Title
Stereospecific Nickel-Catalyzed Cross-Coupling Reactions

Permalink
https://escholarship.org/uc/item/5fc2p3ps

Author
Johnson, Aaron George

Publication Date
2015

UNIVERSITY OF CALIFORNIA,
IRVINE

Stereospecific Nickel-Catalyzed Cross-Coupling Reactions

DISSERTATION

submitted in partial satisfaction of the requirements
for the degree of

DOCTOR OF PHILOSOPHY

in Chemistry

by

Aaron George Johnson

Dissertation Committee:
Professor Elizabeth R. Jarvo, Chair
Professor Christopher D. Vanderwal
Professor James S. Nowick

2015

DEDICATION

For my parents

who taught me to never stop learning

TABLE OF CONTENTS

Page

LIST OF FIGURES vi

LIST OF SCHEMES vii

LIST OF TABLES ix

ACKNOWLEDGMENTS x

CURRICULUM VITAE xii

ABSTRACT OF DISSERTATION xiv

CHAPTER 1: Stereospecific Nickel-Catalyzed Cross-Coupling Reactions of Grignard Reagents with Benzylic Ethers

1.1 Introduction 1

1.2 Results and Discussion 5

1.2.1 Optimization of Cross-Coupling Reaction 5

1.2.2 Reactions with Alkyl Grignard Reagents to From C_{sp^3}–C_{sp^3} Bonds 11

1.2.3 Reactions with Aryl Grignard Reagents to From C_{sp^3}–C_{sp^2} Bonds 14

1.2.4 Demonstration of Stereochemical Outcome 16

1.2.5 Biological Studies 17

1.3 Conclusion 17

1.4 Experimental Section 18

1.4.1 General Procedures 18

1.4.2 Synthesis of Alkyl and Aryl Halides and Organomagnesium Reagents for Cross-Coupling Reactions 19

1.4.3 Preparation of Grignard Reagents 22

1.4.4 Synthesis and Characterization of Substrates 24

1.4.5 Representative Procedure for Cross-Coupling Reactions 31

1.4.6 Characterization Data for Cross-Coupling Products 32

1.4.7 Crystallographic Data 44

Chapter 2: Studies of Pathways Leading to Side-Products of Kumada Type Cross-Coupling Reactions

2.1 Introduction 59

2.2 Optimization of Hydrogenolysis Protocol 62

2.3 Mechanistic Studies 65

2.3.1 Stereochemical and Mechanistic Studies with Compound **2.18** 66

2.3.2 Stereochemical and Mechanistic Studies with Compound **2.19** 70

2.4 Conclusion 73

2.5 Experimental Section 75

2.5.1 General Procedures 75

2.5.2 Preparation of Hydrogenolysis Substrates 76

2.5.3 Hydrogenolysis Reactions 79

2.5.4 Preparation of Mechanistic Probes 81

2.5.5 Representative Mechanistic Experiments..94

Chapter 3: Selective Synthesis of Either Enantiomer of an Anti-Breast Cancer Agent From a Common Enantioenriched Intermediate

3.1 Introduction 97

3.2 Synthesis of Bioactive Triarylmethane 99

3.3 Conclusion..101

3.4 Experimental Section 102

3.4.1 General Procedures...102

3.4.2 Preparation and Characterization of Products 103

APPENDIX A: ^{1}H and ^{13}C NMR Spectra 111

APPENDIX B: SFC Traces 203

LIST OF FIGURES

Figure 1.1. Bioactivity of Compound 1.32 17

Figure 2.1. Mechanistic Probes....................65

Figure 2.2. Diastereomers of Compound 2.18....................66

Figure 2.3. Diastereomers of Compound 2.19....................70

Figure 3.1. Bioactive Triarylmethanes....................97

LIST OF SCHEMES

Scheme 1.1. Substrate Directed Alkyl-Alkyl Cross-Coupling Reactions......................................2

Scheme 1.2. Nickel-Catalyzed Alkyl-Alkyl Cross-Coupling Reaction...2

Scheme 1.3. Stereocontrolled Alkyl-Alkyl Bond Forming Suzuki Reactions 3

Scheme 1.4. Stereoconvergent vs Stereospecific Reactions...3

Scheme 1.5. Examples of Asymmetric Alcohol Synthesis...4

Scheme 1.6. Synthesis of Methyl Ether and Stereospecific Cross-Coupling Reaction...................5

Scheme 1.7. Proposed Hydrogenolysis Pathway...7

Scheme 1.8. Cross-Coupling Reactions with Cyclohexyl Substrate 9

Scheme 1.9. Proposed Formation of Active and Poisoned Catalyst...10

Scheme 1.10. Ni(dppe)Cl_2 as Precatalyst 11

Scheme 1.11. Demonstration of Stereochemical Outcome 16

Scheme 2.1. Hydrogenolysis of Benzhydryl Substrates...59

Scheme 2.2. Use of Barton-McCombie Deoxygenation in Synthesis of Tricycloillicinone 60

Scheme 2.3. Transition Metal-Catalyzed Hydrogenolysis 61

Scheme 2.4. Initial Hydrogenolysis Conditions Applied to Simple Benzylic Substrates 62

Scheme 2.5. Comparison of Bromine and Iodine Counter Ions in the Hydrogenolysis Reaction.63

Scheme 2.6. Hydrogenolysis with Other Substrates...65

Scheme 2.7. Preparation of Alkynyl Napthalene..66

Scheme 2.8. Synthesis of 2.18a. 66

Scheme 2.9. Synthesis of 2.18b 67

Scheme 2.10. Results with Ethers 2.18a and 2.18b 68

Scheme 2.11. Hydrogenolysis with Inversion 69

Scheme 2.12. Mechansim of Elimination 70

Scheme 2.13. Synthesis of Compound 2.19 71

Scheme 2.14. Expected Mechanism of Hydrogenolysis 72

Scheme 2.15 Outcomes of Reactions with 2.20a and 2.20b 72

Scheme 2.16. Mechanisms of β-Hydride Elimination 73

Scheme 3.1. Strategies to Prepare Both Enantiomers of a Triarylmethane form a Common Enantioenriched Intermediate 99

Scheme 3.2. Synthesis of Triarylmethane 3.1 100

LIST OF TABLES

Table 1.1. Effect of Grignard Reagent Age 6

Table 1.2. Comparison of Nickel Sources 7

Table 1.3. Ligand Screen 8

Table 1.4. Variability in Cross-Coupling Results 9

Table 1.5. Effect of Ligand to Nickel Ratio on Reactivity 11

Table 1.6. Alkyl Grignard Reagent Scope 12

Table 1.7. Optimization of Reaction with CF_3 Containing Nucleophile 13

Table 1.8. Effect of Olefin Substitution 14

Table 1.9. Aryl Grignard Reagent Scope. 15

Table 2.1. Efficacy of Grignard Reagents in Hydrogenolysis Reaction 63

Table 2.2. Ligand Screen 64

Table 2.3. Solvent Effects 64

ACKNOWLEDGMENTS

I thank John Wiley and Sons for permission to include Chapter 1, portions of which were originally published in *Angewante Chemie International Addition*. I also thank Elsevier for permission to include Chapter 3, portions of which were originally published in *Tetrahedron Letters*.

I need to thank Stanley Behrens and the University of California, Irvine Graduate Division for awarding me a Stanley Behrens Public Impact Fellowship. The funding and support that came from this fellowship was invaluable to me as I worked to push my research forward and has helped me keep in the forefront of my mind the impact that I, as a chemist, can make on society. I also wish to thank the Graduate Division for awarding me a LaVerne Noyes Fellowship. I wish to honor my great grandfather, Aaron Clayton Parker, whose service to our country in World War I both guaranteed our freedom and qualified me for this award. His sacrifices were great and have not been forgotten. I also wish to thank Jennifer Bentson-Gebel for her continued support of the Gebel award. The recognition and funding that came with this award came at a crucial time for me and was invaluable in pushing me through the third and fourth years of my Ph.D.

I wish to thank the American Chemical Society Green Chemistry Institute and the National Science Foundation for selecting me as a Green Chemistry Scholar, allowing me to attend and present my research at the 17th annual Green Chemistry and Engineering Conference in Bethesda, Maryland. This experience permanently changed the way I think about chemistry and gave me a solid commitment to minimize the environmental impact of my work.

I would like to thank my Ph.D. advisor, Professor Elizabeth Jarvo, for her mentorship and support. I could not be the scientist I have become without her expert hand. I also wish to thank my undergraduate research advisor, Professor Steven Castle, who welcomed me into his lab and ignited my passion for chemistry.

I wish to thank Professors James Nowick, Chris Vanderwal and Dave Van Vranken for insightful discussions on chemistry and life that both enriched my education and, on more than one occasion, pushed me past road blocks in my research.

I want to thank my lab mates in both the Jarvo and the Castle Labs. They have been fantastic mentors and have become great friends. I especially wish to thank Dr. Iva Yonova, Michael Harris, Charlotte Osborne and Lucas Erickson with whom I have shared projects. They have all been great teammates, and I feel privileged to have had the chance to work with them.

I want to thank my parents, Tom and Stephanie Johnson, for their love and support. I thank my father for teaching me how to work hard while maintaining balance. I thank my mother for instilling a deep love of learning within me. I could never have developed the intellect necessary to obtain a Ph.D. without both of them.

I want to thank my brothers, Thomas, Abe, and John for their frequent visits and fantastic adventures.

Finally, I would like to thank my beautiful wife, Annique, whose endless support and unfailing love has pushed me forward more than anything else. In order for me to earn my Ph.D., she has had to make tremendous sacrifices. To my wife, thank you for never letting me even entertain the thought of leaving UCI without finishing my Ph.D. Thank you for being willing to cross state borders to help me achieve my dreams. Thank you for the great memories we have made in California. Thank you for being my best friend and the love of my life.

CURRICULUM VITAE

Aaron George Johnson

EDUCATION:

2010-2015 Ph.D. in Chemistry, University of California, Irvine

2006-2009 B.S., Cum Laude, Biochemistry, Brigham Young University
Minors: Business Management and Asian Studies

RESEARCH EXPERIENCE:

2010-2015 **Doctoral Research** University of California, Irvine; Irvine, CA
Advisor: Professor Elizabeth Jarvo

- Stereospecific nickel-catalyzed cross-coupling reactions of alkyl ethers with alkyl and aryl Grignard reagents
- Mechanistic studies of Kumada-type cross-coupling and major side reactions
- Synthesis of either enantiomer of a bioactive triarylmethane

2008-2009 **Undergraduate Research** Brigham Young University; Provo, UT
Advisor: Professor Steven Castle

- Investigation of the scope of an enantioselective ketone allylation
- Work towards the total synthesis of the natural product hasubanonine

INDUSTRY EXPERIENCE:

2007 Intern: K2 Energy Solutions (battery plant); Shanghai, China

- Translation · interpretation · quality control · global logistics · English instruction

LANGUAGE EXPERIENCE: Mandarin Chinese

2009-2010 Visiting Scholar at Tianjin Normal University; Tianjin, China
2007 K2 Energy Solutions, Technical Interpreter (Internship); Shanghai, China
2006-2009 Minor in Asian Studies including three years of Mandarin language coursework
2004-2006 Brisbane Australia Mission, teaching overseas Chinese nationals in Mandarin Chinese

SAFETY EXPERIENCE:

2011-2015 Jarvo Laboratory Safety On Site Representative

- Identify and correct safety hazards · develop and implement standard operating procedures · train new personnel in best practices · develop safety culture · ensure compliance

TEACHING EXPERIENCE:

2011-2014 Lecture and Laboratory Teaching Assistant: General Chemistry (UCI-4 quarters)
2009-2012 Lecture and Laboratory Teaching Assistant: Organic Chemistry (UCI-8 quarters)
2009-2010 Conversational English (Tianjin Normal University)
2007 English for Battery Manufacturing (K2 Energy Solutions; Shanghai, China)

SOCIETY MEMBERSHIPS:

2014 American Chemical Society
2009 Honors Society of Phi Kappa Phi
2007 Golden Key International Honors Society

ADVOCACY:

2014 UC Graduate Advocacy Day Delegate; Sacramento, CA
  - Selected as a delegate to explain to state legislatures the public impact of academic research

AWARDS AND HONORS:

2014	Stanley Behrens Public Impact Fellow
2013	NSF Green Chemistry and Engineering Conference NSF Scholar
2013	Gebel Award for Excellence in Environmental Chemistry and Community Service
2012	La Verne Noyes Fellow
2011	National Science Foundation Graduate Research Fellowship Honorable Mention
2009	Chinese Government Scholarship for Visiting Scholars
2009	James and Virginia Ott Award for Promise for Success in Research
2006-2009	Brigham Young Scholarship (merit based, full tuition)

PUBLICATIONS:

- **Johnson, A. G.**; Erickson, L. W.; Greene, M. A.; Yonova, I. M.; Taylor, B. L. H.; Jarvo, E. R. “Mechanistic Study of Stereospecific Nickel-Catalyzed Cross-Coupling Reactions.” Manuscript in preparation.
- **Johnson, A. G.**; Tranquilli, M. M.; Harris, M. R.; Jarvo, E. R. “Selective Synthesis of Either Enantiomer of an Anti-Breast Cancer Agent Via a Common Enantioenriched Intermediate.” *Tetrahedron Lett.* **2015**, *56*, 3486.
- **Johnson, A. G.**[‡]; Yonova, I. M.[‡]; Osborne, C. A.; Moore, C. E.; Morrissette, N. S.; Jarvo, E. R. “Stereospecific Nickel-Catalyzed Cross-Coupling Reaction of Alkyl Grignard Reagents and Identification of Selective Anti-Breast-Cancer Agents.” *Angew. Chem. Int. Ed.* 2014, *53*, 2422–2427.
- **Johnson, A. G.**; Loertscher, B. M.; Moeck, A. R.; Matthews S. S.; Ess, D. H.; Castle, S. L. “Experimental and Theoretical Investigation of the Scope of Enantioselective Ketone Allylations Employing Nakamura’s Allylzinc-bisoxazoline Reagent.” *Bioorg. Med. Chem. Lett.* 2011, *21*, 2706–2710.

PRESENTATIONS:

- **Johnson, A. G.**; Yonova, I. M.; Erickson, L. W.; Greene, M. A.; Osborne, C. A.; Jarvo E. R. Stereospecific Nickel-Catalyzed Cross-Coupling of Benzylic Ethers and Grignard Reagents. Presented at the 249th National Meeting of the American Chemical Society. Denver, CO, March 25, 2015 (oral presentation).
- **Johnson, A. G.** The Impact of Molecular Handedness on Drug Discovery and Development. Presented at the 2014 UCI Public Impact Fellows Reception. Irvine, CA, February 3, 2014 (oral presentation).
- **Johnson, A. G.**; Yonova, I. M.; Jarvo, E. R. Stereospecific Nickel-Catalyzed Cross-Coupling of Benzylic Ethers with Grignard Reagents. Presented at the 17th Annual ACS Green Chemistry and Engineering Conference. North Bethesda, MD, June, 19, 2013 (poster presentation).
- **Johnson, A. G.**; Yonova, I. M.; Jarvo, E. R. Stereospecific Nickel-Catalyzed Cross-Coupling of Benzylic Ethers with Grignard Reagents. Presented at the University of California, Irvine, Graduate and Postdoctoral Research Symposium. Irvine, CA, February 22, 2013 (oral presentation).
- **Johnson, A. G.**; Moech, A. R.; Castle, S. L. Asymmetric Allylation of Assorted Ketones Using Nakamura’s Reagent. Presented at the Pacific Northwest Undergraduate Research Symposium on Organic Chemistry and Chemical Biology, Corvallis, OR, August 3-4, 2009 (oral presentation).

ABSTRACT OF DISSERTATION

Stereospecific Nickel-Catalyzed Cross-Coupling Reactions

by

Aaron George Johnson

Doctor of Philosophy in Chemistry

University of California, Irvine, 2015

Professor Elizabeth R. Jarvo, Chair

Transition metal catalyzed cross-coupling reactions have become a staple of organic synthesis and are frequently the most practical strategy for the preparation of medicinal agents and fine chemicals. Catalysts based on the precious metal palladium are commonly used in cross-coupling reactions. Replacing palladium catalysts with nickel catalysts is an active area of research as such advances present significant benefits including increasing the sustainability of transformations and new mechanisms for control of stereochemistry in the construction of C_{sp^3}–C_{sp^3} bonds.

In Chapter 1, a stereospecific nickel-catalyzed cross-coupling reaction of secondary benzylic ethers with a variety of aliphatic and aryl Grignard reagents is presented. The method is highly stereospecific and proceeds with inversion at the benzylic carbon. Products prepared by this method were subject to biological testing, and a thiophene-containing product was shown to selectively inhibit the growth of MCF-7 breast cancer cells.

In Chapter 2, mechanistic studies that provide insight into the mechanism of oxidative addition as well as the mechanisms of major side reactions, hydrogenolysis and β-hydride elimination, are presented. Experiments presented provide evidence that the mechanisms of

cross-coupling, hydrogenolysis, and β-hydride elimination reactions all include a step of oxidative addition with inversion at the benzylic center. Hydrogenolysis was also shown to be stereospecific, proceeding with overall inversion at the stereogenic center.

In Chapter 3, the application of nickel-catalyzed cross-coupling reactions to the synthesis of either enantiomer of a bioactive triaryl methane from a single enantiomer of a precursor alcohol is presented. In the key cross-coupling step a Kumada protocol allows for cross-coupling with inversion at the benzylic carbon, while a Suzuki reaction allows for cross-coupling with retention.

Chapter 1

Stereospecific Nickel-Catalyzed Cross-Coupling Reactions of Grignard Reagents with Benzylic Ethers

1.1 Introduction

Palladium and nickel catalyzed cross-coupling reactions have revolutionized organic chemistry.[1] For C_{sp^2}–C_{sp^2} bond formation, transition-metal catalyzed cross-coupling reactions are likely the first disconnection a chemist will propose. Nonetheless, these reactions remain underdeveloped in forming C_{sp^3}–C_{sp^3} bonds. Two reasons are commonly cited to explain the difficulty of transition metal mediated alkyl-alkyl cross-coupling reactions: oxidative addition to an alkyl electrophile is slower than oxidative addition to an aryl or vinyl electrophile, and β-hydride elimination often outcompetes reductive elimination.[1b] The latter challenge is especially pertinent when both coupling partners contain β-hydrogens. Despite these challenges, recent advances have brought the field closer to realizing the potential of transition metal-catalyzed alkyl-alkyl bond formation. Major milestones in nickel-catalyzed alkyl-alkyl cross-coupling research have included reactions between two primary alkyl groups, reactions between primary and secondary alkyl groups, and stereoconvergent reactions.

The Knochel group demonstrated that alkyl-alkyl bonds between two primary coupling partners could be formed in a nickel-catalyzed reaction when they reported the reaction shown in Scheme 1.1.[2] Reductive elimination to form C_{sp^3}–C_{sp^3} bonds is difficult owing to the electron rich nature of sp^3 carbons. In Knochel's transformation, a pendant olefin promotes reductive elimination by decreasing electron density at the metal center through a backbonding interaction

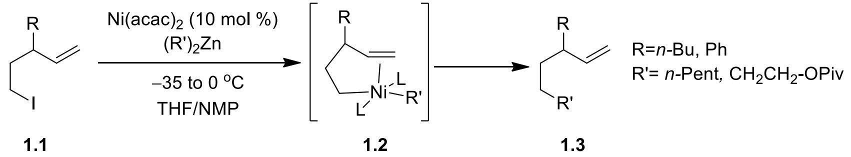
---

[1] (a) Jana, R.; Pathak, T. P.; Sigman, M. S. *Chem. Rev.* **2011**, *111*, 1417. (b) Netherton, M. R.; Fu. G. C. *Adv. Synth. Catal.* **2004**, *346*, 1525. (c) Rudolph, A.; Lautens, M. *Angew. Chem. Int. Ed.* **2009**, *48*, 2656. (d) Johnson, C. R.; De Jong, R. L. *J. Org. Chem.* **1992**, *57*, 594.

[2] (a) Giovannini, R.; Stüdemann, T.; Devasagayaraj, A.; Dussin, G.; Knochel, P. *J. Org. Chem.* **1999**, *64*, 3544. (b) For a more recent example see: Nielsen, D. K.; Huang, C.-Y.; Doyle, A. G. *J. Am. Chem. Soc.* **2013**, *135*, 13605.

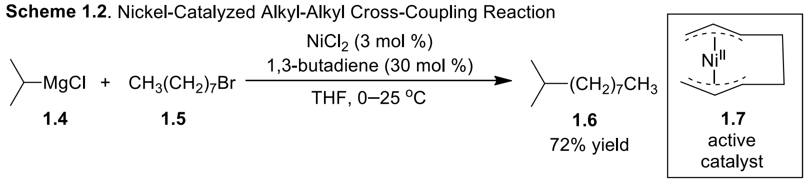
(**1.2**). Other π-accepting functional groups such as ketones, cyanides, or esters also increase reactivity.[3] Knochel's work showcased the potential of using nickel catalysts in alkyl-alkyl cross-coupling reactions.

Scheme 1.1. Substrate Directed Alklyl-Alkyl Cross-Coupling Reactions



Kambe has shown that nickel complexes can catalyze Kumada-type cross-coupling reactions between primary halides and primary and secondary Grignard reagents.[4] In the reaction shown in Scheme 1.2, two butadiene molecules dimerize around the metal center to form a bis-π-allyl Ni^{II} complex (**1.7**) that enters a proposed Ni^{II}–Ni^{IV} catalytic cycle. While initially developed to cross-couple primary alkyl groups, this reaction provides good yields with a secondary Grignard reagent, *i*-PrMgCl (**1.4**).[5]

Scheme 1.2. Nickel-Catalyzed Alkyl-Alkyl Cross-Coupling Reaction



In recent years, research in the Fu group has shown the power of nickel complexes to catalyze stereocontrolled alkyl-alkyl cross-coupling reactions. The Fu group has developed several methods to prepare enantioenriched tertiary products (Scheme 1.3, structure **1.10**) utilizing secondary alkyl halogens (**1.8**).[6] Many of these strategies are stereoselective. These

---

[3] (a) Giovannini, R.; Stüdemann, T.; Dussin, G.; Knochel, P. *Angew. Chem. Int. Ed.* **1998**, *37*, 2387. (b) For an example utilizing exogenous dimethyl fumerate see: Huang, C.-Y.; Doyle, A. G. *J. Am. Chem. Soc.* **2012**, *134*, 9541.

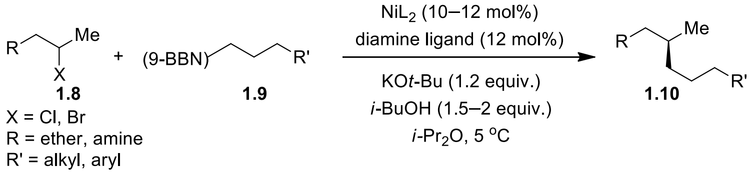
[4] Terao, J.; Watanabe, H.; Ikumi, A.; Kuniyasu, H.; Kambe, N. *J. Am. Chem. Soc.* **2002**, *124*, 4222.

[5] For a realted transformation in which secondary Grignard reagents are coupled to vinyl halides, see: (a) Hayashi, T.; Konishi, M.; Fukushima, M.; Mise, T.; Kagotani, M.; Tajika, M.; Kumada, M. *J. Am. Chem. Soc.* **1982**, *104*, 180. (b) Schwink, L.; Knochel, P. *Chem. Eur. J.* **1998**, *4*, 950.

[6] (a) Lu, Z.; Wilsily, A.; Fu, G. C. *J. Am. Chem. Soc.* **2011**, *133*, 8154. (b) Zhou, J.; Fu, G. C. *J. Am. Chem. Soc.* **2003**, *125*, 14726. (c) Lou, S.; Fu, G. C. *J. Am. Chem. Soc.* **2010**, *132*, 1264. (d) Lundin, P. M.; Fu, G. C. *J. Am.*

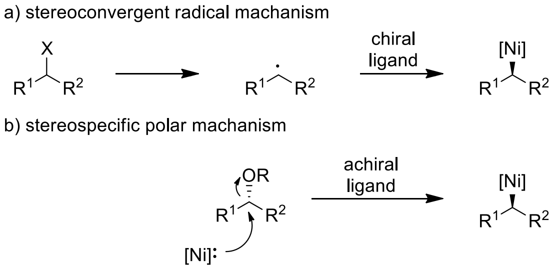
reactions are proposed to go through a radical mechanism and rely on a chiral catalyst to set stereochemistry in a stereoconvergent manner.

Scheme 1.3. Stereocontrolled Alkyl-Alkyl Bond Forming Suzuki Reactions



Stereoconvergent reactions, such as Fu's, represent a strategy that finds high utility when a stereocenter is to be set in a cross-coupling reaction (Scheme 1.4a). However, this strategy is not ideal when stereochemical information is already present at the reactive center of a substrate. In these cases a stereospecific approach, in which stereochemical information is transferred from substrate to product, is desired (Scheme 1.4b). As shown by Fu and others, alkyl halides are expected to go through a radical mechanism of oxidative addition and are not suitable substrates for stereospecific cross-coupling reactions because radical processes scramble stereochemical information.[7]

Scheme 1.4. Stereoconvergent vs Stereospecific Reactions



Ethers are suitable electrophiles for stereospecific nickel catalyzed C_{sp^3}–C_{sp^3} bond formation.[8] The literature of nickel-catalyzed substitution reactions of allylic ethers shows that

---

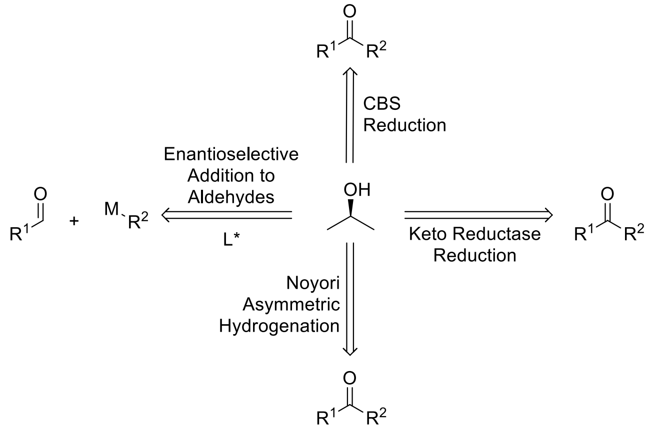
Chem. Soc. **2010**, *132*, 11027. (e) Owston, N. A.; Fu, G. C. *J. Am. Chem. Soc.*, **2010**, *132*, 11908. (f) Saito, B.; Fu. G. C. *J. Am. Chem. Soc.* **2008**, *130*, 6694.

[7] (a) Choi, J.; Martín-Gago, P.; Fu, G. C. *J. Am. Chem. Soc.* **2014**, *136*, 12161. (b) Vechorkin, O.; Csok, Z.; Scopelliti, R.; Hu, X. *Chem. Eur. J.* **2009**, *15*, 3889.; (c) Becker, Y.; Stille, J. K. *J. Am. Chem. Soc.* **1978**, *100*, 838. (d) Hall, T. L.; Lappert, M. F.; Lednor, P. W. *J. Chem. Soc., Dalton Trans* **1980**, 1448.

[8] For a stereospecific palladium catalyzed reaction, see: He, A.; Falck, J. R. *J. Am. Chem. Soc.* **2010**, *132*, 2524.

the oxidative addition of nickel complexes into C–O bonds may proceed through heterolytic bond cleavage.[9] Alcohol derivatives are also an attractive electrophile class owing to the variety of robust methods with which enantioenriched alcohols can be prepared (Scheme 1.5).[10] For these reasons, the cross-coupling of ethers with organometallic nucleophiles is a valuable contribution to the cross-coupling literature.

Scheme 1.5. Examples of Asymmetric Alcohol Synthesis



In 2011, the Jarvo lab demonstrated the utility of using ethers in Kumada-type couplings to install a methyl group.[11,12] An example is shown in Scheme 1.6. First enantioenriched alcohol **1.12** is prepared via a titanium mediated enantioselective addition of diethylzinc to

---

[9] (a) Consiglio, G.; Morandini, F.; Piccolo, O. *J. Am. Chem. Soc.* **1981**, *103*, 1846. (b) Kobayashi, Y; Ikeda, E. *J. Chem. Soc., Chem. Commun.***1994**, 1789. (c) Didiuk, M. T.; Morken, J. P.; Hoveyda, A. H. *Tetrahedron* **1996**, *54*, 1117.

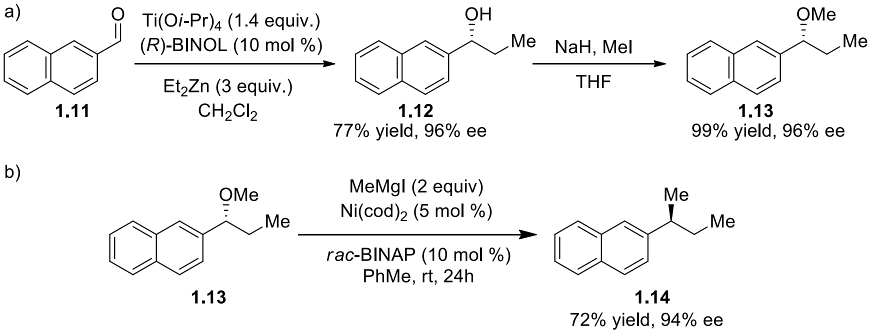
[10] (a) For CBS reduction, see: (i) Corey, E. J. (Nobel Lecture) *Angew. Chem. Int. Ed.* **1991**, *30*, 455. (ii) Corey, E. J.; Helal, C. J. *Angew. Chem. Int. Ed.* **1998**, *37*, 1986. (iii) “Reductions”: Li, J. J.; Limberakis, C.; Pflum, D. A. in *Modern Organic Synthesis in the Laboratory: A Collection of Standard Experimental Proceedures*, Oxford University Press, New York, **2007**, 96–97. (b) for keto reductacses, see: Bohren, K. M.; Bullock, B; Wermuth, B.; Gabbay, K. H. *J. Biol. Chem.* **1989**, *264*, 9547. For Noyori hydrogenation, see: (i) Noyori, R. (Nobel Lecture) *Angew. Chem. Int. Ed.* **2002**, *41*, 2008. (ii) Noyori, R.; Takaya, H. *Acc. Chem. Res.* **1990**, *23*, 345. (d) for assymetric additions to ketones, see: (i) Zhang, F.-Y.; Yip, C.-W.; Cao, R.; Chan, A. S. C. *Tetrahedron: Asymmetry* **1997**, *8*, 585. (ii) Braga, A. L.; Paixão, M. W.; Westermann, B.; Schneider, P. H.; Wessjohann, L. A. *J. Org. Chem.* **2008**, *73*, 2879.

[11] (a) Taylor, B. L. H.; Swift, E. C.; Waetzig, J. D.; Jarvo, E. R. *J. Am. Chem. Soc.* **2011**, *133*, 389. (b) For a variant that does not require an extended π-aromatic system see: Greene, M. A.; Yonova, I. M.; Williams, F. J.; Jarvo, E. R. *Org. Lett.* **2012**, *14*, 4293.

[12] A similar racemic cross-coupling reaction was reported by Shi, see: Guan, B.-T.; Xiang, S.-K.; Wang, B.-Q.; Sun, Z.-P.; Wang, Y.; Zhao, K.-Q.; Shi, Z.-J. *J. Am. Chem. Soc.* **2008**, *130*, 3268.

aldehyde **1.11** (Scheme 1.6a).[13] Methylation of alcohol **1.12** provides methyl ether **1.13** which is capable of undergoing oxidative addition.[14] Under the influence of an achiral catalyst, ether **1.13** will couple with methyl Grignard reagents with overall inversion at the stereogenic center to form enantioenriched target compound **1.14** (Scheme 1.6b).

Scheme 1.6. Synthesis of Methyl Ether and Stereospecific Cross-Coupling Reaction



The Jarvo lab's initial report established that this nickel-catalyzed cross-coupling method is feasible to install a methyl group to a variety of substrates. Herein are reported my efforts aimed to extend the scope of this methodology to include more complex alkyl and aryl Grignard reagents.[15]

1.2 Results and Discussion:

1.2.1 Optimization of Cross-Coupling Reaction

Initial attempts to perform the cross-coupling reaction with a propyl Grignard reagent showed that nickel could catalyze cross-coupling reactions between methyl ether **1.13** and *n*-propylmagnesium iodide to form cross-coupled product **1.15**. Unfortunately, the reaction gave variable yields (14–65%) that seemed to erode proportional to catalyst age (Table 1.1, entry 1).[16]

---

[13] The competing enantiomer conversion method can be used to assign the absolute configuration of secondary alcohols; see: Wagner, A. J.; Rychnovsky, S. D. *J. Org. Chem.* **2013**, *78*, 4594.

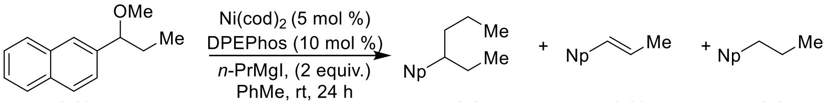
[14] Herrmann, J. M.; König, B. *Eur. J. Org. Chem.* **2013**, 7017.

[15] This chapter will focus on content of the following publication: Yonova, I. M.; Johnson, A. G.; Osborne, C. A.; Moore, C. E.; Morrissette, N. S.; Jarvo, E. R. *Angew. Chem. Int. Ed.* **2014**, *53*, 2422.

[16] Taylor, B. L. H.; Swift, E. C.; Waetzig, J. D.; Jarvo, E. R. *J. Am. Chem. Soc.* **2011**, *133*, 389.

A time-correlated drop in yield could be explained if a co-catalyst was precipitating out of the Grignard reagent solution as the solution aged. We proposed that such a co-catalyst was present in trace amounts in the magnesium source. This hypothesis was tested through a study on Grignard reagent age. Grignard reagents were prepared from magnesium from two sources: standard purity magnesium from Acros, and ultra-pure magnesium from Alfa Aesar (99.98+% Puratronic grade). Reactions run with aged Grignard reagent were expected to show lower yields than reactions run with fresh reagent. In experiments run with pure magnesium, low yields were expected regardless of Grignard reagent age. Surprisingly, in all experiments, both Grignard reagents afforded between 50% and 60% yield (Table 1.1). It was therefore concluded that a co-catalyst was not responsible for the variable yields. Fortuitously, this study also showed that the reaction was reproducible.

Table 1.1. Effect of Grignard Reagent Age



1.13 **1.15** **1.16** **1.17**

Entry	Mg^o grade^b	RMgI age	**1.15** yield (%)^c	**1.16** yield (%)^c	**1.17** yield (%)^c
1^a	Standard	variable	14–64	n.d.^{d}	n.d.^{d}
2	Standard	Fresh	57	31	6
3	Standard	3 Days	61	34	5
4	Standard	6 Days	55	26	5
5	Standard	14 Days	52	39	5
6	Puratronic	Fresh	49	29	<5
7	Puratronic	2 Days	59	15	7
8	Puratronic	5 Days	59	30	7
9	Puratronic	8 Days	54	38	5

^{a}Multiple experiments run by Buck Taylor ^{b}All Grignard reagents were titrated with iodine less than two hours before use. ^{c}Yield determined by ^{1}H NMR spectroscopy by comparison to an internal standard (1,4-dimethoxybenzene). ^{d}Not determined.

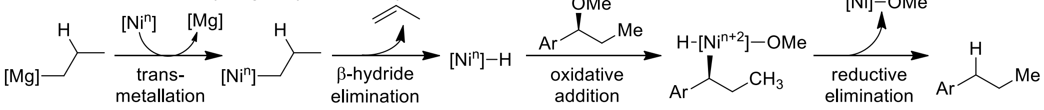
Although the reproducible yields in these experiments were encouraging, these results showed that the products of β-hydride elimination (**1.16**) and hydrogenolysis (**1.17**) were still problematic.[17] Interestingly, hydrogenolysis product **1.17** was not produced when methyl

---

[17] See Chapter 2 for in-depth studies on the mechanism of byproduct formation.

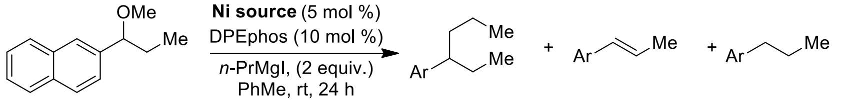
Grignard reagent was used. This result suggests that the reduction pathway arises from β-hydride elimination from the nucleophile prior to oxidative addition (Scheme 1.7).

Scheme 1.7. Proposed Hydrogenolysis Pathway



We next sought to identify conditions that would promote the cross-coupling reaction while suppressing formation of the undesired elimination and hydrogenolysis byproducts. The nickel source was briefly studied. First, a nickel-free positive control showed that the cross-coupling reaction was mediated by the metal catalyst (Table 1.2, entry 1). As has already been shown (vide supra), Ni(cod)$_2$ allows for cross-coupling with an average 56% yield (entry 2). When Ni(acac)$_2$ is used, the cross-coupling reaction proceeded in a comparable 59% yield (entry 3). Because Ni(acac)$_2$ is more stable and less expensive than Ni(cod)$_2$, subsequent studies where performed using Ni(acac)$_2$. Regardless of the nickel source, greater than 36% of starting material underwent undesired hydrogenolysis or β-hydride elimination.

Table 1.2. Comparison of Nickel Sources



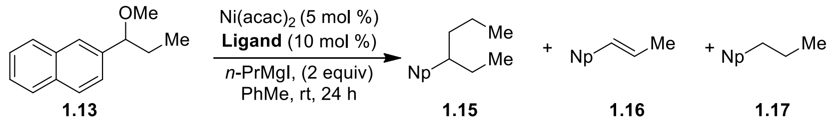
1.13 **1.15** **1.16** **1.17**

Entry	Nickel Source	**1.15** yield (%)[a]	**1.16** yield (%)[a]	**1.17** yield (%)[a]
1[b]	no nickel	0	0	0
2[c]	Ni(cod)$_2$	56	30	6
3	Ni(acac)$_2$	59	37	7

[a] Yield determined by ^{1}H NMR by comparison to an internal standard (1,4-dimethoxybenzene).
[b] 98% starting material recovered. [c]Average of eight experiments.

We postulated that by screening a variety of ligands with varying electronic properties and steric effects, we would be able to improve conversion to desired product **1.15.** To this end we screened a variety of diphosphine ligands (Table 1.3). DPEphos, Xantphos, and racBINAP, all of which give optimal conversion with methyl Grignard reagents, give suboptimal results in reactions with a longer chain Grignard reagent (entries 1–3). Bis-diphenylphosphino ligands with long carbon-chain linkers (dppoctane and dpppentane) promoted the formation of elimination and hydrogenolysis byproducts (entries 4–5). Use of a ligand with a shorter linker (dppp) resulted in a 62% yield of the desired product with most of the mass balance accounted for by elimination and deoxygenation pathways (entry 6). A ligand with a slightly shorter tether, 1,2-bis(diphenylphosphino)ethane (dppe), proved to be an optimal ligand, providing 80% yield of cross-coupling product with minimal byproduct formation (entry 7). The fact that ligands that contain a short tether (dppe and dppp) best promote the reaction suggests that a strongly coordinating bidentate ligand interaction promotes cross-coupling reactivity.

Table 1.3. Ligand Screen

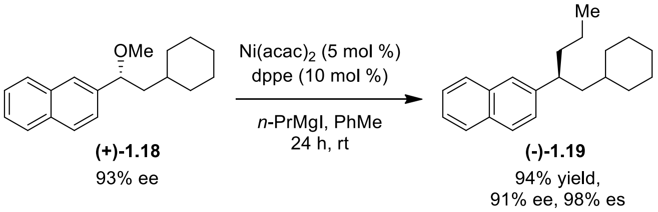


Entry	Ligand	**1.13** recovery (%)[a]	**1.15** yield (%)[a]	**1.16** yield (%)[a]	**1.17** yield (%)[a]
1	DPEphos	0	59	37	7
2	Xantphos	77	14	0	0
3	racBINAP	0	0	0	12
4	dppoctane	0	0	68	26
5	dpppentane	0	0	62	24
6	dppp	0	62	19	16
7	**dppe**	**0**	**80**	**0**	**<5**

[a] Yield determined by ^{1}H NMR spectroscopy by comparison to an internal standard (1,4-dimethoxybenzene).

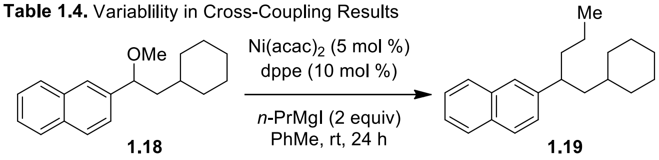
Having established that cross-coupling reactions with a long chain Grignard reagent can proceed in high yield, we turned our attention to the enantiospecificity of the reaction. Despite many attempts, enantiomers of product **1.15** were inseparable by SFC and GC analysis. Therefore an alternative substrate **1.18** was investigated (Scheme 1.8). Methyl ether **1.18** is electronically similar to methyl ether **1.13**, but more sterically congested, a property that we expected to improve separation on a chiral SFC column. The cross-coupling reaction with methyl ether **1.18** afforded desired product **1.19** in 94% yield. Enantiomers of product **1.19** readily separated by chiral column SFC revealing that the reaction proceeds with 98% enantiospecificity.[18]

Scheme 1.8. Cross-Coupling Reactions with Cyclohexyl Substrate



Unfortunately, subsequent experiments showed that the cross-coupling protocol shown in Scheme 1.8 is unreliable. In multiple experiments under "identical" conditions, compound **1.18** was either fully consumed, resulting in nearly quantitative conversion to desired product **1.19**, or no reaction was observed, resulting in quantitative recovery of starting material (Table 1.4).

Table 1.4. Variablility in Cross-Coupling Results



Entry	(**1.18**) recovery (%)[a]	(**1.19**) yield (%)[a]
1	89	0
2	0	89

[a]Determined by 1H NMR agianst an internal standard: 1,4-dimethoxybenzene.

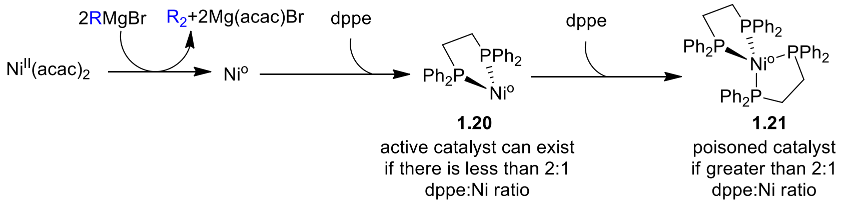
This observed *on-off* effect may be due to subtle differences in the stoichiometry of dppe relative to nickel. Such subtle differences could be caused by random error when weighing small quantities on an analytical scale.[19] It is not uncommon for optimal conditions of nickel-catalyzed cross-coupling reactions to be reported with a 2:1 ligand to nickel ratio.[20] However, the smaller bite angle of dppe, versus DPEphos, BINAP, or other ligands may allow for two dppe ligands to simultaneously coordinate the nickel center if there is an excess of dppe. Indeed, the bis-dppe-

---

[18] Enantiospecificity (es) = $ee_{product}/ee_{starting\ material}$, see, Denmark, S. E.; Vogler, T. *Chem. Eur. J.* **2009**, *15*, 11737.
[19] Wernerova, M.; Hudlicky, T. *Synlett*, **2010**, 2701.
[20] For representative examples, see reference 11 and: (a) Shields, J. D.; Ahneman, D. T.; Graham, T. J. A.; Doyle, A. G. *Org. Lett.* **2014**, *16*, 142. (b) Leowanawat, P.; Zhang, N.; Percec, V. *J. Org. Chem.*, **2012**, *77*, 1018.

nickel complex has been characterized.[21] We hypothesized that the active catalyst is comprised of one nickel atom ligated to one dppe ligand (**1.20**). Complex **1.20** presumably forms after Grignard reagent reduces nickel (II) to nickel (0) (Scheme 1.9). In the presence of excess dppe, a second ligand will bind the nickel atom resulting in complex **1.21**, which we hypothesized is unreactive in the cross-coupling reaction.[22]

Scheme 1.9. Proposed Formation of Active and Poisoned Catalyst



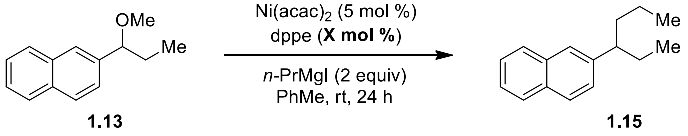
To test these hypotheses, we carried out the experiments shown in Table 1.5. Cross-coupling reactions were executed with 5 mol % Ni(acac)$_2$ and varying amounts of dppe. When dppe is used as ligand, conversion to products is efficient if the dppe:nickel ratio is less than 2:1 (entries 1–6). If the dppe:nickel ratio exceeds 2:1, the catalyst presumably coordinates a second dppe ligand rendering an inactive catalyst (entries 9–10). At a 2:1 dppe:nickel ratio, the reaction is unreliable, presumably because the actual ligand to nickel ratio is very slightly above or very slightly below 2:1 (entries 7–8). These results are consistent with the hypotheses that the active catalyst has one and only one dppe ligand bound to the metal atom.

---

[21] (a) Fisher, K. J.; Alyea, E. C. *Polyhedron* **1998**, *8*, 13. (b) Yamashita, K.-I; Takeda, H.; Kashiwabara, T.; Hua, R.; Shimada, S.; Tanaka, M. *Tetrahedron Lett.* **2007**, *48*, 6655.

[22] Yonova, I. M. Ph.D. Dissertation, University of California, Irvine, 2013.

Table 1.5. Effect of Ligand to Nickel Ratio on Reactivity

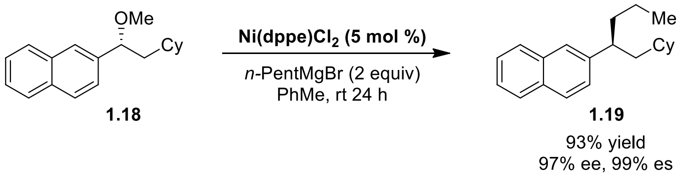


Entry	**ligand load**	[dppe] : [nickel]	**1.13** recovery (%)[a]	**1.15** yield (%)[a]
1	2.5 mol %	0.5 : 1	3	67
2	2.5 mol %	0.5 : 1	0	72
3	5 mol %	1 : 1	0	89
4	5 mol %	1 : 1	0	87
5	7.5 mol %	1.5 : 1	0	87
6	7.5 mol %	1.5 : 1	0	91
7	10 mol %	2 : 1	0	84
8	10 mol %	2 : 1	95	0
9	12.5 mol %	2.5 : 1	97	0
10	12.5 mol %	2.5 : 1	95	0

[a] Yield determined by ^1H NMR spectroscopy by comparison to an internal standard (1,4-dimethoxybenzene).

Because the active catalyst has a 1:1 ligand:nickel ratio, a precatalyst that also exhibits this ratio would be advantageous as it would eliminate the possibility of weighing error. Ni(dppe)Cl_2 displays an inherent 1:1 dppe:nickel ratio. Furthermore, it is stable at room temperature and is not air-sensitive, obviating the need for a glovebox. Initial experiments using Ni(dppe)Cl_2 as precatalyst showed the reagent to be as effective as and easier to work with than Ni(acac)$_2$ (Scheme 1.10). Ni(dppe)Cl_2 was therefore used in all future experiments. With optimized conditions in hand, we turned our attention to reaction scope.

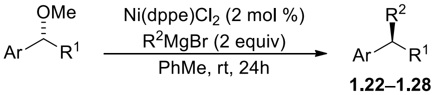
Scheme 1.10. Ni(dppe)Cl_2 as Precatalyst



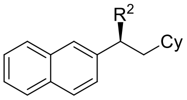
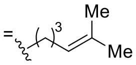
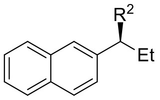
1.2.2. Reactions with Alkyl Grignard Reagents to Form C_{sp^3}–C_{sp^3} bonds.

With regards to scope, we began by studying the scope of alkyl Grignard reagents (Table 1.6). Ni(dppe)Cl_2 catalyzes the coupling of benzylic ethers to a variety of long-chain aliphatic Grignard reagents (entries 1–4). These include functionalized Grignard reagents featuring aromatic rings and olefins (entries 2–3). A pharmaceutically relevant trifluoromethyl moiety was also tolerated (entry 4). Yields are generally high, but somewhat lower with a sterically encumbered nucleophile (entry 5). In all cases, enantiospecificity is greater than 90%.

Table 1.6. Alkyl Grignard Reagent Scope



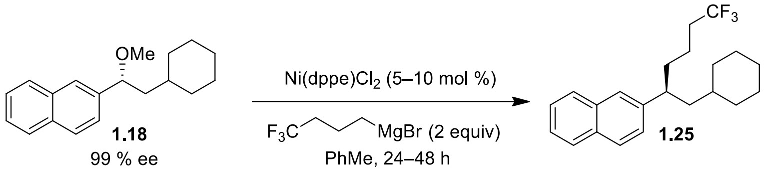
1.22–1.28

entry	product			yield (%)[a]	S.M.*ee* (%)[b]	prod.*ee* (%)[b]	*es* (%)[c]
1		**1.22**	R^2 = *n*-Pent	91	97	97	>99
2		**1.23**	R^2 = $(CH_2)_3Ph$	88	97	97	>99
3[(d)]		**1.24**	R^2 = 	81	97	97	>99
4[(e)]		**1.25**	R^2 = $(CH_2)_3CF_3$	67	>99	97	97
5		**1.26**	R^2 = *i*-Bu	40	97	90	93
6[(d)]		**1.27**	R2 = *n*-Pent	96	>99	96	96
7[(d)]		**1.28**	R^2 = $(CH_2)_3Ph$	93	97	97	>99

[a] Calculated after silica chromatography. [b] Determined by chiral SFC chromatography. [c] 100 x $ee_{product}/ee_{starting\ material}$. [d] $[Ni(dppe)Cl_2]$ (5 mol %). [e] $[Ni(dppe)Cl_2]$ (10 mol %).

Some nucleophiles require mild tuning of reaction conditions to achieve optimal reactivity. In most cases, altering only catalyst loading or temperature is sufficient to realize efficient conversion and high stereospecificity. The cross-coupling reaction with 4,4,4-trifluorobutylmagnesium bromide to form compound **1.25** provides a good example (Table 1.6, entry 4). Most reactions give optimal ee when catalyst loading is 2 mol %; however, inductively electron poor 4,4,4-trifluorobutylmagnesium bromide undergoes poor conversion even at 5 mol % catalyst loading (Table 1.7, entry 1). Heating the reaction boosts yield, but at the expense of ee (entry 2). For the fluorinated nucleophile, optimal results are achieved by doubling catalyst loading to 10 mol % to boost yield while running the reaction at room temperature to maintain high stereochemical fidelity (entry 3). These conditions resulted in an acceptable yield of 68% and an excellent 97% ee. Some Grignard reagents required similar reagent-specific optimization, but in almost all cases, efficient conversion to cross-coupled product was achieved after slight adjustments of temperature or catalyst loading.[23]

Table 1.7. Optimization of Reaction with CF_3 Containing Nucleophile



Entry	Ni(dppe)Cl_2	Temp	**1.18 recovery** (%)[a]	**1.25** yield (%)[b]	ee/es
1	5 mol %	25 °C	48	37	95/95
2	5 mol %	50 °C	0	68	65/65
3	10 mol %	25 °C	4	68	97/97

[a]Determined by 1H NMR against an internal standard, PhTMS. [b]Isolated yield after silica gel flash column chromotography.

Olefin-containing Grignard reagents are exceptionally challenging, and achieving cross-coupling reactivity with them proved more difficult than simply altering concentration or temperature (vide supra, Table 1.6, entry 3). Olefin-containing products are highly attractive as they represent a functional group that can be exploited for further synthetic elaboration. Unfortunately, initial coupling with allyl and terminal olefin-containing Grignard reagents failed to give any cross-coupling product (Table 1.8, entries 1–2). This is not surprising as olefins are known to be ligands for nickel complexes.[24] For example, styrenes have been shown by our lab to have a detrimental effect on nickel-catalyzed Kumada reactions.[25] Steric bulk around the alkene was expected to prevent coordination and preserve reactivity. Unfortunately, a Grignard reagent containing a bulkier *Z*-substituted olefin failed to promote the reaction (entry 3). Fortunately, a trisubstituted olefin underwent cross-coupling to form compound **1.24** in 81% yield and with 97% ee (entry 4). These results suggest that a high degree of olefin substitution is required to prevent coordination of nickel to double bonds.

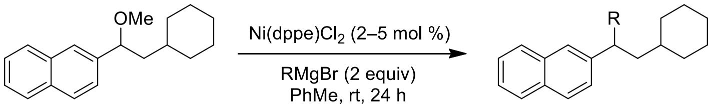
---

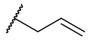
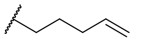
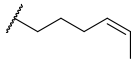
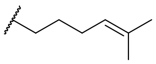
[23] See experimental section.

[24] See reference 2. See also: Yamamoto, T.; Yamamoto, A.; Ikeda, S. *J. Am. Chem. Soc*. **1971**, *93*, 3350.

[25] Taylor, B. L. H.; Swift, E. C.; Waetzig, J. D.; Jarvo, E. R. *J. Am. Chem. Soc.* **2010**, *133*, 389.

Table 1.8. Effect of Olefin Substitution



Entry	R	yield[a]	ee[b]
1		0	N/A
2		0	N/A
3		0	N/A
4		81[c]	97/99

[a]Yield determined by ^{1}H NMR against an internal standard, 1,4-dimethoxybenzene. [b]ee determined by chiral cholum SFC. [c]Isolated yield determined after purification by silica gel flash column chromotography.

1.2.3 Reactions with Aryl Grignard Reagents to Form C_{sp^3}–C_{sp^2} bonds

The primary focus of the project described in this chapter was to develop a facile method for the stereospecific formation of C_{sp^3}–C_{sp^3} bonds. Once optimal conditions for that transformation were identified, we investigated whether or not the same protocol is a general method that could also be applied to the formation of C_{sp^3}–C_{sp^2} bonds. Such a strategy could be used to prepare diarylalkanes,[26,27] a class of molecule that has been shown to have significant biological relevance.[28,29] We therefore investigated if the conditions optimized for C_{sp^3}–C_{sp^3}

---

[26] For similar disconnections see: (a) López-Pérez, A.; Adrio, J; Carretero, J. C.; *Org. Lett.* **2009**, *11*, 5514. (b) Imao, D.; Glasspoole, B. W.; Laberge, V. S.; Crudden, C. M. *J. Am. Chem. Soc.* **2009**, *131*, 5024. (c) Li, J.; Burke, M. D. *J. Am. Chem. Soc.* **2011**, *133*, 13774. (d) Maity, P; Shacklady-McAtee, D. M.; Yap, G. P. A.; Sirianni, E. R.; Watson, M. P. *J. Am. Chem. Soc.* **2013**, *135*, 280. (e) Do, H.-Q.; Chandrashekar, E. R. R.; Fu, G. C. *J. Am. Chem. Soc.* **2013**, *135*, 16288.

[27] For representative alternative strategies for enantioselective synthesis of 1,1-diarylalkanes, see: (a) Wang, Z.; Ai, F.; Wang, Z.; Zhao, W.; Zhu, G.; Lin, Z.; Sun, J. *J. Am. Chem. Soc.* **2015**, *137*, 383. (b) Saini, V.; Liao, L.; Wang, Q.; Jana, R.; Sigman, M. S. *Org. Lett.* **2013**, *15*, 5008. (c) Wang, X.; Guram, A.; Caille, S.; Hu, J.; Preston, J. P.; Ronk, M.; Walker, S. *Org. Lett.* **2011**, *13*, 1881. (d) Fessard, T. C.; Andrews, S. P.; Motoyoshi, H.; Carreira, E. M. *Angew. Chem. Int. Ed.* **2007**, *46*, 9331.

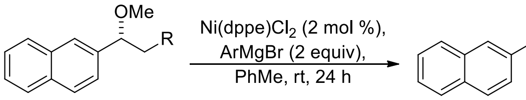
[28] Representative Examples: (a) as ligands for nuclear receptors, see: Kainuma, M.; Kasuga, J.-I.; Hosoda, S.; Wakabayashi, K.-I.; Tanatani, A.; Nagasawa, K.; Miyachi, H.; Makishima, M.; Hashimoto, Y. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 3213. (b) as combretastatin analogues for colon cancer, see: Messaoudi, S.; Hamze, A.; Provot, O.; Tréguier, B.; Rodrigo De Losada, J.; Bignon, J.; Liu, J.-M.; Wdzieczak-Bakala, J.; Thoret, S.; Dubois, J.; Brion, J.-D.; Alami, M. *ChemMedChem* **2011**, *6*, 488. (c) prostate cancer: Hu, Q.; Yin, L.; Jagusch, C.; Hille, U. E.; Hartmann, R. W. *J. Med. Chem.* **2010**, *53*, 5049. (d) diabetes: Chang, J.; Kim, R. M.; Lins, A. R.; Parmee, E. R.; Tan, Q.; Yang, C. International Patent WO 2007111864 A2, October 4, 2007.

[29] For breast cancer, See: (a) Pathak, T. P.; Gligorich, K. M.; Welm, B. E.; Sigman, M. S. *J. Am. Chem. Soc*. **2010**, *132*, 7870. (b) Pathak, T. P.; Osiak, J. G.; Vaden, R. M.; Welm, B. E.; Sigman, M. S. *Tetrahedron* **2012**, *68*, 5203.

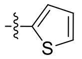
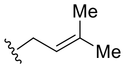
bond formation may represent a general method that is also applicable to stereospecific C_{sp^3}–C_{sp^2} bond formation.

Experiments run using aryl Grignard reagents showed that the reaction is amenable to alkyl-aryl cross-coupling. Results of experiments run with aryl Grignard reagents are shown in Table 1.9. The reaction works well with electron donating groups (entries 2, 5–6). The reaction does not work well with a strongly electron withdrawn para-trifluoromethylphenylmagnesium bromide (not shown) but does work with a para-fluorinated aryl Grignard reagent (entry 3). A heteroaryl Grignard reagent was also amenable to the reaction (entry 4). Analogous to olefin containing nucleophiles, the reactions with aryl Grignard reagents tolerate trisubstituted olefins in the electrophile (entry 6). These results show that the reaction is a general method amenable to the formation of C_{sp^3}–C_{sp^3} bonds as well as C_{sp^3}–C_{sp^2} bonds.

Table 1.9. Aryl Grignard Reagent Scope



1.29–1.34

entry	R	Product	Ar	yield (%)^a	ether ee (%)^b	prod. ee (%)^b	es (%)^c
1	Cy	**1.29**	Ph	67	>99	92	92
2	Cy	**1.30**	(4-OMe)C_6H_4	86	>99	97	97
3	Cy	**1.31**	(4-F)C_6H_4	82	>99	87	88
4^d	Cy	**1.32**		76	>99	93	94
5	Me	**1.33**	(4-NMe$_2$)C_6H_4	80	>99	85	86
6		**1.34**	(4-OMe)C_6H_4	92	96	88	92

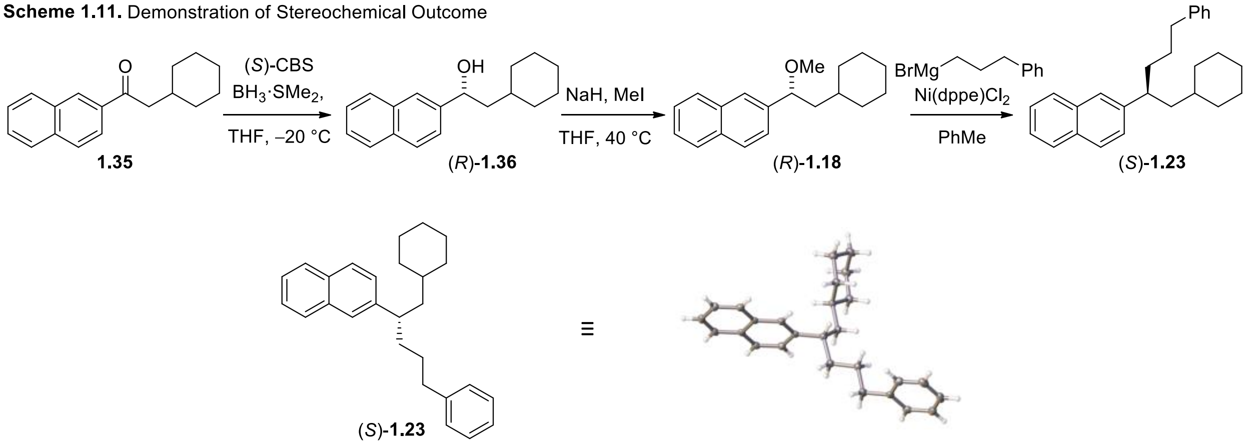
^{a}Isolated yield after silica gel chromatography. ^{b}Determined by chiral SFC chromatography. ^{c}100 x ee$_{\text{product}}$/ee$_{\text{starting material}}$. ^{d} 10 mol % Ni(dppe)Cl$_2$

1.2.4 Demonstration of Stereochemical Outcome

We wanted to be confident that we knew the absolute stereochemistry of products synthesized by this method. Analogous to previously reported nickel-catalyzed cross-coupling reactions involving methyl Grignard reagents,[30] we expected that the Ni(dppe)Cl_2 catalyzed cross-coupling reaction also proceeds with inversion at the benzylic center. Alcohol (*R*)-**1.36** was prepared by CBS reduction of ketone **1.35** (Scheme 1.11). The absolute stereochemistry was assigned as *R* based on the accepted model for CBS reductions[31] and confirmed by competing enantioselective conversion (CEC).[32]

The absolute stereochemistry of the cross-coupled product was confirmed by X-ray crystallography.[33] A crystal of cross-coupled product **1.23** was grown from a methanol/pentane solution by slow evaporation. The x-ray structure was obtained on a Bruker Kappa APEX CCD diffractometer equipped with Cu K_α radiation (λ = 1.5478). The absolute stereochemistry of the crystal structure confirmed that cross-couplings reactions using Ni(dppe)Cl_2 proceed with inversion at the benzylic center.

Scheme 1.11. Demonstration of Stereochemical Outcome



---

[30] See Scheme 1.6.

[31] Corey, E. J.; Helal, C. J. *Angew. Chem. Int. Ed.* **1998**, *37*, 1986.

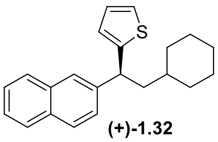
[32] (a) Experiment performed by Alexander J. Wagner using the method described in Wagner, A. J.; David, J. G.; Rychnovsky, S. D. *Org. Lett.* **2011**, *13*, 4470. (b) Wagner, A. J.; Rychnovsky, S. D. *J. Org. Chem.* **2013**, *78*, 4594.

[33] X-ray structure solved by Curtis Moore; see, Yonova, I. M.; Johnson, A. G.; Osborne, C. A.; Moore, C. E.; Morrissette, N. S.; Jarvo, E. R. *Angew. Chem. Int. Ed.* **2014**, *53*, 2422.

1.2.5 Biological Studies

As diarylmethanes are a common motif in pharmaceutically relevant molecules, we were interested in seeing if these compounds show biological activity against various cancer cell lines. Several of the compounds exhibited selective inhibition of MCF-7 breast-cancer cell proliferation. The most potent compound tested, **(+)-1.32**, exhibited an EC_{50} of 5.3 μmol (Figure 1.1).[34] Fortuitously, this compound had no observed effect on non-cancerous MCF-10A cells.

Figure 1.1. Bioactivity of Compound **1.32**



(+)-1.32

EC_{50} = 5.3 ± 1.1μM
against MCF-7 breast cancer cell line
No Activty Against MCF-10A
(non-cancerous) cell line

1.3 Conclusion

In summary, a stereospecific cross-coupling reaction of benzylic ethers with a variety of alkyl and aryl Grignard reagents was developed. It was determined that a 1:1 dppe:nickel ratio was necessary for optimal reactivity; therefore, reaction conditions were optimized using $Ni(dppe)Cl_2$ as the precatalyst. The reaction was shown to be amenable to a broad scope of nucleophiles. An X-ray crystal structure confirmed that the reaction proceeds with inversion at the benzylic center. A diarylmethane synthesized by this method was shown to be active against an MCF-7 breast-cancer cell line.

---

[34] Biological assays performed by Charlotte Osborne; see, Yonova, I. M.; Johnson, A. G.; Osborne, C. A.; Moore, C. E.; Morrissette, N. S.; Jarvo, E. R. *Angew. Chem. Int. Ed.* **2014**, *53*, 2422.

1.4 Experimental Section

1.4.1 General Procedures

All reactions were carried out under an atmosphere of N_2 using glassware that was either oven- or flame-dried prior to use. Hexanes, tetrahydrofuran (THF), diethyl ether (Et_2O), and toluene (PhMe), were degassed with argon and then passed through two 4 x 36 inch columns of anhydrous neutral A-2 alumina (8 x 14 mesh; LaRoche Chemicals; activated under a flow of argon at 350 ºC for 12 h) to remove H_2O. All other solvents utilized were purchased "anhydrous" commercially or purified as described (vide infra). ^1H NMR spectra were recorded on Bruker GN-500 (500 MHz ^1H, 125.7 MHz ^{13}C), CRYO-500 (500 MHz ^1H, 125.7 MHz ^{13}C) or DRX-400 (400 MHz ^1H, 100 MHz ^{13}C) spectrometers. Proton chemical shifts are reported in ppm (δ) relative to internal tetramethylsilane (TMS, δ 0.00). Data are reported as follows: chemical shift (multiplicity [singlet (s), broad singlet (br s), doublet (d), doublet of doublets (dd), triplet (t), doublet of triplets (dt), doublet of doublet of triplets (ddt), triplet of triplets (tt), quartet (q), quintet (quint), multiplet (m), apparent singlet (ap s), apparent doublet (ap d), apparent quartet (ap q), broad doublet (br d) and broad multiplet (br m)], coupling constants [Hz], integration). Carbon chemical shifts are reported in ppm (δ) relative to TMS with the respective solvent resonance as the internal standard ($CDCl_3$, δ 77.16 ppm). Unless otherwise indicated, NMR data were collected at 25 ºC. Analytical thin-layer chromatography (TLC) was performed using Silica Gel 60 F_{254} pre-coated plates (0.25 mm thickness). Visualization was accomplished by irradiation with a UV lamp and/or staining with $KMnO_4$ solution. Flash chromatography was performed using Silica Gel 60Å (170-400 mesh) from Fisher Scientific. Melting points (m.p.) were obtained using a Mel-Temp melting point apparatus and are uncorrected. Infrared spectra were obtained on a Mattson Instruments *Galaxy 5000* (thin film) and Perkin-Elmer Spectrum

1000 FT-IR Systems and are reported in terms of frequency of absorption (cm^{-1}). High resolution mass spectrometry was performed by the University of California, Irvine Mass Spectrometry Center. Optical rotations were measured with a Rudolph Research Analytical Autopol IV Automatic Polarimeter or a Jasco P-1010 digital polarimeter. SFC determinations of enantiopurity were performed on a Berger Analytical instrument using a Daicel™ Chiralpak® column (OD-H, OJ-H, or AD-H; 100 bar, 50 °C, 215 nm).

Ni(cod)$_2$ was purchased from Strem, stored in a glovebox freezer (–20 °C) under an atmosphere of N_2, and used as received. Ni(acac)$_2$ was purchased from Strem, stored in a glovebox under an atmosphere of N_2, and used as received. 1,2-Bis(diphenylphosphino)ethane (dppe) was purchased from Alfa Aesar, stored in a glovebox under an atmosphere of N_2, and used as received. 1,2-Bis(diphenylphosphino)ethane nickel (II) chloride (Ni(dppe)Cl_2) was purchased from Strem and used as received.

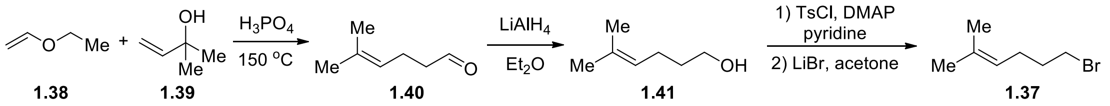
Organomagnesium reagents for substrate synthesis were freshly prepared from the halide precursor in THF, and molarities were determined by titration with I_2.[35] All other chemicals were purchased commercially and used as received.

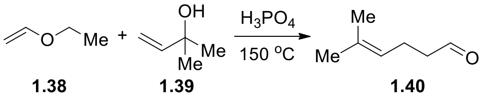
1.4.2 Synthesis of Alkyl and Aryl Halides and Organomagnesium Reagents for Cross-Coupling Reactions

(5-methylhex-4-enyl)magnesium bromide was prepared from **5-methylhex-4-enylbromide (1.37)** which was prepared via the following route:

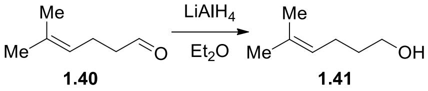
---

[35] Krasovskiy, A.; Knochel, P. *Synthesis* **2006**, 890.





5-methylhex-4-enal (**1.40**) was prepared according to a modified procedure reported by Saucy and co-workers.[36] A sealed tube was charged with ethoxyethene (**1.38**) (11.6 mL, 121 mmol), 2-methylbut-3-en-2-ol (**1.39**) (6.40 mL, 60 mmol), and 85% phosphoric acid (59 µL, 0.60 mmol). The tube was sealed, heated to 150 °C, and allowed to stir for 2.5 h. The reaction mixture was cooled to room temp, opened, and neutralized with triethylamine. Purification by fractional distillation (120 °C, 50 torr) afforded the title compound as a clear, colorless oil (2.41 g, 21.5 mmol, 36%). Analytical data is consistent with literature values.[37]



5-methylhex-4-ene-1-ol (**1.41**) was prepared according to the procedure reported by Heathcock and co-workers.[38] A flame dried round bottom flask was charged with $LiAlH_4$ (1.49 g, 39.4 mmol), put under a nitrogen atmosphere, and cooled to 0 °C. Et_2O (22 mL) was added then aldehyde **1.40** (4.41g, 39.4 mmol) was added as a solution in Et_2O (86 mL). The reaction mixture was allowed to slowly return to room temperature over 3 hours and stirred for an additional 10 hours at which time the reaction mixture was cooled back down to 0 °C. Water (2 mL), 15% NaOH (2 mL), and another aliquot of water (6 mL) were added sequentially. The

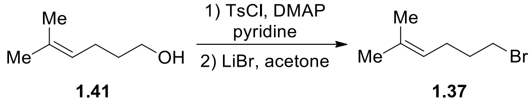
---

[36] (a) Marbet, R.; Saucy, G. *Helv. Chim. Acta* **1967**, *50*, 2095. (b) Liu, C.; Kudo, K; Hashimoto, Y.; Saigo, K. *J. Org. Chem.* **1996**, *61*, 494.

[37] Wei, X.; Lorenz, J. C.; Kapadia, S.; Saha, A.; Haddad, N.; Busacca, C. A.; Senanayake, C. H. *J. Org. Chem.* **2007**, *72*, 4250.

[38] Wallace, G. A.; Heathcock, C. H. *J. Org. Chem.* **2001**, *66*, 450.

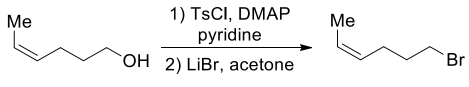
quenched mixture was allowed to return to room temperature. The solid material was filtered and purified by silica gel flash column chromatography to yield the target compound as a clear, colorless oil (3.04g, 26.1 mmol, 68% yield). Analytical data is consistent with literature values.[39]



6-Bromo-2-methylhex-2-ene (**1.37**) was prepared according to a procedure reported by Boyer.[40] A flame dried round bottom flask was charged with alcohol **1.41** (1.26 g, 11.0 mmol) and DMAP (15.2 mg, 0.125 mmol). Pyridine (11 mL) was added, and the reaction mixture was cooled to 0 °C. Tosyl chloride (232 mg, 12.2 mmol) was added in portions, and the reaction mixture was allowed to stir for 2.5 h at 0 °C. The reaction mixture was poured into ice cold water, and the crude mixture was extracted with Et_2O (3 x 10 mL), washed with 10% HCl, washed with a saturated $NaHCO_3$ (aq) solution, and washed with brine. The combined organics were dried with $MgSO_4$ and concentrated in vacuo. With no further purification, the crude tosylate (2.35 g, 9.84 mmol) was loaded into a round bottom flask. LiBr (2.96g, 34.1 mmol) and acetone (23 mL) were added, and the reaction mixture was heated to and stirred at reflux for 1 hour. The reaction mixture was then cooled to room temperature and diluted with a 3:1 mixture of pentane and water. The organic layer was separated and dried with $MgSO_4$. After filtration and concentration, the crude material was purified by silica gel flash column chromatography (100% hexanes) to yield bromide **1.37** as a clear, colorless oil (0.703g, 3.97 mmol, 36% yield from the alcohol). Analytical data was consistent with literature values.[40]

---

[39] Corey, E. J.; Cheng, H.; Baker, C. H.; Matsuda, S. P. T.; Li, D.; Song, X. *J. Am. Chem. Soc.* **1997**, *119*, 1277.
[40] Boyer, F.-D.; Hanna, I. *Org. Lett.* **2007**, *9*, 2293.

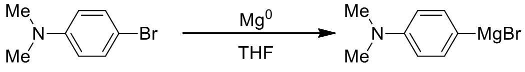


1.42 1.43

(Z)-6-bromohex-2-ene (1.43) was prepared according to the same procedure as **1.37** but starting from the commercially available alcohol **1.42**. Analytical data were consistent with literature values.[41]

All other alkyl and aryl halides were purchased commercially and used as received.

1.4.3 Preparation of Grignard Reagents



1.44 1.45

***p*-(*N,N*-Dimethylamino)phenylmagnesium bromide** (**1.45**) was prepared according to a procedure reported by Jarvo and co-workers.[42] Magnesium turnings (0.18 g, 7.5 mmol) were ground in a mortar and pestle, and then added to a round bottom flask along with one crystal of iodine. The round bottom flask was equipped with a water condenser and put under a nitrogen atmosphere. THF (2.0 mL) was then added. The heterogeneous mixture was heated to reflux, and *p*-(*N,N*-dimethylamino)phenyl bromide (**1.44**) (1.0g in 0.5 mL THF) was added drop wise. The reaction mixture was allowed to stir for 1 h and cooled to room temperature. The Grignard solution was then carefully transferred by syringe to a Schlenk flask in such a way as to leave left-over magnesium solid behind. The Grignard reagent was then concentrated in vacuo on a Schlenk line. Et_2O (1 mL) was added, and the solution was again concentrated in vacuo by

---

[41] Burns, N. Z.; Witten, M. R.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2011**, *133*, 14578.
[42] Taylor, B. L. H.; Harris, M. R.; Jarvo, E. R. *Angew. Chem. Int. Ed.* **2012**, *51*, 7790.

Schlenk technique. This process was repeated five times. The solid Grignard reagent was then transferred to a glove box. Grignard reagent **1.45** was stored and dispensed in the same glove box.

All other Grignard reagents were prepared according to the following general procedure. For satisfactory yields and enantiospecificities in the cross-coupling reactions, the Grignard reagent must be prepared from the alkyl bromide in diethyl ether. In cases were initiation is sluggish, gentle heating by heat gun or oil bath, or the addition of 0.05 mL of 1,2-dibromoethane proved helpful.

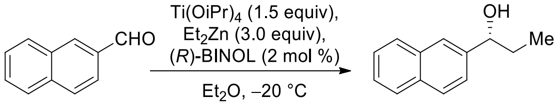
General Procedure for Grignard Reagent Preparation: Magnesium turnings (1.08 g, 45.0 mmol) were added to a vacuum flame-dried round-bottom flask equipped with a stir bar and oven-dried condenser. The reaction apparatus was put under a nitrogen atmosphere. Et_2O (5.0 mL) was added to the reaction apparatus, followed by a single crystal of I_2 (ca. 2 mg). The organohalide[43] (15.0 mmol) was added portion-wise over 30 min. The reaction was stirred at ambient temperature for an additional two hours. The resulting Grignard reagents was typically between 2.0 and 3.0 M as titrated using Knochel's method,[44] and could be stored (sealed, under nitrogen) for at least 4 weeks without detrimental effects.

---

[43] All alkyl and arylhalides were commercially available and used as received without any purification unless otherwise noted.

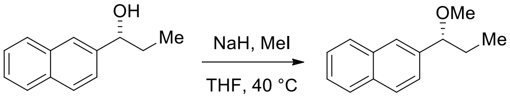
[44] Krasovskiy, A.; Knochel, P. *Synthesis* **2006**, 890.

1.4.4 Synthesis and Characterization of Substrates



1.11 (*R*)-1.12

(*R*)-1-(naphthalen-2-yl)propan-1-ol ((*R*)-1.12) was prepared according to the procedure reported by Jarvo and co-workers.[45] Analytical data is consistent with literature values:[45] **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.80 (m, 3H), 7.73 (s, 1H), 7.45 (m, 3H), 4.72 (t, *J* = 6.8 Hz, 1 H), 2.17 (s, 1H), 1.79–1.90 (m, 2H), 0.91 (t, *J* = 7.5 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 142.0, 133.3, 133.1, 128.3, 128.0, 127.8, 126.2, 125.9, 124.8, 124.2, 76.2, 31.8, 10.3; **$[\alpha]^{24}_D$** +39.5 (*c* 1.01, $CHCl_3$), lit. $[\alpha]^{23}_D$ +41.9 (*c* 1.02, $CHCl_3$, 96% ee);[45] **SFC** analysis (OD-H, 10% IPA, 2.5 mL/min) indicated 95% ee: t_R (minor) = 9.1 minutes, t_R (major) = 9.9 minutes.

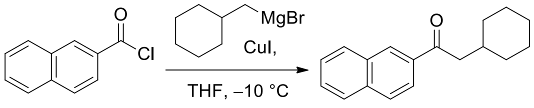


(*R*)-1.12 (*R*)-1.13

(*R*)-2-(1-methoxypropyl)naphthalene ((*R*)-1.13) was Prepared according to the procedure reported by Jarvo and co-workers.[45] Analytical data is consistent with literature values:[45] **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.83 (m, 3H), 7.70 (s, 1H), 7.45 (m, 3H), 4.17 (t, *J* = 6.6 Hz, 1 H), 3.24 (s, 3H), 1.92 (m, 1H), 1.75 (m, 1H), 0.89 (t, *J* = 7.4 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 139.8, 133.3, 133.2, 128.4, 128.0, 127.8, 126.17, 126.16, 125.8, 124.7, 85.8, 56.9, 30.9, 10.4; **$[\alpha]^{24}_D$** +110.5 (*c* 1.07, $CHCl_3$), lit. $[\alpha]^{23}_D$ +92.2 (*c* 1.82, $CHCl_3$);[45] **SFC** analysis (OD-H, 1% IPA, 2.5 mL/min) indicated 95% ee: t_R (minor) = 5.8 minutes, t_R (major) = 6.2 minutes.

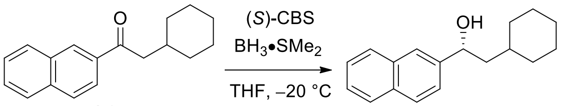
---

[45] Taylor, B. L. H.; Swift, E. C.; Waetzig, J. D.; Jarvo, E. R. *J. Am. Chem. Soc.* **2011**, *133*, 389.



1.46 **1.35**

2-cyclohexyl-1-(naphthalen-2-yl)ethanone (1.35) was prepared according to the procedure reported by Jarvo and co-workers.[46] Analytical data is consistent with literature values:[46] **^{1}H NMR** (500 MHz, CDCl$_3$) δ 8.45 (s, 1H), 8.03 (d, *J* = 9.0 Hz, 1H), 7.97 (d, *J* = 8.0 Hz, 1H), 7.88 (t, *J* = 9.0 Hz, 2H), 7.46–7.61 (m, 2H), 2.95 (d, *J* = 6.5 Hz, 2H), 2.10–1.97 (m, 1H), 1.85–1.75 (m, 2H), 1.70–1.65 (m, 3H), 1.31–1.26 (m, 2H), 1.22–1.17 (m, 1H), 1.15–1.02 (m, 2H); **^{13}C NMR** (125 MHz, CDCl$_3$) δ 200.4, 135.7, 135.0, 132.7, 129.9, 129.7, 128.52, 128.47, 127.9, 126.8, 124.2, 46.4, 34.9, 33.7, 26.4, 26.3.



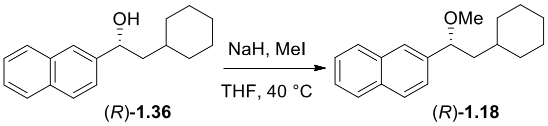
1.35 **(*R*)-1.36**

(*R*)-2-cyclohexyl-1-(naphthalen-2-yl)ethanol ((*R*)-1.36) was prepared according to the procedure reported by Jarvo and co-workers.[46] Analytical data is consistent with literature values:[46] **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.84–7.83 (m, 3H), 7.78 (s, 1H), 7.49–7.45 (m, 3H), 4.97–4.95 (m, 1H), 1.85–1.77 (m, 4H), 1.71–1.60 (m, 4H), 1.51–1.40 (m, 1H), 1.29–1.13 (m, 3H), 1.04–0.92 (m, 2H); **^{13}C NMR** (125 MHz, CDCl$_3$) δ 142.8, 133.5, 133.1, 128.4, 128.1, 127.8, 126.3, 125.9, 124.6, 124.3, 72.4, 47.1, 34.4, 34.1, 33.1, 26.7, 26.4, 26.3; **$[\alpha]^{25}_{D}$** +33.3 (*c* 0.17, CHCl$_3$), lit. $[\alpha]^{28}_{D}$ +23.8 (*c* 1.0, CHCl$_3$, 87% ee);[46] **SFC analysis** (AS-H, 3% IPA, 3 mL/min) indicated 96% ee: t$_R$ (minor) = 12.2 minutes, t$_R$ (major) = 12.8 minutes. Absolute configuration

---

[46] Wisniewska, H. M.; Swift, E. C.; Jarvo, E. R. *J. Am. Chem. Soc.* **2013**, *135*, 9083.

was assigned as *R* based on the accepted model for selectivity in CBS reduction[47] and confirmed by competing enantioselective conversion (CEC).[48]

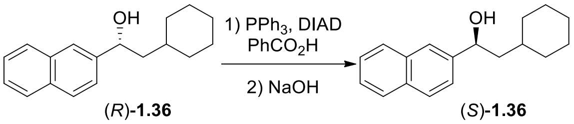


(*R*)-2-(2-cyclohexyl-1-methoxyethyl)naphthalene ((*R*)-1.18): To a solution of NaH (0.514 g, 21.4 mmol) in THF (100 mL) was added (*R*)-**1.36** (2.72 g, 10.7 mmol), and the mixture was stirred at 40 °C for 30 min. MeI (2.00 mL, 32.1 mL) was added, and stirring was continued for 8 h. The reaction was quenched with MeOH, and the solvent was removed in vacuo. The crude mixture was taken up in CH_2Cl_2 (100 mL), washed with sat. $NaCO_3$, brine, dried over $NaSO_4$, and concentrated in vacuo. Purification by silica gel flash column chromatography (5% EtOAc in hexanes) afforded the title compound as a white solid (2.85 g, 10.6 mmol, 99%): **m.p.** 43–47 °C; **TLC R_f** = 0.4 (5% EtOAc in hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.83–7.82 (m, 3H), 7.70 (s, 1H), 7.49–7.43 (m, 3H), 4.36 (dd, *J* = 8.6, 5.7 Hz, 1H), 3.21 (s, 3H), 1.84–1.76 (m, 3H), 1.69–1.62 (m, 3H), 1.54–1.49 (m, 1H), 1.42–1.37 (m, 1H), 1.25–1.10 (m, 3H), 0.99–0.90 (m, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 140.5, 133.4, 133.2, 128.4, 127.9, 127.8, 126.2, 125.9, 125.8, 124.6, 81.9, 56.8, 46.2, 34.3, 34.0, 33.3, 26.7, 26.4, 26.3; **$[\alpha]^{25}_D$** +63.2 (*c* 1.06, $CHCl_3$); **HRMS** (TOF MS CI+) *m / z* calcd for $C_{19}H_{24}O$ $[M]^+$ 268.1827 found 268.1821; **SFC analysis** (OJ-H, 3% IPA, 2.5 mL/min) indicated 97% ee: t_R (minor) = 7.1 minutes, t_R (major) = 8.8 minutes.

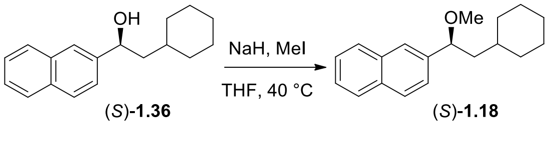
---

[47] Corey, E. J.; Helal, C. J. *Angew. Chem. Int. Ed.* **1998**, *37*, 1986.

[48] (a) Experiment performed by Alexander J. Wagner using the method described in Wagner, A. J.; David, J. G.; Rychnovsky, S. D. *Org. Lett.* **2011**, *13*, 4470. (b) Wagner, A. J.; Rychnovsky, S. D. *J. Org. Chem.* **2013**, *78*, 4594.



(*S*)-2-cyclohexyl-1-(naphthalen-2-yl)ethanol ((*S*)-1.36) was prepared according to a modified procedure reported by Presnell and co-workers.[49] To a cooled (brine ice bath) solution of (*R*)-**1.36** (0.15 g, 0.59 mmol), benzoic acid (0.29 g, 2.4 mmol), and PPh$_3$ (0.62 g, 2.4 mmol) in THF (5 mL) was added DIAD (0.46 mL, 2.4 mmol) drop-wise over 30 min. After the addition was complete the reaction was allowed to warm to room temperature and stir for 12 hours, then heated up to 40 °C and stirred for an additional 3 h. The reaction mixture was diluted with Et$_2$O (10 mL), washed with sat. NaHCO$_3$, dried over NaSO$_4$, and concentrated in vacuo. Trituration with hexanes removed the PPh$_3$ by-products and purification by silica gel flash column chromatography (10% EtOAc in hexanes) afforded the title compound as a white solid (0.112 g, 0.43 mmol, 73%). The product was recrystallized from hexanes to improve enantiopurity. Analytical data is consistent with literature values:[50] **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.84–7.83 (m, 3H), 7.78 (s, 1H), 7.49–7.45 (m, 3H), 4.97–4.95 (m, 1H), 1.85–1.79 (m, 4H), 1.71–1.60 (m, 4H), 1.51–1.40 (m, 1H), 1.29–1.13 (m, 3H), 1.04–0.92 (m, 2H); **^{13}C NMR** (125 MHz, CDCl$_3$) δ 142.8, 133.5, 133.1, 128.4, 128.1, 127.8, 126.3, 125.9, 124.6, 124.3, 72.4, 47.1, 34.4, 34.1, 33.1, 26.7, 26.4, 26.3; **$[\alpha]^{26}_{D}$** –27.4 (*c* 1.02, CHCl$_3$); **SFC analysis** (AS-H, 3% IPA, 3 mL/min) indicated 94% ee: t$_R$ (major) = 11.8 minutes, t$_R$ (minor) = 12.7 minutes.



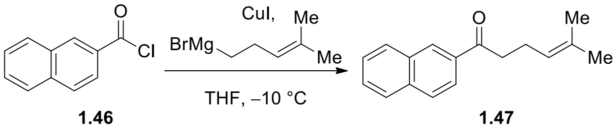
(*S*)-2-(2-cyclohexyl-1-methoxyethyl)naphthalene ((*S*)-1.18) was prepared according to the procedure reported above for (*R*)-**1.18**: **^{1}H NMR** (400 MHz, CDCl$_3$) δ 7.83–7.82 (m, 3H), 7.70

---

[49] Dodge, J. A.; Nissen, J. S.; Presnell, M. *Org. Synth.* **1996**, *73*, 110.

[50] Wisniewska, H. M.; Swift, E. C.; Jarvo, E. R. *J. Am. Chem. Soc.* **2013**, *135*, 9083–9090.

(s, 1H), 7.49–7.43 (m, 3H), 4.36 (dd, *J* = 8.6, 5.7 Hz, 1H), 3.21 (s, 3H), 1.84–1.76 (m, 3H), 1.69–1.62 (m, 3H), 1.54–1.49 (m, 1H), 1.42–1.37 (m, 1H), 1.25–1.10 (m, 3H), 0.99–0.90 (m, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 140.5, 133.4, 133.2, 128.4, 127.9, 127.8, 126.2, 125.9, 125.8, 124.6, 81.9, 56.8, 46.2, 34.3, 34.0, 33.3, 26.7, 26.4, 26.3; **$[\alpha]^{25}_{D}$** –58.1 (*c* 1.30, $CHCl_3$); **SFC analysis** (OJ-H, 3% IPA, 2.5 mL/min) indicated 92% ee: t_R (major) = 7.0 minutes, t_R (minor) = 8.9 minutes.



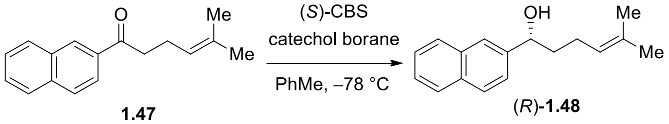
1.46 **1.47**

5-methyl-1-(naphthalen-2-yl)hex-4-en-1-one (1.47) was prepared according to a modified procedure reported by Hultzsch and co-workers.[51] To a cooled (brine/ice bath) solution of CuI (0.059 g, 0.31 mmol) and 2-naphthoyl chloride (**1.46**) (1.19 g, 6.25 mmol) in THF (7 mL) was slowly added (4-methylpent-3-enyl)magnesium bromide (10.9 mL, 6.25 mmol, 0.574 M in THF), and the reaction mixture was stirred for 1 h. The reaction was quenched by the addition of MeOH, and the solvent was removed in vacuo. The crude reaction mixture was taken up in EtOAc (30 mL), washed with 1 N HCl (10 mL), sat. $NaHCO_3$ (10 mL), and brine (10 mL), dried with $NaSO_4$, and concentrated in vacuo. Purification by silica gel flash column chromatography (4% EtOAc in hexanes) afforded the title compound as a colorless oil (1.01 g, 4.22 mmol, 68% yield). This compound has been previously reported.[52] Spectral data is not fully consistent with the reported literature values, therefore full characterization data is provided to support structural assignment shown above: **TLC R_f** = 0.4 (10% EtOAc in hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.46 (s, 1H), 8.03 (d, *J* = 8.8 Hz, 1H), 7.94 (d, *J* = 8.0 Hz, 1H), 7.86 (t, *J* = 7.4 Hz, 2H), 7.57–7.49 (m, 2H), 5.22 (t, *J* = 7.2 Hz, 1H), 3.12 (t, *J* = 7.4 Hz, 2H), 2.48 (q, *J* = 7.4 Hz, 2H), 1.70 (s,

---

[51] Gribkov, D. V.; Hultzsch, K. C.; Hampel, F. *J. Am. Chem. Soc.* **2006**, *128*, 3748.
[52] Narender, T.; Sarkar, S.; Rajendar, K.; Tiwari, S. *Org. Lett.* **2011**, *13*, 6140.

3H), 1.65 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 200.0, 135.6, 134.4, 132.8, 132.6, 129.7, 129.6, 128.43, 128.39, 127.8, 126.8, 124.0, 123.1, 38.9, 25.8, 23.2, 17.8; **IR** (neat) 3058, 2967, 2913, 1678, 1277, 1180, 1123 cm^{-1}; **HRMS** (TOF MS CI+) *m / z* calcd for $C_{17}H_{19}O$ $[M + H]^+$ 239.1436, found 239.1429.

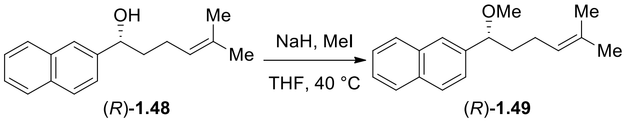


(*R*)-5-methyl-1-(naphthalen-2-yl)hex-4-en-1-ol ((*R*)-1.48) was prepared according to a modified procedure by Okamura and co-workers.[53] A flame dried round bottom flask was charged with (*S*)-2-methyl-CBS-oxazaborolidine (0.12 g, 0.42 mmol), ketone **1.47** (1.01 g, 4.22 mmol), and toluene (20 mL). The mixture was cooled to –78 °C, and catecholborane (0.90 mL, 8.4 mmol) was added dropwise. The reaction mixture was stirred for 20 h, then quenched by slow addition of MeOH (2 mL) followed by sat. NH_4Cl (10 mL). After warming to room temperature, the quenched mixture was extracted with Et_2O (3 x 20 mL). The combined organics were washed with sat. Na_2CO_3, then brine and dried over $NaSO_4$. Solvent was removed in vacuo. Purification by silica gel flash column chromatography (10–20% EtOAc in hexanes) afforded the title compound as a white solid (0.703 g, 2.91 mmol, 69%). The product was recrystallized from hexanes to improve enantiopurity: **m.p.** 53–55 °C; **TLC R$_f$** = 0.5 (20% EtOAc in hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 8.0 Hz, 3H), 7.76 (s, 1H), 7.47–7.43 (m, 3H), 5.16 (t, *J* = 7.0 Hz, 1H), 4.83 (t, *J* = 5.8 Hz, 1H), 2.12–2.04 (m, 3H), 1.94–1.82 (m, 2H), 1.69 (s, 3H), 1.58 (s, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 142.3, 133.4, 133.1, 132.5, 128.4, 128.1, 127.8, 126.2, 125.9, 124.7, 124.3, 123.9, 74.5, 39.0, 25.9, 24.6, 17.9; **IR** (neat) 3263, 2924, 2856, 1059, 1016 cm^{-1}; **HRMS** (TOF MS CI+) *m / z* calcd for $C_{17}H_{20}ONH_4$ $[M + NH_4]^+$ 258.1858, found 258.1847;

---

[53] Lee, A. S.; Norman, A. W.; Okamura, W. H. *J. Org. Chem.* **1992**, *57*, 3846.

[α]^{26}$_{D}$ +4.9 (*c* 1.16, $CHCl_3$); **SFC analysis** (OD-H, 15% IPA, 3 mL/min) indicated 93% ee: t_R (minor) = 4.9 minutes, t_R (major) = 5.3 minutes. Absolute configuration was assigned as *R* based on the accepted model for selectivity in CBS reductions.[54]

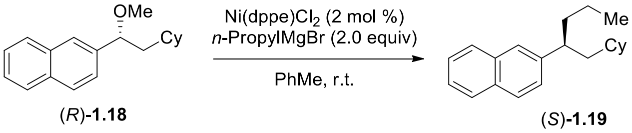


(*R*)-2-(1-methoxy-5-methylhex-4-enyl)naphthalene ((*R*)-1.49): To a suspension of NaH (0.032 g, 1.3 mmol) in THF (3 mL) was added a solution of (*R*)-**1.48** (0.160 g, 0.67 mmol) in THF (3 mL), and the mixture was stirred at 40 °C for 30 min. MeI (0.124 mL, 2.00 mmol) was added and stirring was continued for 5 h. The reaction was quenched with MeOH, and the solvent was removed in vacuo. The crude mixture was taken up in CH_2Cl_2 (10 mL), filtered, and concentrated in vacuo. Purification by silica gel flash column chromatography (5% EtOAc in hexanes) afforded the title compound as a colorless oil (0.164 g, 0.645 mmol, 96%): **TLC R$_f$** = 0.5 (10% EtOAc in hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.84 (app d, *J* = 8.0 Hz, 3H), 7.70 (s, 1H), 7.47–7.43 (m, 3H), 5.12 (t, *J* = 6.8 Hz, 1H), 4.24 (t, *J* = 6.6 Hz, 1H), 3.23 (s, 3H), 2.07–2.02 (m, 2H), 1.96–1.91 (m, 1H), 1.74–1.69 (m, 4H), 1.56 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 140.0, 133.4, 133.2, 132.2, 128.4, 128.0, 127.9, 126.2, 126.1, 125.8, 124.6, 124.0, 83.6, 56.8, 38.1, 25.9, 24.5, 17.9; **IR** (neat) 3055, 2966, 2926, 1445, 1099, 745 cm^{-1}; **HRMS** (TOF MS CI+) *m / z* calcd for $C_{18}H_{22}O$ $[M]^+$ 254.1671, found 254.1652; **[α]^{27}$_{D}$** +30.2 (*c* 1.11, $CHCl_3$); **SFC analysis** (OD-H, 5% IPA, 2.5 mL/min) indicated 94% ee: t_R (minor) = 4.2 minutes, t_R (major) = 4.6 minutes.

---

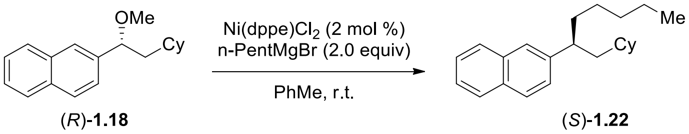
[54] Corey, E. J.; Helal, C. J. *Angew. Chem. Int. Ed.* **1998**, *37*, 1986.

1.4.5 Representative Procedure for Cross-Coupling Reactions

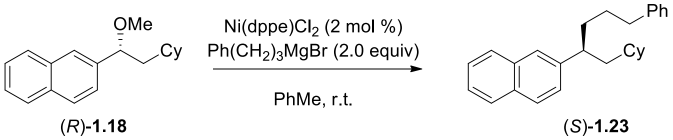


(*S*)-2-(1-cyclohexylpentan-2-yl)naphthalene ((*S*)-1.19): A vial was charged with (*R*)-**1.18** (0.134 g, 0.500 mmol) and Ni(dppe)Cl$_2$ (5.3 mg, 0.010 mmol). The vial was capped, and put under a nitrogen atmosphere. Toluene (3.0 mL) was added, followed by *n*-propylmagnesium bromide (0.44 mL, 1.0 mmol, 2.3 M in Et$_2$O). The reaction was allowed to stir at room temperature for 24 h, at which point the reaction was quenched by the addition of MeOH (1 mL) and run through a silica plug. The solvents were removed in vacuo, and the crude was purified by silica gel flash column chromatography (100% hexanes). The resulting colorless oil (0.137 g) was a mixture of the title compound (93% calculated yield) and the product of elimination (5% calculated yield). Further purification (100% heptanes) afforded a pure sample of (*S*)-**1.19**: **TLC R$_f$** = 0.7 (100% hexanes); **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.80–7.76 (m, 3H), 7.55 (s, 1H), 7.45–7.39 (dquint, *J* = 5.5, 1.2 Hz, 2H), 7.32 (dd, *J* = 8.5, 1.5 Hz, 1H), 2.84–2.79 (dq *J* = 9.3, 5.5 Hz, 1H), 1.84 (d, *J* = 12.8 Hz, 1H), 1.85–1.47 (m, 8H), 1.26–1.05 (m, 6H), 0.91–0.86 (m, 5H); **^{13}C NMR** (500 MHz, CDCl$_3$) δ 144.1, 133.7, 132.3, 128.0, 127.73, 127.65, 126.4, 126.2, 125.8, 125.1, 44.9, 42.7, 39.9, 35.0, 34.4, 33.0, 26.8, 26.4, 26.3, 20.9, 14.3; **IR** (thin film) 3052, 2661, 1915, 1633, 1600 cm^{-1}; **HRMS** (TOF MS CI+) *m / z* calcd for C$_{21}$H$_{28}$ [M]$^+$ 280.2191, found 280.2187; **$[\alpha]^{29}_D$** +17.8 (*c* 1.11, CHCl$_3$); **SFC** analysis (OJ-H, 2% hexanes, 2.0 mL/min) indicated 97% ee: t$_R$ (major) = 11.4 minutes, t$_R$ (minor) = 12.3 minutes.

1.4.6 Characterization Data for Cross-Coupling Products

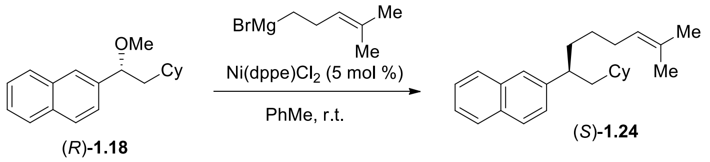


(*S*)-2-(1-cyclohexylheptan-2-yl)naphthalene ((*S*)-1.22) was prepared according to the representative procedure outlined above using the following amounts of reagents: (*R*)-**1.18** (0.134 g, 0.500 mmol), Ni(dppe)Cl_2 (5.3 mg, 0.010 mmol), *n*-pentylmagnesium bromide (0.50 mL, 1.0 mmol, 2.0 M in Et_2O), and toluene (3.0 mL). Purification by flash column chromatography (100% hexanes) afforded a colorless oil (0.147 g) as a mixture of the title compound (91% calculated yield) and the product of elimination (6% calculated yield). Further purification (100% heptanes) afforded a sample of analytically pure material: **R$_f$** = 0.3 (100% hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.80–7.75 (m, 3H), 7.55 (s, 1H), 7.44–7.37 (m, 2H), 7.31 (dd, *J* = 8.4, 1.2 Hz, 1H), 2.83–2.75 (m, 1H), 1.84 (d, *J* = 12.8 Hz, 1H), 1.63–1.44 (m, 8H), 1.21–1.04 (m, 10H), 0.89–0.81 (m, 5H); **^{13}C NMR** (500 MHz, $CDCl_3$) δ 144.2, 133.7, 132.3, 128.0, 127.74, 127.67, 126.4, 126.1, 125.8, 125.1, 45.0, 43.0, 37.6, 35.0, 34.4, 33.0, 32.2, 27.5, 26.8, 26.4, 26.3, 22.7, 14.3; **IR** (neat) 3020, 2920, 2850, 815, 744, 697 cm^{-1}; **HRMS** (TOF MS CI+) *m / z* calcd for $C_{23}H_{32}$ $[M]^+$ 308.2504, found 308.2507; **[α]$^{27}_D$** +9.4 (*c* 1.20, $CHCl_3$); **SFC** analysis (OJ-H, 2% hexanes, 2.0 mL/min) indicated 97% ee: t_R (minor) = 11.4 minutes, t_R (major) = 12.3 minutes.

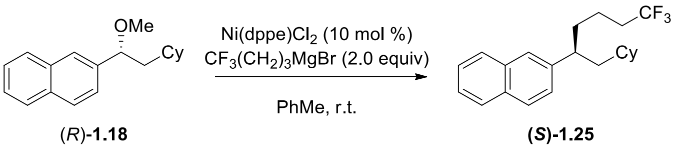


(*S*)-2-(1-cyclohexyl-5-phenylpentan-2-yl)naphthalene ((*S*)-1.23) was prepared according to the representative procedure outlined above using the following amounts of reagents: (*R*)-**1.18**

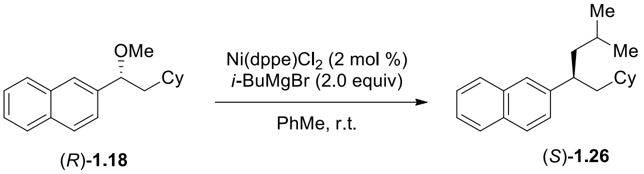
(0.401 g, 1.50 mmol), Ni(dppe)Cl_2 (16 mg, 0.030 mmol), (3-phenylpropyl)magnesium bromide (1.59 mL, 1.89 mmol, 1.19 M in Et_2O), and toluene (22 mL). Purification by flash column chromatography (0–5% EtOAc in hexanes) afforded a colorless oil (0.522 g) as a mixture of the title compound (88% calculated yield) and the product of Wurtz coupling of the organomagnesium reagent (1,6-diphenylhexane). Further purification by flash chromatography (100% pentane) afforded a sample of analytically pure material: **m.p.** 81–81 °C; **TLC R_f** = 0.3 (100% hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.81 (d, *J* = 8.0 Hz, 1H), 7.77 (d, *J* = 8.5 Hz, 2H), 7.54 (s, 1H), 7.46–7.39 (m, 2H), 7.29 (d, *J* = 8.0 Hz, 1H), 7.24–7.20 (m, 2H), 7.13 (t, *J* = 7.5 Hz, 1H), 7.08 (d, *J* = 7.0 Hz, 2H), 2.82 (p, *J* = 5.0 Hz, 1H), 2.60–2.48 (m, 2H), 1.82 (d, *J* = 12.5 Hz, 1H), 1.69–1.43 (br m, 10H), 1.11–1.00 (m, 4H), 0.88–0.82 (m, 2H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 143.7, 142.7, 133.7, 132.3, 128.5, 128.3, 128.0, 127.73, 127.68, 126.4, 126.1, 125.9, 125.7, 125.1, 44.9, 42.9, 37.2, 36.1, 34.9, 34.4, 32.9, 29.6, 26.8, 26.4, 26.3; **IR** (neat) 2918, 2850, 1442, 822, 745, 696 cm^{-1}; **HRMS** (TOF MS CI+) *m / z* calcd for $C_{27}H_{32}$ $[M]^+$ 356.2504, found 356.2509; **$[\alpha]^{20}_D$** +1.0 (*c* 1.03, $CHCl_3$); **SFC** analysis (OJ-H, 20% IPA, 2.5 mL/min) indicated 97% ee: t_R (minor) = 4.2 minutes, t_R (major) = 5.2 minutes. Crystals suitable for X-ray diffraction (vide infra) were grown by slow evaporation of solvent from a solution of the title compound in a mixture of methanol and pentane.



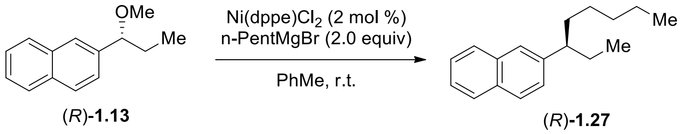
(*S*)-2-(1-cyclohexyl-7-methyloct-6-en-2-yl)naphthalene ((*S*)-1.24) was prepared according to the representative procedure outlined above using the following amounts of reagents: (*R*)-**1.18** (53.7 mg, 0.200 mmol) and Ni(dppe)Cl_2 (5.3 mg, 0.010 mmol), (5-methylhex-4-enyl)magnesium bromide (0.48 mL, 0.40 mmol, 0.83 M in Et_2O), and toluene (3.0 mL). The reaction mixture was stirred for 48 h. Purification by silica gel flash column chromatography (100% pentane) afforded a colorless oil (0.054 g) composed of a mixture of the title compound (81% calculated yield) and the product of elimination (12% calculated yield). Further purification by flash chromatography on silver-impregnated silica (0–3% Et_2O in pentane) afforded a sample of analytically pure material: **TLC R_f** = 0.4 (100% pentane); **^{1}H NMR** (400 MHz, CDCl3) δ 7.81–7.76 (m, 3H), 7.55 (s, 1H), 7.46–7.39 (dp, *J* = 8.4, 1.2 Hz, 2H), 7.31 (dd, *J* = 8.5, 1.5 Hz, 1H), 5.01 (t, *J* = 7.1 Hz, 1H), 2.80 (dq, *J* = 14.8, 5.3 Hz, 1H), 1.96–1.82 (m, 3H), 1.68–1.47 (m, 14H), 1.36–1.18 (m, 2H), 1.16–1.01 (m, 4H), 0.94–0.80 (m, 2H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 144.0, 133.7, 132.3, 131.3, 128.0, 127.7, 127.6, 126.4, 126.1, 125.8, 125.1, 124.9, 44.9, 42.9, 37.2, 35.0, 34.4, 32.9, 28.2, 28.0, 26.8, 26.4, 26.3, 25.8, 17.8; **IR** (neat) 2919, 2850, 1447, 853, 815, 743 cm^{-1}; **HRMS** (TOF MS EI+) *m / z* calcd for $C_{25}H_{34}$ $[M]^+$ 334.2661, found 334.2660; **$[\alpha]^{24}_D$** +11.8 (*c* 5.33, $CHCl_3$) ; **SFC** analysis (OJ-H, 3% IPA, 2.5 mL/min) indicated 97% ee: t_R (minor) = 6.5 minutes, t_R (major) = 6.9 minutes.



