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Forming Quaternary Carbons Using Photoredox Catalysis and Applications in Total Synthesis

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Forming Quaternary Carbons Using Photoredox Catalysis

and Applications in Total Synthesis

DISSERTATION

Submitted in partial satisfaction of the requirements
for the degree of

DOCTOR OF PHILOSOPHY

in Chemistry

by

Gregory Lawrence Lackner

Dissertation Committee:
Prof. Larry E. Overman, Chair
Prof. Christopher D. Vanderwal
Prof. James S. Nowick

2016

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5. **Enantioselective Total Syntheses of *trans*-Clerodane Diterpenoids: Convergent Fragment Coupling Using a *trans*-Decalin Tertiary Radical Generated from a Tertiary Alcohol Precursor.** Slutskyy, Y.; Jamison, C. R.; Lackner, G. L.; Müller D. S.; Dieskau, A. P.; Unteidt, N. L.; Overman, L. E. *J. Org. Chem.* **2016**. *Accepted for publication.*

4. **Constructing Quaternary Carbons from *N*-(Acyloxy)phthalimide Precursors of Tertiary Radicals Using Visible-Light Photocatalysis**. Pratsch, G.; Lackner, G. L.; Overman, L. E. *J. Org. Chem.* **2015**, *80*, 6025–6036.

3. **Fragment Coupling and the Construction of Quaternary Carbons Using Tertiary Radicals Generated From *tert*-Alkyl N-Phthalimidoyl Oxalates By Visible-Light Photocatalysis**. Lackner, G. L.; Quasdorf, K. W.; Pratsch, G.; Overman, L. E. *J. Org. Chem.* **2015**, *80*, 6012–6024.

2. **Constructing Quaternary Stereogenic Centers Using Tertiary Organocuprates and Tertiary Radicals. Total Synthesis of trans-Clerodane Natural Products.** Müller, D. S.; Untiedt, N. L.; Dieskau, A. P.; Lackner, G. L.; Overman, L. E. *J. Am. Chem. Soc.* **2015**, *137*, 660–663.

1. **Direct Construction of Quaternary Carbons from Tertiary Alcohols via Photoredox-Catalyzed Fragmentation of *tert*-Alkyl *N*-Phthalimidoyl Oxalates.** Lackner,G. L.; Quasdorf, K. W.; Overman, L. E. *J. Am. Chem. Soc.* **2013,** *135*, 15342–15345.

Abstract of The Dissertation

Forming Quaternary Carbons Using Photoredox Catalysis

and Applications in Total Synthesis

by

Gregory Lawrence Lackner

Doctor of Philosophy in Chemistry

University of California, Irvine, 2016

Professor Larry E. Overman, Chair

In Chapter 1, the development of *tert*-alkyl *N*-phthalimidoyl oxalates as precursors for generating tertiary carbon radicals and forming quaternary carbons is discussed. The coupling of these radical precursors with conjugate acceptors is determined to be farily general with respect to both oxalate and alkene coupling partners. Studies that elucidate the mechanism of the coupling reaction are also presented. The mechanism of radical termination is found to be directly influenced by the stoichiometric reductant additive included in the reaction.

In Chapter 2, a bimolecular radical fragment coupling is employed as a key step to complete the total syntheses of several *trans*-clerodane diterpenoid natural products as well as one *ent*-halimane diterpenoid natural product. In this context, the tertiary radical is optimally generated from an (*N*-acyloxy)phthalimide substrate rather than the corresponding *tert*-alkyl *N*-phthalimidoyl oxalate.

In Chapter 3, a photoredox-catalyzed radical coupling is used to stereoselectively construct the central C8–C14 bond of the rearranged spongian diterpene macfarlandin C.

An allylic phosphate displacement and intramolecular carbonyl-ene cyclization enable a robust enantioselective synthesis of the decalin fragment. The unexpected intramolecular cyclization of an alkoxycarbonyl radical derived from the (8*S*)-oxalate prompts a revised synthetic approach targeting the (8*R*)-oxalate radical precursor, which couples efficiently with (*S*)-5-methoxyfuran-2-one. Two synthetic routes to the bicyclic lactone moiety of macfarlandin C are investigated on a simple model substrate. These attempts are ultimately foiled by the difficulty in forming a *cis*-alpha, beta-disubstituted butyrolactone that bears a quaternary substituent at the beta-position.

Chapter 1: Forming Quaternary Carbons From Tertiary Alcohol and Tertiary Carboxylic Acid Derivatives Using Photoredox Catalysis

1.1 Introduction

Despite the remarkable evolution of chemical synthesis over the past nearly two centuries, the preparation of organic molecules containing quaternary carbons is still a considerable challenge.[1] These structural motifs are particularly difficult to access in the simplest sense because of the steric repulsion imposed by the substituents often present on the precursor carbon atom. The synthesis of chiral quaternary carbons poses an especially formidable challenge; thus, reliable and straightforward chemical methods to construct quaternary carbon stereocenters are especially valuable.

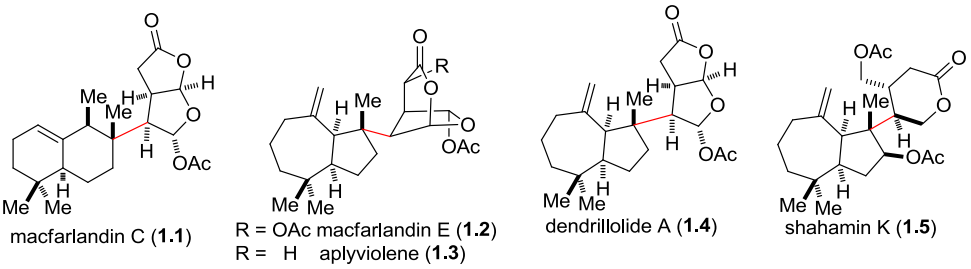
One useful metric of this particular challenge is the infrequency with which quaternary carbons have been incorporated into drugs. Of the top 200 prescription drugs sold in the US in 2011, only 12% contain quaternary carbons.[2] Furthermore, those that do exhibit quaternary carbons are almost certainly prepared by semisynthesis from opioid, steroid, or taxane diterpenoid precursors. One should not interpret this statistic to mean that quaternary carbon-containing molecules do not make effective drugs, however. It has been suggested that both an abundance of sp^3 carbons as well as the presence of chiral carbons confers desirable properties to drug candidates and often correlates with success in clinical testing.[3]

A few chemical transformations have been routinely employed to synthesize molecules containing quaternary carbon centers. In particular, Diels–Alder reactions and alkylation of substituted enolates are among the reactions most frequently utilized for this

purpose.[1a] Many transition metal-catalyzed methods have also emerged in which the quaternary carbon precursor can act as either a nucleophile or an electrophile.[1a,b] Powerful though these reactions may be, each of these approaches suffers from the requirement of vicinal functionality to establish the quaternary carbon center. The most desirable strategy to access these structural motifs would be one in which a tertiary carbon with minimal functionality directly participates in a carbon-carbon bond-forming process to generate the quaternary carbon. A reaction of this type would enable a fundamentally simpler retrosynthetic disconnection in which molecules could be disconnected straightforwardly at a quaternary carbon center. This approach then would permit one to propose a retrosynthetic precursor that does not require redox manipulation or the incorporation of extraneous functionality to introduce the quaternary carbon.

Previous studies in total synthesis carried out in the Overman lab prompted the development of such reactions to more efficiently form quaternary carbons. Several members of the rearranged spongian diterpene family of natural products (Figure 1.1) were recently chosen as the targets of these total synthesis efforts.[4] Many members of this family exhibit unique biological properties that will be discussed in detail in Chapter 3. The rearranged spongian diterpenes in Figure 1.1 consist of a bicyclic hydrocarbon joined to an oxygenated ring system at a central sigma bond. In all of the depicted natural products, this bond joins a chiral quaternary carbon of one ring system to a tertiary stereocenter of the oxygenated fragment. One may note that this bond presents a particularly attractive retrosynthetic disconnection, as dissecting the molecules at this central bond gives rise to two precursors of relatively equal complexity, providing for a convergent synthetic approach. In spite of the appeal of this strategy, however, the

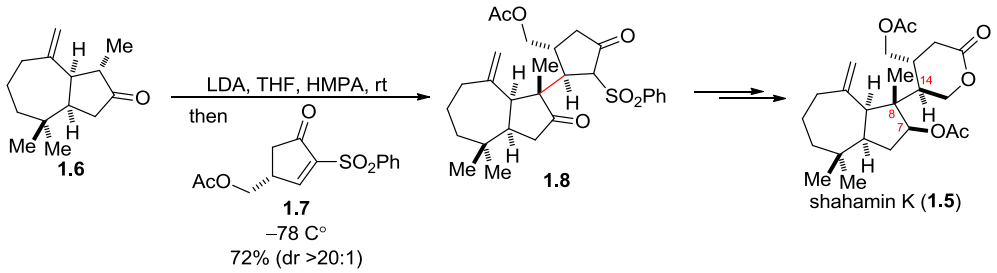
Figure 1.1 Representative rearranged spongian diterpene natural products



intermolecular coupling of two complex fragments and concomitant formation of the vicinal quaternary and tertiary stereocenters is a remarkably challenging task that can be accomplished by few chemical reactions. The evolution of the Overman group's approach to the total synthesis of aplyviolene (**1.3**) served to examine the current state of such bimolecular complex fragment couplings as well as to stimulate the development of more efficient methods for forming quaternary carbons in bimolecular coupling reactions.

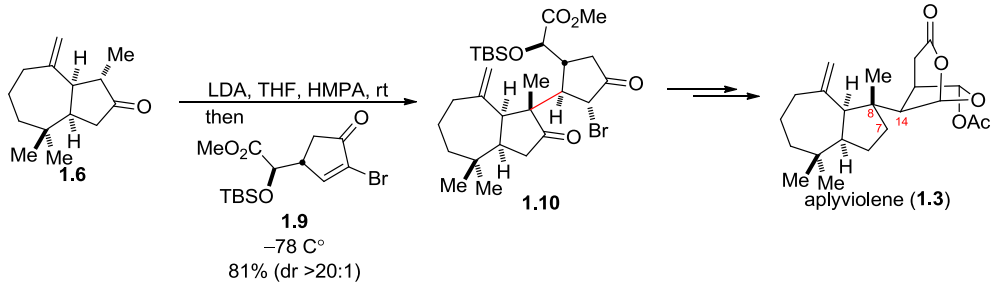
The first approach to the key central bond formation in the total synthesis of aplyviolene was based on a similar strategy utilized in the total synthesis of shahamin K (**1.5**) completed previously by the Overman group.[5] The construction of the C8–C14 bond of shahamin K was accomplished by Michael addition of the thermodynamic enolate of hydroazulenone **1.6** to conjugate acceptor **1.7** (Figure 1.2). The quaternary carbon stereocenter at C8 was formed diastereoselectively as a result of the approach of enone **1.7** from the less-hindered convex face of bicyclic hydroazulene **1.6**. This reaction provided a single adduct **1.8** which could then be processed to shahamin K over several steps.

Figure 1.2 Key Michael addition step in the total synthesis of shahamin K (1.5)



The first-generation total synthesis of aplyviolene (**1.3**) also employed the Michael addition of an enolate to forge the key central C8–C14 bond.[6] In the event, the same thermodynamic enolate generated from hydroazulenone **1.6** underwent diastereoselective addition to enone **1.9**, providing adduct **1.10** in 81% yield (Figure 1.3). A series of steps first developed on a simpler model system[7] successfully converted bromoketone **1.10** to aplyviolene (**1.3**).

Figure 1.3 First-generation Michael addition approach to aplyviolene (1.3)

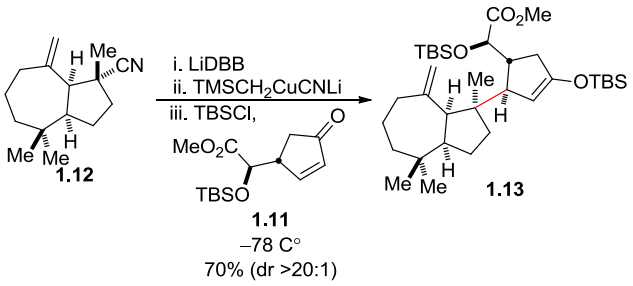


One noteworthy detail in this Michael addition approach to both shahamin K (**1.5**) and aplyviolene (**1.3**) is the eventual fate of the ketone functionality at C7 (aplyviolene and shahamin K numbering) that was necessary to construct the neighboring quaternary carbon. In the synthesis of shahamin K (**1.5**), this functional group is transformed into the acetoxy group present at this position in the natural product.[5] The synthesis of aplyviolene (**1.3**), however, required that this ketone be reductively removed over three

steps to access the unfunctionalized methylene carbon at C7.[6] This undesirable redox manipulation demonstrates that, although high-yielding and diastereoselective, the Michael addition strategy could potentially be revised to incorporate the hydroazulene unit in the correct oxidation state.

One possibility for the direct formation of the C8 quaternary carbon center by an intermolecular coupling was the generation of a tertiary organocuprate that would engage an enone such as **1.11** in a conjugate addition. Spurred by this prospect and the potential general utility of such bimolecular coupling reactions, the Overman group developed a method to access tertiary organocuprates by reductive lithiation of tertiary nitrile precursors followed by transmetalation to copper.[8] This strategy was then applied to the key fragment coupling step in the synthesis of aplyviolene (**1.3**). Surprisingly, the reductive lithiation of nitrile **1.12**, transmetalation to copper and conjugate addition to enone **1.11** resulted in an adduct that was epimeric to aplyviolene (**1.3**) at the newly formed C8 quaternary carbon (Equation 1.1). This result suggested that the intermediate organocuprate underwent addition to enone **1.11** from the more hindered concave face of the hydroazulene and not from the more accessible convex face as was expected. Computational rationalization for this observed diastereoselectivity suggested that the intermediate organocuprate reacted from the more hindered face in order to minimize torsional strain effects within the bicyclic hydroazulene framework.[8]

Equation 1.1

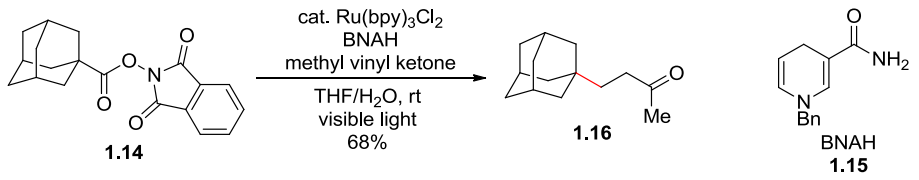


Another option for the direct and diastereoselective introduction of the hydroazulene unit was the addition of a tertiary radical intermediate to a conjugate acceptor.[9] The selection of an appropriate precursor for generating the tertiary radical was nontrivial, and several were initially considered. Although carbon radicals are commonly generated from alkyl halide precursors,[10] the general difficulties associated with synthesizing these substrates[11] advocated that a tertiary radical for use in this coupling might be more efficiently generated from a more stable tertiary carboxylic acid-derived precursor. The most commonly employed carboxylic acid-derived thiohydroxamate esters,[12] or "Barton esters" were initially considered for this purpose, as these intermediates have been widely used for several impressive radical carbon-carbon bond constructions in total synthesis for many years.[10] However, preliminary studies conducted by the Overman group suggested their instability to ambient light made them unfit for general application in complex fragment coupling scenarios.

More appealing was the coupling of a tertiary radical intermediate generated from an (*N*-acyloxy)phthalimide substrate. These carboxylic acid derivatives were first introduced for use in radical addition reactions by Okada in 1991, and were employed to generate primary, secondary and tertiary carbon radicals that coupled with electron-deficient olefins.[13] This transformation likely occurs via electron transfer from the

photocatalyst to the (*N*-acyloxy)phthalimide substrate such as **1.14** (Equation 1.2), promoting homolytic cleavage of the N–O bond and radical decarboxylation to generate the key tertiary radical intermediate. In this reaction, 1-benzyl-1,4-dihydronicotinamide (BNAH, **1.15**) is used as a stoichiometric reductant to facilitate catalyst turnover and termination of the radical addition process. Interestingly, the only example of a tertiary radical coupled in this way included in Okada's report was the 1-adamantanyl radical (Equation 1.2). Nevertheless, the mild photoredox catalysis conditions utilized in this transformation suggested that their use for the coupling of complex functionalized fragments in the context of the total synthesis of aplyviolene (**1.3**) might be successful.

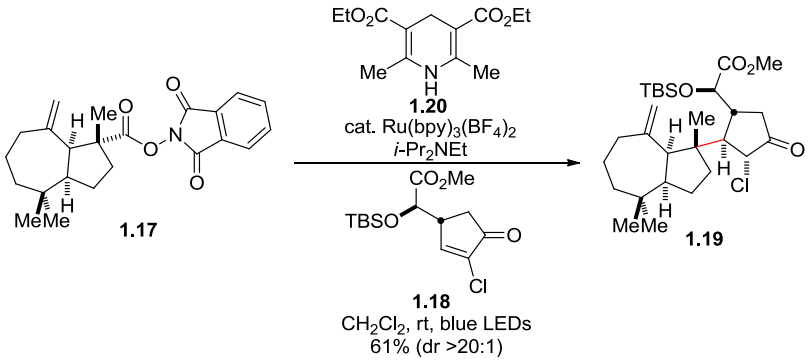
Equation 1.2



The pivotal fragment coupling reaction en route to the total synthesis of aplyviolene (**1.3**) was then attempted using Okada's method for the generation and coupling of tertiary radicals. Subjection of hydroazulene (*N*-acyloxy)phthalimide **1.17** to reductive photoredox catalysis conditions efficiently induced radical coupling with chloroenone **1.18**, giving the desired adduct **1.19** in 61% yield (Equation 1.3). Slightly modified reaction conditions first used by Gagné for the reductive generation of radicals from glucosyl halides were found to be optimial in this transformation.[14] Analysis of the stereochemical outcome of this coupling revealed that addition to the enone acceptor **1.18** had occurred from the less-hindered convex face as was desired. Thus, the diastereoselectivity realized in the course of this radical coupling was complementary to

that previously observed in the case of the analogous tertiary organocuprate and facilitated a second-generation formal synthesis of aplyviolene.

Equation 1.3



The success of Okada's method in stereoselectively coupling highly functionalized structural fragments hinted that this method for forming quaternary carbons may hold considerable untapped potential. Although this approach has been curiously omitted from a recent survey of methods to construct quaternary carbons,[1b] the general use of tertiary radicals to form these structural motifs has several notable advantages. First, the addition of carbon radicals to olefins is calculated to occur with an early transition state, which contributes to a long forming bond (ca. 2.2–2.5 Å) in this transition state, suggesting that these bond formations can succeed in highly hindered steric environments. Tertiary radicals are also known to add to alkenes with higher diastereoselectivity than primary or secondary radicals, advocating their use in the diastereoselective formation of quaternary carbons.[15] Finally, the three alkyl substituents of a tertiary radical confer a "nucleophilic" character to this radical by hyperconjugative donation of electron density. This effect contributes to a higher SOMO and a higher rate of addition of the tertiary radical to electron-deficient olefins than primary and secondary radicals. Despite these attractive features, the adoption of tertiary radicals as useful

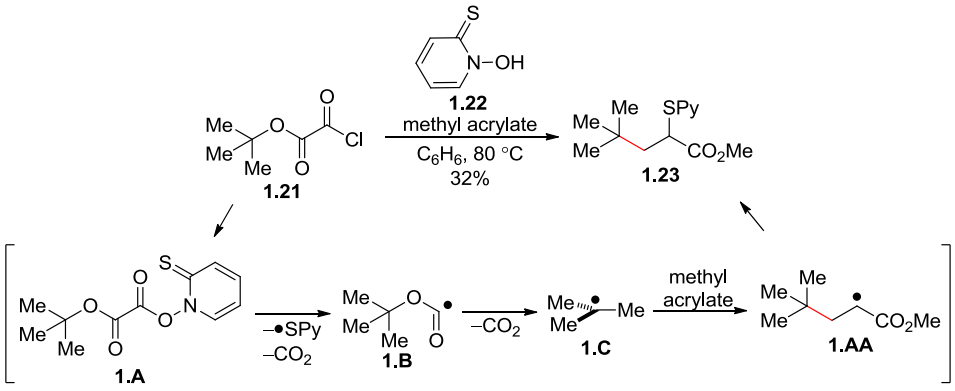
intermediates for forming quaternary carbons has been stagnant, likely because of the lack of convenient precursors and conditions for generating tertiary carbon radicals.

The Overman group's implementation of Okada's radical coupling method to the total synthesis of aplyviolene (**1.3**) established that tertiary (*N*-acyloxy)phthalimide substrates are robust precursors for forming quaternary carbons. One potentially unattractive aspect of the general use of these substrates in total synthesis, however, is that a structural carbon-carbon bond must be incorporated into the substrate only to be subsequently cleaved in the generation of the tertiary radical intermediate. Thus, a quaternary carbon must already be present in the substrate in order to form the desired quaternary carbon in the intermolecular coupling. This requirement can in some cases add several steps to a synthetic route, often requiring cumbersome manipulation of highly hindered tertiary functional groups.[16] A potential improvement to Okada's method envisioned by the Overman group was to utilize instead a radical precursor derived from a tertiary alcohol. Tertiary alcohols are easily constructed by the addition of carbon nucleophiles to ketone substrates, and as a result would be more accessible than the carboxylic acid derivatives employed in Okada's study.

The most common alcohol-derived precursors of carbon radicals are xanthate esters.[17,10b] These substrates have been most widely used to perform deoxygenations of secondary alcohols, however, as tertiary xanthate esters are more prone to elimination. Alternatively, a series of publications by Barton detail the generation of radicals from thiohydroxamate oxalate derivatives of alcohols (Figure 1.4).[18] Much like the analogous thiohydroxamate esters, alkyl radicals are generated by photolysis or thermolysis of these acyloxythiopyridone derivatives **1.A**, promoting homolytic N–O bond cleavage and

decarboxylation. In reactions of thiohydroxamate oxalates, however, generation of the alkyl radical proceeds after two decarboxylation events that occur in a stepwise manner (Figure 1.4). This important distinction provides access to alkyl radicals from alcohols by direct activation of the C–O bond via a decarboxylation process.

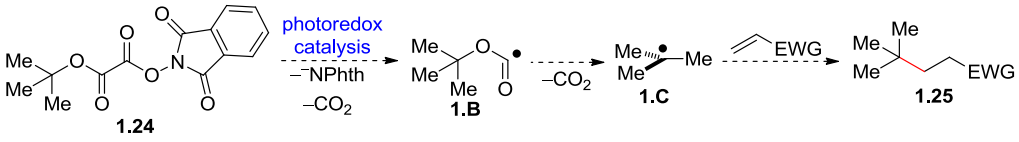
Figure 1.4 Formation of a quaternary carbon from a thiohydroxamate oxalate



Barton's report described the addition of several carbon radicals to electron-deficient olefins by this method; however, the yields of coupling products obtained were disappointingly low. One possible explanation for the inefficiency of these couplings could be the instability of the radical precursor, as the thiohydroxamate oxalates **1.A** must be generated *in situ* during the course of the reaction and presumably cannot be isolated. This characteristic is in stark contrast to the properties of the previously discussed (*N*-acyloxyphthalimides, which are stable to chromatography, ambient light, and prolonged storage at room temperature. Additionally, these phthalimide derivatives are typically crystalline solids that are easily handled. It was reasoned these desirable attributes might be conferred to an alcohol derivative similar to **1.A** by simple replacement of the thiohydroxypyridine moiety by an *N*-hydroxyphthalimide unit. These previously unreported alkyl *N*-phthalimidoyl oxalate substrates could then ideally provide access to

carbon radicals under the same mild photoredox catalysis conditions used to generate radicals from the analogous (*N*-acyloxy)phthalimides such as **1.14**. It was envisioned that formation of the tertiary radical from a phthalimidoyl oxalate should occur in the same manner as observed for the thiohydroxamate oxalates by two decarboxylation steps proceeding through an alkoxycarbonyl intermediate (Figure 1.5). The successful coupling of tertiary radicals generated from alkyl phthalimidoyl oxalates with conjugate acceptors was anticipated to provide a useful method for synthesizing quaternary carbons in a straightforward and synthetically convenient fashion.

Figure 1.5 Proposed reactivity of an alkyl *N*-phthalimidoyl oxalate



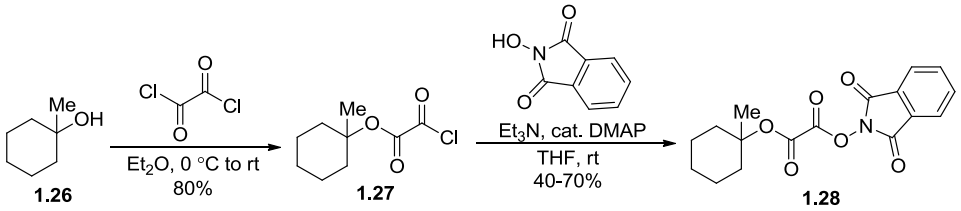
1.2 Results and Discussion

1.2.1 Synthesis of Tertiary Alkyl *N*-Phthalimidoyl Oxalates

The preparation of alkyl phthalimidoyl oxalate radical precursors from their corresponding alcohols was first investigated using 1-methylcyclohexanol (**1.26**) as a simple tertiary alcohol substrate. Since Barton had shown that chlorooxalate esters such as **1.21** could be reliably formed by treatment of the alcohol with oxalyl chloride, it was supposed that incorporation of the phthalimide moiety via this intermediate might be successful. Accordingly, exposure of 1-methylcyclohexanol (**1.26**) to a slight excess of oxalyl chloride in Et_2O at 0 °C, followed by warming to room temperature overnight, afforded chlorooxalate **1.27** in 80% yield (Scheme 1.1). The chlorooxalate was isolated by simply removing the solvent, excess oxalyl chloride, and any remaining traces of

hydrogen chloride under reduced pressure. Introduction of the phthalimidoyl moiety at this stage proved to be significantly challenging owing to the lability of the oxalate products **1.28**. The most effective conditions for this process were found to be addition of chlorooxalate **1.27** to a solution of *N*-hydroxyphthalimide, Et_3N, and DMAP in THF at room temperature for 1 h.

Scheme 1.1 Two-step synthesis of alkyl phthalimidoyl oxalates from tertiary alcohols.

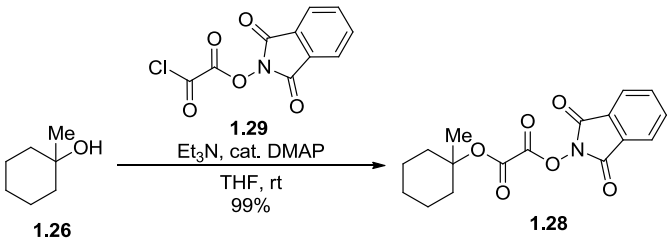


While purification of the crude products by silica gel chromatography was unsuccessful, an aqueous extraction procedure could be employed to obtain the oxalates in high purity. Washing a dilute solution of oxalate **1.28** in Et_2O with aqueous saturated $NaHCO_3$ was required to remove *N*-hydroxyphthalimide from the product mixture, but provided **1.28** in variable yields (Scheme 1.1). Resubjection of pure **1.28** to this purification procedure resulted in substantial cleavage of the phthalimidoyl moiety, confirming the workup as the cause of the inconsistent yields. Although small amounts of **1.28** could be synthesized by this method for use in initial studies, the method was not effective when applied to many other tertiary alcohols and provoked elimination upon acylation of many of the alcohol substrates. A more efficient and general synthesis of the desired radical precursors was then pursued.

The second strategy examined for synthesizing *tert*-alkyl phthalimidoyl oxalates from tertiary alcohols was the direct acylation of a tertiary alcohol substrate with *N*-phthalimidoyl chlorooxalate **1.29**. After careful optimization, a reliable method was

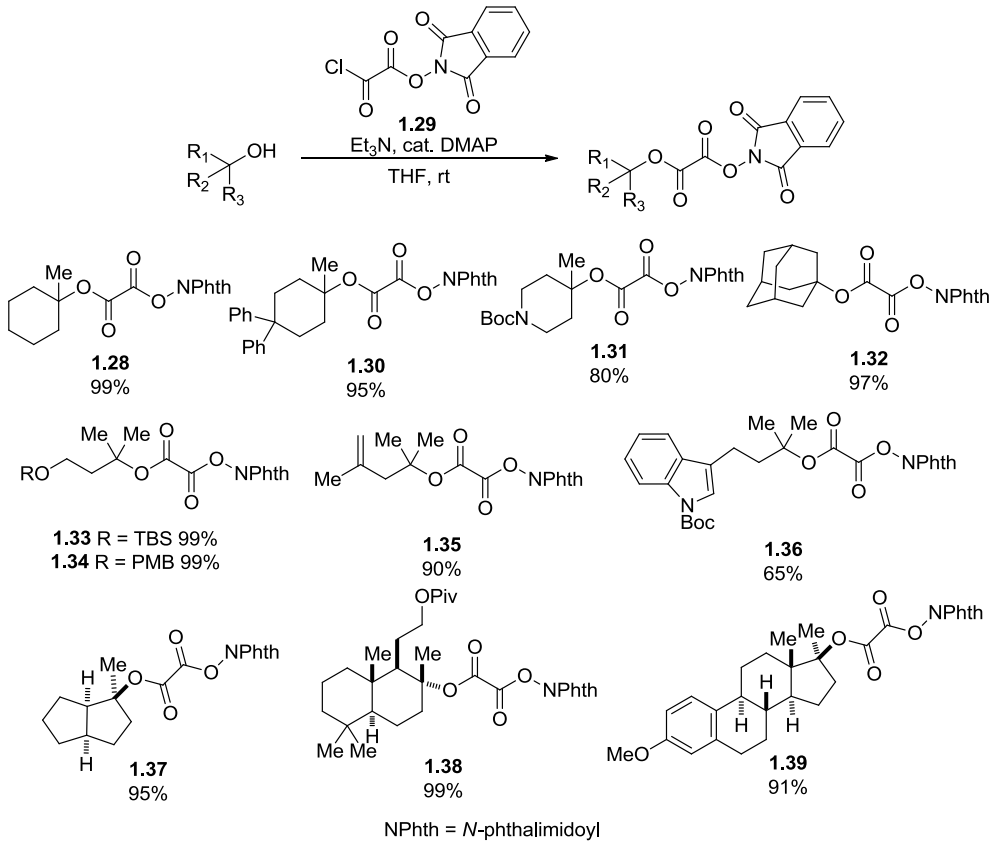
developed to prepare chlorooxalate **1.29** from *N*-hydroxyphthalimide and a large excess of oxalyl chloride by stirring in THF from –78 °C to room temperature overnight.[19] Chlorooxalate **1.29** was then obtained as a colorless solid by concentration of the reaction mixture. This reactive acylating reagent was then most easily manipulated under argon as a 0.06 M solution in THF. The acylation of 1-methylcyclohexanol (**1.26**) proceeded efficiently using two equivalents of chlorooxalate **1.29** in THF in the presence Et_3N and DMAP (Equation 1.4). Phthalimidoyl oxalate **1.28** was purified in this case according to a procedure developed by Dr. Kyle Quasdorf in which the crude product mixture was dissolved in a minimal amount of CH_2Cl_2 and then poured into a large volume of hexanes. This produced a brown suspension that could be filtered through cotton, providing a colorless filtrate solution, which was concentrated to give the phthalimidoyl oxalate **1.28** in quantitative yield and high purity.

Equation 1.4



The preparation of phthalimidoyl oxalate intermediates from tertiary alcohol substrates by this procedure was successfully applied to a variety of structurally diverse tertiary alcohols (Figure 1.6).[20] With most simple substrates, the acylation proceeded to completion in one hour. When significantly hindered tertiary alcohols were employed,

Figure 1.6 Synthesis of alkyl phthalimidoyl oxalates



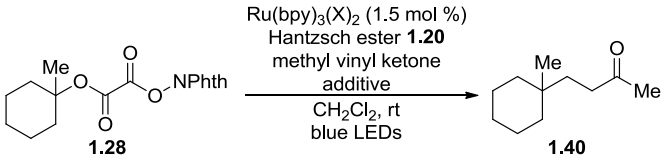
however, the reaction required up to 24 hours. The purification method developed by Dr. Quasdorf was remarkably effective for nearly all oxalates synthesized in this fashion. Oxalates **1.31** and **1.36** which bear nitrogen-based functional groups were isolated in somewhat lower yields, presumably owing to the lack of solubility of these compounds in CH_2Cl_2/hexanes. Most solid oxalates prepared in this way could be stored indefinitely at –20 °C, while those that are oils could typically be stored at this temperature for about one week before decomposition. The structure of these previously unknown esters was confirmed by X-ray single crystal analysis of oxalate **1.32**.[19]

1.2.2 Optimization of the Photoredox-Catalyzed Radical Coupling

With a robust method for preparing alkyl phthalimidoyl oxalates in hand, the photoredox-catalyzed coupling of these intermediates with electron-deficient alkenes was next explored (Table 1.1). For the initial optimization of the photoredox reaction, oxalate **1.28** and methyl vinyl ketone were employed as coupling partners. The first conditions examined in the transformation were those that are typically used for coupling of the related (*N*-acyloxy)phthalimide substrates. Encouragingly, exposure of oxalate **1.28** and methyl vinyl ketone (MVK) to 1.5 mol % $Ru(bpy)_3(BF_4)_2$, Hantzsch dihydropyridine **1.20** and *i*-Pr_2NEt in dichloromethane at room temperature under irradiation with blue LEDs produced adduct **1.40** in 16% yield (entry 1). It was observed that the addition of *i*-Pr_2NEt to the reaction mixture (prior to the addition of the photocatalyst) produced a bright red color, suggesting that it directly interacts with one of the reaction components. After carrying out several control experiments to establish the nature of this reactivity, it was confirmed that this amine rapidly decomposes the substrate oxalate to liberate the red conjugate base of *N*-hydroxyphthalimide. The omission of *i*-Pr_2NEt in the photoredox coupling reaction gave a small increase in yield (entry 2). Including *i*-$Pr_2NEt{\bullet}HBF_4$, an additive that was examined in a related study by Gagné,[14] resulted in a slight improvement to the yield and reproducibility of the reaction (entry 3).[21] A survey of the relative equivalents of the coupling partners employed in the reaction (entries 4–6) revealed that a substantially higher yield of **1.40** could be achieved when the oxalate component was present in slight excess (entry 6). Final optimization of the reaction parameters established that only one equivalent of the ammonium additive was required (entries 8 and 10) and that the use of THF/CH_2Cl_2 as a solvent resulted in a significant

improvement in the yield of **1.40**.[22] Conveniently, the commercially available $Ru(bpy)_3(PF_6)_2$ catalyst performed equally well as $Ru(bpy)_3(BF_4)_2$. Under the optimized reaction conditions, oxalate **1.28** coupled with MVK to give adduct **1.40** in 82% isolated yield (entry 9).

Table 1.1 Optimization of photoredox coupling of 1.28 with MVK



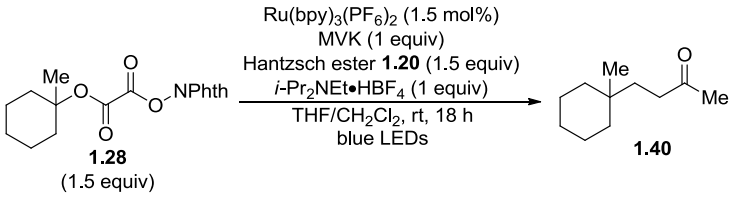
entry	equiv **1.28**	equiv MVK	equiv **1.20**	additive	solvent	X	yield **1.40** (%)
1	1.0	1.5	1.0	*i*-Pr_2NEt^a	CH_2Cl_2	BF_4	19[b]
2	1.0	1.5	1.0	–	CH_2Cl_2	BF_4	36[b]
3	1.0	1.5	1.0	*i*-$Pr_2NEt•HBF_4$[a]	CH_2Cl_2	BF_4	40[b]
4	1.0	5.0	1.0	*i*-$Pr_2NEt•HBF_4$[a]	CH_2Cl_2	BF_4	22[b]
5	1.0	1.0	1.0	*i*-$Pr_2NEt•HBF_4$[a]	CH_2Cl_2	BF_4	56[b]
6	1.5	1.0	1.5	*i*-$Pr_2NEt•HBF_4$[a]	CH_2Cl_2	BF_4	77[b]
7	1.5	1.0	1.5	*i*-$Pr_2NEt•HBF_4$[c]	CH_2Cl_2	BF_4	82[b]
8	1.5	1.0	1.5	*i*-$Pr_2NEt•HBF_4$[c]	THF/ CH_2Cl_2	BF_4	92[b]
9	1.5	1.0	1.5	*i*-$Pr_2NEt•HBF_4$[c]	THF/ CH_2Cl_2	PF_6	92[b], 82[d]
10	1.5	1.0	1.5	–	THF/ CH_2Cl_2	PF_6	65[b]

[a]2.2 equivalents were used. [b]Yield measured by ^1H NMR relative to an internal standard (1,4-dimethoxybenzene). [c]1.0 equivalent was used. [d]Isolated yield.

A series of control reactions was then performed to evaluate the necessity of each reaction component (Table 1.2). Although the coupling reactions were initially carried out for 18 hours because the oxalate substrates were not amenable to TLC analysis, the yield of **1.40** was nearly identical when the reaction was run for only 2 hours (entries 1 and 2). Visible light proved to be essential for reactivity, as no conversion of oxalate **1.28** was observed when the reaction was conducted in the dark (entry 3). Omission of Hantzsch ester **1.20** gave a similar outcome, resulting in complete recovery of **1.28**. Interestingly, significant product formation in the absence of the photocatalyst was

observed (entries 5 and 6). This background reaction was notably slower than the photocatalyzed reaction, producing **1.40** in only 28% yield after 2 hours, although the yield was markedly higher after a reaction time of 18 hours. This reactivity was attributed to being mediated by Hantzsch ester **1.20**, as Okada and co-workers had made a similar observation in their initial studies using a related dihydropyridine.[13] Omitting the ammonium additive resulted in a somewhat depressed yield of **1.40** (entry 7). Finally, revisiting the stoichiometry of coupling substrates in the reaction (entries 8–10) confirmed that the highest yield of **1.40** was obtained when oxalate **1.20** was present in slight excess.

Table 1.2 Control experiments for photoredox coupling

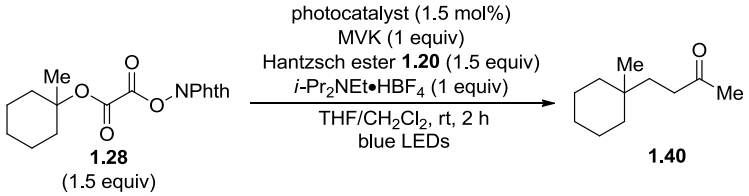


entry	modification	yield of **1.40** (%)[a]
1	--	82
2	reaction time of 2 h	81
3	no light	<5%
4	no Hantzsch ester **1.20**	ND
5	no photocatalyst (2 h)	28
6	no photocatalyst (18 h)	67
7	no *i*-Pr_2NEt•HBF_4	72
8	oxalate **1.28** (1 equiv)	67
9	oxalate **1.28** (1.1 equiv)	68
10	oxalate **1.28** (1 equiv) MVK (1.5 equiv)	57

[a]Isolated yield. ND = not detected.

Several other photoredox catalysts were examined to promote the formation of adduct **1.40** from phthalimidoyl oxalate **1.28** and MVK (Table 1.3). Although no catalyst performed as well as $Ru(bpy)_3^{2+}$ (entry 1), many strongly reducing iridium photoredox catalysts were nearly as effective (entries 2–4).[23] Even $Ru(bpz)_3^{+}$ ($E_{1/2}^{II/I}$ –0.80 V vs SCE),[24] a significantly weaker reductant than $Ru(bpy)_3^{+}$ ($E_{1/2}^{II/I}$ –1.33 V vs SCE), gave a 62% yield (by NMR analysis) of ketone **1.40** (entry 5).

Table 1.3 Coupling of oxalate 1.28 and MVK with various photoredox catalysts



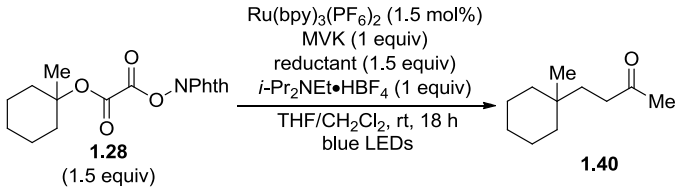
entry	photocatalyst	yield of **1.40** (%)[a]
1	$Ru(bpy)_3(BF_4)_2$	82
2	$Ir(ppy)_3$	75
3	$Ir(dF(CF_3)ppy)_2(dtbbpy)(PF)_6$	74
4	$Ir(dtbbpy)(ppy)_2(PF_6)$	76
5	$Ru(bpz)_3(PF_6)_2$	62

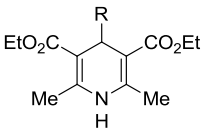
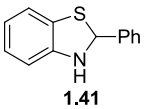
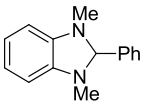
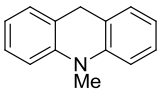
[a]Yield measured by ^1H NMR relative to an internal standard (1,4-dimethoxybenzene).

The replacement of Hantzsch ester **1.20** with several other potential stoichiometric reductants (Table 1.4) was also investigated. Introduction of a substituent at the 4-position of the Hantzsch ester rendered the dihydropyridine unreactive under the reaction conditions (entries 2 and 3). The use of 2-phenylbenzothiazoline (**1.41**)[25] or *N*,*N'*-dimethyl-2-phenylbenzimidazoline (**1.42**)[26] resulted in the formation of product **1.40**, although the yield was somewhat less than that observed under identical conditions

using Hantzsch ester **1.20** (entries 4 and 5). No conversion to adduct **1.40** was observed using *N*-methylacridane (**1.43**), a known reductive quencher of $Ru(bpy)_3^{2+*}$ (entry 6).[27]

Table 1.4 Coupling of oxalate 1.28 and MVK with various reductants



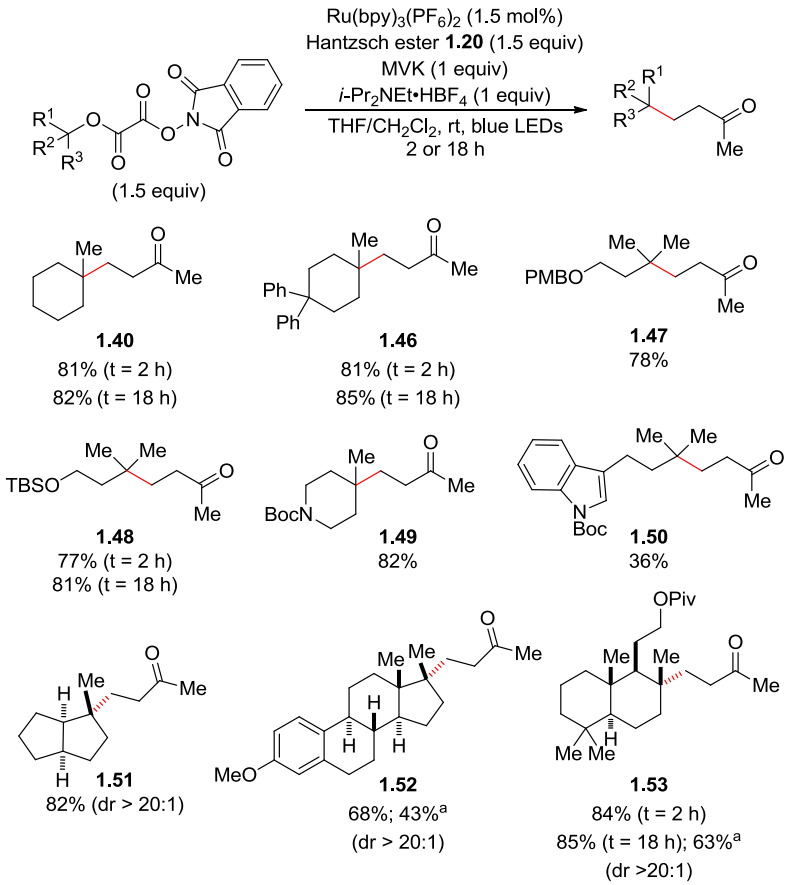
entry	reductant		yield of **1.40** (%)
1		**1.20** R = H	82[a]
2		**1.44** R = Me	ND
3		**1.45** R = Ph	ND
4	 **1.41**		60[b]
5	 **1.42**		73[b]
6	 **1.43**		ND

[a]Isolated yield. [b]Yield measured by ^{1}H NMR relative to an internal standard (1,4-dimethoxybenzene). ND = not detected.

1.2.3 Examining the Scope of the Coupling Reaction

The scope of the photoredox coupling reaction with respect to the oxalate coupling partner was then explored (Figure 1.7). A wide variety of *N*-phthalimidoyl oxalate substrates were tolerated in the transformation, which generally gave good yields of the coupled products. Oxalates derived from both cyclic and linear tertiary alcohols coupled readily with MVK, providing the radical addition products in approximately 80%

Figure 1.7 Coupling of various oxalates with MVK



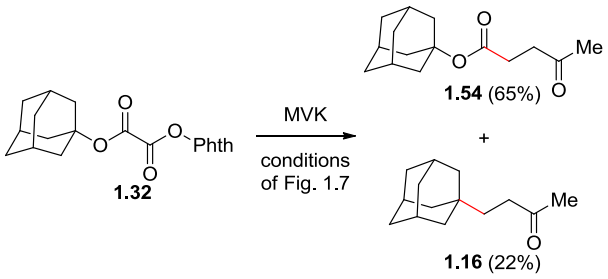
[a]A 1:1 ratio of oxalate:MVK was used.

yield for most substrates. Various common alcohol and amine protecting groups were unaffected by the mild reaction conditions, as demonstrated by the efficient formation of **1.47**, **1.48** and **1.49**. The coupling of an indole-containing oxalate with MVK was less successful, forming **1.50** in only 36% yield. Three chiral *N*-phthalimidoyl oxalates that were examined coupled with MVK from the less-sterically hindered face of the tertiary radical to give products **1.51**, **1.52** and **1.53** with >20:1 diastereoselection. Adducts **1.51** and **1.53** were formed in >80% yield. The yield was somewhat lower in the construction of a quaternary center at C17 in the estrone series (**1.52**, 68%), likely reflecting the demand in forming vicinal quaternary carbon centers. As was observed during

exploratory studies, yields were somewhat lower when equal amounts of the phthalimidoyl oxalate and alkene were employed: 43% vs 68% in forming **1.52** and 63% vs 85% in forming **1.53**. In a number of the coupling reactions summarized in Figure 1.7, the yield was nearly the same when *i*-$Pr_2NEt•HBF_4$ was omitted. Nonetheless, the product yields were more reproducible when this additive is present.

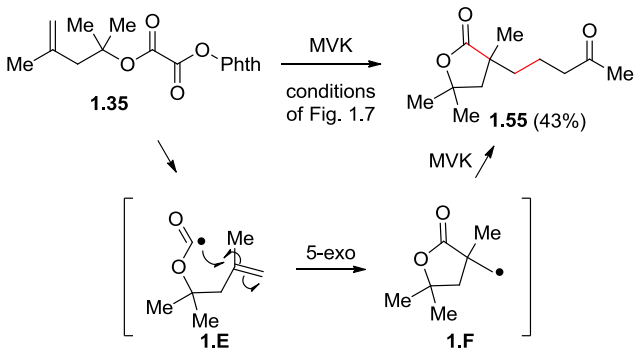
In two cases, the alkoxycarbonyl radical (intermediate **1.B**, Figure 1.4) was trapped by the radical acceptor more rapidly than it underwent decarboxylation to generate the tertiary radical intermediate. Adamantyl phthalimidoyl oxalate (**1.32**) when coupled with MVK gave γ-ketoester **1.54** and the product **1.16** of trapping the adamantyl radical in a 3:1 ratio (Equation 1.5). It is well known that alkoxycarbonyl radicals decarboxylate many orders of magnitude more slowly than carboxy radicals,[28,29] with the activation barrier decreasing with the stability of the carbon radical produced.[30] Trapping of the adamantyl oxycarbonyl radical by MVK to give **1.54** as the major product is a reflection of the higher energy of the non-planar tertiary adamantyl radical than the tertiary radicals generated in the reactions reported in Figure 1.7.

Equation 1.5



In the example illustrated in Scheme 1.2, it is the high rate of 5-exo radical cyclizations (**1.E** → **1.F**) that results in capture of the intermediate alkoxycarbonyl radical to yield lactone **1.55** from phthalimidoyl oxalate **1.35**.[31]

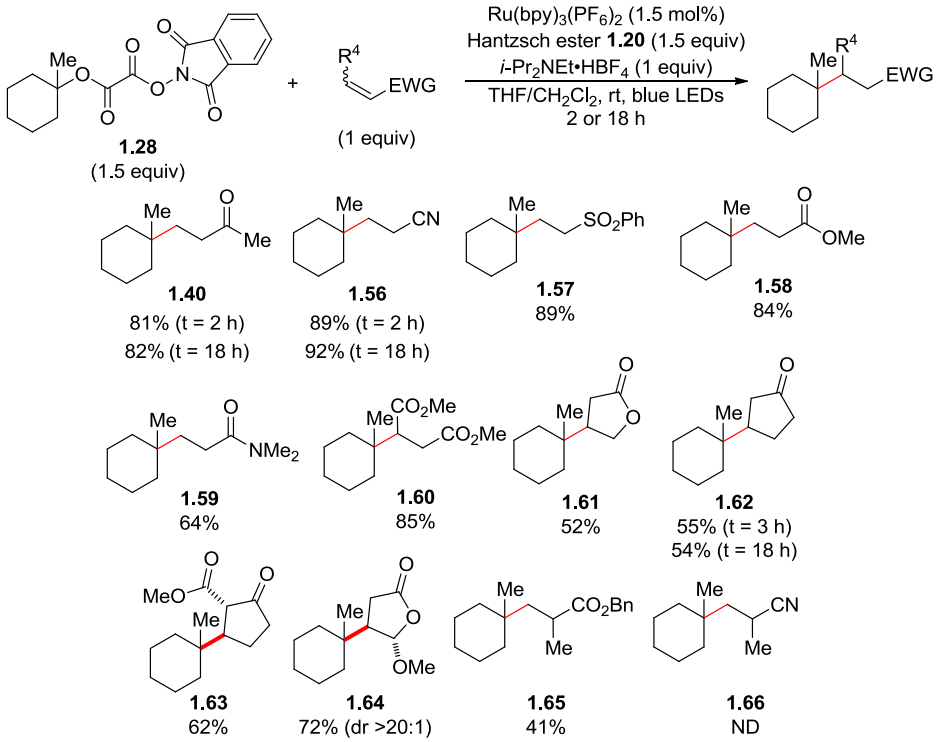
Scheme 1.2 Trapping of an alkoxycarbonyl radical by a 5-exo cyclization



The coupling of oxalate **1.28** with various conjugate acceptors was then surveyed (Figure 1.8). As expected, the highest yields were realized in the coupling reactions with terminal alkenes such as MVK, acrylonitrile and phenyl vinyl sulfone. Several radical acceptors having a substituent at the β-carbon also provided coupled products in good yields. Dimethyl fumarate gave adduct **1.60** in 85% yield, and cyclopenten-2-one coupled with *N*-phthalimidoyl oxalate **1.28** to give product **1.62** in 55% yield. The yield of adduct **1.63** resulting from the coupling of **1.28** with 2-carbomethoxycyclopenten-2-one (62%) was only slightly higher than that observed with cyclopenten-2-one.[32] Butenolides were also competent acceptors, with the presence of a γ-methoxy substituent enhancing the yield of the coupled product (72% for **1.64** vs 52% for **1.61**) and completely regulating face-stereoselectivity.

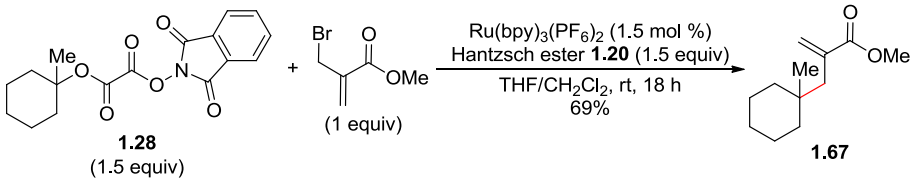
Unfortunately, radical addition to acceptors possessing electron-donating alkyl groups at the α-position was less successful under these conditions. The deactivated acceptor benzyl methacrylate coupled with **1.28** to provide **1.65** in only 41% yield. Product was not detected in the coupling of **1.28** with methacrylonitrile.[33]

Figure 1.8 Coupling oxalate 1.28 with various conjugate acceptors



Radical addition-fragmentation reactions using electron-deficient allylic halides or halomethyl styrenes as the olefin coupling components were subsequently examined by Dr. Gerald Pratsch. These reactions gave the products of formal allylation of the tertiary radical intermediate, as exemplified by the formation of **1.67** from the coupling of oxalate **1.28** and methyl bromomethacrylate (Equation 1.6).[34]

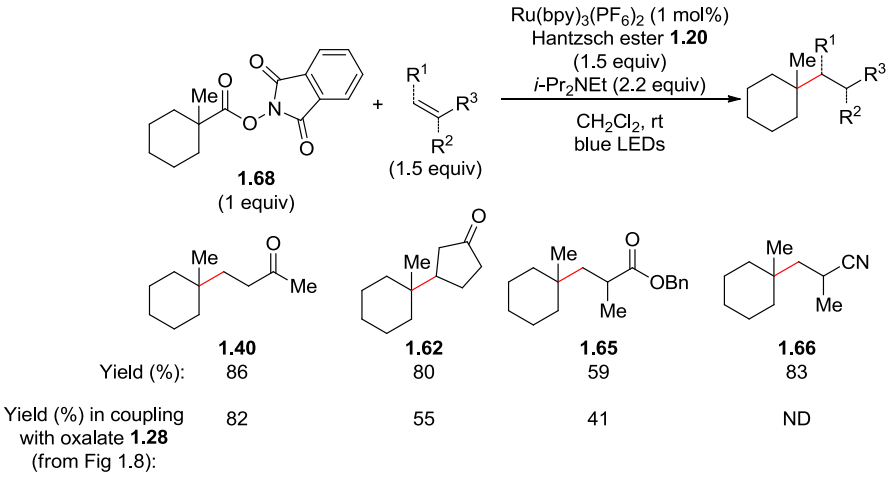
Equation 1.6



1.2.4 Comparing *N*-Phthalimidoyl Oxalate and (*N*-Acyloxy)phthalimide Radical Precursors

To compare the efficiency of the oxalate radical precursors to that of the related (*N*-acyloxy)phthalimides, the coupling of 1-methylcyclohexyl (*N*-acyloxy)phthalimide (**1.68**) with several alkene acceptors (Figure 1.9) was next investigated. To facilitate comparison, the yields obtained in the coupling of oxalate **1.28** with the respective conjugate acceptors from Figure 1.8 are reproduced below in Figure 1.9. Both radical precursors coupled efficiently with MVK, providing adduct **1.40** in over 80% yield. In the case of the remaining acceptors surveyed, however, (*N*-acyloxy)phthalimide **1.68** consistently coupled in higher yield than the corresponding oxalate **1.28**. The addition of

Figure 1.9 Coupling (*N*-acyloxy)phthalimide 1.68 and oxalate 1.28 with various alkenes



a tertiary radical generated from (*N*-acyloxy)phthalimide **1.68** to cyclopentenone and benzyl methacrylate occurred in 80% and 59% yield, respectively, while the analogous reactions of oxalate **1.28** took place in much lower yield. Remarkably, (*N*-acyloxy)phthalimide **1.68** coupled to methacrylonitrile in high yield; oxalate **1.28** gave no product in this transformation.

The consistently higher performance of the (*N*-acyloxy)phthalimide substrates in radical couplings relative to reactions of the oxalate substrates could result from several factors. First, reactions employing the oxalates require that an excess of the oxalate be used to account for decomposition of the substrate over the course of the reaction. The (*N*-acyloxy)phthalimides, by contrast, exhibit superior stability, and therefore the use of one equivalent of these substrates in a given reaction is sufficient to obtain high product yields. Additionally, using only one equivalent of the (*N*-acyloxy)phthalimide radical precursor enables an excess of the acceptor to be employed, which likely results in more efficient coupling of the tertiary radical that is generated in very low concentration.

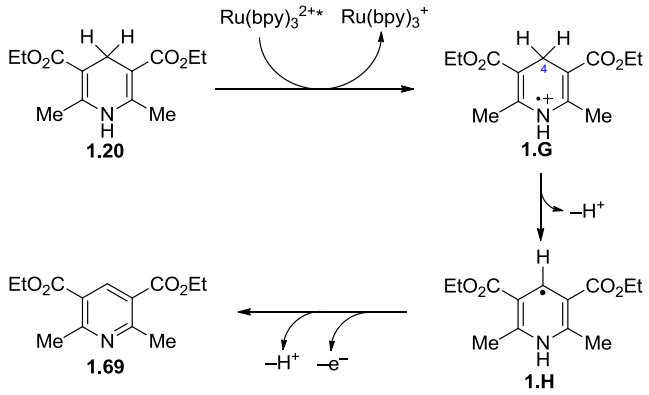
1.2.5 Investigating the Radical Coupling in the Absence of $Ru(bpy)_3^{2+}$.

As described previously, the observation of significant product formation in coupling reactions when $Ru(bpy)_3^{2+}$ was omitted was a surprising result (Table 1.2, entries 5 and 6). In accordance with Okada's proposed mechanism of the reactions of (*N*-acyloxy)phthalimides[13] and the requirement of a dihydropyridine or similar reductant for any reaction progress (Table 1.2, entry 4), it was rationalized that the observed reactivity in the absence of catalyst was mediated by this stoichiometric reductant.

Based on the known reactivity of Hantzsch esters, it was recognized that several possible dihydropyridine intermediates could be involved in single electron transfer to an *N*-phthalimidoyl oxalate substrate. The parent dihydropyridine **1.20** is a known reductive quencher of photoexcited $Ru(bpy)_3^{2+}$.[35] Single-electron oxidation of Hantzsch ester **1.20** by this process would generate radical cation **1.G** (Scheme 1.3). Deprotonation of **1.G** at C4 produces radical intermediate **1.H**, which is a strong one-electron reductant (–0.70 V

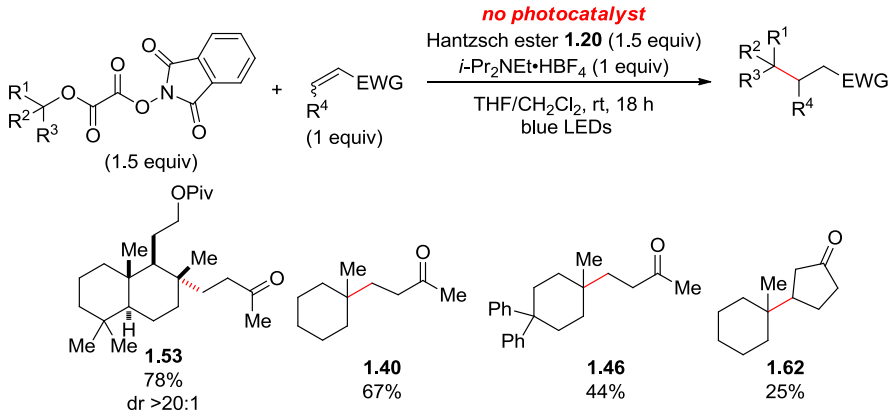
vs SCE).[36] Loss of one electron, followed by deprotonation of the resulting pyridinium intermediate, yields pyridine **1.69**, which is an isolable product of the coupling reactions reported in this account. When a photoredox catalyst is not present, oxidation of Hantzsch ester **1.20** by trace amounts of oxygen is likely responsible for the observed reactivity of *N*-phthalimidoyl oxalates.[37]

Scheme 1.3 Expected reactivity of Hantzsch dihydropyridine 1.20



To determine whether the coupling reaction in the absence of the photocatalyst could be a general method for promoting the desired reactivity, several radical couplings depicted in Figure 1.7 and Figure 1.8 were repeated with omission of the photocatalyst (Figure 1.10). Reasonable yields of products were obtained in the coupling of two oxalates with MVK (67% for **1.40** and 78% for **1.53**). However, the conversion of oxalate substrates to product was typically sluggish and inconsistent, and in two coupling reactions the yields of products obtained were significantly lower than in reactions employing a photocatalyst.

Figure 1.10 Radical coupling reactions in the absence of $Ru(bpy)_3^{2+}$

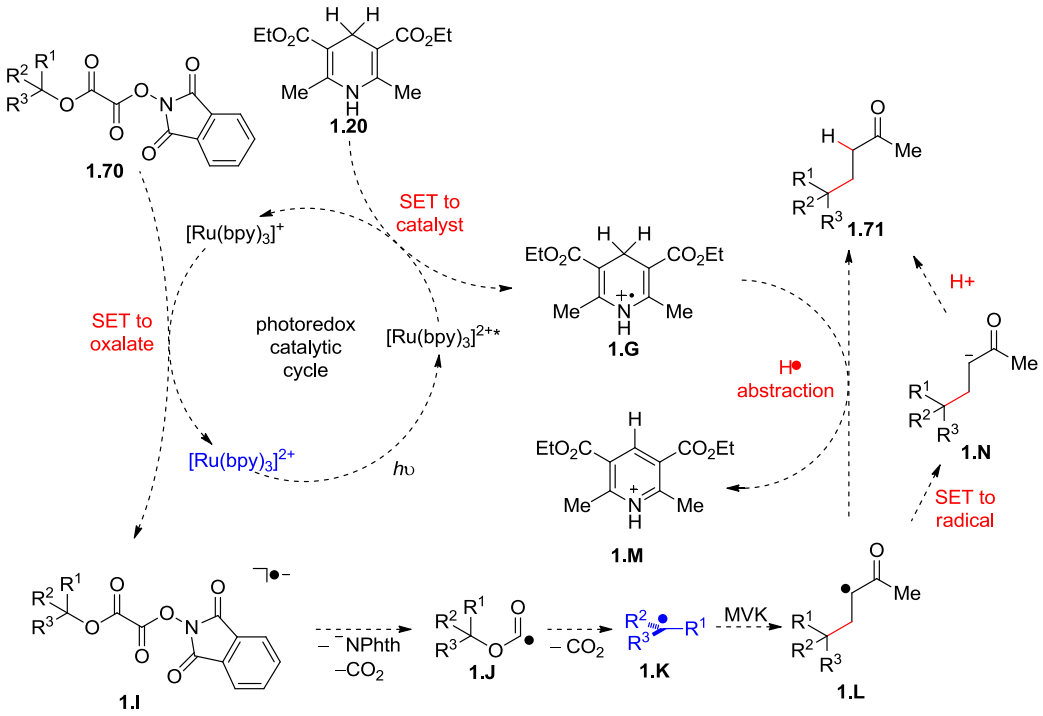


1.2.6 Proposed Reaction Mechanism

At this point, the Overman group's understanding of the reaction mechanism was based on the mechanistic hypotheses proposed by Barton for the coupling of thiohydroxamate oxalates[18] and by Okada for the coupling of (*N*-acyloxy)phthalimide substrates.[13] The proposed mechanism for the photoredox-catalyzed coupling of *N*-phthalimidoyl oxalates with conjugate acceptors is described in Figure 1.11.

The mechanism of the radical coupling of begins with irradiation of $Ru(bpy)_3^{2+}$ with visible light to generate photoexcited species $Ru(bpy)_3^{2+}$*. This catalyst intermediate is then reductively quenched by the dihydropyridine reductant **1.20**, forming $Ru(bpy)_3^{+}$ and radical cation **1.G**. The strong reductant $Ru(bpy)_3^{+}$ likely transfers an electron to the substrate oxalate **1.70**, regenerating the ground state photocatalyst and forming oxalate radical anion **1.I**.[38], This radical anion intermediate **1.I** undergoes N–O homolysis to liberate phthalimide anion (or phthalimide, if protonation occurs first) and subsequently decarboxylates to generate CO_2 and alkoxycarbonyl radical **1.J**. In most cases, alkoxycarbonyl radical **1.J** performs a second decarboxylation to form tertiary radical

Figure 1.11 Proposed photoredox-catalyzed coupling mechanism

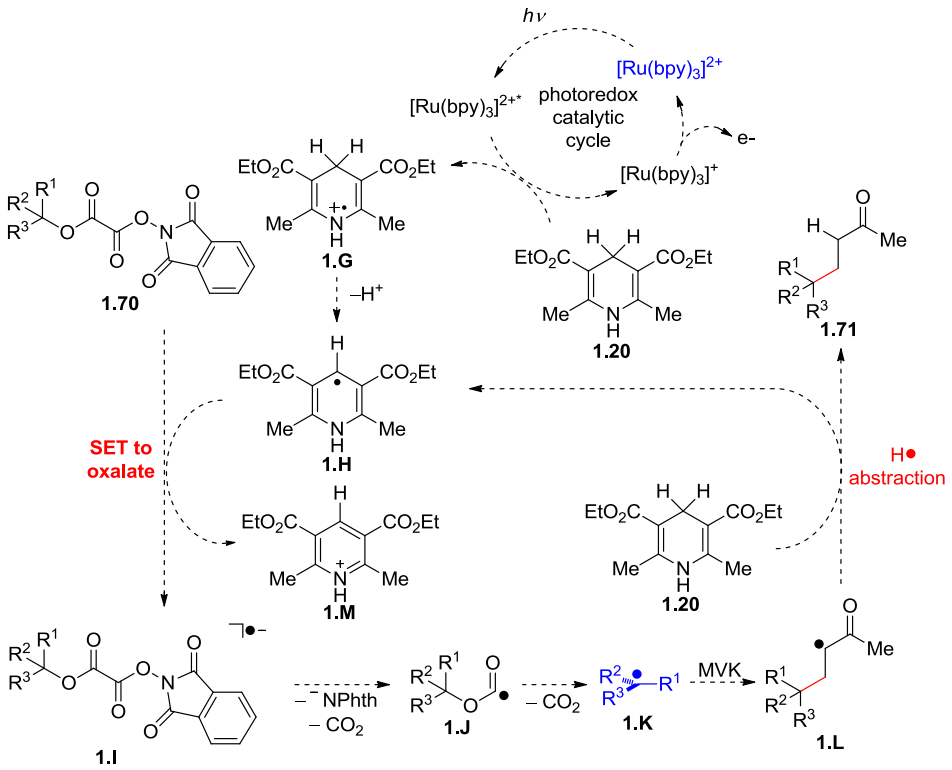


1.K, which readily adds to an electron-deficient olefin such as MVK. The stabilized electrophilic radical **1.L** can then be terminated in one of two ways. One possibility for this process is direct hydrogen atom abstraction from radical cation **1.G** to furnish the addition product **1.71** and concomitantly generate pyridinium **1.M**. Alternatively, single-electron transfer from one of a number of possible intermediates (Scheme 1.3) could provide enolate **1.N**, which would be quickly protonated under the reaction conditions to generate **1.71**.

Okada's mechanistic proposal included speculation that the dihydropyridine reductant, or a downstream intermediate produced by its oxidation, is primarily responsible for reductive fragmentation of the substrate radical precursor.[13] This mode of reactivity in the case of *N*-phthalimidoyl oxalate substrates would account for the substantial reactivity observed in the absence of the photocatalyst discussed previously.

Based on this hypothesis, it is possible that the true mechanism of the coupling of *N*-phthalimidoyl oxalates with conjugate acceptors is more accurately described by the "photoredox-initiated" mechanism shown in Figure 1.12. In this proposed mechanism, dihydropyridine radical cation **1.G** produced by reductive quenching of $Ru(bpy)_3^{2+}$* is deprotonated at C4 to generate dihydropyridine radical **1.H** as shown previously in Scheme 1.3. Reductive fragmentation of the substrate oxalate **1.70** by this intermediate could then occur, with termination of the radical coupling by hydrogen atom abstraction from the parent dihydropyridine **1.20**. This process would regenerate dihydropyridine

Figure 1.12 Proposed "photoredox-initiated" coupling mechanism



radical intermediate **1.H**, effectively constituting a radical chain reaction where $Ru(bpy)_3^{2+}$ serves only to initiate the chain sequence. At this point, the photocatalyst's role in initiating the coupling reaction has not been unambiguously identified. It is also

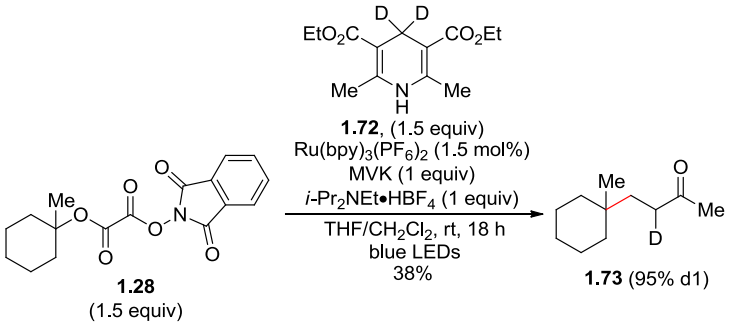
possible that the operative reaction mechanism is some combination of the processes depicted in Figure 1.11 and Figure 1.12.

1.2.7 Investigating the Termination Mechanism

As depicted in Figure 1.11, two mechanistic possibilities exist for the termination of electrophilic radical intermediate **1.L**. Although previous evidence obtained by the Overman group suggested that both mechanistic outcomes are possible[39] it was at this time unclear what factors govern the termination mechanism. It was reasoned that this information would be valuable in future applications of these coupling reactions, and so this mechanistic duality was next examined in detail.

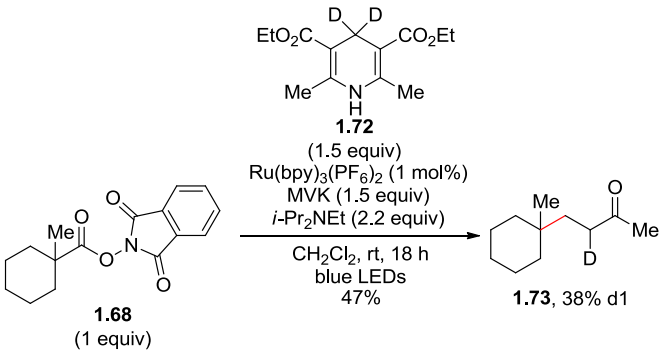
The coupling of both 1-methylcyclohexyl *N*-phthalimidoyl oxalate (**1.28**) and 1-methylcyclohexyl (*N*-acyloxy)phthalimide (**1.68**) with MVK in the presence of dideuterio-Hantzsch ester **1.72** was first investigated. The coupling of oxalate **1.28** under the standard conditions using dihydropyridine **1.72** provided adduct **1.73** in 38% yield (Equation 1.7). This product was determined to have incorporated deuterium in nearly quantitative fashion at the position adjacent to the carbonyl, suggesting that termination is mediated exclusively by the dihydropyridine reductant.[40]

Equation 1.7



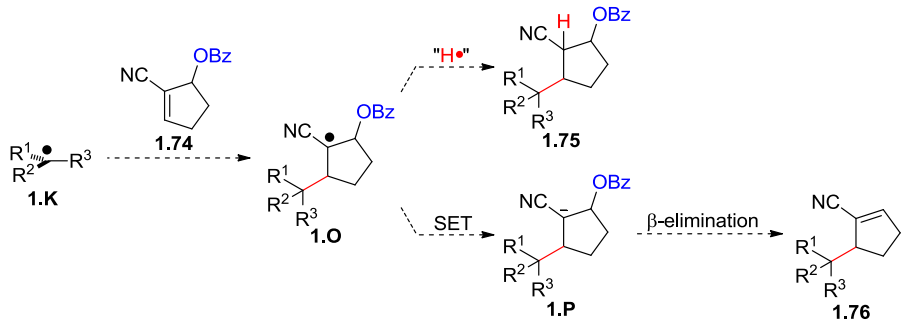
By contrast, the coupling of the related (*N*-acyloxy)phthalimide under the conditions optimized for reactions of these substrates in the presence of dihydropyridine **1.72** resulted in only 38% deuterium incorporation in adduct **1.73**. This result implied that multiple termination pathways may occur under these conditions.

Equation 1.8



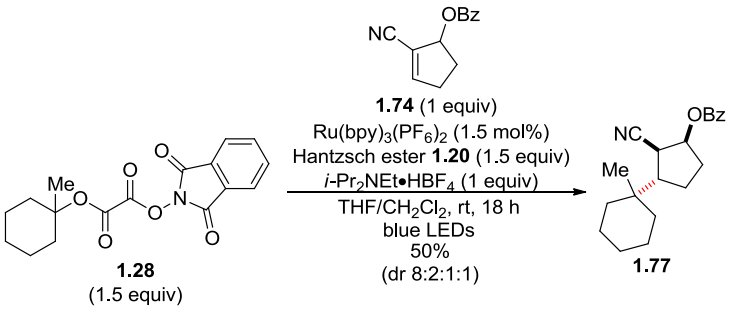
To further probe the termination pathway, a series of experiments was designed in which a tertiary radical intermediate would couple with an acceptor bearing a leaving group at the allylic α' position. Addition of a tertiary radical intermediate **1.K** to cyclopentenenitrile **1.74** would initially provide nitrile-stabilized radical **1.O** (Scheme 1.4). If termination by hydrogen atom abstraction were to occur, the product isolated from the reaction would be **1.75** which retains the benzoate group. Alternatively, single-electron reduction of **1.O** would generate stabilized anion **1.P**, which should rapidly β-eliminate benzoate anion to furnish a product such as **1.76** that exhibits a resulting desaturation. Thus, the termination mechanism could easily be established by simply identifying which products were obtained in a given radical coupling reaction.

Scheme 1.4 Proposed coupling mechanisms of cyclopentene nitrile 1.74



The reaction of *N*-phthalimidoyl oxalate **1.28** with acceptor **1.74** under the previously optimized reaction conditions provided adduct **1.77** in 50% yield. In this coupling, no trace of the β-elimination product **1.78** was seen (Equation 1.9). This result, in accordance with the outcome of the deuterium-labeling experiment described above, establishes that termination of the coupling of phthalimidoyl oxalates occurs by hydrogen atom abstraction from Hantzsch dihydropyridine **1.20**.

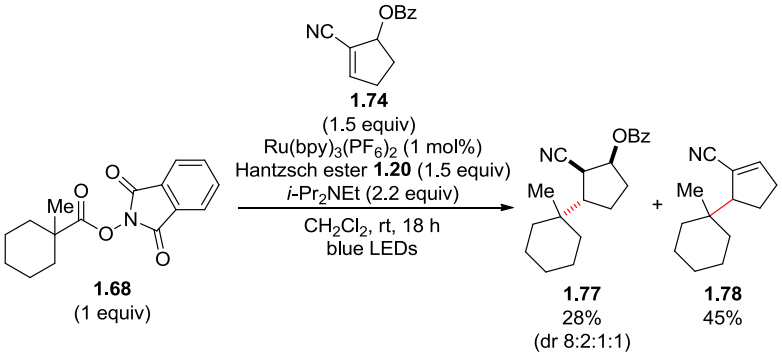
Equation 1.9



Subjecting 1-methylcyclohexyl (*N*-acyloxy)phthalimide (**1.68**) to a radical coupling with acceptor **1.74** under the standard conditions (Equation 1.10) resulted in the formation of adducts **1.77** and **1.78** in 28% and 45% yield, respectively. Addition product **1.77** was undoubtedly formed via hydrogen atom abstraction of the intermediate α-cyano radical, resulting in preservation of the benzoate group. In contrast, olefin **1.78** is likely

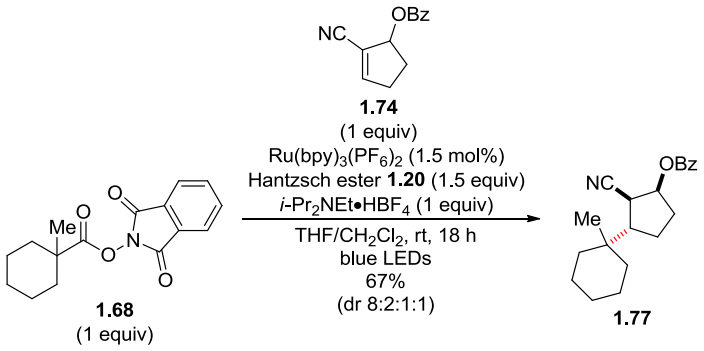
the product of an ionic β-elimination event. These results suggest that under the typical conditions for coupling (*N*-acyloxy)phthalimides with conjugate acceptors, both hydrogen atom abstraction and single-electron transfer followed by protonation occur competitively.[41]

Equation 1.10



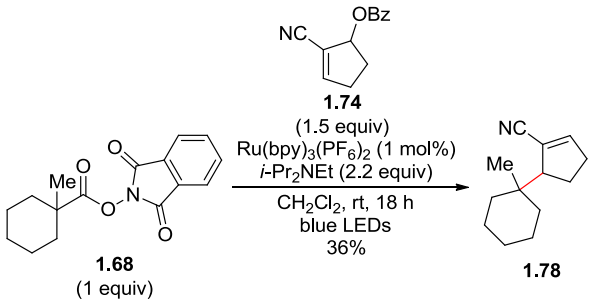
To examine if the radical precursor itself is in some way responsible for regulating the termination mechanism, (*N*-acyloxy)phthalimide **1.68** was subjected to the coupling conditions typically used for the related oxalate substrates (Equation 1.11). Interestingly, only adduct **1.77** was isolated from this reaction, while product **1.78** that would have resulted from β-elimination of an anionic intermediate was not detected. This result was identical to that obtained when oxalate **1.28** was used as the radical source, confirming as expected that both radical precursors terminate via the same mechanism under a given set of conditions.

Equation 1.11



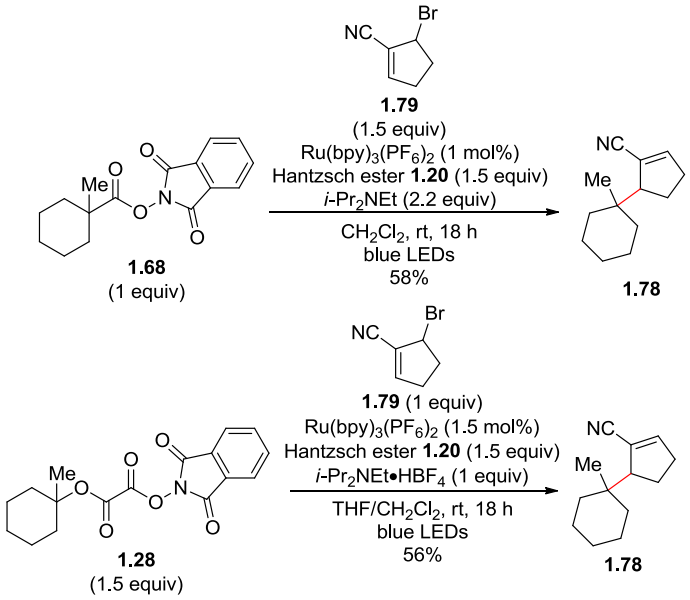
One major difference with respect to the optimized reaction conditions utilizing either radical precursor is that the coupling of (*N*-acyloxy)phthalimides employs *i*-Pr_2NEt as a co-reductant, while the coupling of the related oxalates uses *i*Pr_2NEt•HBF_4 which is presumably redox-inactive. It was thus suspected that the reductant additive was responsible for determining the termination mechanism. The coupling of (*N*-acyloxy)phthalimide **1.68** with acceptor **1.74** was next conducted, omitting Hantzsch ester **1.20** and utilizing only *i*-Pr_2NEt as a terminal reductant (Equation 1.12). This experiment resulted in the exclusive formation of product **1.78** which had been formed by β-elimination to eject the benzoate group.[42] These results implicate the combination[43,44,45] of *i*-Pr_2NEt and photocatalyst as the operative single-electron donors in the reduction of the initially formed product radical, and show that the aminium radical cation generated upon oxidation of the amine during the course of the reaction does not act as a hydrogen atom donor in the termination step. Hydrogen atom transfer to the α-cyano radical by an intermediate derived from *i*-Pr_2NEt[23] would have resulted in the formation of **1.77**, which was not detected in this reaction.

Equation 1.12



As expected, the coupling of either radical precursor under the typical conditions with allylic bromide **1.79** resulted in the exclusive formation of desaturated product **1.78** (Figure 1.13). Addition of the tertiary radical intermediate produced from either substrate to **1.79**, followed by homolytic cleavage of the C–Br bond is the most reasonable mechanism for these two transformations.

Figure 1.13 Coupling of radical precursors with allylic bromide 1.79



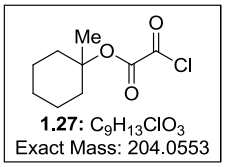
1.3 Conclusions

A new photoredox-catalyzed radical coupling reaction that permits the direct formation of quaternary carbons from tertiary alcohol derivatives was developed. The *N*-phthalimidoyl oxalate radical precursors were easily synthesized from a variety of structurally diverse tertiary alcohols in high yields. Coupling of the oxalates with electron-deficient alkenes was successful for many oxalates and acceptors, generally providing good yields of radical addition products. Importantly, the reaction is successful using only a 1.5:1 ratio of coupling partners, making this process amenable to the coupling of structurally elaborate fragments. The mechanism of the photoredox-catalyzed coupling of both alkyl *N*-phthalimidoyl oxalates and (*N*-acyloxy)phthalimides with conjugate acceptors was also investigated. It was confirmed that the termination pathway is governed by choice of the stoichiometric reductant employed. The coupling reactions of phthalimidoyl oxalate substrates were found to be slightly less efficient than those of the corresponding (*N*-acyloxy)phthalimide radical precursors; however, the synthetic advantage afforded by utilizing an alcohol derivative in the construction a quaternary carbon makes the phthalimidoyl oxalate substrates valuable intermediates for complex molecule synthesis.

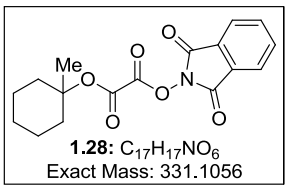
1.4 Experimental Information

Unless stated otherwise, reactions were conducted in oven-dried glassware under an atmosphere of nitrogen or argon using anhydrous solvents (either freshly distilled or passed through activated alumina columns). For all photoredox-catalyzed coupling reactions, THF and CH_2Cl_2 were sparged with argon for 5 minutes prior to use. All commercially obtained reagents were used as received. $Ru(bpy)_3(PF_6)_2$ was obtained from Sigma Aldrich. Methyl vinyl ketone, acrylonitrile, methyl acrylate, *N*,*N*-dimethyl acrylamide, and 2(5*H*)-furanone were distilled neat prior to use. Hantzsch ester **1.20**[46] and *i*-$Pr_2NEt{\bullet}HBF_4$[14] were prepared according to literature procedures. Reaction temperatures were controlled using an IKAmag temperature modulator, and unless stated otherwise, reactions were performed at room temperature (rt, approximately 23 °C). Thin-layer chromatography (TLC) was conducted with E. Merck silica gel 60 F254 pre-coated plates, (0.25 mm) and visualized by exposure to UV light (254 nm) or by anisaldehyde, ceric ammonium molybdate and potassium permanganate staining. EMD silica gel 60 (particle size 0.040–0.063 mm) was used for flash column chromatography. ^{1}H NMR spectra were recorded on Bruker spectrometers (at 500 or 600 MHz) and are reported relative to deuterated solvent signals. Data for ^{1}H NMR spectra are reported as follows: chemical shift (δ ppm), multiplicity, coupling constant (Hz) and integration. ^{13}C NMR spectra were recorded on Bruker spectrometers (at 125 or 150 MHz). Data for ^{13}C NMR spectra are reported in terms of chemical shift. IR spectra were recorded on a Varian 640-IR spectrometer and are reported in terms of frequency of absorption (cm^{-1}). Blue LEDs (30 cm, 1 watt) were purchased from http://www.creativelightings.com and powered by 8 AA batteries. Optical rotations were measured with a Jasco P-1010

polarimeter. High-resolution mass spectra were obtained from the UC Irvine Mass Spectrometry Facility with a Micromass LCT spectrometer. Most data for isolated yield and percent deuterium incorporation reported in the main text are average results of multiple experiments. The data reported in the following experimental information are described for one experiment and may differ from the average yields and percent deuterium incorporation depicted in the main text.

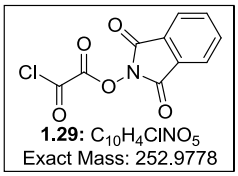


1-Methylcyclohexyl 2-chloro-2-oxoacetate (1.27): A round-bottom flask was charged with 1-methylcyclohexanol **1.26** (2.00 g, 17.5 mmol) and Et_2O (87 mL) under argon. The vessel was then cooled to 0 °C in an ice-water bath. Oxalyl chloride (2.0 mL, 22.8 mmol) was added dropwise over 1 min, and the homogeneous reaction mixture was allowed to warm to rt overnight. After this time, the reaction mixture was concentrated under reduced pressure to provide chlorooxalate ester **1.27** as a colorless oil (2.85 g, 14.0 mmol, 80%) which was used without further purification: ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.22–2.29 (m, 2H), 1.52–1.67 (m, 10H), 1.27–1.38 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.43, 154.3, 89.5, 36.2, 25.1, 24.9, 21.9; IR (thin film) 2939, 2865, 1801, 1751, 1449, 1294, 1273, 1244, 973 cm^{-1}.



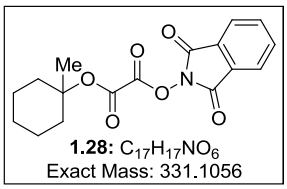
1,3-Dioxoisoindolin-2-yl (1-methylcyclohexyl) oxalate (1.28). Coupling of 1.27 with *N*-hydroxyphthalimide: To a 500 mL round-bottom flask containing *N*-hydroxyphthalimide (2.85 g, 17.5 mmol) and DMAP (213 mg, 1.70 mmol) was added THF (175 mL) and Et_3N (2.4

mL, 17.5 mmol). Chlorooxalate ester **1.27** (3.57 g, 17.5 mmol) was then added as a solution in THF (5 mL) and a colorless precipitate was immediately formed. The mixture was stirred for 1 h at rt, after which it was diluted with Et_2O (200 mL) and was poured into saturated aqueous $NaHCO_3$ (200 mL). The organic layer was separated and washed with additional saturated aqueous $NaHCO_3$ (2 x 200 mL), aqueous 1 N HCl (3 x 100 mL), and brine (2 x 100 mL). The organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure to afford oxalate **1.28** (3.21 g, 9.70 mmol, 55%) as a colorless solid which was used without further purification (typical yields for this reaction ranged from 40-70%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.92–7.90 (m, 2H), 7.83–7.81 (m, 2H), 2.27–2.23 (m, 2H), 1.62 (s, 3H), 1.62–1.52 (m, 7H), 1.35–1.27 (m, 1H); ^{13}C NMR (125 MHz, DMF-d_7) δ 162.5, 156.1, 154.4, 136.9, 129.7, 125.3, 90.2, 36.9, 25.8, 25.6, 22.9; IR (thin film) 2938, 2863, 1824, 1792, 1756, cm^{-1}.[47]

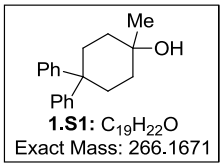


1.29: $C_{10}H_4ClNO_5$
Exact Mass: 252.9778

1,3-Dioxoisoindolin-2-yl 2-chloro-2-oxoacetate (1.29): A round-bottom flask was charged with *N*-hydroxyphthalimide (1.97 g, 12.09 mmol), followed by the addition of THF (200 mL) under argon. The resulting solution was then cooled to –78 °C and oxalyl chloride (5.2 mL, 60.47 mmol) was added dropwise. The solution was then allowed to warm to rt and was stirred for 18 h. After this time, the solution was concentrated under reduced pressure to yield **1.29** as a colorless solid. The crude material was dissolved in THF (200 mL) for use as a 0.06 M solution in the preparation of *tert*-alkyl *N*-phthalimidoyl oxalates; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99–7.91 (m, 2H), 7.90–7.83 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.5, 157.8, 152.4, 135.5, 128.6, 124.7; IR (thin film) 1827, 1791, 1744, 1468, 1354 cm^{-1}.[48]

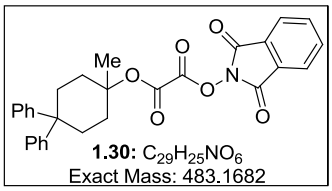


1,3-Dioxoisoindolin-2-yl (1-methylcyclohexyl) oxalate (1.28). Acylation of 1-methylcyclohexanol with 1.29. A round-bottom flask was charged with 1-methylcyclohexanol (690 mg, 6.05 mmol) and DMAP (74 mg, 0.60 mmol) followed by the addition of Et_3N (1.7 mL, 12.09 mmol). A 0.06 M solution of chloro *N*-phthalimidoyl oxalate **1.29** (200 mL, 12.09 mmol) in THF was added via cannula. The resulting heterogeneous mixture was allowed to stir at rt for 1 h. The volatiles were removed under reduced pressure, and the resulting crude residue was dissolved in CH_2Cl_2 (40 mL) then poured into hexanes (1 L). The resulting heterogeneous mixture was filtered through a cotton plug and washed with hexanes (2 x 100 mL). The filtrate was concentrated under reduced pressure to yield oxalate **1.28** as a beige solid (1.90 g, 5.74 mmol, 95%). Characterization data acquired for **1.28** were identical to those reported above.



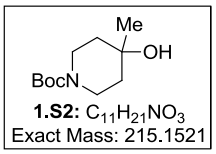
1-Methyl-4,4-diphenylcyclohexan-1-ol (1-S1): A round-bottom flask was charged with 4,4-diphenylcyclohexanone[49] (1.00 g, 3.76 mmol), followed by the addition of THF (38 mL). The resulting solution was then cooled to –78 °C and a solution of methylmagnesium bromide (3.8 mL, 11.28 mmol, 3 M in Et_2O) was added. The reaction was allowed to stir at –78 °C for 1 h, then was allowed to warm to rt and stirred an additional 12 h. The reaction mixture was quenched by slow addition of 3 mL of saturated aqueous NH_4Cl solution and the resulting mixture was transferred to a separatory funnel with Et_2O (75 mL) and saturated aqueous NH_4Cl solution (25 mL). The resulting biphasic mixture was extracted with Et_2O (3 x 50 mL) and the organic layers were combined, dried over $MgSO_4$, filtered through

cotton and concentrated under reduced pressure. The resulting residue was purified by flash chromatography (2:1 hexanes:EtOAc) to yield **1.S1** (802 mg, 3.01 mmol, 80%) as a colorless solid. R_f = 0.31 (2:1 hexanes:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42 (d, *J* = 7.7, 2H), 7.36 (t, *J* = 7.7, 2H), 7.33–7.26 (m, 4H), 7.23 (t, *J* = 7.2, 1H), 7.19–7.12 (m, 1H), 2.55–2.37 (m, 4H), 1.73–1.57 (m, 4H), 1.44 (s, 1H), 1.23 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 128.5, 128.3, 127.5, 126.7, 125.8, 125.6, 69.4, 45.7, 36.1, 32.5, 30.2; IR (thin film) 3361, 3057, 2945, 1597, 1447 cm^{-1}; HRMS (CI) *m/z* calcd for $C_{19}H_{26}NO$ $(M + NH_4)^+$ 284.2014, found 284.2017.

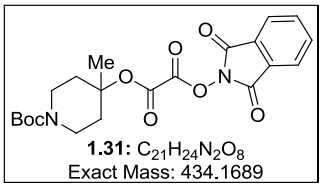


1,3-Dioxoisoindolin-2-yl (1-methyl-4,4-diphenylcyclohexyl) oxalate (1.30): A round-bottom flask was charged with **1.S1** (724 mg, 2.72 mmol) and DMAP (33 mg, 0.272 mmol) followed by the addition of Et_3N (0.75 mL, 5.44 mmol). A 0.06 M solution of chloro *N*-phthalimidoyl oxalate **1.29** (90 mL, 5.44 mmol) in THF was added via cannula. The resulting heterogeneous mixture was allowed to stir at rt for 1.5 h. The volatiles were removed under reduced pressure, and the resulting crude residue was dissolved in CH_2Cl_2 (18 mL) then poured into hexanes (450 mL). The resulting heterogeneous mixture was filtered through a cotton plug and washed with hexanes (2 x 100 mL). The filtrate was concentrated under reduced pressure to yield oxalate **1.30** as a beige solid (1.25 g, 2.59 mmol, 95%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95–7.89 (m, 2H), 7.86–7.79 (m, 2H), 7.43–7.31 (m, 4H), 7.25–7.17 (m, 5H), 7.15–7.07 (m, 1H), 2.50 (d, *J* = 13.3, 2H), 2.43–2.31 (m, 4H), 1.70 (t, *J* = 12.9, 2H), 1.61 (s, 3H); ^{13}C NMR (125 MHz,

$CDCl_3$) δ 161.1, 154.5, 153.1, 135.2, 128.79, 128.75, 128.4, 127.6, 126.5, 126.1, 125.9, 124.4, 88.8, 45.5, 33.1, 32.0, 25.1; IR (thin film) 2951, 1825, 1792, 1756, 1599 cm^{-1}.

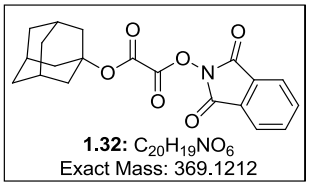


***tert*-Butyl 4-hydroxy-4-methylpiperidine-1-carboxylate (1.S2)**: A round-bottom flask was charged with *N*-Boc-piperidone (1.00 g, 5.03 mmol), followed by the addition of Et_2O (10 mL). The resulting solution was then cooled to –30 °C and a solution of methylmagnesium bromide (1.84 mL, 5.53 mmol, 3 M in Et_2O) was added. The reaction was allowed to stir at –30 °C for 5 min, then was allowed to warm to rt and stirred an additional 12 h. The reaction mixture was quenched by slow addition of 1 mL of saturated NH_4Cl and the resulting mixture was transferred to a separatory funnel with Et_2O (20 mL) and saturated aqueous NH_4Cl solution (15 mL). The resulting biphasic mixture was extracted with Et_2O (3 x 20 mL) and the organic layers were combined, dried over $MgSO_4$, filtered and evaporated under reduced pressure to yield tertiary alcohol **1.S2** (1.07 g, 4.97 mmol, 99%) as a colorless solid: R_f = 0.26 (2:1 hexanes:EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.72–3.63 (m, 2H), 3.26–3.17 (m, 2H), 1.52 (dd, *J* = 7.0, 4.7, 4H), 1.47 (s, 1H), 1.43 (s, 9H), 1.24 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 154.9, 79.5, 68.1, 40.2, 38.5, 30.2, 28.6; IR (thin film) 3434, 2971, 2932, 1670, 1428 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{11}H_{21}NO_3Na$ $(M + Na)^+$ 238.1419, found 238.1420.



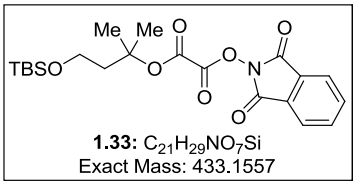
1-(*tert*-Butoxycarbonyl)-4-methylpiperidin-4-yl (1,3-dioxoisoindolin-2-yl) oxalate (1.31): A round-bottom flask

was charged with **1.S2** (430 mg, 2.00 mmol) and DMAP (24 mg, 0.20 mmol) followed by the addition of Et_3N (0.56 mL, 4.00 mmol). A 0.06 M solution of chloro *N*-phthalimidoyl oxalate **1.29** (65 mL, 4.00 mmol) in THF was added via cannula. The resulting heterogeneous mixture was allowed to stir at rt for 2 h. The volatiles were removed under reduced pressure, and the resulting crude residue was dissolved in CH_2Cl_2 (5 mL) then poured into hexanes (250 mL). The resulting heterogeneous mixture was filtered through a cotton plug and washed with hexanes (2 x 100 mL). The filtrate was concentrated under reduced pressure to yield oxalate **1.31** (710 mg, 1.63 mmol, 80%) as a pale yellow solid: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.94–7.91 (m, 2H), 7.84–7.81 (m, 2H), 3.85 (d, *J* = 10.0, 2H), 3.18 (dt, *J* = 12.5, 2.7, 2H), 2.31 (d, *J* = 10.0, 2H), 1.73–1.66 (m, 2H), 1.70 (s, 3H), 1.46 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 161.0, 155.0, 154.3, 153.1, 135.3, 128.9, 124.4, 86.6, 80.5, 35.7, 28.6, 24.9; IR (thin film) 2977, 1825, 1793, 1749, 1686 cm^{-1}.



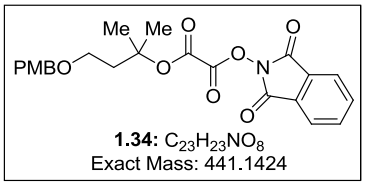
(*rel*-3*s*,5*s*,7*s*)-Adamantan-1-yl (1,3-dioxoisoindolin-2-yl) oxalate (1.32): A round-bottom flask was charged with 1-adamantanol (225 mg, 1.48 mmol) and DMAP (18 mg, 0.15 mmol) followed by the addition of Et_3N (0.41 mL, 2.96 mmol). A 0.06 M solution of chloro *N*-phthalimidoyl oxalate **1.29** (50 mL, 2.96 mmol) in THF was added via cannula. The resulting heterogeneous mixture was allowed to stir at rt for 15 h. The volatiles were removed under reduced pressure, and the resulting crude residue was dissolved in CH_2Cl_2 (6 mL) then poured into hexanes (200 mL). The resulting heterogeneous mixture was filtered through a cotton plug and washed with hexanes (2 x 100 mL). The filtrate was concentrated under reduced pressure to yield oxalate **1.32** (532 mg, 1.44 mmol, 97%) as a

colorless solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94–7.89 (m, 2H), 7.85–7.80 (m, 2H), 2.25 (app. s, 9H), 1.75–1.66 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.1, 154.5, 152.7, 135.2, 128.9, 124.4, 87.7, 41.0, 36.0, 31.2; IR (thin film) 2915, 2855, 1824, 1792, 1748 cm^{-1}. Single crystals suitable for X-ray analysis were obtained by slow evaporation from Et_2O-heptane.[19]

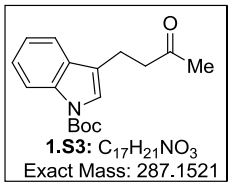


1.33: $C_{21}H_{29}NO_7Si$
Exact Mass: 433.1557

4-((*tert*-Butyldimethylsilyl)oxy)-2-methylbutan-2-yl (1,3-dioxoisoindolin-2-yl) oxalate (1.33): A round-bottom flask was charged with 4-((*tert*-butyldimethylsilyl)oxy)-2-methylbutan-2-ol[50] (250 mg, 1.14 mmol) and DMAP (14 mg, 0.11 mmol) followed by the addition of Et_3N (0.32 mL, 2.29 mmol). A 0.06 M solution of chloro *N*-phthalimidoyl oxalate **1.29** (38 mL, 2.29 mmol) in THF was added via cannula. The resulting heterogeneous mixture was allowed to stir at rt for 1 h. The volatiles were removed under reduced pressure, and the resulting crude residue was dissolved in CH_2Cl_2 (9 mL) then poured into hexanes (180 mL). The resulting heterogeneous mixture was filtered through a cotton plug and washed with hexanes (2 x 100 mL). The filtrate was concentrated under reduced pressure to yield oxalate **1.33** (493 mg, 1.14 mmol, 99%) as a clear oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95–7.89 (m, 2H), 7.85–7.79 (m, 2H), 3.80 (t, *J* = 6.5, 2H), 2.14 (t, *J* = 6.5, 2H), 1.65 (s, 6H), 0.89 (s, 9H), 0.06 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.0, 154.4, 153.1, 135.2, 128.8, 124.3, 89.2, 58.9, 43.1, 26.2, 26.0, 18.3, –5.3; IR (thin film) 2956, 1825, 1793, 1751, 1469 cm^{-1}.

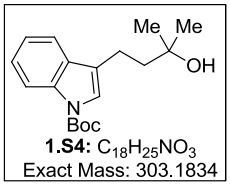


1,3-Dioxoisoindolin-2-yl (4-((4-methoxybenzyl)oxy)-2-methylbutan-2-yl) oxalate (1.34): A round bottom flask was charged with 4-((4-methoxybenzyl)oxy)-2-methylbutan-2-ol[51] (381 mg, 1.70 mmol) and DMAP (21 mg, 0.17 mmol) followed by the addition of Et_3N (0.47 mL, 3.40 mmol). A 0.06 M solution of chloro *N*-phthalimidoyl oxalate **1.29** (56 mL, 3.40 mmol) in THF was added via cannula. The resulting heterogeneous mixture was allowed to stir at rt for 1 h. The volatiles were removed under reduced pressure, and the resulting crude residue was dissolved in CH_2Cl_2 (14 mL) then poured into hexanes (280 mL). The resulting heterogeneous mixture was filtered through a cotton plug and washed with hexanes (2 x 100 mL). The filtrate was concentrated under reduced pressure to yield oxalate **1.34** (781 mg, 1.70 mmol, 99%) as a pale yellow oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92–7.88 (m, 2H), 7.84–7.79 (m, 2H), 7.25 (d, *J* = 8.6, 2H), 6.86 (d, *J* = 8.6, 2H), 4.44 (s, 2H), 3.77 (s, 3H), 3.61 (t, *J* = 6.2, 2H), 2.21 (t, *J* = 6.2, 2H), 1.63 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.0, 159.2, 154.4, 153.3, 135.2, 130.3, 129.4, 128.8, 124.3, 113.8, 88.7, 72.8, 65.5, 55.3, 39.8, 26.2; IR (thin film) 2935, 2866, 1823, 1791, 1748 cm^{-1}.



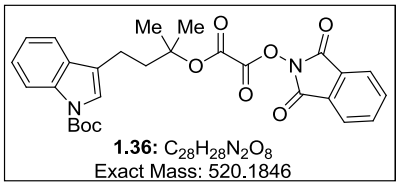
***tert*-Butyl 3-(3-oxobutyl)-1H-indole-1-carboxylate (1.S3)**: A round-bottom flask was charged with 4-(1*H*-3-indolyl)butan-2-one[52] (1.50 g, 8.02 mmol) followed by the addition of CH_2Cl_2 (27 mL). Et_3N (2.2 mL, 16.0 mmol) and DMAP (98 mg, 0.80 mmol) were then added and the solution was cooled to 0 °C. Di-*tert*-butyl dicarbonate (2.10 g, 9.62 mmol) was added in one portion and the resulting solution was allowed to warm to rt and was stirred for 4 h.

The mixture was then transferred to a separatory funnel and the organic layer was washed with H_2O (3 x 50 mL) and brine (1 x 50 mL). The organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude residue obtained was purified by silica gel chromatography (93:7 hexanes:EtOAc to 90:10 hexanes:EtOAc) to yield carbamate **1.S3** (1.54 g, 5.36 mmol, 67%) as a colorless solid: R_f = 0.51 (3:1 hexanes:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.12 (br s, 1H), 7.51 (d, *J* = 8.0, 1H), 7.36 (s, 1H), 7.34–7.29 (t, *J* = 8.0, 1H), 7.24 (t, *J* = 7.3, 1H), 2.97 (t, *J* = 7.7, 2H), 2.85 (t, *J* = 7.7, 2H), 2.18 (s, 3H), 1.67 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 208.0, 149.9, 135.6, 130.4, 124.5, 122.6, 122.5, 119.8, 118.9, 115.4, 83.6, 43.1, 30.2, 28.3, 19.0; IR (thin film) 2978, 2932, 1727, 1454, 1376 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{17}H_{21}NO_3Na$ $(M + Na)^+$ 310.1419, found 310.1425.



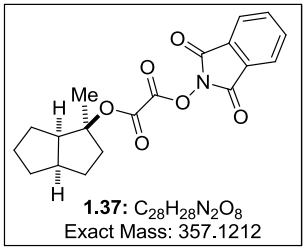
***tert*-Butyl 3-(3-hydroxy-3-methylbutyl)-1*H*-indole-1-carboxylate (1.S4)**: A round-bottom flask was charged with ketone **1.S3** (1.00 g, 3.48 mmol), followed by the addition of Et_2O (17 mL). The resulting solution was then cooled to –78 °C and a solution of methylmagnesium bromide (1.27 mL, 3.83 mmol, 3 M in Et_2O) was added. The reaction was allowed to warm to rt and was stirred for an additional 2 h. After this time, the reaction was cooled to –78 °C and quenched by slow addition of 10 mL of saturated aqueous NH_4Cl solution. The resulting mixture was transferred to a separatory funnel, and the aqueous layer was extracted with Et_2O (3 x 15 mL). The organic layers were combined, dried over $MgSO_4$, filtered and evaporated under reduced pressure. The crude residue was purified by silica gel chromatography (90:10 hexanes:acetone) to yield **1.S4** (980 mg, 3.23 mmol, 93%) as a

pale yellow oil: R_f = 0.38 (3:1 hexanes:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.13 (br s, 1H), 7.54 (d, *J* = 7.9, 1H), 7.37 (s, 1H), 7.32 (t, *J* = 7.9, 1H), 7.24 (t, *J* = 7.9, 1H), 2.81–2.76 (m, 2H), 1.93–1.88 (m, 2H), 1.67 (s, 9H), 1.34 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.9, 135.7, 130.8, 124.4, 122.4, 122.1, 121.3, 119.0, 115.4, 83.4, 71.0, 43.2, 29.4, 28.3, 19.8; IR (thin film) 3396, 2973, 2931, 1731, 1377 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{18}H_{25}NO_3Na$ $(M + Na)^+$ 326.1732, found 326.1730.

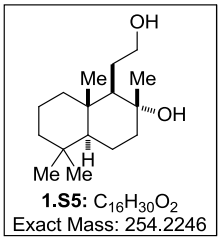


1.36: $C_{28}H_{28}N_2O_8$
Exact Mass: 520.1846

4-(1-(*tert*-Butoxycarbonyl)-1*H*-indol-3-yl)-2-methylbutan-2-yl (1,3-dioxoisoindolin-2-yl) oxalate (1.36): A round-bottom flask was charged with alcohol **1.S4** (500 mg, 1.65 mmol) and DMAP (20 mg, 0.16 mmol) followed by the addition of Et_3N (0.46 mL, 3.30 mmol). A 0.06 M solution of chloro *N*-phthalimidoyl oxalate **1.29** (55 mL, 3.30 mmol) in THF was added via cannula. The resulting heterogeneous mixture was allowed to stir at rt for 1 h. The volatiles were removed under reduced pressure, and the resulting crude residue was dissolved in CH_2Cl_2 (14 mL) then poured into hexanes (250 mL). The resulting heterogeneous mixture was filtered through a cotton plug and washed with hexanes (2 x 100 mL). The filtrate was concentrated under reduced pressure to yield oxalate **1.36** (560 mg, 1.08 mmol, 65%) as a colorless foam: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.12 (br s, 1H), 7.94–7.90 (m, 2H), 7.85–7.80 (m, 2H), 7.55 (d, *J* = 7.9, 1H), 7.39 (s, 1H), 7.30 (t, *J* = 7.5, 1H), 7.24 (t, *J* = 7.5, 1H), 2.85–2.80 (m, 2H), 2.29–2.23 (m, 2H), 1.74 (s, 6H), 1.66 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.1, 154.5, 153.2, 149.9, 135.7, 135.2, 130.5, 128.8, 124.5, 124.4, 122.6, 122.4, 120.1, 119.0, 115.4, 89.3, 83.6, 40.8, 28.3, 25.6, 19.5; IR (thin film) 2979, 2933, 1823, 1791, 1749, 1731 cm^{-1}.

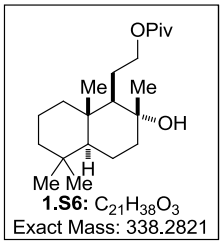


1,3-Dioxoisoindolin-2-yl ((*rel*-1S,3aR,6aR)-1-methyloctahydropentalen-1-yl) oxalate (1.37): A round-bottom flask was charged with (*rel*-1*S*,3a*R*,6a*R*)-1-methyloctahydropentalen-1-ol[53] (392 mg, 2.80 mmol) and DMAP (34 mg, 0.28 mmol) followed by the addition of Et_3N (0.76 mL, 5.59 mmol). A 0.06 M solution of chloro *N*-phthalimidoyl oxalate **1.29** (93 mL, 5.59 mmol) in THF was added via cannula. The resulting heterogeneous mixture was allowed to stir at rt for 1 h. The volatiles were removed under reduced pressure, and the resulting crude residue was dissolved in CH_2Cl_2 (23 mL) then poured into hexanes (460 mL). The resulting heterogeneous mixture was filtered through a cotton plug and washed with hexanes (2 x 100 mL). The filtrate was concentrated under reduced pressure to yield oxalate **1.29** (950 mg, 2.66 mmol, 95%) as a clear oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92–7.89 (m, 2H), 7.83–7.80 (m, 2H), 2.58–2.48 (m, 2H), 2.26–2.17 (m, 1H), 1.93–1.79 (m, 3H), 1.76–1.66 (m, 2H), 1.63 (s, 3H), 1.63–1.55 (m, 1H), 1.50–1.40 (m, 1 H), 1.38–1.27 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.0, 154.6, 153.3, 135.2, 128.9, 124.3, 96.0, 53.6, 41.7, 36.6, 35.2, 29.2, 28.5, 27.2, 23.9; IR (thin film) 2951, 1824, 1792, 1747, 1467, cm^{-1}.



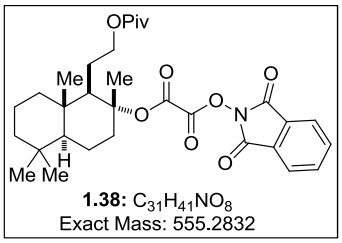
(1*R*,2*R*,4a*S*,8a*S*)-1-(2-Hydroxyethyl)-2,5,5,8a-tetramethyldecahydronaphthalen-2-ol (1.S5): A round-bottom flask was charged with (+)-sclareolide (1.00 g, 4.0 mmol), followed by the addition of THF (20 mL). The resulting solution was then cooled to 0 °C and lithium aluminum hydride (150 mg, 4.0 mmol) was added in one portion. The

reaction temperature was maintained at 0 °C while the heterogeneous mixture was stirred vigorously for 30 min. The reaction mixture was then quenched by the slow addition of 3 mL of EtOAc and the resulting mixture was transferred to a separatory funnel with Et_2O (50 mL) and aqueous 1 M HCl (25 mL). The resulting biphasic mixture was extracted with Et_2O (3 x 50 mL) and the organic layers were combined, dried over $MgSO_4$, filtered and evaporated under reduced pressure to yield **1.S5** (1.00 g, 3.93 mmol, 98%) as a colorless solid: R_f = 0.16 (2:1 hexanes:EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.82–3.77 (m, 1H), 3.51–3.45 (m, 1H), 2.22 (br s, 2H), 1.90 (dt, *J* = 12.0, 3.0, 1H), 1.71–1.62 (m, 4H), 1.62–1.54 (m, 1H), 1.52–1.40 (m, 2H), 1.40–1.35 (m, 1H), 1.33–1.24 (m, 2H), 1.20 (s, 3H), 1.18–1.11 (m, 1H), 0.98–0.90 (m, 2H), 0.88 (s, 3H), 0.79 (s, 6H); $[\alpha]^{25.6}_D$ –16.6, $[\alpha]^{25.8}_{577,}$ –17.8, $[\alpha]^{25.8}_{546}$ –22.4, $[\alpha]^{25.8}_{435}$ –45.8, $[\alpha]^{25.8}_{405}$ –53.5 (*c* = 1.11, $CHCl_3$); Spectral data matched those previously reported.[54]



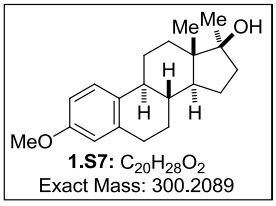
2-((1*R*,2*R*,4a*S*,8a*S*)-2-Hydroxy-2,5,5,8a-tetramethyldecahydronaphthalen-1-yl)ethyl pivalate (1.S6): A round-bottom flask was charged with alcohol **1.S5** (950 mg, 3.77 mmol), followed by the addition of 1,2-dimethoxyethane (DME, 20 mL). The resulting solution was then cooled to 0 °C and NaH (60% dispersion in mineral oil) (151 mg, 3.77 mmol) was added in one portion. The reaction temperature was maintained at 0 °C while the heterogeneous mixture was stirred vigorously for 5 min, after which pivaloyl chloride (462 μL, 3.77 mmol) was added. The reaction mixture was allowed to warm to rt and allowed to stir for 2 h. The flask was again cooled to 0 °C and NaH (60% dispersion in mineral oil) (151 mg, 3.77 mmol) followed by pivaloyl chloride

(392 μL, 3.20 mmol) was added. The reaction vessel was allowed to warm to rt and the mixture was stirred for an additional 12 h. The reaction mixture was quenched by slow addition of 1 mL of saturated aqueous NH_4Cl solution and the resulting mixture was transferred to a separatory funnel with Et_2O (50 mL) and saturated aqueous NH_4Cl solution (20 mL). The resulting biphasic mixture was extracted with Et_2O (3 x 50 mL), and the organic layers were combined, dried over $MgSO_4$, filtered and evaporated under reduced pressure. The crude residue was purified by flash chromatography (2:1 hexanes:Et_2O) to yield **1.S6** (1.27 g, 3.75 mmol, 99%) as a colorless solid: R_f = 0.36 (2:1 hexanes:EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.17–4.10 (m, 1H), 4.09–4.03 (m, 1H), 1.90 (dt, *J* = 12.4, 3.2, 1H), 1.78–1.71 (m, 1H), 1.71–1.53 (m, 5H), 1.48–1.35 (m, 3H), 1.32–1.23 (m, 2H), 1.21 (s, 9H), 1.17 (s, 3H), 1.12–1.07 (m, 1H), 0.96–0.89 (m, 2H), 0.88 (s, 3H), 0.802 (s, 3H), 0.797 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 178.9, 73.7, 66.8, 58.2, 56.3, 44.5, 42.0, 39.8, 38.9, 38.8, 33.5, 33.4, 27.4, 24.5, 24.1, 21.6, 20.6, 18.5, 15.5; IR (thin film) 3484, 2934, 2869, 1726, 1162 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{21}H_{38}O_3Na$ $(M + Na)^+$ 361.2719, found 361.2717; $[\alpha]^{25.7}_D$ +2.5, $[\alpha]^{25.8}_{577}$ +1.7, $[\alpha]^{25.8}_{546}$ –4.0, $[\alpha]^{25.8}_{435}$ –28.3, $[\alpha]^{25.8}_{405}$ –31.6 (*c* = 0.50, $CHCl_3$).



1,3-Dioxoisoindolin-2-yl ((1R,2R,4aS,8aS)-2,5,5,8a-tetramethyl-1-(2-(pivaloyloxy)ethyl)decahydronaphthalen-2-yl) oxalate (1.38): A round-bottom flask was charged with **1.S6** (500 mg, 1.48 mmol) and DMAP (18 mg, 0.15 mmol) followed by the addition of Et_3N (0.41 mL, 2.96 mmol). A 0.06 M solution of chloro *N*-phthalimidoyl oxalate **1.29** (50 mL, 2.96

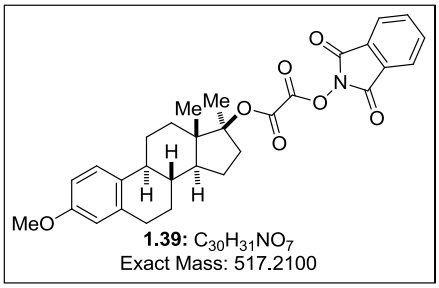
mmol) in THF was added via cannula. The resulting heterogeneous mixture was allowed to stir at rt for 15 h. The volatiles were removed under reduced pressure, and the resulting crude residue was dissolved in CH_2Cl_2 (6 mL) then poured into hexanes (200 mL). The resulting heterogeneous mixture was filtered through a cotton plug and washed with hexanes (2 x 100 mL). The filtrate was concentrated under reduced pressure to yield oxalate **1.38** (818 mg, 1.47 mmol, 99%) as a beige solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.93–7.89 (m, 2H), 7.84–7.78 (m, 2H), 4.27–4.18 (m, 1H), 4.13–4.03 (m, 1H), 2.89 (d, *J* = 11.3, 1H), 1.83–1.71 (m, 5H), 1.69 (s, 3H), 1.63–1.58 (m, 1H), 1.58–1.53 (m, 1H), 1.51–1.44 (m, 1H), 1.43–1.37 (m, 1H), 1.36–1.30 (m, 1H), 1.22–1.16 (m, 1H), 1.12 (s, 9H), 1.04 (d, *J* = 11.8, 1H), 1.01–0.93 (m, 1H), 0.89 (s, 3H), 0.87 (s, 3H), 0.80 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.6, 161.2, 154.4, 152.4, 135.1, 129.0, 124.3, 95.1, 65.6, 55.7, 55.5, 41.9, 39.4, 39.3, 38.9, 38.7, 33.4, 33.3, 27.3, 25.0, 21.5, 20.1, 20.0, 18.4, 15.7; IR (thin film) 2958, 1825, 1793, 1751, 1721 cm^{-1}; $[\alpha]^{26.0}_{D}$ +5.6, $[\alpha]^{26.0}_{577}$ +6.4, $[\alpha]^{26.0}_{546}$ +0.7, $[\alpha]^{25.9}_{435}$ –20.7, $[\alpha]^{25.9}_{405}$ –20.5 (*c* = 0.50, $CHCl_3$).



1.S7: $C_{20}H_{28}O_2$
Exact Mass: 300.2089

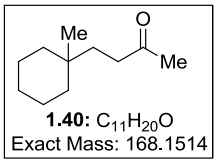
(8*R*,9*S*,13*S*,14*S*,17*S*)-3-Methoxy-13,17-dimethyl-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[a]phenanthren-17-ol (1.S7)[55]: A round-bottom flask fitted with a reflux condenser was charged with (8*R*,9*S*,13*S*,14*S*,17*S*)-3-methoxy-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[a]phenanthren-17-one[56] (830 mg, 2.92 mmol), followed by the addition of benzene (20 mL). A 3 M solution of methylmagnesium bromide (3.8 mL, 11.28 mmol) in Et_2O was added. The reaction was heated to 80 °C and allowed to stir for 2 h. The reaction mixture was then allowed to cool

to rt and was quenched by slow addition of 5 mL of saturated aqueous NH_4Cl solution. The resulting mixture was transferred to a separatory funnel with Et_2O (50 mL), water (20 mL) and aqueous 1 M HCl (10 mL). The resulting biphasic mixture was extracted with Et_2O (3 x 50 mL) and the organic layers were combined, dried over $MgSO_4$, and evaporated under reduced pressure to yield **1.S7** (876 mg, 2.92 mmol, 99%) as a colorless solid: R_f = 0.29 (2:1 hexanes:EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.21 (d, *J* = 8.9, 1H), 6.72 (dd, *J* = 8.9, 2.6 1H), 6.64 (d, *J* = 2.6, 1H), 3.78 (s, 3H), 2.92–2.81 (m, 2H), 2.37–2.29 (m, 1H), 2.21–2.13 (m, 1H), 1.94–1.76 (m, 3H), 1.73–1.60 (m, 2H), 1.57–1.31 (m, 7H), 1.28 (s, 3H), 0.90 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 157.6, 138.1, 132.8, 126.4, 113.9, 111.6, 81.8, 55.3, 49.8, 45.9, 44.0, 39.8, 39.2, 31.8, 30.0, 27.6, 26.4, 26.0, 23.1, 14.0; IR (thin film) 3427, 2933, 2870, 1610, 1500 cm^{-1}; $[\alpha]^{26.1}_{D}$ +56.7, $[\alpha]^{26.1}_{577}$ +58.9, $[\alpha]^{26.2}_{546}$ +63.0, $[\alpha]^{26.2}_{435}$ +93.9, $[\alpha]^{26.2}_{405}$ +116.8 (*c* = 1.00, $CHCl_3$).



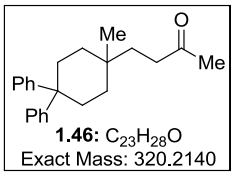
1,3-Dioxoisoindolin-2-yl ((8*R*,9*S*,13*S*,14*S*,17*S*)-3-methoxy-13,17-dimethyl-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[a]phenanthren-17-yl) oxalate (1.39): A round bottom flask was charged with alcohol **1.S7** (500 mg, 1.67 mmol) and DMAP (20 mg, 0.17 mmol, 0.1 equiv) followed by the addition of Et_3N (0.46 mL, 3.33 mmol). A 0.06 M solution of chloro *N*-phthalimidoyl oxalate **1.29** (57 mL, 3.33 mmol) in THF was added via cannula. The resulting heterogeneous mixture was allowed to stir at rt for 4 h. The volatiles were removed under reduced pressure, and the resulting crude residue was dissolved in CH_2Cl_2 (7 mL) then poured into hexanes (200 mL). The resulting

heterogeneous mixture was filtered through a cotton plug and washed with hexanes (2 x 100 mL). The filtrate was concentrated under reduced pressure to yield oxalate **1.39** (786 mg, 1.52 mmol, 91%) as a colorless solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.93–7.90 (m, 2H), 7.85–7.80 (m, 2H), 7.21 (d, *J* = 8.6, 1H), 6.72 (dd, *J* = 8.6, 2.5, 1H), 6.63 (d, *J* = 2.5, 1H), 3.78 (s, 3H), 2.95–2.80 (m, 2H), 2.40–2.16 (m, 4H), 1.96–1.89 (m, 2H), 1.84–1.75 (m, 1H), 1.69–1.29 (m, 6H), 1.64 (s, 3H), 1.00 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.1, 157.6, 154.6, 153.5, 138.0, 135.2, 132.4, 128.9, 126.5, 124.4, 114.0, 111.7, 97.3, 55.4, 48.3, 47.3, 43.8, 39.3, 36.3, 32.0, 29.9, 27.6, 26.2, 23.4, 21.5, 14.5; IR (thin film) 2935, 2874, 1824, 1792, 1748 cm^{-1}; $[\alpha]^{26.0}_{D}$ +33.1, $[\alpha]^{26.0}_{577}$ +34.0, $[\alpha]^{26.0}_{546}$ +34.9, $[\alpha]^{26.0}_{435}$ +47.0, $[\alpha]^{26.0}_{405}$ +59.2 (*c* = 1.00, $CHCl_3$).



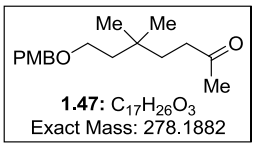
4-(1-Methylcyclohexyl)butan-2-one (1.40). General procedure for the optimization of the coupling of oxalate 1.28 with methyl vinyl ketone: A 1-dram vial was charged with oxalate **1.28** (100 mg, 0.302 mmol), $Ru(bpy)_3(PF_6)_2$ (2.5 mg, 0.003 mmol), Hantzsch ester **1.20** (76 mg, 0.302 mmol), *i*-$Pr_2NEt•HBF_4$ (44 mg, 0.201 mmol), and a magnetic stir bar. A 1:1 mixture of THF:CH_2Cl_2 (2 mL, sparged with Ar for 5 min) was added followed by methyl vinyl ketone (17 μL, 0.201 mmol). The vial was placed in the center of a 30 cm loop of blue LEDs and the mixture was allowed to stir at rt for 14 h. The resulting suspension was filtered through a pad of silica gel, washed with CH_2Cl_2 (10 mL), and the filtrate was concentrated under reduced pressure. The crude residue was purified by silica gel chromatography (98:2 hexanes:EtOAc) to yield ketone **1.40** (27 mg, 0.162 mmol, 80%) as a colorless oil: R_f = 0.45 (9:1 hexanes:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.39–

2.32 (m, 2H), 2.14 (s, 3H), 1.53–1.46 (m, 2H), 1.46–1.16 (m, 10H), 0.83 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 210.0, 38.4, 37.7, 35.5, 32.2, 30.0, 26.5, 24.6, 22.0; IR (thin film) 2926, 2860, 1718, 1448 cm^{-1}; HRMS (CI) *m/z* calcd for $C_{11}H_{24}NO$ $(M + NH_4)^+$ 186.1858, found 186.1862.

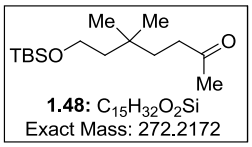


4-(1-Methyl-4,4-diphenylcyclohexyl)butan-2-one (1.46): A 1-dram vial was charged with oxalate **1.30** (146 mg, 0.302 mmol), $Ru(bpy)_3(PF_6)_2$ (2.5 mg, 0.003 mmol), Hantzsch ester **1.20** (76 mg, 0.302 mmol), *i*-$Pr_2NEt•HBF_4$ (44 mg, 0.201 mmol), and a magnetic stir bar. A 1:1 mixture of THF:CH_2Cl_2 (2 mL, sparged with Ar for 5 min) was added followed by methyl vinyl ketone (17 μL, 0.201 mmol). The vial was placed in the center of a 30 cm loop of blue LEDs and the mixture was allowed to stir at rt for 14 h. The suspension was filtered through a pad of silica gel, washed with CH_2Cl_2 (10 mL), and the filtrate was concentrated under reduced pressure. The crude residue was then transferred to a separatory funnel with EtOAc (10 mL) and aqueous 4 M HCl (15 mL). The resulting biphasic mixture was washed with aqueous 4 M HCl (3 x 10 mL) and the organic layer was dried over $MgSO_4$ and evaporated under reduced pressure. The crude residue was purified by flash chromatography (2:1 hexanes:Et_2O) to yield ketone **1.46** (56 mg, 0.175 mmol, 87%) as a clear oil: R_f = 0.45 (9:1 hexanes:EtOAc); ^{1}H NMR (600 MHz, CD_2Cl_2) δ 7.37–7.23 (m, 8H), 7.18–7.09 (m, 2H), 2.45–2.19 (m, 6H), 2.09 (s, 3H) 1.52–1.44 (m, 2H), 1.44–1.30 (m, 4H), 0.90 (s, 3H); ^{13}C NMR (125 MHz, CD_2Cl_2) δ 209.3, 128.7, 128.6, 127.5, 127.0, 125.84, 125.81, 46.2, 38.5, 35.9, 34.3, 32.2, 32.0, 30.1, 24.6; IR (thin

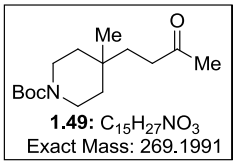
film) 3056, 3029, 2934, 1716 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{23}H_{28}ONa$ $(M + Na)^+$ 343.2038, found 343.2046.



7-((4-Methoxybenzyl)oxy)-5,5-dimethylheptan-2-one (1.47): A 1-dram vial was charged with oxalate **1.34** (133 mg, 0.302 mmol), $Ru(bpy)_3(PF_6)_2$ (2.5 mg, 0.003 mmol), Hantzsch ester **1.20** (76 mg, 0.302 mmol), *i*-$Pr_2NEt•HBF_4$ (44 mg, 0.201 mmol), and a magnetic stir bar. A 1:1 mixture of THF:CH_2Cl_2 (2 mL, sparged with Ar for 5 min) was added followed by methyl vinyl ketone (17 μL, 0.201 mmol). The vial was placed in the center of a 30 cm loop of blue LEDs and the mixture was allowed to stir at rt for 14 h. The suspension was filtered through a pad of silica gel, washed with CH_2Cl_2 (10 mL), and the filtrate was concentrated under reduced pressure. The crude residue was then transferred to a separatory funnel with EtOAc (10 mL) and aqueous 4 M HCl (15 mL). The resulting biphasic mixture was washed with aqueous 4 M HCl (3 x 10 mL) and 2 M NaOH (3 x 10 mL). The organic layer was dried over $MgSO_4$ and evaporated under reduced pressure. The crude residue was purified by flash chromatography (3:1 hexanes:EtOAc) to yield **1.47** as a clear oil (44 mg, 0.158 mmol, 79%): R_f = 0.13 (9:1 hexanes:EtOAc); ^1H NMR (500 MHz, $CDCl_3$) δ 7.24 (d, *J* = 8.5, 2H), 6.87 (d, *J* = 8.5, 2H), 4.40 (s, 2H), 3.80 (s, 3H), 3.48 (t, *J* = 7.5, 2H), 2.43–2.32 (m, 2H), 2.11 (s, 3H), 1.54 (t, *J* = 7.5, 2H), 1.52–1.46 (m, 2H), 0.88 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 209.6, 159.3, 130.8, 129.4, 113.9, 72.9, 67.1, 55.4, 40.8, 39.0, 35.8, 31.9, 30.0, 27.4; IR (thin film) 2955, 2932, 2866, 1714, 1513, cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{17}H_{26}O_3Na$ $(M + Na)^+$ 301.1780, found 301.1769.

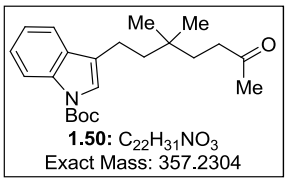


7-((*tert*-Butyldimethylsilyl)oxy)-5,5-dimethylheptan-2-one (1.48): A 1-dram vial was charged with oxalate **1.33** (131 mg, 0.302 mmol), $Ru(bpy)_3(PF_6)_2$ (2.5 mg, 0.003 mmol), Hantzsch ester **1.20** (76 mg, 0.302 mmol), *i*-$Pr_2NEt{\bullet}HBF_4$ (44 mg, 0.201 mmol), and a magnetic stir bar. A 1:1 mixture of THF:CH_2Cl_2 (2 mL, sparged with Ar for 5 min) was added followed by methyl vinyl ketone (17 μL, 0.201 mmol). The vial was placed in the center of a 30 cm loop of blue LEDs and the mixture was allowed to stir at rt for 14 h. The suspension was filtered through a pad of silica gel washed with CH_2Cl_2 (10 mL), and the filtrate concentrated under reduced pressure. The crude residue was purified by flash chromatography (98:2 hexanes:EtOAc) to afford **1.48** as a clear oil (45 mg, 0.165 mmol, 82%): R_f = 0.47 (9:1 hexanes:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.64 (t, *J* = 7.5, 2H), 2.43–2.33 (m, 2H), 2.13 (s, 3H), 1.49–1.43 (m, 4H), 0.87 (s, 15H), 0.03 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 209.5, 60.0, 44.0, 39.1, 35.8, 31.8, 30.0, 27.4, 26.1, 18.4, –5.2; IR (thin film) 2956, 2929, 2857, 1719, 1473 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{15}H_{32}O_2SiNa$ $(M + Na)^+$ 295.2069, found 295.2063.



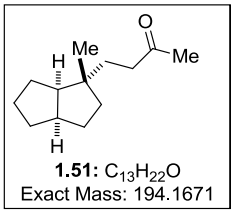
***tert*-Butyl 4-methyl-4-(3-oxobutyl)piperidine-1-carboxylate (1.49)**: A 1-dram vial was charged with oxalate **1.31** (130 mg, 0.302 mmol), $Ru(bpy)_3(PF_6)_2$ (2.5 mg, 0.003 mmol), Hantzsch ester **1.20** (76 mg, 0.302 mmol), *i*-$Pr_2NEt{\bullet}HBF_4$ (44 mg, 0.201 mmol), and a magnetic stir bar. A 1:1 mixture of THF:CH_2Cl_2 (2 mL, sparged with Ar for 5 min) was added followed by methyl vinyl ketone (17 μL, 0.201 mmol). The vial was placed in the center of a 30 cm

loop of blue LEDs and the mixture was allowed to stir at rt for 14 h. The suspension was filtered through a pad of silica gel, washed with CH_2Cl_2 (10 mL), and the filtrate was concentrated under reduced pressure. The crude residue was then transferred to a separatory funnel with EtOAc (10 mL) and aqueous 4 M HCl (15 mL). The resulting biphasic mixture was washed with aqueous 4 M HCl (3 x 10 mL) then 2 M NaOH (3 x 10 mL), the organic layer dried over $MgSO_4$, and evaporated under reduced pressure. The crude residue was purified by flash chromatography (3:1 hexanes:EtOAc) to yield **1.49** (41 mg, 0.166 mmol, 83%) as a clear oil: R_f = 0.13 (9:1 hexanes:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.59–3.51 (m, 2H), 3.19–3.12 (m, 2H), 2.40–2.34 (m, 2H), 2.14 (s, 3H), 1.58–1.49 (m, 2H), 1.43 (s, 9H), 1.35–1.22 (m, 4H), 0.89 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 209.2, 155.1, 79.4, 40.3, 38.0, 36.7, 35.1, 31.0, 30.1, 28.6, 23.1; IR (thin film) 2970, 2927, 1715, 1691, 1422, cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{15}H_{27}NO_3Na$ (M + Na)$^+$ 292.1889, found 292.1888.



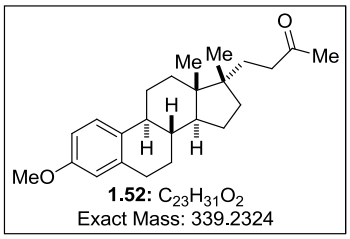
***tert*-Butyl 3-(3,3-dimethyl-6-oxoheptyl)-1*H*-indole-1-carboxylate (1.50)**: A 1-dram vial was charged with oxalate **1.36** (157 mg, 0.302 mmol), $Ru(bpy)_3(PF_6)_2$ (2.5 mg, 0.003 mmol), Hantzsch ester **1.20** (76 mg, 0.302 mmol), *i*-$Pr_2NEt•HBF_4$ (44 mg, 0.201 mmol), and a magnetic stir bar. A 1:1 mixture of THF:CH_2Cl_2 (2 mL, sparged with Ar for 5 min) was added followed by methyl vinyl ketone (17 μL, 0.201 mmol). The vial was placed in the center of a 30 cm loop of blue LEDs and the mixture was allowed to stir at rt for 14 h. The suspension was filtered through a pad of silica gel, washed with CH_2Cl_2 (10 mL), and the filtrate was concentrated under reduced pressure. The crude residue was then

transferred to a separatory funnel with EtOAc (10 mL) and 4 M HCl (15 mL). The resulting biphasic mixture was washed with aqueous 4 M HCl (3 x 10 mL) then aqueous 2 M NaOH (3 x 10 mL). The organic layer was then dried over $MgSO_4$ and evaporated under reduced pressure. The crude residue was purified by flash chromatography (95:5 hexanes:EtOAc to 90:10 hexanes:EtOAc) to afford **1.50** as a clear oil (32 mg, 0.090 mmol, 44%): R_f = 0.28 (9:1 hexanes:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.12 (br s, 1H), 7.49 (d, *J* = 7.9, 1H), 7.34 (br s, 1H), 7.31 (t, *J* = 7.9, 1H), 7.24 (t, *J* =7.5, 1H), 2.68–2.57 (m, 2H), 2.49–2.38 (m, 2H), 2.17 (s, 3H), 1.67 (s, 9H), 1.64–1.57 (m, 4H), 0.98 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 209.6, 150.0, 135.7, 130.8, 124.4, 122.4, 122.0, 121.8, 119.0, 115.4, 83.4, 41.4, 39.1, 35.3, 32.6, 30.2, 26.9, 19.6; IR (thin film) 2956, 2932, 1728, 1453, cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{22}H_{31}NO_3Na$ $(M + Na)^+$ 380.2202, found 380.2192.



4-((*rel*-1*S*,3a*R*,6a*R*)-1-Methyloctahydropentalen-1-yl)butan-2-one (1.51): A 1-dram vial was charged with oxalate **1.37** (107 mg, 0.302 mmol), $Ru(bpy)_3(PF_6)_2$ (2.5 mg, 0.003 mmol), Hantzsch ester **1.20** (76 mg, 0.302 mmol), *i*-$Pr_2NEt•HBF_4$ (44 mg, 0.201 mmol), and a magnetic stir bar. A 1:1 mixture of THF:CH_2Cl_2 (2 mL, sparged with Ar for 5 min) was added followed by methyl vinyl ketone (17 μL, 0.201 mmol). The vial was placed in the center of a 30 cm loop of blue LEDs and the mixture was allowed to stir at rt for 14 h. The suspension was filtered through a pad of silica gel, washed with CH_2Cl_2 (10 mL), and the filtrate was concentrated under reduced pressure. The crude residue was purified by silica gel chromatography (97:3 hexanes:EtOAc) to yield ketone **1.51** (32 mg, 0.165 mmol, 82%)

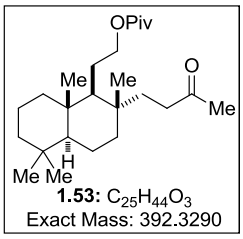
as a clear oil as a single diastereomer: R_f = 0.39 (9:1 hexanes:EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.48–2.41 (m, 1H), 2.40–2.36 (m, 2H), 2.14 (s, 3H), 1.93 (q, *J* = 9 Hz, 1H), 1.88–1.81 (m, 1H), 1.80–1.74 (m, 1H), 1.63–1.58 (m, 1H), 1.55–1.45 (m, 3H), 1.41–1.28 (m, 3H), 1.25–1.16 (m, 2H), 1.14–1.08 (m, 1H), 0.87 (s, 3H). Spectral data matched those previously reported.[9]



1.52: $C_{23}H_{31}O_2$
Exact Mass: 339.2324

((8*R*,9*S*,13*S*,14*S*,17*R*)-3-Methoxy-13,17-dimethyl-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[a]phenanthren-17-yl) butan-2-one (1.52): A 1-dram vial was charged with oxalate **1.39** (156 mg, 0.302 mmol), $Ru(bpy)_3(PF_6)_2$ (2.5 mg, 0.003 mmol), Hantzsch ester **1.20** (76 mg, 0.302 mmol), *i*-$Pr_2NEt•HBF_4$ (44 mg, 0.201 mmol), and a magnetic stir bar. A 1:1 mixture of THF:CH_2Cl_2 (2 mL, sparged with Ar for 5 min) was added followed by methyl vinyl ketone (17 μL, 0.201 mmol). The vial was placed in the center of a 30 cm loop of blue LEDs and the mixture was allowed to stir at rt for 14 h. The suspension was filtered through a pad of silica gel, washed with CH_2Cl_2 (10 mL), and the filtrate was concentrated under reduced pressure. The crude residue was then transferred to a separatory funnel with EtOAc (10 mL) and aqueous 4 M HCl (15 mL). The resulting biphasic mixture was washed with aqueous 4 M HCl (3 x 10 mL) then aqueous 2 M NaOH (3 x 10 mL). The organic layer was dried over $MgSO_4$ and evaporated under reduced pressure. The crude residue was purified by silica gel chromatography (2:1 hexanes:EtOAc) to yield ketone **1.52** (49 mg, 0.144 mmol, 72%) as a clear oil as a single diastereomer: R_f = 0.33 (2:1 hexanes:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.21 (d, *J* =

8.6, 1H), 6.71 (dd, *J* = 8.6, 2.3, 1H), 6.63 (d, *J* = 2.3, 1H), 3.78 (s, 3H), 2.94–2.78 (m, 2H), 2.54–2.37 (m, 2H) 2.32–2.24 (m, 1H), 2.18 (s, 3H), 1.92–1.84 (m, 1H), 1.73–1.59 (m, 3H), 1.59–1.23 (m, 10H), 0.87 (s, 3H), 0.77 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 210.1, 157.5, 138.2, 133.1, 126.4, 113.9, 111.5, 55.3, 49.5, 46.0, 45.4, 43.8, 40.2, 39.6, 33.5, 31.8, 30.4, 30.3, 30.1, 28.3, 26.5, 24.8, 20.8, 16.3; IR (thin film) 2937, 2869, 1716, 1500 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{24}H_{34}O_2Na$ $(M + Na)^+$ 377.2456, found 377.2461; $[\alpha]^{26.0}_D$ +37.3, $[\alpha]^{26.2}_{577}$ +38.4, $[\alpha]^{26.2}_{546}$ +40.3, $[\alpha]^{26.2}_{435}$ +58.7, $[\alpha]^{26.2}_{405}$ +75.2 (*c* = 1.00, $CHCl_3$).

