.4
SPOFF1             0.00 Hz
SPOFF2             0.00 Hz

======= CHANNEL f2 =======
CPDPRG2          waltz16
NUC2                 1H
PCPD2             100.00 usec
PL2                1.60 dB
PL12              24.60 dB
SFO2        500.2225011 MHz

===== GRADIENT CHANNEL ====
GPNAM1           SINE.100
GPNAM2           SINE.100
GPX1                0.00 %
GPX2                0.00 %
GPY1                0.00 %
GPY2                0.00 %
GPZ1               30.00 %
GPZ2               50.00 %
p15               500.00 usec
p16              1000.00 usec

F2 - Processing parameters
SI                   65536
SF          125.7804190 MHz
WDW                  EM
SSB                  0
LB                 1.00 Hz
GB                   0
PC                 2.00

1D NMR plot parameters
CX                 22.80 cm
CY                 15.65 cm
F1P               230.637 ppm
F1                29009.68 Hz
F2P               -10.287 ppm
F2               -1293.96 Hz
PPMCM             10.56688 ppm/cm
HZCM           1329.10706 Hz/cm
```


1H spectrum
OTES
Me
H
O
Me
H
Current Data Parameters
USER roosen
NAME pcr3.017_isolate
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20131205
Time 11:11
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.244226 Hz
AQ 1.9998451 sec
RG 4.5
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 7.50 usec
PL1 1.60 dB
SFO1 500.2235015 MHz
F2 - Processing parameters
SI 65536
SF 500.2200066 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00
0.076
0.551
0.681
0.696
0.712
0.727
0.965
0.981
0.997
1.035
1.047
1.072
1.086
1.222
1.247
1.260
1.565
1.592
1.641
1.735
1.748
1.772
1.800
2.007
2.032
2.058
2.189
2.350
2.373
2.739
2.761
5.087
7.270
9.175
15.997
4.254
4.367
3.391
3.882
3.177
3.218
1.513
1.276
1.173
1.126
ppm

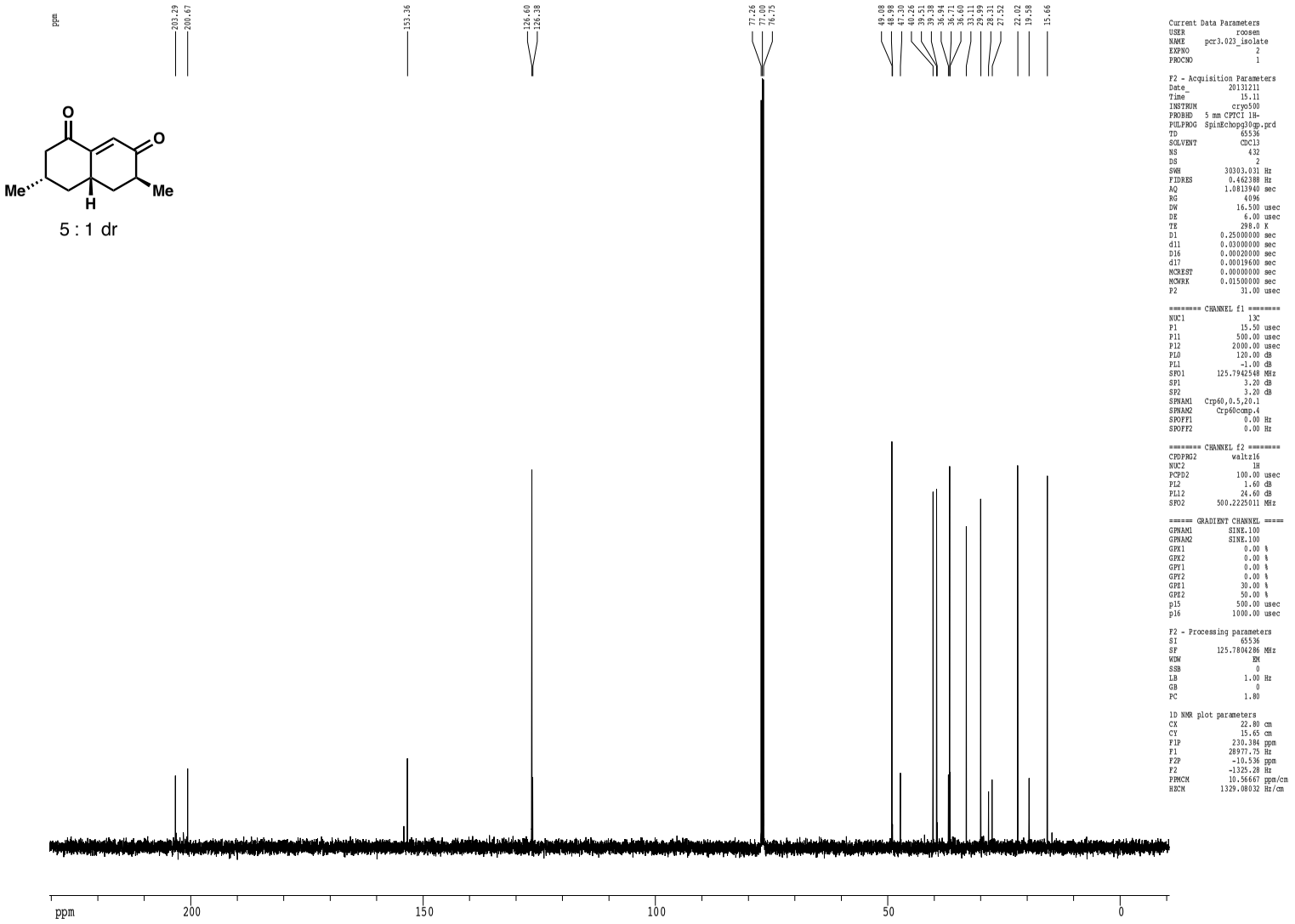
Z-restored spin-echo 13C spectrum with 1H decoupling

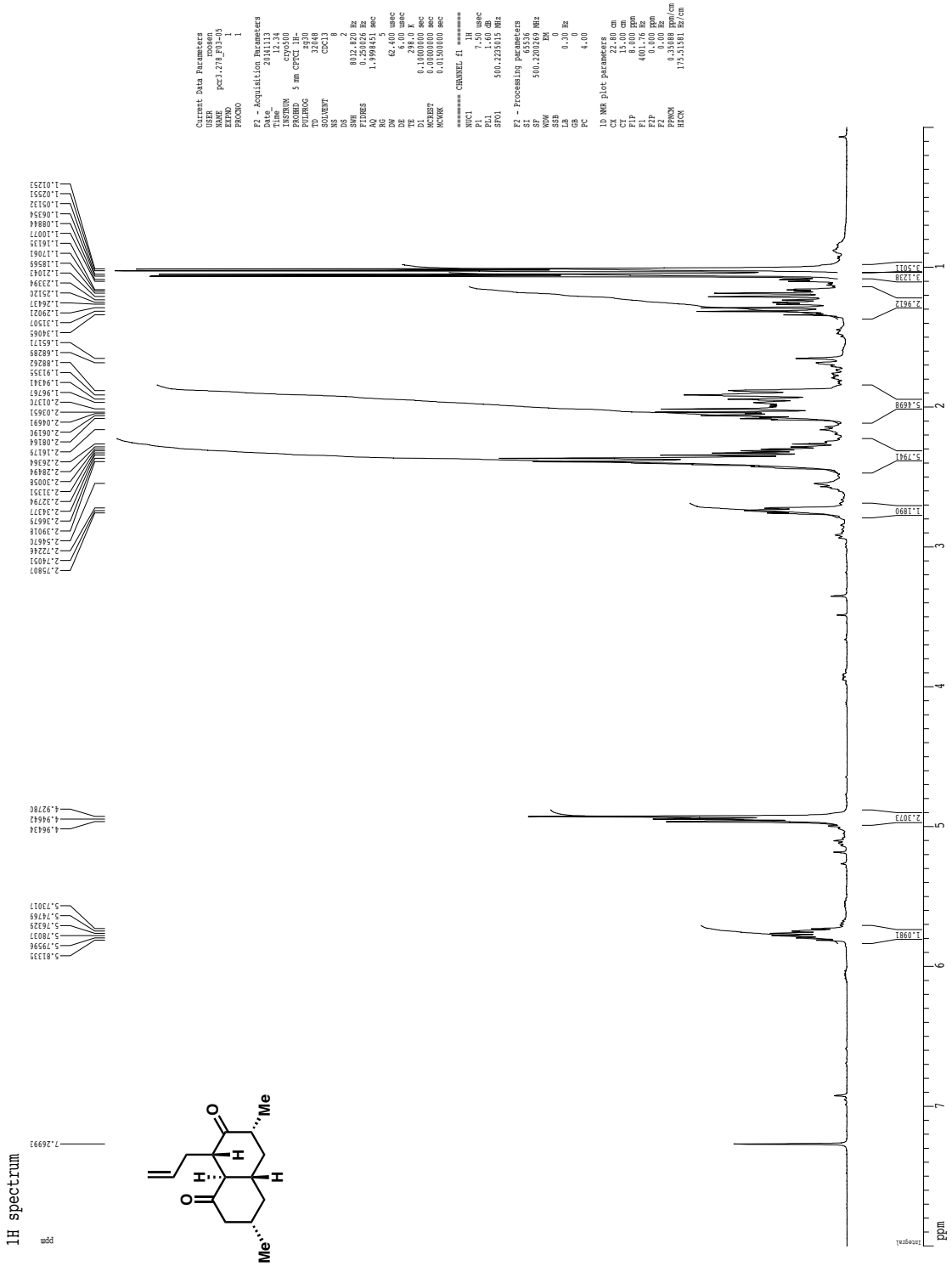



```
Current Data Parameters
USER                roosen
NAME          pcr3.017_isolate
EXPNO                    2
PROCNO                   1

F2 - Acquisition Parameters
Date_              20131205
Time                 11.13
INSTRUM            cryo500
PROBHD    5 mm CPTCI 1H-
PULPROG   SpinEchopg30gp.prd
TD                   65536
SOLVENT              CDCl3
NS                     152
DS                       2
SWH              30303.031 Hz
FIDRES               0.462388 Hz
AQ                1.0813940 sec
RG                  11585.2
DW                   16.500 usec
DE                    6.00 usec
TE                   298.0 K
D1              0.25000000 sec
d11             0.03000000 sec
D16             0.00020000 sec
d17             0.00019600 sec
MCREST          0.00000000 sec
MCWRK           0.01500000 sec
P2                   31.00 usec

======= CHANNEL f1 =======
NUC1                   13C
P1                   15.50 usec
P11                 500.00 usec
P12                2000.00 usec
PL0                 120.00 dB
PL1                  -1.00 dB
SFO1          125.7942548 MHz
SP1                  3.20 dB
SP2                  3.20 dB
SPNAM1    Crp60,0.5,20.1
SPNAM2       Crp60comp.4
SFOFF1               0.00 Hz
SFOFF2               0.00 Hz

======= CHANNEL f2 =======
CPDPRG2            waltz16
NUC2                   1H
PCPD2               100.00 usec
PL2                  1.60 dB
PL12                24.60 dB
SFO2          500.2225011 MHz

===== GRADIENT CHANNEL ====
GPNAM1             SINE.100
GPNAM2             SINE.100
GPX1                 0.00 %
GPX2                 0.00 %
GPY1                 0.00 %
GPY2                 0.00 %
GPZ1                30.00 %
GPZ2                50.00 %
p15                500.00 usec
p16               1000.00 usec

F2 - Processing parameters
SI                   65536
SF            125.7804190 MHz
WDW                    EM
SSB                     0
LB                   1.00 Hz
GB                      0
PC                   2.00

1D NMR plot parameters
CX                   22.80 cm
CY                   15.65 cm
F1P                 230.637 ppm
F1                29009.68 Hz
F2P                -10.287 ppm
F2                -1293.96 Hz
PPMCM             10.56688 ppm/cm
HZCM           1329.10706 Hz/cm
```

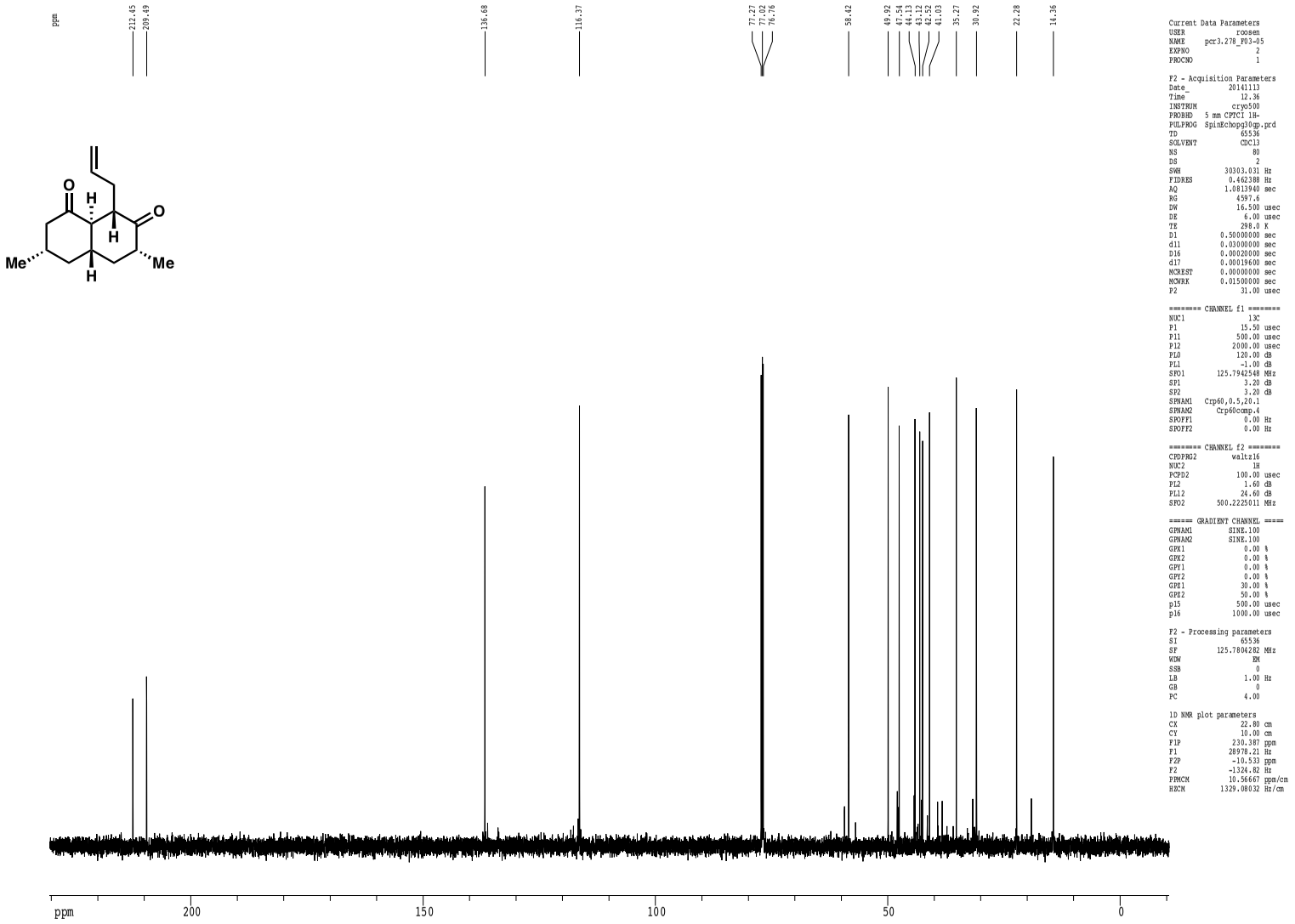

1H spectrum
ppm
5 : 1 dr
Me
H
Me
O
O
Current Data Parameters
USER zocoen
NAME pcr3.023_isolate
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20131211
Time 15.07
INSTRUM crys500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 32048
SOLVENT CDCl3
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.250026 Hz
AQ 1.9998451 sec
RG 64
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======= CHANNEL f1 =======
NUC1 1H
P1 7.50 usec
PL1 1.00 dB
SFO1 500.2235913 MHz
F2 - Processing parameters
SI 65536
SF 500.2200260 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00
1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 10.000 ppm
F1 5002.23 Hz
F2P -1.000 ppm
F2 -500.22 Hz
PPMCM 0.48246 ppm/cm
HZCM 241.33423 Hz/cm
7.27005
6.40279
6.39796
6.36501
2.82116
2.76356
2.71344
2.60613
2.59858
2.50039
2.46774
2.21005
2.07082
2.04540
1.99808
1.98976
1.97908
1.97035
1.84312
1.72989
1.61386
1.28619
1.26184
1.23172
1.21275
1.19860
1.17797
1.16260
1.14606
1.10928
1.08715
3.68604
0.83460
4.38427
1.73015
0.42322
0.50239
4.13427
2.71725
0.81746
1.78279
1.37886
1.42555
0.45627
1.09613
0.27346
ppm

Z-restored spin-echo 13C spectrum with 1H decoupling

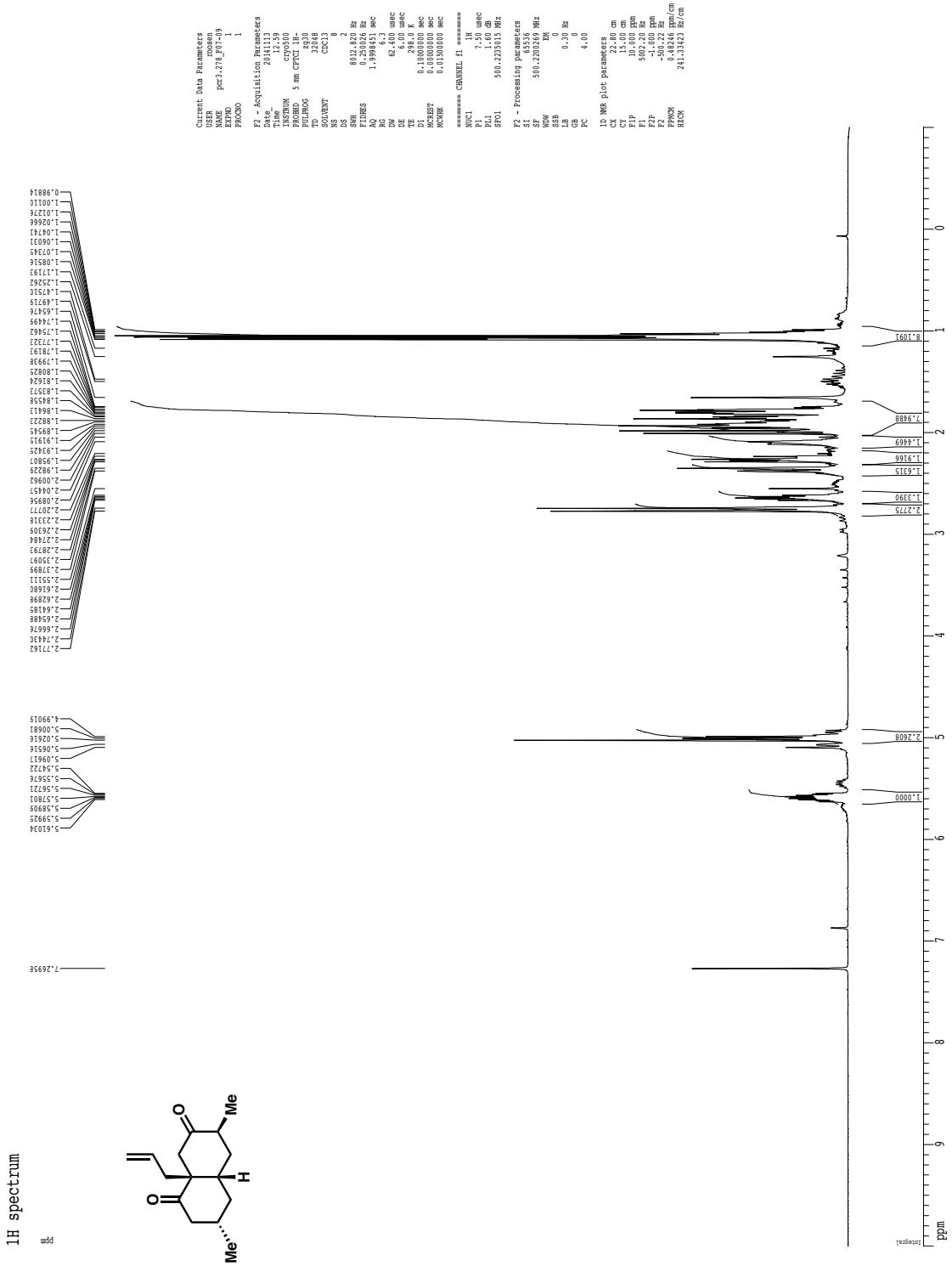



1H spectrum
Current Data Parameters
USER zocoen
NAME pcc3.278_F03-05
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20141113
Time 12.34
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 32048
SOLVENT CDCl3
NS 8
DS 2
SWH 8012.820 Hz
FIDRES 0.250026 Hz
AQ 1.9998451 sec
RG 64
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======= CHANNEL f1 =======
NUC1 1H
P1 7.50 usec
PL1 1.50 dB
SFO1 500.2235913 MHz
F2 - Processing parameters
SI 65536
SF 500.2200269 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00
1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 8.000 ppm
F1 4001.76 Hz
F2P 0.000 ppm
F2 0.00 Hz
PPMCM 0.35088 ppm/cm
HZCM 175.51581 Hz/cm
7.26993
5.81335
5.79596
5.78027
5.76329
5.74769
5.73017
4.96434
4.94642
4.92780
3.5011
3.1238
2.9612
5.4698
5.7941
1.1890
2.3073
1.0981
ppm

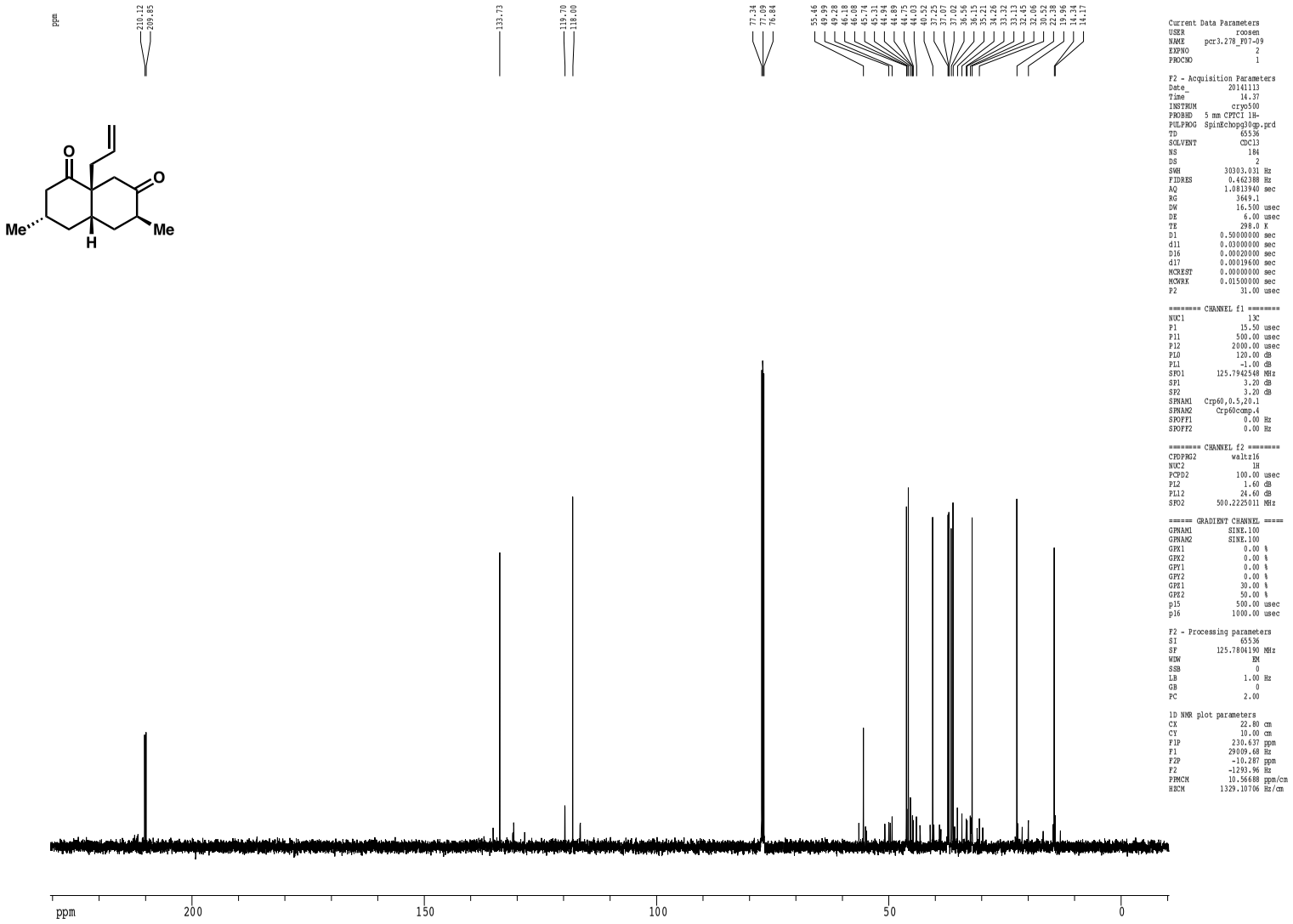
Z-restored spin-echo 13C spectrum with 1H decoupling




```
Current Data Parameters
USER                 roosen
NAME          pcr3.278_F03-05
EXPNO                     2
PROCNO                    1

F2 - Acquisition Parameters
Date_              20141113
Time                 12.36
INSTRUM             cryo500
PROBHD    5 mm CPTCI 1H-
PULPROG   SpinEchopg30gp.prd
TD                   65536
SOLVENT              CDCl3
NS                      80
DS                       2
SWH              30303.031 Hz
FIDRES           0.462388 Hz
AQ               1.0813940 sec
RG                  4597.6
DW                 16.500 usec
DE                  6.00 usec
TE                 298.0 K
D1           0.50000000 sec
d11          0.03000000 sec
D16          0.00020000 sec
d17          0.00019600 sec
MCREST       0.00000000 sec
MCWRK        0.01500000 sec
P2                 31.00 usec

======= CHANNEL f1 =======
NUC1                 13C
P1                 15.50 usec
P11               500.00 usec
P12              2000.00 usec
PL0               120.00 dB
PL1                -1.00 dB
SFO1         125.7942548 MHz
SP1                3.20 dB
SP2                3.20 dB
SPNAM1   Crp60,0.5,20.1
SPNAM2      Crp60comp.4
SPOFF1              0.00 Hz
SPOFF2              0.00 Hz

======= CHANNEL f2 =======
CPDPRG2          waltz16
NUC2                 1H
PCPD2             100.00 usec
PL2                1.60 dB
PL12              24.60 dB
SFO2        500.2225011 MHz

===== GRADIENT CHANNEL ====
GPNAM1           SINE.100
GPNAM2           SINE.100
GPX1                0.00 %
GPX2                0.00 %
GPY1                0.00 %
GPY2                0.00 %
GPZ1               30.00 %
GPZ2               50.00 %
p15               500.00 usec
p16              1000.00 usec

F2 - Processing parameters
SI                   65536
SF          125.7804282 MHz
WDW                  EM
SSB                  0
LB                 1.00 Hz
GB                   0
PC                 4.00

1D NMR plot parameters
CX                 22.80 cm
CY                 10.00 cm
F1P               230.387 ppm
F1                28978.21 Hz
F2P               -10.533 ppm
F2                -1324.82 Hz
PPMCM             10.56667 ppm/cm
HZCM          1329.08032 Hz/cm
```

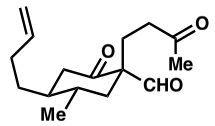

1H spectrum
ppm
Me
H
O
O
Me
Current Data Parameters
USER zoosen
NAME pcr3.278_F07-09
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20141113
Time 12.59
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 32048
SOLVENT CDCl3
NS 8
DS 2
SWH 8012.820 Hz
FIDRES 0.250026 Hz
AQ 1.9998451 sec
RG 6.3
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======= CHANNEL f1 =======
NUC1 1H
P1 7.50 usec
PL1 1.50 dB
SFO1 500.2235913 MHz
F2 - Processing parameters
SI 65536
SF 500.2200249 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00
1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 10.000 ppm
F1 5002.23 Hz
F2P -1.000 ppm
F2 -500.22 Hz
PPMCM 0.48246 ppm/cm
HZCM 241.33423 Hz/cm
8.1091
7.9488
1.4469
1.9166
1.6315
1.3390
3.2775
2.2608
1.0000
7.26958
0.98814
1.00110
1.01276
1.02666
1.04741
1.06031
1.07345
1.08516
1.11793
1.25262
1.47510
1.49719
1.65476
1.74499
1.75662
1.77323
1.78193
1.79938
1.80825
1.81624
1.83573
1.86558
1.86613
1.88223
1.89545
1.91915
1.93425
1.95807
1.98229
2.00962
2.04457
2.08956
2.20777
2.23118
2.26309
2.27484
2.28793
2.35097
2.37899
2.55111
2.61660
2.62898
2.64185
2.65488
2.66676
2.71462
2.77162
4.99019
5.00681
5.02616
5.06516
5.09617
5.54732
5.55676
5.56721
5.57801
5.58909
5.59925
5.61034

Z-restored spin-echo 13C spectrum with 1H decoupling




```
Current Data Parameters
USER                roosen
NAME        pcr3.278_F07-09
EXPNO                    2
PROCNO                   1

F2 - Acquisition Parameters
Date_              20141113
Time                  14.37
INSTRUM             cryo500
PROBHD    5 mm CPTCI 1H-
PULPROG   SpinEchopg30gp.prd
TD                    65536
SOLVENT               CDCl3
NS                      184
DS                        2
SWH               30303.031 Hz
FIDRES            0.462388 Hz
AQ                1.0813940 sec
RG                   3649.1
DW                  16.500 usec
DE                   6.00 usec
TE                  298.0 K
D1              0.50000000 sec
d11             0.03000000 sec
D16             0.00020000 sec
d17             0.00019600 sec
MCREST          0.00000000 sec
MCWRK           0.01500000 sec
P2                  31.00 usec

======= CHANNEL f1 =======
NUC1                   13C
P1                  15.50 usec
P11                500.00 usec
P12               2000.00 usec
PL0                120.00 dB
PL1                 -1.00 dB
SFO1          125.7942548 MHz
SP1                 3.20 dB
SP2                 3.20 dB
SPNAM1    Crp60,0.5,20.1
SPNAM2       Crp60comp.4
SFOFF1                0.00 Hz
SFOFF2                0.00 Hz

======= CHANNEL f2 =======
CPDPRG2           waltz16
NUC2                   1H
PCPD2              100.00 usec
PL2                  1.60 dB
PL12                24.60 dB
SFO2         500.2225011 MHz

===== GRADIENT CHANNEL ====
GPNAM1           SINE.100
GPNAM2           SINE.100
GPX1                 0.00 %
GPX2                 0.00 %
GPY1                 0.00 %
GPY2                 0.00 %
GPZ1                30.00 %
GPZ2                50.00 %
p15                500.00 usec
p16               1000.00 usec

F2 - Processing parameters
SI                    65536
SF            125.7804190 MHz
WDW                     EM
SSB                      0
LB                   1.00 Hz
GB                       0
PC                    2.00

1D NMR plot parameters
CX                   22.80 cm
CY                   10.00 cm
F1P                 230.637 ppm
F1                29009.68 Hz
F2P                -10.287 ppm
F2                -1293.96 Hz
PPMCM             10.56688 ppm/cm
HZCM           1329.10706 Hz/cm
```

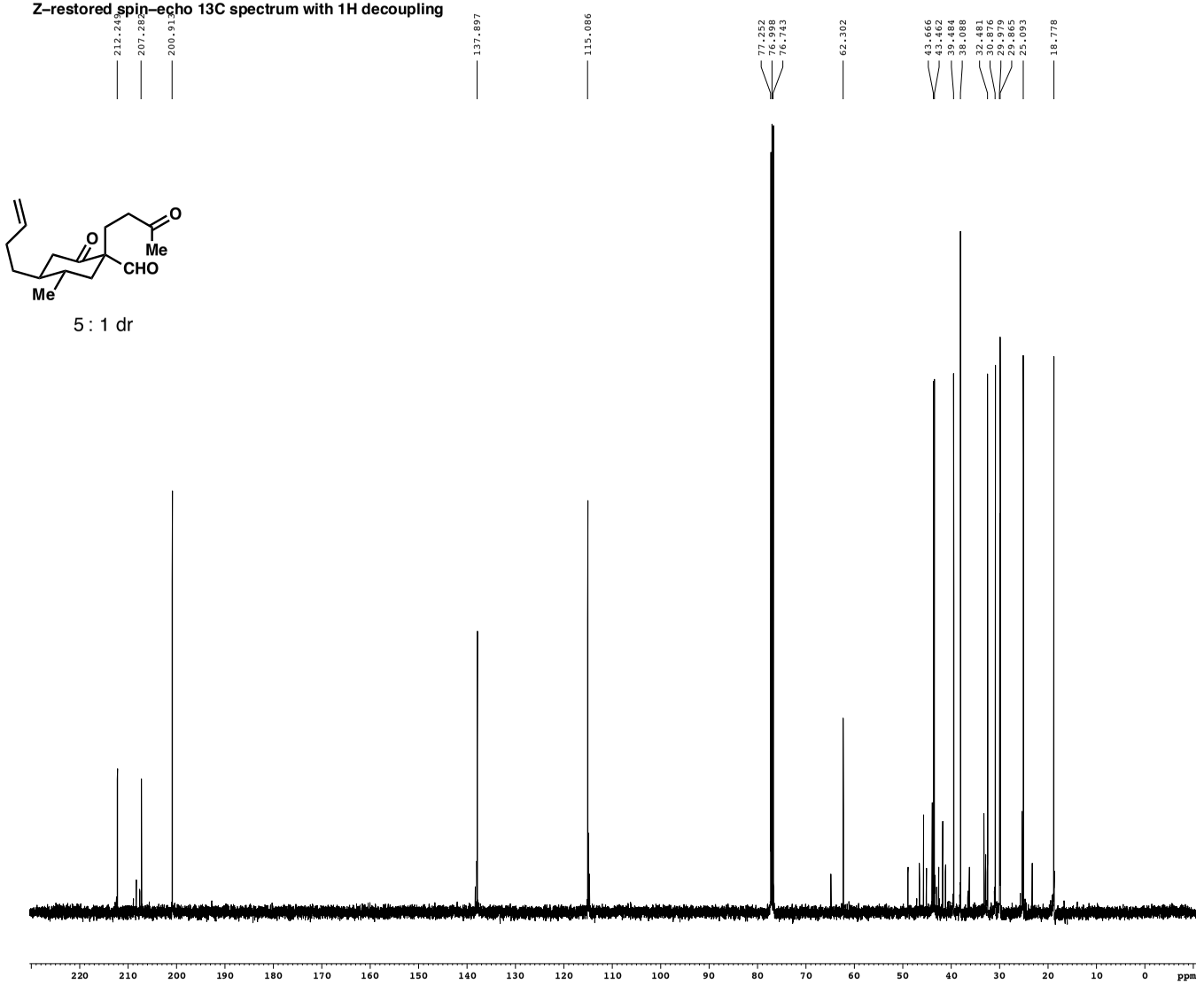
1H spectrum



5 : 1 dr

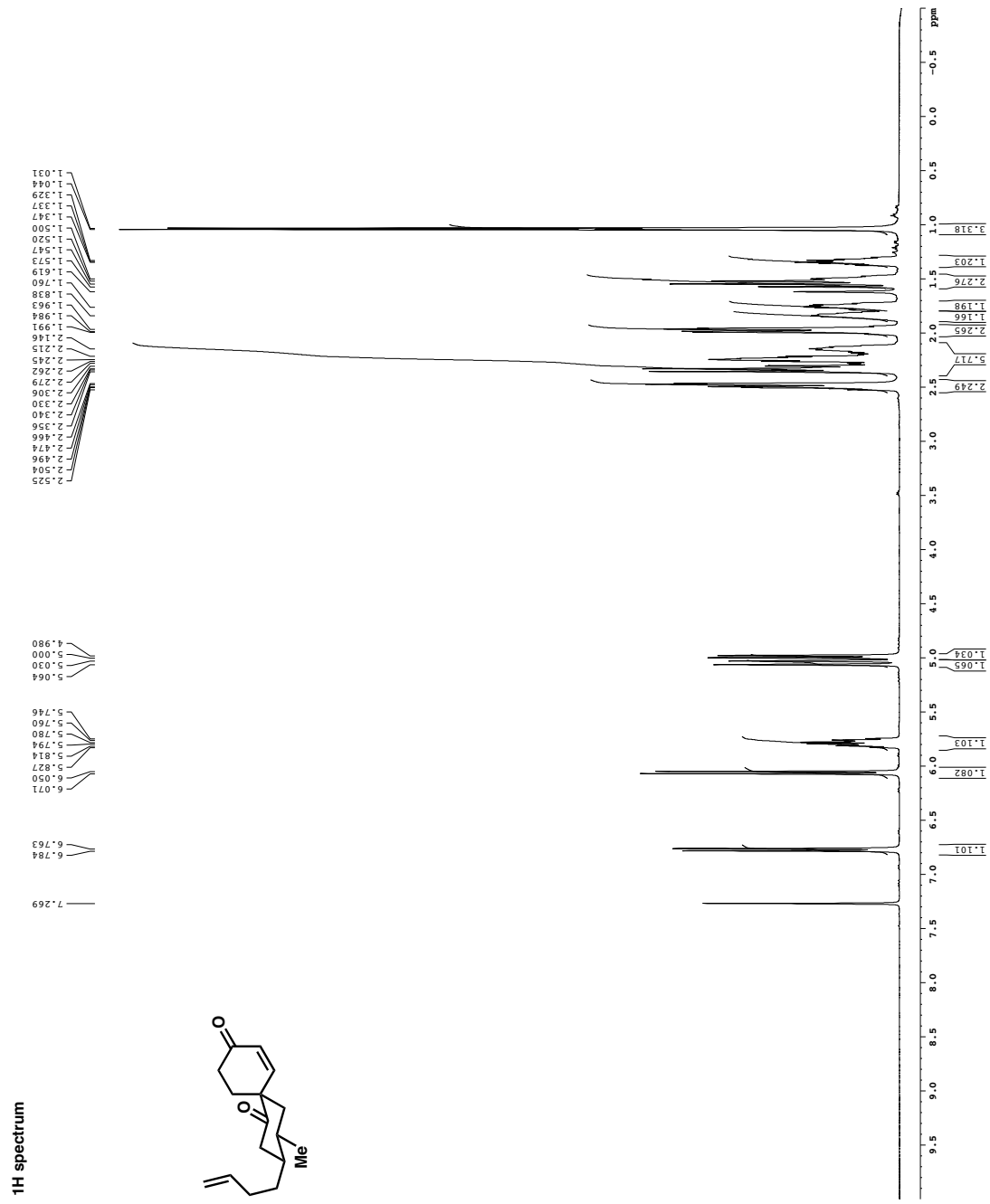

```
Current Data Parameters
USER                 rcosen
NAME         pcr3.053_f3-7
EXPNO                     1
PROCNO                    1

F2 - Acquisition Parameters
Date_             20140206
Time                 15.35
INSTRUM              cryo500
PROBHD    5 mm CPTCI 1H-
PULPROG                zg30
TD                    32048
SOLVENT               CDCl3
NS                       16
DS                        2
SWH                8012.820 Hz
FIDRES             0.250026 Hz
AQ                 1.9998451 sec
RG                       5.7
DW                  62.400 usec
DE                   6.00 usec
TE                  298.0 K
D1                0.10000000 sec
MCREST            0.00000000 sec
MCWRK             0.01500000 sec

======== CHANNEL f1 ========
NUC1                     1H
P1                    7.50 usec
PL1                   1.60 dB
SFO1          500.2235015 MHz

F2 - Processing parameters
SI                       65536
SF            500.2200260 MHz
WDW                      EM
SSB                       0
LB                     0.30 Hz
GB                        0
PC                     4.00
```

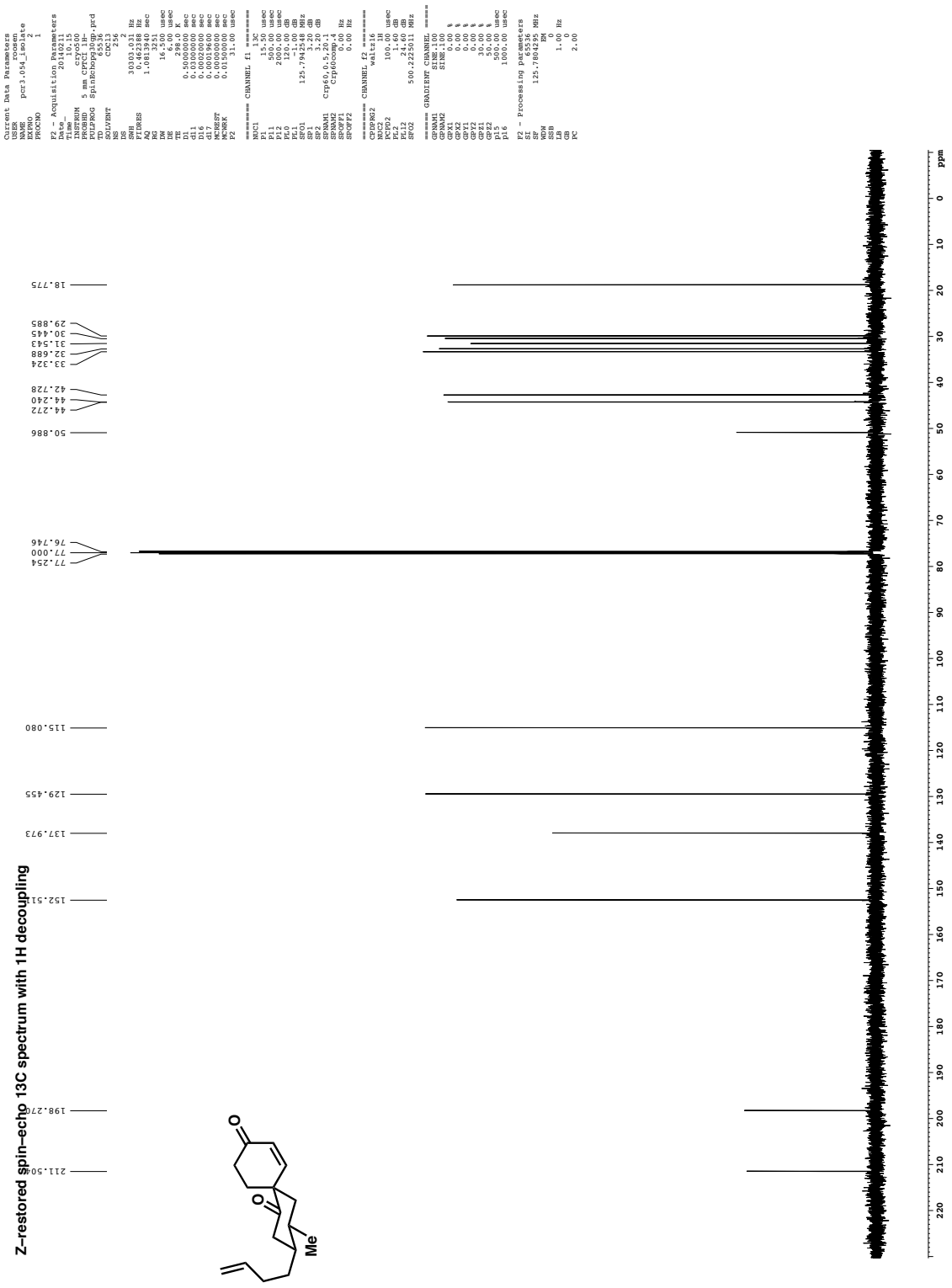
Z–restored spin–echo 13C spectrum with 1H decoupling



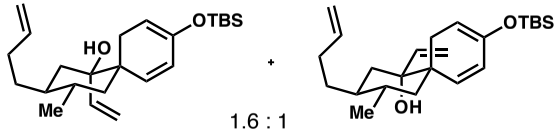
5 : 1 dr

```
Current Data Parameters
USER                 roosen
NAME          pcr3.053_f3-7
EXPNO                      2
PROCNO                     1

F2 - Acquisition Parameters
Date_              20140206
Time                  15.39
INSTRUM             cryo500
PROBHD    5 mm CPTCI 1H-
PULPROG   SpinEchopg30gp.prd
TD                    65536
SOLVENT                CDCl3
NS                       504
DS                         2
SWH                30303.031 Hz
FIDRES             0.462388 Hz
AQ                 1.0813940 sec
RG                    1625.5
DW                    16.500 usec
DE                     6.00 usec
TE                    298.0 K
D1                 0.50000000 sec
d11                0.03000000 sec
D16                0.00020000 sec
d17                0.00019600 sec
MCREST             0.00000000 sec
MCWRK              0.01500000 sec
P2                    31.00 usec

======= CHANNEL f1 =======
NUC1                     13C
P1                    15.50 usec
P11                  500.00 usec
P12                 2000.00 usec
PL0                  120.00 dB
PL1                   -1.00 dB
SFO1           125.7942548 MHz
SP1                    3.20 dB
SP2                    3.20 dB
SPNAM1    Crp60,0.5,20.1
SPNAM2        Crp60comp.4
SPOFF1                 0.00 Hz
SPOFF2                 0.00 Hz

======= CHANNEL f2 =======
CPDPRG2              waltz16
NUC2                     1H
PCPD2                100.00 usec
PL2                    1.60 dB
PL12                  24.60 dB
SFO2           500.2225011 MHz

===== GRADIENT CHANNEL =====
GPNAM1             SINE.100
GPNAM2             SINE.100
GPX1                   0.00 %
GPX2                   0.00 %
GPY1                   0.00 %
GPY2                   0.00 %
GPZ1                  30.00 %
GPZ2                  50.00 %
p15                  500.00 usec
p16                 1000.00 usec

F2 - Processing parameters
SI                    65536
SF             125.7804305 MHz
WDW                      EM
SSB                       0
LB                     1.00 Hz
GB                        0
PC                     2.50
```


Current Data Parameters
USER pcr
NAME pcr3.054_isolate
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20140211
Time 10.12
INSTRUM cryo500
PROBHD 5 mm CPCI 1H-
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.250026 Hz
AQ 1.9998641 sec
RG 64.3
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCWEGT 0.10000000 sec
MCWRK 0.01500000 sec
nnnnnnnn CHANNEL f1 nnnnnnnn
NUC1 1H
P1 7.50 usec
PL1 1.60 dB
SFO1 500.2235015 MHz
F2 - Processing parameters
SI 65536
SF 500.2200268 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00
1H spectrum
Me
ppm


Z–restored spin–echo 13C spectrum with 1H decoupling
Me
211.504
198.276
152.512
137.973
129.455
115.080
77.254
77.000
76.746
50.886
44.272
44.240
42.728
33.324
32.688
31.543
30.445
29.885
18.775
ppm

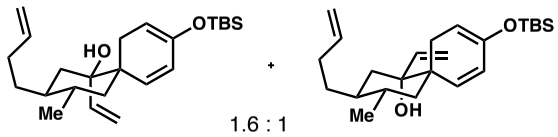
1H spectrum



1.6 : 1


```
Current Data Parameters
USER                  roosen
NAME          pcr1.237_F06-14
EXPNO                      1
PROCNO                     1

F2 - Acquisition Parameters
Date_              20121019
Time                  10.36
INSTRUM              cryo500
PROBHD    5 mm CPTCI 1H-
PULPROG                zg30
TD                    80126
SOLVENT               CDCl3
NS                       16
DS                        2
SWH                8012.820 Hz
FIDRES                0.100003 Hz
AQ                 4.9999123 sec
RG                        4
DW                   62.400 usec
DE                    6.00 usec
TE                   298.0 K
D1                0.10000000 sec
MCREST            0.00000000 sec
MCWRK             0.01500000 sec

======== CHANNEL f1 ========
NUC1                      1H
P1                    7.50 usec
PL1                   1.60 dB
SFO1           500.2235015 MHz

F2 - Processing parameters
SI                       65536
SF             500.2200265 MHz
WDW                      EM
SSB                       0
LB                    0.30 Hz
GB                        0
PC                    4.00
```

Z–restored spin–echo 13C spectrum with 1H decoupling



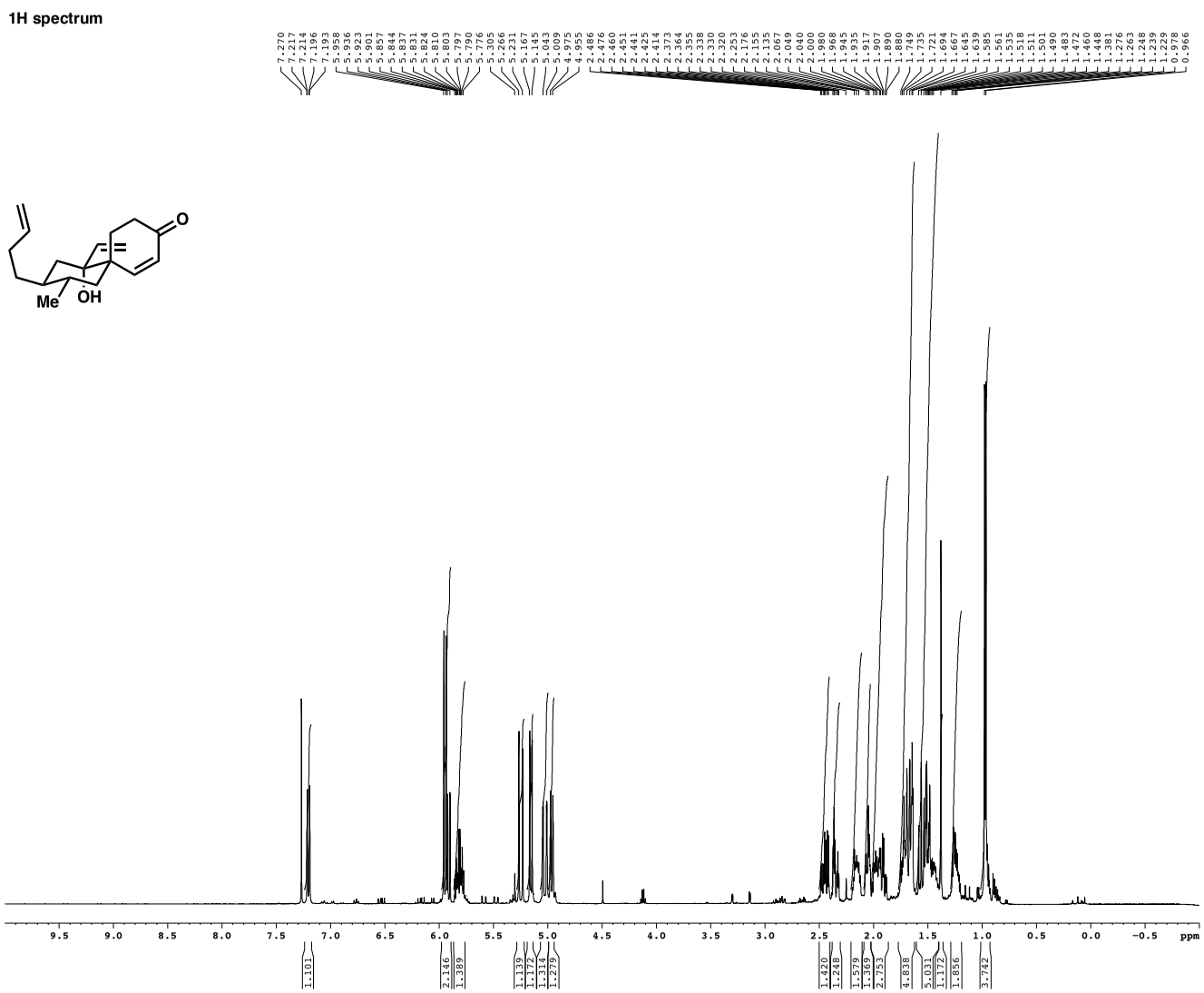
1.6 : 1

147.231
146.700
143.936
141.266
139.186
138.922
134.678
134.081
127.008
125.614
114.343
114.199
113.905
112.715
101.906
100.428
77.856
77.256
77.002
76.748
76.086
42.229
42.069
41.697
39.934
39.845
39.026
37.711
37.557
32.765
32.336
31.565
31.058
30.533
30.515
30.466
29.094
27.626
25.908
25.842
25.737
25.682
19.638
19.452
18.034
18.007
-4.426
-4.454
-4.488

220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

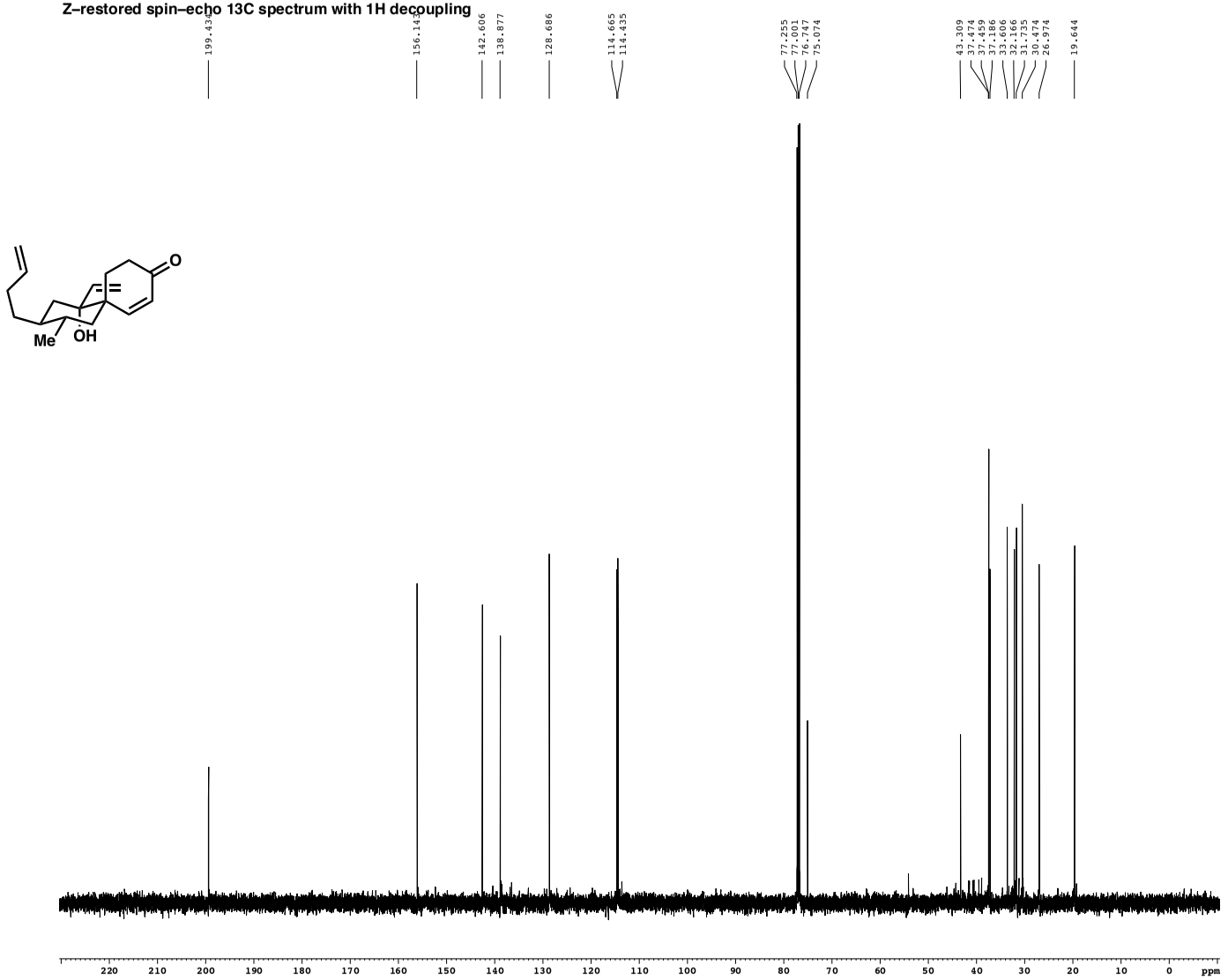
```
Current Data Parameters
USER                 roosen
NAME       pcr1.237_F06-14
EXPNO                     2
PROCNO                    1

F2 - Acquisition Parameters
Date_             20121019
Time                 10.38
INSTRUM              cryo500
PROBHD     5 mm CPTCI 1H-
PULPROG    SpinEchopg30gp.prd
TD                   65536
SOLVENT              CDCl3
NS                     424
DS                      16
SWH              30303.031 Hz
FIDRES           0.462388 Hz
AQ               1.0813940 sec
RG                  7298.2
DW                  16.500 usec
DE                   6.00 usec
TE                  298.0 K
D1             0.25000000 sec
d11            0.03000000 sec
D16            0.00020000 sec
d17            0.00019600 sec
MCREST         0.00000000 sec
MCWRK          0.01500000 sec
P2                  31.00 usec

======= CHANNEL f1 =======
NUC1                  13C
P1                  15.50 usec
P11                500.00 usec
P12               2000.00 usec
PL0                120.00 dB
PL1                 -1.00 dB
SFO1          125.7942548 MHz
SP1                  3.20 dB
SP2                  3.20 dB
SPNAM1     Crp60,0.5,20.1
SPNAM2       Crp60comp.4
SPOFF1               0.00 Hz
SPOFF2               0.00 Hz

======= CHANNEL f2 =======
CPDPRG2             waltz16
NUC2                    1H
PCPD2              100.00 usec
PL2                  1.60 dB
PL12                24.60 dB
SFO2          500.2225011 MHz

===== GRADIENT CHANNEL =====
GPNAM1            SINE.100
GPNAM2            SINE.100
GPX1                 0.00 %
GPX2                 0.00 %
GPY1                 0.00 %
GPY2                 0.00 %
GPZ1                30.00 %
GPZ2                50.00 %
p15                500.00 usec
p16               1000.00 usec

F2 - Processing parameters
SI                   65536
SF            125.7804282 MHz
WDW                    EM
SSB                     0
LB                   1.00 Hz
GB                      0
PC                   2.00
```

1H spectrum

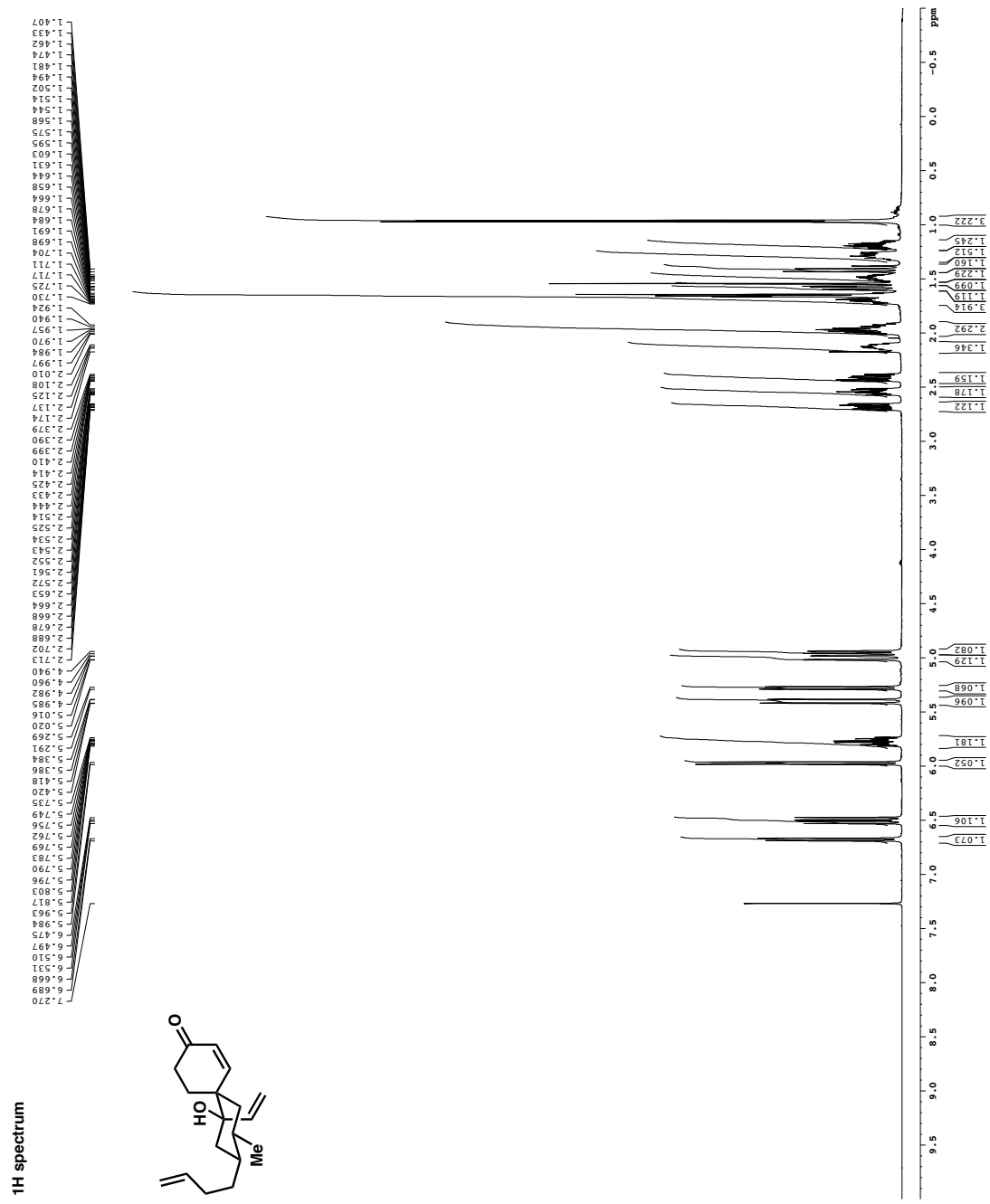


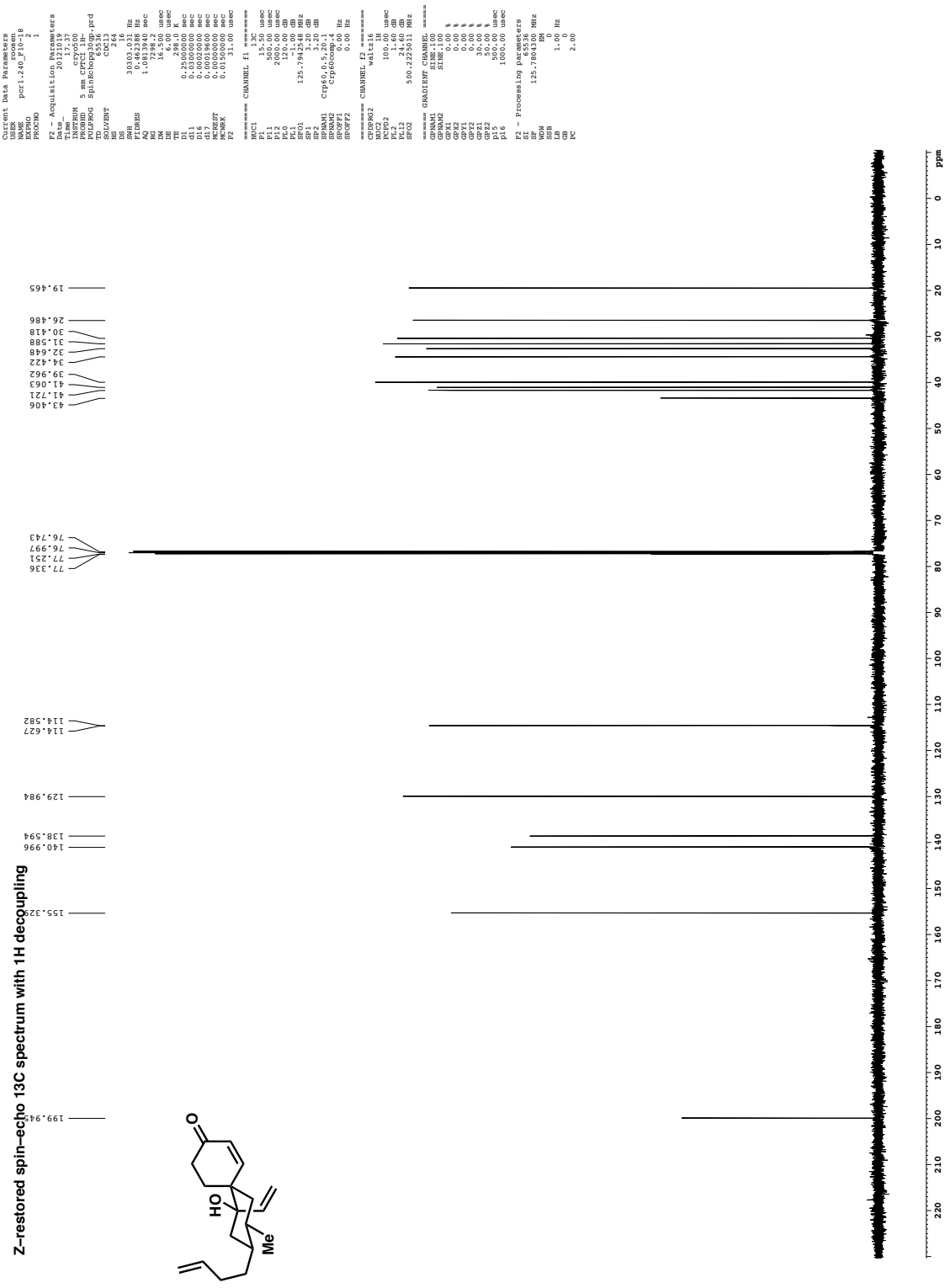

```
Current Data Parameters
USER                  roosen
NAME          pcr1.240_F04-07
EXPNO                      1
PROCNO                     1

F2 - Acquisition Parameters
Date_              20121019
Time                  15.27
INSTRUM              cryo500
PROBHD    5 mm CPTCI 1H-
PULPROG                zg30
TD                    80126
SOLVENT               CDCl3
NS                        8
DS                        2
SWH                8012.820 Hz
FIDRES            0.100003 Hz
AQ                4.9999123 sec
RG                        4
DW                   62.400 usec
DE                    6.00 usec
TE                   298.0 K
D1              0.10000000 sec
MCREST          0.00000000 sec
MCWRK           0.01500000 sec

======== CHANNEL f1 ========
NUC1                      1H
P1                    7.50 usec
PL1                   1.60 dB
SFO1           500.2235015 MHz

F2 - Processing parameters
SI                    65536
SF             500.2200268 MHz
WDW                      EM
SSB                       0
LB                    0.30 Hz
GB                        0
PC                    4.00
```

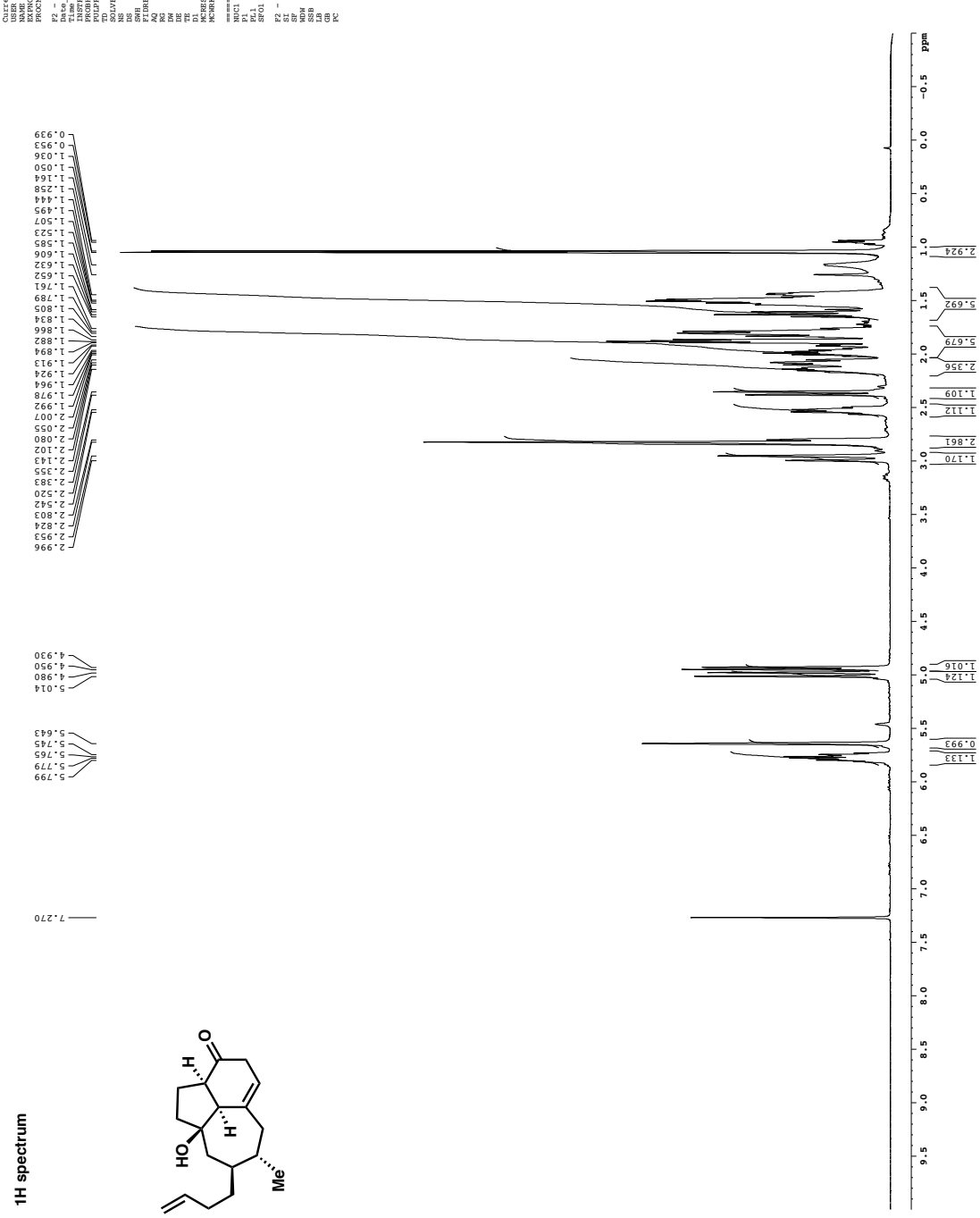
Z–restored spin–echo 13C spectrum with 1H decoupling

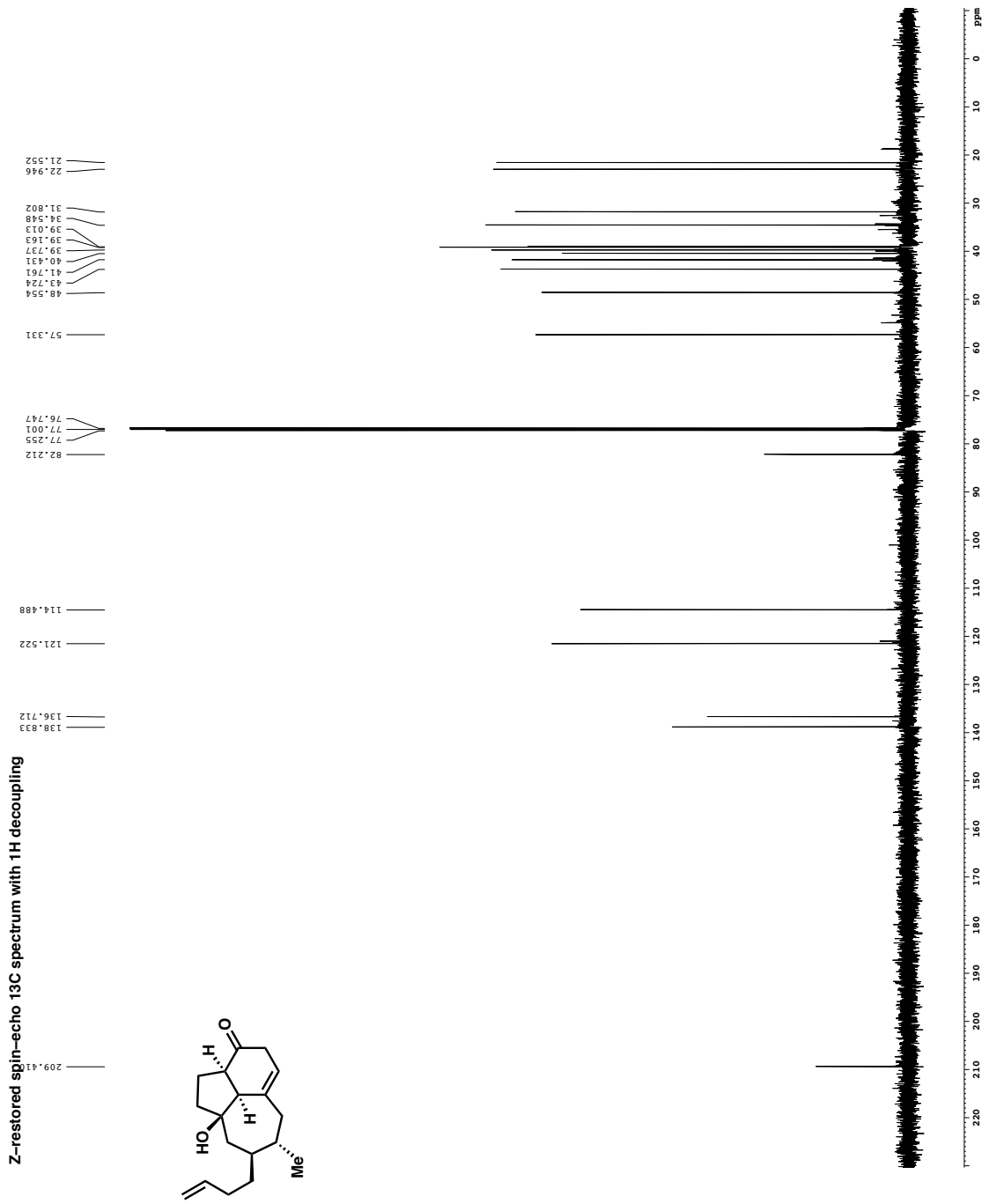



```
Current Data Parameters
USER                 roosen
NAME      pcr1.240_F04-07
EXPNO                     2
PROCNO                    1

F2 - Acquisition Parameters
Date_             20121019
Time                 15.29
INSTRUM           cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD                   65536
SOLVENT               CDCl3
NS                      120
DS                       16
SWH               30303.031 Hz
FIDRES            0.462388 Hz
AQ                1.0813940 sec
RG                    8192
DW                  16.500 usec
DE                   6.00 usec
TE                  298.0 K
D1             0.25000000 sec
d11            0.03000000 sec
D16            0.00020000 sec
d17            0.00019600 sec
MCREST         0.00000000 sec
MCWRK          0.01500000 sec
P2                  31.00 usec

======= CHANNEL f1 ========
NUC1                   13C
P1                   15.50 usec
P11                 500.00 usec
P12                2000.00 usec
PL0                 120.00 dB
PL1                  -1.00 dB
SFO1          125.7942548 MHz
SP1                   3.20 dB
SP2                   3.20 dB
SPNAM1    Crp60,0.5,20.1
SPNAM2        Crp60comp.4
SPOFF1                0.00 Hz
SPOFF2                0.00 Hz

======= CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                    1H
PCPD2               100.00 usec
PL2                   1.60 dB
PL12                 24.60 dB
SFO2          500.2225011 MHz

===== GRADIENT CHANNEL =====
GPNAM1            SINE.100
GPNAM2            SINE.100
GPX1                  0.00 %
GPX2                  0.00 %
GPY1                  0.00 %
GPY2                  0.00 %
GPZ1                 30.00 %
GPZ2                 50.00 %
p15                 500.00 usec
p16                1000.00 usec

F2 - Processing parameters
SI                   65536
SF            125.7804291 MHz
WDW                     EM
SSB                      0
LB                    1.00 Hz
GB                       0
PC                    2.00
```

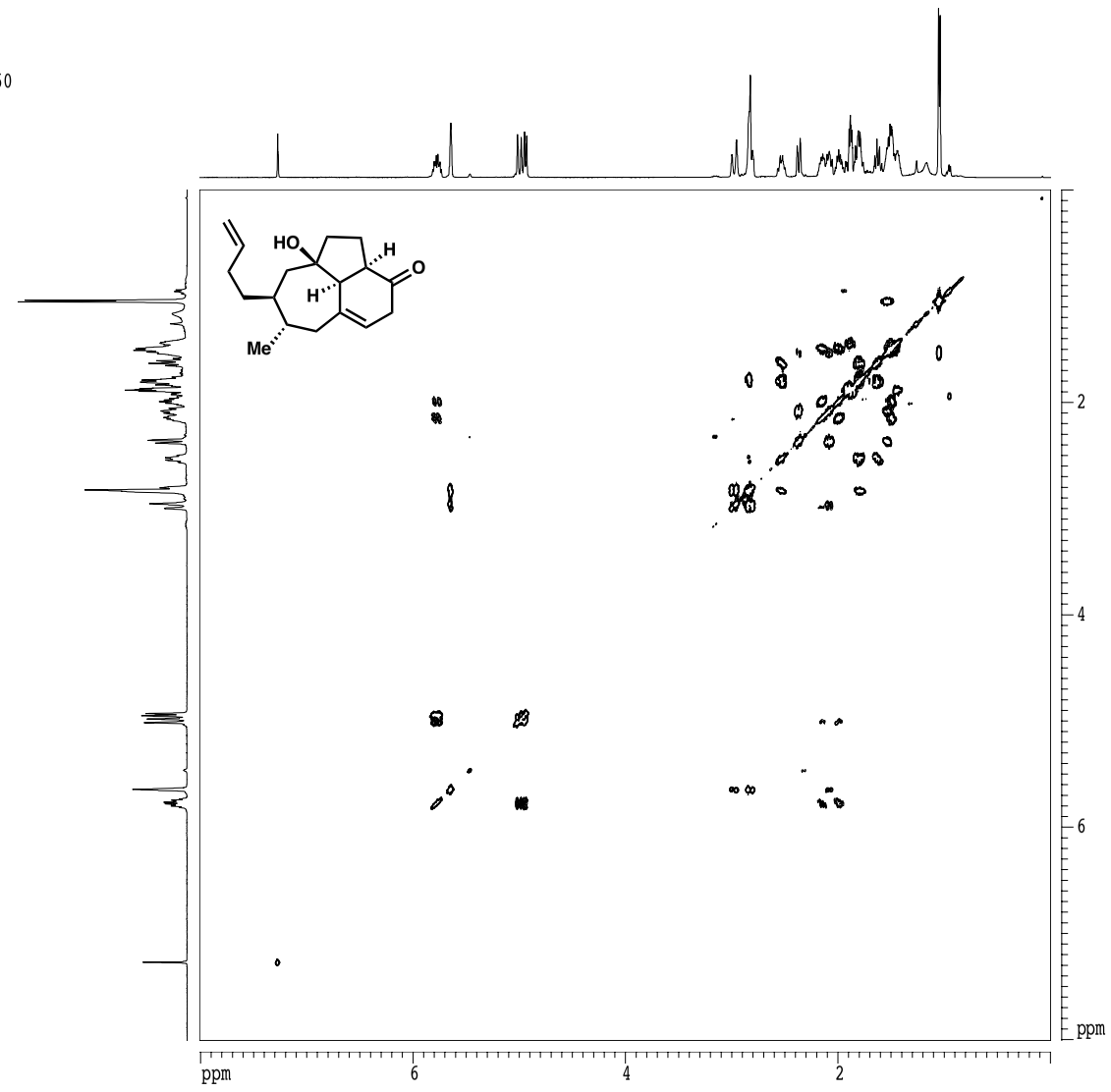

1H spectrum
HO
Me
O


Z–restored spin–echo 13C spectrum with 1H decoupling
199.945
155.325
140.996
138.594
129.984
114.627
114.582
76.743
76.997
77.251
77.336
43.406
41.721
41.063
39.962
34.422
32.648
31.588
30.418
26.486
19.465
O
HO
Me
ppm


1H spectrum
Current Data Parameters
USER pcr
NAME pcr3.069_isolate
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20140301
Time 11.10
INSTRUM spect
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.250026 Hz
AQ 1.9999615 sec
RG 71
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCWEGT 0.10000000 sec
MCREK 0.01500000 sec
==== CHANNEL f1 ====
NUC1 1H
P1 7.50 usec
PL1 1.60 dB
SFO1 500.2235015 MHz
F2 - Processing parameters
SI 65536
SF 500.2200262 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00
7.270
5.799
5.779
5.765
5.745
5.643
5.014
4.980
4.950
4.930
2.996
2.953
2.824
2.803
2.542
2.520
2.383
2.355
2.143
2.102
2.080
2.055
2.007
1.992
1.978
1.964
1.924
1.913
1.894
1.882
1.866
1.834
1.805
1.789
1.761
1.652
1.632
1.606
1.585
1.523
1.507
1.495
1.444
1.258
1.164
1.050
1.036
0.953
0.939
1.133
0.993
1.124
1.016
1.170
2.861
1.112
1.109
2.356
5.679
5.692
2.924
ppm
O
H
H
HO
Me


Z–restored spin–echo 13C spectrum with 1H decoupling
209.410
138.833
136.712
121.522
114.488
82.212
77.255
77.001
76.747
57.331
48.554
43.724
41.761
40.431
39.737
39.163
39.013
34.548
31.802
22.946
21.552
ppm
HO
H
H
O
Me

gcosy60



Current Data Parameters

USER	roosen
NAME	pcr3.069_isolate
EXPNO	5
PROCNO	1

F2 - Acquisition Parameters

Date_	20140301
Time	11.36
INSTRUM	cryo500
PROBHD	5 mm CPTCI 1H-
PULPROG	cosygp60.prd
TD	2048
SOLVENT	CDCl3
NS	2
DS	2
SWH	4006.410 Hz
FIDRES	1.956255 Hz
AQ	0.2556404 sec
RG	143.7
DW	124.800 usec
DE	6.00 usec
TE	298.0 K
d0	0.00000300 sec
D1	1.00000000 sec
d13	0.00000300 sec
D16	0.00020000 sec
IN0	0.00024960 sec

======= CHANNEL f1 =======

NUC1	1H
P1	7.50 usec
PL1	1.60 dB
SFO1	500.2220271 MHz

====== GRADIENT CHANNEL =====

GPNAM1	sine.100
GPNAM2	sine.100
GPX1	0.00 %
GPX2	0.00 %
GPY1	0.00 %
GPY2	0.00 %
GPZ1	17.00 %
GPZ2	17.00 %
P16	1000.00 usec

F1 - Acquisition parameters

ND0	1
TD	252
SFO1	500.222 MHz
FIDRES	15.898454 Hz
SW	8.009 ppm
FnMODE	undefined

F2 - Processing parameters

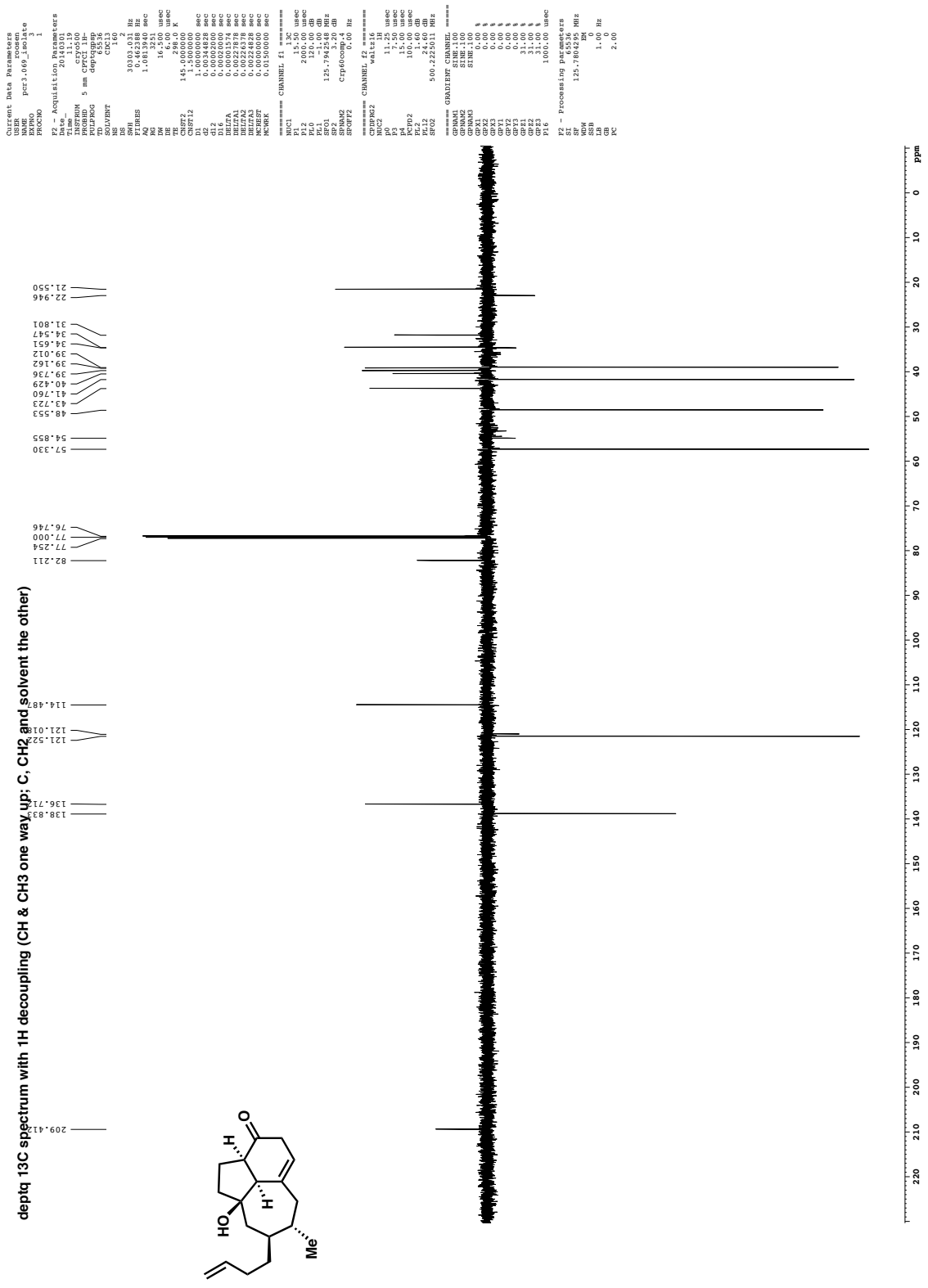
SI	1024
SF	500.2200248 MHz
WDW	SINE
SSB	0
LB	0.00 Hz
GB	0
PC	4.00

F1 - Processing parameters

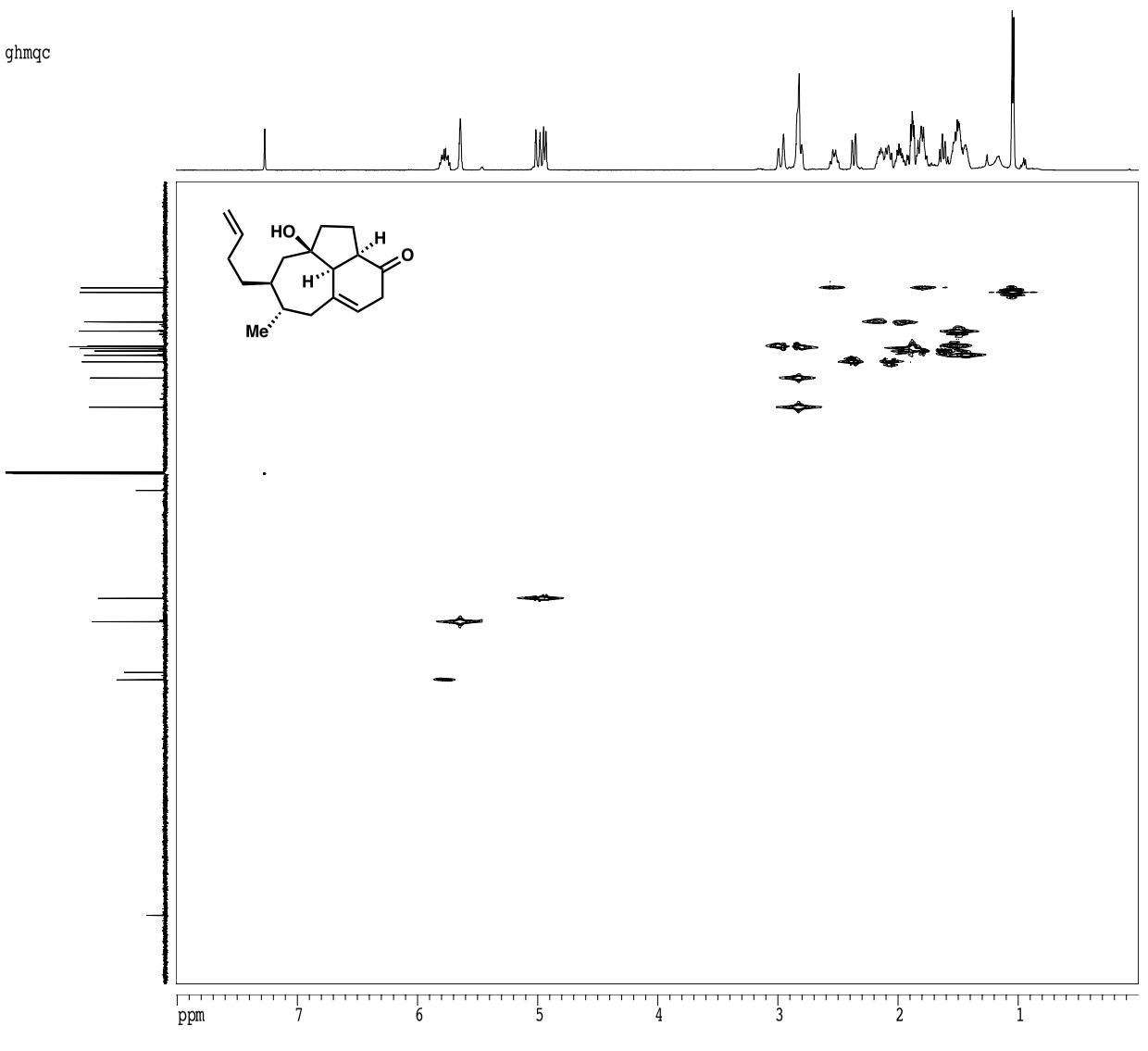
SI	1024
MC2	QF
SF	500.2200245 MHz
WDW	SINE
SSB	0
LB	0.00 Hz
GB	0

2D NMR plot parameters

CX2	15.00 cm
CX1	15.00 cm
F2PLO	8.007 ppm
F2LO	4005.51 Hz
F2PHI	-0.002 ppm
F2HI	-0.90 Hz
F1PLO	8.008 ppm
F1LO	4005.84 Hz
F1PHI	-0.001 ppm
F1HI	-0.57 Hz
F2PPMCM	0.53395 ppm/cm
F2HZCM	267.09402 Hz/cm
F1PPMCM	0.53395 ppm/cm
F1HZCM	267.09402 Hz/cm


deptq 13C spectrum with 1H decoupling (CH & CH3 one way up; C, CH2 and solvent the other)
209.412
138.837
136.718
121.522
121.018
114.487
82.211
77.254
77.000
76.746
57.330
54.855
48.553
43.723
41.760
40.429
39.736
39.162
39.012
34.651
34.547
31.801
22.946
21.550
HO
H
H
Me
O
ppm

ghmqc



Current Data Parameters

USER	roosen
NAME	pcr3.069_isolate
EXPNO	4
PROCNO	1

F2 - Acquisition Parameters

Date_	20140301
Time	11.22
INSTRUM	cryo500
PROBHD	5 mm CPTCI 1H-
PULPROG	inv4gp.wu
TD	2048
SOLVENT	CDCl3
NS	2
DS	2
SWH	4006.410 Hz
FIDRES	1.956255 Hz
AQ	0.2556404 sec
RG	11585.2
DW	124.800 usec
DE	6.50 usec
TE	298.0 K
CNST2	145.0000000
d0	0.00000300 sec
D1	1.00000000 sec
d2	0.00344828 sec
d12	0.00002000 sec
d13	0.00000300 sec
D16	0.00020000 sec
d20	0.00242528 sec
IN0	0.00001656 sec

======= CHANNEL f1 =======

NUC1	1H
P1	7.50 usec
p2	15.00 usec
PL1	1.60 dB
SFO1	500.2220271 MHz

======= CHANNEL f2 =======

CPDPRG2	garp
NUC2	13C
P3	15.50 usec
PCPD2	65.00 usec
PL2	-1.00 dB
PL12	11.30 dB
SFO2	125.7942568 MHz

====== GRADIENT CHANNEL =====

GPNAM1	sine.100
GPNAM2	sine.100
GPNAM3	sine.100
GPX1	0.00 %
GPX2	0.00 %
GPX3	0.00 %
GPY1	0.00 %
GPY2	0.00 %
GPY3	0.00 %
GPZ1	30.00 %
GPZ2	18.00 %
GPZ3	24.00 %
P16	1000.00 usec

F1 - Acquisition parameters

ND0	2
TD	320
SFO1	125.7943 MHz
FIDRES	94.339622 Hz
SW	239.985 ppm
FnMODE	undefined

F2 - Processing parameters

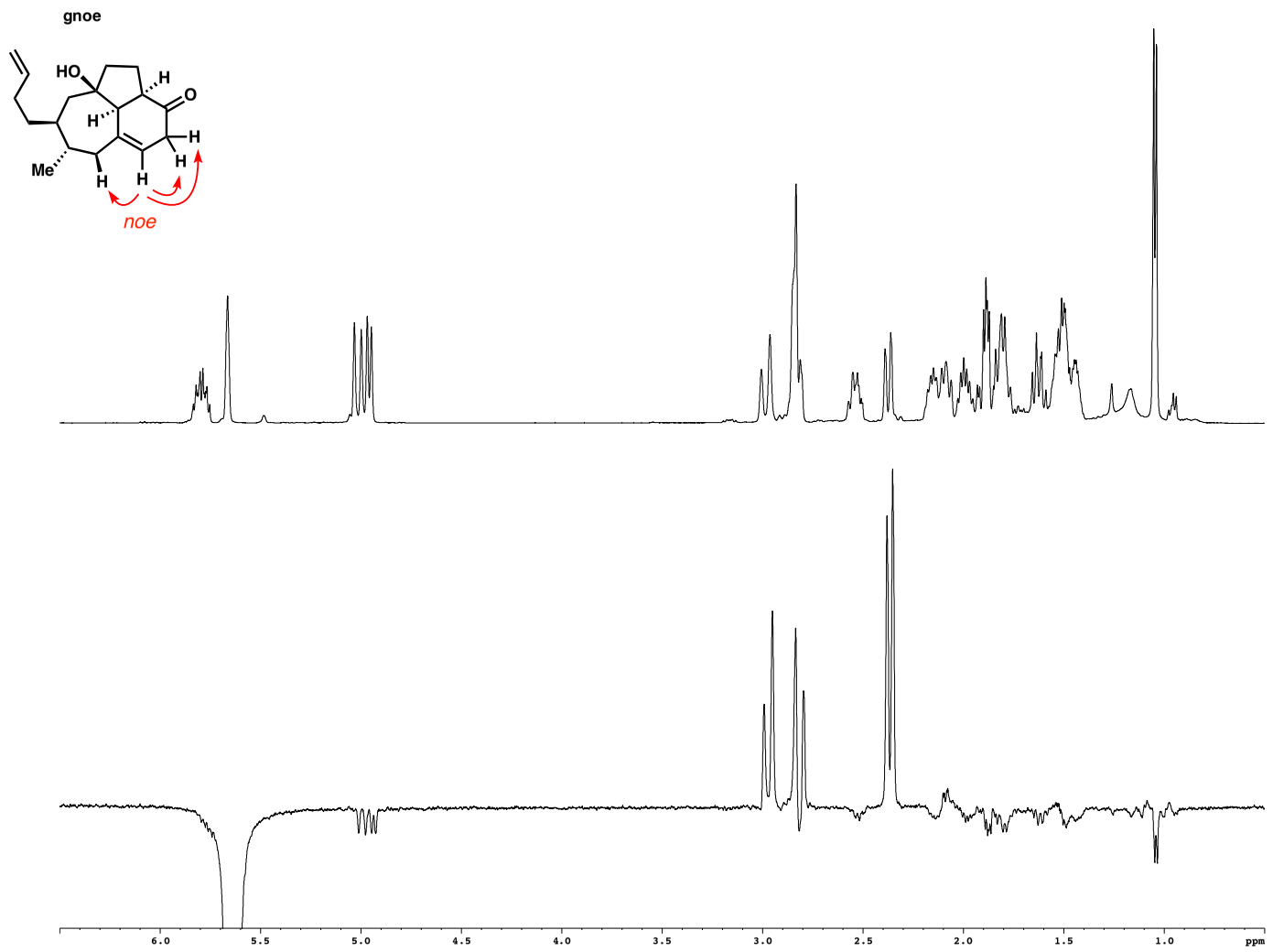
SI	1024
SF	500.2200234 MHz
WDW	EM
SSB	0
LB	5.00 Hz
GB	0
PC	4.00

F1 - Processing parameters

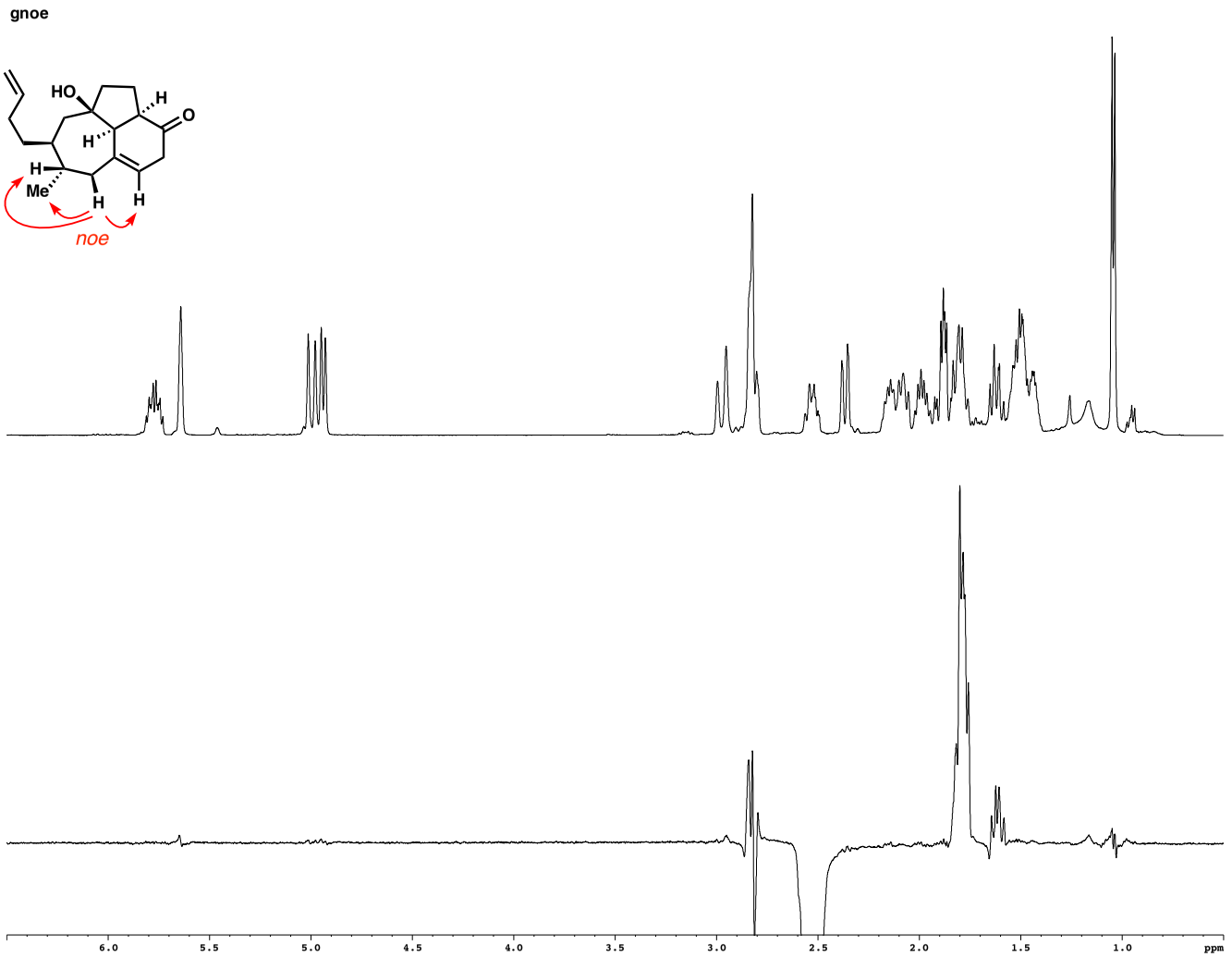
SI	1024
MC2	QF
SF	125.7804350 MHz
WDW	QSINE
SSB	3
LB	0.00 Hz
GB	0

2D NMR plot parameters

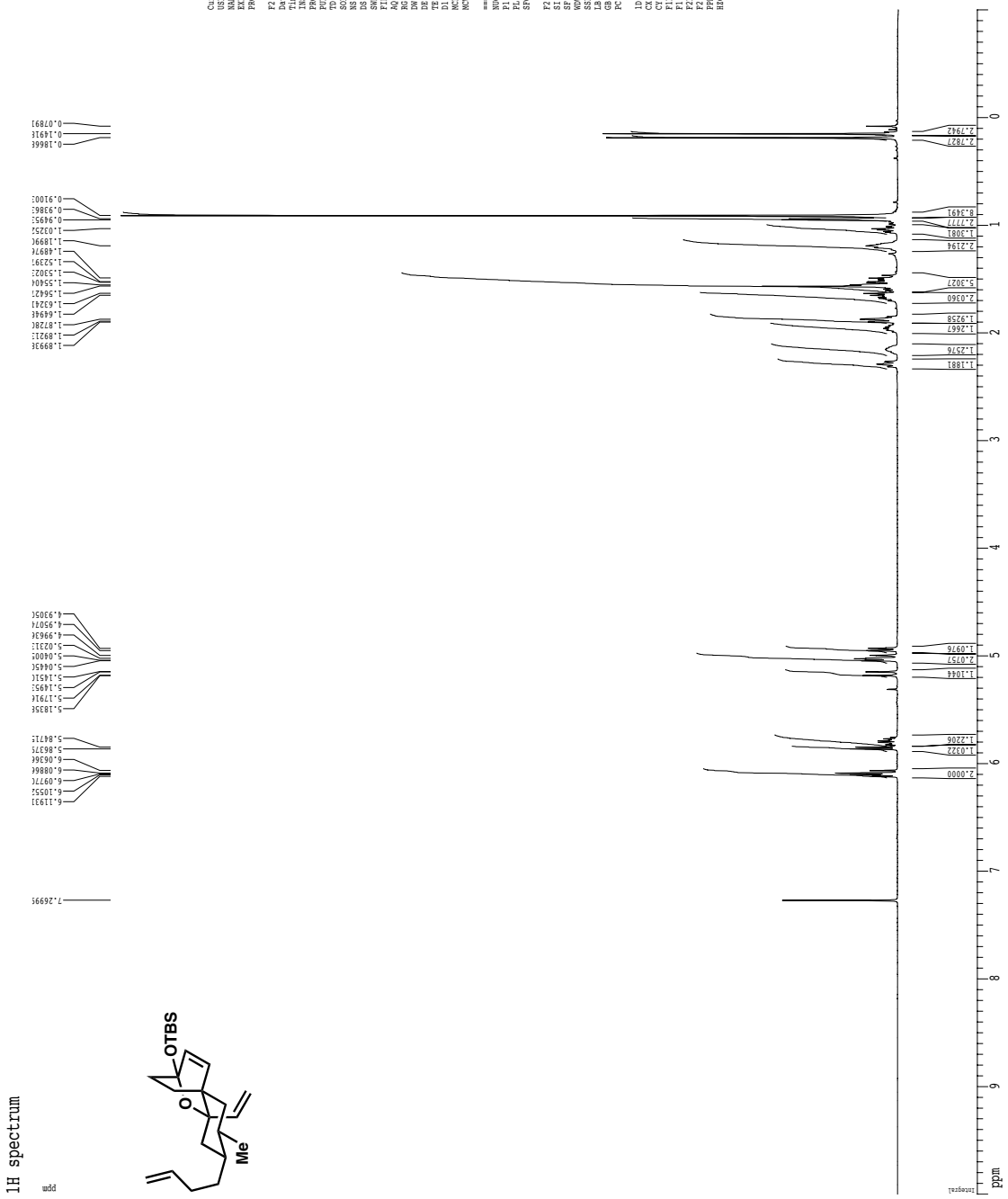
CX2	18.00 cm
CX1	15.00 cm
F2PLO	8.010 ppm
F2LO	4006.87 Hz
F2PHI	0.001 ppm
F2HI	0.46 Hz
F1PLO	229.878 ppm
F1LO	28914.16 Hz
F1PHI	-10.133 ppm
F1HI	-1274.52 Hz
F2PPMCM	0.44496 ppm/cm
F2HZCM	222.57834 Hz/cm
F1PPMCM	16.00073 ppm/cm
F1HZCM	2012.57849 Hz/cm



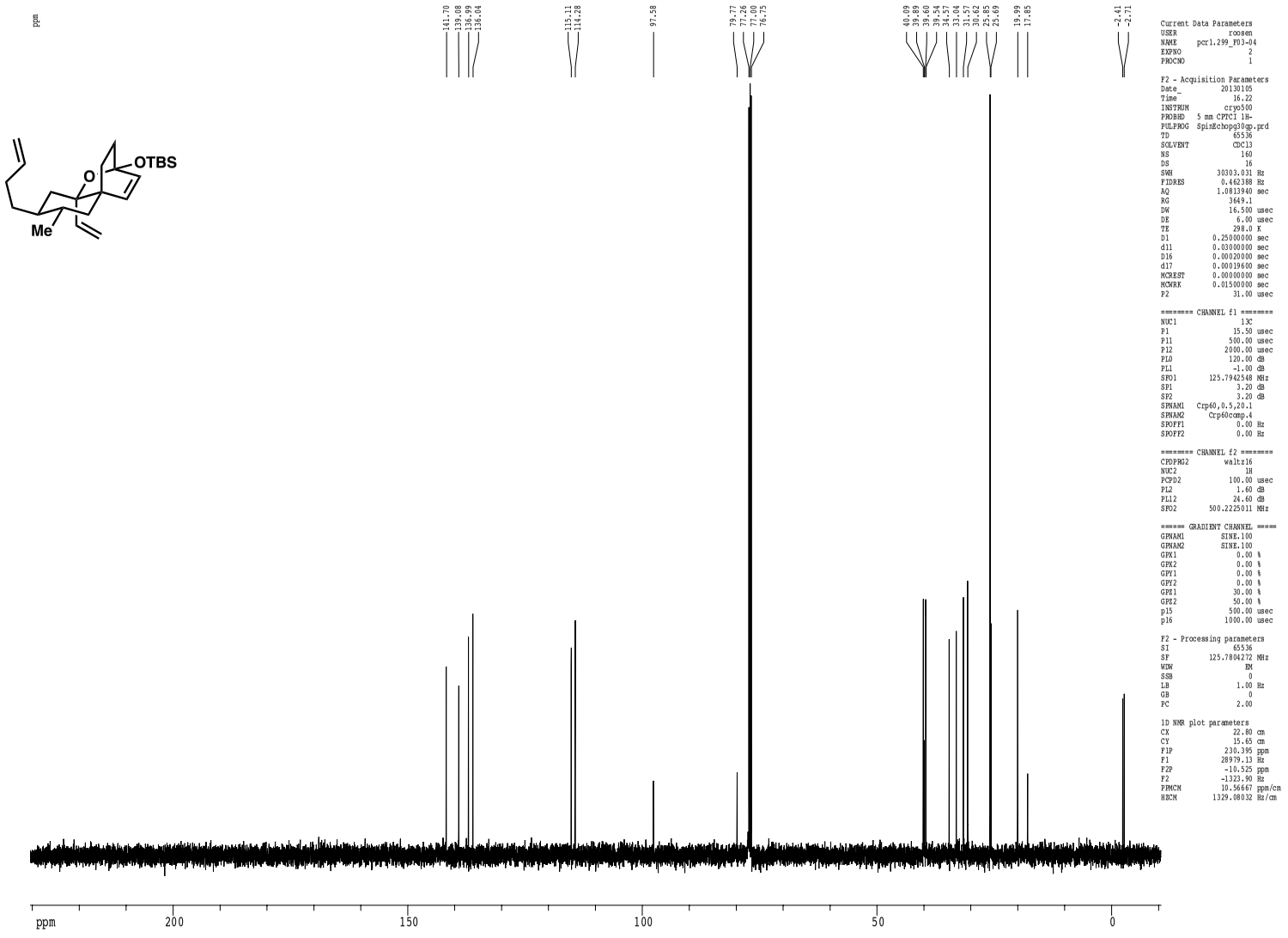