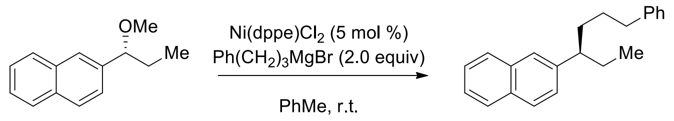
(*S*)-2-(1-cyclohexyl-6,6,6-trifluorohexan-2-yl)naphthalene ((*S*)-1.25) was prepared according to the representative procedure outlined above using the following amounts of reagents: (*R*)-**1.18** (53.7 mg, 0.200 mmol), Ni(dppe)Cl_2 (10.6 mg, 0.0200 mmol), (4,4,4-trifluorobutyl)magnesium bromide (0.20 mL, 0.40 mmol, 2.0 M in Et_2O), and toluene (3.0 mL). The reaction mixture was stirred for a period of 48 h. Purification by silica gel flash column chromatography (100% pentane) afforded a colorless oil (54 mg) as a mixture of the title compound (67% calculated yield) and the product of elimination (15% calculated yield). Further purification by silica gel flash column chromatography on silver-impregnated silica (100% pentane) afforded a sample of analytically pure material: **TLC R$_f$** = 0.4 (100% pentane); **^{1}H NMR** (400 MHz, CDCl3) δ 7.82–7.78 (m, 3H), 7.55 (s, 1H), 7.44 (dp, *J* = 6.9, 1.3 Hz, 2H), 7.29 (dd, *J* = 8.5, 1.5 Hz, 1H), 2.81 (dq, *J* = 14.8, 4.9 Hz, 1H), 2.11–1.90 (m, 2H), 1.83 (d, *J* = 12.9 Hz, 1H), 1.75–1.25 (m, 10H), 1.15–1.01 (m, 4H), 0.93–0.81 (m, 2H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 142.9, 133.7, 132.4, 128.3, 127.8, 127.7, 126.4, 126.0, 125.7, 125.3, 44.8, 42.8, 36.5, 34.9, 34.3, 33.9 (q, *J* = 28.3 Hz, 1C), 32.9, 26.7, 26.7, 26.3, 26.2, 20.3 (q, *J* = 2.8 Hz, 1C); **IR** (neat) 2920, 2850, 1448, 1253, 1131, 816, 744 cm^{-1}; **HRMS** (TOF MS EI+) *m / z* calcd for $C_{22}H_{27}F_3$ $[M]^+$ 348.2065, found 348.2065; **$[\alpha]^{26}_D$** +19.7 (*c* 1.2, $CHCl_3$); **SFC** analysis (OJ-H, 10% hexanes, 2.5 mL/min) indicated 97% ee: t_R (major) = 4.7 minutes, t_R (minor) = 5.3 minutes.



(*S*)-2-(1-cyclohexyl-4-methylpentan-2-yl)naphthalene ((*S*)-1.26) was prepared according to the representative procedure outlined above using the following amounts of reagents: (*R*)-**1.18** (0.134 g, 0.500 mmol), Ni(dppe)Cl_2 (5.3 mg, 0.010 mmol), *i*-butylmagnesium bromide (0.40 mL, 1.0 mmol, 2.5 M in Et_2O), and toluene (3.0 mL). Purification by flash column chromatography (100% hexanes) afforded a colorless oil (0.067 g) as a mixture of the title compound (40% calculated yield), the product of hydrogenolysis (8% calculated yield), and the product of elimination (7% calculated yield). Further purification (100% heptanes) afforded a sample of analytically pure material: **TLC R$_f$** = 0.7 (100% hexanes); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.79 (q, *J* = 7.5 Hz, 3H), 7.56 (s, 1H), 7.46–7.41 (m, 2H), 7.32 (d, *J* = 9.0 Hz, 1H), 2.92 (hept, *J* = 5.0 Hz, 1H), 1.85 (d, *J* = 12.5 Hz, 1H), 1.66–1.54 (m, 6H), 1.49–1.39 (m, 2H), 1.35–1.33 (m, 1H), 1.14–1.03 (m, 4H), 0.92–0.84 (m, 5H), 0.80 (d, *J* = 6.5 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 144.2, 133.7, 132.3, 128.0, 127.7, 127.6, 126.3, 126.1, 125.8, 125.1, 46.9, 45.4, 40.5, 34.9, 34.3, 33.0, 26.8, 26.4, 26.3, 25.5, 23.7, 22.0; **IR** (neat) 2919, 2849, 1447, 853, 813, 743 cm^{-1}; **HRMS** (TOF MS EI+) *m / z* calcd for $C_{22}H_{30}$ [M]$^+$ 294.2347, found 294.2350; **[α]^{27}$_D$** +14.9 (*c* 0.80, $CHCl_3$); **SFC** analysis (OJ-H, 2% hexanes, 2.0 mL/min) indicated 90% ee: t_R (major) = 7.0 minutes, t_R (minor) = 8.4 minutes.

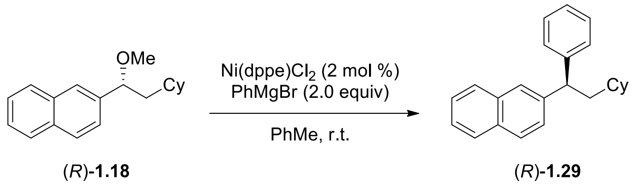


(*R*)-2-(octan-3-yl)naphthalene ((*R*)-1.27) was prepared according to the representative procedure outlined above using the following amounts of reagents: (*R*)-**1.13** (0.100 g, 0.500 mmol), Ni(dppe)Cl_2 (5.3 mg, 0.010 mmol), *n*-pentylmagnesium bromide (0.60 mL, 1.0 mmol, 1.7 M in Et_2O), and toluene (3.0 mL). Purification by flash column chromatography (100% hexanes) afforded a colorless oil (0.118 g) as a mixture of the title compound (96% calculated yield), the product of hydrogenolysis (2% calculated yield), and the product of elimination (1% calculated yield). Further purification (100% heptanes) afforded a sample of analytically pure material: **TLC R$_f$** = 0.6 (100% hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.80–7.76 (m, 3H), 7.56 (s, 1H), 7.46–7.38 (m, 2H), 7.30 (dd, *J* = 8.4, 0.8 Hz, 1H), 2.60–2.52 (m, 1H), 1.78–1.60 (m, 4H), 1.26–1.10 (m, 6H), 0.83–0.76 (m, 6H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 143.7, 133.7, 132.2, 127.9, 127.7, 127.6, 126.5, 126.2, 125.8, 125.1, 48.2, 36.6, 32.2, 29.8, 27.5, 22.7, 14.2, 12.4; **IR** (neat) 3056, 2981, 2918, 2850, 1107, 1067 cm^{-1}; **HRMS** (TOF MS CI+) *m / z* calcd for $C_{18}H_{24}$ [M]$^+$ 240.1878, found 240.1871; **[α]^{27}$_D$** –1.6 (*c* 1.83, $CHCl_3$); **SFC** analysis (OJ-H, 2% hexanes, 2 mL/min) indicated 96% ee: t_R (minor) = 10.0 minutes, t_R (major) = 10.6 minutes.

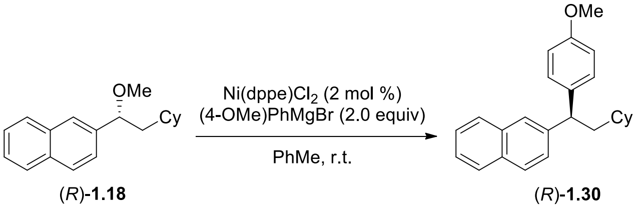


(*R*)-**1.13** (*R*)-**1.28**

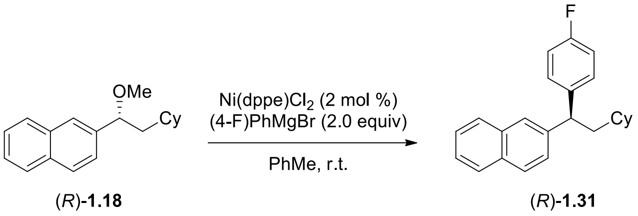
(*R*)-2-(6-phenylhexan-3-yl)naphthalene ((*R*)-1.28) was prepared according to the representative procedure outlined above using the following amounts of reagents: (*R*)-**1.13** (40 mg, 0.20 mmol), Ni(dppe)Cl_2 (5.3 mg, 0.010 mmol), (3-phenylpropyl)magnesium bromide (0.24 mL, 0.40 mmol, 1.7 M in Et_2O), and toluene (3.0 mL). Purification by flash column chromatography (100% heptanes) afforded a colorless oil (0.054 g) as a mixture of the title compound (93% calculated yield) and the product of Wurtz coupling of the organomagnesium reagent (1,6-diphenylhexane). Further purification (flash column chromatography in 100% pentanes) afforded a sample of analytically pure material: **TLC R_f** = 0.6 (100% hexanes); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.1 Hz, 1H), 7.77 (d, *J* = 8.4 Hz, 2H), 7.54 (s, 1H), 7.42 (dt, J = 17.4, 6.7 Hz, 2H), 7.28 (d, *J* = 8.3 Hz, 1H), 7.23–7.20 (m, 2H), 7.14–7.11 (m, 1H), 7.08 (d, *J* = 7.3 Hz, 2H), 2.61–2.49 (m, 3H), 1.79–1.59 (m, 4H), 1.57–1.41 (m, 2H), 0.77 (t, *J* = 7.3Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 143.3, 142.7, 133.7, 132.4, 128.5, 128.3, 128.3, 128.0, 127.72, 127.65, 126.6, 126.1, 125.9, 125.7, 125.2, 48.1, 36.23, 36.15, 29.8, 29.6, 12.4; **IR** (neat) 3024, 2928, 2856, 815, 743 cm^{-1}; **HRMS** (TOF MS CI+) *m / z* calcd for $C_{22}H_{24}$ $[M]^+$ 288.1878, found 288.1880; **$[\alpha]^{24}_D$** –15.1 (*c* 1.08, $CHCl_3$); **SFC** analysis (OJ-H, 15% IPA, 2.0 mL/min) indicated 97% ee: t_R (minor) = 6.3 minutes, t_R (major) = 7.8 minutes.



(*R*)-2-(2-cyclohexyl-1-phenylethyl)naphthalene ((*R*)-1.29) was prepared according to the representative procedure outlined above using the following amounts of reagents: (*R*)-**1.18** (0.134 g, 0.500 mmol), Ni(dppe)Cl_2 (5.3 mg, 0.010 mmol), phenylmagnesium bromide (0.37 mL, 1.0 mmol, 2.7 M in Et_2O), and toluene (7.5 mL). The reaction was stirred for a period of 24 h. Purification by flash column chromatography (100% pentane) afforded the title compound as a colorless oil (0.105 g, 0.33 mmol, 67%): **TLC R_f** = 0.2 (100% pentane); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.77 (t, *J* = 8.1 Hz, 2H), 7.72 (d, *J* = 8.5 Hz, 1H), 7.69 (s, 1H), 7.41 (quintd, *J* = 6.9, 1.3 Hz, 2H), 7.34 (dd, *J* = 8.5, 1.6 Hz, 1H), 7.29–7.24 (m, 4H), 7.17–7.14 (m, 1H), 4.23 (t, *J* = 7.9 Hz, 1H), 2.08–1.95 (m, 2H), 1.80 (t, *J* = 11.7 Hz, 2H), 1.66–1.58 (m, 3H), 1.26–1.05 (m, 4H), 1.01–0.93 (m, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 145.5, 143.0, 133.7, 132.3, 128.5, 128.1, 127.9, 127.7, 127.0, 126.2, 126.0, 125.4, 48.2, 43.5, 35.0, 33.7, 33.5, 26.8, 26.3; **IR** (neat) 2919, 2849, 1448, 3055, 1490, 743, 698 cm^{-1}; **HRMS** (TOF MS EI+) *m / z* calcd for $C_{24}H_{26}$ $[M]^+$ 314.2035, found 314.2030; **$[\alpha]^{25}_D$** –10.8 (*c* 1.99, $CHCl_3$); **SFC** analysis (OJ-H, 15% IPA, 2.5 mL/min) indicated 92% ee: t_R (major) = 6.1 minutes, t_R (minor) = 6.9 minutes.

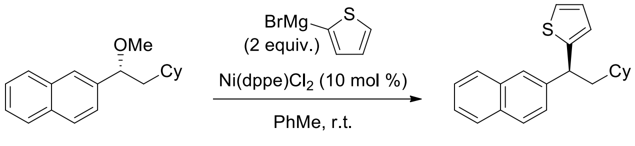


(*R*)-2-(2-cyclohexyl-1-(4-methoxyphenyl)ethyl)naphthalene ((*R*)-1.30) was prepared according to the representative procedure outlined above using the following amounts of reagents: (*R*)-**1.18** (0.134 g, 0.500 mmol) and Ni(dppe)Cl_2 (5.3 mg, 0.010 mmol), 4-methoxyphenylmagnesium bromide (0.53 mL, 1.0 mmol, 1.9 M in Et_2O), and toluene (7.5 mL). The reaction mixture was stirred for a period of 24 h. Purification by silica gel flash column chromatography (5% Et_2O in pentane) afforded a mixture of the title compound (86% calculated yield) and the starting material (15% calculated yield) as a colorless oil (0.157 g total mass). Further purification by silica gel flash column chromatography (1–15% benzene in hexanes) afforded a pure sample of the title compound: **TLC R$_f$** = 0.7 (5% EtOAc in hexanes); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.77 (t, *J* = 9.3 Hz, 2H), 7.72 (d, *J* = 8.5 Hz, 1H), 7.66 (s, 1H), 7.45–7.35 (m, 2H), 7.32 (d, *J* = 8.5 Hz, 1H), 7.18 (d, *J* = 8.5 Hz, 2H), 6.83 (d, *J* = 9.0 Hz, 2H), 4.18 (t, *J* = 7.3 Hz, 1H), 3.74 (s, 3H), 2.02–1.94 (m, 2H), 1.80–1.78 (m, 2H), 1.70–1.55 (m, 3H), 1.23–1.04 (m, 4H), 1.02–0.91 (m, 2H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 157.9, 143.4, 137.6, 133.7, 132.2, 129.0, 128.5, 128.1, 127.8, 127.7, 127.0, 126.0, 125.8, 125.4, 113.9, 55.3, 47.2, 43.7, 35.0, 33.62, 33.57, 26.8, 26.3; **IR** (neat) 2919, 2848, 1509, 1447, 1245, 1177, 1037 cm^{-1}; **HRMS** (TOF MS CI+) *m / z* calcd for $C_{25}H_{28}O$ $[M]^+$ 344.2140, found 344.2131; **$[\alpha]^{24}_D$** –6.3 (*c* 1.17, $CHCl_3$); **SFC** analysis (AD-H, 15% IPA, 3.0 mL/min) indicated 97% ee: t_R (major) = 9.0 minutes, t_R (minor) = 9.6 minutes.



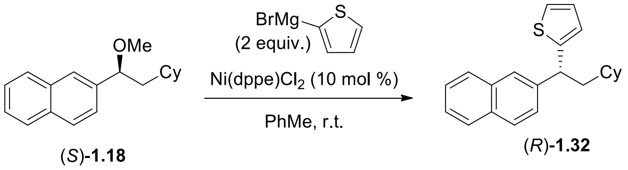
(*R*)-2-(2-cyclohexyl-1-(4-fluorophenyl)ethyl)naphthalene ((*R*)-1.31) was prepared according to the representative procedure outlined above using the following amounts of reagents: (*R*)-**1.18** (0.134 g, 0.500 mmol), Ni(dppe)Cl_2 (5.3 mg, 0.010 mmol), 4-flourophenylmagnesium bromide

(0.46 mL, 1.0 mmol, 2.2 M in Et_2O), and toluene (7.5 mL). The reaction mixture was stirred for a period of 48 h. Purification by silica gel flash column chromatography (100% hexanes) afforded a mixture of the title compound (82% calculated yield) and the product of Wurtz coupling of the organomagnesium reagent as a colorless oil (0.147 g total mass). Further purification by column chromatography (100% pentane) afforded a pure sample of (*R*)-**1.31**: **TLC R_f** = 0.8 (5% EtOAc in hexanes); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.78 (t, *J* = 7.5 Hz, 2H), 7.74 (d, *J* = 8.5 Hz, 1H), 7.66 (s, 1H), 7.46–7.40 (m, 2H), 7.31 (d, *J* = 8.5 Hz, 1H), 7.22 (dd, *J* = 8.5, 6.0 Hz, 2H), 6.95 (app t, *J* = 8.5 Hz, 2H), 4.21 (t, *J* = 8.0 Hz, 1H), 2.02 (quint, *J* = 7.1 Hz, 1H), 1.94 (quint, *J* = 7.0 Hz, 1H), 1.79 (t, *J* = 12.3 Hz, 2H), 1.70–1.56 (m, 3H), 1.22–1.04 (m, 4H), 1.01–0.96 (m, 2H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 161.4 (d, *J* = 242.5 Hz, 1C), 142.8, 141.1 (d, *J* = 3.3 Hz, 1C), 133.7, 132.2, 129.5 (d, *J* = 7.8 Hz, 2C), 128.2, 127.8, 127.7, 126.8, 126.1, 125.9, 125.5, 115.3 (d, *J* = 84.0 Hz, 2C), 47.3, 43.6, 35.0, 33.6, 33.5, 26.7, 26.2; **IR** (neat) 3053, 2920, 2850, 1506, 1222, 793 cm^{-1}; **HRMS** (TOF MS CI+) *m / z* calcd for $C_{24}H_{25}F$ $[M]^+$ 332.1940, found 332.1930; **$[\alpha]^{20}_D$** –11.1 (*c* 0.91, $CHCl_3$); **SFC** analysis (OJ-H, 15% IPA, 2.5 mL/min) indicated 87% ee: t_R (major) = 4.3 minutes, t_R (minor) = 5.6 minutes.

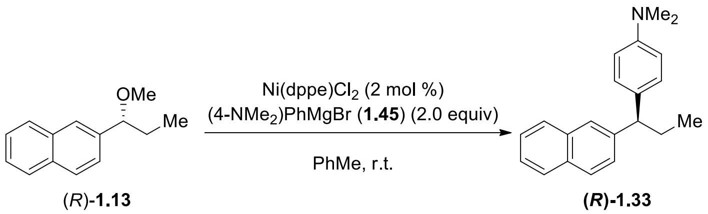


(*R*)-**1.18** (*S*)-**1.32**

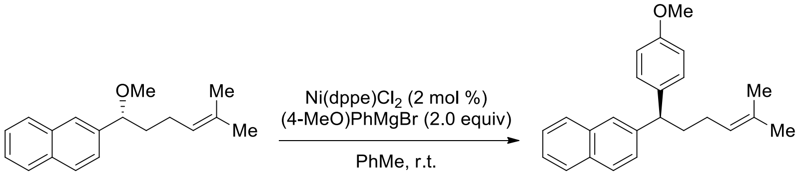
(*S*)-2-(2-cyclohexyl-1-(naphthalen-2-yl)ethyl)thiophene ((*S*)-1.32) was prepared according to the representative procedure outlined above using the following amounts of reagents: (*R*)-**1.18** (54 mg, 0.20 mmol), $Ni(dppe)Cl_2$ (10.6 mg, 0.0200 mmol), 2-thienylmagnesium bromide (0.15 mL, 0.40 mmol, 2.6 M in Et_2O), and toluene (3.0 mL). The reaction mixture was stirred for a period of 48 h. Purification by flash column chromatography (2% Et_2O in pentane) afforded the title compound as a yellow oil (49 mg, 0.15 mmol, 76%): **TLC R_f** = 0.5 (100% hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.78 (t, *J* = 9.0 Hz, 3H), 7.70 (s, 1H), 7.47–7.38 (m, 3H), 7.12 (d, *J* = 4.4 Hz, 1H), 6.91 (dd, *J* = 5.2, 3.2 Hz, 1H), 6.83 (d, *J* = 3.2 Hz, 1H), 4.45 (t, *J* = 8.0 Hz, 1H), 2.05 (t, *J* = 7.4 Hz, 2H), 1.85 (d, *J* = 12.4 Hz, 1H), 1.73 (d, *J* = 12.4 Hz, 1H), 1.64–1.50 (m, 3H), 1.30–0.96 (m, 6H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 150.2, 142.5, 133.7, 132.5, 128.4, 127.9, 127.8, 126.7, 126.3, 126.2, 126.1, 125.6, 123.9, 123.6, 45.1, 43.9, 35.1, 33.8, 33.1, 26.7, 26.3, 26.2; **IR** (neat) 3026, 2922, 2853, 1453, 743, 697 cm^{-1}; **HRMS** (TOF MS CI+) *m / z* calcd for $C_{22}H_{24}SH$ $[M + H]^+$ 321.1677, found 321.1672; **$[\alpha]^{24}_D$** +42.4 (*c* 1.20, $CHCl_3$); **SFC** analysis (OD-H, 20% hexanes, 3.0 mL/min) indicated 93% ee: t_R (minor) = 14.9 minutes, t_R (major) = 17.5 minutes.



(*R*)-2-(2-cyclohexyl-1-(naphthalen-2-yl)ethyl)thiophene ((*R*)-1.32) was prepared according to the representative procedure outlined above using the following amounts of reagents: (*S*)-**1.18** (39 mg, 0.15 mmol), Ni(dppe)Cl_2 (7.7 mg, 0.015 mmol), 2-thienylmagnesium bromide (0.17 mL, 0.29 mmol, 2.0 M in Et_2O), and toluene (2.2 mL). The reaction mixture was stirred for a period of 48 h. Purification by flash column chromatography (2% Et_2O in pentane) afforded the title compound as a yellow oil (33 mg, 0.10 mmol, 70%): **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.78 (t, *J* = 8.6 Hz, 3H), 7.70 (s, 1H), 7.42 (m, 3H), 7.13 (d, *J* = 5.2 Hz, 1H), 6.91 (dd, *J* = 5.2, 3.6 Hz, 1H), 6.84 (d, *J* = 3.6 Hz, 1H), 4.45 (t, *J* = 8.0 Hz, 1H), 2.05 (t, *J* = 7.4 Hz, 2H), 1.86 (d, *J* = 12.8 Hz, 1H), 1.73 (d, *J* = 12.4 Hz, 1H), 1.64–1.54 (m, 3H), 1.26–0.96 (m, 6H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 150.2, 142.5, 133.7, 132.5, 128.4, 127.9, 127.8, 126.7, 126.3, 126.14, 126.09, 125.6, 123.9, 123.6, 45.1, 43.8, 35.1, 33.8, 33.1, 26.7, 26.25, 26.21; **[α]^{24}D** –42.9 (*c* 0.98, CHCl$_3$); **SFC** analysis (OD-H, 20% hexanes, 3.0 mL/min) indicated 92% ee: t$_R$ (major) = 14.3 minutes, t$_R$ (minor) = 17.5 minutes.



(*R*)-*N,N*-dimethyl-4-(1-(naphthalen-2-yl)propyl)aniline ((*R*)-1.33): A 7 mL vial was equipped with a stir bar, flame dried, and pumped into a glove box while still warm. (*R*)-**1.13** (0.040 g, 0.20 mmol), Ni(dppe)Cl$_2$ (5.3 mg, 0.010 mmol), and 4-(*N*,*N*-dimethylamino) phenylmagnesium bromide (**1.45**) (0.133 g, 0.400 mmol) were added. The vial was capped, removed from the glove box and put under a nitrogen atmosphere. Toluene (3 mL) was added and the reaction mixture was stirred for 24 h at which point the reaction was quenched with an excess of methanol. The crude mixture was eluted through a silica plug (100% Et$_2$O) and concentrated in vacuo. Purification by flash column chromatography (1% Et$_3$N, 5% Et$_2$O in pentane) afforded the title compound as a yellow oil (0.047 g, 0.16 mmol, 80% yield). Trace amounts (<5%) of Wurtz coupling product of the organomagnesium reagent could not be separated from the product. **TLC R$_f$** = 0.2 (1% Et$_3$N, 5% EtOAc in hexanes); **^{1}H NMR** (400 MHz, CDCl$_3$) δ 7.77 (t, *J* = 8.0 Hz, 2H), 7.71 (d, *J* = 8.4 Hz, 1H), 7.68 (s, 1H), 7.40 (quint, *J* = 8.0 Hz, 2H), 7.33 (d, *J* = 8.4 Hz, 1H), 7.14 (d, *J* = 8.4 Hz, 2H), 6.75 (d, *J* = 8.4 Hz, 2H), 3.87 (t, *J* = 7.6 Hz, 1H), 2.89 (s, 6H), 2.17–2.08 (quint, *J* = 7.2 Hz, 2H), 0.93 (t, *J* = 7.4 Hz, 3H); **^{13}C NMR** (125 MHz, CDCl$_3$) δ 149.2, 143.6, 133.7, 133.3, 132.2, 128.7, 128.0, 127.8, 127.7, 127.1, 125.9, 125.8, 125.2, 112.9, 52.4, 40.9, 28.6, 13.0; **[α]^{26}D** –3.4 (*c* 1.17, CHCl$_3$); **IR** (neat) 2958, 2928, 2871, 2797, 1613, 1564, 1818, 1345, 811, 780, 747; **HRMS** (TOF MS ES+) *m / z* calcd for $C_{21}H_{23}NH$ $[M + H]^+$ 290.1909, found 290.1903; **$[\alpha]^{25}_D$** –3.4 (*c* 1.16, $CHCl_3$); **SFC** analysis (AD-H, 20% IPA, 2.5 mL/min) indicated 85% ee: t_R (major) = 6.1 minutes, t_R (minor) = 7.4 minutes.



(*R*)-**1.49** (*R*)-**1.34**

(*R*)-2-(1-(4-methoxyphenyl)-5-methylhex-4-enyl)naphthalene ((*R*)-1.34): A flame dried 20 mL dram vial was charged with (*R*)-**1.49** (127 mg, 0.50mmol) and $Ni(dppe)Cl_2$ (5.3 mg, 0.010 mmol). The vial was capped and put under a nitrogen atmosphere. Toluene (7.5 mL) was added followed by (4-methoxy)phenylmagnesium bromide (0.57 mL, 1.0 mmol, 1.8 M in Et_2O). The reaction mixture was stirred for a period of 24 h at which point the reaction vessel was briefly opened to air and another 5.3 mg (0.010 mmol) of $Ni(dppe)Cl_2$ were added. The reaction mixture was then allowed to stir for a second 24 hour period then run through a silica plug (100% Et_2O). Purification of the crude material by silica gel flash column chromatography (2% Et_2O in pentane) yielded a mixture of the title compound (92% calculated yield) and the product of Wurtz coupling of the organomagnesium reagent as an oil (151 mg total mass). Further purification by silica gel flash column chromatography (1% Et_2O in pentane) afforded a pure sample of (*R*)-**1.34**: **TLC R_f** = 0.7 (2% EtOAc in hexanes); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.78 (t, *J* = 8.3 Hz, 2H), 7.72 (d, *J* = 8.0 Hz, 1H), 7.68 (s, 1H), 7.45–7.38 (m, 2H), 7.31 (d, *J* = 8.5 Hz, 1H), 7.19 (d, *J* = 9.0 Hz, 2H), 6.81 (d, *J* = 9.0 Hz, 2H), 5.17 (t, *J* = 7.0 Hz, 1H), 4.02 (t, *J* = 7.8 Hz, 1H), 3.75 (s, 3H), 2.17–2.11 (m, 2H), 1.97 (app q, *J* = 7.5 Hz, 2H), 1.69 (s, 3H), 1.48 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 158.0, 143.1, 137.3, 133.7, 132.22, 132.16, 129.1, 128.1, 127.8, 127.7, 126.9, 126.0, 125.9, 125.4, 124.3, 113.9, 55.3, 49.9, 35.8, 26.5, 25.9, 17.9; **IR** (neat) 2925, 1608, 1509, 1440, 1245 cm^{-1}; **HRMS** (TOF MS CI+) *m / z* calcd for $C_{24}H_{26}O$ $[M]^+$ 330.1984, found 330.1986; **$[\alpha]^{20}_D$** –2.7 (*c* 1.06, $CHCl_3$); **SFC** analysis (AD-H, 10% IPA, 3.0 mL/min) indicated 88% ee: t_R (major) = 8.2 minutes, t_R (minor) = 8.9 minutes.

1.4.7 Crystallographic Data[55]

The single crystal X-ray diffraction studies were carried out on a Bruker Kappa APEX CCD diffractometer equipped with Cu K_α radiation (λ = 1.5478). Crystals of the subject compound were grown by slow evaporation of a 1:1 methanol:pentane solution. A 0.217 x 0.095 x 0.053 mm colorless needle was mounted on a Cryoloop with Paratone oil. Data were collected in a nitrogen gas stream at 90(2) K using ϕ and ϖ scans. Data was collected at two crystal-to-detector distances, 45mm or 60mm, using variable exposure time (2s-10s) depending on θ with a scan width of 1.0°. Data collection was 98.7% complete to 68.00° in θ. A total of 57312 reflections were collected covering the indices, --7<=h<=7, -16<=k<=16, -17<=l<=17. 7355 reflections were found to be symmetry independent, with a R_{int} of 0.0524. Indexing and unit cell refinement indicated a primitive, triclinic lattice. The space group was found to be *P*1. The data were integrated using the Bruker SAINT software program and scaled using the SADABS software program. Solution by direct methods (SHELXT) produced a complete phasing model consistent with the proposed structure.

All nonhydrogen atoms were refined anisotropically by full-matrix least-squares (SHELXL-2013). All hydrogen atoms were placed using a riding model. Their positions were

---

[55] Crystal Structure solved and X-Ray data compiled by Curtis E. Moore at the University of California, San Diego.

constrained relative to their parent atom using the appropriate HFIX command in SHELXL-2013. Crystallographic data are summarized in Table 1.10.

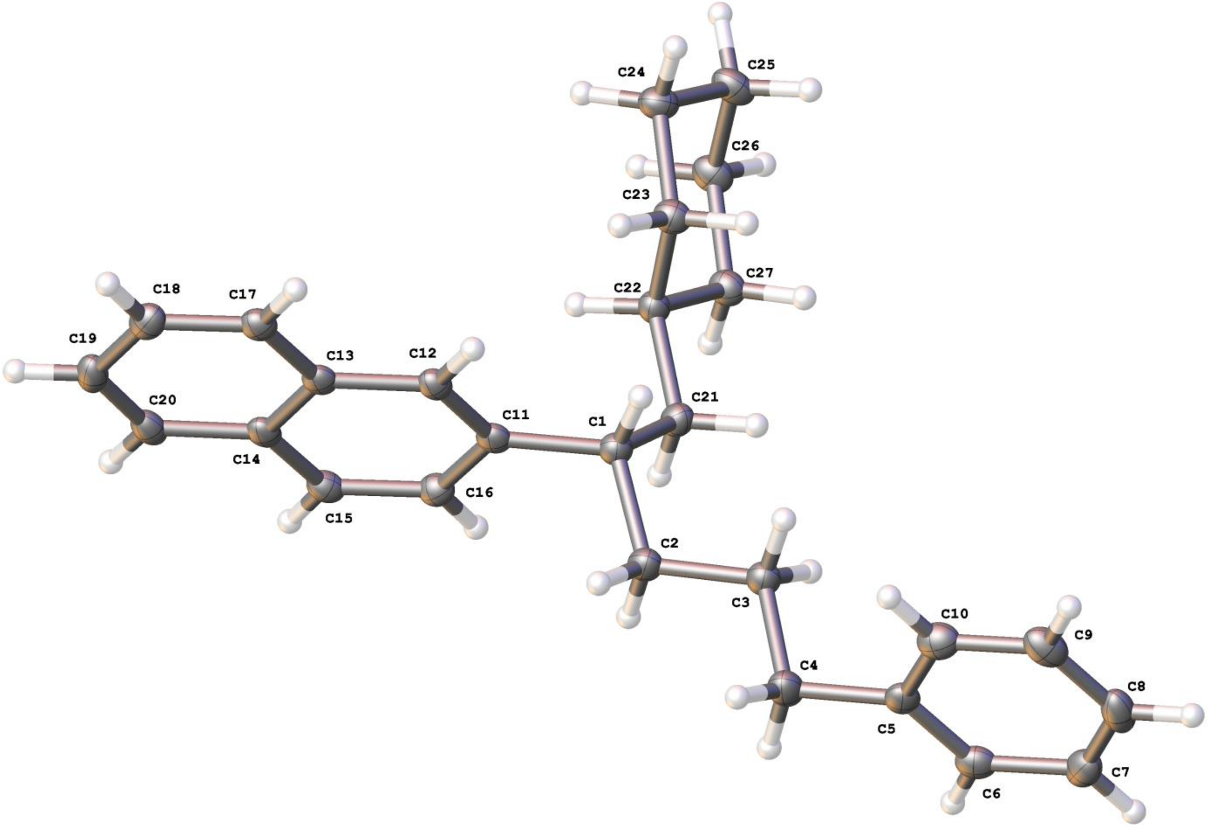


Table 1.10. Crystal Data and Structure Refinement for Jarvo02.

Identification code	ERJ-14	
Empirical formula	C27 H32	
Molecular formula	C27 H32	
Formula weight	356.52	
Temperature	90 K	
Wavelength	1.54178 Å	
Crystal system	Triclinic	
Space group	P 1	
Unit cell dimensions	a = 5.9031(2) Å	α= 106.3499(15)°.
	b = 13.8552(5) Å	β= 98.3273(14)°.
	c = 14.0936(5) Å	γ = 101.5540(15)°.
Volume	1058.56(7) Å^3	
Z	2	
Density (calculated)	1.119 Mg/m^3	
Absorption coefficient	0.463 mm^{-1}	
F(000)	388	
Crystal size	0.217 x 0.095 x 0.053 mm^3	
Crystal color, habit	Colorless Needle	
Theta range for data collection	3.345 to 69.358°.	
Index ranges	-7<=h<=7, -16<=k<=16, -17<=l<=17	
Reflections collected	57312	
Independent reflections	7355 [R(int) = 0.0524]	
Completeness to theta = 68.000°	98.7 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7532 and 0.7017	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	7355 / 3 / 487	
Goodness-of-fit on F^2	1.029	
Final R indices [I>2sigma(I)]	R1 = 0.0312, wR2 = 0.0787	
R indices (all data)	R1 = 0.0324, wR2 = 0.0799	
Absolute structure parameter	0.065(347)	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.120 and -0.172 e.Å^{-3}	

Table 1.11. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3) for Jarvo02. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
C(1)	8627(3)	2712(2)	9759(1)	20(1)
C(2)	8982(4)	1839(2)	10204(2)	23(1)
C(3)	9335(3)	883(2)	9445(1)	21(1)
C(4)	10054(4)	108(2)	9944(2)	27(1)
C(5)	10507(3)	-808(2)	9186(1)	21(1)
C(6)	8896(3)	-1776(2)	8845(2)	23(1)
C(7)	9312(4)	-2603(2)	8126(2)	27(1)
C(8)	11349(4)	-2473(2)	7748(2)	29(1)
C(9)	12964(4)	-1513(2)	8083(2)	28(1)
C(10)	12546(4)	-689(2)	8797(2)	26(1)
C(11)	8776(3)	3692(2)	10609(1)	18(1)
C(12)	10775(3)	4502(2)	10932(1)	18(1)
C(13)	11023(3)	5399(2)	11773(1)	18(1)
C(14)	9133(3)	5458(2)	12292(1)	19(1)
C(15)	7078(3)	4622(2)	11945(1)	21(1)
C(16)	6901(3)	3768(2)	11136(1)	20(1)
C(17)	13086(3)	6234(2)	12111(1)	20(1)
C(18)	13267(3)	7090(2)	12923(2)	23(1)
C(19)	11385(4)	7148(2)	13438(2)	24(1)
C(20)	9373(4)	6355(2)	13131(2)	22(1)
C(21)	6322(3)	2349(2)	8940(2)	21(1)
C(22)	5748(3)	3152(2)	8446(1)	19(1)
C(23)	7800(3)	3596(2)	8012(2)	22(1)
C(24)	7172(4)	4332(2)	7439(2)	24(1)
C(25)	4963(4)	3801(2)	6602(2)	27(1)
C(26)	2893(3)	3389(2)	7036(2)	25(1)
C(27)	3503(3)	2646(2)	7602(2)	22(1)
C(1')	9460(3)	671(2)	3372(1)	21(1)
C(2')	10172(4)	1568(2)	2946(2)	24(1)
C(3')	11922(4)	2533(2)	3706(2)	23(1)
C(4')	12998(4)	3309(2)	3205(2)	28(1)

C(5')	14500(4)	4307(2)	3977(2)	23(1)
C(6')	13548(4)	5157(2)	4278(2)	25(1)
C(7')	14867(4)	6067(2)	5020(2)	28(1)
C(8')	17162(4)	6145(2)	5474(2)	29(1)
C(9')	18138(4)	5304(2)	5183(2)	28(1)
C(10')	16815(4)	4395(2)	4438(2)	26(1)
C(11')	7920(3)	-281(2)	2526(1)	19(1)
C(12')	8759(3)	-1134(2)	2159(1)	19(1)
C(13')	7410(3)	-2009(2)	1326(1)	18(1)
C(14')	5111(3)	-1999(2)	863(1)	19(1)
C(15')	4255(3)	-1114(2)	1263(2)	21(1)
C(16')	5600(3)	-288(2)	2066(2)	21(1)
C(17')	8279(3)	-2891(2)	942(1)	20(1)
C(18')	6937(4)	-3720(2)	136(2)	23(1)
C(19')	4663(3)	-3706(2)	-327(2)	23(1)
C(20')	3773(3)	-2862(2)	29(2)	22(1)
C(21')	8305(3)	988(2)	4284(2)	22(1)
C(22')	7554(3)	139(2)	4758(1)	19(1)
C(23')	9615(3)	-298(2)	5085(2)	23(1)
C(24')	8856(4)	-1122(2)	5585(2)	26(1)
C(25')	7787(4)	-692(2)	6486(2)	28(1)
C(26')	5719(4)	-262(2)	6172(2)	27(1)
C(27')	6475(3)	559(2)	5667(2)	24(1)

Table 1.12. Bond lengths [Å] and angles [°] for Jarvo02.

C(1)-H(1)	1.0000	C(16)-H(16)	0.9500
C(1)-C(2)	1.546(3)	C(17)-H(17)	0.9500
C(1)-C(11)	1.514(3)	C(17)-C(18)	1.370(3)
C(1)-C(21)	1.542(3)	C(18)-H(18)	0.9500
C(2)-H(2A)	0.9900	C(18)-C(19)	1.415(3)
C(2)-H(2B)	0.9900	C(19)-H(19)	0.9500
C(2)-C(3)	1.523(3)	C(19)-C(20)	1.366(3)
C(3)-H(3A)	0.9900	C(20)-H(20)	0.9500
C(3)-H(3B)	0.9900	C(21)-H(21A)	0.9900
C(3)-C(4)	1.533(3)	C(21)-H(21B)	0.9900
C(4)-H(4A)	0.9900	C(21)-C(22)	1.536(3)
C(4)-H(4B)	0.9900	C(22)-H(22)	1.0000
C(4)-C(5)	1.510(3)	C(22)-C(23)	1.533(3)
C(5)-C(6)	1.388(3)	C(22)-C(27)	1.538(3)
C(5)-C(10)	1.392(3)	C(23)-H(23A)	0.9900
C(6)-H(6)	0.9500	C(23)-H(23B)	0.9900
C(6)-C(7)	1.389(3)	C(23)-C(24)	1.534(3)
C(7)-H(7)	0.9500	C(24)-H(24A)	0.9900
C(7)-C(8)	1.384(3)	C(24)-H(24B)	0.9900
C(8)-H(8)	0.9500	C(24)-C(25)	1.522(3)
C(8)-C(9)	1.382(3)	C(25)-H(25A)	0.9900
C(9)-H(9)	0.9500	C(25)-H(25B)	0.9900
C(9)-C(10)	1.384(3)	C(25)-C(26)	1.526(3)
C(10)-H(10)	0.9500	C(26)-H(26A)	0.9900
C(11)-C(12)	1.373(3)	C(26)-H(26B)	0.9900
C(11)-C(16)	1.424(3)	C(26)-C(27)	1.533(3)
C(12)-H(12)	0.9500	C(27)-H(27A)	0.9900
C(12)-C(13)	1.421(3)	C(27)-H(27B)	0.9900
C(13)-C(14)	1.423(3)	C(1')-H(1')	1.0000
C(13)-C(17)	1.416(3)	C(1')-C(2')	1.539(3)
C(14)-C(15)	1.415(3)	C(1')-C(11')	1.519(3)
C(14)-C(20)	1.420(3)	C(1')-C(21')	1.538(3)
C(15)-H(15)	0.9500	C(2')-H(2'A)	0.9900
C(15)-C(16)	1.366(3)	C(2')-H(2'B)	0.9900

C(2')-C(3')	1.524(3)	C(21')-H(21C)	0.9900
C(3')-H(3'A)	0.9900	C(21')-H(21D)	0.9900
C(3')-H(3'B)	0.9900	C(21')-C(22')	1.531(3)
C(3')-C(4')	1.531(3)	C(22')-H(22')	1.0000
C(4')-H(4'A)	0.9900	C(22')-C(23')	1.533(3)
C(4')-H(4'B)	0.9900	C(22')-C(27')	1.533(3)
C(4')-C(5')	1.505(3)	C(23')-H(23C)	0.9900
C(5')-C(6')	1.391(3)	C(23')-H(23D)	0.9900
C(5')-C(10')	1.392(3)	C(23')-C(24')	1.530(3)
C(6')-H(6')	0.9500	C(24')-H(24C)	0.9900
C(6')-C(7')	1.385(3)	C(24')-H(24D)	0.9900
C(7')-H(7')	0.9500	C(24')-C(25')	1.524(3)
C(7')-C(8')	1.381(3)	C(25')-H(25C)	0.9900
C(8')-H(8')	0.9500	C(25')-H(25D)	0.9900
C(8')-C(9')	1.388(3)	C(25')-C(26')	1.524(3)
C(9')-H(9')	0.9500	C(26')-H(26C)	0.9900
C(9')-C(10')	1.386(3)	C(26')-H(26D)	0.9900
C(10')-H(10')	0.9500	C(26')-C(27')	1.531(3)
C(11')-C(12')	1.369(3)	C(27')-H(27C)	0.9900
C(11')-C(16')	1.425(3)	C(27')-H(27D)	0.9900
C(12')-H(12')	0.9500		
C(12')-C(13')	1.422(3)	C(2)-C(1)-H(1)	107.4
C(13')-C(14')	1.423(2)	C(11)-C(1)-H(1)	107.4
C(13')-C(17')	1.417(3)	C(11)-C(1)-C(2)	109.61(15)
C(14')-C(15')	1.421(3)	C(11)-C(1)-C(21)	113.87(16)
C(14')-C(20')	1.413(3)	C(21)-C(1)-H(1)	107.4
C(15')-H(15')	0.9500	C(21)-C(1)-C(2)	110.96(16)
C(15')-C(16')	1.366(3)	C(1)-C(2)-H(2A)	108.7
C(16')-H(16')	0.9500	C(1)-C(2)-H(2B)	108.7
C(17')-H(17')	0.9500	H(2A)-C(2)-H(2B)	107.6
C(17')-C(18')	1.369(3)	C(3)-C(2)-C(1)	114.19(16)
C(18')-H(18')	0.9500	C(3)-C(2)-H(2A)	108.7
C(18')-C(19')	1.411(3)	C(3)-C(2)-H(2B)	108.7
C(19')-H(19')	0.9500	C(2)-C(3)-H(3A)	109.1
C(19')-C(20')	1.373(3)	C(2)-C(3)-H(3B)	109.1
C(20')-H(20')	0.9500	C(2)-C(3)-C(4)	112.66(16)

H(3A)-C(3)-H(3B)	107.8
C(4)-C(3)-H(3A)	109.1
C(4)-C(3)-H(3B)	109.1
C(3)-C(4)-H(4A)	109.3
C(3)-C(4)-H(4B)	109.3
H(4A)-C(4)-H(4B)	107.9
C(5)-C(4)-C(3)	111.74(16)
C(5)-C(4)-H(4A)	109.3
C(5)-C(4)-H(4B)	109.3
C(6)-C(5)-C(4)	121.28(18)
C(6)-C(5)-C(10)	118.54(19)
C(10)-C(5)-C(4)	120.17(19)
C(5)-C(6)-H(6)	119.8
C(5)-C(6)-C(7)	120.47(19)
C(7)-C(6)-H(6)	119.8
C(6)-C(7)-H(7)	119.8
C(8)-C(7)-C(6)	120.3(2)
C(8)-C(7)-H(7)	119.8
C(7)-C(8)-H(8)	120.2
C(9)-C(8)-C(7)	119.6(2)
C(9)-C(8)-H(8)	120.2
C(8)-C(9)-H(9)	120.0
C(8)-C(9)-C(10)	120.0(2)
C(10)-C(9)-H(9)	120.0
C(5)-C(10)-H(10)	119.5
C(9)-C(10)-C(5)	121.0(2)
C(9)-C(10)-H(10)	119.5
C(12)-C(11)-C(1)	120.95(17)
C(12)-C(11)-C(16)	118.36(18)
C(16)-C(11)-C(1)	120.57(18)
C(11)-C(12)-H(12)	119.0
C(11)-C(12)-C(13)	121.99(17)
C(13)-C(12)-H(12)	119.0
C(12)-C(13)-C(14)	118.84(17)
C(17)-C(13)-C(12)	122.18(17)
C(17)-C(13)-C(14)	118.98(18)
C(15)-C(14)-C(13)	118.46(18)
C(15)-C(14)-C(20)	122.61(18)
C(20)-C(14)-C(13)	118.94(18)
C(14)-C(15)-H(15)	119.4
C(16)-C(15)-C(14)	121.24(18)
C(16)-C(15)-H(15)	119.4
C(11)-C(16)-H(16)	119.4
C(15)-C(16)-C(11)	121.12(18)
C(15)-C(16)-H(16)	119.4
C(13)-C(17)-H(17)	119.6
C(18)-C(17)-C(13)	120.76(18)
C(18)-C(17)-H(17)	119.6
C(17)-C(18)-H(18)	119.9
C(17)-C(18)-C(19)	120.16(19)
C(19)-C(18)-H(18)	119.9
C(18)-C(19)-H(19)	119.8
C(20)-C(19)-C(18)	120.5(2)
C(20)-C(19)-H(19)	119.8
C(14)-C(20)-H(20)	119.7
C(19)-C(20)-C(14)	120.66(19)
C(19)-C(20)-H(20)	119.7
C(1)-C(21)-H(21A)	108.3
C(1)-C(21)-H(21B)	108.3
H(21A)-C(21)-H(21B)	107.4
C(22)-C(21)-C(1)	116.10(16)
C(22)-C(21)-H(21A)	108.3
C(22)-C(21)-H(21B)	108.3
C(21)-C(22)-H(22)	108.5
C(21)-C(22)-C(27)	109.54(16)
C(23)-C(22)-C(21)	111.91(15)
C(23)-C(22)-H(22)	108.5
C(23)-C(22)-C(27)	109.80(15)
C(27)-C(22)-H(22)	108.5
C(22)-C(23)-H(23A)	109.1
C(22)-C(23)-H(23B)	109.1
C(22)-C(23)-C(24)	112.37(15)

H(23A)-C(23)-H(23B)	107.9
C(24)-C(23)-H(23A)	109.1
C(24)-C(23)-H(23B)	109.1
C(23)-C(24)-H(24A)	109.3
C(23)-C(24)-H(24B)	109.3
H(24A)-C(24)-H(24B)	108.0
C(25)-C(24)-C(23)	111.43(17)
C(25)-C(24)-H(24A)	109.3
C(25)-C(24)-H(24B)	109.3
C(24)-C(25)-H(25A)	109.6
C(24)-C(25)-H(25B)	109.6
C(24)-C(25)-C(26)	110.29(16)
H(25A)-C(25)-H(25B)	108.1
C(26)-C(25)-H(25A)	109.6
C(26)-C(25)-H(25B)	109.6
C(25)-C(26)-H(26A)	109.4
C(25)-C(26)-H(26B)	109.4
C(25)-C(26)-C(27)	110.99(16)
H(26A)-C(26)-H(26B)	108.0
C(27)-C(26)-H(26A)	109.4
C(27)-C(26)-H(26B)	109.4
C(22)-C(27)-H(27A)	109.1
C(22)-C(27)-H(27B)	109.1
C(26)-C(27)-C(22)	112.43(17)
C(26)-C(27)-H(27A)	109.1
C(26)-C(27)-H(27B)	109.1
H(27A)-C(27)-H(27B)	107.9
C(2')-C(1')-H(1')	107.3
C(11')-C(1')-H(1')	107.3
C(11')-C(1')-C(2')	109.48(15)
C(11')-C(1')-C(21')	113.10(16)
C(21')-C(1')-H(1')	107.3
C(21')-C(1')-C(2')	112.20(17)
C(1')-C(2')-H(2'A)	108.7
C(1')-C(2')-H(2'B)	108.7
H(2'A)-C(2')-H(2'B)	107.6
C(3')-C(2')-C(1')	114.09(16)
C(3')-C(2')-H(2'A)	108.7
C(3')-C(2')-H(2'B)	108.7
C(2')-C(3')-H(3'A)	109.1
C(2')-C(3')-H(3'B)	109.1
C(2')-C(3')-C(4')	112.48(16)
H(3'A)-C(3')-H(3'B)	107.8
C(4')-C(3')-H(3'A)	109.1
C(4')-C(3')-H(3'B)	109.1
C(3')-C(4')-H(4'A)	109.3
C(3')-C(4')-H(4'B)	109.3
H(4'A)-C(4')-H(4'B)	107.9
C(5')-C(4')-C(3')	111.69(16)
C(5')-C(4')-H(4'A)	109.3
C(5')-C(4')-H(4'B)	109.3
C(6')-C(5')-C(4')	120.02(19)
C(6')-C(5')-C(10')	118.34(19)
C(10')-C(5')-C(4')	121.6(2)
C(5')-C(6')-H(6')	119.5
C(7')-C(6')-C(5')	120.91(19)
C(7')-C(6')-H(6')	119.5
C(6')-C(7')-H(7')	119.9
C(8')-C(7')-C(6')	120.3(2)
C(8')-C(7')-H(7')	119.9
C(7')-C(8')-H(8')	120.2
C(7')-C(8')-C(9')	119.6(2)
C(9')-C(8')-H(8')	120.2
C(8')-C(9')-H(9')	120.0
C(10')-C(9')-C(8')	119.99(19)
C(10')-C(9')-H(9')	120.0
C(5')-C(10')-H(10')	119.5
C(9')-C(10')-C(5')	120.9(2)
C(9')-C(10')-H(10')	119.5
C(12')-C(11')-C(1')	120.97(17)
C(12')-C(11')-C(16')	118.38(18)
C(16')-C(11')-C(1')	120.59(18)

C(11')-C(12')-H(12')	118.9
C(11')-C(12')-C(13')	122.11(17)
C(13')-C(12')-H(12')	118.9
C(12')-C(13')-C(14')	118.90(18)
C(17')-C(13')-C(12')	122.20(17)
C(17')-C(13')-C(14')	118.90(18)
C(15')-C(14')-C(13')	118.23(18)
C(20')-C(14')-C(13')	119.09(18)
C(20')-C(14')-C(15')	122.68(17)
C(14')-C(15')-H(15')	119.4
C(16')-C(15')-C(14')	121.23(17)
C(16')-C(15')-H(15')	119.4
C(11')-C(16')-H(16')	119.4
C(15')-C(16')-C(11')	121.13(18)
C(15')-C(16')-H(16')	119.4
C(13')-C(17')-H(17')	119.6
C(18')-C(17')-C(13')	120.72(18)
C(18')-C(17')-H(17')	119.6
C(17')-C(18')-H(18')	119.8
C(17')-C(18')-C(19')	120.34(19)
C(19')-C(18')-H(18')	119.8
C(18')-C(19')-H(19')	119.9
C(20')-C(19')-C(18')	120.27(19)
C(20')-C(19')-H(19')	119.9
C(14')-C(20')-H(20')	119.7
C(19')-C(20')-C(14')	120.68(18)
C(19')-C(20')-H(20')	119.7
C(1')-C(21')-H(21C)	108.4
C(1')-C(21')-H(21D)	108.4
H(21C)-C(21')-H(21D)	107.5
C(22')-C(21')-C(1')	115.48(16)
C(22')-C(21')-H(21C)	108.4
C(22')-C(21')-H(21D)	108.4
C(21')-C(22')-H(22')	108.1
C(21')-C(22')-C(23')	112.32(15)
C(21')-C(22')-C(27')	110.28(16)
C(23')-C(22')-H(22')	108.1
C(23')-C(22')-C(27')	109.76(15)
C(27')-C(22')-H(22')	108.1
C(22')-C(23')-H(23C)	109.3
C(22')-C(23')-H(23D)	109.3
H(23C)-C(23')-H(23D)	107.9
C(24')-C(23')-C(22')	111.76(15)
C(24')-C(23')-H(23C)	109.3
C(24')-C(23')-H(23D)	109.3
C(23')-C(24')-H(24C)	109.4
C(23')-C(24')-H(24D)	109.4
H(24C)-C(24')-H(24D)	108.0
C(25')-C(24')-C(23')	111.14(18)
C(25')-C(24')-H(24C)	109.4
C(25')-C(24')-H(24D)	109.4
C(24')-C(25')-H(25C)	109.4
C(24')-C(25')-H(25D)	109.4
C(24')-C(25')-C(26')	110.98(17)
H(25C)-C(25')-H(25D)	108.0
C(26')-C(25')-H(25C)	109.4
C(26')-C(25')-H(25D)	109.4
C(25')-C(26')-H(26C)	109.5
C(25')-C(26')-H(26D)	109.5
C(25')-C(26')-C(27')	110.94(17)
H(26C)-C(26')-H(26D)	108.0
C(27')-C(26')-H(26C)	109.5
C(27')-C(26')-H(26D)	109.5
C(22')-C(27')-H(27C)	109.2
C(22')-C(27')-H(27D)	109.2
C(26')-C(27')-C(22')	112.16(17)
C(26')-C(27')-H(27C)	109.2
C(26')-C(27')-H(27D)	109.2
H(27C)-C(27')-H(27D)	107.9

Table 1.13. Anisotropic displacement parameters ($Å^2$x 10^3) for Jarvo02. The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2 a^{*2}U^{11} + ... + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(1)	23(1)	19(1)	18(1)	7(1)	3(1)	6(1)
C(2)	30(1)	20(1)	18(1)	7(1)	2(1)	7(1)
C(3)	24(1)	20(1)	19(1)	7(1)	3(1)	7(1)
C(4)	38(1)	24(1)	21(1)	9(1)	6(1)	13(1)
C(5)	26(1)	20(1)	17(1)	9(1)	1(1)	9(1)
C(6)	22(1)	27(1)	22(1)	13(1)	2(1)	8(1)
C(7)	34(1)	22(1)	20(1)	6(1)	-4(1)	5(1)
C(8)	41(1)	31(1)	18(1)	5(1)	2(1)	20(1)
C(9)	27(1)	39(1)	24(1)	14(1)	7(1)	16(1)
C(10)	24(1)	28(1)	26(1)	12(1)	1(1)	4(1)
C(11)	21(1)	21(1)	16(1)	9(1)	1(1)	8(1)
C(12)	20(1)	21(1)	16(1)	8(1)	3(1)	9(1)
C(13)	22(1)	21(1)	16(1)	10(1)	2(1)	9(1)
C(14)	24(1)	22(1)	15(1)	10(1)	3(1)	11(1)
C(15)	21(1)	26(1)	20(1)	11(1)	6(1)	9(1)
C(16)	20(1)	21(1)	19(1)	8(1)	1(1)	4(1)
C(17)	21(1)	23(1)	18(1)	10(1)	2(1)	8(1)
C(18)	24(1)	21(1)	21(1)	7(1)	-3(1)	5(1)
C(19)	32(1)	21(1)	16(1)	4(1)	-1(1)	12(1)
C(20)	28(1)	28(1)	16(1)	10(1)	6(1)	15(1)
C(21)	25(1)	18(1)	19(1)	6(1)	1(1)	5(1)
C(22)	22(1)	18(1)	16(1)	6(1)	3(1)	7(1)
C(23)	22(1)	25(1)	21(1)	9(1)	4(1)	7(1)
C(24)	28(1)	26(1)	24(1)	13(1)	7(1)	9(1)
C(25)	30(1)	36(1)	19(1)	13(1)	5(1)	12(1)
C(26)	23(1)	31(1)	21(1)	10(1)	1(1)	9(1)
C(27)	22(1)	25(1)	19(1)	7(1)	2(1)	5(1)
C(1')	24(1)	21(1)	18(1)	8(1)	4(1)	5(1)
C(2')	30(1)	22(1)	18(1)	7(1)	3(1)	4(1)
C(3')	28(1)	22(1)	20(1)	8(1)	4(1)	3(1)

C(4')	36(1)	25(1)	21(1)	9(1)	5(1)	2(1)
C(5')	28(1)	24(1)	19(1)	12(1)	6(1)	3(1)
C(6')	26(1)	29(1)	21(1)	12(1)	2(1)	6(1)
C(7')	37(1)	25(1)	24(1)	10(1)	5(1)	9(1)
C(8')	36(1)	26(1)	19(1)	9(1)	0(1)	-2(1)
C(9')	22(1)	39(1)	22(1)	14(1)	1(1)	2(1)
C(10')	29(1)	30(1)	24(1)	13(1)	10(1)	9(1)
C(11')	21(1)	21(1)	16(1)	10(1)	4(1)	4(1)
C(12')	18(1)	23(1)	17(1)	10(1)	3(1)	4(1)
C(13')	21(1)	21(1)	15(1)	10(1)	5(1)	5(1)
C(14')	19(1)	24(1)	17(1)	11(1)	4(1)	5(1)
C(15')	18(1)	27(1)	20(1)	12(1)	3(1)	8(1)
C(16')	24(1)	21(1)	22(1)	9(1)	7(1)	10(1)
C(17')	20(1)	23(1)	19(1)	9(1)	3(1)	7(1)
C(18')	28(1)	22(1)	21(1)	8(1)	7(1)	8(1)
C(19')	24(1)	24(1)	16(1)	4(1)	0(1)	2(1)
C(20')	20(1)	27(1)	18(1)	9(1)	2(1)	6(1)
C(21')	28(1)	18(1)	19(1)	6(1)	4(1)	6(1)
C(22')	22(1)	18(1)	17(1)	5(1)	4(1)	4(1)
C(23')	23(1)	27(1)	23(1)	11(1)	7(1)	9(1)
C(24')	27(1)	29(1)	26(1)	15(1)	7(1)	10(1)
C(25')	30(1)	36(1)	23(1)	15(1)	8(1)	11(1)
C(26')	27(1)	33(1)	25(1)	12(1)	11(1)	9(1)
C(27')	27(1)	23(1)	22(1)	6(1)	7(1)	8(1)

Table 1.14. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^{3}) for Jarvo02.

	x	y	z	U(eq)
H(1)	9972	2865	9422	24
H(2A)	10378	2122	10774	27
H(2B)	7583	1624	10479	27
H(3A)	10576	1106	9092	25
H(3B)	7846	532	8931	25
H(4A)	11504	466	10479	32
H(4B)	8780	-144	10268	32
H(6)	7500	-1873	9104	27
H(7)	8192	-3260	7893	32
H(8)	11636	-3041	7260	35
H(9)	14362	-1419	7824	33
H(10)	13667	-32	9025	31
H(12)	12031	4461	10582	22
H(15)	5797	4654	12280	25
H(16)	5504	3215	10921	24
H(17)	14359	6200	11771	24
H(18)	14659	7645	13142	27
H(19)	11522	7743	14001	28
H(20)	8121	6405	13482	27
H(21A)	6416	1730	8401	25
H(21B)	4988	2127	9248	25
H(22)	5437	3736	8972	23
H(23A)	8240	3016	7546	26
H(23B)	9192	3979	8572	26
H(24A)	6906	4953	7920	29
H(24B)	8515	4567	7142	29
H(25A)	5272	3218	6086	32
H(25B)	4559	4303	6268	32
H(26A)	1488	3019	6480	30
H(26B)	2496	3980	7506	30

H(27A)	3735	2022	7114	27
H(27B)	2157	2418	7901	27
H(1')	10945	490	3617	25
H(2'A)	10880	1318	2357	29
H(2'B)	8727	1763	2700	29
H(3'A)	13209	2320	4063	28
H(3'B)	11102	2878	4216	28
H(4'A)	13979	2994	2755	33
H(4'B)	11710	3462	2783	33
H(6')	11971	5113	3971	30
H(7')	14190	6640	5217	34
H(8')	18067	6770	5981	34
H(9')	19713	5351	5495	34
H(10')	17498	3824	4239	31
H(12')	10291	-1142	2470	22
H(15')	2720	-1095	966	25
H(16')	4978	291	2321	25
H(17')	9809	-2908	1246	24
H(18')	7540	-4306	-113	27
H(19')	3744	-4283	-886	27
H(20')	2243	-2859	-289	26
H(21C)	9433	1592	4813	26
H(21D)	6892	1219	4068	26
H(22')	6310	-444	4239	23
H(23C)	10234	-608	4486	28
H(23D)	10908	277	5567	28
H(24C)	7677	-1729	5083	31
H(24D)	10247	-1361	5815	31
H(25C)	9015	-132	7019	34
H(25D)	7232	-1251	6771	34
H(26C)	5121	53	6777	32
H(26D)	4417	-837	5696	32
H(27C)	7651	1167	6169	28
H(27D)	5081	796	5439	28

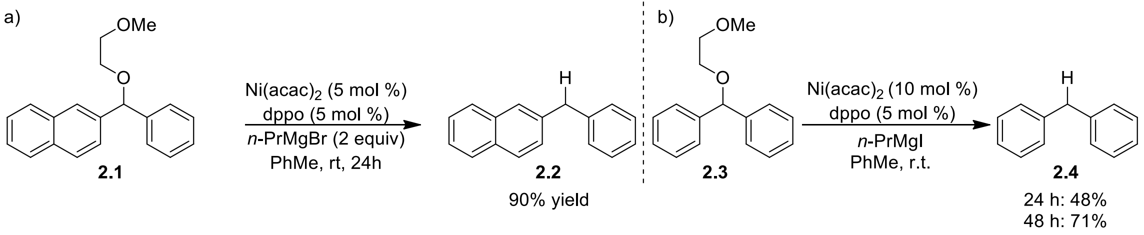
Chapter 2

Studies of Pathways Leading to Side-Products of Kumada-Type Cross-Coupling Reactions

2.1 Introduction

Chapter 1 described a cross-coupling reaction in which $Ni(acac)_2$ in the presence of dppe catalyzes the cross-coupling of benzylic ethers with aryl and alkyl Grignard reagents. Additionally, $Ni(acac)_2$ in the presence of a longer-chain ligand, dppo, was shown to promote major side-reactions: hydrogenolysis and elimination.[1] While attempting to identify conditions that were amenable to the cross-coupling of benzhydryl substrates, we saw a similar but more pronounced trend. $Ni(acac)_2$ in the presence of dppo and *n*-propylmagnesium iodide catalyzes the nearly quantitative hydrogenolysis of substrate **2.1** to form hydrocarbon **2.2** (Scheme 2.1a). The catalytic system also effectively performs hydrogenolysis on substrate **2.3** to form hydrocarbon **2.4** (Scheme 2.1b). If rendered a general method this reaction would be an interesting and useful reaction in its own right. We therefore studied the application of this protocol as a general method for the hydrogenolysis of benzylic ethers.

Scheme 2.1. Hydrogenolysis of Benzhydryl Substrates



One of the most prolific hydrogenolysis protocols is the Barton-McCombie deoxygenation.[2] This reaction has found ample application in late stage synthesis.[3] For example, as shown in Scheme 2.2, Barton-McCombie deoxygenation is the last step in the total synthesis

---

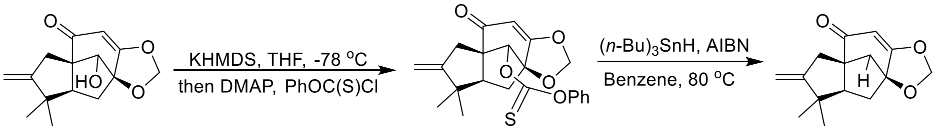
[1] See Table 1.3, entry 4.

[2] (a) Barton, D. H. R.; McCombie, S. W. *J. Chem. Soc., Perkin Trans. 1* **1975**, 1574. (b) Hartwig, W. *Tetrahedron* **1983**, *39*, 2609. (c)Hong, F.-T.; Paquette, L. A. *Chemtracts* **1998**, *11*, 67.

[3] For representative examples, see (a) Singh, V.; Prathap, S.; Porinchu, M. *J. Org. Chem.*, **1998**, *63*, 4011. (b) Luzzio, F. A.; Fitch, R. W.; *J. Org. Chem.* **1999**, *64*, 5485. (c) Schlessinger, R. H.; Gillman, K. W. *Tetrahedron Lett.* **1996**, *37*, 1331.

of tricycloillicinone (**2.7**).[4] Barton-McCombie deoxygenations are carried out through a two-step process: first an alcohol is converted to a thiocarbonyl derivative, and second, the intermediate is reduced by a tin hydride reagent in a radical hydrogenolysis reaction. The reaction lends itself to late stage deoxygenation due to its superb functional group tolerance.[5] The reaction proceeds with primary and tertiary substrates, but works particularly well with secondary alcohols. Unfortunately, the tin reagents are toxic making tin-free alternatives attractive.[6]

Scheme 2.2. Use of Barton-McCombie Deoxygenation in Synthesis of Tricycloillicinone



2.5

2.6
90% yield

tricycloillicinone (2.7)
42% yield

Among alternatives to the Barton-McCombie deoxygenation, few nickel-catalyzed reactions have been reported. Recent nickel-catalyzed advances that have been reported primarily allow for the deoxygenation of phenols and the hydrogenolysis of aryl ethers (Scheme 2.3a).[7] Rhodium-based catalysts have been more successful in the hydrogenolysis of alkyl C–O bonds.[8] For instance rhodium based Wilkinson's catalyst will promote hydrogenolysis of a benzylic ester (Scheme 2.3b).[9] Unfortunately, with a commodity price of greater than $1000 per

---

[4] Pettus, T. R. R.; Inoue, M.; Chen, X.-T.; Danishefsky, S. J. *J. Am. Chem. Soc.* **2000**, *122*, 6160.

[5] (a) Zard, S. Z. *Angew. Chem. Int. Ed.* **1997**, *36*, 672. (b) Chatgilialoglu, C.; Ferreri, C.; *Res. Chem. Intermed.* **1993**, *19*, 755. (b) Barton, D. H. R.; Jang, D. O.; Jaszberenyi, J. C. *J. Org. Chem.* **1993**, *58*, 6838. (c) Barton, D. H. R.; Jang, D. O.; Jaszberenyi, J. C.; Joseph, C. *Synlett* **1991**, 435. (d) Barton, D. H. R.; Motherwell, W. B.; Stange, A. *Synthesis* **1981**, 743.

[6] Kimbrough, R. D. *Environ. Health. Perspect.* **1976**, *14*, 51.

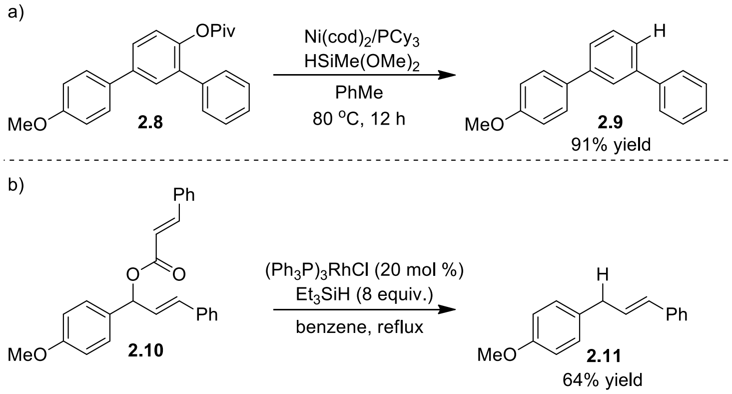
[7] (a) Sasaki, K; Sakai, M; Sakakibara, Y.; Takagi, K. *Chem. Lett.* **1991**, *20*, 2017. (b) Sasaki, K. Kubo, T.; Sakai, M.; Kuroda, Y. *Chem. Lett.*, **1997**, *26*, 617. (c) Sergeev, A. G.; Hartwig, J. F. *Science* **2011**, *332*, 439. (d) Sergeev, A. G.; Webb, J. D.; Hartwig, J. F. *J. Am. Chem. Soc.* **2012**, *134*, 20226. (e) Tobisu, M.; Yamakawa, K.; Shimasaki, T.; Chatani, N. *Chem. Commun.* **2011**, *47*, 2946. (f) Lipshutz, B. H.; Frieman, B. A.; Butler, T.; Kogan, V. *Angew. Chem. Int. Ed.* **2006**, *45*, 800.

[8] (a) Maruyama, Y.; Sezaki, T.; Tekawa, M.; Sakamoto, T.; Shimizu, I.; Yamamoto, A. *J. Organomet. Chem.* **1994**, *473*, 257. (b) Kang, S.-K.; Kim, D.-Y.; Rho, H.-S.; Yoon, S.-H.; Ho, P.-S. *Synth. Commun.* **1996**, *26*, 1485.

[9] Liu, H.-J.; Zhu, B.-Y. *Synth. Commun.* **1990**, *20*, 557.

ounce, rhodium is expensive.[10] In contrast, nickel carries a commodity price of less than $10 per pound.[11] A method of hydrogenolysis catalyzed by an earth-abundant nickel catalyst would be an attractive alternative to rhodium based methods.

Scheme 2.3. Transition Metal-Catalyzed Hydrogenolysis



We envisioned that a catalytic system comprised of Ni(acac)$_2$ and dppo may be a general catalyst for the hydrogenolysis of benzylic ethers. Analogous to the cross-coupling chemistry discussed in Chapter 1, we envisioned that this reaction would go through a two-electron mechanism. If so, in addition to providing an alternative to the Barton-McCombie reaction, the dppo ligated nickel catalyst may allow for the stereospecific installation of deuterium for labeling studies. In this chapter, I present my efforts to develop a general hydrogenolysis protocol as well as to identify the stereochemical outcome of hydrogenolysis reactions. Although we found that the Ni(acac)$_2$, dppo catalytic system is not a general method, these studies provided insight into the mechanism of both hydrogenolysis and elimination pathways, and insight into the mechanism of polar cross-coupling reactions in general.

---

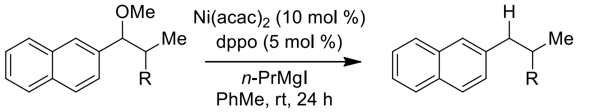
[10] Kitco. http://www.kitco.com/charts/historicalrhodium.html (accessed 21 April, 2015).

[11] InvestmentMine. Nickel Prices and Nickel Price Charts. http://www.infomine.com/investment/metal-prices/nickel/ (accessed 21 April, 2015).

2.2 Optimization of Hydrogenolysis Protocol

We set out to investigate if the hydrogenolysis reaction we discovered with benzhydryl ether **2.1** might represent a general method for the hydrogenolysis of alkyl ethers. In particular, we wanted to extend the methodology to benzylic ethers similar to the substrates discussed in Chapter 1. Unfortunately, subjecting benzylic substrates **2.12** and **2.14** to conditions that are identical to those that worked with benzhydryl substrates resulted in less than 50% yield of hydrogenolysis product (Scheme 2.4).

Scheme 2.4. Initial Hydrogenolysis Conditions Applied Simple Benzylic Substrates



R = H **2.12** R = H **2.13** 36% yield
R = Me **2.14** R = Me **2.15** 42% yiled

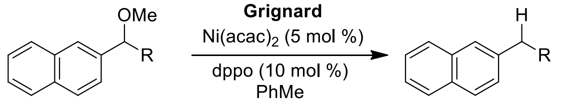
Because we had proposed that the Grignard reagent was the hydride source,[12] we hypothesized that certain Grignard reagents may allow for more facile formation of a nickel hydride complex. We therefore studied the effect of various Grignard reagents on hydrogenolysis. Isopropylmagnesium bromide and 2-phenylethylmagnesium bromide were chosen because they were expected to undergo faster β-hydride elimination than *n*-alkyl Grignard reagents. Isopropylmagnesium bromide has six rather than two β-hydrogens, and β-hydride elimination from 2-phenylethylmagnesium bromide would give a stable styrene. As shown in Table 2.1, none of the organomagnesium bromide reagents were effective at performing hydrogenolysis on simple benzylic ethers (entries 1–7) although several were effective at performing hydrogenolysis on benzhydryl ethers (entries 8–11).[13]

---

[12] See Chapter 1, Scheme 1.7

[13] With Lucas Erickson

Table 2.1. Efficacy of Grignard Reagents in Hydrogenolysis Reaction



2.14 R = *i*-Pr
2.16 R = Ph

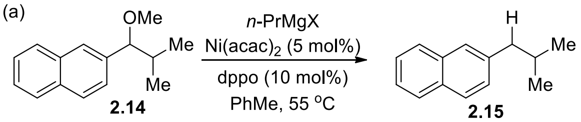
2.15 R = *i*-Pr
2.17 R = Ph

Entry	R	Grignard	Temperature	SM (%)[a]	Hydrogenolysis (%)[a]
1	*i*-Pr	*i*-PrMgBr	r.t.	95	0
2	*i*-Pr	Ph(CH$_2$)$_2$Mg Br	r.t.	95	0
4	*i*-Pr	Ph(CH$_2$)$_3$MgBr	60°C	89	0
5	*i*-Pr	cyclopentylMgBr	60°C	73	9
6	*i*-Pr	*n*-OctylMgBr	r.t.	76	0
7	*i*-Pr	EtMgBr	r.t.	96	0
8	Ph	Ph(CH2)2MgBr	r.t.	97	0
9	Ph	Ph(CH$_2$)$_3$MgBr	r.t.	7	80
10	Ph	cyclopentylMgBr	r.t.	0	75
11	Ph	*n*-OctylMgBr	r.t.	0	79

[a]Determined by ^{1}H NMR against an internal standard, phenyltrimethylsilane (PhTMS)

We wanted to see if the identity of the halogen on the Grignard reagent had any effect on reactivity. Interestingly, *i*-PrMgI was far better at promoting hydrogenolysis from ether **2.14** than *i*-PrMgBr (Scheme 2.5). Therefore, *i*-PrMgI was used in subsequent studies. Unfortunately, with substrate **2.14**, high yield was only accomplished at elevated temperatures.[14]

Scheme 2.5. Comparison of Bromine and Iodine Counter Ions in the Hydrogenolysis Reaction



2.14

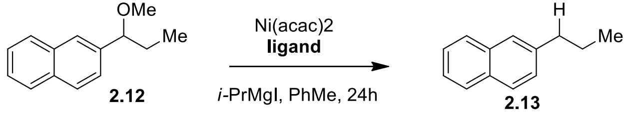
2.15
X = Br, <2%
X = I, 60%

In an attempt to achieve high yields at room temperature, we performed a ligand screen. Bidentate ligands do not efficiently promote hydrogenolysis (Table 2.2, entries 1–6). Bisphosphine ligands with long carbon-chain linkers better promote the hydrogenolysis reaction (entries 7–9). Due to the high degree of freedom of these long linkers, these ligands likely acts as monodentate ligands. Monophosphine ligands were therefore studied and shown to give higher yields of hydrogenolysis product (entries 10–12). Among monodentate ligands, PPh_3 gives the highest yield (33%, entry 12). PPh_3 was therefore used in subsequent studies.

---

[14] Reactions studying halogen effect run by Lucas Erickson

Table 2.2. Ligand Screen

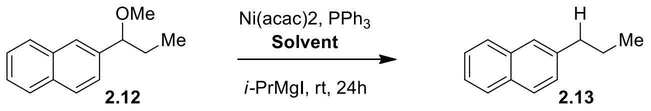


Entry	lignad	SM (%)^{a}	Hydrogenolysis (%)^{a}	Elimination (%)^{a}
1	DPEPhos	0	10	16
2	racBINAP	54	7	0
3	Xantphos	8	11	13
4	dppf	8	9	6
5	dppe	78	4	7
6	dppp	50	5	32
7	dpppent	0	25	56
8	dpphex	0	25	64
9	dppo	0	24	60
10	Ph_2PPr	5	25	52
11	Ph_2Pi-Pr	0	29	59
12	**PPh_3**	**0**	**33**	**44**

^{a}Determined by ^{1}H NMR against an internal standard, PhTMS.

We were interested in seeing what solvent effects might be at play in this reaction. A study of solvent effects is shown in Table 2.3. The reaction does not proceed in the presence of THF and DCM (entries 1–3). Hydrocarbon solvents, toluene and *n*-hexane, both provide hydrogenolysis product in 33% yield (entries 4–5). The use of diethyl ether improved yield to 42% (entry 6). The best result, 51% yield, was achieved with triethylamine (TEA) (entry 7). A small ligand screen run in TEA showed that regardless of solvent, hydrogenolysis is most efficient when PPh_3 is used as ligand (entries 7–10).

Table 2.3. Solvent Effects

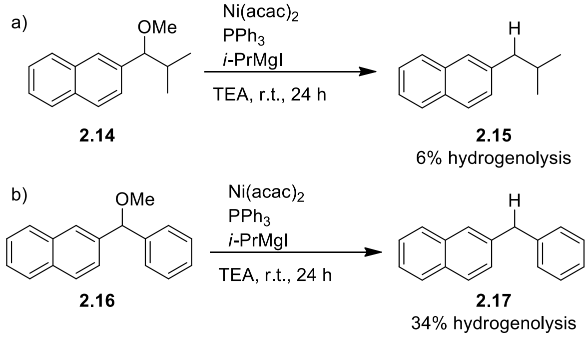


Entry	Solvent	ligand	Hydrogenolysis (%)^{a}	Elimination (%)^{a}	SM (%)^{a}
1	THF	PPh_3	3	1	86
2	1:1 THF: Tol	PPh_3	3	1	91
3	DCM	PPh_3	0	0	88
4	Tol	PPh_3	33	44	0
5	n-hexane	PPh_3	33	40	0
6	Et_2O	PPh_3	42	43	4
7	**TEA**	**PPh_3**	**51**	**27**	**18**
8	TEA	Ph_2PPr	29	59	0
9	TEA	dpphexane	25	64	0
10	TEA	dppo	24	60	0

^{a}Determined by ^{1}H NMR against an internal standard, PhTMS.

We wanted to see if we were converging on a general hydrogenolysis method that could be applied to compounds other than ether **2.12**. To test for generality, we ran the optimized reaction against benzylic substrate **2.14** and benzhydryl substrate **2.16** (Scheme 2.6). Unfortunately, the optimized conditions for hydrogenolysis of **2.12** proved to be suboptimal for the other two ethers. Because we did not appear to be converging on a general method, we shifted our focus to mechanistic studies.

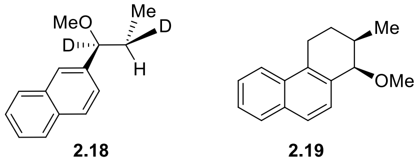
Scheme 2.6. Hydrogenolysis with Other Substrates



2.3 Mechanistic Studies

From the inception of this project we sought to develop a stereospecific method for deuterium incorporation. To test for stereospecificity, we needed to design molecules that would allow for the differentiation of deuterated diastereomers. Ethers **2.18** and **2.19** were selected because diastereomers of the products of hydrogenolysis were expected to give discernable differences in *J*-coupling as defined by the Karplus equation.[15] Additionally, experiments run with these compounds provided evidence for a mechanism of oxidative addition with inversion at the benzylic center.

Figure 2.1. Mechanistic Probes

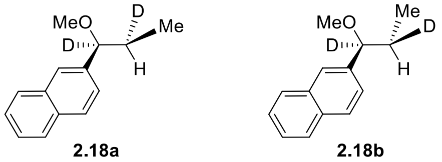


---

[15] Karplus, M. *J. Chem. Phys.* **1959**, *30*, 11

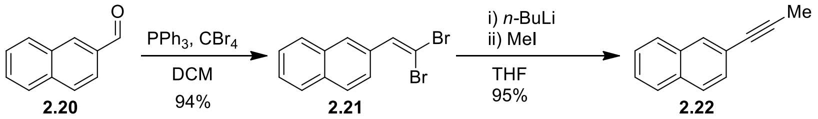
2.3.1 Stereochemical and Mechanistic Studies with Compound 2.18

Figure 2.2. Diastereomers of Compound **2.18**



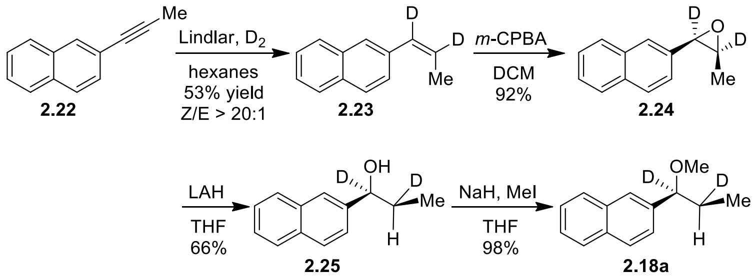
Studies on diastereomeric compounds **2.18a** and **2.18b** (Figure 2.2) provided insight into both the mechanism of oxidative addition and the stereochemical course of hydrogenolysis. These compounds were prepared as shown in Schemes 2.7–2.9. Synthesis of both **2.18a** and **2.18b** went through common alkynyl intermediate **2.22** which was prepared by a Corey-Fuchs protocol (Scheme 2.7).[16] Trapping the acetylide with MeI allowed for the facile synthesis of the methylated alkyne.

Scheme 2.7. Preparation of Alkynyl Napthalene



Ether **2.18a** was prepared from acetylene **2.22** as shown in Scheme 2.8. *Syn*-deuteration was achieved by treatment with Lindlar catalyst under a D_2 atmosphere. *m*-CPBA epoxidation to form epoxide **2.24** followed by ring-opening with LAH afforded alcohol **2.25**.[17] Finally, *o*-methylation of **2.25** in the presence of NaH and MeI yielded the desired mechanistic probe **2.18a**.

Scheme 2.8. Synthesis of **2.18a**



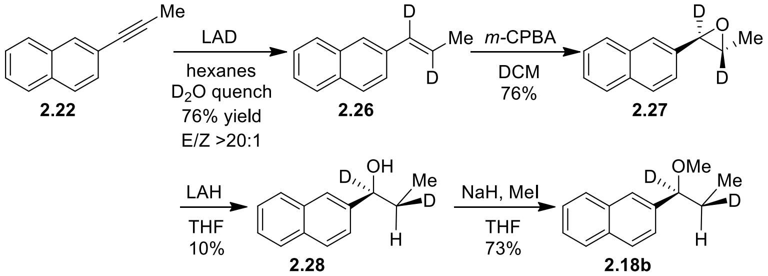
---

[16] Corey, E. J.; Fuchs, P. L. *Tetrahedron Lett.* **1972**, *13*, 3769.

[17] Zhou, Q.; Srinivas, H. D.; Dasgupta, S.; Watson, M. P. *J. Am. Chem. Soc.* **2013**, *135*, 3307.

Compound **2.18b** was prepared by a similar procedure, differing primarily in the deuteration of the alkyne (Scheme 2.9). Treatment of **2.22** with lithium aluminum deuteride afforded the desired trans olefin in 76% yield with a greater than 20:1 E/Z ratio.[18] To achieve high deuterium incorporation at the benzylic position, it was important that this step was quenched with D_2O from a freshly opened ampule. The remainder of the synthesis of **2.18b** is analogous to the procedures used for **2.18a**. Oddly, epoxide opening with LAH is far less effective on *trans*-epoxide **2.27** than with c*is*-epoxide **2.24**. Ring opening of epoxide **2.27** suffers from attack at the benzylic position resulting in formation of the homobenzylic alcohol as the major product.

Scheme 2.9. Synthesis of **2.18b**

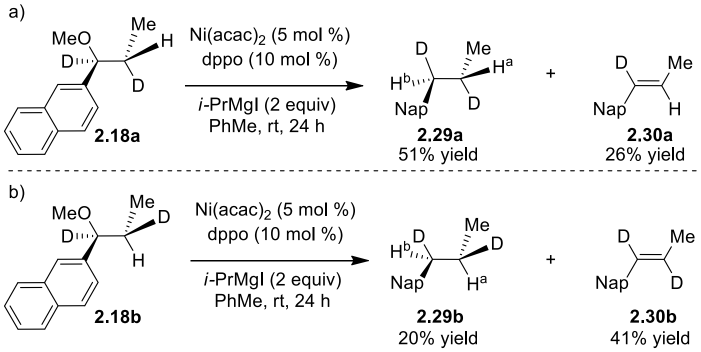


With deuterated compounds **2.18a** and **2.18b** in hand, we were ready to perform studies on the stereochemical outcome of the hydrogenolysis reaction. The outcome of experiments run with **2.18a** and **2.18b** in the presence of $Ni(acac)_2$ and dppo are shown in Scheme 2.10. A discussion of the mechanistic implications of these results follows. In the presence of $Ni(acac)_2$ and dppo, diastereomers of **2.18** undergo both hydrogenolysis and elimination processes. The mechanistic implications of these processes will each be discussed in turn.

---

[18] Magoon, E. F.; Slaugh, L. H. *Tetrahedron*, **1967**, *23*, 4509.

Scheme 2.10. Results with Ethers **2.18a** and **2.18b**

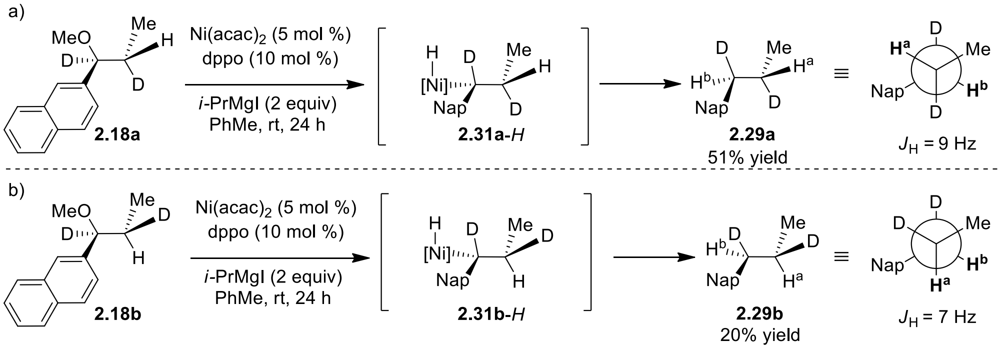


Mechanistic insights gained from hydrogenolysis will be discussed first. An explanation of the results of hydrogenolysis using both diastereomers of ether **2.18** is provided in Scheme 2.11. Oxidative addition with inversion into diastereomer **2.18a** followed by reductive elimination from **2.31a**-*H* was expected to result in deuterated hydrocarbon **2.29a** (Scheme 2.11a). In its most stable s-trans conformation, **2.29a** bears hydrogen atoms, H^a and H^b, which are anti to each other and should therefore exhibit a large $J_{\mathrm{H^a}\text{–}\mathrm{H^b}}$ coupling (see Newman projection). If diastereomer **2.18b** were subject to the same reaction, product **2.29b** would exhibit hydrogens that, in the s-trans conformation, exhibit H^a and H^b in a gauche orientation (Scheme 2.11b). Diastereomer **2.29b** would therefore be expected to exhibit a smaller $J_{\mathrm{H^a}\text{–}\mathrm{H^b}}$ coupling value than **2.29a**. A *J*-coupling of 8 Hz or greater is indicative of protons on adjacent carbons that are predominantly in a trans orientation relative to one another, and a *J*-coupling value of 7 Hz or less is typical of a gauche orientation.[19] As expected **2.29a** gave a *J*-coupling value greater than 8 Hz and **2.29b** gave a J-coupling value of 7 Hz. These results show that the hydrogenolysis process delivers a hydride stereospecifically with inversion at the benzylic center.

---

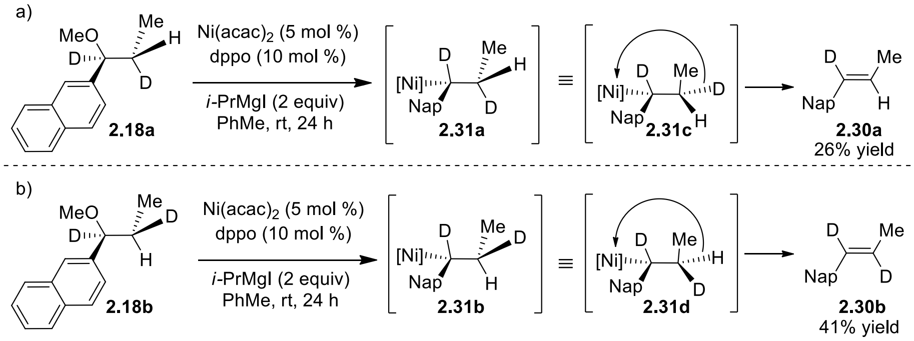
[19] (a) Silverstein, R. M.; Webster, F. X.; Kiemle, D. J. *Spectrometric Identification of Organic Compounds,* 7th ed; John Wiley and Sons: Hoboken, NJ, 2005; 171–172. (b) Bock, P. L.; Boschetto, D. J.; Rasmussen, J. R.; Demers, J. P.; Whitesides, G. M. *J. Am. Chem. Soc.* **1974**, *96*, 2814. (c) Whitesides, G. M.; Sevenair, J. P.; Goetz, R. W. *J. Am. Chem. Soc.* 1967, 89, 1135. For similar experiments, see: (d) Ridgway, B. H.; Woerpel, K. A. *J. Org. Chem.* **1998**, *63,* 458. (e) Matos, K.; Soderquist, J. A. *J. Org. Chem.* **1998**, *63*, 461. (f) Taylor, B. L. H.; Jarvo, E. R. *J. Org. Chem.* **2011**, *76*, 7573.

Scheme 2.11. Hydrogenolysis with Inversion



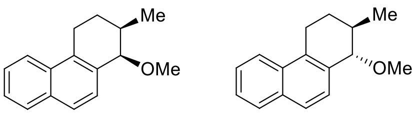
Under the conditions used in this experiment, the product of β-hydride elimination was also a major product (vide supra, Scheme 2.10). Interestingly, both diastereomers underwent elimination to give very different yields. This difference in yield can be explained by a kinetic isotope effect that is consistent with a mechanism of oxidative addition with inversion followed by β-hydride elimination. When diastereomer **2.18a** undergoes oxidative addition with inversion, intermediate **2.31a** forms (Scheme 2.12a). To avoid a steric interaction between the methyl and naphthyl groups, reductive elimination will proceed from rotamer **2.31c**. Because β-deuteride elimination proceeds from this rotamer, a slow rate is expected and observed. In contrast, when diastereomer **2.18b** is subject to eliminating conditions, oxidative addition leads to intermediate **2.31b** (Scheme 2.12b). Sterics are minimized in rotamer **2.31d** from which β-hydride elimination can occur. The kinetic isotope effect is seen as β-deuteride elimination from **2.31c** proceeds slower than β-hydride elimination from **2.31d**. These results provide evidence that elimination and hydrogenolysis mechanisms begin with a polar S$_N$2-like mechanism of oxidative addition which proceeds with inversion at the reactive center.

Scheme 2.12. Mechanism of Elimination



2.3.2 Stereochemical and Mechanistic Studies with Compound 2.19

Figure 2.3. Diastereomers of **2.19**



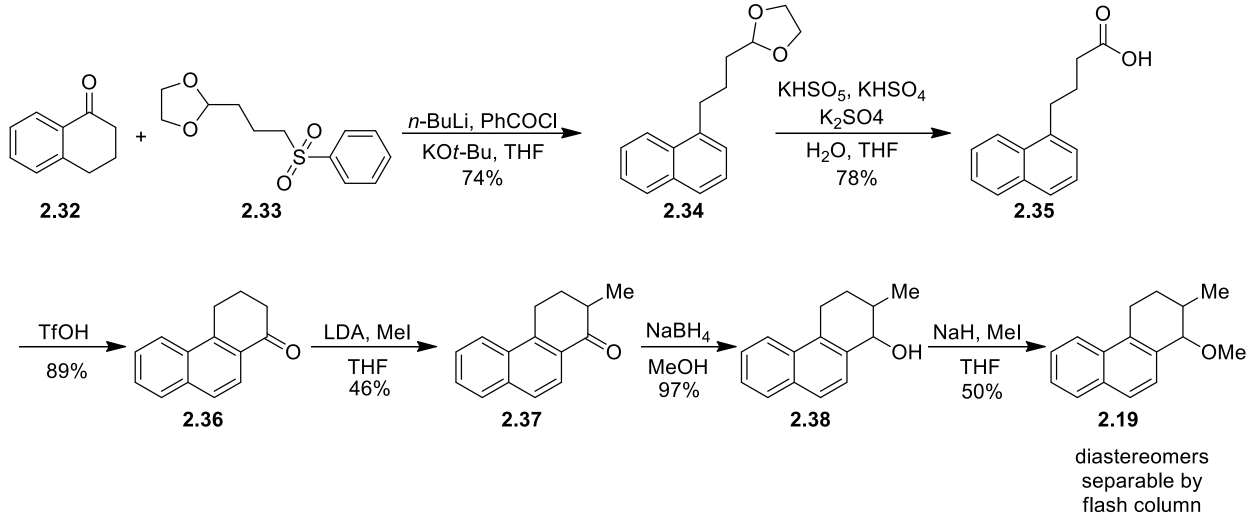
2.19a **2.19b**

Diastereomers of compound **2.19** (Figure 2.3) were also designed to probe the stereochemical outcome of hydrogenolysis and the mechanism of β-hydride elimination. Both diastereomers of compound **2.19** were obtained via the synthesis outlined in Scheme 2.13. Addition of deprotonated sulfone **2.33** into ketone **2.32** resulted in dioxolane **2.34**. Oxidizing conditions revealed carboxylic acid **2.35**. A Friedel-Crafts type cyclization gave tetralone **2.36**.[20] Reaction of the enolate of **2.36** with methyl iodide resulted in methylated ketone **2.37** which could be reduced to alcohol **2.38**. Finally, *o*-methylation of alcohol **2.38** completed the synthesis of the desired mechanistic probe **2.19** as a mixture of diastereomers which were readily separated by silica gel flash column chromatography.

---

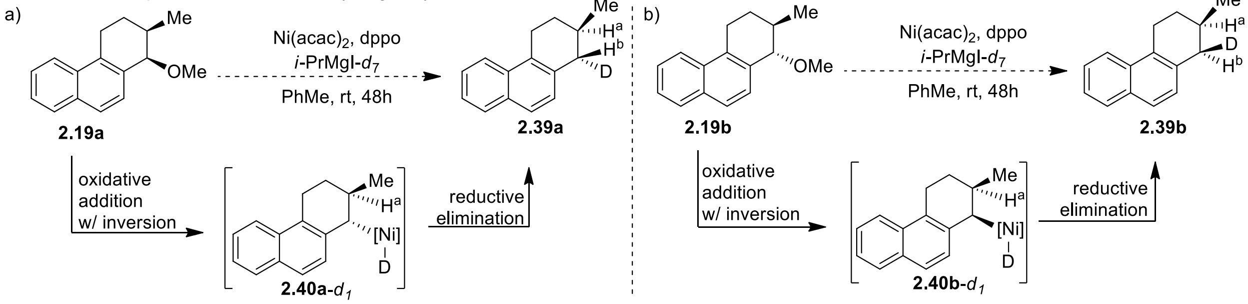
[20] Orita, A.; Yaruva, J.; *Angew. Chem. Int. Ed.* **1999**, *38*, 2267.

Scheme 2.13. Synthesis of Compound **2.19**

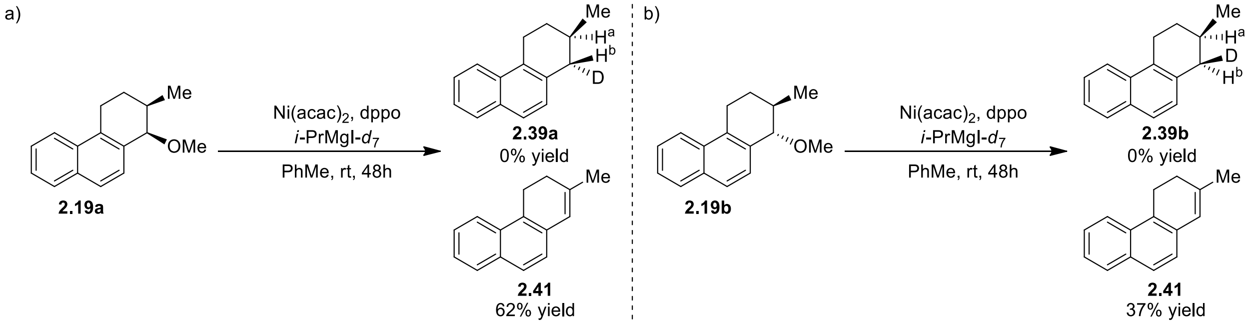


Compound **2.19** was chosen to study the hydrogenolysis stereochemical course because hydrogenolysis of the diastereomers of **2.19** were expected to yield diastereomeric products **2.39a** or **2.39b**, which should exhibit distinct differences in the magnitude $J_{\mathrm{H^a–H^b}}$-couplings (Scheme 2.14). Starting from **2.19a**, oxidative addition with inversion would give intermediate **2.40a**-d_1, which could undergo reductive elimination to give hydrogenolysis product **2.39a** (Scheme 2.14a). In its most stable conformation, compound **2.39a** would present hydrogen $\mathrm{H^a}$ anti to hydrogen $\mathrm{H^b}$, and would be expected to give a large value for the $J_{\mathrm{H^a–H^b}}$ coupling. Hydrogenolysis of **2.19b** should give product **2.39b** in which $\mathrm{H^a}$ is gauche to $\mathrm{H^b}$ (Scheme 2.14b). This confirmation would be expected to exhibit a small value for the $J_{\mathrm{H^a–H^b}}$ coupling. Unexpectedly, no hydrogenolysis product was observed with either of these substrates. Rather, the major observed product was that of β-hydride elimination (Scheme 2.15).

Scheme 2.14. Expected Mechanism of Hydrogenolysis

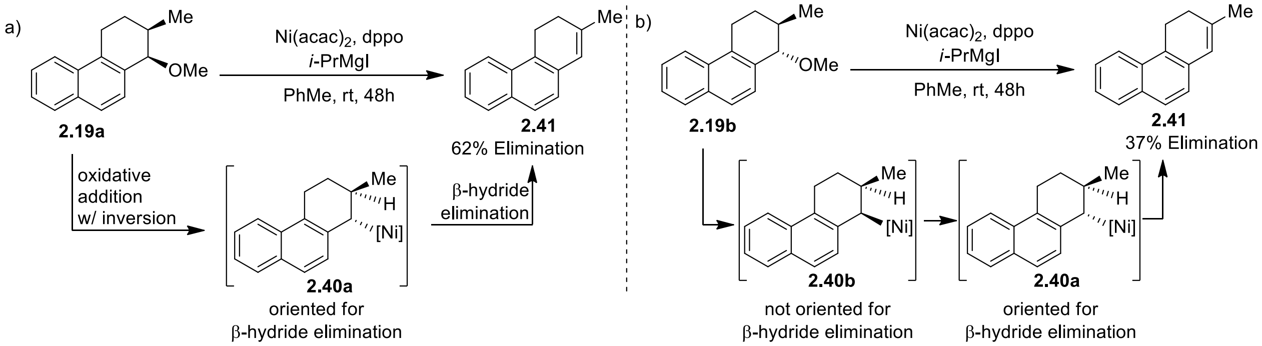


Scheme 2.15. Outcomes of Reactions with **2.19a** and **2.19b**



Although the stereochemical course of hydrogenolysis could not be determined in the above studies, experiments using the diastereomers of **2.19** provided valuable insight into the mechanisms of oxidative addition and subsequent elimination processes. The conformational rigidity of **2.19** would be expected to define β-hydride elimination reactivity. Oxidative addition with inversion into diastereomer **2.19a** would result in a nickel complex (**2.40a**) in which nickel is in a syn orientation to the only adjacent hydride (Scheme 2.16a). In this orientation, complex **2.40a** should readily undergo β-hydride elimination to form elimination product **2.41**. Indeed, elimination is observed at 62% yield. In contrast, if diastereomer **2.19b** is used, oxidative addition with inversion would result in complex **2.40b** in which nickel is anti to the only adjacent hydride (Scheme 2.16b). β-hydride elimination should not be possible from complex **2.40b**. When we ran experiments with **2.19b** we were surprised to observe 37% yield of the elimination product. This result can be explained, however, if after oxidative addition with inversion to form complex **2.40b**, a second nickel complex attacks **2.40b**, again with inversion, resulting in complex **2.40a**. Complex **2.40a** can then undergo β-hydride elimination. In support of this bimetallic mechanism, we have shown that there is an inverse correlation between nickel catalyst concentration and cross-coupled product ee.[21] These results are consistent with an overall oxidative addition with inversion, followed by β-hydride elimination. Taken together, the results of all mechanistic studies discussed in this report provide evidence that cross-coupling, hydrogenolysis, and elimination mechanisms all include a fundamental mechanistic step of S_N2-like oxidative addition with inversion at the benzylic carbon.

Scheme 2.16. Mechanisms of β-Hydride Elimination



2.4 Conclusion

In conclusion, we sought to identify a general method for the hydrogenolysis of benzylic and benzhydryl ethers. With dppo as ligand, the reaction works well with benzhydryl ethers, but provides marginal conversion with simple benzylic ethers. Attempts to optimize the hydrogenolysis reaction with ether **2.12** showed that in the presence of PPh_3 and with triethylamine as solvent, compound **2.12** undergoes hydrogenolysis at 51% yield. Unfortunately, these optimized conditions are not applicable to a broad range of substrates.

Studies were conducted to better understand the polar mechanism of these reactions. Deuterium labeling studies showed that the nickel-catalyzed hydrogenolysis reaction delivers a hydride in a stereospecific manner with inversion at the benzylic center. Additionally, results of

---

[21] Yonova, I. M.; Johnson, A. G.; Osborne, C. A.; Moore, C. E.; Morrissette, N. S.; Jarvo, E. R. *Angew. Chem. Int. Ed.* **2014**, *53*, 2422.

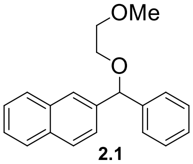
elimination reactions are consistent with a mechanism of oxidative addition with inversion followed by β-hydride elimination.

2.5 Experimental Section

2.5.1 General Procedures

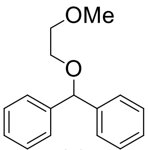
All reactions were carried out under an atmosphere of N_2 using glassware that was either oven- or flame-dried prior to use. Methanol (MeOH) was purchased commercially and used without further purification. *N*,*N*-Dimethylformamide (DMF), tetrahydrofuran (THF), and toluene (PhMe) were degassed with argon and then passed through two 4 x 36 inch columns of anhydrous neutral A-2 alumina (8 x 14 mesh; LaRoche Chemicals; activated under a flow of argon at 350 ºC for 12 h) to remove H_2O. All other solvents utilized were purchased "anhydrous" commercially, or purified as described (vide infra). ^{1}H NMR spectra were recorded on Bruker GN-500 (500 MHz ^{1}H, 125.7 MHz ^{13}C), CRYO-500 (500 MHz ^{1}H, 125.7 MHz ^{13}C) or DRX-400 (400 MHz ^{1}H, 100 MHz ^{13}C) spectrometers. Proton chemical shifts are reported in ppm (δ) relative to internal tetramethylsilane (TMS, δ 0.00). Data are reported as follows: chemical shift (multiplicity [singlet (s), broad singlet (br s), doublet (d), triplet (t), quartet (q), quintet (quin), sextet, septet (sep), multiplet (m), doublet of doublets (dd), doublet of triplets (dt), apparent doublet (ap d), apparent triplet (ap t), apparent septet (ap sep), apparent quintet (ap q), apparent doublet of doublets (ap dd), apparent quintet of doublets, (ap quin)], coupling constants [Hz], integration). Carbon chemical shifts are reported in ppm (δ) relative to TMS with the respective solvent resonance as the internal standard ($CDCl_3$, δ 77.16 ppm). Analytical thin-layer chromatography (TLC) was performed using Silica Gel 60 F_{254} pre-coated plates (0.25 mm thickness). Visualization was accomplished by irradiation with a UV lamp. Flash chromatography was performed using Silica Gel 60Å (170-400 mesh) from Fisher Scientific. Melting points (m.p.) were obtained using a Mel-Temp melting point apparatus and are uncorrected. Infrared spectra were obtained on a Nicolet™ iS™5 FT-IR spectrometer system and are reported in terms of frequency of absorption (cm^{-1}). High resolution mass spectrometry was performed by the University of California, Irvine Mass Spectrometry Center. Optical rotations were measured with a Rudolph Research Analytical Autopol IV Automatic Polarimeter or a Jasco P-1010 digital polarimeter. SFC determinations of enantiopurity were performed on a Berger Analytical instrument using a Daicel™ Chiralpak® column (AD-H; 100 bar, 50 °C, 254 nm).