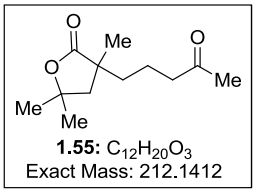


2-((1*S*,2*S*,4a*S*,8a*S*)-2,5,5,8a-Tetramethyl-2-(3-oxobutyl)decahydronaphthalen-1-yl)ethyl pivalate (1.53): A 1-dram vial was charged with oxalate **1.38** (168 mg, 0.302 mmol), $Ru(bpy)_3(PF_6)_2$ (2.5 mg, 0.003 mmol), Hantzsch ester **1.20** (76 mg, 0.302 mmol), *i*-$Pr_2NEt•HBF_4$ (44 mg, 0.201 mmol), and a magnetic stir bar. A 1:1 mixture of THF:CH_2Cl_2 (2 mL, sparged with Ar for 5 min) was added followed by methyl vinyl ketone (17 μL, 0.201 mmol). The vial was placed in the center of a 30 cm loop of blue LEDs and the mixture was allowed to stir at rt for 14 h. The suspension was filtered through a pad of silica gel, washed with CH_2Cl_2 (10 mL), and the filtrate was concentrated under reduced pressure. The crude residue was then transferred to a separatory funnel with EtOAc (10 mL) and aqueous 4 M HCl (15 mL). The resulting biphasic mixture was washed with aqueous 4 M HCl (3 x 10 mL), the organic layer dried over $MgSO_4$, and evaporated under reduced pressure. The crude residue was purified by silica gel chromatography (9:1 hexanes:EtOAc) to yield ketone **1.53** (68 mg, 0.173 mmol,

86%) as a colorless solid as a single diastereomer: R_f = 0.30 (9:1 hexanes:EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.05–3.99 (m, 1H), 3.94–3.87 (m, 1H), 2.39–2.33 (m, 2H), 2.15 (s, 3H), 1.71–1.63 (m, 2H), 1.58–1.45 (m, 5H), 1.45–1.26 (m, 5H), 1.19 (s, 9H), 1.16–1.09 (m, 2H), 0.88–0.82 (m, 1 H), 0.86 (s, 3H), 0.85 (s, 3H), 0.81 (s, 3H), 0.79 (s, 3H), 0.70 (t, *J* = 3.6, 1H); ^{13}C NMR (150 MHz, C_6D_6) δ 206.6, 178.0, 66.6, 56.3, 56.0, 42.3, 40.1, 39.3, 39.1, 38.8, 37.7, 37.4, 37.1, 33.5, 33.4, 29.5, 27.5, 25.9, 21.8, 19.5, 18.8, 18.6, 16.2; IR (thin film) 2958, 2930, 2869, 1723, 1479 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{25}H_{44}O_3Na$ $(M + Na)^+$ 415.3188, found 415.3170; $[\alpha]^{25.8}_D$ +3.6, $[\alpha]^{25.8}_{577}$ +2.3, $[\alpha]^{25.9}_{546}$ –2.5, $[\alpha]^{25.9}_{435}$ –23.7, $[\alpha]^{25.9}_{405}$ –25.0 (*c* = 0.50, $CHCl_3$). Single crystals suitable for X-ray analysis were obtained by slow evaporation from Et_2O-hexanes.[19]

4-((*rel*-3*r*,5*r*,7*r*)-Adamantan-1-yl)butan-2-one (1.16) and (*rel*-3*s*,5*s*,7*s*)-adamantan-1-yl 4-oxopentanoate (1.54): A 1-dram vial was charged with oxalate **1.32** (111 mg, 0.302 mmol), $Ru(bpy)_3(PF_6)_2$ (2.5 mg, 0.003 mmol), Hantzsch ester **1.20** (76 mg, 0.302 mmol), *i*-Pr_2NEt•HBF_4 (44 mg, 0.201 mmol), and a magnetic stir bar. A 1:1 mixture of THF:CH_2Cl_2 (2 mL, sparged with Ar for 5 min) was added followed by methyl vinyl ketone (17 μL, 0.201 mmol). The vial was placed in the center of a 30 cm loop of blue LEDs and the mixture was allowed to stir at rt for 14 h. The suspension was filtered through a pad of silica gel, washed with CH_2Cl_2 (10 mL), and the filtrate was concentrated under reduced pressure. The crude residue was then transferred to a separatory funnel with EtOAc (10 mL) and aqueous 4 M HCl (15 mL). The resulting biphasic mixture was washed with aqueous 4 M HCl (3 x 10 mL), the

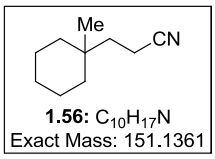
organic layer dried over $MgSO_4$, and evaporated under reduced pressure. The crude residue was purified by flash chromatography (4:1 hexanes:Et_2O) to yield **1.16** (10 mg, 0.048 mmol, 24%) as a clear oil: R_f = 0.45 (4:1 hexanes:Et_2O); ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.42–2.36 (m, 2H), 2.16 (s, 3H), 1.96 (s, 3H), 1.71 (d, *J* = 12.0, 3H), 1.62 (d, *J* = 12.0, 3H), 1.46 (s, 6H), 1.39–1.33 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 210.2, 42.3, 37.9, 37.6, 37.2, 31.9, 30.1, 28.7; IR (thin film) 2903, 2846, 1719, 1451 cm^{-1}; HRMS (CI) *m/z* calcd for $C_{14}H_{26}ON$ $(M + NH_4)^+$ 224.2014, found 224.2005. Purification by flash chromatography (4:1 hexanes:Et_2O) also afforded **1.54** as a clear oil (34 mg, 0.136 mmol, 68%): R_f = 0.20 (4:1 hexanes:Et_2O); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.66 (app. t, *J* = 6.5, 2H), 2.48 (app. t, *J* = 6.5, 2H), 2.17 (s, 3H), 2.13 (br s, 3H), 2.08 (s, 6H), 1.68–1.57 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 207.1, 171.9, 80.8, 41.4, 38.2, 36.3, 30.9, 30.1, 29.5; IR (thin film) 2914, 2854, 1721, 1456 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{15}H_{22}O_3Na$ $(M + Na)^+$ 273.1467, found 273.1459.



1.55: $C_{12}H_{20}O_3$
Exact Mass: 212.1412

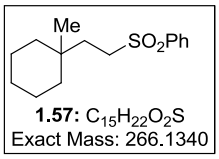
3,5,5-Trimethyl-3-(4-oxopentyl)dihydrofuran-2(3*H*)-one (1.55): A 1-dram vial was charged with oxalate **1.35** (100 mg, 0.302 mmol), $Ru(bpy)_3(PF_6)_2$ (2.5 mg, 0.003 mmol), Hantzsch ester **1.20** (76 mg, 0.302 mmol, 1.5 equiv), *i*-Pr_2NEt HBF_4 (44 mg, 0.201 mmol, 1 equiv), and a magnetic stir bar. A 1:1 mixture of THF:CH_2Cl_2 (2 mL, sparged with Ar for 5 min) was added followed by methyl vinyl ketone (17 μL, 0.201 mmol). The vial was placed in the center of a 30 cm loop of blue LEDs and the mixture was allowed to stir at rt for 14 h. The suspension was filtered through a pad of silica gel, washed with CH_2Cl_2 (10 mL), and the filtrate was concentrated under reduced pressure. The crude residue was then

transferred to a separatory funnel with EtOAc (10 mL) and aqueous 4 M HCl (15 mL). The resulting biphasic mixture was washed with aqueous 4 M HCl (3 x 10 mL) then aqueous 2 M NaOH (3 x 10 mL). The organic layer was dried over $MgSO_4$ and evaporated under reduced pressure. The crude residue was purified by flash chromatography (9:1 hexanes:acetone) to yield **1.55** oil (18 mg, 0.086 mmol, 43%) as a clear: R_f = 0.14 (3:1 hexanes:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.45 (t, *J* = 6.6, 2H), 2.16, (d, *J* = 13.3, 1H), 2.13 (s, 3H), 1.90 (d, *J* = 13.3, 1H), 1.75–1.65 (m, 1H), 1.57–1.51 (m, 2H), 1.50-1.45 (m, 1H), 1.44 (s, 3H), 1.43 (s, 3H), 1.31 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 208.4, 181.6, 81.2, 46.2, 45.2, 43.4, 38.8, 30.23, 30.22, 30.18, 25.9, 18.7; IR (thin film) 2974, 2937, 2876, 1758, 1715 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{12}H_{20}O_3Na$ $(M + Na)^+$ 235.1310, found 235.1310.

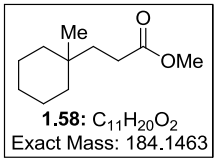


3-(1-Methylcyclohexyl)propanenitrile (1.56): A 1-dram vial was charged with oxalate **1.28** (100 mg, 0.302 mmol), $Ru(bpy)_3(PF_6)_2$ (2.5 mg, 0.003 mmol), Hantzsch ester **1.20** (76 mg, 0.302 mmol), *i*-$Pr_2NEt{\bullet}HBF_4$ (44 mg, 0.201 mmol), and a magnetic stir bar. A 1:1 mixture of THF:CH_2Cl_2 (2 mL, sparged with Ar for 5 min) was added followed by acrylonitrile (13 μL, 0.201 mmol). The vial was placed in the center of a 30 cm loop of blue LEDs and the mixture was allowed to stir at rt for 14 h. The suspension was filtered through a pad of silica gel washed with CH_2Cl_2 (10 mL), and the filtrate was concentrated under reduced pressure. The crude residue was purified by flash chromatography (98:2 hexanes:EtOAc) to yield nitrile **1.56** (28 mg, 0.185 mmol, 92%) as a clear oil: R_f = 0.40 (9:1 hexanes: EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.28–2.24 (m, 2H), 1.67–1.62 (m, 2H), 1.50–1.42

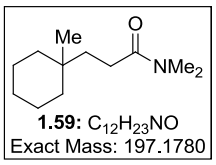
(m, 5H), 1.36–1.30 (m, 1H), 1.30–1.20 (m, 4H), 0.88 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 120.9, 37.6, 37.2, 32.7, 26.3, 24.2, 21.9, 11.8; IR (thin film) 2928, 2856, 2249, 1454 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{10}H_{17}NNa$ $(M + Na)^+$ 174.1259, found 174.1260.



((2-(1-Methylcyclohexyl)ethyl)sulfonyl)benzene (1.57): A 1-dram vial was charged with oxalate **1.28** (100 mg, 0.302 mmol), $Ru(bpy)_3(PF_6)_2$ (2.5 mg, 0.003 mmol), Hantzsch ester **1.20** (76 mg, 0.302 mmol), *i*-Pr_2NEt•HBF_4 (44 mg, 0.201 mmol), phenyl vinyl sulfone (34 mg, 0.201 mmol), and a magnetic stir bar. A 1:1 mixture of THF:CH_2Cl_2 (2 mL, sparged with Ar for 5 min) was then added. The vial was placed in the center of a 30 cm loop of blue LEDs and the mixture was allowed to stir at rt for 14 h. The suspension was filtered through a pad of silica gel washed with CH_2Cl_2 (10 mL), and the filtrate concentrated under reduced pressure. The crude residue was then transferred to a separatory funnel with EtOAc (10 mL) and aqueous 4 M HCl (15 mL). The resulting biphasic mixture was washed with aqueous 4 M HCl (3 x 10 mL). The organic layer dried over $MgSO_4$ and evaporated under reduced pressure. The crude residue was purified by flash chromatography (2:1 hexanes:Et_2O) to yield **1.57** (49 mg, 0.182 mmol, 91%) as a clear oil: R_f = 0.31 (2:1 hexanes:Et_2O); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.92 (d, *J* = 7.9, 2H), 7.66 (t, *J* = 7.2, 1H), 7.58 (t, *J* = 7.9, 2H), 3.07–3.01 (m, 2H), 1.66–1.60 (m, 2H), 1.44–1.33 (m, 5H), 1.31–1.24 (m, 1H), 1.24–1.14 (m, 4 H), 0.80 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.3, 133.7, 129.4, 128.1, 52.1, 37.5, 33.7, 32.4, 26.2, 24.6, 21.8; IR (thin film) 2926, 2857, 1447, 1304, 1148 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{10}H_{17}O_2SNa$ $(M + Na)^+$ 289.1238, found 289.1246.

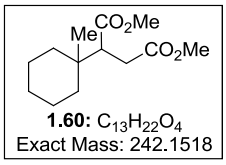


Methyl 3-(1-methylcyclohexyl)propanoate (1.58): A 1-dram vial was charged with oxalate **1.28** (100 mg, 0.302 mmol), $Ru(bpy)_3(PF_6)_2$ (2.5 mg, 0.003 mmol), Hantzsch ester **1.20** (76 mg, 0.302 mmol), *i*-$Pr_2NEt{\bullet}HBF_4$ (44 mg, 0.201 mmol), and a magnetic stir bar. A 1:1 mixture of THF:CH_2Cl_2 (2 mL, sparged with Ar for 5 min) was added followed by methyl acrylate (21 μL, 0.201 mmol). The vial was placed in the center of a 30 cm loop of blue LEDs and the mixture was allowed to stir at rt for 14 h. The suspension was filtered through a pad of silica gel, washed with CH_2Cl_2 (10 mL), and the filtrate was concentrated under reduced pressure. The crude residue was purified by flash chromatography (4:1 hexanes:Et_2O) to yield **1.58** (32 mg, 0.173 mmol, 86%) as a clear oil: R_f = 0.56 (3:1 hexanes:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.66 (s, 3H), 2.27–2.24 (m, 2H), 1.59–1.55 (m, 2H), 1.47–1.35 (m, 5H), 1.35–1.27 (m, 1H), 1.26–1.20 (m, 4H), 0.84 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.2, 51.7, 37.6, 36.8, 32.4, 28.9, 26.5, 24.5, 22.0; IR (thin film) 2925, 2852, 1741, 1436, 1167 cm^{-1}; HRMS (CI) *m/z* calcd for $C_{11}H_{21}O_2$ $(M + H)^+$ 185.1542, found 185.1544.



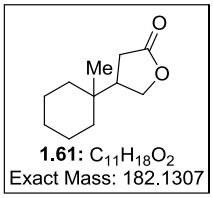
***N,N*-Dimethyl-3-(1-methylcyclohexyl)propanamide (1.59)**: A 1-dram vial was charged with oxalate **1.28** (100 mg, 0.302 mmol), $Ru(bpy)_3(PF_6)_2$ (2.5 mg, 0.003 mmol), Hantzsch ester **1.20** (76 mg, 0.302 mmol), *i*-$Pr_2NEt{\bullet}HBF_4$ (44 mg, 0.201 mmol), and a magnetic stir bar. A 1:1 mixture of THF:CH_2Cl_2 (2 mL, sparged with Ar for 5 min) was added followed by *N*,*N*-dimethylacrylamide (21 μL, 0.201 mmol). The vial was placed in the center of a 30 cm loop of blue LEDs and the mixture was allowed to stir at rt for 14 h. The suspension was

filtered through a pad of silica gel, washed with CH_2Cl_2 (10 mL), and the filtrate was concentrated under reduced pressure. The crude residue was then transferred to a separatory funnel with EtOAc (10 mL) and aqueous 4 M HCl (15 mL). The resulting biphasic mixture was washed with aqueous 4 M HCl (3 x 10 mL) then aqueous 2 M NaOH (3 x 10 mL). The organic layer was dried over $MgSO_4$ and evaporated under reduced pressure. The crude residue was purified by flash chromatography (1:1 hexanes:EtOAc) to yield **1.59** (27 mg, 0.137 mmol, 68%) as a clear oil: R_f = 0.33 (1:1 hexanes:EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.01 (s, 3H), 2.93 (s, 3H), 2.27–2.22 (m, 2H), 1.58–1.53 (m, 2H), 1.49–1.37 (m, 5H), 1.34–1.28 (m, 1H) 1.25 (t, *J* = 6.0, 4H), 0.87 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.1, 37.7, 37.5, 37.1, 35.6, 32.5, 28.0, 26.6, 24.8, 22.1; IR (thin film) 2926, 2858, 1643, 1452 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{12}H_{23}O_4NNa$ $(M + Na)^+$ 220.1677, found 220.1676.



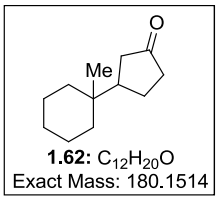
Dimethyl 2-(1-methylcyclohexyl)succinate (1.60): A 1-dram vial was charged with oxalate **1.28** (100 mg, 0.302 mmol), $Ru(bpy)_3(PF_6)_2$ (2.5 mg, 0.003 mmol), Hantzsch ester **1.20** (76 mg, 0.302 mmol), *i*-$Pr_2NEt{\bullet}HBF_4$ (44 mg, 0.201 mmol), dimethyl fumarate (29 mg, 0.201 mmol), and a magnetic stir bar. A 1:1 mixture of THF:CH_2Cl_2 (2 mL, sparged with Ar for 5 min) was then added. The vial was placed in the center of a 30 cm loop of blue LEDs and the mixture was allowed to stir at rt for 14 h. The suspension was filtered through a pad of silica gel, washed with CH_2Cl_2 (10 mL), and the filtrate was concentrated under reduced pressure. The crude residue was then transferred to a separatory funnel with EtOAc (10 mL) and aqueous 4 M HCl (15 mL). The resulting biphasic mixture was washed with

aqueous 4 M HCl (3 x 10 mL). The organic layer was dried over $MgSO_4$ and evaporated under reduced pressure. The crude residue was purified by flash chromatography (2:1 hexanes:Et_2O) to yield **1.60** (45 mg, 0.186 mmol, 88%) as a clear oil: R_f = 0.40 (2:1 hexanes:Et_2O); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.68 (s, 3H), 3.65 (s, 3H), 2.84–2.72 (m, 2H), 2.52–2.41 (m, 1H), 1.64–1.55 (m, 1H), 1.54–1.33 (m, 6H) 1.32–1.18 (m, 3H), 0.91 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.9, 173.5, 51.9, 51.5, 36.4, 35.3, 31.8, 26.1, 21.84, 21.78, 21.0; IR (thin film): 2933, 2856, 1733, 1438 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{13}H_{22}O_4Na$ $(M + Na)^+$ 265.1416, found 265.1417.

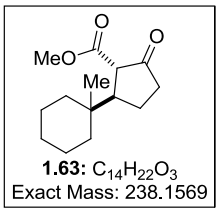


4-(1-Methylcyclohexyl)dihydrofuran-2(3*H*)-one (1.61): A 1-dram vial was charged with oxalate **1.28** (100 mg, 0.302 mmol), $Ru(bpy)_3(PF_6)_2$ (2.5 mg, 0.003 mmol), Hantzsch ester **1.20** (76 mg, 0.302 mmol), *i*-Pr_2NEt•HBF_4 (44 mg, 0.201 mmol), and a magnetic stir bar. A 1:1 mixture of THF:CH_2Cl_2 (2 mL, sparged with Ar for 5 min) was added followed by 2(5*H*)-furanone (14 μL, 0.201 mmol). The vial was placed in the center of a 30 cm loop of blue LEDs and the mixture was allowed to stir at rt for 14 h. The suspension was filtered through a pad of silica gel, washed with CH_2Cl_2 (10 mL), and the filtrate was concentrated under reduced pressure. The crude residue was then transferred to a separatory funnel with EtOAc (10 mL) and aqueous 4 M HCl (15 mL). The resulting biphasic mixture was washed with aqueous 4 M HCl (3 x 10 mL) then aqueous 2 M NaOH (3 x 10 mL). The organic layer was dried over $MgSO_4$ and evaporated under reduced pressure. The crude residue was purified by silica gel chromatography (95:5 hexanes:EtOAc) to yield **1.61** (19 mg, 0.106 mmol, 53%) as a clear oil: R_f 0.39 (9:1

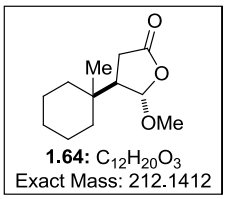
hexanes:EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.30 (app. t, *J* = 8.7, 1H), 4.13 (app. t, *J* = 8.7, 1H), 2.53 (p, *J* = 9.0, 1H), 2.44–2.33 (m, 2H), 1.60–1.54 (m, 1H), 1.54–1.48 (m, 1H), 1.48–1.40 (m, 2H), 1.33–1.27 (m, 2H), 1.27–1.16 (m, 4H), 0.89 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.7, 69.3, 35.9, 35.4, 33.9, 29.2, 26.2, 21.58, 21.55; IR (thin film) 2926, 2855, 1780, 1462 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{11}H_{18}O_2Na$ $(M + Na)^+$ 205.1205, found 205.1207.



3-(1-Methylcyclohexyl)cyclopentan-1-one (1.62): A 1-dram vial was charged with oxalate **1.28** (100 mg, 0.302 mmol), $Ru(bpy)_3(PF_6)_2$ (2.5 mg, 0.003 mmol), Hantzsch ester **1.20** (76 mg, 0.302 mmol), *i*-$Pr_2NEt{\cdot}HBF_4$ (44 mg, 0.201 mmol), and a magnetic stir bar. A 1:1 mixture of THF:CH_2Cl_2 (2 mL, sparged with Ar for 5 min) was added followed by cyclopentenone (17 μL, 0.201 mmol). The vial was placed in the center of a 30 cm loop of blue LEDs and the mixture was allowed to stir at rt for 14 h. The suspension was filtered through a pad of silica gel, washed with CH_2Cl_2 (10 mL), and the filtrate was concentrated under reduced pressure. The crude residue was purified by flash chromatography (4:1 hexanes:Et_2O) to yield **1.62** (20 mg, 0.111 mmol, 56%) as a clear oil: R_f = 0.35 (4:1 hexanes:Et_2O); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.36–2.28 (m, 1H), 2.22–2.06 (m, 3H), 2.00–1.90 (m, 2H), 1.65–1.58 (m, 1H), 1.58–1.38 (m, 5H), 1.38–1.31 (m, 1H), 1.30–1.20 (m, 4H), 0.86 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 220.2, 39.7, 39.4, 36.6, 36.0, 34.2, 26.5, 23.3, 21.89, 21.86; IR (thin film) 2925, 2850, 1743, 1446, 1157 cm^{-1}; HRMS (CI) *m/z* calculated for $C_{12}H_{24}NO$ $(M + NH_4)^+$ 189.1858, found 198.1850.

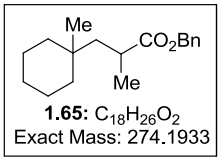


Methyl (*rel*-1*S*,2*R*)-2-(1-methylcyclohexyl)-5-oxocyclopentane-1-carboxylate (1.63): A 1-dram vial was charged with oxalate **1.28** (100 mg, 0.302 mmol), $Ru(bpy)_3(PF_6)_2$ (2.5 mg, 0.003 mmol), Hantzsch ester **1.20** (76 mg, 0.302 mmol), *i*-$Pr_2NEt{\bullet}HBF_4$ (44 mg, 0.201 mmol), 2-carboxymethyl-2-cyclopenten-1-one[57] (28 mg, 0.201 mmol) and a magnetic stir bar. A 1:1 mixture of THF:CH_2Cl_2 (2 mL, sparged with Ar for 5 min) was then added. The vial was placed in the center of a 30 cm loop of blue LEDs and the mixture was allowed to stir at rt for 14 h. The suspension was filtered through a pad of silica gel, washed with CH_2Cl_2 (10 mL), and the filtrate was concentrated under reduced pressure. The crude residue was then transferred to a separatory funnel with EtOAc (10 mL) and aqueous 4 M HCl (15 mL). The resulting biphasic mixture was washed with aqueous 4 M HCl (3 x 10 mL). The organic layer was dried over $MgSO_4$ and evaporated under reduced pressure. The crude residue was purified by flash chromatography (2:1 hexanes:Et_2O) to yield **1.63** (30.5 mg, 0.128 mmol, 64%) as a clear oil: R_f = 0.41 (9:1 Hexanes:EtOAc); ^1H NMR (600 MHz, $CDCl_3$) δ 3.73 (s, 3H), 3.06 (d, *J* = 11.4, 1H), 2.74–2.65 (m, 1H), 2.46–2.29 (m, 2H), 2.09–2.01 (m, 1H), 1.66–1.58 (m, 1H), 1.56–1.48 (m, 3H), 1.46–1.35 (m, 3H), 1.30–1.24 (m, 2H), 1.23–1.19 (m, 2H), 0.88 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 212.9, 171.4, 56.9, 52.6, 38.9, 36.5, 36.1, 34.9, 26.3, 21.8, 21.7, 21.5; IR (thin film) 2927, 2853, 1757, 1728 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{14}H_{22}O_3Na$ $(M + Na)^+$ 261.1467, found 261.1471.



1.64: $C_{12}H_{20}O_3$
Exact Mass: 212.1412

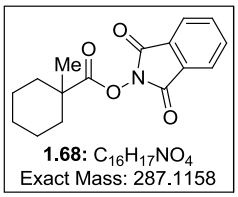
(*rel*-4*R*,5*S*)-5-Methoxy-4-(1-methylcyclohexyl)dihydrofuran-2(3*H*)-one (1.64): A 1-dram vial was charged with oxalate **1.28** (100 mg, 0.302 mmol), $Ru(bpy)_3(PF_6)_2$ (2.5 mg, 0.003 mmol), Hantzsch ester **1.20** (76 mg, 0.302 mmol), *i*-$Pr_2NEt{\bullet}HBF_4$ (44 mg, 0.201 mmol), 5-methoxy-2(5*H*)-furanone (23 mg, 0.201 mmol), and a magnetic stir bar. A 1:1 mixture of THF:CH_2Cl_2 (2 mL, sparged with Ar for 5 min) was then added. The vial was placed in the center of a 30 cm loop of blue LEDs and the mixture was allowed to stir at rt for 14 h. The suspension was filtered through a pad of silica gel, washed with CH_2Cl_2 (10 mL), and the filtrate was concentrated under reduced pressure. The crude residue was then transferred to a separatory funnel with EtOAc (10 mL) and aqueous 4 M HCl (15 mL). The resulting biphasic mixture was washed with aquous 4 M HCl (3 x 10 mL). The organic layer was dried over $MgSO_4$ and evaporated under reduced pressure. The crude residue was purified by flash chromatography (2:1 hexanes:Et_2O) to yield **1.64** (31 mg, 0.147 mmol, 73%) as a clear oil: R_f = 0.31 (9:1 Hexanes:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.22 (d, *J* = 2.8, 1H), 3.48 (s, 3H), 2.62 (dd, *J* = 18.4, 10.0, 1H), 2.36 (dd, *J* = 18.4, 6.0, 1H), 2.27 (ddd, *J* = 18.4, 6.0, 2.8, 1H), 1.60–1.38 (m, 5H), 1.36–1.14 (m, 5H), 0.86 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.4, 106.9, 57.0, 35.5, 35.3, 33.8, 29.0, 26.1, 21.49, 21.47; IR (thin film) 2927, 2853, 1785, 1113 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{12}H_{20}O_3Na$ $(M + Na)^+$ 235.1310, found 235.1316.



1.65: $C_{18}H_{26}O_2$
Exact Mass: 274.1933

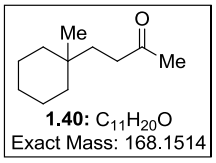
Benzyl 2-methyl-3-(1-methylcyclohexyl)propanoate (1.65): A 1-dram vial was charged with oxalate **1.28** (100 mg, 0.302 mmol),

$Ru(bpy)_3(PF_6)_2$ (2.6 mg, 0.003 mmol), Hantzsch ester **1.20** (76 mg, 0.302 mmol), *i*-$Pr_2NEt•HBF_4$ (44 mg, 0.201 mmol) and a magnetic stir bar under argon. After sequential addition of CH_2Cl_2, (1 mL, sparged with Ar for 5 min), THF (1 mL, sparged with Ar for 5 min), and benzyl methacrylate (34 μL, 0.201 mmol), the vial was capped and placed in the center of a 30 cm loop of blue LEDs. The reaction mixture was stirred for 18 h, after which it was concentrated under reduced pressure. The yield of product obtained was determined by comparison of diagnostic ^{1}H NMR signals to those of an internal standard (1,4-dimethoxybenzene). An analytically pure sample of **1.65** was obtained by silica gel chromatography (2.5% EtOAc/hexanes) to provide **1.65** as a clear oil: R_f = 0.57 (10% EtOAc/hexanes); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.38–7.30 (m, 5H), 5.12–5.07 (m, 2H), 2.61–2.55 (m, 1H), 1.90 (dd, *J* = 14.2, 9.0, 1H), 1.44–1.31 (m, 5H), 1.28–1.15 (m, 9H), 0.83 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.0, 136.3, 128.6, 128.4, 128.2, 66.3, 38.1, 37.7, 35.4, 33.3, 26.5, 22.11, 22.10, 20.7; IR (thin film) 2925, 2850, 1736, 1455, 1145.cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{18}H_{26}O_2Na$ $(M + Na)^+$ 297.1830, found 297.1835.

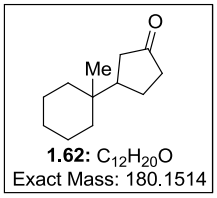


1,3-Dioxoisoindolin-2-yl 1-methylcyclohexane-1-carboxylate (1.68): A round bottom flask was charged with 1-methyl-1-cyclohexanecarboxylic acid (5.00 g, 35.2 mmol), *N*-hydroxyphthalimide (8.61 g, 52.8 mmol) and *N, N'*-dicyclohexylcarbodiimide (10.88 g, 52.8 mmol) under argon. After sequential addition of THF (350 mL) and DMAP (430 mg, 3.5 mmol), the reaction mixture was stirred at rt overnight. After this time, the heterogeneous mixture was concentrated under reduced pressure and the resulting residue suspended in Et_2O (400 mL). The mixture was filtered through cotton, transferred to a

separatory funnel, and washed with saturated aqueous NH_4Cl solution (3 x 200 mL). The organic layer was dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude residue obtained was purified by silica gel chromatography (7% EtOAc/hexanes) to give (*N*-acyloxy)phthalimide **1.68** (9.05 g, 31.5 mmol, 90%) as a colorless solid: R_f = 0.26 (10% EtOAc/hexanes); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.90–7.84 (m, 2H), 7.79–7.75 (m, 2H), 2.26–2.20 (m, 2H), 1.69–1.51 (m, 5H), 1.42 (s, 3H), 1.40–1.34 (m, 2H), 1.33–1.23 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.7, 162.3, 134.7, 129.2, 123.9, 43.2, 35.8, 26.8, 25.5, 23.1; IR (thin film) 2934, 2860, 1807, 1782, 1743 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{16}H_{17}NO_4Na$ $(M + Na)^+$ 310.1055, found 310.1051.

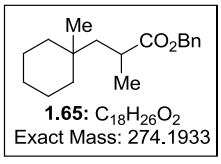


4-(1-Methylcyclohexyl)butan-2-one (1.40). Coupling of (*N*-acyloxy)phthalimide 1.68 with methyl vinyl ketone: A 1-dram vial was charged with (*N*-acyloxy)phthalimide **1.68** (75 mg, 0.261 mmol), $Ru(bpy)_3(PF_6)_2$ (2 mg, 0.003 mmol), Hantzsch ester **1.20** (100 mg, 0.39 mmol) and a magnetic stir bar under argon. After sequential addition of CH_2Cl_2 (1.75 mL, sparged with Ar for 5 min), methyl vinyl ketone (33 μL, 0.39 mmol) and *i*-Pr_2NEt (100 μL, 0.57 mmol), the vial was capped and placed in the center of a 30 cm loop of blue LEDs. The reaction mixture was stirred for 1.5 h at rt, after which it was concentrated under reduced pressure. The crude residue was purified by silica gel chromatography (2.5% EtOAc/hexanes) to provide ketone **1.40** (40 mg, 0.237 mmol, 91%) as a clear oil. Spectral data obtained for **1.40** matched those reported above.



1.62: $C_{12}H_{20}O$
Exact Mass: 180.1514

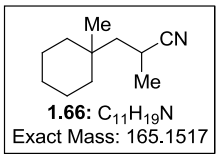
3-(1-Methylcyclohexyl)cyclopentan-1-one (1.62). Coupling of (*N*-acyloxy)phthalimide 1.68 with cyclopentenone: A 1-dram vial was charged with (*N*-acyloxy)phthalimide **1.68** (75 mg, 0.261 mmol), $Ru(bpy)_3(PF_6)_2$ (2 mg, 0.003 mmol), Hantzsch ester **1.20** (100 mg, 0.39 mmol) and a magnetic stir bar under argon. After sequential addition of CH_2Cl_2 (1.75 mL, sparged with Ar for 5 min), cyclopentenone (33 μL, 0.39 mmol) and *i*-Pr_2NEt (100 μL, 0.57 mmol), the vial was capped and placed in the center of a 30 cm loop of blue LEDs. The reaction mixture was stirred for 2 h at rt, after which it was concentrated under reduced pressure. The crude residue was purified by silica gel chromatography (2.5% EtOAc/hexanes) to provide **1.62** (37 mg, 0.208 mmol, 80%) as a clear oil. Spectral data obtained for **1.62** matched those reported above.



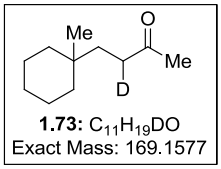
1.65: $C_{18}H_{26}O_2$
Exact Mass: 274.1933

Benzyl 2-methyl-3-(1-methylcyclohexyl)propanoate (1.65). Coupling of (*N*-acyloxy)phthalimide 1.68 with benzyl methacrylate: A 1-dram vial was charged with (*N*-acyloxy)phthalimide **1.68** (75 mg, 0.261 mmol), $Ru(bpy)_3(PF_6)_2$ (2 mg, 0.003 mmol), Hantzsch ester **1.20** (100 mg, 0.39 mmol) and a magnetic stir bar under argon. After sequential addition of CH_2Cl_2 (1.75 mL, sparged with Ar for 5 min), benzyl methacrylate (66 μL, 0.39 mmol) and *i*-Pr_2NEt (100 μL, 0.57 mmol), the vial was capped and placed in the center of a 30 cm loop of blue LEDs. The reaction mixture was stirred for 18 h at rt, after which 1,4-dimethoxybenzene (36 mg, 0.261 mmol, 1 equiv) was added as an NMR internal standard and the reaction mixture was concentrated. The yield of product obtained (0.154 mmol, 59%) was determined by examining the relative integration of

NMR signals using the internal standard (1,4-dimethoxybenzene). An analytically pure sample of **1.65** was obtained by silica gel chromatography (2.5% EtOAc/hexanes) to provide **1.65** as a clear oil. Spectral data obtained for **1.65** matched those reported above.

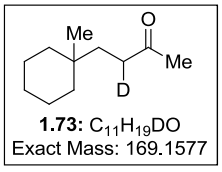


2-Methyl-3-(1-methylcyclohexyl)propanenitrile (1.66): A 1-dram vial was charged with (*N*-acyloxy)phthalimide **1.68** (75 mg, 0.261 mmol), $Ru(bpy)_3(PF_6)_2$ (2 mg, 0.003 mmol), Hantzsch ester **1.20** (100 mg, 0.39 mmol) and a magnetic stir bar under argon. After sequential addition of CH_2Cl_2 (1.75 mL, sparged with Ar for 5 min), methacrylonitrile (33 μL, 0.39 mmol) and *i*-Pr_2NEt (100 μL, 0.57 mmol), the vial was capped and placed in the center of a 30 cm loop of blue LEDs. The reaction mixture was stirred for 18 h at rt, after which it was concentrated under reduced pressure. The crude residue was purified by silica gel chromatography (2.5% EtOAc/hexanes) to provide nitrile **1.66** (36 mg, 0.217 mmol, 83%) as a clear oil. R_f = 0.47 (10% EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.64–2.57 (m, 1H), 1.77 (dd, *J* = 14.1, 13.4, 1H), 1.58–1.4 (m, 5H), 1.39–1.22 (m, 8H), 0.97 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 124.5, 38.0, 37.6, 33.2, 26.3, 22.0, 21.9, 20.8, 20.2; IR (thin film) 2927, 2853, 2237, 1455, 1382 cm^{-1}; HRMS-ESI *m/z* $(M + Na)^+$ calcd for $C_{11}H_{19}NNa$ 188.1415, found 188.1408.



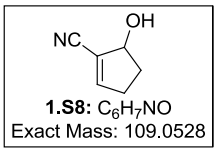
4-(1-Methylcyclohexyl)butan-2-one-3-*d* (1.73). Coupling of phthalimidoyl oxalate 1.28 with methyl vinyl ketone in the presence of 4,4-d_2-Hantzsch ester 1.72: A 1-dram vial was charged with oxalate **1.28** (100 mg, 0.302 mmol), $Ru(bpy)_3(PF_6)_2$ (2 mg, 0.003 mmol), 4,4-d_2-

Hantzsch ester **1.72** (77 mg, 0.302 mmol)[58], *i*-Pr_2NEt•HBF_4 (44 mg, 0.201 mmol) and a magnetic stir bar under argon. After sequential addition of CH_2Cl_2, (1 mL, sparged with Ar for 5 min), THF (1 mL, sparged with Ar for 5 min), and methyl vinyl ketone (17 μL, 0.201 mmol), the vial was capped and placed in the center of a 30 cm loop of blue LEDs. The reaction mixture was stirred for 18 h at rt, after which it was concentrated under reduced pressure. Purification of the crude residue by silica gel chromatography (2.5% EtOAc/Hx) provided ketone **1.73** (13 mg, 0.07 mmol, 37%) as a colorless oil: R_f = 0.43 (10% EtOAc/hexanes); ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.39–2.30 (m, 1H), 2.15 (s, 3H), 1.49 (d, *J* = 8.4, 2 H), 1.46–1.38 (m, 5H), 1.33–1.20 (m, 5H), 0.83 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 210.2, 38.1 (t, *J* = 20.2), 37.7, 32.3, 30.0, 29.8, 26.5, 24.7, 22.1; IR (thin film) 2925, 2853, 1716, 1356 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{11}H_{19}DONa$ $(M + Na)^+$ 192.1475, found 192.1484.

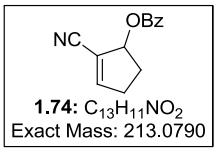


4-(1-Methylcyclohexyl)butan-2-one-3-*d* (1.73). Coupling of (*N*-acyloxy)phthalimide 1.68 with methyl vinyl ketone in the presence of 4,4-*d*$_2$-Hantzsch ester 1.72: A 1-dram vial was charged with (*N*-acyloxy)phthalimide **1.68** (75 mg, 0.26 mmol), $Ru(bpy)_3(PF_6)_2$ (2 mg, 0.003 mmol), 4,4-*d*$_2$-Hantzsch ester **1.72** (100 mg, 0.39 mmol) and a magnetic stir bar under argon. After sequential addition of CH_2Cl_2 (1.75 mL, sparged with Ar for 5 min), methyl vinyl ketone (32 μL, 0.39 mmol) and *i*-Pr_2NEt (100 μL, 0.57 mmol), the vial was capped and placed in the center of a 30 cm loop of blue LEDs. The reaction mixture was stirred for 18 h at rt, after which it was concentrated under reduced pressure. Purification by silica gel chromatography (2.5 EtOAc/hexanes) provided ketone **1.73** (21 mg, 0.13 mmol, 48%) as

a colorless oil. Spectral data acquired for **1.73** matched those described previously. Analysis of the compound by ^{1}H NMR confirmed that the deuterium incorporation was 38%.

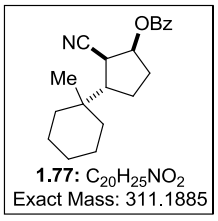


5-Hydroxycyclopent-1-ene-1-carbonitrile (1.S8): A solution of 2,5-dimethoxytetrahydrofuran (3.2 mL, 24.7 mmol, mixture of *cis* and *trans*) in aqueous 0.6 M HCl (20 mL) was heated to 70 °C for 2 h. The mixture was cooled to rt and sat. aqueous $KHCO_3$ solution (14 mL) was added to neutralize the reaction mixture. Diethyl cyanomethylphosphonate (4.00 mL, 24.7 mmol) was added, followed by aqueous 5 M K_2CO_3 (10 mL), and the mixture was stirred at rt for 48 h. After this time, the solution was transferred to a separatory funnel and extracted with EtOAc (3 x 50 mL). The organic layers were combined, dried over $MgSO_4$ and filtered through cotton. Concentration of the filtrate under reduced pressure provided a crude residue which was purified by silica gel chromatography (25–50% EtOAc/hexanes) to yield alcohol **1.S8** (2.25 g, 20.7 mmol, 84%) as a colorless oil. Spectral data acquired for **1.S8** matched that previously reported.[59]



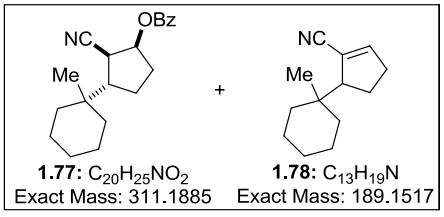
2-Cyanocyclopent-2-en-1-yl benzoate (1.74): A round-bottom flask was charged with alcohol **1.S8** (500 mg, 4.58 mmol), and Et_3N (1.3 mL, 9.17 mmol), DMAP (56 mg, 0.45 mmol) and THF (15 mL) were added sequentially under argon. The solution was cooled to 0 °C and BzCl (1.1 mL, 9.17 mmol) was added dropwise. The cloudy suspension was stirred while warming to rt over 18 h. After this time, the reaction mixture was cooled to 0 °C and quenched with

saturated aqueous NH_4Cl solution (10 mL). The contents of the flask were transferred to a separatory funnel, diluted with Et_2O (50 mL) and the layers separated. The organic layer was washed with saturated aqueous NH_4Cl solution (3 x 40 mL), aqueous 1 N NaOH (3 x 40 mL), and brine (2 x 40 mL). The organic layer was dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude residue was purified by silica gel chromatography (10-20% EtOAc/hexanes) to provide **1.74** (862 mg, 4.04 mmol, 88%) as a clear oil: R_f = 0.14 (10% EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (d, *J* = 7.9, 2H), 7.57 (t, *J* = 7.9, 1 H), 7.44 (t, *J*= 7.9, 2H) 7.03–7.00 (m, 1H), 6.08–6.04 (m, 1H), 2.81–2.73 (m, 1H), 2.64–2.56 (m, 2H), 2.09–2.02 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.8, 154.3, 133.3, 129.7, 129.5, 128.4, 115.1, 114.9, 79.3, 32.1, 30.6; IR (thin film) 3069, 2950, 2226, 1972, 1915, 1720 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{13}H_{11}NO_2Na$ $(M + Na)^+$ 236.0687, found 236.0678.



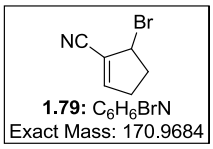
(*rel*-1*S*,2*S*,3*S*)-2-Cyano-3-(1-methylcyclohexyl)cyclopentyl benzoate (1.77). Coupling of *N*-phthalimidoyl oxalate 1.28 with cyclopentene nitrile 1.74: A 1-dram vial was charged with oxalate **1.28** (100 mg, 0.302 mmol), $Ru(bpy)_3(PF_6)_2$ (3 mg, 0.003 mmol), Hantzsch ester **1.20** (76 mg, 0.302 mmol), *i*-Pr_2NEt•HBF_4 (44 mg, 0.20 mmol) and a magnetic stir bar under argon. After sequential addition of CH_2Cl_2 (1 mL, sparged with Ar for 5 min), THF (1 mL, sparged with Ar for 5 min), and cyclopentene nitrile **1.74** (43 mg, 0.20 mmol), the vial was capped and placed in the center of a 30 cm loop of blue LEDs. The reaction mixture was stirred for 18 h at rt, after which it was diluted with Et_2O (30 mL) and transferred to a separatory funnel. The ether layer was washed with aqueous 4 N HCl (4 x

20 mL) and aqueous 2 N NaOH (3 x 20 mL) and was dried over $MgSO_4$. The organic layer was filtered and concentrated under reduced pressure. The crude residue was subjected to silica gel chromatography (4% acetone/hexanes) to provide **1.77** (34 mg, 0.110 mmol, 55%) as a colorless oil: Data for major diastereomer (**8**:2:1:1): R_f = 0.40 (10% EtOAc/hexanes); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.10 (d, *J* = 8.0, 2 H), 7.58 (t, *J* = 7.4, 1 H), 7.45 (t, *J* = 8.0, 2H), 5.30 (app. q, *J* = 7.6, 1H), 3.42–3.39 (m, 1H), 2.31–2.24 (m, 1H), 2.10–1.96 (m, 3H), 1.82–1.76 (m, 1H), 1.60–1.55 (m, 2H), 1.53–1.45 (m, 6H), 1.31–1.22 (m, 2H), 1.14 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.2, 133.5, 130.0, 129.6, 128.6, 118.6, 74.4, 37.01, 37.0, 35.3, 34.5, 28.2, 26.2, 21.9, 21.62, 21.61; IR (thin film) 2925, 2853, 1722, 1271 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{20}H_{25}NO_2Na$ $(M + Na)^+$ 334.1783, found 334.1789. Data for minor diastereomer (8:**2**:1:1): R_f = 0.44 (10% EtOAc/hexanes); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.00 (d, *J* = 8.1, 2H), 7.6 (t, *J* = 7.6, 1H), 7.46 (t, *J* = 7.6, 2H), 5.52–5.50 (m, 1H), 3.08–3.05 (m, 1H), 2.53–2.46 (m, 1H), 2.25–2.19 (m, 1H), 1.96–1.78 (m, 3H), 1.60–1.45 (m, 8H), 1.34–1.23 (m, 2H), 1.13 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.6, 133.5, 129.8, 129.7, 128.6, 119.9, 78.5, 37.5, 37.1, 36.9, 34.1, 30.6, 26.3, 23.1, 22.0, 21.7. The relative stereochemistry of the major and minor diastereomers was assigned by nOe analysis.



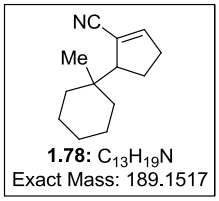
(*rel*-1*S*,2*S*,3*S*)-2-Cyano-3-(1-methylcyclohexyl)cyclopentyl benzoate (1.77) and 5-(1-Methylcyclohexyl)cyclopent-1-ene-1-carbonitrile (1.78). Coupling of (*N*-acyloxy)phthalimide 1.68 with cyclopentene nitrile 1.74: A 1-dram vial was charged with (*N*-acyloxy)phthalimide **1.68** (75 mg, 0.261 mmol), $Ru(bpy)_3(PF_6)_2$ (2 mg, 0.003 mmol), Hantzsch ester **1.20** (100 mg, 0.39 mmol)

and a magnetic stir bar under argon. After sequential addition of CH_2Cl_2 (1.75 mL, sparged with Ar for 5 min), cyclopentene nitrile **1.74** (84 mg, 0.39 mmol) and *i*-Pr_2NEt (100 μL, 0.57 mmol), the vial was capped and placed in the center of a 30 cm loop of blue LEDs. The reaction mixture was stirred for 18 h at rt, after which it was diluted with Et_2O (30 mL) and transferred to a separatory funnel. The organic layer was washed with aqueous 4 N HCl (4 x 20 mL) and aqueous 2 N NaOH (3 x 20 mL) and was dried over $MgSO_4$. The organic layer was filtered and concentrated under reduced pressure. The crude residue was subjected to silica gel chromatography (4% acetone/hexanes) to provide **1.77** (23 mg, 0.07 mmol, 29%, dr 8:2:1:1) and **1.78** (25 mg, 0.13 mmol, 51%) as clear oils. Spectral data acquired for **1.77** matched those reported above. Data for **1.78**: R_f = 0.47 (10% EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.79–6.76 (m, 1H), 2.89–2.83 (m, 1H), 2.50–2.34 (m, 2H), 2.01–1.92 (m, 1H), 1.87–1.79 (m, 1H), 1.64–1.38 (m, 7H), 1.36–1.18 (m, 3H), 0.88 (s, 3H);^{13}C NMR (125 MHz, $CDCl_3$) δ 152.4, 118.7, 116.7, 36.7, 36.1, 36.0, 33.0, 26.3, 25.2, 22.0, 21.8 ; IR (thin film) 2926, 2853, 2215, 1459 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{13}H_{19}NNa$ $(M + Na)^+$ 212.1415, found 212.1405.

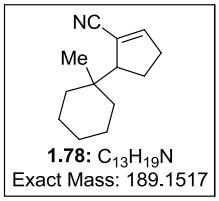


5-Bromocyclopent-1-ene-1-carbonitrile (1.79): A round-bottom flask was charged with alcohol **1.S8** (400 mg, 3.67 mmol), and Et_2O (16 mL) and CBr_4 (2.43 g, 7.34 mmol) were added sequentially under argon. The solution was cooled to 0 °C and PPh_3 (1.92 g, 7.34 mmol) was added in one portion. The resulting heterogeneous mixture was allowed to warm to rt while stirring for 3 h. After this time, the reaction mixture was filtered through a plug of Celite and the filtrate was concentrated under reduced pressure. The crude residue was purified by silica

gel chromatography (10-15% EtOAc/hexanes) to yield **1.79** (304 mg, 1.78 mmol, 48%) as a clear oil: R_f = 0.26 (10% EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.87–6.82 (m, 1H), 5.09–5.04 (m, 1H), 2.86–2.75 (m, 1H), 2.63–2.52 (m, 2H), 2.50–2.42 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.9, 119.1, 114.7, 53.1, 35.5, 32.3; IR (thin film) 2927, 2227, 1607, 1189, 1010 cm^{-1}; HRMS (ESI) *m/z* calculated for C_6H_7BrN $(M + H)^+$ 193.9581, found 193.9582.



5-(1-Methylcyclohexyl)cyclopent-1-ene-1-carbonitrile (1.78). Coupling of oxalate 1.28 with bromocyclopentene nitrile 1.79: A 1-dram vial was charged with oxalate **1.28** (100 mg, 0.302 mmol), $Ru(bpy)_3(PF_6)_2$ (3 mg, 0.003 mmol), Hantzsch ester **1.20** (76 mg, 0.302 mmol), *i*-$Pr_2NEt•HBF_4$ (44 mg, 0.20 mmol) and a magnetic stir bar under argon. After sequential addition of CH_2Cl_2 (1 mL, sparged with Ar for 5 min), THF (1 mL, sparged with Ar for 5 min), and bromocyclopentene nitrile **1.79** (34 mg, 0.20 mmol), the vial was capped and placed in the center of a 30 cm loop of blue LEDs. The reaction mixture was stirred for 18 h at rt, after which it was concentrated under reduced pressure. The crude residue was subjected to silica gel chromatography (2% EtOAc/hexanes) to provide **1.78** (22 mg, 0.114 mmol, 57%) as a colorless oil. Spectral data for **1.78** matched those reported above.

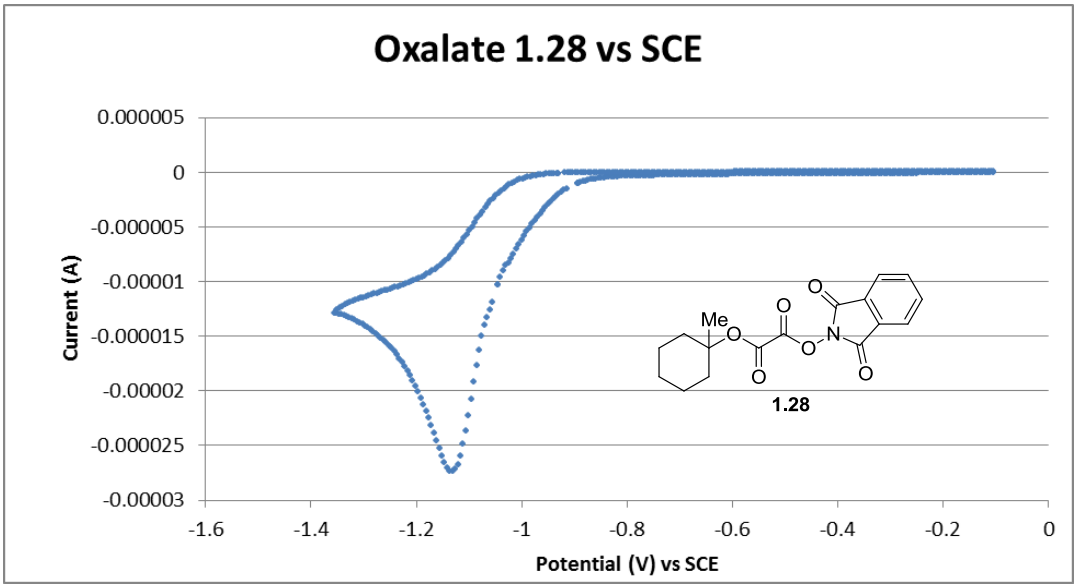


5-(1-Methylcyclohexyl)cyclopent-1-ene-1-carbonitrile (1.78). Coupling of (*N*-acyloxy)phthalimide 1.68 with bromocyclopentene nitrile 1.79: A 1-dram vial was charged with (*N*-acyloxy)phthalimide **1.68** (75 mg, 0.261 mmol), $Ru(bpy)_3(PF_6)_2$ (2 mg, 0.003 mmol), Hantzsch ester **1.20** (100

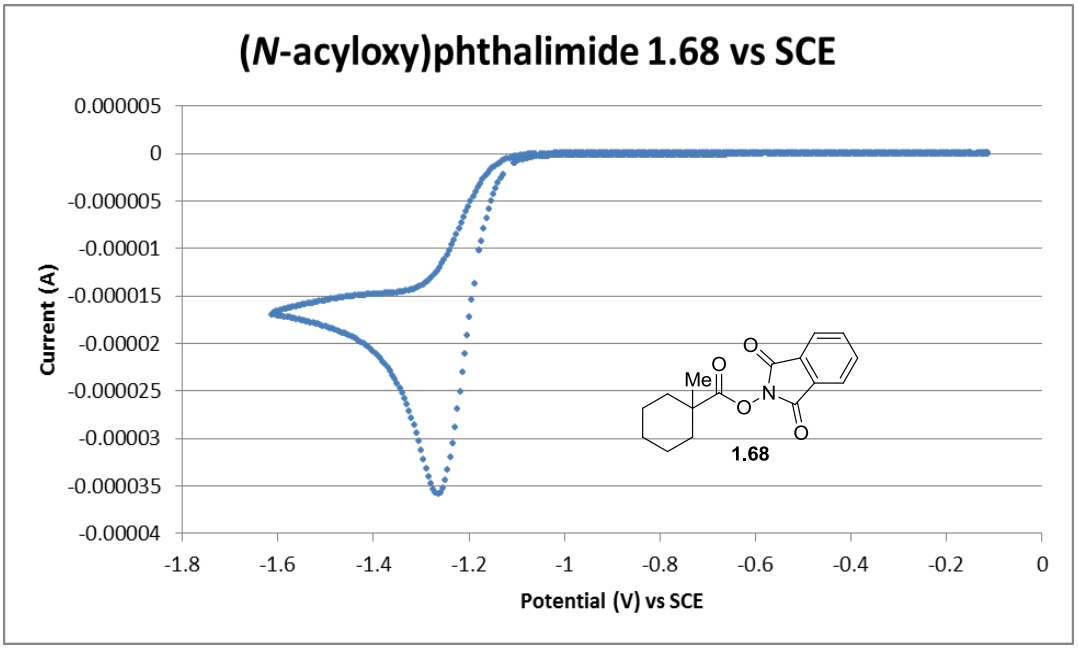
mg, 0.39 mmol) and a magnetic stir bar under argon. After sequential addition of CH_2Cl_2 (1.75 mL, sparged with Ar for 5 min), bromocyclopentene nitrile **1.79** (67 mg, 0.39 mmol) and *i*-Pr_2NEt (100 μL, 0.57 mmol), the vial was capped and placed in the center of a 30 cm loop of blue LEDs. The reaction mixture was stirred for 18 h at rt, after which it was concentrated under reduced pressure. The crude residue was subjected to silica gel chromatography (2% EtOAc/hexanes) to provide **1.78** (30 mg, 0.156 mmol, 60%) as a clear oil. Spectral data acquired for **1.78** matched those reported above.

1.5 Cyclic Voltammetry Experiments

Cyclic Voltammetry was conducted using a Pine Research Instruments Wavedriver potentiostat, a glassy carbon disk working electrode, a glassy carbon rod counter electrode, and a Ag/Ag^+ reference electrode (Vycor tip). Samples were prepared with a substrate concentration of 0.01 M in a 0.1 M Bu_4NBF_4 in MeCN electrolyte solution. Data was collected with a sweep rate of 100 mV/s. Reduction potentials were measured in reference to ferrocene and were converted to reference the saturated calomel electrode (SCE) using the reported reduction potential of ferrocene ($E_{1/2}$ = +0.38 V vs SCE, reported in the following publication: Zanello, P.; Cinquantini, A.; Mangiani, S.; Opromolla, G.; Pardi, L.; Janiak, C.; Rausch, M. D. *J. Organomet. Chem.* **1994**, *471*, 171–177.).



$E_{1/2}$ = –1.14 V vs SCE



$E_{1/2}$ = –1.26 V vs SCE

1.6 References and Notes

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11. The preparation of tertiary halides is often complicated by undesired elimination. See ref. 9.

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20. These studies were conducted in collaboration with Dr. Kyle Quasdorf.

21. The ammonium additive was originally introduced by Gagné to aid in proton transfer during the course of the reaction. Its use in this reaction appears to promote consistent results in the radical couplings of phthalimidoyl oxalates.

22. When oxalate **1.28** was allowed to stand in CH_2Cl_2 at rt overnight, substantial decomposition was observed. These substrates exhibit much improved stability in THF/CH_2Cl_2.

23. For a comprehensive review of visible-light photocatalysis, which discusses the reactivity and electrochemical potentials of common photoredox catalysts, see: Prier C. K.; Rankic, D. A.; MacMillan, D. W. C. *Chem. Rev.* **2013**, *113*, 5322–5363.

24. Reduction potentials are reported vs the saturated calomel electrode (SCE) and were determined in acetonitrile unless noted otherwise.

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32. The isolation of **1.63** as a single stereoisommer likely results from the acidic (4 M HCl) workup promoting isomerization to yield the more stable *trans* stereoisomer.

33. The failure of this reaction is attributed to polymerization of methyl methacrylate, as similar photoredox catalysis conditions have been employed to initiate radical polymerization of methacrylates. See: Fors, B. F.; Hawker, C. J. *Angew. Chem., Int. Ed.*, **2012**, *51*, 8850–8853.

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38. Reductive fragmentation of either a phthalimidoyl oxalate or (*N*-acyloxy)phthalimide is the most likely mechanism for radical generation. The reduction potential of oxalate **1.28** in MeCN was measured to be –1.14 V vs SCE, and the reduction potential of (*N*-acyloxy)phthalimide **1.68** in MeCN was measured to be –1.26 V vs SCE. See experimental section for details.

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40. Since the C4 hydrogens of the Hantzsch ester can be potentially donated as either protons or hydrogen atoms (see Scheme 1.3), this result alone does not unambiguously reveal if deuterium was incorporated via enolate protonation or hydrogen atom abstraction.

41. Resubjection of **1.77** to the reaction conditions did not result in the formation of **1.78** and only provided recovered **1.77**, confirming that **1.78** is not produced from **1.77** under the reaction conditions.

42. Unreacted (*N*-acyloxy)phthalimide **1.68** was recovered in 60% yield.

43. $Ru(bpy)_3^+$ is the most reasonable electron-transfer agent under these conditions, as its reduction potential is more negative ($E_{1/2}$ = –1.33 V vs. SCE) than the amine (For Et_3N, the corresponding $E_{1/2}$ = +1.0 V vs. SCE, see ref 44) or the corresponding α-amino radical (For Et_3N, the corresponding $E_{1/2}$ = –1.12 V vs. SCE, see ref 45)

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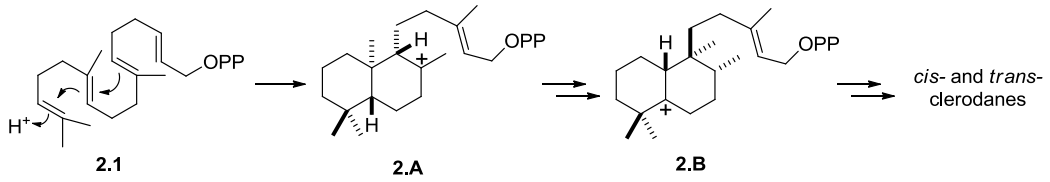
Chapter 2: Total Synthesis of *trans*-Clerodane and *ent*-Halimane Diterpenoids via a Stereoselective Radical 1,6-Addition

2.1 Introduction

The clerodane diterpenoids are a large family of natural products isolated primarily from dicotyledonous plants.[1] Many of these secondary metabolites exhibit antifeedant activity,[1] although the biological activity of certain clerodane diterpenes is more extensive.[2] This scaffold is thought to originate biosynthetically from geranylgeranyl pyrophosphate (**2.1**) via a series of enzymatic cyclizations (Figure 2.1). Intermediate **2.A**, which has been implicated in this biosynthetic pathway, provides a point of divergence from which the clerodanes and related labdane diterpenoids can both be derived.[1a] A series of hydride and methyl migrations is then thought to ensue from intermediate **2.A** to generate a common precursor **2.B** from which both the *cis*- and *trans*-clerodane diterpeoids can be formed, depending on which of the geminal methyl groups migrates in the following step.[1a]

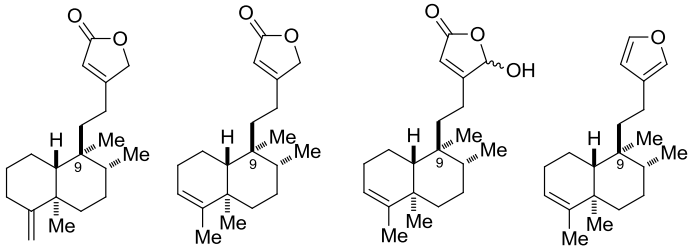
Figure 2.1 Proposed biosynthesis of clerodane diterpenoids



The *trans*-clerodane subset of this family of natural products, represented by **2.2**,[3] solidagolactone (**2.3**),[3] 16-hydroxycleroda-3,13-dien-15,16-olide (**2.4**, referred to as PL3 or HCD),[2,4] and annonene (**2.5**)[5] (Figure 2.2), is structurally characterized by a *trans*-decalin core bearing four contiguous stereocenters, two of which are 1,3-related

quaternary carbons. As a result of this structural complexity, early total syntheses of *trans*-clerodanes, including those of PL3 (**2.4**)[6] and annonene (**2.5**),[6,7] required lengthy sequences to install the contiguous stereocenters and fashion the C9 quaternary carbon.[8]

Figure 2.2 Representative trans-clerodane natural products



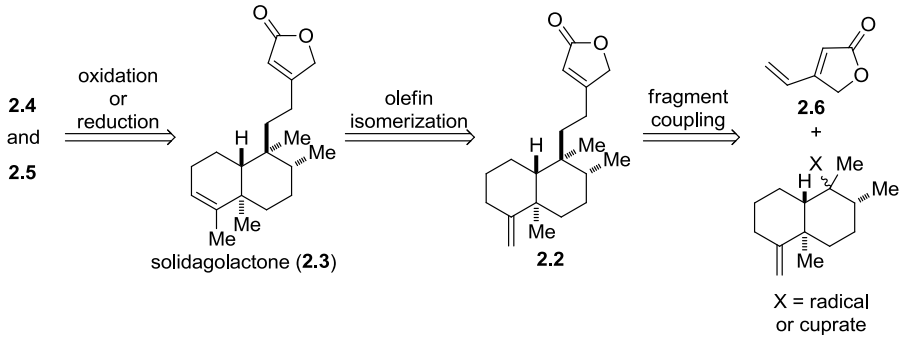
Despite the substantial previous work in the total synthesis of *trans*-clerodane natural products,[1b] a concise route to diterpenes of this family remained elusive. It was envisioned that recent studies in the Overman group involving the construction of quaternary carbons via tertiary radical[9,10] and tertiary organometallic[11] intermediates could enable efficient construction of the C9 quaternary carbon of these diterpenoids and provide for efficient syntheses of *trans*-clerodanes **2.2–2.5**. Importantly, this total synthesis venture would also enable investigation of the diastereoselectivity of tertiary radical and tertiary organometallic couplings using a decalin substrate, as previous investigations in the Overman group suggested that the diastereoselectivity in such reactions can be divergent depending on the nature of the reactive intermediate employed.[10,11]

2.2 Retrosynthetic Analysis

The projected total synthesis (Figure 2.3) was initially outlined to target *trans*-clerodane **2.2**, the simplest member of the exemplary natural products depicted in Figure

2.2. It was assumed that by isomerization of the exocyclic olefin and redox manipulation of the butenolide moiety, solidagolactone (**2.3**), PL3 (**2.4**), and annonene (**2.5**) would be directly accessible from **2.2**.[12] The key quaternary carbon stereocenter present in **2.2** would be formed at this late stage by the coupling of the corresponding structurally complex tertiary radical or tertiary organometallic intermediate with an electron-deficient olefinic acceptor.

Figure 2.3 Endgame retrosynthesis for *trans*-clerodane diterpenoids



Several options for the choice of an appropriate conjugate acceptor were considered. Methyl vinyl ketone, a simple and competent substrate in such radical addition reactions,[9] was initially considered, as elaboration of the ketone functional group over several steps would form the butenolide moiety of **2.2**–**2.5**.[13] More attractive was the direct incorporation of the entire ethanobutenolide fragment via a 1,6-addition to 4-vinylfuranone (**2.6**). Since 1,6-additions of organocuprates are well-known in the literature,[14] coupling the decalin and vinylbutenolide units was expected to occur readily, providing that access to the required tertiary organometallic intermediate was obtained. By contrast, the analogous radical 1,6-additions of this type held only modest precedent,[15] perhaps due to the difficulty of terminating the highly stabilized allylic radical intermediate using classical radical chain transfer chemistry. However, it was

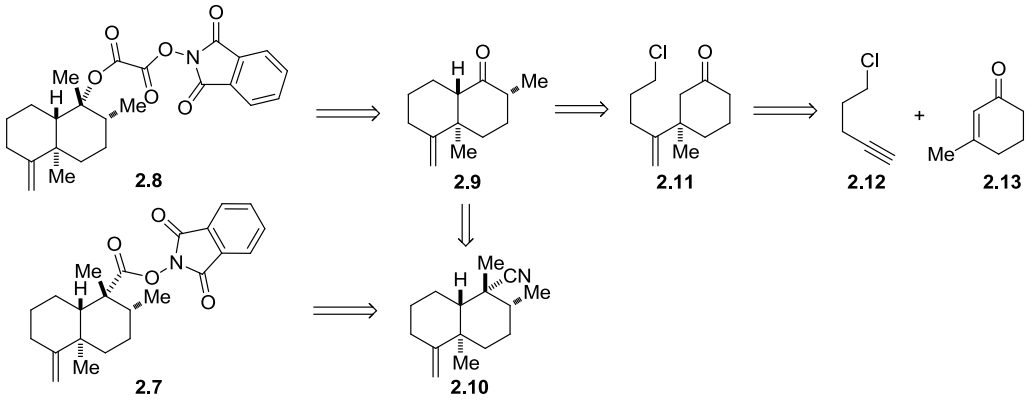
anticipated that mechanistic knowledge regarding photoredox-catalyzed radical couplings garnered in the previous exploratory studies would enable the development of a synthetically viable radical 1,6-addition reaction.[9b,c]

Significant literature precedent suggested that coupling via the tertiary radical intermediate would occur from the less-hindered equatorial face, avoiding destabilizing interactions with the axial angular methyl group and carbon substituents neighboring the radical-bearing carbon.[9,10] The stereoselectivity of the coupling of the corresponding tertiary organocuprate was less predictable, as previous studies advocated that tertiary organocuprates in some instances react from the more-hindered faces of bicyclic ring systems.[11] Thus, access to both a tertiary radical and a tertiary organometallic intermediate at this stage of the synthesis would allow a comparison of the diastereoselectivity observed in either a radical or anionic coupling in the case of a decalin substrate.

A final consideration was the precursor from which a tertiary radical would be generated. Recent results from the Overman group had established that tertiary radicals are efficiently generated and coupled from tertiary carboxylic acid-derived (*N*-acyloxy)phthalimides[9c, 10] such as **2.7** as well as tertiary alcohol-derived *tert*-alkyl-(*N*-phthalimidoyl)oxalates such as **2.8**.[9a,b] It was inferred that both of these radical precursors would be accessible from a common intermediate **2.9** (Figure 2.4). Decalone **2.9** could be synthesized using straightforward chemistry developed by Piers.[16] Closure of the decalin ring would be accomplished by intramolecular alkylation of chloroketone **2.11**, which in turn could be formed via copper-catalyzed conjugate addition of a vinylalane derived from **2.12** to 3-methylcyclohexenone (**2.13**). The use of a chiral Ag-NHC ligand

developed by Hoveyda and coworkers in this conjugate organometallic addition would ideally enable the execution of the total synthesis in enantioselective fashion.[17] The preparation of a tertiary organometallic precursor with which to investigate the key coupling reaction was also pursued by a similar route.[18]

Figure 2.4 Retrosynthetic analysis of radical precursors

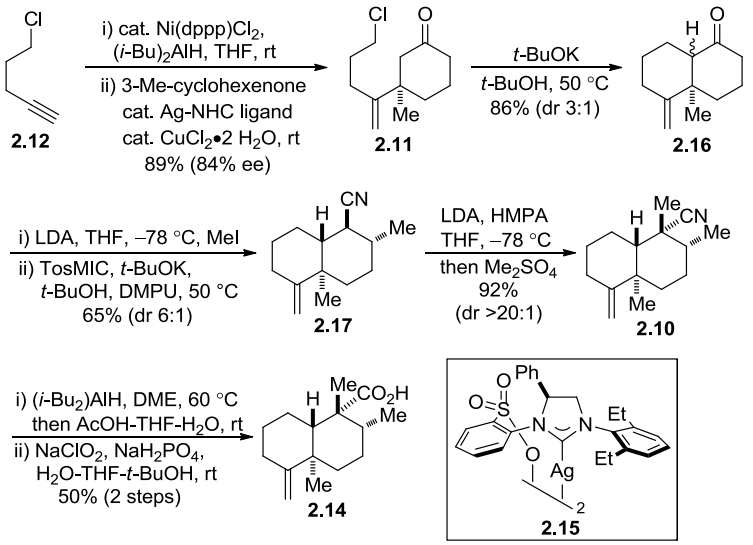


2.3 Results and Discussion

2.3.1 Synthesis of a Radical Precursor

Because the synthetic utility of both (*N*-acyloxy)phthalimides and *tert*-alkyl-(*N*-phthalimidoyl) oxalates had not yet been fully explored at the onset of these studies, both of these substrates were initially sought to investigate the key radical fragment coupling. The synthesis of decalin carboxylic acid **2.14** is summarized in Scheme 2.1.[19] Regioselective hydroalumination of 5-chloro-1-pentyne (**2.12**) using diisobutylaluminum hydride (DIBAL-H) and catalytic Ni(dppp)Cl_2 in THF generated a branched vinylaluminum species that underwent enantioselective conjugate addition to 3-methylcyclohexeneone (**2.13**) in the presence of $CuCl_2$•2 H_2O and chiral Ag-NHC ligand **2.15**.[17] When using 0.25 mol% of the $CuCl_2$/Ag-NHC catalyst system, ketone **2.11** was formed in 89% yield and 84% *ee*. Importantly, since the Ag-NHC ligand required several

Scheme 2.1 Synthesis of carboxylic acid 2.14

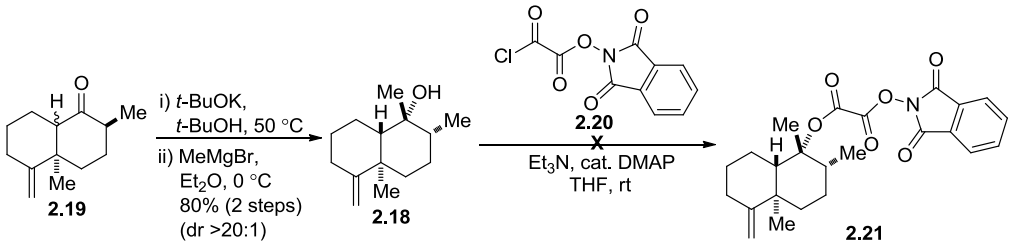


steps to synthesize, the catalyst loading was optimized in order to prepare the maximum amount of ketone **2.11** per amount of ligand. These studies conducted by Dr. André Dieskau confirmed that using 0.1 mol% of this $CuCl_2$/Ag-NHC catalyst system in the conjugate addition reaction was sufficient to generate ketone **2.11** in 50–55% yield and comparable enantioselectivity. Intramolecular alkylation of **2.11** mediated by *t*-BuOK in *t*-BuOH formed decalone **2.16** in 86% yield as a 3:1 mixture of *trans*:*cis* decalin diastereomers. Both decalones were then methylated in high yield via the kinetic enolate of **2.16** using LDA and MeI. Although alkylation occurred predominantly from the β-face of decalones **2.16**, this methyl-bearing stereocenter as well as the decalin ring fusion were equilibrated to give the stereochemistry required for the *trans*-clerodanes at these positions in the ensuing reductive cyanation reaction, which provided secondary nitriles **2.17** as a mixture of epimers at only the nitrile-bearing carbon. As expected, these diastereomers converged after methylation to form tertiary nitrile **2.10**. After many failed attempts to hydrolyze the sterically hindered nitrile **2.10**, a two-step sequence of

reduction of **2.10** to the intermediate aldehyde, followed by Lindgren-Kraus oxidation was employed to provide carboxylic acid **2.14** in 50% yield over two steps.

Tertiary alcohol **2.18** was also synthesized by Dr. Nick Untiedt in 2 steps and 80% yield from ketone **2.19** (Scheme 2.2).[20] Because the synthesis of this alcohol is considerably shorter than that of carboxylic acid **2.14**, it was reasoned that a radical precursor derived from **2.18** would be the most attractive substrate to use in the key coupling reaction. Unfortunately, Dr. Untiedt's attempted acylation of **2.18** with *N*-phthalimidoyl chlorooxalate **2.20** returned only the unreacted substrate, suggesting that this alcohol may be too sterically hindered to access the corresponding alkyl *N*-phthalimidoyl oxalate **2.21**.

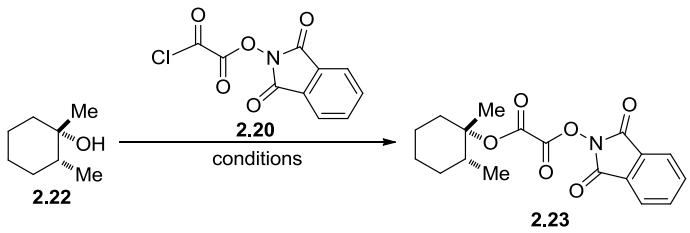
Scheme 2.2 Attempted synthesis of oxalate 2.21



A series of studies examining the acylation of 1,2-dimethylcyclohexan-1-ol (**2.22**) was then initiated to determine whether more forcing conditions could be used to prepare *tert*-alkyl *N*-phthalimidoyl oxalates from severely hindered tertiary alcohols when the standard conditions (Scheme 2.2) failed. Accordingly, subjection of **2.22** to the acylation conditions depicted in Scheme 2.2 resulted in only 72% conversion to the desired oxalate **2.23** (Table 2.1, entry 1). Heating the reaction mixture to 40 °C (entry 2) or employing additional **2.20**, Et_3N and DMAP (entry 3) failed to improve conversion. Unfortunately, trituration purification of **2.23** was unsuccessful in these cases where conversion was

incomplete. In an attempt to improve conversion, alcohol **2.22** was treated with either NaH or *n*-BuLi (entries 4 and 5) to initially generate a sodium or lithium alkoxide, respectively, followed by exposure to acyl chloride **2.20**. Analysis of the crude reaction mixtures by ^{1}H NMR revealed that nearly all of the substrate had been consumed, although multiple decomposition products were present in addition to the desired oxalate **2.23**.

Table 2.1 Acylation of 1,2-dimethylcyclohexan-1-ol (2.22) with 2.20.



entry	conditions	conversion (%) by ^{1}H NMR
1	**2.20** (2 equiv), Et_3N (2 equiv), DMAP (0.1 equiv), THF, rt, 24 h	72
2	**2.20** (2 equiv), Et_3N (2 equiv), DMAP (0.1 equiv), THF, 40 °C, 24 h	72
3	**2.20** (4 equiv), Et_3N (4 equiv), DMAP (0.2 equiv), THF, rt, 7 h	74
4	NaH (1 equiv), THF/DMF, 20 min, rt then **2.20** (2 equiv), rt, 24 h	_[a]
5	*n*-BuLi (1 equiv), THF, 0 °C, 15 min then **2.20** (2 equiv), 0 °C to rt, 24 h	_[a]

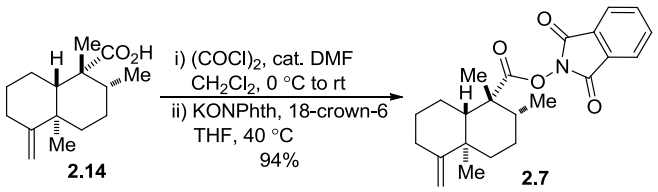
[a]A complex mixture of products was observed by ^{1}H NMR.

Ultimately, clean conversion of **2.22** to its phthalimidoyl oxalate could not be realized. These results underscored a general limitation to the use of phthalimidoyl oxalates in complex settings in that the synthesis and purification of these radical precursors can be problematic depending on the nature and reactivity of the tertiary alcohol substrate. Because these sensitive intermediates are prone to decomposition, no

purification methods attempted could successfully isolate the desired oxalates in cases when conversion from the tertiary alcohol is incomplete. Thus, conversion of a tertiary alcohol to its phthalimidoyl oxalate must occur cleanly under the standard conditions (Table 2.1, entry 1) in order to isolate oxalate products of acceptable purity.

An (*N*-acyloxy)phthalimide radical precursor derived from carboxylic acid **2.14** was then pursued for use in the key radical fragment coupling. This intermediate was formed most efficiently by first generating the acyl chloride of **2.14**, followed by subjection of this intermediate to KONPhth and 18-crown-6 in THF at 40 °C (Equation 2.1). The (*N*-acyloxy)phthalimide **2.7** so formed was stable to silica gel chromatography using pH 7-buffered silica gel. With access to a radical precursor for use in the key coupling reaction, the optimization of a radical 1,6-addition was next investigated.

Equation 2.1

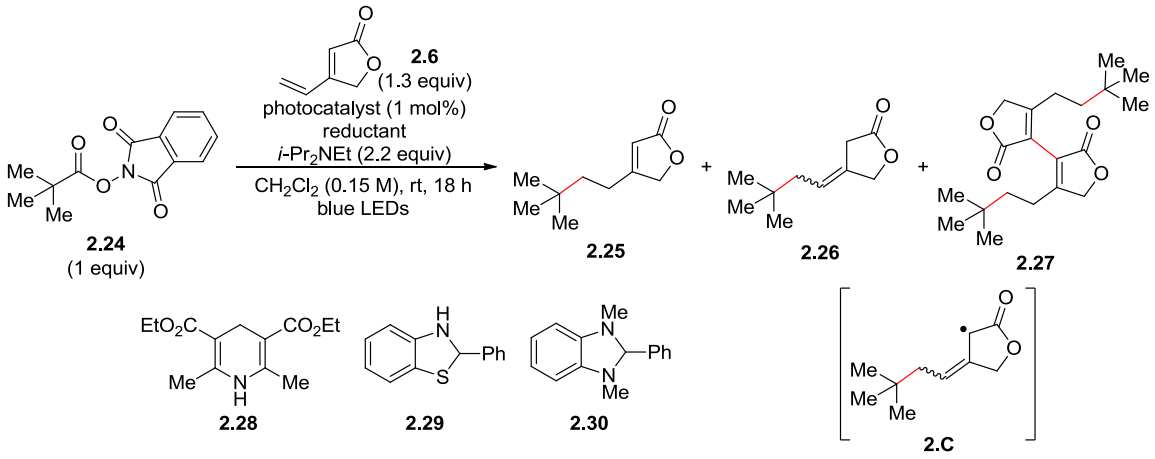


2.3.2 Optimization of a Radical 1,6-Addition

The initial development of the key radical coupling was conducted using a simple (*N*-acyloxy)phthalimide substrate **2.24** derived from trimethylacetic acid (Table 2.2). Using conditions optimized for the 1,4-addition of tertiary radicals to electron-deficient alkenes,[9c] **2.24** coupled with 4-vinylfuranone (**2.6**) to form adduct **2.25** accompanied by trace amounts of β,γ-unsaturated lactones **2.26** (entry 1). This product distribution would be inconsequential, as treatment with base had been previously shown to converge

regioisomeric products of this type. More problematic was the formation of a significant amount of a product containing two *tert*-butyl butenolide fragments, **2.27**. Such a product

Table 2.2 Optimization of radical 1,6-addition



entry	photocatalyst	reductant (equiv)	yield **2.25** (%)[b]	yield **2.26** (%)[b]	yield **2.27** (%)[b]
1	$Ru(bpy)_3(BF_4)_2$	**2.28** (1.5)	36	<5	30
2[c]	$Ir(ppy)_3$	**2.28** (1.5)	0	0	0
3	$Ir(dF(CF_3)ppy)_2(dtbbpy)PF_6$	**2.28** (1.5)	24	0	42
4[c]	$Ir(dtbbpy)ppy_2PF_6$	**2.28** (1.5)	25	0	33
5	$Ru(bpz)_3(PF_6)_2$	**2.28** (1.5)	0	0	0
6	$Ru(bpy)_3(BF_4)_2$	**2.29** (1.5)	27	20	9
7	$Ru(bpy)_3(BF_4)_2$	**2.30** (1.5)	66	9	<5
8	$Ru(bpy)_3(BF_4)_2$	**2.28** (5)	46	<5	34
9[d]	$Ru(bpy)_3(BF_4)_2$	**2.28** (5)	25	75	0

[a]Conditions unless otherwise noted: **2.24** (1 equiv), **2.6** (1.3 equiv), photocatalyst (0.01 equiv), *i*-Pr_2NEt (2.2 equiv), reductant (1.5 or 5 equiv), 0.15 M (with respect to **2.24**) in CH_2Cl_2, rt, 18 h, blue LEDs. [b]Determined by ^1H NMR integration relative to an internal standard (1,4-dimethoxybenzene). [c]A compact fluorescent light was used in place of blue LEDs. [d]The concentration of **2.24** was 0.02 M.

could arise from dimerization of the highly delocalized allylic radical intermediate **2.C** at the carbon adjacent to the carbonyl group, followed by isomerization of the double bonds

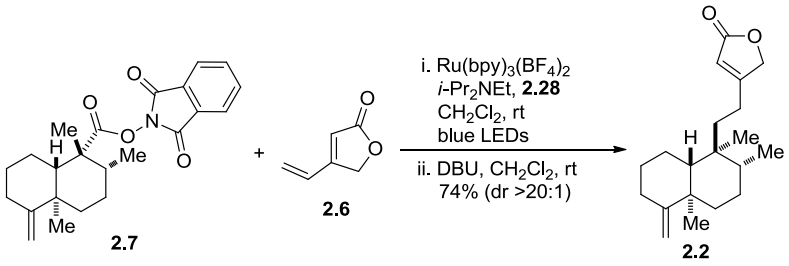
into conjugation with the lactone carbonyls. Speculating that the reduction potential of the catalyst might affect the termination sequence, several common photoredox catalysts were screened in an attempt to minimize the formation of **2.27**. Of the iridium photocatalysts examined, $Ir(ppy)_3$ did not promote the reaction, whereas $Ir(dF(CF_3)ppy)_2(dtbbpy)PF_6$ provided primarily dimer **2.27** (entries 2–4). $Ru(bpz)_3(BF_4)_2$, whose +1 oxidation state is a much poorer reductant than $Ru(bpy)_3^{+}$,[21] also did not promote reactivity (entry 5). In addition to Hantzsch ester **2.28** the use of two other reductive quenchers, **2.29**[22] and **2.30**,[23] with $Ru(bpy)_3(BF_4)_2$ was examined. Both reduced the formation of dimer **2.27** (entries 6 and 7), with **2.30** delivering a 75% overall yield of 1,6-addition products. Ultimately, it was found that the highest yields of adducts **2.25** and **2.26** were obtained, while avoiding the formation dimer **2.27**, by conducting the reaction at higher dilution (0.02M) using an excess of the dihydropyridine reductant **2.28** (entry 9). With optimal conditions for the key radical fragment coupling identified, the radical 1,6-addition was next attempted using the structurally complex radical precursor **2.7** synthesized previously.

2.3.3 Key Radical and Cuprate Fragment Couplings

The direct application of the optimized conditions to the coupling of decalin tertiary radical formed from (*N*-acyloxy)phthalimide **2.7** gave the desired 1,6-adducts in high yield as a mixture of double bond isomers (Equation 2.2). Equilibration of these crude products with DBU afforded the *trans*-clerodane diterpenoid **2.2** as a single stereoisomer at the newly formed C9 quaternary carbon stereocenter. As expected,[10] this

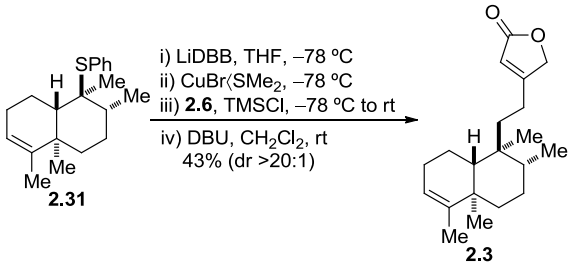
coupling took place exclusively from the less-hindered face of the *trans*-decalin tertiary radical intermediate.

Equation 2.2



The coupling of a structurally similar tertiary organocuprate intermediate was performed by Dr. Daniel Müller in the racemic series (Equation 2.3). In the key coupling event, reductive lithiation of phenyl thioether **2.31** followed by transmetalation and 1,6-conjugate addition of the resulting organocuprate to 4-vinylfuranone provided a mixture of regioisomeric olefin products that converged upon treatment with DBU to solidagolactone (**2.3**). The yield of 1,6-addition product in the coupling of this organocuprate was notably lower than that obtained via the radical coupling.

Equation 2.3



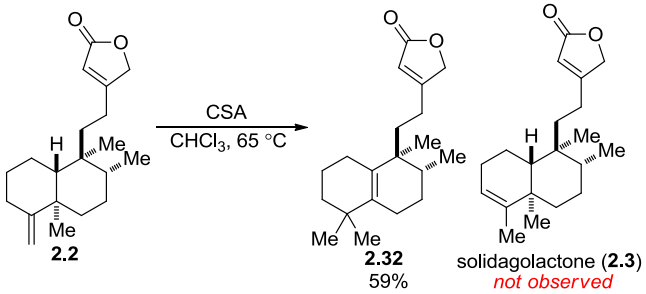
The quaternary carbon was formed with complete diastereoselectivity in this cuprate coupling with addition occurring from the less-hindered face of the decalin ring system. Although the Overman group's prior investigations suggested that coupling from the more-hindered face of the decalin might be reasonable or even preferred,[11] the

observed stereoselectivity was attributed in this case to the severe 1,3-diaxial interaction between the angular methyl group and the incoming electrophile that such a bond formation would incur.

2.3.4 Unexpected Structural Rearrangement of Exocyclic Olefin 2.2

The conversion of *trans*-clerodane diterpene **2.2** to solidagolactone (**2.3**), PL3 (**2.4**), and annonene (**2.5**) required that the exocyclic olefin be isomerized to the internal position. In a first attempt to enact this transformation, **2.2** was exposed to CSA in $CHCl_3$ at elevated temperature for three days.[24] Unexpectedly, the single product isolated from the reaction was not the desired solidagolactone (**2.3**) but the *ent*-halimane diterpenoid **2.32** (Equation 2.4).[3]

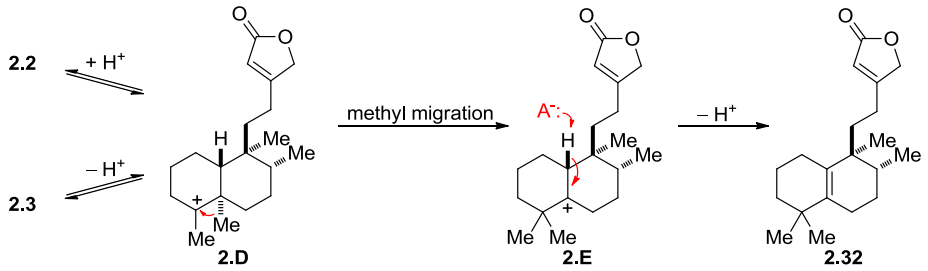
Equation 2.4



Tetrasubstituted olefin **2.32** is perhaps the result of the cationic rearrangement depicted in Figure 2.5. Protonation of the exocyclic olefin of **2.2** generates a tertiary carbocation **2.D** which can reversibly form the endocyclic olefin **2.3**. Alternatively, migration of the angular methyl group of **2.D** can occur to alleviate 1,3-diaxial interaction with the methyl substituent at C9, forming a tertiary carbocation **2.E** that can generate tetrasubstituted olefin **2.32** by action of a conjugate base present in solution. Not surprisingly, *ent*-halimane **2.32** has been co-isolated with several *trans*-clerodane

diterpenoids,[3] suggesting that certain *trans*-clerodanes may be biosynthetic precursors to *ent*-halimanes via a similar structural rearrangement.[25]

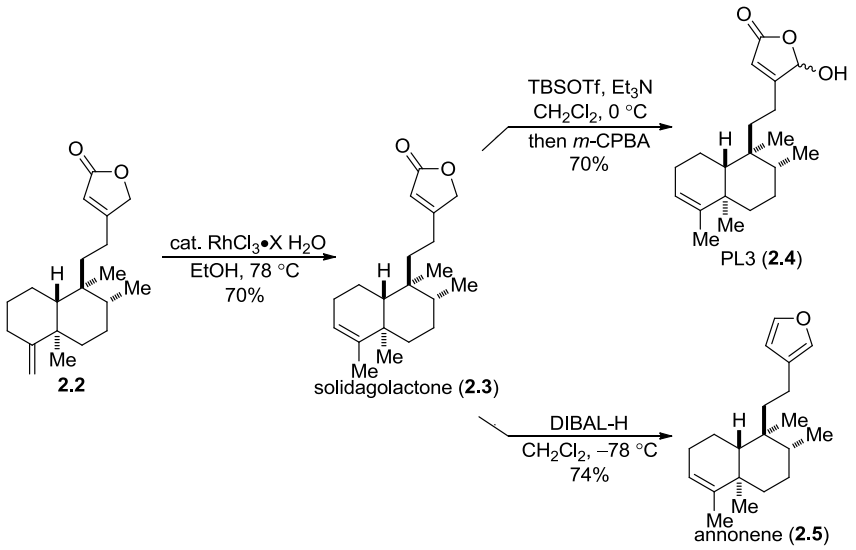
Figure 2.5 Proposed rearrangement mechanism



2.3.5 Olefin Isomerization and Synthesis Endgame

After noting that exposure of exocyclic olefin **2.2** to acid in the presence of heat provoked a structural rearrangement, alternative isomerization conditions were then explored. Fortunately, subjection of **2.2** to a catalytic amount of $RhCl_3$ in refluxing EtOH promoted clean isomerization of the exocyclic alkene to provide solidagolactone (**2.3**) with no observable rearrangement product **2.32** detected (Scheme 2.3).[26] Installation of the butenolide hydroxyl group required to complete the synthesis of PL3 (**2.4**) was accomplished by soft enolization to form the corresponding silyloxyfuran, followed by oxidation with *m*-CPBA.[27] Conversion of solidagolactone (**2.3**) to annonene (**2.5**) occurred smoothly by treatment of **2.3** with DIBAL-H in CH_2Cl_2 at low temperature.[28] Completion of the total syntheses was confirmed by comparison of ^1H and ^{13}C NMR spectra obtained for the natural products with those published previously for **2.2**,[3] solidagolactone (**2.3**),[3] PL3 (**2.4**)[2c], and annonene (**2.5**).[6]

Scheme 2.3 Synthesis endgame



2.4 Conclusions

The late-stage coupling of either a structurally elaborate tertiary radical or tertiary organocuprate intermediate with a vinylbutenolide conjugate acceptor was a successful strategy for stereoselectively forming the key central quaternary carbon present in several *trans*-clerodane natural products. In both fragment couplings, addition occured from the less hindered face of the nucleophilic decalin intermediate. This selectivity is likely due to the avoidance of unfavorable steric interactions present in the transition states corresponding to approach of the electrophile from the more hindered decalin face. The superior yield obtained in the fragment coupling of the tertiary radical intermediate compared to that of the tertiary organocuprate intermediate validates the radical coupling approach as a general means to unite structurally elaborate molecular fragments. This convergent coupling approach permitted efficient enantioselective syntheses of four *trans*-clerodane diterpenes: **2.2**, solidagolactone (**2.3**), PL3 (**2.4**), and annonene (**2.5**). In

addition, a cationic rearrangement allowed a biosynthetically related *ent*-halimane diterpene, **2.32**, to be synthesized via this route.

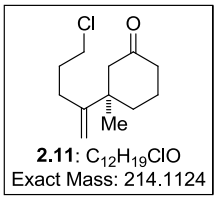
The inability to access *tert*-alkyl *N*-phthalimidoyl oxalate **2.8** for use in the coupling reaction reveals a limitation to the general utility of these radical precursors in complex molecule synthesis. Although these substrates can be prepared from many easily accessible tertiary alcohols, the instability of oxalates such as **2.23** under both harsh acylation conditions and various purification techniques is a critical liability that complicates their further application to total synthesis.

Since the completion of the work described in this chapter, novel tertiary alcohol-derived radical precursors have been developed in the Overman and MacMillan laboratories that exhibit much greater stability than phthalimidoyl oxalates.[29] These advances have allowed much streamlined syntheses of **2.2** and **2.3**, and will be drawn upon in the succeeding chapter.[29,30]

2.5 Experimental Information

Unless stated otherwise, reactions were conducted in oven-dried glassware under an atmosphere of argon using anhydrous solvents (either freshly distilled or passed through activated alumina columns). *t*-BuOH was dried over $MgSO_4$ for 18 h and distilled prior use. DMPU and HMPA were purified by distillation under a vacuum (~0.1 torr) over CaH_2. All other commercially obtained reagents were used as received. Thin-layer chromatography (TLC) was conducted with E. Merck silica gel 60 F254 pre-coated plates, (0.25 mm) and visualized by exposure to UV light (254 nm) or stained with anisaldehyde, ceric ammonium molybdate, or potassium permanganate. Flash chromatography and filtration were performed using 40–63 μm EMD Chemicals Silica Gel 60 Å Geduran silica gel. ^{1}H NMR spectra were recorded on Bruker spectrometers (at 500 or 600 MHz) and are reported relative to deuterated solvent signals. Data for ^{1}H NMR spectra are reported as follows: chemical shift (δ ppm), multiplicity, coupling constant (Hz) and integration. ^{13}C NMR spectra were recorded on Bruker Spectrometers (at 125 or 150 MHz). Data for ^{13}C NMR spectra are reported in terms of chemical shift. IR spectra were recorded on a Varian 640-IR spectrometer and are reported in terms of frequency of absorption (cm-1). High resolution mass spectra were obtained from the UC Irvine Mass Spectrometry Facility with a Micromass LCT spectrometer. Blue LEDs (30 cm, 1 watt) were purchased from http://www.creativelightings.com (product code CL-FRS5050-12WP-12V) and powered by 8 AA batteries. Enantiomeric excess for compound **2.11** was determined by gas chromatography (GC) and was performed using a Hewlett Packard Series II 5890 Series with a Chiraldex™ B-DM 30 mm x 0.25 mm x 0.12

μm column (50–180 °C at 15 °C/min). See JOC Standard Abbreviations and Acronyms for abbreviations. Available at: http://pubs.acs.org/userimages/ContentEditor/1218717864819/joceah_abbreviations.pdf

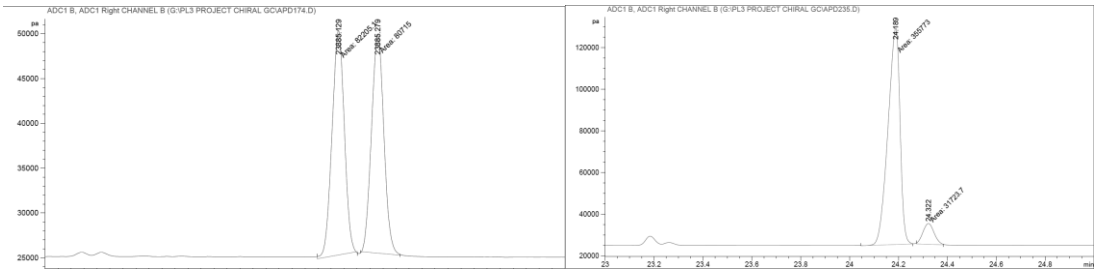


2.11: $C_{12}H_{19}ClO$
Exact Mass: 214.1124

(–)-(*R*)-3-(5-Chloropent-1-en-2-yl)-3-methylcyclohexan-1-one (2.11). *Preparation of the vinylaluminum stock solution:* A round-bottom flask was charged with Ni(dppp)Cl_2 (0.30 g, 0.54 mmol) and THF (22 mL). DIBAL-H (neat, 3.2 mL, 18 mmol) was added slowly to the mixture to form a black solution (temperature increase, gas evolution). The reaction was maintained for 15 min at rt and then the vessel was cooled to 0 °C in an ice-water bath. 5-Chloro-1-pentyne (1.9 mL, 18 mmol) was then *slowly** added dropwise to the solution over ca. 40 min; after complete addition, the reaction was maintained at 0 °C for 5 min. The reaction was then allowed to warm to rt and stir for 3 h (concentration = 0.8 *M*). **** Note**: If alkyne is added too quickly, a substantial amount of the linear β-vinylaluminum species is formed.*

Enantioselective conjugate addition: A round-bottom flask was charged with $CuCl_2 \cdot 2H_2O$ (3.0 mg, 0.014 mmol) and Ag-NHC **2.15**[17] (9.0 mg, 0.014 mmol) in a glove box under a N_2 atmosphere. The flask was sealed with a rubber septum and removed from the glove box, THF was added (10 mL), and the blue solution was stirred for 5 min. The vinylaluminum reagent in THF (21 mL, 16.5 mmol, 0.8 M) was added slowly via syringe, followed by dropwise addition of 3-methylcyclohex-2-ene-1-one (0.62 mL, 5.5 mmol) and the black reaction mixture was stirred at rt overnight. The reaction was quenched with a saturated aqueous solution of Rochelle's salt (10 mL), the aqueous phase

was extracted with Et_2O (3 x 100 mL) and the organic layers were combined, dried over $MgSO_4$ and concentrated *in vacuo* to produce a yellow syrup that was purified by flash column chromatography (100% hexanes to 20% EtOAc/hexanes) to obtain **2.11** as a clear yellow oil (1.05 g, 4.9 mmol, 89%, 84% *ee* determined by chiral GLC: CHIRALDEX B, 30 psi, 50 °C → 180 °C, @ 15 °C/min, injection volume 1 μL): R_f = 0.68 (40% EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.92 (s, 1H), 4.87 (s, 1H), 3.59 (t, *J* = 6.4 Hz, 2H), 2.62 (d, *J* = 14.2 Hz, 4H), 2.08–2.33 (m, 5H), 1.93–2.00 (m, 3H), 1.60–1.80 (m, 3H), 1.11 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 211.8, 152.7, 110.5, 52.8, 45.0, 44.5, 41.0, 35.0, 31.9, 27.8, 27.0, 22.1; IR (thin film) 3096, 2957, 2871, 1714, 1635, 1455, 903 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{12}H_{20}ClO$, $(M + H)^+$ 232.1468, found 232.1476; $[\alpha]^{26.7}_D$ -29.1, $[\alpha]^{26.8}_{577}$ -32.3, $[\alpha]^{26.8}_{546}$ -37.3, $[\alpha]^{26.8}_{435}$ -64.5, $[\alpha]^{26.8}_{405}$ -81.0 (*c* = 1.04, $CHCl_3$).



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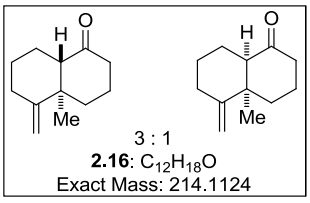
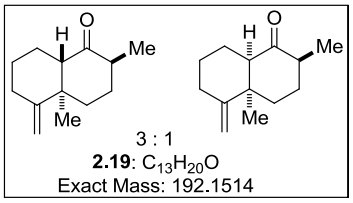
2	24.322	MM	0.0530	3.17237e4	9976.63379	8.1868



4a-Methyl-5-methylene-octahydronaphthalen-1(2H)-ones (2.16): The general procedure of Piers was followed.[16a] A round-bottom flask was charged with chloroketone **2.11** (2.0 g,

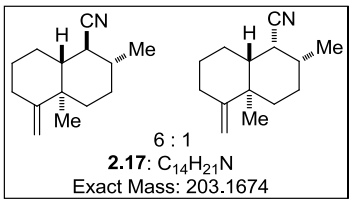
9.32 mmol), *t*-BuOH (19 mL), and *t*-BuOK* (2.1 g, 18.6 mmol). The vessel was placed in a sand bath, heated to 50 °C and maintained for 4 h. The reaction was then allowed to cool to rt and quenched with aqueous 2 N HCl (18 mL), extracted with Et_2O (3 x 100 mL) and the organic layers were combined, dried over $MgSO_4$, and concentrated *in vacuo* to produce a yellow oil. The oil was purified by flash column chromatography (100% hexanes to 20% EtOAc/hexanes) to obtain a 3:1 diastereomeric mixture of **2.16**, as a clear yellow oil (1.43 g, 8.03 mmol, 86%). The *trans* configuration of the major diastereomer was previously assigned by Piers[16c] on the basis of diagnostic nOe correlations; ^{1}H NMR, IR and mass spectrometry data for **2.16** were consistent with those previously reported:[16c] R_f = 0.48 (10% EtOAc/hexanes); ^{13}C NMR (125 MHz, $CDCl_3$, mixture of diastereomers): δ 214.2, 212.3, 155.7, 152.9, 107.8, 105.8, 59.1, 58.3, 44.7, 42.7, 41.3, 38.1, 35.7, 32.7, 32.3, 32.2, 26.6, 26.2, 26.0, 25.9, 22.4, 22.1, 20.9, 18.9.

**Note: It is very important to use freshly sublimed (or a new batch) of t-BuOK as well as dried and distilled t-BuOH to get satisfactory and reproducible yields.*



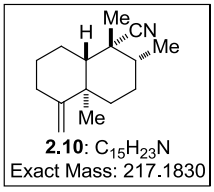
2,4a-Dimethyl-5-methylene-octahydronaphthalen-1(2H)-ones (2.19). A round-bottom flask was charged with *i*-Pr_2NH (2.8 mL, 19.7 mmol), THF (23 mL), and cooled to –78 °C in an acetone/dry ice bath. A solution of *n*-BuLi in hexanes (2.65 M, 7.4 mL, 19.7 mmol) was added dropwise to the cooled solution. After complete addition the reaction was allowed to warm to 0 °C in an ice bath and maintained for 20 min. The solution was cooled to –78 °C in a dry ice-acetone bath and a 3:1 mixture of **2.16** (3.18 g, 17.9 mmol) in THF (3.3 mL) was added dropwise. The solution was stirred for 30 min at –78 °C,

after which MeI (5.6 mL, 89.5 mmol) was added dropwise. The vessel was removed from the dry ice-acetone bath, allowed to warm to rt, and maintained at rt for 2 h. The reaction mixture was then quenched with a saturated aqueous solution of NH_4Cl (70 mL), extracted with Et_2O (3 x 120 mL) and the organic layers were combined, dried over Na_2SO_4, and concentrated *in vacuo*. The resulting yellow oil was purified by flash column chromatography (100% hexanes to 20% EtOAc/hexanes) to obtain a 3:1 diastereomeric mixture of **2.19** as a clear yellow oil (3.17 g, 16.5 mmol, 92%). A third diastereomer present in trace amount is visible by inspection of the ^{13}C NMR spectrum. This impurity was carried through the formation of tertiary nitrile **2.10** and was removed by silica gel chromatography at that stage. R_f = 0.5 (10% EtOAc/hexanes). Spectral data for minor diastereomer was consistent with previously reported data.[16a] Major diastereomer ***trans*-2.19**: ^1H NMR (600 MHz, $CDCl_3$) δ 4.75 (s, 1H), 4.73 (s, 1H), 2.54 (dddd, *J* = 6.4, 6.4, 6.4, 6.4 Hz, 1H), 2.43 (dd, *J* = 3.5, 12.1 Hz, 1H), 2.43 (ddd, *J* = 5.0, 13.9, 13.9 Hz, 1H), 2.08–2.19 (m, 3H), 1.87–1.91 (m, 1H), 1.65–1.77 (m, 3H) 1.58 (dddd, *J* = 3.9, 13.5, 13.5, 13.5 Hz, 1H), 1.24–1.32 (m, 1H), 2.43 (d, *J* = 7.4 Hz, 3H), 0.94 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 216.5, 156.0, 106.0, 53.5, 45.0, 43.9, 32.4, 31.0, 28.5, 26.8, 21.0, 19.0, 18.3; IR (thin film) 2934, 2861, 1704, 1640, 1456, 997, 879 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{13}H_{21}O$, $(M + H)^+$ 193.1592, found 193.1585. X-ray quality crystals of a racemic sample of the major diastereomer were obtained by slow evaporation from 1:1 THF:heptane, confirming the relative configuration of this isomer.[12]



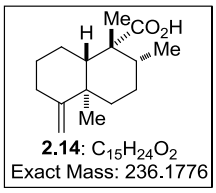
2,4a-Dimethyl-5-methylene-trans-decahydronaphthalene-1-carbonitriles (2.17). The procedure by Piers was followed with minor modification.[16a] A scintillation vial was charged with a 3:1 mixture of **2.19** (0.528 g, 2.75 mmol), TosMIC (1.61 g, 8.24 mmol), DMPU (9.2 mL), and *t*-BuOH (0.28 mL, 3.0 mmol). The mixture was stirred until homogenous (sonication helpful) and then KO*t*-Bu (2.22 g, 19.8 mmol) was added. The vessel was sealed with a Teflon-coated cap, wrapped with Teflon tape, placed in a sand bath, and heated at 50 °C for 5 d. The reaction was then allowed to cool to rt and was quenched with aqueous 2 N HCl (10 mL), extracted with Et_2O (3 x 25 mL) and the organic layers were combined, dried over Na_2SO_4, and concentrated *in vacuo* to produce a yellow oil. The oil was purified by flash column chromatography (100% hexanes to 20% EtOAc/hexanes) to obtain a 6:1 diastereomeric mixture of **2.17** as clear yellow oil (0.352 g, 1.73 mmol, 65%). A third diastereomer present in trace amount is visible by inspection of the ^{13}C NMR spectrum. This impurity was carried through the formation of tertiary nitrile **2.10** and was removed by silica gel chromatography at that stage. The relative configuration of the major diastereomer was previously assigned by Piers on the basis of coupling constants observed in diagnostic ^1H NMR resonances;[16a] ^1H NMR and mass spectrometry data were consistent with previously reported data:[16a] R_f = 0.54 (10% EtOAc/hexanes); ^{13}C NMR (125 MHz, $CDCl_3$, major diastereomer) δ 156.0, 121.7, 105.7, 47.3, 39.1, 38.7, 36.4, 35.6, 32.4, 29.6, 27.4, 26.7, 21.0, 17.2.

**Note: It is very important to use freshly sublimed (or a new batch) of KOt-Bu as well as dried and distilled t-BuOH to get satisfactory and reproducible yields.*



2.10: $C_{15}H_{23}N$
Exact Mass: 217.1830

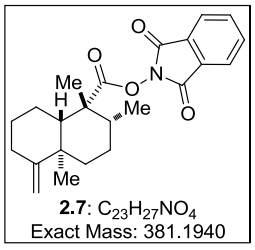
(+)-1,2,4a-Trimethyl-5-methylene-trans-decahydronaphthalene-1-carbonitrile (2.10). A round-bottom flask was charged with *i*-Pr_2NH (252 μL, 1.8 mmol) and THF (8 mL), and was cooled to –78 °C in an acetone/dry ice bath. A solution of *n*-BuLi in hexanes (2.6 M, 730 μL, 1.9 mmol) was added dropwise and the solution was allowed to warm to 0 °C and maintained for 20 min. HMPA (310 μL, 1.8 mmol) was added followed by dropwise addition of a solution of secondary nitriles **2.17** (183 mg, 0.9 mmol) in THF (700 μL) and the reaction was allowed to stir at 0 °C for 40 min. Me_2SO_4 (170 μL, 1.8 mmol) was added dropwise and the vessel was removed from the ice-water bath, allowed to warm to rt and maintained for 16 h. The reaction was then quenched with a saturated aqueous solution of NH_4Cl (10 mL) and extracted with Et_2O (3 x 20 mL). The organic layers were combined, dried over Na_2SO_4, and concentrated *in vacuo* to produce a yellow oil that was purified by flash column chromatography (100% hexanes to 20% EtOAc/hexanes) to obtain tertiary nitrile **2.10** as a clear colorless oil (193 mg, 0.89 mmol, 92%): R_f = 0.54 (10% EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.61 (s, 1H), 4.57 (s, 1H), 2.38–2.45 (m, 1H), 2.12–2.16 (m, 1H), 1.94–1.99 (m, 1H), 1.87–1.92 (m, 1H), 1.67–1.76 (m, 2H), 1.63–1.66 (m, 1H), 1.51–1.57 (m, 1H), 1.37–1.27 (m, 2H), 1.35 (br s, 3H), 1.25 (br s, 3H), 1.17 (d, *J* = 6.6 Hz, 3H), 1.07 (dd, *J* = 3.1, 12.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.1, 123.1, 104.5, 53.1, 41.8, 40.7, 40.3, 36.4, 32.4, 28.6, 28.0, 25.1, 23.4, 18.9, 18.1; IR (thin film) 3086, 2929, 2860, 2360, 2341, 2229, 1639, 1455, 1379, 982, 893 cm^{-1}; HRMS (GC) *m*/*z* calcd for $C_{15}H_{27}N_2$, $(M + NH_4)^+$ 235.2174, found 235.2181; $[\alpha]^{24.4}_D$ +62.5, $[\alpha]^{24.6}_{577}$ +64.9, $[\alpha]^{24.7}_{546}$ +72.1, $[\alpha]^{24.8}_{435}$ +121.2, $[\alpha]^{24.8}_{405}$ +150.5 (*c* = 1.15, $CHCl_3$).



(+)-1,2,4a-Trimethyl-5-methylene-trans-decahydronaphthalene-1-carboxylic acid (2.14). A flame dried round-bottom flask was charged with tertiary nitrile **2.10** (200 mg, 0.92 mmol) and DME (13 mL). The solution was treated with DIBAL-H (neat, 0.7 mL, 3.68 mmol) and the reaction was stirred and heated at 60 °C for 6 h. The clear solution was then allowed to cool to rt and was pipetted into a stirred saturated aqueous solution of Rochelle's salt (45 mL). The aqueous layer was extracted with Et_2O (4 x 100 mL) and the combined organics were dried over Na_2SO_4, and concentrated *in vacuo*. The residue was dissolved in THF (5.8 mL), AcOH (1.9 mL) and H_2O (0.29 mL) and stirred at rt overnight. The reaction was then concentrated *in vacuo*, the residue was dissolved in Et_2O, and washed with a saturated aqueous $NaHCO_3$ solution, and brine. The organic phase was dried over $MgSO_4$, filtered and concentrated *in vacuo* to give the tertiary aldehyde, which was used without further purification. Data for aldehyde: R_f = 0.62 (10% EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.96 (s, 1H), 4.58 (br s, 2H), 2.28 (ddd, *J* = 5.0, 13.5, 13.5 Hz, 1H), 2.09–2.13 (m, 1H), 1.83–1.92 (m, 3H), 1.83–1.92 (m, 3H), 1.27 (s, 3H), 1.07 (s, 1H), 1.02 (d, *J* = 7.1 Hz, 3H), 1.01 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 207.7, 158.7, 104.0, 56.4, 52.6, 40.9, 40.2, 37.0, 32.9, 28.9, 28.0, 22.7, 21.4, 21.3, 17.4; IR (thin film) 3085, 2929, 2858, 1717, 1637, 1448, 1376, 892 cm^{-1}; HRMS (GC) *m*/*z* calcd for $C_{15}H_{25}O$, $(M + H)^+$ 221.1905, found 221.1908.

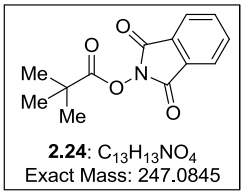
The crude tertiary aldehyde (219 mg, 0.99 mmol) was then dissolved in H_2O (20 mL), THF (20 mL), and *t*-BuOH (5 mL). 2-Methyl-2-butene (5 mL), NaH_2PO_4 (1.37 g, 9.9 mmol), and $NaClO_2$ (477 mg, 5 mmol) were added and the reaction was stirred at rt

for 24 h. The reaction was then quenched with a saturated aqueous solution of NH_4Cl (10 mL), extracted with EtOAc (3 x 30 mL) and the organic layers were combined, dried over Na_2SO_4, filtered and concentrated *in vacuo* to produce a colorless solid. The solid was purified by flash column chromatography (100% hexanes to 20% EtOAc/hexanes) to obtain the title compound as a colorless solid (116 mg, 0.49 mmol, 50%): R_f = 0.41 (10:1 hexanes/EtOAc,); ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.57 (s, 1H), 4.55 (s, 1H), 2.33 (ddd, *J* = 4.6, 11.8, 11.8 Hz, 1H), 2.10–2.17 (m, 2H), 1.90–1.98 (m, 2H), 1.73 (ddd, *J* = 2.8, 2.8, 10.7 Hz, 1H), 1.56–1.63 (m, 2H), 1.48 (dddd, *J* = 3.2, 3.2, 3.2, 6.3 Hz, 1H), 1.22–1.33 (m, 2H), 1.27 (s, 3H), 1.16 (dd, *J* = 1.6, 10.4 Hz, 1H), 1.09 (d, *J* = 5.7 Hz, 3H), 1.06 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 180.2, 159.9, 103.8, 55.7, 48.2, 42.8, 40.6, 37.7, 33.1, 29.0, 27.9, 25.8, 24.0, 18.8, 17.4; IR (thin film) 2930, 2858, 1696, 1447, 1258, 892 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{15}H_{23}O_2$, $(M - H)^-$ 235.1698, found 235.1696; $[\alpha]^{25.7}_D$ +66.5, $[\alpha]^{25.7}_{577}$ +69.6, $[\alpha]^{25.7}_{546}$ +78.6, $[\alpha]^{25.8}_{435}$ +133.2, $[\alpha]^{25.8}_{405}$ +165.5 (*c* = 1.04, $CHCl_3$).



(1*R*,2*R*,4a*R*,8a*S*)-(–)-1,3-Dioxoisoindolin-2-yl-1,2,4a-trimethyl-5-methylene-trans-decahydronaphthalene-1-carboxylate (2.7). A flame-dried round-bottom flask was charged with tertiary acid **2.14** (20 mg, 0.085 mmol) and CH_2Cl_2 (85 μL) and the solution was cooled to 0 °C. Oxalyl chloride (11 μL, 0.13 mmol) was added followed by two drops of DMF (gas evolution occurred), and the reaction was removed from the cooling bath and stirred for 1 h at rt. Toluene (100 μL) was added and the reaction was concentrated *in vacuo* to give a yellow oil. In a scintillation vial, this yellow oil was

dissolved in THF (85 μL) and potassium phthalimide *N*-oxide (17 mg, 0.085 mmol) and 18-crown-6 (22 mg, 0.085 mmol) were added sequentially. The vial was capped and the heterogeneous brick-red solution was heated with stirring at 40 °C. After 20 h, the cloudy yellow solution was diluted with hexanes (2 mL) and passed through a small plug of Celite®. The filtrate was concentrated and the residue was purified by silica gel chromatography using pH 7-buffered silica gel (10% EtOAc/hexanes) to obtain (*N*-acyloxy)phthalimide **2.7** as a colorless solid (30 mg, 0.08 mmol, 94%): R_f = 0.43 (10% EtOAc /hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.87–7.89 (m, 2H), 7.78–7.81 (m, 2H), 4.57 (br s, 2H), 2.44 (dt, *J* = 13.8, 4.6 Hz, 1H), 1.95–2.17 (m, 5H), 1.74 (dt, *J* = 3.2, 13.0 Hz, 1H), 1.53–1.65 (m, 2H), 1.51 (s, 3H), 1.38–1.47 (m, 1H), 1.26–1.34 (m, 2H), 1.13 (d, *J* = 6.9 Hz, 3H), 1.10 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.4, 162.4, 159.7, 134.8, 129.2, 124.0, 103.7, 55.4, 48.6, 43.7, 40.6, 37.3, 32.9, 28.9, 27.7, 25.2, 23.8, 18.8, 17.0; IR (thin film) 2932, 2866, 1781, 1746, 1467, 1014, 879 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{23}H_{27}NO_4Na$, $(M + Na)^+$ 404.1838, found 404.1842; $[\alpha]^{24.9}_D$ –3.2, $[\alpha]^{24.9}_{577}$ –3.5, $[\alpha]^{25.0}_{546}$ –3.5, $[\alpha]^{25.1}_{435}$ –5.9, $[\alpha]^{25.1}_{405}$ –8.0 (*c* = 1.02, $CHCl_3$).



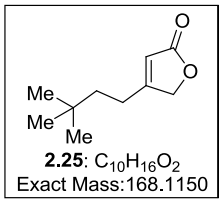
2.24: $C_{13}H_{13}NO_4$
Exact Mass: 247.0845

1,3-Dioxoisoindolin-2-yl pivalate (2.24): Pivalic acid (2.00 g, 19.6 mmol) and *N*-hydroxyphthalimide (4.80 g, 29.4 mmol) were dissolved in THF (200 mL) under an argon atmosphere. After sequential addition of dicyclohexylcarbodiimide (6.07 g, 29.4 mmol) and DMAP (120 mg, 0.98 mmol), the reaction mixture was stirred for 18 h at rt. The mixture was concentrated under reduced pressure, the resulting residue was suspended in Et_2O (200

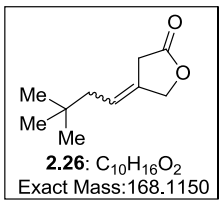
mL) and transferred to a separatory funnel. The organic layer was washed with saturated aqueous NH_4Cl solution (3 x 150 mL) and brine (2 x 150 mL) and was dried over $MgSO_4$. The drying agent was removed by filtration and the filtrate was concentrated under reduced pressure. The crude residue obtained was purified by silica gel chromatography (7% EtOAc/hexanes) to provide (*N*-acyloxy)phthalimide **2.24** (3.68 g, 14.9 mmol, 76%) as a colorless solid. Characterization data matched that previously reported.[31]

4-(3,3-Dimethylbutyl)furan-2(5H)-one (2.25), *E*- and *Z*- 4-(3,3-Dimethylbutylidene)-dihydrofuran-2(3*H*)-one (2.26), and 4,4'-bis(3,3-dimethylbutyl)-[3,3'-bifuran]-2,2'(5*H*,5'*H*)-dione (2.27); General procedure for 1,6-radical addition optimization reported in Table 2.2. (Table 2.2, entry 1 is described): A solution of 4-vinylfuran-2-one (**2.6**)[32] in Et_2O (0.53 M, 610 μL, 0.34 mmol) was added to a 1-dram vial and the solution was concentrated under reduced pressure. The residue was immediately dissolved in CH_2Cl_2 (1.5 mL, previously sparged with Ar for 5 min) under an argon atmosphere. After sequential addition of (*N*-acyloxy)phthalimide **2.24** (64 mg, 0.26 mmol), Hantzsch ester **2.28**[33] (100 mg, 0.39 mmol), *i*-Pr_2NEt (100 μL, 0.57 mmol) and a solution of $Ru(bpy)_3(BF_4)_2$[10] in CH_2Cl_2 (0.01 M, 260 μL, 0.003 mmol) under Ar, the 1-dram vial was capped and placed in the center of a 30-cm loop of blue LEDs. The reaction mixture was stirred at rt under visible light irradiation for 18 h, after which a solution of 1,4-dimethoxybenzene (36 mg, 0.26 mmol, 1 equiv) in CH_2Cl_2 (1 mL) was added. The reaction mixture was stirred for 1 min and a small aliquot was removed and concentrated under reduced pressure. ^1H NMR analysis of the residue and

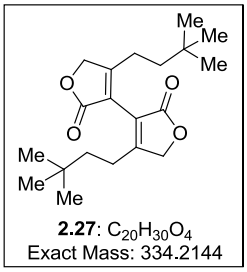
comparison of relative peak integrations using 1,4-dimethoxybenzene as an internal standard was used to determine the yield of products obtained. Silica gel chromatography (10% acetone/hexanes) of the crude mixture provided analytically pure samples of **2.25**, **2.26**, and **2.27**.



4-(3,3-Dimethylbutyl)furan-2(5*H*)-one (2.25): R_f = 0.16 (10% acetone/hexanes); ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.80–5.83 (m, 1H), 4.74 (s, 2H), 2.32–2.38 (m, 2H), 1.43–1.48 (m, 2H), 0.93 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.3, 171.4, 115.1, 73.2, 41.2, 30.4, 29.2, 24.2; IR (thin film) 2955, 2868, 1781, 1748, 1638, 1027 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{10}H_{16}O_2Na$, $(M + Na)^+$ 191.1048, found 191.1054.

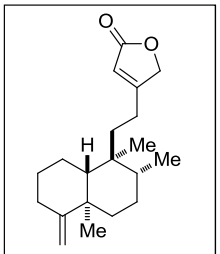


***E*- and *Z*- 4-(3,3-Dimethylbutylidene)dihydrofuran-2(3*H*)-one (2.26, a 2.6:1 mixture of double-bond isomers)**: R_f = 0.3 (10% acetone/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$, mixture of isomers) δ 5.50–5.60 (m, 1H, major and minor isomers), 4.85–4.88 (m, 2H, major and minor isomers), 3.22–3.25 (m, 2H, major isomer), 3.13–3.15 (m, 2H, minor isomer), 1.90 (d, *J* = 7.5 Hz, 2H, minor isomer), 1.82 (d, *J* = 7.5 Hz, 2H, major isomer), 0.91 (s, 9H, major and minor isomers); ^{13}C NMR (125 MHz, $CDCl_3$, mixture of isomers): δ 175.9, 175.8, 130.1, 129.6, 122.7, 122.2, 72.5, 70.7, 43.9, 42.6, 34.0, 31.9, 31.73, 31.68, 29.34, 29.29; IR (thin film) 2955, 1785, 1364, 1163, 1028 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{10}H_{16}O_2Na$, $(M + Na)^+$ 191.1048, found 191.1057.



2.27: $C_{20}H_{30}O_4$
Exact Mass: 334.2144

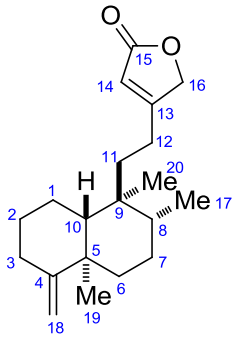
4,4'-bis(3,3-Dimethylbutyl)-[3,3'-bifuran]-2,2'(5*H*,5'*H*)-dione (2.27): R_f = 0.12 (10% acetone/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.87 (s, 4H), 2.45–2.50 (m, 4H), 1.38–1.44 (m, 4H), 0.91 (s, 18H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.1, 169.7, 117.3, 72.2, 41.6, 30.7, 29.1, 24.4; IR (thin film) 2955, 1756, 1620, 1157, 1030 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{20}H_{30}O_4Na$, $(M + Na)^+$ 357.2042, found 357.2043.



2.2: $C_{20}H_{30}O_2$
Exact Mass: 302.2246

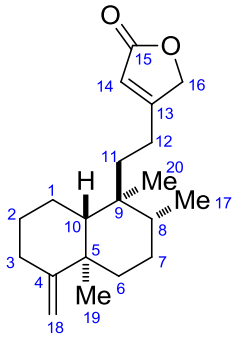
(1*R*,2*R*,4a*R*,8a*S*)-(+)-4-(2-(1,2,4a-Trimethyl-5-methylenedecahydronaphthalen-1-yl)ethyl)furan-2(5H)-one (2.2). A 1-dram vial was charged with (*N*-acyloxy)phthalimide **2.7** (20 mg, 0.05 mmol) and a magnetic stir bar under argon. A solution of 4-vinylfuran-2-one **2.6** (105 μL, 0.068 mmol) in CH_2Cl_2 (1 mL) was added, followed by CH_2Cl_2 (1.6 mL). After sequential addition of Hantzsch ester **2.28** (66 mg, 0.26 mmol), $Ru(bpy)_3(BF_4)_2$[10] (0.01 M in CH_2Cl_2, 50 μL, 5 μmol) and *i*-Pr_2NEt (20 μL, 0.1 mmol), the vial was capped and placed in the center of a 30-cm loop of blue LEDs. The heterogeneous reaction mixture was stirred for 18 h, after which it was transferred to a separatory funnel containing Et_2O (30 mL). The organic layer was washed with aqueous 4 M HCl (4 x 20 mL) and aqueous 2 M NaOH (3 x 20 mL), and was dried over $MgSO_4$. The ether layer was filtered and concentrated in vacuo to provide a yellow crude solid mixture that was suspended in 7% EtOAc/hexanes and filtered through a plug of silica gel (eluting with 200 mL 7% EtOAc/hexanes). Concentration of the filtrate provided a mixture of butenolide **2.2** and the corresponding β,γ-unsaturated lactone products (a mixture of *E*- and *Z*- olefins). The product mixture was dissolved in CH_2Cl_2 (2 mL) and DBU (9 μL, 0.06 mmol) was added.

The colorless solution was maintained at rt for 10 min, after which it was diluted with Et_2O (30 mL) and washed with aqueous 2 M HCl (3 x 20 mL). The ether layer was dried over $MgSO_4$, filtered, and concentrated in vacuo to give butenolide **2.2** (11 mg, 0.038 mmol, 74%, dr >20:1) as a thin film. Spectral data were consistent with previously reported data:[3] R_f = 0.40 (25% EtOAc/hexanes); ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.80 (s, 1H), 4.70 (s, 2H), 4.50 (s, 2H), 2.32–2.21 (m, 2H), 2.15–2.07 (m, 2H), 1.92–1.87 (m, 1H), 1.64–1.55 (m, 2H), 1.54–1.44 (m, 6H), 1.44–1.37 (m, 1H), 1.34–1.26 (m, 1H), 1.05 (s, 3H), 1.09–1.02 (m, 1H), 0.80 (d, *J* = 6.7 Hz, 3H), 0.78 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.2, 171.2, 160.2, 115.0, 103.0, 73.2, 48.8, 40.1, 39.4, 37.3, 36.8, 35.3, 33.0, 28.7, 27.4, 22.3, 21.9, 20.9, 18.1, 16.1. $[\alpha]^{22.4}_{D}$ +6.2, $[\alpha]^{22.5}_{577}$ +5.5, $[\alpha]^{22.6}_{546}$ +8.0, $[\alpha]^{22.7}_{435}$ +13.3, $[\alpha]^{22.8}_{405}$ +14.0 (*c* = 0.35, $CHCl_3$).



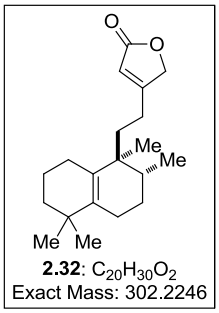
^{1}H NMR Data

position	literature **2.2**[3] (500 MHz)	synthetic **2.2** (600 MHz)	Δδ
1	not reported	1.54–1.44 (m, 2H),	--
2	not reported	1.92–1.87 (m, 1H) and 1.34–1.26 (m, 1H)	--
3	not reported	2.32–2.21 (m, 1H), and 2.15–2.07 (m, 1H)	--
6	not reported	1.64–1.55 (m, 1H), and 1.54–1.44 (m, 1H),	--
7	not reported	1.54–1.44 (m, 2H),	--
8	not reported	1.54–1.44 (m, 1H),	--
10	not reported	1.09–1.02 (m, 1H)	--
11	not reported	1.44–1.37 (m, 1H) and 1.64–1.55 (m, 1H),	--
12	not reported	2.32–2.21 (m, 1H), and 2.15–2.07 (m, 1H)	--
14	5.81 (s)	5.80 (br s, 1H)	–0.01
16	4.72 (s)	4.70 (br s, 3 H)	–0.02
17	0.82 (d, *J* = 6.2 Hz)	0.80 (d, *J* = 6.7 Hz, 3H),	–0.02
18	4.51 (s)	4.50 (br s, 2H)	–0.01
19	1.06 (s)	1.05 (s, 3H)	–0.01
20	0.79 (s)	0.78 (s, 3H)	–0.02



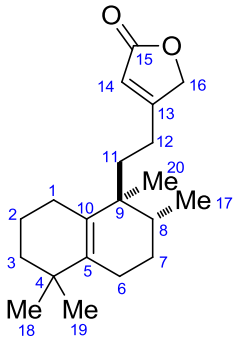
^{13}C NMR Data

position	literature **2.2**[4d] (100.6 MHz)	literature **2.2**[3] (125 MHz)	synthetic **2.2** (126 MHz)	Δδ [Lit. 3]
1	21.8	21.7	21.9	0.2
2	22.2*	32.9*	28.7	0.1
3	32.9	28.6*	33.0	0.1
4	160.4	160.1	160.2	0.1
5	39.3*	40.0	40.1	0.1
6	27.4*	37.2	37.3	0.1
7	37.3*	27.3	27.4	0.1
8	36.8	36.7	36.8	0.1
9	40.0*	39.2	39.4	0.2
10	48.8	48.7	48.8	0.1
11	28.6*	35.2	35.3	0.1
12	35.3*	22.3	22.3	0.0
13	170.9	171.1	171.2	0.1
14	115.0	114.9	115.0	0.1
15	174.0	174.0	174.2	0.2
16	73.0	73.0	73.2	0.2
17	15.9	16.0	16.1	0.1
18	102.8	102.8	103.0	0.2
19	18.3*	20.7	20.9	0.2
20	20.8*	17.9	18.1	0.2



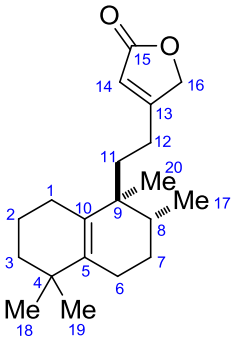
4-(2-((1*S*,2*R*)-1,2,5,5-Tetramethyl-1,2,3,4,5,6,7,8-octahydronaphthalen-1-yl)ethyl)furan-2(5*H*)-one (2.32): A 1-dram vial was charged with exocyclic olefin **2.2** (11 mg, 0.036 mmol), $CHCl_3$ (200 μL) and camphorsulfonic acid (10 mg, 0.044 mmol). The

vial was capped, sealed with Teflon tape, and was placed in an aluminum block preheated to 65 °C. The reaction mixture was maintained at this temperature for 66 h and then removed from the aluminum block and allowed to cool to rt. The vial was opened and the reaction mixture was diluted with Et_2O (20 mL), washed with aqueous 2 N NaOH (2 x 15 mL) and brine (2 x 15 mL). The organic layer was dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue obtained was purified by silica gel chromatography to provide *ent*-halimane diterpenoid **2.32** as a colorless oil (6.4 mg, 0.021 mmol, 59%): R_f = 0.58 (10% EtOAc/hexanes); ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.82 (s, 1H), 4.73 (s, 2H), 2.34–2.26 (m, 1 H), 2.07–2.00 (m, 1 H), 2.05–1.99 (m, 2H), 1.99–1.91 (m, 1H), 1.66–1.57 (m, 1H), 1.66–1.52 (m, 4H), 1.59–1.51 (m, 3H), 1.40–1.30 (m, 3H), 0.99 (s, 3H), 0.97 (s, 3H), 0.86 (s, 3H), 0.86 (d, *J* = 7.0 Hz, 3H), ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.3, 171.6, 138.7, 131.3, 115.0, 73.3, 40.8, 40.0, 34.7, 33.8, 33.4, 29.4, 27.7, 27.2, 25.9, 25.4, 23.8, 21.0, 20.0, 16.3; IR (thin film) 2925, 2866, 1779, 1749, 1458, 1168; HRMS (ESI) *m*/*z* calcd for $C_{20}H_{30}O_2Na$, $(M + Na)^+$ 325.2144, found 325.2136; $[\alpha]^{21.9}_D$ +12.5, $[\alpha]^{21.9}_{577}$ +11.6, $[\alpha]^{21.9}_{546}$ +12.9, $[\alpha]^{21.8}_{435}$ +16.2, $[\alpha]^{21.9}_{405}$ +24.0 (*c* = 0.50, MeOH).



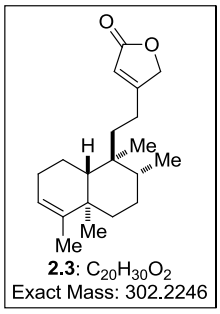
^{1}H NMR Data

position	literature **2.32** (500 MHz)	synthetic **2.32** (600 MHz)	Δδ
1	not reported	2.05–1.99 (m, 2H)	--
2	not reported	1.66–1.52 (m, 2H)	--
3	not reported	1.59–1.51 (m, 1H) and 1.40–1.30 (m, 1H)	--
6	not reported	1.99–1.91 (m, 1H) and 1.66–1.57 (m, 1H)	--
7	not reported	1.59–1.51 (m, 1H) and 1.40–1.30 (m, 1H)	--
8	not reported	1.59–1.51 (m, 1H) and 1.40–1.30 (m, 1H)	--
11	not reported	1.66–1.52 (m, 2H)	--
12	not reported	2.34–2.26 (m, 1 H) and 2.07–2.00 (m, 1 H)	--
14	5.83 (s)	5.82 (s, 1H)	–0.01
16	4.74 (s)	4.73 (s, 2H)	–0.01
17	0.86 (d, *J* = 6.3 Hz)	0.86 (d, *J* = 7.0 Hz, 3H)	0.00
18	0.97 (s)	0.97 (s, 3H)	0.00
19	0.99 (s)	0.99 (s, 3H)	0.00
20	0.87 (s)	0.86 (s, 3H)	–0.01



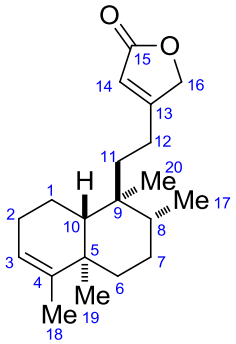
^{13}C NMR Data

position	literature **2.32**[3] (125 MHz)	synthetic **2.32** (126 MHz)	Δδ
1	25.2	25.4	+0.2
2	19.8	20.0	+0.2
3	39.8	40.0	+0.2
4	34.5	34.7	+0.2
5	138.6	138.7	+0.1
6	25.8	25.9	+0.1
7	27.0	27.2	+0.2
8	33.7	33.8	+0.1
9	40.7	40.8	+0.1
10	131.1	131.3	+0.2
11	33.3	33.4	+0.1
12	23.6	23.8	+0.2
13	171.4	171.6	+0.2
14	114.9	115.0	+0.1
15	174.0	174.3	+0.3
16	73.1	73.3	+0.2
17	16.1	16.3	+0.2
18	27.6	27.7	+0.1
19	29.2	29.4	+0.2
20	20.9	21.0	+0.1



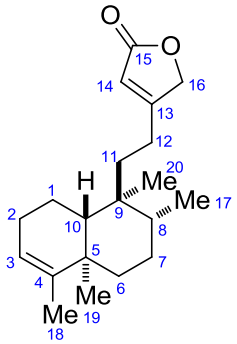
2.3: $C_{20}H_{30}O_2$
Exact Mass: 302.2246

(–)-4-1,2,4a,5-Tetramethyl-1,2,3,4,4a,7,8,8a-octahydronap-hthalen-1-yl)ethyl)furan-2(5*H*)-one ((–)-solidagolactone) (2.3). A 1-dram vial was charged with exocyclic olefin **2.2** (19 mg, 0.062 mmol), $RhCl_3$ hydrate (3 mg, 38–41% Rh), and a magnetic stir bar. After the addition of EtOH (1.3 mL), the vial was capped with a Teflon®-coated cap and sealed with Teflon® tape. The black heterogeneous mixture was heated to 80 °C and stirred for 18 h. The vial was then allowed to cool to rt and the reaction mixture was concentrated under reduced pressure. The crude residue obtained was purified by silica gel chromatography (10% EtOAc/hexanes) to provide (–)-solidagolactone (**2.3**) (13 mg, 0.044 mmol, 70%) as a thin film. Spectral data were in excellent agreement with previously reported data:[3] R_f = 0.40 (3:1 hexanes:EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.81 (s, 1H), 5.17 (s, 1H), 4.71 (s, 2H), 2.32–2.24 (m, 1H), 2.22–2.14 (m, 1H), 2.09–2.03 (m, 1H), 1.99–1.90 (m, 1H), 1.71 (apt d, *J* = 12.7 Hz, 1H), 1.65 (apt d, *J* = 13.6, 4.9 Hz, 1H), 1.56 (s, 3H), 1.54–1.38 (m, 6H), 1.30 (dd, *J* = 10.2, 3.5 Hz, 1H), 1.20–1.12 (m, 1H), 0.99 (s, 3H), 0.79 (d, *J* = 5.2 Hz, 3H), 0.75 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.2, 171.4, 144.4, 120.4, 115.0, 73.2, 46.5, 38.7, 38.2, 36.8, 36.4, 35.3, 27.4, 26.9, 22.3, 20.0, 18.4, 18.2, 18.1, 16.1. $[\alpha]^{23.0}_{D}$ –26.3, $[\alpha]^{23.0}_{577}$ –25.9, $[\alpha]^{23.0}_{546}$ –28.1, $[\alpha]^{23.0}_{435}$ –53.4, $[\alpha]^{23.0}_{405}$ –67.9 (*c* = 0.32, $CHCl_3$).



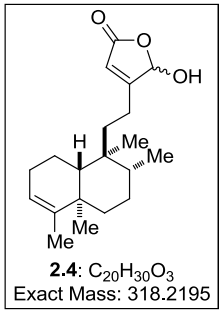
^{1}H NMR Data

position	literature **2.3**[3] (500 MHz)	synthetic **2.3** (600 MHz)	Δδ
1	not reported	1.54–1.38 (m, 2H),	--
2	not reported	1.99–1.90 (m, 1H), and 2.09–2.03 (m, 1H)	--
3	5.19 (br s, 1H)	5.17 (br s, 1H)	–0.02
6	not reported	1.71 (apt d, *J* = 12.7 Hz, 1H), and 1.20–1.12 (m, 1H),	--
7	not reported	1.54–1.38 (m, 2H),	--
8	not reported	1.54–1.38 (m, 1H),	--
10	not reported	1.30 (dd, *J* = 10.2, 3.5 Hz, 1H),	--
11	not reported	1.65 (apt td, *J* = 13.6, 4.9 Hz, 1H) and 1.54–1.38 (m, 1H),	--
12	not reported	2.32–2.24 (m, 1H) and 2.22–2.14 (m, 1H)	--
14	5.83 (s, 1H)	5.81 (s, 1H)	–0.02
16	4.73 (s, 2H)	4.71 (s, 2 H)	–0.02
17	0.82 (d, *J* = 6.2 Hz, 3H)	0.79 (d, *J* = 5.2 Hz, 3H),	–0.03
18	1.59 (s, 3H)	1.56 (s, 3H)	–0.03
19	1.01 (s, 3H)	0.99 (s, 3H)	–0.02
20	0.78 (s, 3H)	0.75 (s, 3H)	–0.03



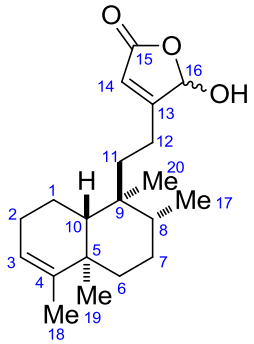
^{13}C NMR Data

position	literature **2.3**[3] (125 MHz)	synthetic **2.3** (126 MHz)	Δδ
1	18.3	18.4	+0.1
2	26.8	26.9	+0.1
3	120.2	120.4	+0.2
4	144.4	144.4	+0.0
5	38.7	38.7	+0.0
6	36.7	36.8	+0.1
7	27.3	27.4	+0.1
8	36.3	36.4	+0.1
9	38.2	38.2	0.0
10	46.5	46.5	0.0
11	35.3	35.3	0.0
12	22.3	22.3	0.0
13	171.2	171.4	+0.2
14	115.0	115.0	0.0
15	174.0	174.2	+0.2
16	73.1	73.2	+0.1
17	16.0	16.1	+0.1
18	17.9	18.1	+0.2
19	19.9	20.0	+0.1
20	18.1	18.2	+0.1



2.4: $C_{20}H_{30}O_3$
Exact Mass: 318.2195

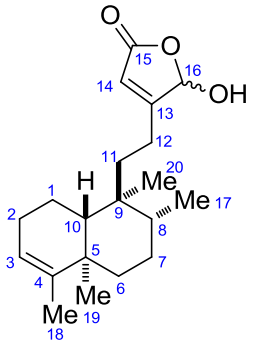
(–)-16-Hydroxycleroda-3,13 (14)Z-dien-15,16-olide, (–)-PL3 (2.4). To a stirred solution of (–)-solidagolactone (**2.3**) (45 mg, 0.15 mmol) in CH_2Cl_2 (0.5 mL) was added at rt a solution of NEt_3 (29 μL, 0.21 mmol) in CH_2Cl_2 (0.4 mL). After 3 min, a solution of TBSOTf (38 μL, 0.16 mmol) in CH_2Cl_2 (0.4 mL) was added and stirring at rt was continued for an additional 30 min, after which a solution of 2-methyl-2-butene (6 μL, 0.06 mmol) in CH_2Cl_2 (0.2 mL) was added. The reaction mixture was cooled to 0 °C, a solution of *m*-CPBA (49 mg, 0.22 mmol; technical grade ~70% purity) was added and stirring was continued for 30 min at this temperature. The reaction mixture was allowed to warm to rt, diluted with Et_2O (20 mL) and washed with aqueous $NaHCO_3$ (0.3 M, 4 x 2 mL), aqueous 2 N HCl (2 mL), dried over Na_2SO_4 and concentrated *in vacuo*. This residue was purified by column chromatography (7:1 hexanes:acetone) to obtain **2.4** as a colorless amorphous solid (33 mg, 0.11 mmol, 70%). Spectral data were consistent with previously reported data:[2d,3] R_f = 0.30 (2:1 hexanes:acetone); ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.00 (d, *J* = 6.0 Hz, 1H), 5.84 (br s, 1H), 5.19 (br s, 1H), 4.39 (d, *J* = 4.0 Hz, 1H), 2.43–2.10 (m, 2H), 2.10–1.92 (m, 2H), 1.72 (apt d, *J* = 12.5 Hz, 1H), 1.69–1.63 (m, 1H), 1.58 (s, 3H), 1.56–1.49 (m, 3H), 1.49–1.40 (m, 3H), 1.34 (apt d, *J* = 11.6 Hz, 1H), 1.21–1.13 (m, 1H), 1.00 (s, 3H), 0.81 (s, 3H), 0.77 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.7, 170.71,* 170.66,* 144.52,* 144.46,* 120.55,* 120.48,* 117.18,* 117.15,* 99.16,* 99.14,* 46.6, 38.82,* 38.79,* 38.3, 36.8, 36.48,* 36.44,* 34.93,* 34.88,* 27.5, 26.9, 21.50,* 21.47,* 20.0, 18.4, 18.3, 18.1, 16.1 (*Two sets of carbons observed as a result of 1:1 mixture of epimers at C16); mp = 163 °C; $[\alpha]^{23.0}_{D}$ –21.4, $[\alpha]^{23.0}_{577}$ –26.6, $[\alpha]^{23.0}_{546}$ –30.7, $[\alpha]^{23.0}_{435}$ –52.4, $[\alpha]^{23.0}_{405}$ –70.8 (*c* = 0.23, $CHCl_3$).



