Total Synthesis of Divergolides E and H and an Investigation into the Oxidative Rearrangement to Divergolides C and D

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Total Synthesis of Divergolides E and H and an Investigation into the Oxidative Rearrangement to Divergolides C and D

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This thesis describes the first total syntheses of divergolides **E** and **H.** Construction of the core bridged bicyclic acetal unit was accomplished using a hetero-Diels–Alder (HDA) reaction and oxidative carbon-hydrogen bond cleavage to couple two highly functionalized subunits. Additional highlights of this convergent synthesis include a chelation-controlled alkenylzinc addition, amide formation between a hindered aniline and an acylating agent prone to ketene formation, and a challenging macrolactonization. Model studies showed effective oxidation of the core structure using a hypervalent iodine species which sets the stage for rearrangement into divergolides **C** and **D**.

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LIST OF ABBREVIATIONS

9-BBN	9-borabicyclo[3.3.1]nonane
Ac	acetyl
CAN	ceric ammonium nitrate
CM	cross metathesis
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
BTI	[bis(trifluoroacetoxy)iodo]benzene
DCC	N,N-dicyclohexylcarbodiimide
DCM	dichloromethane
DDQ	2,3-Dichloro-5,6-dicyano-1,4-benzoquinone
DIBAL	diisobutylaluminum hydride
DIPEA	diisopropyl ethyl amine
DIPT	diisopropyl tartrate
DMSO	dimethylsulfoxide
HDA	hetero-Diels-Alder
HWE	Horner-Wadsworth-Emmons
IBX	2-iodoxybenzoic acid
IR	infrared
KIE	kinetic isotope effect

LAB	lithium ammonia borane
LAH	lithium aluminum hydride
LDA	lithium diisopropyl amine
MS	molecular sieves
NMR	nuclear magnetic resonance
N.R.	no reaction
PMB	p-methoxybenzyl
PPM	parts per million
RCM	ring closing metathesis
SAE	Sharpless asymmetric epoxidation
TBAF	tetra-*n*-butyl ammonium fluoride
TBAI	tetrabutylammonium iodide
TBS	*tert*-butyldimethylsilyl
TES	triethylsilyl
TFA	trifluoroacetic acid
THF	tetrahydrofuran
TLC	thin layer chromatography

1.0 DDQ OXIDATION

Carbon-carbon bond formation is fundamental to organic synthesis and is often achieved through activation by functional groups, transforming unreactive starting materials into reactive coupling partners. The idea of directly functionalizing carbon-hydrogen bonds is an attractive option that avoids additional steps to implement a functional group, making syntheses concise and atom economical. The Floreancig group has developed a strategy for carbon-carbon bond formation using the reagent 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) to cleave a specific carbon-hydrogen bond (Figure 1). This protocol avoids the use of harsher conditions typically found in alternative methods for oxocarbenium ion formation such as acid-mediated Prins-type reactions.[1,2] Herein, we demonstrate the method is more effective than both the Saegusa[3] and 2-iodoxybenzoic acid (IBX)[4] oxidation, two common methods for the oxidation of enol silanes.

Three possible mechanisms have been proposed for DDQ oxidation of benzylic ethers to oxocarbenium ions (Figure 1): direct hydride transfer; electron transfer followed by hydrogen atom transfer; electron transfer followed by proton transfer then a second electron transfer.

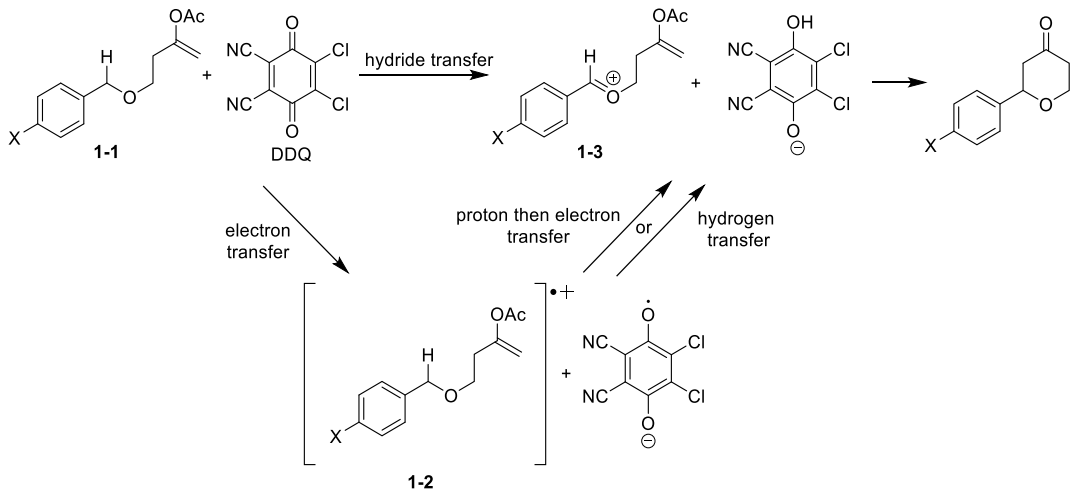

Figure 1: Possible Mechanisms for DDQ Oxidation

In 1967, Trost and coworkers used deuterated acenaphthenes to determine that DDQ oxidation proceeded through a stepwise, direct hydride transfer process to form a carbocation, in which carbon-hydrogen bond cleavage was the rate determining step.[5] However, Trost's work focused specifically on aromatization of all carbon systems and has limited applicability to oxocarbenium ion formation, the main focus in this synthesis. To investigate DDQ oxidation in oxocarbenium ion formation, the Floreancig group studied intermolecular and intramolecular kinetic isotope effects (KIE) in benzylic and allylic ethers (Figure 2).[6]

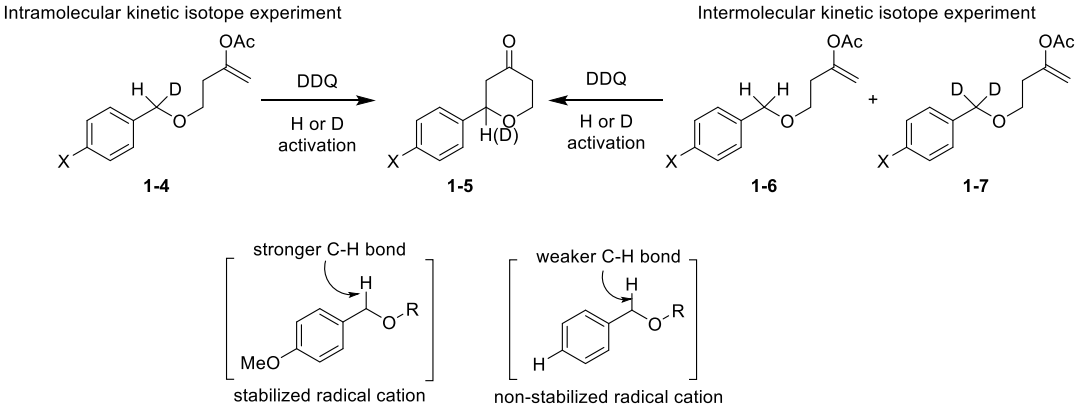

Figure 2: Kinetic Isotope Experiments

In the study, all substrates showed a KIE indicating carbon-hydrogen bond cleavage was the rate determining step. In addition, the magnitude of the KIE was consistent in both intramolecular (compound **1-4**) and intermolecular (compounds **1-6**, **1-7**) reactions indicating there was no formation of a reactive intermediate prior to bond cleavage that was rate limiting. Recently, DFT calculations provided compelling support for the direct hydride transfer mechanism and indicates that reactivity is determined by stability of the oxocarbenium ion intermediate, the amount of charge transfer in the transition state, and π orbital overlap between DDQ and the forming cation in the substrate.[7] Interestingly, direct transfer to either oxygen or carbon was calculated to have similar activation barriers and should be taken into consideration (Figure 3).

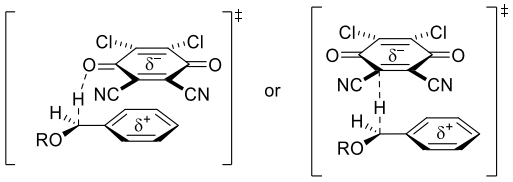

Figure 3: Direct Hydride Transfer Transition State to Either Oxygen or Carbon

Although DDQ is most commonly used to cleave *p*-methoxybenzyl (PMB) groups, significant advances towards its use in carbon-carbon bond formation began in 1987 by Mukaiyama and coworkers who oxidized several allylic ethers to oxocarbenium ions, which then underwent nucleophilic addition (Figure 4).[8]

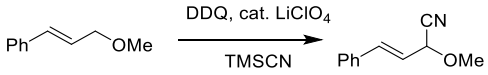

Figure 4: Mukaiyama's Oxidation of Allylic Ethers

A catalytic amount of $LiClO_4$ was found to greatly improve the yield. Initial oxidation affords an oxocarbenium ion and a hydroquinone anion (Figure 1, **1-3**), which can be replaced with $LiClO_4$. Phenyl and furyl groups attached to the allylic ether also improve the yield due to stabilization of

the resulting oxocarbenium ion through resonance. Mukaiyama studied various nucleophiles including silyl enol ethers, allyltrimethylsilane, and organotin reagents.

Recently, the Floreancig group has greatly expanded the scope to include substrates with many types of functionalities (Figure 5).

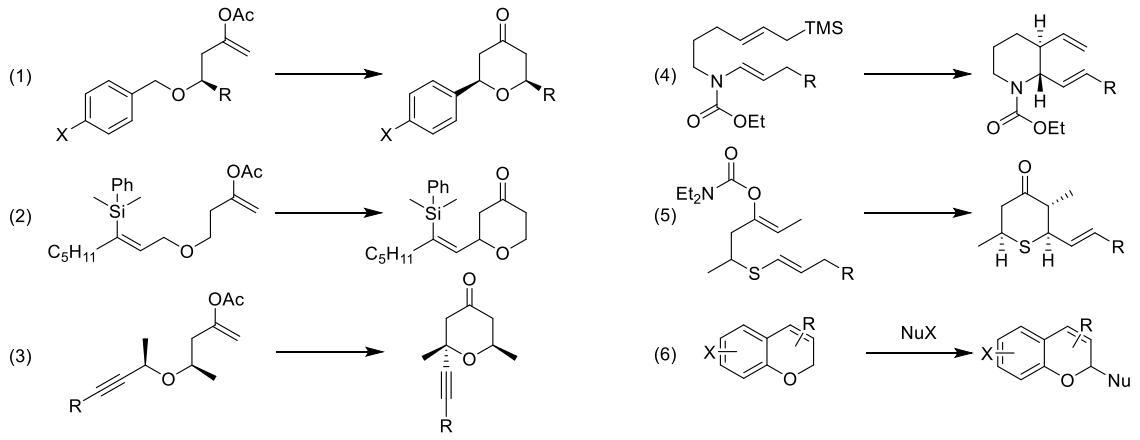

Figure 5: The Floreancig Group Investigation of DDQ Oxidation

In 2008, the substrate scope was expanded to oxidation of the benzylic position which underwent intramolecular nucleophilic attack by enol acetate (eq 1).[9] The formation of a six membered ring also allowed for excellent stereochemical control through the chair conformation. The utility of the reaction was demonstrated in the total synthesis of the macrolide ring neopeltolide.[10] Vinyl silanes and alkynes were also found to be suitable directing groups (eq 2, 3).[11,12,12b] Interestingly, an alkynyl group showed a preference to occupy the axial position on a six membered ring due to the electrostatic attraction between the π electrons and oxocarbenium ion. DDQ was also effective when other heteroatoms were used as demonstrated in the formation of acyliminium ions to synthesize cyclic vinyl oxaolidinones[13] and functionalized enamides, (eq 4)[14] as well as formation of thiocarbenium ions from vinyl sulfides (eq 5).[15] Chromene derivatives were found to be excellent substrates in bimolecular reactions as they provide greater stability to the oxocarbenium ion intermediate (eq 6).[16,17] The bimolecular reactions required a

balance between oxocarbenium ion formation (oxidation potential/concentration of the intermediate) and rapid nucleophilic addition to drive the reaction forward. The mildness of DDQ oxidation was demonstrated in the synthesis of clavosolide where the oxocarbenium ion was generated in proximity to a cyclopropane ring.[18]

In 2014, our group applied the methodology to form the spiroacetal structure in bistramide A using a three step, one pot sequence (Figure 6).[19] The sequence involved coupling silyl enol ether **1-9** and aldehyde **1-8** through a hetero-Diels–Alder (HDA) reaction to yield **1-10** followed by oxidation with DDQ to form the dihydropyrone **1-12** then TES ether cleavage to achieve cyclization to **1-13** in 58% yield over 3 steps (one pot).

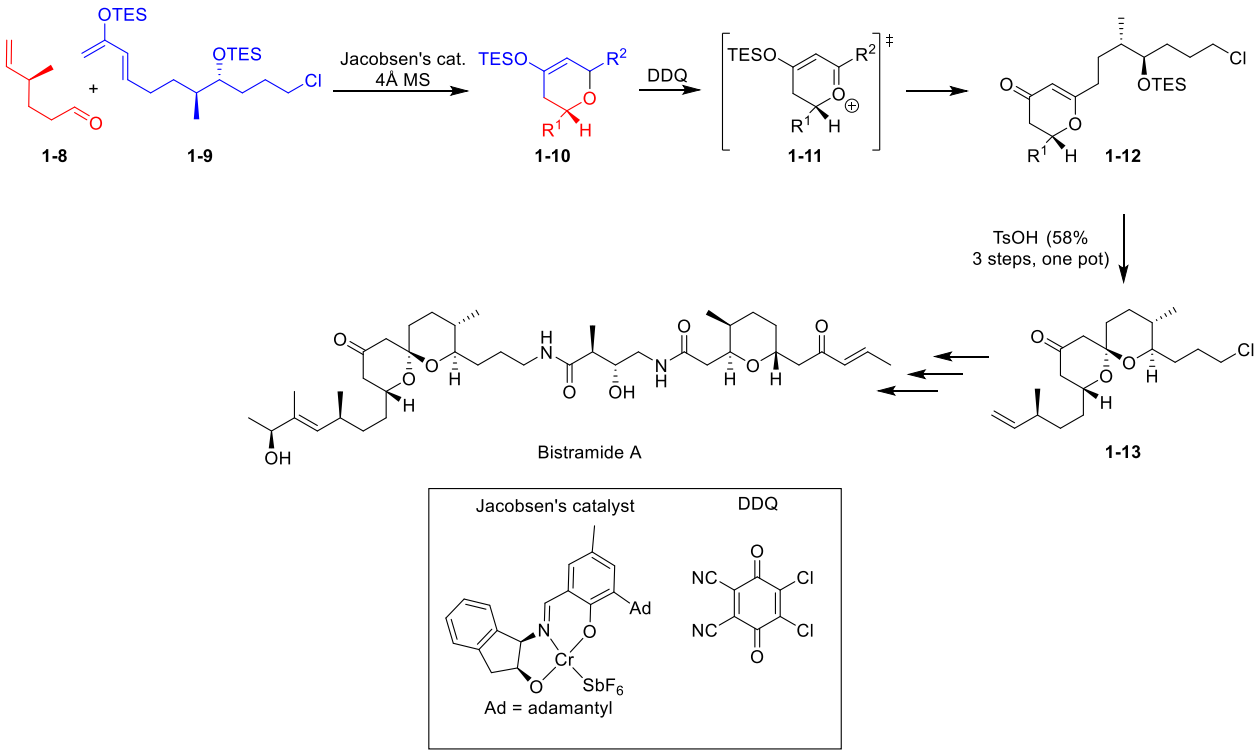

Figure 6: Synthesis of Bistramide A using a Three Step Telescoped Sequence

The key step in the synthesis of divergolide **E** will build on this telescoped sequence. The pendant nucleophile on the silyl enol ether unit (Figure 6) will instead be placed on the aldehyde unit, which will allow for the synthesis of bridged bicyclic acetals (model studies: Figure 13, 14).

2.0 THE DIVERGOLIDES

2.1 ISOLATION AND STRUCTURE

Actinomycetes have produced a wide variety of ansa macrolides (ansamycins) prominent for their large macrolide ring fused to a cyclic aromatic core. Several notable ansamycins are strong antibacterial[20], antitumor[21] and HSP90 inhibitor[22] agents. In 2011, Hertweck and coworkers isolated four novel ansa macrolides (Figure 7, divergolides **A**-**D**) from the endophyte *Streptomyces* sp. found on the mangrove tree *Bruguiera gynorrhiza*.[23]

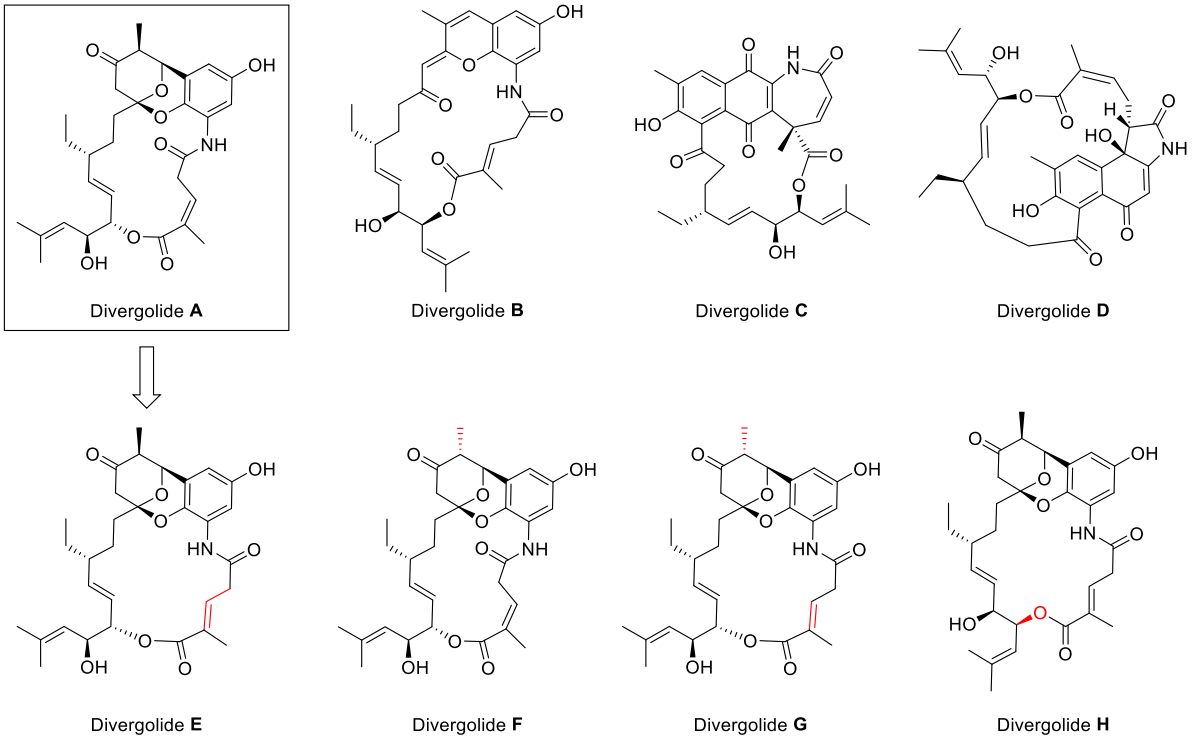

Figure 7: Divergolides A-H

Further investigation into this diverse group of natural products led to the discovery of additional isomers of divergolide **A**[24] and divergolide **C**[25] all of which derive biosynthetically from a common polyketide (Figure 9). The structural complexity and promising biological activity has attracted interest from the synthetic community with several synthetic studies (section 2.4)[26,27,28,29] and the first total synthesis of divergolide **I**, recently reported by Trauner.[30] The Floreancig group's interest arises from the desire to access the uncommon, bicyclic bridged acetal core using a one pot hetero-Diels–Alder (HDA) reaction, oxidative carbon-hydrogen bond cleavage using 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ), and cyclization (model studies: Figure 13, 14). Although DDQ has been extensively studied by the Floreancig group this will be the first example in the formation of a bridged O-heterocyclic natural product, the complexity of which will test the limits of the reaction.[18,10,19] In addition, the structural similarities between divergolides **E**, **C**, and **D** provides the unique possibility of accessing these and structurally similar compounds from a common intermediate.

2.2 BIOLOGICAL ACTIVITY

Investigation into biologically active and cytotoxic compounds has become increasingly important due to the growing prevalence of drug resistant infectious agents. The diverse group of ansa macrolides have shown prominent biological activity and are important targets for study. Galdanamycin and its derivatives are potent inhibitors of the chaperone protein HSP90, an important target for anticancer agents (Figure 8).[31] Rifamycin inhibits a broad range of bacteria through its strong binding to DNA-dependent RNA polymerase in many prokaryotes.[20]

Maytansinoid is potent towards a variety of tumor cells including L-1210 and P-388 leukemias, Lewis lung carcinoma, as well as towards other eukaryotic systems.[21,32]

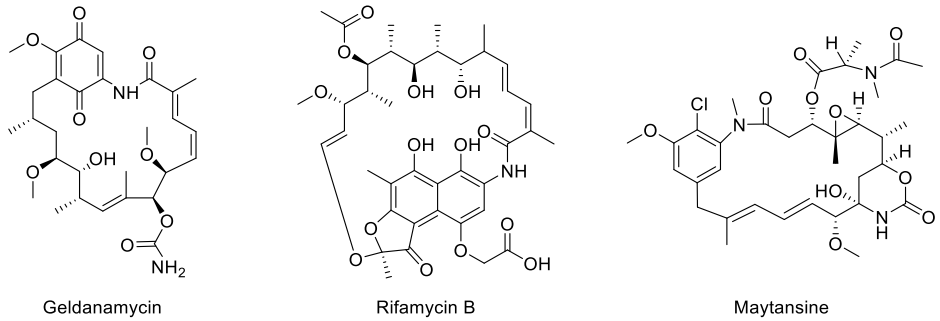

Figure 8: Notable Ansamycin Natural Products

Divergolides **A**-**D** and their isomers have shown promising biological activity during preliminary screening, most notably towards antibiotic resistant strains (Table 1). Divergolide **A** shows the strongest activity towards *Mycobacterium vaccae*. Divergolide **C** has moderate activity against *Enterococcus faecalis*, while divergolide **D** shows activity towards *Bacillus subtilis*, *Staphylococcus aureus*, and several tumor cell lines (IC_{50} of 1-2 μM) including lung, renal, pancreatic, and sarcoma cancers.[23]

Table 1. Antibacterial and Cytotoxic Activity of Divergolides A-D[23]

	Test strains (mm inhibition zone)[a]				
Divergolide	*Bacillus subtilis*	*Mycobacterium vaccae*	Methicillin resistant *Staphylococcus aureus*	vancomycin-resistant *Enterococcus faecalis*	Cytotoxicity Mean IC_{50} [μM][b]
A	11	19	11	0	>10
B	10	12	0	0	>10
C	13	11	13	14	>10
D	19	12	19	0	2.4

[a] Data in diameter; 50 mg per paper disk, d=7 mm. [b] Test concentration in 10 half-log steps up to 10 mM.

2.3 PROPOSED BIOSYNTHESIS

Although the divergolide cores each have different cyclic structures, they can be traced back biosynthetically to a common polyketide chain. This extraordinary pathway exemplifies how diversification is accomplished using divergent polyketide synthesis. Hertweck and coworkers describe a plausible biosynthesis originating from a 3-amino-5-hydroxybenzoic acid starter unit **2-1** (Figure 9).[23,33] Polyketide synthase would elongate the polyketide chain at the carboxylic acid position using a branched isobutyryl-malonyl-CoA extender unit.[34] A Baeyer-Villiger oxygenase could disrupt the polyketide chain and implement the ester linkage, which could then undergo an optional acyl migration with the adjacent hydroxyl group on **2-4**.[35] This common polyketide intermediate could then cyclize at various positions to obtain the divergolide core structures. Attack by the phenolic hydroxyl group on the nearby ketones of **2-5** and **2-6** leads to divergolides **B** and **A** respectively. The phenol could also be oxidized to quinone **2-7** then undergo enolate attack to form a six membered aromatic ring. Further enolate attack by the amide on quinone **2-8** and **2-9** then forms the third ring to complete divergolides **C** and **D** respectively.

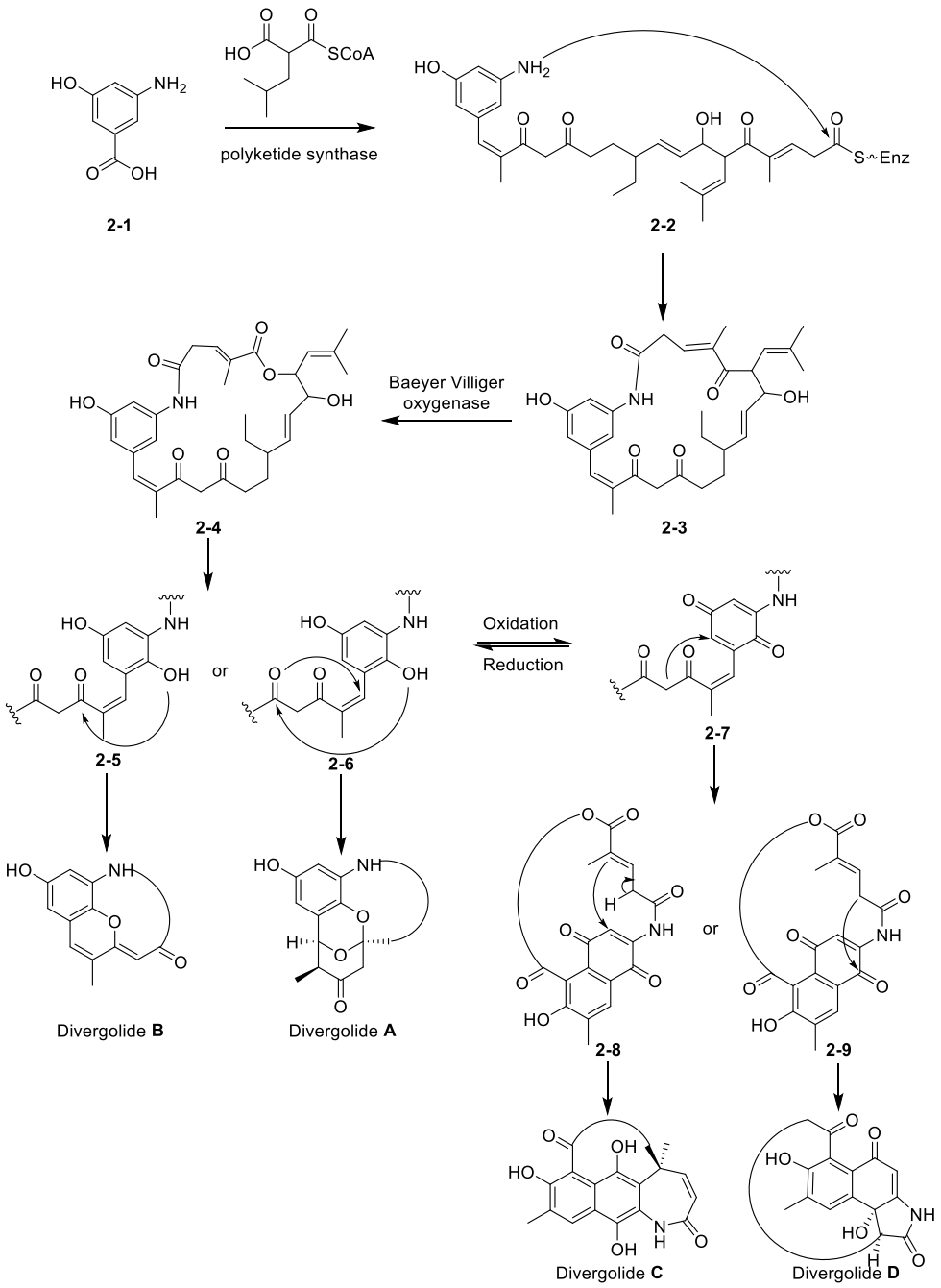

Figure 9: Proposed Biosynthesis of Divergolides A-D

2.4 PREVIOUS SYNTHETIC STUDIES

Several partial syntheses have been published for divergolides **C** and **D** that construct the bicyclic core[29,28,26] while only a small fragment of divergolide **A** has been synthesized.[27] The common method to synthesize the cores of divergolides **C** and **D** is a Diels-Alder reaction (Figure 10). The groups of Trauner[29] and Rasapalli[26] each perform a Diels-Alder between Danishefsky's diene **2-10** and quinone **2-11**, envisioning the lactam to arise from enolate attack into the quinone (Figure 10, A). Trauner has recently completed the total synthesis of divergolide **I**, the acyl migrated isomer of divergolide **C**.[30] Moody and coworkers (Figure 10, B)[28] first form the bicyclic lactam-aromatic ring **2-15** starting from aromatic core **2-14**. An intramolecular Diels-Alder reaction with **2-17** would then construct the tricyclic core and macrolide ring simultaneously.

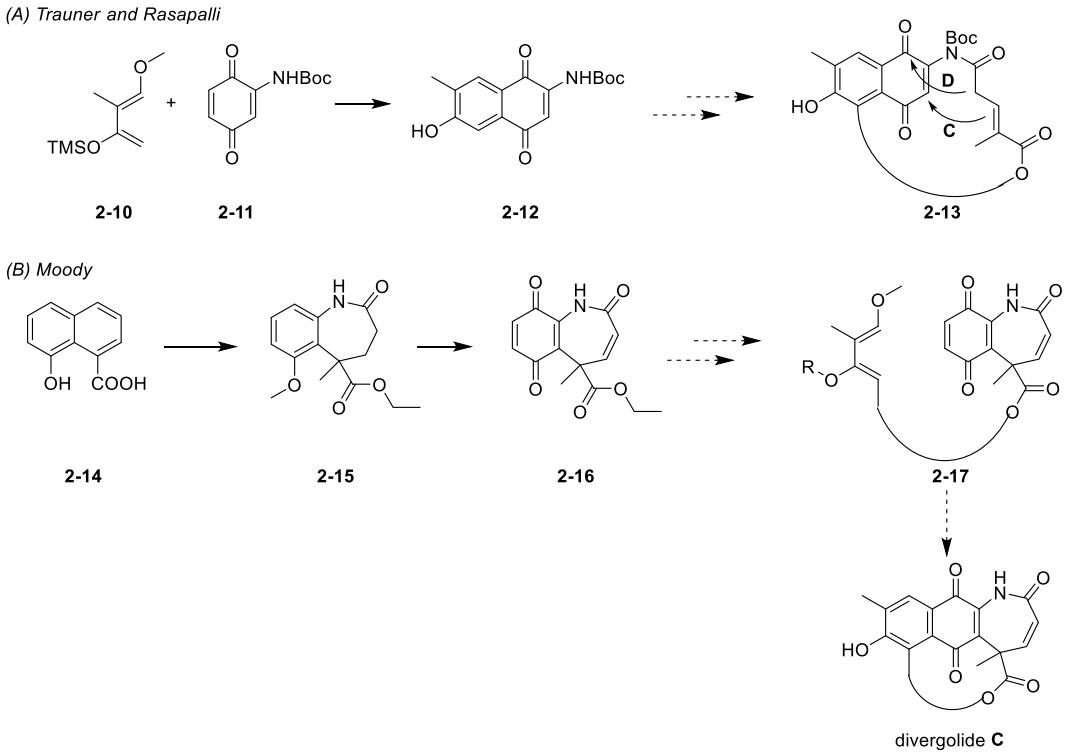

Figure 10: Trauner, Rasapalli, and Moody's Partial Synthesis of Diverolides C and D Using a Diels-Alder Reaction

Wei-Min Dai and coworkers foresee constructing divergolide **A** by first forming the macrolide ring using a ring closing metathesis (RCM) (Figure 11).[27,36] The acetal group of the bridged tricyclic core would then arise from condensation of a ketone with corresponding hydroxyl groups.

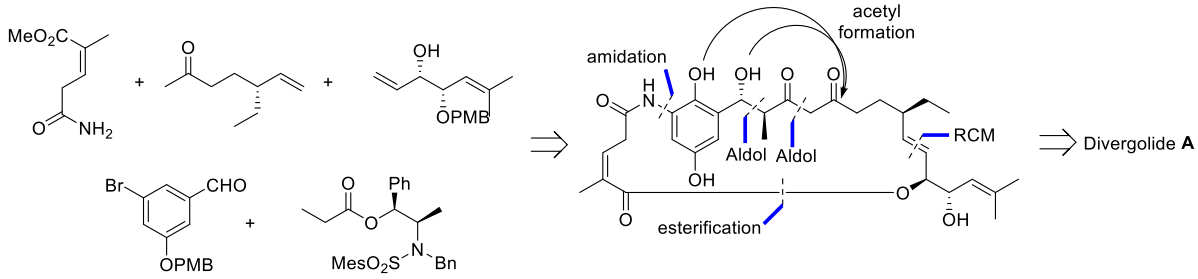

Figure 11: Wei-Min Dai's Retrosynthetic Analysis

3.0 MODEL STUDIES

3.1 HETERO-DIELS–ALDER AND DDQ OXIDATION

Model studies of the core of divergolide **E** began with the synthesis of diene **3-2** and aldehyde **3-4** (Figure 12, A). Methylation of 5-hexene-1-ol followed by cross metathesis with ethyl vinyl ketone yielded enone **3-1.** Treatment of **3-1** with triethylsilyl trifluoromethanesulfonate (TESOTf) and triethylamine yielded diene **3-2**.[37] Aldehyde **3-4** was prepared through formylation of 4-methoxyphenol to yield **3-3**,[38] followed by acylation with acetic anhydride to yield **3-4** (Figure 12, B).

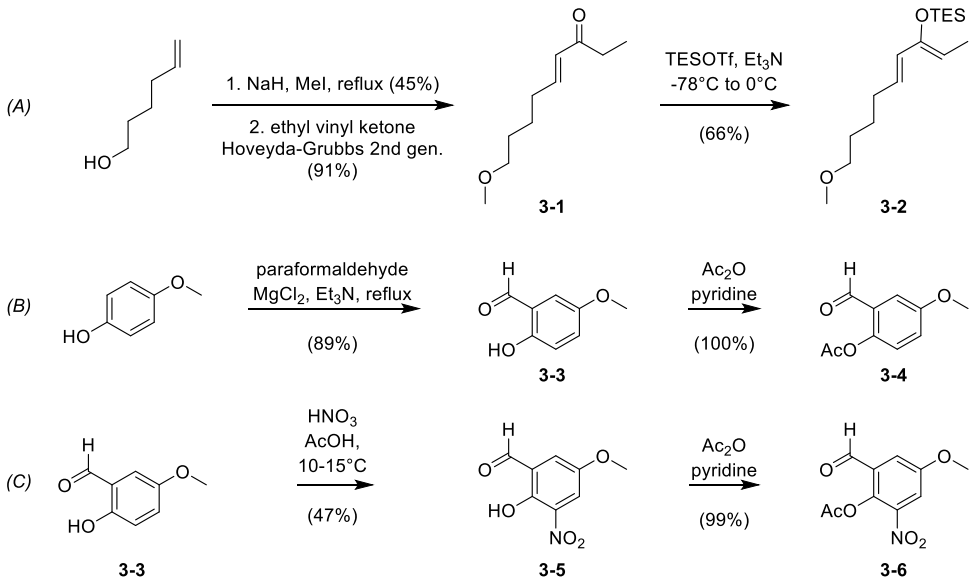

Figure 12: Synthesis of Diene 3-2 and Aldehydes 3-4 and 3-6

Jacobsen's catalyst was chosen as the HDA catalyst due to its high reported yields and enantioselectivity in relatively unactivated substrates.[39] However, attempts to couple aldehyde **3-4** with diene **3-2** proved ineffective with Jacobsen's catalyst (Cl) and only proceeded if the stronger Lewis acid dimethylaluminum chloride was used (Figure 13).[40] The isomeric mixture of the product silyl enol ether **3-7** was successfully reacted with DDQ to yield dihydropyrone **3-8** (45% over 2 steps). Deprotection of the acyl group produced a mixture of uncyclized **3-9** and cyclized **3-10** which could be cyclized upon stirring with a catalytic amount of trifluoroacetic acid (TFA). NMR analysis showed the disappearance of both the phenol and alkene (of the dihydropyrone) hydrogens confirming the product as **3-10**, the bridged tricyclic core of divergolide **E**.

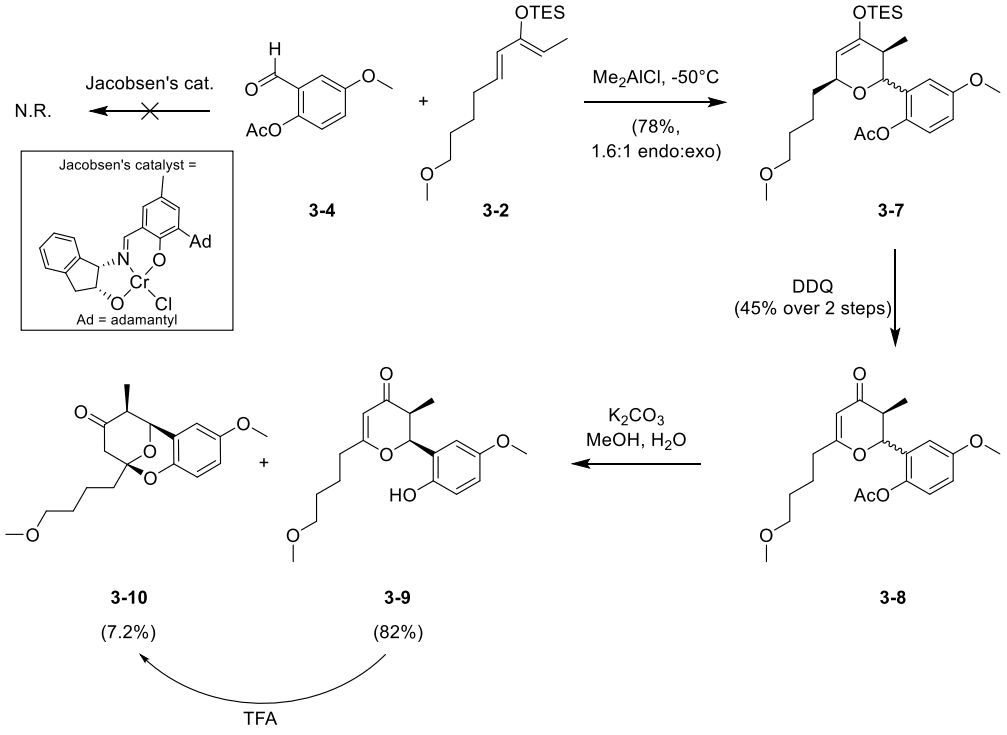

Figure 13: Model Studies: Racemic Synthesis of Core Structure 3-10

3.2 NITRO GROUP ACTIVATION

In order to use Jacobsen's catalyst, either the diene or aldehyde had to be activated. Since the natural product contains an amino group, a nitro group was used to activate the aldehyde which could later be reduced to the amine. The activated aldehyde **3-6** was prepared (Figure 12, C) through nitration of **3-3** to yield **3-5**, which was then acylated to compound **3-6**. Compound **3-6** was successfully coupled to diene **3-2** using Jacobsen's catalyst (Cl) (Figure 14) to give **3-11** in 75% yield.

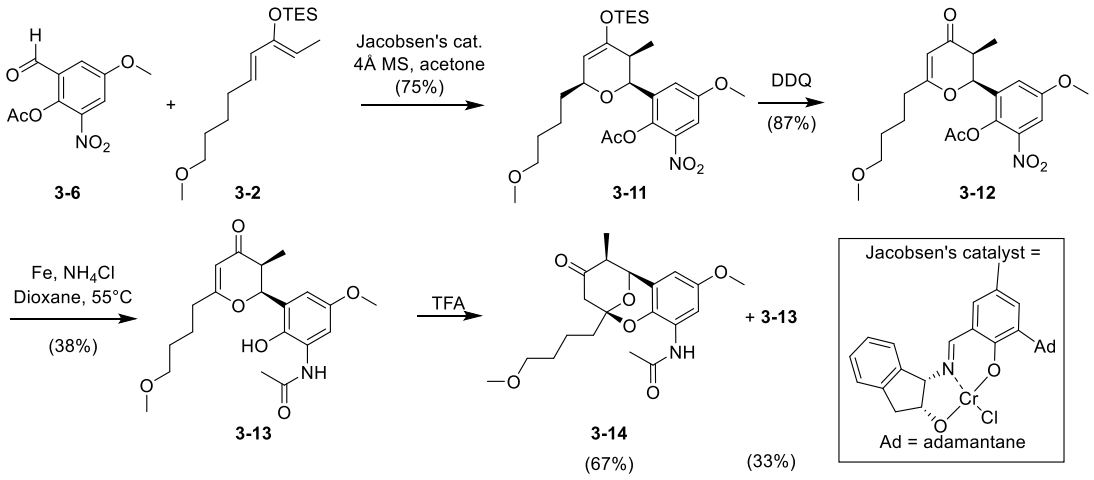

Figure 14: Model Studies: Synthesis of Core Structure 3-14

Reaction of **3-11** with DDQ yielded the desired dihydropyrone **3-12** in 87% yield and required 6.5 h to reach completion. The nitro group of **3-12** was successfully reduced using the relatively mild conditions of activated iron and ammonium chloride.[41] During the reduction step, the acyl group had migrated to form the amide and free hydroxyl group on **3-13** that cyclized in the presence of catalytic TFA to produce **3-14**.

3.3 OXIDATIVE REARRANGEMENT

With successful construction of the divergolide **E** core, investigations began to convert it to the core of divergolides **C** and **D**. Oxidative rearrangement was initially attempted on cyclized **3-10** using ceric ammonium nitrate (CAN) but only resulted in decomposition (Figure 15, A).[42,43] Switching to the hypervalent iodine reagent [bis(trifluoroacetoxy)iodo]benzene (BTI) proved equally ineffective on the cyclized core **3-10** leaving largely starting material.[44] However, BTI reacted very rapidly with the uncyclized core **3-9** to produce two products **3-15** and **3-16** (Figure 15, B).

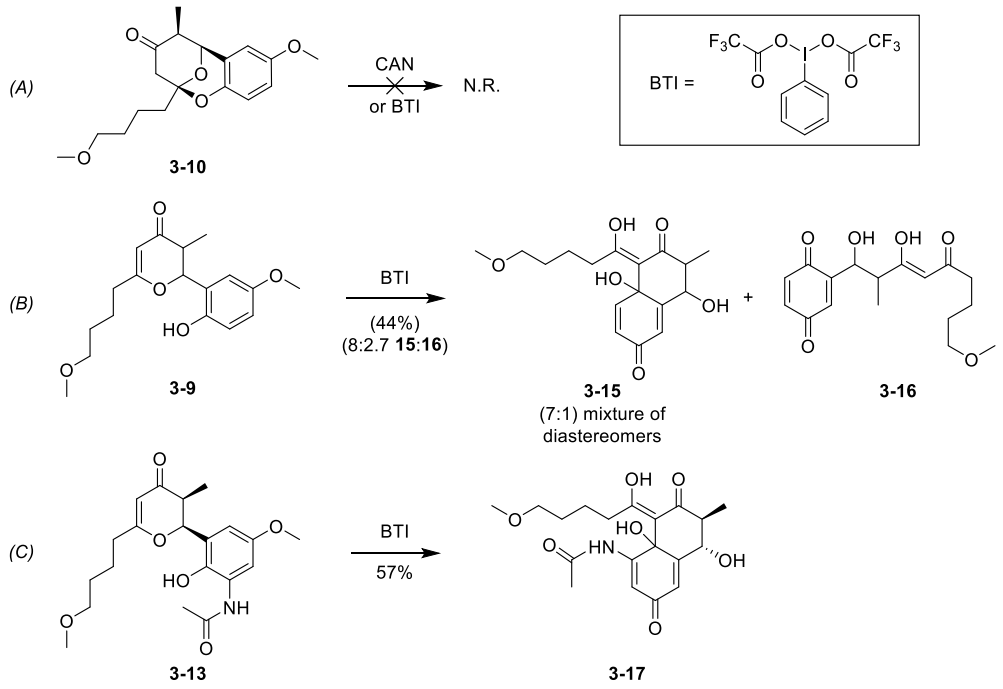

Figure 15: Oxidative Rearrangement of the Core Structure

NMR analysis of the products **3-15** and **3-16** showed no phenol or methoxy hydrogens confirming oxidation to the quinone (confirmed by LRMS, Experimental Section). The lack of

enol hydrogen in **3-15**, which was found in **3-16**, suggests that enolate attack and cyclization had occurred. However, three alkene (formerly aromatic) hydrogens were still present in both products indicating the molecule had not undergone 1,4-addition. Low resolution mass spectrometry produced a mass consistent with the 1,2-addition product **3-15** and without elimination of the hydroxyl group (however, the dehydration product cannot be completely ruled out). Similar reactivity was observed when uncyclized core **3-13** was oxidized with BTI, this time without isolation of any uncyclized material (Figure 15, C). The reaction produced a single compound with an NMR similar to **3-15** and consistent with **3-17**.

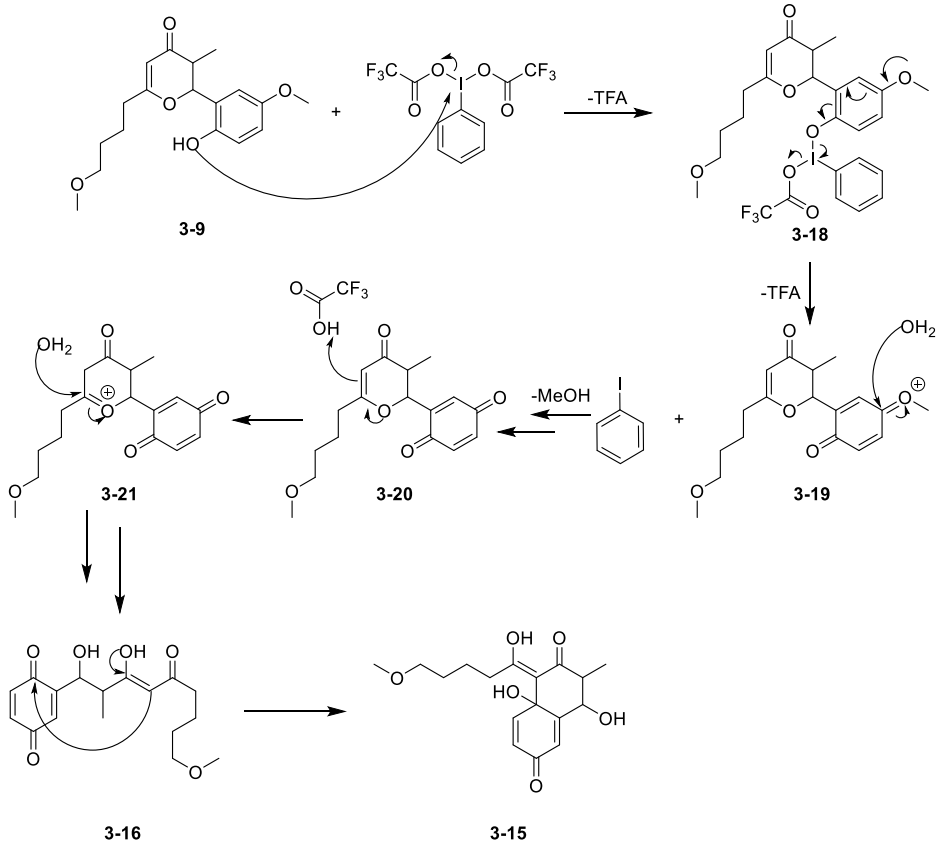

Figure 16: Proposed Mechanism of BTI Oxidation of 3-9

A proposed mechanism for the oxidation to the quinone is shown in Figure 16. The phenol of compound **3-9** attacks the hypervalent iodine reagent BTI releasing TFA and for **3-18**. Departure of the second TFA and iodobenzene facilitates the formation of oxocarbenium ion **3-**

19. Attack by H_2O on the oxocarbenium ion of **3-19** and loss of methanol leads to a dihydropyrone-quinone intermediate **3-20**. TFA can facilitate opening of the dihydropyrone on **3-20** resulting in compound **3-16**, which can attack the quinone and form compound **3-15.** The resulting rearranged products **3-15** and **3-17** had not undergone the 1,4-addition as hoped but instead 1,2-addition. The long macrolide chain may act as a tether in the natural product to control the regiochemistry upon addition to the quinone. Rearrangement of the initially formed 1,2-addition product to the 1,4-addition product may also be possible under certain conditions. In the future, a more extensive investigation will build on these preliminary results to further explore this oxidative-rearrangement process. With the core structure successfully synthesized attention turned to the full natural product.

4.0 INITIAL SYNTHETIC SEQUENCE

4.1 INITIAL RETROSYNTHETIC ANALYSIS

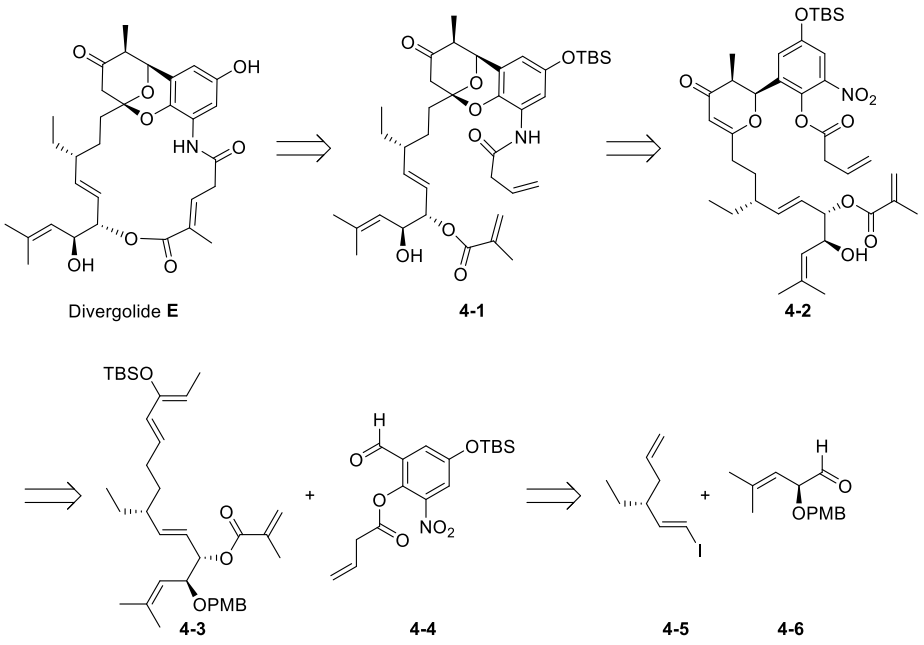

Figure 17: **Initial Retrosynthetic Analysis of Divergolide E**

Work on the synthesis of divergolide **E** began with the retrosynthetic analysis in Figure 17. The macrolide ring would be formed last using a RCM of compound **4-1**, which would in turn arise from nitro group reduction with subsequent acyl migration of compound **4-2**. The bridged bicyclic acetal core could be formed via acid or base catalyzed 1,4-addition. The key steps in the synthesis will be the stereoselective HDA reaction between diene **4-3** and aldehyde **4-4** using Jacobsen's catalyst[39,45] followed by DDQ oxidation to dihydropyrone **4-2**. Diene **4-3** could be derived from a chelation-controlled organozinc addition of vinyl iodide **4-5** and

aldehyde **4-6**. The stereocenter on vinyl iodide **4-5** will be implemented using a chiral auxiliary, while a desymmetrizing Sharpless epoxidation will set the stereocenter on aldehyde **4-6**.