2.5.2 Preparation of Hydrogenolysis Substrates



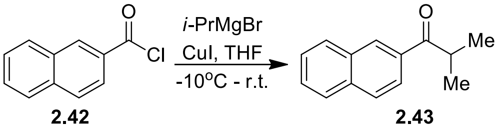
2.1

2-((2-Methoxyethoxy)(phenyl)methyl)naphthalene (2.1) was prepared as described by Jarvo.[22]



2.3

((2-Methoxyethoxy)methylene)dibenzene (2.3) was prepared as described by Jarvo.[23]

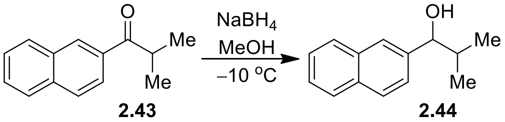


2-Methyl-1-(naphthalen-2-yl)propan-1-one (2.43): In a glove box, a flame-dried round bottom flask was charged with CuI (0.141 g, 0.711 mmol, 0.551 equiv.), then removed and 2-naphthoyl chloride **2.42** (2.46 g, 12.9 mmol, 1.00 equiv.) was added as a solution in THF (25 mL). The reaction mixture was cooled to –10 °C and isopropylmagnesium bromide (1.52 M in THF, 8.50

---

[22] Taylor, B. L. H.; Harris, M. R.; Jarvo, E. R. *Angew. Chem. Int. Ed.* **2012**, *51*, 7790.
[23] Greene, M. A.; Yonova, I. M.; Williams, F. J.; Jarvo, E. R. *Org. Lett.* **2012**, *14*, 4293.

mL, 12.9 mmol, 1.00 equiv.) was added dropwise. The mixture was warmed to room temperature and stirred for 1 h. The crude mixture was concentrated in vacuo then quenched with HCl (20 mL, 1M) and extracted with Et_2O (3 x 20 mL). The crude mixture was then washed with brine (20 mL) and dried over $MgSO_4$. Purification by flash column chromatography (5% EtOAc in hexanes) yielded **2.43** as a yellow oil (2.23 g, 11.2 mmol, 87% yield). Spectral data are consistent with literature values.[24]

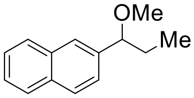


2-Methyl-1-(naphthalen-2-yl)propan-1-ol (2.44): A round bottom flask was charged with sodium borohydride (0.303 g, 8.0 mmol) and cooled to –10 ºC. **2.43** (0.793 g, 4.0 mmol) and methanol (80 mL) were added to the reaction flask, and the reaction mixture was stirred for 1 h. The reaction was quenched with $NaHCO_3$ (20 mL), extracted with EtOAc (3 x 30 mL), washed with brine (40 mL), and dried over Na_2SO_4. The crude mixture was then concentrated in vacuo and purified by flash column chromatography (20% Et_2O in hexanes) to afford the title compound as a yellow oil (0.375 g, 1.87 mmol, 47% yield). Analytical data are consistent with literature values:[25] **TLC R_f** = 0.3 (20% Et_2O in hexanes); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.82 (m, 3H), 7.74 (s, 1H), 7.46 (m, 3H), 4.52 (d, *J* = 6.8 Hz, 1H), 2.06 (sx, *J* = 6.6 Hz, 1H), 1.96 (s, 1H), 1.03 (d, *J* = 6.5 Hz, 3H), 0.83 (d, *J* = 6.7 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 141.4, 133.5, 133.3, 128.3, 128.2, 128.0, 126.4, 126.1, 125.7, 125.0, 80.5, 35.5, 19.5, 18.6.

---

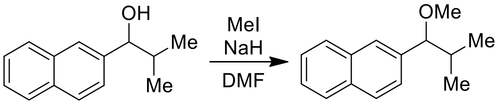
[24] Lee, S. W.; Lee, K.; Seomoon, D.; Kim, S.; Kim, H.; Kim, H.; Shim, E.; Lee, M.; Lee, S.; Kim, M.; Lee, P. H. *J. Org. Chem.* **2004**, *69*, 4852.

[25] Kulasegaram, S.; Kulawiec, R. J. *J. Org. Chem.* **1997**, *62*, 6547.



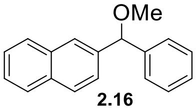
2.12

2-(1-Methoxypropyl)naphthalene (2.12) was prepared as described by Jarvo.[26]



2.44 **2.14**

2-(1-Methoxy-2-methylpropyl)naphthalene (2.14): A round bottom flask was charged with NaH (348 mg, 14.5 mmol, 1.8 equiv.). Alcohol **2.44** (1.61 g, 8.05 mmol, 1.00 equiv.) was then added as a solution in THF (25 mL), and the reaction mixture was allowed to stir for 1 h. MeI (0.85 mL, 14 mmol, 1.7 equiv.) was added and the reaction mixture was allowed to stir overnight. The reaction was quenched with saturated aqueous NH_4Cl, extracted with EtOAc (3 x 20 mL), washed with brine, and dried over $MgSO_4$. The crude mixture was then concentrated in vacuo. Purification of the crude mixture by silica gel flash column chromatography (2% Et_2O in pentanes) yielded **2.14** as a clear, colorless oil (1.51 g, 7.06 mmol, 88% yield): **TLC R$_f$** = 0.6 (2% Et_2O in pentanes); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.82 (d, *J* = 6.4 Hz, 3H), 7.67 (s, 1H), 7.48–7.40 (m, 2H), 7.41 (d, *J* = 8.1 Hz, 1H), 3.89 (d, *J* = 7.3 Hz, 1H), 3.22 (s, 3H), 2.02 (sextet, *J* = 6.8 Hz, 1H), 1.05 (d, *J* = 6.8 Hz, 3H), 0.75 (d, *J* = 6.8 Hz, 3H); **^{13}C NMR** δ (125 MHz, $CDCl_3$) δ 138.8, 133.21, 133.18, 128.04 127.96, 127.8, 126.9, 126.1, 125.8, 125.3, 90.1, 57.2,. 34.8, 19.23, 19.20; **IR** (neat) 3055, 2957, 2927, 2919, 1468, 1383, 1135, 1089, 815, 773 cm^{-1}; **HRMS** (TOF MS CI+) *m / z* calcd for $C_{15}H_{18}ONH_4$ $[M + NH_4]^+$ 232.1701, found 232.1704.



2.16

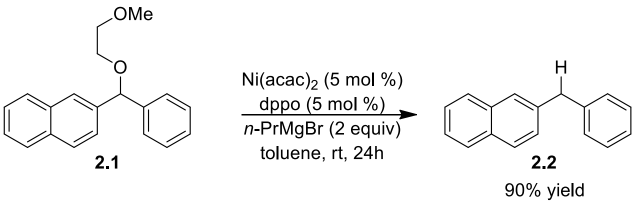
2-(Methoxy(phenyl)methyl)naphthalene (2.16) was prepared as described by Jarvo.[22]

---

[26] Taylor, B. L. H.; Swift, E. C.; Waetzig, J. D.; Jarvo, E. R. *J. Am. Chem. Soc.* **2011**, *133*, 389.

2.5.3 Hydrogenolysis Reactions

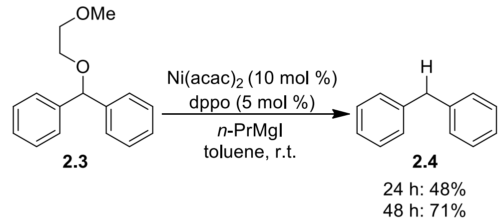
Hydrogenolysis Representative Procedure A



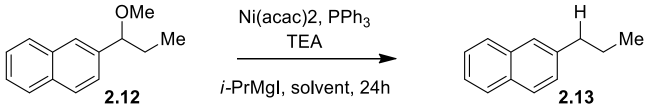
2-Benzylnaphthalene (2.2): In a glove box, a flame-dried 7 mL vial was charged with 1,8-bis(diphenylphosphino)octane (dppo) (4.8 mg, 0.010 mmol, 0.10 equiv.). Ni (acac)$_2$ (1.3 mg, 0.0050 mmol, 0.050 equiv.) was added as a stock solution in toluene (1 mL, 5.06 x 10^{-3} M). The vial was capped and removed from the box but kept under a nitrogen atmosphere. Ether **2.1** (28 mg, 0.10 mmol, 1.0 equiv.) was also added from a stock solution in toluene (0.5 mL, 0.191 M). *n*-Propylmagnesium bromide (0.090 mL, 0.20 mmol, 2.2 M, 2.2 equiv.) was added, and the reaction mixture was allowed to stir for 24 h. The reaction was quenched with MeOH and run through a silica plug (100% Et$_2$O as eluent). Analysis by ^{1}H NMR with an internal standard (1,2-dimethoxybenzne) revealed that the reaction proceeded to give 19 mg of hydrogenolysis product (0.087 mmol, 87% yield). Purification by silica gel flash column chromatography (20% DCM in hexanes) yielded a pure sample. Analytical data is consistent with literature values:[27] **TLC R$_f$** = 0.7 (20% DCM in hexanes); **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.77 (m, 3H), 7.64 (s, 1H), 7.44 (quint, *J* = 7.5 Hz, 2H), 7.30 (quint, *J* = 7.3 Hz, 3H), 7.23 (m, 3H), 4.15 (s, 3H); **^{13}C NMR** (125 MHz, CDCl$_3$) δ 141.3, 138.9, 133.9, 132.4, 129.4, 128.8, 128.4, 127.97, 127.95, 127.8, 127.4, 126.5, 126.3, 125.7, 42.4.

---

[27] Cho, C.-H.; Sun, M.; Seo, Y.-S.; Kim, C.-B.; Park, K. *J. Org. Chem.* **2005**, *70*, 1482.



Diphenylmethane (2.4) was prepared according to Representative Procedure A described above using the following amounts of reagents: **2.3** (23 μL, 0.010mmol, 1 equiv.), Ni(acac)$_2$ (1.3 mg, 0.0049 mmol, 0.050 equiv.), dppo (4.7 mg, 0.010 mmol, 0.10 equiv.), *n*-PrMgI (0.079 mL, 0.20 mmol, 2.0 equiv.), and toluene (1.5 ml). Analysis by ^{1}H NMR with an internal standard (PhTMS) revealed 71% conversion to the product of hydrogenolysis. Analytical data are consistent with literature values.[28]

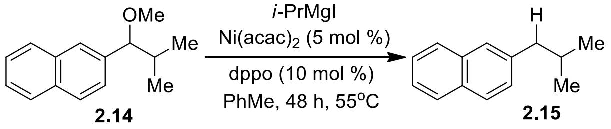


2-Propylnaphthalene (2.13) was prepared according to Representative Procedure A using the following amounts of reagents: ether **2.12** (40 mg, 0.20 mmol, 1.0 equiv.), Ni(acac)$_2$ (2.6 mg, 0.010 mmol, 0.050 equiv.), PPh$_3$ (5.3 mg, 0.020 mmol, 0.10 equiv.), *i*-PrMgI (0.26 mL, 0.40 mmol, 1.5 M, 2.0 equiv.), and TEA (1.5 mL). Analysis by ^{1}H NMR with an internal standard (PhTMS) revealed 51% conversion to the product of hydrogenolysis. Analytical data was consistent with literature values.[29]

---

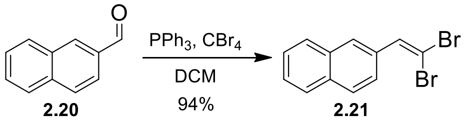
[28] Peña-López, M.; Ayán-Varela, M.; Sarandeses, L. A.; Sestelo, J. P. *Chem. Eur. J.* **2010**, *16*, 9905.

[29] Guan, B.-T.; Xiang, S.-K.; Wang, B.-Q.; Sun, Z.-P.; Wang, Y.; Zhao, K.-Q.; Shi, Z.-J. *J. Am. Chem. Soc.* **2008**, *130*, 3268.



2-Isobutylnaphthalene (2.15) was prepared according to Representative Procedure A outlined above with the follow reagents: **2.14** (43 mg, 0.20 mmol, 1.00 equiv.), Ni(acac)$_2$ (2.6 mg, 0.010 mmol, 0.050 equiv.), dppo (9.7 mg, 0.020 mmol, 0.10 equiv.), *i*-PrMgI (1.43 M in ether, 0.28 mL, 0.40 mmol, 2.0 equiv.) and toluene (1.5 mL). The crude mixture was purified by silica gel flash column chromatography (20% DCM in hexanes) to give **2.15** as a clear colorless oil (27 mg, 0.15 mmol, 71% yield). Spectral data are consistent with literature values:[30] **TLC R$_f$** = 0.9 (20% DCM in hexanes); **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.82 (d, *J* = 7.8 Hz, 1H), 7.79 (t, *J* = 8.7 Hz, 2H), 7.59 (s, 1H), 7.49–7.38 (m, 2H), 7.32 (dd, *J* = 8.4, 1.5 Hz, 1H), 2.65 (d, *J* = 7.3 Hz, 2H), 2.00 (septet, *J* = 6.7 Hz, 1H), 0.97 (d, *J* = 6.6 Hz, 6H); **^{13}C NMR** (125 MHz, CDCl$_3$) δ 139.6, 133.9, 132.3, 128.3, 127.93, 127.90, 127.8, 127.5, 126.1, 125.3, 46.0, 30.5, 22.8.

2.5.4 Preparation of Mechanistic Probes



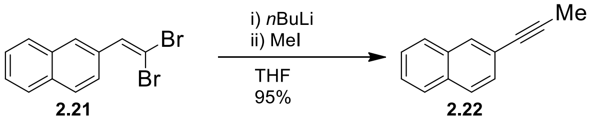
2-(2,2-Dibromovinyl)naphthalene (2.21) was prepared according to a modified procedure as described by Rao.[31] A flame dried round bottom flask was charged with triphenylphosphine (13.4 g, 51.2 mmol, 4.00 equiv.) and put under a nitrogen atmosphere. Dichloromethane (DCM, 46 mL) was added, and the reaction mixture was cooled to 0 °C. Tetrabromomethane (8.5g, 26 mmol, 2.0 equiv.) was then added as a solution in DCM (12 mL). The reaction mixture was allowed to stir for 3 min, and 2-naphthaldehyde (**2.20**) (2.00 g, 12.8 mmol, 1.00 equiv.) was

---

[30] Limmert, M. E.; Roy, A. H.; Hartwig, J. F. *J. Org. Chem.* **2005**, *70,* 9364

[31] Rao, M. L. N.; Jadhav, D. N.; Dasgupta, P. *Org. Lett.* **2010**, *12,* 2048.

added as a solution in DCM (11 mL). The reaction mixture was stirred for 10 additional min then run through a silica plug. Purification by silica gel flash column chromatography (5–50% EtOAc in hexanes) yielded the title compound as a white solid (3.47g, 11.1 mmol, 94% yield). Spectral data are consistent with literature values:[32] **m.p.** = 103–105 °C; **TLC R$_f$** = 0.8 (10% EtOAc in hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.99 (s, 1H), 7.84–7.79 (m, 3H), 7.64–7.62 (m, 2H), 7.52–7.46 (m, 2H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 137.1, 133.12, 133.11, 132.9, 128.4, 128.3, 128.1, 127.8, 126.9, 126.6, 125.8, 90.0; **IR** (neat) 3011, 1595, 1506, 1272, 834 cm^{-1}; **HRMS** (TOF MS CI+) *m / z* calcd for $C_{12}H_8Br_2$ $[M]^+$ 309.8993, found 309.8995.

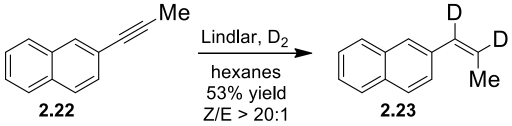


2-(Prop-1-yn-1-yl)naphthalene (2.22) was prepared by Corey-Fuchs protocol.[33] A flame dried round bottom flask was charged with dibromide **2.21** (2.90 g, 9.15 mmol, 1.00 equiv.) and put under a nitrogen atmosphere. THF was added, and the reaction vessel was cooled to –78 °C. *n*-BuLi (12.3 mL, 18.3 mmol, 1.49 M in Et_2O, 2.00 equiv.) was added, and the reaction mixture was stirred for 1 hour at –78 °C. The reaction mixture was heated to room temperature, and the reaction was allowed to stir for an additional 1 h. Methyl iodide (1.25 mL, 20.1 mmol, 2.20 equiv.) was added dropwise followed by an excess of MeOH, also added dropwise. An excess of H_2O was added, and the aqueous layer was separated from the organic layer. The aqueous layer was extracted with Et_2O (3 x 30 mL). The combined organics layers were dried with $MgSO_4$, filtered, and purified by silica gel flash column chromatography (100% hexanes) to yield the title compound as a reluctant solid (1.39 g, 8.57 mmol, 94% yield): **m.p.** = 28–29 °C; **TLC R$_f$** = 0.4 (100% hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.89 (s, 1H), 7.80–7.73 (m, 3H); 7.46–7.43 (m,

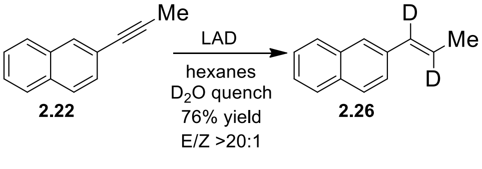
---

[32] Rao, M. L. N.; Jadhav, D. N.; Dasgupta, P. *Org. Lett.* **2010**, *12*, 2048.
[33] Corey, E. J.; Fuchs, P. L. *Tetrahedron Lett.* **1972**, *13,* 3769.

3H), 2.10 (s, 3H); **^{13}C NMR** (125 MHz, CDCl$_3$) δ 133.2, 132.6, 131.1, 128.8, 128.0, 127.8, 127.7, 126.5, 126.4, 121.5, 86.4, 80.2, 4.6; **IR** (neat) 3056, 2914, 2235, 1596, 1500 cm^{-1}; **HRMS** (TOF MS CI+) *m / z* calcd for $C_{13}H_{10}$ [M]$^+$ 184.1126, found 184.1122.



***d*₂-(*Z*)-2-(Prop-1-en-1-yl)naphthalene (2.23)**: In a glove box, a flame-dried 7 mL vial was loaded with acetylene **2.22** (50 mg, 0.30 mmol, 1.0 equiv.) and Lindlar catalyst (5% pd, 3.0 mg, 0.0010 mmol Pd, 0.0050 equiv.). The vial was capped and connected to a Schlenk line. The reaction vessel was evacuated and back filled with D_2 gas (x 5). The reaction mixture was stirred under a deuterium atmosphere for 7 h at which point the reaction vessel was again evacuated and back filled with nitrogen (x 6). The reaction mixture was filtered through Celite to yield the title compound as a clear colorless oil (163 mg, 0.959 mmol, 53% yield): **TLC R$_f$** = 0.6 (100% hexanes); **^{1}H NMR** (400 MHz, CDCl$_3$) δ 7.81–7.78 (m, 3H), 7.73 (s, 1H), 7.47–7.41 (m, 3H), 1.97 (s, 3H); **^{13}C NMR** (125 MHz, CDCl$_3$) δ 135.2, 133.5, 132.2, 129.6 (t, *J* = 23.6 Hz, 1C), 128.0, 127.71, 127.69, 127.59, 127.4, 126.9 (t, *J* = 23.6 Hz, 1C), 126.1, 125.8, 14.8; **IR** (neat) 3053, 2938, 2243, 1503, 1372 cm^{-1}; **HRMS** (TOF MS CI+) *m / z* calcd for $C_{13}H_{10}D_2$ [M]$^+$ 170.1064, found 170.1069.

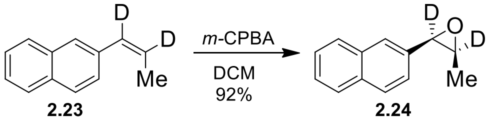


(*E*)-2-(1,2-Dideuteroprop-1-enyl)naphthalene (2.26) was prepared according to a modified procedure reported by Magoon.[34] In a glove box, a flame-dried round bottom flask was charged with lithium aluminum deuteride (141 mg, 3.35 mmol, 1.70 equiv.). The reaction vessel was

---

[34] Magoon, E. F.; Slaugh, L. H. *Tetrahedron* **1967**, *23*, 4509.

fitted with a water condenser, capped, removed from the glove box, and kept under a nitrogen atmosphere. Alkyne **2.22** (327 mg, 1.97 mmol, 1.00 equiv.) was added as a solution in dry THF (6 mL). The reaction mixture was heated to a gentle reflux and allowed to stir for 24 h. The reaction was quenched with D_2O (1.40 mL, 19.4 mmol, 9.85 equiv.) from a sealed ampule. The reaction mixture was run down a silica plug with 100% Et_2O as eluent. The crude material was purified by silica gel flash column chromatography (100% hexanes) to yield the title compound as a white solid (255 mg, 1.50 mmol, 76% yield, 97% D incorporation, > 20:1 *E*/*Z*): **m.p.** 43–44 ^{o}C; **TLC R$_f$** = 0.6 (100% hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.78–7.74 (m, 3H), 7.65 (s, 1H), 7.56 (d, *J* = 8.4 Hz, 1H), 7.41 (ap quin, *J* = 8.1 Hz, 2H), 1.93 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 135.5, 133.9, 132.7, 130.9 (t, *J* = 23.1 Hz, 1C), 128.2, 128.0, 127.8, 126.2, 125.9 (t, *J* = 22.7 Hz, 1C), 125.5, 125.3, 123.6, 18.6; **IR** (neat) 3051, 2906, 2846, 2226, 1508, 1445 cm^{-1}; **HRMS** (TOF MS CI+) *m / z* calcd for $C_{13}H_{10}D_2NH_4$ $[M + NH_4]^+$ 188.1408 found 188.1409.

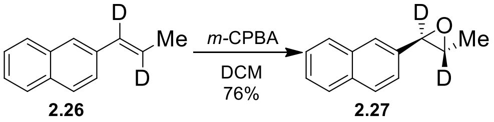


(*cis*)-2-Methyl-1,2-dideutero-3-(naphthalen-2-yl)oxirane (2.24) was prepared according to a modified procedure as reported by Watson.[35] A round bottom flask was charged with a stir bar and *m*-CPBA (898 mg, 4.01 mmol, 1.20 equiv.) then put under a nitrogen atmosphere. DCM (25 mL) was added followed by olefin **2.23** (562 mg, 3.34 mmol, 1.00 equiv.) as a solution in DCM (13 mL). The reaction mixture was stirred for 35 min then quenched with saturated Na_2SO_4. The crude mixture was diluted with brine and the organic layer was separated from the aqueous layer. The organic layer was dried with Na_2SO_4, filtered, and purified by flash column chromatography (5% Et_2O in hexanes) to give the product as a clear colorless oil (568 mg, 3.08

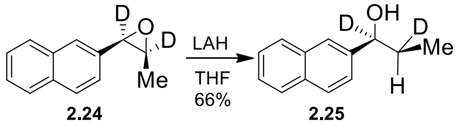
---

[35] Zhou, Q.; Srinivas, H. D.; Dasgupta, S.; Watson, M. P. *J. Am. Chem. Soc.* **2013**, *135,* 3307.

mmol, 92% yield): **TLC R$_f$** = 0.2 (2% EtOAc in hexanes); **^{1}H NMR** (400 MHz, CDCl$_3$) δ 7.85–7.82 (m, 3H), 7.76 (s, 1H), 7.51–7.41 (m, 3H), 1.11 (s, 3H); **^{13}C NMR** (125 MHz, CDCl$_3$) δ 133.11, 133.10, 133.0, 128.0, 127.9, 127.8, 126.4, 126.0, 125.6, 124.6, 57.4 (t, *J* = 26.4 Hz, 1C), 55.1 (t, *J* = 26.4 Hz, 1C), 12.5; **IR** (neat) 3055, 2963, 2927, 2207, 1602, 1389 cm^{-1}; **HRMS** (TOF MS CI+) *m / z* calcd for $C_{13}H_{10}D_2ONH_4$ $[M + NH_4]^+$ 204.1357, found 204.1366.



(*trans*)-2-Methyl-1,2-dideutero-3-(naphthalen-2-yl)oxirane (2.27) was prepared according to the same epoxidation procedure as compound **2.24** (vide supra) using the following amounts of reagents: *m*-CPBA (363 mg, 1.62 mmol, 1.40 equiv.), **2.26** (197 mg, 1.16 mmol, 1.00 equiv. in 5 mL DCM), and 10 additional mL of DCM. Purification by flash column chromatography (5% Et$_2$O in hexanes) yielded the title compound as a white solid (165 mg, 0.886 mmol, 76% yield): **m.p.** 51–53 °C; **TLC R$_f$** = 0.2 (2% EtOAc in hexanes); **^{1}H NMR** (400 MHz, CDCl$_3$) δ 7.81 (ap d, *J* = 8.15 Hz, 3H), 7.76 (s, 1H), 7.49–7.44 (m, 2H), 7.32 (dd, *J* = 7.0, 1.5 Hz, 1H), 1.49 (s. 3H); **^{13}C NMR** (125 MHz, CDCl$_3$) δ 135.3, 133.4, 133.3, 128.4, 127.9, 126.4, 126.1, 125.1, 123.1, 59.4 (t, *J* = 26.8 Hz, 1C), 58.8 (t, *J* = 26.4 Hz, 1C), 17.9; **IR** (neat) 3055, 2974, 2926, 2226, 1600, 1505 cm^{-1}; **HRMS** (TOF MS CI+) *m / z* calcd for $C_{13}H_{10}D_2ONH_4$ $[M + NH_4]^+$ 204.1357, found 204.1345.

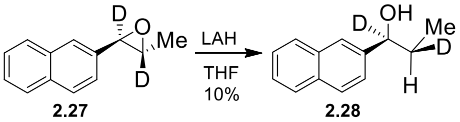


***threo*-1-(Naphthalen-2-yl)-1,2-dideuteropropan-1-ol (2.25)** was prepared according to a modified procedure reported by Watson.[36] A flame-dried round bottom flask was charged with

---

[36] Zhou, Qi; Srinivas, H. D.; Dasgupta, S.; Watson, M. P. *J. Am. Chem. Soc.* **2013**, *135*, 3307.

$LiAlH_4$ (524 mg, 13.7 mmol, 4.50 equiv.) and put under a nitrogen atmosphere. Dry THF (20 mL) was added and the vessel was cooled to 0 °C. Epoxide **2.24** (568 mg, 3.05 mmol, 1.00 equiv) was then added dropwise as a solution in THF (5 mL). The reaction mixture was allowed to return to room temperature and stirred for an additional 2 h. The reaction was quenched with saturated aqueous NH_4Cl and washed with brine. The organic layer was dried with $MgSO_4$ and purified by silica gel flash column chromatography (17% Et_2O in hexanes) to yield the title compound as a white solid (376 mg, 2.00 mmol, 66% yield): **m.p.** 31–32 °C; **TLC R$_f$** = 0.6 (20% EtOAc in hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.84–7.82 (m, 3H), 7.78 (s, 1H), 7.45–7.44 (m, 3H), 1.92–1.85 (m, 2H), 0.93 (d, *J* = 7.3 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 142.0, 133.3, 133.1, 128.3, 128.0, 127.8, 126.2, 125.9, 124.8, 124.2, 75.7 (t, *J* = 21.7, 1C), 31.3 (t, *J* = 19.4 Hz, 1C), 10.12; **IR** (neat) 3254, 3052, 2967, 1600, 1452 cm^{-1}; **HRMS** (TOF MS CI+) *m / z* calcd for $C_{13}H_{12}D_2O$ $[M]^+$ 188.1170, found 188.1174.

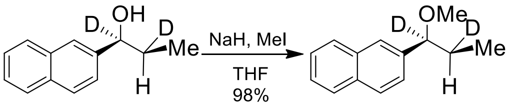


***erythro*-1-(Naphthalen-2-yl)-1,2-dideuteropropan-1-ol (2.28)** was prepared according to a modified procedure reported by Watson.[37] In a glove box, a flame-dried round bottom flask was charged with lithium aluminum hydride (117 mg, 3.09 mmol, 4.50 equiv.) and dry THF (1 mL). The reaction vessel was capped, removed from the glove box, and kept under a nitrogen atmosphere. Epoxide **2.27** (128 mg, 0.687 mmol, 1.00 equiv) was added as a solution in THF (4 mL). The reaction mixture was allowed to stir for 4 h at room temperature and then quenched with H_2O and run through a silica plug. Purification by silica gel flash column chromatography (10% EtOAc in hexanes) yielded the title compound as an oil (13 mg, 0.069 mmol, 10% yield):

---

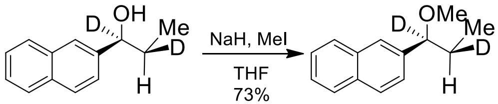
[37] Zhou, Qi; Srinivas, H. D.; Dasgupta, S.; Watson, M. P. *J. Am. Chem. Soc.* **2013**, *135,* 3307.

TLC R$_f$ = 0.6 (20% EtOAc in Hexanes); **^{1}H NMR** (600 MHz, CDCl$_3$) δ 7.84–7.82 (m, 3H), 7.77 (s, 1H), 7.49–7.44 (m, 3H), 1.90–1.80 (m, 2H), 0.93 (d, *J* = 7.5 Hz, 3H); **^{13}C NMR** (125 MHz, CDCl$_3$) δ 142.0, 133.4, 133.1, 128.4, 128.1, 127.8, 126.2, 125.9, 124.9, 124.3, 75.8 (t, *J* = 21.7 Hz, 1C), 31.4 (t, *J* = 19.4 Hz, 1C), 10.1; **IR** (neat) 3352, 3054, 2963, 2937, 1127, 1018 cm^{-1}; **HRMS** (TOF MS CI+) *m / z* calcd for $C_{13}H_{12}D_2O$ [M]$^+$ 188.1170, found 188.1306.



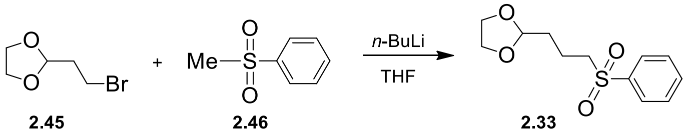
2.25 **2.18a**

***threo*-2-(1-Methoxy-1,2-dideuteropropyl)naphthalene (2.18a)**: In a glove box, a flame-dried round bottom flask was charged with NaH (82 mg, 3.4 mmol, 1.8 equiv.). The reaction vessel was capped, removed from the glove box, and put under a nitrogen atmosphere. THF (5 mL) was added, followed by alcohol **2.25** (360 mg, 1.91 mmol, 1.00 equiv.) as a solution in THF (4 mL). The reaction mixture was stirred for 1 h, at which point MeI (0.202 mL, 3.25 mmol, 1.78 equiv.) was added. The reaction mixture was stirred overnight then the reaction was quenched with an excess of saturated aqueous NH_4Cl. The aqueous phase was extracted with EtOAc (4 x 10 mL), and the combined organics were dried with $MgSO_4$, filtered, and concentrated in vacuo. The crude material was purified by silica gel flash column chromatography to yield the title compound as a clear, colorless oil (380 mg, 1.88 mmol, 98% yield): **TLC R$_f$** = 0.7 (10% EtOAc in hexanes); **^{1}H NMR** (400 MHz, CDCl$_3$) δ 7.85–7.83 (m, 3H), 7.71 (ap d, *J* = 1.4 Hz, 1H), 7.49–7.43 (m, 3H), 3.25 (s, 3H), 1.89 (q, *J* = 7.4 Hz, 1H), 0.89 (d, *J* = 7.3 Hz, 3H); **^{13}C NMR** (125 MHz, CDCl$_3$) δ 139.7, 133.3, 133.2, 128.4, 128.0, 127.9, 126.18, 126.16, 125.8, 124.7, 85.3 (t, *J* = 21.7 Hz, 1C), 56.8, 30.4 (t, *J* = 19.4 Hz, 1C), 10.3; **IR** (neat) 3055, 2971, 2929, 2816, 1460 cm^{-1}; **HRMS** (TOF MS CI+) *m / z* calcd for $C_{14}H_{14}D_2O$ [M]$^+$ 202.1327, found 202.1325.



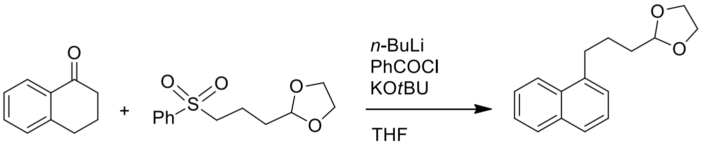
2.28 2.18b

***erythro*-2-(1-Methoxy-1,2-dideuteropropyl)naphthalene (2.18b)** was prepared by the same procedure as **2.18a** with the following amounts of reagents: NaH (7.2 mg, 0.30 mmol, 4.0 equiv.), alcohol **2.28** (14 mg, 0.07 mmol, 1.0 equiv.), MeI (0.050 mL, 0.82 mmol, 11 equiv.). Purification by silica gel flash column chromatography (10% EtOAc in hexanes) afforded the title compound as an oil (11 mg, 0.050 mmol, 73% yield): **TLC R$_f$** = 0.7 (10% EtOAc in hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.85–7.82 (m, 3H), 7.71 (s, 1H), 7.49–7.43 (m, 3H), 3.25 (s, 3H), 1.73 (q, *J* = 7.4 Hz, 1H), 0.88 (d, *J* = 7.4 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 139.7, 133.3, 133.2, 128.4, 128.0, 127.9, 126.2 (2C), 125.8, 124.7, 85.3 (t, *J* = 21.7 Hz, 1C), 56.8, 30.4 (t, *J* = 19.4 Hz, 1C), 10.2; **IR** (neat) 3055, 2969, 2929, 2817, 1454, 1086 cm^{-1}; **HRMS** (TOF MS CI+) *m / z* calcd for $C_{14}H_{14}D_2O$ [M]$^+$ 202.1327, found 202.1323.



2.45 2.46 2.33

2-(3-(Phenylsulfonyl)propyl)-1,3-dioxolane (2.33) was prepared according to the procedure reported by LeBel.[38]



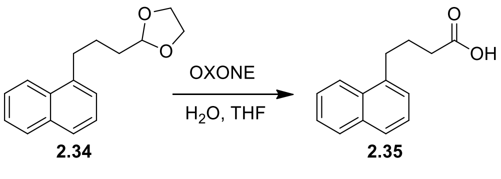
2.32 2.33 2.34

2-(3-(Naphthalen-1-yl)propyl)-1,3-dioxolane (2.34) was prepared according to a modified procedure reported by Otera.[39] A flame-dried round bottom flask was charged with sulfone **2.33** (1.95g, 7.61 mmol, 1.40 equiv.) and put under a nitrogen atmosphere. THF (31 mL) was added,

---

[38] LeBel, N. A.; Balasubramanian, N. *J. Am. Chem. Soc.* **1989**, *111*, 3363.
[39] Orita, A.; Yaruva, J.; Otera, J. *Angew. Chem. Int. Ed.* **1999**, *38*, 2267.

and the vessel was cooled to –78 °C. *n*-BuLi (4.2 mL, 6.5 mmol, 1.6 M in hexanes, 1.2 equiv.) was added and the reaction mixture was stirred for 30 min. α-Tetralone (**2.32**) (795 mg, 5.44 mmol, 1.00 equiv.) and benzoyl chloride (0.95 mL, 8.2 mmol, 1.5 equiv.) were then added. The reaction mixture was allowed to warm to room temperature and stirred for 3 h. Potassium *tert*-butoxide (3.05 g, 27.2 mmol, 5.00 equiv.) was added and the reaction mixture was stirred at reflux for another 3 h. The reaction was quenched with saturated aqueous NH_4Cl. The organic layer was separated and the aqueous layer was extracted with Et_2O (3 x 20 mL). The combined organic layers were dried with Na_2SO_4, filtered through a fritted funnel, and concentrated in vacuo. The crude mixture was purified by flash chromatography (5% Et_2O in Hexanes) to yield **2.34** as a yellow oil (608 mg, 2.51 mmol, 46% yield): **TLC R$_f$** = 0.1 (3% EtOAc in Hexanes); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.99 (d, *J* = 8.2 Hz, 1H), 7.77 (d, *J* = 7.9 Hz, 1H), 7.63 (d, *J* = 8.0 Hz, 1H), 7.42 (t, *J* = 7.25 Hz, 1H), 7.38 (t, *J* = 7.3 Hz, 1H), 7.31 (t, *J* = 7.5 Hz, 1H), 7.25 (d, *J* = 6.8 Hz, 1H), 4.81 (t, *J* = 4.4 Hz, 1H), 3.84–3.77 (m, 2H), 3.71–3.64 (m, 2H), 3.05 (t, *J* = 7.6 Hz, 2H), 1.85 (quin, *J* = 7.6 Hz, 2H), 1.77–1.73 (m, 2H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 138.4, 134.0, 132.0, 128.9, 126.7, 126.1, 125.9, 125.6, 125.5, 124.0, 104.6, 65.0 (2C), 33.9, 32.9, 25.1; **IR** (neat) 2924, 1733, 1394, 1133, 1029 cm^{-1}; **HRMS** (TOF MS CI+) *m / z* calcd for $C_{16}H_{18}O_2$ $[M]^+$ 242.1307, found 242.1302.

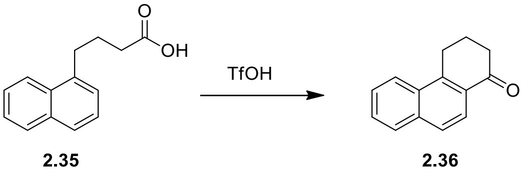


4-(Naphthalen-1-yl)butanoic acid (2.35) was prepared according to a modified procedure reported by Otera.[40] A flame-dried round bottom flask was charged with dioxolane **2.34** (54 mg, 0.22 mmol, 1.0 equiv.) and THF (0.67 mL). In a second flame-dried round bottom flask was

---

[40] Orita, A.; Yaruva, J.; Otera, J. *Angew. Chem. Int. Ed.* **1999**, *38*, 2267.

prepared a solution of potassium peroxymonosulfate (OXONE®) (205 mg, 0.67 mmol, 3 equiv.) in H_2O (0.7 mL). The OXONE® solution was added to the solution of dioxolane **2.34**, and the resulting mixture was stirred for 12 h. The reaction was quenched by a mixture of H_2O and EtOAc. The organic layer was separated, and the aqueous layer was washed three times with EtOAc. The combined organic layers were dried with Na_2SO_4, filtered, and concentrated in vacuo. The crude material was purified by flash column chromatography (30% EtOAc in hexanes) to yield the title compound as a white solid (705 mg, 3.29 mmol; 78% yield): **m.p.** 109–110 °C; **TLC R_f** = 0.2 (30% EtOAc in hexanes); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 11.33 (br s, 1H), 8.05 (d, *J* = 8.3 Hz, 1H), 7.85 (d, *J* = 8.0 Hz, 1H), 7.72 (d, *J* = 8.1 Hz, 1H), 7.52 (t, *J* = 7.2 Hz, 1H), 7.47 (t, *J* = 6.8 Hz, 1H), 7.40 (t, *J* = 7.6 Hz, 1H), 7.32 (d, *J* = 6.7 Hz, 1H), 3.14 (t, *J* = 7.6 Hz, 2H), 2.47 (t, *J* = 7.3 Hz, 2H), 2.11 (quin, *J* = 7.4 Hz, 2H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 179.6, 137.4, 134.0, 131.9, 128.9, 127.1, 126.4, 126.1, 125.7, 125.6, 123.8, 33.7, 32.3, 25.6; **IR** (neat) 2951, 1705, 1428, 1408 cm^{-1}; **HRMS** (TOF MS ES-) *m / z* calcd for $C_{14}H_{13}O_2$ $[M–H]^-$ 213.0916, found 213.0909.

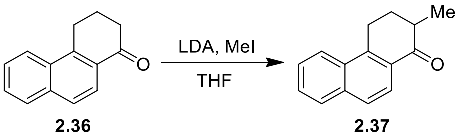


3,4-Dihydrophenanthren-1(2H)-one (2.36) was prepared according to a modified procedure reported by Otera and coworkers.[41] A flamed dried round bottom flask was charged with carboxylic acid **2.35** (705mg, 3.29 mmol, 1.00 equiv) and cooled to 0 °C. Trifluoromethanesulfonic acid (3.29 mL, 37.2 mmol, 11.3 equiv.) was then added. The reaction mixture was slowly allowed to warm to room temperature over 2 h while stirring. Ice-cold H_2O

---

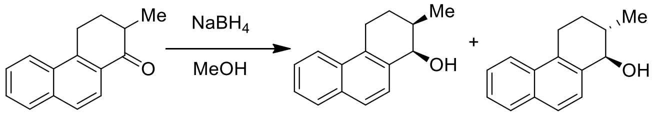
[41] Orita, A.; Yaruva, J.; Otera, J. *Angew. Chem. Int. Ed.* **1999**, *38*, 2267.

was added and the aqueous phase was extracted with ethyl acetate (3 x 10 mL). The combined organics were washed with brine, dried over Na_2SO_4, and purified by silica gel flash column chromatography (10% EtOAc in hexanes) to yield the title compound as a white solid (577 mg, 2.94 mmol, 89% yield): **m.p.** 89–90 ^oC; **TLC R_f** = 0.4 (10% EtOAc in hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.16–8.11 (m, 2H), 7.88–7.86 (m, 1H), 7.76 (d, *J* = 8.7 Hz, 1H), 7.64–7.57 (m, 2H), 3.40 (t, *J* = 6.2 Hz, 2H), 2.75 (ap t, *J* = 6.7 Hz, 2H), 2.31 (quin, *J* = 6.4 Hz, 2H); **^{13}C NMR** (125 Hz, $CDCl_3$) δ 198.7, 143.1, 135.9, 131.6, 130.2, 128.9, 128.4, 127.1, 126.8, 125.0, 122.9, 38.5, 25.8, 22.9; **I.R.** (neat) 2947, 1668, 1618, 1460, 1105 cm^{-1}; **HRMS** (TOF MS ES+) *m / z* calcd for $C_{14}H_{12}ONa$ $[M + Na]^+$ 219.0786, found 219.0781.



3,4-Dihydrophenanthren-1(2H)-one (2.37): A flame-dried round bottom flask was charged with distilled diisopropyl amine (0.33 mL, 2.4 mmol, 1.0 equiv.) and dry THF (4.7 mL). The reaction was cooled to –78 ^oC, and a solution of *n*-BuLi (1.6 mL, 2.4 mmol, 1.5 M in hexanes, 1.0 equiv.) was added. The reaction mixture was warmed to 0 ^oC and stirred for 1 h. The reaction mixture was again cooled to –78 ^oC and ketone **2.36** (462 mg, 2.35 mmol, 1.00 equiv.) was added as a solution in THF. The reaction mixture was warmed to 0 ^oC and stirred for 3 h, at which point methyl iodide (0.29 mL, 4.7 mmol, 2.0 equiv.) was added. The reaction mixture was stirred for an additional 2 h at 0 ^oC, and the reaction was quenched with saturated aqueous $NaHCO_3$. The aqueous layer was extracted with Et_2O (3 x 10 mL) and the combined organics were washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude mixture was purified by silica gel flash column chromatography (2% EtOAc in hexanes) to yield the title compound as a white solid (495 mg, 2.35 mmol, 46% yield): **m.p.** 67–68 ^oC; **TLC R_f** =

0.2 (2% EtOAc in hexanes); **^{1}H NMR** (400 MHz, CDCl$_3$) δ 8.11–8.08 (m, 2H), 7.83 (ap dd, *J* = 6.4, 2.2 Hz, 1H), 7.72 (d, *J* = 8.7 Hz, 1H), 7.59–7.53 (m, 2H), 3.50 (dt, *J* = 17.4, 4.2 Hz, 1H), 3.27–3.19 (m, 1H), 2.66 (ap sep, *J* = 5.9 Hz, 1H), 2.38–2.32 (m, 1H), 2.02–1.95 (m, 1H), 1.31 (d, *J* = 6.7 Hz, 3H); **^{13}C NMR** (100 MHz, CDCl$_3$) δ 201.1, 142.4, 135.6, 131.5, 129.8, 128.8, 128.2, 127.0, 126.7, 124.8, 123.2, 41.7, 30.8, 25.1, 15.4; **IR** (neat) 3060, 2930, 2862, 1674 cm^{-1}; **HRMS** (TOF MS ES+) *m / z* calcd for $C_{15}H_{14}ONa$ [M + Na]$^{+}$ 233.0942, found 233.0951.

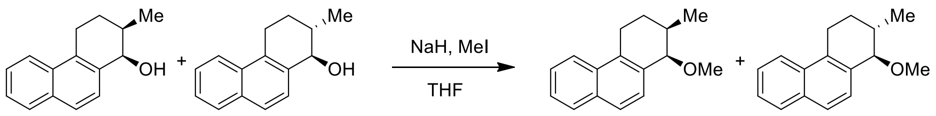


2.37 **2.38**

1:1.5 mixture of diastereomers

2-Methyl-1,2,3,4-tetrahydrophenanthren-1-ol (2.38): In a glove box, a flame-dried round bottom flask was charged with ketone **2.37** (219 mg, 1.04 mmol, 1.00 equiv.) and NaBH$_4$ (79 mg, 2.1 mmol, 2.0 equiv.). The flask was removed from the glove box and kept under a nitrogen atmosphere. The reaction vessel was cooled to –10 °C and methanol (21 mL) was added. The reaction was stirred for 25 min at –10 °C. The reaction was quenched with a mixture of saturated aqueous NaHCO$_3$. Dichloromethane was added, and the aqueous and organic layers were separated. The aqueous layer was extracted with dichloromethane (3 x 25 mL) and the combined organic layers were dried with MgSO$_4$ then filtered through a fritted funnel. The crude mixture was purified by silica gel flash column chromatography to yield **2.38** as a white solid. The product was an inseparable mixture of diastereomers (215 mg, 1.01 mmol, 97% yield): **m.p.** 84–92 °C.; **TLC R$_f$** = 0.3 (10% EtOAc in hexanes); **^{1}H NMR** (400 MHz, CDCl$_3$) δ7.96 (t, *J* = 9.3 Hz, 2H), 7.79 (d, *J* = 7.8 Hz, 2H), 7.68 (ap t, *J* = 7.0 Hz, 2H), 7.62 (ap d, *J* = 8.6 Hz, 1H), 7.52–7.42 (m, 5H), 4.64 (d, *J* = 3.1 Hz, 1H), 4.43 (d, *J* = 7.3 Hz, 1H), 3.29 (dt, *J* = 17.4, 4.2 Hz, 1H), 3.17–2.91 (m, 3H), 2.13–2.06 (m, 1H), 1.98–1.80 (m, 5H), 1.70–1.60 (m, 2H), 1.17 (d, *J* = 6.8

Hz, 3H), 1.14 (d, *J* = 6.7 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 135.8, 135.6, 133.3, 132.9, 132.5, 132.2, 132.1, 132.0, 128.6, 128.5, 128.1, 126.8, 126.7, 126.21 (2C), 126.17, 125.9, 125.7, 123.7, 123.6, 75.5, 72.1, 37.0, 33.9, 27.7, 25.8, 24.7, 24.6, 18.1, 17.1; **IR** (neat) 3312, 2955, 2926, 2872 cm^{-1}; **HRMS** (TOF MS CI+) *m / z* calcd for $C_{15}H_{16}O$ $[M]^+$ 212.1201, found 212.1199.



2.38

mixture of diastereomers

2.19a **2.19b**

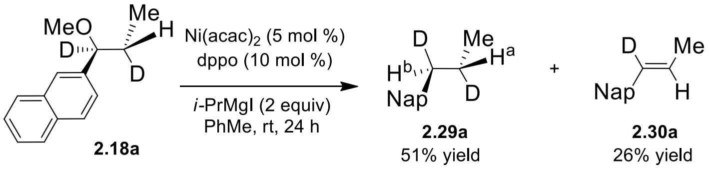
separable by silica gel flash column chromatography

1-Methoxy-2-methyl-1,2,3,4-tetrahydrophenanthrene (2.19): In a glove box, a flame-dried round bottom flask was charged with alcohol **2.38** as a mixture of diastereomers (270 mg, 1.27 mmol, 1.00 equiv.). NaH (55 mg, 2.3 mmol, 1.8 equiv) was added, and the reaction vessel was capped, removed from the glove box, and kept under a nitrogen atmosphere. Dry THF (3.8 mL) was added, and the reaction was stirred for 1 h. Methyl iodide (0.13 mL, 2.2 mmol, 1.7 equiv.) was then added, and the reaction mixture was stirred overnight. The reaction was quenched with saturated aqueous NH_4Cl, extracted with ethyl acetate (3 x 5 mL), and washed with brine. The crude mixture was dried over $MgSO_4$, filtered through a fritted funnel and concentrated in vacuo. Purification by silica gel flash column chromatography (2–5% Et_2O in pentane) yielded each diastereomer pure, both as clear, colorless oils (85% combined yield).

2.19a (100 mg, 0.442 mmol, 35% yield): **TLC R$_f$** = 0.5 (5% Et_2O in pentane); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.2 Hz, 1H), 7.79 (d, *J* = 7.6 Hz, 1H), 7.67 (d, *J* = 8.4 Hz, 1H), 7.50–7.42 (m, 3H), 4.23 (d, *J* = 3.3 Hz, 1H), 3.51 (s, 3H), 3.27 (dt, *J* = 17.6, 5.6 Hz, 1H), 3.03 (dt, *J* = 17.6, 7.6 Hz, 1H), 2.16–2.13 (m, 1H), 2.09–2.00 (m, 1H), 1.89–1.81 (m, 1H), 1.11 (d, *J* = 6.8 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 133.9, 133.2, 132.4, 132.2, 128.5, 127.6, 126.0, 125.9, 125.6, 123.7, 81.4, 57.9, 32.2, 25.5, 24.6, 15.8; **IR** (neat) 3049, 2927, 2817, 1457, 1088, 818 cm^{-1}; **HRMS** (TOF MS ES+) *m / z* calcd for $C_{16}H_{18}ONa$ [M + Na]$^+$ 249.1255, found 249.1249.

2.19b (145 mg, 0.642 mmol, 50% yield): **TLC R$_f$** = 0.4 (5% Et_2O in pentane); **^{1}H NMR** (400MHz, $CDCl_3$) δ 7.96 (d, *J* = 8.1 Hz, 1H), 7.79 (d, *J* = 8.3 Hz, 1H), 7.68 (d, *J* = 8.5 Hz, 1H), 7.50–7.44 (m, 3H), 4.21 (d, *J* = 6.3 Hz, 1H), 3.36 (s, 3H), 3.10 (t, *J* = 6.4 Hz, 2H), 2.24–2.15 (m, 2H), 1.70–1.67 (m, 1H), 1.06 (d, *J* = 6.8 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 133.2, 133.01, 132.98, 132.2, 128.5, 127.1, 126.3, 126.0, 125.6, 123.5, 83.2, 55.2, 30.9, 26.7, 23.7, 17.3; **IR** (neat) 3052, 2926, 1508, 1456, 1083, 815 cm^{-1}; **HRMS (TOF MS ES+)** *m / z* calcd for $C_{16}H_{18}ONa$ [M + Na]$^+$ 249.1255, found 249.1248.

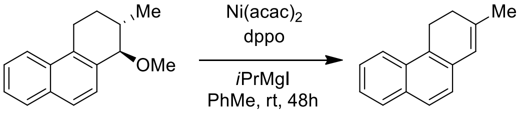
2.5.5 Representative Mechanistic Experiments



2-(1,2-Dideuteropropyl)naphthalene (2.29a) and **(*E*)-2-(prop-1-en-1-yl-1-d)naphthalene (2.30a)**: In a glove box, a flame-dried 7mL vial was charged with $Ni(acac)_2$ (2.5 mg, 0.010 mmol, 0.050 equiv.), dppo (9.8 mg, 0.020 mmol, 0.10 equiv.), and ether **2.18a** (41.0 mg, 0.200 mmol, 1.00 equiv.). Toluene (1.5 mL) was then added. The reaction vessel was removed from the glove box and kept under a nitrogen atmosphere. The reaction mixture was stirred for 10 min, then isopropylmagnesium iodide (0.25 mL, 1.7M, 0.41 mmol, 2.0 equiv.) was added. The reaction mixture was allowed to stir for 24 hours, quenched with methanol, then run down a silica plug (100% Et_2O as eluent). Purification by silica gel flash column chromatography (100% pentanes) yielded **2.29a** as an oil and **2.30a** as a white solid.

2.29a (18 mg, 0.095 mmol, 51% yield): **TLC R_f** = 0.6 (100% pentane); **^{1}H NMR** (400 MHz, CDCl$_3$) δ 7.81–7.75 (m, 3H), 7.61 (s, 1H), 7.42 (ap quin, J = 7.5, 1.3 Hz, 2H), 7.33 (dd, J = 8.4, 1.5 Hz, 1H), 2.72 (d, J = 8.6 Hz, 1 H), 1.71 (quin, J = 7.4 Hz, 1H), 0.96 (d, J = 7.3 Hz, 3H); **^{13}C NMR** (125 MHz, CDCl$_3$) δ 140.3, 133.8, 132.1, 127.8, 127.7, 127.6, 127.5, 126.5, 125.9, 125.1, 37.9 (t, J = 19.4 Hz, 1C), 24.1 (J = 19.4 Hz, 1C), 13.9; **IR** (neat) 3050, 2957, 2910, 2871, 1507 cm^{-1}; **HRMS** (TOF MS CI+) m / z calcd for C$_{13}$H$_{12}$D$_2$ [M]$^+$ 172.1221, found 172.1216.

2.30a (8.9 mg, 0.052 mmol, 26% yield): **m.p.** 40–42 °C; **TLC R_f** = 0.5 (100% pentane); **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.78–7.74 (m, 3H), 7.65 (s, 1H), 7.56 (dd, J = 8.6, 1.6 Hz, 1H), 7.45–7.38 (m, 2H), 6.36 (qt, J = 6.6, 2.2 Hz, 1H), 1.93 (d, J = 6.7 Hz, 3H); **^{13}C NMR** (125 MHz, CDCl$_3$) δ 135.5, 133.9, 132.8, 131.0 (t, J = 23.1 Hz, 1C), 128.2, 128.0, 127.8, 126.24, 126.23, 125.5, 125.3, 123.6, 18.7; **IR** (thin film) 3052, 2906, 2847, 2225, 1596, 1507, 1445 cm^{-1}; **HRMS** (TOF MS CI+) m / z calcd for C$_{11}$H$_{11}$D [M]$^+$ 169.1002, found 169.1004.



2.19a **2.41**

2-Methyl-3,4-dihydrophenanthrene (2.41): In a glove box, a flame-dried 7 mL vial was charged with Ni(acac)$_2$ (2.6 mg, 0.010 mmol, 0.050 equiv.), dppo (9.7 mg, 0.020 mmol, 0.10 equiv.), and **2.19a** (45.3 mg, 0.200 mmol, 1.00 equiv.). The reaction vessel was capped, removed from the glove box and kept under a nitrogen atmosphere. Toluene (1.5 mL) was added and the reaction mixture was stirred for 10 min. Isopropylmagnesium iodide (0.23 mL, 1.7M, 0.40 mmol, 2.0 equiv.) was added then the reaction mixture was stirred for 48 h. The reaction was quenched with an excess of methanol and run through a silica plug (100% Et$_2$O). Analysis by ^{1}H NMR with an internal standard (PhTMS) revealed 62% yield of product. Purification by silica-gel flash column chromatography provided a small amount of analytically pure material: **TLC R_f** = 0.4 (100% hexanes); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.00 (d, *J* = 8.6 Hz, 1H), 7.77 (d, *J* = 8.3 Hz, 1H), 7.64 (d, *J* = 8.2 Hz, 1H), 7.47 (ap t, *J* = 7.6 Hz, 1H), 7.37 (ap t, *J* = 7.5 Hz, 1H), 7.17 (d, *J* = 8.3 Hz, 1H), 6.31 (s, 1H), 3.24 (t, *J* = 8.7 Hz, 2H), 2.40 (t, *J* = 8.7 Hz, 2H), 1.98 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 138.1, 132.9, 132.2, 131.5, 128.7, 128.4, 126.4, 126.0, 125.3, 124.6, 123.4, 123.3, 28.9, 23.5, 23.3; **IR** (thin film in $CDCl_3$) 3047, 2960, 2920, 2828, 1434 cm^{-1}; **HRMS** (TOF MS CI+) *m / z* calcd for $C_{14}H_{15}$ $[M + H]^+$ 195.1174, found 195.1080.

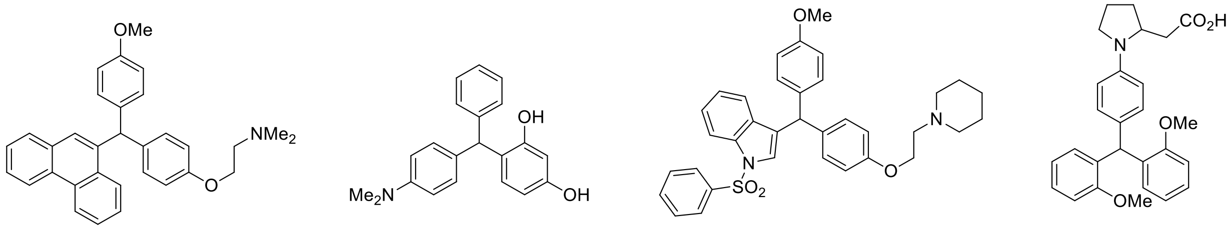
Chapter 3

Selective Synthesis of Either Enantiomer of an Anti Breast Cancer Agent from a Common Enantioenriched Intermediate

3.1. Introduction

Triarylmethanes are important targets owing to their application in materials[1] and medicinal chemistry (Figure 3.1).[2] In particular, the triarylmethane motif is found in anti-cancer lead compounds.[2b] One such compound is anti breast cancer agent **3.1.**[2bi] In 2006, (±)-**3.1** was shown by Panda and co-workers to inhibit proliferation of the MCF-7 breast cancer cell line, with an in vitro IC_{50} of 3.88 μM. In vivo, (±)-**3.1** was shown to inhibit tumor growth and induce significant regression of mammary tumors in mice. Synthetic access to enantioenriched samples of triarylmethanes is critical for their evaluation as medicinal agents and in determining three-dimensional structure-activity relationships.

Figure 3.1. Bioactive Triarylmethanes



anti breast cancer agent (**3.1**)
Ref. 2bi

anti ovarian cancer agent
Ref. 2bii

anti tuberculosis agent
Ref. 2ci

diabetes treatment
Ref. 2d

---

[1] (a) Duxbury, D. F. *Chem. Rev.* **1993**, *93*, 381. (b) Shchepinov, M. S.; Korshun, V. A. *Chem. Soc. Rev.* **2003**, *32*, 170. (c) Xu, Y.-Q.; Lu, J.-M.; Li, N.-J.; Yan, F.; Xia, X.-W.; Xu, Q.-F. *Eur. Polym. J.* **2008**, *44*, 2404. (d) Herron, N.; Johansson, G. A.; Radu, N. S.; US Patent Application 2005/0187364A1, Aug 25, 2005.

[2] (a) For an overview of synthesis and medicinal properties of triarylmethanes, see: Mondal, F. S.; Panda, G. *RSC Adv.* **2014**, *4*, 28317. (b) Anti-cancer: (i) Shagufta; Srivastava, A. K.; Sharma, R.; Mishra, R.; Balapure, A. K.; Murthy, P. S. R.; Panda, G. *Bioorg. Med. Chem.* **2006**, *14*, 1497. (ii) Finer, J. T.; Chabala, J. C.; Lewis, E. US Patent Application 2004/0132830 A1, Jul 8, 2004. (iii) Palchaudhuri, R.; Nesterenko, V.; Hergenrother, P. J. *J. Am. Chem. Soc.* **2008**, *130*, 10274. (c) Anti-tuberculosis: (i) Panda, G.; Parai, M. K.; Das, S. K.; Shagufta; Manish, S.; Chaturvedi, V.; Srivastava, A. K.; Manju, Y. S.; Gaikwad, A. N.; Sinha, S. *Eur. J. Med. Chem.* **2007**, *42*, 410. (ii) Parai, M. K.; Panda, G.; Chaturvedi, V.; Manju, Y. K.; Sinha, S. *Bioorg. Med. Chem. Lett.* **2008**, *18*, 289. (d) Anti-diabetes: Ellsworth, B. A.; Ewing, W. R.; Jurica, E. U.S. Patent Application 2011/0082165 A1, Apr 7, 2011. (e) Anti-implantation: Srivastava, N.; Sangita; Ray, S.; Singh, M. M.; Dwivedi, A.; Kumar, A. *Bioorg. Med. Chem.* **2004**, *12*, 1011.

Traditional syntheses of triarylmethanes, including **3.1**, have relied on Friedel-Crafts reactions that lead to racemic products.[3,4] To broaden substrate scope beyond electron-rich aromatic compounds, access alternative regioisomers, and achieve stereocontrol, new methods have been developed.[5,6] Recent advances include methods that utilize chiral Brønsted acids and C–H bond activation.[7] Approaches that develop Suzuki and Kumada cross-coupling reactions have further increased access to enantioenriched triarylmethanes. Crudden and co-workers have demonstrated a palladium-catalyzed Suzuki reaction of enantioenriched boronic esters and aryl iodides.[8] Our group has developed the umpolung approach in which benzylic ethers or esters are coupled with arylmetal reagents.[9]

The contributions of the Jarvo laboratory provide a strategy to prepare both enantiomers of a triarylmethane from a common enantiomer of an alcohol intermediate (Scheme 3.1). In 2012, our group reported a stereospecific nickel-catalyzed Kumada cross-coupling reaction that allows for the preparation of optically active triarylmethanes from enantioenriched benzylic ethers such as **3.3**. The reaction proceeds with inversion at the benzylic center. This Kumada

---

[3] (a) Nair, V.; Thomas, S.; Mathew, S. C.; Abhilash, K. G. *Tetrahedron* **2006**, *62*, 6731. (b) Pratt, E. F.; Green, L. Q. *J. Am. Chem. Soc.* **1953**, *75*, 275. (c) Muthyala, R; Katritzky, A. R.; Lan, X. *Dyes Pigm.* **1994**, *25*, 303.

[4] For more recent advances in transition-metal catalyzed Friedel-Crafts reactions, see: (a) Lin, S.; Lu, X. *J. Org. Chem.* **2007**, *72*, 9757. (b) Esquivias, J; Arrayás, R. G.; Carretero, J. C. *Angew. Chem., Int. Ed.* **2006**, *45*, 629. (c) Iovel, I.; Mertins, K.; Kischel, J.; Zapf, A.; Beller, M. *Angew. Chem., Int. Ed.* **2005**, *44*, 3913.

[5] (a) Nambo, M.; Crudden, C. M. *Angew. Chem., Int. Ed.* **2014**, *53*, 742. (b) Xia, Y.; Hu, F.; Liu, Z.; Qu, P.; Ge, R.; Ma, C.; Zhang, Y.; Wang, J. *Org. Lett.* **2013**, *15*, 1784.

[6] For cross-coupling strategies that provide racemic products, see: (a) Molander, G. A.; Elia, M. D. *J. Org. Chem.* **2006**, *71*, 9198. (b) Yu, J.-Y.; Kuwano, R. *Org. Lett.* **2008**, *10*, 973. (c) Tabuchi, S.; Hirano, K.; Satoh, T.; Miura, M. *J. Org. Chem.* **2014**, *79*, 5401.

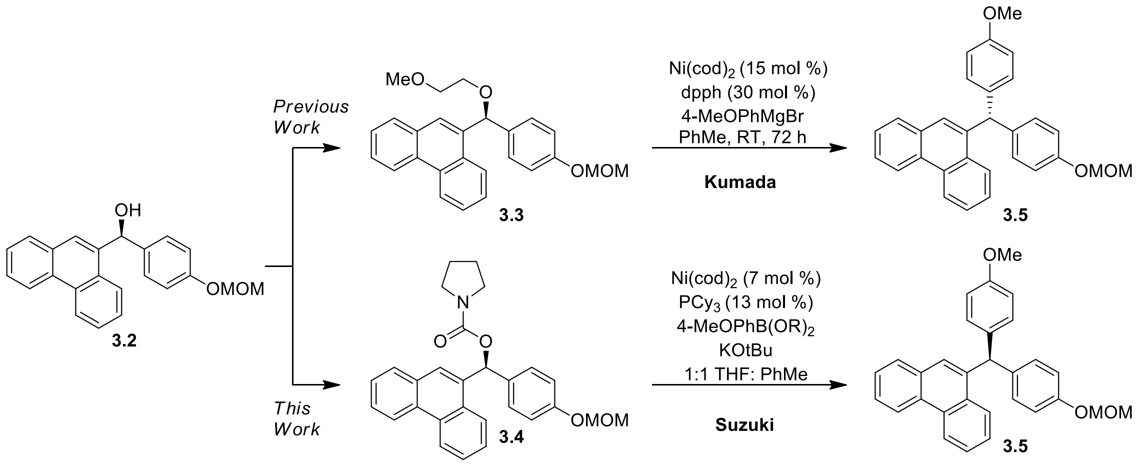
[7] (a) Sun, F.-L.; Zheng, X.-J.; Gu, Q.; He, Q.-L., You, S.-L. *Eur. J. Org. Chem.* **2010**, 47. (b) Zhuo, M.-H.; Jiang, Y.-J.; Fan, Y.-S.; Gao, Y.; Liu, S.; Zhang, S. *Org. Lett.* **2014**, *16*, 1096. (c) Saha, S.; Alamsetti, S. K.; Schneider, C. *Chem. Commun.* **2015**, *51*, 1461. (d) Shi, B.-F.; Maugel, N.; Zhang, Y.-H.; Yu, J.-Q. *Angew. Chem., Int. Ed.* **2008**, *47*, 4882. (e) Li, Y.-Z.; Li, B.-J.; Lu, X.-Y.; Lin, S.; Shi, Z.-J. *Angew. Chem., Int. Ed.* **2009**, *48*, 3817. (f) McGrew, G. I.; Temaismithi, J.; Carroll, P. J.; Walsh, P. J. *Angew. Chem., Int. Ed.* **2010**, *49*, 5541. (g) Zhang, J.; Bellomo, A.; Creamer, A. D.; Dreher, S. D.; Walsh, P. J. *J. Am. Chem. Soc.* **2012**, *134*, 13765. (h) Zhang, J.; Bellomo, A.; Trongsiriwat, N.; Jia, T.; Carroll, P. J.; Dreher, S. D.; Tudge, M. T.; Yin, H.; Robinson, J. R.; Schelter, E. J.;Walsh, P. J. *J. Am. Chem. Soc.* **2014**, *136*, 6276. (i) Niwa, T.; Yorimitsu, H.; Oshima, K. *Org. Lett.* **2007**, *9*, 2373.

[8] Matthew, S. C.; Glasspoole, B. W.; Eisenberger, P.; Crudden, C. M. *J. Am. Chem. Soc.* **2014**, *136*, 5828.

[9] (a) Taylor, B. L. H.; Harris, M. R.; Jarvo, E. R. *Angew. Chem., Int. Ed.* **2012**, *51*, 7790. (b) Harris, M. R.; Hanna, L. E.; Greene, M. A.; Moore, C. E.; Jarvo, E. R. *J. Am. Chem. Soc.* **2013**, *135*, 3303. (c) For a related transformation, see: Zhou, Q.; Srinivas, H. D.; Dasgupta, S.; Watson, M. P. *J. Am. Chem. Soc.* **2013**, *135*, 3307.

method was employed in an enantioselective synthesis of **3.1**.[10] In 2013 our group reported a nickel-catalyzed stereospecific Suzuki-Miyaura reaction of enantioenriched diaryl carbamates, such as **3.4,** with arylboronic esters.[11] In contrast to the Kumada protocol, the Suzuki reaction can proceed with retention of configuration at the benzylic center if tricyclohexylphosphine is used as ligand or inversion if SIMes is employed. Together, the Kumada and Suzuki reactions provide complementary methods to synthesize both enantiomers of **3.1** from the same enantiomer of alcohol **3.2**. Herein we report the synthesis of the opposite enantiomer of **3.1** via the Suzuki reaction.[12]

Scheme 3.1. Strategies to Prepare Both Enantiomers of a Triarylmethane from a Common Enantioenriched Intermediate



3.2. Synthesis of a Bioactive Triarylmethane

The synthesis was carried out as described in Scheme 3.2. Enantioenriched alcohol **3.2** was prepared from commercially available boronic acid **3.6** and phenanthrene-9-carboxaldehyde **3.7** via an asymmetric arylation using chiral aziridine catalyst **3.8**. [9a, 13] Alcohol **3.2** is the common intermediate for both the Kumada and Suzuki protocols. The Kumada protocol requires

---

[10] Taylor, B. L. H.; Harris, M. R.; Jarvo, E. R. *Angew. Chem., Int. Ed.* **2012**, *51*, 7790.

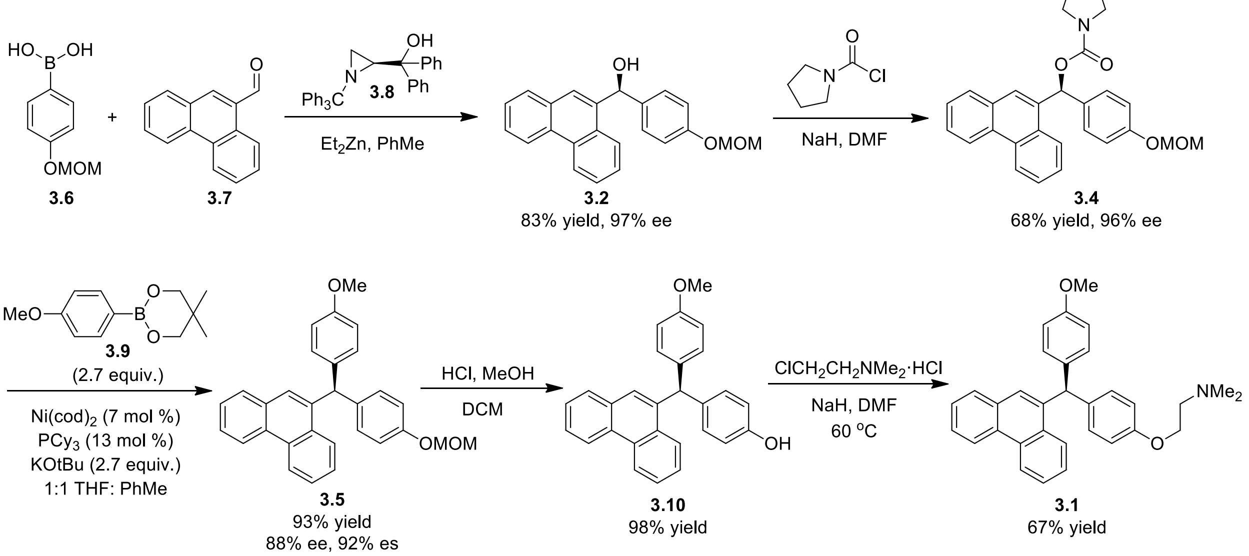
[11] Harris, M. R.; Hanna, L. E.; Greene, M. A.; Moore, C. E.; Jarvo, E. R. *J. Am. Chem. Soc.* **2013**, *135*, 3303.

[12] This chapter will focus on content from the following publication: Johnson, A. G.; Tranquilli, M. M.; Harris, M. R.; Jarvo, E. R. *Tetrahedron Lett.* **2015**, [online early access]. DOI: 10.1016/j.tetlet.2015.02.121. Published Online: March 2, 2015. http://www.sciencedirect.com/science/article/pii/S0040403915004141 (accessed May 4, 2015).

[13] (a) Braga, A. L.; Paixão, M. W.; Westermann, B.; Schneider, P. H.; Wessjohann, L. A. *J. Org. Chem.* **2008**, *73*, 2879. (b) Bolm, C.; Rudolph, J. *J. Am. Chem. Soc.* **2002**, *124*, 14850.

that the alcohol be converted into a methoxyethyl ether leaving group. The Suzuki reaction is more efficient if the alcohol is converted to an electron-withdrawing carbamate. The carbamate is installed by treatment of **3.2** with sodium hydride and 1-pyrrolidinecarbonyl chloride resulting in compound **3.4**.

Scheme 3.2. Synthesis of Triarylmethane **3.1**



With carbamate **3.4** in hand, we were poised to test the key step, the stereospecific Suzuki cross-coupling reaction. Subjection of **3.4** to Suzuki conditions with tricyclohexylphosphine as ligand led to the efficient formation of triarylmethane **3.5** in 93% yield and 88% ee (92% es).[14] Importantly, analysis of the reaction product by chiral SFC chromatography and comparison to material obtained by the Kumada route confirmed that the Suzuki reaction proceeds with overall retention. To achieve the highest yield, **3.4** was recrystallized prior to the cross-coupling reaction, as residual alcohol **3.2** diminishes the yield in the Suzuki coupling. Interestingly, when PCy_3 is replaced with SIMes, compound **3.4** provides low yields of the desired Suzuki product.[15]

---

[14] es = enantiospecificity = (ee starting material)/(ee product) see, Denmark, S. E.; Vogler, T. *Chem. Eur. J.* **2009**, *15,* 11737.

[15] Although effective with many benzhydryl carbamates, subjection of carbamate **3.4** to cross-coupling conditions using a catalyst prepared in situ from $Ni(cod)_2$ and SIMes resulted in only 10% yield of triarylmethane **3.5**. See reference 11.

Completion of the synthesis was achieved by introduction of the requisite side chain. In the penultimate step of the synthesis the MOM group was removed under acidic conditions to form phenol **3.10**. Finally, alkylation of the phenol by treatment with sodium hydride and 2-dimethylaminoethylchloride hydrochloride afforded target compound **3.1**.[16] This synthesis allowed for the preparation of **3.1** in 34% overall yield and 88% ee.

3.3. Conclusion

In summary, either enantiomer of anti-cancer triarylmethane **3.1** can be synthesized using a complementary pair of nickel-catalyzed cross-coupling reactions from a common enantiomer of a chiral alcohol intermediate. For the synthesis of anti-cancer agent **3.1**, when the Kumada protocol is followed, the reaction occurs with inversion at the benzylic stereogenic center. When the Suzuki protocol is followed, the reaction occurs with retention at the benzylic stereogenic center, providing the opposite enantiomer of **3.1**. These syntheses allow for efficient and selective preparation of either enantiomer of triarylmethanes for biological testing. With the exception of the alcohol protection and the subsequent nickel-catalyzed cross-coupling steps, both syntheses are identical and provide optically active **3.1** in five synthetic steps from commercially available starting materials.

---

[16] McCague, R.; Leclercq, G.; Jordan, V. C. *J. Med. Chem.* **1988**, *31*, 1285.

3.4. Experimental Section

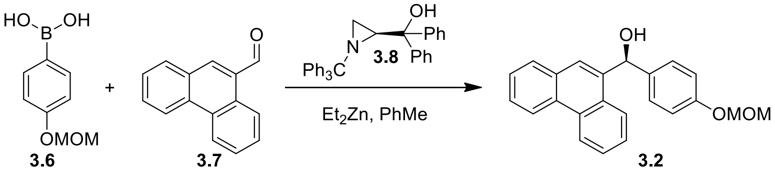
3.4.1. General Procedures

All reactions were carried out under an atmosphere of N_2 using glassware that was either oven- or flame-dried prior to use. Methanol (MeOH) was purchased commercially and used without further purification. *N*,*N*-dimethylformamide (DMF), tetrahydrofuran (THF), and toluene (PhMe) were degassed with argon and then passed through two 4 x 36 inch columns of anhydrous neutral A-2 alumina (8 x 14 mesh; LaRoche Chemicals; activated under a flow of argon at 350 ºC for 12 h) to remove H_2O. All other solvents utilized were purchased anhydrous commercially, or purified as described (vide infra). ^{1}H NMR spectra were recorded on Bruker GN-500 (500 MHz ^{1}H, 125.7 MHz ^{13}C), CRYO-500 (500 MHz ^{1}H, 125.7 MHz ^{13}C) or DRX-400 (400 MHz ^{1}H, 100 MHz ^{13}C) spectrometers. Proton chemical shifts are reported in ppm (δ) relative to internal tetramethylsilane (TMS, δ 0.00). Data are reported as follows: chemical shift (multiplicity [singlet (s), broad singlet (br s), doublet (d), triplet (t), multiplet (m), apparent doublet (ap d), apparent triplet (ap t)], coupling constants [Hz], integration). Carbon chemical shifts are reported in ppm (δ) relative to TMS with the respective solvent resonance as the internal standard ($CDCl_3$, δ 77.16 ppm). Analytical thin-layer chromatography (TLC) was performed using Silica Gel 60 F_{254} pre-coated plates (0.25 mm thickness). Visualization was accomplished by irradiation with a UV lamp. Flash chromatography was performed using Silica Gel 60Å (170-400 mesh) from Fisher Scientific. Melting points (m.p.) were obtained using a Mel-Temp melting point apparatus and are uncorrected. Infrared spectra were obtained on a Nicolet™ iS™5 FT-IR spectrometer system and are reported in terms of frequency of absorption (cm^{-1}). High resolution mass spectrometry was performed by the University of California, Irvine Mass Spectrometry Center. Optical rotations were measured with a Rudolph Research Analytical

Autopol IV Automatic Polarimeter or a Jasco P-1010 digital polarimeter. SFC determinations of enantiopurity were performed on a Berger Analytical instrument using a Daicel™ Chiralpak® column (AD-H; 100 bar, 50 °C, 254 nm).

(*S*)-α,α-diphenyl-1-(triphenylmethyl)-2-aziridinemethanol (**3.8**) was prepared according to a procedure described by Braga.[17] *p*-[(Methoxymethyl)oxy]phenylboronic acid (**3.6**) was prepared from the corresponding methoxymethyl protected aryl bromide.[18] 2-(4-Methoxyphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (**3.9**) was prepared from the corresponding boronic acid and 2,2-dimethylpropane-1,3-diol.[19] 4-Methoxymethoxybenzaldehyde was prepared from the corresponding 4-hydroxybenzaldehyde and chloromethyl methyl ether.[20] $Ni(cod)_2$ was purchased from Strem, stored in a glove box freezer (–20 °C) under an atmosphere of N_2, and used as received. Tricyclohexylphosphine (PCy_3) was purchased from Strem, stored in a glove box, and used as received. All other chemicals were purchased commercially and used as received.

3.4.2. Preparation and Characterization of Products



(4-(Methoxymethoxy)phenyl)(phenanthren-9-yl)methanol (3.2) was prepared according to a procedure reported by Jarvo modified from a procedure developed by Braga.[21] A flame-dried

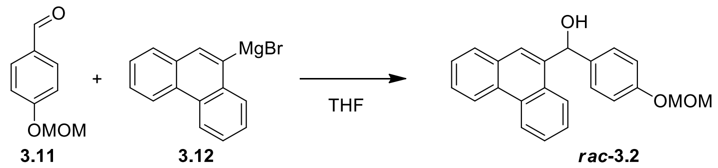
---

[17] Braga, A. L.; Paixão, M. W.; Westermann, B.; Schneider, P. H.; Wessjohann, L. A. *J. Org. Chem.* **2008**, *73*, 2879.
[18] Choshi, T.; Yamada, S.; Sugino, E.; Kuwada, T.; Hibino, S. *J. Org. Chem.* **1995**, *60*, 5899.
[19] Tivola, P. B.; Deagostino, A.; Prandi, C.; Venturello, P. *Org. Lett.* **2002**, *4*, 1275.
[20] Fruit, C.; Turck, A.; Plé, N.; Mojovic, L.; Quéguiner, G. *Tetrahedron* **2001**, *57*, 9435.
[21] Taylor, B. L. H.; Harris, M. R.; Jarvo, E. R. *Angew. Chem. Int. Ed.* **2012**, *51*, 7790.

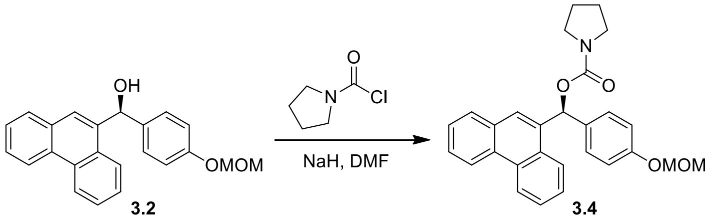
round bottom flask was charged with boronic acid **3.6** (717 mg, 3.94 mmol, 1.63 equiv.). Toluene (6.5 mL) was added, followed by a solution of Et_2Zn in PhMe (22.3 mL, 22.3 mmol 1.00 M, 9.20 equiv.). The reaction mixture was heated to 60 °C and allowed to stir for 12 hours, then cooled to room temperature. A solution of (*S*)-α,α-diphenyl-1-(triphenylmethyl)-2-aziridinemethanol (**3.8**) (113 mg, 0.240 mmol, 0.100 equiv.) in toluene (5 mL) was added and the reaction was stirred for 15 minutes. A solution of phenanthrene-9-carbaldehyde **3.7** (499 mg, 2.42 mmol, 1.00 equiv.) in toluene (4.8 mL) was added and the reaction was stirred for 14 hours at room temperature. The reaction was quenched with an excess of 1 M HCl. The crude mixture was extracted with EtOAc (3 x 30 mL), washed with brine, dried over Na_2SO_4, and purified by silica gel flash column chromatography (1% EtOAc/benzene) to afford the target compound as a white solid (820 mg, 2.38 mmol, 98% yield, 94% ee): **$[\alpha]^{23}_{D}$** +79.1 (*c* 1.35, $CHCl_3$). The product was recrystallized in a mixture of 20:1 Et_2O:H_2O to improve ee. After recrystallization, SFC analysis indicated 97% ee (689 mg, 2.00 mmol, 83% yield, 97% ee). Analytical data are consistent with literature values:[22] **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.73 (d, *J* = 8.2 Hz, 1H), 8.67 (d, *J* = 8.1 Hz, 1H), 8.01 (s, 1H), 7.99 (d, *J* = 8.2 Hz, 1H), 7.92 (d, *J* = 7.9 Hz, 1H), 7.68–7.59 (m, 3H), 7.51 (t, *J* = 7.1 Hz, 1H), 7.36 (d, *J* = 8.6 Hz, 2H), 6.99 (d, *J* = 8.7 Hz, 2H), 6.50 (d, *J* = 3.4 Hz, 1H), 5.14 (s, 2H), 3.45 (s, 3H), 2.31 (d, *J* = 3.8 Hz, 1H); **SFC** analysis (AD-H, 35% MeOH, 3.5 mL/min, 254 nm) indicated 97% ee: t_R (major) = 4.4 min, t_R (minor) = 6.2 min.

---

[22] Taylor, B. L. H.; Harris, M. R.; Jarvo, E. R. *Angew. Chem. Int. Ed.* **2012**, *51*, 7790.



***racemic*-(4-(Methoxymethoxy)phenyl)(phenanthren-9-yl)methanol (*rac*-3.2)** was prepared according to a procedure reported by Jarvo.[23] To a solution of 4-(methoxymethoxy)benzaldehyde **3.11** (1.66 g, 10.0 mmol, 1.00 equiv.) in THF (10 mL) was added 9-phenanthrenylmagnesium bromide **3.12** (12 mL, 12 mmol, 1.0 M in THF, 1.2 equiv.) at 0 ^{o}C. The mixture was warmed to room temperature and stirred for 4 hours. Saturated aqueous NH_4Cl was added, and the aqueous layer was extracted with EtOAc (3 x 20 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The crude reaction mixture was purified by silica gel flash column chromatography (10–20% EtOAc/hexanes) to afford the title compound as a white solid (1.80 g, 5.23 mmol, 52% yield). Analytical data are consistent with the values listed above for compound **3.2**.



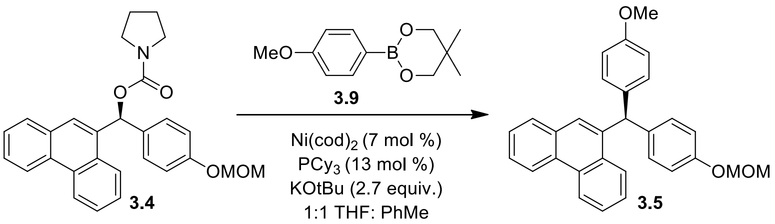
4-(Methoxymethoxy)phenyl)(phenanthren-9-yl)methyl pyrrolidine-1-carboxylate (3.4) was prepared according to a modified procedure reported by Ishihara and co-workers.[24] A flame-dried round bottom flask was charged with NaH (86 mg, 3.6 mmol, 1.8 equiv.) and alcohol **3.2** (689 mg, 2.00 mmol, 1.00 equiv.) and cooled to 0 ^{o}C. DMF (3 mL) was added to the reaction vessel at 0 ^{o}C, and the reaction mixture was allowed to stir for 1 hour at 0 ^{o}C. 1-

---

[23] Taylor, B. L. H.; Harris, M. R.; Jarvo, E. R. *Angew. Chem. Int. Ed.* **2012**, *51*, 7790.

[24] Ishihara, K.; Kosugi, Y.; Umemura, S; Sakakura, A. *Org. Lett.* **2008**, *10*, 3191.

Pyrrolidinecarbonyl chloride (0.243 mL, 2.20 mmol, 1.10 equiv.) was then added. The reaction mixture was stirred for an additional 3 hours at room temperature and quenched with an excess of saturated aqueous NH_4Cl. The crude mixture was extracted with EtOAc (4 x 5 mL), and the combined organic layers were washed with brine and dried over Na_2SO_4. Silica gel flash column chromatography (20% EtOAc/hexanes) followed by recrystallization from hexanes afforded the target compound as a white solid (604 mg, 1.37 mmol, 68% yield, 96% ee): **m.p.** = 54–57 ^{o}C; **TLC R_f** = 0.5 (30% EtOAc in hexanes); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.72 (d, *J* = 8.3 Hz, 1H), 8.67 (d, *J* = 8.2 Hz, 1H), 8.07 (d, *J* = 8.3 Hz, 1H), 7.90–7.87 (m, 2H), 7.67–7.58 (m, 3H), 7.53–7.50 (m, 2H), 7.35 (d, *J* = 8.7 Hz, 2H), 6.97 (d, *J* = 8.7 Hz, 2H), 5.14 (s, 2H), 3.56–3.40 (m, 7H), 1.92–1.83 (m, 4H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 157.0, 154.4, 134.5, 133.9, 131.3, 131.0, 130.6, 129.9, 129.1, 129.0, 127.0, 126.8, 126.74, 126.70, 126.4, 125.5, 123.2, 122.6, 116.2, 94.5, 75.3, 56.2, 46.5, 46.0, 25.9, 25.1; **IR** (neat) 2951, 2876, 1696, 1409, 1509, 1078 cm^{-1}; **HRMS** (TOF MS ES+) *m / z* calcd for $C_{28}H_{27}NO_4Na$ $[M + Na]^+$ 464.1838, found 464.1830; **$[\alpha]^{25}_{D}$** +52.9 (*c* 5.00, $CDCl_3$); **SFC** analysis (AD-H 30% MeOH, 2.5 mL/min, 254 nm) indicated 96% ee: t_R (major) = 7.8 min, t_R (minor) = 8.7 min.

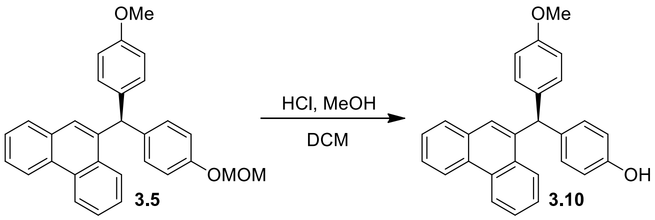


9-((4-(Methoxymethoxy)phenyl)(4-methoxyphenyl)methyl)phenanthrene (3.5) was prepared according to a modified procedure reported by Jarvo.[25] In a glove box, a 7 mL vial was charged with carbamate **3.4** (200 mg, 0.450 mmol, 1.00 equiv.), boronic ester **3.9** (266 mg, 1.21 mmol, 2.66 equiv.), and KO*t*-Bu (135 mg, 1.21 mmol, 2.66 equiv.). PCy_3 as a solution in 1:1

---

[25] Harris, M. R.; Hanna, L. E.; Greene, M. A.; Moore, C. E.; Jarvo, E. R. *J. Am. Chem. Soc.* **2013**, *135*, 3303.

THF:PhMe (0.020 M, 3.0 mL, 0.060 mmol, 0.13 equiv.) was added followed by Ni(cod)$_2$ as a solution in 1:1 THF:PhMe (0.010 M, 3.0 mL, 0.030 mmol, 0.070 equiv.). The reaction was then stirred for 24 h in the glove box. The reaction vessel was removed from the glove box, and the crude mixture was passed through a silica plug with 1:1 Et$_2$O:hexanes. Silica gel flash column chromatography (100% benzene) afforded a mixture of desired product and boronic ester. A second flash column (100% benzene) afforded a pure sample of the target compound as a white solid (182 mg, 0.419 mmol, 93% yield, 88% ee). NMR data are consistent with the values previously reported by Jarvo:[26] **^{1}H NMR** (400 MHz, CDCl$_3$) δ 8.72, (d, *J* = 8.3 Hz, 1H), 8.65 (d, *J* = 8.3 Hz, 1H), 8.04 (d, *J* = 8.3 Hz, 1H), 7.68 (d, *J* = 7.9 Hz, 1H), 7.61 (t, *J* = 1.5 Hz, 2 H), 7.60–7.47 (m, 2H), 7.16 (s, 1H), 7.07 (apt d, *J* = 8.5 Hz, 4H), 6.96 (d, *J* = 8.7 Hz, 2H), 6.82 (d, *J* = 8.7 Hz, 2H), 6.15 (s, 1H), 5.15 (s, 2H), 3.78 (s, 3H) 3.48 (s, 3H); **$[\alpha]^{23}_D$** –3.3 (*c* 3.8, CHCl$_3$)[27]; **SFC** analysis (AD-H, 10% MeOH, 3.5 mL/min, 254 nm) indicated 88% ee, 92% es: t_R (major) = 13.3 min, t_R (minor) = 14.0 min.



4-((4-Methoxyphenyl)(phenanthren-9-yl)methyl)phenol (3.10) was prepared according to a procedure reported by Jarvo.[28] To a solution of triarylmethane **3.5** (182 mg, 0.419 mmol, 1.00 equiv.) in DCM (12.1 mL) was added a solution of HCl in MeOH (2.00 M, 12.1 mL). The reaction mixture was stirred overnight and then quenched with an excess of NaHCO$_3$. The crude

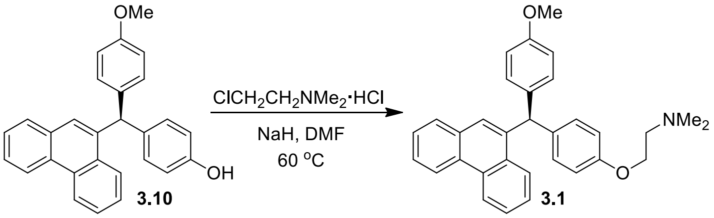
---

[26] Taylor, B. L. H.; Harris, M. R.; Jarvo, E. R. *Angew. Chem. Int. Ed.* **2012**, *51*, 7790.

[27] Optical rotation data are inconsistent with literature values (ref. 26). SFC data, however, are consistent with formation of the opposite enantiomer (vide infra).

[28] See reference 26.

mixture was extracted with EtOAc (3 x 30 mL), washed with brine, and dried over Na_2SO_4. Purification by silica gel flash column chromatography (30% EtOAc/hexanes) yielded the target compound as a white solid (160 mg, 0.410 mmol, 98% yield, 88% ee). NMR data are consistent with literature values:[29] **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.72 (d, *J* = 8.4 Hz, 1H), 8.65 (d, *J* = 8.3 Hz, 1H), 8.03 (d, *J* = 8.3 Hz, 1H), 7.68 (d, *J* = 7.8 Hz, 1H), 7.63–7.57 (m, 2H), 7.54–7.46 (m, 2H), 7.15 (s, 1H), 7.06 (d, *J* = 8.6 Hz, 2H), 7.02 (d, *J* = 8.5 Hz, 2H), 6.83 (d, *J* = 8.7 Hz, 2H), 6.75 (d, *J* = 8.6 Hz, 2H), 6.14 (s, 1H), 4.65 (br s, 1H), 3.77 (s, 3H); **$[\alpha]^{23}_D$** –2.6 (*c* 1.5, $CDCl_3$)[30]; **SFC** analysis (AD-H, 25% MeOH, 2.5 mL/min, 254 nm) indicated 88% ee: t_R (major) = 9.0 min, t_R (minor) = 11.0 min.



2-(4-((4-Methoxyphenyl)(phenanthren-9-yl)methyl)phenoxy)-*N*,*N*-dimethylethanamine (3.1) was prepared according to a procedure reported by Jarvo, adapted from McCague.[31,32] In a glove box, a flame dried round bottom flask was charged with NaH (129 mg, 5.38 mmol, 15.0 equiv.). The reaction vessel was removed from the box and phenol **3.10** (140 mg, 0.359 mmol, 1.00 equiv.) was added as a solution in DMF (7.0 mL). The reaction mixture was heated to 60 °C and stirred for 10 min. The reaction mixture was allowed to cool to room temperature before addition of 2-dimethylaminoethylchloride hydrochloride (211 mg, 1.47 mmol, 4.10 equiv.) as a slurry in DMF (7.0 mL; a large gauge needle is recommended to prevent clogging of the syringe).

---

[29] Taylor, B. L. H.; Harris, M. R.; Jarvo, E. R. *Angew. Chem. Int. Ed.* **2012**, *51*, 7790.
[30] Optical rotation data are inconsistent with literature values (ref. 29). SFC data, however, are consistent with formation of the opposite enantiomer (vide infra).
[31] See reference 29.
[32] McCague, R.; Leclercq, G.; Jordan, V. C. *J. Med. Chem.* **1988**, *31*, 1285.

The reaction mixture was again heated to 60 °C and stirred for 4 hours, at which time the mixture was allowed to cool to room temperature. The reaction was then quenched with an excess of isopropanol. The crude mixture was diluted with H_2O, and extracted with EtOAc (4 x 10 mL). The combined organic layers were washed with brine and dried over Na_2SO_4. Purification by silica gel flash column chromatography (3% Et_3N/EtOAc) yielded the target compound as an off-white solid (110 mg, 0.239 mmol, 67% yield). NMR data are consistent with reported values:[33] **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.72 (d, *J* = 8.1 Hz, 1H), 8.65 (d, *J* = 8.2 Hz, 1H), 8.04 (d, *J* = 8.2 Hz, 1H), 7.67 (d, *J* = 7.8 Hz, 1H), 7.60 (t, *J* = 7.1 Hz, 2H), 7.58–7.48 (m, 2H), 7.15 (s, 1H), 7.07–7.04 (m, 4H), 6.83 (apt t, *J* = 8.2 Hz, 4H), 6.14 (s, 1H), 4.04 (t, *J* = 5.8 Hz, 2H), 3.78 (s, 3H), 2.71 (t, *J* = 5.8 Hz, 2H), 2.32 (s, 6H); **$[\alpha]^{25}_D$** –0.06 (*c* 8.83 $CHCl_3$).[34]

---

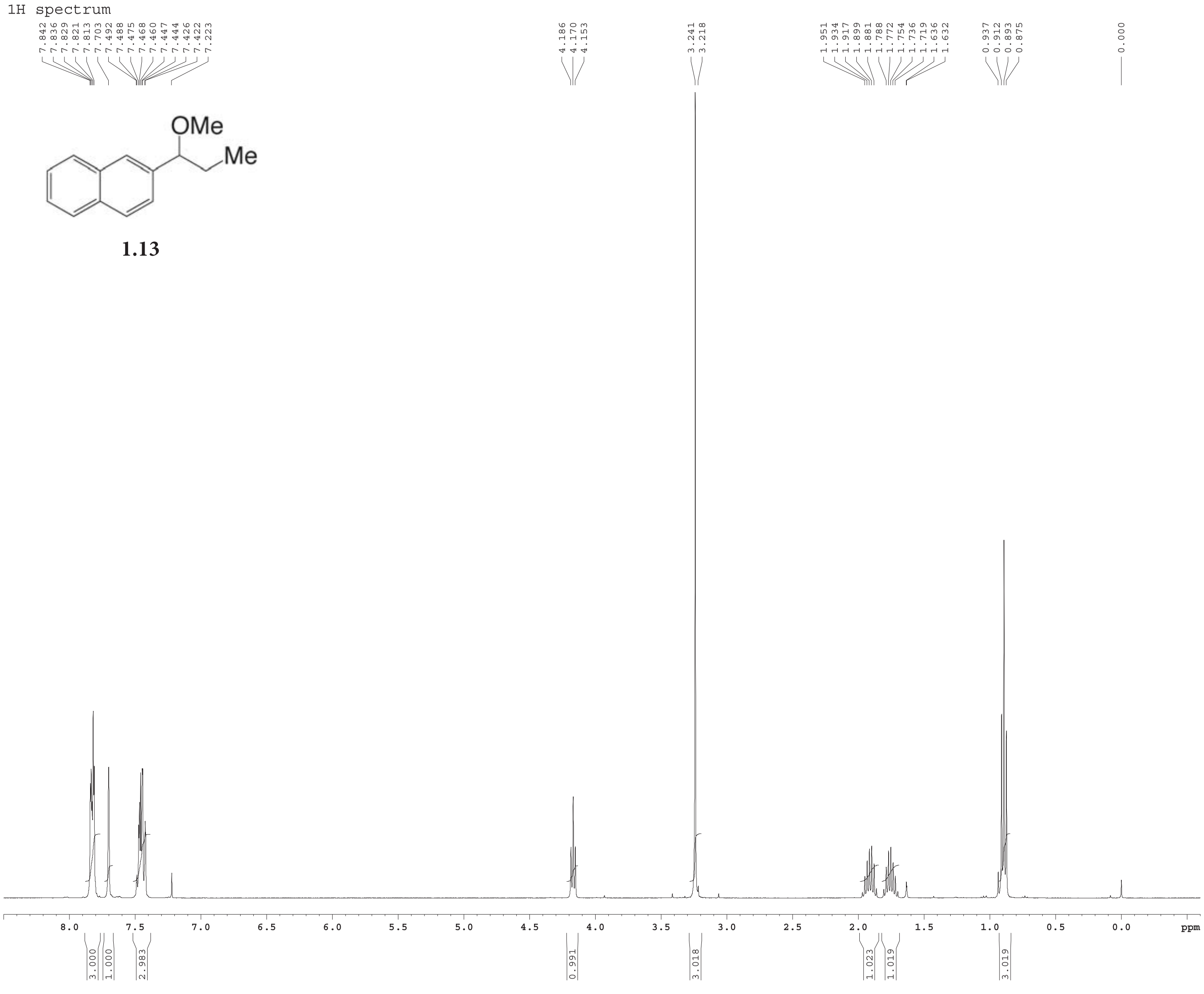
[33] Taylor, B. L. H.; Harris, M. R.; Jarvo, E. R. *Angew. Chem. Int. Ed.* **2012**, *51*, 7790.

[34] Optical rotation data are inconsistent with literature values (ref. 33). SFC data, however, are consistent with formation of the opposite enantiomer (vide infra).