```
Current Data Parameters
USER                 roosen
NAME      pcr3.069_isolate
EXPNO                    6
PROCNO                   1

F2 - Acquisition Parameters
Date_             20140301
Time                 13.22
INSTRUM             cryo500
PROBHD    5 mm CPTCI 1H-
PULPROG        gnoelcc.wu
TD                   65536
SOLVENT                CDCl3
NS                      64
DS                       2
SWH                8012.820 Hz
FIDRES             0.122266 Hz
AQ                 4.0894966 sec
RG                     161.3
DW                    62.400 usec
DE                     6.00 usec
TE                    298.0 K
D1              1.00000000 sec
D8              0.50000000 sec
D16             0.00020000 sec
d21             0.33376500 sec
d22             0.16399699 sec
p2                    15.00 usec

======== CHANNEL f1 ========
NUC1                     1H
P1                     7.50 usec
p3                    22.50 usec
p4                    30.00 usec
p5                    20.00 usec
P12                40000.00 usec
PL1                    1.60 dB
SFO1           500.2228475 MHz
SP1                   61.60 dB
SPNAM1          gauss1.512
SPOFF1                 0.00 Hz

====== GRADIENT CHANNEL =====
GPNAM1              sine.100
GPNAM2              sine.100
GPNAM3              sine.100
GPNAM4              sine.100
GPX1                   0.00 %
GPX2                   0.00 %
GPX3                   0.00 %
GPX4                   0.00 %
GPY1                   0.00 %
GPY2                   0.00 %
GPY3                   0.00 %
GPY4                   0.00 %
GPZ1                   7.00 %
GPZ2                   3.00 %
GPZ3                   2.30 %
GPZ4                  -2.30 %
P16                 1000.00 usec

F2 - Processing parameters
SI                       65536
SF             500.2200274 MHz
WDW                         EM
SSB                          0
LB                      1.00 Hz
GB                           0
PC                      1.00
```

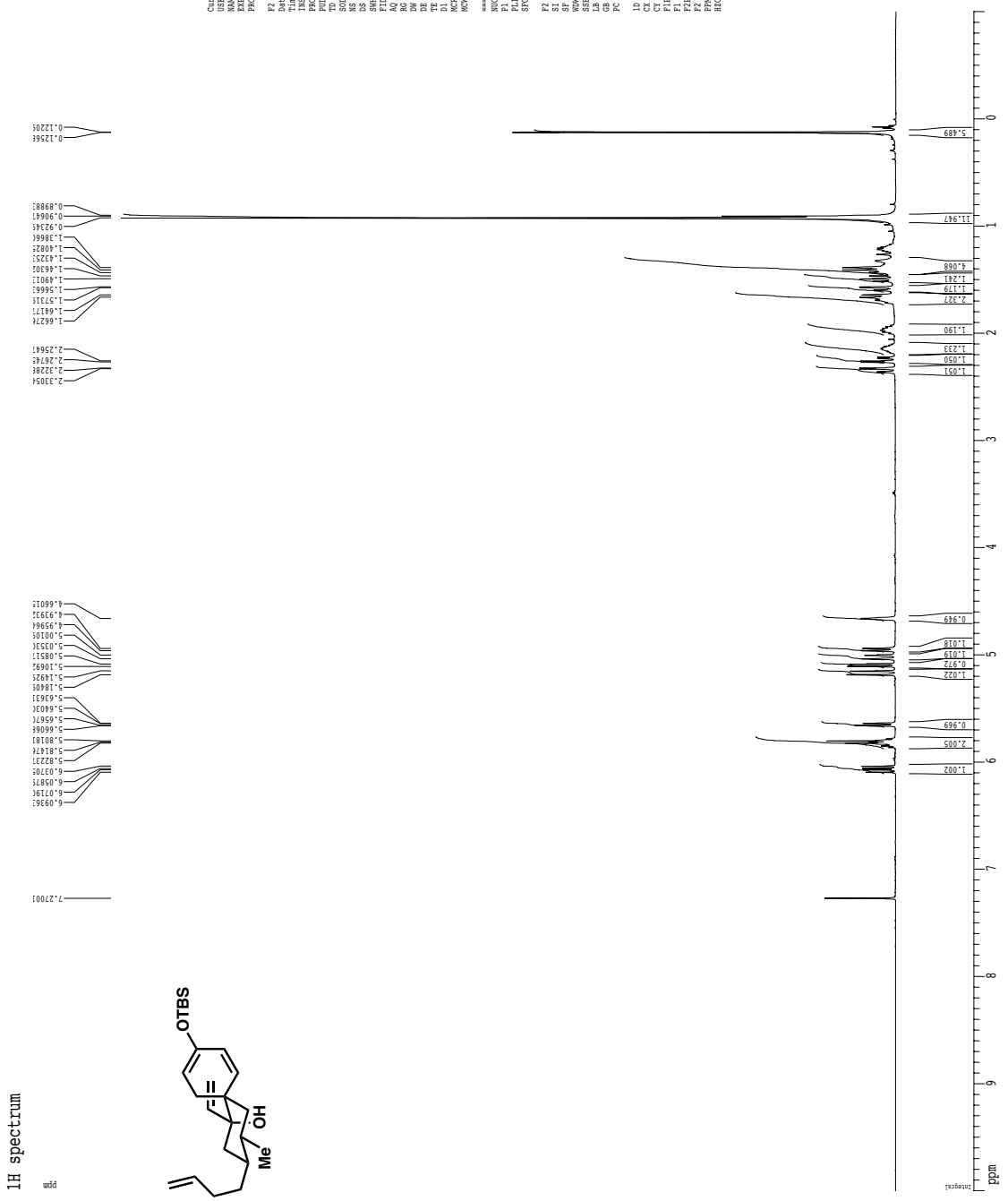



```
Current Data Parameters
USER                 roosen
NAME      pcr3.069_isolate
EXPNO                    8
PROCNO                   1

F2 - Acquisition Parameters
Date_             20140301
Time                 13.37
INSTRUM            cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG        gnoelcc.wu
TD                   65536
SOLVENT               CDCl3
NS                       64
DS                        2
SWH                8012.820 Hz
FIDRES             0.122266 Hz
AQ                 4.0894966 sec
RG                     161.3
DW                    62.400 usec
DE                     6.00 usec
TE                    298.0 K
D1              1.00000000 sec
D8              0.50000000 sec
D16             0.00020000 sec
d21             0.33376500 sec
d22             0.16399699 sec
p2                    15.00 usec

======== CHANNEL f1 ========
NUC1                     1H
P1                     7.50 usec
p3                    22.50 usec
p4                    30.00 usec
p5                    20.00 usec
P12                40000.00 usec
PL1                    1.60 dB
SFO1          500.2212979 MHz
SP1                   61.60 dB
SPNAM1          gauss1.512
SPOFF1                 0.00 Hz

====== GRADIENT CHANNEL =====
GPNAM1              sine.100
GPNAM2              sine.100
GPNAM3              sine.100
GPNAM4              sine.100
GPX1                   0.00 %
GPX2                   0.00 %
GPX3                   0.00 %
GPX4                   0.00 %
GPY1                   0.00 %
GPY2                   0.00 %
GPY3                   0.00 %
GPY4                   0.00 %
GPZ1                   7.00 %
GPZ2                   3.00 %
GPZ3                   2.30 %
GPZ4                  -2.30 %
P16                 1000.00 usec

F2 - Processing parameters
SI                       65536
SF            500.2200285 MHz
WDW                         EM
SSB                          0
LB                      1.00 Hz
GB                           0
PC                      1.00
```

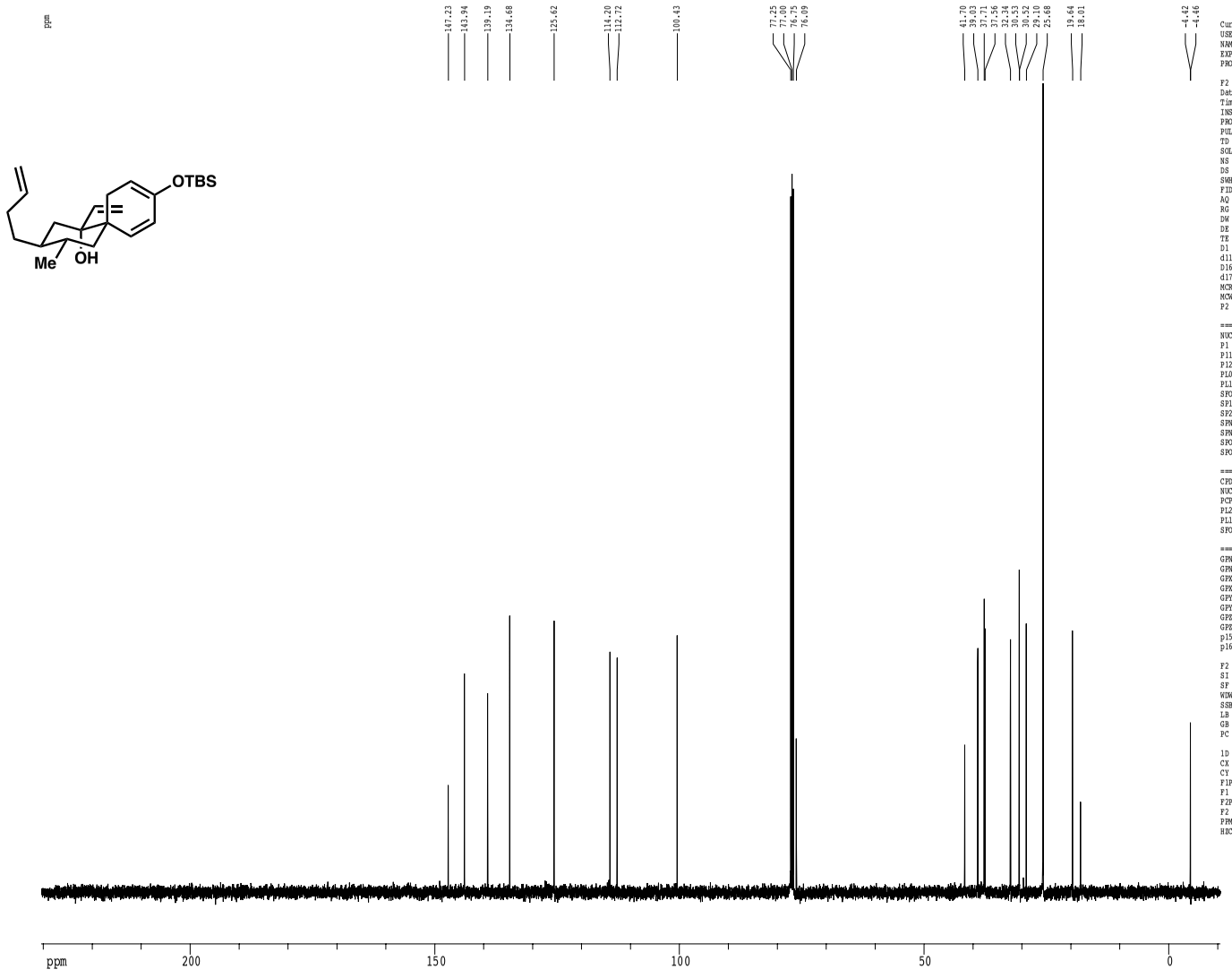

1H spectrum
OTBS
O
Me
ppm

Z-restored spin-echo 13C spectrum with 1H decoupling

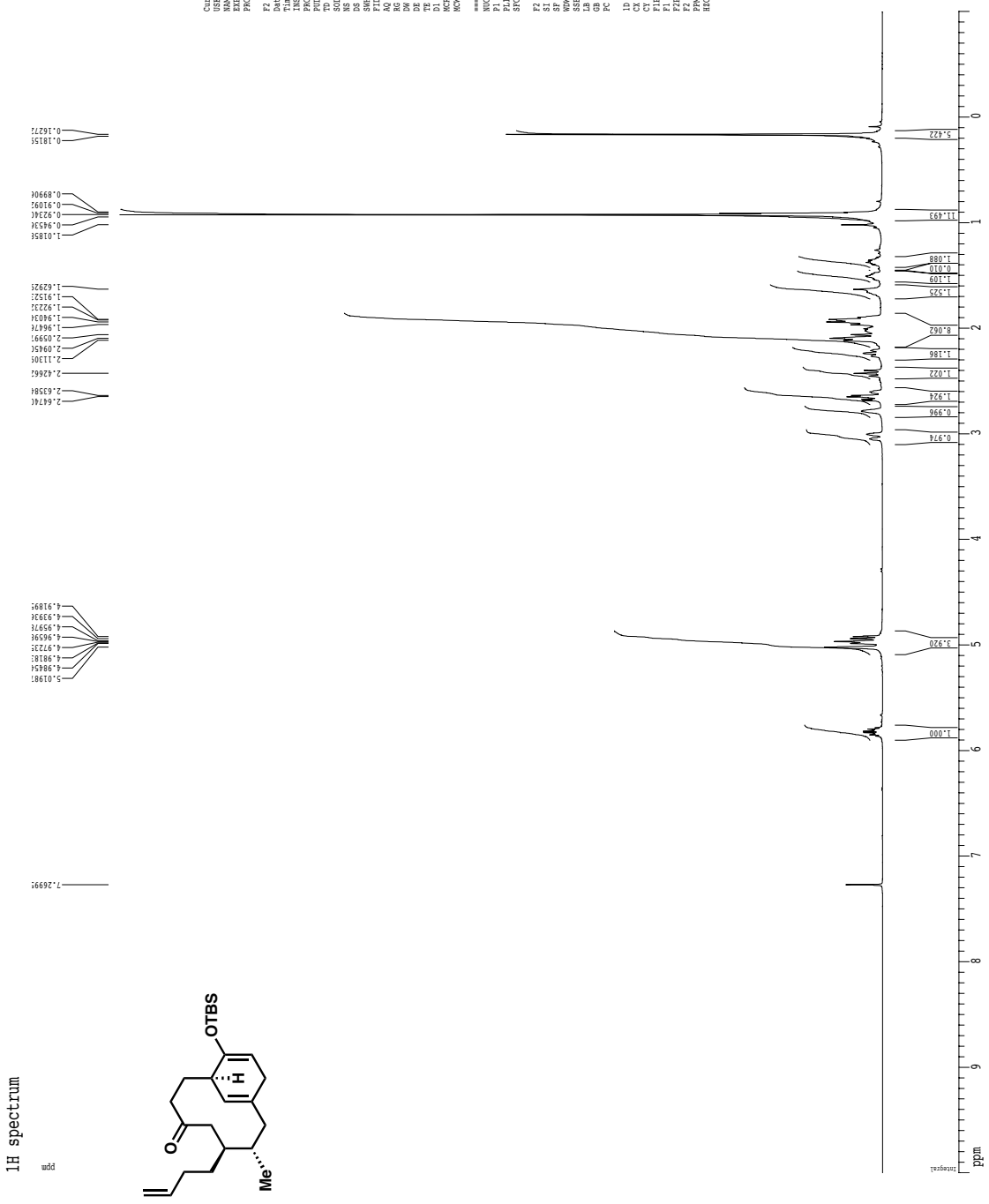



1H spectrum
OTBS
Me
OH
ppm

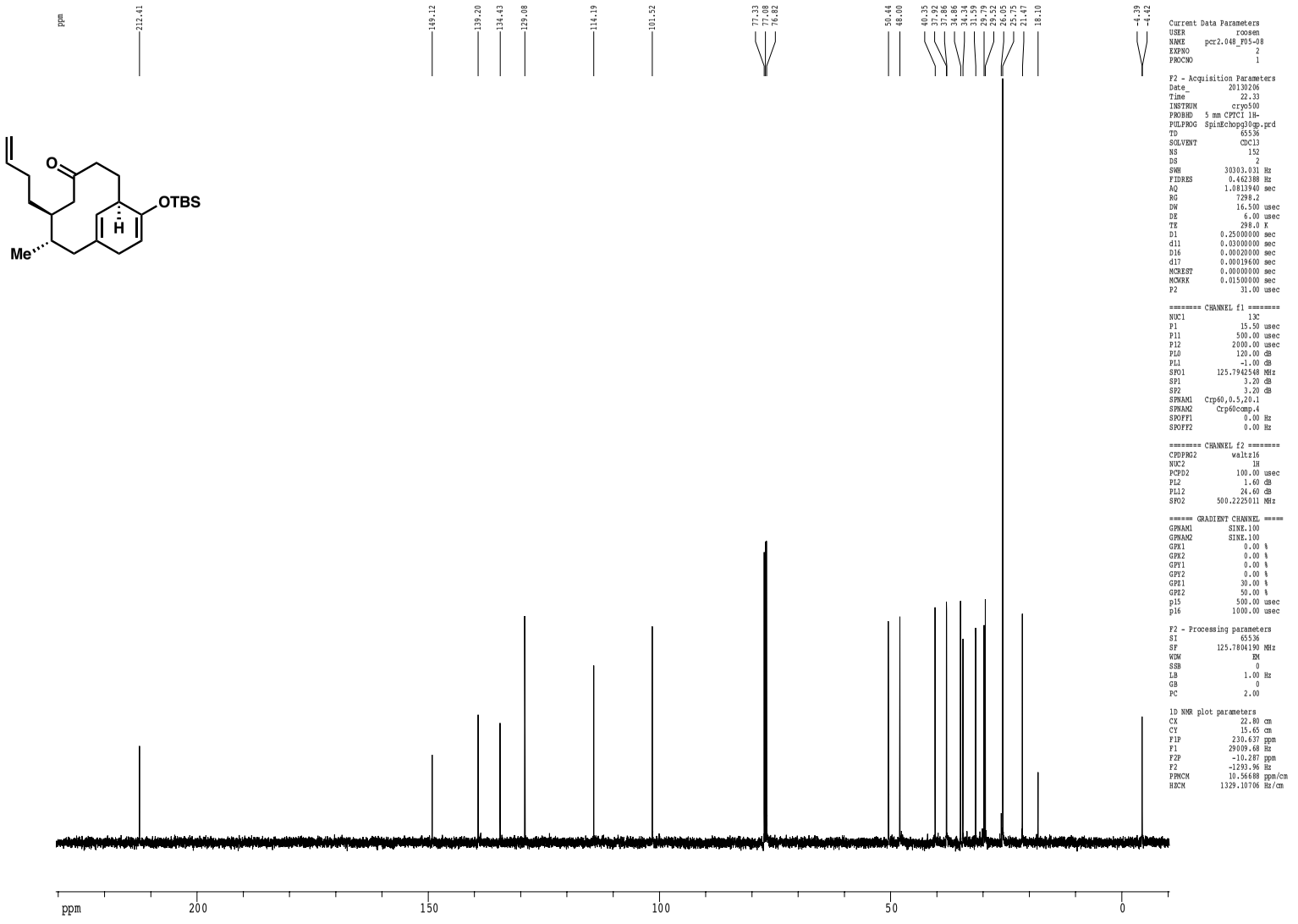
Z-restored spin-echo 13C spectrum with 1H decoupling




```
Current Data Parameters
USER              roosen
NAME      pcr1.292_F04-07
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_          20121221
Time              14.37
INSTRUM         cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD                65536
SOLVENT            CDCl3
NS                   160
DS                     2
SWH           30303.031 Hz
FIDRES        0.462388 Hz
AQ           1.0813940 sec
RG              7298.2
DW               16.500 usec
DE                6.00 usec
TE              298.0 K
D1           0.25000000 sec
d11          0.03000000 sec
D16          0.00020000 sec
d17          0.00019600 sec
MCREST       0.00000000 sec
MCWRK        0.01500000 sec
P2               31.00 usec

======= CHANNEL f1 =======
NUC1               13C
P1                15.50 usec
P11              500.00 usec
P12             2000.00 usec
PL0              120.00 dB
PL1               -1.00 dB
SFO1        125.7942548 MHz
SP1               3.20 dB
SP2               3.20 dB
SPNAM1   Crp60,0.5,20.1
SPNAM2      Crp60comp.4
SPOFF1               0.00 Hz
SPOFF2               0.00 Hz

======= CHANNEL f2 =======
CPDPRG2          waltz16
NUC2                1H
PCPD2            100.00 usec
PL2               1.60 dB
PL12             24.60 dB
SFO2        500.2225011 MHz

===== GRADIENT CHANNEL ====
GPNAM1          SINE.100
GPNAM2          SINE.100
GPX1              0.00 %
GPX2              0.00 %
GPY1              0.00 %
GPY2              0.00 %
GPZ1             30.00 %
GPZ2             50.00 %
p15             500.00 usec
p16            1000.00 usec

F2 - Processing parameters
SI                65536
SF          125.7804282 MHz
WDW                  EM
SSB                   0
LB                1.00 Hz
GB                    0
PC                2.00

1D NMR plot parameters
CX               22.80 cm
CY               15.65 cm
F1P             230.387 ppm
F1              28978.21 Hz
F2P             -10.533 ppm
F2              -1324.82 Hz
PPMCM           10.56667 ppm/cm
HZCM         1329.08032 Hz/cm
```


1H spectrum
ppm
OTBS
H
O
Me
Integral
ppm

Z-restored spin-echo 13C spectrum with 1H decoupling



Current Data Parameters
USER roosen
NAME pcr2.048_F05-08
EXPNO 2
PROCNO 1

F2 - Acquisition Parameters
Date_ 20130206
Time 22.33
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG SpinEchopg30gp.prd
TD 65536
SOLVENT CDCl3
NS 152
DS 2
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0813940 sec
RG 7298.2
DW 16.500 usec
DE 6.00 usec
TE 298.0 K
D1 0.25000000 sec
d11 0.03000000 sec
D16 0.00020000 sec
d17 0.00019600 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
P2 31.00 usec

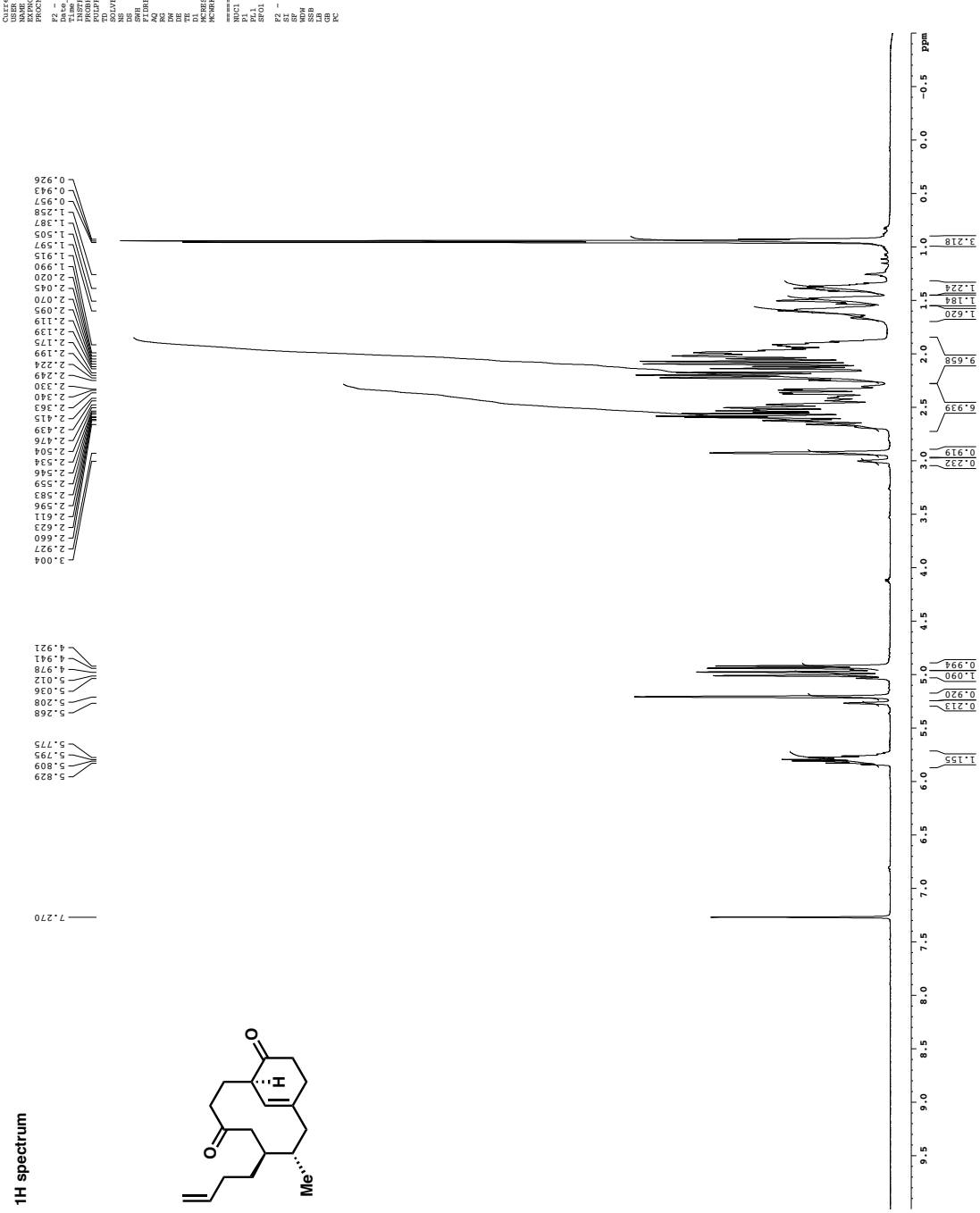
======= CHANNEL f1 =======
NUC1 13C
P1 15.50 usec
P11 500.00 usec
P12 2000.00 usec
PL0 120.00 dB
PL1 -1.00 dB
SFO1 125.7942548 MHz
SP1 3.20 dB
SP2 3.20 dB
SPNAM1 Crp60,0.5,20.1
SPNAM2 Crp60comp.4
SPOFF1 0.00 Hz
SPOFF2 0.00 Hz

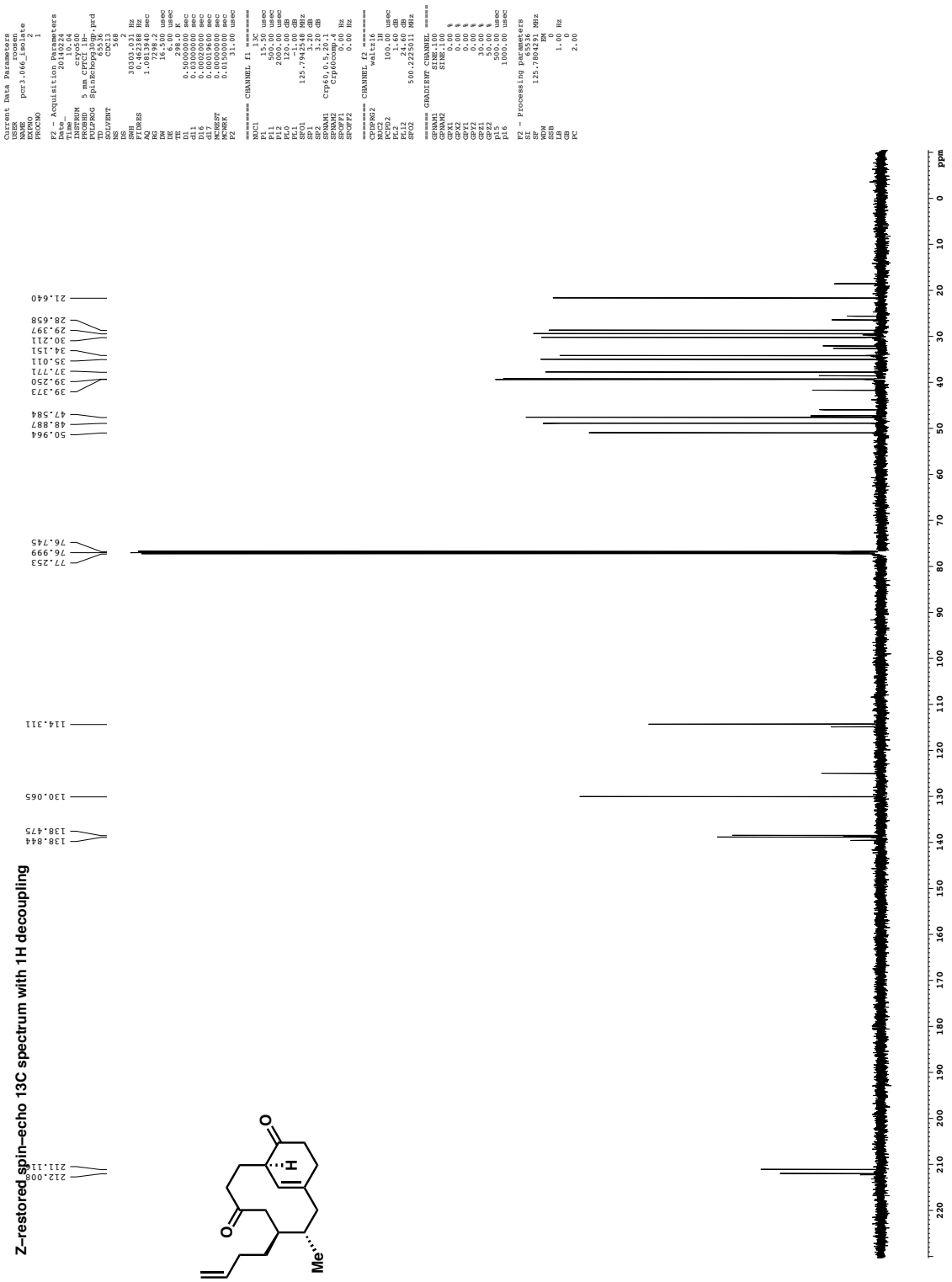
======= CHANNEL f2 =======
CPDPRG2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 1.60 dB
PL12 24.60 dB
SFO2 500.2225011 MHz

===== GRADIENT CHANNEL ====
GPNAM1 SINE.100
GPNAM2 SINE.100
GPX1 0.00 %
GPX2 0.00 %
GPY1 0.00 %
GPY2 0.00 %
GPZ1 30.00 %
GPZ2 50.00 %
p15 500.00 usec
p16 1000.00 usec

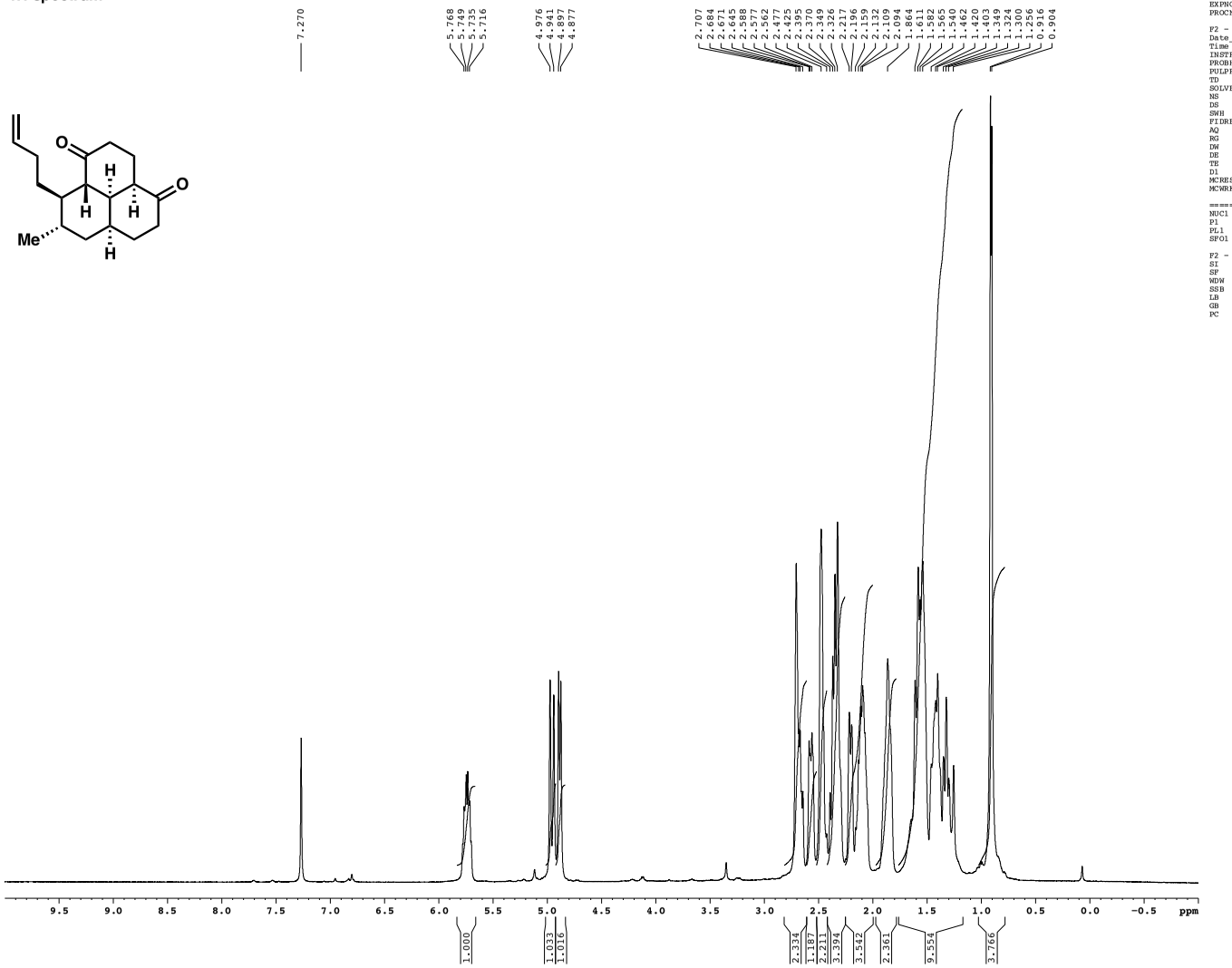
F2 - Processing parameters
SI 65536
SF 125.7804190 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00

1D NMR plot parameters
CX 22.80 cm
CY 15.65 cm
F1P 230.637 ppm
F1 29009.68 Hz
F2P -10.287 ppm
F2 -1293.96 Hz
PPMCM 10.56688 ppm/cm
HZCM 1329.10706 Hz/cm

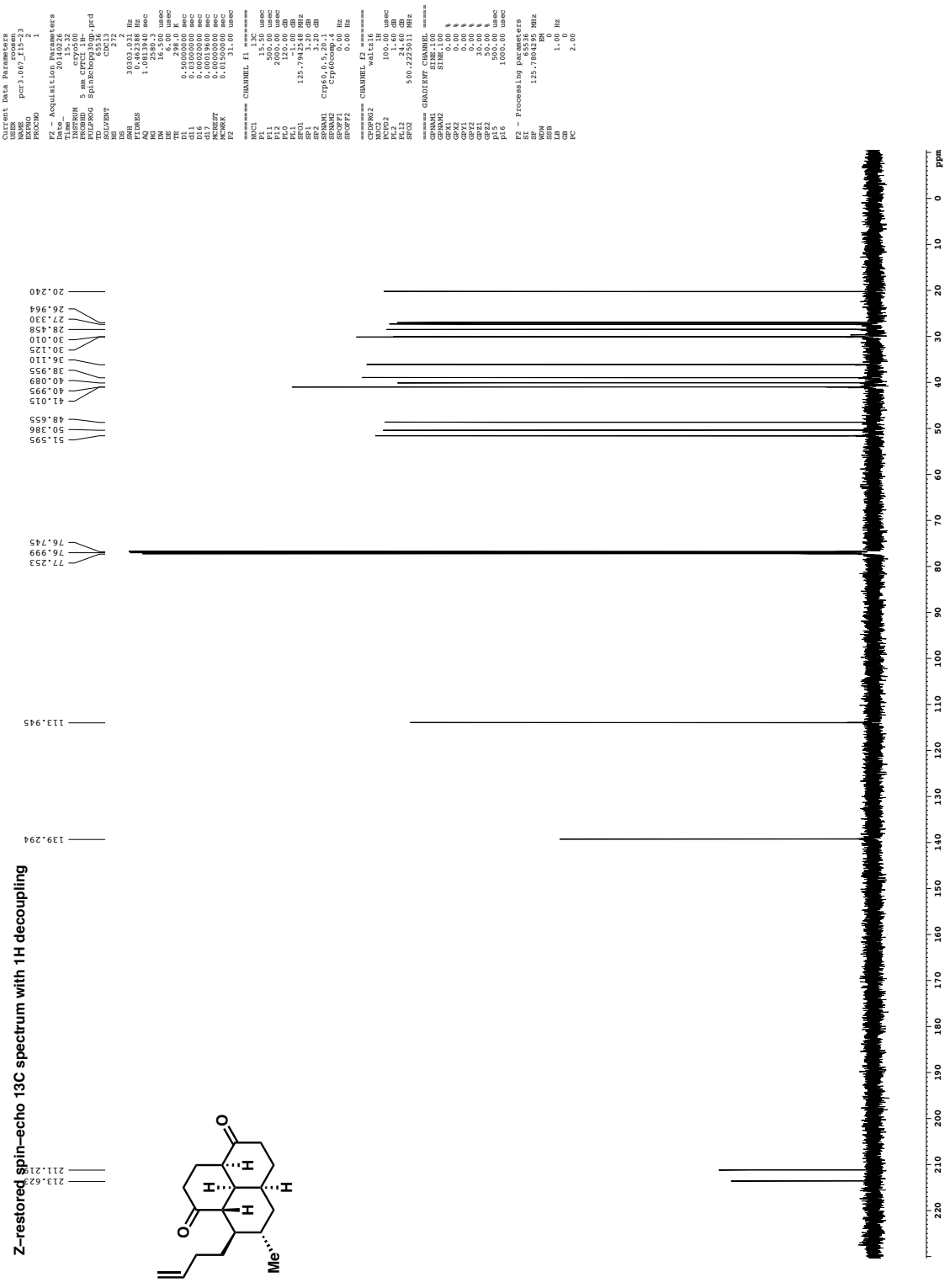

1H spectrum
Current Data Parameters
USER
NAME
EXPNO
PROCNO
F2 - Acquisition Parameters
Date_
Time
INSTRUM
PROBHD
PULPROG
TD
SOLVENT
NS
DS
SWH
FIDRES
AQ
RG
DW
DE
TE
D1
MCREST
MCWRK
=========
NUC1
P1
PL1
SFO1
F2 - Processing parameters
SI
SF
WDW
SSB
LB
GB
PC
ppm
Me
O
O
H

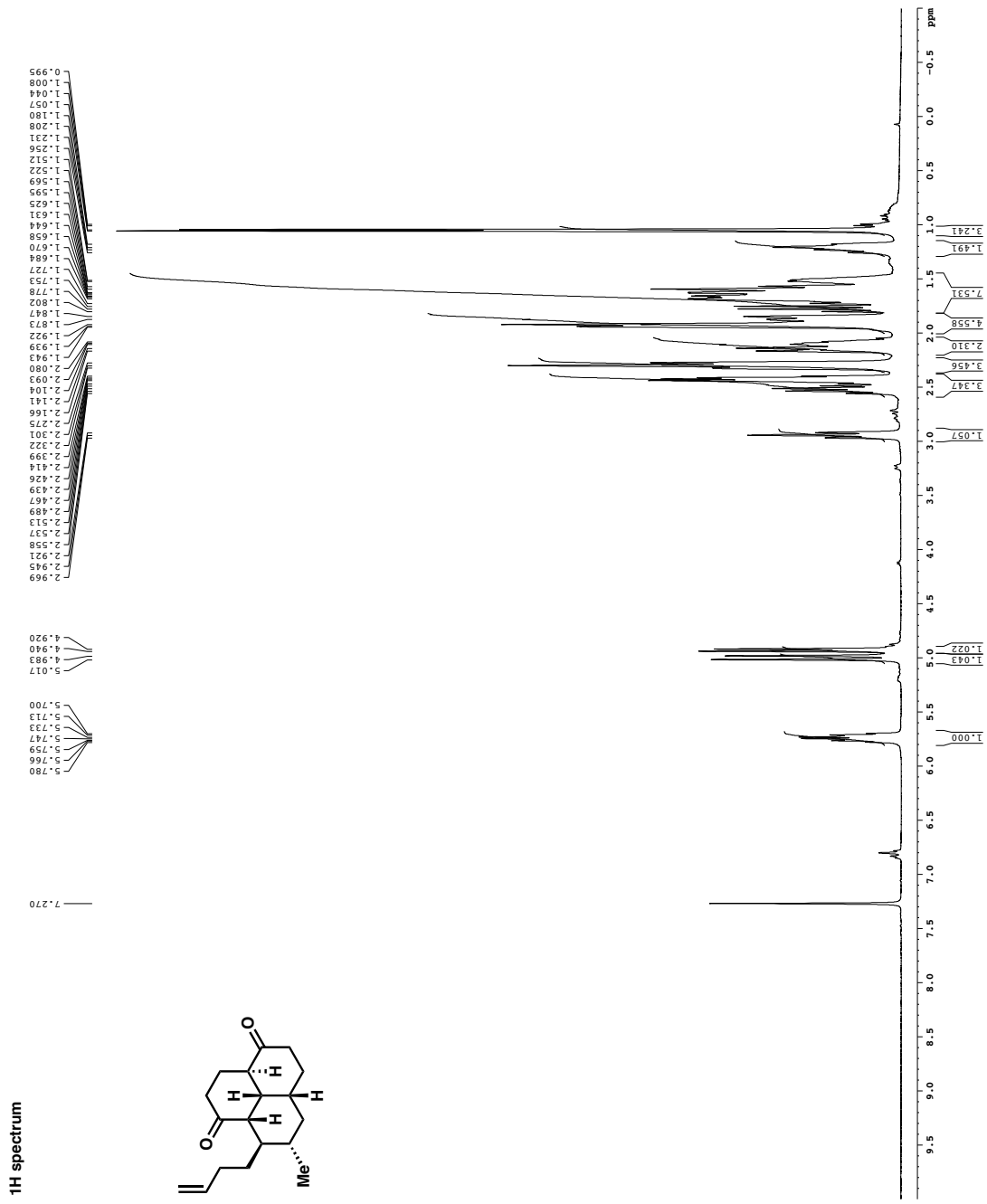

Z–restored spin–echo 13C spectrum with 1H decoupling
Me
ppm

1H spectrum

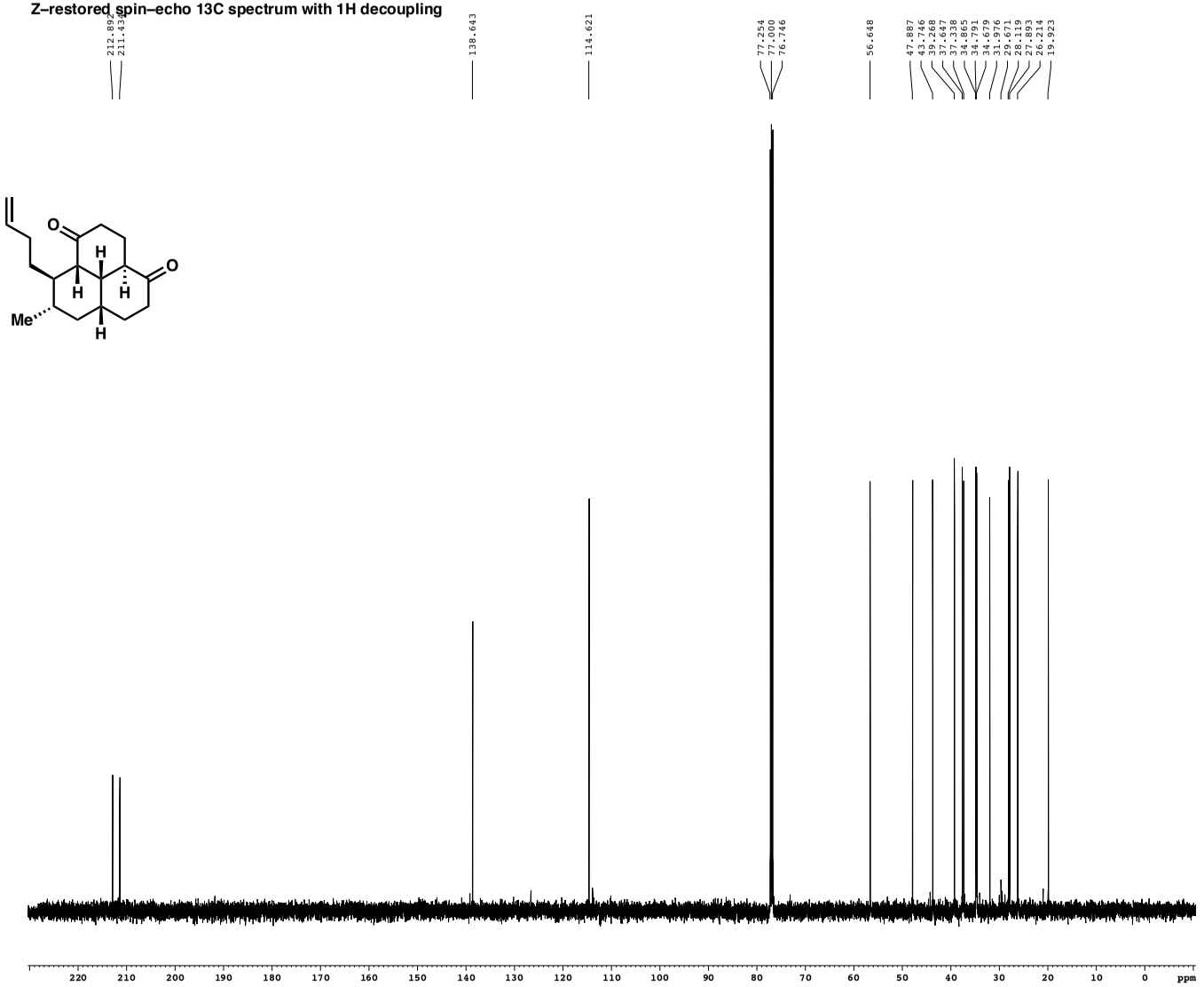



```
Current Data Parameters
USER                 roosen
NAME       pcr3.067_f15-23
EXPNO                     1
PROCNO                    1

F2 - Acquisition Parameters
Date_             20140226
Time                 15.30
INSTRUM            cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG              zg30
TD                  32048
SOLVENT              CDCl3
NS                      16
DS                       2
SWH              8012.820 Hz
FIDRES           0.250026 Hz
AQ               1.9998451 sec
RG                     4.5
DW                  62.400 usec
DE                   6.00 usec
TE                  298.0 K
D1             0.10000000 sec
MCREST         0.00000000 sec
MCWRK          0.01500000 sec

======== CHANNEL f1 ========
NUC1                   1H
P1                   7.50 usec
PL1                  1.60 dB
SFO1          500.2235015 MHz

F2 - Processing parameters
SI                    65536
SF            500.2200265 MHz
WDW                      EM
SSB                       0
LB                     0.30 Hz
GB                        0
PC                     4.00
```

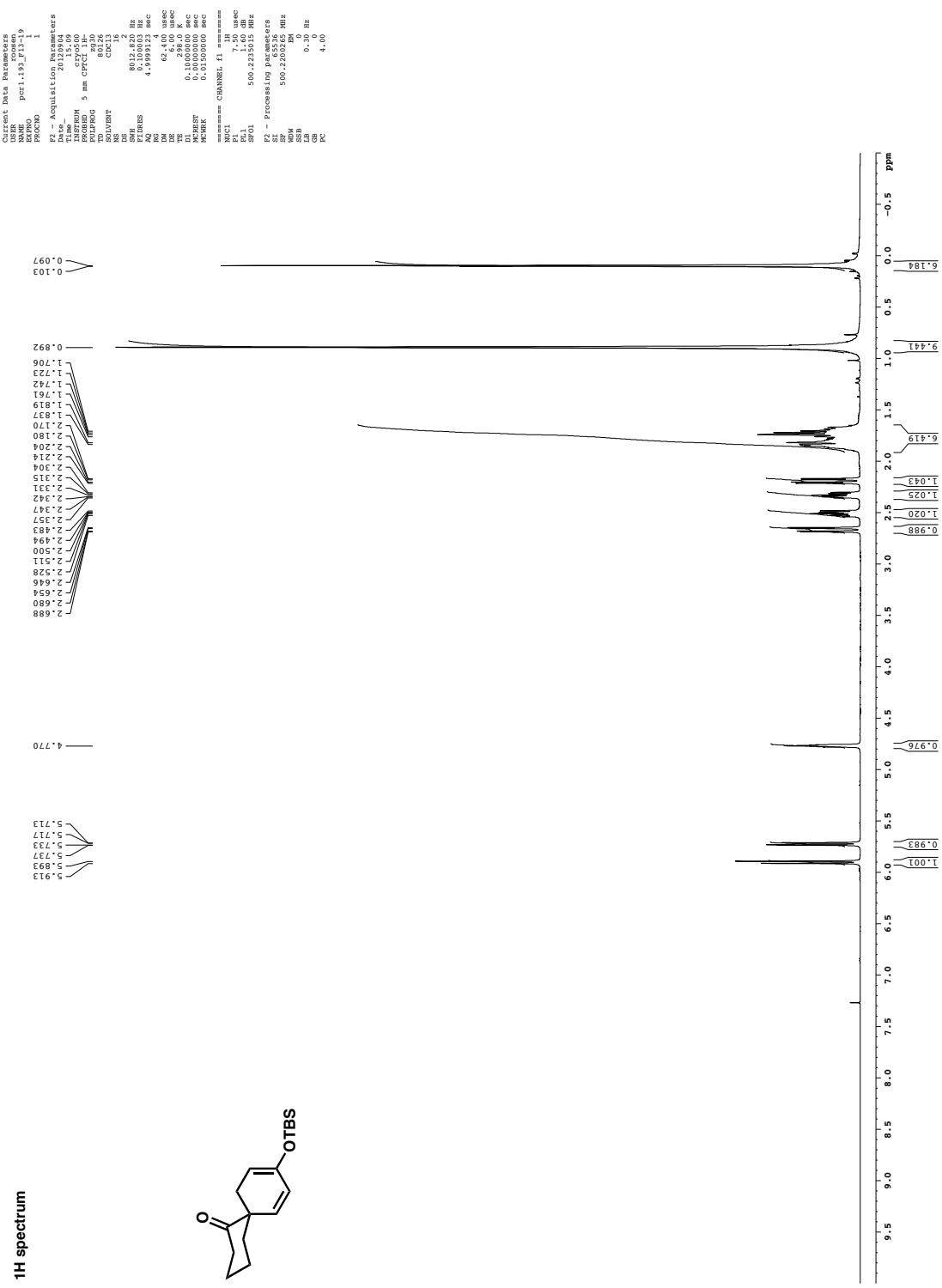

Z–restored spin–echo 13C spectrum with 1H decoupling
Current Data Parameters
USERA2 pcr3.067_f15-23
NAME pcr3.067_f15-23
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20141230
Time 15.32
INSTRUM cryo1in
PROBHD 5 mm CPCI cryo1in
PULPROG SpinEchopg30gp.pcd
TD 65536
SOLVENT CDCl3
NS 272
DS 2
SWH 30303.031 Hz
FIDRES 0.462308 Hz
AQ 1.0813440 sec
RG 2580.3
DW 16.500 usec
DE 6.00 usec
TE 298.0 K
D1 0.50000000 sec
D11 0.03000000 sec
D16 0.00020000 sec
d17 0.00019600 sec
MCWRGHT 0.00000000 sec
MCWRK 0.01500000 sec
P2 31.00 usec
======== CHANNEL f1 ========
NUC1 13C
P1 15.50 usec
P11 500.00 usec
PL2 2000.00 usec
PL10 120.00 dB
PL1 -1.00 dB
SFO1 125.7942548 MHz
SP1 3.00 dB
SP2 3.20 dB
SPNAM1 Crp60,0.5,20.1
SPNAM2 Crp60comp.4
SPOFF1 0.00 Hz
SPOFF2 0.00 Hz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 1.60 dB
PL12 24.60 dB
SFO2 500.2225011 MHz
====== GRADIENT CHANNEL =====
GPNAM1 SINE.100
GPNAM2 SINE.100
GPZ1 0.00 %
GPZ2 0.00 %
GPZ3 0.00 %
GPZ4 0.00 %
GPZ5 30.00 %
GPZ6 50.00 %
p15 500.00 usec
p16 1000.00 usec
F2 - Processing parameters
SI 65536
SF 125.7804282 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00
20.240
26.964
27.330
28.458
30.010
30.125
36.110
38.955
40.089
40.995
41.015
48.655
50.386
51.595
77.253
76.999
76.745
113.945
139.294
213.623
211.215
Me
H
H
H
H
O
O
ppm


1H spectrum
Me

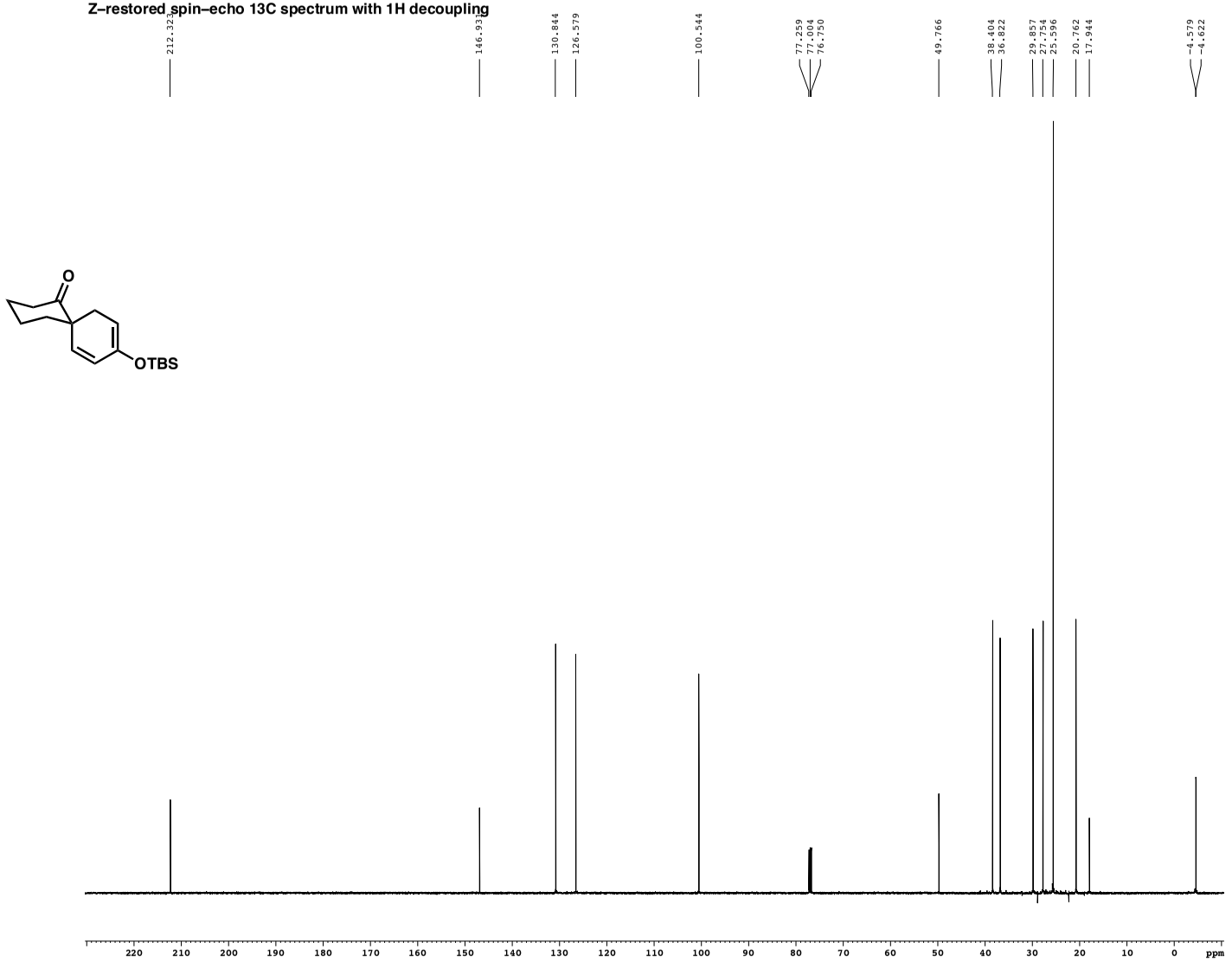
Z–restored spin–echo 13C spectrum with 1H decoupling




```
Current Data Parameters
USER                 roosen
NAME      pcr3.067_f28-39
EXPNO                     2
PROCNO                    1

F2 - Acquisition Parameters
Date_            20140226
Time                15.45
INSTRUM           cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD                  65536
SOLVENT               CDCl3
NS                      248
DS                        2
SWH              30303.031 Hz
FIDRES           0.462388 Hz
AQ               1.0813940 sec
RG                  3649.1
DW                  16.500 usec
DE                   6.00 usec
TE                  298.0 K
D1              0.50000000 sec
d11             0.03000000 sec
D16             0.00020000 sec
d17             0.00019600 sec
MCREST          0.00000000 sec
MCWRK           0.01500000 sec
P2                  31.00 usec

======= CHANNEL f1 ========
NUC1                   13C
P1                   15.50 usec
P11                 500.00 usec
P12                2000.00 usec
PL0                 120.00 dB
PL1                  -1.00 dB
SFO1          125.7942548 MHz
SP1                   3.20 dB
SP2                   3.20 dB
SPNAM1    Crp60,0.5,20.1
SPNAM2       Crp60comp.4
SPOFF1                0.00 Hz
SPOFF2                0.00 Hz

======= CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                    1H
PCPD2                100.00 usec
PL2                   1.60 dB
PL12                 24.60 dB
SFO2          500.2225011 MHz

===== GRADIENT CHANNEL =====
GPNAM1             SINE.100
GPNAM2             SINE.100
GPX1                  0.00 %
GPX2                  0.00 %
GPY1                  0.00 %
GPY2                  0.00 %
GPZ1                 30.00 %
GPZ2                 50.00 %
p15                 500.00 usec
p16                1000.00 usec

F2 - Processing parameters
SI                    65536
SF            125.7804295 MHz
WDW                     EM
SSB                      0
LB                    1.00 Hz
GB                       0
PC                    2.00
```

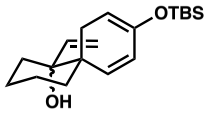

1H spectrum
OTBS
O
Current Data Parameters
NAME pcr1.193_F13-19
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20120904
TIME 15.09
INSTRUM cryo500
PROBHD 5 mm CPCI
PULPROG zg30
TD 80128
SOLVENT CDCl3
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.100803 Hz
AQ 4.999913 sec
RG 4
DW 62.400 usec
DE 6.00 usec
TE 296.0 K
D1 0.10000000 sec
MCWEGT 0.10000000 sec
MCWRK 0.01500000 sec
nnnnnnn CHANNEL f1 nnnnnnn
NUC1 1H
P1 7.50 usec
PL1 1.00 dB
SFO1 500.2235015 MHz
F2 - Processing parameters
SI 65536
SF 500.2200265 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00
0.097
0.103
0.892
1.706
1.723
1.742
1.761
1.819
1.837
2.170
2.180
2.204
2.214
2.304
2.315
2.331
2.342
2.347
2.357
2.483
2.494
2.500
2.511
2.528
2.646
2.654
2.680
2.688
4.770
5.713
5.717
5.733
5.737
5.893
5.913
6.184
9.441
6.419
1.043
1.025
1.020
0.988
0.976
0.983
1.001
ppm

Z–restored spin–echo 13C spectrum with 1H decoupling




```
Current Data Parameters
USER                roosen
NAME      pcr1.193_F13-19
EXPNO                    2
PROCNO                   1

F2 - Acquisition Parameters
Date_            20120904
Time                15.12
INSTRUM           cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD                  65536
SOLVENT               CDCl3
NS                      128
DS                       16
SWH              30303.031 Hz
FIDRES           0.462388 Hz
AQ               1.0813940 sec
RG                   5160.6
DW                   16.500 usec
DE                    6.00 usec
TE                   298.0 K
D1              0.25000000 sec
d11             0.03000000 sec
D16             0.00020000 sec
d17             0.00019600 sec
MCREST          0.00000000 sec
MCWRK           0.01500000 sec
P2                   31.00 usec

======= CHANNEL f1 =======
NUC1                    13C
P1                   15.50 usec
P11                 500.00 usec
P12                2000.00 usec
PL0                 120.00 dB
PL1                  -1.00 dB
SFO1          125.7942548 MHz
SP1                   3.20 dB
SP2                   3.20 dB
SPNAM1    Crp60,0.5,20.1
SPNAM2       Crp60comp.4
SPOFF1               0.00 Hz
SPOFF2               0.00 Hz

======= CHANNEL f2 =======
CPDPRG2             waltz16
NUC2                    1H
PCPD2               100.00 usec
PL2                   1.60 dB
PL12                 24.60 dB
SFO2          500.2225011 MHz

===== GRADIENT CHANNEL =====
GPNAM1            SINE.100
GPNAM2            SINE.100
GPX1                 0.00 %
GPX2                 0.00 %
GPY1                 0.00 %
GPY2                 0.00 %
GPZ1                30.00 %
GPZ2                50.00 %
p15                500.00 usec
p16               1000.00 usec

F2 - Processing parameters
SI                  65536
SF            125.7804319 MHz
WDW                    EM
SSB                     0
LB                   1.00 Hz
GB                      0
PC                   2.00
```

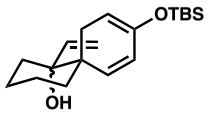
1H spectrum



5.4 : 1 dr

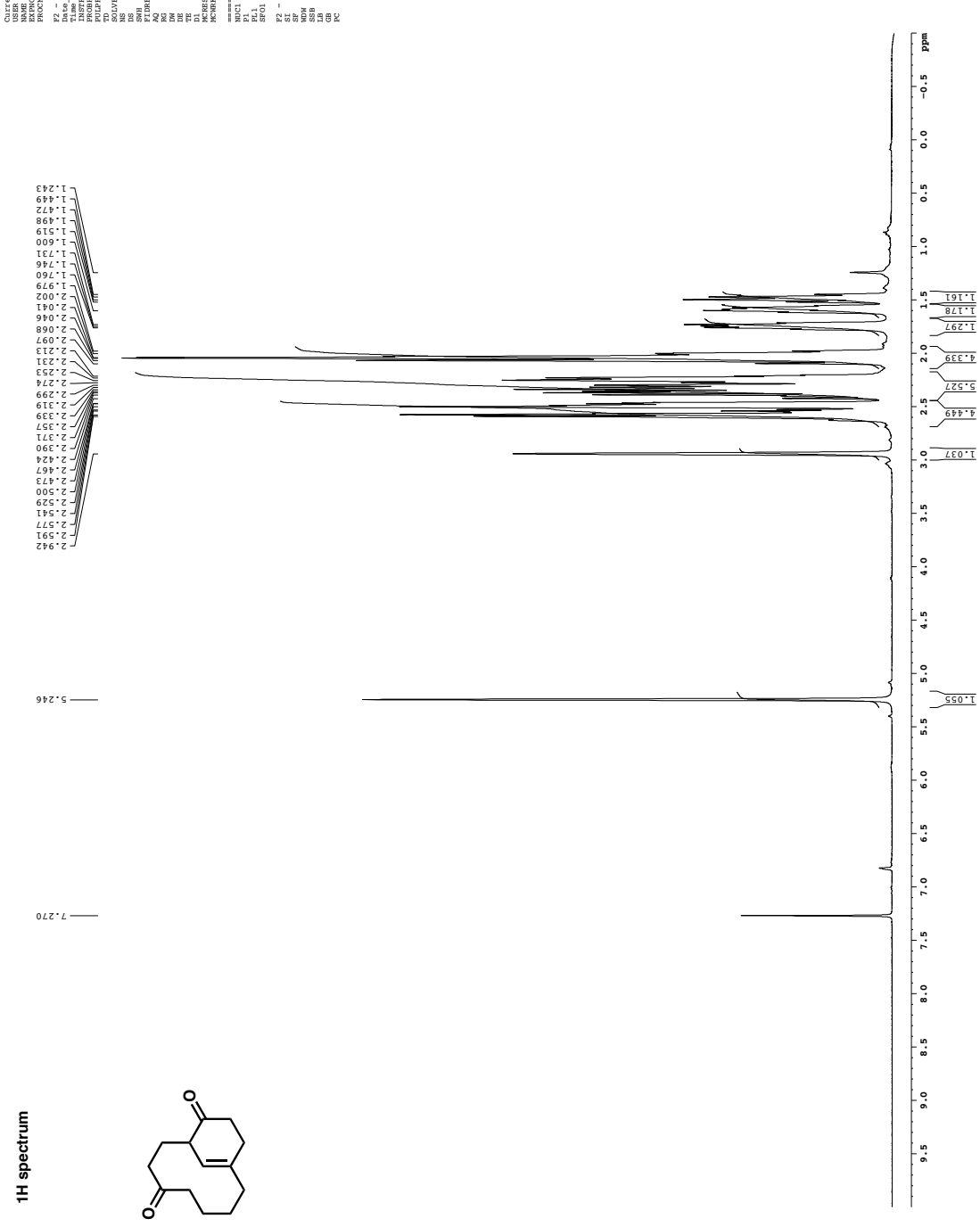

```
Current Data Parameters
USER                 roosen
NAME       pcr1.196_F11-19
EXPNO                     1
PROCNO                    1

F2 - Acquisition Parameters
Date_             20120907
Time                 10.09
INSTRUM              cryo500
PROBHD    5 mm CPTCI 1H-
PULPROG                zg30
TD                    80126
SOLVENT               CDCl3
NS                       16
DS                        2
SWH                6009.615 Hz
FIDRES             0.075002 Hz
AQ                 6.6665330 sec
RG                        5
DW                   83.200 usec
DE                    6.00 usec
TE                   298.0 K
D1              0.10000000 sec
MCREST          0.00000000 sec
MCWRK           0.01500000 sec

======== CHANNEL f1 ========
NUC1                     1H
P1                    7.50 usec
PL1                   1.60 dB
SFO1           500.2225011 MHz

F2 - Processing parameters
SI                    65536
SF             500.2200262 MHz
WDW                      EM
SSB                       0
LB                     0.30 Hz
GB                        0
PC                     4.00
```

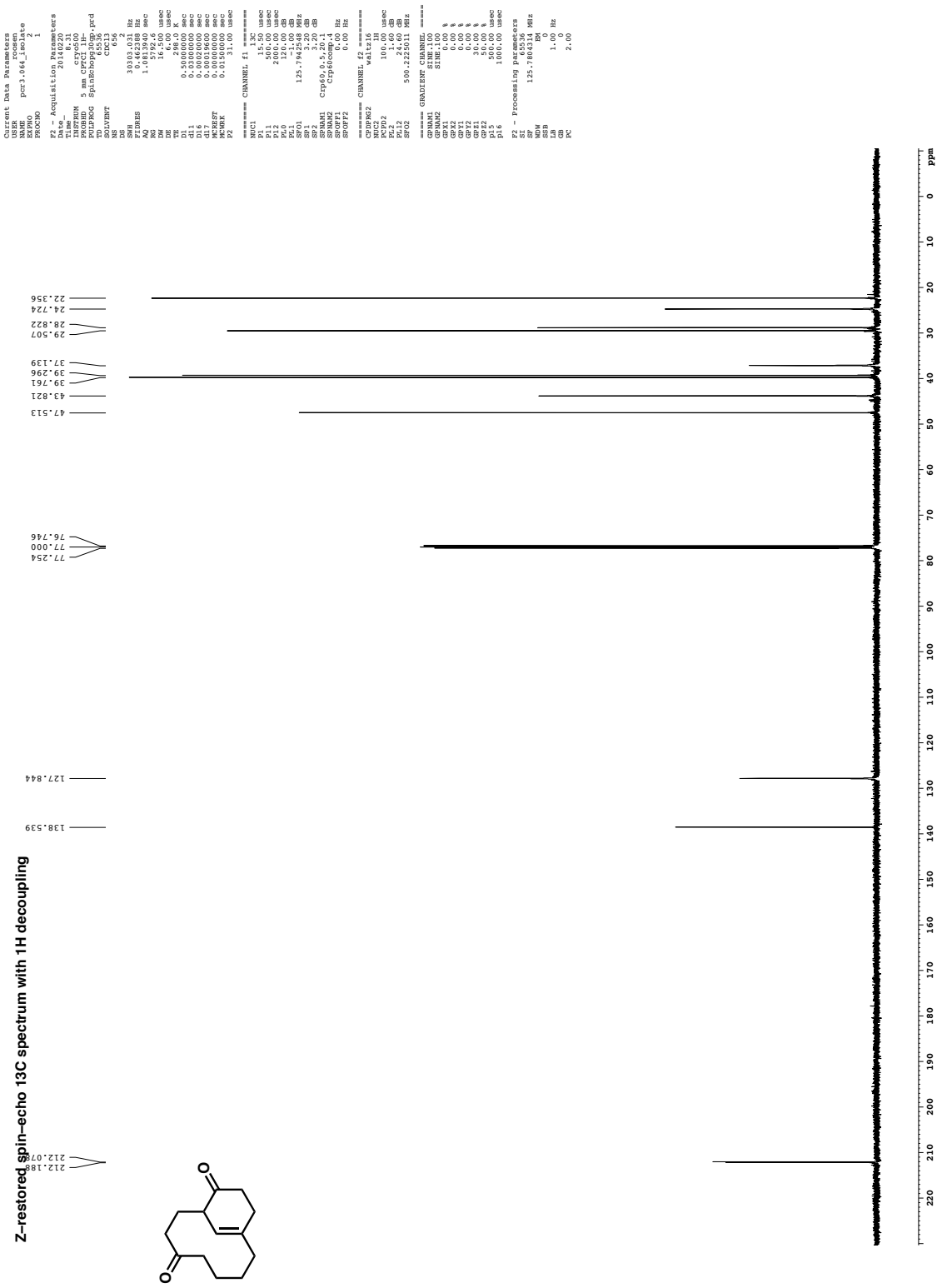
Z–restored spin–echo 13C spectrum with 1H decoupling



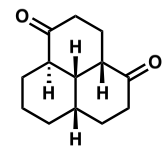
5.4 : 1 dr


```
Current Data Parameters
USER                 roosen
NAME      pcr1.196_F11-19
EXPNO                     2
PROCNO                    1

F2 - Acquisition Parameters
Date_             20120907
Time                 10.12
INSTRUM              cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD                   65536
SOLVENT              CDCl3
NS                     384
DS                      16
SWH              30303.031 Hz
FIDRES           0.462388 Hz
AQ               1.0813940 sec
RG                  4597.6
DW                  16.500 usec
DE                   6.00 usec
TE                  298.0 K
D1              0.25000000 sec
d11             0.03000000 sec
D16             0.00020000 sec
d17             0.00019600 sec
MCREST          0.00000000 sec
MCWRK           0.01500000 sec
P2                  31.00 usec

======= CHANNEL f1 =======
NUC1                  13C
P1                  15.50 usec
P11                500.00 usec
P12               2000.00 usec
PL0                120.00 dB
PL1                 -1.00 dB
SFO1         125.7942548 MHz
SP1                 3.20 dB
SP2                 3.20 dB
SPNAM1    Crp60,0.5,20.1
SPNAM2       Crp60comp.4
SPOFF1              0.00 Hz
SPOFF2              0.00 Hz

======= CHANNEL f2 =======
CPDPRG2           waltz16
NUC2                   1H
PCPD2              100.00 usec
PL2                 1.60 dB
PL12               24.60 dB
SFO2         500.2225011 MHz

===== GRADIENT CHANNEL =====
GPNAM1           SINE.100
GPNAM2           SINE.100
GPX1                0.00 %
GPX2                0.00 %
GPY1                0.00 %
GPY2                0.00 %
GPZ1               30.00 %
GPZ2               50.00 %
p15               500.00 usec
p16              1000.00 usec

F2 - Processing parameters
SI                   65536
SF           125.7804282 MHz
WDW                    EM
SSB                     0
LB                   1.00 Hz
GB                      0
PC                   2.00
```


1H spectrum
Current Data Parameters
USER pcr
NAME pcr3.064_isolate
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20140220
TIME 8.29
INSTRUM cpc-250
PROBHD 5 mm CPCI 1H-
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.250026 Hz
AQ 1.999881 sec
RG 5
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCWEGT 0.10000000 sec
MCWERK 0.01500000 sec
CHANNEL f1
NUC1 1H
P1 7.50 usec
PL1 1.60 dB
SFO1 500.2235015 MHz
F2 - Processing parameters
SI 65536
SF 500.2200268 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00
7.270
5.246
2.942
2.591
2.577
2.541
2.529
2.500
2.473
2.467
2.424
2.390
2.371
2.357
2.339
2.319
2.299
2.274
2.253
2.231
2.213
2.097
2.068
2.046
2.041
2.002
1.979
1.760
1.746
1.731
1.600
1.519
1.498
1.472
1.449
1.243
1.055
1.037
4.449
5.527
4.339
1.297
1.178
1.161
ppm

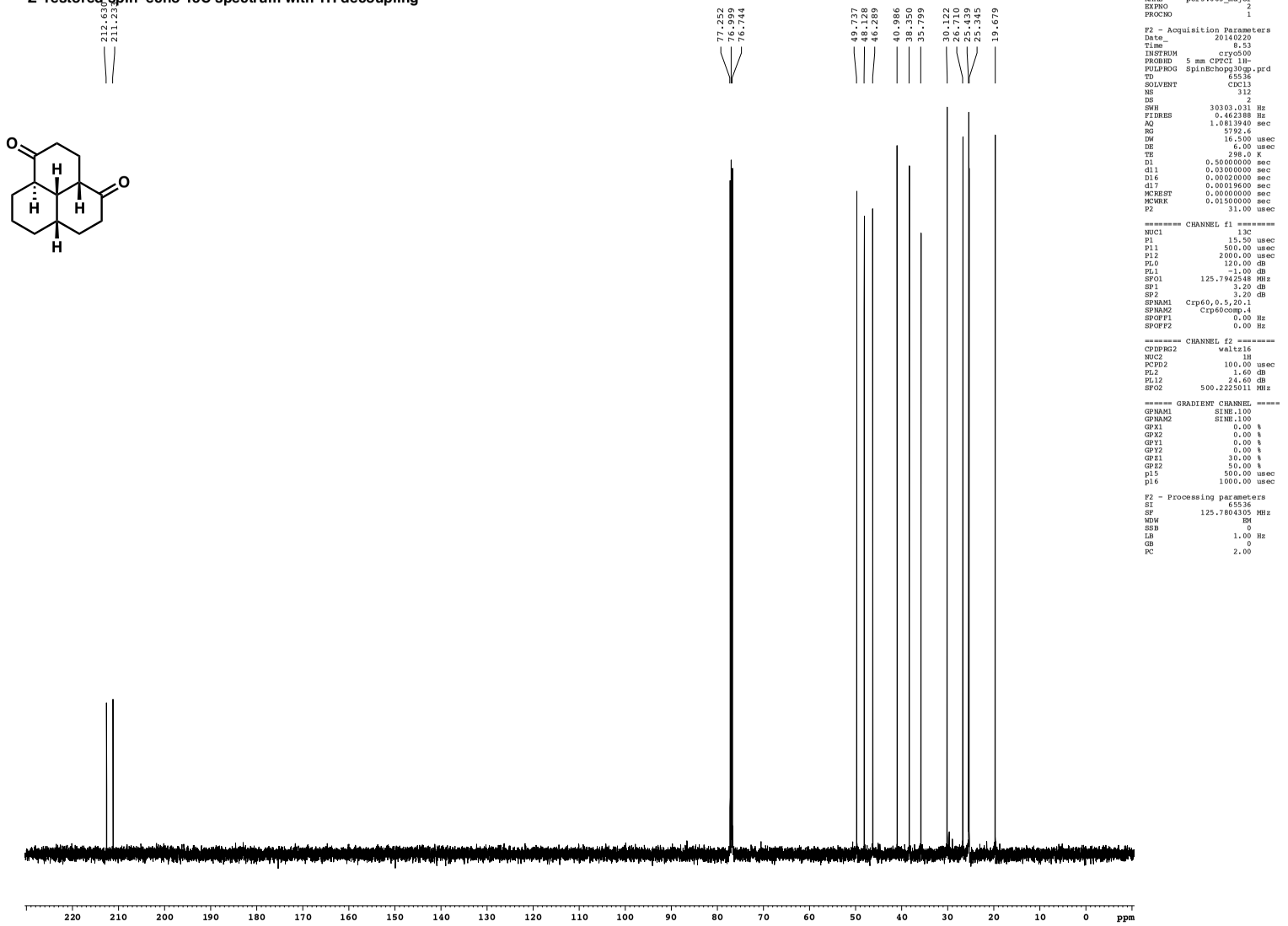

Z–restored spin–echo 13C spectrum with 1H decoupling
212.078
212.188
138.539
127.844
77.254
77.000
76.746
47.513
43.821
39.761
39.296
37.139
29.507
28.822
24.724
22.356
ppm

1H spectrum

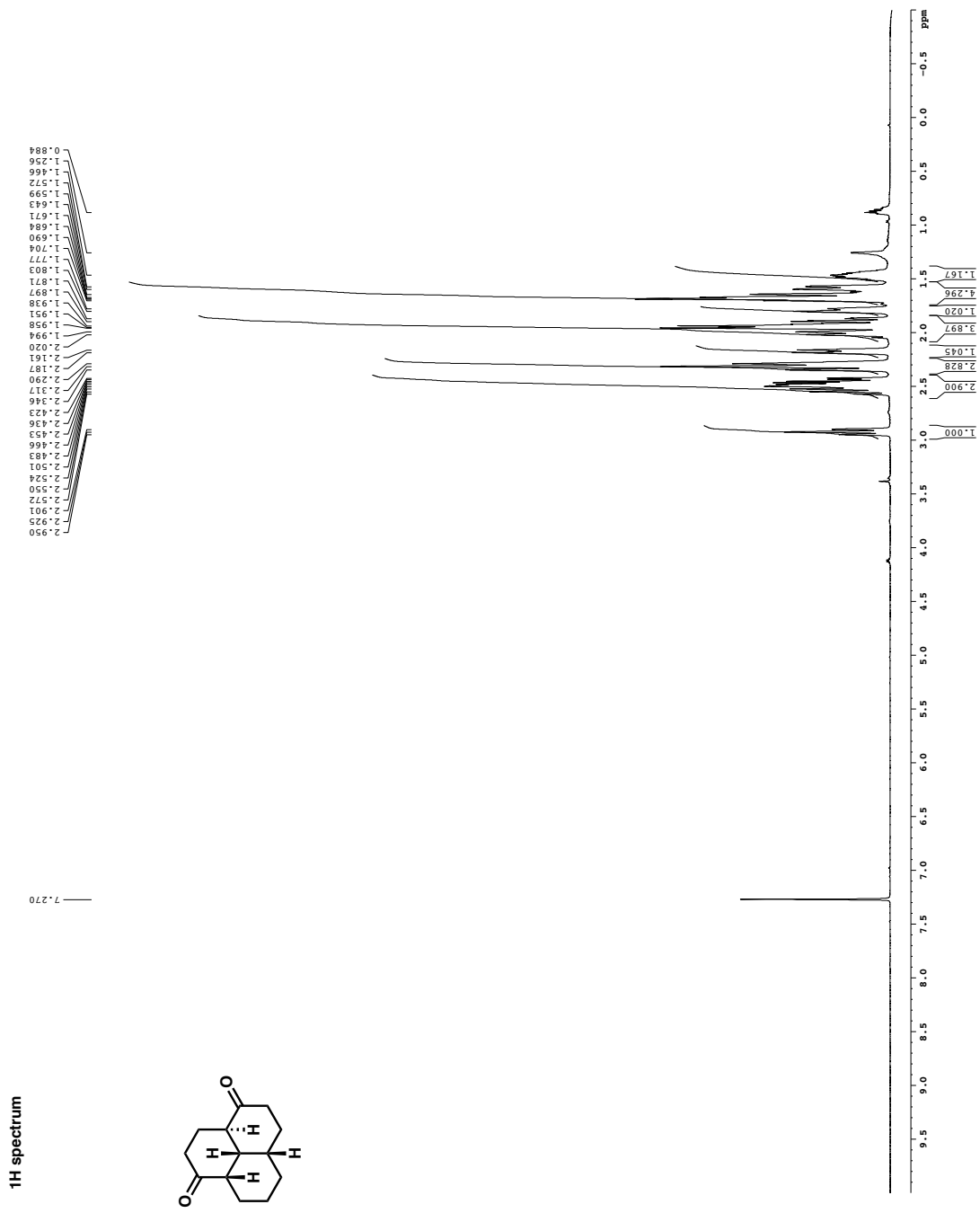



```
Current Data Parameters
USER                  roosen
NAME          pcr3.063_major
EXPNO                      1
PROCNO                     1

F2 - Acquisition Parameters
Date_              20140220
Time                   8.50
INSTRUM              cryo500
PROBHD    5 mm CPTCI 1H-
PULPROG                zg30
TD                    32048
SOLVENT               CDCl3
NS                       16
DS                        2
SWH                8012.820 Hz
FIDRES             0.250026 Hz
AQ                 1.9998451 sec
RG                       7.1
DW                    62.400 usec
DE                     6.00 usec
TE                    298.0 K
D1                 0.10000000 sec
MCREST             0.00000000 sec
MCWRK              0.01500000 sec

======== CHANNEL f1 ========
NUC1                      1H
P1                     7.50 usec
PL1                    1.60 dB
SFO1           500.2235015 MHz

F2 - Processing parameters
SI                       65536
SF             500.2200267 MHz
WDW                       EM
SSB                        0
LB                      0.30 Hz
GB                         0
PC                      4.00
```

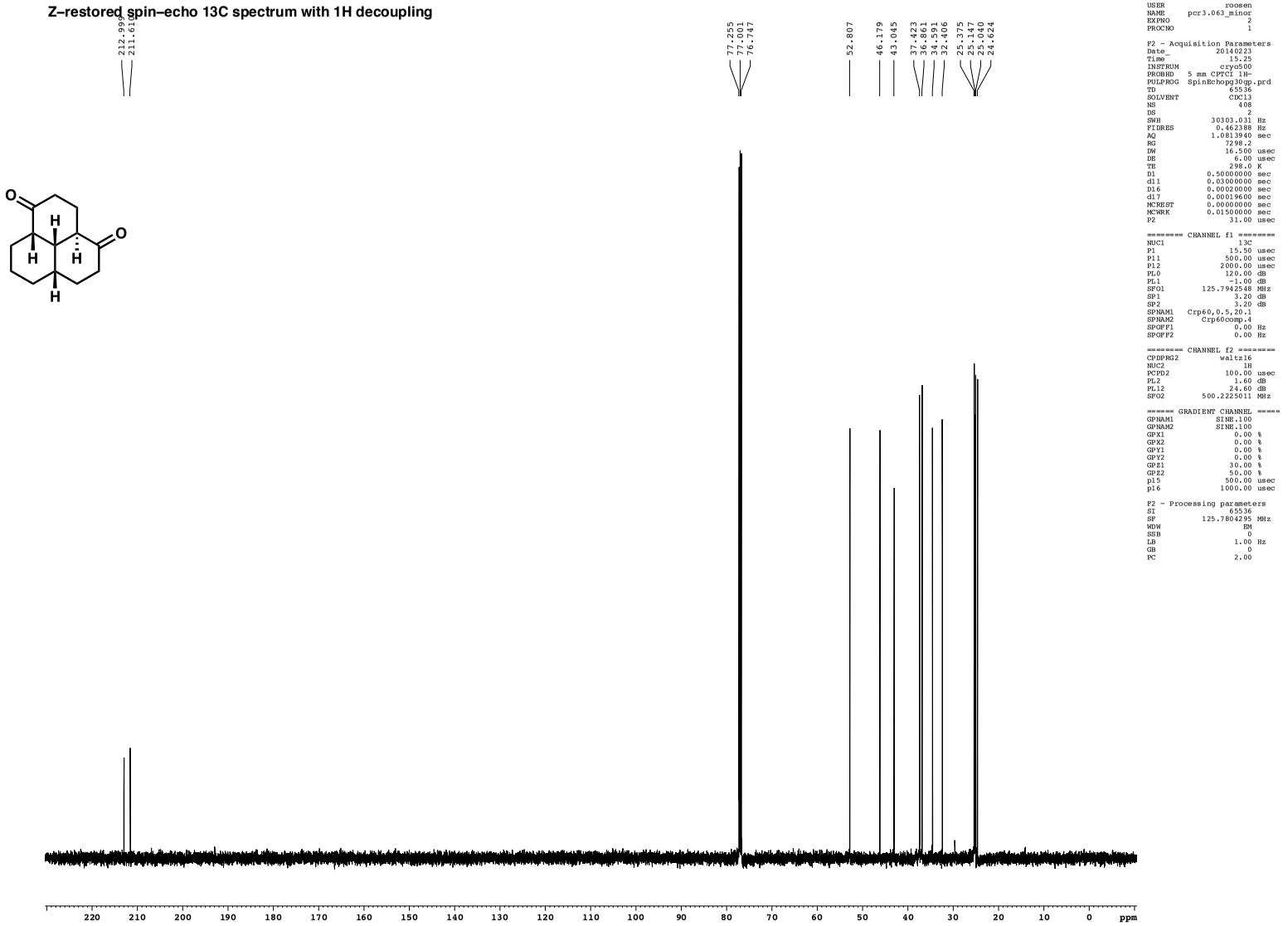
Z–restored spin–echo 13C spectrum with 1H decoupling