4.2 INITIAL ROUTE TO DIENE 4-3

The total synthesis of divergolide **E** began with aldehyde **4-6** as shown in Figure 18. The stereocenter was set through desymmetrization of 1,4-pentadien-3-ol using a modified Sharpless asymmetric epoxidation to yield **4-7** as a single enantiomer (60% yield, >99% e.e., confirmed by Mosher ester analysis)[46,47] Attempts to prepare and react 2,6-dimethyl-2,5-heptadien-4-ol only provided a rearranged by-product and was therefore too unstable to use (Figure 18, bottom). PMB protection of alcohol **4-7**[48] followed by cross metathesis with isobutylene afforded **4-8**.[49,50] The epoxide **4-8** was opened under basic conditions and the resulting diol cleaved to quantitatively yield aldehyde **4-6** using sodium periodate.[51]

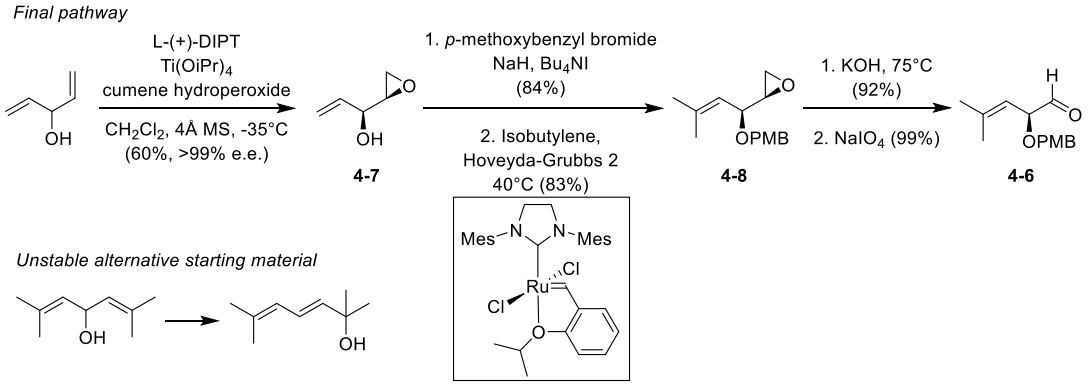

Figure 18: Synthesis of Aldehyde 4-6

With aldehyde **4-6** synthesized, focus shifted to vinyl iodide **4-5** (Figure 19). The alkyl stereocenter was introduced through an asymmetric allylation of compound **4-10** using Evan's oxazolidinone to produce known compound **4-11** in 98% yield.[52] Cleavage of **4-11** by lithium aluminum hydride (LAH)[53] followed by Swern oxidation[54] afforded aldehyde **4-12**. Takai's iodomethylenation of **4-12** using catalytic $CrCl_3$ provided only low yields of vinyl iodide **4-5** (<25%).[55] Utilizing Auge's method with chromium(III) chloride hexahydrate as a stoichiometric reagent improved the yield of **4-5** to 57%.[56]

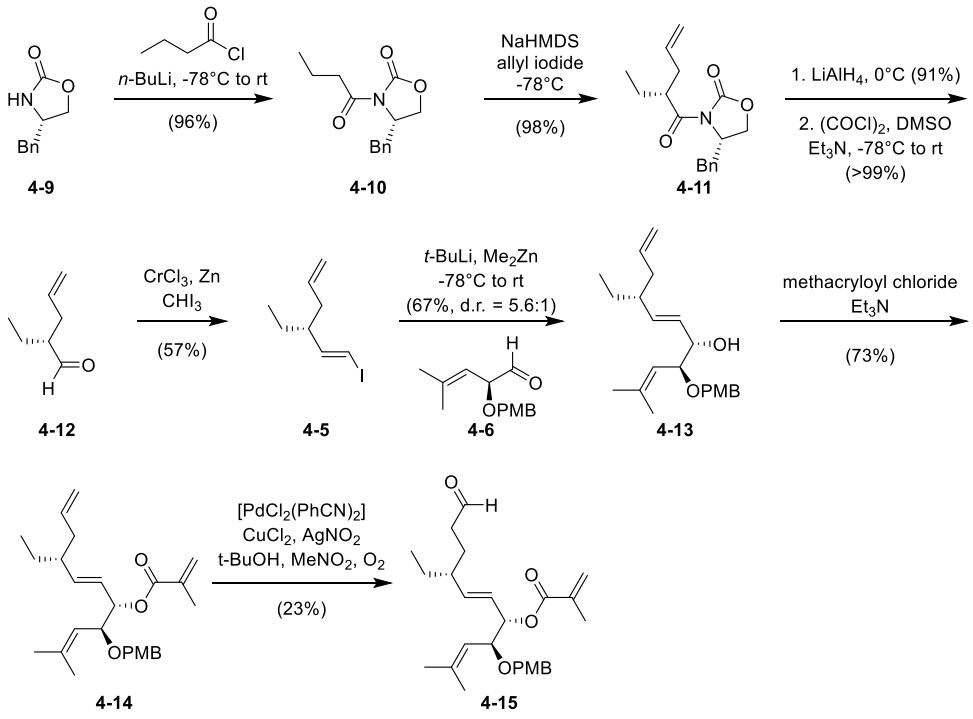

Figure 19: Initial Attempt at the Synthesis of Diene 4-3

The chelation-controlled organometallic addition between vinyl iodide **4-5** and aldehyde **4-6** was initially attempted by a metal-halogen exchange with isopropyl magnesium chloride in the presence of lithium chloride but only resulted in low yields.[57,58] Significant stereoselectivity has been achieved using CH_2Cl_2 as the solvent instead of THF in organomagnesium reactions.[59] A Lithium-iodine exchange of compound **4-5** was accomplished with *tert*-butyllithium followed

by metal-metal exchange with magnesium bromide to yield the organomagnesium reagent of **4-5**.[60] However, attempts to remove the THF *in vacuo* at –78 °C and replace with CH_2Cl_2 without losing the *trans* stereochemistry of the alkene were unsuccessful. Therefore, we turned to the less reactive organozinc reagent to achieve stereoselectivity. A successful reaction was finally achieved through a lithium-iodine exchange of compound **4-5** using *tert*-buyllithium followed by lithium-zinc exchange with dimethylzinc. The organozinc reagent of **4-5** underwent chelation-controlled addition to aldehyde **4-6** to yield alcohol **4-13** (67% yield, d.r.=5.6:1, major stereoisomer confirmed by Mosher ester analysis[61] of the analogous compound **4-19**) and a minor side product resulting from methyl addition.[62] After methacryloyl protection of compound **4-13**,[63] the resulting tetraene **4-14** proved to be exceedingly difficult to functionalize at the terminal olefin. The Wacker-type oxidation of **4-14** published by Grubbs suffered from long reaction times (>24 hours), incomplete conversion (77%), and low yield (23%).[64] Increasing the concentration, O_2 saturation, and catalyst loading offered better conversion but lower yields (13%) due to side reaction with the other alkenes (loss of alkene protons in the NMR). Reaction of **4-14** with 9-borabicyclo[3.3.1]nonane (9-BBN) was also ineffective leading us to conclude that the terminal alkene of **4-14** may exist in a hindered conformation (possibly due to interactions between the π-bonds). The difficulty in functionalizing tetraene **4-14** prompted a revision of the sequence to circumvent this problem.

4.3 REVISED SYNTHESIS OF DIENE 4-3

Instead of oxidizing tetraene **4-14** later in the sequence the oxygen could be introduced prior to the organozinc addition. The revised synthetic sequence to diene **4-3** is shown in Figure 20, in which the stereocenter would be set by an asymmetric alkylation using Myers auxiliary.

The synthesis of alkyne **4-18** was based on a route developed by Fürstner and co-workers.[65] Asymmetric alkylation of amide **4-16** with the known alkyliodide, *tert*-butyl(3-iodopropoxy)dimethylsilane, proceeded in 92% yield with a d.r. of 97:3 (confirmed by conversion to the oxazolium triflate derivative).[66] This was followed by cleavage with lithium ammonia-borane (LAB)[65] and oxidation to furnish aldehyde **4-17**.[67,66,68] Unlike before, the sensitive vinyl iodide **4-5** was avoided by converting aldehyde **4-17** to alkyne **4-18** in 74% yield using the Ohira-Bestmann reagent,[69] which was then directly used in the subsequent organometallic addition step. Conversion to the alkyne also avoids the use of stoichiometric chromium required to transformation aldehyde **4-12** to vinyl iodide **4-5** (Figure 19) and allows for long term storage of the stable alkyne **4-18** to investigate other divergent routes.

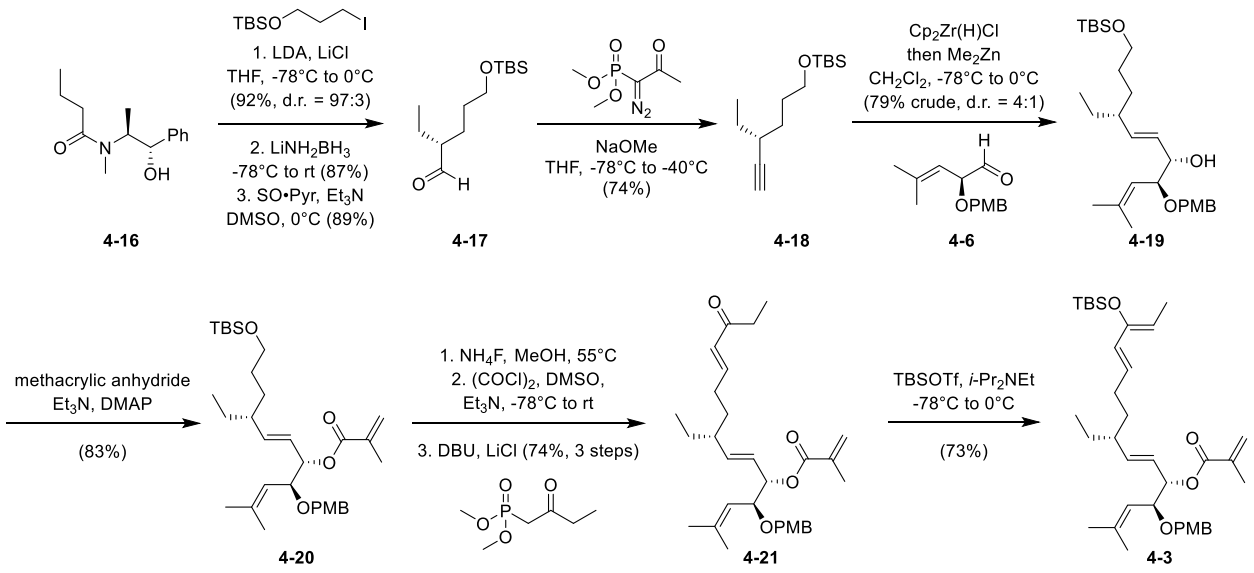

Figure 20: Revised Synthesis of Diene 4-3

Hydrozirconation of alkyne **4-18** with the Schwartz reagent was followed by transmetallation with Me_2Zn.[70] Chelation-controlled addition[71] of the vinylzincate to aldehyde **4-6** yielded alcohol **4-19** (79% crude, d.r. = 4:1, major stereoisomer confirmed by Mosher ester analysis).[46] The Mosher ester analysis of compound **4-19** also confirmed the integrity of the preexisting stereocenters. This step scales easily to gram quantities and avoids the use of hazardous organolithium reagents for the lithium-iodine exchange. The methacryloyl group was then installed on compound **4-19** to yield **4-20**. The TBS group on **4-20** was deprotected with ammonium fluoride[72] and the resulting crude alcohol underwent Swern oxidation followed by the HWE reaction to yield compound **4-21** in 74% over 3 steps. Similar to the synthesis of diene **3-2**, silyl enol ether **4-3** was successfully synthesized as a single isomer (confirmed by positive NOE correlation of analogous **6-11**) by treatment of **4-21** with *tert*-butyldimethylsilyl trifluoromethanesulfonate (TBSOTf) and *i*-Pr_2NEt.

4.4 SYNTHESIS OF ALDEHYDE 4-4

With diene **4-3** in hand, the remaining coupling partner for the HDA reaction, aldehyde **4-4**, was synthesized (Figure 21). Methyl ether deprotection of 2,5-dimethoxybenzaldehyde with BBr_3 afforded compound **4-22** followed by mono-TBS protection to produce **4-23**.[73,74] Nitration of aldehyde **4-23** using copper(II) nitrate produced a modest yield of compound **4-24** (63%) along with unreacted starting material **4-23** (8%).[75] Additionally, a minor side product with a similar Rf value was observed on TLC, which could result from nitration of a different position on the aromatic ring. Esterification of phenol **4-24** was achieved using vinyl acetic anhydride (synthesized from dicyclohexylcarbodiimide (DCC) and vinyl acetic acid) and pyridine to yield **4-4**.[76] Because the ester on **4-4** is located between two electron withdrawing groups, care had to be taken to prevent hydrolysis; the reaction had to be quenched under acidic conditions (saturated aqueous NH_4Cl) and all the pyridine needed to be removed prior to concentration of the product. In addition, complete consumption of the starting material was required because it had the same Rf value as the product and could not be separated.

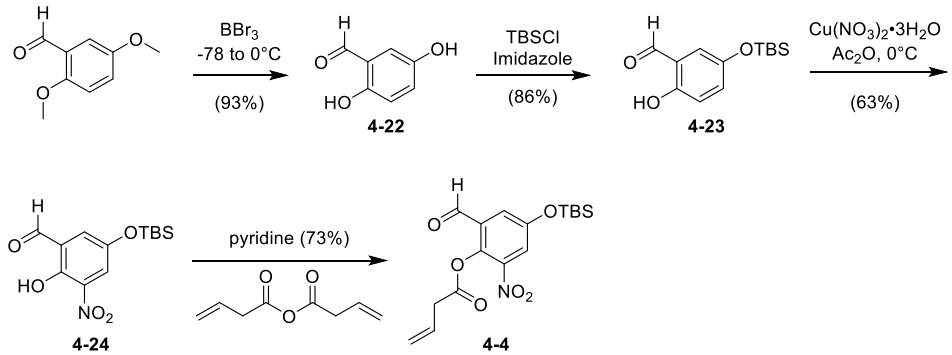

Figure 21: Synthesis of Aldehyde 4-4

4.5 HETERO-DIELS–ALDER, DDQ OXIDATION, AND ATTEMPTED RING CLOSING METATHESIS

The completion of diene **4-3** and aldehyde **4-4** led to the key step in the sequence (Figure 22). In this HDA reaction, the structurally more complex diene **4-3** would be the limiting reagent. Because of this, the TBS enolsilane (rather than TES enolsilane) was used to minimize the regeneration of enone **4-21** by adventitious water. The HDA reaction between **4-3** and **4-4** did not occur when using Jacobsen's catalyst with chlorine as the anion. However, full conversion to **4-25** was achieved within 18 hours when the chlorine anion was replaced with SbF_6. Unfortunately, dilution of the reaction with CH_2Cl_2 and directly adding solid DDQ to **4-25** only resulted in minimal product along with baseline decomposition on TLC. Fortunately, running the DDQ reaction of **4-25** under dilute conditions prevented decomposition and furnished dihydropyrone **4-26** in 40% combined yield (see section 7.2 for discussion of the HDA-DDQ reaction)

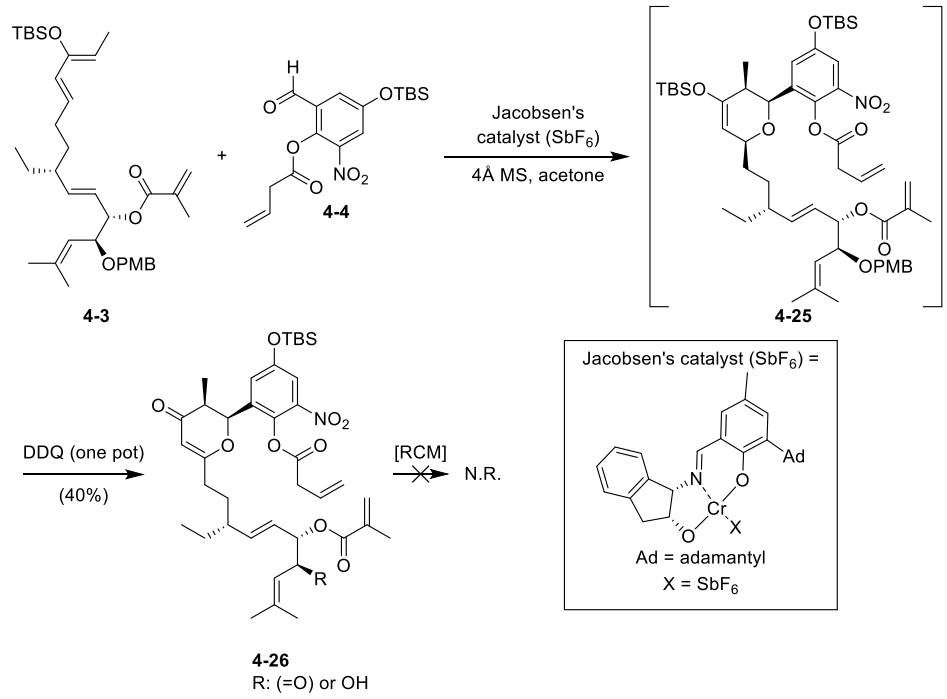

Figure 22: HDA-DDQ Reaction and Attempted RCM

We envisioned the PMB protecting group on **4-25** would be removed upon reaction with DDQ and save a step in the sequence. However, due to the unexpectedly long DDQ reaction time (discussion in section 7.2), the allylic alcohol on **4-26** (labeled as R) had undergone partial oxidation (seen in the NMR as a reduction in signal of the ether hydrogen). However, the material was moved forward to investigate the RCM step.

Successful RCM in large rings has been achieved in asymmetric dienes where one alkene is unperturbed and the other is sterically and electronically deactivated.[77] In substrate **4-26**, The ruthenium catalyst would initially react at the more reactive terminal alkene then with the less active methacrylate.

Investigations began with **4-26** and Grubb's second generation catalyst using 10% catalyst in CH_2Cl_2. Unfortunately, only starting material was recovered even after refluxing overnight and allowing the reaction to concentrate. Attention was next turned to reacting **4-26** with the more reactive Hoveyda-Grubbs second generation catalyst in toluene to allow heating at

higher temperature. Despite the more active catalyst and prolonged heating at 100° C, no reactivity was achieved up until **4-26** began decomposing. The lack of any metathesis products from any of the alkenes in the molecule or even dimerization by-products became a major concern (no loss of the terminal alkene protons was seen in the ^{1}H-NMR). The primary culprit is believed to be trapping and loss of the catalyst to a potential 5-membered chelate that could arise at the amide carbonyl. Chelation with proximal functional groups can be a major issue in metathesis reactions but has occasionally been solved using mild Lewis acid additives.[78,79] Unfortunately, the classic additive titanium(IV) isopropoxide did not improve the results.

The success of the HDA-DDQ reaction illustrated the viability of coupling two highly functionalized molecules in the key step. However, because of the unsuccessful RCM the macrocyclization strategy was revised to a macrolactonization, one of the most widely used bond disconnects to build large macrocycles.

5.0 SECOND SYNTHETIC SEQUENCE

5.1 SECOND RETROSYNTHETIC ANALYSIS

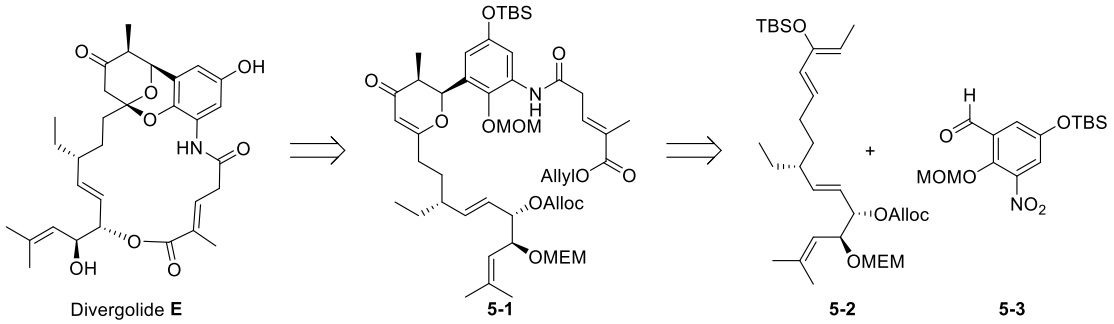

Figure 23: Second Retrosynthesis

The initial synthesis of divergolide **E** was revised to the retrosynthesis shown in Figure 23, where the macrocycle could now be formed through deallylation then macrolactonization of compound **5-1**. The new route would utilize allyl ester and allyl carbonate (alloc) protecting groups in order to remove both simultaneously in preparation for the macrolactonization. The dicarbonyl amide in **5-1** would be installed after the HDA-DDQ reaction which would occur between diene **5-2** and aldehyde **5-3**. Because of the divergent nature of the route, diene **5-2** will arise from the same aldehyde **4-6** and alkyne **4-18** using the chelation-controlled organozinc addition. The previously PMB protected allylic alcohol would now possess a 2-methoxyethoxymethyl (MEM) protecting group (compound **5-2**) to prevent interference with the key DDQ step. Ideally, the aldehyde used in the HDA step would possess a product relevant ester (**5-4**) which could undergo migration during nitro reduction (as seen in model studies,

Figure 14). Unfortunately, cyclization readily occurs with the adjacent aldehyde on **5-4** (Figure 24) due to the high acidity of the alpha proton which arises from it being a vinylogous β-dicarbonyl group (confirmed by NMR and loss of the aldehyde signal).

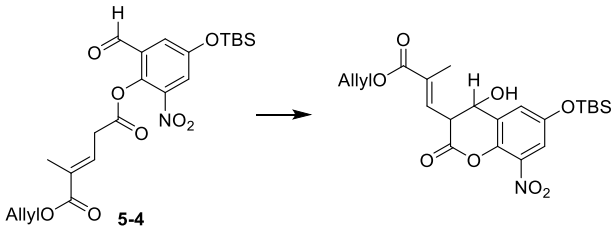

Figure 24: Cyclization By-product of Aldehyde 5-4

Any acyl group on the phenol adjacent to the nitro group on **5-3** would migrate during the reduction step, therefore, the phenol had to be protected as an ether. The methoxymethyl (MOM) protecting group on **5-3** was chosen due to its small size (less steric interference during the macrocyclization) and its removal under conditions similar to the MEM group.

5.2 SYNTHESIS OF DIENE 5-2 AND ALDEHYDE 5-3

Synthesis of the new diene began by alloc protection of alcohol **4-19**, which had been stored for use in divergent routes, to produce **5-5** (Figure 25, A). At this point, the PMB group on **5-5** was removed using DDQ and reprotected as the MEM ether **5-6**. It is important to note no oxidation of the allylic alcohol occurred during the protecting group swap, however, care had to be taken to prevent intramolecular cyclization of the unprotected allylic alcohol with the adjacent alloc group. Using the same sequence as before, removal of the TBS group on **5-6** was followed by oxidation, the HWE reaction, then treatment with TBSOTf and *i*-Pr_2NEt to yield diene **5-2**.

The aldehyde for the HDA reaction was prepared by treatment of aldehyde **4-24** with chloromethyl methyl ether and *i*-Pr_2NEt (Figure 25, B) to yield **5-3**.

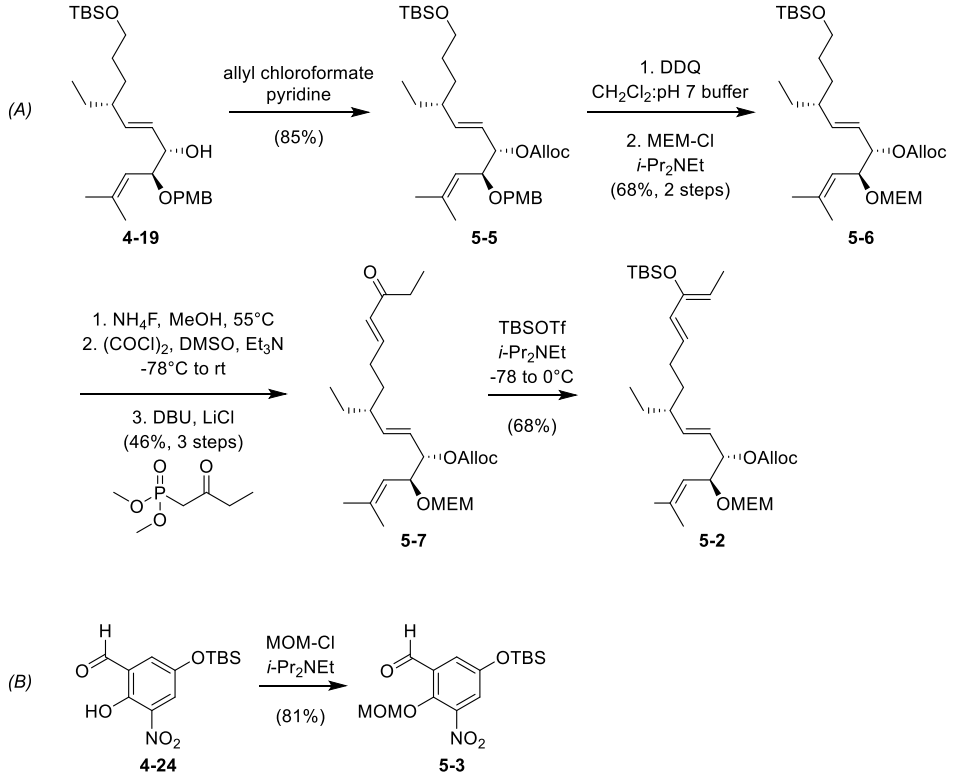

Figure 25: Synthesis of Diene 5-2 and Aldehyde 5-3

5.3 HDA-DDQ REACTION AND NITRO REDUCTION

With diene **5-2** and aldehyde **5-3** in hand, attention again turned towards the HDA-DDQ reaction (Figure 26). Although the steric environment around both substrates is similar to the previous substrates **4-3** and **4-4**, the electronic environment of aldehyde **5-3** is quite different. Switching the acyl group on **4-4** to the MOM protecting group in **5-3** increases the electron density of the aromatic ring evidenced by an upfield shift in the aromatic protons in the ^{1}H-NMR (δ 7.74, 7.57 to 7.53, 7.51 respectively, see Experimental Section). This increase in electron

density in turn decreases the compounds activity. This is reflected in the long reaction time required for the HDA step between **5-2** and **5-3**, which required 7 days compared to 18 hours as seen previously (Figure 22). However, full conversion was achieved to yield **5-8** along with small amounts of hydrolyzed diene **5-2**. Although the DDQ reaction still required long reaction times (discussion in section 7.2), full conversion was achieved to yield dihydropyrone **5-8** (39%, one pot).

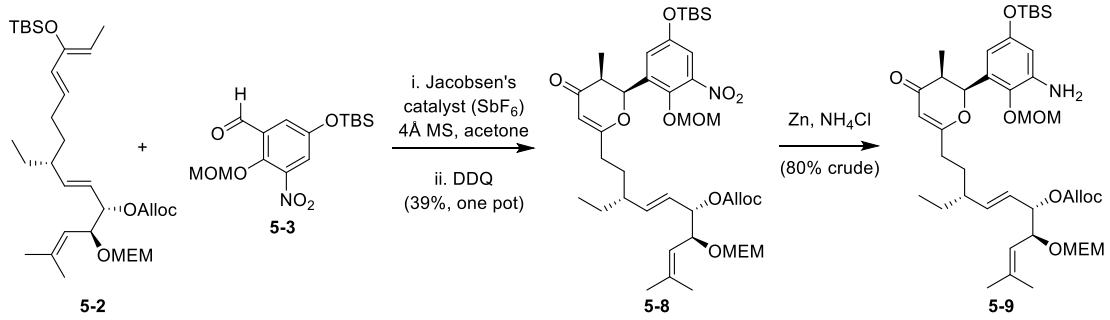

Figure 26: HDA-DDQ Reaction Between Diene 5-2 and Aldehyde 5-3

Reduction of the nitro group proved to be more difficult in the fully functionalized substrate **5-8** than in the model system **3-12** presumably due to the increased steric environment. An extensive investigation of reduction conditions were first examined on simpler model substrates that possessed a similar electronic environment to **5-8**. A variety of conditions were successful on the simpler model systems including Lindlar's catalyst, Fe/NH_4Cl[41], $SnCl_2$, and $HSiCl_3/i\text{-}Pr_2NEt$[80]. However, the conditions proved ineffective on compound **5-8**. No reduction of the nitro group on **5-8** occurred using Lindlar's catalyst, Fe/NH_4Cl, or $HSiCl_3/i\text{-}Pr_2NEt$ and largely left unreacted starting material ($HSiCl_3/i\text{-}Pr_2NEt$ removed the TBS group on **5-8**). Reaction of **5-8** and $SnCl_2$ was partially successfully but produced multiple spots on TLC possibly due to incomplete reduction. Drawing inspiration from previous literature, the best condition to reduce **5-8** was found to be Zn and NH_4Cl (Figure 26).[81] The fact that many of the reduction conditions worked on the simpler model substrates with similar electronics but not on

the complex substrates points towards steric interference provided by the dihydropyrone ring and bulky side chain on **5-8** which could be folded in a conformation that blocks one face of the aromatic ring.

5.4 AMIDATION

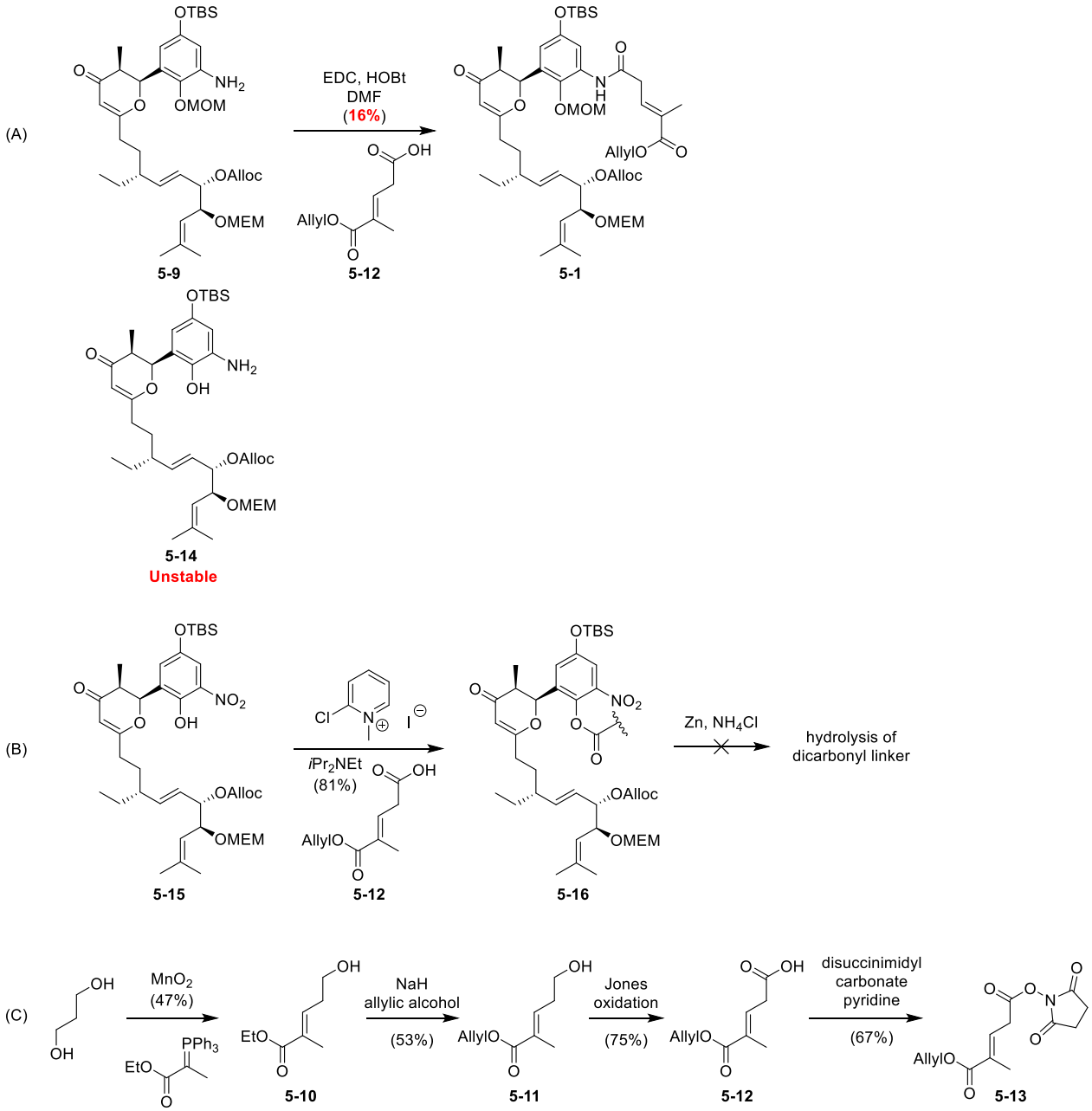

Figure 27: Initial Amidation Studies and Synthesis of Succinimidyl Ester 5-13

Initially, a longer more conservative approach was used to synthesize the dicarbonyl linker **5-12**, but the route was optimized to the more concise synthesis shown in Figure 27, C. A

one-pot oxidation of 1,3-propanediol and Wittig reaction with commercially available (carbethoxyethylidene)triphenylphosphorane delivered ester **5-10**.[82] Transesterification of **5-10** with the sodium salt of allyl alcohol implemented the allylic group in **5-11**. The Jones oxidation was found to be the optimal conditions to cleanly oxidize **5-11** to carboxylic acid **5-12**.

The amidation of aniline **5-9** with carboxylic acid **5-12** proved to be a very difficult transformation (Figure 27, A). The use of standard coupling conditions including EDC/HOBT, BOPCl, and HATU all yielded poor conversion of the aniline. A large excess of reagent added over the course of the reaction was the only way to fully consume **5-9**, at the cost of low and inconsistent isolated yields (on average ~20%). In addition, large amounts of the activated carboxylic acid **5-12** were lost to decomposition (loss of the conjugated alkene in the NMR). Decomposition of the activated ester of **5-12** presumably occurs through ketene formation because of the high acidity of the alpha proton, being contained within a vinylogous β-dicarbonyl group. Consequently, if the *Z* isomer of the conjugated alkene in carboxylic acid **5-12** is used in the amidation step (towards the synthesis of divergolide **A**) facile isomerization to the *E* isomer is observed (seen as a noticeable shift of the alkene hydrogen in the NMR). The complications of this facile isomerization is also described by Trauner in the total synthesis of divergolide **I**.[30]

Carboxylic acid **5-12** could however successfully couple with more nucleophilic anilines (3,5-dimethylaniline, ammonia). Therefore, to increase the nucleophilicity of aniline **5-9**, the adjacent protecting group was removed to decrease the steric environment and increase the electron density. Unfortunately, compound **5-14** proved to be too electron rich and rapidly decomposed. Attempts at a route similar to the model studies was also investigated (Figure 27, B). Compound **5-15** can undergo esterification using Mukaiyama's salt,[83] however, the product ester **5-16** readily hydrolyzes under the nitro reduction conditions. Although Mukaiyama's

conditions worked well for the esterification, direct amidation of aniline **5-9** was unsuccessful and only yielded large amounts of decomposed **5-12**.

Various leaving groups were also investigated for carboxylic acid **5-12** (Figure 28). The most promising, shown on the left include the succinimidyl ester **5-13**, OBt ester, and activation by Mukaiyama's salt. The succinimidyl ester **5-13** proved to be the easiest to synthesize and isolate and was even stable under mildly basic conditions (2,6-lutidine). Unfortunately, it did not react with **5-9** only with stronger nucleophiles (e.g. 3,5-dimethylaniline). Partial decomposition occurred during the synthesis and reaction of the OBt ester with **5-9**, however, some product **5-1** could be isolated.

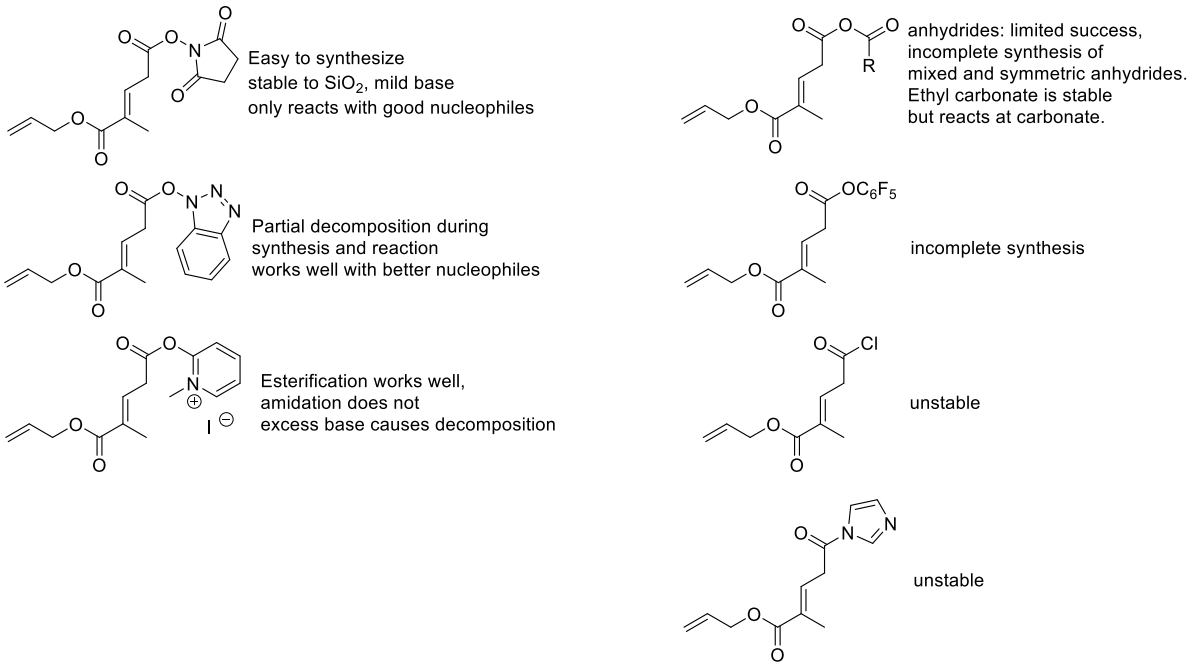

Figure 28: Leaving Group Investigation

The compounds on the right of Figure 28 all proved to be either unstable or could not be readily synthesized and include: anhydrides (mixed and symmetric), pentafluorophenyl, acyl chloride, and acyl imidazole.

Despite the low conversion and low yield of the amidation step, enough of product **5-1** was obtained to examine the macrolactonization (Figure 29).

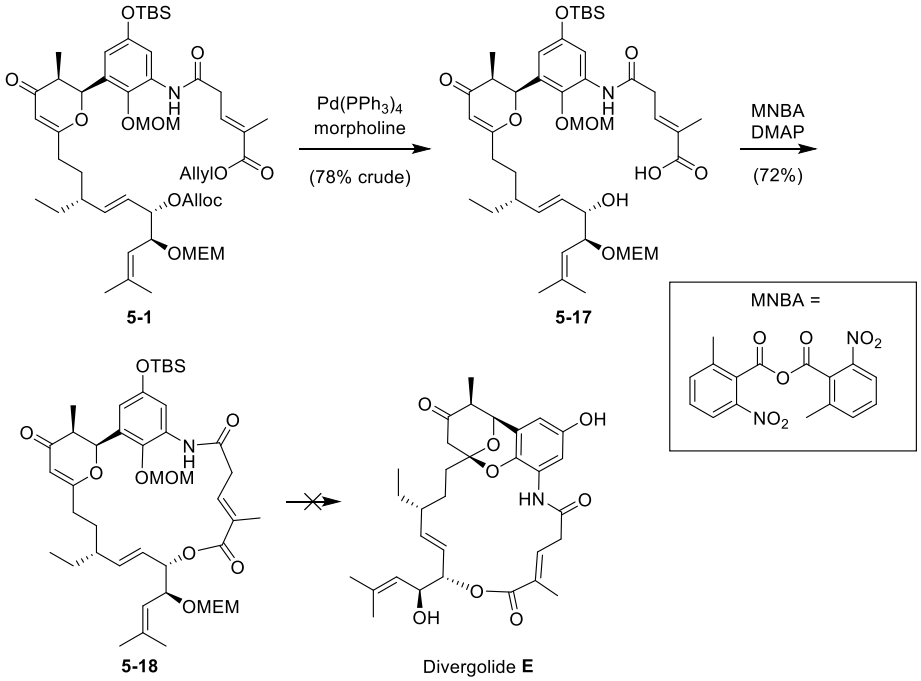

Figure 29: Macrolactonization and Attempted Completion of the Synthesis

Deallylation of **5-1** proceeded with tetrakis(triphenylphosphine)palladium(0) using morpholine as the allyl scavenger to produce seco-acid **5-17**. One of the most widely used macrolactonization conditions is the Yamaguchi protocol,[84] however, initial attempts on **5-17** only resulted in decomposition. Fortunately, switching to the mild macrolactonization strategy developed by Shiina successfully converted **5-17** to macrocycle **5-18** in 72% yield, which was confirmed by mass spectrometry and NMR analysis.[85]

To remove the protecting groups, Bronsted acid conditions (both aqueous and nonaqueous) were first investigated to remove the MOM and MEM groups on compound **5-18**, but only resulted in decomposition. The poor and inconsistent yields of the amidation step (Figure 27, A) became a major hindrance to the completion of the synthesis; enough of

compound **5-1** couldn't be synthesized for a thorough investigation of deprotection conditions. It now became apparent that a reliable solution was necessary.

Although unable to complete the synthesis through this synthetic route, discovery of a successful condition for the macrolactonization was a major breakthrough. In addition, the succinimidyl group proved to be a promising leaving group to activate carboxylic acid **5-12**, being both stable and reactive towards good nucleophiles. Two potential solutions for a successful amidation will be investigated in the following section. One solution could involve increasing the reactivity of the aniline by stabilizing compound **5-14**. A second potential solution could include limiting the impact of the poor amidation yield by implementing the amidation reaction before the HDA-DDQ step off of the longest linear sequence. Both potential solutions will be investigated using model systems in the following section along with a revision of the protecting group strategy.

6.0 INVESTIGATING SOLUTIONS TO THE AMIDATION REACTION

6.1 SYNTHESIS AND AMIDATION OF ANILINE 6-4

One potential solution to improving the low and inconsistent yield of the amidation reaction is to increase the nucleophilicity of aniline **5-9**. This could be achieved by removing the steric interference from the adjacent protecting group. However, after nitro reduction the resulting aniline-phenol (compounds like **5-14**) must also be stabilized, which can be achieved by decreasing the electron density of the aromatic ring. Switching the electron donating TBS group on compound **5-14** with an electron withdrawing acyl group provides the target model aniline **6-4** (Figure 30).

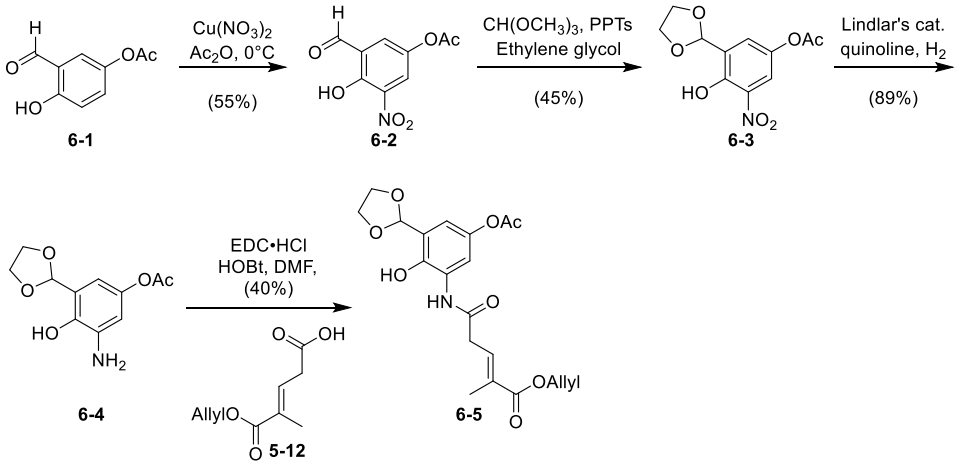

Figure 30: Synthesis of Amide 6-5

The synthesis commenced with nitration of known compound **6-1** to yield **6-2** (see discussion of compound **4-24**).[86] The aldehyde **6-2** proved to be unstable during the nitro reduction and was

protected as an acetal to yield **6-3**. Unlike compound **5-8**, the nitro group in the simpler model system **6-3** could be reduced using Lindlar's catalyst to yield aniline **6-4**. Although still prone to decomposition if left exposed to the atmosphere, aniline **6-4** proved stable enough to successfully undergo amidation with carboxylic acid **5-12** using EDC/HOBt in a moderate, but consistent 40% yield. In addition, preliminary experiments showed successful coupling of aniline **6-4** with succinimidyl ester **5-13**, compared to the unreactive aniline **5-9**.

Success of the amidation reaction using a more nucleophilic and stable aniline **6-4** shows promise for amidation of the fully functionalized system. In the following section, amide **6-5** will be functionalized and investigated as a substrate for the HDA-DDQ reaction.

6.2 INVESTIGATING THE HDA REACTION OF ALDEHYDES 6-7 AND 6-8

Previous experiments conducted in this thesis (Figure 14, 26) shows the HDA reaction proceeds more efficiently with an electron deficient aldehyde. Therefore, electron withdrawing acyl groups were used to mitigate the electron donating oxygen and nitrogen on **6-5**. Two substrates were synthesized: the di-acylated compound **6-7** and tri-acylated compound **6-8**. The synthesis commenced with removal of the acetal from the amidation product **6-5** to provide aldehyde **6-6** followed by acylation to either **6-7** or **6-8** (Figure 31, A). A mixture of di- and tri-acylated material (**6-7** and **6-8** respectively) was used in the HDA reaction in order to compare their relative reactivities, however, the reaction conditions can be modified to provide preference for either compound. Reaction of **6-6** with acetic anhydride and pyridine provides di-acylated compound **6-7** (90% yield, 94% purity), while addition of catalytic amounts of *N*-

methylimidazole acylates the less reactive amide to give tri-acylated compound **6-8** (78% yield, 90% purity). [87]

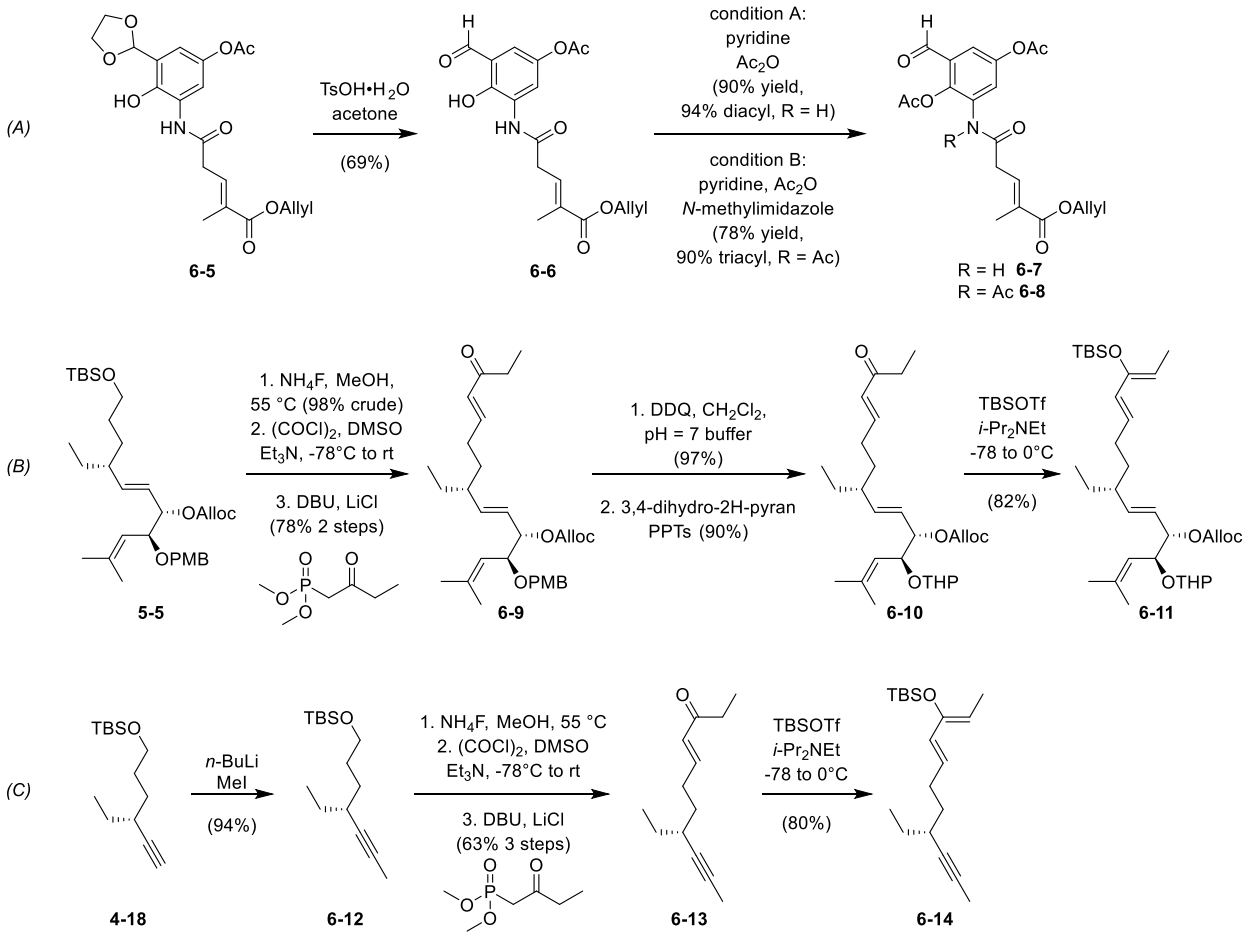

Figure 31: Synthesis of Aldehydes 6-7, 6-8 and Dienes 6-11, 6-14

Three dienes were investigated in the HDA reaction: the full diene **6-11** with the PMB group replaced with a THP group, the model diene **3-2**, and a truncated diene **6-14** which could be used to explore the possibility of a ring closing alkyne metathesis (RCAM). The synthesis of diene **6-11** commenced similar to before with removal of the TBS group from compound **5-5**, followed by Swern oxidation, and the HWE reaction to yield enone **6-9** (Figure 31, B). The PMB group on **6-9** was then removed by treatment with DDQ and replaced as the THP ether on **6-10**, which is more labile than the MEM group on **5-2** that was used previously. Notably, no oxidation

of the allylic alcohol or cyclization with the adjacent alloc group was observed, both of which could be issues in this type of system. In principle, the THP group could be introduced earlier in the sequence onto compound **4-7** (Figure 18), unfortunately, the cross metathesis to form the THP analogue of compound **4-8** proceeded very inefficiently especially on large scale. The lack of activity is presumably due to coordination of the catalyst with the ring oxygen of the THP ring. Interestingly, this reduction in catalytic activity seemed to only be pronounced in one of the THP isomers as seen by an unequal loss of the alkene signals in the NMR. Treatment of **6-10** with TBSOTf and *i*-Pr_2NEt yielded diene **6-11** (stereochemistry of the alkenes confirmed by a positive NOE correlation, see Experimental Section). The truncated diene **6-14** was synthesized by methylation of alkyne **4-18**, followed by the same protocol as above to yield **6-14** (Figure 31, C).

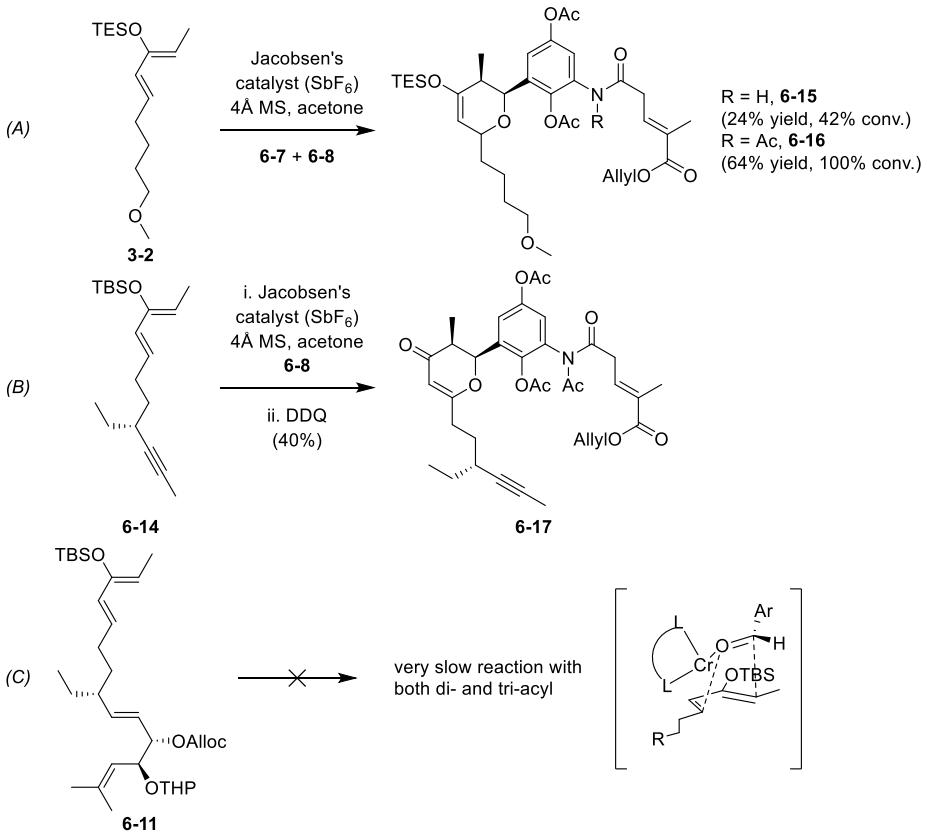

Figure 32: Investigating the HDA Reaction

The HDA reaction was initially tested on a mixture of aldehydes **6-7, 6-8** and model diene **3-2** (Figure 32, A). All of the tri-acyl **6-8** was consumed and yielded 64% of **6-16**, while only 42% of di-acyl **6-7** was consumed and yielded 24% of **6-15**. This reflects the increased reactivity of electron deficient aldehydes seen during previous HDA reactions (section 5.3). Highly electron withdrawing ether protecting groups (sulfonyl protecting group) on the phenol of **6-6** were unreactive in the HDA reaction. When the fully functionalized diene **6-11** was tested, the reaction proceeded extremely slowly with both di- and tri-acylated aldehyde (Figure 32, C). The difference in activity between dienes **6-11** and **3-2**/**6-14** is most likely due to interference between the large functionality at the end of diene **6-11** and Jacobsen's catalyst as depicted in Figure 32. Similar to the shorter diene **3-2**, the truncated diene **6-14** successfully reacted with the tri-acylated aldehyde **6-8** to give **6-17** in 40% combined yield after the DDQ reaction (Figure 32, B). Unfortunately, attempts at removing the acyl protecting groups on **6-17** only resulted in loss of the dicarbonyl linker and isolation of compounds **6-18** and **6-19** (Figure 33).