APPENDEX A

^{1}H and ^{13}C NMR Spectra

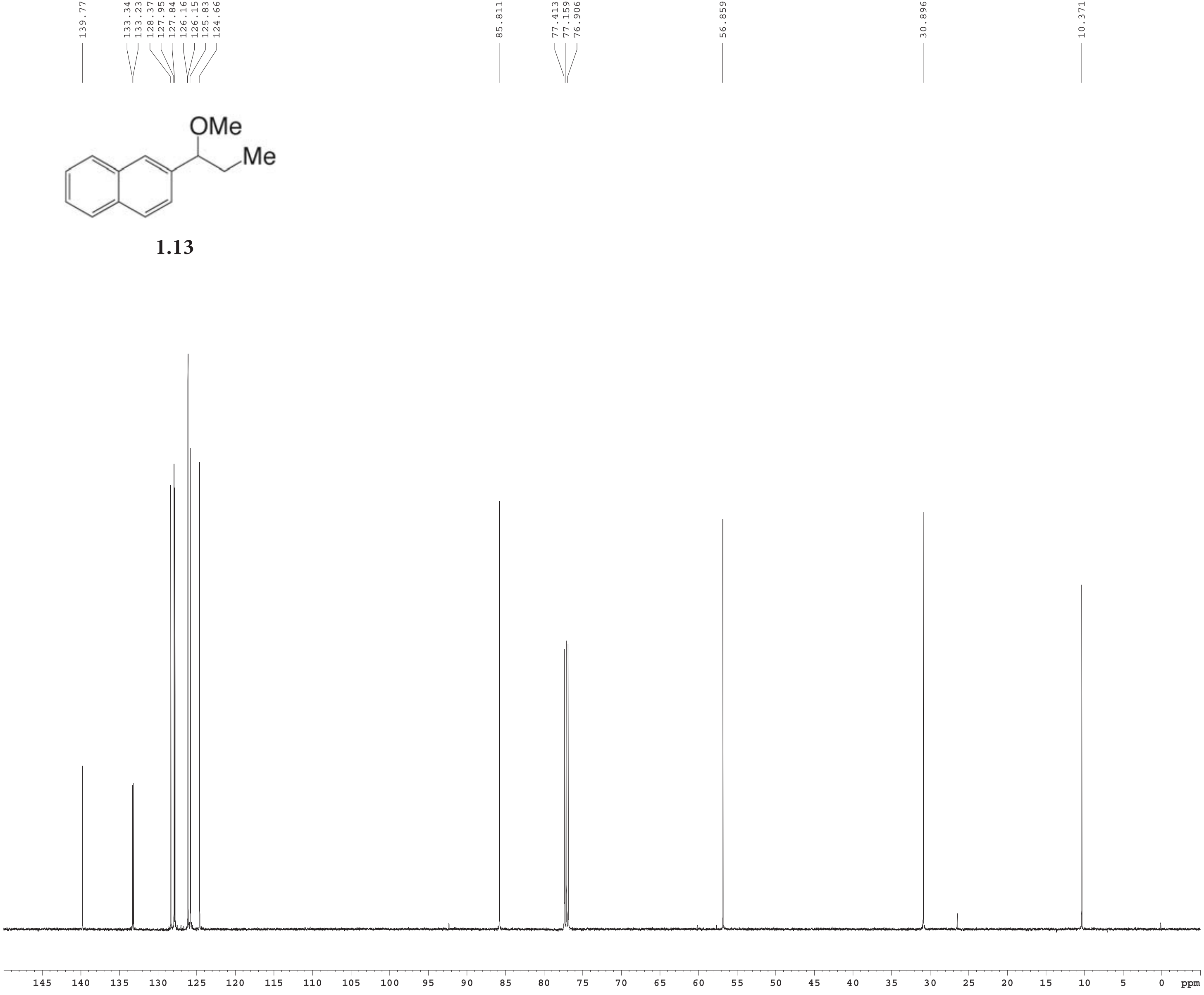
1H spectrum



1.13

```
Current Data Parameters
USER             aaronj
NAME     AGJ_1_79_14-20
EXPNO                 1
PROCNO                1

F2 - Acquisition Parameters
Date_          20110927
Time              19.13
INSTRUM          drx400
PROBHD   5 mm QNP H/F/P
PULPROG            zg30
TD                65536
SOLVENT           CDCl3
NS                    8
DS                    2
SWH            6410.256 Hz
FIDRES         0.097813 Hz
AQ            5.1118579 sec
RG                 90.5
DW               78.000 usec
DE                 4.50 usec
TE                298.0 K
D1           0.10000000 sec
MCREST       0.00000000 sec
MCWRK        0.01500000 sec

======== CHANNEL f1 ========
NUC1                 1H
P1                12.00 usec
PL1               -0.60 dB
SFO1        400.1328009 MHz

F2 - Processing parameters
SI                65536
SF          400.1300364 MHz
WDW                  EM
SSB                   0
LB                 0.30 Hz
GB                    0
PC                 2.00
```

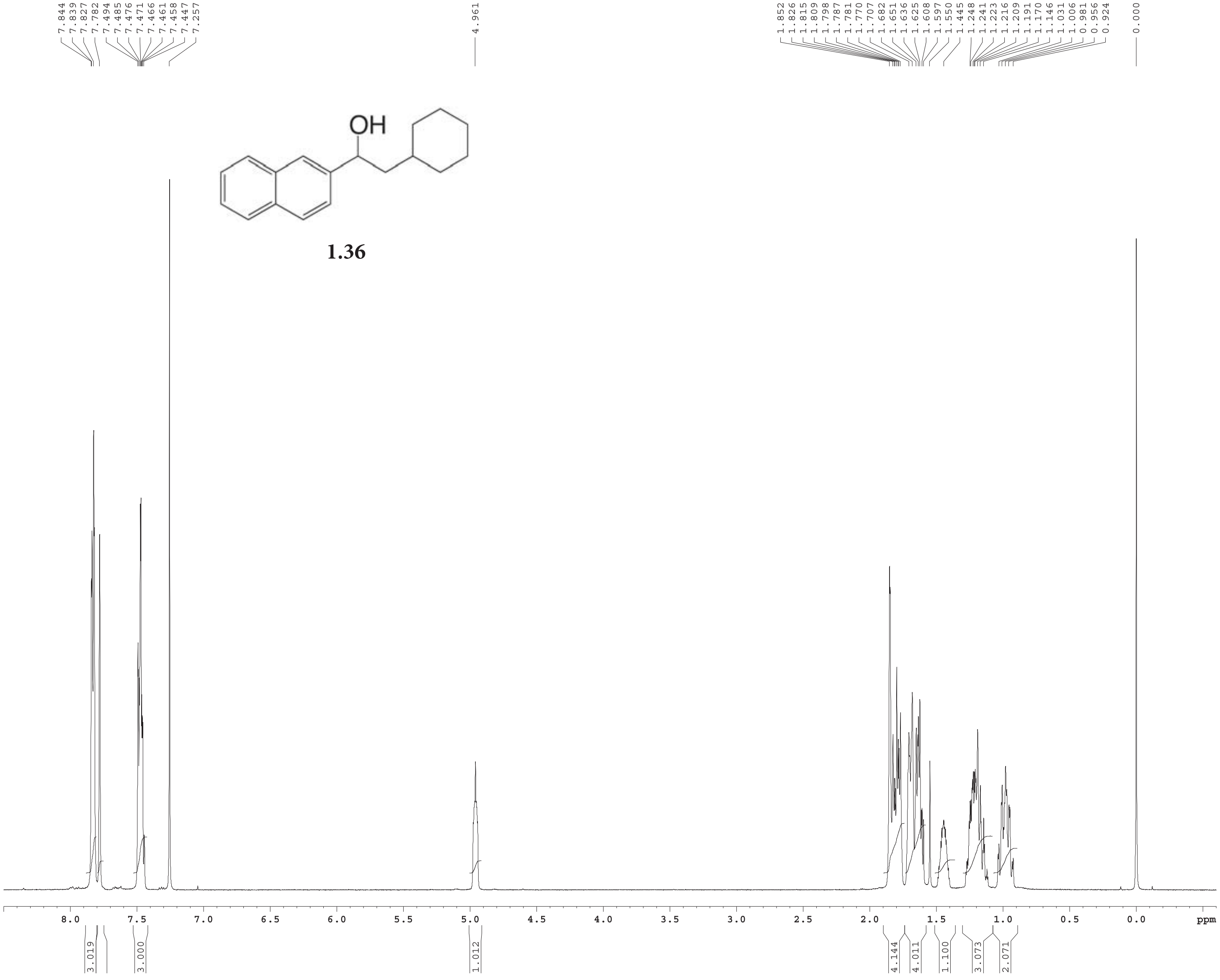
Z-restored spin-echo 13C spectrum with 1H decoupling



1.13

```
Current Data Parameters
USER             aaronj
NAME          AGJ_1_79
EXPNO                1
PROCNO               1

F2 - Acquisition Parameters
Date_         20111105
Time              0.31
INSTRUM        cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD               65536
SOLVENT          CDCl3
NS                 988
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               300.5 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         125.7804108 MHz
WDW                 EM
SSB                  0
LB                1.00 Hz
GB                   0
PC                2.00
```

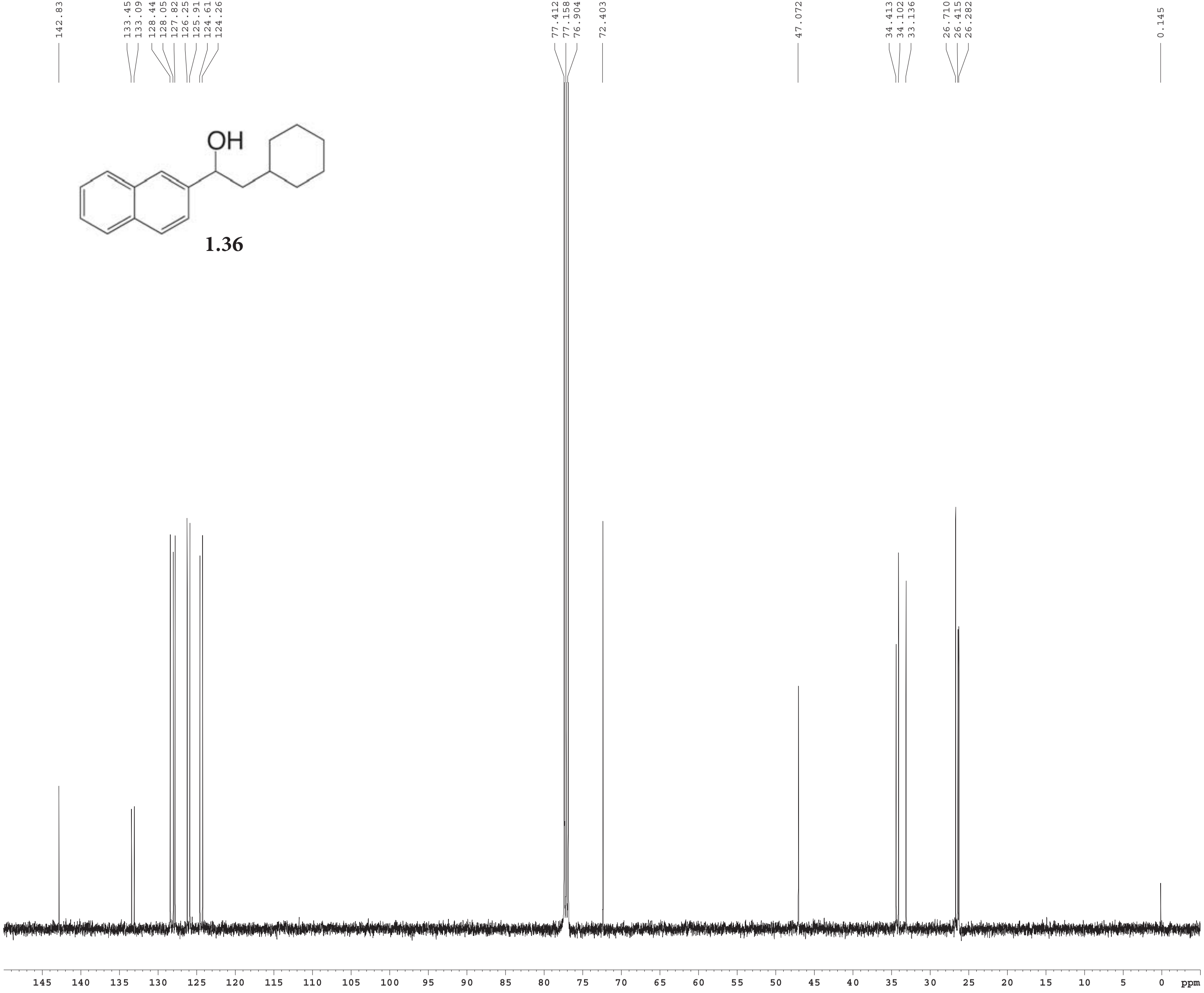
1H spectrum



1.36

```
Current Data Parameters
USER              aaronj
NAME     AGJ_1_Nap_Cy_OH
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20120502
Time               22.56
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                 1.60 dB
SFO1         500.2235015 MHz

F2 - Processing parameters
SI                 65536
SF           500.2200338 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  4.00
```

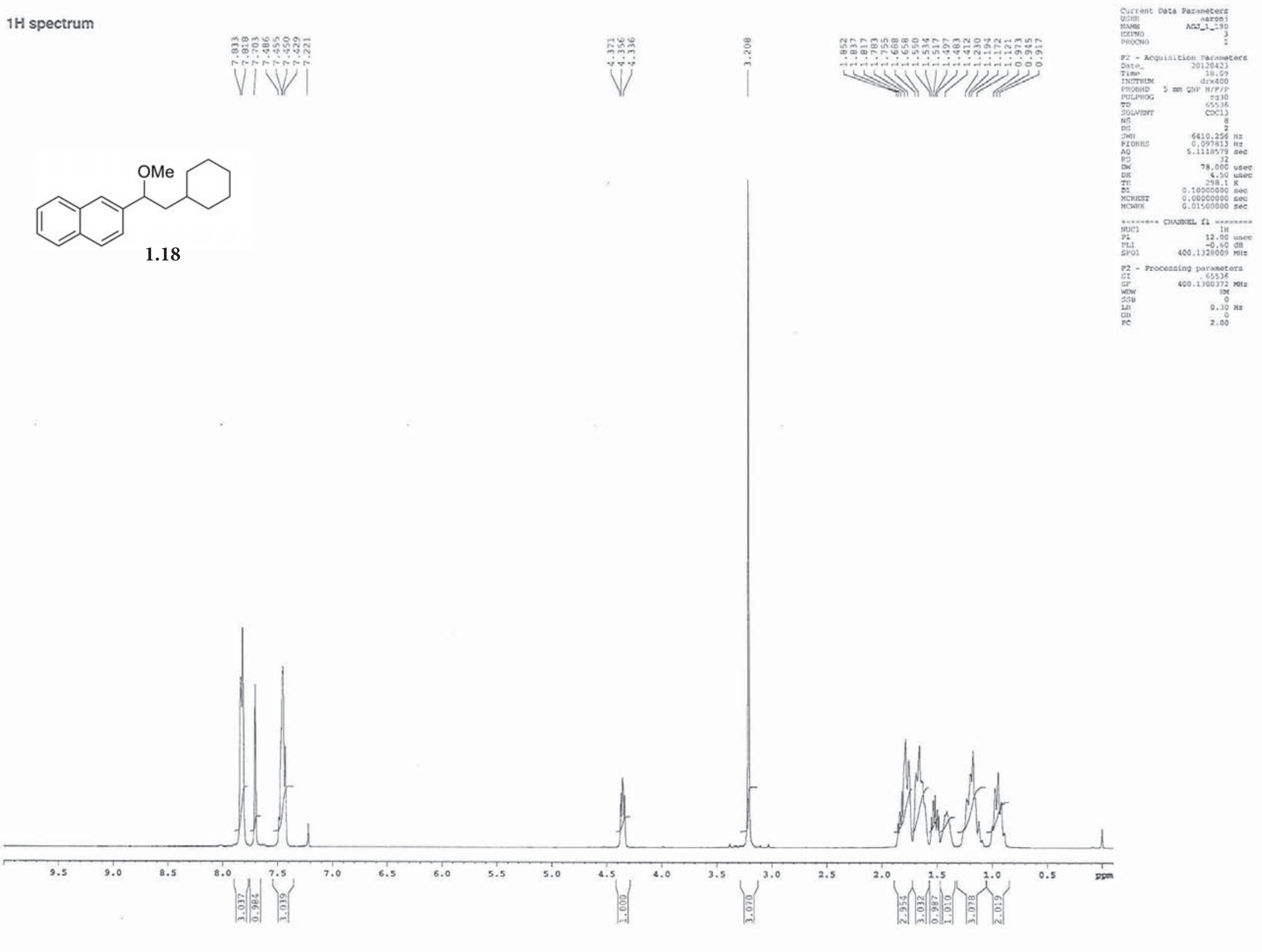
Z-restored spin-echo 13C spectrum with 1H decoupling



1.36

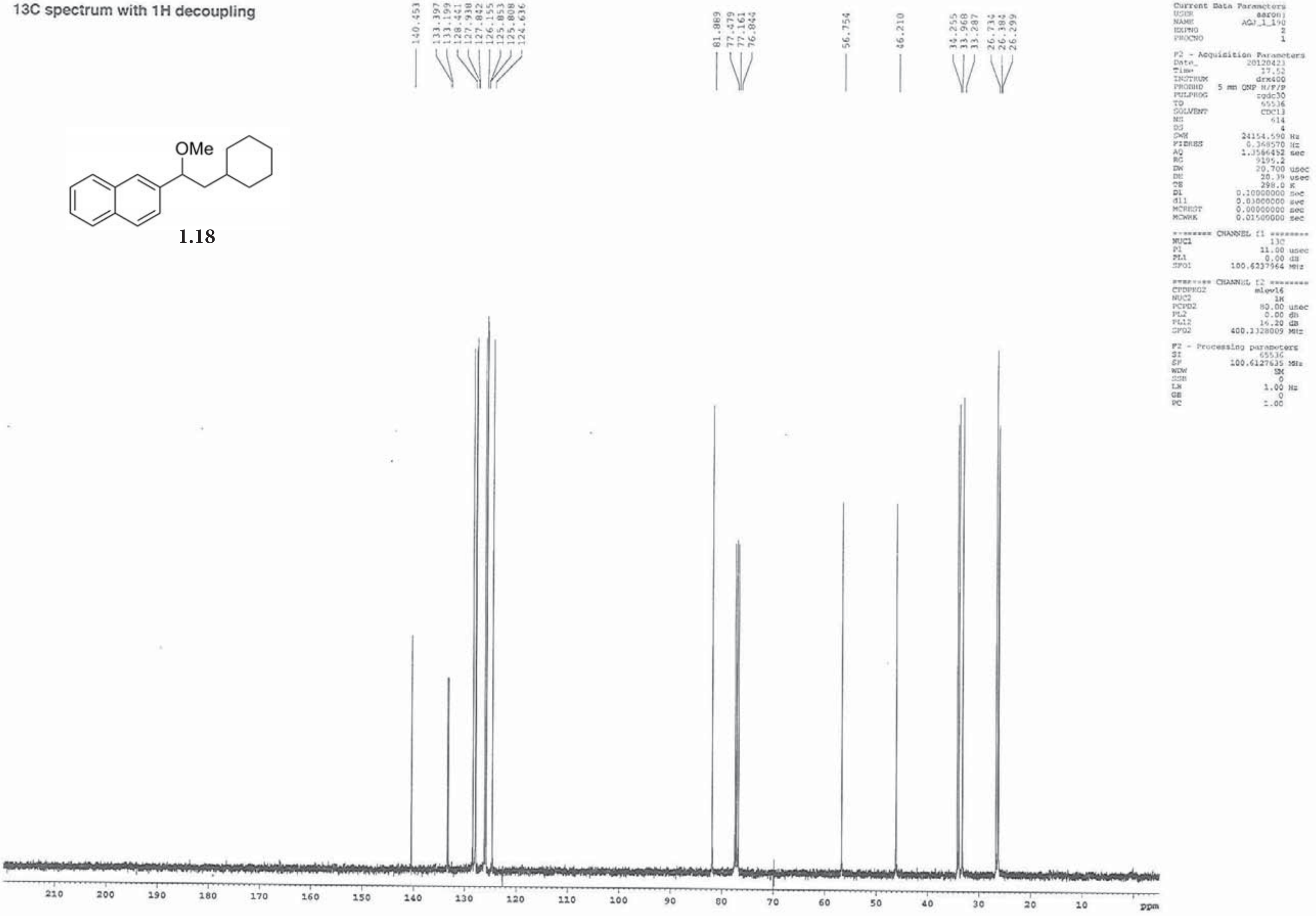
```
Current Data Parameters
USER               aaronj
NAME      AGJ_1_Nap_Cy_OH
EXPNO                   3
PROCNO                  1

F2 - Acquisition Parameters
Date_            20120502
Time                23.01
INSTRUM          cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD                  65536
SOLVENT             CDCl3
NS                    709
DS                     16
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            125.7804090 MHz
WDW                    EM
SSB                     0
LB                   1.00 Hz
GB                      0
PC                   2.00
```

1H spectrum



1.18

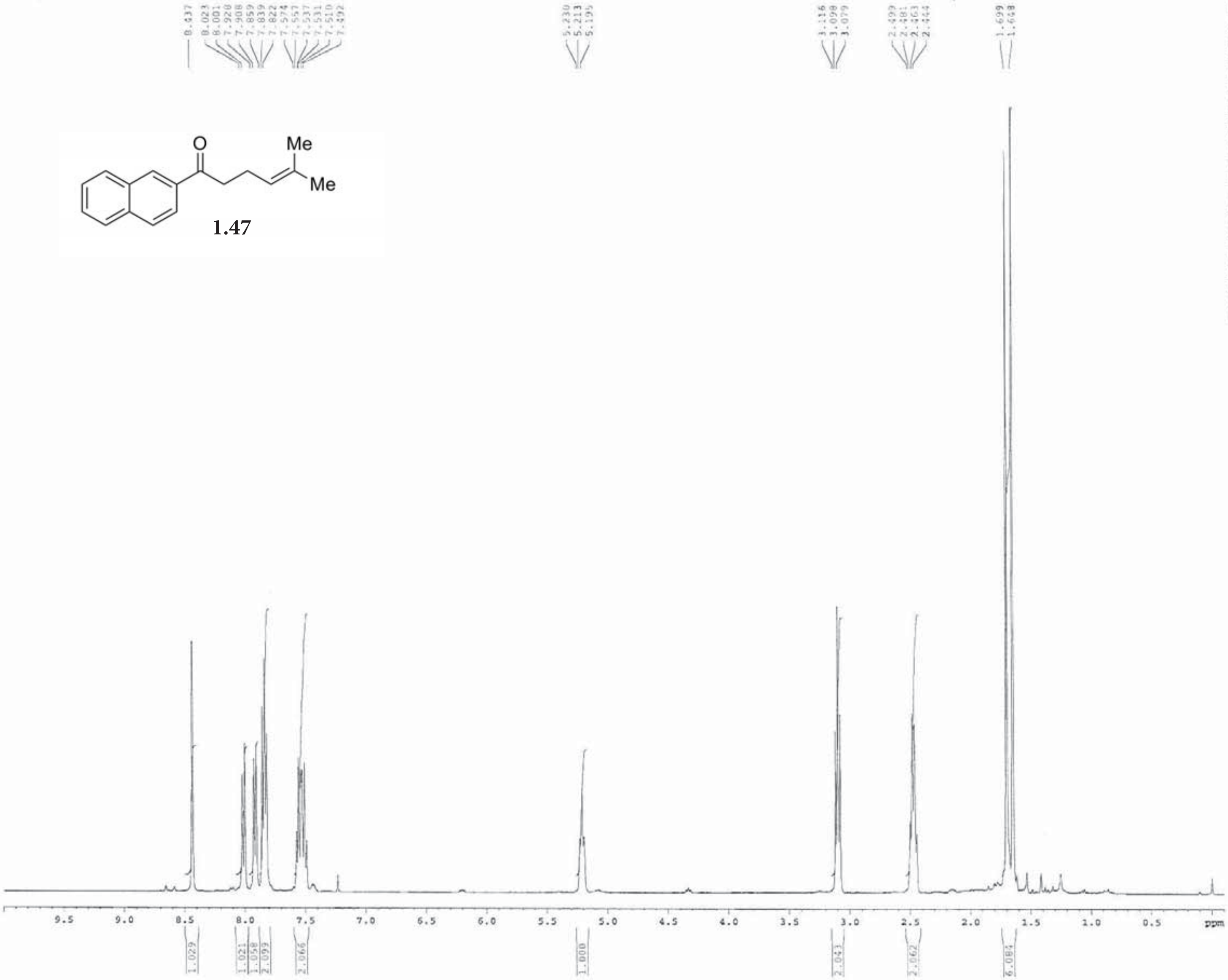
13C spectrum with 1H decoupling



1.18

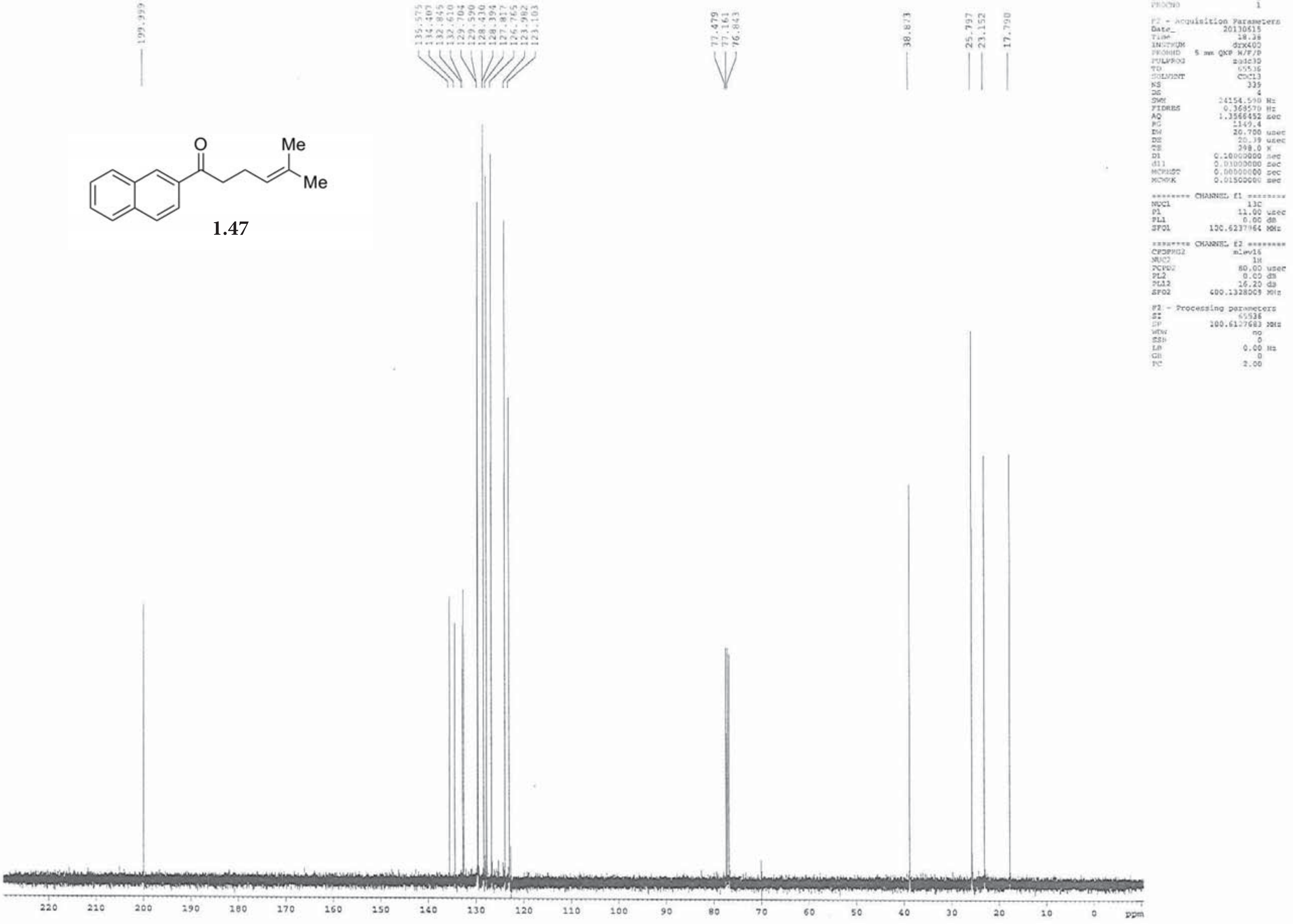
```
Current Data Parameters
USER                aaronj
NAME             AGJ_1_190
EXPNO                    2
PROCNO                   1

F2 - Acquisition Parameters
Date_             20120423
Time                 17.52
INSTRUM             drx400
PROBHD     5 mm QNP H/F/P
PULPROG            zgdc30
TD                   65536
SOLVENT              CDCl3
NS                     614
DS                       4
SWH            24154.590 Hz
FIDRES          0.368570 Hz
AQ             1.3566452 sec
RG                  9195.2
DW                  20.700 usec
DE                   20.39 usec
TE                   298.0 K
D1            0.10000000 sec
d11           0.03000000 sec
MCREST        0.00000000 sec
MCWRK         0.01500000 sec

======== CHANNEL f1 ========
NUC1                   13C
P1                   11.00 usec
PL1                   0.00 dB
SFO1           100.6237964 MHz

======== CHANNEL f2 ========
CPDPRG2             mlev16
NUC2                    1H
PCPD2                80.00 usec
PL2                   0.00 dB
PL12                 16.20 dB
SFO2           400.3328009 MHz

F2 - Processing parameters
SI                   65536
SF             100.6127635 MHz
WDW                     EM
SSB                      0
LB                    1.00 Hz
GB                       0
PC                    1.00
```

1H spectrum


1.47

```
Current Data Parameters
USER             yonova
NAME    imyh - AGJ-3-45
EXPNO                 1
PROCNO                1

F2 - Acquisition Parameters
Date_          20130815
Time              18.33
INSTRUM          drx400
PROBHD   5 mm QNP H/F/P
PULPROG            zg30
TD                65536
SOLVENT           CDCl3
NS                    8
DS                    2
SWH            6410.256 Hz
FIDRES         0.097813 Hz
AQ            5.1118579 sec
RG                   32
DW               78.000 usec
DE                 4.50 usec
TE                298.1 K
D1           0.10000000 sec
MCREST       0.00000000 sec
MCWRK        0.01500000 sec

======== CHANNEL f1 ========
NUC1                 1H
P1                12.00 usec
PL1               -0.60 dB
SFO1        400.1328009 MHz

F2 - Processing parameters
SI                65536
SF          400.1300312 MHz
WDW                  EM
SSB                   0
LB                 0.30 Hz
GB                    0
PC                 1.00
```

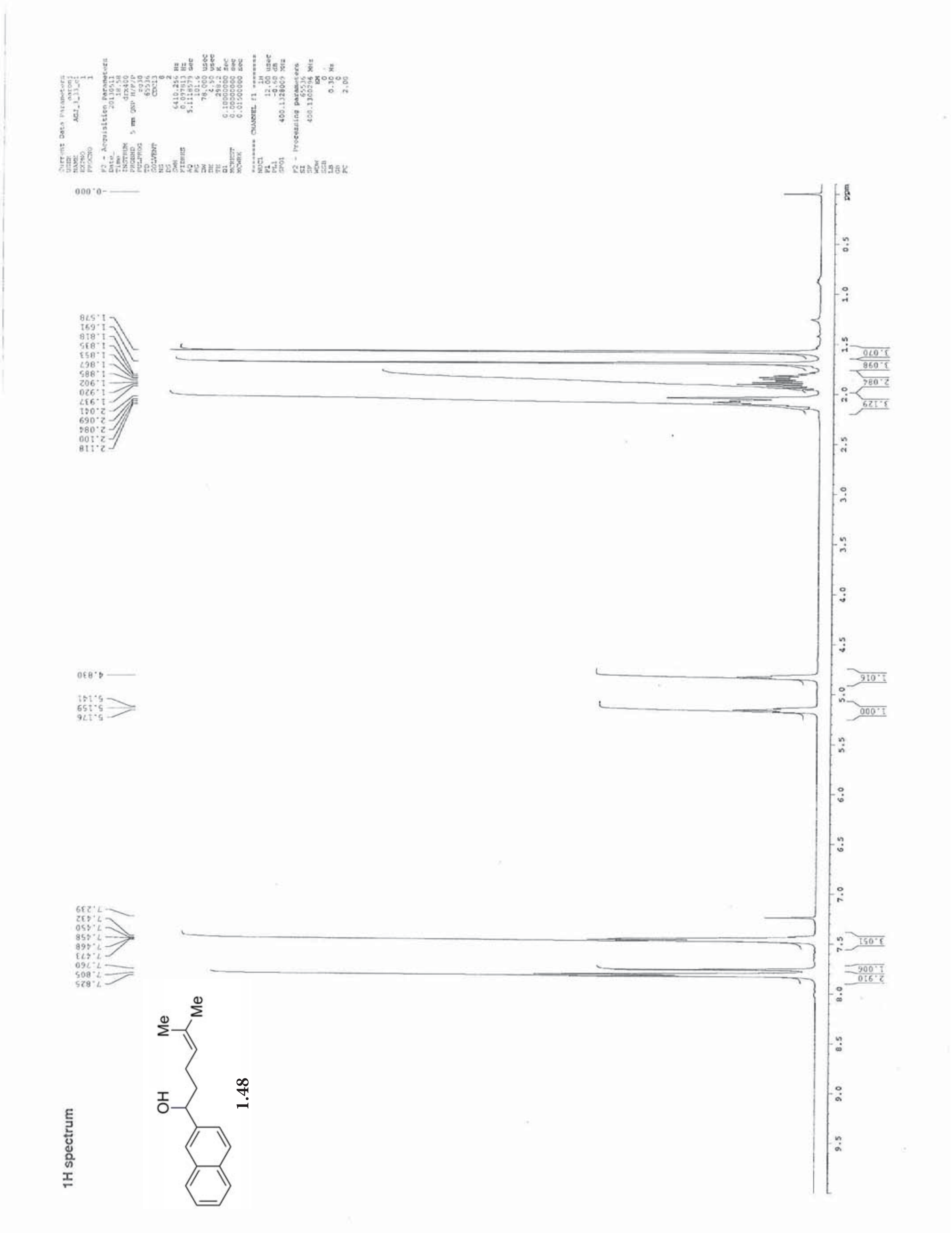
13C spectrum with 1H decoupling



1.47

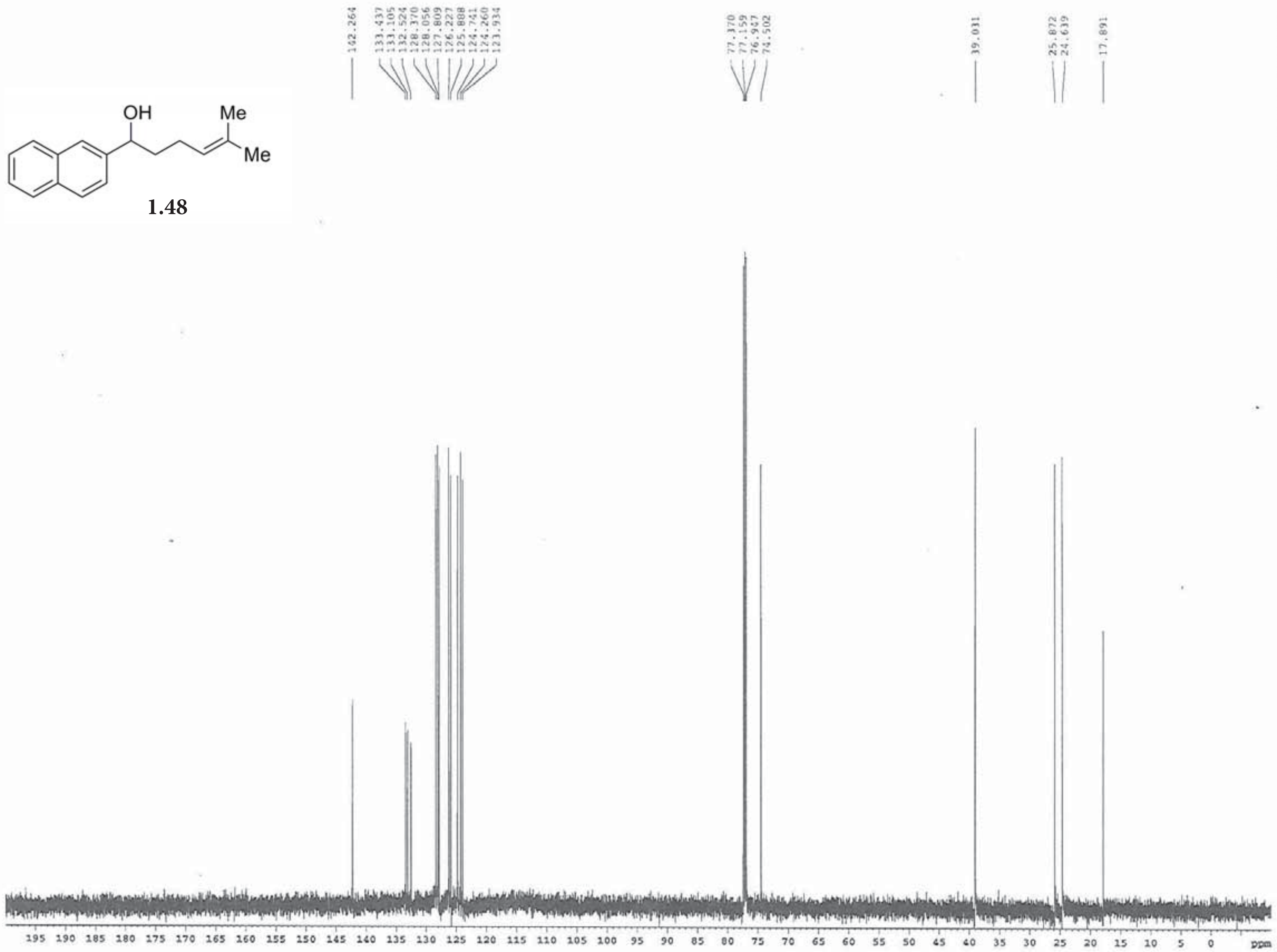
```
Current Data Parameters
USER              yonova
NAME      lmy5 - ACJ-3-45
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20130615
Time               18.36
INSTRUM           drx400
PROBHD   5 mm QNP H/F/P
PULPROG          zgdc30
TD                 65536
SOLVENT            CDCl3
NS                   335
DS                     4
SWH          24154.590 Hz
FIDRES        0.368570 Hz
AQ           1.3566452 sec
RG                1149.4
DW              20.700 usec
DE               20.39 usec
TE               298.0 K
D1          0.10000000 sec
d11         0.03000000 sec
MCREST      0.00000000 sec
MCWRK       0.01500000 sec

======== CHANNEL f1 ========
NUC1                 13C
P1               11.00 usec
PL1               0.00 dB
SFO1       100.6237964 MHz

======== CHANNEL f2 ========
CPDPRG2           mlev16
NUC2                  1H
PCPD2            80.00 usec
PL2               0.00 dB
PL12             16.20 dB
SFO2       400.1328009 MHz

F2 - Processing parameters
SI                 65536
SF         100.6127683 MHz
WDW                   no
SSB                    0
LB                0.00 Hz
GB                     0
PC                  2.00
```

1H spectrum



1.48

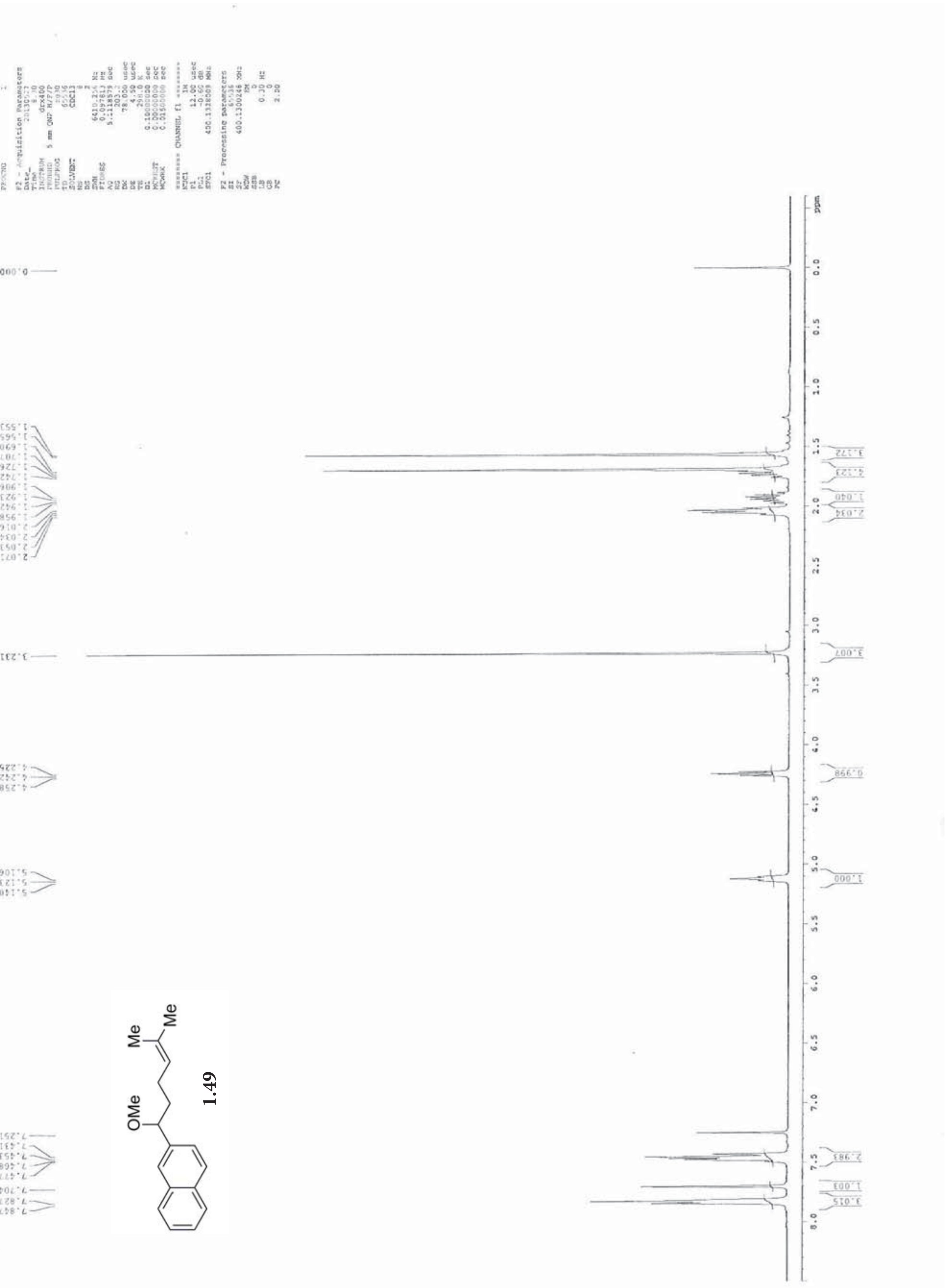
11B spectrum with 1H decoupling, using composite pulse for background suppression



1.48

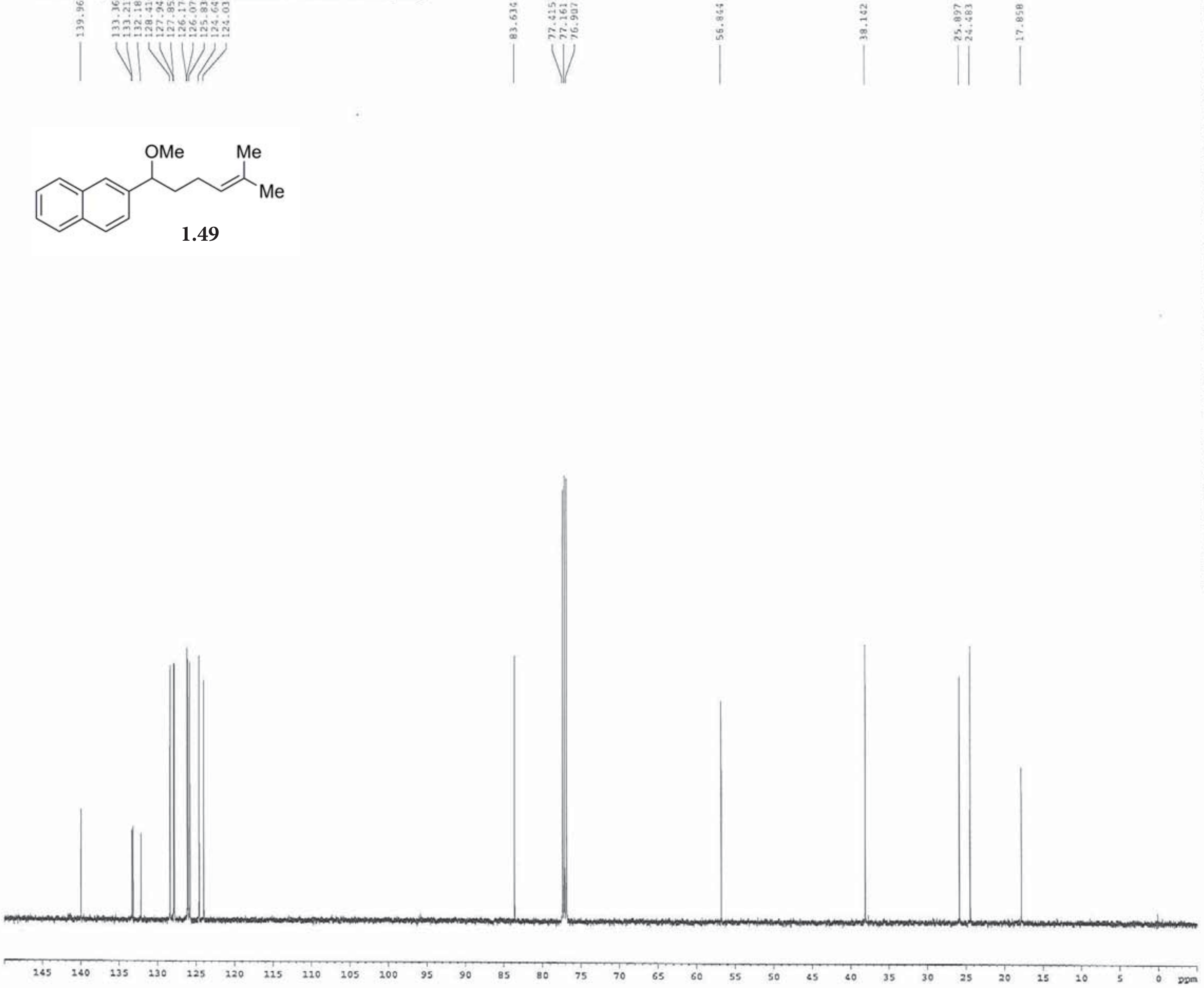
```
Current Data Parameters
USER              aaron1
NAME             ACJ_3_33
EXPNO                   5
PROCNO                  1

F2 - Acquisition Parameters
Date_            20130511
Time                19.24
INSTRUM             av600
PROBHD   5 mm TBI 1H/13
PULPROG           zgdc30
TD                 65400
SOLVENT            CDCl3
NS                   550
DS                     4
SWH            36231.883 Hz
FIDRES          0.554004 Hz
AQ             0.9025700 sec
RG                  1030
DW                13.800 usec
DE                  6.00 usec
TE                 298.1 K
D1            0.40000001 sec
D11           0.03000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                 13C
P1                 15.00 usec

F2 - Processing parameters
SI                 65536
SF           150.9027969 MHz
WDW                   EM
SSB                    0
LB                  1.00 Hz
GB                     0
PC                  1.00
```

1H spectrum



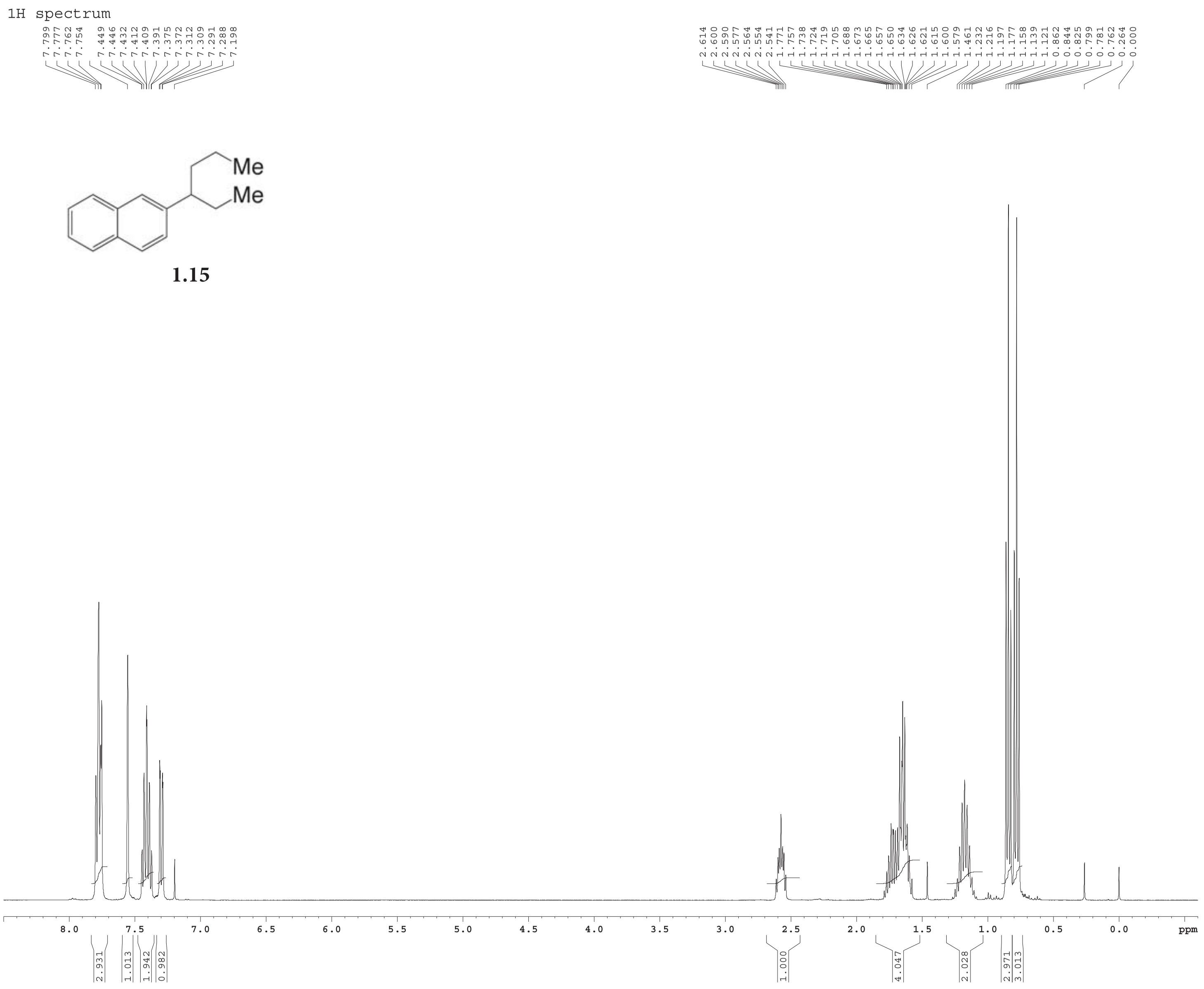
1.49

Z–restored spin–echo 13C spectrum with 1H decoupling



1.49

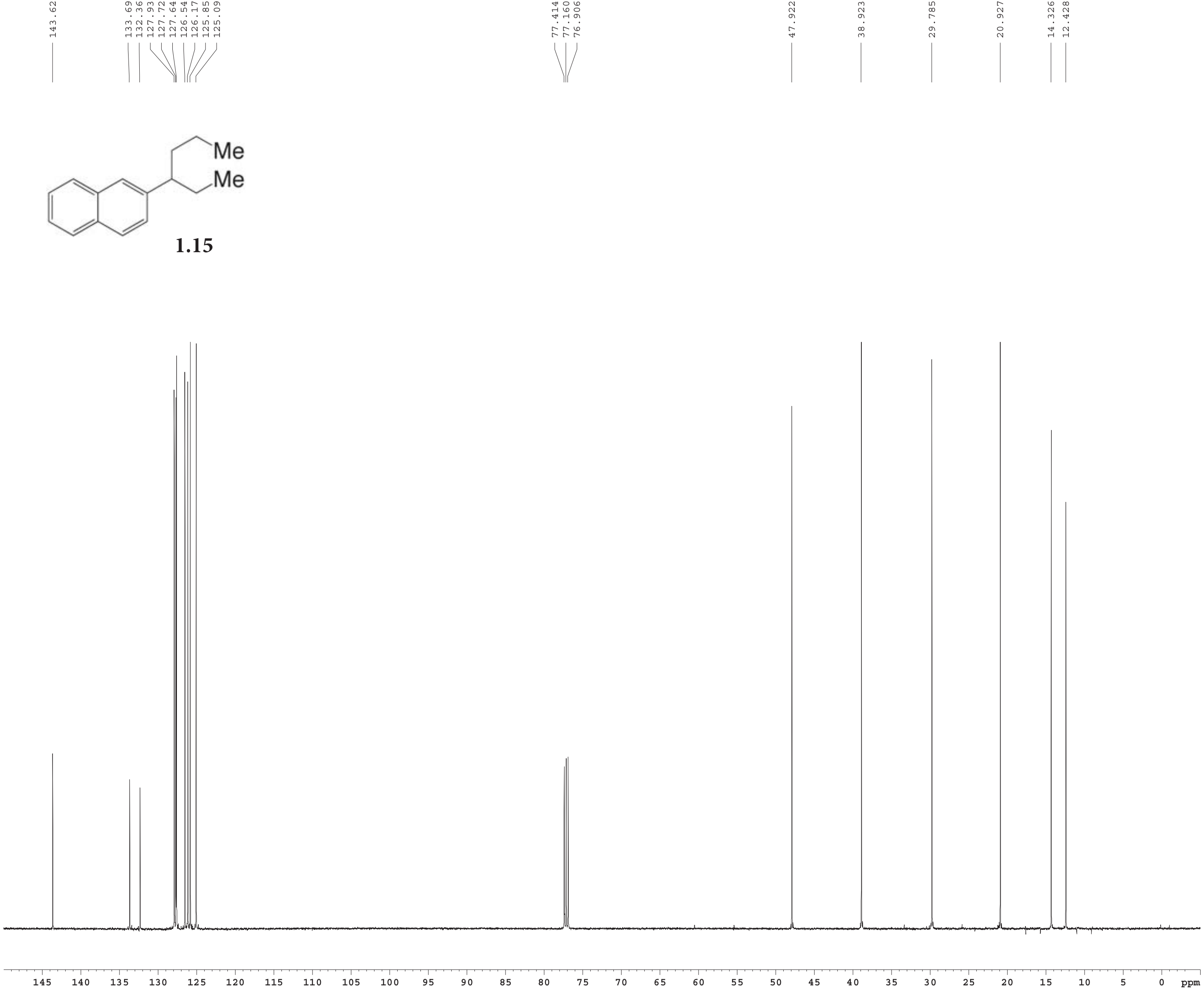
```
Current Data Parameters
USER              aaronj
NAME            AGJ_3_39
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20130527
Time                8.48
INSTRUM          cryo500
PROBHD    5 mm CPTCI 1H-
PULPROG  Spinechopg30gp.prd
TD                 65536
SOLVENT            CDCl3
NS                   400
DS                    16
SWH            30303.031 Hz
FIDRES          0.462388 Hz
AQ             1.0814105 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           125.7804085 MHz
WDW                   EM
SSB                    0
LB                  1.00 Hz
GB                     0
PC                  2.00
```



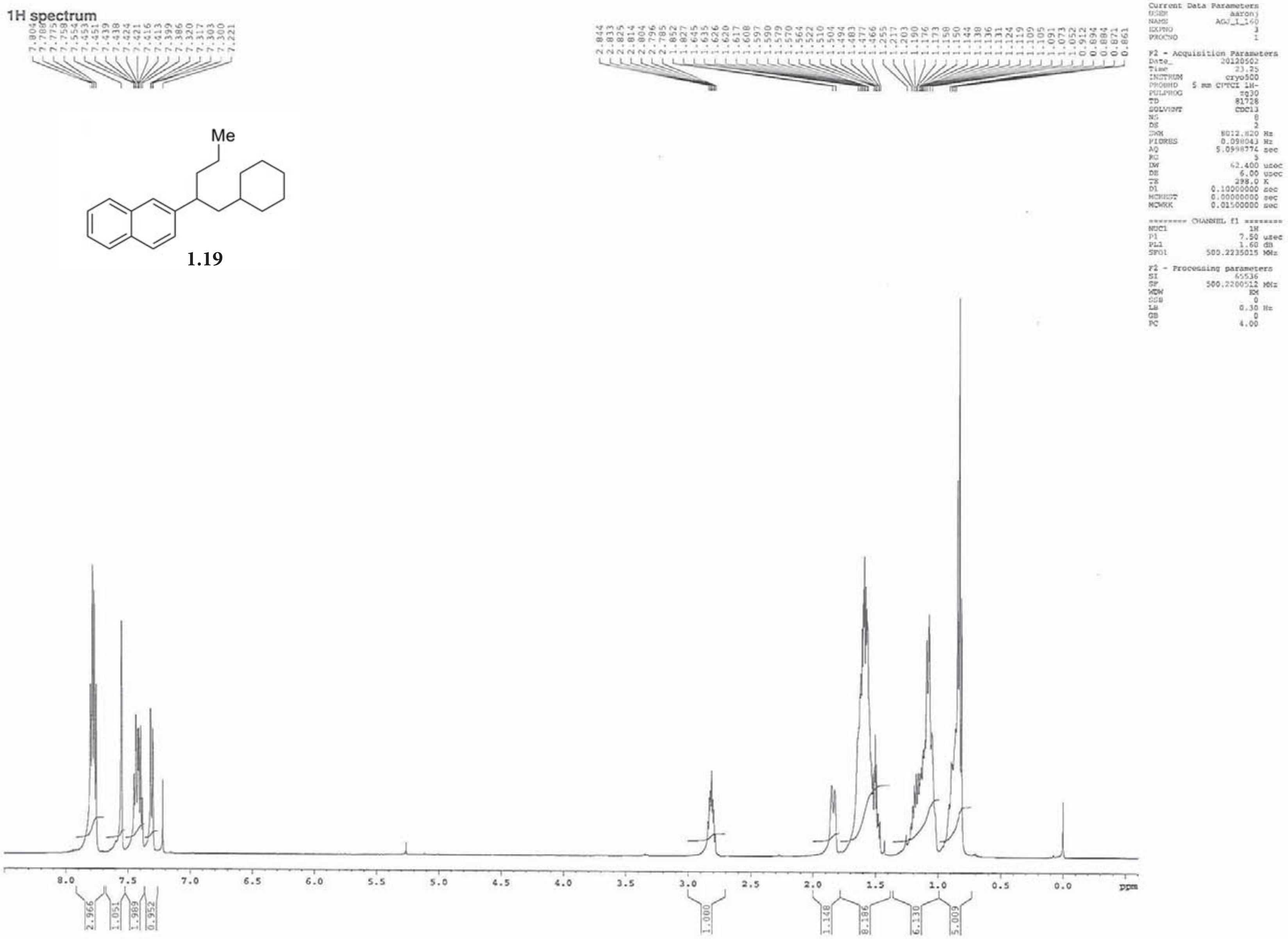
1.15

```
Current Data Parameters
USER                aaronj
NAME      AGJ_1_propyl_6-7
EXPNO                    1
PROCNO                   1

F2 - Acquisition Parameters
Date_             20110830
Time                 18.01
INSTRUM             drx400
PROBHD   5 mm QNP H/F/P
PULPROG               zg30
TD                   65536
SOLVENT              CDCl3
NS                       8
DS                       2
SWH               6410.256 Hz
FIDRES            0.097813 Hz
AQ               5.1118579 sec
RG                    71.8
DW                  78.000 usec
DE                    4.50 usec
TE                   297.9 K
D1              0.10000000 sec
MCREST          0.00000000 sec
MCWRK           0.01500000 sec

======== CHANNEL f1 ========
NUC1                    1H
P1                   12.00 usec
PL1                  -0.60 dB
SFO1           400.1328009 MHz

F2 - Processing parameters
SI                   65536
SF             400.1300464 MHz
WDW                     EM
SSB                      0
LB                    0.30 Hz
GB                       0
PC                    2.00
```

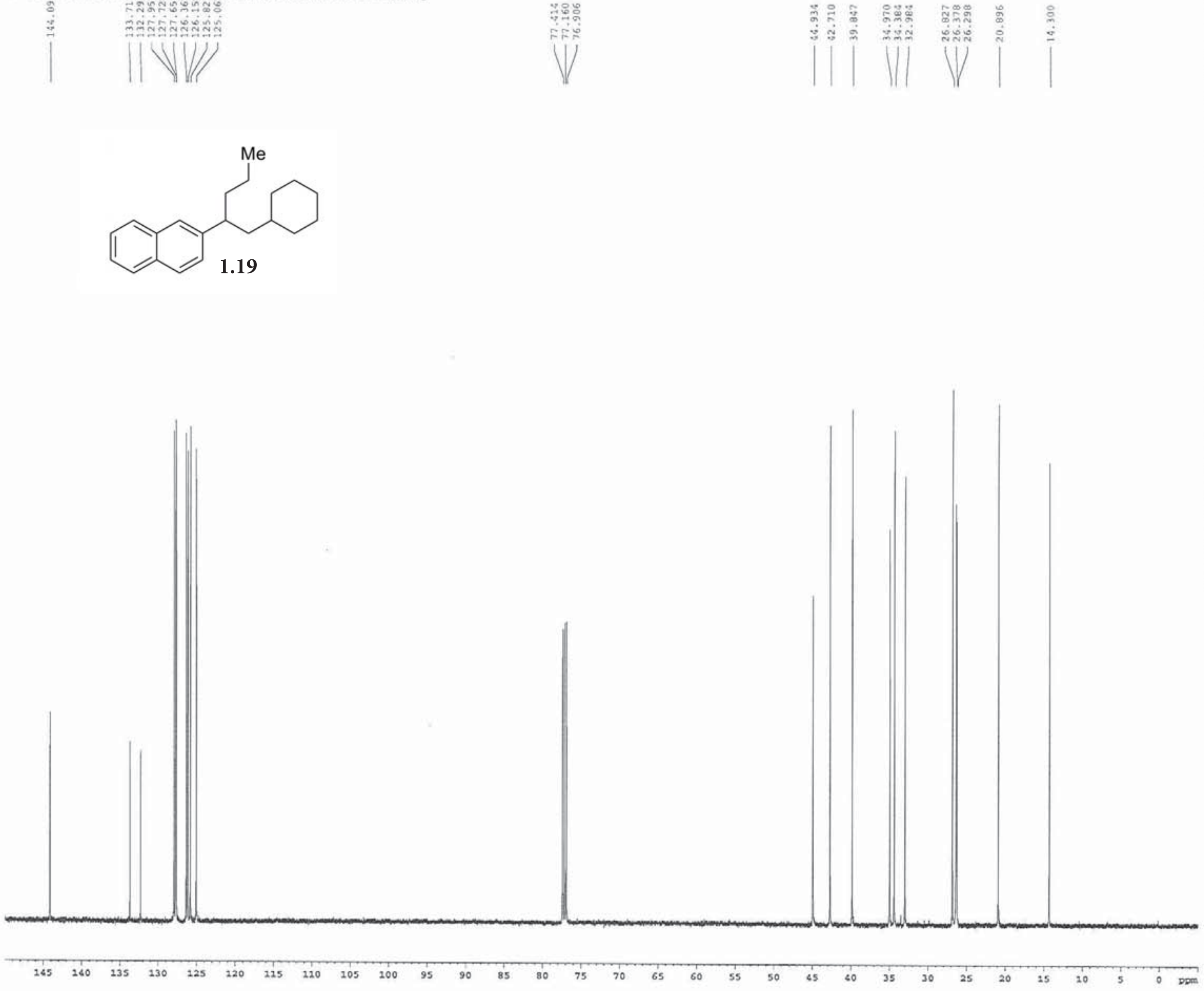
Z-restored spin-echo 13C spectrum with 1H decoupling



```
Current Data Parameters
USER              aaronj
NAME     AGJ_1_prop_6-7
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20111105
Time                0.07
INSTRUM          cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD                 65536
SOLVENT            CDCl3
NS                   999
DS                    16
SWH            30303.031 Hz
FIDRES          0.462388 Hz
AQ             1.0813940 sec
RG                  4096
DW                16.500 usec
DE                  6.00 usec
TE                 300.5 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           125.7804131 MHz
WDW                   EM
SSB                    0
LB                  1.00 Hz
GB                     0
PC                  2.00
```

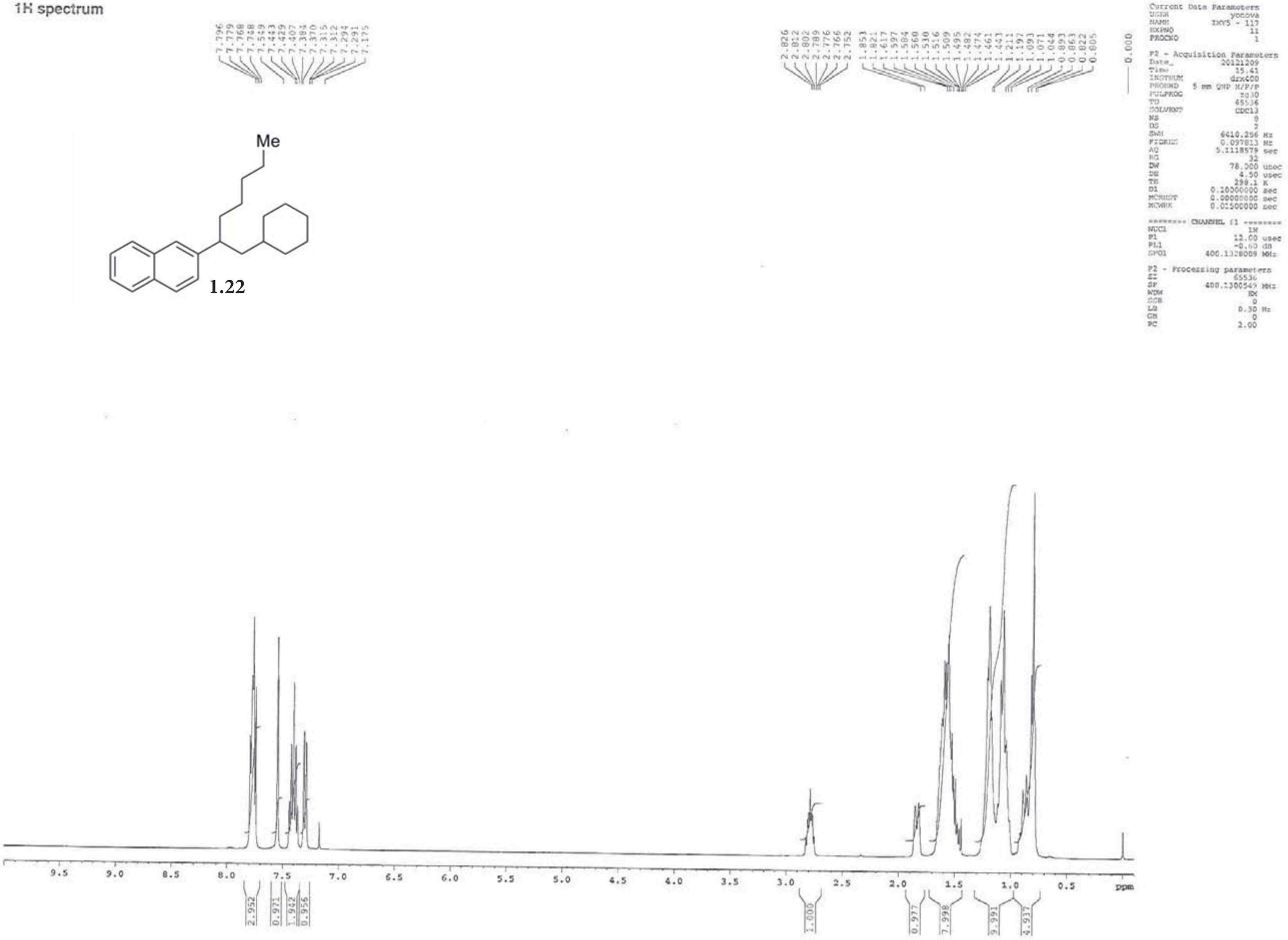

1H spectrum
7.804
7.788
7.775
7.558
7.554
7.453
7.451
7.439
7.438
7.424
7.421
7.416
7.413
7.399
7.386
7.320
7.317
7.303
7.300
7.221
Me
1.19
2.844
2.833
2.825
2.814
2.804
2.796
2.785
1.852
1.827
1.645
1.635
1.626
1.620
1.617
1.608
1.597
1.590
1.579
1.570
1.564
1.522
1.510
1.504
1.494
1.483
1.477
1.466
1.255
1.217
1.203
1.190
1.176
1.173
1.158
1.150
1.144
1.138
1.136
1.131
1.124
1.119
1.109
1.105
1.091
1.073
1.052
0.912
0.894
0.884
0.871
0.861
Current Data Parameters
USER aaronj
NAME AGJ_1_140
EXPNO 3
PROCNO 1
F2 - Acquisition Parameters
Date_ 20120502
Time 23.25
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
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 500.2200512 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00
8.0
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
0.0
ppm
2.966
1.051
1.989
0.952
1.000
1.148
8.186
6.130
5.009

Z–restored spin–echo 13C spectrum with 1H decoupling



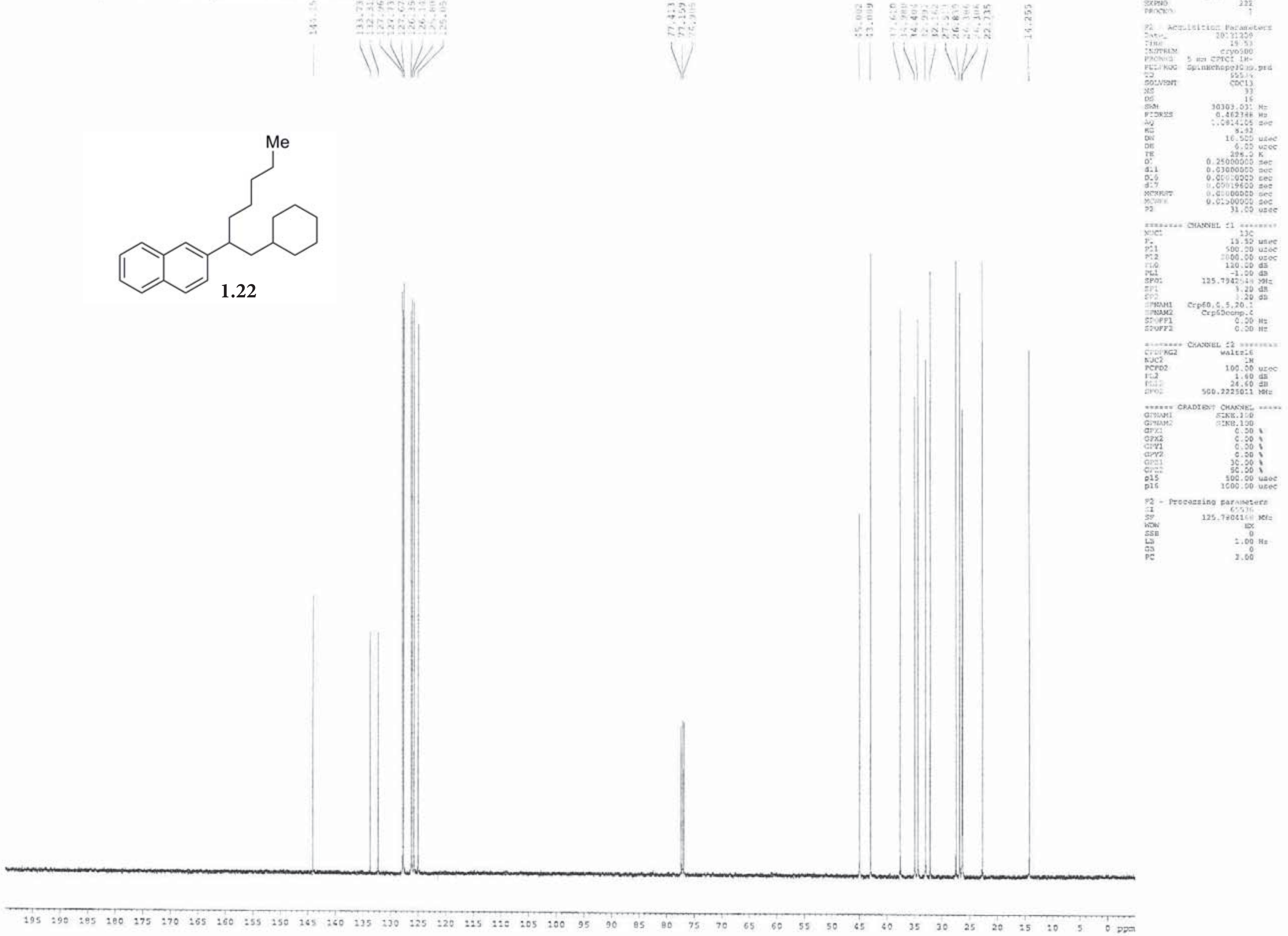
```
Current Data Parameters
USER               aaronj
NAME           AGJ_1_160
EXPNO                  4
PROCNO                 1

F2 - Acquisition Parameters
Date_           20120502
Time               21.32
INSTRUM          cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD                 65536
SOLVENT            CDCl3
NS                   412
DS                    16
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            0.25000000 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           125.7804122 MHz
WDW                   EM
SSB                    0
LB                  1.00 Hz
GB                     0
PC                  2.00
```

1H spectrum



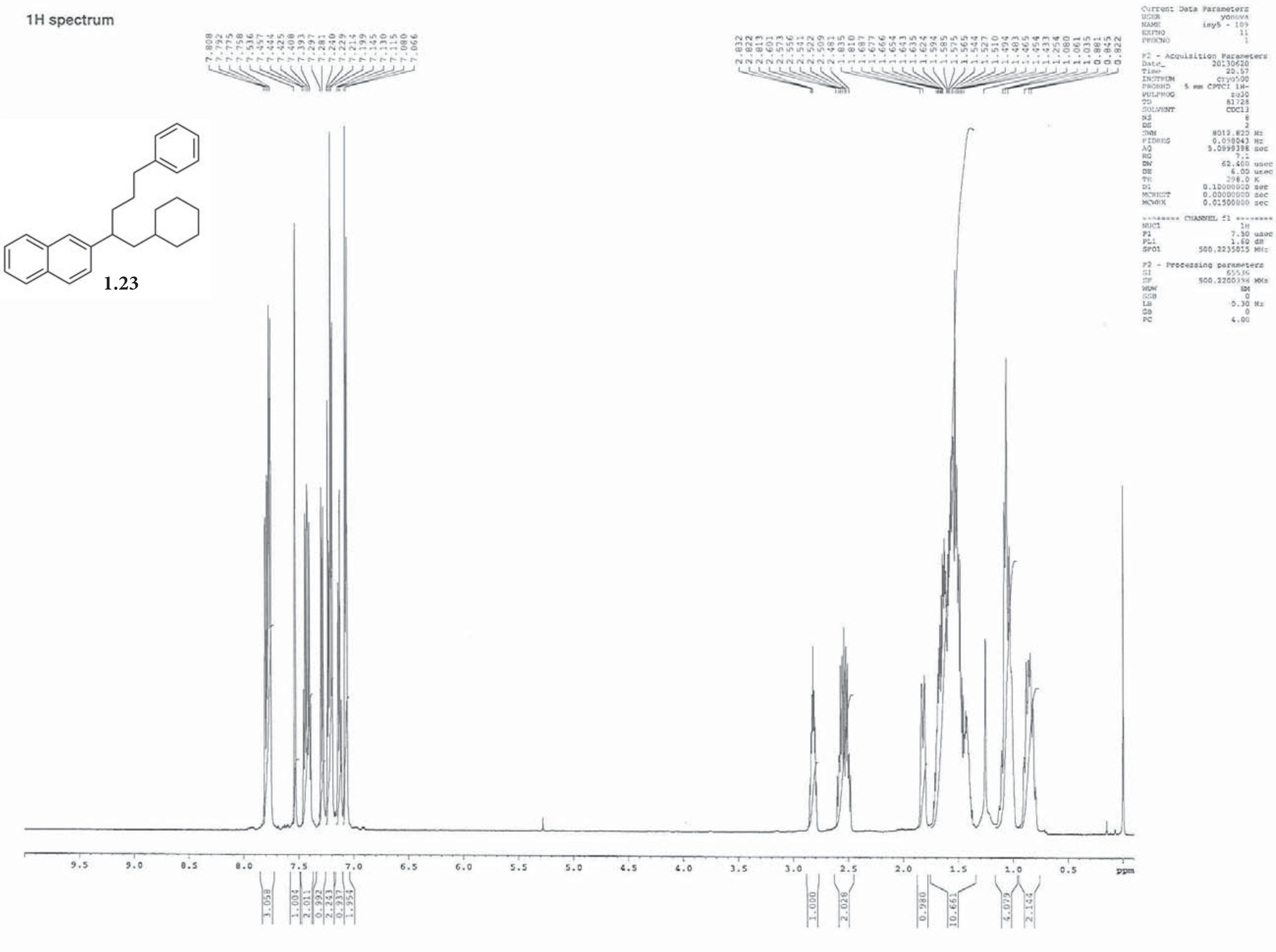
1.22

Z-restored spin-echo 13C spectrum with 1H decoupling

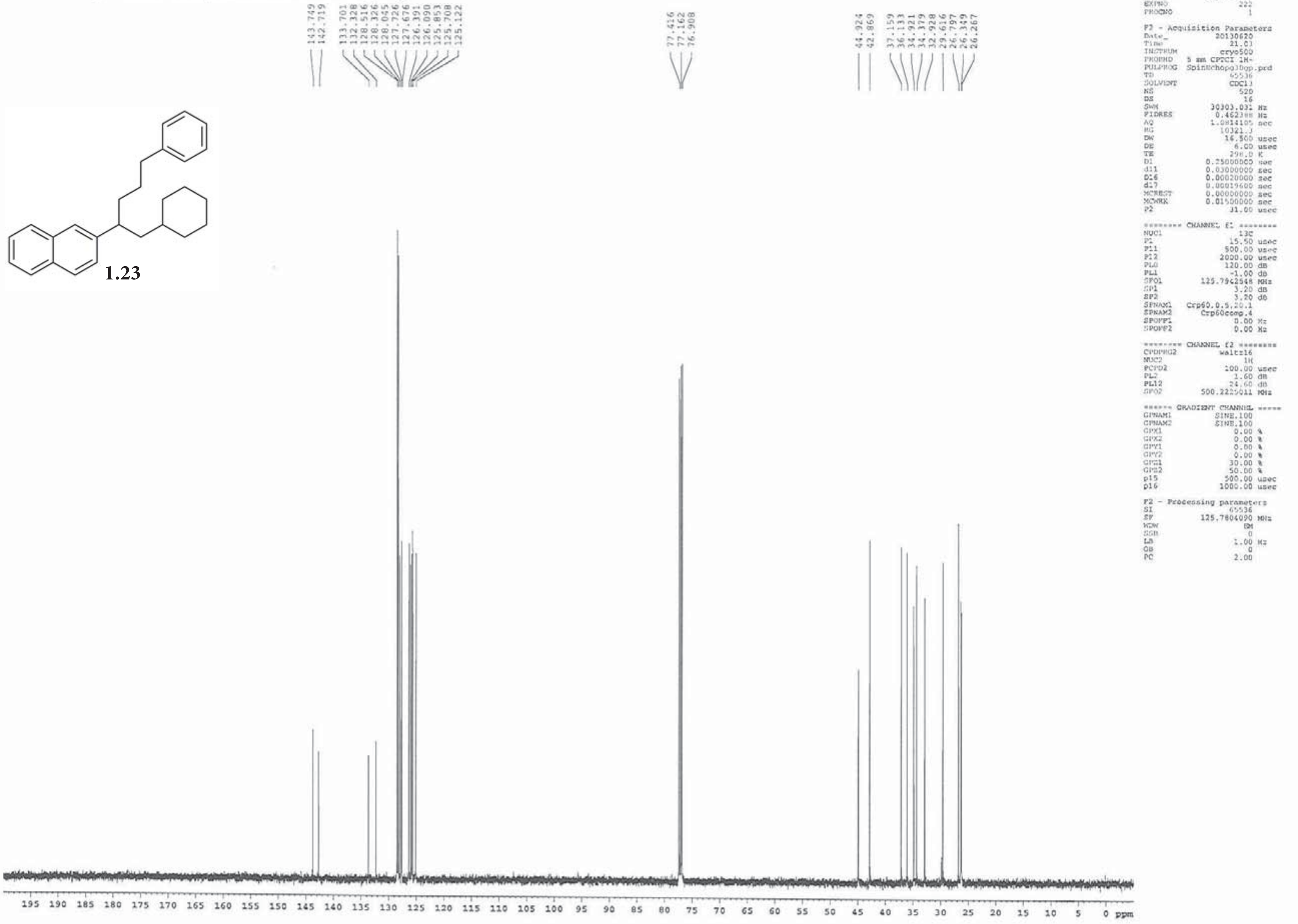


1.22

1H spectrum

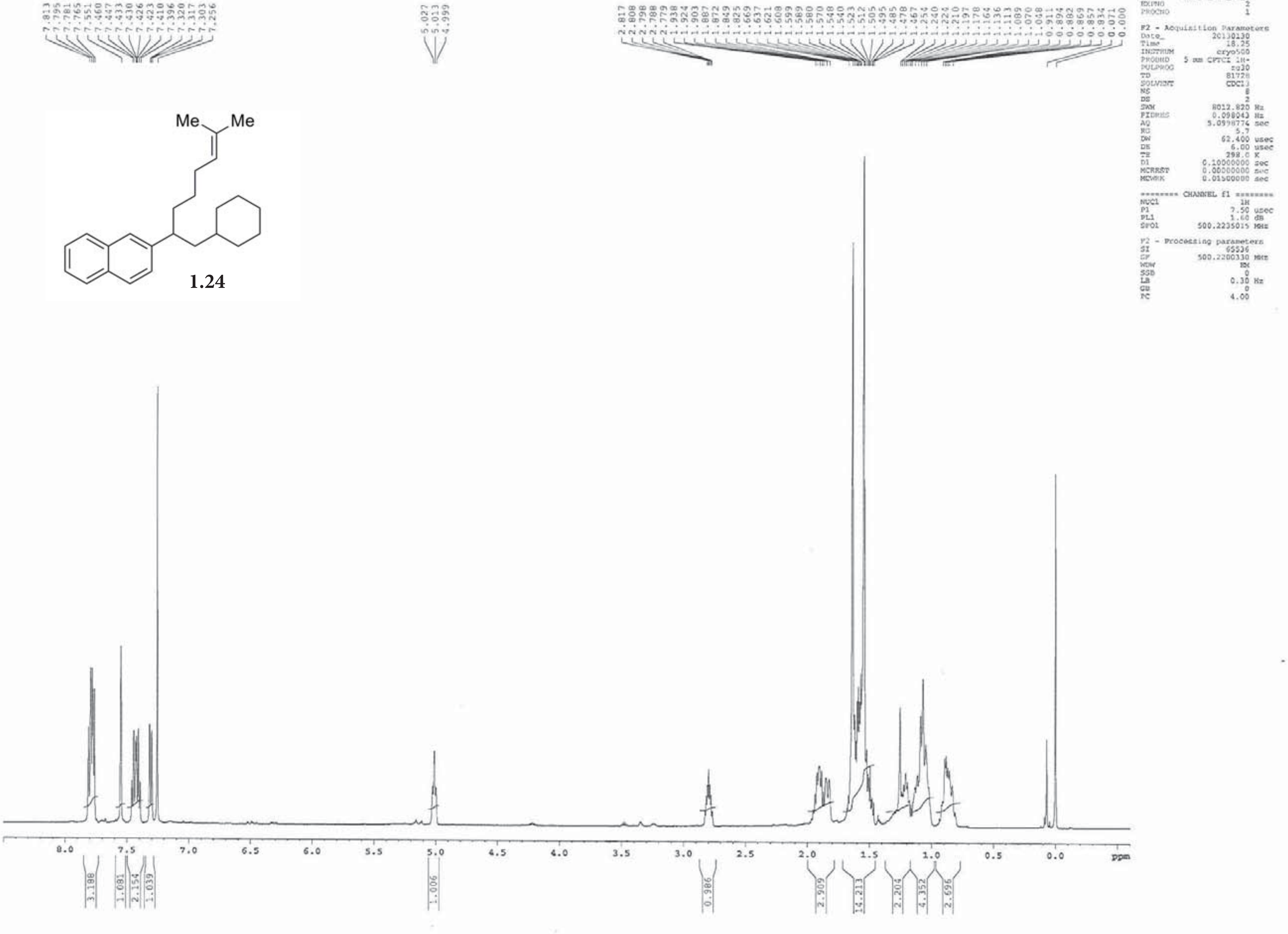

1.23

Z–restored spin–echo 13C spectrum with 1H decoupling

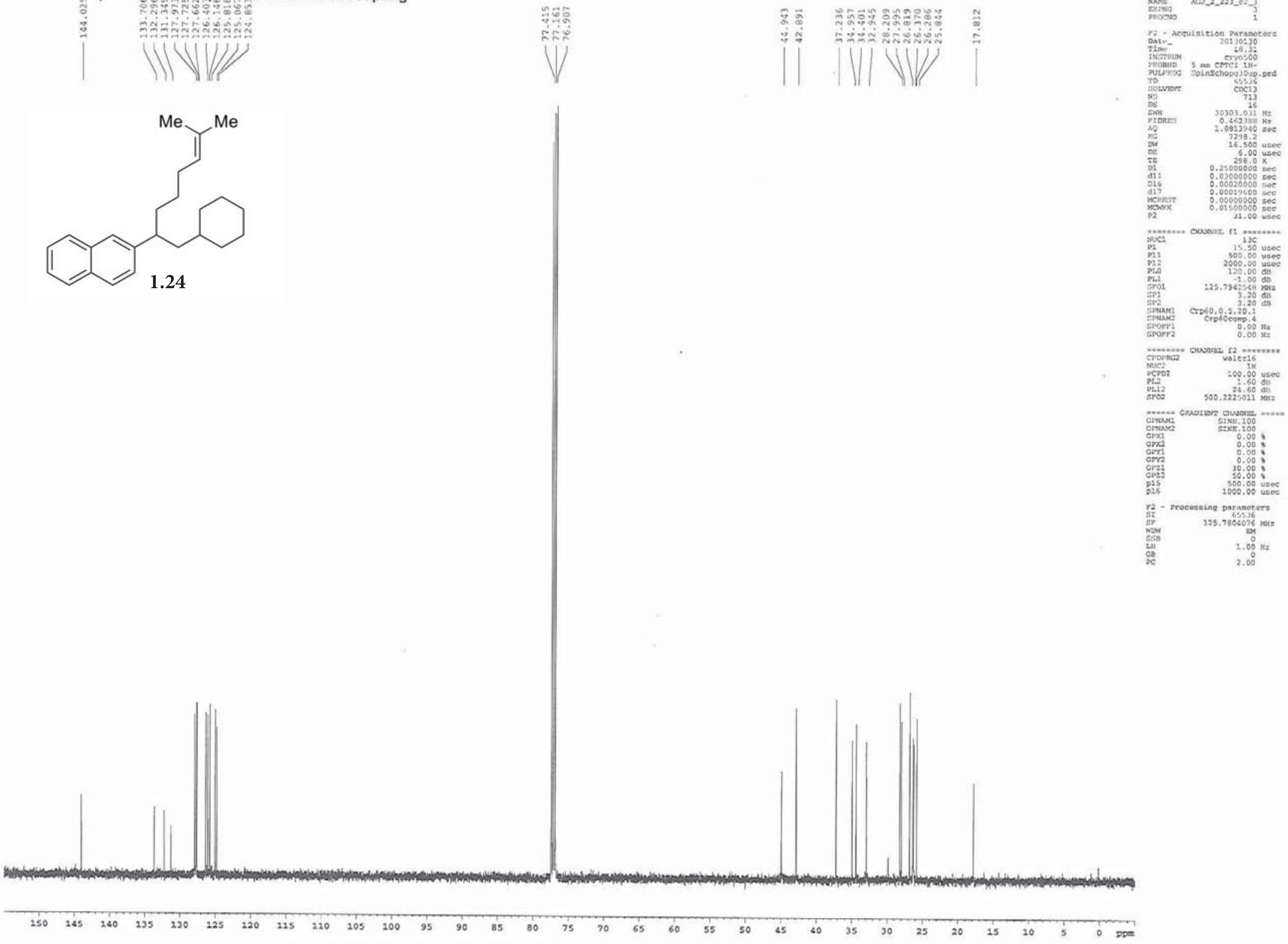


```
Current Data Parameters
USER              ybnovo
NAME           lmy5 - 109
EXPNO                 222
PROCNO                  1

F2 - Acquisition Parameters
Date_            20130620
Time                21.03
INSTRUM           cryo500
PROBHD    5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD                  65536
SOLVENT             CDCl3
NS                    520
DS                     16
SWH          30303.031 Hz
FIDRES        0.462388 Hz
AQ           1.0814105 sec
RG                10321.3
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
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        125.7804090 MHz
WDW                    EM
SSB                     0
LB               1.00 Hz
GB                      0
PC                   2.00
```

1H spectrum


7.813
7.795
7.781
7.765
7.551
7.460
7.447
7.433
7.430
7.426
7.423
7.410
7.396
7.320
7.317
7.303
7.256
5.027
5.013
4.999
2.817
2.808
2.798
2.788
2.779
1.938
1.924
1.903
1.887
1.872
1.849
1.825
1.669
1.637
1.621
1.608
1.599
1.589
1.580
1.570
1.548
1.540
1.523
1.512
1.505
1.495
1.485
1.478
1.467
1.254
1.240
1.224
1.210
1.197
1.178
1.164
1.136
1.113
1.089
1.070
1.048
0.911
0.894
0.882
0.869
0.857
0.834
0.071
0.000
Me
Me
1.24
Current Data Parameters
USER aaronj
NAME AGJ_2_223_c2_j
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20130130
Time 18.25
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 1.60 dB
SFO1 500.2235015 MHz
F2 - Processing parameters
SI 65536
SF 500.2200330 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00
8.0
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
0.0
ppm
3.188
1.081
2.154
1.039
1.006
0.986
2.909
14.213
2.204
4.352
2.696

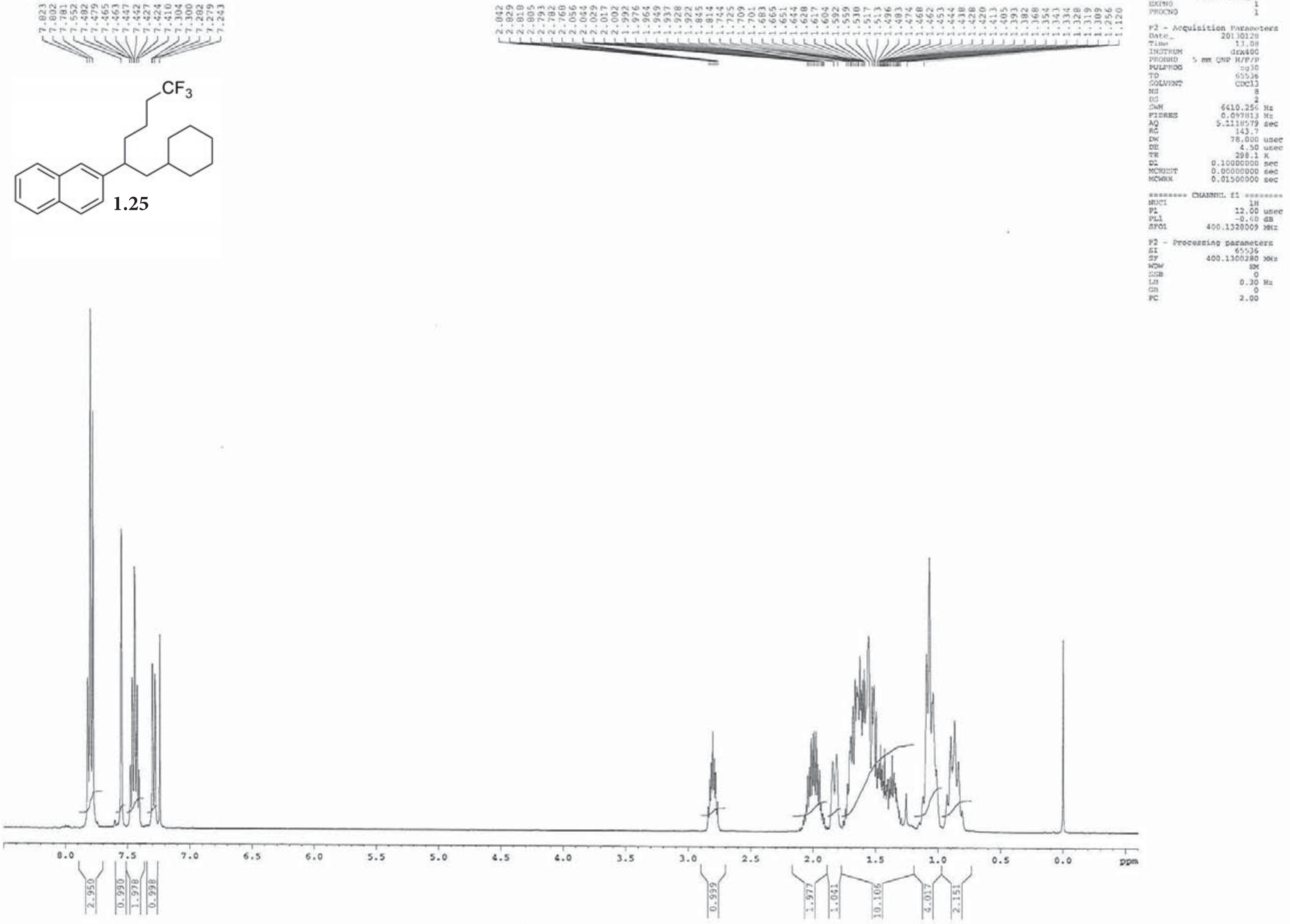
Z–restored spin–echo 13C spectrum with 1H decoupling



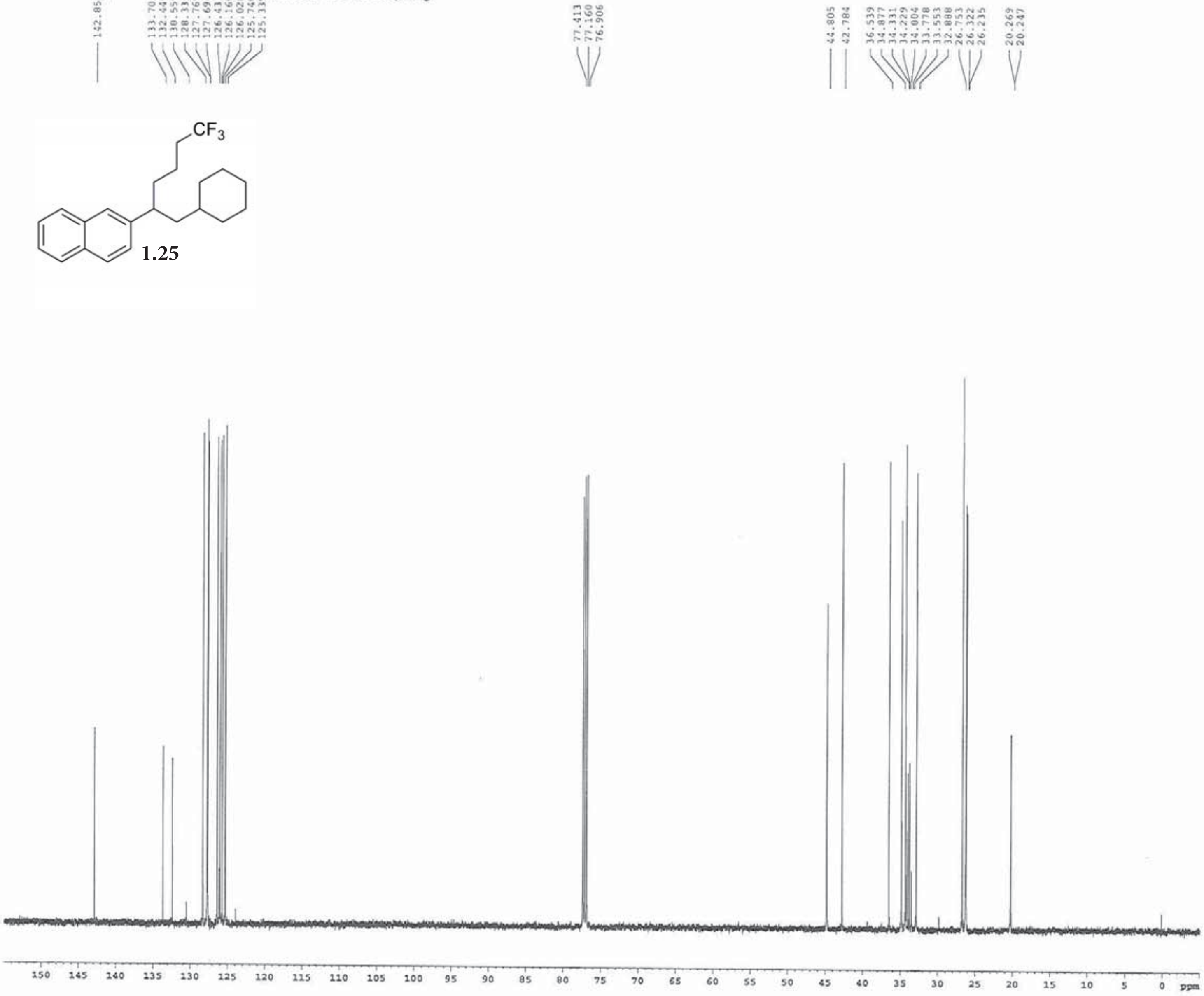
1.24

```
Current Data Parameters
USER             aaronj
NAME      AGJ_2_223_c2_j
EXPNO                 3
PROCNO                1

F2 - Acquisition Parameters
Date_          20130130
Time              18.31
INSTRUM         cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30sp.prd
TD                65536
SOLVENT           CDCl3
NS                  713
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          0.00019400 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          125.7804076 MHz
WDW                  EM
SSB                   0
LB                 1.00 Hz
GB                    0
PC                 2.00
```

1H spectrum

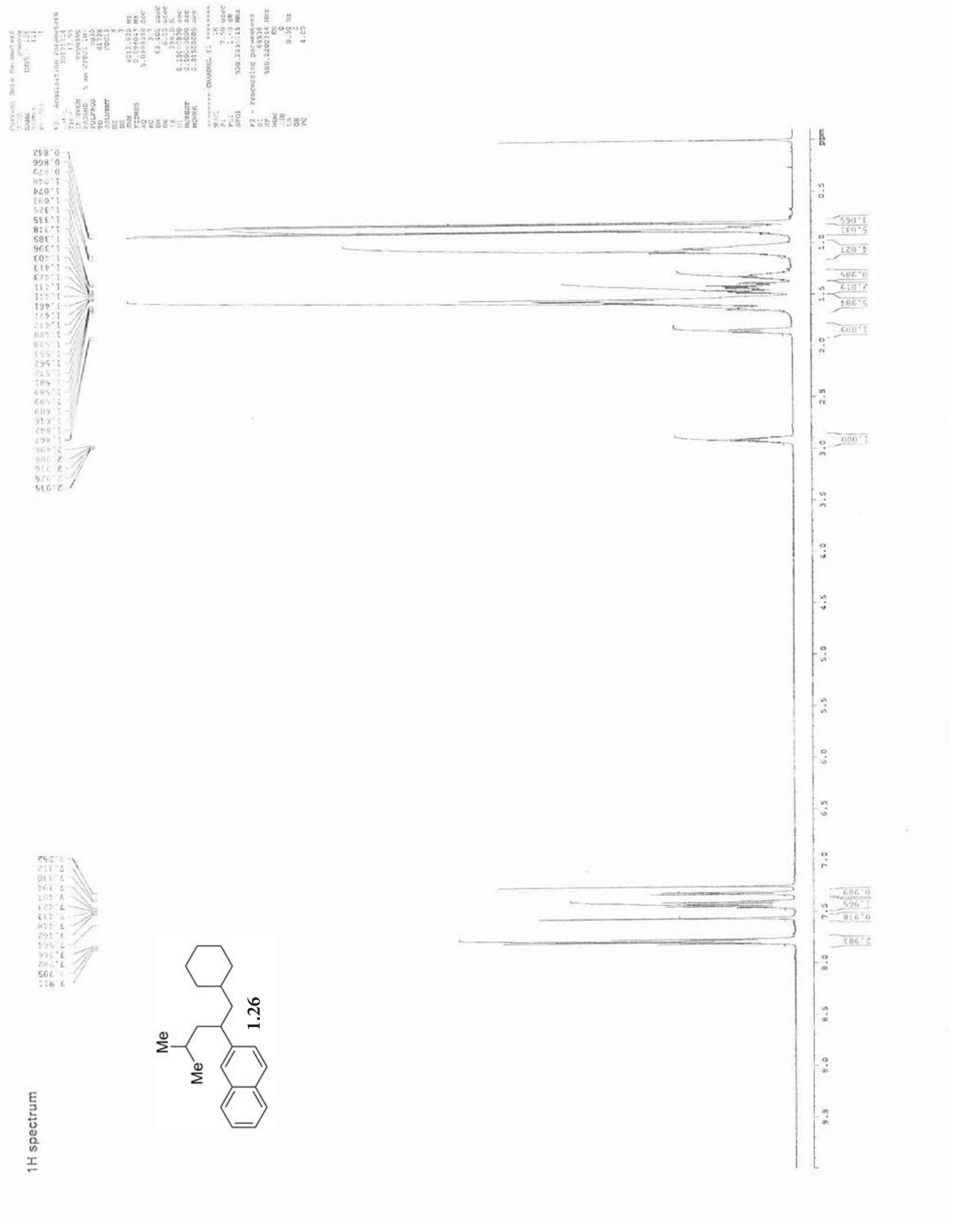

1.25

Z-restored spin-echo 13C spectrum with 1H decoupling



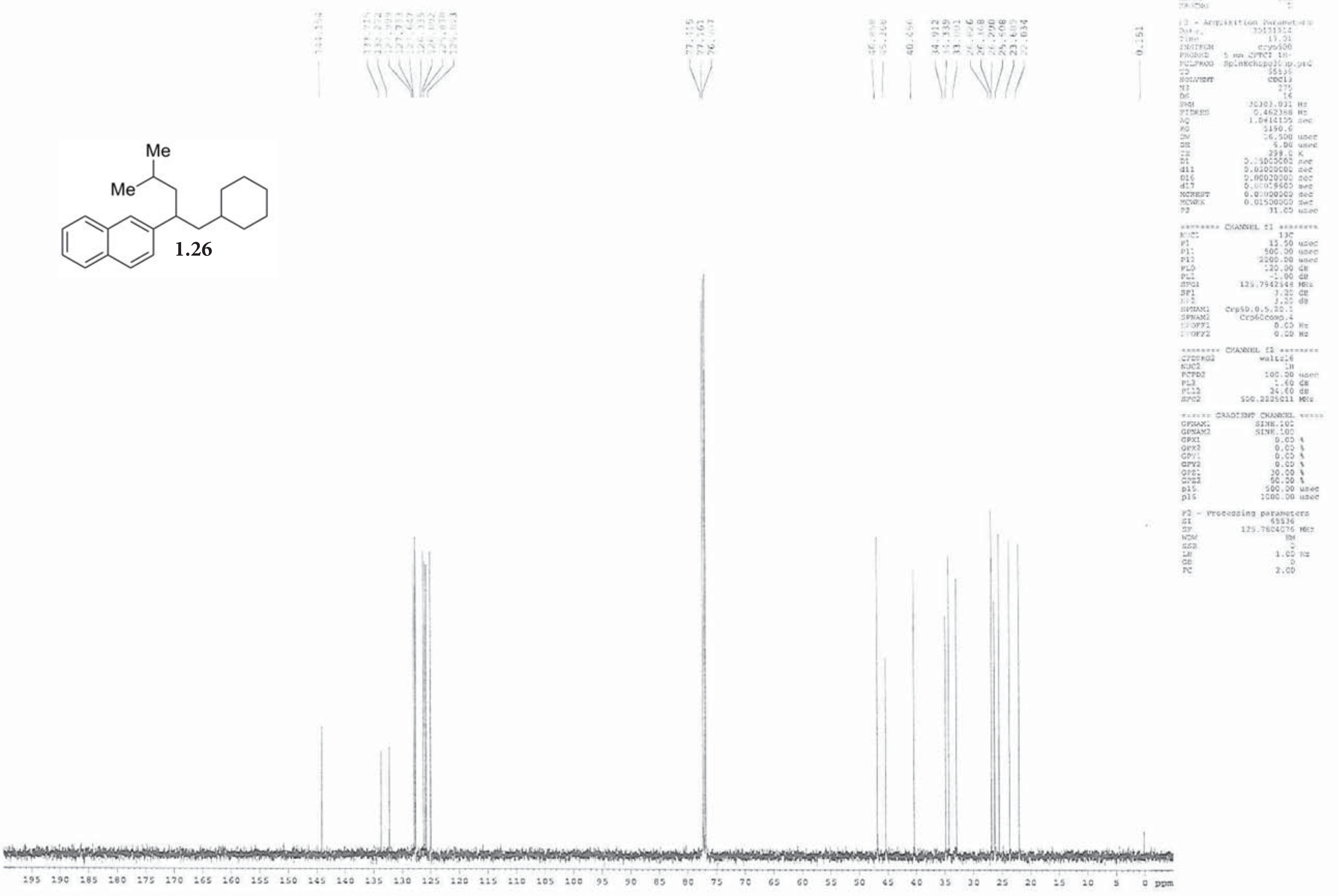
```
Current Data Parameters
USER             aaronj
NAME       AGJ_2_235_c2_j
EXPNO                 1
PROCNO                1

F2 - Acquisition Parameters
Date_          20130129
Time               8.29
INSTRUM         cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD                65536
SOLVENT           CDCl3
NS                  641
DS                   16
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
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          125.7804090 MHz
WDW                  EM
SSB                   0
LB                 1.00 Hz
GB                    0
PC                 2.00
```