```
Current Data Parameters
USER                 roosen
NAME      pcr3.063_major
EXPNO                     2
PROCNO                    1

F2 - Acquisition Parameters
Date_              20140220
Time                   8.53
INSTRUM              cryo500
PROBHD    5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD                    65536
SOLVENT                CDCl3
NS                       312
DS                         2
SWH                30303.031 Hz
FIDRES             0.462388 Hz
AQ                 1.0813940 sec
RG                    5792.6
DW                    16.500 usec
DE                     6.00 usec
TE                     298.0 K
D1              0.50000000 sec
d11             0.03000000 sec
D16             0.00020000 sec
d17             0.00019600 sec
MCREST          0.00000000 sec
MCWRK           0.01500000 sec
P2                    31.00 usec

======= CHANNEL f1 ========
NUC1                    13C
P1                    15.50 usec
P11                  500.00 usec
P12                 2000.00 usec
PL0                  120.00 dB
PL1                   -1.00 dB
SFO1           125.7942548 MHz
SP1                    3.20 dB
SP2                    3.20 dB
SPNAM1    Crp60,0.5,20.1
SPNAM2       Crp60comp.4
SPOFF1                 0.00 Hz
SPOFF2                 0.00 Hz

======= CHANNEL f2 ========
CPDPRG2              waltz16
NUC2                    1H
PCPD2                100.00 usec
PL2                    1.60 dB
PL12                  24.60 dB
SFO2           500.2225011 MHz

===== GRADIENT CHANNEL =====
GPNAM1             SINE.100
GPNAM2             SINE.100
GPX1                   0.00 %
GPX2                   0.00 %
GPY1                   0.00 %
GPY2                   0.00 %
GPZ1                  30.00 %
GPZ2                  50.00 %
p15                  500.00 usec
p16                 1000.00 usec

F2 - Processing parameters
SI                    65536
SF             125.7804305 MHz
WDW                      EM
SSB                       0
LB                     1.00 Hz
GB                        0
PC                     2.00
```

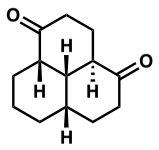

1H spectrum
Current Data Parameters
NAME pcr3.063_minor
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20140223
Time 15.23
INSTRUM spect
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.250026 Hz
AQ 1.999951 sec
RG 7.1
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCWEGT 0.10000000 sec
MCREK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 7.50 usec
PL1 1.60 dB
SFO1 500.2235015 MHz
F2 - Processing parameters
SI 65536
SF 500.2200261 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00
7.270
2.950
2.925
2.901
2.572
2.550
2.524
2.501
2.483
2.466
2.453
2.436
2.423
2.346
2.317
2.290
2.187
2.161
2.020
1.994
1.958
1.938
1.897
1.871
1.803
1.777
1.704
1.690
1.684
1.671
1.643
1.599
1.572
1.466
1.256
0.884
1.000
2.900
2.828
1.045
3.897
1.020
4.296
1.167
ppm

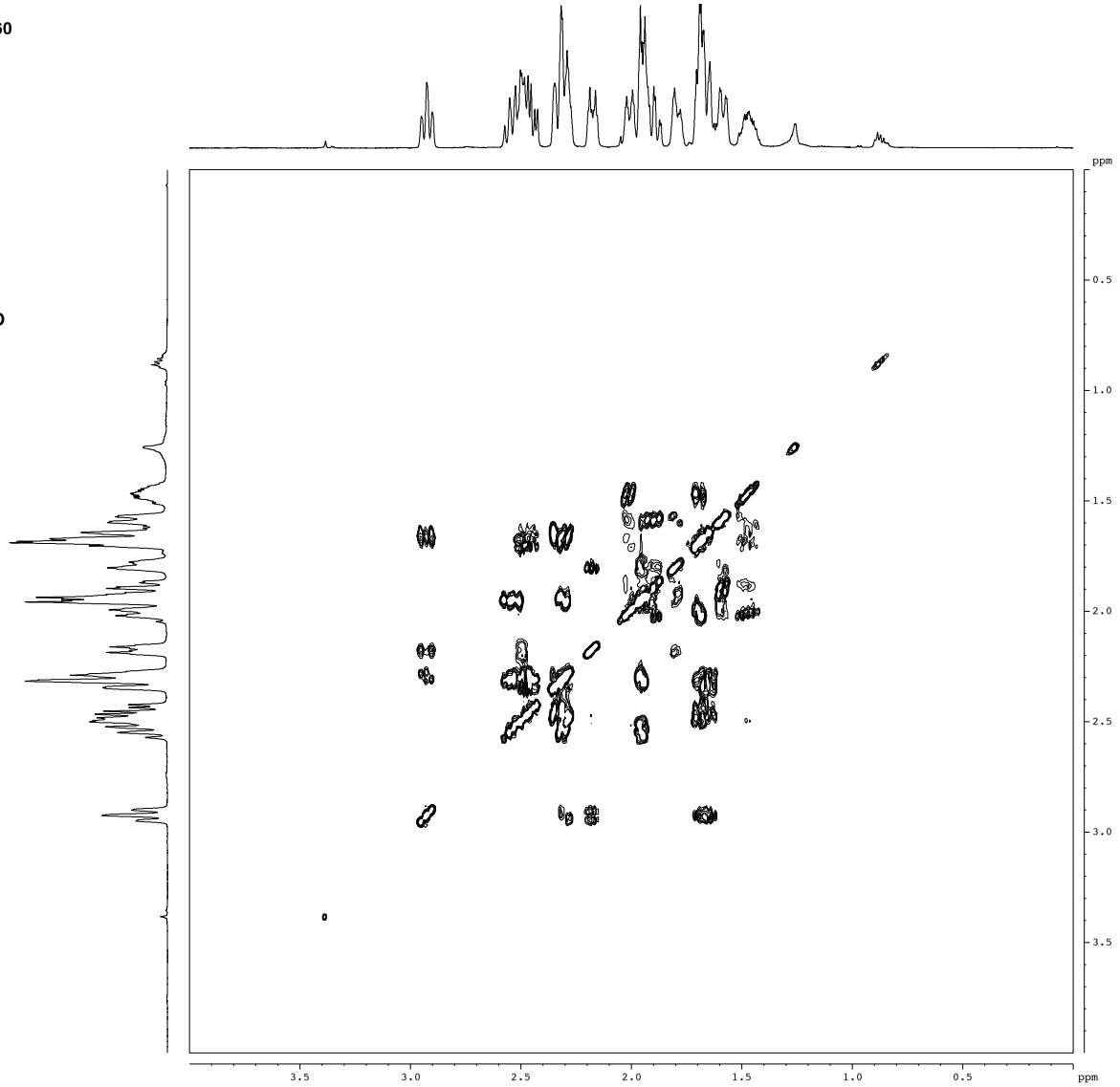
Z–restored spin–echo 13C spectrum with 1H decoupling




```
Current Data Parameters
USER                 roosen
NAME      pcr3.063_minor
EXPNO                     2
PROCNO                    1

F2 - Acquisition Parameters
Date_             20140223
Time                 15.25
INSTRUM           cryo500
PROBHD    5 mm CPTCI 1H-
PULPROG   SpinEchopg30gp.prd
TD                   65536
SOLVENT              CDCl3
NS                     408
DS                       2
SWH              30303.031 Hz
FIDRES           0.462388 Hz
AQ               1.0813940 sec
RG                  7298.2
DW                  16.500 usec
DE                   6.00 usec
TE                  298.0 K
D1              0.50000000 sec
d11             0.03000000 sec
D16             0.00020000 sec
d17             0.00019600 sec
MCREST          0.00000000 sec
MCWRK           0.01500000 sec
P2                  31.00 usec

======= CHANNEL f1 ========
NUC1                  13C
P1                  15.50 usec
P11                500.00 usec
P12               2000.00 usec
PL0                120.00 dB
PL1                 -1.00 dB
SFO1         125.7942548 MHz
SP1                 3.20 dB
SP2                 3.20 dB
SPNAM1    Crp60,0.5,20.1
SPNAM2       Crp60comp.4
SPOFF1              0.00 Hz
SPOFF2              0.00 Hz

======= CHANNEL f2 ========
CPDPRG2           waltz16
NUC2                   1H
PCPD2              100.00 usec
PL2                 1.60 dB
PL12               24.60 dB
SFO2         500.2225011 MHz

===== GRADIENT CHANNEL =====
GPNAM1           SINE.100
GPNAM2           SINE.100
GPX1                0.00 %
GPX2                0.00 %
GPY1                0.00 %
GPY2                0.00 %
GPZ1               30.00 %
GPZ2               50.00 %
p15               500.00 usec
p16              1000.00 usec

F2 - Processing parameters
SI                   65536
SF           125.7804295 MHz
WDW                    EM
SSB                     0
LB                   1.00 Hz
GB                      0
PC                   2.00
```

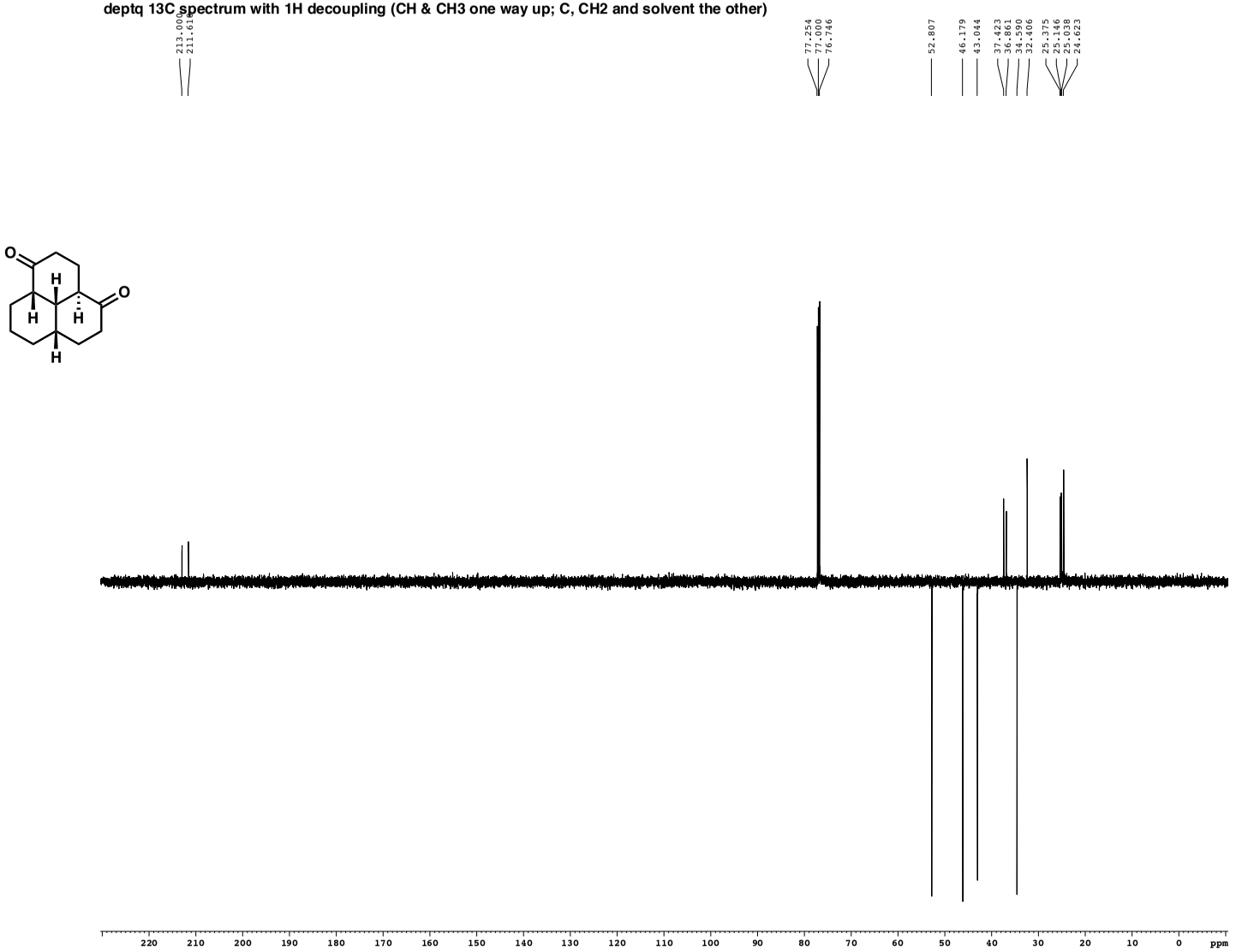
gcosy60



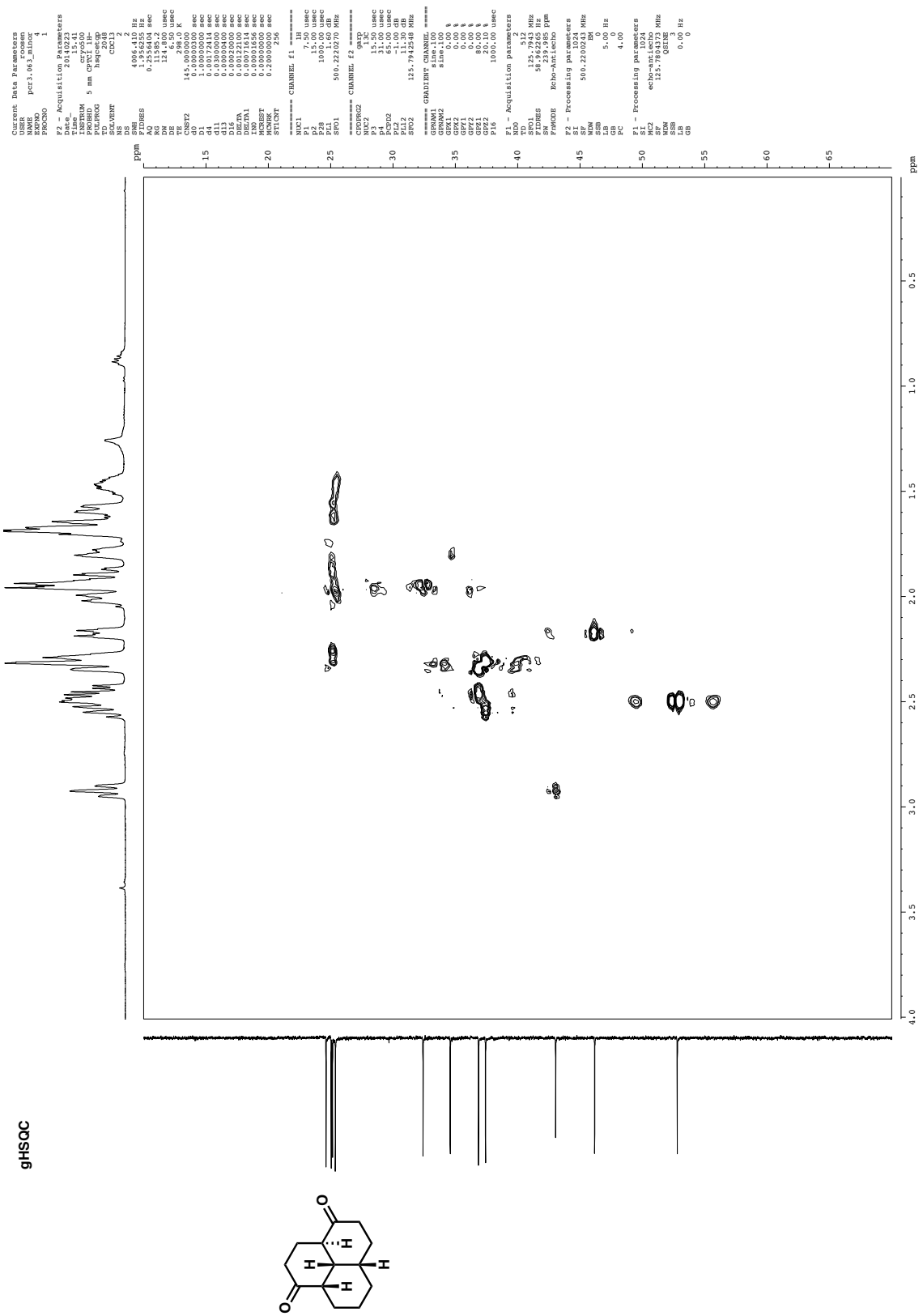


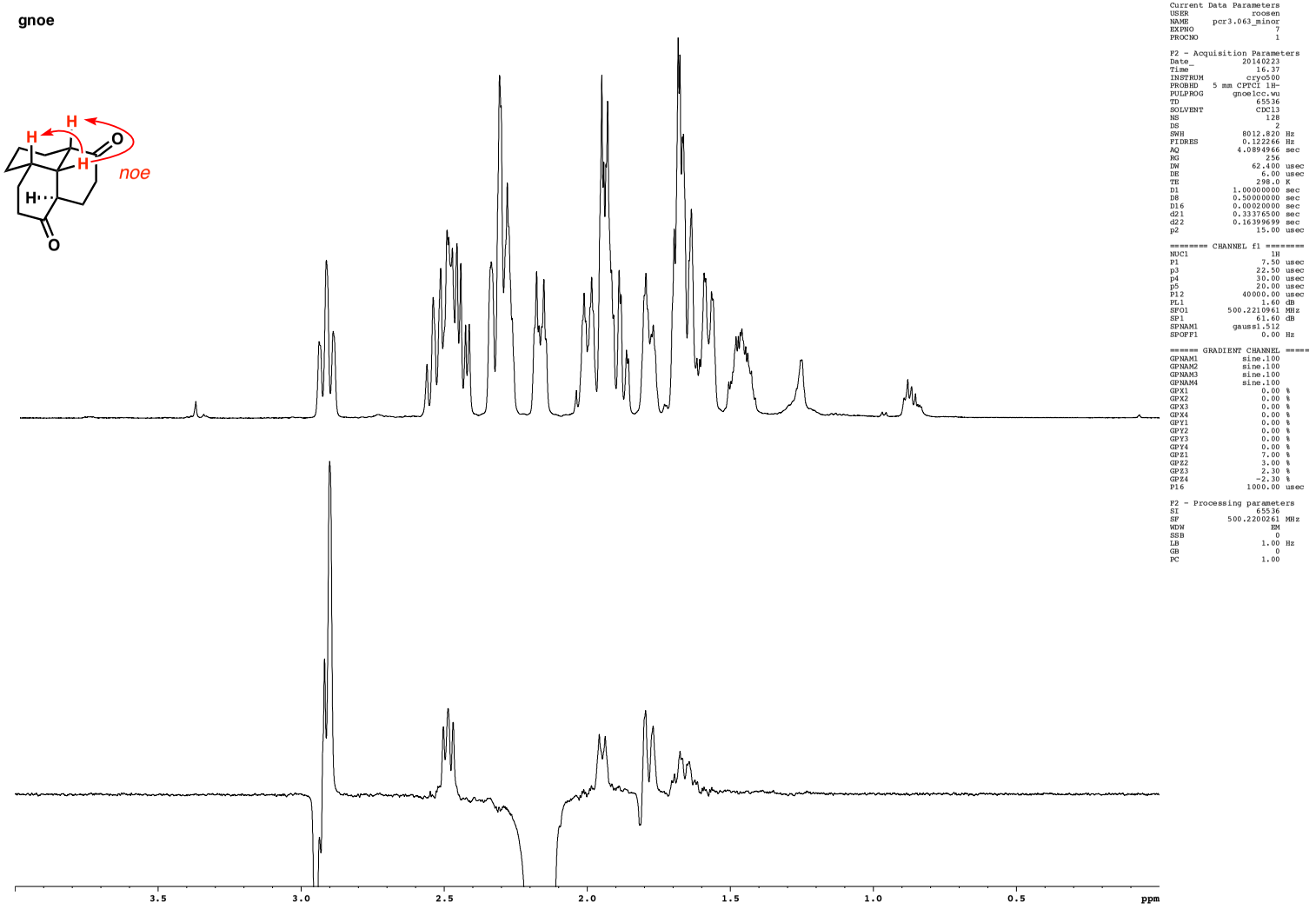

```
Current Data Parameters
USER                 roosen
NAME       pcr3.063_minor
EXPNO                     5
PROCNO                    1

F2 - Acquisition Parameters
Date_              20140223
Time                  16.03
INSTRUM             cryo500
PROBHD    5 mm CPTCI 1H-
PULPROG      cosygp60.prd
TD                     2048
SOLVENT              CDCl3
NS                        2
DS                        2
SWH                4006.410 Hz
FIDRES             1.956255 Hz
AQ                 0.2556404 sec
RG                     228.1
DW                   124.800 usec
DE                     6.00 usec
TE                   298.0 K
d0                0.00000300 sec
D1                1.00000000 sec
d13               0.00000300 sec
D16               0.00020000 sec
IN0               0.00024960 sec

======== CHANNEL f1 ========
NUC1                      1H
P1                      7.50 usec
PL1                     1.60 dB
SFO1           500.2220270 MHz

====== GRADIENT CHANNEL =====
GPNAM1             sine.100
GPNAM2             sine.100
GPX1                    0.00 %
GPX2                    0.00 %
GPY1                    0.00 %
GPY2                    0.00 %
GPZ1                   17.00 %
GPZ2                   17.00 %
P16                  1000.00 usec

F1 - Acquisition parameters
MD0                       1
TD                      256
SFO1               500.222 MHz
FIDRES            15.650040 Hz
SW                    8.009 ppm
FnMODE            undefined

F2 - Processing parameters
SI                     1024
SF              500.2200257 MHz
WDW                    SINE
SSB                       0
LB                     0.00 Hz
GB                        0
PC                     4.00

F1 - Processing parameters
SI                     1024
MC2                      QF
SF              500.2200255 MHz
WDW                    SINE
SSB                       0
LB                     0.00 Hz
GB                        0
```

deptq 13C spectrum with 1H decoupling (CH & CH3 one way up; C, CH2 and solvent the other)



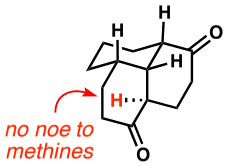

```
Current Data Parameters
USER                 roosen
NAME          pcr3.063_minor
EXPNO                     3
PROCNO                    1

F2 - Acquisition Parameters
Date_              20140223
Time                  15.37
INSTRUM             cryo500
PROBHD    5 mm CPTCI 1H-
PULPROG          deptqgpsp
TD                    65536
SOLVENT                CDCl3
NS                      176
DS                        2
SWH                30303.031 Hz
FIDRES             0.462388 Hz
AQ                 1.0813940 sec
RG                     2048
DW                   16.500 usec
DE                    6.00 usec
TE                   298.0 K
CNST2             145.0000000
CNST12              1.5000000
D1                  1.00000000 sec
d2                  0.00344828 sec
d12                 0.00002000 sec
D16                 0.00020000 sec
DELTA               0.00001574 sec
DELTA1              0.00227878 sec
DELTA2              0.00226378 sec
DELTA3              0.00224828 sec
MCWEST              0.00000000 sec
MCWRK               0.01500000 sec

======= CHANNEL f1 =======
NUC1                     13C
P1                     15.50 usec
P12                  2000.00 usec
PL0                   120.00 dB
PL1                    -1.00 dB
SFO1            125.7942548 MHz
SP2                    3.20 dB
SPNAM2          Crp60comp.4
SPOFF2                 0.00 Hz

======= CHANNEL f2 =======
CPDPRG2              waltz16
NUC2                     1H
p0                     11.25 usec
P3                      7.50 usec
p4                     15.00 usec
PCPD2                 100.00 usec
PL2                    1.60 dB
PL12                  24.60 dB
SFO2            500.2225011 MHz

===== GRADIENT CHANNEL =====
GPNAM1              SINE.100
GPNAM2              SINE.100
GPNAM3              SINE.100
GPX1                   0.00 %
GPX2                   0.00 %
GPX3                   0.00 %
GPY1                   0.00 %
GPY2                   0.00 %
GPY3                   0.00 %
GPZ1                  31.00 %
GPZ2                  31.00 %
GPZ3                  31.00 %
P16                 1000.00 usec

F2 - Processing parameters
SI                    65536
SF              125.7804295 MHz
WDW                      EM
SSB                       0
LB                     1.00 Hz
GB                        0
PC                     2.00
```


gHSQC
Current Data Parameters
USERA2 pcr3.063_minor
PROCNO 1
F2 - Acquisition Parameters
Date_ 20140223
TD 32768
SOLVENT CDCl3
NS 2
DS 4
SWH 4006.410 Hz
FIDRES 0.122284 Hz
AQ 4.0894640 sec
RG 114
DW 124.800 usec
DE 6.50 usec
TE 298.0 K
D1 1.00000000 sec
D11 0.03000000 sec
D16 0.00020000 sec
D17 0.00002000 sec
D20 0.00071614 sec
NUC1 1H
P1 7.50 usec
P2 15.00 usec
PL1 1.00 dB
SFO1 500.2220270 MHz
CPDPRG2 garp
NUC2 13C
P3 13.50 usec
P4 31.00 usec
PCPD2 65.00 usec
PL2 1.00 dB
PL12 11.30 dB
SFO2 125.79422548 MHz
GPNAM1 sine.100
GPX1 0.00 %
GPY1 0.00 %
GPZ1 20.10 %
GPZ2 80.20 %
P16 1000.00 usec
ND0 2
TD0 512
SFO1 125.7943 MHz
FIDRES 58.962265 Hz
SW 31.847134 ppm
FnMODE Echo-AntiEcho
SI 1024
SF 500.2200243 MHz
WDW 0
SSB 5.00 Hz
LB 0 Hz
GB 4.00
PC
SI 1024
MC2 echo-antiecho
SF01 125.7942173 MHz
WDW QSINE
SSB 3
LB 0.00 Hz
GB 0
ppm
ppm

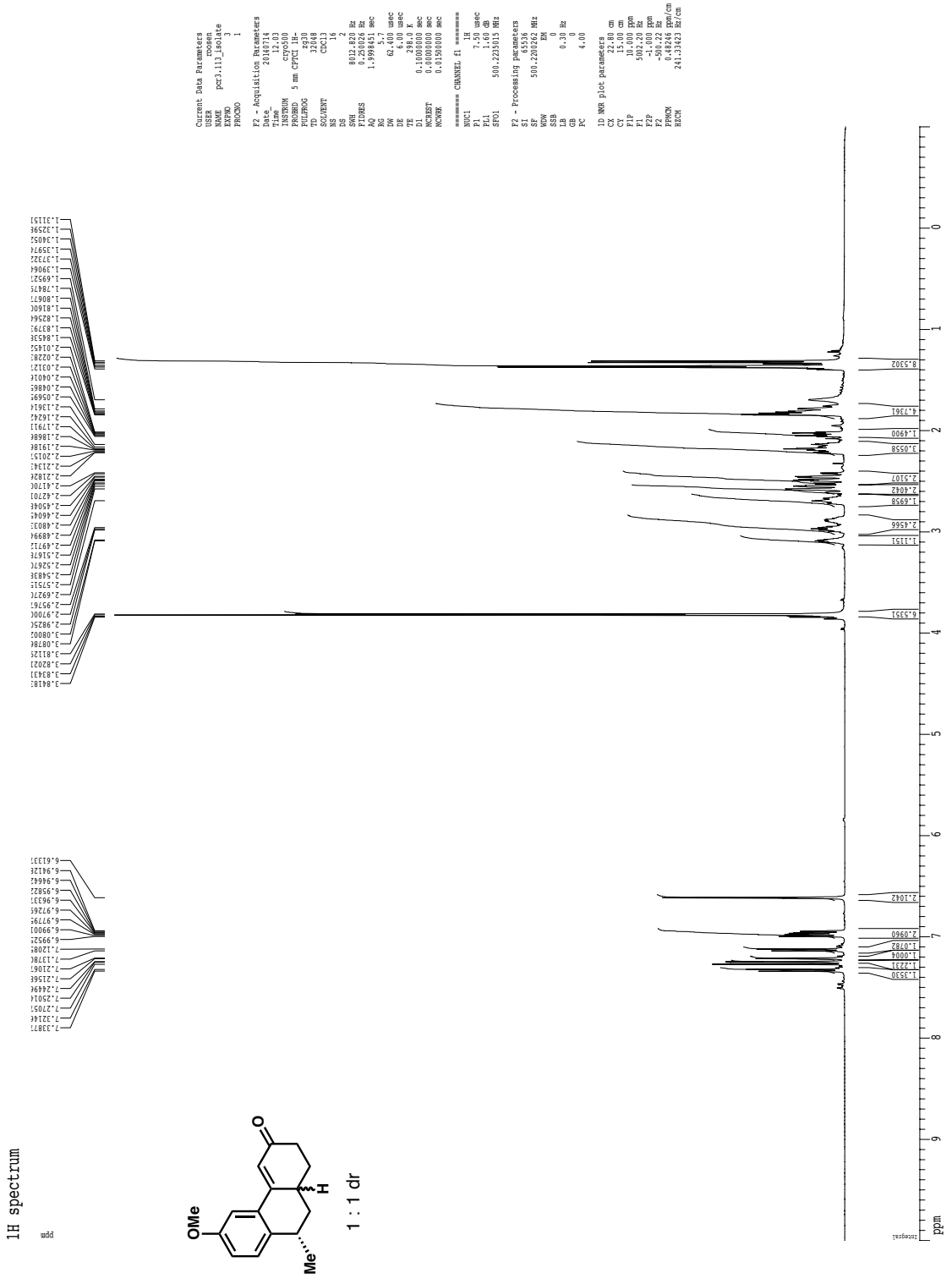



```
Current Data Parameters
USER                  roosen
NAME      pcr3.063_minor
EXPNO                      7
PROCNO                     1

F2 - Acquisition Parameters
Date_              20140223
Time                  16.37
INSTRUM             cryo500
PROBHD    5 mm CPTCI 1H-
PULPROG         gnoelcc.wu
TD                     65536
SOLVENT                CDCl3
NS                       128
DS                         2
SWH                 8012.820 Hz
FIDRES              0.122266 Hz
AQ                  4.0894966 sec
RG                       256
DW                    62.400 usec
DE                     6.00 usec
TE                    298.0 K
D1                 1.00000000 sec
D8                 0.50000000 sec
D16                0.00020000 sec
d21                0.33376500 sec
d22                0.16399699 sec
p2                    15.00 usec

======== CHANNEL f1 ========
NUC1                      1H
P1                     7.50 usec
p3                    22.50 usec
p4                    30.00 usec
p5                    20.00 usec
P12                40000.00 usec
PL1                    1.60 dB
SFO1           500.2210961 MHz
SP1                   61.60 dB
SPNAM1          gauss1.512
SPOFF1                 0.00 Hz

====== GRADIENT CHANNEL =====
GPNAM1              sine.100
GPNAM2              sine.100
GPNAM3              sine.100
GPNAM4              sine.100
GPX1                   0.00 %
GPX2                   0.00 %
GPX3                   0.00 %
GPX4                   0.00 %
GPY1                   0.00 %
GPY2                   0.00 %
GPY3                   0.00 %
GPY4                   0.00 %
GPZ1                   7.00 %
GPZ2                   3.00 %
GPZ3                   2.30 %
GPZ4                  -2.30 %
P16                 1000.00 usec

F2 - Processing parameters
SI                     65536
SF             500.2200261 MHz
WDW                       EM
SSB                        0
LB                      1.00 Hz
GB                         0
PC                      1.00
```

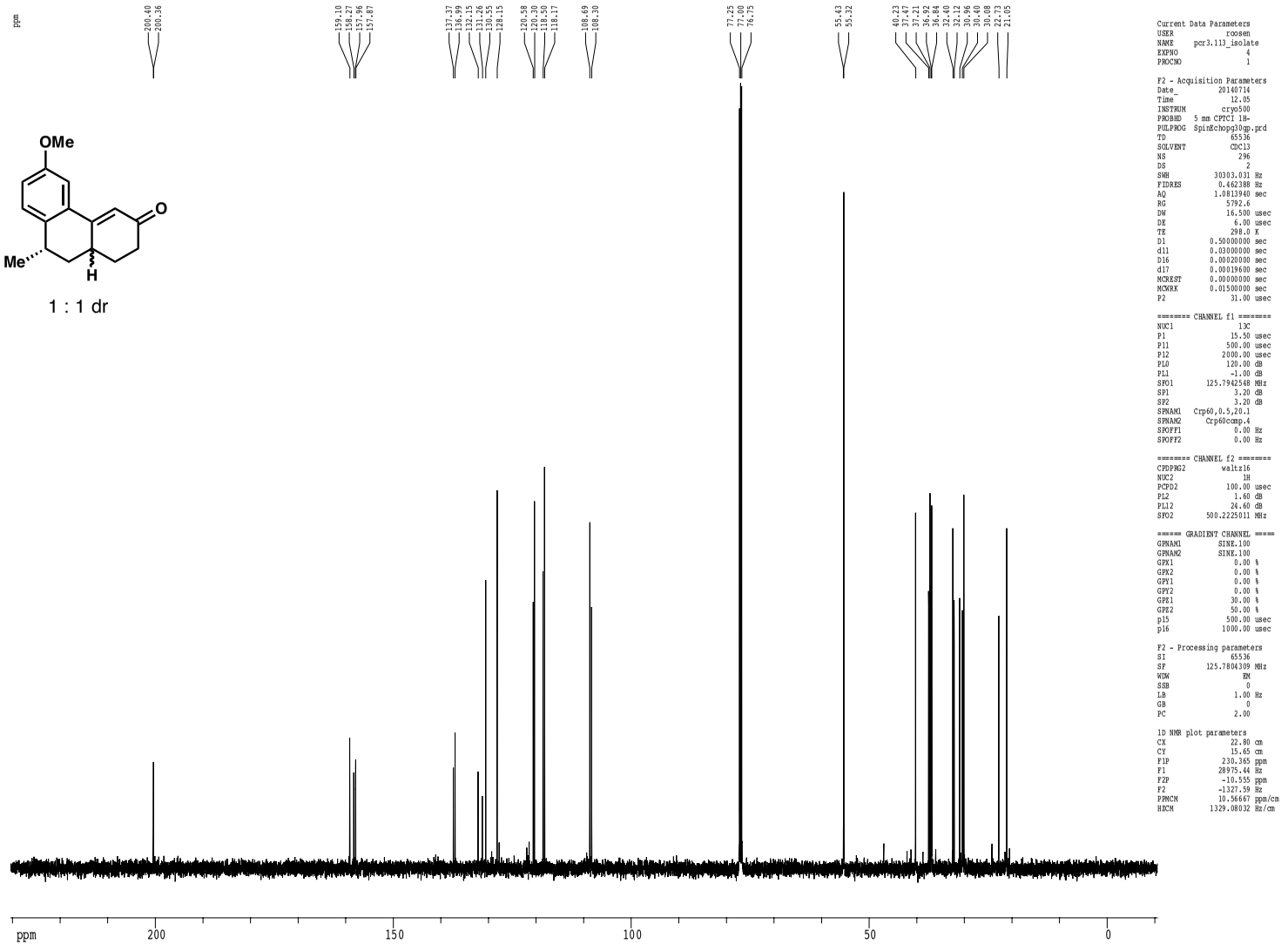
gnoe



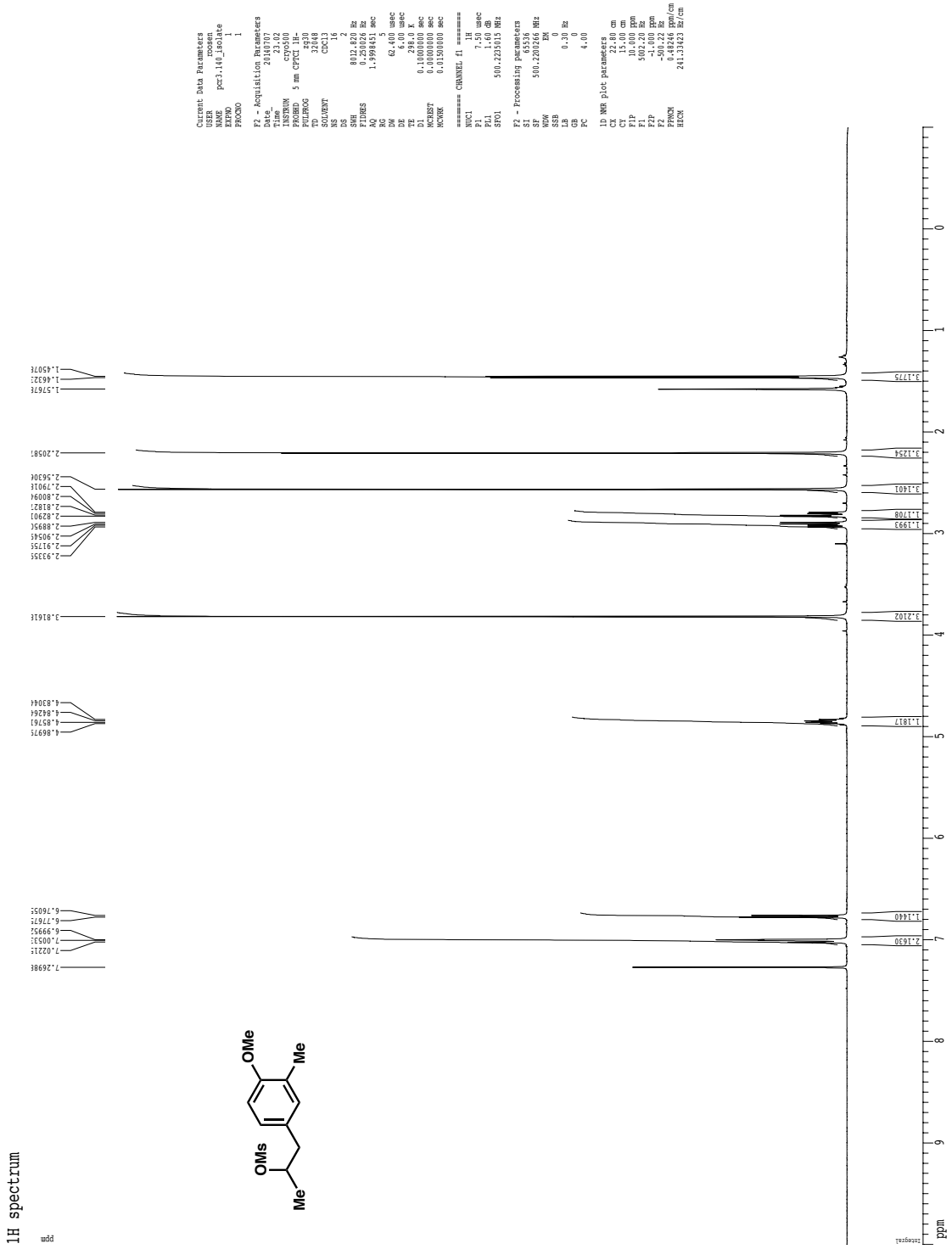

```
Current Data Parameters
USER                  roosen
NAME          pcr3.063_minor
EXPNO                      6
PROCNO                     1

F2 - Acquisition Parameters
Date_              20140223
Time                  16.20
INSTRUM             cryo500
PROBHD    5 mm CPTCI 1H-
PULPROG          gnoelcc.wu
TD                    65536
SOLVENT               CDCl3
NS                      128
DS                        2
SWH                8012.820 Hz
FIDRES             0.122266 Hz
AQ                 4.0894966 sec
RG                     161.3
DW                    62.400 usec
DE                     6.00 usec
TE                    298.0 K
D1              1.00000000 sec
D8              0.50000000 sec
D16             0.00020000 sec
d21             0.33376500 sec
d22             0.16399699 sec
p2                    15.00 usec

======== CHANNEL f1 ========
NUC1                      1H
P1                      7.50 usec
p3                     22.50 usec
p4                     30.00 usec
p5                     20.00 usec
P12                 40000.00 usec
PL1                     1.60 dB
SFO1           500.2214905 MHz
SP1                    61.60 dB
SPNAM1          gauss1.512
SPOFF1                  0.00 Hz

====== GRADIENT CHANNEL =====
GPNAM1              sine.100
GPNAM2              sine.100
GPNAM3              sine.100
GPNAM4              sine.100
GPX1                    0.00 %
GPX2                    0.00 %
GPX3                    0.00 %
GPX4                    0.00 %
GPY1                    0.00 %
GPY2                    0.00 %
GPY3                    0.00 %
GPY4                    0.00 %
GPZ1                    7.00 %
GPZ2                    3.00 %
GPZ3                    2.30 %
GPZ4                   -2.30 %
P16                 1000.00 usec

F2 - Processing parameters
SI                        65536
SF             500.2200263 MHz
WDW                        EM
SSB                         0
LB                       1.00 Hz
GB                          0
PC                       1.00
```


1H spectrum
ppm
OMe
Me
H
O
1 : 1 dr

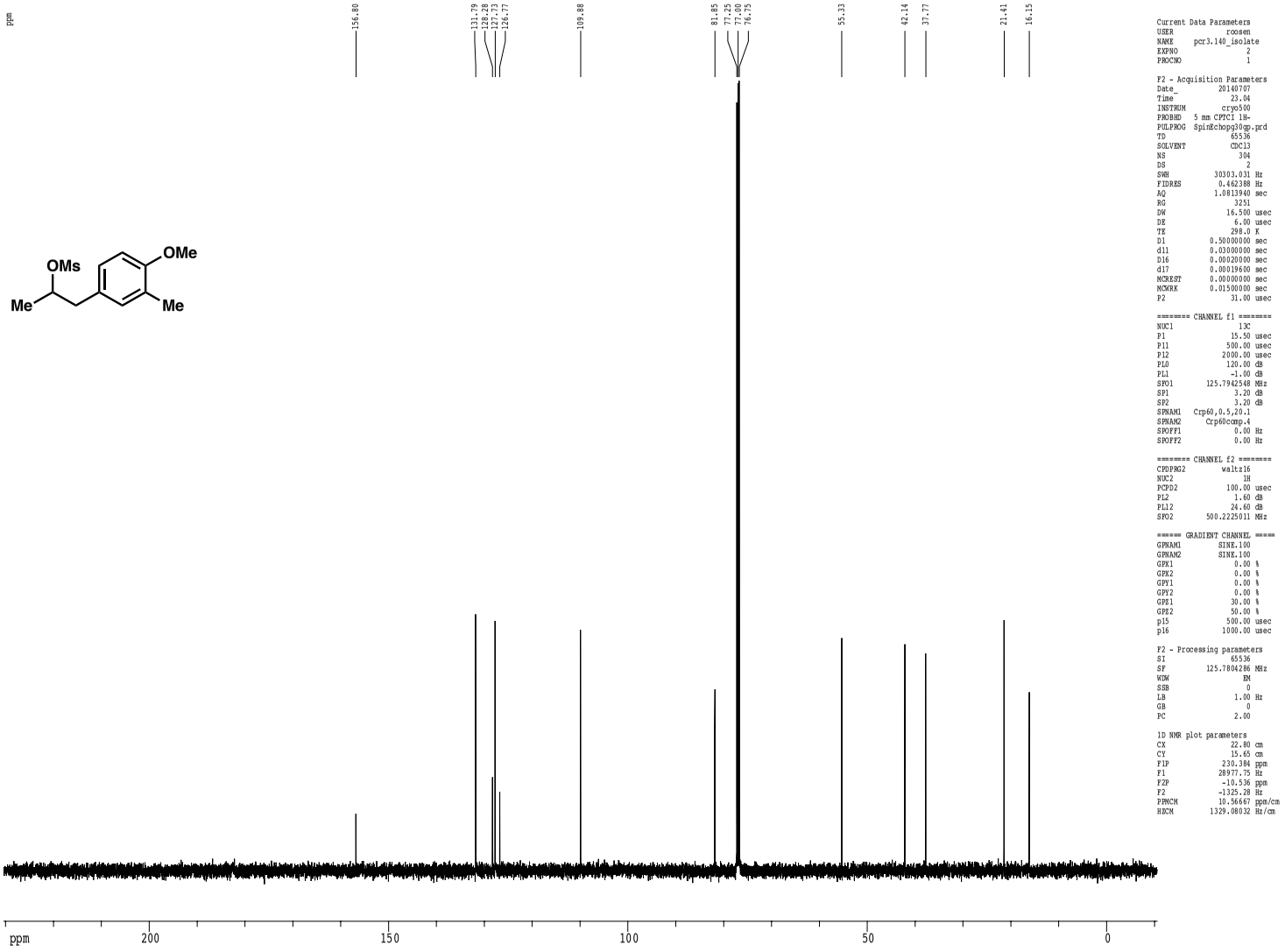
Z-restored spin-echo 13C spectrum with 1H decoupling




```
Current Data Parameters
USER              roosen
NAME      pcr3.113_isolate
EXPNO                    4
PROCNO                   1

F2 - Acquisition Parameters
Date_           20140714
Time              12.05
INSTRUM          cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD                 65536
SOLVENT             CDCl3
NS                    296
DS                      2
SWH           30303.031 Hz
FIDRES        0.462388 Hz
AQ            1.0813940 sec
RG               5792.6
DW               16.500 usec
DE                6.00 usec
TE               298.0 K
D1           0.50000000 sec
d11          0.03000000 sec
D16          0.00020000 sec
d17          0.00019600 sec
MCREST       0.00000000 sec
MCWRK        0.01500000 sec
P2               31.00 usec

======= CHANNEL f1 =======
NUC1                13C
P1                15.50 usec
P11              500.00 usec
P12             2000.00 usec
PL0              120.00 dB
PL1               -1.00 dB
SFO1        125.7942548 MHz
SP1               3.20 dB
SP2               3.20 dB
SPNAM1   Crp60,0.5,20.1
SPNAM2      Crp60comp.4
SPOFF1               0.00 Hz
SPOFF2               0.00 Hz

======= CHANNEL f2 =======
CPDPRG2          waltz16
NUC2                1H
PCPD2            100.00 usec
PL2               1.60 dB
PL12             24.60 dB
SFO2        500.2225011 MHz

===== GRADIENT CHANNEL ====
GPNAM1          SINE.100
GPNAM2          SINE.100
GPX1              0.00 %
GPX2              0.00 %
GPY1              0.00 %
GPY2              0.00 %
GPZ1             30.00 %
GPZ2             50.00 %
p15             500.00 usec
p16            1000.00 usec

F2 - Processing parameters
SI                 65536
SF          125.7804309 MHz
WDW                   EM
SSB                    0
LB                1.00 Hz
GB                     0
PC                2.00

1D NMR plot parameters
CX               22.80 cm
CY               15.65 cm
F1P             230.365 ppm
F1              28975.44 Hz
F2P             -10.555 ppm
F2              -1327.59 Hz
PPMCM          10.56667 ppm/cm
HZCM         1329.08032 Hz/cm
```


1H spectrum
OMe
Me
OMs
Me
ppm

Z-restored spin-echo 13C spectrum with 1H decoupling



Current Data Parameters
USER roosen
NAME pcr3.140_isolate
EXPNO 2
PROCNO 1

F2 - Acquisition Parameters
Date_ 20140707
Time 23.04
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG SpinEchopg30gp.prd
TD 65536
SOLVENT CDCl3
NS 304
DS 2
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0813940 sec
RG 3251
DW 16.500 usec
DE 6.00 usec
TE 298.0 K
D1 0.50000000 sec
d11 0.03000000 sec
D16 0.00020000 sec
d17 0.00019600 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
P2 31.00 usec

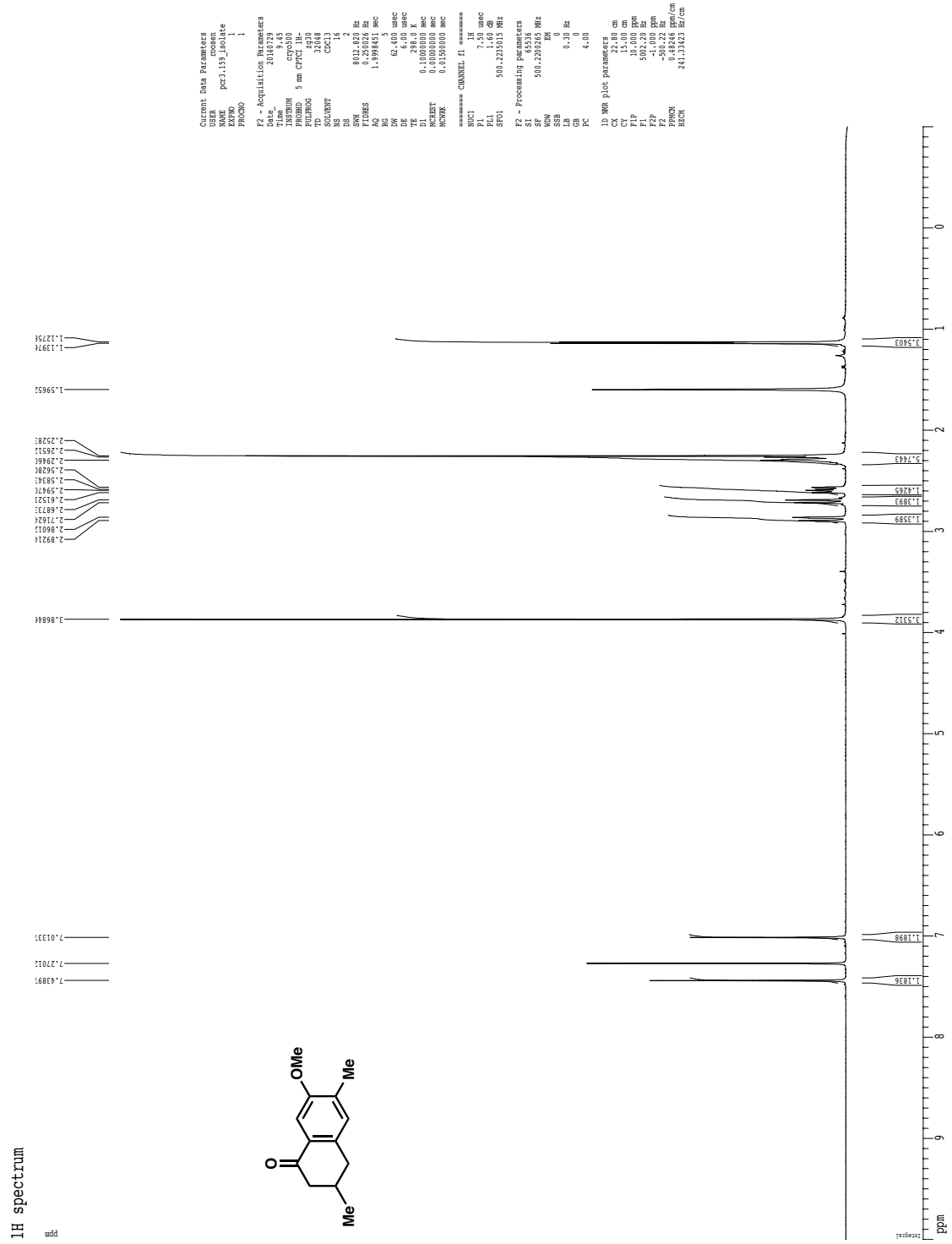
======= CHANNEL f1 =======
NUC1 13C
P1 15.50 usec
P11 500.00 usec
P12 2000.00 usec
PL0 120.00 dB
PL1 -1.00 dB
SFO1 125.7942548 MHz
SP1 3.20 dB
SP2 3.20 dB
SPNAM1 Crp60,0.5,20.1
SPNAM2 Crp60comp.4
SPOFF1 0.00 Hz
SPOFF2 0.00 Hz

======= CHANNEL f2 =======
CPDPRG2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 1.60 dB
PL12 24.60 dB
SFO2 500.2225011 MHz

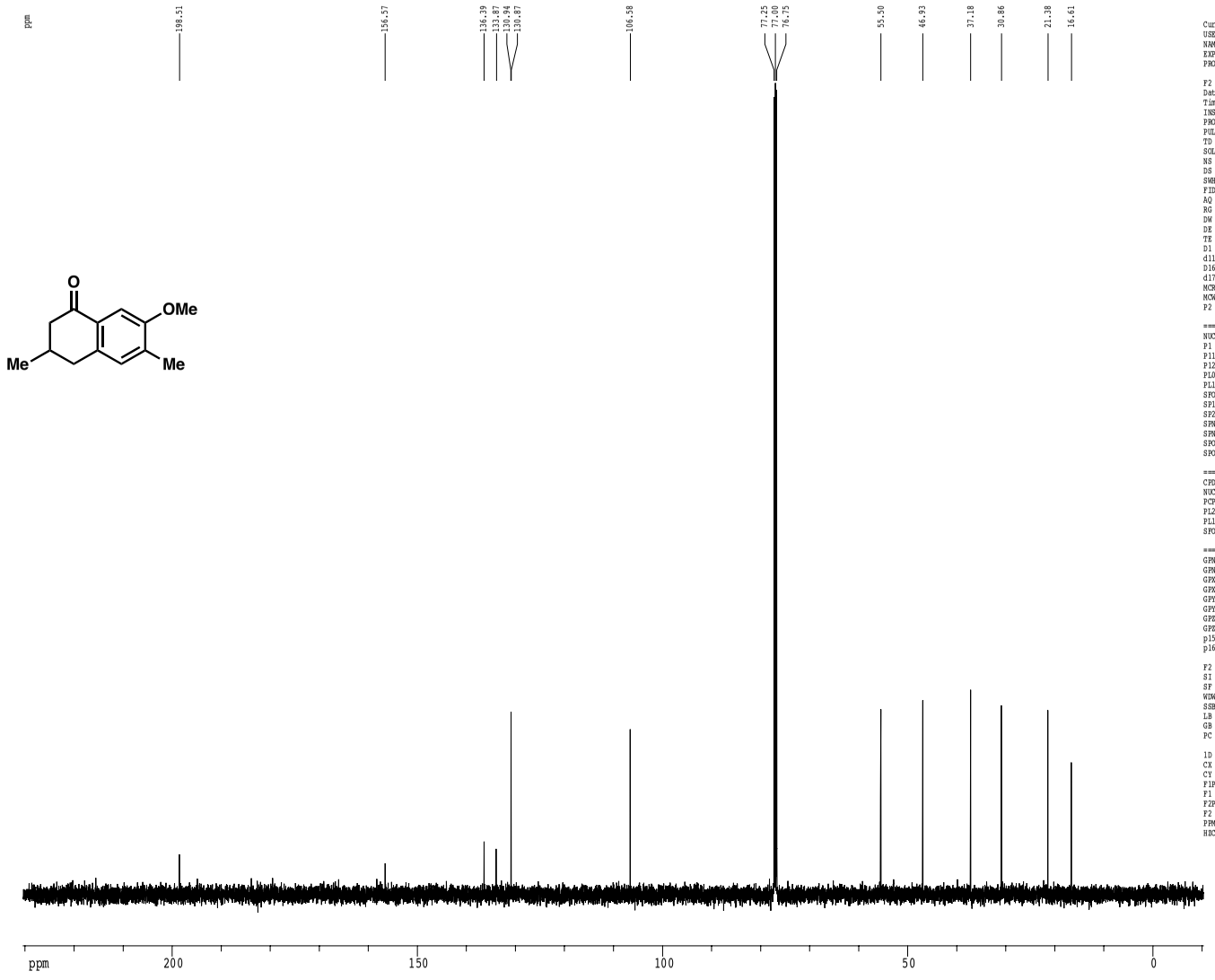
===== GRADIENT CHANNEL ====
GPNAM1 SINE.100
GPNAM2 SINE.100
GPX1 0.00 %
GPX2 0.00 %
GPY1 0.00 %
GPY2 0.00 %
GPZ1 30.00 %
GPZ2 50.00 %
p15 500.00 usec
p16 1000.00 usec

F2 - Processing parameters
SI 65536
SF 125.7804286 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00

1D NMR plot parameters
CX 22.80 cm
CY 15.65 cm
F1P 230.384 ppm
F1 28977.75 Hz
F2P -10.536 ppm
F2 -1325.28 Hz
PPMCM 10.56667 ppm/cm
HZCM 1329.08032 Hz/cm


1H spectrum
OMe
Me
Me
O
ppm

Z-restored spin-echo 13C spectrum with 1H decoupling



Current Data Parameters
USER roosen
NAME pcr3.159_isolate
EXPNO 2
PROCNO 1

F2 - Acquisition Parameters
Date_ 20140729
Time 9.48
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG SpinEchopg30gp.prd
TD 65536
SOLVENT CDCl3
NS 232
DS 2
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0813940 sec
RG 7298.2
DW 16.500 usec
DE 6.00 usec
TE 298.0 K
D1 0.50000000 sec
d11 0.03000000 sec
D16 0.00020000 sec
d17 0.00019600 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
P2 31.00 usec

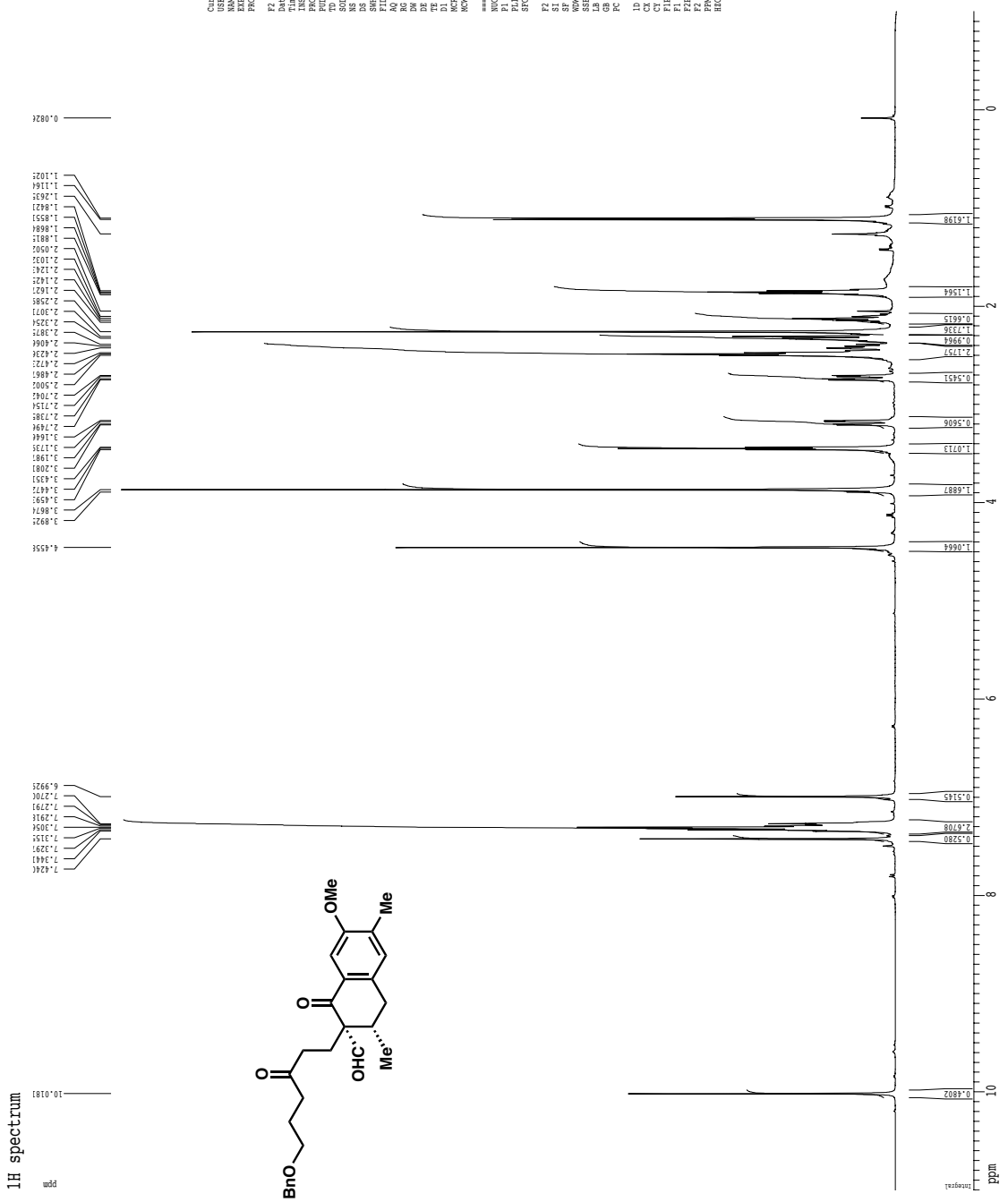
======= CHANNEL f1 =======
NUC1 13C
P1 15.50 usec
P11 500.00 usec
P12 2000.00 usec
PL0 120.00 dB
PL1 -1.00 dB
SFO1 125.7942548 MHz
SP1 3.20 dB
SP2 3.20 dB
SPNAM1 Crp60,0.5,20.1
SPNAM2 Crp60comp.4
SPOFF1 0.00 Hz
SPOFF2 0.00 Hz

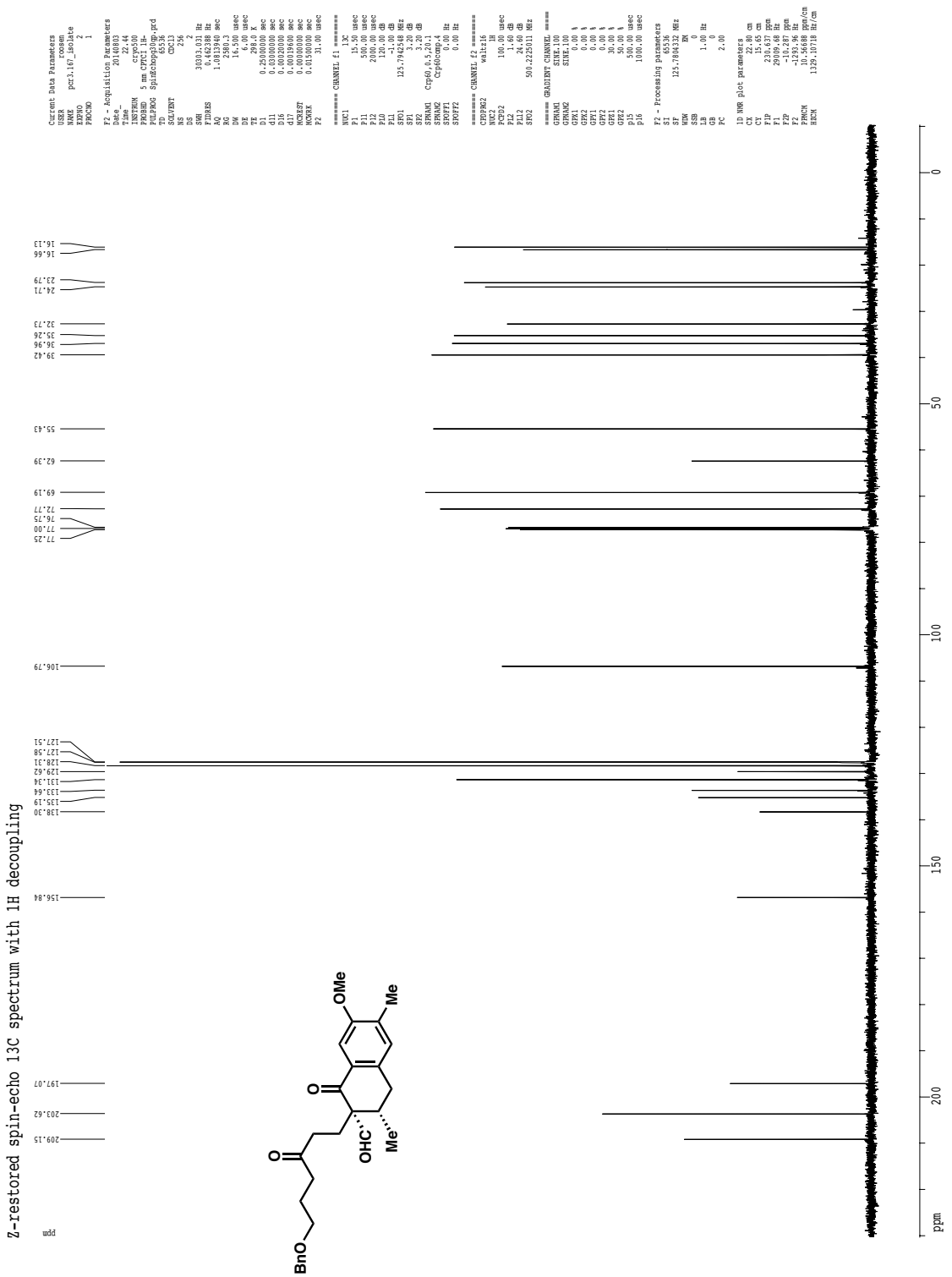
======= CHANNEL f2 =======
CPDPRG2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 1.60 dB
PL12 24.60 dB
SFO2 500.2225011 MHz

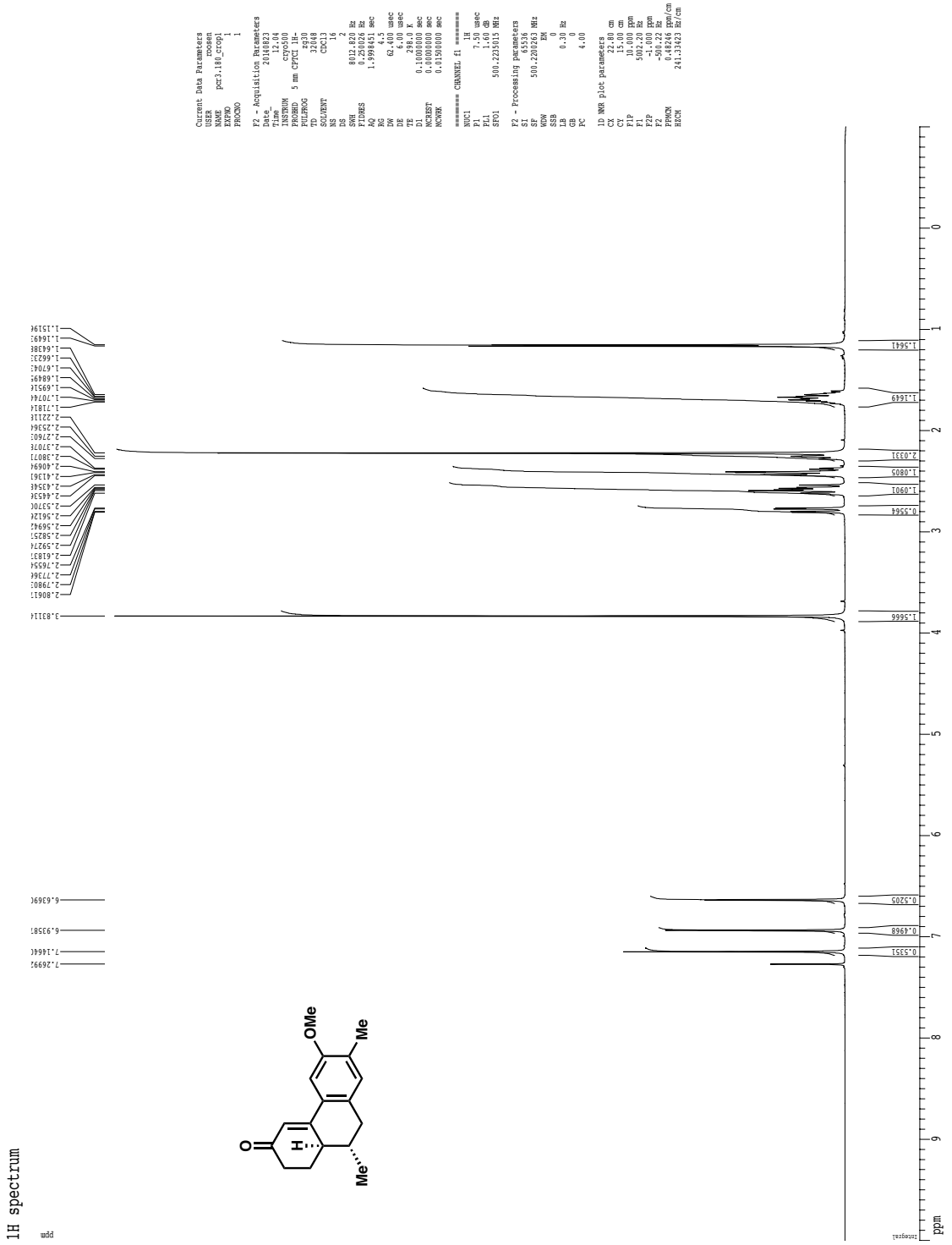
===== GRADIENT CHANNEL ====
GPNAM1 SINE.100
GPNAM2 SINE.100
GPX1 0.00 %
GPX2 0.00 %
GPY1 0.00 %
GPY2 0.00 %
GPZ1 30.00 %
GPZ2 50.00 %
p15 500.00 usec
p16 1000.00 usec

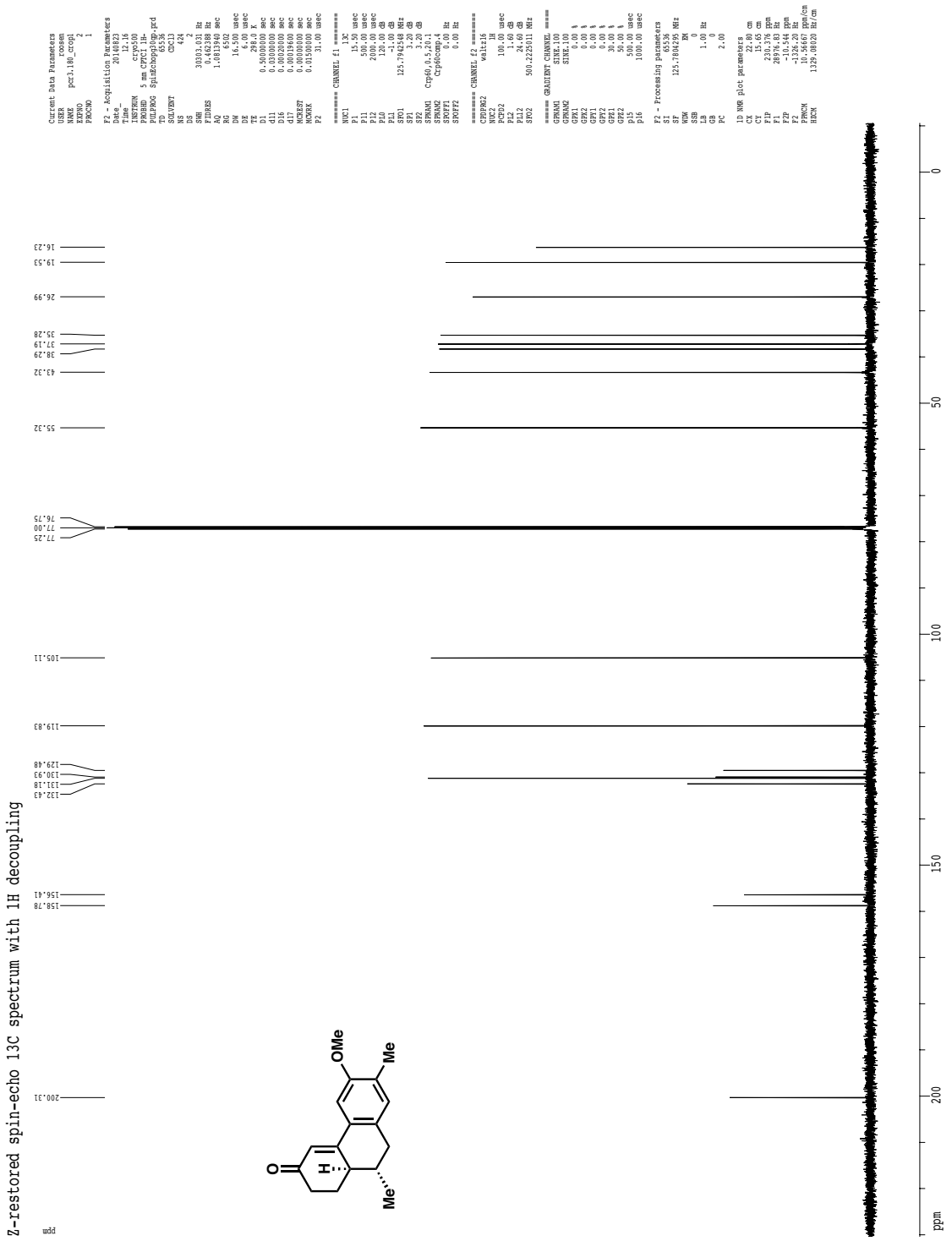
F2 - Processing parameters
SI 65536
SF 125.7804282 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00

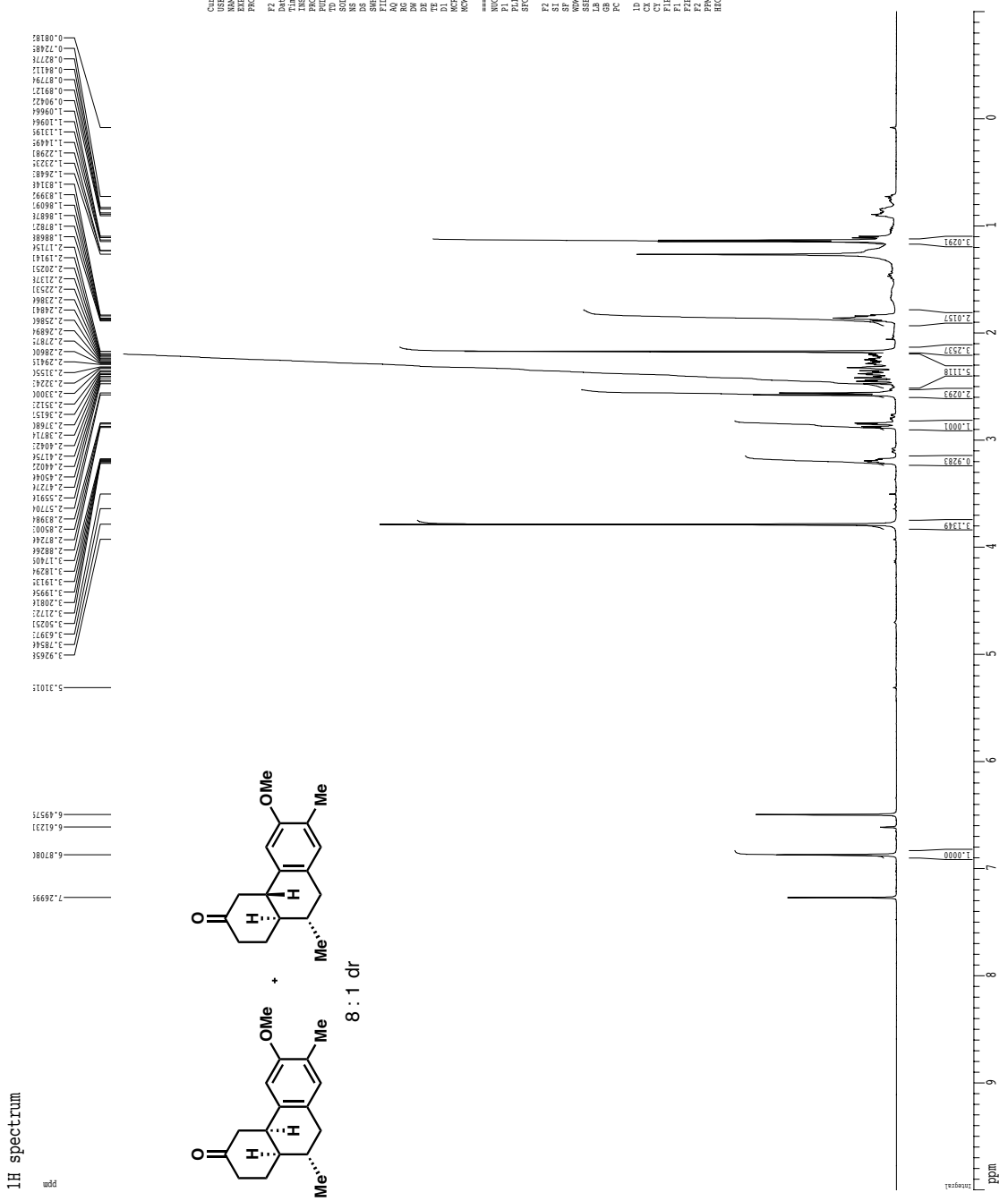
1D NMR plot parameters
CX 22.80 cm
CY 15.65 cm
F1P 230.637 ppm
F1 29009.68 Hz
F2P -10.287 ppm
F2 -1293.96 Hz
PPMCM 10.56688 ppm/cm
HZCM 1329.10718 Hz/cm


1H spectrum
OMe
Me
O
OHC
Me
O
BnO

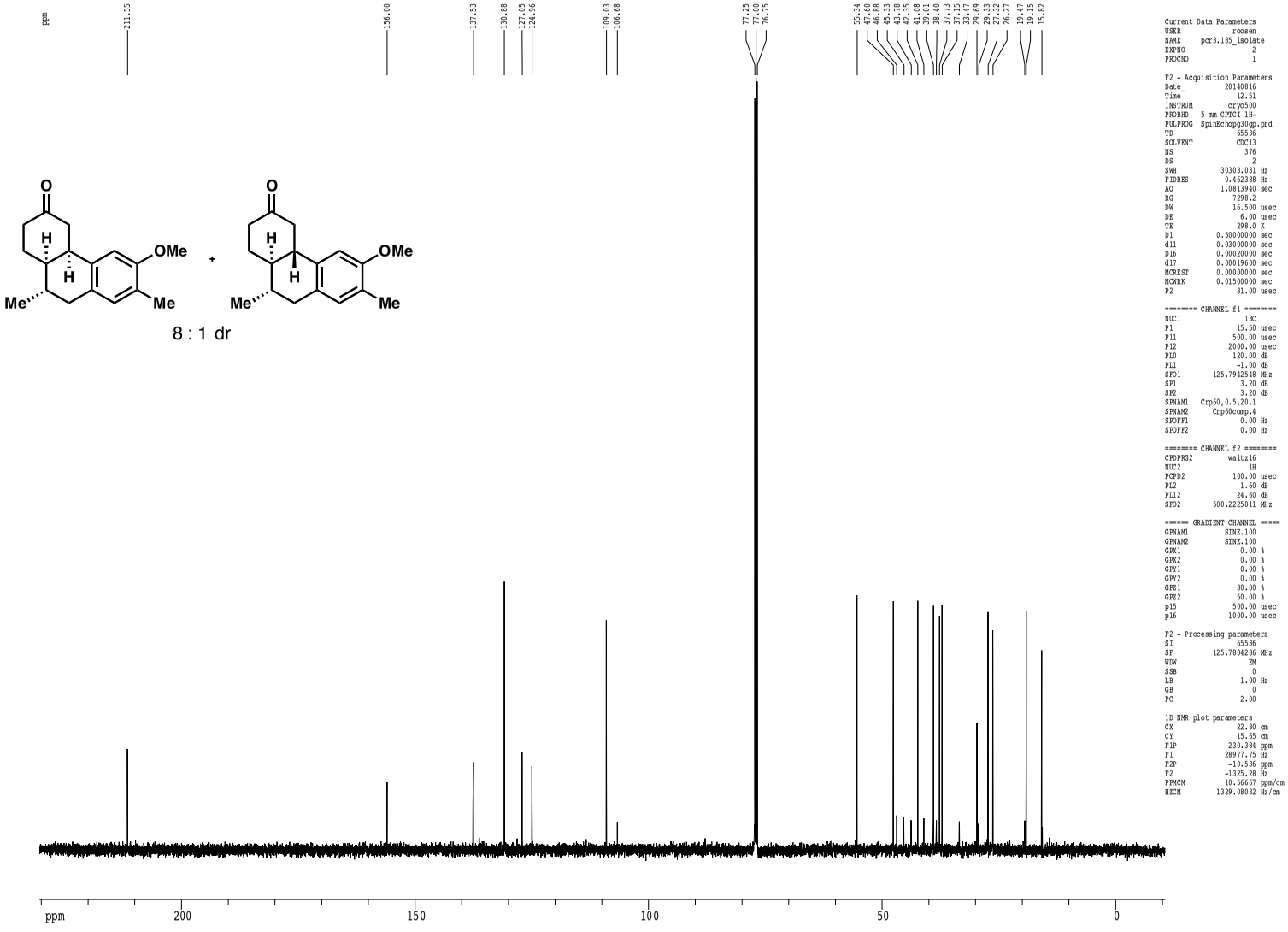

Z-restored spin-echo 13C spectrum with 1H decoupling
OMe
Me
O
OHC
Me
O
BnO
ppm
0
50
100
150
200
209.15
203.62
197.07
156.84
138.30
135.19
133.64
131.34
129.62
128.31
127.58
127.51
106.79
77.25
77.00
76.75
72.77
69.19
62.39
55.43
39.42
36.96
35.26
32.73
24.71
23.79
16.66
16.13


1H spectrum
OMe
Me
Me
O
H
ppm


Z-restored spin-echo 13C spectrum with 1H decoupling
ppm
200.31
158.78
156.61
132.43
131.18
130.93
129.68
119.83
105.11
77.25
77.00
76.75
55.32
43.32
38.29
37.19
35.28
26.99
19.53
16.23
OMe
Me
O
H
Me
Current Data Parameters
USER roosen
NAME pcc3.180_cropl 2
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20140123
Time 12.16
INSTRUM cryo500
PROBHD 5 mm CPPCI 1H-
PULPROG SpinEchopg180p.pcd
TD 65536
SOLVENT CDCl3
NS 424
DS 2
SWH 31013.131 Hz
FIDRES 0.473098 Hz
AQ 1.0613940 sec
RG 6502
DW 16.500 usec
DE 6.00 usec
TE 298.0 K
D1 0.50000000 sec
d11 0.03000000 sec
D16 0.00020000 sec
d12 0.00001000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
F2 31.00 usec
======= CHANNEL f1 =======
NUC1 13C
P1 15.50 usec
P11 500.00 usec
P12 2000.00 usec
PL0 120.00 dB
PL1 -1.00 dB
SFO1 125.7742548 MHz
SF01 3.20 dB
SF02 3.20 dB
SPNAM1 Crp60,0.5,20.1
SPNAM2 Crp60comp.4
SPOFF1 0.00 Hz
SPOFF2 0.00 Hz
======= CHANNEL f2 =======
CPDPRG2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 1.60 dB
PL12 24.60 dB
SFO2 500.2225011 MHz
===== GRADIENT CHANNEL =====
GPNAM1 SINE.100
GPNAM2 SINE.100
GPZ1 0.00 %
GPZ2 0.00 %
GPZ3 0.00 %
GPZ4 30.00 %
GPZ5 50.00 %
p15 500.00 usec
p16 1000.00 usec
F2 - Processing parameters
SI 65536
SF 125.7704295 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00
1D NMR plot parameters
CX 22.80 cm
CY 15.45 cm
F1P 230.376 ppm
F1 28976.83 Hz
F2P -10.544 ppm
F2 -1326.20 Hz
PPMCM 10.56667 ppm/cm
HZCM 1329.08020 Hz/cm
0
50
100
150
200
ppm

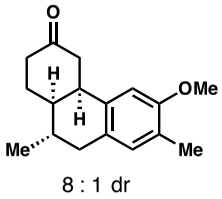

1H spectrum
OMe
Me
H
H
O
Me
+
8 : 1 dr
OMe
Me
H
H
O
Me
Current Data Parameters
F2 - Acquisition Parameters
F2 - Processing parameters
1D NMR plot parameters
ppm

Z-restored spin-echo 13C spectrum with 1H decoupling




```
Current Data Parameters
USER              roosen
NAME      pcr3.185_isolate
EXPNO                    2
PROCNO                   1

F2 - Acquisition Parameters
Date_           20140816
Time              12.51
INSTRUM          cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD                 65536
SOLVENT             CDCl3
NS                    376
DS                      2
SWH           30303.031 Hz
FIDRES        0.462388 Hz
AQ            1.0813940 sec
RG               7298.2
DW               16.500 usec
DE                6.00 usec
TE               298.0 K
D1            0.50000000 sec
d11           0.03000000 sec
D16           0.00020000 sec
d17           0.00019600 sec
MCREST        0.00000000 sec
MCWRK         0.01500000 sec
P2               31.00 usec

======= CHANNEL f1 =======
NUC1                13C
P1                15.50 usec
P11              500.00 usec
P12             2000.00 usec
PL0              120.00 dB
PL1               -1.00 dB
SFO1         125.7942548 MHz
SP1               3.20 dB
SP2               3.20 dB
SPNAM1    Crp60,0.5,20.1
SPNAM2      Crp60comp.4
SPOFF1               0.00 Hz
SPOFF2               0.00 Hz

======= CHANNEL f2 =======
CPDPRG2          waltz16
NUC2                1H
PCPD2            100.00 usec
PL2                1.60 dB
PL12              24.60 dB
SFO2         500.2225011 MHz

===== GRADIENT CHANNEL ====
GPNAM1          SINE.100
GPNAM2          SINE.100
GPX1                0.00 %
GPX2                0.00 %
GPY1                0.00 %
GPY2                0.00 %
GPZ1               30.00 %
GPZ2               50.00 %
p15              500.00 usec
p16             1000.00 usec

F2 - Processing parameters
SI                 65536
SF           125.7804286 MHz
WDW                   EM
SSB                    0
LB                  1.00 Hz
GB                     0
PC                  2.00

1D NMR plot parameters
CX                 22.80 cm
CY                 15.65 cm
F1P              230.384 ppm
F1               28977.75 Hz
F2P              -10.536 ppm
F2               -1325.28 Hz
PPMCM            10.56667 ppm/cm
HZCM          1329.08032 Hz/cm
```

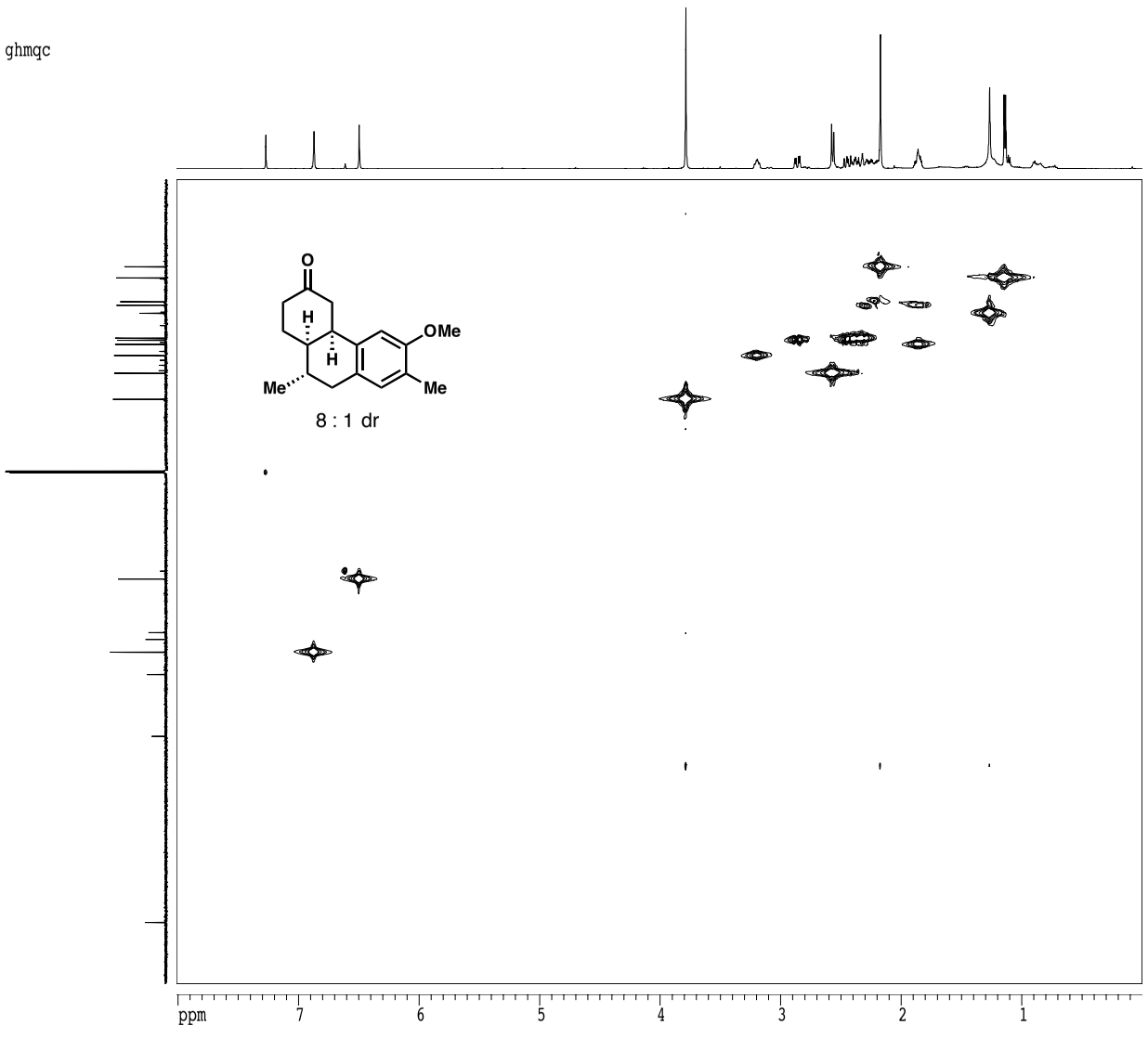
deptq 13C spectrum with 1H decoupling (CH & CH3 one way up; C, CH2 and solvent the other)



8 : 1 dr


```
Current Data Parameters
USER                roosen
NAME      pcr3.185_isolate
EXPNO                   3
PROCNO                  1

F2 - Acquisition Parameters
Date_          20140816
Time               13.00
INSTRUM          cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG        deptqgpsp
TD                 65536
SOLVENT             CDCl3
NS                    152
DS                      2
SWH             30303.031 Hz
FIDRES          0.462388 Hz
AQ              1.0813940 sec
RG                 5160.6
DW                16.500 usec
DE                 6.00 usec
TE                298.0 K
CNST2         145.0000000
CNST12          1.5000000
D1              1.00000000 sec
d2              0.00344828 sec
d12             0.00002000 sec
D16             0.00020000 sec
DELTA           0.00001574 sec
DELTA1          0.00227878 sec
DELTA2          0.00226378 sec
DELTA3          0.00224828 sec
MCREST          0.00000000 sec
MCWRK           0.01500000 sec

======== CHANNEL f1 ========
NUC1                  13C
P1                 15.50 usec
P12              2000.00 usec
PL0                120.00 dB
PL1                 -1.00 dB
SFO1         125.7942549 MHz
SP2                 3.20 dB
SPNAM2       Crp60comp.4
SPOFF2              0.00 Hz

======== CHANNEL f2 ========
CPDPRG2            waltz16
NUC2                   1H
p0                 11.25 usec
P3                  7.50 usec
p4                 15.00 usec
PCPD2             100.00 usec
PL2                 1.60 dB
PL12               24.60 dB
SFO2         500.2225011 MHz

====== GRADIENT CHANNEL =====
GPNAM1           SINE.100
GPNAM2           SINE.100
GPNAM3           SINE.100
GPX1                0.00 %
GPX2                0.00 %
GPX3                0.00 %
GPY1                0.00 %
GPY2                0.00 %
GPY3                0.00 %
GPZ1               31.00 %
GPZ2               31.00 %
GPZ3               31.00 %
P16              1000.00 usec

F2 - Processing parameters
SI                 65536
SF           125.7804272 MHz
WDW                   EM
SSB                    0
LB                  1.00 Hz
GB                     0
PC                  2.00