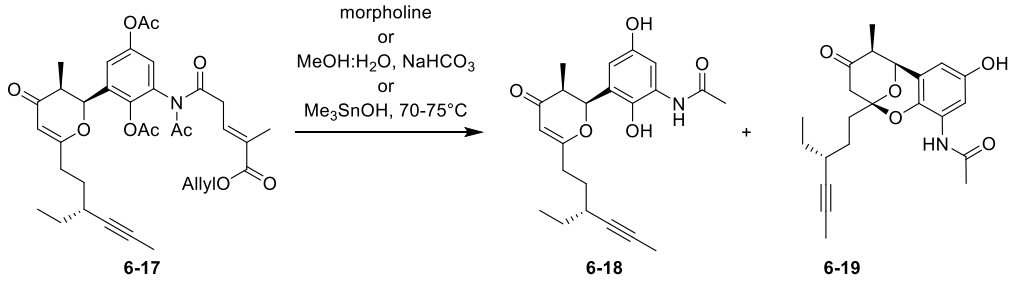

Figure 33: Attempted Removal of Acyl Groups

Although the HDA reaction between the full diene **6-11** and aldehydes **6-7**/**6-8** was unsuccessful, aniline **6-4** not only proved to be stable but also a reliable pathway to the amidation product. The success of this model system led to the final pathway and completion of the total synthesis.

7.0 FINAL SYNTHETIC ROUTE

7.1 RETROSYNTHESIS

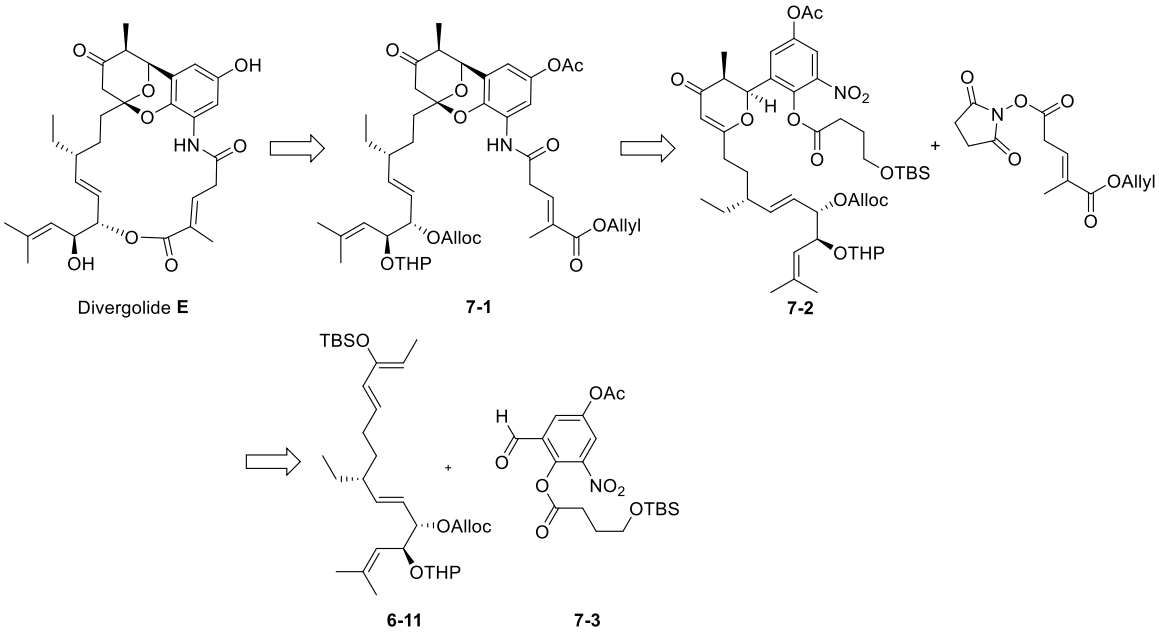

Figure 34: Final Retrosynthesis

Culmination of the knowledge learned from all of the previous research led to the final retrosynthesis, depicted in Figure 34. The macrocycle will be formed by deallylation then macrolactonization of compound **7-1** using Shiina's protocol. The secondary alcohol on divergolide **E** will be protected by an acid-labile THP group while the phenol will be protected by an acyl group. The challenging amidation reaction will occur after the HDA-DDQ reaction using an aniline with only a single acyl protecting group on the aromatic ring. This can be

accessed from compound **7-2** by selective deprotection of the unusual acyl protecting group with the attached primary TBS ether. The HDA-DDQ reaction will couple diene **6-11** with electron deficient aldehyde **7-3**.

7.2 SYNTHESIS OF ALDEHYDE 7-3 AND THE HDA-DDQ REACTON

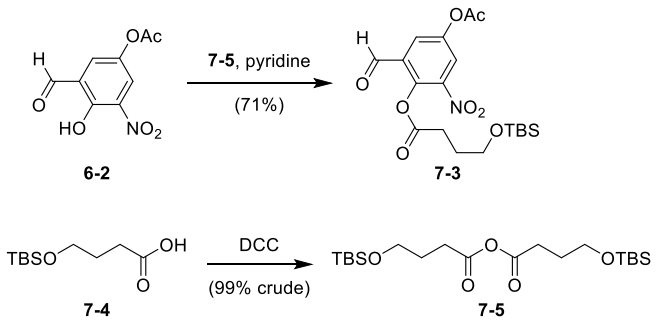

Figure 35: Synthesis of Aldehyde 7-3

Experiments throughout the course of this project illustrated that electron deficient aldehydes were more reactive in the HDA reaction. Therefore, the target aldehyde for the HDA reaction is compound **7-3**, which contains a nitro group with the phenols protected by acyl groups. The unusual acyl protecting group adjacent to the nitro group on **7-3** can be selectively deprotected by removal of the TBS group and subsequent lactone formation to release the nitro-phenol. In previous trials of the HDA reaction, separation of the diene and aldehyde into two separate layers greatly hampered conversion to the product. This particular group was an attractive option because the TBS group would increase the miscibility of aldehyde **7-3** with diene **6-11** in the HDA step (run concentrated, with only minimal acetone). Concurrently, attachment of the TBS group onto the end of the long chain would hopefully keep it far enough from the aldehyde on **7-3** to minimize steric interference with the catalyst. Anhydride **7-5**,

prepared through the dehydrative coupling of known carboxylic acid **7-4**,[88] was used to acylate compound **6-2** to yield compound **7-3** (Figure 35). Because the unusual acyl group is between two electron withdrawing groups, it proved to be somewhat sensitive to hydrolysis. However, isolation of pure **7-3** was accomplished by dehydrating the silica gel before purifying by chromatography.

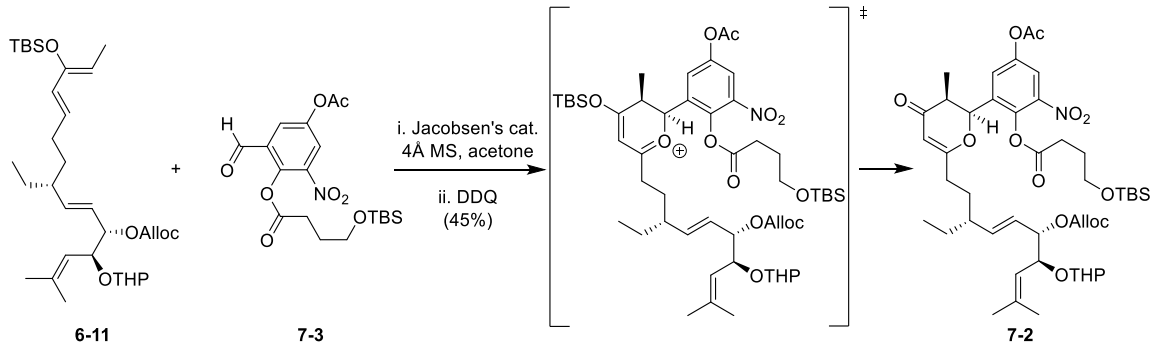

Figure 36: HDA-DDQ Reaction Between Diene 6-11 and Aldehyde 7-3

The HDA reaction successfully coupled diene **6-11** and aldehyde **7-3** to yield **7-2** in 45% yield (one pot), however, the reaction proceeded slower than expected and required two days to reach completion (Figure 36). In comparison, the HDA reaction using aldehyde **4-4** (Figure 22), which contains one acyl and one ether protecting group, was complete within 18 hours. Again, the SbF_6 anion of Jacobsen's catalyst was used to provide increased reactivity and the TBS enolsilane on **6-11** to minimize reversion to enone **6-10** by adventitious water. Despite this, small amounts of enone **6-10** was generated which reduced the yield of the HDA reaction. Although aldehyde **7-3** is electron deficient, the unusual acyl protecting group is larger and may sterically interfere with coordination of the catalyst. A positive NOE correlation between the alpha methyl group and aromatic hydrogens on **7-2** confirms their relative positions. In addition, comparison of the NMR spectra of the synthesized Divergolide **E** to the isolated natural product confirms that their stereochemistry is identical (see p.90, Experimental Section). Similar to previous

experiments, the DDQ reaction proceeded slowly requiring 24 hours to reach completion (45% yield, one pot). Interestingly, the rate of the reaction was independent of the concentration. A couple factors could be interfering with the rate of the DDQ reaction. The stability of the positively charged oxocarbenium ion intermediate in Figure 36 may be diminished due to the electron deficient nature of the arene. In addition, steric effects from the large acyl group and full side chain on diene **6-11**, both of which slowed the HDA reaction, may be lowering the rate of oxidation by blocking the approach of DDQ. The ability of DDQ to successfully oxidize such a complex system that also utilizes a TBS enolsilane is notable when compared to alternative oxidation methods. Attempts to increase the oxidation rate using Larock's variant of the Saegusa oxidation resulted in alloc cleavage with no oxidation.[3] The difficulty to utilize TBS enolsilanes as substrates is also reflected in the inability of IBX, another common reagent for this transformation, to form the critical oxygen-iodine bond from an OTBS group rather than the commonly employed OTMS group.[4] It's important to note that these substrates (Figures 22, 26, 32, 36) are some of the most complex that have been used in either Jacobsen's HDA reaction or DDQ oxidation and a suitable yield of **7-2** was obtained to move forward with this route.

7.3 NITRO REDUCTION AND AMIDATION REACTION TO COMPOUND 7-1

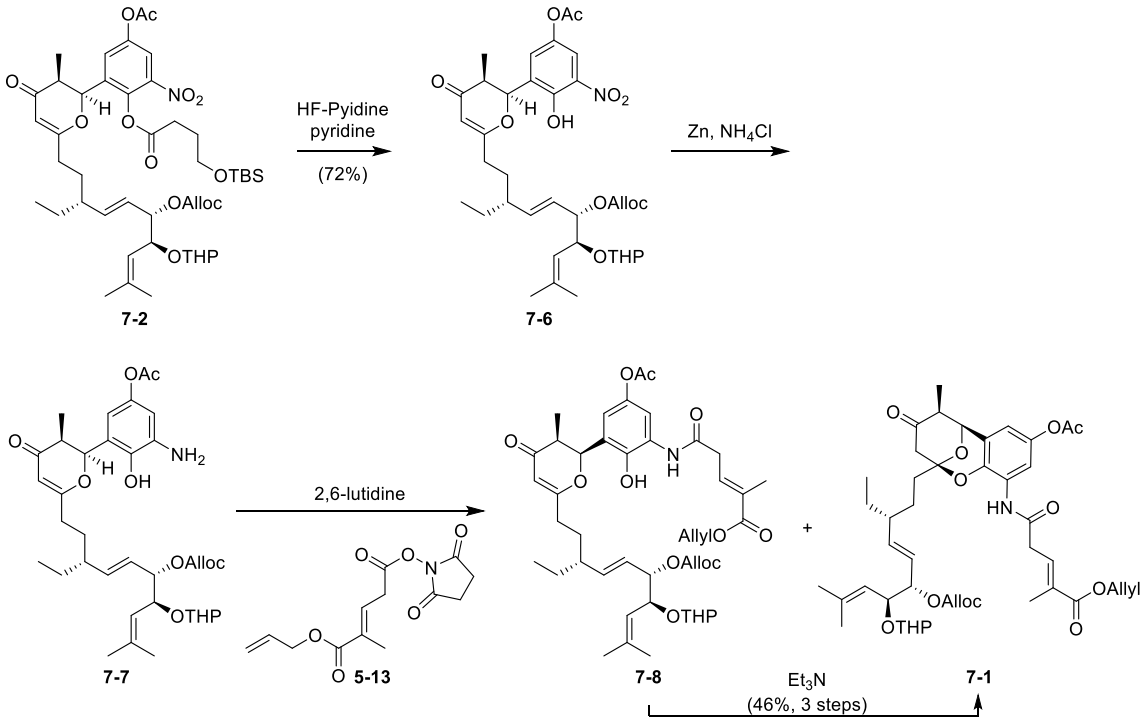

Figure 37: Synthesis of Amide 7-1

Removal of the unusual acyl group from **7-2** was facilitated by deprotection of the TBS ether using HF-pyridine (THP groups are stable to these conditions), with subsequent deacylation through lactone formation to yield **7-6** (Figure 37). Nitro-phenol **7-6** was reduced by treatment with Zn and NH_4Cl, as used previously (discussion in section 5.3), to yield the important target aniline **7-7**.

The stability and reactivity of aniline **7-7** mimicked the model aniline **6-4** and coupled with succinimidyl ester **5-13** to initially yield predominantly uncyclized **7-8**, which could be cyclized to compound **7-1** (46% yield over 3 steps) using a catalytic amount of triethylamine (see section 5.4 and 6.1 for discussion of the amidation reaction).

7.4 MACROCYCLIZATION AND COMPLETION OF THE SYNTHESIS

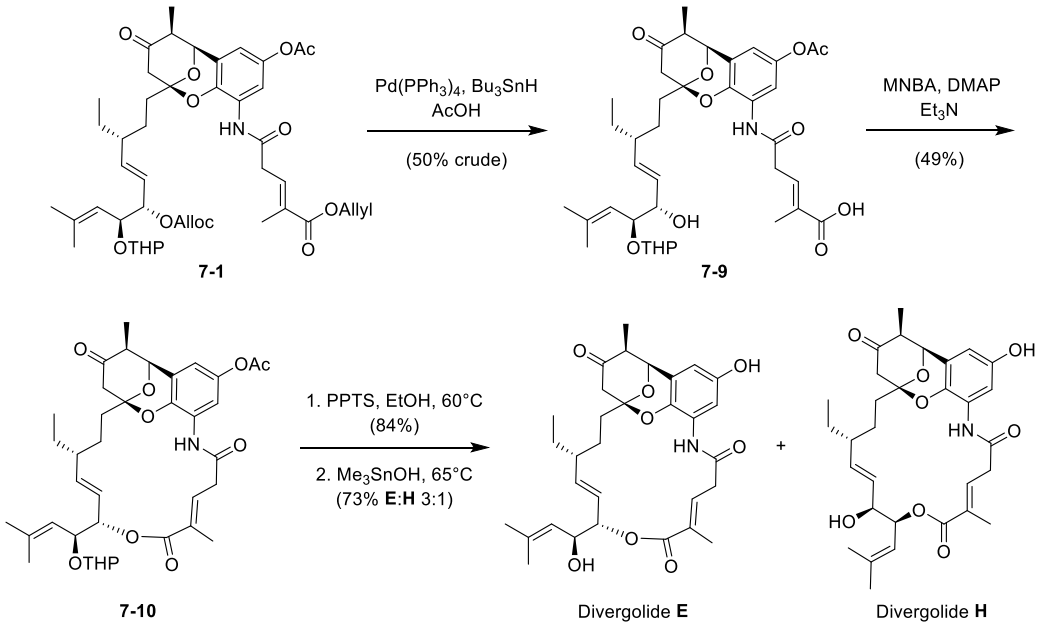

Figure 38: Synthesis of Divergolides E and H

The previous deallylation conditions were modified for compound **7-1** (Figure 38). Bu_3SnH was used as the allyl scavenger instead of morpholine to avoid interference with the acyl protecting group, which would result in having to work with an extremely polar compound. The tin byproducts from the reaction can be removed using chromatography, however, the product seco-acid **7-9** remains contaminated with triphenylphosphine oxide.

The crude-seco acid **7-9** was then subjected to Shiina's macrolactonization[85] to give compound **7-10** in 49% yield. Attempting the macrolactonization on the uncyclized core **7-8** only resulted in complete baseline decomposition. To complete the synthesis, compound **7-10** was subjected to mild acidic conditions to remove the THP group followed by deacylation using Me_3SnOH[89] to yield divergolide **E** and the acyl migration natural product divergolide **H** in a 3:1 ratio. Comparison of the NMR data and mass spectra to the isolated natural products confirms the identity of the natural products and are available in the Experimental Section (p.90).

Interestingly, the acyl migrated natural product divergolide **H**, only appeared in the final step despite the similarity of the deprotection conditions. Fortunately, the natural products can be separated and are stable at room temperature.

8.0 CONCLUSION

The first total syntheses of divergolides **E** and **H** have been achieved. Through the course of this thesis, significant difficulties were overcome to transition from simpler model systems to the fully functionalized substrates. Long range steric interference played a surprising role in reactivity, particularly in the HDA reaction where the bulky side chain at the far end of the diene noticeably interfered with Jacobsen's catalyst. Long range interference also seemed to be an important factor in the nitro reduction of the fully functionalized substrates.

Success of the DDQ reaction illustrates the mild and functional group tolerance of this methodology. The ability to utilize TBS enolsilanes as substrates is notable in comparison to other common methods.[3-4] In addition, these substrates are some of the most complex that have been used in either Jacobsen's HDA reaction or DDQ oxidation and probes their limits both electronically and sterically.

This synthesis also describes difficulties in the decomposition prone vinylogous β-dicarbonyl motif. An effective coupling strategy involved decreasing the reactivity of the electrophile while increasing the reactivity of the nucleophile.

Preliminary work was conducted on the oxidative rearrangement of model systems in preparation for the conversion of divergolide **E** to divergolides **C** and **D**. Subsequent work will focus on applying the oxidative rearrangement to divergolide **E** as well as exploring the structure activity relationship of these natural products.

APPENDIX A: EXPERIMENTAL SECTION

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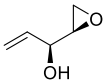
General Experimental

Tetrahydrofuran and diethyl ether were distilled over sodium/benzophenone under N_2. Dichloromethane was distilled from CaH_2 under N_2. Acetone was dried over $CaSO_4$, then distilled under Ar over fresh $CaSO_4$ immediately before use. Benzene, acetonitrile, 1,2-dichloroethane, and methanol were stored over 3 Å MS. Diisopropylethylamine, triethylamine, and 1,8-diazabicycloundec-7-ene were distilled from CaH_2, and diisopropylamine from NaH. Anhydrous dimethylsulfoxide, dimethylformamide, 1,4-dioxane, and pyridine were purchased from Sigma Aldrich. LiCl was dried under high vacuum (4 mmHg) at 140 °C for 24 hours.

Analytical TLC was performed on Merck pre-coated silica gel 60 F_{254} plates and visualized using UV light (254 nm), anisaldehyde stain, and $KMnO_4$ stain. Flash chromatography was performed using SiliCycle SiliaFlash P60, 40-63μm, 60 Å silica gel. Reagent grade ethyl acetate, hexanes, diethyl ether, and pentane were purchased from Fischer Scientific and used as received for chromatography of larger scale reactions. HPLC grade solvent was used for workup and chromatography of all late stage, small scale reactions to minimize the accumulation of grease. All other reagents were purchased through Fischer Scientific or Sigma Aldrich and used as received, unless noted otherwise. All reactions were performed in oven or flame dried glassware under a positive pressure of inert gas (Ar or N_2) unless noted otherwise.

Proton (^{1}H) NMRs were recorded on Bruker Avance spectrometers at 300, 400, 600, and 700 MHz. Carbon (^{13}C) NMR were recorded on Bruker Avance spectrometers at 75, 100, 150, and 176 MHz. The chemical shifts are recorded in parts per million (ppm) on the delta (δ) scale, using solvent peaks as the reference: ^{1}H-NMR, $CDCl_3$ = 7.26 ppm, benzene = 7.16 ppm; ^{13}C-NMR, $CDCl_3$ = 77.16 ppm. The coupling data are reported as follows: s = singlet; d = doublet; t = triplet; q = quartet; quint = quintet; br = broad; app = apparent. Infrared spectra were collected on a Nicolet IR200 FT-IR spectrometer using NaCl plates. Optical rotations $[\alpha]_{\mathrm{D}}^{T} = 100\alpha/cl$ were measured on a Perkin-Elmer 241 polarimeter with a sodium lamp (589 nm, D) at ambient temperature (T in °C) with a 1 dm path length (l) cell. Concentration (c) is expressed in g/100 mL. High and low resolution mass spectra were collected on one of the following: Q-Tof Ultima API, Micromass UK Limited; Q-Exactive, Thermo Scientific; LCMS-2020, Shimadzu Instrument.

Final Synthetic Route: Synthesis of Aldehyde 4-6



(*S*)-1-((*R*)-Oxiran-2-yl)prop-2-en-1-ol (4-7)

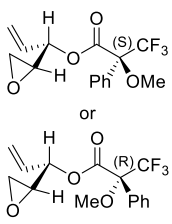
Titanium tetraisopropoxide (2.82 mL, 2.71 g, 9.54 mmol) and L-(+)-diisopropyltartrate (2.60 mL, 2.90 g, 12.4 mmol) were added sequentially via syringe to a stirred suspension of CH_2Cl_2 (96 mL) and powdered 4Å MS (3.23 g) at –35 °C under Ar. After stirring 30 min, penta-1,4-dien-3-ol (8.09 g, 96.1 mmol) was added dropwise followed by cumene hydroperoxide (80%, 35.5 mL, 36.6 g, 192 mmol). The reaction was stirred for 36 h at –35 °C, then saturated aqueous Na_2SO_4 (8 mL) and Et_2O (80 mL) were added. The mixture was warmed to rt and stirred 3 h. The resulting slurry was filtered through a pad of Celite using a fritted funnel and carefully concentrated *in vacuo* (no high vacuum). Excess cumene hydroperoxide/alcohol were removed by flash chromatography (5% to 30 % Et_2O in CH_2Cl_2) to yield **4-7** as a single enantiomer (5.70 g, 60 %, e.e. >99%, confirmed by the following Mosher ester analysis[61]) contaminated with L-(+)-diisopropyltartrate. If desired, the epoxide can be further purified by Kugelrohr distillation (130 °C, 12 mmHg).

^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.84 (ddd, *J* = 17.2, 10.4, 6.4 Hz, 1H), 5.38 (dt, *J* = 17.2, 0.8 Hz, 1H), 5.26 (dt, *J* = 10.4, 1.2 Hz, 1H), 4.33-4.32 (m, 1H), 3.09 (app q, *J* = 3.2 Hz, 1H), 2.80 (dd, *J* = 2.8, 4.8 Hz, 1H), 2.75 (dd, *J* = 4.0, 4.8 Hz, 1H), 2.19 (br s, 1H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ 135.6, 117.7, 70.3, 54.0, 43.6

Optical Rotation: $[\alpha]_D^{18}$ = + 62.3 (*c* = 0.92, $CHCl_3$)

These data are consistent with literature values. [48, 90]



(*S*)-1-((*R*)-Oxiran-2-yl)allyl-(*S* or *R*)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoate (S1)

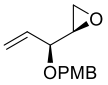
Pyridine (25 μL, 25 mg, 0.31 mmol) was added via syringe to a 1 dram vial containing **4-7** (10 mg, 0.10 mmol) and CH_2Cl_2 (1 mL) under ambient air. Either [(S)-(+)]- or [(R)-(–)]-α-methoxy-α-(trifluoromethyl)phenylacetyl chloride (MTPA-Cl) (58 μL, 78 mg, 0.19 mmol) was added via syringe, then the reaction capped and stirred at rt for 2 h. The reaction was quenched with H_2O and extracted three times with Et_2O. The combined organic layer was dried over Na_2SO_4 then concentrated *in vacuo*. NMR analysis of the crude product revealed diastereomerically pure **S1** (ee >99%), confirmed to be the desired stereoisomer after purification by flash chromatography (20% ethyl acetate in hexanes) and analysis using the advanced Mosher method (δS – δR).[61]

^{1}H-NMR ((R)-Mosher Ester, $CDCl_3$, 400 MHz): δ 7.62-7.37 (m, 5H), 5.85 (ddd, *J* = 17.2, 10.4, 7.2 Hz, 1H), 5.53 (dd, *J* = 6.8, 4.0 Hz, 1H), 5.48 (d, *J* = 17.2 Hz, 1H), 5.39 (d, *J* = 10.4 Hz, 1H), 3.53 (s, 3H), 3.07 (app q, *J* = 3.6 Hz, 1H), 2.70 (dd, *J* = 4.8, 4.4 Hz, 1H), 2.59 (dd, *J* = 4.8, 2.4 Hz, 1H).

^{1}H-NMR ((S)-Mosher Ester, $CDCl_3$, 400 MHz): δ 7.51-7.37 (m, 5H), 5.76 (ddd, *J* = 17.2, 10.4, 6.8 Hz, 1H), 5.57 (dd, *J* = 6.8, 3.6 Hz, 1H), 5.37 (d, *J* = 17.2 Hz, 1H), 5.32 (d, *J* = 10.4 Hz, 1H), 3.54 (s, 3H), 3.15 (app q, *J* = 3.6 Hz, 1H), 2.75 (t, *J* = 5.2 Hz, 1H), 2.70 (dd, *J* = 4.8, 2.4 Hz, 1H).

Table 2 Mosher Ester Analysis of Epoxide S1 Using the Advanced Mosher Method (δS – δR)

H#	δ (S)-MTPA ester	δ (R)-MTPA ester	Δδ = δS – δR
2	5.759	5.834	-0.075
4	5.3755	5.4765	-0.101
5	5.325	5.387	-0.062
7	3.155	3.069	+0.086
8	2.754	2.695	+0.059
9	2.699	2.586	+0.113



(*R*)-2-((*S*)-1-((4-Methoxybenzyl)oxy)allyl)oxirane (S2)

Preparation of 1-(bromomethyl)-4-methoxybenzene (PMBBr):[91] PBr_3 (2.0 mL, 5.9 g, 22 mmol) was added via syringe to a solution of (4-methoxyphenyl)methanol (6.00 g, 43.4 mmol) in Et_2O (50 mL) at 0 °C under N_2. The reaction was stirred at 0 °C for 2 h then was poured into saturated aqueous $NaHCO_3$ at 0 °C. The organic layer was washed twice with saturated aqueous $NaHCO_3$ and brine, then was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to yield the title compound (8.34 g, 96%), which was used immediately.

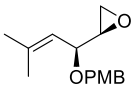
(*R*)-2-((*S*)-1-((4-Methoxybenzyl)oxy)allyl)oxirane (**S2**): Freshly prepared PMBBr (10.9 g, 54.5 mmol) was added via syringe to a solution of crude epoxide **4-7** (3.17 g, 31.6 mmol, contaminated with L-(+)-diisopropyltartrate), tetrabutylammonium iodide (0.21g, 0.569 mmol), and THF (85 mL) at 0 °C under Ar. In a separate round bottom flask under Ar, NaH (60 % w/w in mineral oil, 2.03 g, 50.6 mmol) was washed three times with dry hexanes (stored over 4Å MS) using syringes, then dried under high vacuum. The NaH was quickly added as a solid to the reaction flask in several small portions under a positive flow of Ar. The reaction was warmed to rt and stirred overnight. The mixture was cooled to 0 °C, diluted with Et_2O, and carefully quenched by dropwise addition of H_2O. The organic layer was washed with H_2O, saturated aqueous NH_4Cl, and twice with brine, then was dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude material was purified by flash chromatography (20 % Et_2O in hexanes) to yield compound **S2** (5.88 g, 84 %) as a clear liquid.

^{1}H-NMR ($CDCl_3$, 300 MHz): δ 7.26 (d, *J* = 8.4 Hz, 2H), 6.88 (d, *J* = 8.4 Hz, 2H), 5.82 (m, 1H), 5.37 (s, 1H), 5.32 (d, *J* = 6.6 Hz, 1H), 4.57 (d, *J* = 11.4 Hz, 1H), 4.40 (d, *J* = 11.4 Hz, 1H), 3.81 (s, 3H), 3.78 (dd, *J* = 7.5, 4.5 Hz, 1H), 3.06 (dt, *J* = 4.2, 3.0 Hz, 1H), 2.77 (app t, *J* = 5.1, 1H), 2.66 (dd, *J* = 5.4, 2.7 Hz, 1H)

^{13}C-NMR ($CDCl_3$, 75 MHz): δ 159.4, 134.8, 130.4, 129.5, 119.5, 114.0, 79.2, 70.5, 55.4, 53.4, 45.0

Optical Rotation: $[\alpha]_D^{19}$ = + 30.5 (*c* = 1.52, $CHCl_3$)

These data are consistent with literature values.[91]



(*R*)-2-((*S*)-1-((4-Methoxybenzyl)oxy)-3-methylbut-2-en-1-yl)oxirane (4-8)

Reaction apparatus:

Ace glass #25 thick-walled, threaded tube. The screw cap, containing a threaded hole, was attached to a valve. The valve was connected to a 3-way glass stopcock, via Nalgene tubing. One line of the 3-way stopcock was attached to a high vacuum line while the other was attached to a lecture bottle of isobutylene.

Reaction procedure: *Warning – this reaction generates pressure and the proper glassware must be used behind a blast shield and with proper precautions upon opening the vessel.*

Hoveyda-Grubbs second generation metathesis catalyst (0.124 g, 0.198 mmol, 1 mol %) was added as a solid to compound **S2** (4.36 g, 19.8 mmol) in the Ace glass #25 reaction vessel. The tube was capped, placed under high vacuum, then cooled to –78 °C. Isobutylene (~190 mL at –78 °C) was condensed into the tube by alternating the stopcock between the vacuum and isobutylene lecture bottle. The valve was closed and the reaction vessel was warmed to rt behind a blast shield. The reaction was further warmed to 40 °C in an oil bath and stirred 24 h. An additional 1 mol % of Hoveyda-Grubbs second generation catalyst (0.124 g, 0.198 mmol) was

added as a solid to the reaction at –78 °C, then warmed to 40 °C and stirred 24 h. This step was repeated once more followed by addition of DMSO (6.3 mL, 7.0 g, 89.1 mmol). The reaction was stirred 12 h at rt, cooled to –78 °C, and diluted with hexanes (~400 mL). The mixture was warmed to rt then was directly purified by flash chromatography (10% to 30% EtOAc in hexanes) to yield **4-8** (4.09 g, 83%) as a clear oil.

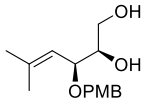
IR (cm^{-1}, neat): 3050, 2988, 1675, 1612, 1513, 1463, 1301, 1248, 1173, 1073, 1035, 927, 886, 824

^{1}H-NMR ($CDCl_3$, 300 MHz): δ 7.25 (d, *J* = 8.4 Hz, 2H), 6.87 (d, *J* = 8.7 Hz, 2H), 5.17 (dt, *J* = 9.0, 1.2 Hz, 1H), 4.53 (d, *J* = 11.4 Hz, 1H), 4.36 (d, *J* = 11.4 Hz, 1H), 4.10 (dd, *J* = 9.0, 3.9 Hz, 1H), 3.80 (s, 3H), 3.05 (dt, *J* = 4.2, 2.7 Hz, 1H), 2.75 (dd, *J* = 5.1, 3.9 Hz, 1H), 2.65 (dd, *J* = 5.4, 2.7 Hz, 1H), 1.79 (d, *J* = 1.2 Hz, 3H), 1.63 (d, *J* = 1.2 Hz, 3H)

^{13}C-NMR ($CDCl_3$, 100 MHz): δ = 159.1, 138.9, 130.6, 129.3, 121.5, 113.8, 74.0, 69.7, 55.3, 53.7, 44.7, 26.0, 18.5

MS: HRMS (ESI+) *m/z* calcd for $C_{14}H_{17}O_2$ $[M - OCH_3]^+$ 217.1246, found 217.1229

Optical Rotation: $[\alpha]_D^{18}$ = + 35.1 (*c* = 1.13, $CHCl_3$)



(2R,3S)-3-((4-methoxybenzyl)oxy)-5-methylhex-4-ene-1,2-diol (S3)

KOH (2.46 g, 43.8 mmol) was added as a solid in one portion to compound **4-8** (2.72 g, 10.9 mmol) in DMSO:H_2O (1:1 v/v, 55 mL) at rt under ambient atmosphere. The reaction was stirred for 5 min at rt then was warmed to 75 °C and stirred for 4 h. The reaction was cooled to rt and poured into 0.1 M aqueous HCl (500 mL). The aqueous layer was extracted six times with EtOAc. The combined organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude material was purified by flash chromatography (10% EtOAc in

hexanes to 30% hexanes in EtOAc) to yield diol **S3** (2.67 g, 92%) as a viscous liquid which solidified to a white solid upon storage in the freezer.

IR (cm^{-1}, neat): 3400, 3154, 2913, 1612, 1513, 1443, 1248, 1174, 1035, 820, 650

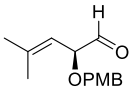
^{1}H-NMR ($CDCl_3$, 300 MHz): δ 7.22 (d, *J* = 8.7 Hz, 2H), 6.87 (d, *J* = 8.7 Hz, 2H), 5.17 (dt, *J* = 9.3, 1.2 Hz, 1H), 4.53 (d, *J* = 11.4 Hz, 1H), 4.26 (d, *J* = 11.4 Hz, 1H), 4.21 (dd, *J* = 9.3, 5.1 Hz, 1H), 3.80 (s, 3H), 3.80-3.56 (m, 3H), 2.39 (br s, 2H), 1.82 (d, *J* = 0.9 Hz, 3H), 1.67 (d, *J* = 0.9 Hz, 3H)

^{13}C-NMR ($CDCl_3$, 75 MHz): δ 159.4, 139.9, 130.4, 129.5, 122.2, 114.0, 77.4, 73.5, 70.0, 63.7, 55.4, 26.2, 18.7

MS: HRMS (ESI) *m/z* calcd for $C_{15}H_{23}O_4$ $[M+H]^+$ 267.1591, found 267.1583

Optical Rotation: $[\alpha]_D^{19}$ = + 44.9 (*c* = 0.68, $CHCl_3$)

Melting Point Range: 28-30 °C



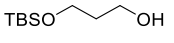
(S)-2-((4-methoxybenzyl)oxy)-4-methylpent-3-enal (4-6)

$NaIO_4$ (2.15 g, 10.0 mmol) was added as a solid in one portion to a solution of diol **S3** (2.23 g, 8.37 mmol) in THF:H_2O (0.75:1 v/v, 110 mL) at 0 °C under ambient atmosphere. After 5 min the solution was warmed to rt and stirred 2 h. The reaction mixture was diluted with H_2O and extracted four times with Et_2O:hexanes (9:1). The combined organic layer was washed with H_2O:brine (1:1), dried over Na_2SO_4, concentrated *in vacuo*, then left on the high vacuum 30 min to yield aldehyde **4-6** (1.94 g, 99%) which was immediately used in the next step without further purification.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ 9.52 (d, *J* = 2.0 Hz, 1H), 7.28 (d, *J* = 8.8 Hz, 2H), 6.89 (d, *J* = 8.8 Hz, 2H), 5.12 (dt, *J* = 8.8, 1.6 Hz, 1H), 4.58 (d, *J* = 11.6 Hz, 1H), 4.51-4.46 (m, 2H), 3.82 (s, 3H), 1.83 (s, 3H), 1.71 (s, 3H)

Optical Rotation: $[\alpha]_D^{19}$ = + 124 (*c* = 1.00, $CHCl_3$)

Final Synthetic Route: Synthesis of Alkyne 4-18

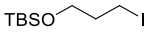


3-((*tert*-Butyldimethylsilyl)oxy)propan-1-ol (S4)

Tert-butyldimethylsilyl chloride (31.7 g, 210 mmol) in CH_2Cl_2 (84 mL) was added to propane-1,3-diol (16 g, 210 mmol), Et_3N (29.3 mL, 21.3 g, 210 mmol), and CH_2Cl_2 (630 mL) at rt under Ar. The reaction was stirred for 17 h then was washed with 10% aqueous $NaHCO_3$, H_2O, then brine. The organic layer was dried over Na_2SO_4 and concentrated *in vacuo*. The crude material was purified by flash chromatography (0% to 30% EtOAc in hexanes) to yield the mono-protected product **S4** (29.8 g, 75%) contaminated with a small amount of the double TBS protected material.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ 3.85-3.78 (m, 4H), 2.56 (t, *J* = 5.6 Hz, 1H), 1.77 (quint, *J* = 5.6 Hz, 2H), 0.90 (s, 9H), 0.07 (s, 6H)

These data are consistent with literature values.[65]



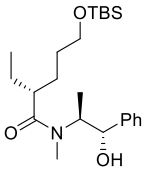
***tert*-Butyl(3-iodopropoxy)dimethylsilane (S5)**

A three neck round bottom flask was equipped with a septum, dropping funnel, and Ar inlet. The flask was charged with PPh_3 (22.6 g, 86.2 mmol) and CH_2Cl_2 (215 mL) and placed under Ar. Imidazole (7.33 g, 108 mmol) then I_2 (23.7 g, 93.3 mmol) were added as solids to the quickly

stirring solution. To the reaction was slowly added **S4** (13.7 g, 71.8 mmol) in CH_2Cl_2 (86 mL) via the dropping funnel. The reaction was stirred 4 h in the dark, then was filtered and concentrated *in vacuo*. The brown residue was extracted 3x with 20% EtOAc in hexanes. The combined extracts were filtered through a plug of SiO_2 gel and concentrated *in vacuo* to yield **S5** (18.4 g, 85%). The crude product was used in the next step without further purification.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ 3.67 (t, *J* = 5.6 Hz, 2H), 3.28 (t, *J* = 6.8 Hz, 2H), 1.99 (quint, *J* = 6.4 Hz, 2H), 0.90 (s, 9H), 0.07 (s, 6H)

These data are consistent with literature values.[65]



(*R*)-5-((*tert*-Butyldimethylsilyl)oxy)-2-ethyl-N-((1S,2S)-1-hydroxy-1-phenylpropan-2-yl)-N-methylpentanamide (S6)

A three-neck round bottom flask was equipped with a septum, thermometer, and Ar inlet. Dry LiCl was added and the flask was placed under Ar. THF (68 mL) was added followed by diisopropylamine (17.9 mL, 12.9 g, 127 mmol). The reaction was cooled to –78 °C and *n*-butyllithium (1.6 M in hexanes, 74.5 mL, 119 mmol) was added slowly via syringe. The mixture was warmed to rt, stirred 10 min, then cooled back to –78 °C. Compound **4-16**[92] (13.4 g, 56.8 mmol) in THF (180 mL) at 0 °C was added via cannula over 30 min. The reaction was stirred 1.5 h at –78 °C then warmed to 0 °C and stirred 30 min. **S5** (25.6 g, 85.1 mmol) in THF (350 mL) at 0 °C was added via cannula over 1.5 h. The reaction was stirred 3 h then was quenched with saturated aqueous NH_4Cl. The aqueous layer was extracted three times with EtOAc. The combined organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Hexanes (~ 400 mL) was added and the white precipitate that formed was filtered out. The solvent was removed *in vacuo* and the crude material was purified by flash chromatography (5% EtOAc in

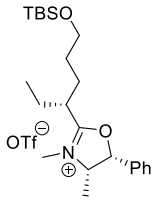
hexanes to 20% hexanes in EtOAc) to yield compound **S6** (21.3 g, 92%) with a diastereomeric ratio of 97:3 determined through the following conversion to the oxazolium triflate derivative.[66]

^{1}H-NMR ($CDCl_3$, 400 MHz, 5:1 rotamer ratio, major rotamer): δ 7.36-7.22 (m, 5H), 4.61 (t, *J* = 7.2 Hz, 1H), 4.41 (br s, 1H), 3.58 (m, 2H), 2.85 (s, 3H), 2.52 (tt, *J* = 8.4, 5.6 Hz, 1H), 1.70-1.33 (m, 6H), 1.15 (d, *J* = 6.8 Hz, 3H), 0.88 (m, 12H), 0.03 (s, 6H)

^{13}C-NMR ($CDCl_3$, 100 MHz, asterisk denotes minor rotamer peaks): δ 178.6, 142.8, 128.9*, 128.5*, 128.4, 127.6, 127.1*, 126.4, 77.4, 76.5, 63.2, 43.7, 30.6, 29.0, 26.1, 26.1, 26.0, 18.5, 14.7, 12.0, –5.2

Optical Rotation: $[\alpha]_D^{21}$ = + 53.4 (*c* = 1.57, $CHCl_3$)

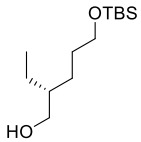
These data are consistent with literature values.[65]



(4S,5R)-2-((R)-6-((tert-butyldimethylsilyl)oxy)hexan-3-yl)-3,4-dimethyl-5-phenyl-4,5-dihydrooxazol-3-iumtrifluoromethane sulfonate[66]

To a solution of compound **S6** (20 mg, 49 μmol) in CH_2Cl_2 (1.2 mL) at 0 °C under Ar, was added pyridine (12 μL, 12 mg, 150 μmol) followed by trifluoromethanesulfonic anhydride (17 μL, 27 mg, 98 μmol) via syringe. The reaction was stirred 2 min at 0 °C then was concentrated *in vacuo* at rt and placed under high vacuum for 1 h at rt. NMR of the crude mixture revealed the title compound with a 97:3 diastereomeric ratio.

^{1}H-NMR ($CDCl_3$, 300 MHz, asterisk denotes minor diastereomer): δ 7.44-7.19 (m, 5H + pyridine), 6.50 (d, *J* = 10.2 Hz, 1H), 5.09 (dq, *J* = 10.2, 6.9 Hz, 1H), 3.68-3.55 (m, 1.95 H), 3.48 (s, 3H), 3.05 (quint, *J* = 6.9 Hz, 0.97 H), 2.94 (br s, 0.03 H)*, 1.93-1.77 (m, 3.89 H), 1.64-1.55 (m, 1.97 H), 1.39 (m, 0.1 H)*, 1.06 (t, *J* = 7.2 Hz, 3H), 0.97 (d, *J* = 6.9 Hz, 2.96 H), 0.87 (s, 0.3H)*, 0.83 (s, 8.75 H), 0.03 (s, 0.12 H)*, 0.00 (s, 5.72 H)



(*R*)-5-((*tert*-Butyldimethylsilyl)oxy)-2-ethylpentan-1-ol (S7)

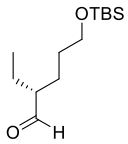
A two-neck round bottom flask was equipped with a septum and powder addition funnel containing ammonia-borane complex (90%, 3.20 g, 93.2 mmol). The reaction flask was placed under N_2 then charged with diisopropylamine (13.7 mL, 9.90 g, 97.9 mmol) and THF (100 mL). The flask was cooled to –78 °C and *n*-butyllithium (1.6 M in hexanes, 56.8 mL, 90.9 mmol) was added dropwise via syringe. The reaction was stirred for 10 min at –78 °C, warmed to 0 °C and stirred 10 min. Ammonia-borane complex from the powder addition funnel was added slowly at 0 °C and the reaction was warmed to rt. After stirring 30 min at rt, the powder addition funnel was replaced with a liquid addition funnel under a positive pressure of N_2. The reaction was cooled to 0 °C and compound **S6** (9.5 g, 23.3 mmol) in THF (160 mL) was added via the liquid addition funnel. The reaction was warmed to rt and stirred 3 h. Saturated aqueous NH_4Cl was added and the mixture was stirred for 30 min. The aqueous layer was extracted three times with Et_2O. The combined organic layer was washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The crude material was purified by flash chromatography (10% to 50% EtOAc in hexanes) to yield alcohol **S7** (5.01 g, 87%) as a clear oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ 3.60 (t, *J* = 6.4 Hz, 2H), 3.54 (br d, *J* = 4.0 Hz, 2H), 1.57-1.50 (m, 2H), 1.46-1.25 (m, 6H), 0.89 (m, 12H), 0.04 (s, 6H)

^{13}C-NMR ($CDCl_3$, 100 MHz): δ 65.3, 63.5, 41.8, 29.9, 26.5, 26.0, 23.5, 18.4, 11.1, –5.3

Optical Rotation: $[\alpha]_D^{21}$ = + 0.65 (*c* = 1.38, $CHCl_3$)

These data are consistent with literature values.[65]



(*R*)-5-((*tert*-Butyldimethylsilyl)oxy)-2-ethylpentanal (4-17)[65]

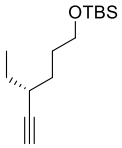
Et_3N (28.3 mL, 20.8 g, 203 mmol) was added via syringe to a solution of alcohol **S7**

(5.01 g, 20.3 mmol), dimethylsulfoxide (28.9 mL), and CH_2Cl_2 (60 mL) at 0 °C under N_2. Sulfur trioxide pyridine complex, technical grade (12.9 g, 81.3 mmol) was added as a solid and the reaction was stirred for 2.5 h at 0 °C. The reaction was quenched with saturated aqueous $NaHCO_3$:H_2O (3:5). The aqueous layer was extracted three times with Et_2O. The combined organic layer was dried over Na_2SO_4 and concentrated *in vacuo*. The crude material was purified by flash chromatography (0% to 10% EtOAc in hexanes) to yield aldehyde **4-17** (4.40 g, 89%) as a clear oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ 9.61 (d, *J* = 2.8 Hz, 1H), 3.64 (t, *J* = 6.4 Hz, 2 H), 2.23 (m, 1H), 1.76-1.64 (m, 2H), 1.61-1.50 (m, 4H), 0.95 (t, *J* = 7.6 Hz, 3H), 0.92 (s, 9H), 0.07 (s, 6H)

^{13}C-NMR ($CDCl_3$, 100 MHz): δ 205.5, 62.8, 53.0, 30.1, 25.9, 24.7, 21.8, 18.3, 11.4, –5.3

Optical Rotation: $[\alpha]_D^{18}$ = – 0.93 (*c* = 2.79, $CHCl_3$)



(R)-tert-butyl((4-ethylhex-5-yn-1-yl)oxy)dimethylsilane (4-18)

A solution of 2.29 M NaOMe was freshly prepared by adding Na (1.58 g) to MeOH (30 mL) under N_2 at 0 °C, followed by stirring 2 h at rt. The 2.29 M NaOMe solution (22.7 mL, 51.9 mmol) was slowly added via syringe to quickly stirring Ohira–Bestmann reagent[93] (10.5 g, 54.6 mmol) in THF (180 mL) at –78 °C, under N_2. The reaction was stirred 15 min then aldehyde **4-17** (6.68 g, 27.3 mmol) in THF (120 mL) at –78 °C was added via cannula over 1 h. The reaction was allowed to warm slowly to –40 °C over ~1.5 h then was quenched with saturated aqueous NH_4Cl. The aqueous layer was extracted 3x with Et_2O. The combined organic layer was washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The crude material was purified by flash column (0% to 5% Et_2O in hexanes) to yield alkyne **4-18** (4.86 g, 74%) as a clear oil.

IR (cm^{-1}, neat): 3312, 2113, 1729, 1462, 1386, 1361, 1254, 1099, 969, 836, 775, 628

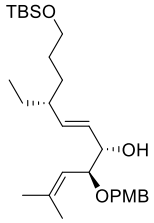
^{1}H-NMR ($CDCl_3$, 300 MHz): δ 3.63 (t, *J* = 6.0 Hz, 2H), 2.33-2.23 (m, 1H), 2.04 (d, *J* = 2.4 Hz, 1H), 1.81-1.38 (m, 6H), 1.01 (t, *J* = 7.5 Hz, 3H), 0.89 (s, 9H), 0.05 (s, 6H)

^{13}C-NMR ($CDCl_3$, 100 MHz): δ 87.8, 69.2, 63.0, 32.9, 30.8, 30.5, 28.0, 26.0, 18.4, 11.6, -5.3

MS: HRMS (ESI+) *m/z* calcd for $C_{14}H_{29}OSi$ $[M+H]^+$ 241.1943, found 241.1963

Optical Rotation: $[\alpha]_D^{19}$ = – 6.94 (*c* = 1.80, $CHCl_3$)

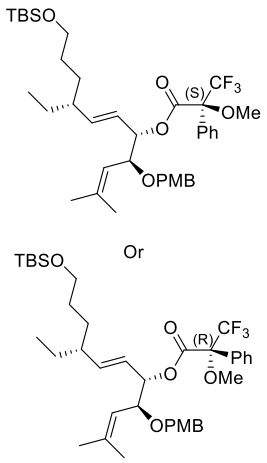
Final Synthetic Route: Synthesis of Diene 4-3



(4*S*,5*S*,8*R*,*E*)-11-((*tert*-Butyldimethylsilyl)oxy)-8-ethyl-4-((4-methoxybenzyl)oxy)-2-methylundeca-2,6-dien-5-ol (4-19):

Alkyne **4-18** (1.90 g, 7.90 mmol) in CH_2Cl_2 (24 mL) was added to $Cp_2Zr(H)Cl$ (2.24 g, 8.69 mmol), prepared according to literature,[94] under Ar, at rt, wrapped in Al foil. The reaction was stirred 10 min until the mixture was homogeneous, then was cooled to –65 °C. Me_2Zn (1.2 M in toluene, 9.2 mL, 11 mmol) was added dropwise (0.17 mL/min). The reaction was cooled to –78 °C, followed by addition of aldehyde **4-6** (1.48 g, 6.32 mmol) in CH_2Cl_2 (24 mL) dropwise (0.2-0.3 mL/min). The reaction was allowed to slowly warm to 0 °C over 3 h then was poured into ice cold saturated aqueous $NaHCO_3$. The aqueous layer was extracted three times with Et_2O. The combined organic extracts were washed with saturated aqueous NH_4Cl and brine, then were dried over Na_2SO_4 and filtered through a plug of silica gel (eluted with 30% EtOAc in hexanes). The eluent was concentrated *in vacuo* to yield the crude product **4-19** (2.38 g, 79%, dr = 4:1) contaminated with the alkene byproduct of alkyne **4-18**,

which was stored and used in the next step without further purification. The stereochemistry was confirmed by the following Mosher ester analysis.[61]



(4*S*,5*S*,8*R*,*E*)-11-((*tert*-Butyldimethylsilyl)oxy)-8-ethyl-4-((4-methoxybenzyl)oxy)-2-methylundeca-2,6-dien-5-yl-(*S* or *R*)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoate (S8)

Pyridine (3.0 μL, 3.0 mg, 38 μmol) was added via syringe to **4-19** (0.7 mg, 1.5 μmol) in $CDCl_3$ (50 μL) in a small vial under ambient air. Either [(*S*)-(+)] or [(*R*)-(–)]-α-methoxy-α-(trifluoromethyl)phenylacetyl chloride (3.0 μL, 4.1 mg, 16 μmol) was added via syringe. The mixture was stirred at rt for 6 h then $CDCl_3$ (~0.6 mL) was added. ^{1}H NMR of the crude material was acquired for both the (*R*)- and (*S*)-Mosher esters and confirmed the presence of the desired diastereomer.

^{1}H-NMR ((*S*)-Mosher Ester, $CDCl_3$, 400 MHz)

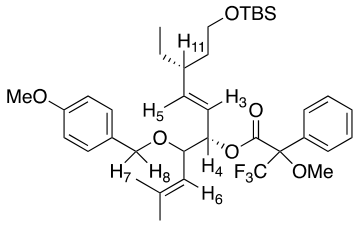
[aromatic hydrogens obscured by MTPA, pyridine] – δ 7.16 (d, *J* = 8.8 Hz, 2H), 6.80 (d, *J* = 8.4 Hz, 2H), 5.47 (m, 1H), 5.47 (m, 1H), 5.16 (dd, *J* = 15.6, 8.4 Hz, 1H), 5.00 (d, *J* = 10.0 Hz, 1H), 4.50 (d, *J* = 11.6 Hz, 1H), 4.25 (d, *J* = 11.6 Hz, 1H), 4.21 (t, *J* = 9.2 Hz, 1H), 3.78 (s, 3H), – [hydrogens obscured by MTPA] – 1.78-1.77 (m, 1H), 1.74 (s, 3H), 1.59 (s, 3H), 1.40-1.03 (m, 6H), 0.872 (s, 9H), 0.76 (t, *J* = 7.6 Hz, 3H), 0.02 (s, 6H).

^{1}H-NMR (((R)-Mosher Ester, $CDCl_3$, 400 MHz)

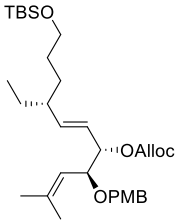
[aromatic hydrogens obscured by MTPA, pyridine] – δ 7.02 (d, *J* = 8.4 Hz, 2H), 6.75 (d, *J* = 8.4 Hz, 2H), 5.53 (dd, *J* = 15.2, 9.2 Hz, 1H), 5.49 (t, *J* = 8.4 Hz, 1H), 5.30 (dd, *J* = 15.6, 8.8 Hz, 1H), 4.95 (d, *J* = 9.6 Hz, 1H), 4.39 (d, *J* = 11.6 Hz, 1H), 4.15 (d, *J* = 11.6 Hz, 1H), 4.12 (dd, *J* =

9.2, 8.0 Hz, 1H), 3.76 (s, 3H) – [hydrogens obscured by MTPA] – 1.81 (m, 1H), 1.71 (s, 3H), 1.54 (s, 3H), 1.40-1.01 (m, 6H), 0.86 (s, 9H), 0.75 (t, *J* = 7.2 Hz, 3H), 0.01 (s, 6H).