1H spectrum



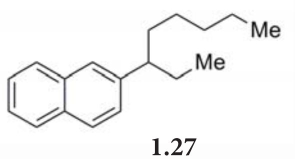
1.26

Z-restored spin-echo 13C spectrum with 1H decoupling

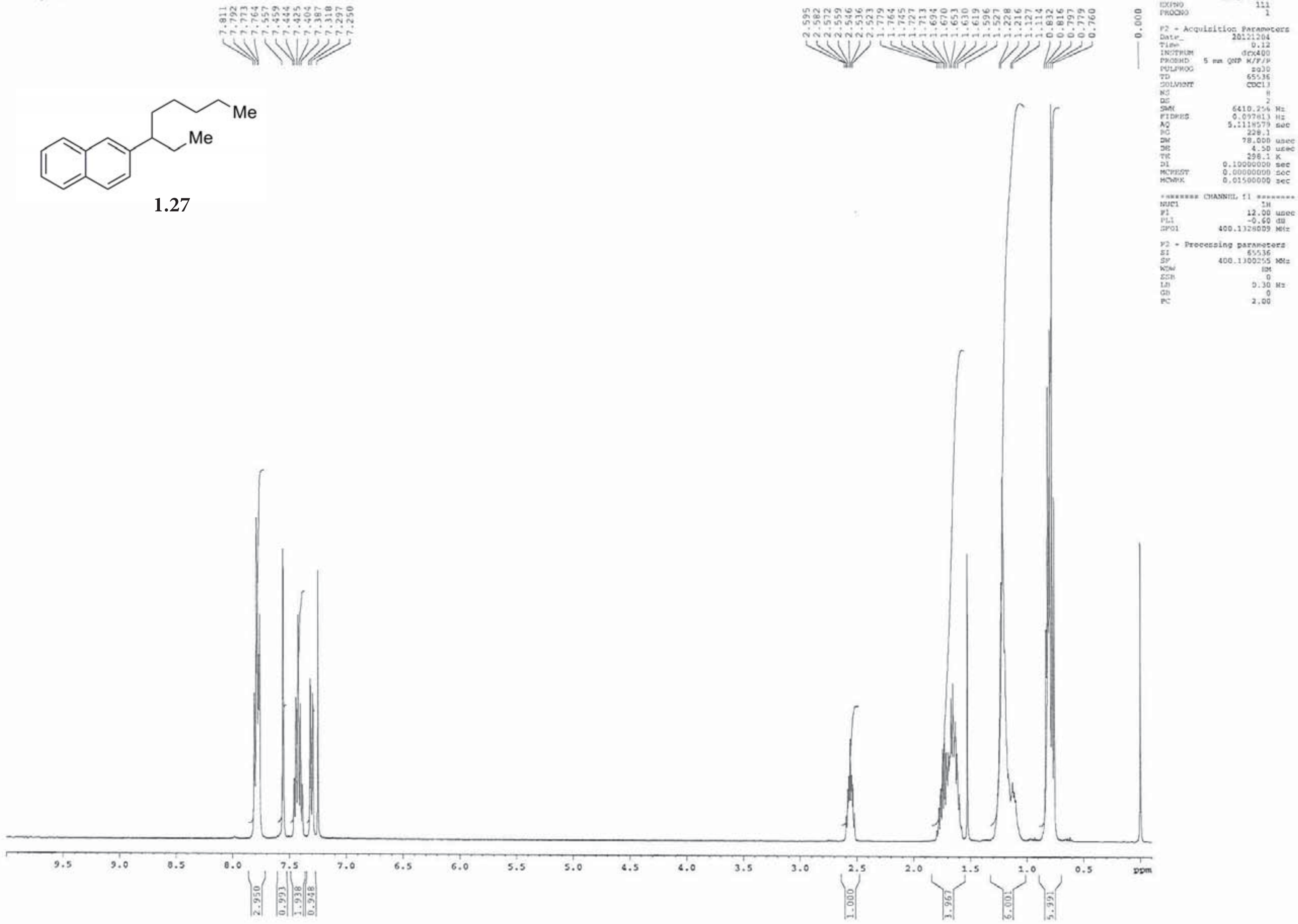


1.26

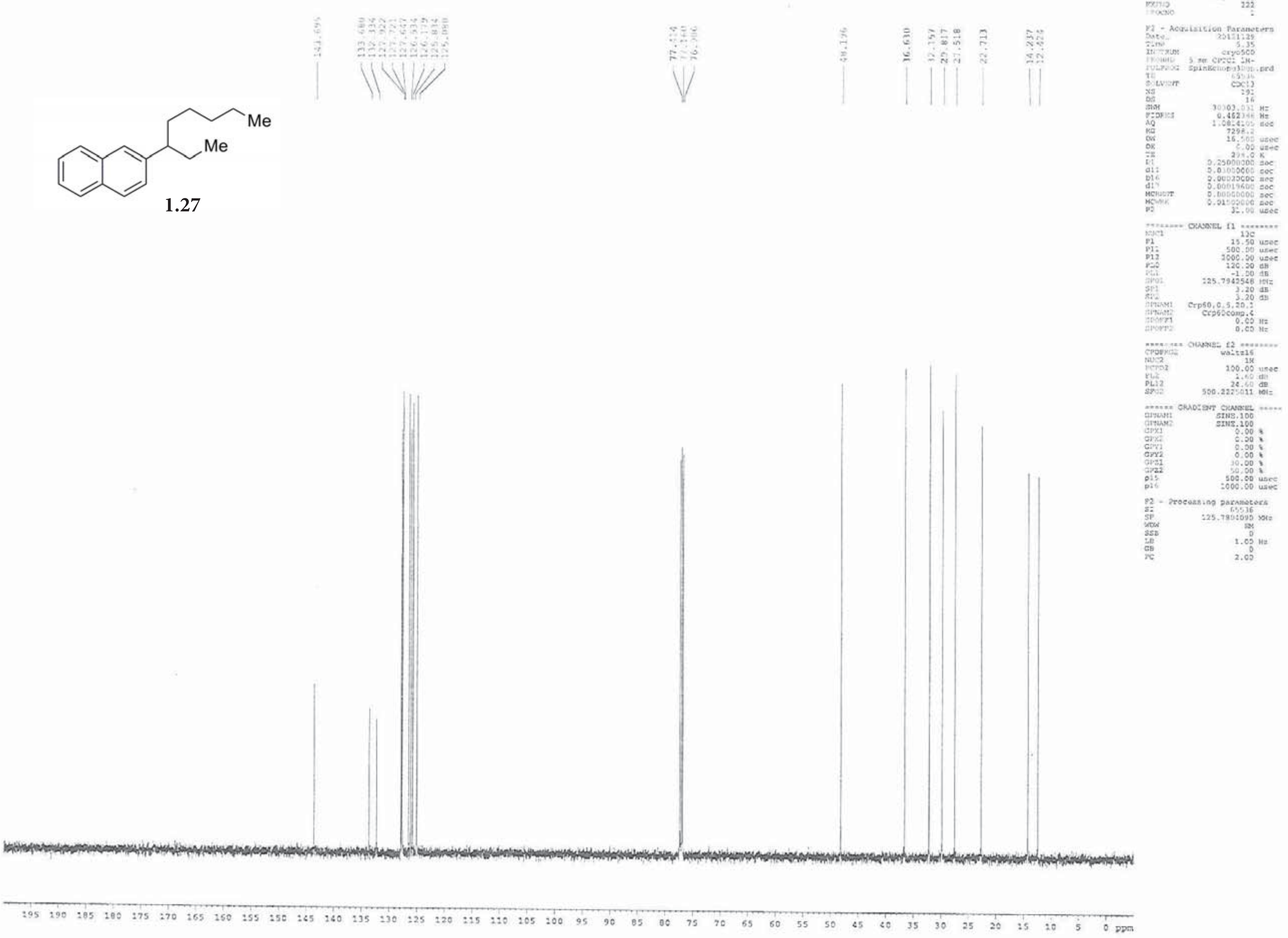
1H spectrum



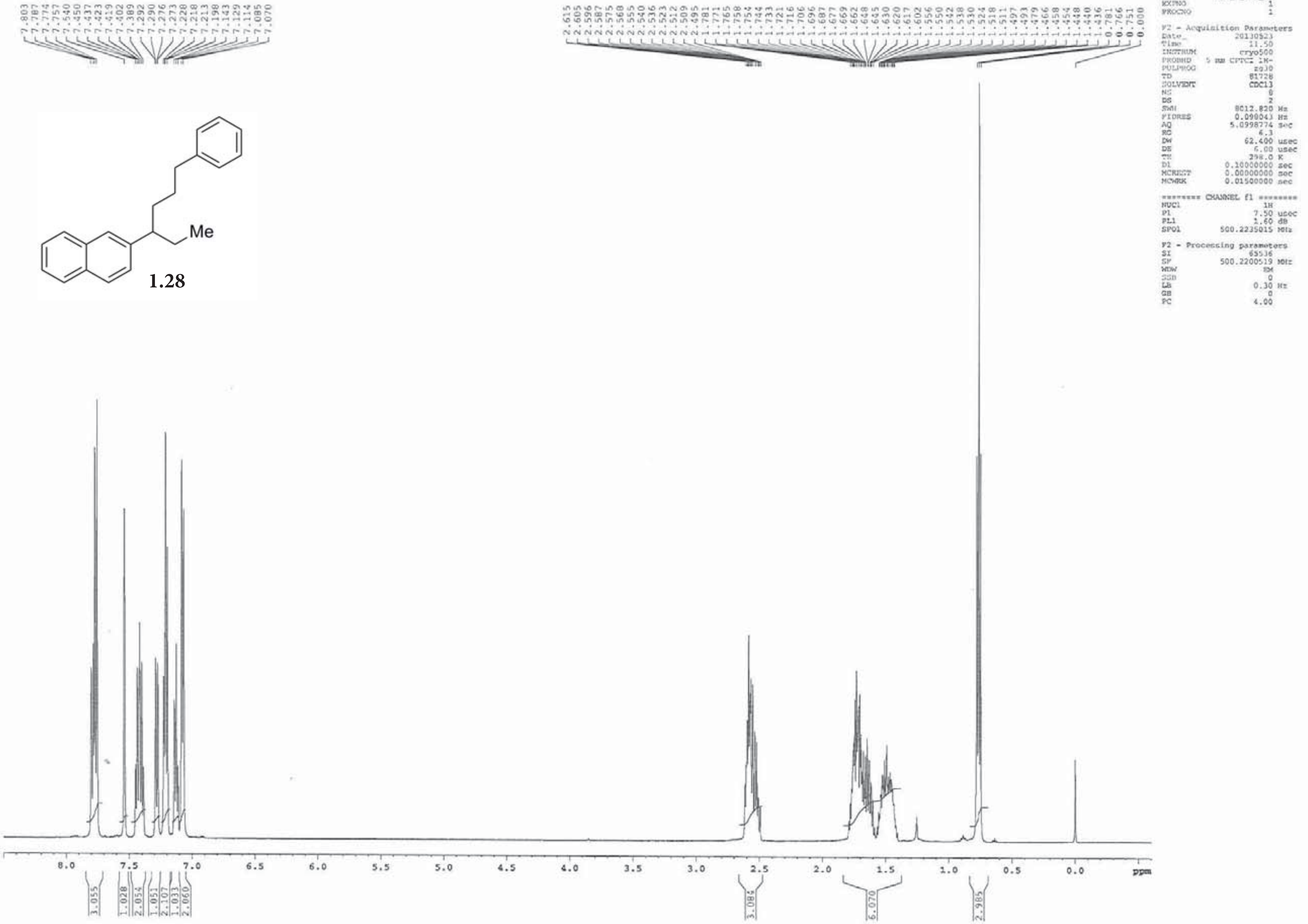
1.27

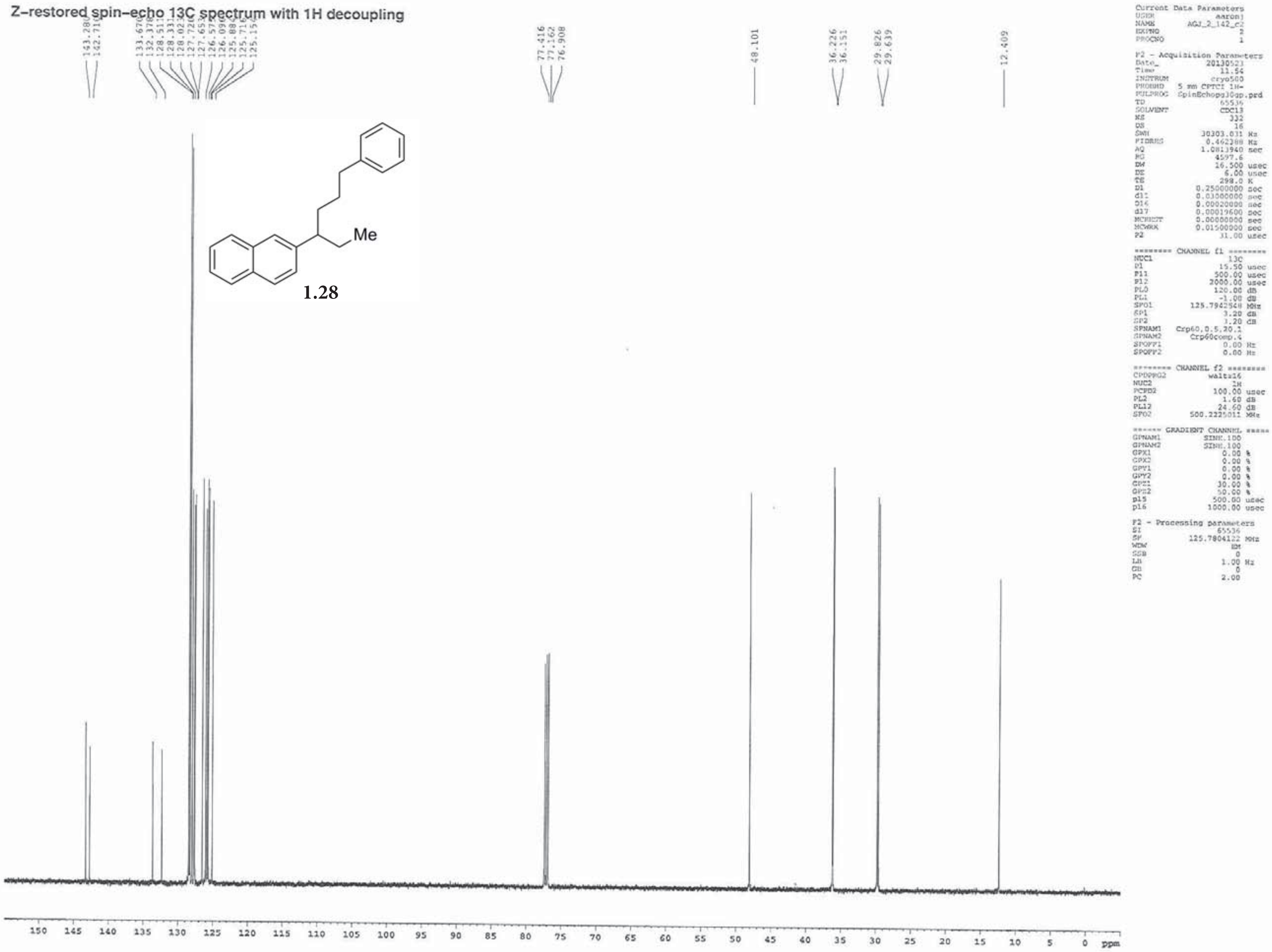


Z-restored spin-echo 13C spectrum with 1H decoupling



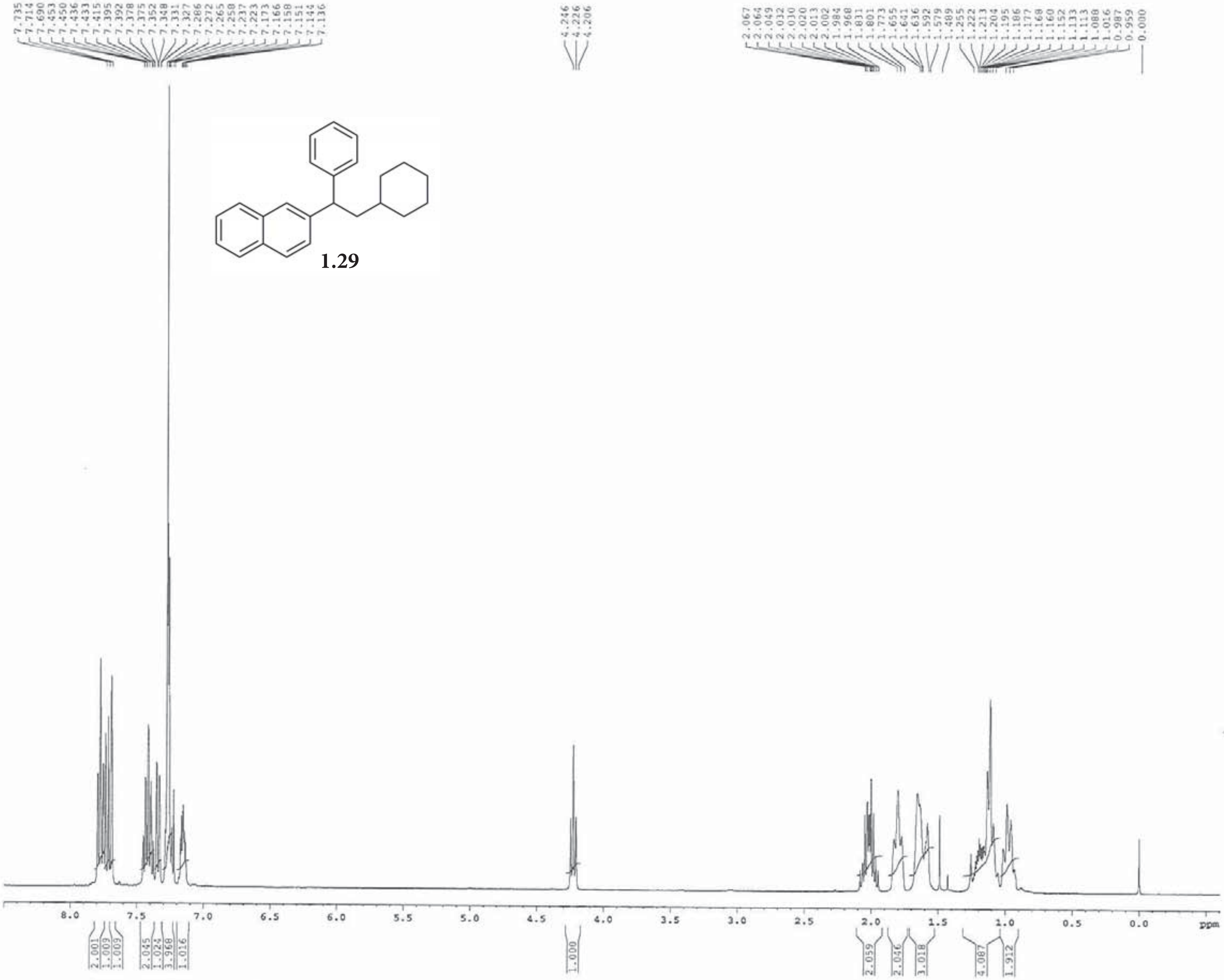
1H spectrum


1.28

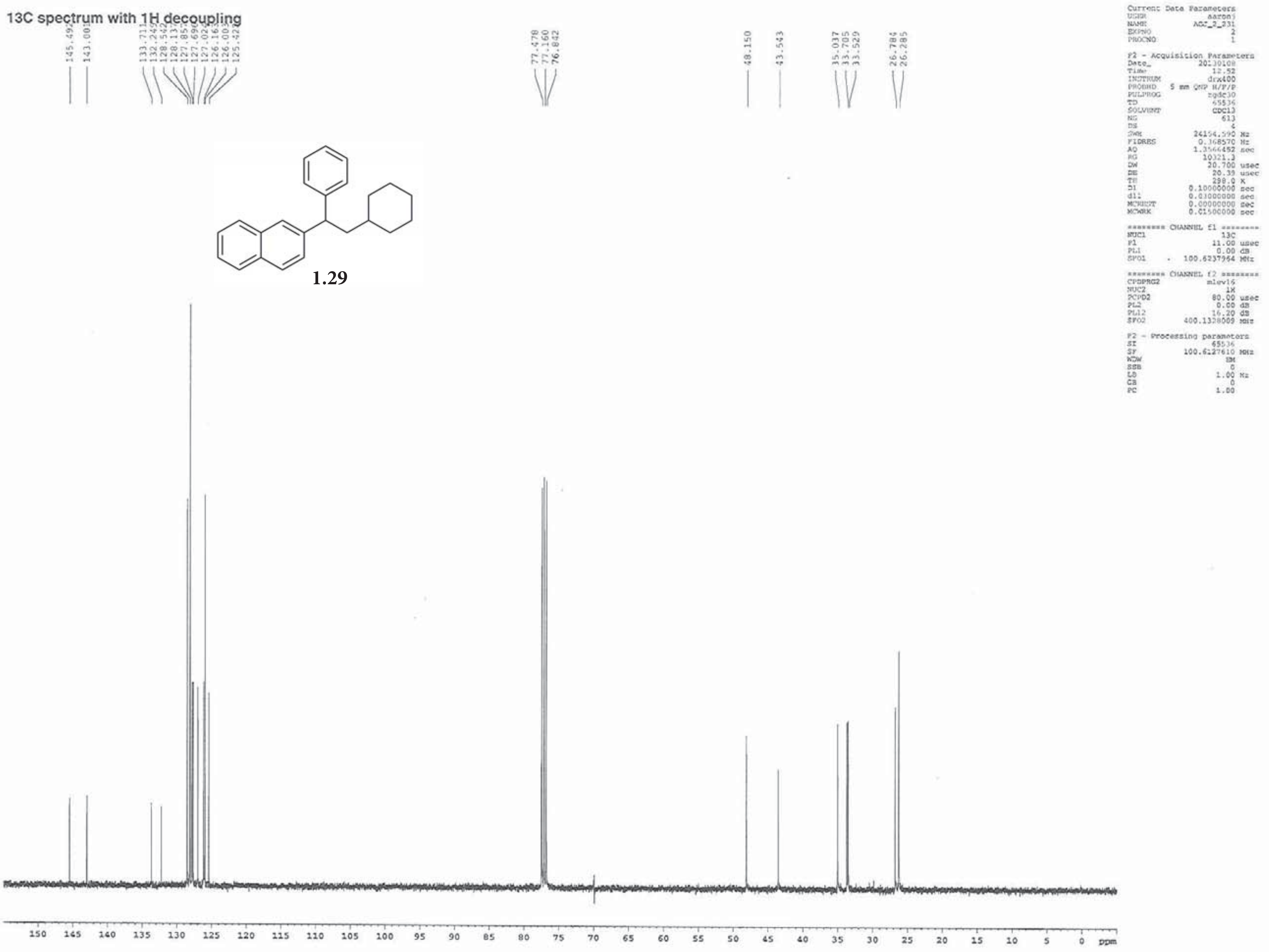

Z–restored spin–echo 13C spectrum with 1H decoupling

1.28

1H spectrum

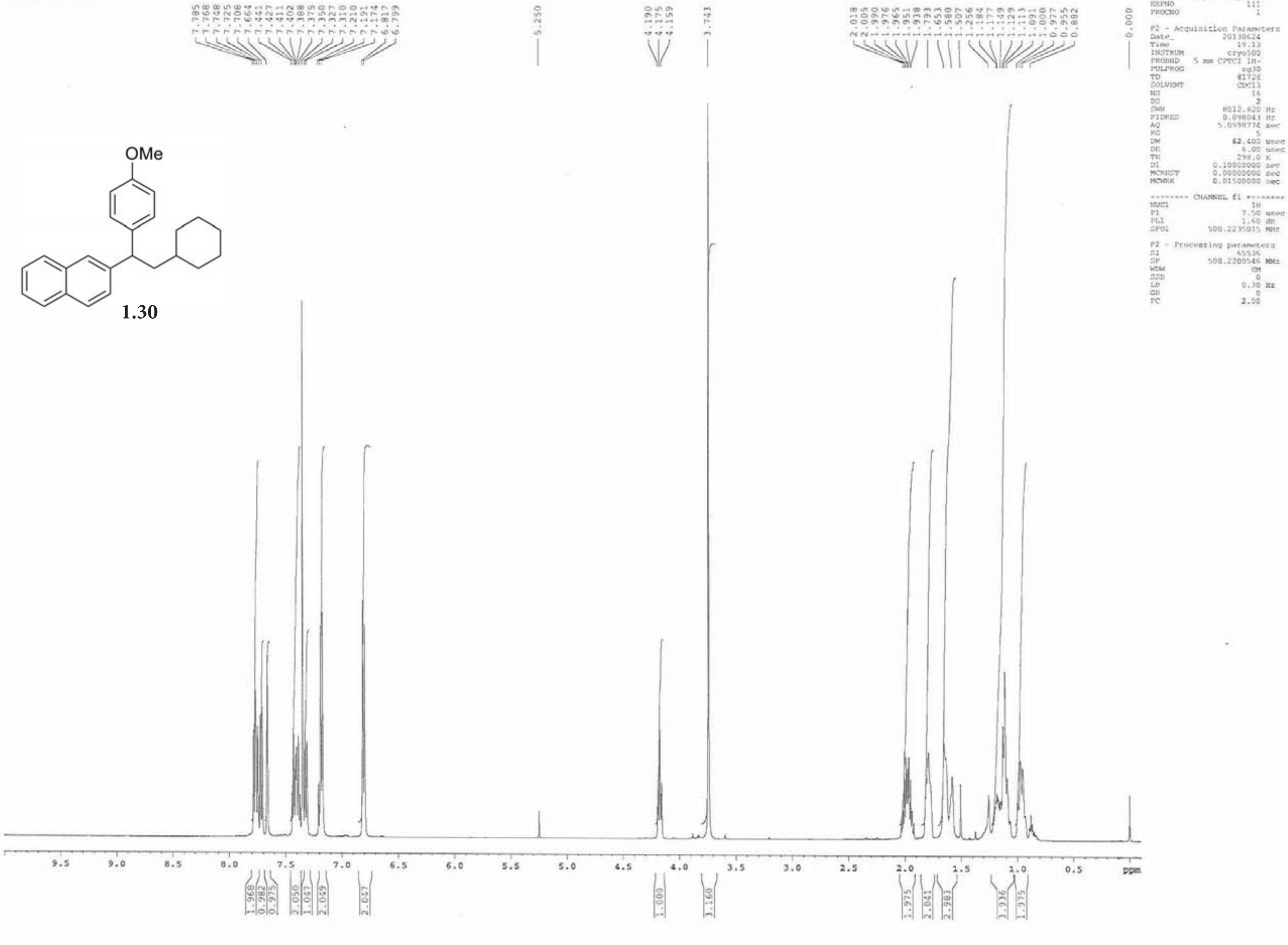


```
Current Data Parameters
USER              aaronj
NAME          AGJ_2_231
EXPNO                 1
PROCNO                1

F2 - Acquisition Parameters
Date_          20130108
Time              11.57
INSTRUM          drx400
PROBHD   5 mm QNP H/F/P
PULPROG            zg30
TD                65536
SOLVENT           CDCl3
NS                    8
DS                    2
SWH            6410.256 Hz
FIDRES         0.097813 Hz
AQ            5.1118579 sec
RG                  114
DW               78.000 usec
DE                 4.50 usec
TE                298.0 K
D1           0.10000000 sec
MCREST       0.00000000 sec
MCWRK        0.01500000 sec

======== CHANNEL f1 ========
NUC1                 1H
P1                12.00 usec
PL1               -0.60 dB
SFO1        400.1328009 MHz

F2 - Processing parameters
SI                65536
SF          400.1300361 MHz
WDW                  EM
SSB                   0
LB                 0.30 Hz
GB                    0
PC                 2.00
```

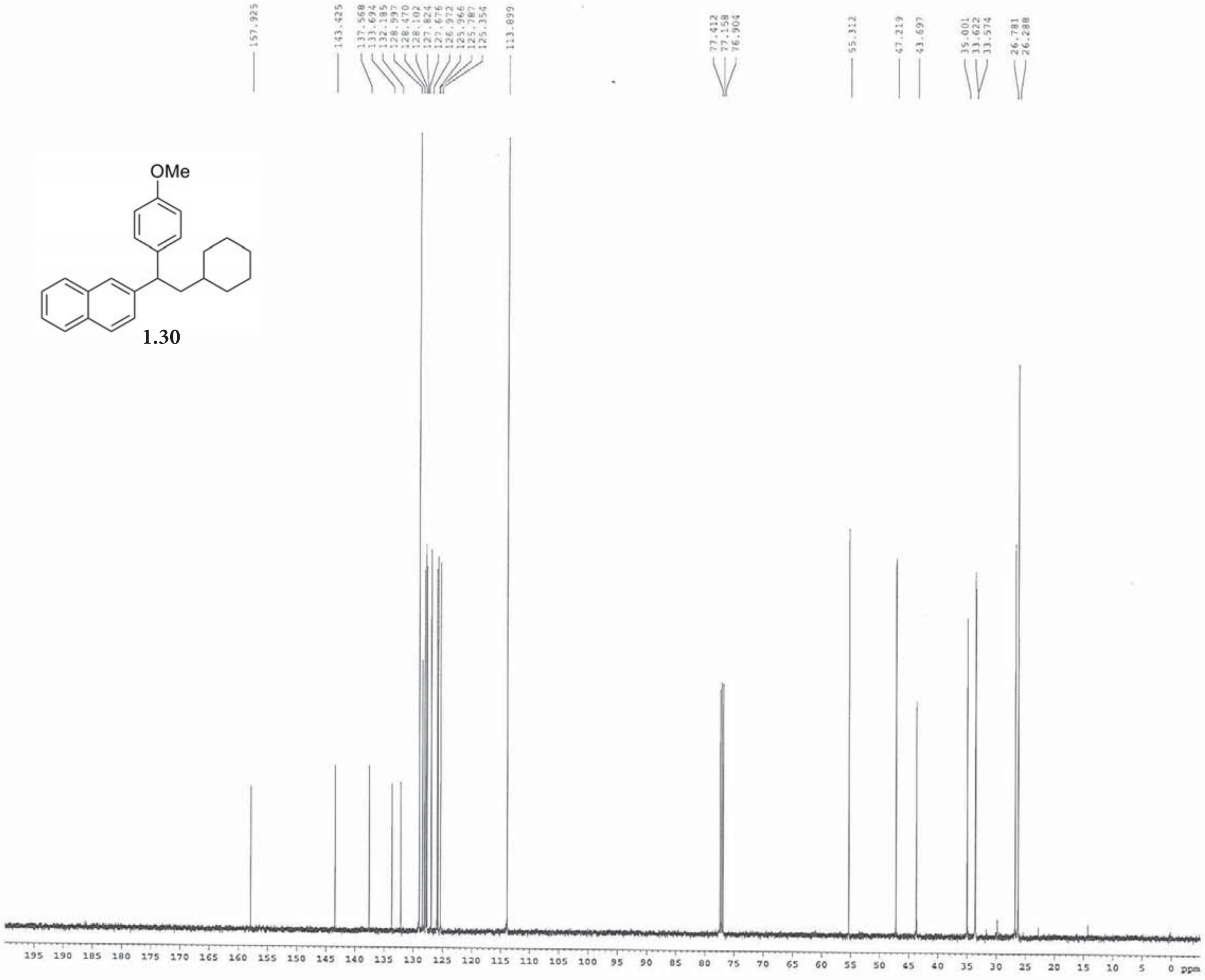

13C spectrum with 1H decoupling

1.29

1H spectrum


1.30

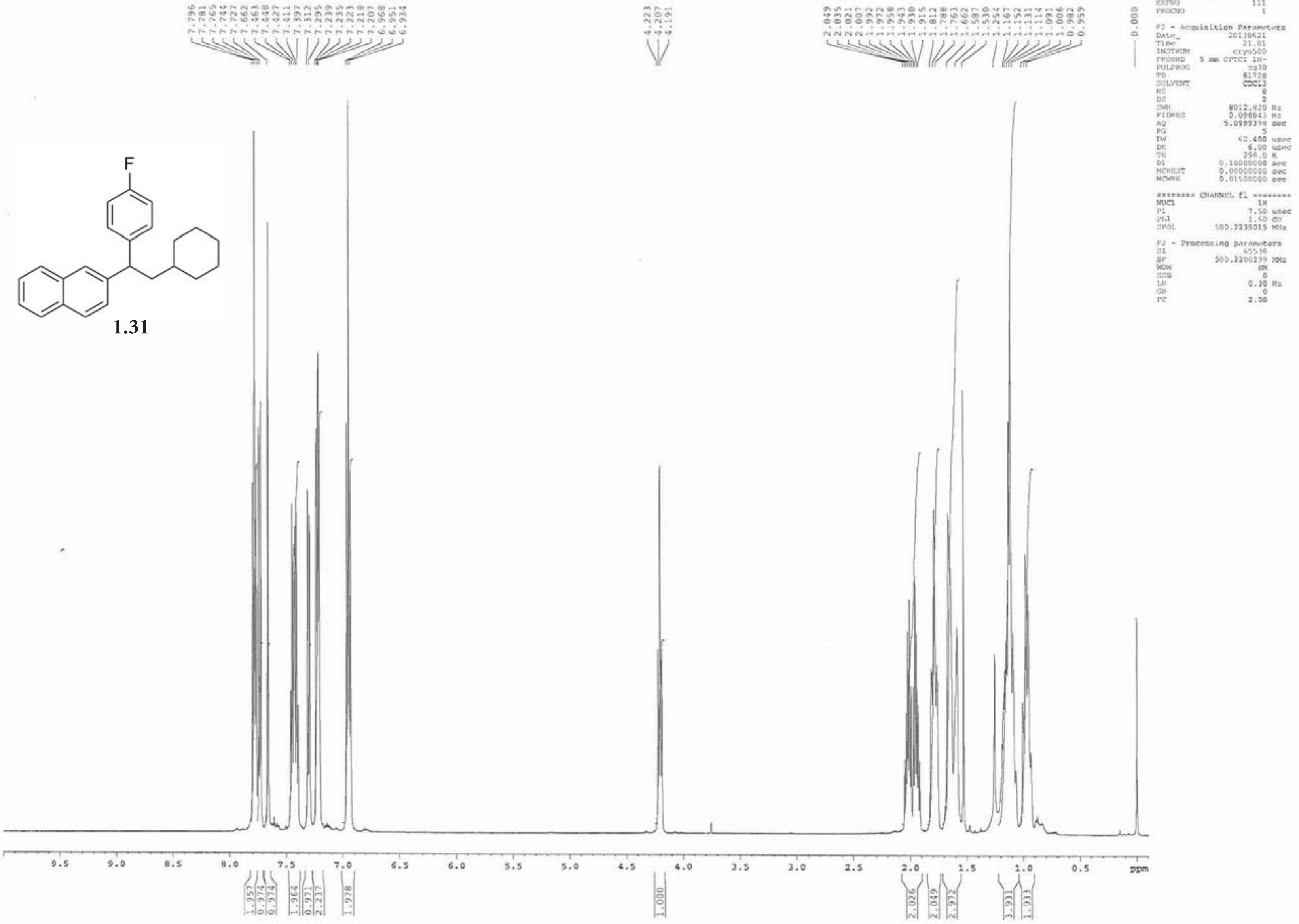
Z–restored spin–echo 13C spectrum with 1H decoupling



1.30

```
Current Data Parameters
USER            yonova
NAME     imy5 - agj2-272
EXPNO              222
PROCNO               1

F2 - Acquisition Parameters
Date_          20130624
Time              19.20
INSTRUM         cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD                65536
SOLVENT           CDCl3
NS                  207
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          125.7804140 MHz
WDW                  EM
SSB                   0
LB                 1.00 Hz
GB                    0
PC                 4.00
```

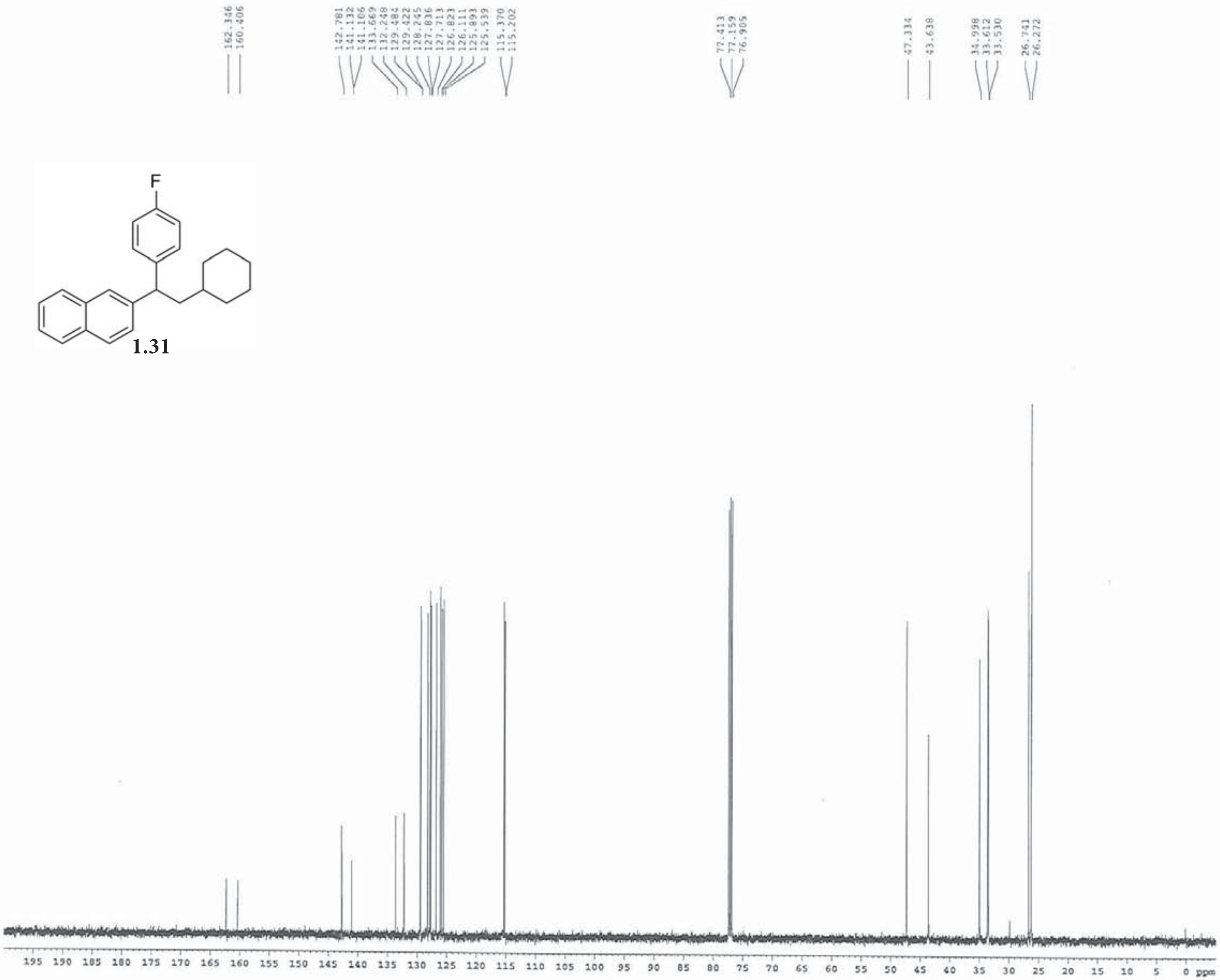
1H spectrum



```
Current Data Parameters
USER              yonova
NAME      lmy5 - agj2-281
EXPNO                111
PROCNO                 1

F2 - Acquisition Parameters
Date_           20130621
Time               21.01
INSTRUM          cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG             zg30
TD                 61728
SOLVENT            CDCl3
NS                     8
DS                     2
SWH             8012.820 Hz
FIDRES          0.098043 Hz
AQ             5.0999398 sec
RG                     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           500.2200399 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  2.00
```

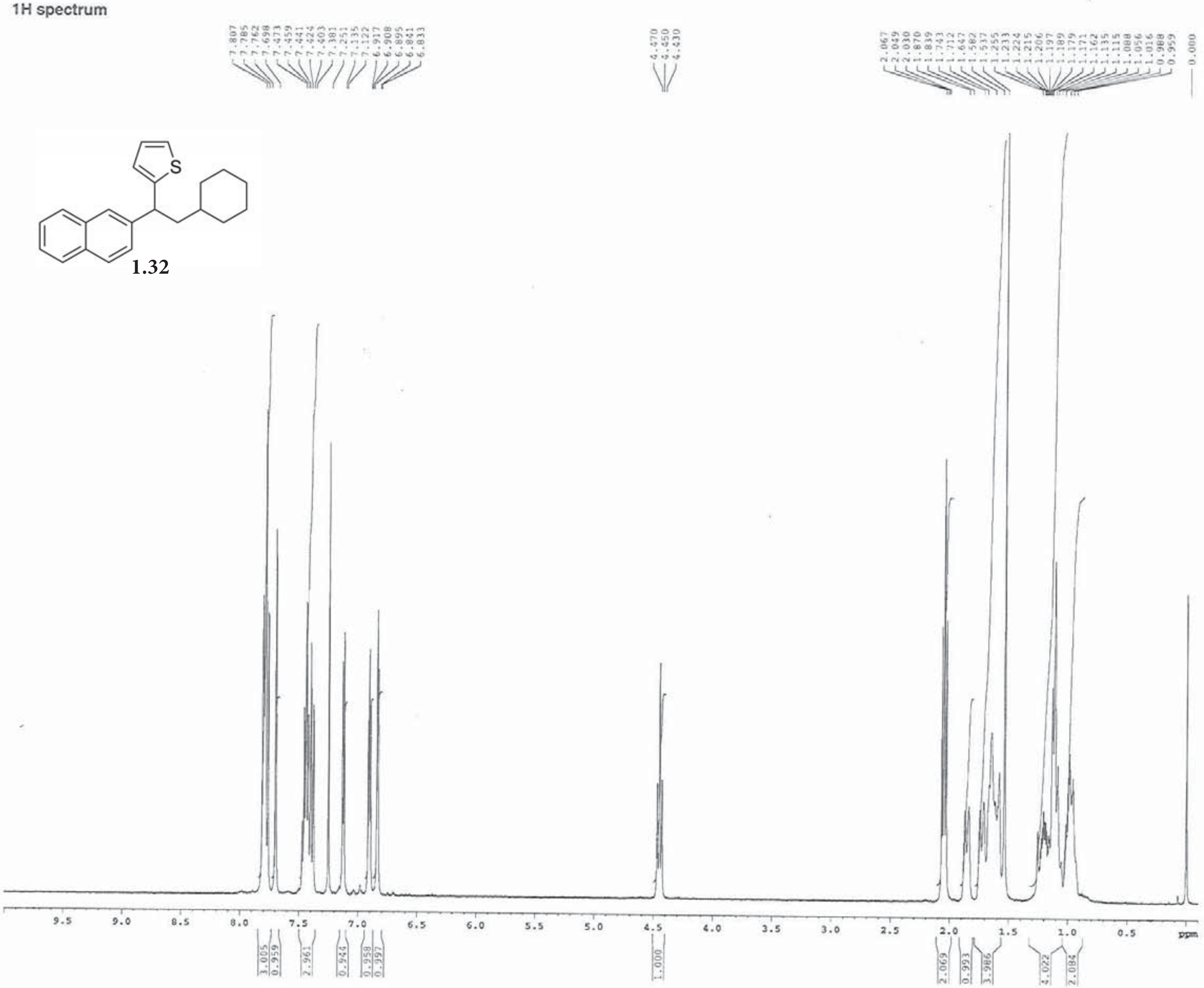
Z–restored spin–echo 13C spectrum with 1H decoupling

1.31



```
Current Data Parameters
USER              yonova
NAME      imy5 - agj2-281
EXPNO                222
PROCNO                 1

F2 - Acquisition Parameters
Date_           20130621
Time               21.07
INSTRUM          cryo500
PROBHD     5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD                 65536
SOLVENT            CDCl3
NS                   238
DS                    16
SWH            30303.031 Hz
FIDRES          0.462388 Hz
AQ             1.0814105 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         125.7942546 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           125.7804094 MHz
WDW                   EM
SSB                    0
LB                  1.00 Hz
GB                     0
PC                  2.00
```

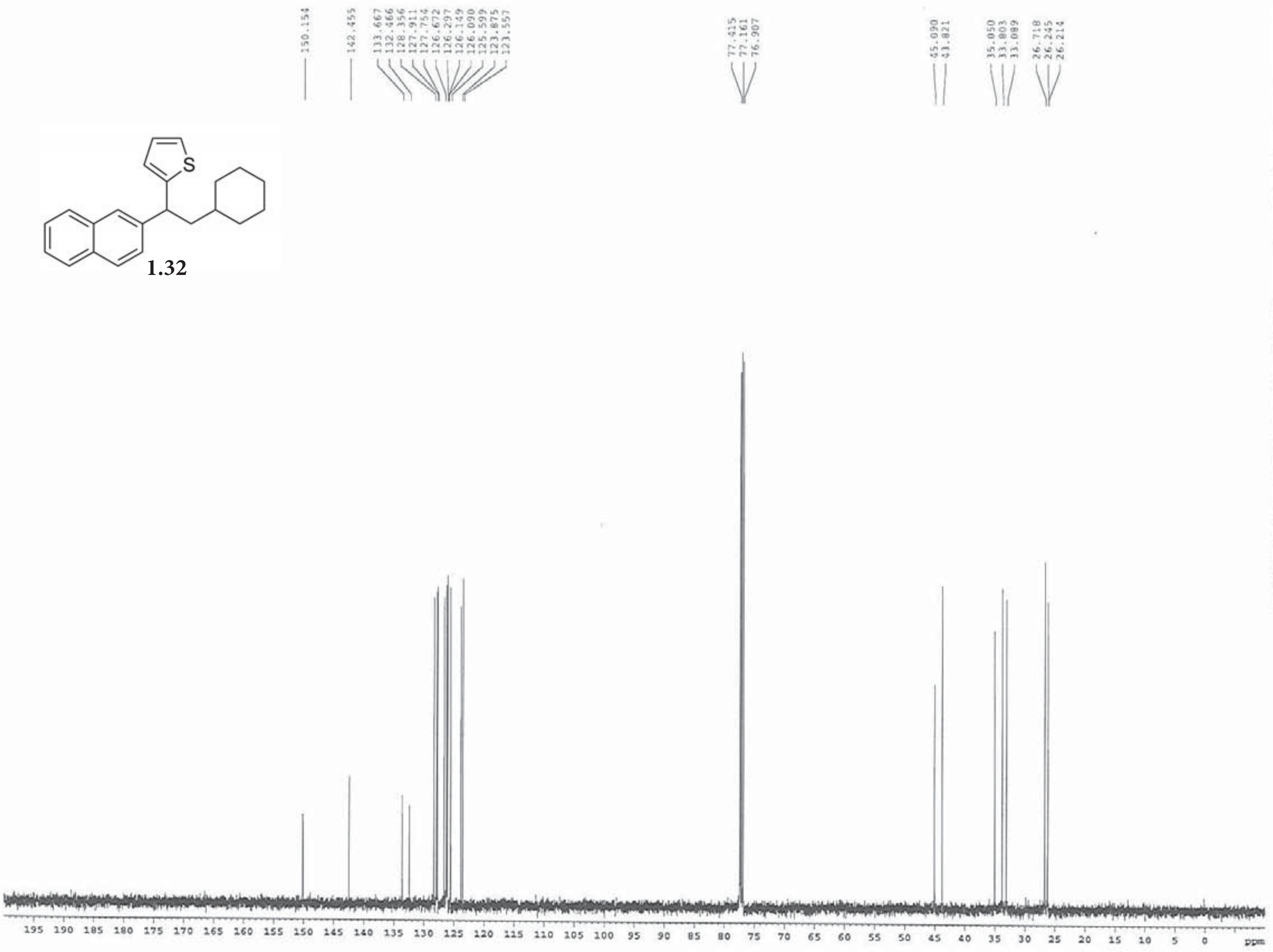
1H spectrum



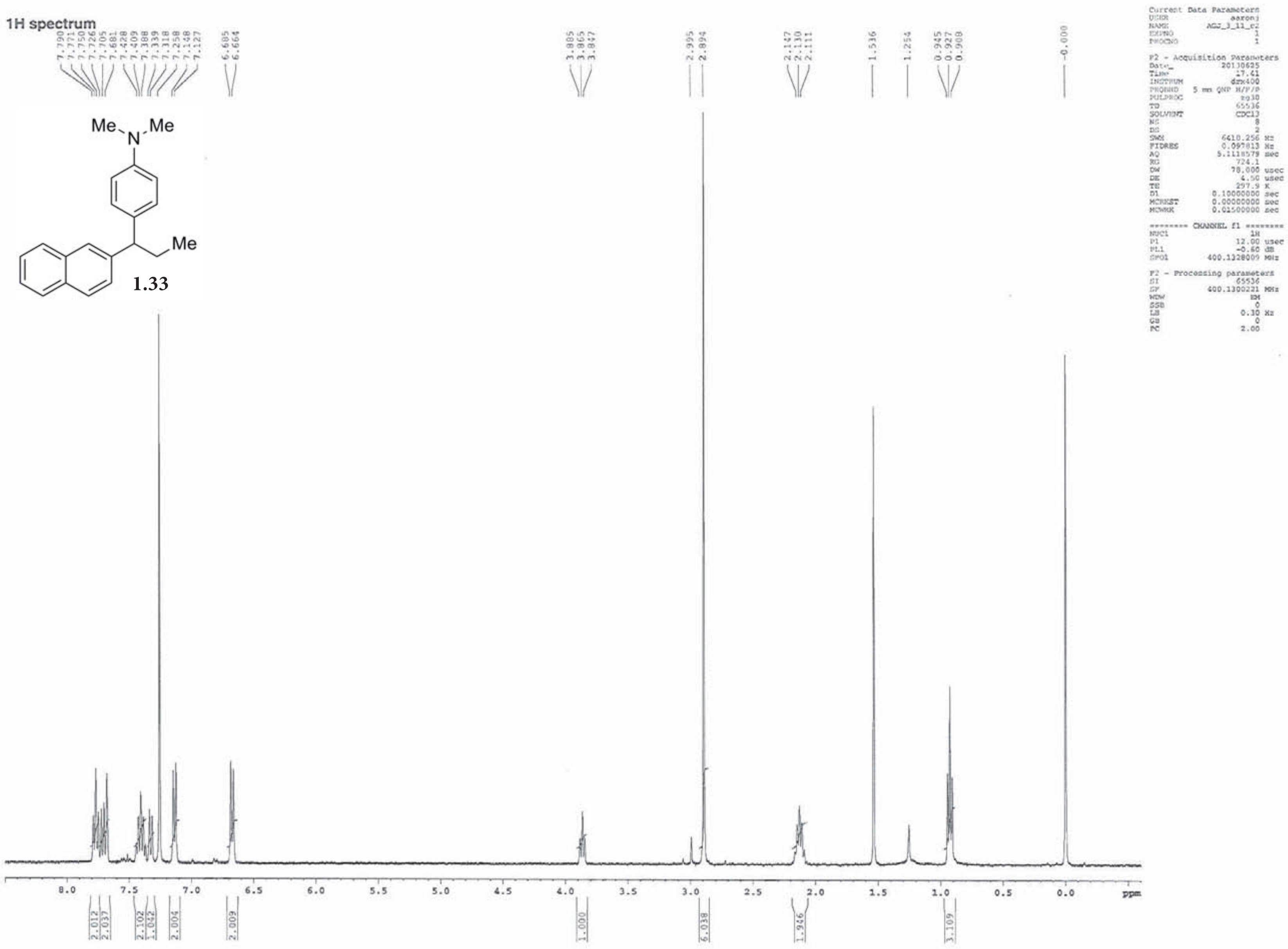
1.32

```
Current Data Parameters
USER              yonova
NAME           imy5 - 243
EXPNO                  17
PROCNO                  1

F2 - Acquisition Parameters
Date_            20130509
Time                13.57
INSTRUM            drx400
PROBHD   5 mm QNP H/F/P
PULPROG              zg30
TD                  65536
SOLVENT             CDCl3
NS                      8
DS                      2
SWH              6410.256 Hz
FIDRES           0.097813 Hz
AQ              5.1118579 sec
RG                  287.4
DW                 78.000 usec
DE                   4.50 usec
TE                  298.1 K
D1             0.10000000 sec
MCREST         0.00000000 sec
MCWRK          0.01500000 sec

======== CHANNEL f1 ========
NUC1                   1H
P1                  12.00 usec
PL1                 -0.60 dB
SFO1          400.1328009 MHz

F2 - Processing parameters
SI                  65536
SF            400.1300249 MHz
WDW                    EM
SSB                     0
LB                   0.30 Hz
GB                      0
PC                   2.00
```

Z–restored spin–echo 13C spectrum with 1H decoupling

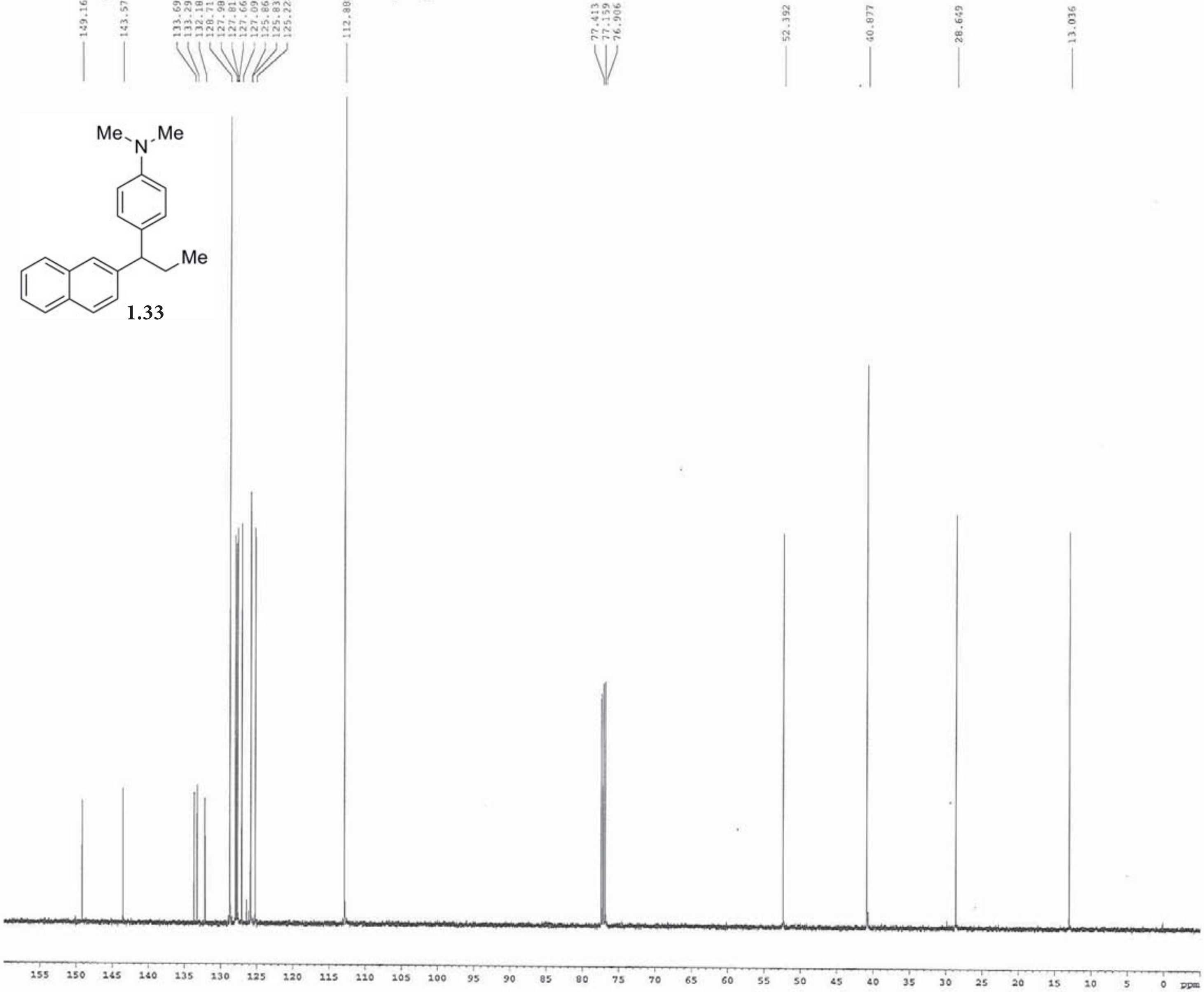

1.32

```
Current Data Parameters
USER               yonova
NAME            imy5 - 243
EXPNO                  222
PROCNO                   1

F2 - Acquisition Parameters
Date_             20130510
Time                 14.26
INSTRUM            cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD                   65536
SOLVENT              CDCl3
NS                     325
DS                      16
SWH              30303.031 Hz
FIDRES            0.462388 Hz
AQ               1.0814105 sec
RG                  5792.6
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             125.7804094 MHz
WDW                     EM
SSB                      0
LB                    1.00 Hz
GB                       0
PC                    2.00
```


1H spectrum

1.33

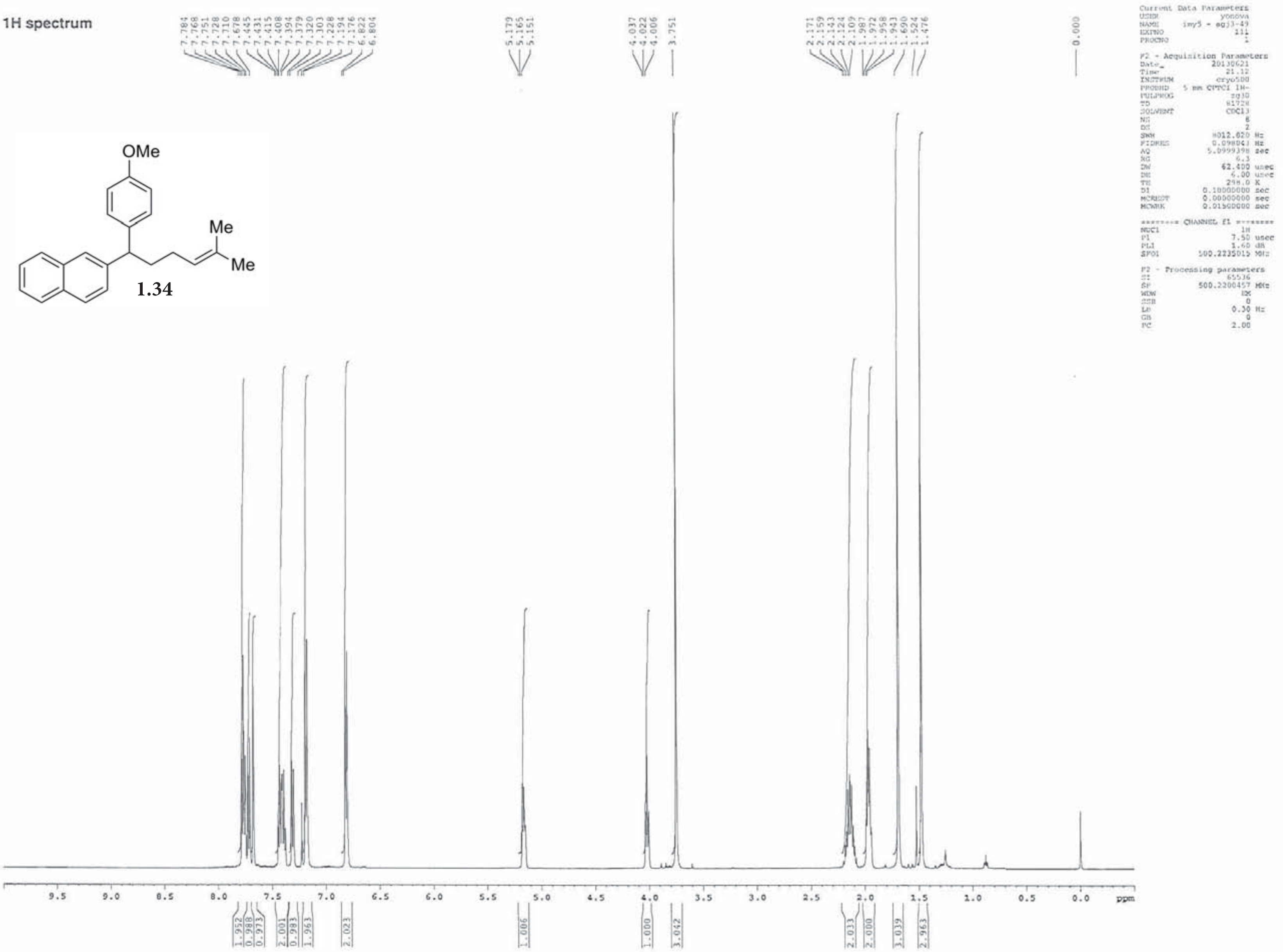
Z-restored spin-echo 13C spectrum with 1H decoupling



1.33

```
Current Data Parameters
USER                aaronj
NAME              AGJ_3_11
EXPNO                    5
PROCNO                   1

F2 - Acquisition Parameters
Date_             20130625
Time                 18.40
INSTRUM            cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopgJ0gp.prd
TD                   65536
SOLVENT              CDCl3
NS                     440
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             125.7804127 MHz
WDW                     EM
SSB                      0
LB                    1.00 Hz
GB                       0
PC                    2.00
```

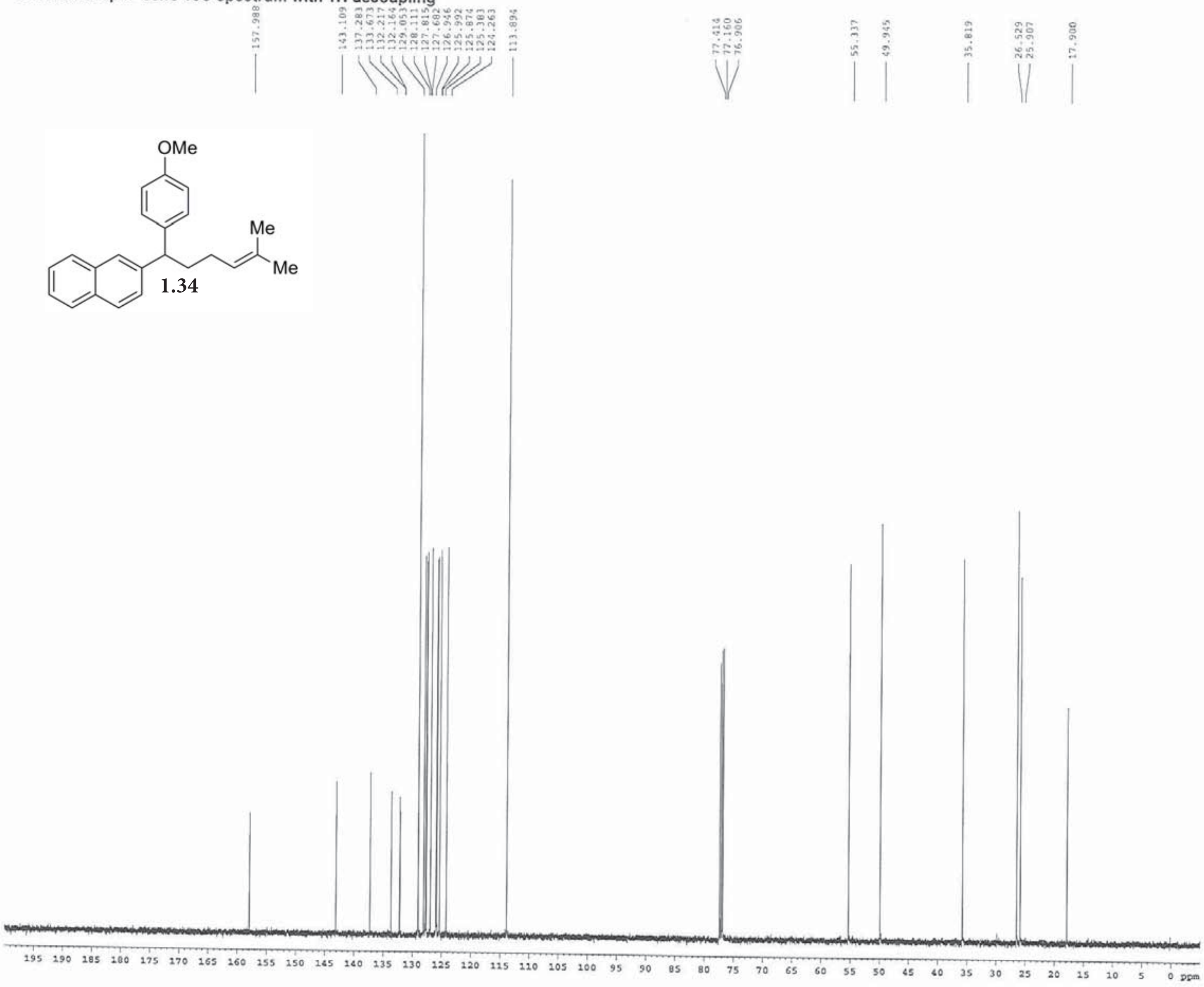
1H spectrum



1.34

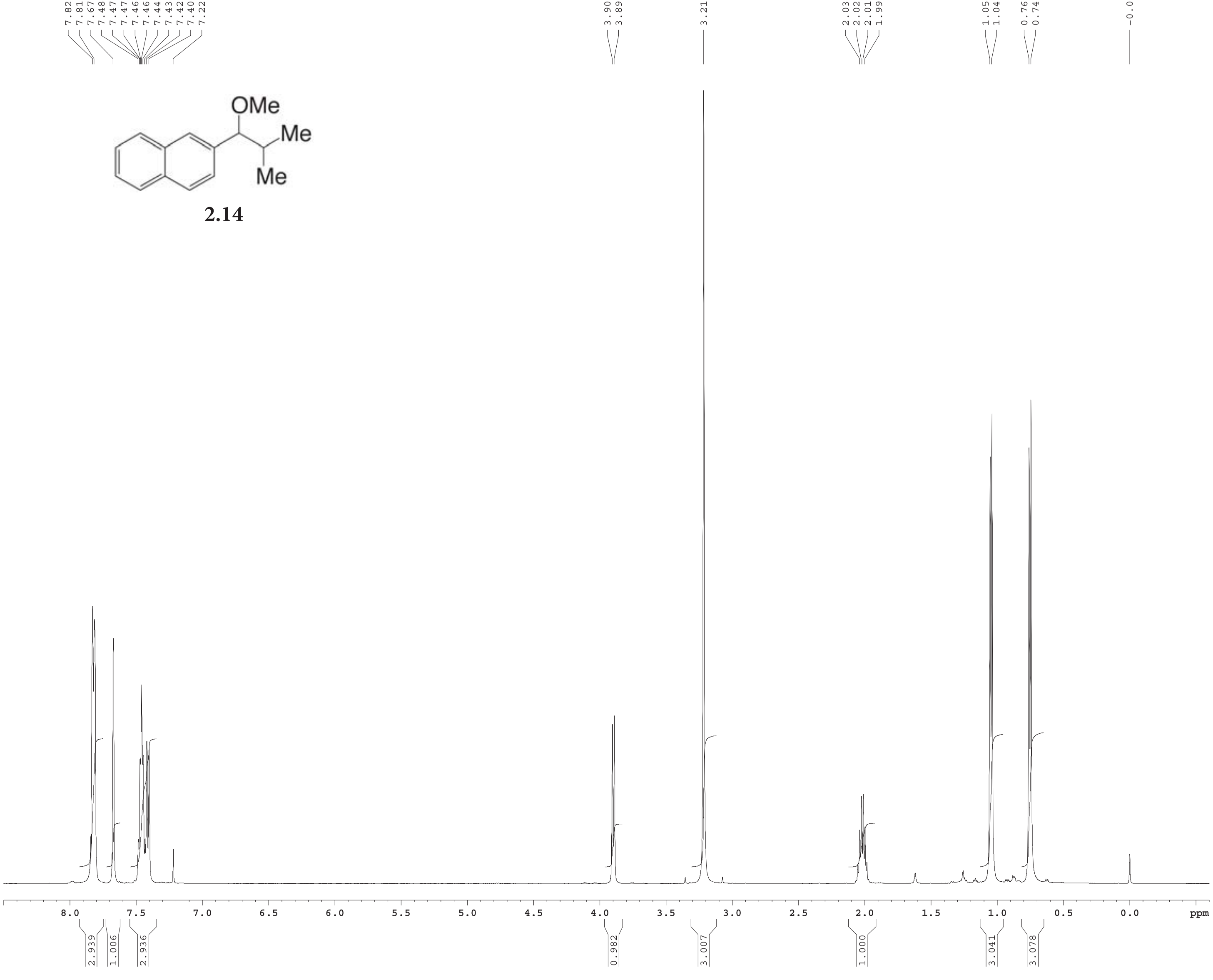
```
Current Data Parameters
USER              yonova
NAME       imy5 - egj3-49
EXPNO                111
PROCNO                 1

F2 - Acquisition Parameters
Date_           20130621
Time               21.12
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            5.0999398 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           500.2200457 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  2.00
```

Z–restored spin–echo 13C spectrum with 1H decoupling



```
Current Data Parameters
USER              yonova
NAME      imy5 - agj3-49
EXPNO                222
PROCNO                 1

F2 - Acquisition Parameters
Date_           20130621
Time               21.20
INSTRUM          cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG Spinechopg30gp.prd
TD                 65536
SOLVENT            CDCl3
NS                   276
DS                    16
SWH            30303.031 Hz
FIDRES          0.462388 Hz
AQ             1.0814105 sec
RG                5792.6
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           125.7804113 MHz
WDW                   EM
SSB                    0
LB                  1.00 Hz
GB                     0
PC                  4.00
```

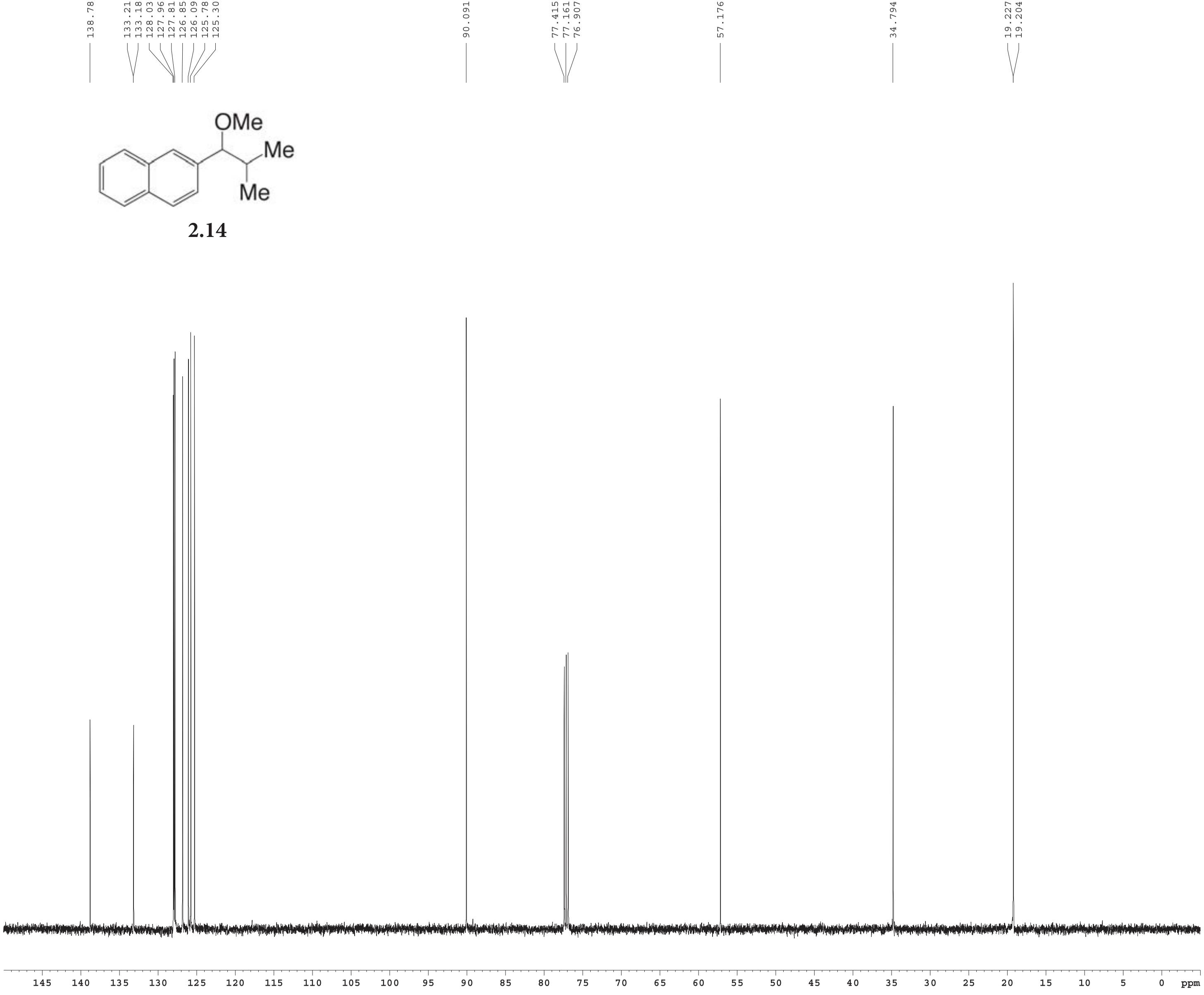
1H spectrum



2.14

```
Current Data Parameters
USER             lucase
NAME      LWE-I-fy-niet-2h
EXPNO                 1
PROCNO                1

F2 - Acquisition Parameters
Date_          20131120
Time               8.44
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          500.2200505 MHz
WDW                  EM
SSB                   0
LB                 0.30 Hz
GB                    0
PC                 4.00
```

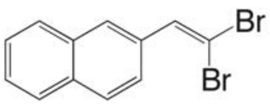
Z-restored spin-echo 13C spectrum with 1H decoupling



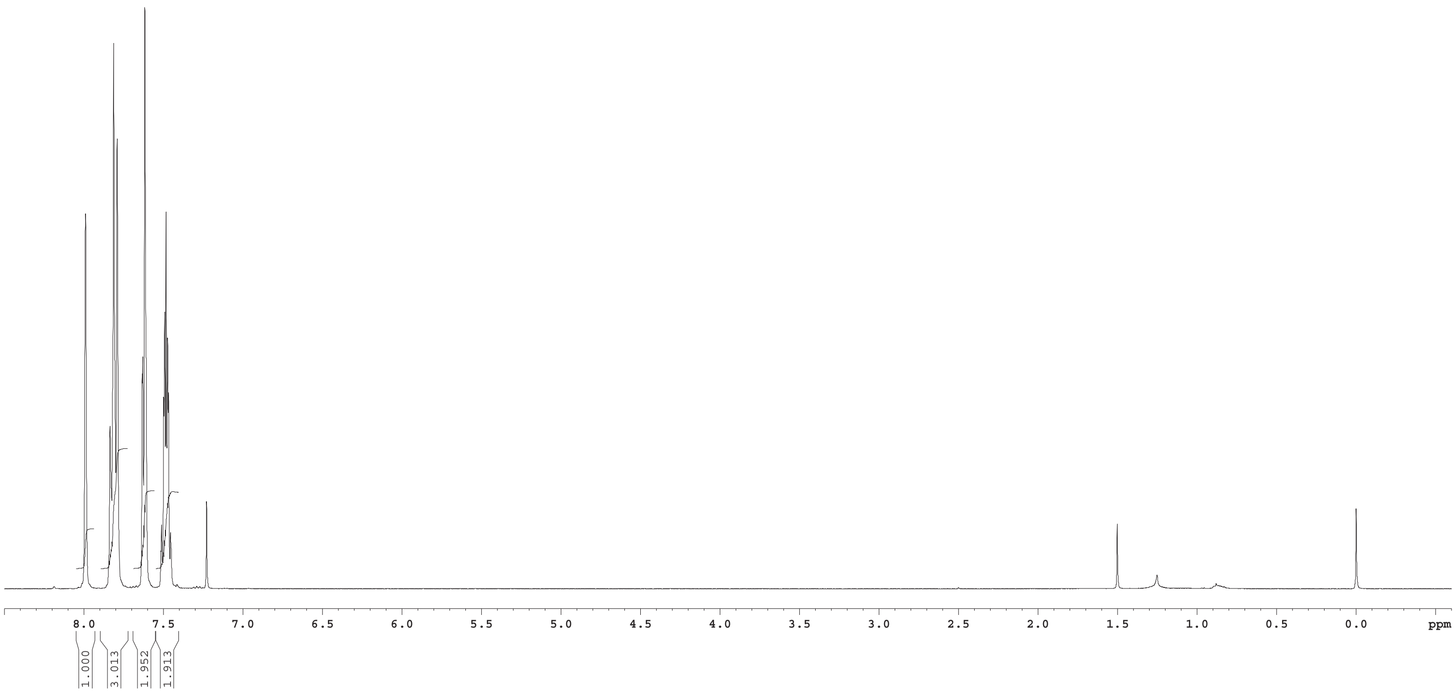
2.14

```
Current Data Parameters
USER                lucase
NAME       LWE-I-fy-niet-2c
EXPNO                    1
PROCNO                   1

F2 - Acquisition Parameters
Date_             20131120
Time                  8.46
INSTRUM            cryo500
PROBHD     5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD                   65536
SOLVENT              CDCl3
NS                      39
DS                       8
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
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             125.7804136 MHz
WDW                     EM
SSB                      0
LB                    1.00 Hz
GB                       0
PC                    2.00
```

1H spectrum

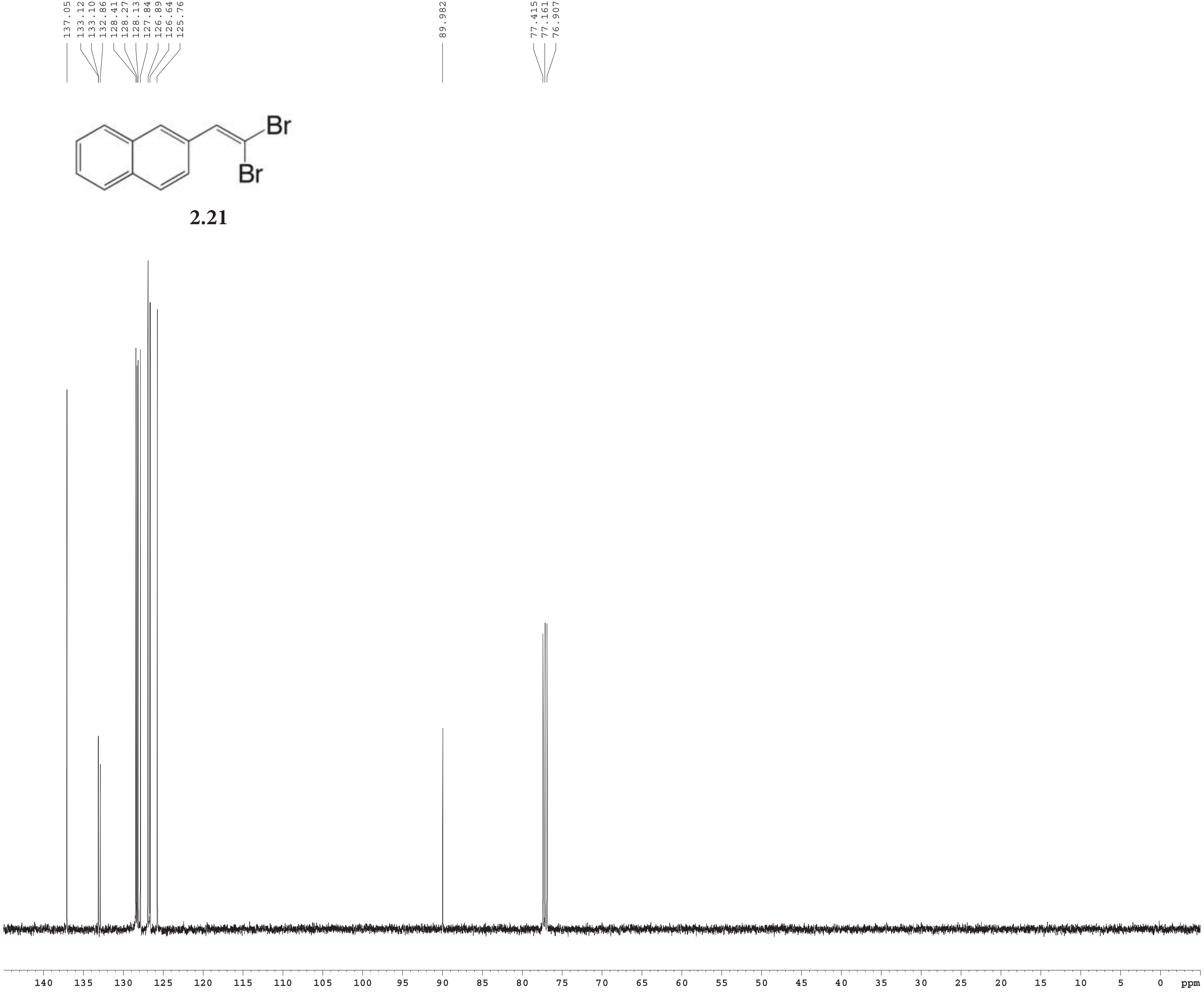


2.21



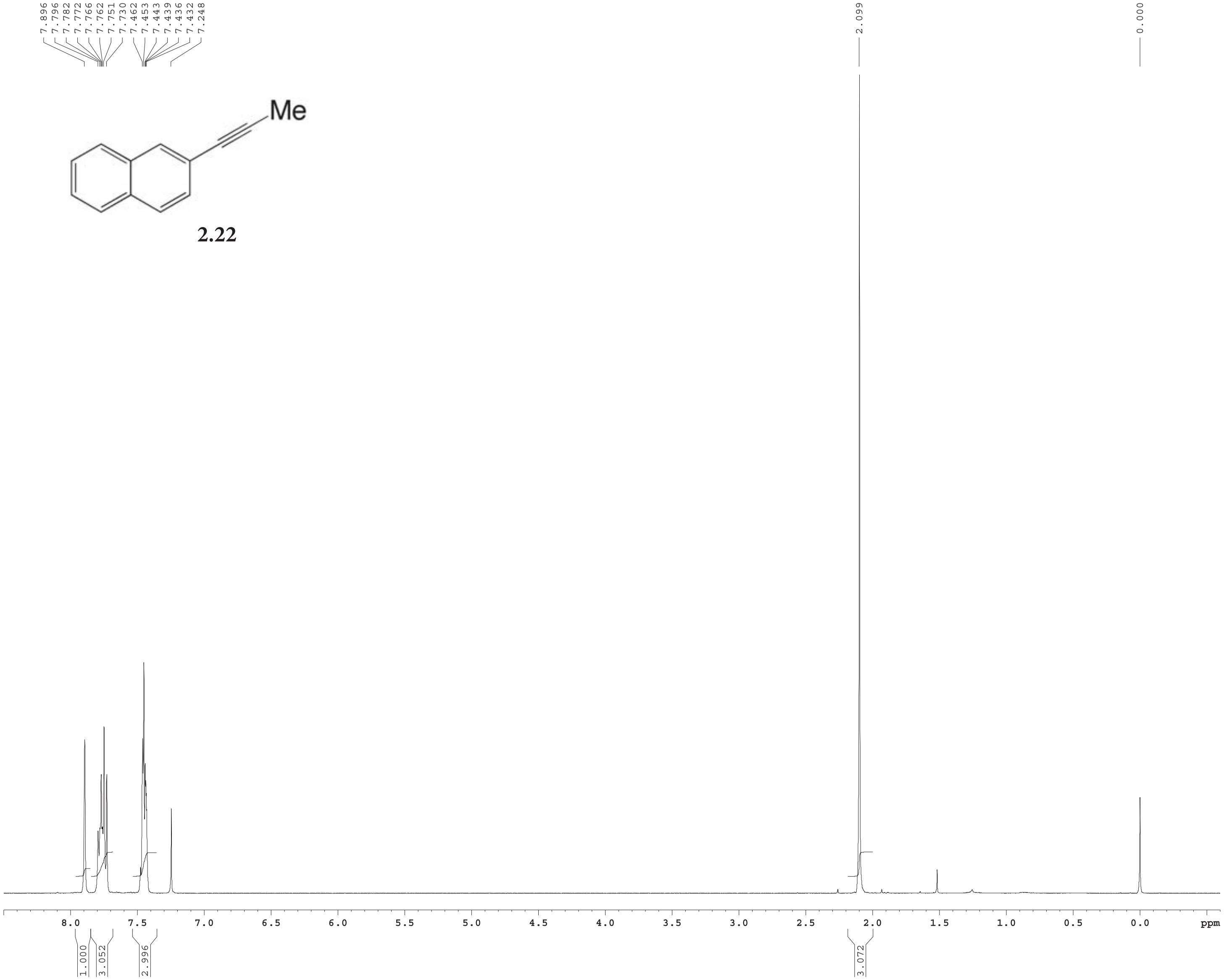
```
Current Data Parameters
USER              aaronj
NAME         AGJ_3_262_c1
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20140414
Time               10.36
INSTRUM           drx400
PROBHD   5 mm QNP H/F/P
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                     8
DS                     2
SWH             6410.256 Hz
FIDRES          0.097813 Hz
AQ             5.1118579 sec
RG                 203.2
DW                78.000 usec
DE                  4.50 usec
TE                 298.0 K
D1            0.10000000 sec
MCREST        0.00000000 sec
MCWRK         0.01500000 sec

======== CHANNEL f1 ========
NUC1                  1H
P1                 12.00 usec
PL1                 0.00 dB
SFO1         400.1328009 MHz

F2 - Processing parameters
SI                 65536
SF           400.1300339 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  2.00
```

Z-restored spin-echo 13C spectrum with 1H decoupling


2.21

```
Current Data Parameters
USER               aaronj
NAME         AGJ_3_262_c1
EXPNO                   3
PROCNO                  1

F2 - Acquisition Parameters
Date_            20140414
Time                11.04
INSTRUM           cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD                  65536
SOLVENT             CDCl3
NS                    160
DS                     16
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            125.7804117 MHz
WDW                    EM
SSB                     0
LB                   1.00 Hz
GB                      0
PC                   2.00
```

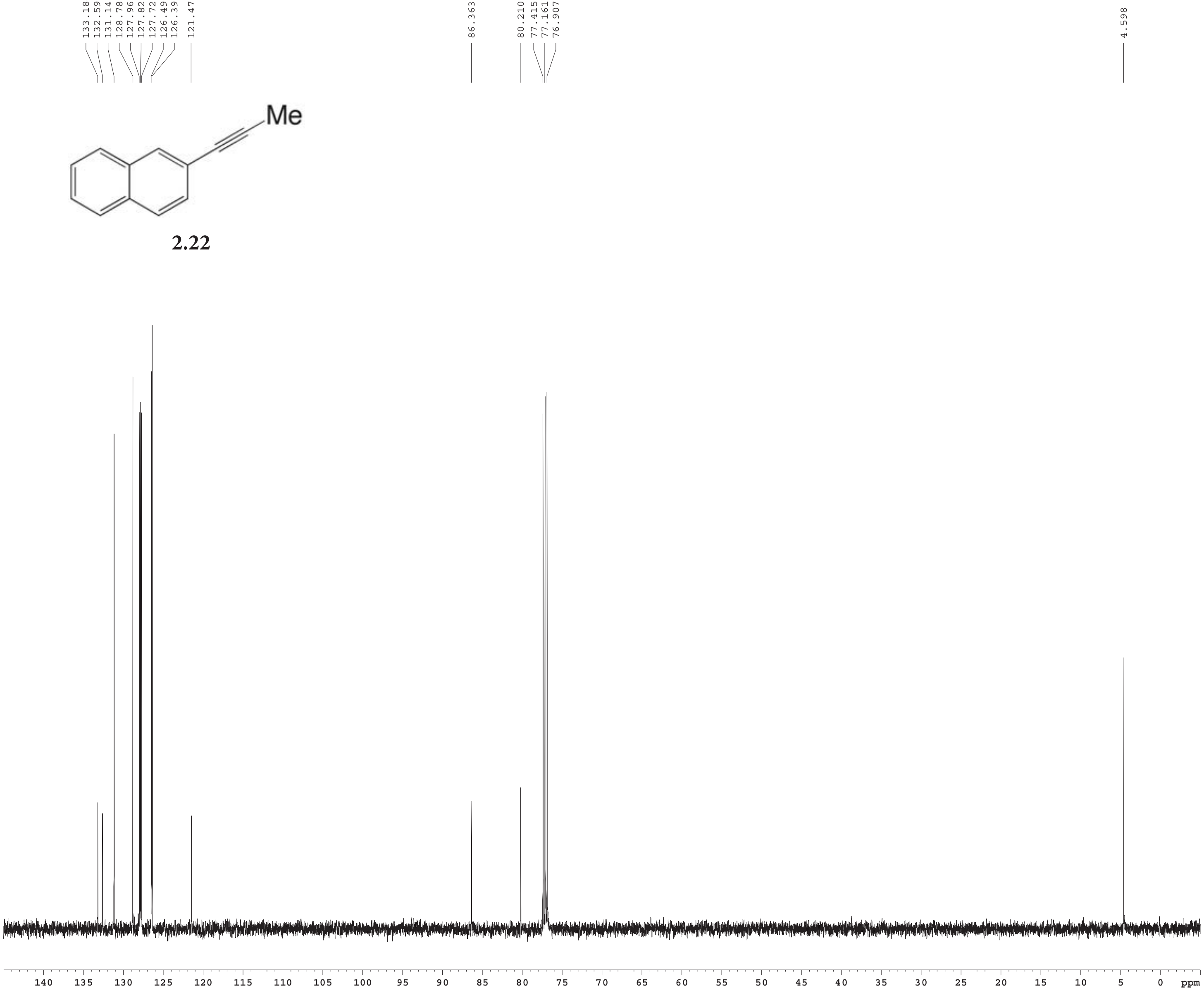
1H spectrum



2.22

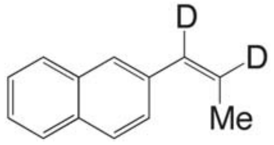
```
Current Data Parameters
USER              aaronj
NAME         AGJ_3_263_c1
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20140415
Time               16.08
INSTRUM           drx400
PROBHD   5 mm QNP H/F/P
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                     8
DS                     2
SWH             6410.256 Hz
FIDRES          0.097813 Hz
AQ             5.1118579 sec
RG                   362
DW                78.000 usec
DE                  4.50 usec
TE                 298.0 K
D1            0.10000000 sec
MCREST        0.00000000 sec
MCWRK         0.01500000 sec

======== CHANNEL f1 ========
NUC1                  1H
P1                 12.00 usec
PL1                 0.00 dB
SFO1         400.1328009 MHz

F2 - Processing parameters
SI                 65536
SF           400.1300266 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  2.00
```

Z-restored spin-echo 13C spectrum with 1H decoupling

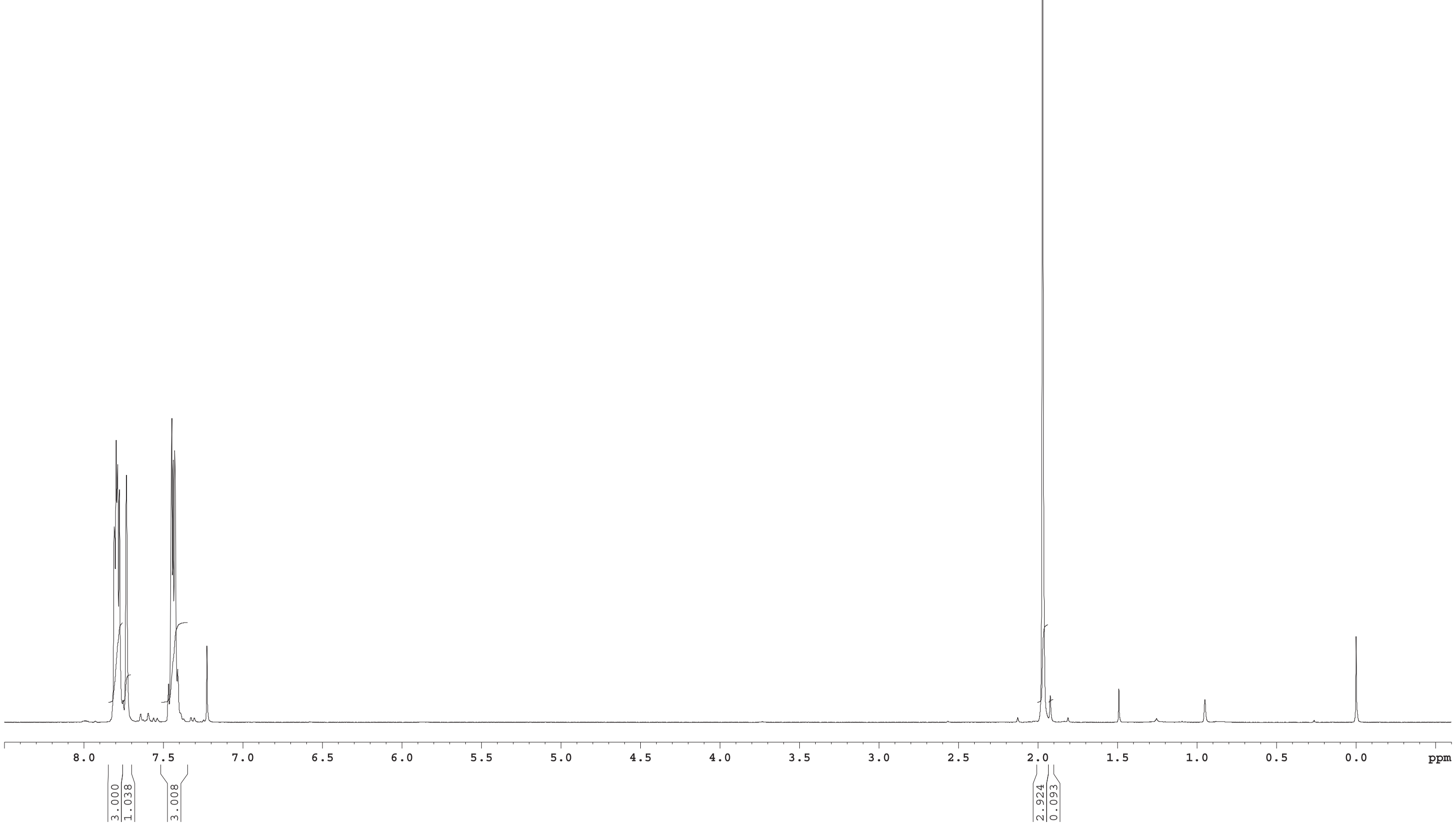


```
Current Data Parameters
USER              aaronj
NAME         AGJ_3_263_c1
EXPNO                  4
PROCNO                 1

F2 - Acquisition Parameters
Date_           20140415
Time               17.47
INSTRUM          cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD                 65536
SOLVENT            CDCl3
NS                   248
DS                    16
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
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           125.7804090 MHz
WDW                   EM
SSB                    0
LB                  1.00 Hz
GB                     0
PC                  2.00
```

1H spectrum

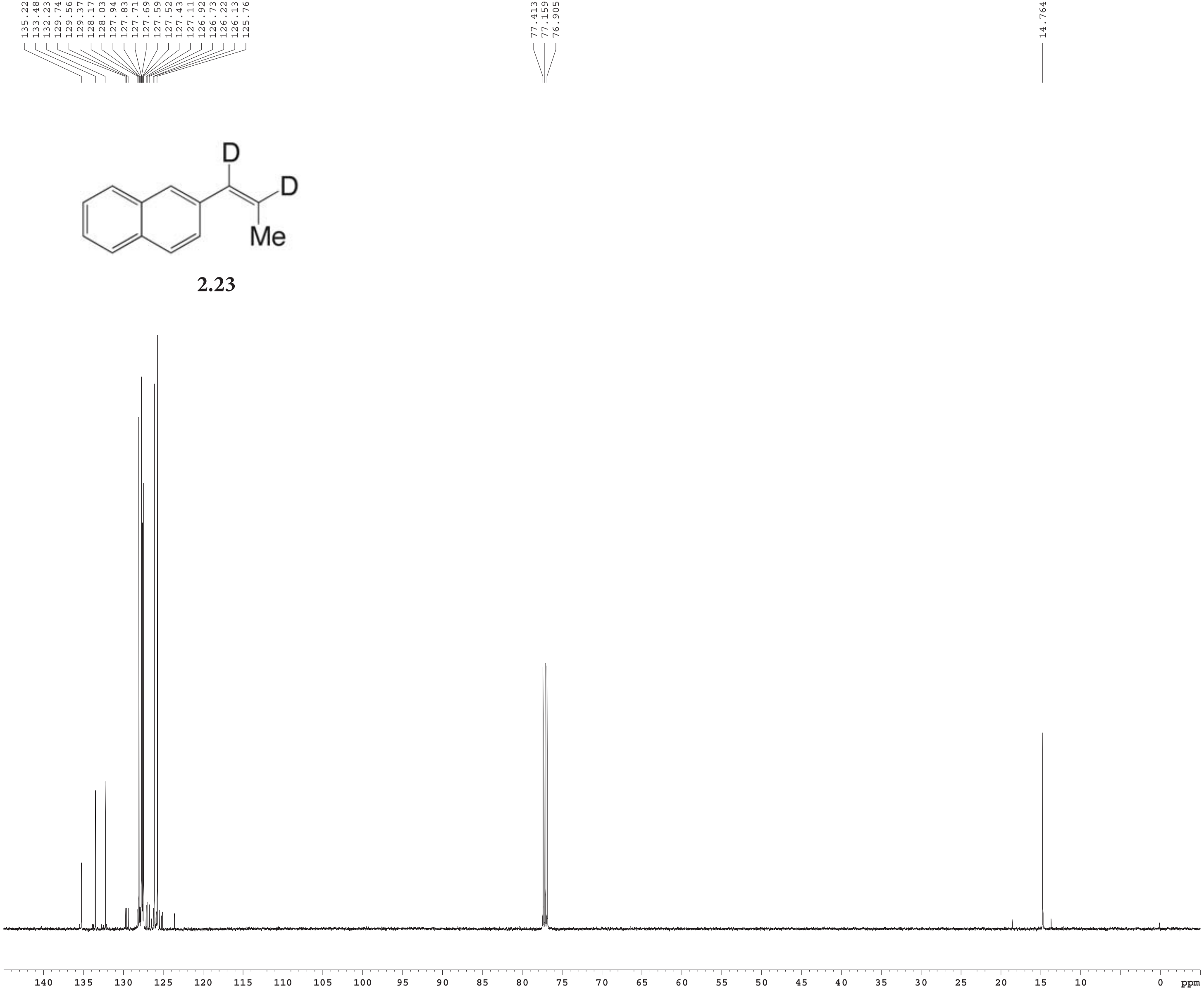


2.23

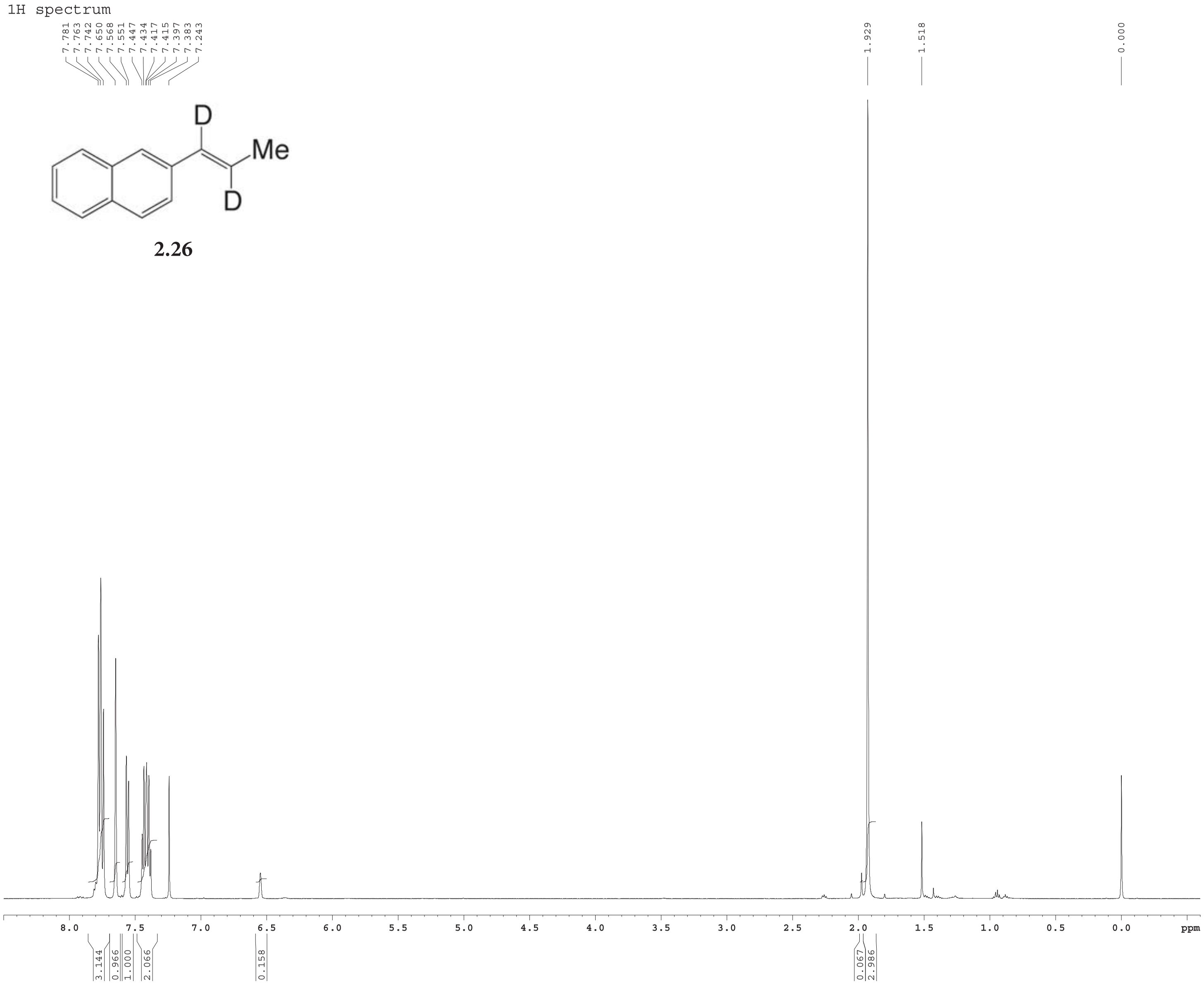


```
Current Data Parameters
USER              aaronj
NAME         AGJ_3_264_c1_1
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20140419
Time               18.35
INSTRUM           drx400
PROBHD    5 mm QNP H/F/P
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                     8
DS                     2
SWH             6410.256 Hz
FIDRES          0.097813 Hz
AQ             5.1118579 sec
RG                 203.2
DW                78.000 usec
DE                  4.50 usec
TE                 298.1 K
D1            0.10000000 sec
MCREST        0.00000000 sec
MCWRK         0.01500000 sec

======== CHANNEL f1 ========
NUC1                  1H
P1                 12.00 usec
PL1                 0.00 dB
SFO1        400.1328009 MHz

F2 - Processing parameters
SI                 65536
SF          400.1300348 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  2.00
```

Z-restored spin-echo 13C spectrum with 1H decoupling

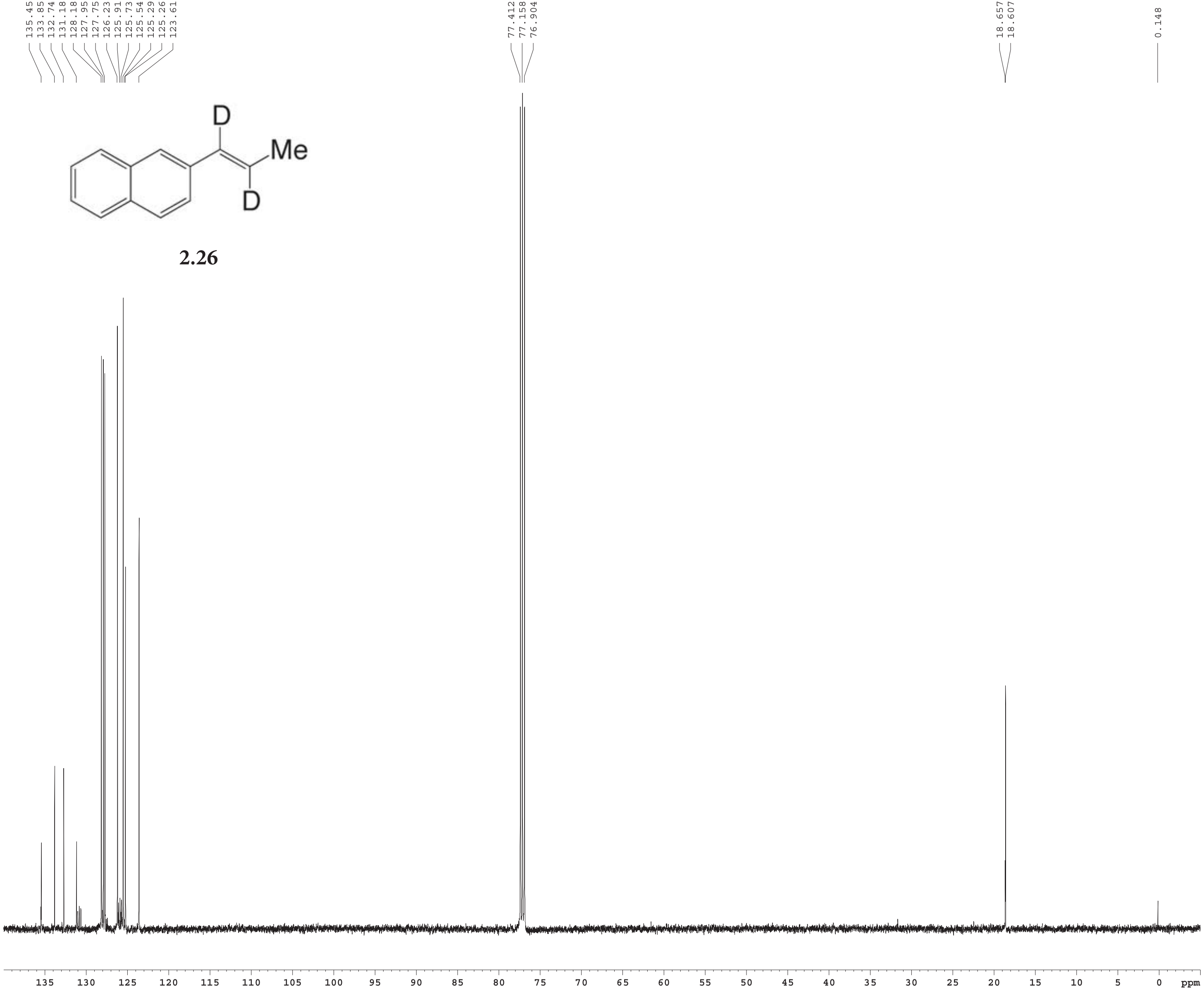


```
Current Data Parameters
USER                aaronj
NAME          AGJ_3_264_c1
EXPNO                    3
PROCNO                   1

F2 - Acquisition Parameters
Date_             20140422
Time                 15.46
INSTRUM            cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD                   65536
SOLVENT              CDCl3
NS                     792
DS                      16
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             125.7804159 MHz
WDW                     EM
SSB                      0
LB                    1.00 Hz
GB                       0
PC                    2.00
```



```
Current Data Parameters
USER                aaronj
NAME           AGJ_3_297_c2
EXPNO                    1
PROCNO                   1

F2 - Acquisition Parameters
Date_             20140528
Time                  9.43
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                   1.60 dB
SFO1           500.2235015 MHz

F2 - Processing parameters
SI                   65536
SF             500.2200409 MHz
WDW                     EM
SSB                      0
LB                    0.30 Hz
GB                       0
PC                    4.00
```

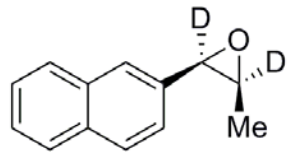
Z-restored spin-echo 13C spectrum with 1H decoupling



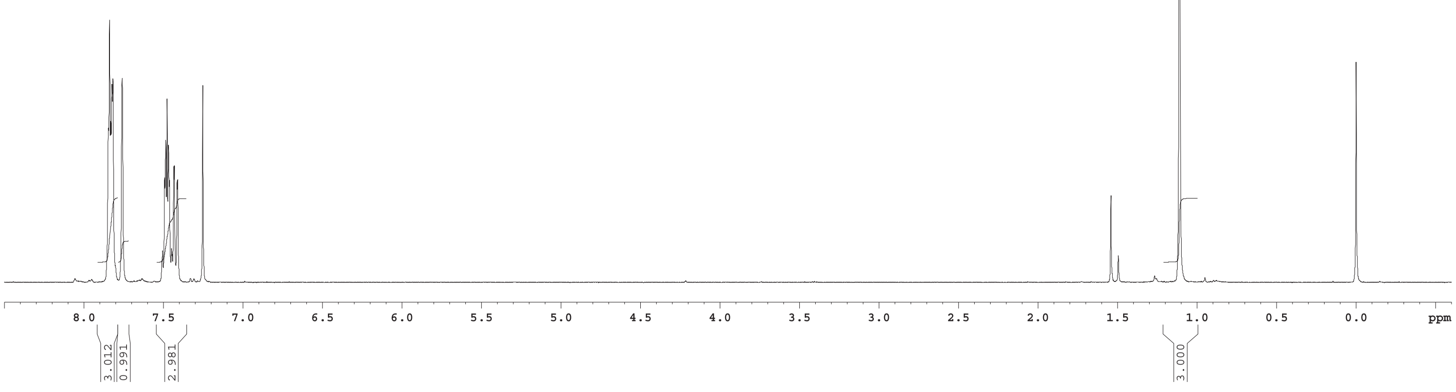
2.26

```
Current Data Parameters
USER                aaronj
NAME          AGJ_3_297_c2
EXPNO                    2
PROCNO                   1

F2 - Acquisition Parameters
Date_             20140528
Time                  9.49
INSTRUM            cryo500
PROBHD    5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD                   65536
SOLVENT              CDCl3
NS                     976
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             125.7804103 MHz
WDW                     EM
SSB                      0
LB                    1.00 Hz
GB                       0
PC                    2.00
```

1H spectrum

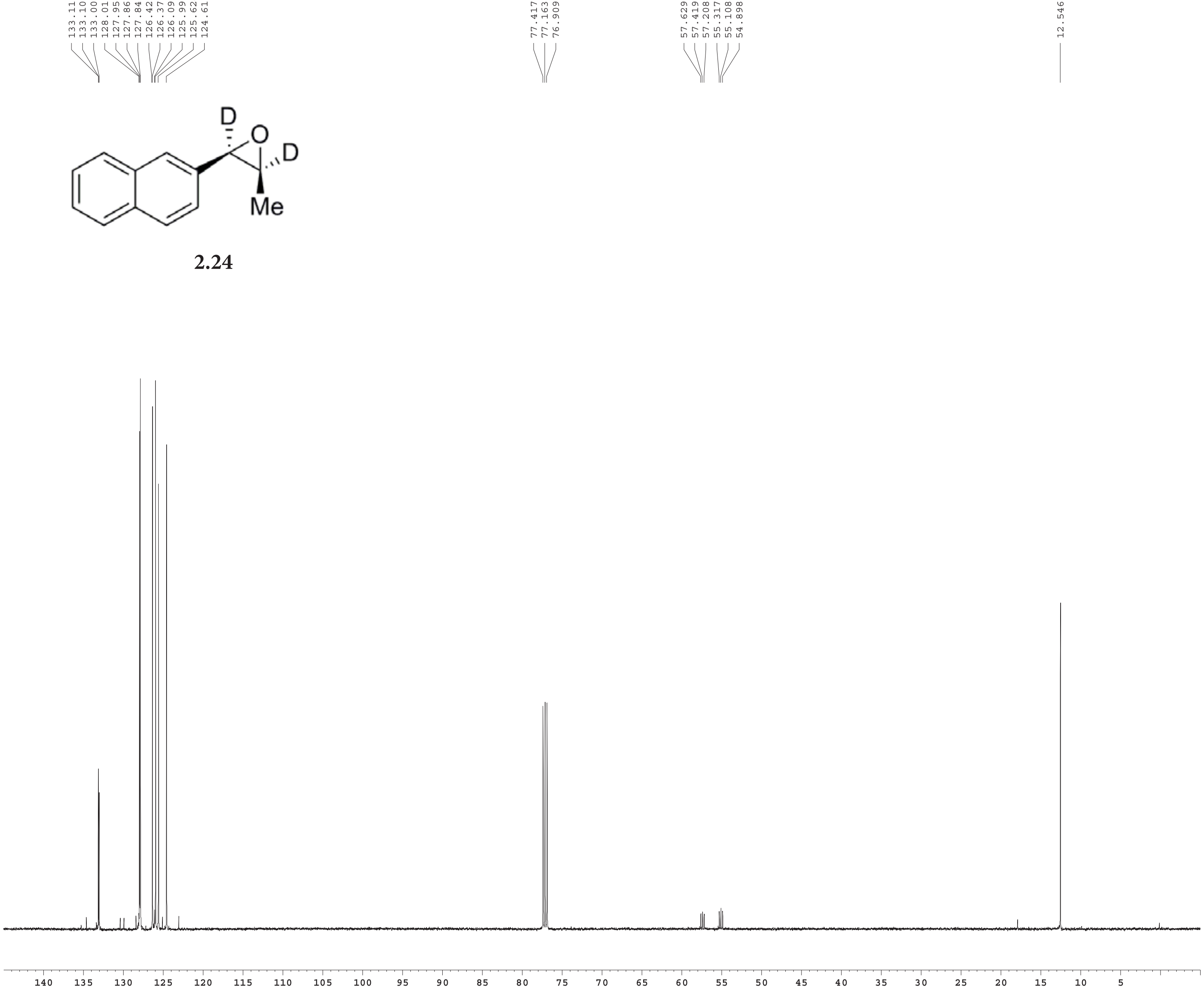


2.24



```
Current Data Parameters
USER              aaronj
NAME         AGJ_3_268_C1
EXPNO                  3
PROCNO                 1

F2 - Acquisition Parameters
Date_           20140423
Time               20.34
INSTRUM           drx400
PROBHD   5 mm QNP H/F/P
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                     8
DS                     2
SWH             6410.256 Hz
FIDRES          0.097813 Hz
AQ             5.1118579 sec
RG                 456.1
DW                78.000 usec
DE                  4.50 usec
TE                 298.0 K
D1            0.10000000 sec
MCREST        0.00000000 sec
MCWRK         0.01500000 sec

======== CHANNEL f1 ========
NUC1                  1H
P1                 12.00 usec
PL1                 0.00 dB
SFO1         400.1328009 MHz

F2 - Processing parameters
SI                 65536
SF           400.1300243 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  2.00
```