1D NMR plot parameters
CX                 22.80 cm
CY                  7.50 cm
F1P               230.395 ppm
F1              28979.14 Hz
F2P              -10.525 ppm
F2             -1323.89 Hz
PPMCM           10.56667 ppm/cm
HZCM          1329.08032 Hz/cm
```

ghmqc



Current Data Parameters

USER	roosen
NAME	pcr3.185_isolate
EXPNO	4
PROCNO	1

F2 - Acquisition Parameters

Date_	20140816
Time	13.03
INSTRUM	cryo500
PROBHD	5 mm CPTCI 1H-
PULPROG	inv4gp.wu
TD	2048
SOLVENT	CDCl3
NS	2
DS	16
SWH	4006.410 Hz
FIDRES	1.956255 Hz
AQ	0.2556404 sec
RG	11585.2
DW	124.800 usec
DE	6.50 usec
TE	298.0 K
CNST2	145.0000000
d0	0.00000300 sec
D1	1.00000000 sec
d2	0.00344828 sec
d12	0.00002000 sec
d13	0.00000300 sec
D16	0.00020000 sec
d20	0.00242528 sec
IN0	0.00001656 sec

======= CHANNEL f1 =======

NUC1	1H
P1	7.50 usec
p2	15.00 usec
PL1	1.60 dB
SFO1	500.2220272 MHz

======= CHANNEL f2 =======

CPDPRG2	garp
NUC2	13C
P3	15.50 usec
PCPD2	65.00 usec
PL2	-1.00 dB
PL12	11.30 dB
SFO2	125.7942568 MHz

====== GRADIENT CHANNEL =====

GPNAM1	sine.100
GPNAM2	sine.100
GPNAM3	sine.100
GPX1	0.00 %
GPX2	0.00 %
GPX3	0.00 %
GPY1	0.00 %
GPY2	0.00 %
GPY3	0.00 %
GPZ1	30.00 %
GPZ2	18.00 %
GPZ3	24.00 %
P16	1000.00 usec

F1 - Acquisition parameters

ND0	2
TD	128
SFO1	125.7943 MHz
FIDRES	235.849060 Hz
SW	239.985 ppm
FnMODE	undefined

F2 - Processing parameters

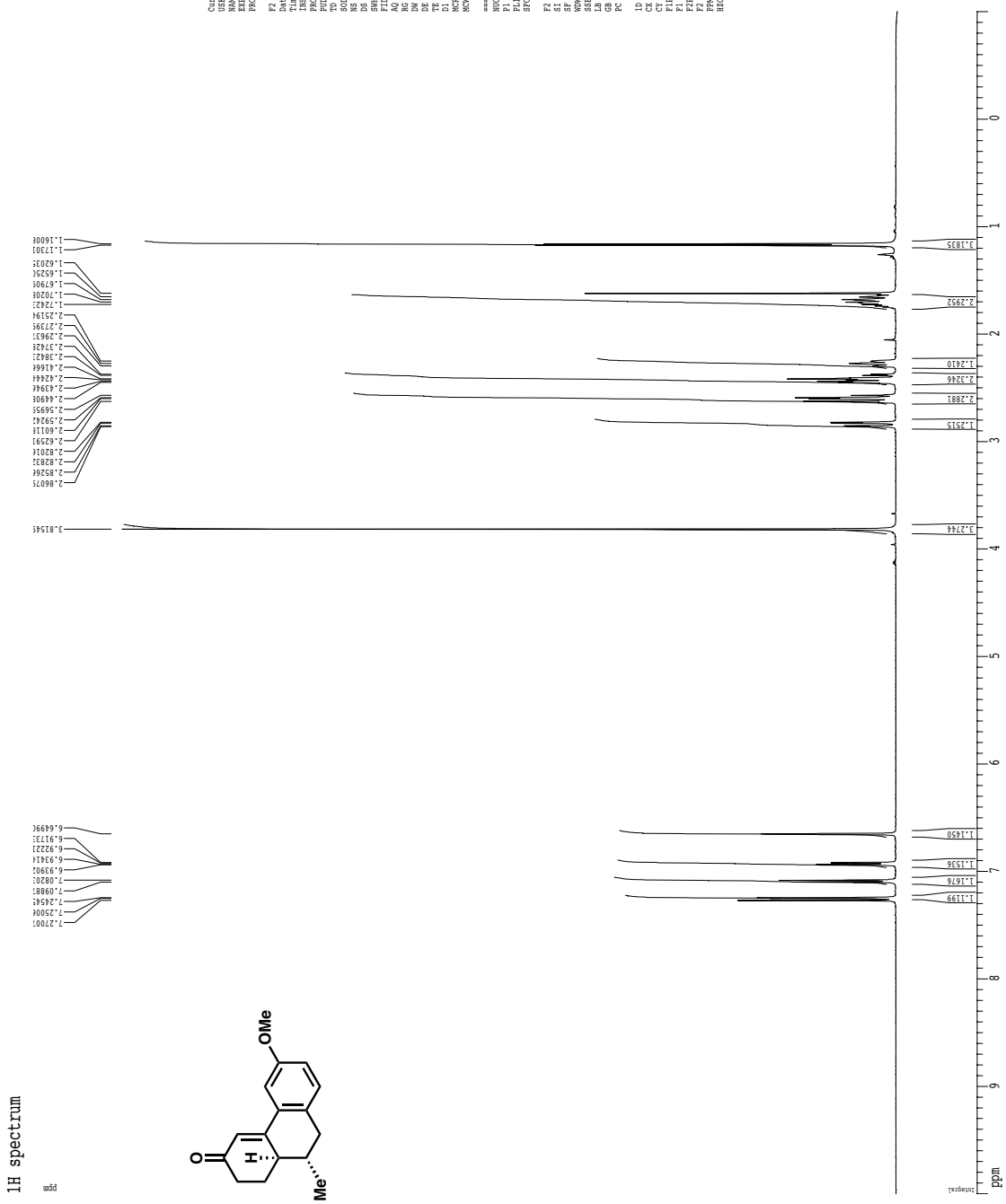
SI	1024
SF	500.2200233 MHz
WDW	EM
SSB	0
LB	5.00 Hz
GB	0
PC	4.00

F1 - Processing parameters

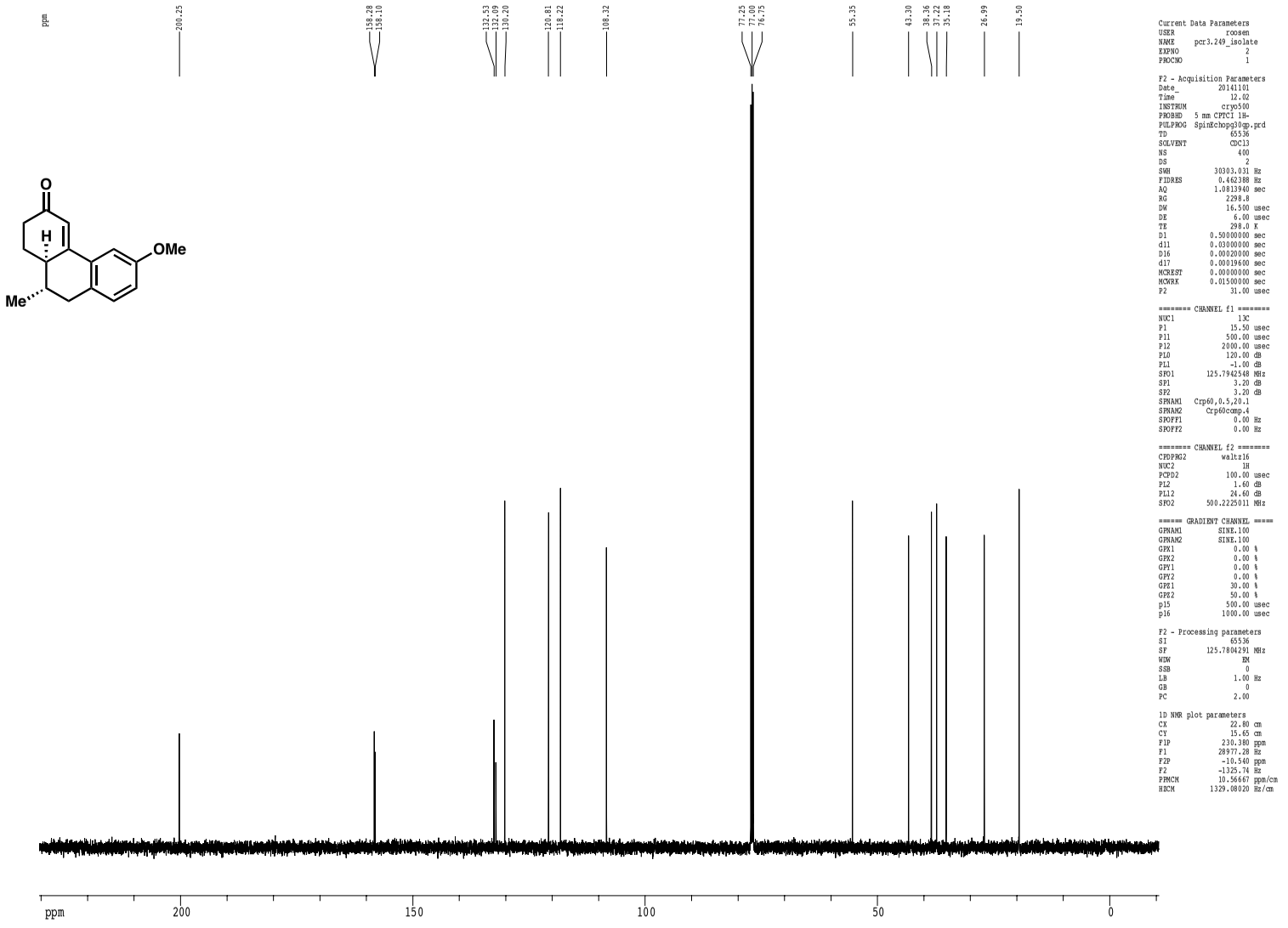
SI	1024
MC2	QF
SF	125.7804394 MHz
WDW	QSINE
SSB	3
LB	0.00 Hz
GB	0

2D NMR plot parameters

CX2	18.00 cm
CX1	15.00 cm
F2PLO	8.011 ppm
F2LO	4007.11 Hz
F2PHI	0.001 ppm
F2HI	0.70 Hz
F1PLO	229.844 ppm
F1LO	28909.83 Hz
F1PHI	-10.167 ppm
F1HI	-1278.85 Hz
F2PPMCM	0.44496 ppm/cm
F2HZCM	222.57834 Hz/cm
F1PPMCM	16.00073 ppm/cm
F1HZCM	2012.57849 Hz/cm


1H spectrum
ppm
OMe
O
H
Me

Z-restored spin-echo 13C spectrum with 1H decoupling



Current Data Parameters
USER roosen
NAME pcr3.249_isolate
EXPNO 2
PROCNO 1

F2 - Acquisition Parameters
Date_ 20141101
Time 12.02
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG SpinEchopg30gp.prd
TD 65536
SOLVENT CDCl3
NS 400
DS 2
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0813940 sec
RG 2298.8
DW 16.500 usec
DE 6.00 usec
TE 298.0 K
D1 0.50000000 sec
d11 0.03000000 sec
D16 0.00020000 sec
d17 0.00019600 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
P2 31.00 usec

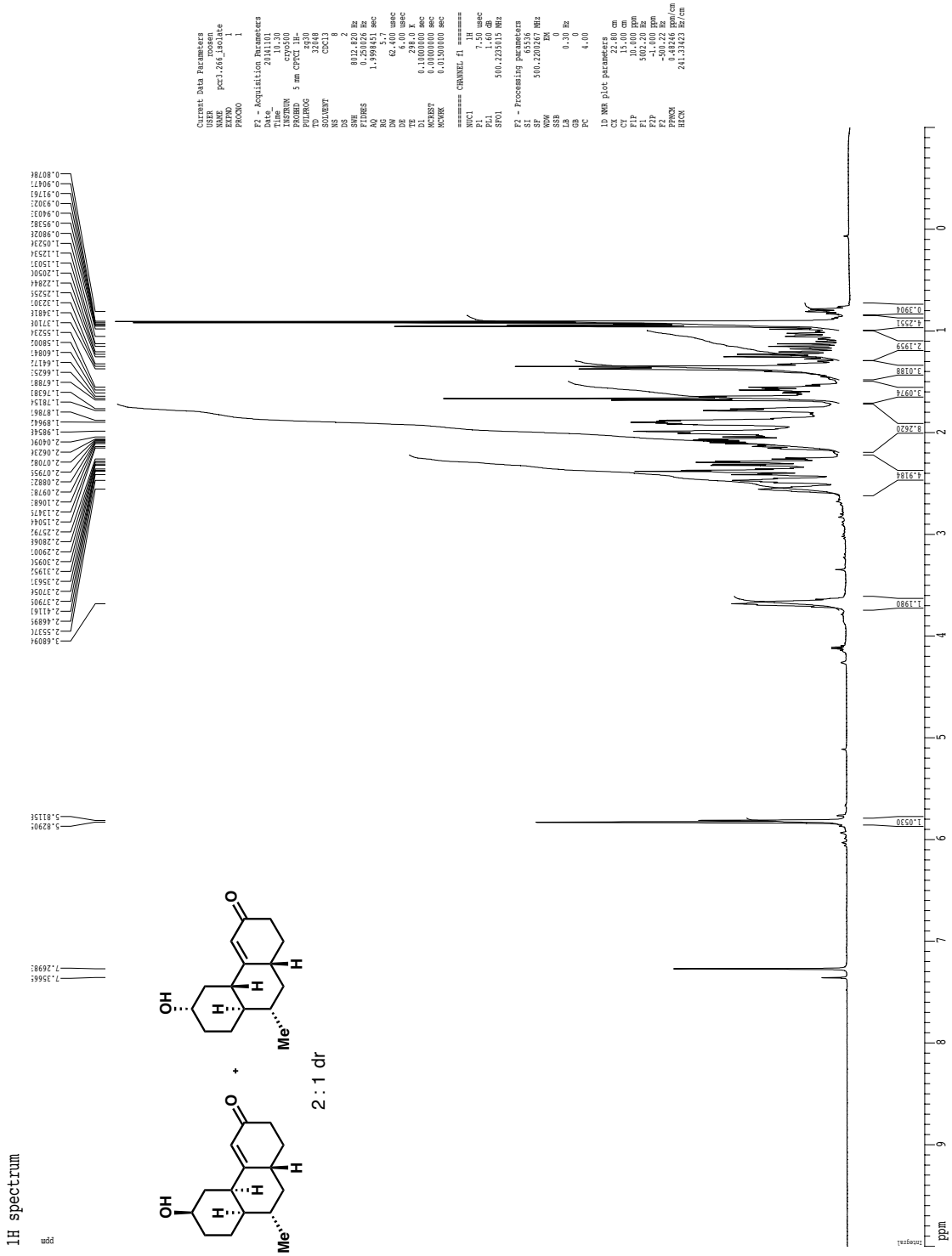
======= CHANNEL f1 =======
NUC1 13C
P1 15.50 usec
P11 500.00 usec
P12 2000.00 usec
PL0 120.00 dB
PL1 -1.00 dB
SFO1 125.7942548 MHz
SP1 3.20 dB
SP2 3.20 dB
SPNAM1 Crp60,0.5,20.1
SPNAM2 Crp60comp.4
SPOFF1 0.00 Hz
SPOFF2 0.00 Hz

======= CHANNEL f2 =======
CPDPRG2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 1.60 dB
PL12 24.60 dB
SFO2 500.2225011 MHz

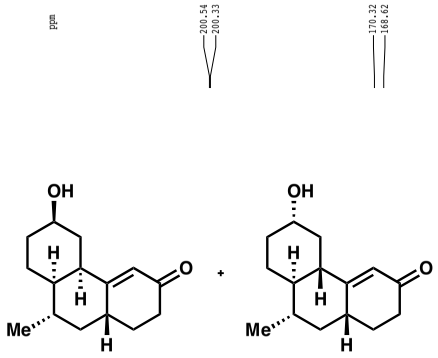
===== GRADIENT CHANNEL ====
GPNAM1 SINE.100
GPNAM2 SINE.100
GPX1 0.00 %
GPX2 0.00 %
GPY1 0.00 %
GPY2 0.00 %
GPZ1 30.00 %
GPZ2 50.00 %
p15 500.00 usec
p16 1000.00 usec

F2 - Processing parameters
SI 65536
SF 125.7804291 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00

1D NMR plot parameters
CX 22.80 cm
CY 15.65 cm
F1P 230.380 ppm
F1 28977.28 Hz
F2P -10.540 ppm
F2 -1325.74 Hz
PPMCM 10.56667 ppm/cm
HZCM 1329.08020 Hz/cm

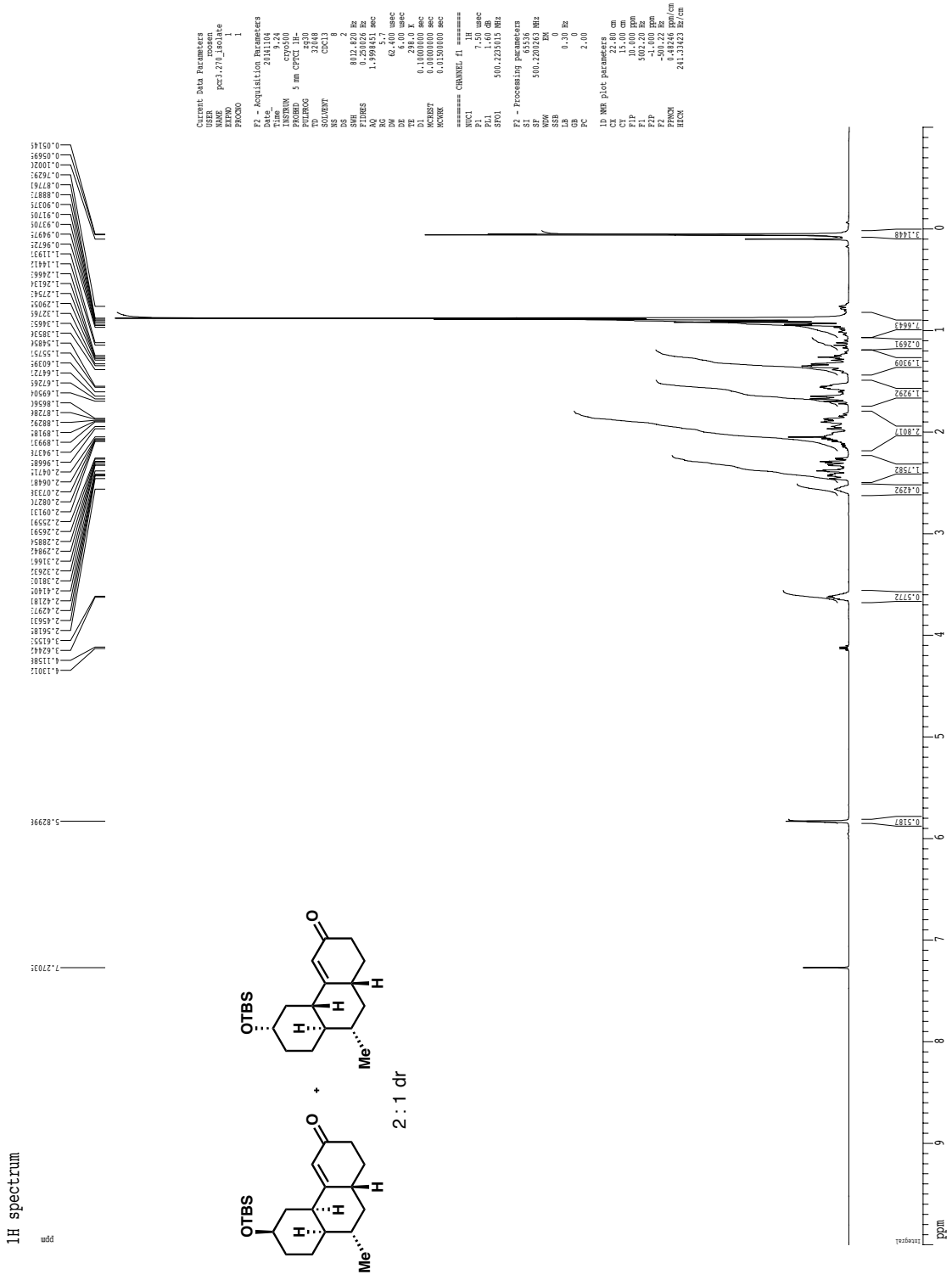

1H spectrum
ppm
Integral
OH
H
Me
2 : 1 dr

Z-restored spin-echo 13C spectrum with 1H decoupling

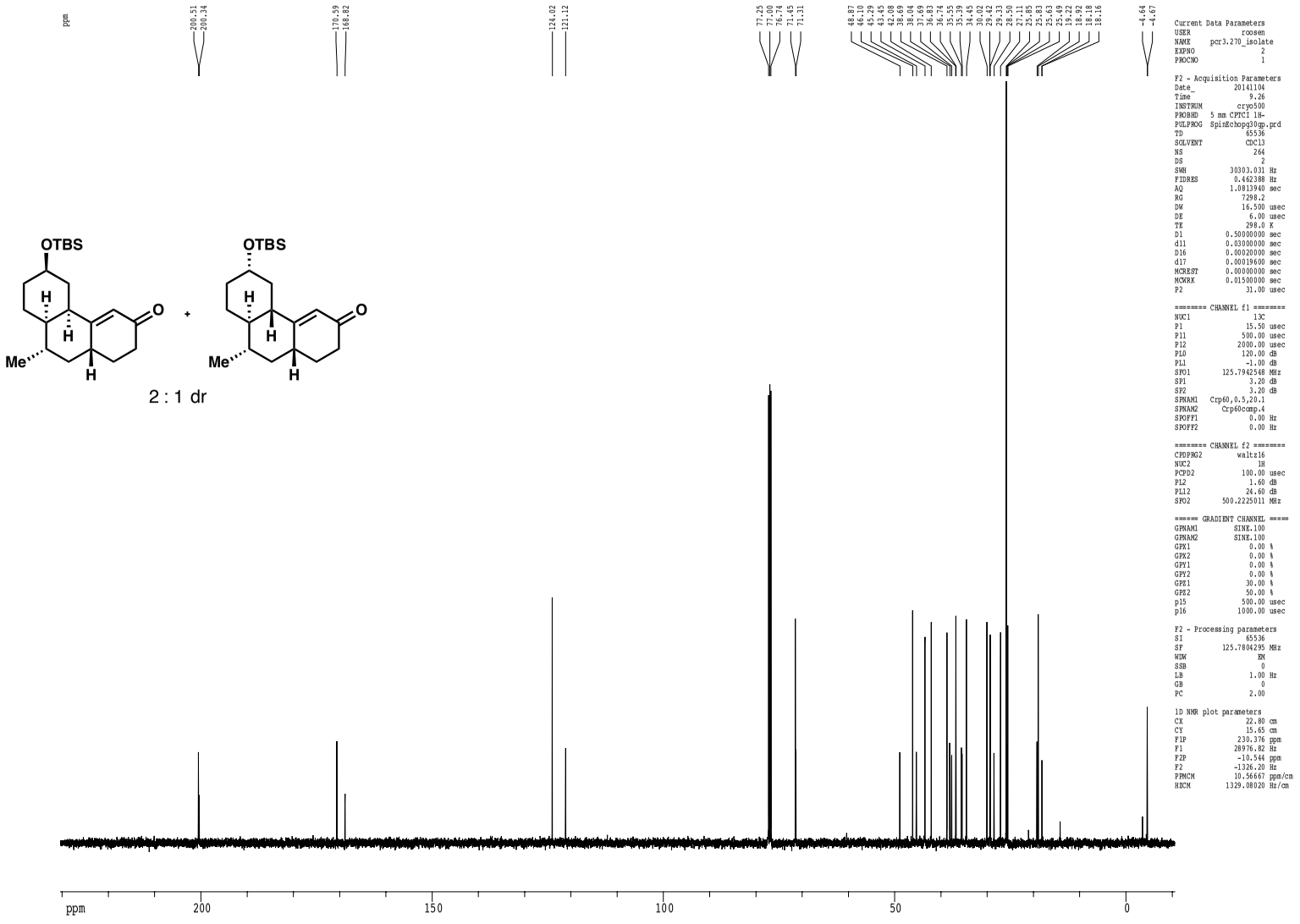


2 : 1 dr


```
Current Data Parameters
USER              roosen
NAME      pcr3.266_isolate
EXPNO                   2
PROCNO                  1

F2 - Acquisition Parameters
Date_           20141101
Time              10.37
INSTRUM          cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD                65536
SOLVENT           CDCl3
NS                  288
DS                    2
SWH           30303.031 Hz
FIDRES        0.462388 Hz
AQ            1.0813940 sec
RG               3649.1
DW                16.500 usec
DE                 6.00 usec
TE               298.0 K
D1            0.50000000 sec
d11           0.03000000 sec
D16           0.00020000 sec
d17           0.00019600 sec
MCREST        0.00000000 sec
MCWRK         0.01500000 sec
P2                31.00 usec

======= CHANNEL f1 =======
NUC1                13C
P1                15.50 usec
P11              500.00 usec
P12             2000.00 usec
PL0              120.00 dB
PL1               -1.00 dB
SFO1         125.7942548 MHz
SP1               3.20 dB
SP2               3.20 dB
SPNAM1    Crp60,0.5,20.1
SPNAM2      Crp60comp.4
SPOFF1               0.00 Hz
SPOFF2               0.00 Hz

======= CHANNEL f2 =======
CPDPRG2          waltz16
NUC2                1H
PCPD2            100.00 usec
PL2                1.60 dB
PL12              24.60 dB
SFO2         500.2225011 MHz

===== GRADIENT CHANNEL ====
GPNAM1           SINE.100
GPNAM2           SINE.100
GPX1                0.00 %
GPX2                0.00 %
GPY1                0.00 %
GPY2                0.00 %
GPZ1               30.00 %
GPZ2               50.00 %
p15              500.00 usec
p16             1000.00 usec

F2 - Processing parameters
SI                  65536
SF           125.7804319 MHz
WDW                    EM
SSB                    0
LB                  1.00 Hz
GB                     0
PC                  2.00

1D NMR plot parameters
CX                 22.80 cm
CY                 15.65 cm
F1P              230.358 ppm
F1              28974.50 Hz
F2P              -10.562 ppm
F2              -1328.53 Hz
PPMCM           10.56667 ppm/cm
HZCM          1329.08032 Hz/cm
```


1H spectrum
OTBS
Me
H
O
+
2 : 1 dr
ppm

Z-restored spin-echo 13C spectrum with 1H decoupling



Current Data Parameters
USER roosen
NAME pcr3.270_isolate
EXPNO 2
PROCNO 1

F2 - Acquisition Parameters
Date_ 20141104
Time 9.26
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG SpinEchopg30gp.prd
TD 65536
SOLVENT CDCl3
NS 264
DS 2
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0813940 sec
RG 7298.2
DW 16.500 usec
DE 6.00 usec
TE 298.0 K
D1 0.50000000 sec
d11 0.03000000 sec
D16 0.00020000 sec
d17 0.00019600 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
P2 31.00 usec

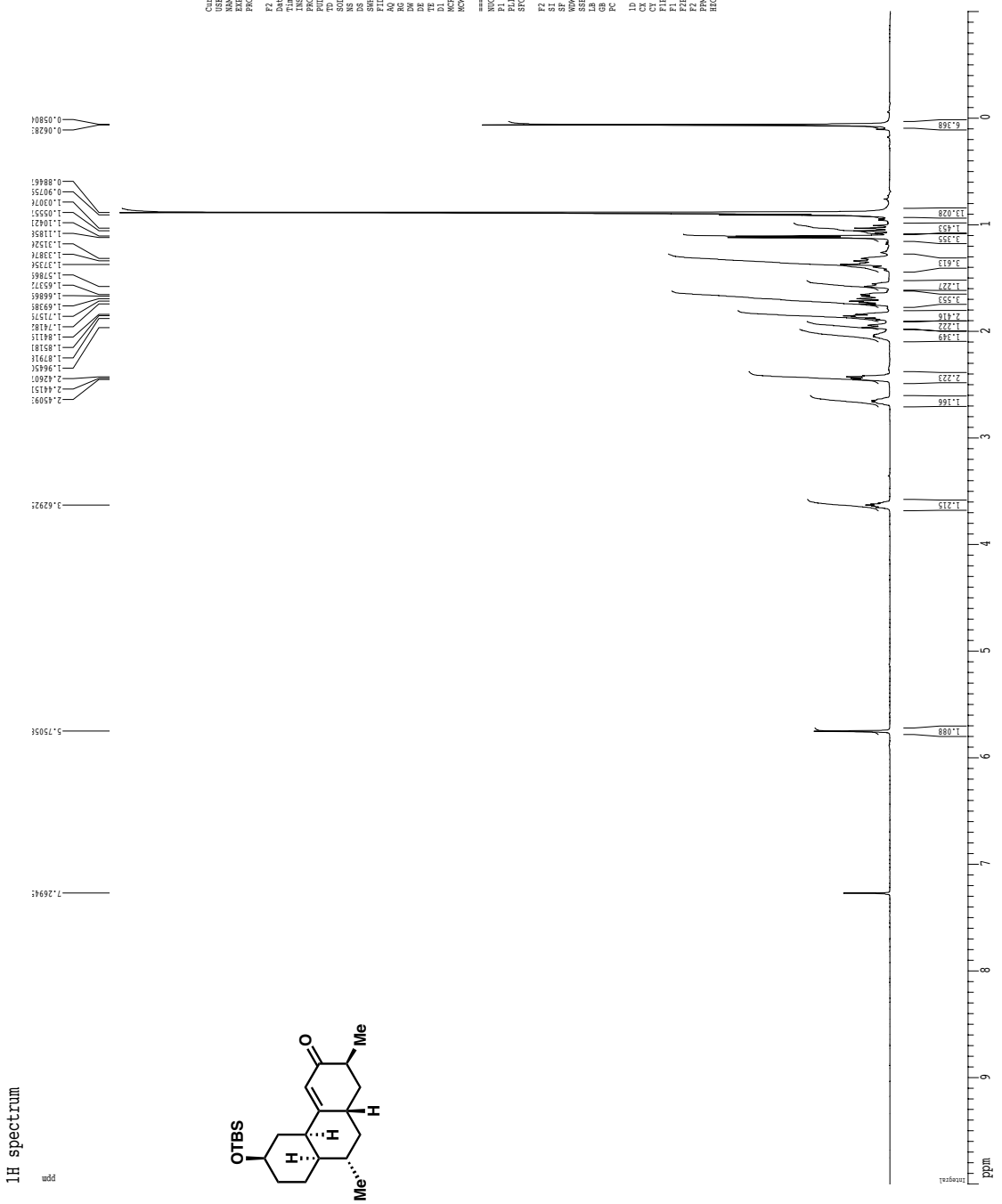
======= CHANNEL f1 =======
NUC1 13C
P1 15.50 usec
P11 500.00 usec
P12 2000.00 usec
PL0 120.00 dB
PL1 -1.00 dB
SFO1 125.7942548 MHz
SP1 3.20 dB
SP2 3.20 dB
SPNAM1 Crp60,0.5,20.1
SPNAM2 Crp60comp.4
SPOFF1 0.00 Hz
SPOFF2 0.00 Hz

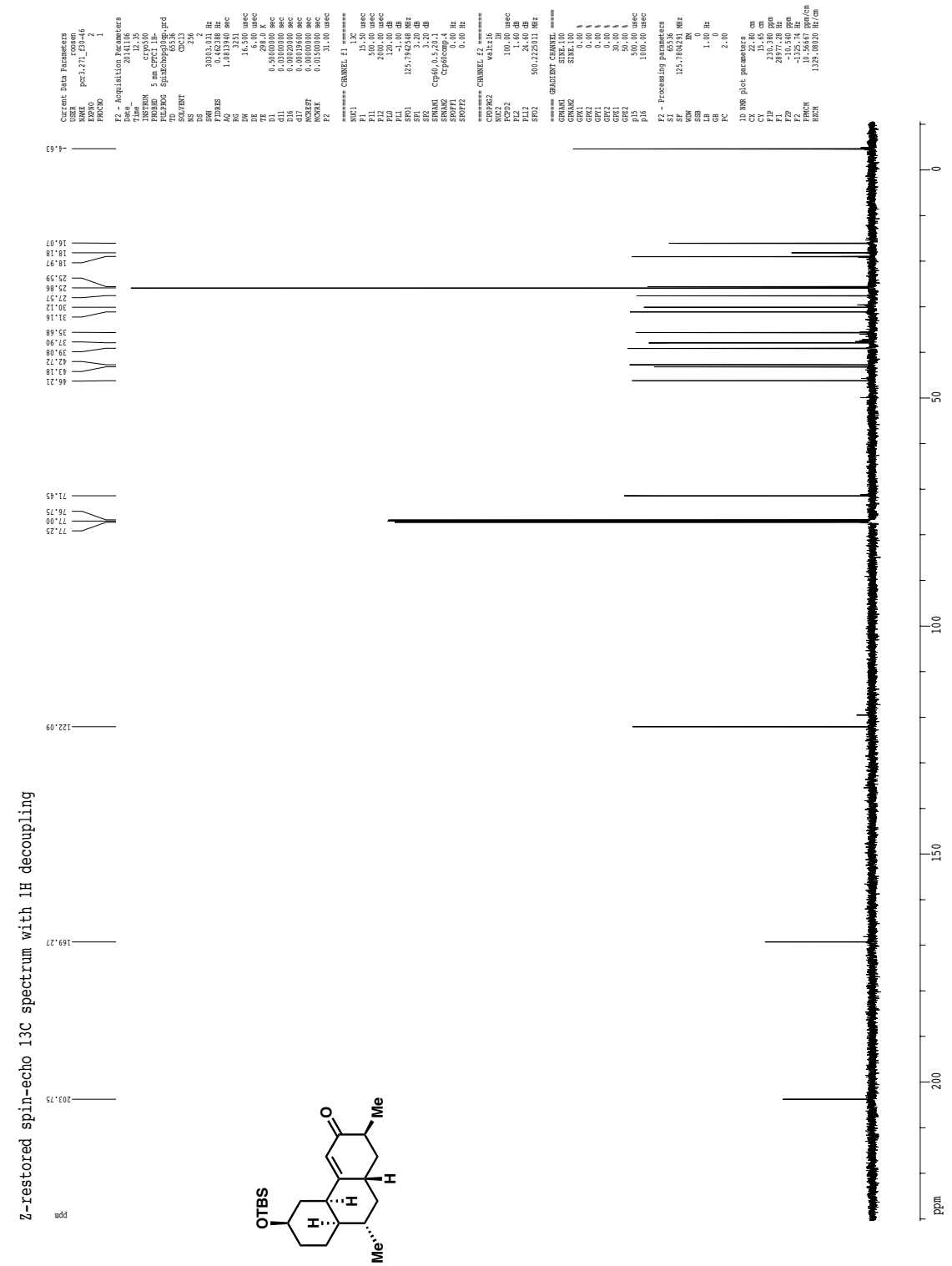
======= CHANNEL f2 =======
CPDPRG2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 1.60 dB
PL12 24.60 dB
SFO2 500.2225011 MHz

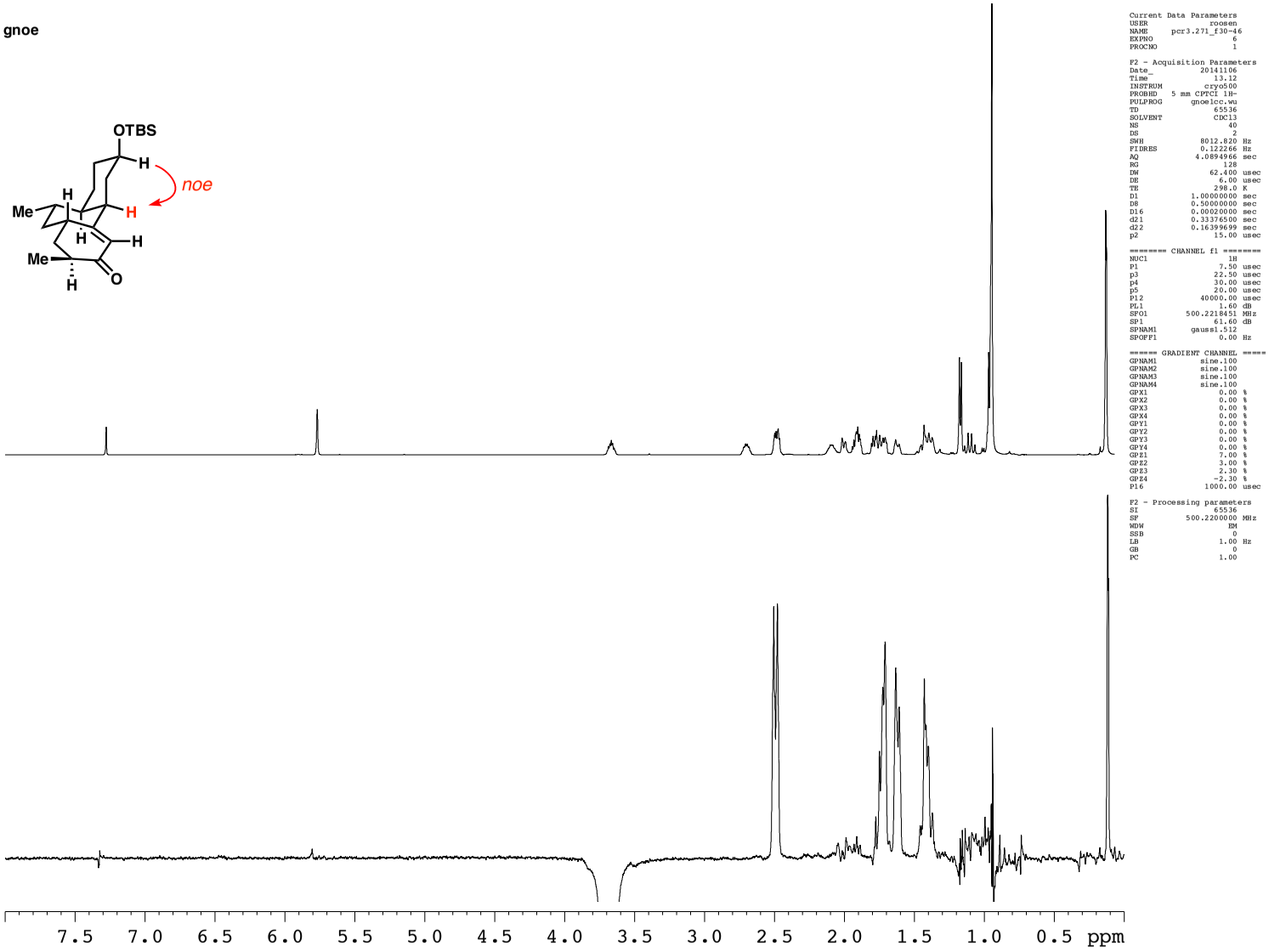
===== GRADIENT CHANNEL ====
GPNAM1 SINE.100
GPNAM2 SINE.100
GPX1 0.00 %
GPX2 0.00 %
GPY1 0.00 %
GPY2 0.00 %
GPZ1 30.00 %
GPZ2 50.00 %
p15 500.00 usec
p16 1000.00 usec

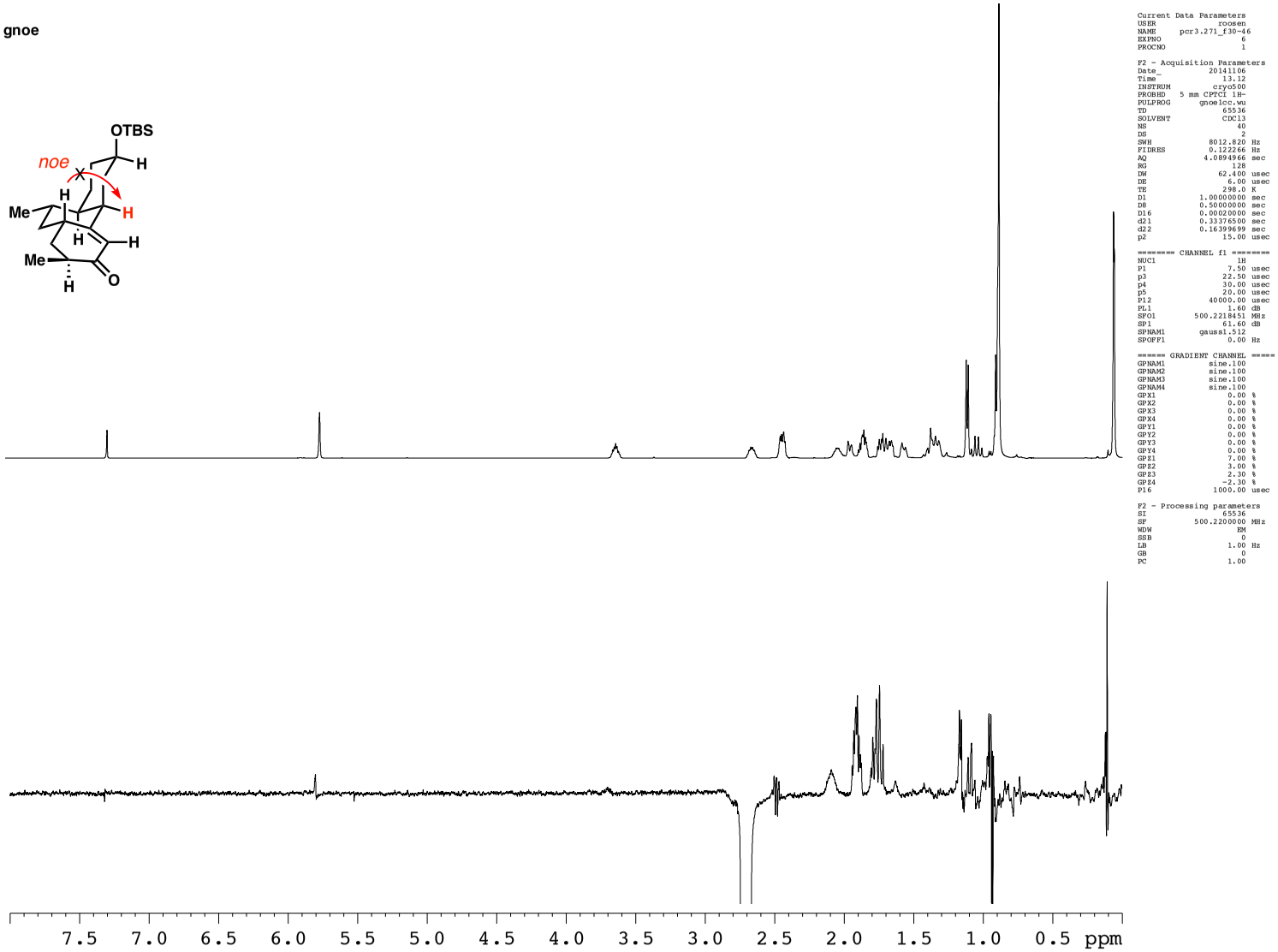
F2 - Processing parameters
SI 65536
SF 125.7804295 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00

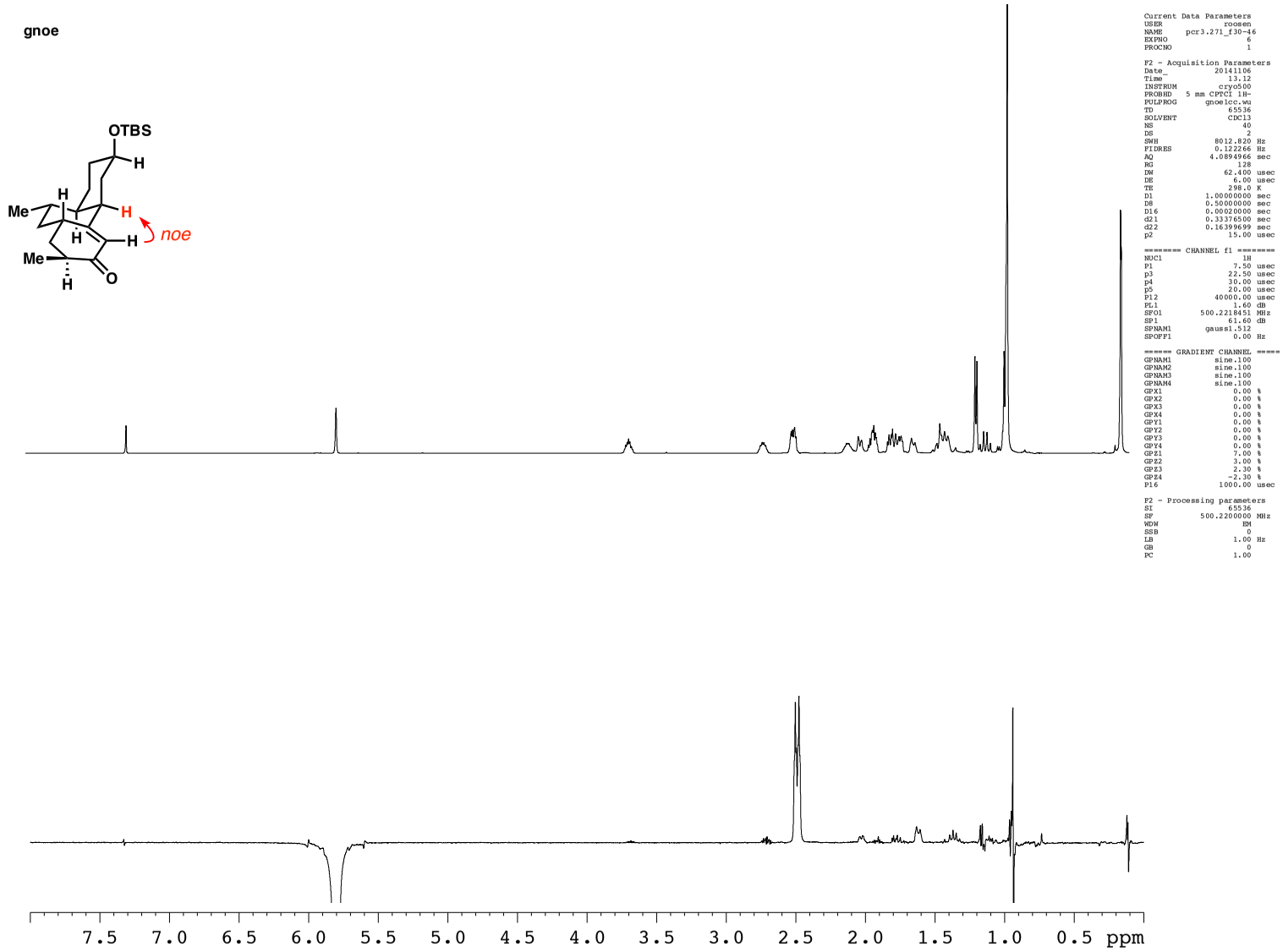
1D NMR plot parameters
CX 22.80 cm
CY 15.65 cm
F1P 230.376 ppm
F1 28976.82 Hz
F2P -10.544 ppm
F2 -1326.20 Hz
PPMCM 10.56667 ppm/cm
HZCM 1329.08020 Hz/cm

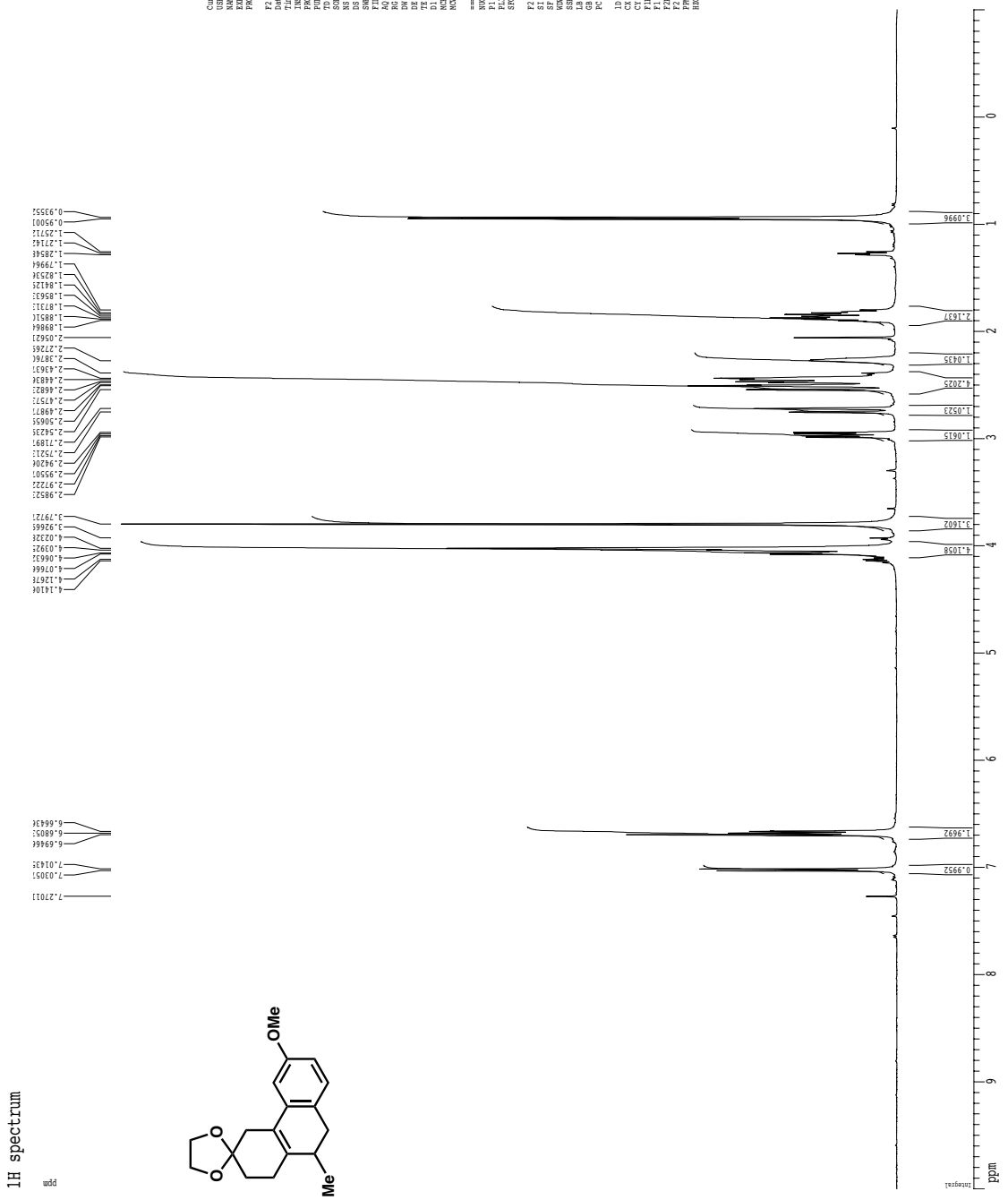

1H spectrum
ppm
Integral
OTBS
Me
Me
H
H
H

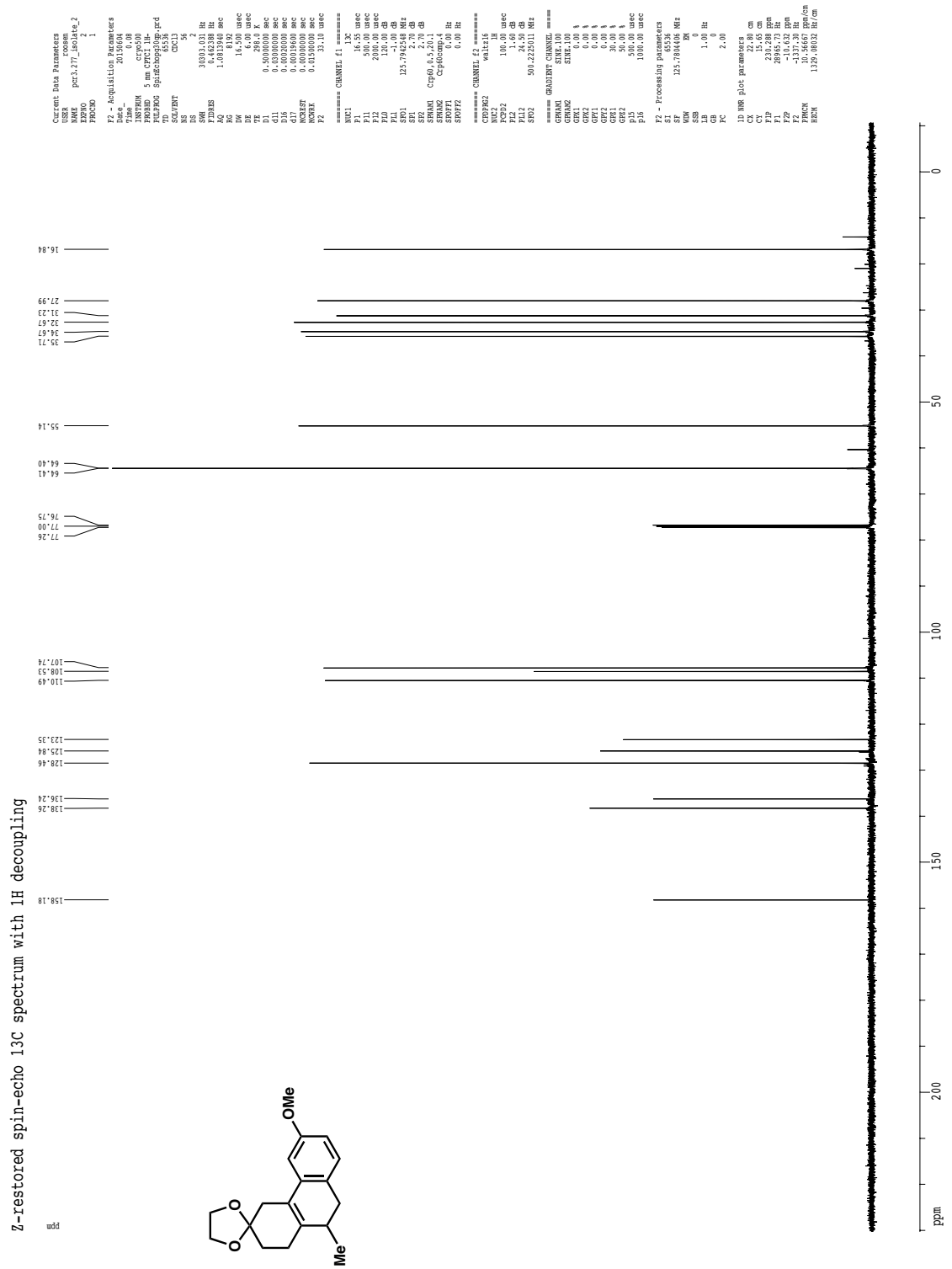

Z-restored spin-echo 13C spectrum with 1H decoupling
OTBS
Me
Me
H
H
H
O
ppm

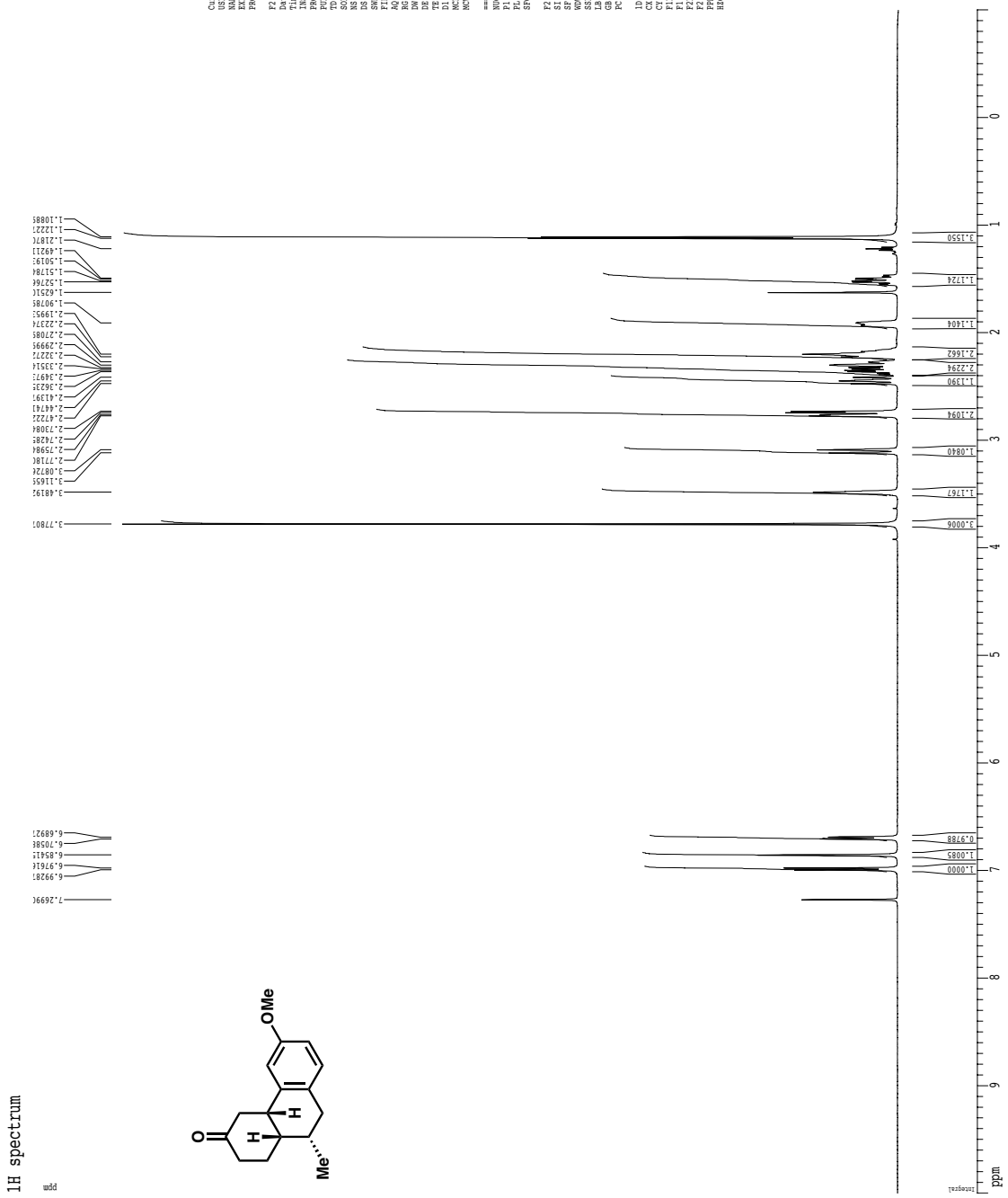

gnoe
OTBS
H
noe
Me
H
H
H
H
Me
O
H
Current Data Parameters
USER roosen
NAME pcr3.271_f30-46
EXPNO 6
PROCNO 1
F2 - Acquisition Parameters
Date_ 20141106
Time 13.12
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG gnoelcc.wu
TD 65536
SOLVENT CDCl3
NS 40
DS 2
SWH 8012.820 Hz
FIDRES 0.122266 Hz
AQ 4.0894966 sec
RG 128
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 1.00000000 sec
D8 0.50000000 sec
D16 0.00020000 sec
d21 0.33376500 sec
d22 0.16399699 sec
p2 15.00 usec
======= CHANNEL f1 =======
NUC1 1H
P1 7.50 usec
p3 22.50 usec
p4 30.00 usec
p5 20.00 usec
P12 40000.00 usec
PL1 1.60 dB
SFO1 500.2218451 MHz
SP1 61.60 dB
SPNAM1 gauss1.512
SPOFF1 0.00 Hz
===== GRADIENT CHANNEL =====
GPNAM1 sine.100
GPNAM2 sine.100
GPNAM3 sine.100
GPNAM4 sine.100
GPX1 0.00 %
GPX2 0.00 %
GPX3 0.00 %
GPX4 0.00 %
GPY1 0.00 %
GPY2 0.00 %
GPY3 0.00 %
GPY4 0.00 %
GPZ1 7.00 %
GPZ2 3.00 %
GPZ3 2.30 %
GPZ4 -2.30 %
P16 1000.00 usec
F2 - Processing parameters
SI 65536
SF 500.2200000 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.00
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm

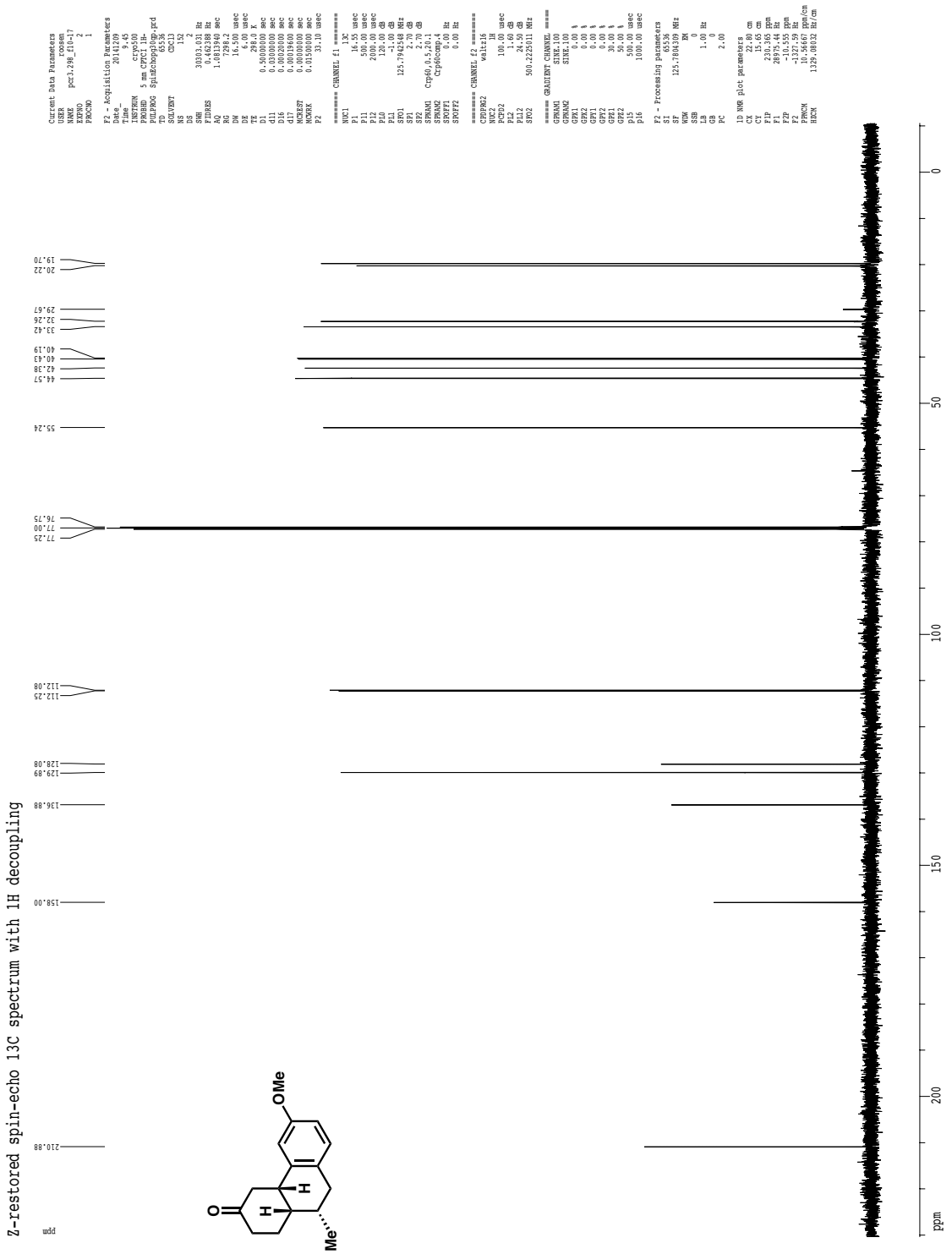

gnoe
OTBS
noe
H
H
Me
H
H
H
Me
H
O
Current Data Parameters
USER roosen
NAME pcr3.271_f30-46
EXPNO 6
PROCNO 1
F2 - Acquisition Parameters
Date_ 20141106
Time 13.12
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG gnoelcc.wu
TD 65536
SOLVENT CDCl3
NS 40
DS 2
SWH 8012.820 Hz
FIDRES 0.122266 Hz
AQ 4.0894966 sec
RG 128
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 1.00000000 sec
D8 0.50000000 sec
D16 0.00020000 sec
d21 0.33376500 sec
d22 0.16399699 sec
p2 15.00 usec
======= CHANNEL f1 =======
NUC1 1H
P1 7.50 usec
p3 22.50 usec
p4 30.00 usec
p5 20.00 usec
P12 40000.00 usec
PL1 1.60 dB
SFO1 500.2218451 MHz
SP1 61.60 dB
SPNAM1 gauss1.512
SPOFF1 0.00 Hz
===== GRADIENT CHANNEL =====
GPNAM1 sine.100
GPNAM2 sine.100
GPNAM3 sine.100
GPNAM4 sine.100
GPX1 0.00 %
GPX2 0.00 %
GPX3 0.00 %
GPX4 0.00 %
GPY1 0.00 %
GPY2 0.00 %
GPY3 0.00 %
GPY4 0.00 %
GPZ1 7.00 %
GPZ2 3.00 %
GPZ3 2.30 %
GPZ4 -2.30 %
P16 1000.00 usec
F2 - Processing parameters
SI 65536
SF 500.2200000 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.00
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm

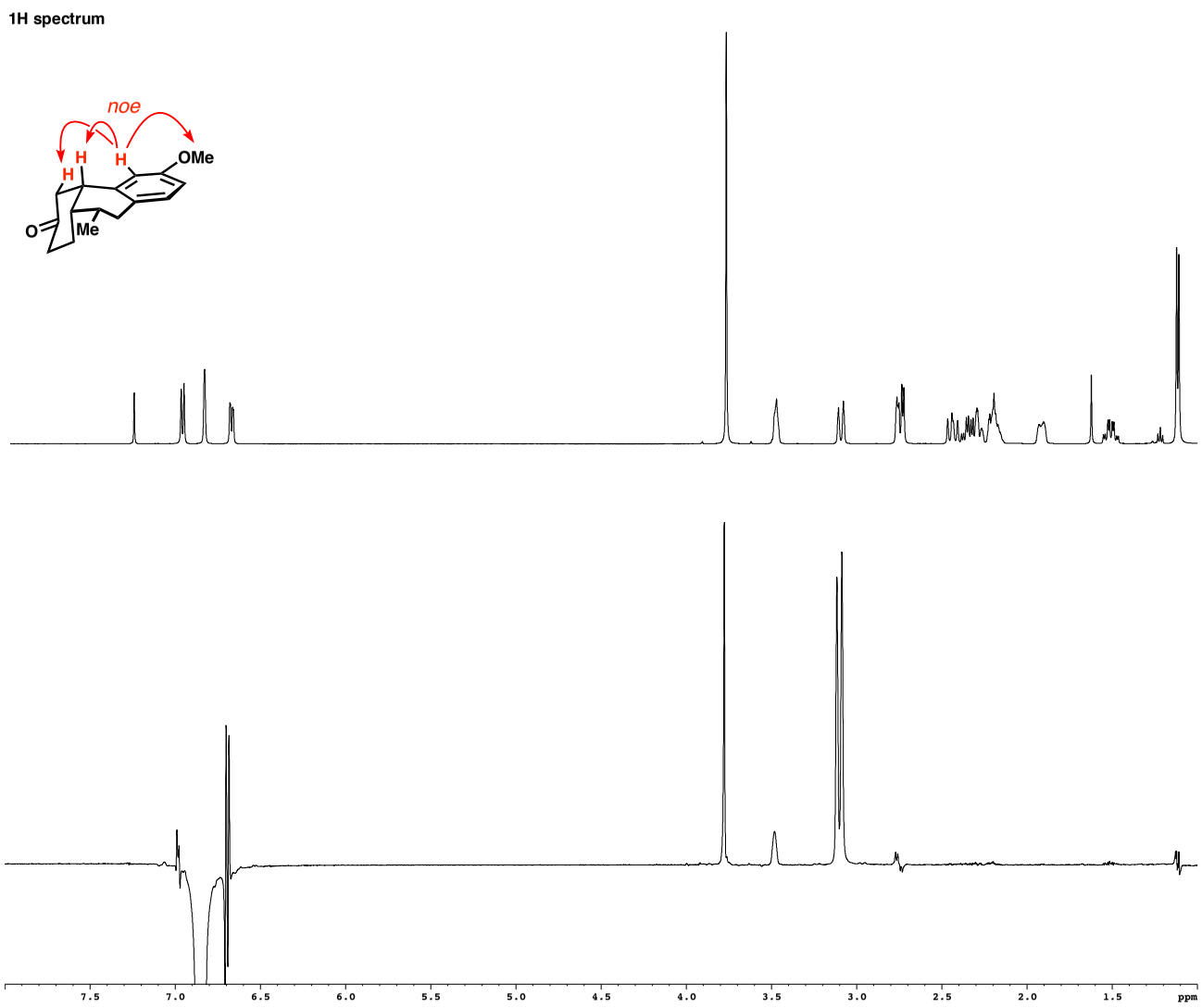

gnoe
OTBS
H
Me
H
H
H
noe
H
Me
H
O
Current Data Parameters
USER roosen
NAME pcr3.271_f30-46
EXPNO 6
PROCNO 1
F2 - Acquisition Parameters
Date_ 20141106
Time 13.12
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG gnoelcc.wu
TD 65536
SOLVENT CDCl3
NS 40
DS 2
SWH 8012.820 Hz
FIDRES 0.122266 Hz
AQ 4.0894966 sec
RG 128
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 1.00000000 sec
D8 0.50000000 sec
D16 0.00020000 sec
d21 0.33376500 sec
d22 0.16399699 sec
p2 15.00 usec
======= CHANNEL f1 =======
NUC1 1H
P1 7.50 usec
p3 22.50 usec
p4 30.00 usec
p5 20.00 usec
P12 40000.00 usec
PL1 1.60 dB
SFO1 500.2218451 MHz
SP1 61.60 dB
SPNAM1 gauss1.512
SPOFF1 0.00 Hz
===== GRADIENT CHANNEL =====
GPNAM1 sine.100
GPNAM2 sine.100
GPNAM3 sine.100
GPNAM4 sine.100
GPX1 0.00 %
GPX2 0.00 %
GPX3 0.00 %
GPX4 0.00 %
GPY1 0.00 %
GPY2 0.00 %
GPY3 0.00 %
GPY4 0.00 %
GPZ1 7.00 %
GPZ2 3.00 %
GPZ3 2.30 %
GPZ4 -2.30 %
P16 1000.00 usec
F2 - Processing parameters
SI 65536
SF 500.2200000 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.00
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm


1H spectrum
ppm
OMe
Me

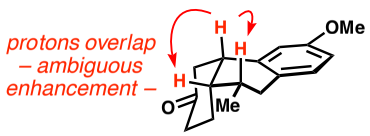

Z-restored spin-echo 13C spectrum with 1H decoupling
ppm
OMe
Me
16.84
27.99
31.23
32.67
34.67
35.71
55.14
64.40
64.41
76.75
77.00
77.26
107.74
108.53
110.49
123.35
125.84
128.46
136.24
138.26
158.18
0
50
100
150
200


1H spectrum
ppm
OMe
H
H
O
Me


Z-restored spin-echo 13C spectrum with 1H decoupling
Current Data Parameters
USER rossen
NAME pcc3.298_f10-17
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20141209
Time 9.45
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG SpinEchopg30gp.pcd
TD 65536
SOLVENT CDCl3
NS 152
DS 2
SWH 31013.131 Hz
FIDRES 0.473098 Hz
AQ 1.0013940 sec
RG 7298.2
DW 16.500 usec
DE 6.00 usec
TE 298.0 K
D1 0.50000000 sec
d11 0.03000000 sec
D16 0.00120000 sec
d12 0.00001000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
F2 33.10 usec
======= CHANNEL f1 =======
NUC1 13C
P1 16.55 usec
P11 500.00 usec
P12 2000.00 usec
PL0 120.00 dB
PL1 -1.00 dB
SFO1 125.7742548 MHz
SF01 2.70 dB
SF02 Crp60,0.5,20.1
SFRAM1 Crp60comp.4
SFRAM2 0.00 Hz
SFOFF1 0.00 Hz
SFOFF2
======= CHANNEL f2 =======
CPDPRG2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 1.60 dB
PL12 24.50 dB
SFO2 500.2225011 MHz
===== GRADIENT CHANNEL =====
GPRAM1 SINE.100
GPRAM2 SINE.100
GPZ1 0.00 %
GPZ2 0.00 %
GPZ1 0.00 %
GPZ2 0.00 %
GPZ1 30.00 %
GPZ2 50.00 %
p15 500.00 usec
p16 1000.00 usec
F2 - Processing parameters
SI 65536
SF 125.7804309 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00
1D NMR plot parameters
CX 22.80 cm
CY 15.45 cm
F1P 230.965 ppm
F1 29035.44 Hz
F2P -10.555 ppm
F2 -1327.59 Hz
PPMCM 10.56667 ppm/cm
HZCM 1329.08032 Hz/cm
210.88
158.00
136.88
129.89
128.08
112.25
112.08
77.25
77.00
76.75
55.24
44.57
42.38
40.43
40.19
33.42
32.26
29.67
20.22
19.70
OMe
O
H
H
Me
ppm
0
50
100
150
200

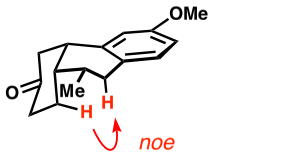

1H spectrum
noe
H
H
H
OMe
O
Me
Current Data Parameters
USER roosen
NAME pcr3.298_f10-17
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20141209
Time 15.56
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 32048
SOLVENT CDCl3
NS 8
DS 2
SWH 8012.820 Hz
FIDRES 0.250026 Hz
AQ 1.9998451 sec
RG 6.3
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 7.50 usec
PL1 1.60 dB
SFO1 500.2235015 MHz
F2 - Processing parameters
SI 65536
SF 500.2200268 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00
1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 10.000 ppm
F1 5002.20 Hz
F2P -1.000 ppm
F2 -500.22 Hz
PPMCM 0.48246 ppm/cm
HZCM 241.33423 Hz/cm
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
ppm

1H spectrum

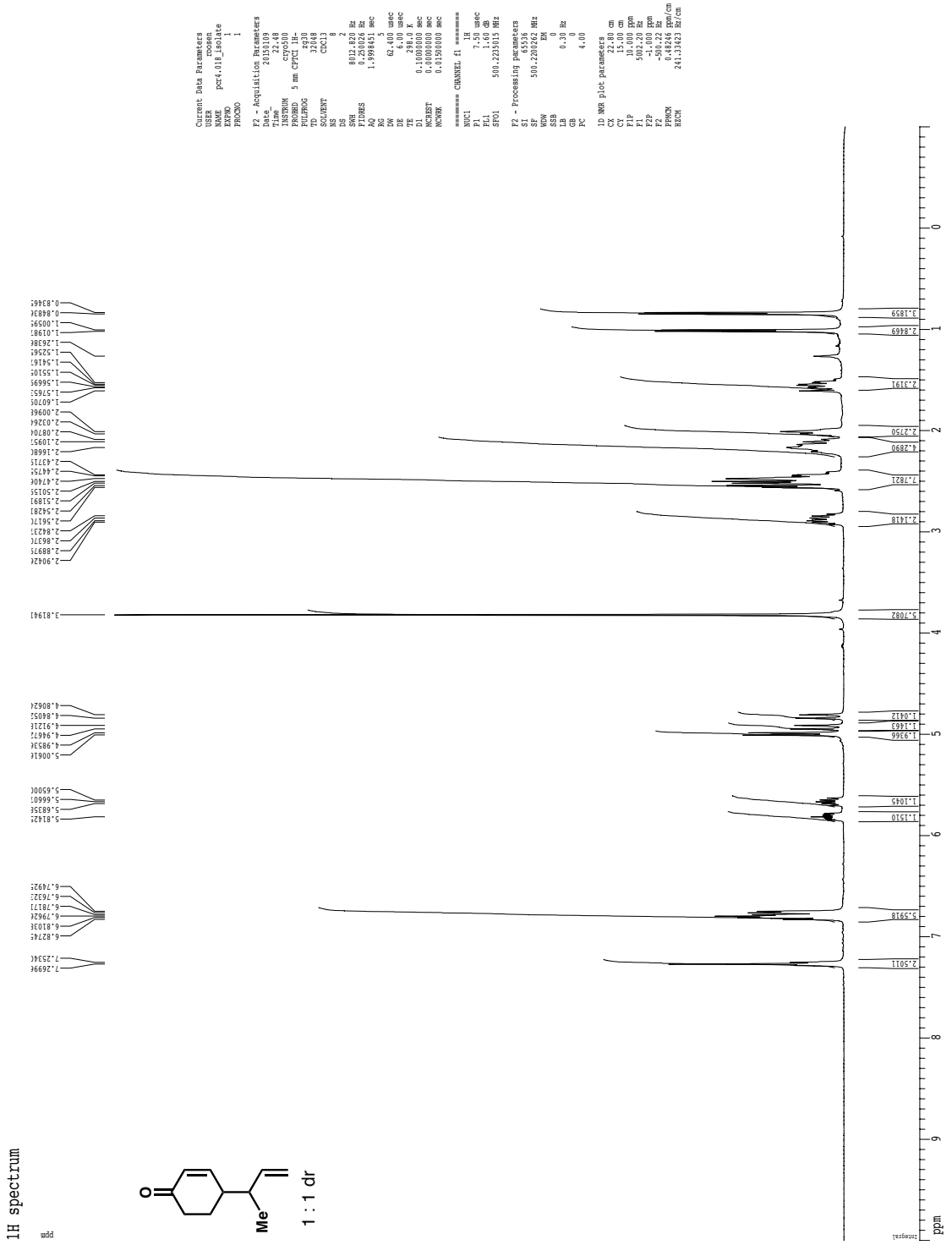



```
Current Data Parameters
USER                 roosen
NAME       pcr3.298_f10-17
EXPNO                     1
PROCNO                    1

F2 - Acquisition Parameters
Date_              20141209
Time                  15.56
INSTRUM             cryo500
PROBHD    5 mm CPTCI 1H-
PULPROG               zg30
TD                   32048
SOLVENT              CDCl3
NS                       8
DS                       2
SWH               8012.820 Hz
FIDRES            0.250026 Hz
AQ                1.9998451 sec
RG                     6.3
DW                  62.400 usec
DE                   6.00 usec
TE                  298.0 K
D1              0.10000000 sec
MCREST          0.00000000 sec
MCWRK           0.01500000 sec

======== CHANNEL f1 ========
NUC1                   1H
P1                   7.50 usec
PL1                  1.60 dB
SFO1          500.2235015 MHz

F2 - Processing parameters
SI                    65536
SF             500.2200268 MHz
WDW                      EM
SSB                       0
LB                     0.30 Hz
GB                        0
PC                     4.00

1D NMR plot parameters
CX                    22.80 cm
CY                    15.00 cm
F1P                  10.000 ppm
F1                 5002.20 Hz
F2P                 -1.000 ppm
F2                 -500.22 Hz
PPMCM               0.48246 ppm/cm
HZCM              241.33423 Hz/cm
```

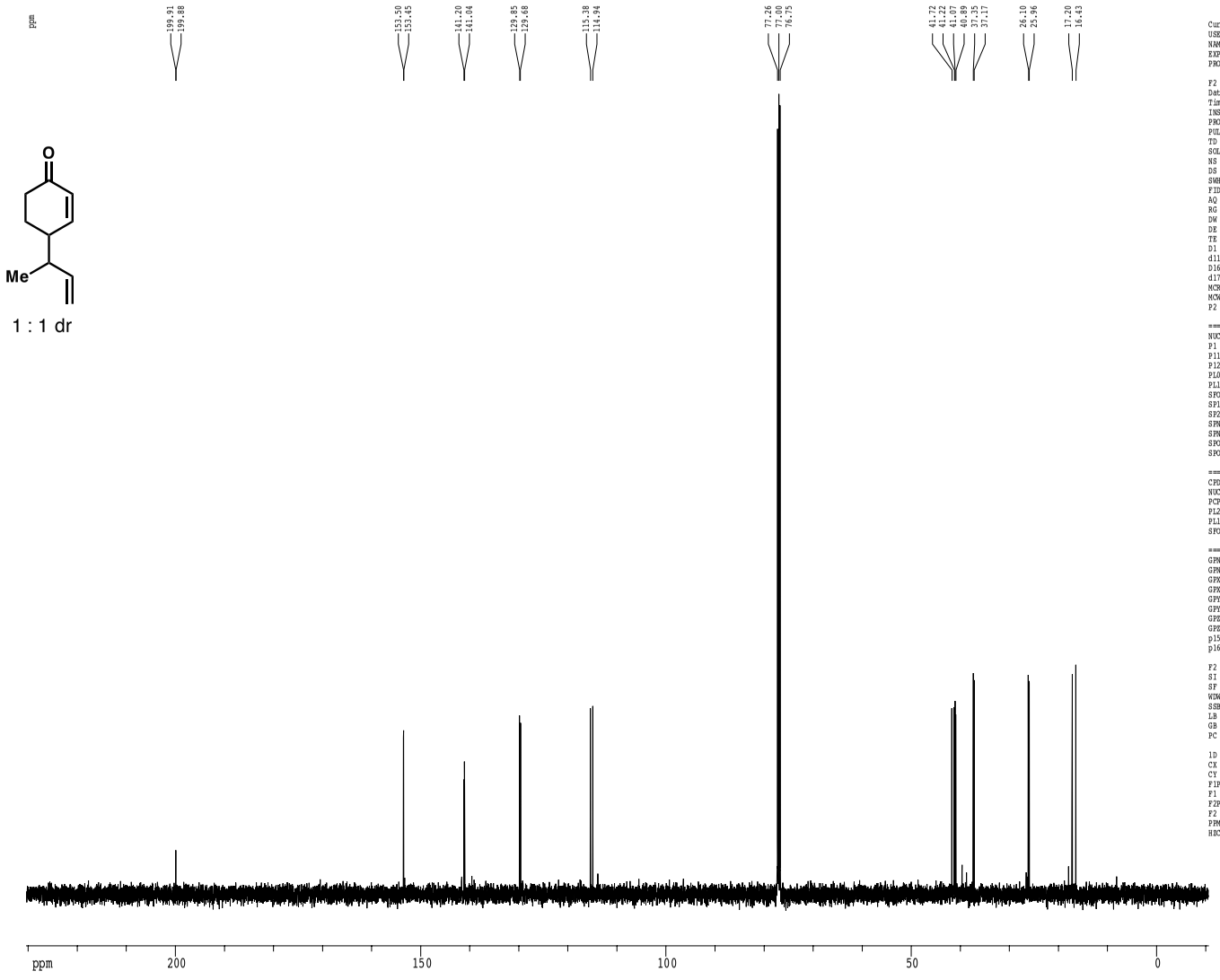
1H spectrum



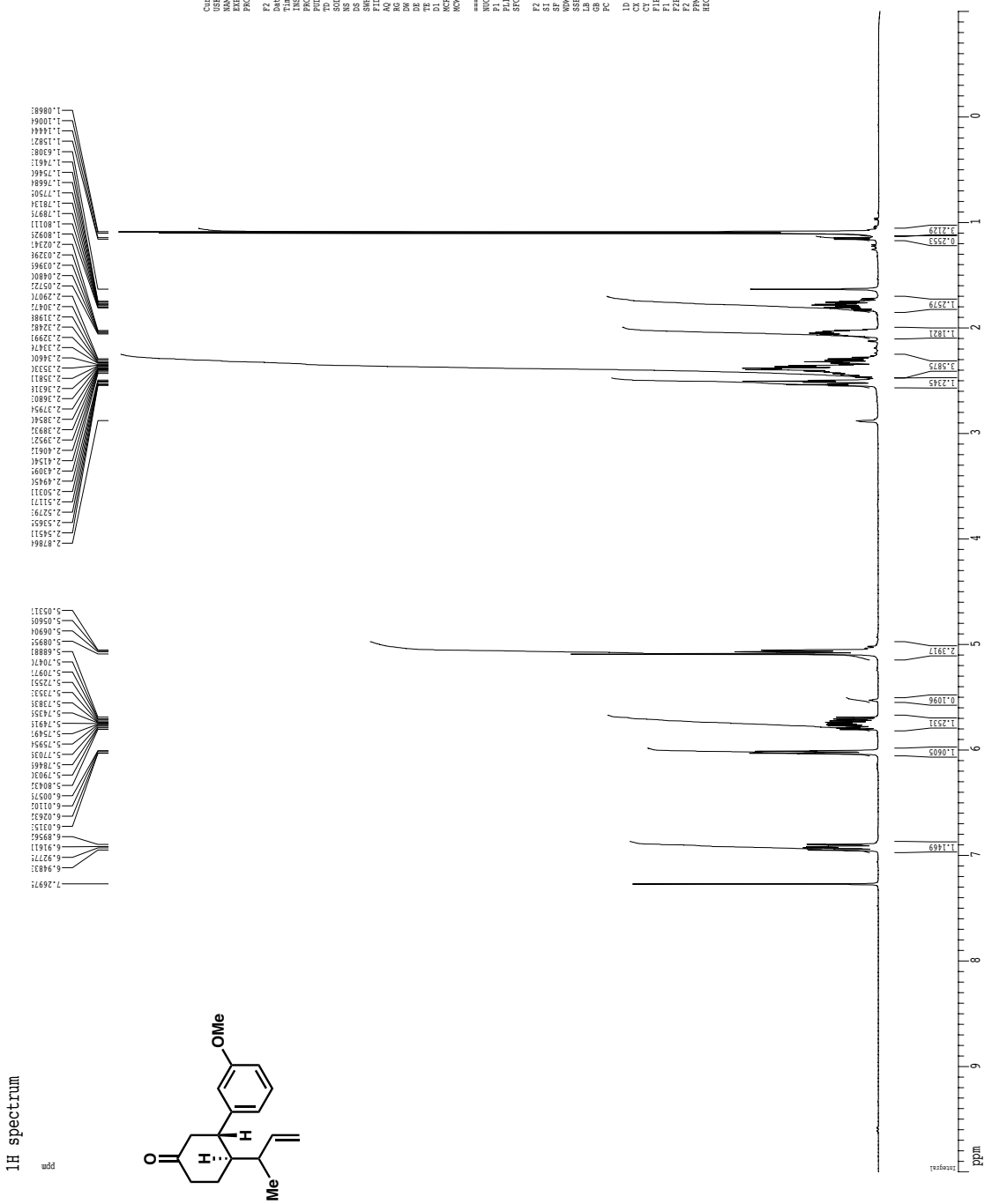

```
Current Data Parameters
USER                  roosen
NAME      pcr3.298_f10-17
EXPNO                      1
PROCNO                     1

F2 - Acquisition Parameters
Date_              20141209
Time                  15.56
INSTRUM             cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG                zg30
TD                    32048
SOLVENT               CDCl3
NS                        8
DS                        2
SWH                8012.820 Hz
FIDRES             0.250026 Hz
AQ                 1.9998451 sec
RG                       6.3
DW                    62.400 usec
DE                     6.00 usec
TE                    298.0 K
D1                0.10000000 sec
MCREST            0.00000000 sec
MCWRK             0.01500000 sec

======== CHANNEL f1 ========
NUC1                      1H
P1                     7.50 usec
PL1                    1.60 dB
SFO1           500.2235015 MHz

F2 - Processing parameters
SI                       65536
SF             500.2200268 MHz
WDW                         EM
SSB                          0
LB                        0.30 Hz
GB                           0
PC                        4.00

1D NMR plot parameters
CX                       22.80 cm
CY                       15.00 cm
F1P                     10.000 ppm
F1                    5002.20 Hz
F2P                    -1.000 ppm
F2                    -500.22 Hz
PPMCM                  0.48246 ppm/cm
HZCM                 241.33423 Hz/cm
```


1H spectrum
O
Me
1 : 1 dr
ppm

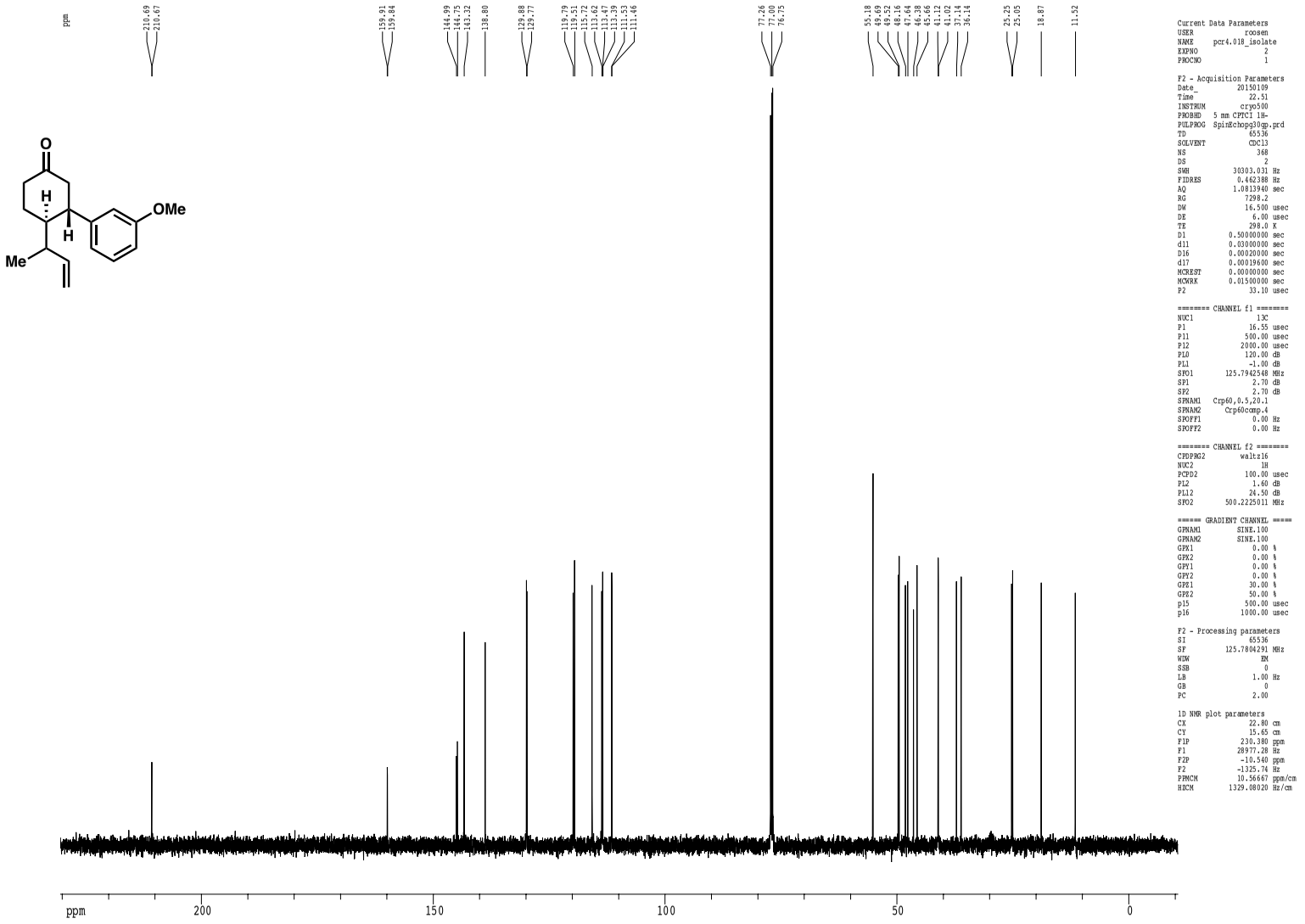
Z-restored spin-echo 13C spectrum with 1H decoupling



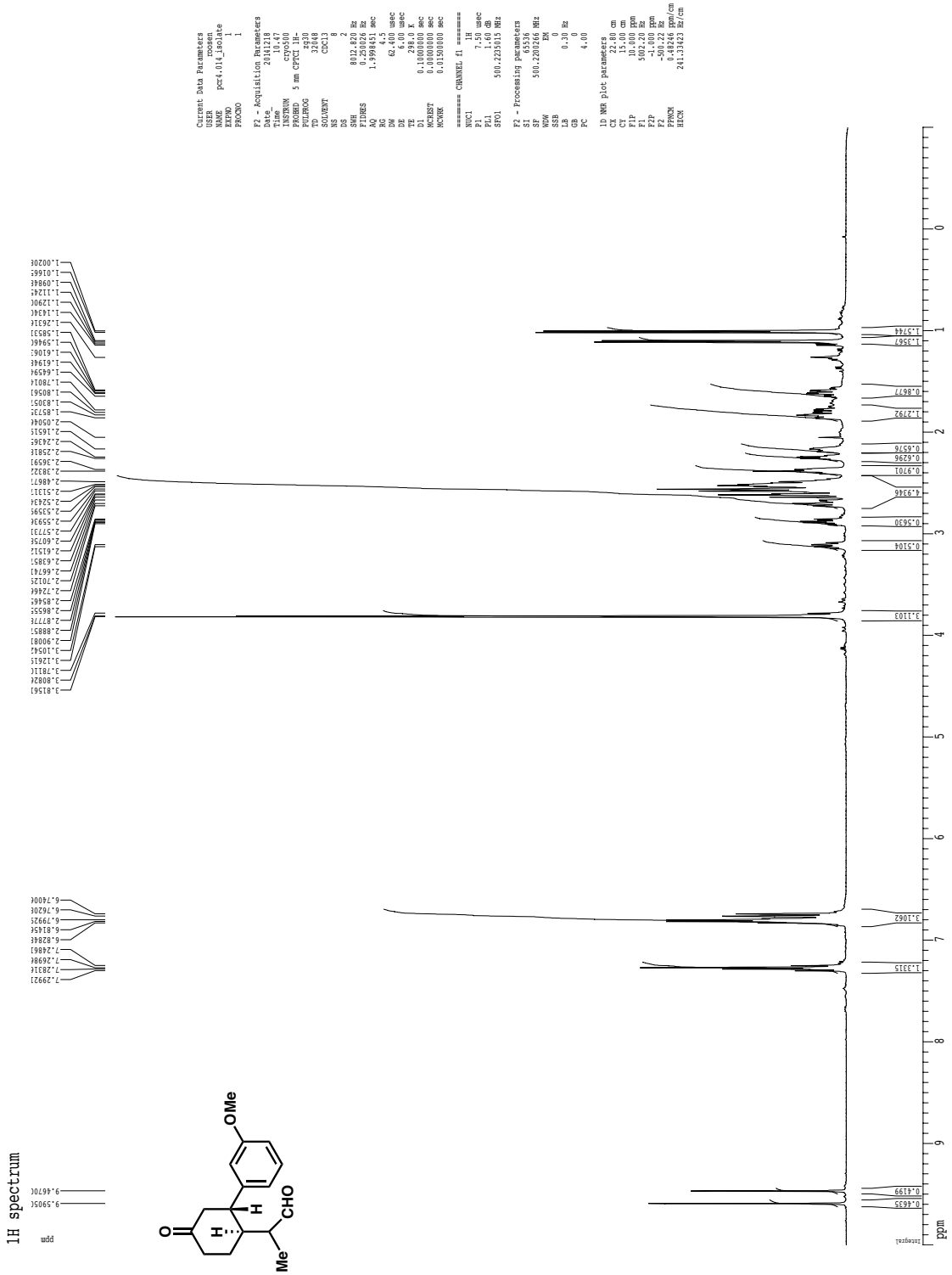

```
Current Data Parameters
USER              roosen
NAME      pcr4.115_77-80
EXPNO                2
PROCNO               1

F2 - Acquisition Parameters
Date_          20150417
Time              13.45
INSTRUM          cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD                65536
SOLVENT           CDCl3
NS                  144
DS                    2
SWH           30303.031 Hz
FIDRES        0.462388 Hz
AQ           1.0813940 sec
RG              7298.2
DW               16.500 usec
DE                6.00 usec
TE              298.0 K
D1          0.50000000 sec
d11         0.03000000 sec
D16         0.00020000 sec
d17         0.00019600 sec
MCREST      0.00000000 sec
MCWRK       0.01500000 sec
P2               33.10 usec

======= CHANNEL f1 =======
NUC1               13C
P1               16.55 usec
P11             500.00 usec
P12            2000.00 usec
PL0             120.00 dB
PL1              -1.00 dB
SFO1       125.7942548 MHz
SP1              2.70 dB
SP2              2.70 dB
SPNAM1   Crp60,0.5,20.1
SPNAM2     Crp60comp.4
SPOFF1              0.00 Hz
SPOFF2              0.00 Hz

======= CHANNEL f2 =======
CPDPRG2          waltz16
NUC2               1H
PCPD2           100.00 usec
PL2               1.60 dB
PL12             24.50 dB
SFO2       500.2225011 MHz

===== GRADIENT CHANNEL ====
GPNAM1          SINE.100
GPNAM2          SINE.100
GPX1                0.00 %
GPX2                0.00 %
GPY1                0.00 %
GPY2                0.00 %
GPZ1               30.00 %
GPZ2               50.00 %
p15              500.00 usec
p16             1000.00 usec

F2 - Processing parameters
SI                 65536
SF         125.7804286 MHz
WDW                  EM
SSB                  0
LB                1.00 Hz
GB                   0
PC                2.00

1D NMR plot parameters
CX               22.80 cm
CY               15.65 cm
F1P            230.384 ppm
F1             28977.75 Hz
F2P            -10.536 ppm
F2             -1325.28 Hz
PPMCM          10.56667 ppm/cm
HZCM        1329.08032 Hz/cm
```


1H spectrum
ppm
OMe
H
H
O
Me

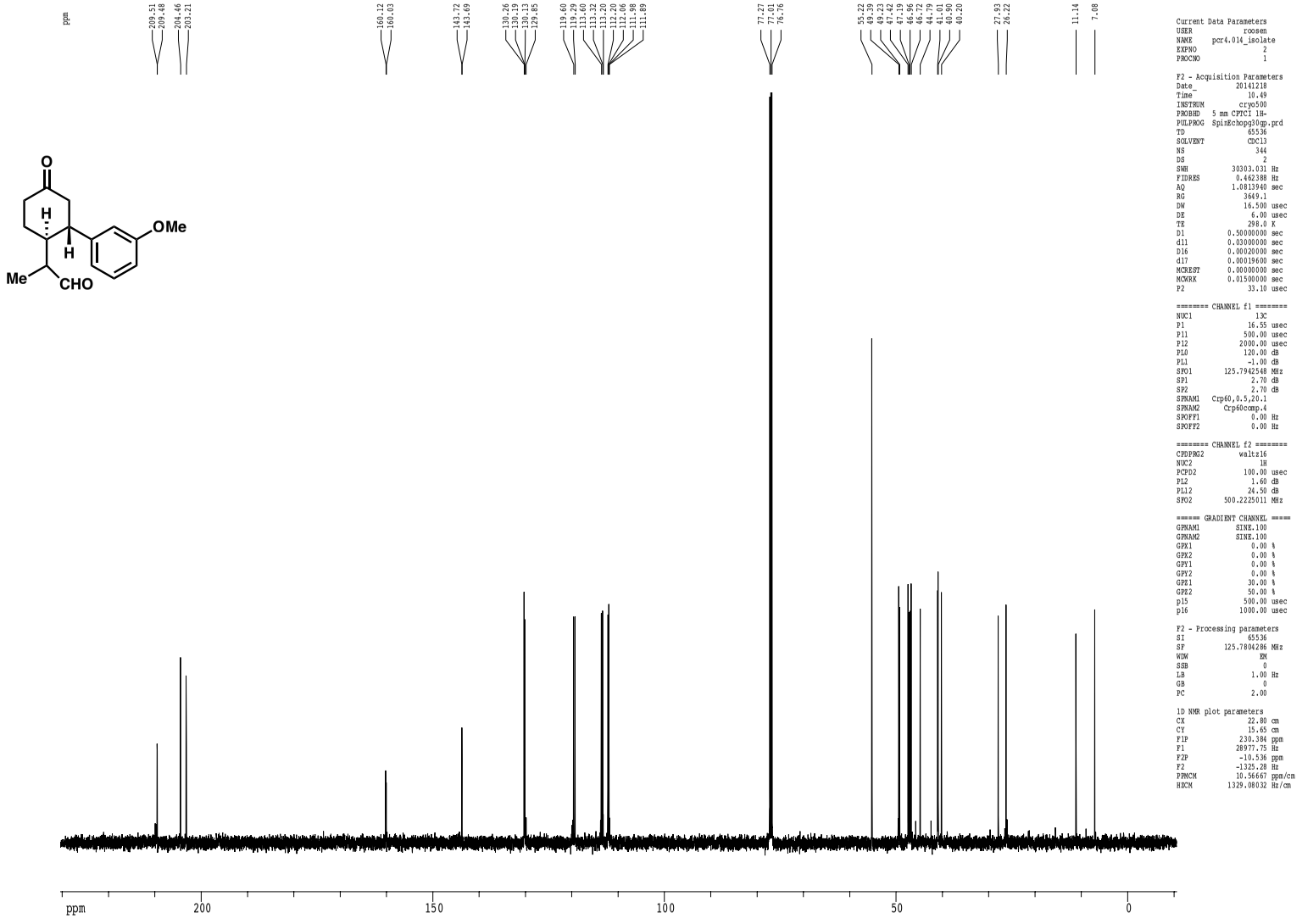
Z-restored spin-echo 13C spectrum with 1H decoupling