^{1}H NMR Data

position	literature **2.4**[2d] (300 MHz)[a]	synthetic **2.4** (600 MHz)	$\Delta\delta^b$
1	1.52 (m, 2H)	1.56–1.49 (m, 2H)	+0.01
2	2.04 (m, 2H)	2.10–1.91 (m, 2H)	–0.04
3	5.18 (br s, 1H)	5.19 (s, 1H),	–0.01
6	1.75 (m, 1H) and 1.18 (m, 1H)	1.72 (apt d, *J* = 12.5 Hz, 1H) and 1.22–1.13 (m, 1H)	–0.03
7	1.44 (m, 2H),	1.49–1.40 (m, 2H)	0.00
8	1.45 (m, 1H)	1.49–1.40 (m, 1H)	0.00
10	1.34 (m, 1H)	1.34 (apt d, *J* = 11.6 Hz, 1H)	0.00
11	1.70 (m, 1H) and 1.52 (m, 1H)	1.72 (d, *J* = 12.5 Hz, 1H) and 1.56–1.49 (s, 1H)	+0.01
12	2.26 (m, 2H)	2.44–2.10 (m, 2H)	--
14	5.85 (s, 1H)	5.84 (s, 1H)	–0.01
16	6.07(s, 1H)	6.00 (d, *J* = 6.0 Hz, 1H)	–0.07[c]
17	0.81 (d, *J* = 6.4 Hz, 3H)	0.81 (br s, 3H)	0.00
18	1.58 (s, 3H)	1.58 (s, 3H)	0.00
19	1.00 (s, 3H)	1.00 (s, 3H)	0.00
20	0.77 (s, 3H)	0.77 (s, 3H)	0.00
C16-OH	not reported	4.39 (d, *J* = 4.0 Hz, 1H)	--

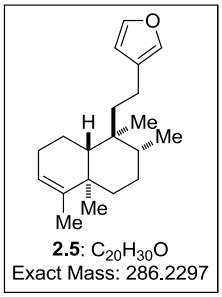
[a]Reported as the 16*S* isomer.[2d] [b]When a multiplet is reported as a range of chemical shifts, the center of the range is used in this comparison. [c]This is attributed this larger difference to the synthetic product being a 1:1 mixture of 16-hydroxy epimers.



^{13}C NMR Data

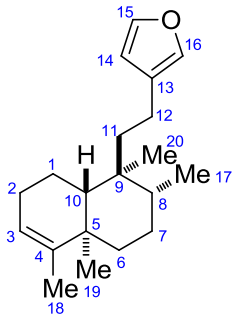
position	literature **2.4**[2d] (75 MHz)[a]	literature **2.4**[3] (125 MHz)[b,c]	synthetic **2.4** (126 MHz)[c]	$\Delta\delta^d$
1	18.4	18.3	18.4	+0.1
2	26.9	26.8	26.9	+0.1
3	120.5	120.3, 120.4	120.55, 120.48*	+0.2
4	144.5	144.3, 144.3	144.52, 144.46*	+0.2
5	38.3	38.1	38.3	+0.2
6	36.9	36.7	36.8	+0.1
7	27.5	27.4	27.5	+0.1
8	36.5	36.3. 36.3	36.48, 36.44*	+0.1
9	38.8	38.6, 38.7	38.82, 38.79*	+0.2
10	46.6	46.5	46.60	+0.1
11	35.0	34.8, 34.8	34.93, 34.88*	+0.1
12	21.5	21.3, 21.4	21.50, 21.47*	+0.2
13	170.4	171.0	170.71, 170.66*	–0.3
14	117.6	116.8	117.18, 117.15*	–0.4
15	172.0	172.0	171.7	–0.3
16	101.8[e]	99.3	99.16, 99.14*	–0.1
17	16.1	15.9	16.1	+0.2
18	18.1	17.9	18.1	+0.2
19	20.0	19.9	20.0	+0.1
20	18.3	18.1	18.3	+0.2

[a]Reported as the 16*S* isomer.[2d] [b]Reported as a 1:1 mixture of 16-hydroxy epimers.[3] [c]Asterisk indicates that two signals are observed for this carbon in the 1:1 mixture of 16-hydroxy epimers. [d]This comparison is for the natural and synthetic 1:1 mixture of 16-hydroxy epimers. [e]The larger chemical shift of this carbon is undoubtedly a result of this sample being a single hydroxyl epimer, whereas the signals reported in columns 3 and 4 are for this carbon of a 1:1 mixture of hydroxyl epimers.



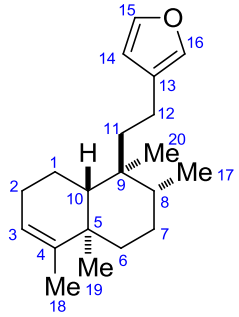
2.5: $C_{20}H_{30}O$
Exact Mass: 286.2297

(–)-3-(2-(1,2,4a,5-Tetramethyl-1,2,3,4,4a,7,8,8aoctahydronaphthalen-1yl)ethyl)-furan; (–)-annonene (2.5). To a solution of (–)-solidagolactone (**2.3**) (23 mg, 0.076 mmol) in CH_2Cl_2 (1.5 mL) was added at −78 °C DIBAL-H (150 μL, 0.150 mmol, 1.0 M solution in hexanes). After 30 min, MeOH was added and the acetone/dry ice bath was removed. The reaction was allowed to warm to 0 °C and aqueous 2 N HCl (270 μL, 0.530 mmol) was added. The mixture was stirred for 30 min at rt. The organic phase was diluted with Et_2O (10 mL), washed with H_2O (2 x 5 mL), dried over Na_2SO_4 and concentrated *in vacuo*. The resulting residue was purified by flash chromatography (20:1 to 10:1 hexanes:EtOAc) to obtain (–)-annonene (**2.5**) as a colorless oil (16 mg, 0.056 mmol, 74%). Spectral data were consistent with previously reported data:[6,34] R_f = 0.69 (10:1 hexanes:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 (s, 1H), 7.21 (s, 1H), 6.27 (s, 1H), 5.21 (s, 1H), 2.36–2.18 (m, 2H), 2.11–1.94 (m, 2H), 1.75–1.41 (m, 9H), 1.61 (s, 3H), 1.24–1.17 (m, 1H), 1.01 (s, 3H), 0.83 (d, *J* = 6.7 Hz, 3H), 0.74 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 144.7, 142.8, 138.5, 126.0, 120.6, 111.2, 46.6, 38.9, 38.7, 38.3, 37.0, 36.4, 27.6, 27.0, 20.1, 18.44, 18.43, 18.3, 18.2, 16.2; $[\alpha]^{23.0}_{D}$ –28.9, $[\alpha]^{23.0}_{577}$ –29.2, $[\alpha]^{23.0}_{546}$ –31.6, $[\alpha]^{23.0}_{435}$ –56.4, $[\alpha]^{23.0}_{405}$ –68.9 (*c* = 0.71, $CHCl_3$).



^{1}H NMR Data

position	literature **2.5**[6] (100.6 MHz)	synthetic **2.5** (500 MHz)	Δδ
1	1.27–2.47 (m, 2H)	1.75–1.41 (m, 2H)	--
2	1.27–2.47 (m, 2H)	2.11–1.94 (m, 2H)	--
3	5.20 (br s, 1H)	5.21 (s, 1H)	+0.01
6	1.27–2.47 (m, 2H)	1.75–1.41 (m, 2H)	--
7	1.27–2.47 (m, 2H)	1.75–1.41 (m, 2H)	--
8	1.27–2.47 (m, 1H)	1.24–1.17 (m, 1H)	--
10	1.27–2.47 (m, 1H)	1.75–1.41 (m, 1H)	--
11	1.27–2.47 (m, 2H)	1.75–1.41 (m, 2H)	--
12	1.27–2.47 (m, 2H)	2.36–2.18 (m, 2H)	--
14	6.27 (br s, 1H)	6.27 (br s, 1H),	--
15	7.37 (t, *J* = 2 Hz, 1H)	7.35 (br s, 1H),	–0.02
16	7.22 (br s, 1H)	7.21 (br s, 1H)	–0.01
17	0.83 (d *J* = 5 Hz, 3H)	0.83 (d, *J* = 6.7 Hz, 3H)	–0.00
18	1.59 (d, *J* = 2 Hz, 3H)	1.61 (s, 3H)	–0.02
19	1.00 (s, 3H)	0.99 (s, 3H)	–0.01
20	0.75 (s, 3H)	0.75 (s, 3H)	0.00



^{13}C NMR Data

position	literature **2.5**[34] (125 MHz)	synthetic **2.5** (126 MHz)	Δδ
1	18.2	18.3	+ 0.1
2	26.7	27.0	+ 0.3
3	120.6	120.6	0
4	143.7	144.7	+1.0[a]
5	37.9	38.3	+ 0.4
6	36.6	37.0	+ 0.4
7	27.4	27.6	+ 0.2
8	36.2	36.4	+ 0.2
9	38.4	38.7	+ 0.3
10	46.1	46.6	+ 0.5
11	38.5	38.9	+ 0.4
12	18.2	18.44	+ 0.24
13	125.2	126.0	+ 0.8
14	110.7	111.2	+ 0.5
15	142.3	142.8	+ 0.5
16	138.0	138.5	+ 0.5
17	16.1	16.2	+ 0.1
18	17.9	18.43	+ 0.53
19	19.8	20.1	+ 0.3
20	18.2	18.2	0

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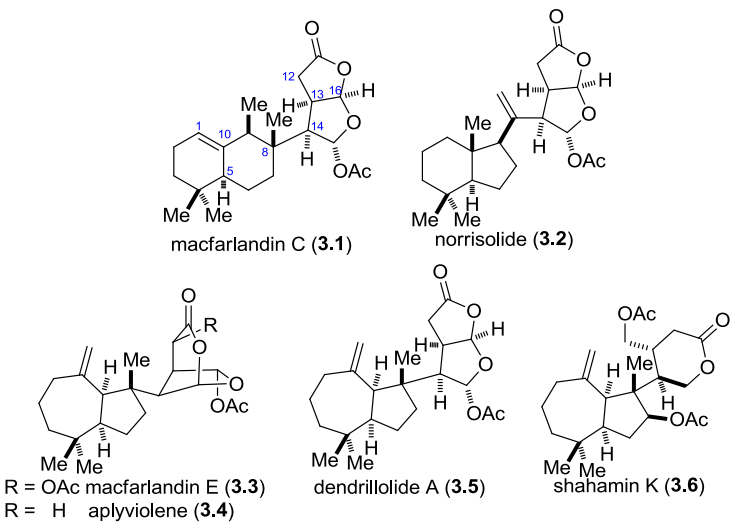
Chapter 3: Studies Toward the Total Synthesis of Macfarlandin C

3.1 Introduction

Macfarlandin C (**3.1**) is a rearranged spongian diterpene first isolated from the marine nudibranch *Chromodoris macfarlandi* in 1986 by Faulkner, Clardy and coworkers.[1] Like many related members of this natural product family (Figure 3.1), macfarlandin C exhibits a bicyclic hydrocarbon unit joined to a dioxabicyclooctanone moiety via the central C8–C14 bond.[2] Although this general feature is common among most rearranged spongian diterpenes, the two conjoined bicycles can exist in various

Figure 3.1 Representative rearranged spongian diterpenes

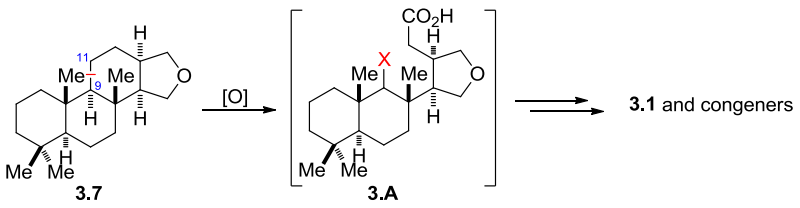


different permutations. For example, the hydrophobic unit present in macfarlandin C is a functionalized octahydronaphthalene ring system, whereas many other rearranged spongian diterpenes bear a *cis*-perhydroazulene or *trans*-hydrindane fragment, among other possibilities. Additionally, the highly oxygenated portion of these diterpenes can vary greatly; two of the notably more complex motifs are the dioxabicyclo[3.3.0]octan-3-

one (macfarlandin C (**3.1**), norrisolide (**3.2**) and dendrillolide A (**3.5**)), and dioxabicyclo[3.2.1]octan-3-ones (macfarlandin E (**3.3**) and aplyviolene (**3.4**)).

The structural similarity between the many known rearranged spongian diterpenes has prompted speculation that they share a common biosynthetic precursor.[2] As many spongian diterpenes have been isolated that possess the general skeleton **3.7**, it has been proposed that enzymatic oxidations and structural rearrangements from precursors such as **3.7** account for the variety of diverse natural products in this family. A commonly invoked biosynthetic process is oxidative cleavage of the C9–C11 bond in **3.7**.[2] This bond cleavage is thought to lead to an oxidized intermediate such as **3.A**, which is a proposed intermediate in the biosynthetic pathway of several rearranged spongian diterpenes.[2,3,4] Further enzymatic processing of **3.A** could then occur, with a skeletal shift displacing leaving group "X" to form the fused perhydroazulene unit present in dendrillolide A (**3.5**) or alternatively the octahydronaphthalene fragment found in macfarlandin C (**3.1**). The bicyclic lactone moiety could similarly be formed via extensive oxidation of the tetrahydrofuran ring.[2,4]

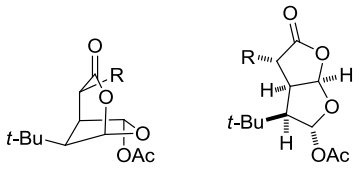
Figure 3.2: Proposed biosynthetic pathway



A diverse array of biological activities has been reported for members of the rearranged spongian diterpene family.[1,2] In particular, the Overman group's interest in this category of natural products arose not only from the structural complexity of these diterpenes but also from the remarkable effects that several members exhibit on the Golgi

apparatus.[5] Specifically, norrisolide (**3.2**) and simplified analogs have been reported to fragment the Golgi ribbon into stacks that are then dispersed throughout the cytosol.[5,6] By contrast, recent collaborative studies between the Overman and Sütterlin groups at UC Irvine revealed that macfarlandin E also acts to induce considerable alterations of Golgi structure in normal rat kidney (NRK) cells; however, these fragments remain localized in the pericentriolar region of the cell.[5] This disruption of Golgi structure was also demonstrated to affect protein secretion via blockage of Golgi to membrane transport.[5] Speculating that the highly oxidized bicyclooctanone moiety was responsible for the observed biological effects, synthetic analogs (**3.8**) and (**3.9**) were prepared, which are effectively simplified congeners of macfarlandin E (**3.3**) and aplyviolene (**3.4**) in which the *cis*-perhydroazulene moiety has been replaced with a simple *tert*-butyl group.[5,7] Related analogs (**3.10**) and (**3.11**) were also synthesized, which are simplified forms of macfarlandin C (**3.1**) and dendrillolide A (**3.5**). Analog **3.10** bears an additional acetoxy group adjacent to the lactone carbonyl (Figure 3.3).

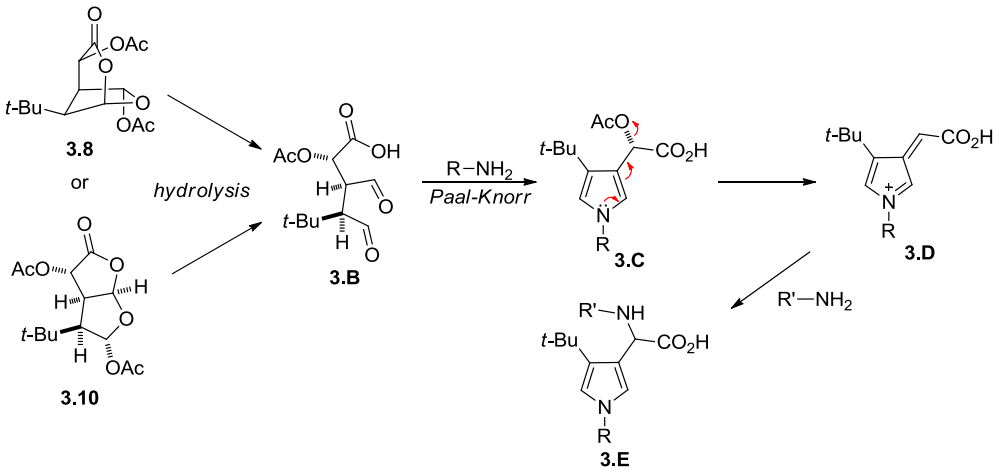
Figure 3.3: Simplified rearranged spongian diterpene analogs



A Golgi phenotype nearly identical to that effected by macfarlandin E (**3.3**) was observed for **3.8**, while compound **3.9** induced no Golgi modification.[5,7] Not surprisingly, the bicyclo[3.3.0]octanones **3.10** and **3.11** exhibited the same trend, where treatment of NRK cells with acetoxylated bicycle **3.10** caused significant disruption of Golgi

structure.[7] Des-acetoxy congener **3.11**, however, elicited no biological response. These results suggested that the acetoxy group adjacent to the carbonyl plays a critical role in inducing the Golgi phenotype observed.[5,7] Bioconjugation studies conducted by the Overman group subsequently contributed evidence for the precise role of this functional group, suggesting that conjugation may occur via the mechanism depicted in Figure 3.4. Degradation of either the dioxabicylclo[3.2.1]octanone or the dioxabicyclo[3.3.0]octanone ring systems by a cellular nucleophile may first occur to generate dialdehyde intermediate **3.B**, which engages in Paal–Knorr pyrrole formation with the primary amine group of enzymatic lysine residues. The acetoxy group of **3.C** could then be ejected in a gramine-type fragmentation, generating electrophilic intermediate **3.D** that was shown to be intercepted by additional amino groups in bioconjugation experiments to provide amines such as **3.E**.[7]

Figure 3.4: Proposed bioconjugation mechanism

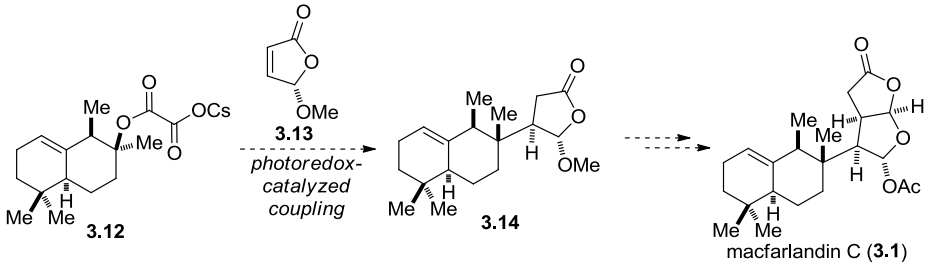


The effect of macfarlandin C (**3.1**) on Golgi structure and function has not yet been studied. Based on the proposed mechanism of action of macfarlandin E (**3.3**) and the simplified analogs depicted in Figure 3.4, it is expected that macfarlandin C (**3.1**) will not

elicit the Golgi fragmentation phenotype, as it lacks an acetoxy group at C12. In order to assess the *in vitro* activity of macfarlandin C, the Overman lab chose to prepare this molecule, potentially as well as C12-acetoxylated variants, by total synthesis. Access to significant amounts of macfarlandin C (**3.1**) would enable the comparison of any observed biological activity to that exhibited by previously studied members of the rearranged spongian diterpene family.

Central to the proposed synthetic approach toward macfarlandin C was stereoselective construction of the key C8–C14 bond by a photoredox-catalyzed radical coupling.[8,9] Recent advances in the development of tertiary alcohol-derived radical precursors strongly suggested that generation of the required tertiary carbon radical would be possible via the corresponding hemioxalate salt **3.12**[9] in the coupling reaction with butenolide **3.13**[10] depicted in Figure 3.5.

Figure 3.5: Proposed key radical coupling step

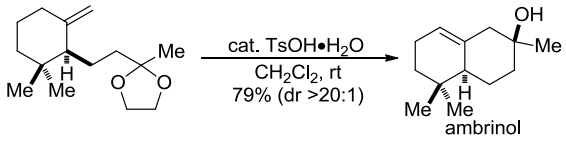


3.2 Previous work: Decalin Synthesis

To obtain radical precursor **3.12** for the key radical coupling step, an efficient synthesis of the corresponding decalin tertiary alcohol was required. At the onset, it was speculated that the hemioxalate salt of either epimer of the precursor alcohol would be effective for generating a tertiary radical to couple with butenolide **3.13**, so the intitial

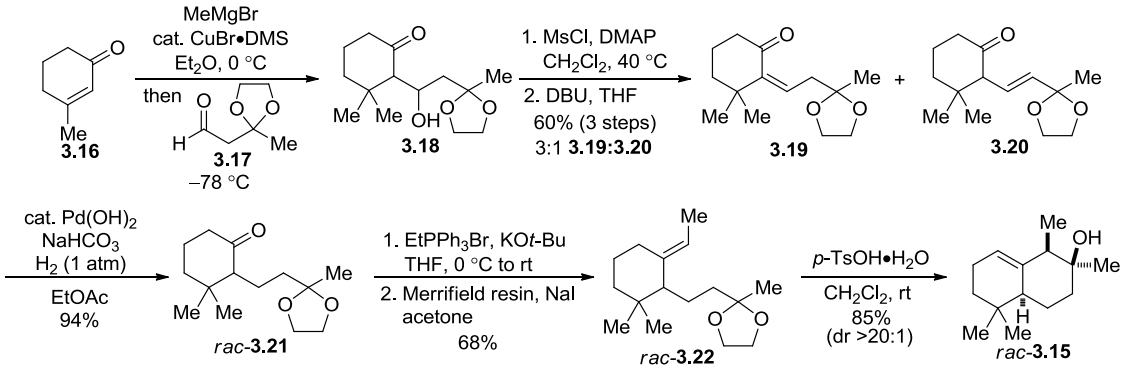
synthesis plan targeted either epimer of the alcohol (or a mixture of the epimers if they were obtained). The synthesis of the decalin framework itself was not expected to be straightforward, as the trisubstituted olefin of carbons C1 and C10 gives the bicyclic ring system a bent shape significantly departed from a typical *cis*- or *trans*- decalin. The consequence of this ring shape is that the molecule does not have well-defined axial and equatorial positions, preventing one from drawing on established reactivity to functionalize *cis*- or *trans*- decalin ring systems. Interestingly, however, an attractive carbonyl-ene cyclization had been previously used by Oltra and co-workers to construct a similar decalin ring system (Equation 3.1).[11] It was anticipated that a nearly identical substrate bearing an additional alkenyl methyl group would cyclize stereoselectively to directly provide the tertiary alcohol required to access a radical precursor.

Equation 3.1



Dr. André Dieskau designed an expedient route to synthesize racemic tertiary alcohol *rac*-**3.15** using a similar carbonyl-ene cyclization (Scheme 3.1).[12] The synthesis of *rac*-**3.15** begins with conjugate methyl cuprate addition to 3-methylcyclohexenone (**3.16**) to generate an enolate which was subsequently trapped with aldehyde **3.17** to provide a mixture of alcohols **3.18**. Mesylation of the aldol products and elimination with DBU afforded a mixture of regioisomeric olefins **3.19** and **3.20** in 60% yield over the three steps. This mixture of olefins converged in the ensuing hydrogenation step mediated by $Pd(OH)_2$, forming ketone *rac*-**3.21** in high yield. Cyclization precursor *rac*-

Scheme 3.1 Synthesis of alcohol *rac*-3.15



3.22 was then generated as a single olefin isomer by Wittig ethylidenation of *rac*-**3.21** followed by resin-assisted purification. The critical carbonyl-ene reaction proceeded readily in the presence of catalytic *p*-toluenesulfonic acid in wet CH_2Cl_2 at room termperature after *in situ* ketal deprotection to provide tertiary alcohol *rac*-**3.15** in 85% yield as a single diastereomer.[13] It was anticipated that the synthesis of this decalin fragment could be rendered enantioselective by performing an enantioselective hydrogenation of enone **3.19**.[14]

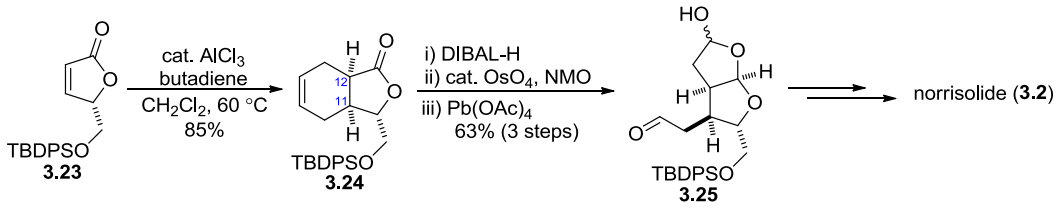
3.3 Previous Work: Bicyclic Lactone Synthesis

The dioxabicyclo[3.3.0]octan-3-one fragment of macfarlandin C (**3.1**) also poses a considerable synthetic challenge. In particular, establishing the relative stereochemistry of substituents on the lower tetrahydrofuran ring would require careful execution. The bicyclic lactone of macfarlandin C (**3.1**) as well as those of dendrillolide A (**3.5**) and norrisolide (**3.2**) are significantly challenging due to the presence of a large substituent (either the decalin, *cis*-perhydroazulene, or vinylhydrindane, respectively) on the concave face of the bicyclooctanone. The steric interaction of these substituents with the bicyclic

lactone framework is maximized when this substituent resides on the concave face, and as a result complicates the synthesis of these structural motifs.

To date, two total syntheses of norrisolide (**3.2**) have been completed that demonstrate successful methods for constructing dioxabicyclo[3.3.0]octan-3-one units. The first synthesis of norrisolide was published in 2004 by Theodorakis and co-workers, and featured a Diels–Alder cycloaddition of butenolide **3.23** with butadiene to establish the *cis*-stereochemistry of the C12 and C11 substituents (norrisolide numbering).[15,16] Oxidative degradation of the cyclohexene ring of **3.24** then generated two methylcarboxaldehyde moieties that were differentiated by cyclization of the C12-substituent with a lactol, thus stereoselectively forming the framework of the [3.3.0] bicycle. Incorporation of the hydrindane unit was then accomplished over several steps from **3.25** to complete Theodorakis's synthesis of norrisolide (**3.2**).

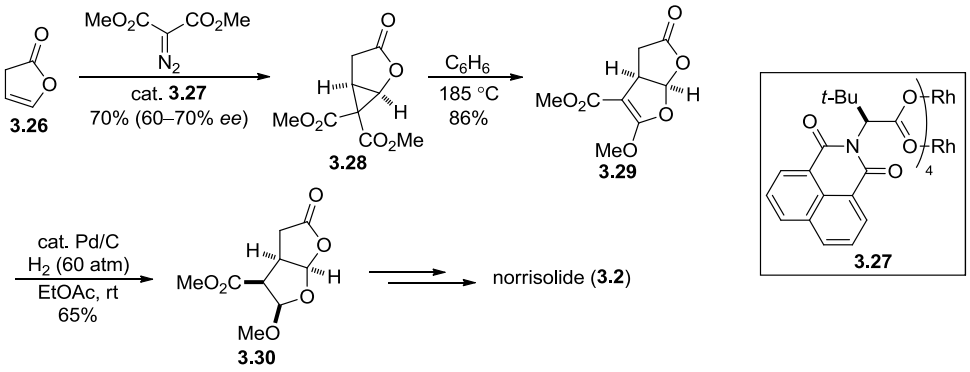
Scheme 3.2: Theodorakis's Diels-Alder approach toward norrisolide (3.2)



The Snapper group utilized a much different approach to the bicyclic lactone in their synthesis of norrisolide reported in 2012 (Scheme 3.3).[17,18] The absolute configuration of the bicyclic lactone is established by enantioselective cyclopropanation of **3.26** using dimethyl diazomalonate and dirhodium catalyst **3.27** to give cyclopropane **3.28** in 70% yield, albeit in low enantioselectivity. Cyclopropane opening and intramolecular trapping of the resulting oxocarbenium ion under thermal conditions then formed bicyclooctanone **3.29** in 86% yield. This intermediate was hydrogenated using

Pd/C at 60 atm H_2, forming **3.30** in which the carbomethoxy and methoxy groups reside on the concave face of the bicycle. Although the stereochemistry at the methoxy-bearing carbon would be erased later in the synthesis, this strategy proved successful for establishing the critical C11 and C12 stereocenters.

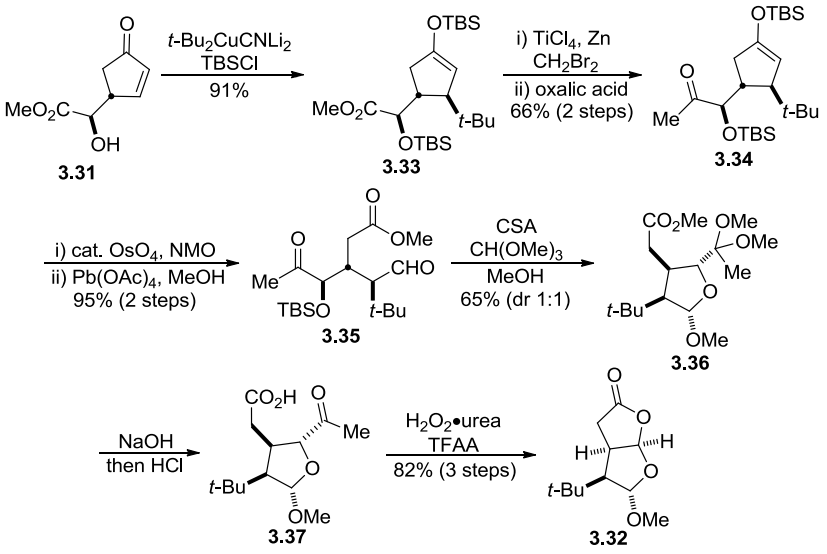
Scheme 3.3 Snapper's cyclopropanation-hydrogenation approach to norrisolide (3.2)



The Overman group has also developed novel approaches to the synthesis of both dioxabicyclo[3.2.1]octan-3-ones and dioxabicyclo[3.3.0]octan-3-ones. The simplified rearranged spongian diterpene analogs described in Figure 3.3 were prepared via a divergent route from enone **3.31**; the synthesis of bicyclooctanone **3.32** is depicted in Scheme 3.4. The synthesis of bicyclic lactone **3.32** commences with conjugate *tert*-butyl cyanocuprate addition to **3.31** and silyl protection of both the free alcohol and the intermediate enolate to provide **3.33** in excellent yield. Transformation of the ester group to a methyl ketone was carried out in 66% yield over two steps, generating enoxysilane **3.34** which was cleaved under oxidative conditions to form tricarbonyl **3.35**. This intermediate engaged in acid-promoted cyclization after *in situ* deprotection of the silyl ether to yield tetrahydrofuran **3.36** in 65% yield as a mixture of methoxy epimers. Deprotection of the methyl ester and dimethoxy ketal groups to provide ketone **3.37**,

followed by Baeyer–Villiger oxidation and lactonization efficiently gave the bicyclic lactone in 83% yield over three steps. The analogous dioxabicyclo[3.2.1]octan-3-ones were synthesized in divergent fashion from tricarbonyl **3.35**.

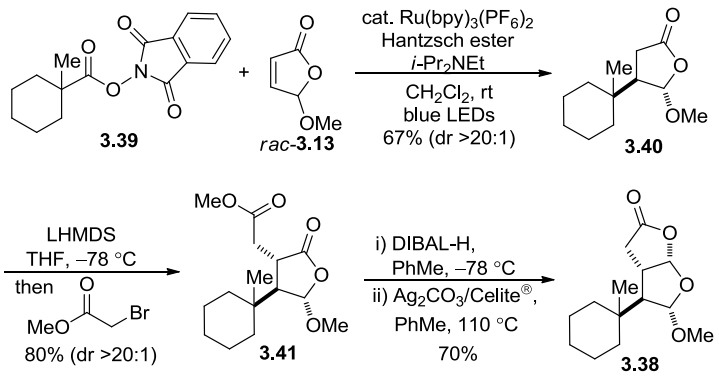
Scheme 3.4 Overman's synthesis of bicyclic lactone 3.32



More recently, the Overman group has developed a streamlined approach for the synthesis of dioxabicyclo[3.3.0]octanones that employs a DIBAL-H reduction-cyclization cascade of a carboxymethyl-substituted lactone.[19] A variety of substituted bicyclic lactones have been synthesized to date according to the general strategy shown in Scheme 3.5 specifically for bicyclic lactone **3.38**. The sequence begins with diastereoselective coupling of a tertiary radical intermediate generated from any of a variety of possible precursors (*N*-acyloxyphthalimide **3.39** is shown arbitrarily) with 5-methoxyfuran-2-one *rac*-**3.13** to provide lactone **3.40**. Alkylation of the lithium enolate of **3.40** with methyl bromoacetate installs the methyl carboxymethyl side chain diastereoselectively, with the electrophile approaching from the face opposite the 1-methylcyclohexyl group. Treatment of substituted lactone **3.41** with DIBAL-H results in

hydride delivery to the lactone carbonyl, generating a presumed metalated lactol intermediate that cyclizes on the pendant ester. In many cases, the bicyclic lactone so formed is in turn reduced with excess DIBAL-H present in the reaction, so the product mixture is treated with Ag_2CO_3/Celite® to oxidize any bicyclic lactol formed to the desired lactone **3.38**.

Scheme 3.5 Overman's DIBAL-H reduction-cyclization cascade



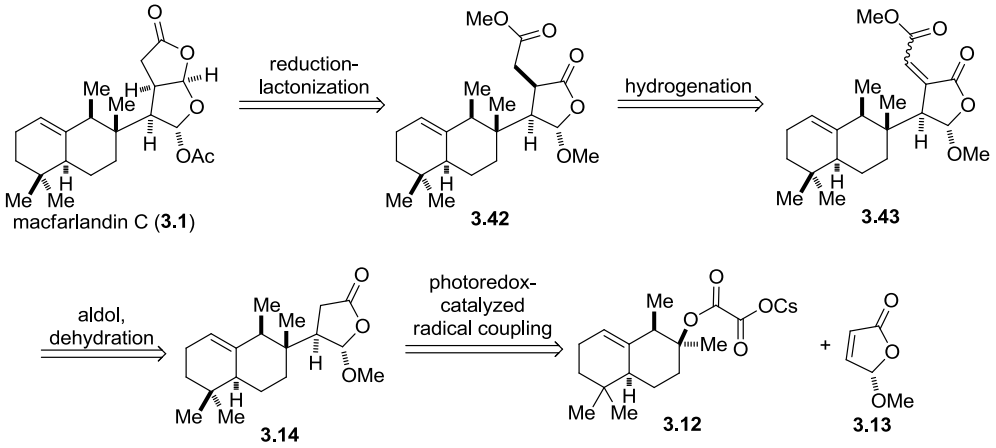
While the synthetic process described above can be used to construct bicyclic lactones such as **3.38** rapidly from coupling products such as **3.40**, the stereoselectivity of the alkylation of lactone **3.40** suggests that only dioxabicyclo[3.3.0]octanones bearing the quaternary substituent on the convex face of the bicycle can be accessed via this sequence of steps. Thus, in order to apply the expedient DIBAL-H reduction-cyclization reaction to the total synthesis of macfarlandin C (**3.1**), it would be necessary to establish the stereochemistry of the carbon center adjacent to the lactone carbonyl by another means prior to the reductive cascade.

3.4 Retrosynthetic Analysis

The reduction-lactonization cascade was expected to be carried out late-stage, followed by exchange of the methoxy acetal for an acetoxy group to provide

macfarlandin C (**3.1**) (Figure 3.6). It was anticipated that this cyclization precursor **3.42** might be generated by diastereoselective and chemoselective hydrogenation of unsaturated lactone **3.43**, which in turn could arise from aldol condensation of lactone **3.14** with methyl glyoxylate. Lactone **3.14** could be formed by the photoredox-catalyzed coupling of cesium oxalate **3.12** with methoxybutenolide **3.13**.

Figure 3.6 Retrosynthetic analysis for macfarlandin C (3.1)



The major objectives that required consideration at the onset of this total synthesis project were the synthesis of the decalin fragment in enantioselective fashion and the stereoselective synthesis of the bicyclic lactone unit, likely initially employing a simpler model system.

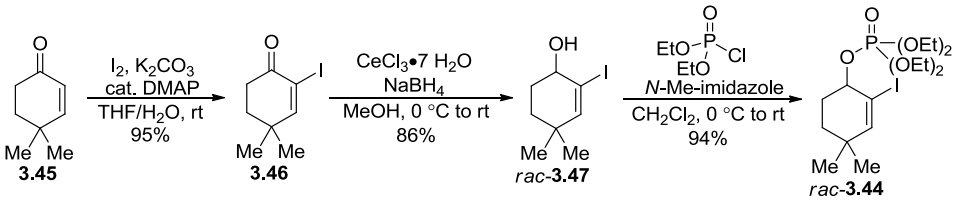
3.5 Results and Discussion

3.5.1 Enantioselective Synthesis of the Decalin Fragment

It was projected that the route to racemic alcohol *rac*-**3.15** developed by Dr. André Dieskau could be made enantioselective by employing an asymmetric hydrogenation of exocyclic enone **3.19**.[14] Evaluating this approach required access to regioisomerically pure enone **3.19**, however. A brief survey of various conditions for dehydrating aldol

adduct **3.18** were explored with no success. It was then decided that the absolute configuration of the ketone **3.21** should be set by an alternative strategy. A two-step method for forming substituted cyclohexanones in enantiopure form developed by the Knochel group was most attractive, as they had shown that even highly hindered neopentylic carbon stereocenters can be formed adjacent to ketones in a stereospecific manner.[20] This two-step procedure consists of displacement of an allylic phosphate group by an organocuprate nucleophile, followed by oxidative installation of the carbonyl group. To evaluate this sequence for the enantioselective preparation of ketone **3.21**, allylic phosphates *rac*-**3.44** and **3.44** were prepared in racemic (Scheme 3.6) and enantiopure (Scheme 3.7) form, respectively. The synthesis of both phosphates commenced with iodination of commercially available 4,4'-dimethylcyclohexen-1-one (**3.45**), which occurs in high yield. Iodoenone **3.46** was then reduced using sodium borohydride in the presence of cerium trichloride to give racemic alcohol *rac*-**3.47** in good yield. Phosphorylation of *rac*-**3.47** proceeded in nearly quantitative yield, providing allylic phosphate *rac*-**3.44**.

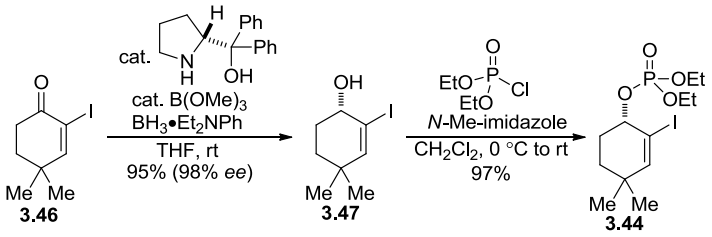
Scheme 3.6 Synthesis of allylic phosphate *rac*-3.44.



Enantiopure phosphate **3.44** was accessed in a similar manner, with the stereocontrolled formation of allylic alcohol **3.47** accomplished using a Corey–Bakshi–Shibata reduction.[20b] The highest yields and enantioselectivities were obtained using Knochel's protocol, which required *in situ* generation of the active catalyst from (*R*)-

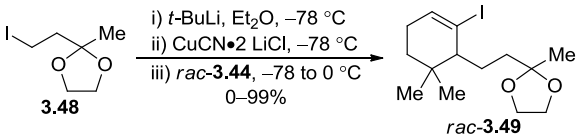
diphenylprolinol and trimethylborate.[20b] The use of borane-diethylaniline complex as a hydride donor was also found to be optimal. Phosphorylation of **3.47** occurred uneventfully, yielding allylic phosphate **3.44**. Using this three-step sequence, quantities of enantiopure phosphate **3.44** in excess of 15 g could be routinely prepared.

Scheme 3.7 Synthesis of enantiopure phosphate 3.44



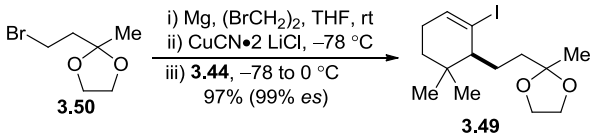
The stereospecific allylic phosphate displacement was then examined under a variety of conditions. Although Knochel and coworkers demonstrated that organocuprates derived from the corresponding organozinc halides were effective in this transformation, the preparation of an organozinc halide on small scale to test the displacement reaction was exceptionally challenging. Numerous literature reports, however, described similar allylic displacement reactions using organocuprates generated from either organolithiums[21] or Grignard reagents,[21,22] and so these two classes of organometallic nucleophiles were examined first. The organolithium intermediate required for formation of the cuprate was efficiently generated by lithium-halogen exchange with iodide **3.48** using *t*-BuLi (Equation 3.2). Transmetalation of the resulting organolithium using CuCN and various other copper sources was somewhat unreliable, providing in some instances displacement of the allylic phosphate of *rac*-**3.44** to provide *rac*-**3.49** in encouraging yield. However, this reaction suffered from poor reproducibility, especially as the scale of the reaction was increased.

Equation 3.2



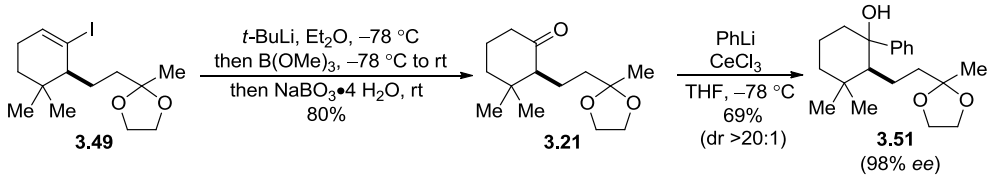
In a control experiment, the intermediate organolithium generated from **3.48** was trapped with benzaldehyde in high yield, confirming that lithium-halogen exchange occurred efficiently. It was inferred that the transmetalation step was responsible for the disappointing results obtained with this reaction. Because lithium-halogen exchange using *t*-BuLi cannot typically be carried out in THF, this process was conducted in Et_2O, which resulted in thick, viscous solutions of the intermediate organocuprate. It was speculated that the use of a Grignard reagent, in place of the organolithium, which could be easily generated in THF and would result in more reproducible cuprate formation. Accordingly, the preparation of an alkyl Grignard reagent from bromide **3.50** and excess magnesium in THF at room temperature, followed by transmetalation of the intermediate organomagnesium halide with CuCN at –78 °C generated a cyanocuprate reagent that efficiently displaced the allylic phosphate moiety of either *rac*-**3.44** or **3.44** (Equation 3.3). When three equivalents of the bromide precursor with respect to the phosphate were used, the reaction proceeded in nearly quantitative yield. As expected, the reaction of enantioenriched phosphate **3.44** occurred with perfect stereospecificity to yield vinyl iodide **3.49** in 99% *ee*. In addition, this transformation could be easily carried out on a 10 g scale with respect to phosphate **3.44** with no loss of product yield or enantiopurity.

Equation 3.3



Vinyl iodide **3.49** was then converted to the corresponding ketone by Knochel's one-pot protocol (Scheme 3.8).[20c] Exposure of **3.49** to excess *t*-BuLi in Et_2O at low temperature generated a vinyllithium that added readily to trimethyl borate. The organoboron intermediate generated in this way was subsequently oxidized *in situ* to provide ketone **3.21** in 80% yield.

Scheme 3.8 Synthesis and derivitization of ketone 3.21



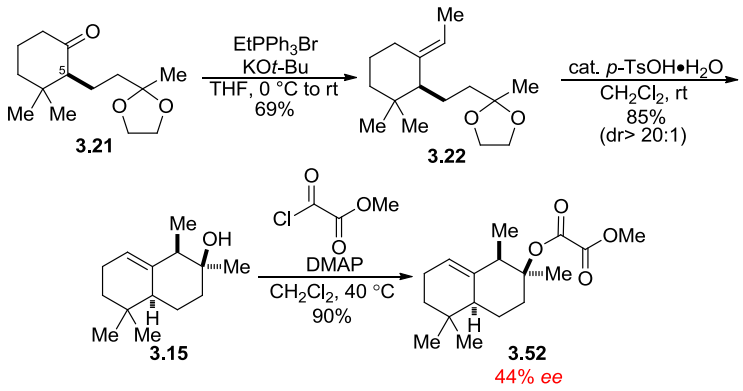
To confirm that the transformation of vinyl iodide **3.49** to ketone **3.21** resulted in no loss of enantiopurity, ketone **3.21** was analyzed by HPLC and GC using chiral stationary phases. The resolution of *rac*-**3.21** by these techniques was unsuccessful, so derivatization of ketone **3.21** was explored**.**[23] Initial attempts to condense ketone **3.21** with a hydrazine derivative under neutral conditions to form the corresponding hydrazone were unsuccessful, likely because of the hindered nature of **3.21** and the omission of an acid catalyst in an attempt to avoid epimerization. Fortunately, the diastereoselective addition of phenyllithium to ketone **3.21** in the presence of cerium trichloride gave tertiary alcohol **3.51**, which bears a suitable chromophore for HPLC analysis. Examination of both *rac*-**3.51** and **3.51** by HPLC revealed that tertiary alcohol **3.51** was

formed in 98% *ee*, and therefore no epimerization had occurred in the conversion of vinyl iodide **3.49** to ketone **3.21**.

3.5.2 Wittig Olefination of Ketone 3.21

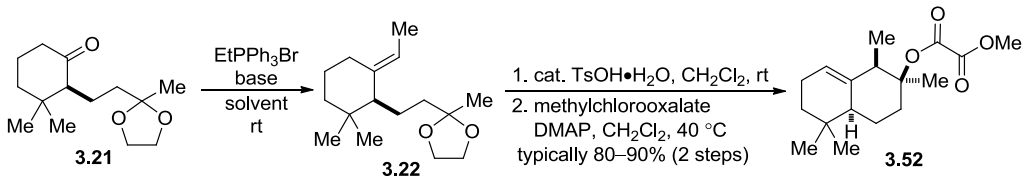
After developing a concise and enantioselective route to ketone **3.21**, procedures developed by Dr. André Dieskau were employed to convert **3.21** to a tertiary radical precursor for use in the key coupling step (Scheme 3.9). Ketone **3.21** was subjected to Wittig olefination under the conditions first developed by Dr. Dieskau to form trisubstituted alkene **3.22** in 69% yield. Carbonyl-ene cyclization then successfully converted ketal **3.22** to tertiary alcohol **3.15** as a single diastereomer in 86% yield. After a brief survey of conditions to acylate **3.15**, it was determined that the formation of methyl oxalate **3.52** occurred most efficiently when stoichiometric DMAP was employed in dichloromethane at 40 °C. Surprisingly, analysis of methyl oxalate **3.52** by HPLC using a chiral stationary phase revealed that the enantiomeric purity of **3.52** was significantly diminished. Since the C5 (macfarlandin C numbering) methine stereocenter is not particularly labile during either the carbonyl-ene or acylation steps, it was suspected that racemization of the substrate was occurring during the course of the Wittig reaction.[24] In an attempt to suppress this undesired epimerization process, numerous alternative conditions for the ethylidenation of ketone **3.21** were examined (Table 3.1).[25]

Scheme 3.9: Synthesis of methyl oxalate 3.52



A variety of solvents and bases were employed in the olefination of ketone **3.21**. All ethylidenation reactions described in Table 3.1 were conducted using ethyltriphenylphosphonium bromide as the phosphorus ylide precursor. The ketone substrate **3.21** was added to a solution of preformed ylide at room temperature in all cases, as it was speculated that heating the reaction mixture would lead to epimerization of **3.21**. The olefination was surprisingly effective in nearly every solvent examined, and even proceeded to give **3.22** in high yield in solvents such as hexanes (entry 3). Of all bases investigated, potassium *tert*-butoxide (entries 1–5) and potassium hexamethyldisilazide (entry 6) were the only bases that promoted ethylidenation. When *n*-butyllithium or LHMDS were used to generate the phosphorus ylide, no reactivity of ketone **3.21** was observed. Unfortunately, every set of conditions that resulted in successful olefination of ketone **3.21** also caused racemization to a certain extent. Methyl oxalate **3.52** was obtained in highest enantiomeric purity (56% *ee*) when the respective Wittig reaction was conducted using potassium *tert*-butoxide as a base and toluene as the solvent (entry 4).

Table 3.1 Wittig ethylidenation of ketone 3.21

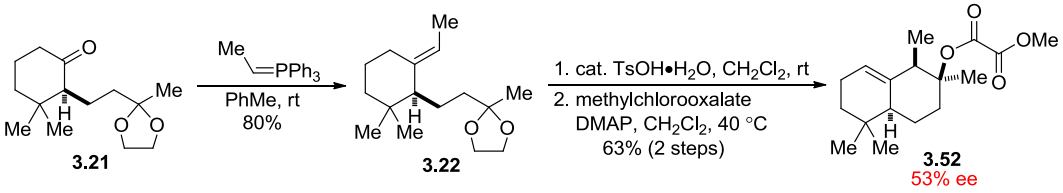


entry	solvent	base	yield **3.22** (%)	*ee* **3.52** (%)
1	THF	KO*t*-Bu	69	44
2	Et_2O	KO*t*-Bu	80	5
3	hexanes	KO*t*-Bu	94	6
4	PhMe	KO*t*-Bu	89	56
5	DME	KO*t*-Bu	93	28
6	PhMe	KHMDS	99	24

After evaluating several conditions for the olefination of **3.21**, it was still not evident which specific reagent or intermediate was promoting epimerization of the substrate. The base employed in every Wittig reaction described is certainly capable of racemizing ketone **3.21**; however, it is well-known that phosphorus ylides such as the one presumably generated in this reaction are also sufficiently basic and capable of racemizing the substrate.[24] To directly examine if the phosphonium ylide intermediate generated in these reactions epimerized the ketone substrate in the absence of exogenous base, a "salt- and base-free" Wittig reaction was conducted.[26] Ketone **3.21** was exposed to a homogeneous solution of the ylide generated from ethyltriphenylphosphonium bromide and sodamide in toluene,[27] providing exocyclic olefin **3.22** in 80% yield (Scheme 3.10). However, conversion of olefin **3.22** to the corresponding methyl oxalate **3.52** over two steps revealed a significant loss of enantiopurity. This result suggested that the ylide intermediate generated under any set of conditions could likely promote

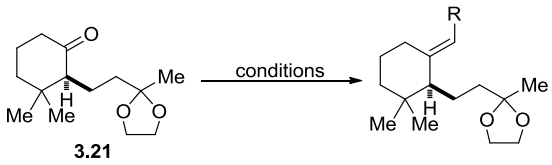
racemization and that the Wittig reaction would not be a useful method for the preparation of a radical precursor in enantiopure form.

Scheme 3.10 Salt- and base-free Wittig reaction of ketone 3.21



Various other reactions using less basic olefinating agents were then briefly examined with ketone **3.21** (Table 3.2**)**. Horner–Wadsworth–Emmons[28] olefination of ketone **3.21** with the stabilized ylide derived from trimethylphosphonoacetate (entry 1) resulted in only poor conversion of **3.21**, giving unacceptable yields of the α,β-

Table 3.2 Attempted olefination of ketone 3.21



entry	conditions	R	result
1	$MeO_2CCH_2P(O)(OMe)_2$, NaH, THF, 0 °C to rt	CO_2Me	<20% conversion
2	$EtSO_2Ph$, LHMDS, THF, 0–65 °C	Me	no conversion
3	$EtSO_2$(benzothiazole), LHMDS, THF, 0–65 °C	Me	no conversion
4	$EtSO_2$(2-phenyltetrazole), LHMDS, THF, 0–65 °C	Me	no conversion
5	$CrCl_2$, CHI_3, THF, rt	I	no conversion
6	I_2CHCH_3, Zn, $PbCl_2$, $TiCl_4$, THF, rt	Me	no conversion

unsaturated ester product. Similarly, attempted Julia olefination[29] (entry 2) or "modified" Julia olefination[30] (entries 3 and 4) of ketone **3.21** was unsuccessful, returning only

unreacted **3.21**. Takai–Utimoto iodomethylenation[31] (entry 5) or ethylidenation[32] (entry 6) reactions also to failed to convert ketone **3.21** to a synthetically useful product. Unable to advance ketone **3.21** to the desired methyl oxalate radical precursor **3.52** in enantiopure form, the use of ketone **3.21** as a synthetic intermediate was abandoned.

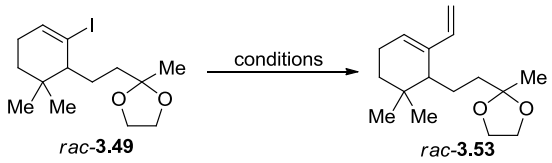
3.5.3 Vinyl Coupling and 1,4-Hydrogenation

The efficiency and high enantioselectivity in which vinyl iodide **3.49** could be prepared suggested that an alternative synthetic pathway to transform **3.49** to carbonyl-ene precursor **3.22** would be worth investigating. Installation of the ethyl moiety directly from vinyl iodide **3.49**, while avoiding labile ketone intermediate **3.21**, was at this time the most attractive and logical strategy for preventing undesired racemization of the substrate. It was reasoned that appendage of a vinyl unit followed by functionalization of the resulting diene intermediate might be successful in converting iodide **3.49** to cyclization precursor **3.22**.

The vinylation of iodide *rac*-**3.49** via a transition metal-catalyzed cross-coupling was next examined under several conditions (Table 3.3).[33] Kumada coupling[34] (entry 1) of *rac*-**3.49** with vinylmagnesium bromide in the presence of 5 mol % $PdCl_2(PPh_3)_2$ resulted in 50% conversion of iodide *rac*-**3.49** to diene *rac*-**3.53**. Increasing the catalyst loading to 10 mol % (entry 2) gave full conversion of the starting material, and diene *rac*-**3.53** was isolated in 64% yield. However, the product obtained in this reaction was contaminated with a significant amount of protodeiodinated starting material. It was speculated that replacing the reactive Grignard reagent employed in this coupling with a milder nucleophile might result in cleaner reactivity of iodide *rac*-**3.49**. A brief survey of

other established cross-coupling methods using alternative organometallic coupling partners was then conducted. Specifically, the Stille[35] (entry 4), Suzuki[36] (entry 5) and Negishi[37] (entries 6 and 7) couplings were examined. The Negishi coupling was found to give exceptionally clean reactivity of iodide *rac*-**3.49**, perhaps because it could be executed at room temperature. Using 10 mol % of catalyst $Pd(PPh_3)_4$ promoted full conversion of the iodide starting material and provided diene **3.53** in 93% isolated yield.[38] As expected, enantiopure vinyl iodide **3.49** reacted identically under these conditions to provide enantiopure diene **3.53**.

Table 3.3 Vinylation of iodide *rac*-3.49



rac-**3.49** → *rac*-**3.53**

entry	conditions	ratio *rac*-**3.49** : *rac*-**3.53**	yield of *rac*-**3.53** (%)
1[a]	$CH_2CHMgBr$, cat. $PdCl_2(PPh_3)_2$ THF, 0 °C to rt	1 : 1	-
2[b]	$CH_2CHMgBr$, cat. $PdCl_2(PPh_3)_2$ THF, 0 °C to rt	0 : 1	64
3[a]	$CH_2CHMgBr$, cat. $Pd(PPh_3)_4$ THF, 0 °C to rt	1.7 : 1	-
4[a]	$CH_2CHSn(nBu)_3$, cat. $Pd(dppf)Cl_2$ DMF, 90 °C	1 : 1.7	-
5[b]	CH_2CHBF_3K, cat. $Pd(dppf)Cl_2$ Cs_2CO_3, THF/H_2O, 85 °C	0 : 1	64
6[a]	$CH_2CHMgBr$, $ZnCl_2$, cat. $Pd(PPh_3)_4$, DMF/THF, 0 °C to rt	1 : 2	-
7[b]	$CH_2CHMgBr$, $ZnCl_2$, cat. $Pd(PPh_3)_4$, DMF/THF, 0 °C to rt	0 : 1	93

[a]The catalyst loading was 5 mol %. [b]The catalyst loading was 10 mol %.

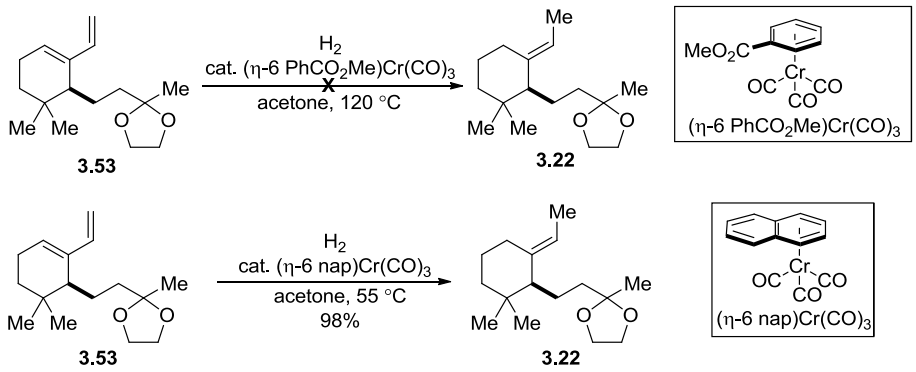
Although several known 1,4-functionalizations of diene **3.53** were initially considered,[39,40] the most direct way to transform diene **3.53** to carbonyl-ene precursor

3.22 in a single step was presumed to be the net delivery of hydrogen to the 1- and 4-positions. Hydrogenations of this type are known to be effected by chromium η-6 arene tricarbonyl complexes, but the application of this strategy in total synthesis is extremely limited.[40] Nevertheless, the appeal of directly converting diene **3.53** to exocyclic olefin **3.22** warranted exploration of this approach.

A variety of chromium η-6 arene tricarbonyl complexes participate in 1,4-hydrogenations of dienes, but the most widely used catalysts are (η-6 methylbenzoate)chromium tricarbonyl ((η-6 $PhCO_2Me)Cr(CO)_3$) and (η-6 naphthalene)chromium tricarbonyl ((η-6 nap)$Cr(CO)_3$).[40] The generally accepted mechanism for these transformations is that dissociation of the arene moiety from chromium first occurs to generate a 12-electron chromium tricarbonyl intermediate that coordinates to the diene in an s-*cis* fashion. Association of hydrogen to the complex is then followed by regioselective delivery of hydrogen to the 1- and 4- positions. Importantly, since the diene must coordinate to the catalyst in an s-*cis* orientation, the geometry of the resulting olefin is completely controlled in these processes.[40]

Subjection of diene **3.53** to 20 mol % (η-6 methylbenzoate)chromium tricarbonyl under 75 atmospheres of hydrogen pressure in acetone at 130 °C for 18 h resulted only in the recovery of starting material (Scheme 3.11). The related (η-6 naphthalene)chromium tricarbonyl catalyst, which is known to react efficiently at much lower temperatures,[40] was then examined. Hydrogenation of diene **3.53** mediated by this catalyst under 75 atmospheres of hydrogen pressure in acetone at 55 °C resulted in quantitative conversion

Scheme 3.11 Hydrogenation of diene 3.53

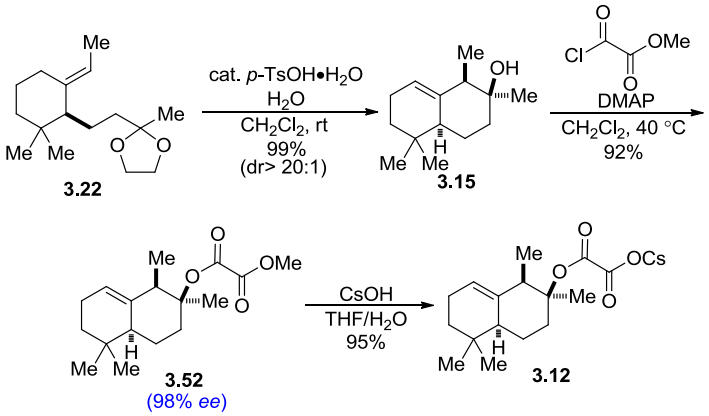


to exocyclic olefin **3.22**, which was confirmed to be a single olefin isomer by ^{1}H NMR analysis. A brief assessment of the reaction parameters revealed that this hydrogenation could be run under one atmosphere of hydrogen pressure; however, conversion of diene **3.53** to product was variable under these conditions. The addition of reagents to the Parr bomb apparatus in a glove box as well as the use of rigorously degassed acetone ensured highly reproducible results.

3.5.4 Synthesis and Attempted Coupling of (8*S*)-Cesium Oxalate 3.12

With the 1,4-hydrogenation of diene **3.53** providing access to carbonyl-ene substrate **3.22**, cesium oxalate **3.12** could then be prepared in enantiopure form for use in the key radical coupling reaction (Scheme 3.12). Cyclization of olefin **3.22** was carried out as previously mentioned using catalytic *p*-toluenesulfonic acid in wet dichloromethane at room temperature. The addition of one equivalent of water to the reaction mixture facilitated clean ketal deprotection and cyclization, providing tertiary alcohol **3.15** in quantitative yield. Acylation of alcohol **3.15** as previously discussed

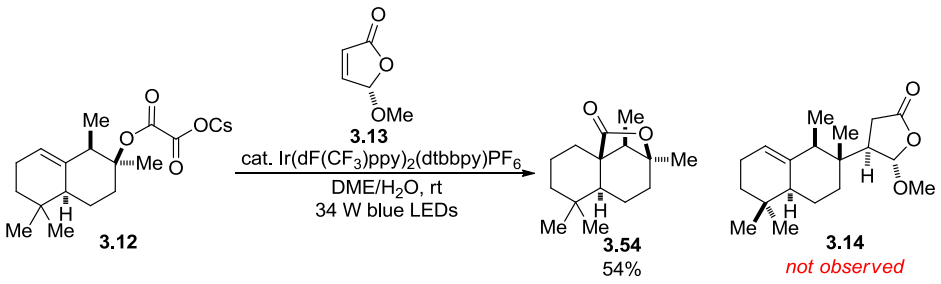
Scheme 3.12 Synthesis of cesium oxalate 3.12



gave methyl oxalate **3.52**, which was pleasingly determined to be enantiopure by HPLC analysis using a chiral stationary phase. Oxalate ester **3.52** was easily saponified using 1 equiv of cesium hydroxide in tetrahydrofuran/water at room temperature to yield the radical precursor **3.12**.

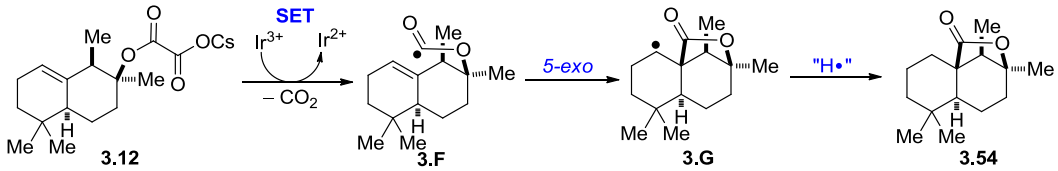
The attempted radical coupling of cesium oxalate **3.12** with (*S*)-5-methoxyfuran-2-one (**3.13**) was met with a surprising result. Reaction of a slight molar excess (1.1 equiv) of cesium oxalate **3.12** with butenolide **3.13** in the presence of 1 mol % of $Ir(dF(CF_3)ppy)_2(dtbbpy)PF_6$ and 10 equiv H_2O in DME at room temperature produced lactone **3.54** in 54% yield with no trace of the desired coupling product **3.14** (Equation 3.4).

Equation 3.4



Lactone **3.54** is likely formed via cyclization of intermediate alkoxycarbonyl **3.F** radical produced after the first decarboxylation event onto the trisubstituted olefin, followed by hydrogen atom abstraction by secondary radical **3.G** (Scheme 3.13).[41]

Scheme 3.13 Proposed mechanism for the formation of 3.54



After cesium oxalate **3.12** was proven to be an ineffective substrate for the generation of the required tertiary radical intermediate, alternative precursors from which a tertiary radical might be more easily accessed for use in the coupling were then considered.

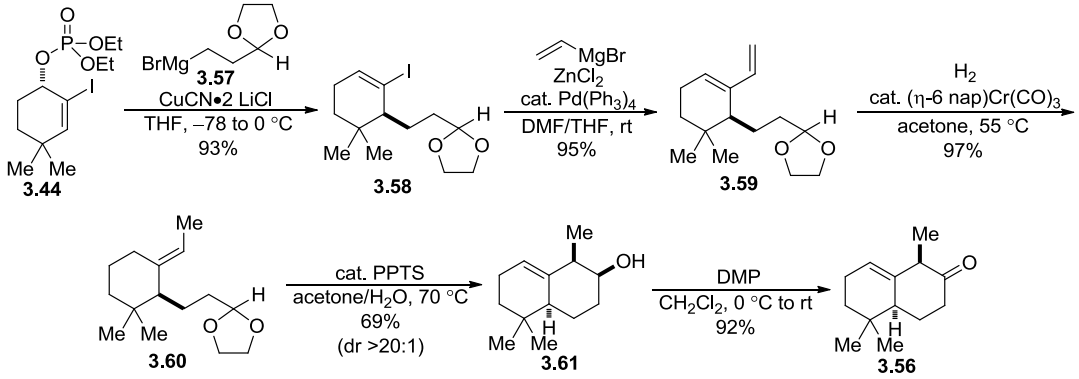
3.5.5 Accessing (8*R*)-Tertiary Alcohol 3.55

The failure of cesium oxalate **3.12** to generate a tertiary radical was attributed to the proximity of the postulated intermediate alkoxycarbonyl radical to the trisubstituted olefin. A potential straightforward solution to this problem was to access the epimeric tertiary alcohol **3.55**, which should be more distant from the trisubstituted olefin, and attempt to employ its corresponding cesium oxalate in a radical coupling reaction.

It was anticipated that (8*R*)-tertiary alcohol **3.55** could be formed by addition of a methyl organometallic nucleophile to the precursor ketone **3.56**. A sequence similar to that developed for the synthesis of (8*S*)-tertiary alcohol **3.15** was used to access ketone **3.56** (Scheme 3.14). Phosphate **3.44,** an intermediate prepared in the synthesis of (8*S*)-**3.12**, was subjected to an allylic displacement reaction using as a nucleophile the cuprate

derived from acetal-bearing Grignard reagent **3.57**. Vinylation of iodide **3.58** and 1,4-hydrogenation of the resulting diene **3.59** occurred smoothly as observed with previous substrates. The carbonyl-ene cyclization of acetal **3.60** was significantly more troublesome than the cyclization of its ketal-bearing analog **3.22**. The most successful conditions for promoting this cyclization were found to be exposure of acetal **3.60** to 0.3 equiv of PPTS in acetone/water at 70 °C. This transformation provided secondary alcohol **3.61** as a single diastereomer in 69% yield.[42] Alcohol **3.61** was then oxidized in high yield using Dess–Martin periodinane[43] to ketone **3.56**.[44]

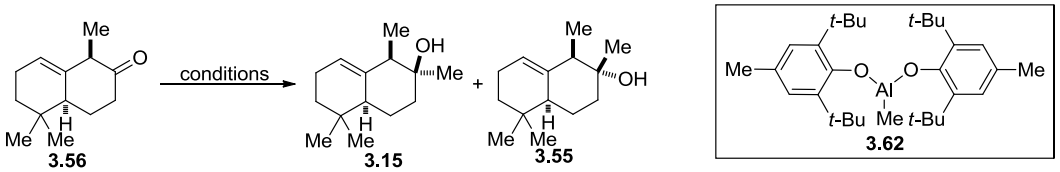
Scheme 3.14 Synthesis of ketone 3.56



The addition of a methyl nucleophile to ketone **3.56** was next examined (Table 3.4). The "bent" shape of the decalin scaffold of **3.56** significantly complicated conformational analyses to predict the diastereoselectivity of the transformation, although the neighboring secondary methyl group was expected to exhibit some steric influence. Addition of methylmagnesium bromide to ketone **3.56** in Et_2O at low temperature (entry 1) gave a mixture of diastereomeric alcohols **3.15** and **3.55**; however, the undesired (8*S*)-tertiary alcohol **3.15** predominated. The reaction of **3.56** with either methyllithium (entry 2) or the organocerium species derived from methyllithium and cerium trichloride (entry

3) gave only the (8*S*)-alcohol **3.15**. The use of Yamamoto's bulky Lewis acid bis[2,6-bis(1,1-dimethylethyl)-4-methylphenolato]methylaluminum ("MAD," **3.62**), which is proposed to invert the diastereoselectivity typically observed in organometallic additions by coordinating to and blocking the less-hindered face of a carbonyl substrate, was then examined.[45] Employing this Lewis acid additive with methyllithium (entry 4) was not successful in providing alcohol **3.55**, as a complex mixture of products was observed by ^{1}H NMR. By contrast, the addition of methylmagnesium bromide to ketone **3.56** in the presence of **3.62** (entry 5) was exceptionally clean and completely selective for the (8*R*)-alcohol **3.55**. Methyl addition under these conditions provided alcohol **3.55** in 62% isolated yield.

Table 3.4 Methyl addition to ketone 3.56



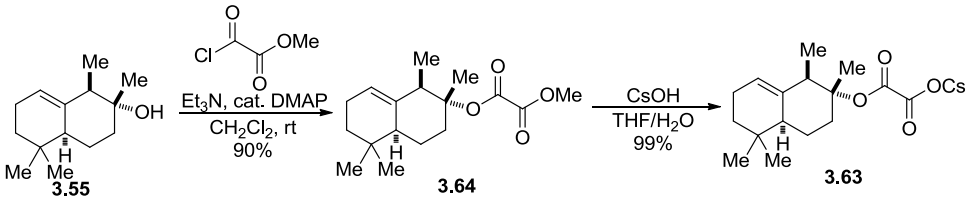
entry	conditions	ratio[a] **3.15** : **3.55**	yield **3.55** (%)
1	MeMgBr Et_2O, –78 °C	1.4 : 1	24
2	MeLi Et_2O, –78 °C	1 : 0	-
3	MeLi, CeCl3 THF, –78 to 0 °C	11 : 1	-
4	**3.62**, MeLi PhMe/Et_2O, –78 °C	-[b]	-
5	**3.62**, MeMgBr PhMe/Et_2O, –78 °C	0 : 1	62

[a]Determined by ^{1}H NMR analysis of the crude reaction mixture. [b]A complex mixture of products was obtained.

3.5.6 Radical Coupling with (8*R*)-Oxalate 3.63

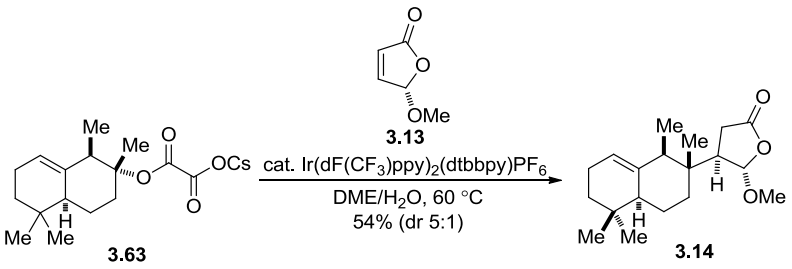
The synthesis of radical precursor (8*R*)-**3.63** was carried out in straightforward manner from tertiary alcohol **3.55** (Scheme 3.15). Acylation of **3.55** with methylchlorooxalate in the presence of triethylamine and catalytic DMAP in dichloromethane at room temperature provided methyl oxalate **3.64** in 90% yield. The oxalate ester **3.64** was then selectively saponified with cesium hydroxide to give cesium oxalate **3.63** in quantitative yield.

Scheme 3.15 Synthesis of cesium oxalate 3.63



Oxalate salt **3.63** coupled readily with (*S*)-5-methoxyfuran-2-one (**3.13**) (Equation 3.5). Pleasingly, no trace of a lactone product arising from intramolecular cyclization of the intermediate alkoxycarbonyl radical onto the trisubstituted olefin was observed. Exposure of oxalate **3.63** and butenolide **3.13** to 1 mol % $Ir(dF(CF_3)ppy)_2(dtbbpy)PF_6$ in DME/H_2O under visible light irradiation for 24 h provided adduct **3.14** in 54% yield as a 5:1 mixture of diastereomers.

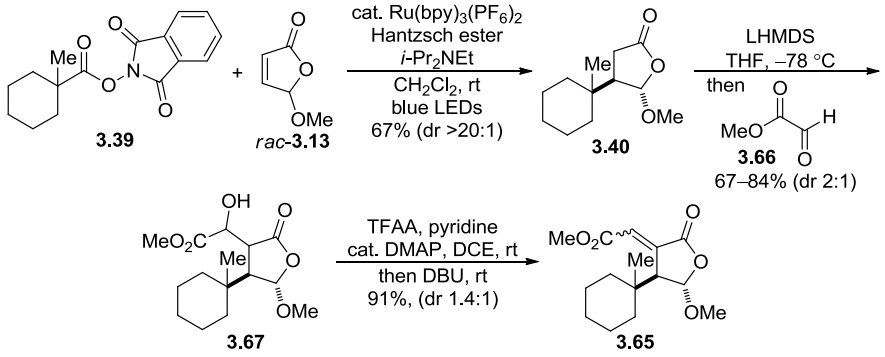
Equation 3.5



3.5.7 Hydrogenation Studies with Unsaturated Lactones 3.65

At this point, the construction of the bicyclic lactone unit of macfarlandin C (**3.1**) was explored using a model substrate bearing a simpler 1-methylcyclohexyl group in place of the decalin fragment. This lactone could be accessed in gram quantities by the reductive coupling of 1-methylcyclohexyl (*N*-acyloxy)phthalimide (**3.39**) with racemic 5-methoxyfuran-2-one (**3.13**) catalyzed by $Ru(bpy)_3(PF_6)_2$ (Scheme 3.16). The lactone enolate generated by treatment of **3.40** with LHMDS in THF at low temperature engaged in aldol coupling with methyl glyoxylate (**3.66**), which was itself generated *in situ* via ozonolysis of dimethyl maleate.[46] Aldol adducts **3.67** were obtained in variable yield in this reaction, likely due to the instability of methyl glyoxylate that was meticulously prepared and distilled prior to use. Dehydration of alcohols **3.67** was accomplished most efficiently by conversion to the trifluoroacetate derivatives and *in situ* elimination with DBU. This sequence provided useful quantities of unsaturated lactone **3.65** as mixtures of olefin isomers that were expected to converge upon hydrogenation.

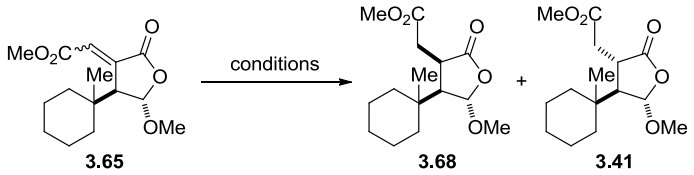
Scheme 3.16 Preparation of unsaturated lactones 3.65



The hydrogenation of olefins **3.65** was examined under a variety of conditions (Table 3.5). Several heterogeneous catalysts were initially employed, anticipating that a metal hydrogenation catalyst would approach from the lactone face opposite the sterically

encumbered 1-methylcyclohexyl group. Unfortunately, hydrogenation of unsaturated lactones **3.65** with Pd/C (entry 1), PtO_2 (entry 3), and Rh/Al_2O_3 (entry 4) occurred to provide predominantly the undesired α,β-*trans*-disubstituted lactone **3.41** rather than the desired *cis*-substituted lactone **3.68**.[19] Pearlman's catalyst and rhodium on carbon were

Table 3.5 Hydrogenation of unsaturated lactones 3.65



entry	conditions	ratio[a] **3.68** : **3.41**
1	cat. Pd/C, H_2 (1 atm), MeOH, rt	1 : 7
2	cat. $Pd(OH)_2$, $NaHCO_3$, H_2 (1 atm), EtOAc, rt	-[b]
3	PtO_2, H_2 (1 atm), EtOAc, rt	1 : 1.4
4	cat. Rh/Al_2O_3, H_2 (15 atm), EtOAc, rt	1 : 3
5	cat. Rh/C, H_2 (85 atm) THF, rt	-[b]
6	cat. $Rh(PPh_3)_3Cl$, H_2 (7 atm) C_6H_6, rt	-[b]
7	cat. $[Ir(COD)(pyr)PCy_3](PF_6)$ H_2 (85 atm), CH_2Cl_2, rt	-[b]
8	Raney Ni, THF, rt	-[b]
9	H_2NNH_2, $PhI(OAc)_2$ H_2O/CH_2Cl_2, rt	-[b]
10	IPr-CuCl, NaO*t*-Bu, PMHS PhMe, rt	0 : 1
11	Red-Al, CuI, 2-butanol, THF/PhMe, –78 to –20 °C	1.3 : 1
12	$NaBH_4$, $NiCl_2$, MeOH 0 °C	1 : 2
13	L-selectride, THF, –78 °C	0 : 1

[a]Determined by ^1H NMR analysis of the crude reaction mixture. [b]No conversion of the starting material was observed. IPr-CuCl = *N*,*N*-bis(2,6diisopropylphenyl)imidazol-2-ylidene copper(I) chloride. PMHS = polymethylhydrosiloxane.

inactive in the transformation (entries 2 and 5 respectively). Hydrogenations with Wilkinson's catalyst (entry 6) and Crabtree's catalyst (entry 7) were also unsuccessful, giving no product even after subjection to high pressure of hydrogen. More exotic reducing conditions using Raney nickel (entry 8), diimide (entry 9) or an NHC-copper-hydride species[47] (entry 10) failed as well. Not surprisingly, good conversion of the electron-deficient olefin substrate was observed with nucleophilic metal-hydride reagents (entries 11–13). However, the ratio of *cis*:*trans* substituted lactones was at best 1.3:1 when using Red-Al/CuI (entry 11). This reaction gave a mixture of several products in addition to lactones **3.68** and **3.41**, so it was likely unfeasible for application to the more complex decalin-bearing substrate without extensive optimization.

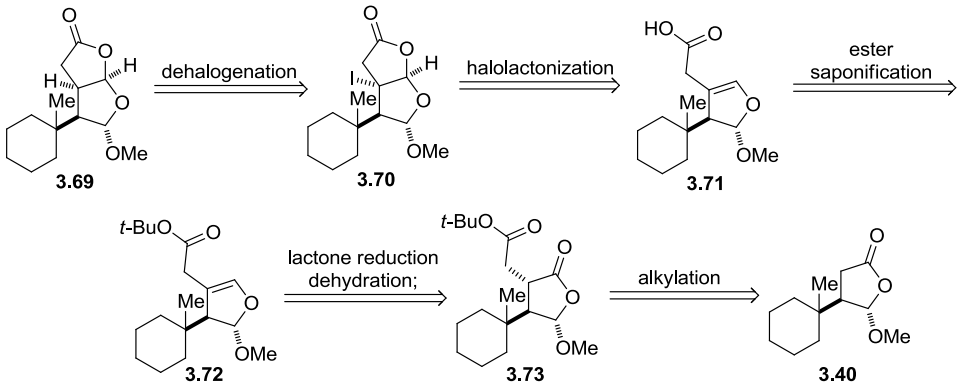
The hydrogenation of olefins **3.65** under the conditions examined could not be stereochemically controlled as was initially desired. Clearly, the bulky quaternary carbon substituent and the methyl carboxymethyl lactone side chain exhibit a severe steric interaction in the diastereomeric hydrogenation transition state that would result in placing these substituents on the same face of the lactone. Even though the hydrogenation of a very similar substrate has been successfully accomplished to establish a *cis*-relationship between α- and β-substituents,[47b] the large quaternary β-substituent present in this case likely obstructs the desired stereochemical outcome.

3.5.8 Iodolactonization Approach to the Bicyclic Lactone

With the hydrogenation of exocyclic olefins **3.65** showing little promise in reliably establishing the relative stereochemistry of the bicyclic lactone of macfarlandin C (**3.1**), various alternative approaches to access this structural fragment were considered.

Inspiration for revising the synthetic route was taken from studies[19] carried out concurrently in the Overman group that confirmed that enolates derived from lactones such as **3.40** undergo highly diastereoselective alkylation from the lactone face opposite the quaternary substituent. The bicyclic lactone of macfarlandin C (**3.1**) has a proton present on this face at C13 however, so alkylation of lactone **3.40** would presumably give the incorrect stereochemistry at C13. Instead, a proton equivalent such as a halide could be introduced at this position from the less-hindered lactone face, orienting the carboxymethyl group on the correct face. This halide could subsequently be stereoselectively converted to a hydrogen atom via radical dehalogenation once the dioxabicyclo[3.3.0]octanone framework was constructed to provide bicyclic lactone **3.69** with the appropriate relative configuration (Figure 3.7). It was inferred that diastereoselective electrophilic halogenation and concomitant cyclization might occur to form iodolactone **3.70** from a precursor such as carboxylic acid **3.71**.[48] Ester-bearing dihydrofuran **3.72** could derive from reduction of the corresponding lactone **3.73** to a lactol, followed by dehydration. The *tert*-butyl carboxymethyl side chain of **3.73** would

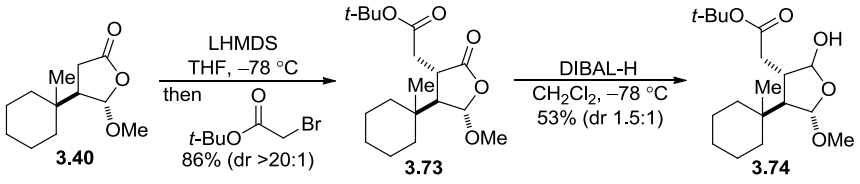
Figure 3.7 Retrosynthetic analysis for halolactonization approach



be introduced via alkylation of the enolate of lactone **3.40**, with the stereochemical outcome of this alkylation being inconsequential.

The assessment of the halolactonization strategy began with alkylation of the enolate of lactone **3.40** with *tert*-butyl bromoacetate, which occurred in high yield (Scheme 3.17). Reduction of the lactone to the corresponding lactol proved to be significantly troublesome. Exposure of lactone **3.73** to DIBAL-H in a variety of solvents at –78 °C frequently gave complex mixtures of products corresponding to unselective reduction of the dicarbonyl substrate. The best results were obtained when the reduction was carried out in dichloromethane as solvent. Although greater than one equivalent of DIBAL-H was typically required to consume the substrate, it was necessary to add the reagent portionwise to realize clean reactivity. Lactols **3.74** were isolated in 53% as an anomeric mixture using this protocol.[49] All attempts to improve this reduction by employing other substrates bearing various bulky esters in place of the *tert*-butyl ester were unsuccessful.

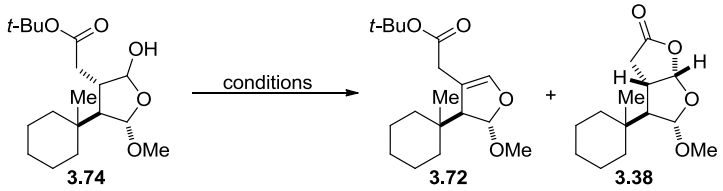
Scheme 3.17 Synthesis of lactols 3.74



The dehydration of lactols **3.74** to form dihydrofuran **3.72** (Table 3.6) was also problematic. As one might expect, activation of the lactol to generate an oxocarbenium intermediate in most cases invited closure of the lactone ring by attack of the pendant *tert*-butyl ester. The lactol functionality of **3.74** also appeared to be sterically hindered, as it was unreactive under many conditions typically employed in lactol dehydrations.

Treatment of lactols **3.74** with methanesulfonyl chloride and triethylamine in dichloromethane at –20 °C, followed by heating at 40 °C (entry 1) gave only a small amount of dihydrofuran **3.72**. The substrate was more reactive towards phosphorus oxychloride, although the formation of bicyclic lactone byproduct **3.38** could not be avoided (entries 2 and 3). Other common dehydrating agents thionyl chloride and the Burgess reagent failed to react with lactols **3.74** (entries 4 and 5). Whereas conversion of the substrate to the corresponding triflate gave a complex mixture of products (entry 6), the trifluoroacetate analog proved to be more useful (entries 7 and 8). Employing

Table 3.6 Dehydration of lactols 3.74



3.74 **3.72** **3.38**

entry	conditions	ratio **3.72** : **3.38**[a]	comment
1	MsCl, Et_3N CH_2Cl_2, –20 to 40 °C	-	complex mixture
2	$POCl_3$, pyridine, 70 °C	1 : 3	
3	$POCl_3$, pyridine CH_2Cl_2, 0 °C to rt	0 : 1	
4	$SOCl_2$, pyridine 0–70 °C	-	low conversion
5	Burgess reagent MeCN, rt–50 °C	-	no conversion
6	Tf_2O, Et_3N, cat. DMAP CH_2Cl_2, –78 to 0 °C	-	complex mixture
7	TFAA, pyridine, cat. DMAP THF, 0–65 °C	1 : 3.4	
8	TFAA, Et_3N, cat. DMAP THF, 0–65 °C	2.3 : 1	isolated 35% **3.72**

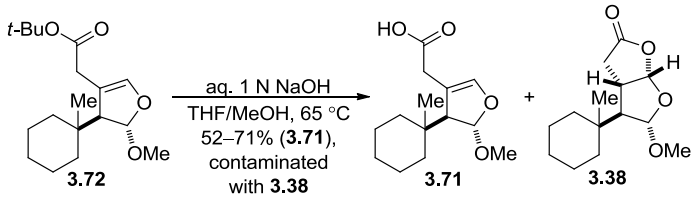
[a]Determined by ^{1}H NMR analysis of the crude reaction mixture.

triethylamine as the auxiliary base in this reaction shifted the product distribution towards the desired dihydrofuran **3.72**, although the isolated yield of this product was poor (entry

8). All attempts to effect the dehydration of lactols **3.74** under various other conditions were unproductive.

The dehydration of lactols **3.74** could fortunately be conducted on a 300 mg scale to provide sufficient material to test the halolactonization strategy. Prior to cyclization, *tert*-butyl ester **3.72** was first saponified using aqueous sodium hydroxide in methanol/tetrahydrofuran at 65 °C (Equation 3.6). Hydrolysis of this ester occurred cleanly; however, acidification of the carboxylate obtained by this method provoked cyclization to form bicyclic lactone **3.38** which bears the undesired relative configuration on the tetrahydrofuran ring. Because of this complication, carboxylic acid **3.71** could rarely be isolated in pure form. Even after silica gel chromatography, purified acid **3.71** was observed to undergo lactonization on standing in $CDCl_3$.

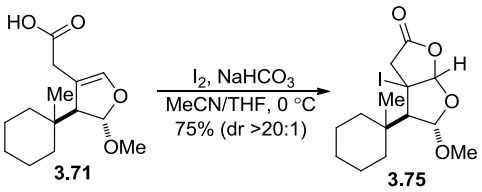
Equation 3.6



A reasonably pure sample of carboxylic acid **3.71** obtained by the above hydrolysis reaction was submitted to iodolactonization on small scale. Subjection of **3.71** to excess iodine in the presence of sodium bicarbonate in acetonitrile/tetrahydrofuran at 0 °C induced rapid iodolactonization (Equation 3.7). Complete regioselectivity in this reaction was observed as expected, with the tetrahydrofuran oxygen presumably facilitating the opening of the transient iodonium intermediate. The transformation was also highly stereoselective, providing a single diastereomer of bicyclic lactone **3.75**.

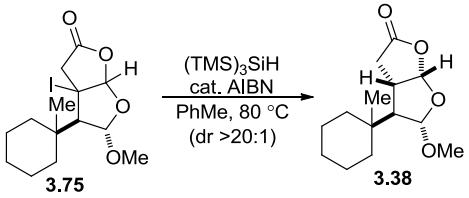
Unfortunately, attempts to establish the relative stereochemistry of lactone **3.75** via NOESY or ^{1}H nOe NMR experiments were not informative.

Equation 3.7



To confirm the relative configuration of bicyclic lactone **3.75**, this intermediate was dehalogenated to enable comparison with a known compound.[19] Exposure of a small sample of **3.75** to tris(trimethylsilyl)silane and a catalytic amount of azobisisobutyronitrile in toluene at 80 °C produced solely bicyclooctanone **3.38** exhibiting a *trans*- relationship between the lactone ring and 1-methylcyclohexyl groups (Equation 3.8).

Equation 3.8



The relative stereochemistry of this product at the angular positions of the bicyclooctanone is unfortunately opposite to that required for the synthesis of macfarlandin C. At the moment it is unclear why iodolactonization of dihydrofuran **3.71** occurs with this stereochemical outcome. If the formation of the iodonium intermediate is reversible, this reaction may proceed under thermodynamic control to place the iodine atom on the concave face of the bicycle. In this configuration, the long carbon-iodine bond likely contributes to a lesser steric interaction between the iodide and the quaternary

substituent than would be present between the lactone carbons and the quaternary substituent were the iodide on the opposite convex face. Alternatively, the acetal methoxy group may exhibit more steric influence than previously expected.

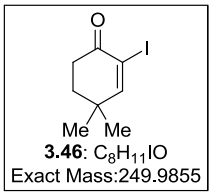
Although only one set of conditions was evaluated for the halolactonization of dihydrofuran **3.71**, the development of this strategy to construct the bicyclooctanone moiety of macfarlandin C was terminated. The troublesome chemoselective reduction of dicarbonyl **3.73** as well as the propensity of several intermediates in this route to prematurely lactonize contributed to low yields in almost every step. The inefficiency of this route thus obstructed a comprehensive evaluation of halolactonization conditions.

3.6 Conclusions

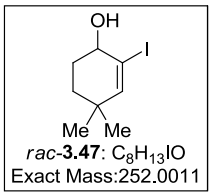
An enantioselective synthesis of the decalin moiety of macfarlandin C was developed, allowing the preparation of radical precursor cesium oxalate **3.63** in 11 steps and 26% overall yield from dimethylcyclohexenone **3.45**. Oxalate **3.63** coupled in moderate yield and good diastereoselectivity with methoxybutenolide **3.13** to construct the central C8–C14 bond of macfarlandin C. Two approaches for forming the bicyclic lactone moiety were explored on a simpler model compound; however, these efforts were complicated by the difficulty of establishing the correct relative stereochemistry at the position corresponding to the C13 stereocenter of macfarlandin C. A well-precedented kinetic protonation approach[50] is currently under investigation and, if successful, will ideally enable completion of the total synthesis.

3.7 Experimental Information

Unless stated otherwise, reactions were conducted in oven-dried glassware under an atmosphere of argon using anhydrous solvents (either freshly distilled or passed through activated alumina columns). All commercially obtained reagents were used as received. Thin layer chromatography (TLC) was conducted on EMD Chemicals silica gel 60 F254 plates and visualization was carried out by exposing plates to UV light or staining plates with anisaldehyde or $KMnO_4$. Flash chromatography and filtration were performed using 40–63 μm EMD Chemicals Silica Gel 60 Å Geduran silica gel. ^{1}H NMR spectra were recorded on Bruker spectrometers (at 500 or 600 MHz) and are reported relative to deuterated solvent signals. Data for ^{1}H NMR spectra are reported as follows: chemical shift (δ ppm), multiplicity, coupling constant (Hz) and integration. ^{13}C NMR spectra were recorded on Bruker Spectrometers (at 125 or 150 MHz). Data for ^{13}C NMR spectra are reported in terms of chemical shift. IR spectra were recorded on a Varian 640-IR spectrometer and are reported in terms of frequency of absorption (cm^{-1}). High resolution mass spectra were obtained from the UC Irvine Mass Spectrometry Facility with a Micromass LCT spectrometer. Enantiomeric excess for compounds **3.47**, **3.49**, **3.51** and **3.52** was determined by HPLC using an Agilent 1100 Series analytical HPLC. Two "Kessil KSH150B LED Grow Light 150, Blue" were purchased from http://www.amazon.com for use in photoredox-catalyed coupling reactions. See JOC Standard Abbreviations and Acronyms for abbreviations. Available at: http://pubs.acs.org/userimages/ContentEditor/1218717864819/joceah_abbreviations.pdf

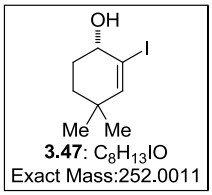


2-Iodo-4,4-dimethyl-2-cyclohexenone (3.46): To a solution of 4,4-dimethylcyclohex-2-ene-1-one (9.5 mL, 72.2 mmol) in THF (180 mL) and H_2O (180 mL) at rt was added sequentially K_2CO_3 (17.96 g, 130.0 mmol), I_2 (40.31 g, 158.8 mmol) and DMAP (2.646 g, 21.7 mmol). The purple heterogeneous solution was stirred vigorously for 18 h at rt. After this time, additional K_2CO_3 (4.49 g, 32.5 mmol), I_2 (10.07 g, 39.7 mmol) and DMAP (0.66 g, 5.41 mmol) were added sequentially. After stirring for an additional 5 h at rt, EtOAc (300 mL) was added and the biphasic mixture was transferred to a separatory funnel. The organic layer was separated, washed with saturated aqueous $Na_2S_2O_3$ solution (3 x 300 mL), aqueous 0.1 N HCl (3 x 300 mL), and brine (2 x 300 mL), and dried over Na_2SO_4. The drying agent was removed by filtration and the filtrate was concentrated to provide a viscous yellow oil. The crude product was loaded onto a short plug of silica gel and was quickly eluted into a single round-bottom flask using Et_2O (700 mL). Removal of the solvent under reduced pressure gave iodoenone **3.46** (17.26 g, 69.0 mmol, 96%) as an orange oil that solidified upon storage at –20 °C. Spectral data acquired for the compound matched those previously reported.[51]



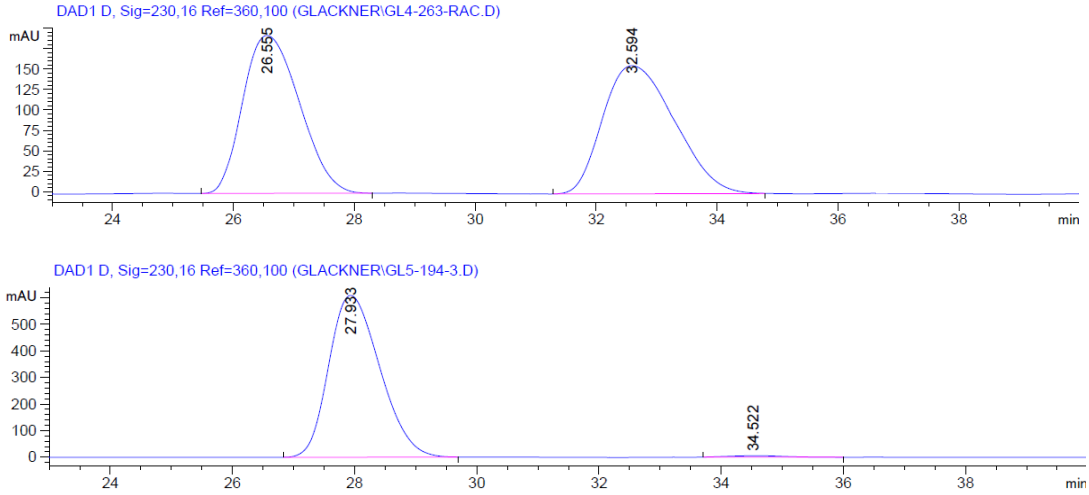
2-Iodo-4,4-dimethyl-2-cyclohexenol (*rac*-3.47): A round-bottom flask containing 2-iodo-4,4-dimethyl-2-cyclohexenone (**3.46**) (500 mg, 2.00 mmol), $CeCl_3$•6 H_2O (890 mg, 2.40 mmol) and MeOH (8 mL) was cooled to 0 °C under argon. To the solution was then added $NaBH_4$ (90 mg, 2.40 mmol) in one portion. The suspension was allowed to warm to rt while stirring for 18 h. After this time, aqueous 1 N HCl (5 mL) was added, and the resulting biphasic mixture

was extracted with Et_2O (3 x 15 mL). The combined organic layers were washed with brine (2 x 25 mL), dried over $MgSO_4$, filtered through cotton, and concentrated under reduced pressure. The residue obtained was purified by silica gel chromatography (10% EtOAc/hexanes) to provide alcohol *rac*-**3.47** (499 mg, 1.98 mmol, 99%) as a colorless oil. Spectral data acquired for *rac*-**3.47** matched those reported previously.[20b]



(*S*)-2-Iodo-4,4-dimethyl-2-cyclohexenol (3.47): The procedure of Knochel was adopted with the exception that *D*-diphenylprolinol was employed to synthesize the (*S*)-configured secondary alcohol.[20b] To a solution of *D*-diphenylprolinol[52] (253 mg, 1.0 mmol) in THF (21 mL) under argon at rt was added $B(OMe)_3$ (110 μL, 1.0 mmol, 0.05 equiv) under argon. The resulting colorless solution was maintained at rt for 1 h. After this time, BH_3•Et_2NPh (3.56 mL, 20.0 mmol) was added via syringe. A solution of enone **3.46** (5.00 g, 20.0 mmol) in THF (21 mL) was then added over 1 h using a syringe pump. After the addition was complete, the homogeneous solution was maintained at rt for an additional 3 h. Methanol (10 mL) was then added and the reaction mixture was concentrated under reduced pressure. The residue obtained was diluted with Et_2O (200 mL) and washed with saturated aqueous Na_2CO_3 (3 x 150 mL), saturated aqueous $KHSO_4$ (3 x 150 mL), and brine (3 x 150 mL). The organic layer was dried over $MgSO_4$, filtered and concentrated to provide a crude residue that was purified by silica gel chromatography (20% EtOAc/hexanes) to give alcohol **3.47** (4.576 g, 18.16 mmol, 91%) as a colorless oil. Spectral data acquired for **3.47** matched those reported previously.[20b] Analysis by HPLC confirmed that the compound was obtained in 98% *ee*: OD-H column, 215 nm, 2% IPA/*n*-hexane, 0.3

mL/min. t_R: 26.555 min (major), 32.594 min, (minor). $[\alpha]^{26.7}_{D}$ –39.8, $[\alpha]^{26.7}_{577}$ –42.0, $[\alpha]^{26.7}_{546}$ –49.3, $[\alpha]^{26.7}_{435}$ –92.2, $[\alpha]^{26.7}_{405}$ –117.1 (*c* = 1.28, $CHCl_3$). The absolute configuration of (*R*)-**3.47** was previously assigned by Knochel.[20b]



Signal 3: DAD1 D, Sig=230,16 Ref=360,100

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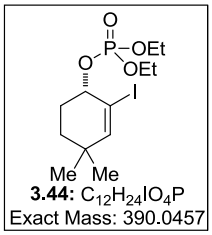
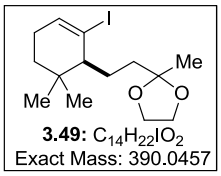


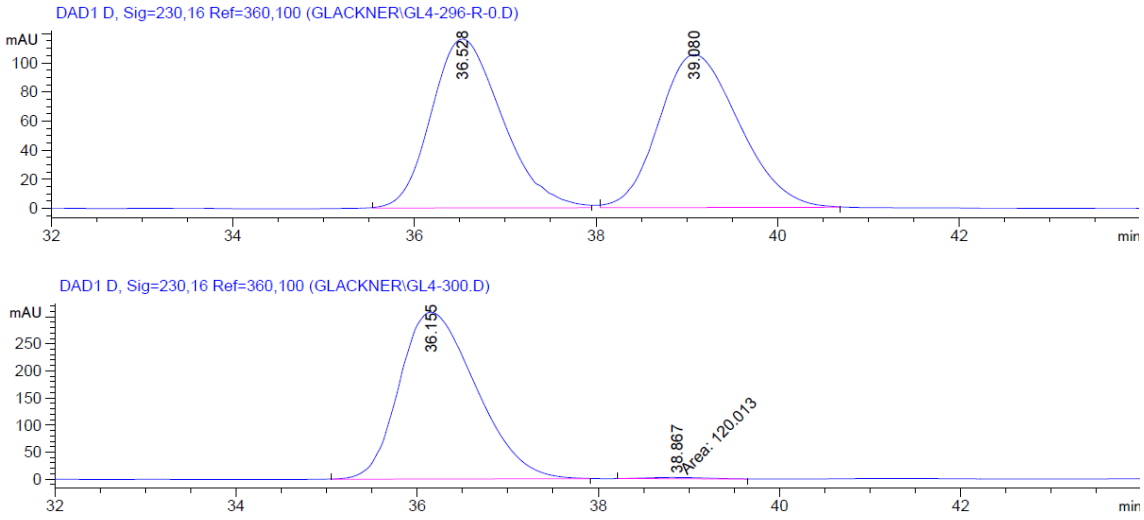
(*S*)-Diethyl (2-iodo-4,4-dimethylcyclohex-2-en-1-yl) phosphate (3.44): The procedure of Knochel was slightly modified.[20b] To a solution of alcohol **3.47** (4.58 g, 18.16 mmol) in CH_2Cl_2 (48 mL) at 0 °C was added sequentially *N*-methylimidazole (2.9 mL, 36.3 mmol) and diethyl chlorophosphate (27.2 mL, 27.2 mmol). The mixture was allowed to warm to rt and was maintained at this temperature for 18 h. Brine (50 mL) was added and the biphasic mixture was transferred to a separatory funnel. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 x 50 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated. The residue obtained was purified by silica gel chromatography (25–

50% EtOAc/hexanes) to provide phosphate **3.44** (6.78 g, 17.5 mmol, 96%) as a colorless oil. Spectral data acquired for the compound matched those previously reported.[20b] $[\alpha]^{26.7}_{D}$ –27.2, $[\alpha]^{26.7}_{577}$ –29.8, $[\alpha]^{26.7}_{546}$ –34.1, $[\alpha]^{26.7}_{435}$ –63.8, $[\alpha]^{26.7}_{405}$ –79.6 (*c* = 1.10, $CHCl_3$).



(*S*)-2-(2-(2-Iodo-6,6-dimethylcyclohex-2-en-1-yl)ethyl)-2-methyl-1,3-dioxolane (3.49): A solution of 2-(2-bromoethyl)-2-methyl-1,3-dioxolane[53] (6.00 g, 30.9 mmol) and 1,2-dibromoethane (0.6 mL) in THF (20 mL) was added to a suspension of Mg turnings (2.25 g, 92.8 mmol) in THF (45 mL). The mixture was briefly warmed with a heat gun for 10 seconds, and was then stirred for 2 h at rt. The resulting black suspension was transferred via cannula to a round-bottom flask containing a stir bar under argon. The mixture was cooled to –78 °C and a homogeneous solution of CuCN (2.77 g, 30.9 mmol) and LiCl (2.62 g, 61.85 mmol) in THF (31 mL) was added via syringe. After stirring vigorously for 15 minutes at –78 °C, a solution of phosphate **3.44** (4.00 g, 10.3 mmol) in THF (20 mL) was added. The suspension was stirred for 30 minutes at –78 °C, then was allowed to warm to 0 °C while stirring for an additional 30 minutes. Saturated aqueous NH_4Cl solution (150 mL) was added and the biphasic mixture was transferred to a separatory funnel. The aqueous layer was extracted with Et_2O (3 x 200 mL) and the combined organic layers were washed with brine (2 x 300 mL), dried over $MgSO_4$, filtered and concentrated. The residue obtained was purified by silica gel chromatography (7% EtOAc/hexanes) to provide vinyl iodide **3.49** (3.49 g, 9.97 mmol, 97%) as a colorless oil. Spectral data acquired for the compound matched those previously reported.[20b] Analysis by HPLC confirmed that the compound was present in 99% *ee*: AD

column, 215 nm, 0.5% IPA/*n*-hexane, 0.15 mL/min. t_R: 36.528 min (major), 39.080 min (minor). $[\alpha]^{26.7}_{D}$ –58.5, $[\alpha]^{26.7}_{577}$ –61.8, $[\alpha]^{26.7}_{546}$ –70.7, $[\alpha]^{26.7}_{435}$ –123.2, $[\alpha]^{26.7}_{405}$ –152.6 (*c* = 0.58, CH_2Cl_2).



Signal 4: DAD1 D, Sig=230,16 Ref=360,100

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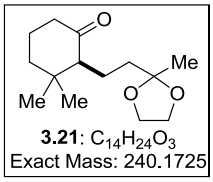
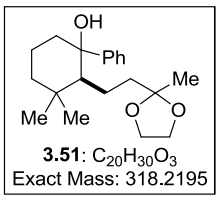


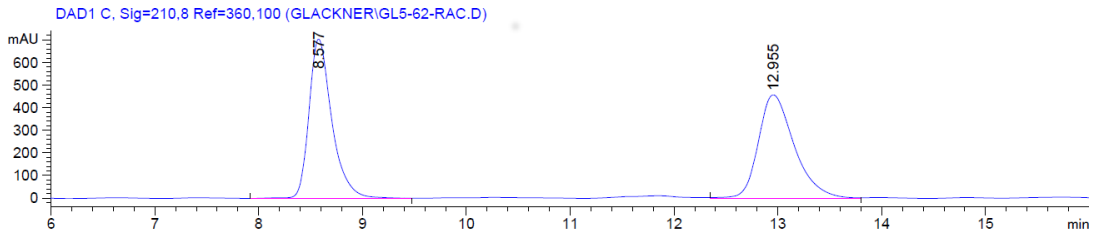
(*S*)-3,3-Dimethyl-2-(2-(2-methyl-1,3-dioxolan-2-yl)ethyl)cyclohexan-1-one (3.21): A round-bottom flask was charged with vinyl iodide **3.49** (1.50 g, 4.28 mmol) and Et_2O (14 mL) under Ar. The reaction mixture was cooled to –78 °C and a solution of *t*-BuLi (6.0 mL, 9.00 mmol, 1.5 M in pentane) was added slowly. The homogeneous solution was maintained at this temperature for 45 min, after which $B(OMe)_3$ (1.2 mL, 10.71 mmol) was added in one portion. The reaction mixture was then allowed to warm to rt and was maintained at this temperature for 3 h. After this time, THF (15 mL), $NaBO_3$•4 H_2O (6.59 g, 42.85

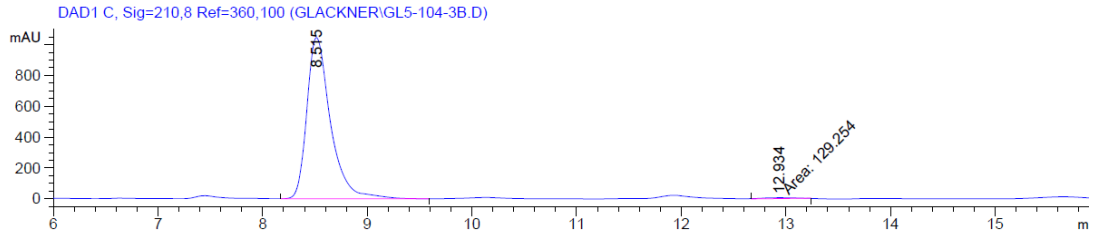
mmol) and H_2O (15 mL) were added sequentially. The heterogeneous mixture was stirred at rt for 24 h, after which it was diluted with H_2O (40 mL) and extracted with Et_2O (3 x 50 mL). The combined organic layers were washed with brine (2 x 100 mL) and dried over $MgSO_4$. The suspension was filtered through cotton to remove the drying agent and the filtrate was concentrated under reduced pressure. The residue obtained was purified by silica gel chromatography (10–15% EtOAc/hexanes) to provide ketone **3.21** (830 mg, 3.45 mmol, 80%) as a colorless oil: R_f = 0.36 (25% EtOAc/hexanes); ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.97–3.90 (m, 4H), 2.35–2.32 (m, 1H), 2.28–2.23 (m, 1H), 2.12 (apt. d, *J* = 11.0 Hz, 1H), 1.91–1.87 (m, 1H), 1.84–1.80 (m, 1H), 1.77–1.65 (m, 2H), 1.64–1.59 (m, 2H), 1.47–1.38 (m, 2H), 1.32 (s, 3H), 1.05 (s, 3H), 0.79 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 213.6, 110.1, 64.7, 64.6, 61.1, 41.2, 39.8, 39.0, 37.8, 29.5, 23.8, 23.3, 22.5, 18.9; IR (thin film) 2962, 2874, 1708, 1459, 1370, 1259, 1222, 1058, 868 cm^{-1}; HRMS (CI) *m*/*z* calcd for $C_{12}H_{25}O_3$ $(M + H)^+$ 241.1804, found 241.1798; $[\alpha]^{24.9}_D$ +11.3, $[\alpha]^{24.9}_{577}$ +12.6, $[\alpha]^{25.0}_{546}$ +14.9, $[\alpha]^{25.1}_{435}$ +47.5, $[\alpha]^{25.1}_{405}$ +75.6 (*c* = 1.00, $CHCl_3$).



(*S*)-2-(2-(6,6-Dimethyl-2-vinylcyclohex-2-en-1-yl)ethyl)-2-methyl-1,3-dioxolane (3.51): In a glove box, anhydrous $CeCl_3$ (178 mg, 0.724 mmol) was placed in a round-bottom flask. The flask was sealed and removed from the glove box. Under an atmosphere of argon, THF (1 mL) was added, and the resulting suspension was cooled to –78 °C. A solution of PhLi (0.4 mL, 0.724 mmol, 1.9 M in Bu_2O) was added slowly, and the reaction mixture was stirred at –78 °C for 2 h. After this time, ketone **3.21** (58 mg, 0.241 mmol) in THF (0.75 mL) was added, and the reaction vessel was transferred to an ice-water bath and was allowed to

warm to 0 °C over 2 h. After this time, saturated aqueous NH_4Cl solution (300 μL) was added, and the mixture was extracted with Et_2O (3 x 10 mL). The combined organic layers were washed with brine (2 x 15 mL), dried over $MgSO_4$, filtered through cotton, and concentrated under reduced pressure. The residue obtained was purified by silica gel chromatography (10–15–20% EtOAc/hexanes) to yield alcohol **3.51** (53 mg, 0.165 mmol, 69%) as a colorless solid. HPLC analysis confirmed that the alcohol was present in 98% *ee*: R_f = 0.71 (25% EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46 (d, *J* = 7.6 Hz, 2H), 7.32 (t, *J* = 8.2 Hz, 2H), 7.19 (t, *J* = 7.0 Hz, 1H), 3.79–3.69 (m, 2H), 3.66–3.61 (m, 1H), 3.52–3.47 (m, 1H), 1.94–1.85 (m, 2H), 1.74–1.65 (m, 1H), 1.61–1.49 (m, 3H), 1.42–1.33 (m, 2H), 1.33–1.26 (m, 1H), 1.26–1.17 (m, 2H), 1.10 (s, 3H), 1.00 (s, 3H), 0.94 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.7, 128.0, 126.4, 125.4, 109.8, 77.6, 64.3, 64.2, 54.2, 41.9, 41.6, 40.8, 35.3, 32.4, 23.0, 21.8, 20.5, 18.6; IR (thin film) 3474, 2954, 1201, 845 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{20}H_{30}O_3Na$ $(M + Na)^+$ 341.2093, found 341.2091; $[\alpha]^{24.9}_D$ –7.4, $[\alpha]^{24.9}_{577}$ –7.2, $[\alpha]^{25.0}_{546}$ –8.1, $[\alpha]^{25.1}_{435}$ –9.6, $[\alpha]^{25.1}_{405}$ –9.4 (*c* = 1.03, $CHCl_3$); AD column, 5% IPA/hexanes, 1 mL/min. t_R: 8.577 min (major), 12.934 min (minor).





Signal 3: DAD1 C, Sig=210,8 Ref=360,100

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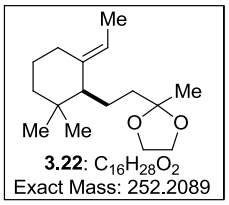
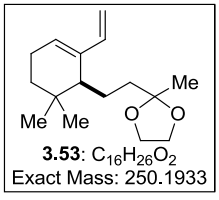


3.22: $C_{16}H_{28}O_2$
Exact Mass: 252.2089

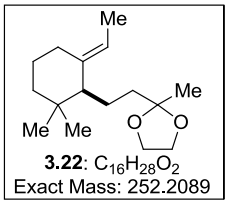
(2*S*)-3,3-Dimethyl-2-(2-(2-methyl-1,3-dioxolan-2-yl)ethyl)-1-phenylcyclohexan-1-ol (3.22). Wittig ethylidenation of ketone 3.21: A round bottom flask was charged with $EtPPh_3Br$ (1.32 g, 3.57 mmol) and THF (5.3 mL) under argon. To the flask was added KO*t*-Bu (365 mg, 3.25 mmol) in one portion, and the orange mixture was stirred at rt for 30 min. The reaction mixture was then cooled to 0 °C, and ketone **3.21** (104 mg, 0.43 mmol) was added as a solution in THF (4.3 mL). The reaction mixture was allowed to warm to rt and was maintained at this temperature for 18 h. After this time, the reaction vessel was heated to 60 °C in a sand bath, and was maintained at this temperature for 6 h. The reaction mixture was then allowed to cool to rt and saturated aqueous NH_4Cl solution (5 mL) was added. The aqueous and organic layers were separated, and the aqueous layer was extracted with Et_2O (3 x 10 mL). The combined organic layers were washed with brine (2 x 15 mL), dried over $MgSO_4$, filtered through cotton, and concentrated under reduced pressure. The crude solid obtained was then dissolved in acetone (3 mL), and Merrifield's resin (219 mg) and NaI (130 mg) were added. The mixture was stirred vigorously for 18

h at rt, and was subsequently filtered through Celite®. The pad of Celite® was washed with THF (8 mL), CH_2Cl_2 (8 mL), H_2O (8 mL), acetone (8 mL) and MeOH (8 mL). This washing sequence was repeated a second time, washing the pad of Celite® with THF (8 mL), CH_2Cl_2 (8 mL), H_2O (8 mL), acetone (8 mL) and MeOH (8 mL). The organic solvents were removed from the biphasic mixture under reduced pressure, and the resulting aqueous layer was extracted with Et_2O (3 x 30 mL). The combined organic layers were washed with brine (2 x 50 mL), dried over $MgSO_4$, filtered through cotton, and concentrated under reduced pressure. The residue obtained was purified by silica gel chromatography (3% EtOAc/hexanes) to give exocyclic olefin **3.22** (75 mg, 0.30 mmol, 69%) as a colorless oil: R_f = 0.46 (3% EtOAc/hexanes); ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.07 (q, *J* = 6.7 Hz, 1H), 3.95–3.90 (m, 4H), 2.25 (dt, *J* = 14.1, 3.5 Hz, 1H), 1.78–1.74 (m, 1H), 1.60 (d, *J* = 6.6 Hz, 3H), 1.55–1.50 (m, 5H), 1.45–1.39 (m, 2H), 1.35–1.34 (m, 1H), 1.32 (s, 3H), 1.20–1.18 (m, 1H), 0.88 (s, 3H), 0.86 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.2, 117.7, 110.6, 64.67, 64.72, 55.9, 37.9, 35.8, 34.9, 28.3, 27.9, 24.0, 23.9, 23.0, 21.1, 12.8; IR (thin film) 2953, 2926, 2864, 1449, 1376, 1238, 1220, 1063, 864, 825 cm^{-1}; HRMS (CI) *m/z* calcd for $C_{16}H_{29}O_2$, $(M + H)^+$ 253.2168, found 253.2161. Conversion of **3.22** to oxalate **3.52** and analysis of oxalate **3.52** by HPLC revealed that the enantiomeric purity of **3.22** was significantly diminished.



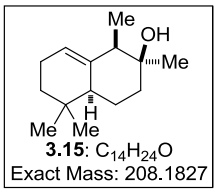
(*S*)-2-(2-(6,6-Dimethyl-2-vinylcyclohex-2-en-1-yl)ethyl)-2-methyl-1,3-dioxolane (3.53): A solution of vinylmagnesium bromide (4.6 mL, 2.86 mmol, 0.62 M in THF) was added to a solution of $ZnCl_2$ (8.56 mL, 4.28 mmol, 0.5 M in THF) at –78 °C. The suspension was then allowed to

warm to rt while stirring for 1.5 h. After this time, a solution of iodide **3.49** (500 mg, 1.43 mmol) and $Pd(PPh_3)_4$ (165 mg, 0.143 mmol) in THF (3.3 mL) and DMF (3.3 mL) was added slowly. The reaction mixture was allowed to stir at rt for 36 h, after which saturated aqueous NH_4Cl solution (10 mL) and Et_2O (50 mL) were added. The organic layer was separated, washed with brine (2 x 40 mL), dried over $MgSO_4$, filtered through cotton, and concentrated under reduced pressure. The residue obtained was purified by silica gel chromatography (3–5% EtOAc/hexanes) to provide diene **3.53** (333 mg, 1.33 mmol, 93%) as a colorless oil: R_f = 0.49 (10% EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.23 (dd, *J* = 17.8, 11.0 Hz, 1H), 5.61 (t, *J* = 3.8 Hz, 1H), 5.05 (d, *J* = 17.8 Hz, 1H), 4.89 (d *J* = 11.0 Hz, 1H), 3.95–3.86 (m, 4H), 2.15–2.10 (m, 2H), 1.90–1.86 (m, 1H), 1.79–1.65 (m, 2H), 1.64–1.52 (m, 2H), 1.41–1.32 (m, 1H), 1.28 (s, 3H), 1.18–1.12 (m, 1H), 0.99 (s, 3H), 0.84 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 140.05, 140.04, 127.3, 109.9, 109.1, 63.94, 63.92, 42.3, 32.0, 30.0, 28.4, 26.7, 26.3, 23.5, 23.0; IR (thin film) 3088, 2953, 2872, 1375, 1060 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{16}H_{27}O_2$ $(M + H)^+$ 251.2011, found 251.1920; $[\alpha]^{24.9}_D$ –72.0, $[\alpha]^{24.9}_{577}$ –75.4, $[\alpha]^{25.0}_{546}$ –85.5, $[\alpha]^{25.1}_{435}$ –146.5, $[\alpha]^{25.1}_{405}$ –177.8 (*c* = 1.14, $CHCl_3$).



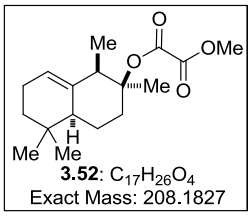
(2*S*)-3,3-Dimethyl-2-(2-(2-methyl-1,3-dioxolan-2-yl)ethyl)-1-phenylcyclohexan-1-ol (3.22). Hydrogenation of diene 3.53: In a glove box under a N_2 atmosphere, a stainless steel Parr bomb containing a stir bar was charged with (η^6-naphthalene)chromium tricarbonyl[54] (106 mg, 0.40 mmol), diene **3.53** (500 mg, 2.00 mmol) and acetone (20 mL, degassed in a Schlenk tube by 3 freeze-pump-thaw cycles prior to bringing into the glove box). The Parr bomb

was sealed, removed from the glove box, and quickly purged with H_2 gas three times before being pressurized to 75 atm (~1100 psi) H_2. The apparatus was then placed in a sand bath preheated to 55 °C and was maintained at this temperature while stirring for 18 h. The H_2 pressure was released and the reaction mixture was transferred to a round-bottom flask and concentrated under reduced pressure. Silica gel chromatography (2–4% EtOAc/hexanes) of the residue provided exocyclic olefin **3.22** (496 mg, 1.97 mmol, 98%) as a colorless oil. Spectral data acquired for the compound matched those reported above. $[\alpha]^{24.9}_{D}$ +24.7, $[\alpha]^{24.9}_{577}$ +24.9, $[\alpha]^{25.0}_{546}$ +27.7, $[\alpha]^{25.1}_{435}$ +45.3, $[\alpha]^{25.1}_{405}$ +56.1 (*c* = 1.04, $CHCl_3$).



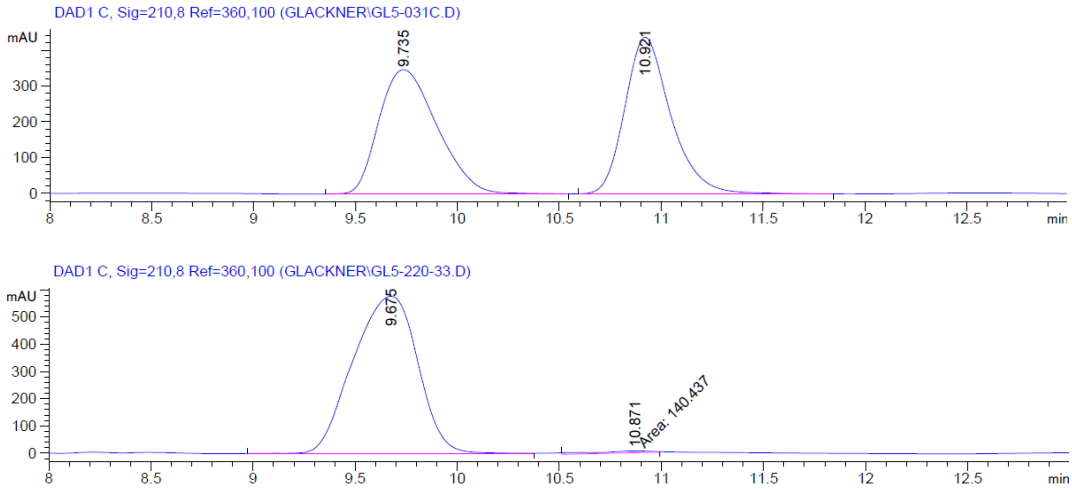
(1*R*,2*S*,4a*S*)-1,2,5,5-Tetramethyl-1,2,3,4,4a,5,6,7-octahydronaphthalen-2-ol (3.15): To a 1-dram vial containing a stir bar and ketal **3.22** (50 mg, 0.20 mmol) at rt was added sequentially CH_2Cl_2 (8 mL), H_2O (4 μL, 0.2 mmol), and TsOH•H_2O (8 mg, 0.04 mmol). The homogeneous reaction mixture was maintained at rt for 3 h, after which it was diluted with H_2O (10 mL). The aqueous layer was extracted with CH_2Cl_2 (3 x 15 mL), and the combined organic layers were washed with brine (2 x 20 mL), dried over Na_2SO_4, filtered through cotton and concentrated under reduced pressure. The residue was purified by silica gel chromatography (5% EtOAc/hexanes) to provide alcohol **3.15** (41 mg, 0.20 mmol, 99%) as a colorless oil: R_f = 0.41 (10% EtOAc/hexanes); ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.44 (br s, 1H), 2.09–2.04 (m, 3H), 1.77–1.70 (m, 2H), 1.63 (s, 1H), 1.53 (td, *J* = 13.4, 4.3 Hz, 1H), 1.47 (br d, *J* = 12.9 Hz, 1H), 1.43–1.38 (m, 1H), 1.28–1.22 (m, 1H), 1.21 (s, 3H), 1.18–1.15 (m, 1H), 1.00 (d, *J* = 6.5 Hz, 3H), 0.90 (s, 3H), 0.88 (s, 3H); ^{13}C

NMR (125 MHz, $CDCl_3$) δ 141.9, 119.0, 72.5, 49.2, 47.9, 40.7, 31.9, 31.3, 27.6, 27.5, 26.7, 26.5, 23.1, 10.7; IR (thin film) 2925, 2866, 1454, 1380, 1363, 1271, 1246, 999, 948, 909, 724 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{14}H_{25}O$ $(M + H)^+$ 209.1905, found 209.1907; $[\alpha]^{24.9}_{D}$ –78.6, $[\alpha]^{24.9}_{577}$ –83.2, $[\alpha]^{25.0}_{546}$ –95.0, $[\alpha]^{25.1}_{435}$ –163.8, $[\alpha]^{25.1}_{405}$ –200.1 (*c* = 1.24, $CHCl_3$).



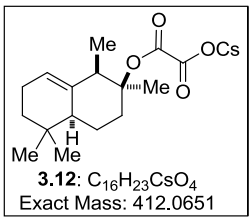
Methyl ((1*R*,2*S*,4a*S*)-1,2,5,5-tetramethyl-1,2,3,4,4a,5,6,7-octahydronaphthalen-2-yl) oxalate (3.52): Tertiary alcohol **3.15** (81 mg, 0.38 mmol) and DMAP (71 mg, 0.58 mmol) were dissolved in CH_2Cl_2 (4 mL) in a scintillation vial under argon. After the addition of methyl chlorooxacetate (71 μL, 0.77 mmol), the vial was sealed with a Teflon-coated cap and was placed in an aluminum block preheated to 40 °C. The homogeneous mixture was maintained at this temperature for 2 h. After this time, the vial was removed from the block and allowed to cool to rt. Additional portions of DMAP (71 mg, 0.58 mmol) and methyl chlorooxacetate (71 μL, 0.77 mmol) were added, and the vial was capped, placed in the aluminum heating block at 40 °C, and maintained at this temperature for a further 3 h. The vial was then allowed to cool to rt and the reaction mixture was quenched with saturated aqueous NH_4Cl solution (2 mL). The biphasic mixture was transferred to a separatory funnel and diluted with H_2O (10 mL). The aqueous layer was extracted with CH_2Cl_2 (3 x 20 mL), and the combined organic layers were washed with brine (2 x 30 mL), dried over Na_2SO_4, filtered through cotton, and concentrated under reduced pressure. The residue obtained was purified by silica gel chromatography (5% EtOAc/hexanes) to provide methyl oxalate ester **3.52** (105 mg, 0.35 mmol, 92%) as a

colorless oil. HPLC analysis confirmed that the compound was present in 98% *ee*: R_f = 0.45 (10% EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.45 (s, 1H), 3.83 (s, 3H), 2.85 (br d, *J* = 15.0 Hz, 1H), 2.07–2.00 (m, 2H), 2.00–1.96 (m, 1H), 1.69–1.64 (m, 1H), 1.63–1.55 (m, 1H), 1.60 (s, 3H), 1.50 (td, *J* = 14.4, 3.7 Hz, 1H), 1.38–1.31 (m, 1H), 1.20–1.14 (m, 2H), 1.12 (d, *J* = 6.6 Hz, 3H), 0.91 (s, 3H), 0.82 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.2, 157.2, 138.5, 119.2, 88.7, 53.2, 48.4, 48.0, 35.2, 33.7, 31.5, 28.2, 25.8, 24.7, 24.3, 23.0, 10.9; IR (thin film) 2951, 2919, 1766, 1739, 1452, 1331, 1208, 1164, 1100, 873 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{17}H_{26}O_4Na$ $(M + Na)^+$ 317.1729, found 317.1736; $[\alpha]^{24.9}_D$ –12.9, $[\alpha]^{24.9}_{577}$ –13.3, $[\alpha]^{25.0}_{546}$ –14.9, $[\alpha]^{25.1}_{435}$ –20.3, $[\alpha]^{25.1}_{405}$ –29.3 (*c* = 1.15, $CHCl_3$); AD column, 1% IPA/*n*-hexane, 0.5 mL/min. t_R: 9.735 min (major), 10.921 min (minor).



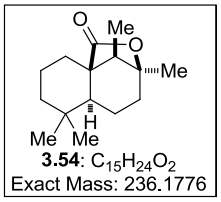
Signal 3: DAD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.675	BB	0.3512	1.27364e4	577.63605	98.9094
2	10.871	MM	0.3569	140.43681	6.55890	1.0906



3.12: $C_{16}H_{23}CsO_4$
Exact Mass: 412.0651

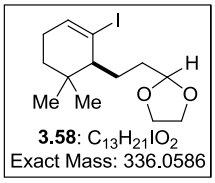
Cesium 2-oxo-2-(((1*R*,2*S*,4a*S*)-1,2,5,5-tetramethyl-1,2,3,4,4a,5,6,7-octahydronaphthalen-2-yl)oxy)acetate (3.12): A 1-dram vial containing a stir bar was charged with methyl oxalate ester **3.52** (101 mg, 0.340 mmol) and THF (340 μL). To this colorless solution was added dropwise aqueous 1 N CsOH (340 μL, 0.340 mmol) with vigorous stirring. The progress of the reaction was monitored by TLC during addition of the aqueous CsOH solution. After complete addition of the aqueous CsOH solution, the reaction mixture was transferred to a round-bottom flask and was concentrated under reduced pressure at 50 °C to yield cesium oxalate salt **3.12** (133 mg, 0.322 mmol, 95%) as a colorless powder. The oxalate was dried under vacuum for 18 h before use: ^{1}H NMR (600 MHz, DMSO-d_6) δ 5.27 (br s, 1H), 2.74–2.69 (m, 1H), 1.95–1.86 (m, 2H), 1.85–1.78 (m, 1H), 1.56–1.47 (m, 2H), 1.41 (s, 3H), 1.34 (dt, *J* = 13.8, 3.6 Hz, 1H), 1.29–1.23 (m, 1H), 1.22–1.14 (m, 1H), 1.31–1.08 (m, 1H), 0.98 (d, *J* = 6.9 Hz, 3H), 0.85 (s, 3H), 0.75 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 168.0, 163.7, 139.5, 117.3, 81.6, 47.7, 47.3, 34.8, 34.2, 31.1, 28.5, 24.84, 24.76, 23.4, 22.4, 10.8 ; HRMS (ESI) *m*/*z* calcd for $C_{16}H_{23}O_4$ $(M - Cs)^-$ 279.1596, found 279.1588.



3.54: $C_{15}H_{24}O_2$
Exact Mass: 236.1776

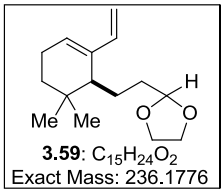
(3*S*,5a*S*,9a*R*,10*R*)-3,6,6,10-Tetramethyloctahydro-1H-3,9a-methanobenzo[c]oxepin-1-one (3.54): To a 1-dram vial was added sequentially (*S*)-5-methoxyfuranone (**3.13**) (13 mg, 0.110 mmol), cesium oxalate salt **3.12** (50 mg, 0.121 mmol), Ir(dF(CF_3)ppy)$_2$(dtbbpy)PF_6 (1 mg, 0.001 mmol), DME (550 μL) and H_2O (20 μL, 1.11 mmol). The yellow reaction mixture was sparged with argon for 5 minutes, after which it was placed in the center of two 34 W

blue LED lamps and stirred vigorously for 36 h. Air was blown on the vial to prevent an increase in temperature due to the LED lamps. After 36 h, the reaction mixture was diluted with CH_2Cl_2 (1 mL) and flushed through a pipette plug of Na_2SO_4. The yellow solution was concentrated under reduced pressure to obtain a crude residue that was purified by silica gel chromatography (3% EtOAc/hexanes), providing lactone **3.54** (16 mg, 0.066 mmol, 54% based on the cesium oxalate) as a colorless oil: R_f = 0.44 (10% EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.13–2.02 (m, 1H), 1.95–1.87 (m, 3H), 1.71 (q, *J* = 7.1 Hz, 1H), 1.63–1.57 (m, 2H), 1.52–1.43 (m, 2H), 1.34 (dd, *J* = 12.2, 5.0 Hz, 1H), 1.28 (s, 3H), 1.18–1.08 (m, 2H), 0.91–0.88 (m, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 180.2, 83.6, 53.8, 50.5, 50.4, 41.8, 36.5, 34.1, 32.2, 29.3, 21.9, 21.6, 20.3, 18.7, 10.4; IR (thin film) 2932, 1754, 1136 cm^{-1}; HRMS (CI) *m*/*z* calcd for $C_{15}H_{28}NO_2$ $(M + NH_4)^+$ 254.2120, found 254.2111; $[\alpha]^{24.9}_D$ –3.4, $[\alpha]^{24.9}_{577}$ –3.2, $[\alpha]^{25.0}_{546}$ –3.9, $[\alpha]^{25.1}_{435}$ –4.8, $[\alpha]^{25.1}_{405}$ –3.3 (*c* = 1.29, $CHCl_3$).



(*S*)-2-(2-(2-Iodo-6,6-dimethylcyclohex-2-en-1-yl)ethyl)-1,3-dioxolane (3.58): A solution of 2-(2-bromoethyl)-1,3-dioxolane [55] (6.96 g, 38.7 mmol) and 1,2-dibromoethane (0.7 mL) in THF (25 mL) was added to a suspension of Mg turnings (2.82 g, 116 mmol) in THF (55 mL). The mixture was briefly warmed with a heat gun for 10 seconds, and was then stirred for 2 h at rt. The resulting black suspension was transferred via cannula to a round-bottom flask containing a stir bar under argon. The mixture was cooled to –78 °C and a homogeneous solution of CuCN (3.46 g, 38.7 mmol) and LiCl (3.28 g, 77.3 mmol) in THF (40 mL) was added via syringe. After stirring vigorously for 15 minutes at –78 °C, a solution of

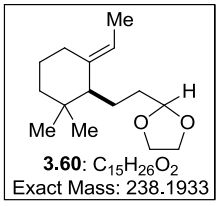
phosphate **3.44** (5.00 g, 12.8 mmol) in THF (25 mL) was added. The suspension was stirred for 30 minutes at –78 °C, then was allowed to warm to 0 °C while stirring for an additional 30 minutes. Saturated aqueous NH_4Cl solution (150 mL) was added and the biphasic mixture was transferred to a separatory funnel. The aqueous layer was extracted with Et_2O (3 x 200 mL) and the combined organic layers were washed with brine (2 x 300 mL), dried over $MgSO_4$, filtered and concentrated. The residue obtained was purified by silica gel chromatography (5% EtOAc/hexanes) to provide vinyl iodide **3.58** (4.03 g, 11.9 mmol, 93%) as a colorless oil. Spectral data acquired for the compound matched those previously reported:[20b] $[\alpha]^{24.9}_{D}$ –59.2, $[\alpha]^{24.9}_{577}$ –62.6, $[\alpha]^{25.0}_{546}$ –70.5, $[\alpha]^{25.1}_{435}$ –126.5, $[\alpha]^{25.1}_{405}$ –155.8 (*c* = 1.02, $CHCl_3$).



3.59: $C_{15}H_{24}O_2$
Exact Mass: 236.1776

(*S*)-2-(2-(6,6-Dimethyl-2-vinylcyclohex-2-en-1-yl)ethyl)-1,3-dioxolane (3.59): A solution of vinylmagnesium bromide (22.5 mL, 22.5 mmol, 1 M in THF) was added to a solution of $ZnCl_2$ (48 mL, 33.7 mmol, 0.7 M in THF) and THF (19 mL) at –78 °C. The suspension was then allowed to warm to rt while stirring for 1.5 h. After this time, a solution of iodide **3.58** (3.78 g, 11.2 mmol) and $Pd(PPh_3)_4$ (1.30 g, 1.12 mmol) in THF (25 mL) and DMF (25 mL) was added slowly. The reaction mixture was allowed to stir at rt for 36 h, after which saturated aqueous NH_4Cl solution (100 mL) was added. The mixture was extracted with Et_2O (3 x 150 mL), and the organic layer was separated, washed with brine (2 x 200 mL), dried over $MgSO_4$, filtered through cotton, and concentrated under reduced pressure. The residue obtained was purified by silica gel chromatography (3–7% EtOAc/hexanes) to provide diene **3.59** (2.54 g, 10.7 mmol, 95%) as a colorless oil: R_f =

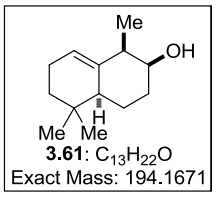
0.61 (10% EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.29 (dd, *J* = 17.7, 10.8 Hz, 1H), 5.64–5.61 (m, 1H), 5.06 (d, *J* = 17.7 Hz, 1H), 4.88 (d, *J* = 11.1 Hz, 1H), 4.75 (t, *J* = 4.8 Hz, 1H), 3.98–3.91 (m, 2H), 3.84–3.79 (m, 2H), 2.15–2.10 (m, 2H), 1.96–1.92 (m, 1H), 1.76–1.69 (m, 2H), 1.66–1.57 (m, 2H), 1.42–1.34 (m, 1H), 1.18–1.12 (m, 1H), 1.00 (s, 3H), 0.85 (s 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.5, 140.2, 127.9, 109.8, 105.1, 64.95, 64.92, 43.0, 34.7, 32.5, 30.5, 28.8, 27.0, 26.8, 23.7; IR (thin film) 2954, 2870, 1647, 1406, 1139, 1034, 893 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{15}H_{28}NO_2$ $(M + NH_4)^+$ 254.2120, found 254.2129; $[\alpha]^{22.4}_{D}$ –87.4, $[\alpha]^{22.4}_{577}$ –93.7, $[\alpha]^{22.4}_{546}$ –105.4, $[\alpha]^{22.4}_{435}$ –182.8, $[\alpha]^{22.4}_{405}$ –219.1 (*c* = 1.02, $CHCl_3$).



3.60: $C_{15}H_{26}O_2$
Exact Mass: 238.1933

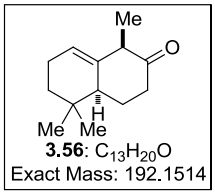
(*S*,*E*)-2-(2-(6-Ethylidene-2,2-dimethylcyclohexyl)ethyl)-1,3-dioxolane (3.60): In a glove box under a N_2 atmosphere, a stainless steel Parr bomb containing a stir bar was charged with (η^6-naphthalene)chromium tricarbonyl[54] (565 mg, 2.1 mmol), diene **3.59** (2.52 g, 10.7 mmol) and acetone (107 mL, degassed in a Schlenk tube by 3 freeze-pump-thaw cycles prior to bringing into the glove box). The Parr bomb was sealed, removed from the glove box, and quickly purged with H_2 gas three times before being pressurized to 75 atm (~1100 psi) H_2. The apparatus was then placed in a sand bath preheated to 55 °C and was maintained at this temperature while stirring for 18 h. The H_2 pressure was released and the reaction mixture was transferred to a round-bottom flask and concentrated. Silica gel chromatography (2% EtOAc/hexanes) of the residue provided exocyclic olefin **3.60** (2.47 g, 10.4 mmol, 97%) as a colorless oil: R_f = 0.67 (10% EtOAc/hexanes); ^{1}H NMR (500

MHz, $CDCl_3$) δ 5.08 (q, *J* = 6.4 Hz, 1H), 4.82 (t, *J* = 4.4 Hz, 1H), 3.98–3.95 (m, 2H), 3.87–3.82 (m, 2H), 2.28–2.25 (m, 1H), 1.76–1.71 (m, 1H), 1.61–1.58 (m, 1H), 1.59 (dd, *J* = 6.7, 1.0 Hz, 3H), 1.56–1.47 (m, 5H), 1.45–1.35 (m, 2H), 1.23–1.17 (m, 1H), 0.88 (s, 3H), 0.85 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.9, 118.0, 105.2, 65.0, 64.9, 55.7, 35.6, 34.8, 32.8, 28.2, 28.0, 23.8, 22.9, 21.2, 12.8; IR (thin film) 2951, 2926, 1460, 1408, 1382, 1364, 1140, 1037, 955, 891, 907, 824 cm^{-1}; HRMS (CI) *m*/*z* calcd for $C_{15}H_{26}O_2$ $(M)^+$ 238.1933, found 238.1942; $[\alpha]^{22.7}_D$ +32.8, $[\alpha]^{22.7}_{577}$ +33.3, $[\alpha]^{22.7}_{546}$ +38.2, $[\alpha]^{22.7}_{435}$ +60.8, $[\alpha]^{22.7}_{405}$ +74.5 (*c* = 0.96, $CHCl_3$).



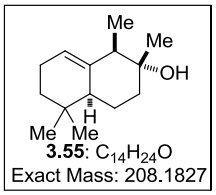
(1*R*,2*S*,4a*S*)-1,5,5-Trimethyl-1,2,3,4,4a,5,6,7-octahydronaphthalen-2-ol (3.61): A round-bottom flask containing a stir bar was charged with exocyclic olefin **3.60** (1.42 g, 9.95 mmol), acetone (53 mL) and H_2O (20 mL). To the mixture was added PPTS (450 mg, 1.79 mmol), and the flask was placed in a sand bath pre-heated to 70 °C. The reaction mixture was stirred at this temperature for 20 h, after which it was allowed to cool to rt. The mixture was diluted with H_2O (30 mL) and extracted with Et_2O (3 x 60 mL). The combined organic layers were washed with brine (2 x 100 mL), dried over $MgSO_4$, filtered through cotton, and concentrated under reduced pressure. The residue obtained was purified by silica gel chromatography (10% EtOAc/hexanes) to provide alcohol **3.61** (796 mg, 4.1 mmol, 69%) as a colorless oil that solidified upon storage at –20 °C: R_f = 0.40 (10% EtOAc/hexanes); ^1H NMR (600 MHz, $CDCl_3$) δ 5.38 (br s, 1H), 3.77 (br s, 1H), 2.28–2.24 (m, 1H), 2.05–2.02 (m, 2H), 1.92 (dq, *J* = 13.7, 3.2 Hz, 1 H), 1.69–1.65 (m, 1H), 1.60 (tdd, *J* = 13.6,

4.5, 2.4 Hz, 1H), 1.53–1.50 (m, 1H), 1.41–1.34 (m, 2H), 1.32 (qd, *J* = 12.9, 4.0 Hz, 1H), 1.17 (dt, *J* = 13.0, 4.7 Hz, 1H), 1.06 (d, *J* = 6.9 Hz, 3H), 0.90 (s, 3H), 0.86 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.0, 119.6, 72.4, 49.1, 43.7, 33.9, 32.7, 31.4, 27.8, 27.0, 24.4, 23.0, 14.3; IR (thin film) 2911, 2867, 2360, 2340, 1452, 1382, 1363, 1186, 1093, 969, 940, 714 cm^{-1}; HRMS (CI) *m*/*z* calcd for $C_{13}H_{22}O$ $(M)^+$ 194.1671, found 194.1672; $[\alpha]^{22.5}_D$ –84.8, $[\alpha]^{22.5}_{577}$ –89.2, $[\alpha]^{22.5}_{546}$ –101.2, $[\alpha]^{22.5}_{435}$ –174.0, $[\alpha]^{22.5}_{405}$ –208.4 (*c* = 1.14, $CHCl_3$).