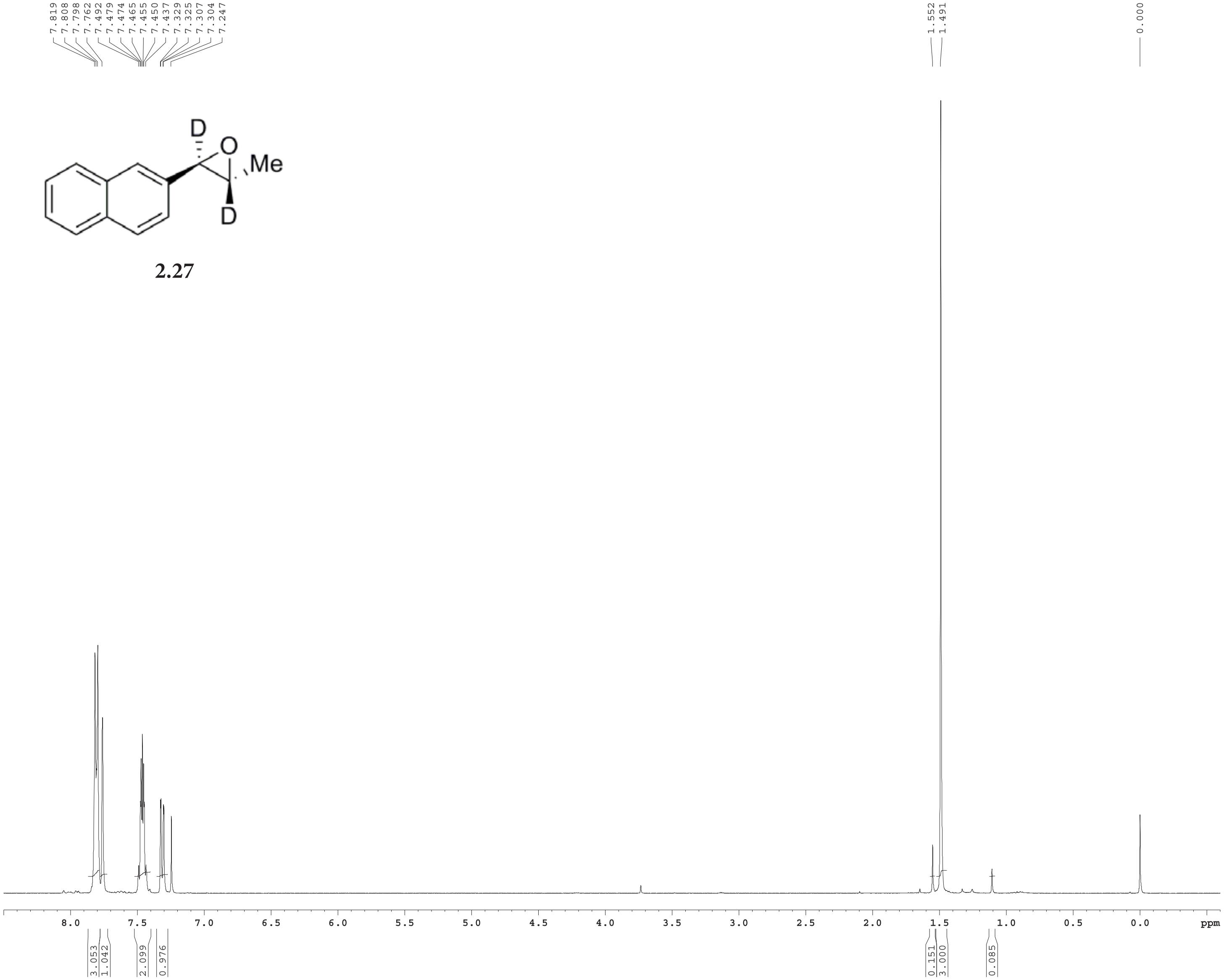
Z-restored spin-echo 13C spectrum with 1H decoupling



2.24

```
Current Data Parameters
USER              aaronj
NAME         AGJ_3_267_c1
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20140423
Time               19.51
INSTRUM          cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD                 65536
SOLVENT            CDCl3
NS                  1024
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           125.7804145 MHz
WDW                   EM
SSB                    0
LB                  1.00 Hz
GB                     0
PC                  2.00
```

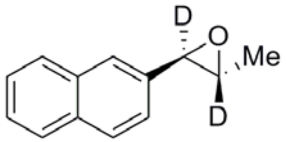
1H spectrum



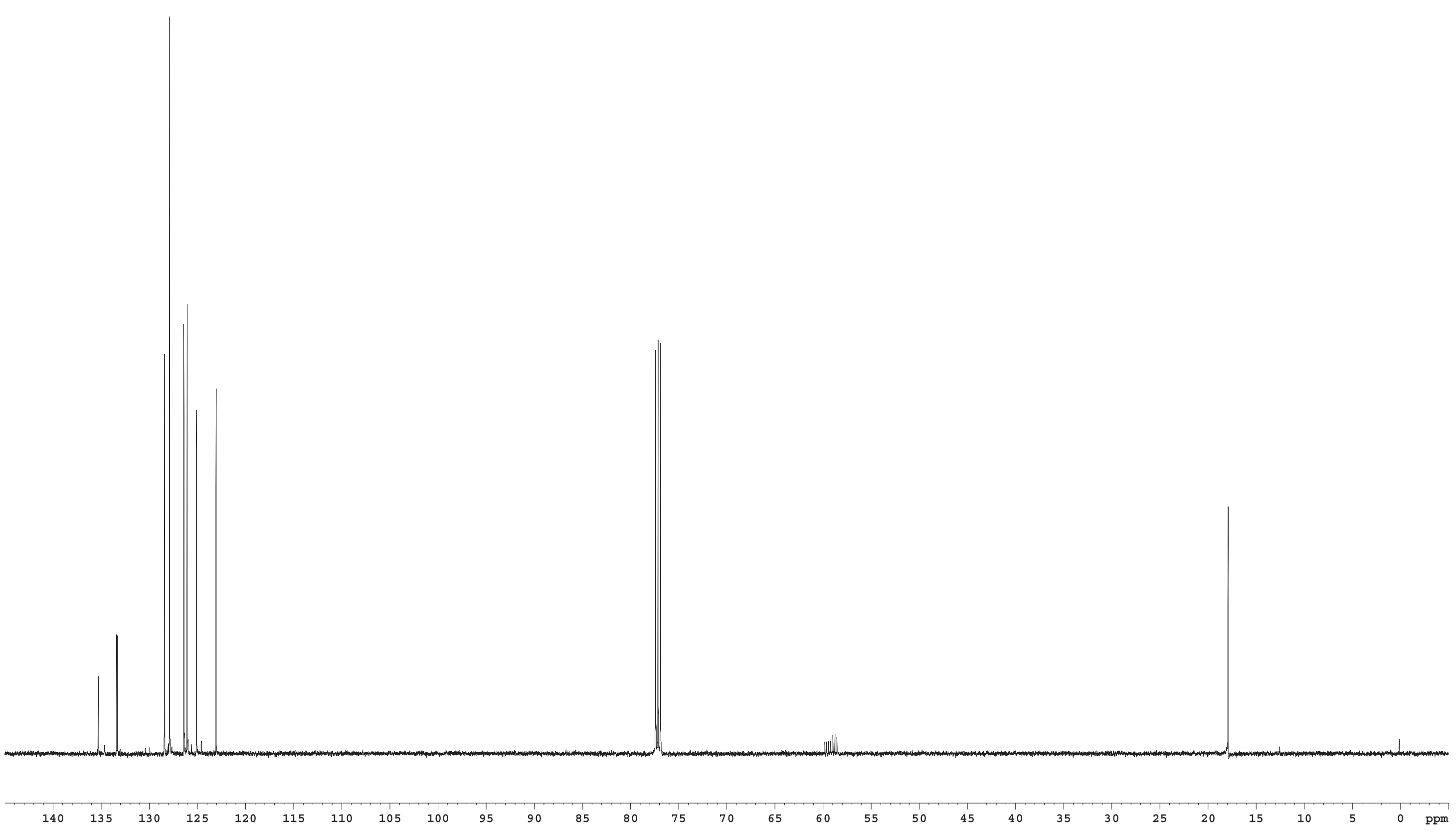
2.27

```
Current Data Parameters
USER              aaronj
NAME        AGJ_3_294_c1
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20140610
Time               14.35
INSTRUM           drx400
PROBHD   5 mm QNP H/F/P
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                     8
DS                     2
SWH             6410.256 Hz
FIDRES          0.097813 Hz
AQ             5.1118579 sec
RG                 322.5
DW                78.000 usec
DE                  4.50 usec
TE                 298.0 K
D1           0.10000000 sec
MCREST       0.00000000 sec
MCWRK        0.01500000 sec

======== CHANNEL f1 ========
NUC1                  1H
P1                 12.00 usec
PL1                 0.00 dB
SFO1         400.1328009 MHz

F2 - Processing parameters
SI                 65536
SF           400.1300258 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  2.00
```

Z-restored spin-echo 13C spectrum with 1H decoupling

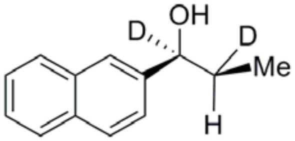


2.27



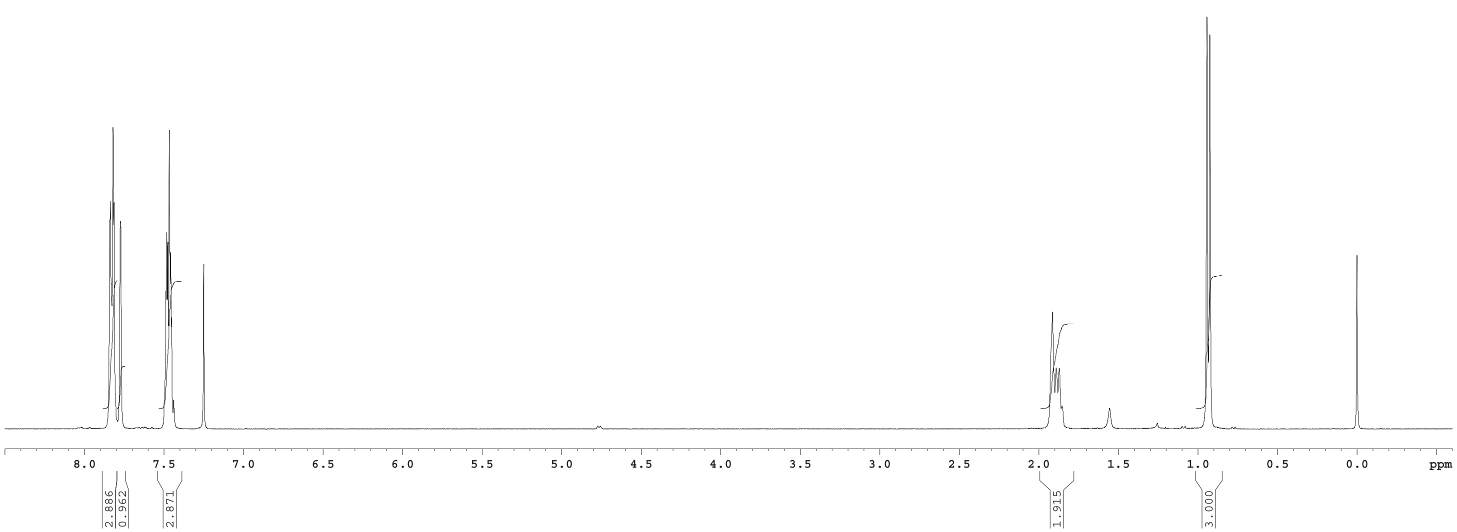
```
Current Data Parameters
USER              aaronj
NAME         AGJ_3_294_c1
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20140610
Time               15.04
INSTRUM          cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD                 65536
SOLVENT            CDCl3
NS                   608
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           125.7804113 MHz
WDW                   EM
SSB                    0
LB                  1.00 Hz
GB                     0
PC                  2.00
```

1H spectrum

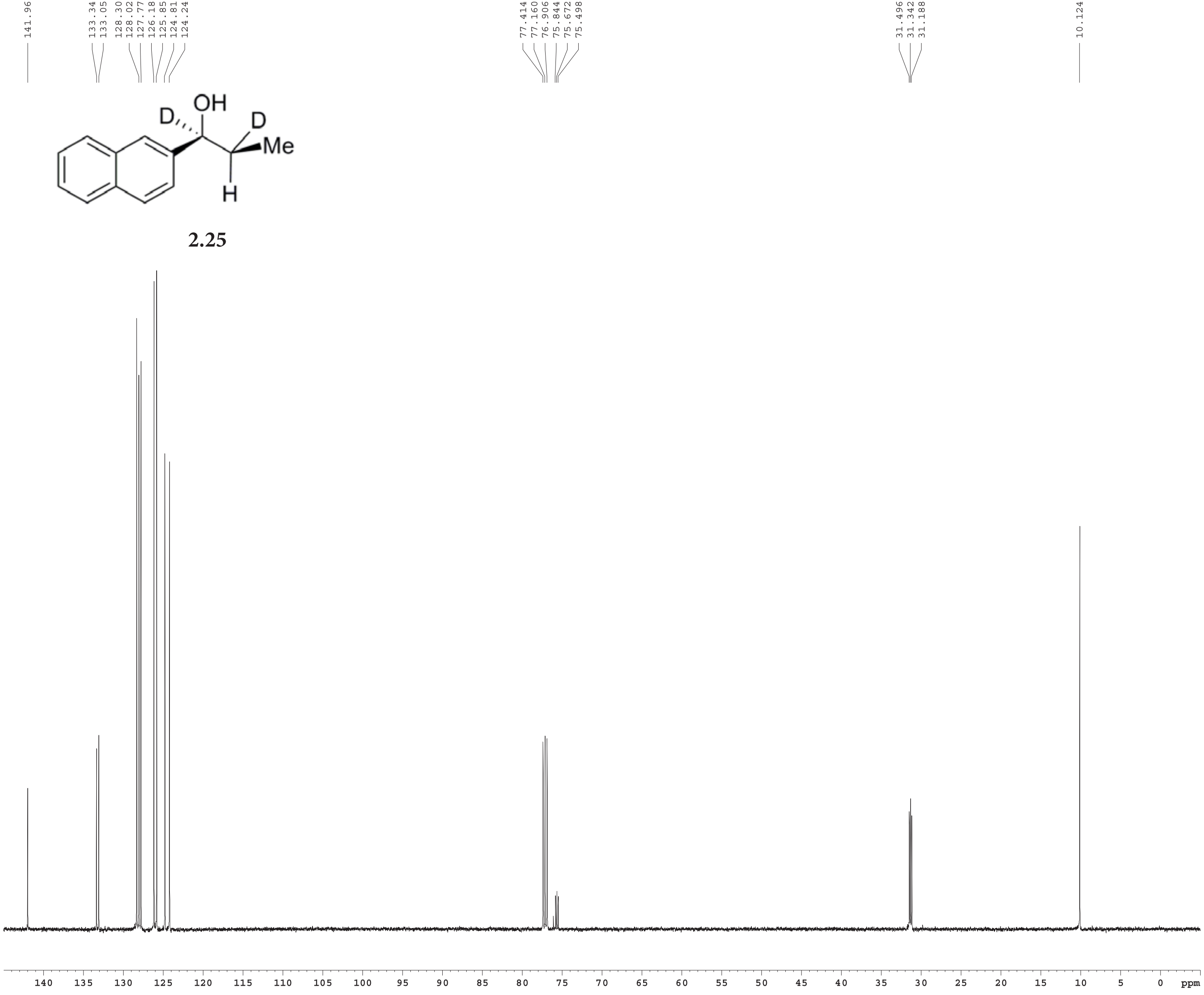


2.25

```
Current Data Parameters
USER              aaronj
NAME          AGJ_3_269_c1
EXPNO                  5
PROCNO                 1

F2 - Acquisition Parameters
Date_           20140425
Time                9.09
INSTRUM           drx400
PROBHD   5 mm QNP H/F/P
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                     8
DS                     2
SWH             6410.256 Hz
FIDRES          0.097813 Hz
AQ             5.1118579 sec
RG                 406.4
DW                78.000 usec
DE                  4.50 usec
TE                 298.0 K
D1           0.10000000 sec
MCREST       0.00000000 sec
MCWRK        0.01500000 sec

======== CHANNEL f1 ========
NUC1                  1H
P1                 12.00 usec
PL1                 0.00 dB
SFO1        400.1328009 MHz

F2 - Processing parameters
SI                 65536
SF          400.1300252 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  2.00
```



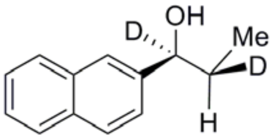
Z-restored spin-echo 13C spectrum with 1H decoupling



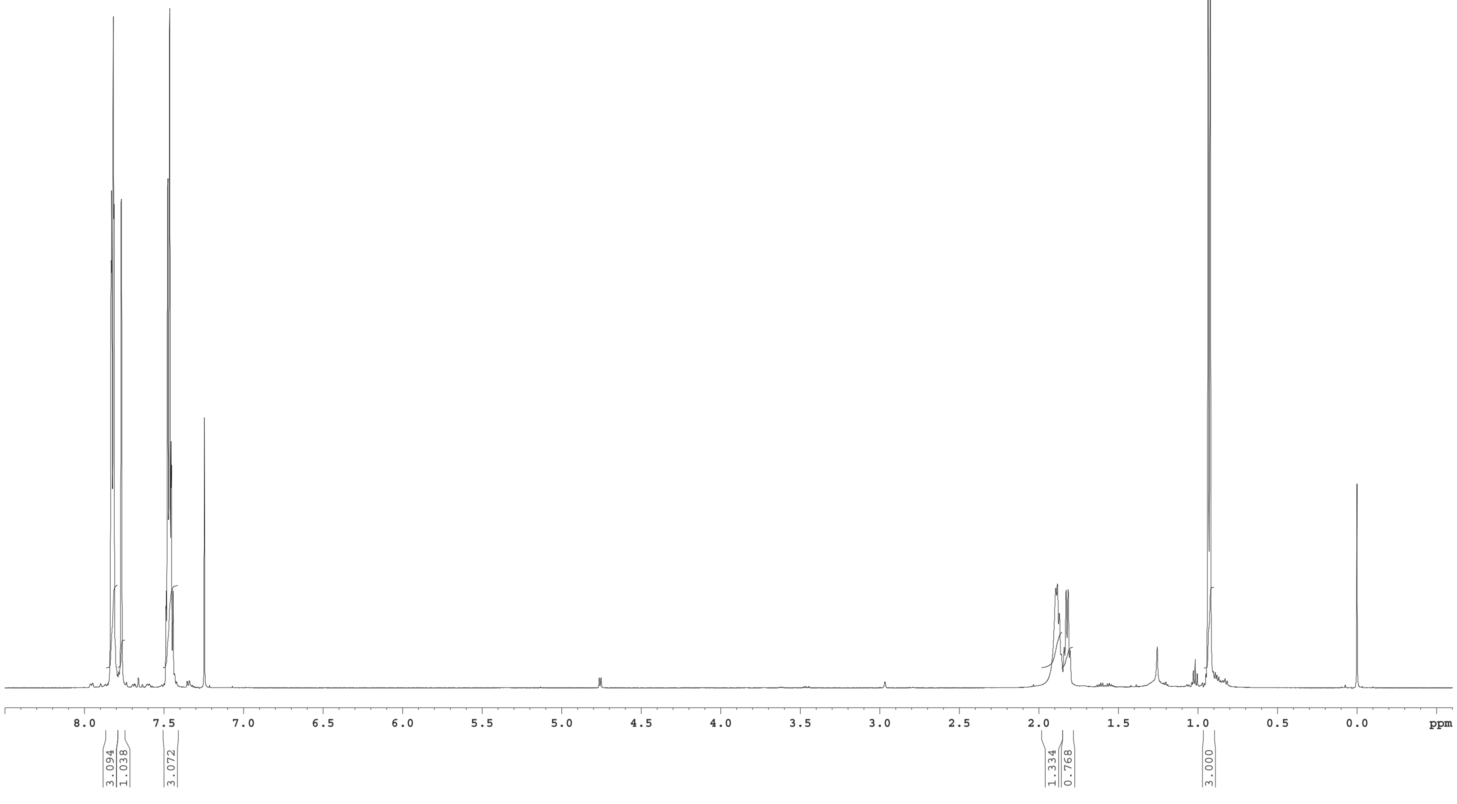
2.25

```
Current Data Parameters
USER                aaronj
NAME          AGJ_3_269_c1
EXPNO                    4
PROCNO                   1

F2 - Acquisition Parameters
Date_             20140425
Time                  8.26
INSTRUM            cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD                   65536
SOLVENT              CDCl3
NS                     400
DS                      16
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              0.25000000 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             125.7804187 MHz
WDW                     EM
SSB                      0
LB                    1.00 Hz
GB                       0
PC                    2.00
```

1H spectrum

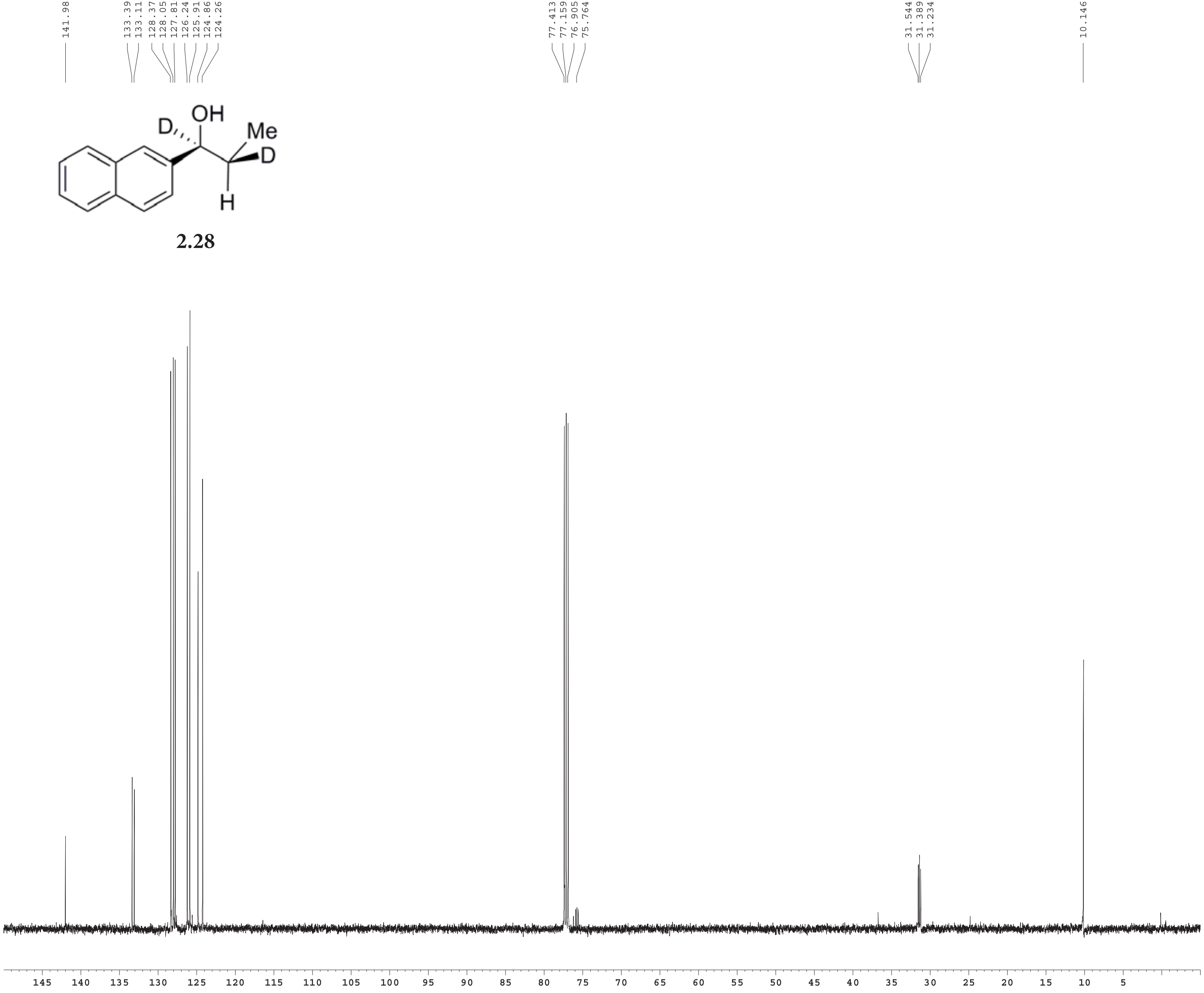


2.28



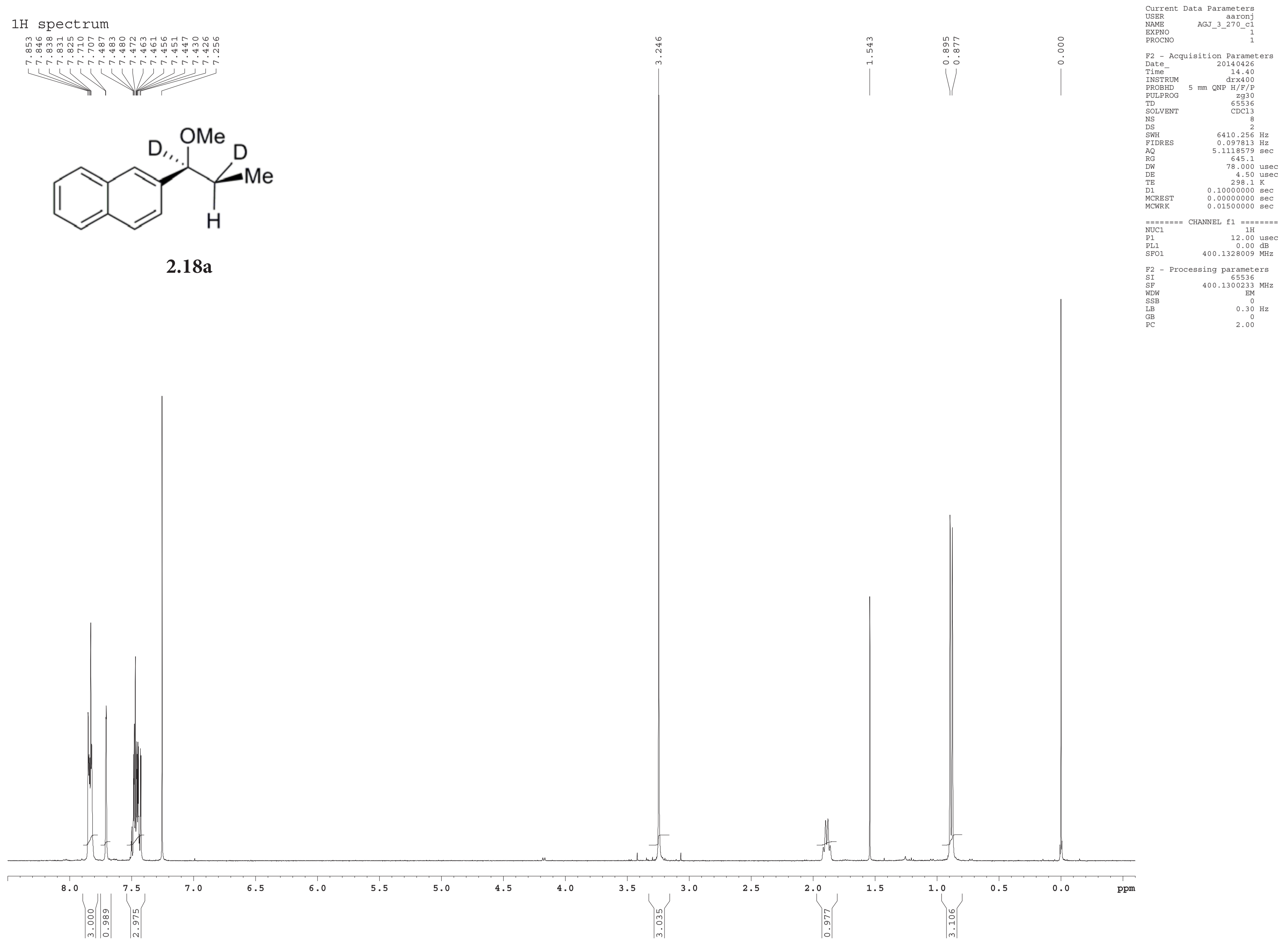
```
Current Data Parameters
USER              aaronj
NAME          AGJ_4_51_c2
EXPNO                   2
PROCNO                  1

F2 - Acquisition Parameters
Date_            20140730
Time                14.34
INSTRUM             av600
PROBHD   5 mm TBI 1H/13
PULPROG              zg30
TD                  98074
SOLVENT             CDCl3
NS                      8
DS                      2
SWH              9615.385 Hz
FIDRES           0.098042 Hz
AQ              5.0998979 sec
RG                    144
DW                 52.000 usec
DE                  14.54 usec
TE                  298.0 K
D1            0.10000000 sec
TD0                     1

======== CHANNEL f1 ========
SFO1         600.1342009 MHz
NUC1                   1H
P1                   8.00 usec

F2 - Processing parameters
SI                  65536
SF           600.1300416 MHz
WDW                    EM
SSB                     0
LB                   0.30 Hz
GB                      0
PC                   1.00
```

Z-restored spin-echo 13C spectrum with 1H decoupling



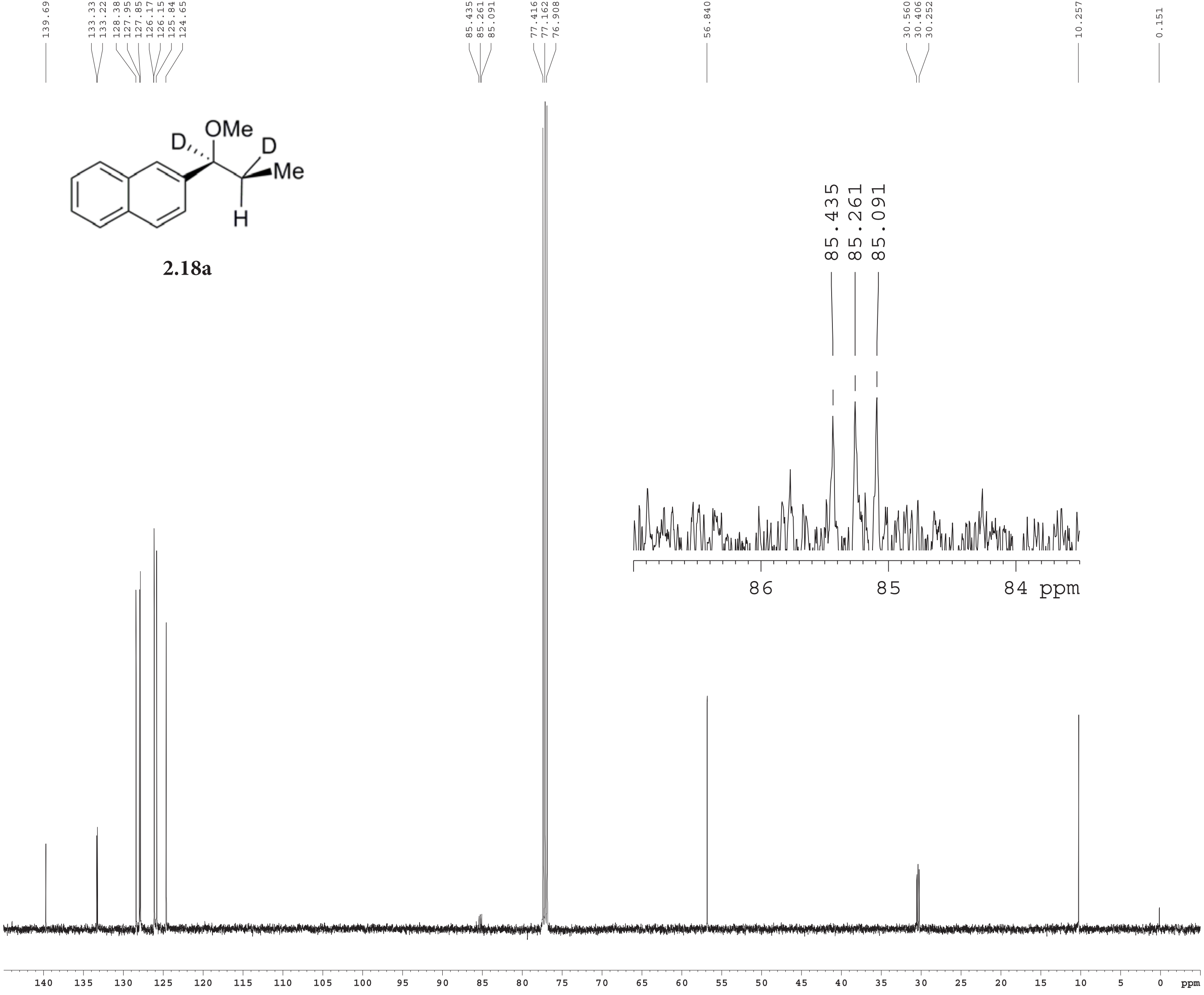
2.28

```
Current Data Parameters
USER              aaronj
NAME         AGJ_4_51_c3
EXPNO                  4
PROCNO                 1

F2 - Acquisition Parameters
Date_           20140730
Time               16.54
INSTRUM          cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD                 65536
SOLVENT            CDCl3
NS                   592
DS                    16
SWH            30303.031 Hz
FIDRES          0.462388 Hz
AQ             1.0813940 sec
RG               10321.3
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
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           125.7804094 MHz
WDW                   EM
SSB                    0
LB                  1.00 Hz
GB                     0
PC                  2.00
```


1H spectrum
7.853
7.846
7.838
7.831
7.825
7.710
7.707
7.487
7.483
7.480
7.472
7.463
7.461
7.456
7.451
7.447
7.430
7.426
7.256
3.246
1.543
0.895
0.877
0.000
OMe
D
D
Me
H
Current Data Parameters
USER aaronj
NAME AGJ_3_270_c1
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20140426
Time 14.40
INSTRUM drx400
PROBHD 5 mm QNP H/F/P
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 8
DS 2
SWH 6410.256 Hz
FIDRES 0.097813 Hz
AQ 5.1118579 sec
RG 645.1
DW 78.000 usec
DE 4.50 usec
TE 298.1 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 12.00 usec
PL1 0.00 dB
SFO1 400.1328009 MHz
F2 - Processing parameters
SI 65536
SF 400.1300233 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 2.00
8.0
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
0.0
ppm
3.000
0.989
2.975
3.035
0.977
3.106

2.18a

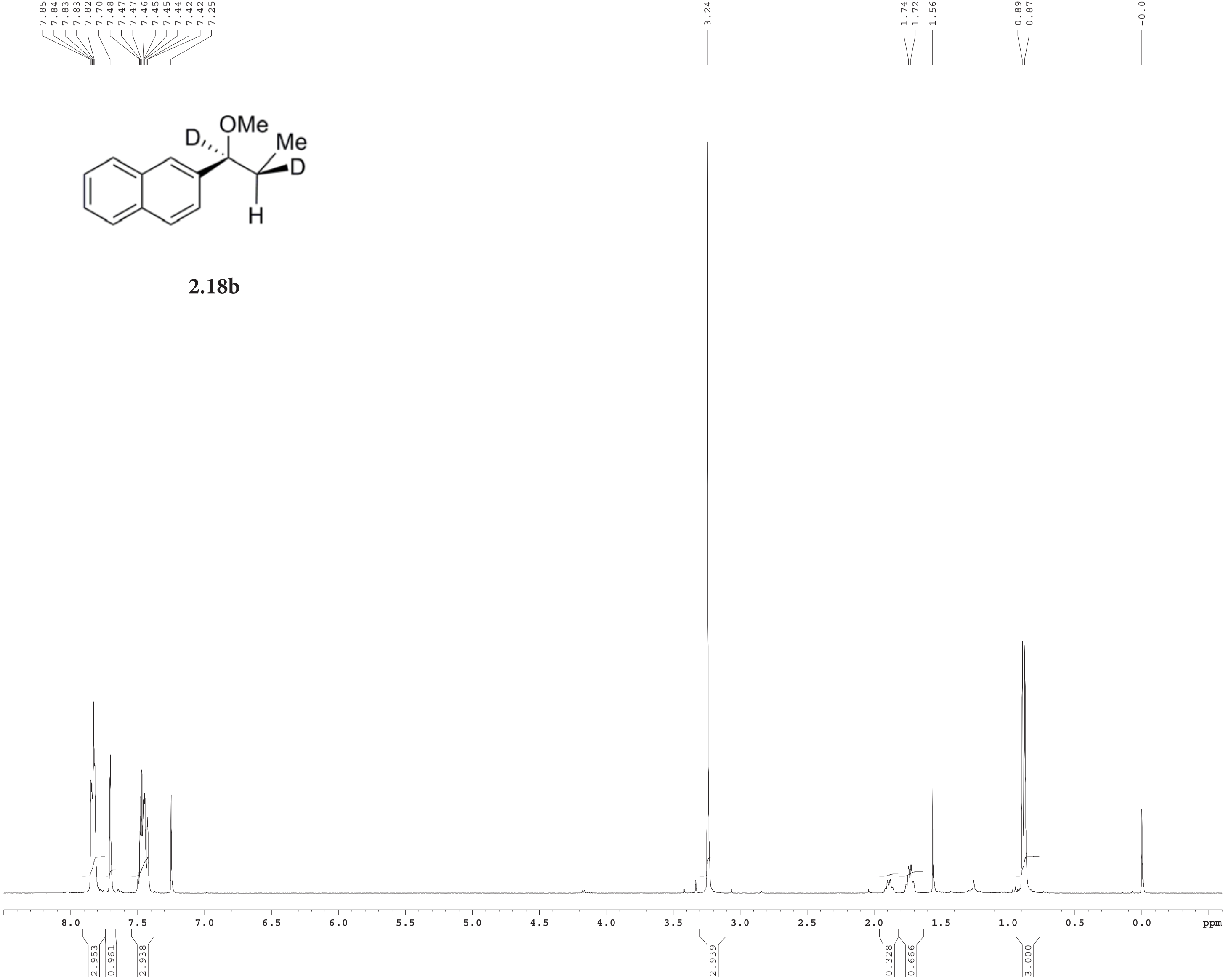
Z-restored spin-echo 13C spectrum with 1H decoupling



2.18a

```
Current Data Parameters
USER                aaronj
NAME          AGJ_3_270_c1
EXPNO                    2
PROCNO                   1

F2 - Acquisition Parameters
Date_             20140426
Time                 15.14
INSTRUM            cryo500
PROBHD    5 mm CPTCI 1H-
PULPROG   SpinEchopg30gp.prd
TD                   65536
SOLVENT              CDCl3
NS                    1400
DS                      16
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
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             125.7804085 MHz
WDW                     EM
SSB                      0
LB                    1.00 Hz
GB                       0
PC                    1.30
```

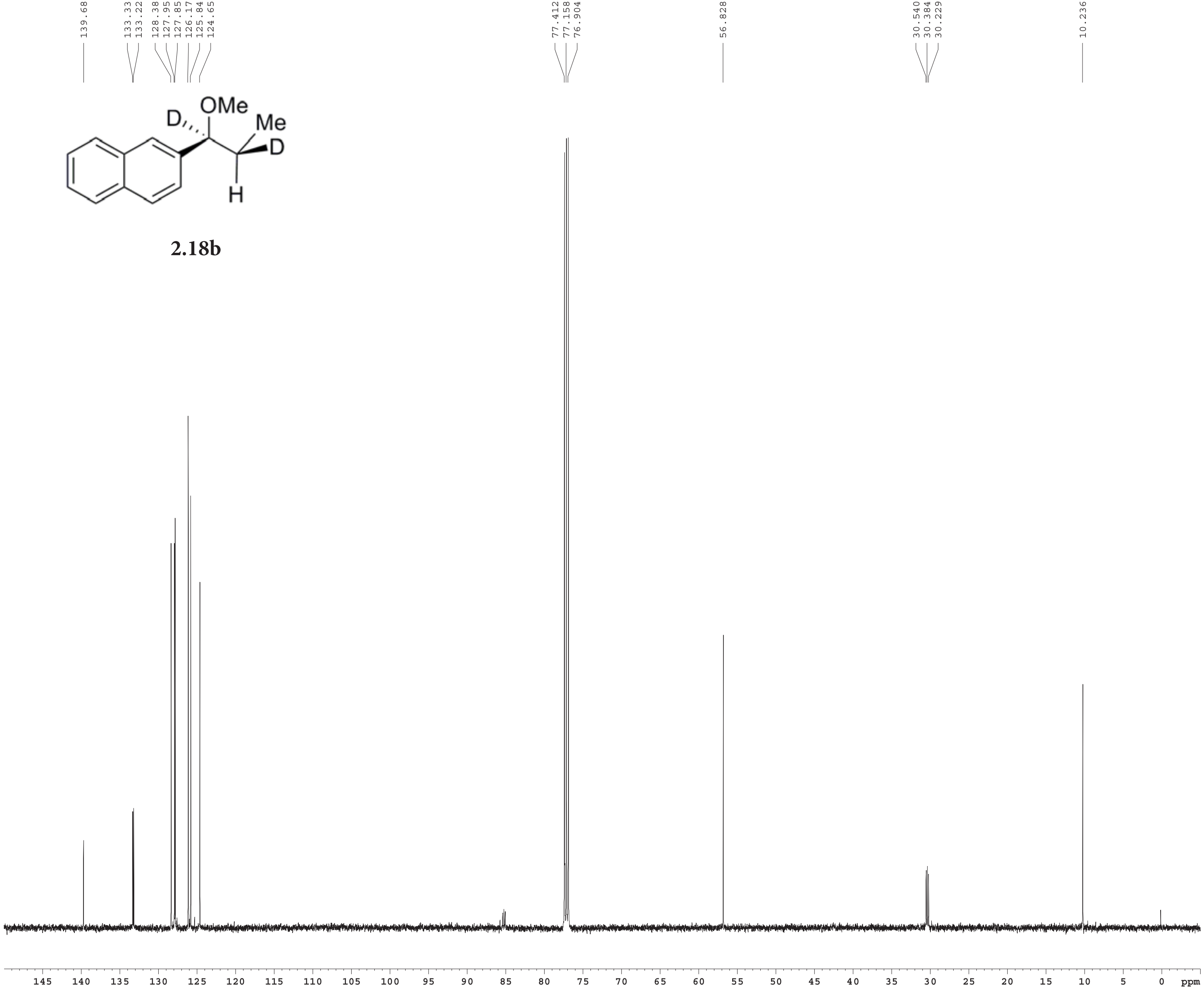
1H spectrum



2.18b

```
Current Data Parameters
USER              aaronj
NAME         AGJ_4_54_c1
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20140804
Time               12.02
INSTRUM           drx400
PROBHD   5 mm QNP H/F/P
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                     8
DS                     2
SWH             6410.256 Hz
FIDRES          0.097813 Hz
AQ             5.1118579 sec
RG                 322.5
DW                78.000 usec
DE                  4.50 usec
TE                 298.1 K
D1            0.10000000 sec
MCREST        0.00000000 sec
MCWRK         0.01500000 sec

======== CHANNEL f1 ========
NUC1                  1H
P1                 12.00 usec
PL1                 0.00 dB
SFO1         400.1328009 MHz

F2 - Processing parameters
SI                 65536
SF           400.1300007 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  2.00
```

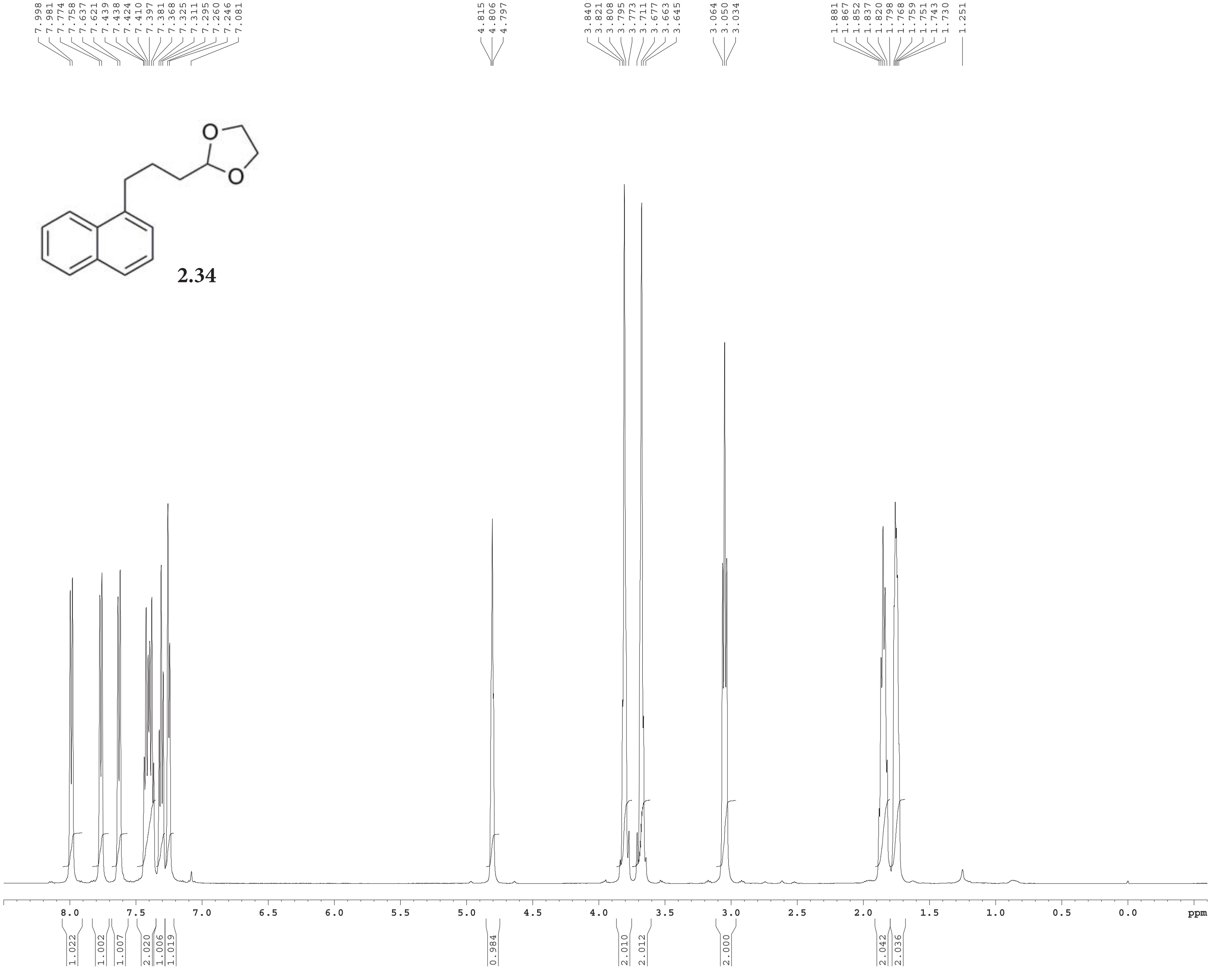
Z-restored spin-echo 13C spectrum with 1H decoupling



2.18b

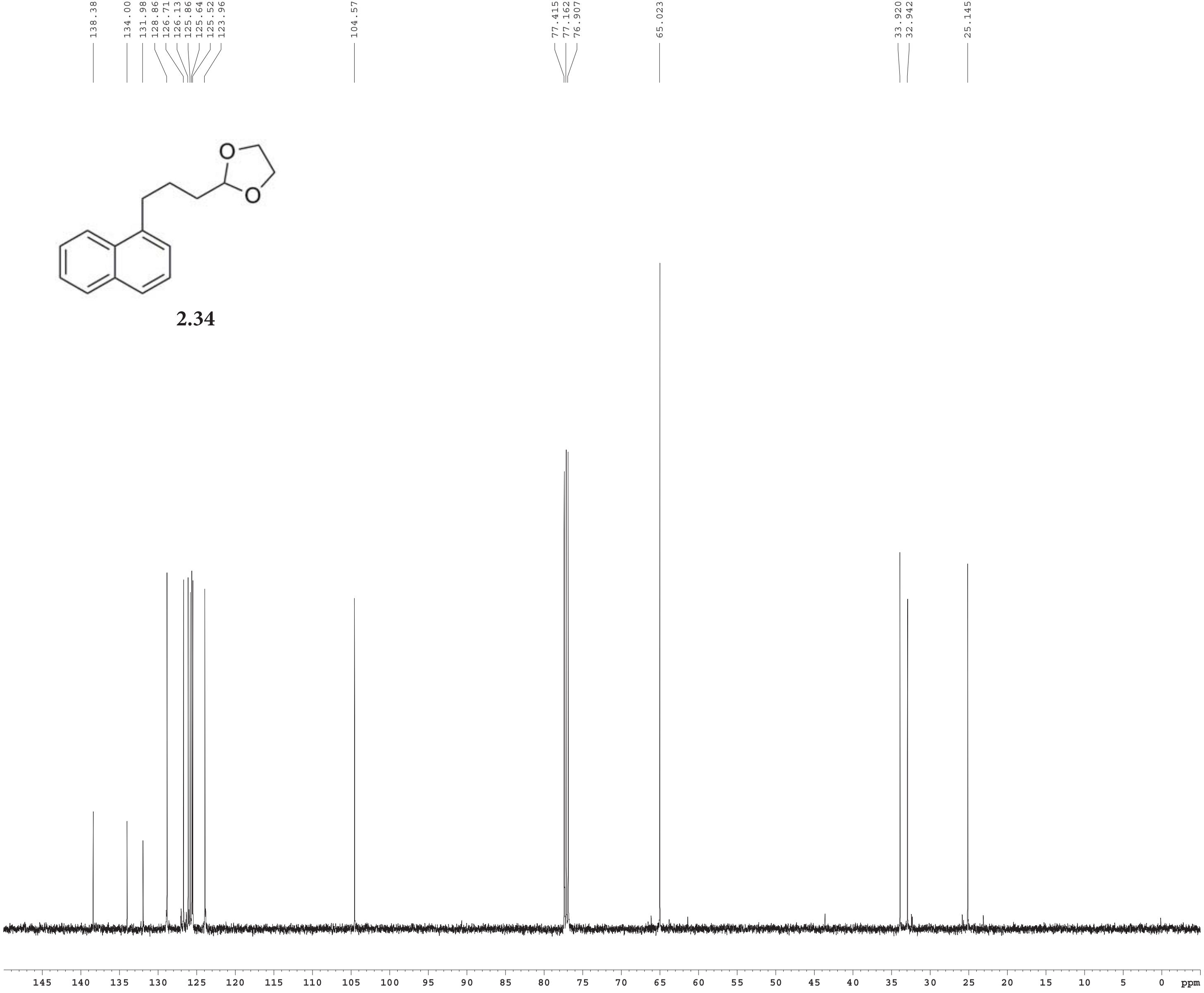
```
Current Data Parameters
USER              aaronj
NAME         AGJ_4_54_c1
EXPNO                  3
PROCNO                 1

F2 - Acquisition Parameters
Date_           20140804
Time               13.23
INSTRUM          cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD                 65536
SOLVENT            CDCl3
NS                  1024
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           125.7804085 MHz
WDW                   EM
SSB                    0
LB                  1.00 Hz
GB                     0
PC                  2.00
```

1H spectrum


2.34

```
Current Data Parameters
USER              aaronj
NAME         AGJ_3_117_C1
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20131105
Time               17.50
INSTRUM            gn500
PROBHD   5 mm broadband
PULPROG             zg30
TD                 81728
SOLVENT            CDCl3
NS                     8
DS                     2
SWH             8012.820 Hz
FIDRES          0.098043 Hz
AQ             5.0998774 sec
RG                    18
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                 12.20 usec
PL1                -5.00 dB
SFO1         499.2934950 MHz

F2 - Processing parameters
SI                 65536
SF           499.2901165 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.00
```

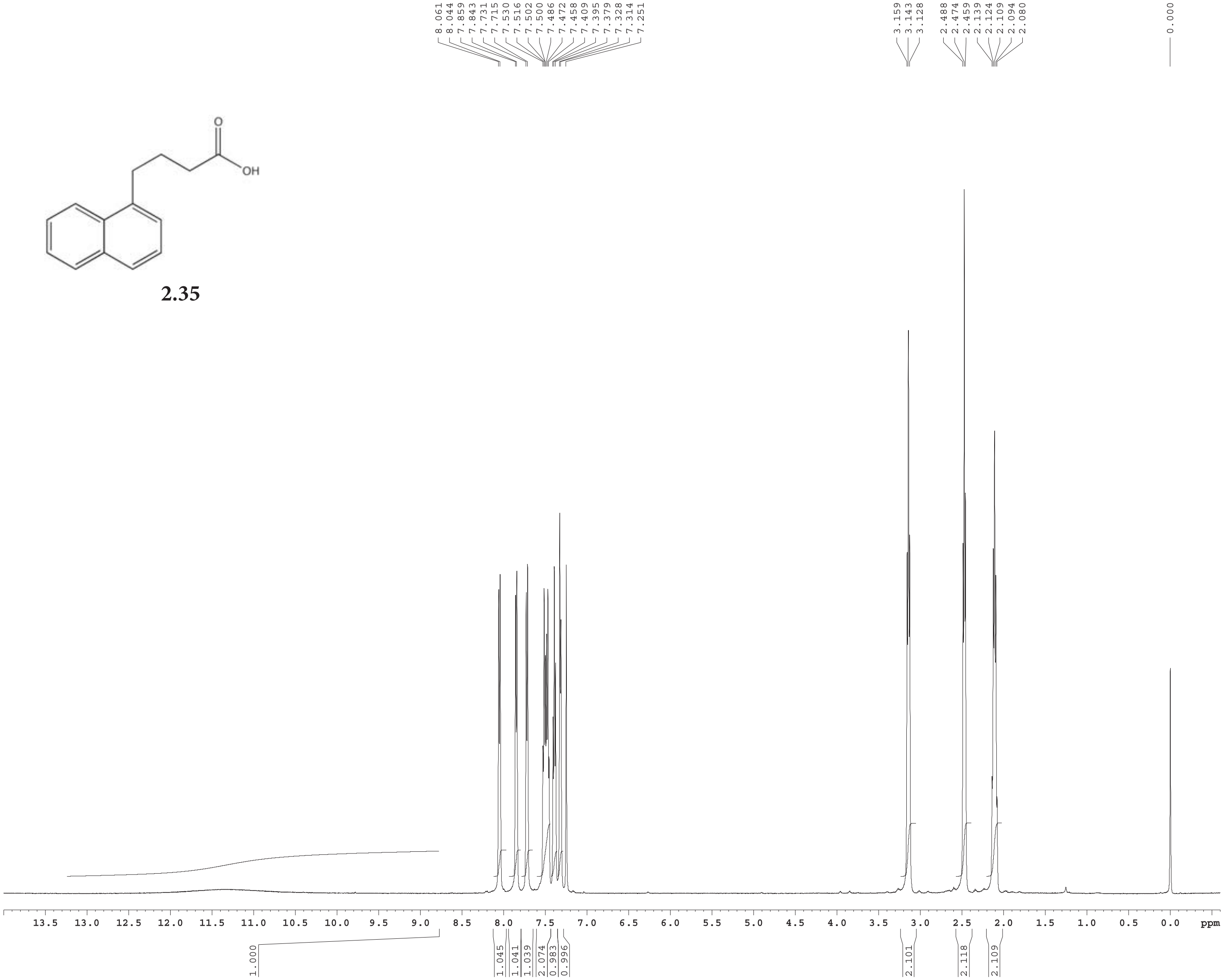
Z-restored spin-echo 13C spectrum with 1H decoupling



2.34

```
Current Data Parameters
USER              aaronj
NAME          AGJ_3_diox
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20140331
Time               15.22
INSTRUM          cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD                 65536
SOLVENT            CDCl3
NS                   400
DS                    16
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            0.25000000 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           125.7804099 MHz
WDW                   EM
SSB                    0
LB                  1.00 Hz
GB                     0
PC                  2.00
```

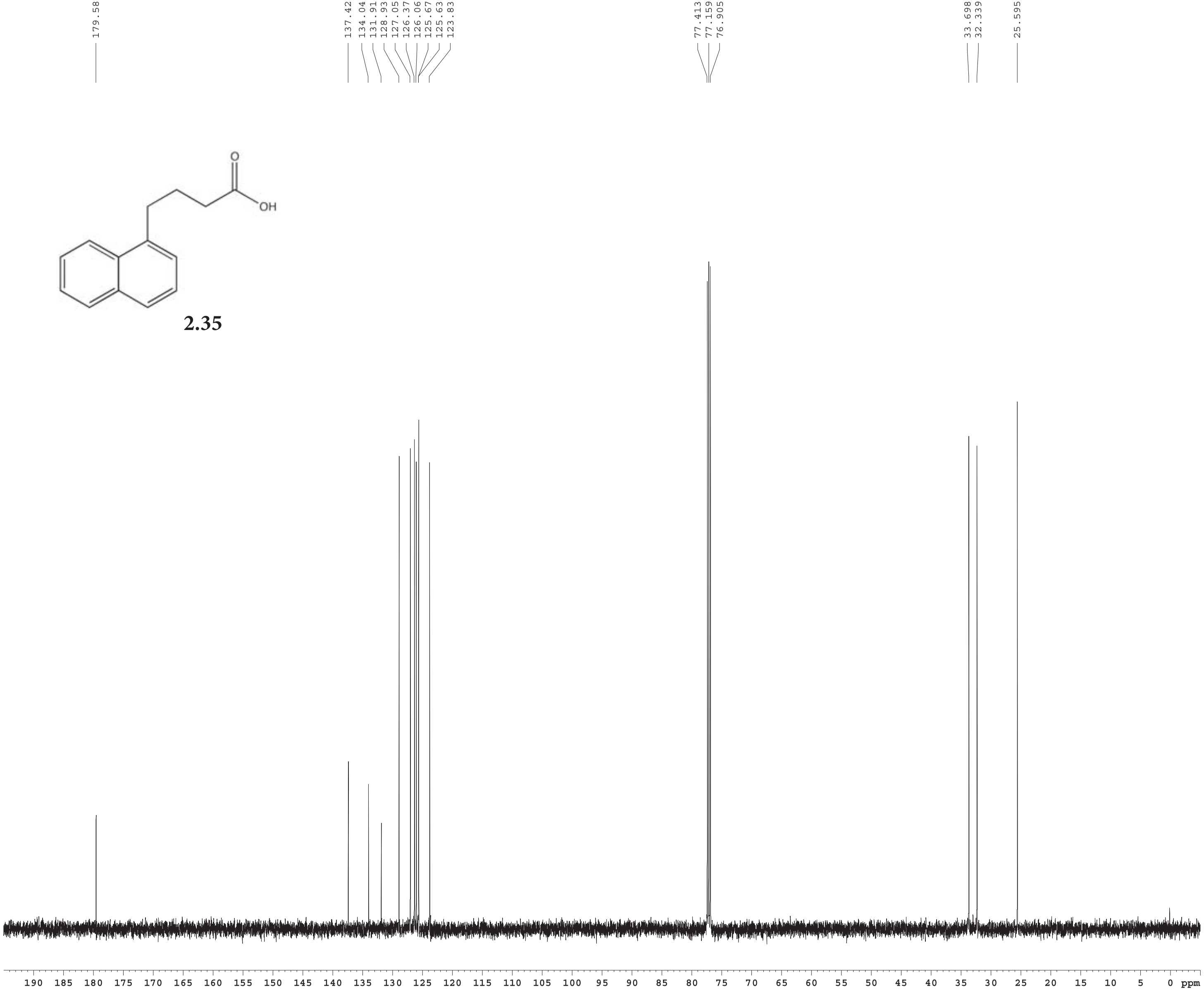
1H spectrum



2.35

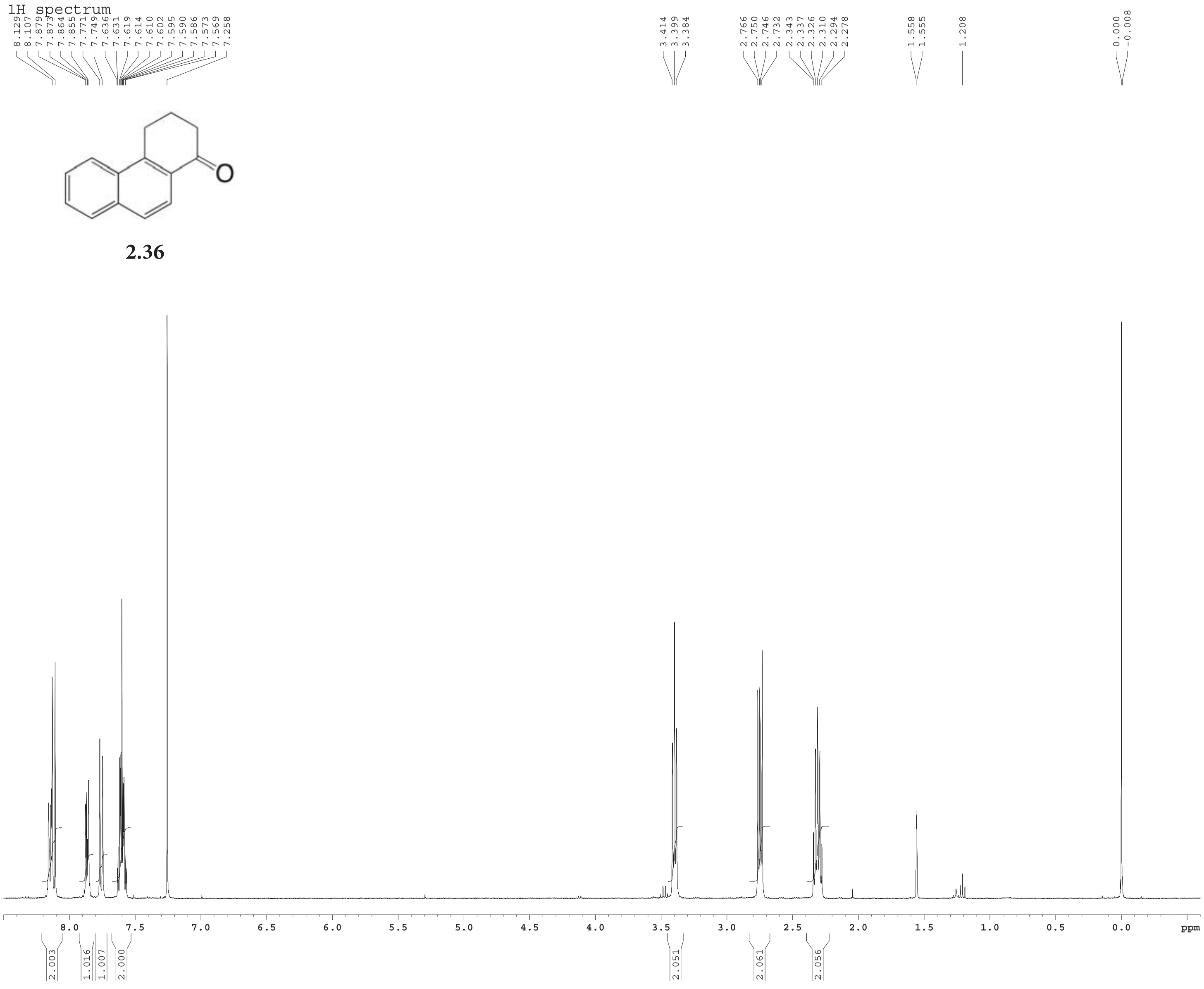
```
Current Data Parameters
USER              aaronj
NAME      AGJ_3_carboxacid
EXPNO                  3
PROCNO                 1

F2 - Acquisition Parameters
Date_           20140402
Time               15.24
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                1.60 dB
SFO1        500.2235015 MHz

F2 - Processing parameters
SI                65536
SF          500.2200349 MHz
WDW                  EM
SSB                   0
LB                 0.30 Hz
GB                    0
PC                 4.00
```

Z-restored spin-echo 13C spectrum with 1H decoupling



2.35

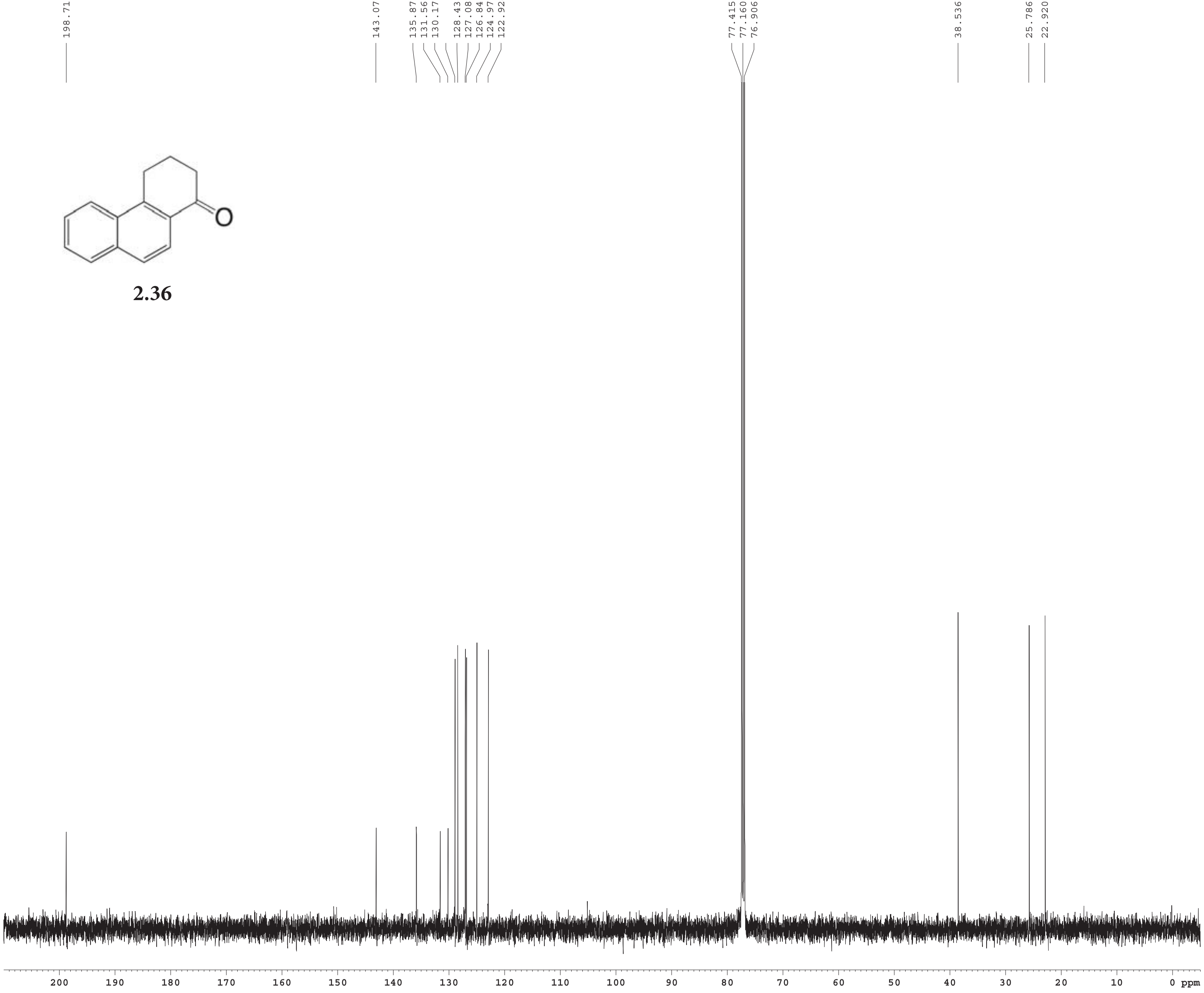
```
Current Data Parameters
USER                 aaronj
NAME      AGJ_3_carboxacid
EXPNO                     4
PROCNO                    1

F2 - Acquisition Parameters
Date_              20140402
Time                  15.30
INSTRUM             cryo500
PROBHD    5 mm CPTCI 1H-
PULPROG   SpinEchopg30gp.prd
TD                    65536
SOLVENT               CDCl3
NS                      344
DS                       16
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
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              125.7804090 MHz
WDW                      EM
SSB                       0
LB                     1.00 Hz
GB                        0
PC                     2.00
```



2.36

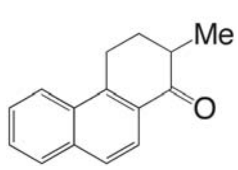
```
Current Data Parameters
USER              aaronj
NAME         AGJ_3_123_c1
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20131109
Time               16.34
INSTRUM           drx400
PROBHD   5 mm QNP H/F/P
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                     8
DS                     2
SWH             6410.256 Hz
FIDRES          0.097813 Hz
AQ             5.1118579 sec
RG                 574.7
DW                78.000 usec
DE                  4.50 usec
TE                 298.0 K
D1            0.10000000 sec
MCREST        0.00000000 sec
MCWRK         0.01500000 sec

======== CHANNEL f1 ========
NUC1                  1H
P1                 12.00 usec
PL1                 0.00 dB
SFO1         400.1328009 MHz

F2 - Processing parameters
SI                 65536
SF           400.1300225 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  2.00
```

13C spectrum with 1H decoupling

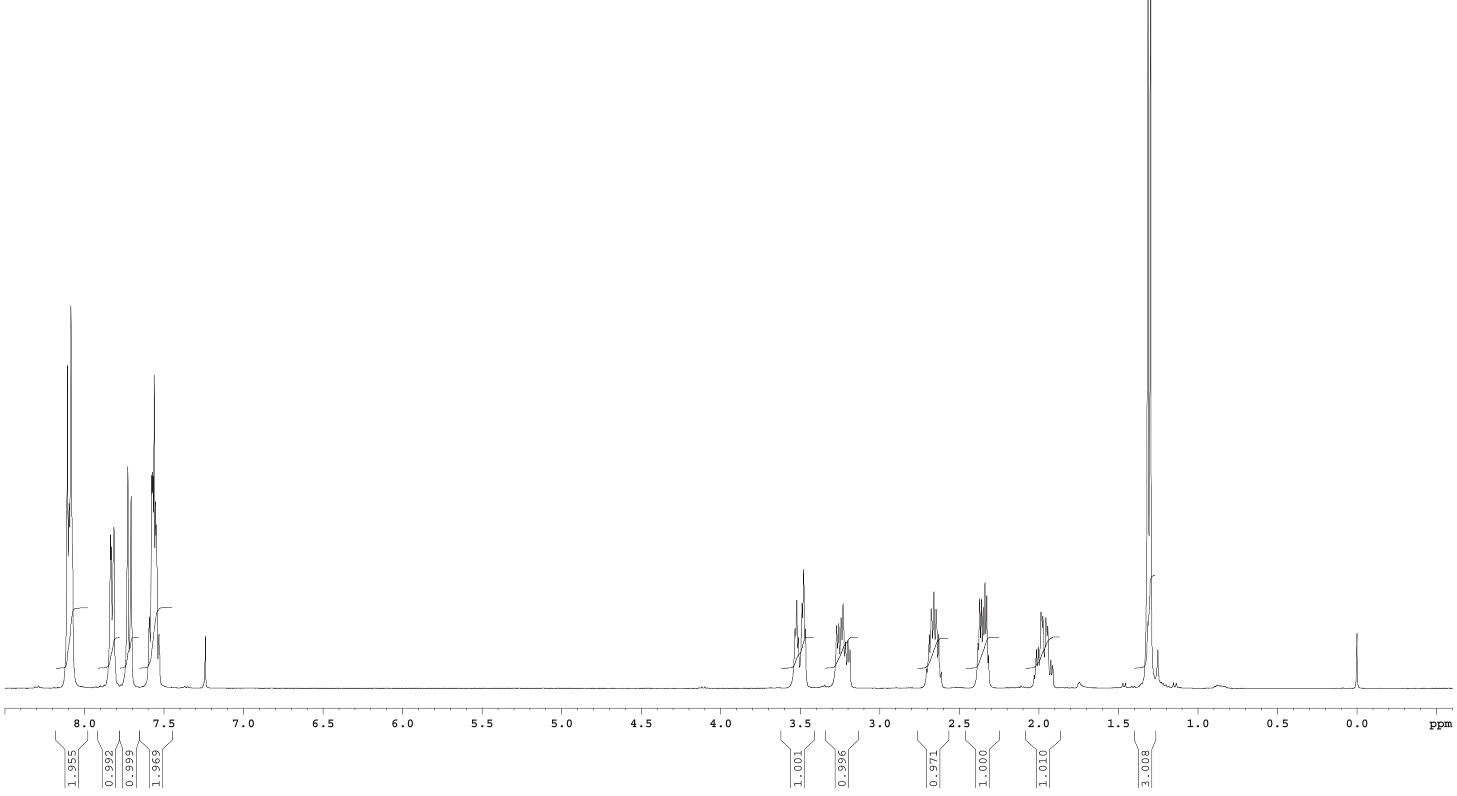

2.36

```
Current Data Parameters
USER              aaronj
NAME        AGJ_3_ketone
EXPNO                  4
PROCNO                 1

F2 - Acquisition Parameters
Date_           20140401
Time               17.21
INSTRUM            gn500
PROBHD   5 mm broadband
PULPROG           zgdc30
TD                 65536
SOLVENT            CDCl3
NS                   640
DS                     4
SWH          30303.031 Hz
FIDRES        0.462388 Hz
AQ           1.0813940 sec
RG             41285.1
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          125.5465574 MHz
WDW                   EM
SSB                    0
LB                  1.00 Hz
GB                     0
PC                  2.00
```

1H spectrum

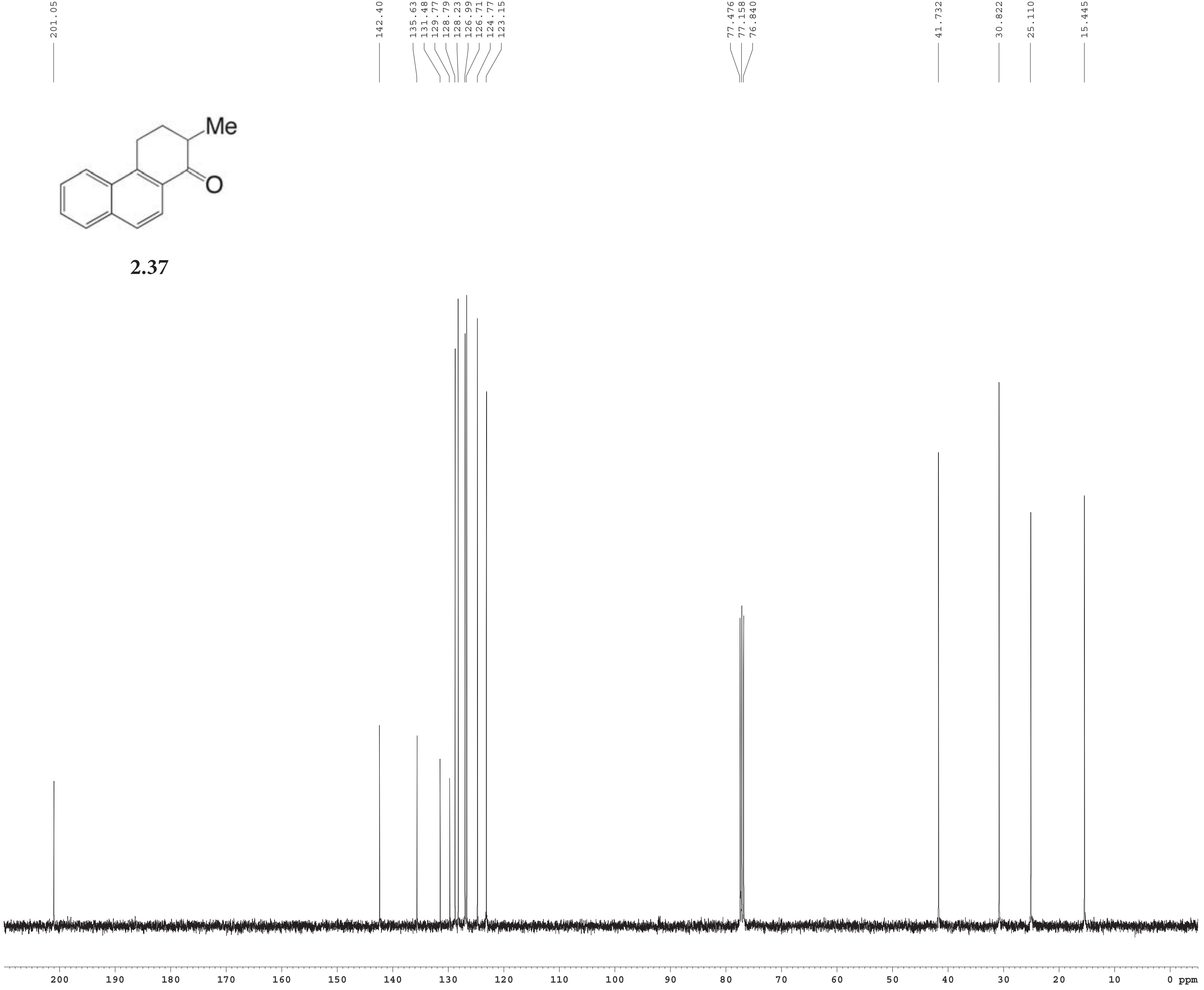


2.37



```
Current Data Parameters
USER              aaronj
NAME            AGJ_3_125
EXPNO                   1
PROCNO                  1

F2 - Acquisition Parameters
Date_            20131113
Time                13.54
INSTRUM            drx400
PROBHD   5 mm QNP H/F/P
PULPROG              zg30
TD                  65536
SOLVENT             CDCl3
NS                      8
DS                      2
SWH              6410.256 Hz
FIDRES           0.097813 Hz
AQ              5.1118579 sec
RG                   80.6
DW                 78.000 usec
DE                   4.50 usec
TE                  298.0 K
D1             0.10000000 sec
MCREST         0.00000000 sec
MCWRK          0.01500000 sec

======== CHANNEL f1 ========
NUC1                   1H
P1                  12.00 usec
PL1                  0.00 dB
SFO1          400.1328009 MHz

F2 - Processing parameters
SI                  65536
SF            400.1300289 MHz
WDW                    EM
SSB                     0
LB                   0.30 Hz
GB                      0
PC                   2.00
```

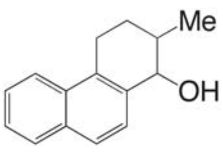
13C spectrum with 1H decoupling



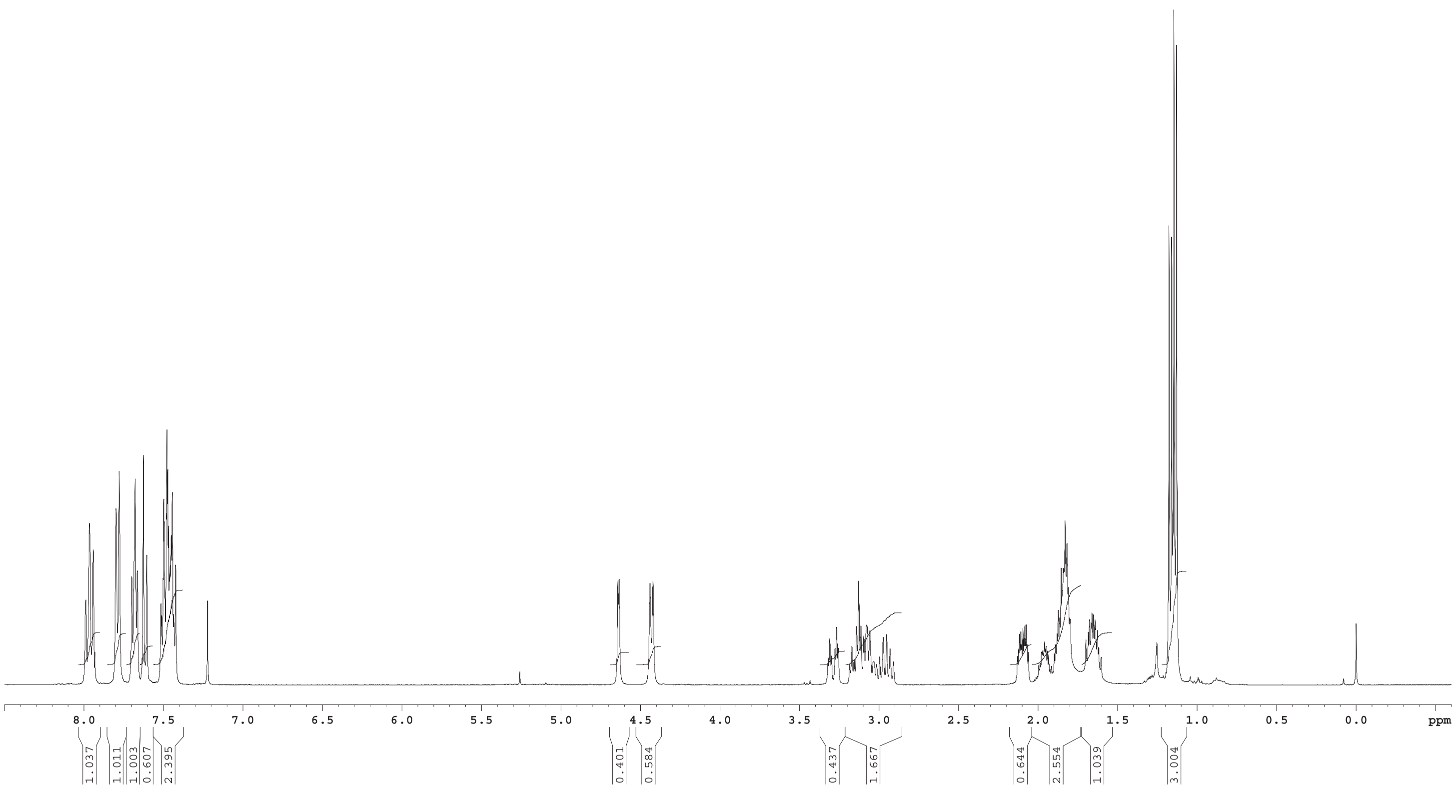
2.37

```
Current Data Parameters
USER              aaronj
NAME           AGJ_3_125
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20131113
Time               13.59
INSTRUM           drx400
PROBHD   5 mm QNP H/F/P
PULPROG           zgdc30
TD                 65536
SOLVENT            CDCl3
NS                   478
DS                     4
SWH            24154.590 Hz
FIDRES          0.368570 Hz
AQ             1.3566452 sec
RG                7298.2
DW                20.700 usec
DE                 20.39 usec
TE                 298.1 K
D1            0.10000000 sec
d11           0.03000000 sec
MCREST        0.00000000 sec
MCWRK         0.01500000 sec

======== CHANNEL f1 ========
NUC1                 13C
P1                  7.75 usec
PL1                -3.00 dB
SFO1         100.6237964 MHz

======== CHANNEL f2 ========
CPDPRG2           mlev16
NUC2                  1H
PCPD2              90.00 usec
PL2                 0.00 dB
PL12               17.70 dB
SFO2         400.1328009 MHz

F2 - Processing parameters
SI                 65536
SF           100.6127654 MHz
WDW                   EM
SSB                    0
LB                  1.00 Hz
GB                     0
PC                  1.00
```

1H spectrum

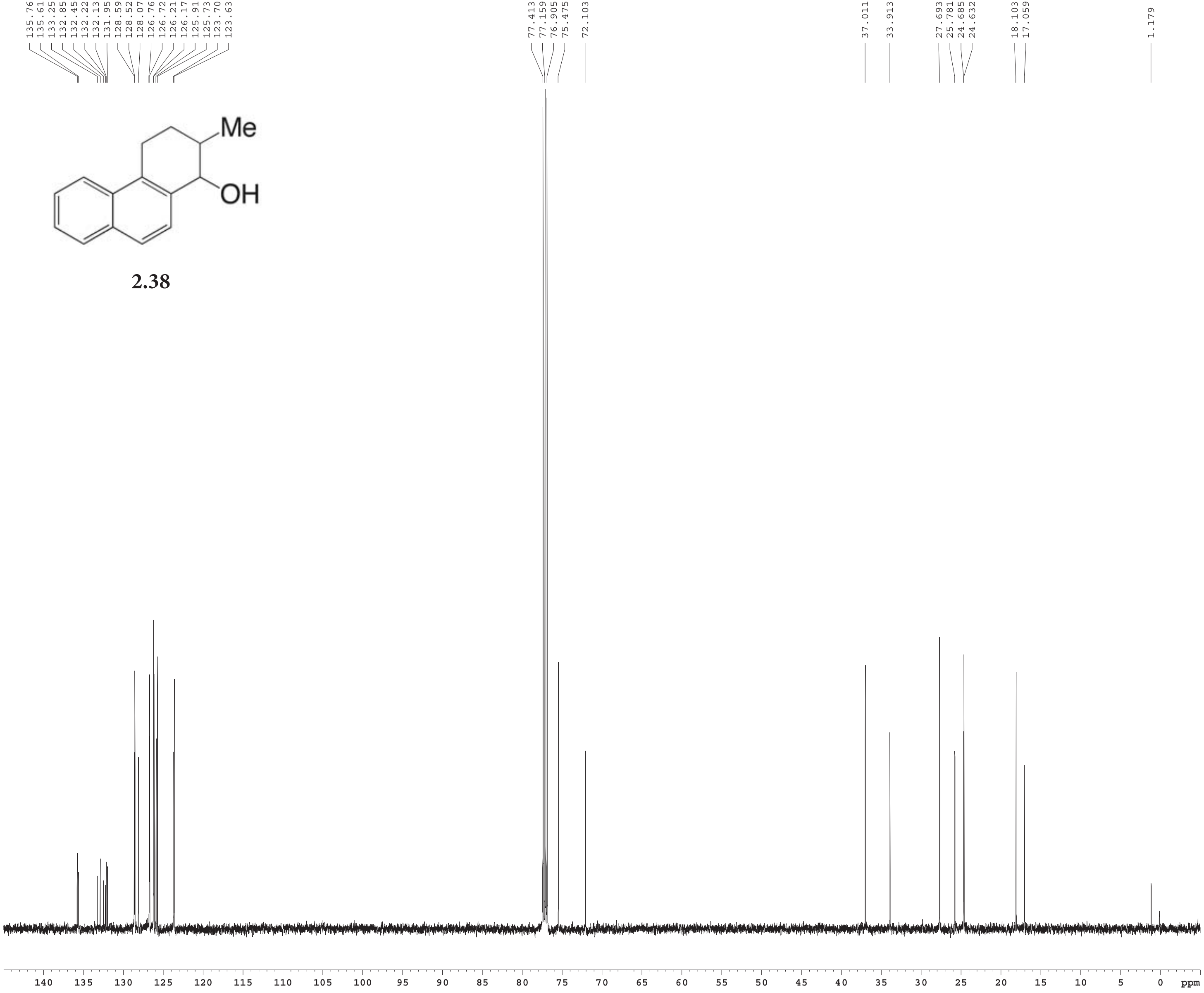


2.38



```
Current Data Parameters
USER                aaronj
NAME             AGJ_3_126
EXPNO                    1
PROCNO                   1

F2 - Acquisition Parameters
Date_             20131114
Time                 18.05
INSTRUM             drx400
PROBHD   5 mm QNP H/F/P
PULPROG               zg30
TD                   65536
SOLVENT              CDCl3
NS                       8
DS                       2
SWH               6410.256 Hz
FIDRES            0.097813 Hz
AQ               5.1118579 sec
RG                   101.6
DW                  78.000 usec
DE                    4.50 usec
TE                   298.0 K
D1              0.10000000 sec
MCREST          0.00000000 sec
MCWRK           0.01500000 sec

======== CHANNEL f1 ========
NUC1                    1H
P1                   12.00 usec
PL1                   0.00 dB
SFO1           400.1328009 MHz

F2 - Processing parameters
SI                   65536
SF             400.1300361 MHz
WDW                     EM
SSB                      0
LB                    0.30 Hz
GB                       0
PC                    2.00
```

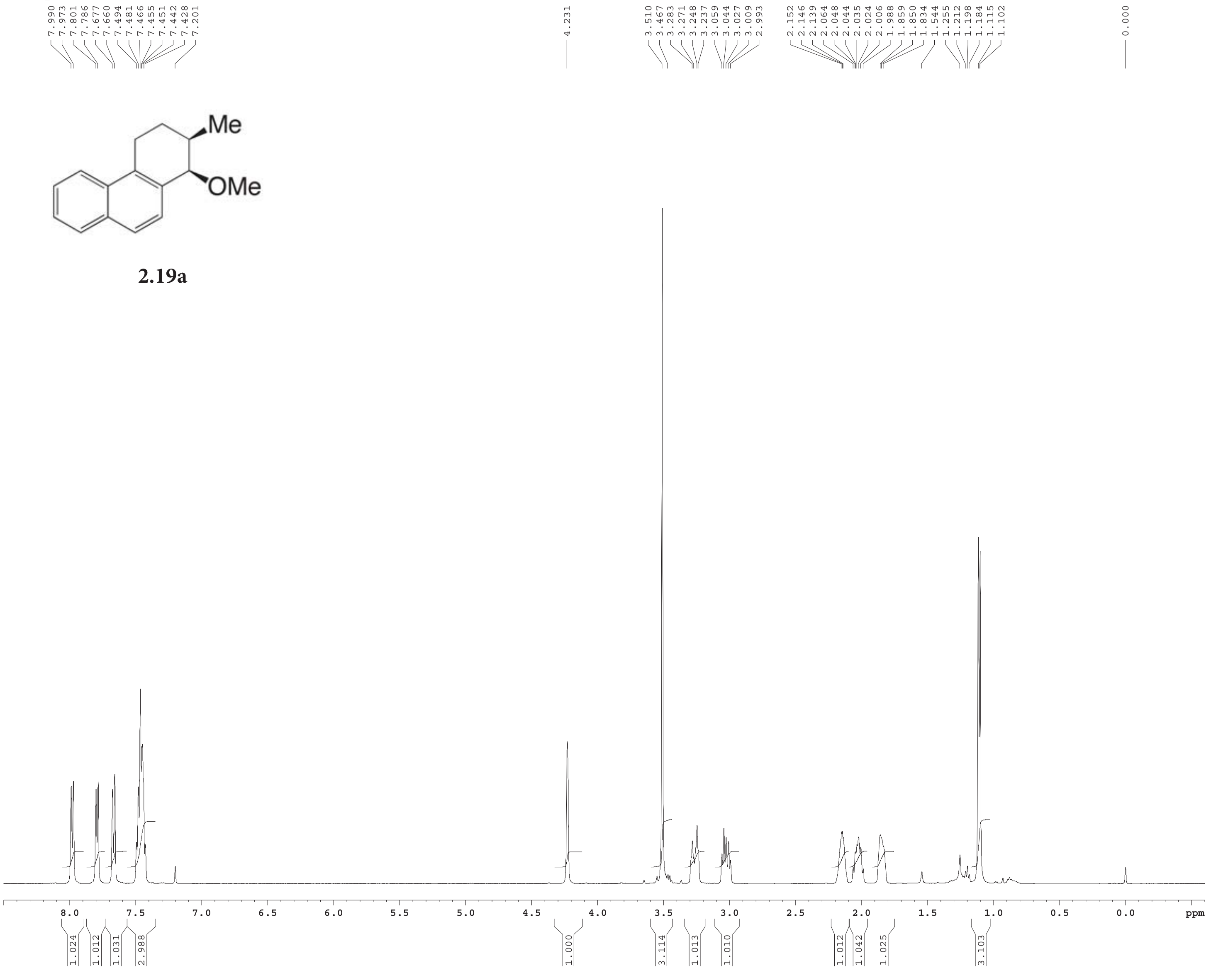
Z-restored spin-echo 13C spectrum with 1H decoupling



2.38

```
Current Data Parameters
USER              aaronj
NAME       AGJ_3_125_char
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20140315
Time               16.04
INSTRUM          cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD                 65536
SOLVENT            CDCl3
NS                  1024
DS                    16
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            0.25000000 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           125.7804090 MHz
WDW                   EM
SSB                    0
LB                  1.00 Hz
GB                     0
PC                  2.00
```

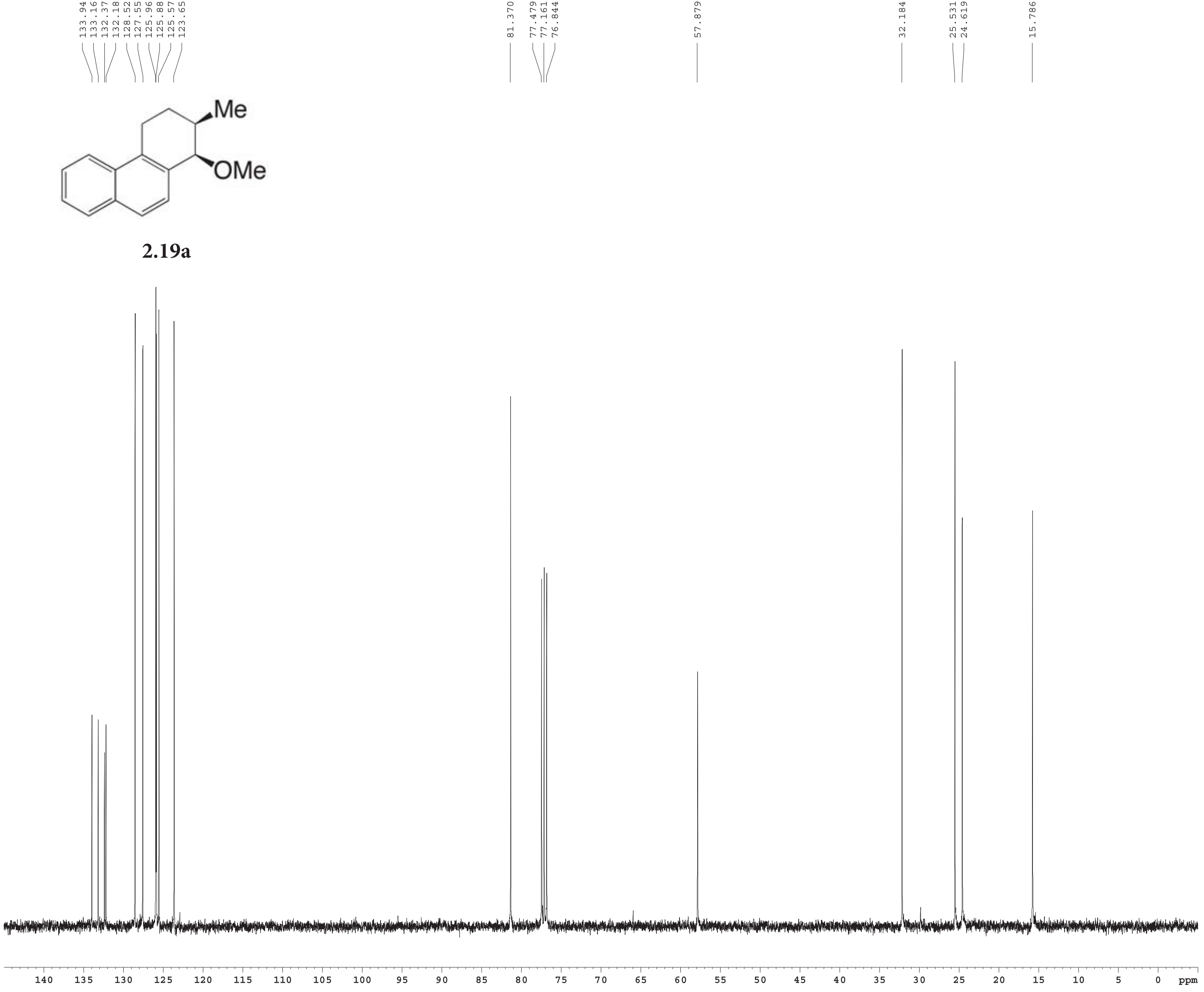
1H spectrum



2.19a

```
Current Data Parameters
USER              aaronj
NAME      AGJ_3_128_C1_1
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20131121
Time                7.21
INSTRUM            gn500
PROBHD   5 mm broadband
PULPROG             zg30
TD                 81728
SOLVENT            CDCl3
NS                     8
DS                     2
SWH             8012.820 Hz
FIDRES          0.098043 Hz
AQ             5.0998774 sec
RG                  40.3
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                 12.20 usec
PL1                -5.00 dB
SFO1         499.2934950 MHz

F2 - Processing parameters
SI                 65536
SF           499.2900583 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.00
```

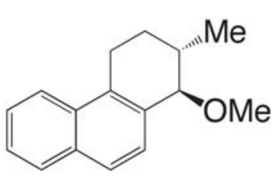
13C spectrum with 1H decoupling



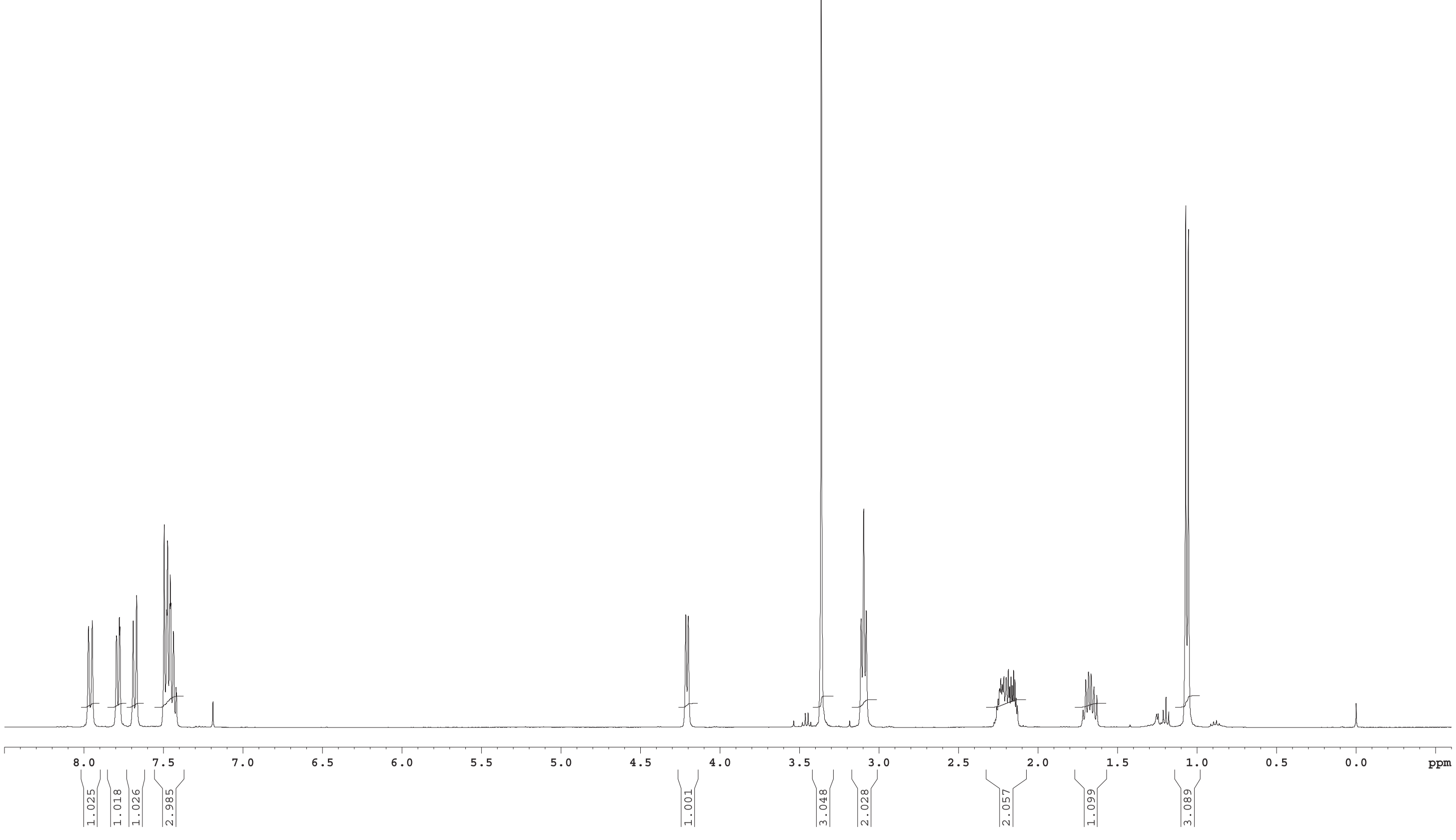
2.19a

```
Current Data Parameters
USER              aaronj
NAME      AGJ_3_128_c1_1
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20131121
Time               15.56
INSTRUM           drx400
PROBHD   5 mm QNP H/F/P
PULPROG          zgdc30
TD                 65536
SOLVENT            CDCl3
NS                   400
DS                     4
SWH           24154.590 Hz
FIDRES         0.368570 Hz
AQ            1.3566452 sec
RG                 16384
DW                20.700 usec
DE                 20.39 usec
TE                 298.0 K
D1            0.10000000 sec
d11           0.03000000 sec
MCREST        0.00000000 sec
MCWRK         0.01500000 sec

======== CHANNEL f1 ========
NUC1                 13C
P1                  7.75 usec
PL1                -3.00 dB
SFO1        100.6237964 MHz

======== CHANNEL f2 ========
CPDPRG2           mlev16
NUC2                  1H
PCPD2              90.00 usec
PL2                 0.00 dB
PL12               17.70 dB
SFO2        400.1328009 MHz

F2 - Processing parameters
SI                 65536
SF          100.6127650 MHz
WDW                   EM
SSB                    0
LB                  1.00 Hz
GB                     0
PC                  1.00
```

1H spectrum

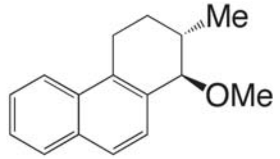


2.19b

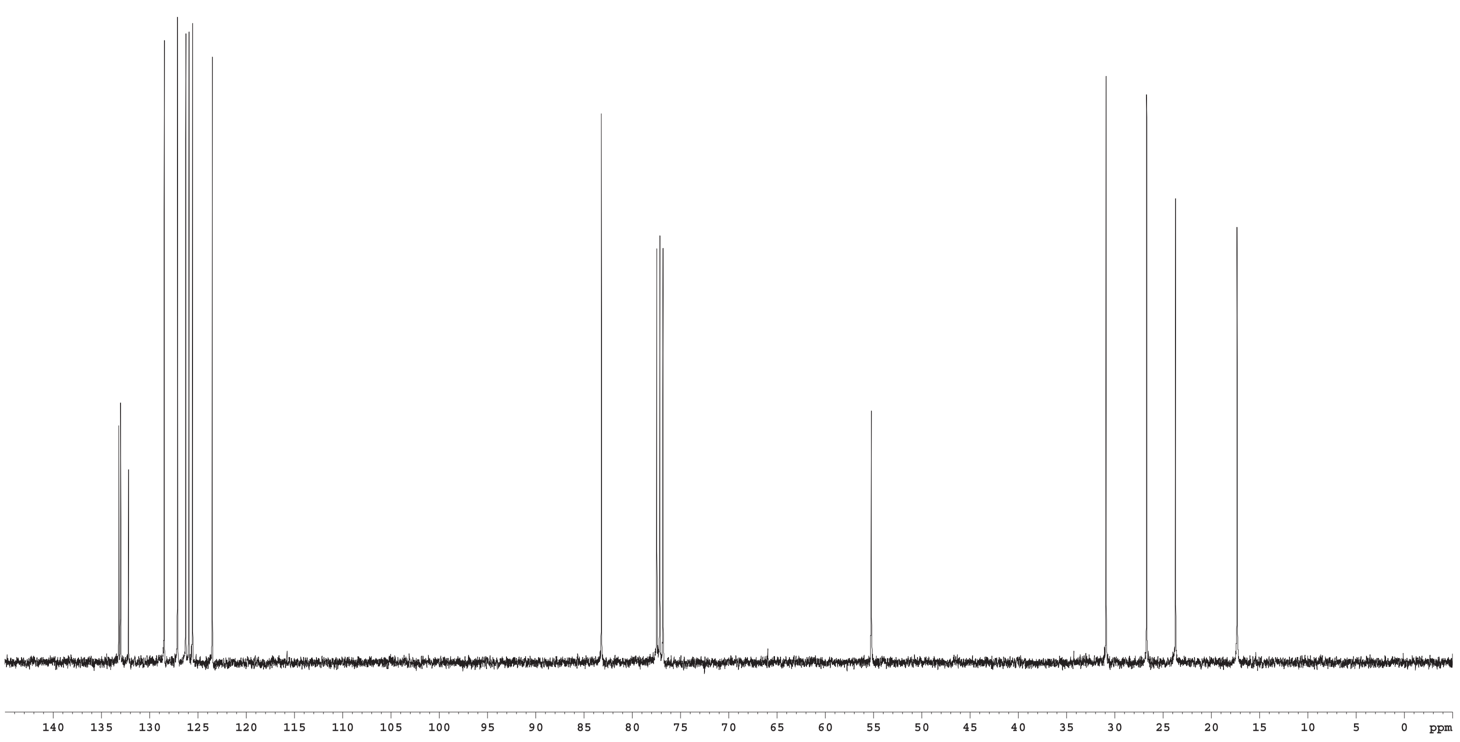


```
Current Data Parameters
USER              aaronj
NAME      AGJ_3_128_c1_2
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20131120
Time               13.06
INSTRUM           drx400
PROBHD   5 mm QNP H/F/P
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                     8
DS                     2
SWH             6410.256 Hz
FIDRES          0.097813 Hz
AQ             5.1118579 sec
RG                  50.8
DW                78.000 usec
DE                  4.50 usec
TE                 298.0 K
D1            0.10000000 sec
MCREST        0.00000000 sec
MCWRK         0.01500000 sec

======== CHANNEL f1 ========
NUC1                  1H
P1                 12.00 usec
PL1                 0.00 dB
SFO1         400.1328009 MHz

F2 - Processing parameters
SI                 65536
SF           400.1300496 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  2.00
```