Table 3 Mosher ester analysis of the S8 diastereomers using the advanced Mosher method



H#	δ(S)-MTPA ester	δ(R)-MTPA ester	Δδ = δS – δR
3	5.471	5.5355	–0.0645
5	5.163	5.3025	–0.1395
11	1.772	1.810	–0.038
9	4.206	4.1265	+0.0795
7	4.5015	4.3875	+0.114
8	4.2485	4.1485	+0.1
6	5.0064	4.954	+0.0525



Allyl ((4*S*,5*S*,8*R*,*E*)-11-((*tert*-butyldimethylsilyl)oxy)-8-ethyl-4-((4-methoxybenzyl)oxy)-2-methylundeca-2,6-dien-5-yl) carbonate (5-5)

Anhydrous pyridine (7.0 mL, 6.8 g, 8.6 mmol) was added to crude alcohol **4-19** (3.73 g, 7.82 mmol) in THF (40 mL) at 0 °C under N_2. Allyl chloroformate (8.3 mL, 9.4 g, 78 mmol) was added dropwise and the reaction was warmed to rt and stirred 2 h. The reaction was quenched with 10% aqueous $NaHCO_3$ at 0 °C. The aqueous layer was extracted three times with Et_2O. The combined organic layer was washed with saturated aqueous NH_4Cl and brine, then was dried over Na_2SO_4, and concentrated *in vacuo*. The crude product was purified by three rounds of flash chromatography (5.5 inches SiO_2, 2.5% to 10% EtOAc in hexanes) to yield the desired, major diastereomer of **5-5** (3.00 g, 68% of total starting material, 85% of the major isomer) as a clear oil.

IR (cm^{-1}, neat): 2955, 2931, 2857, 1747, 1613, 1513, 1462, 1251, 1095, 836, 777

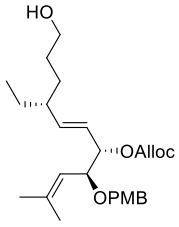
^{1}H-NMR ($CDCl_3$, 500 MHz): δ 7.22 (d, *J* = 9.0 Hz, 2H), 6.84 (d, *J* = 8.5 Hz, 2H), 5.93 (ddt, *J* = 16.5, 10.5, 5.5 Hz, 1H), 5.48 (dd, *J* = 15, 8.5 Hz, 1H), 5.36-5.28 (m, 2H), 5.23 (dd, *J* = 10.5, 1.0 Hz, 1H), 5.12 (t, *J* = 7.5 Hz, 1H), 5.05 (d, *J* = 10.0 Hz, 1H), 4.61 (dd, *J* = 5.5, 1.0 Hz, 2H), 4.53

(d, *J* = 11.5 Hz, 1H), 4.31 (d, *J* = 11.5 Hz, 1H), 4.15 (dd, *J* = 9.5, 7.5 Hz, 1H), 3.80 (s, 3H), 3.54 (t, *J* = 5.5 Hz, 2H), 1.83 (m, 1H), 1.75 (d, *J* = 0.5 Hz, 3H), 1.60 (d, *J* = 0.5 Hz, 3H), 1.47-1.32 (m, 4H), 1.25-1.14 (m, 2H), 0.88 (s, 9H), 0.79 (t, *J* = 7.5 Hz, 3H), 0.03 (s, 6H)

^{13}C-NMR ($CDCl_3$, 125 MHz): δ 159.2, 154.7, 140.8, 138.8, 132.1, 131.1, 129.2, 124.7, 121.9, 118.6, 113.8, 81.0, 76.3, 69.7, 68.3, 63.4, 55.4, 44.5, 30.9, 30.6, 28.0, 26.1, 18.8, 18.5, 11.7, -5.2

MS: HRMS (ESI+) *m/z* calcd for $C_{32}H_{53}O_6Si$ $[M+H]^+$ 561.3606, found 561.3606

Optical Rotation: $[\alpha]_D^{20}$ = + 34.5 (*c* = 1.03, $CHCl_3$)



Allyl ((4*S*,5*S*,8*R*,*E*)-8-ethyl-11-hydroxy-4-((4-methoxybenzyl)oxy)-2-methylundeca-2,6-dien-5-yl) carbonate (S9)

NH_4F (4.35 g, 117 mmol) was added to compound **5-5** (2.99 g, 5.34 mmol) dissolved in MeOH (100 mL) at rt. The reaction was warmed to 55 °C and stirred for 7.5 h. H_2O was added and the aqueous layer was extracted twice with Et_2O then once with EtOAc. The combined organic layer was washed with brine, dried over $MgSO_4$, filtered, concentrated *in vacuo*, then was left on the high vacuum overnight to yield crude alcohol **S9** (2.35 g, 98%).

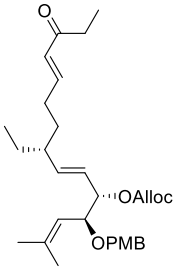
IR (cm^{-1}, neat): 3443, 2933, 1746, 1612, 1513, 1250, 1036, 821, 787

^{1}H-NMR ($CDCl_3$, 500 MHz): δ 7.22 (d, *J* = 8.5 Hz, 2H), 6.85 (d, *J* = 8.5 Hz, 2H), 5.93 (ddt, *J* = 16.5, 11.0, 6.0 Hz, 1H), 5.49 (dd, *J* = 15.0, 8.5 Hz, 1H), 5.36-5.32 (m, 2H), 5.24 (d, *J* = 10.5 Hz, 1H), 5.12 (t, *J* = 7.5 Hz, 1H), 5.07 (d, *J* = 10.0 Hz, 1H), 4.61 (d, *J* = 5.5 Hz, 2H), 4.53 (d, *J* = 11.5 Hz, 1H), 4.31 (d, *J* = 11.5 Hz, 1H), 4.16 (dd, *J* = 9.5, 7.0 Hz, 1H), 3.80 (s, 3H), 3.57 (br s, 2H), 1.85 (qt, *J* = 9.5, 4.5 Hz, 1H), 1.76 (s, 3H), 1.61 (s, 3H), 1.51-1.36 (m, 4H), 1.27-1.18 (m, 2H), 1.18 (br s, 1H), 0.80 (t, *J* = 7.5 Hz, 3H)

^{13}C-NMR ($CDCl_3$, 125 MHz): δ 159.2, 154.7, 140.4, 138.8, 132.1, 131.0, 129.3, 124.9, 121.8, 118.6, 113.8, 80.8, 76.1, 69.7, 68.4, 63.2, 55.4, 44.5, 30.9, 30.6, 28.0, 26.1, 18.8, 11.7

MS: HRMS (ESI+) *m/z* calcd for $C_{26}H_{42}O_6N$ $[M+NH_4]^+$ 464.3007, found 464.3008

Optical Rotation: $[\alpha]_D^{20}$ = + 43.3 (*c* = 0.52, $CHCl_3$)



Allyl ((4*S*,5*S*,6*E*,8*R*,11*E*)-8-ethyl-4-((4-methoxybenzyl)oxy)-2-methyl-13-oxopentadeca-2,6,11-trien-5-yl) carbonate (6-9)

Oxidation

Dimethylsulfoxide (0.48 mL, 0.53 g, 6.8 mmol) in CH_2Cl_2 (5.3 mL) was added dropwise (0.15 mL/min) to oxalyl chloride (248 µL, 0.427 g, 3.38 mmol) in CH_2Cl_2 (11.8 mL) at –78 °C under N_2. The reaction was stirred 10 min at –78 °C then alcohol **S9** (1.26 g, 2.82 mmol) in CH_2Cl_2 (3.7 mL) was added dropwise (0.12 mL/min). The reaction was stirred for 1 h at –78 °C followed by dropwise addition (0.03 mL/min) of Et_3N (1.18 mL, 0.856 g, 8.46 mmol). The mixture was warmed slowly to rt in a glass pyrex container over 2 h, then was quenched with H_2O. The aqueous layer was extracted three times with CH_2Cl_2. The combined organic extracts were washed twice with saturated aqueous NH_4Cl, once with brine, dried over Na_2SO_4, then concentrated *in vacuo* to yield the crude aldehyde (1.27 g).

HWE reaction

$EtC(O)CH_2P(O)(OMe)_2$[95] (0.975 g, 5.42 mmol) in MeCN (2 mL) was added to a suspension of LiCl (0.23 g, 5.4 mmol) and MeCN (27 mL) under N_2 at rt. A solution of 1,8-diazabicycloundec-7-ene (0.619 g, 4.06 mmol) in MeCN (2 mL) was added and the reaction was stirred 30 min. Crude aldehyde from the above oxidation was dissolved in MeCN (1.5 mL) then was added to the reaction. After stirring for 2 h at rt, H_2O was added. The aqueous layer was extracted three

times with Et_2O then once with EtOAc. The combined organic layer was washed with saturated aqueous NH_4Cl, brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude material was purified by flash chromatography (2.5% to 30% EtOAc in hexanes) to yield enone **6-9** (1.09 g, 78% over 2 steps) as a clear oil.

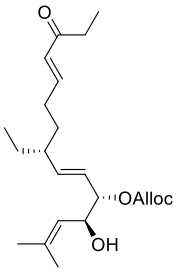
IR (cm^{-1}, neat): 2965, 2933, 2880, 1746, 1673, 1513, 1250, 1035, 822, 788

^{1}H-NMR ($CDCl_3$, 500 MHz): δ 7.22 (d, *J* = 8.5 Hz, 2H), 6.84 (d, *J* = 8.5 Hz, 2H), 6.76 (dt, *J* = 16.0, 7.0 Hz, 1H), 6.05 (d, *J* = 16.0 Hz, 1H), 5.92 (ddt, *J* = 16.0, 10.5, 5.5 Hz, 1H), 5.47 (dd, *J* = 15.5, 9.0 Hz, 1H), 5.37-5.32 (m, 2H), 5.24 (dd, *J* = 10.5, 1.0 Hz, 1H), 5.13 (t, *J* = 7.0 Hz, 1H), 5.07 (d, *J* = 9.5 Hz, 1H), 4.61 (d, *J* = 5.5 Hz, 2H), 4.53 (d, *J* = 11.5 Hz, 1H), 4.31 (d, *J* = 12.0 Hz, 1H), 4.17 (dd, *J* = 9.5, 7.0 Hz, 1H), 3.80 (s, 3H), 2.53 (q, *J* = 7.5 Hz, 2H), 2.17-2.10 (m, 1H), 2.02 (dq, *J* = 16.5, 8.0 Hz, 1H), 1.86 (qt, *J* = 9.0, 4.5 Hz, 1H), 1.75 (s, 3H), 1.61 (s, 3H), 1.53-1.47 (m, 1H), 1.43-1.30 (m, 2H), 1.29-1.20 (m, 1H), 1.09 (t, *J* = 7.0 Hz, 3H), 0.80 (t, *J* = 7.5 Hz, 3H)

^{13}C-NMR ($CDCl_3$, 125 MHz): δ 201.1, 159.2, 154.6, 146.9, 139.7, 138.9, 132.0, 130.9, 130.2, 129.3, 125.5, 121.8, 118.7, 113.8, 80.7, 76.0, 69.7, 68.4, 55.4, 44.3, 33.4, 33.2, 30.2, 28.0, 26.2, 18.8, 11.7, 8.3

MS: HRMS (ESI+) *m/z* calcd for $C_{30}H_{43}O_6$ $[M+H]^+$ 499.3054, found 499.3052

Optical Rotation: $[\alpha]_D^{20}$ = + 26.8 (*c* = 0.56, $CHCl_3$)



Allyl ((4*S*,5*S*,6*E*,8*R*,11*E*)-8-ethyl-4-hydroxy-2-methyl-13-oxopentadeca-2,6,11-trien-5-yl) carbonate (S10)

To a solution of **6-9** (1.97 g, 3.95 mmol) in CH_2Cl_2:0.1 M pH 7 sodium phosphate buffer (18:1, 47 mL) at 0 °C was added 2,3-dichloro-5,6-dicyano-*p*-

benzoquinone (1.17 g, 5.14 mmol) slowly as a solid. The reaction was warmed to rt and stirred for 1 h. The crude mixture was directly loaded onto a silica gel column with a top layer of $MgSO_4$:sand (1:1, 0.5 inches). Elution with 5% to 30% EtOAc in hexanes yielded compound **S10** (1.45 g, 97%), that was immediately reprotected in the next step to prevent cyclization of the secondary alcohol with the allyl carbonate protecting group.

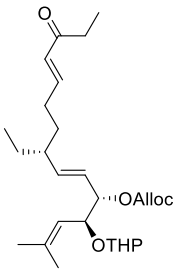
IR (cm^{-1}, neat): 3466, 2969, 2931, 2880, 1746, 1672, 1255, 975

^{1}H-NMR ($CDCl_3$, 500 MHz): δ 6.77 (dt, *J* = 15.5, 6.5 Hz, 1H), 6.06 (d, *J* = 16.0 Hz, 1H), 5.93 (ddt, *J* = 16.5, 11.0, 6.0 Hz, 1H), 5.53 (dd, *J* = 15.5, 9.0 Hz, 1H), 5.37-5.31 (m, 2H), 5.26 (d, *J* = 10.5 Hz, 1H), 5.14 (d, *J* = 9.0 Hz, 1H), 4.95 (t, *J* = 7.5 Hz, 1H), 4.63-4.62 (m, 2H), 4.42 (t, *J* = 8.5 Hz, 1H), 2.54 (q, *J* = 7.0 Hz, 2H), 2.19-2.12 (m, 1H), 2.04 (dq, *J* = 15.5, 7.5 Hz, 1H), 1.98 (br s, 1H), 1.89 (qt, *J* = 9.0, 4.5 Hz, 1H), 1.72 (s, 3H), 1.70 (s, 3H), 1.56-1.49 (m, 1H), 1.45-1.32 (m, 2H), 1.29-1.22 (m, 1H), 1.09 (t, *J* = 7.5 Hz, 3H), 0.81 (t, *J* = 7.5 Hz, 3H)

^{13}C-NMR ($CDCl_3$, 125 MHz): δ 201.1, 154.6, 146.7, 140.8, 138.9, 131.8, 130.2, 125.3, 122.7, 119.0, 82.5, 70.0, 68.6, 44.3, 33.5, 33.2, 30.2, 27.9, 26.1, 18.8, 11.7, 8.3

MS: HRMS (ESI+) *m/z* calcd for $C_{22}H_{38}O_5N$ $[M+NH_4]^+$ 396.2745, found 396.2752

Optical Rotation: $[\alpha]_D^{20}$ = + 35.3 (*c* = 0.34, $CHCl_3$)



Allyl ((4*S*,5*S*,6*E*,8*R*,11*E*)-8-ethyl-2-methyl-13-oxo-4-((tetrahydro-2H-pyran-2-yl)oxy)pentadeca-2,6,11-trien-5-yl) carbonate (6-10)

To a solution of alcohol **S10** (1.51 g, 3.99 mmol) in 1,2-dichloroethane (28 mL) under N_2 was added 3,4-dihydro-2H-pyran (0.91 mL, 0.84 g, 10 mmol). Pyridinium *p*-toluenesulfonate (0.100 g, 0.399 mmol) was added as a solid in one portion and the reaction was stirred overnight. The mixture was diluted with Et_2O, washed twice with brine:H_2O

(1:1), dried over Na_2SO_4, and concentrated *in vacuo*. The crude material was purified by flash chromatography (5% to 30% EtOAc in hexanes) to yield compound **6-10** (1.59 g, 90%) as a clear oil.

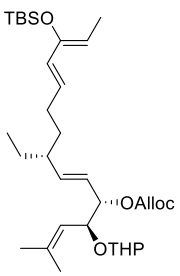
IR (cm^{-1}, neat): 2937, 2875, 1748, 1674, 1252, 1115, 1020, 975

^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 6.77 (dt, *J* = 15.2, 6.8 Hz, 1H), 6.05 (d, *J* = 16.0 Hz, 1H), 5.97-5.86 (m, 1H), 5.50-5.41 (m, 1H), 5.39-5.29 (m, 2H), 5.25-5.21 (m, 1H), 5.17-5.05 (m, 1.5H), 4.92 (d, *J* = 10.0 Hz, 0.5H), 4.81 (t, *J* = 3.2 Hz, 0.5H), 4.64-4.59 (m, 2.5H), 4.48 (dd, *J* = 10.0, 8.0 Hz, 0.5H), 4.38 (dd, *J* = 9.6, 8.0 Hz, 0.5H), 3.91 (td, *J* = 11.2, 2.8 Hz, 0.5H), 3.79 (td, *J* = 11.2, 2.8 Hz, 0.5H), 3.50 (br d, *J* = 10.8 Hz, 0.5H), 3.44-3.41 (m, 0.5H), 2.53 (q, *J* = 7.6 Hz, 2H), 2.20-2.10 (m, 1H), 2.02 (dq, *J* = 16.8, 8.4 Hz, 1H), 1.91-1.81 (m, 1H), 1.71 (s, 1.5H), 1.70 (s, 1.5H), 1.67 (s, 3H), 1.64-1.59 (m, 1H), 1.55-1.46 (m, 6H), 1.42-1.30 (m, 2H), 1.29-1.18 (m, 1H), 1.08 (t, *J* = 7.2 Hz, 3H), 0.80 (t, *J* = 7.2 Hz, 1.5H), 0.79 (t, *J* = 7.2 Hz, 1.5H)

^{13}C-NMR ($CDCl_3$, 125 MHz, asterisk denotes THP isomer): δ = 201.1, 154.7, 154.5*, 146.9, 146.8*, 140.0, 139.8, 139.6*137.0*, 132.0, 131.9*, 130.1, 125.7, 125.4*, 122.0, 120.8*, 118.8, 118.6*, 99.4, 93.3*, 81.3, 80.5*, 75.0, 71.7*, 68.3, 68.3*, 62.2, 61.1*, 44.3, 44.2*, 33.4, 33.1, 30.7, 30.5*, 30.2, 28.0, 26.2, 25.8, 25.5*, 19.4, 18.7*, 18.7, 18.6*, 11.7, 8.3

MS: HRMS (ESI+) *m/z* calcd for $C_{27}H_{42}O_6Na$ $[M+Na]^+$ 485.2874, found 485.2893

Optical Rotation: $[\alpha]_D^{18}$ = + 22.6 (*c* = 0.62, $CHCl_3$)



Allyl ((4*S*,5*S*,6*E*,8*R*,11*E*,13*Z*)-13-((*tert*-butyldimethylsilyl)oxy)-8-ethyl-2-methyl-4-((tetrahydro-2H-pyran-2-yl)oxy)pentadeca-2,6,11,13-tetraen-5-yl) carbonate (6-11)

Diisopropylethylamine (1.99 mL, 1.47 g, 11.4 mmol) then *tert*-butyldimethylsilyl

trifluoromethanesulfonate (1.84 mL, 2.12 g, 8.02 mmol) were added sequentially via syringe to compound **6-10** and Et_2O (9.4 mL) at –78 °C under Ar. The reaction was warmed to 0 °C over 1.5 h then was placed in an ice/water bath and stirred for 15 min. The reaction was quenched with saturated aqueous $NaHCO_3$ at 0 °C. The aqueous layer was extracted three times with Et_2O. The combined organic extracts were washed with brine, dried over Na_2SO_4, filtered, then concentrated *in vacuo*. The crude material was purified by flash chromatography (4 inches SiO_2, 0% to 10% EtOAc in hexanes) to yield diene **6-11** (0.63 g, 82%) as a clear oil.

IR (cm^{-1}, neat): 2965, 2930, 2857, 1749, 1626, 1253, 1115, 1021, 969

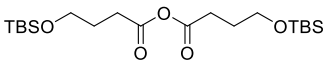
^{1}H-NMR ($CDCl_3$, 500 MHz): δ 5.93 (ddt, *J* = 16.5, 10.5, 6.0 Hz, 0.5H), 5.92 (ddt, *J* = 16, 10.5, 5.5 Hz, 0.5H), 5.78 (d, *J* = 16.0 Hz, 1H), 5.68 (dt, *J* = 14.0, 7.0 Hz, 1H), 5.48 (dd, *J* = 15.5, 9.0 Hz, 0.5H), 5.45 (dd, *J* = 15.5, 9.0 Hz, 0.5H), 5.37-5.27 (m, 2H), 5.25-5.22 (m, 1H), 5.17-5.12 (m, 1H), 5.08 (t, *J* = 7.5 Hz, 0.5H), 4.93 (d, *J* = 10.0 Hz, 0.5H), 4.82 (t, *J* = 3.5 Hz, 0.5H), 4.71 (q, *J* = 6.5 Hz, 1H), 4.66 (t, *J* = 3.0 Hz, 0.5H), 4.64-4.60 (m, 2H), 4.49 (dd, *J* = 10.0, 8.0 Hz, 0.5H), 4.38 (dd, *J* = 9.5, 8.5 Hz, 0.5H), 3.93 (ddd, *J* = 13.5, 11.0, 2.5 Hz, 0.5H), 3.82 (ddd, *J* = 11.0, 8.5, 2.5 Hz, 0.5H), 3.50 (br d, *J* = 11.0 Hz, 0.5H), 3.43 (dt, *J* = 10.5, 4.5 Hz, 0.5H), 2.07-1.97 (m, 1H), 1.92-1.84 (m, 2H), 1.72 (s, 1.5H), 1.71 (s, 1.5H), 1.68 (s, 1.5H), 1.67 (s, 1.5H), 1.65-1.60 (m, 2H), 1.61 (d, *J* = 7.0 Hz, 3H), 1.60-1.44 (m, 4H), 1.44-1.34 (m, 2H), 1.31-1.18 (m, 2H), 1.0 (s, 9H), 0.80 (t, *J* = 7.5 Hz, 1.5H), 0.79 (t, *J* = 7.5 Hz, 1.5H), 0.10 (s, 6H)

^{13}C-NMR ($CDCl_3$, 125 MHz, asterisk denotes THP isomer): δ 154.8, 154.6*, 149.3, 140.7, 140.6*, 139.9, 136.9*, 132.1, 132.0*, 128.9, 128.7, 128.7*, 125.1, 124.9*, 122.1, 120.9*, 118.7, 118.6*, 107.4, 99.4, 93.3*, 81.7, 80.9*, 75.2, 71.8*, 68.3, 68.3*, 62.2, 61.0*, 44.2, 34.5, 30.8, 30.5*, 29.9, 28.0, 26.2, 26.2, 25.8, 25.6, 19.5, 18.7*, 18.7, 18.7*, 18.6, 11.8, 11.7*, -3.4

MS: HRMS (ESI+) *m/z* calculated for $C_{33}H_{57}O_6Si$ $[M+H]^+$ 577.3919, found 577.3906

Optical Rotation: $[\alpha]_D^{18}$ = + 23.5 (*c* = 0.66, $CHCl_3$)

Final Synthetic Route: Synthesis of Aldehyde 7-3



4-((*tert*-Butyldimethylsilyl)oxy)butanoic anhydride (7-5)

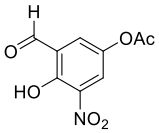
To a solution of 4-((*tert*-butyldimethylsilyl)oxy)butanoic acid[88] (2.00 g, 9.16 mmol) in CH_2Cl_2 (9.4 mL) at rt under N_2 was added *N,N'*-Dicyclohexylcarbodiimide (0.90 g, 4.36 mmol) in CH_2Cl_2 (19 mL) dropwise over 40 min. The reaction was stirred for 3 h, then was filtered and concentrated *in vacuo*. The residue was redissolved in Et_2O, filtered, then concentrated *in vacuo* to yield the title anhydride (1.8 g, 99%) as a clear oil, which was used crude without further purification.

IR (cm^{-1}, neat): 2929, 2859, 1821, 1752, 1256, 1112

^{1}H-NMR ($CDCl_3$, 400 MHz): δ 3.66 (t, *J* = 6.0 Hz, 4H), 2.55 (t, *J* = 7.2 Hz, 4H), 1.86 (tt, *J* = 7.2, 6.4 Hz, 4H), 0.88 (s, 18H), 0.04 (s, 12H)

^{13}C-NMR ($CDCl_3$, 100 MHz): δ 169.6, 61.6, 31.9, 27.4, 26.0, 18.4, -5.3

MS: HRMS (ESI+) *m/z* calcd for $C_{20}H_{43}O_5Si_2$ $[M+H]^+$ 419.2644, found 419.2645



3-Formyl-4-hydroxy-5-nitrophenyl acetate (6-2)

To a solution of copper(II) nitrate trihydrate (1.79 g, 7.42 mmol) in acetic anhydride (14.8 mL) at 0 °C under Ar was added dropwise 3-formyl-4-hydroxyphenyl acetate[86] (2.43 g, 13.5 mmol) in acetic anhydride (14.6 mL). The reaction was stirred for 1 h at 0 °C then was warmed to rt and stirred for 30 min. The reaction was quenched with ice water at and the aqueous layer was extracted three times with Et_2O. The combined organic layer was washed with

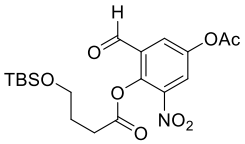
H_2O and brine, then was filtered through SiO_2 gel eluting with Et_2O. After concentrating *in vacuo*, the crude material was purified by flash chromatography (5% to 50% EtOAc in hexanes) to yield nitrophenol **6-2** (1.67 g, 55%) as a bright yellow solid.

IR (cm^{-1}, neat): 3248, 3085, 2876, 1769, 1688, 1547, 1460, 1430, 1367, 1247, 1198, 1021, 932, 864, 779

^{1}H-NMR ($CDCl_3$, 400 MHz): δ 11.21 (s, 1H), 10.39 (s, 1H), 8.11 (d, *J* = 2.8 Hz, 1H), 7.86 (d, *J* = 2.8 Hz, 1H), 2.33 (s, 3H)

^{13}C-NMR ($CDCl_3$, 100 MHz): δ 188.0, 169.0, 154.3, 142.4, 134.9, 130.4, 126.1, 124.4, 20.9

MS: HRMS (ESI–) *m/z* calcd for $C_9H_6O_6N$ $[M–H]^-$ 224.0190, found 224.0213



4-Acetoxy-2-formyl-6-nitrophenyl 4-((*tert*-butyldimethylsilyl)oxy)butanoate (7-3)

To a solution of nitrophenol **6-2** (0.597 g, 2.65 mmol) in 1,2-dichloroethane (14.9 mL) at 0 °C under N_2, was added **7-5** (4.44 g, 10.6 mmol) via syringe using 1,2-dichloroethane (1 mL) to transfer. Pyridine (0.235 mL, 0.231 g, 2.92 mmol) was added and the reaction was warmed to rt. After stirring for 4 h, saturated aqueous NH_4Cl was added followed by EtOAc. The organic layer was washed three times with saturated aqueous $CuSO_4$ and brine, dried over Na_2SO_4, and concentrated *in vacuo*. The crude material was purified by flash chromatography (SiO_2 dried at 130 °C under high vacuum for 30 min, 5% to 30% EtOAc in hexanes – $MgSO_4$ was mixed in with the sand (1:1) above the silica gel) to yield aldehyde **7-3** (0.805 g, 71%). The product is a stable, white solid but readily hydrolyzes on wet silica gel. The starting anhydride was recovered (2.62 g, 59%) and could be reused for additional acylations.

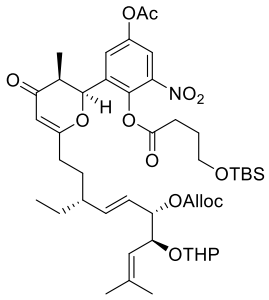
IR (cm^{-1}, neat): 3090, 2931, 2857, 1778, 1703, 1613, 1588, 1544, 1464, 1350, 1257, 1186, 1101, 1020, 919, 838, 778, 709

^{1}H-NMR ($CDCl_3$, 400 MHz): δ 10.16 (s, 1H), 8.11 (d, *J* = 3.2 Hz, 1H), 7.93 (d, *J* = 2.8 Hz, 1H), 3.74 (t, *J* = 6.0 Hz, 2H), 2.85 (t, *J* = 7.2 Hz, 2H), 2.37 (s, 3H), 2.01 (tt, *J* = 7.2, 6.0 Hz, 2H), 0.91 (s, 9H), 0.07 (s, 6H)

^{13}C-NMR ($CDCl_3$, 100 MHz): δ 185.6, 171.2, 168.4, 148.0, 143.4, 142.8, 131.4, 127.5, 124.6, 61.7, 30.6, 27.6, 26.1, 21.0, 18.5, –5.2

MS: HRMS (ESI+) *m/z* calcd for $C_{19}H_{28}O_8NSi$ $[M+H]^+$ 426.1579, found 426.1580

Final Synthetic Route: Synthesis of Cyclized Amide 7-1



4-Acetoxy-2-((2*S*,3*S*)-6-((3*R*,6*S*,7*S*,*E*)-6-(((allyloxy)carbonyl)oxy)-3-ethyl-9-methyl-7-((tetrahydro-2H-pyran-2-yl)oxy)deca-4,8-dien-1-yl)-3-methyl-4-oxo-3,4-dihydro-2H-pyran-2-yl)-6-nitrophenyl 4-((*tert*-butyldimethylsilyl)oxy)butanoate (7-2)

Diene **6-11** (100 mg, 0.173 mmol) and aldehyde **7-3** (88.5 mg, 0.208 mmol) were loaded into a 2 mL vial using THF to transfer then placed under high vacuum for 2 h. Jacobsen's catalyst (SbF_6)[39] (11.9 mg, 17.3 μmol), 4Å MS (17 mg), and a stir bar were added. The vial was placed under high vacuum for 30 min, then backfilled with Ar (balloon). Acetone (34 μL) was added via syringe. The Ar balloon was removed and the entire vial cap was wrapped in parafilm. The vial was placed in a larger vessel fitted with a septum, backfilled with N_2 (manifold), and wrapped in aluminum foil. The reaction was then stirred overnight. Additional Jacobsen's catalyst (6.0 mg, 8.7 μmol) and acetone (5 μL) were added. The reaction vial was backfilled with Ar (balloon), placed in the larger vessel (backfilled with N_2) then stirred

overnight. The reaction mixture was diluted with dry CH_2Cl_2 (4.3 mL) and added to a separate round bottom flask containing 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (70.8 mg, 0.312 mmol) and $NaHCO_3$ (52.4 mg, 0.624 mmol) at 0 °C under N_2. The reaction was warmed to rt and stirred overnight. The mixture was filtered (syringe filter) onto a flash column (SiO_2 dried for 30 min, 140 °C, high vacuum) and eluted with 5% MeOH in CH_2Cl_2. The crude material was purified by flash column (SiO_2 dried 30 min, 140 °C, high vacuum, 5% to 40% EtOAc in hexanes) to yield dihydropyrone **7-2** (69.4 mg, 45%) as a dark yellow oil.

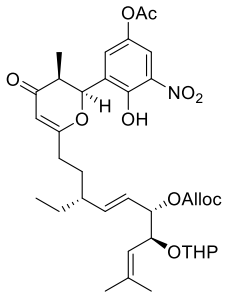
IR (cm^{-1}, neat): 2932, 2857, 1777, 1747, 1673, 1611, 1542, 1346, 1254, 1185, 1110, 838, 781

^{1}H-NMR ($CDCl_3$, 400 MHz): δ 7.92 (d, *J* = 2.8 Hz, 1H), 7.63 (d, *J* = 3.2, Hz, 0.5H), 7.62 (d, *J* = 3.6 Hz, 0.5H), 5.98-5.87 (m, 1H), 5.53 (br s, 1H), 5.49 (dd, *J* = 6.8, 2.8 Hz, 0.5H), 5.45 (dd, *J* = 6.8, 2.4 Hz, 0.5H), 5.42 (dd, *J* = 6.8, 2.4 Hz, 0.5H), 5.37-5.32 (m, 2.5H), 5.24 (br d, *J* = 10.5 Hz, 1H), 5.17 (t, *J* = 7.6 Hz, 0.5H), 5.14 (d, *J* = 9.6 Hz, 0.5H), 5.09 (t, *J* = 7.2 Hz, 0.5H), 4.95 (d, *J* = 9.6 Hz, 0.5H), 4.82 (br s, 0.5H), 4.65-4.61 (m, 2.5H), 4.51 (t, *J* = 8.0 Hz, 0.5H), 4.40 (dd, *J* = 9.6, 8.4 Hz, 0.5H), 3.92 (app t, *J* = 10.0 Hz, 0.5H), 3.80 (app t, *J* = 9.2 Hz, 0.5H), 3.69 (t, *J* = 6.0 Hz, 2H), 3.52-3.49 (m, 0.5H), 3.45-3.42 (m, 0.5H), 2.73 (t, *J* = 8.0 Hz, 2H), 2.53-2.51 (m, 1H), 2.37 (s, 3H), 2.33-2.28 (m, 1H), 2.20-2.11 (m, 1H), 1.94 (quint, *J*= 6.8 Hz, 2H), 1.90-1.85 (m, 1H), 1.78-1.68 (m, 9H), 1.54-1.37 (m, 6H), 1.34-1.25 (m, 1H), 0.89 (br s, 12H), 0.83 (q, *J* = 7.2 Hz, 1.5H), 0.82 (q, *J* = 7.2 Hz, 1.5H), 0.06 (s, 3H), 0.05 (s, 3H)

^{13}C-NMR ($CDCl_3$, 125 MHz, asterisk denotes THP isomer): δ 196.0, 176.5, 171.0, 168.5, 154.7, 154.5*, 147.8, 142.1, 140.2, 139.0, 138.9*, 138.1, 137.1*, 133.9, 131.9, 131.9*, 126.6, 126.2, 126.0*, 122.0, 120.7*, 119.2, 118.8, 118.7*, 103.3, 99.4, 93.4*, 81.1, 80.3*, 78.1, 78.0*, 75.0, 71.7*, 68.4, 68.4*, 62.2, 61.7, 61.2*, 44.4, 43.0, 32.4, 31.3, 30.7, 30.5*, 28.0, 27.6, 26.1, 26.1, 25.8, 25.7, 25.5, 21.1, 19.4, 18.8*, 18.7, 18.6*, 18.4, 11.7, 10.6*, –2.9, –5.2*

MS: HRMS (ESI+) *m/z* calcd for $C_{46}H_{67}O_{14}NNaSi$ $[M+Na]^+$ 908.4223, found 908.4181

Optical Rotation: $[\alpha]_D^{18}$ = – 3.71 (*c* = 0.35, $CHCl_3$)



3-((2*S*,3*S*)-6-((3*R*,6*S*,7*S*,*E*)-6-(((Allyloxy)carbonyl)oxy)-3-ethyl-9-methyl-7-((tetrahydro-2H-pyran-2-yl)oxy)deca-4,8-dien-1-yl)-3-methyl-4-oxo-3,4-dihydro-2H-pyran-2-yl)-4-hydroxy-5-nitrophenyl acetate (7-6)

A solution of dihydropyrone **7-2** (0.245 g, 0.276 mmol) in THF (2 mL) was added via syringe to a plastic reaction vessel charged with THF (3.9 mL), pyridine (1.5 mL), and HF-pyridine (70% HF, 0.32 mL) at rt. The mixture was stirred for 5.5 h then was diluted with Et_2O followed by 0.1 M pH 7 sodium phosphate buffer. The aqueous layer was extracted three times with EtOAc. The combined organic layers were washed three times with saturated aqueous $CuSO_4$ and once with brine, then was dried over Na_2SO_4 and concentrated *in vacuo*. After drying overnight on the high vacuum, the crude material was purified by flash chromatography (4.5 inches SiO_2, 5% to 50% EtOAc in hexanes) to yield nitrophenol **7-6** (0.136 g, 72%) as a bright yellow oil.

IR (cm^{-1}, neat): 3257, 3096, 2934, 2875, 1771, 1747, 1671, 1609, 1544, 1434, 1371, 1253, 1196, 1021, 973, 868, 756

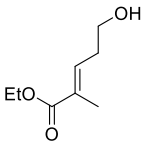
^{1}H-NMR ($CDCl_3$, 400 MHz): δ 10.84 (s, 1H), 7.90 (d, *J* = 2.8 Hz, 1H), 7.58 (d, *J* = 3.2 Hz, 1H), 5.98-5.87 (m, 1H), 5.78 (d, *J* = 2.8 Hz, 1H), 5.53-5.41 (m, 1.5H), 5.36-5.32 (m, 2.5H), 5.24 (br d, *J* = 10.4 Hz, 1H), 5.18 (t, *J* = 7.6 Hz, 0.5H), 5.14 (d, *J* = 10.0 Hz, 0.5H), 5.10 (t, *J* = 7.6 Hz, 0.5H), 4.94 (d, *J* = 10.0 Hz, 0.5H), 4.82 (br s, 0.5H), 4.64-4.60 (m, 2.5H), 4.50 (dd, *J* = 10.0, 8.0 Hz, 0.5H), 4.40 (t, *J* = 9.2 Hz, 0.5H), 3.95 (app t, *J* = 10.8 Hz, 0.5H), 3.80 (app t, *J* = 8.4 Hz, 0.5H), 3.50 (br d, *J* = 11.2 Hz, 0.5H), 3.44-3.41 (m, 0.5H), 2.81-2.76 (m, 1H), 2.35 (s, 3H), 2.35-

2.28 (m, 1H), 2.21-2.12 (m, 1H), 1.90 (qt, *J* = 8.4, 4.0 Hz, 1H), 1.80-1.60 (m, 3H), 1.72 (s, 1.5H), 1.70 (s, 1.5H), 1.68 (s, 3H), 1.55-1.38 (m, 6H), 1.34-1.28 (m, 1H), 0.88 (d, *J* = 7.2 Hz, 3H), 0.82 (t, *J* = 7.2 Hz, 1.5H), 0.81 (t, *J* = 7.2 Hz, 1.5H)

^{13}C-NMR ($CDCl_3$, 150 MHz, asterisk denotes THP isomer): δ 196.7, 176.4, 169.2, 154.7, 154.5*, 149.0, 142.5, 140.2, 140.1*, 139.1, 139.0*, 137.2, 133.2, 131.9, 131.8*, 129.4, 129.3*, 126.2, 126.0*, 122.0, 120.7*, 118.9, 118.8*, 117.3, 103.4, 99.4, 93.3*, 81.1, 80.3*, 77.9, 74.9, 71.6*, 68.4, 68.4*, 62.3, 61.2*, 44.4, 44.4*, 41.9, 41.8*, 32.4, 31.4, 31.4*, 30.7, 30.5, 28.0, 28.0*, 26.2, 25.7, 25.5*, 21.1, 19.5, 18.8*, 18.7, 18.6*, 11.8, 10.6*

MS: HRMS (ESI+) *m/z* calcd for $C_{36}H_{48}O_{12}N$ $[M+H]^+$ 686.3171, found 686.3159

Optical Rotation: $[\alpha]_D^{18}$ = – 16.5 (*c* = 1.30, $CHCl_3$)

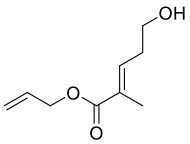


Ethyl (*E*)-5-hydroxy-2-methylpent-2-enoate (5-10)

To a solution of (carbethoxyethylidene)triphenylphosphorane (2.28 g, 6.31 mmol), MnO_2 (4.57 g, 52.6 mmol, 10 μm, 90%) in CH_2Cl_2 (94 mL) at rt under N_2 was added 1,3-propanediol (0.19 mL, 0.2 g, 2.63 mmol) via syringe. The reaction was stirred 24 h at rt then was filtered through Celite. The filtrate was washed with CH_2Cl_2 then the combined organic layer was concentrated *in vacuo*. The crude product was purified by flash chromatography (5% to 40% EtOAc in hexanes) to yield compound **5-10** (0.197 g, 47%).

^{1}H-NMR ($CDCl_3$, 400 MHz): δ 6.78 (td, *J* = 7.2, 1.2 Hz, 1H), 4.19 (q, *J* = 7.2 Hz, 2H), 3.76 (q, *J* = 6.4 Hz, 2H), 2.46 (qd, *J* = 6.4, 0.8 Hz, 2H), 1.87 (d, *J* = 1.2 Hz, 3H), 1.51 (t, *J* = 5.2 Hz, 1H), 1.29 (t, *J* = 7.2 Hz, 3H)

These data are consistent with literature values[82]



Allyl (*E*)-5-hydroxy-2-methylpent-2-enoate (5-11)

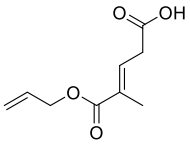
A stock solution of NaOAllyl/HOAllyl was freshly prepared by adding NaH (0.125 g, 60% in mineral oil) to allyl alcohol (9.52 mL, dried over 3Å MS) under N_2. To compound **5-10** (0.365 g, 2.31 mmol) at rt under N_2 was added the stock solution (7 mL, 2.31 mmol NaOAllyl) and the reaction was stirred for 24 h. The reaction was diluted with EtOAc then H_2O. The organic layer was washed twice with H_2O and brine, then was dried over Na_2SO_4 and concentrated *in vacuo*. The crude product was purified by flash chromatography (10% to 40% EtOAc in hexanes) to yield compound **5-11** (0.206 g, 53%) as a clear liquid.

IR (cm^{-1}, neat): 3424, 2953, 1629, 1648, 1444, 1274, 1130, 1049, 928, 744

^{1}H-NMR ($CDCl_3$, 500 MHz): δ 6.82 (td, *J* = 7.5, 1.5 Hz, 1H), 5.95 (ddt, *J* = 16.0, 11.0, 5.5 Hz, 1H), 5.33 (dd, *J* = 17.0, 1.0 Hz, 1H), 5.23 (dd, *J* = 10.5, 1.0 Hz, 1H), 4.65 (d, *J* = 5.5 Hz, 2H), 3.76 (t, *J* = 5.5 Hz, 2H), 2.47 (q, *J* = 6.5 Hz, 2H), 1.89 (s, 3H), 1.56 (br s, 1H)

^{13}C-NMR ($CDCl_3$, 125 MHz): δ 167.7, 138.4, 132.6, 130.2, 118.1, 65.4, 61.6, 32.3, 12.7

MS: HRMS (ESI+) *m/z* calcd for $C_9H_{15}O_3$ $[M+H]^+$ 171.1016, found 171.1012



(*E*)-5-(Allyloxy)-4-methyl-5-oxopent-3-enoic acid (5-12)

A 2M aqueous solution of Jones reagent was freshly prepared by adding H_2O (total volume = 10 mL) to CrO_3 (2.0 g, 20 mmol) and H_2SO_4 (2.1 mL, 40 mmol) in a 10 mL volumetric flask at 0 °C.

Jones reagent (5.94 mL, 2 eq) was added dropwise to compound **5-11** (1.01 g, 5.93 mmol) in acetone (83 mL) at 0 °C. The reaction was stirred for 20 min at 0 °C then additional Jones reagent (1.5 mL, 0.5 eq) was added. The reaction was stirred for 20 min at 0 °C, quenched with 2-propanol, then was diluted with H_2O. The aqueous layer was extracted seven times with

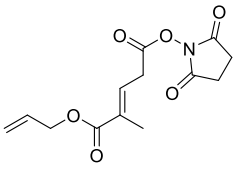
EtOAc. The combined organic layer was washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The crude product was purified by flash chromatography (20% to 80% EtOAc in hexanes) to yield acid **5-12** (0.809 g, 75%) as a clear oil.

IR (cm^{-1}, neat): 3424, 2942, 1712, 1651, 1422, 1261, 1125, 908, 733

^{1}H-NMR ($CDCl_3$, 400 MHz): δ 6.93 (tq, *J* = 7.2, 1.6 Hz, 1H), 5.96 (ddt, *J* = 17.2, 10.4, 5.6 Hz, 1H), 5.34 (dq, *J* = 17.2, 1.6 Hz, 1H), 5.25 (dq, *J* = 10.8, 1.6 Hz, 1H), 4.66 (dt, *J* = 5.6, 1.2 Hz, 2H), 3.29 (dd, *J* = 7.2, 0.8 Hz, 2H), 1.89 (d, *J* = 1.2 Hz, 3H)

^{13}C-NMR ($CDCl_3$, 100 MHz): δ 176.6, 167.1, 132.3, 132.3, 131.2, 118.3, 65.6, 34.0, 12.9

MS: HRMS (ESI+) *m/z* calcd for $C_9H_{13}O_4$ $[M+H]^+$ 185.0808, found 185.0807



1-Allyl 5-(2,5-dioxopyrrolidin-1-yl) (*E*)-2-methylpent-2-enedioate (5-13)

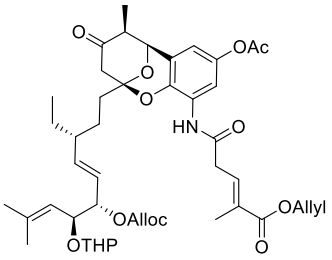
Acid **5-12** (0.25 g, 1.36 mmol) in MeCN (4 mL) was added to *N,N'*-disuccinimidyl carbonate (0.382 g, 1.49 mmol) at rt under N_2. Pyridine (109 µL, 0.107 g, 1.36 mmol) was added and the reaction was stirred for 5h. The reaction was diluted with EtOAc and H_2O. The organic layer was washed with brine, dried over Na_2SO_4, then concentrated *in vacuo*. The crude product was purified by flash chromatography (5% to 50% EtOAc in hexanes) to yield succinimidyl ester **5-13** (0.263 g, 67%) as a clear oil.

IR (cm^{-1}, neat): 2948, 1816, 1784, 1740, 1650, 1366, 1259, 1207, 1077, 994.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ 6.92 (tq, *J* = 6.8, 1.2 Hz, 1H), 5.95 (ddt, *J* = 17.2, 10.4, 5.6 Hz, 1H), 5.34 (dq, *J* = 17.2, 1.2 Hz, 1H), 5.25 (dq, *J* = 10.4, 1.2 Hz, 1H), 4.66 (dt, *J* = 5.6, 1.2 Hz, 2H), 2.54 (dd, *J* = 7.2, 1.2 Hz, 2H), 2.85 (br s, 4H), 1.92 (d, *J* = 1.2 Hz, 3H)

^{13}C-NMR ($CDCl_3$, 100 MHz): δ 169.1, 166.6, 165.9, 132.6, 132.2, 129.9, 118.3, 65.6, 30.8, 25.7, 13.0

MS: HRMS (ESI–) *m/z* calcd for $C_{13}H_{14}O_6N$ $[M-H]^-$ 280.0816, found 280.0820



Allyl (*E*)-5-(((2*S*,5*S*,6*S*)-8-acetoxy-2-((3*R*,6*S*,7*S*,*E*)-6-(((allyloxy)carbonyl)oxy)-3-ethyl-9-methyl-7-((tetrahydro-2H-pyran-2-yl)oxy)deca-4,8-dien-1-yl)-5-methyl-4-oxo-3,4,5,6-tetrahydro-2H-2,6-epoxybenzo[b]oxocin-10-yl)amino)-2-methyl-5-oxopent-2-enoate (7-1)

Nitro group reduction

Powdered Zn was activated by washing sequentially with 2 x 2% HCl, 3 x H_2O, 2 x MeOH, and 1 x Et_2O, then allowed to dry overnight on the high vacuum.

1,4-Dioxane:H_2O (6:1, 1.6 mL) was added to nitro-phenol **7-6** (34.8 mg, 50.7 µmol) in a vial at rt. NH_4Cl (0.271 g, 5.07 mmol) was added to the reaction vial followed by activated powdered Zn (0.332 g, 5.07 mmol) and the reaction was vigorously stirred for 1 h. The mixture was diluted with EtOAc then decanted five times. The combined organic layer was filtered (syringe filter), washed once with 3% ethylenediaminetetraacetic acid disodium salt, dried over Na_2SO_4, and concentrated *in vacuo*. The product was dried on the high vacuum 15 min to yield crude aniline **7-7** (37.2 mg), that was immediately used in the next step without further purification (product is unstable if stored for long periods of time).

Amidation

Anhydrous 1,4-dioxane was degassed using the freeze-pump-thaw method then stored under Ar. Under an Ar atmosphere, crude aniline **7-7** (50.7 µmol) was dissolved in 1,4-dioxane (0.46 mL) then added via gas tight syringe to succinimidyl ester **5-13** (71.3 mg, 0.254 mmol) in a 1 dram vial under Ar. To the mixture was added 2,6-lutidine (6.5 µL, 6.0 mg, 56 µmol) via syringe,

which was then stirred overnight. The reaction was diluted with EtOAc, washed twice with H_2O and once with saturated aqueous $NaHCO_3$ and brine, then was dried over Na_2SO_4 and concentrated *in vacuo*. Unreacted succinimidyl ester **5-13** was removed by flash chromatography (5% to 40% EtOAc in benzene) to yield uncyclized amide **7-8** (5 mg) and a crude mixture containing **7-8** and cyclized amide **7-1** (31.6 mg).

Cyclization

To the crude mixture of **7-8** and **7-1** was added 1,2-dichloroethane (3.8 mL) followed by Et_3N (1.0 µL, 0.78 mg, 7.7 µmol) under N_2. The reaction was stirred for 24 h then was diluted with EtOAc. The organic layer was washed with 2 x 1% aqueous HCl, saturated aqueous $NaHCO_3$ and brine, then was dried over Na_2SO_4 and concentrated *in vacuo*. The crude product was purified by flash chromatography (5 inches SiO_2, 5% to 30% EtOAc in benzene) to yield cyclized amide **7-1** (total: 19.2 mg, 46% over 3 steps) as a slightly yellow oil.

IR (cm^{-1}, neat): 3355, 2934, 1747, 1721, 1535, 1445, 1369, 1253, 1204, 1116, 1019, 972, 786, 734

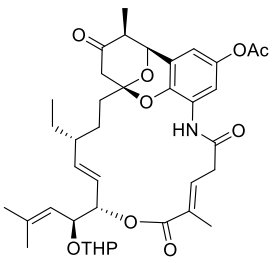
^{1}H-NMR ($CDCl_3$, 500 MHz): δ 8.08 (br s, 0.5H), 8.06 (br s, 0.5H), 7.60 (br s, 0.5H), 7.51 (br s, 0.5H), 7.01 (t, *J* = 7.5 Hz, 1H), 6.41 (d, *J* = 1.5 Hz, 1H), 6.00-5.87 (m, 2H), 5.59-5.43 (m, 2H), 5.41-5.31 (m, 2H), 5.26-5.22 (m, 2H), 5.20-5.14 (m, 1H), 5.11 (t, *J* = 7.0 Hz, 0.5H), 5.08 (d, *J* = 5.5 Hz, 1H), 4.96 (d, *J* = 9.5 Hz, 0.5H), 4.81 (br d, *J* = 2.5 Hz, 0.5H), 4.66 (d, *J* = 5.5 Hz, 2H), 4.65-4.59 (m, 2.5H), 4.51 (t, *J* = 7.0 Hz, 0.5H), 4.40 (t, *J* = 7.5 Hz, 0.5H), 3.92 (br t, *J* = 11.0 Hz, 0.5H), 3.80 (br t, *J* = 9.5 Hz, 0.5H), 3.50 (app dd, *J* = 9.5, 3.5 Hz, 0.5H), 3.43 (app dd, *J* = 10.0, 5.0 Hz, 0.5H), 3.32 (d, *J* = 7.0 Hz, 2H), 3.06 (quint, *J* = 6.5 Hz, 1H), 2.71-2.59 (m, 2H), 2.24 (s, 3H), 1.94 (s, 3H), 1.94-1.87 (m, 1H), 1.83-1.75 (m, 2H), 1.73-1.62 (m, 9H), 1.48-1.38 (m, 6H), 1.34-1.28 (m, 1H), 1.06 (d, *J* = 7.0 Hz, 3H), 0.84 (t, *J* = 7.5 Hz, 1.5H), 0.83 (t, *J* = 7.0 Hz, 1.5H)

^{13}C-NMR ($CDCl_3$, 150 MHz, asterisk denotes THP isomer): δ 205.2, 169.7, 167.1, 166.9, 154.7, 154.6*, 143.3, 140.0, 139.3, 139.2*, 137.0, 136.3, 133.1, 133.1*, 132.3, 132.3*, 131.9, 131.8*, 126.8, 126.8*, 125.7, 125.5*, 121.9, 120.7*, 118.9, 118.8*, 118.5, 118.5, 118.4*, 114.5, 113.5, 104.7, 99.4, 93.4*, 81.0, 80.3*, 75.9, 75.0, 71.8*, 68.5, 68.4*, 65.7, 62.3, 61.3*, 50.7, 50.3*, 49.0, 44.3, 44.3*, 38.4, 37.6, 30.7, 30.5*, 27.9, 27.6, 26.2, 25.8, 25.5*, 21.2, 19.5, 18.8*, 18.7, 13.1, 11.8, 9.9

MS: HRMS (ESI+) *m/z* calcd for $C_{45}H_{60}O_{13}N$ $[M+H]^+$ 822.4059, found 822.4013

Optical Rotation: $[\alpha]_D^{18}$ = + 22.0 (*c* = 0.41, $CHCl_3$)

Final Synthetic Route: Synthesis of Divergolides E and H



Compound 7-10

Deallylation:

Amide **7-1** (18.3 mg, 22.3 μmol) in 1,2-dichloroethane (0.78 mL) was added to a 1 dram vial containing $Pd(PPh_3)_4$ (1.0 mg, 0.89 μmol) under N_2. Freshly distilled Bu_3SnH (13.2 μL, 14.3 g, 49.0 μmol) was added via syringe followed by glacial AcOH (3.8 μL, 4.0 mg, 67 μmol). The reaction was stirred for 15 min at rt then diluted with EtOAc. The organic layer was washed three times with H_2O and brine, then was dried over Na_2SO_4 and concentrated *in vacuo*. The tin by-products were removed using flash chromatography (20% to 40% EtOAc in hexanes followed by 1:80:9 to 1:99:0, MeOH:EtOAc:hexanes) to yield crude seco acid **7-9** (7.8 mg, 50% crude yield) as a clear gel, contaminated with triphenylphosphine oxide. The crude product was used in the next step without further purification.