```
Current Data Parameters
USER              roosen
NAME      pcr4.018_isolate
EXPNO                    2
PROCNO                   1

F2 - Acquisition Parameters
Date_           20150109
Time              22.51
INSTRUM          cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD                 65536
SOLVENT             CDCl3
NS                    368
DS                      2
SWH           30303.031 Hz
FIDRES        0.462388 Hz
AQ            1.0813940 sec
RG               7298.2
DW                16.500 usec
DE                 6.00 usec
TE               298.0 K
D1          0.50000000 sec
d11         0.03000000 sec
D16         0.00020000 sec
d17         0.00019600 sec
MCREST      0.00000000 sec
MCWRK       0.01500000 sec
P2                33.10 usec

======= CHANNEL f1 =======
NUC1                 13C
P1                 16.55 usec
P11               500.00 usec
P12              2000.00 usec
PL0               120.00 dB
PL1                -1.00 dB
SFO1        125.7942548 MHz
SP1                2.70 dB
SP2                2.70 dB
SPNAM1   Crp60,0.5,20.1
SPNAM2     Crp60comp.4
SPOFF1               0.00 Hz
SPOFF2               0.00 Hz

======= CHANNEL f2 =======
CPDPRG2          waltz16
NUC2                1H
PCPD2             100.00 usec
PL2                1.60 dB
PL12              24.50 dB
SFO2        500.2225011 MHz

===== GRADIENT CHANNEL ====
GPNAM1          SINE.100
GPNAM2          SINE.100
GPX1                0.00 %
GPX2                0.00 %
GPY1                0.00 %
GPY2                0.00 %
GPZ1               30.00 %
GPZ2               50.00 %
p15               500.00 usec
p16              1000.00 usec

F2 - Processing parameters
SI                 65536
SF          125.7804291 MHz
WDW                   EM
SSB                    0
LB                  1.00 Hz
GB                     0
PC                  2.00

1D NMR plot parameters
CX                 22.80 cm
CY                 15.65 cm
F1P              230.380 ppm
F1               28977.28 Hz
F2P               -10.540 ppm
F2               -1325.74 Hz
PPMCM             10.56667 ppm/cm
HZCM           1329.08020 Hz/cm
```


1H spectrum
ppm
OMe
H
H
CHO
Me
O
Integral
ppm

Z-restored spin-echo 13C spectrum with 1H decoupling



Current Data Parameters
USER roosen
NAME pcr4.014_isolate
EXPNO 2
PROCNO 1

F2 - Acquisition Parameters
Date_ 20141218
Time 10.49
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG SpinEchopg30gp.prd
TD 65536
SOLVENT CDCl3
NS 344
DS 2
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0813940 sec
RG 3649.1
DW 16.500 usec
DE 6.00 usec
TE 298.0 K
D1 0.50000000 sec
d11 0.03000000 sec
D16 0.00020000 sec
d17 0.00019600 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
P2 33.10 usec

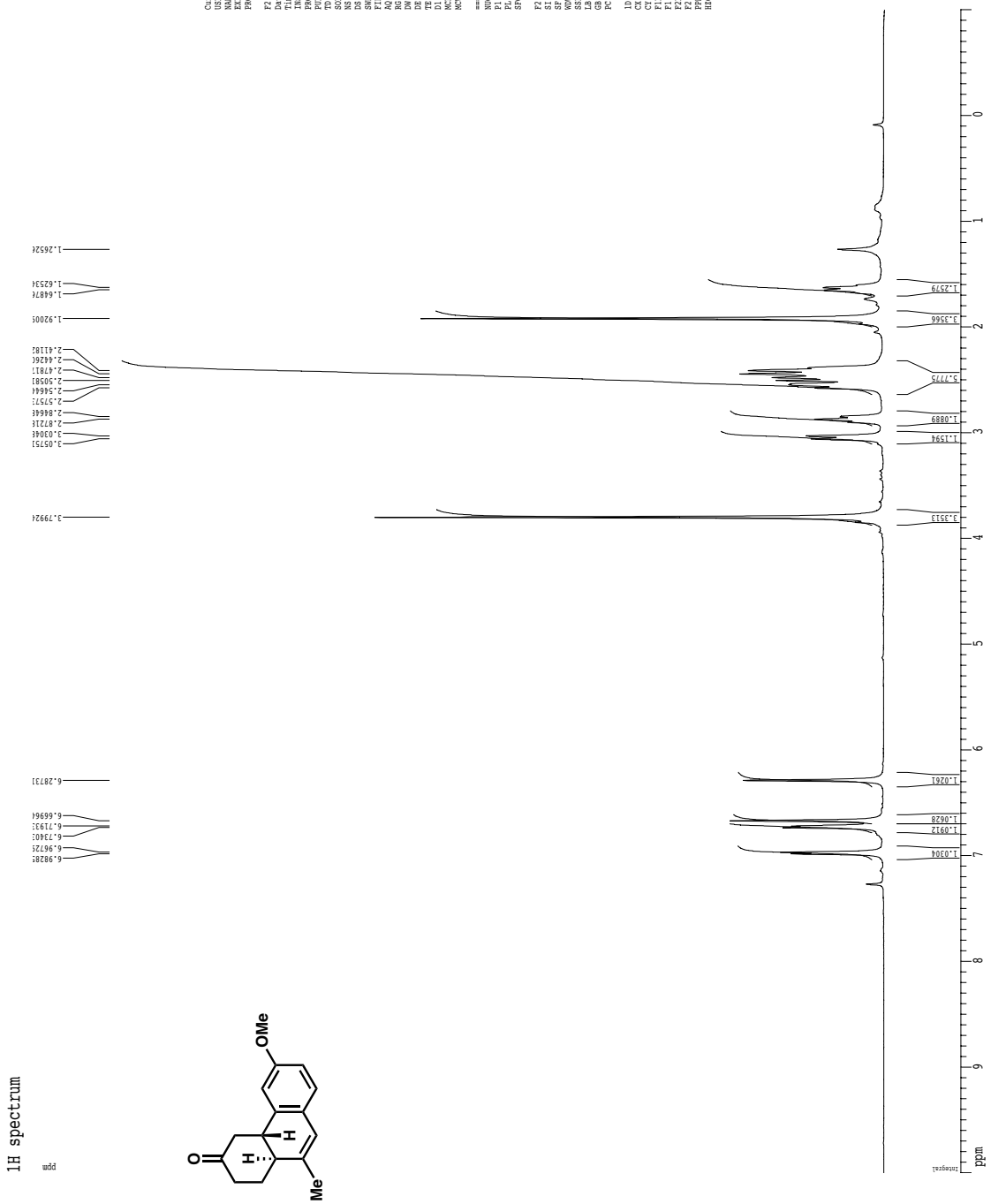
======= CHANNEL f1 =======
NUC1 13C
P1 16.55 usec
P11 500.00 usec
P12 2000.00 usec
PL0 120.00 dB
PL1 -1.00 dB
SFO1 125.7942548 MHz
SP1 2.70 dB
SP2 2.70 dB
SPNAM1 Crp60,0.5,20.1
SPNAM2 Crp60comp.4
SPOFF1 0.00 Hz
SPOFF2 0.00 Hz

======= CHANNEL f2 =======
CPDPRG2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 1.60 dB
PL12 24.50 dB
SFO2 500.2225011 MHz

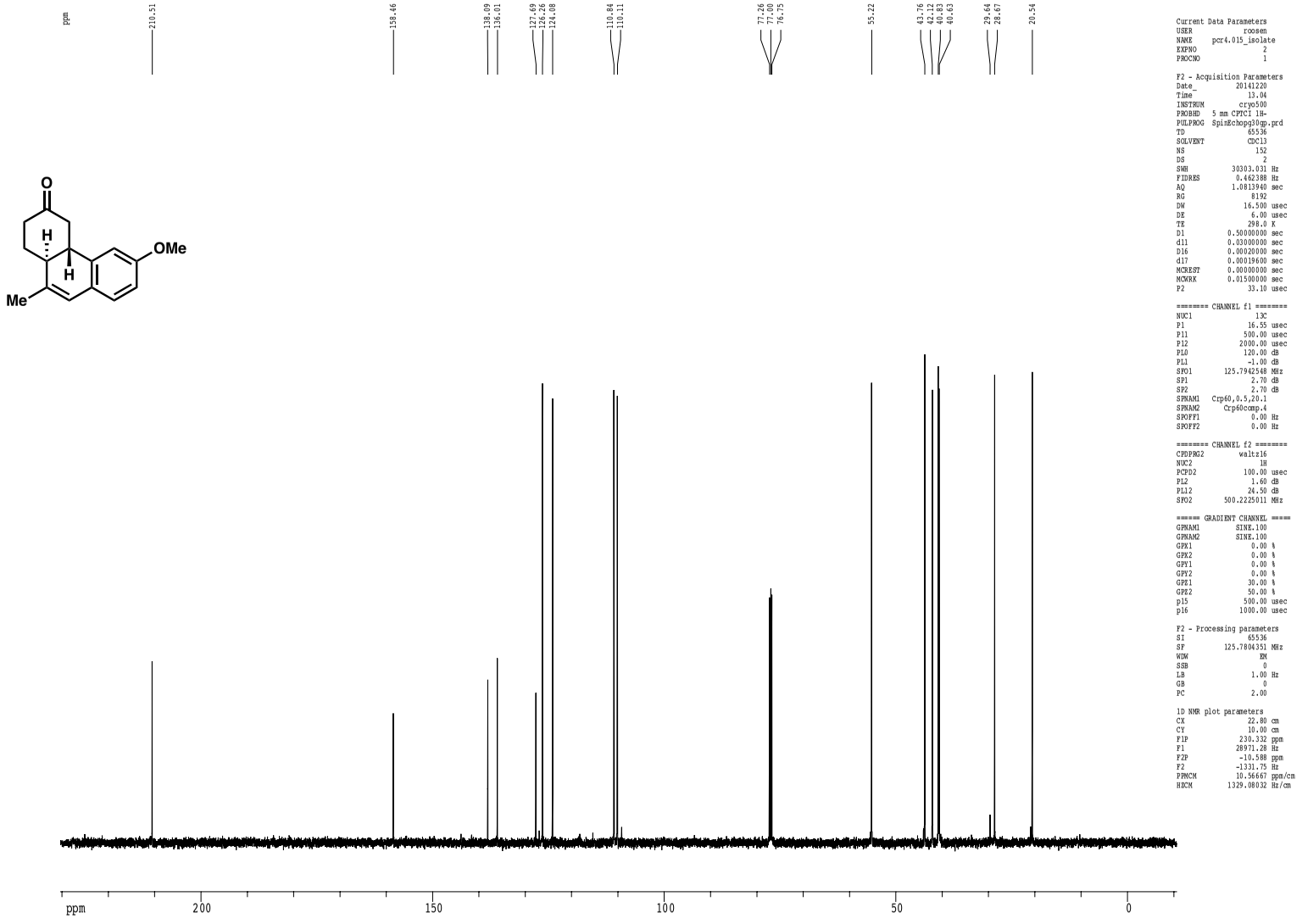
===== GRADIENT CHANNEL ====
GPNAM1 SINE.100
GPNAM2 SINE.100
GPX1 0.00 %
GPX2 0.00 %
GPY1 0.00 %
GPY2 0.00 %
GPZ1 30.00 %
GPZ2 50.00 %
p15 500.00 usec
p16 1000.00 usec

F2 - Processing parameters
SI 65536
SF 125.7804286 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00

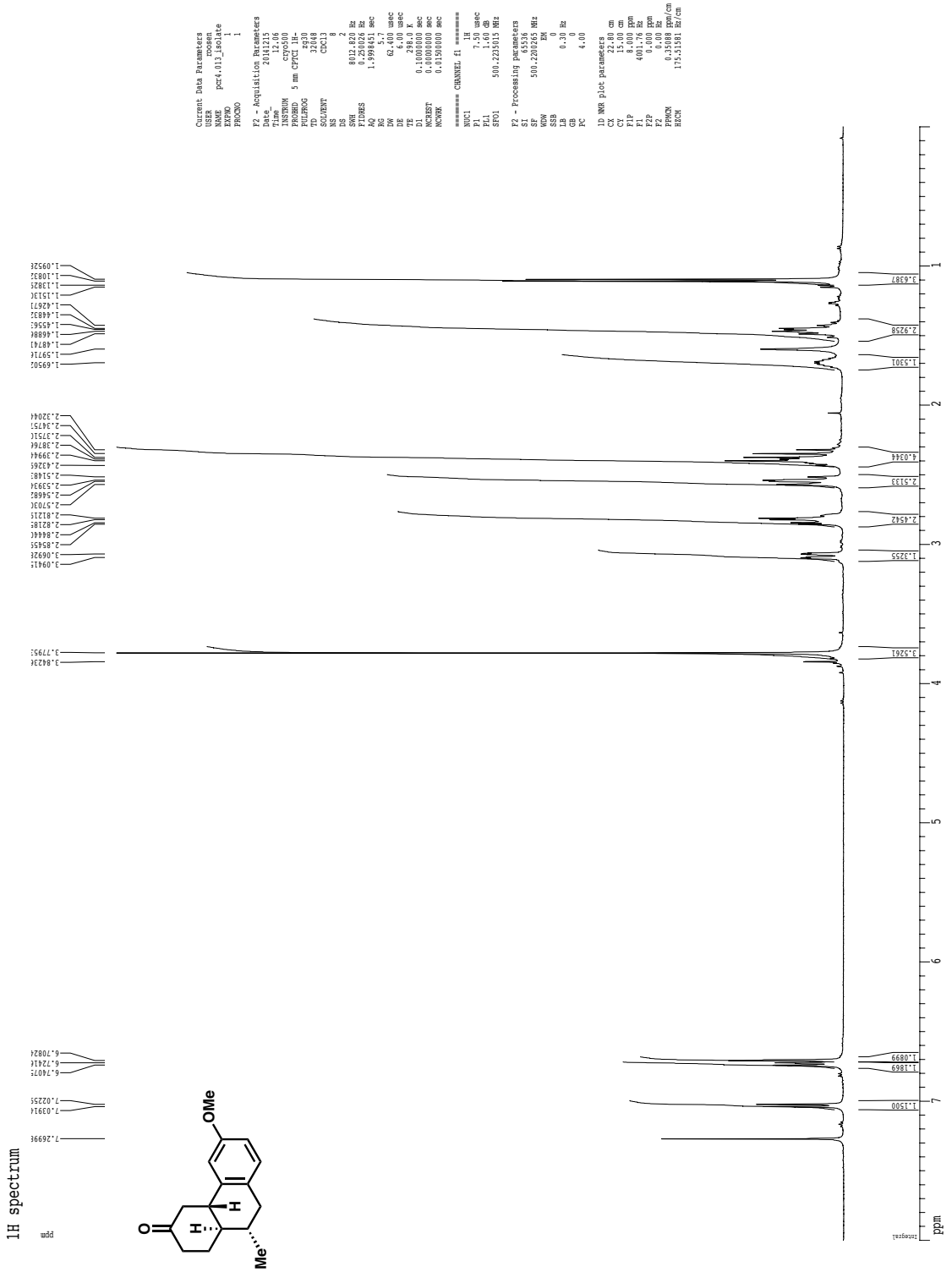
1D NMR plot parameters
CX 22.80 cm
CY 15.65 cm
F1P 230.384 ppm
F1 28977.75 Hz
F2P -10.536 ppm
F2 -1325.28 Hz
PPMCM 10.56667 ppm/cm
HZCM 1329.08032 Hz/cm


1H spectrum
ppm
OMe
H
H
O
Me
Current Data Parameters
NAME pcr4.015_isolate
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20141220
Time 13.02
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 8
DS 0
SWH 8012.820 Hz
FIDRES 0.244592 Hz
AQ 1.9998451 sec
RG 4.5
DW 62.400 usec
DE 6.00 usec
TE 298.1 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 7.50 usec
PL1 1.60 dB
SFO1 500.2235015 MHz
F2 - Processing parameters
SI 65536
SF 500.2200266 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00
1D NMR plot parameters
CX 27.80 cm
CY 10.00 cm
F1P 10.000 ppm
F1 5002.20 Hz
F2P -1.000 ppm
F2 -500.22 Hz
PPMCM 0.48246 ppm/cm
HZCM 241.33423 Hz/cm
1.2579
3.3566
5.7775
1.0889
1.1594
3.3513
1.0261
1.0628
1.0912
1.0304
3.7992
3.0751
3.0704
2.8721
2.8664
2.5571
2.5464
2.5058
2.4781
2.4626
2.4118
1.9200
1.6534
1.6487
1.2652
Integral
ppm

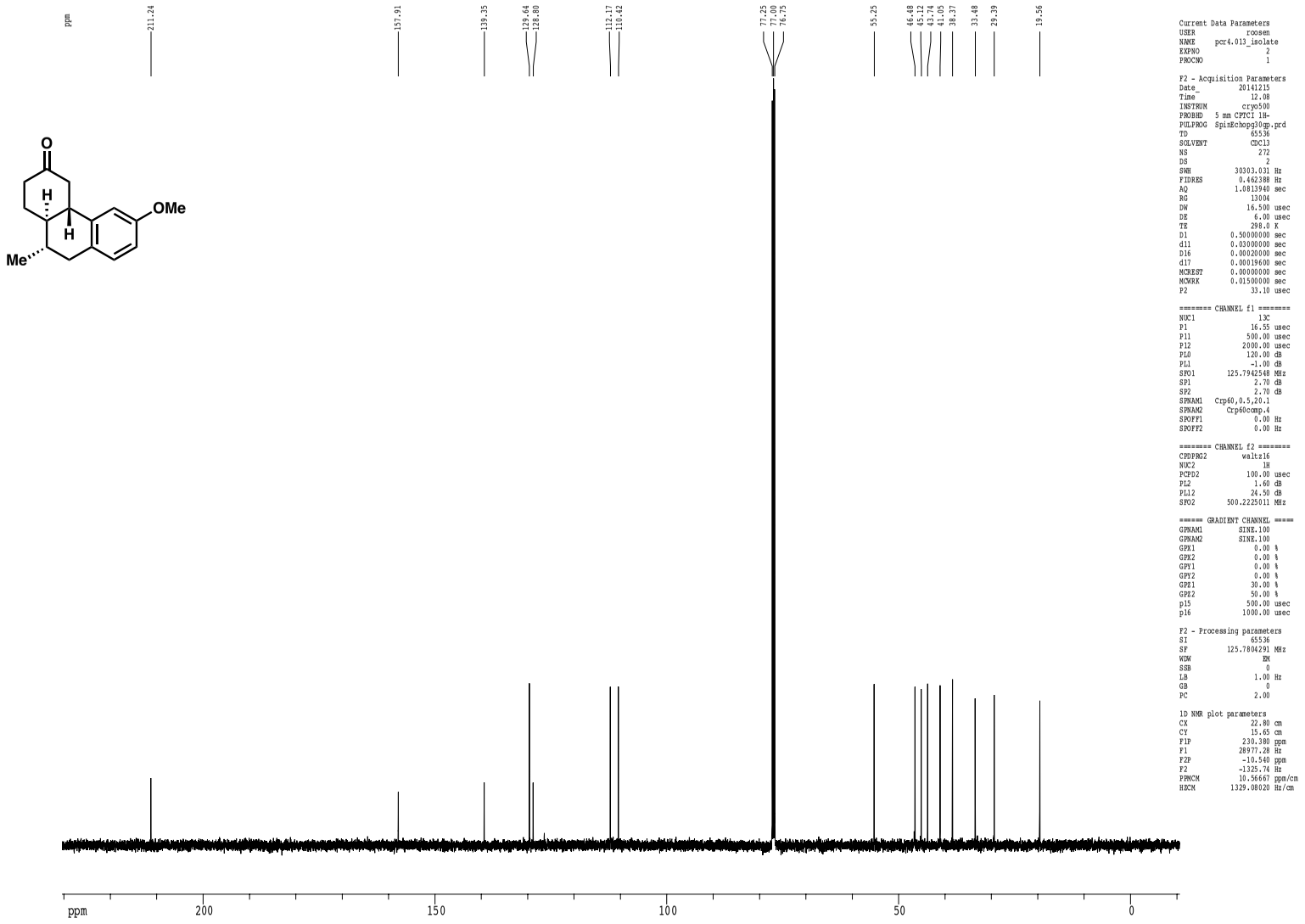
Z-restored spin-echo 13C spectrum with 1H decoupling




```
Current Data Parameters
USER              roosen
NAME      pcr4.015_isolate
EXPNO                    2
PROCNO                   1

F2 - Acquisition Parameters
Date_           20141220
Time              13.04
INSTRUM         cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD                65536
SOLVENT           CDCl3
NS                  152
DS                    2
SWH           30303.031 Hz
FIDRES        0.462388 Hz
AQ            1.0813940 sec
RG                 8192
DW               16.500 usec
DE                6.00 usec
TE               298.0 K
D1           0.50000000 sec
d11          0.03000000 sec
D16          0.00020000 sec
d17          0.00019600 sec
MCREST       0.00000000 sec
MCWRK        0.01500000 sec
P2               33.10 usec

======= CHANNEL f1 =======
NUC1                13C
P1                16.55 usec
P11              500.00 usec
P12             2000.00 usec
PL0              120.00 dB
PL1               -1.00 dB
SFO1        125.7942548 MHz
SP1               2.70 dB
SP2               2.70 dB
SPNAM1   Crp60,0.5,20.1
SPNAM2      Crp60comp.4
SPOFF1               0.00 Hz
SPOFF2               0.00 Hz

======= CHANNEL f2 =======
CPDPRG2          waltz16
NUC2                1H
PCPD2            100.00 usec
PL2               1.60 dB
PL12             24.50 dB
SFO2        500.2225011 MHz

===== GRADIENT CHANNEL ====
GPNAM1          SINE.100
GPNAM2          SINE.100
GPX1              0.00 %
GPX2              0.00 %
GPY1              0.00 %
GPY2              0.00 %
GPZ1             30.00 %
GPZ2             50.00 %
p15             500.00 usec
p16            1000.00 usec

F2 - Processing parameters
SI                65536
SF          125.7804351 MHz
WDW                  EM
SSB                   0
LB                1.00 Hz
GB                    0
PC                2.00

1D NMR plot parameters
CX               22.80 cm
CY               10.00 cm
F1P             230.332 ppm
F1             28971.28 Hz
F2P             -10.588 ppm
F2             -1331.75 Hz
PPMCM          10.56667 ppm/cm
HZCM         1329.08032 Hz/cm
```

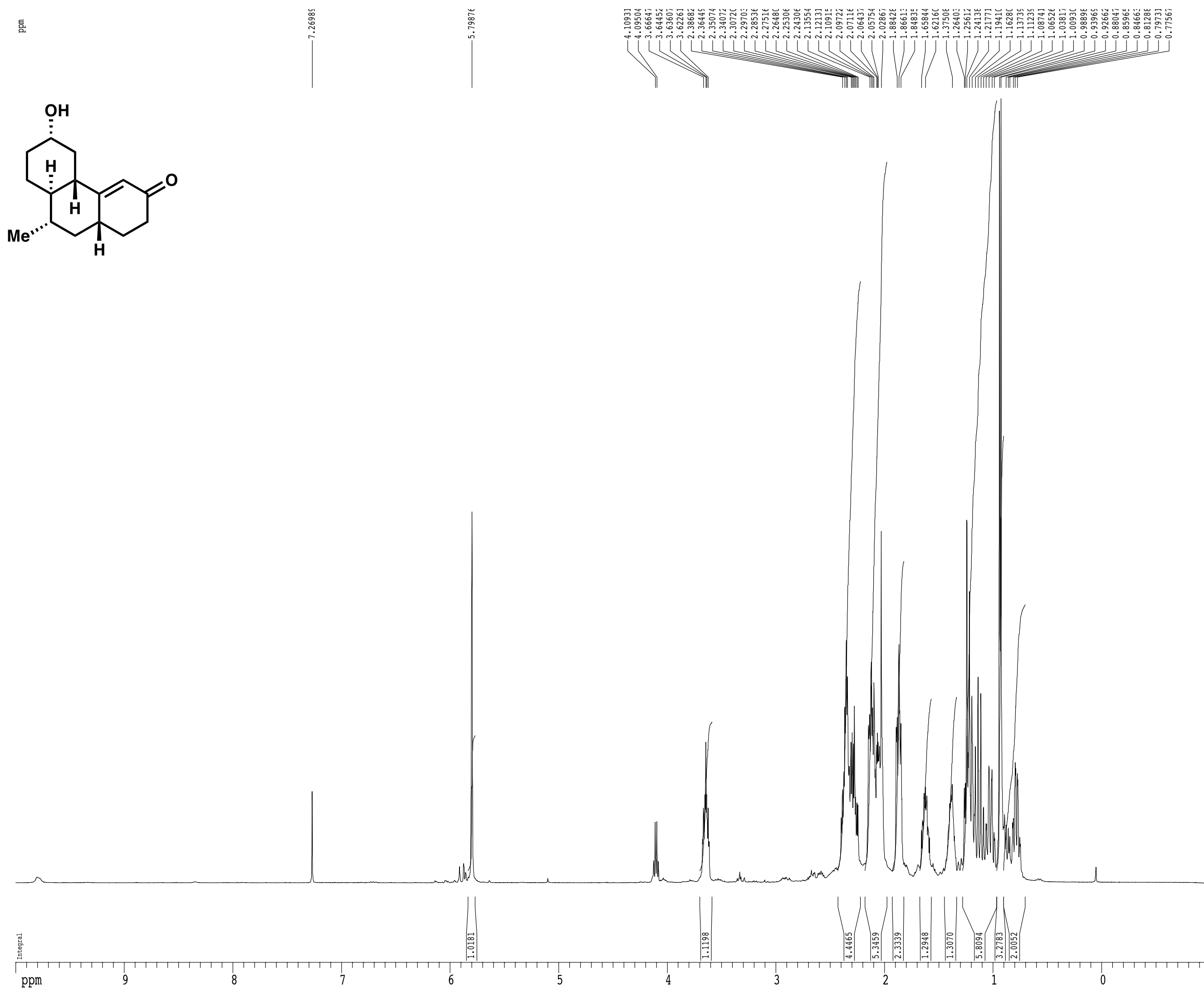

1H spectrum
ppm
OMe
H
H
O
Me
Integral
ppm

Z-restored spin-echo 13C spectrum with 1H decoupling



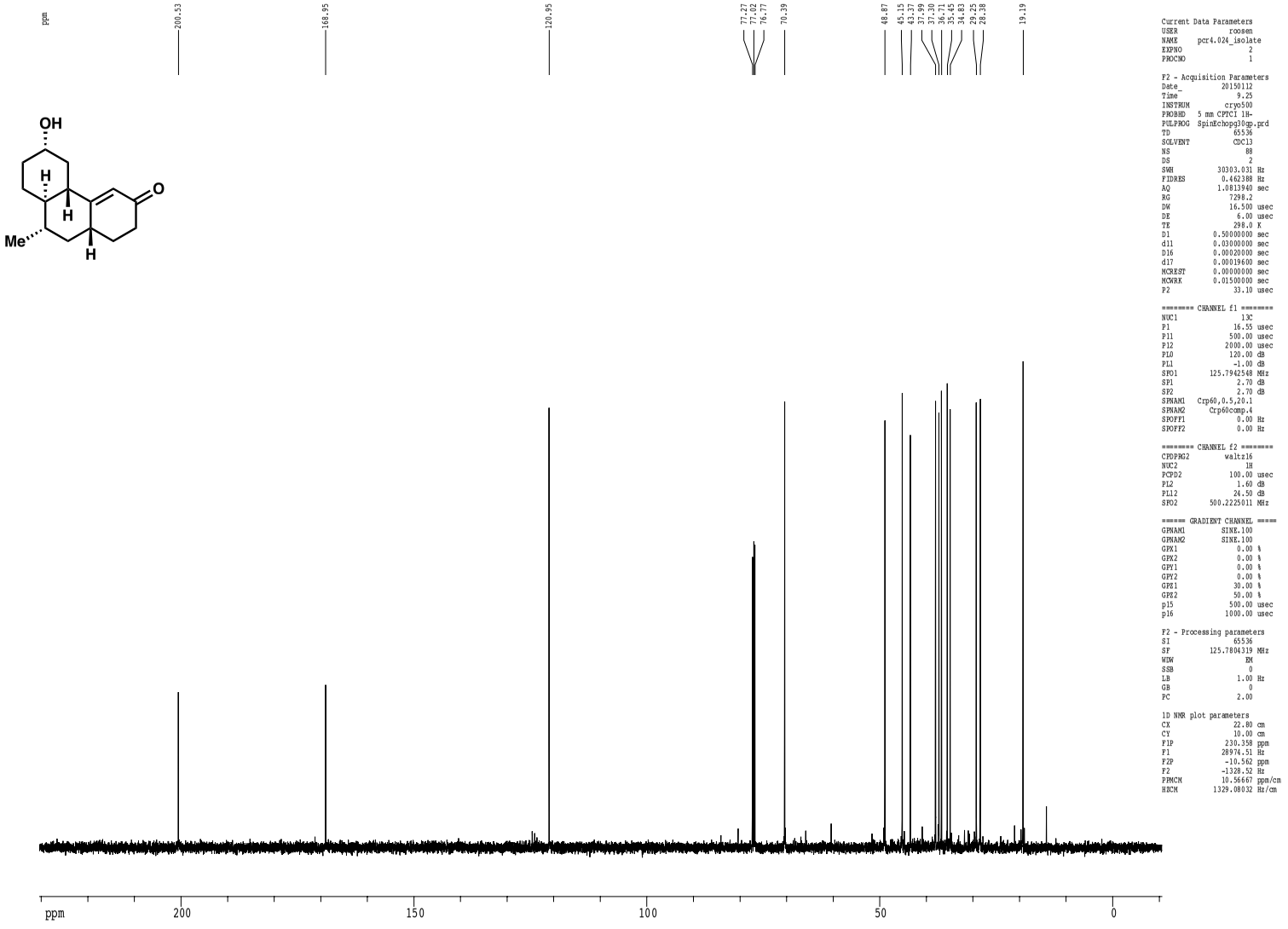

```
Current Data Parameters
USER              roosen
NAME      pcr4.013_isolate
EXPNO                    2
PROCNO                   1

F2 - Acquisition Parameters
Date_          20141215
Time              12.08
INSTRUM          cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD                 65536
SOLVENT             CDCl3
NS                    272
DS                      2
SWH           30303.031 Hz
FIDRES         0.462388 Hz
AQ           1.0813940 sec
RG                 13004
DW              16.500 usec
DE               6.00 usec
TE              298.0 K
D1          0.50000000 sec
d11         0.03000000 sec
D16         0.00020000 sec
d17         0.00019600 sec
MCREST      0.00000000 sec
MCWRK       0.01500000 sec
P2             33.10 usec

======= CHANNEL f1 =======
NUC1                13C
P1               16.55 usec
P11             500.00 usec
P12            2000.00 usec
PL0             120.00 dB
PL1              -1.00 dB
SFO1       125.7942548 MHz
SP1              2.70 dB
SP2              2.70 dB
SPNAM1   Crp60,0.5,20.1
SPNAM2     Crp60comp.4
SPOFF1              0.00 Hz
SPOFF2              0.00 Hz

======= CHANNEL f2 =======
CPDPRG2          waltz16
NUC2                1H
PCPD2           100.00 usec
PL2               1.60 dB
PL12             24.50 dB
SFO2       500.2225011 MHz

===== GRADIENT CHANNEL ====
GPNAM1          SINE.100
GPNAM2          SINE.100
GPX1                0.00 %
GPX2                0.00 %
GPY1                0.00 %
GPY2                0.00 %
GPZ1               30.00 %
GPZ2               50.00 %
p15              500.00 usec
p16             1000.00 usec

F2 - Processing parameters
SI                 65536
SF         125.7804291 MHz
WDW                   EM
SSB                    0
LB                  1.00 Hz
GB                     0
PC                  2.00

1D NMR plot parameters
CX                 22.80 cm
CY                 15.65 cm
F1P              230.380 ppm
F1              28977.28 Hz
F2P              -10.540 ppm
F2              -1325.74 Hz
PPMCM           10.56667 ppm/cm
HZCM          1329.08020 Hz/cm
```

1H spectrum

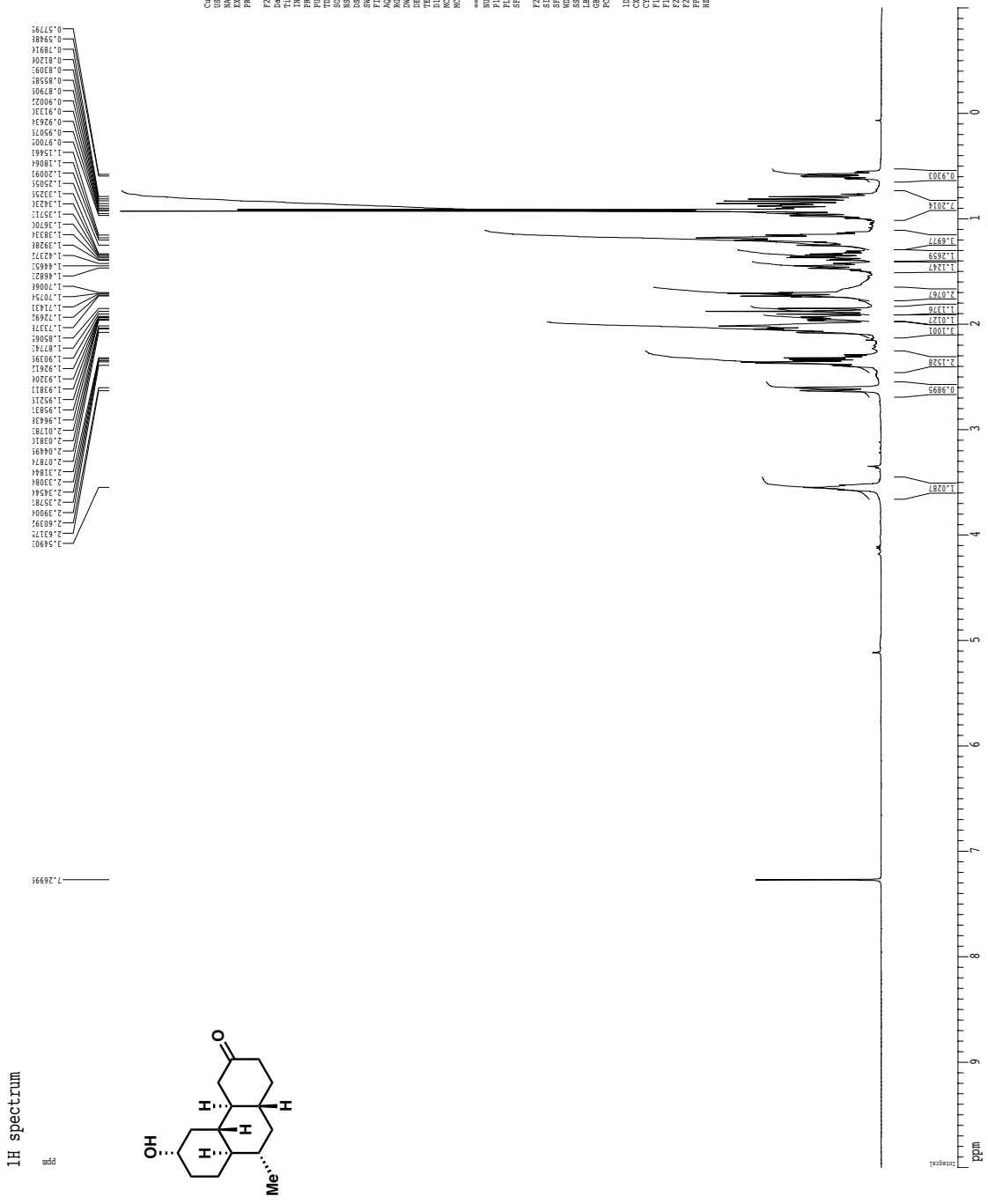



```
Current Data Parameters
USER            roosen
NAME     pcr4.024_isolate
EXPNO               1
PROCNO              1

F2 - Acquisition Parameters
Date_        20150112
Time             9.23
INSTRUM       cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG          zg30
TD              32048
SOLVENT         CDCl3
NS                  8
DS                  2
SWH          8012.820 Hz
FIDRES       0.250026 Hz
AQ          1.9998451 sec
RG                4.5
DW             62.400 usec
DE               6.00 usec
TE              298.0 K
D1         0.10000000 sec
MCREST     0.00000000 sec
MCWRK      0.01500000 sec

======== CHANNEL f1 ========
NUC1               1H
P1               7.50 usec
PL1              1.60 dB
SFO1      500.2235015 MHz

F2 - Processing parameters
SI              65536
SF        500.2200262 MHz
WDW                EM
SSB                 0
LB               0.30 Hz
GB                  0
PC               4.00

1D NMR plot parameters
CX              22.80 cm
CY              15.00 cm
F1P            10.000 ppm
F1            5002.20 Hz
F2P            -1.000 ppm
F2            -500.22 Hz
PPMCM         0.48246 ppm/cm
HZCM        241.33423 Hz/cm
```

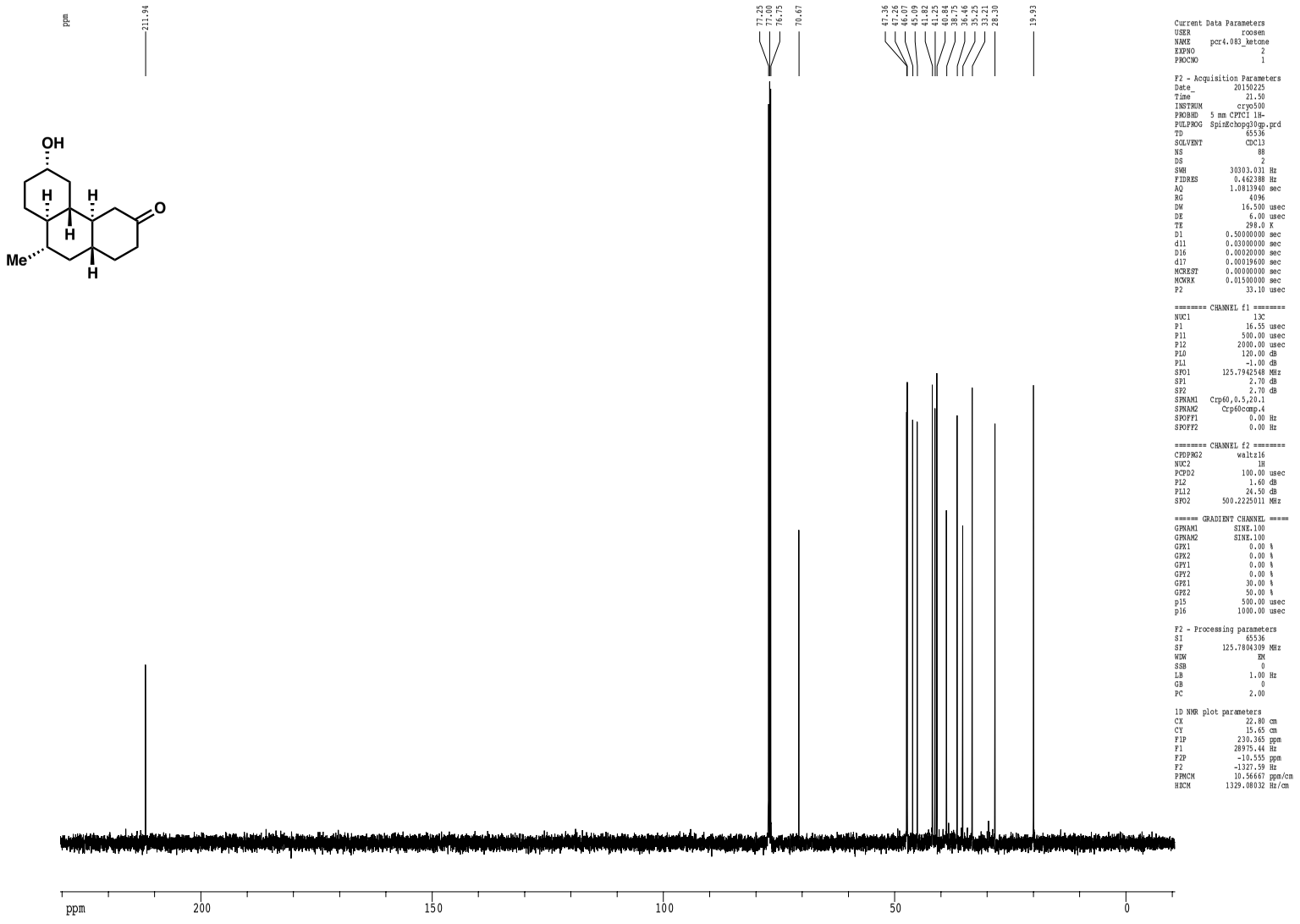
Z-restored spin-echo 13C spectrum with 1H decoupling



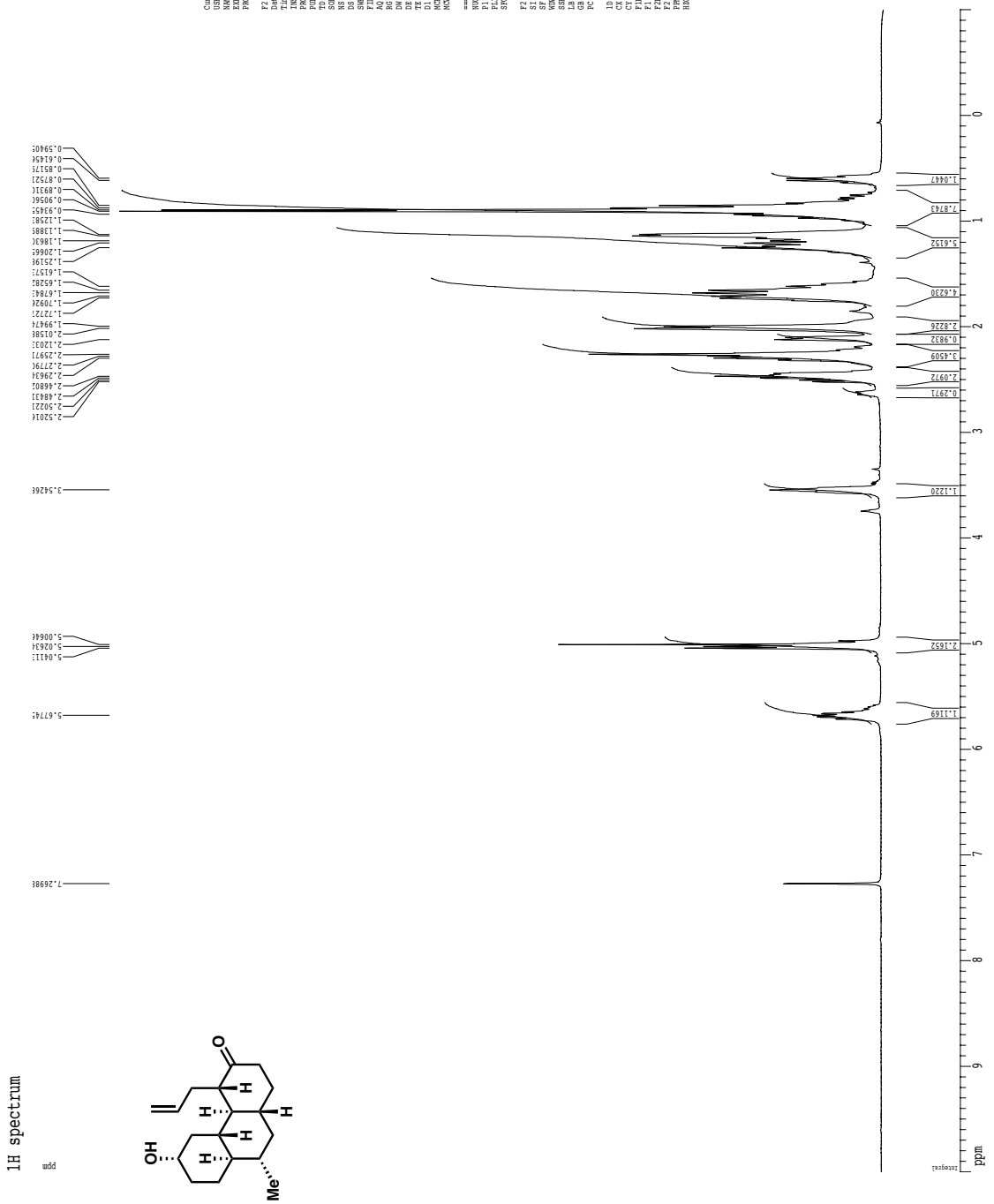

```
Current Data Parameters
USER              roosen
NAME      pcr4.024_isolate
EXPNO                   2
PROCNO                  1

F2 - Acquisition Parameters
Date_          20150112
Time              9.25
INSTRUM         cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD                65536
SOLVENT           CDCl3
NS                   88
DS                    2
SWH           30303.031 Hz
FIDRES        0.462388 Hz
AQ           1.0813940 sec
RG              7298.2
DW               16.500 usec
DE                6.00 usec
TE              298.0 K
D1          0.50000000 sec
d11         0.03000000 sec
D16         0.00020000 sec
d17         0.00019600 sec
MCREST      0.00000000 sec
MCWRK       0.01500000 sec
P2               33.10 usec

======= CHANNEL f1 =======
NUC1               13C
P1               16.55 usec
P11             500.00 usec
P12            2000.00 usec
PL0             120.00 dB
PL1              -1.00 dB
SFO1       125.7942548 MHz
SP1              2.70 dB
SP2              2.70 dB
SPNAM1   Crp60,0.5,20.1
SPNAM2     Crp60comp.4
SPOFF1              0.00 Hz
SPOFF2              0.00 Hz

======= CHANNEL f2 =======
CPDPRG2         waltz16
NUC2               1H
PCPD2           100.00 usec
PL2               1.60 dB
PL12             24.50 dB
SFO2       500.2225011 MHz

===== GRADIENT CHANNEL ====
GPNAM1         SINE.100
GPNAM2         SINE.100
GPX1              0.00 %
GPX2              0.00 %
GPY1              0.00 %
GPY2              0.00 %
GPZ1             30.00 %
GPZ2             50.00 %
p15             500.00 usec
p16            1000.00 usec

F2 - Processing parameters
SI                65536
SF         125.7804319 MHz
WDW                  EM
SSB                   0
LB                1.00 Hz
GB                    0
PC                2.00

1D NMR plot parameters
CX               22.80 cm
CY               10.00 cm
F1P            230.358 ppm
F1             28974.51 Hz
F2P            -10.562 ppm
F2             -1328.52 Hz
PPMCM          10.56667 ppm/cm
HZCM        1329.08032 Hz/cm
```


1H spectrum
ppm
integral
Current Data Parameters
NAME pcr4.083_ketone
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20151225
Time 21.53
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 8
DS 2
SWH 8012.820 Hz
FIDRES 0.244409 Hz
AQ 1.9998451 sec
RG 11.3
DW 62.400 usec
DE 6.00 usec
TE 298.1 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 7.50 usec
PL1 1.60 dB
SFO1 500.2235015 MHz
F2 - Processing parameters
SI 65536
SF 500.2200269 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00
1D NMR plot parameters
CX 22.00 cm
CY 15.00 cm
F1P 10.000 ppm
F1 5002.20 Hz
F2P -1.000 ppm
F2 -500.22 Hz
PPMCM 0.48246 ppm/cm
HZCM 241.33423 Hz/cm
0.9303
7.2014
3.6977
1.2659
1.1247
2.0767
1.1376
1.0127
3.1001
2.1528
0.9895
1.0287
7.26995
OH
H
H
H
H
Me
O

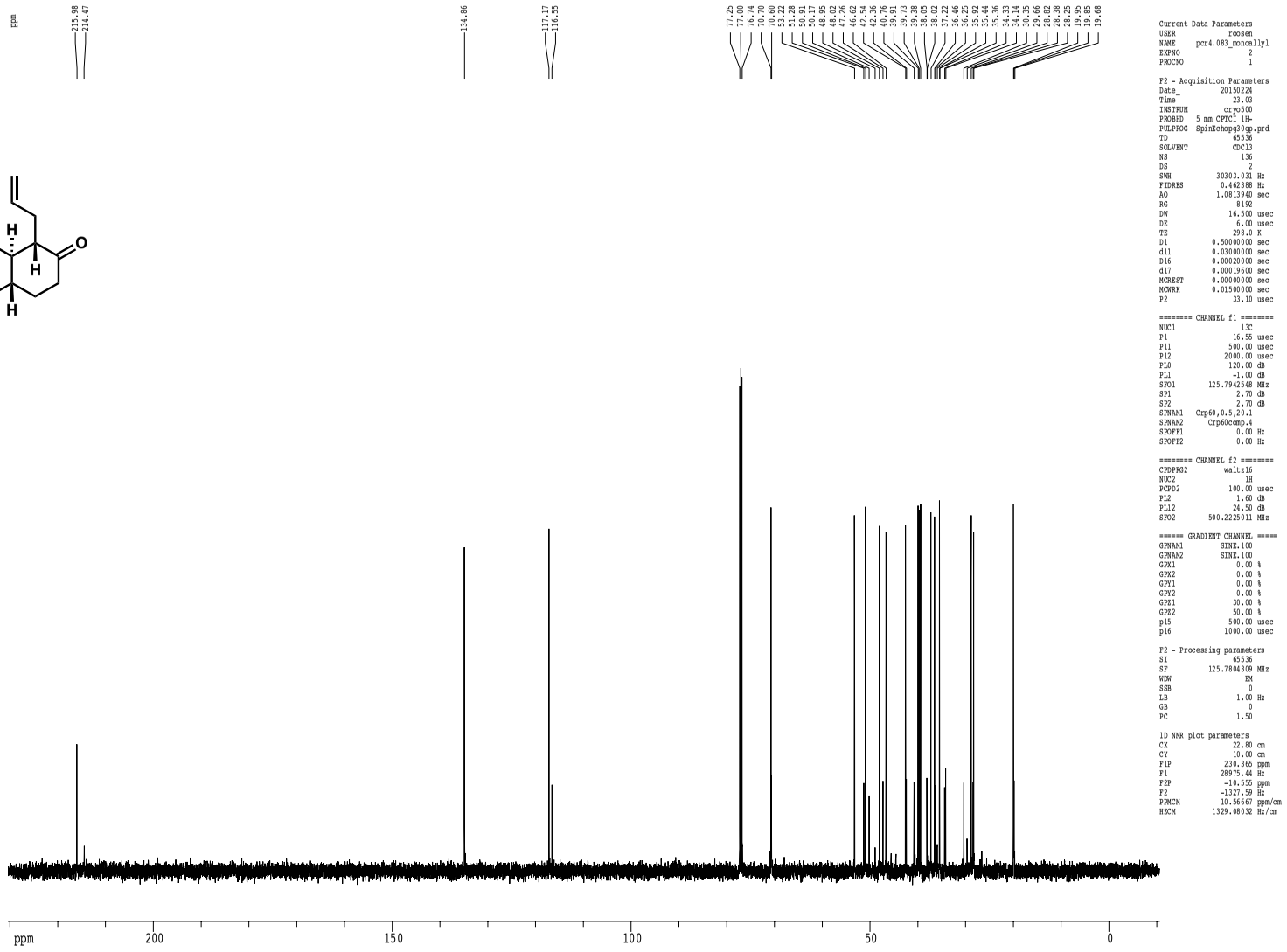
Z-restored spin-echo 13C spectrum with 1H decoupling

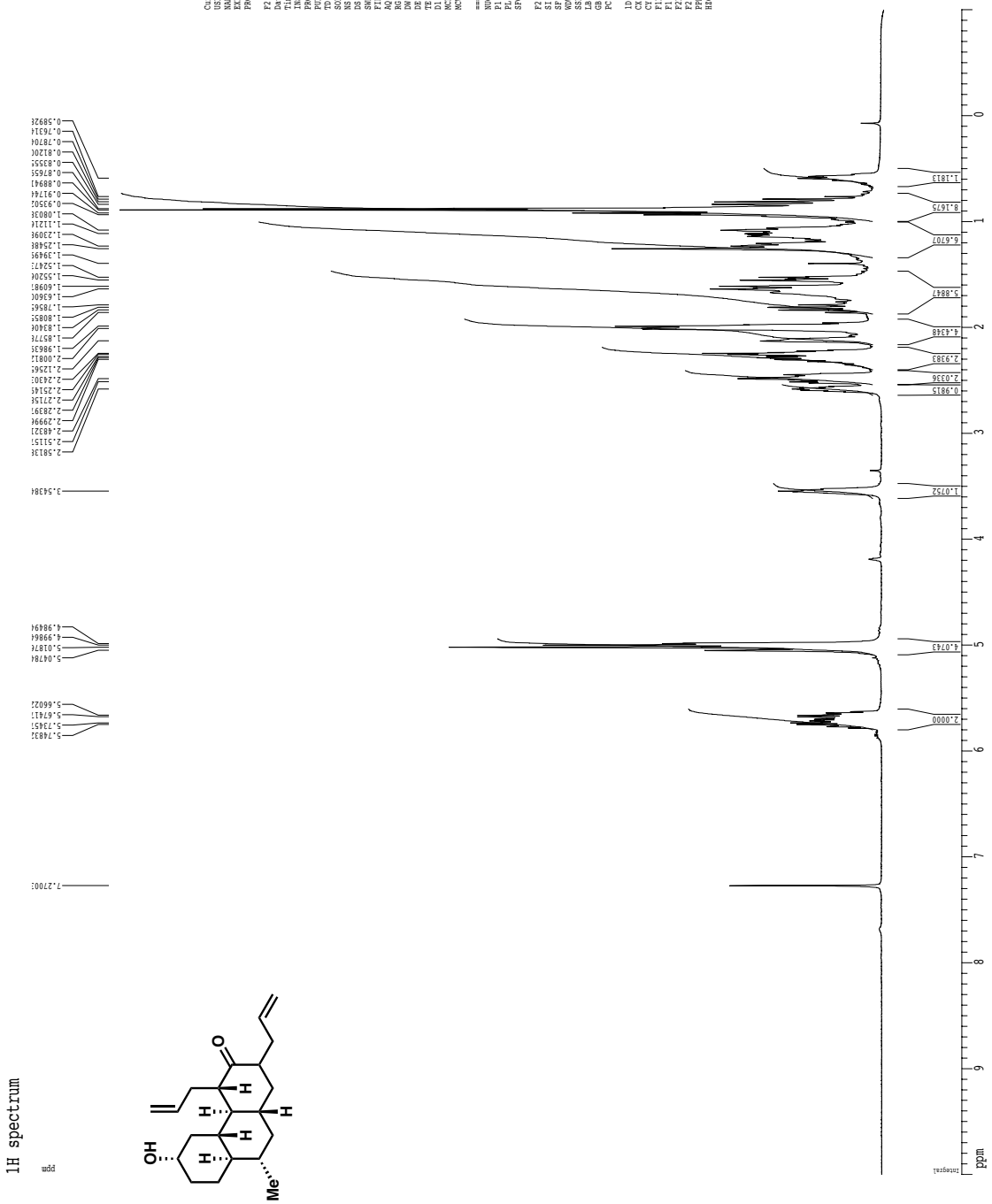



```
Current Data Parameters
USER              roosen
NAME      pcr4.083_ketone
EXPNO                   2
PROCNO                  1

F2 - Acquisition Parameters
Date_           20150225
Time              21.50
INSTRUM          cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD                65536
SOLVENT           CDCl3
NS                   88
DS                    2
SWH           30303.031 Hz
FIDRES        0.462388 Hz
AQ            1.0813940 sec
RG                 4096
DW               16.500 usec
DE                6.00 usec
TE               298.0 K
D1            0.50000000 sec
d11           0.03000000 sec
D16           0.00020000 sec
d17           0.00019600 sec
MCREST        0.00000000 sec
MCWRK         0.01500000 sec
P2               33.10 usec

======= CHANNEL f1 =======
NUC1                13C
P1                16.55 usec
P11              500.00 usec
P12             2000.00 usec
PL0              120.00 dB
PL1               -1.00 dB
SFO1        125.7942548 MHz
SP1               2.70 dB
SP2               2.70 dB
SPNAM1   Crp60,0.5,20.1
SPNAM2      Crp60comp.4
SPOFF1               0.00 Hz
SPOFF2               0.00 Hz

======= CHANNEL f2 =======
CPDPRG2          waltz16
NUC2                1H
PCPD2            100.00 usec
PL2                1.60 dB
PL12              24.50 dB
SFO2        500.2225011 MHz

===== GRADIENT CHANNEL ====
GPNAM1          SINE.100
GPNAM2          SINE.100
GPX1                0.00 %
GPX2                0.00 %
GPY1                0.00 %
GPY2                0.00 %
GPZ1               30.00 %
GPZ2               50.00 %
p15              500.00 usec
p16             1000.00 usec

F2 - Processing parameters
SI                  65536
SF          125.7804309 MHz
WDW                    EM
SSB                    0
LB                  1.00 Hz
GB                     0
PC                  2.00

1D NMR plot parameters
CX                 22.80 cm
CY                 15.65 cm
F1P              230.365 ppm
F1               28975.44 Hz
F2P              -10.555 ppm
F2               -1327.59 Hz
PPMCM            10.56667 ppm/cm
HZCM          1329.08032 Hz/cm
```

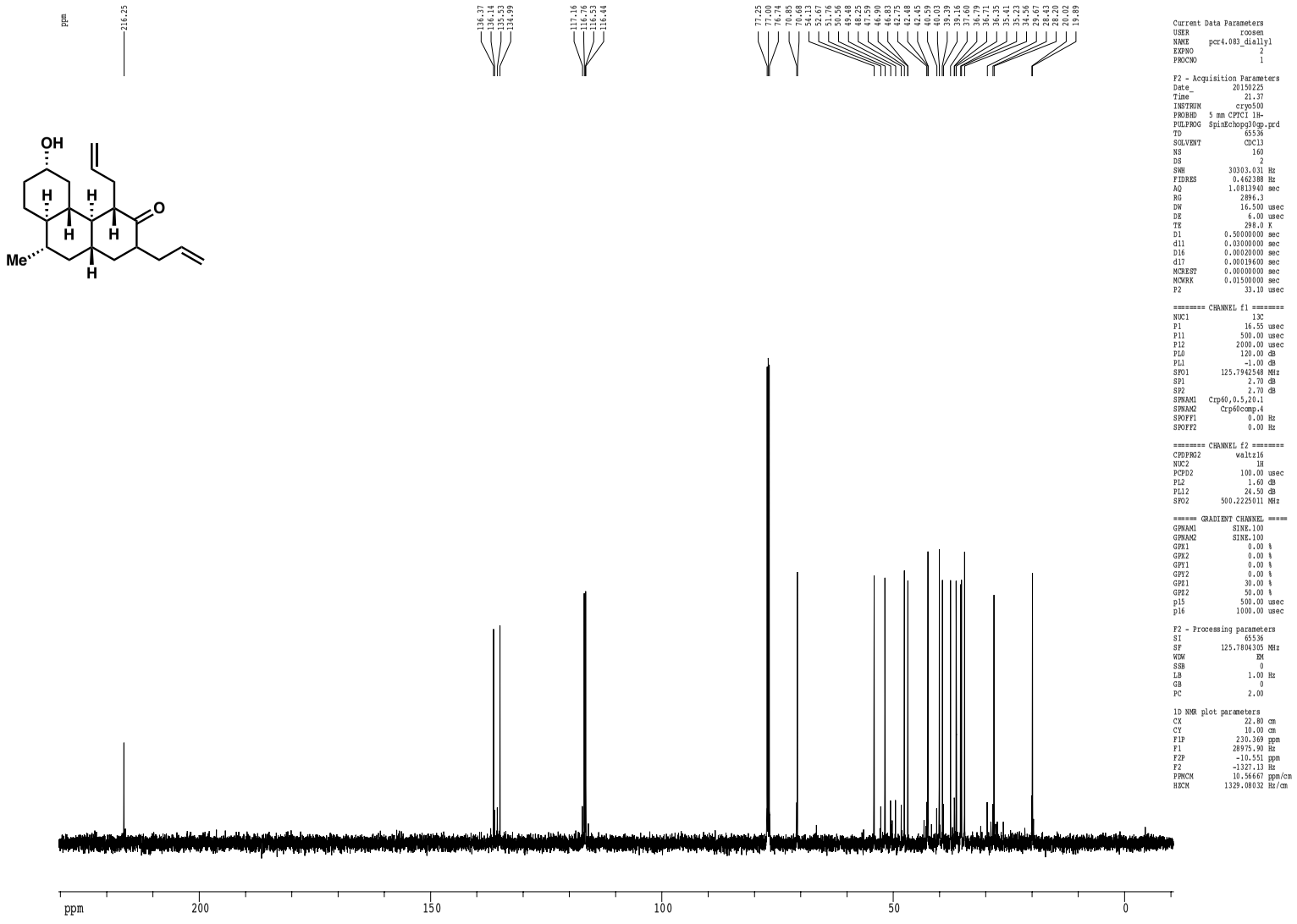

1H spectrum
ppm
Integral
OH
Me
H
O

Z-restored spin-echo 13C spectrum with 1H decoupling




1H spectrum
ppm
Integral
Current Data Parameters
NAME pcr4.083_diallyl
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20151225
Time 21.46
INSTRUM cryo500
PROBHD 5 mm CPPCI 1H-
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 8
DS 2
SWH 8012.820 Hz
FIDRES 0.244409 Hz
AQ 1.9998451 sec
RG 4.5
DW 62.400 usec
DE 6.00 usec
TE 298.1 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 7.50 usec
PL1 1.60 dB
SFO1 500.2235015 MHz
F2 - Processing parameters
SI 65536
SF 500.2200260 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00
1D NMR plot parameters
CX 27.00 cm
CY 15.00 cm
F1P 10.000 ppm
F1 5002.20 Hz
F2P -1.000 ppm
F2 -500.22 Hz
PPMCM 0.48246 ppm/cm
HZCM 241.33423 Hz/cm
7.27001
5.76832
5.74651
5.67417
5.66021
5.06784
5.01874
4.99864
4.98694
3.56384
2.58134
2.51157
2.48321
2.29990
2.28397
2.27154
2.25141
2.12565
2.02430
2.00812
1.98635
1.85774
1.83404
1.80855
1.78567
1.63601
1.60983
1.55204
1.52472
1.39491
1.25468
1.23094
1.11214
1.08038
0.93502
0.89941
0.87651
0.83555
0.81204
0.78704
0.76314
0.58924
1.1813
8.1675
6.6707
5.8847
4.4348
2.9383
2.0336
0.9815
1.0752
4.0743
2.0000
0
1
2
3
4
5
6
7
8
9
ppm
OH
Me
H
H
H
H
O

Z-restored spin-echo 13C spectrum with 1H decoupling



Current Data Parameters

USER	roosen
NAME	pcr4.083_diallyl
EXPNO	2
PROCNO	1

F2 - Acquisition Parameters

Date_	20150225
Time	21.37
INSTRUM	cryo500
PROBHD	5 mm CPTCI 1H-
PULPROG	SpinEchopg30gp.prd
TD	65536
SOLVENT	CDCl3
NS	160
DS	2
SWH	30303.031 Hz
FIDRES	0.462388 Hz
AQ	1.0813940 sec
RG	2896.3
DW	16.500 usec
DE	6.00 usec
TE	298.0 K
D1	0.50000000 sec
d11	0.03000000 sec
D16	0.00020000 sec
d17	0.00019600 sec
MCREST	0.00000000 sec
MCWRK	0.01500000 sec
P2	33.10 usec

======= CHANNEL f1 =======

NUC1	13C
P1	16.55 usec
P11	500.00 usec
P12	2000.00 usec
PL0	120.00 dB
PL1	-1.00 dB
SFO1	125.7942548 MHz
SP1	2.70 dB
SP2	2.70 dB
SPNAM1	Crp60,0.5,20.1
SPNAM2	Crp60comp.4
SPOFF1	0.00 Hz
SPOFF2	0.00 Hz

======= CHANNEL f2 =======

CPDPRG2	waltz16
NUC2	1H
PCPD2	100.00 usec
PL2	1.60 dB
PL12	24.50 dB
SFO2	500.2225011 MHz

===== GRADIENT CHANNEL ====

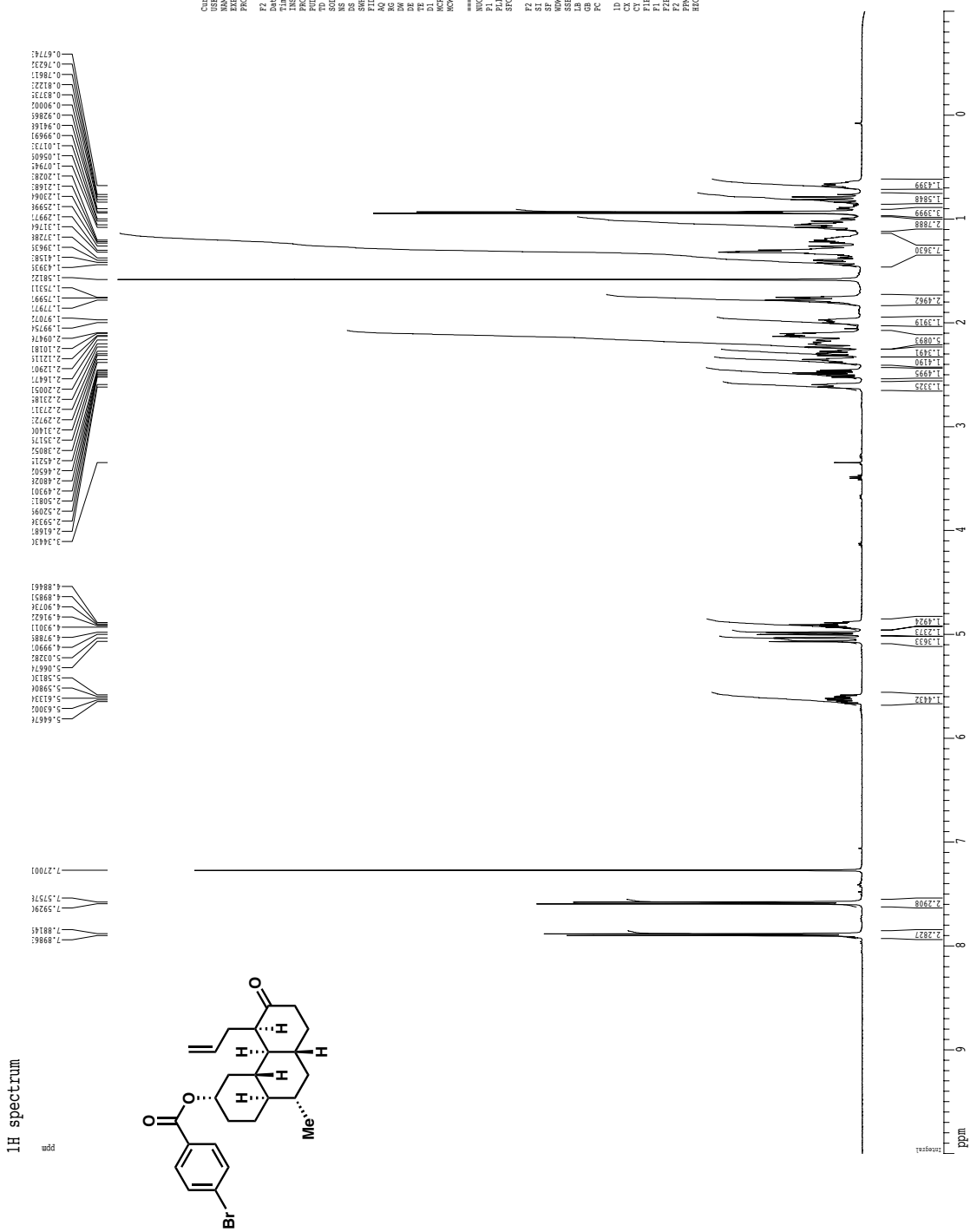
GPNAM1	SINE.100
GPNAM2	SINE.100
GPX1	0.00 %
GPX2	0.00 %
GPY1	0.00 %
GPY2	0.00 %
GPZ1	30.00 %
GPZ2	50.00 %
p15	500.00 usec
p16	1000.00 usec

F2 - Processing parameters

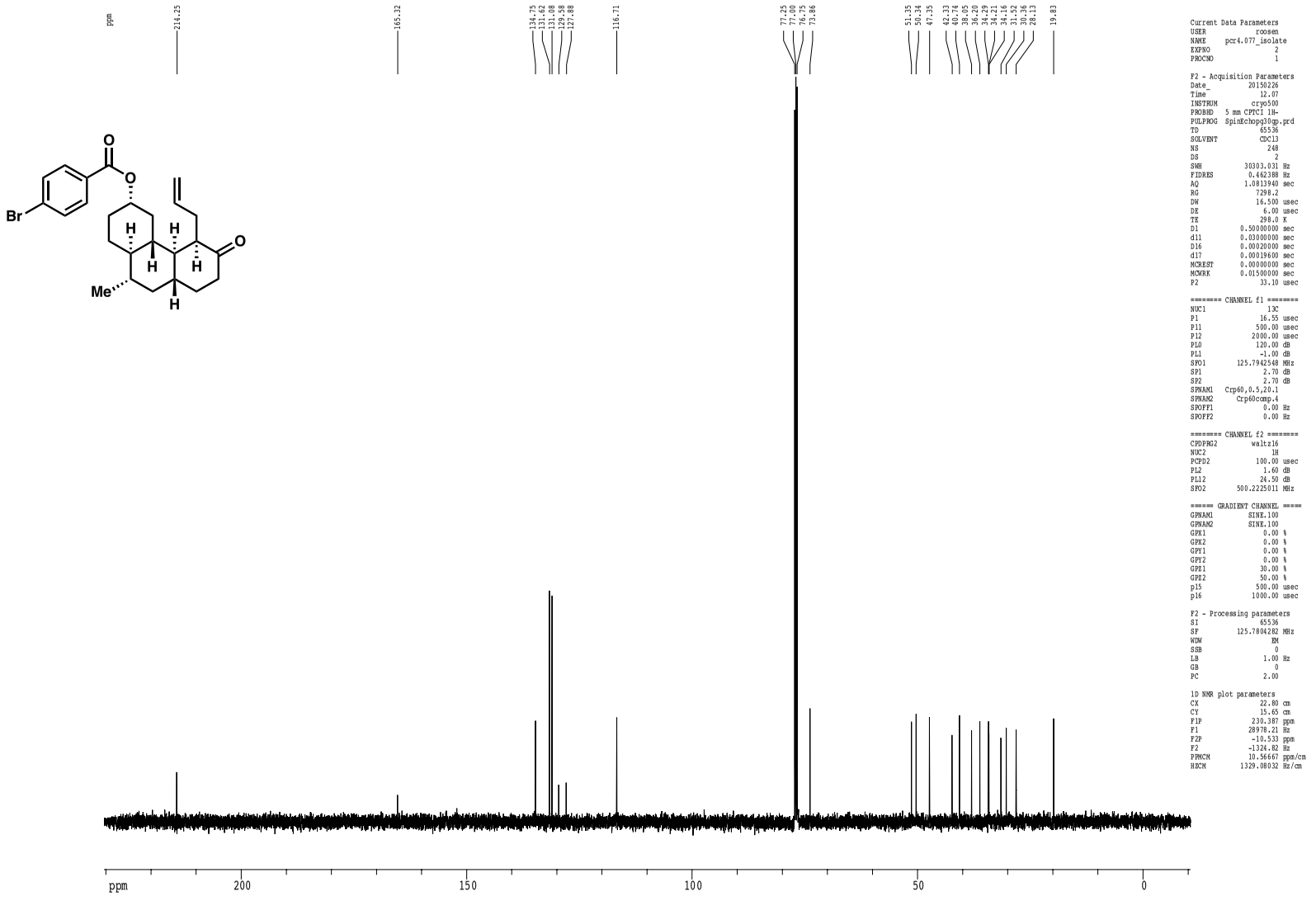
SI	65536
SF	125.7804305 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	2.00

1D NMR plot parameters

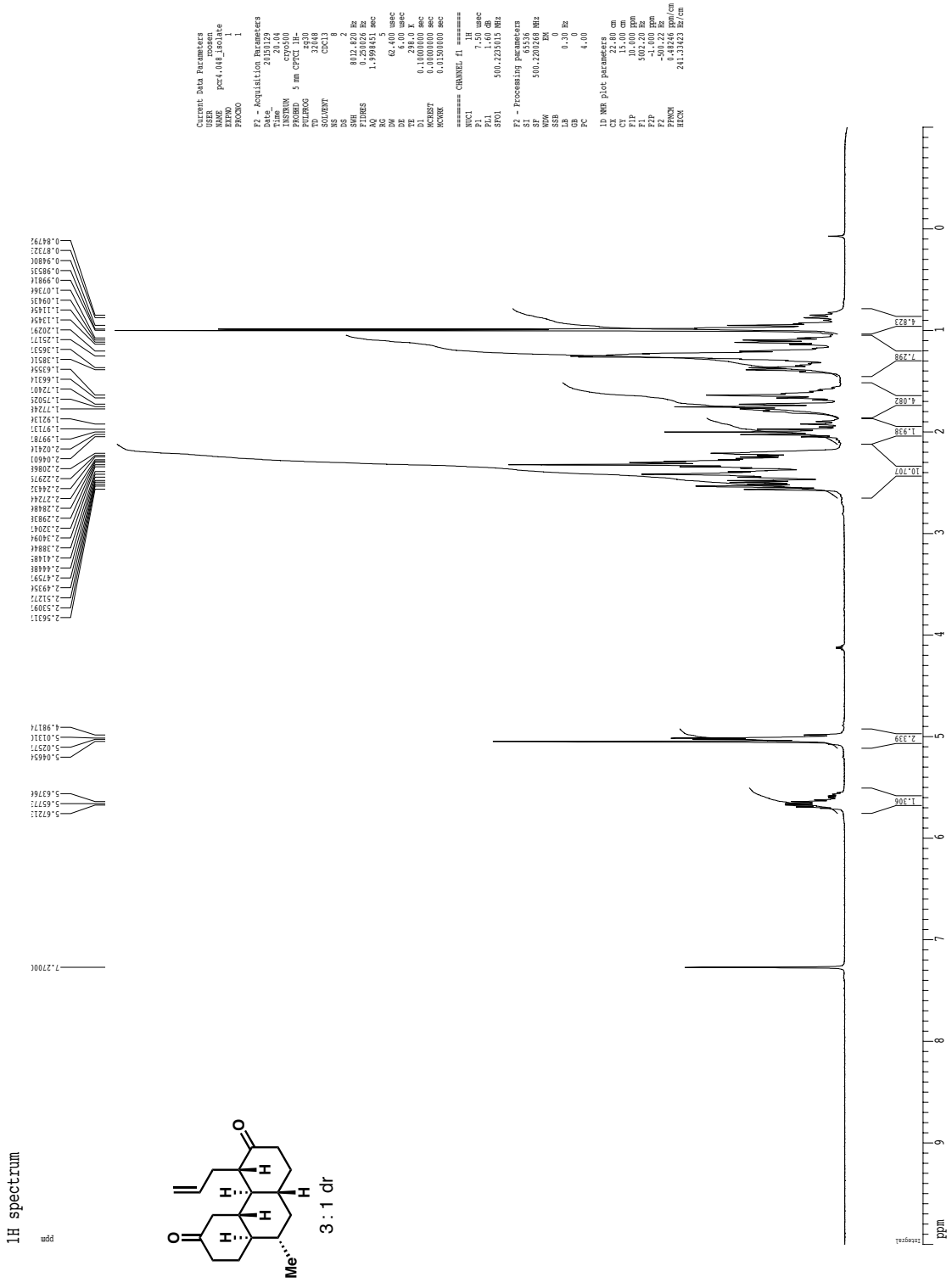
CX	22.80 cm
CY	10.00 cm
F1P	230.369 ppm
F1	28975.90 Hz
F2P	-10.551 ppm
F2	-1327.13 Hz
PPMCM	10.56667 ppm/cm
HZCM	1329.08032 Hz/cm


1H spectrum
ppm
Integral
Current Data Parameters
NAME pcr4.077_isolate
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20151226
Time 12.05
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 8
DS 2
SWH 8012.820 Hz
FIDRES 0.244409 Hz
AQ 1.9998451 sec
RG 8
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 7.50 usec
PL1 1.60 dB
SFO1 500.2235015 MHz
F2 - Processing parameters
SI 65536
SF 500.2200268 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00
1D NMR plot parameters
CX 27.00 cm
CY 15.00 cm
F1P 10.000 ppm
F1 5002.20 Hz
F2P -1.000 ppm
F2 -500.02 Hz
PPMCM 0.48246 ppm/cm
HZCM 241.33423 Hz/cm
Me
Br

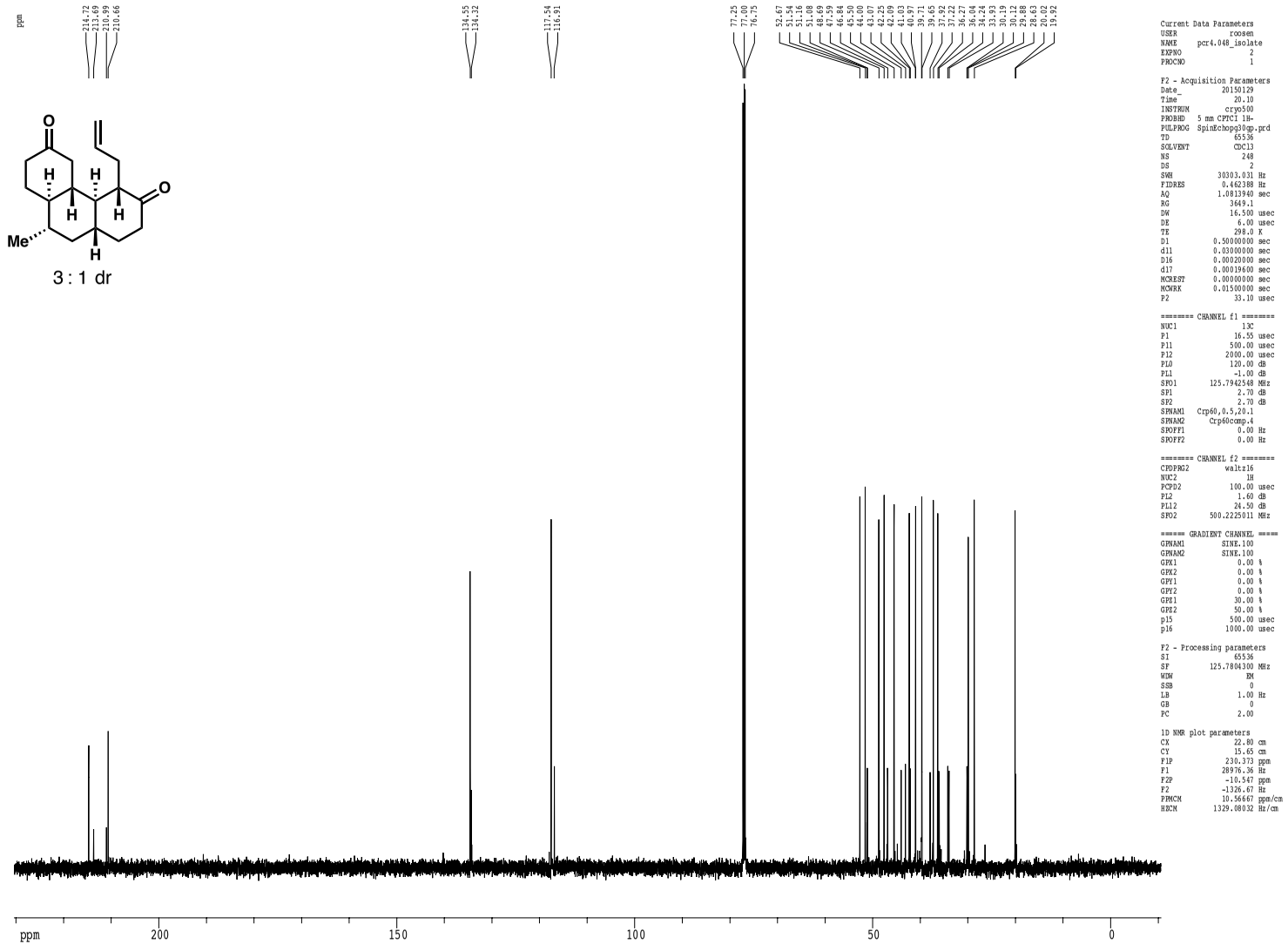
Z-restored spin-echo 13C spectrum with 1H decoupling




```
Current Data Parameters
USER              roosen
NAME      pcr4.077_isolate
EXPNO                    2
PROCNO                   1

F2 - Acquisition Parameters
Date_           20150226
Time              12.07
INSTRUM          cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD                 65536
SOLVENT             CDCl3
NS                    248
DS                      2
SWH           30303.031 Hz
FIDRES        0.462388 Hz
AQ            1.0813940 sec
RG               7298.2
DW               16.500 usec
DE                6.00 usec
TE               298.0 K
D1          0.50000000 sec
d11         0.03000000 sec
D16         0.00020000 sec
d17         0.00019600 sec
MCREST      0.00000000 sec
MCWRK       0.01500000 sec
P2               33.10 usec

======= CHANNEL f1 =======
NUC1                13C
P1                16.55 usec
P11              500.00 usec
P12             2000.00 usec
PL0              120.00 dB
PL1               -1.00 dB
SFO1        125.7942548 MHz
SP1               2.70 dB
SP2               2.70 dB
SPNAM1   Crp60,0.5,20.1
SPNAM2     Crp60comp.4
SPOFF1               0.00 Hz
SPOFF2               0.00 Hz

======= CHANNEL f2 =======
CPDPRG2          waltz16
NUC2                1H
PCPD2            100.00 usec
PL2               1.60 dB
PL12             24.50 dB
SFO2        500.2225011 MHz

===== GRADIENT CHANNEL ====
GPNAM1          SINE.100
GPNAM2          SINE.100
GPX1                0.00 %
GPX2                0.00 %
GPY1                0.00 %
GPY2                0.00 %
GPZ1               30.00 %
GPZ2               50.00 %
p15              500.00 usec
p16             1000.00 usec

F2 - Processing parameters
SI                 65536
SF          125.7804282 MHz
WDW                   EM
SSB                    0
LB                  1.00 Hz
GB                     0
PC                  2.00

1D NMR plot parameters
CX                 22.80 cm
CY                 15.65 cm
F1P              230.387 ppm
F1              28978.21 Hz
F2P              -10.533 ppm
F2              -1324.82 Hz
PPMCM           10.56667 ppm/cm
HZCM          1329.08032 Hz/cm
```


1H spectrum
ppm
Integral
Me
3 : 1 dr

Z-restored spin-echo 13C spectrum with 1H decoupling



Current Data Parameters
USER roosen
NAME pcr4.048_isolate
EXPNO 2
PROCNO 1

F2 - Acquisition Parameters
Date_ 20150129
Time 20.10
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG SpinEchopg30gp.prd
TD 65536
SOLVENT CDCl3
NS 248
DS 2
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0813940 sec
RG 3649.1
DW 16.500 usec
DE 6.00 usec
TE 298.0 K
D1 0.50000000 sec
d11 0.03000000 sec
D16 0.00020000 sec
d17 0.00019600 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
P2 33.10 usec

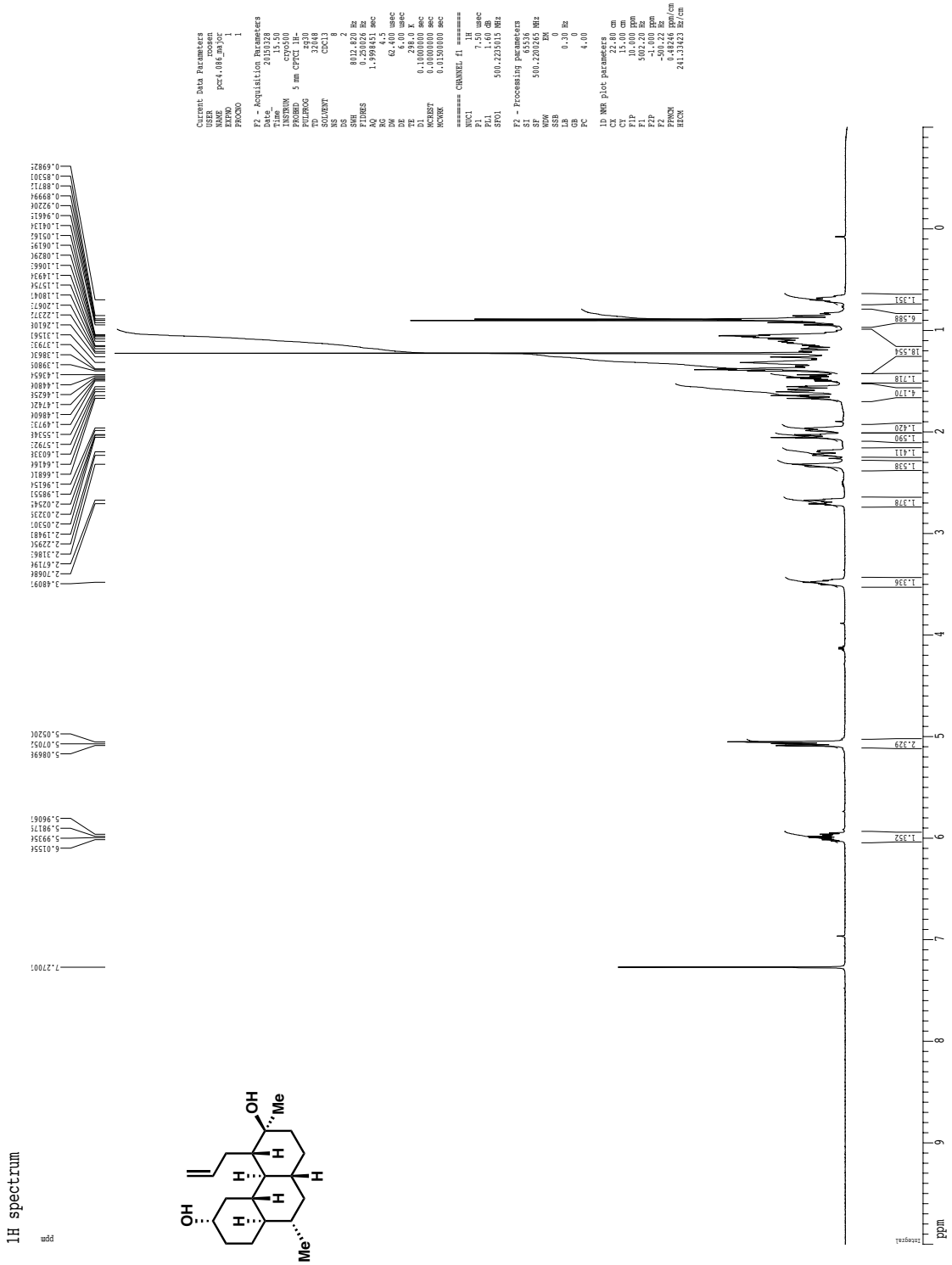
======= CHANNEL f1 =======
NUC1 13C
P1 16.55 usec
P11 500.00 usec
P12 2000.00 usec
PL0 120.00 dB
PL1 -1.00 dB
SFO1 125.7942548 MHz
SP1 2.70 dB
SP2 2.70 dB
SPNAM1 Crp60,0.5,20.1
SPNAM2 Crp60comp.4
SPOFF1 0.00 Hz
SPOFF2 0.00 Hz

======= CHANNEL f2 =======
CPDPRG2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 1.60 dB
PL12 24.50 dB
SFO2 500.2225011 MHz

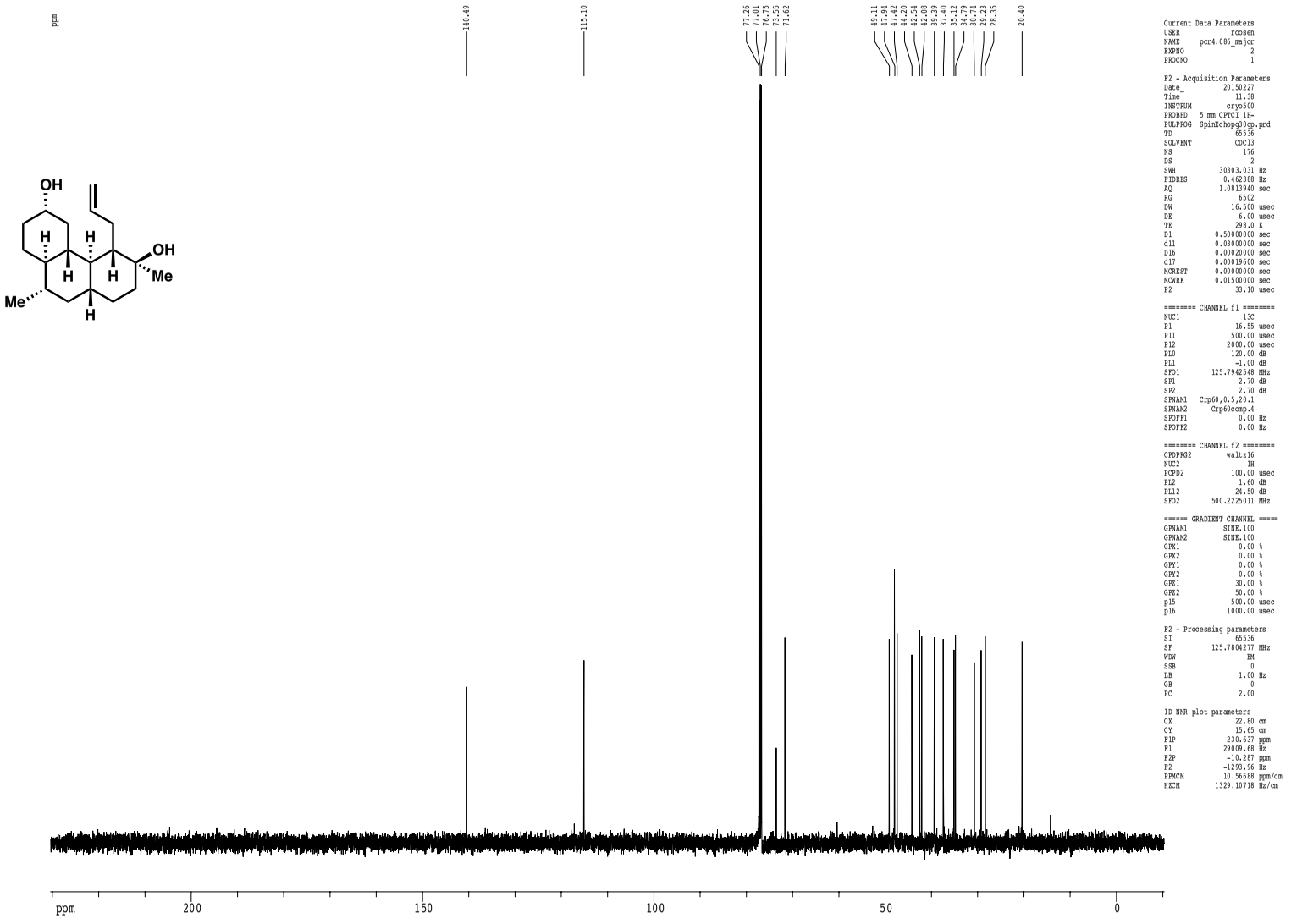
===== GRADIENT CHANNEL ====
GPNAM1 SINE.100
GPNAM2 SINE.100
GPX1 0.00 %
GPX2 0.00 %
GPY1 0.00 %
GPY2 0.00 %
GPZ1 30.00 %
GPZ2 50.00 %
p15 500.00 usec
p16 1000.00 usec

F2 - Processing parameters
SI 65536
SF 125.7804300 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00

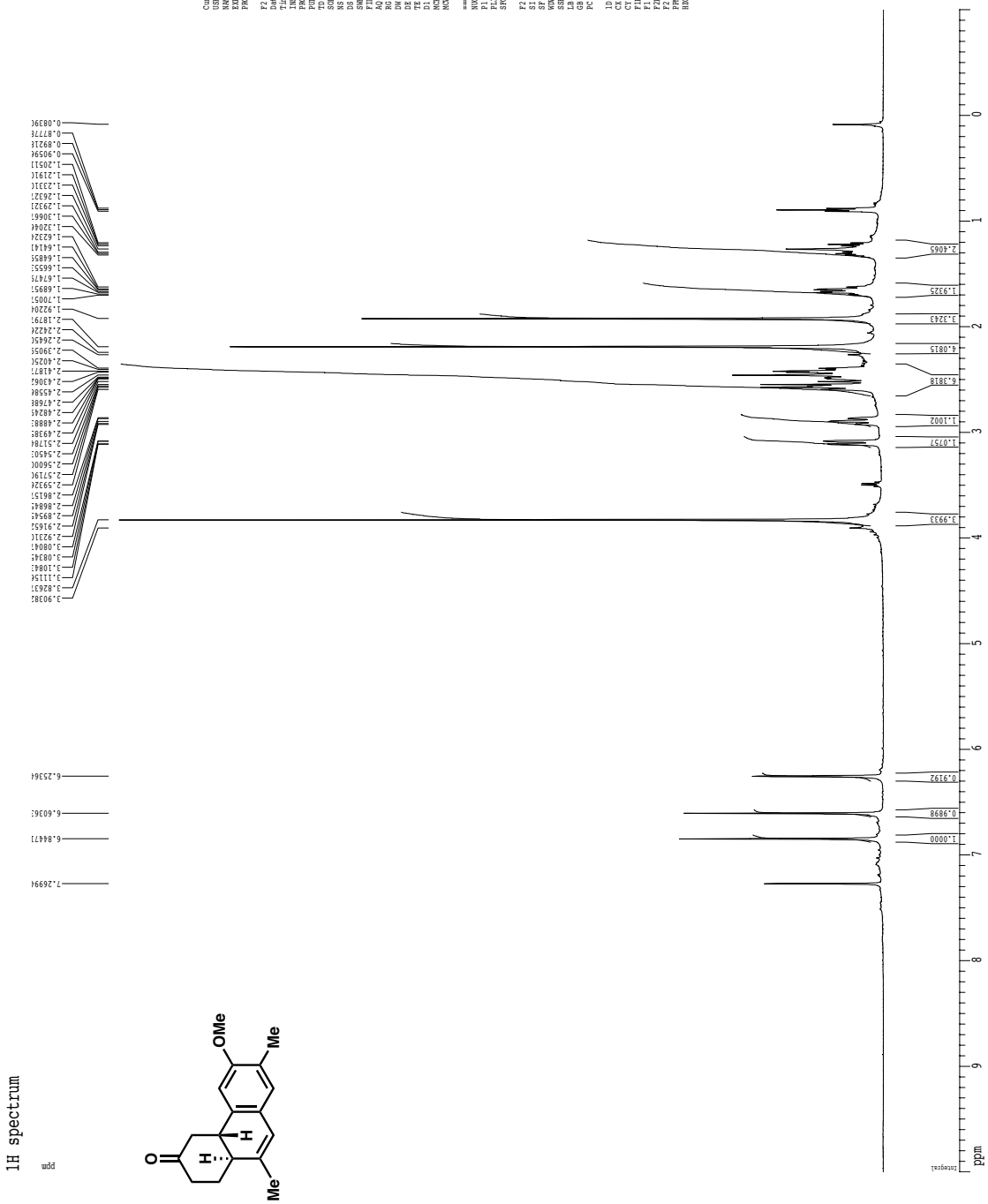
1D NMR plot parameters
CX 22.80 cm
CY 15.65 cm
F1P 230.373 ppm
F1 28976.36 Hz
F2P -10.547 ppm
F2 -1326.67 Hz
PPMCM 10.56667 ppm/cm
HZCM 1329.08032 Hz/cm

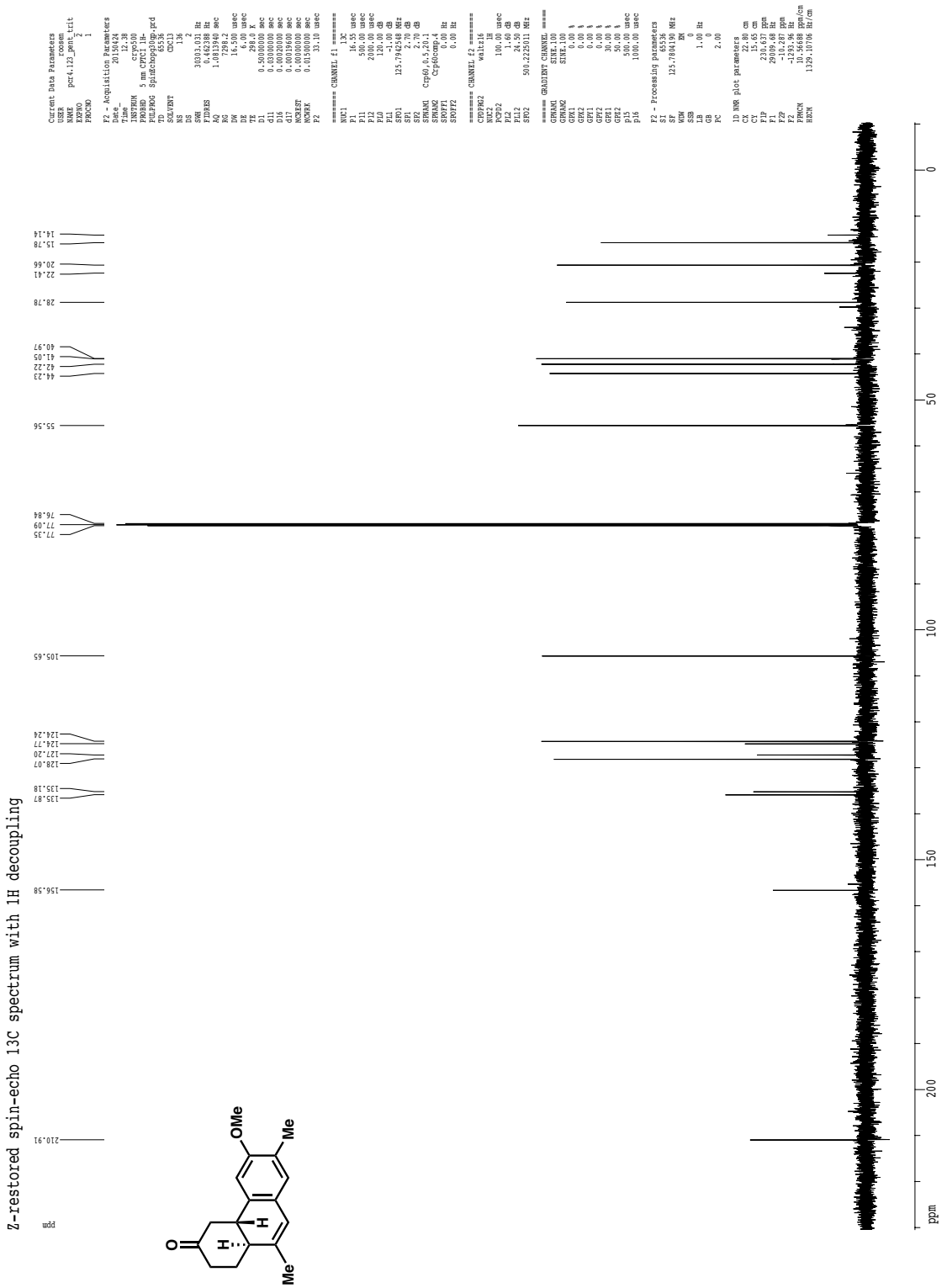

1H spectrum
ppm
OH
Me
H
H
H
H
H
OH
Me
Integral
ppm

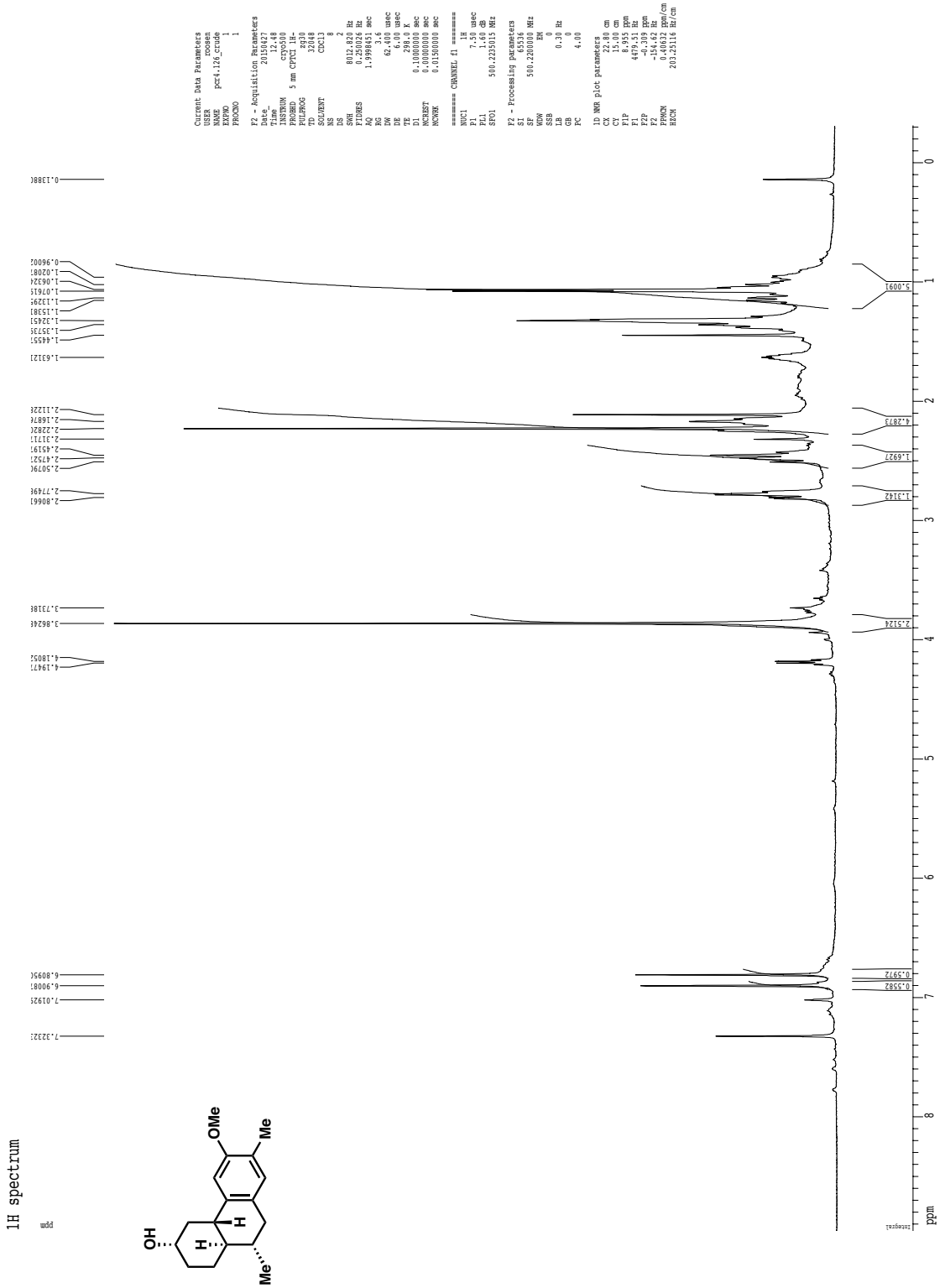
Z-restored spin-echo 13C spectrum with 1H decoupling



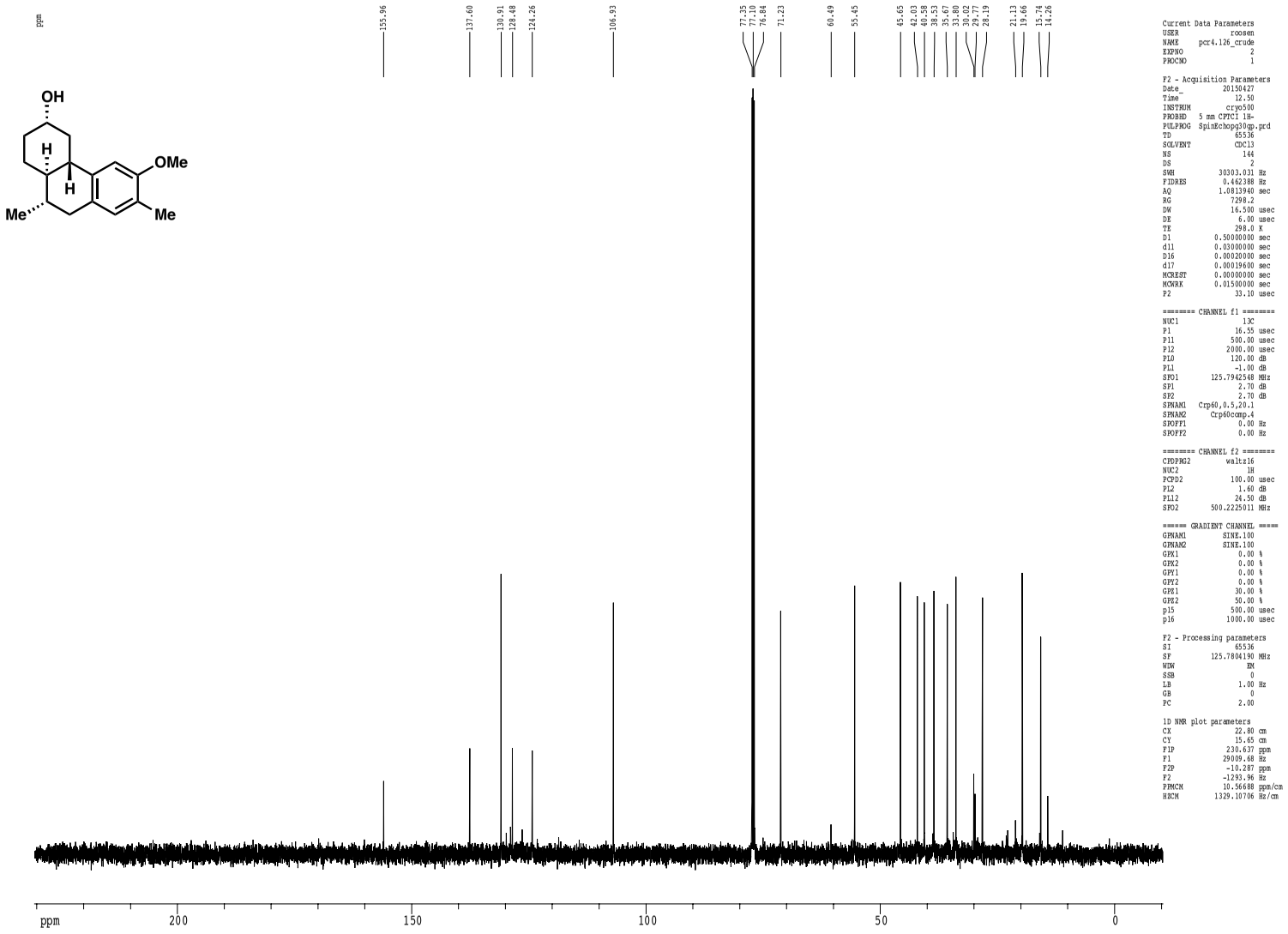