13C spectrum with 1H decoupling

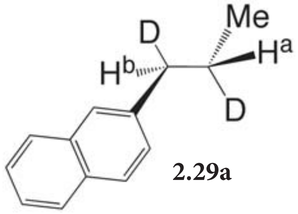


2.19b

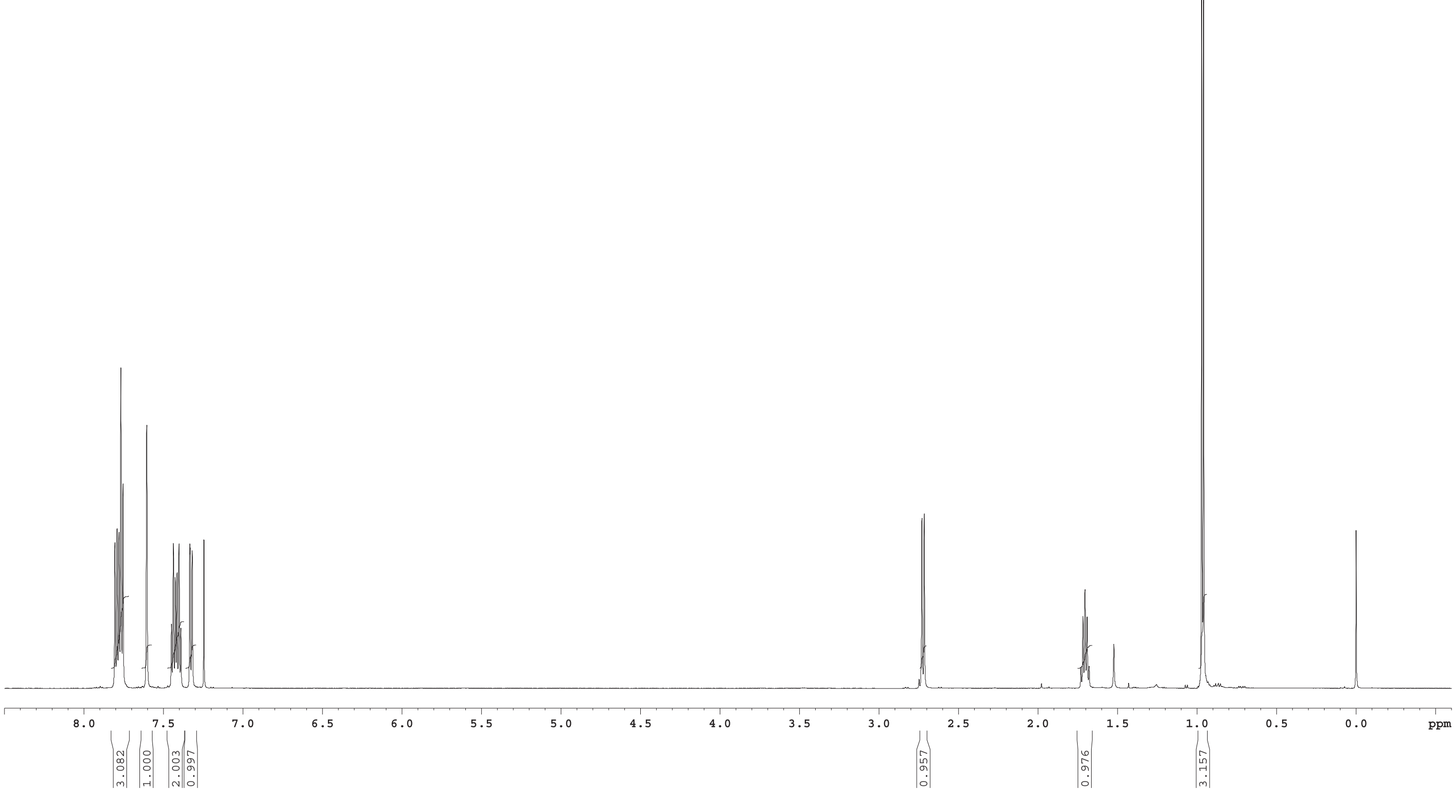


```
Current Data Parameters
USER              aaronj
NAME      AGJ_3_128_c1_2
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20131120
Time               13.10
INSTRUM           drx400
PROBHD   5 mm QNP H/F/P
PULPROG          zgdc30
TD                 65536
SOLVENT            CDCl3
NS                   241
DS                     4
SWH           24154.590 Hz
FIDRES         0.368570 Hz
AQ            1.3566452 sec
RG                9195.2
DW                20.700 usec
DE                 20.39 usec
TE                 298.0 K
D1            0.10000000 sec
d11           0.03000000 sec
MCREST        0.00000000 sec
MCWRK         0.01500000 sec

======== CHANNEL f1 ========
NUC1                 13C
P1                  7.75 usec
PL1                -3.00 dB
SFO1        100.6237964 MHz

======== CHANNEL f2 ========
CPDPRG2           mlev16
NUC2                  1H
PCPD2              90.00 usec
PL2                 0.00 dB
PL12               17.70 dB
SFO2        400.1328009 MHz

F2 - Processing parameters
SI                 65536
SF           100.6127683 MHz
WDW                   EM
SSB                    0
LB                  1.00 Hz
GB                     0
PC                  1.00
```

1H spectrum

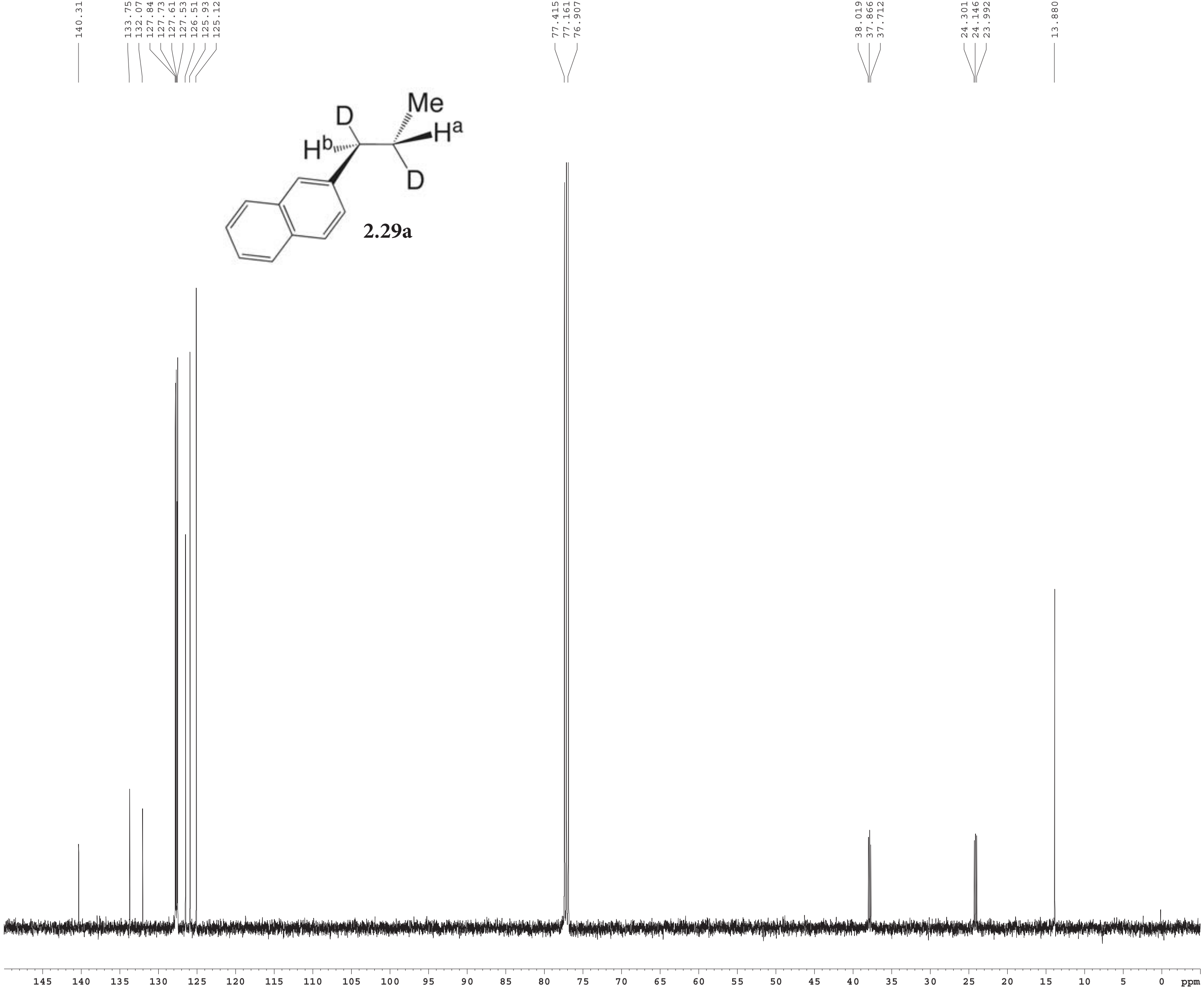


2.29a

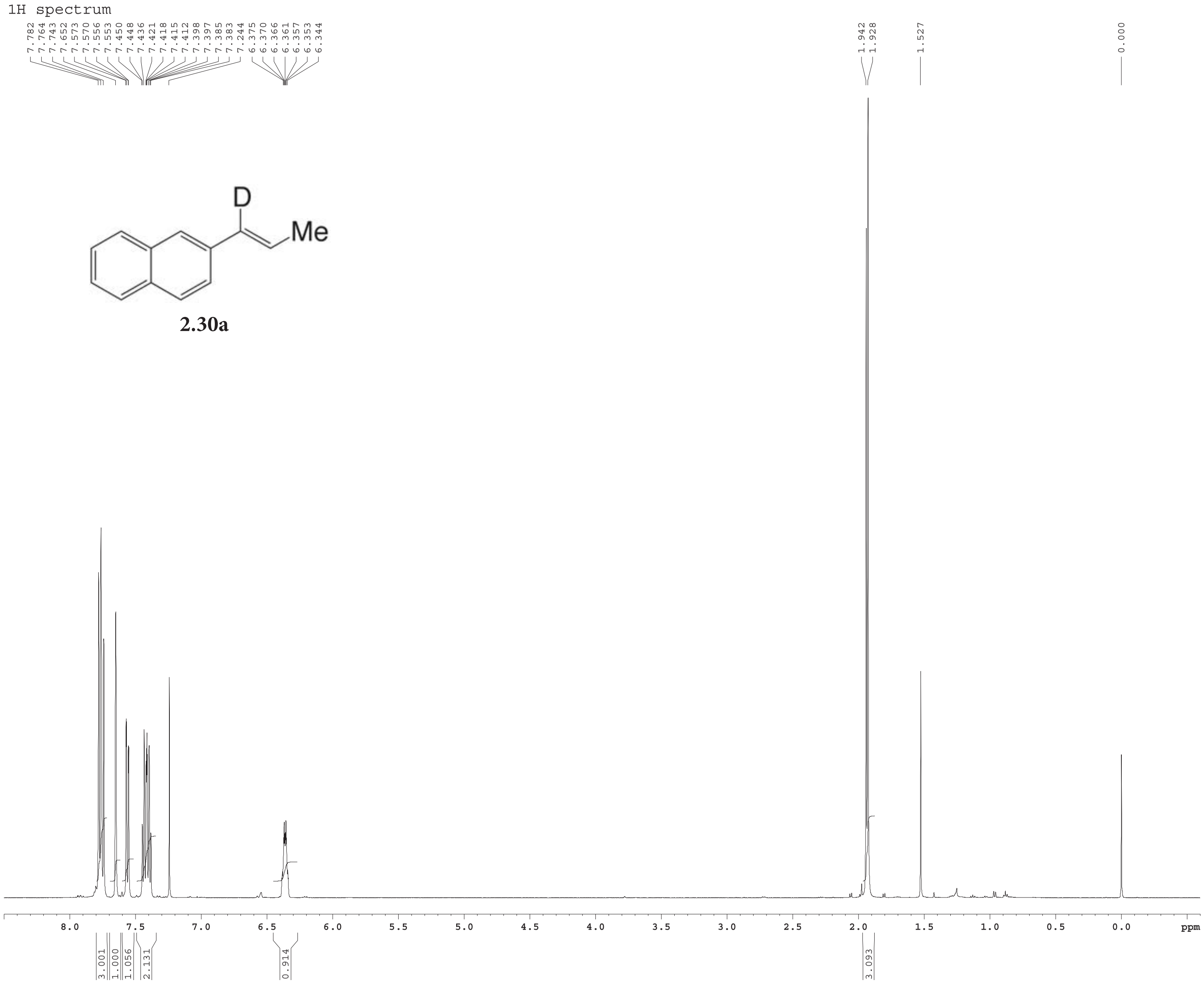


```
Current Data Parameters
USER              aaronj
NAME            AGJ_3_271
EXPNO                   3
PROCNO                  1

F2 - Acquisition Parameters
Date_            20140501
Time                11.32
INSTRUM             av600
PROBHD   5 mm TBI 1H/13
PULPROG          zg1h2h.2
TD                  98074
SOLVENT             CDCl3
NS                      8
DS                      2
SWH              9615.385 Hz
FIDRES           0.098042 Hz
AQ              5.0998979 sec
RG                    114
DW                 52.000 usec
DE                  11.13 usec
TE                  294.6 K
D1             4.00000000 sec
D11            0.03000000 sec
D12            0.00002000 sec
TD0                     1

======== CHANNEL f1 ========
SFO1         600.1342009 MHz
NUC1                   1H
P1                   8.00 usec

F2 - Processing parameters
SI                  65536
SF          600.1300415 MHz
WDW                    EM
SSB                     0
LB                   0.30 Hz
GB                      0
PC                   1.00
```

Z-restored spin-echo 13C spectrum with 1H decoupling



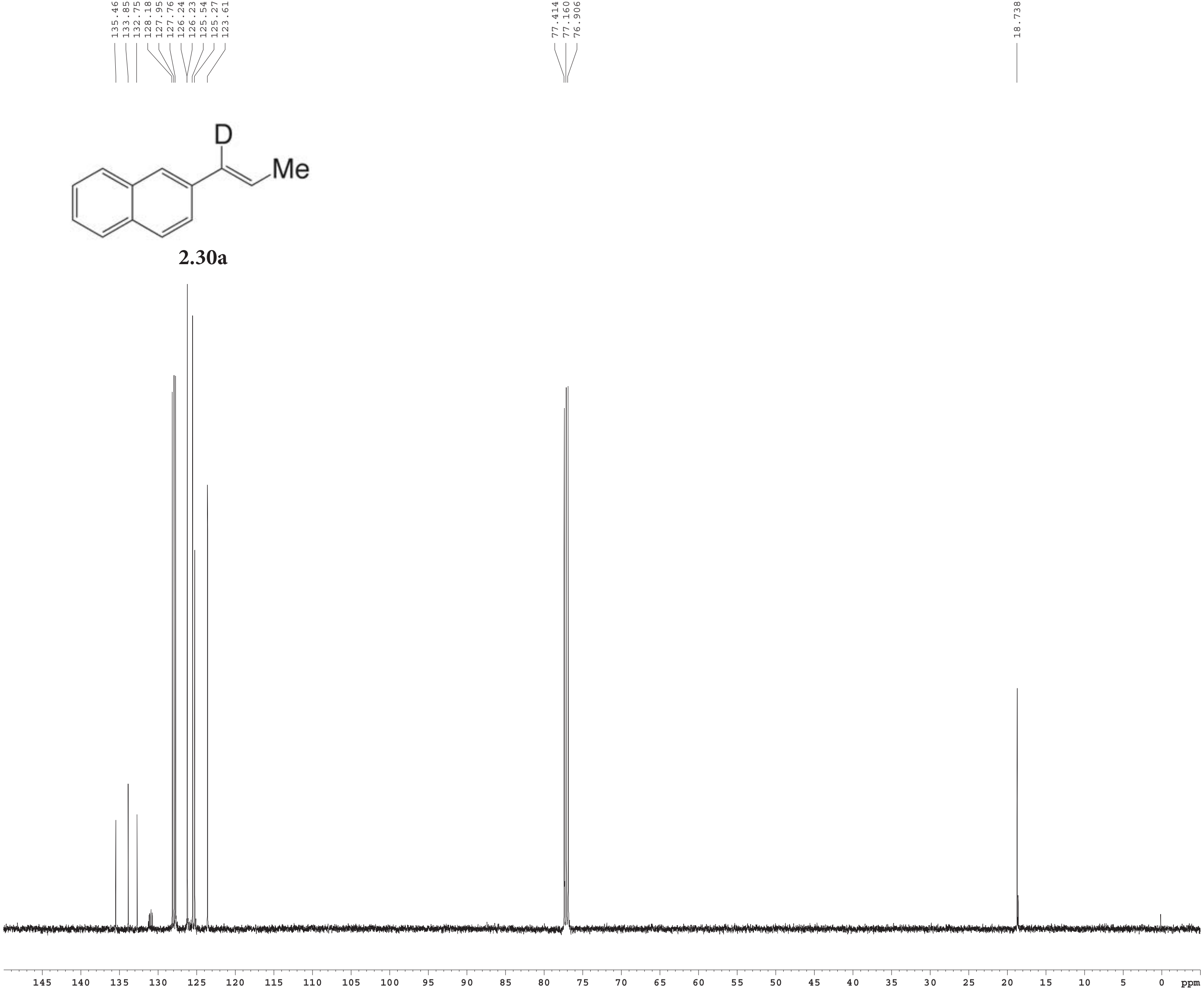
```
Current Data Parameters
USER                aaronj
NAME          AGJ_3_271_c1
EXPNO                    4
PROCNO                   1

F2 - Acquisition Parameters
Date_             20140501
Time                 11.50
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             125.7804094 MHz
WDW                     EM
SSB                      0
LB                    1.00 Hz
GB                       0
PC                    2.00
```



2.30a

```
Current Data Parameters
USER             aaronj
NAME        AGJ_4_176_c1
EXPNO                 5
PROCNO                1

F2 - Acquisition Parameters
Date_          20150527
Time              13.10
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                  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          500.2200395 MHz
WDW                  EM
SSB                   0
LB                 0.30 Hz
GB                    0
PC                 2.00
```

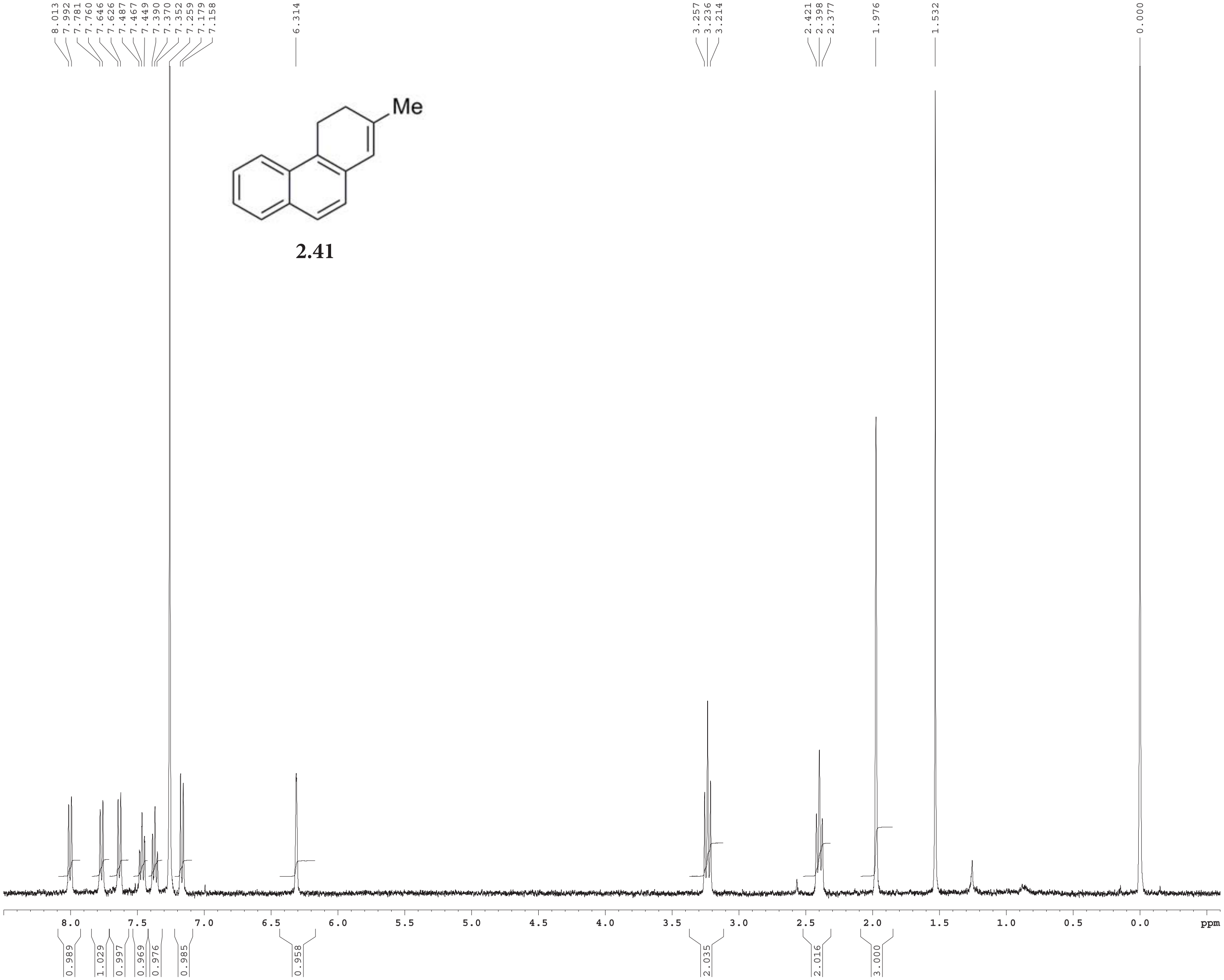
Z-restored spin-echo 13C spectrum with 1H decoupling



2.30a

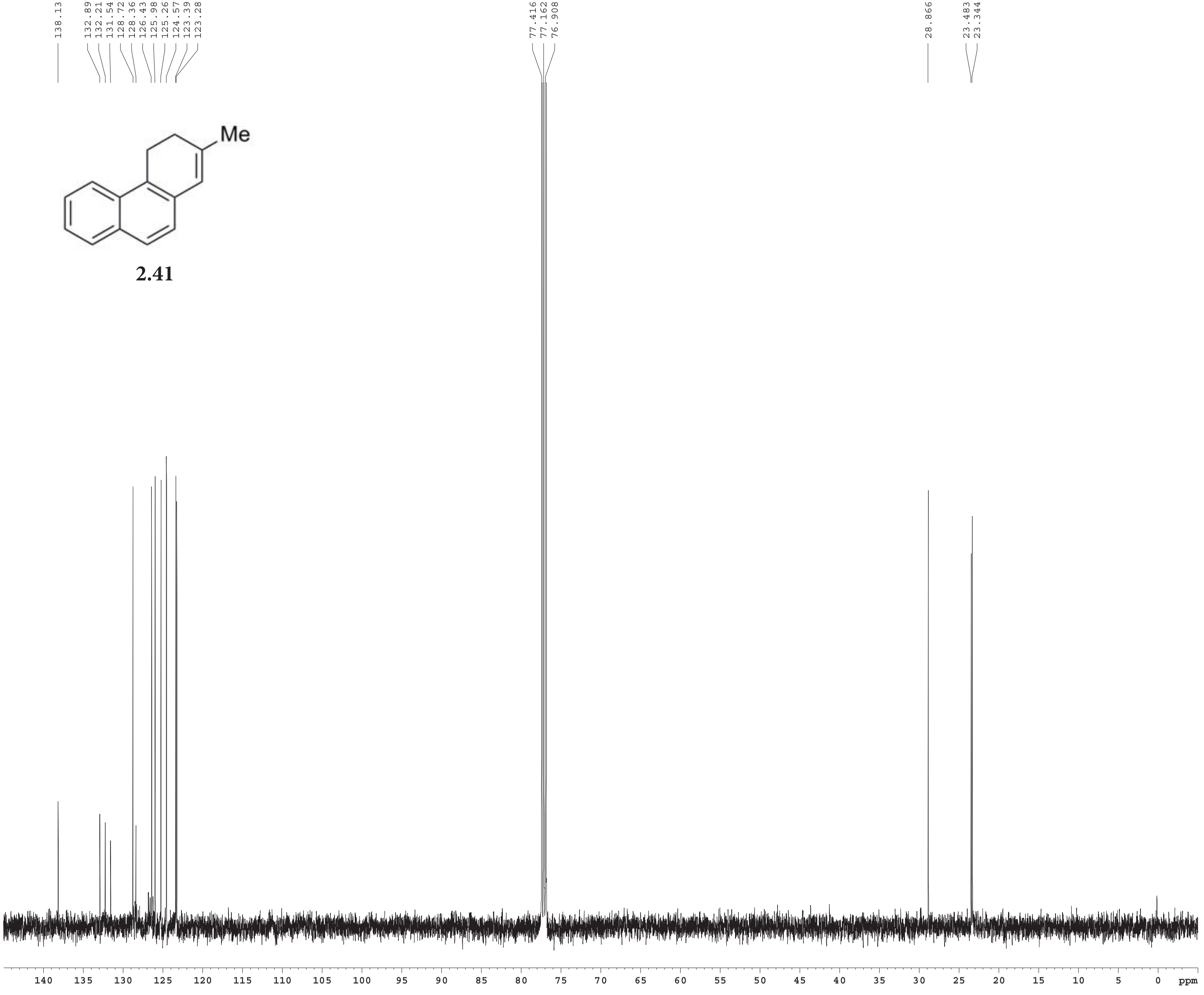
```
Current Data Parameters
USER                aaronj
NAME          AGJ_4_176_c1
EXPNO                    6
PROCNO                   1

F2 - Acquisition Parameters
Date_             20150527
Time                 13.29
INSTRUM            cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD                   65536
SOLVENT              CDCl3
NS                    1024
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                   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             125.7804094 MHz
WDW                     EM
SSB                      0
LB                    1.00 Hz
GB                       0
PC                    2.00
```

1H spectrum

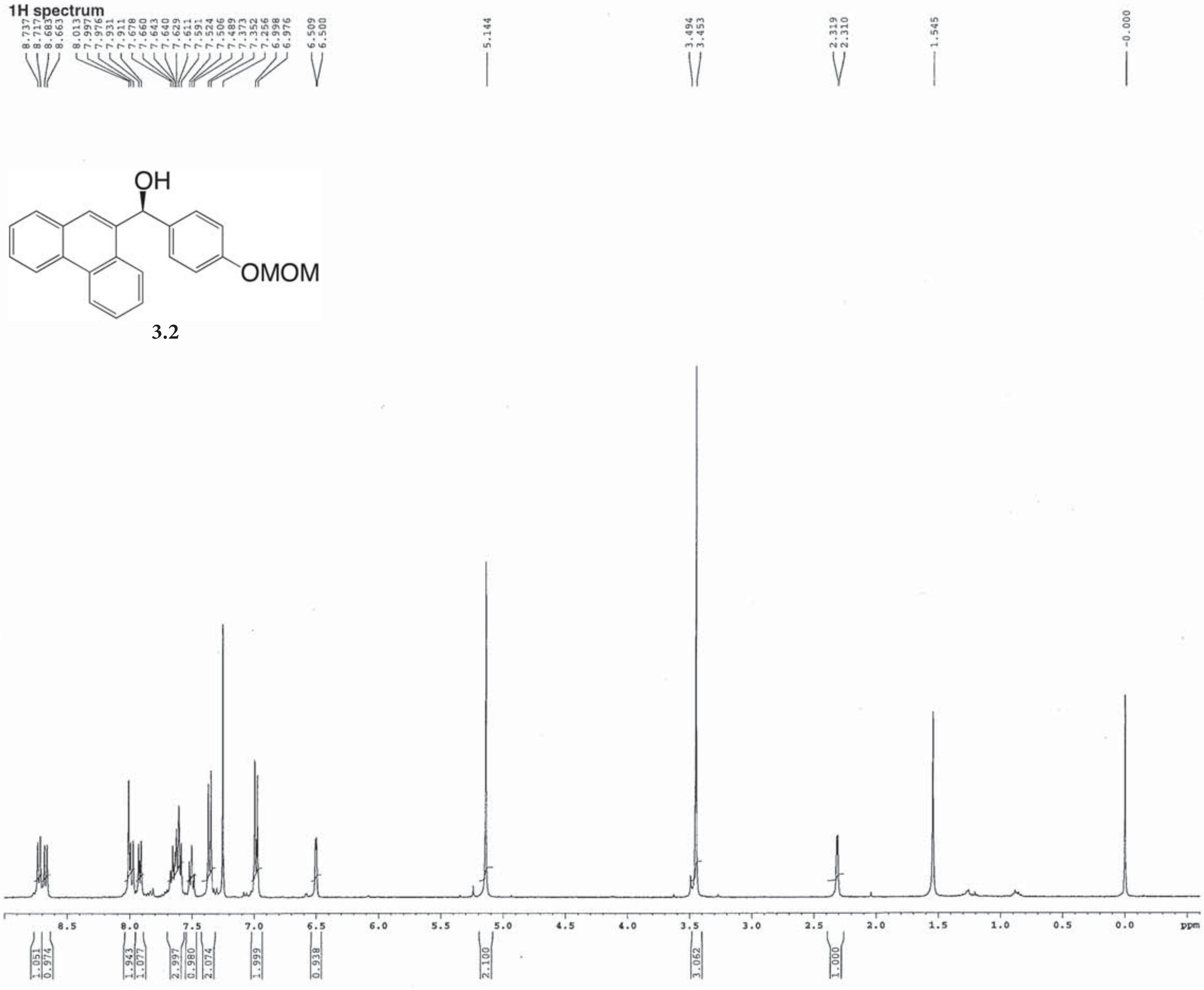

2.41

```
Current Data Parameters
USER              aaronj
NAME         AGJ_3_258_c4
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20140411
Time               17.44
INSTRUM           drx400
PROBHD   5 mm QNP H/F/P
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                     8
DS                     2
SWH             6410.256 Hz
FIDRES          0.097813 Hz
AQ             5.1118579 sec
RG                1625.5
DW                78.000 usec
DE                  4.50 usec
TE                 298.0 K
D1            0.10000000 sec
MCREST        0.00000000 sec
MCWRK         0.01500000 sec

======== CHANNEL f1 ========
NUC1                  1H
P1                 12.00 usec
PL1                 0.00 dB
SFO1         400.1328009 MHz

F2 - Processing parameters
SI                 65536
SF           400.1300221 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  4.00
```

Z-restored spin-echo 13C spectrum with 1H decoupling

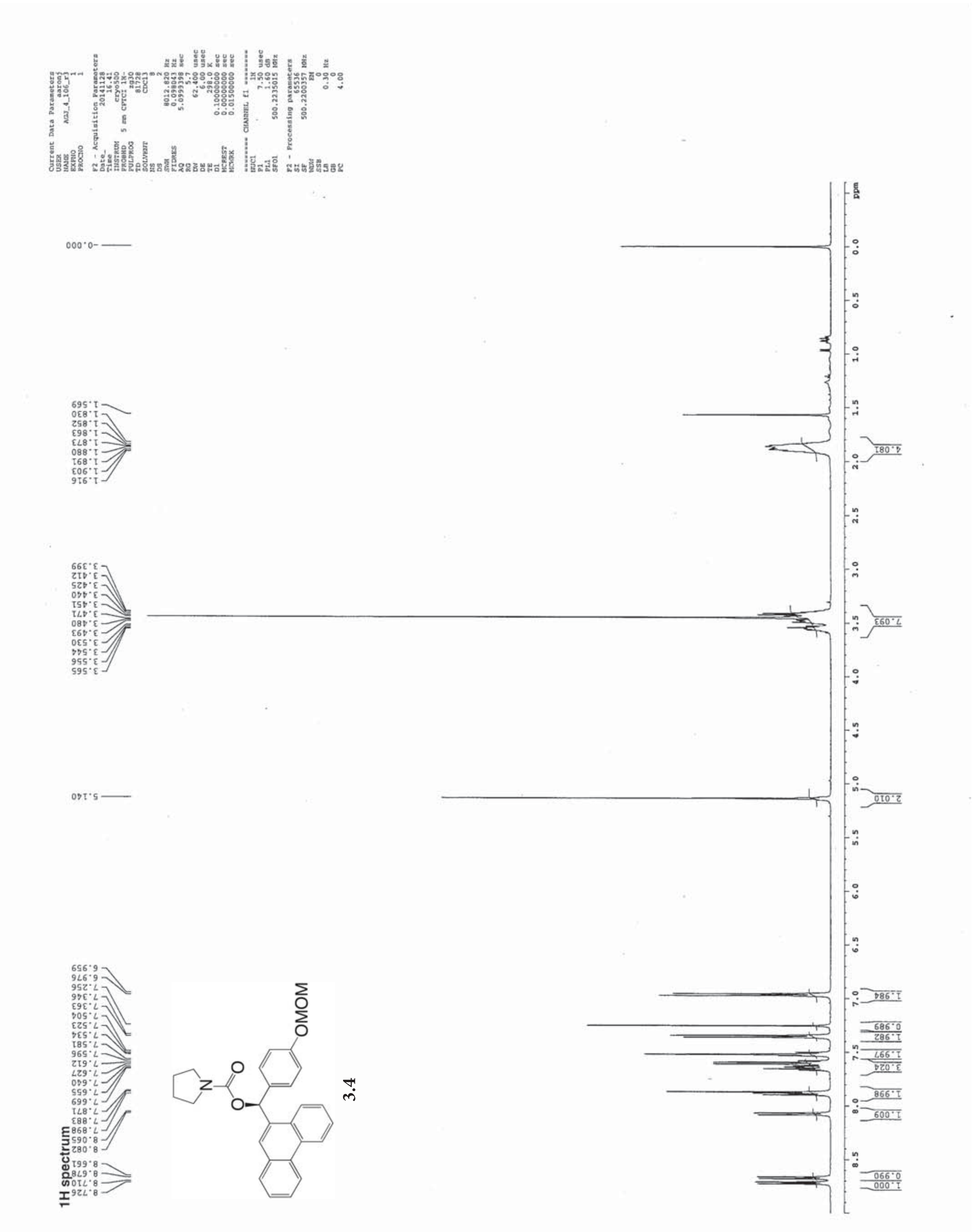

2.41

```
Current Data Parameters
USER              aaronj
NAME         AGJ_3_258_c4
EXPNO                  4
PROCNO                 1

F2 - Acquisition Parameters
Date_           20140412
Time               12.03
INSTRUM          cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD                 65536
SOLVENT            CDCl3
NS                  1024
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           125.7804066 MHz
WDW                   EM
SSB                    0
LB                  1.00 Hz
GB                     0
PC                  2.00
```



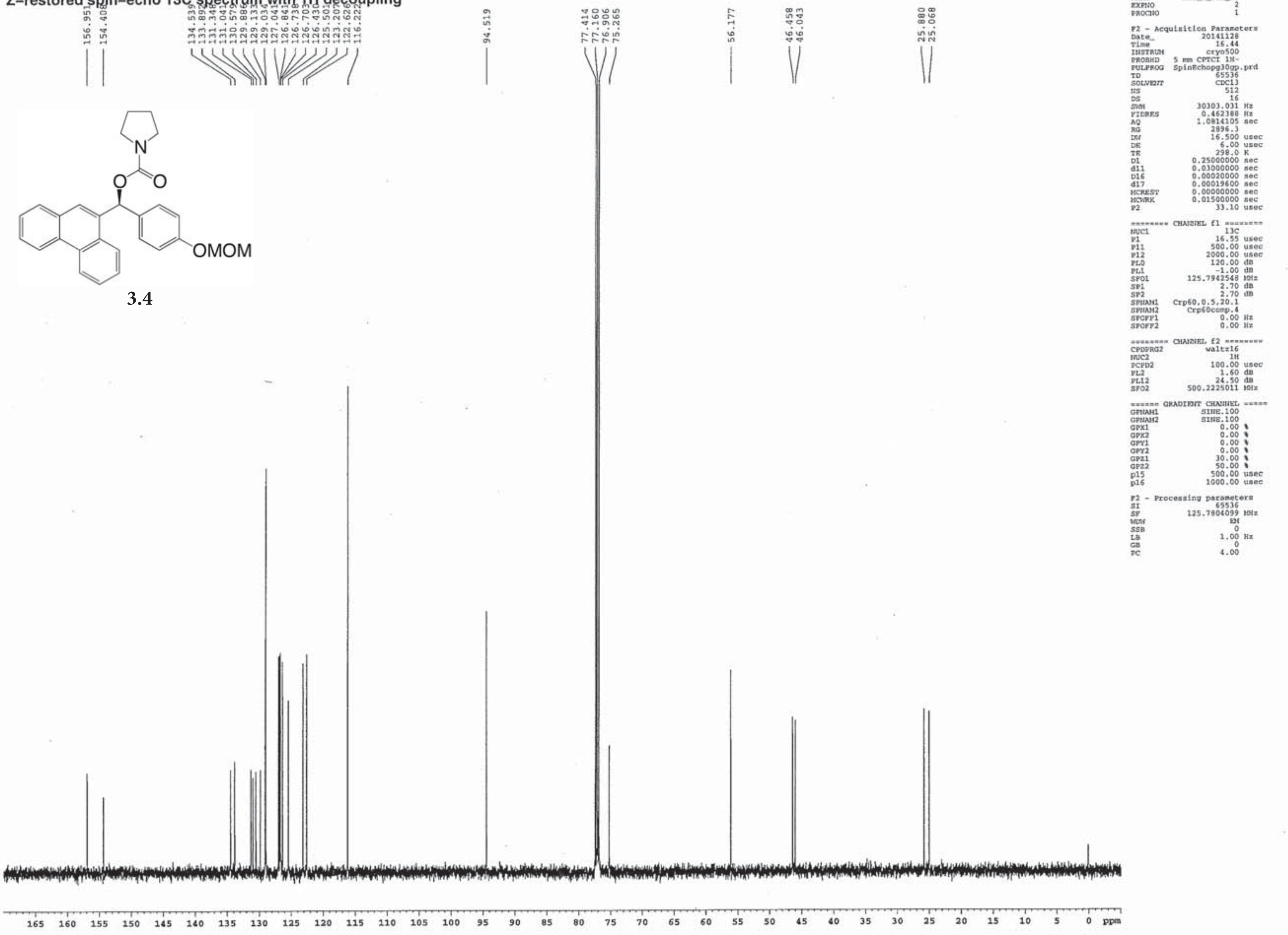
3.2

```
Current Data Parameters
USER                aaronj
NAME           AGJ_4_Benz_OH
EXPNO                    3
PROCNO                   1

F2 - Acquisition Parameters
Date_             20141129
Time                 18.59
INSTRUM             drx400
PROBHD    5 mm QNP H/F/P
PULPROG               zg30
TD                   65536
SOLVENT              CDCl3
NS                       8
DS                       2
SWH             6410.256 Hz
FIDRES          0.097813 Hz
AQ             5.1118579 sec
RG                   645.1
DW                  78.000 usec
DE                    4.50 usec
TE                   298.1 K
D1             0.10000000 sec
MCREST         0.00000000 sec
MCWRK          0.01500000 sec

======== CHANNEL f1 ========
NUC1                    1H
P1                   12.00 usec
PL1                   0.00 dB
SFO1        400.1328009 MHz

F2 - Processing parameters
SI                   65536
SF          400.1300221 MHz
WDW                     EM
SSB                      0
LB                    0.30 Hz
GB                       0
PC                    2.00
```


1H spectrum
OMOM
N
O
O
O
Current Data Parameters
USER aaronj
NAME AGJ_4_106_r3
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20141128
Time 16.41
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 5.0999398 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 500.2200357 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00
-0.000
1.569
1.830
1.852
1.863
1.873
1.880
1.891
1.903
1.916
3.399
3.412
3.425
3.440
3.451
3.471
3.480
3.493
3.530
3.544
3.556
3.565
5.140
6.959
6.976
7.256
7.346
7.363
7.504
7.523
7.534
7.581
7.596
7.612
7.627
7.640
7.655
7.669
7.871
7.883
7.898
8.065
8.082
8.661
8.678
8.710
8.726
ppm
0.0
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
8.0
8.5
4.081
7.093
2.010
1.984
0.989
1.982
1.997
3.024
1.998
1.009
0.990
1.000

3.4

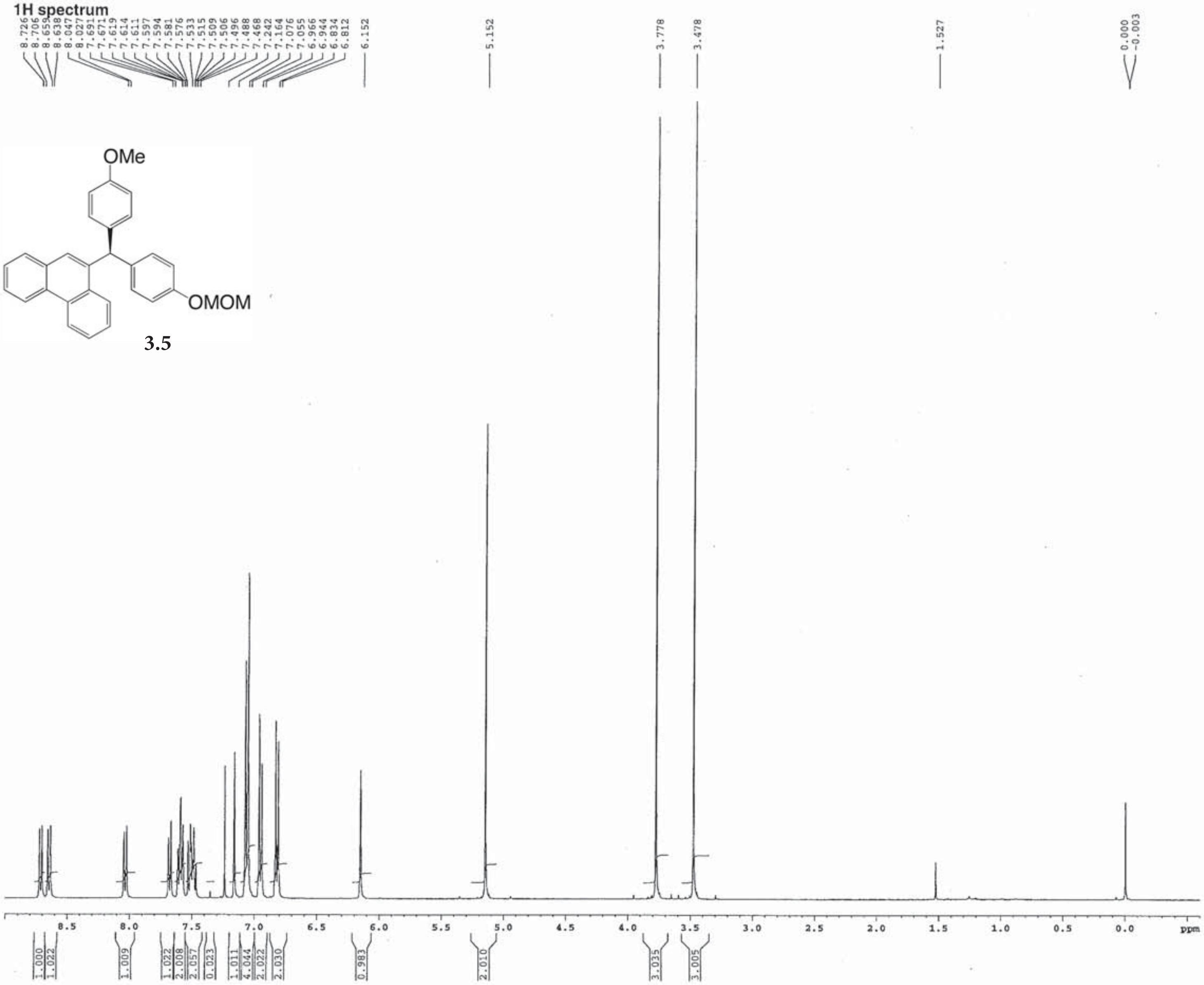
Z–restored spin–echo 13C spectrum with 1H decoupling



3.4

```
Current Data Parameters
USER               aaronj
NAME         AGJ_4_106_r3
EXPNO                   2
PROCNO                  1

F2 - Acquisition Parameters
Date_            20141128
Time                16.44
INSTRUM           cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD                  65536
SOLVENT             CDCl3
NS                    512
DS                     16
SWH             30303.031 Hz
FIDRES           0.462388 Hz
AQ              1.0814105 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                  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            125.7804099 MHz
WDW                    EM
SSB                     0
LB                   1.00 Hz
GB                      0
PC                   4.00
```

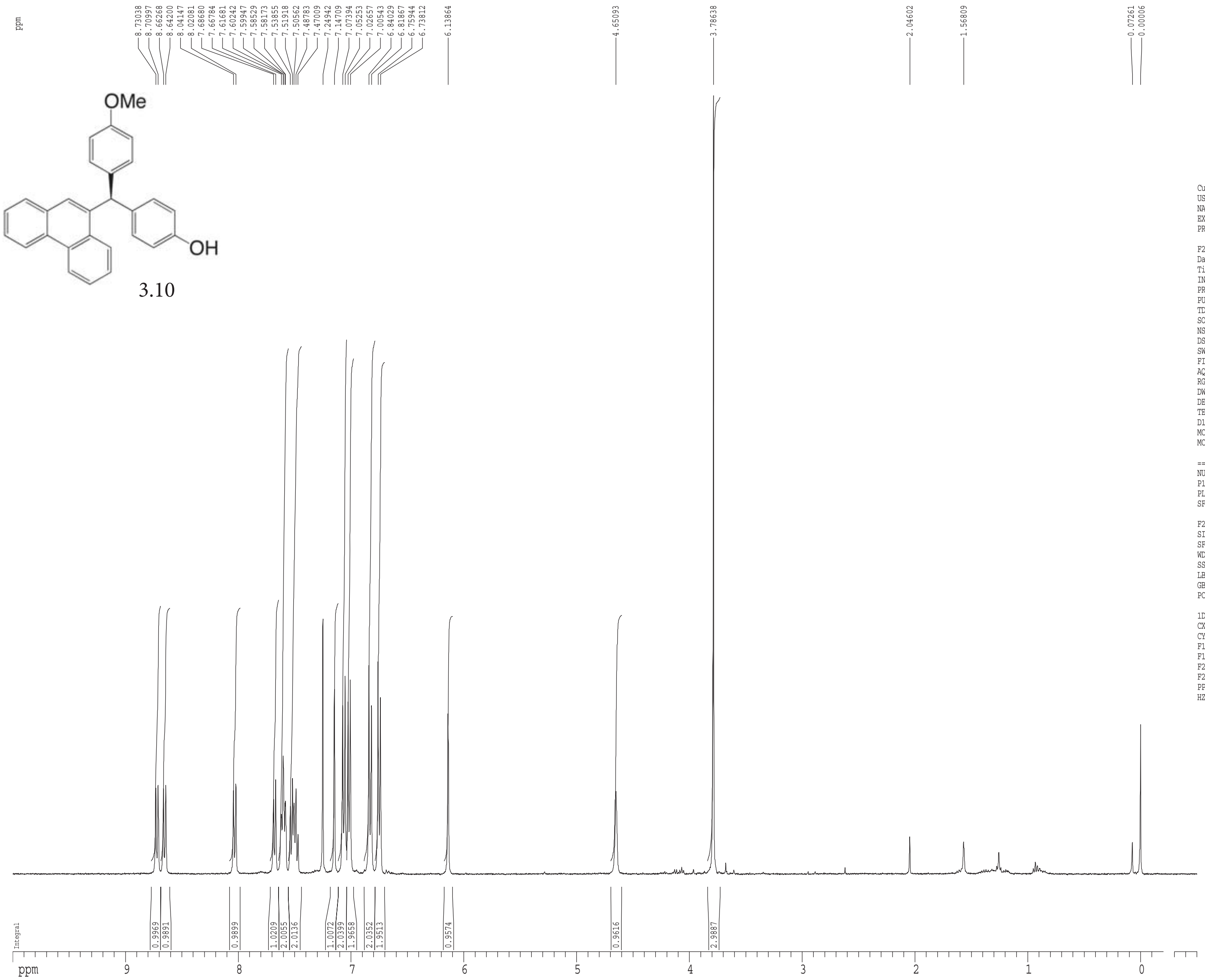
1H spectrum



3.5

```
Current Data Parameters
USER                aaronj
NAME           AGJ_4_130_c2
EXPNO                    2
PROCNO                   1

F2 - Acquisition Parameters
Date_             20141125
Time                 20.36
INSTRUM             drx400
PROBHD   5 mm QNP H/F/P
PULPROG               zg30
TD                   65536
SOLVENT              CDCl3
NS                       8
DS                       2
SWH               6410.256 Hz
FIDRES            0.097813 Hz
AQ               5.1118579 sec
RG                     256
DW                  78.000 usec
DE                    4.50 usec
TE                   298.0 K
D1              0.10000000 sec
MCREST          0.00000000 sec
MCWRK           0.01500000 sec

======== CHANNEL f1 ========
NUC1                    1H
P1                   12.00 usec
PL1                   0.00 dB
SFO1           400.1328009 MHz

F2 - Processing parameters
SI                   65536
SF             400.1300281 MHz
WDW                     EM
SSB                      0
LB                    0.30 Hz
GB                       0
PC                    2.00
```

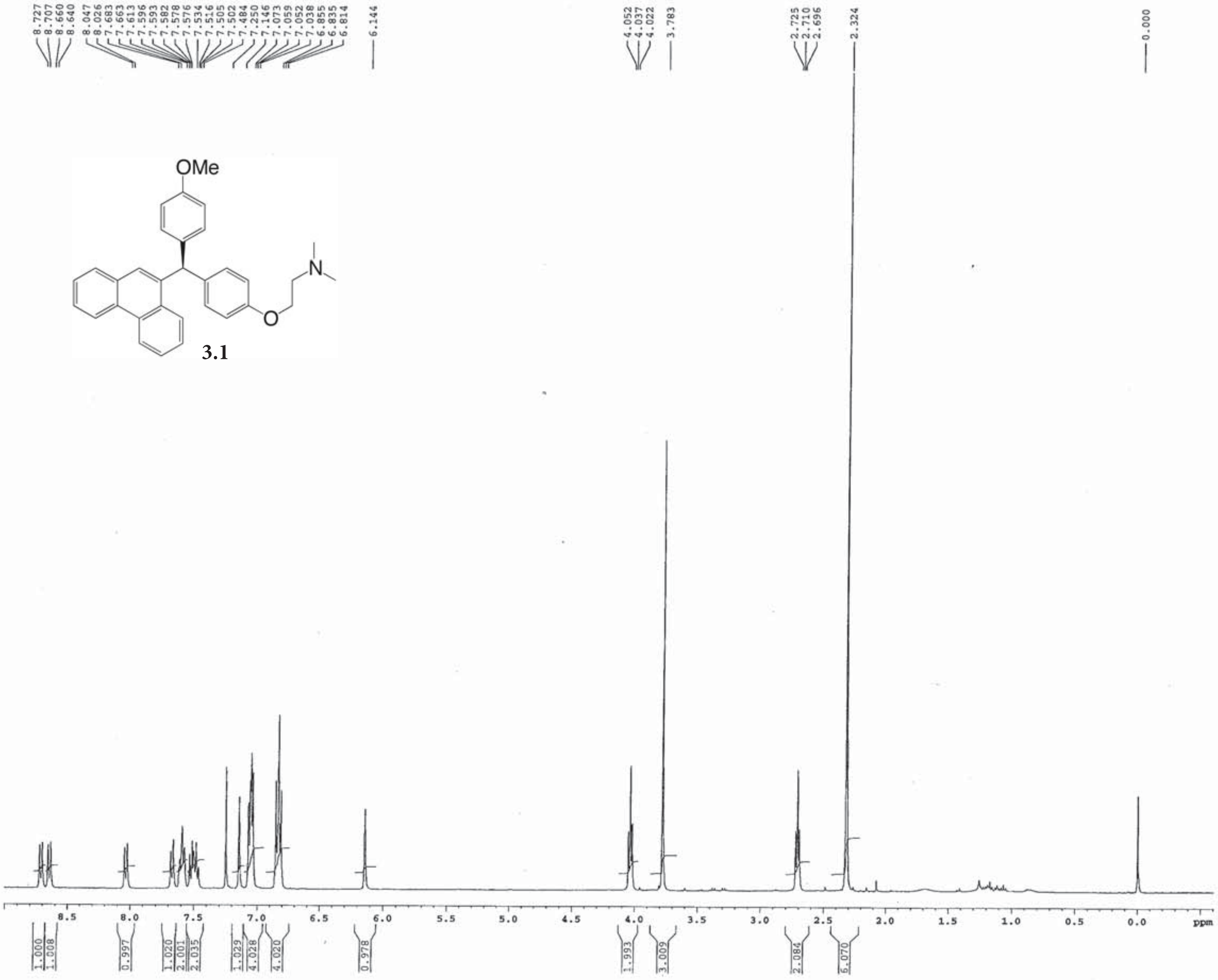
1H spectrum



3.10

```
Current Data Parameters
USER              taylor
NAME          BLT-6-014-A
EXPNO                  4
PROCNO                 1

F2 - Acquisition Parameters
Date_           20120113
Time               13.03
INSTRUM           drx400
PROBHD   5 mm QNP H/F/P
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                     8
DS                     2
SWH             6410.256 Hz
FIDRES          0.097813 Hz
AQ             5.1118579 sec
RG                   362
DW                78.000 usec
DE                  4.50 usec
TE                 298.0 K
D1            0.10000000 sec
MCREST        0.00000000 sec
MCWRK         0.01500000 sec

======== CHANNEL f1 ========
NUC1                  1H
P1                 12.00 usec
PL1                -0.60 dB
SFO1         400.1328009 MHz

F2 - Processing parameters
SI                 65536
SF           400.1300259 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               4001.30 Hz
F2P               -0.500 ppm
F2               -200.07 Hz
PPMCM            0.46053 ppm/cm
HZCM           184.27042 Hz/cm
```

1H spectrum

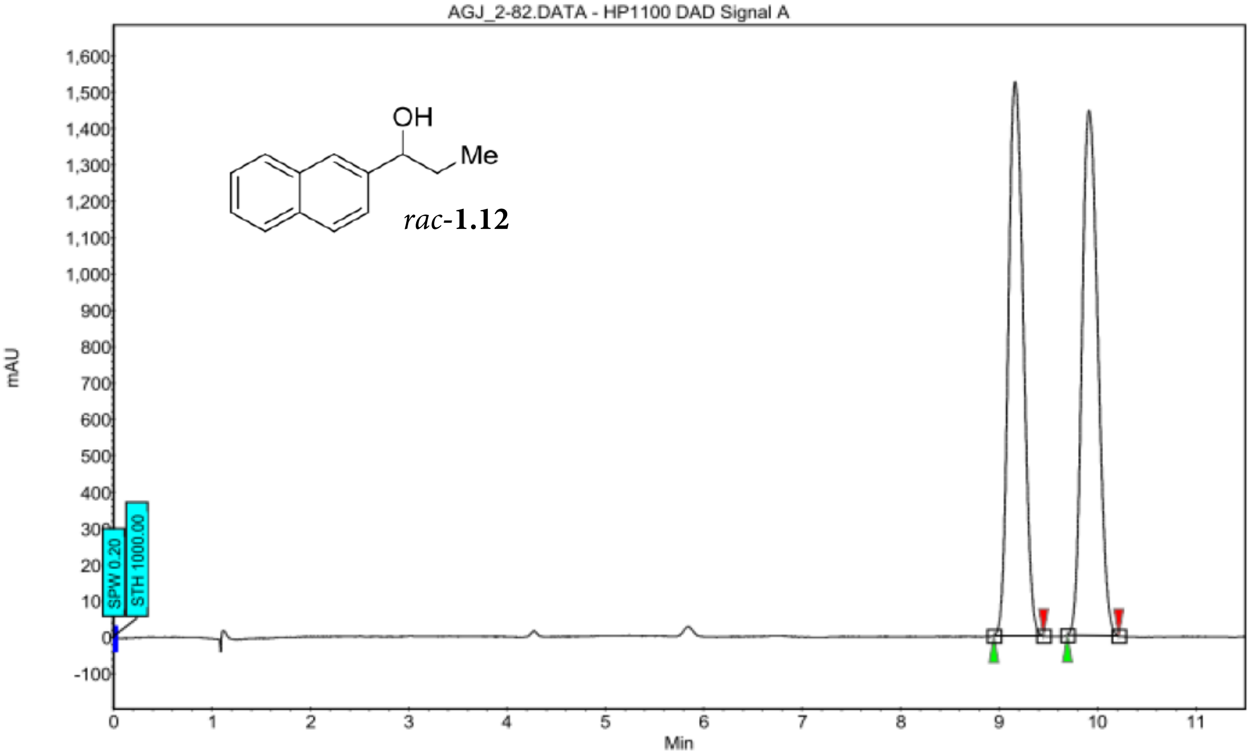


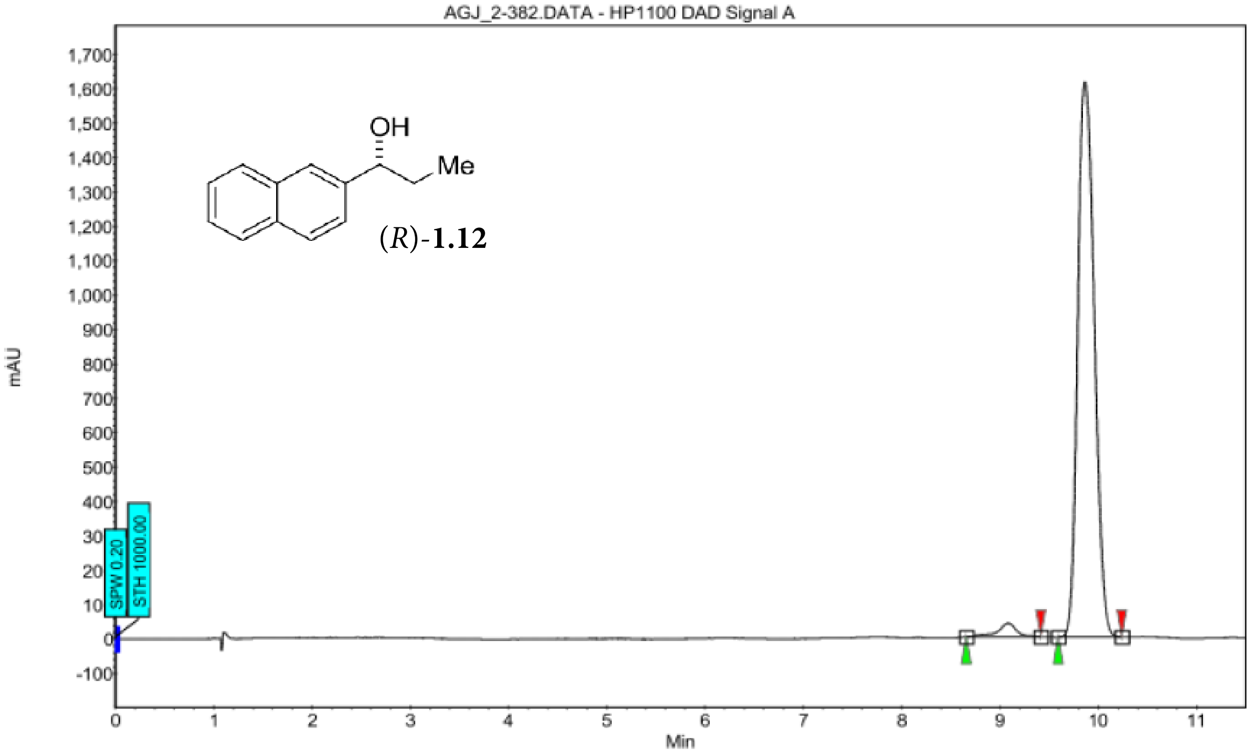
3.1

```
Current Data Parameters
USER              aaronj
NAME         AGJ_4_133_c3
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20141128
Time               12.43
INSTRUM           drx400
PROBHD   5 mm QNP H/F/P
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                     8
DS                     2
SWH             6410.256 Hz
FIDRES          0.097813 Hz
AQ             5.1118579 sec
RG                 287.4
DW                78.000 usec
DE                  4.50 usec
TE                 298.0 K
D1            0.10000000 sec
MCREST        0.00000000 sec
MCWRK         0.01500000 sec

======== CHANNEL f1 ========
NUC1                  1H
P1                 12.00 usec
PL1                 0.00 dB
SFO1         400.1328009 MHz

F2 - Processing parameters
SI                 65536
SF           400.1300246 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  2.00
```

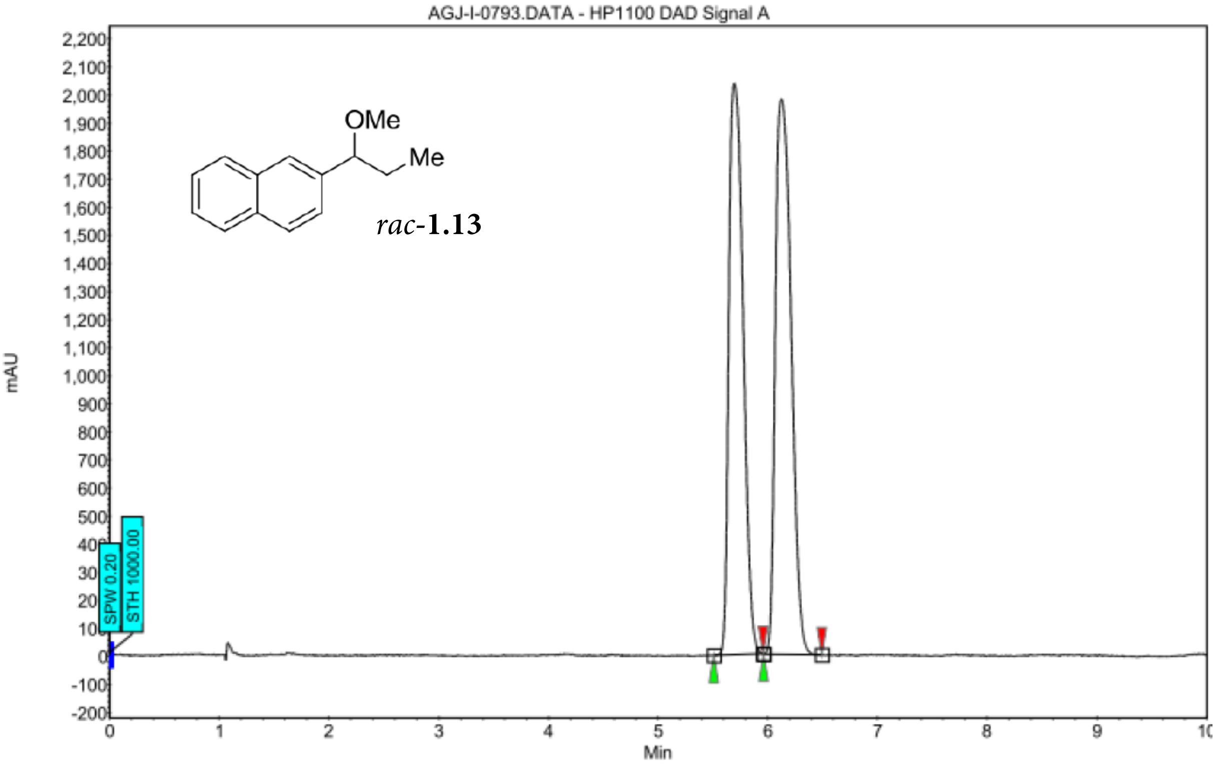
APPENDEX B

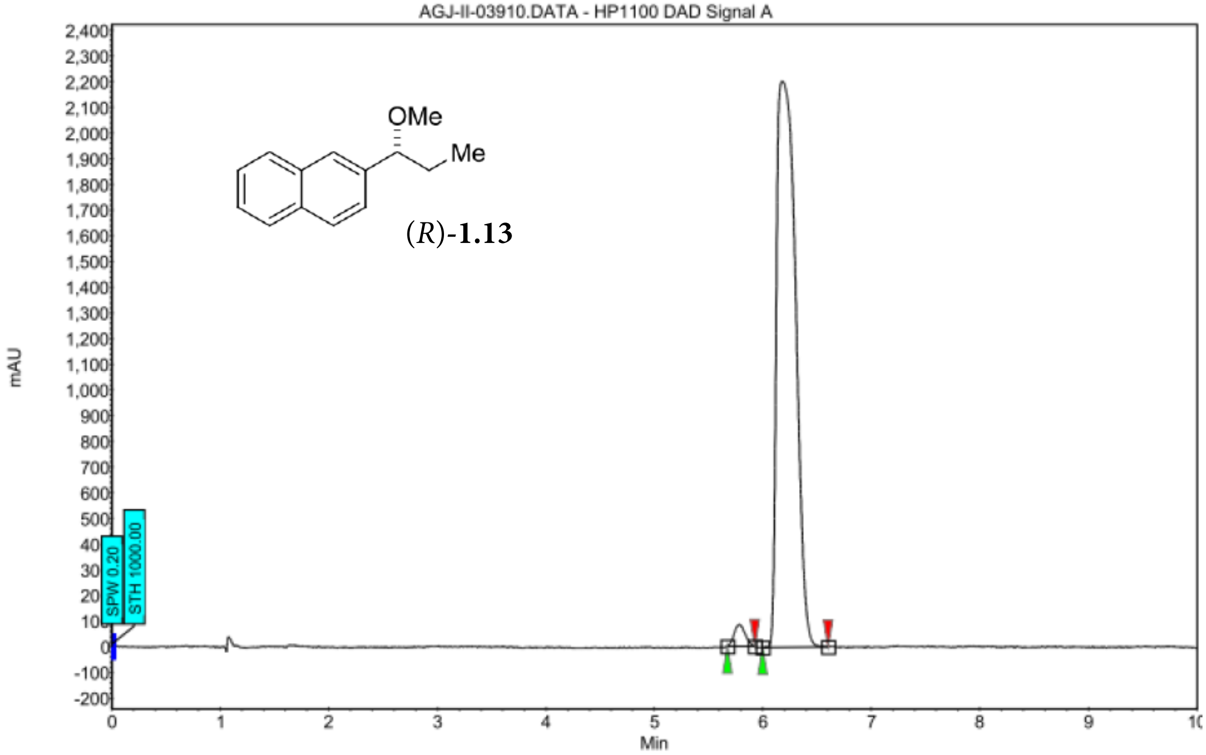
SFC Traces



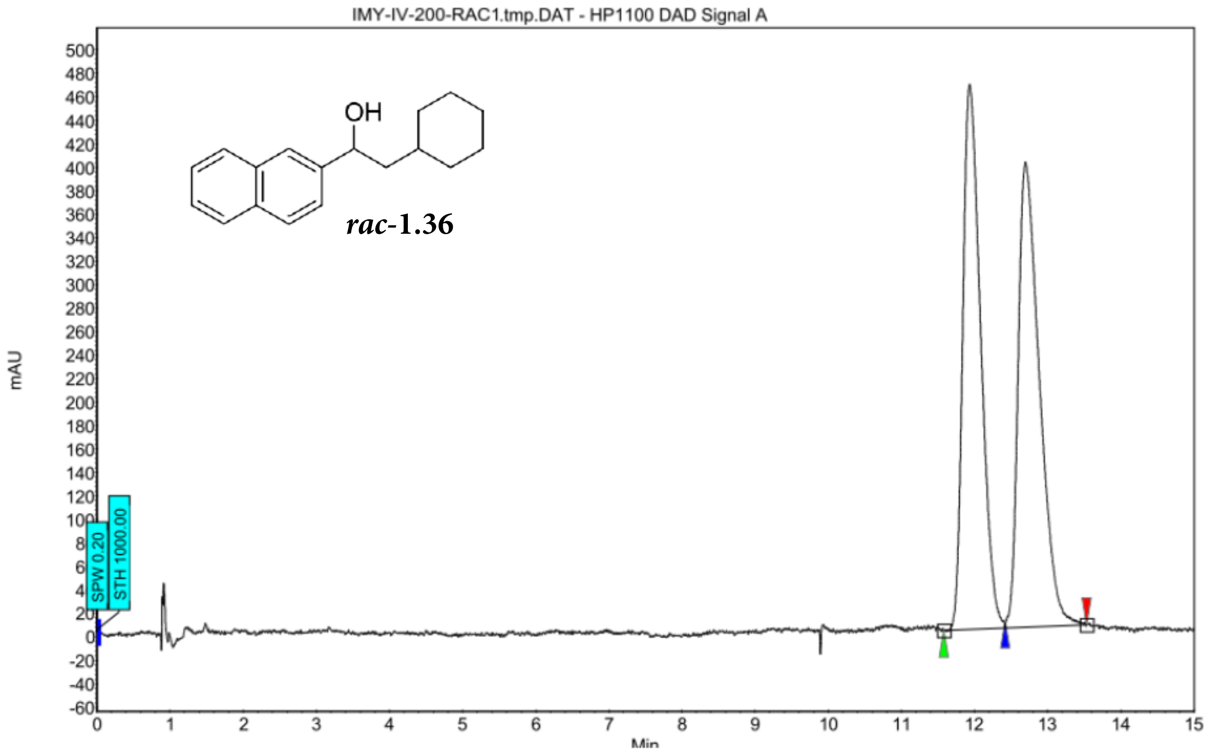


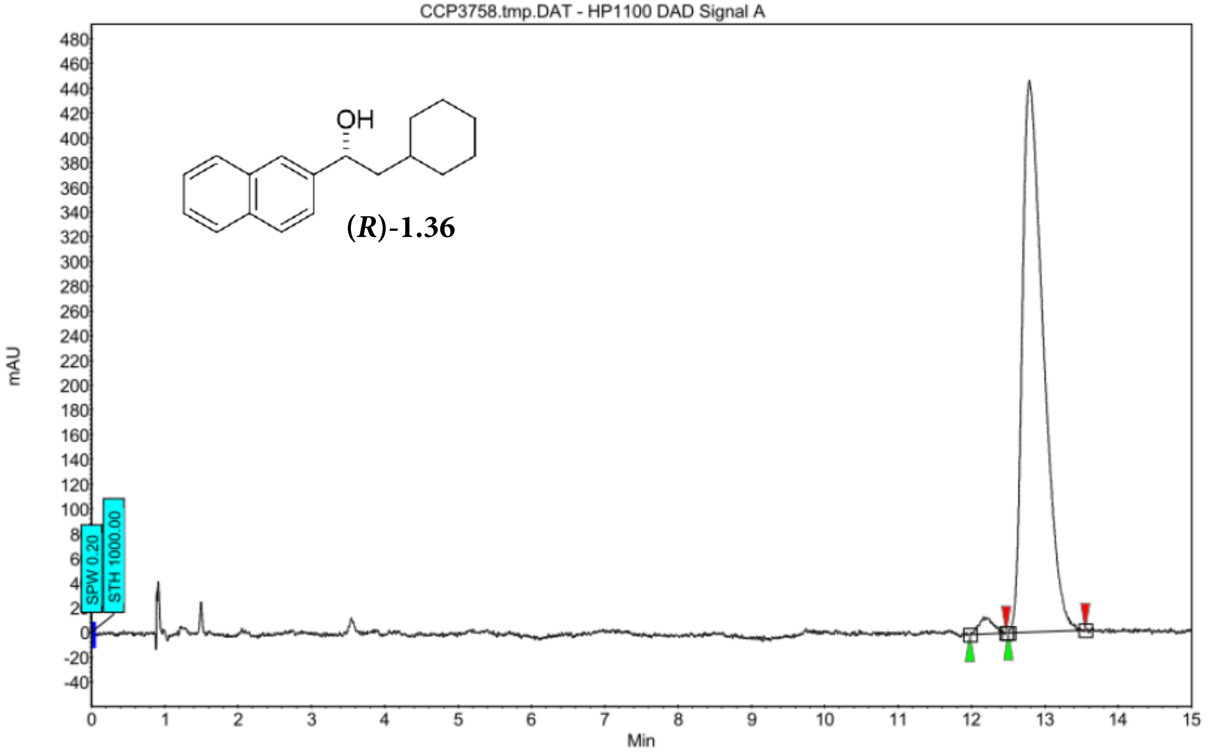
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
2	UNKNOWN	8.66	9.08	9.42	0.00	2.69	39.6	8.8	2.691
1	UNKNOWN	9.60	9.86	10.24	0.00	97.31	1613.2	316.9	97.309
Total						100.00	1652.8	325.7	100.000



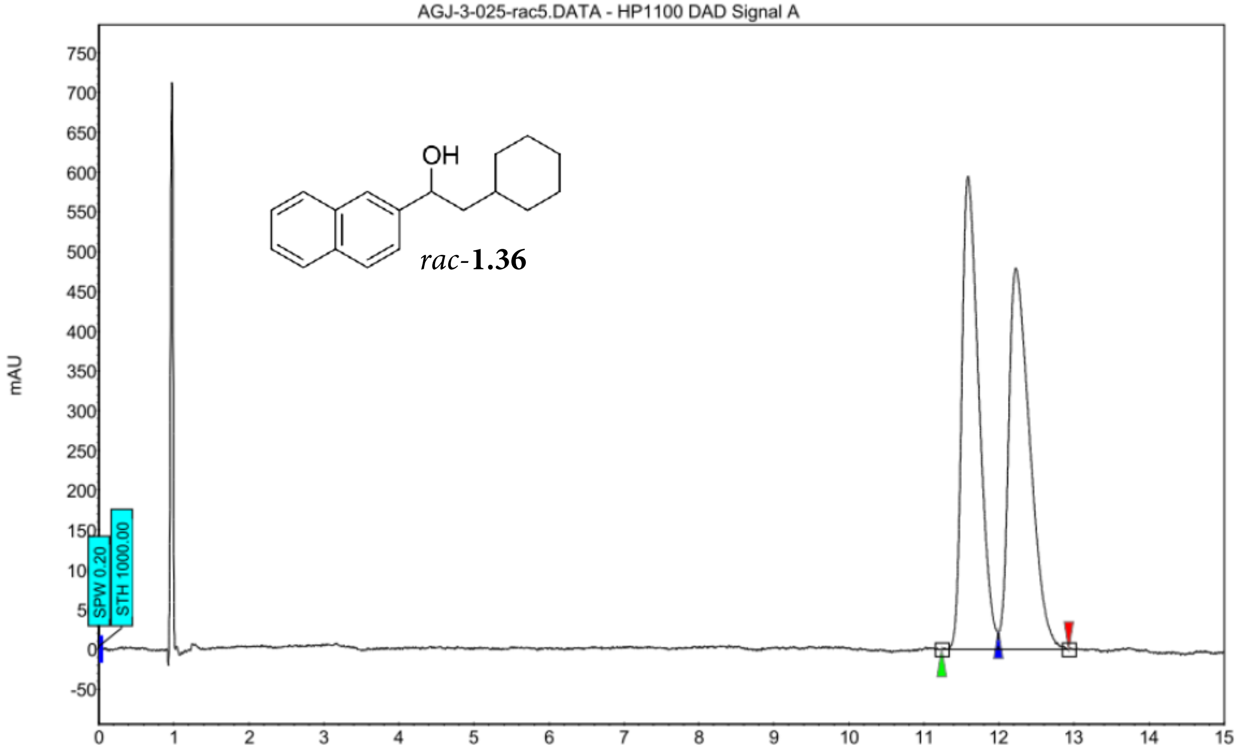


Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
2	UNKNOWN	5.67	5.78	5.93	0.00	2.19	84.6	10.0	2.186
1	UNKNOWN	6.00	6.18	6.60	0.00	97.81	2204.3	445.6	97.814
Total						100.00	2288.8	455.6	100.000

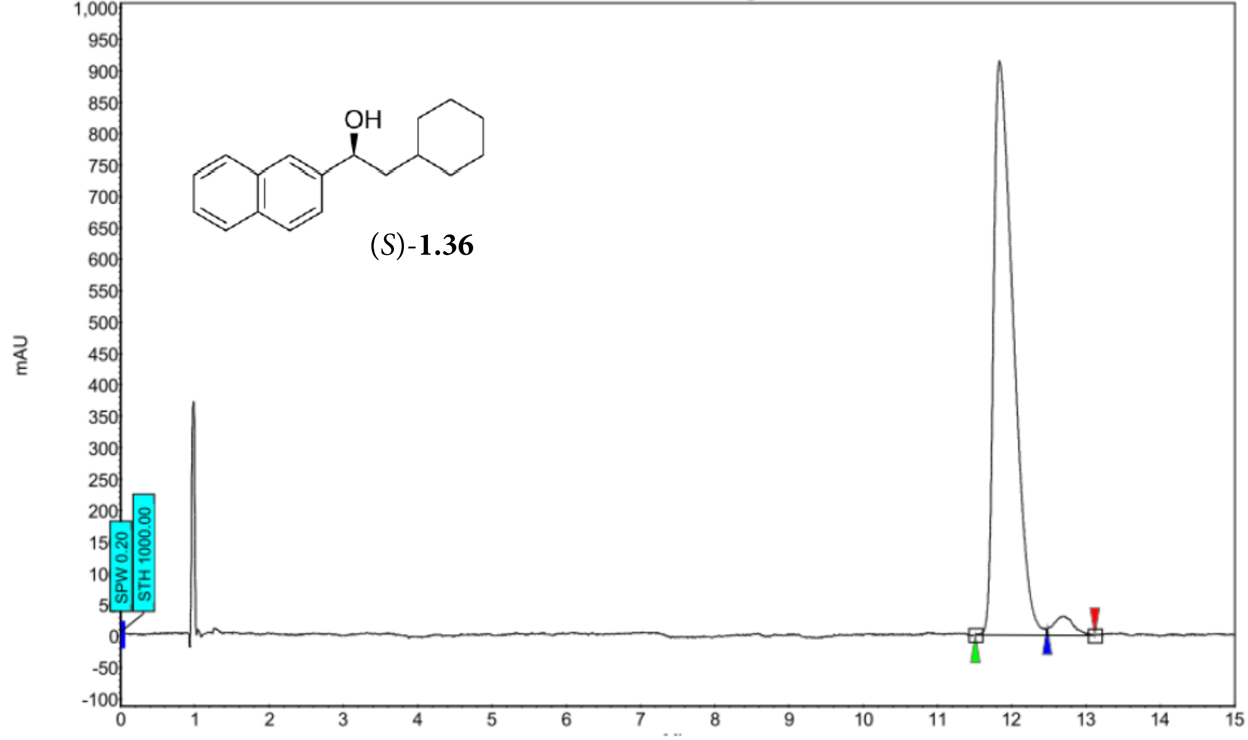




Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	11.98	12.17	12.47	0.00	2.01	13.9	3.0	2.010
2	UNKNOWN	12.50	12.79	13.55	0.00	97.99	445.8	147.3	97.990
Total						100.00	459.7	150.3	100.000

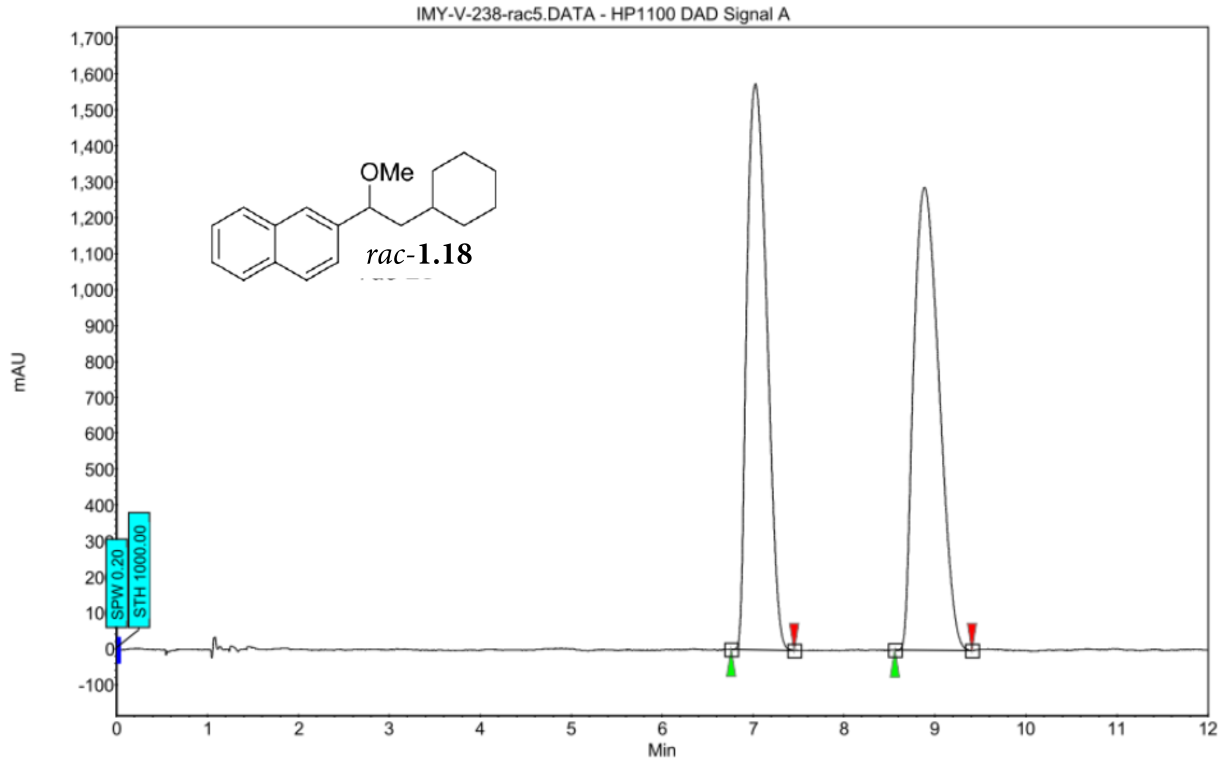


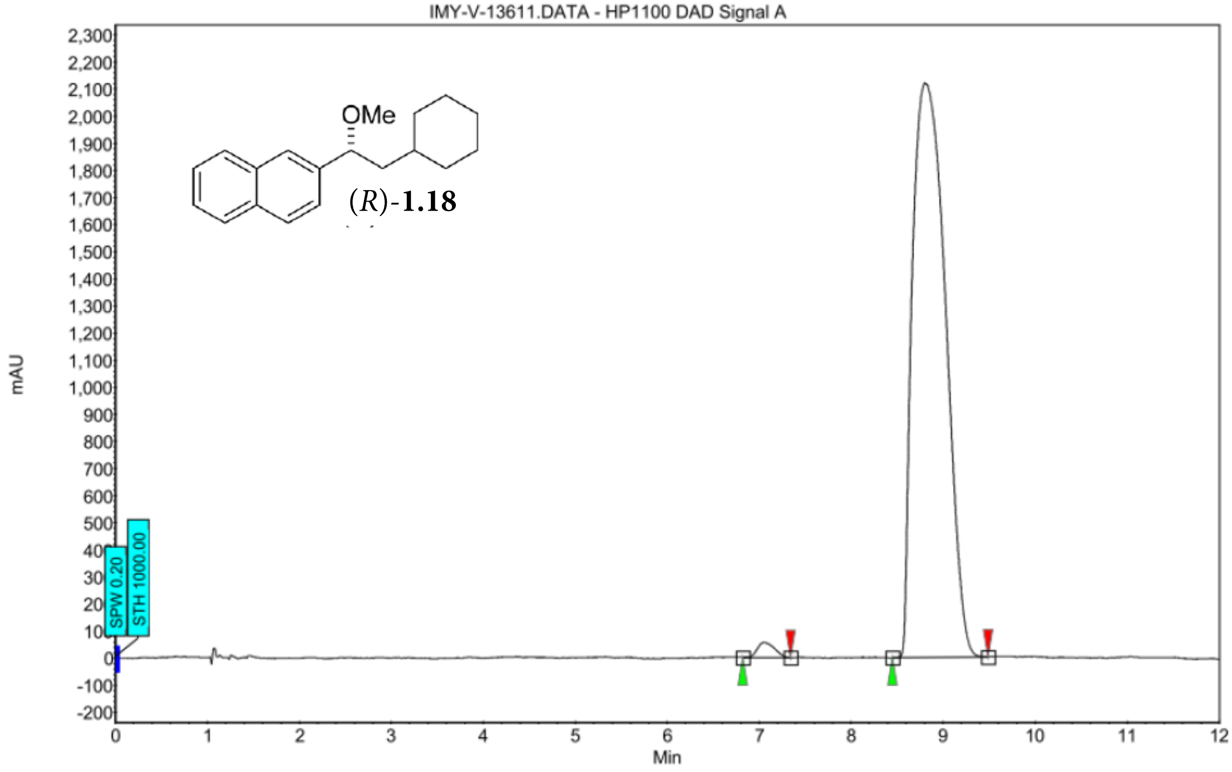
rac-**1.36**



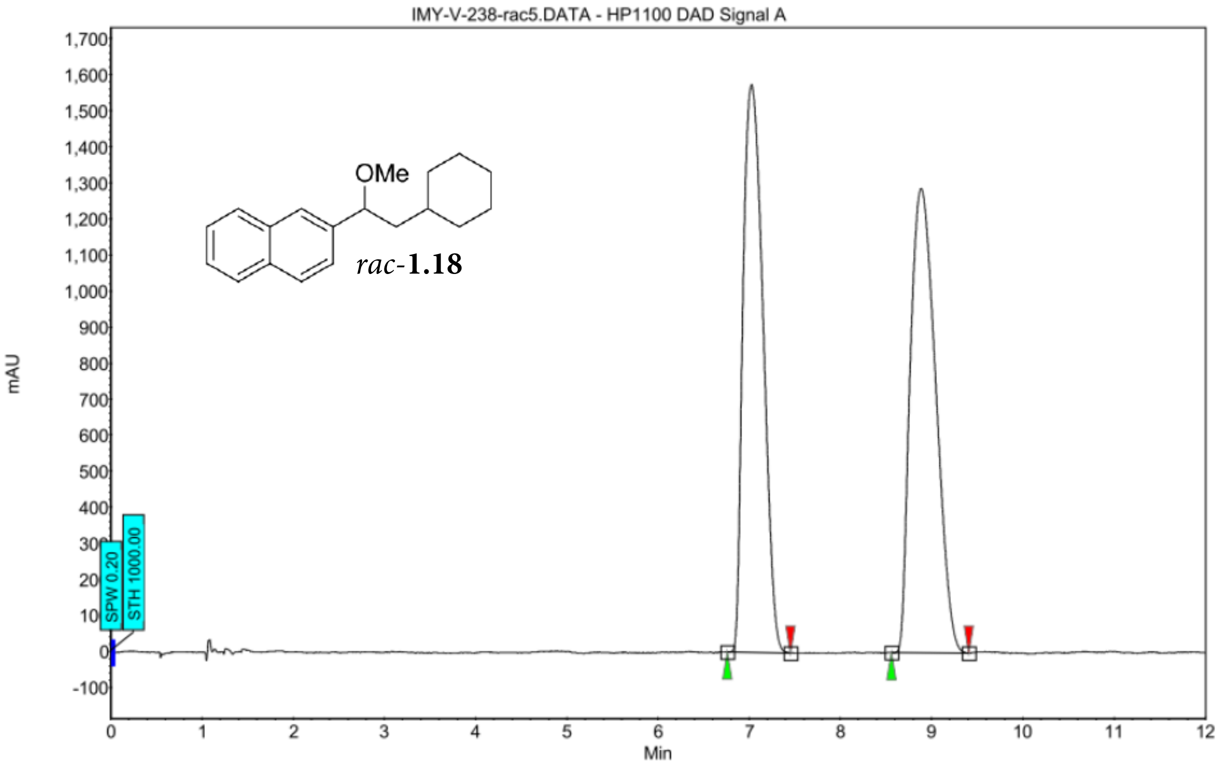
(*S*)-**1.36**

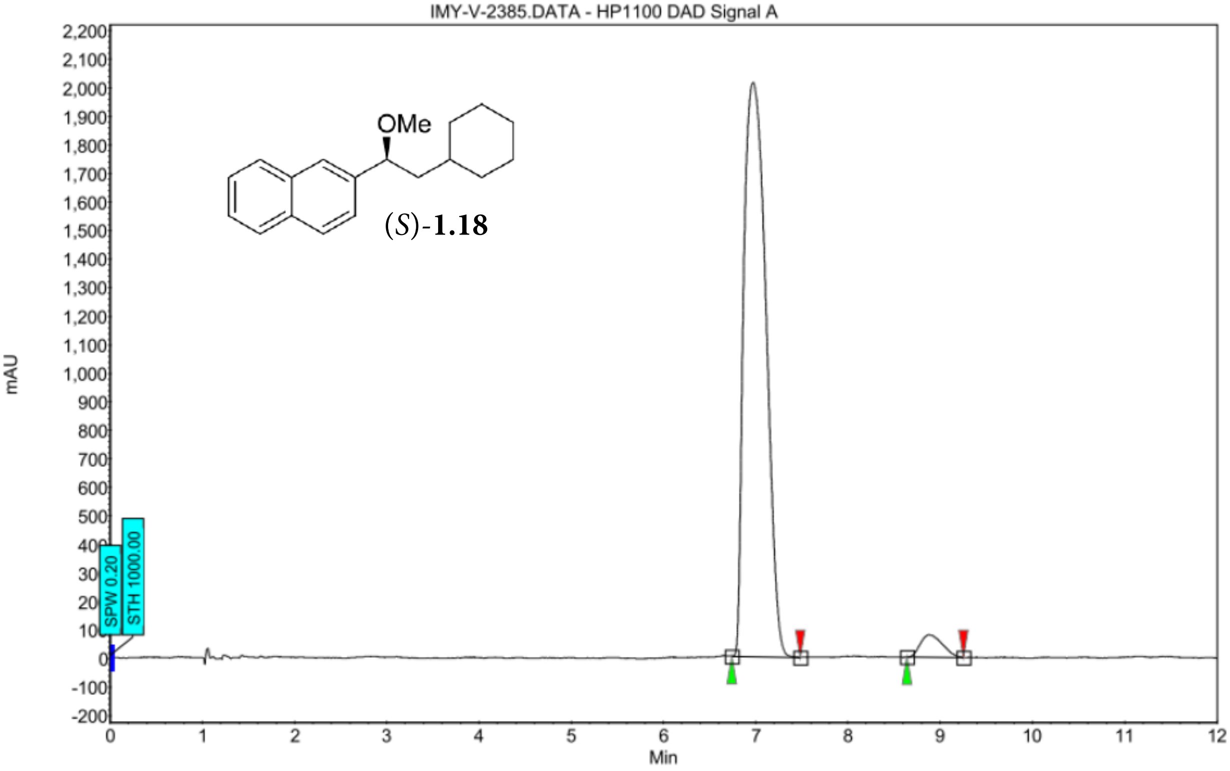
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	11.51	11.83	12.47	0.00	96.72	913.1	279.8	96.723
2	UNKNOWN	12.47	12.70	13.11	0.00	3.28	30.9	9.5	3.277
Total						100.00	944.0	289.3	100.000



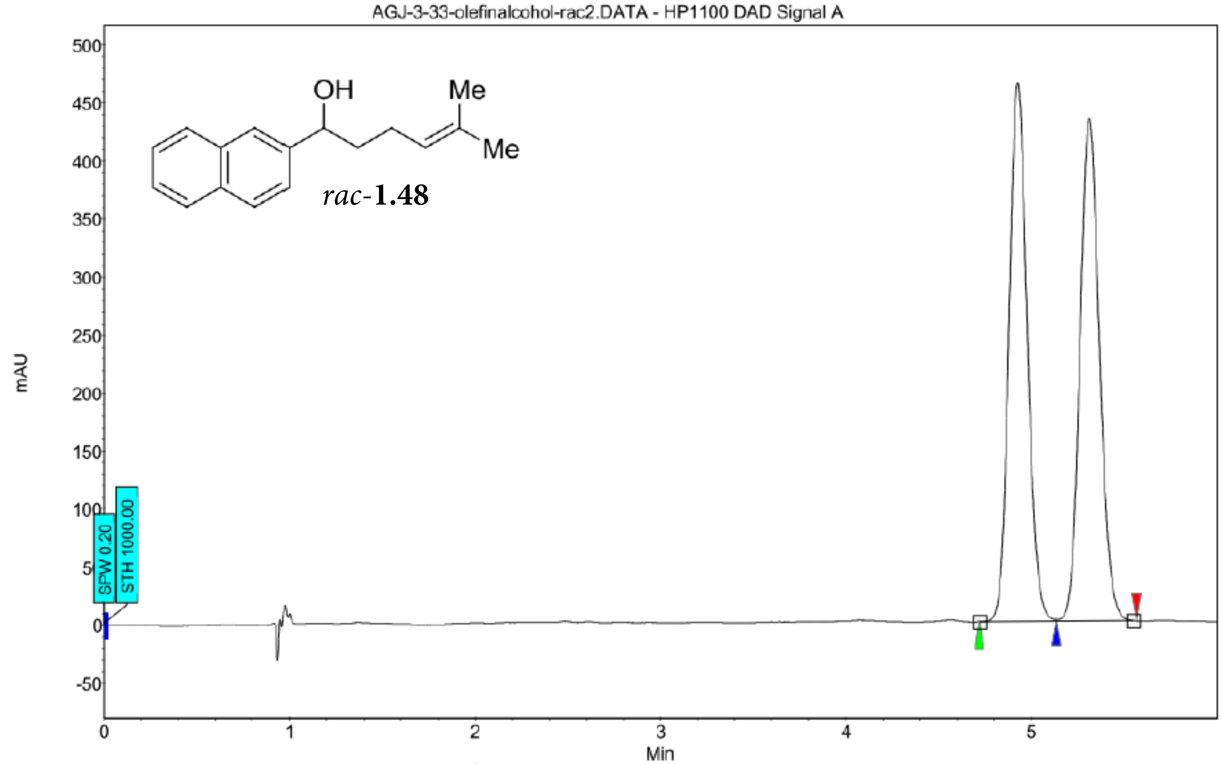


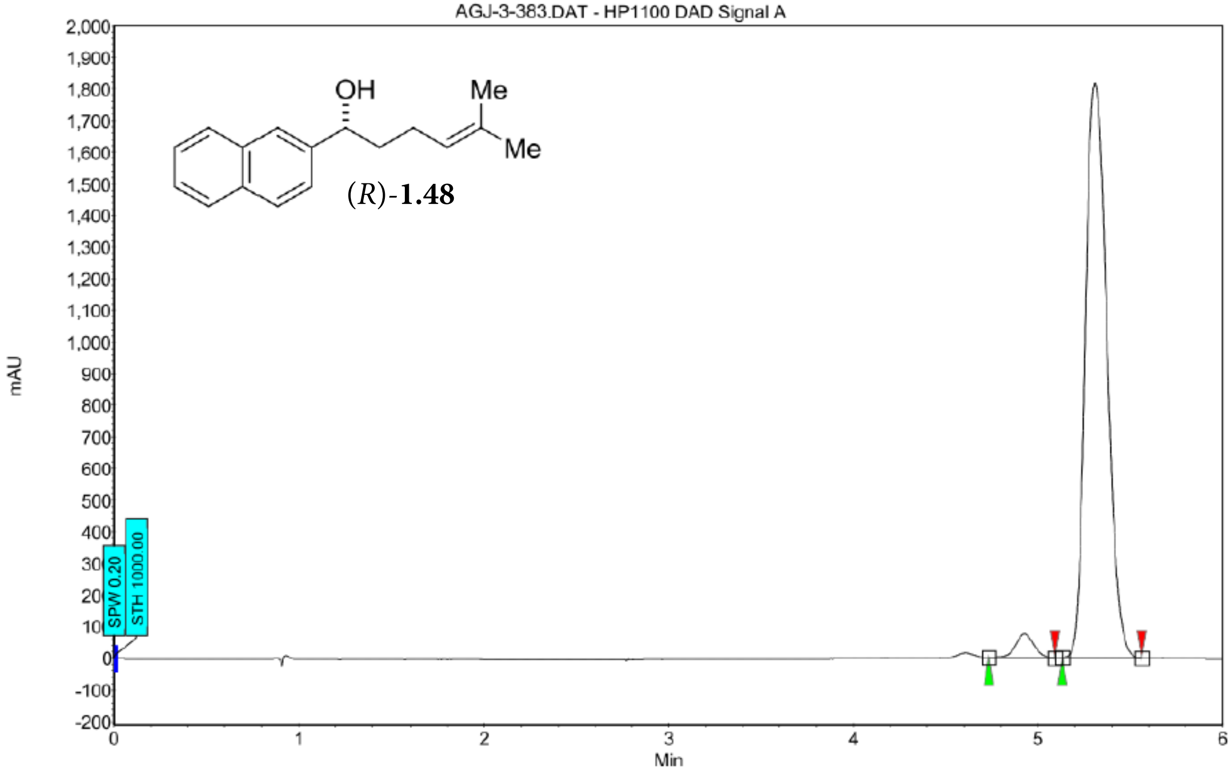
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
2	UNKNOWN	6.82	7.05	7.34	0.00	1.35	56.2	12.1	1.352
1	UNKNOWN	8.45	8.80	9.49	0.00	98.65	2120.6	879.3	98.648
Total						100.00	2176.8	891.4	100.000



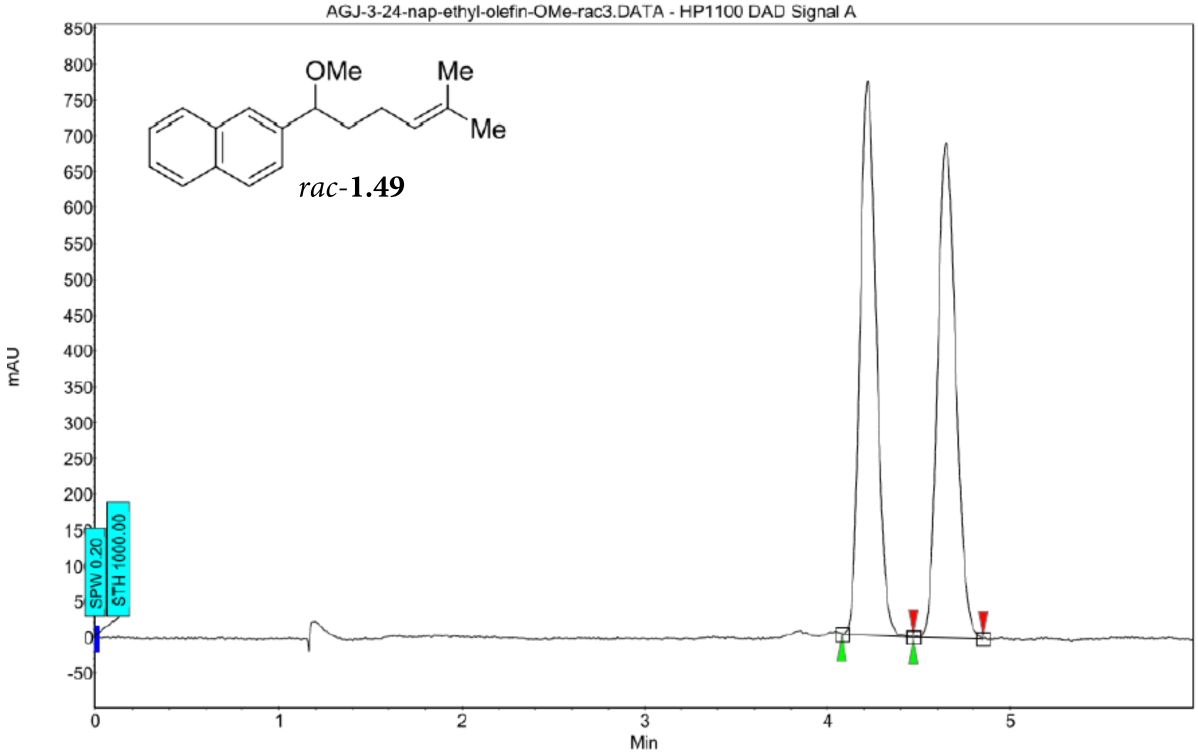


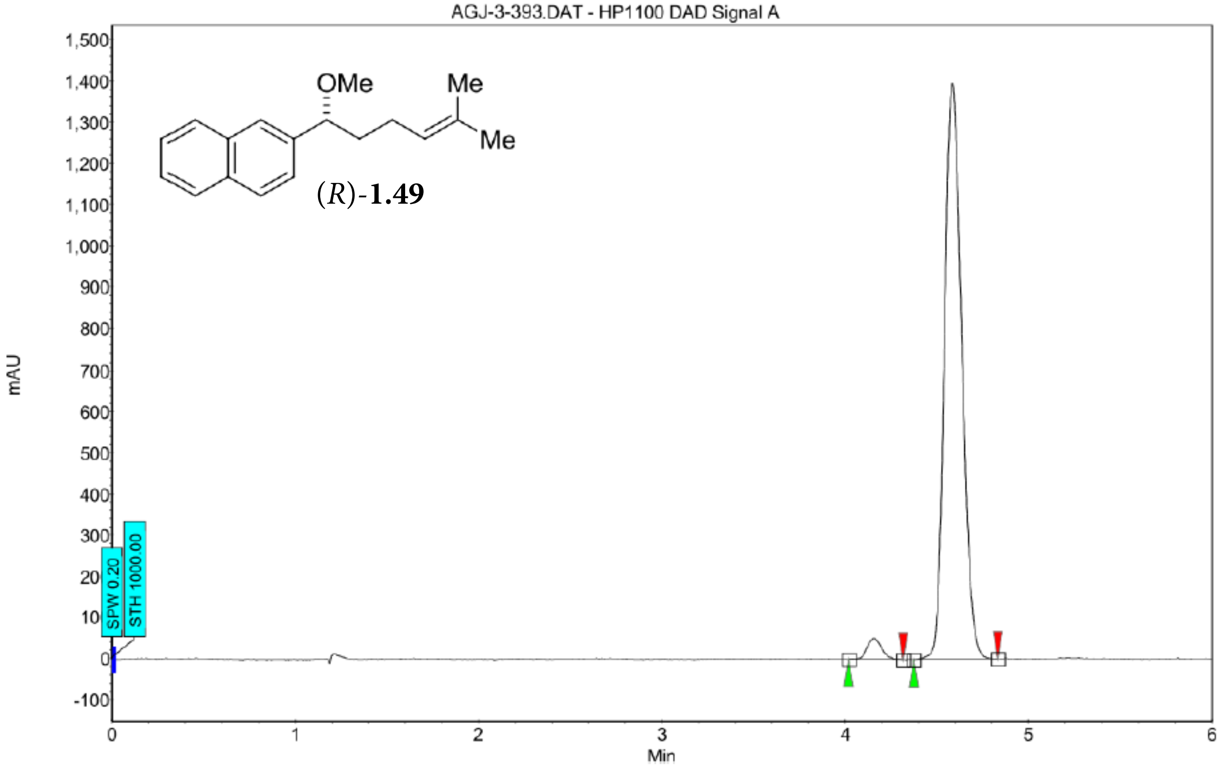
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	6.75	6.98	7.49	0.00	96.23	2011.3	558.6	96.229
2	UNKNOWN	8.64	8.87	9.25	0.00	3.77	78.5	21.9	3.771
Total						100.00	2089.9	580.5	100.000



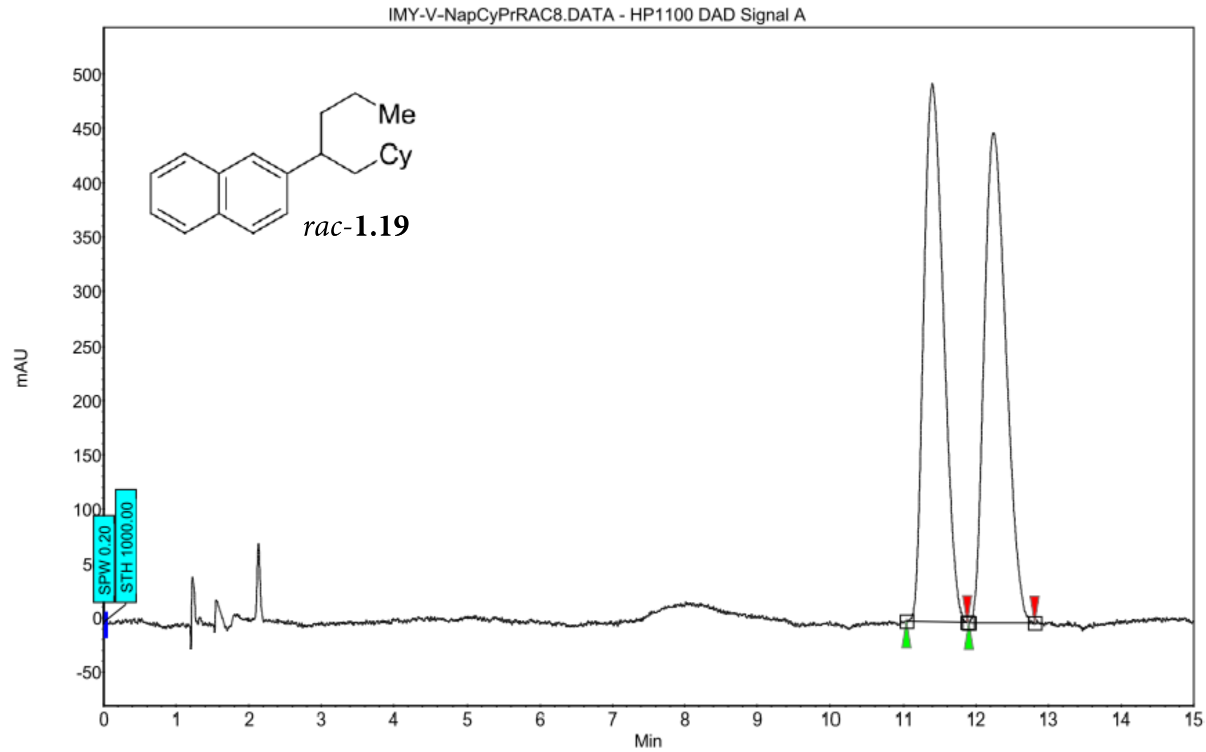


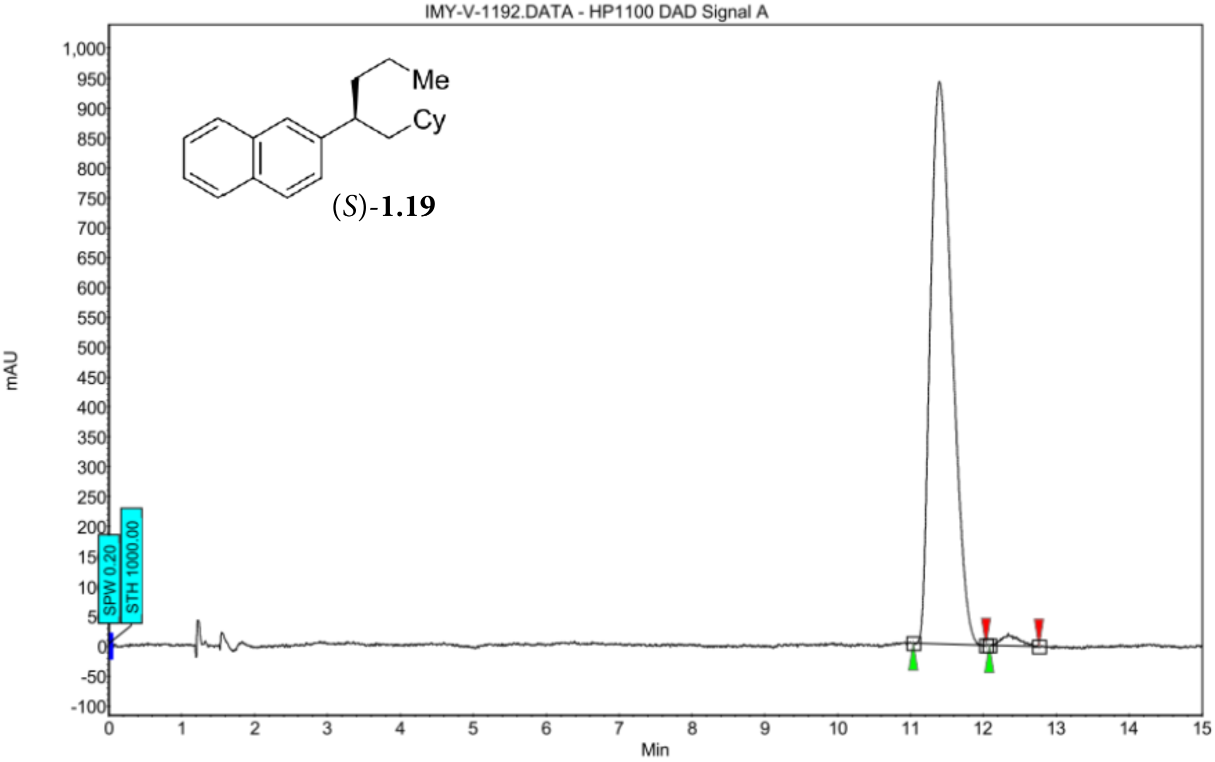
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
2	UNKNOWN	4.73	4.93	5.09	0.00	3.37	75.0	8.6	3.373
1	UNKNOWN	5.13	5.31	5.56	0.00	96.63	1816.9	245.2	96.627
Total						100.00	1891.9	253.8	100.000