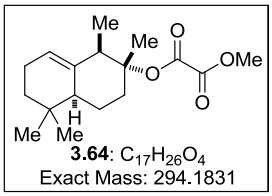
(1*R*,4a*S*)-1,5,5-Trimethyl-3,4,4a,5,6,7-hexahydronaphthalen-2(1*H*)-one (3.56): To a round-bottom flask containing a stir bar and alcohol **3.61** (500 mg, 2.57 mmol) was added CH_2Cl_2 (26 mL) under argon. The solution was cooled to 0 °C and Dess-Martin periodinane[43] (1.31 g, 3.09 mmol) was added in one portion. The reaction mixture was allowed to warm to rt and was maintained at this temperature for 2 h. After this time, Et_2O (26 mL) was added and the solution was flushed through a pad of Celite®. The pad of Celite® was washed with Et_2O (300 mL), and the filtrate was concentrated under reduced pressure. The solid residue obtained was suspended in 10% EtOAc/hexanes (10 mL) and flushed through a small plug of silica gel. The plug of silica gel was eluted with 10% EtOAc/hexanes (100 mL), and the filtrate was concentrated to obtain ketone **3.56** (454 mg, 2.36 mmol, 92%) as a colorless oil. Ketone **3.56** was used immediately in the next step: R_f = 0.48 (10% EtOAc/hexanes); ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.41 (br s, 1H), 3.04–3.00 (m, 1H), 2.48 (ddd, *J* = 14.5, 5.1, 3.5 Hz, 1H), 2.41 (dddd, *J* =14.6, 12.3, 6.2, 1.0 Hz, 1H), 2.11–2.04 (m, 2H), 2.04–1.98 (m, 2H), 1.48–1.42 (m, 1H), 1.41–1.36 (m, 1H), 1.27–1.22 (m, 1H),

1.16 (d, J = 6.6 Hz, 3H), 1.00 (s, 3H), 0.92 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 210.9, 139.0, 118.5, 52.2, 48.0, 41.1, 32.9, 31.8, 28.1, 27.7, 26.5, 23.1, 10.5; IR (thin film) 2953, 2869, 1717, 1673, 1453, 1365, 1337, 1174, 953, 849 cm^{-1}; HRMS (EI) *m*/*z* calcd for $C_{13}H_{20}O$ $(M)^+$ 192.1514, found 192.1519; $[\alpha]^{22.5}_D$ –139.3, $[\alpha]^{22.5}_{577}$ –147.9, $[\alpha]^{22.5}_{546}$ –171.4, $[\alpha]^{22.5}_{435}$ –333.2, $[\alpha]^{22.5}_{405}$ –72.8 (c = 1.05, $CHCl_3$).



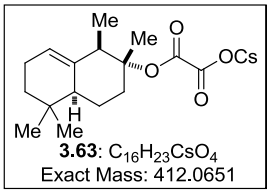
(1*R*,2*R*,4a*S*)-1,2,5,5-Tetramethyl-1,2,3,4,4a,5,6,7-octahydronaphthalen-2-ol (3.55): A round-bottom flask containing a stir bar was charged with 2,6-di-*tert*-butyl-4-methylphenol (3.09 g, 14.04 mmol) and PhMe (23 mL) under argon. A solution of $AlMe_3$ (3.5 mL, 7.03 mmol, 2 M in PhMe) was added slowly via syringe at rt and vigorous gas evolution was observed. The homogeneous light yellow solution was maintained at rt for 1 h, after which it was cooled to –78 °C. Ketone **3.56** (450 mg, 2.34 mmol) was added slowly as a solution in PhMe (7 mL) and the solution was maintained at –78 °C for 5 minutes. A solution of MeMgBr (2.4 mL, 7.03 mmol, 3.0 M in Et_2O) was added slowly, and the solution was maintained at –78 °C for 1.5 h. After this time, the solution was allowed to warm to 0 °C over 20 min. The reaction mixture was then quenched with saturated aqueous NH_4Cl solution (20 mL) and the layers were separated. The aqueous layer was extracted with Et_2O (3 x 30 mL), and the combined organic layers were washed with brine (2 x 40 mL), dried over $MgSO_4$, filtered through cotton, and concentrated under reduced pressure. The residue obtained was purified by silica gel chromatography (10% EtOAc/hexanes) to provide alcohol **3.55** (304 mg, 1.46 mmol, 62%) as a colorless solid: R_f = 0.30 (10% EtOAc/hexanes); ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.35 (br s, 1H), 2.07–

1.98 (m, 3H), 1.84 (dt, *J* = 12.8, 3.7 Hz, 1H), 1.76 (dq, *J* = 13.3, 4.4 Hz, 1H), 1.61–1.53 (m, 2H), 1.45–1.35 (br s, 1H), 1.35–1.29 (m, 1H), 1.20–1.15 (m, 1H), 1.11 (qd, *J* = 13.1, 4.0 Hz, 1H), 1.04 (d, *J* = 6.9 Hz, 3H), 0.96 (s, 3H), 0.91 (s, 3H), 0.83 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.9, 117.8, 74.5, 48.9, 48.5, 42.8, 34.0, 31.4, 28.4, 26.0, 23.0, 20.2, 10.6; IR (thin film) 3307, 2947, 2922, 2845, 1454, 1374, 1126, 1001, 948 cm^{-1}; $[\alpha]^{22.4}_{D}$ –88.5, $[\alpha]^{22.4}_{577}$ –91.6, $[\alpha]^{22.4}_{546}$ –108.8, $[\alpha]^{22.4}_{435}$ –180.6, $[\alpha]^{22.4}_{405}$ –212.5 (*c* = 0.04, $CHCl_3$). Several attempts to acquire HRMS data for **3.55** using ESI and CI ionization techniques were unsuccessful.



Methyl ((1*R*,2*R*,4a*S*)-1,2,5,5-tetramethyl-1,2,3,4,4a,5,6,7-octahydronaphthalen-2-yl) oxalate (3.64): A scintillation vial containing a stir bar was charged with tertiary alcohol **3.55** (304 mg, 1.46 mmol), DMAP (18 mg, 0.15 mmol) and CH_2Cl_2 (7 mL) under argon. After sequential addition of Et_3N (410 μL, 2.92 mmol) and methyl chlorooxacetate (270 μL, 2.92 mmol), the reaction mixture was maintained at rt for 2 h. After this time, saturated aqueous NH_4Cl solution (4 mL) was added and the layers were separated. The aqueous layer was extracted with Et_2O (3 x 10 mL), and the combined organic layers were washed with brine (2 x 20 mL), dried over $MgSO_4$, filtered through cotton, and concentrated under reduced pressure. The residue obtained was purified by silica gel chromatography (3% EtOAc/hexanes) to provide methyl oxalate ester **3.64** (385 mg, 1.31 mmol, 90%) as a colorless oil: R_f = 0.57 (10% EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.43 (s, 1H), 3.86 (s, 3H), 2.65–2.55 (m 2H), 2.03–1.98 (m, 2H), 1.89 (td, *J* = 13.2, 4.0 Hz, 1H), 1.83–1.77 (m, 1H), 1.64–1.57 (m, 1H), 1.33 (s, 3H), 1.32–1.28 (m, 1H), 1.23–1.16 (m,

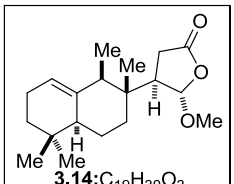
1H), 1.16–1.07 (m, 1H), 1.05 (d, *J* = 7.1 Hz, 3H), 0.90 (s, 3H), 0.82 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.2, 156.8, 139.3, 119.7, 91.2, 53.4, 48.2, 46.1, 36.7, 34.0, 31.4, 28.4, 25.7, 25.4, 23.0, 17.3, 10.9; IR (thin film) 2951, 2919, 1772, 1741, 1200, 1168 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{17}H_{26}O_4Na$ $(M + Na)^+$ 217.1729, found 317.1732; $[\alpha]^{22.4}_D$ –103.0, $[\alpha]^{22.4}_{577}$ –100.8, $[\alpha]^{22.4}_{546}$ –108.5, $[\alpha]^{22.4}_{435}$ –187.3, $[\alpha]^{22.4}_{405}$ –221.9 (*c* = 0.22, $CHCl_3$).



3.63: $C_{16}H_{23}CsO_4$
Exact Mass: 412.0651

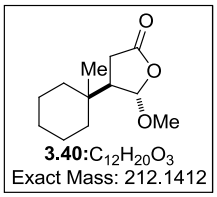
Cesium 2-oxo-2-(((1*R*,2*R*,4a*S*)-1,2,5,5-tetramethyl-1,2,3,4,4a,5,6,7-octahydronaphthalen-2-yl)oxy)acetate (3.63): A scintillation vial containing a stir bar was charged with methyl oxalate ester **3.64** (379 mg, 1.29 mmol) and THF (2.6 mL). A solution of CsOH (1.29 mL, 1.29 mmol, 1 N in H_2O) was added in 100 μL portions with vigorous stirring. After a total of 900 μL had been added, the remaining CsOH solution was added in 50 μL portions and the progress of the reaction was checked by TLC after each addition. After the addition was complete, the solution was transferred to a pear-shaped flask and concentrated under reduced pressure at 50 °C. The residue obtained was dried under vacuum overnight to produce a colorless solid. This solid was washed with *n*-pentane (3 x 2 mL) and further dried 1 h under vacuum to provide cesium oxalate salt **3.63** (525 mg, 1.27 mmol, 99%) as a colorless powder: ^{1}H NMR (500 MHz, DMSO-d_6) δ 5.36 (br s, 1H), 2.56–2.52 (m, 1H), 2.41–2.35 (m, 1H), 2.00–1.93 (m, 2H), 1.84 (td, *J* = 13.6, 3.5 Hz, 1H), 1.75–1.69 (m, 1H), 1.61–1.55 (m, 1H), 1.33–1.26 (m, 1H), 1.18–1.14 (m, 1H), 1.12 (s, 3H), 1.05 (qd, *J* = 13.7, 3.8 Hz, 1H), 0.93 (d, *J* = 7.0 Hz, 3H), 0.88 (s, 3H), 0.80

(s, 3H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 167.5, 163.4, 139.8, 118.0, 83.7, 47.6, 45.3, 36.4, 33.6, 30.9, 28.1, 25.3, 24.8, 22.4, 17.5, 10.5; HRMS (ESI) *m*/*z* calcd for $C_{16}H_{23}O_4$ $(M - Cs)^-$ 279.1596, found 279.1602.

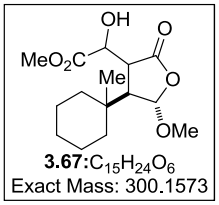


(4*R*,5*S*)-5-Methoxy-4-((1*S*,2*R*,4a*S*)-1,2,5,5-tetramethyl-1,2,3,4,4a,5,6,7-octahydronaphthalen-2-yl)dihydrofuran-2(3*H*)-one (3.14): To a one-dram vial containing a stir bar was added sequentially (*S*)-5-methoxyfuranone (**3.13**) (11 mg, 0.097 mmol), cesium oxalate salt **3.63** (40 mg, 0.097 mmol), Ir(dF(CF_3)ppy)$_2$(dtbbpy)PF_6 (1 mg, 0.97 μmol), DME (1 mL), and H_2O (17 μL, 0.97 mmol). The heterogeneous yellow solution was sparged with argon for 5 minutes, then the vial was sealed with a Teflon-lined cap and the vial was placed in the center of two 34 W blue LED lamps. The reaction mixture was stirred vigorously for 24 h, and was then dilued with H_2O (0.5 mL) and extracted with Et_2O (4 x 2 mL). The combined organic layers were washed with brine (2 x 5 mL), dried over $MgSO_4$, filtered through cotton and concentrated under reduced pressure. The residue obtained was purified by silica gel chromatography to provide lactone **3.14** (16 mg, 0.052 mmol, 54%) as a colorless oil and as a 5:1 mixture of diastereomers: R_f = 0.37 (10% EtOAc/hexanes); ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.37 (d, *J* = 2.1, 1H), 5.35–5.31 (m, 1H), 3.49 (s, 3H), 2.68 (dd, *J* = 18.4, 10.3 Hz, 1H), 2.54–2.50 (m, 1H), 2.38 (dd, *J* = 18.4, 4.7 Hz, 1H), 2.13–2.08 (m, 1H), 2.06–1.99 (m, 2H), 1.72–1.67 (m, 1H), 1.64–1.54 (m, 1H), 1.48–1.41 (m, 2H), 1.38–1.32 (m, 1H), 1.30–1.21 (m, 1H), 1.21–1.14 (m, 1H), 0.95 (d, *J* = 6.9 Hz, 3H), 0.89 (s, 3H), 0.84 (s, 3H), 0.66 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 176.8, 140.6, 118.5, 106.2, 57.0, 49.3, 48.9, 43.4, 39.2, 33.2, 32.7, 31.4, 29.7,

28.0, 26.6, 24.7, 23.1, 17.5, 11.3; IR (thin film) 2931, 1786, 1451, 1168, 947 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{19}H_{30}O_3Na$ $(M + Na)^+$ 329.2093, found 329.2099; $[\alpha]^{22.6}_D$ –43.7, $[\alpha]^{22.6}_{577}$ –45.4, $[\alpha]^{22.6}_{546}$ –52.2, $[\alpha]^{22.6}_{435}$ –93.1, $[\alpha]^{22.6}_{405}$ –111.3 (*c* = 0.60, $CHCl_3$). The relative stereochemistry of the major diastereomer was assigned based on analogy to the products of several diastereoselective coupling reactions conducted in Chapter 1.

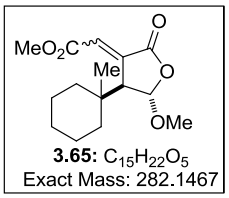


(*rel*-4*R*,5*S*)-5-Methoxy-4-(1-methylcyclohexyl)dihydrofuran-2(3*H*)-one (3.40): A round-bottom flask was charged with 5-methoxyfuranone (2.01 g, 17.62 mmol), (*N*-acyloxy)phthalimide **3.39**[56] (4.60 g, 16.02 mmol), Hantzsch ester (6.09 g, 24.03 mmol), and $Ru(bpy)_3(PF_6)_2$ (138 mg, 0.16 mmol). Under argon, CH_2Cl_2 (107 mL, previously sparged with argon for 15 min) and *i*-Pr_2NEt (6.2 mL, 35.24 mmol) were added sequentially, and the flask was placed in the center of a 30 cm strip of blue LEDs. The heterogeneous reaction mixture was stirred for 24 h, after which it was diluted with Et_2O (500 mL). The solution was washed with aqueous 4 N HCl (3 x 300 mL), aqueous 2 N NaOH (3 x 300 mL) and brine (2 x 400 mL). The organic layer was dried over $MgSO_4$, filtered through cotton and concentrated under reduced pressure. The residue obtained was purified by silica gel chromatography (10% acetone/hexanes) to provide lactone **3.40** (2.27 g, 10.69 mmol, 67%) as a colorless oil. Spectral data acquired for the compound matched those reported previously in Chapter 1.



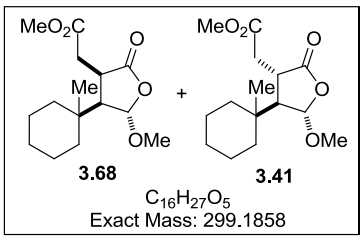
Methyl 2-hydroxy-2-((*rel*-4*R*,5*S*)-5-methoxy-4-(1-methylcyclohexyl)-2-oxotetrahydrofuran-3-yl)acetate (3.67): A solution of lactone **3.40** (500 mg, 2.36 mmol) in THF (12 mL) was cooled to –78 °C, and a solution of LHMDS (2.8 mL, 2.8 mmol, 1 M in THF) was added dropwise. The resulting yellow solution was maintained at –78 °C for 15 min, after which a solution of freshly prepared and distilled methyl glyoxylate (**3.66**)[46] (30 mL, 24.0 mmol, 0.81 M in THF) was added. The reaction mixture was maintained at –78 °C for 1 h and was subsequently quenched by the addition of saturated aqueous NH_4Cl solution (7 mL). The layers were separated and the aqueous layer was extracted with Et_2O (3 x 15 mL). The combined organic layers were washed with brine (2 x 30 mL), dried over $MgSO_4$, filtered through cotton, and concentrated under reduced pressure. The residue obtained was purified by silica gel chromatography (25–30–40% EtOAc/hexanes) to obtain alcohol **3.67** (492 mg, 1.64 mmol, 69%) as a colorless oil and as a 2:1 mixture of diastereomers: R_f = 0.36 (25% EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$, mixture of diastereomers) δ 5.22 (br s, 1H, minor), 5.16 (d, *J* = 3.1 Hz, 1H, major), 4.67 (dd, *J* = 9.4, 3.1 Hz, 1H, minor), 4.37–4.34 (m, 1H, major), 3.84 (s, 3H, major), 3.75 (s, 3H, minor), 3.50 (s, 3H, minor), 3.49 (s, 3H, major), 3.48–3.47 (m, 1H, minor), 3.26 (d, *J* = 4.3 Hz, 1H, major), 3.06 (dd, *J* = 6.5, 3.2 Hz, 1H, major), 2.91–2.89 (m, 1H, minor), 2.38–2.33 (m, 1H, major), 2.11–2.07 (m, 1H, minor), 1.60–1.16 (m, 10H, major and minor), 0.90 (s, 3H, major), 0.81 (s, 3H, major); ^{13}C NMR (125 MHz, $CDCl_3$, mixture of diastereomers) δ 176.2, 174.8, 172.9, 172.8, 106.0, 105.4, 70.8, 70.6, 57.3, 56.9, 53.2, 52.6, 52.3, 52.1, 45.9, 45.5, 35.6, 35.4, 34.9, 34.6, 34.5, 34.0, 26.02, 25.96, 21.45, 21.38, 21.3, 20.3, 19.5;

IR (thin film) 2929, 2854, 1777, 1747, 1446, 1124, 964 cm^{-1}; HRMS (CI) *m*/*z* calcd for $C_{15}H_{25}O_6$ $(M + H)^+$ 301.1651, found 301.1658.

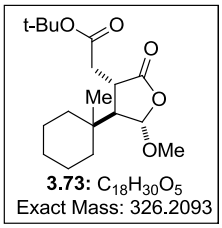


Methyl 2-((*rel*-4*S*,5*S*)-5-methoxy-4-(1-methylcyclohexyl)-2-oxodihydrofuran-3(2*H*)-ylidene)acetate (3.65): A scintillation vial containing a stir bar was charged with alcohol **3.67** (486 mg, 1.62 mmol), DMAP (20 mg, 0.16 mmol) and 1,2-dichloroethane (11 mL) under argon. After sequential addition of pyridine (520 μL, 6.48 mmol) and trifluoroacetic anhydride (460 μL, 3.24 mmol), the reaction mixture was maintained at rt for 45 minutes when complete consumption of the starting material was observed by TLC. After this time, DBU (1.45 mL, 9,72 mmol) was added by syringe and the reaction mixture was stirred at rt for 1 h. The reaction mixture was then quenched by the addition of saturated aqueous NH_4Cl solution (6 mL) and the layers were separated. The aqueous layer was extracted with Et_2O (3 x 15 mL) and the combined organic layers were washed with brine (2 x 30 mL), dried over $MgSO_4$, filtered through cotton and concentrated under reduced pressure. The residue obtained was purified by silica gel chromatography (20% EtOAc/hexanes) to provide alkene **3.65** (415 mg, 1.47 mmol, 91%) as a colorless oil and as a 1.4:1 mixture of olefin isomers: R_f = 0.68 and 0.50 (25% EtOAc/hexanes); ^1H NMR (500 MHz, $CDCl_3$, mixture of olefin isomers) δ 6.90 (s, 1H, major), 6.28 (s, 1H, minor), 5.39 (s, 1H, major), 5.27 (s, 1H, minor), 3.83 (s, 3H, minor), 3.78 (s, 3H, major), 3.49–3.46 (m, 1H), 3.48 (s, 3H), 3.47 (s, 3H), 2.70 (br s, 1H), 1.64–1.04 (m, 10H, major and minor), 0.93 (s, 3H, major), 0.86 (s, 3H, minor); ^{13}C NMR (125 MHz, $CDCl_3$, mixture of diastereomers) δ 170.5, 167.3, 165.7, 165.6, 141.7, 133.5, 130.2, 127.6, 105.1, 104.2, 56.63, 56.59, 55.9,

52.6, 52.2, 38.1, 35.8, 35.3, 35.1, 34.6, 34.3, 25.97, 25.93, 21.7, 21.6, 21.50, 21.46, 20.5, 19.8 ; IR (thin film) 2931, 2858, 1774, 1731, 1214, 938, 911 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{15}H_{22}O_5Na$ $(M + Na)^+$ 305.1365, found 305.1362.

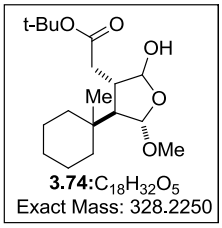


Methyl 2-((*rel*-3*R*,4*R*,5*S*)-5-methoxy-4-(1-methylcyclohexyl)-2-oxotetrahydrofuran-3-yl)acetate (3.68) and Methyl 2-((*rel*-3*S*,4*R*,5*S*)-5-methoxy-4-(1-methylcyclohexyl)-2-oxotetrahydrofuran-3-yl)acetate 3.41. Exemplary procedure for the hydrogenation of α,β-unsaturated lactone 3.65. Table 3.5, entry 1 is described: A 1-dram vial containing a stir bar was charged with alkene **3.65** (11 mg, 0.041 mmol), 10% Pd/C (4 mg) and MeOH (410 μL). The vial was evacuated and backfilled with H_2 using a balloon of H_2 gas. The vial was equipped with the hydrogen balloon and the reaction mixture was stirred vigorously for 3 h at rt. After this time, the reaction mixture was filtered through a plug of Celite® and the plug was then washed with CH_2Cl_2 (3 mL). The filtrate was concentrated under reduced pressure and the crude residue was analyzed by ^1H NMR. Inspection of the ^1H NMR spectrum and comparison to ^1H NMR data previously obtained[19] for **3.68** and **3.41** revealed that compounds **3.68** and **3.41** were present in a 1:7 ratio.



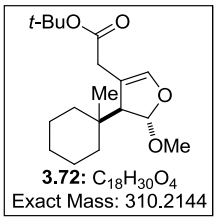
***tert*-Butyl 2-((*rel*-3*S*,4*R*,5*S*)-5-methoxy-4-(1-methylcyclohexyl)-2-oxotetrahydrofuran-3-yl)acetate (3.73)**: A solution of lactone **3.40** (1.37 g, 6.46 mmol) in THF (32 mL) was cooled to –78 °C, and a

solution of LHMDS (7.4 mL, 7.4 mmol, 1 M in THF) was added dropwise. The yellow solution was maintained at this temperature for 15 minutes, after which *tert*-butyl bromoacetate (1.4 mL, 9.69 mmol) was added via syringe. The reaction mixture was maintained at –78 °C for 2 h, after which saturated aqueous NH4Cl solution (20 mL) was added. The layers were separated and the aqueous layer was extracted with Et_2O (3 x 50 mL). The combined organic layers were washed with brine (2 x 80 mL), dried over $MgSO_4$, filtered through cotton and concentrated under reduced pressure. The residue obtained was purified by silica gel chromatography (10% EtOAc/hexanes) to provide lactone **3.73** (1.82 g, 5.57 mmol, 86%) as a colorless oil: R_f = 0.21 (10% EtOAc/hexanes); ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.18 (d, *J* = 2.7 Hz, 1H), 3.49 (s, 3H), 2.83 (q, *J* = 6.1 Hz, 1H), 2.73 (dd, *J* = 16.1, 7.1 Hz, 1H), 2.62 (dd, *J* = 16.1, 5.5 Hz, 1H), 2.08–2.05 (m, 1H), 1.59–1.18 (m, 10H), 1.46 (s, 9H), 0.89 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 178.0, 170.0, 106.0, 81.7, 57.1, 38.4, 38.1, 35.6, 34.3, 28.1, 26.1, 21.55, 21.49, 20.4; IR (thin film) 2929, 2857, 1776, 1730, 1367, 1151, 952 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{18}H_{30}O_5Na$ $(M + Na)^+$ 349.1991, found 349.1997.



***tert*-Butyl 2-((*rel*-3*S*,4*R*,5*S*)-2-hydroxy-5-methoxy-4-(1-methylcyclohexyl)tetrahydrofuran-3-yl)acetate (3.74)**: A solution of lactone **3.73** (1.82 g, 5.57 mmol) in CH_2Cl_2 (56 mL) was cooled to –78 °C and a solution of DIBAL-H (6.1 mL, 6.1 mmol, 1 M in hexanes) was added dropwise. The reaction mixture was maintained at –78 °C for 1 h, after which additional solution of DIBAL-H (6.1 mL, 6.1 mmol, 1 M in hexanes) was added dropwise. The reaction mixture was maintained at –78 °C for 1 h 45 min and was

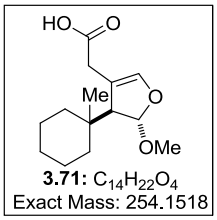
then quenched with MeOH (20 mL). The reaction mixture was allowed to warm to rt and saturated aqueous Rochelle's salt solution (30 mL) and Et_2O (30 mL) were added. The suspension was stirred vigorously at rt for 45 min and was then extracted with Et_2O (3 x 100 mL). The combined organic layers were washed with brine (2 x 200 mL), dried over MgSO4, filtered through cotton and concentrated under reduced pressure. The residue obtained was purified by silica gel chromatography (15% EtOAc/hexanes) to provide lactols **3.74** (972 mg, 2.96 mmol, 53%) as a colorless oil and a 1.4:1 mixture of lactol diastereomers: R_f = 0.37 (25% EtOAc/hexanes); ^{1}H NMR (500 MHz, C_6D_6) δ 5.82 (dd, *J* = 8.2, 5.8 Hz, 1H, major), 5.51–5.47 (m, 1H, minor), 4.92 (d, *J* = 2.3 Hz, 1H, minor), 4.77 (d, *J* = 1.9 Hz, 1H, major), 3.42 (d, *J* = 5.4 Hz, 1H, minor), 3.28 (s, 3H, minor), 3.22 (s, 3H, major), 3.09 (d, *J* = 8.3 Hz, 1H, major), 2.81 (dd, *J* = 16.7, 11.0 Hz, 1H, major), 2.66–2.59 (m, 1H, major), 2.52–2.44 (m, 2H), 2.42–2.35 (m, 1H, minor), 1.42 (s, 9H, major), 1.39 (s, 9H, minor), 1.39–0.97 (m, 10H, major and 10H, minor), 0.90 (s, 3H, minor), 0.68 (s, 3H, major) ; ^{13}C NMR (125 MHz, C_6D_6, mixture of diastereomers) δ 172.1, 171.8, 108.2, 106.0, 103.8, 101.8, 80.4, 79.9, 55.0, 54.9, 43.9, 40.6, 40.3, 37.3, 36.6, 36.5, 36.1, 35.9, 28.17, 28.10, 26.5, 26.4, 22.0, 21.96, 21.94, 21.88; IR (thin film) 3448, 2927, 2859, 1730, 1367, 1155, 1106 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{18}H_{32}O_5Na$ $(M + Na)^+$ 351.2148, found 351.2159. *Note: Lactol **3.74** decomposed rapidly when dissolved in commercial $CDCl_3$, so it was more suitable for NMR analysis in C_6D_6.*



3.72: $C_{18}H_{30}O_4$
Exact Mass: 310.2144

***tert*-Butyl 2-((*rel*-4*S*,5*S*)-5-methoxy-4-(1-methylcyclohexyl)-4,5-dihydrofuran-3-yl)acetate (3.72)**: A 1-dram vial containing a stir bar

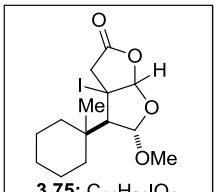
was charged with lactol **3.74** (100 mg, 0.30 mmol), DMAP (4 mg, 0.03 mmol) and THF (1.5 mL) under argon. The vial was cooled to 0 °C, and pyridine (230 μL, 3.05 mmol) and trifluoroacetic anhydride (210 μL, 1.5 mmol) were added sequentially. The vial was then capped with a Teflon-lined cap and was placed in an aluminum block preheated to 65 °C. The brown reaction mixture was stirred for 1 h, after which it was allowed to cool to rt. The reaction mixture was quenched with saturated aqueous NH_4Cl solution (1 mL) and the layers were separated. The aqueous layer was extracted with Et_2O (3 x 2 mL), and the combined organic layers were washed with brine (2 x 5 mL), dried over $MgSO_4$, filtered through cotton and concentrated under reduced pressure. The residue obtained was purified by silica gel chromatography (2–3–5% EtOAc/hexanes) to provide dihydrofuran **3.72** (34 mg, 0.11 mmol, 36%) as a colorless oil: R_f = 0.79 (10% EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.33 (s, 1H), 5.14 (d, *J* = 2.3 Hz, 1H), 3.41 (s, 3H), 3.07 (dd, *J* = 29.9, 17.0 Hz, 2H), 2.66 (s, 1H), 1.58–1.20 (m, 10H), 1.44 (s, 9H), 0.84 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.7, 143.2, 109.0, 108.9, 80.8, 55.2, 36.4, 36.1, 35.5, 34.5, 28.2, 26.3, 21.9, 21.8; IR (thin film) 2928, 2857, 1732, 1368, 1148, 1081 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{18}H_{30}O_4Na$ $(M + Na)^+$ 333.2042, found 333.2036.



3.71: $C_{14}H_{22}O_4$
Exact Mass: 254.1518

2-((*rel*-4*S*,5*S*)-5-Methoxy-4-(1-methylcyclohexyl)-4,5-dihydrofuran-3-yl)acetic acid (3.71): A 1-dram vial containing a stir bar was charged with ester **3.72** (33 mg, 0.11 mmol), MeOH (1 mL) and THF (1 mL). Aqueous 1 N NaOH (1 mL, 1 mmol) was added and the reaction mixture was heated to 65 °C in an aluminum block for 18 h. After this time, the solution was allowed to cool to rt and aqueous 1 N HCl (1.5 mL) was added. The

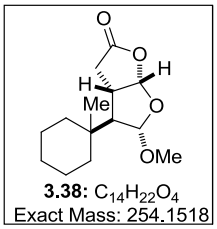
mixture was extracted with EtOAc (4 x 3 mL), and the combined organic layers were washed with brine (2 x 5 mL), dried over MgSO4, filtered through cotton and concentrated under reduced pressure. The residue obtained was purified by silica gel chromatography (20% acetone/hexanes then 100% EtOAc) to obtain a mixture of carboxylic acid **3.71** and bicyclic lactone **3.38**. Repeated chromatography under these conditions eventually gave a trace amount of carboxylic acid **3.71** that was pure by ^{1}H NMR analysis: ^{1}H NMR (600 MHz, CD_2Cl_2) δ 6.35 (s, 1H), 5.16 (d, *J* = 2.2 Hz, 1H), 3.40 (s, 3H), 3.29 (d, *J* = 17.5 Hz, 1H), 3.20 (d, *J* = 17.5 Hz, 1H), 2.66 (s, 1H), 1.57–1.21 (m, 10H), 0.85 (s, 3H). Carboxylic acid **3.71** was used immediately after preparation in the subsequent reaction. Repeating the above procedure to obtain analytically pure carboxylic acid **3.71** for characterization purposes was unsuccessful due to the propensity of **3.71** to spontaneously cyclize to form **3.38**.



3.75: $C_{14}H_{21}IO_4$
Exact Mass: 380.0485

(*rel*-4*R*,5*S*)-3a-Iodo-5-methoxy-4-(1-methylcyclohexyl)tetrahydrofuro[2,3-b]furan-2(3*H*)-one (3.75): A 1-dram vial containing a stir bar was added sequentially carboxylic acid **3.71** (6 mg, 0.025 mmol), $NaHCO_3$ (10 mg, 0.12 mmol), THF (120 μL) and MeCN (250 μL) under argon. The reaction mixture was cooled to 0 °C and I_2 (20 mg, 0.08 mmol) was added in one portion. The resulting heterogeneous purple solution was stirred at 0 °C for 15 minutes, after which it was diluted with Et_2O (20 mL) and transferred to a separatory funnel. The solution was washed with saturated aqueous $Na_2S_2O_3$ solution (3 x 15 mL) and brine (2 x 15 mL). The organic layer was dried over $MgSO_4$, filtered through cotton and concentrated under reduced pressure. The residue

obtained was purified by silica gel chromatography (10% EtOAc/hexanes) to provide iodolactone **3.75** (7 mg, 0.02 mmol, 75%) as a colorless oil: R_f = 0.41 (10% EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.28 (s, 1H), 5.24 (d, *J* = 5.9 Hz, 1H), 3.57 (d, *J* = 18.1 Hz, 1H), 3.45 (s, 3H), 3.34 (d, *J*= 18.1 Hz, 1H), 1.73 (d, *J* = 5.9 Hz, 1H), 1.70–1.41 (m, 9H), 1.37 (td, *J* = 12.3, 3.9 Hz, 1H), 1.19 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.0, 117.0, 109.8, 62.3, 56.5, 52.0, 38.0, 35.9, 35.1, 33.6, 25.9, 21.6, 21.3, 19.9; IR (thin film) 2928, 1793, 1100, 895, 692 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{14}H_{21}IO_4Na$ $(M + Na)^+$ 403.0382, found 403.0367.



3.38: $C_{14}H_{22}O_4$
Exact Mass: 254.1518

(*rel*-3a*S*,4*R*,5*S*,6a*S*)-5-Methoxy-4-(1-methylcyclohexyl)tetrahydrofuro[2,3-b]furan-2(3*H*)-one (3.38): A 1-dram vial containing a stir bar was charged with iodolactone **3.75** (4 mg, 10 μmol) and PhMe (100 μL) under argon. After sequential addition of $(TMS)_3SiH$ (6 μL) and AIBN solution (16 μL, 1 μmol, 61 mM in PhMe), the vial was capped and placed in an aluminum block preheated to 80 °C. The reaction mixture was maintained at this temperature for 40 minutes, after which it was allowed to cool to rt and was concentrated under reduced pressure. Analysis of the residue by ^{1}H NMR confirmed that the bicyclic lactone was formed as a single diastereomer.[19]

3.8 References and Notes

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26. The salt present in solution can affect the outcome of a Wittig reaction. See: Vedejs, E.; Cabaj, J.; Peterson, M. J. *J. Org. Chem.* **1993**, *58*, 6509–6512 and references therein.

27. In this procedure, the ylide is first generated by deprotonation of ethyltriphenylphosphonium bromide with sodamide in toluene at high temperature. After

ylide formation evidenced by a red color, the solution is allowed to cool to room temperature to precipitate the salt byproducts as well as unreacted sodamide. Filtration of the supernatant under an inert atmosphere then provides a solution of the ylide intermediate free from salt and excess base.

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33. This optimization was carried out using *rac*-**3.49** as the substrate. Identical results were obtained in all cases when enantioenriched vinyl iodide **3.49** was used in place of *rac*-**3.49**.

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35. Milstein, D.; Stille, J. K.; *J. Am. Chem. Soc.* **1978**, *100*, 3636–3638.

36. Miyaura, N.; Suzuki, A. *J. Chem. Soc., Chem. Commun.* **1979**, 866–867.

37. Baba, S.; Negishi, E. *J. Am. Chem. Soc.* **1976**, *98*, 6729–6731.

38. This compound was stable when stored neat at –20 °C and showed no signs of decomposition.

39. (a) Wu, J. Y.; Moreau, B.; Ritter, T. *J. Am. Chem. Soc.* **2009**, *131*, 12915–12917. (b) Ely, R. J.; Morken, J. P. *J. Am. Chem. Soc.* **2010**, *132*, 2534–2535.

40. Sodeoka, M.; Shibasaki, M. *Synthesis* **1993**, 643–658.

41. The mechanism of catalyst turnover by this process is unclear, as previous experiments established that catalyst turnover requires a single-electron reduction of the substrate to regenerate the ground-state photocatalyst.

42. The relative configuration of the secondary methyl group of this intermediate was assigned based on analogy to the stereochemistry established by carbonyl-ene cyclization of ketal *rac*-**3.22**. The stereochemistry at the hydroxyl-bearing carbon was established by ^{1}H NMR analysis, even though it is inconsequential in this case as the alcohol is oxidized in the next step.

43. Dess, D. B.; Martin, J. C. *J. Org. Chem.* **1983**, *48*, 4155–4156.

44. This β,γ-unsaturated ketone was prone to olefin isomerization, forming the respective α,β-unsaturated carbonyl compound under acidic or basic conditions or prolonged storage at room temperature. As a consequence, ketone **3.56** was always used immediately after preparation in the ensuing reactions.

45. Maruoka, K.; Itoh, T.; Yamamoto, H. *J. Am. Chem. Soc.* **1985**, *107*, 4573–4576.

46. Jung, M. E.; Shishido, K.; Davis, L. H. *J. Org. Chem.* **1982**, *47*, 892–893.

47. (a) Jurkauskas, V.; Sadighi, J. P.; Buchwald, S. L. *Org. Lett.* **2003**, *5*, 2417–2420. (b) Bui The Thuong, M.; Sottocornola, S.; Prestat, G.; Broggini, G.; Madec. D.; Poli, G. *Synlett* **2007**, 1521–1524.

48. For an informative review of seleno- and iodolactonizations, see: Ranganathan, S.; Muraleedharan, K. M.; Vaish, N. K.; Jayaraman, N. *Tetrahedron* **2004**, *60*, 5273–5308.

49. Surprisingly, the lactols **3.74** rapidly decomposed in $CDCl_3$, likely from trace amounts of HCl present, so NMR analysis of **3.74** was conducted using C_6D_6.

50. Rashid, S.; Bhat, B. A.; Mehta, G. *Org. Lett.* **2015**, *17*, 3604–3607.

51. Pandey, G.; Balakrishnan, M. *J. Org. Chem.* **2008**, *73*, 8128–8131.

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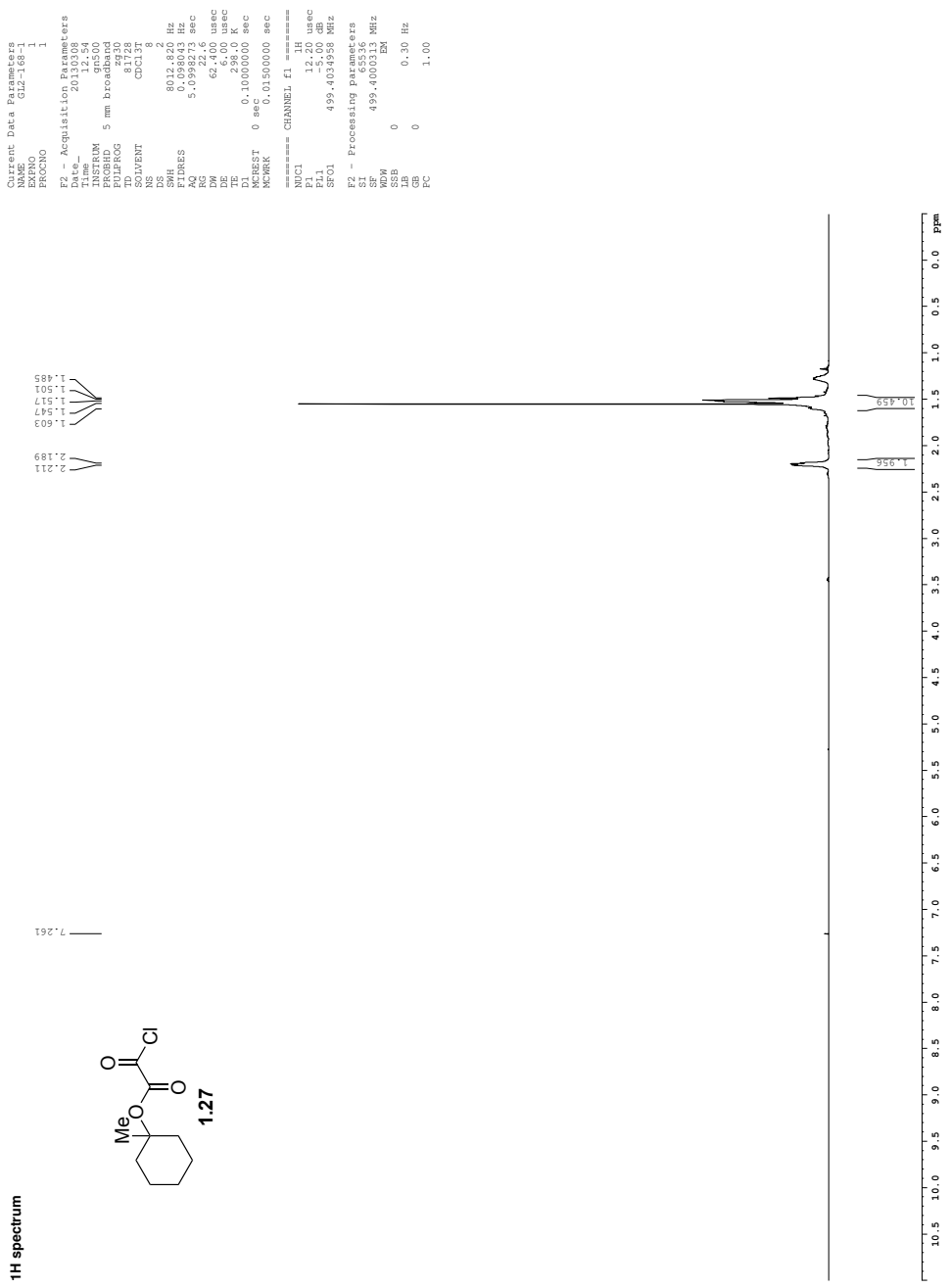
53. Singh, S.; Guiry, P. J. *J. Org. Chem.* **2009**, *74*, 5758–5761.

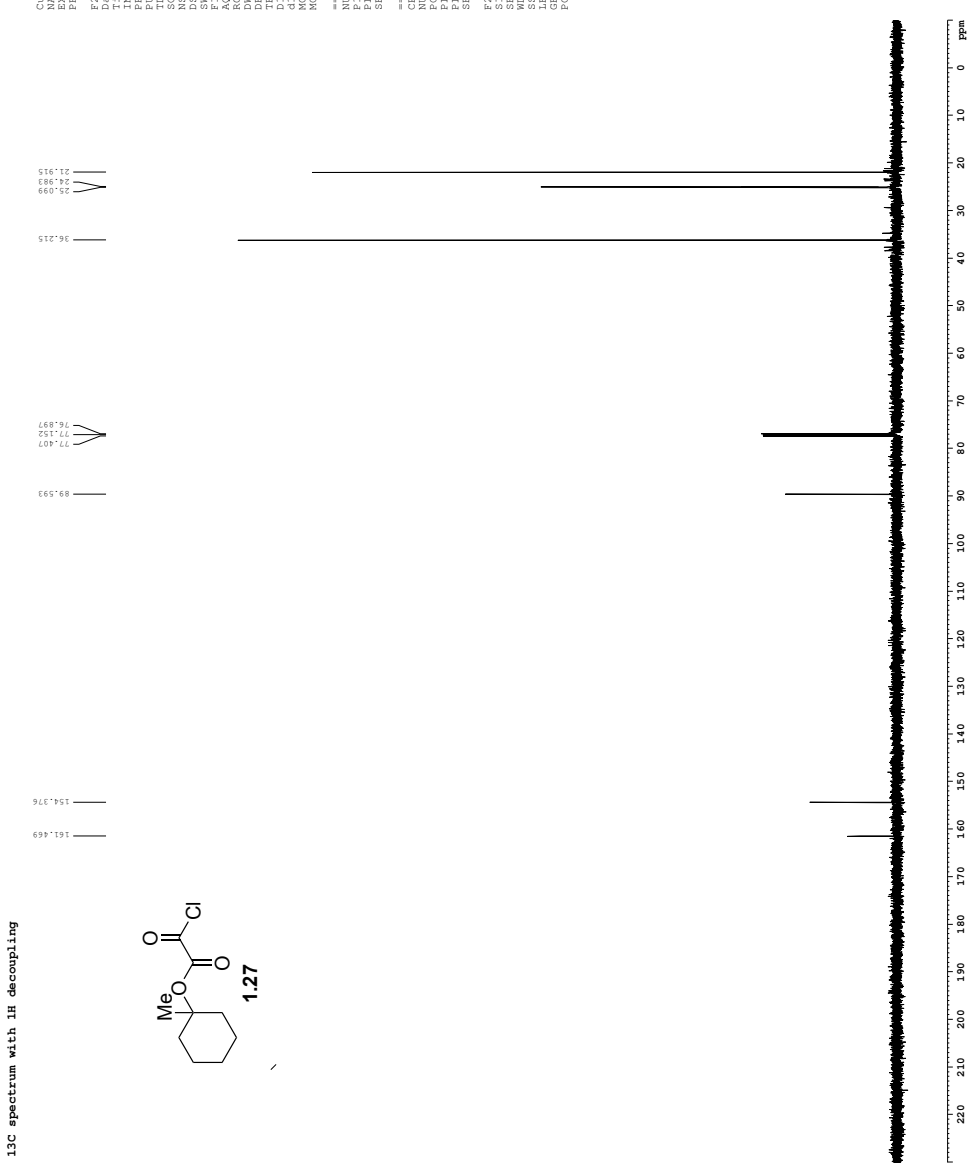
54. Uemura, M.; Minami, T.; Hirotsu, K.; Hayashi, Y. *J. Org. Chem.* **1989**, *54*, 469–477.

55. Hsung, R. P. *Synth. Commun.* **1990**, *20*, 1175–1179.

56. See Chapter 1 for the preparation of this radical precursor.

Appendix A: NMR Spectra




13C spectrum with 1H decoupling
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PROCNO 1
F2 - Acquisition Parameters
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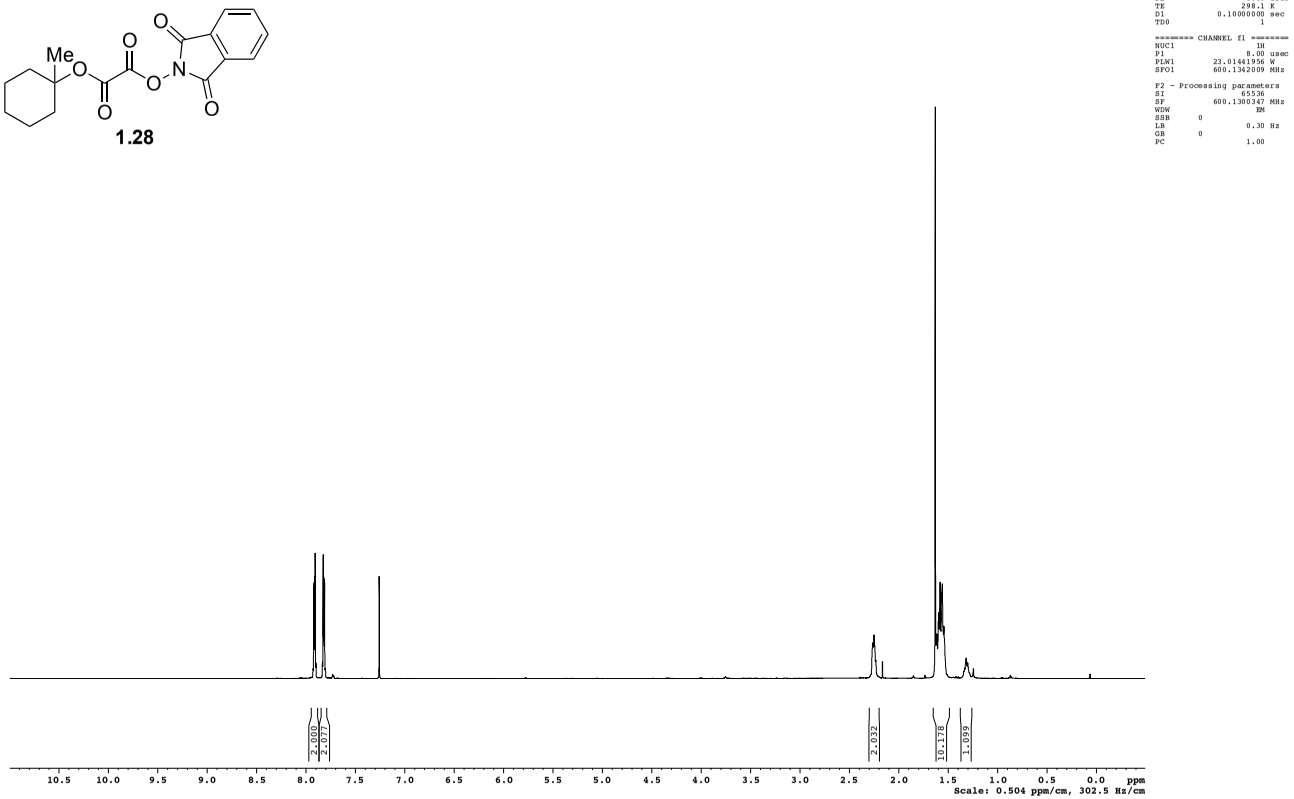
Time 12.54
INSTRUM qnp500
PROBHD 5 mm broadband
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 11
DS 4
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0813440 sec
RG 5792.6
DW 16.500 usec
DE 4.50 usec
TE 298.0 K
D1 0.25000000 sec
D11 0.03000000 sec
MCREST 0 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 13C
P1 7.70 usec
PL1 0 dB
SFO1 125.5880432 MHz
======== CHANNEL f2 ========
CPDPRG[2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 -3.00 dB
PL12 13.20 dB
SFO2 499.4024970 MHz
F2 - Processing parameters
SI 65536
SF 125.5742250 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00
161.469
154.376
89.593
77.407
77.152
76.897
36.215
25.099
24.983
21.915
ppm
1.27

1H spectrum

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PROCNO                          1

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PULPROG                 zg30
TD                     98074
SOLVENT                CDCl3
NS                             8
DS                             2
SWH                 9615.385 Hz
FIDRES              0.098042 Hz
AQ                  5.0998979 sec
RG                           575
DW                    52.000 usec
DE                     6.00 usec
TE                     298.1 K
D1                 0.10000000 sec
TD0                            1

======== CHANNEL f1 ========
NUC1                           1H
P1                          8.00 usec
PLW1                23.01441956 W
SFO1                600.1342009 MHz

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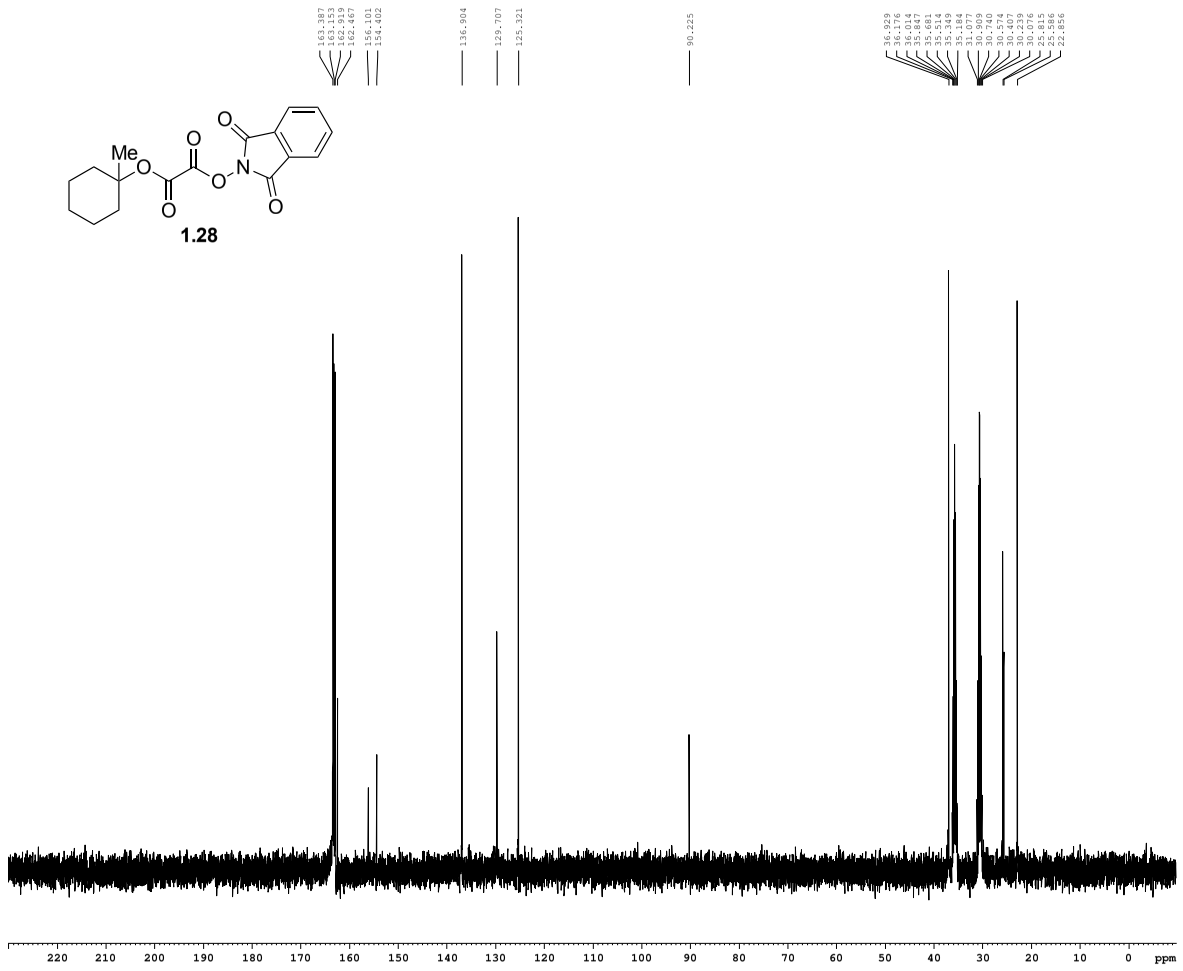
WDW                            EM
SSB                 0
LB                          0.30 Hz
GB                  0
PC                          1.00
```

13C spectrum with 1H decoupling

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PROCNO                 1

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PROBHD   5 mm broadband
PULPROG          zgdc30
TD                65536
SOLVENT           CDCl3
NS                   73
DS                    4
SWH           30303.031 Hz
FIDRES        0.462388 Hz
AQ            1.0813440 sec
RG              11585.2
DW               16.500 usec
DE                4.50 usec
TE                298.0 K
D1           0.25000000 sec
d11          0.03000000 sec
MCREST    0 sec
MCWRK        0.01500000 sec

======== CHANNEL f1 ========
NUC1                 13C
P1                  7.70 usec
PL1        0 dB
SFO1        125.5880432 MHz

======== CHANNEL f2 ========
CPDPRG[2          waltz16
NUC2                 1H
PCPD2              80.00 usec
PL2                -3.00 dB
PL12               13.20 dB
SFO2        499.4024970 MHz

F2 - Processing parameters
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SF          125.5741202 MHz
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SSB        0
LB                  1.00 Hz
GB         0
PC                  2.00
```
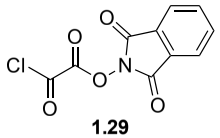

Crude Product



1.29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PROCNO                      1

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PULPROG                 zg30
TD                     81728
SOLVENT                CDCl3
NS                          7
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 sec
MCWRK               0.01500000 sec

======== CHANNEL f1 ========
NUC1                       1H
P1                      7.50 usec
PL1                     1.60 dB
SFO1               500.2235015 MHz

F2 - Processing parameters
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SF                 500.2200259 MHz
WDW                           EM
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GB          0
PC                      4.00
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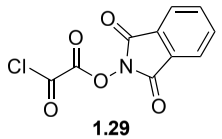
Crude Product



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PROCNO                  1

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PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD                  65536
SOLVENT              CDCl3
NS                     389
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 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 Hz
SPOFF2   0 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 =====
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GPNAM2           SINE.100
GPX1      0 %
GPX2      0 %
GPY1      0 %
GPY2      0 %
GPZ1                30.00 %
GPZ2                50.00 %
p15                500.00 usec
p16               1000.00 usec

F2 - Processing parameters
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SF            125.7804088 MHz
WDW                    EM
SSB       0
LB                   1.00 Hz
GB        0
PC                   2.00
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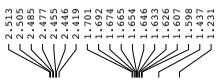
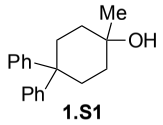
Purified Product





1.S1

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EXPNO                      2
PROCNO                     1

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PULPROG                zg30
TD                    81728
SOLVENT               CDCl3
NS                        21
DS                         0
SWH                8012.820 Hz
FIDRES             0.098043 Hz
AQ                 5.0998774 sec
RG                       4.5
DW                    62.400 usec
DE                     6.00 usec
TE                    298.0 K
D1                 0.10000000 sec
MCREST    0 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             500.2200222 MHz
WDW                       EM
SSB       0
LB        0 Hz
GB        0
PC                     4.00
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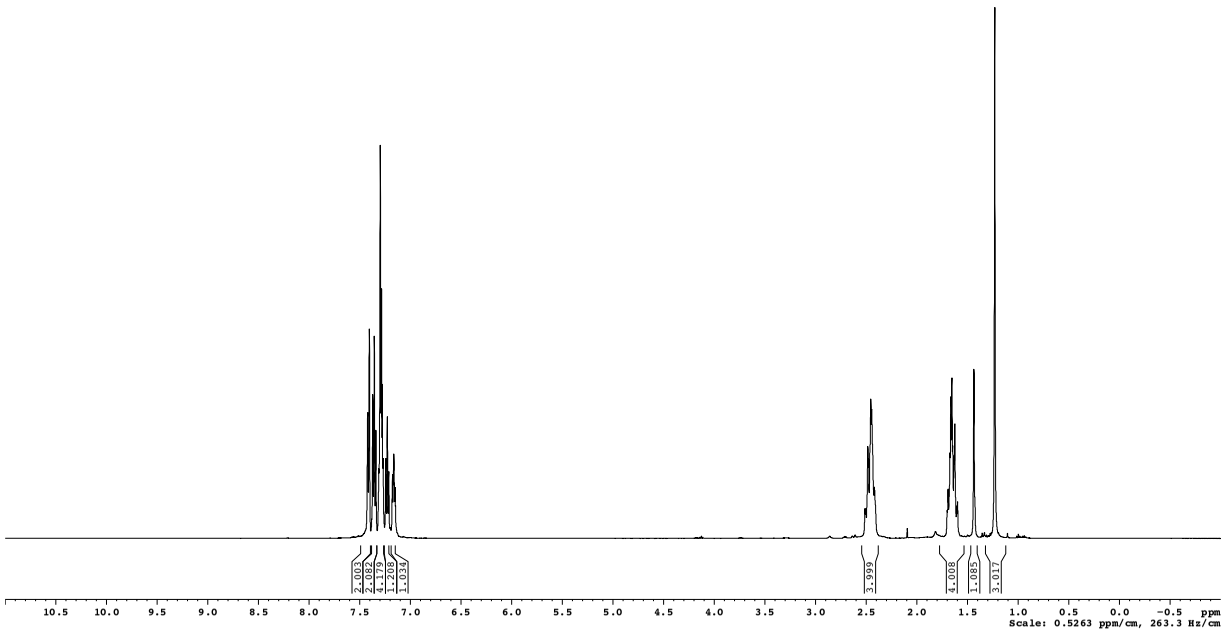

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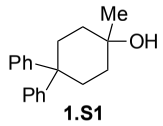

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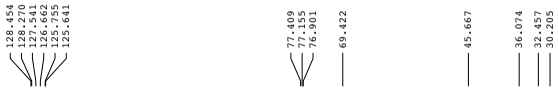

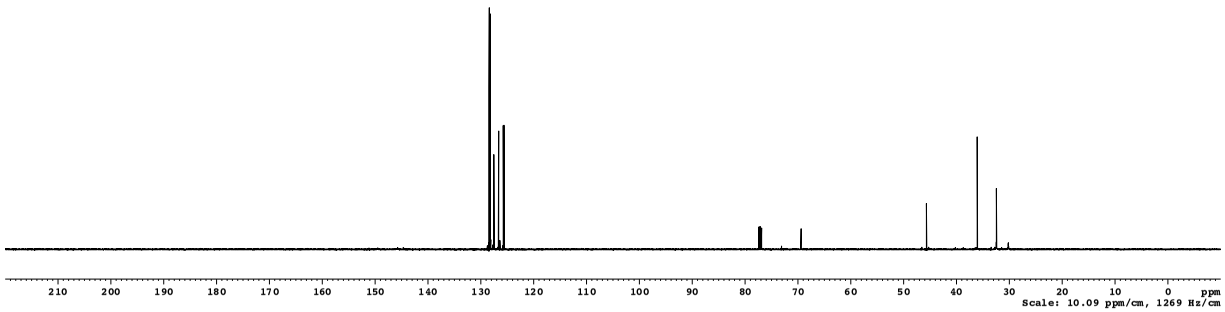


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PROCNO                     1

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PULPROG  SpinEchopg30gp.prd
TD                    65536
SOLVENT                CDCl3
NS                       158
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 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 Hz
SPOFF2   0 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 =====
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GPNAM2            SINE.100
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GPX2      0 %
GPY1      0 %
GPY2      0 %
GPZ1                  30.00 %
GPZ2                  50.00 %
p15                 500.00 usec
p16                1000.00 usec

F2 - Processing parameters
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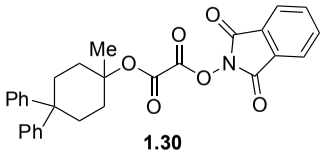
SF             125.7804226 MHz
WDW                      EM
SSB       0
LB        0 Hz
GB        0
PC                     2.00
```

Crude Product



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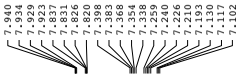

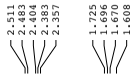


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PROCNO                     1

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PROBHD   5 mm CPTCI 1H-
PULPROG                zg30
TD                    81728
SOLVENT               CDCl3
NS                         7
DS                         0
SWH                8012.820 Hz
FIDRES             0.098043 Hz
AQ                 5.0998774 sec
RG                         5
DW                    62.400 usec
DE                     6.00 usec
TE                    291.3 K
D1                 0.10000000 sec
MCREST    0 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             500.2200318 MHz
WDW                        EM
SSB       0
LB        0 Hz
GB        0
PC                     4.00
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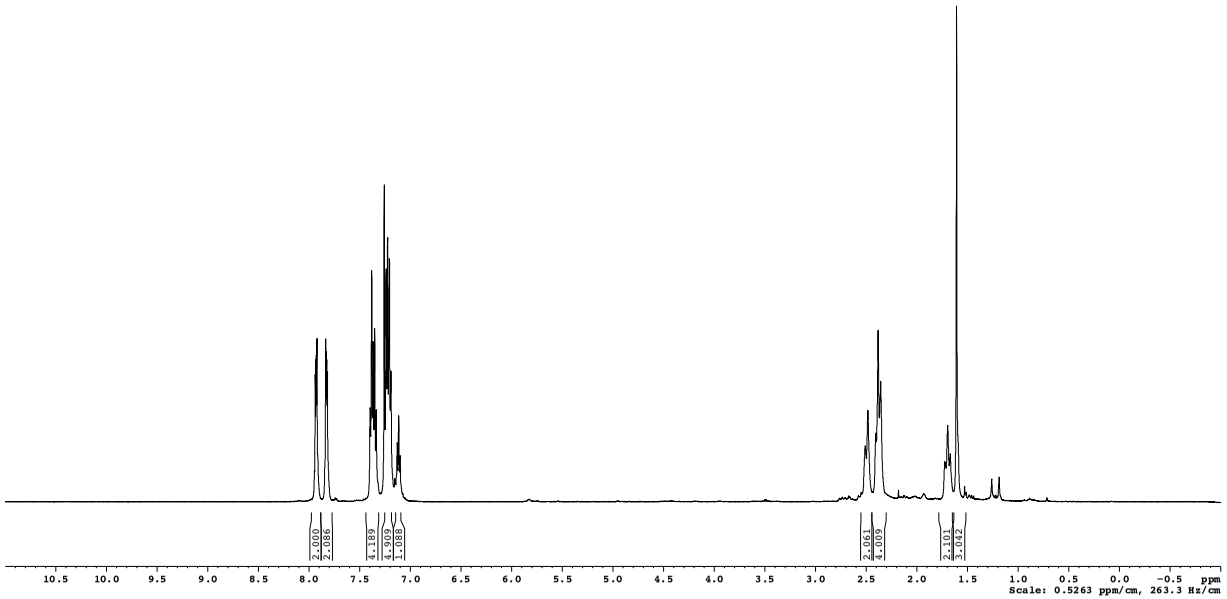
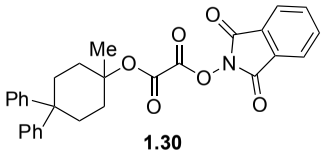


Crude Product



1.30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PROCNO                     1

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Time                  17.24
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TD                     65536
SOLVENT                CDCl3
NS                       187
DS                         0
SWH                30303.031 Hz
FIDRES             0.462388 Hz
AQ                 1.0813940 sec
RG                    2896.3
DW                   16.500 usec
DE                    6.00 usec
TE                   291.3 K
D1                0.25000000 sec
d11               0.03000000 sec
D16               0.00020000 sec
d17               0.00019600 sec
MCREST    0 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 Hz
SPOFF2    0 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 %
GPX2      0 %
GPY1      0 %
GPY2      0 %
GPZ1                 30.00 %
GPZ2                 50.00 %
p15                 500.00 usec
p16                1000.00 usec

F2 - Processing parameters
SI                     65536
SF           125.7804153 MHz
WDW                       EM
SSB       0
LB        0 Hz
GB        0
PC                     2.00
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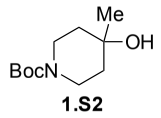
Purified Product



1.S2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Current Data Parameters
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EXPNO                       2
PROCNO                      1

F2 - Acquisition Parameters
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Time                   15.40
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                      40.3
DW                   52.000 usec
DE                    6.00 usec
TE                   293.8 K
D1                 0.10000000 sec
TD0                         1

======== CHANNEL f1 ========
NUC1                       1H
P1                      8.00 usec
PLW1              23.01441956 W
SFO1             600.1342009 MHz

F2 - Processing parameters
SI                      65536
SF               600.1300358 MHz
WDW                        EM
SSB          0
LB           0 Hz
GB           0
PC                       1.00
```
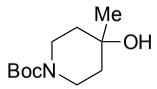
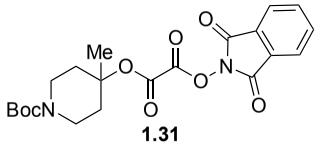

Purified Product



1.S2


```
Current Data Parameters
NAME                  KQ2-136
EXPNO                       3
PROCNO                      1

F2 - Acquisition Parameters
Date_              20130629
Time                   15.48
INSTRUM                av600
PROBHD   5 mm TBI 1H/13
PULPROG                zgdc30
TD                      65536
SOLVENT                CDCl3
NS                        555
DS                          0
SWH                36231.883 Hz
FIDRES              0.552855 Hz
AQ                  0.9044468 sec
RG                        645
DW                   13.800 usec
DE                    6.00 usec
TE                    294.4 K
D1                 0.40000001 sec
D11                0.03000000 sec
TD0                         1

======== CHANNEL f1 ========
NUC1                      13C
P1                    15.00 usec
PLW1             107.15190125 W
SFO1             150.91940880 MHz

======== CHANNEL f2 ========
CPDPRG2                waltz16
NUC2                       1H
PCPD2                 70.00 usec
PLW2          0 W
PLW12            0.30199519 W
SFO2             600.1330010 MHz

F2 - Processing parameters
SI                        65536
SF               150.9027983 MHz
WDW                          EM
SSB           0
LB                     2.00 Hz
GB            0
PC                     1.00
```

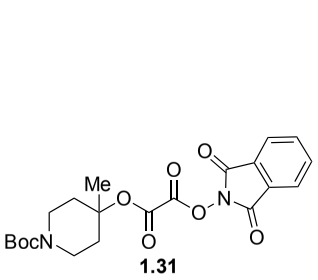
Crude Product



1.31


```
Current Data Parameters
NAME                  KQ2-138
EXPNO                       2
PROCNO                      1

F2 - Acquisition Parameters
Date_              20130702
Time                   18.56
INSTRUM                av600
PROBHD   5 mm TBI 1H/13
PULPROG                zg30
TD                     98074
SOLVENT                CDCl3
NS                         8
DS                         0
SWH                 9615.385 Hz
FIDRES              0.098042 Hz
AQ                  5.0998979 sec
RG                       228
DW                    52.000 usec
DE                     6.00 usec
TE                    298.0 K
D1                 0.10000000 sec
TD0                         1

======== CHANNEL f1 ========
NUC1                       1H
P1                      8.00 usec
PLW1               23.01441956 W
SFO1               600.1342009 MHz

F2 - Processing parameters
SI                      65536
SF                 600.1300355 MHz
WDW                        EM
SSB          0
LB           0 Hz
GB           0
PC                       1.00
```

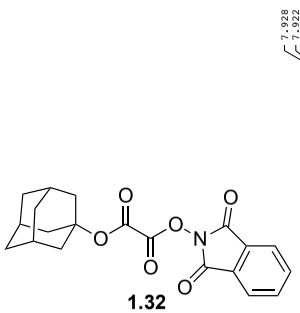
Crude Product



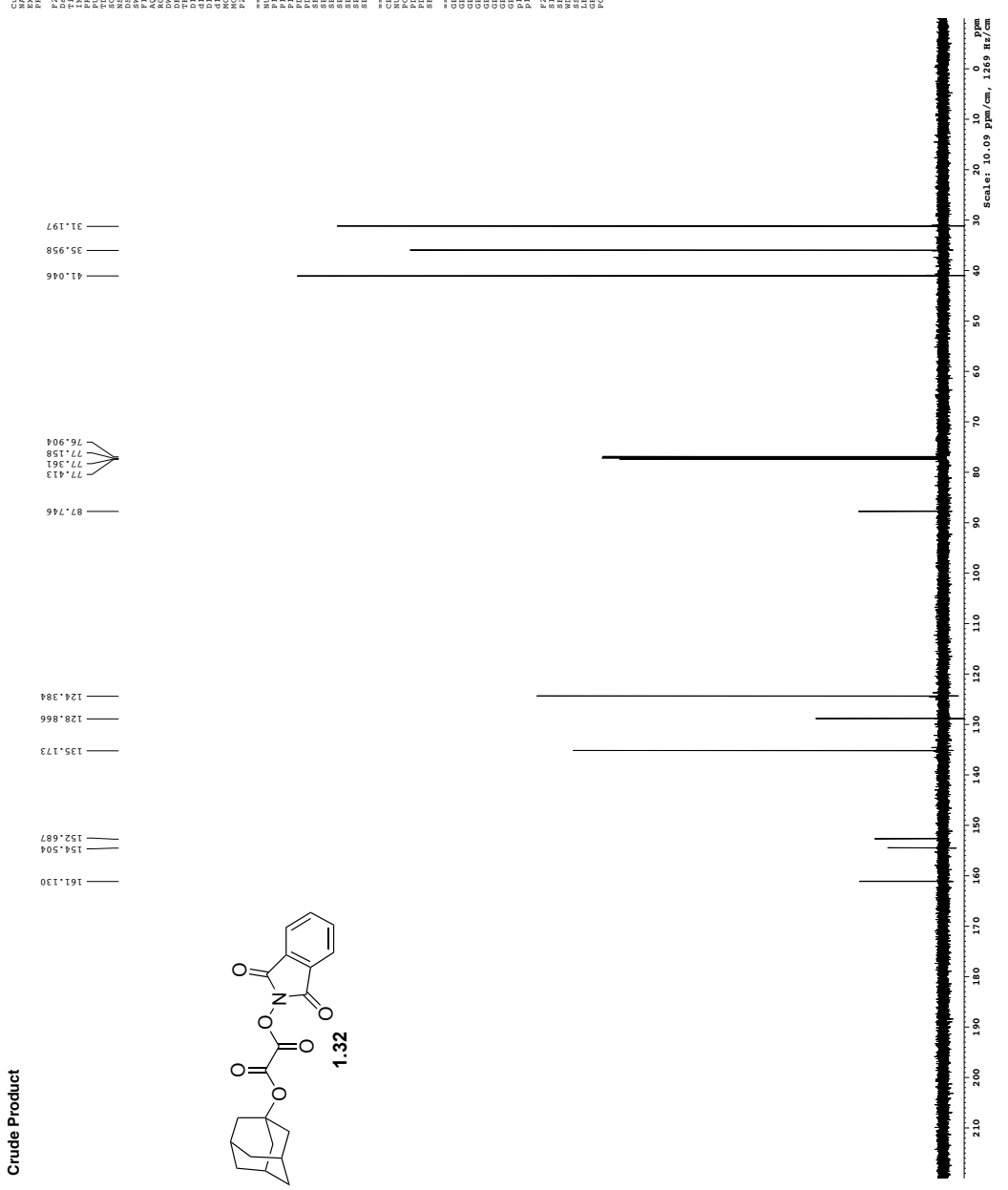
1.31

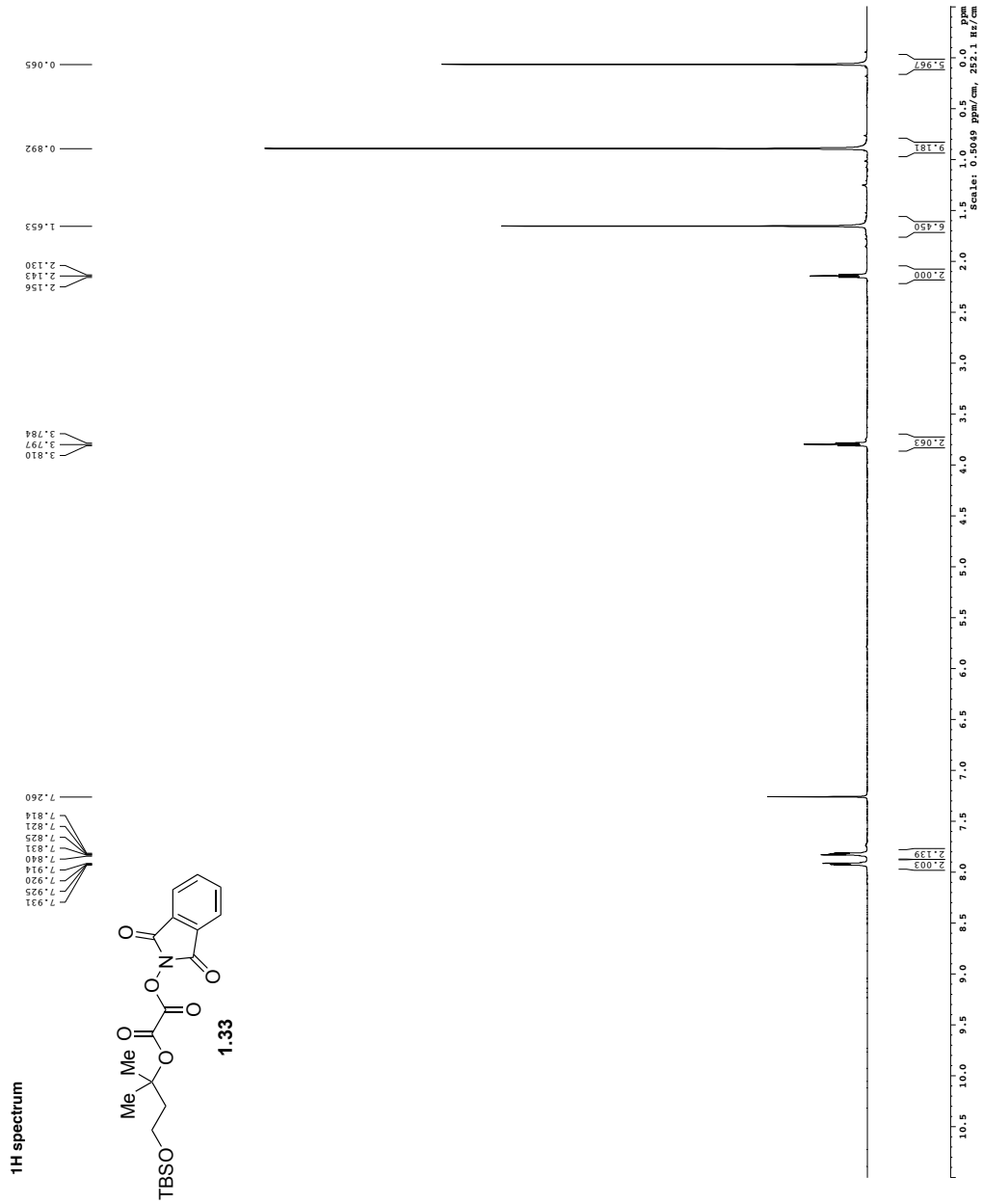

```
Current Data Parameters
NAME              KQ2-138
EXPNO                   4
PROCNO                  1

F2 - Acquisition Parameters
Date_           20130702
Time                19.05
INSTRUM             av600
PROBHD   5 mm TBI 1H/13
PULPROG           zgdc30
TD                 65536
SOLVENT             CDCl3
NS                    511
DS                      0
SWH             36231.883 Hz
FIDRES          0.552855 Hz
AQ              0.9044468 sec
RG                    456
DW                 13.800 usec
DE                  6.00 usec
TE                298.3 K
D1              0.40000001 sec
D11             0.03000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                  13C
P1                  15.00 usec
PLW1        107.15190125 W
SFO1        150.9194080 MHz

======== CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                    1H
PCPD2               70.00 usec
PLW2      0 W
PLW12       0.30199519 W
SFO2        600.1330010 MHz

F2 - Processing parameters
SI                    65536
SF          150.9027935 MHz
WDW                     EM
SSB       0
LB        0 Hz
GB        0
PC                    1.00
```

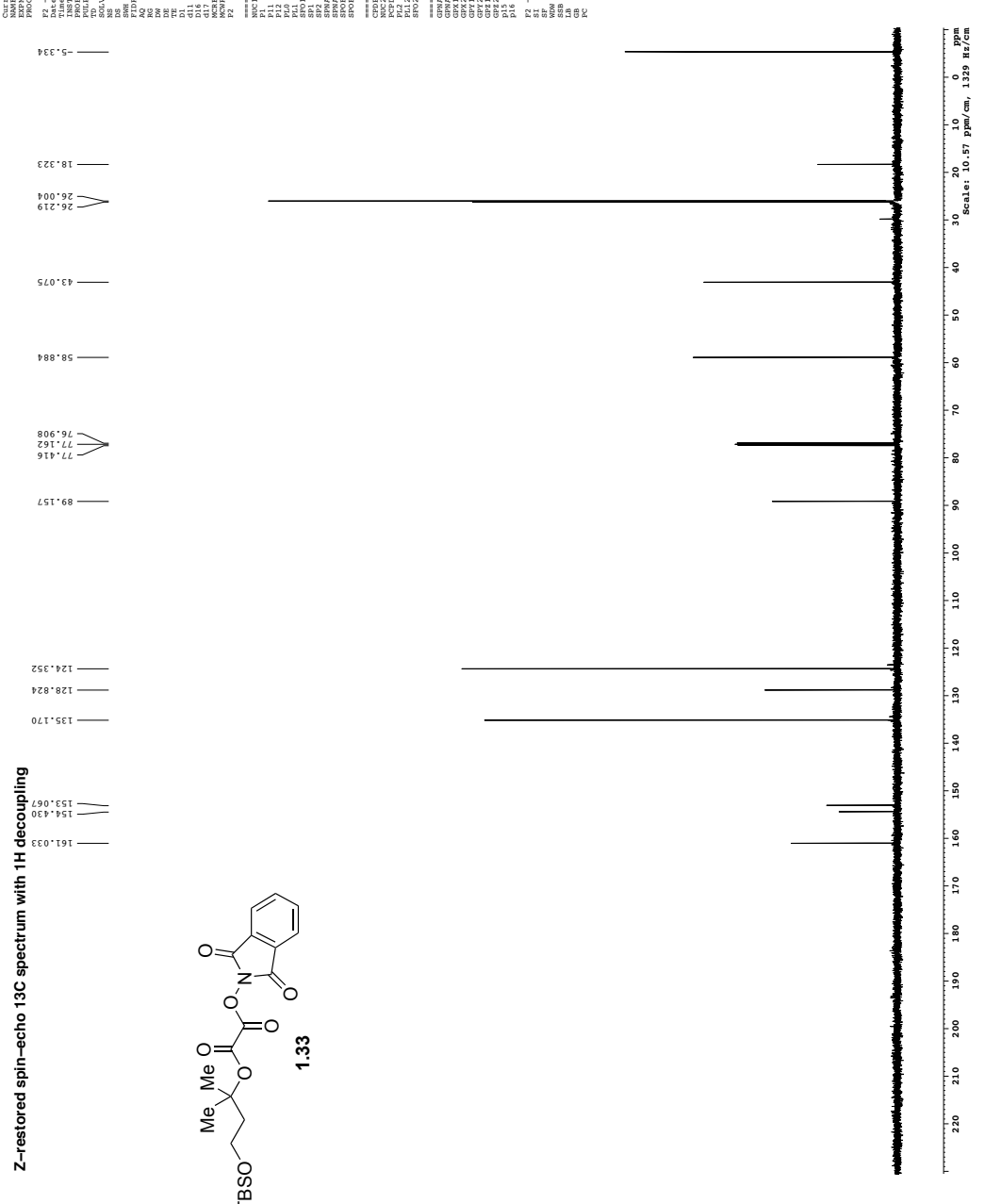
Crude Product



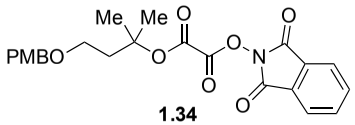

```
Current Data Parameters
NAME                  KQ2-129
EXPNO                       3
PROCNO                      1

F2 - Acquisition Parameters
Date_              20130623
Time                   14.24
INSTRUM             cryo500
PROBHD    5 mm CPTCI 1H-
PULPROG                zg30
TD                    81728
SOLVENT               CDCl3
NS                        7
DS                        0
SWH                8012.820 Hz
FIDRES             0.098043 Hz
AQ                 5.0998774 sec
RG                        8
DW                   62.400 usec
DE                    6.00 usec
TE                  298.0 K
D1                  0.10000000 sec
MCREST    0 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             500.2200302 MHz
WDW                       EM
SSB       0
LB        0 Hz
GB        0
PC                     2.00
```


Crude Product
1.32
31.197
35.958
41.046
76.904
77.158
77.361
77.413
87.746
124.384
128.866
135.173
152.687
154.504
161.130
Scale: 10.09 ppm/cm, 1269 Hz/cm
ppm


1H spectrum
1.33
TBSO
Me
Me
Current Data Parameters
NAME GDP-295-2
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20170703
Time 15.18
INSTRUM spect
PROBHD 5 mm broadband
PULPROG zg30
TD 81536
SOLVENT CDCl3
NS 8
DS 2
SWH 8012.820 Hz
FIDRES 0.098254 Hz
AQ 5.1098774 sec
RG 645.1
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0 sec
MCWRK 0.01500000 sec
NUC1 1H
P1 12.20 usec
PL1 -1.00 dB
SFO1 499.2934950 MHz
F2 - Processing parameters
SI 65536
SF 499.2900000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
7.260
7.814
7.821
7.825
7.831
7.840
7.914
7.920
7.925
7.931
3.784
3.797
3.810
2.130
2.143
2.156
1.653
0.892
0.065
2.139
2.003
2.063
2.000
6.450
9.181
5.967
Scale: 0.5049 ppm/cm, 252.1 Hz/cm
ppm

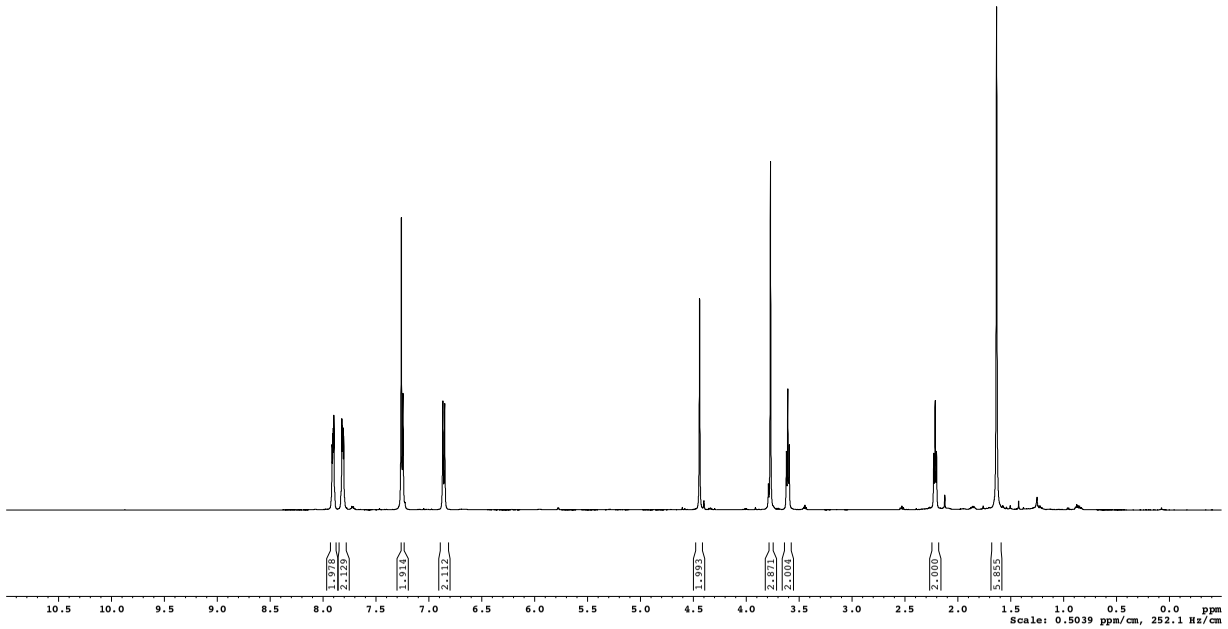

Z–restored spin–echo 13C spectrum with 1H decoupling
-5.334
18.323
26.004
26.219
43.075
58.884
76.908
77.162
77.416
89.157
124.352
128.824
135.170
153.067
154.430
161.033
Me
Me
TBSO
1.33
Scale: 10.57 ppm/cm, 1329 Hz/cm
ppm

1H spectrum

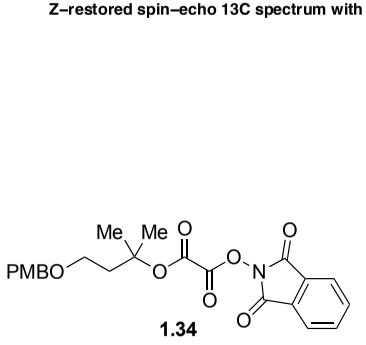


1.34


```
Current Data Parameters
NAME                  GLJ-10-2
EXPNO                        1
PROCNO                       1

F2 - Acquisition Parameters
Date_              20130711
Time                    16.11
INSTRUM                cryo500
PROBHD     5 mm CPTCI 1H-
PULPROG                  zg30
TD                      81728
SOLVENT                CDCl3T
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 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                 500.2200307 MHz
WDW                          EM
SSB          0
LB                      0.30 Hz
GB           0
PC                      4.00
```



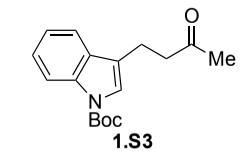
Z–restored spin–echo 13C spectrum with 1H decoupling



1.34

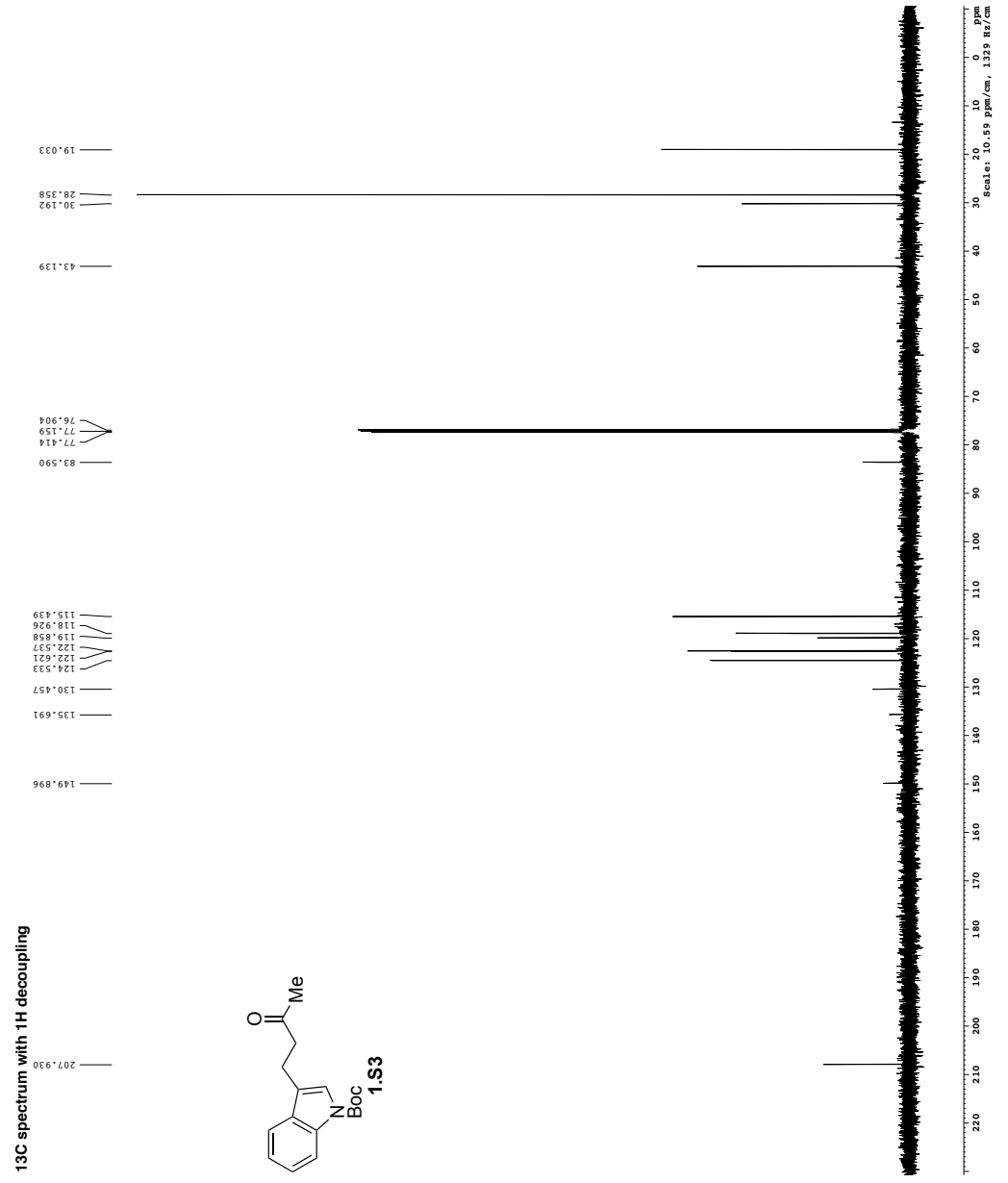

```
Current Data Parameters
NAME            GL3-10-2
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20130711
Time               16.13
INSTRUM          cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD                 65536
SOLVENT             CDCl3
NS                    42
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 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 Hz
SPOFF2    0 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 %
GPX2      0 %
GPY1      0 %
GPY2      0 %
GPZ1             30.00 %
GPZ2             50.00 %
p15             500.00 usec
p16            1000.00 usec

F2 - Processing parameters
SI                 65536
SF          125.7804156 MHz
WDW                   EM
SSB       0
LB                 1.00 Hz
GB        0
PC                 2.00
```

1H spectrum

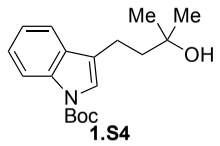


1.S3


```
Current Data Parameters
NAME       GL2-304-3-3-3
EXPNO                 1
PROCNO                1

F2 - Acquisition Parameters
Date_          20130813
Time              15.13
INSTRUM           qn500
PROBHD   5 mm broadband
PULPROG           zg30
TD               81728
SOLVENT          CDCl3T
NS                    8
DS                    2
SWH           8012.820 Hz
FIDRES        0.098043 Hz
AQ            5.0998774 sec
RG                161.3
DW               62.400 usec
DE                6.00 usec
TE               298.0 K
D1            0.10000000 sec
MCREST    0 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           499.2900287 MHz
WDW                     EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

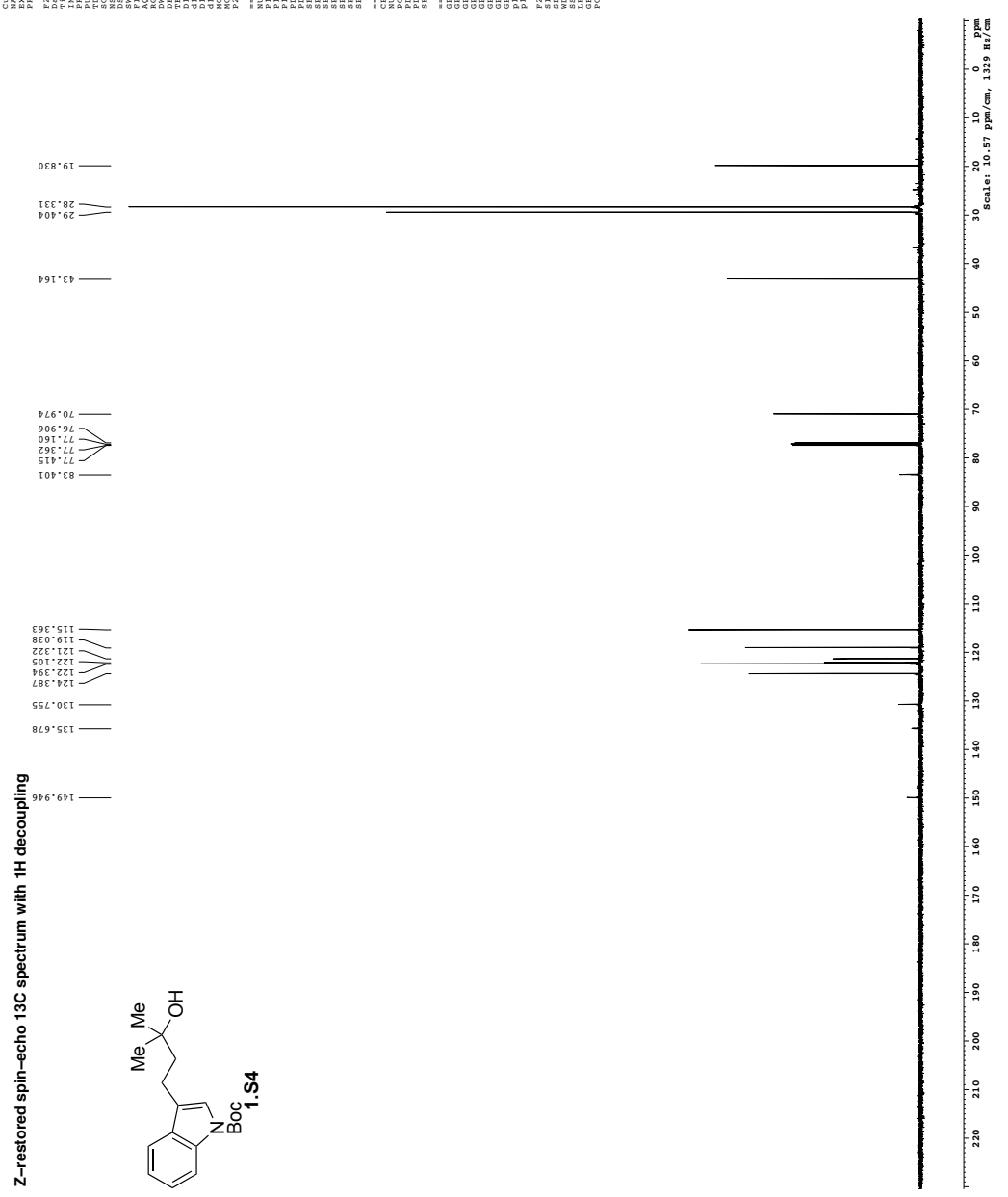

13C spectrum with 1H decoupling
1.S3
Me
O
N
Boc
207.930
149.896
135.691
130.457
124.533
122.621
122.537
119.858
118.926
115.439
83.590
77.414
77.159
76.904
43.139
30.192
28.358
19.033
Scale: 10.59 ppm/cm, 1329 Hz/cm

1H spectrum

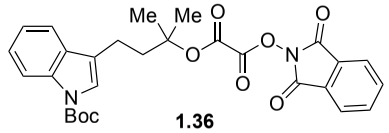


1.S4


```
Current Data Parameters
NAME                  GL3-9-3H
EXPNO                        1
PROCNO                       1

F2 - Acquisition Parameters
Date_              20130813
Time                   19.35
INSTRUM                gn500
PROBHD   5 mm broadband
PULPROG                zg30
TD                    81728
SOLVENT               CDCl3T
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 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              499.2900290 MHz
WDW                        EM
SSB          0
LB                      0.30 Hz
GB           0
PC                      1.00
```


Z–restored spin–echo 13C spectrum with 1H decoupling
Me
Me
OH
N
Boc
1.S4
149.946
135.678
130.755
124.387
122.394
122.105
121.322
119.038
115.363
83.401
77.415
77.362
77.160
76.906
70.974
43.164
29.404
28.331
19.830
Scale: 10.57 ppm/cm, 1329 Hz/cm
ppm

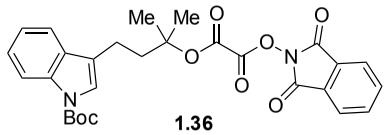
1H spectrum



1.36

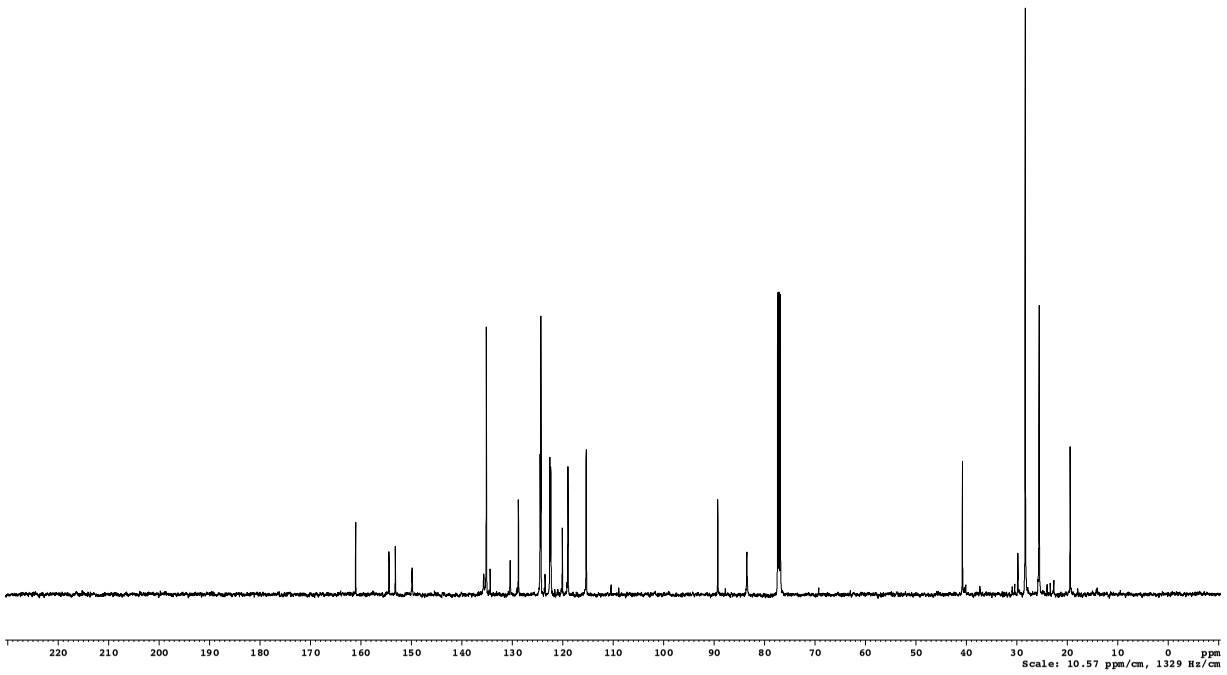

```
Current Data Parameters
NAME                  GL3-11-2
EXPNO                        1
PROCNO                       1

F2 - Acquisition Parameters
Date_              20130711
Time                    16.04
INSTRUM                 cryo500
PROBHD     5 mm CPTCI 1H-
PULPROG                 zg30
TD                      81728
SOLVENT                 CDCl3T
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 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                  500.2200315 MHz
WDW                         EM
SSB          0
LB                       0.30 Hz
GB           0
PC                       4.00
```

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



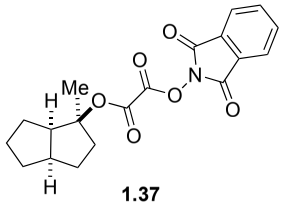
1.36

161.066
154.465
153.219
149.884
135.704
135.171
130.438
128.313
124.506
124.362
122.588
122.394
121.112
118.992
115.374
89.289
83.523
77.413
77.159
76.905
40.790
28.340
25.583
19.448

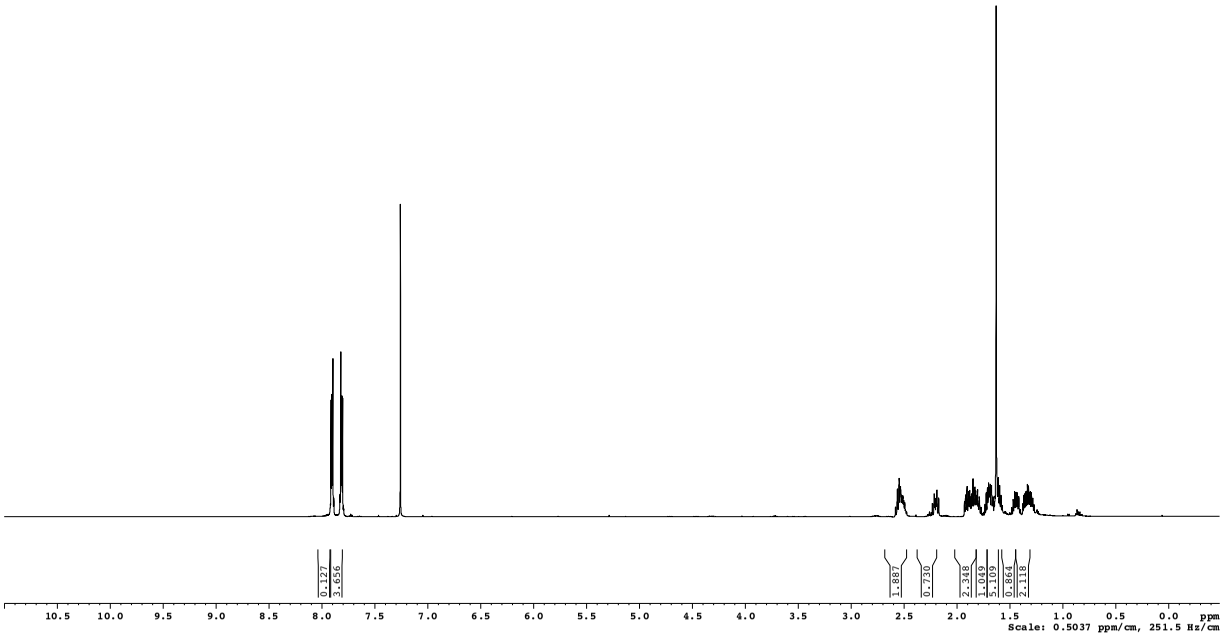



```
Current Data Parameters
NAME          GL3-11-2-23
EXPNO                   2
PROCNO                  1

F2 - Acquisition Parameters
Date_           20130824
Time              17.26
INSTRUM           cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG   SpinEchopg30qp.prd
TD                65536
SOLVENT           CDCl3
NS                  416
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 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 Hz
SPOFF2    0 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 %
GPX2      0 %
GPY1      0 %
GPY2      0 %
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                5.00 Hz
GB        0
PC                2.00
```

1H spectrum



1.37

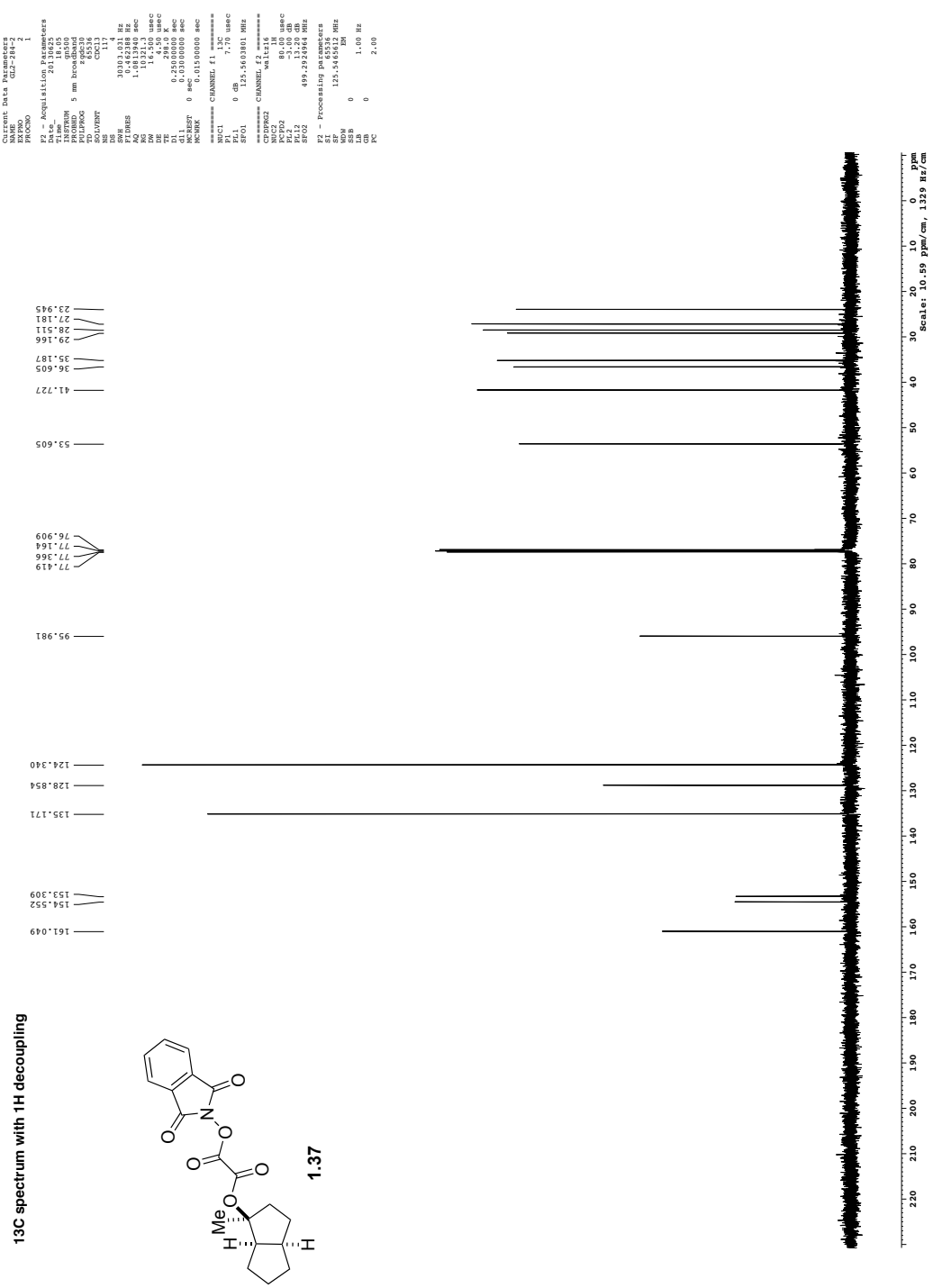


Current Data Parameters
NAME GL2-284-2
EXPNO 1
PROCNO 1

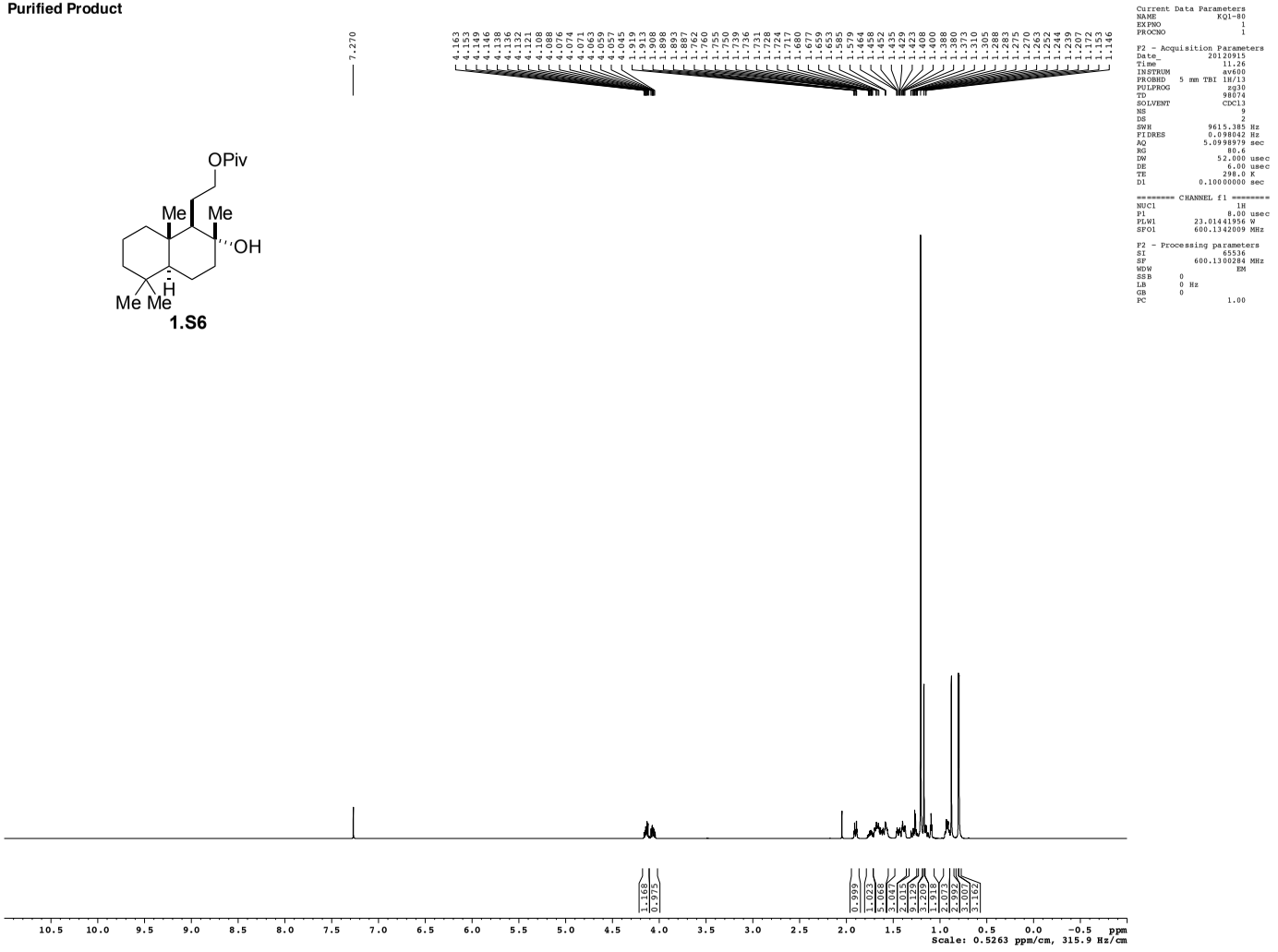
F2 - Acquisition Parameters
Date_ 20130625
Time 18.04
INSTRUM qn500
PROBHD 5 mm broadband
PULPROG zg30
TD 81728
SOLVENT CDCl3T
NS 8
DS 2
SWH 8012.820 Hz
FIDRES 0.098043 Hz
AQ 5.0998774 sec
RG 71.8
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0 sec
MCWRK 0.01500000 sec

======== CHANNEL f1 ========
NUC1 1H
P1 12.20 usec
PL1 -5.00 dB
SFO1 499.2934950 MHz

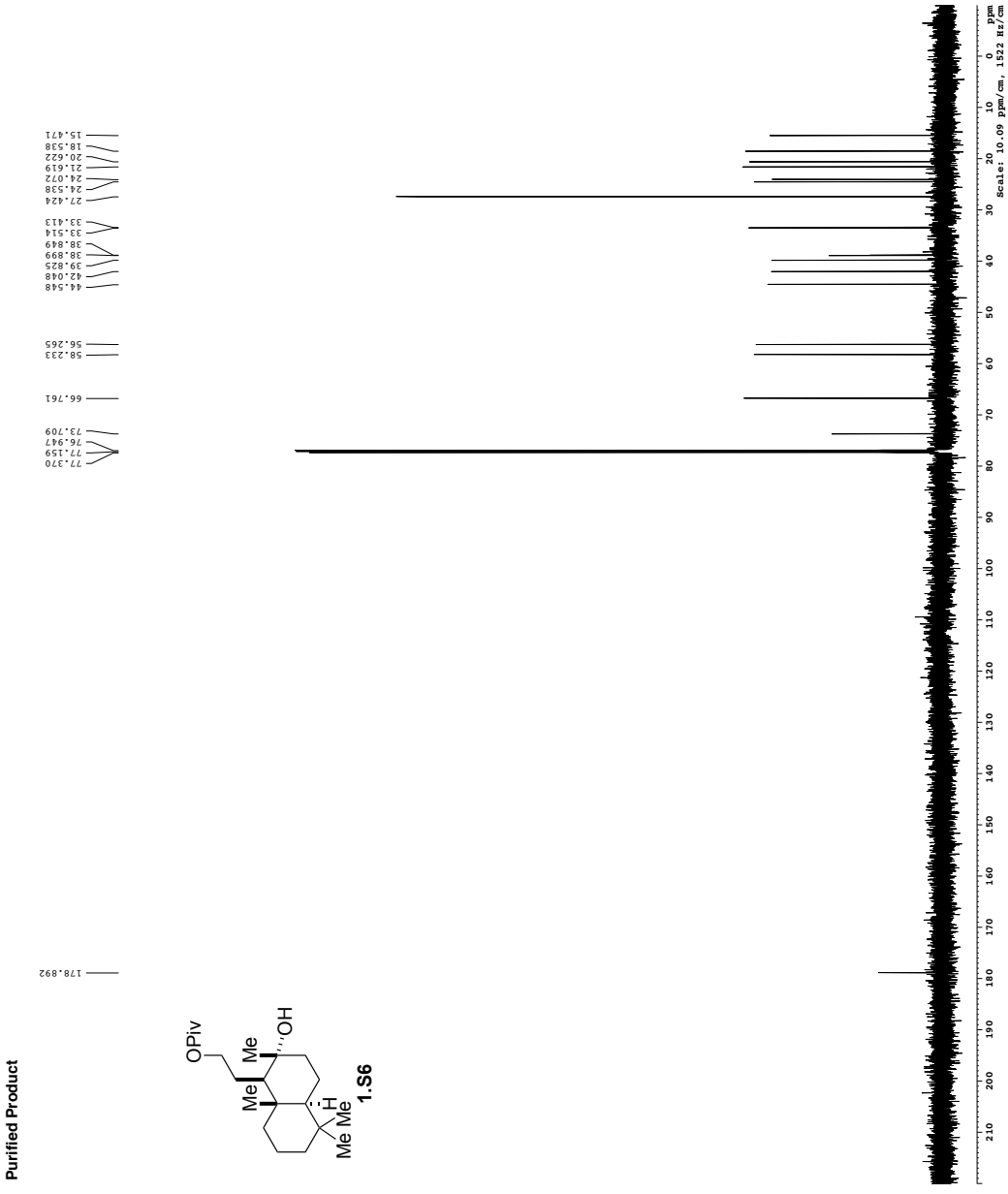
F2 - Processing parameters
SI 65536
SF 499.2900290 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00


13C spectrum with 1H decoupling
1.37
Me
H
H
O
N
Scale: 10.59 ppm/cm, 1329 Hz/cm
ppm

Purified Product

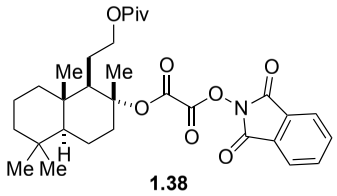


Purified Product

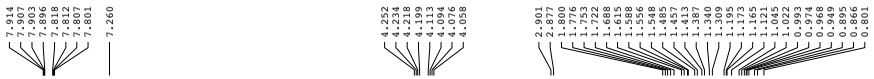


1.S6

Crude Product



1.38

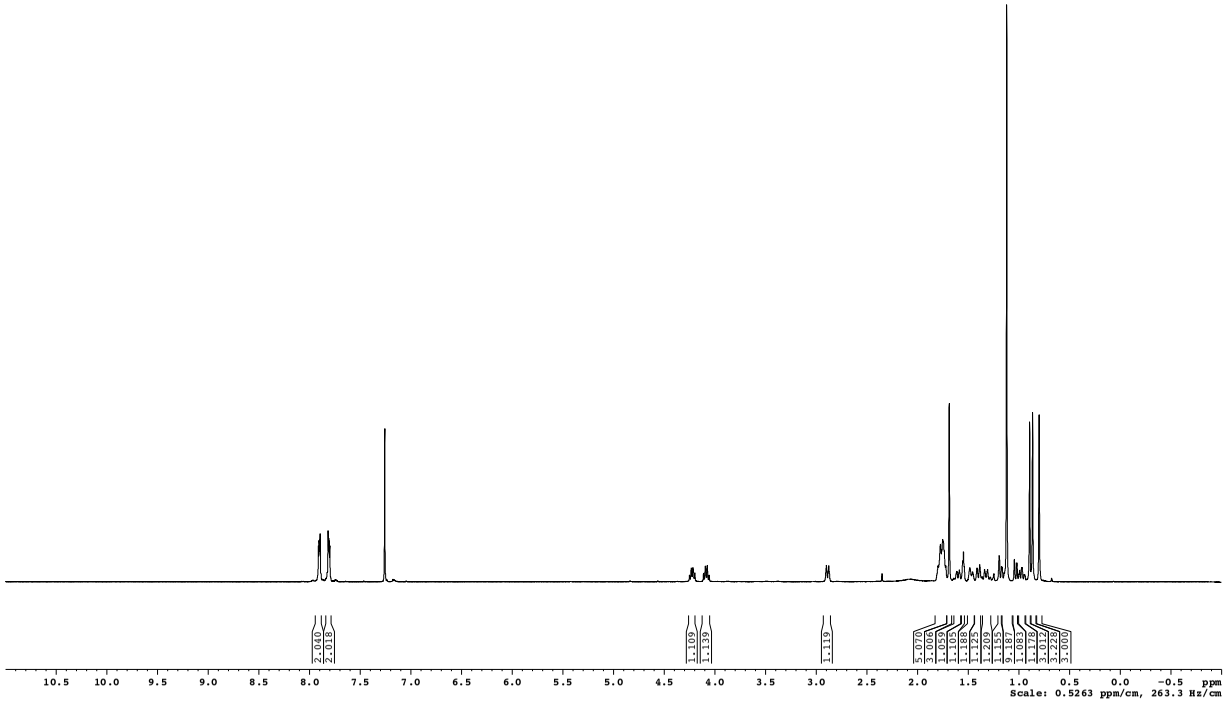


Current Data Parameters
NAME KQ2-128
EXPNO 3
PROCNO 1

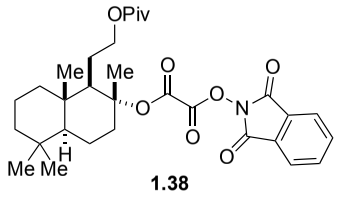
F2 - Acquisition Parameters
Date_ 20130623
Time 14.13
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 81728
SOLVENT CDCl3
NS 7
DS 0
SWH 8012.820 Hz
FIDRES 0.098043 Hz
AQ 5.0998774 sec
RG 5.7
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0 sec
MCWRK 0.01500000 sec

======== CHANNEL f1 ========
NUC1 1H
P1 7.50 usec
PL1 1.60 dB
SFO1 500.2235015 MHz

F2 - Processing parameters
SI 65536
SF 500.2200299 MHz
WDW EM
SSB 0
LB 0 Hz
GB 0
PC 4.00



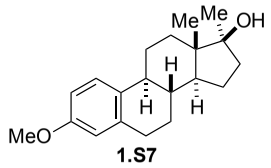
Crude Product



1.38


```
Current Data Parameters
NAME                  KQ2-128
EXPNO                       4
PROCNO                      1

F2 - Acquisition Parameters
Date_              20130623
Time                    14.15
INSTRUM                 cryo500
PROBHD     5 mm CPTCI 1H-
PULPROG    SpinEchopg30gp.prd
TD                      65536
SOLVENT                 CDCl3
NS                        291
DS                          0
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 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               125.7925480 MHz
SP1                      3.20 dB
SP2                      3.20 dB
SPNAM1     Crp60,0.5,20.1
SPNAM2       Crp60comp.4
SPOFF1     0 Hz
SPOFF2     0 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 %
GPX2       0 %
GPY1       0 %
GPY2       0 %
GPZ1                    30.00 %
GPZ2                    50.00 %
p15                    500.00 usec
p16                   1000.00 usec

F2 - Processing parameters
SI                        65536
SF                 125.7804073 MHz
WDW                          EM
SSB        0
LB         0 Hz
GB         0
PC                       2.00
```

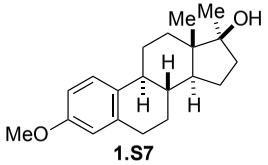
Purified Product



1.S7


```
Current Data Parameters
NAME                  KQ2-144
EXPNO                       2
PROCNO                      1

F2 - Acquisition Parameters
Date_              20130711
Time                   11.01
INSTRUM                av600
PROBHD    5 mm TBI 1H/13
PULPROG                zg30
TD                     98074
SOLVENT                CDCl3
NS                        10
DS                         0
SWH                9615.385 Hz
FIDRES             0.098042 Hz
AQ                 5.0998979 sec
RG                       456
DW                    52.000 usec
DE                     6.00 usec
TE                    298.0 K
D1                 0.10000000 sec
TD0                         1

======== CHANNEL f1 ========
NUC1                       1H
P1                      8.00 usec
PLW1              23.01441956 W
SFO1             600.1342009 MHz

F2 - Processing parameters
SI                       65536
SF                600.1300348 MHz
WDW                         EM
SSB                0
LB                 0 Hz
GB                 0
PC                      1.00
```

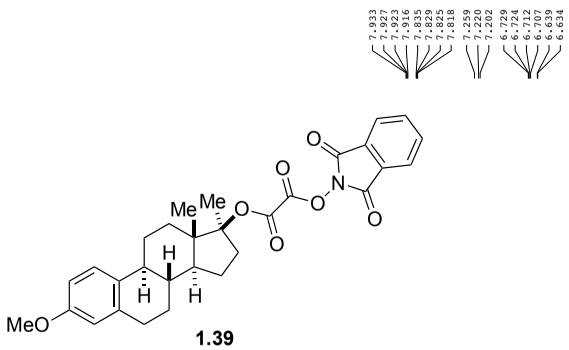
Purified Product



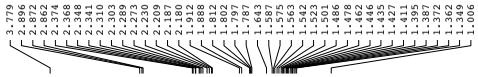
1.S7


```
Current Data Parameters
NAME                  KQ2-144
EXPNO                       3
PROCNO                      1

F2 - Acquisition Parameters
Date_              20130711
Time                   11.04
INSTRUM                av600
PROBHD   5 mm TBI 1H/13
PULPROG             zgdc30
TD                      65536
SOLVENT                 CDCl3
NS                        707
DS                          0
SWH                36231.883 Hz
FIDRES              0.552855 Hz
AQ                  0.9044468 sec
RG                       90.5
DW                     13.800 usec
DE                      6.00 usec
TE                     298.0 K
D1                 0.40000001 sec
D11                0.03000000 sec
TD0                         1

======== CHANNEL f1 ========
NUC1                      13C
P1                      15.00 usec
PLW1             107.15190125 W
SFO1             150.9194080 MHz

======== CHANNEL f2 ========
CPDPRG2                waltz16
NUC2                       1H
PCPD2                   70.00 usec
PLW2             0 W
PLW12            0.30199519 W
SFO2             600.1330010 MHz

F2 - Processing parameters
SI                      65536
SF                150.9027971 MHz
WDW                        EM
SSB          0
LB                      3.00 Hz
GB           0
PC                      1.00
```

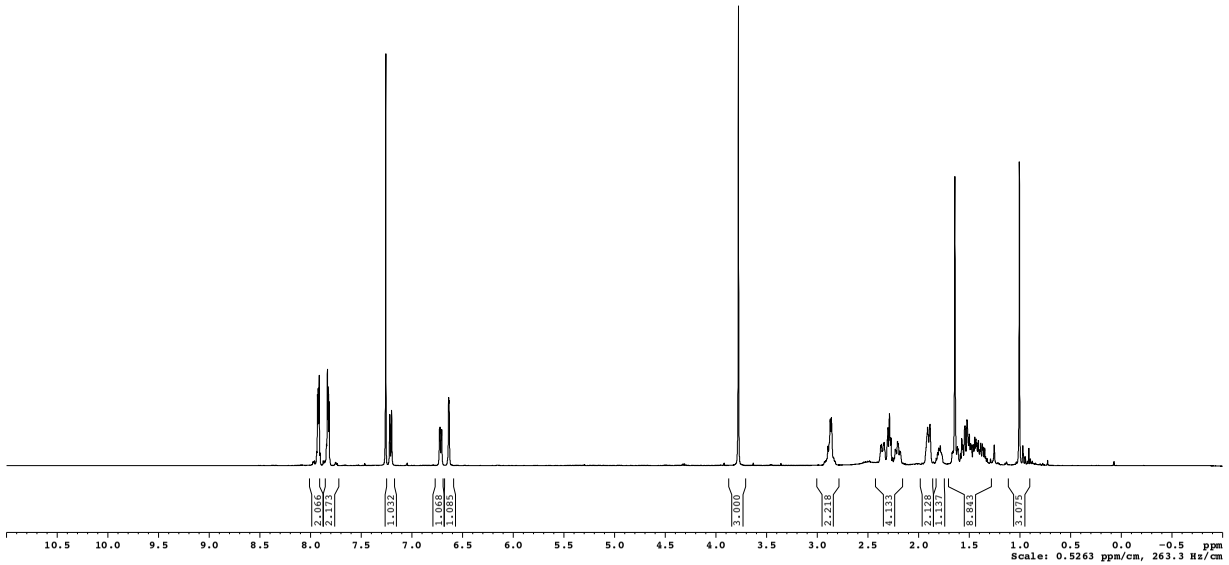
Crude Product



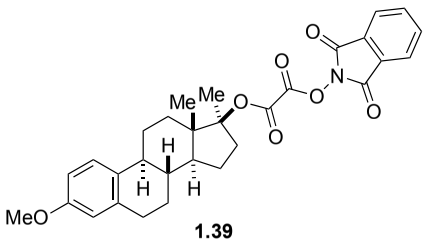
1.39




```
Current Data Parameters
NAME                  KQ2-146
EXPNO                       3
PROCNO                      1

F2 - Acquisition Parameters
Date_               20130711
Time                   19.35
INSTRUM              cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG                zg30
TD                    81728
SOLVENT               CDCl3
NS                       16
DS                        0
SWH                8012.820 Hz
FIDRES             0.098043 Hz
AQ                 5.0998774 sec
RG                      12.7
DW                   62.400 usec
DE                    6.00 usec
TE                   298.0 K
D1                2.00000000 sec
MCREST    0 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             500.2200318 MHz
WDW                         EM
SSB       0
LB        0 Hz
GB        0
PC                    4.00
```

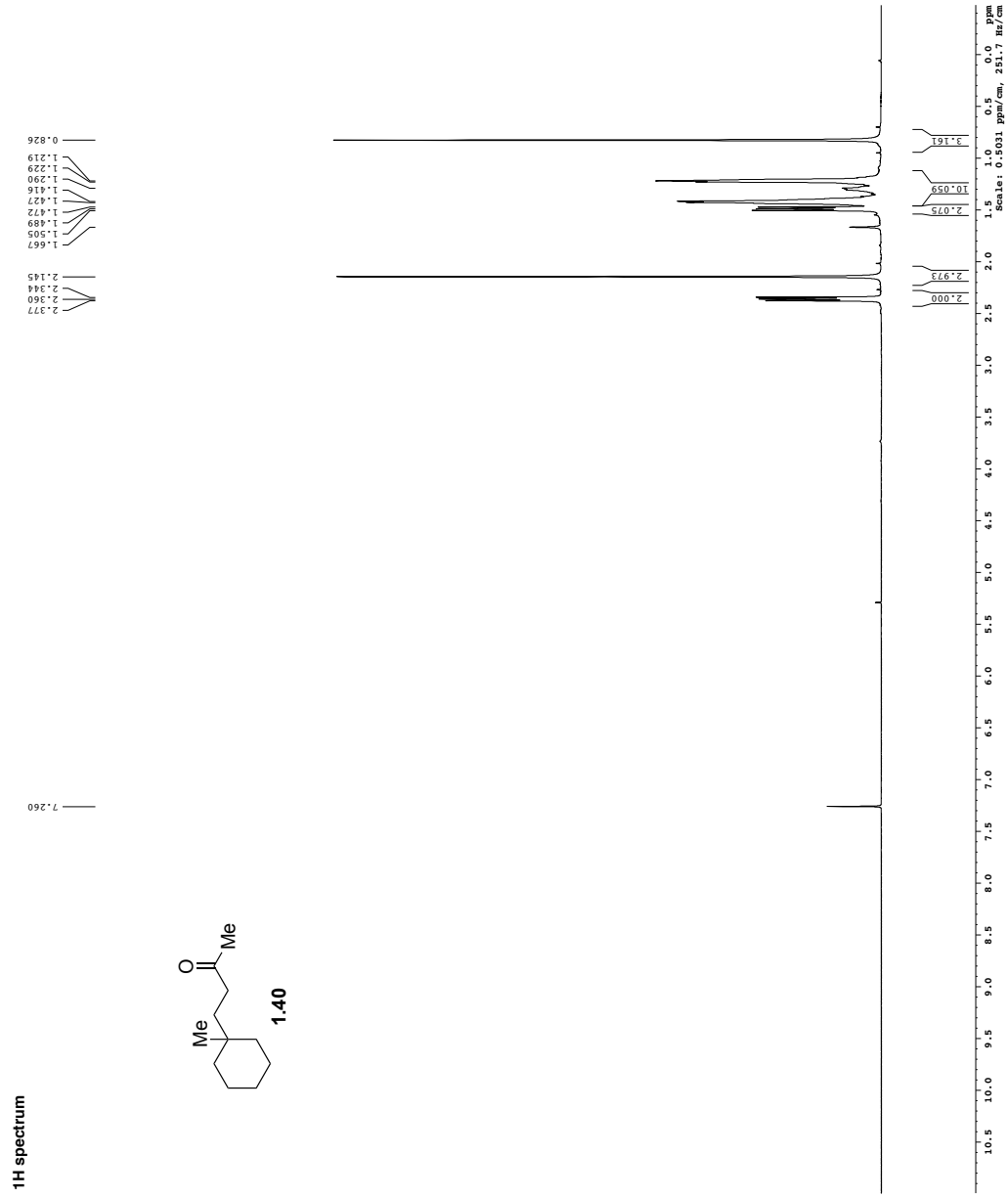


Crude Product

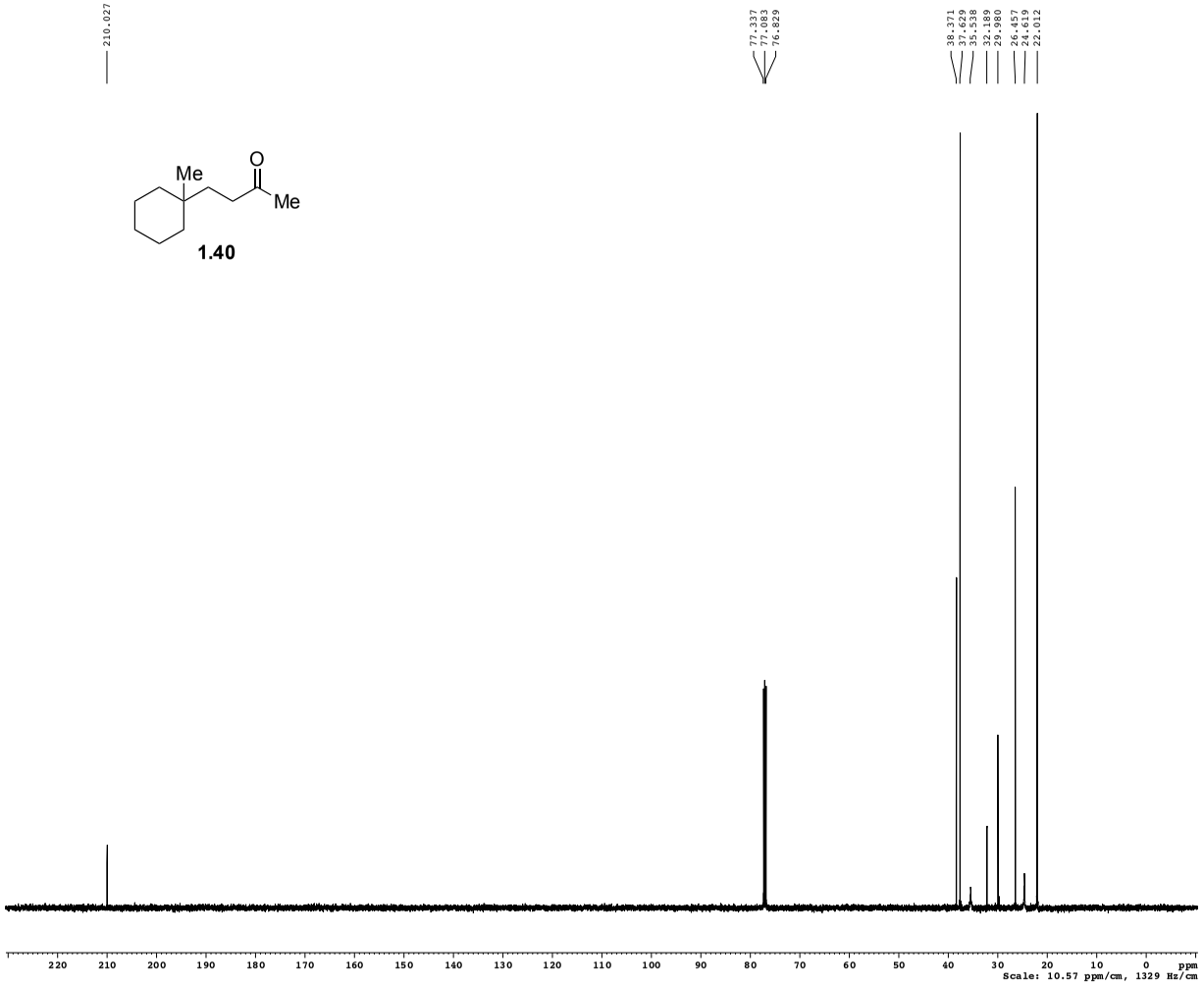


1.39


```
Current Data Parameters
NAME              KQ2-146
EXPNO                   4
PROCNO                  1

F2 - Acquisition Parameters
Date_           20130711
Time              19.30
INSTRUM         cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD                65536
SOLVENT           CDCl3
NS                  471
DS                    0
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 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 Hz
SPOFF2   0 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 %
GPX2      0 %
GPY1      0 %
GPY2      0 %
GPZ1               30.00 %
GPZ2               50.00 %
p15               500.00 usec
p16              1000.00 usec

F2 - Processing parameters
SI                 65536
SF           125.7804097 MHz
WDW                   EM
SSB       0
LB                 1.00 Hz
GB        0
PC                 2.00
```

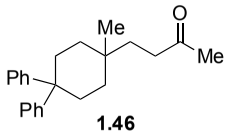

1H spectrum
Me
O
Me
Me
1.40
7.260
2.377
2.360
2.344
2.145
1.667
1.505
1.489
1.472
1.427
1.416
1.290
1.229
1.219
0.826
3.161
10.059
2.075
2.973
2.000
ppm
Scale: 0.5031 ppm/cm, 251.7 Hz/cm

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



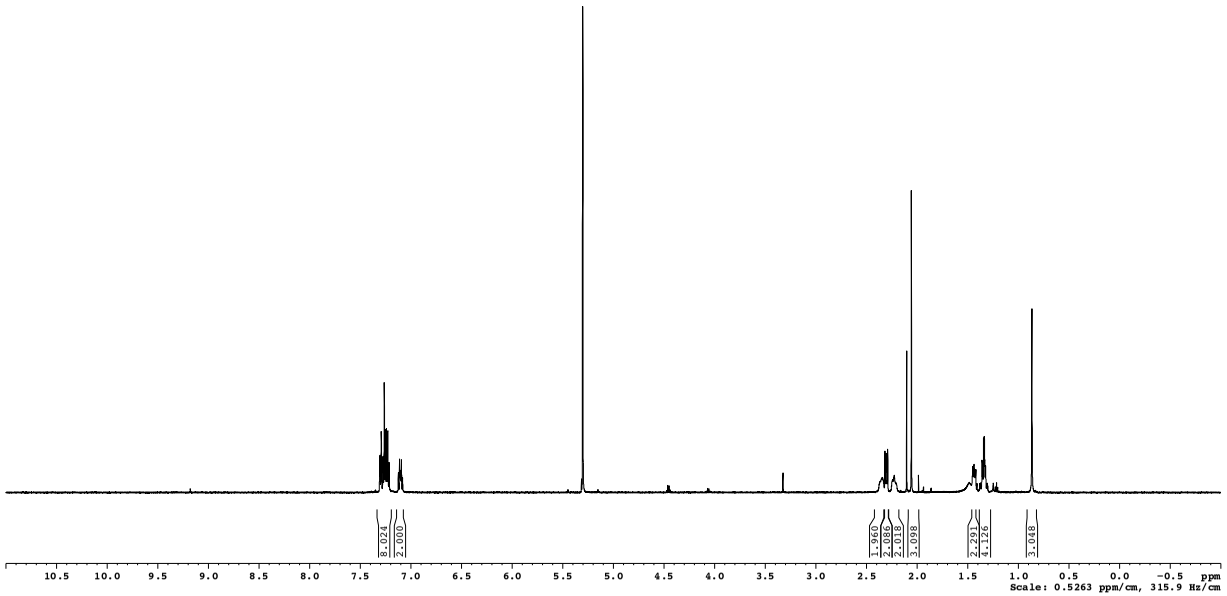

```
Current Data Parameters
NAME          GL2-244-3-3
EXPNO                   2
PROCNO                  1

F2 - Acquisition Parameters
Date_          20130612
Time               9.25
INSTRUM          cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD               65536
SOLVENT          CDCl3
NS                 180
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 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 Hz
SPOFF2   0 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 %
GPX2     0 %
GPY1     0 %
GPY2     0 %
GPZ1            30.00 %
GPZ2            50.00 %
p15           500.00 usec
p16          1000.00 usec

F2 - Processing parameters
SI               65536
SF         125.7804190 MHz
WDW                EM
SSB      0
LB              1.00 Hz
GB       0
PC              2.00
```

Purified Product

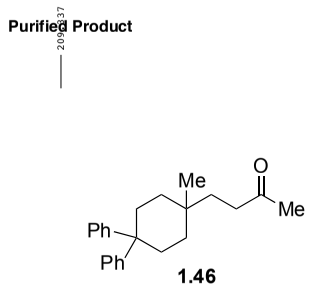


1.46


```
Current Data Parameters
NAME                  KQ2-120
EXPNO                       2
PROCNO                      1

F2 - Acquisition Parameters
Date_              20130614
Time                  16.42
INSTRUM              av600
PROBHD    5 mm TBI 1H/13
PULPROG               zg30
TD                    98074
SOLVENT             CD2Cl2
NS                        38
DS                         0
SWH                9615.385 Hz
FIDRES             0.098042 Hz
AQ                 5.0998979 sec
RG                      2050
DW                   52.000 usec
DE                    6.00 usec
TE                   298.1 K
D1                0.10000000 sec
TD0                         1

======== CHANNEL f1 ========
NUC1                      1H
P1                     8.00 usec
PLW1             23.01441956 W
SFO1             600.1342009 MHz