Macrolactonization:

A stock solution of 4-(dimethylamino)pyridine (3.7 mg/0.69 mL CH_2Cl_2) was freshly prepared under N_2. To a solution of 2-methyl-6-nitrobenzoic anhydride (4.9 mg, 14 µmol) in CH_2Cl_2 (4 mL) at rt under N_2, was added 50 µL of the 4-(dimethylamino)pyridine stock solution (0.27 mg, 2.2 µmol). Et_3N (4.3 µL, 3.1 mg, 31 µmol) was added followed by a solution of seco acid **7-9** (6.0 mg, 8.6 µmol) in CH_2Cl_2 (2 mL) added dropwise over 3 h. The reaction was stirred for an additional 1 h then was diluted with EtOAc. The organic layer was washed with 2% aqueous HCl, saturated aqueous $NaHCO_3$, and brine, then was dried over Na_2SO_4 and concentrated *in vacuo*. The crude material was purified by flash chromatography (4 inches SiO_2, 5% to 50% EtOAc in hexanes) to yield compound **7-10** (2.9 mg, 49%) as a clear gel which solidifies to a white-yellow crystal upon storage in the freezer. The ^{1}H-NMR shows a potential minor isomer.

IR (cm^{-1}, neat): 3393, 2933, 2873, 1764, 1719, 1532, 1445, 1363, 1205, 1118, 1019, 980, 737

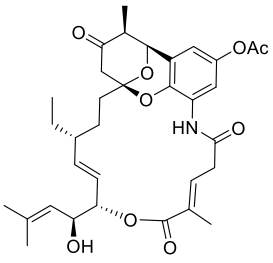
^{1}H-NMR ($CDCl_3$, 600 MHz, major product): δ 8.11 (d, *J* = 2.4 Hz, 0.5H), 8.10 (d, *J* = 3.0 Hz, 0.5H), 7.81 (br s, 0.5H), 7.80 (br s, 0.5H), 6.98 (t, *J* = 9.0 Hz, 1H), 6.39 (d, *J* = 2.4 Hz, 1H), 5.68-5.55 (m, 1.5H), 5.37-5.34 (m, 0.5H), 5.32-5.24 (m, 1H), 5.21 (d, *J* = 10.2 Hz, 0.5H), 5.07 (d, *J* = 5.4 Hz, 1H), 5.00 (d, *J* = 9.6 Hz, 0.5H), 4.88 (t, *J* = 3.0 Hz, 0.5H), 4.66 (t, *J* = 2.4 Hz, 0.5H), 4.53 (dd, *J* = 9.6, 7.8 Hz, 0.5H), 4.45 (dd, *J* = 9.0, 7.8 Hz, 0.5H), 3.93 (td, *J* = 11.4, 1.8 Hz, 0.5H), 3.80 (td, *J* = 10.8, 1.8 Hz, 0.5H), 3.56-3.41 (m, 2H), 3.36-3.24 (m, 1H), 3.06 (dq, *J* = 13.2, 6.6 Hz, 1H), 2.65 (d, *J* = 1.2 Hz, 1H), 2.64 (s, 1H), 2.25 (s, 1.5H), 2.24 (s, 1.5H), 1.97 (s, 1.5H), 1.96 (s, 1.5H), 1.81-1.72 (m, 9H), 1.69-1.63 (m, 3H), 1.57-1.49 (m, 5H), 1.39-1.33 (m, 1H), 1.28-1.21 (m, 1H), 1.05 (d, *J* = 7.2 Hz, 1.5H), 1.03 (d, *J* = 7.2 Hz, 1.5H), 0.83 (t, *J* = 7.2 Hz, 3H)

^{13}C-NMR ($CDCl_3$, 150 MHz, asterisk denotes THP isomer): δ 205.0, 169.8, 166.0, 165.9, 143.2, 139.9, 137.0*, 136.8, 136.4, 136.3*, 135.8, 135.7*, 131.3, 131.1*, 127.8, 127.7*, 126.7, 126.7*,

121.7, 120.5*, 118.3, 114.5, 113.0, 104.6, 99.1, 93.6*, 76.1, 76.0*, 75.1, 75.0*, 74.0, 72.3*, 62.1, 61.3*, 52.0, 49.0, 43.7, 43.6*, 38.6, 37.9*, 37.6, 37.5*, 30.7, 30.6*, 28.9, 28.9*, 27.8, 27.7*, 26.2, 25.8, 25.6*, 21.2, 19.3, 18.9*, 18.7, 13.1, 11.9, 9.9

MS: HRMS (ESI+) *m/z* calcd for $C_{38}H_{50}O_{10}N$ $[M+H]^+$ 680.3429, found 680.3416

Optical Rotation: $[\alpha]_D^{22}$ = + 30.5 (*c* = 0.41, $CHCl_3$)



Compound S11

A stock solution of pyridinium *p*-toluenesulfonate (7.1 mg/0.32 mL EtOH) was freshly prepared under N_2. To a solution of compound **7-10** (6.0 mg, 8.8 µmol) in EtOH (0.46 mL) in a small vial under N_2, was added 20 µL of the pyridinium *p*-toluenesulfonate stock solution (0.44 mg, 1.8 µmol). The cap was wrapped in parafilm and the reaction was warmed to 60 °C. After stirring for 8 h, the reaction was diluted with Et_2O and washed twice with brine:H_2O (1:1). The organic layer was dried over Na_2SO_4 and concentrated *in vacuo* to yield the crude product **S11** (4.4 mg, 84%) as a slightly yellow solid. The crude product was used in the following step without further purification.

The simplified spectrum, without the THP isomers, confirms the presence of an isomer (1/3 total mass).

IR (cm^{-1}, neat): 3390, 2925, 2854, 1761, 1714, 1536, 1446, 1362, 1206, 1127, 1018, 981, 927, 736

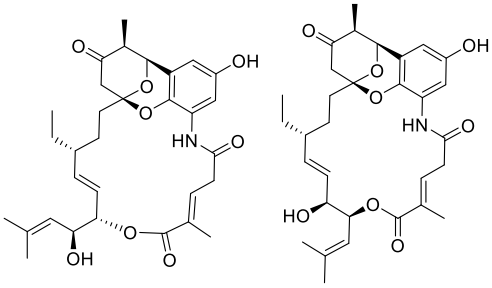
^{1}H-NMR ($CDCl_3$, 400 MHz, major product): δ 8.11 (d, *J* = 2.4 Hz, 1H), 7.81 (br s, 1H), 7.01 (t, *J* = 8.0 Hz, 1H), 6.39 (d, *J* = 2.8 Hz, 1H), 5.59 (dd, *J* = 15.6, 4.8 Hz, 1H), 5.30 (dd, *J* = 15.6, 9.2 Hz, 1H), 5.22-5.17 (m, 2H), 5.07 (d, *J* = 5.2 Hz, 1H), 4.46 (t, *J* = 8.8 Hz, 1H), 3.46 (dd, *J* = 17.2,

8.8 Hz, 1H), 3.32 (dd, *J* = 17.2, 7.6 Hz, 1H), 3.06 (m, 1H), 2.65 (s, 2H), 2.25 (s, 3H), 1.98 (s, 3H), 1.77-1.71 (m, 9H), 1.64-1.54 (m, 2H), 1.43-1.35 (m, 1H), 1.35-1.19 (m, 1H + grease), 1.02 (d, *J* = 6.8 Hz, 3H), 0.83 (t, *J* = 7.2 Hz, 3H)

^{13}C-NMR ($CDCl_3$, 150 MHz): δ 205.1, 169.8, 166.2, 165.8, 143.2, 139.2, 137.1, 136.7, 135.7, 131.7, 127.5, 126.7, 122.1, 118.3, 114.5, 113.0, 104.5, 76.8, 76.0, 70.5, 52.0, 49.0, 43.7, 38.5, 37.5, 28.9, 27.7, 26.1, 21.2, 18.9, 13.2, 11.9, 9.9

MS: HRMS (ESI+) *m/z* calcd for $C_{33}H_{42}O_9N$ $[M+H]^+$ 596.2854, found 596.2841

Optical Rotation: $[\alpha]_D^{22}$ = + 23.7 (*c* = 0.44, $CHCl_3$)



Divergolides E and H

A solution of compound **S11** (2.8 mg, 4.7 µmol) in 1,2-dichloroethane (0.45 mL) was added to Me_3SnOH (25.6 mg, 0.14 mmol) in a small vial at rt under N_2. The cap was wrapped in parafilm and the reaction warmed to 65 °C. After 2 h, the reaction was cooled to rt and concentrated *in vacuo*. The residue was redissolved in EtOAc and washed five times with 0.01 M aqueous $KHSO_4$, brine, dried over Na_2SO_4, then concentrated *in vacuo*. The crude product was purified by flash chromatography (40% to 80% EtOAc in hexanes) to yield divergolide **E** (1.4 mg) and the acyl migrated natural product, divergolide **H** (0.5 mg – further purified by flash chromatography 20% to 60% EtOAc in benzene) each as white solids (total: 1.9 mg, 73%).

Divergolide E:

^{1}H-NMR ($CDCl_3$, 700 MHz): δ 8.21 (d, *J* = 2.8 Hz, 1H), 8.09 (br s, 1H), 7.91 (s, 1H), 7.00 (t, *J* = 7.7 Hz, 1H), 6.19 (d, *J* = 2.1 Hz, 1H), 5.58 (dd, *J* = 15.4, 4.9 Hz, 1H), 5.32 (dd, *J* = 15.4, 9.1 Hz,

1H), 5.21-5.19 (m, 2H), 5.03 (d, *J* = 5.6 Hz, 1H), 4.46 (t, *J* = 8.4 Hz, 1H), 3.49 (dd, *J* = 16.8, 8.4 Hz, 1H), 3.33 (dd, *J* = 16.8, 7.7 Hz, 1H), 3.04 (m, 1H), 2.62 (d, *J* = 15.4 Hz, 1H), 2.59 (d, *J* = 15.4 Hz, 1H), 1.97 (s, 3H), 1.80-1.75 (m, 4H) 1.76 (s, 3H), 1.71 (s, 3H), 1.41-1.36 (m, 1H), 1.25-1.21 (m, 1H), 1.16-1.13 (m, 1H), 1.05 (d, *J* = 7.0 Hz, 3H), 0.82 (t, *J* = 7.0 Hz, 3H)

^{13}C-NMR ($CDCl_3$, 176 MHz): δ 205.4, 167.2, 166.1, 150.0, 139.2, 137.1, 136.2, 132.3, 131.0, 127.4, 125.7, 122.0, 118.8, 108.5, 107.2, 103.8, 76.6, 76.1, 70.6, 52.1, 49.1, 43.8, 38.6, 37.2, 28.8, 27.7, 26.1, 18.9, 13.3, 12.0, 9.9

MS: HRMS (ESI+) *m/z* calcd for $C_{31}H_{40}O_8N$ $[M+H]^+$ 554.2748, found 554.2743

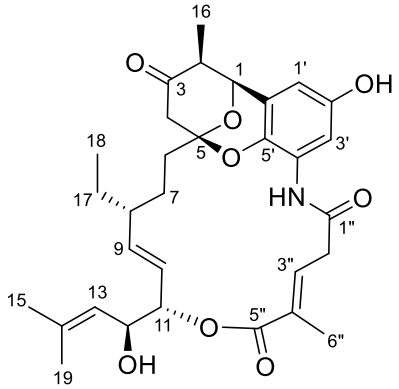
Optical Rotation: $[\alpha]_D^{25}$ = + 31.8 (*c* = 0.085, MeOH)

Divergolide H:

^{1}H-NMR ($CDCl_3$, 600 MHz): δ 7.93 (d, *J* = 2.4 Hz, 1H), 7.62 (s, 1H), 6.84 (td, *J* = 7.8, 0.6 Hz, 1H), 6.18 (d, *J* = 3.0 Hz, 1H), 5.66 (dd, *J* =9.0, 3.0 Hz, 1H), 5.48 (dd, *J* = 15.6, 5.4 Hz, 1H), 5.44 (dd, *J* = 16.2, 7.2 Hz, 1H), 5.27 (br d, *J* = 9.0 Hz, 1H), 5.06 (d, *J* = 5.4 Hz, 1H), 4.34 (m, 1H), 3.45 (dd, *J* = 16.8, 9.6 Hz, 1H), 3.27 (dd, *J* = 17.4, 7.2 Hz, 1H), 3.08 (m, 1H), 2.70 (d, *J* = 15.6 Hz, 1H), 2.61 (d, *J* = 15.0 Hz, 1H), 1.97 (s, 3H), 1.89-1.84 (m, 1H), 1.84 (s, 3H), 1.80 (s, 3H), 1.77-1.72 (m, 2H), 1.43-1.39 (m, 1H), 1.33-1.27 (m, 3H + grease), 1.08 (d, *J* = 7.2 Hz, 3H), 0.89 (t, *J* = 7.2 Hz, 3H)

MS: HRMS (ESI+) *m/z* calculated for $C_{31}H_{40}O_8N$ $[M+H]^+$ 554.2754, found 554.2735

Comparison Between Natural and Synthetic NMR Data



Divergolide **E**

Table 4 Comparison of the NMR data of the isolated (Hertweck)[24] and synthetic (this work) natural products.

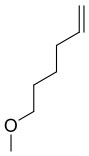
Atom numbering as originally defined by Hertweck.

	Divergolide **E**				Divergolide **H**	
	^{1}H-NMR, δ (*J* in Hz) *		^{13}C-NMR, δ		^{1}H-NMR, δ (*J* in Hz) *	
Position	Natural	Synthetic	Natural	Synthetic	Natural	Synthetic
1’	6.17 (d, 2.7)	6.19 (d, 2.1)	108.3	108.5	6.18 (d, 2.7)	6.18 (d, 3.0)
2’	-	-	149.8	150.0	-	-
3’	8.19 (d, 2.7)	8.21 (d, 2.8)	107.1	107.2	8.13 (d, 2.6)	7.93 (d, 2.4)
4’	-	-	125.6	125.7	-	-
5’	-	-	132.2	132.3	-	-
6’	-	-	118.7	118.8	-	-
1	5.01 (d, 5.4)	5.03 (d, 5.6)	76.0	76.1	5.04 (d, 5.4)	5.06 (d, 5.4)
2	3.02 (m)	3.04 (m)	49.0	49.1	3.06 (m)	3.08 (m)
3	-	-	205.2	205.4	-	-
4	2.61 (15.8), 2.53 (15.8)	2.62 (15.4) 2.59 (15.4)	51.9	52.1	2.68 (15.0) 2.59 (15.0)	2.70 (d, 15.6) 2.61 (d, 15.0)
5	-	-	103.6	103.8	-	-
6	1.75 (m)	1.80-1.75 (m)	38.5	38.6	1.76 (m)	1.77-1.72 (m)
7	1.73 (m), 1.13 (m)	1.80-1.75 (m) 1.16-1.13	27.6	27.7	1.32 (m)	1.33-1.27 (m)

		(m)				
8	1.75 (m)	1.80-1.75 (m)	43.6	43.8	1.85 (m)	1.89-1.84 (m)
9	5.30 (dd, 15.9, 9.4)	5.32 (dd, 15.4, 9.1)	137.0	137.1	5.42 (dd, 15.8, 7.3)	5.44 (dd, 16.2, 7.2
10	5.56 (dd, 15.7, 4.9)	5.58 (dd, 15.4, 4.9)	127.2	127.4	5.46 (dd, 15.8, 5.4)	5.48 (dd, 15.6, 5.4)
11	5.18 (m)	5.21-5.19 (m)	76.7	76.6	4.32 (dd, 5.3, 3.2)	4.34 (m)
12	4.44 (t, 8.9)	4.46 (t, 8.4)	70.4	70.6	5.64 (dd, 9.6, 3.1)	5.66 (dd, 9.0, 3.0)
13	5.19 (m)	5.21-5.19 (m)	121.9	122.0	5.24 (m)	5.27 (br d, 9.0)
14	-	-	139.0	139.2	-	-
15	1.74 (s)	1.76 (s)	25.9	26.1	1.83 (d, 1.1)	1.84 (s)
16	1.03 (d, 6.9)	1.05 (d, 7.0)	9.8	9.9	1.06 (d, 6.9)	1.08 (d, 7.2)
17	1.39-1.20 (m)	1.41-1.36 (m) 1.25-1.21 (m)	28.7	28.8	1.40 (m) 1.27 (m)	1.43-1.39 (m) 1.33-1.27 (m)
18	0.80 (t, 7.4)	0.82 (t, 7.0)	11.8	12.0	0.87 (t, 7.4)	0.89 (t, 7.2)
19	1.69 (s)	1.71 (s)	18.7	18.9	1.78 (d, 1.1)	1.80 (s)
1”	-	-	167.0	167.2	-	-
2”	3.48 (dd, 17.5, 8.5); 3.31 (dd, 17.4, 7.8)	3.49 (dd, 16.8, 8.4); 3.33 (dd, 16.8, 7.7	37.1	37.2	3.41 (dd, 17.2, 9.4); 3.22 (dd, 17.5, 6.7)	3.45 (dd, 16.8, 9.6) 3.27 (dd, 17.4, 7.2)
3”	6.98 (ddd, 8.5, 7.7, 1.1)	7.00 (t, 7.7)	130.9	131.0	6.82 (td, 8.5, 1.4)	6.84 (td, 7.8, 0.6)
4”	-	-	136.0	136.2	-	-
5”	-	-	165.9	166.1	-	-
6”	1.95 (d, 1.1)	1.97 (s)	13.0	13.3	1.95 (d, 1.0)	1.97 (s)
NH	7.89 (s)	7.91 (s)	-	-	7.62 (s)	7.62 (s)
Ar-OH	8.08 (br s)	8.09 (br s)	-	-	-	-

*Chemical shifts calibrated to residual $CHCl_3$ peak. ^{1}H-NMR: Hertweck = 7.24 ppm; Floreancig = 7.26 ppm.

Model Studies: Synthesis of Diene 3-2

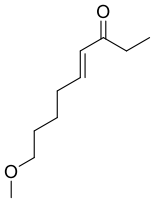


6-methoxyhex-1-ene[96]

A two-neck round bottom flask, equipped with a reflux condenser, was charged with NaH (60% w/w in mineral oil, 1.60 g, 40.0 mmol). The flask was placed under Ar and dry hexanes (10 mL, dried over 4Å MS) was added followed by 5-hexen-1-ol (4.8 mL, 4.0 g, 40 mmol). The mixture was refluxed 3 h then cooled to rt. Methyl iodide (3.2 mL, 7.4 g, 52 mmol) was added dropwise via syringe and the apparatus was wrapped in aluminum foil. The reaction was refluxed for 2 h, cooled to rt, then quenched with H_2O. The aqueous layer was extracted three times with Et_2O. The combined organic layer was dried over Na_2SO_4, then careful concentrated via rotary evaporation to remove most of the solvent. The crude material was purified by fractional distillation (45 °C (70 °C bath)/80 mmHg) to yield the title compound (2.04 g, 45%)

^{1}H-NMR ($CDCl_3$, 400 MHz): δ 5.79 (ddt, *J* = 16.8, 10.4, 6.8 Hz, 1H), 4.99 (dd, *J* =17.2, 1.6 Hz, 1H), 4.93 (dd, *J* = 10.4, 0.8 Hz, 1H), 3.35 (t, *J* = 6.4 Hz, 2 H), 3.31 (s, 3H), 2.05 (q, *J* = 7.2 Hz, 2H), 1.60-1.53 (m, 2H), 1.46-1.39 (m, 2H).

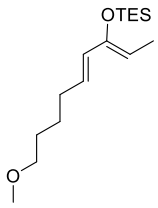
These data are consistent with literature values.[96]



(*E*)-9-methoxynon-4-en-3-one (3-1)[97]

Hoveyda-Grubbs second generation metathesis catalyst (5.48 mg, 8.75 μmol) was added to a solution of 6-methoxyhex-1-ene (0.20 g, 1.75 mmol), ethyl vinyl ketone (0.52 mL, 0.44 g, 5.3 mmol), and CH_2Cl_2 (7.5 mL) under Ar. The reaction was stirred 3 h at rt then concentrated *in vacuo*. The crude material was purified by flash chromatography (neutral alumina, 5% EtOAc in hexanes) to yield compound **3-1** (0.271 g, 91%).

^{1}H-NMR (C_6D_6, 300 MHz): δ 6.57 (dt, *J* = 15.9, 6.9 Hz, 1H), 5.94 (dt, *J* = 15.9, 1.5 Hz, 1H), 3.11 (s, 3H), 3.10 (t, *J* = 6.0 Hz, 2H), 2.15 (q, *J* = 7.2 Hz, 2H), 1.81 (qd, *J* = 7.2, 1.5 Hz, 2H), 1.43-1.23 (m, 4H), 1.03 (t, *J* = 7.2 Hz, 3H).

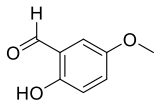


(((2*Z*,4*E*)-9-methoxynona-2,4-dien-3-yl)oxy)triethylsilane (3-2)[37]

Triethylsilyl trifluoromethanesulfonate (0.4 mL, 0.46 g, 1.8 mmol) was added via syringe to a stirred solution of compound **3-1** (0.228 g, 1.34 mmol), Et_3N (0.38 mL, 0.27 g, 2.7 mmol), and Et_2O (30 mL) under N_2 at –78 °C. The reaction was warmed to 0 °C and stirred for 70 min. Aqueous saturated $NaHCO_3$ was added and the aqueous layer was extracted three times with EtOAc. The combined organic layer was washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The crude material was purified by flash chromatography (neutral alumina, 0% to 2% EtOAc in hexanes) to yield the desired product **3-2** (0.253 g, 66%).

^{1}H-NMR (C_6D_6, 400 MHz): δ6.00-5.88 (m, 2H), 4.70 (q, *J* = 6.8 Hz, 1H), 3.17 (t, *J* = 6.4 Hz, 2H), 3.10 (s, 3H), 2.03 (q, *J* = 7.2 Hz, 2H), 1.67 (d, *J* = 7.2 Hz, 3H), 1.60-1.42 (m, 4H), 1.14 (t, *J* = 8.0 Hz, 9 H), 0.74 (q, *J* = 8.0 Hz, 6 H).

Model Studies: Synthesis of Aldehyde 3-4 and Core Structure 3-10



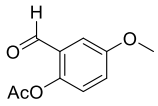
2-hydroxy-5-methoxybenzaldehyde (3-3)[38b]

A two-neck round bottom flask, equipped with a condenser, was charged with 4-methoxyphenol (0.817 g, 6.58 mmol) and anhydrous $MgCl_2$ (0.940 g, 9.87 mmol) then placed under N_2. Acetonitrile (50 mL) was added followed by Et_3N (3.4 mL, 2.5 g, 25 mmol).

Paraformaldehyde (1.38 g, 46.1 mmol) was quickly added as a solid. The reaction was refluxed for 2 h then quenched with 5% aqueous HCl (100 mL) at rt. The aqueous layer was extracted three times with Et_2O. The combined organic layer was dried over Na_2SO_4 then concentration *in vacuo*. The crude material was purified by flash chromatography (20% EtOAc in hexanes) to yield compound **3-3** (0.888 g, 89%) as a clear yellow liquid.

^{1}H-NMR ($CDCl_3$, 300 MHz): δ 10.65 (s, 1H), 9.86 (s, 1H), 7.15 (dd, *J* = 9.0, 3.0 Hz, 1H), 7.00 (d, *J* = 3.0 Hz, 1H), 6.94 (d, *J* = 9.0 Hz, 1H), 3.82 (s, 3H).

These data are consistent with literature values.[38b]

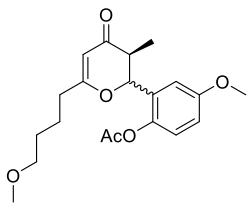


2-formyl-4-methoxyphenyl acetate (3-4)

Acetic anhydride (0.109 mL, 0.118 g, 1.15 mmol) was added to a solution of compound **3-3** (0.157 g, 1.03 mmol) and pyridine (0.66 mL, 0.65 g, 8.2 mmol) at 0 °C under N_2. The reaction was warmed to rt and stirred overnight. H_2O was added and the aqueous layer was extracted three times with EtOAc. The combined organic layer was washed with 10% aqueous HCl, brine, dried over Na_2SO_4, then concentrated *in vacuo* to yield compound **3-4** (0.20 g, 100%) as a yellow solid.

^{1}H-NMR ($CDCl_3$, 300 MHz): δ 10.09 (s, 1H), 7.36 (d, *J* = 3.0 Hz, 1H), 7.17 (dd, *J* = 8.7, 3.0 Hz, 1H), 7.10 (d, *J* = 9.0 Hz, 1H), 3.86 (s, 3H), 2.38 (s, 3H).

These data are consistent with literature values.[98]



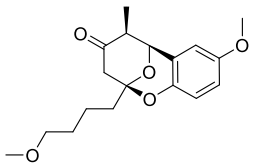
4-methoxy-2-(6-(4-methoxybutyl)-3-methyl-4-oxo-3,4-dihydro-2H-pyran-2-yl)phenyl acetate (3-8)

Me_2AlCl (1M in hexanes, 0.27 mL, 0.27 mmol) was added via syringe to a

solution of aldehyde **3-4** (0.350 g, 1.80 mmol) and diene **3-2** (0.559 g, 1.97 mmol) in toluene (35 mL) at –50 °C under N_2. The reaction was stirred 2 h then quenched with aqueous saturated $NaHCO_3$ at –50 °C. The reaction was warmed to rt then diluted with additional aqueous saturated $NaHCO_3$. The aqueous layer was extracted three times with Et_2O. The combined organic layer was washed with brine, dried over Na_2SO_4, then concentrated *in vacuo* to give crude **3-7** (0.63 g, 73%)

The crude intermediate **3-7** was dissolved in CH_2Cl_2 (20 mL) under air atmosphere and DDQ (0.491 g, 2.16 mmol) was added as a solid in one portion. After TLC showed complete reaction (several minutes), the crude material was directly loaded onto a SiO_2 column and purified by flash chromatography (20% to 40% EtOAc in hexanes) to yield compound **3-8** (0.331 g, 51%, endo:exo 1.61:1).

^{1}H-NMR (C_6D_6, 400 MHz, endo + exo): δ 7.33 (endo, d, *J* = 3.2 Hz, 0.6H), 6.95 (exo, d, *J* = 2.8 Hz, 0.4H), 6.92 (d, *J* = 8.8 Hz, 1H), 6.59-6.54 (endo + exo, m, 1H), 5.59 (endo, d, *J* = 3.2 Hz, 0.6H), 5.48 (exo, s, 0.4H), 5.37 (endo, s, 0.6H), 5.10 (exo, d, *J* = 13.2 Hz, 0.4H), 3.29 (endo, s, 1.8H), 3.23 (exo, s, 1.2H), 3.07-3.02 (m, 5H), 2.75 (endo, qd, *J* = 7.6, 2.8 Hz, 0.6H), 2.65 (exo, dq, *J* = 13.6, 6.8 Hz, 0.4H), 1.89 (t, *J* = 6.4 Hz, 2H), 1.68 (exo, s, 1.2H), 1.63 (endo, s, 1.8H), 1.47-1.33 (m, 4H), 1.07 (exo, d, *J* = 6.8 Hz, 1.2H), 0.94 (endo, d, *J* = 7.2 Hz, 1.8H).



(2*S*,5*S*,6*S*)-8-methoxy-2-(4-methoxybutyl)-5-methyl-2,3,5,6-tetrahydro-4H-2,6-epoxybenzo[b]oxocin-4-one (3-10)

To a solution of K_2CO_3 (0.262 g, 1.90 mmol) in 5:1 MeOH:H_2O (5 mL) was added **3-8** (0.316 g, 0.872 mmol, endo:exo 1.61:1). The reaction was stirred 20 min at rt then diluted with aqueous saturated NH_4Cl. The aqueous layer was extracted three times with EtOAc.

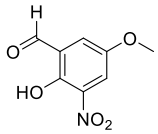
The combined organic layer was washed with brine, dried over Na_2SO_4, then concentrated *in vacuo*. The crude material was purified by flash chromatography (50% EtOAc in hexanes) to yield cyclized **3-10** (0.021 g, 7.5%) and uncyclized **3-9** (0.228 g, 82%), which can be converted to **3-10** by treatment with trifluoroacetic acid (~5 µL, 7.4 mg, 65 µmol) in CH_2Cl_2 over 1.5 days.

^{1}H-NMR ($CDCl_3$, 400 MHz - major diastereomer, uncyclized **3-9**: δ 8.20 (br s, 1H), 6.98 (d, *J* = 2.8 Hz, 1H), 6.80 (d, *J* = 8.8 Hz, 1H), 6.69 (dd, *J* = 8.8, 3.2 Hz, 1H), 5.71 (d, *J* = 3.2 Hz, 1H), 5.39 (s, 1H), 3.75 (s, 3H), 3.38 (t, *J* = 6.0 Hz, 2H), 3.30 (s, 3H), 2.96 (qd, *J* = 7.2, 2.8 Hz, 1H), 2.38 (t, *J* = 6.8 Hz, 2H), 1.72-1.58 (m, 4H), 0.75 (d, *J* = 7.6 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz - major diastereomer, uncyclized **3-9**: δ 200.9, 178.7, 153.0, 146.6, 124.2, 116.0, 113.2, 113.2, 102.7, 79.6, 72.2, 58.6, 55.8, 41.2, 34.7, 29.0, 23.3, 10.7

^{1}H-NMR ($CDCl_3$, 400 MHz - major diastereomer, cyclized **3-10**: δ 6.73-6.66 (m, 2H), 6.41 (d, *J* = 2.0 Hz, 1H), 4.92 (s, 1H), 3.70 (s, 3H), 3.41-3.37 (m, 2H), 3.31 (s, 3H), 2.76 (d, *J* = 16.8 Hz, 1H), 2.60 (q, *J* = 7.6 Hz, 1H), 2.50 (d, *J* = 16.8 Hz, 1H), 1.92-1.89 (m, 2H), 1.64-1.61 (m, 4H), 1.37 (d, *J* = 7.2 Hz, 3H).

Model Studies: Synthesis of Aldehyde 3-6 and Core Structure 3-14



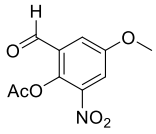
2-hydroxy-5-methoxy-3-nitrobenzaldehyde (3-5)[99]

To a solution of compound **3-3** (1.00 g, 6.57 mmol) in glacial acetic acid (5.5 mL) at 10-15 °C (water bath, cooled with a few ice cubes) was added dropwise a solution of 70% HNO_3 (0.62 mL) in glacial acetic acid (6 mL). The reaction was stirred 1 h at 10-15 °C and turns a viscous orange. The reaction was diluted with H_2O (12 mL) and the yellow precipitate was

filtered. The crude material was purified by flash chromatography (20% to 50% EtOAc in hexanes to yield compound **3-5** (0.607 g, 47%) as a yellow solid.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ 10.89 (s, 1H), 10.45 (s, 1H), 7.85 (d, *J* = 3.2 Hz, 1H), 7.72 (d, *J* = 3.6 Hz, 1H), 3.88 (s, 3H).

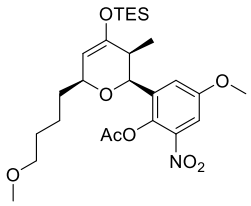
These data are consistent with literature values.[100]



2-formyl-4-methoxy-6-nitrophenyl acetate (3-6)

Acetic anhydride (0.44 mL, 0.48 g, 4.7 mmol) was added via syringe to a bright yellow solution of **3-5** (0.229 g, 1.16 mmol) and pyridine (0.187 mL, 0.184 g, 2.32 mmol) in CH_2Cl_2 (25 mL) at 0 °C under N_2. The reaction was warmed to rt and stirred for 24 h during which the solution turns pale yellow. Aqueous saturated NH_4Cl was added and the aqueous layer was extracted three times with EtOAc. The organic layer was washed with 10% aqueous HCl, brine, dried over Na_2SO_4 and concentrated *in vacuo*. The crude material was purified by flash chromatography (40% EtOAc in hexanes) to yield compound **3-6** (0.274 g, 99%) as a pale-yellow solid. The solution should remain nearly clear/pale yellow throughout the workup.

^{1}H-NMR ($CDCl_3$, 300 MHz): δ 10.15 (s, 1H), 7.83 (d, *J* = 3.0 Hz, 1H), 7.66 (d, *J* = 3.3 Hz, 1H), 3.93 (s, 3H), 2.45 (s, 3H).



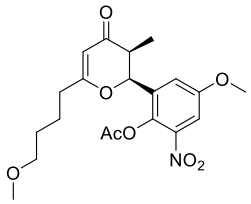
4-methoxy-2-((2*S*,3*S*,6*S*)-6-(4-methoxybutyl)-3-methyl-4-((triethylsilyl)oxy)-3,6-dihydro-2H-pyran-2-yl)-6-nitrophenyl acetate (3-11)

A 1-dram vial fitted with a septum screw cap was charged with Jacobsen's catalyst - Cl anion (12 mg, 26 μmol, 7 mol%), 4Å MS (0.1 g), and aldehyde **3-6** (0.089 g, 0.37 mmol) and placed

under Ar. Diene **3-2** (0.159 g, 0.559 mmol) was added via syringe followed by acetone (40 µL). The reaction was stirred 5 days after which TLC showed no aldehyde remaining. The crude material was directly loaded onto a silica gel column (0% to 20% EtOAc in hexanes) to yield silyl enol ether **3-11** (0.145 g, 75%) as a single diastereomer.

^{1}H-NMR (C_6D_6, 400 MHz): δ 7.68 (d, *J* = 3.2 Hz, 1 H), 7.22 (d, J = 2.8 Hz, 1H), 4.98 (d, *J* = 2.8 Hz, 1H), 4.77 (s, 1H), 4.17 (br s, 1H), 3.21 (t, *J* = 6.0 Hz, 2H), 3.13 (s, 3 H), 3.04 (s, 3H), 2.56 (br s, 1H), 1.85 (s, 3H), 1.65-1.55 (m, 6H), 1.00 (t, *J* = 8.0, 12 H), 0.68 (q, *J* = 7.6 Hz, 6H)

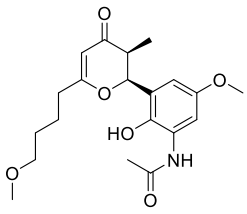
^{13}C-NMR (C_6D_6, 100 MHz): δ 199.7, 168.2, 157.0, 153.7, 142.4, 137.8, 134.5, 120.4, 108.1, 104.3, 74.8, 74.1, 72.6, 58.2, 55.1, 38.3, 36.5, 30.1, 22.2, 20.0, 13.3, 6.8, 5.3



4-methoxy-2-((2*S*,3*S*)-6-(4-methoxybutyl)-3-methyl-4-oxo-3,4-dihydro-2H-pyran-2-yl)-6-nitrophenyl acetate (3-12)

DDQ (0.051 g, 0.225 mmol) was added as a solid in one portion to a solution of **3-11** (0.107 g, 0.204 mmol) in CH_2Cl_2 (6 mL) at rt under Ar. The reaction was stirred for 6.5 h then directly loaded onto a silica gel column (40% EtOAc in hexanes) to yield dihydropyrone **3-12** (72 mg, 87%).

^{1}H-NMR (C_6D_6, 400 MHz): δ 7.38 (d, *J* = 2.4 Hz, 1H), [Ar-H hidden behind benzene], 5.48 (d, *J* = 3.2 Hz, 1H), 5.33 (s, 1H), 3.06 (s, 3H), 3.05 (t, *J* = 5.6 Hz, 2H), 2.97 (s, 3H), 2.67-2.65 (m, 1H), 1.86-1.82 (m, 2H), 1.72 (s, 3H), 1.45-1.29 (m, 4H), 0.80 (d, *J* = 7.6 Hz, 3H).



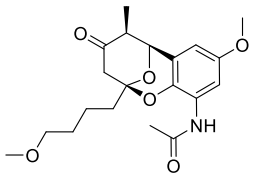
***N*-(2-hydroxy-5-methoxy-3-((2*S*,3*S*)-6-(4-methoxybutyl)-3-methyl-4-oxo-3,4-dihydro-2H-pyran-2-yl)phenyl)acetamide (3-13)**

Iron powder (0.35 g, 6.27 mmol) and conc. 12.1 M HCl (0.05 mL, 0.61

mmol) in H_2O (0.1 mL) was heated for 2 h at 65 °C in a pear-shaped round bottom flask. A scupula tip of the activated iron (black slurry) was added to **3-12** (70 mg, 0.17 mmol) in p-dioxane (2 mL) followed by 25% aqueous NH_4Cl (0.15 mL). The reaction was stirred at 55 °C for 3 h then cooled to 40 °C. Ethanol (20 mL) was added and solution was filtered over celite. The celite pad was washed with additional ethanol and the filtrate was concentrated *in vacuo*. The crude material was suspended in EtOAc, washed with brine, dried over Na_2SO_4, and concentrated *in vacuo.* The crude material was purified by flash chromatography (80% EtOAc in hexanes) to yield compound **3-13** (25 mg, 38%).

^{1}H-NMR ($CDCl_3$, 400 MHz): δ 8.58 (br s, 1H), 8.46 (br s, 1H), 6.91 (s, 1H), 6.55 (s, 1H), 5.77 (s, 1H), 5.33 (s, 1H), 3.73 (s, 3H), 3.37 (t, *J* = 6.0 Hz, 2H), 3.30 (s, 3H), 2.80-2.69 (m, 1H), 2.35 (t, *J* = 6.4 Hz, 2H), 2.23 (s, 3H), 1.68-1.61 (m, 4H), 0.78 (d, *J* = 7.2 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ 198.9, 177.3, 170.9, 152.9, 139.4, 128.3, 126.2, 111.2, 106.9, 103.0, 79.5, 72.2, 58.6, 55.8, 42.2, 34.5, 29.0, 23.5, 23.3, 10.6.

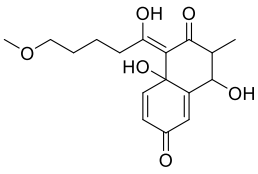


_N_-((2_S_,5_S_,6_S_)-8-methoxy-2-(4-methoxybutyl)-5-methyl-4-oxo-3,4,5,6-tetrahydro-2H-2,6-epoxybenzo[b]oxocin-10-yl)acetamide (3-14)

In a TLC scale test reaction, a small drop of TFA (using a 10 μL syringe) was added to a few milligrams of **3-13** in CH_2Cl_2 (1 mL) under Ar. The reaction was stirred 4 d at rt after which equilibrium had been reached. The reaction was quenched with aqueous saturated $NaHCO_3$ and extracted three times with CH_2Cl_2. ^{1}H-NMR of the crude material showed a 2:1 ratio of cyclized product **3-14** to un-cyclized starting material **3-13** (an isomer or rotamer is apparent in the crude nmr).

^{1}H-NMR ($CDCl_3$, 400 MHz – major, cyclized product): δ 7.95 (d, *J* = 2.0 Hz, 1H), 7.41 (br s, 1H), 6.12 (d, *J* = 2.0 Hz, 1H), 5.02 (d, *J* = 5.2 Hz, 1H), 3.70 (s, 3H), 3.39 (t, *J* = 5.2 Hz, 2H), 3.31 (s, 3H), 3.05 (quin, J = 6.8 Hz, 1H), 2.69 (d, *J* = 15.6 Hz, 1H), 2.63 (d, *J* = 15.2 Hz, 1H), 2.15 (s, 3H), 1.96 (t, *J* = 8.0 Hz, 2H), 1.70-1.57 (m, 4H), 1.05 (d, *J* = 6.8 Hz, 3H).

Model Studies: Oxidative Rearrangement to Compounds 3-15 and 3-16



(*Z*)-4,8a-dihydroxy-1-(1-hydroxy-5-methoxypentylidene)-3-methyl-1,3,4,8a-tetrahydronaphthalene-2,6-dione (3-15)

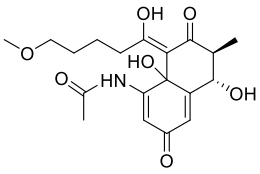
H_2O (1 mL) was added to **3-9** (47 mg, 0.15 mmol). Just enough acetonitrile (several drops) was added until the solution was homogeneous. [Bis(trifluoroacetoxy)iodo]benzene (0.158 g, 0.367 mmol) was added as a solid in one po at rt. The reaction was stirred 5 min then extracted three times with EtOAc. The combined organic layer was washed with brine and concentrated *in vacuo*. The crude material was purified by prep TLC (30% EtOAc in benzene) to yield compounds **3-15a** (major diastereomer):**3-15b** (minor diastereomer):**3-16** - (7:1:2.7, 21 mg, 44%). The dehydration product is also a possible structure for the cyclized compounds.

^{1}H-NMR (C_6D_6, 400 MHz, **3-15a** - major diastereomer): δ 6.40 (d, *J* = 1.6 Hz, 1H), 5.92-5.85 (m, 2H), 4.68 (d, *J* = 12.8 Hz, 1H), 3.08 (t, *J* = 6.0 Hz, 2H), 3.06 (s, 3H), 2.34 (dt, *J* = 14.0, 7.2 Hz, 1H), 2.23 (dt, *J* = 14.8, 7.6 Hz, 1H), 2.12 (dq, *J* = 14.0, 6.8 Hz, 1H), 1.59-1.50 (m, 2H), 1.44-1.38 (m, 2H), 0.74 (d, *J* = 7.2 Hz, 3H)

^{13}C-NMR (C_6D_6, 100 MHz, **3-15a** - major diastereomer): δ 186.3, 184.9, 171.3, 143.1, 135.6, 135.5, 133.7, 111.4, 78.0, 71.9, 58.2, 44.2, 32.3, 29.3, 22.9, 10.6

MS: LCMS (ES) *m/z* calculated for $C_{17}H_{23}O_6$ $[M+H]^+$ 323, found 323.

^{1}H-NMR (C_6D_6, 400 MHz, **3-16** - linear, uncyclized): δ 6.75 (app t, *J* = 2.0 Hz, 1H), 5.98 (dd, *J* = 10.4, 2.4 Hz, 1H), 5.90 (d, *J* = 10.0 Hz, 1H), 5.28 (s, 1H), 5.09 (dd, *J* = 2.8, 1.6 Hz, 1H), 3.10 (2, 3H), 3.07 (t, *J* = 6.0 Hz, 2H), 2.72 (qd, *J* = 7.2, 2.8 Hz, 1H), 1.81 (t, *J* = 6.8 Hz, 2H), 1.46-1.31 (m, 4H), 0.66 (d, *J* = 7.6 Hz, 3H).



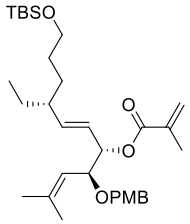
***N*-((5*S*,6*S*)-5-hydroxy-8-(5-methoxypentanoyl)-6-methyl-3,7-dioxo-3,5,6,7-tetrahydronaphthalen-1-yl)acetamide (3-17)**

H_2O (1 mL) was added to **3-13** (14 mg, 37 µmol) at rt. Acetonitrile (several drops) was added until the solution was homogeneous. [Bis(trifluoroacetoxy)iodo]benzene (39 mg, 91 µmol) was added as a solid in one portion at rt. The reaction was stirred for 5 min then extracted three times with EtOAc. The combined organic layer was washed with brine and concentrated *in vacuo* to give compound **3-17** (8 mg, 57%). The dehydration product is also a possible structure.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ 7.99 (br s, 1H), 7.61 (d, *J* = 2.4 Hz, 1H), 6.89 (app t, *J* = 2.0 Hz, 1H), 5.44 (dd, *J* = 2.4, 1.6 Hz, 1H), 3.37 (t, *J* = 6.0 Hz, 2H), 3.31 (s, 3H), 2.87 (qd, *J* = 7.2, 2.8 Hz, 1H), 2.64 (t, *J* = 7.6 Hz, 2H), 2.24 (s, 3H), 1.76-1.68 (m, 2H), 1.65-1.58 (m, 2H), 1.53 (s, 3H), 0.96 (d, *J* = 7.2 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ 188.1, 186.9, 181.3, 172.3, 169.3, 139.6, 138.2, 134.6, 114.9, 111.1, 72.0, 58.7, 42.6, 32.3, 29.7, 29.2, 24.9, 22.9, 10.5

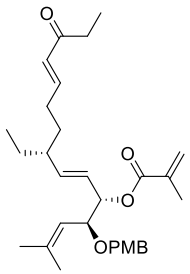
Unproductive Routes: Synthesis of Diene 4-3 and Aldehyde 4-4



(4*S*,5*S*,8*R*,*E*)-11-((*tert*-butyldimethylsilyl)oxy)-8-ethyl-4-((4-methoxybenzyl)oxy)-2-methylundeca-2,6-dien-5-yl methacrylate (4-20)

Crude compound **4-19** (2.38 g, 4.99 mmol) in CH_2Cl_2 (60 mL) was added to 4-(dimethylamino)pyridine (0.128 g, 1.05 mmol) under Ar at rt. The solution was cooled to 0 °C and Et_3N (2.1 mL, 1.5 g, 15 mmol) was added followed by methacrylic anhydride (94% pure, 1.9 mL, 2.0 g, 13 mmol). The reaction was stirred overnight at rt then quenched by addition of saturated aqueous $NaHCO_3$ followed by H_2O (1:9 $NaHCO_3$ solution:H_2O). The aqueous layer was extracted three times with CH_2Cl_2. The combined organic layer was washed with saturated aqueous NH_4Cl, brine, dried over Na_2SO_4, then concentrated *in vacuo*. The crude material was purified by flash chromatography (0% to 7.5% EtOAc in hexanes) to yield compound **4-20** (2.24 g, 83%).

^{1}H-NMR ($CDCl_3$, 400 MHz): δ 7.20 (d, *J* = 8.4 Hz, 2H), 6.84 (d, *J* = 8.4 Hz, 2H), 6.10 (s, 1H), 5.55 (s, 1H), 5.46-5.28 (m, 3H), 5.07 (d, *J* = 9.6 Hz, 1H), 4.53 (d, *J* = 12.0 Hz, 1H), 4.30 (d, *J* = 12.0 Hz, 1H), 4.14 (dd, *J* = 9.6, 7.2 Hz, 1H), 3.79 (s, 3H), 3.54 (t, *J* = 6.0 Hz, 2H), 1.94 (s, 3H), 1.85-1.76 (m, 1H), 1.76 (s, 3H), 1.60 (s, 3H), 1.47-1.13 (m, 6H), 0.88 (s, 9H), 0.78 (t, *J* = 7.2 Hz, 3H), 0.03 (s, 6H)



(4*S*,5*S*,6*E*,8*R*,11*E*)-8-ethyl-4-((4-methoxybenzyl)oxy)-2-methyl-13-oxopentadeca-2,6,11-trien-5-yl methacrylate (4-21)

Prepared analogously to compound **6-9**.

Deprotection:

From compound **4-20** (1.39 g, 2.55 mmol), NH_4F (2.08 g, 56.1 mmol) and MeOH (50 mL). The crude alcohol (1.09 g, 99% crude) was used in the next step without further purification.

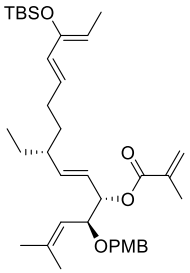
Oxidation:

From the crude alcohol (500 mg, 1.16 mmol) in CH_2Cl_2 (1.5 mL); oxalyl chloride (117 µL, 176 mg, 1.39 mmol) in CH_2Cl_2 (5.4 mL); dimethylsulfoxide (198 µL, 218 mg, 2.78 mmol) in CH_2Cl_2 (0.78 mL); and Et_3N (0.49 mL, 0.35 g, 3.5 mmol). The crude aldehyde (0.497 g, 99% crude) was used in the next step without further purification.

HWE Reaction:

From the crude aldehyde (0.494 g, 1.15 mmol), $EtC(O)CH_2P(O)(OMe)_2$[95] (0.375 g, 2.09 mmol), 1,8-diazabicycloundec-7-ene (0.265 g, 1.74 mmol), LiCl (88.4 mg, 2.09 mmol) and MeCN (14 mL). The crude material was purified by flash chromatography (1 inch SiO_2, 5% to 20% EtOAc in hexanes) to yield compound **4-21** (0.421 g, 74% over 3 steps).

^{1}H-NMR ($CDCl_3$, 400 MHz): δ 7.20 (d, *J* = 8.8 Hz, 2H), 6.83 (d, *J* = 8.8 Hz, 2H), 6.76 (dt, *J* = 16.0, 7.2 Hz, 1H), 6.10 (br s, 1H), 6.04 (dt, *J* = 16.0, 1.6 Hz, 1H), 5.56 (app t, *J* = 1.6 Hz, 1H), 5.43-5.32 (m, 3H), 5.08 (dt, *J* = 9.6, 1.2 Hz, 1H), 4.53 (d, *J* = 12.0 Hz, 1H), 4.30 (d, *J* = 12.0 Hz, 1H), 4.16 (dd, *J* = 9.6, 6.8 Hz, 1H), 3.79 (s, 3H), 2.53 (q, *J* = 7.2 Hz, 2H), 2.19-1.97 (m, 2H), 1.94 (s, 3H), 1.84 (qt, *J* = 8.8, 4.4 Hz, 1H), 1.75 (d, *J* = 0.8 Hz, 3H), 1.60 (d, *J* = 0.8 Hz, 3H), 1.53-1.29 (m, 4H), 1.09 (t, *J* = 7.2 Hz, 3H), 0.79 (t, *J* = 7.6 Hz, 3H).

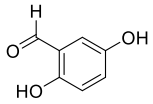


(4*S*,5*S*,6*E*,8*R*,11*E*,13*Z*)-13-((*tert*-butyldimethylsilyl)oxy)-8-ethyl-4-((4-methoxybenzyl)oxy)-2-methylpentadeca-2,6,11,13-tetraen-5-yl methacrylate (4-3)

Prepared analogously to compound **6-11**. From compound **4-21** (54.9 mg, 0.114

mmol), *tert*-butyldimethylsilyl trifluoromethanesulfonate (157 µL, 0.180 g, 0.683 mmol), *N*,*N*-diisopropylethylamine (169 µL, 0.125 g, 0.967 mmol), and Et_2O (0.7 mL). The crude material was purified by flash chromatography (1.5 inches SiO_2, 0% to 10% EtOAc in hexanes) to yield compound **4-3** (49.5 mg, 73%).

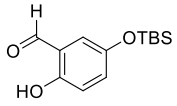
^{1}H-NMR ($CDCl_3$, 300 MHz): δ 7.21 (d, *J* = 11.6 Hz, 2H), 6.84 (d, *J* = 11.6 Hz, 2H), 6.10 (s, 1H), 5.81-5.63 (m, 2H), 5.49 (app t, *J* = 2.4 Hz, 1H), 5.46-5.27 (m, 3H), 5.09 (dt, *J* = 13.2, 2.0 Hz, 1H), 4.71 (q, *J* = 8.8 Hz, 1H), 4.54 (d, *J* = 16.0 Hz, 1H), 4.31 (d, *J* = 16.0 Hz, 1H), 4.16 (dd, *J* = 12.8, 9.2 Hz, 1H), 3.79 (s, 3H), 2.05-1.81 (m, 3H), 1.95 (s, 3H), 1.75 (d, *J* = 1.2 Hz, 3H), 1.61 (d, *J* = 6.4 Hz, 3H), 1.60 (d, *J* = 2.0 Hz, 3H), 1.43-1.16 (m, 4H), 1.00 (s, 9H), 0.77 (t, *J* = 9.6 Hz, 3H), 0.10 (s, 6H).



2,5-dihydroxybenzaldehyde (4-22)

BBr_3 solution (1M in CH_2Cl_2, 38 mL, 38 mmol) was added slowly dropwise to 2,5-dimethoxybenzaldehyde (3.00 g, 18.1 mmol) in CH_2Cl_2 (18 mL) at –78 °C under Ar. The reaction was stirred 50 min at –78 °C, warmed to 0 °C then stirred an additional 1h. H_2O was slowly added and the aqueous layer was extracted three times with Et_2O. The combined organic layer was washed with brine, dried over Na_2SO_4, then concentrated *in vacuo*. The crude material was purified by flash chromatography (dry load onto SiO_2, 30% EtOAc in hexanes) to yield compound **4-22** (2.27 g, 93%) as a yellow solid.

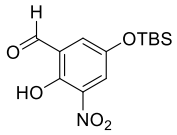
^{1}H-NMR ($CDCl_3$, 400 MHz): δ 10.60 (s, 1H), 9.83 (s, 1H), 7.07 (dd, *J* = 8.8, 2.8 Hz, 1H), 7.00 (d, *J* = 3.2 Hz, 1H), 6.90 (d, *J* = 8.8 Hz, 1H), 4.56 (s, 1H).



5-((*tert*-butyldimethylsilyl)oxy)-2-hydroxybenzaldehyde (4-23)

Tert-butyldimethylsilyl chloride (2.64 g, 17.5 mmol) was added as a solid in portions to a solution of compound **4-22** (2.27 g, 16.7mmol), imidazole (1.71 g, 25.1 mmol), and CH_2Cl_2 (67 mL) at 0 °C under Ar. The reaction was stirred overnight at rt then diluted with CH_2Cl_2 (400 mL) and washed three times with H_2O, twice with brine, dried over Na_2SO_4, then concentrated *in vacuo*. The crude material was purified by flash chromatography (10% to 30% EtOAc in hexanes) to yield compound **4-23** (3.61 g, 86%).

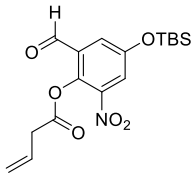
^{1}H-NMR ($CDCl_3$, 400 MHz): δ 10.63 (s, 1H), 9.81 (s, 1H), 7.05 (dd, *J* = 8.8 2.8 Hz, 1H), 6.97 (d, *J* = 3.2 Hz, 1H), 6.87 (d, *J* = 8.8 Hz, 1H), 0.99 (s, 9H), 0.19 (s, 6H).