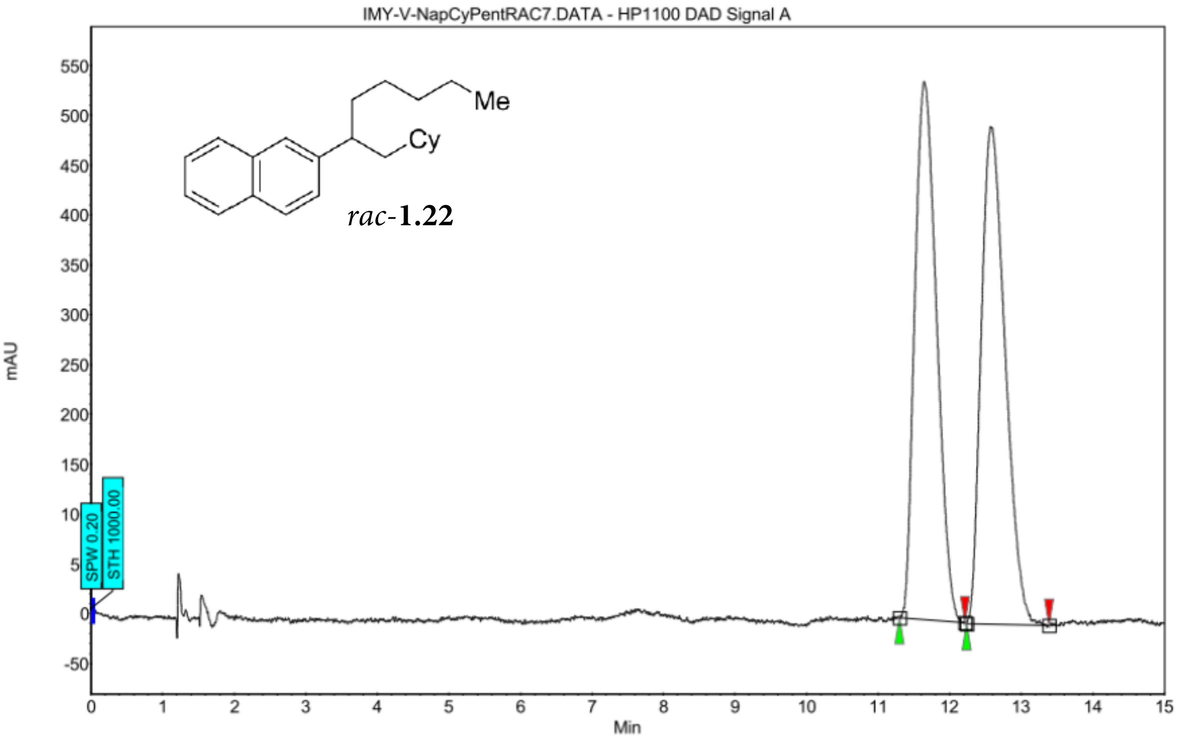


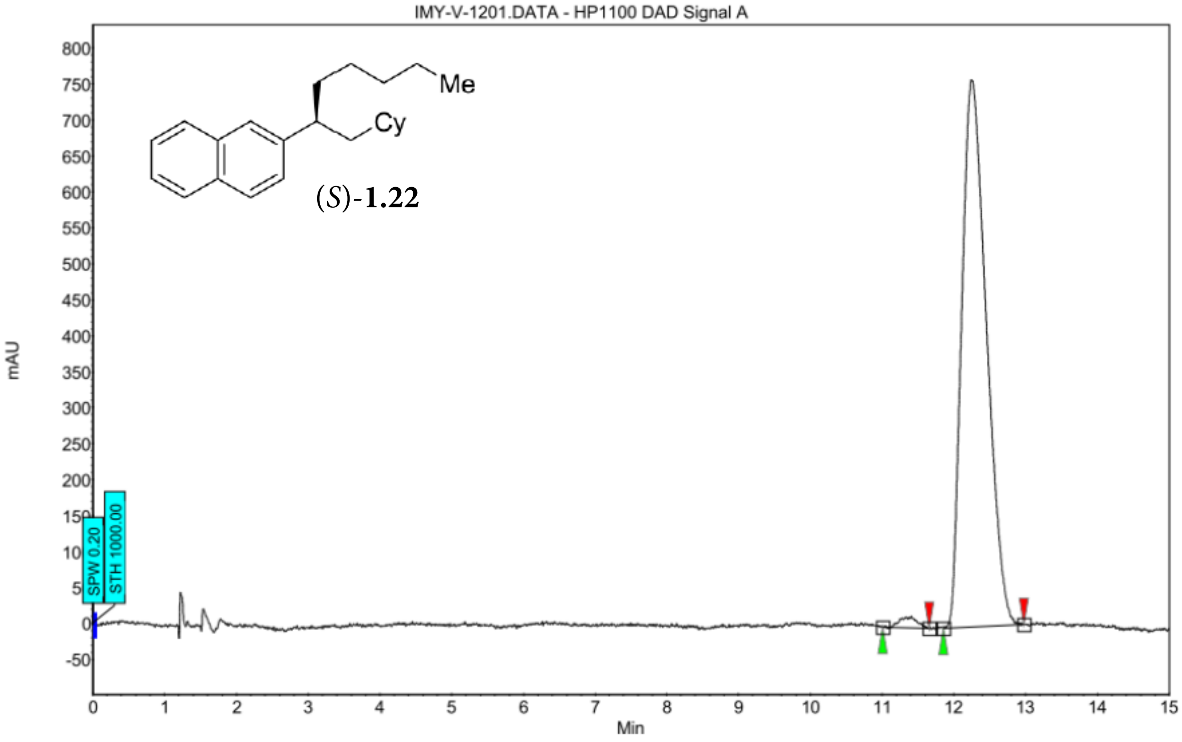
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
2	UNKNOWN	4.02	4.16	4.32	0.00	3.08	51.8	4.9	3.080
1	UNKNOWN	4.37	4.58	4.83	0.00	96.92	1396.8	153.4	96.920
Total						100.00	1448.6	158.2	100.000



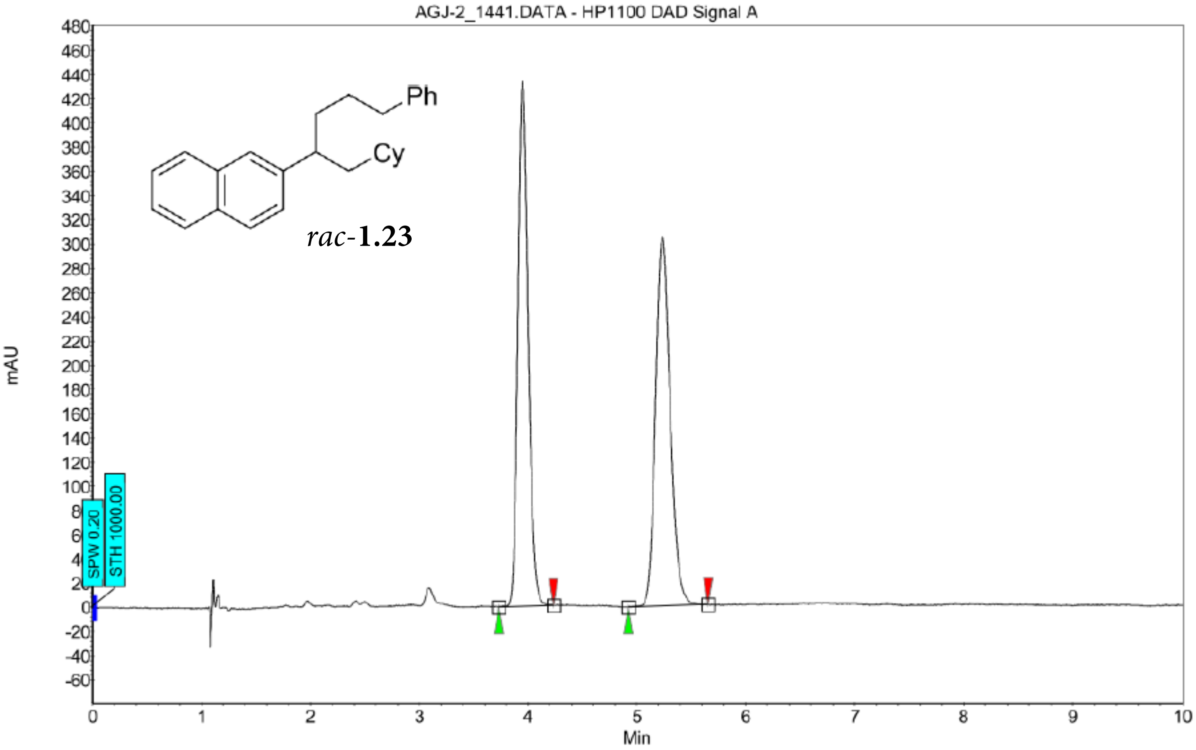


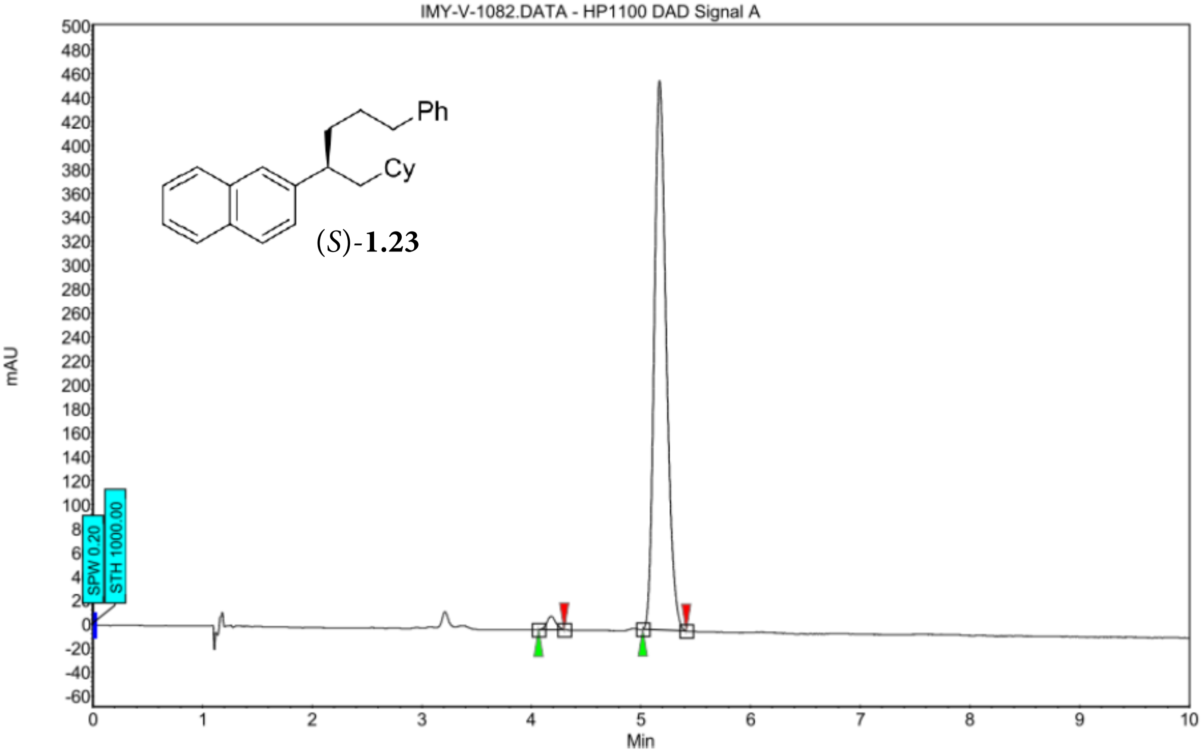
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	11.04	11.40	12.03	0.00	98.37	939.8	323.2	98.367
2	UNKNOWN	12.08	12.34	12.76	0.00	1.63	20.8	5.4	1.633
Total						100.00	960.6	328.6	100.000



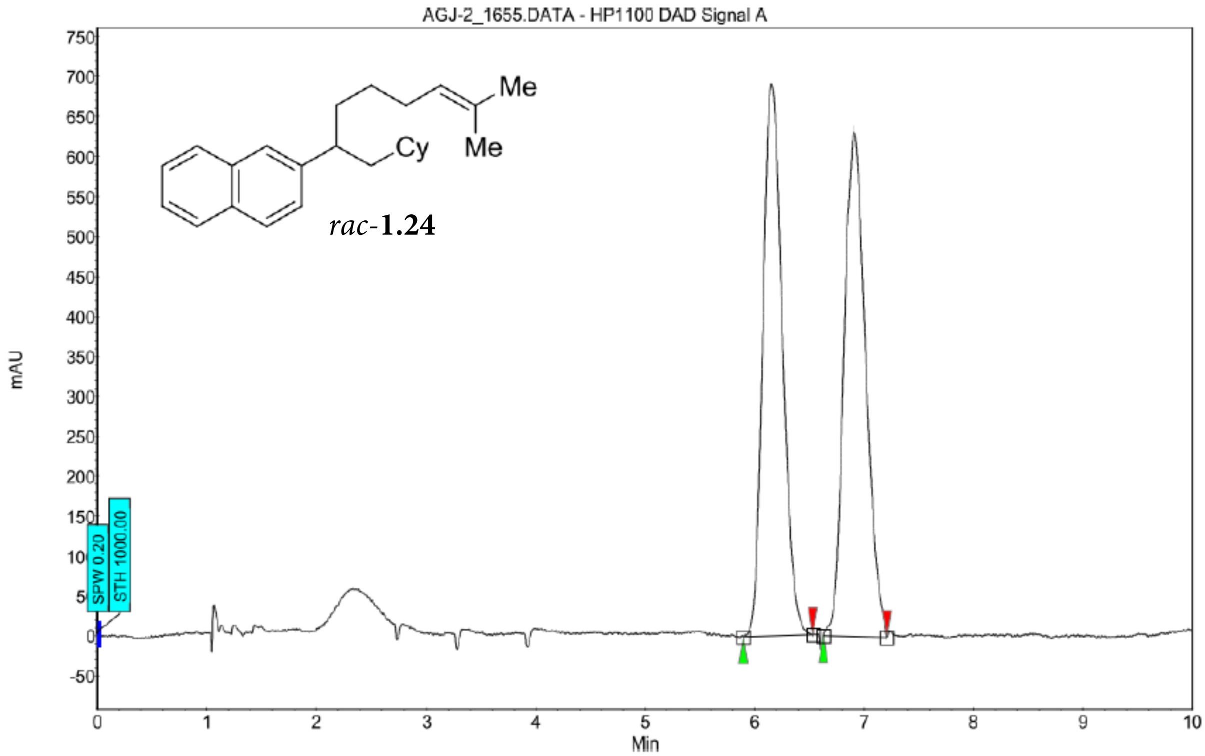


Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
2	UNKNOWN	11.01	11.41	11.66	0.00	1.44	16.2	4.4	1.435
1	UNKNOWN	11.85	12.25	12.98	0.00	98.56	759.8	301.9	98.565
Total						100.00	776.0	306.3	100.000

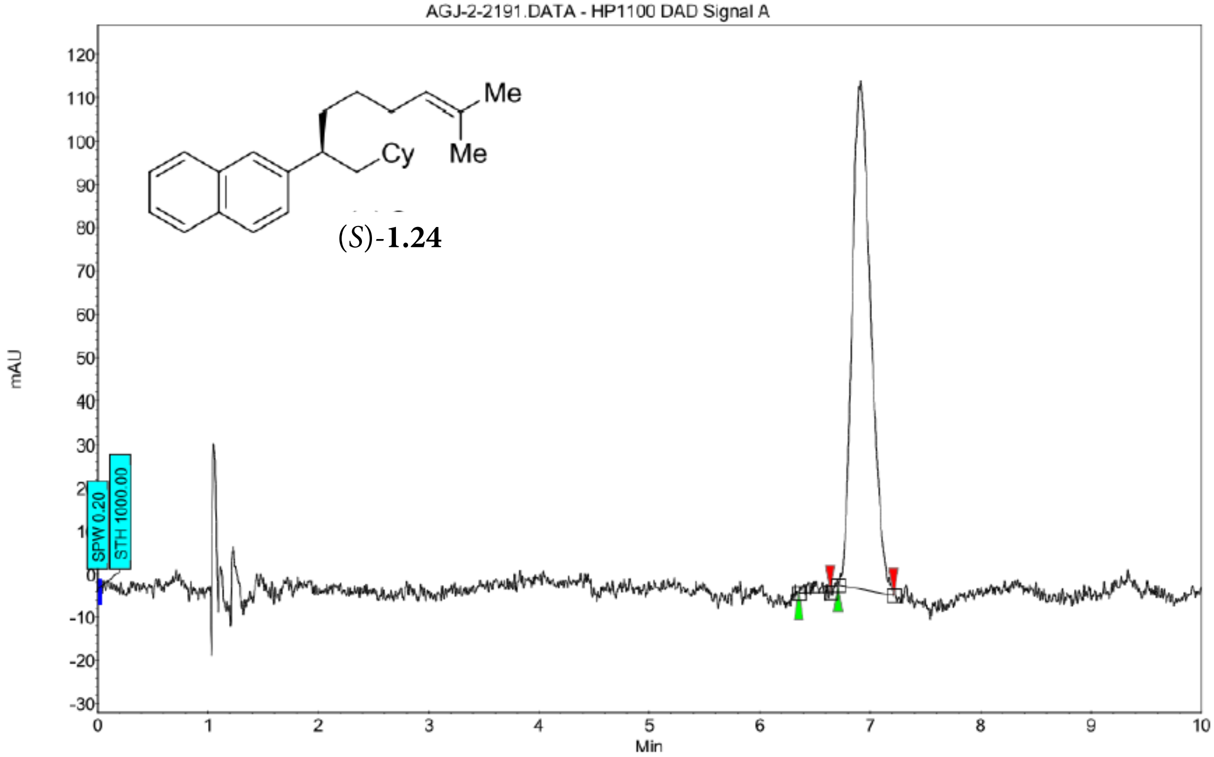




Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	4.07	4.18	4.30	0.00	1.74	11.2	1.0	1.735
2	UNKNOWN	5.02	5.17	5.42	0.00	98.26	458.7	58.1	98.265
Total						100.00	469.9	59.1	100.000

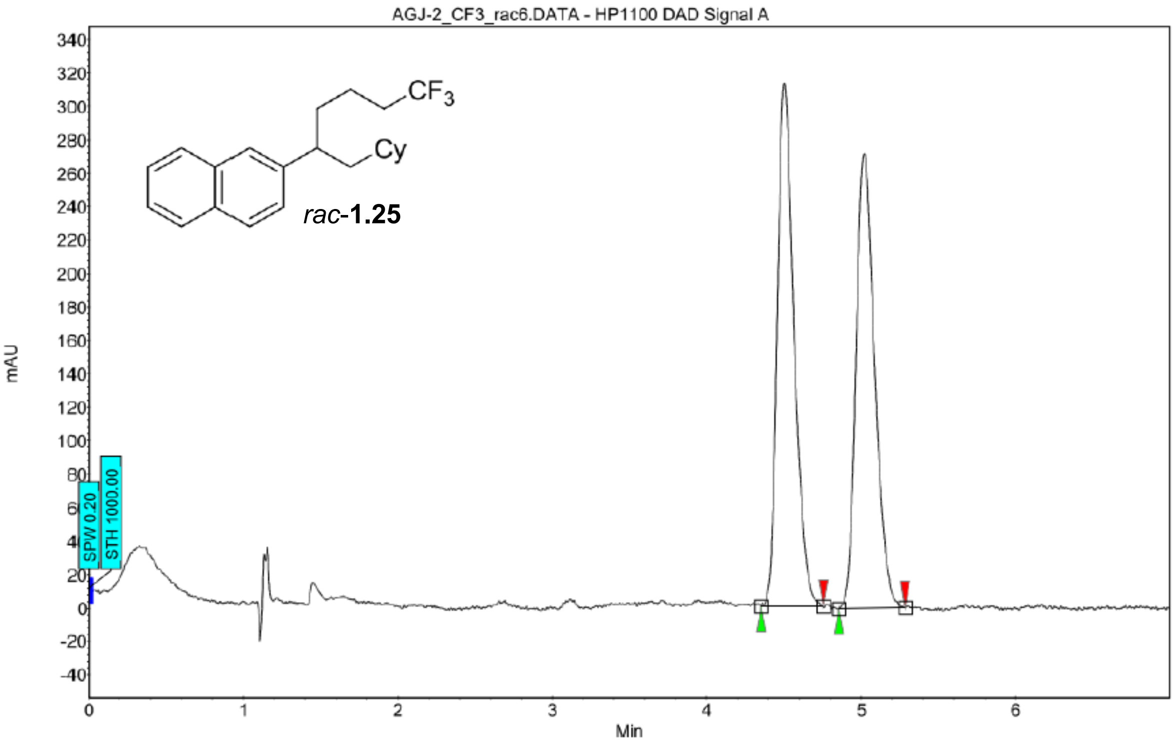


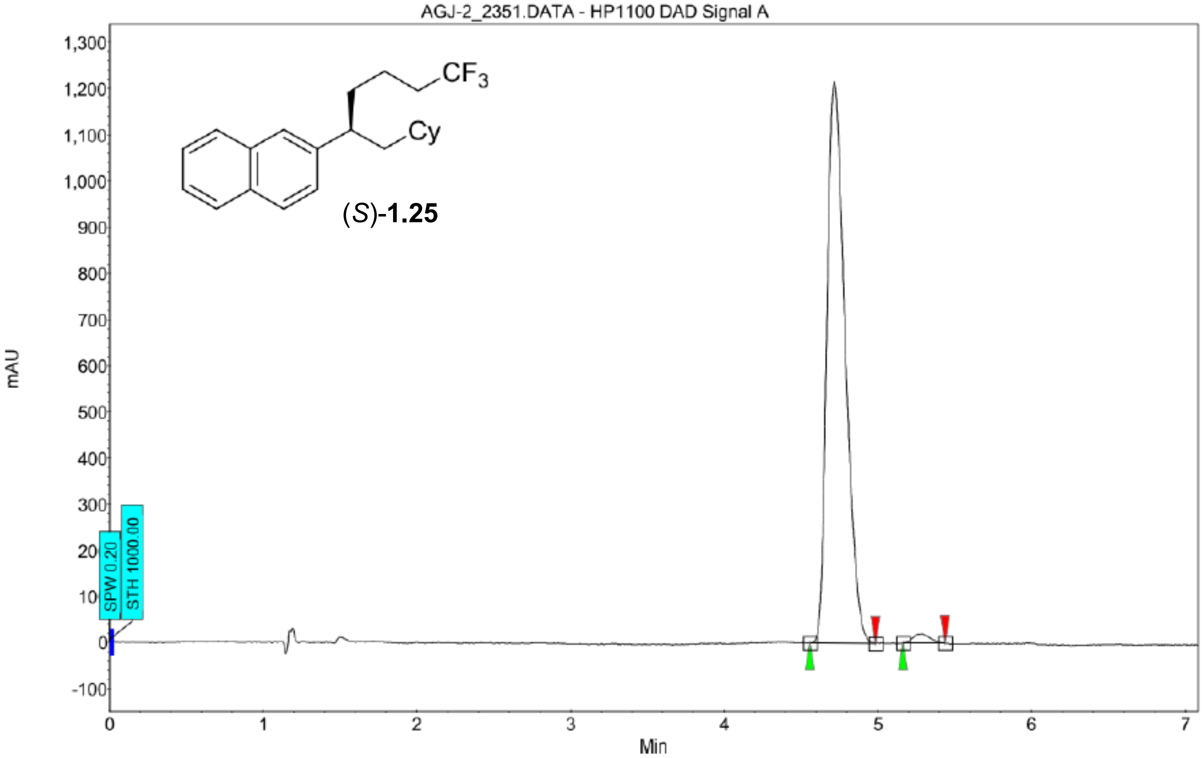
rac-**1.24**



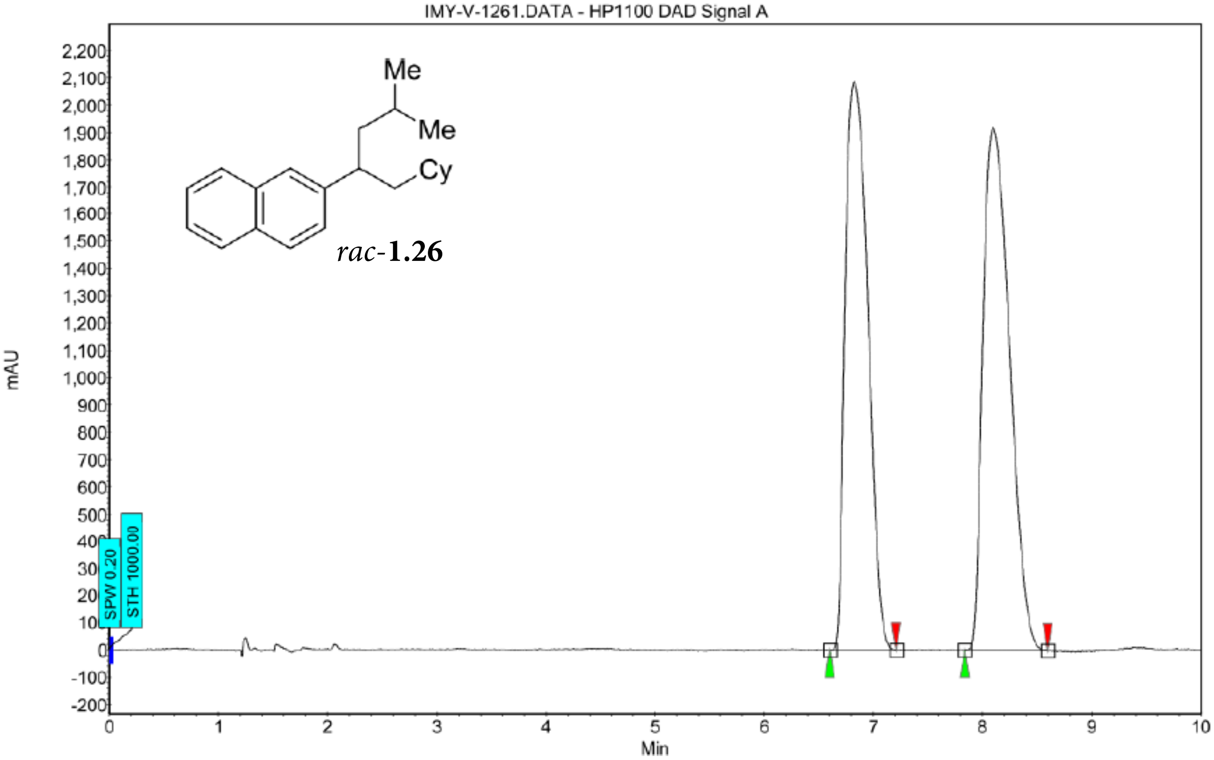
(*S*)-**1.24**

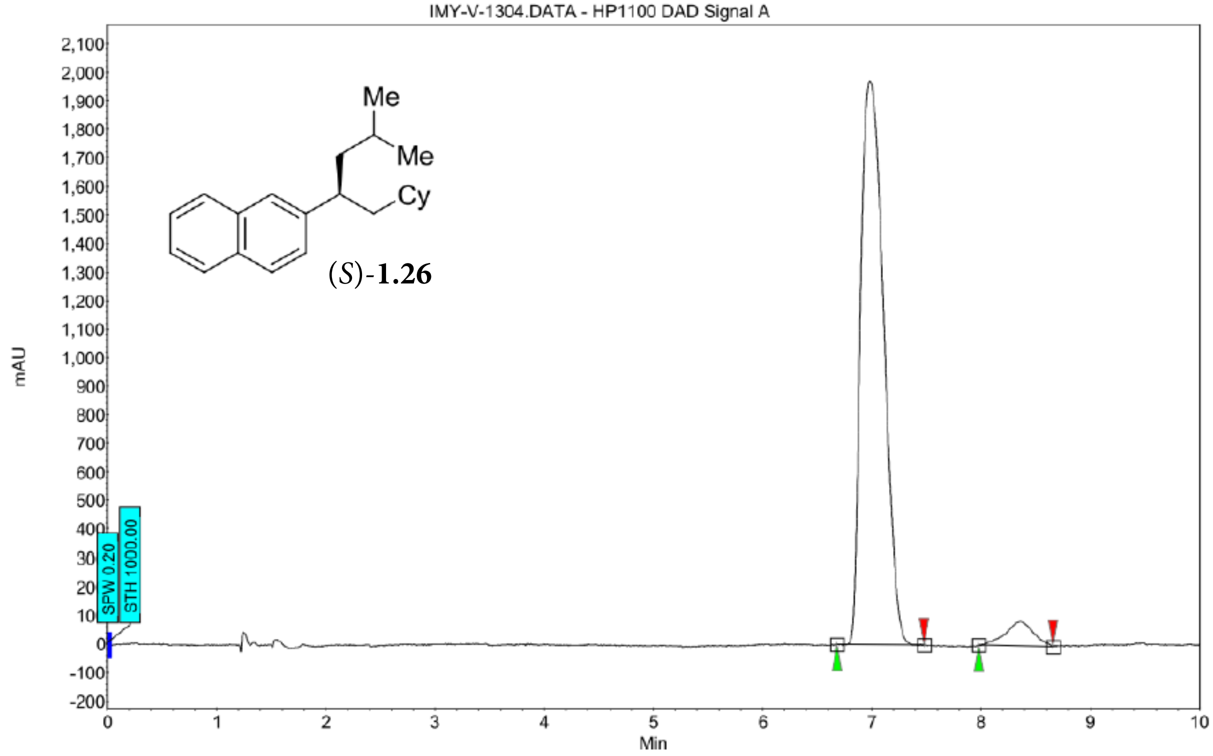
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
2	UNKNOWN	6.35	6.49	6.64	0.00	1.12	2.2	0.3	1.119
1	UNKNOWN	6.71	6.92	7.21	0.00	98.88	117.2	23.0	98.881
Total						100.00	119.4	23.3	100.000



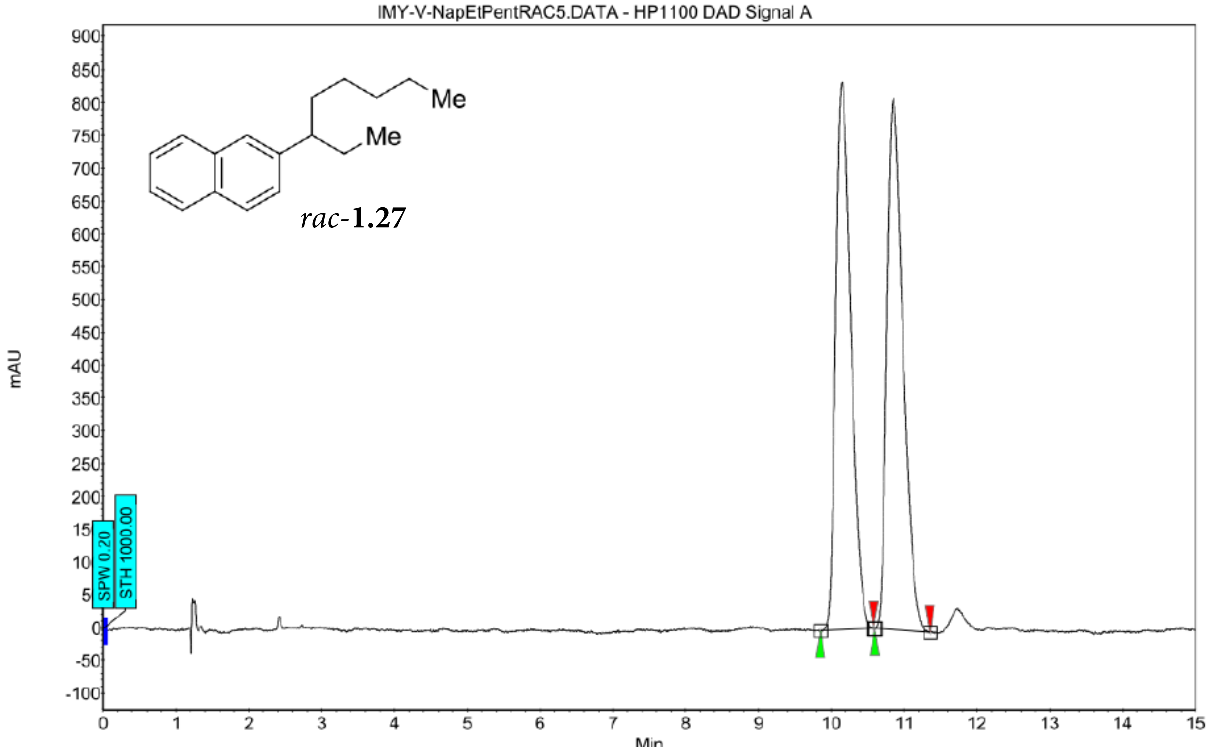


Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	4.56	4.72	4.99	0.00	98.50	1215.7	167.4	98.504
2	UNKNOWN	5.16	5.29	5.44	0.00	1.50	20.2	2.5	1.496
Total						100.00	1235.9	169.9	100.000

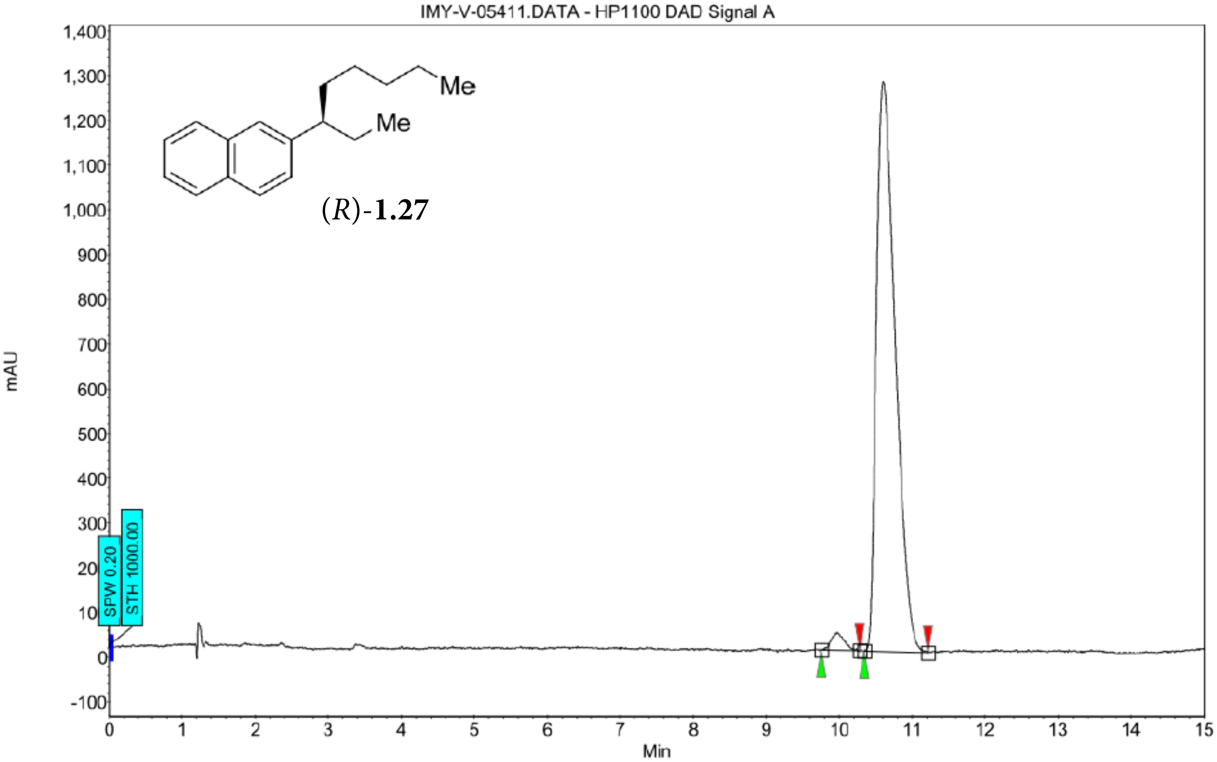




Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	6.68	6.98	7.48	0.00	94.98	1972.0	477.3	94.985
2	UNKNOWN	7.98	8.36	8.66	0.00	5.02	86.7	25.2	5.015
Total						100.00	2058.6	502.5	100.000

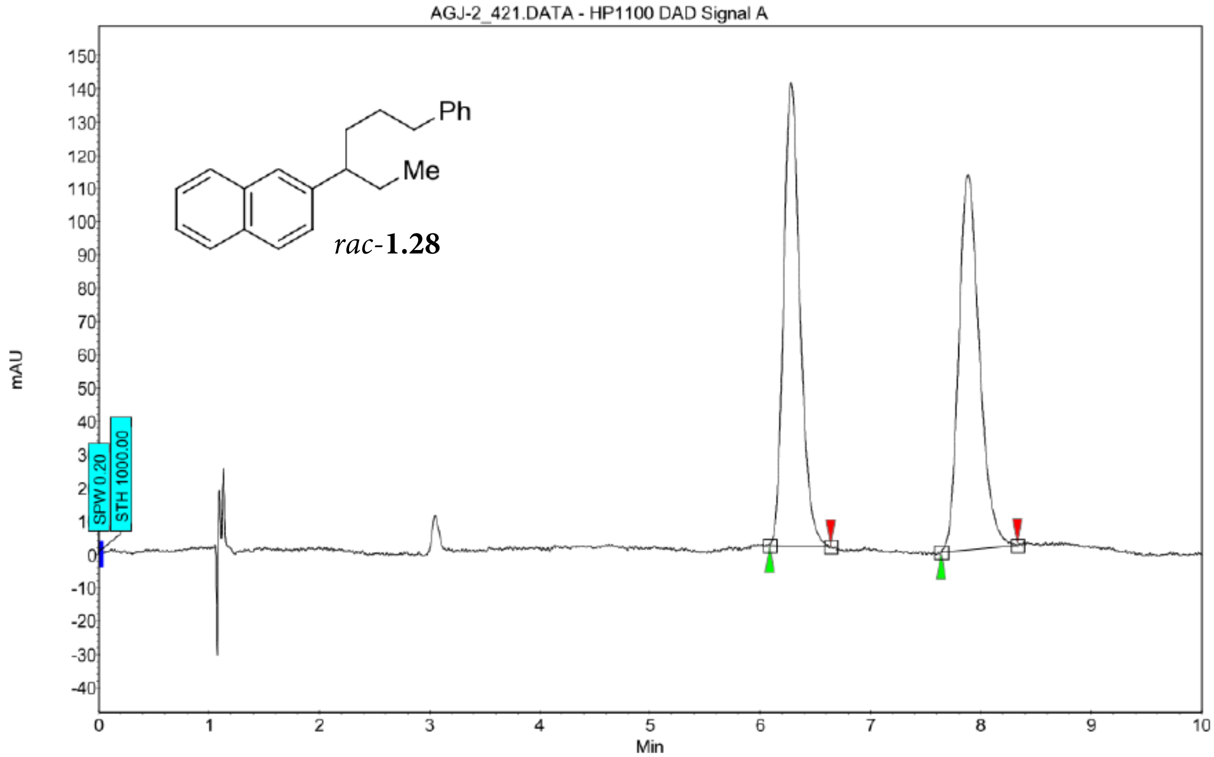


rac-**1.27**

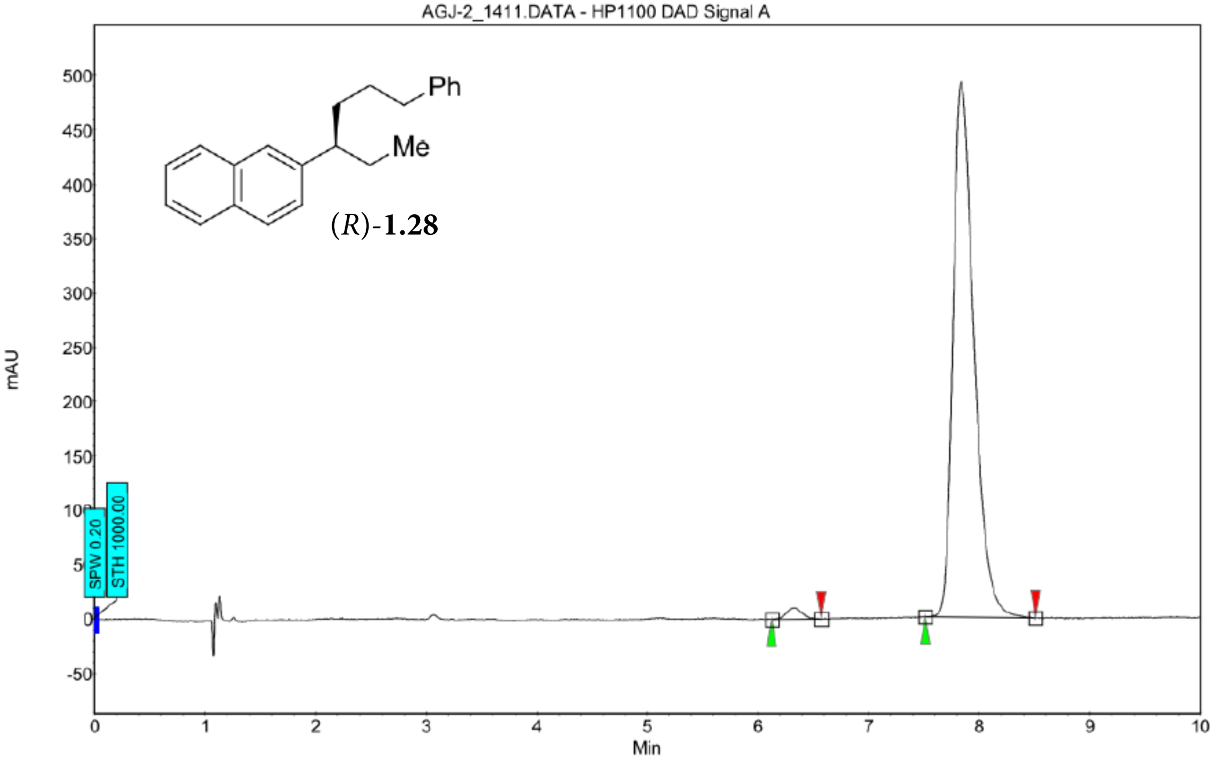


(*R*)-**1.27**

Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	9.76	9.97	10.28	0.00	1.97	38.7	7.7	1.972
2	UNKNOWN	10.34	10.61	11.22	0.00	98.03	1272.5	380.8	98.028
Total						100.00	1311.2	388.5	100.000

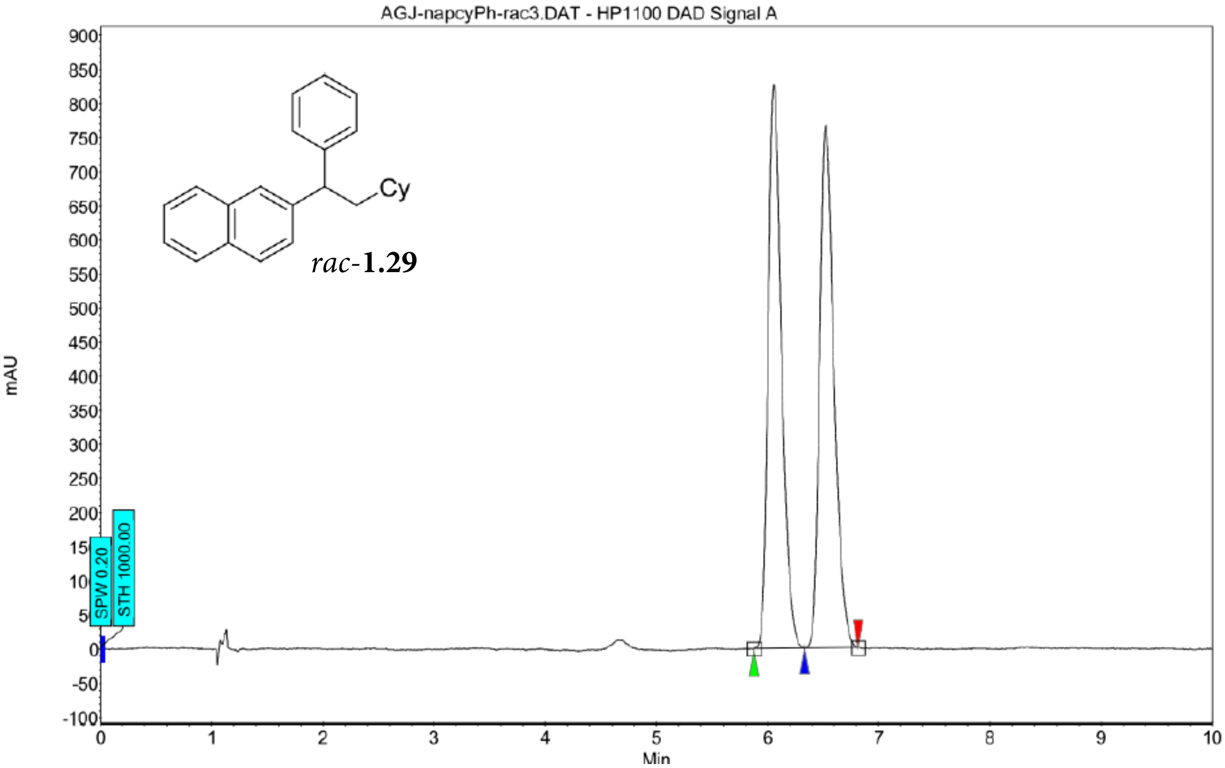


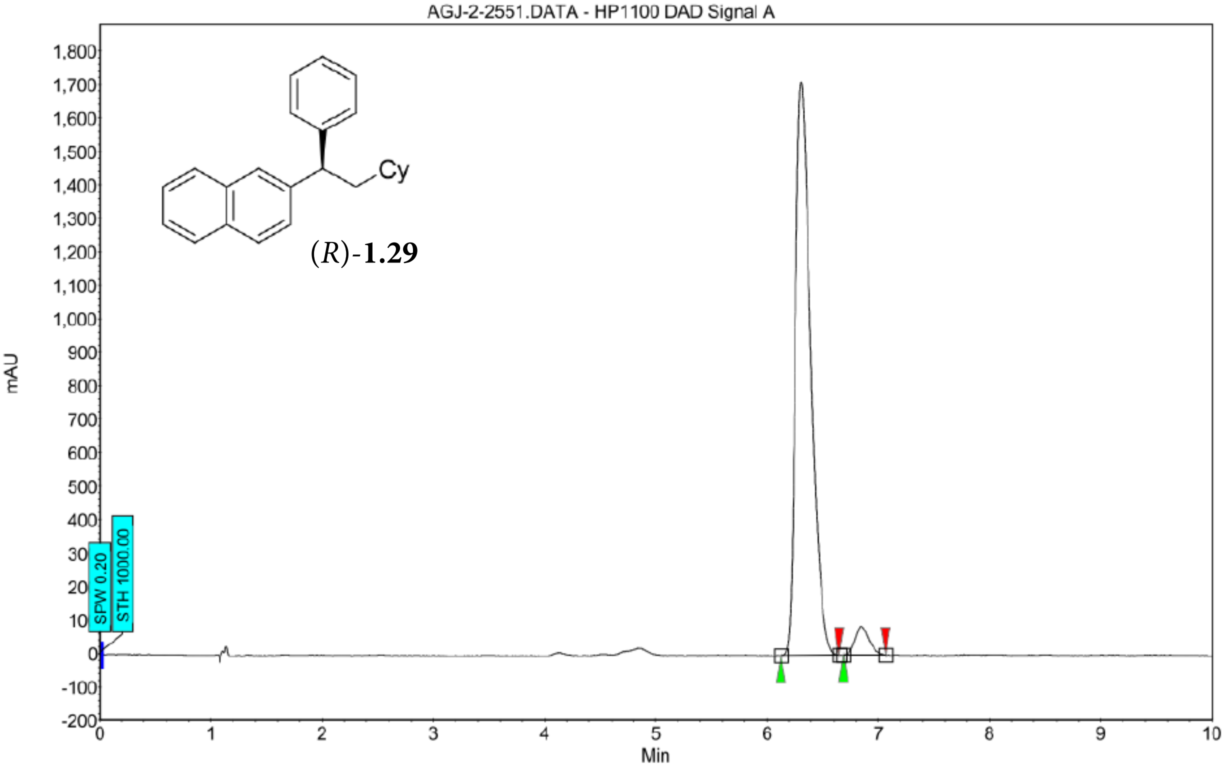
rac-**1.28**



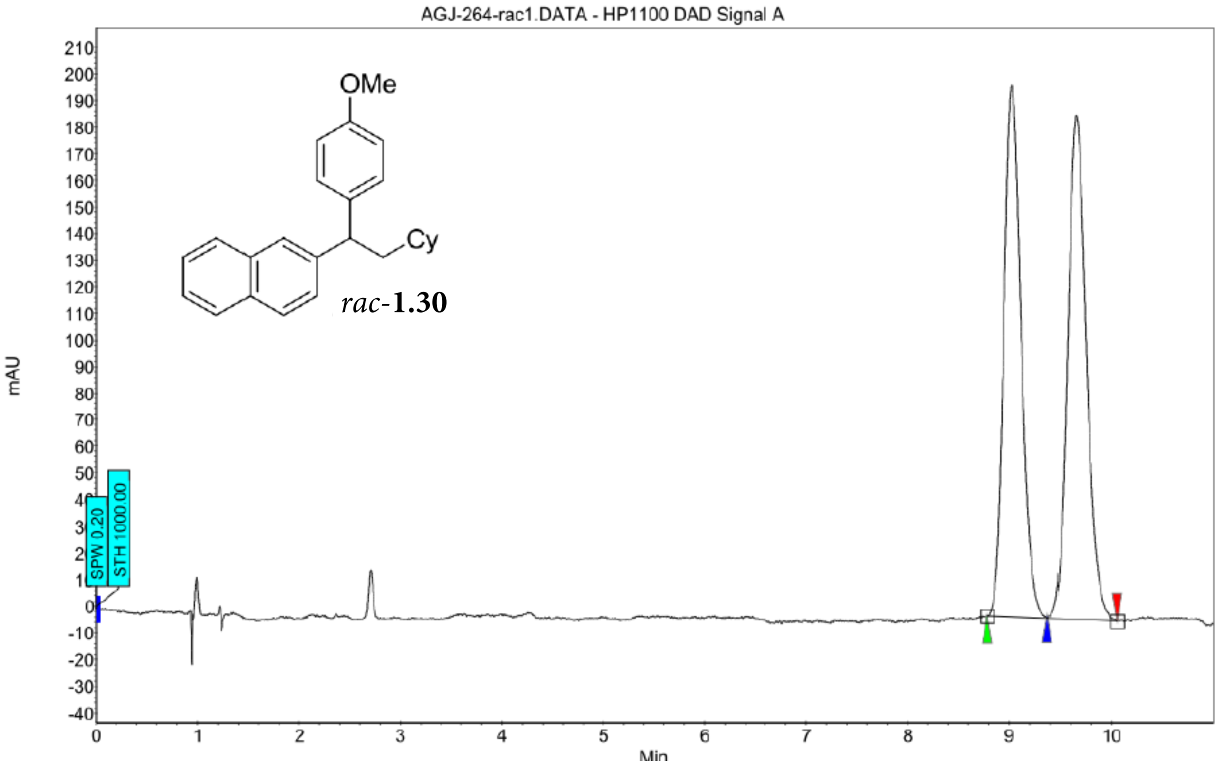
(*R*)-**1.28**

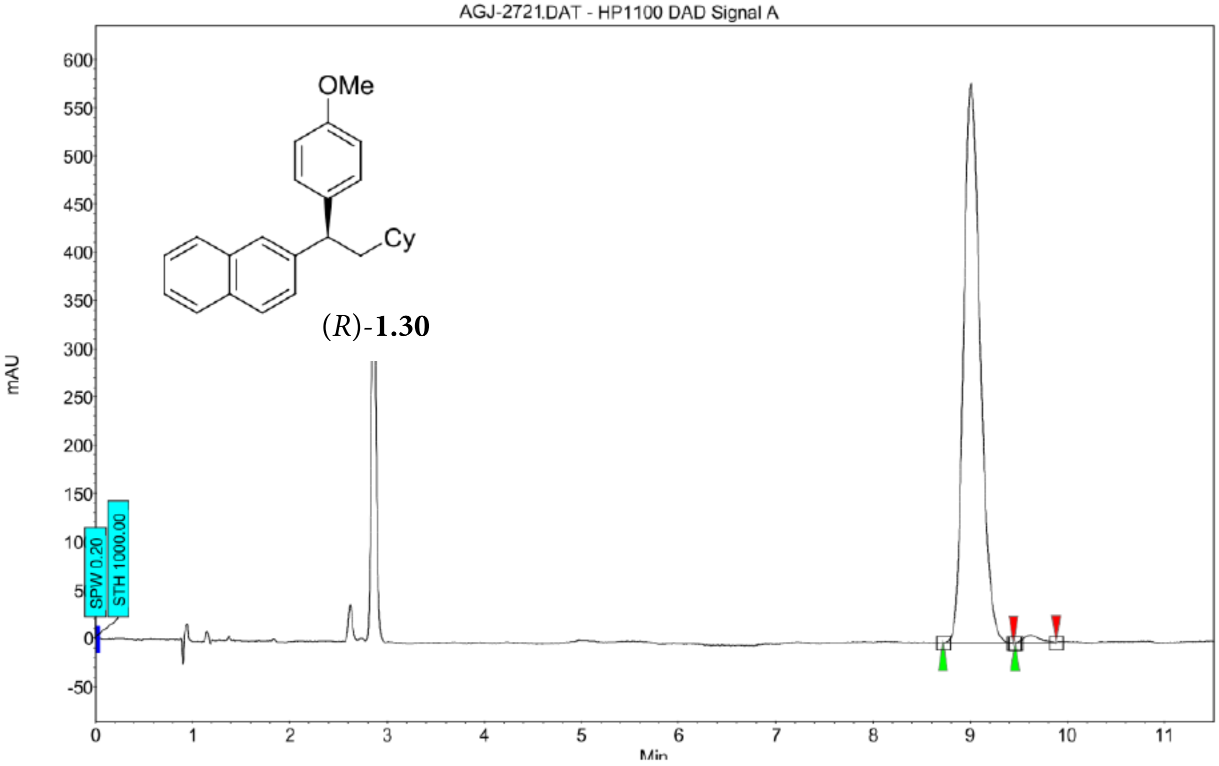
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	6.12	6.32	6.57	0.00	1.49	10.0	1.6	1.489
2	UNKNOWN	7.51	7.84	8.51	0.00	98.51	492.5	107.7	98.511
Total						100.00	502.5	109.3	100.000



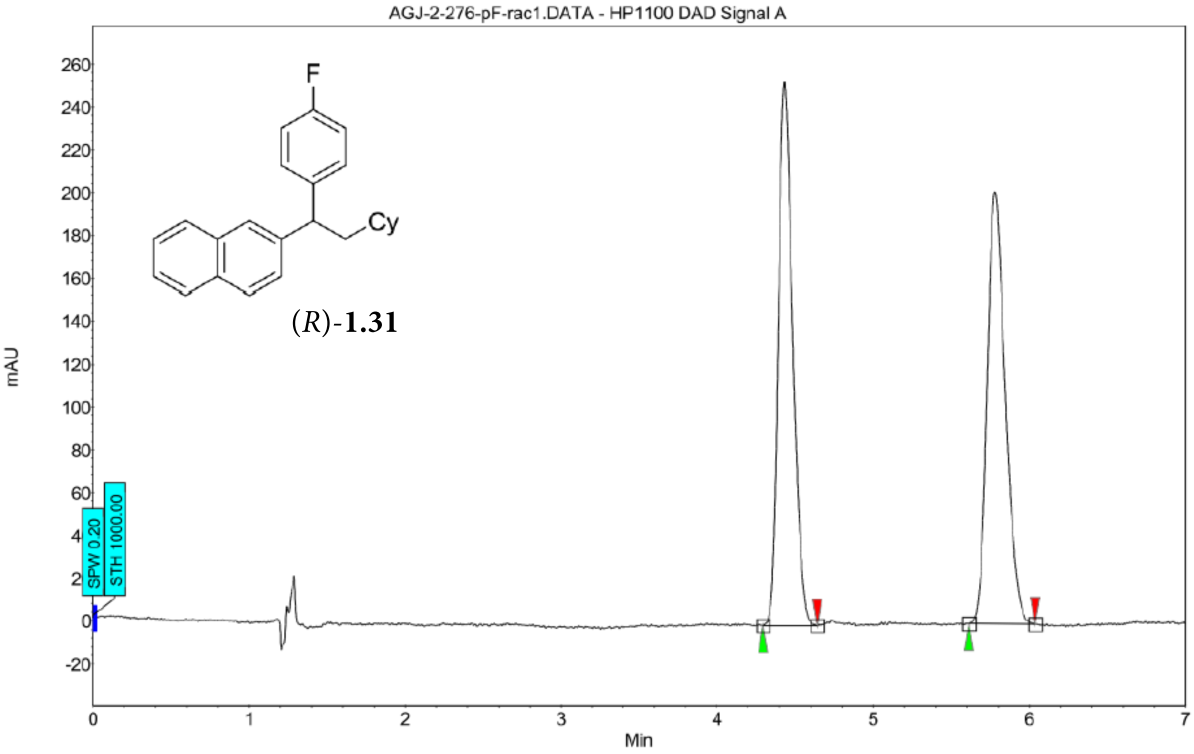


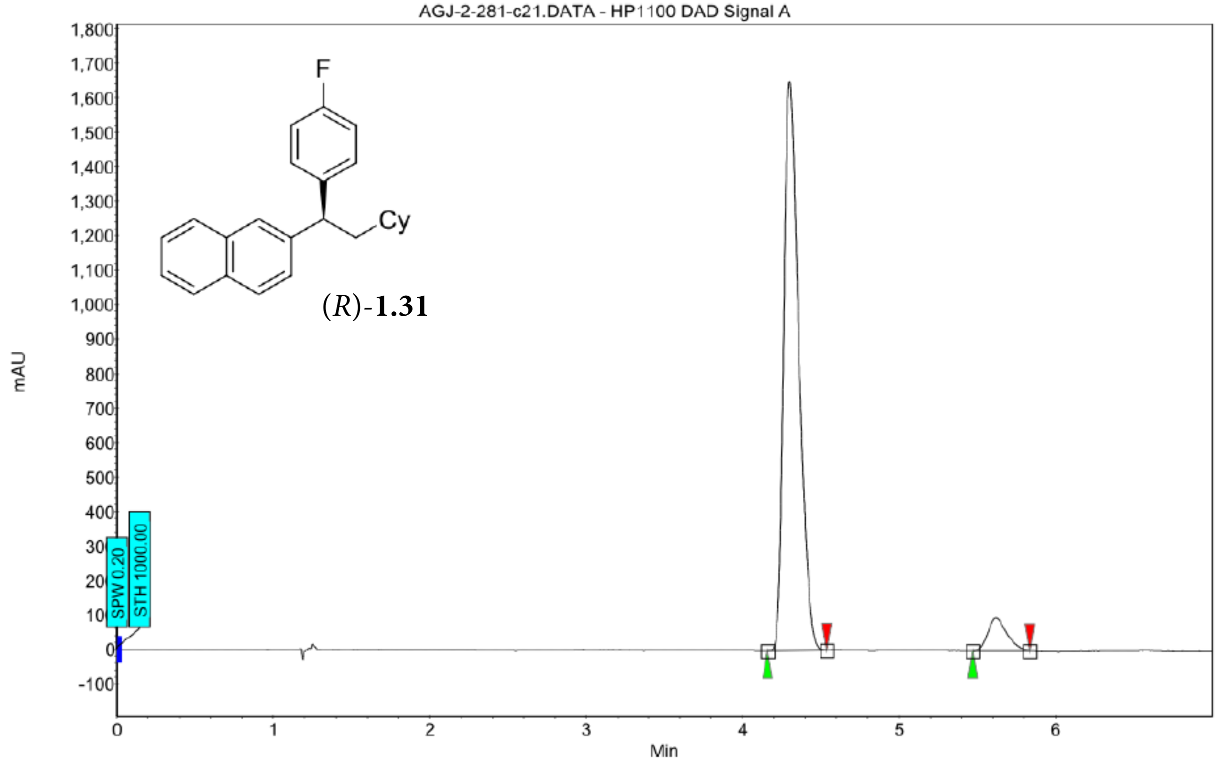
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	6.13	6.31	6.65	0.00	95.60	1711.1	272.1	95.596
2	UNKNOWN	6.69	6.85	7.07	0.00	4.40	85.5	12.5	4.404
Total						100.00	1796.6	284.6	100.000



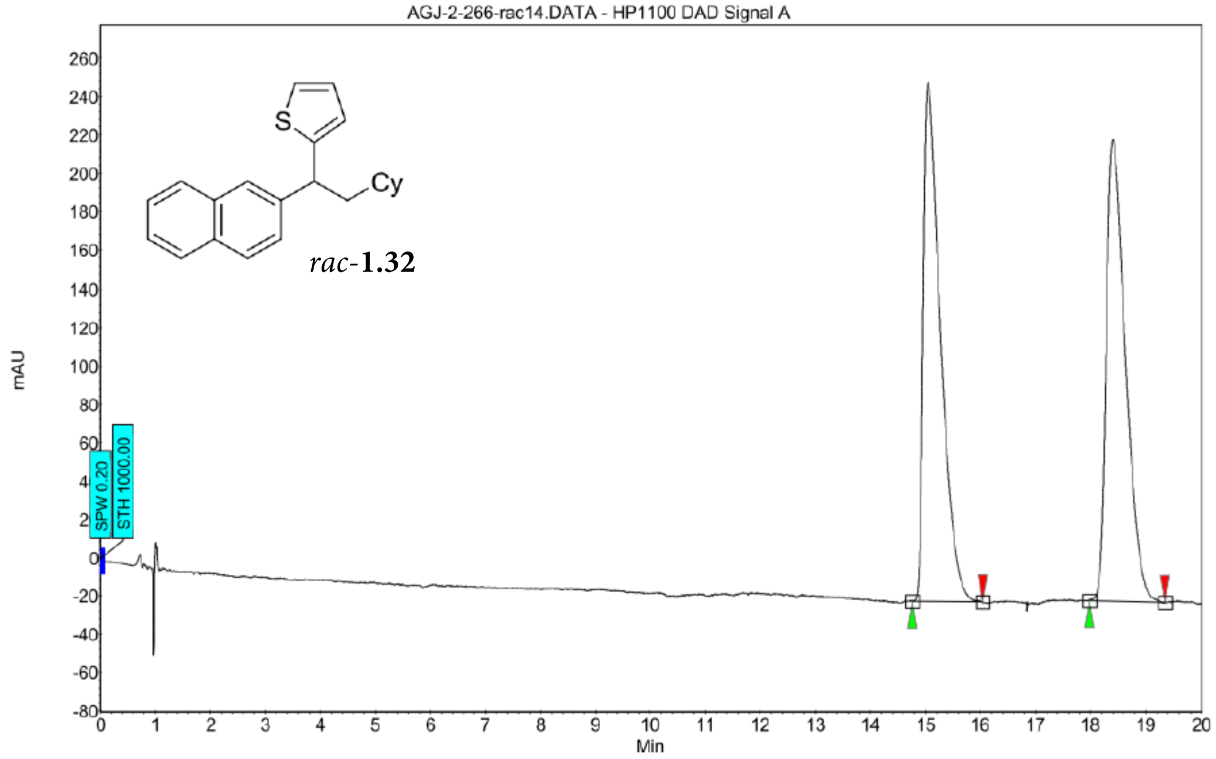


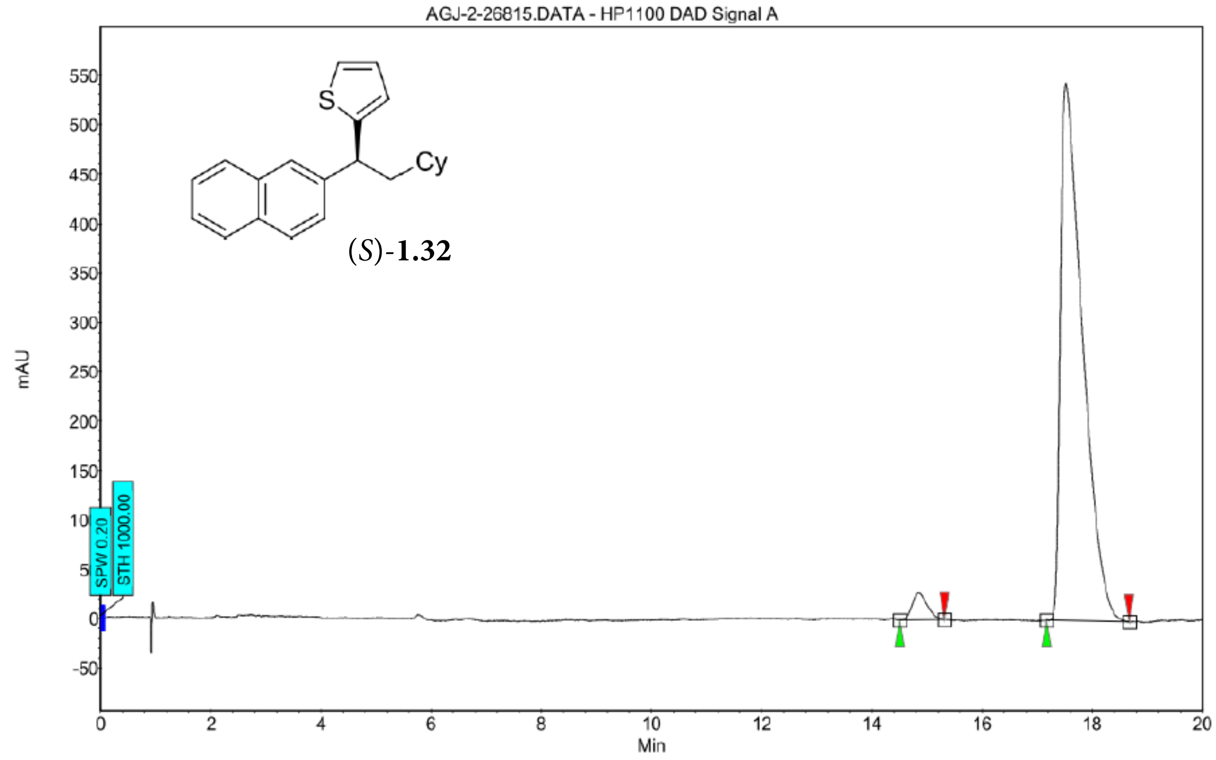
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	8.72	9.01	9.44	0.00	98.68	579.9	115.5	98.681
2	UNKNOWN	9.46	9.63	9.88	0.00	1.32	8.0	1.5	1.319
Total						100.00	587.9	117.0	100.000



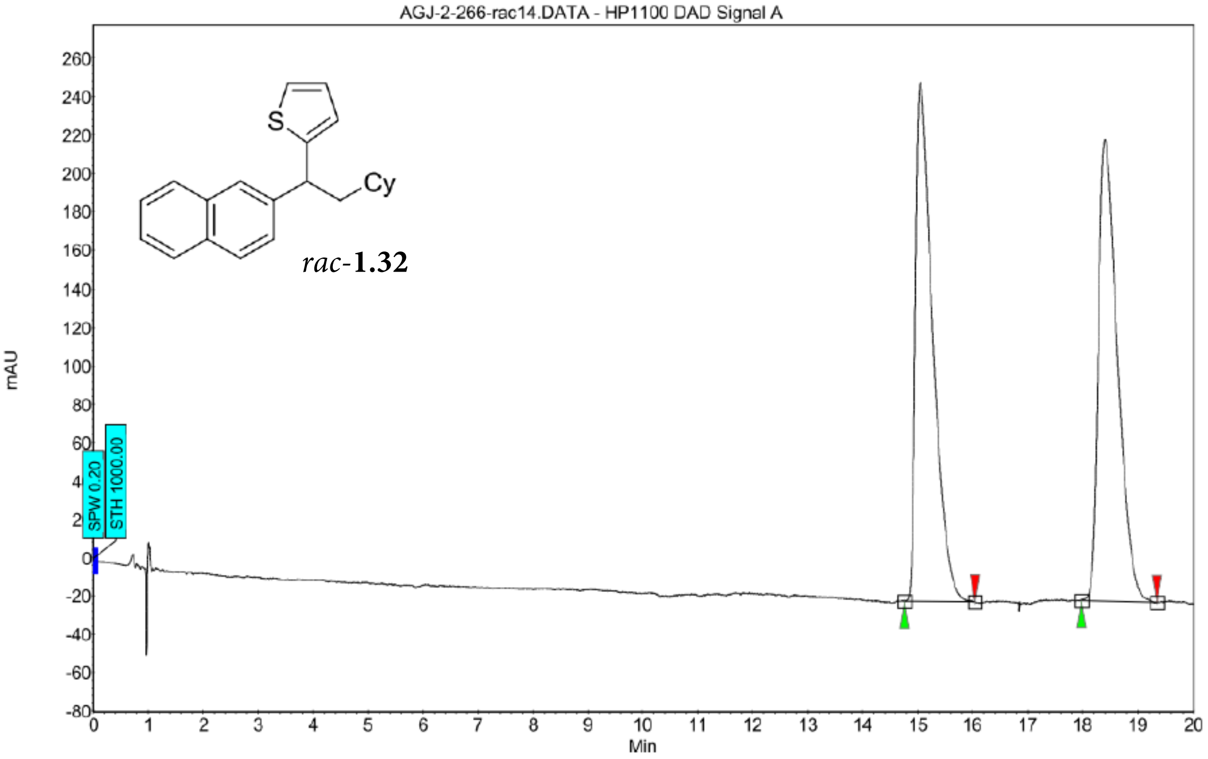


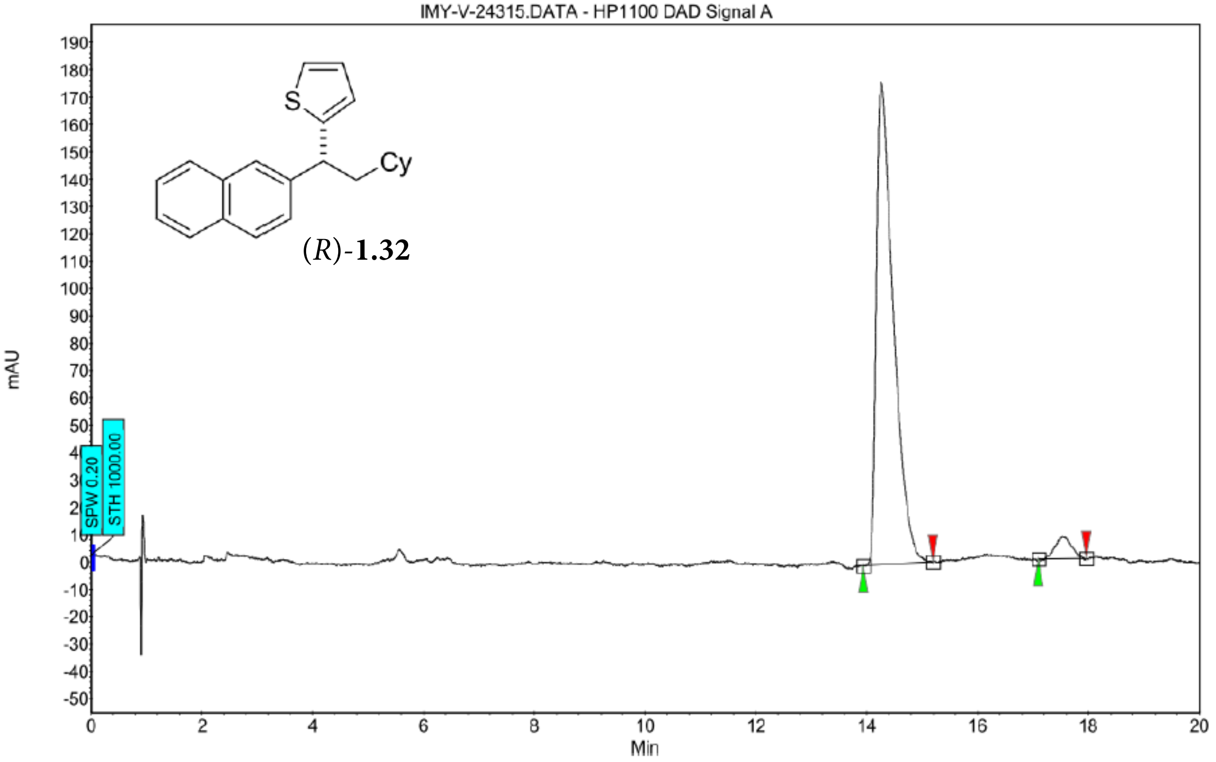
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	4.16	4.30	4.54	0.00	93.26	1651.3	185.9	93.264
2	UNKNOWN	5.47	5.62	5.84	0.00	6.74	94.7	13.4	6.736
Total						100.00	1746.0	199.4	100.000



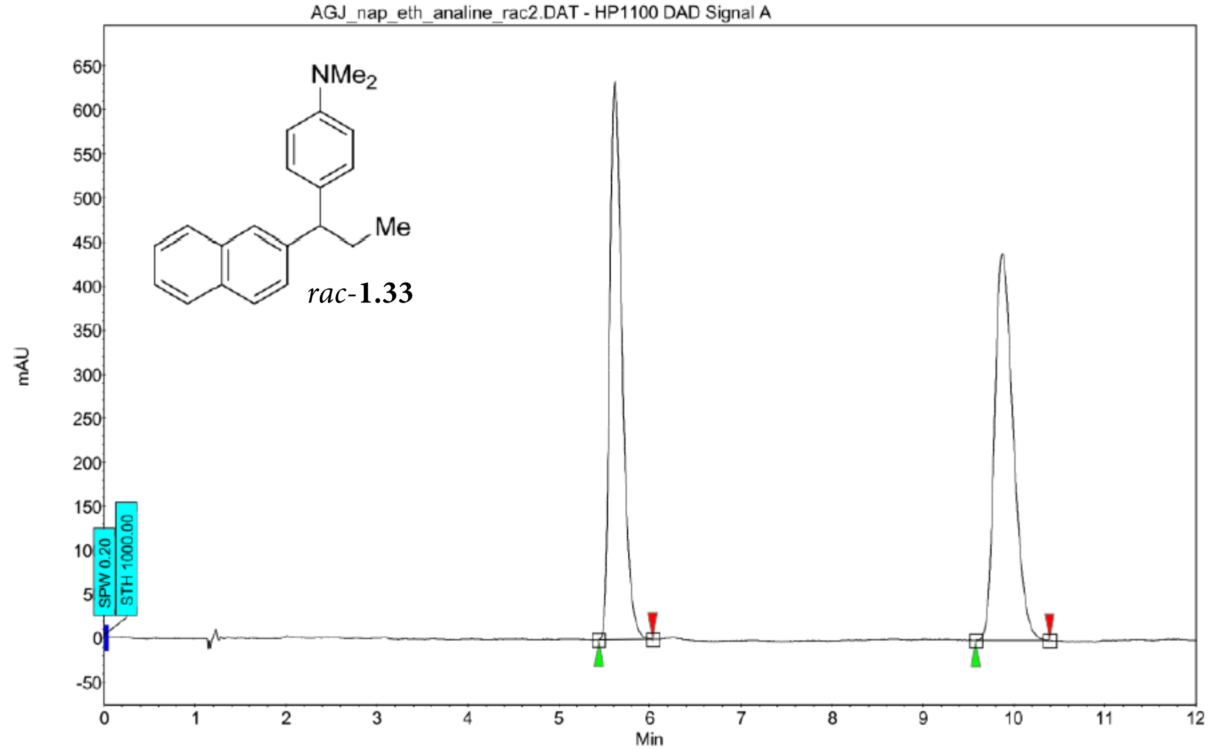


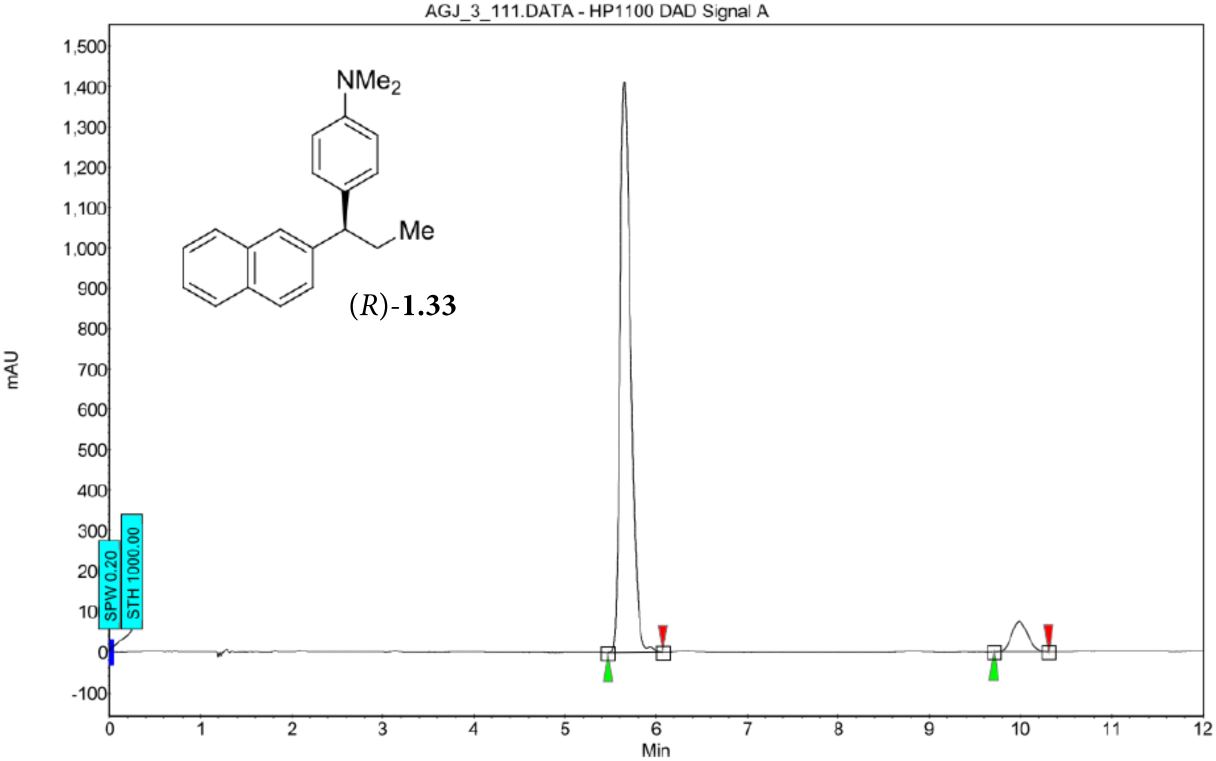
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
2	UNKNOWN	14.50	14.85	15.31	0.00	3.24	26.9	8.4	3.236
1	UNKNOWN	17.17	17.52	18.67	0.00	96.76	543.4	252.1	96.764
Total						100.00	570.3	260.5	100.000



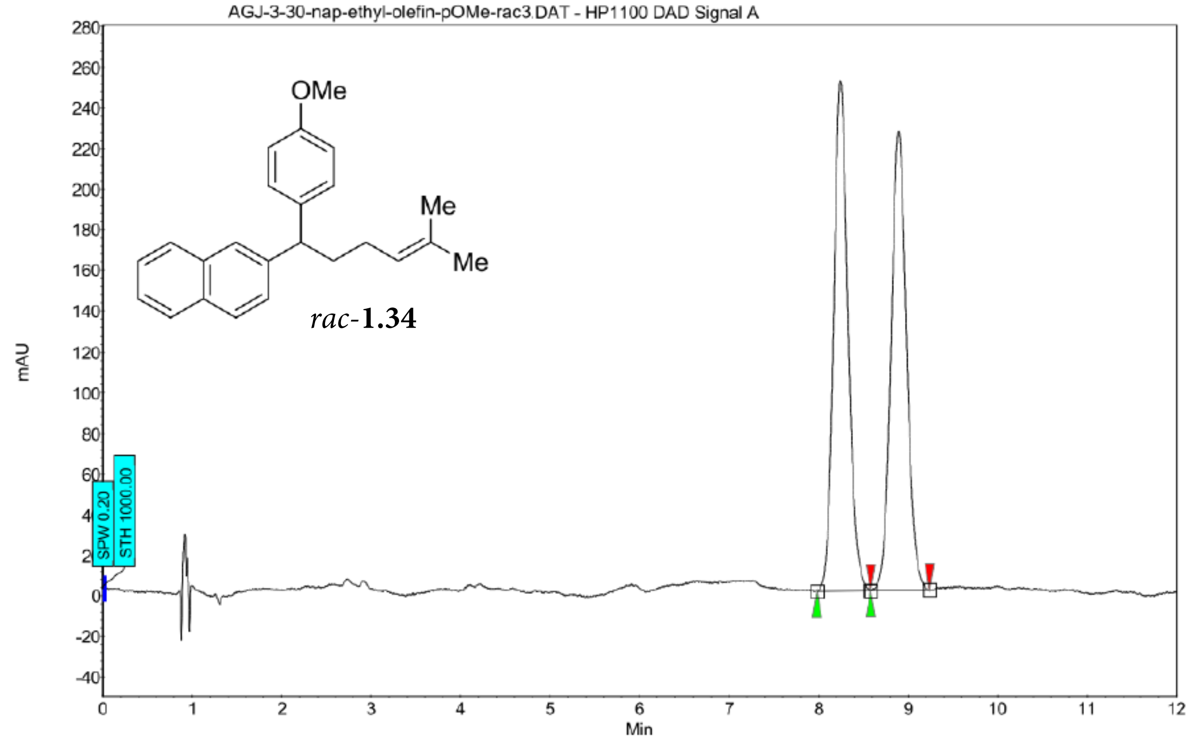


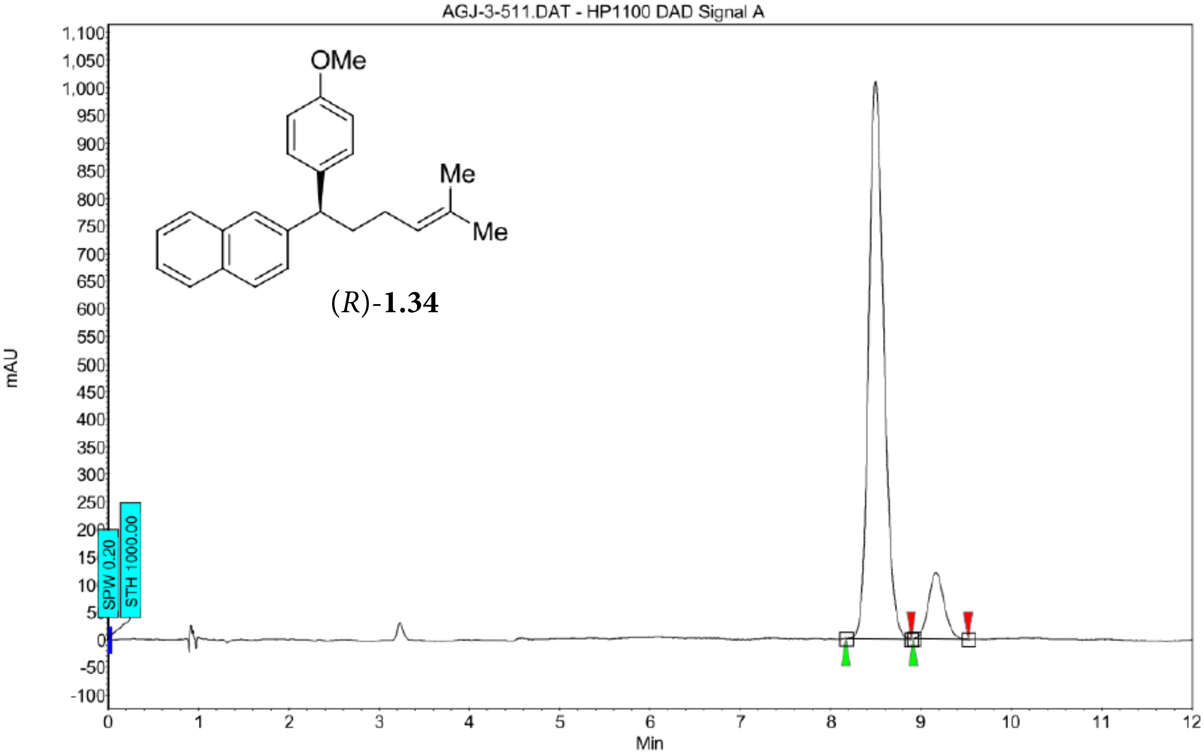
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	13.94	14.26	15.20	0.00	95.79	176.7	62.8	95.788
2	UNKNOWN	17.10	17.53	17.96	0.00	4.21	8.4	2.8	4.212
Total						100.00	185.2	65.6	100.000





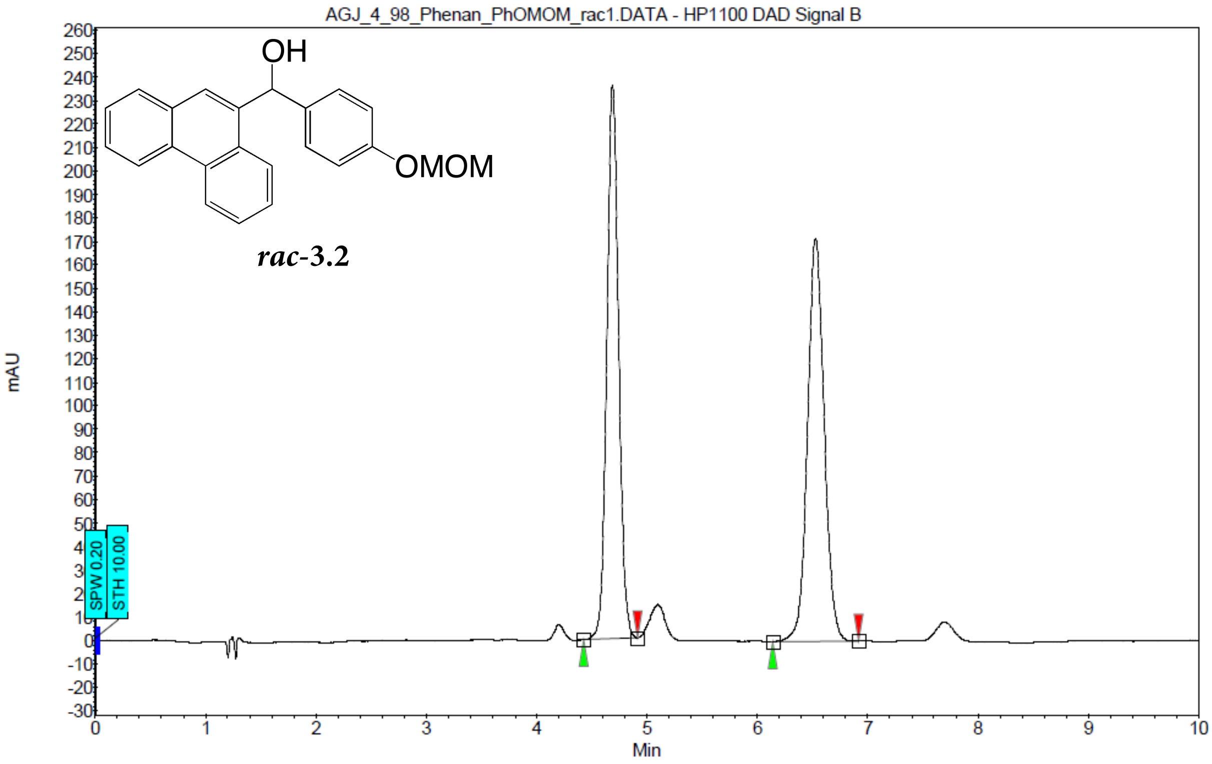
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	5.47	5.65	6.08	0.00	92.72	1414.5	200.0	92.717
2	UNKNOWN	9.71	9.98	10.31	0.00	7.28	75.1	15.7	7.283
Total						100.00	1489.6	215.7	100.000



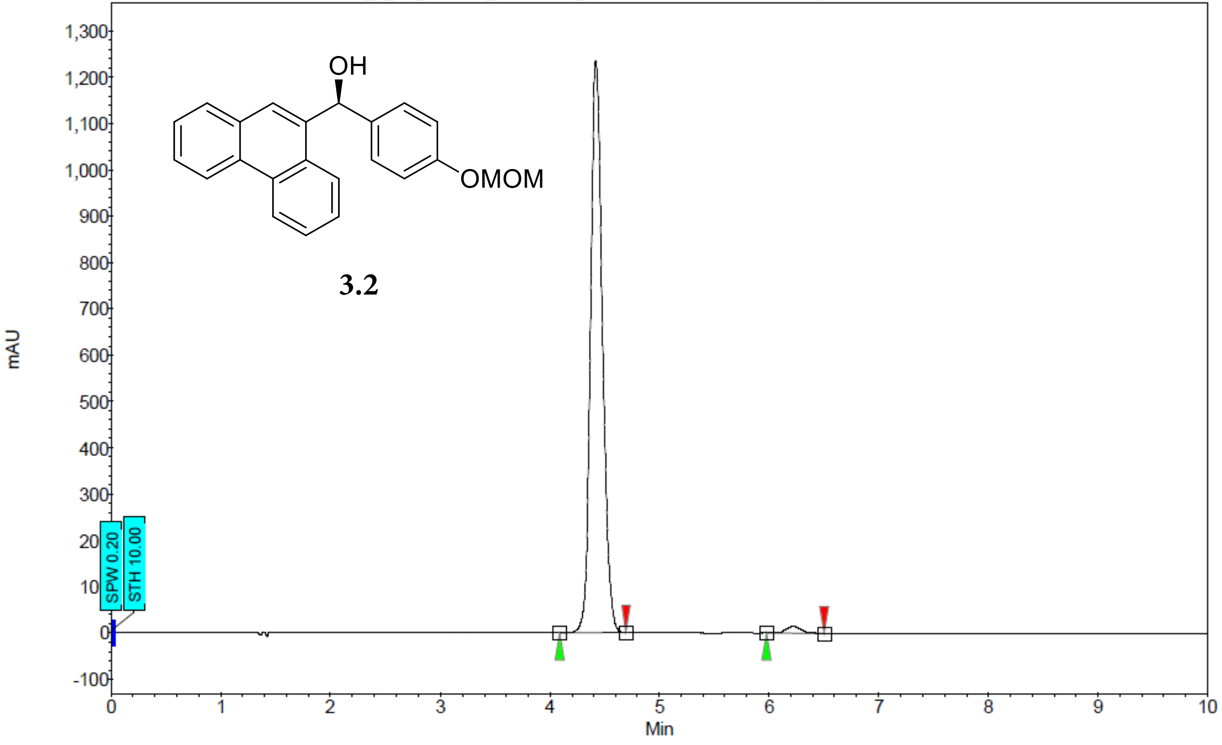


Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	8.17	8.50	8.89	0.00	89.04	1009.3	195.4	89.036
2	UNKNOWN	8.91	9.17	9.52	0.00	10.96	119.6	24.1	10.964
Total						100.00	1128.9	219.5	100.000

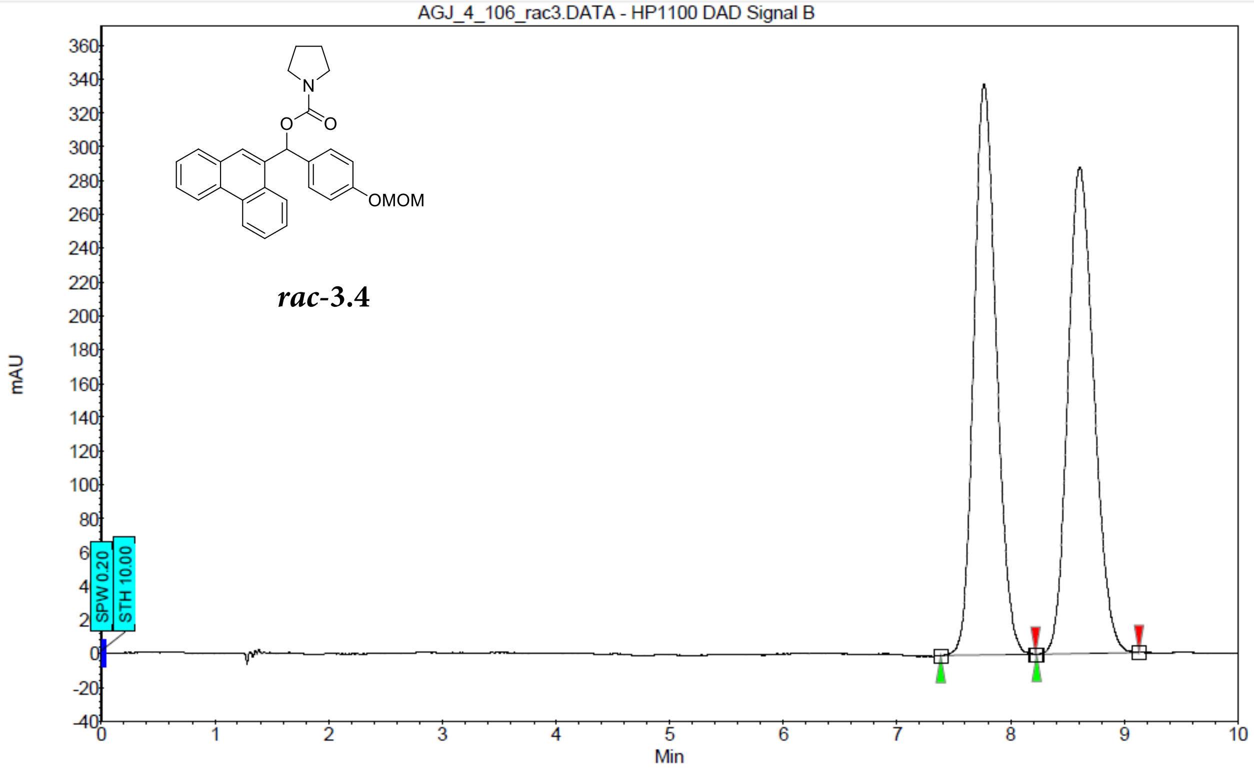
AGJ_4_98_Phenan_PhOMOM_rac1.DATA - HP1100 DAD Signal B

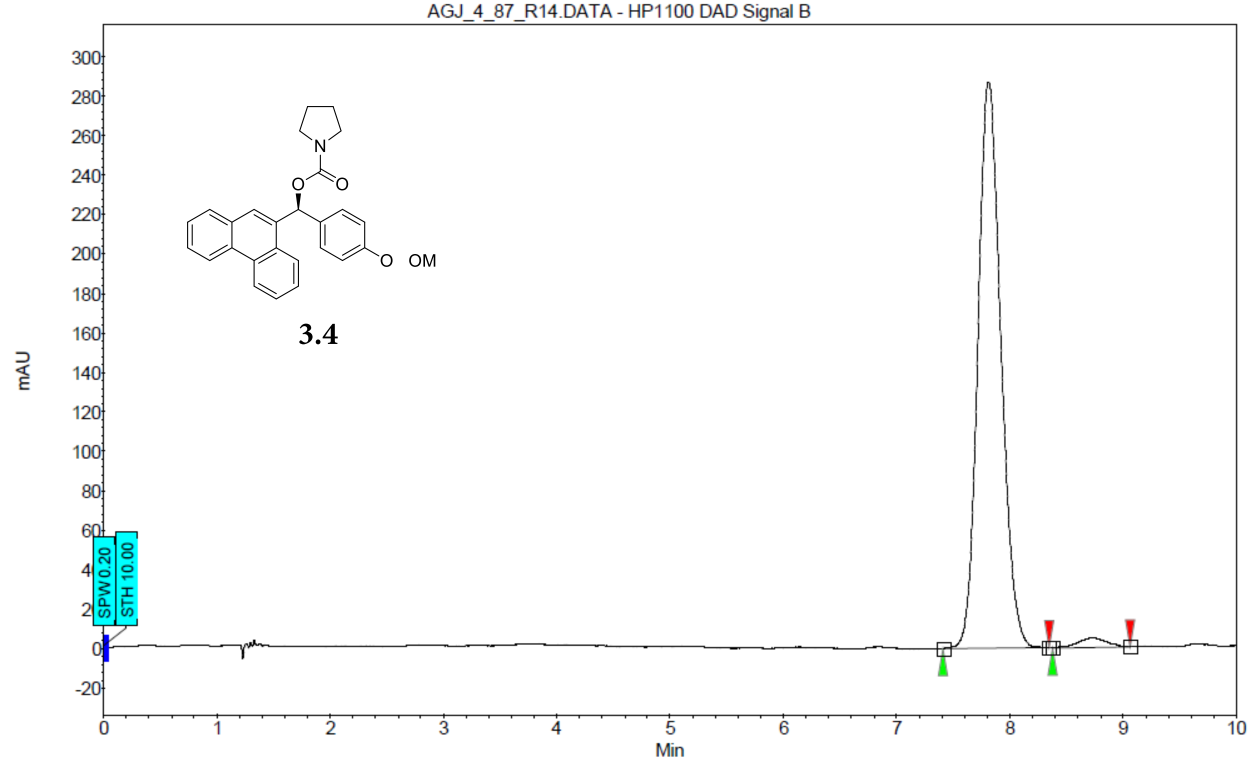


AGJ_4_85_Phenan_PhOMOM_R41.DATA - HP1100 DAD Signal B

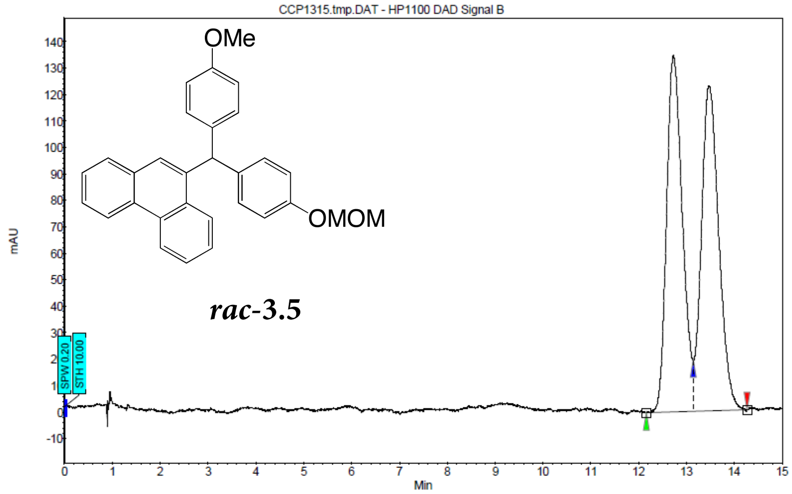


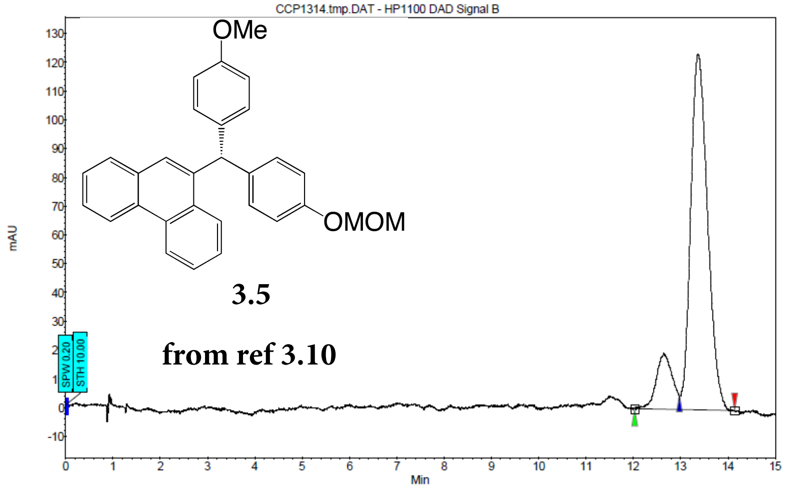
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	4.09	4.42	4.69	0.00	98.41	1236.6	155.9	98.410
2	UNKNOWN	5.98	6.22	6.50	0.00	1.59	14.7	2.5	1.590
Total						100.00	1251.3	158.4	100.000



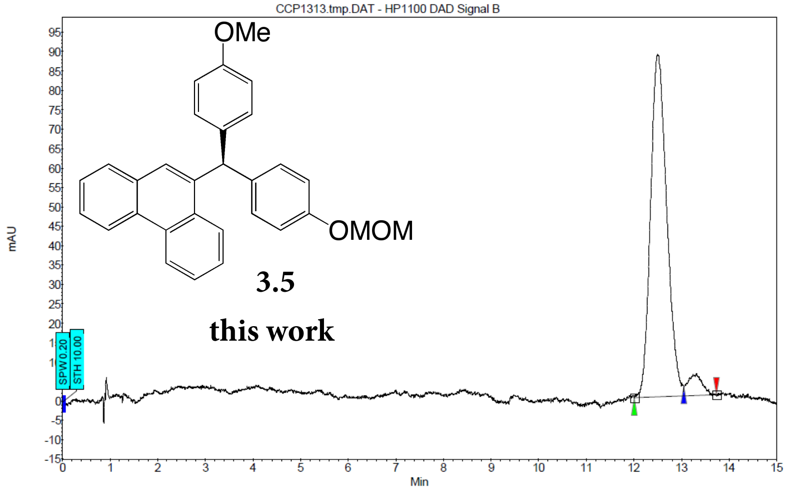


Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	7.41	7.81	8.35	0.00	97.94	286.9	67.5	97.943
2	UNKNOWN	8.37	8.70	9.06	0.00	2.06	4.9	1.4	2.057
Total						100.00	291.7	68.9	100.000

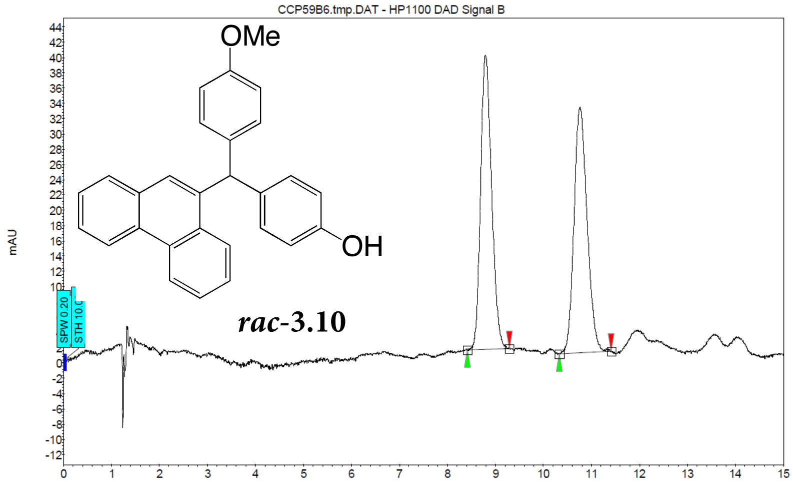


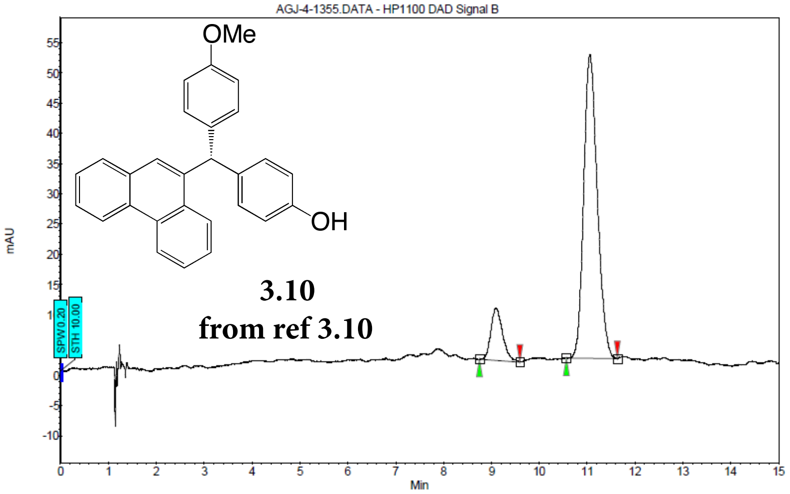


Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	12.03	12.64	12.97	0.00	12.98	19.4	7.6	12.978
2	UNKNOWN	12.97	13.37	14.14	0.00	87.02	123.8	51.0	87.022
Total						100.00	143.1	58.7	100.000

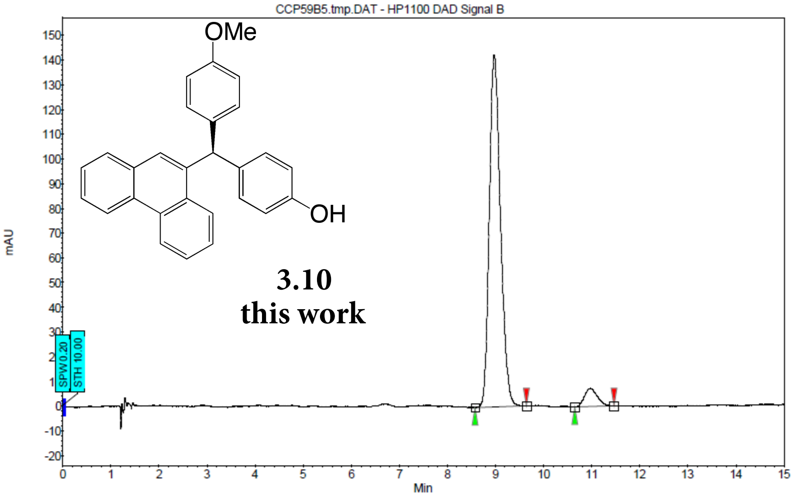


Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	12.01	12.50	13.05	0.00	94.82	88.3	34.9	94.824
2	UNKNOWN	13.05	13.32	13.73	0.00	5.18	5.6	1.9	5.176
Total						100.00	93.9	36.8	100.000





Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	8.75	9.09	9.60	0.00	13.00	8.7	2.5	12.997
2	UNKNOWN	10.57	11.06	11.63	0.00	87.00	50.2	16.5	87.003
Total						100.00	58.9	18.9	100.000



Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	8.58	8.98	9.65	0.00	94.42	142.5	38.3	94.421
2	UNKNOWN	10.65	10.98	11.47	0.00	5.58	7.4	2.3	5.579
Total						100.00	149.9	40.5	100.000