F2 - Processing parameters
SI                        65536
SF               600.1300355 MHz
WDW                         EM
SSB          0
LB           0 Hz
GB           0
PC                        1.00
```

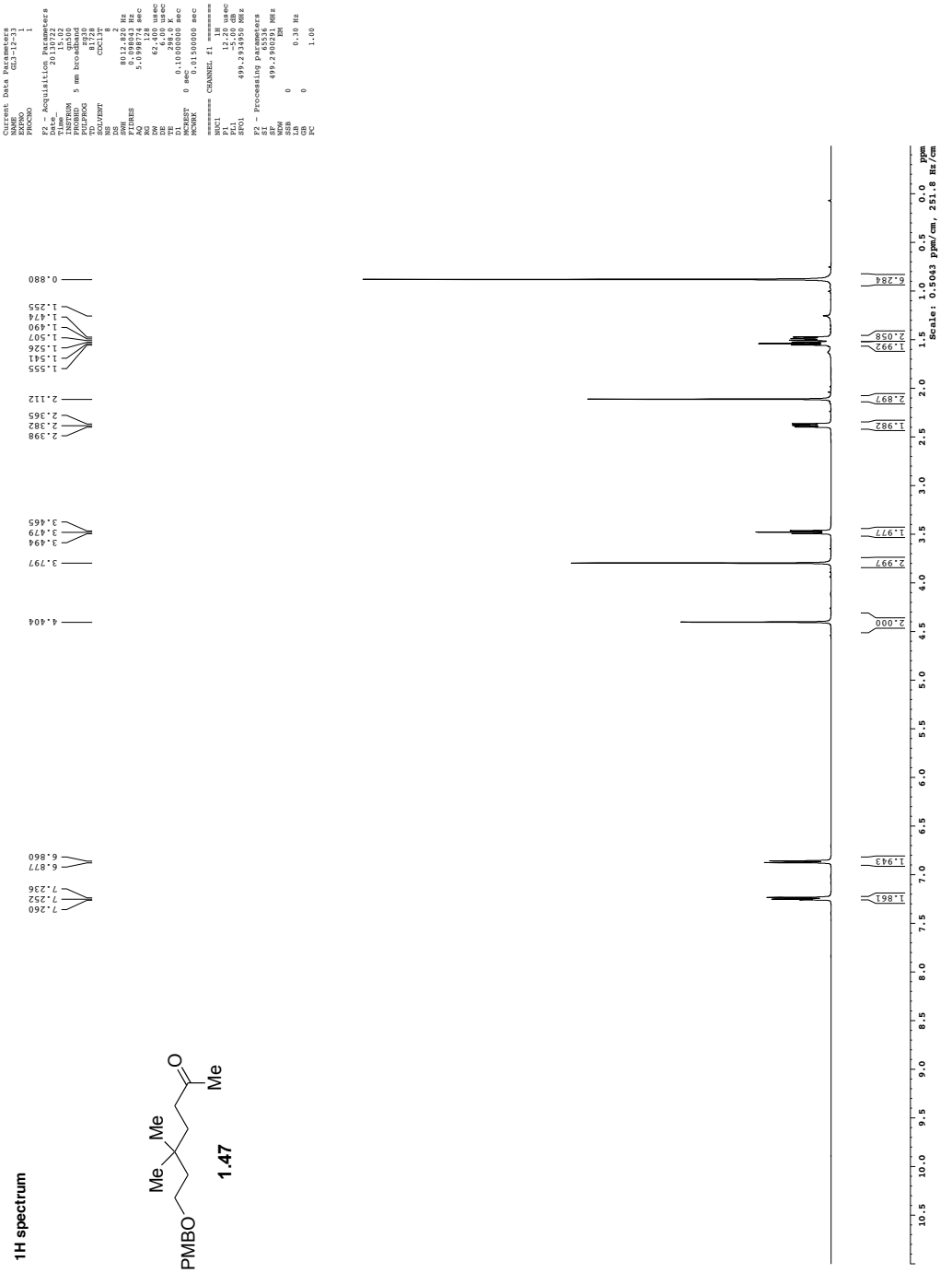


Purified Product



1.46

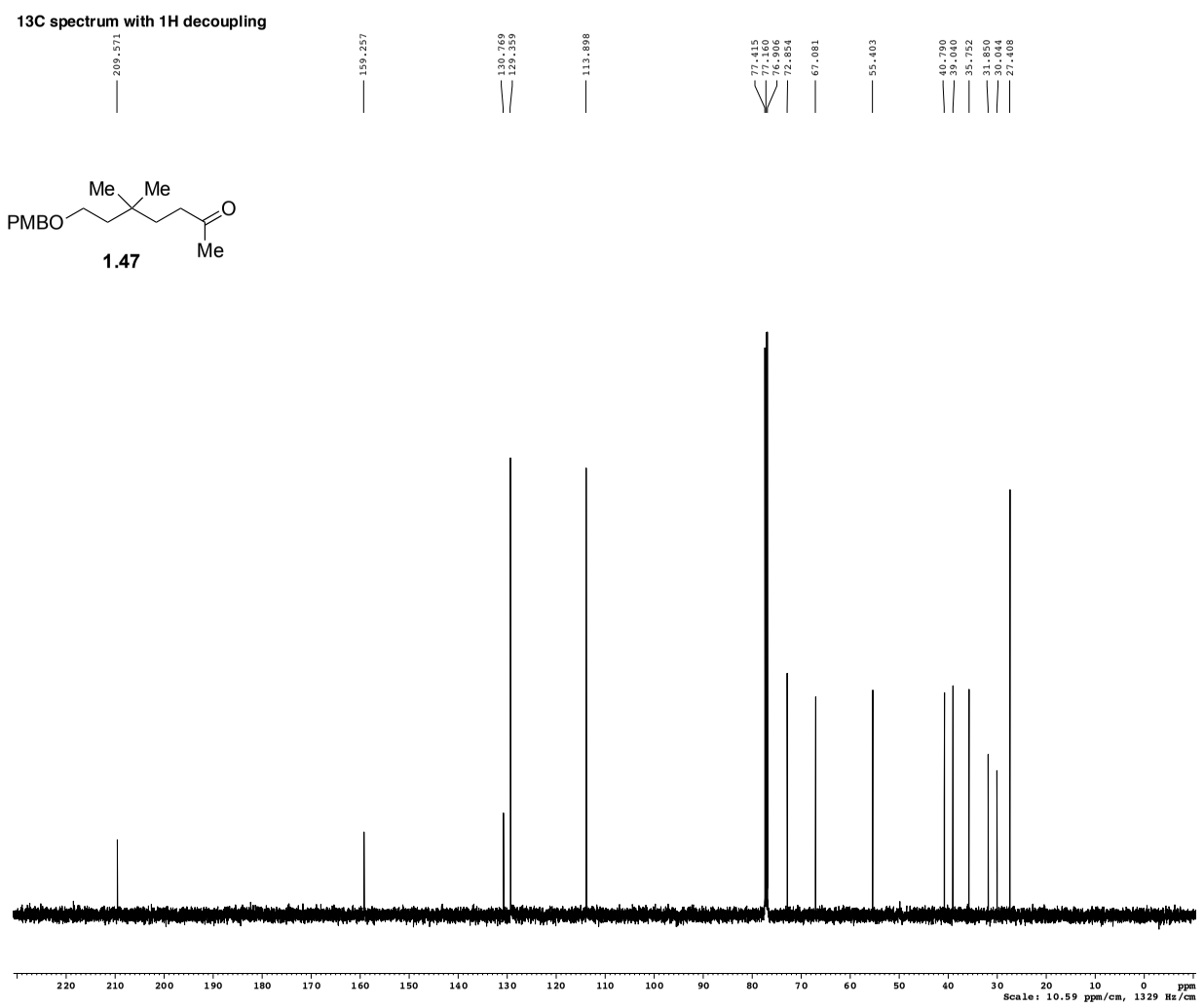

```
Current Data Parameters
NAME              KQ2-120
EXPNO                   8
PROCNO                  1

F2 - Acquisition Parameters
Date_           20130616
Time              17.43
INSTRUM          cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG   SpinEchopg30gp.prd
TD                65536
SOLVENT            CDCl3
NS                   798
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 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 Hz
SPOFF2    0 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 %
GPX2      0 %
GPY1      0 %
GPY2      0 %
GPZ1              30.00 %
GPZ2              50.00 %
p15              500.00 usec
p16             1000.00 usec

F2 - Processing parameters
SI                65536
SF           125.7803730 MHz
WDW                  EM
SSB       0
LB                 5.00 Hz
GB        0
PC                 2.00
```


1H spectrum
Current Data Parameters
NAME cds_12-2-13
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20131222
Time 15.02
INSTRUM spt300
PROBHD 5 mm broadband
PULPROG zg30
TD 81728
SOLVENT CDCl3
NS 8
DS 2
SWH 8012.820 Hz
FIDRES 0.098063 Hz
AQ 5.0999774 sec
RG 128
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0 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 499.2900251 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
0.880
1.255
1.474
1.490
1.507
1.526
1.541
1.555
2.112
2.365
2.382
2.398
3.465
3.479
3.494
3.797
4.404
6.860
6.877
7.236
7.252
7.260
1.861
1.943
2.000
2.997
1.977
1.982
2.897
1.992
2.058
6.284
ppm
Scale: 0.5043 ppm/cm, 251.8 Hz/cm

Me
Me
O
Me
PMBO

1.47

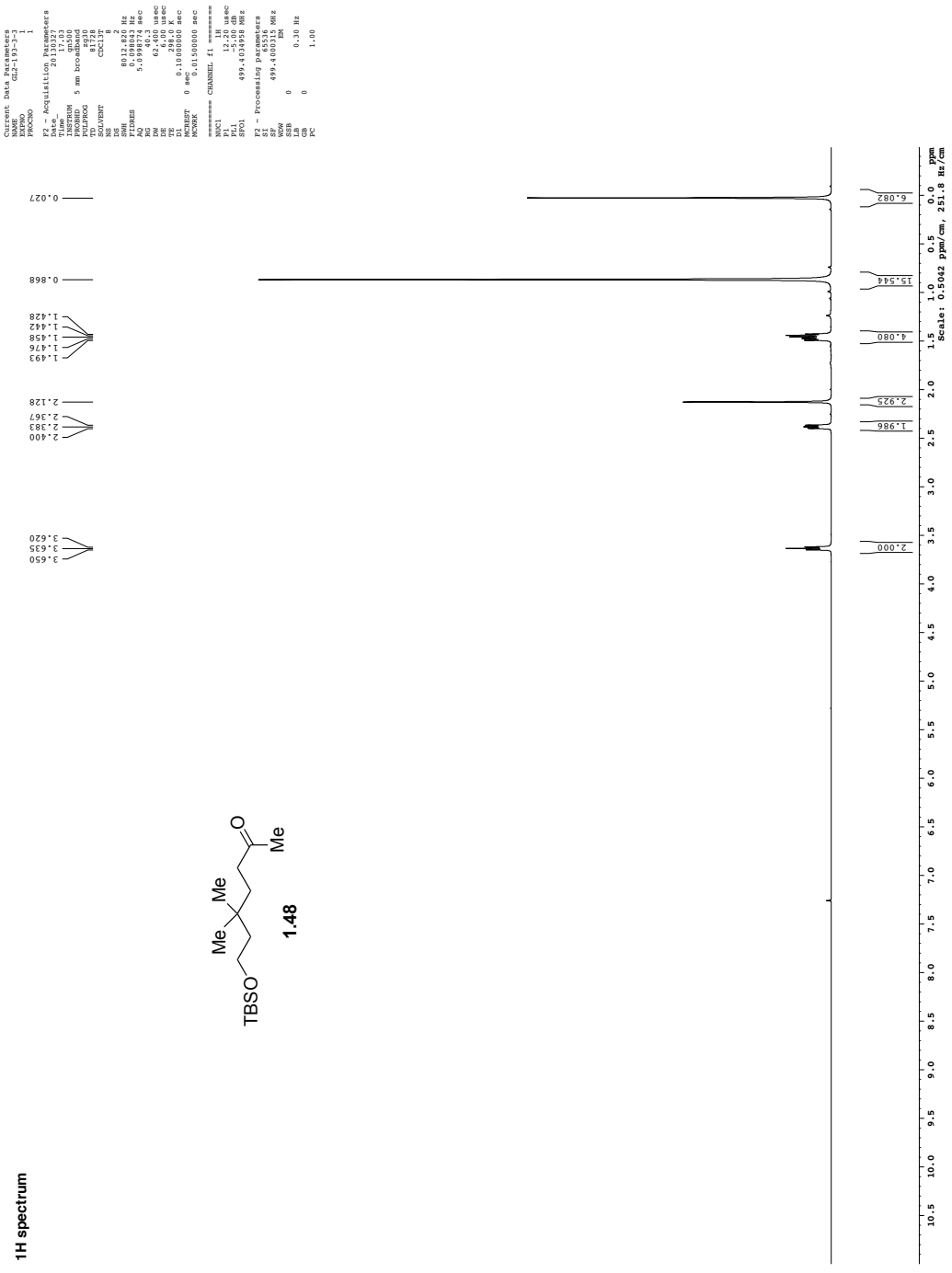
13C spectrum with 1H decoupling



1.47

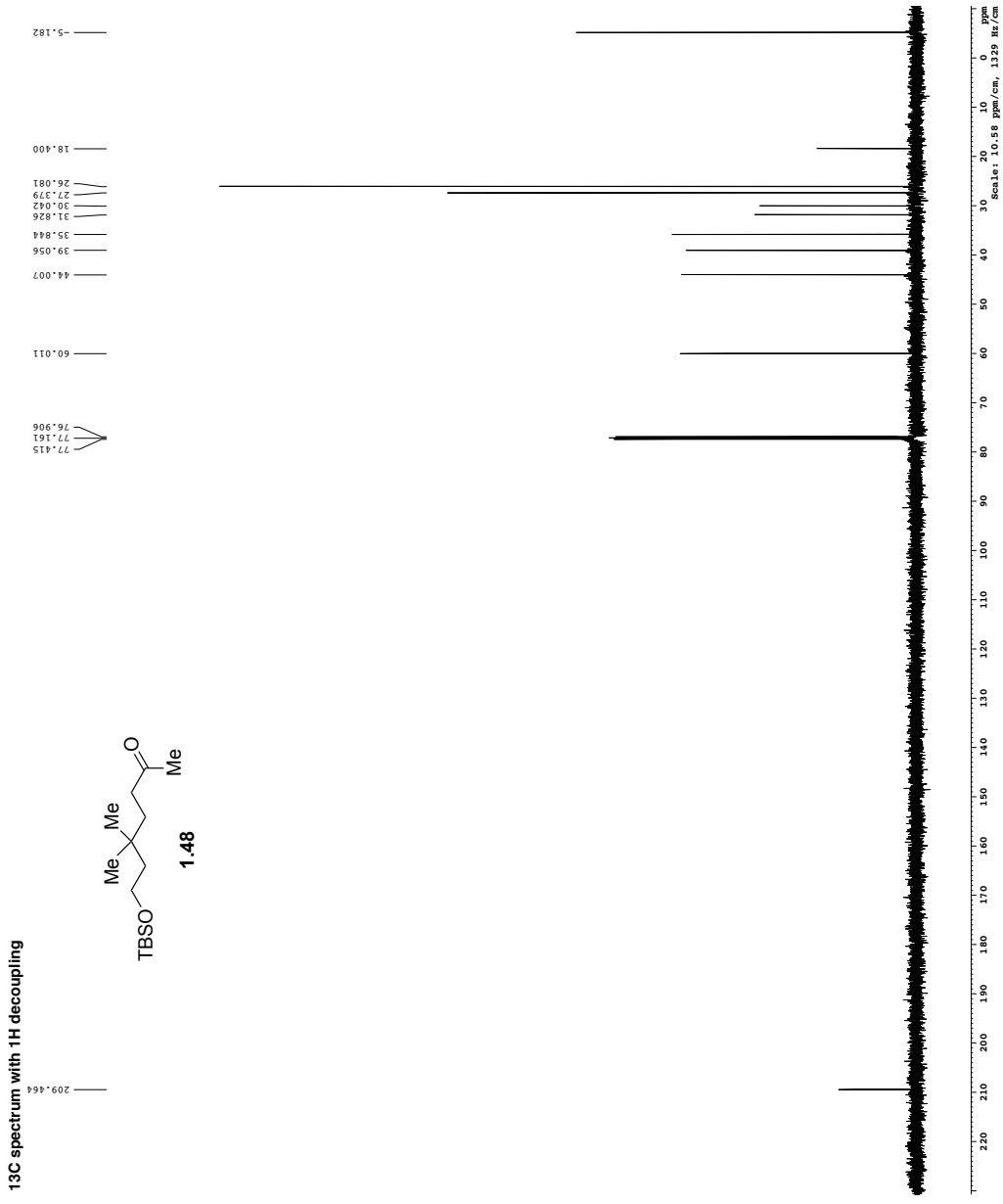
```
Current Data Parameters
NAME              GL3-12-33
EXPNO                     2
PROCNO                    1

F2 - Acquisition Parameters
Date_           20130722
Time                15.03
INSTRUM             qn500
PROBHD   5 mm broadband
PULPROG           zgdc30
TD                 65536
SOLVENT            CDCl3
NS                   265
DS                     4
SWH             30303.031 Hz
FIDRES          0.462388 Hz
AQ              1.0813940 sec
RG                4597.6
DW                16.500 usec
DE                 4.50 usec
TE                298.0 K
D1              0.25000000 sec
d11             0.03000000 sec
MCREST    0 sec
MCWRK           0.01500000 sec

======== CHANNEL f1 ========
NUC1                  13C
P1                  7.70 usec
PL1        0 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            125.5465590 MHz
WDW                   EM
SSB        0
LB                 1.00 Hz
GB         0
PC                 2.00
```

1H spectrum

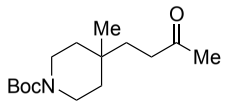


1.48

13C spectrum with 1H decoupling

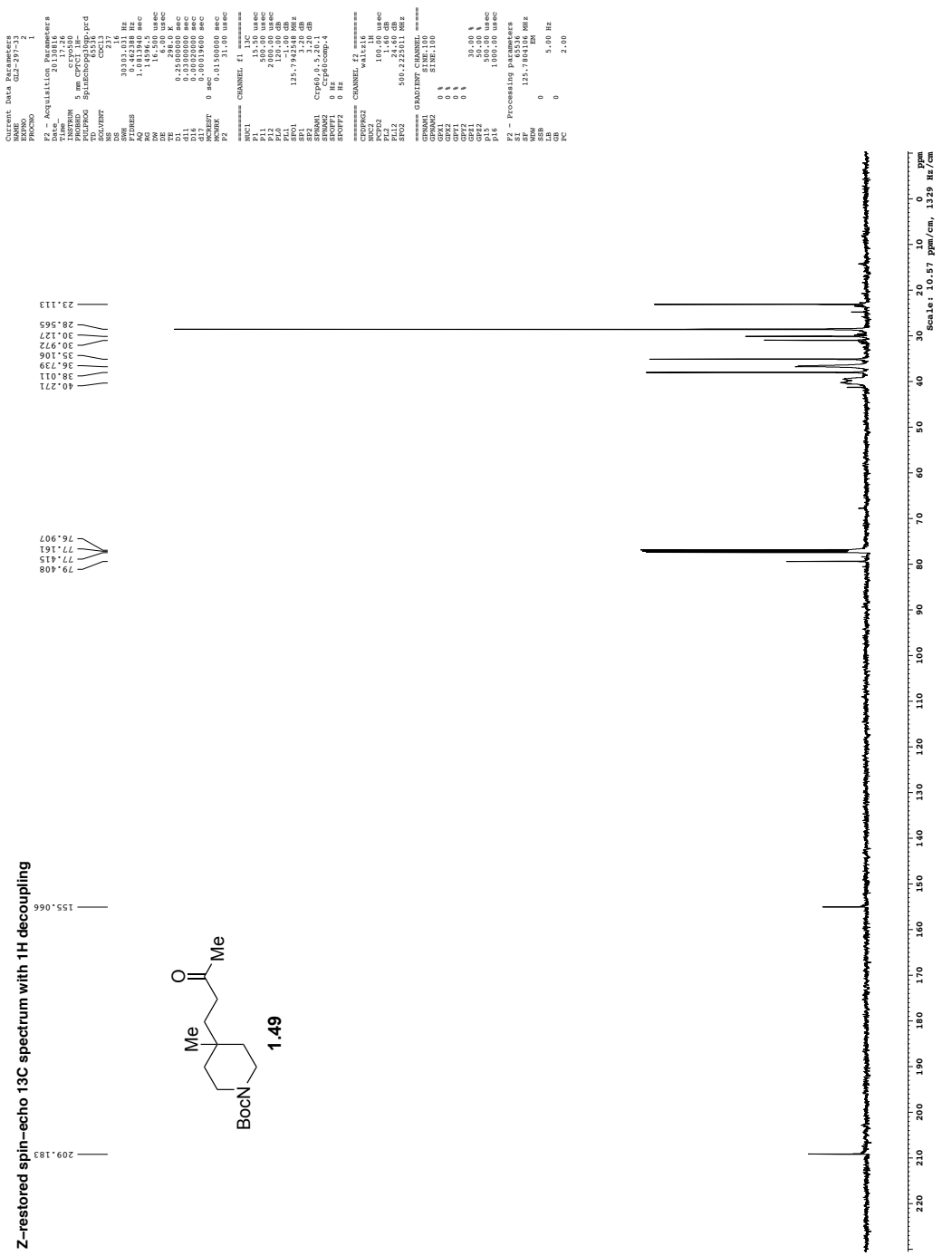


1H spectrum

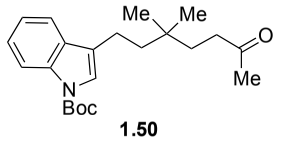


1.49


```
Current Data Parameters
NAME                GL2-297-33
EXPNO                        1
PROCNO                       1

F2 - Acquisition Parameters
Date_              20130816
Time                   17.22
INSTRUM              cryo500
PROBHD    5 mm CPTCI 1H-
PULPROG                 zg30
TD                     81728
SOLVENT               CDCl3T
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 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               500.2200314 MHz
WDW                        EM
SSB       0
LB                      0.30 Hz
GB        0
PC                      4.00
```


Z-restored spin-echo 13C spectrum with 1H decoupling
209.183
155.066
79.408
77.415
77.161
76.907
40.271
38.011
36.739
35.106
30.972
30.127
28.565
23.113
Me
O
Me
Me
BocN
1.49

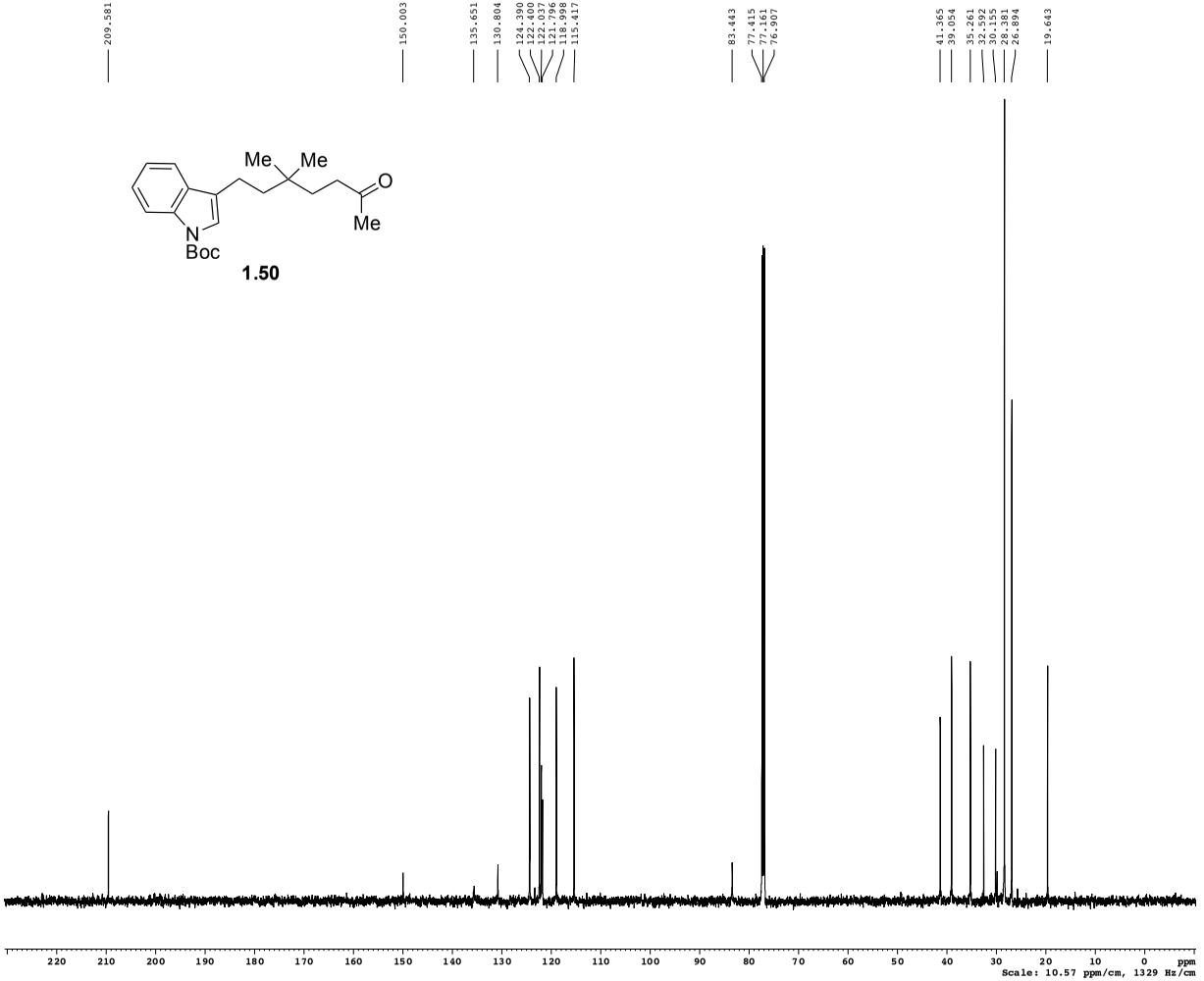
1H spectrum



1.50

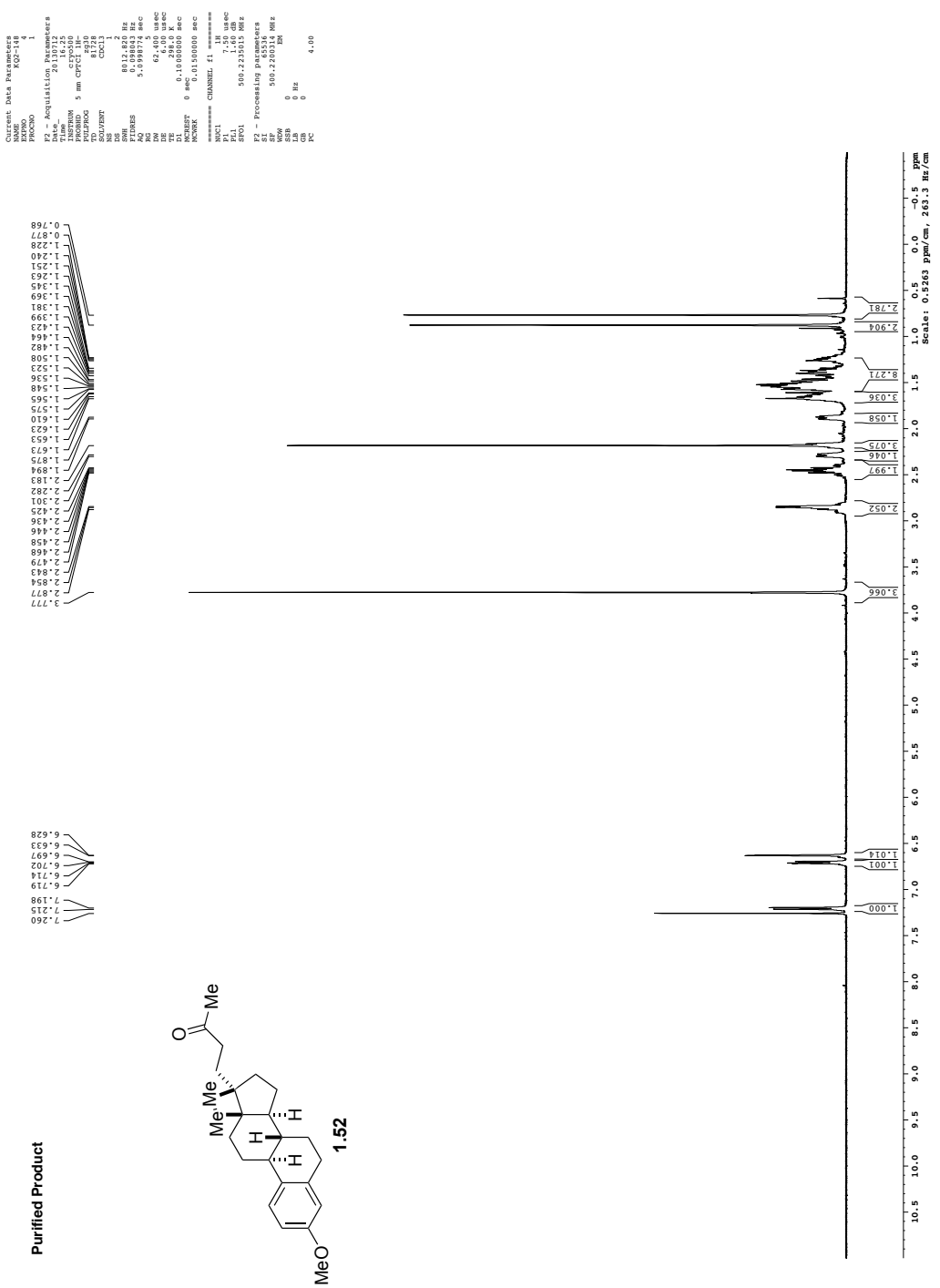

```
Current Data Parameters
NAME            GLJ-13-33r
EXPNO                    1
PROCNO                   1

F2 - Acquisition Parameters
Date_             20130814
Time                 12.22
INSTRUM           cryo500
PROBHD    5 mm CPTCI 1H-
PULPROG              zg30
TD                  81728
SOLVENT             CDCl3T
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 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           500.2200315 MHz
WDW                    EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 4.00
```

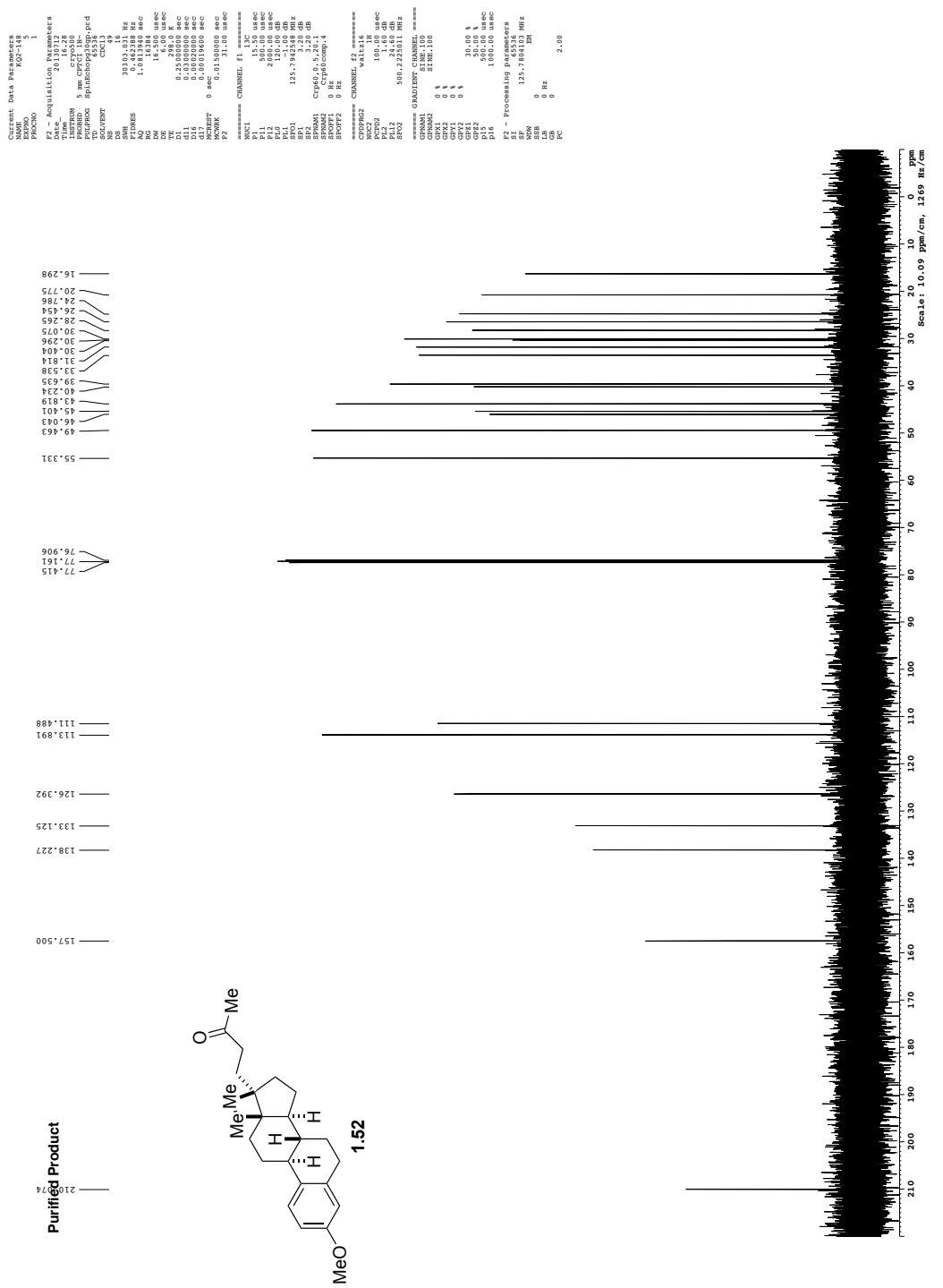
Z–restored spin–echo 13C spectrum with 1H decoupling



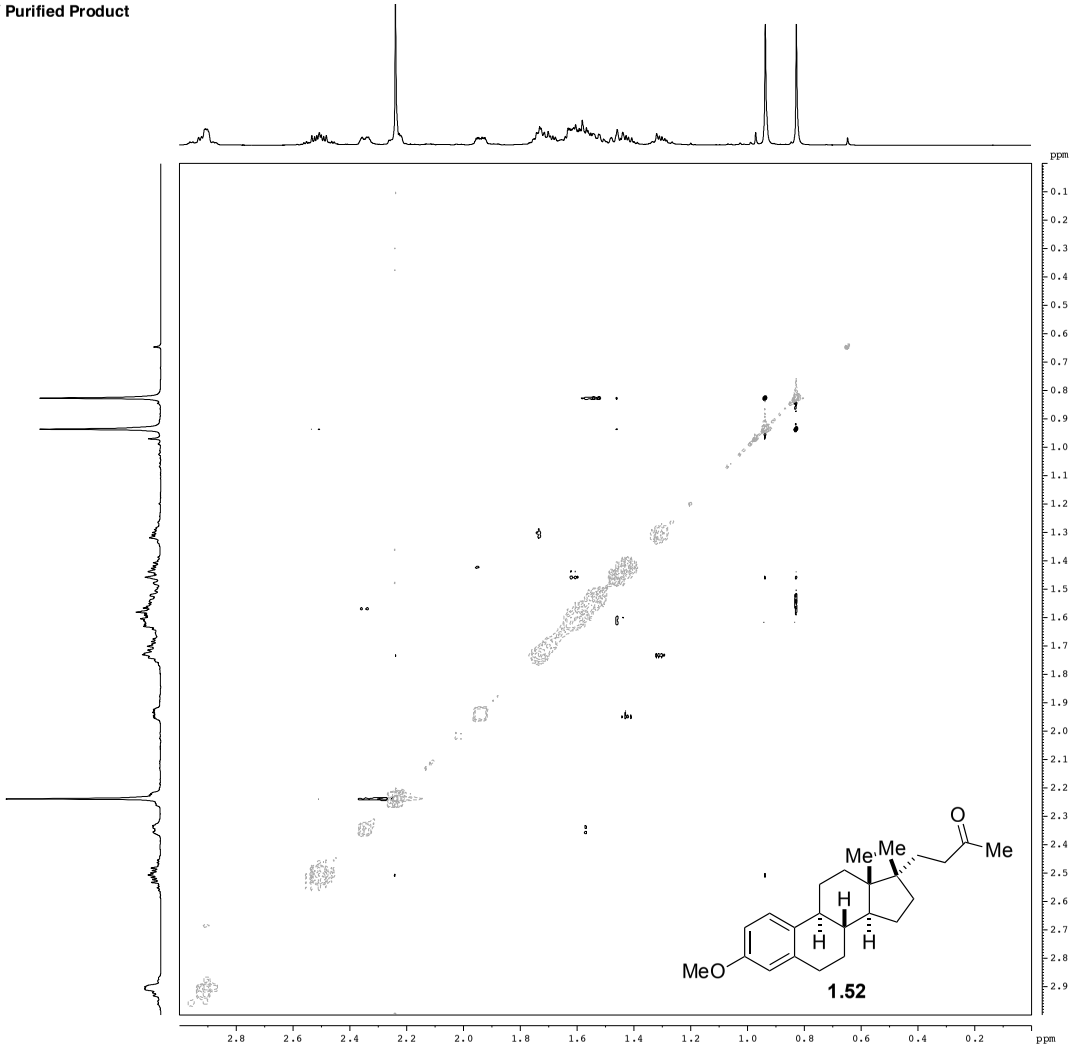
1.50

```
Current Data Parameters
NAME                 GL3-13-33r
EXPNO                         2
PROCNO                        1

F2 - Acquisition Parameters
Date_              20130814
Time                   12.23
INSTRUM              cryo500
PROBHD    5 mm CPTCI 1H-
PULPROG   SpinEchopg30gp.prd
TD                    65536
SOLVENT               CDCl3
NS                      293
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 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 Hz
SPOFF2    0 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 %
GPX2      0 %
GPY1      0 %
GPY2      0 %
GPZ1                   30.00 %
GPZ2                   50.00 %
p15                   500.00 usec
p16                  1000.00 usec

F2 - Processing parameters
SI                    65536
SF             125.7804093 MHz
WDW                      EM
SSB       0
LB                      3.00 Hz
GB        0
PC                      2.00
```


Purified Product
1.52
Me
O
Me
Me
H
H
H
MeO
Current Data Parameters
NAME KQO-148
EXPNO 4
PROCNO 1
F2 - Acquisition Parameters
Date_ 20130712
Time 16.25
INSTRUM spect
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 81920
SOLVENT CDCl3
NS 1
DS 2
SWH 8012.821 Hz
FIDRES 0.097843 Hz
AQ 5.1099774 sec
RG 5
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
D12 0.00002000 sec
MCREST 0.01500000 sec
MCWRK
======== CHANNEL f1 ========
NUC1 1H
P1 7.10 usec
PL1 1.40 dB
SFO1 500.2235615 MHz
F2 - Processing parameters
SI 65536
SF 500.2200314 MHz
WDW EM
SSB 0
LB 0 Hz
GB 0
PC 4.00
7.260
7.215
7.198
6.719
6.714
6.697
6.702
6.633
6.628
3.777
2.877
2.854
2.843
2.479
2.468
2.458
2.446
2.436
2.425
2.301
2.282
2.183
1.894
1.875
1.653
1.623
1.610
1.575
1.565
1.548
1.536
1.523
1.508
1.482
1.464
1.423
1.399
1.381
1.369
1.345
1.263
1.251
1.240
1.228
0.877
0.768
1.000
1.001
1.014
2.052
1.997
1.046
3.075
1.058
3.036
8.271
2.904
2.781
3.066
10.5
10.0
9.5
9.0
8.5
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
-0.5
ppm
Scale: 0.5263 ppm/cm, 265.3 Hz/cm


Purified Product
1.52
MeO
Me
Me
H
H
H
O
Me
Scale: 10.09 ppm/cm, 1269 Hz/cm
ppm

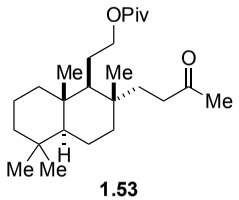
NOESY Purified Product



1.52

```
Current Data Parameters
NAME                  KQ2-148
EXPNO                      11
PROCNO                      1

F2 - Acquisition Parameters
Date_               20130826
Time                   17.03
INSTRUM                av600
PROBHD    5 mm TBI 1H/13
PULPROG          noesygpph
TD                      2048
SOLVENT                CDCl3
NS                         2
DS                        16
SWH                 2400.768 Hz
FIDRES              1.172250 Hz
AQ                  0.4265801 sec
RG                        203
DW                  208.267 usec
DE                    8.38 usec
TE                    298.1 K
D0                  0.00019808 sec
D1                  2.00000000 sec
D8                  1.00000000 sec
D16                 0.00020000 sec
IN0                 0.00041655 sec

======== CHANNEL f1 ========
NUC1                       1H
P1                       8.00 usec
P2                      16.00 usec
PLW1               23.01441956 W
SFO1               600.1306000 MHz

====== GRADIENT CHANNEL =====
GPNAM1                SINE.100
GPZ1                     40.00 %
P16                    1000.00 usec

F1 - Acquisition parameters
TD                          512
SFO1                600.1306 MHz
FIDRES              4.689001 Hz
SW                      4.000 ppm
FnMODE           States-TPPI

F2 - Processing parameters
SI                         1024
SF                600.1300000 MHz
WDW                       QSINE
SSB                           2
LB           0 Hz
GB           0
PC                         1.00

F1 - Processing parameters
SI                         1024
MC2              States-TPPI
SF                600.1300000 MHz
WDW              States-TPPI
SSB                           2
LB           0 Hz
GB           0
```

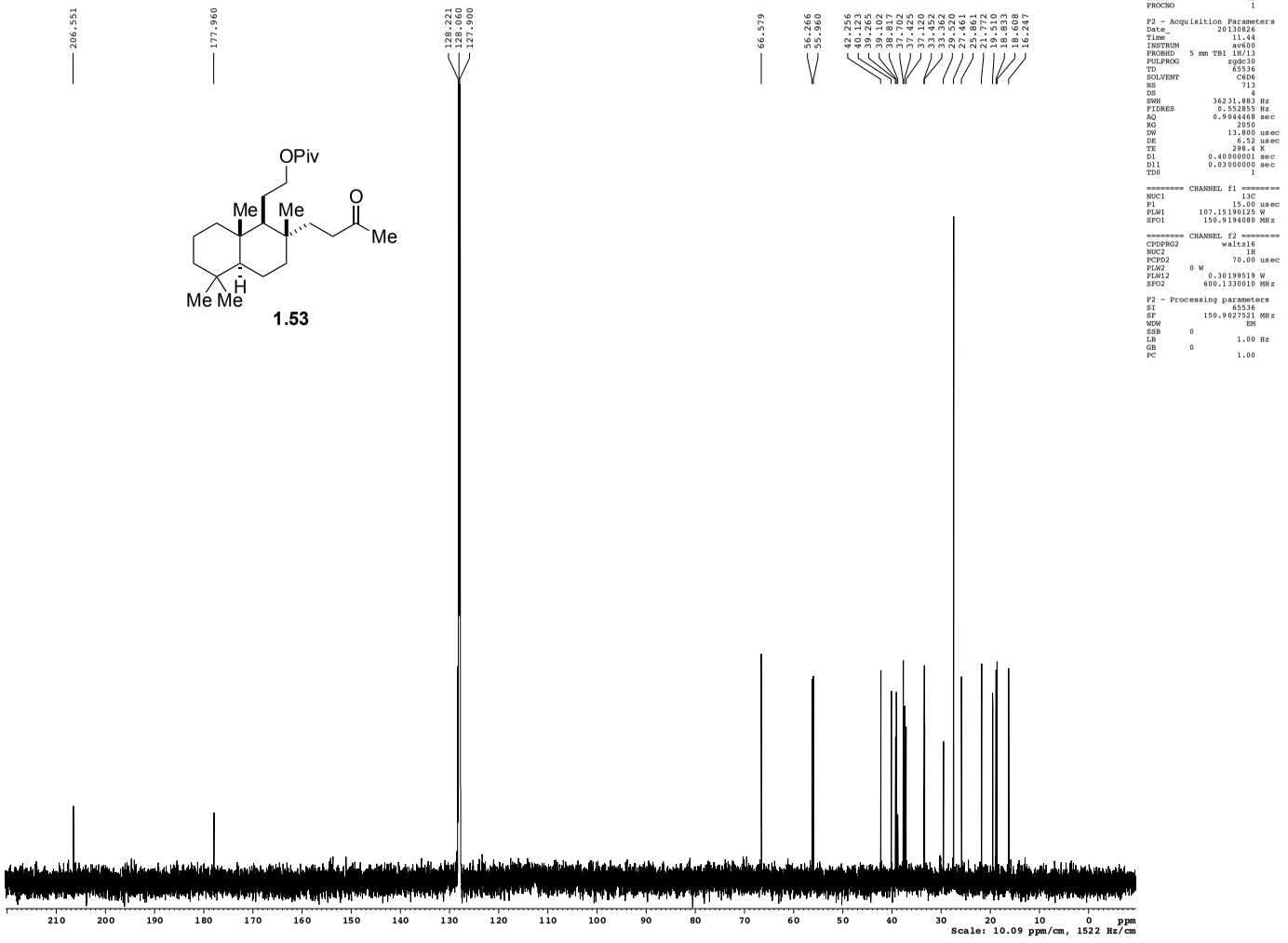
Purified Product



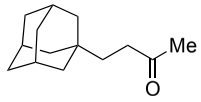
1.53


```
Current Data Parameters
NAME                  KQ1-188
EXPNO                      12
PROCNO                      1

F2 - Acquisition Parameters
Date_              20121207
Time                  13.39
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                      456
DW                 52.000 usec
DE                  6.00 usec
TE                  298.0 K
D1              0.10000000 sec

======== CHANNEL f1 ========
NUC1                      1H
P1                     8.00 usec
PLW1           23.01441956 W
SFO1           600.1342009 MHz

F2 - Processing parameters
SI                        65536
SF             600.1300346 MHz
WDW                       EM
SSB       0
LB        0 Hz
GB        0
PC                      1.00
```

Purified Product



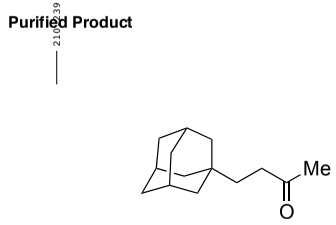
Purified Product



1.16

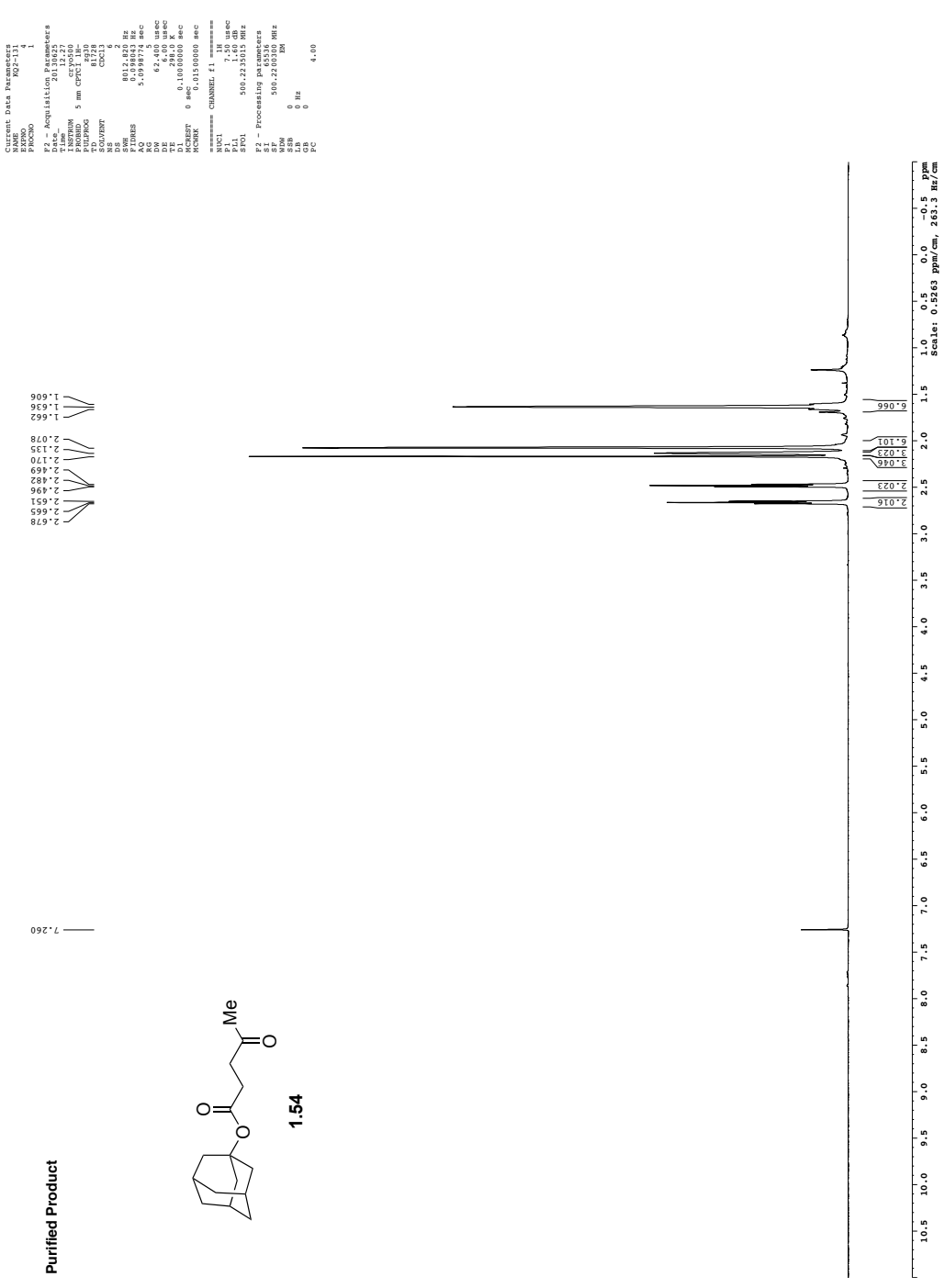

```
Current Data Parameters
NAME                  KQ1-162
EXPNO                       3
PROCNO                      1

F2 - Acquisition Parameters
Date_              20121109
Time                   15.14
INSTRUM                av600
PROBHD   5 mm TBI 1H/13
PULPROG                zg30
TD                     98074
SOLVENT              CDCl3T
NS                         21
DS                          2
SWH                 9615.385 Hz
FIDRES              0.098042 Hz
AQ                  5.0998979 sec
RG                        724
DW                   52.000 usec
DE                    6.00 usec
TE                    298.0 K
D1                 0.10000000 sec

======== CHANNEL f1 ========
NUC1                       1H
P1                    8.00 usec
PLW1             23.01441956 W
SFO1             600.1342009 MHz

F2 - Processing parameters
SI                         65536
SF               600.1300284 MHz
WDW                           EM
SSB          0
LB                     0.30 Hz
GB           0
PC                     1.00
```

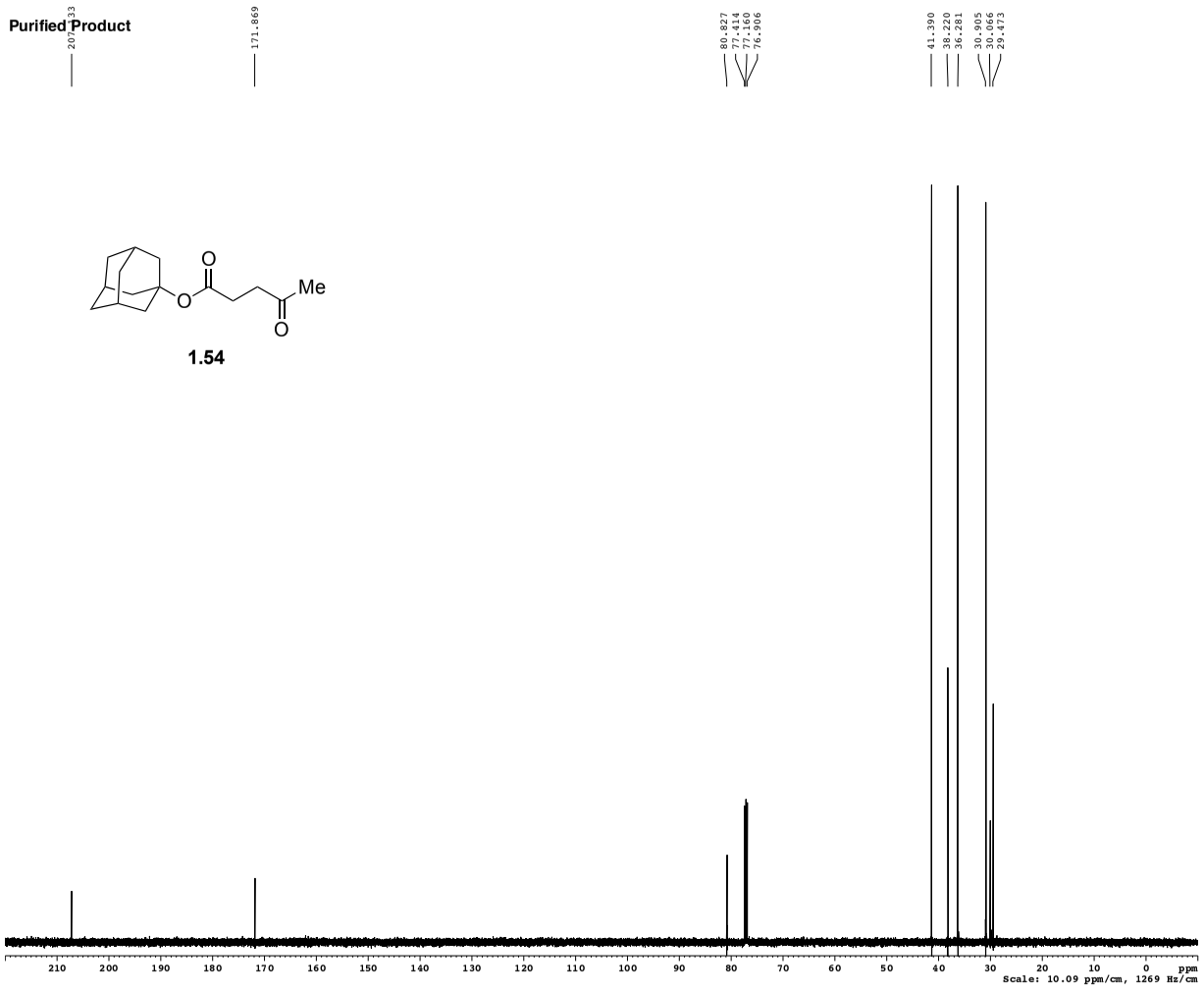
Purified Product



1.16

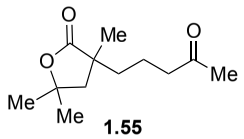

```
Current Data Parameters
NAME                  KQ1-162
EXPNO                      11
PROCNO                      1

F2 - Acquisition Parameters
Date_              20130818
Time                   17.06
INSTRUM                cryo500
PROBHD     5 mm CPTCI 1H-
PULPROG    SpinEchopg30gp.prd
TD                     65536
SOLVENT                CDCl3
NS                      1144
DS                         0
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 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 Hz
SPOFF2     0 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 %
GPX2       0 %
GPY1       0 %
GPY2       0 %
GPZ1                   30.00 %
GPZ2                   50.00 %
p15                   500.00 usec
p16                  1000.00 usec

F2 - Processing parameters
SI                     65536
SF              125.7804074 MHz
WDW                       EM
SSB        0
LB                      1.00 Hz
GB         0
PC                      2.00
```


Purified Product
1.54
Me
O
O
O
7.260
2.678
2.665
2.651
2.496
2.482
2.469
2.170
2.135
2.078
1.662
1.636
1.606
6.066
2.023
2.016
1.101
1.023
1.046
Current Data Parameters
NAME RQ2-13
EXPNO 4
PROCNO 1
F2 - Acquisition Parameters
Date_ 20111027
Time 13.27
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 81728
SOLVENT CDCl3
NS 6
DS 2
SWH 8012.820 Hz
FIDRES 0.098043 Hz
AQ 5.0987344 sec
RG 5
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0 sec
MCWRK 0.01500000 sec
========== CHANNEL f1 ==========
NUC1 1H
P1 7.50 usec
PL1 0.00 dB
SFO1 500.2235615 MHz
F2 - Processing parameters
SI 65536
SF 500.2200300 MHz
WDW EM
SSB 0 Hz
LB 0 Hz
GB 0
PC 4.00
10.5 10.0 9.5 9.0 8.5 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 -0.5 ppm
Scale: 0.5263 ppm/cm, 263.3 Hz/cm



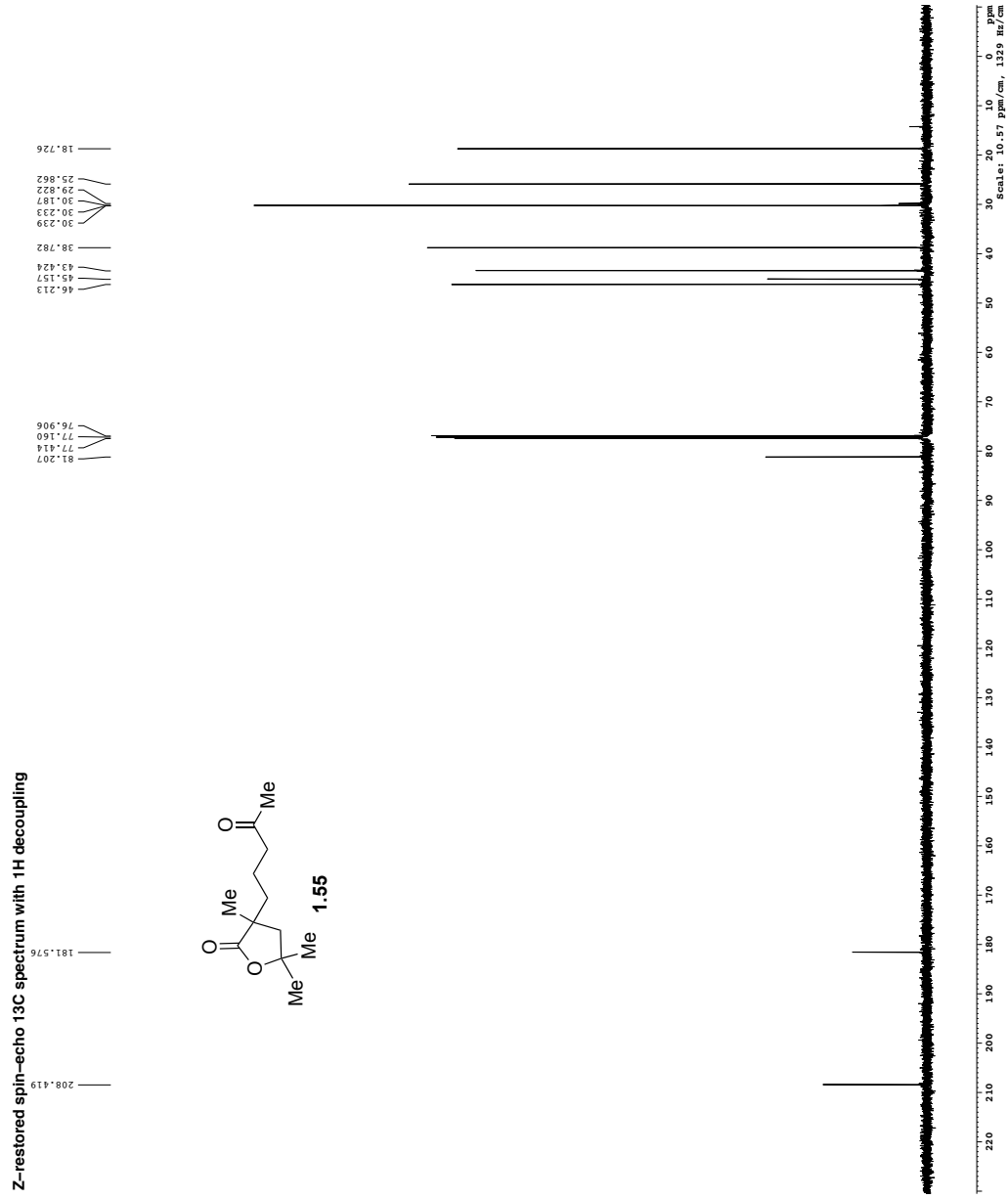

```
Current Data Parameters
NAME                  KQ2-131
EXPNO                       5
PROCNO                      1

F2 - Acquisition Parameters
Date_              20130625
Time                   12.30
INSTRUM              cryo500
PROBHD    5 mm CPTCI 1H-
PULPROG   SpinEchopg30gp.prd
TD                     65536
SOLVENT                CDCl3
NS                       136
DS                         0
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 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 Hz
SPOFF2    0 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 %
GPX2       0 %
GPY1       0 %
GPY2       0 %
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         0 Hz
GB         0
PC                     4.00
```

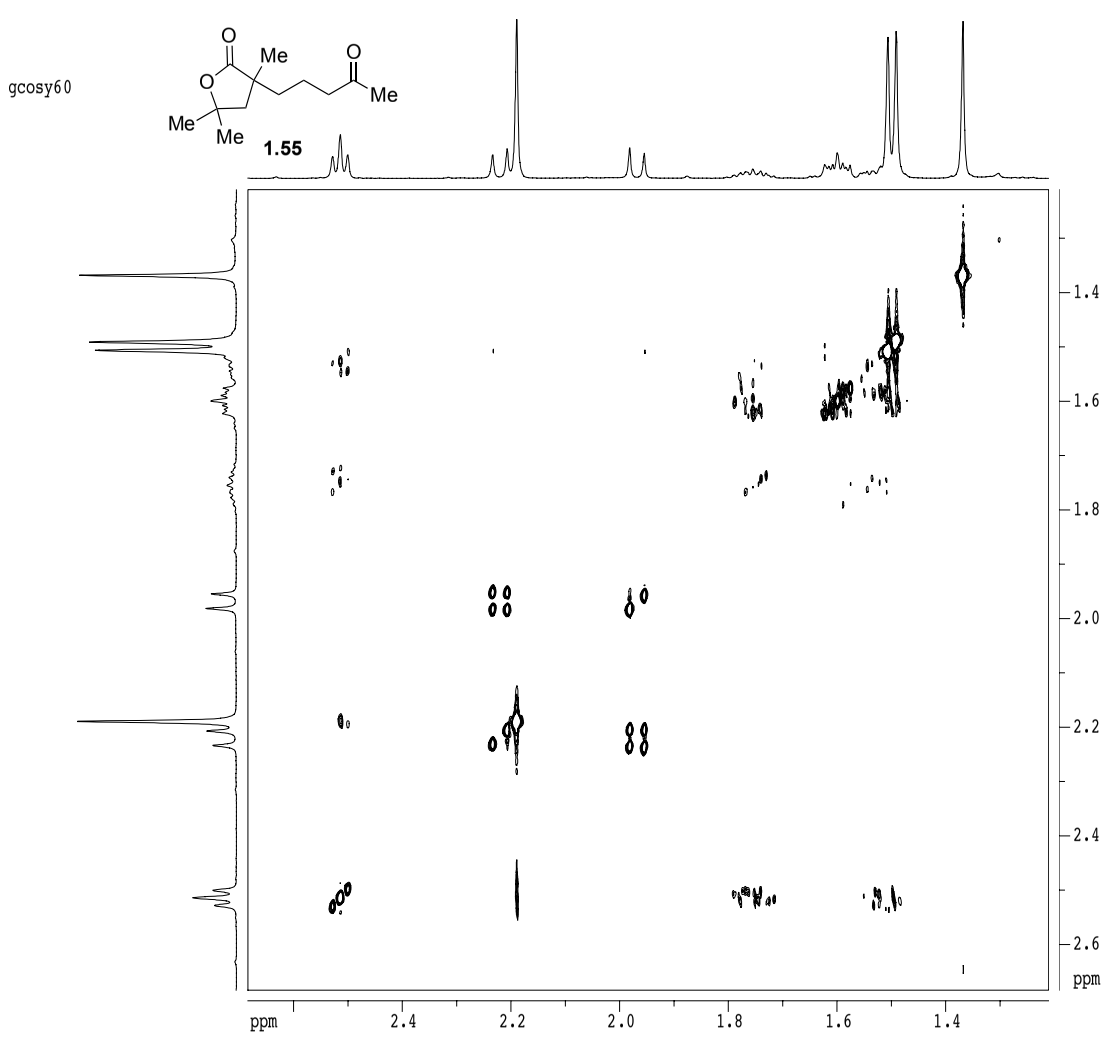
1H spectrum



1.55

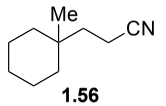

```
Current Data Parameters
NAME                  GL2-289-3-33
EXPNO                            1
PROCNO                           1

F2 - Acquisition Parameters
Date_                     20130817
Time                         10.34
INSTRUM                   cryo500
PROBHD     5 mm CPTCI 1H-
PULPROG                       zg30
TD                           81728
SOLVENT                     CDCl3T
NS                               8
DS                               2
SWH                    8012.820 Hz
FIDRES                 0.098043 Hz
AQ                     5.0998774 sec
RG                             6.3
DW                        62.400 usec
DE                         6.00 usec
TE                          298.0 K
D1                     0.10000000 sec
MCREST     0 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                  500.2200315 MHz
WDW                             EM
SSB          0
LB                          0.30 Hz
GB           0
PC                          4.00
```


Z-restored spin-echo 13C spectrum with 1H decoupling
1.55
Me
Me
Me
O
O
O
Me
208.419
181.576
81.207
77.414
77.160
76.906
46.213
45.157
43.424
38.782
30.239
30.233
30.187
29.822
25.862
18.726
ppm
Scale: 10.157 ppm/cm, 1329 Hz/cm




```
      Current Data Parameters
USER              gregll
NAME       GL2-197B-3-2d
EXPNO                 2
PROCNO                1

      F2 - Acquisition Parameters
Date_          20130402
Time               8.55
INSTRUM         cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG     cosygp60.prd
TD                 2048
SOLVENT           CDCl3
NS                    2
DS                   16
SWH             737.028 Hz
FIDRES          0.359877 Hz
AQ              1.3894132 sec
RG                143.7
DW                678.400 usec
DE                  6.00 usec
TE                298.0 K
d0            0.00000300 sec
D1            1.00000000 sec
d13           0.00000300 sec
D16           0.00020000 sec
IN0           0.00135680 sec

     ======== CHANNEL f1 ========
NUC1                 1H
P1                 7.50 usec
PL1                1.60 dB
SFO1         500.2209741 MHz

     ====== GRADIENT CHANNEL =====
GPNAM1           sine.100
GPNAM2           sine.100
GPX1                0.00 %
GPX2                0.00 %
GPY1                0.00 %
GPY2                0.00 %
GPZ1               17.00 %
GPZ2               17.00 %
P16              1000.00 usec

      F1 - Acquisition parameters
ND0                   1
TD                   79
SFO1            500.221 MHz
FIDRES          9.329473 Hz
SW                1.473 ppm
FnMODE        undefined

      F2 - Processing parameters
SI                 1024
SF          500.2200000 MHz
WDW                SINE
SSB                   0
LB                 0.00 Hz
GB                    0
PC                 2.00

      F1 - Processing parameters
SI                 1024
MC2                  QF
SF          500.2200000 MHz
WDW                SINE
SSB                   0
LB                 0.00 Hz
GB                    0

      2D NMR plot parameters
CX2               15.00 cm
CX1               15.00 cm
F2PLO              2.684 ppm
F2LO             1342.62 Hz
F2PHI              1.211 ppm
F2HI              605.60 Hz
F1PLO              2.684 ppm
F1LO             1342.62 Hz
F1PHI              1.211 ppm
F1HI              605.60 Hz
F2PPMCM         0.09823 ppm/cm
F2HZCM         49.13522 Hz/cm
F1PPMCM         0.09823 ppm/cm
F1HZCM         49.13522 Hz/cm
```

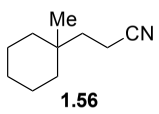
Purified Product



1.56


```
Current Data Parameters
NAME                  KQ2-106
EXPNO                       2
PROCNO                      1

F2 - Acquisition Parameters
Date                 20130604
Time                    18.56
INSTRUM                av600
PROBHD     5 mm TBI 1H/13
PULPROG                 zg30
TD                      98074
SOLVENT                 CDCl3
NS                          6
DS                          0
SWH                  9615.385 Hz
FIDRES               0.098042 Hz
AQ                   5.0998979 sec
RG                        181
DW                     52.000 usec
DE                      6.00 usec
TE                      298.1 K
D1                0.10000000 sec
TD0                         1

======== CHANNEL f1 ========
NUC1                       1H
P1                      8.00 usec
PLW1                23.01441956 W
SFO1                600.1342009 MHz

F2 - Processing parameters
SI                        65536
SF                600.1300356 MHz
WDW                        EM
SSB          0
LB           0 Hz
GB           0
PC                        1.00
```

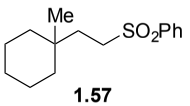
Purified Product



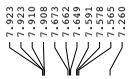
1.56

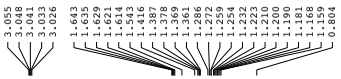

```
Current Data Parameters
NAME            KQ2-106
EXPNO                 3
PROCNO                1

F2 - Acquisition Parameters
Date_          20130606
Time              10.52
INSTRUM          cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD                65536
SOLVENT           CDCl3
NS                  328
DS                    0
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 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 Hz
SPOFF2    0 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 %
GPX2      0 %
GPY1      0 %
GPY2      0 %
GPZ1             30.00 %
GPZ2             50.00 %
p15             500.00 usec
p16            1000.00 usec

F2 - Processing parameters
SI                65536
SF           125.7804100 MHz
WDW                  EM
SSB       0
LB                5.00 Hz
GB        0
PC                2.00
```

Purified Product

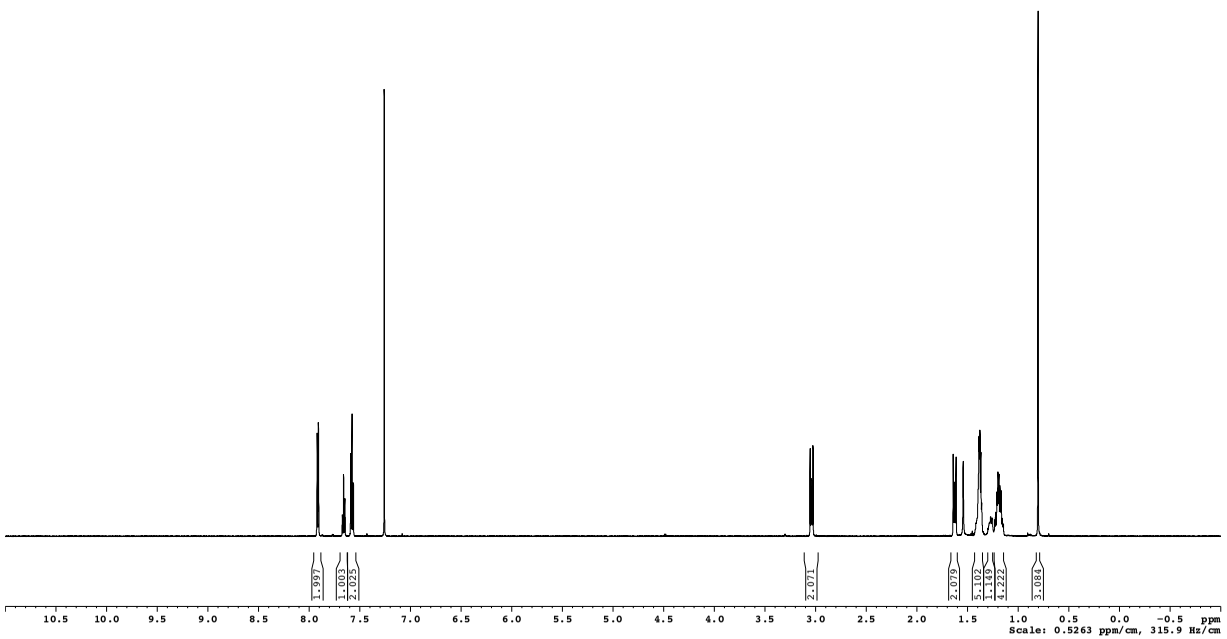


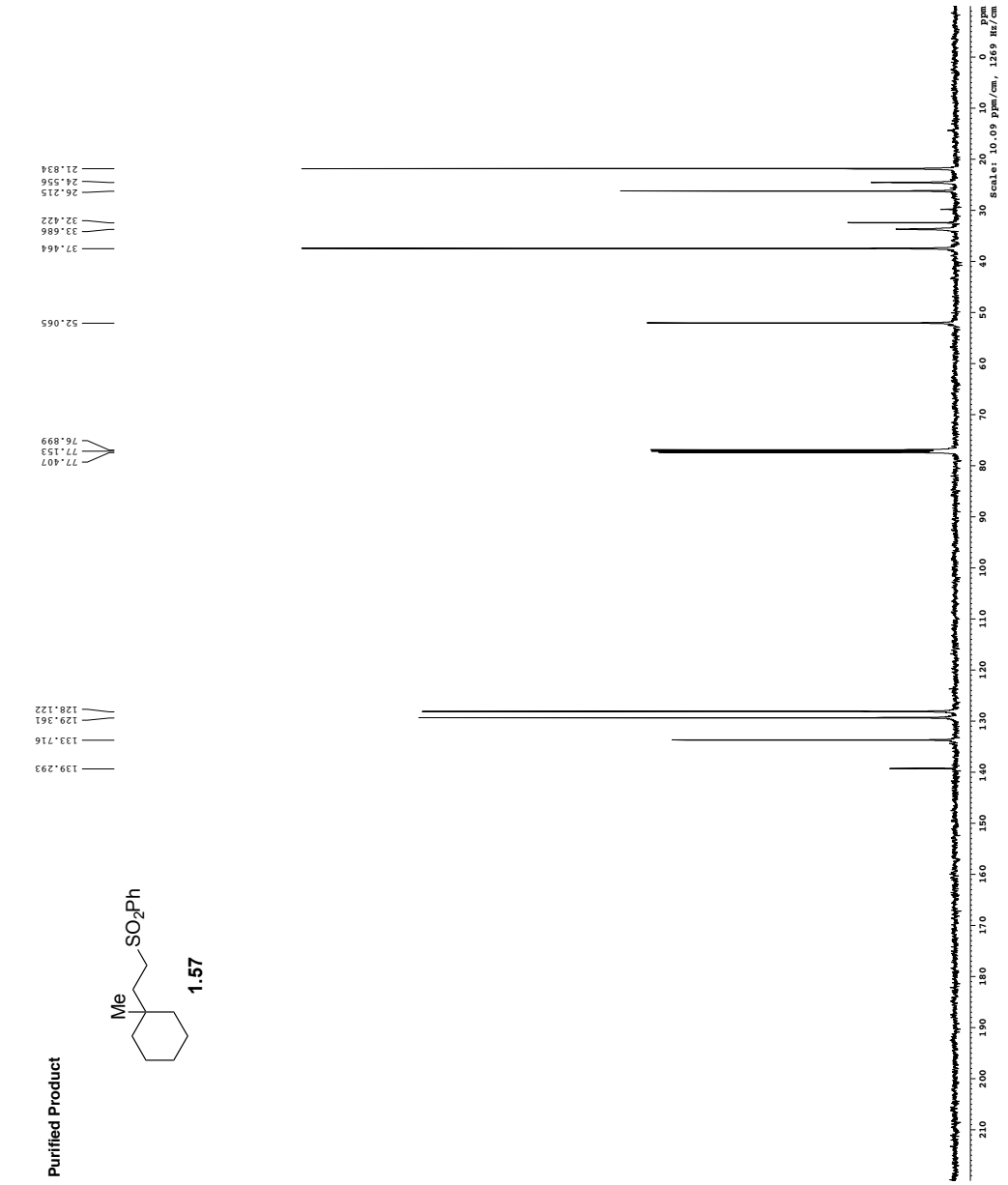
1.57



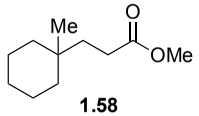



```
Current Data Parameters
NAME                  KQ2-108
EXPNO                       3
PROCNO                      1

F2 - Acquisition Parameters
Date_              20130605
Time                   18.17
INSTRUM                av600
PROBHD     5 mm TBI 1H/13
PULPROG                zg30
TD                     98074
SOLVENT                CDCl3
NS                        10
DS                         0
SWH                 9615.385 Hz
FIDRES              0.098042 Hz
AQ                  5.0998979 sec
RG                       456
DW                    52.000 usec
DE                     6.00 usec
TE                     298.0 K
D1                0.10000000 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      1H
P1                     8.00 usec
PLW1             23.01441956 W
SFO1             600.1342009 MHz

F2 - Processing parameters
SI                        65536
SF               600.1300355 MHz
WDW                        EM
SSB                        0
LB                     0 Hz
GB                         0
PC                      1.00
```




Purified Product
Me
SO2Ph
1.57
139.293
133.716
129.361
128.122
77.407
77.153
76.899
52.065
37.464
33.686
32.422
26.215
24.556
21.834
Scale: 10.09 ppm/cm, 1269 Hz/cm

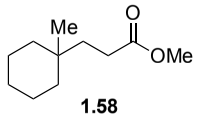
1H spectrum



1.58


```
Current Data Parameters
NAME                  GL2 248 34
EXPNO                          1
PROCNO                         1

F2 - Acquisition Parameters
Date_                   20130622
Time                       15.43
INSTRUM                    qns500
PROBHD    5 mm broadband
PULPROG                    zg30
TD                         81728
SOLVENT                    CDCl3T
NS                             8
DS                             2
SWH                     8012.820 Hz
FIDRES                  0.098043 Hz
AQ                      5.0998774 sec
RG                         574.7
DW                        62.400 usec
DE                         6.00 usec
TE                        298.0 K
D1                      0.10000000 sec
MCREST    0 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                  499.2900293 MHz
WDW                           EM
SSB       0
LB                         0.30 Hz
GB        0
PC                         1.00
```

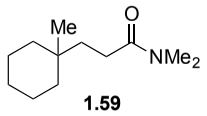
13C spectrum with 1H decoupling



1.58


```
Current Data Parameters
NAME          GL2-248-34
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20130622
Time              15.45
INSTRUM           qn500
PROBHD   5 mm broadband
PULPROG         zgdc30
TD               65536
SOLVENT          CDCl3
NS                 684
DS                   4
SWH          30303.031 Hz
FIDRES        0.462388 Hz
AQ            1.0813940 sec
RG               29193
DW              16.500 usec
DE               4.50 usec
TE              298.0 K
D1           0.25000000 sec
d11          0.03000000 sec
MCREST    0 sec
MCWRK        0.01500000 sec

======== CHANNEL f1 ========
NUC1                13C
P1                 7.70 usec
PL1        0 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          125.5465566 MHz
WDW                   EM
SSB        0
LB                 4.00 Hz
GB         0
PC                 2.00
```

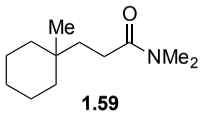
Purified Product



1.59

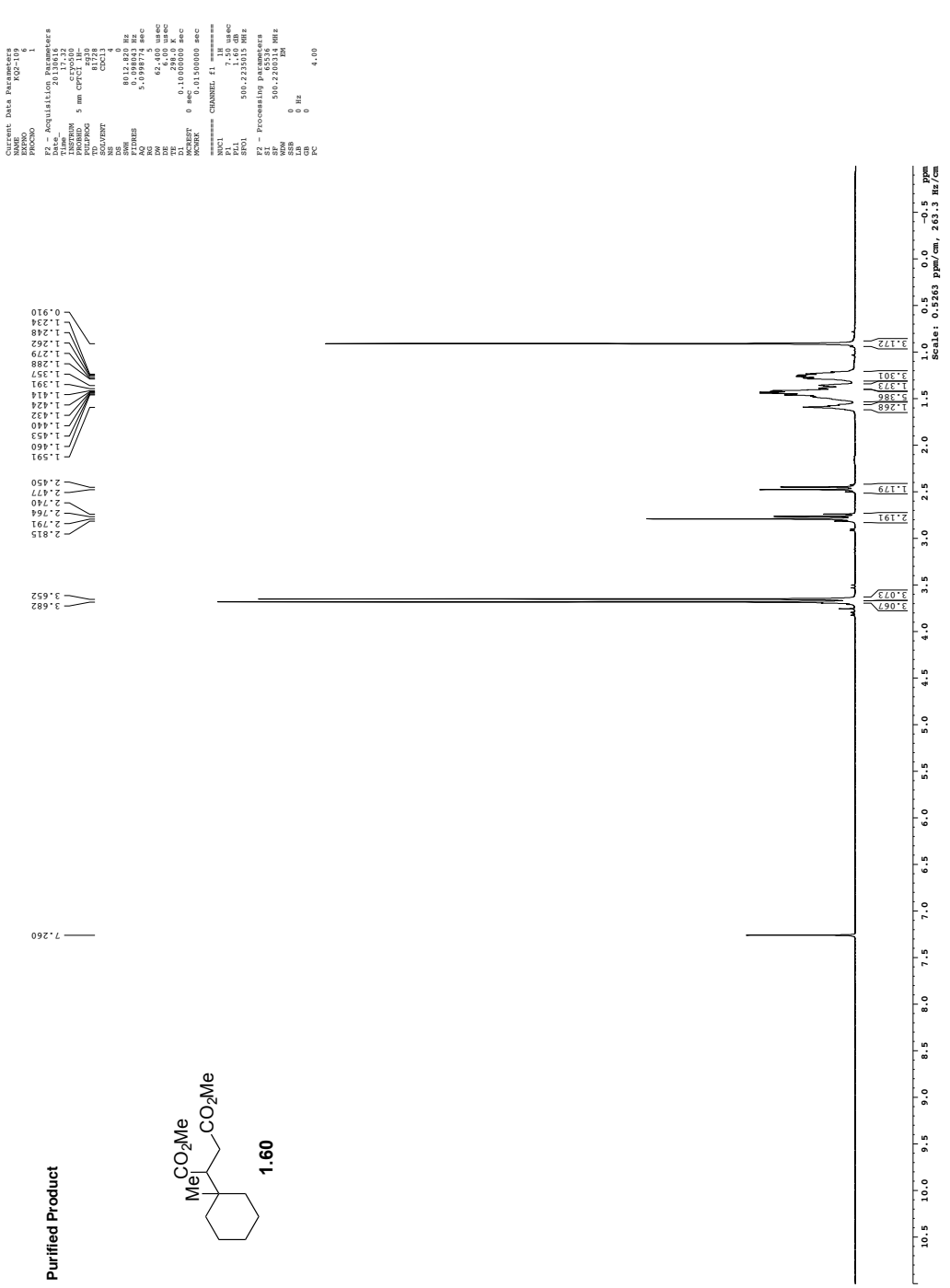

```
Current Data Parameters
NAME                  KQ2-124
EXPNO                      10
PROCNO                      1

F2 - Acquisition Parameters
Date_               20130617
Time                   21.12
INSTRUM                av600
PROBHD    5 mm TBI 1H/13
PULPROG                 zg30
TD                     98074
SOLVENT                CDCl3
NS                         8
DS                         0
SWH                 9615.385 Hz
FIDRES              0.098042 Hz
AQ                  5.0998979 sec
RG                       456
DW                    52.000 usec
DE                     6.00 usec
TE                    298.1 K
D1                 0.10000000 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      1H
P1                     8.00 usec
PLW1              23.01441956 W
SFO1              600.1342009 MHz

F2 - Processing parameters
SI                        65536
SF              600.1300359 MHz
WDW                        EM
SSB                 0
LB                  0 Hz
GB                  0
PC                       1.00
```

Purified Product

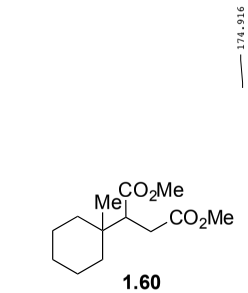


1.59


```
Current Data Parameters
NAME                  KQ2-124
EXPNO                      12
PROCNO                      1

F2 - Acquisition Parameters
Date_               20130618
Time                    9.15
INSTRUM                cryo500
PROBHD     5 mm CPTCI 1H-
PULPROG    SpinEchopg30gp.prd
TD                      65536
SOLVENT                 CDCl3
NS                        443
DS                          0
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 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 Hz
SPOFF2     0 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 %
GPX2       0 %
GPY1       0 %
GPY2       0 %
GPZ1                    30.00 %
GPZ2                    50.00 %
p15                    500.00 usec
p16                   1000.00 usec

F2 - Processing parameters
SI                        65536
SF                 125.7804084 MHz
WDW                          EM
SSB        0
LB                       5.00 Hz
GB         0
PC                       2.00
```


Purified Product
1.60
CO2Me
Me
CO2Me
Current Data Parameters
NAME KQ2-109
EXPNO 6
PROCNO 1
F2 - Acquisition Parameters
Date_ 20130616
Time 17:32
INSTRUM spect
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 81928
SOLVENT CDCl3
NS 4
DS 0
SWH 8012.821 Hz
FIDRES 0.097853 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 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 7.40 usec
PL1 1.60 dB
SFO1 500.2235015 MHz
F2 - Processing parameters
SI 65536
SF 500.2200314 MHz
WDW EM
SSB 0
LB 0 Hz
GB 0
PC 4.00
7.260
3.682
3.652
2.815
2.791
2.764
2.740
2.477
2.450
1.591
1.460
1.453
1.440
1.432
1.424
1.414
1.391
1.357
1.288
1.279
1.262
1.248
1.234
0.910
3.172
3.301
1.373
5.386
1.268
1.179
2.191
3.073
3.067
ppm
Scale: 0.5263 ppm/cm, 263.3 Hz/cm

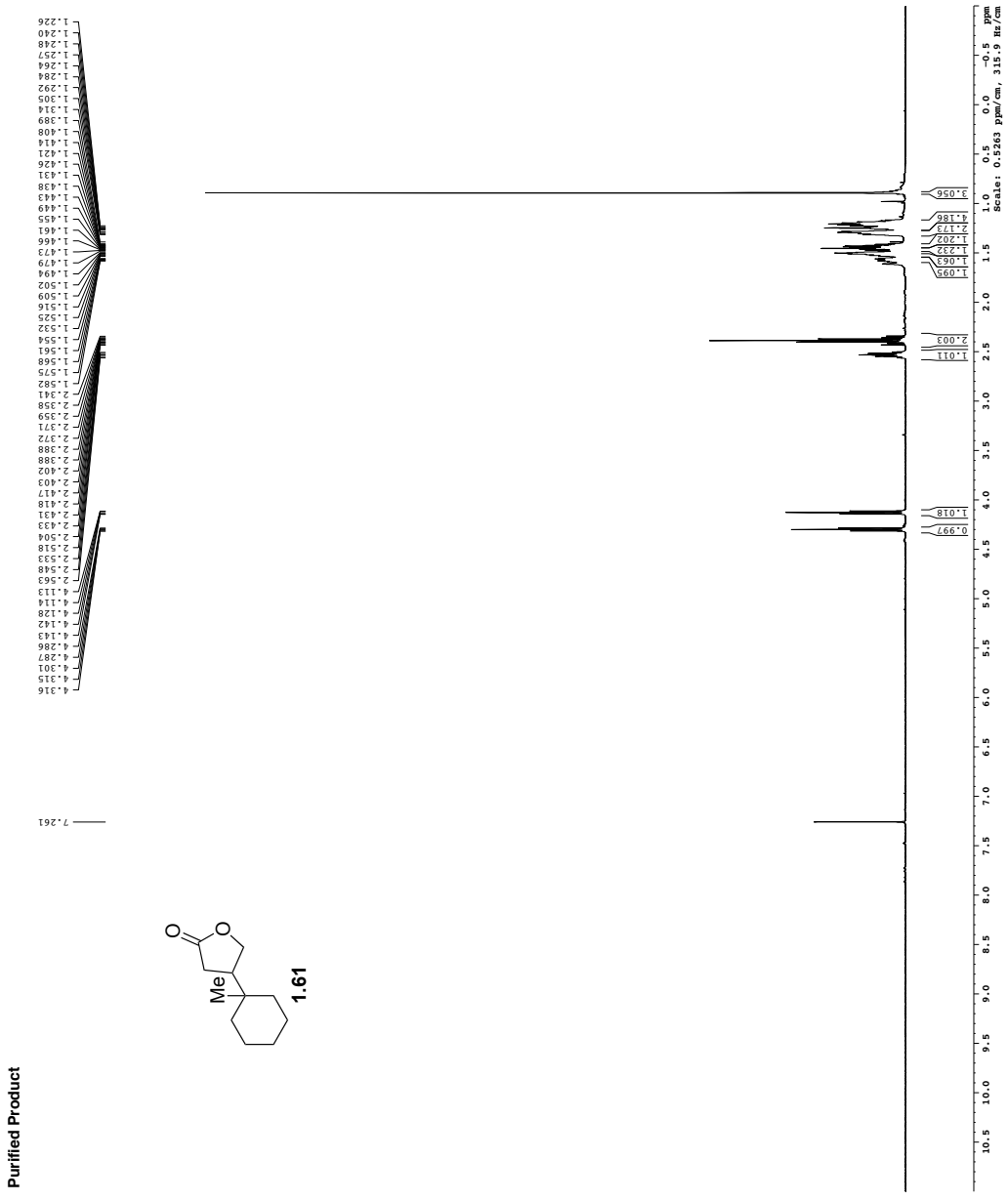
Purified Product



1.60

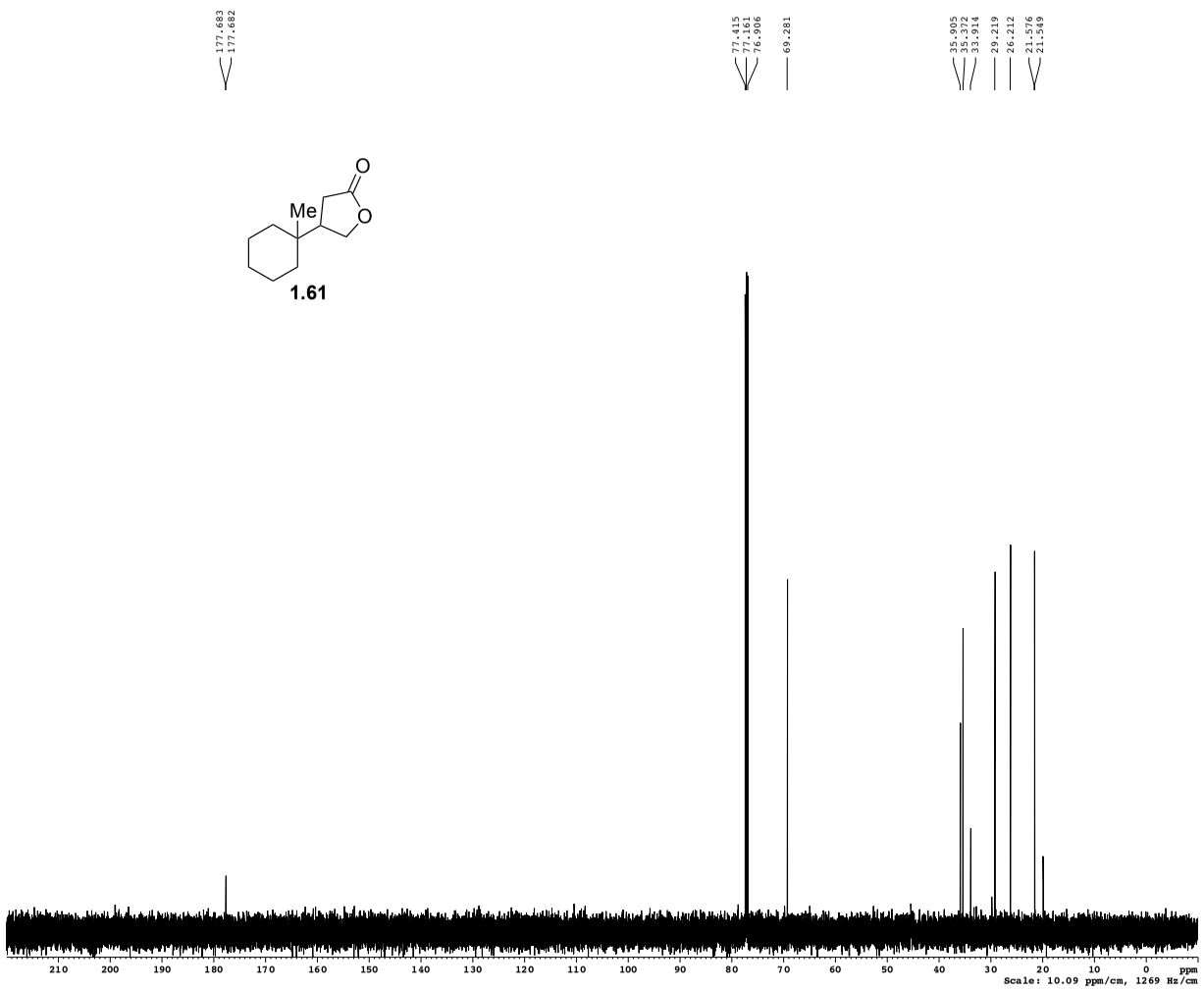

```
Current Data Parameters
NAME              KQ2-109
EXPNO                   7
PROCNO                  1

F2 - Acquisition Parameters
Date_           20130616
Time              17.33
INSTRUM          cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30qp.prd
TD                65536
SOLVENT           CDCl3
NS                  136
DS                   16
SWH           30303.031 Hz
FIDRES         0.462388 Hz
AQ             1.081940 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 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 Hz
SPOFF2   0 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 %
GPX2     0 %
GPY1     0 %
GPY2     0 %
GPZ1            30.00 %
GPZ2            50.00 %
p15            500.00 usec
p16           1000.00 usec

F2 - Processing parameters
SI                65536
SF          125.7804079 MHz
WDW                   EM
SSB      0
LB       0 Hz
GB       0
PC              2.00
```

Purified Product



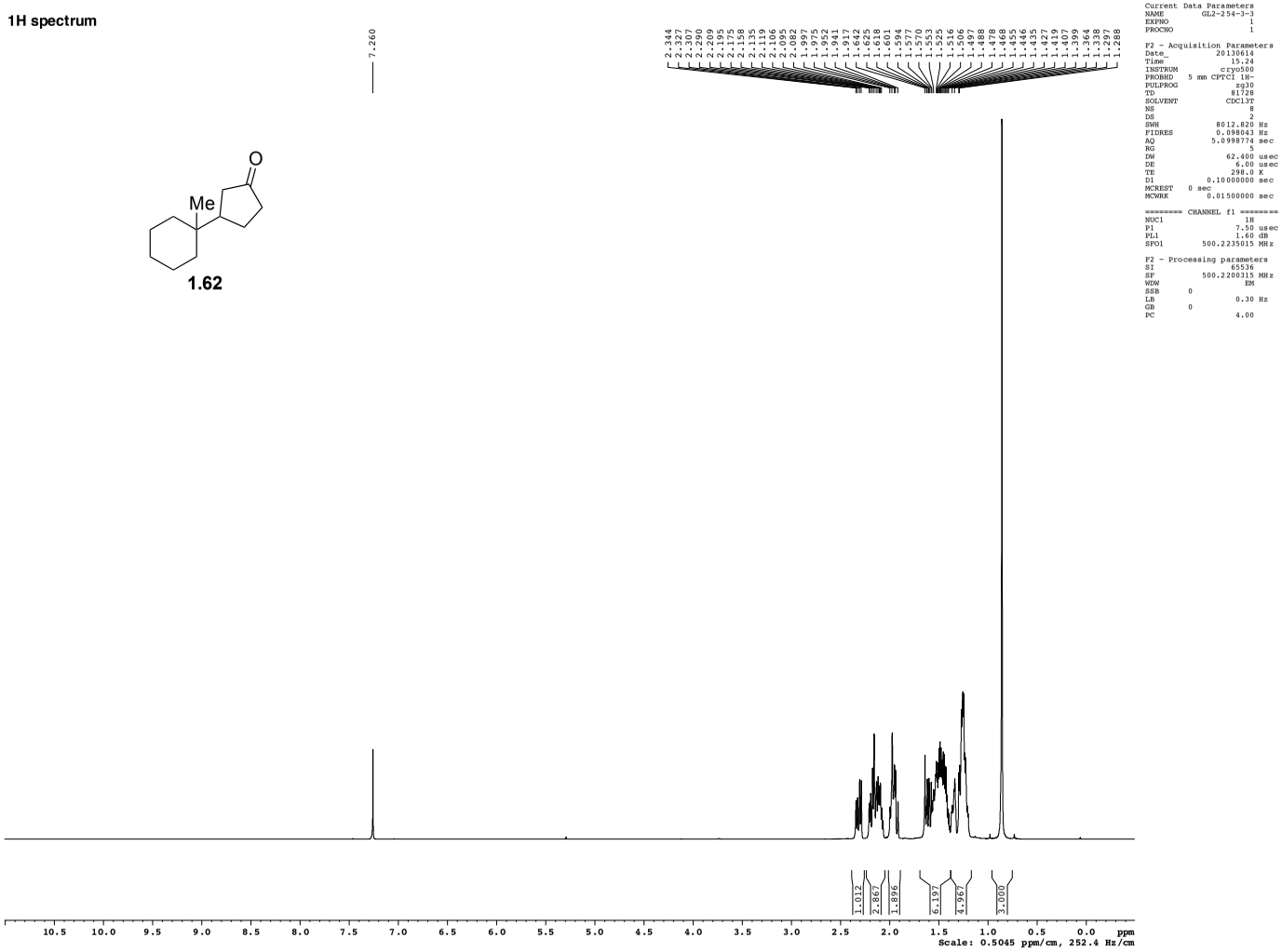
1.61

Purified Product

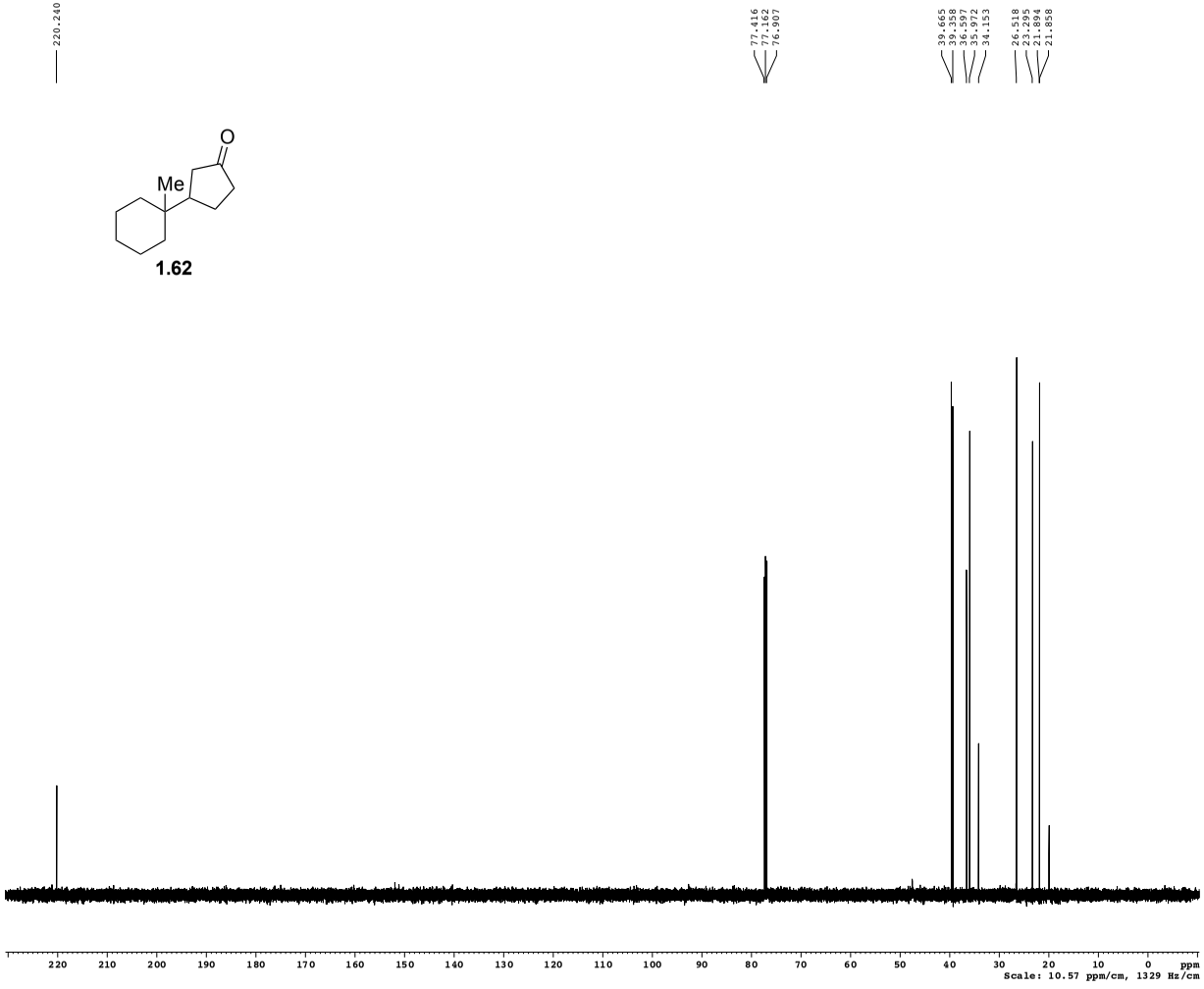



```
Current Data Parameters
NAME              KQ2-132
EXPNO                   5
PROCNO                  1

F2 - Acquisition Parameters
Date_           20130626
Time              16.11
INSTRUM         cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30qp.prd
TD                65536
SOLVENT           CDCl3
NS                   34
DS                    0
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 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 Hz
SPOFF2   0 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 %
GPX2      0 %
GPY1      0 %
GPY2      0 %
GPZ1              30.00 %
GPZ2              50.00 %
p15              500.00 usec
p16             1000.00 usec

F2 - Processing parameters
SI                65536
SF           125.7804088 MHz
WDW                  EM
SSB       0
LB        0 Hz
GB        0
PC                 2.00
```

1H spectrum


7.260
2.344
2.327
2.307
2.290
2.269
2.195
2.175
2.158
2.135
2.119
2.106
2.095
2.082
1.997
1.975
1.952
1.941
1.917
1.642
1.625
1.618
1.601
1.594
1.577
1.570
1.553
1.525
1.516
1.506
1.497
1.488
1.478
1.468
1.455
1.446
1.435
1.427
1.419
1.407
1.390
1.364
1.338
1.297
1.288
O
Me
1.62
Current Data Parameters
NAME GL2-254-3-3
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20130614
Time 15.24
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 81728
SOLVENT CDCl3T
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 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 500.2200315 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00
1.012
2.867
1.896
6.197
4.967
3.000
10.5 10.0 9.5 9.0 8.5 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
Scale: 0.5045 ppm/cm, 252.4 Hz/cm

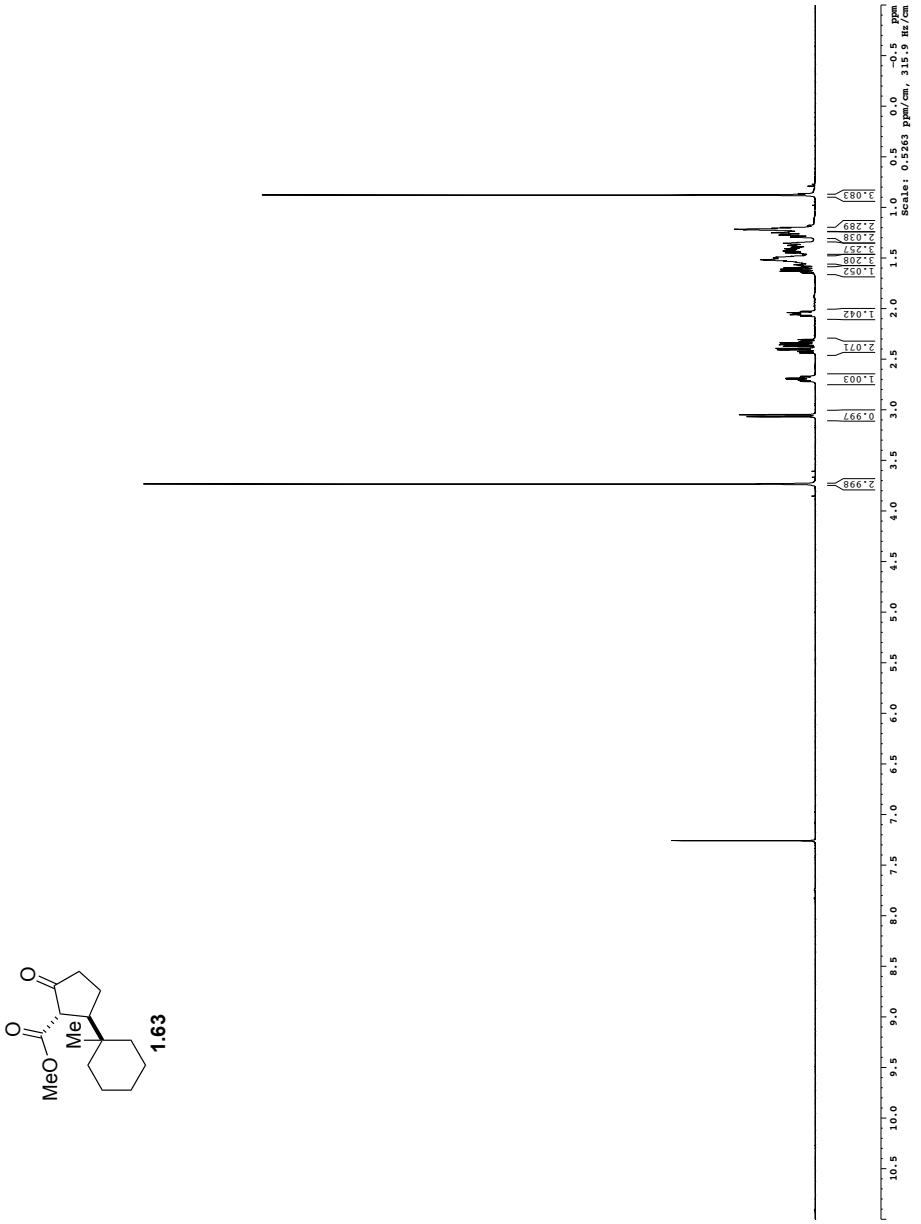
Z restored spin echo 13C spectrum with 1H decoupling



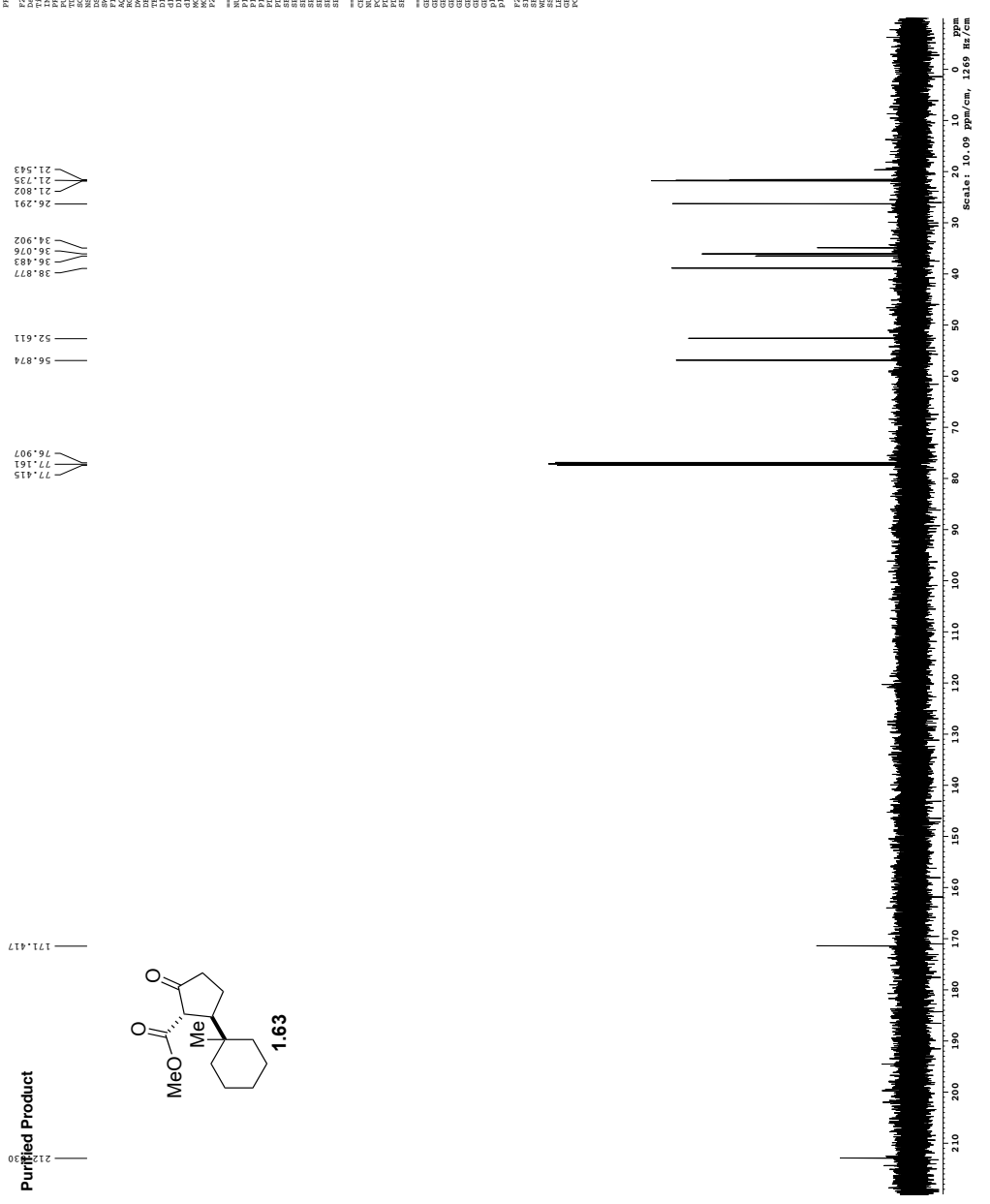
1.62

```
Current Data Parameters
NAME          GL2 254 3  3
EXPNO                    2
PROCNO                   1

F2   Acquisition Parameters
Date_          20130614
Time              15.28
INSTRUM          cryo500
PROBHD   5 mm CPTCI 1H
PULPROG  SpinEchopg30gp.prd
TD               65536
SOLVENT           CDCl3
NS                  193
DS                   16
SWH           30303.031 Hz
FIDRES        0.462398 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
MCWEST   0 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 Hz
SPOFF2   0 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 %
GPX2     0 %
GPY1     0 %
GPY2     0 %
GPZ1              30.00 %
GPZ2              50.00 %
p15              500.00 usec
p16             1000.00 usec

F2   Processing parameters
SI                65536
SF           125.7804086 MHz
WDW                  EM
SSB      0
LB       0 Hz
GB       0
PC                 2.00
```

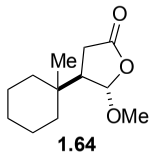
Purified Product



1.63

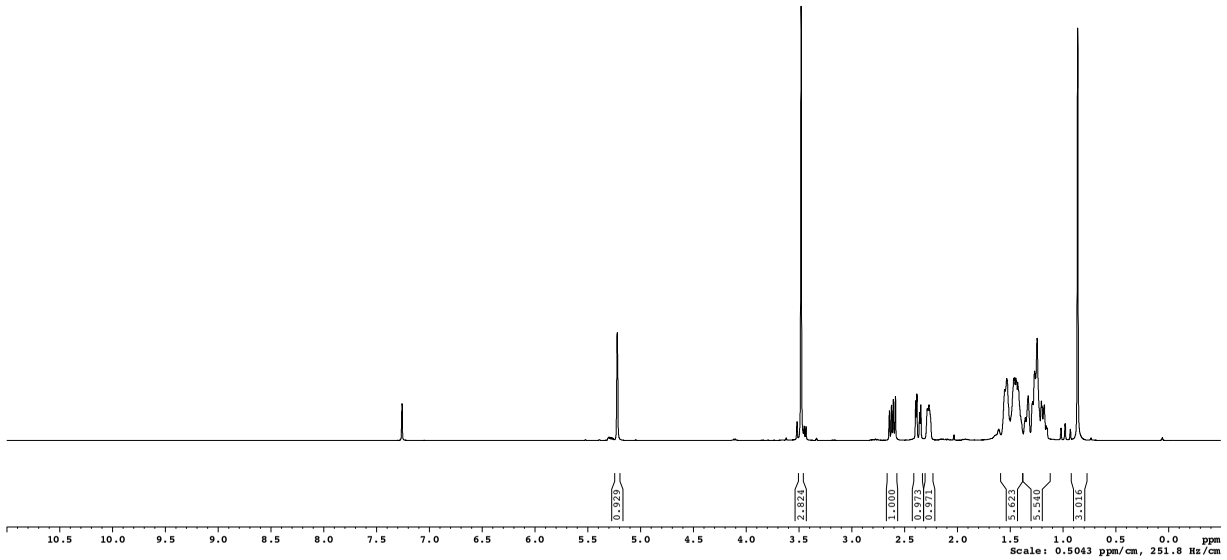

Purified Product
MeO
Me
1.63
212.330
171.417
77.415
77.161
76.907
56.874
52.611
38.877
36.483
36.076
34.902
26.291
21.802
21.735
21.543
Scale 10.09 ppm/cm, 1269 Hz/cm
ppm

1H spectrum

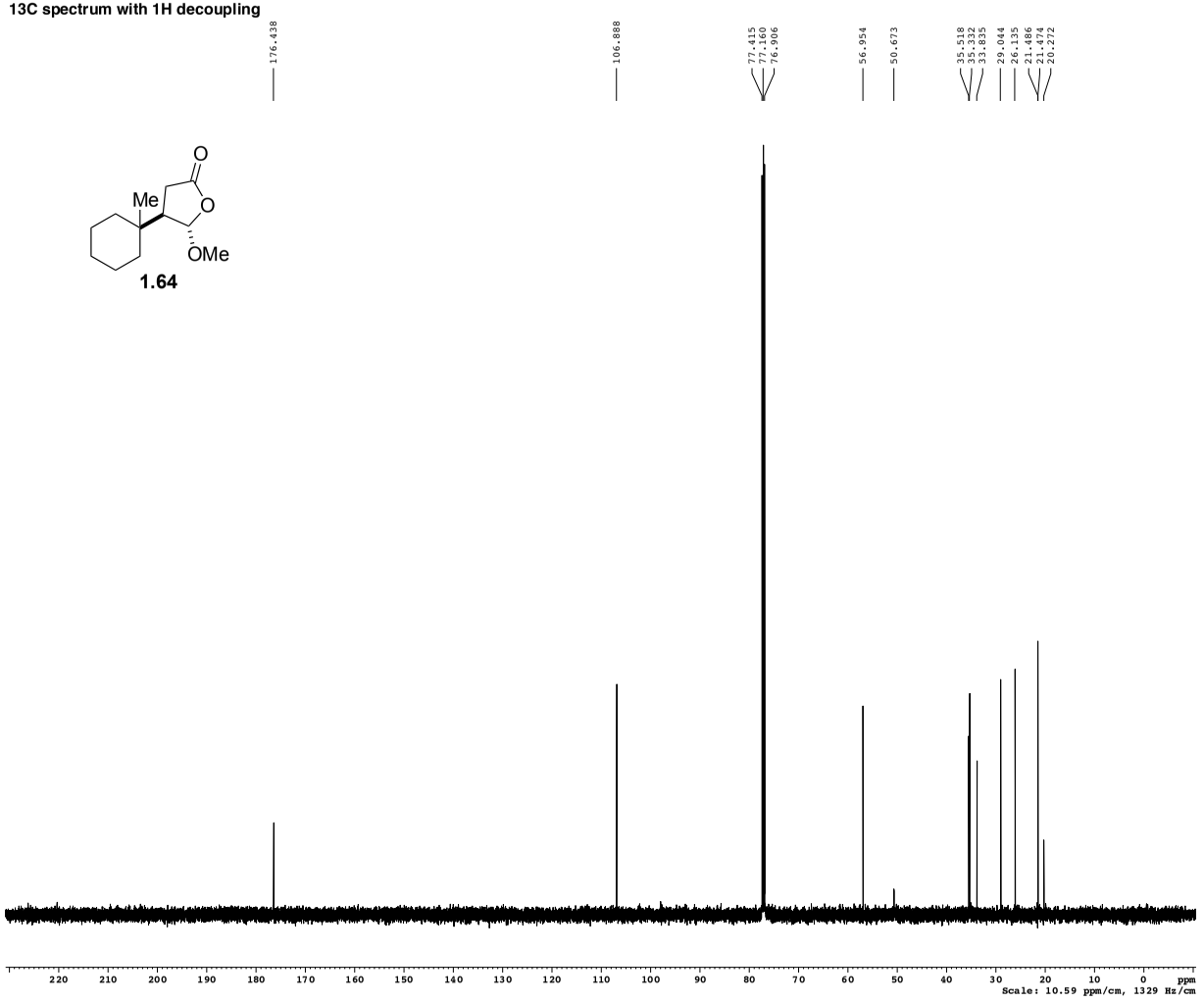


1.64

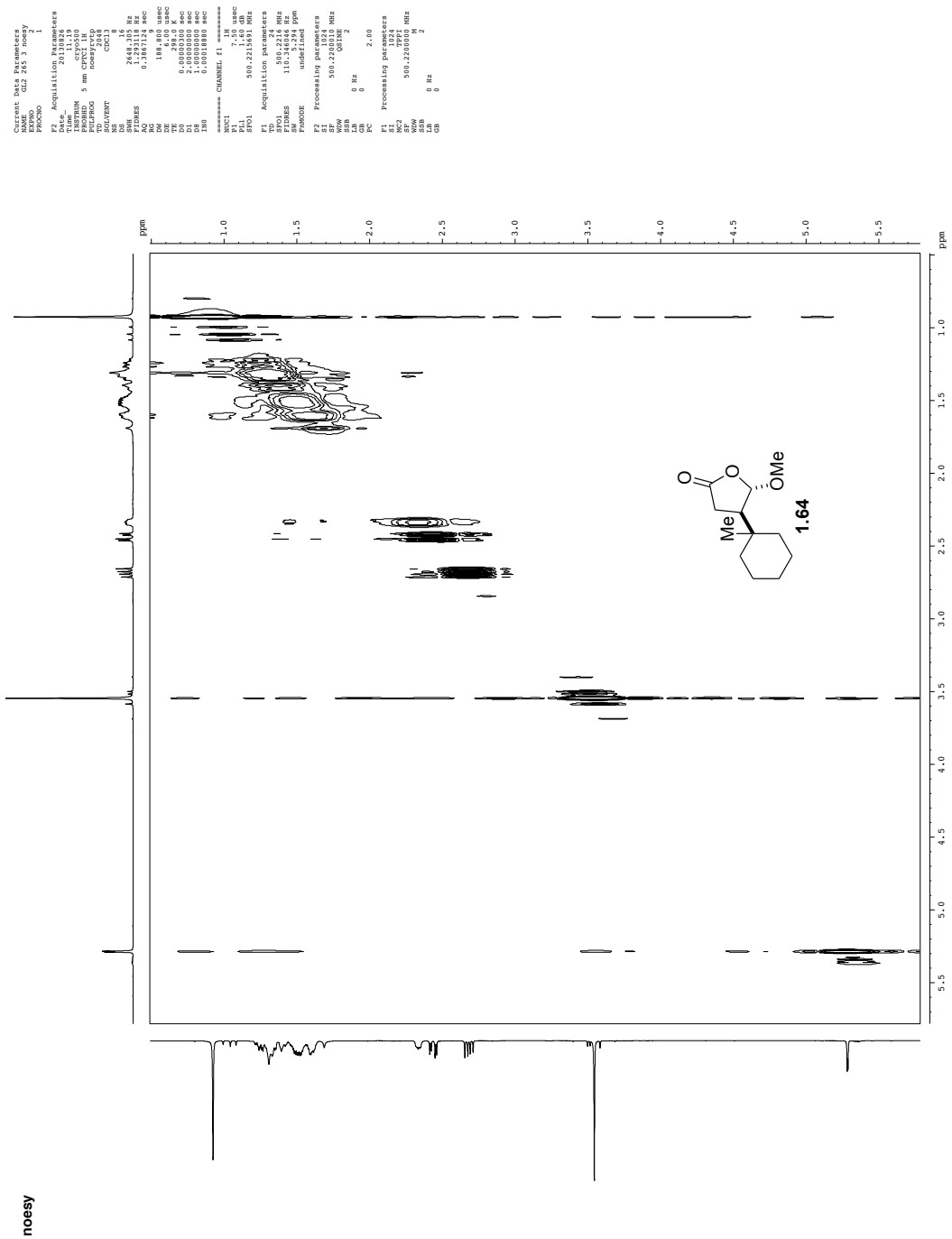

```
Current Data Parameters
NAME            GL2-265-33
EXPNO                    1
PROCNO                   1

F2 - Acquisition Parameters
Date_           20130821
Time                 9.50
INSTRUM             gn500
PROBHD   5 mm broadband
PULPROG              zg30
TD                  81728
SOLVENT             CDCl3T
NS                       8
DS                       2
SWH              8012.820 Hz
FIDRES           0.098043 Hz
AQ               5.0998774 sec
RG                    90.5
DW                 62.400 usec
DE                  6.00 usec
TE                 298.0 K
D1              0.10000000 sec
MCREST   0 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            499.2900293 MHz
WDW                    EM
SSB          0
LB                   0.30 Hz
GB           0
PC                   1.00
```

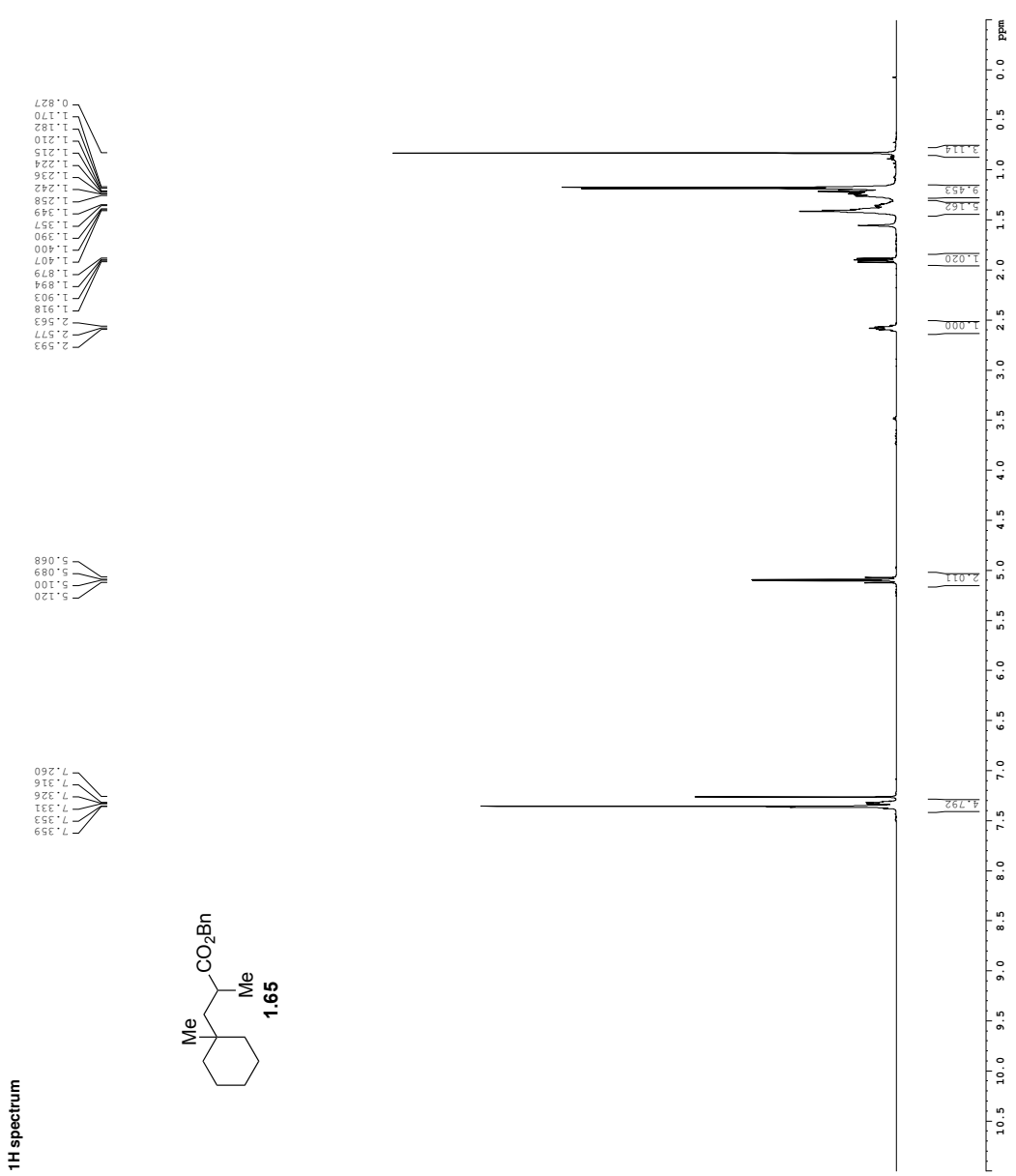


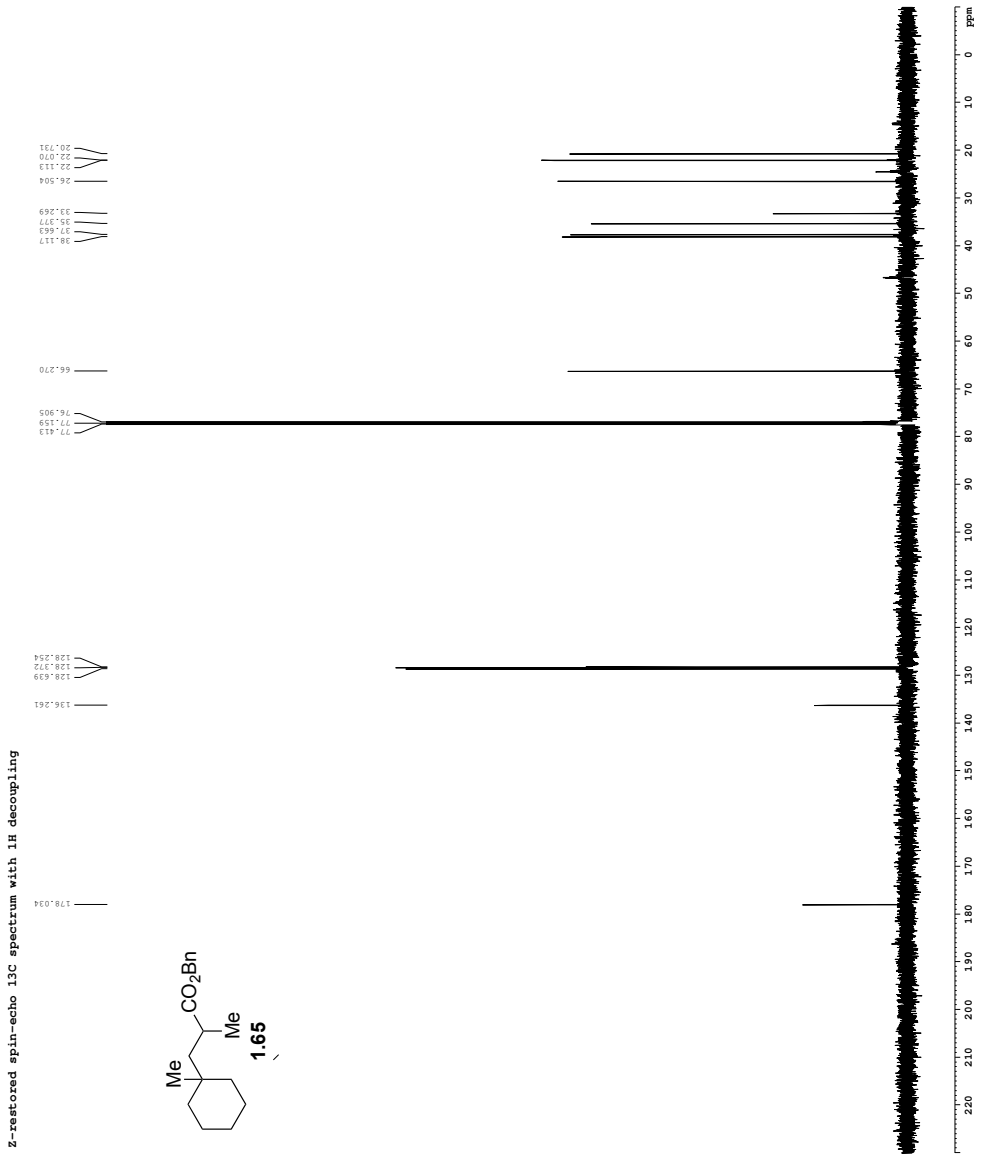
13C spectrum with 1H decoupling



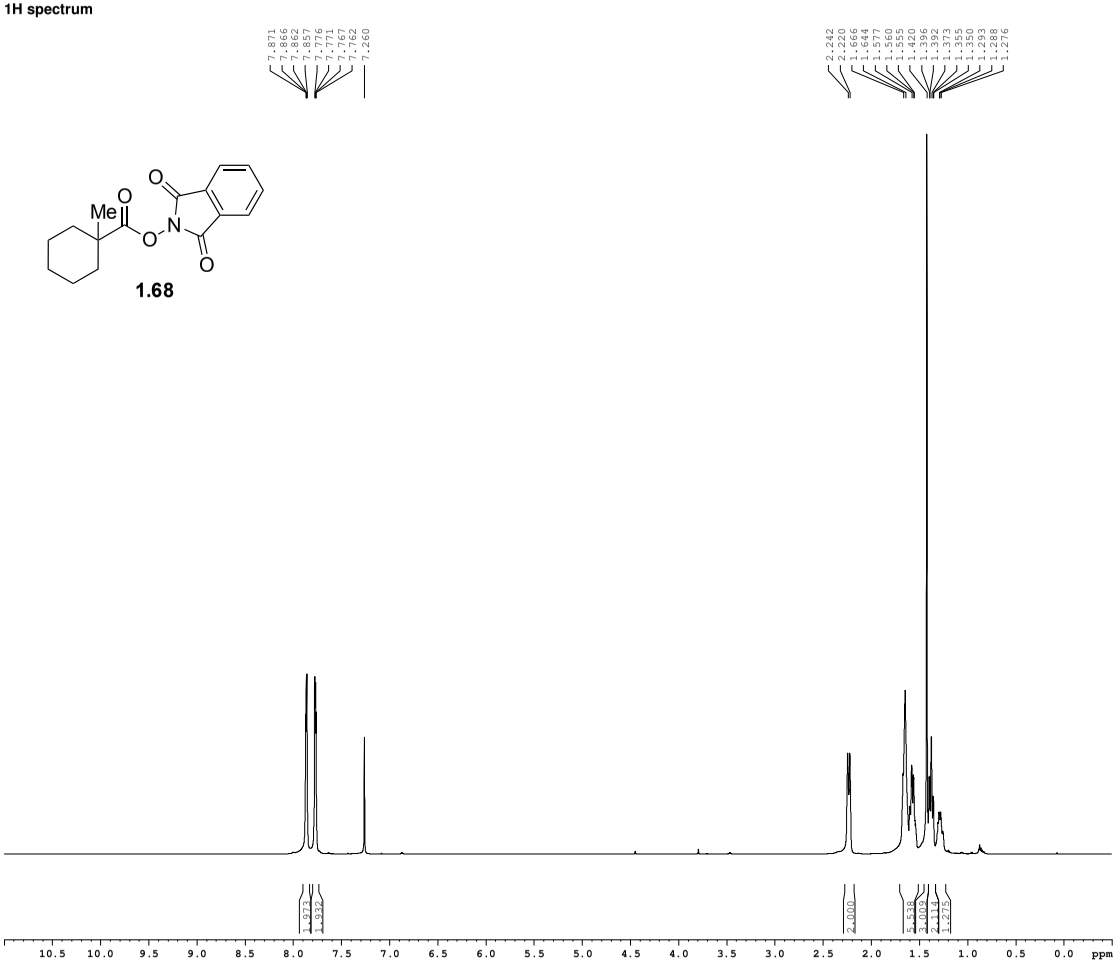

```
Current Data Parameters
NAME              GL2-265-33
EXPNO                      2
PROCNO                     1

F2 - Acquisition Parameters
Date_           20130821
Time                9.52
INSTRUM             qn500
PROBHD   5 mm broadband
PULPROG           zgdc30
TD                 65536
SOLVENT             CDCl3
NS                    257
DS                      4
SWH             30303.031 Hz
FIDRES          0.462388 Hz
AQ              1.0813940 sec
RG                  46341
DW                16.500 usec
DE                 4.50 usec
TE                298.0 K
D1             0.25000000 sec
d11            0.03000000 sec
MCREST    0 sec
MCWRK          0.01500000 sec

======== CHANNEL f1 ========
NUC1                  13C
P1                   7.70 usec
PL1        0 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            125.5465590 MHz
WDW                      EM
SSB       0
LB                    0.50 Hz
GB        0
PC                    2.00
```


Current Data Parameters
NAME GL2 265 3 noesy
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20130826
Time 13
INSTRUM crycon10
PROBHD 5 mm CPTCI 1H
PULPROG noesygpph
TD 2048
SOLVENT CDCl3
NS 8
DS 16
SWH 2648.305 Hz
FIDRES 1.293118 Hz
AQ 0.3867114 sec
RG 181
DW 188.800 usec
DE 6.50 usec
TE 298.0 K
D0 0.00000300 sec
D1 2.00000000 sec
D8 1.00000000 sec
IN0 0.00001880 sec
======== CHANNEL f1 ========
NUC1 1H
P1 7.50 usec
PL1 -1.00 dB
SFO1 500.2215691 MHz
F1 - Acquisition parameters
TD 1024
SFO1 500.2274 MHz
FIDRES 110.346046 Hz
SW 2.27364 ppm
FnMODE undefined
F2 - Processing parameters
SI 1024
SF01 500.2215691 MHz
WDW QSINE
SSB 2
LB 0 Hz
GB 0
PC 2.00
F1 - Processing parameters
SI 1024
MC2 TPPI
SF01 500.2215691 MHz
WDW QSINE
SSB 2
LB 0 Hz
GB 0
ppm
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
O
O
OMe
Me
1.64
noesy

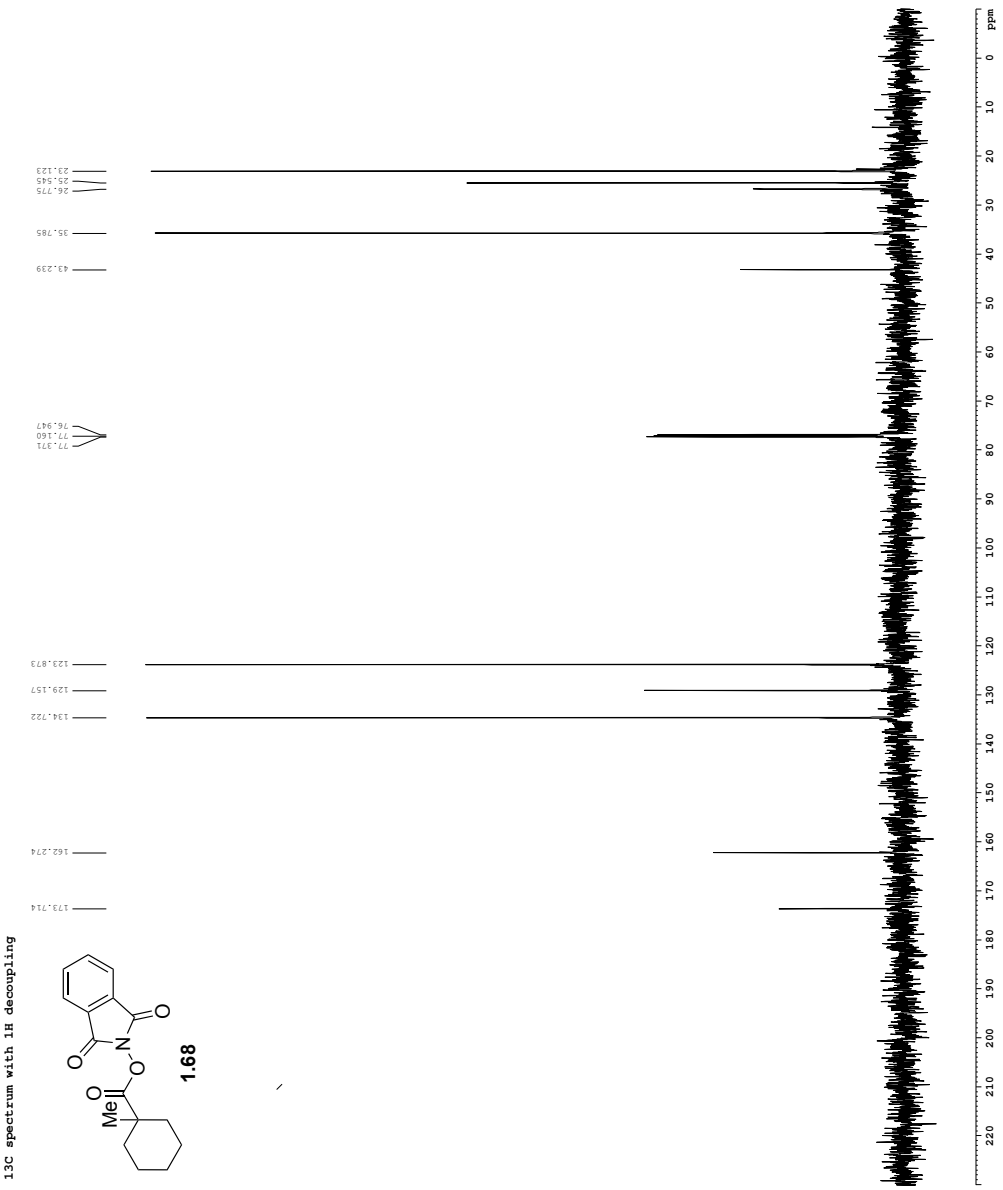

1H spectrum
Current Data Parameters
NAME GL4-44-33sh
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20140729
Time 20.35
INSTRUM av600
PROBHD 5 mm TBI 1H/13
PULPROG zg30
TD 96074
SOLVENT CDCl3
NS 8
DS 2
SWH 9615.385 Hz
FIDRES 0.098042 Hz
AQ 5.0998478 sec
RG 228
DW 52.000 usec
DE 14.54 usec
TE 298.1 K
D1 0.10000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 600.1342009 MHz
NUC1 1H
P1 8.00 usec
PLW1 23.01441956 W
F2 - Processing parameters
SI 65536
SF 600.1300343 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
7.359
7.353
7.331
7.326
7.316
7.260
5.120
5.100
5.089
5.068
2.593
2.577
2.563
1.918
1.903
1.894
1.879
1.407
1.400
1.390
1.357
1.349
1.258
1.242
1.236
1.224
1.215
1.210
1.182
1.170
0.827
4.792
2.011
1.000
1.020
1.162
9.453
3.114
Me
CO2Bn
Me
1.65
10.5
10.0
9.5
9.0
8.5
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


Z-restored spin-echo 13C spectrum with 1H decoupling
Me
CO2Bn
Me
1.65
178.034
136.261
128.639
128.372
128.254
77.413
77.159
76.905
66.270
38.117
37.663
35.377
33.269
26.504
22.113
22.070
20.731
ppm

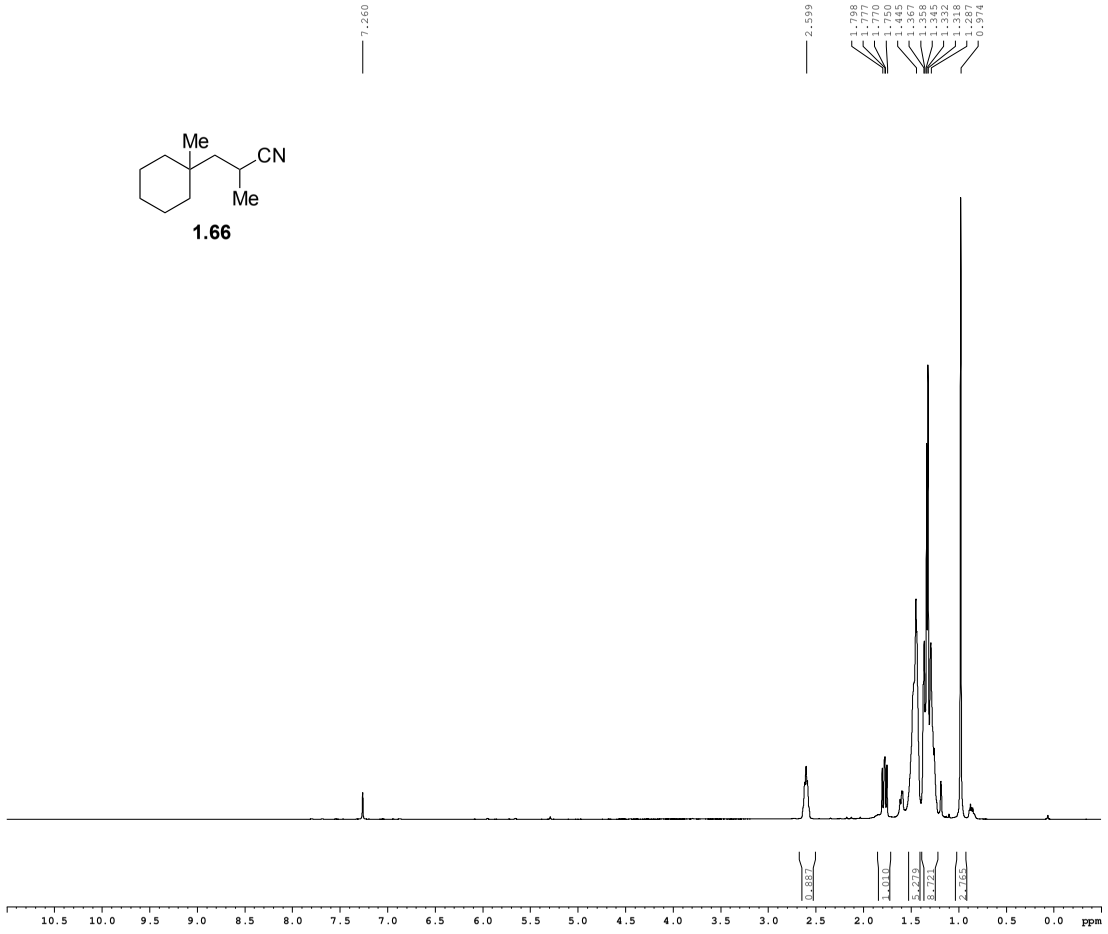
1H spectrum



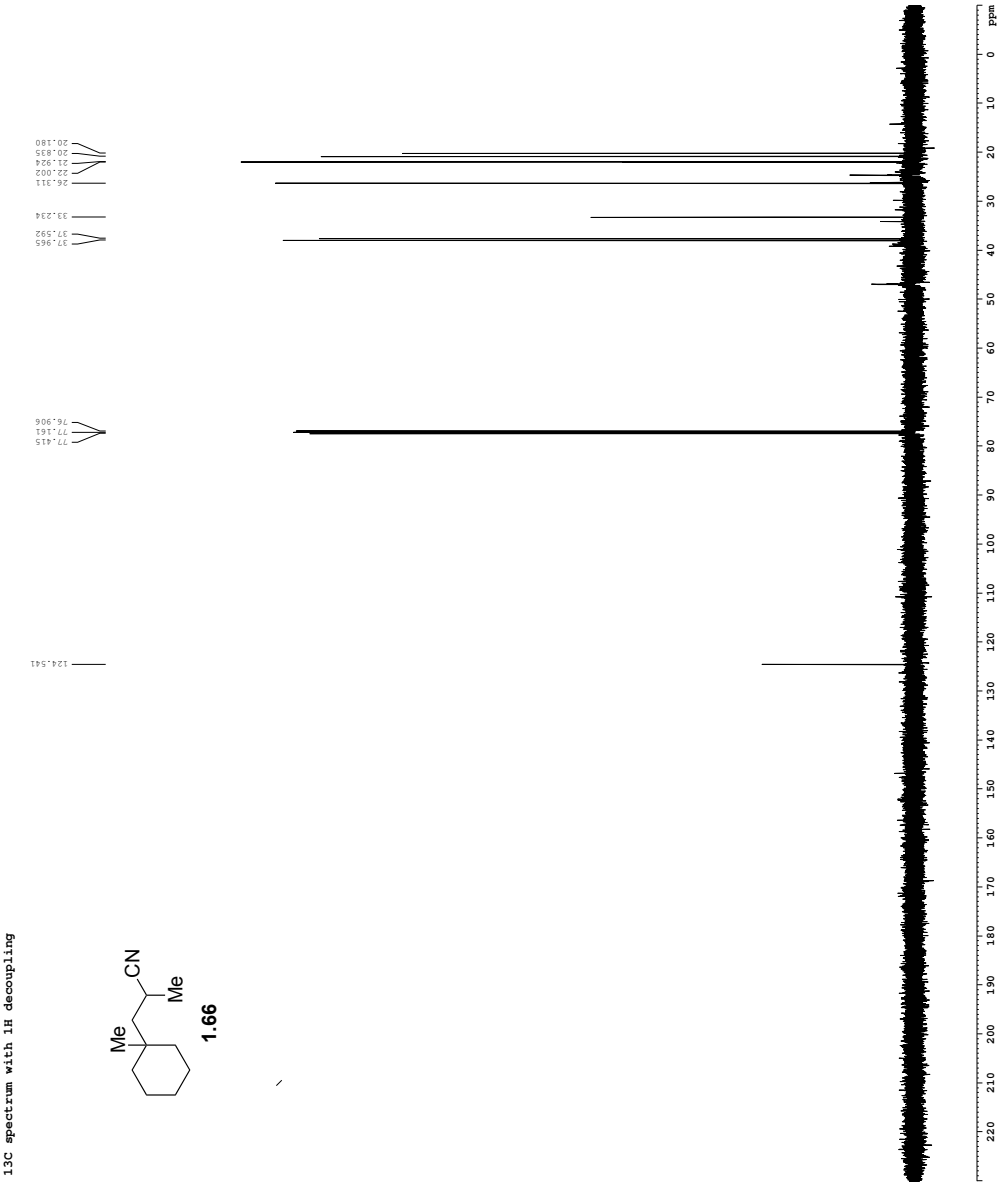