```
Current Data Parameters
USER              roosen
NAME      pcr4.086_major
EXPNO                   2
PROCNO                  1

F2 - Acquisition Parameters
Date_           20150227
Time              11.38
INSTRUM          cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD                 65536
SOLVENT             CDCl3
NS                    176
DS                      2
SWH           30303.031 Hz
FIDRES        0.462388 Hz
AQ           1.0813940 sec
RG                 6502
DW               16.500 usec
DE                6.00 usec
TE               298.0 K
D1          0.50000000 sec
d11         0.03000000 sec
D16         0.00020000 sec
d17         0.00019600 sec
MCREST      0.00000000 sec
MCWRK       0.01500000 sec
P2               33.10 usec

======= CHANNEL f1 =======
NUC1                13C
P1                16.55 usec
P11              500.00 usec
P12             2000.00 usec
PL0              120.00 dB
PL1               -1.00 dB
SFO1        125.7942548 MHz
SP1               2.70 dB
SP2               2.70 dB
SPNAM1   Crp60,0.5,20.1
SPNAM2     Crp60comp.4
SPOFF1               0.00 Hz
SPOFF2               0.00 Hz

======= CHANNEL f2 =======
CPDPRG2          waltz16
NUC2                1H
PCPD2            100.00 usec
PL2               1.60 dB
PL12             24.50 dB
SFO2        500.2225011 MHz

===== GRADIENT CHANNEL ====
GPNAM1          SINE.100
GPNAM2          SINE.100
GPX1                0.00 %
GPX2                0.00 %
GPY1                0.00 %
GPY2                0.00 %
GPZ1               30.00 %
GPZ2               50.00 %
p15              500.00 usec
p16             1000.00 usec

F2 - Processing parameters
SI                 65536
SF          125.7804277 MHz
WDW                   EM
SSB                    0
LB                  1.00 Hz
GB                     0
PC                  2.00

1D NMR plot parameters
CX                 22.80 cm
CY                 15.65 cm
F1P              230.637 ppm
F1               29009.68 Hz
F2P              -10.287 ppm
F2               -1293.96 Hz
PPMCM            10.56688 ppm/cm
HZCM          1329.10718 Hz/cm
```


1H spectrum
OMe
Me
H
H
O
Me


Z-restored spin-echo 13C spectrum with 1H decoupling
ppm
210.91
156.58
135.87
135.18
128.07
127.20
124.77
124.24
105.65
77.35
77.09
76.84
55.56
44.23
42.22
41.05
40.97
28.78
22.41
20.66
15.78
14.14
OMe
Me
H
H
O
Me
Current Data Parameters
USER rossen
NAME pcr4.123_pent_trit
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20150424
Time 12.38
INSTRUM cryo500
PROBHD 5 mm CPPCI 1H-
PULPROG SpinEchopg13dp.pcd
TD 65536
SOLVENT CDCl3
NS 136
DS 2
SWH 31013.131 Hz
FIDRES 0.473098 Hz
AQ 1.0013940 sec
RG 7298.2
DW 16.500 usec
DE 6.00 usec
TE 294.0 K
D1 0.50000000 sec
d11 0.03000000 sec
D16 0.00020000 sec
d12 0.00001000 sec
NUCLEUS 0.00000000 sec
NUCWRK 0.01500000 sec
F2 33.10 usec
======= CHANNEL f1 =======
NUC1 13C
P1 16.55 usec
P11 500.00 usec
P12 2000.00 usec
PL0 120.00 dB
PL1 -1.00 dB
SFO1 125.7742548 MHz
SF01 2.70 dB
SF02 Crp60,0.5,20.1
SFRAMP1 Crp60comp.4
SFRAMP2 0.00 Hz
SFOFF1 0.00 Hz
SFOFF2
======= CHANNEL f2 =======
CPDPRG2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 1.60 dB
PL12 24.50 dB
SFO2 500.2225011 MHz
===== GRADIENT CHANNEL =====
GPNAM1 SINE.100
GPNAM2 SINE.100
GPZ1 0.00 %
GPZ2 0.00 %
GPZ3 0.00 %
GPZ11 30.00 %
GPZ12 50.00 %
p15 500.00 usec
p16 1000.00 usec
F2 - Processing parameters
SI 65536
SF 125.7704190 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00
1D NMR plot parameters
CX 22.80 cm
CY 15.65 cm
F1P 230.637 ppm
F1 29000.68 Hz
F2P -10.197 ppm
F2 -1293.96 Hz
PPMCM 10.56688 ppm/cm
HZCM 1329.10706 Hz/cm
0
50
100
150
200
ppm

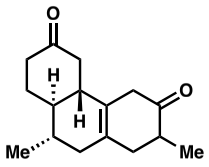

1H spectrum
ppm
OMe
Me
OH
H
H
Me

Z-restored spin-echo 13C spectrum with 1H decoupling




```
Current Data Parameters
USER              roosen
NAME      pcr4.126_crude
EXPNO                 2
PROCNO                1

F2 - Acquisition Parameters
Date_          20150427
Time              12.50
INSTRUM         cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD                65536
SOLVENT           CDCl3
NS                  144
DS                    2
SWH           30303.031 Hz
FIDRES        0.462388 Hz
AQ            1.0813940 sec
RG               7298.2
DW               16.500 usec
DE                6.00 usec
TE              298.0 K
D1           0.50000000 sec
d11          0.03000000 sec
D16          0.00020000 sec
d17          0.00019600 sec
MCREST       0.00000000 sec
MCWRK        0.01500000 sec
P2               33.10 usec

======= CHANNEL f1 =======
NUC1                13C
P1                16.55 usec
P11              500.00 usec
P12             2000.00 usec
PL0              120.00 dB
PL1               -1.00 dB
SFO1        125.7942548 MHz
SP1               2.70 dB
SP2               2.70 dB
SPNAM1   Crp60,0.5,20.1
SPNAM2      Crp60comp.4
SPOFF1               0.00 Hz
SPOFF2               0.00 Hz

======= CHANNEL f2 =======
CPDPRG2          waltz16
NUC2                1H
PCPD2            100.00 usec
PL2                1.60 dB
PL12              24.50 dB
SFO2        500.2225011 MHz

===== GRADIENT CHANNEL ====
GPNAM1          SINE.100
GPNAM2          SINE.100
GPX1                0.00 %
GPX2                0.00 %
GPY1                0.00 %
GPY2                0.00 %
GPZ1               30.00 %
GPZ2               50.00 %
p15              500.00 usec
p16             1000.00 usec

F2 - Processing parameters
SI                  65536
SF          125.7804190 MHz
WDW                    EM
SSB                    0
LB                  1.00 Hz
GB                     0
PC                  2.00

1D NMR plot parameters
CX                 22.80 cm
CY                 15.65 cm
F1P              230.637 ppm
F1               29009.68 Hz
F2P              -10.287 ppm
F2               -1293.96 Hz
PPMCM            10.56688 ppm/cm
HZCM          1329.10706 Hz/cm
```

1H spectrum



1.6 : 1 dr

Current Data Parameters
USER roosen
NAME pcr4.137_isolate
EXPNO 1
PROCNO 1

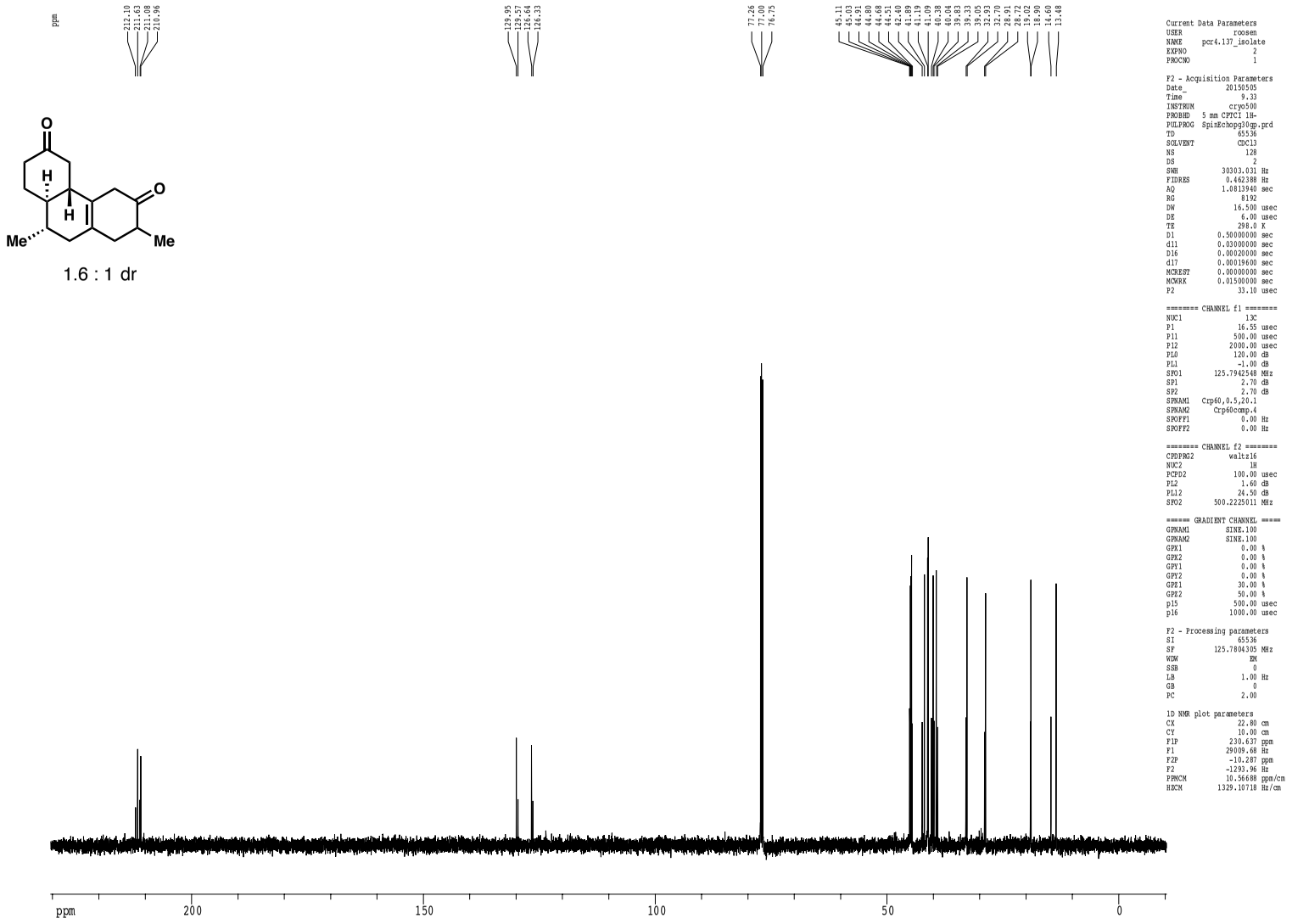
F2 - Acquisition Parameters
Date_ 20150505
Time 9.31
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 32048
SOLVENT CDCl3
NS 8
DS 2
SWH 8012.820 Hz
FIDRES 0.250026 Hz
AQ 1.9998451 sec
RG 3.6
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec

======= CHANNEL f1 =======
NUC1 1H
P1 7.50 usec
PL1 1.60 dB
SFO1 500.2235015 MHz

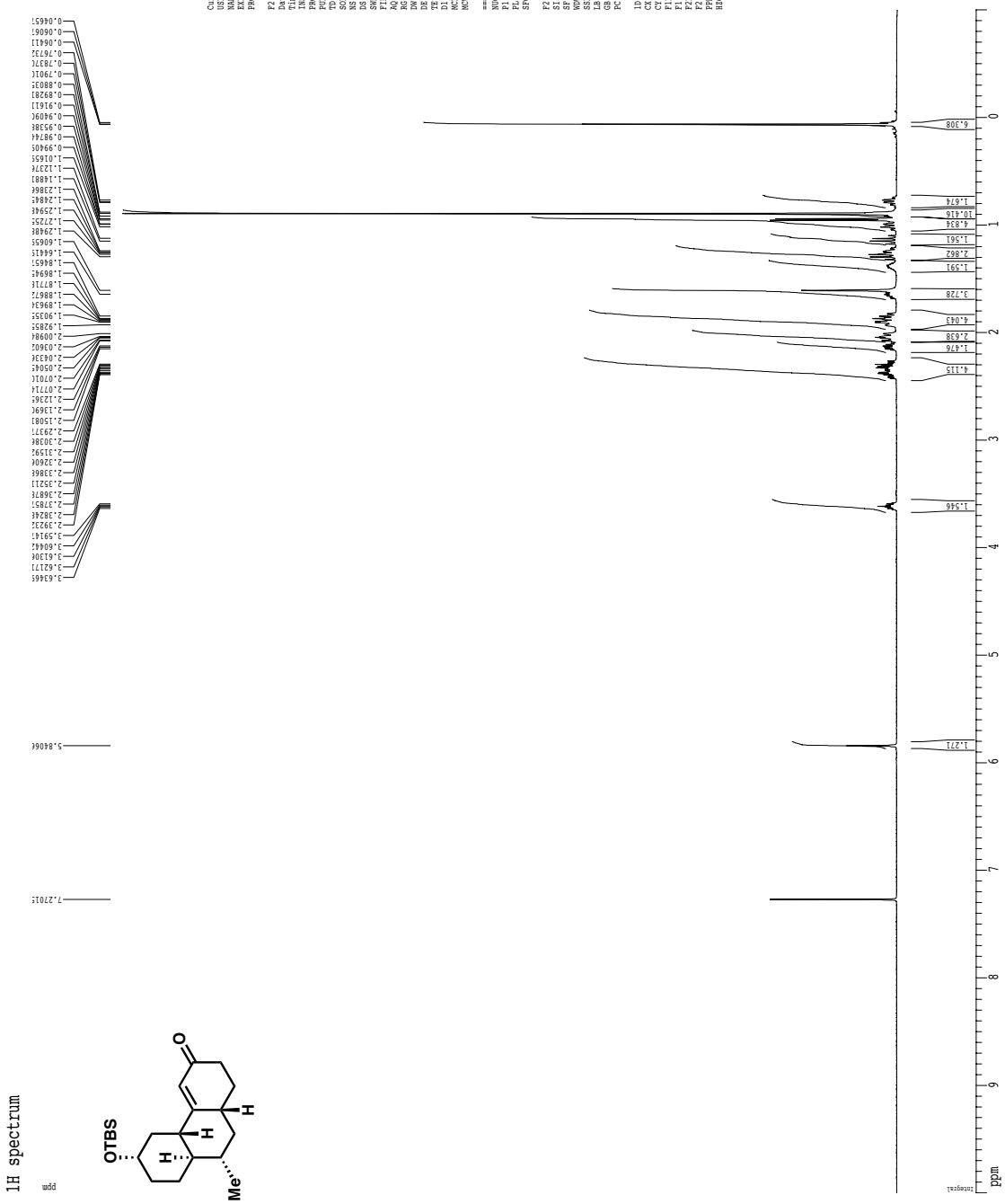
F2 - Processing parameters
SI 65536
SF 500.2200269 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00

1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 10.000 ppm
F1 5002.20 Hz
F2P -1.000 ppm
F2 -500.22 Hz
PPMCM 0.48246 ppm/cm
HZCM 241.33423 Hz/cm

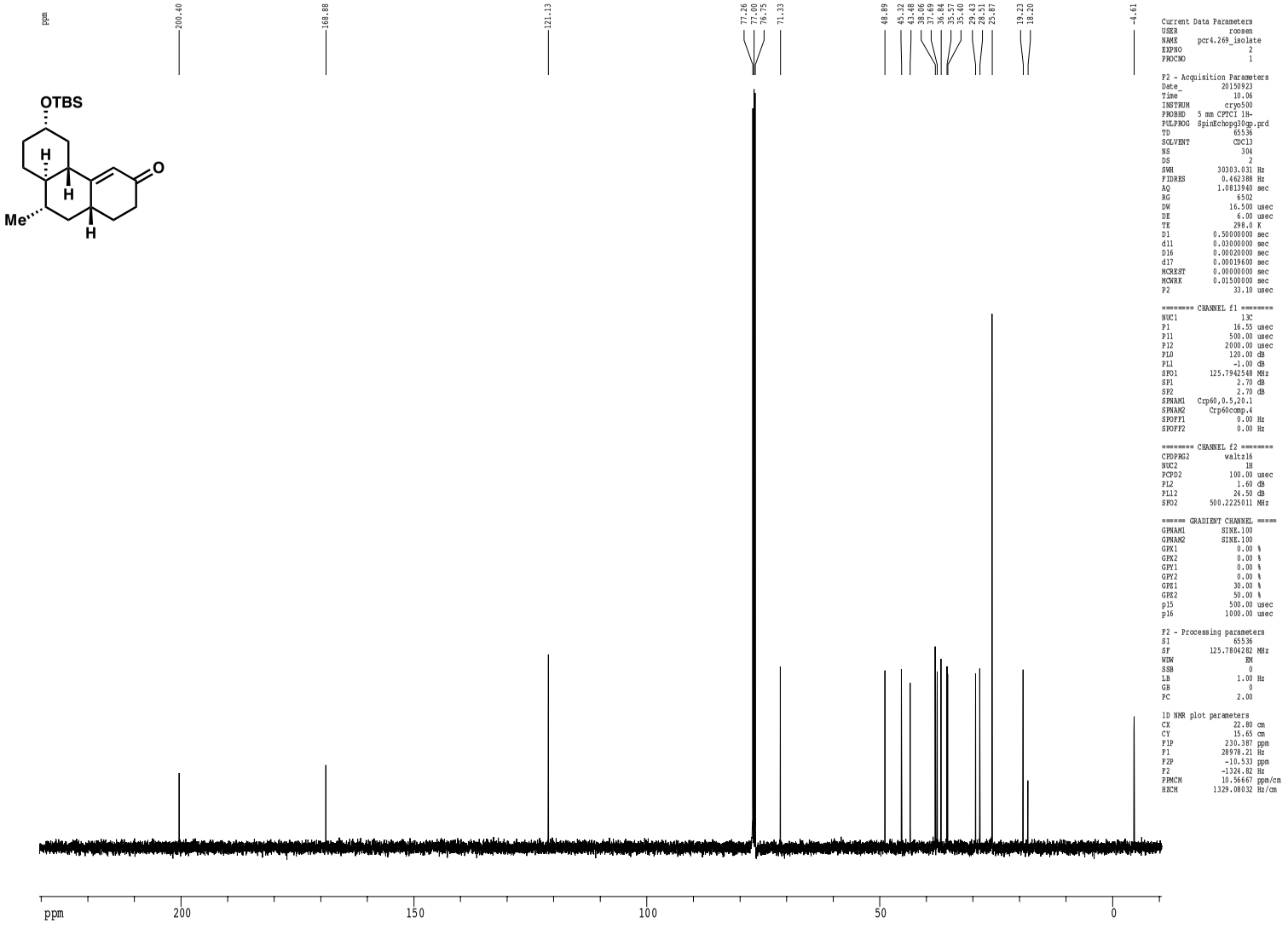
Z-restored spin-echo 13C spectrum with 1H decoupling



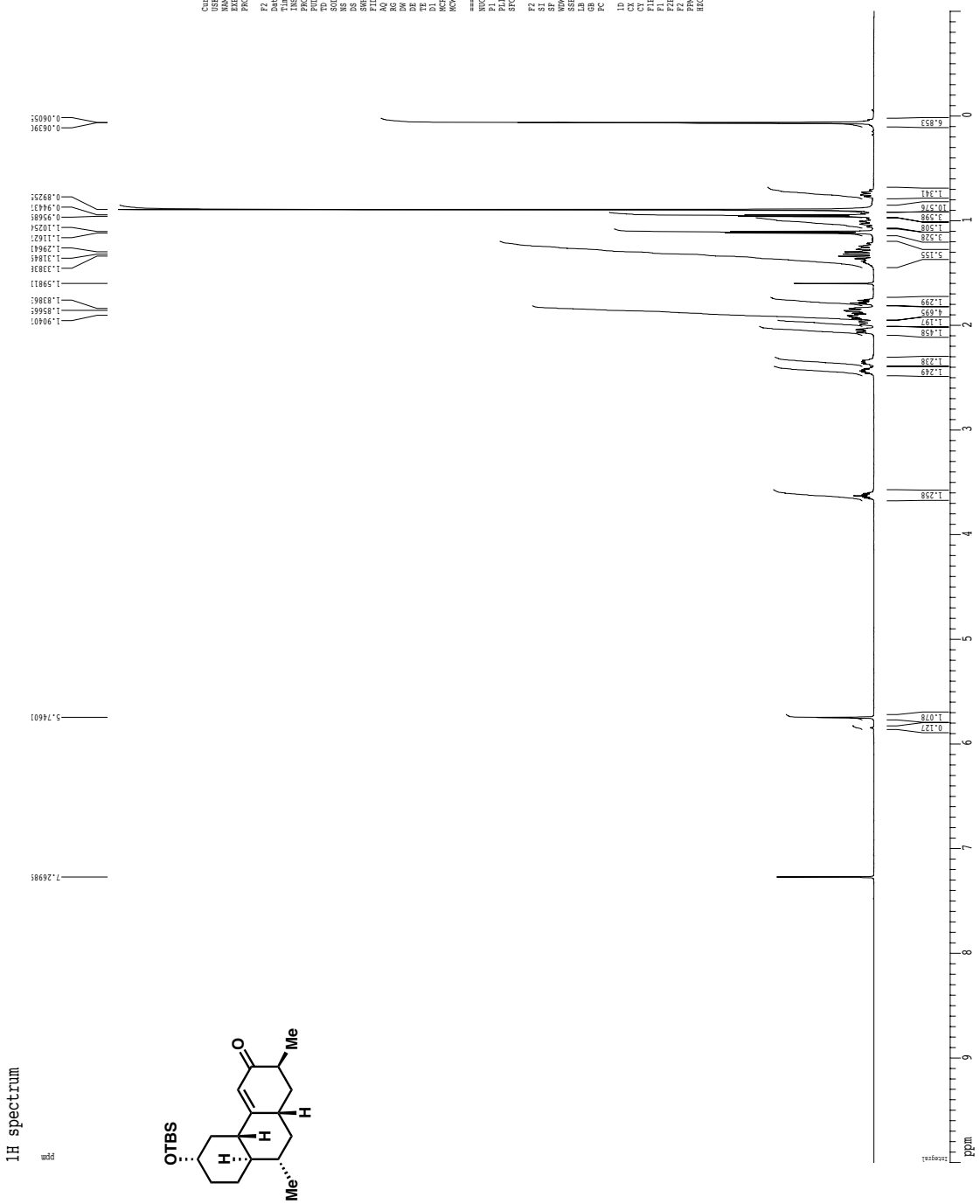

```
Current Data Parameters
USER              roosen
NAME      pcr4.137_isolate
EXPNO                    2
PROCNO                   1

F2 - Acquisition Parameters
Date_          20150505
Time               9.33
INSTRUM          cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD                 65536
SOLVENT             CDCl3
NS                    128
DS                      2
SWH             30303.031 Hz
FIDRES          0.462388 Hz
AQ              1.0813940 sec
RG                   8192
DW                 16.500 usec
DE                  6.00 usec
TE                298.0 K
D1           0.50000000 sec
d11          0.03000000 sec
D16          0.00020000 sec
d17          0.00019600 sec
MCREST       0.00000000 sec
MCWRK        0.01500000 sec
P2                 33.10 usec

======= CHANNEL f1 =======
NUC1                 13C
P1                 16.55 usec
P11               500.00 usec
P12              2000.00 usec
PL0               120.00 dB
PL1                -1.00 dB
SFO1         125.7942548 MHz
SP1                 2.70 dB
SP2                 2.70 dB
SPNAM1   Crp60,0.5,20.1
SPNAM2      Crp60comp.4
SPOFF1              0.00 Hz
SPOFF2              0.00 Hz

======= CHANNEL f2 =======
CPDPRG2          waltz16
NUC2                1H
PCPD2             100.00 usec
PL2                1.60 dB
PL12              24.50 dB
SFO2         500.2225011 MHz

===== GRADIENT CHANNEL ====
GPNAM1          SINE.100
GPNAM2          SINE.100
GPX1                0.00 %
GPX2                0.00 %
GPY1                0.00 %
GPY2                0.00 %
GPZ1               30.00 %
GPZ2               50.00 %
p15               500.00 usec
p16              1000.00 usec

F2 - Processing parameters
SI                 65536
SF           125.7804305 MHz
WDW                   EM
SSB                    0
LB                  1.00 Hz
GB                     0
PC                  2.00

1D NMR plot parameters
CX                 22.80 cm
CY                 10.00 cm
F1P              230.637 ppm
F1               29009.68 Hz
F2P              -10.287 ppm
F2               -1293.96 Hz
PPMCM            10.56688 ppm/cm
HZCM          1329.10718 Hz/cm
```


1H spectrum
ppm
OTBS
Me
H
H
H
O
Current Data Parameters
USERA2 processed
NAME pcr4.269_isolate
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20151023
Time 10.04
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 8
DS 2
SWH 8012.820 Hz
FIDRES 0.122040 Hz
AQ 1.9998451 sec
RG 6.3
DW 62.400 usec
DE 6.00 usec
TE 298.1 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 7.50 usec
PL1 1.60 dB
SFO1 500.2235015 MHz
F2 - Processing parameters
SI 65536
SF 500.2200266 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
1D NMR plot parameters
CX 27.00 cm
CY 15.00 cm
F1P 10.000 ppm
F1 5002.20 Hz
F2P -1.000 ppm
F2 -500.22 Hz
PPMCM 0.48246 ppm/cm
HZCM 241.33423 Hz/cm
integral
6.308
1.674
10.516
4.634
1.561
2.862
1.591
3.728
4.043
2.638
1.476
4.115
1.546
1.271
7.270
5.846
0.465
0.606
0.964
0.767
0.783
0.790
0.880
0.892
0.916
0.940
0.953
0.987
0.994
1.016
1.127
1.148
1.238
1.246
1.294
1.272
1.294
1.606
1.644
1.866
1.869
1.877
1.886
1.896
1.903
1.928
2.009
2.060
2.063
2.050
2.070
2.077
2.126
2.136
2.150
2.293
2.303
2.315
2.326
2.352
2.368
2.378
2.382
2.392
3.591
3.604
3.613
3.621
3.646

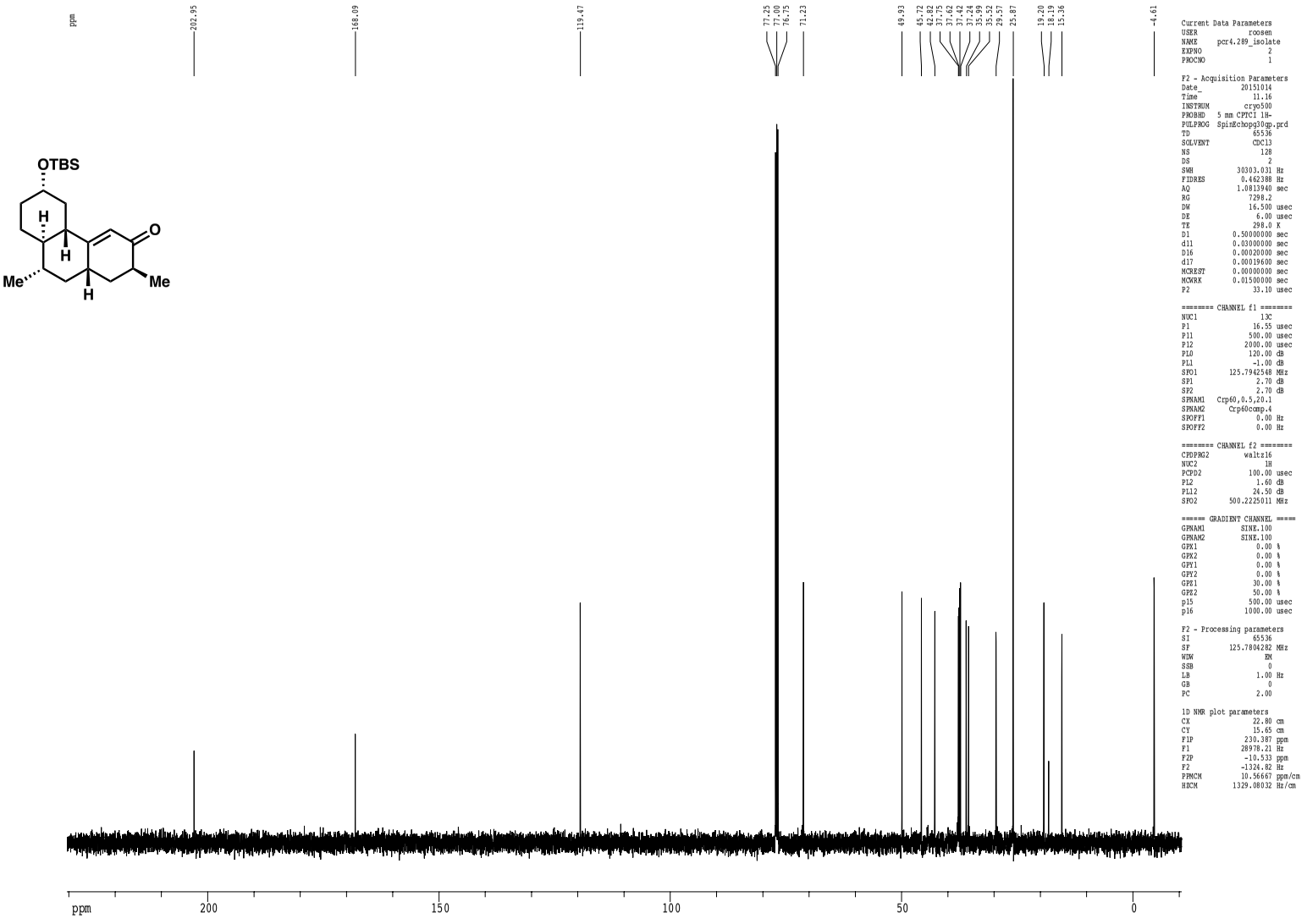
Z-restored spin-echo 13C spectrum with 1H decoupling



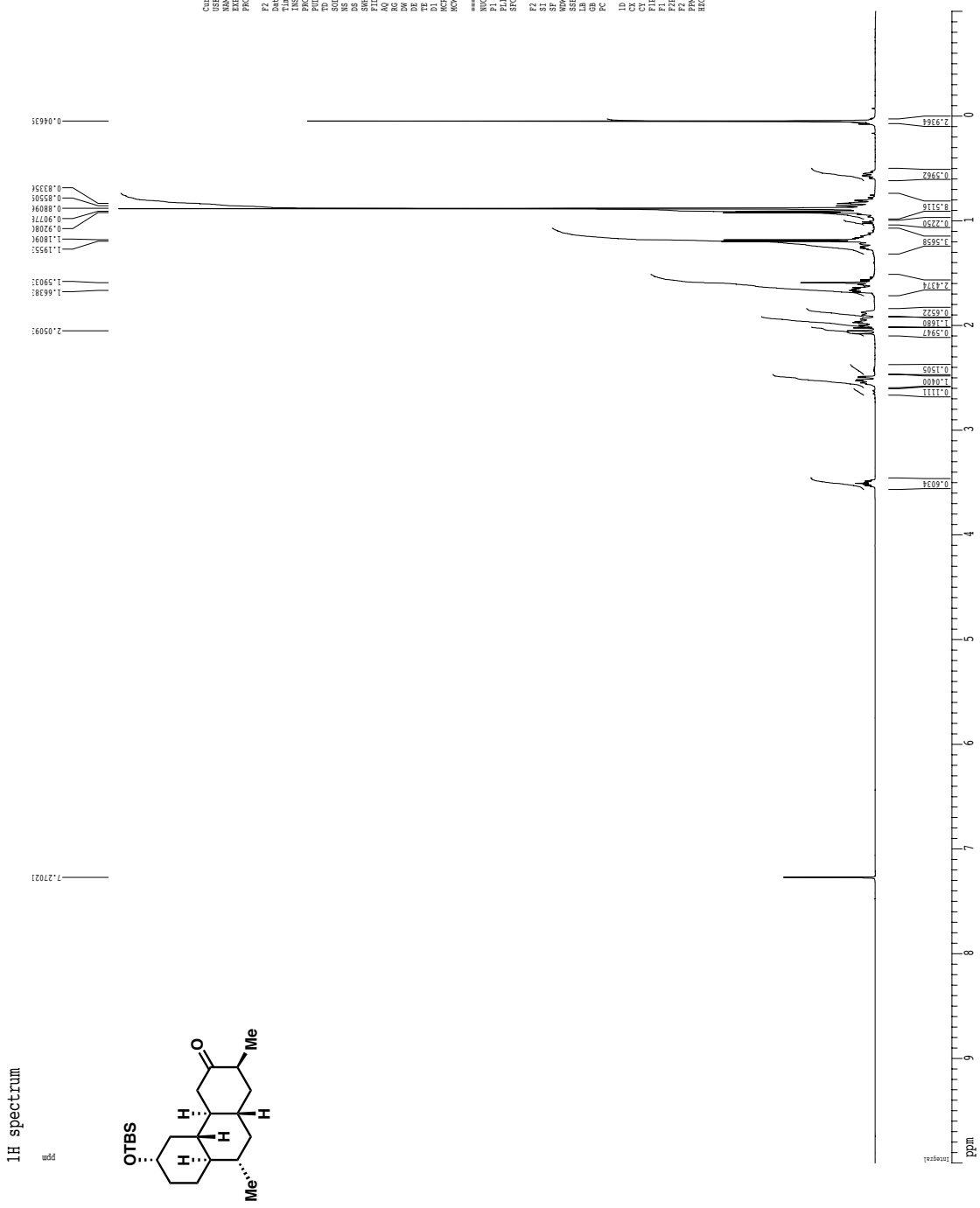

```
Current Data Parameters
USER              roosen
NAME      pcr4.269_isolate
EXPNO                    2
PROCNO                   1

F2 - Acquisition Parameters
Date_          20150923
Time              10.06
INSTRUM          cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD                 65536
SOLVENT             CDCl3
NS                    304
DS                      2
SWH           30303.031 Hz
FIDRES        0.462388 Hz
AQ            1.0813940 sec
RG                 6502
DW               16.500 usec
DE                6.00 usec
TE               298.0 K
D1           0.50000000 sec
d11          0.03000000 sec
D16          0.00020000 sec
d17          0.00019600 sec
MCREST       0.00000000 sec
MCWRK        0.01500000 sec
P2               33.10 usec

======= CHANNEL f1 =======
NUC1                13C
P1                16.55 usec
P11              500.00 usec
P12             2000.00 usec
PL0              120.00 dB
PL1               -1.00 dB
SFO1        125.7942548 MHz
SP1               2.70 dB
SP2               2.70 dB
SPNAM1   Crp60,0.5,20.1
SPNAM2     Crp60comp.4
SPOFF1               0.00 Hz
SPOFF2               0.00 Hz

======= CHANNEL f2 =======
CPDPRG2          waltz16
NUC2                1H
PCPD2            100.00 usec
PL2               1.60 dB
PL12             24.50 dB
SFO2        500.2225011 MHz

===== GRADIENT CHANNEL ====
GPNAM1          SINE.100
GPNAM2          SINE.100
GPX1                0.00 %
GPX2                0.00 %
GPY1                0.00 %
GPY2                0.00 %
GPZ1               30.00 %
GPZ2               50.00 %
p15              500.00 usec
p16             1000.00 usec

F2 - Processing parameters
SI                 65536
SF          125.7804282 MHz
WDW                   EM
SSB                    0
LB                  1.00 Hz
GB                     0
PC                  2.00

1D NMR plot parameters
CX                 22.80 cm
CY                 15.65 cm
F1P              230.387 ppm
F1               28978.21 Hz
F2P               -10.533 ppm
F2               -1324.82 Hz
PPMCM            10.56667 ppm/cm
HZCM          1329.08032 Hz/cm
```


1H spectrum
OTBS
Me
H
H
H
Me
O
ppm

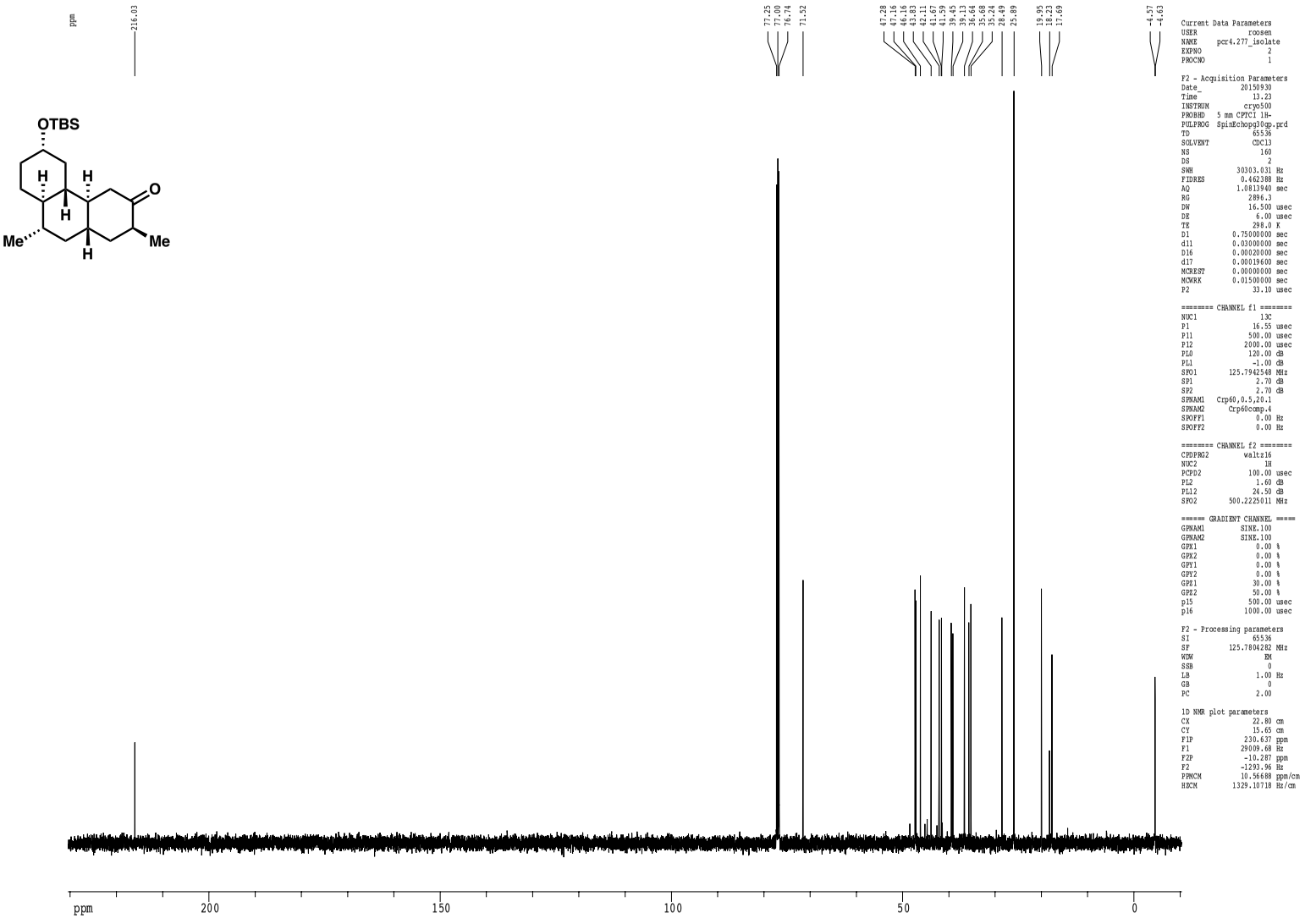
Z-restored spin-echo 13C spectrum with 1H decoupling




```
Current Data Parameters
USER              roosen
NAME      pcr4.289_isolate
EXPNO                    2
PROCNO                   1

F2 - Acquisition Parameters
Date_           20151014
Time              11.16
INSTRUM          cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD                 65536
SOLVENT             CDCl3
NS                    128
DS                      2
SWH           30303.031 Hz
FIDRES        0.462388 Hz
AQ            1.0813940 sec
RG               7298.2
DW               16.500 usec
DE                6.00 usec
TE               298.0 K
D1          0.50000000 sec
d11         0.03000000 sec
D16         0.00020000 sec
d17         0.00019600 sec
MCREST      0.00000000 sec
MCWRK       0.01500000 sec
P2               33.10 usec

======= CHANNEL f1 =======
NUC1                13C
P1               16.55 usec
P11             500.00 usec
P12            2000.00 usec
PL0             120.00 dB
PL1              -1.00 dB
SFO1       125.7942548 MHz
SP1              2.70 dB
SP2              2.70 dB
SPNAM1   Crp60,0.5,20.1
SPNAM2     Crp60comp.4
SPOFF1              0.00 Hz
SPOFF2              0.00 Hz

======= CHANNEL f2 =======
CPDPRG2          waltz16
NUC2                1H
PCPD2           100.00 usec
PL2               1.60 dB
PL12             24.50 dB
SFO2       500.2225011 MHz

===== GRADIENT CHANNEL ====
GPNAM1          SINE.100
GPNAM2          SINE.100
GPX1                0.00 %
GPX2                0.00 %
GPY1                0.00 %
GPY2                0.00 %
GPZ1               30.00 %
GPZ2               50.00 %
p15             500.00 usec
p16            1000.00 usec

F2 - Processing parameters
SI                 65536
SF         125.7804282 MHz
WDW                   EM
SSB                    0
LB                  1.00 Hz
GB                     0
PC                  2.00

1D NMR plot parameters
CX                 22.80 cm
CY                 15.65 cm
F1P              230.387 ppm
F1              28978.21 Hz
F2P              -10.533 ppm
F2              -1324.82 Hz
PPMCM           10.56667 ppm/cm
HZCM         1329.08032 Hz/cm
```


1H spectrum
OTBS
Me
Me
H
H
H
H
ppm
Integral

Z-restored spin-echo 13C spectrum with 1H decoupling



Current Data Parameters

USER	roosen
NAME	pcr4.277_isolate
EXPNO	2
PROCNO	1

F2 - Acquisition Parameters

Date_	20150930
Time	13.23
INSTRUM	cryo500
PROBHD	5 mm CPTCI 1H-
PULPROG	SpinEchopg30gp.prd
TD	65536
SOLVENT	CDCl3
NS	160
DS	2
SWH	30303.031 Hz
FIDRES	0.462388 Hz
AQ	1.0813940 sec
RG	2896.3
DW	16.500 usec
DE	6.00 usec
TE	298.0 K
D1	0.75000000 sec
d11	0.03000000 sec
D16	0.00020000 sec
d17	0.00019600 sec
MCREST	0.00000000 sec
MCWRK	0.01500000 sec
P2	33.10 usec

======= CHANNEL f1 =======

NUC1	13C
P1	16.55 usec
P11	500.00 usec
P12	2000.00 usec
PL0	120.00 dB
PL1	-1.00 dB
SFO1	125.7942548 MHz
SP1	2.70 dB
SP2	2.70 dB
SPNAM1	Crp60,0.5,20.1
SPNAM2	Crp60comp.4
SPOFF1	0.00 Hz
SPOFF2	0.00 Hz

======= CHANNEL f2 =======

CPDPRG2	waltz16
NUC2	1H
PCPD2	100.00 usec
PL2	1.60 dB
PL12	24.50 dB
SFO2	500.2225011 MHz

===== GRADIENT CHANNEL ====

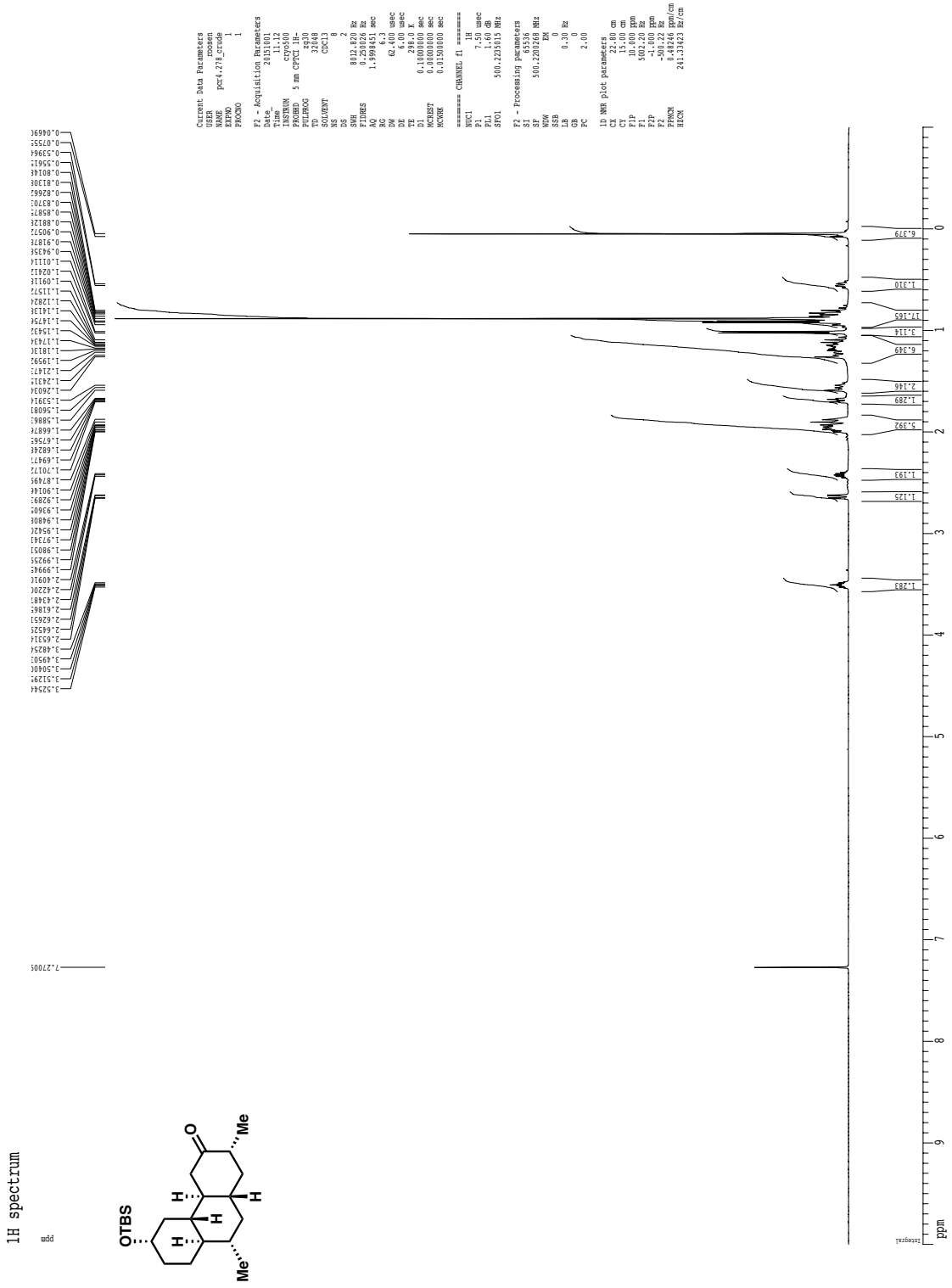
GPNAM1	SINE.100
GPNAM2	SINE.100
GPX1	0.00 %
GPX2	0.00 %
GPY1	0.00 %
GPY2	0.00 %
GPZ1	30.00 %
GPZ2	50.00 %
p15	500.00 usec
p16	1000.00 usec

F2 - Processing parameters

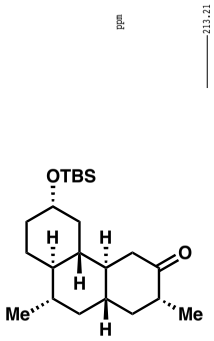
SI	65536
SF	125.7804282 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	2.00

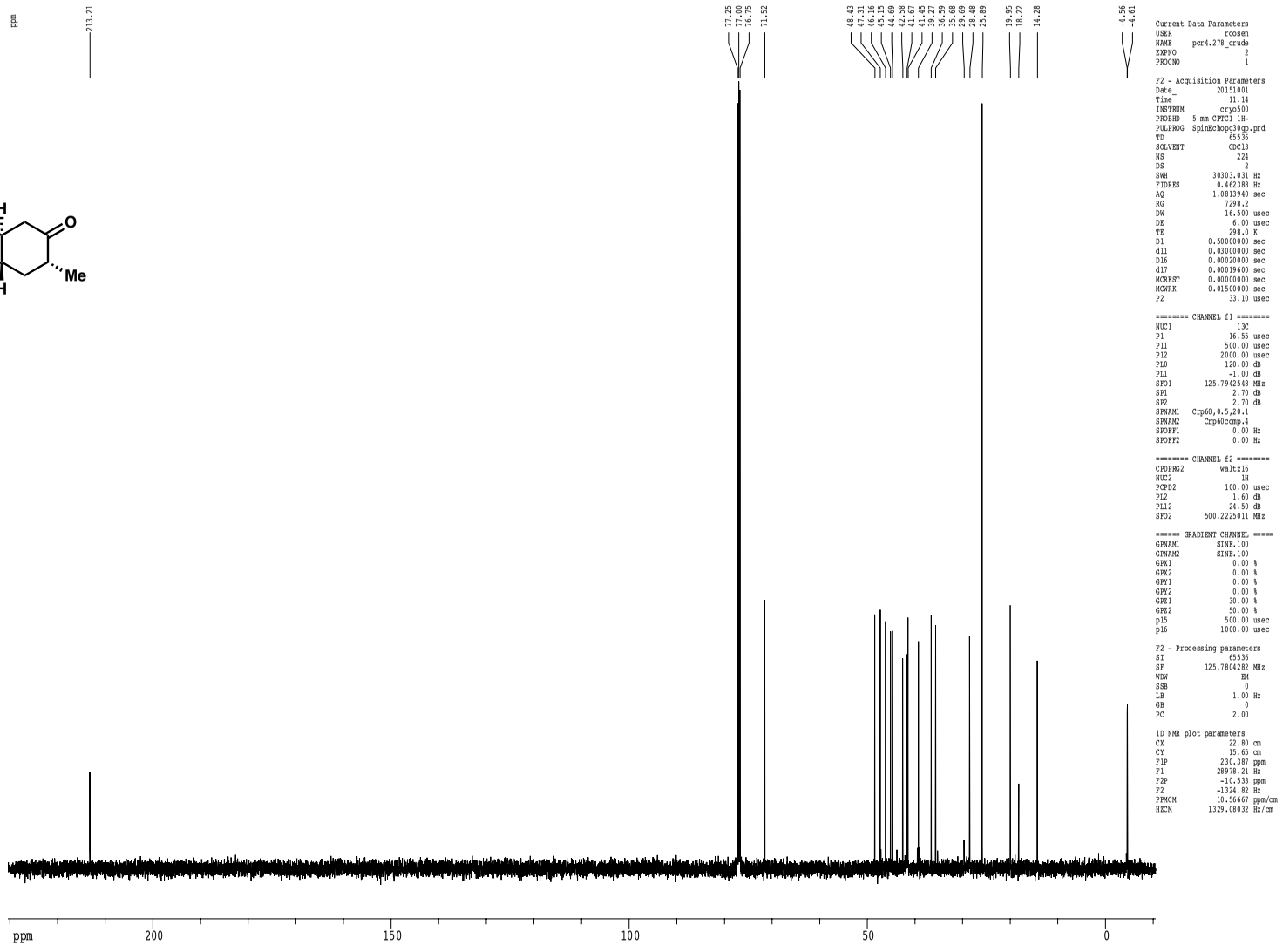
1D NMR plot parameters

CX	22.80 cm
CY	15.65 cm
F1P	230.637 ppm
F1	29009.68 Hz
F2P	-10.287 ppm
F2	-1293.96 Hz
PPMCM	10.56688 ppm/cm
HZCM	1329.10718 Hz/cm

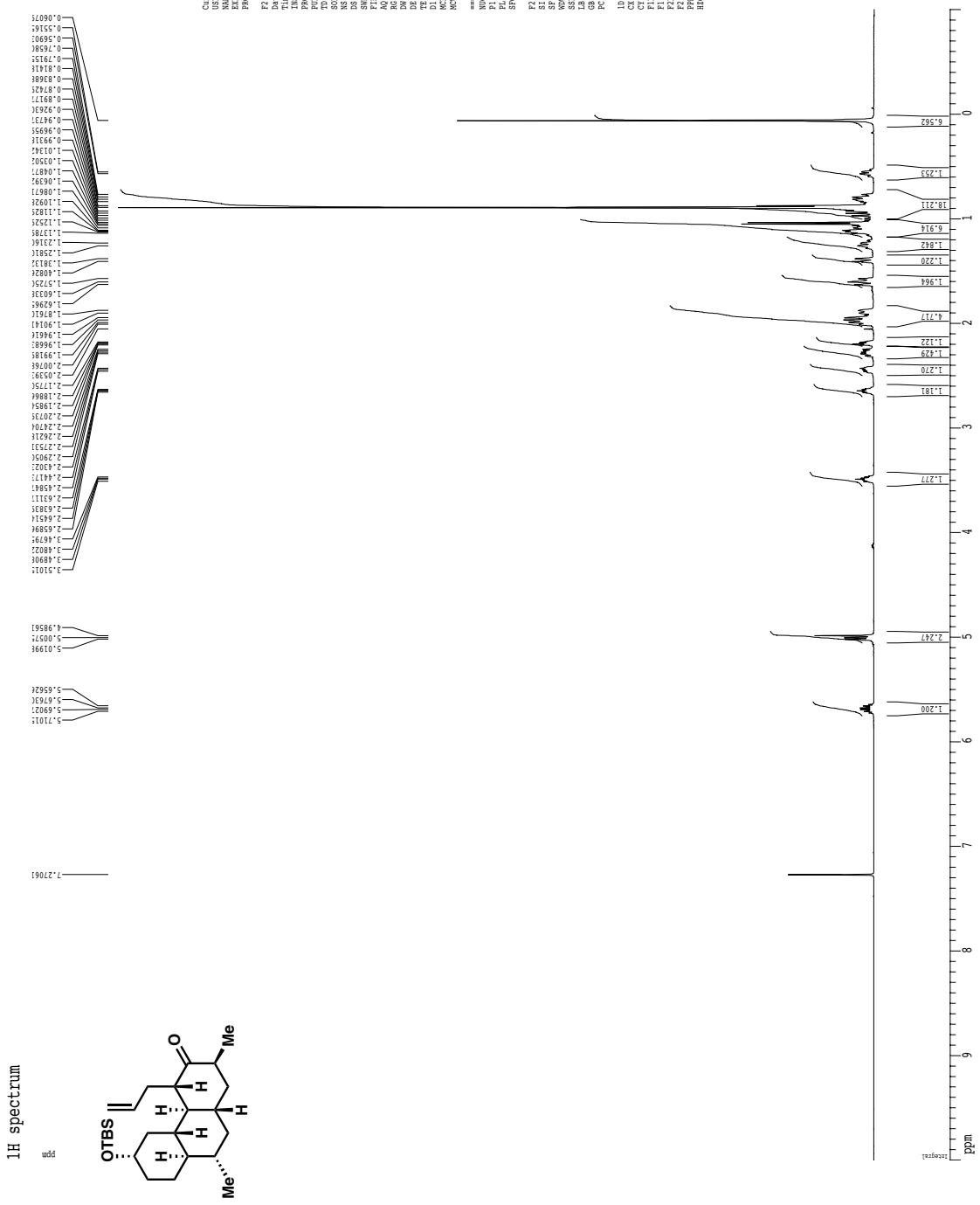

1H spectrum
ppm
OTBS
Me
Me
H
H
H
H
O
Current Data Parameters
NAME pcr4.278_crude
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20151001
Time 11.12
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 8
DS 2
SWH 8012.820 Hz
FIDRES 0.244409 Hz
AQ 1.9998451 sec
RG 6.3
DW 62.400 usec
DE 6.00 usec
TE 298.1 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 7.50 usec
PL1 1.60 dB
SFO1 500.2235015 MHz
F2 - Processing parameters
SI 65536
SF 500.2200268 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 2.00
1D NMR plot parameters
CX 27.00 cm
CY 15.00 cm
F1P 10.000 ppm
F1 5002.20 Hz
F2P -1.000 ppm
F2 -500.22 Hz
PPMCM 0.48246 ppm/cm
HZCM 241.33423 Hz/cm
6.379
1.310
17.165
3.114
6.349
2.146
1.289
5.392
1.193
1.125
1.283
7.270
Integral
ppm

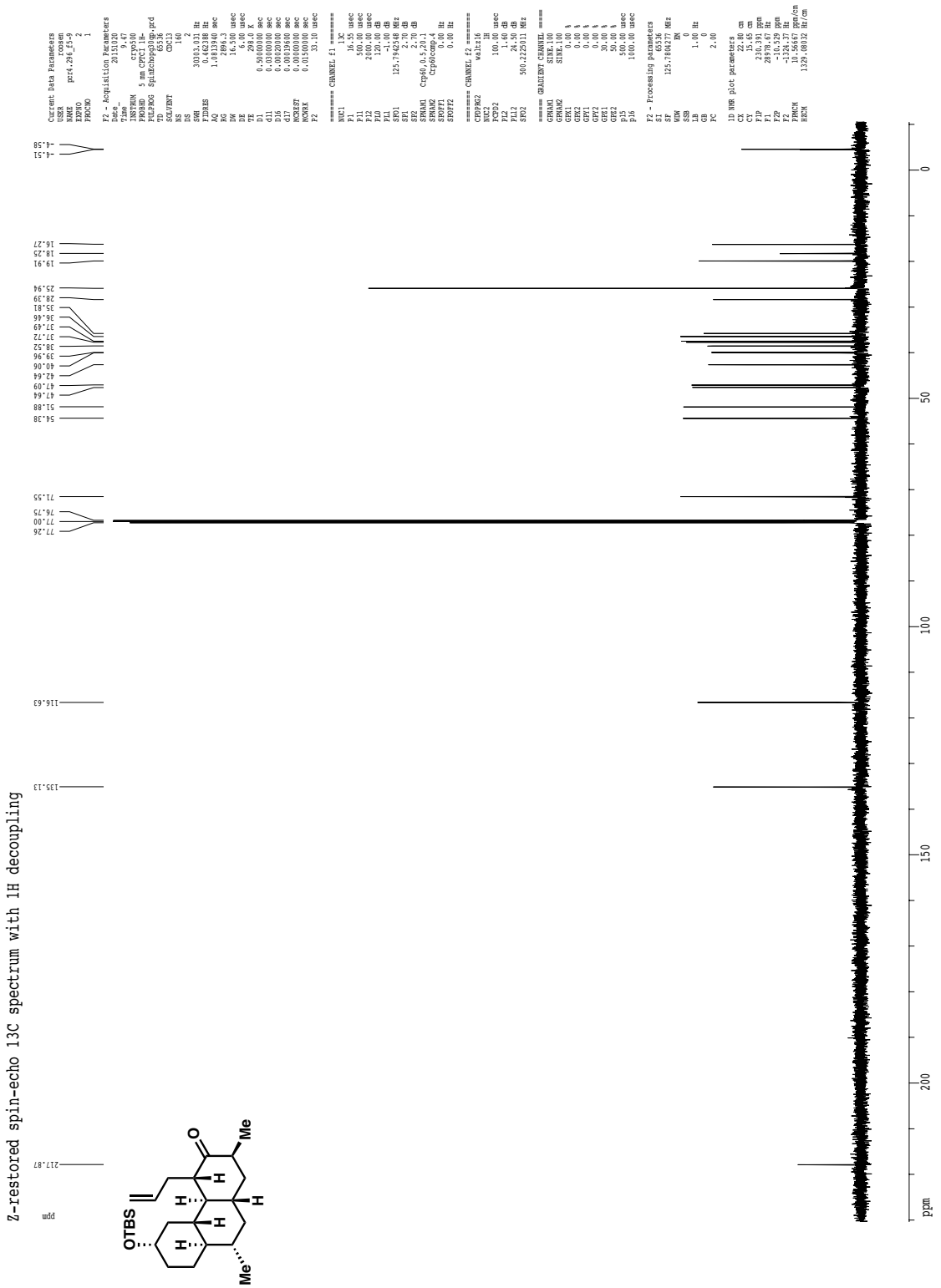
Z-restored spin-echo 13C spectrum with 1H decoupling

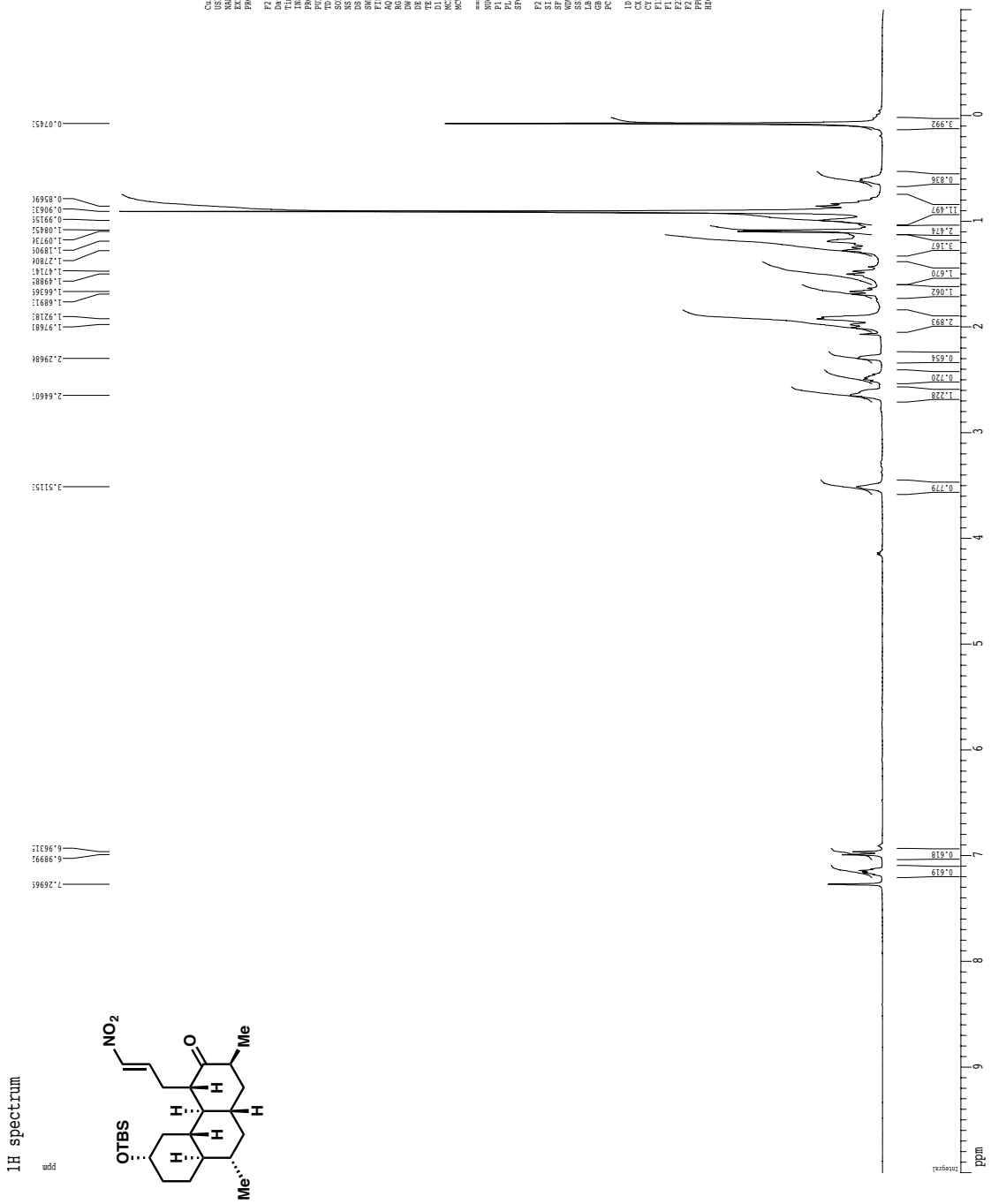




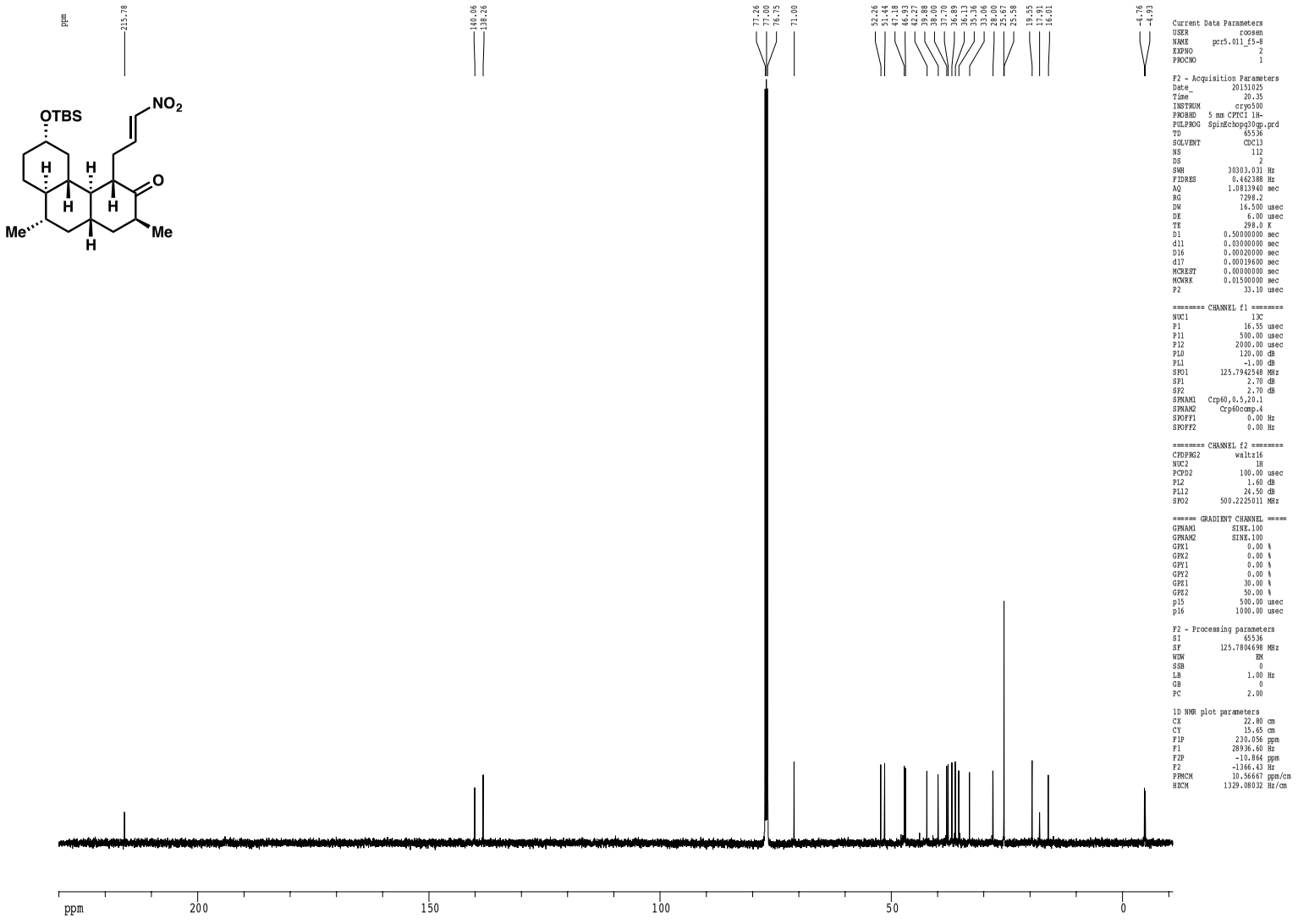

```
Current Data Parameters
USER              roosen
NAME      pcr4.278_crude
EXPNO                 2
PROCNO                1

F2 - Acquisition Parameters
Date_          20151001
Time              11.14
INSTRUM          cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD                65536
SOLVENT           CDCl3
NS                  224
DS                    2
SWH           30303.031 Hz
FIDRES        0.462388 Hz
AQ            1.0813940 sec
RG               7298.2
DW                16.500 usec
DE                 6.00 usec
TE               298.0 K
D1           0.50000000 sec
d11          0.03000000 sec
D16          0.00020000 sec
d17          0.00019600 sec
MCREST       0.00000000 sec
MCWRK        0.01500000 sec
P2                33.10 usec

======= CHANNEL f1 =======
NUC1                13C
P1                16.55 usec
P11              500.00 usec
P12             2000.00 usec
PL0              120.00 dB
PL1               -1.00 dB
SFO1        125.7942548 MHz
SP1               2.70 dB
SP2               2.70 dB
SPNAM1   Crp60,0.5,20.1
SPNAM2      Crp60comp.4
SPOFF1               0.00 Hz
SPOFF2               0.00 Hz

======= CHANNEL f2 =======
CPDPRG2          waltz16
NUC2                1H
PCPD2            100.00 usec
PL2                1.60 dB
PL12              24.50 dB
SFO2        500.2225011 MHz

===== GRADIENT CHANNEL ====
GPNAM1          SINE.100
GPNAM2          SINE.100
GPX1               0.00 %
GPX2               0.00 %
GPY1               0.00 %
GPY2               0.00 %
GPZ1              30.00 %
GPZ2              50.00 %
p15              500.00 usec
p16             1000.00 usec

F2 - Processing parameters
SI                65536
SF          125.7804282 MHz
WDW                  EM
SSB                   0
LB                 1.00 Hz
GB                    0
PC                 2.00

1D NMR plot parameters
CX                22.80 cm
CY                15.65 cm
F1P             230.387 ppm
F1              28978.21 Hz
F2P              -10.533 ppm
F2              -1324.82 Hz
PPMCM           10.56667 ppm/cm
HZCM         1329.08032 Hz/cm
```


1H spectrum
ppm
OTBS
Me
Me
H
H
H
H
O

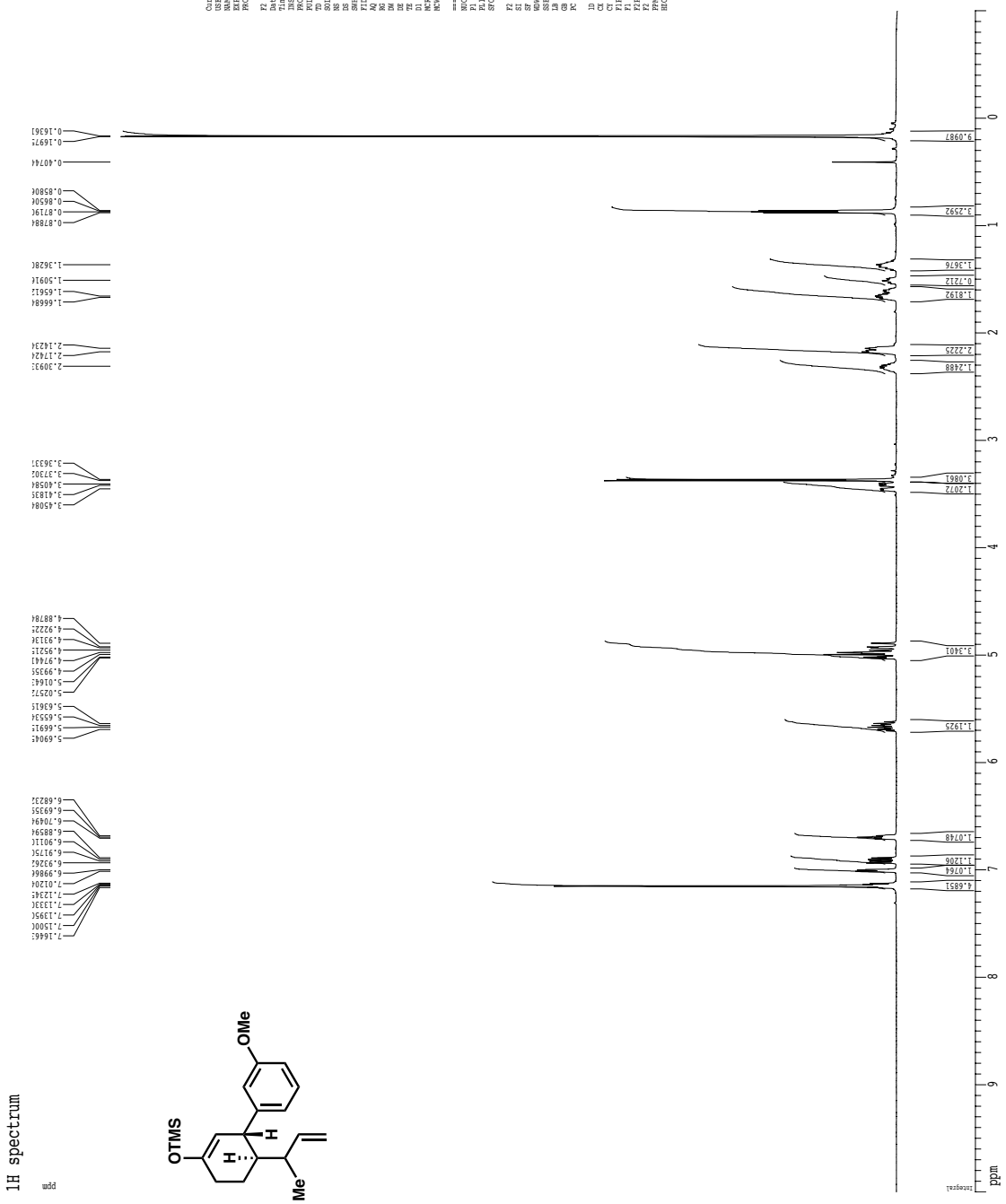

2-restored spin-echo 13C spectrum with 1H decoupling
Current Data Parameters
USER roosen
NAME pc4.29d_f3-9
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20151120
Time 9.47
INSTRUM cryo500
PROBHD 5 mm CPPCI 1H-
PULPROG SpinEchopg13dp.pcd
TD 65536
SOLVENT CDCl3
NS 160
DS 2
SWH 31013.101 Hz
FIDRES 0.473098 Hz
AQ 1.0013940 sec
RG 2896.3
DW 16.500 usec
DE 6.00 usec
TE 298.0 K
D1 0.50000000 sec
d11 0.03000000 sec
D16 0.00120000 sec
d12 0.00001000 sec
d17 0.00001000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
P2 33.10 usec
======= CHANNEL f1 =======
NUC1 13C
P1 16.55 usec
P11 500.00 usec
P12 2000.00 usec
PL0 120.00 dB
PL1 -1.00 dB
SFO1 125.7742548 MHz
SPL1 2.70 dB
SP2 2.70 dB
SPNAM1 Crp60,0.5,20.1
SPNAM2 Crp60comp.4
SPOFF1 0.00 Hz
SPOFF2 0.00 Hz
======= CHANNEL f2 =======
CPDPRG2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 1.60 dB
PL12 24.50 dB
SFO2 500.2225011 MHz
===== GRADIENT CHANNEL =====
GPNAM1 SINE.100
GPNAM2 SINE.100
GPZ1 0.00 %
GPZ2 0.00 %
GPZ1 0.00 %
GPZ2 80.00 %
GPZ1 50.00 %
p15 500.00 usec
p16 1000.00 usec
F2 - Processing parameters
SI 65536
SF 125.7804277 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00
1D NMR plot parameters
CX 22.80 cm
CY 15.65 cm
F1P 230.991 ppm
F1 29038.57 Hz
F2P -10.529 ppm
F2 -1324.37 Hz
PPMCM 10.56667 ppm/cm
HZCM 1329.08032 Hz/cm
-4.58
-4.51
16.27
18.25
19.91
25.94
28.39
35.81
36.46
37.49
37.72
38.52
39.96
40.06
42.64
47.09
47.64
51.88
54.38
71.55
76.75
77.00
77.26
116.63
135.13
217.87
ppm
0
50
100
150
200
OTBS
Me
Me
H
H
H
H
H

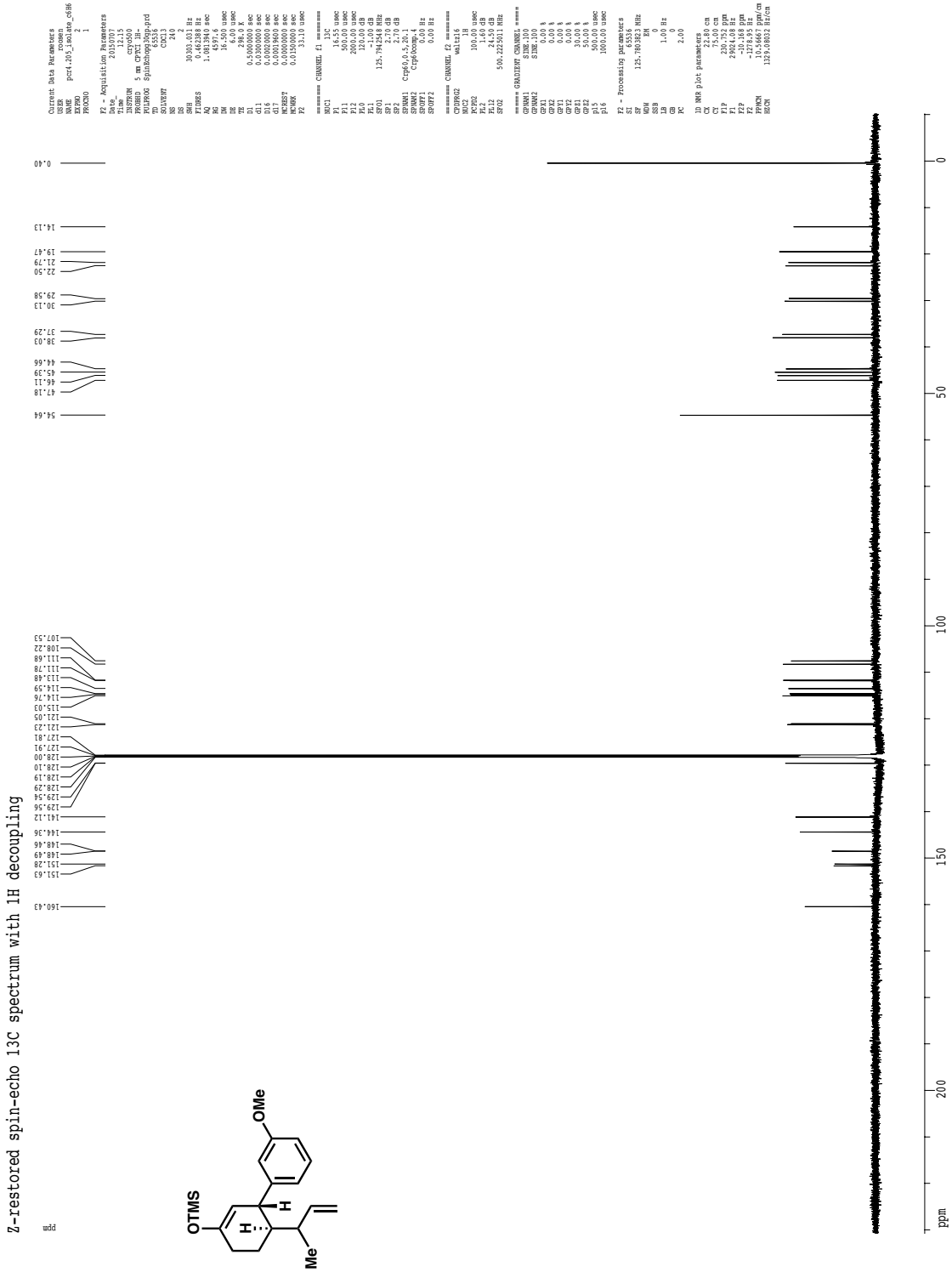

1H spectrum
ppm
NO2
O
Me
OTBS
Me
H
H
H
H
H
Current Data Parameters
NAME pcr5.011_f5-8
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20151021
Time 20.33
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 8
DS 2
SWH 8012.820 Hz
FIDRES 0.244409 Hz
AQ 1.9998451 sec
RG 5.7
DW 62.400 usec
DE 6.00 usec
TE 298.1 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 7.50 usec
PL1 1.60 dB
SFO1 500.2235015 MHz
F2 - Processing parameters
SI 65536
SF 500.2200266 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00
1D NMR plot parameters
CX 27.00 cm
CY 15.00 cm
F1P 10.000 ppm
F1 5002.20 Hz
F2P -1.000 ppm
F2 -500.22 Hz
PPMCM 0.48246 ppm/cm
HZCM 241.33423 Hz/cm
0.0745
0.8569
0.9063
0.9915
1.0864
1.0973
1.1890
1.2780
1.6716
1.6988
1.6636
1.6891
1.9218
1.9768
2.2968
2.6660
3.5115
6.9631
6.9899
7.2696
3.992
0.836
11.497
2.474
3.167
1.670
1.062
2.893
0.654
0.720
1.228
0.779
0.618
0.619
Integral
ppm

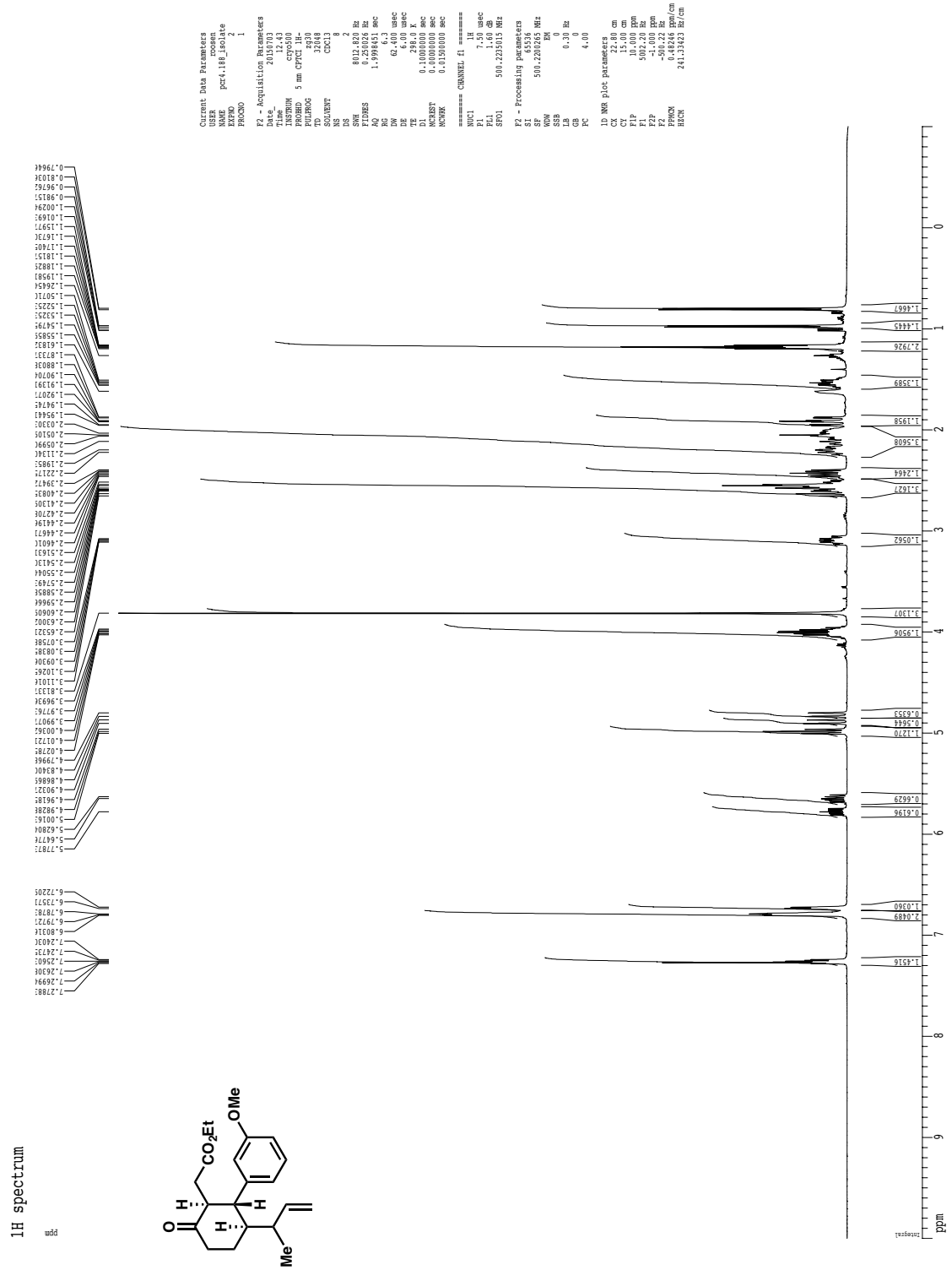
Z-restored spin-echo 13C spectrum with 1H decoupling



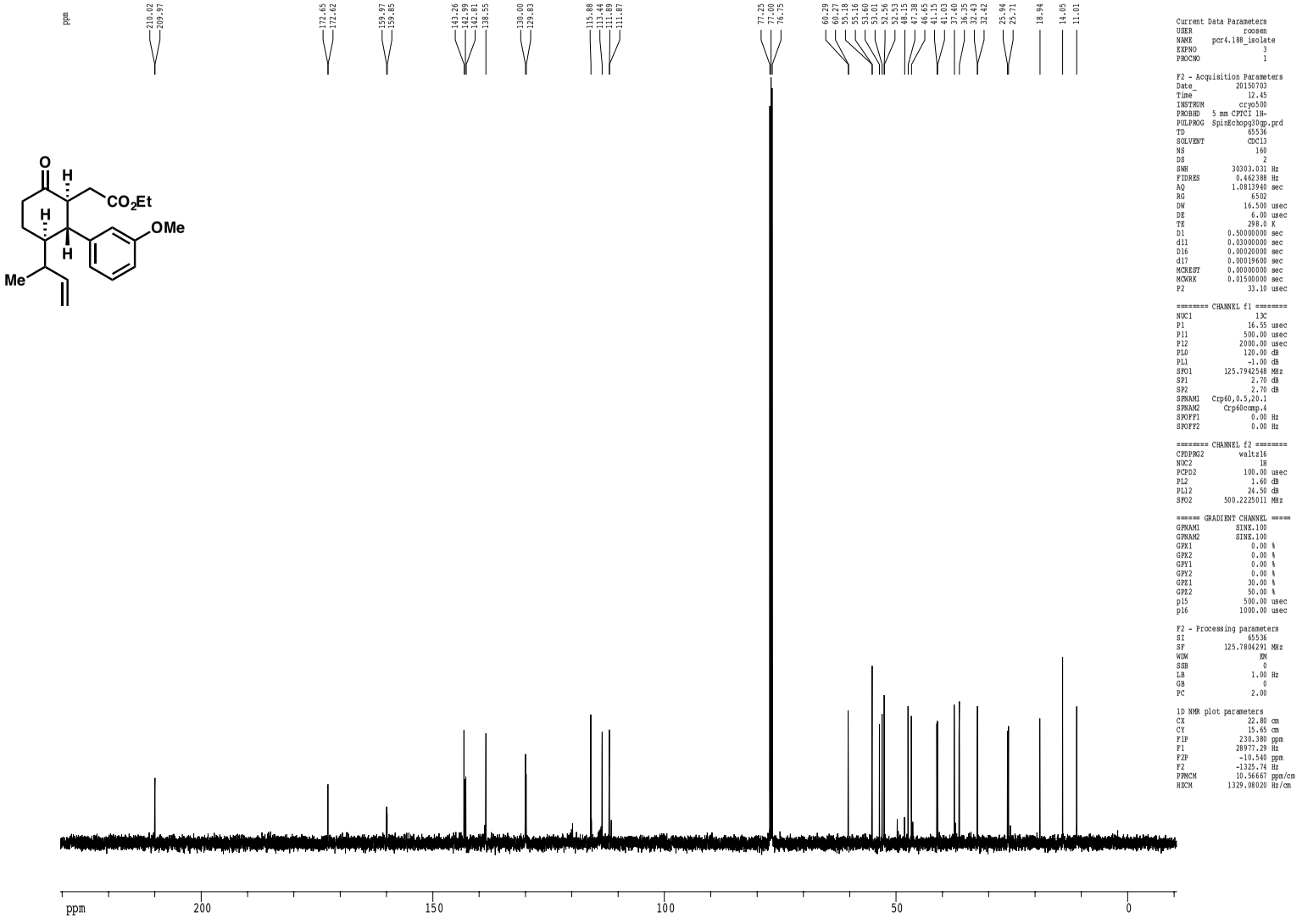