5-((*tert*-butyldimethylsilyl)oxy)-2-hydroxy-3-nitrobenzaldehyde (4-24)

Prepared analogous to compound **6-2**. From compound **4-23** (3.61 g, 14.3 mmol) in acetic anhydride (15 mL); copper(II) nitrate trihydrate (1.90 g, 7.86 mmol) in acetic anhydride (15 mL). The crude material was purified by flash chromatography (5% EtOAc in hexanes) to yield compound **4-24** (2.70 g, 63%) along with starting material **4-23** (0.183 g, 8%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ 10.92 (s, 1H), 10.41 (s, 1H), 7.78 (d, *J* = 4.4 Hz, 1H), 7.61 (d, *J* = 4.0 Hz, 1H), 0.99 (s, 9H), 0.23 (s, 6H)



4-((*tert*-butyldimethylsilyl)oxy)-2-formyl-6-nitrophenyl but-3-enoate (4-4)

Preparation of 3-butenoic anhydride:

N,N'-dicyclohexylcarbodiimide (0.856 g, 4.15 mmol) in CH_2Cl_2 (18 mL) was added (0.55 mL/min) to 3-butenoic acid (0.75 g, 8.7 mmol) in CH_2Cl_2 (9 mL) at rt under Ar. The reaction was stirred 3 h, filtered, then concentrated *in vacuo*. The material was redissolved in a

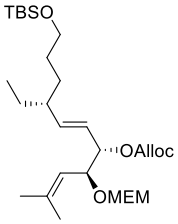
small amount of Et_2O. The precipitate was filtered then the solvent removed *in vacuo* to yield the anhydride (0.50 g), which was used in the next step without further purification.

Preparation of Compound **4-4**:

3-Butenoic anhydride (0.166 g, 1.08 mmol) in CH_2Cl_2 (1.62 mL) was added to compound **4-24** (80.0 mg, 0.269 mmol) at 0 °C under Ar. Pyridine (43 µL, 43 mg, 0.54 mmol) was added and the reaction was stirred 4 h at rt. Saturated aqueous NH_4Cl was added and the aqueous layer was extracted three times with CH_2Cl_2. The combined organic layer was washed twice with 1% aqueous HCl, brine, dried over Na_2SO_4, then concentrated *in vacuo*. The crude material was purified by flash chromatography (2 inches SiO_2, 10% EtOAc in hexanes) followed by heating 4 h at 55 °C under high vacuum (to remove excess acid/anhydride) to yield compound **4-4** (71.4 mg, 73%)

^{1}H-NMR ($CDCl_3$, 400 MHz): δ 10.10 (s, 1H), 7.74 (d, *J* = 3.2 Hz, 1H), 7.57 (d, *J* = 3.2 Hz, 1H), 6.04 (ddt, *J* = 17.2, 10.4, 7.2 Hz, 1H), 5.36 (dq, *J* = 13.2, 1.6 Hz, 1H), 5.32 (dq, *J* = 6.0, 1.2 Hz, 1H), 3.50 (dt, *J* = 7.2, 1.2 Hz, 2H), 1.00 (s, 9H), 0.28 (s, 6H).

Unproductive Routes: Synthesis of Diene 5-2 and Aldehyde 5-3



allyl ((8*S*,9*S*,12*R*,*E*)-12-ethyl-17,17,18,18-tetramethyl-8-(2-methylprop-1-en-1-yl)-2,5,7,16-tetraoxa-17-silanonadec-10-en-9-yl) carbonate (5-6)

PMB deprotection:

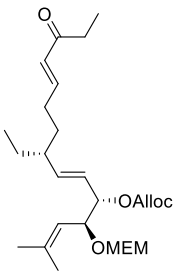
Prepared analogously to compound **S10**. From compound **5-5** (0.607 g, 1.08 mmol), 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (0.295 g, 1.30 mmol), and CH_2Cl_2:pH 7 phosphate buffer (18:1, 13mL). The crude reaction mixture was directly loaded onto a 1 inch

plug of SiO_2 and eluted with 30% EtOAc in hexanes to yield the crude alcohol (0.624 g), which was quickly reprotected in the next step to prevent cyclization of the alcohol with the adjacent allyl carbonate group.

MEM protection:

N,*N*-diisopropylethylamine (0.79 mL, 0.59 g, 4.5 mmol) was added to the above alcohol (0.476 g, 1.08 mmol) in CH_2Cl_2 (3.8 mL) followed quickly by 2-methoxyethoxymethyl chloride (0.50 mL, 0.54 g, 4.3 mmol) at 0 °C under Ar. The reaction was stirred 2 h at rt then quenched by addition of 10% aqueous $NaHCO_3$. The aqueous layer was extracted three times with CH_2Cl_2. The combined organic layer was washed with saturated aqueous NH_4Cl, brine, dried over Na_2SO_4, then concentrated *in vacuo*. The crude material was purified by flash chromatography (0% to 1.5% EtOAc in hexanes) to yield compound **5-6** (0.386 g, 68% over 2 steps).

^{1}H-NMR ($CDCl_3$, 400 MHz): δ 5.90 (ddt, *J* = 16.4, 10.8, 6.0 Hz, 1H), 5.49 (dd, *J* = 15.6, 9.2 Hz, 1H), 5.35-5.21 (m, 3H), 5.06 (t, *J* = 8.0 Hz, 1H), 4.95 (d, *J* = 9.6 Hz, 1H), 4.70 (d, *J* = 6.8 Hz, 1H), 4.63-4.59 (m, 3H), 4.42 (dd, *J* = 10.0, 8.0 Hz, 1H), 3.80 (dd, *J* = 4.8 Hz, 1H), 3.59-3.49 (m, 5H), 3.38 (s, 3H), 1.89-1.79 (m, 1H), 1.71 (d, *J* = 1.2 Hz, 3H), 1.67 (d, *J* = 1.2 Hz, 3H), 1.47-1.30 (m, 4H), 1.27-1.13 (2H), 0.87 (s, 9H), 0.78 (t, *J* = 7.2 Hz, 3H), 0.02 (s, 6H).



allyl ((4*S*,5*S*,6*E*,8*R*,11*E*)-8-ethyl-4-((2-methoxyethoxy)methoxy)-2-methyl-13-oxopentadeca-2,6,11-trien-5-yl) carbonate (5-7)

Prepared analogously to compound **6-9**.

TBS deprotection:

From compound **5-6** (0.208 g, 0.393 mmol), NH_4F (0.321 g, 8.65 mmol) and MeOH (7.8 mL). The crude alcohol (0.147 g, 90% crude) was used in the next step without further purification.

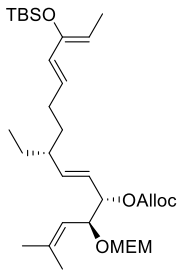
Swern oxidation:

From the crude alcohol (0.147 g, 0.355 mmol) in CH_2Cl_2 (0.46 mL); oxalyl chloride (36 µL, 54 mg, 0.43 mmol) in CH_2Cl_2 (1.6 mL); dimethylsulfoxide (60 µL, 67 mg, 0.85 mmol) in CH_2Cl_2 (0.66 mL); and Et_3N (148 µL, 108 mg, 1.06 mmol). The crude aldehyde was used in the next step without further purification.

HWE reaction:

From the crude aldehyde (146 mg, 0.355 mmol), $EtC(O)CH_2P(O)(OMe)_2$[95] (140 mg, 0.777 mmol), 1,8-diazabicycloundec-7-ene (81.0 mg, 0.532 mmol), LiCl (32 mg, 0.76 mmol), and MeCN (4.3 mL). The crude material was purified by flash chromatography (1 inch SiO_2, 0% to 20% EtOAc in hexanes) to yield compound **5-7** (85.2 mg, 51% over 2 steps)

^{1}H-NMR ($CDCl_3$, 400 MHz): δ 6.76 (dt, *J* = 15.6, 6.8 Hz, 1H), 6.04 (d, *J* = 15.6 Hz, 1H), 5.90 (ddt, *J* = 16.0, 10.4, 5.6 Hz, 1H), 5.47 (dd, *J* = 15.2, 8.8 Hz, 1H), 5.35-5.29 (m, 2H), 5.23 (app dd, *J* = 10.4, 1.2 Hz, 1H), 5.07 (t, *J* = 7.6 Hz, 1H), 4.95 (app d, *J* = 9.6 Hz, 1H), 4.70 (d, *J* = 6.8 Hz, 1H), 4.63-4.59 (m, 3H), 4.44 (dd, *J* = 10.0, 8.0 Hz, 1H), 3.80 (dd, *J* = 7.6, 4.8 Hz, 1H), 3.59-3.49 (m, 3H), 3.37 (s, 3H), 2.53 (q, *J* = 7.2 Hz, 2H), 2.17-1.96 (m, 2H), 1.92-1.82 (m, 1H), 1.70 (d, *J* = 1.2 Hz, 3H), 1.68 (d, *J* = 1.2 Hz, 3H), 1.55-1.45 (m, 1H), 1.44-1.30 (m, 2H), 1.29-1.18 (m, 1H), 1.08 (t, *J* = 7.2 Hz, 3H), 0.79 (t, *J* = 7.6 Hz, 3H).

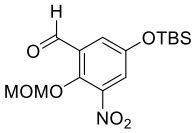


allyl ((8*S*,9*S*,10*E*,12*R*,15*E*,17*Z*)-12-ethyl-17-ethylidene-19,19,20,20-tetramethyl-8-(2-methylprop-1-en-1-yl)-2,5,7,18-tetraoxa-19-silahenicosa-10,15-dien-9-yl) carbonate (5-2)

Prepared analogously to compound **6-11**. From compound **5-7** (200 mg, 0.428 mmol), *tert*-butyldimethylsilyl trifluoromethanesulfonate (0.59 mL, 0.68 g, 2.6 mmol), *N*,*N*-

diisopropylethylamine (0.64 mL, 0.47 g, 3.6 mmol), and Et_2O (3 mL). The crude material was purified by flash chromatography (1.5 inches SiO_2, 0% to 10% EtOAc in hexanes) to yield compound **5-2** (0.168 g, 68%).

^{1}H-NMR ($CDCl_3$, 400 MHz): δ 5.92 (ddt, *J* = 16.0, 10.4, 5.6 Hz, 1H), 5.78 (d, *J* = 15.6 Hz, 1H), 5.68 (dt, *J* = 13.6, 6.8 Hz, 1H), 5.48 (dd, *J* = 15.2, 9.2 Hz, 1H), 5.36-5.23 (m, 2H), 5.24 (app dd, 10.4, 1.2 Hz, 1H), 5.08 (t, *J* = 8.0 Hz, 1H), 4.97 (dt, *J* = 10.0, 1.2 Hz, 1H), 4.72 (d, *J* = 6.8 Hz, 2H), 4.64-4.60 (m, 3H), 4.44 (dd, *J* = 9.6, 8.0 Hz, 1H), 3.82 (dd, *J* = 7.6, 4.8 Hz, 1H), 3.76-3.73 (m, 1H), 3.60-3.50 (m, 2H), 3.39 (s, 3H), 2.05-1.95 (m, 1H), 1.92-1.82 (m, 2H), 1.72 (d, *J* = 1.2 Hz, 3H), 1.69 (d, *J* = 1.2 Hz, 3H), 1.61 (d, *J* = 7.2 Hz, 3H), 1.45-1.33 (m, 2H), 1.31-1.19 (m, 2H), 1.00 (s, 9H), 0.79 (t, *J* = 7.6 Hz, 3H), 0.10 (s, 6H).

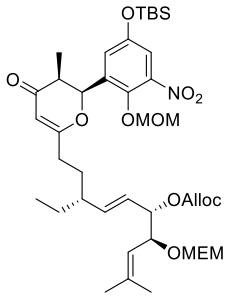


5-((*tert*-butyldimethylsilyl)oxy)-2-(methoxymethoxy)-3-nitrobenzaldehyde (5-3)

N,*N*-diisopropylethylamine (249 µL, 185 mg, 1.43 mmol) then methoxymethyl chloride (technical grade, 96 µL, 102 mg, 1.26 mmol) were added to compound **4-24** (250 mg, 0.841 mmol) under Ar at 0 °C. The reaction was stirred 1 h at rt then quenched by addition of saturated aqueous NH_4Cl at 0 °C. The aqueous layer was extracted three times with CH_2Cl_2. The combined organic layer was washed with brine, dried over Na_2SO_4, then concentrated *in vacuo*. The crude material was purified by flash chromatography (2 inches SiO_2, 5% to 20% EtOAc in hexanes) to yield compound **5-3** (0.232 g, 81%) which solidifies to a yellow solid upon storing in the freezer.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ 10.30 (s, 1H), 7.53 (d, *J* = 3.2 Hz, 1H), 7.51 (d, *J* = 3.2 Hz, 1H), 5.16 (s, 2H), 3.58 (s, 3H), 0.99 (s, 9H), 0.25 (s, 6H).

Unproductive Routes: HDA-DDQ Reaction to Compound 5-8



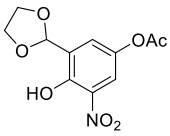
allyl ((4*S*,5*S*,8*R*,*E*)-10-((2*S*,3*S*)-2-(5-((*tert*-butyldimethylsilyl)oxy)-2-(methoxymethoxy)-3-nitrophenyl)-3-methyl-4-oxo-3,4-dihydro-2H-pyran-6-yl)-8-ethyl-4-((2-methoxyethoxy)methoxy)-2-methyldeca-2,6-dien-5-yl) carbonate (5-8)

Aldehyde **5-3** (168 mg, 0.289 mmol), Jacobsen's catalyst [SbF_6][39] (29.8 mg, 43.4 µmol), 4Å MS (43 mg), and a stir bar were added to diene **5-2** (168 mg, 0.289 mmol) in a 1 dram vial. The vial was placed on the high vacuum then backfilled with Ar. Acetone (15 µL) was added and the cap was wrapped in parafilm and the entire vial wrapped in aluminum foil. The reaction was stirred 3 d then additional freshly prepared Jacobsen's catalyst (29.8 mg, 43.4 µmol) was added. The reaction was stirred 3 d then diluted with CH_2Cl_2 (100 mL). To the reaction was added 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (78.9 mg, 0.347 mmol) in CH_2Cl_2 (10 mL). The reaction was stirred 3 d then loaded directly onto a SiO_2 gel column (10% to 30% EtOAc in hexanes) to yield compound **5-8** (89.7 mg, 39%) and recovered enone **5-7** (22.3 mg, 17%).

^{1}H-NMR ($CDCl_3$, 400 MHz): δ 7.30 (d, *J* = 2.8 Hz, 1H), 7.23 (d, *J* = 2.8 Hz, 1H), 5.91 (ddt, *J* = 16.0, 10.4, 5.6 Hz, 1H), 5.80 (d, *J* = 3.2 Hz, 1H), 5.49 (dd, *J* = 15.6, 9.2 Hz, 1H), 5.39-5.31(m, 3H), 5.30 (s, 1H), 5.24 (app dd, 10.4, 1.2 Hz, 1H), 5.11-5.06 (m, 2H), 5.00 (d, *J* = 6.8 Hz, 1H), 4.97 (app dd, *J* = 10.0, 1.2 Hz, 1H), 4.70 (d, *J* = 6.8 Hz, 1H), 4.64-4.61 (m, 3H), 4.46 (dd, *J* = 9.6, 8.0 Hz, 1H), 3.80 (dd, *J* = 7.6, 4.8 Hz, 1H), 3.60-3.51 (m, 3H), 3.49 (s, 3H), 3.38 (s, 3H), 2.78 (qd, *J* = 6.8, 2.4 Hz, 1H), 2.36-2.26 (m, 1H), 2.22-2.10 (m, 1H), 1.95-1.84 (m, 1H), 1.72 (s,

3H), 1.69 (d, *J* = 1.2 Hz, 3H), 1.60-1.38 (m, 3H), 1.34-1.27 (m, 1H), 1.00 (s, 9H), 0.86 (d, *J* = 7.2 Hz, 3H), 0.82 (t, *J* = 7.2 Hz, 3H), 0.24 (s, 6H)

Unproductive Routes: Investigating Solutions to the Amidation Reaction - Synthesis of Amide 6-5 and Aldehydes 6-7/6-8

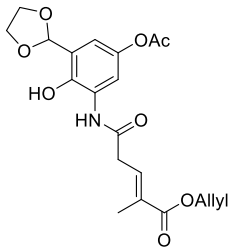


3-(1,3-dioxolan-2-yl)-4-hydroxy-5-nitrophenyl acetate (6-3)

Toluene (3.7 mL) and ethylene glycol (0.83 mL, 0.92 g, 14.8 mmol) were added to compound **6-2** (0.835 g, 3.71 mmol) under Ar at rt. Trimethyl orthoformate (1.6 mL, 1.6 g, 15 mmol) was added followed by pyridinium *p*-toluenesulfonate (100 mg, 0.371 mmol) as a solid. The reaction was warmed to 60 °C and stirred 3 h. TLC showed no starting material so the reaction was cooled to rt and allowed to stir overnight. The reaction was quenched by addition of pH 7 phosphate buffer and the aqueous layer was extracted three times with EtOAc. The combined organic extract was washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The crude material was purified by flash chromatography (5% to 40% EtOAc in hexanes) to unexpectedly yield the dimethyl acetal (0.635 g, 57%).

To the dimethyl acetal (0.271 g, 1 mmol) at rt under Ar was added toluene (1 mL) and ethylene glycol (220 µL, 248 mg, 4 mmol). Pyridinium *p*-toluenesulfonate (25.1 mg, 0.1 mmol) was added as a solid and the reaction stirred 24 h at rt. The reaction was quenched with pH 7 phosphate buffer and the aqueous layer extracted three times with EtOAc. The combined organic layer was washed with brine, dried over Na_2SO_4, then concentrated *in vacuo*. The crude material was purified by flash chromatography (5% to 40% EtOAc in hexanes) to yield compound **6-3** (0.211 g, 78%).

^{1}H-NMR ($CDCl_3$, 400 MHz): δ 10.87 (s, 1H), 7.90 (d, *J* = 3.2 Hz, 1H), 7.63 (d, *J* = 2.8 Hz, 1H), 6.20 (s, 1H), 4.15-4.06 (m, 4H), 2.31 (s, 3H)



allyl (*E*)-5-((5-acetoxy-3-(1,3-dioxolan-2-yl)-2-hydroxyphenyl)amino)-2-methyl-5-oxopent-2-enoate (6-5)

Nitro Reduction:

Lindlar's catalyst (5% Pd, 106 mg) was added to a 2-neck round bottom flask and backfilled with H_2. In a separate round bottom flask, THF (5.3 mL) then quinoline (53 µL) was added to compound **6-3** (200 mg, 0.743 mmol) under Ar. The solution was then added via syringe to the flask containing Lindlar's catalyst and the reaction was stirred 4 h. The reaction was diluted with THF, filtered (syringe filter), then concentrated *in vacuo*. The crude aniline **6-4** (0.242 g, 89%), contaminated with quinoline, was used immediately in the next step without further purification.

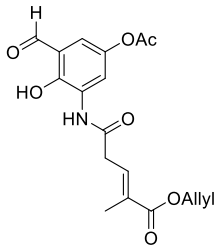
Amidation:

Dimethylformamide (DMF) was degassed using the freeze-pump-thaw method.

N-(3-dimethylaminopropyl)-*N'*-ethylcarbodiimide hydrochloride (EDC·HCl, 168 mg, 0.878 mmol) and a stir bar were placed under N_2 and cooled to 0 °C. In a separate flask carboxylic acid **5-12** (162 mg, 0.878 mmol) and 1-hydroxybenzotriazole hydrate (137 mg, 0.878 mmol) were placed under Ar. DMF (7 mL) was added and the solution was added via gastight syringe to the first flask containing the EDC·HCl at 0 °C. The reaction was stirred and crude aniline **6-4** (70 mg, 0.29 mmol) in DMF (4 mL) was added via gastight syringe. The reaction was stirred 24 h at rt then quenched by addition of brine:H_2O (1:4). The aqueous layer was extracted once with Et_2O, the three times with EtOAc. The combined organic layer was washed with brine, dried

over Na_2SO_4, then concentrated *in vacuo* (high vacuum overnight). The crude material was purified by flash chromatography (10% to 60% EtOAc in hexanes) to yield amide **6-5** (48 mg, 40%) and recovered carboxylic acid **5-12** (85.3 mg)

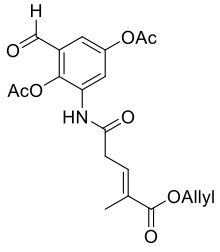
^{1}H-NMR ($CDCl_3$, 400 MHz): δ 8.05 (d, *J* = 2.4 Hz, 1H), 7.86 (br s, 1H), 7.02 (td, *J* = 7.6, 1.2 Hz, 1H), 6.76 (d, *J* = 2.8 Hz, 1H), 6.01-5.91 (m, 2H), 5.35 (dq, *J* = 17.2, 1.6 Hz, 1H), 5.24 (app dd, *J* = 10.4, 1.2 Hz, 1H), 4.67 (dt, *J* = 5.6, 1,2 Hz, 2H), 4.13-4.05 (m, 4H), 3.33 (d, *J* = 7.6 Hz, 2H), 2.25 (s, 3H), 1.95 (s, 3H)



allyl (*E*)-5-((5-acetoxy-3-formyl-2-hydroxyphenyl)amino)-2-methyl-5-oxopent-2-enoate (6-6)

Toluenesulfonic acid monohydrate (22.0 mg, 0.116 mmol) was added as a solid to compound **6-5** (470 mg, 1.16 mmol) in acetone (5.8 mL) at rt under air atmosphere. The reaction was stirred 30 min then diluted with CH_2Cl_2 and saturated aqueous $NaHCO_3$:H_2O (1:1). The aqueous layer was extracted three times with CH_2Cl_2. The combined organic layer was washed with brine, dried over Na_2SO_4, then concentrated *in vacuo*. The crude material was purified by flash chromatography (5% to 40% EtOAc in hexanes) to yield compound **6-6** (0.289 g, 69%)

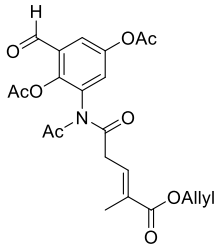
^{1}H-NMR ($CDCl_3$, 400 MHz): δ 11.40 (s, 1H), 9.84 (s, 1H), 8.46 (d, *J* = 2.8 Hz, 1H), 7.87 (br s, 1H), 7.10 (d, *J* = 2.8 Hz, 1H), 7.03 (qt, *J* = 7.2, 1.6 Hz, 1H), 5.97 (ddt, *J* = 17.2, 10.4, 5.6 Hz, 1H), 5.35 (dq, *J* = 17.2, 1.2 Hz, 1H), 5.25 (dq, *J* = 10.4, 1.2 Hz, 1H), 4.68 (dt, *J* = 5.6, 1.2 Hz, 2H), 3.37 (dd, *J* = 7.2, 0.8 Hz, 2H), 2.30 (s, 3H), 1.96 (d, *J* = 1.2 Hz, 3H).



(*E*)-2-(5-(allyloxy)-4-methyl-5-oxopent-3-enamido)-6-formyl-1,4-phenylene diacetate (6-7)

Acetic anhydride (13.1 µL 14.1 mg, 0.138 mmol) was added to compound **6-6** (12.5 mg, 34.6 µmol) in 1,2-dichloroethane (0.21 mL) at 0 °C under N_2. Pyridine (4.2 µL, 4.1 mg, 52 µmol) was added and the reaction was stirred 3 h at rt. Saturated aqueous NH_4Cl was added and the aqueous layer was extracted three times with EtOAc. The combined organic layer was washed three times with 1% aqueous HCl, brine, dried over Na_2SO_4, then concentrated *in vacuo*. The crude material was left on the high vacuum overnight to yield compound **6-7** (12.5 mg, 90% yield, 94% diacyl).

^{1}H-NMR ($CDCl_3$, 400 MHz): δ 9.85 (s, 1H), 8.40 (d, *J* = 2.4 Hz, 1H), 7.53 (br s, 1H), 7.33 (d, *J* = 2.8 Hz, 1H), 6.96 (td, *J* = 7.6, 1.6 Hz, 1H), 5.96 (ddt, *J* = 17.2, 10.4, 6.0 Hz, 1H), 5.35 (dq, *J* = 17.2, 1.6 Hz, 1H), 5.26 (dq, *J* = 10.4, 1.2 Hz, 1H), 4.68 (dt, *J* = 5.6, 1.2 Hz, 2H), 3.33 (d, *J* = 7.6 Hz, 2H), 2.39 (s, 3H), 2.32 (s, 3H), 1.95 (s, 3H).



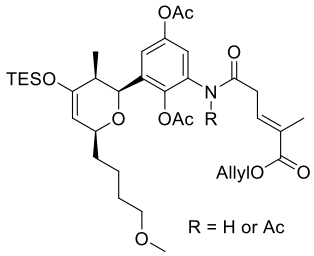
(*E*)-2-(N-acetyl-5-(allyloxy)-4-methyl-5-oxopent-3-enamido)-6-formyl-1,4-phenylene diacetate (6-8)

Acetic anhydride (92 µL, 99 mg, 970 µmol) was added to compound **6-6** (35 mg, 97 µmol) in 1,2-dichloroethane (1 mL) at 0 °C under Ar. Pyridine (47 µL, 46 mg, 580 µmol) was added followed by 1-methylimidazole (0.8 µL, 0.8 mg, 10 µmol). The reaction was stirred 2.5 h at rt then quenched by addition of saturated aqueous NH_4Cl. The aqueous layer was extracted three times with EtOAc. The combined organic layer was washed three times with 1% aqueous HCl, brine, dried over Na_2SO_4, then concentrated *in vacuo*. The

crude material was left on the high vacuum overnight to yield compound **6-8** (33.7 mg, 78% yield, 90% triacyl).

^{1}H-NMR ($CDCl_3$, 400 MHz): δ 9.98 (s, 1H), 7.72 (d, *J* = 2.8 Hz, 1H), 7.35 (d, *J* = 2.8 Hz, 1H), 6.96 (tq, *J* = 6.8, 1.2 Hz, 1H), 5.94 (ddt, *J* = 17.2, 10.4, 5.6 Hz, 1H), 5.33 (dq, *J* = 17.2, 1.6 Hz, 1H), 5.23 (dq, *J* = 10.4, 1.2 Hz, 1H), 4.64 (dt, *J* = 5.6, 1.2 Hz, 2H), 3.57 (app t, *J* = 7.6 Hz, 2H), 2.34 (s, 6H), 2.23 (3H), 1.82 (d, *J* = 1.2 Hz, 3H).

Unproductive Routes: Investigating Solutions to the Amidation Reaction – HDA Reaction to Compound 6-15 and 6-16



Compounds 6-15 (diacyl) and 6-16 (triacyl)

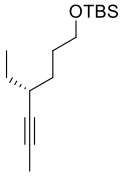
A mixture of di- and tri-acylated aldehyde **6-7**:**6-8**, 2.8:1 (14.0 mg, 34.7 μmol) was loaded into a small vial (with a septum cap) using THF to transfer. The solvent was removed by high vacuum then diene **3-2** (19.7 mg, 69.4 μmol), Jacobsen's catalyst [SbF_6][39] (4.8 mg, 6.9 μmol), 4Å MS (5.2 mg), and a stir bar were added. The vial was placed under Ar then acetone (7 μL) was added. The cap was wrapped in parafilm and the entire vial wrapped in aluminum foil. The reaction was stirred 4 d then directly loaded onto a SiO_2 gel column (0% to 40% EtOAc in hexanes) to yield diacyl product **6-15** (4.2 mg, 24%), triacyl product **6-16** (4.2 mg, 64%) and the diacyl aldehyde **6-7** (5.7 mg 58% recovered).

^{1}H-NMR ($CDCl_3$, 400 MHz, diacyl product **6-15**): δ 7.83 (d, *J* = 2.4 Hz, 1H), 7.10 (d, *J* = 2.8 Hz, 1H), 7.09 (br s, 1H), 6.95 (td, *J* = 7.6, 1.2 Hz, 1H), 5.96 (ddt, *J* = 16.4, 11.2, 6.0 Hz, 1H), 5.35 (dd, *J* = 16.8, 1.2 Hz, 1H), 5.26 (app d, *J* = 10.4 Hz, 1H), 4.69-4.64 (m, 4H), 4.22 (br s, 1H), 3.39

(t, *J* = 6.4 Hz, 2H), 3.34 (s, 3H), 3.30 (d, *J* = 7.2 Hz, 2H), 2.29 (s, 3H), 2.28 (s, 3H), 2.15-2.09 (m, 1H), 1.95 (s, 3H), 1.63-1.53 (m, 6H), 0.99 (t, *J* = 8.0 Hz, 9H), 0.74 (d, *J* = 6.8 Hz, 3H), 0.69 (q, *J* = 8.0 Hz, 6H)

^{1}H-NMR ($CDCl_3$, 400 MHz, triacyl product, nmr shows potential rotamer peaks, **6-16**): δ 7.42 (d, *J* = 2.8 Hz, 1H), 7.02-6.95 (m, 2H), 5.95 (ddt, *J* = 17.2, 10.8, 6.0 Hz, 1H), 5.32 (dq, *J* = 17.2, 1.6 Hz, 1H), 5.22 (app dd, *J* = 10.4, 1.2 Hz, 1H), 4.71-4.69 (m, 2H), 4.64 (d, *J* = 5.6 Hz, 2H), 4.24 (br s, 1H), 3.40 (t, *J* = 6.4 Hz, 2H), 3.34-3.30 (m, 5H), 2.31 (s, 6H), 2.21 (s, 3H), 2.19-2.13 (m, 1H), 1.83 (s, 1.5H), 1.81 (s, 1.5H), 1.64-1.52 (m, 6H), 0.98 (t, *J* = 8.0 Hz, 9H), 0.75 (d, *J* = 6.8 Hz, 3H), 0.68 (q, *J* = 7.6 Hz, 6H).

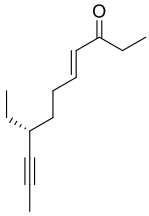
Unproductive Routes: Synthesis of Diene 6-14



(*R*)-*tert*-butyl((4-ethylhept-5-yn-1-yl)oxy)dimethylsilane (6-12)

To a solution of compound **4-18** (0.500 g, 2.08 mmol) in THF (20 mL) at –78 °C under Ar was added *n*-butyllithium solution (1.6M in hexanes, 1.56 mL, 2.5 mmol) dropwise via syringe. The reaction was stirred 15 min at –78 °C followed by dropwise addition of MeI (0.91 mL, 2.1 g, 15 mmol). The reaction was slowly warmed to rt over 3 h then quenched by addition of saturated aqueous NH_4Cl. The mixture was diluted with H_2O and the aqueous layer was extracted three times with EtOAc. The combined organic layer was washed with brine, dried over Na_2SO_4, then concentrated *in vacuo*. The crude material was purified by flash chromatography (0% to 3% EtOAc in hexanes) to yield compound **6-12** (0.498 g, 94%).

^{1}H-NMR ($CDCl_3$, 400 MHz): δ 3.62 (t, *J* = 6.8 Hz, 2H), 2.24-2.15 (m, 1H), 1.80 (d, *J* = 2.4 Hz, 3H), 1.76-1.54 (m, 2H), 1.52-1.32 (m, 4H), 0.97 (t, *J* = 7.2 Hz, 3H), 0.90 (s, 9H), 0.05 (s, 6H)



(*R*,*E*)-8-ethylundec-4-en-9-yn-3-one (6-13)

Prepared analogously to compound **6-9**.

TBS deprotection:

From compound **6-12** (0.490 g, 1.93 mmol), NH_4F (1.57 g, 42.4 mmol) and MeOH (39 mL). The crude alcohol (0.253 g, 94% crude) was used in the next step without further purification.

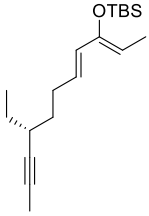
Swern oxidation:

From the crude alcohol (0.250 g, 1.78 mmol) in CH_2Cl_2 (2.3 mL); oxalyl chloride (180 µL, 270 mg, 2.14 mmol) in CH_2Cl_2 (7.5 mL); dimethylsulfoxide (0.30 mL, 0.33 g, 4.3 mmol) in CH_2Cl_2 (3.3 mL); and Et_3N (0.74 mL, 0.54 g, 5.3 mmol). The crude aldehyde (0.257 g) was used in the next step without further purification.

HWE reaction:

From the crude aldehyde (0.246 g, 1.78 mmol), $EtC(O)CH_2P(O)(OMe)_2$[95] (0.642 g, 3.57 mmol), 1,8-diazabicycloundec-7-ene (0.40 mL, 0.41 g, 2.67 mmol), LiCl (0.15 g, 3.6 mmol), and MeCN (21 mL). The crude material was purified by flash chromatography (1 inch SiO_2, 0% to 10% EtOAc in hexanes) to yield compound **6-13** (0.235 g, 63% over 3 steps)

^{1}H-NMR ($CDCl_3$, 400 MHz): δ 6.84 (dt, *J* = 15.6, 6.8 Hz, 1H), 6.12 (d, *J* = 16.0 Hz, 1H), 2.55 (q, *J* = 7.2 Hz, 2H), 2.42 (dq, *J* = 15.2, 7.2 Hz, 1H), 2.29 (dq, *J* = 8.0 Hz, 1H), 2.24-2.17 (m, 1H), 1.80 (d, *J* = 2.0 Hz, 3H), 1.59-1.37 (m, 4H), 1.09 (t, *J* = 7.2 Hz, 3H), 0.98 (t, *J* = 7.2 Hz, 3H).



***tert*-butyl(((*R*,2*Z*,4*E*)-8-ethylundeca-2,4-dien-9-yn-3-yl)oxy)dimethylsilane (6-14)**

Prepared analogously to compound **6-11**. From compound **6-13** (36.4 mg, 0.189 mmol), *tert*-butyldimethylsilyl trifluoromethanesulfonate (0.26 mL, 0.30 g, 1.1 mmol), *N*,*N*-

diisopropylethylamine (0.28 mL, 0.21 g, 1.6 mmol), and Et_2O (1.3 mL). The crude material was purified by flash chromatography (3 inches SiO_2, 0% to 5% EtOAc in hexanes) to yield compound **6-14** (46.7 g, 80%).

^{1}H-NMR ($CDCl_3$, 400 MHz): δ 5.86 (d, *J* = 15.6 Hz, 1H), 5.73 (dt, *J* = 14.0, 6.8 Hz, 1H), 4.74 (q, *J* = 7.2 Hz, 1H), 2.31-2.09 (m, 3H), 1.81 (d, *J* = 2.4 Hz, 3H), 1.61 (d, *J* = 6.8 Hz, 3H), 1.49-1.35 (m, 4H), 1.00 (s, 9H), 0.97 (t, *J* = 7.6 Hz, 3H), 0.10 (s, 6H).

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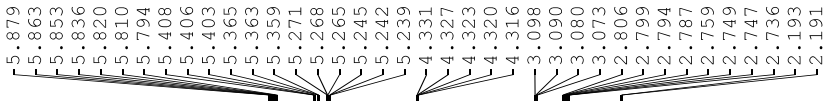

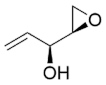


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PC                1.00
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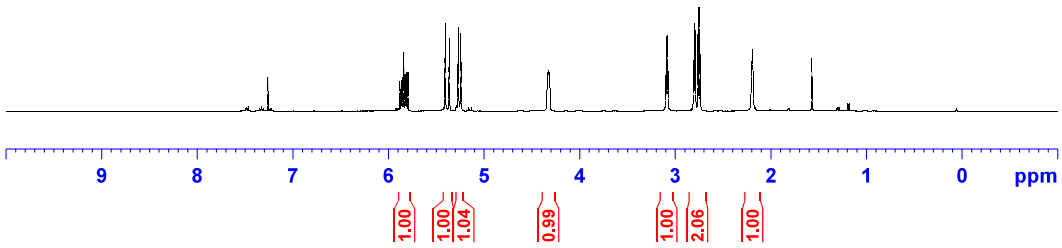
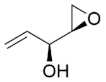
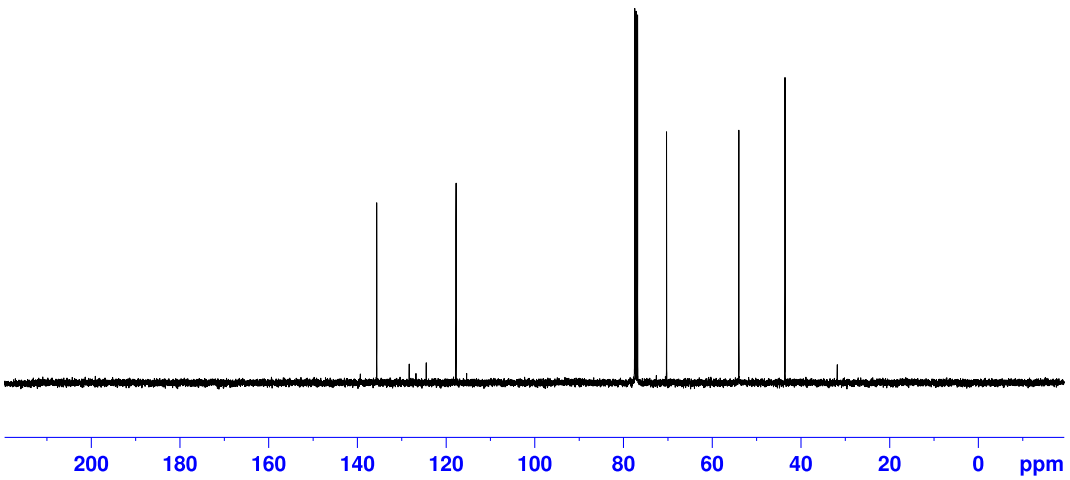


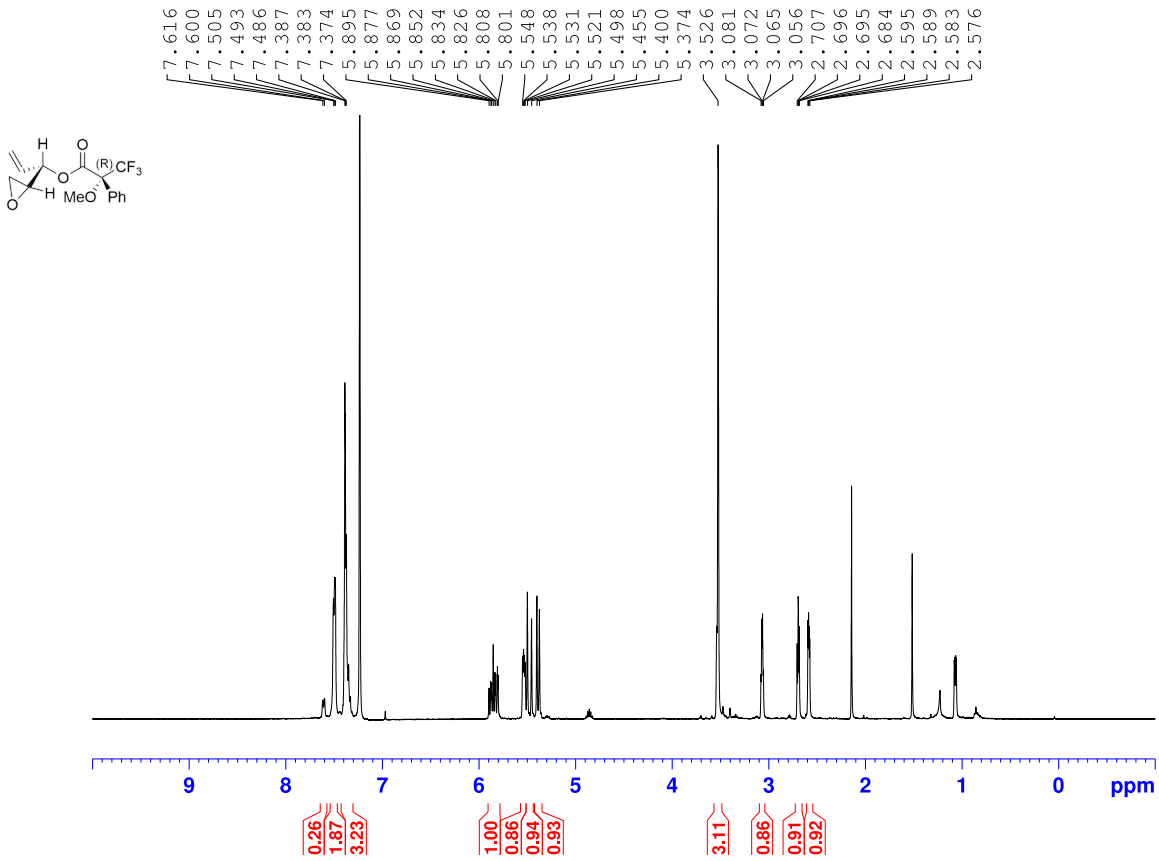
p.226-3 kugelrohr fr 1




```
Current Data Parameters
NAME          Scott SAE
EXPNO                20
PROCNO                1

F2 - Acquisition Parameters
Date_          20180420
Time              11.39
INSTRUM           spect
PROBHD   5 mm PABBO BB-
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                  200
DS                    4
SWH           24038.461 Hz
FIDRES         0.366798 Hz
AQ             1.3631488 sec
RG                  181
DW               20.800 usec
DE                6.50 usec
TE              2243.6 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                   1

======== CHANNEL f1 ========
SFO1         100.6228293 MHz
NUC1                 13C
P1               10.00 usec
PLW1         56.13299942 W

======== CHANNEL f2 ========
SFO2         400.1316005 MHz
NUC2                 1H
CPDPRG[2         waltz16
PCPD2             90.00 usec
PLW2         12.01700020 W
PLW12         0.31191999 W
PLW13         0.25266001 W

F2 - Processing parameters
SI                32768
SF           100.6127590 MHz
WDW                  EM
SSB       0
LB                1.00 Hz
GB        0
PC                1.40
```

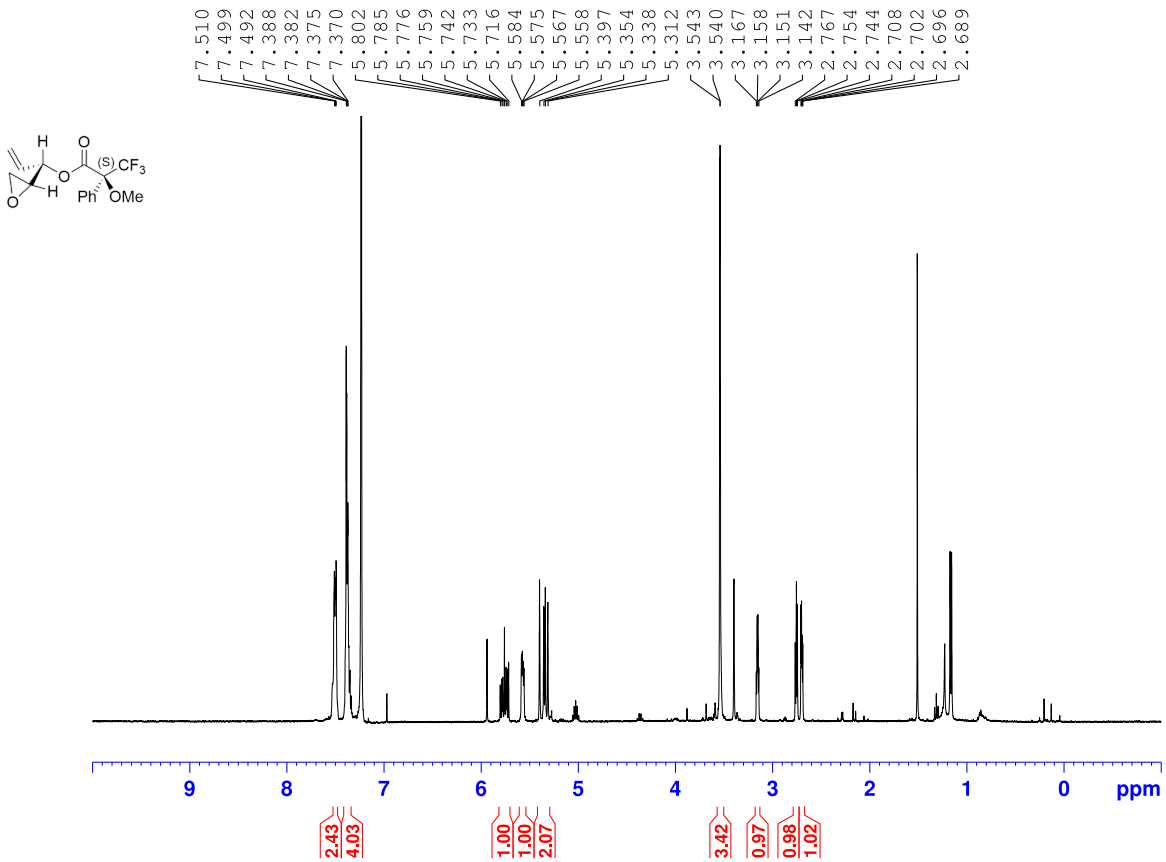


P.124 (R) 2



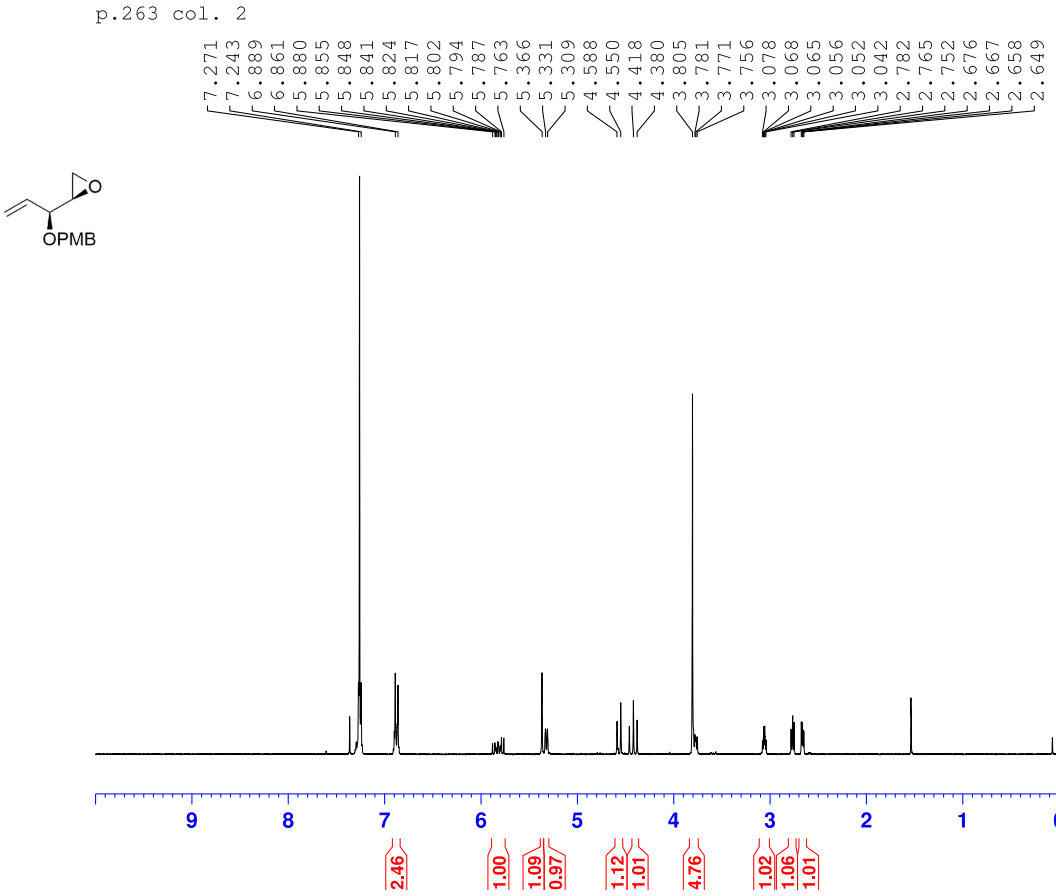

```
Current Data Parameters
NAME      Scott Mosher Ester
EXPNO                 10
PROCNO                 1

F2 - Acquisition Parameters
Date_           20131115
Time               16.51
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    25
DS                     2
SWH             8223.685 Hz
FIDRES          0.125483 Hz
AQ              3.9845889 sec
RG                   114
DW                60.800 usec
DE                 6.50 usec
TE                297.6 K
D1             1.00000000 sec

======== CHANNEL f1 ========
NUC1                  1H
P1                13.75 usec
PLW1         12.01700020 W
SFO1         400.1324710 MHz

F2 - Processing parameters
SI                 65536
SF          400.1300207 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

p.124 (s) 1



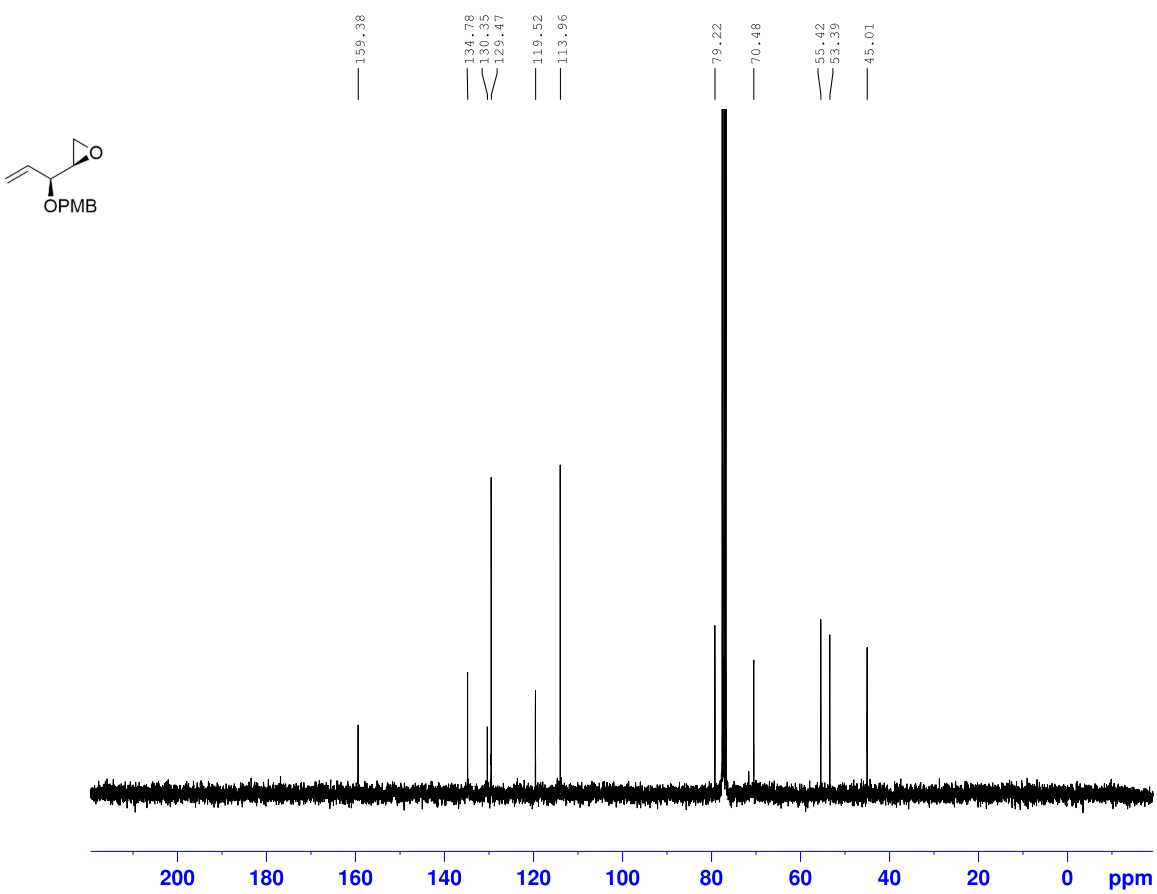

```
Current Data Parameters
NAME      Scott Mosher Ester
EXPNO                 52
PROCNO                 1

F2 - Acquisition Parameters
Date_           20131119
Time               19.41
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    25
DS                     2
SWH             8223.685 Hz
FIDRES          0.125483 Hz
AQ              3.9845889 sec
RG                   144
DW                60.800 usec
DE                 6.50 usec
TE                298.0 K
D1             1.00000000 sec

======== CHANNEL f1 ========
NUC1                  1H
P1                13.75 usec
PLW1         12.01700020 W
SFO1         400.1324710 MHz