```
Current Data Parameters
NAME          GL2-165-33
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20140717
Time               17.43
INSTRUM             av600
PROBHD   5 mm TBI 1H/13
PULPROG             zg30
TD                 98074
SOLVENT           CDCl3T
NS                     8
DS                     2
SWH             9615.385 Hz
FIDRES          0.098042 Hz
AQ              5.0998478 sec
RG                    64
DW                52.000 usec
DE                 14.54 usec
TE                298.1 K
D1             0.10000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         600.1342009 MHz
NUC1                   1H
P1                  8.00 usec
PLW1        23.01441956 W

F2 - Processing parameters
SI                 65536
SF           600.1300343 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```


13C spectrum with 1H decoupling
Current Data Parameters
NAME GL2-165-3
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20130306
Time 19.33
INSTRUM 400QNP
PROBHD 5 mm TBI 1H/13
PULPROG zgdc30
TD 65536
SOLVENT CDCl3
NS 4
DS 4
SWH 36231.883 Hz
FIDRES 0.552855 Hz
AQ 0.9043968 sec
RG 362
DW 13.800 usec
DE 6.00 usec
TE 298.0 K
D1 0.40000001 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 15.00 usec
PLW1 107.15190125 W
SFO1 150.9194080 MHz
======== CHANNEL f2 ========
CPDPRG[2 waltz16
NUC2 1H
PCPD2 70.00 usec
PLW2 0 W 0.30199519 W
PLW12 600.1330010 MHz
SFO2
F2 - Processing parameters
SI 65536
SF 150.9028024 MHz
WDW EM
SSB 0
LB 5.00 Hz
GB 0
PC 1.00
173.714
162.274
134.722
129.157
123.873
77.371
77.160
76.947
43.239
35.785
26.775
25.545
23.123
1.68
ppm

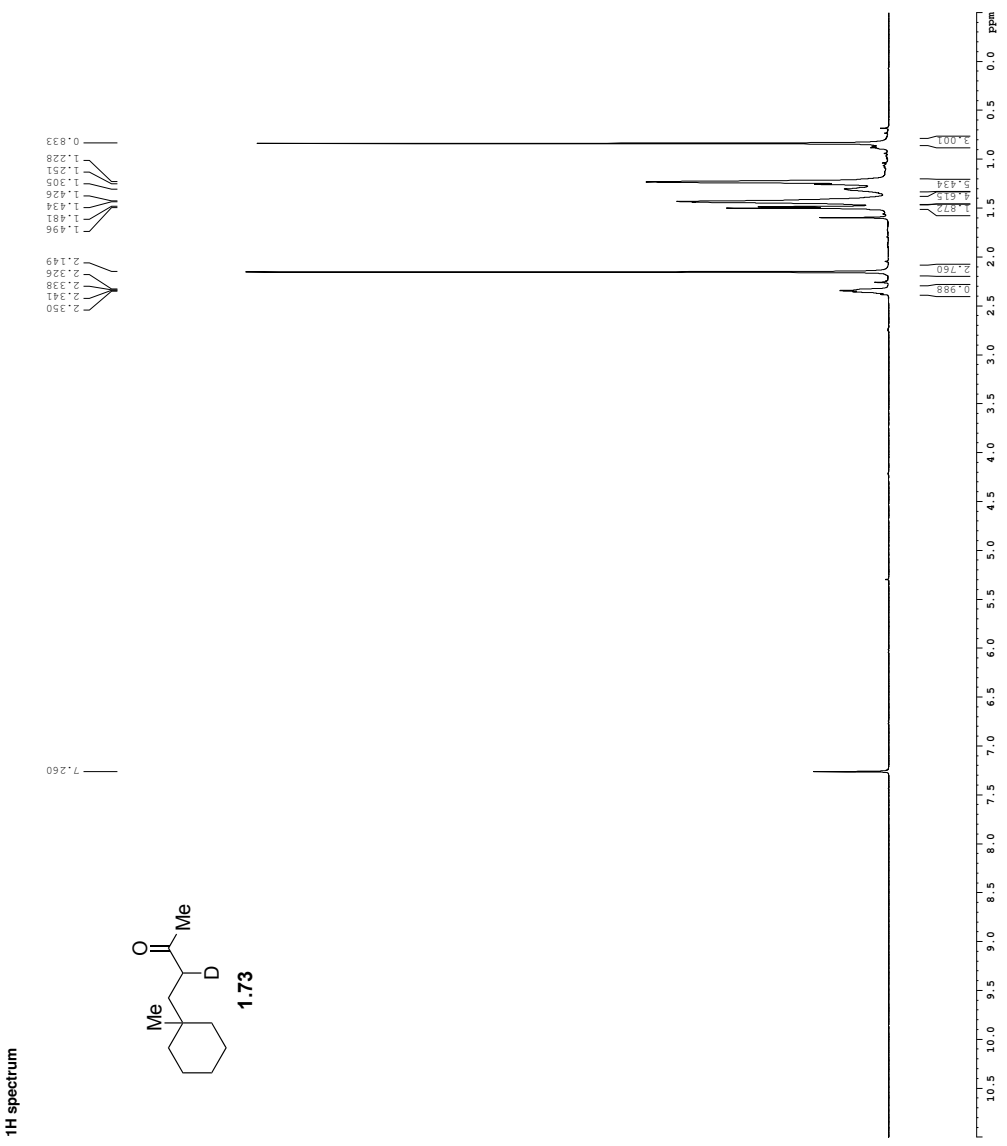
1H spectrum

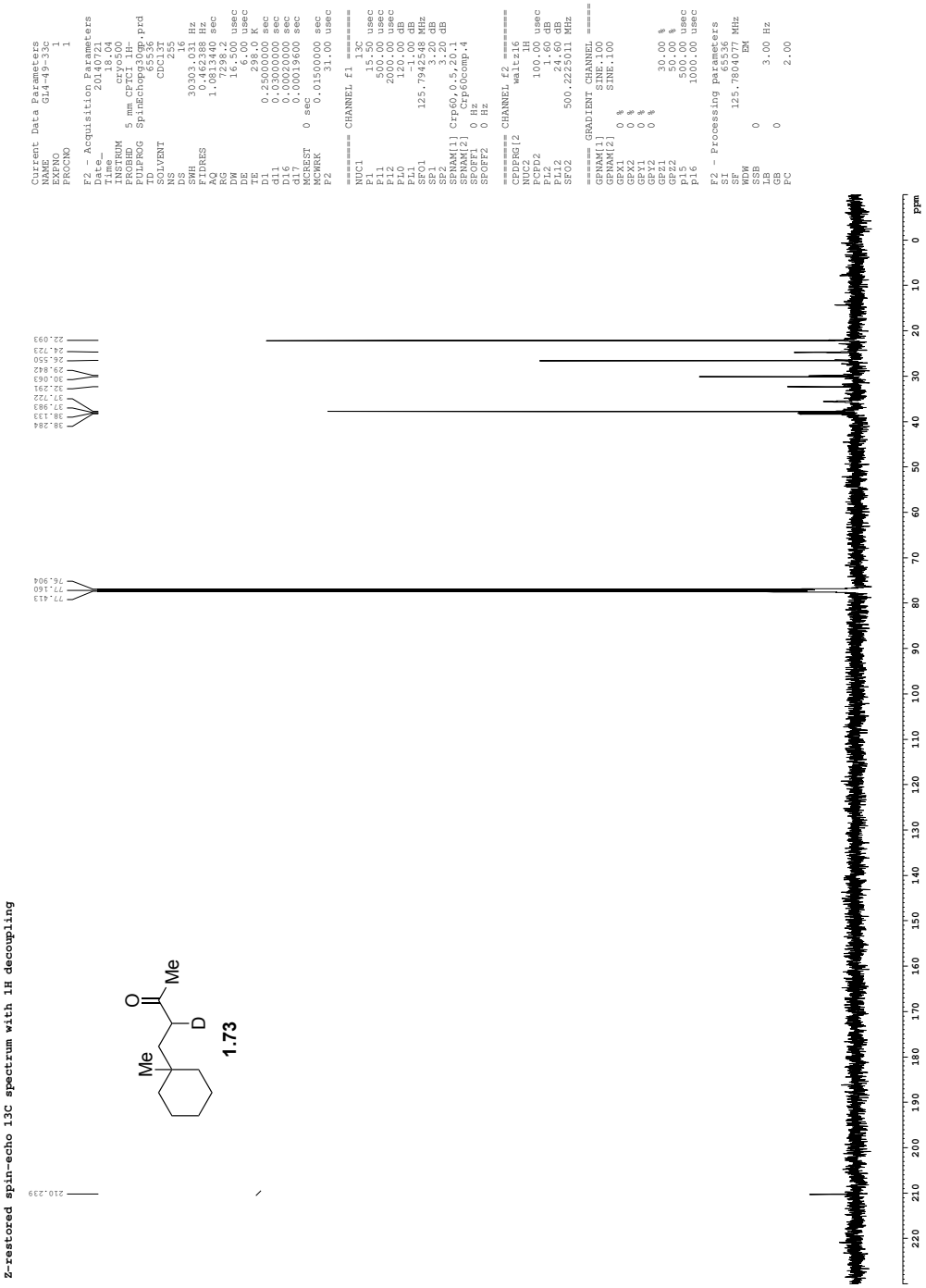



```
Current Data Parameters
NAME            GL3-74-3
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_          20131011
Time              10.03
INSTRUM           gn500
PROBHD   5 mm broadband
PULPROG            zg30
TD                81728
SOLVENT           CDCl3T
NS                     8
DS                     2
SWH            8012.820 Hz
FIDRES         0.098043 Hz
AQ             5.0998273 sec
RG                  40.3
DW                62.400 usec
DE                 6.00 usec
TE                298.0 K
D1           0.10000000 sec
MCREST    0 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           499.2900294 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

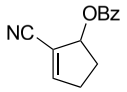

13C spectrum with 1H decoupling
Current Data Parameters
NAME GI3-74-3
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20131011
Time 10.05
INSTRUM DPX300
PROBHD 5 mm broadband
PULPROG zgdc30
TD 65536
SOLVENT CDCl3
NS 151
DS 4
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0813440 sec
RG 115.2
DW 16.500 usec
DE 4.50 usec
TE 298.0 K
D1 0.25000000 sec
D11 0.03000000 sec
MCREST 0 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 13C
P1 7.70 usec
PL1 0 dB
SFO1 125.5603801 MHz
======== CHANNEL f2 ========
CPDPRG[2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 -3.00 dB
PL12 3.20 dB
SFO2 499.2929464 MHz
F2 - Processing parameters
SI 65536
SF 125.5465620 MHz
WDW EM
SSB 0
LB 0.10 Hz
GB 0
PC 2.00
124.541
77.415
77.161
76.906
37.965
37.592
33.234
26.311
22.002
21.924
20.835
20.180
Me
CN
Me
1.66
ppm

1H spectrum


Current Data Parameters
NAME GL4-49-3
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20140704
Time 12.15
INSTRUM av600
PROBHD 5 mm TBI 1H/13
PULPROG zg30
TD 98074
SOLVENT CDCl3T
NS 8
DS 2
SWH 9615.385 Hz
FIDRES 0.098042 Hz
AQ 5.0998478 sec
RG 645
DW 52.000 usec
DE 14.65 usec
TE 298.0 K
D1 0.10000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 600.1342009 MHz
NUC1 1H
P1 8.00 usec
PLW1 23.01441956 W
F2 - Processing parameters
SI 65536
SF 600.1300345 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
7.260
0.833
1.228
1.251
1.305
1.426
1.434
1.481
1.496
2.149
2.326
2.338
2.341
2.350
3.001
5.434
4.615
1.872
2.760
0.988
ppm
Me
O
Me
D
1.73

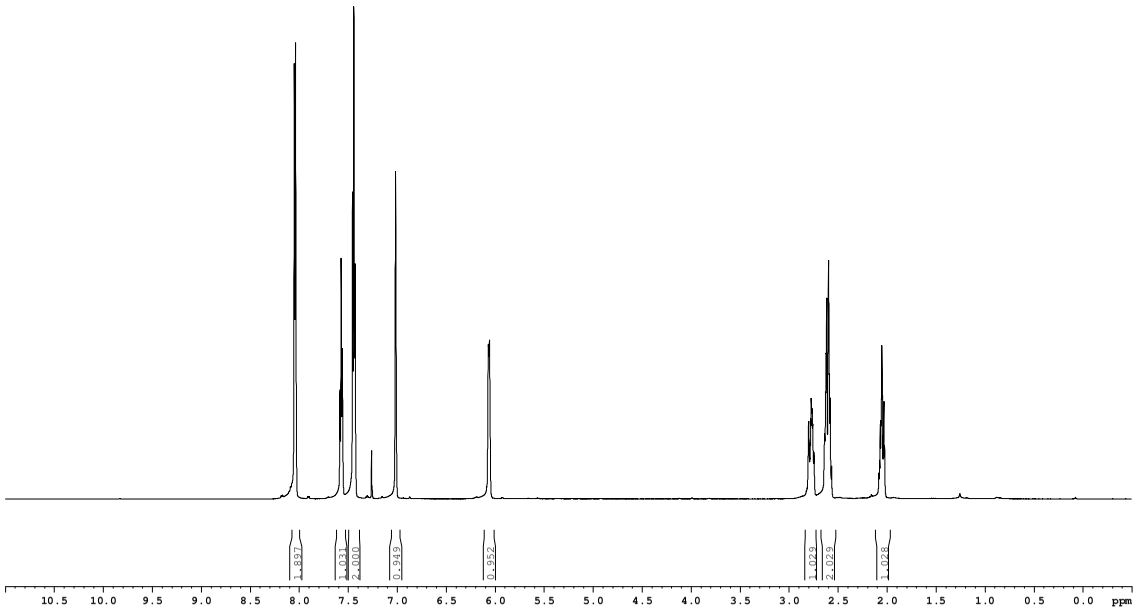

Z-restored spin-echo 13C spectrum with 1H decoupling
Me
O
Me
D
Me
1.73
ppm

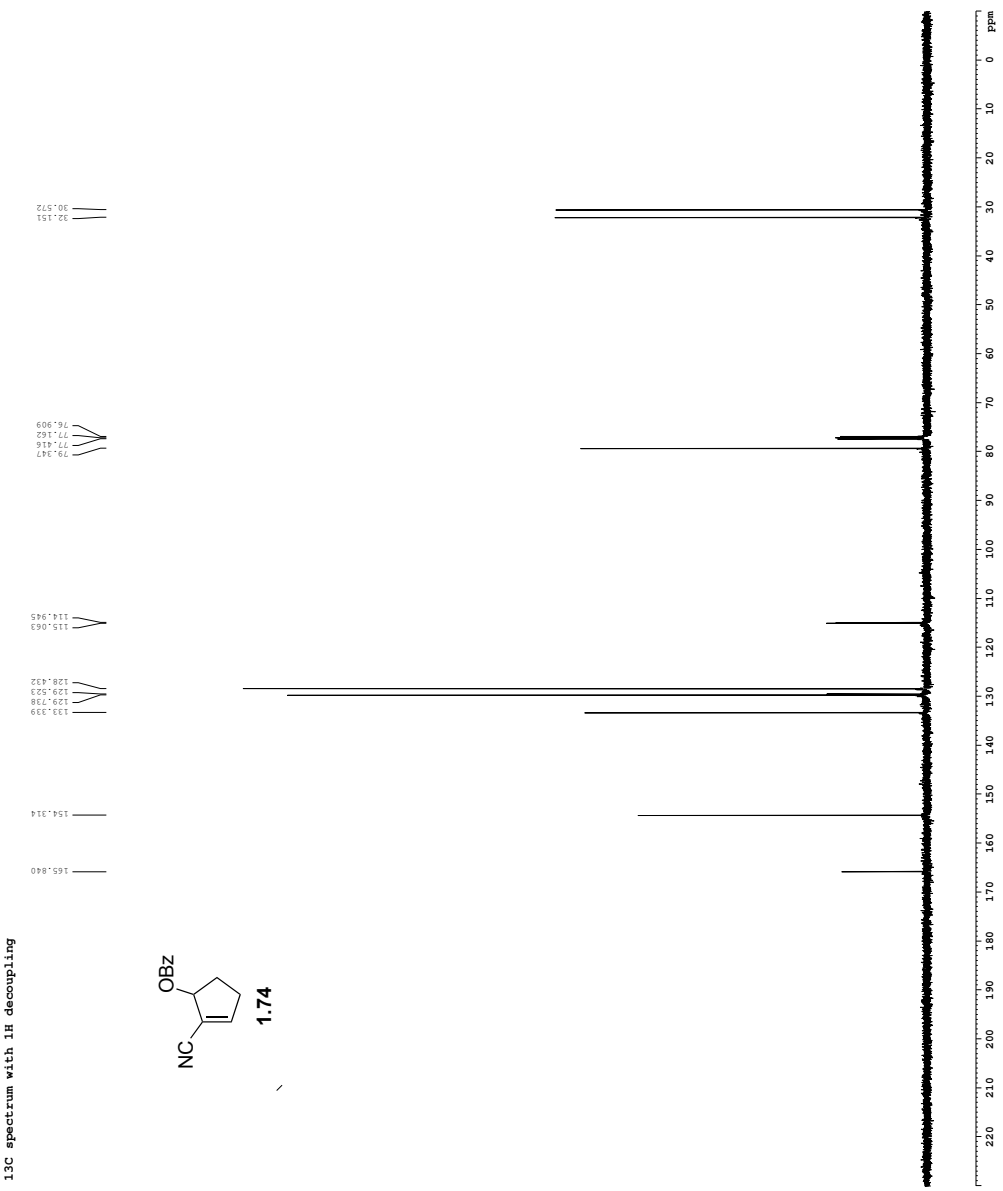
1H spectrum



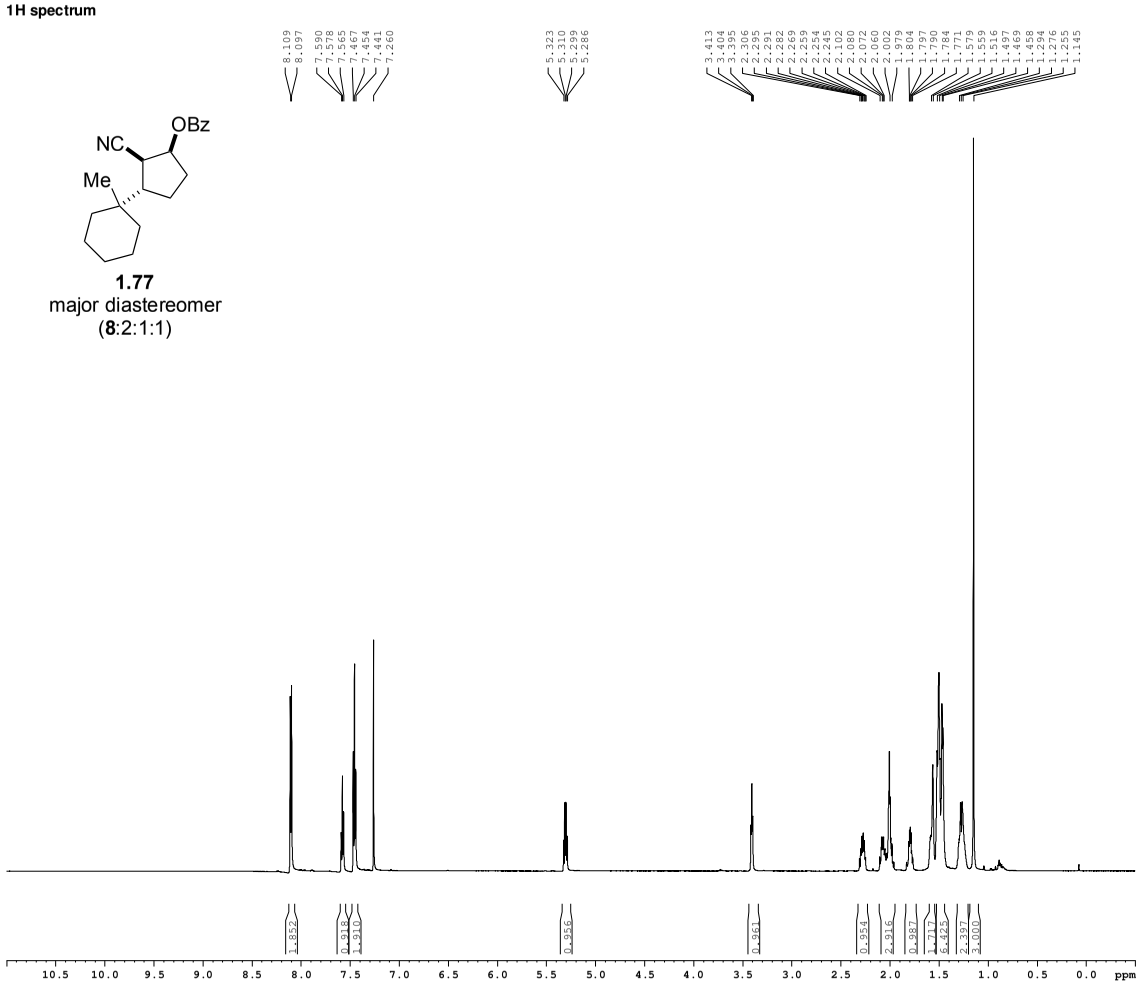
1.74

```
Current Data Parameters
NAME          GL3-272-3H
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20140722
Time               9.18
INSTRUM           av600
PROBHD   5 mm TBI 1H/13
PULPROG            zg30
TD                98074
SOLVENT           CDC13T
NS                     8
DS                     2
SWH            9615.385 Hz
FIDRES        0.098042 Hz
AQ            5.0998478 sec
RG                   101
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
PLW1       23.01441956 W

F2 - Processing parameters
SI                 65536
SF          600.1300343 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```




13C spectrum with 1H decoupling
Current Data Parameters
NAME GL3-272-3c
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20140721
Time 10.50
INSTRUM spect
PROBHD 5 mm broadband
PULPROG zgdc30
TD 65536
SOLVENT CDCl3
NS 4
DS 4
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0813440 sec
RG 16.004
DW 16.500 usec
DE 4.50 usec
TE 298.0 K
D1 0.25000000 sec
D11 0.03000000 sec
MCREST 0 sec
MCWRK 0.01500000 sec
CHANNEL f1
NUC1 13C
P1 9.00 usec
PL1 -0.60 dB
SFO1 125.5603801 MHz
CHANNEL f2
CPDPRG[2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 -3.00 dB
PL12 24.80 dB
SFO2 499.2924964 MHz
F2 - Processing parameters
SI 65536
SF 125.5465791 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00
OBz
NC
1.74
165.840
154.314
133.399
129.738
129.523
128.432
115.063
114.945
79.347
77.456
77.162
76.909
32.151
30.572
ppm

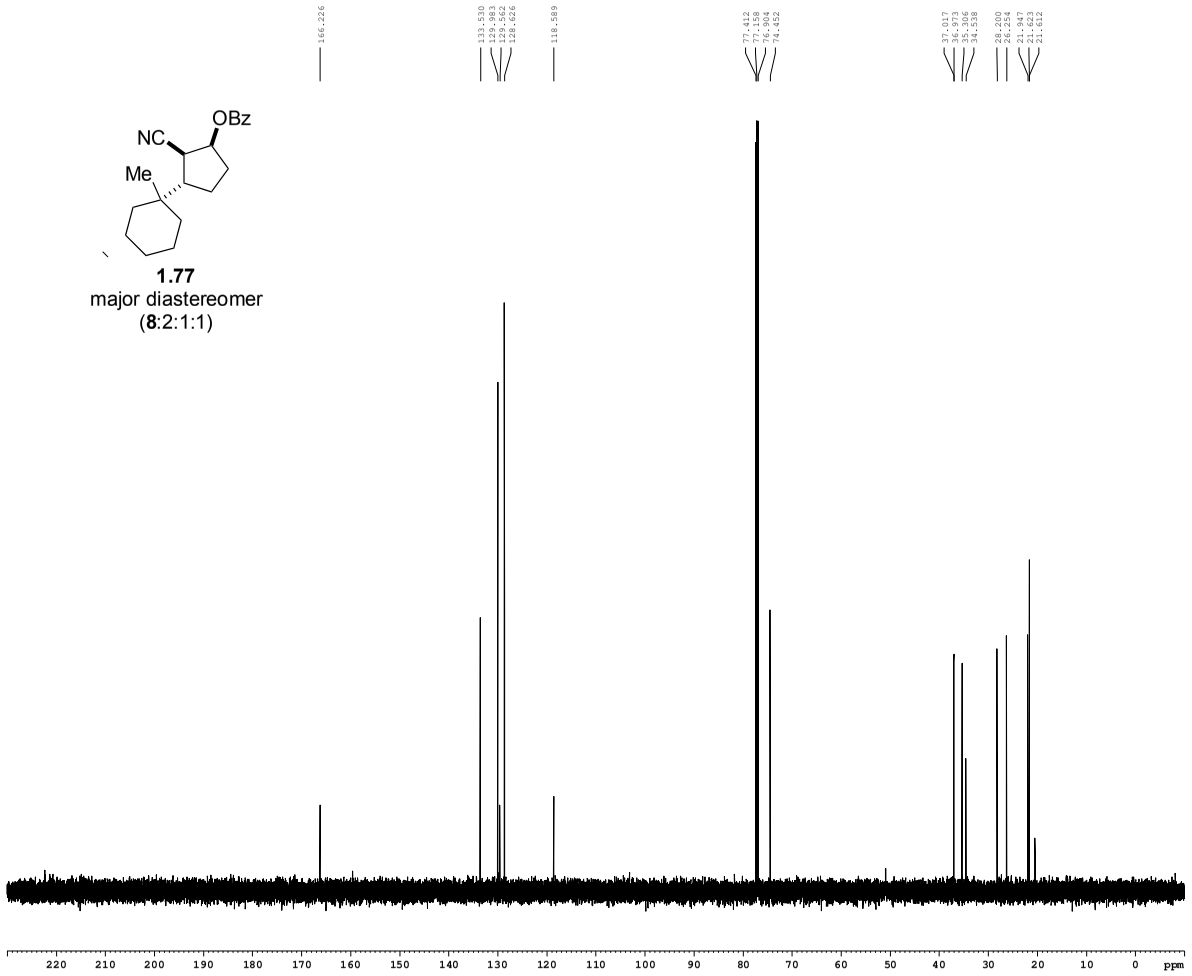
1H spectrum



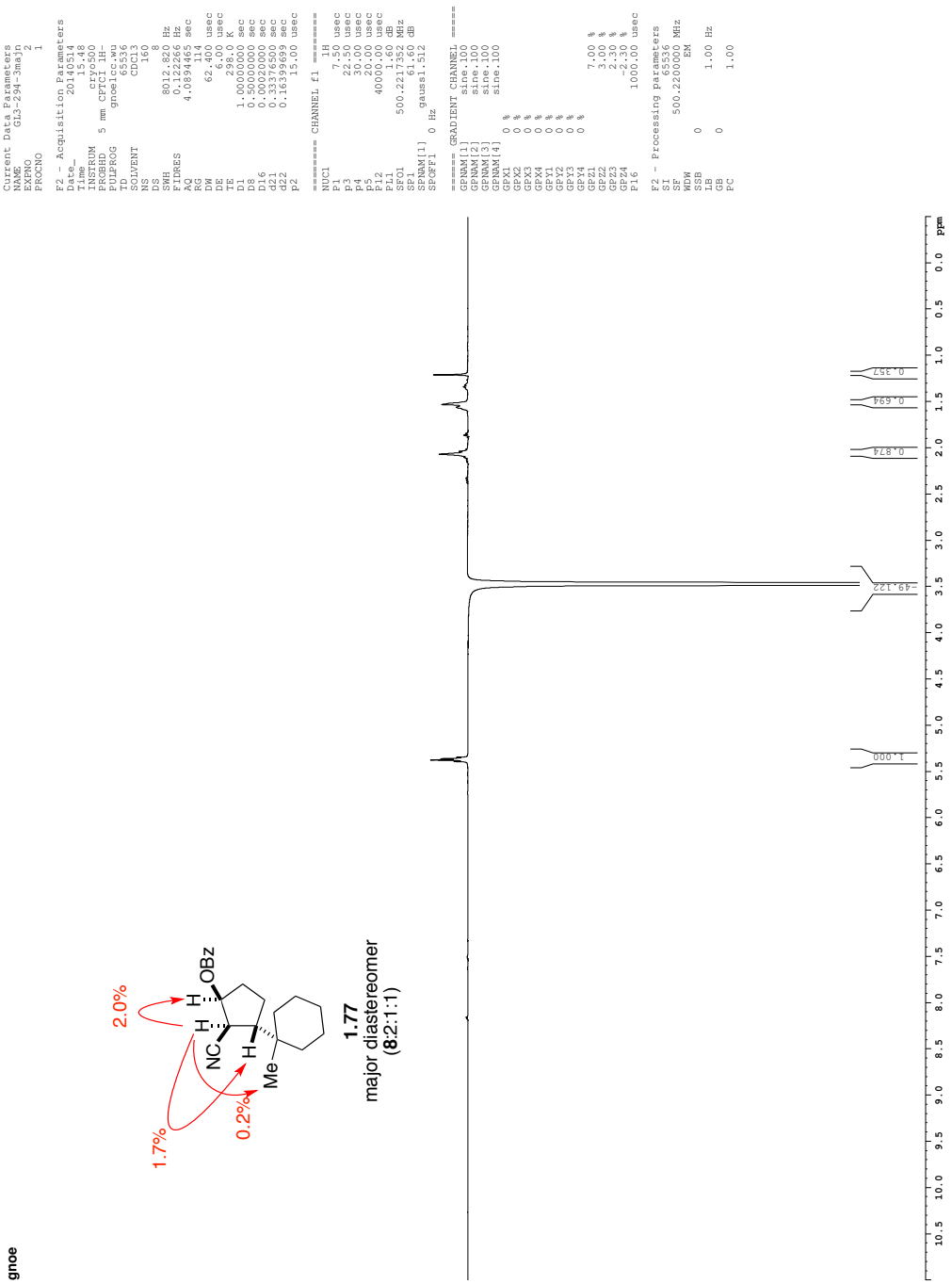
1.77
major diastereomer
(**8**:2:1:1)

```
Current Data Parameters
NAME      GL3-274-33-majh
EXPNO                   1
PROCNO                  1

F2 - Acquisition Parameters
Date_           20140730
Time               14.25
INSTRUM            av600
PROBHD   5 mm TBI 1H/13
PULPROG             zg30
TD                 98074
SOLVENT           CDC13T
NS                     8
DS                     2
SWH             9615.385 Hz
FIDRES          0.098042 Hz
AQ              5.0998478 sec
RG                   203
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
PLW1         23.01441956 W

F2 - Processing parameters
SI                 65536
SF            600.1300343 MHz
WDW                   EM
SSB        0
LB                  0.50 Hz
GB         0
PC                  1.00
```

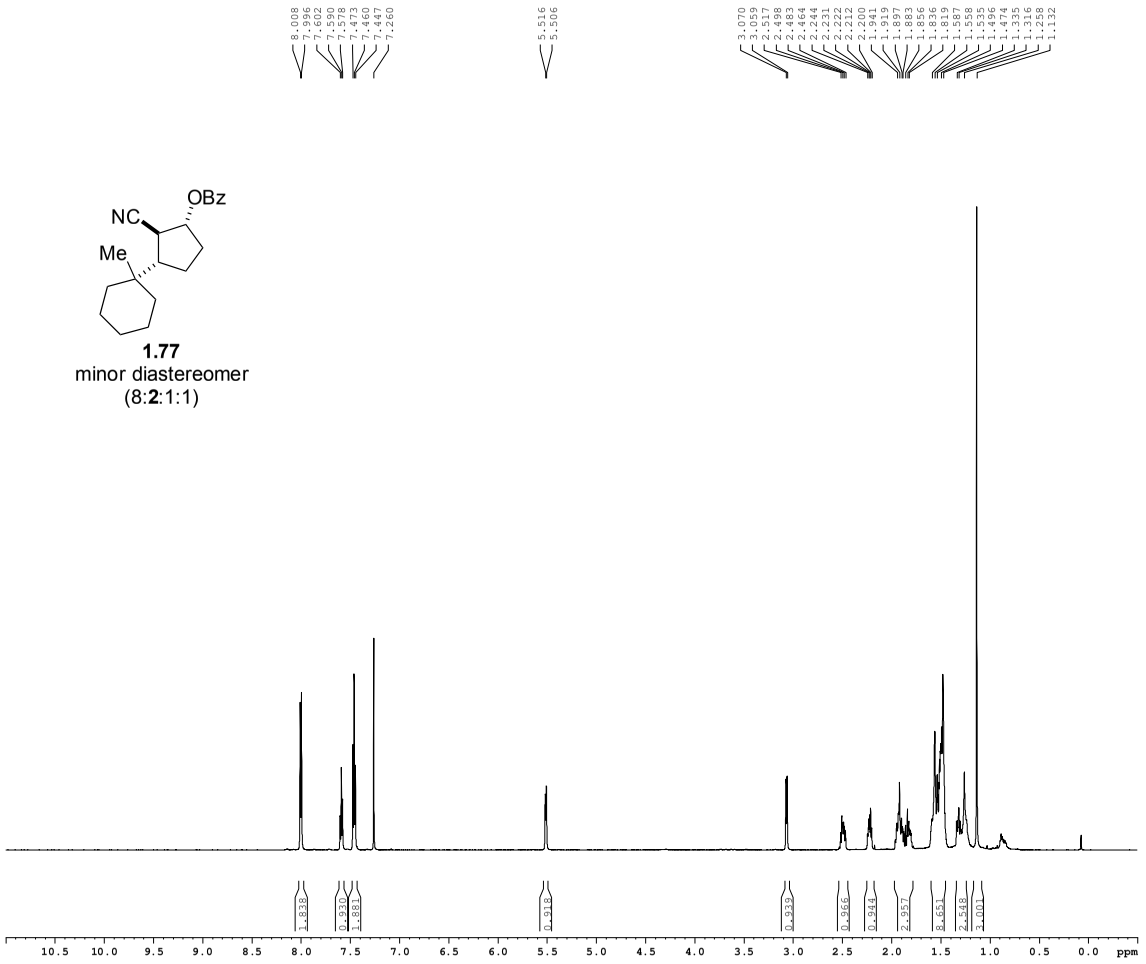
Z-restored spin-echo 13C spectrum with 1H decoupling




```
Current Data Parameters
NAME      GL3-274-33-majc
EXPNO                   1
PROCNO                  1

F2 - Acquisition Parameters
Date_          20140730
Time              14.34
INSTRUM          cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD                65536
SOLVENT           CDCl3T
NS                  215
DS                   16
SWH           30303.031 Hz
FIDRES         0.462388 Hz
AQ             1.0813440 sec
RG                2580.3
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 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
SPNAM[1] Crp60,0.5,20.1
SPNAM[2]    Crp60comp.4
SPOFF1   0 Hz
SPOFF2   0 Hz

======== CHANNEL f2 ========
CPDPRG[2         waltz16
NUC2                1H
PCPD2             100.00 usec
PL2                1.60 dB
PL12              24.60 dB
SFO2         500.2225011 MHz

====== GRADIENT CHANNEL =====
GPNAM[1]        SINE.100
GPNAM[2]        SINE.100
GPX1     0 %
GPX2     0 %
GPY1     0 %
GPY2     0 %
GPZ1              30.00 %
GPZ2              50.00 %
p15              500.00 usec
p16             1000.00 usec

F2 - Processing parameters
SI                65536
SF           125.7804082 MHz
WDW                  EM
SSB      0
LB                 0.10 Hz
GB       0
PC                 2.00
```

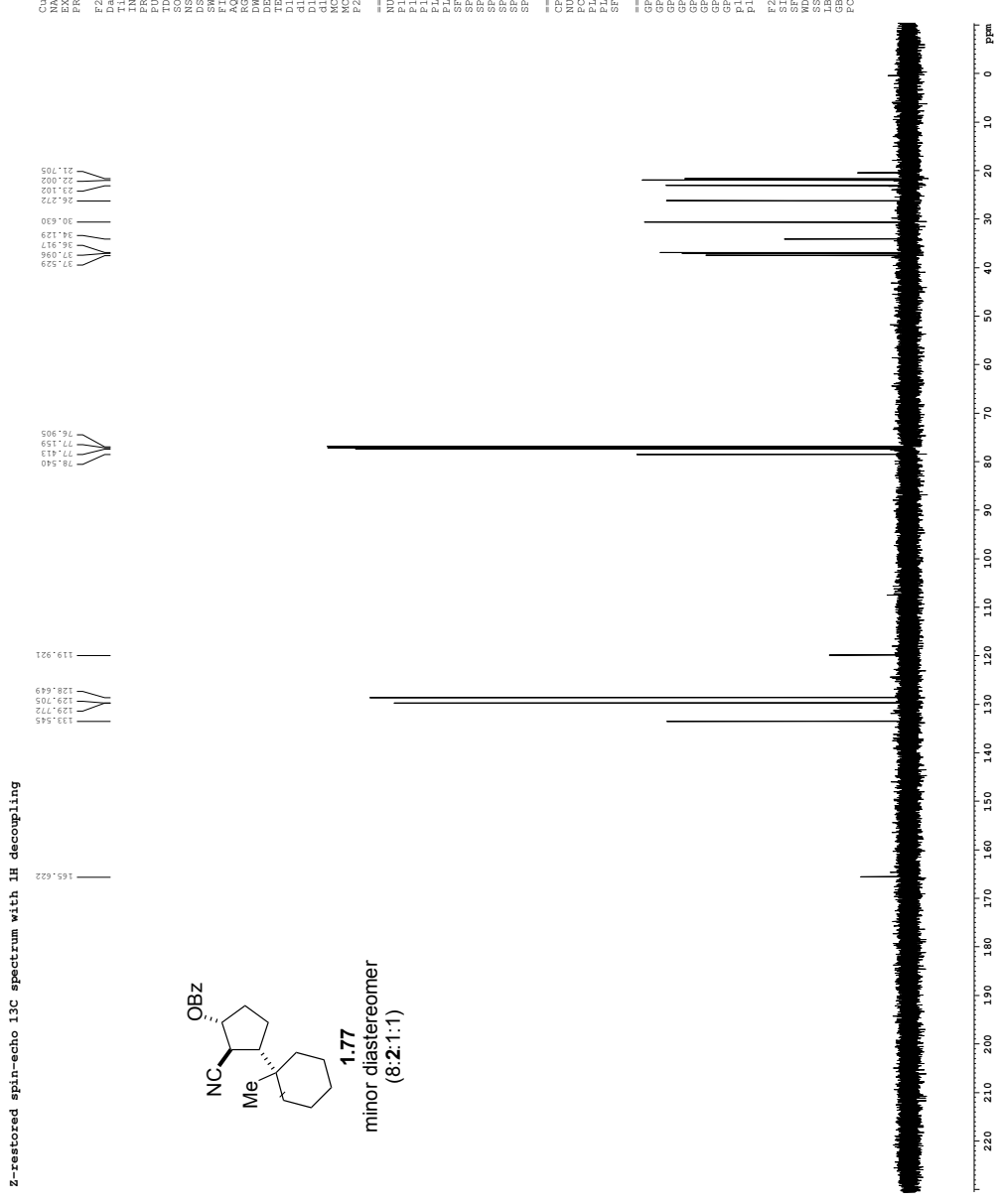

gnoe
Current Data Parameters
NAME GL3-294-3majn
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20140514
Time 15.48
INSTRUM cryo500
PROBHD 5 mm CPCI 1H-
PULPROG gncelicc.wu
TD 65536
SOLVENT CDCl3
NS 160
DS 8
SWH 8012.820 Hz
FIDRES 0.122266 Hz
AQ 4.0894465 sec
RG 114
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 1.00000000 sec
D8 0.50000000 sec
D16 0.00020000 sec
d21 0.03350000 sec
d22 0.16399699 sec
p2 15.00 usec
======== CHANNEL f1 ========
NUC1 1H
P1 7.50 usec
p3 22.50 usec
p4 30.00 usec
P5 20.00 usec
P12 40000.00 usec
P11 1.60 dB
SFO1 500.22173352 MHz
SP1 61.60 dB
SPNAM[1] gauss1.512
SPOFF1 0 Hz
====== GRADIENT CHANNEL =====
GPNAM[1] sine.100
GPNAM[2] sine.100
GPNAM[3] sine.100
GPNAM[4] sine.100
GPX1 0 %
GPX2 0 %
GPX3 0 %
GPX4 0 %
GPY1 0 %
GPY2 0 %
GPY3 0 %
GPY4 0 %
GPZ1 7.00 %
GPZ2 3.00 %
GPZ3 2.30 %
GPZ4 -2.30 %
P16 1000.00 usec
F2 - Processing parameters
SI 65536
SF 500.2200000 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.00
2.0%
1.7%
0.2%
NC
H
OBz
H
H
Me
1.77
major diastereomer
(8:2:1:1)
1.000
49.122
0.874
0.694
0.357
10.5
10.0
9.5
9.0
8.5
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

1H spectrum

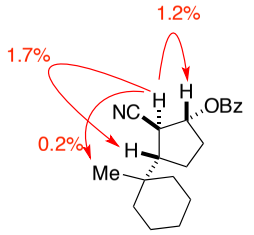


1.77
minor diastereomer
(8:**2**:1:1)

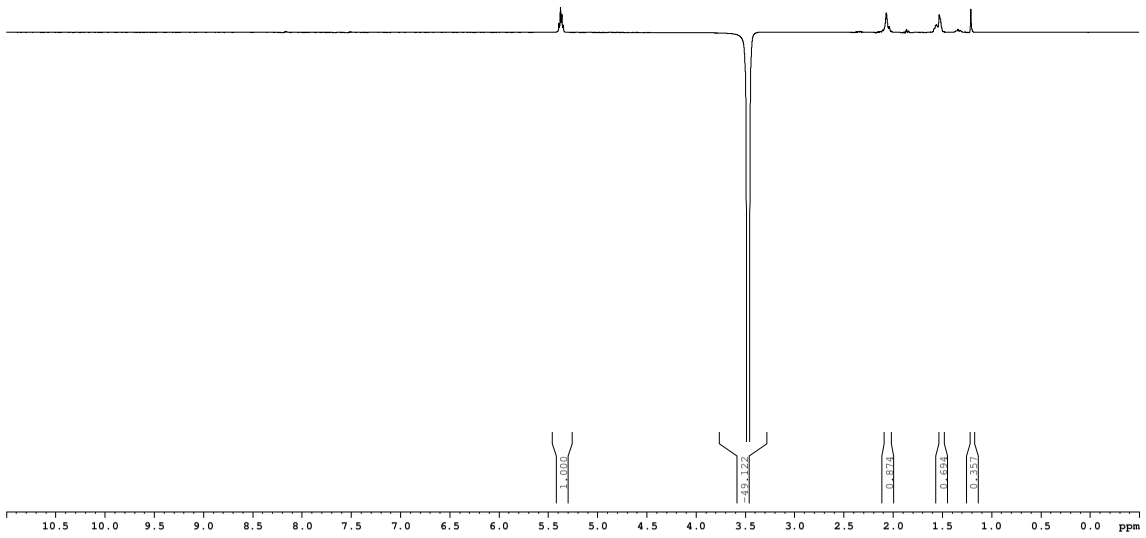
```
Current Data Parameters
NAME      GL3-273-274-topsp-3
EXPNO                       1
PROCNO                      1

F2 - Acquisition Parameters
Date_              20140730
Time                  12.14
INSTRUM               av600
PROBHD    5 mm TBI 1H/13
PULPROG               zg30
TD                   98074
SOLVENT            CDCl3T
NS                        8
DS                        2
SWH                9615.385 Hz
FIDRES            0.098042 Hz
AQ                5.0998478 sec
RG                      287
DW                   52.000 usec
DE                    14.54 usec
TE                    299.6 K
D1              0.10000000 sec
TD0                       1

======== CHANNEL f1 ========
SFO1            600.1342009 MHz
NUC1                      1H
P1                     8.00 usec
PLW1           23.01441956 W

F2 - Processing parameters
SI                    65536
SF              600.1300343 MHz
WDW                     EM
SSB       0
LB                     0.30 Hz
GB        0
PC                     1.00
```


z-restored spin-echo 13C spectrum with 1H decoupling
OBz
NC
Me
1.77
minor diastereomer
(8:2:1:1)
ppm

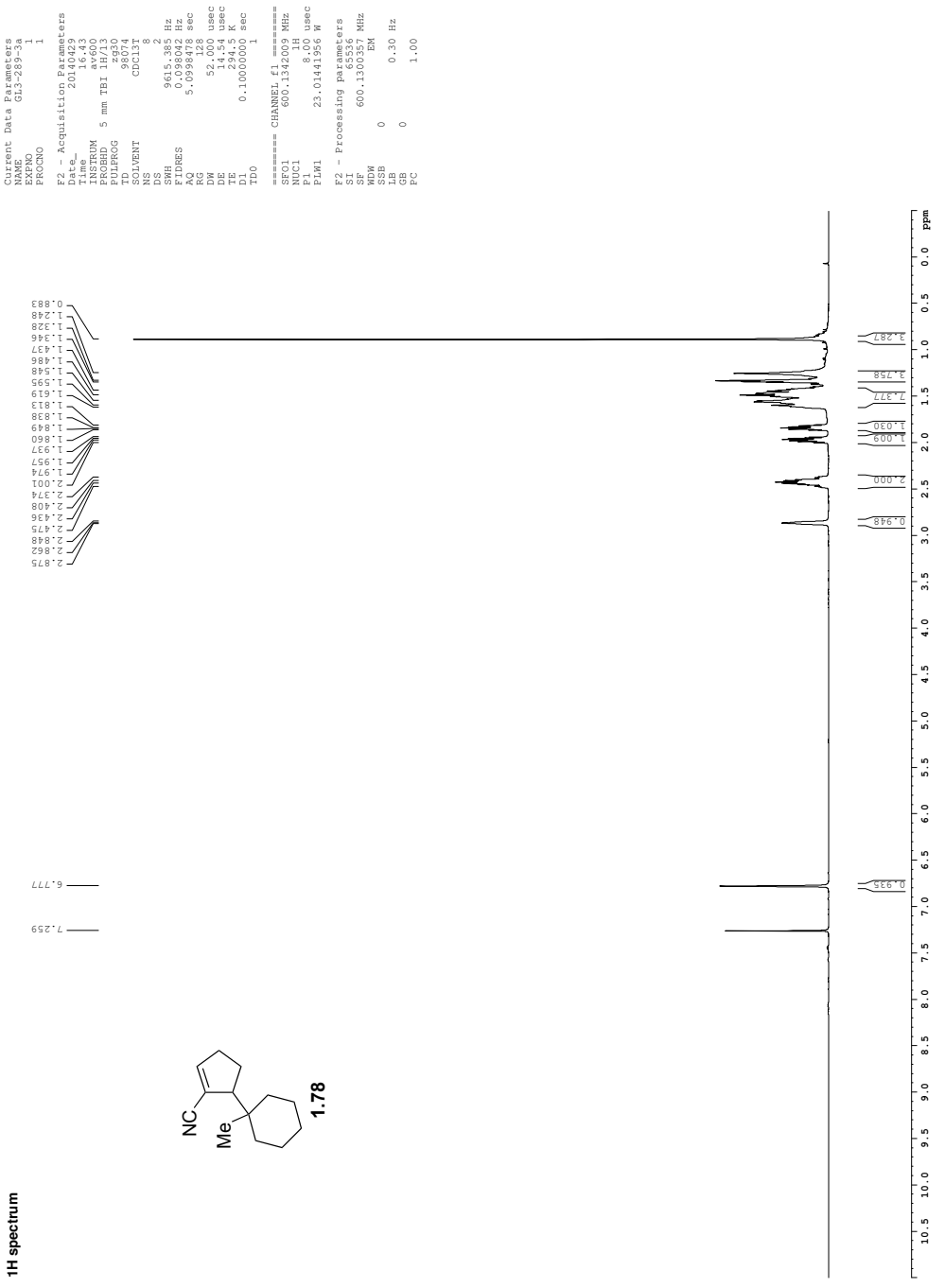
gnoe



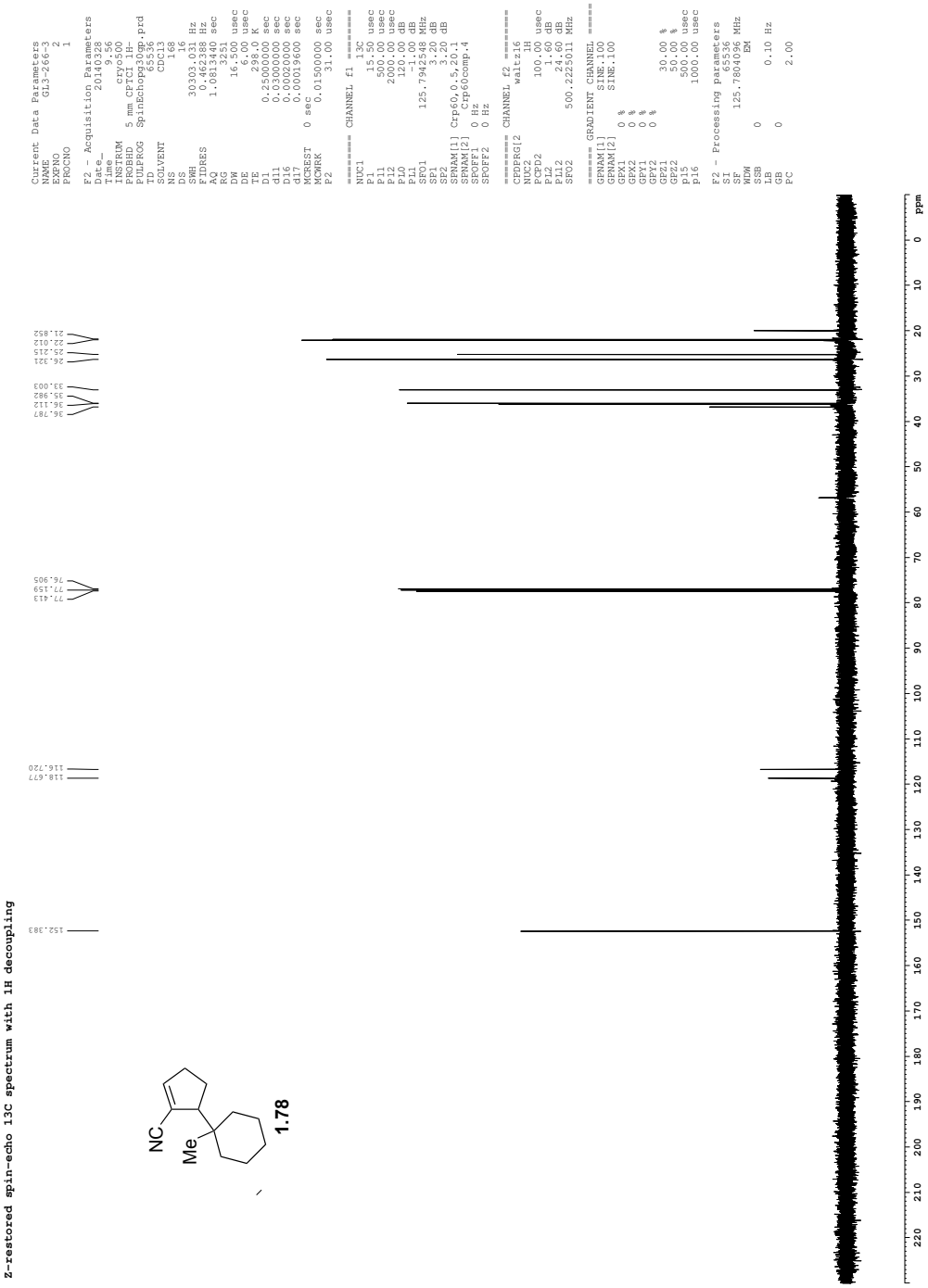
1.77
minor diastereomer
(8:**2**:1:1)



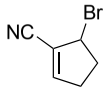

```
Current Data Parameters
NAME       GL3-294-3majn
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20140514
Time              15.48
INSTRUM         cryo500
PROBHD    5 mm CPTCI 1H-
PULPROG       gnoelcc.wu
TD                65536
SOLVENT           CDCl3
NS                  160
DS                    8
SWH            8012.820 Hz
FIDRES            0.122266 Hz
AQ             4.0894465 sec
RG                  114
DW               62.400 usec
DE                6.00 usec
TE                298.0 K
D1           1.00000000 sec
D8           0.50000000 sec
D16          0.00020000 sec
d21          0.33376500 sec
d22          0.16399699 sec
p2               15.00 usec

======== CHANNEL f1 ========
NUC1                 1H
P1                7.50 usec
p3               22.50 usec
p4               30.00 usec
p5               20.00 usec
P12           40000.00 usec
PL1                1.60 dB
SFO1        500.2217352 MHz
SP1               61.60 dB
SPNAM[1]      gauss1.512
SPOFF1    0 Hz

====== GRADIENT CHANNEL =====
GPNAM[1]        sine.100
GPNAM[2]        sine.100
GPNAM[3]        sine.100
GPNAM[4]        sine.100
GPX1      0 %
GPX2      0 %
GPX3      0 %
GPX4      0 %
GPY1      0 %
GPY2      0 %
GPY3      0 %
GPY4      0 %
GPZ1               7.00 %
GPZ2               3.00 %
GPZ3               2.30 %
GPZ4              -2.30 %
P16             1000.00 usec

F2 - Processing parameters
SI                65536
SF          500.2200000 MHz
WDW                 EM
SSB       0
LB                1.00 Hz
GB        0
PC                1.00
```


Current Data Parameters
NAME GL3-289-3a
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20140429
Time 16.43
INSTRUM spect
PROBHD 5 mm TBI 1H/13
PULPROG zg30
TD 98074
SOLVENT CDCl3T
NS 8
DS 2
SWH 9615.385 Hz
FIDRES 0.098042 Hz
AQ 5.0998478 sec
RG 128
DW 52.000 usec
DE 14.54 usec
TE 294.5 K
D1 0.10000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 600.1342009 MHz
NUC1 1H
P1 8.00 usec
PLW1 23.01441956 W
F2 - Processing parameters
SI 65536
SF 600.1300357 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
0.883
1.248
1.328
1.346
1.437
1.486
1.548
1.595
1.619
1.813
1.838
1.849
1.860
1.937
1.957
1.974
2.001
2.374
2.408
2.436
2.475
2.848
2.862
2.875
7.259
6.777
0.935
1.287
1.758
1.377
1.030
1.009
2.000
0.948
NC
Me
1.78
ppm

1H spectrum

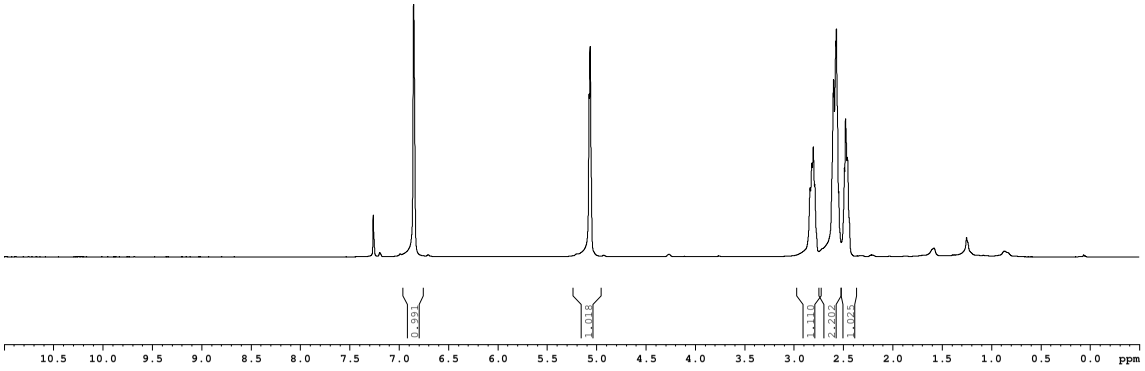

Z-restored spin-echo 13C spectrum with 1H decoupling
NC
Me
1.78
ppm

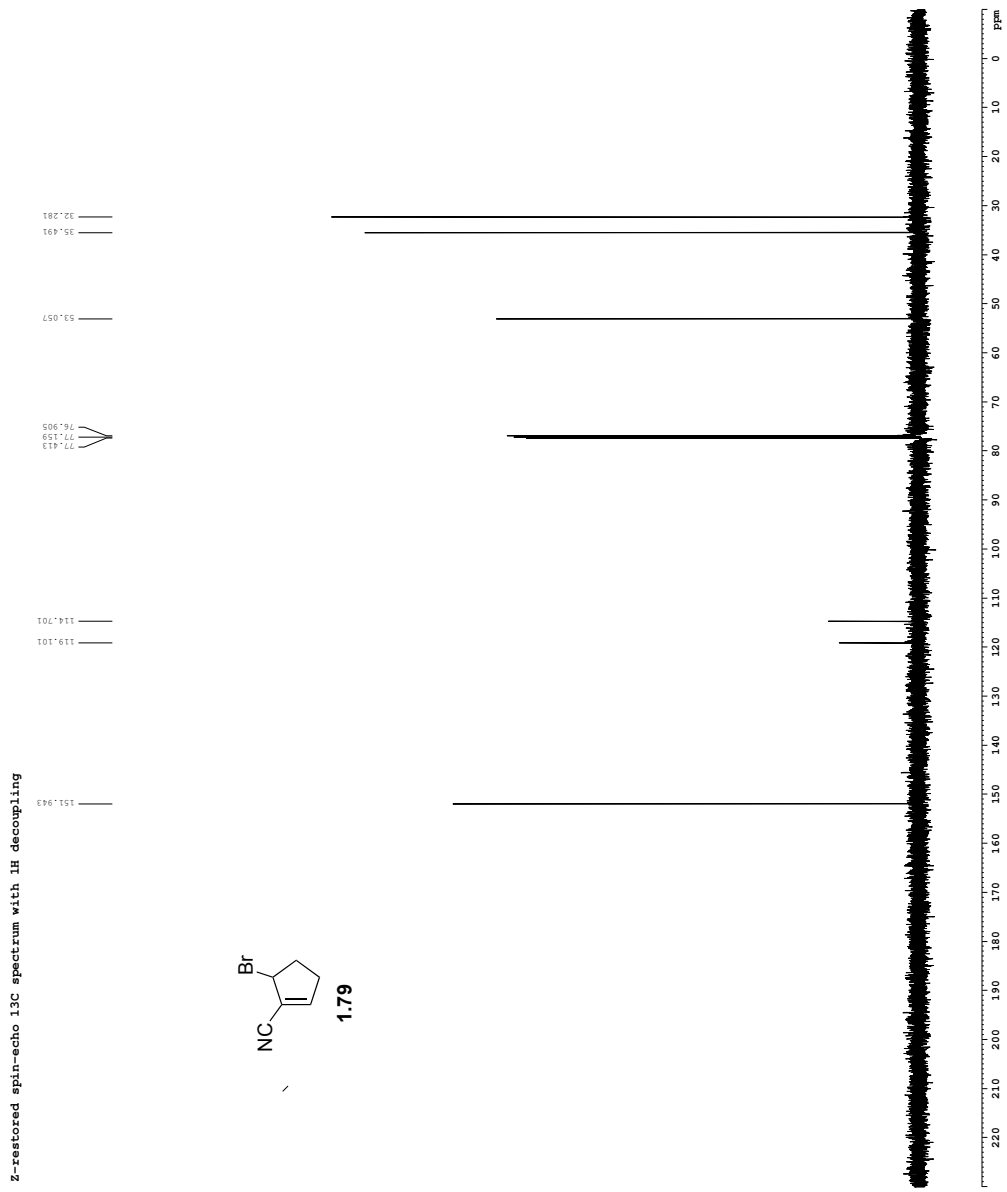
1H spectrum

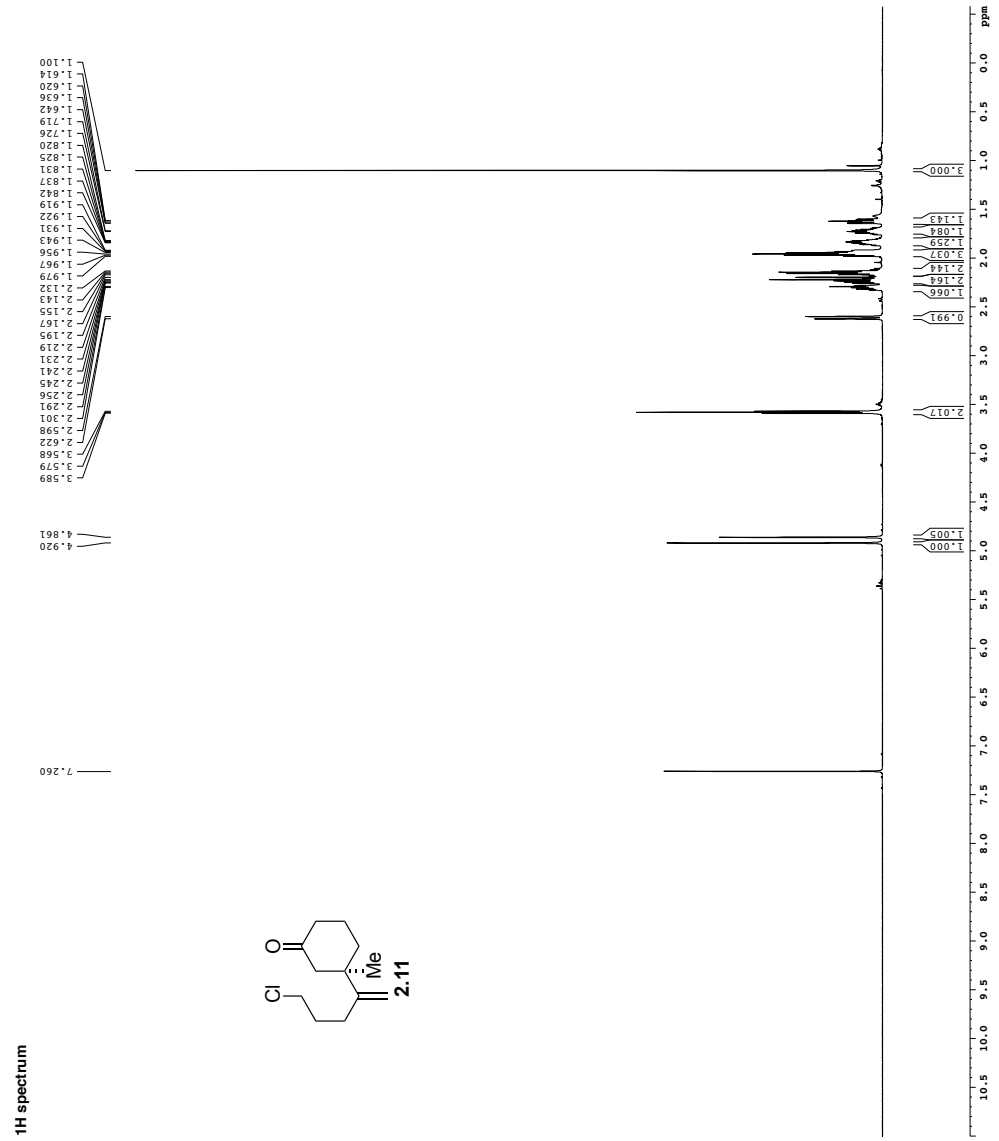


1.79

```
Current Data Parameters
NAME          GL3-291-3r
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20140722
Time               11.53
INSTRUM            av600
PROBHD   5 mm TBI 1H/13
PULPROG             zg30
TD                 98074
SOLVENT           CDCl3T
NS                     8
DS                     2
SWH             9615.385 Hz
FIDRES          0.098042 Hz
AQ              5.0998478 sec
RG                   228
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
PLW1         23.01441956 W

F2 - Processing parameters
SI                 65536
SF           600.1300341 MHz
WDW                   EM
SSB       0
LB                  2.00 Hz
GB        0
PC                  1.00
```

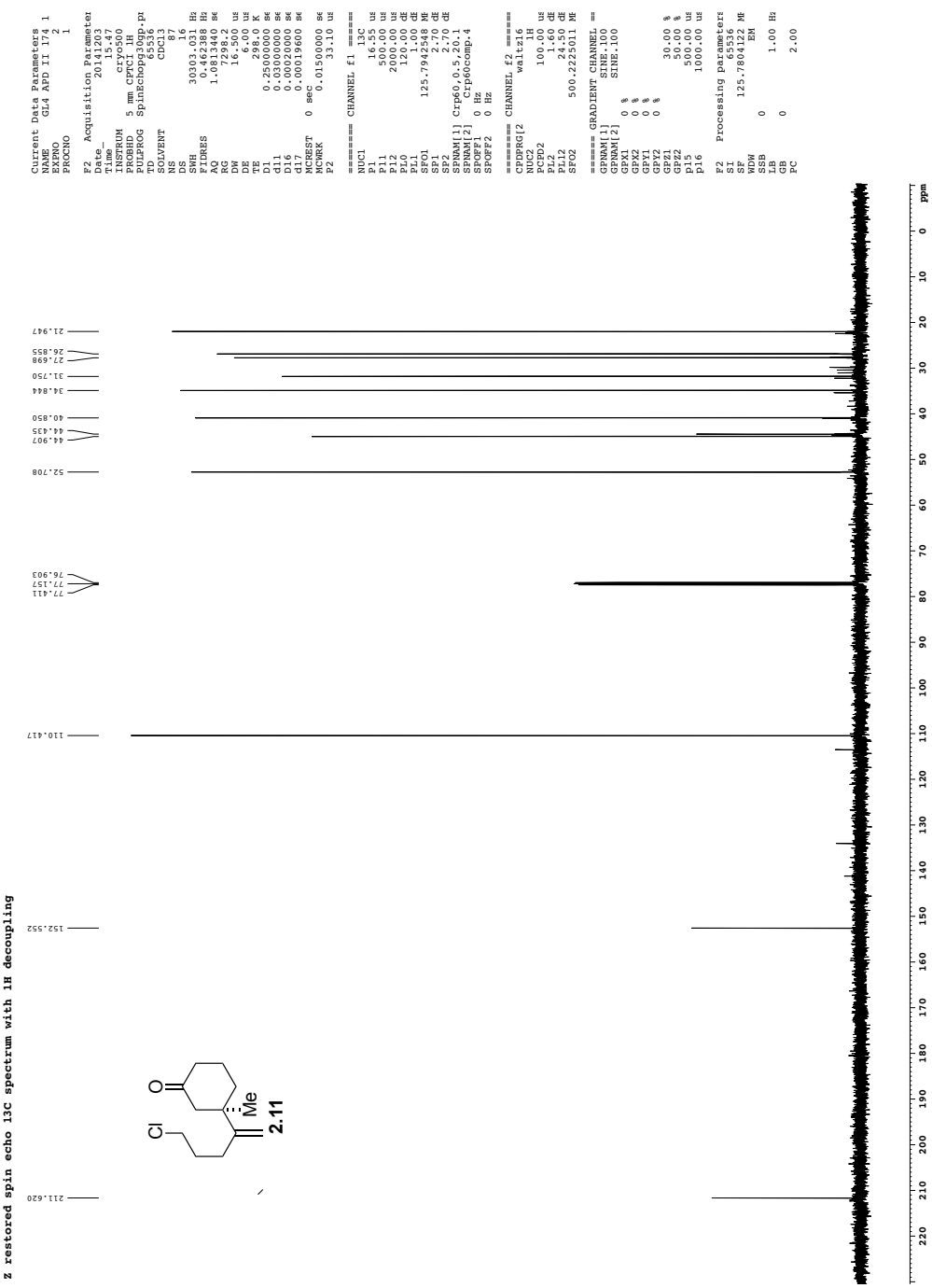



Z-restored spin-echo 13C spectrum with 1H decoupling
Br
NC
1.79
151.943
119.101
114.701
77.413
77.159
76.905
53.057
35.491
32.281
ppm

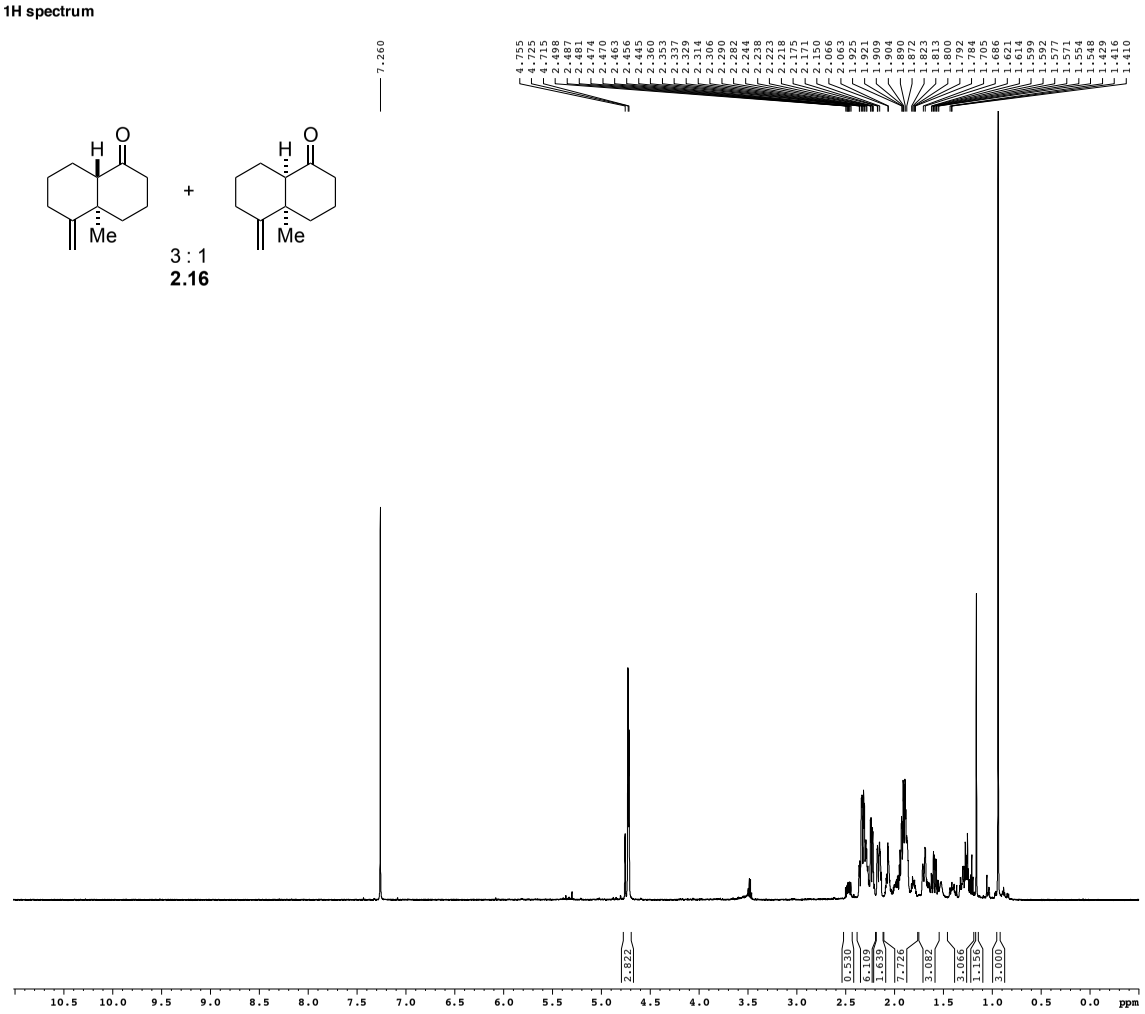


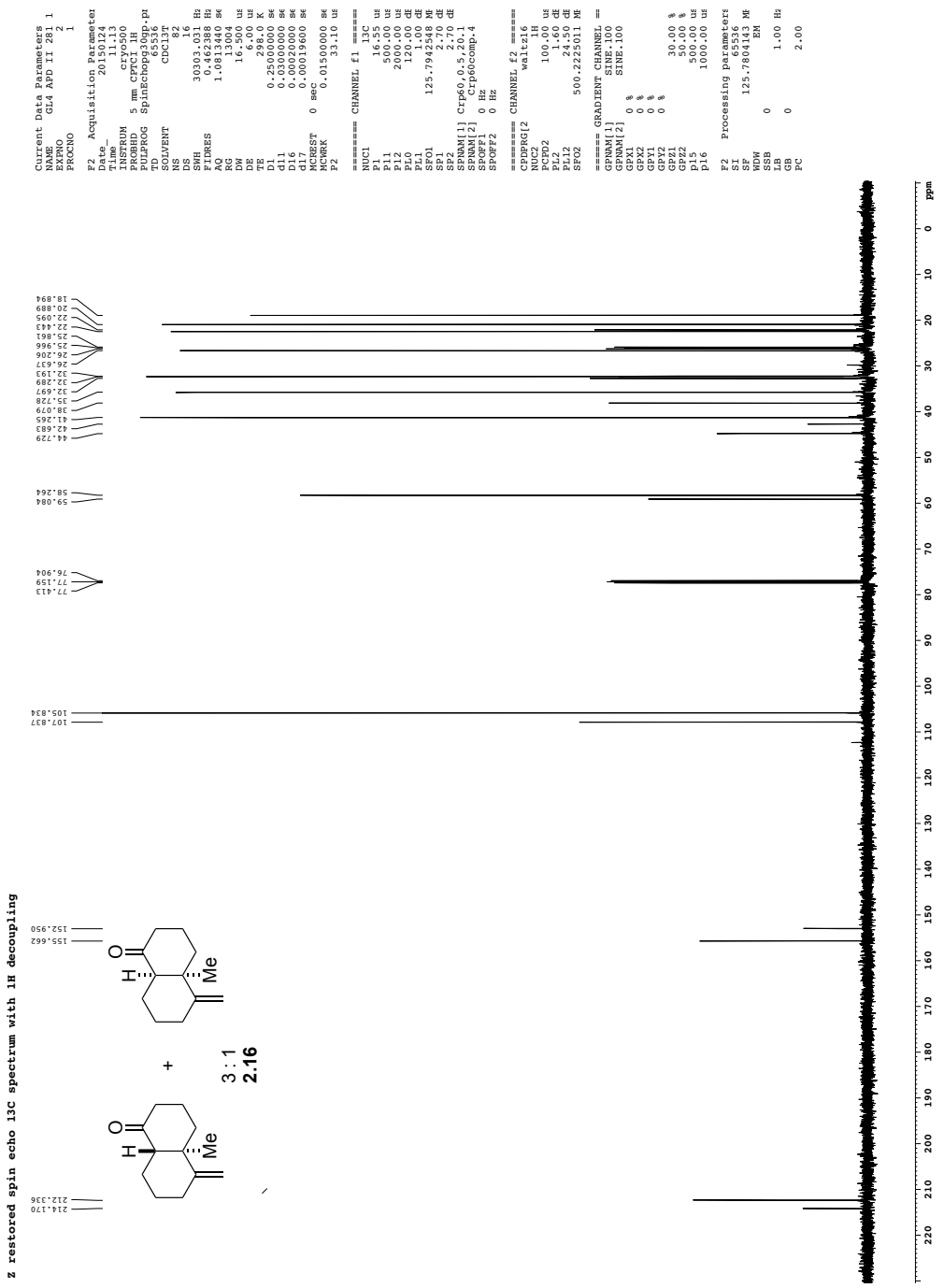
1H spectrum

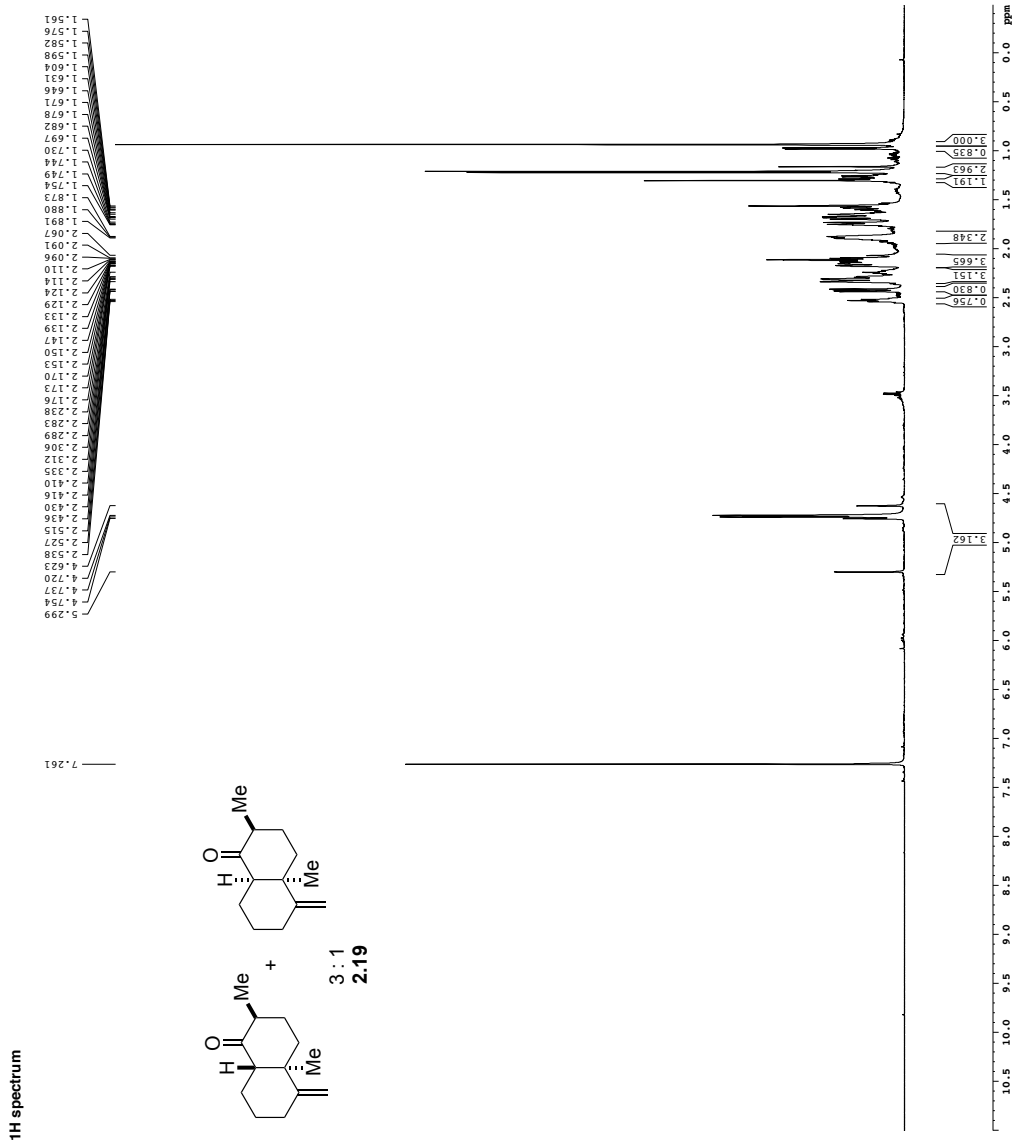
2.11


z restored spin echo 13C spectrum with 1H decoupling
Current Data Parameters
NAME GL4 APD 11 174 1
EXPNO 2
PROCNO 1
F2 - Acquisition Parameter
Date_ 20141203
Time 15.47
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H
PULPROG SpinEchopg30gp.pr
TD 65536
SOLVENT CDCl3
NS 87
DS 16
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0813440 sec
RG 2798.2
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 sec 0.01500000 sec
MCWRK 33.10 usec
P2
======== 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
SPNAM[1] Crp60,0.5,20.1
SPNAM[2] Crp60comp.4
SPOFF1 0 Hz
SPOFF2 0 Hz
======== CHANNEL f2 ======
CPDPRG[2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 1.00 dB
PL12 24.50 dB
SFO2 500.2225011 MHz
====== GRADIENT CHANNEL =
GPNAM[1] SINE.100
GPNAM[2] SINE.100
GPX1 0 %
GPX2 0 %
GPY1 0 %
GPY2 0 %
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
211.620
152.552
110.417
77.411
77.157
76.903
52.708
44.907
44.635
40.850
34.844
31.750
27.698
26.855
21.947
Cl
O
Me
2.11
ppm

1H spectrum


7.260
4.755
4.725
4.715
2.498
2.487
2.481
2.474
2.470
2.463
2.456
2.445
2.360
2.353
2.337
2.329
2.314
2.306
2.290
2.282
2.244
2.238
2.223
2.218
2.175
2.171
2.150
2.066
2.063
1.925
1.921
1.909
1.904
1.890
1.872
1.823
1.813
1.800
1.792
1.784
1.705
1.686
1.621
1.614
1.599
1.592
1.577
1.571
1.554
1.548
1.429
1.416
1.410
H
O
Me
+
H
O
Me
3 : 1
2.16
Current Data Parameters
NAME APD II 240 1
EXPNO 1
PROCNO 1
F2 Acquisition Parameters
Date_ 20131108
Time 15.12
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 5.0998478 sec
RG 812
DW 52.000 usec
DE 14.54 usec
TE 298.1 K
D1 0.10000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 8.00 usec
PLW1 23.01441956 W
SFO1 600.1342009 MHz
F2 Processing parameters
SI 65536
SF 600.1300358 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
2.822
0.530
6.109
1.639
7.726
3.082
3.066
1.156
3.000
10.5 10.0 9.5 9.0 8.5 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

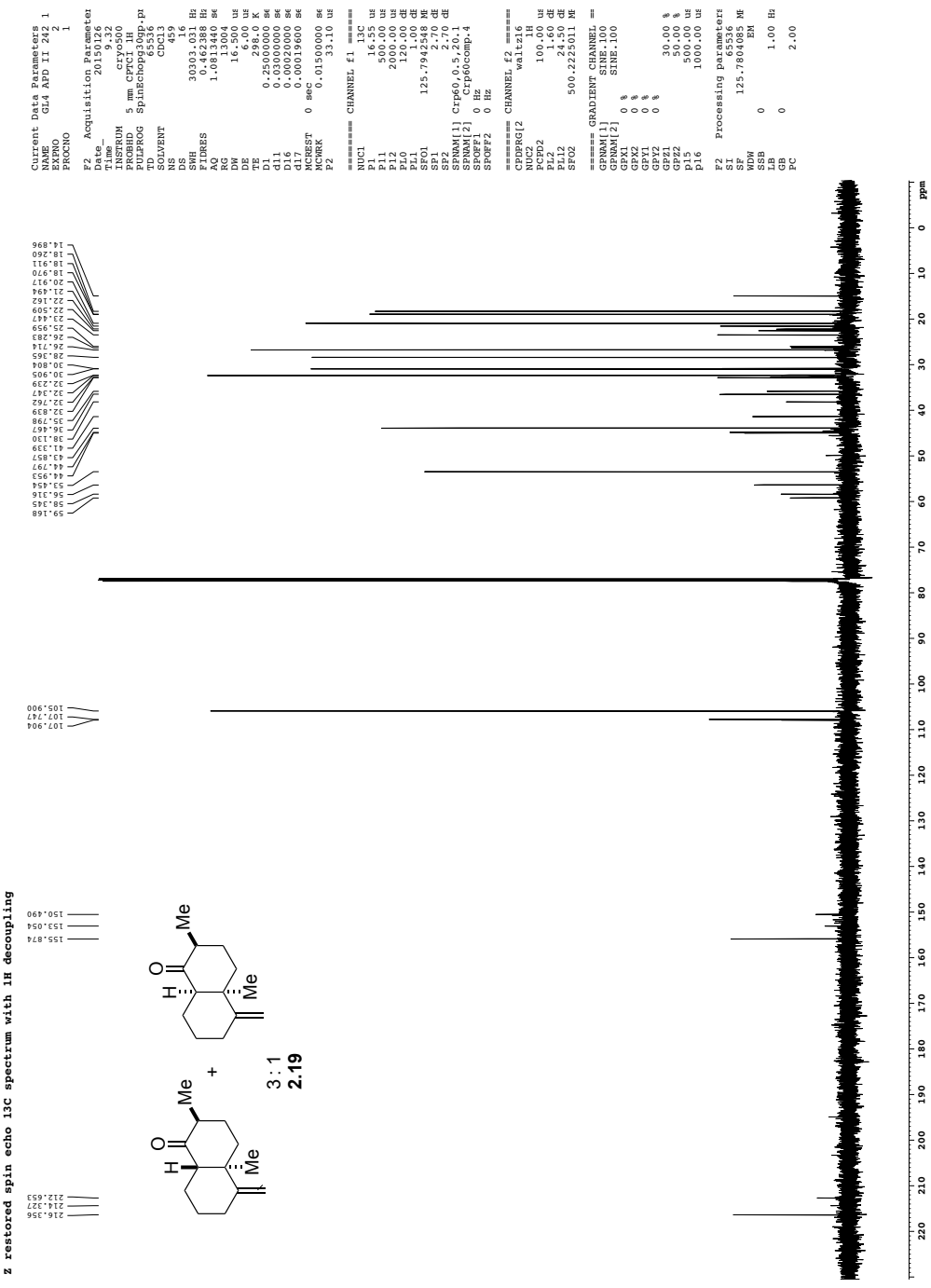

z restored spin echo 13C spectrum with 1H decoupling
Current Data Parameters
NAME Gl4 APD 11 28 1
EXPNO 2 1
PROCNO 1
F2 - Acquisition Parameter
Date_ 20150724
Time 11.13
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H
PULPROG SpinEchopg3dgp.pt
TD 65536
SOLVENT CDCl3
NS 82
DS 16
SWH 30303.031 Hz
FIDRES 0.462080 Hz
AQ 1.0813440 sec
RG 13004
DW 16.500 us
DE 6.00 us
TE 298.0 K
D1 0.25000000 sec
d11 0.03000000 sec
d16 0.00020000 sec
d17 0.00019600 sec
MCREST 0 sec 0.01500000 sec
MCWRK 0.01500000 sec
P2 33.10 us
======== CHANNEL f1 ======
NUC1 13C
P1 16.15 us
PL1 500.00 us
P12 2000.00 us
PL0 120.00 dB
PL1 1.00 dB
SFO1 125.7942564 MHz
SP1 2.70 dB
SP2 2.70 dB
SPNAM[1] Crp60,0.5,20.1
SPNAM[2] Crp60comp.4
SPOFF1 0 Hz
SPOFF2 0 Hz
======== CHANNEL f2 ======
CPDPRG[2 waltz16
NUC2 1H
PCPD2 100.00 us
PL2 1.60 dB
PL12 24.50 dB
SFO2 500.2225011 MHz
====== GRADIENT CHANNEL ==
GPNAM[1] SINE.100
GPNAM[2] SINE.100
GPX1 0 %
GPX2 0 %
GPY1 0 %
GPY2 0 %
GPZ1 30.00 %
GPZ2 50.00 %
p15 500.00 us
p16 1000.00 us
F2 - Processing parameters
SI 65536
SF 125.7804143 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00
214.170
212.336
155.662
152.950
107.837
105.834
77.413
77.159
76.904
59.084
58.264
44.729
42.683
41.265
38.079
35.728
32.697
32.289
32.193
26.637
26.206
25.966
25.861
22.643
22.095
20.889
18.894
O
H
Me
+
3 : 1
2.16
ppm

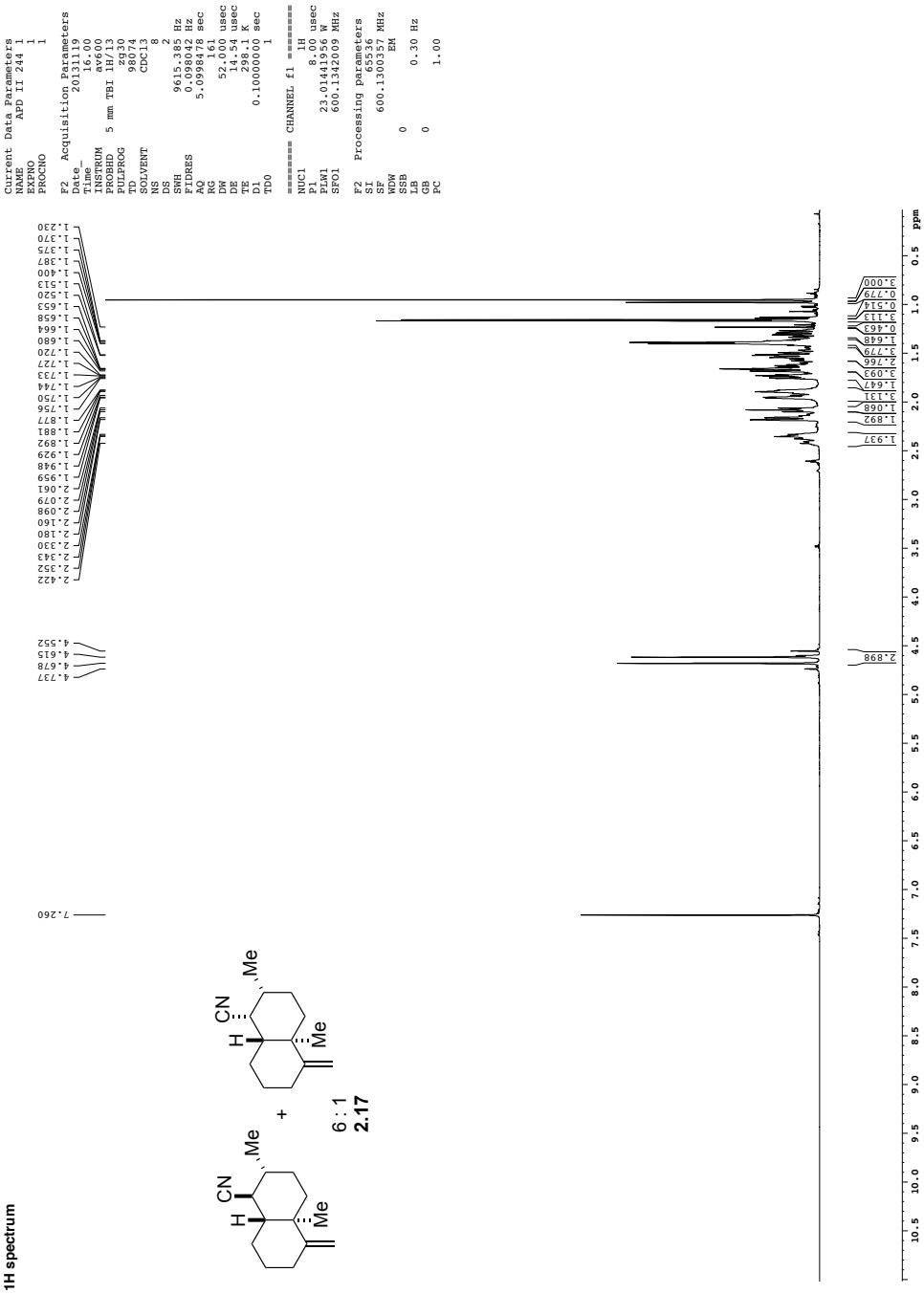


1H spectrum

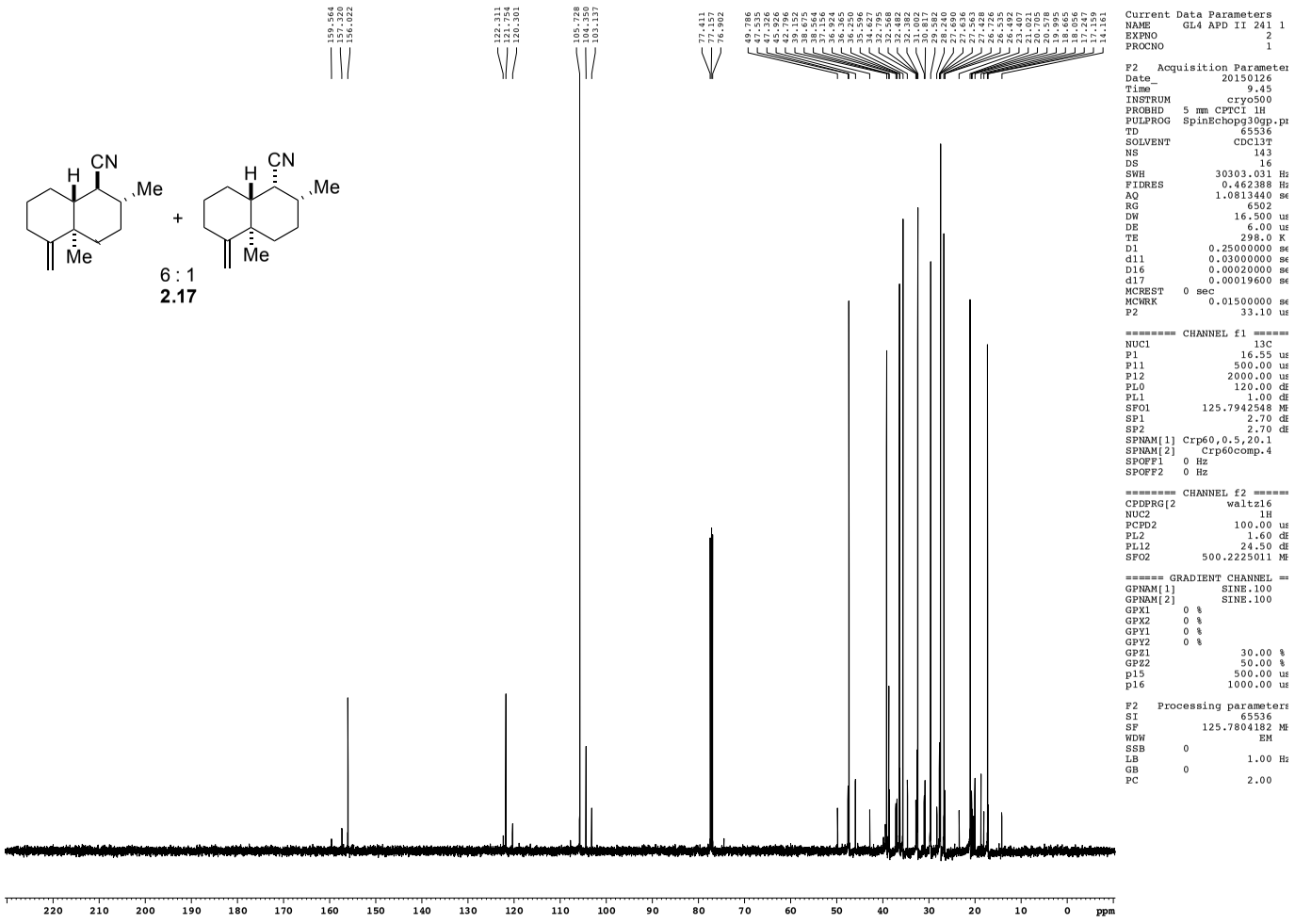
3 : 1

2.19

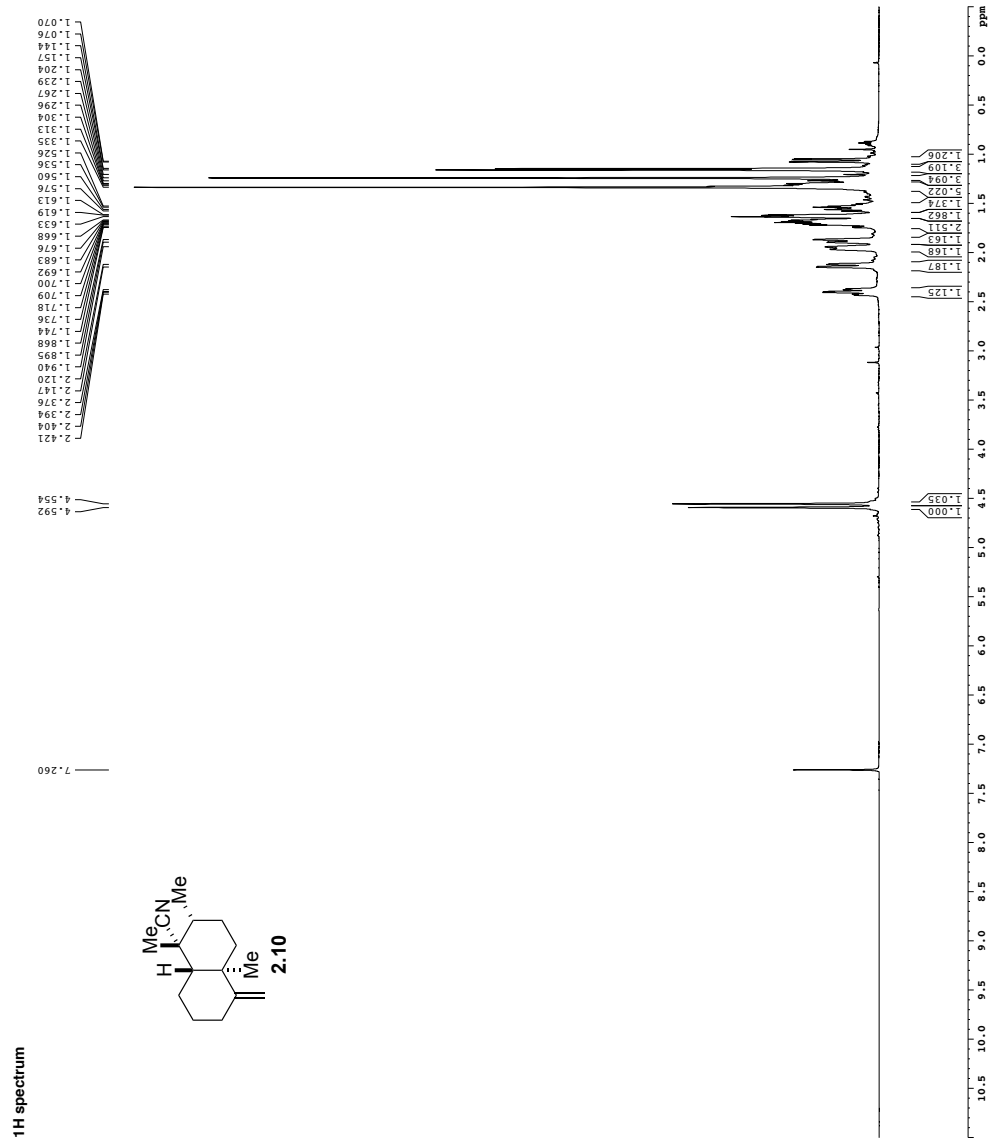

z restored spin echo 13C spectrum with 1H decoupling
Me
O
H
Me
Me
+
3 : 1
2.19
ppm

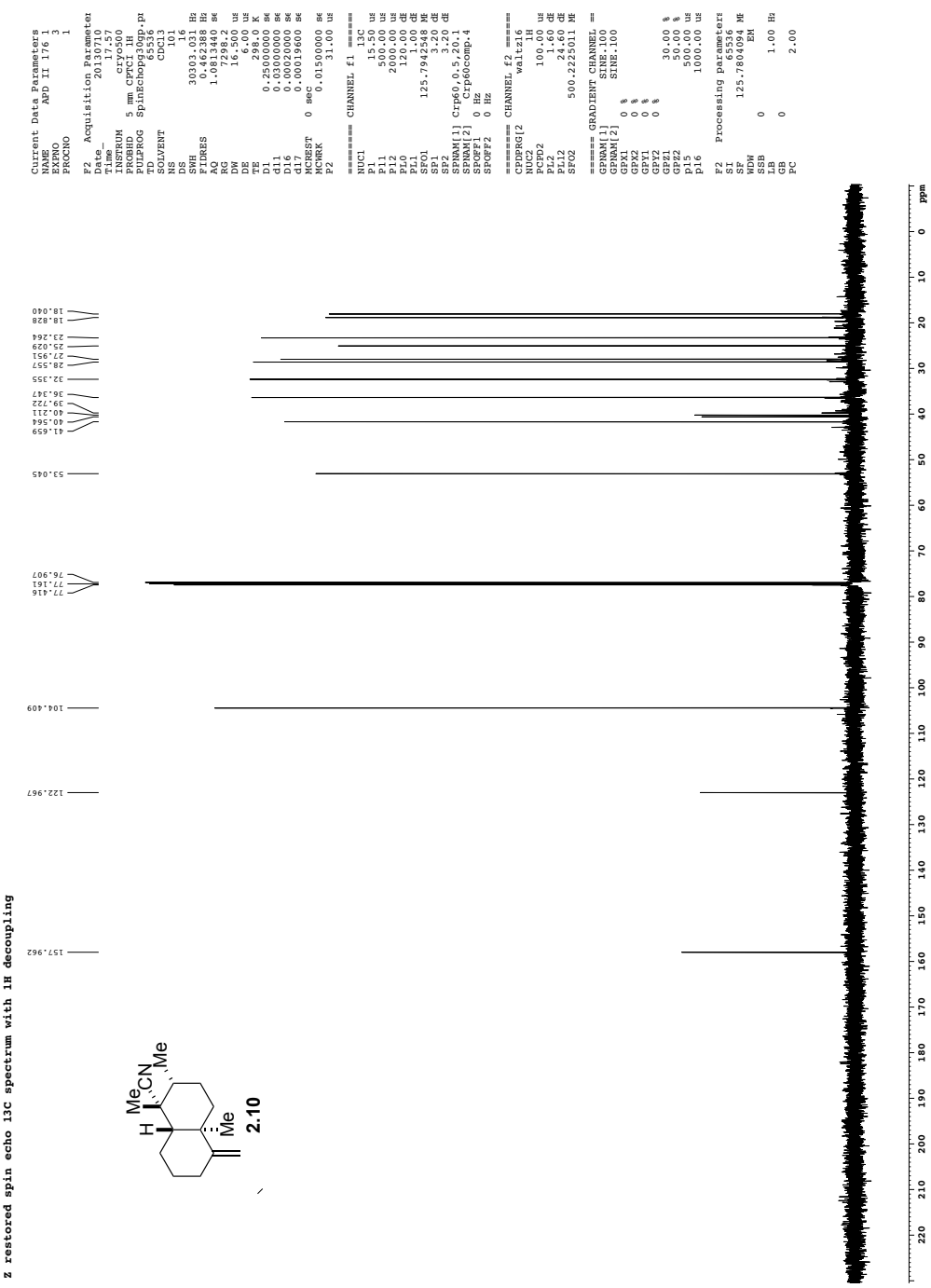

1H spectrum
Current Data Parameters
NAME
EXPNO
PROCNO
F2 Acquisition Parameters
Date_
Time
INSTRUM
PROBHD
PULPROG
TD
SOLVENT
NS
DS
SWH
FIDRES
AQ
RG
DW
DE
TE
D1
TD0
======== CHANNEL f1 ========
NUC1
P1
PLW1
SFO1
F2 Processing parameters
SI
SF
WDW
SSB
LB
GB
PC
7.260
4.737
4.678
4.615
4.552
2.898
1.937
1.892
1.068
3.131
1.647
3.093
2.766
3.779
1.648
0.463
3.113
0.514
0.779
3.000
CN
Me
H
Me
+
CN
Me
H
Me
6 : 1
2.17
ppm

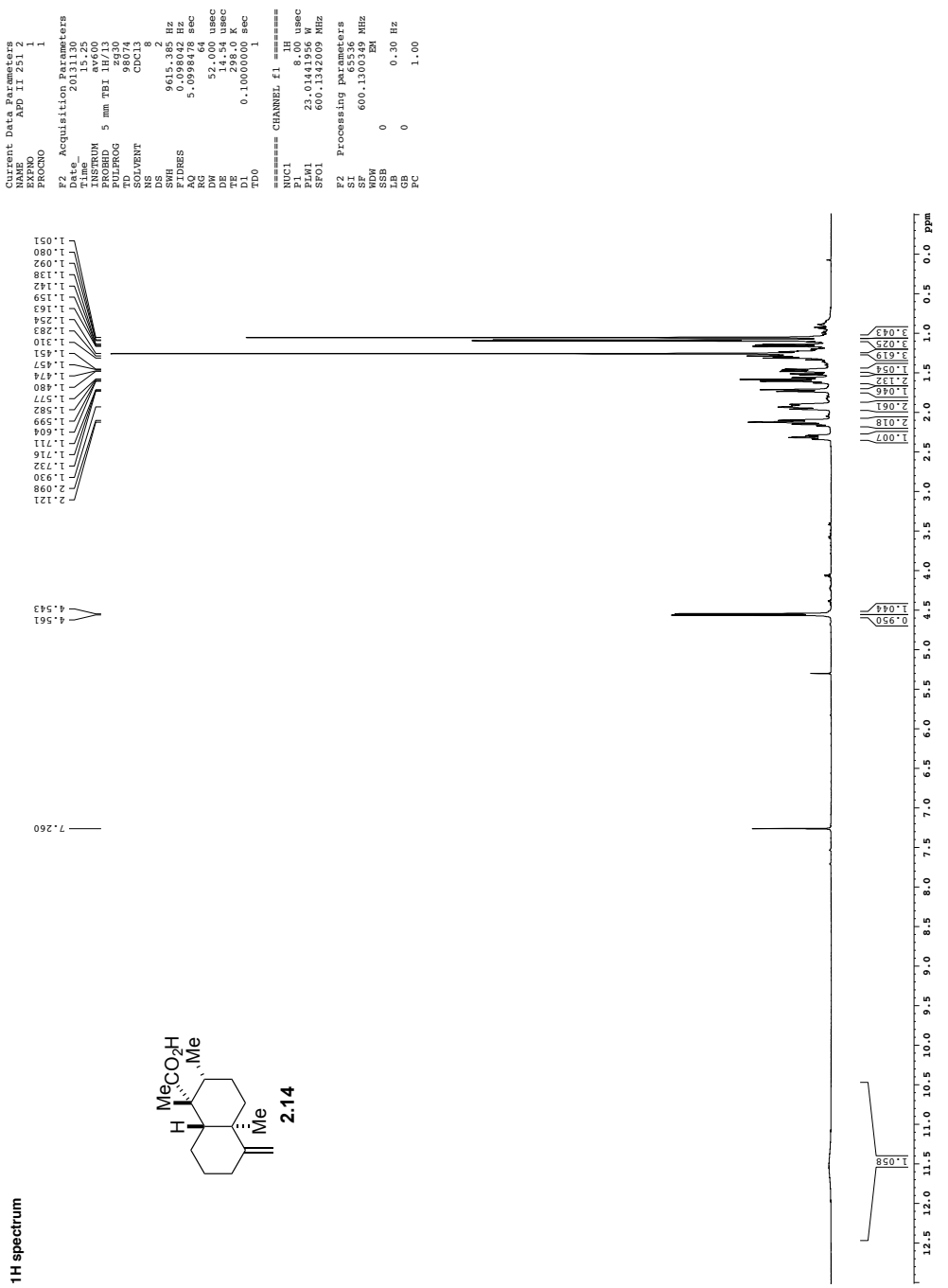
Z restored spin echo 13C spectrum with 1H decoupling

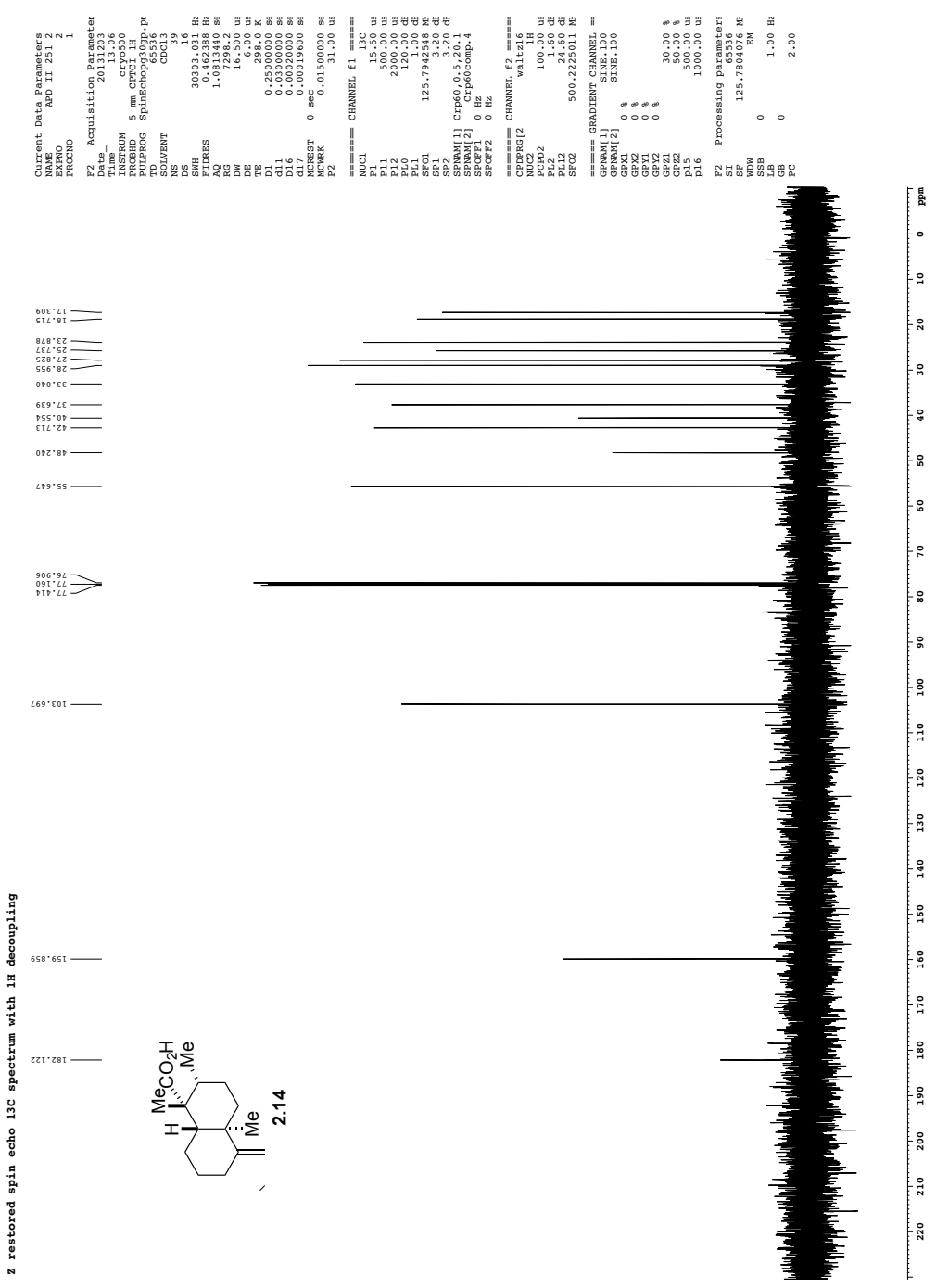


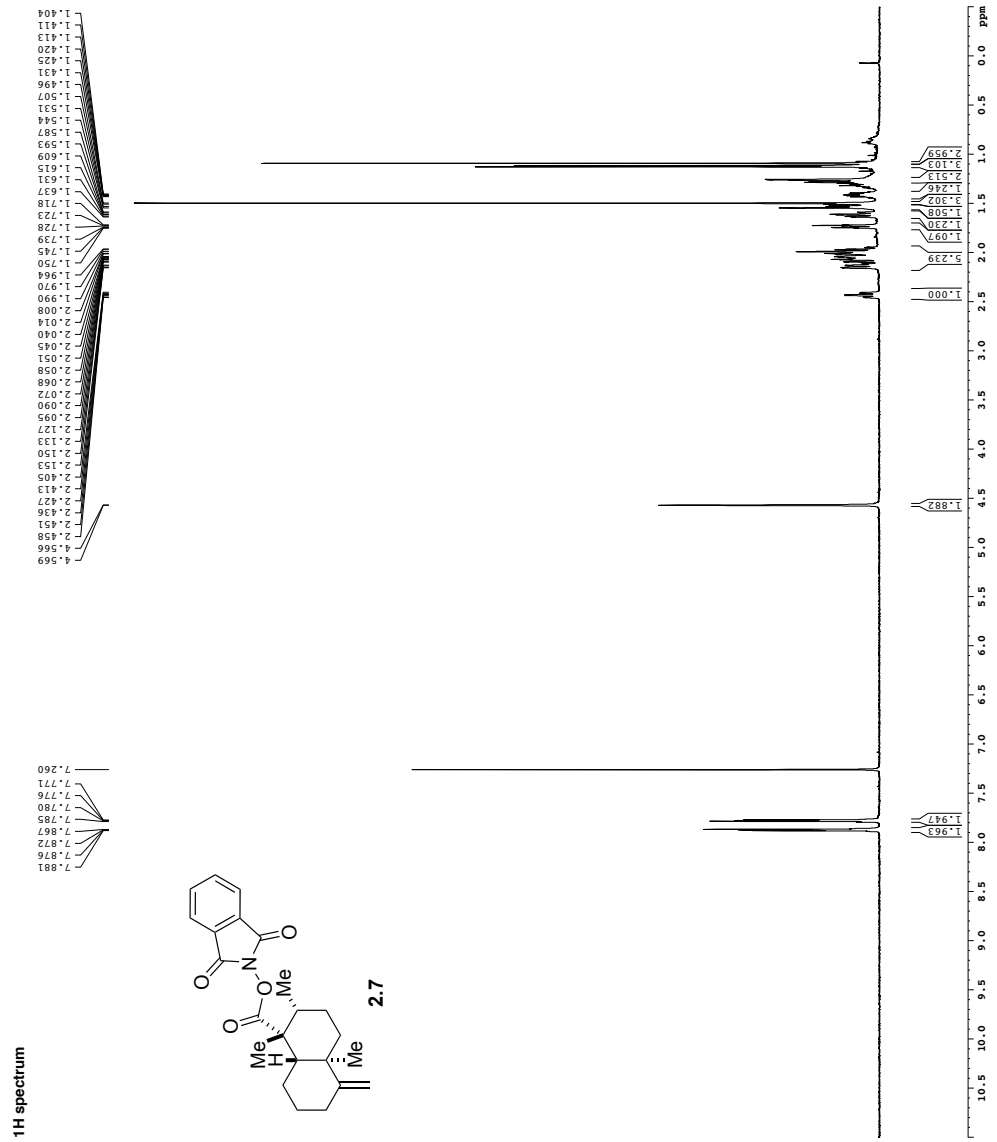

```
Current Data Parameters
NAME        GL4 APD II 241 1
EXPNO                     2
PROCNO                    1

F2   Acquisition Parameter
Date_           20150126
Time                9.45
INSTRUM          cryo500
PROBHD   5 mm CPTCI 1H
PULPROG  SpinEchopg30gp.pr
TD                 65536
SOLVENT            CDCl3T
NS                   143
DS                    16
SWH             30303.031 Hz
FIDRES              0.462388 Hz
AQ                  1.0813440 se
RG                   6502
DW                 16.500 us
DE                  6.00 us
TE                298.0 K
D1              0.25000000 se
d11             0.03000000 se
D16             0.00020000 se
d17             0.00019600 se
MCREST   0 sec
MCWRK           0.01500000 se
P2                 33.10 us

======== CHANNEL f1 ======
NUC1                 13C
P1                 16.55 us
P11               500.00 us
P12              2000.00 us
PL0               120.00 dB
PL1                 1.00 dB
SFO1         125.7942548 MH
SP1                 2.70 dB
SP2                 2.70 dB
SPNAM[1] Crp60,0.5,20.1
SPNAM[2]    Crp60comp.4
SPOFF1   0 Hz
SPOFF2   0 Hz

======== CHANNEL f2 ======
CPDPRG[2         waltz16
NUC2                 1H
PCPD2             100.00 us
PL2                 1.60 dB
PL12               24.50 dB
SFO2         500.2225011 MH

====== GRADIENT CHANNEL ==
GPNAM[1]         SINE.100
GPNAM[2]         SINE.100
GPX1     0 %
GPX2     0 %
GPY1     0 %
GPY2     0 %
GPZ1               30.00 %
GPZ2               50.00 %
p15               500.00 us
p16              1000.00 us

F2   Processing parameters
SI                 65536
SF          125.7804182 MH
WDW                   EM
SSB      0
LB                  1.00 Hz
GB       0
PC                  2.00
```

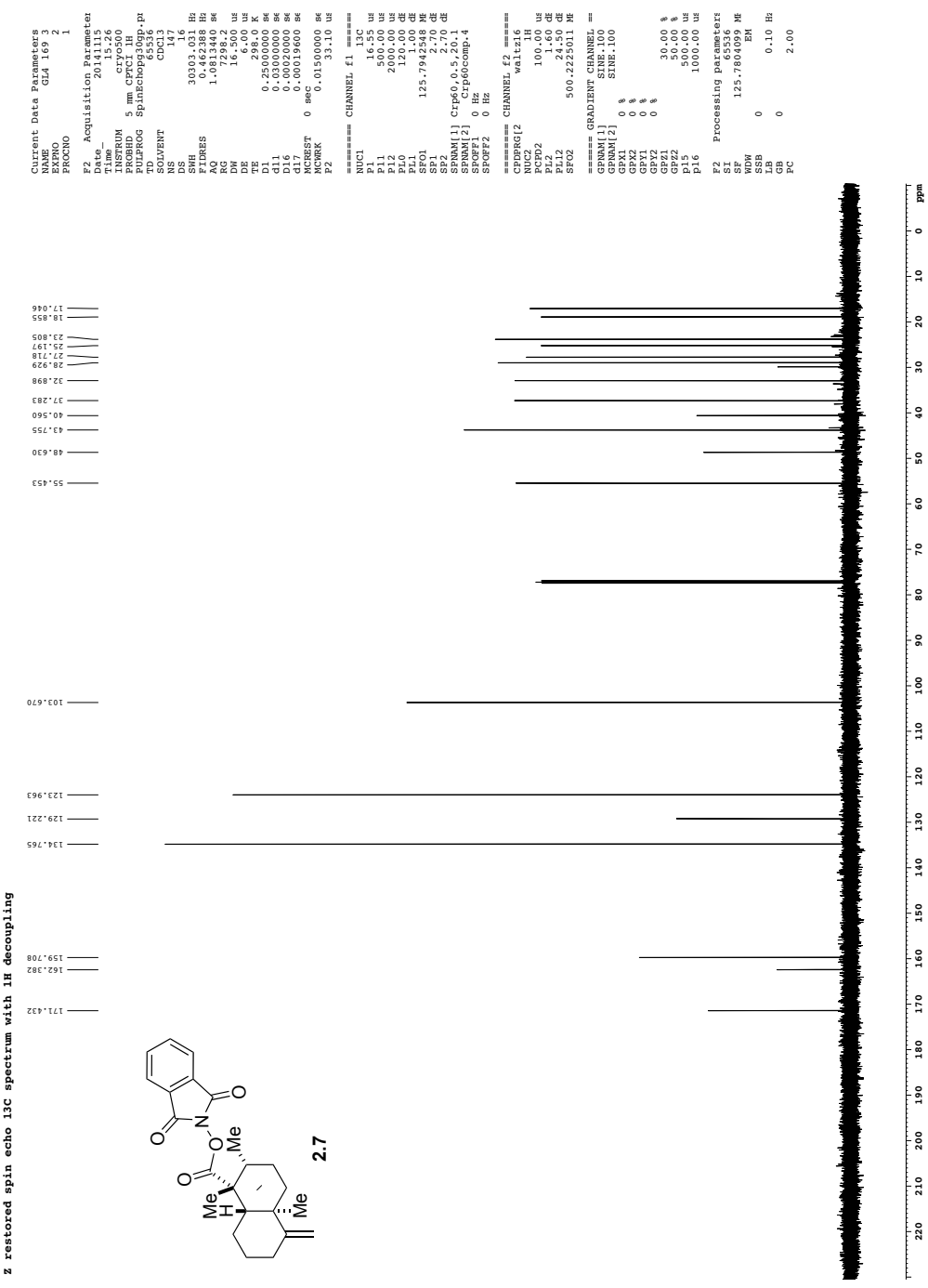

1H spectrum
Current Data Parameters
NAME AFD II 176 1
EXPNO 1
PROCNO 1
F2 Acquisition Parameters
Date_ 20170710
Time 17.43
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H
PULPROG zg30
TD 81728
SOLVENT CDCl3
NS 8
DS 2
SWH 8012.820 Hz
FIDRES 0.098603 Hz
AQ 5.0998273 sec
RG 3.6
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0 sec 0.01500000 sec
MCWRK
======== CHANNEL f1 ========
NUC1 1H
P1 7.50 usec
PL1 1.60 dB
SFO1 500.2235015 MHz
F2 Processing parameters
SI 65536
SF 500.2200317 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00
7.260
4.592
4.554
2.421
2.404
2.394
2.376
2.147
2.120
1.940
1.895
1.868
1.744
1.736
1.718
1.709
1.700
1.692
1.683
1.676
1.668
1.639
1.619
1.613
1.576
1.560
1.536
1.526
1.335
1.313
1.304
1.296
1.267
1.239
1.204
1.157
1.144
1.076
1.070
1.000
1.035
1.125
1.187
1.168
1.163
2.511
1.862
1.374
5.022
3.094
3.109
1.206
Me
CN
Me
H
Me
2.10
ppm

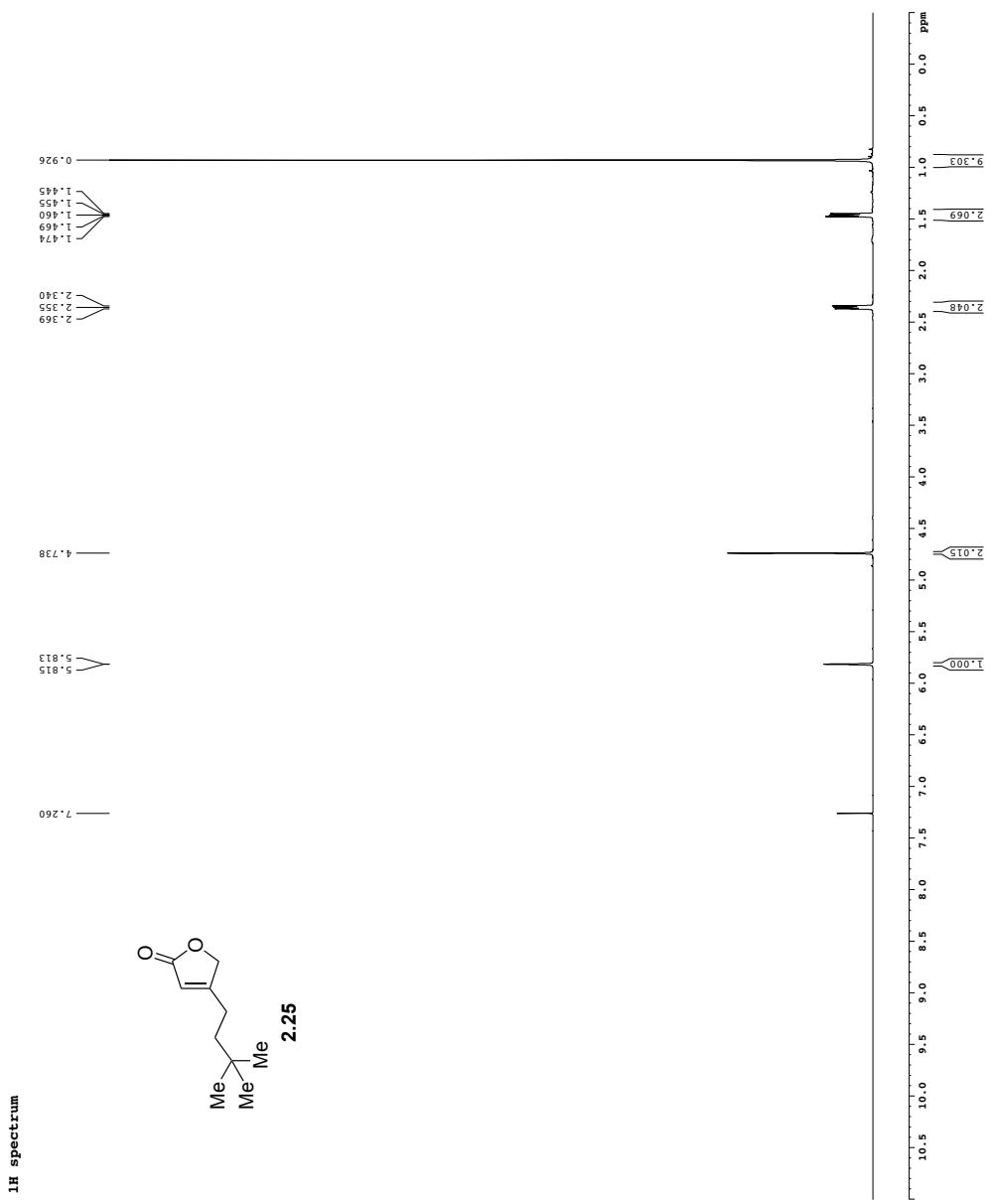

z restored spin echo 13C spectrum with 1H decoupling
Current Data Parameters
NAME
EXPNO
PROCNO
F2 - Acquisition Parameter
Date_
Time
INSTRUM
PROBHD
PULPROG
TD
SOLVENT
NS
DS
SWH
FIDRES
AQ
RG
DW
DE
TE
D1
d11
D16
d17
MCREST
MCWRK
P2
======== CHANNEL f1 ======
NUC1
P1
PL1
PL12
PL0
PL1
SFO1
SP1
SP2
SPNAM[1]
SPNAM[2]
SPOFF1
SPOFF2
======== CHANNEL f2 ======
CPDPRG[2
NUC2
PCPD2
PL2
PL12
SFO2
====== GRADIENT CHANNEL
GPNAM[1]
GPNAM[2]
GPX1
GPX2
GPY1
GPY2
GPZ1
GPZ2
p15
p16
F2 - Processing parameters
SI
SF
WDW
SSB
LB
GB
PC
ppm
Me
Me
Me
2.10

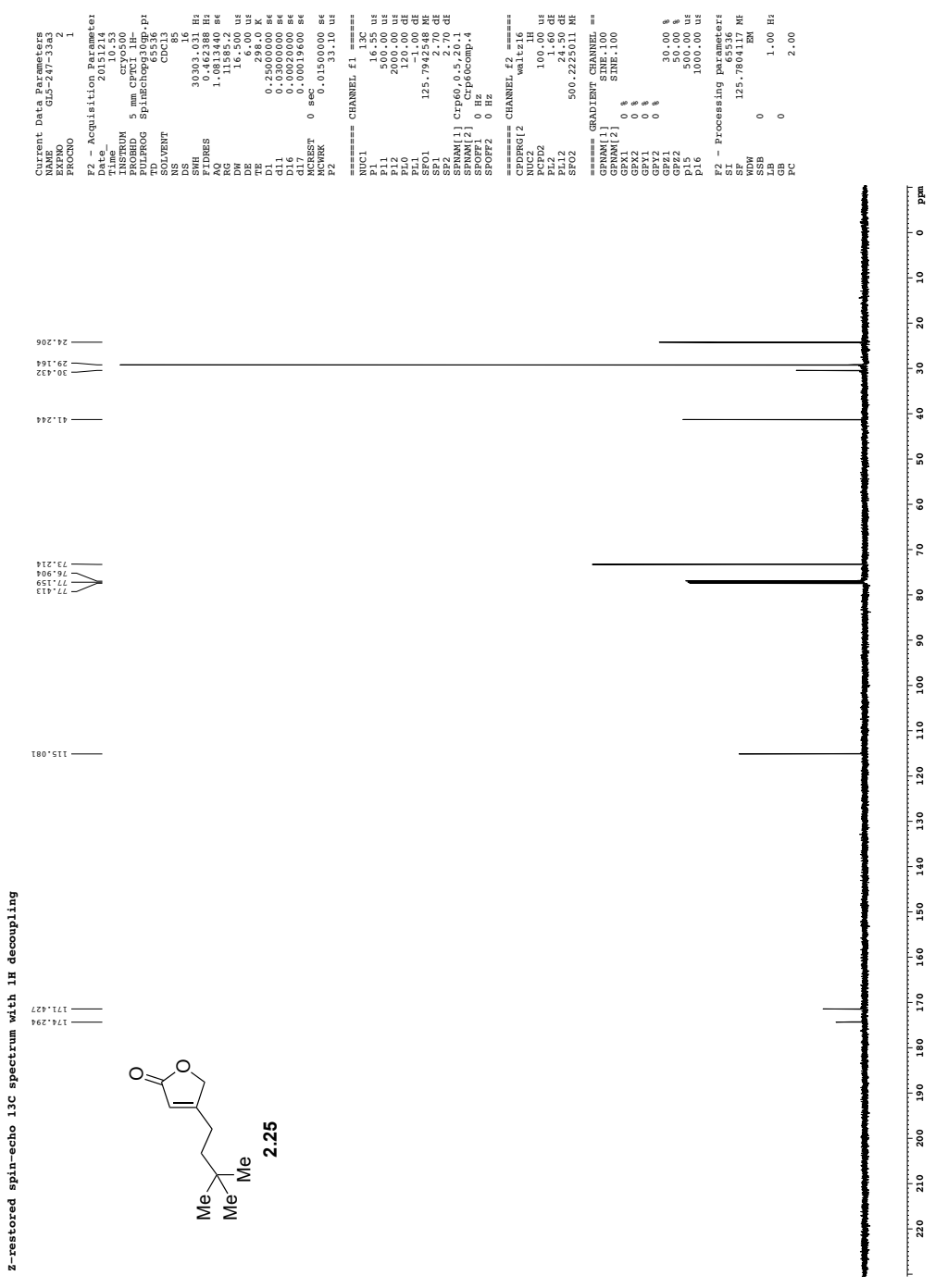

1H spectrum
Current Data Parameters
NAME APD II 251 2
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20131130
Time_ 15.25
INSTRUM av600
PROBHD 5 mm TBI 1H/13
PULPROG zg30
TD 98074
SOLVENT CDCl3
NS 8
DS 2
SWH 9615.385 Hz
FIDRES 0.098042 Hz
AQ 5.0998478 sec
RG 64
DW 52.000 usec
DE 14.50 usec
TE 298.0 K
D1 0.10000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 8.00 usec
PLW1 23.01441956 W
SFO1 600.1342009 MHz
F2 - Processing parameters
SI 65536
SF 600.1300349 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
7.260
4.561
4.543
2.121
2.098
1.930
1.732
1.716
1.711
1.604
1.599
1.582
1.577
1.474
1.480
1.457
1.451
1.310
1.283
1.254
1.163
1.159
1.142
1.138
1.092
1.080
1.051
0.950
1.044
1.007
2.018
2.061
1.046
2.132
1.054
3.619
3.025
3.043
1.058
Me
CO2H
Me
H
Me
2.14
ppm

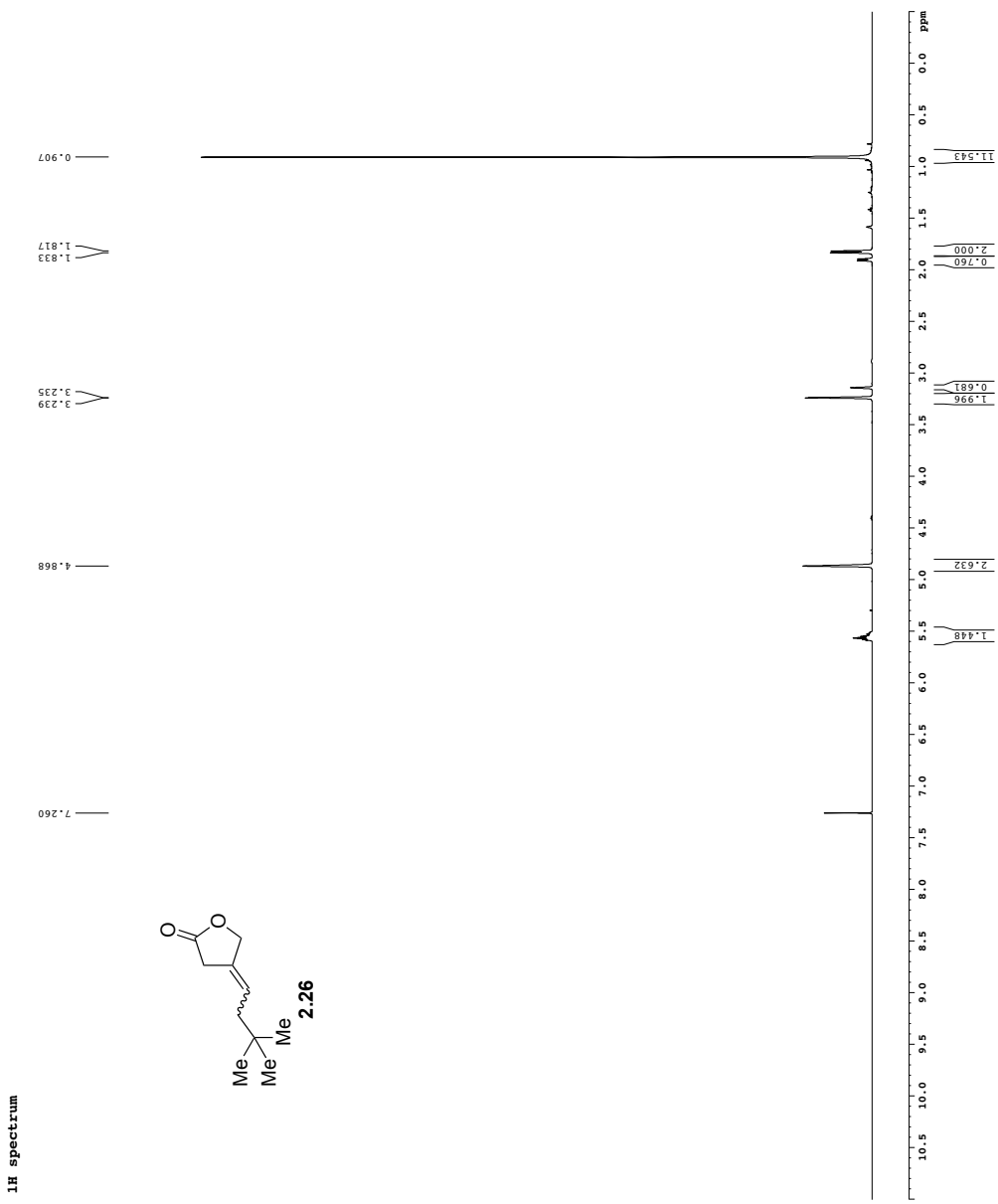

z restored spin echo 13C spectrum with 1H decoupling
Current Data Parameters
NAME 2
EXPNO 2
PROCNO 1
F2 - Acquisition Parameter
Date_ 20112008
Time_ 13.06
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H
PULPROG SpinEchopg30gp.pt
TD 65536
SOLVENT CDCl3
NS 16
DS 16
SWH 30303.031 Hz
FIDRES 0.462280 Hz
AQ 1.0813440 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 sec 0.01500000 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 125.7942568 MHz
SP1 3.20 dB
SP2 3.20 dB
SPNAM[1] Crp60,0.5,20.1
SPNAM[2] Crp60comp.4
SPOFF1 0 Hz
SPOFF2 0 Hz
======== CHANNEL f2 ======
CPDPRG[2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 1.60 dB
PL12 24.60 dB
SFO2 500.2225011 MHz
====== GRADIENT CHANNEL ==
GPNAM[1] SINE.100
GPNAM[2] SINE.100
GPX1 0 %
GPX2 0 %
GPY1 0 %
GPY2 0 %
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
182.122
159.859
103.697
77.414
77.160
76.906
55.647
48.240
42.713
40.554
37.639
33.040
28.955
27.825
25.737
23.878
18.715
17.309
Me
CO2H
Me
H
Me
2.14
ppm

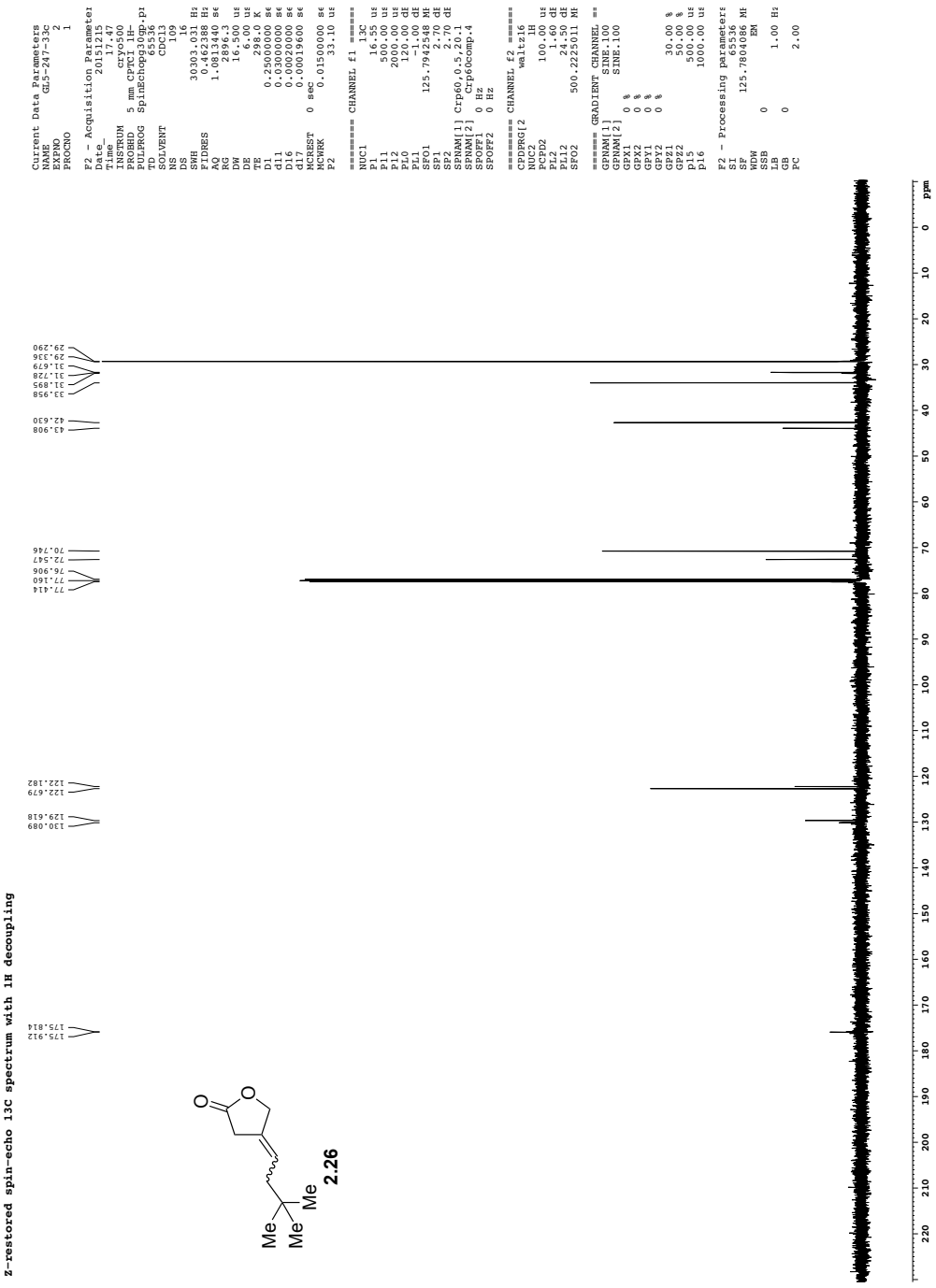

Current Data Parameters
NAME gl4 175 3
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20141125
Time 14.32
INSTRUM av600
PROBHD 5 mm TBI 1H/13
PULPROG zg30
TD 98074
SOLVENT CDCl3T
NS 8
DS 2
SWH 9615.385 Hz
FIDRES 0.098047 Hz
AQ 5.0998478 sec
RG 912
DW 52.000 usec
DE 14.54 usec
TE 298.0 K
D1 0.10000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 600.1342009 MHz
NUC1 1H
P1 8.00 usec
PLW1 23.01441956 W
F2 - Processing parameters
SI 65536
SF 600.1300342 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
1H spectrum
2.7
Me
Me
H
Me
O
O
N
O
O
Me
1.963
1.947
1.882
1.000
5.239
1.097
1.239
1.508
3.302
1.246
2.513
3.103
2.959
ppm