```
Current Data Parameters
USER              roosen
NAME       pcr5.011_f5-8
EXPNO                 2
PROCNO                1

F2 - Acquisition Parameters
Date_          20151025
Time              20.35
INSTRUM         cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD                65536
SOLVENT           CDCl3
NS                  112
DS                    2
SWH           30303.031 Hz
FIDRES        0.462388 Hz
AQ            1.0813940 sec
RG               7298.2
DW                16.500 usec
DE                 6.00 usec
TE               298.0 K
D1            0.50000000 sec
d11           0.03000000 sec
D16           0.00020000 sec
d17           0.00019600 sec
MCREST        0.00000000 sec
MCWRK         0.01500000 sec
P2                33.10 usec

======= CHANNEL f1 =======
NUC1                13C
P1                16.55 usec
P11              500.00 usec
P12             2000.00 usec
PL0              120.00 dB
PL1               -1.00 dB
SFO1        125.7942548 MHz
SP1                2.70 dB
SP2                2.70 dB
SPNAM1    Crp60,0.5,20.1
SPNAM2      Crp60comp.4
SPOFF1               0.00 Hz
SPOFF2               0.00 Hz

======= CHANNEL f2 =======
CPDPRG2          waltz16
NUC2                1H
PCPD2             100.00 usec
PL2                1.60 dB
PL12              24.50 dB
SFO2        500.2225011 MHz

===== GRADIENT CHANNEL ====
GPNAM1          SINE.100
GPNAM2          SINE.100
GPX1               0.00 %
GPX2               0.00 %
GPY1               0.00 %
GPY2               0.00 %
GPZ1              30.00 %
GPZ2              50.00 %
p15              500.00 usec
p16             1000.00 usec

F2 - Processing parameters
SI                 65536
SF          125.7804698 MHz
WDW                   EM
SSB                    0
LB                  1.00 Hz
GB                     0
PC                  2.00

1D NMR plot parameters
CX                 22.80 cm
CY                 15.65 cm
F1P              230.056 ppm
F1               28936.60 Hz
F2P              -10.864 ppm
F2               -1366.43 Hz
PPMCM            10.56667 ppm/cm
HZCM          1329.08032 Hz/cm
```


1H spectrum
OMe
OTMS
H
H
Me
ppm


Z-restored spin-echo 13C spectrum with 1H decoupling
OTMS
OMe
H
H
Me
ppm


1H spectrum
ppm
Integral
Current Data Parameters
NAME pcr4.188_isolate
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20151701
Time 12.43
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 8
DS 2
SWH 8012.820 Hz
FIDRES 0.244409 Hz
AQ 1.9998451 sec
RG 6.3
DW 62.400 usec
DE 6.00 usec
TE 298.1 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 7.50 usec
PL1 1.60 dB
SFO1 500.2235015 MHz
F2 - Processing parameters
SI 65536
SF 500.2200265 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00
1D NMR plot parameters
CX 27.00 cm
CY 15.00 cm
F1P 10.000 ppm
F1 5002.20 Hz
F2P -1.000 ppm
F2 -500.22 Hz
PPMCM 0.48246 ppm/cm
HZCM 241.33423 Hz/cm
1.4667
1.4445
2.7926
1.3589
1.1958
3.5608
1.2464
1.1627
1.0562
3.1307
1.9506
1.1270
0.5644
0.6353
0.6196
0.6679
1.0360
2.0489
1.4516
OMe
CO2Et
H
H
H
O
Me

Z-restored spin-echo 13C spectrum with 1H decoupling



Current Data Parameters
USER roosen
NAME pcr4.188_isolate
EXPNO 3
PROCNO 1

F2 - Acquisition Parameters
Date_ 20150703
Time 12.45
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG SpinEchopg30gp.prd
TD 65536
SOLVENT CDCl3
NS 160
DS 2
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0813940 sec
RG 6502
DW 16.500 usec
DE 6.00 usec
TE 298.0 K
D1 0.50000000 sec
d11 0.03000000 sec
D16 0.00020000 sec
d17 0.00019600 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
P2 33.10 usec

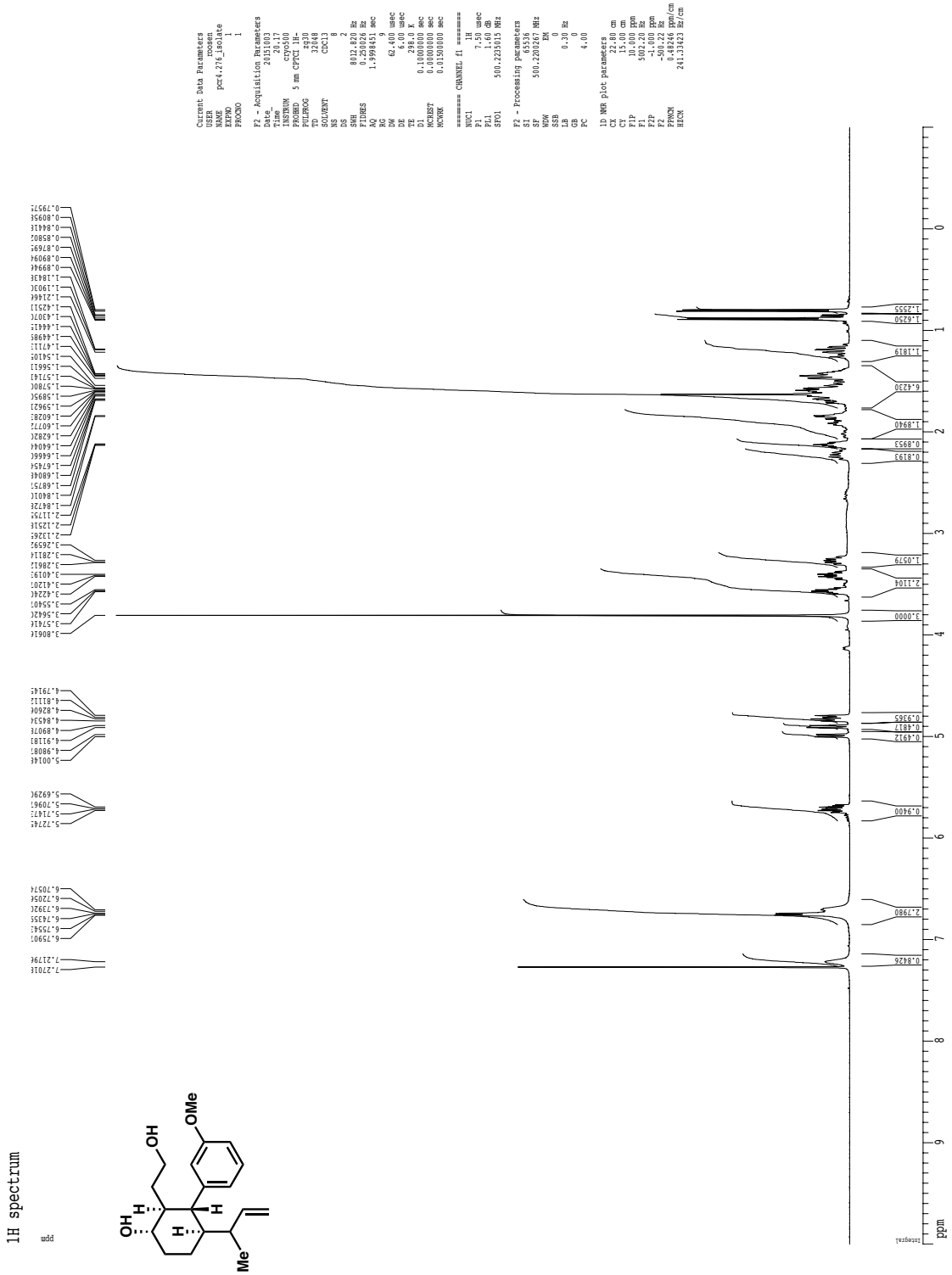
======= CHANNEL f1 =======
NUC1 13C
P1 16.55 usec
P11 500.00 usec
P12 2000.00 usec
PL0 120.00 dB
PL1 -1.00 dB
SFO1 125.7942548 MHz
SP1 2.70 dB
SP2 2.70 dB
SPNAM1 Crp60,0.5,20.1
SPNAM2 Crp60comp.4
SPOFF1 0.00 Hz
SPOFF2 0.00 Hz

======= CHANNEL f2 =======
CPDPRG2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 1.60 dB
PL12 24.50 dB
SFO2 500.2225011 MHz

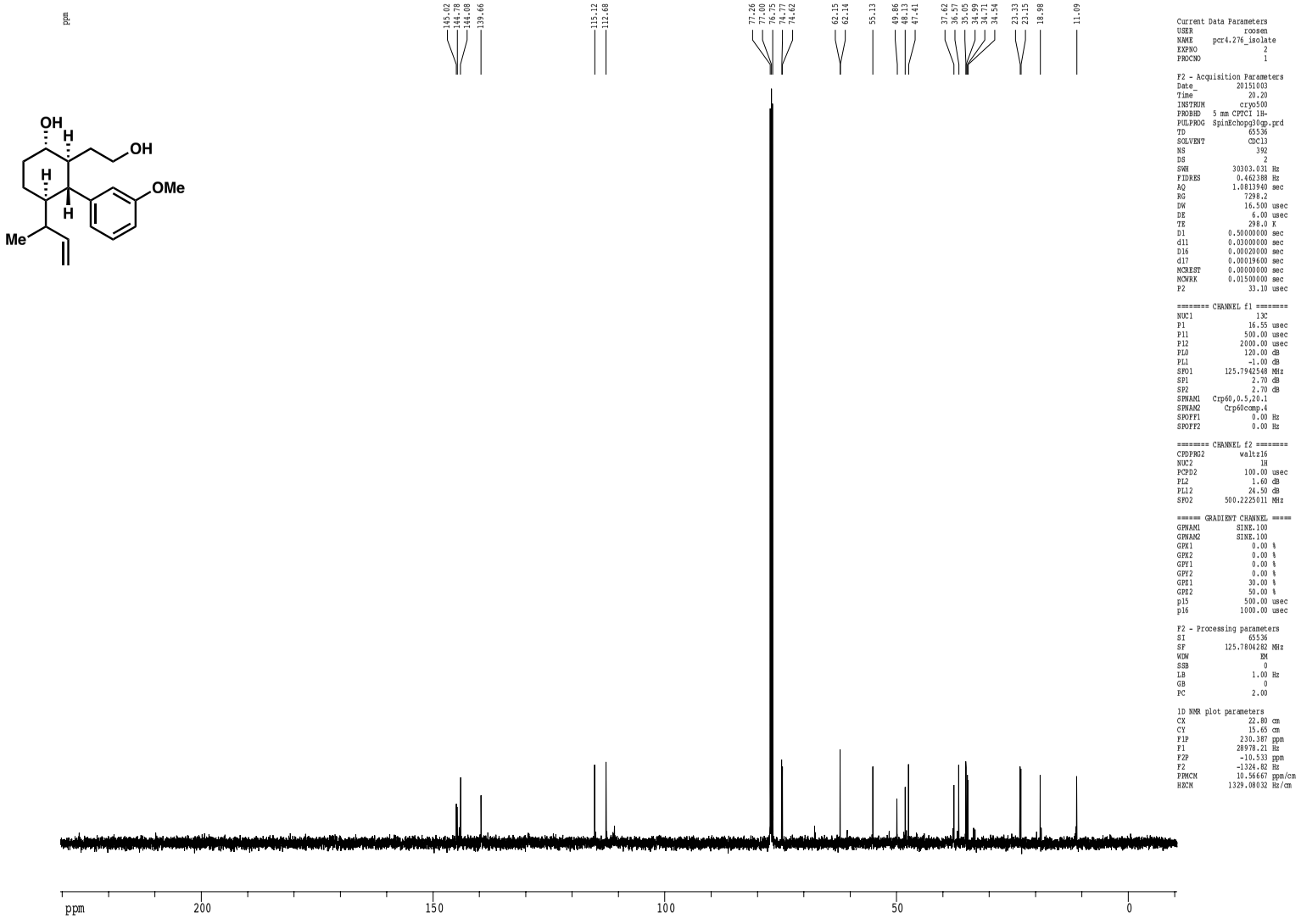
===== GRADIENT CHANNEL ====
GPNAM1 SINE.100
GPNAM2 SINE.100
GPX1 0.00 %
GPX2 0.00 %
GPY1 0.00 %
GPY2 0.00 %
GPZ1 30.00 %
GPZ2 50.00 %
p15 500.00 usec
p16 1000.00 usec

F2 - Processing parameters
SI 65536
SF 125.7804291 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00

1D NMR plot parameters
CX 22.80 cm
CY 15.65 cm
F1P 230.380 ppm
F1 28977.29 Hz
F2P -10.540 ppm
F2 -1325.74 Hz
PPMCM 10.56667 ppm/cm
HZCM 1329.08020 Hz/cm


1H spectrum
ppm
OH
OMe
H
H
H
Me

Z-restored spin-echo 13C spectrum with 1H decoupling



Current Data Parameters

USER	roosen
NAME	pcr4.276_isolate
EXPNO	2
PROCNO	1

F2 - Acquisition Parameters

Date_	20151003
Time	20.20
INSTRUM	cryo500
PROBHD	5 mm CPTCI 1H-
PULPROG	SpinEchopg30gp.prd
TD	65536
SOLVENT	CDCl3
NS	392
DS	2
SWH	30303.031 Hz
FIDRES	0.462388 Hz
AQ	1.0813940 sec
RG	7298.2
DW	16.500 usec
DE	6.00 usec
TE	298.0 K
D1	0.50000000 sec
d11	0.03000000 sec
D16	0.00020000 sec
d17	0.00019600 sec
MCREST	0.00000000 sec
MCWRK	0.01500000 sec
P2	33.10 usec

======= CHANNEL f1 =======

NUC1	13C
P1	16.55 usec
P11	500.00 usec
P12	2000.00 usec
PL0	120.00 dB
PL1	-1.00 dB
SFO1	125.7942548 MHz
SP1	2.70 dB
SP2	2.70 dB
SPNAM1	Crp60,0.5,20.1
SPNAM2	Crp60comp.4
SPOFF1	0.00 Hz
SPOFF2	0.00 Hz

======= CHANNEL f2 =======

CPDPRG2	waltz16
NUC2	1H
PCPD2	100.00 usec
PL2	1.60 dB
PL12	24.50 dB
SFO2	500.2225011 MHz

===== GRADIENT CHANNEL ====

GPNAM1	SINE.100
GPNAM2	SINE.100
GPX1	0.00 %
GPX2	0.00 %
GPY1	0.00 %
GPY2	0.00 %
GPZ1	30.00 %
GPZ2	50.00 %
p15	500.00 usec
p16	1000.00 usec

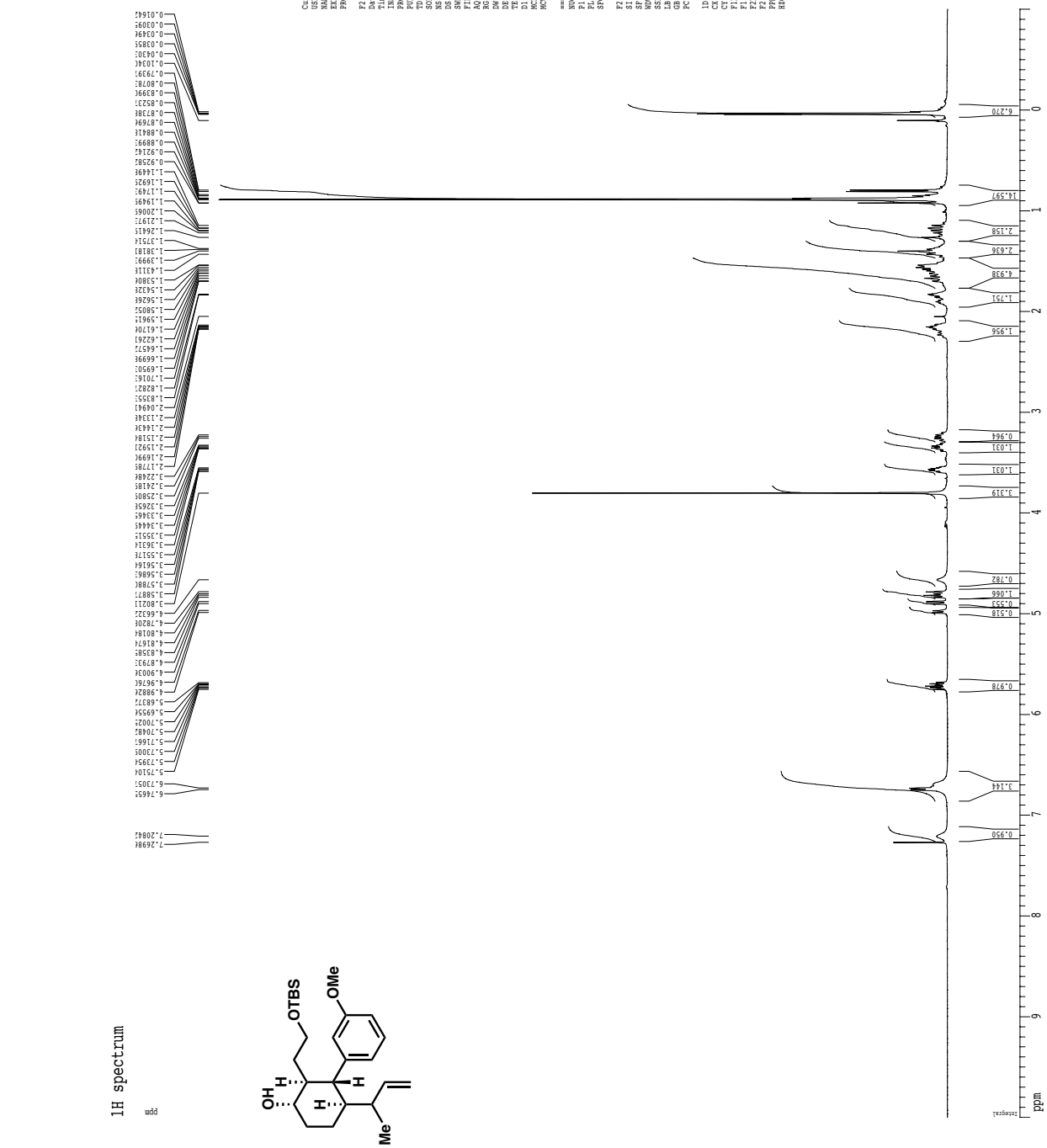
F2 - Processing parameters

SI	65536
SF	125.7804282 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	2.00

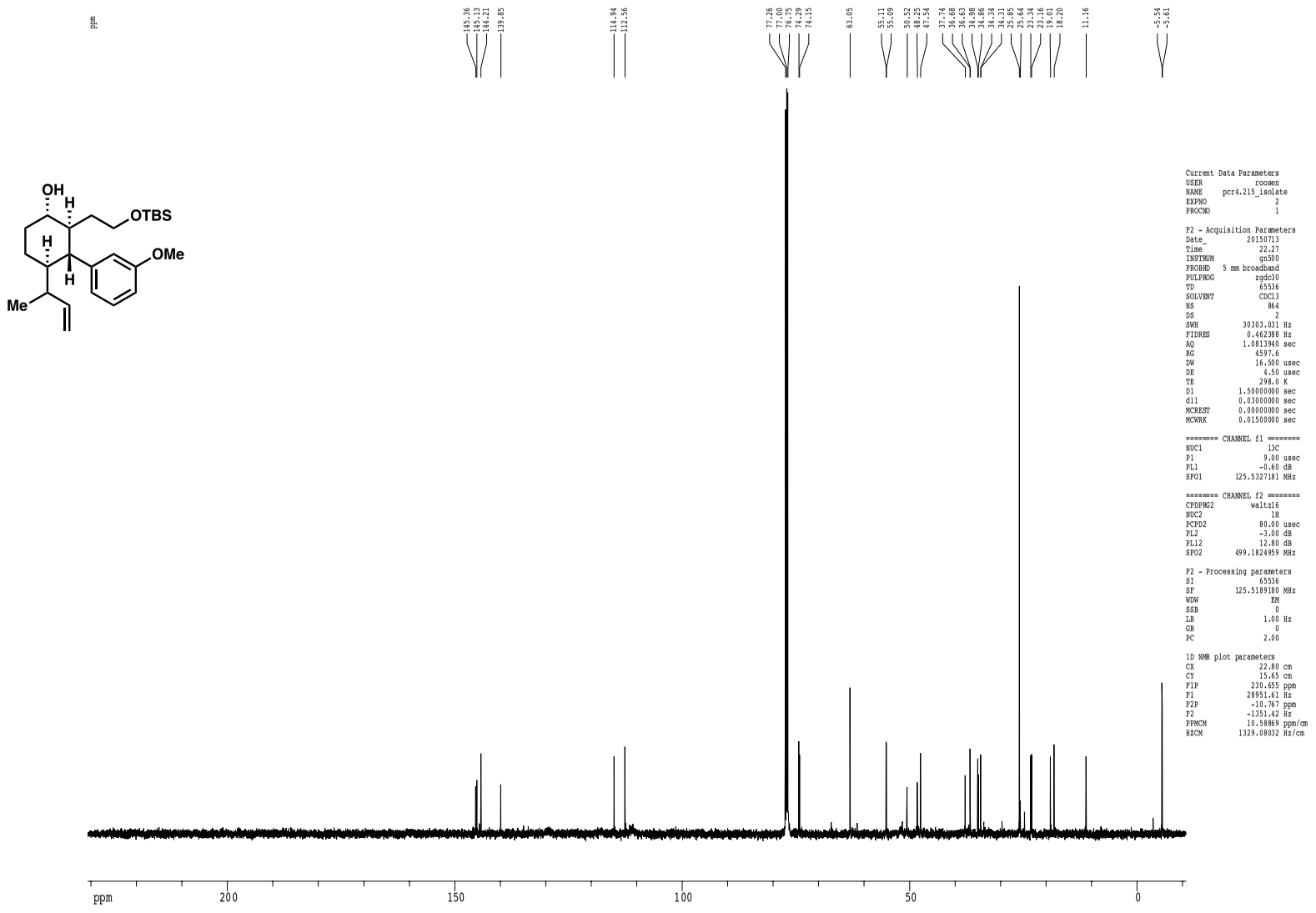
1D NMR plot parameters

CX	22.80 cm
CY	15.65 cm
F1P	230.387 ppm
F1	28978.21 Hz
F2P	-10.533 ppm
F2	-1324.82 Hz
PPMCM	10.56667 ppm/cm
HZCM	1329.08032 Hz/cm

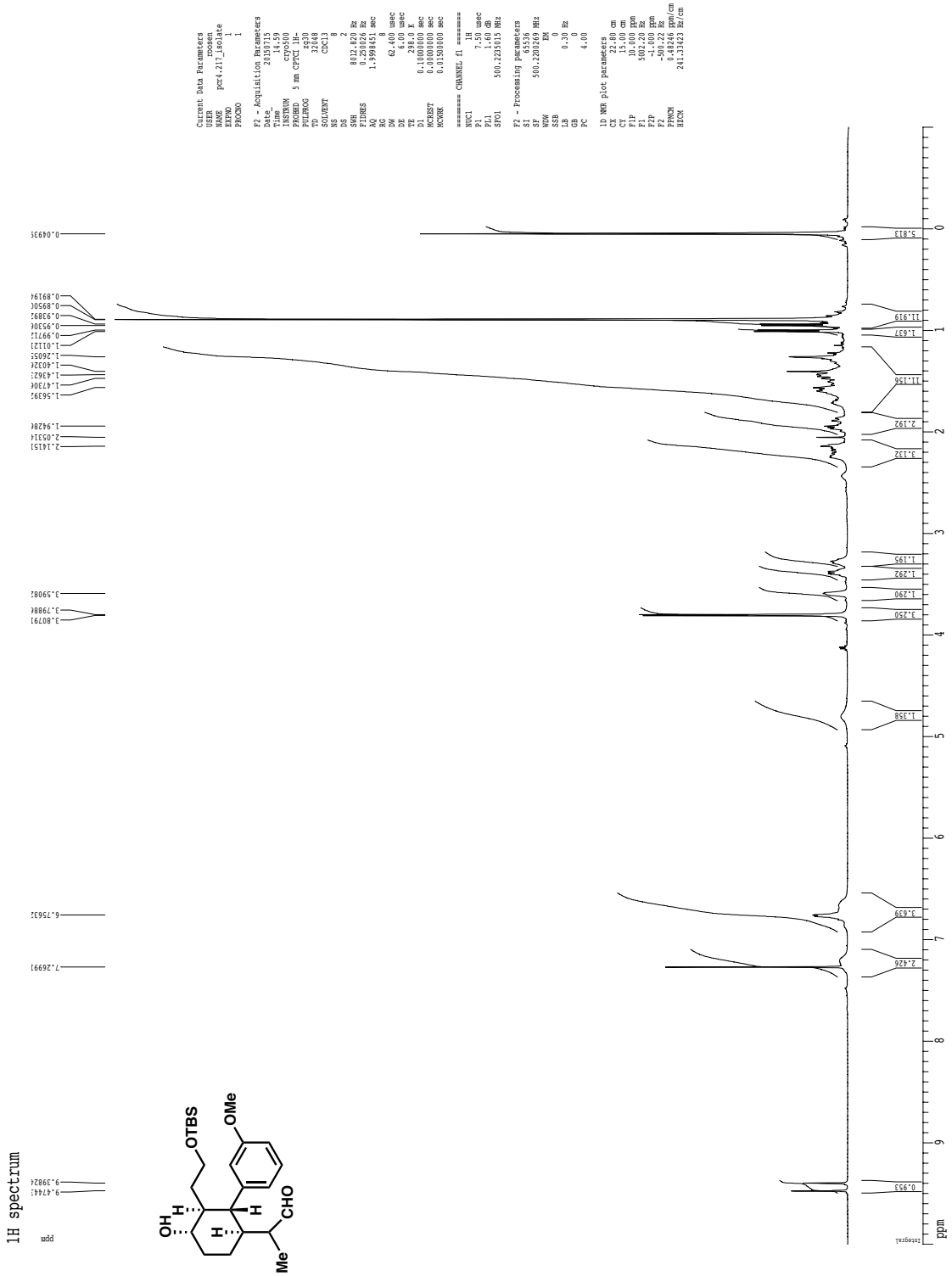
1H spectrum



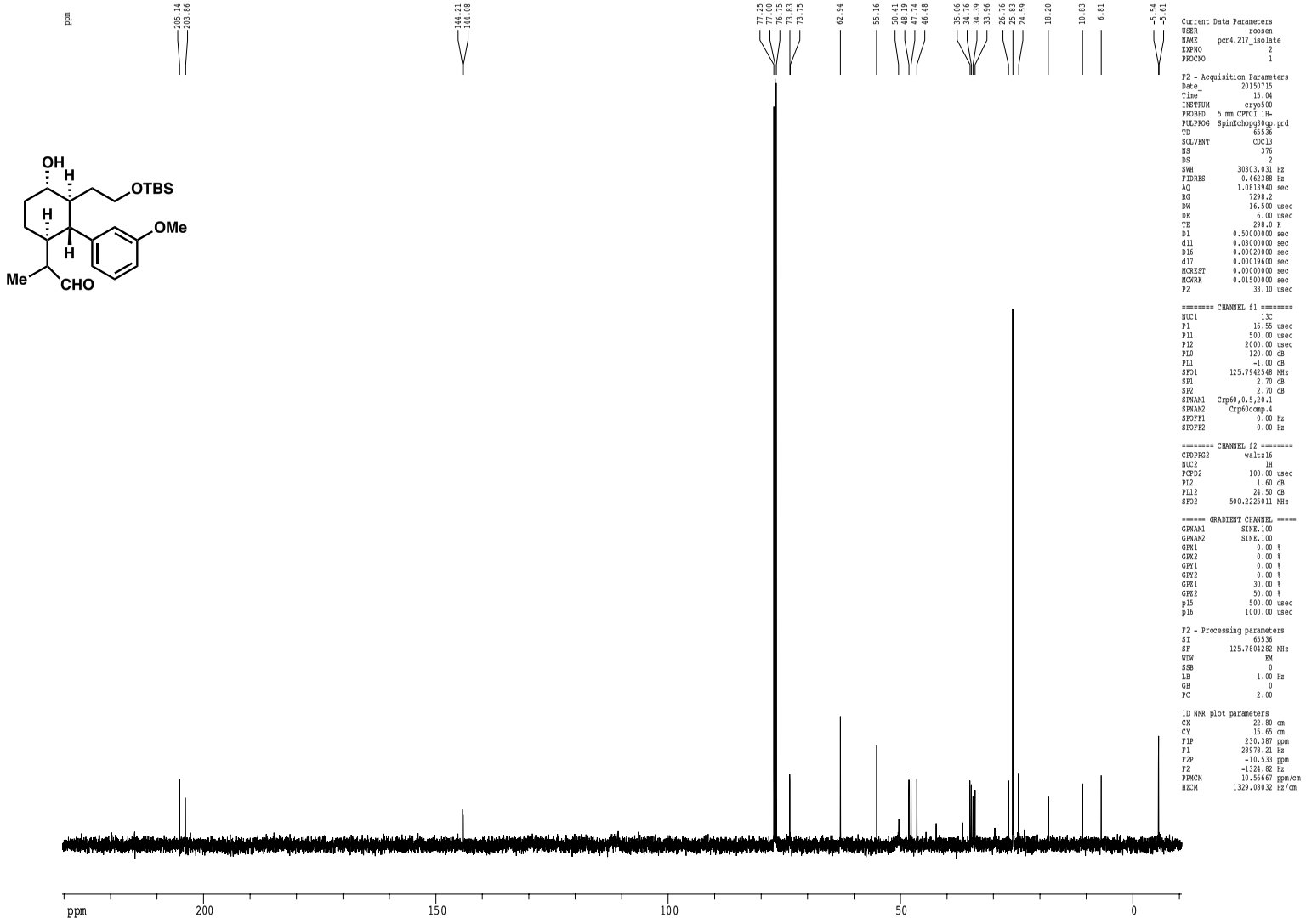
13C spectrum with 1H decoupling

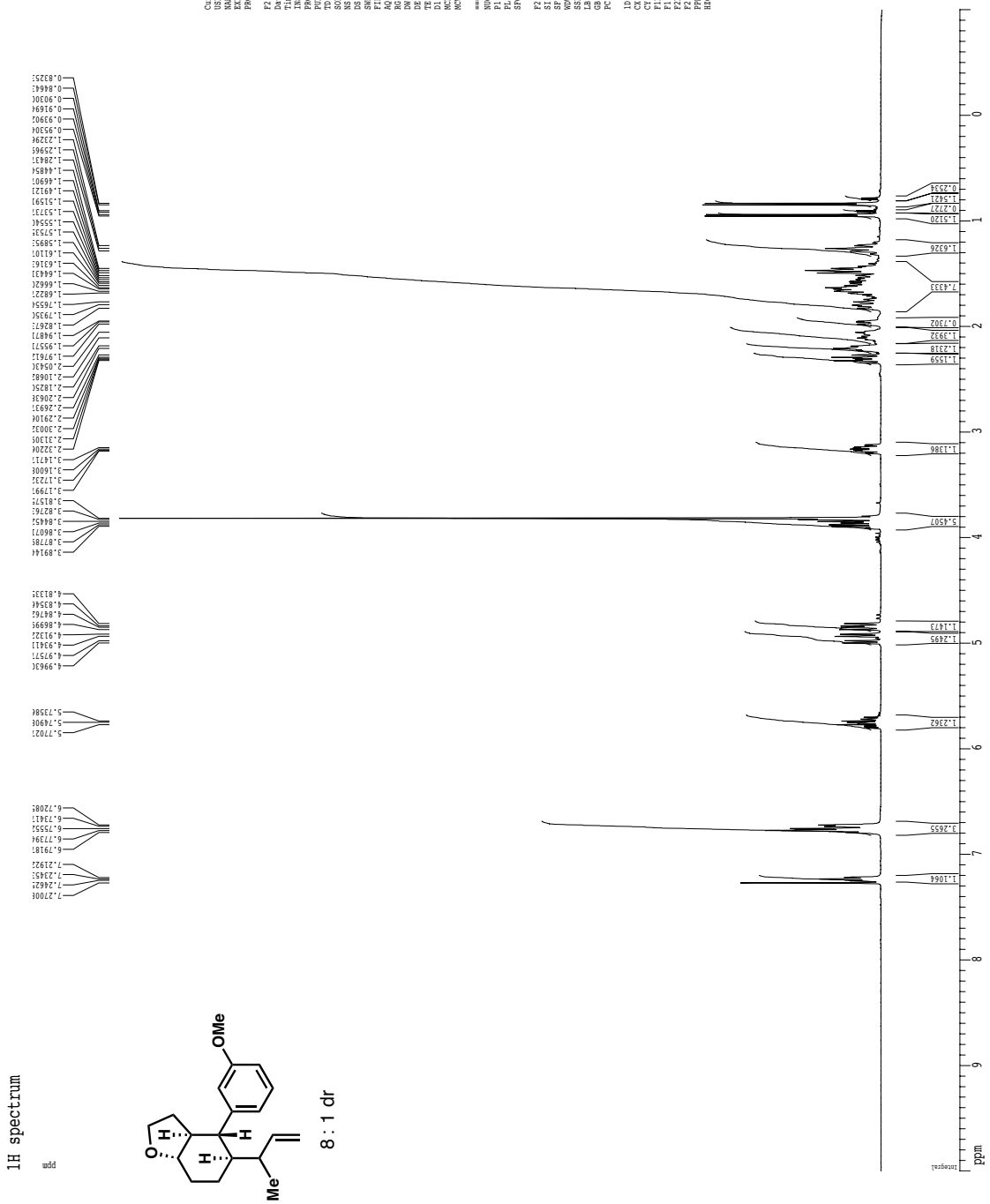



```
Current Data Parameters
USER                roosen
NAME       pcr4.215_isolate
EXPNO                    2
PROCNO                   1

F2 - Acquisition Parameters
Date_             20150713
Time                 22.27
INSTRUM              qn500
PROBHD   5 mm broadband
PULPROG           zgdc30
TD                  65536
SOLVENT             CDCl3
NS                    864
DS                      2
SWH             30303.031 Hz
FIDRES          0.462388 Hz
AQ              1.0813940 sec
RG                 4597.6
DW                16.500 usec
DE                 4.50 usec
TE                298.0 K
D1              1.50000000 sec
d11             0.03000000 sec
MCREST          0.00000000 sec
MCWRK           0.01500000 sec

======== CHANNEL f1 ========
NUC1                  13C
P1                   9.00 usec
PL1                 -0.60 dB
SFO1         125.5327181 MHz

======== CHANNEL f2 ========
CPDPRG2           waltz16
NUC2                   1H
PCPD2               80.00 usec
PL2                 -3.00 dB
PL12                12.80 dB
SFO2         499.1824959 MHz

F2 - Processing parameters
SI                  65536
SF           125.5189180 MHz
WDW                    EM
SSB                     0
LB                   1.00 Hz
GB                      0
PC                   2.00

1D NMR plot parameters
CX                  22.80 cm
CY                  15.65 cm
F1P               230.655 ppm
F1                28951.61 Hz
F2P               -10.767 ppm
F2                -1351.42 Hz
PPMCM             10.58869 ppm/cm
HZCM          1329.08032 Hz/cm
```

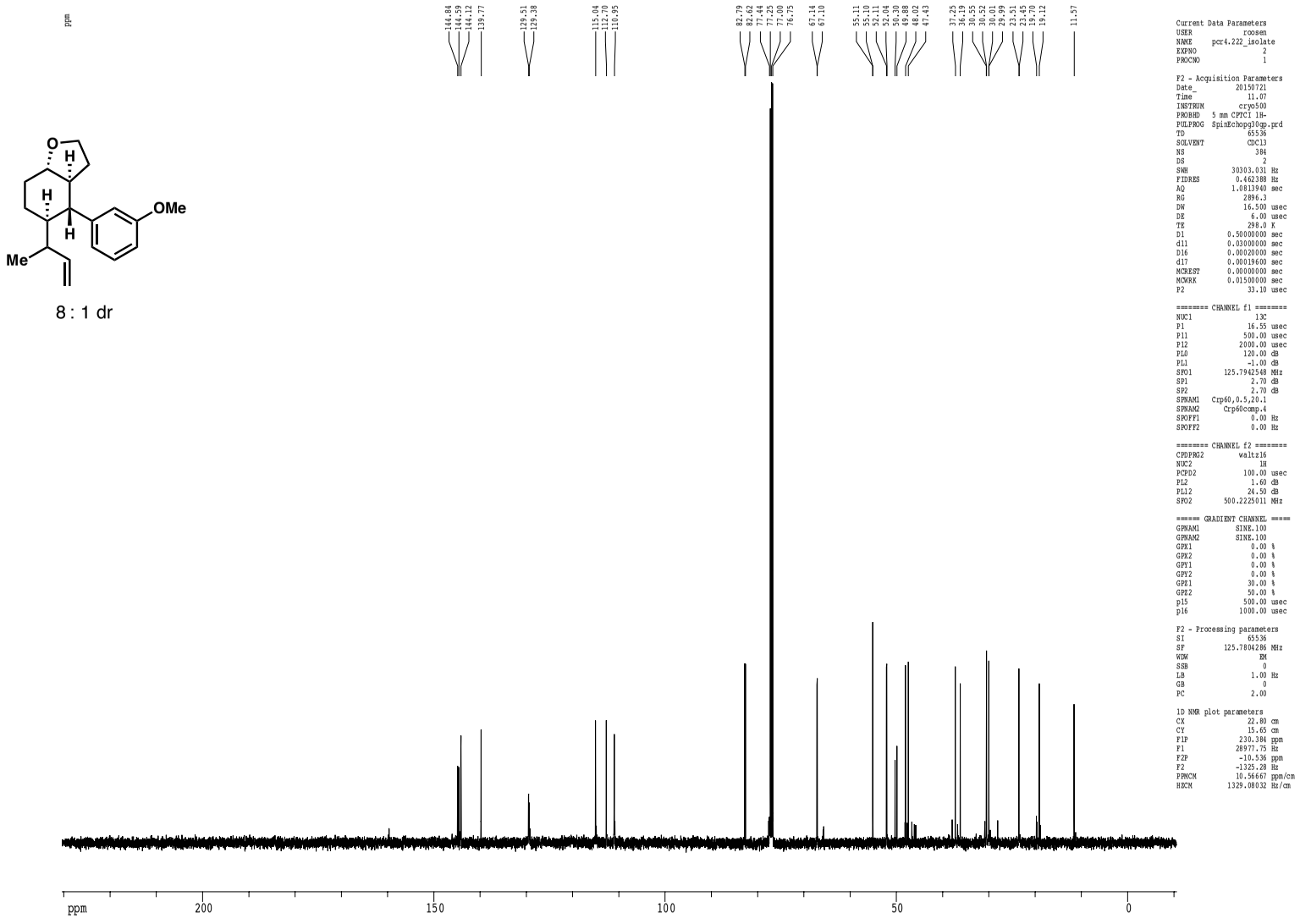

1H spectrum
ppm
OH
H
H
H
OTBS
OMe
CHO
Me
Current Data Parameters
NAME pcr4.217_isolate
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20151015
Time 14.59
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 8
DS 0
SWH 8012.820 Hz
FIDRES 0.244409 Hz
AQ 1.9998451 sec
RG 8
DW 62.400 usec
DE 6.00 usec
TE 298.1 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 7.50 usec
PL1 1.60 dB
SFO1 500.2235015 MHz
F2 - Processing parameters
SI 65536
SF 500.2200269 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00
1D NMR plot parameters
CX 27.00 cm
CY 15.00 cm
F1P 10.000 ppm
F1 5002.20 Hz
F2P -1.000 ppm
F2 -500.22 Hz
PPMCM 0.48246 ppm/cm
HZCM 241.33423 Hz/cm
0.04935
0.89194
0.89506
0.93892
0.95306
0.99712
1.01121
1.26055
1.40326
1.43621
1.47306
1.56391
1.94286
2.05314
2.14151
3.59082
3.79884
3.80791
6.75632
7.26991
9.39824
9.47441
5.813
11.919
1.637
11.156
2.192
3.132
1.195
1.292
1.290
3.250
1.358
3.639
2.426
0.953
Integral
ppm

Z-restored spin-echo 13C spectrum with 1H decoupling




1H spectrum
ppm
OMe
H
H
H
O
Me
8 : 1 dr

Z-restored spin-echo 13C spectrum with 1H decoupling



Current Data Parameters
USER roosen
NAME pcr4.222_isolate
EXPNO 2
PROCNO 1

F2 - Acquisition Parameters
Date_ 20150721
Time 11.07
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG SpinEchopg30gp.prd
TD 65536
SOLVENT CDCl3
NS 384
DS 2
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0813940 sec
RG 2896.3
DW 16.500 usec
DE 6.00 usec
TE 298.0 K
D1 0.50000000 sec
d11 0.03000000 sec
D16 0.00020000 sec
d17 0.00019600 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
P2 33.10 usec

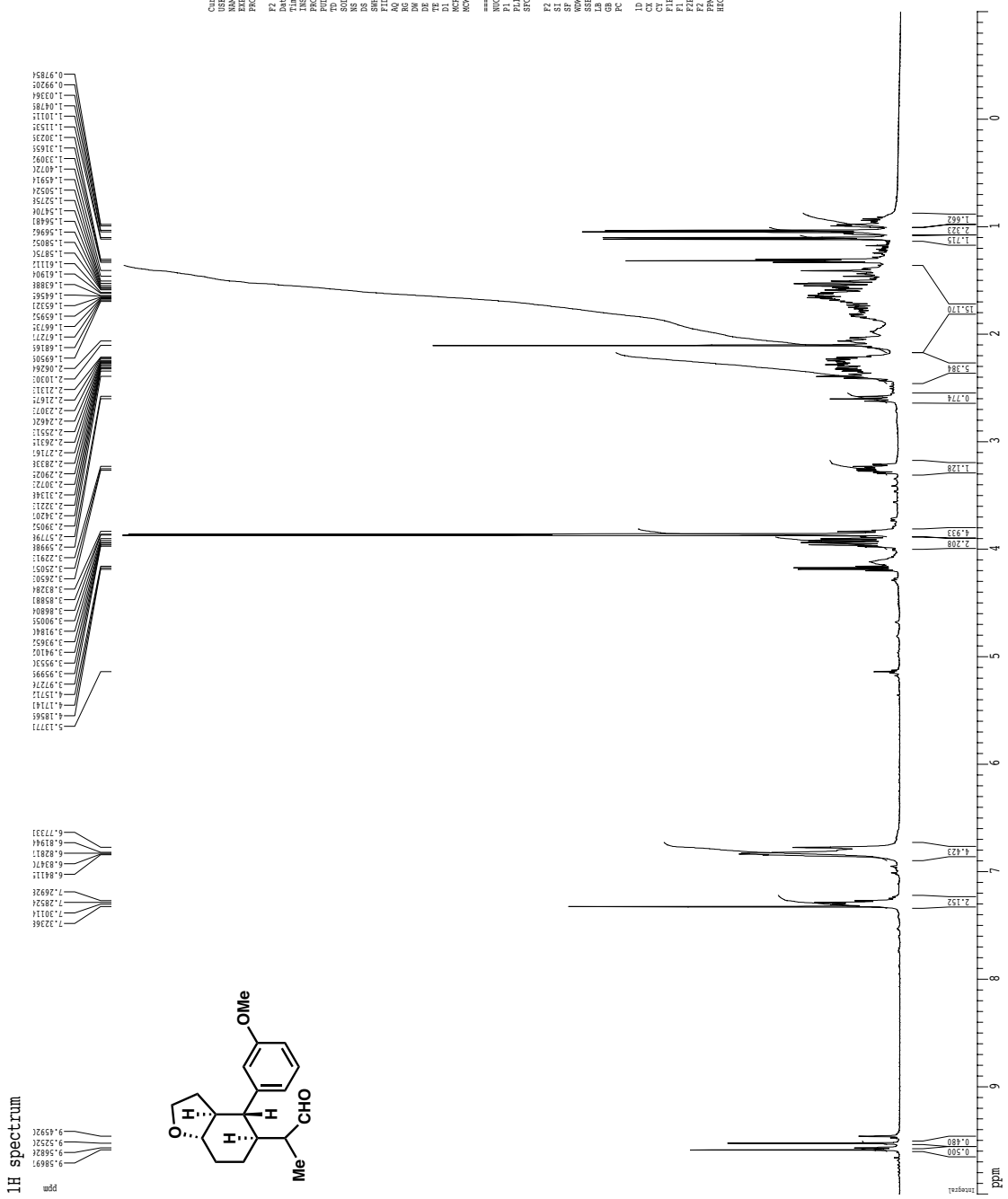
======= CHANNEL f1 =======
NUC1 13C
P1 16.55 usec
P11 500.00 usec
P12 2000.00 usec
PL0 120.00 dB
PL1 -1.00 dB
SFO1 125.7942548 MHz
SP1 2.70 dB
SP2 2.70 dB
SPNAM1 Crp60,0.5,20.1
SPNAM2 Crp60comp.4
SPOFF1 0.00 Hz
SPOFF2 0.00 Hz

======= CHANNEL f2 =======
CPDPRG2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 1.60 dB
PL12 24.50 dB
SFO2 500.2225011 MHz

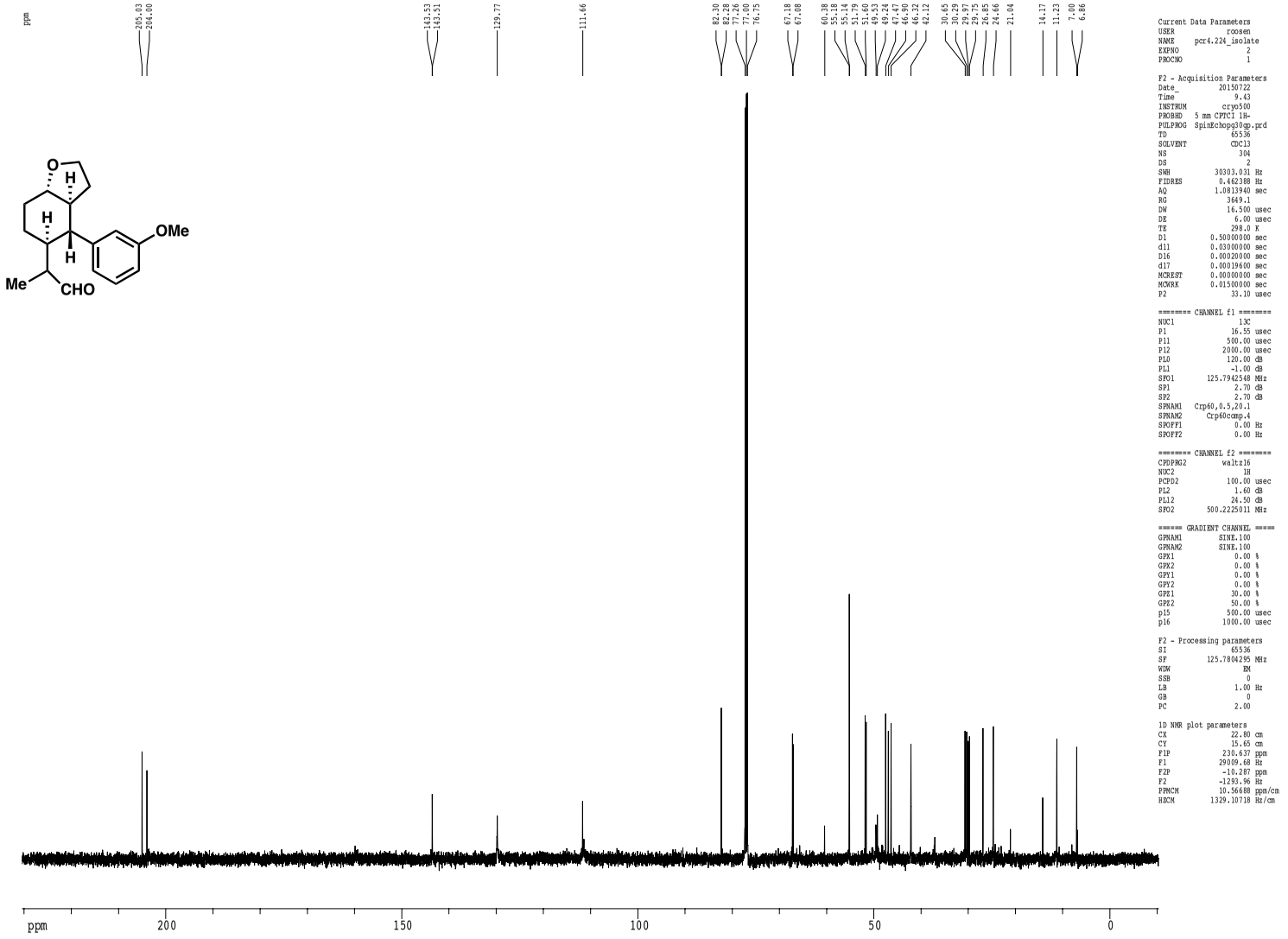
===== GRADIENT CHANNEL ====
GPNAM1 SINE.100
GPNAM2 SINE.100
GPX1 0.00 %
GPX2 0.00 %
GPY1 0.00 %
GPY2 0.00 %
GPZ1 30.00 %
GPZ2 50.00 %
p15 500.00 usec
p16 1000.00 usec

F2 - Processing parameters
SI 65536
SF 125.7804286 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00

1D NMR plot parameters
CX 22.80 cm
CY 15.65 cm
F1P 230.384 ppm
F1 28977.75 Hz
F2P -10.536 ppm
F2 -1325.28 Hz
PPMCM 10.56667 ppm/cm
HZCM 1329.08032 Hz/cm


1H spectrum
OMe
H
H
H
O
Me
CHO
ppm
Integral

Z-restored spin-echo 13C spectrum with 1H decoupling



Current Data Parameters
USER roosen
NAME pcr4.224_isolate
EXPNO 2
PROCNO 1

F2 - Acquisition Parameters
Date_ 20150722
Time 9.43
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG SpinEchopg30gp.prd
TD 65536
SOLVENT CDCl3
NS 304
DS 2
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0813940 sec
RG 3649.1
DW 16.500 usec
DE 6.00 usec
TE 298.0 K
D1 0.50000000 sec
d11 0.03000000 sec
D16 0.00020000 sec
d17 0.00019600 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
P2 33.10 usec

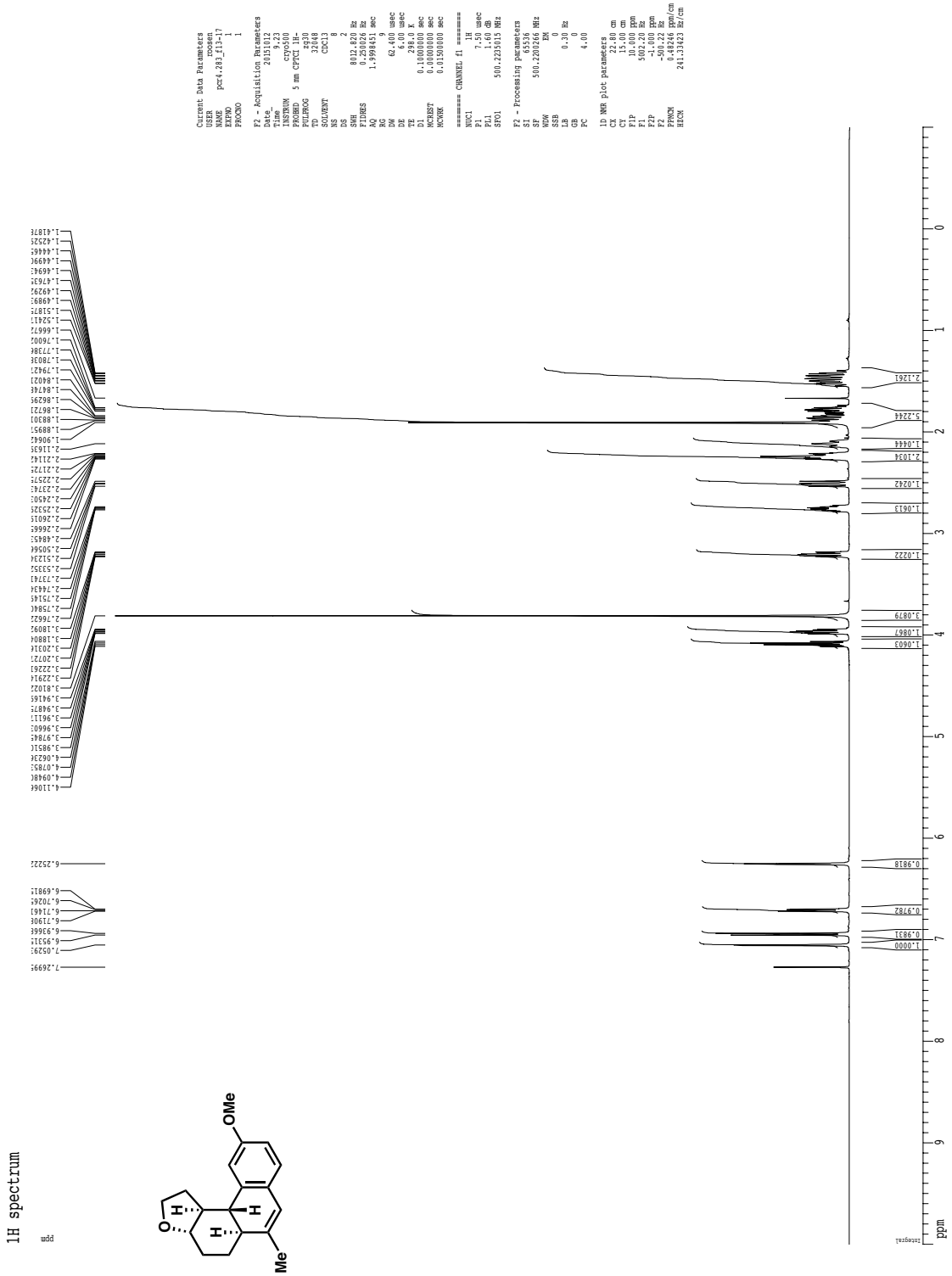
======= CHANNEL f1 =======
NUC1 13C
P1 16.55 usec
P11 500.00 usec
P12 2000.00 usec
PL0 120.00 dB
PL1 -1.00 dB
SFO1 125.7942548 MHz
SP1 2.70 dB
SP2 2.70 dB
SPNAM1 Crp60,0.5,20.1
SPNAM2 Crp60comp.4
SPOFF1 0.00 Hz
SPOFF2 0.00 Hz

======= CHANNEL f2 =======
CPDPRG2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 1.60 dB
PL12 24.50 dB
SFO2 500.2225011 MHz

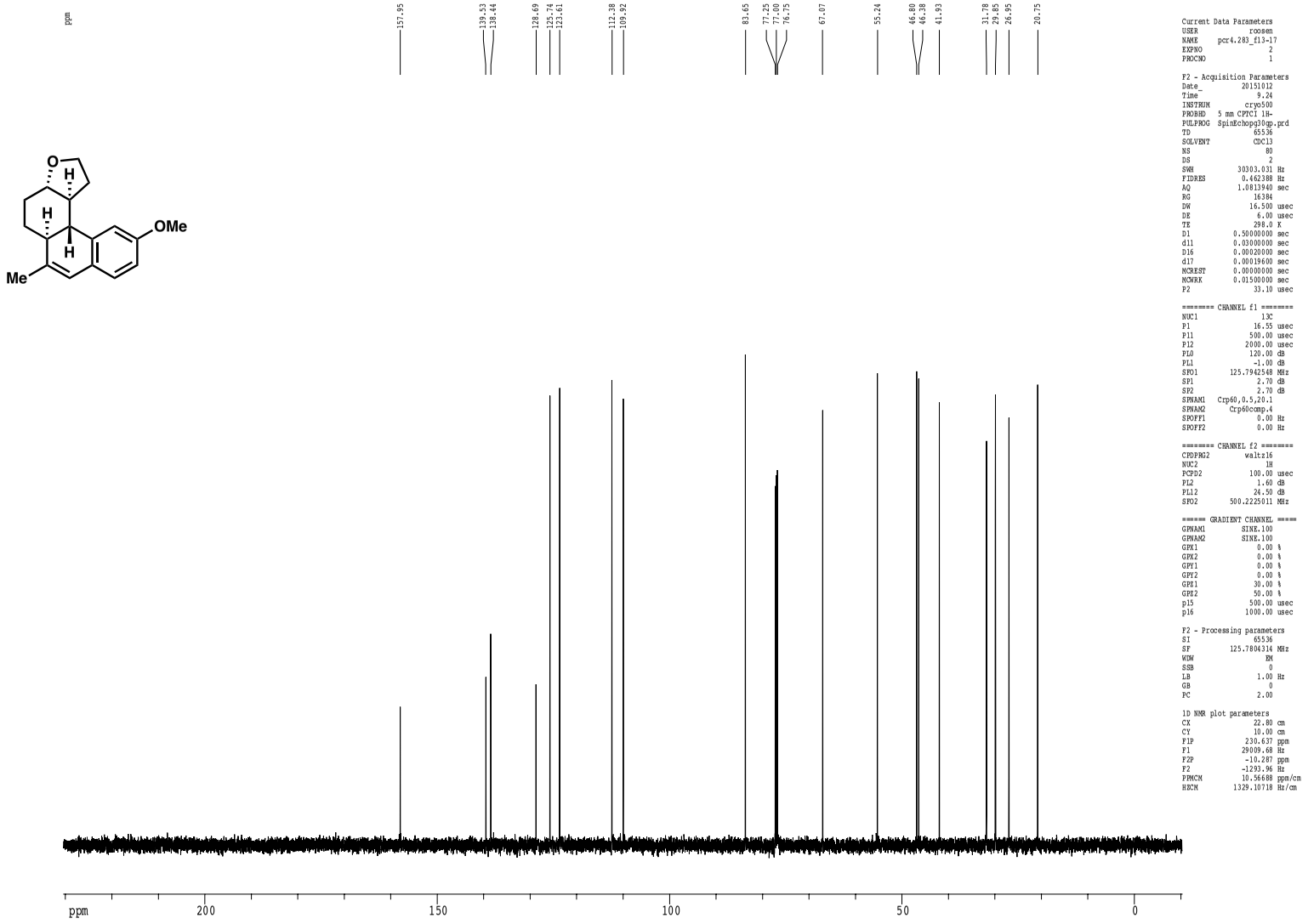
===== GRADIENT CHANNEL ====
GPNAM1 SINE.100
GPNAM2 SINE.100
GPX1 0.00 %
GPX2 0.00 %
GPY1 0.00 %
GPY2 0.00 %
GPZ1 30.00 %
GPZ2 50.00 %
p15 500.00 usec
p16 1000.00 usec

F2 - Processing parameters
SI 65536
SF 125.7804295 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00

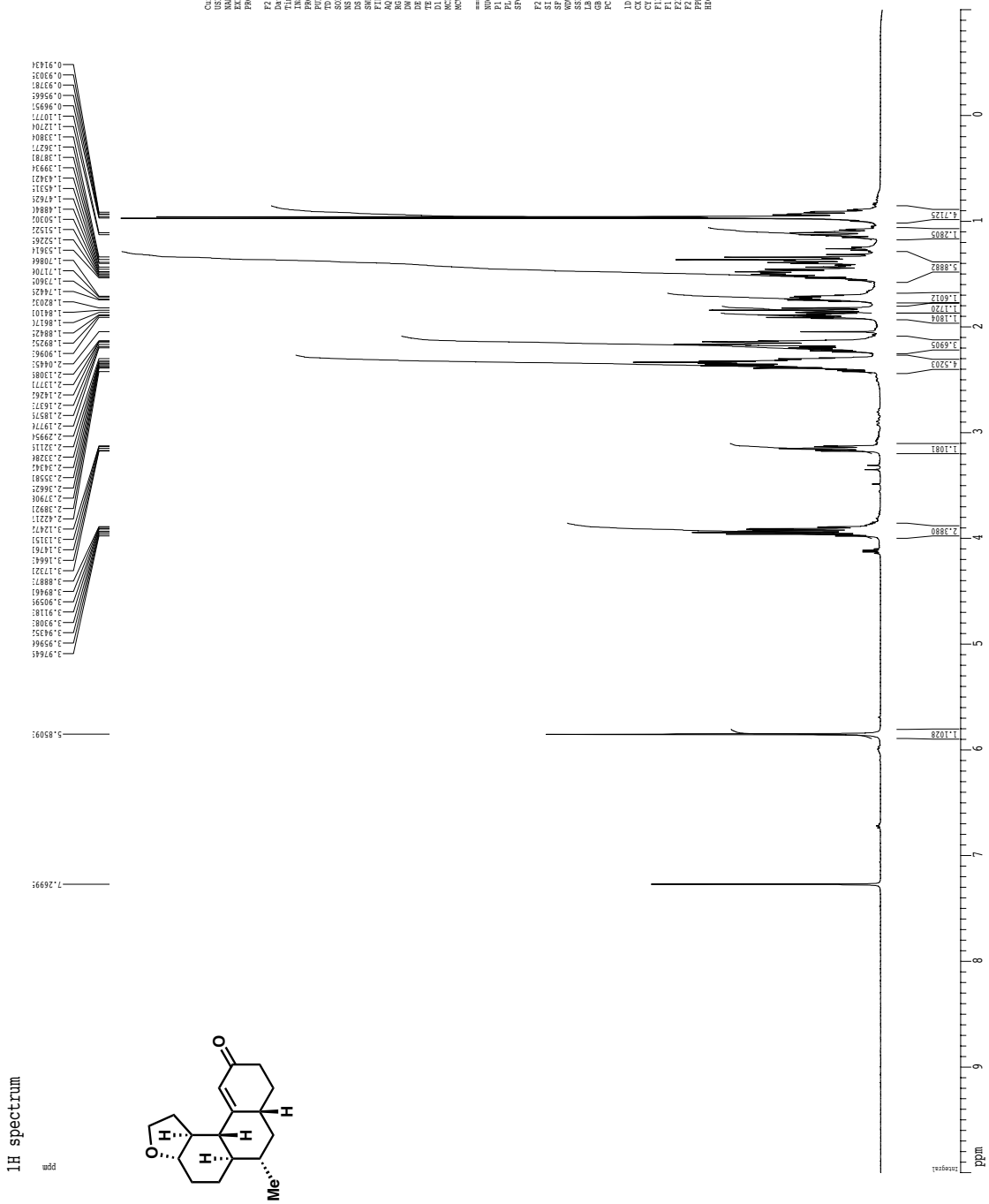
1D NMR plot parameters
CX 22.80 cm
CY 15.65 cm
F1P 230.637 ppm
F1 29009.68 Hz
F2P -10.287 ppm
F2 -1293.96 Hz
PPMCM 10.56688 ppm/cm
HZCM 1329.10718 Hz/cm


1H spectrum
ppm
OMe
H
H
H
O
Me
Integral
ppm

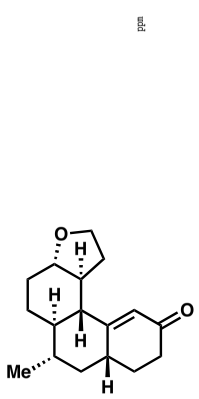
Z-restored spin-echo 13C spectrum with 1H decoupling

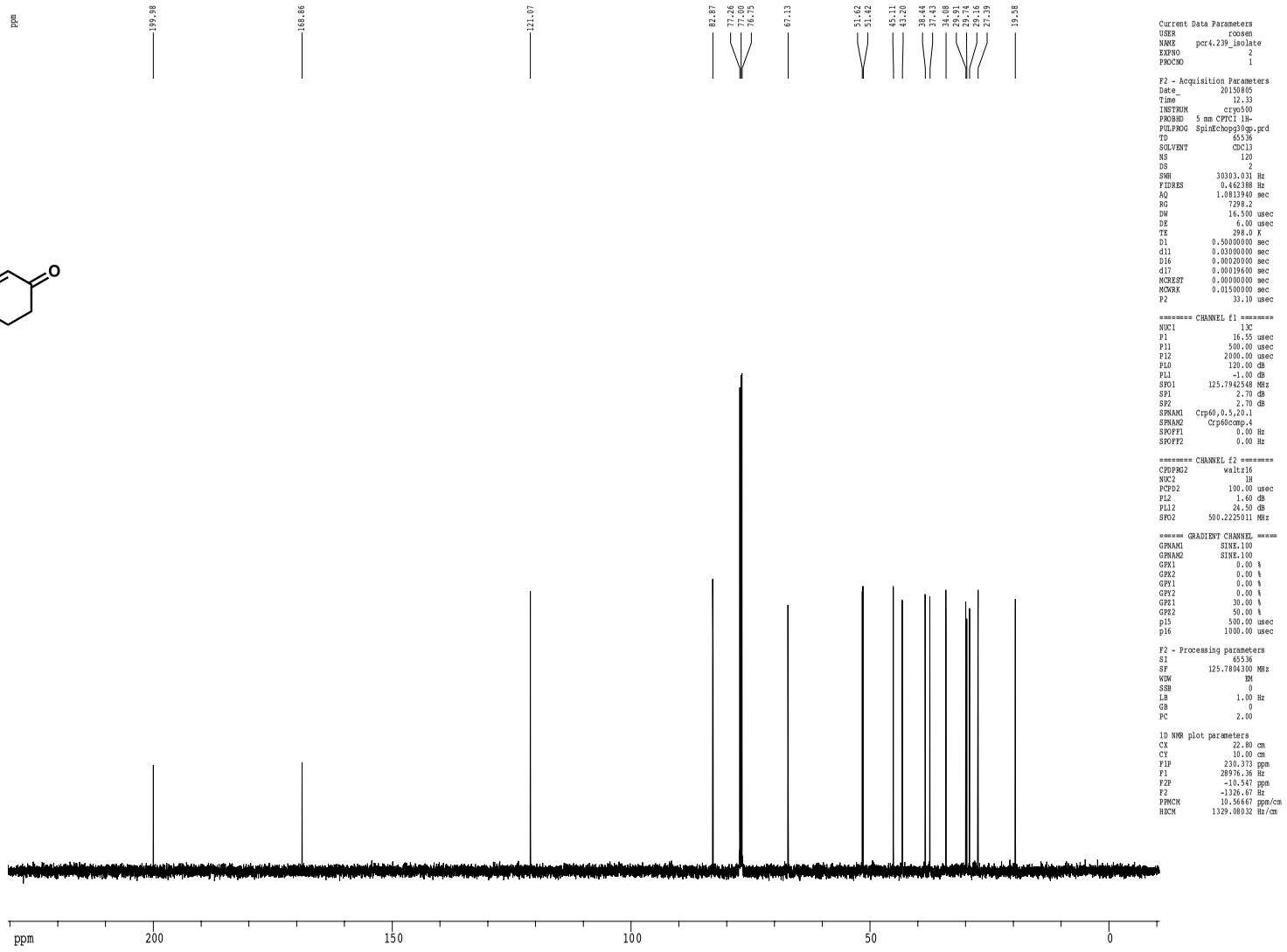



```
Current Data Parameters
USER              roosen
NAME      pcr4.283_f13-17
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_          20151012
Time              9.24
INSTRUM         cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD               65536
SOLVENT          CDCl3
NS                  80
DS                   2
SWH           30303.031 Hz
FIDRES        0.462388 Hz
AQ            1.0813940 sec
RG               16384
DW               16.500 usec
DE                6.00 usec
TE              298.0 K
D1           0.50000000 sec
d11          0.03000000 sec
D16          0.00020000 sec
d17          0.00019600 sec
MCREST       0.00000000 sec
MCWRK        0.01500000 sec
P2               33.10 usec

======= CHANNEL f1 =======
NUC1               13C
P1               16.55 usec
P11             500.00 usec
P12            2000.00 usec
PL0             120.00 dB
PL1              -1.00 dB
SFO1        125.7942548 MHz
SP1              2.70 dB
SP2              2.70 dB
SPNAM1   Crp60,0.5,20.1
SPNAM2     Crp60comp.4
SPOFF1              0.00 Hz
SPOFF2              0.00 Hz

======= CHANNEL f2 =======
CPDPRG2          waltz16
NUC2                1H
PCPD2           100.00 usec
PL2               1.60 dB
PL12             24.50 dB
SFO2        500.2225011 MHz

===== GRADIENT CHANNEL ====
GPNAM1          SINE.100
GPNAM2          SINE.100
GPX1                0.00 %
GPX2                0.00 %
GPY1                0.00 %
GPY2                0.00 %
GPZ1               30.00 %
GPZ2               50.00 %
p15              500.00 usec
p16             1000.00 usec

F2 - Processing parameters
SI                 65536
SF          125.7804314 MHz
WDW                   EM
SSB                    0
LB                  1.00 Hz
GB                     0
PC                  2.00

1D NMR plot parameters
CX                 22.80 cm
CY                 10.00 cm
F1P              230.637 ppm
F1               29009.68 Hz
F2P              -10.287 ppm
F2               -1293.96 Hz
PPMCM            10.56688 ppm/cm
HZCM          1329.10718 Hz/cm
```

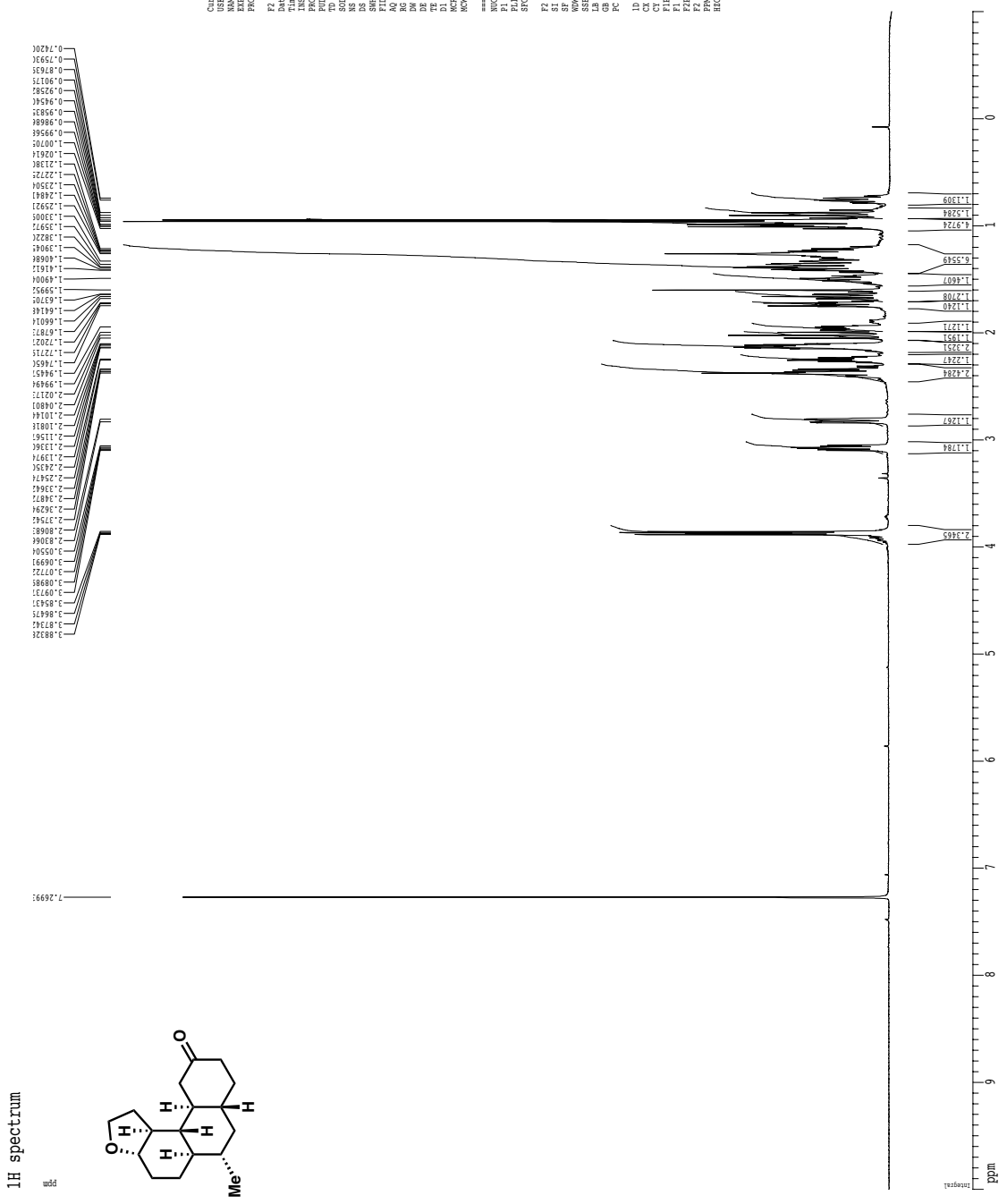

1H spectrum
ppm
Integral
Me

Z-restored spin-echo 13C spectrum with 1H decoupling

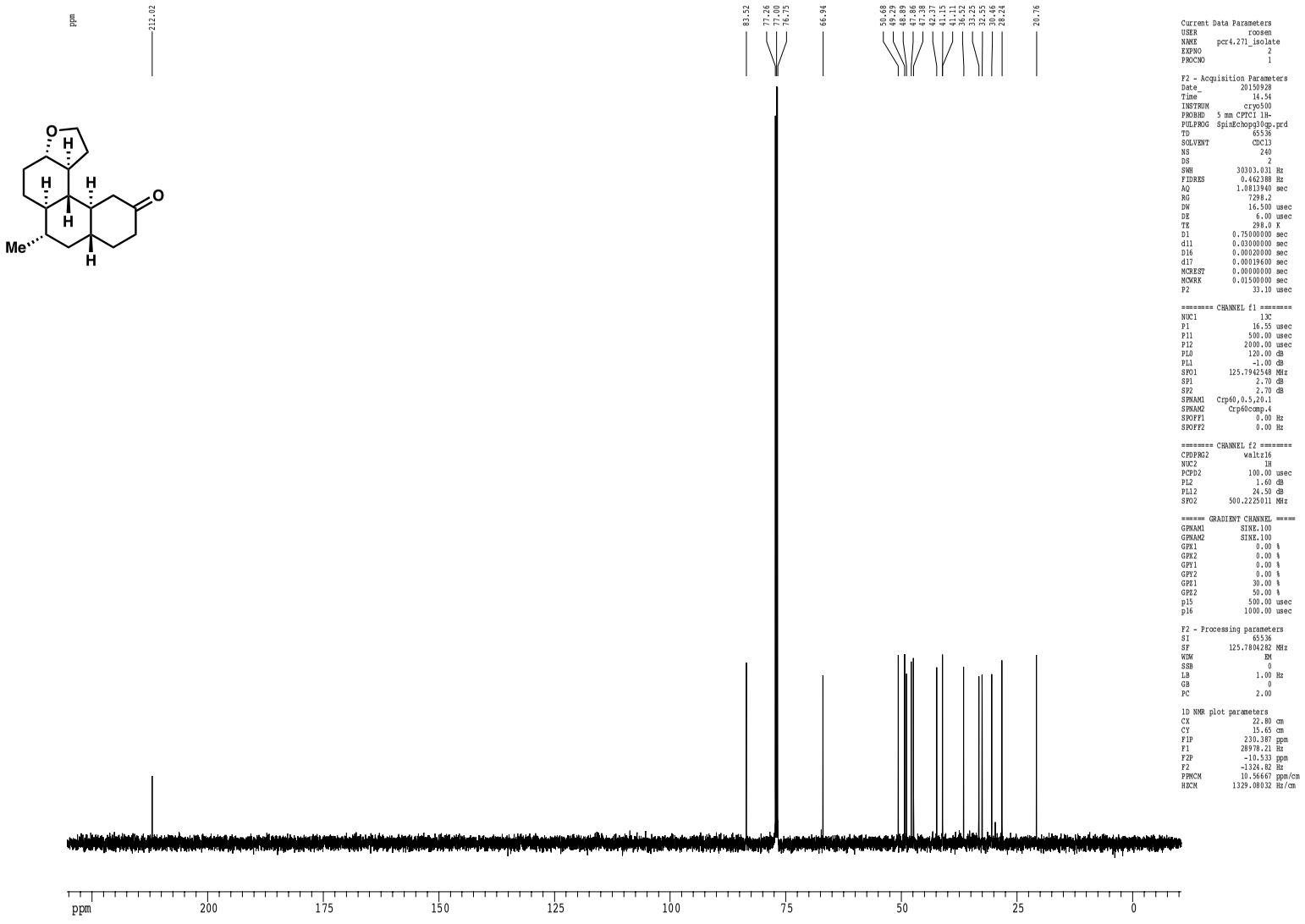





```
Current Data Parameters
USER              roosen
NAME      pcr4.239_isolate
EXPNO                   2
PROCNO                  1

F2 - Acquisition Parameters
Date_          20150805
Time              12.33
INSTRUM          cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD                65536
SOLVENT            CDCl3
NS                   120
DS                     2
SWH           30303.031 Hz
FIDRES        0.462388 Hz
AQ            1.0813940 sec
RG               7298.2
DW               16.500 usec
DE                6.00 usec
TE               298.0 K
D1          0.50000000 sec
d11         0.03000000 sec
D16         0.00020000 sec
d17         0.00019600 sec
MCREST      0.00000000 sec
MCWRK       0.01500000 sec
P2               33.10 usec

======= CHANNEL f1 =======
NUC1               13C
P1               16.55 usec
P11             500.00 usec
P12            2000.00 usec
PL0             120.00 dB
PL1              -1.00 dB
SFO1       125.7942548 MHz
SP1              2.70 dB
SP2              2.70 dB
SPNAM1   Crp60,0.5,20.1
SPNAM2     Crp60comp.4
SPOFF1             0.00 Hz
SPOFF2             0.00 Hz

======= CHANNEL f2 =======
CPDPRG2         waltz16
NUC2               1H
PCPD2           100.00 usec
PL2               1.60 dB
PL12             24.50 dB
SFO2       500.2225011 MHz

===== GRADIENT CHANNEL ====
GPNAM1          SINE.100
GPNAM2          SINE.100
GPX1              0.00 %
GPX2              0.00 %
GPY1              0.00 %
GPY2              0.00 %
GPZ1             30.00 %
GPZ2             50.00 %
p15             500.00 usec
p16            1000.00 usec

F2 - Processing parameters
SI                65536
SF         125.7804300 MHz
WDW                  EM
SSB                   0
LB                 1.00 Hz
GB                    0
PC                 2.00

1D NMR plot parameters
CX                22.80 cm
CY                10.00 cm
F1P             230.373 ppm
F1              28976.36 Hz
F2P             -10.547 ppm
F2              -1326.67 Hz
PPMCM          10.56667 ppm/cm
HZCM         1329.08032 Hz/cm
```


1H spectrum
Current Data Parameters
NAME pcr4.271_isolate
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20151028
Time 14.52
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 8
DS 2
SWH 8012.820 Hz
FIDRES 0.244466 Hz
AQ 1.9998451 sec
RG 10.1
DW 62.400 usec
DE 6.00 usec
TE 298.1 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 7.50 usec
PL1 1.60 dB
SFO1 500.2235015 MHz
F2 - Processing parameters
SI 65536
SF 500.2200265 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00
1D NMR plot parameters
CX 27.80 cm
CY 15.00 cm
F1P 10.000 ppm
F1 5002.20 Hz
F2P -1.000 ppm
F2 -500.22 Hz
PPMCM 0.48246 ppm/cm
HZCM 241.33423 Hz/cm
1.1309
1.3284
4.9724
6.5549
1.4607
1.2708
1.1240
1.1271
1.1951
2.3251
1.2247
2.4284
1.1267
1.1784
2.3465
Me
O
H
ppm
Integral

Z-restored spin-echo 13C spectrum with 1H decoupling



Current Data Parameters
USER roosen
NAME pcr4.271_isolate
EXPNO 2
PROCNO 1

F2 - Acquisition Parameters
Date_ 20150928
Time 14.54
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG SpinEchopg30gp.prd
TD 65536
SOLVENT CDCl3
NS 240
DS 2
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0813940 sec
RG 7298.2
DW 16.500 usec
DE 6.00 usec
TE 298.0 K
D1 0.75000000 sec
d11 0.03000000 sec
D16 0.00020000 sec
d17 0.00019600 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
P2 33.10 usec

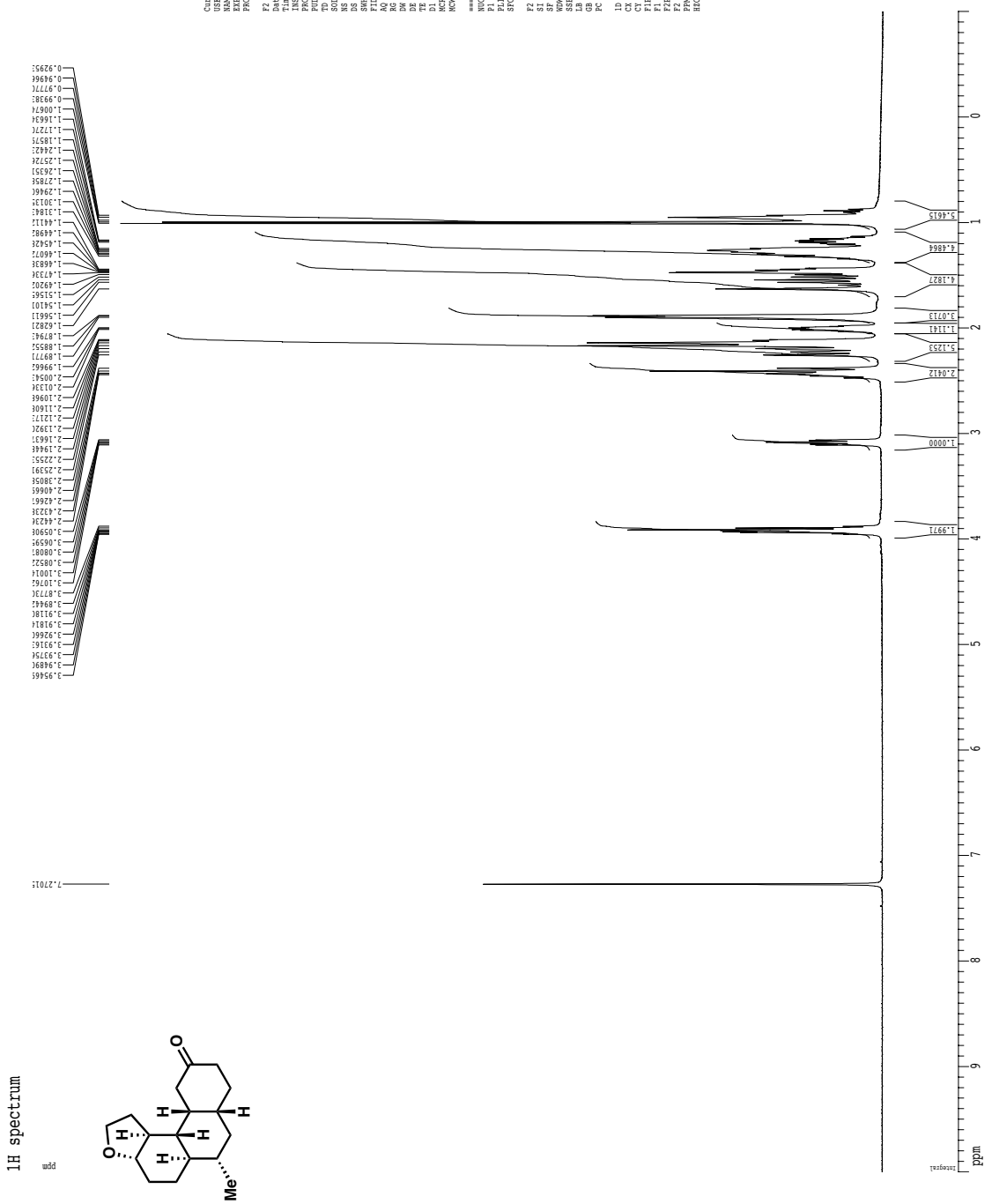
======= CHANNEL f1 =======
NUC1 13C
P1 16.55 usec
P11 500.00 usec
P12 2000.00 usec
PL0 120.00 dB
PL1 -1.00 dB
SFO1 125.7942548 MHz
SP1 2.70 dB
SP2 2.70 dB
SPNAM1 Crp60,0.5,20.1
SPNAM2 Crp60comp.4
SPOFF1 0.00 Hz
SPOFF2 0.00 Hz

======= CHANNEL f2 =======
CPDPRG2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 1.60 dB
PL12 24.50 dB
SFO2 500.2225011 MHz

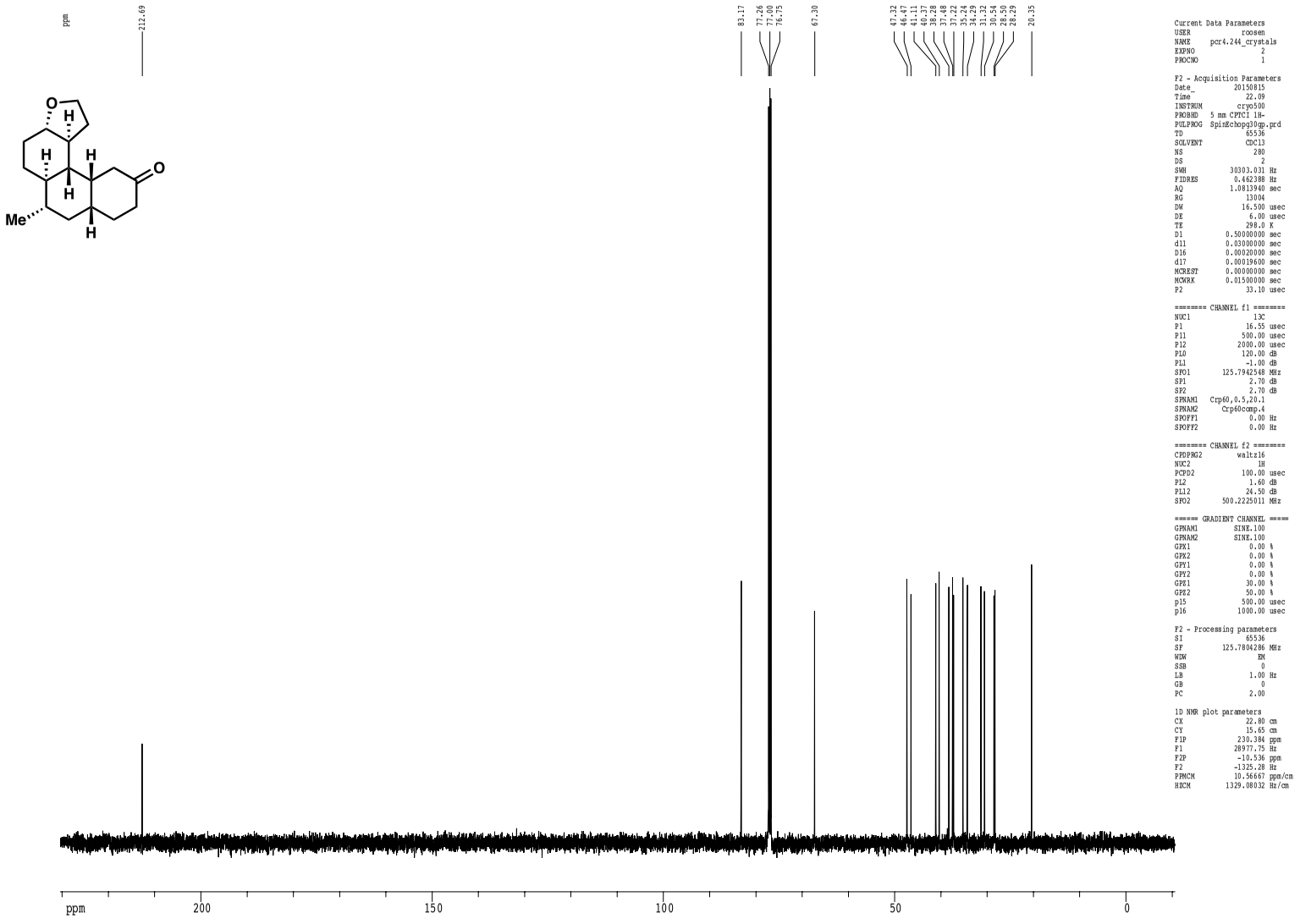
===== GRADIENT CHANNEL ====
GPNAM1 SINE.100
GPNAM2 SINE.100
GPX1 0.00 %
GPX2 0.00 %
GPY1 0.00 %
GPY2 0.00 %
GPZ1 30.00 %
GPZ2 50.00 %
p15 500.00 usec
p16 1000.00 usec

F2 - Processing parameters
SI 65536
SF 125.7804282 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00

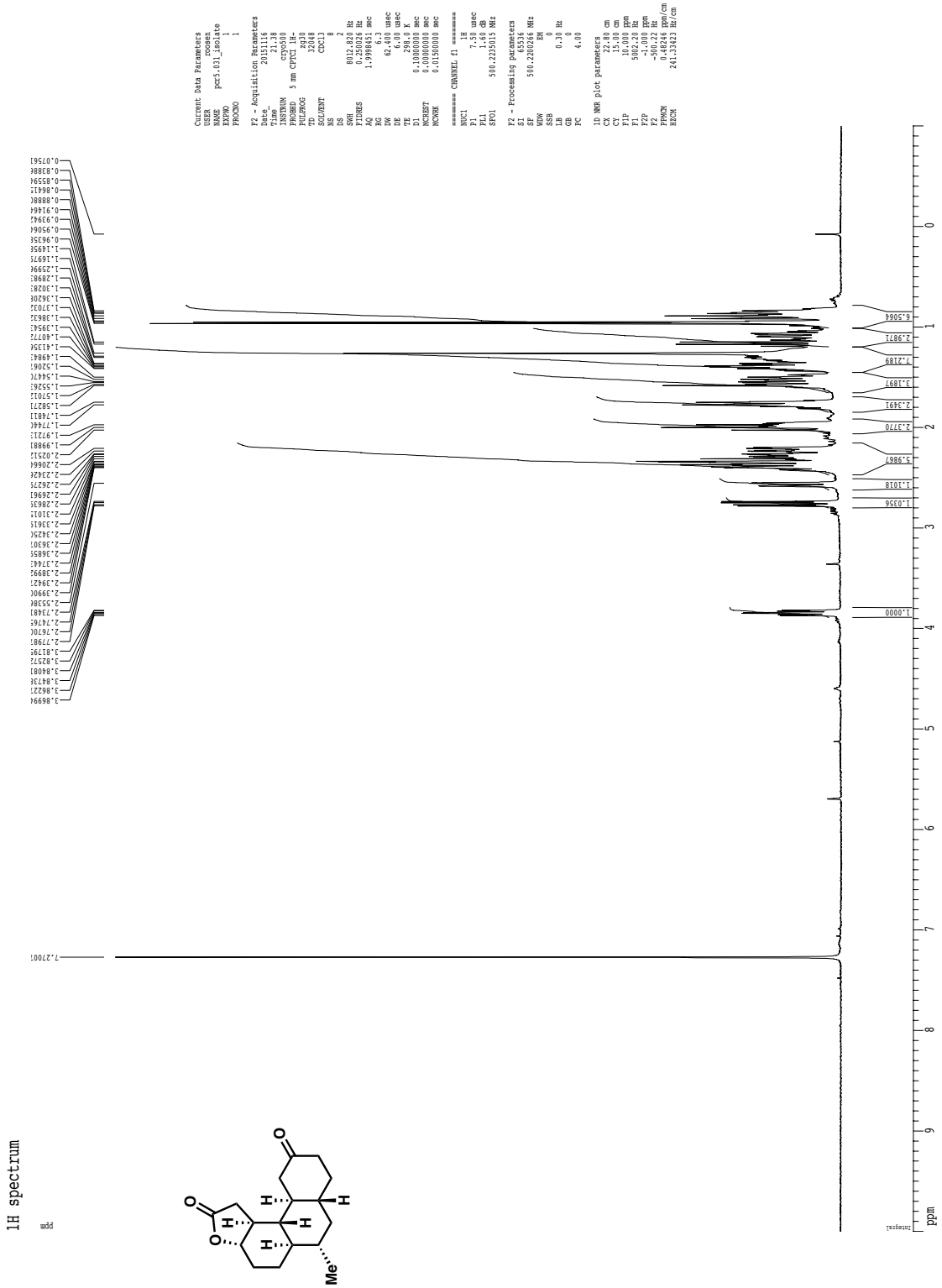
1D NMR plot parameters
CX 22.80 cm
CY 15.65 cm
F1P 230.387 ppm
F1 28978.21 Hz
F2P -10.533 ppm
F2 -1324.82 Hz
PPMCM 10.56667 ppm/cm
HZCM 1329.08032 Hz/cm


1H spectrum
ppm
Integral
Me
5.4615
4.4864
4.1827
3.0713
1.1141
5.1253
2.0412
1.0000
1.9971

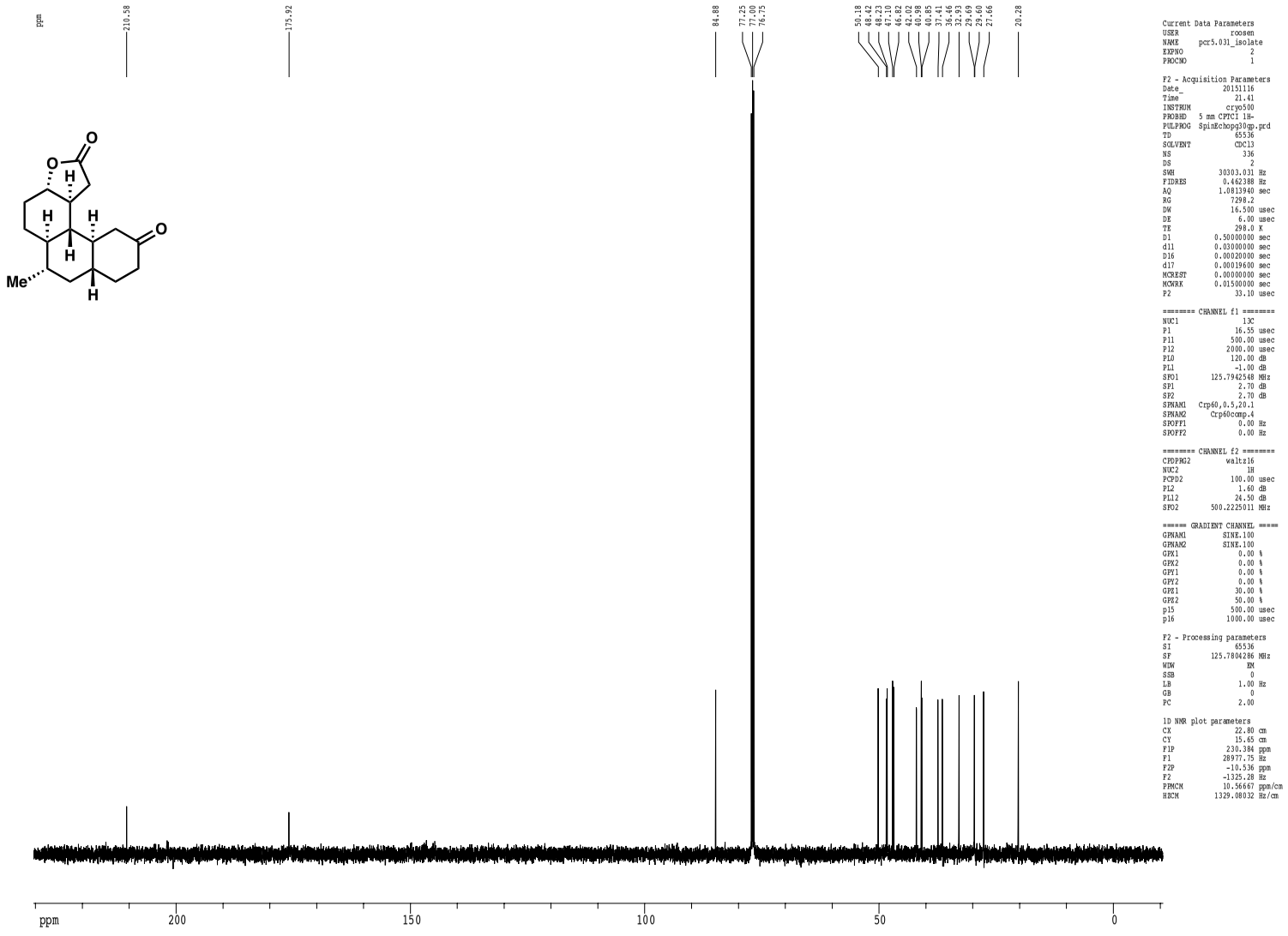
Z-restored spin-echo 13C spectrum with 1H decoupling