F2 - Processing parameters
SI                 65536
SF          400.1300202 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

p.263 col. 2



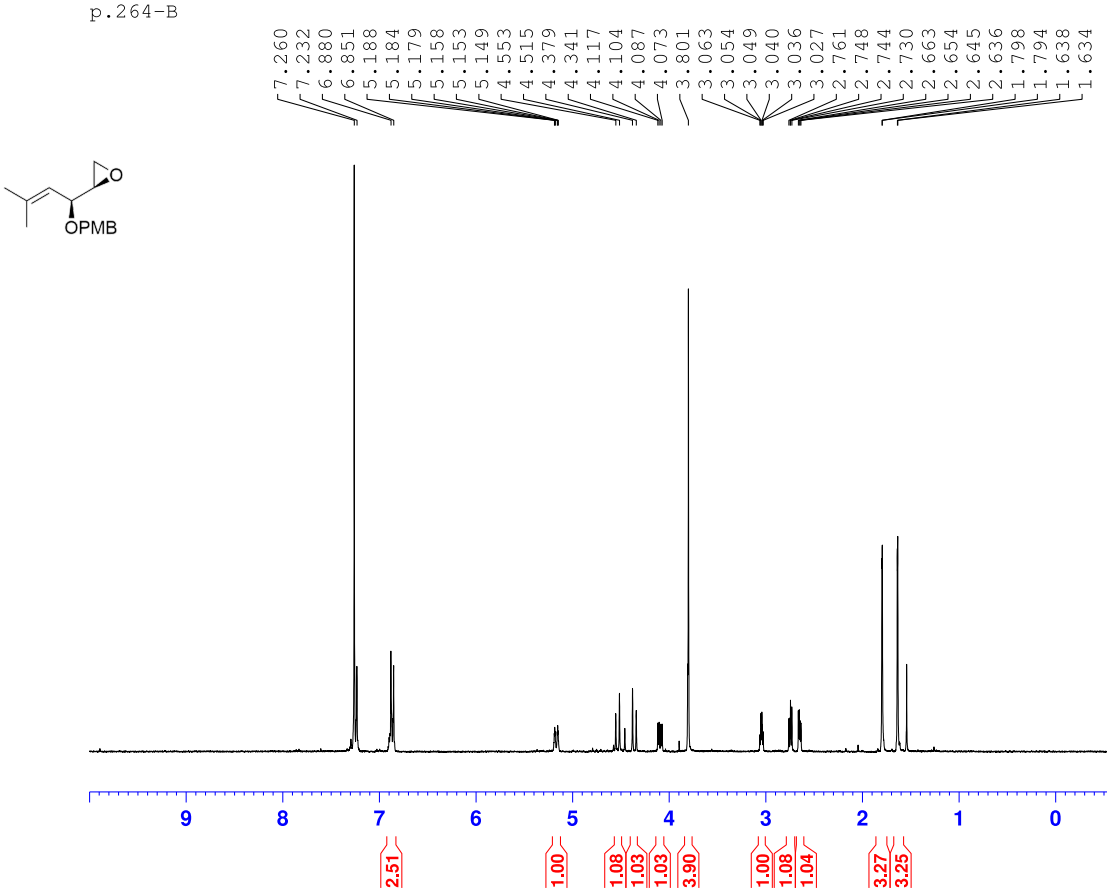

```
Current Data Parameters
NAME            Scott PMB
EXPNO                  30
PROCNO                  1

F2 - Acquisition Parameters
Date_           20140619
Time               13.30
INSTRUM            spect
PROBHD   5 mm QNP  1H/1
PULPROG            zg30
TD                32768
SOLVENT           CDCl3
NS                   16
DS                    2
SWH           6188.119 Hz
FIDRES        0.188846 Hz
AQ            2.6476543 sec
RG                  322
DW               80.800 usec
DE                6.50 usec
TE               -925.2 K
D1           1.00000000 sec

======== CHANNEL f1 ========
NUC1                1H
P1                12.71 usec
PLW1        18.19700050 W
SFO1       300.2318540 MHz

F2 - Processing parameters
SI                 32768
SF          300.2300092 MHz
WDW                   EM
SSB       0
LB                0.10 Hz
GB        0
PC                1.00
```

p.276



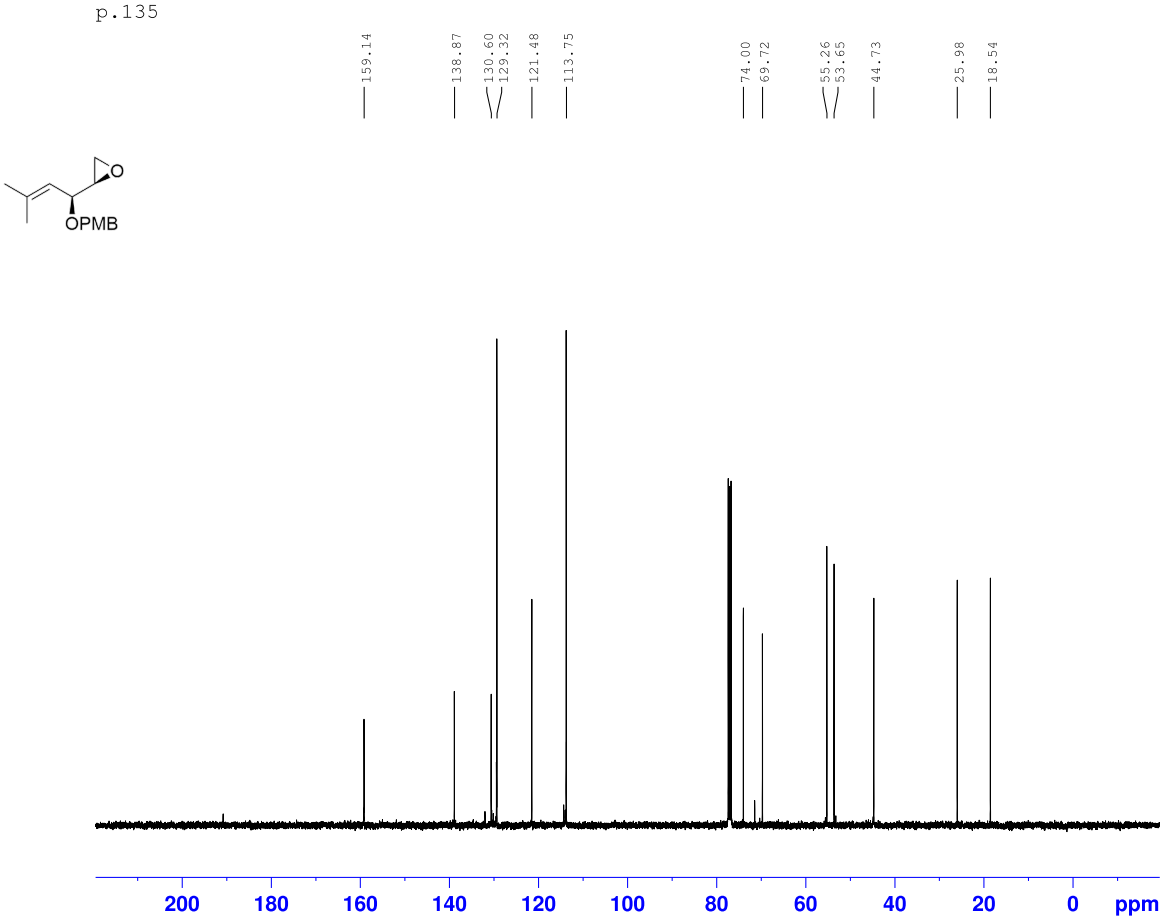

```
Current Data Parameters
NAME            Scott PMB
EXPNO                  51
PROCNO                  1

F2 - Acquisition Parameters
Date_           20140930
Time               16.02
INSTRUM            spect
PROBHD   5 mm QNP  1H/1
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                  220
DS                    4
SWH           18028.846 Hz
FIDRES        0.275098 Hz
AQ            1.8175317 sec
RG                  203
DW               27.733 usec
DE                6.50 usec
TE               -923.6 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                   1

======== CHANNEL f1 ========
SFO1        75.5004428 MHz
NUC1               13C
P1                12.00 usec
PLW1        31.62299919 W

======== CHANNEL f2 ========
SFO2       300.2312009 MHz
NUC2                1H
CPDPRG[2         waltz16
PCPD2             90.00 usec
PLW2        18.19700050 W
PLW12        0.36291999 W
PLW13        0.29396001 W

F2 - Processing parameters
SI                 32768
SF          75.4928837 MHz
WDW                   EM
SSB       0
LB                1.00 Hz
GB        0
PC                1.40
```

p.264-B



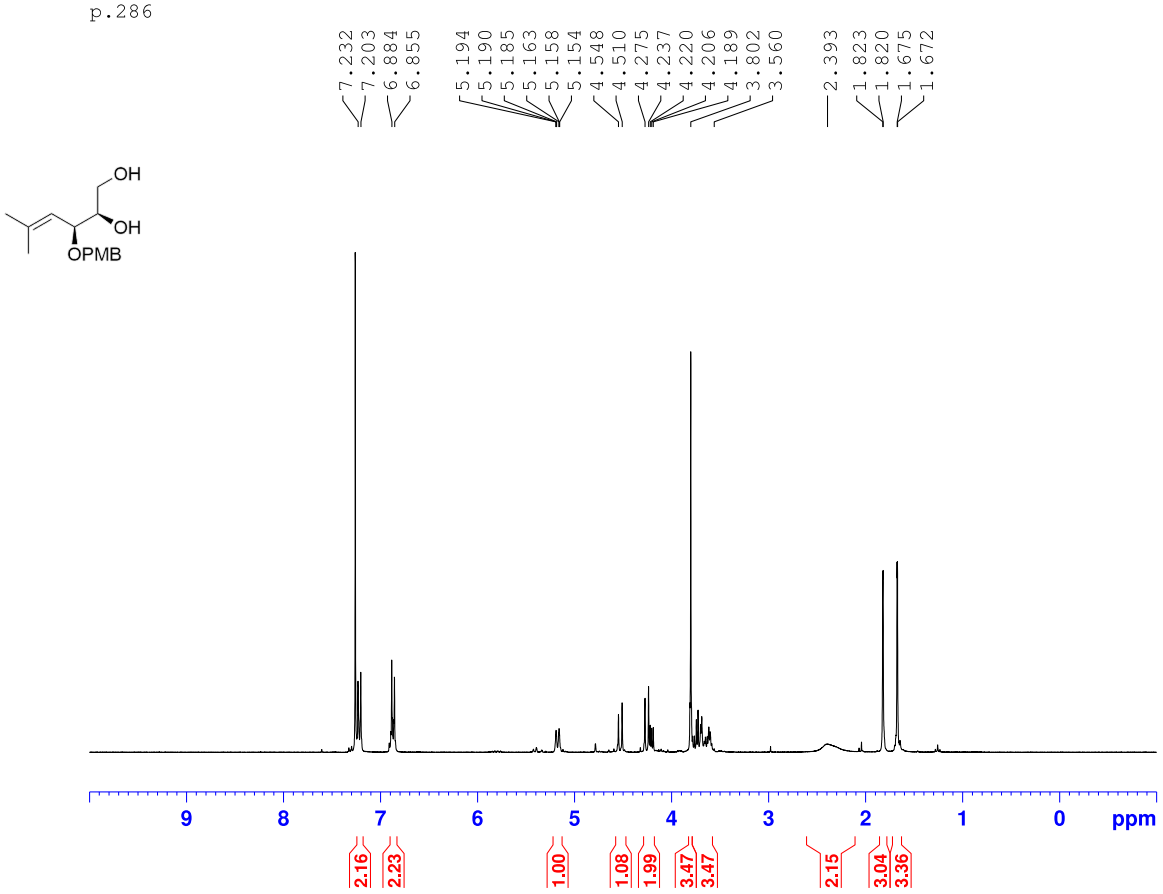

```
Current Data Parameters
NAME      Scott Metathesis
EXPNO                   70
PROCNO                   1

F2 - Acquisition Parameters
Date_           20140624
Time              16.04
INSTRUM           spect
PROBHD   5 mm QNP  1H/1
PULPROG            zg30
TD                32768
SOLVENT           CDCl3
NS                   16
DS                    2
SWH            6188.119 Hz
FIDRES          0.188846 Hz
AQ             2.6476543 sec
RG                  322
DW               80.800 usec
DE                6.50 usec
TE              -932.0 K
D1           1.00000000 sec

======== CHANNEL f1 ========
NUC1                 1H
P1                12.71 usec
PLW1        18.19700050 W
SFO1       300.2318540 MHz

F2 - Processing parameters
SI                32768
SF           300.2300094 MHz
WDW                  EM
SSB       0
LB                0.10 Hz
GB        0
PC                1.00
```

p.135



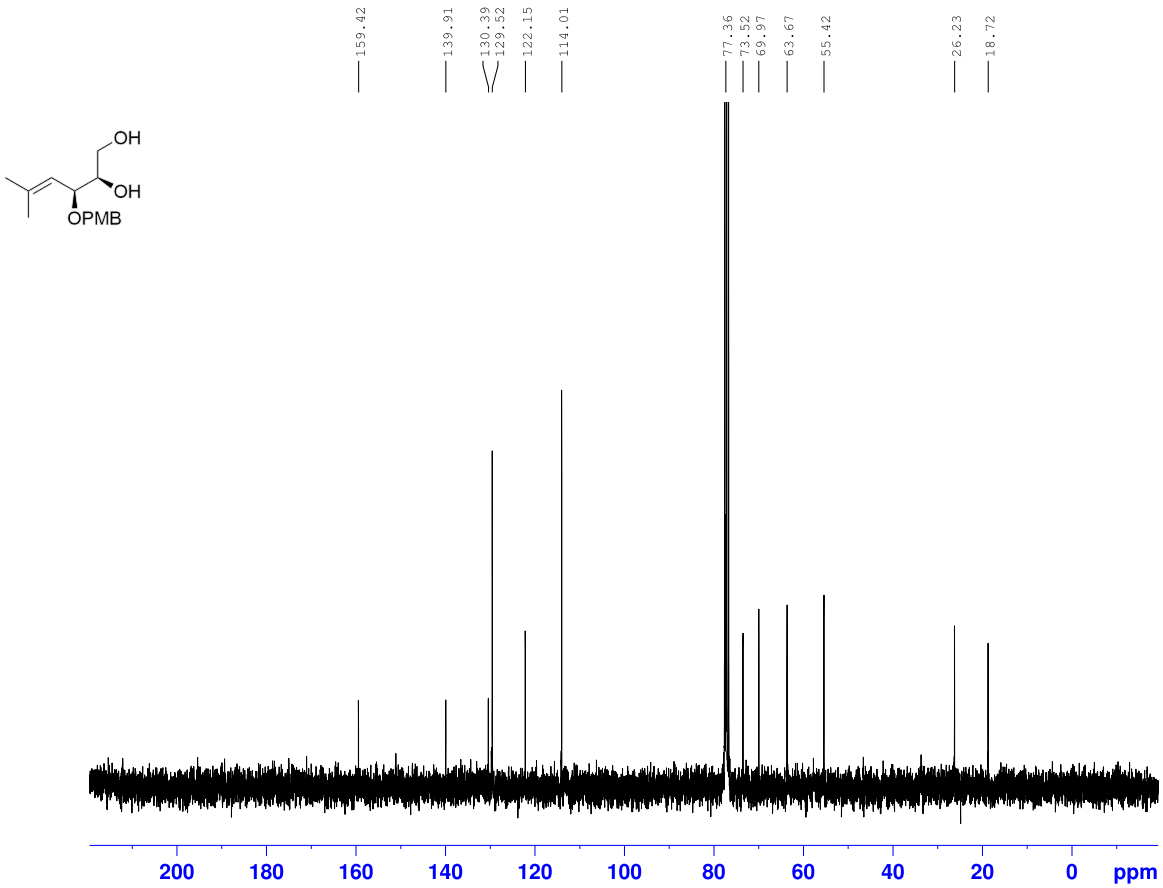

```
Current Data Parameters
NAME      Scott Metathesis
EXPNO                   52
PROCNO                   1

F2 - Acquisition Parameters
Date_           20131202
Time              12.50
INSTRUM           spect
PROBHD   5 mm PABBO BB-
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                  250
DS                    4
SWH           24038.461 Hz
FIDRES         0.366798 Hz
AQ             1.3631488 sec
RG                  203
DW               20.800 usec
DE                6.50 usec
TE                298.7 K
D1           2.00000000 sec
D11          0.03000000 sec

======== CHANNEL f1 ========
NUC1                13C
P1                10.00 usec
PLW1        56.13299942 W
SFO1       100.6228293 MHz

======== CHANNEL f2 ========
CPDPRG[2         waltz16
NUC2                 1H
PCPD2             90.00 usec
PLW2        12.01700020 W
PLW12        0.29076999 W
PLW13    0 W
SFO2       400.1316005 MHz

F2 - Processing parameters
SI                32768
SF           100.6127690 MHz
WDW                  EM
SSB       0
LB                1.00 Hz
GB        0
PC                1.40
```

p.286



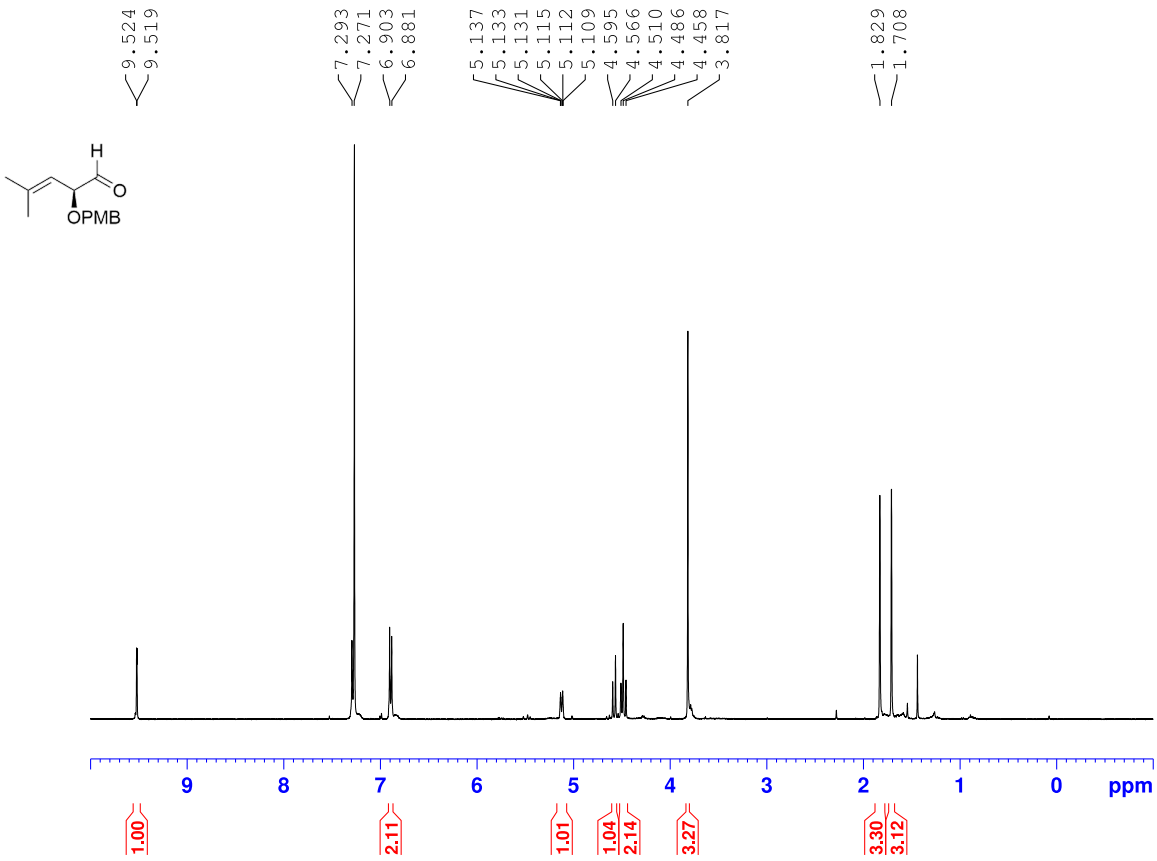

```
Current Data Parameters
NAME            Scott KOH
EXPNO                  10
PROCNO                  1

F2 - Acquisition Parameters
Date_           20141001
Time               14.02
INSTRUM            spect
PROBHD    5 mm QNP  1H/1
PULPROG             zg30
TD                 32768
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             6188.119 Hz
FIDRES          0.188846 Hz
AQ             2.6476543 sec
RG                   144
DW                80.800 usec
DE                 6.50 usec
TE                -922.0 K
D1           1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         300.2318540 MHz
NUC1                   1H
P1                 12.71 usec
PLW1         18.19700050 W

F2 - Processing parameters
SI                 32768
SF            300.2300084 MHz
WDW                   EM
SSB       0
LB                 0.10 Hz
GB        0
PC                 1.00
```

p.286



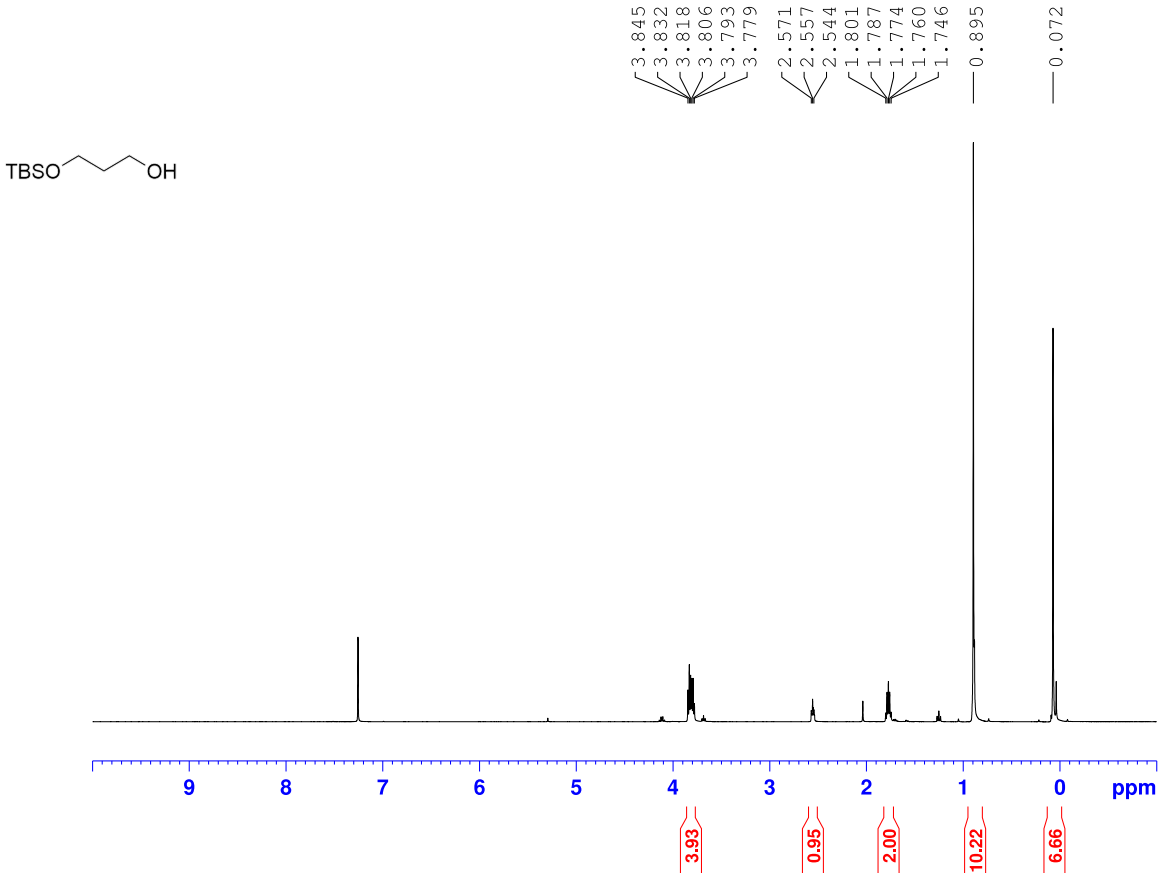

```
Current Data Parameters
NAME            Scott KOH
EXPNO                  11
PROCNO                  1

F2 - Acquisition Parameters
Date_           20141001
Time               14.18
INSTRUM            spect
PROBHD    5 mm QNP  1H/1
PULPROG          zgpg30
TD                 65536
SOLVENT            CDCl3
NS                   220
DS                     4
SWH            18028.846 Hz
FIDRES          0.275098 Hz
AQ             1.8175317 sec
RG                   181
DW                27.733 usec
DE                 6.50 usec
TE                -921.9 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         75.5004428 MHz
NUC1                  13C
P1                12.00 usec
PLW1         31.62299919 W

======== CHANNEL f2 ========
SFO2         300.2312009 MHz
NUC2                   1H
CPDPRG[2         waltz16
PCPD2             90.00 usec
PLW2         18.19700050 W
PLW12         0.36291999 W
PLW13         0.29396001 W

F2 - Processing parameters
SI                 32768
SF            75.4928835 MHz
WDW                   EM
SSB       0
LB                 1.00 Hz
GB        0
PC                 1.40
```

p.175-B



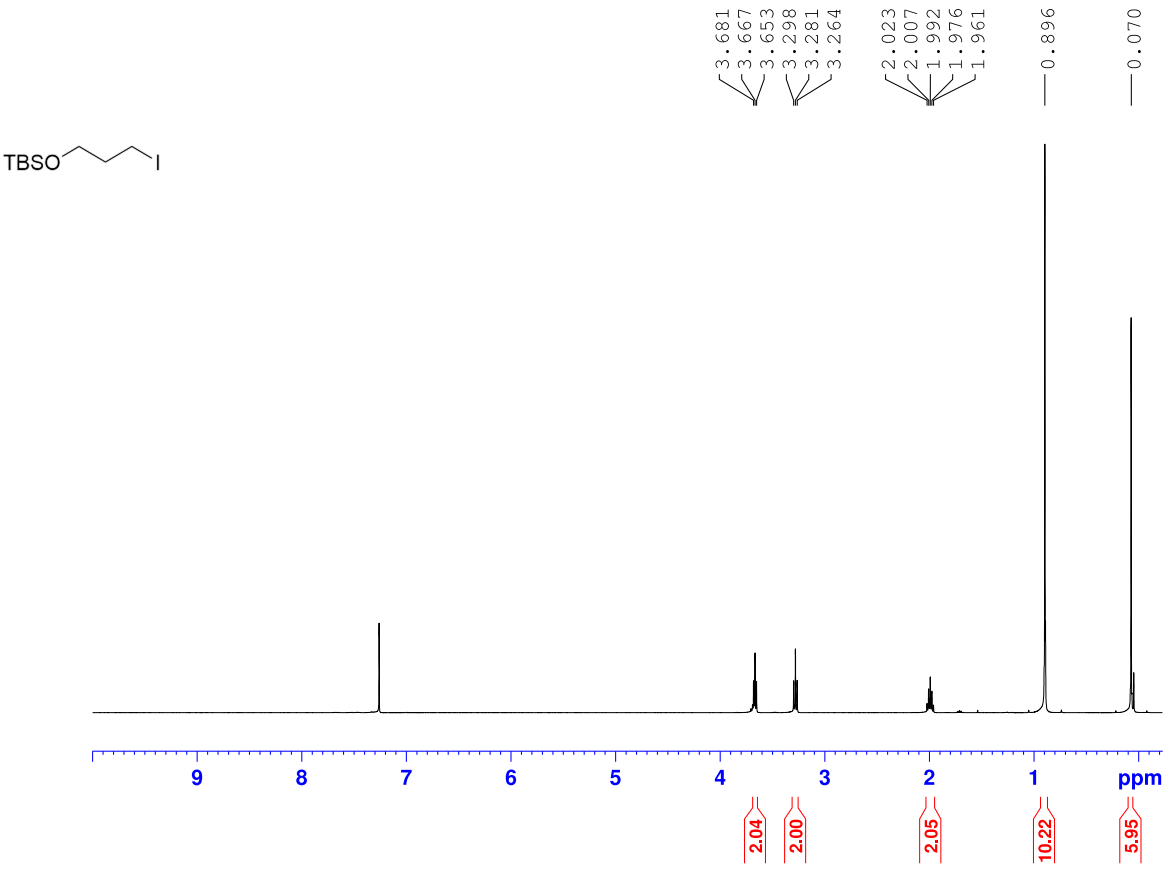

```
Current Data Parameters
NAME      Scott Sodium Periodate
EXPNO                 90
PROCNO                 1

F2 - Acquisition Parameters
Date_           20140306
Time              13.05
INSTRUM           spect
PROBHD   5 mm PABBO BB-
PULPROG           zg30
TD               65536
SOLVENT          CDCl3
NS                  16
DS                   2
SWH            8223.685 Hz
FIDRES        0.125483 Hz
AQ            3.9845889 sec
RG                 181
DW              60.800 usec
DE               6.50 usec
TE              307.9 K
D1           1.00000000 sec

======== CHANNEL f1 ========
NUC1                1H
P1               13.75 usec
PLW1        12.01700020 W
SFO1       400.1324710 MHz

F2 - Processing parameters
SI               65536
SF          400.1300075 MHz
WDW                 EM
SSB       0
LB              0.30 Hz
GB        0
PC              1.00
```

p.54-2



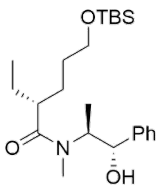

```
Current Data Parameters
NAME          Scott TBS
EXPNO                50
PROCNO                1

F2 - Acquisition Parameters
Date_          20141202
Time              10.49
INSTRUM           spect
PROBHD   5 mm PABBO BB-
PULPROG           zg30
TD               65536
SOLVENT          CDCl3
NS                  16
DS                   2
SWH           8223.685 Hz
FIDRES        0.125483 Hz
AQ            3.9845889 sec
RG                 101
DW              60.800 usec
DE               6.50 usec
TE               92.2 K
D1           1.00000000 sec

======== CHANNEL f1 ========
NUC1                1H
P1              13.75 usec
PLW1       12.01700020 W
SFO1      400.1324710 MHz

F2 - Processing parameters
SI               65536
SF          400.1300119 MHz
WDW                 EM
SSB       0
LB              0.30 Hz
GB        0
PC              1.00
```

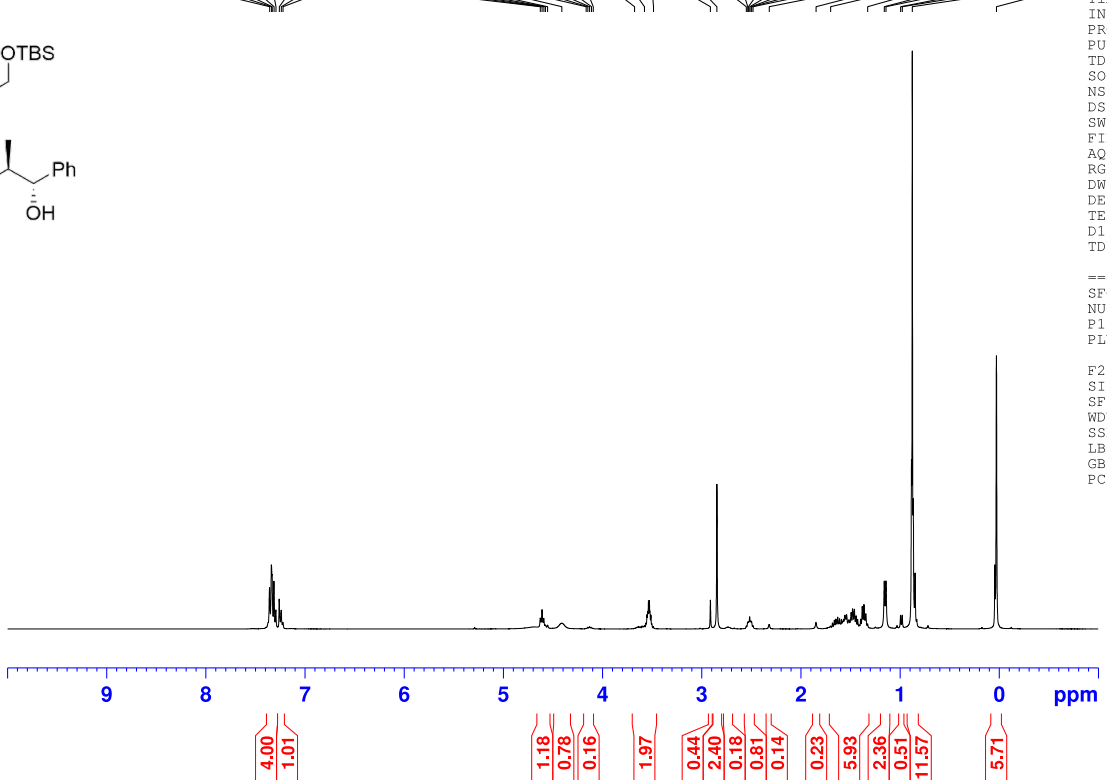
p.55-2,b crude




```
Current Data Parameters
NAME      Scott Myers Aux
EXPNO                 80
PROCNO                 1

F2 - Acquisition Parameters
Date_          20141211
Time               9.43
INSTRUM           spect
PROBHD   5 mm PABBO BB-
PULPROG           zg30
TD               65536
SOLVENT          CDCl3
NS                  16
DS                   2
SWH           8223.685 Hz
FIDRES        0.125483 Hz
AQ            3.9845889 sec
RG                 114
DW              60.800 usec
DE               6.50 usec
TE              -466.1 K
D1           1.00000000 sec

======== CHANNEL f1 ========
NUC1                1H
P1              13.75 usec
PLW1       12.01700020 W
SFO1      400.1324710 MHz

F2 - Processing parameters
SI               65536
SF          400.1300099 MHz
WDW                 EM
SSB       0
LB              0.30 Hz
GB        0
PC              1.00
```

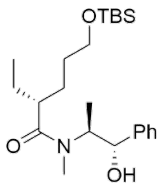
p.7-2

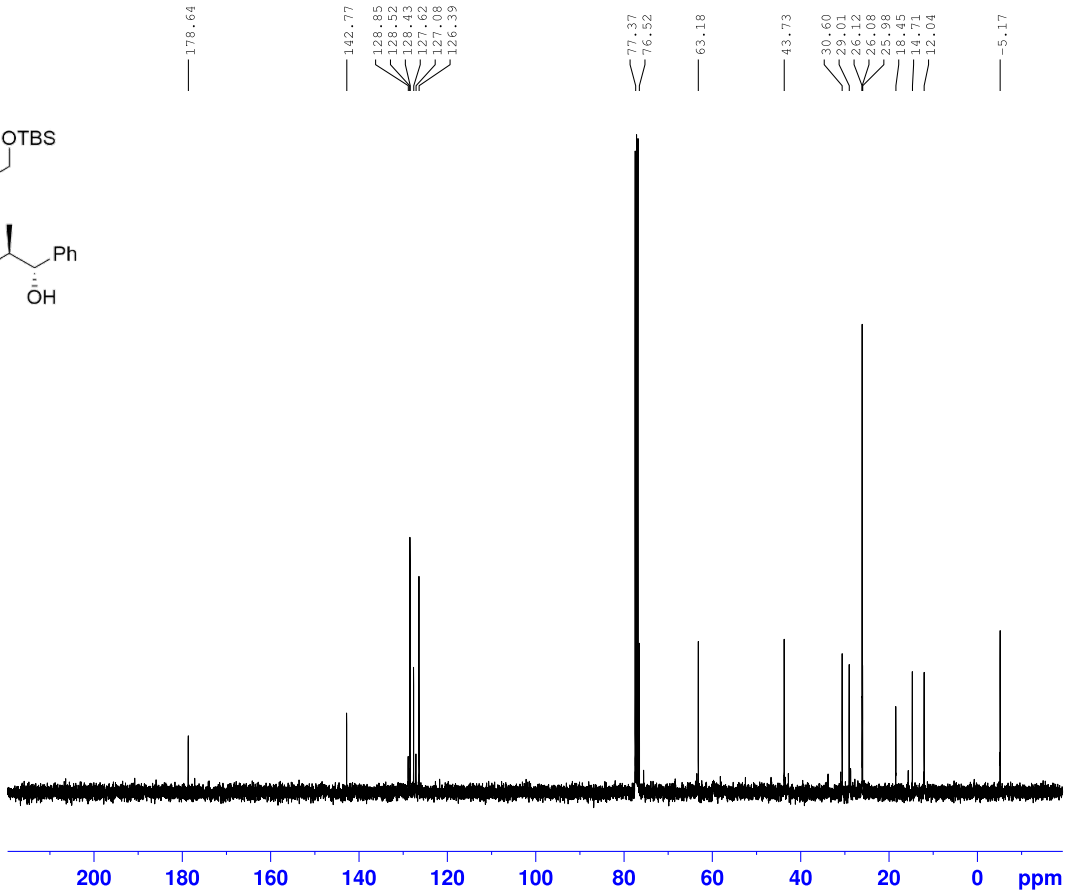





```
Current Data Parameters
NAME      Scott Myers Aux
EXPNO                 20
PROCNO                 1

F2 - Acquisition Parameters
Date_           20180330
Time                9.34
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8012.820 Hz
FIDRES             0.122266 Hz
AQ              4.0894465 sec
RG                    32
DW                62.400 usec
DE                 6.50 usec
TE                2508.0 K
D1             1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1          400.1324710 MHz
NUC1                  1H
P1                 14.50 usec
PLW1          12.01700020 W

F2 - Processing parameters
SI                 65536
SF            400.1300097 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

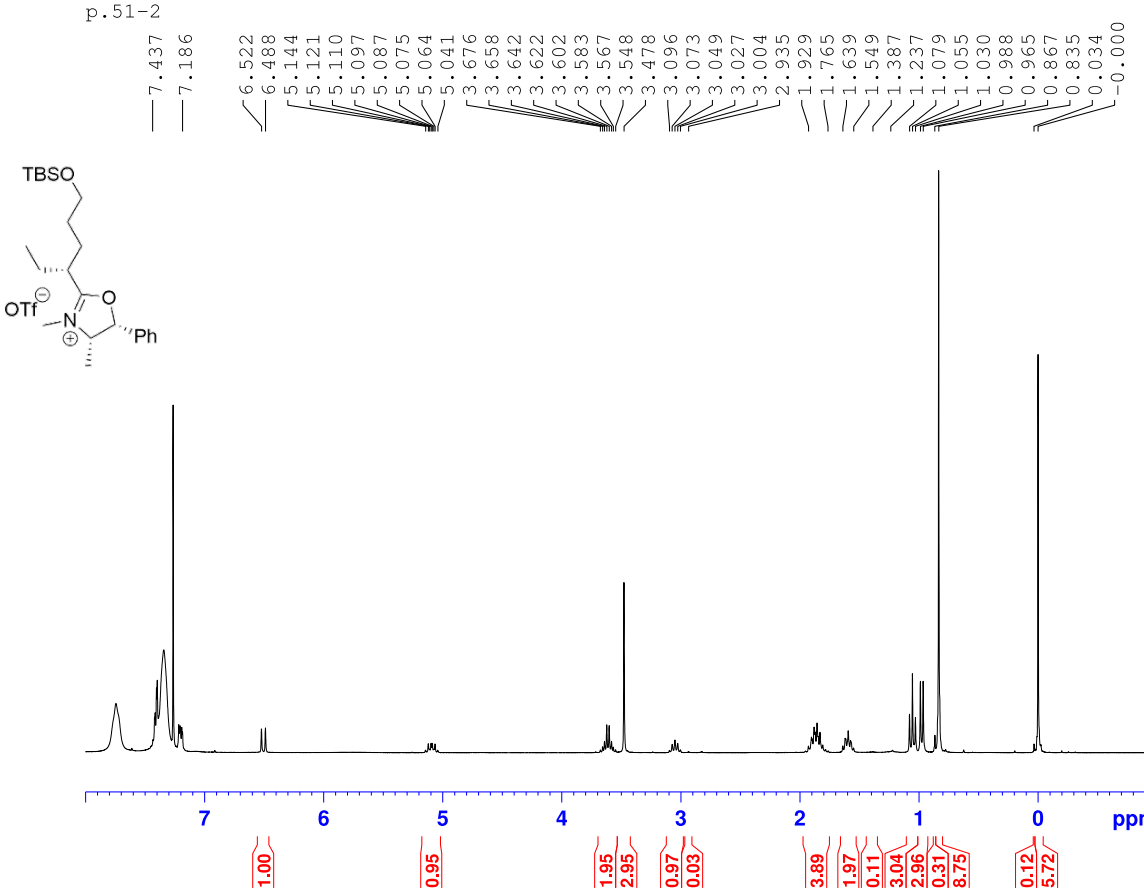
p.7-2





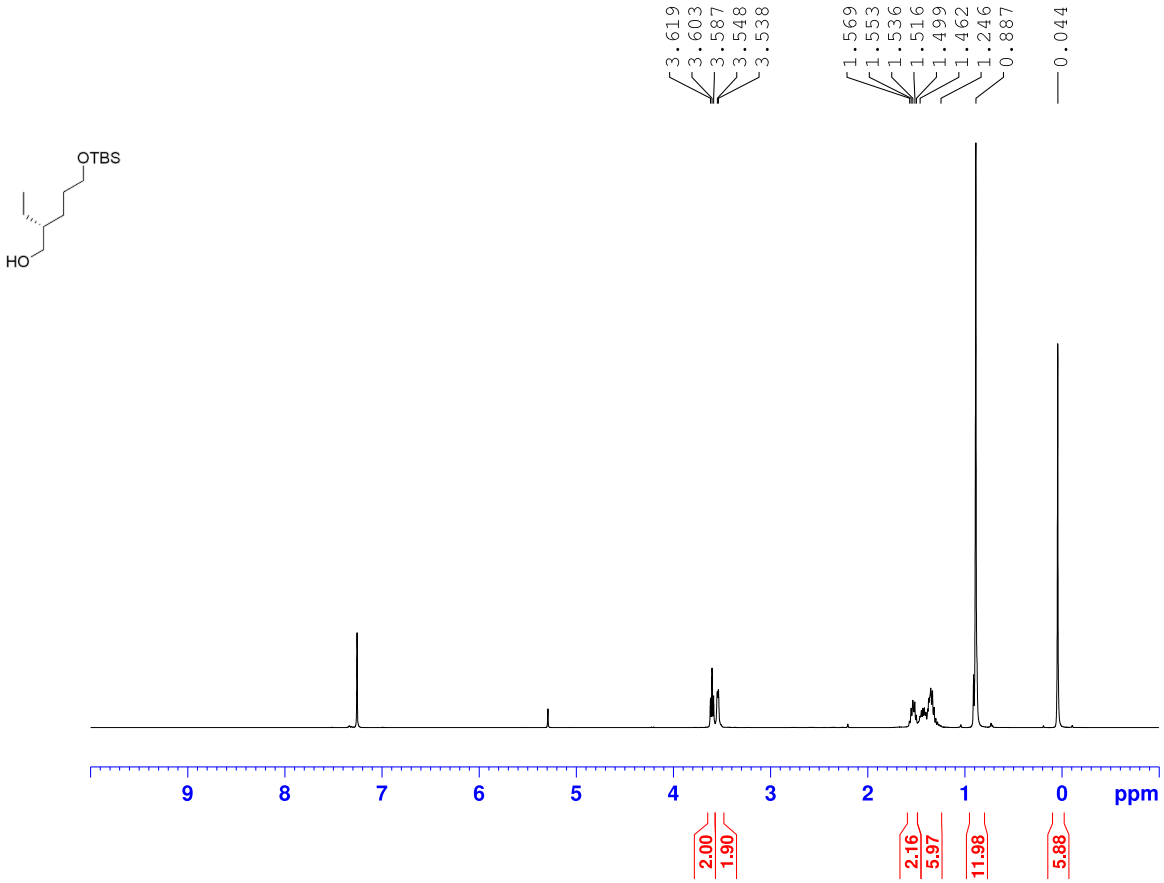

```
Current Data Parameters
NAME      Scott Myers Aux
EXPNO                 22
PROCNO                 1

F2 - Acquisition Parameters
Date_           20180330
Time                9.51
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG           zgpg30
TD                 65536
SOLVENT            CDCl3
NS                   150
DS                     4
SWH            24038.461 Hz
FIDRES             0.366798 Hz
AQ              1.3631488 sec
RG                   203
DW                20.800 usec
DE                 6.50 usec
TE                2743.5 K
D1             2.00000000 sec
D11            0.03000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1          100.6228293 MHz
NUC1                  13C
P1                 10.00 usec
PLW1          56.13299942 W

======== CHANNEL f2 ========
SFO2          400.1316005 MHz
NUC2                  1H
CPDPRG[2          waltz16
PCPD2              90.00 usec
PLW2          12.01700020 W
PLW12          0.31191999 W
PLW13          0.25266001 W

F2 - Processing parameters
SI                 32768
SF            100.6127568 MHz
WDW                   EM
SSB       0
LB                 1.00 Hz
GB        0
PC                 1.40
```

p.51-2



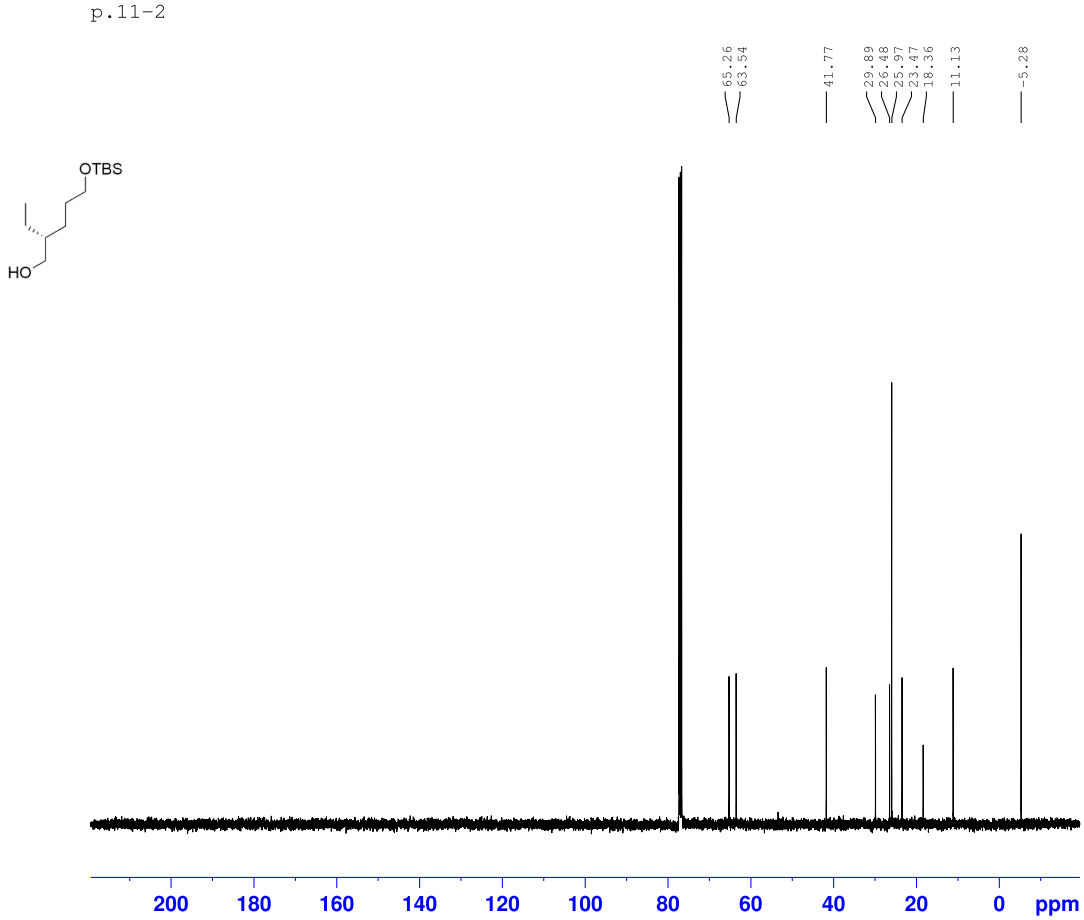

```
Current Data Parameters
NAME      Scott Myers DE
EXPNO                 10
PROCNO                 1

F2 - Acquisition Parameters
Date_           20141024
Time               20.16
INSTRUM            spect
PROBHD    5 mm QNP  1H/1
PULPROG             zg30
TD                 32768
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             6188.119 Hz
FIDRES          0.188846 Hz
AQ             2.6476543 sec
RG                    64
DW                80.800 usec
DE                 6.50 usec
TE                -924.0 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         300.2318540 MHz
NUC1                   1H
P1                 12.71 usec
PLW1         18.19700050 W

F2 - Processing parameters
SI                 32768
SF           300.2300068 MHz
WDW                   EM
SSB       0
LB                 0.10 Hz
GB        0
PC                 1.00
```

p.11-2



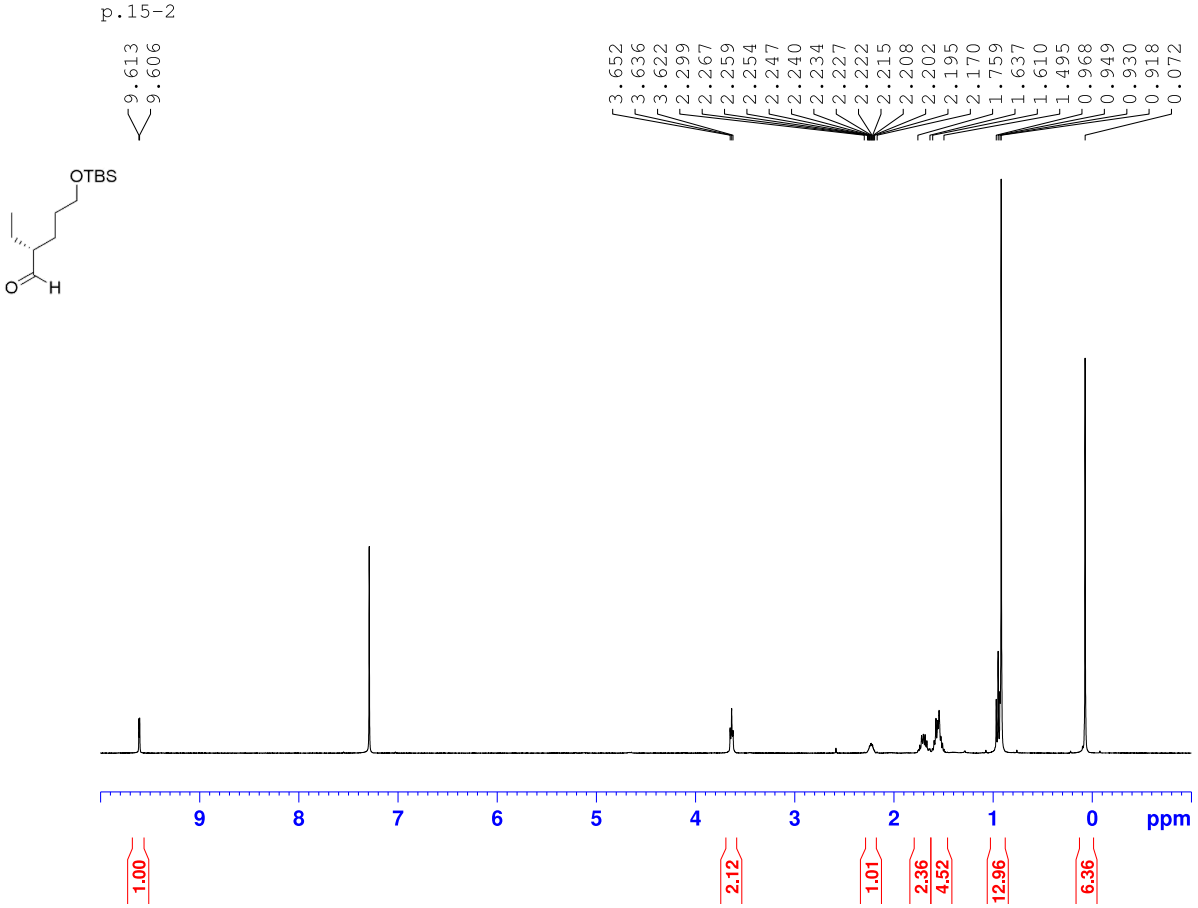

```
Current Data Parameters
NAME            Scott LAB
EXPNO                  20
PROCNO                  1

F2 - Acquisition Parameters
Date_            20140917
Time                16.12
INSTRUM             spect
PROBHD    5 mm PABBO BB-
PULPROG              zg30
TD                  65536
SOLVENT             CDCl3
NS                     16
DS                      2
SWH              8223.685 Hz
FIDRES           0.125483 Hz
AQ               3.9845889 sec
RG                     32
DW                60.800 usec
DE                 6.50 usec
TE                 94.9 K
D1              1.00000000 sec

======== CHANNEL f1 ========
NUC1                   1H
P1                  13.75 usec
PLW1          12.01700020 W
SFO1         400.1324710 MHz

F2 - Processing parameters
SI                  65536
SF           400.1300120 MHz
WDW                    EM
SSB       0
LB                  0.30 Hz
GB        0
PC                  1.00
```

p.11-2



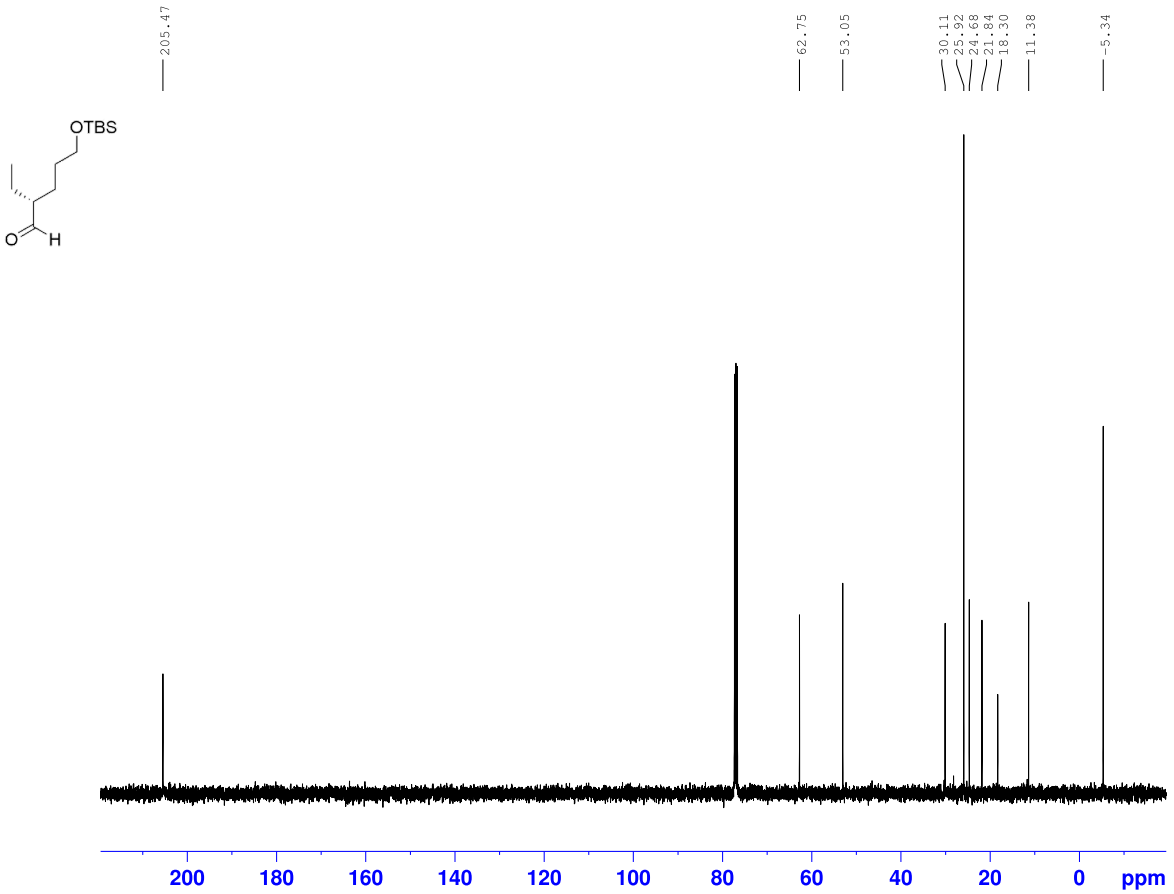