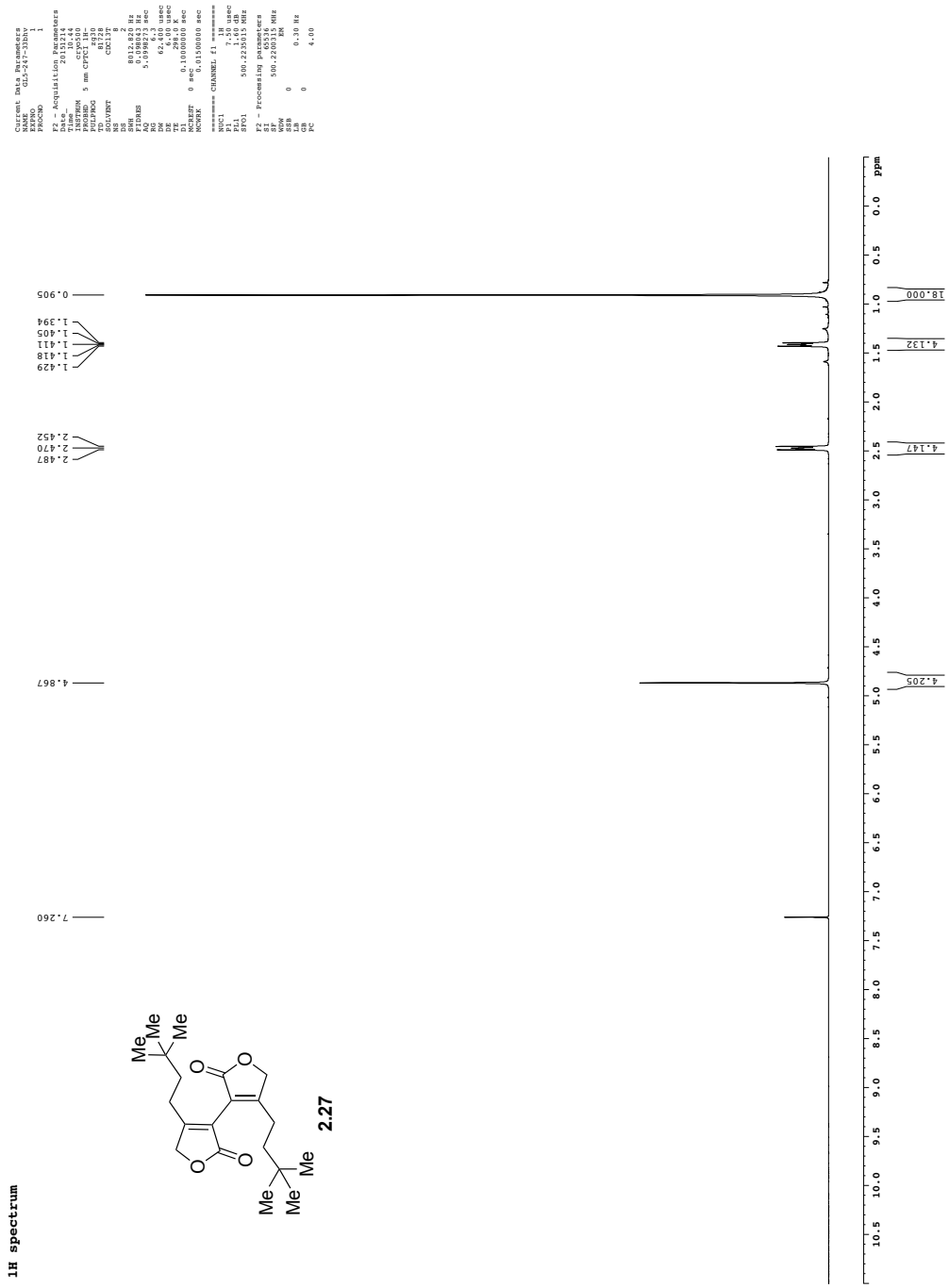

z restored spin echo 13C spectrum with 1H decoupling
Current Data Parameters
NAME GL4 169 3
EXPNO 2
PROCNO 1
F2 - Acquisition Parameter
Date_ 20141115
Time 15.26
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H
PULPROG SpinEchopg30gp.pi
TD 65536
SOLVENT CDCl3
NS 16
DS 16
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0813440 sec
RG 7282.2
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 sec 0.01500000 sec
MCWRK 0.01500000 sec
P2 33.10 usec
======== CHANNEL f1 ======
NUC1 13C
P1 16.55 usec
PL1 500.00 dB
PL12 2000.00 dB
PL0 120.00 dB
PL1 1.00 dB
SFO1 125.7942548 MHz
SF1 125.7700000 MHz
SP2 2.70 dB
SPNAM[1] Crp60,0.5,20.1
SPNAM[2] Crp60comp.4
SPOFF1 0 Hz
SPOFF2 0 Hz
======== CHANNEL f2 ======
CPDPRG[2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 1.60 dB
PL12 24.50 dB
SFO2 500.2225011 MHz
====== GRADIENT CHANNEL =
GPNAM[1] SINE.100
GPNAM[2] SINE.100
GPX1 0 %
GPX2 0 %
GPY1 0 %
GPY2 0 %
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 0.10 Hz
GB 0
PC 2.00
17.046
18.855
23.805
25.197
27.718
28.929
32.898
37.283
40.560
43.755
48.630
55.453
103.670
123.963
129.221
134.765
159.708
162.382
171.432
Me
Me
H
Me
2.7
ppm

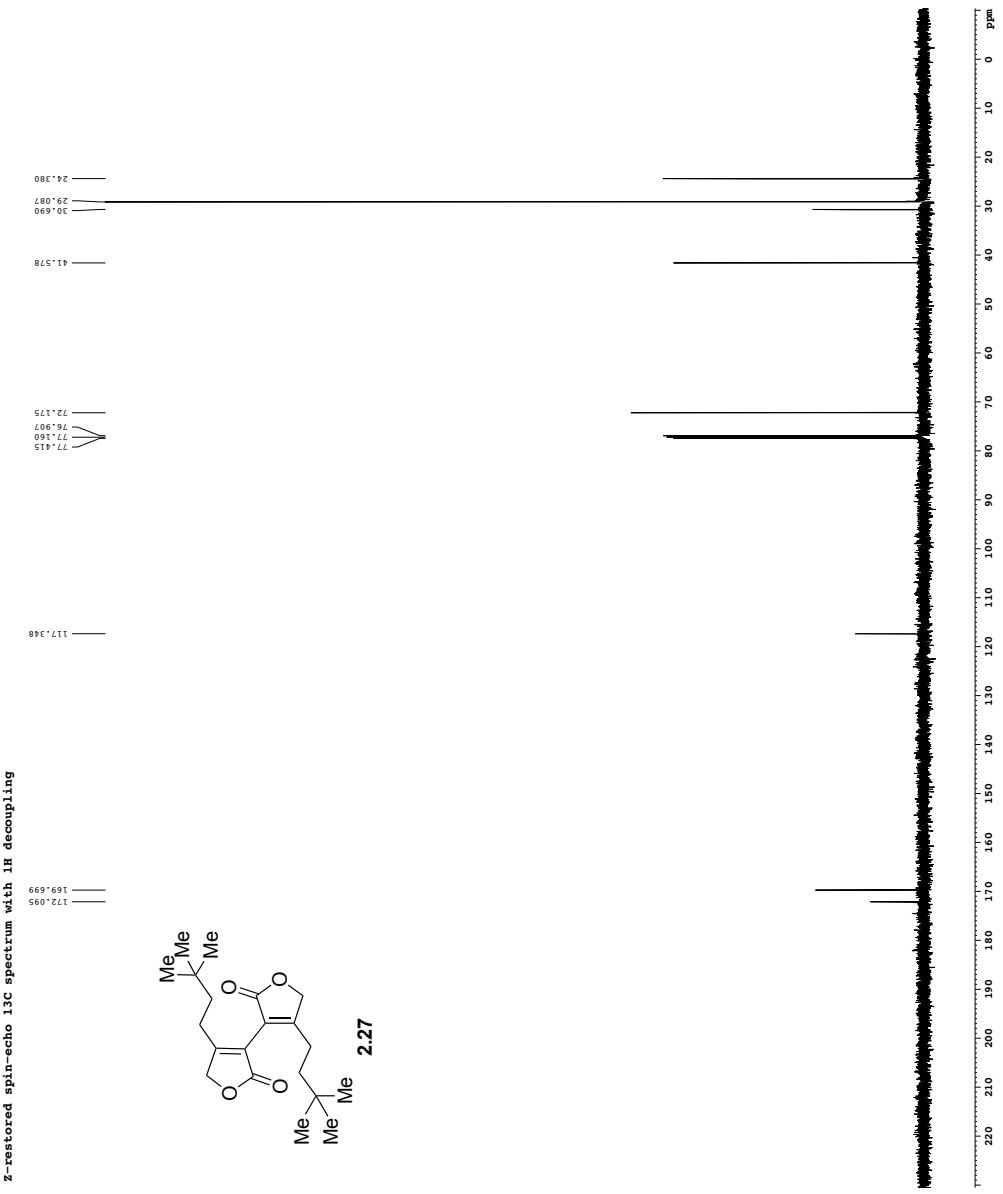

1H spectrum
Current Data Parameters
NAME GLS-247-33a33
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20111228
Time 14.58
INSTRUM av600
PROBHD 5 mm TBI BB-H-D-
PULPROG zg30
TD 65536
SOLVENT CDCl3F
NS 2
DS 2
SWH 9615.385 Hz
FIDRES 0.146802 Hz
AQ 5.0998478 sec
RG 287.27
DW 52.000 usec
DE 6.50 usec
TE 293.0 K
D1 0.10000000 sec
TD1 1
======== CHANNEL f1 ========
SFO1 600.1342009 MHz
NUC1 1H
P1 8.00 usec
PLW1 24.00000000 W
F2 - Processing parameters
SI 65536
SF 600.1300356 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
7.260
5.815
5.813
4.738
2.369
2.355
2.340
1.474
1.469
1.460
1.455
1.445
0.926
9.303
2.069
2.048
2.015
1.000
ppm
O
O
Me
Me
Me
2.25

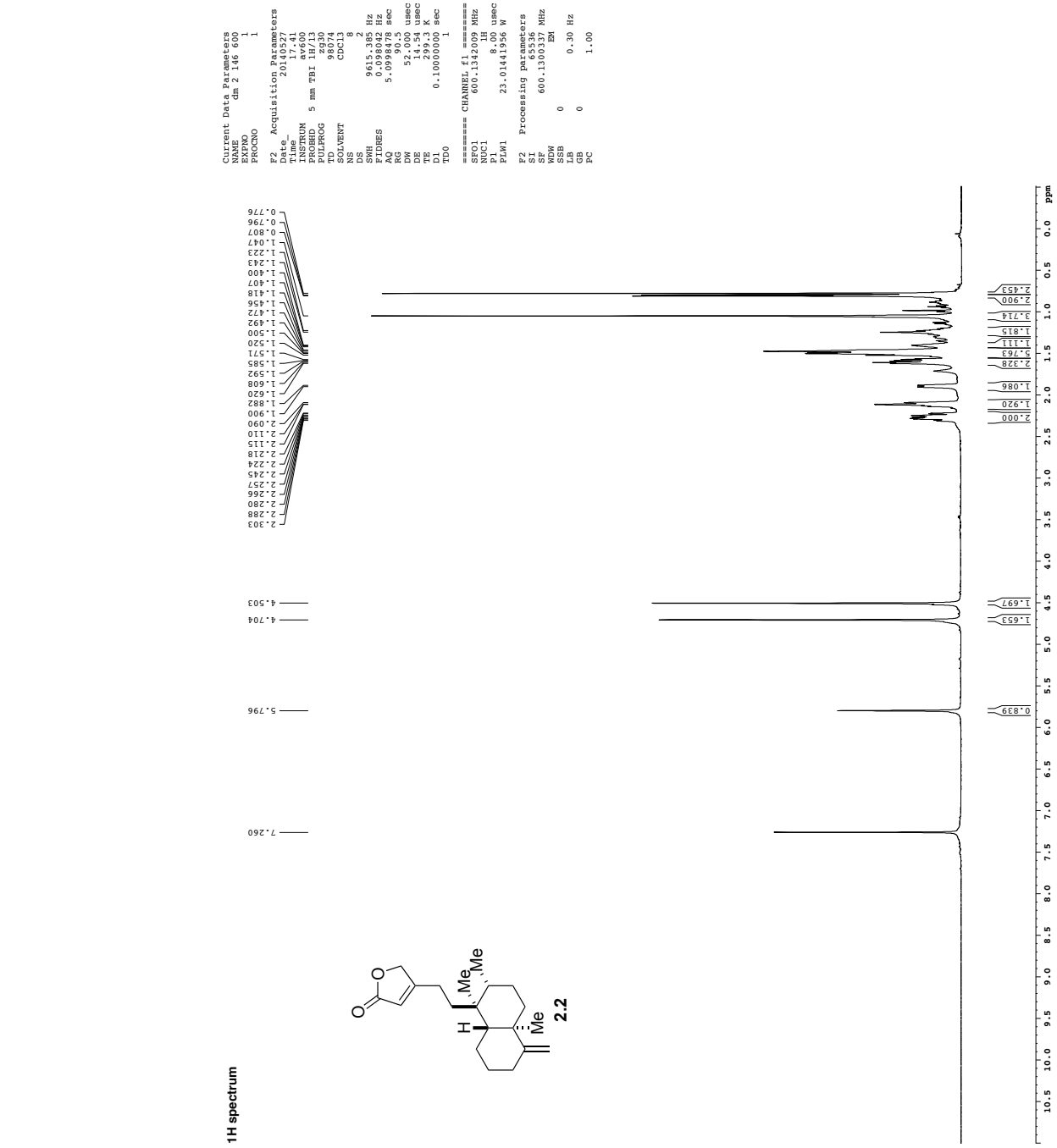

Z-restored spin-echo 13C spectrum with 1H decoupling
Current Data Parameters
NAME GLS-247-3a2
EXPNO 2
PROCNO 1
F2 - Acquisition Parameter
Date_ 20112714
Time_ 10.53
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG SpinEchopg30gp.p1
TD 65536
SOLVENT CDCl3
NS 85
DS 16
SWH 30303.031 Hz
FIDRES 0.462288 Hz
AQ 1.0813440 sec
RG 11585.2
DW 16.500 us
DE 6.00 us
TE 298.0 K
D1 0.25000000 sec
D11 0.03000000 sec
D16 0.00020000 sec
d17 0.00019600 sec
MCREST 0 sec
MCWRK 0.01500000 sec
P2 33.10 us
======== CHANNEL f1 ======
NUC1 13C
P1 16.55 us
P11 500.00 us
P12 2000.00 us
PL0 120.00 dB
PL1 -1.00 dB
SFO1 125.7992460 MHz
SP1 2.70 dB
SP2 2.70 dB
SPNAM[1] Crp60,0.5,20.1
SPNAM[2] Crp60comp.4
SPOFF1 0 Hz
SPOFF2 0 Hz
======== CHANNEL f2 ======
CPDPRG[2 waltz16
NUC2 1H
PCPD2 100.00 us
PL2 1.60 dB
PL12 24.50 dB
SFO2 500.2225011 MH
====== GRADIENT CHANNEL ==
GPNAM[1] SINE.100
GPNAM[2] SINE.100
GPX1 0 %
GPX2 0 %
GPY1 0 %
GPY2 0 %
GPZ1 30.00 %
GPZ2 50.00 %
P15 500.00 us
P16 1000.00 us
F2 - Processing parameters
SI 65536
SF 125.7804117 MH
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00
174.294
171.427
115.081
77.413
77.159
76.904
73.214
41.244
30.432
29.164
24.206
Me
Me
Me
2.25
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

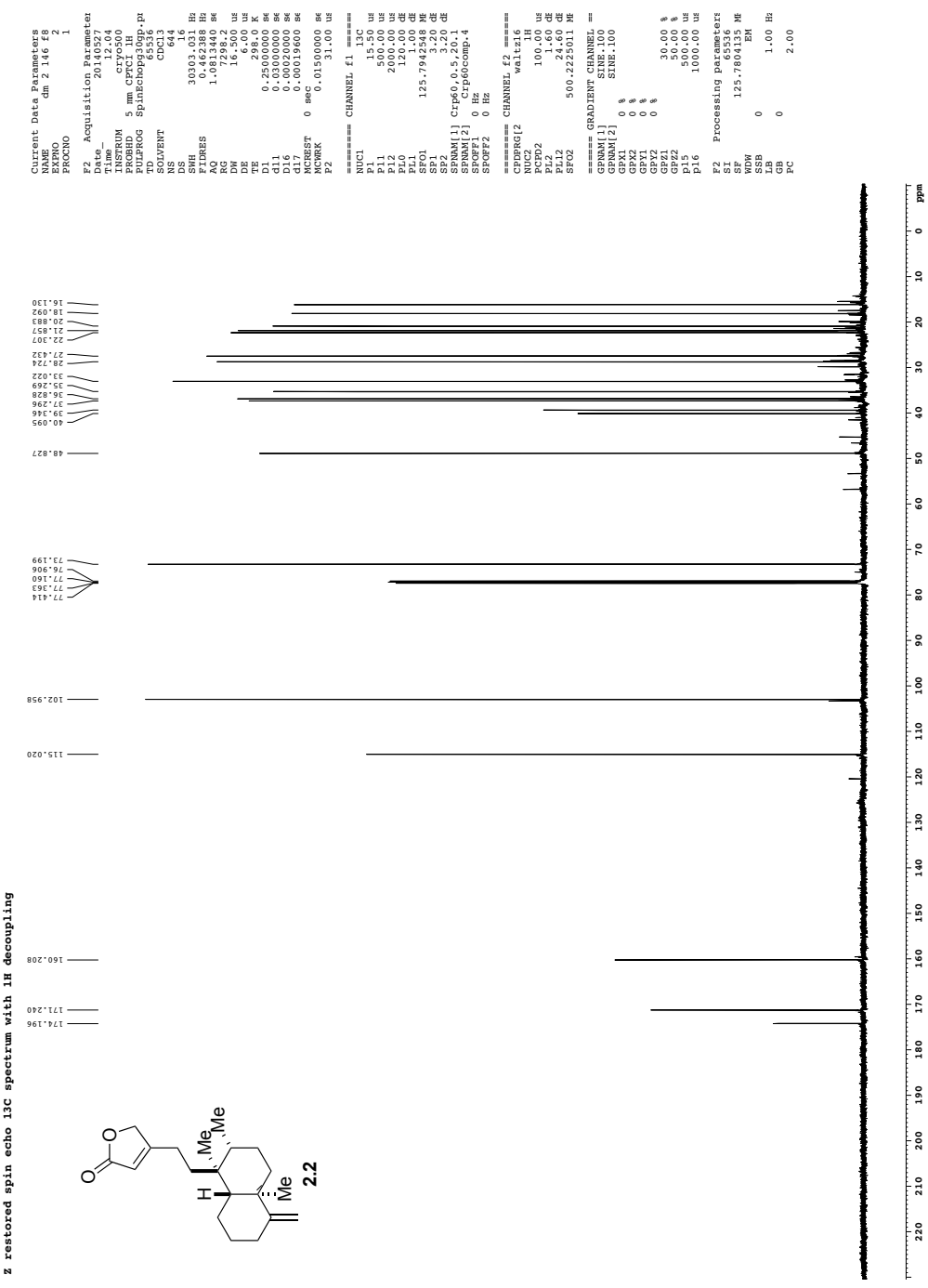

1H spectrum
Current Data Parameters
NAME GLS-247-33c
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20151215
Time 17.46
INSTRUM cryo500
PROBHD 5 mm CPTC 1H-
PULPROG zg30
TD 81728
SOLVENT CDCl3
NS 8
DS 2
SWH 8012.820 Hz
FIDRES 0.098273 Hz
AQ 6.0 sec
RG 62.000
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
D12 0.00002000 sec
MCREV 0 sec 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 7.50 usec
PL1 1.40 dB
SFO1 500.2235015 MHz
F2 - Processing parameters
SI 65536
SF 500.2200316 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00
7.260
4.868
3.239
3.235
1.833
1.817
0.907
1.448
2.632
1.543
2.000
0.760
1.996
0.681
ppm
2.26
Me
Me
Me
O
O

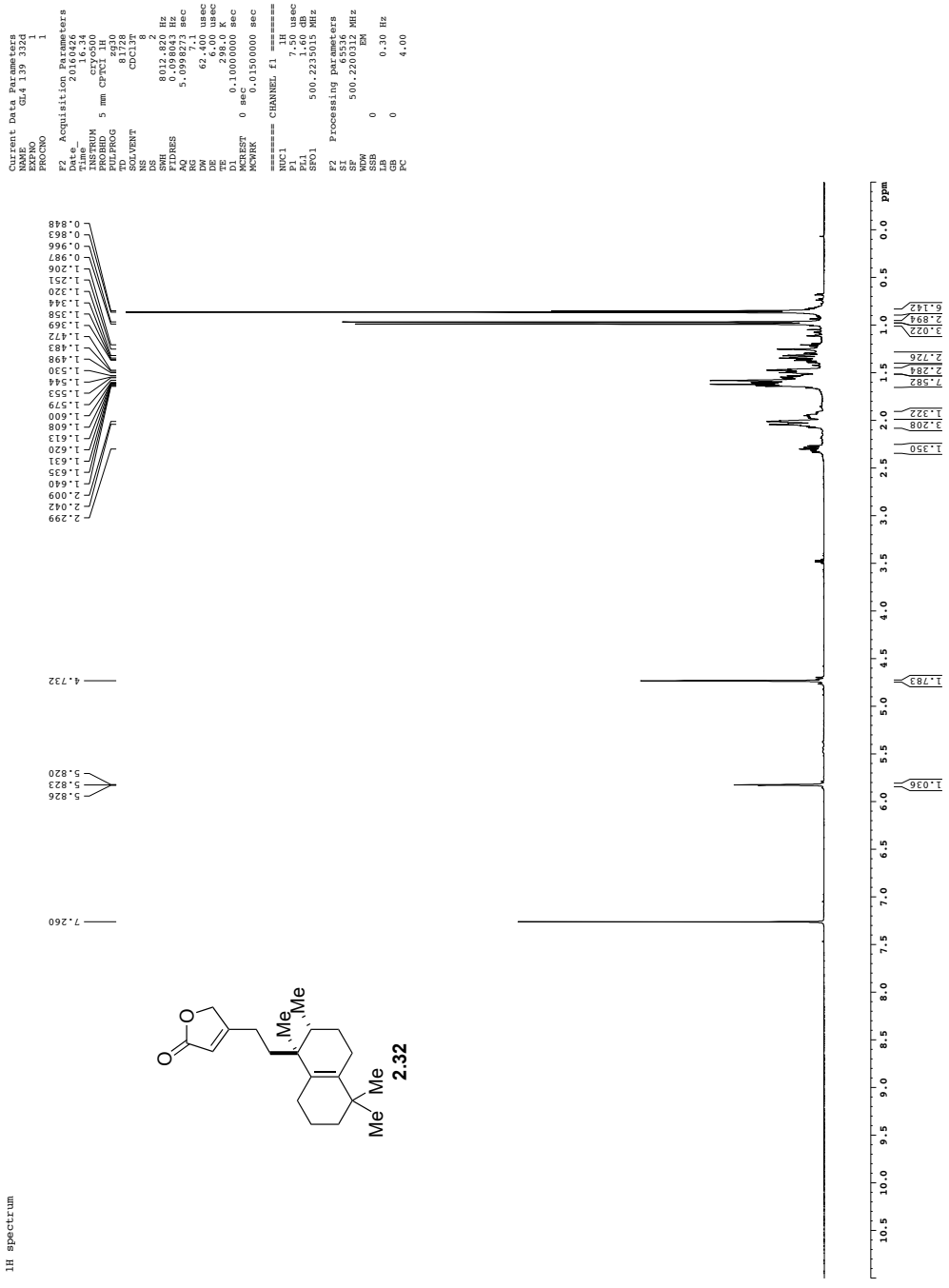

Z-restored spin-echo 13C spectrum with 1H decoupling
Current Data Parameters
NAME GL5-247-33c
EXPNO 2
PROCNO 1
F2 - Acquisition Parameter
Date_ 20151215
Time 17.47
INSTRUM cryo
PROBHD 5 mm CPTCI 1H-
PULPROG SpinEchopg30gp.p1
TD 65536
SOLVENT CDCl3
NS 1024
DS 16
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0813440 sec
RG 228.3
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 sec 0.01500000 sec
MCWRK 0.01500000 sec
P2 33.10 usec
======== CHANNEL f1 ======
NUC1 13C
P1 16.55 usec
PL1 500.00 usec
PL2 2000.00 dB
PL0 120.00 dB
PL1 -1.00 dB
SFO1 125.7942548 MHz
SP1 2.70 dB
SP2 2.70 dB
SPNAM[1] Crp60,0.5,20.1
SPNAM[2] Crp60comp.4
SPOFF1 0 Hz
SPOFF2 0 Hz
======== CHANNEL f2 ======
CPDPRG[2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 1.60 dB
PL12 24.50 dB
SFO2 500.2225011 MHz
====== GRADIENT CHANNEL ==
GPNAM[1] SINE.100
GPNAM[2] SINE.100
GPX1 0 %
GPX2 0 %
GPY1 0 %
GPY2 0 %
GPZ1 30.00 %
GPZ2 50.00 %
p15 500.00 usec
p16 1000.00 usec
F2 - Processing parameters
SI 65536
SF 125.7804086 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00
175.912
175.814
130.089
129.618
122.679
122.182
77.414
77.160
76.906
72.547
70.746
43.908
42.630
33.958
31.895
31.728
31.679
29.336
29.290
O
O
Me
Me
Me
2.26
ppm

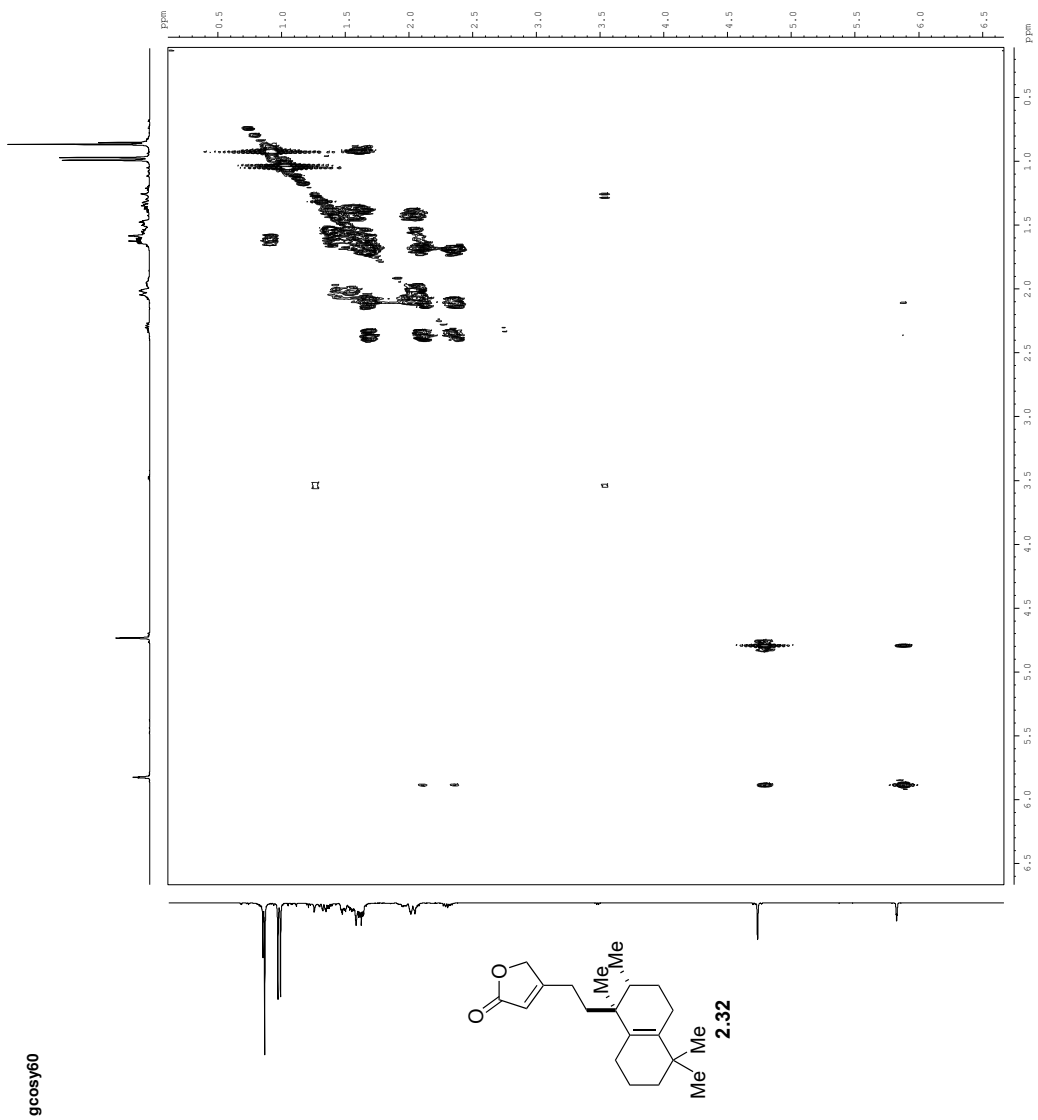

1H spectrum
Current Data Parameters
NAME GLS-247-33bhr
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20131214
Time 11.44
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 2
DS 2
SWH 8012.820 Hz
FIDRES 0.122283 Hz
AQ 5.0990273 sec
RG 1
DW 62.400 usec
DE 6.00 usec
TE 293.0 K
D1 0.10000000 sec
D11 0.03000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 7.50 usec
PL1 3.00 dB
SFO1 500.2230013 MHz
F2 - Processing parameters
SI 65536
SF 500.2200376 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00
0.905
1.394
1.405
1.411
1.418
1.429
2.452
2.470
2.487
4.867
7.260
18.000
4.132
4.147
4.205
ppm
2.27

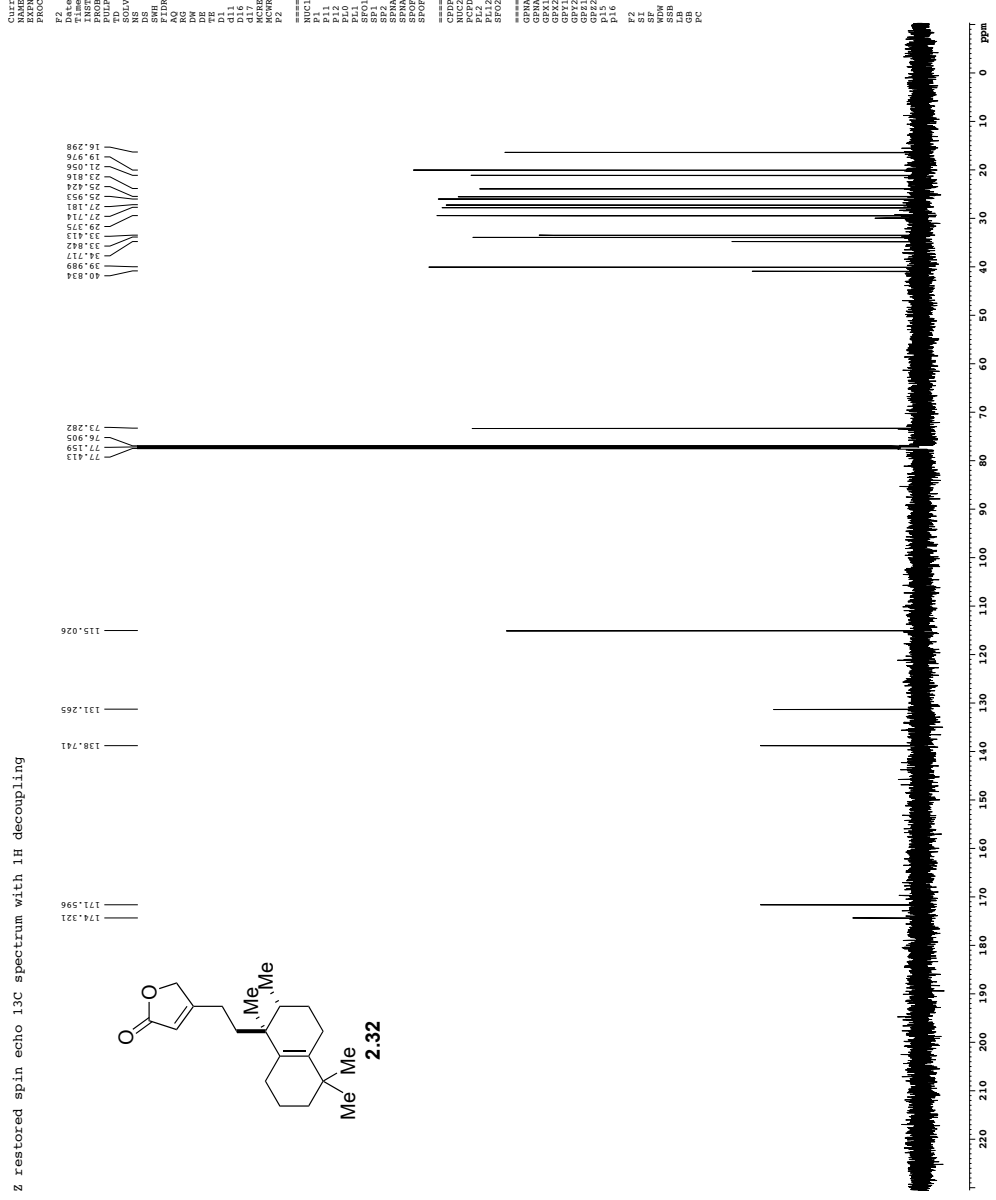

Z-restored spin-echo 13C spectrum with 1H decoupling
Current Data Parameters
NAME GL5-247-33bhv
EXPNO 2
PROCNO 1
F2 - Acquisition Parameter
Date_ 20151214
Time 10.45
INSTRUM cryo
PROBHD 5 mm CPTCI 1H-
PULPROG SpinEchopg30gp.p1
TD 65536
SOLVENT CDCl3
NS 16
DS 16
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0813440 sec
RG 11585.2
DW 16.500 us
DE 6.00 us
TE 298.0 K
D1 0.25000000 sec
d11 0.03000000 sec
D16 0.00020000 sec
d17 0.00019600 sec
MCREST 0 sec 0.01500000 sec
MCWRK 0.01500000 sec
P2 33.10 us
======== CHANNEL f1 ======
NUC1 13C
P1 16.55 us
PL1 500.00 us
PL2 2000.00 dB
PL0 120.00 dB
PL1 -1.00 dB
SFO1 125.7942548 MHz
SP1 2.70 dB
SP2 2.70 dB
SPNAM[1] Crp60,0.5,20.1
SPNAM[2] Crp60comp.4
SPOFF1 0 Hz
SPOFF2 0 Hz
======== CHANNEL f2 ======
CPDPRG[2 waltz16
NUC2 1H
PCPD2 100.00 us
PL2 1.60 dB
PL12 24.50 dB
SFO2 500.2225011 MHz
====== GRADIENT CHANNEL ==
GNAM[1] STD5.100
GNAM[2] SINE.100
GPX1 0 %
GPX2 0 %
GPY1 0 %
GPY2 0 %
GPZ1 30.00 %
GPZ2 50.00 %
p15 500.00 us
p16 1000.00 us
F2 - Processing parameters
SI 65536
SF 125.7804090 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00
172.095
169.699
117.348
77.415
77.160
76.907
72.175
41.578
30.690
29.087
24.380
ppm
Me
Me
Me
Me
Me
Me
O
O
O
O
2.27

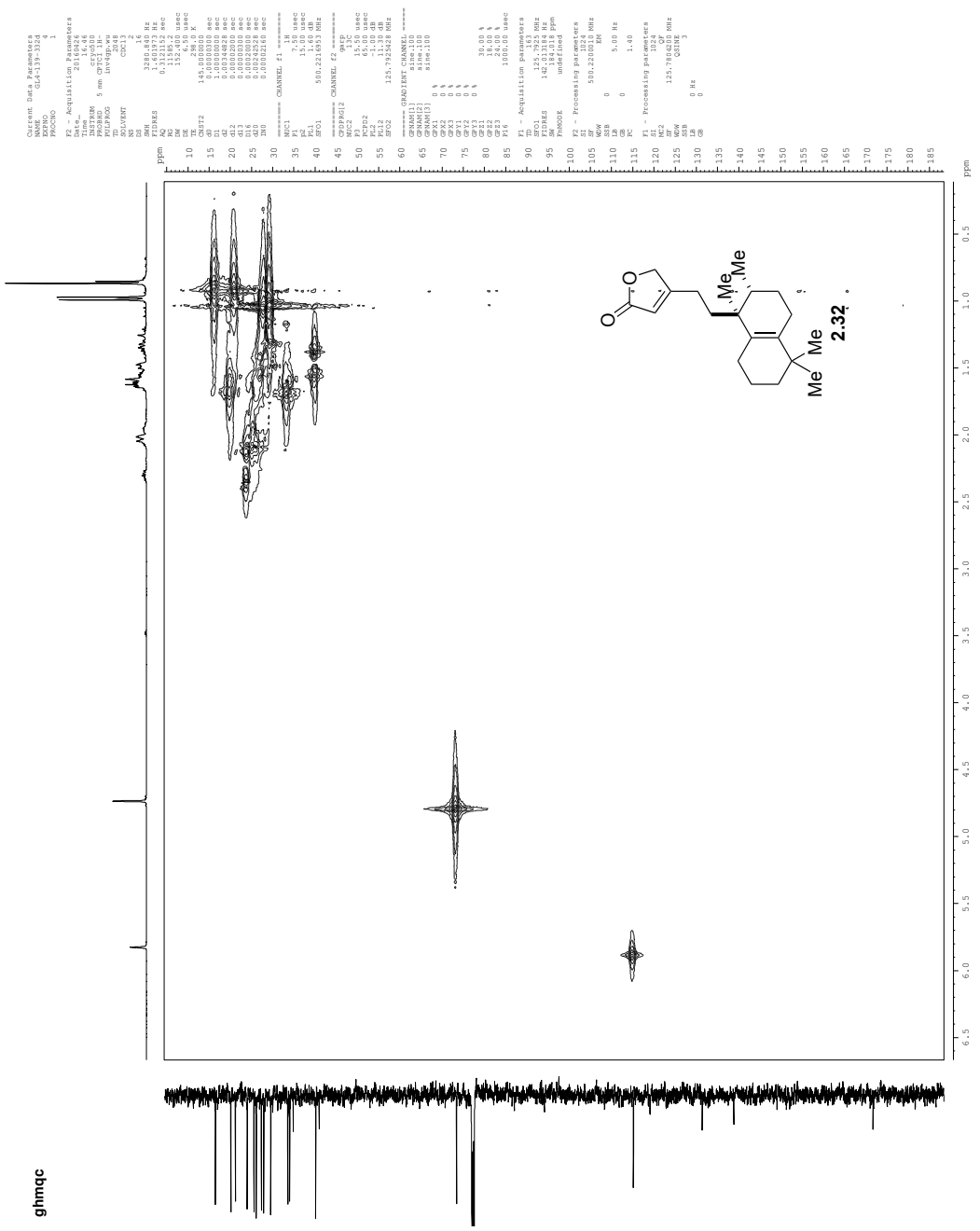

Current Data Parameters
NAME
EXPNO
PROCNO
F2 - Acquisition Parameters
Date_
Time
INSTRUM
PROBHD
PULPROG
TD
SOLVENT
NS
DS
SWH
FIDRES
AQ
RG
DW
DE
TE
D1
TD0
======== CHANNEL f1 ========
SFO1
NUC1
P1
PLW1
F2 - Processing parameters
SI
SF
WDW
SSB
LB
GB
PC
1H spectrum
2.2
Me
Me
H
Me
O
O
ppm

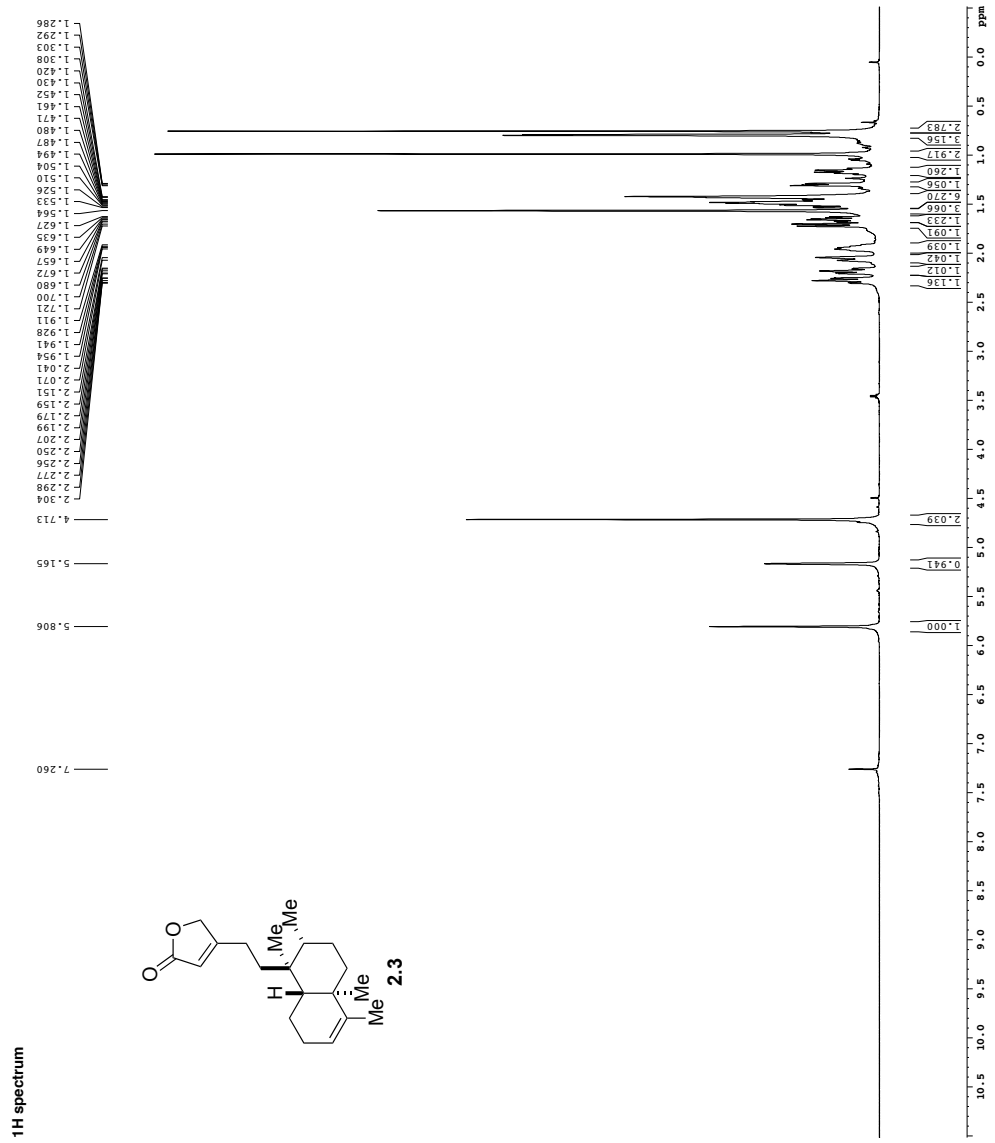

z restored spin echo 13C spectrum with 1H decoupling
2.2
Me
Me
Me
H
O
O
Current Data Parameters
NAME dm 2 146 f8
EXPNO 2
PROCNO 1
F2 - Acquisition Parameter
Date_ 20140527
Time 7.04
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H
PULPROG SpinEchopg30gp.pi
TD 65536
SOLVENT CDCl3
NS 644
DS 16
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.08213440 sec
RG 77982.2
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 sec 0.01500000 sec
MCWRK 0.01500000 sec
P2 31.00 usec
======== CHANNEL f1 ======
NUC1 13C
P1 15.50 usec
PL1 500.00 usec
PL12 2000.00 usec
PL0 120.00 dB
PL1 1.00 dB
SFO1 125.7942548 MHz
SF1 125.7804135 MHz
SP2 3.20 dB
SPNAM[1] Crp60,0.5,20.1
SPNAM[2] Crp60comp.4
SPOFF1 0 Hz
SPOFF2 0 Hz
======== CHANNEL f2 ======
CPDPRG[2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 1.60 dB
PL12 24.60 dB
SFO2 500.2225011 MHz
====== GRADIENT CHANNEL =
GPNAM[1] SINE.100
GPNAM[2] SINE.100
GPX1 0 %
GPX2 0 %
GPY1 0 %
GPY2 0 %
GPZ1 30.00 %
GPZ2 50.00 %
p15 500.00 usec
p16 1000.00 usec
F2 - Processing parameters
SI 65536
SF 125.7804135 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00
16.130
18.092
20.883
21.857
22.307
27.432
28.724
33.022
35.269
36.828
37.296
39.346
40.095
48.827
73.199
76.906
77.160
77.363
77.414
102.958
115.020
160.208
171.240
174.196
ppm

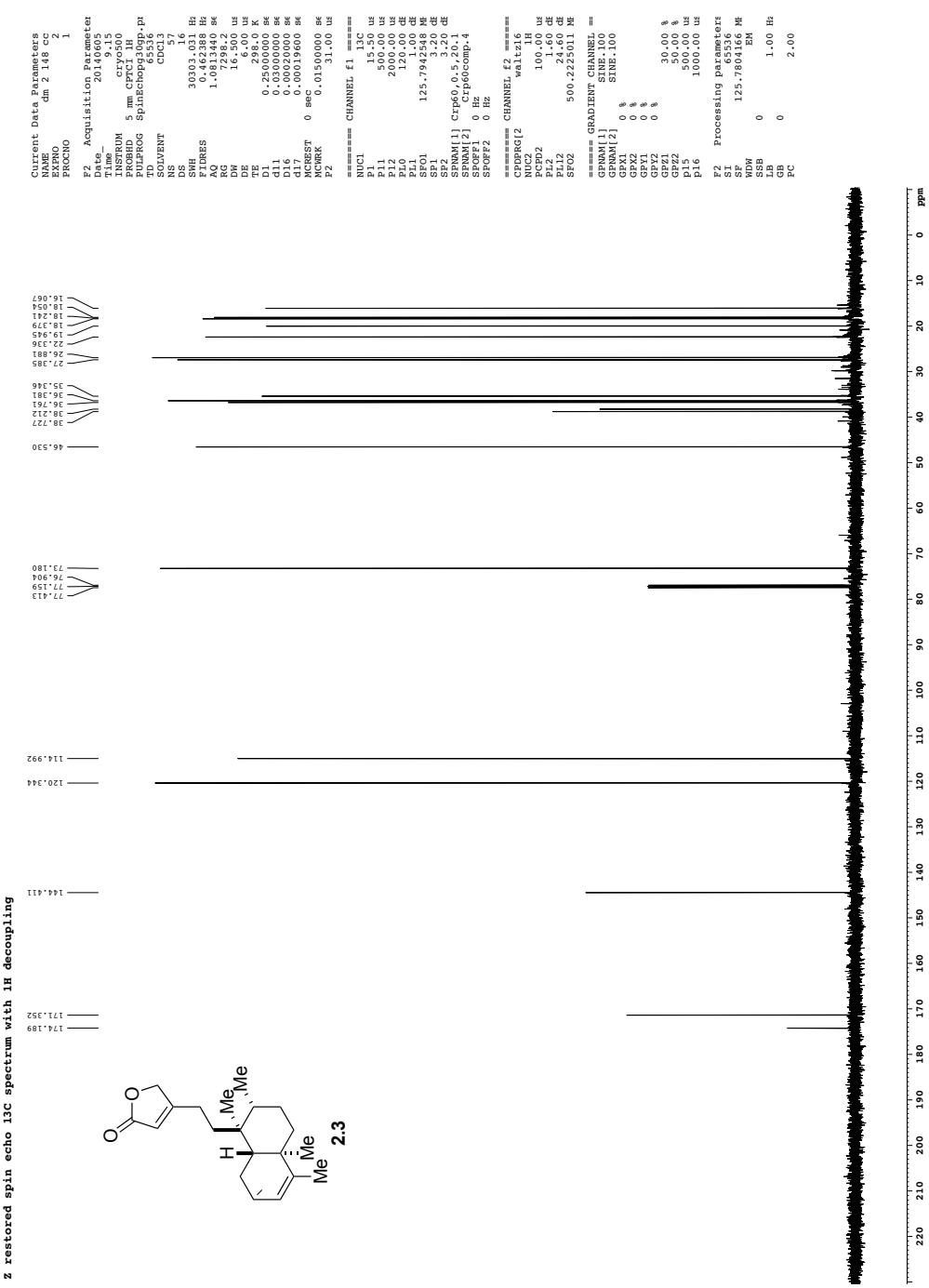

1H spectrum
Current Data Parameters
NAME GL4139 3324
EXPNO 1
PROCNO 1
F2 Acquisition Parameters
Date_ 20160426
Time 16.34
INSTRUM ccy-600
PROBHD 5 mm CPTCI 1H
PULPROG zg30
TD 81728
SOLVENT CDCl3
NS 8
DS 2
SWH 8012.820 Hz
FIDRES 0.098023 Hz
AQ 5.1099221 sec
RG 7.1
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 7.50 usec
PL1 1.00 dB
SFO1 500.2235015 MHz
F2 Processing parameters
SI 65536
SF 500.2200312 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00
0.848
0.863
0.966
0.987
1.206
1.251
1.320
1.344
1.358
1.369
1.472
1.483
1.498
1.530
1.544
1.553
1.579
1.600
1.608
1.613
1.620
1.631
1.635
1.640
2.009
2.042
2.299
4.732
5.820
5.823
5.826
7.260
1.036
1.783
1.350
1.322
3.208
1.582
2.284
2.726
3.022
2.894
6.142
ppm
Me
Me
Me
Me
2.32

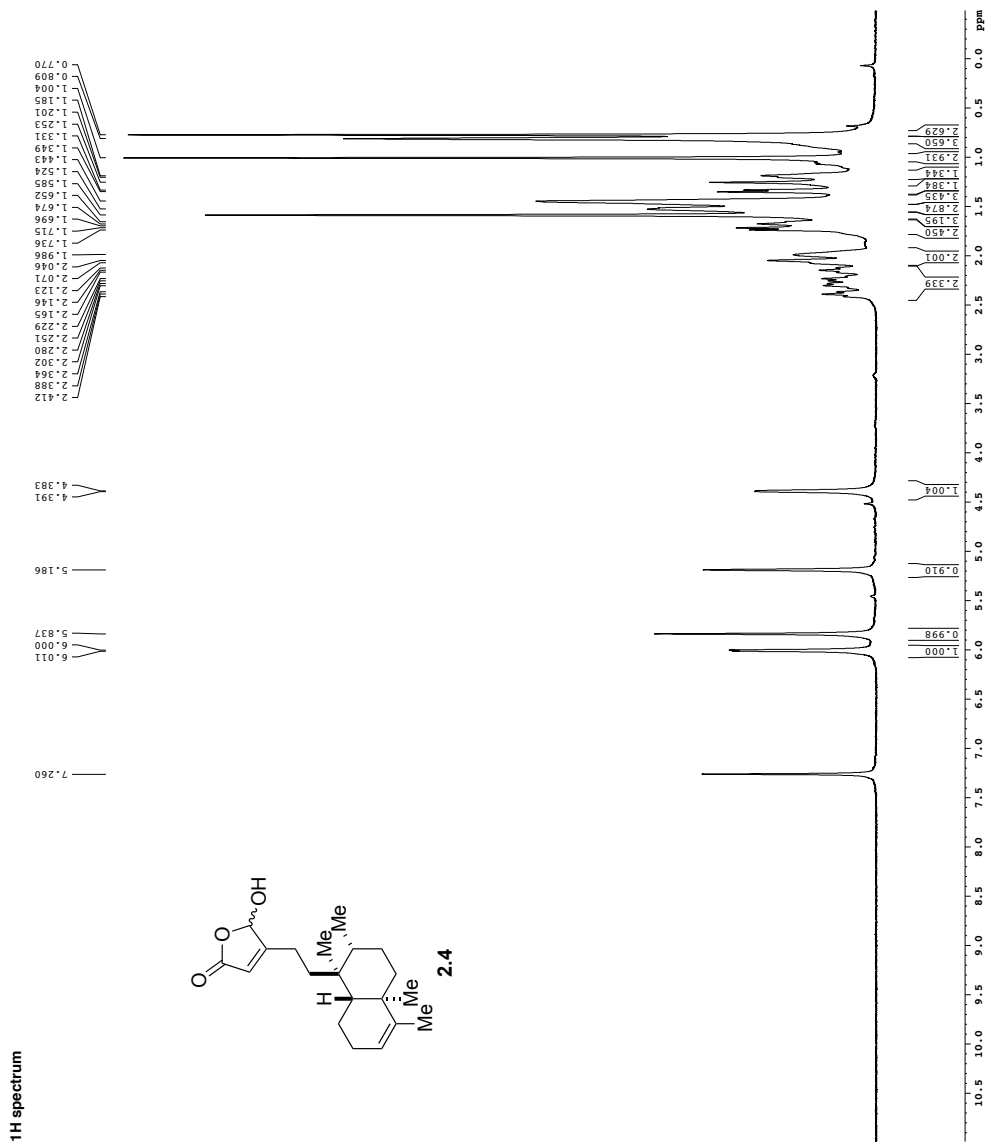

gcosy60
Me
Me
Me
Me
2.32

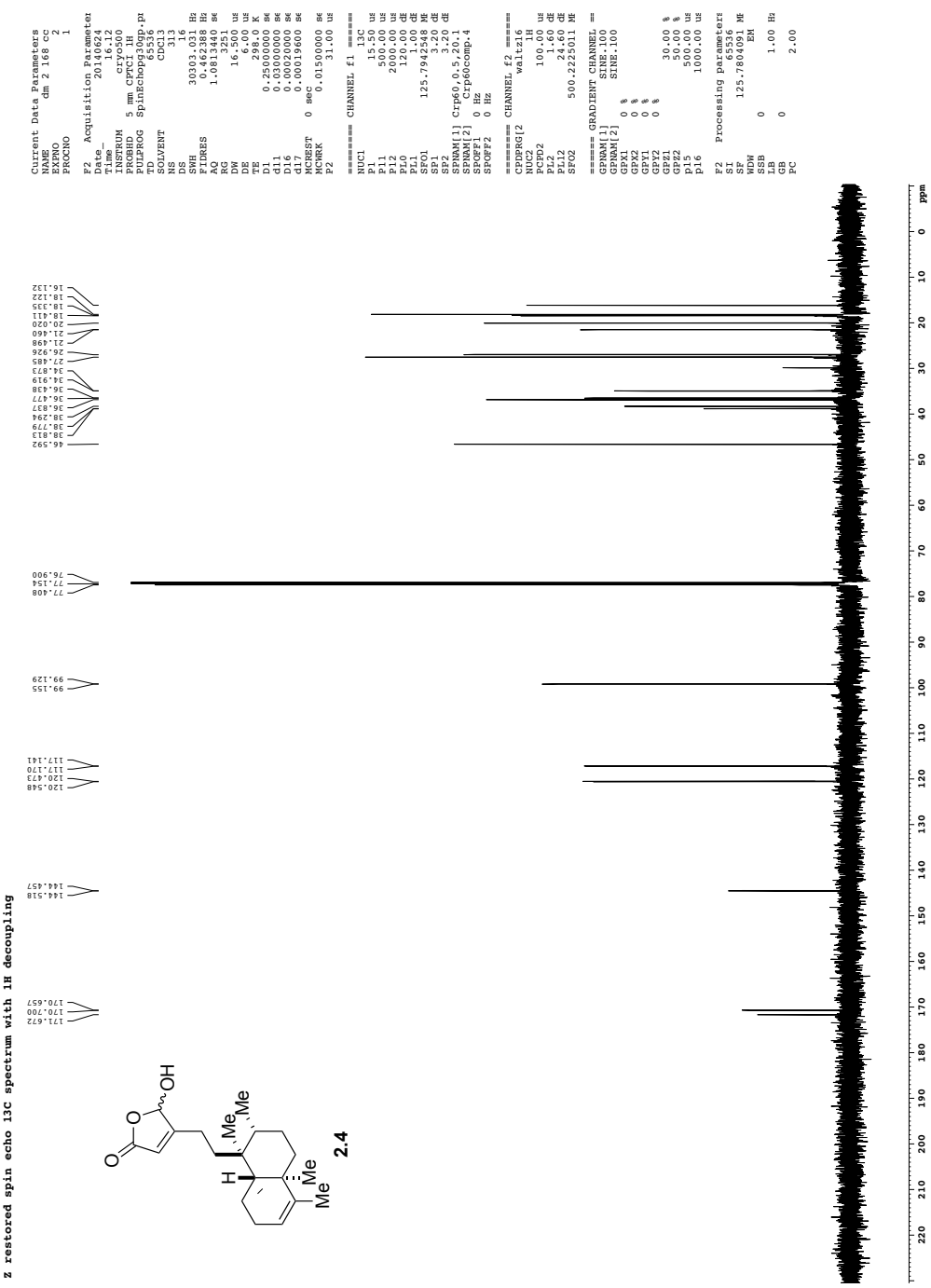

Z restored spin echo 13C spectrum with 1H decoupling
2.32
Me
Me
Me
Me
O
O
174.321
171.596
138.741
131.265
115.026
77.413
77.159
76.905
73.282
60.834
39.989
34.717
33.413
33.042
29.375
27.714
25.953
22.181
21.424
21.056
19.816
16.298
ppm

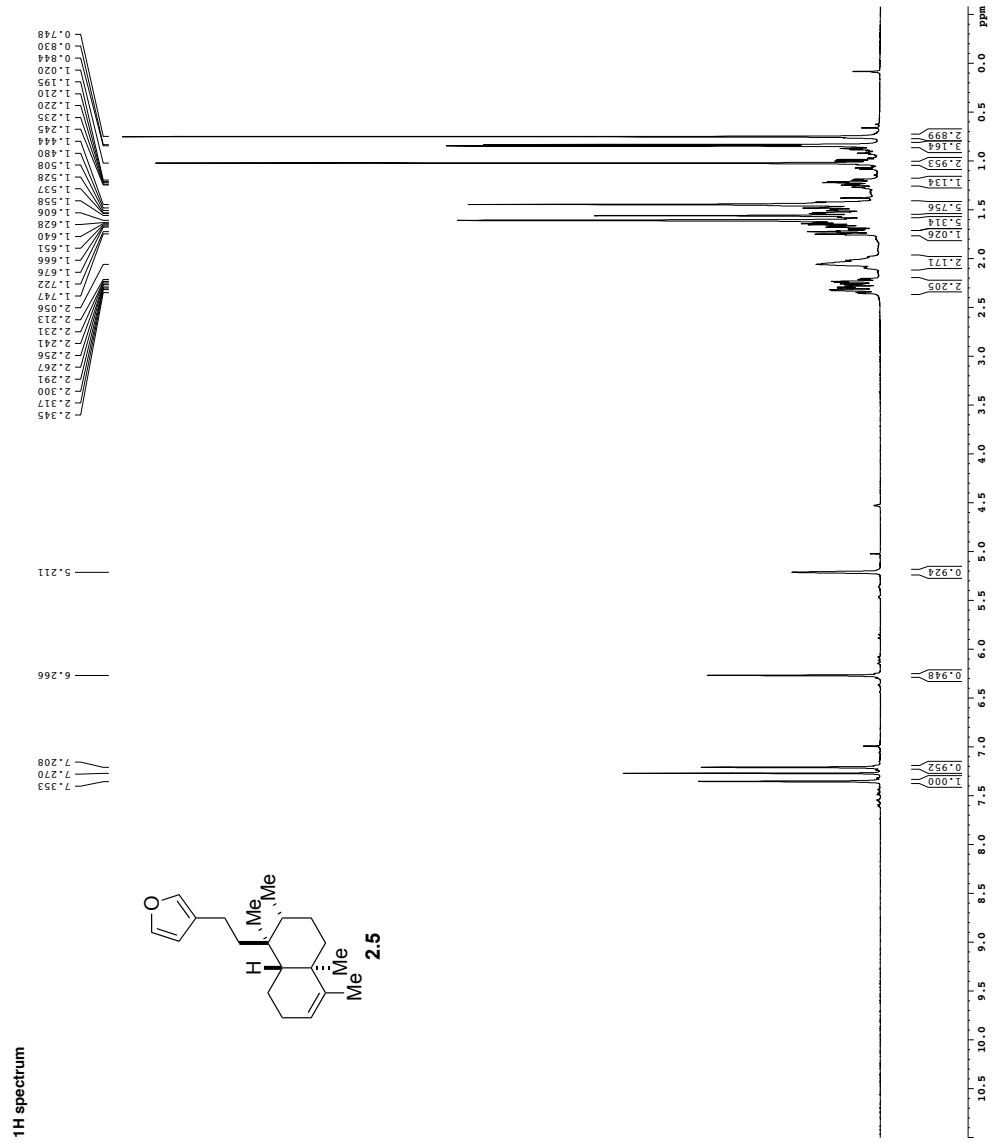

ghmqc
Me
Me
Me
Me
2.32


Current Data Parameters
NAME dm 2 148 600a
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20140604
Time 17.32
INSTRUM av600
PROBHD 5 mm TBI 1H/13
PULPROG zg30
TD 98074
SOLVENT CDCl3
NS 8
DS 2
SWH 9615.385 Hz
FIDRES 0.098047 Hz
AQ 5.0998478 sec
RG 32
DW 52.000 usec
DE 14.54 usec
TE 298.1 K
D1 0.10000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 600.1342009 MHz
NUC1 1H
P1 8.00 usec
PLW1 23.01441956 W
F2 - Processing parameters
SI 65536
SF 600.1300342 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
1H spectrum
2.304
2.298
2.277
2.256
2.250
2.207
2.199
2.179
2.159
2.151
2.071
2.041
1.954
1.941
1.928
1.911
1.721
1.700
1.680
1.672
1.657
1.649
1.635
1.627
1.564
1.533
1.526
1.510
1.504
1.494
1.487
1.480
1.471
1.461
1.452
1.430
1.420
1.308
1.303
1.292
1.286
7.260
5.806
5.165
4.713
2.039
0.941
1.000
1.136
1.012
1.042
1.039
1.091
1.233
3.066
6.270
1.056
1.260
2.917
3.156
2.783
ppm
2.3
Me
Me
H
Me
Me
O
O


z restored spin echo 13C spectrum with 1H decoupling
Current Data Parameters
NAME dm 2 148 cc
EXPNO 2
PROCNO 1
F2 - Acquisition Parameter
Date_ 20140605
Time 9.15
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H
PULPROG SpinEchopg30gp.pi
TD 65536
SOLVENT CDCl3
NS 32
DS 16
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0813440 sec
RG 72792.2
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 sec
MCWRK 0.01500000 sec
P2 31.00 usec
======== CHANNEL f1 ======
NUC1 13C
P1 15.50 usec
PL1 500.00 usec
PL12 2000.00 usec
PL0 120.00 dB
PL1 1.00 dB
SFO1 125.7942548 MHz
SP1 3.20 dB
SPNAM[1] Crp60,0.5,20.1
SPNAM[2] Crp60comp.4
SPOFF1 0 Hz
SPOFF2 0 Hz
======== CHANNEL f2 ======
CPDPRG[2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 1.60 dB
PL12 24.60 dB
SFO2 500.2225011 MHz
====== GRADIENT CHANNEL =
GPNAM[1] SINE.100
GPNAM[2] SINE.100
GPX1 0 %
GPX2 0 %
GPY1 0 %
GPY2 0 %
GPZ1 30.00 %
GPZ2 50.00 %
p15 500.00 usec
p16 1000.00 usec
F2 - Processing parameters
SI 65536
SF 125.7804166 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00
38.727
38.212
36.761
36.381
35.346
27.385
26.881
22.336
19.945
18.379
18.241
18.054
16.067
46.530
77.413
77.159
76.904
73.180
114.992
120.344
144.411
171.352
174.189
ppm
Me
Me
H
Me
Me
2.3

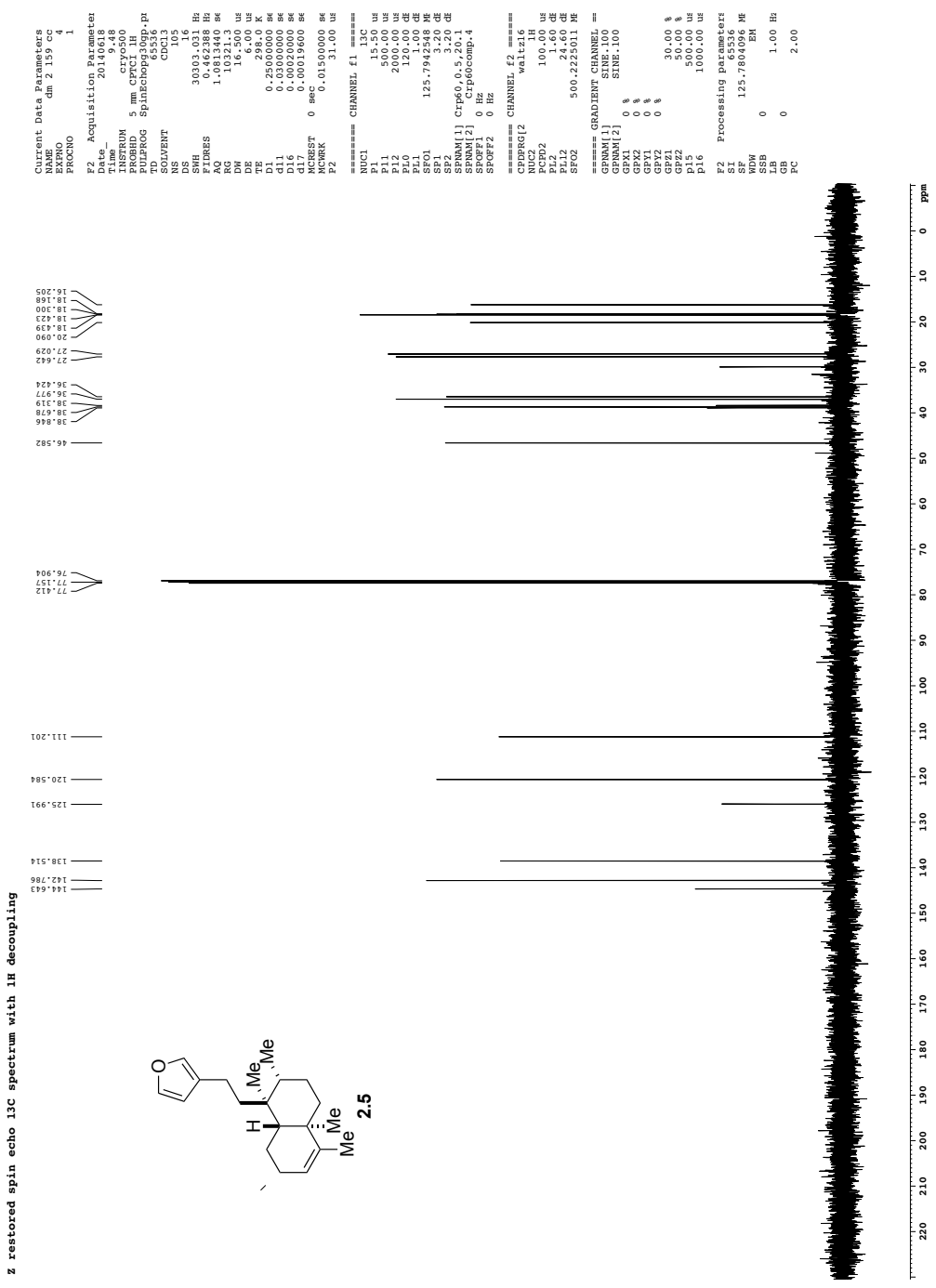

Current Data Parameters
NAME
EXPNO 1
PROCNO 1
F2 Acquisition Parameters
Date_ 20140624
Time_ 16.03
INSTRUM av600
PROBHD 5 mm TBI 1H/13
PULPROG zg30
TD 98074
SOLVENT CDCl3
NS 8
DS 2
SWH 9615.385 Hz
FIDRES 0.098042 Hz
AQ 5.0998478 sec
RG 128
DW 52.000 usec
DE 14.50 usec
TE 298.0 K
D1 0.10000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 600.1342009 MHz
NUC1 1H
P1 8.00 usec
PLW1 23.01441956 W
F2 Processing parameters
SI 65536
SF 600.1300337 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
7.260
6.011
6.000
5.837
5.186
4.391
4.383
2.412
2.388
2.364
2.302
2.280
2.251
2.229
2.165
2.146
2.123
2.071
2.046
1.986
1.736
1.715
1.696
1.674
1.652
1.585
1.524
1.443
1.349
1.331
1.253
1.201
1.185
1.004
0.809
0.770
1.000
0.998
0.910
1.004
2.339
2.001
2.450
3.195
2.874
2.435
1.384
1.344
2.931
3.650
2.629
ppm
1H spectrum
O
OH
Me
Me
H
Me
Me
2.4


z restored spin echo 13C spectrum with 1H decoupling
Current Data Parameters
NAME dm 2 168 cc
EXPNO 2
PROCNO 1
F2 - Acquisition Parameter
Date_ 20140624
Time 16.12
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H
PULPROG SpinEchopg30gp.pi
TD 65536
SOLVENT CDCl3
NS 16
DS 16
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0813440 sec
RG 325.1
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 sec 0.01500000 sec
MCWRK 31.00 usec
P2
======== CHANNEL f1 ======
NUC1 13C
P1 15.50 usec
PL1 500.00 usec
PL12 2000.00 usec
PL0 120.00 dB
PL1 1.00 dB
SFO1 125.7942548 MHz
SP1 3.20 dB
SP2 Crp60,0.5,20.1 dB
SPNAM[1] Crp60comp.4
SPNAM[2]
SPOFF1 0 Hz
SPOFF2 0 Hz
======== CHANNEL f2 ======
CPDPRG[2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 1.60 dB
PL12 24.60 dB
SFO2 500.2225011 MHz
====== GRADIENT CHANNEL =
GPNAM[1] SINE.100
GPNAM[2] SINE.100
GPX1 0 %
GPX2 0 %
GPY1 0 %
GPY2 0 %
GPZ1 30.00 %
GPZ2 50.00 %
p15 500.00 usec
p16 1000.00 usec
F2 - Processing parameters
SI 65536
SF 125.7804091 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00
171.672
170.700
170.657
144.518
144.457
120.548
120.473
117.170
117.141
99.155
99.129
77.408
77.154
76.900
46.592
38.813
38.779
38.294
36.837
36.677
36.438
34.919
34.873
27.485
26.926
21.498
20.020
18.411
18.122
16.132
OH
O
O
Me
Me
H
Me
Me
2.4
ppm

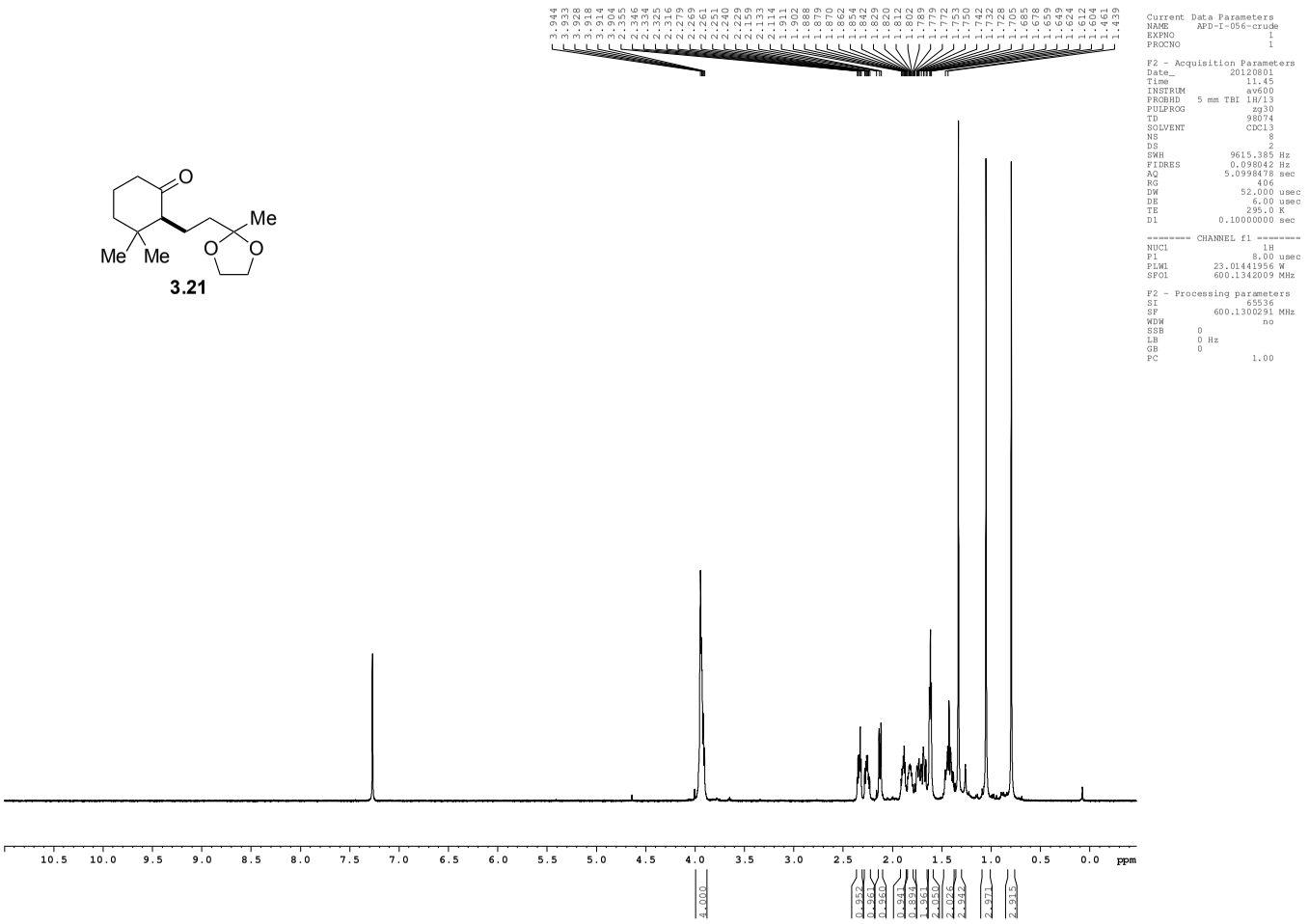


1H spectrum

2.5

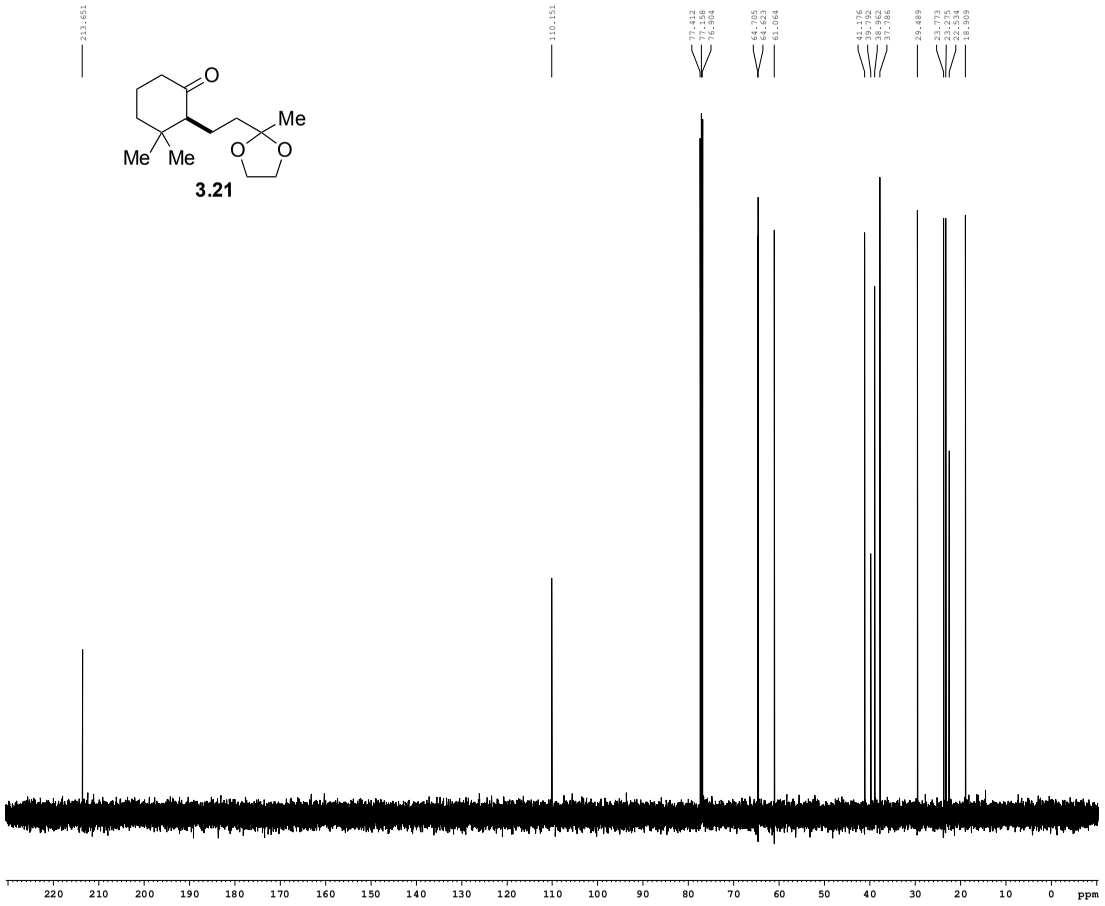

z restored spin echo 13C spectrum with 1H decoupling
2.5
Me
Me
Me
H
O
Current Data Parameters
NAME cm 2 159 cc
EXPNO 4
PROCNO 1
F2 - Acquisition Parameter
Date_ 20140617
Time 9.48
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H
PULPROG SpinEchopg30gp.pt
TD 65536
SOLVENT CDCl3
NS 105
DS 16
SWH 30303.031 Hz
FIDRES 0.462080 Hz
AQ 1.0813440 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 sec 0.01500000 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 1.50 dB
SFO1 125.7942564 MHz
SP1 3.20 dB
SP2 3.20 dB
SPNAM[1] Crp60,0.5,20.1
SPNAM[2] Crp60comp.4
SPOFF1 0 Hz
SPOFF2 0 Hz
======== CHANNEL f2 ======
CPDPRG[2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 1.60 dB
PL12 24.60 dB
SFO2 500.2225011 MHz
====== GRADIENT CHANNEL ==
GPNAM[1] SINE.100
GPNAM[2] SINE.100
GPX1 0 %
GPX2 0 %
GPY1 0 %
GPY2 0 %
GPZ1 30.00 %
GPZ2 50.00 %
P15 500.00 usec
P16 1000.00 usec
F2 - Processing parameters
SI 65536
SF 125.7804096 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00
16.205
18.168
18.300
18.423
18.439
20.090
27.029
27.642
36.424
36.977
38.319
38.678
38.846
46.582
76.904
77.157
77.412
111.201
120.584
125.991
138.514
142.786
144.643
ppm

1H spectrum

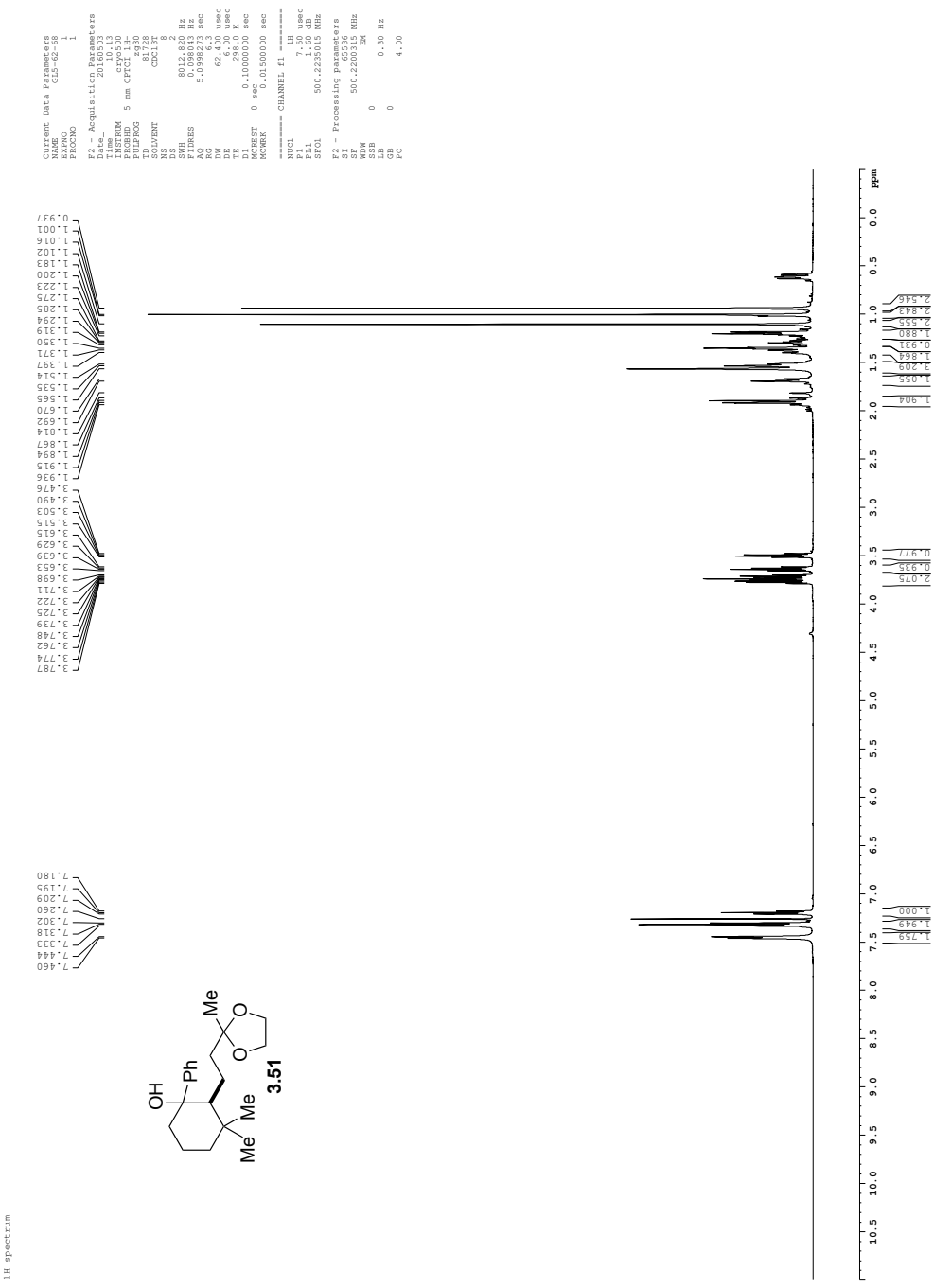


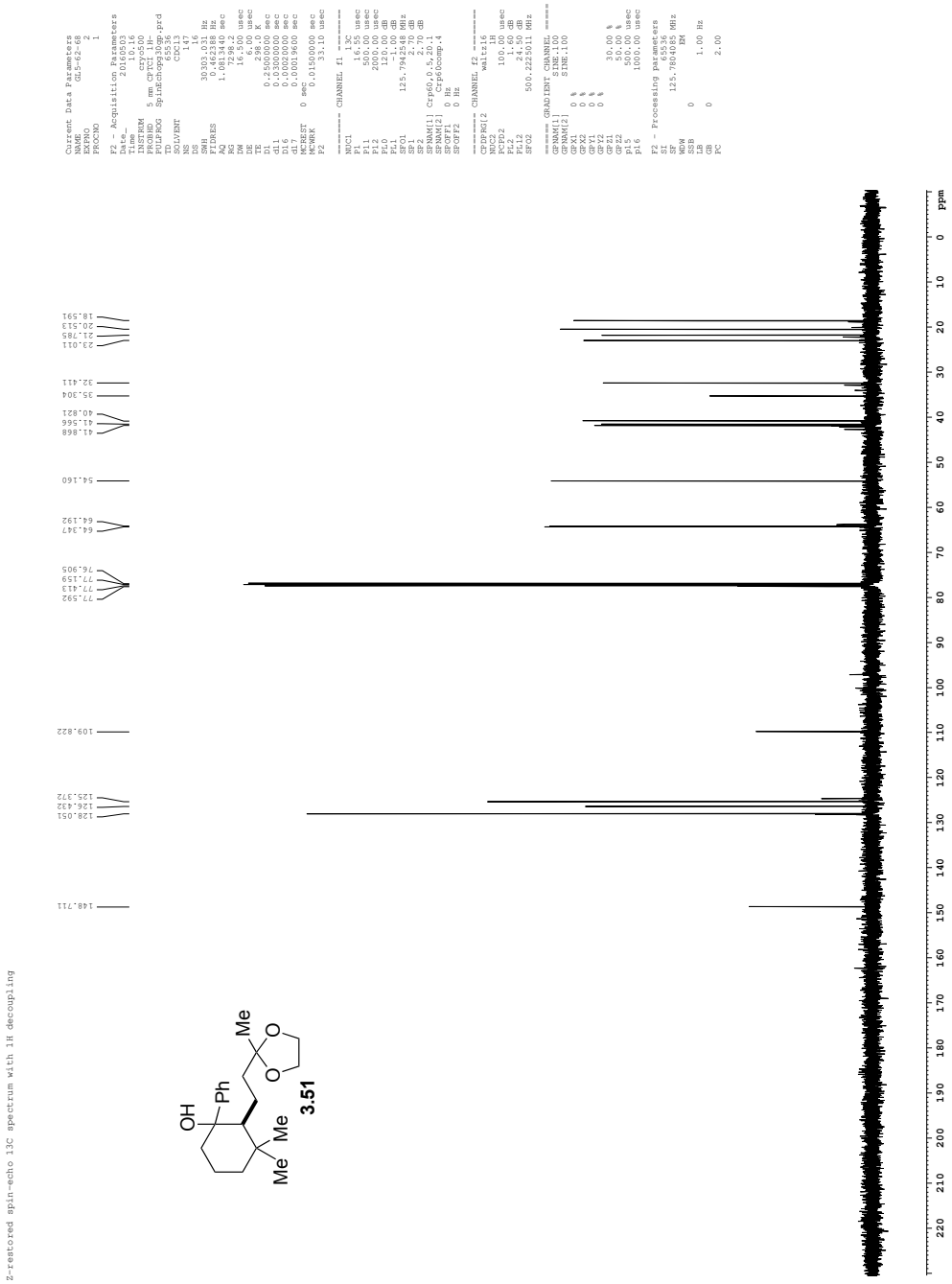

```
Current Data Parameters
NAME      APD-I-056-crude
EXPNO                   1
PROCNO                  1

F2 - Acquisition Parameters
Date_            20120801
Time                11.45
INSTRUM            av600
PROBHD   5 mm TBI 1H/13
PULPROG             zg30
TD                 98074
SOLVENT            CDC13
NS                     8
DS                     2
SWH             9615.385 Hz
FIDRES          0.098042 Hz
AQ              5.0998478 sec
RG                   406
DW                52.000 usec
DE                 6.00 usec
TE                295.0 K
D1           0.10000000 sec

======== CHANNEL f1 ========
NUC1                  1H
P1                 8.00 usec
PLW1         23.01441956 W
SFO1         600.1342009 MHz

F2 - Processing parameters
SI                 65536
SF          600.1300291 MHz
WDW                   no
SSB       0
LB        0 Hz
GB        0
PC                  1.00
```

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

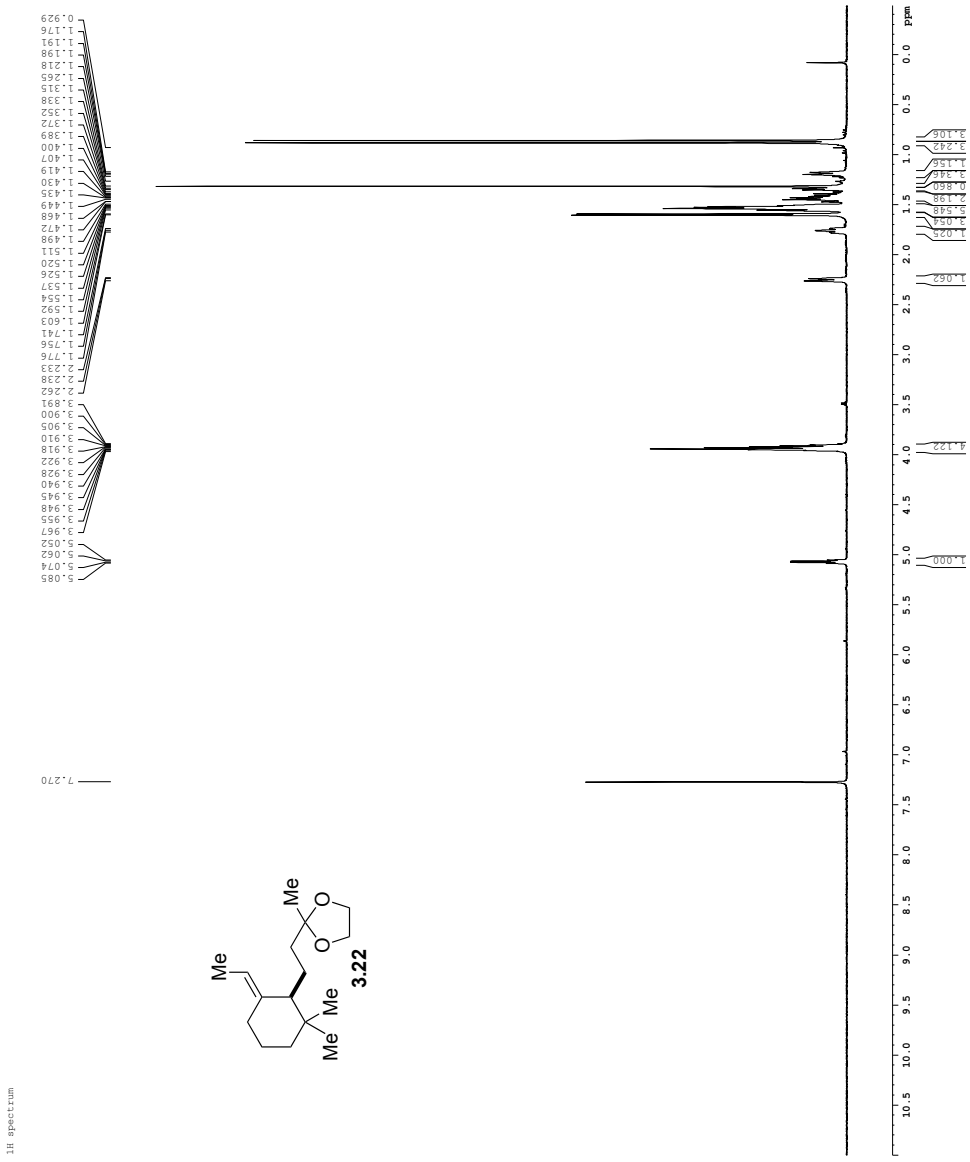



```
Current Data Parameters
NAME      APD-I-056-crude
EXPNO                   2
PROCNO                  1

F2 - Acquisition Parameters
Date_          20120801
Time              18.29
INSTRUM         cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD              65536
SOLVENT          CDCl3
NS                 266
DS                  16
SWH           30303.031 Hz
FIDRES        0.462388 Hz
AQ            1.0813440 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 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
SPNAM[1] Crp60,0.5,20.1
SPNAM[2]    Crp60comp.4
SPOFF1   0 Hz
SPOFF2   0 Hz

======= CHANNEL f2 =======
CPDPRG[2          waltz16
NUC2                1H
PCPD2          100.00 usec
PL2             1.60 dB
PL12           24.60 dB
SFO2       500.2225011 MHz

====== GRADIENT CHANNEL ====
GPNAM[1]        SINE.100
GPNAM[2]        SINE.100
GPX1     0 %
GPX2     0 %
GPY1     0 %
GPY2     0 %
GPZ1            30.00 %
GPZ2            50.00 %
p15           500.00 usec
p16          1000.00 usec

F2 - Processing parameters
SI                65536
SF         125.7804086 MHz
WDW                  no
SSB      0
LB       0 Hz
GB       0
PC              2.00
```


1H spectrum
Current Data Parameters
NAME GLS-62-68
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20160503
Time 10.13
INSTRUM spect
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 87728
SOLVENT CDCl3
NS 8
DS 2
SWH 8012.820 Hz
FIDRES 0.091643 Hz
AQ 5.4998273 sec
RG 64
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MC-REST 0 sec
MC-WORK 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 500.2200315 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00
7.460
7.444
7.333
7.318
7.302
7.260
7.209
7.195
7.180
3.787
3.774
3.762
3.748
3.739
3.725
3.722
3.711
3.698
3.653
3.639
3.629
3.615
3.515
3.503
3.490
3.476
1.936
1.915
1.894
1.867
1.814
1.692
1.670
1.565
1.535
1.514
1.397
1.371
1.350
1.319
1.294
1.285
1.275
1.223
1.200
1.183
1.102
1.016
1.001
0.937
1.759
1.949
1.000
0.977
0.939
2.075
1.904
1.055
3.209
1.864
0.931
1.880
4.843
4.855
4.848
4.846
ppm
OH
Ph
Me
Me
Me
O
O
3.51

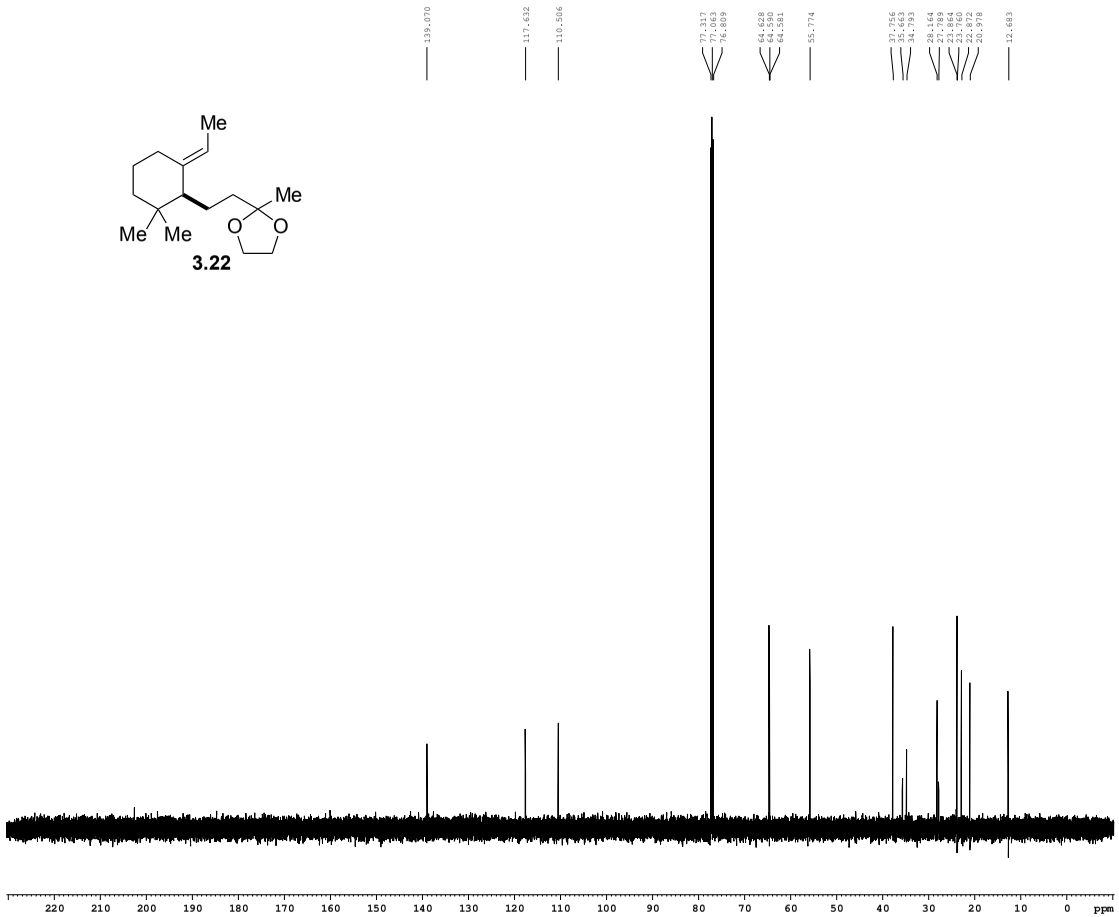


Z-restored spin-echo 13C spectrum with 1H decoupling

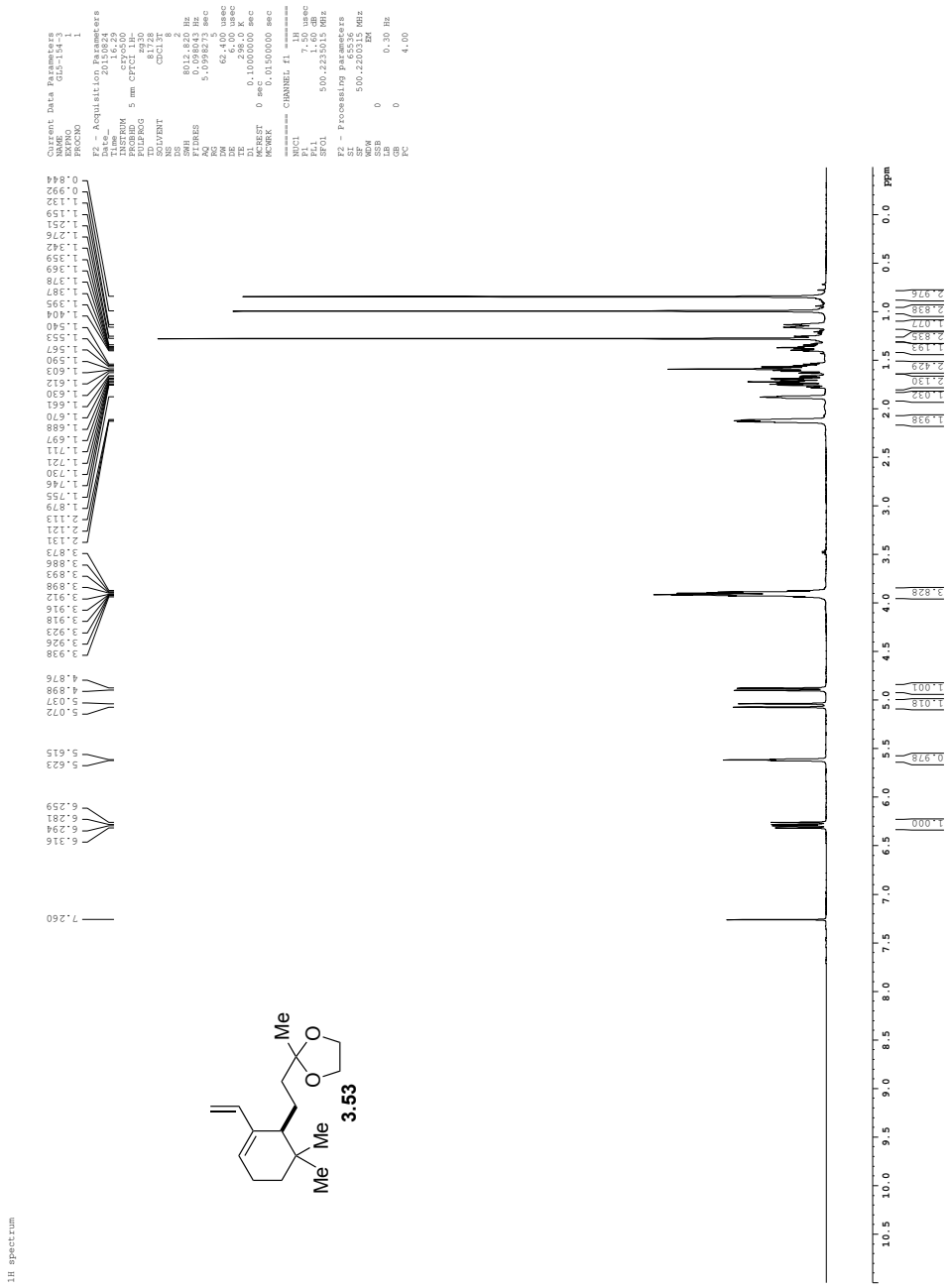

Current Data Parameters
NAME AYD-I-081-1
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20100922
Time 19.22
INSTRUM av600
PROBHD 5 mm TBI 1H/13
PULPROG zg30
TD 98074
SOLVENT CDCl3
NS 8
DS 2
SWH 9615.385 Hz
FIDRES 0.098042 Hz
AQ 5.098478 sec
RG 20
DW 52.000 usec
DE 6.00 usec
TE 298.1 K
D1 0.10000000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 8.00 usec
PL1 23.01466 dB
SFO1 600.1342009 MHz
F2 - Processing parameters
SI 65536
SF 600.1300283 MHz
WDW no
SSB 0
LB 0 Hz
GB 0
PC 1.00
7.270
5.085
5.074
5.062
5.052
3.967
3.955
3.948
3.945
3.940
3.928
3.922
3.918
3.910
3.905
3.900
3.891
2.662
2.238
2.233
1.776
1.756
1.741
1.603
1.592
1.554
1.537
1.526
1.520
1.511
1.498
1.472
1.468
1.449
1.435
1.430
1.419
1.407
1.400
1.389
1.372
1.352
1.338
1.315
1.265
1.218
1.198
1.191
1.176
0.929
Me
Me
Me
Me
O
O
3.22
1.000
4.122
1.062
1.025
3.054
5.548
4.198
0.860
3.346
1.156
3.242
3.108
ppm

1H spectrum

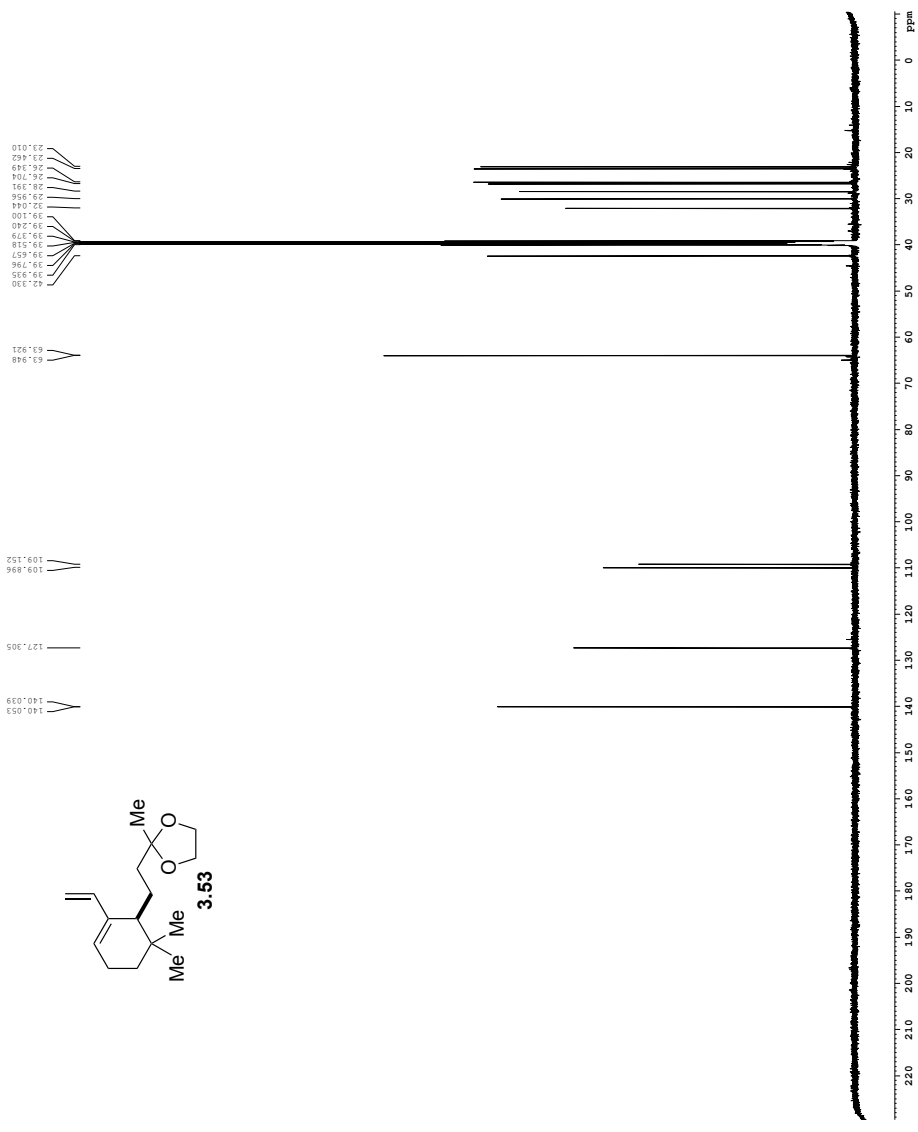
Z-restored spin-echo 13C spectrum with 1H decoupling




```
Current Data Parameters
NAME          APD-I-081-1
EXPNO                   2
PROCNO                  1

F2 - Acquisition Parameters
Date_          20120820
Time              19.30
INSTRUM          cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD               65536
SOLVENT          CDCl3
NS                 446
DS                  16
SWH           30303.031 Hz
FIDRES        0.462388 Hz
AQ            1.0813440 sec
RG                4096
DW              16.500 usec
DE               6.00 usec
TE              298.0 K
D1           0.25000000 sec
d11          0.03000000 sec
D16          0.00020000 sec
d17          0.00019600 sec
MCREST    0 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
SPNAM[1] Crp60,0.5,20.1
SPNAM[2]    Crp60comp.4
SPOFF1   0 Hz
SPOFF2   0 Hz

======= CHANNEL f2 =======
CPDPRG[2         waltz16
NUC2               1H
PCPD2           100.00 usec
PL2              1.60 dB
PL12            24.60 dB
SFO2       500.2225011 MHz

===== GRADIENT CHANNEL =====
GPNAM[1]         SINE.100
GPNAM[2]         SINE.100
GPX1      0 %
GPX2      0 %
GPY1      0 %
GPY2      0 %
GPZ1             30.00 %
GPZ2             50.00 %
p15             500.00 usec
p16            1000.00 usec

F2 - Processing parameters
SI               65536
SF         125.7804190 MHz
WDW                 no
SSB       0
LB        0 Hz
GB        0
PC               2.00
```

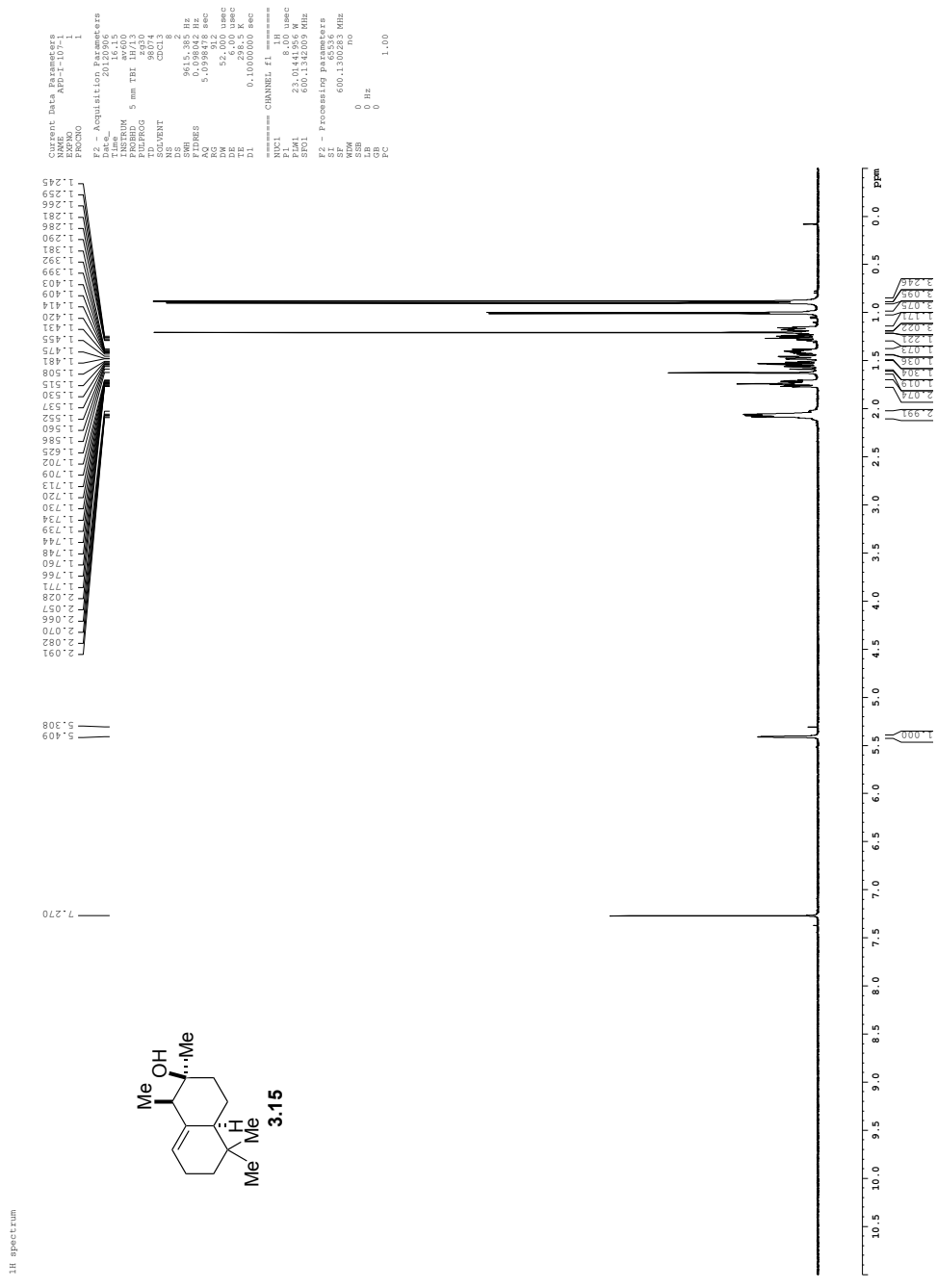

Current Data Parameters
NAME GL5-154-3
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20150824
Time 16.29
INSTRUM spect
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 81728
SOLVENT CDCl3
NS 8
DS 2
SWH 8012.820 Hz
FIDRES 0.098043 Hz
AQ 5.0998673 sec
RG 5
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0 sec
MCWRK 0.01500000 sec
CHANNEL f1
NUC1 1H
P1 7.60 usec
PL1 1.50 dB
SFO1 500.2235015 MHz
F2 - Processing parameters
SI 65536
SF 500.2200013 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00
7.260
6.316
6.294
6.281
6.259
5.623
5.615
5.072
5.037
4.898
4.876
3.938
3.926
3.923
3.918
3.916
3.912
3.898
3.893
3.886
3.873
2.131
2.121
2.113
1.879
1.755
1.746
1.730
1.721
1.711
1.697
1.688
1.670
1.650
1.641
1.612
1.603
1.590
1.567
1.553
1.540
1.404
1.395
1.387
1.378
1.369
1.359
1.342
1.276
1.251
1.159
1.132
0.992
0.844
Me
Me
Me
O
O
3.53
ppm
3.828
1.938
1.032
2.130
2.429
1.193
2.838
1.077
2.838
2.976
1.018
1.001
0.978
1.000

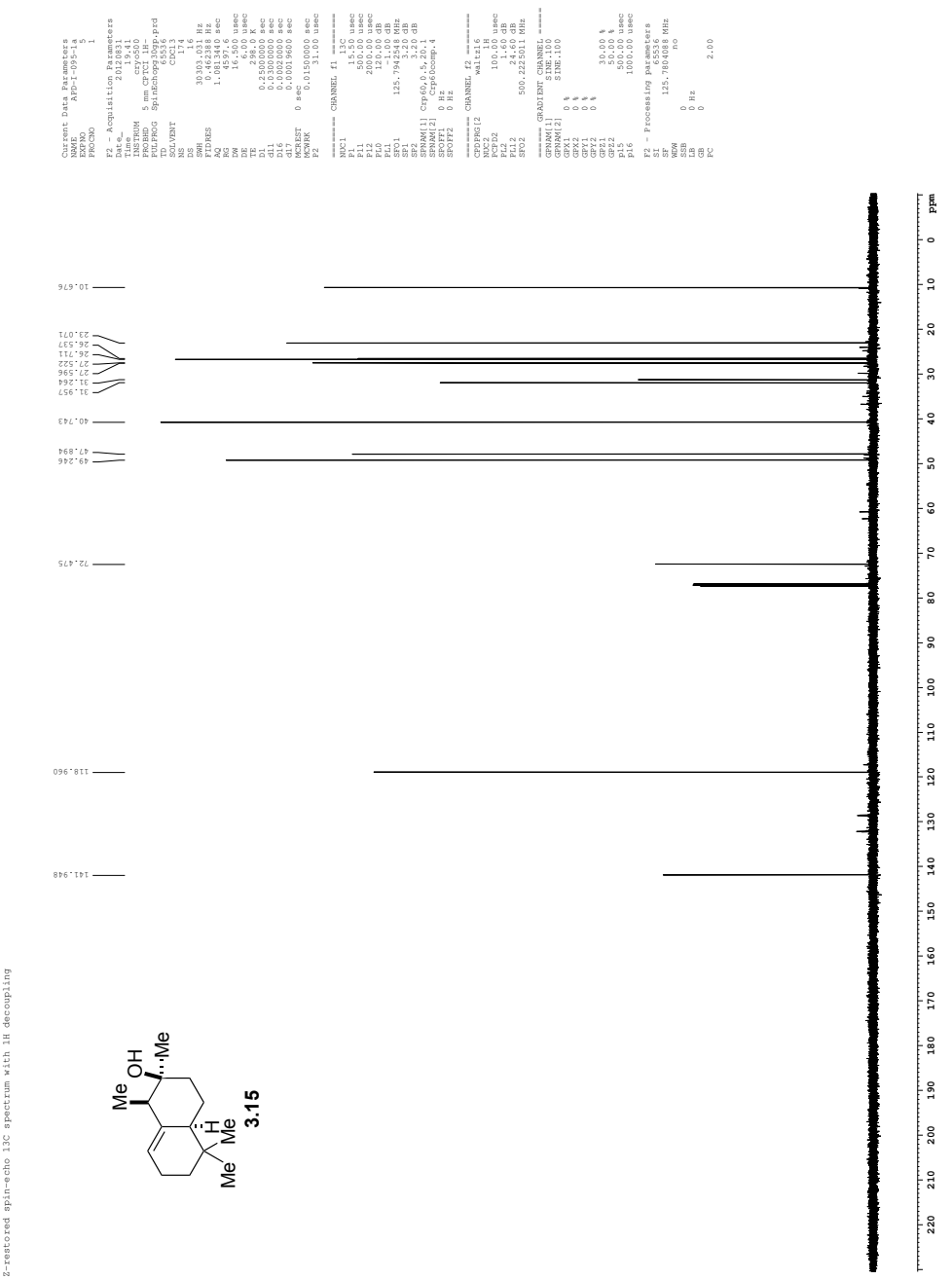
1H spectrum

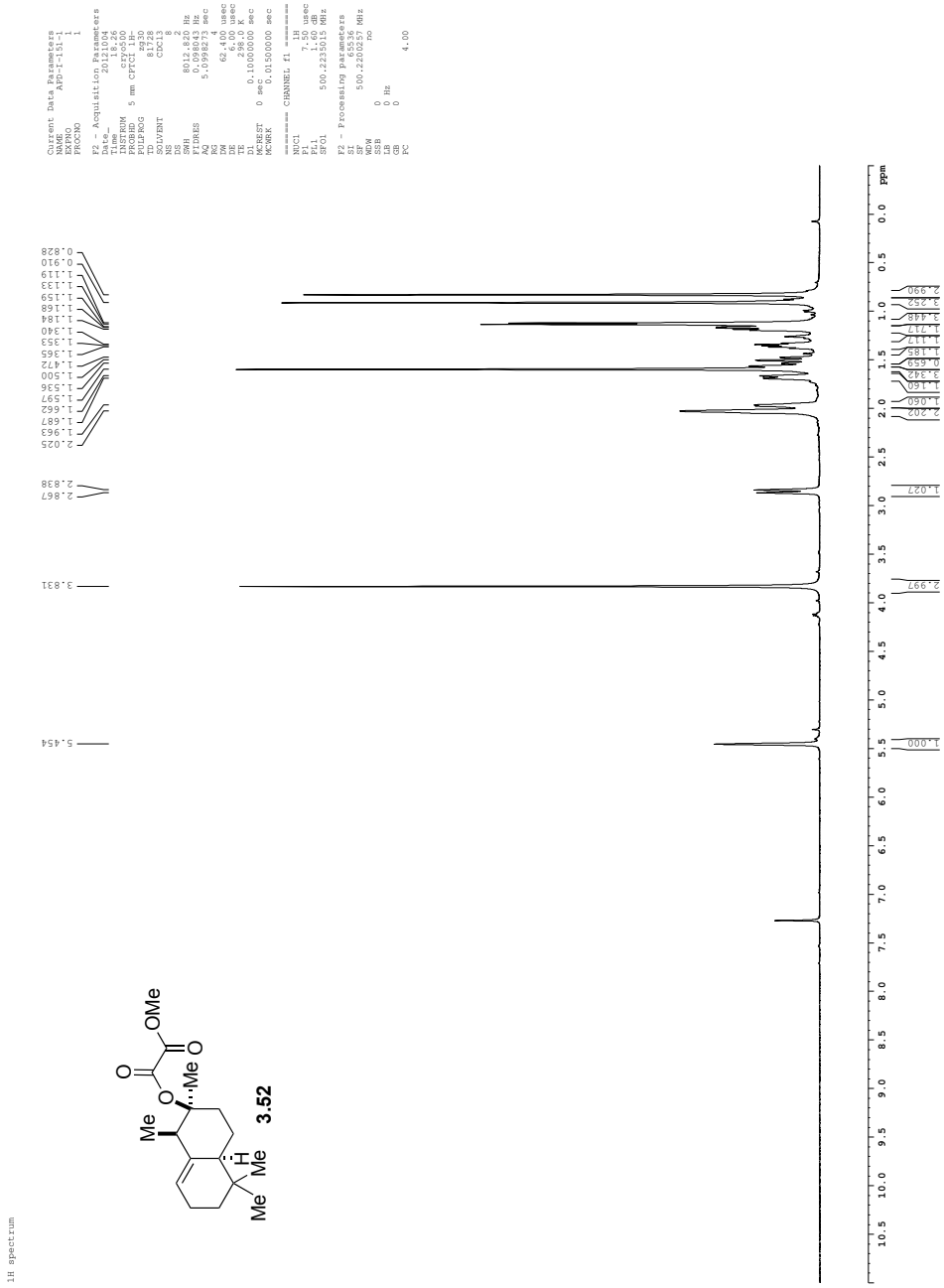

Current Data Parameters
NAME GL5-162-3dmso 2
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20160512
Time 13.31
INSTRUM av600
PROBHD 5 mm CPBBO BB-
PULPROG zgpg30
TD 65536
SOLVENT DMSO
NS 341
DS 4
SWH 36231.883 Hz
FIDRES 0.552835 Hz
AQ 0.9043968 sec
RG 2050
DW 13.800 usec
DE 19.65 usec
TE 298.0 K
D1 0.40000001 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 150.9194075 MHz
NUC1 13C
P1 10.00 usec
PLW1 64.00000000 W
======== CHANNEL f2 ========
SFO2 600.1330010 MHz
NUC2 1H
CPDPRG2 waltz16
PCPD2 80.00 usec
PLW2 20.00000000 W
PLW12 0.74000001 W
F2 - Processing parameters
SI 65536
SF 150.9028809 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.00
63.948
63.921
42.390
39.935
39.796
39.657
39.518
39.379
39.240
39.100
32.044
29.956
28.391
26.704
26.349
23.462
23.010
140.053
140.039
127.305
109.896
109.152
ppm

Me
O
O
Me
Me

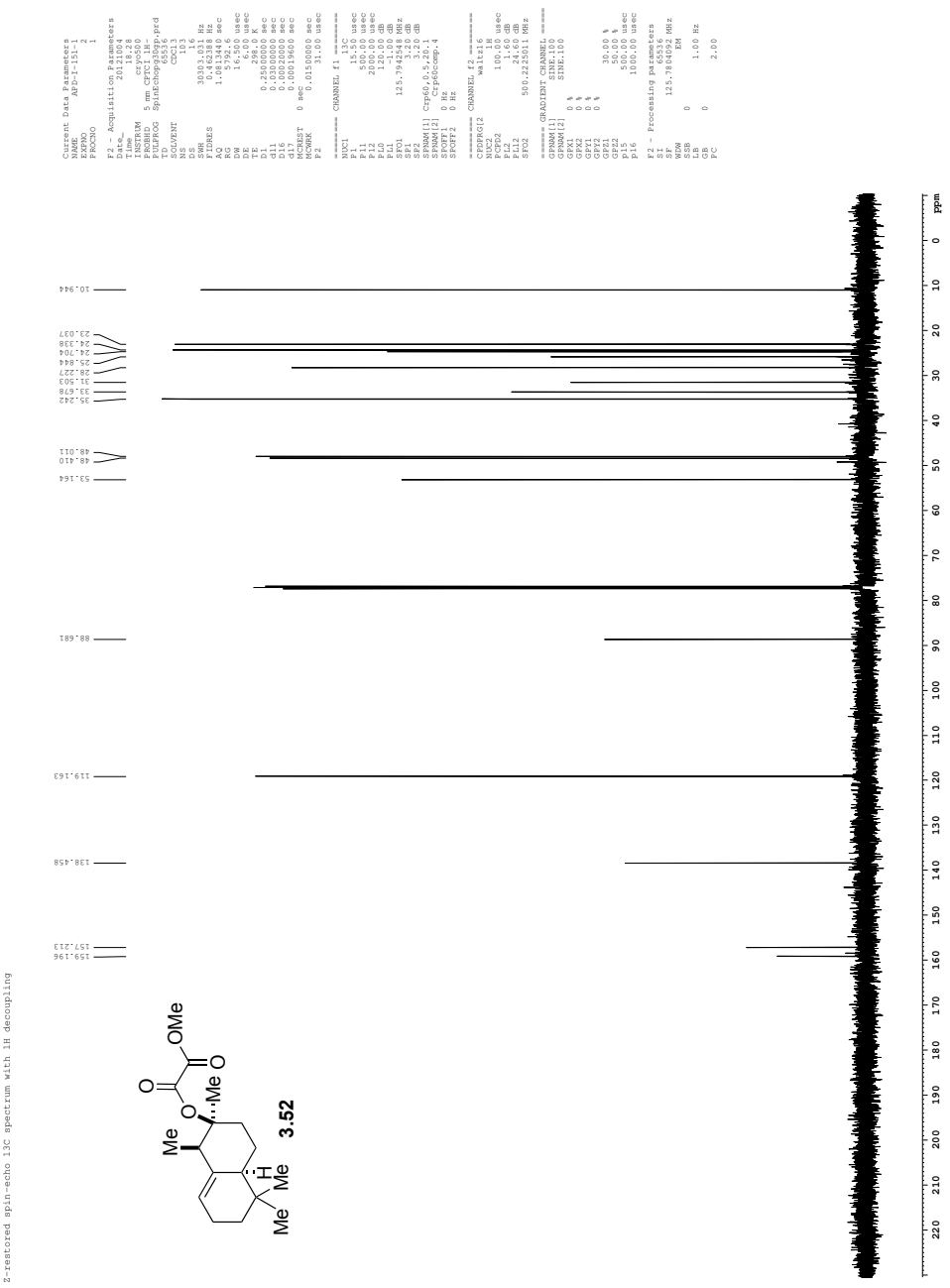
3.53

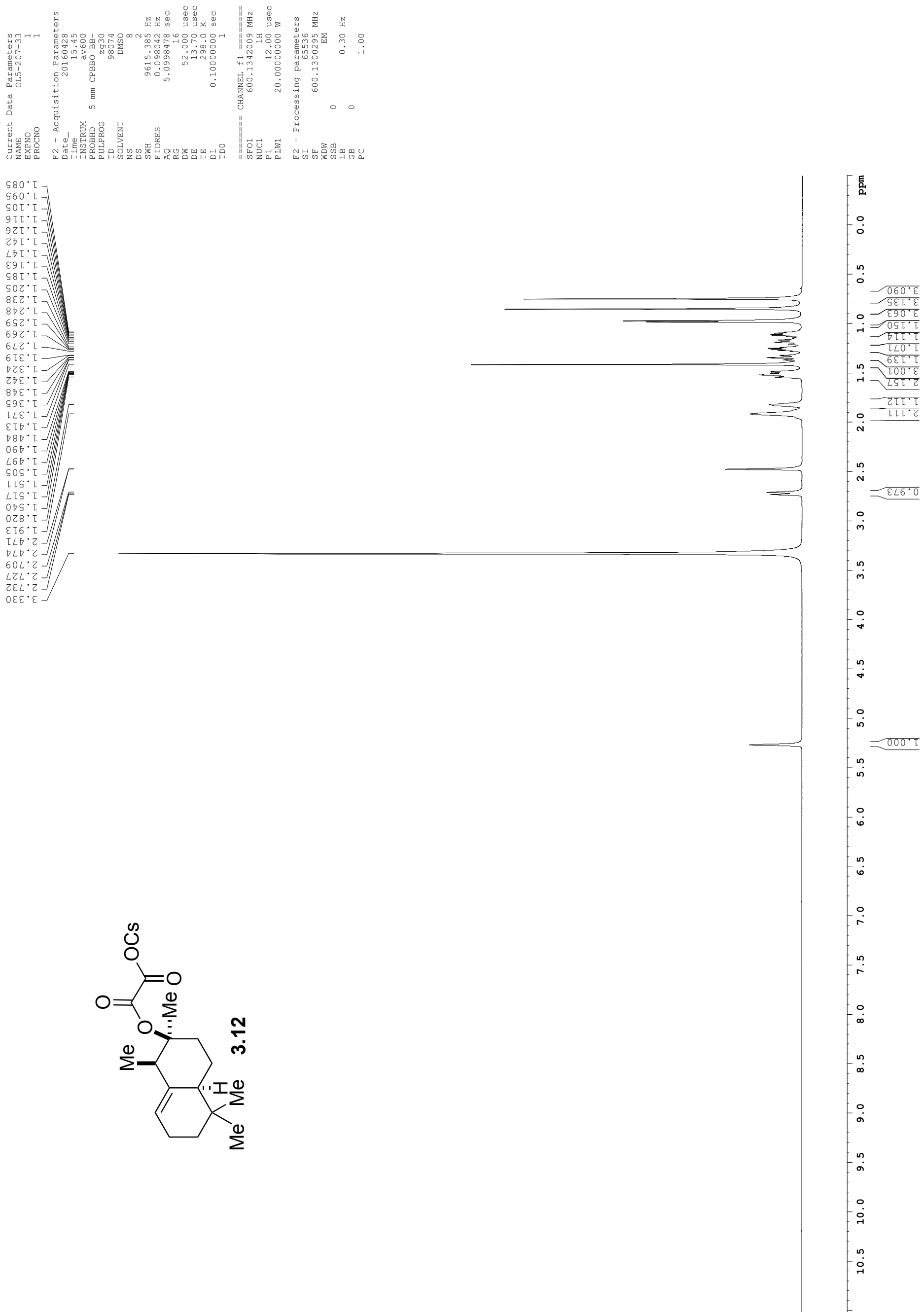

1H spectrum
Current Data Parameters
NAME AFD-I-107-1
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20100906
Time 16:15
INSTRUM av600
PROBHD 5 mm TBI 1H/13
PULPROG zg30
TD 98074
SOLVENT CDCl3
NS 8
DS 2
SWH 9615.385 Hz
FIDRES 0.098042 Hz
AQ 5.098478 sec
RG 52.000
DW 52.000 usec
DE 6.00 usec
TE 298.1 K
D1 0.10000000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 8.00 usec
PL1 23.01466 dB
SFO1 600.1342009 MHz
F2 - Processing parameters
SI 65536
SF 600.1300283 MHz
WDW no
SSB 0
LB 0 Hz
GB 0
PC 1.00
7.270
5.409
5.308
2.091
2.082
2.070
2.057
2.028
1.771
1.766
1.760
1.748
1.744
1.739
1.734
1.730
1.720
1.713
1.709
1.702
1.625
1.586
1.560
1.552
1.537
1.530
1.515
1.508
1.481
1.475
1.455
1.431
1.420
1.414
1.409
1.403
1.392
1.381
1.290
1.286
1.281
1.266
1.259
1.245
1.000
2.991
2.074
1.919
1.304
1.156
1.073
1.023
1.221
1.171
1.075
1.095
1.246
ppm
Me
OH
Me
H
Me
Me
3.15

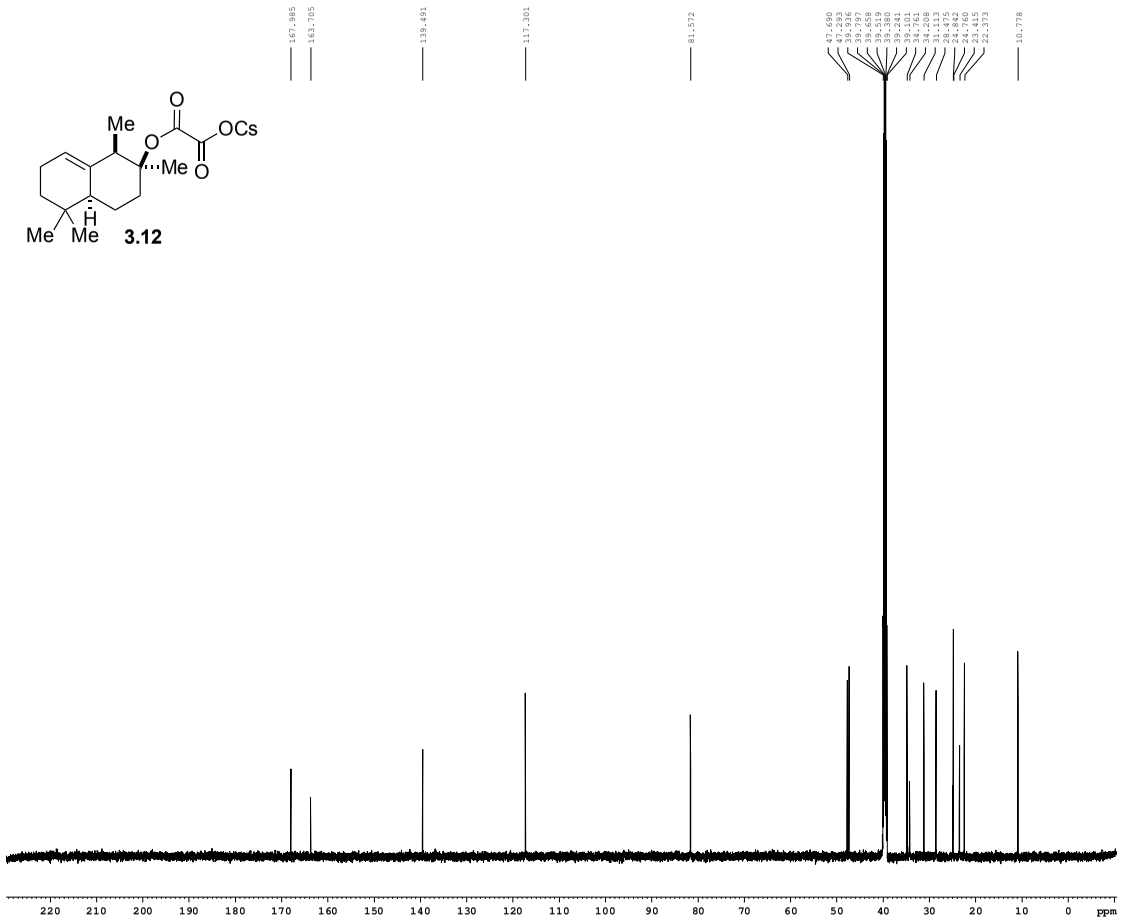

Current Data Parameters
NAME AP1-095-a
EXPNO 5
PROCNO 1
F2 - Acquisition Parameters
Date_ 20120831
Time 9.41
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG spiecho2pg.prd
TD 65536
SOLVENT CDCl3
NS 116
DS 16
SWH 30303.031 Hz
FIDRES 0.462381 Hz
AQ 1.0813440 sec
RG 45.6
DW 16.500 usec
DE 6.00 usec
TE 298.0 K
D1 0.25000000 sec
d11 0.03000000 sec
d12 0.00002000 sec
d17 0.00019600 sec
MCREST 0 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 1.60 dB
SFO1 125.7942548 MHz
SP1 3.20 dB
SP2 3.20 dB
SPNAM[1] Crp60,0.5,20.1
SPNAM[2] Crp60comp.4
SPOFF1 0 Hz
SPOFF2 0 Hz
======== CHANNEL f2 ========
CPDPRG[2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 1.60 dB
PL12 2.40 dB
SFO2 500.2250161 MHz
====== GRADIENT CHANNEL =====
GPNAM[1] SINE.100
GPNAM[2] SINE.100
GPX1 0 %
GPX2 0 %
GPY1 0 %
GPY2 0 %
GPZ1 30.00 %
GPZ2 50.00 %
p16 600.000 usec
p16 1000.00 usec
F2 - Processing parameters
SI 65536
SF 125.7804088 MHz
WDW no
SSB 0
LB 0 Hz
GB 0
PC 2.00
10.676
23.071
26.537
26.711
27.528
27.596
31.264
31.957
40.743
47.894
49.246
72.475
118.960
141.948
ppm
Me
OH
Me
H
Me
Me
3.15
Z-restored spin-echo 13C spectrum with 1H decoupling


Current Data Parameters
NAME APD-1-151-1
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20121004
Time 17.56
INSTRUM cry-600
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 81728
SOLVENT CDCl3
NS 8
DS 2
SWH 8012.820 Hz
FIDRES 0.098613 Hz
AQ 5.0998273 sec
RG 4
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0 sec
MCWRK 0.01500000 sec
CHANNEL f1
NUC1 1H
P1 7.50 usec
PL1 1.60 dB
SFO1 500.2235015 MHz
F2 - Processing parameters
SI 65536
SF 500.2200257 MHz
WDW no
SSB 0
LB 0 Hz
GB 0
PC 4.00
0.828
0.910
1.119
1.135
1.159
1.168
1.184
1.340
1.353
1.385
1.472
1.500
1.536
1.597
1.662
1.687
1.963
2.025
2.838
2.867
3.831
5.454
1.000
2.997
1.027
2.202
1.060
1.160
3.342
0.659
1.185
1.717
1.748
3.448
2.252
2.990
ppm
Me
O
O
OMe
Me
Me
Me
H
3.52

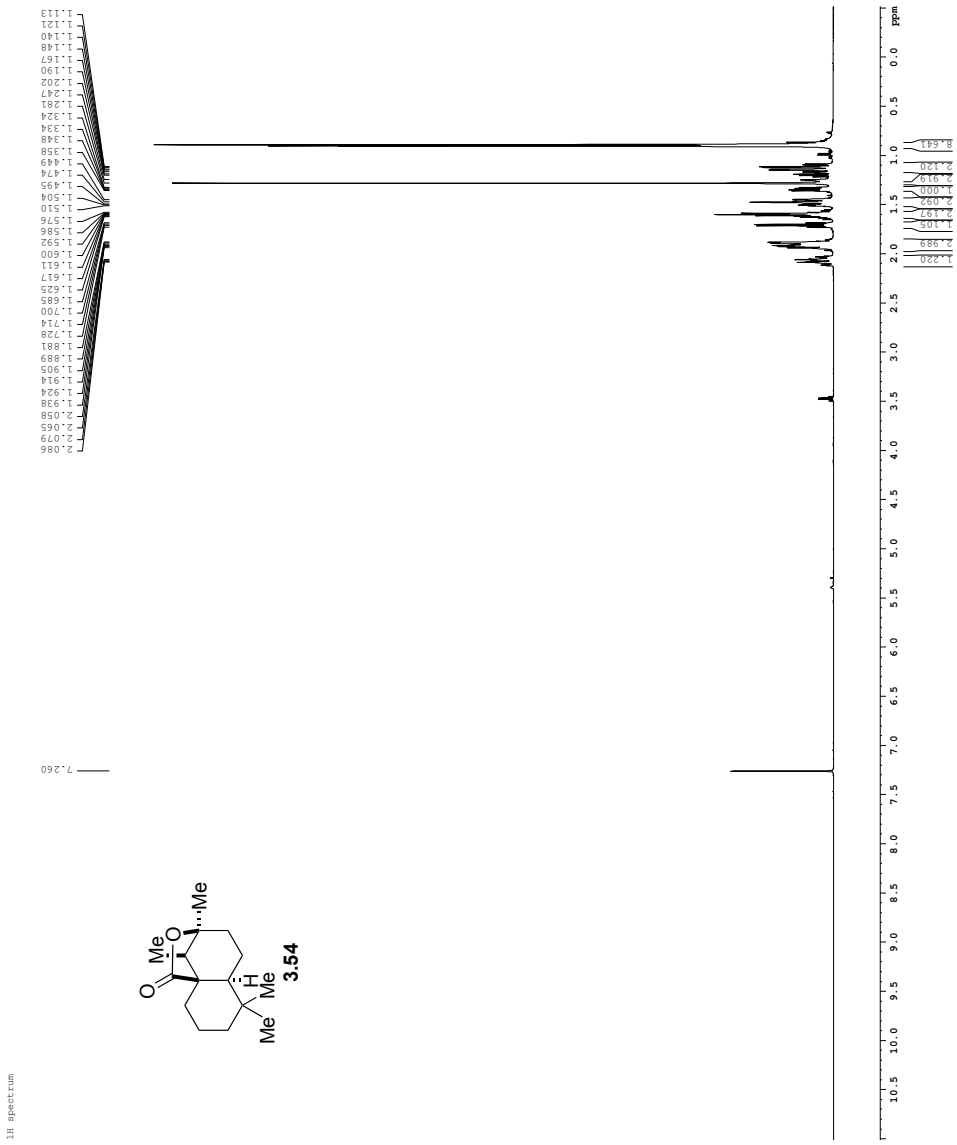
1H spectrum

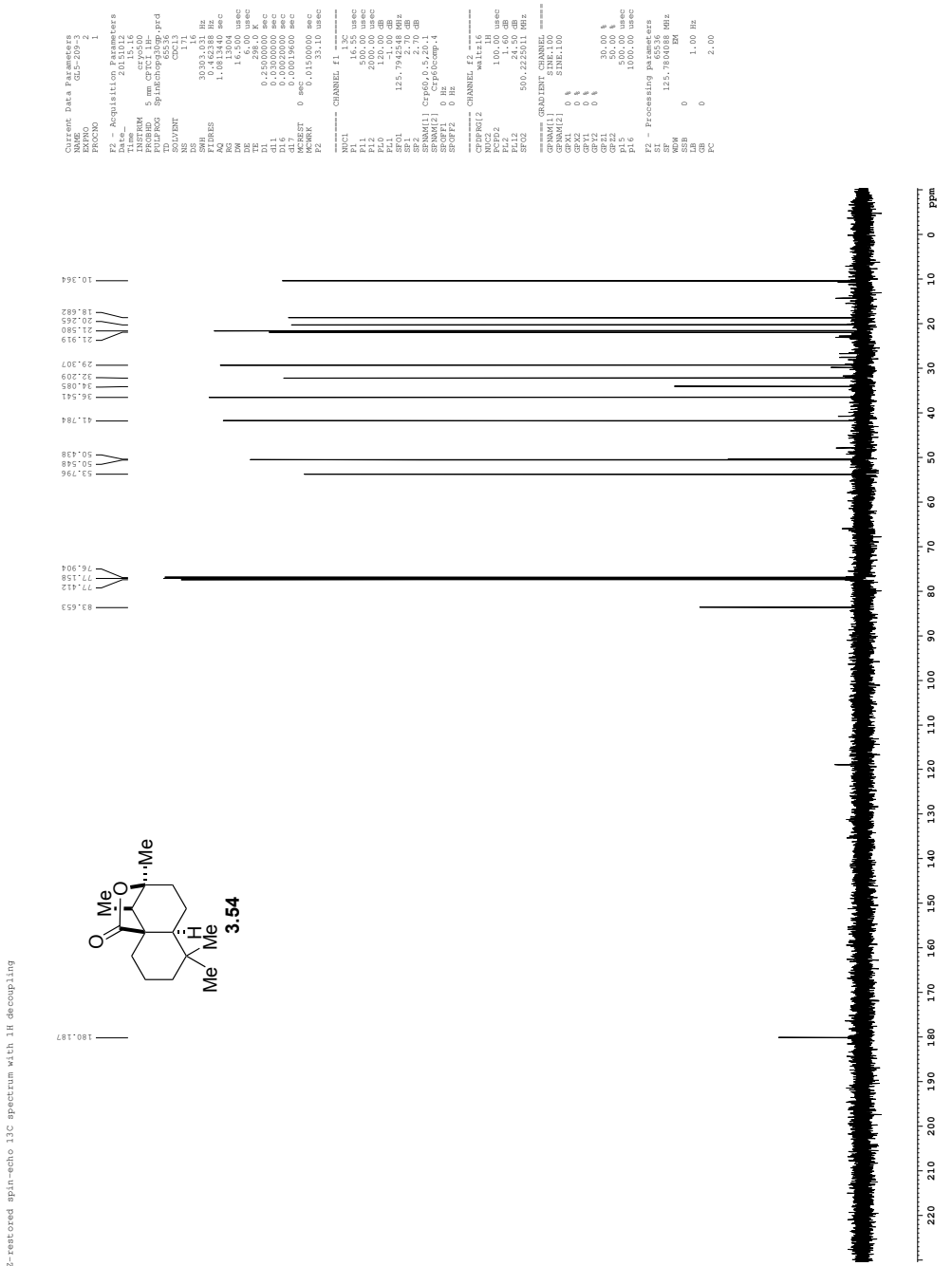

Z--restored spin-echo 13c spectrum with 1H decoupling
Current Data Parameters
NAME AFD-I-151-1
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20121004
Time 18:28
INSTRUM spect
PROBHD 5 mm CPTCI 1H
PULPROG SpinEchopg30pprd
TD 65536
SOLVENT CDCl3
NS 1024
DS 16
SWH 30303.031 Hz
FIDRES 0.462238 Hz
AQ 1.0848448 sec
RG 5792.6
DW 16.500 usec
DE 6.50 usec
TE 298.0 K
D1 0.25000000 sec
D11 0.03000000 sec
D16 0.00002000 sec
d13 0.00019400 sec
MCREST 0 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
PL2 120.00 dB
PL0 120.0 dB
PL1 1.00 dB
SFO1 125.7941148 MHz
SP1 3.20 dB
SPNAM[1] Crp60,0.5,20.1
SPNAM[2] Crp60comp.4
SPOFF1 0 Hz
SPOFF2 0 Hz
======== CHANNEL f2 ========
CPDPRG[2 waltz16
NUC2 1H
PCPD2 100.10 usec
PL2 1.60 dB
PL12 24.60 dB
SFO2 500.2228911 MHz
======== GRADIENT CHANNEL ====
GNAM[1] SINE.100
GNAM[2] SINE.100
GPX1 0 %
GPY1 0 %
GPZ1 0 %
GPX2 30.00 %
GPY2 50.00 %
GPZ2 80.00 %
DLS 1000.00 usec
P16
F2 - Processing parameters
SI 65536
SF 125.7804092 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00
159.196
157.213
138.458
119.163
88.681
53.164
48.410
48.011
35.242
33.678
31.503
28.227
25.844
24.704
24.338
23.037
10.944
Me
O
O
OMe
O
Me
H
Me
Me
3.52
ppm