```
Current Data Parameters
USER              roosen
NAME      pcr4.244_crystals
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_          20150815
Time              22.09
INSTRUM          cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD                65536
SOLVENT           CDCl3
NS                  280
DS                    2
SWH           30303.031 Hz
FIDRES        0.462388 Hz
AQ            1.0813940 sec
RG                13004
DW               16.500 usec
DE                6.00 usec
TE               298.0 K
D1           0.50000000 sec
d11          0.03000000 sec
D16          0.00020000 sec
d17          0.00019600 sec
MCREST       0.00000000 sec
MCWRK        0.01500000 sec
P2               33.10 usec

======= CHANNEL f1 =======
NUC1                13C
P1                16.55 usec
P11              500.00 usec
P12             2000.00 usec
PL0              120.00 dB
PL1               -1.00 dB
SFO1        125.7942548 MHz
SP1               2.70 dB
SP2               2.70 dB
SPNAM1   Crp60,0.5,20.1
SPNAM2      Crp60comp.4
SPOFF1               0.00 Hz
SPOFF2               0.00 Hz

======= CHANNEL f2 =======
CPDPRG2          waltz16
NUC2                1H
PCPD2            100.00 usec
PL2               1.60 dB
PL12             24.50 dB
SFO2        500.2225011 MHz

===== GRADIENT CHANNEL ====
GPNAM1          SINE.100
GPNAM2          SINE.100
GPX1              0.00 %
GPX2              0.00 %
GPY1              0.00 %
GPY2              0.00 %
GPZ1             30.00 %
GPZ2             50.00 %
p15             500.00 usec
p16            1000.00 usec

F2 - Processing parameters
SI                65536
SF          125.7804286 MHz
WDW                  EM
SSB                   0
LB                1.00 Hz
GB                    0
PC                2.00

1D NMR plot parameters
CX               22.80 cm
CY               15.65 cm
F1P             230.384 ppm
F1              28977.75 Hz
F2P             -10.536 ppm
F2              -1325.28 Hz
PPMCM           10.56667 ppm/cm
HZCM         1329.08032 Hz/cm
```


1H spectrum
ppm
Integral
Me

Z-restored spin-echo 13C spectrum with 1H decoupling



Current Data Parameters
USER roosen
NAME pcr5.031_isolate
EXPNO 2
PROCNO 1

F2 - Acquisition Parameters
Date_ 20151116
Time 21.41
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG SpinEchopg30gp.prd
TD 65536
SOLVENT CDCl3
NS 336
DS 2
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0813940 sec
RG 7298.2
DW 16.500 usec
DE 6.00 usec
TE 298.0 K
D1 0.50000000 sec
d11 0.03000000 sec
D16 0.00020000 sec
d17 0.00019600 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
P2 33.10 usec

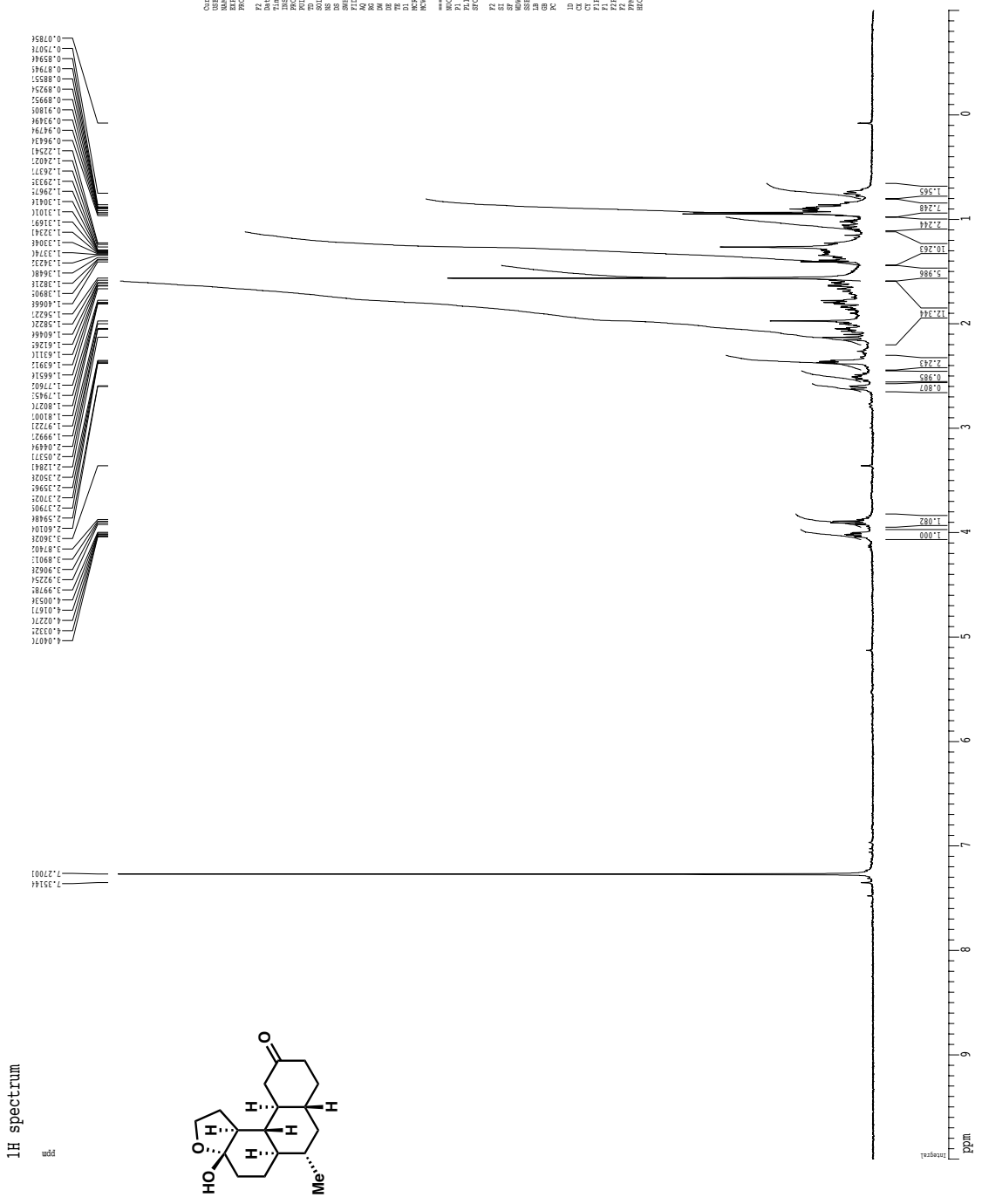
======= CHANNEL f1 =======
NUC1 13C
P1 16.55 usec
P11 500.00 usec
P12 2000.00 usec
PL0 120.00 dB
PL1 -1.00 dB
SFO1 125.7942548 MHz
SP1 2.70 dB
SP2 2.70 dB
SPNAM1 Crp60,0.5,20.1
SPNAM2 Crp60comp.4
SPOFF1 0.00 Hz
SPOFF2 0.00 Hz

======= CHANNEL f2 =======
CPDPRG2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 1.60 dB
PL12 24.50 dB
SFO2 500.2225011 MHz

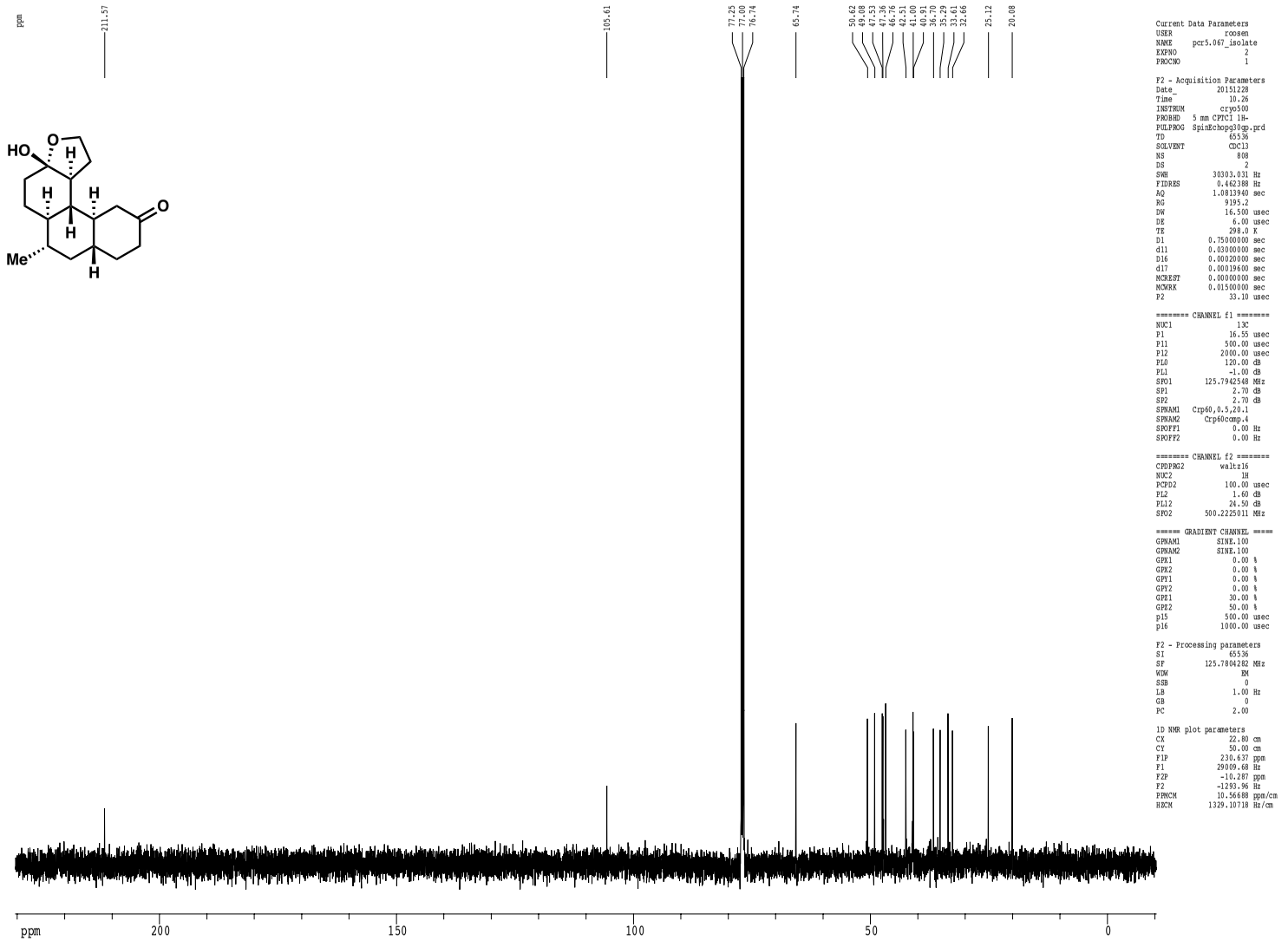
===== GRADIENT CHANNEL ====
GPNAM1 SINE.100
GPNAM2 SINE.100
GPX1 0.00 %
GPX2 0.00 %
GPY1 0.00 %
GPY2 0.00 %
GPZ1 30.00 %
GPZ2 50.00 %
p15 500.00 usec
p16 1000.00 usec

F2 - Processing parameters
SI 65536
SF 125.7804286 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00

1D NMR plot parameters
CX 22.80 cm
CY 15.65 cm
F1P 230.384 ppm
F1 28977.75 Hz
F2P -10.536 ppm
F2 -1325.28 Hz
PPMCM 10.56667 ppm/cm
HZCM 1329.08032 Hz/cm


1H spectrum
ppm
Integral
Current Data Parameters
NAME pct_061_60_Deuterpot
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20151218
Time 13.48 h
INSTRUM qnp500
PROBHD 5 mm broadband
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.244604 Hz
AQ 1.0944643 sec
RG 1625.1
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
CHANNEL f1
NUC1 1H
P1 12.40 usec
PL1 -5.80 dB
SFO1 499.1834943 MHz
F2 - Processing parameters
SI 65536
SF 499.1800223 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 10.000 ppm
F1 4991.83 Hz
F2P -1.000 ppm
F2 -499.18 Hz
PPMCM 0.43917 ppm/cm
HZCM 240.83241 Hz/cm
7.27001
7.35144
4.06076
4.03326
4.01671
4.02776
3.99783
3.90626
3.89013
3.87602
3.36026
3.03574
2.59484
2.37905
2.37026
2.35026
2.12841
2.05371
2.04494
1.99926
1.97226
1.81006
1.80276
1.79451
1.77602
1.66514
1.63912
1.61261
1.60466
1.58226
1.56226
1.40666
1.38926
1.38216
1.36486
1.34232
1.33746
1.33046
1.32346
1.31691
1.31016
1.30416
1.29672
1.29326
1.26371
1.22541
0.96434
0.94794
0.93494
0.91806
0.89252
0.89952
0.88551
0.87946
0.85944
0.75074
0.07854
1.565
7.248
2.244
10.263
5.986
12.344
2.243
0.985
0.807
1.082
1.000
0
1
2
3
4
5
6
7
8
9
ppm

Z-restored spin-echo 13C spectrum with 1H decoupling



Current Data Parameters
USER roosen
NAME pcr5.067_isolate
EXPNO 2
PROCNO 1

F2 - Acquisition Parameters
Date_ 20151228
Time 10.26
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG SpinEchopg30gp.prd
TD 65536
SOLVENT CDCl3
NS 808
DS 2
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0813940 sec
RG 9195.2
DW 16.500 usec
DE 6.00 usec
TE 298.0 K
D1 0.75000000 sec
d11 0.03000000 sec
D16 0.00020000 sec
d17 0.00019600 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
P2 33.10 usec

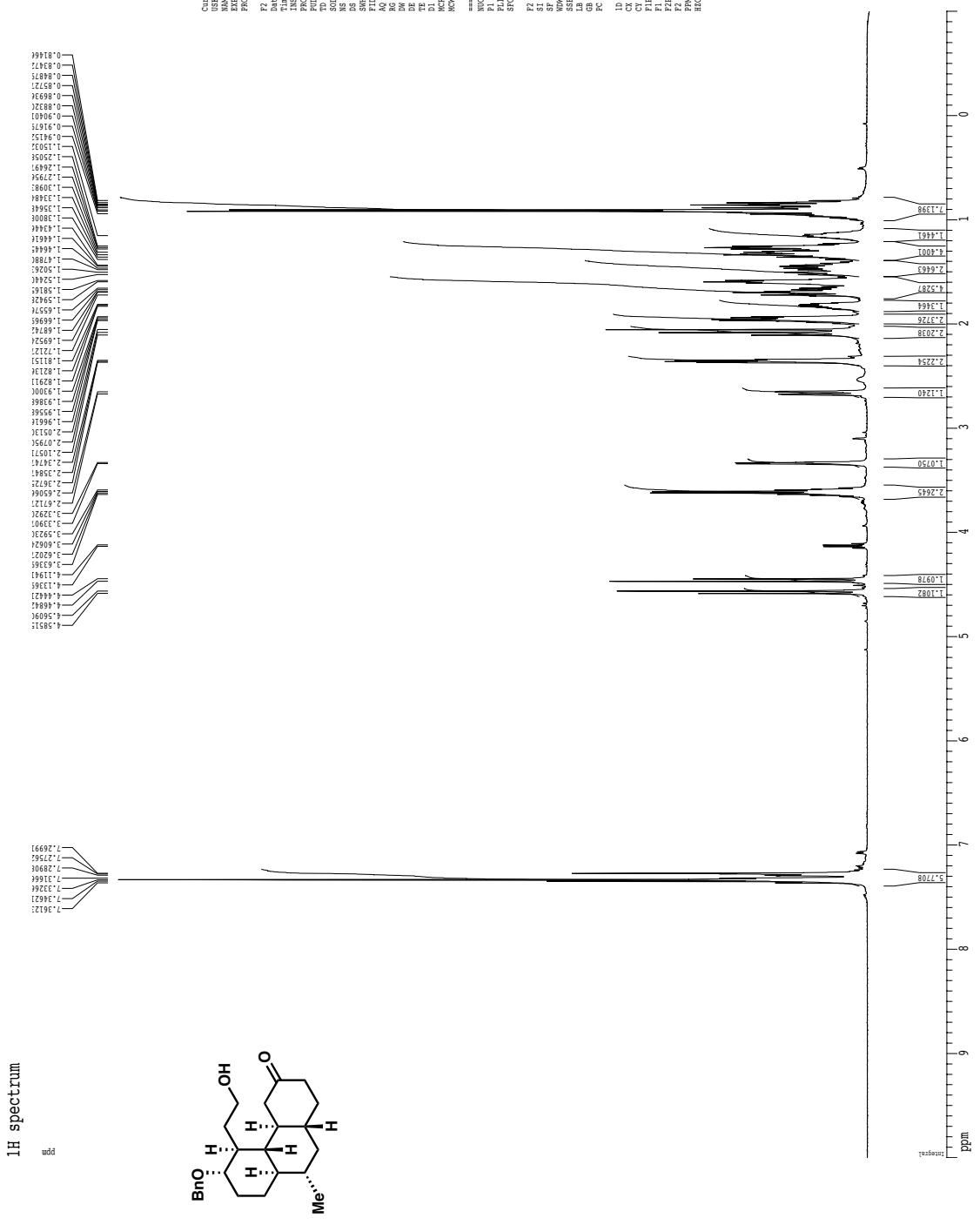
======= CHANNEL f1 =======
NUC1 13C
P1 16.55 usec
P11 500.00 usec
P12 2000.00 usec
PL0 120.00 dB
PL1 -1.00 dB
SFO1 125.7942548 MHz
SP1 2.70 dB
SP2 2.70 dB
SPNAM1 Crp60,0.5,20.1
SPNAM2 Crp60comp.4
SPOFF1 0.00 Hz
SPOFF2 0.00 Hz

======= CHANNEL f2 =======
CPDPRG2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 1.60 dB
PL12 24.50 dB
SFO2 500.2225011 MHz

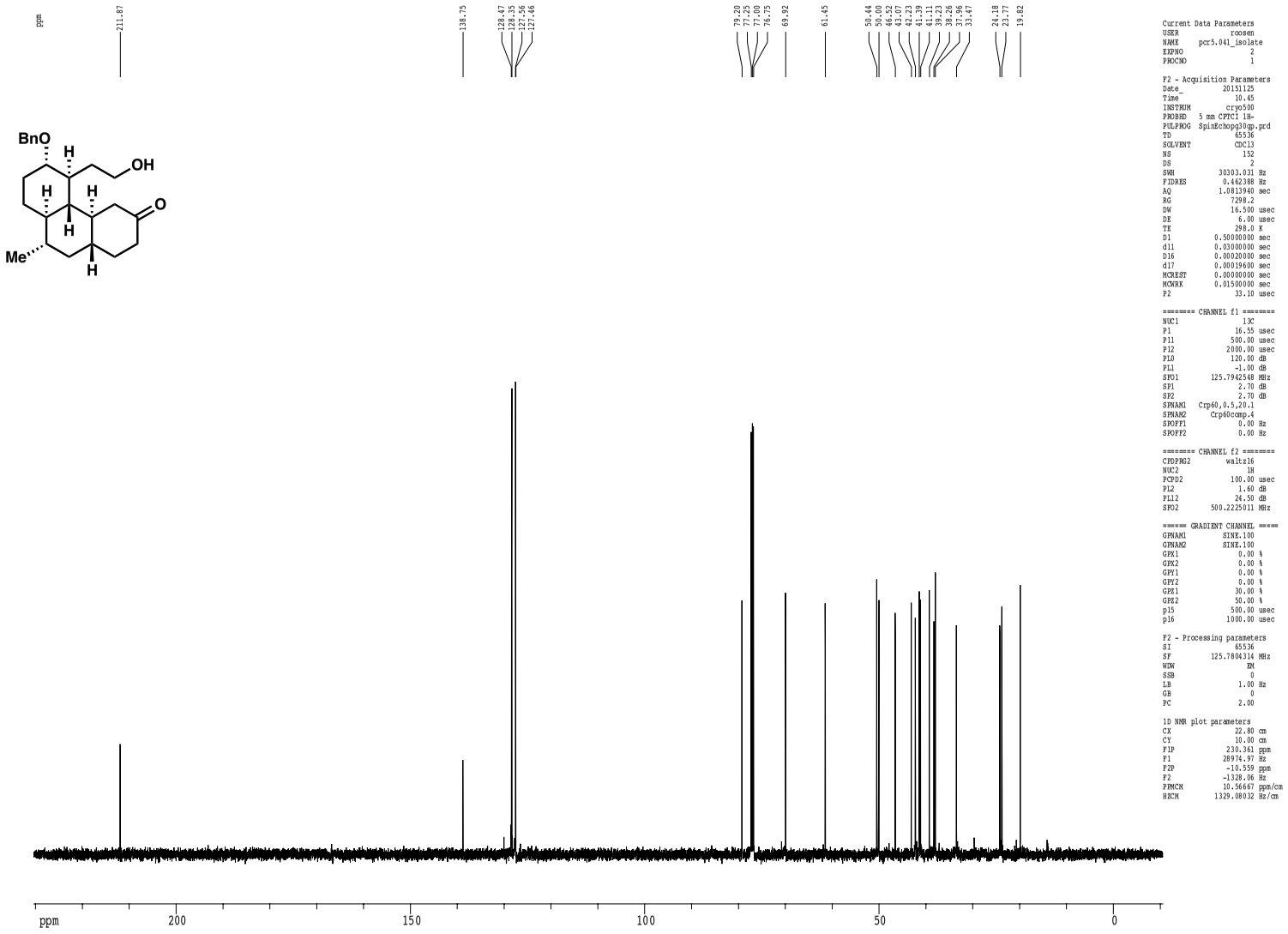
===== GRADIENT CHANNEL ====
GPNAM1 SINE.100
GPNAM2 SINE.100
GPX1 0.00 %
GPX2 0.00 %
GPY1 0.00 %
GPY2 0.00 %
GPZ1 30.00 %
GPZ2 50.00 %
p15 500.00 usec
p16 1000.00 usec

F2 - Processing parameters
SI 65536
SF 125.7804282 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00

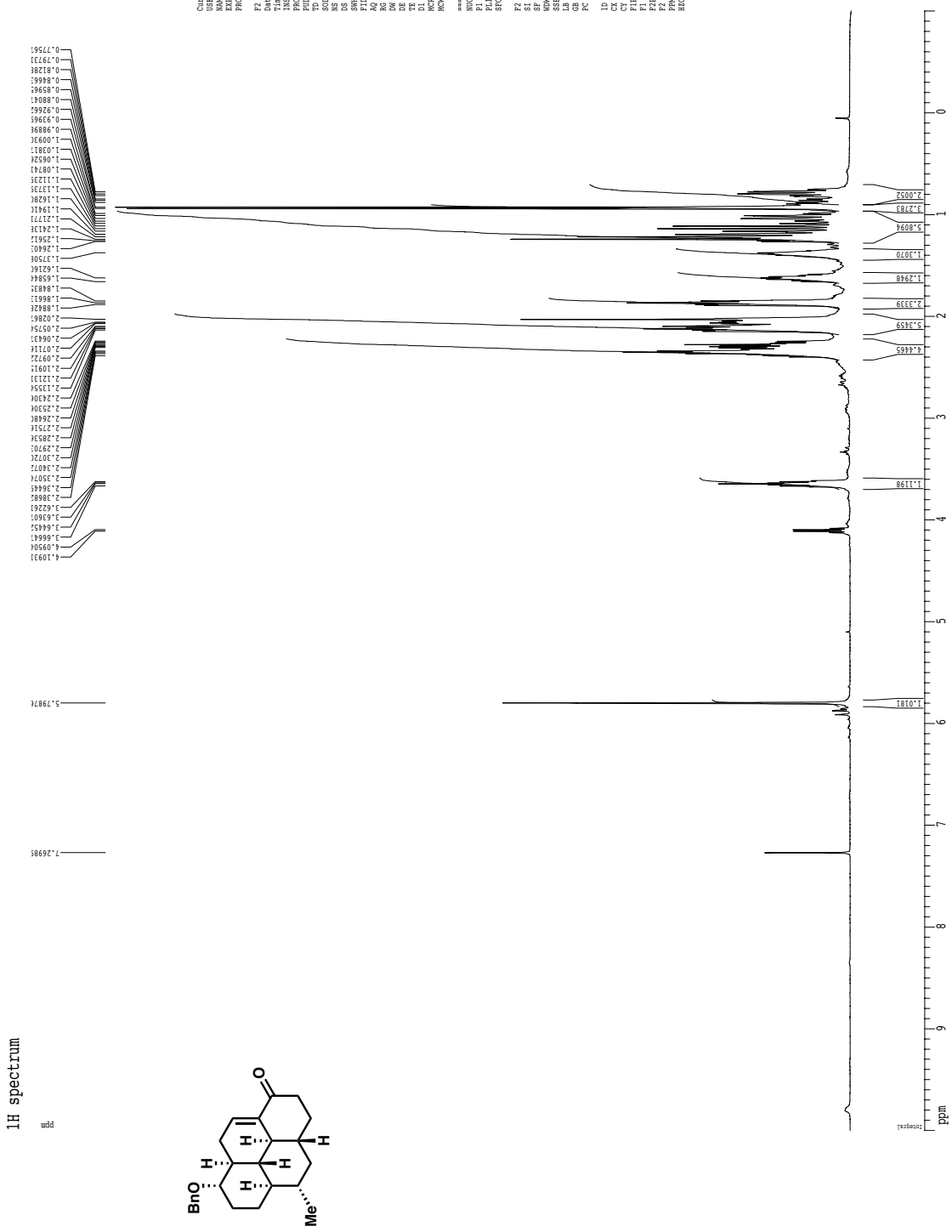
1D NMR plot parameters
CX 22.80 cm
CY 50.00 cm
F1P 230.637 ppm
F1 29009.68 Hz
F2P -10.287 ppm
F2 -1293.96 Hz
PPMCM 10.56688 ppm/cm
HZCM 1329.10718 Hz/cm


1H spectrum
ppm
Integral
BnO
OH
O
Me
H

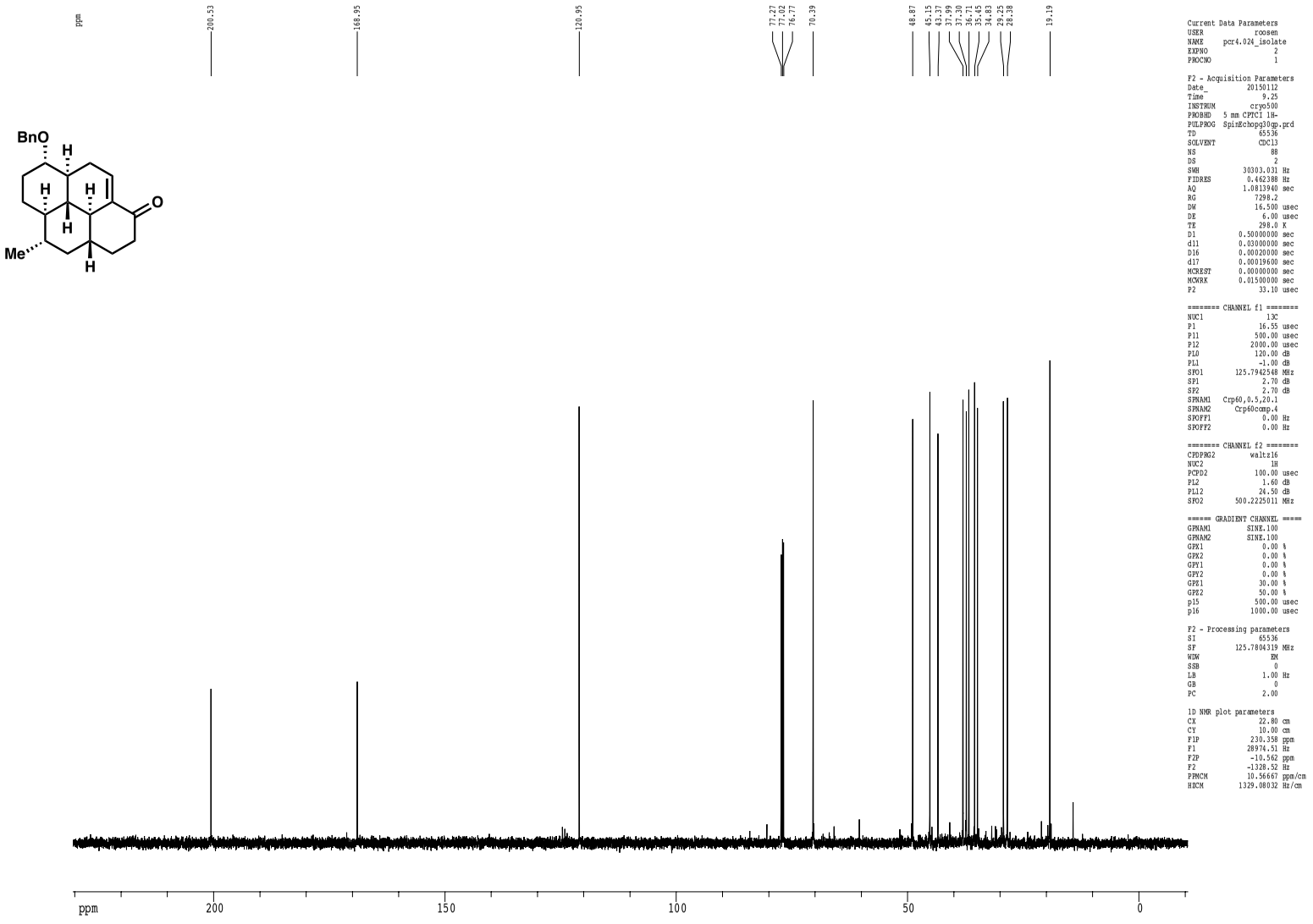
Z-restored spin-echo 13C spectrum with 1H decoupling




```
Current Data Parameters
USER              roosen
NAME      pcr5.041_isolate
EXPNO                   2
PROCNO                  1

F2 - Acquisition Parameters
Date_           20151125
Time              10.45
INSTRUM          cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD                65536
SOLVENT            CDCl3
NS                   152
DS                     2
SWH           30303.031 Hz
FIDRES        0.462388 Hz
AQ            1.0813940 sec
RG               7298.2
DW                16.500 usec
DE                 6.00 usec
TE               298.0 K
D1          0.50000000 sec
d11         0.03000000 sec
D16         0.00020000 sec
d17         0.00019600 sec
MCREST      0.00000000 sec
MCWRK       0.01500000 sec
P2                33.10 usec

======= CHANNEL f1 =======
NUC1                13C
P1                16.55 usec
P11              500.00 usec
P12             2000.00 usec
PL0              120.00 dB
PL1               -1.00 dB
SFO1        125.7942548 MHz
SP1               2.70 dB
SP2               2.70 dB
SPNAM1   Crp60,0.5,20.1
SPNAM2     Crp60comp.4
SPOFF1               0.00 Hz
SPOFF2               0.00 Hz

======= CHANNEL f2 =======
CPDPRG2          waltz16
NUC2                1H
PCPD2            100.00 usec
PL2               1.60 dB
PL12             24.50 dB
SFO2        500.2225011 MHz

===== GRADIENT CHANNEL ====
GPNAM1          SINE.100
GPNAM2          SINE.100
GPX1                0.00 %
GPX2                0.00 %
GPY1                0.00 %
GPY2                0.00 %
GPZ1               30.00 %
GPZ2               50.00 %
p15              500.00 usec
p16             1000.00 usec

F2 - Processing parameters
SI                  65536
SF          125.7804314 MHz
WDW                    EM
SSB                    0
LB                  1.00 Hz
GB                     0
PC                  2.00

1D NMR plot parameters
CX                 22.80 cm
CY                 10.00 cm
F1P              230.361 ppm
F1               28974.97 Hz
F2P              -10.559 ppm
F2               -1328.06 Hz
PPMCM            10.56667 ppm/cm
HZCM          1329.08032 Hz/cm
```


1H spectrum
ppm
Integral
BnO
Me
H
O

Z-restored spin-echo 13C spectrum with 1H decoupling



Current Data Parameters
USER roosen
NAME pcr4.024_isolate
EXPNO 2
PROCNO 1

F2 - Acquisition Parameters
Date_ 20150112
Time 9.25
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG SpinEchopg30gp.prd
TD 65536
SOLVENT CDCl3
NS 88
DS 2
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0813940 sec
RG 7298.2
DW 16.500 usec
DE 6.00 usec
TE 298.0 K
D1 0.50000000 sec
d11 0.03000000 sec
D16 0.00020000 sec
d17 0.00019600 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
P2 33.10 usec

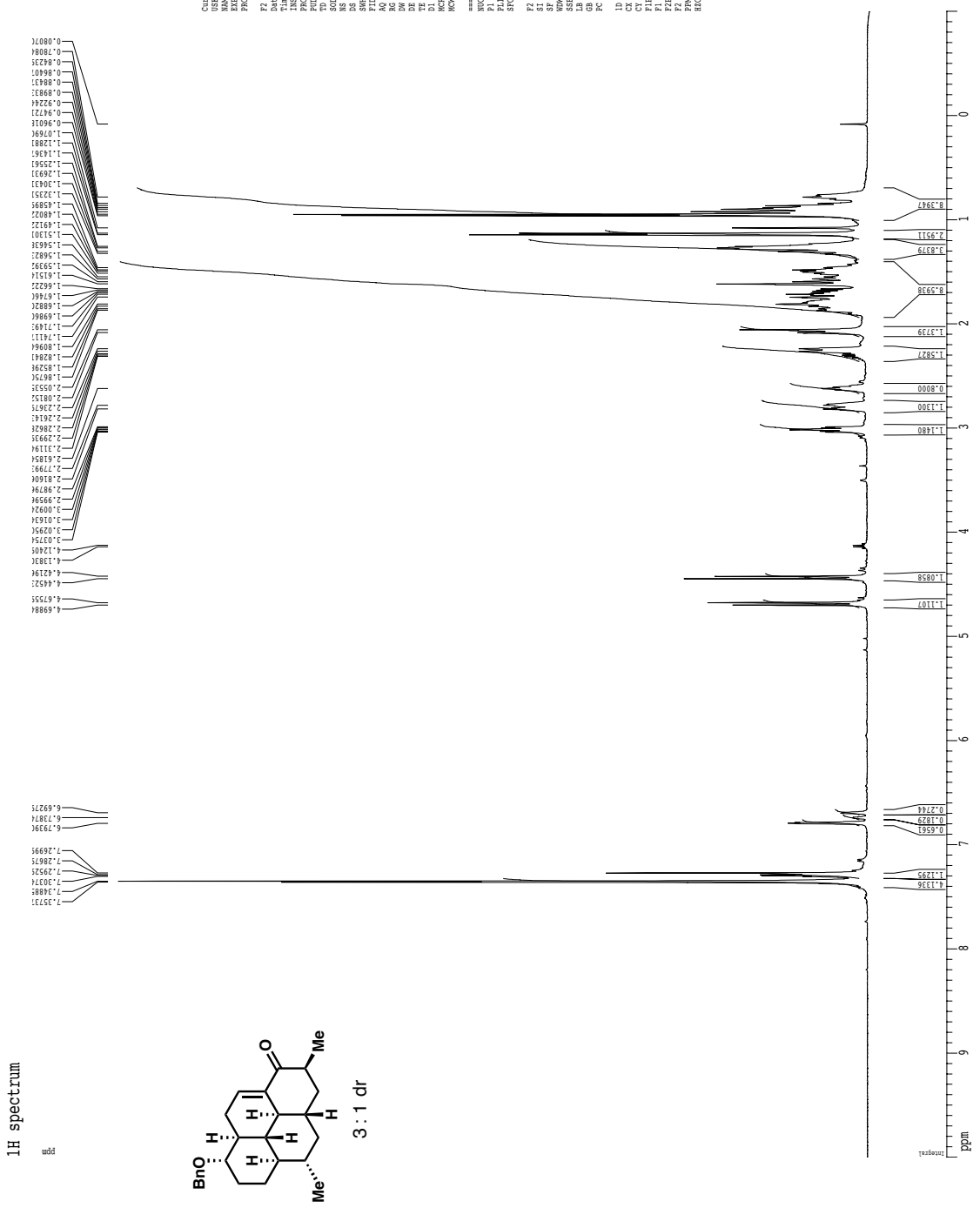
======= CHANNEL f1 =======
NUC1 13C
P1 16.55 usec
P11 500.00 usec
P12 2000.00 usec
PL0 120.00 dB
PL1 -1.00 dB
SFO1 125.7942548 MHz
SP1 2.70 dB
SP2 2.70 dB
SPNAM1 Crp60,0.5,20.1
SPNAM2 Crp60comp.4
SPOFF1 0.00 Hz
SPOFF2 0.00 Hz

======= CHANNEL f2 =======
CPDPRG2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 1.60 dB
PL12 24.50 dB
SFO2 500.2225011 MHz

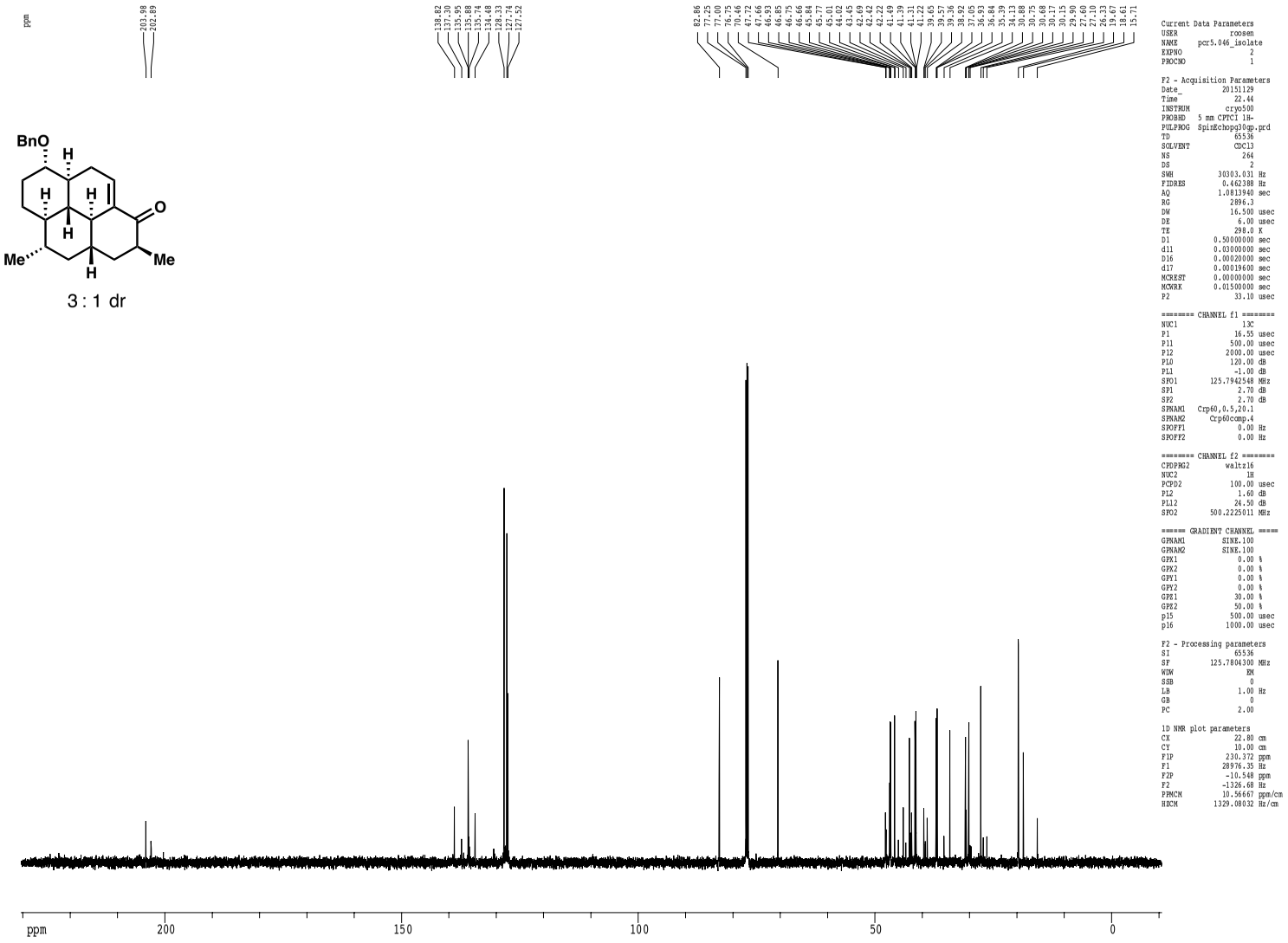
===== GRADIENT CHANNEL ====
GPNAM1 SINE.100
GPNAM2 SINE.100
GPX1 0.00 %
GPX2 0.00 %
GPY1 0.00 %
GPY2 0.00 %
GPZ1 30.00 %
GPZ2 50.00 %
p15 500.00 usec
p16 1000.00 usec

F2 - Processing parameters
SI 65536
SF 125.7804319 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00

1D NMR plot parameters
CX 22.80 cm
CY 10.00 cm
F1P 230.358 ppm
F1 28974.51 Hz
F2P -10.562 ppm
F2 -1328.52 Hz
PPMCM 10.56667 ppm/cm
HZCM 1329.08032 Hz/cm


1H spectrum
ppm
Integral
3 : 1 dr
BnO
Me
Me
O
H
H
H
H
H

Z-restored spin-echo 13C spectrum with 1H decoupling



Current Data Parameters

USER	roosen
NAME	pcr5.046_isolate
EXPNO	2
PROCNO	1

F2 - Acquisition Parameters

Date_	20151129
Time	22.44
INSTRUM	cryo500
PROBHD	5 mm CPTCI 1H-
PULPROG	SpinEchopg30gp.prd
TD	65536
SOLVENT	CDCl3
NS	264
DS	2
SWH	30303.031 Hz
FIDRES	0.462388 Hz
AQ	1.0813940 sec
RG	2896.3
DW	16.500 usec
DE	6.00 usec
TE	298.0 K
D1	0.50000000 sec
d11	0.03000000 sec
D16	0.00020000 sec
d17	0.00019600 sec
MCREST	0.00000000 sec
MCWRK	0.01500000 sec
P2	33.10 usec

======= CHANNEL f1 =======

NUC1	13C
P1	16.55 usec
P11	500.00 usec
P12	2000.00 usec
PL0	120.00 dB
PL1	-1.00 dB
SFO1	125.7942548 MHz
SP1	2.70 dB
SP2	2.70 dB
SPNAM1	Crp60,0.5,20.1
SPNAM2	Crp60comp.4
SPOFF1	0.00 Hz
SPOFF2	0.00 Hz

======= CHANNEL f2 =======

CPDPRG2	waltz16
NUC2	1H
PCPD2	100.00 usec
PL2	1.60 dB
PL12	24.50 dB
SFO2	500.2225011 MHz

===== GRADIENT CHANNEL ====

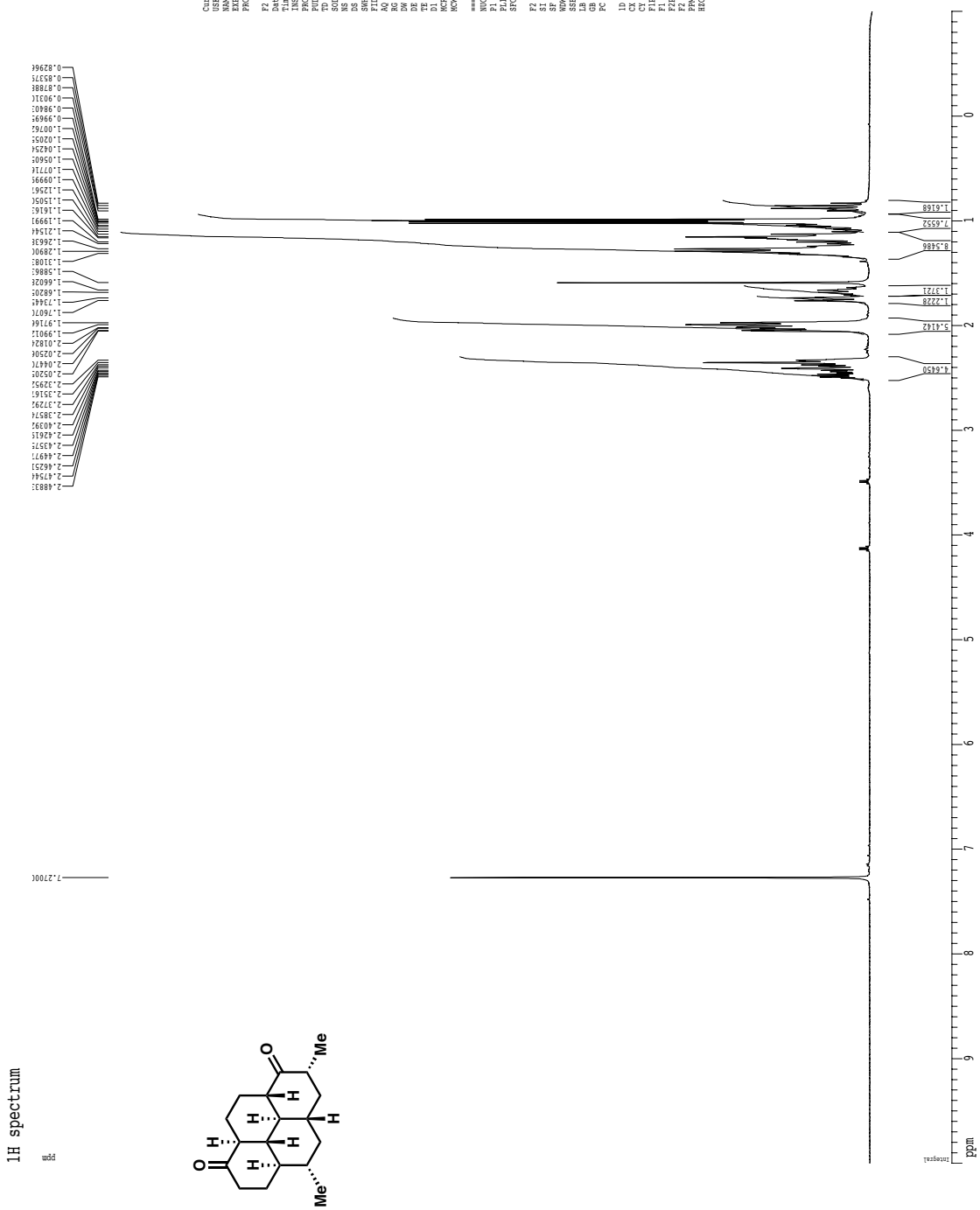
GPNAM1	SINE.100
GPNAM2	SINE.100
GPX1	0.00 %
GPX2	0.00 %
GPY1	0.00 %
GPY2	0.00 %
GPZ1	30.00 %
GPZ2	50.00 %
p15	500.00 usec
p16	1000.00 usec

F2 - Processing parameters

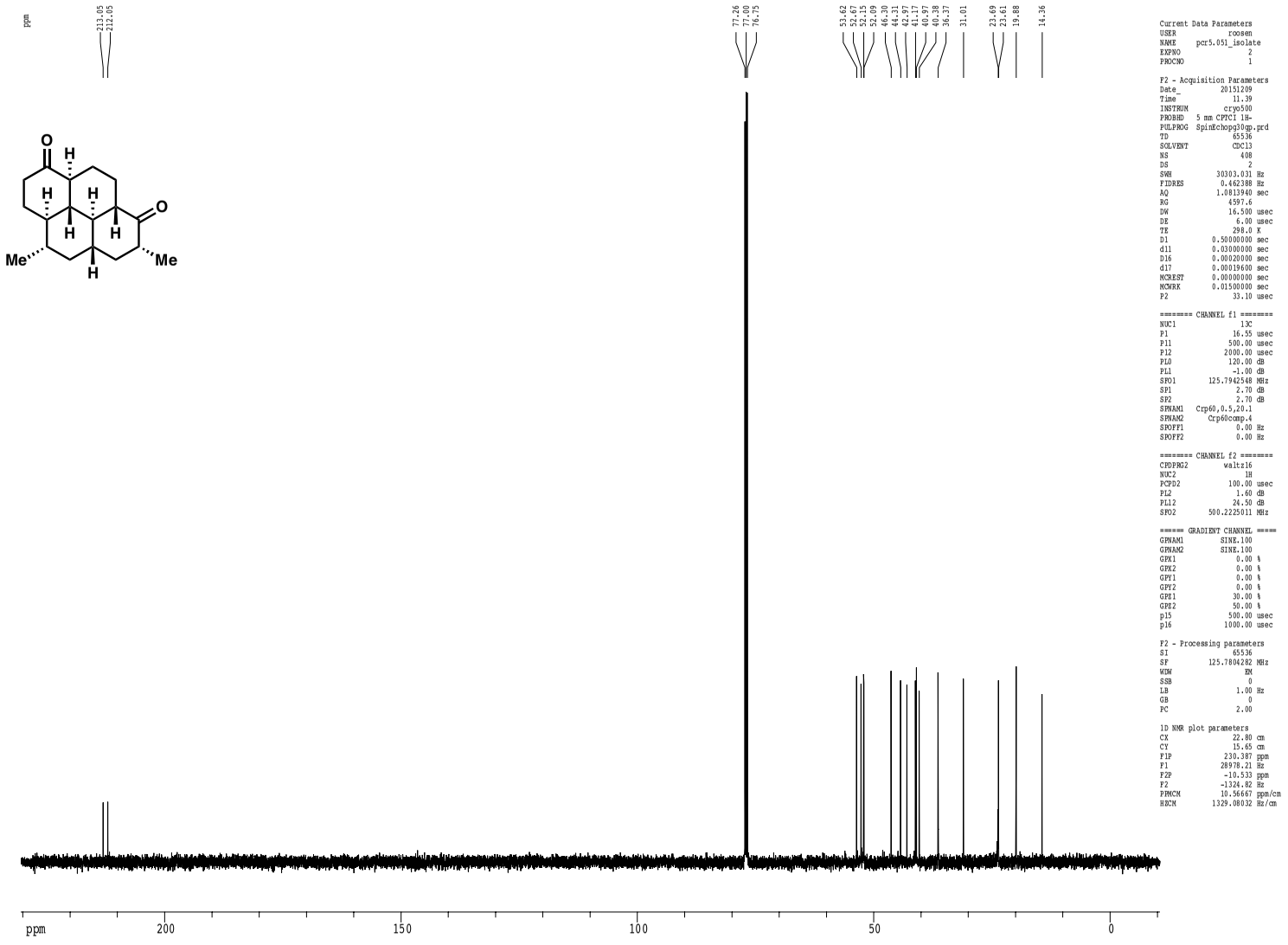
SI	65536
SF	125.7804300 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	2.00

1D NMR plot parameters

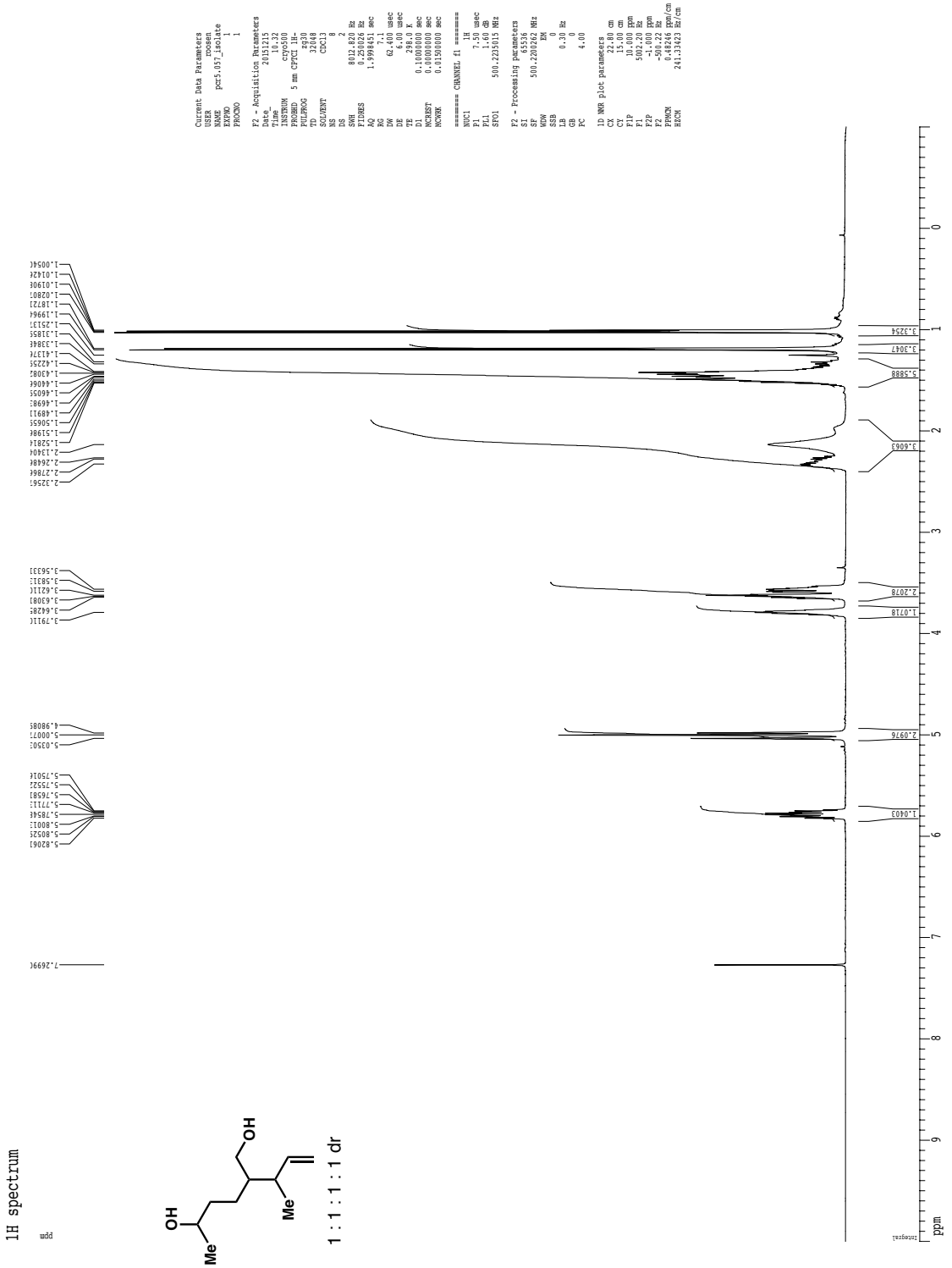
CX	22.80 cm
CY	10.00 cm
F1P	230.372 ppm
F1	28976.35 Hz
F2P	-10.548 ppm
F2	-1326.68 Hz
PPMCM	10.56667 ppm/cm
HZCM	1329.08032 Hz/cm


1H spectrum
ppm
Integral
7.27006
1.61688
7.65520
8.54864
1.37210
1.22280
5.41420
4.66500
Me
Me
H
O
O

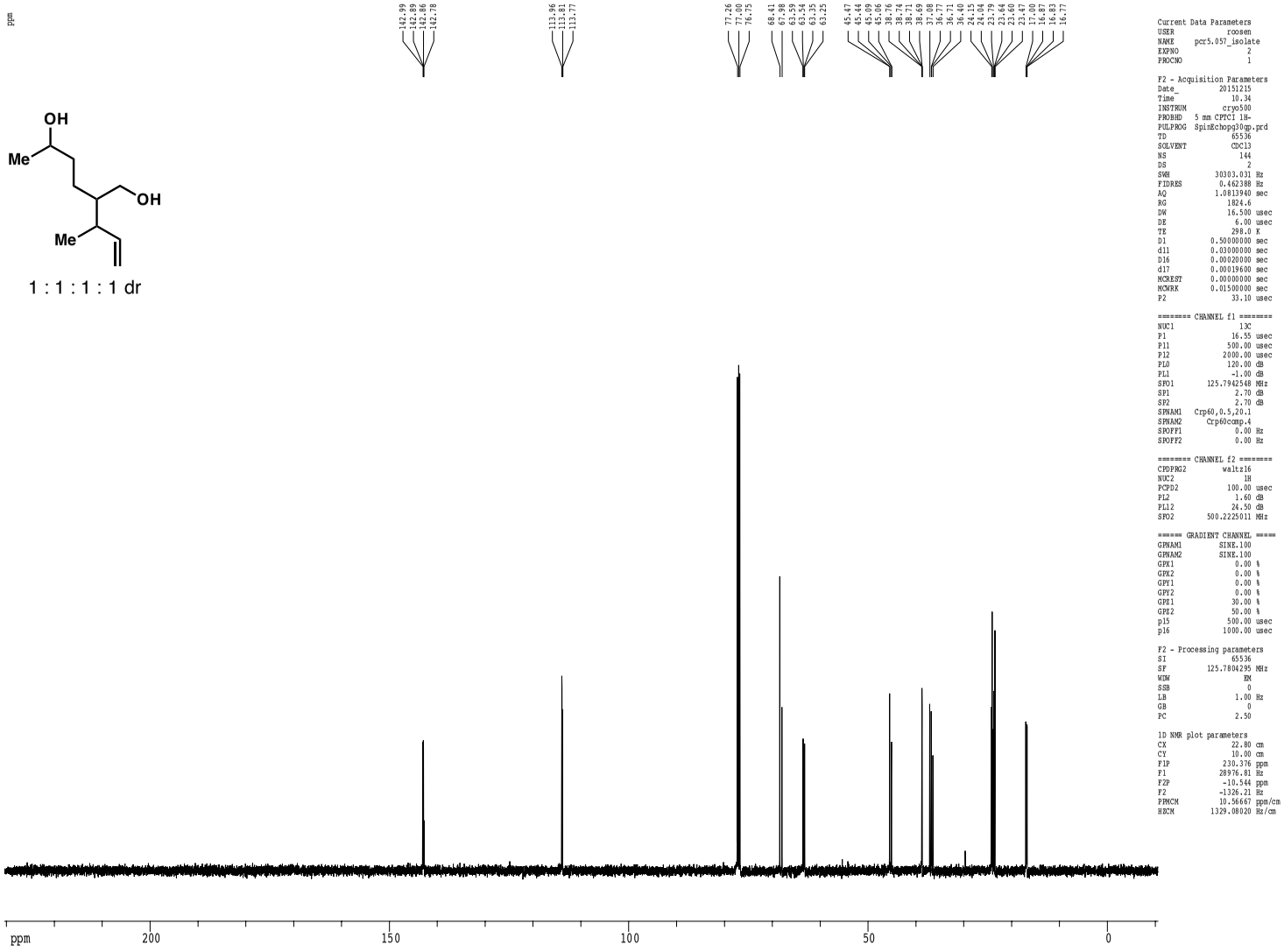
Z-restored spin-echo 13C spectrum with 1H decoupling




```
Current Data Parameters
USER              roosen
NAME      pcr5.051_isolate
EXPNO                   2
PROCNO                  1

F2 - Acquisition Parameters
Date_           20151209
Time              11.39
INSTRUM          cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD                65536
SOLVENT            CDCl3
NS                   408
DS                     2
SWH           30303.031 Hz
FIDRES        0.462388 Hz
AQ           1.0813940 sec
RG              4597.6
DW               16.500 usec
DE                6.00 usec
TE              298.0 K
D1          0.50000000 sec
d11         0.03000000 sec
D16         0.00020000 sec
d17         0.00019600 sec
MCREST      0.00000000 sec
MCWRK       0.01500000 sec
P2               33.10 usec

======= CHANNEL f1 =======
NUC1               13C
P1               16.55 usec
P11             500.00 usec
P12            2000.00 usec
PL0             120.00 dB
PL1              -1.00 dB
SFO1       125.7942548 MHz
SP1              2.70 dB
SP2              2.70 dB
SPNAM1   Crp60,0.5,20.1
SPNAM2     Crp60comp.4
SPOFF1             0.00 Hz
SPOFF2             0.00 Hz

======= CHANNEL f2 =======
CPDPRG2         waltz16
NUC2               1H
PCPD2           100.00 usec
PL2               1.60 dB
PL12             24.50 dB
SFO2       500.2225011 MHz

===== GRADIENT CHANNEL ====
GPNAM1         SINE.100
GPNAM2         SINE.100
GPX1              0.00 %
GPX2              0.00 %
GPY1              0.00 %
GPY2              0.00 %
GPZ1             30.00 %
GPZ2             50.00 %
p15             500.00 usec
p16            1000.00 usec

F2 - Processing parameters
SI                65536
SF         125.7804282 MHz
WDW                  EM
SSB                   0
LB                 1.00 Hz
GB                    0
PC                 2.00

1D NMR plot parameters
CX                22.80 cm
CY                15.65 cm
F1P             230.387 ppm
F1              28978.21 Hz
F2P              -10.533 ppm
F2              -1324.82 Hz
PPMCM           10.56667 ppm/cm
HZCM         1329.08032 Hz/cm
```


1H spectrum
ppm
OH
Me
OH
Me
1 : 1 : 1 : 1 dr
Integral
ppm

Z-restored spin-echo 13C spectrum with 1H decoupling



Current Data Parameters

USER	roosen
NAME	pcr5.057_isolate
EXPNO	2
PROCNO	1

F2 - Acquisition Parameters

Date_	20151215
Time	10.34
INSTRUM	cryo500
PROBHD	5 mm CPTCI 1H-
PULPROG	SpinEchopg30gp.prd
TD	65536
SOLVENT	CDCl3
NS	144
DS	2
SWH	30303.031 Hz
FIDRES	0.462388 Hz
AQ	1.0813940 sec
RG	1824.6
DW	16.500 usec
DE	6.00 usec
TE	298.0 K
D1	0.50000000 sec
d11	0.03000000 sec
D16	0.00020000 sec
d17	0.00019600 sec
MCREST	0.00000000 sec
MCWRK	0.01500000 sec
P2	33.10 usec

======= CHANNEL f1 =======

NUC1	13C
P1	16.55 usec
P11	500.00 usec
P12	2000.00 usec
PL0	120.00 dB
PL1	-1.00 dB
SFO1	125.7942548 MHz
SP1	2.70 dB
SP2	2.70 dB
SPNAM1	Crp60,0.5,20.1
SPNAM2	Crp60comp.4
SPOFF1	0.00 Hz
SPOFF2	0.00 Hz

======= CHANNEL f2 =======

CPDPRG2	waltz16
NUC2	1H
PCPD2	100.00 usec
PL2	1.60 dB
PL12	24.50 dB
SFO2	500.2225011 MHz

===== GRADIENT CHANNEL ====

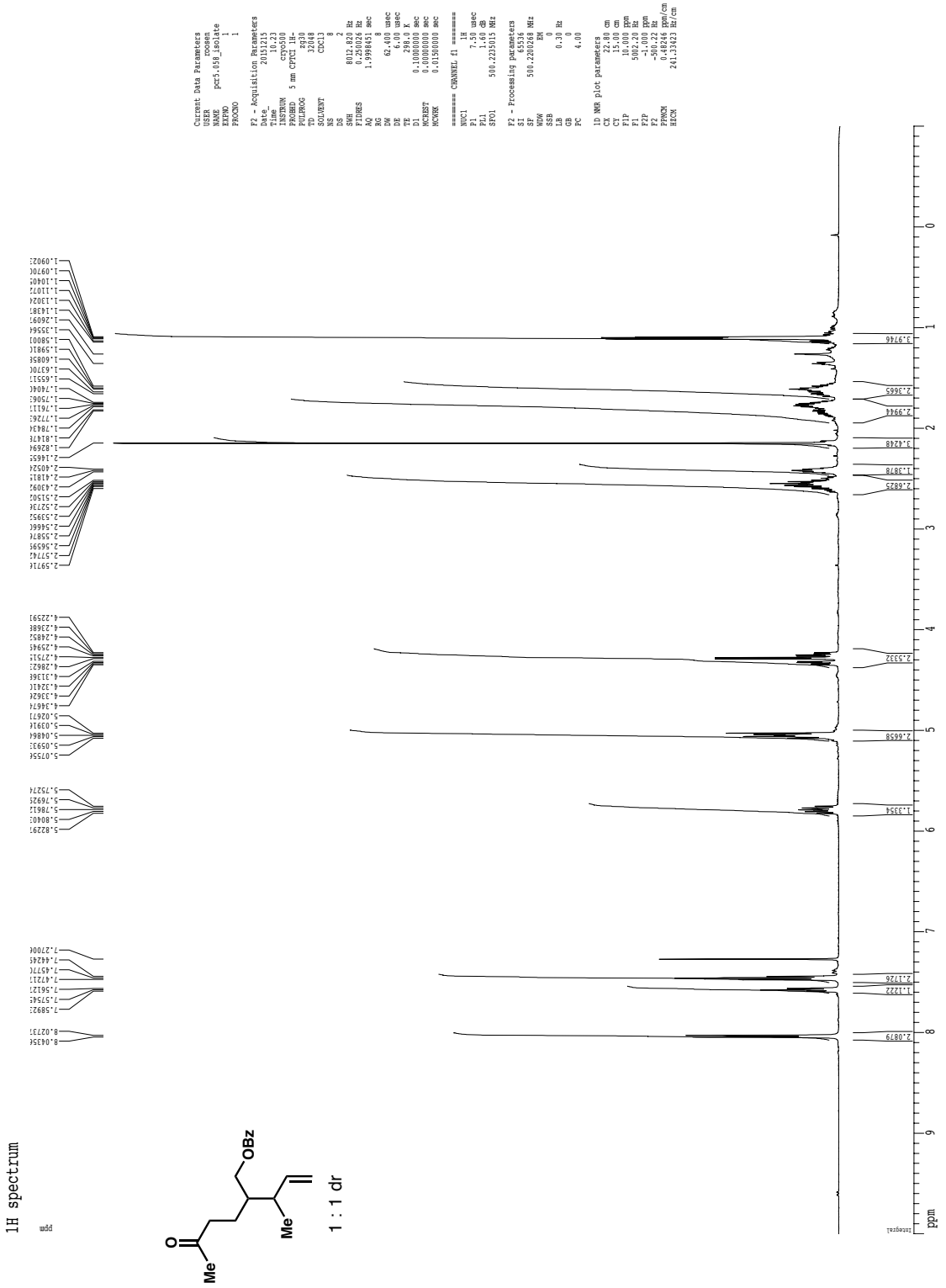
GPNAM1	SINE.100
GPNAM2	SINE.100
GPX1	0.00 %
GPX2	0.00 %
GPY1	0.00 %
GPY2	0.00 %
GPZ1	30.00 %
GPZ2	50.00 %
p15	500.00 usec
p16	1000.00 usec

F2 - Processing parameters

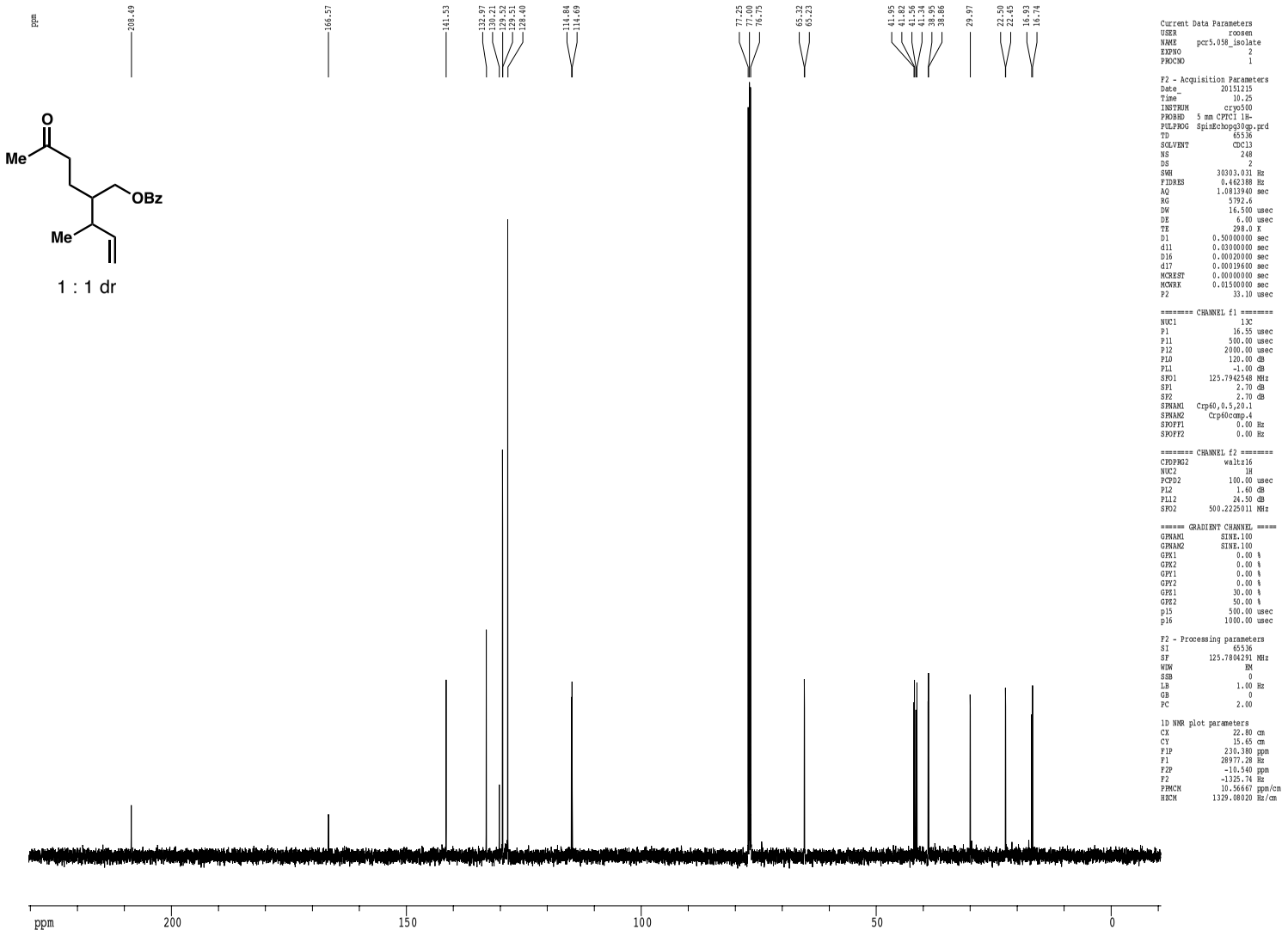
SI	65536
SF	125.7804295 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	2.50

1D NMR plot parameters

CX	22.80 cm
CY	10.00 cm
F1P	230.376 ppm
F1	28976.81 Hz
F2P	-10.544 ppm
F2	-1326.21 Hz
PPMCM	10.56667 ppm/cm
HZCM	1329.08020 Hz/cm


1H spectrum
ppm
Me
OBz
Me
1 : 1 dr

Z-restored spin-echo 13C spectrum with 1H decoupling



Current Data Parameters
USER roosen
NAME pcr5.058_isolate
EXPNO 2
PROCNO 1

F2 - Acquisition Parameters
Date_ 20151215
Time 10.25
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG SpinEchopg30gp.prd
TD 65536
SOLVENT CDCl3
NS 248
DS 2
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0813940 sec
RG 5792.6
DW 16.500 usec
DE 6.00 usec
TE 298.0 K
D1 0.50000000 sec
d11 0.03000000 sec
D16 0.00020000 sec
d17 0.00019600 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
P2 33.10 usec

======= CHANNEL f1 =======
NUC1 13C
P1 16.55 usec
P11 500.00 usec
P12 2000.00 usec
PL0 120.00 dB
PL1 -1.00 dB
SFO1 125.7942548 MHz
SP1 2.70 dB
SP2 2.70 dB
SPNAM1 Crp60,0.5,20.1
SPNAM2 Crp60comp.4
SPOFF1 0.00 Hz
SPOFF2 0.00 Hz

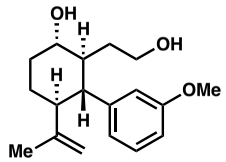
======= CHANNEL f2 =======
CPDPRG2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 1.60 dB
PL12 24.50 dB
SFO2 500.2225011 MHz

===== GRADIENT CHANNEL ====
GPNAM1 SINE.100
GPNAM2 SINE.100
GPX1 0.00 %
GPX2 0.00 %
GPY1 0.00 %
GPY2 0.00 %
GPZ1 30.00 %
GPZ2 50.00 %
p15 500.00 usec
p16 1000.00 usec

F2 - Processing parameters
SI 65536
SF 125.7804291 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00

1D NMR plot parameters
CX 22.80 cm
CY 15.65 cm
F1P 230.380 ppm
F1 28977.28 Hz
F2P -10.540 ppm
F2 -1325.74 Hz
PPMCM 10.56667 ppm/cm
HZCM 1329.08020 Hz/cm

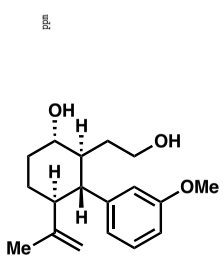
1H spectrum



7 : 1 dr

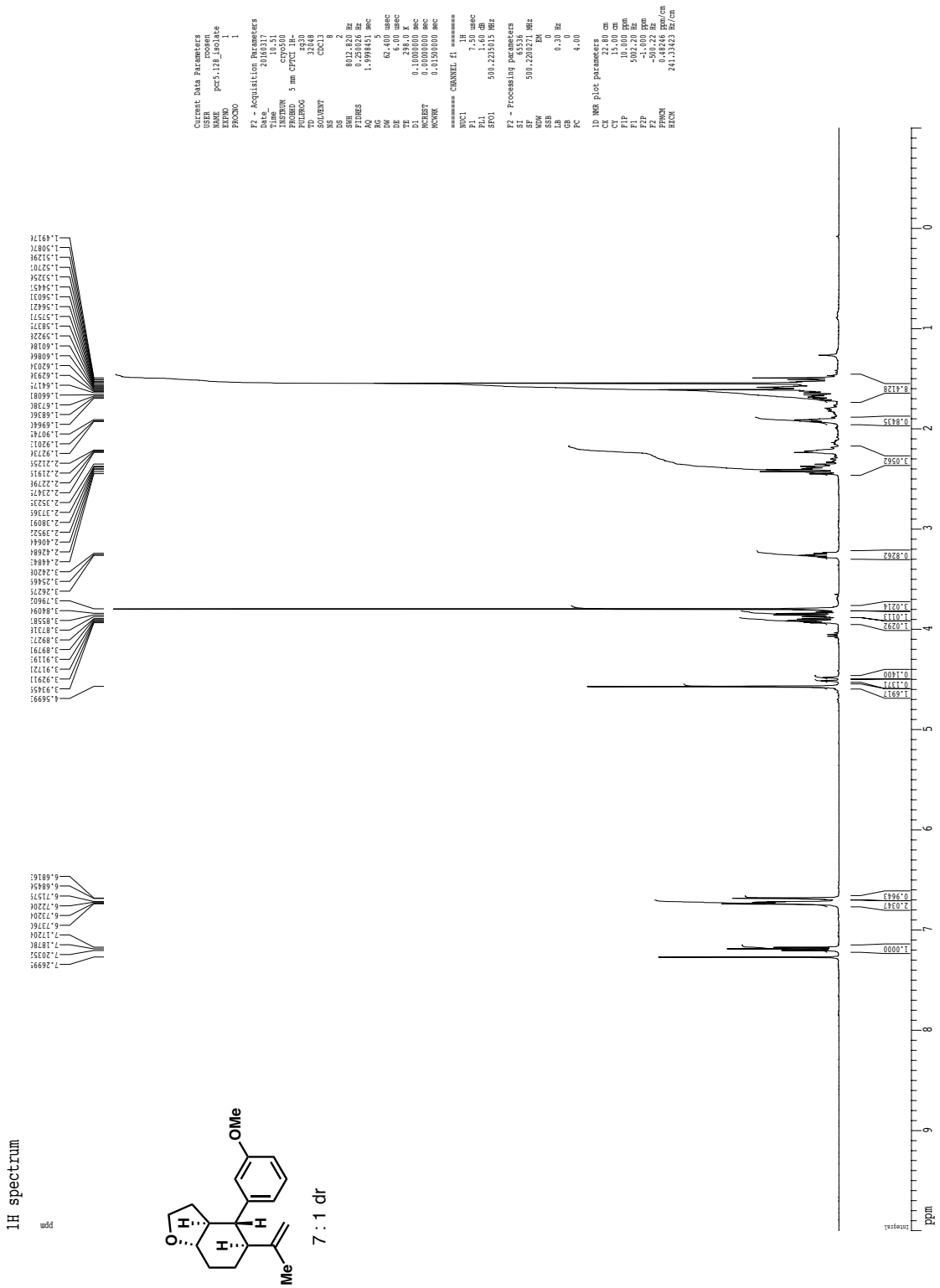

```
Current Data Parameters
USER                roosen
NAME          pcr5.125_isolate
EXPNO                    1
PROCNO                   1

F2 - Acquisition Parameters
Date_              20160309
Time                 10.43
INSTRUM            cryo500
PROBHD    5 mm CPTCI 1H-
PULPROG               zg30
TD                   32048
SOLVENT              CDCl3
NS                       8
DS                       2
SWH                8012.820 Hz
FIDRES             0.250026 Hz
AQ                 1.9998451 sec
RG                       3.2
DW                  62.400 usec
DE                   6.00 usec
TE                  298.0 K
D1                0.10000000 sec
MCREST            0.00000000 sec
MCWRK             0.01500000 sec

======== CHANNEL f1 ========
NUC1                     1H
P1                    7.50 usec
PL1                   1.60 dB
SFO1           500.2235015 MHz

F2 - Processing parameters
SI                       65536
SF             500.2200257 MHz
WDW                      EM
SSB                      0
LB                    0.30 Hz
GB                       0
PC                    4.00

1D NMR plot parameters
CX                   22.80 cm
CY                   15.00 cm
F1P                 10.000 ppm
F1                 5002.20 Hz
F2P                -1.000 ppm
F2                 -500.22 Hz
PPMCM              0.48246 ppm/cm
HZCM             241.33423 Hz/cm
```

Z-restored spin-echo 13C spectrum with 1H decoupling

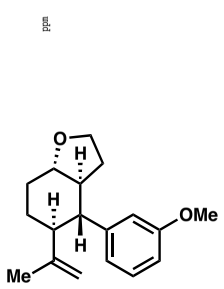


7 : 1 dr


```
Current Data Parameters
USER              roosen
NAME      pcr5.125_isolate
EXPNO                    2
PROCNO                   1

F2 - Acquisition Parameters
Date_          20160309
Time              10.45
INSTRUM          cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD                65536
SOLVENT           CDCl3
NS                   88
DS                    2
SWH           30303.031 Hz
FIDRES        0.462388 Hz
AQ            1.0813940 sec
RG               2580.3
DW                16.500 usec
DE                 6.00 usec
TE               298.0 K
D1            0.50000000 sec
d11           0.03000000 sec
D16           0.00020000 sec
d17           0.00019600 sec
MCREST        0.00000000 sec
MCWRK         0.01500000 sec
P2                33.10 usec

======= CHANNEL f1 =======
NUC1                 13C
P1                 16.55 usec
P11               500.00 usec
P12              2000.00 usec
PL0               120.00 dB
PL1                -1.00 dB
SFO1         125.7942548 MHz
SP1                2.70 dB
SP2                2.70 dB
SPNAM1    Crp60,0.5,20.1
SPNAM2      Crp60comp.4
SPOFF1               0.00 Hz
SPOFF2               0.00 Hz

======= CHANNEL f2 =======
CPDPRG2          waltz16
NUC2                 1H
PCPD2             100.00 usec
PL2                1.60 dB
PL12              24.50 dB
SFO2         500.2225011 MHz

===== GRADIENT CHANNEL ====
GPNAM1           SINE.100
GPNAM2           SINE.100
GPX1                0.00 %
GPX2                0.00 %
GPY1                0.00 %
GPY2                0.00 %
GPZ1               30.00 %
GPZ2               50.00 %
p15               500.00 usec
p16              1000.00 usec

F2 - Processing parameters
SI                  65536
SF           125.7804379 MHz
WDW                    EM
SSB                    0
LB                  1.00 Hz
GB                     0
PC                  2.00

1D NMR plot parameters
CX                 22.80 cm
CY                 10.00 cm
F1P              230.310 ppm
F1               28968.50 Hz
F2P              -10.610 ppm
F2               -1334.53 Hz
PPMCM            10.56667 ppm/cm
HZCM          1329.08032 Hz/cm
```


1H spectrum
ppm
OMe
H
H
H
O
Me
7 : 1 dr

Z-restored spin-echo 13C spectrum with 1H decoupling



7 : 1 dr


```
Current Data Parameters
USER              roosen
NAME      pcr5.128_isolate
EXPNO                    2
PROCNO                   1

F2 - Acquisition Parameters
Date_           20160317
Time              10.54
INSTRUM           cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD                65536
SOLVENT           CDCl3
NS                  240
DS                    2
SWH           30303.031 Hz
FIDRES        0.462388 Hz
AQ            1.0813940 sec
RG              14596.5
DW                16.500 usec
DE                 6.00 usec
TE               298.0 K
D1           0.50000000 sec
d11          0.03000000 sec
D16          0.00020000 sec
d17          0.00019600 sec
MCREST       0.00000000 sec
MCWRK        0.01500000 sec
P2                33.10 usec

======= CHANNEL f1 =======
NUC1                13C
P1                16.55 usec
P11              500.00 usec
P12             2000.00 usec
PL0              120.00 dB
PL1               -1.00 dB
SFO1        125.7942548 MHz
SP1               2.70 dB
SP2               2.70 dB
SPNAM1   Crp60,0.5,20.1
SPNAM2     Crp60comp.4
SPOFF1               0.00 Hz
SPOFF2               0.00 Hz

======= CHANNEL f2 =======
CPDPRG2          waltz16
NUC2                1H
PCPD2            100.00 usec
PL2                1.60 dB
PL12              24.50 dB
SFO2        500.2225011 MHz

===== GRADIENT CHANNEL ====
GPNAM1          SINE.100
GPNAM2          SINE.100
GPX1               0.00 %
GPX2               0.00 %
GPY1               0.00 %
GPY2               0.00 %
GPZ1              30.00 %
GPZ2              50.00 %
p15              500.00 usec
p16             1000.00 usec

F2 - Processing parameters
SI                65536
SF          125.7804291 MHz
WDW                  EM
SSB                   0
LB                 1.00 Hz
GB                    0
PC                 2.00

1D NMR plot parameters
CX                22.80 cm
CY                15.65 cm
F1P             230.380 ppm
F1              28977.28 Hz
F2P              -10.540 ppm
F2              -1325.75 Hz
PPMCM          10.56667 ppm/cm
HZCM         1329.08032 Hz/cm
```

APPENDIX B: X-ray Crystallographic Data

Figure B1. X-Ray Structure for **3.37**.

Table B1. Crystal Data and Structure Refinement for **3.37**.

Identification code	CCDC #1033631 (cdv24)	
Empirical formula	$C_{18}\ H_{26}\ O_2$	
Formula weight	274.39	
Temperature	143(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	$P2_1/c$	
Unit cell dimensions	a = 5.9268(6) Å	a= 90°.
	b = 33.959(4) Å	b= 105.1645(12)°.
	c = 7.8335(8) Å	g = 90°.
Volume	1521.7(3) Å^3	
Z	4	
Density (calculated)	1.198 Mg/m^3	
Absorption coefficient	0.076 mm^{-1}	
F(000)	600	
Crystal color	colorless	
Crystal size	0.284 x 0.265 x 0.152 mm^3	
Theta range for data collection	2.399 to 28.281°	
Index ranges	$-7 \le h \le 7$, $-43 \le k \le 43$, $-9 \le l \le 10$	
Reflections collected	17594	
Independent reflections	3575 [R(int) = 0.0253]	
Completeness to theta = 25.500°	99.8 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.8621 and 0.8088	
Refinement method	Full-matrix least-squares on F^2	

Data / restraints / parameters	3575 / 0 / 285
Goodness-of-fit on F^2	1.040
Final R indices [I>2sigma(I) = 3045 data]	R1 = 0.0390, wR2 = 0.1012
R indices (all data, 0.75 Å)	R1 = 0.0466, wR2 = 0.1064
Extinction coefficient	n/a
Largest diff. peak and hole	0.400 and -0.180 e.Å^{-3}

Figure B2. X-Ray Structure for **3.58**.

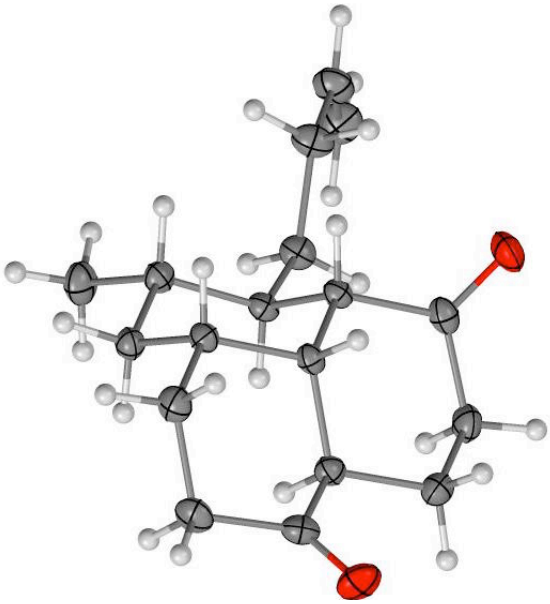


Table B2. Crystal Data and Structure Refinement for **3.58**.

Identification code	CCDC #1033632 (cdv27)	
Empirical formula	$C_{18}H_{26}O_2$	
Formula weight	274.39	
Temperature	143(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	$P2_1/c$	
Unit cell dimensions	a = 8.5541(7) Å	a= 90°.
	b = 8.9646(8) Å	b= 101.7717(11)°.
	c = 20.1698(17) Å	g = 90°.
Volume	1514.2(2) Å^3	
Z	4	
Density (calculated)	1.204 Mg/m^3	
Absorption coefficient	0.076 mm^{-1}	
F(000)	600	
Crystal color	colorless	
Crystal size	0.388 x 0.362 x 0.166 mm^3	

Theta range for data collection	2.063 to 27.094°
Index ranges	$-10 \leq h \leq 10$, $-11 \leq k \leq 11$, $-25 \leq l \leq 25$
Reflections collected	11171
Independent reflections	3309 [R(int) = 0.0255]
Completeness to theta = 25.500°	99.9 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.8621 and 0.8061
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3309 / 0 / 285
Goodness-of-fit on F^2	1.023
Final R indices [I>2sigma(I) = 2684 data]	R1 = 0.0401, wR2 = 0.1000
R indices (all data, ? Å)	R1 = 0.0520, wR2 = 0.1072
Largest diff. peak and hole	0.322 and -0.169 e.Å^{-3}

Figure B3. X-Ray Structure for **3.64**.

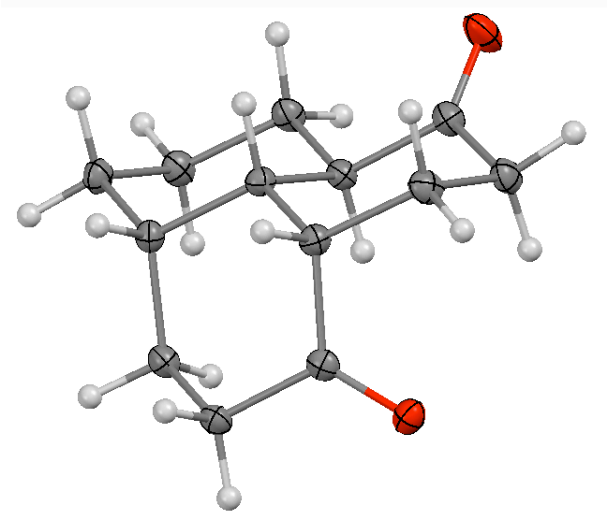


Table B3. Crystal Data and Structure Refinement for **3.64**.

Identification code	CCDC #1033633 (cdv25)	
Empirical formula	C_{13} H_{18} O_2	
Formula weight	206.27	
Temperature	83(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	$P\bar{1}$	
Unit cell dimensions	a = 7.4167(5) Å	a= 104.2514(8)°.
	b = 8.7830(6) Å	b= 98.7965(8)°.
	c = 9.1296(7) Å	g = 110.1474(7)°.
Volume	522.34(6) Å^3	
Z	2	

Density (calculated)	1.311 Mg/m^3
Absorption coefficient	0.086 mm^{-1}
F(000)	224
Crystal color	colorless
Crystal size	0.405 x 0.324 x 0.312 mm^3
Theta range for data collection	2.385 to 28.865°
Index ranges	$-9 \leq h \leq 10$, $-11 \leq k \leq 11$, $-12 \leq l \leq 11$
Reflections collected	6268
Independent reflections	2486 [R(int) = 0.0111]
Completeness to theta = 25.500°	99.1 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.8621 and 0.8158
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2486 / 0 / 208
Goodness-of-fit on F^2	1.084
Final R indices [I>2sigma(I) = 2311 data]	R1 = 0.0391, wR2 = 0.1147
R indices (all data, 0.74 Å)	R1 = 0.0411, wR2 = 0.1168
Extinction coefficient	n/a
Largest diff. peak and hole	0.390 and -0.206 $e.Å^{-3}$

Figure B4. X-Ray Structure for **5.70**.

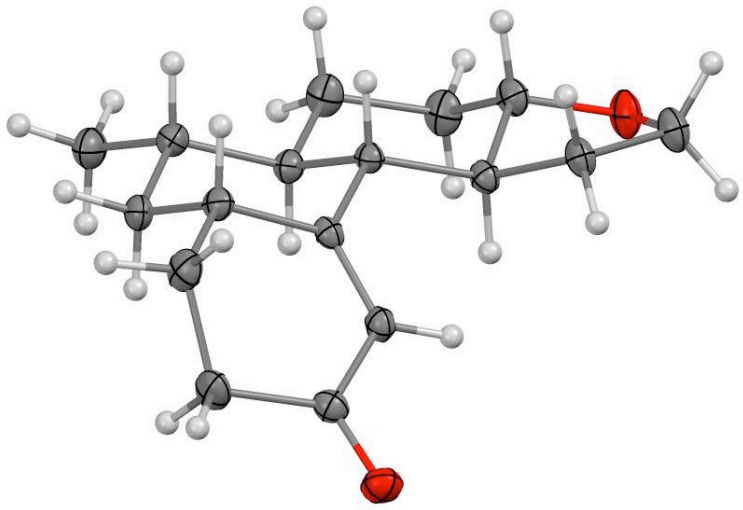


Table B4. Crystal Data and Structure Refinement for **5.70**.

Identification code	CCDC #1474440 (cdv39)
Empirical formula	$C_{17}H_{24}O_2$
Formula weight	260.36
Temperature	133(2) K
Wavelength	0.71073 Å
Crystal system	Triclinic

Space group	$P\bar{1}$	
Unit cell dimensions	a = 7.0946(5) Å	a= 91.4370(8)°.
	b = 10.4299(7) Å	b= 109.1829(8)°.
	c = 10.7084(7) Å	g = 107.5789(8)°.
Volume	706.60(8) $Å^3$	
Z	2	
Density (calculated)	1.224 Mg/m^3	
Absorption coefficient	0.078 mm^{-1}	
F(000)	284	
Crystal color	colorless	
Crystal size	0.464 x 0.277 x 0.255 mm^3	
Theta range for data collection	2.033 to 28.669°	
Index ranges	$-9 \le h \le 9, -13 \le k \le 13, -14 \le l \le 13$	
Reflections collected	8518	
Independent reflections	3351 [R(int) = 0.0142]	
Completeness to theta = 26.000°	99.7 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.8621 and 0.8062	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3351 / 0 / 172	
Goodness-of-fit on F^2	1.035	
Final R indices [I>2sigma(I) = 2954 data]	R1 = 0.0397, wR2 = 0.1086	
R indices (all data, 0.74 Å)	R1 = 0.0444, wR2 = 0.1131	
Largest diff. peak and hole	0.351 and -0.224 $e.Å^{-3}$	

Figure B5. X-Ray Structure for **5.74**.

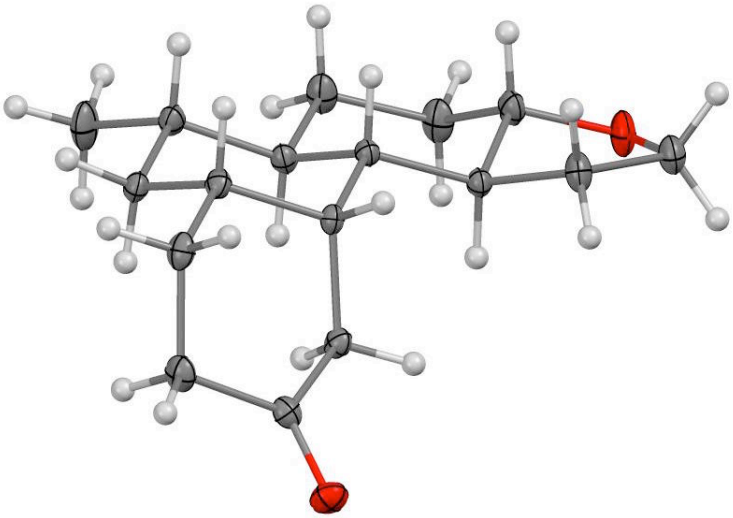


Table B5. Crystal Data and Structure Refinement for **5.74**.

Identification code	CCDC #1474441 (cdv40)	
Empirical formula	$C_{17}H_{26}O_2$	
Formula weight	262.38	
Temperature	88(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	$P2_1$	
Unit cell dimensions	a = 6.9229(3) Å	a= 90°.
	b = 7.1568(4) Å	b= 95.9776(7)°.
	c = 14.6894(7) Å	g = 90°.
Volume	723.84(6) $Å^3$	
Z	2	
Density (calculated)	1.204 Mg/m^3	
Absorption coefficient	0.076 mm^{-1}	
F(000)	288	
Crystal color	colorless	
Crystal size	0.433 x 0.297 x 0.156 mm^3	
Theta range for data collection	2.788 to 29.179°	
Index ranges	$-9 \le h \le 9$, $-9 \le k \le 9$, $-19 \le l \le 20$	
Reflections collected	9092	
Independent reflections	3603 [R(int) = 0.0154]	
Completeness to theta = 26.000°	99.9 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7458 and 0.6904	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3603 / 1 / 173	
Goodness-of-fit on F^2	1.033	
Final R indices [I>2sigma(I) = 3427 data]	R1 = 0.0324, wR2 = 0.0864	
R indices (all data, 0.73 Å)	R1 = 0.0344, wR2 = 0.0882	
Absolute structure parameter	0.0(3)	
Largest diff. peak and hole	0.319 and -0.171 $e.Å^{-3}$	