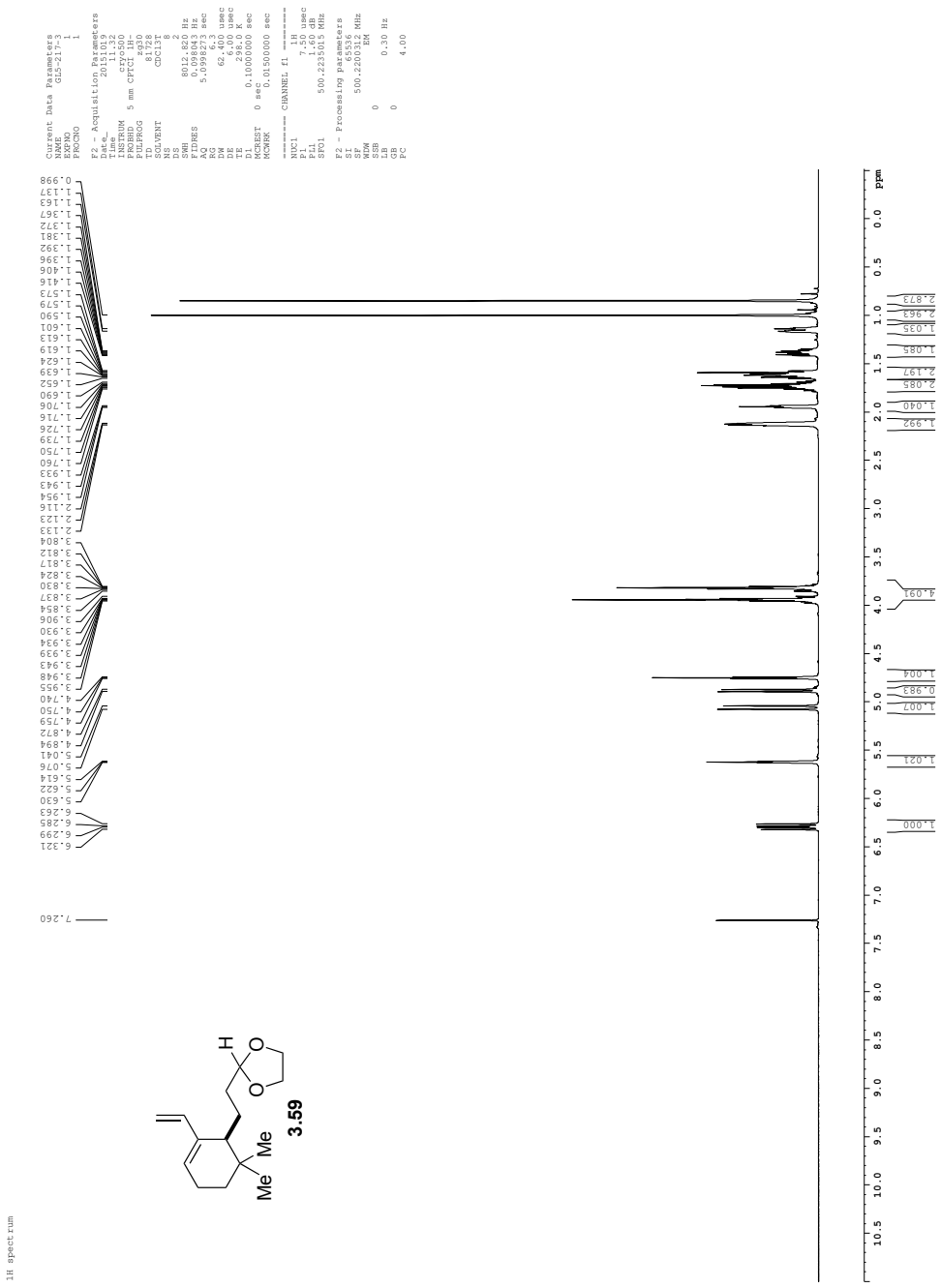

Me
O
OCs
Me
O
Me
H
Me
3.12
3.330
2.732
2.727
2.709
2.474
2.471
1.913
1.820
1.540
1.517
1.511
1.505
1.497
1.490
1.484
1.413
1.371
1.365
1.348
1.342
1.324
1.319
1.279
1.269
1.259
1.248
1.238
1.205
1.185
1.163
1.147
1.142
1.126
1.116
1.105
1.095
1.085
Current Data Parameters
NAME GL5-207-33
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20160428
Time 15.45
INSTRUM av600
PROBHD 5 mm CPBBO BB-
PULPROG zg30
TD 98074
SOLVENT DMSO
NS 8
DS 2
SWH 9615.385 Hz
FIDRES 0.098042 Hz
AQ 5.0998478 sec
RG 16
DW 52.000 usec
DE 13.70 usec
TE 298.0 K
D1 0.10000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 600.1342009 MHz
NUC1 1H
P1 12.00 usec
PLW1 20.00000000 W
F2 - Processing parameters
SI 65536
SF 600.1300295 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
10.5 10.0 9.5 9.0 8.5 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
1.000
0.973
2.111
1.112
2.157
3.001
1.139
1.071
1.114
1.150
3.063
3.135
3.090



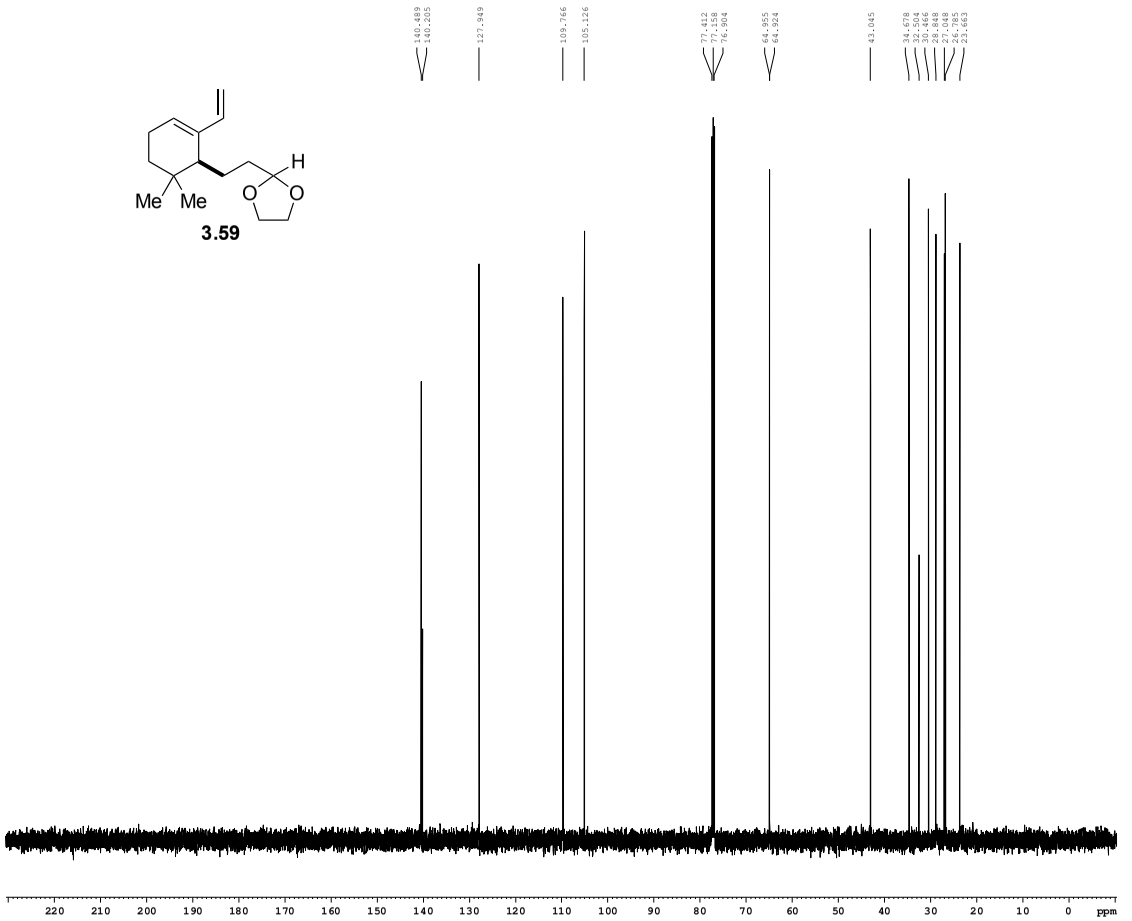

```
Current Data Parameters
NAME                 GL5-207-33
EXPNO                         2
PROCNO                        1

F2 - Acquisition Parameters
Date_               20160428
Time                     15.48
INSTRUM                  av600
PROBHD    5 mm CPBBO BB-
PULPROG                zgdc30
TD                      65536
SOLVENT                  DMSO
NS                         90
DS                          4
SWH                 36231.883 Hz
FIDRES              0.552855 Hz
AQ                  0.9043968 sec
RG                       2050
DW                     13.800 usec
DE                     19.65 usec
TE                     298.0 K
D1                  0.40000001 sec
D11                 0.03000000 sec
TD0                         1

======== CHANNEL f1 ========
SFO1               150.9194075 MHz
NUC1                       13C
P1                       10.00 usec
PLW1               64.00000000 W

======== CHANNEL f2 ========
SFO2               600.1330010 MHz
NUC2                       1H
CPDPRG[2                waltz16
PCPD2                    80.00 usec
PLW2               20.00000000 W
PLW12               0.36000001 W

F2 - Processing parameters
SI                       65536
SF                 150.9028796 MHz
WDW                         EM
SSB          0
LB                       1.00 Hz
GB           0
PC                       1.00
```


Current Data Parameters
NAME GL5-209-3
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20151012
Time 15:13
INSTRUM spect
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 8192
SOLVENT CDCl3T
NS 8
DS 2
SWH 8012.820 Hz
FIDRES 0.978943 Hz
AQ 5.0922752 sec
RG 5.7
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0 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 500.2200052 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00
7.260
8.641
7.120
7.919
1.000
2.092
2.197
1.105
2.989
1.220
ppm
1H spectrum
Me
O
Me
O
H
Me
Me
3.54

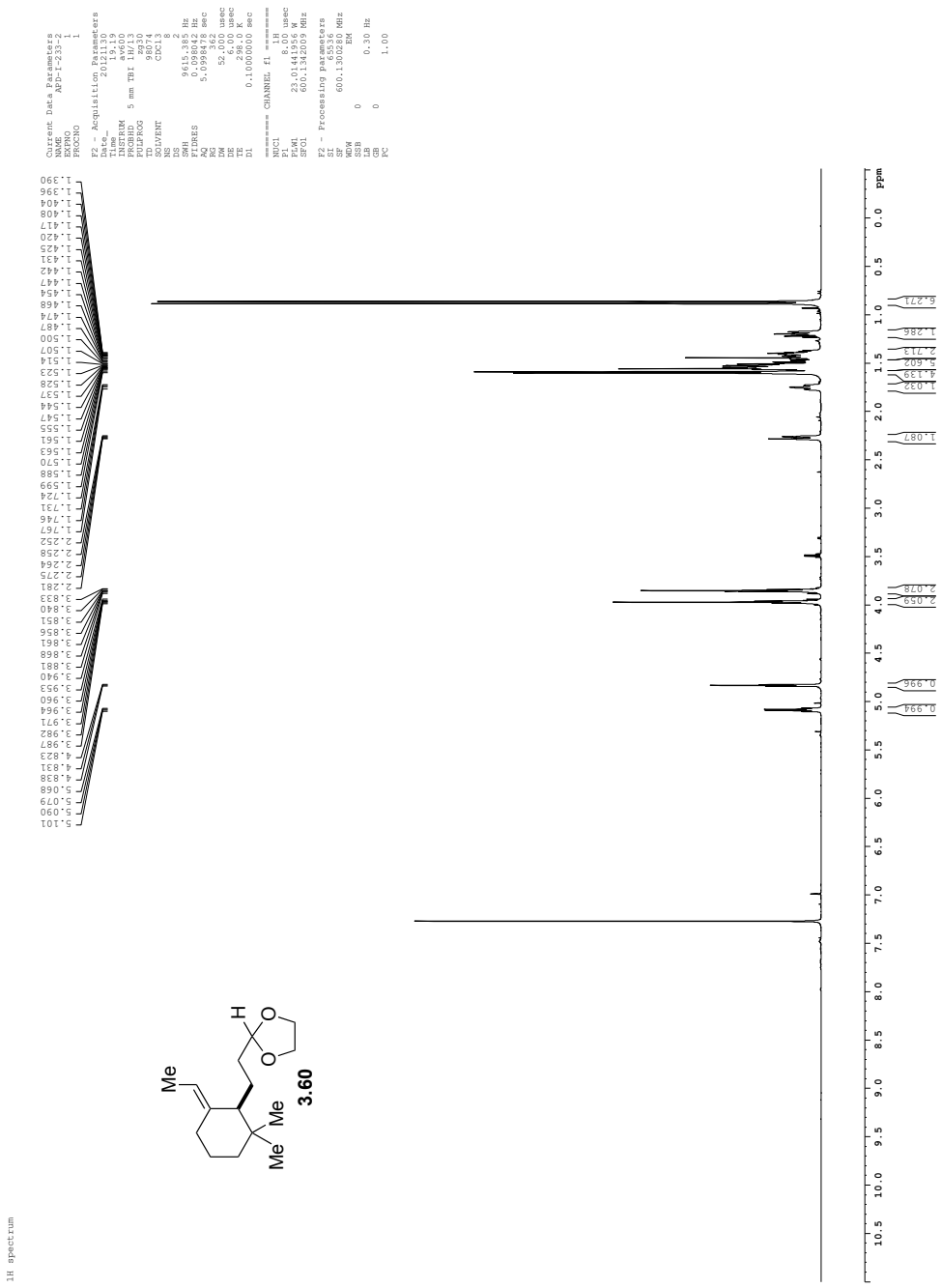

Current Data Parameters
NAME GLS-209-3
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20151012
Time 15.16
INSTRUM cryo600
PROBHD 5 mm CPTCI 1H-
PULPROG Spinechopgp30gp.prd
TD 65536
SOLVENT CDCl3
NS 171
DS 16
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0813440 sec
RG 13004
DW 16.500 usec
DE 6.00 usec
TE 298.0 K
D1 0.25000000 sec
d11 0.03000000 sec
D16 0.00020000 sec
d17 0.00019600 sec
MC2REST 1 sec
MCWRK 0.015000000 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 21.00 dB
SFO1 125.7942548 MHz
SP1 2.70 dB
SP2 2.70 dB
SPNAM[1] Crp60,0.5,20.1
SPNAM[2] Crp60comp.4
SPOFF1 0 Hz
SPOFF2 0 Hz
======== CHANNEL f2 ========
waltz16
CPDPRG[2
NUC2 1H
PCPD2 100.00 usec
PL2 1.60 dB
PL12 24.41 dB
SFO2 500.2225011 MHz
===== GRADIENT CHANNEL =====
GFNAM[1] SINE.100
GFNAM[2] SINE.100
GPX1 0 %
GPX2 0 %
GPY1 0 %
GPY2 0 %
GPZ1 30.00 %
GPZ2 50.00 %
P15 500.00 usec
P16 1000.00 usec
F2 - Processing parameters
SI 65536
SF 125.7804088 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00
10.364
18.682
20.265
21.580
21.919
29.307
32.209
34.085
36.541
41.784
50.438
50.548
53.796
76.904
77.158
77.412
83.653
180.187
Me
O
Me
O
H
Me
Me
3.54
ppm
2-testcored spin-echo 13C spectrum with 1H decoupling


Current Data Parameters
NAME G15-217-3
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20151002
Time 11.32
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 81728
SOLVENT CDCl3
NS 8
DS 2
SWH 8012.822 Hz
FIDRES 0.098043 Hz
AQ 5.099827 sec
RG 64
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0 sec 0.01500000 sec
MCWRK
CHANNEL f1
NUC1 1H
P1 7.50 usec
PL1 1.60 dB
SFO1 500.2235015 MHz
F2 - Processing parameters
SI 65536
SF 500.2200312 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00
7.260
6.321
6.299
6.285
6.263
5.630
5.622
5.614
5.076
5.041
4.894
4.872
4.759
4.750
4.740
3.955
3.948
3.943
3.939
3.934
3.930
3.906
3.854
3.837
3.830
3.824
3.817
3.812
3.804
2.133
2.123
2.116
1.954
1.943
1.933
1.760
1.750
1.739
1.726
1.716
1.706
1.690
1.652
1.639
1.624
1.619
1.613
1.601
1.590
1.579
1.573
1.416
1.406
1.396
1.392
1.381
1.372
1.367
1.163
1.137
0.998
H
O
O
Me
Me
3.59
4.091
1.004
0.983
1.007
1.021
1.000
1.992
1.040
2.085
2.197
1.085
1.035
2.963
2.873
ppm
1H spect.rum

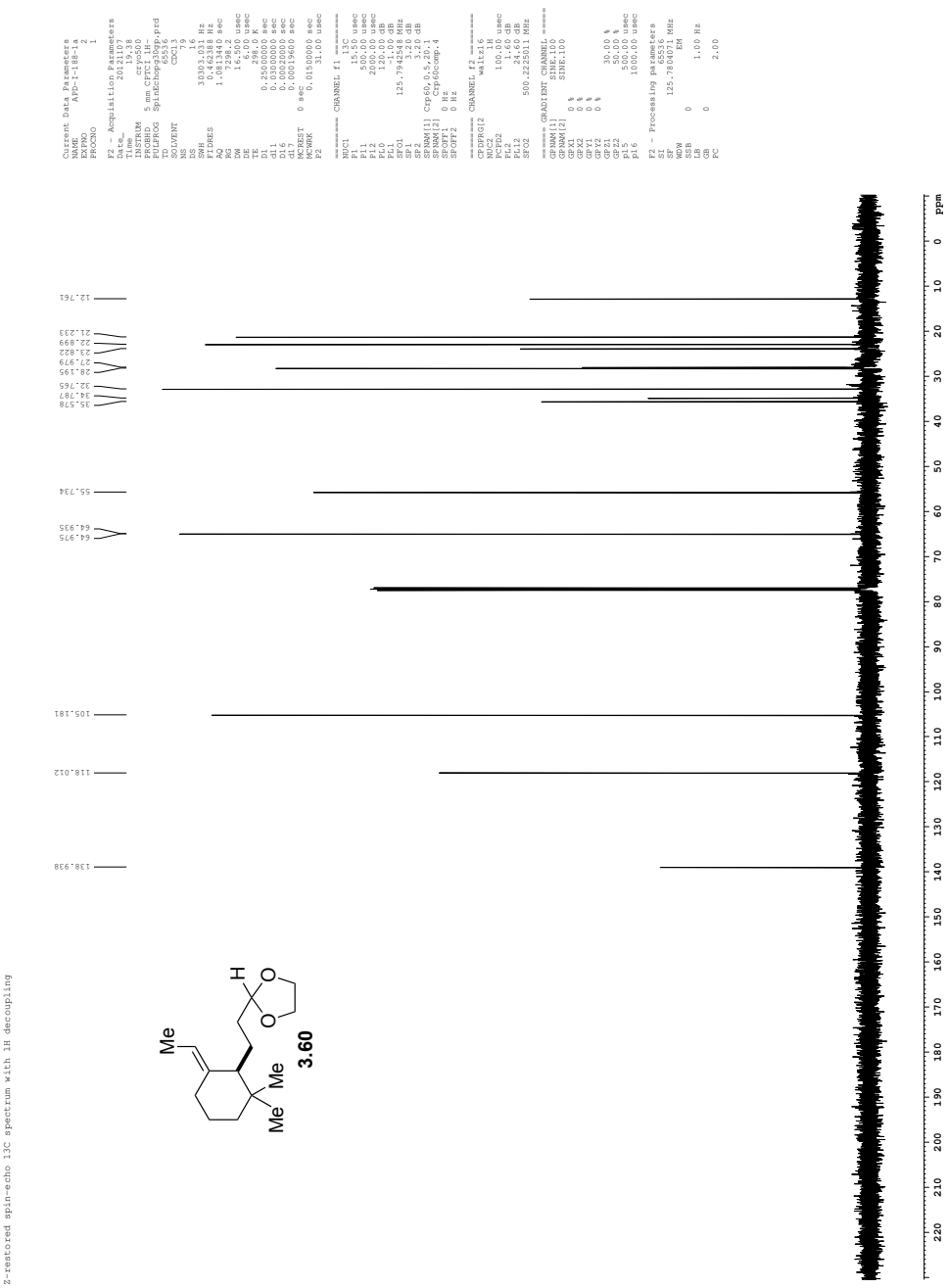
Z-restored spin-echo 13C spectrum with 1H decoupling

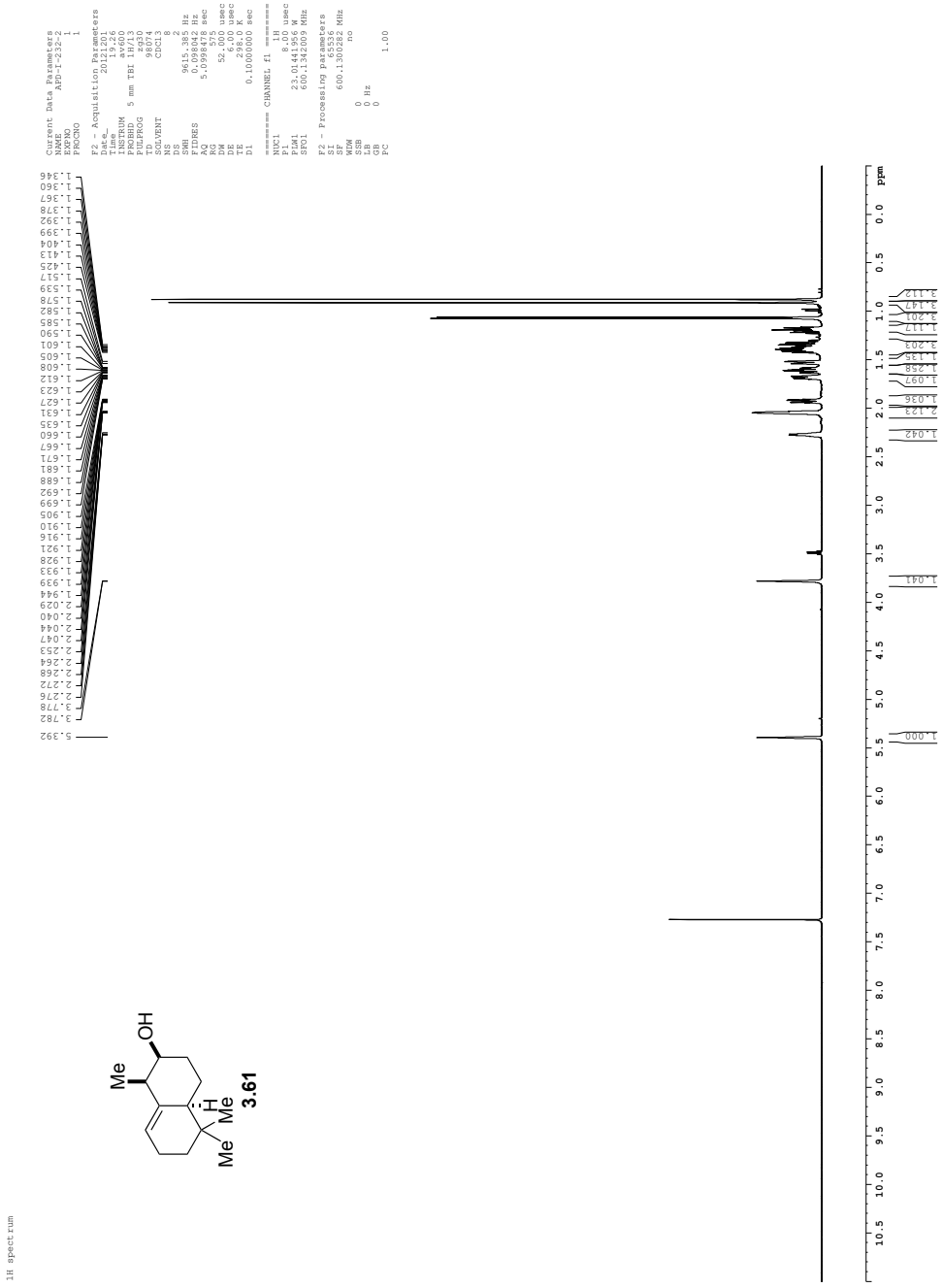



```
Current Data Parameters
NAME              GL5-217-3
EXPNO                     2
PROCNO                    1

F2 - Acquisition Parameters
Date_          20151019
Time              11.34
INSTRUM           cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD                65536
SOLVENT           CDCl3
NS                   85
DS                   16
SWH           30303.031 Hz
FIDRES        0.462388 Hz
AQ            1.0813440 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 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
SPNAM[1] Crp60,0.5,20.1
SPNAM[2]    Crp60comp.4
SPOFF1    0 Hz
SPOFF2    0 Hz

======= CHANNEL f2 =======
CPDPRG[2          waltz16
NUC2                 1H
PCPD2             100.00 usec
PL2               1.60 dB
PL12             24.50 dB
SFO2        500.2225011 MHz

===== GRADIENT CHANNEL =====
GPNAM[1]          SINE.100
GPNAM[2]          SINE.100
GPX1      0 %
GPX2      0 %
GPY1      0 %
GPY2      0 %
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
```

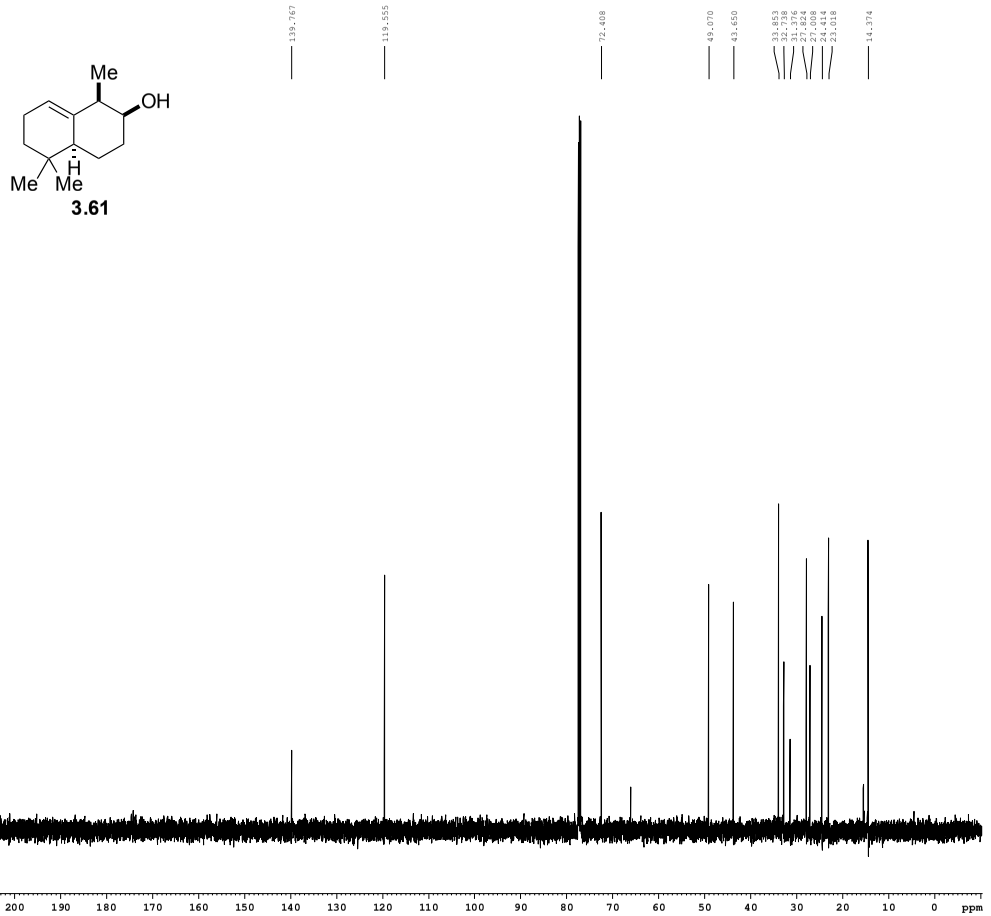

Current Data Parameters
NAME AFP-1-233-2
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20110210
Time 19.19
INSTRUM av600
PROBHD 5 mm TBI 1H/13
PULPROG zg30
TD 98074
SOLVENT CDCl3
NS 8
DS 2
SWH 9615.385 Hz
FIDRES 0.098442 Hz
AQ 5.0998478 sec
RG 52.000
DW 52.000 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 8.00 usec
PL1 23.01446152 W
SFO1 600.1324109 MHz
F2 - Processing parameters
SI 65536
SF 600.1300280 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
Me
Me
Me
H
O
O
3.60
6.271
1.286
2.713
9.602
4.139
1.032
1.087
2.059
2.078
0.996
0.994
ppm

1H spectrum

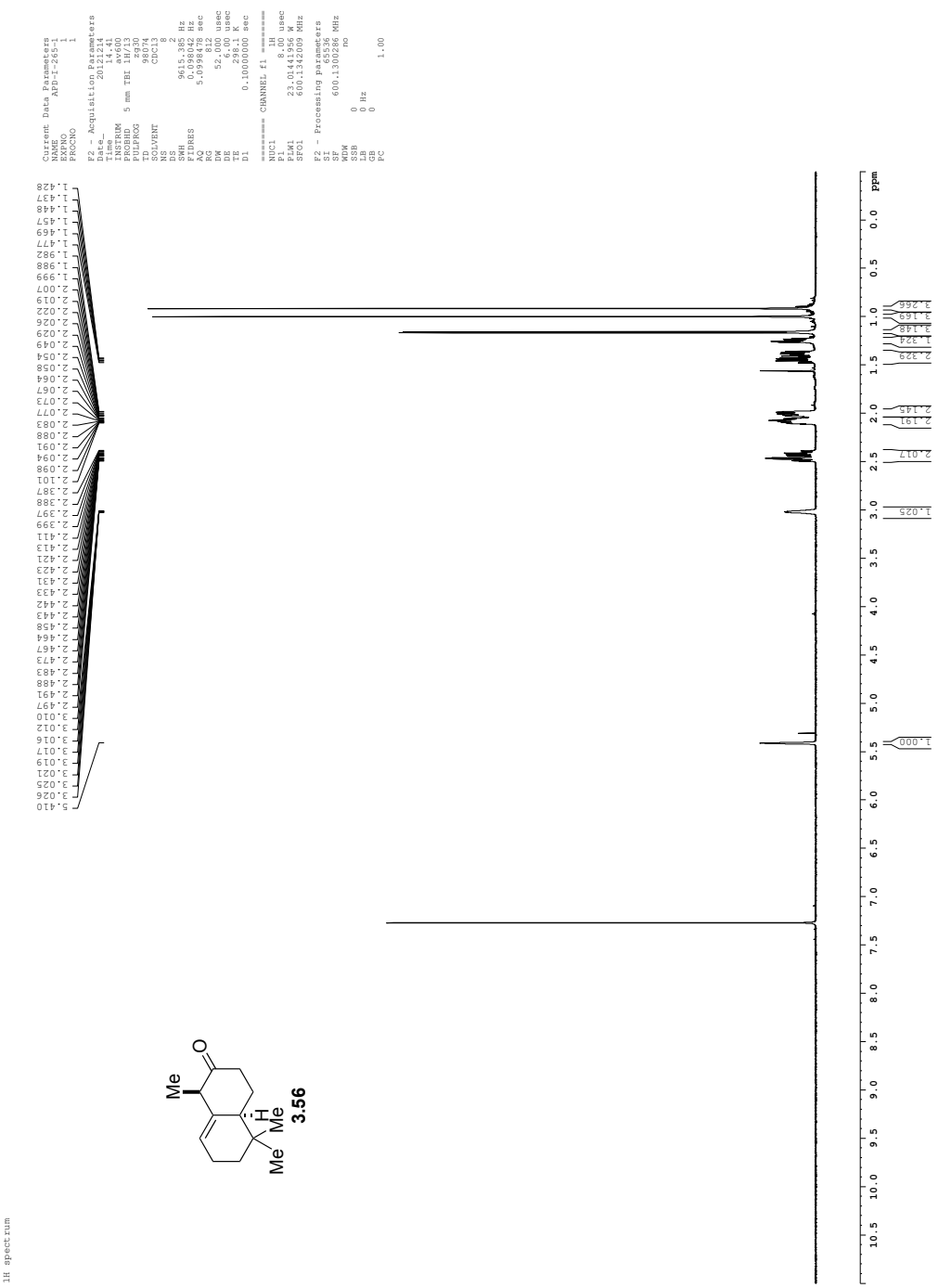

Z-restored spin-echo 13C spectrum with 1H decoupling
Me
Me
Me
H
O
O
3.60
12.761
21.233
22.899
23.822
27.979
28.195
32.765
34.787
35.578
55.734
64.935
64.975
105.181
118.012
138.938
ppm

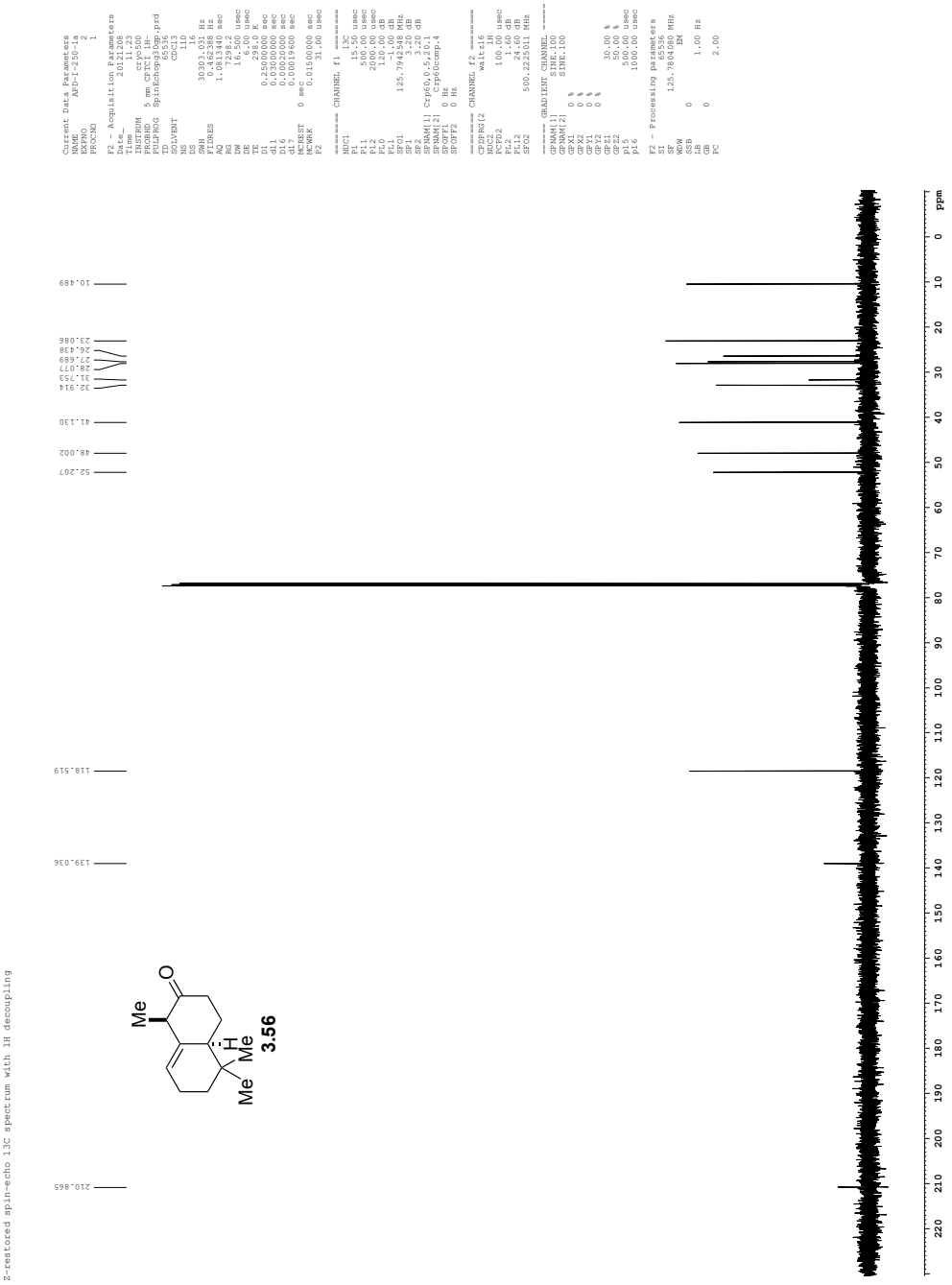

Current Data Parameters
NAME AKD-I-232-2
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20171026
Time 19.26
INSTRUM av600
PROBHD 5 mm TBI 1H/13
PULPROG zg30
TD 98074
SOLVENT CDCl3
NS 8
DS 0
SWH 9615.385 Hz
FIDRES 0.098042 Hz
AQ 5.0998478 sec
RG 52.000
DW 52.000 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 8.00 usec
PL1 23.01466 dB
SFO1 600.1342009 MHz
F2 - Processing parameters
SI 65536
SF 600.1300282 MHz
WDW no
SSB 0
LB 0 Hz
GB 0
PC 1.00
1H spect.rum
Me
OH
H
Me
Me
3.61
ppm

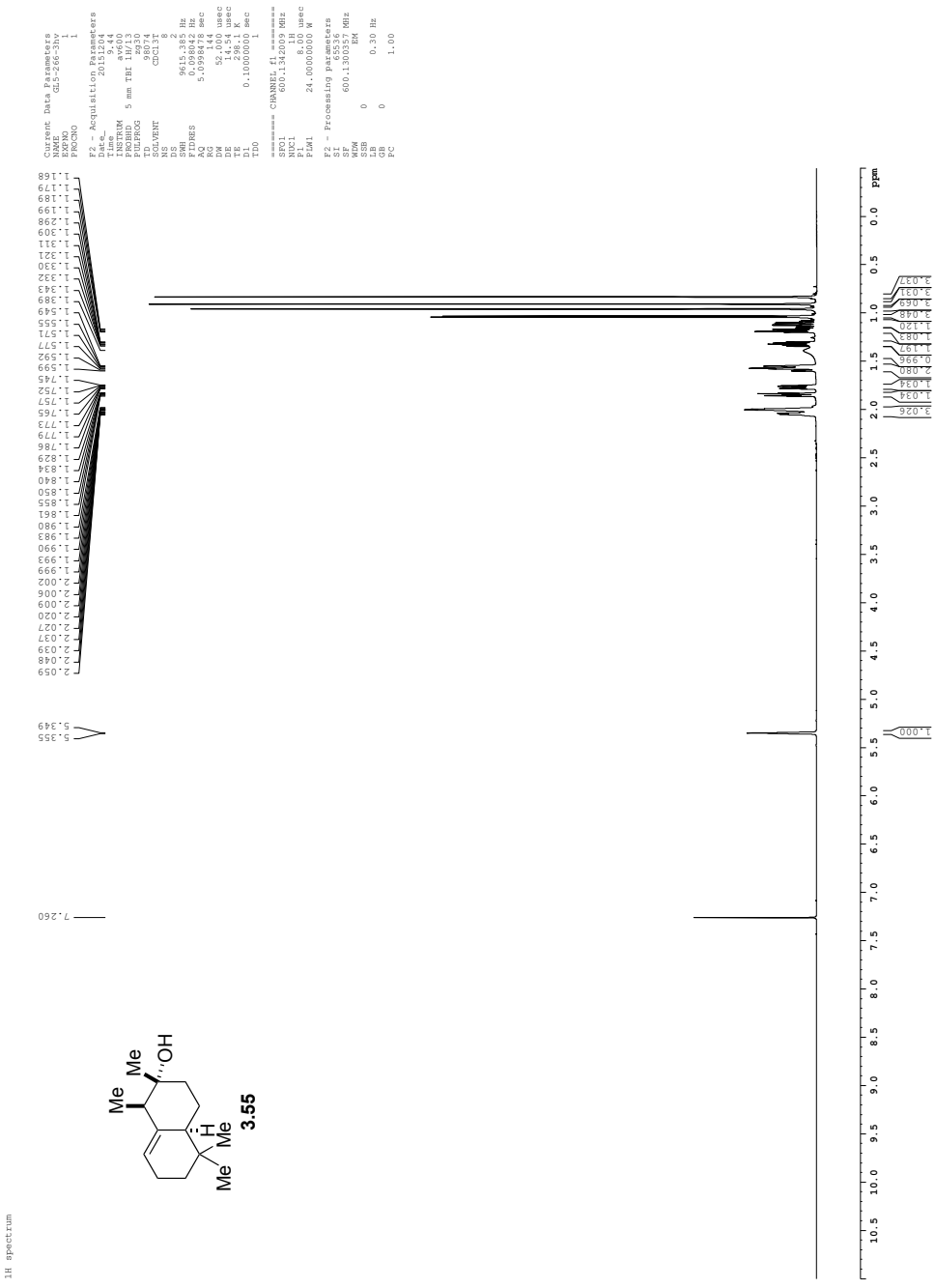
Z-restored spin-echo 13C spectrum with 1H decoupling



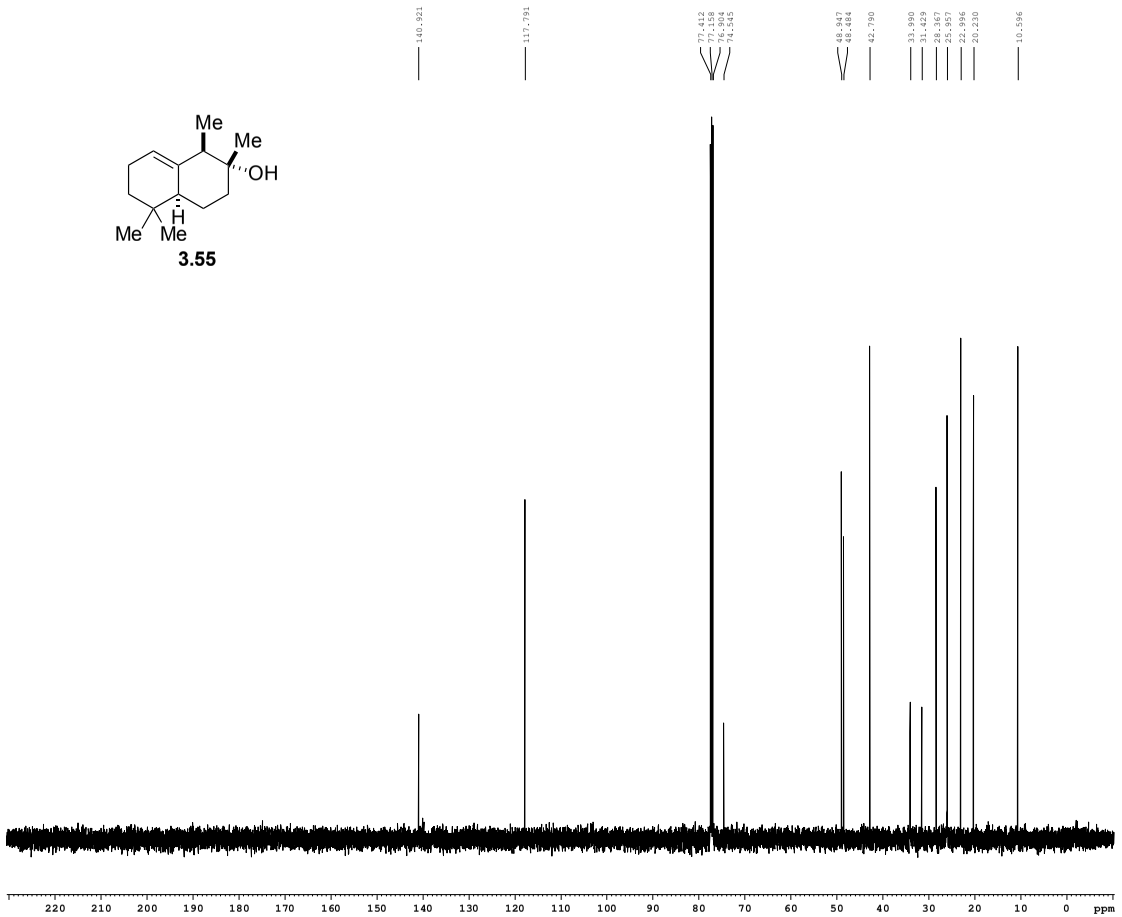

```
Current Data Parameters
NAME            APD-I-195-2
EXPNO                     2
PROCNO                    1

F2 - Acquisition Parameters
Date_          20121112
Time               15.57
INSTRUM          cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD                 65536
SOLVENT             CDCl3
NS                   137
DS                    16
SWH           30303.031 Hz
FIDRES        0.462388 Hz
AQ            1.0813440 sec
RG               7296.2
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 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
SPNAM[1] Crp60,0.5,20.1
SPNAM[2]    Crp60comp.4
SPOFF1    0 Hz
SPOFF2    0 Hz

======= CHANNEL f2 =======
CPDPRG[2          waltz16
NUC2                 1H
PCPD2             100.00 usec
PL2                1.60 dB
PL12              24.60 dB
SFO2         500.2225011 MHz

===== GRADIENT CHANNEL =====
GPNAM[1]         SINE.100
GPNAM[2]         SINE.100
GPX1      0 %
GPX2      0 %
GPY1      0 %
GPY2      0 %
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
Current Data Parameters
NAME APD-I-265-1
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20120414
Time 14.41
INSTRUM av600
PROBHD 5 mm TBI 1H/13
PULPROG zg30
TD 98074
SOLVENT CDCl3
NS 8
DS 2
SWH 9615.385 Hz
FIDRES 0.098084 Hz
AQ 5.0998478 sec
RG 812
DW 52.000 usec
DE 6.00 usec
TE 298.1 K
D1 0.10000000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 8.00 usec
PLW1 23.01441956 W
SFO1 600.1342009 MHz
F2 - Processing parameters
SI 65536
SF 600.1300266 MHz
WDW no
SSB 0
LB 0 Hz
GB 0
PC 1.00
Me
O
H
Me
Me
3.56
1.000
1.025
2.017
2.145
2.191
2.329
1.124
1.148
1.169
1.266
ppm

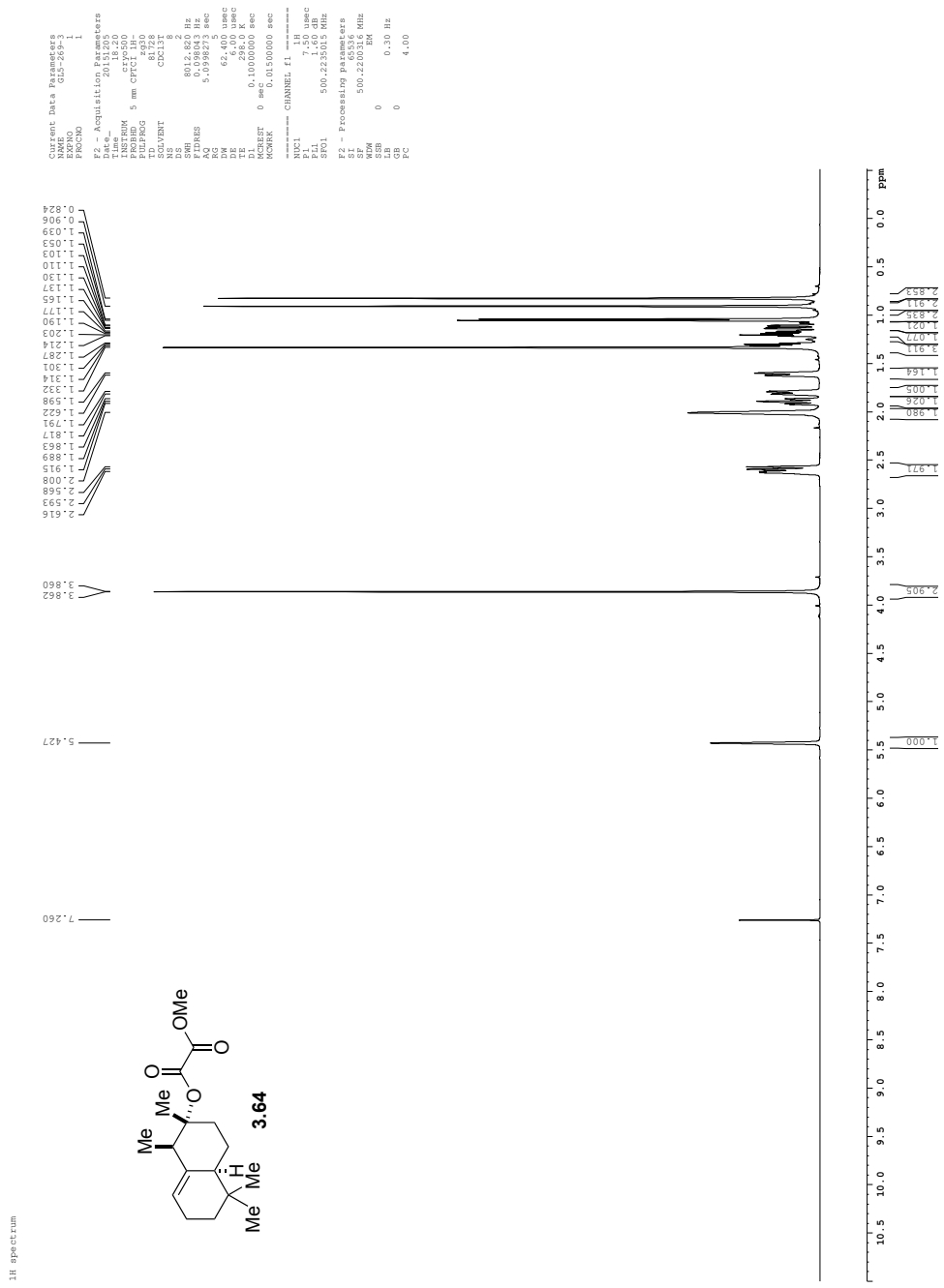

Z-restored spin-echo 13C spectrum with 1H decoupling
Me
O
H
Me
Me
3.56
Current Data Parameters
NAME AFD-I-250-1a
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20121208
Time 11:23
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG SpinEch-pg.prd
TD 65536
SOLVENT CDCl3
NS 110
DS 16
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0913440 sec
RG 7298.2
DW 16.500 usec
DE 6.00 usec
TE 298.0 K
D1 0.23000000 sec
d11 0.03000000 sec
D16 0.00020000 sec
d1 0.00019600 sec
MCREST 0 sec
MCWRK 0.01500000 sec
P2 31.00 usec
======== CHANNEL f1 ========
NUC1 13C
P1 15.50 usec
PL1 500.00 usec
PL2 2000.00 usec
PL12 120.00 dB
PL1 -1.00 dB
SFO1 125.7942548 MHz
SP1 3.20 dB
SP2 3.20 dB
SPNAM[1] Crp60,0.5,20.1
SPNAM[2] cpdprg_waltz16
SPOFF1 0 Hz
SPOFF2 0 Hz
======== CHANNEL f2 ========
CPDPRG[2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 1.60 dB
PL12 24.60 dB
SFO2 500.2225011 MHz
====== GRADIENT CHANNEL =====
GPNAM[1] SINE.100
GPNAM[2] SINE.100
GPZ1 0 %
GPZ2 0 %
GPY1 0 %
GPY2 0 %
GPZ1 30.00 %
GPZ2 50.00 %
P15 500.00 usec
P16 1000.00 usec
F2 - Processing parameters
SI 65536
SF 125.7804080 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00
210.865
139.036
118.519
41.130
52.207
48.002
32.914
31.753
28.077
27.689
26.438
23.086
10.489
ppm


1H spectrum
Current Data Parameters
NAME
EXPNO
PROCNO
F2 - Acquisition Parameters
Date_
Time
INSTRUM
PROBHD
PULPROG
TD
SOLVENT
NS
DS
SWH
FIDRES
AQ
RG
DW
DE
TE
D1
TD0
======== CHANNEL f1 ========
SFO1
NUC1
P1
PLW1
F2 - Processing parameters
SI
SF
WDW
SSB
LB
GB
PC
Me
Me
OH
H
Me
Me
3.55
ppm

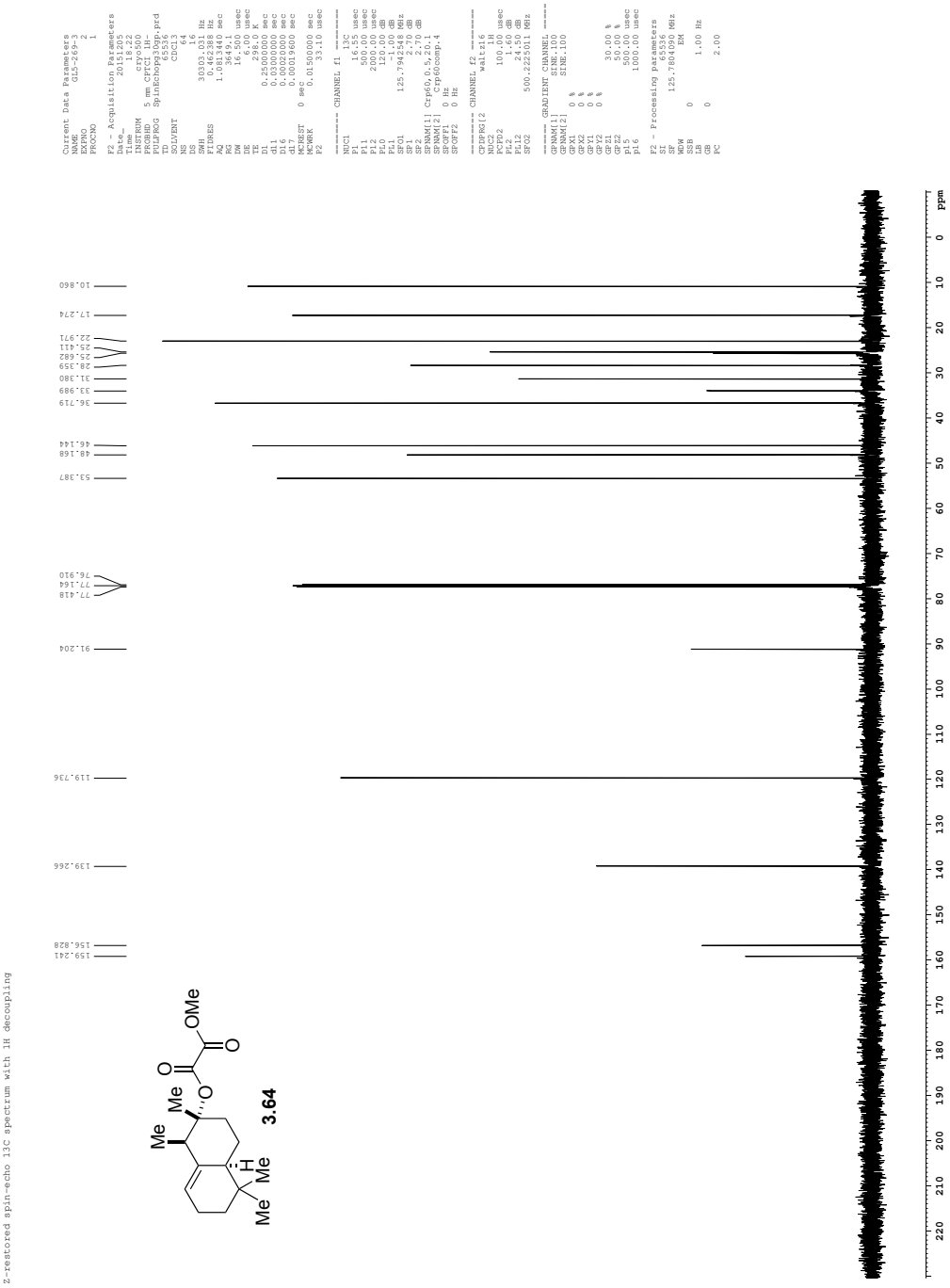
Z-restored spin-echo 13C spectrum with 1H decoupling



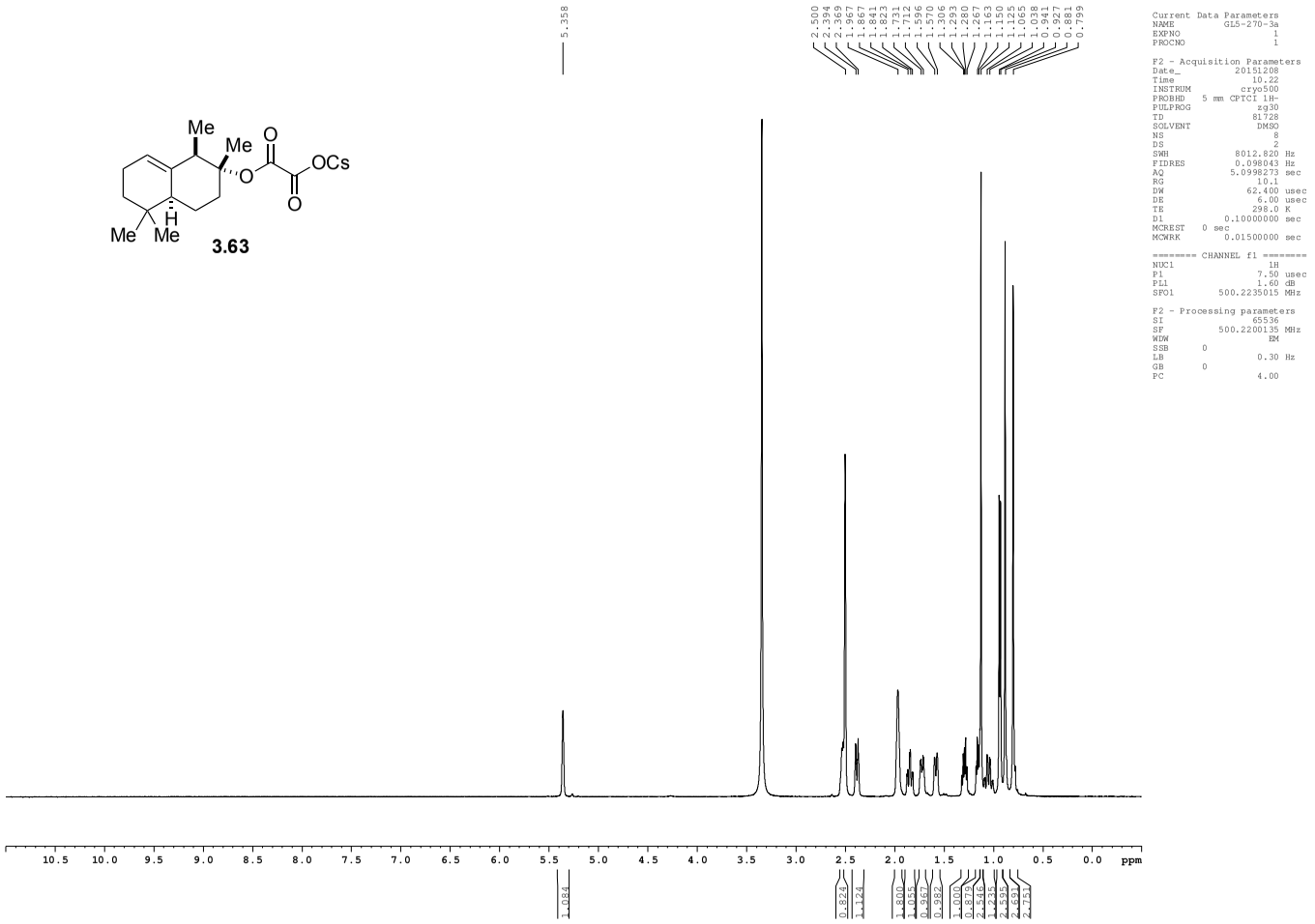

```
Current Data Parameters
NAME            GL5-266-3
EXPNO                   2
PROCNO                  1

F2 - Acquisition Parameters
Date_           20151203
Time                15.35
INSTRUM           cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD                  65536
SOLVENT             CDCl3
NS                    143
DS                     16
SWH             30303.031 Hz
FIDRES          0.462388 Hz
AQ              1.0813440 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 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
SPNAM[1]  Crp60,0.5,20.1
SPNAM[2]     Crp60comp.4
SPOFF1    0 Hz
SPOFF2    0 Hz

======== CHANNEL f2 ========
CPDPRG[2            waltz16
NUC2                   1H
PCPD2             100.00 usec
PL2                1.60 dB
PL12              24.50 dB
SFO2         500.2225011 MHz

====== GRADIENT CHANNEL =====
GPNAM[1]          SINE.100
GPNAM[2]          SINE.100
GPX1       0 %
GPX2       0 %
GPY1       0 %
GPY2       0 %
GPZ1              30.00 %
GPZ2              50.00 %
p15              500.00 usec
p16             1000.00 usec

F2 - Processing parameters
SI                  65536
SF           125.7804080 MHz
WDW                   EM
SSB        0
LB                 1.00 Hz
GB         0
PC                 2.00
```


Current Data Parameters
NAME G15-269-3
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20111020
Time 18.20
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 81728
SOLVENT CDCl3
NS 8
DS 2
SWH 8012.822 Hz
FIDRES 0.098043 Hz
AQ 5.098227 sec
RG 64
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0 sec 0.01500000 sec
MCWRK
CHANNEL f1
NUC1 1H
P1 7.50 usec
PL1 1.60 dB
SFO1 500.2250151 MHz
F2 - Processing parameters
SI 65536
SF 500.2200331 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00
0.824
0.906
1.039
1.053
1.103
1.110
1.130
1.137
1.165
1.177
1.190
1.203
1.214
1.287
1.301
1.314
1.332
1.598
1.622
1.791
1.817
1.863
1.889
1.915
2.008
2.568
2.593
2.616
3.860
3.862
5.427
7.260
Me
Me
O
O
OMe
O
H
Me
Me
3.64
ppm
1.000
2.905
1.971
1.980
1.026
1.005
1.164
1.911
1.077
1.021
2.835
2.911
2.853

1H spectrum

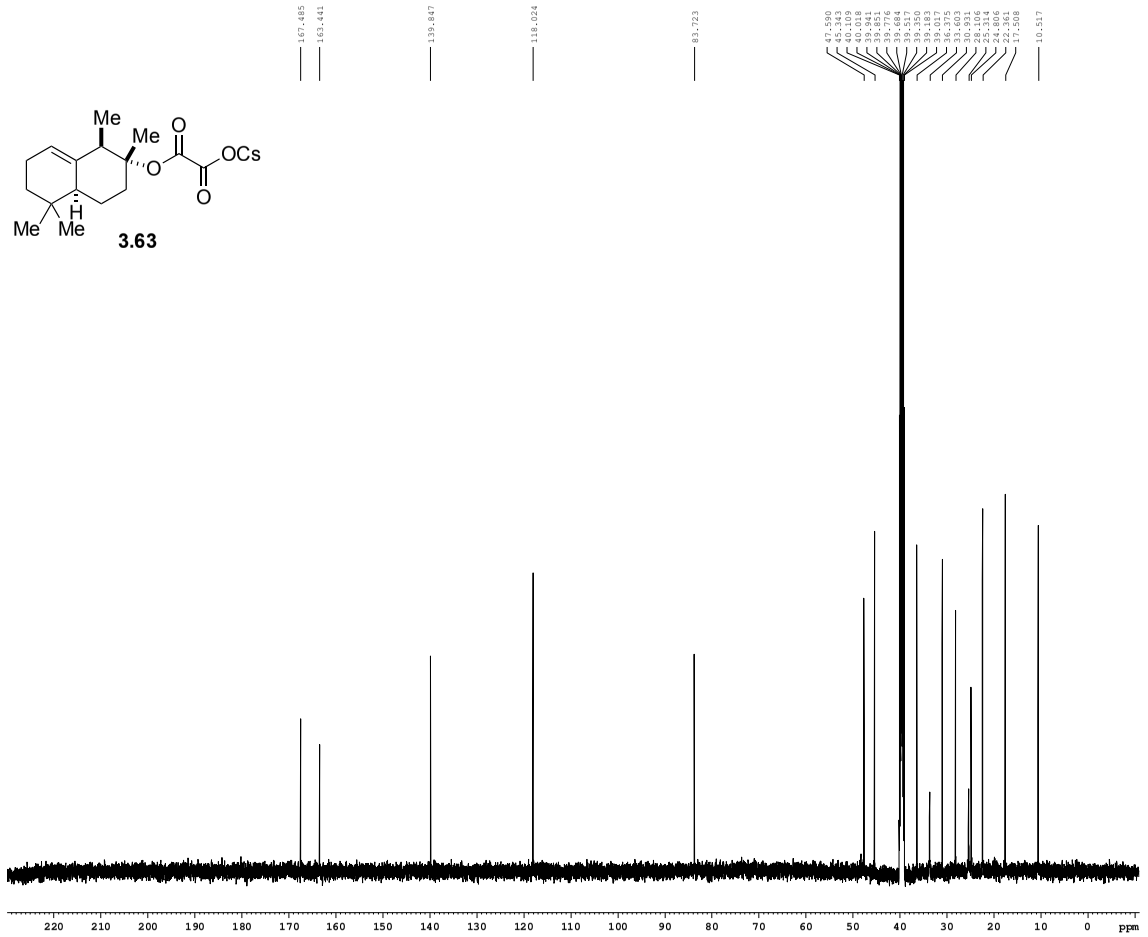

Current Data Parameters
NAME GLS-269-3
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20151025
Time 18.22
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG SpinEchopz30gp.prd
TD 65536
SOLVENT CDCl3
NS 64
DS 16
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0813440 sec
RG 161.5
DW 16.500 usec
DE 6.00 usec
TE 298.0 K
D1 0.25000000 sec
d11 0.03000000 sec
d12 0.00020000 sec
d16 0.00010800 sec
MCREST 0 sec 0.01500000 sec
MCWRK 0.01500000 sec
F2 - 39.10 usec
======== CHANNEL f1 ========
NUC1 13C
P1 16.35 usec
P11 500.00 usec
P12 2000.00 usec
PL0 120.00 dB
PL1 -1.00 dB
SFO1 125.7942548 MHz
SF1 125.7600000 MHz
SP2 2.70 dB
SPNAM[1] Crp60,0.5,20.1
SPNAM[2] CPPrecomp.4
SFOFF1 0 Hz
SFOFF2 0 Hz
======== CHANNEL f2 ========
CPDPRG[2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 1.60 dB
PL12 24.50 dB
SFO2 500.2235011 MHz
====== GRADIENT CHANNEL =====
GPNAM[1] SINE.100
GPNAM[2] SINE.100
GPX1 0 %
GPX2 0 %
GPY1 0 %
GPY2 0 %
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
10.860
17.274
22.971
25.411
25.682
28.359
31.380
33.989
36.719
46.144
48.168
53.387
76.910
77.164
77.418
91.204
119.736
139.266
156.828
159.241
ppm
Me
Me
O
O
OMe
O
O
H
Me
Me
3.64
Z-restored spin-echo 13C spectrum with 1H decoupling

1H spectrum

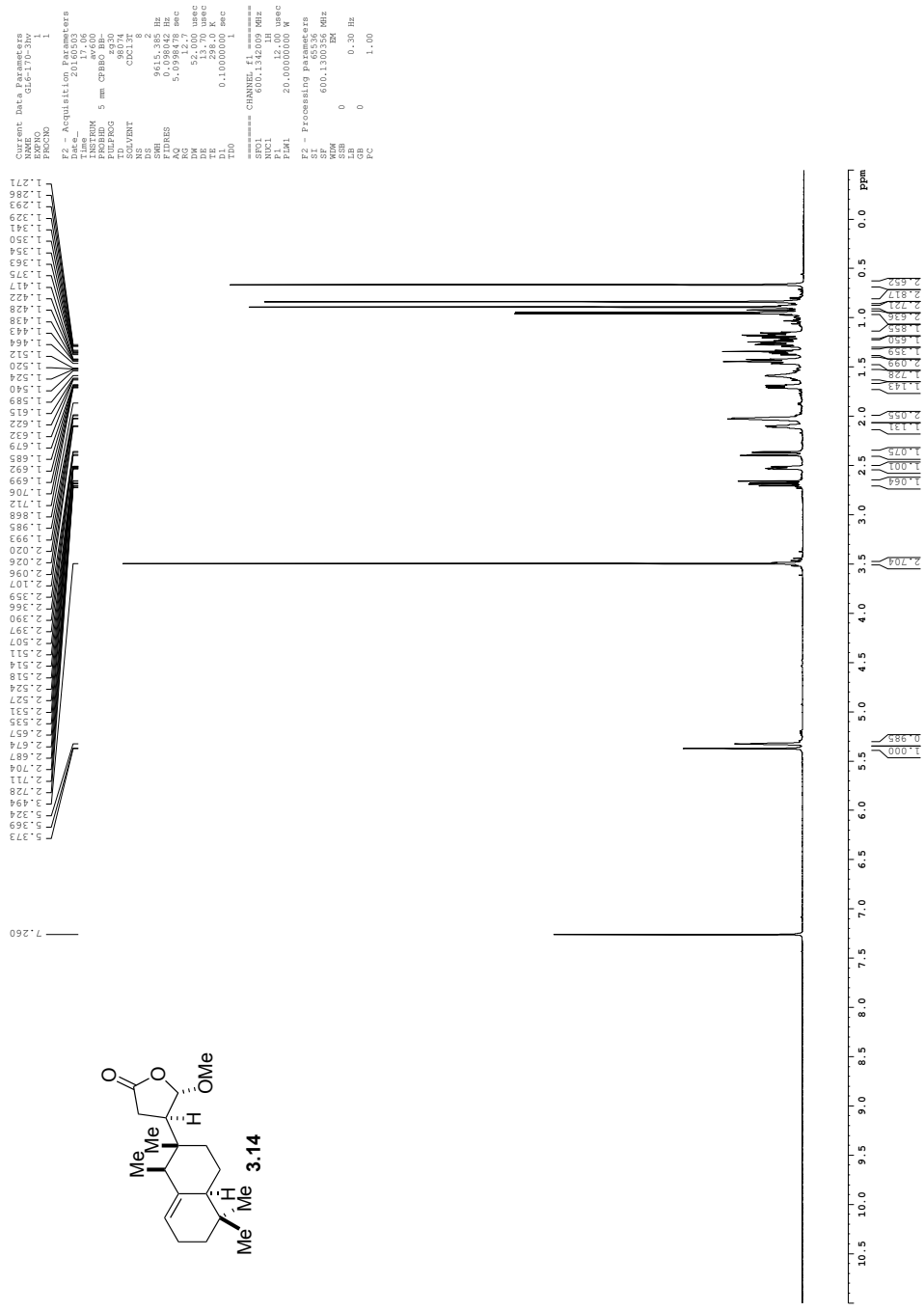



```
Current Data Parameters
NAME                  GLS-270-3a
EXPNO                          1
PROCNO                         1

F2 - Acquisition Parameters
Date_                   20151208
Time                       10.22
INSTRUM                  cryo500
PROBHD    5 mm CPTCI 1H-
PULPROG                    zg30
TD                        81728
SOLVENT                    DMSO
NS                             8
DS                             2
SWH                     8012.820 Hz
FIDRES                  0.098043 Hz
AQ                      5.0998273 sec
RG                          10.1
DW                        62.400 usec
DE                         6.00 usec
TE                        298.0 K
D1                   0.10000000 sec
MCREST    0 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                  500.2200135 MHz
WDW                           EM
SSB       0
LB                         0.30 Hz
GB        0
PC                         4.00
```

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




```
Current Data Parameters
NAME            GL5-270-3a
EXPNO                    2
PROCNO                   1

F2 - Acquisition Parameters
Date_          20151208
Time               10.25
INSTRUM          cryo500
PROBHD    5 mm CPTCI 1H-
PULPROG   SpinEchopg30gp.prd
TD                 65536
SOLVENT              CDCl3
NS                     603
DS                      16
SWH            30303.031 Hz
FIDRES          0.462388 Hz
AQ              1.0813440 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
MCWREST   0 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
SPNAM[1] Crp60,0.5,20.1
SPNAM[2]    Crp60comp.4
SPOFF1    0 Hz
SPOFF2    0 Hz

======= CHANNEL f2 =======
CPDPRG[2          waltz16
NUC2                  1H
PCPD2             100.00 usec
PL2                1.60 dB
PL12              24.50 dB
SFO2         500.2225011 MHz

===== GRADIENT CHANNEL ====
GPNAM[1]         SINE.100
GPNAM[2]         SINE.100
GPX1      0 %
GPX2      0 %
GPY1      0 %
GPY2      0 %
GPZ1              30.00 %
GPZ2              50.00 %
p15              500.00 usec
p16             1000.00 usec

F2 - Processing parameters
SI                 65536
SF           125.7804792 MHz
WDW                   EM
SSB       0
LB                 1.00 Hz
GB        0
PC                 2.00
```


Current Data Parameters
NAME GL6-170-3hv
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20160503
Time 17.06
INSTRUM spect
PROBHD 5 mm CPBBO BB-
PULPROG zg30
TD 98304
SOLVENT CDCl3
NS 8
DS 2
SWH 9615.385 Hz
FIDRES 0.098042 Hz
AQ 5.0998147 sec
RG 287.5
DW 52.000 usec
DE 13.10 usec
TE 298.2 K
D1 0.10000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 600.1342009 MHz
NUC1 1H
P1 12.00 usec
PLW1 20.00000000 W
F2 - Processing parameters
SI 65536
SF 600.1300256 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
7.260
5.373
5.369
5.324
3.494
2.728
2.711
2.704
2.687
2.674
2.657
2.535
2.531
2.527
2.524
2.518
2.514
2.511
2.507
2.397
2.390
2.366
2.359
2.107
2.096
2.026
2.020
1.993
1.985
1.868
1.712
1.706
1.699
1.692
1.685
1.679
1.632
1.622
1.615
1.589
1.540
1.524
1.520
1.512
1.464
1.443
1.438
1.428
1.422
1.417
1.375
1.363
1.354
1.350
1.341
1.329
1.293
1.271
2.704
1.064
1.001
1.079
1.131
2.055
1.143
1.728
2.099
1.359
1.650
1.858
1.838
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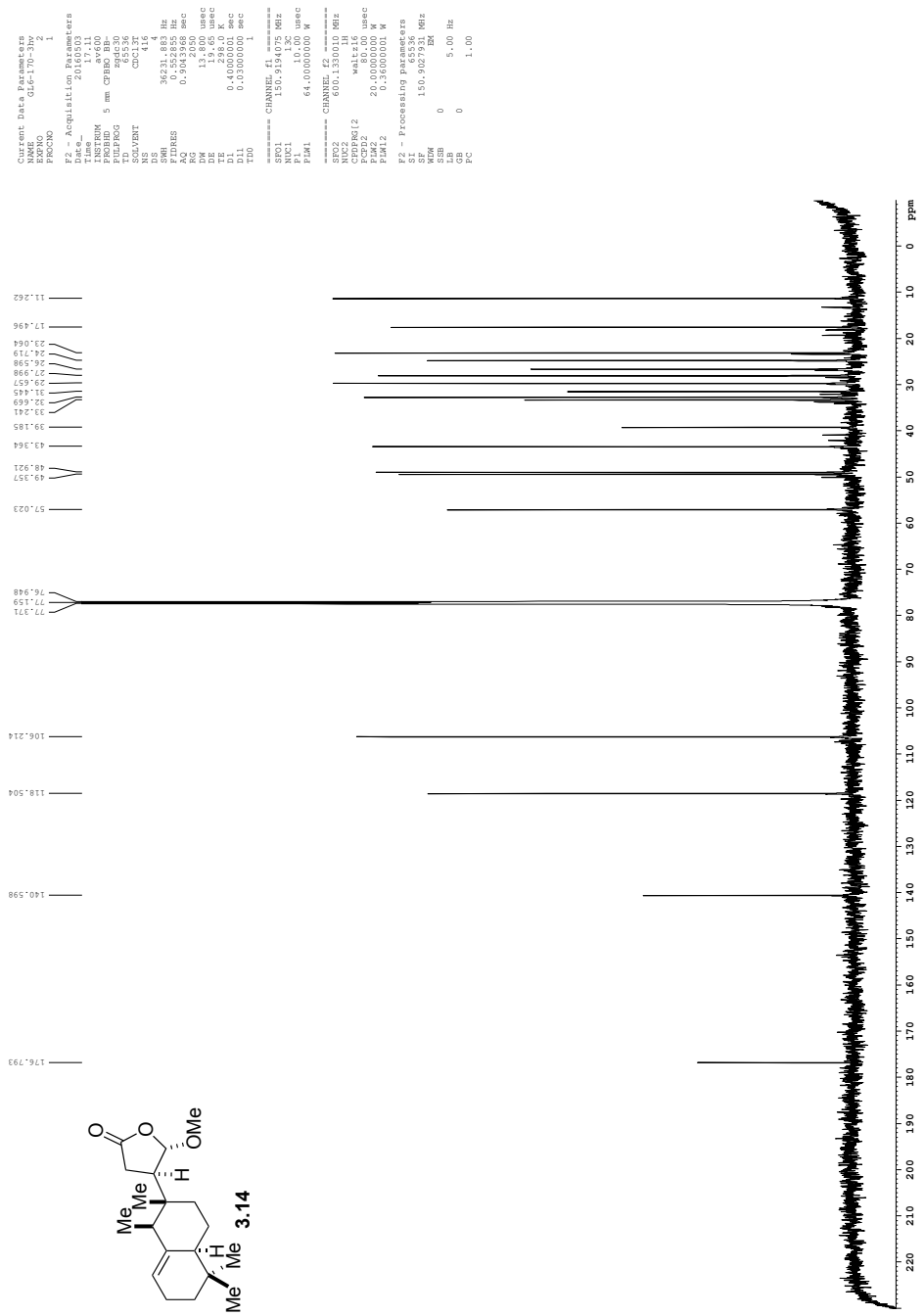
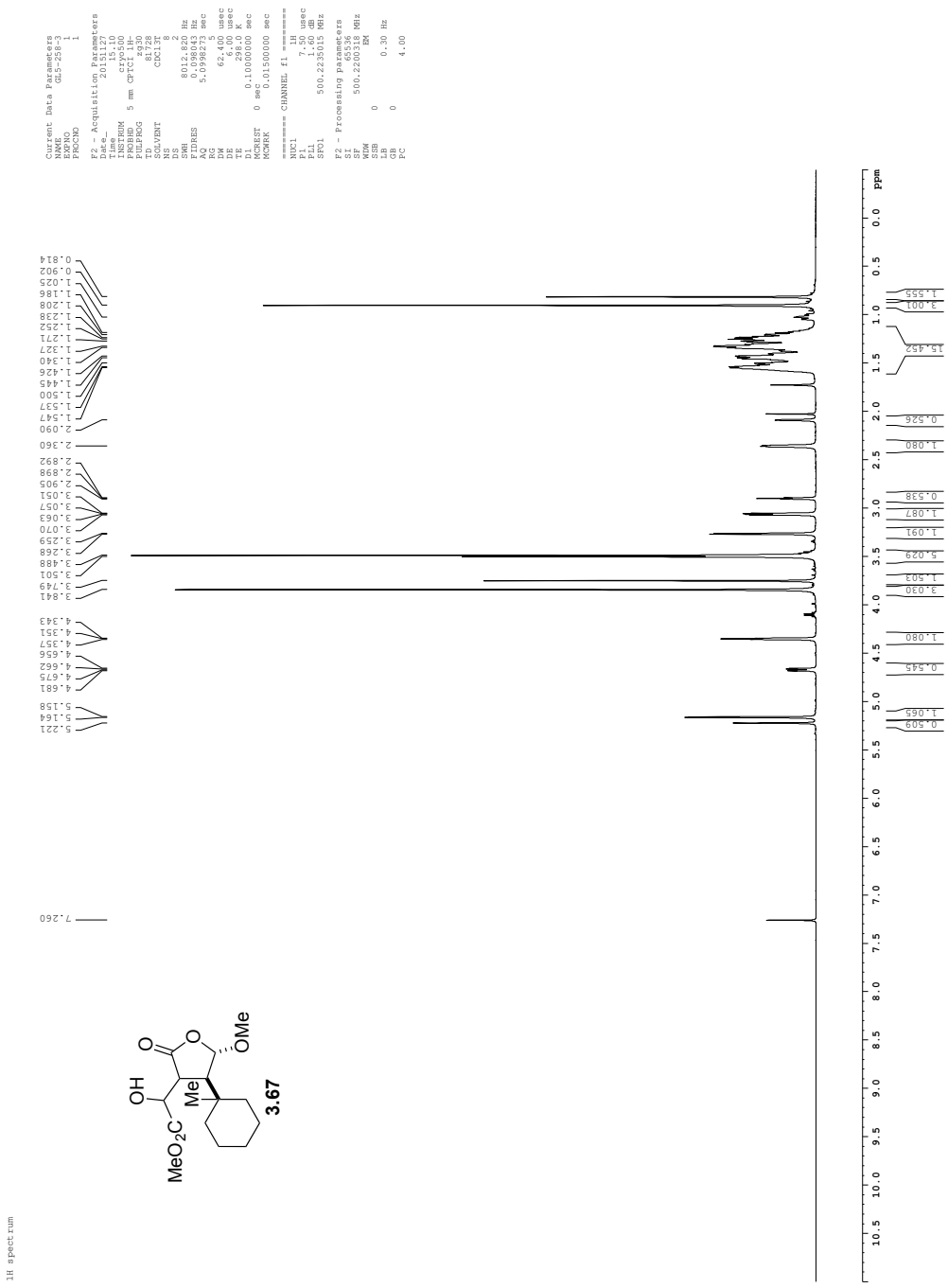
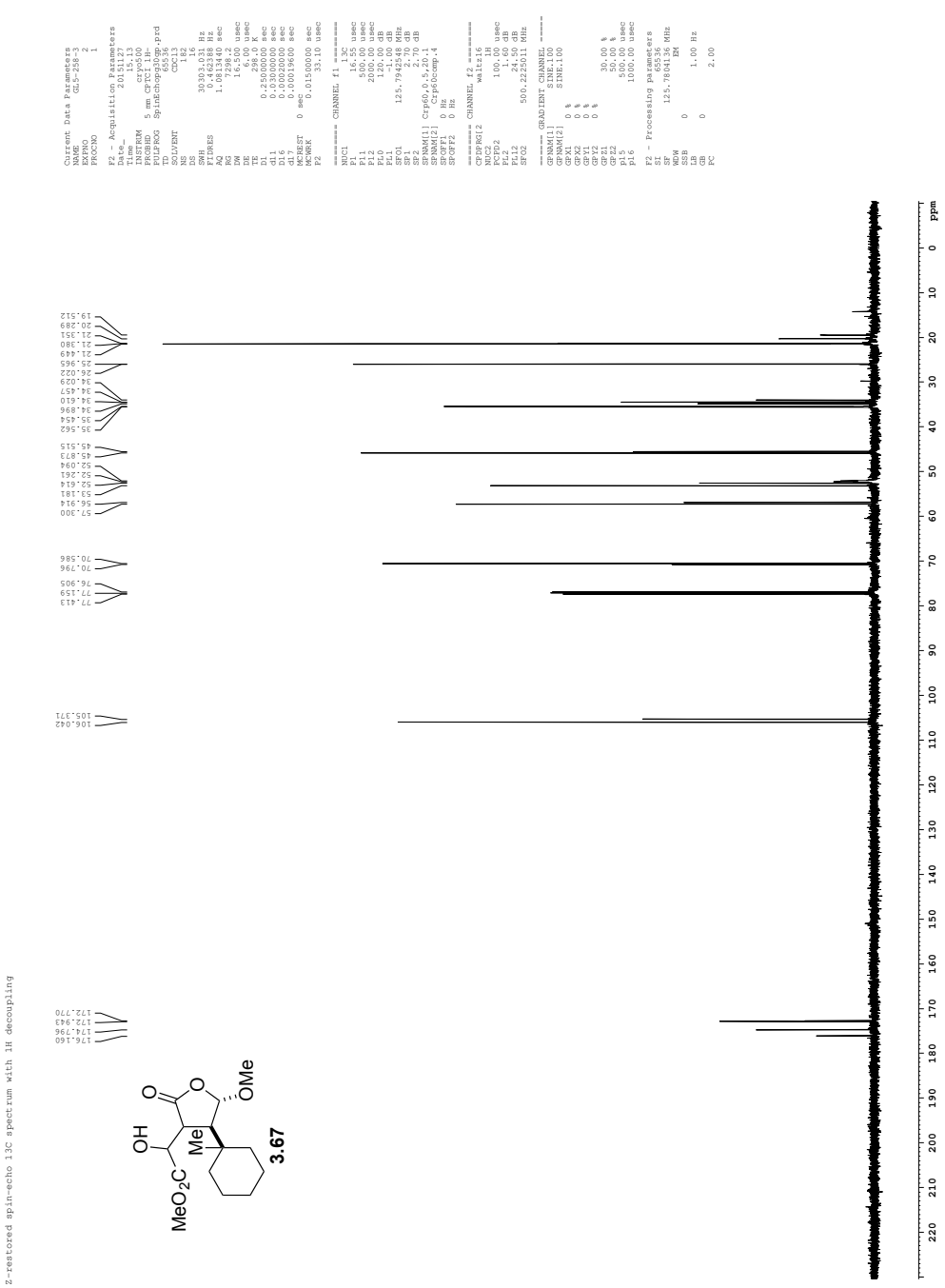
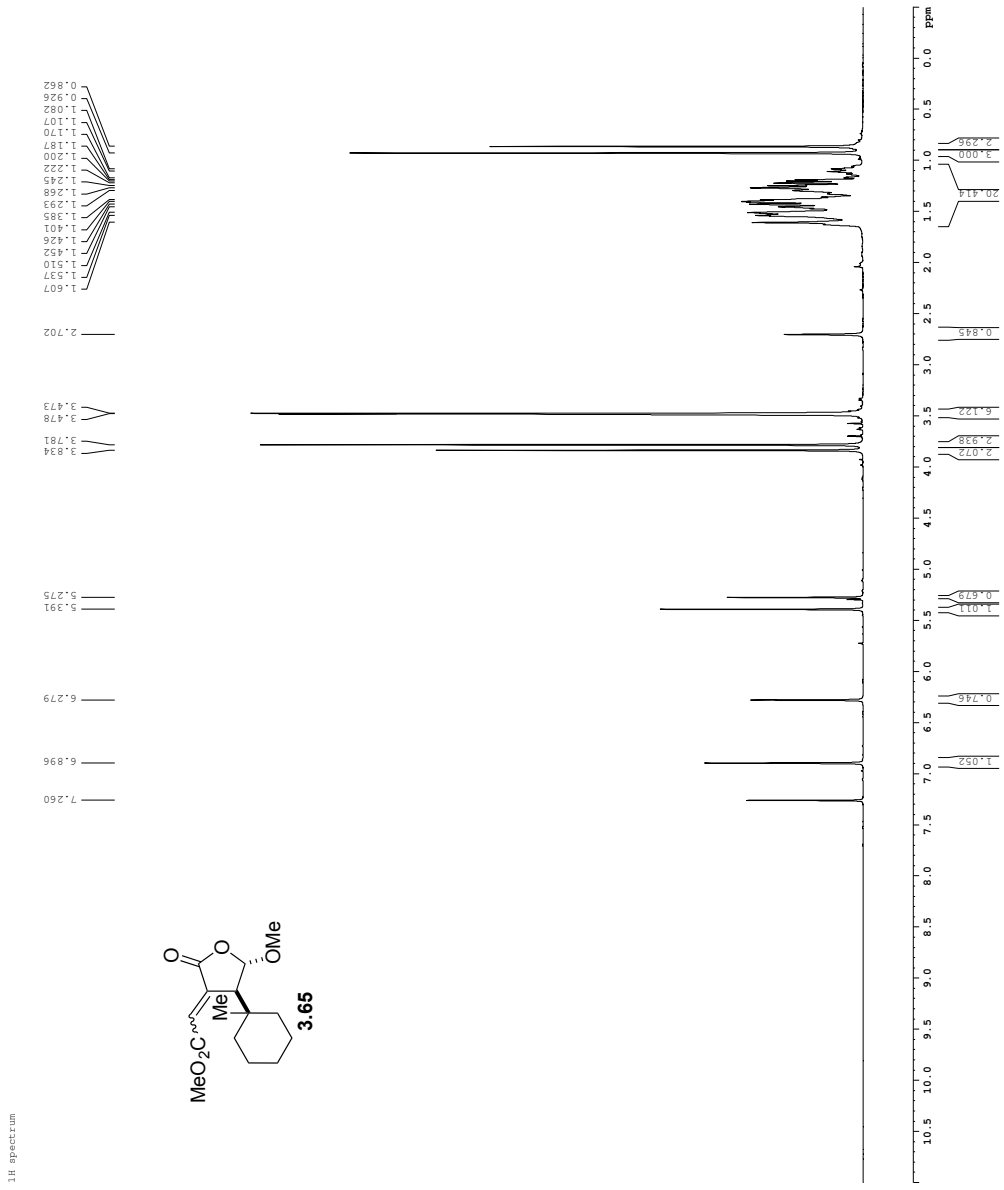
2.652
1.000
0.985
ppm
Me
Me
H
OMe
H
Me
Me
3.14


Current Data Parameters
NAME GL6-170-3hv
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20160503
Time 17.11
INSTRUM av600
PROBHD 5 mm CPBBO BB-
PULPROG zgdc30
TD 65536
SOLVENT CDCl3
NS 416
DS 4
SWH 36231.883 Hz
FIDRES 0.552855 Hz
AQ 0.9043968 sec
RG 203
DW 13.800 usec
DE 19.65 usec
TE 298.0 K
D1 0.40000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 150.9194075 MHz
NUC1 13C
P1 10.00 usec
PLW1 64.00000000 W
======== CHANNEL f2 ========
SFO2 600.1330010 MHz
NUC2 1H
CPDPRG2 waltz16
PCPD2 80.00 usec
PLW2 20.00000000 W
PLW12 0.36000001 W
F2 - Processing parameters
SI 65536
SF 150.9027931 MHz
WDW EM
SSB 0
LB 5.00 Hz
GB 0
PC 1.00
11.262
17.496
23.064
24.719
26.598
27.998
29.657
31.445
32.669
33.241
39.185
43.364
48.921
49.357
57.023
76.948
77.159
77.371
106.214
118.504
140.598
176.793
ppm
O
O
OMe
H
Me
Me
H
Me
Me
3.14

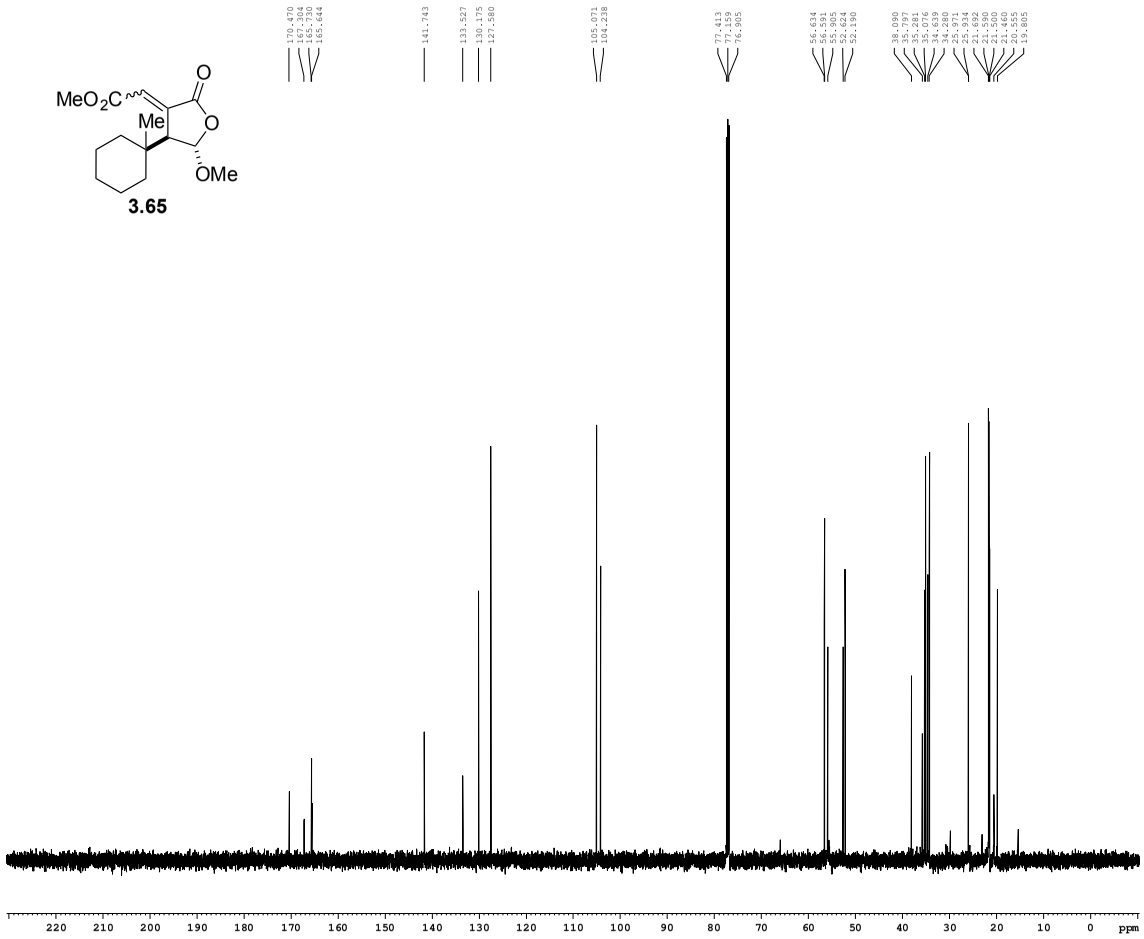

1H spectrum
Current Data Parameters
NAME GDS-259-3
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20151127
Time 15.10
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 81728
SOLVENT CDCl3T
NS 2
DS 2
SWH 8012.820 Hz
FIDRES 0.098043 Hz
AQ 5.0858752 sec
RG 5
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
WCHEST 0 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 500.2200318 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00
7.260
5.221
5.164
5.158
4.681
4.675
4.662
4.656
4.357
4.351
4.343
3.841
3.749
3.501
3.488
3.268
3.259
3.070
3.063
3.057
3.051
2.905
2.898
2.892
2.360
2.090
1.547
1.537
1.500
1.445
1.426
1.340
1.327
1.271
1.252
1.238
1.208
1.186
1.025
0.902
0.814
OH
O
O
OMe
Me
MeO2C
3.67
ppm
1.955
3.001
15.452
0.526
1.080
0.538
1.087
1.091
5.029
1.503
3.030
1.080
0.545
1.065
0.509


z-restored spin-echo 13C spectrum with 1H decoupling
3.67
MeO2C
Me
OH
OMe
O
O
ppm


Current Data Parameters
NAME GDZ-29C-1
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20160105
Time 11.55
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 5.0983274 sec
RG 5.7
DW 62.400 usec
DE 6.50 usec
TE 298.0 K
D1 0.10000000 sec
NUCLEST 0 sec
MCWREK 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 500.2200300 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00
7.260
6.896
6.279
5.391
5.275
3.834
3.781
3.478
3.473
2.702
1.607
1.537
1.510
1.452
1.426
1.401
1.385
1.293
1.268
1.245
1.222
1.200
1.187
1.170
1.107
1.082
0.926
0.862
2.296
3.000
20.414
0.845
6.122
2.938
2.072
0.679
1.011
0.746
1.052
ppm
MeO2C
Me
O
O
OMe
3.65

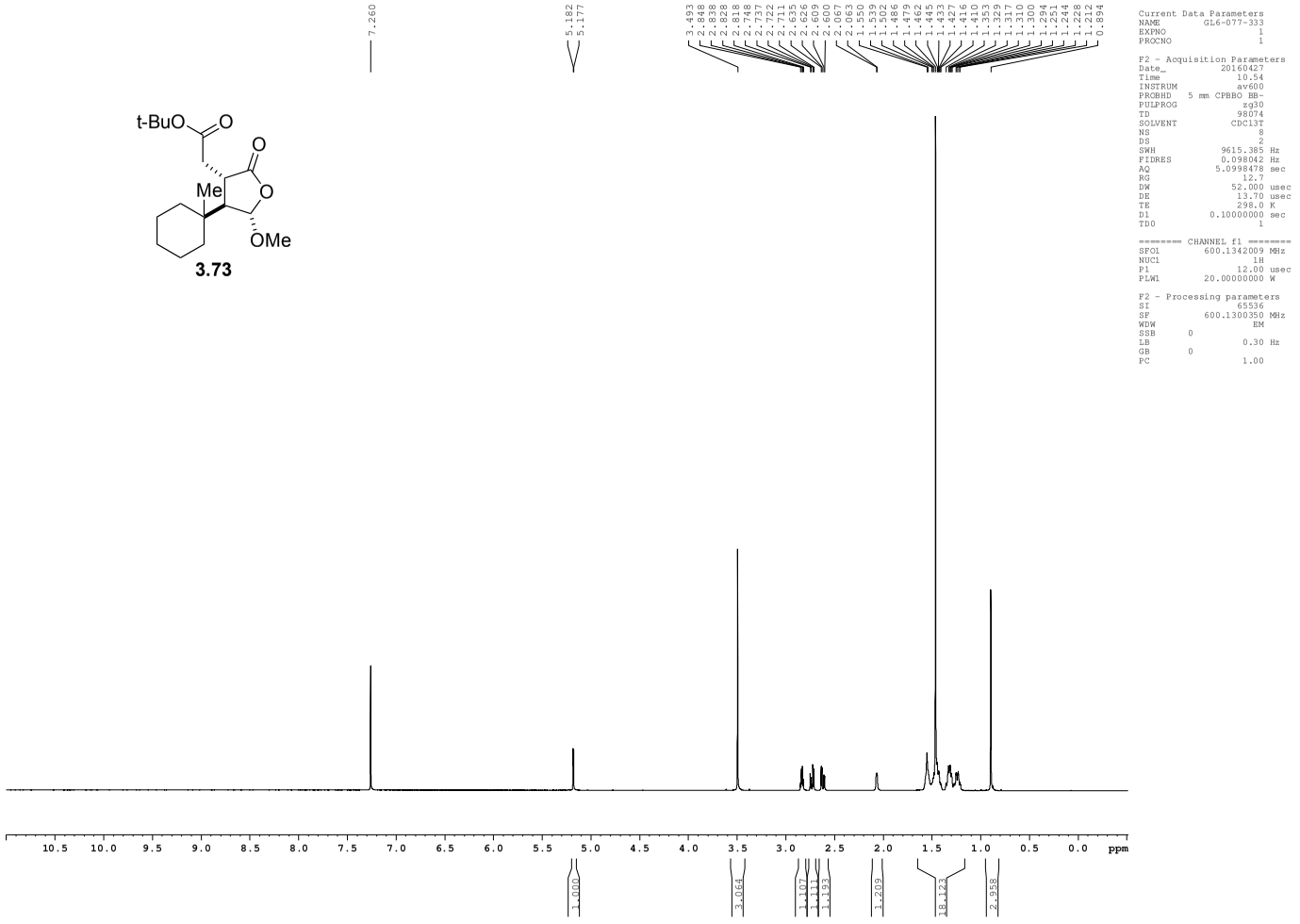
1H spectrum

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

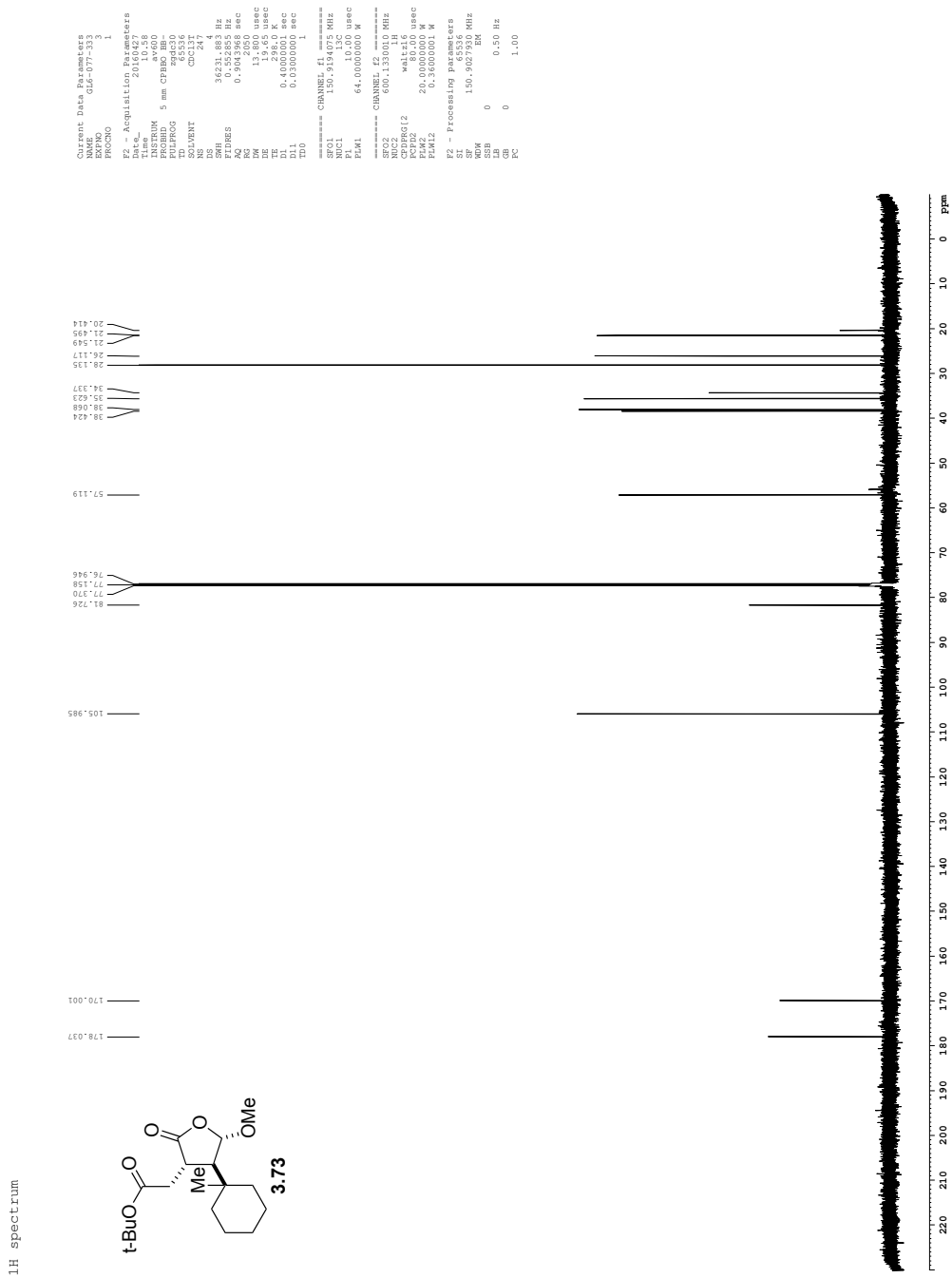



```
Current Data Parameters
NAME                GL5-290-3
EXPNO                       2
PROCNO                      1

F2 - Acquisition Parameters
Date_              20160105
Time                   11.57
INSTRUM                cryo500
PROBHD     5 mm CPTCI 1H-
PULPROG    SpinEchopg30gp.prd
TD                      65536
SOLVENT                CDCl3
NS                        365
DS                         16
SWH                30303.031 Hz
FIDRES             0.462388 Hz
AQ                 1.0813440 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 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
SPNAM[1] Crp60,0.5,20.1
SPNAM[2]    Crp60comp.4
SPOFF1     0 Hz
SPOFF2     0 Hz

======== CHANNEL f2 ========
CPDPRG[2              waltz16
NUC2                      1H
PCPD2                  100.00 usec
PL2                      1.60 dB
PL12                    24.50 dB
SFO2               500.2225011 MHz

====== GRADIENT CHANNEL =====
GPNAM[1]          SINE.100
GPNAM[2]          SINE.100
GPX1       0 %
GPX2       0 %
GPY1       0 %
GPY2       0 %
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
```

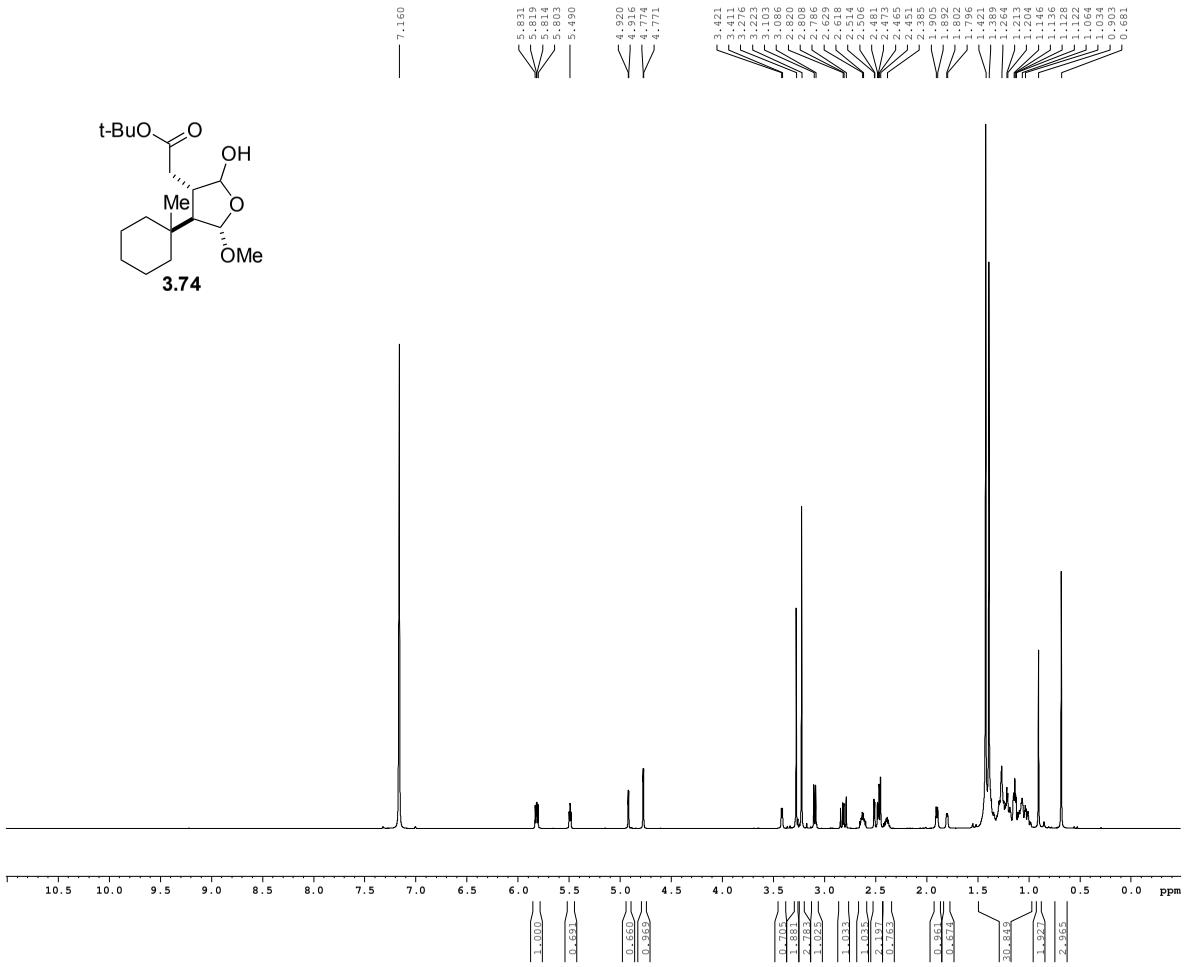
1H spectrum


7.260
5.182
5.177
3.493
2.848
2.838
2.828
2.818
2.748
2.737
2.722
2.711
2.635
2.626
2.609
2.600
2.067
2.063
1.550
1.539
1.502
1.486
1.479
1.462
1.445
1.433
1.427
1.416
1.410
1.353
1.329
1.317
1.310
1.300
1.294
1.251
1.244
1.228
1.212
0.894
t-BuO
O
O
Me
O
OMe
3.73
Current Data Parameters
NAME GL6-077-333
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20160427
Time 10.54
INSTRUM av600
PROBHD 5 mm CPBBO BB-
PULPROG zg30
TD 98074
SOLVENT CDCl3T
NS 8
DS 2
SWH 9615.385 Hz
FIDRES 0.098042 Hz
AQ 5.0998478 sec
RG 12.7
DW 52.000 usec
DE 13.70 usec
TE 298.0 K
D1 0.10000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 600.1342009 MHz
NUC1 1H
P1 12.00 usec
PLW1 20.00000000 W
F2 - Processing parameters
SI 65536
SF 600.1300350 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
10.5 10.0 9.5 9.0 8.5 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
1.000
3.064
1.107
1.111
1.193
1.209
18.123
2.958

1H spectrum

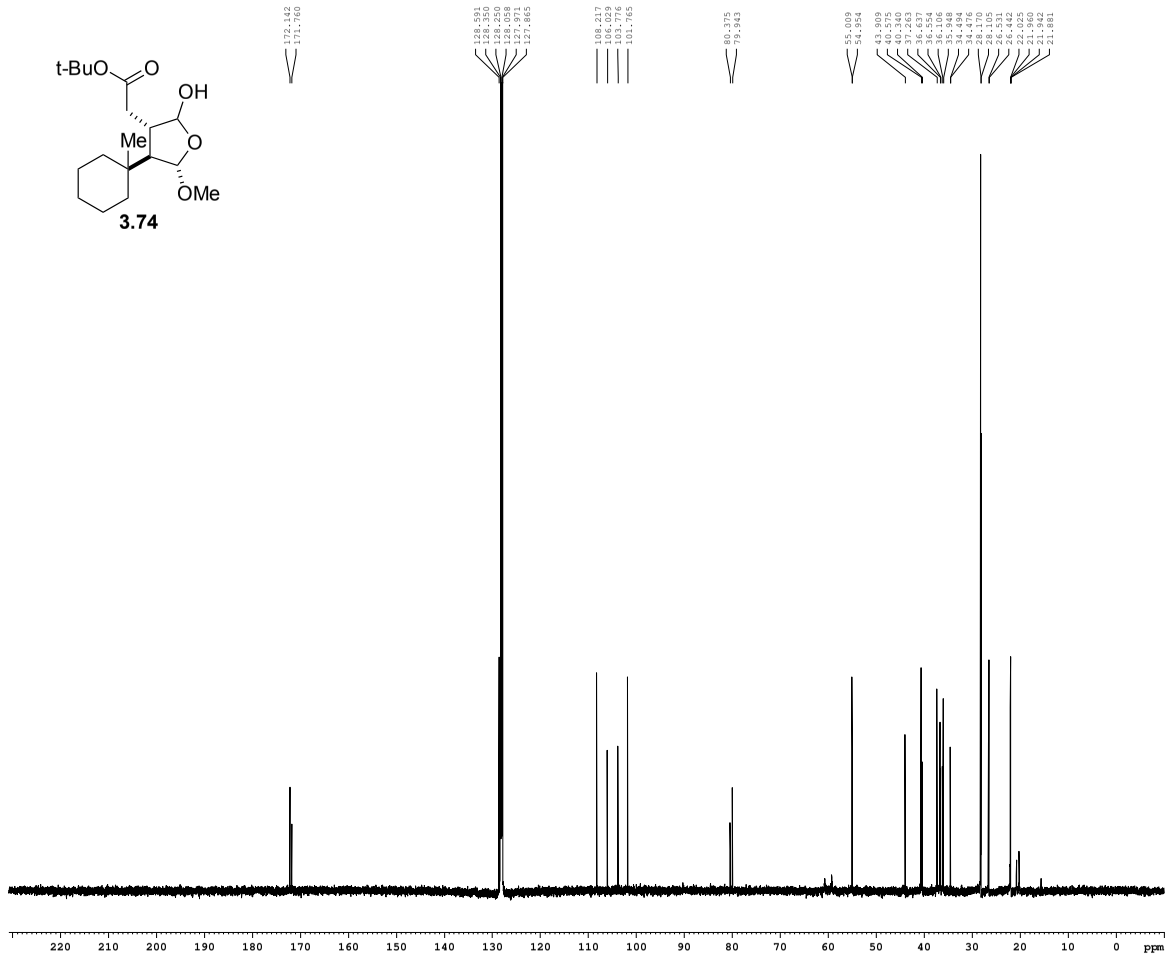

Current Data Parameters
NAME G65-077-S3
EXPNO 3
PROCNO 1
F2 - Acquisition Parameters
Date_ 20160427
Time 10.58
INSTRUM spect
PROBHD 5 mm CPBBO BB-
PULPROG zgdc30
TD 65536
SOLVENT CDCl3F
NS 247
DS 4
SWH 36231.883 Hz
FIDRES 0.552855 Hz
AQ 0.9043200 sec
RG 203
DW 13.800 usec
DE 19.65 usec
TE 298.1 K
D1 0.40000001 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 150.9194475 MHz
NUC1 13C
P1 10.00 usec
PLW1 64.00000000 W
======== CHANNEL f2 ========
SFO2 600.1330010 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 80.00 usec
PLW2 20.00000000 W
PLW12 0.36000001 W
F2 - Processing parameters
SI 65536
SF 150.9027930 MHz
WDW EM
SSB 0
LB 0.50 Hz
GB 0
PC 1.00
178.037
170.001
105.985
81.726
77.370
77.158
76.946
57.119
38.424
38.068
35.623
34.337
28.135
26.117
21.495
21.549
20.414
ppm
t-BuO
Me
OMe
3.73

1H spectrum

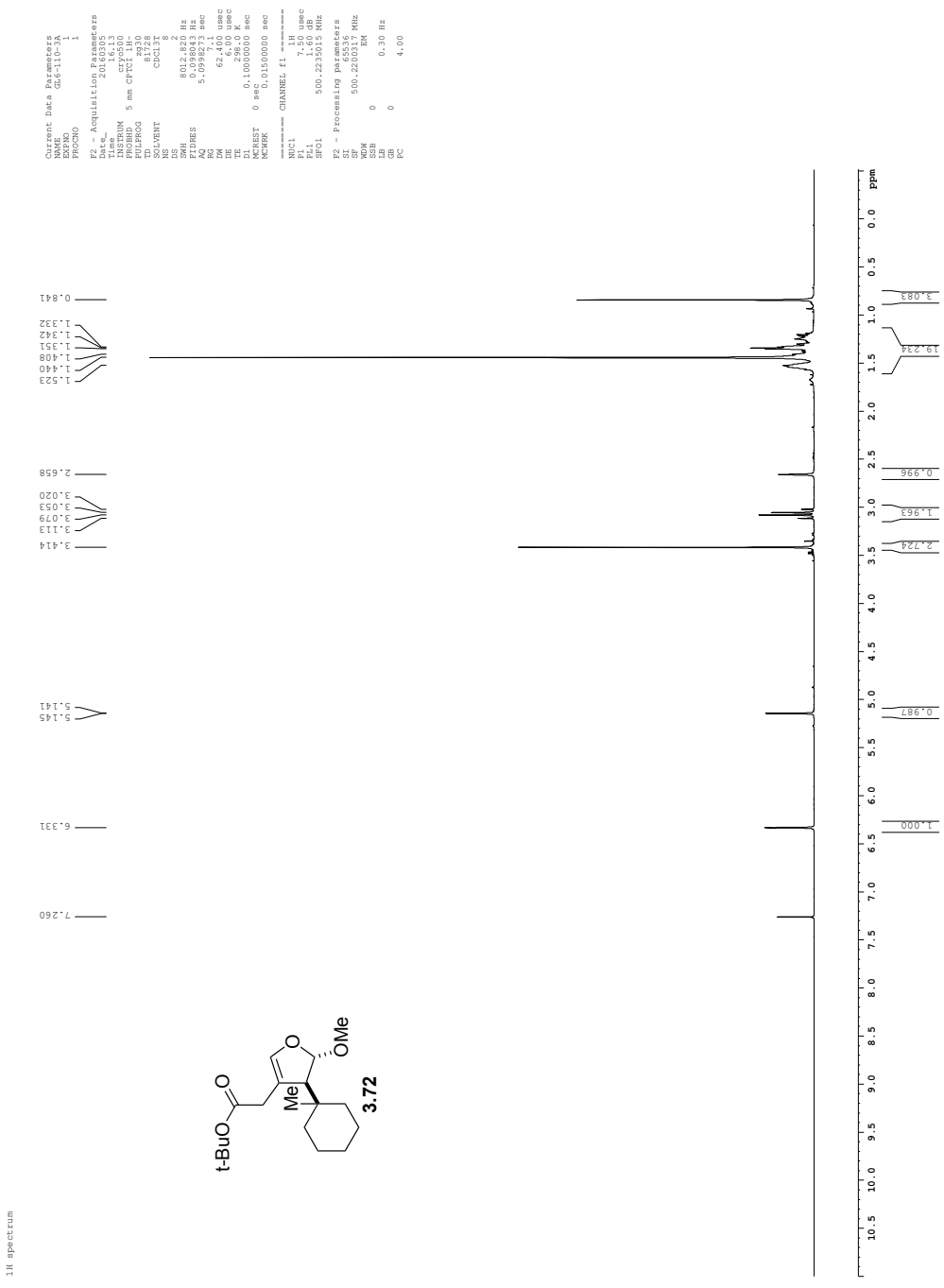



```
Current Data Parameters
NAME          GL6-124-hv
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20160325
Time               17.35
INSTRUM          cryo500
PROBHD    5 mm CPTCI 1H-
PULPROG             zg30
TD                 81728
SOLVENT             C6D6
NS                     8
DS                     2
SWH           8012.820 Hz
FIDRES        0.098043 Hz
AQ            5.0998273 sec
RG                     5
DW               62.400 usec
DE                6.00 usec
TE                298.0 K
D1          0.10000000 sec
MCREST    0 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          500.2199979 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 4.00
```

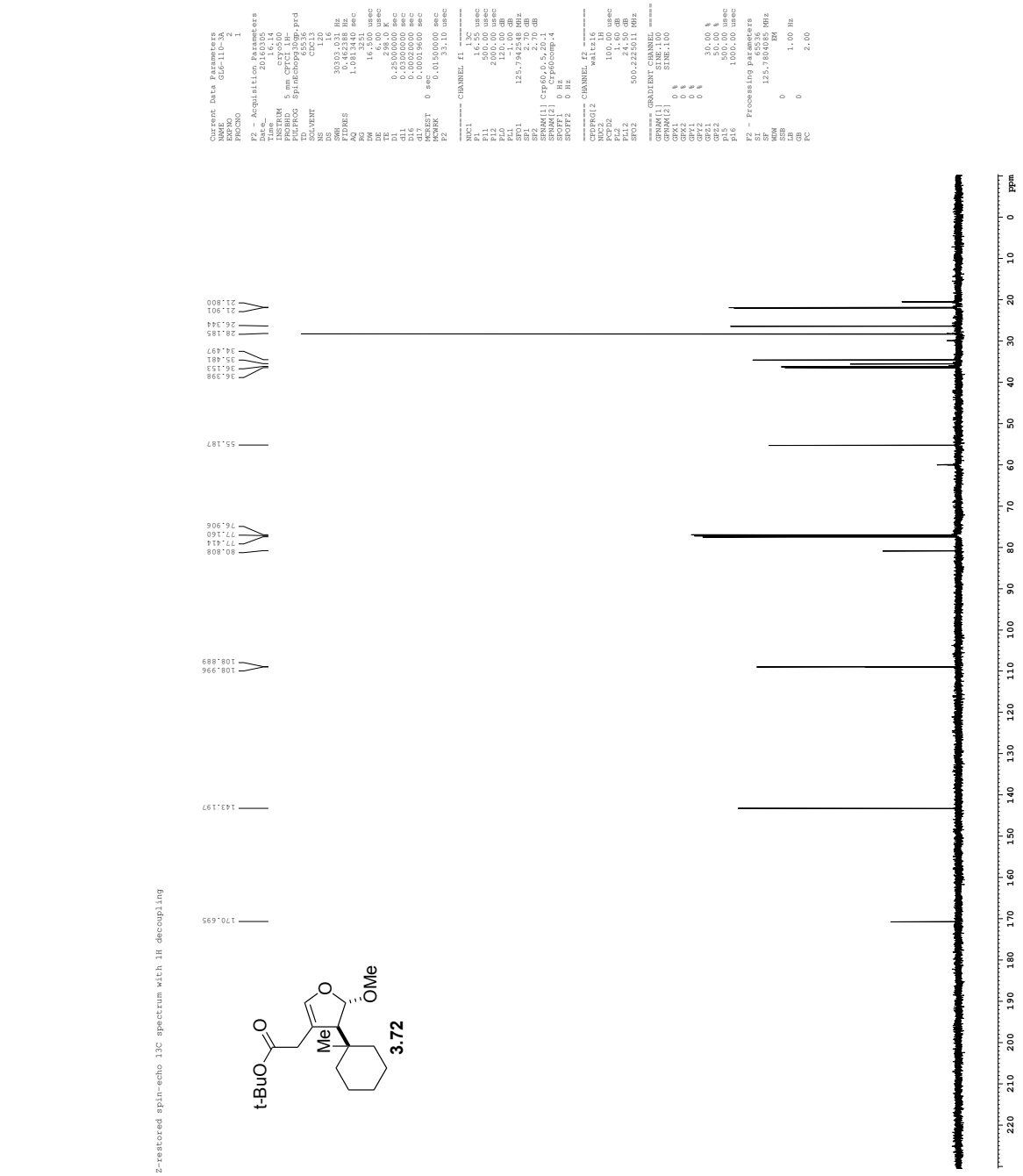
Z-restored spin-echo 13C spectrum with 1H decoupling



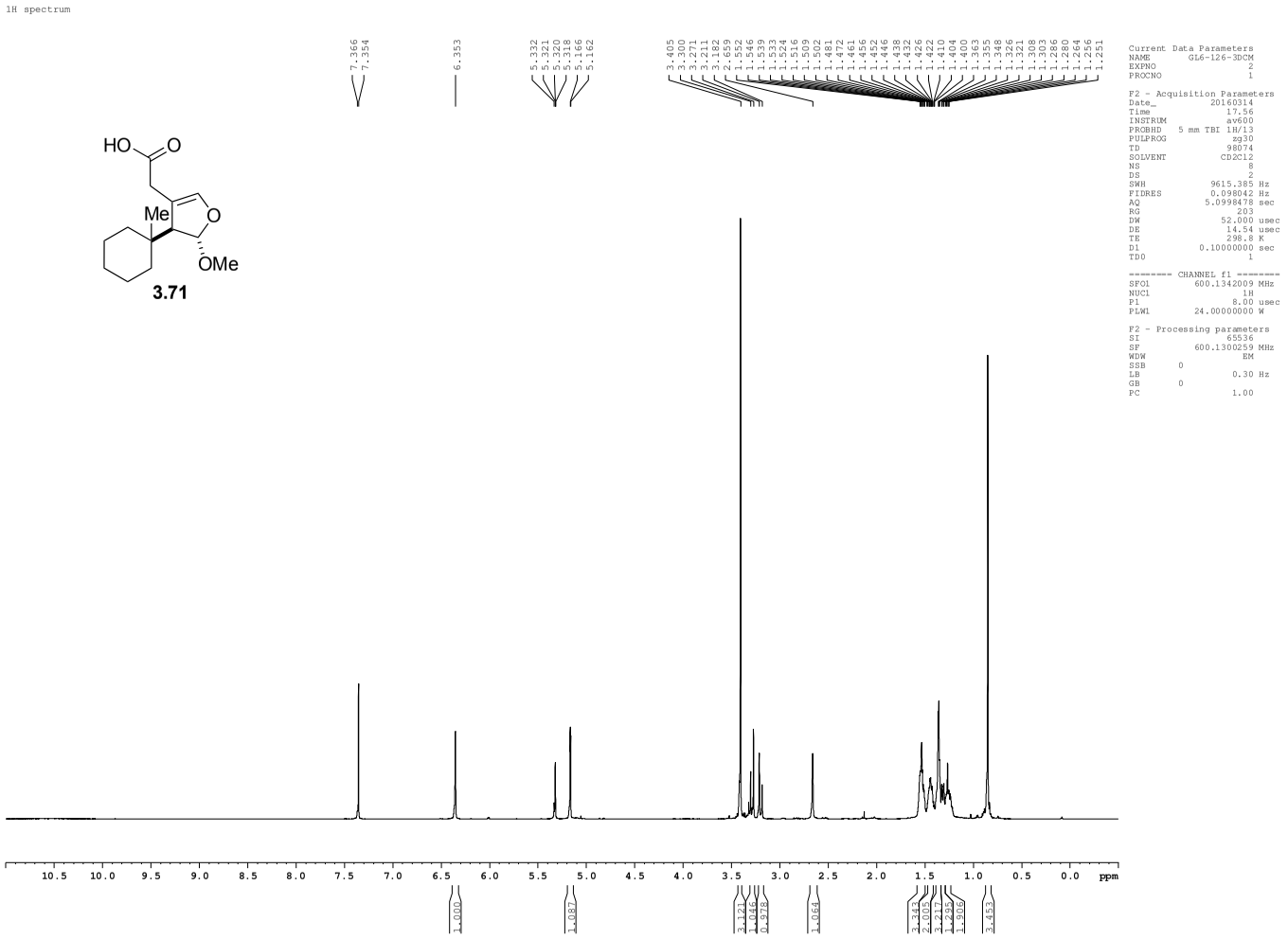

```
Current Data Parameters
NAME            GL6-124-hv
EXPNO                    2
PROCNO                   1

F2 - Acquisition Parameters
Date_          20160325
Time               17.37
INSTRUM            cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD                 65536
SOLVENT              CDCl3
NS                     145
DS                      16
SWH            30303.031 Hz
FIDRES         0.462388 Hz
AQ             1.0813440 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 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
SPNAM[1]  Crp60,0.5,20.1
SPNAM[2]     Crp60comp.4
SPOFF1    0 Hz
SPOFF2    0 Hz

======== CHANNEL f2 ========
CPDPRG[2          waltz16
NUC2                 1H
PCPD2             100.00 usec
PL2                1.60 dB
PL12              24.50 dB
SFO2         500.2225011 MHz

====== GRADIENT CHANNEL =====
GPNAM[1]          SINE.100
GPNAM[2]          SINE.100
GPX1      0 %
GPX2      0 %
GPY1      0 %
GPY2      0 %
GPZ1              30.00 %
GPZ2              50.00 %
p15              500.00 usec
p16             1000.00 usec

F2 - Processing parameters
SI                 65536
SF           125.7803743 MHz
WDW                   EM
SSB       0
LB                 1.00 Hz
GB        0
PC                 2.00
```

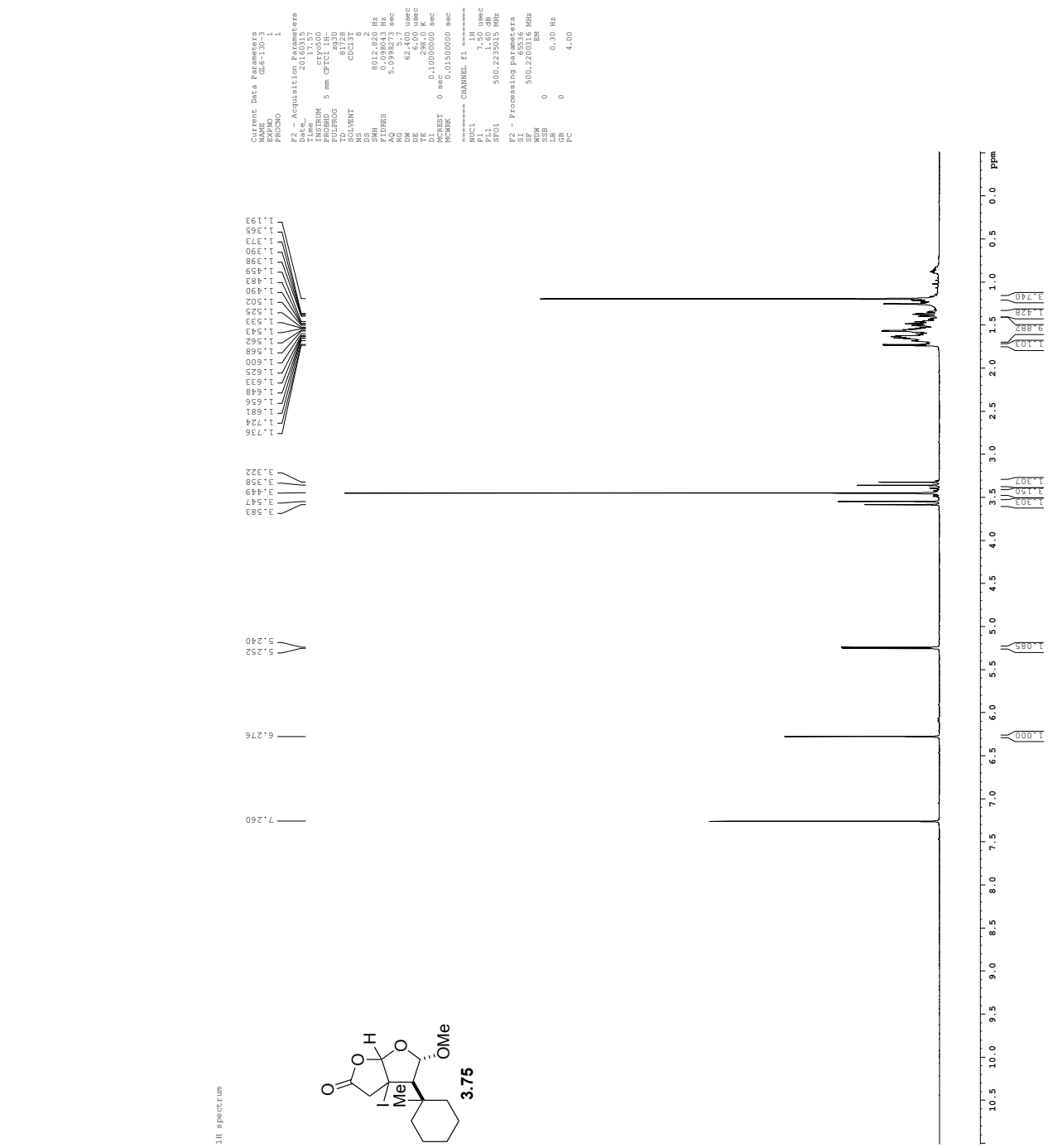

Current Data Parameters
NAME rdc1105A
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20160305
Time 16.13
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 81728
SOLVENT CDCl3
NS 8
DS 2
SWH 8012.820 Hz
FIDRES 0.098043 Hz
AQ 5.099827 sec
RG 7.1
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0 sec
MCWRK 0.01500000 sec
NUC1 1H
P1 7.50 usec
PL1 1.60 dB
SFO1 500.2235015 MHz
F2 - Processing parameters
SI 65536
SF 500.2200317 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00
0.841
1.332
1.342
1.351
1.408
1.440
1.523
2.658
3.020
3.053
3.079
3.113
3.414
5.141
5.145
6.331
7.260
t-BuO
O
Me
OMe
3.72
ppm
3.083
19.234
0.996
1.963
2.724
0.987
1.000

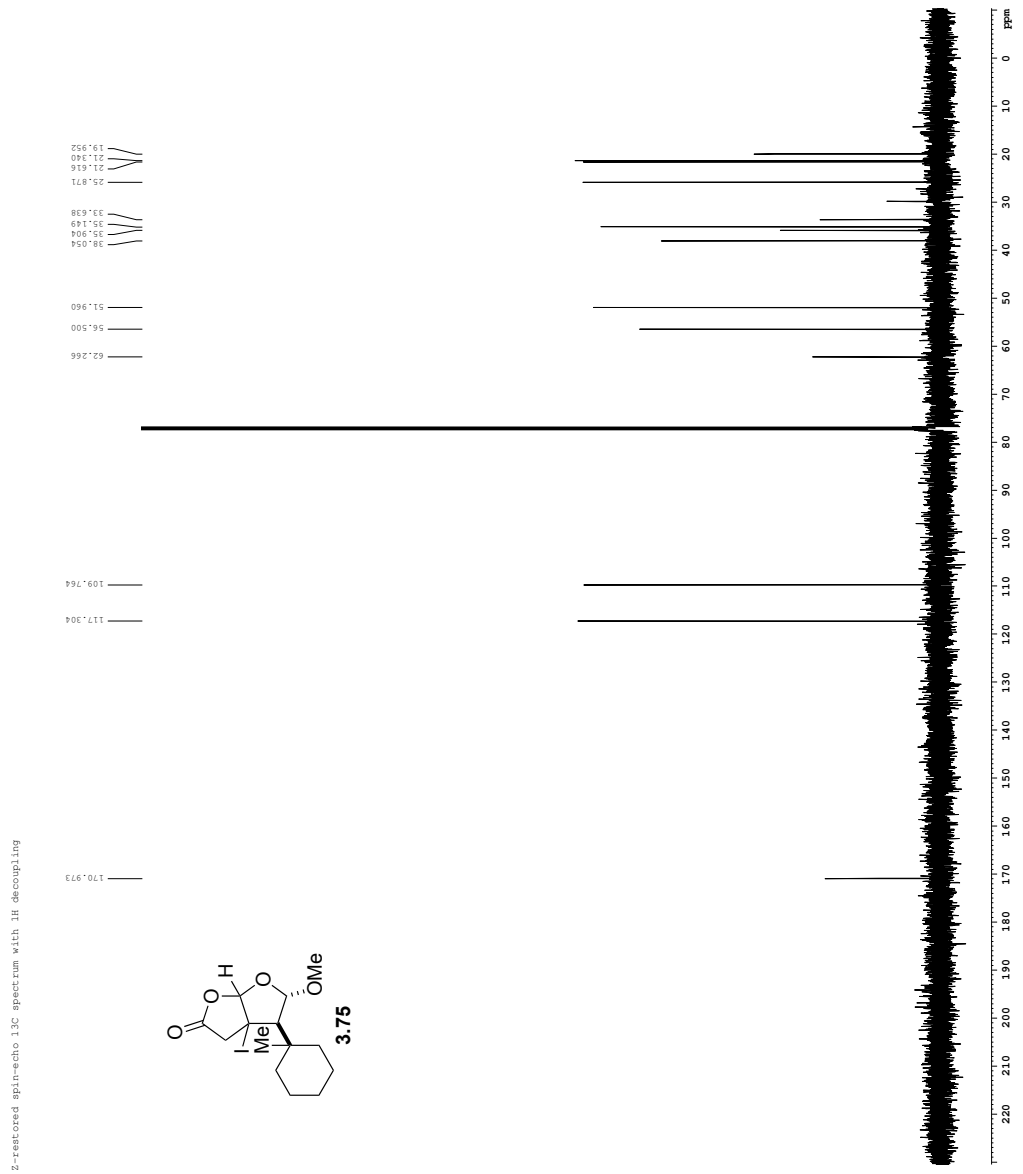
1H spectrum



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


1H spectrum
7.366
7.354
6.353
5.332
5.321
5.320
5.318
5.166
5.162
3.405
3.300
3.271
3.211
3.182
2.659
1.552
1.546
1.539
1.533
1.524
1.516
1.509
1.502
1.481
1.472
1.461
1.456
1.452
1.446
1.438
1.432
1.426
1.422
1.410
1.404
1.400
1.363
1.355
1.348
1.326
1.321
1.308
1.303
1.286
1.280
1.264
1.256
1.251
HO
O
Me
O
OMe
3.71
Current Data Parameters
NAME GL6-126-3DCM
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20160314
Time 17.56
INSTRUM av600
PROBHD 5 mm TBI 1H/13
PULPROG zg30
TD 98074
SOLVENT CD2Cl2
NS 8
DS 2
SWH 9615.385 Hz
FIDRES 0.098042 Hz
AQ 5.0998478 sec
RG 203
DW 52.000 usec
DE 14.54 usec
TE 298.8 K
D1 0.10000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 600.1342009 MHz
NUC1 1H
P1 8.00 usec
PLW1 24.00000000 W
F2 - Processing parameters
SI 65536
SF 600.1300259 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
10.5 10.0 9.5 9.0 8.5 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
1.000
1.087
3.121
1.046
0.978
1.064
2.343
2.005
1.211
1.882
1.890
3.453


1H spectrum
Current Data Parameters
NAME GL6-130-3
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20160315
Time 17.57
INSTRUM spect
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 81728
SOLVENT CDCl3
NS 8
DS 2
SWH 8012.800 Hz
FIDRES 0.098043 Hz
AQ 5.099273 sec
RG 57
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0 sec 0.01500000 sec
MCWRK
======== CHANNEL f1 ========
NUC1 1H
P1 7.60 usec
PL1 1.00 dB
SFO1 500.2235015 MHz
F2 - Processing parameters
SI 65536
SF 500.2200316 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00
7.260
6.276
5.252
5.240
3.583
3.547
3.449
3.358
3.322
1.736
1.724
1.681
1.656
1.648
1.633
1.625
1.600
1.568
1.562
1.543
1.533
1.525
1.502
1.490
1.483
1.459
1.398
1.390
1.373
1.365
1.193
1.000
1.085
1.307
1.303
1.150
1.103
9.882
1.428
3.740
ppm
3.75


Current Data Parameters
NAME GL6-130-3
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20161015
Time 17.59
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG SpinEchopy30gp.prd
TD 65536
SOLVENT CDCl3
NS 16
DS 16
SWH 30303.031 Hz
FIDRES 0.462338 Hz
AQ 1.08134440 sec
RG 72.98.2
DW 16.500 usec
DE 6.00 usec
TE 298.0 K
D1 0.25000000 sec
D11 0.03000000 sec
D16 0.00020000 sec
CNST2 0.00019600 sec
MCREST 0 sec
MCWRK 0.01500000 sec
P2 33.10 usec
======== CHANNEL f1 ========
NUC1 13C
P1 6.25 usec
P11 500.00 usec
P12 2000.00 usec
PL1 120.00 dB
PL1 -1.00 dB
SFO1 125.7942548 MHz
SP1 2.70 dB
SP2 2.70 dB
SPNAM[1] Crp60,0.5,20.1
SPNAM[2] cpdprgcomp.4
SPOFF1 0 Hz
SPOFF2 0 Hz
======== CHANNEL f2 ========
CPDPRG[2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 1.60 dB
PL12 24.50 dB
SFO2 500.2229011 MHz
GPNAM[1] SINE.100
GPNAM[2] SINE.100
GPX1 0 %
GPX2 0 %
GPY1 0 %
GPY2 0 %
GPZ1 30.00 %
GPZ2 50.00 %
P15 500.00 usec
P16 1000.00 usec
F2 - Processing parameters
SI 65536
SF 125.7800000 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00
25.871
21.616
21.340
19.952
33.638
38.054
35.904
35.149
51.960
56.500
62.266
109.764
117.304
170.973
ppm
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
210
220
O
O
H
O
OMe
O
Me
I
3.75
Z-restored spin-echo 13C spectrum with 1H decoupling