```
Current Data Parameters
NAME            Scott LAB
EXPNO                  21
PROCNO                  1

F2 - Acquisition Parameters
Date_            20140917
Time                16.28
INSTRUM             spect
PROBHD    5 mm PABBO BB-
PULPROG           zgpg30
TD                  65536
SOLVENT             CDCl3
NS                    250
DS                      4
SWH             24038.461 Hz
FIDRES           0.366798 Hz
AQ               1.3631488 sec
RG                    181
DW                20.800 usec
DE                 6.50 usec
TE                 94.8 K
D1              2.00000000 sec
D11             0.03000000 sec

======== CHANNEL f1 ========
NUC1                  13C
P1                  10.00 usec
PLW1          56.13299942 W
SFO1         100.6228293 MHz

======== CHANNEL f2 ========
CPDPRG[2          waltz16
NUC2                   1H
PCPD2               90.00 usec
PLW2          12.01700020 W
PLW12          0.29076999 W
PLW13     0 W
SFO2         400.1316005 MHz

F2 - Processing parameters
SI                  32768
SF           100.6127690 MHz
WDW                    EM
SSB       0
LB                  1.00 Hz
GB        0
PC                  1.40
```

p.15-2



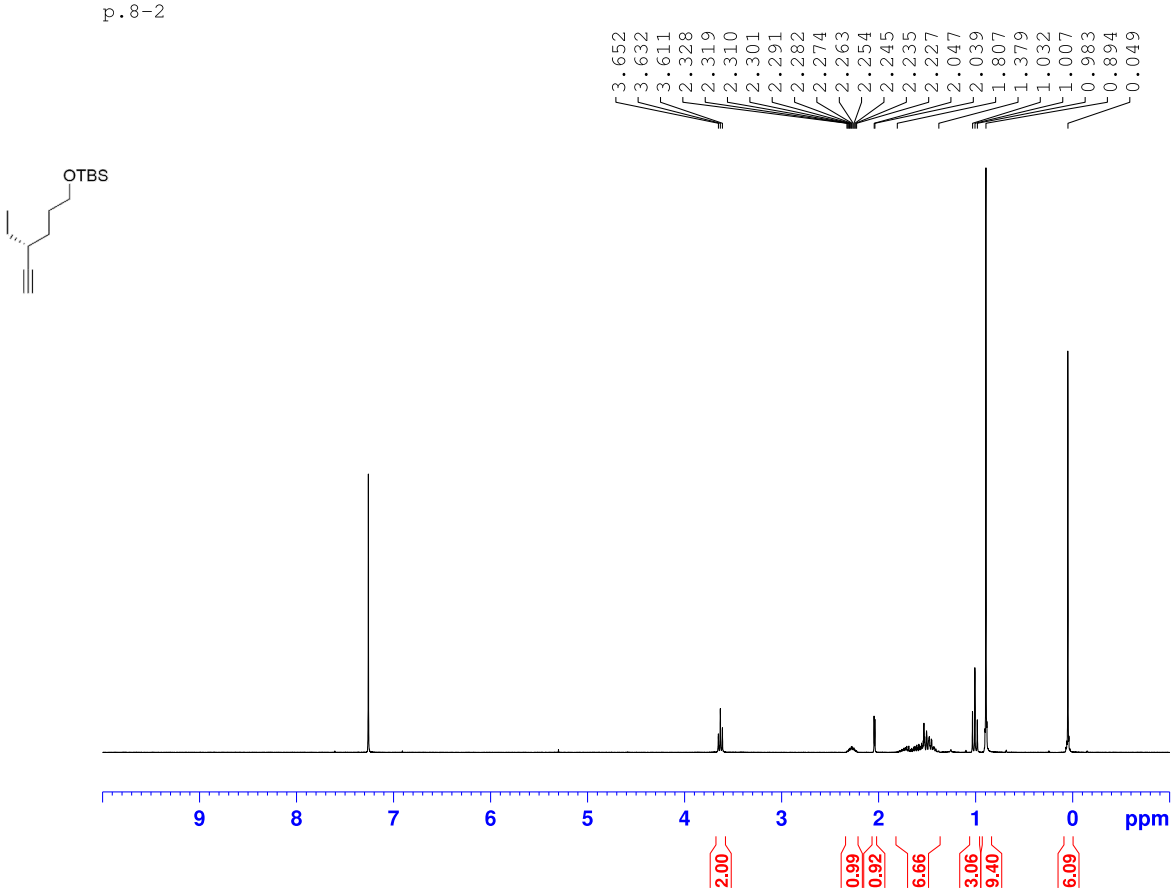

```
Current Data Parameters
NAME      Scott Oxidation
EXPNO                 120
PROCNO                  1

F2 - Acquisition Parameters
Date_           20140807
Time                9.40
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8223.685 Hz
FIDRES          0.125483 Hz
AQ              3.9845889 sec
RG                   128
DW                60.800 usec
DE                 6.50 usec
TE                 95.9 K
D1            1.00000000 sec

======== CHANNEL f1 ========
NUC1                  1H
P1                13.75 usec
PLW1         12.01700020 W
SFO1         400.1324710 MHz

F2 - Processing parameters
SI                 65536
SF           400.1299985 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

p.49-2



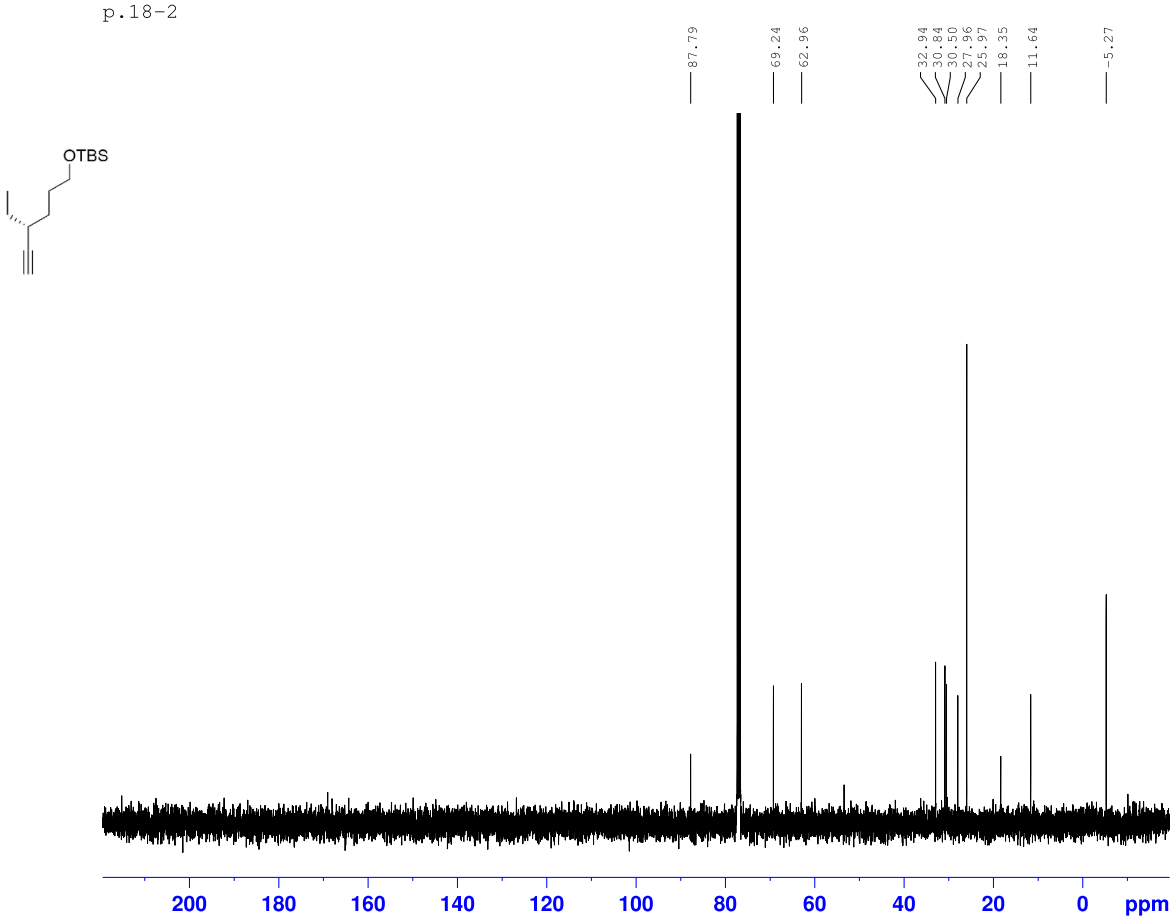

```
Current Data Parameters
NAME      Scott Oxidation
EXPNO                 140
PROCNO                  1

F2 - Acquisition Parameters
Date_           20141024
Time               14.31
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG          zgpg30
TD                 65536
SOLVENT            CDCl3
NS                   100
DS                     4
SWH            24038.461 Hz
FIDRES          0.366798 Hz
AQ              1.3631488 sec
RG                   203
DW                20.800 usec
DE                 6.50 usec
TE                -372.8 K
D1            2.00000000 sec
D11           0.03000000 sec

======== CHANNEL f1 ========
NUC1                 13C
P1                10.00 usec
PLW1         56.13299942 W
SFO1         100.6228293 MHz

======== CHANNEL f2 ========
CPDPRG[2          waltz16
NUC2                  1H
PCPD2             90.00 usec
PLW2         12.01700020 W
PLW12         0.29076999 W
PLW13     0 W
SFO2         400.1316005 MHz

F2 - Processing parameters
SI                 32768
SF           100.6127690 MHz
WDW                   EM
SSB       0
LB                 1.00 Hz
GB        0
PC                 1.40
```

p.8-2



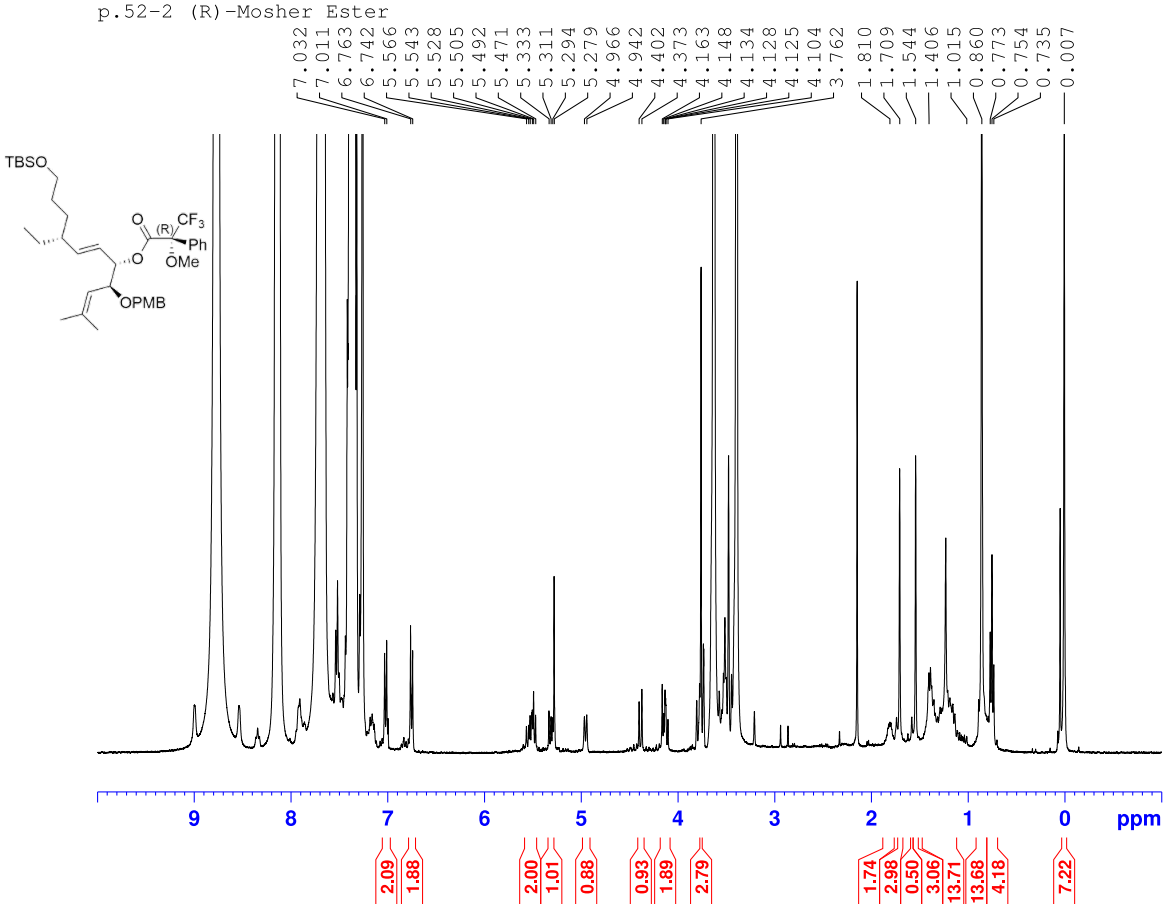

```
Current Data Parameters
NAME       Scott THP-TBS
EXPNO                 10
PROCNO                 1

F2 - Acquisition Parameters
Date_           20140725
Time               15.09
INSTRUM            spect
PROBHD   5 mm QNP  1H/1
PULPROG            zg30
TD                32768
SOLVENT           CDCl3
NS                   16
DS                    2
SWH            6188.119 Hz
FIDRES        0.188846 Hz
AQ            2.6476543 sec
RG                  322
DW               80.800 usec
DE                6.50 usec
TE               -925.1 K
D1            1.00000000 sec

======== CHANNEL f1 ========
NUC1                1H
P1                12.71 usec
PLW1        18.19700050 W
SFO1       300.2318540 MHz

F2 - Processing parameters
SI                32768
SF           300.2300084 MHz
WDW                  EM
SSB       0
LB                0.10 Hz
GB        0
PC                1.00
```

p.18-2



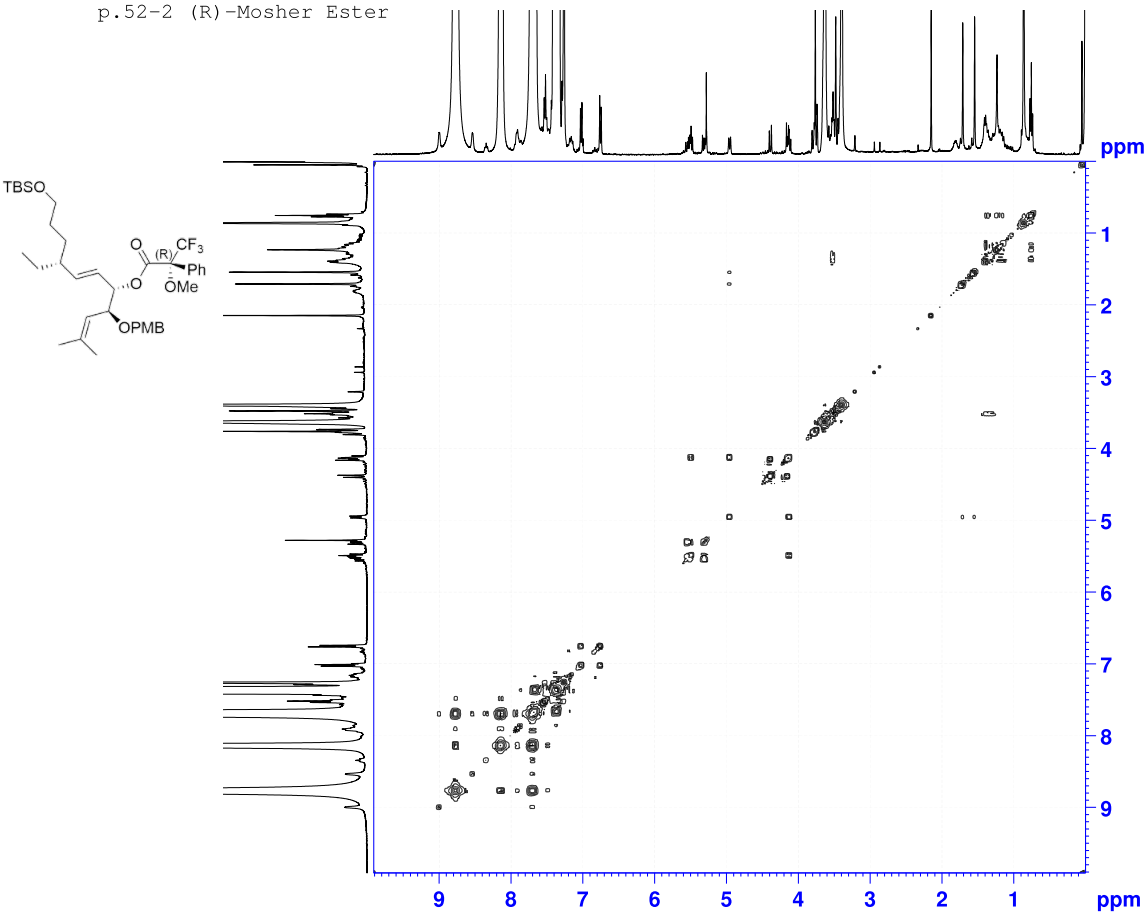

```
Current Data Parameters
NAME     Scott Ohira Bestmann
EXPNO                 101
PROCNO                  1

F2 - Acquisition Parameters
Date_           20140819
Time               12.47
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                  250
DS                    4
SWH           24038.461 Hz
FIDRES        0.366798 Hz
AQ            1.3631488 sec
RG                  203
DW               20.800 usec
DE                6.50 usec
TE                92.1 K
D1            2.00000000 sec
D11           0.03000000 sec

======== CHANNEL f1 ========
NUC1                13C
P1                10.00 usec
PLW1        56.13299942 W
SFO1       100.6228293 MHz

======== CHANNEL f2 ========
CPDPRG[2         waltz16
NUC2                1H
PCPD2             90.00 usec
PLW2        12.01700020 W
PLW12        0.29076999 W
PLW13    0 W
SFO2       400.1316005 MHz

F2 - Processing parameters
SI                32768
SF           100.6127690 MHz
WDW                  EM
SSB       0
LB                1.00 Hz
GB        0
PC                1.40
```

p.52-2 (R)-Mosher Ester



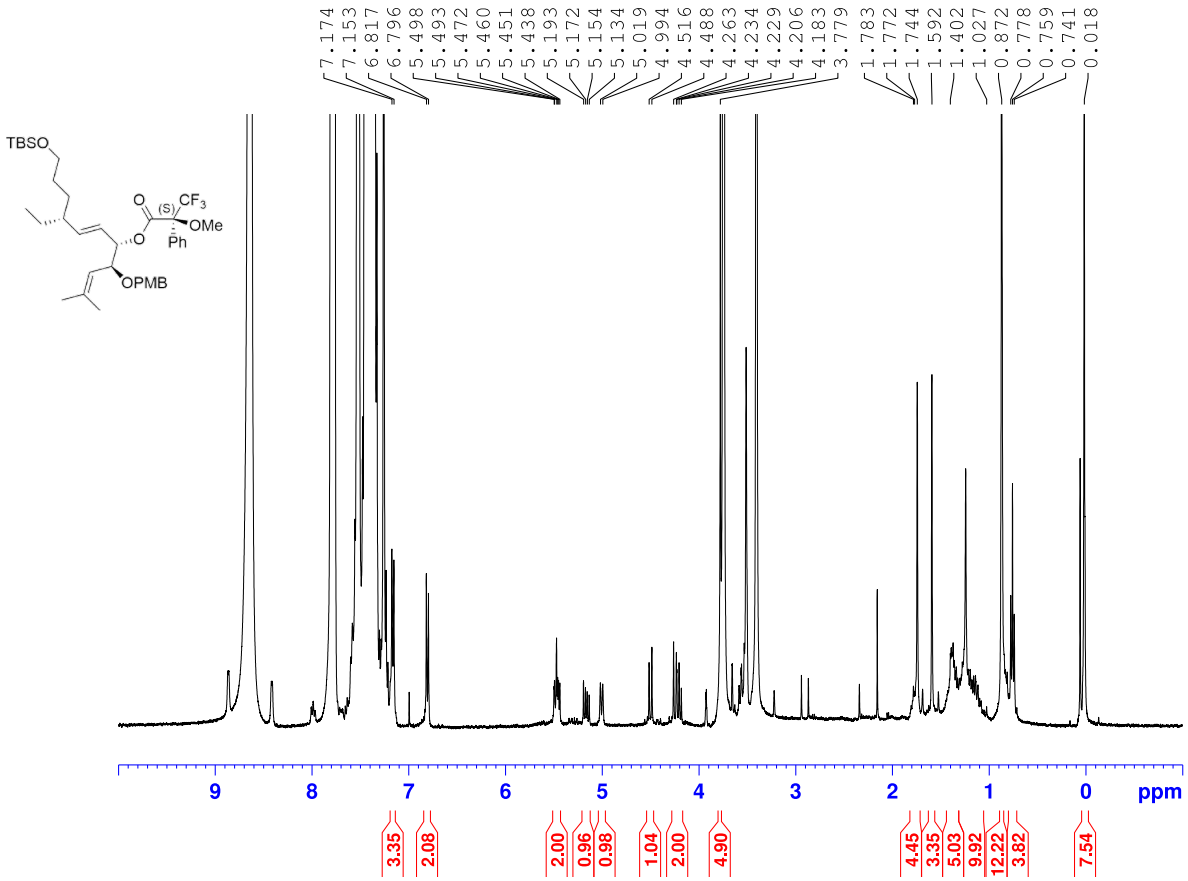

```
Current Data Parameters
NAME      Scott Mosher Ester
EXPNO                   80
PROCNO                   1

F2 - Acquisition Parameters
Date_           20141029
Time                6.24
INSTRUM           spect
PROBHD    5 mm PABBO BB-
PULPROG           zg30
TD               65536
SOLVENT          CDC13
NS                 500
DS                   2
SWH           8223.685 Hz
FIDRES         0.125483 Hz
AQ            3.9845889 sec
RG                90.5
DW              60.800 usec
DE               6.50 usec
TE             -1772.6 K
D1          1.00000000 sec

======== CHANNEL f1 ========
NUC1                1H
P1               13.75 usec
PLW1        12.01700020 W
SFO1        400.1324710 MHz

F2 - Processing parameters
SI               65536
SF          400.1300111 MHz
WDW                 EM
SSB       0
LB                0.30 Hz
GB        0
PC                1.00
```

p.52-2 (R)-Mosher Ester



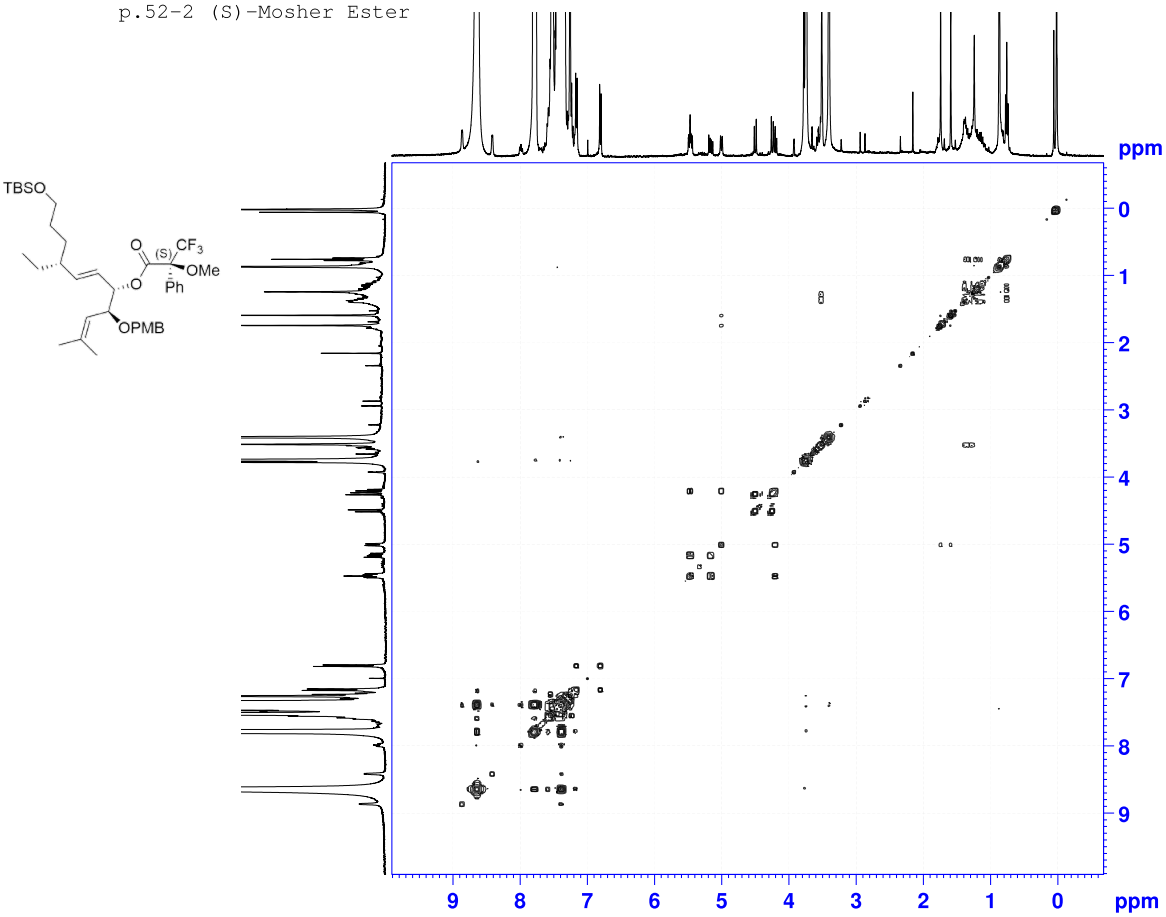

```
Current Data Parameters
NAME      Scott Mosher Ester
EXPNO                   81
PROCNO                   1

F2 - Acquisition Parameters
Date_           20141029
Time                6.26
INSTRUM           spect
PROBHD    5 mm PABBO BB-
PULPROG       cosygpppqf
TD                 2048
SOLVENT          CDC13
NS                   10
DS                    8
SWH           3968.254 Hz
FIDRES        1.937624 Hz
AQ            0.2580480 sec
RG                50.8
DW              126.000 usec
DE               6.50 usec
TE             -1873.9 K
D0          0.00000300 sec
D1          1.93364501 sec
D11         0.03000000 sec
D12         0.00002000 sec
D13         0.00000400 sec
D16         0.00020000 sec
IN0         0.00025200 sec

======== CHANNEL f1 ========
NUC1                1H
P0               13.75 usec
P1               13.75 usec
P17            2500.00 usec
PLW1        12.01700020 W
PLW10        3.48410010 W
SFO1        400.1319943 MHz

====== GRADIENT CHANNEL =====
GPNAM[1]      SMSQ10.100
GPZ1              10.00 %
P16             1000.00 usec

F1 - Acquisition parameters
TD                  128
SFO1          400.132 MHz
FIDRES       62.002967 Hz
SW             9.917 ppm
FnMODE              QF

F2 - Processing parameters
SI                1024
SF          400.1300090 MHz
WDW               QSINE
SSB       0
LB        0 Hz
GB        0
PC                1.40

F1 - Processing parameters
SI                1024
MC2                 QF
SF          400.1300105 MHz
WDW               QSINE
SSB       0
LB        0 Hz
GB        0
```

p.52-2 (S)-Mosher Ester



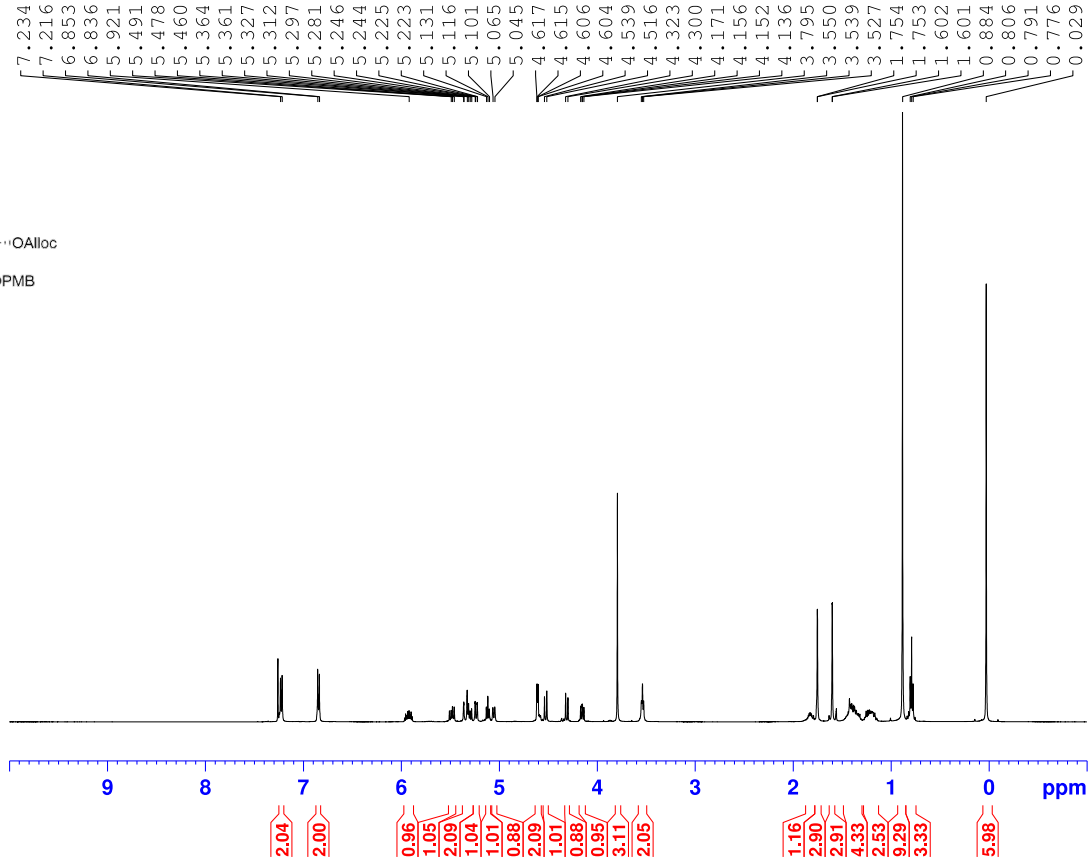

```
Current Data Parameters
NAME      Scott Mosher Ester
EXPNO                 90
PROCNO                 1

F2 - Acquisition Parameters
Date_           20141029
Time              16.35
INSTRUM           spect
PROBHD    5 mm PABBO BB-
PULPROG           zg30
TD               65536
SOLVENT          CDCl3
NS                 170
DS                   2
SWH           8223.685 Hz
FIDRES        0.125483 Hz
AQ            3.9845889 sec
RG                 101
DW              60.800 usec
DE               6.50 usec
TE              482.2 K
D1           1.00000000 sec

======== CHANNEL f1 ========
NUC1                1H
P1              13.75 usec
PLW1       12.01700020 W
SFO1      400.1324710 MHz

F2 - Processing parameters
SI               65536
SF        400.1300110 MHz
WDW                EM
SSB       0
LB              0.30 Hz
GB        0
PC              1.00
```

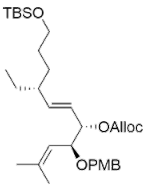
p.52-2 (S)-Mosher Ester




```
Current Data Parameters
NAME      Scott Mosher Ester
EXPNO                 91
PROCNO                 1

F2 - Acquisition Parameters
Date_           20141029
Time              16.36
INSTRUM           spect
PROBHD    5 mm PABBO BB-
PULPROG       cosygpppqf
TD                2048
SOLVENT          CDCl3
NS                   3
DS                   8
SWH           4237.288 Hz
FIDRES        2.068988 Hz
AQ            0.2416640 sec
RG                  64
DW             118.000 usec
DE               6.50 usec
TE               8.7 K
D0         0.00000300 sec
D1         1.95002902 sec
D11        0.03000000 sec
D12        0.00002000 sec
D13        0.00000400 sec
D16        0.00020000 sec
IN0        0.00023600 sec

======== CHANNEL f1 ========
NUC1                1H
P0              13.75 usec
P1              13.75 usec
P17           2500.00 usec
PLW1       12.01700020 W
PLW10       3.48410010 W
SFO1      400.1318571 MHz

====== GRADIENT CHANNEL =====
GPNAM[1]      SMSQ10.100
GPZ1             10.00 %
P16            1000.00 usec

F1 - Acquisition parameters
TD                  128
SFO1          400.1319 MHz
FIDRES        66.207626 Hz
SW              10.590 ppm
FnMODE                QF

F2 - Processing parameters
SI                 1024
SF        400.1300104 MHz
WDW              QSINE
SSB       0
LB        0 Hz
GB        0
PC              1.40

F1 - Processing parameters
SI                 1024
MC2                QF
SF        400.1300093 MHz
WDW              QSINE
SSB       0
LB        0 Hz
GB        0
```

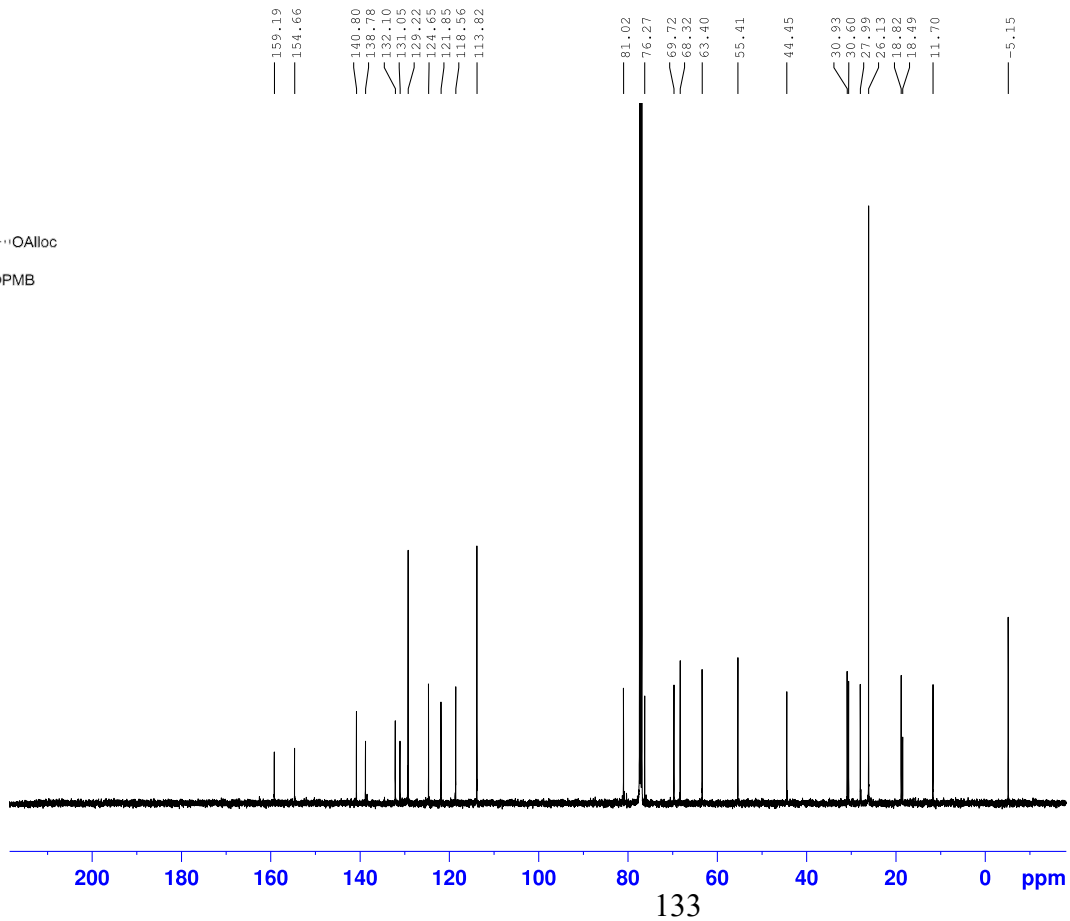
p.244-4

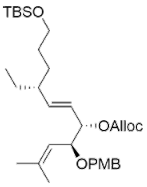





```
Current Data Parameters
NAME         Scott Alloc
EXPNO                 10
PROCNO                 1

F2 - Acquisition Parameters
Date_           20180413
Time                3.59
INSTRUM            spect
PROBHD   5 mm PABBO BB/
PULPROG            zg30
TD                65536
SOLVENT           CDCl3
NS                   16
DS                    2
SWH           10000.000 Hz
FIDRES            0.152588 Hz
AQ             3.2767999 sec
RG                   64
DW                50.000 usec
DE                 6.50 usec
TE                301.6 K
D1             1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         500.1630887 MHz
NUC1                 1H
P1                11.50 usec
PLW1         18.00000000 W

F2 - Processing parameters
SI                65536
SF           500.1600120 MHz
WDW                  EM
SSB       0
LB                0.30 Hz
GB        0
PC                1.00
```

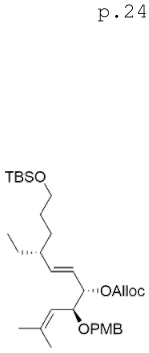
p.244-4

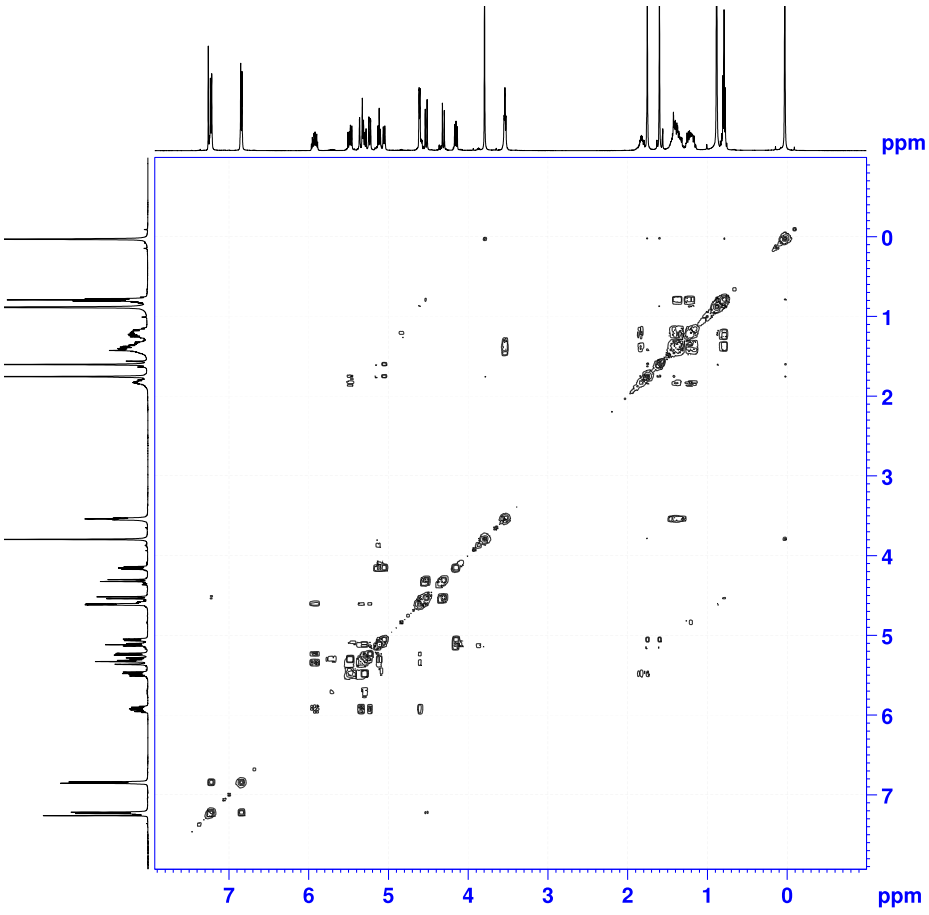





```
Current Data Parameters
NAME         Scott Alloc
EXPNO                 12
PROCNO                 1

F2 - Acquisition Parameters
Date_           20180413
Time                5.25
INSTRUM            spect
PROBHD   5 mm PABBO BB/
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                 1500
DS                    2
SWH           29761.904 Hz
FIDRES            0.454131 Hz
AQ             1.1010048 sec
RG                  203
DW                16.800 usec
DE                 6.50 usec
TE                303.4 K
D1             2.00000000 sec
D11            0.03000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         125.7779086 MHz
NUC1                 13C
P1                10.50 usec
PLW1        110.00000000 W

======== CHANNEL f2 ========
SFO2         500.1620006 MHz
NUC2                 1H
CPDPRG[2          waltz16
PCPD2             80.00 usec
PLW2         18.00000000 W
PLW12         0.37195000 W
PLW13         0.23805000 W

F2 - Processing parameters
SI                32768
SF           125.7653101 MHz
WDW                  EM
SSB       0
LB                1.00 Hz
GB        0
PC                1.40
```

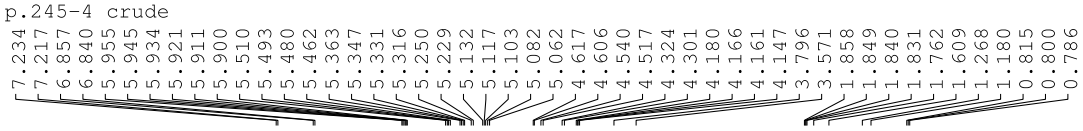
p.244-4

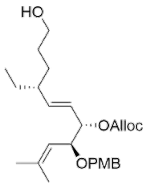


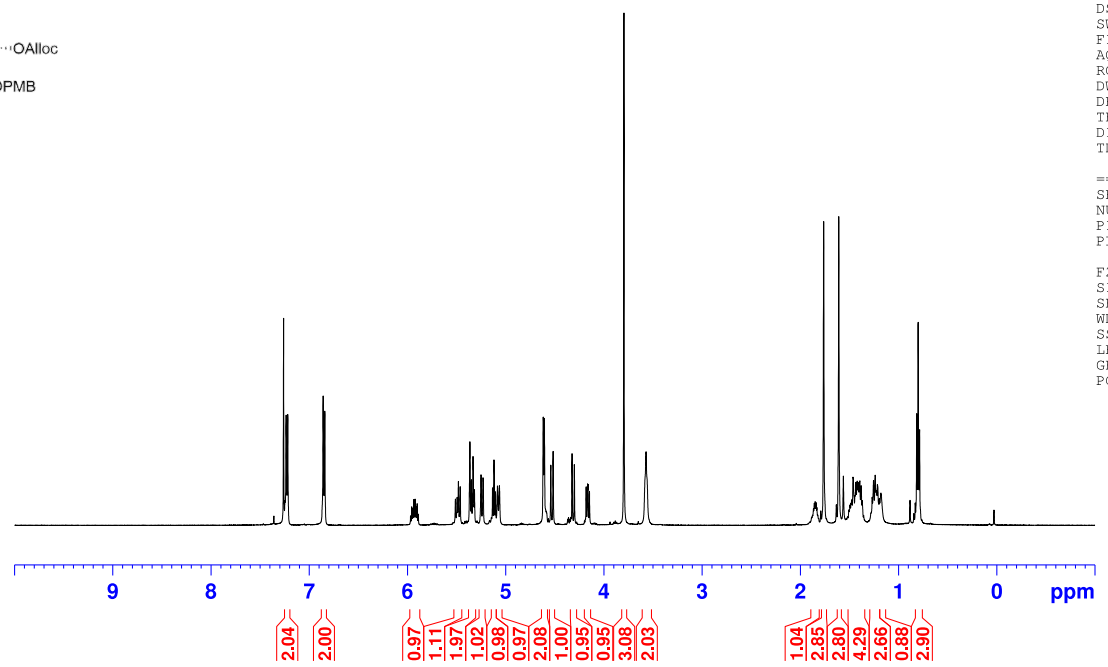



```
Current Data Parameters
NAME          Scott Alloc
EXPNO                  11
PROCNO                  1

F2 - Acquisition Parameters
Date_            20180413
Time                 4.00
INSTRUM             spect
PROBHD    5 mm PABBO BB/
PULPROG       cosygpppqf
TD                   2048
SOLVENT             CDCl3
NS                      1
DS                      8
SWH              4464.286 Hz
FIDRES           2.179827 Hz
AQ               0.2293760 sec
RG                   40.3
DW                112.000 usec
DE                  6.50 usec
TE                301.5 K
D0             0.00000300 sec
D1             1.92381406 sec
D11            0.03000000 sec
D12            0.00002000 sec
D13            0.00000400 sec
D16            0.00020000 sec
IN0            0.00022400 sec

======== CHANNEL f1 ========
SFO1          500.1617480 MHz
NUC1                    1H
P0                  11.50 usec
P1                  11.50 usec
P17               2500.00 usec
PLW1         18.00000000 W
PLW10         3.52139997 W

====== GRADIENT CHANNEL =====
GPNAM[1]       SMSQ10.100
GPZ1                10.00 %
P16               1000.00 usec

F1 - Acquisition parameters
TD                     128
SFO1            500.1617 MHz
FIDRES          69.754463 Hz
SW                 8.926 ppm
FnMODE                 QF

F2 - Processing parameters
SI                     1024
SF            500.1600133 MHz
WDW                  QSINE
SSB       0
LB        0 Hz
GB        0
PC                   1.40

F1 - Processing parameters
SI                     1024
MC2                    QF
SF            500.1600127 MHz
WDW                  QSINE
SSB       0
LB        0 Hz
GB        0
```

p.245-4 crude

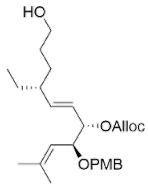


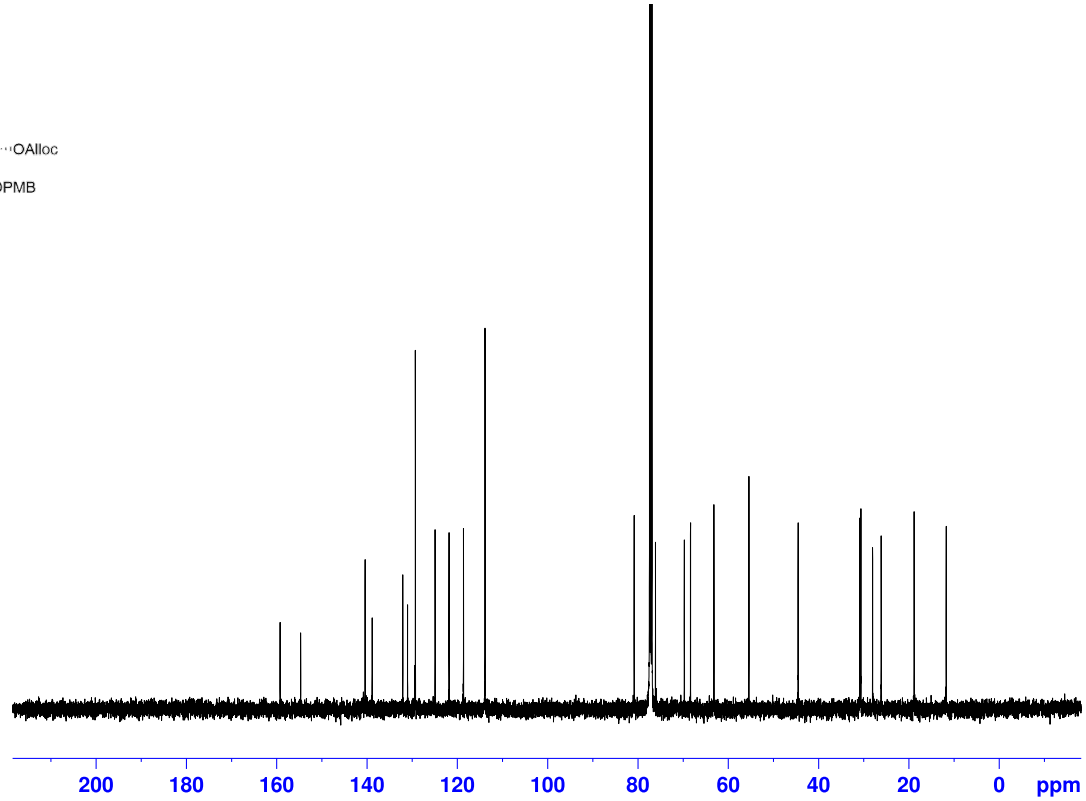





```
Current Data Parameters
NAME          Scott NH4F
EXPNO                 10
PROCNO                 1

F2 - Acquisition Parameters
Date_           20180413
Time                5.35
INSTRUM            spect
PROBHD   5 mm PABBO BB/
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH            10000.000 Hz
FIDRES             0.152588 Hz
AQ              3.2767999 sec
RG                  90.5
DW                 50.000 usec
DE                  6.50 usec
TE                302.2 K
D1             1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1          500.1630887 MHz
NUC1                  1H
P1                 11.50 usec
PLW1          18.00000000 W

F2 - Processing parameters
SI                 65536
SF            500.1600120 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

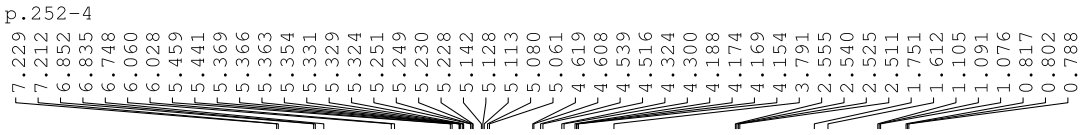
p.245-4 crude

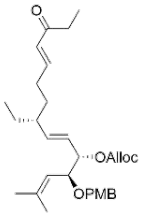


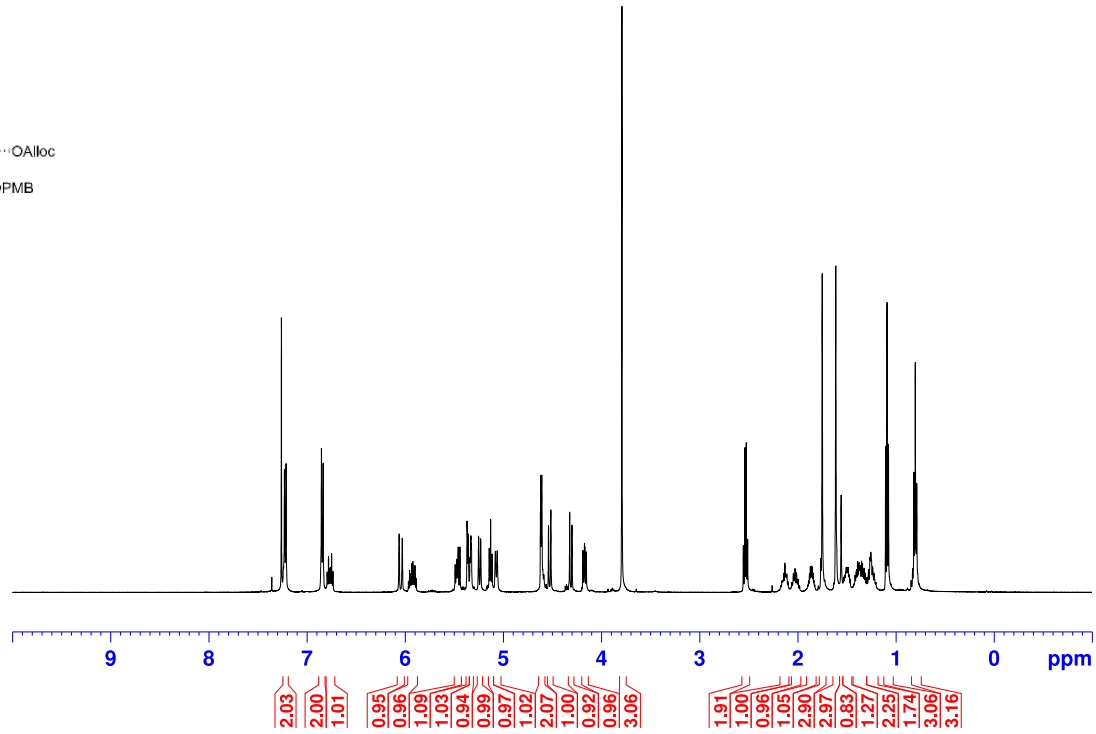



```
Current Data Parameters
NAME          Scott NH4F
EXPNO                 11
PROCNO                 1

F2 - Acquisition Parameters
Date_           20180413
Time                6.55
INSTRUM            spect
PROBHD   5 mm PABBO BB/
PULPROG           zgpg30
TD                 65536
SOLVENT            CDCl3
NS                  1500
DS                     2
SWH            29761.904 Hz
FIDRES             0.454131 Hz
AQ              1.1010048 sec
RG                   203
DW                 16.800 usec
DE                  6.50 usec
TE                303.6 K
D1             2.00000000 sec
D11            0.03000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1          125.7779086 MHz
NUC1                  13C
P1                 10.50 usec
PLW1         110.00000000 W

======== CHANNEL f2 ========
SFO2          500.1620006 MHz
NUC2                  1H
CPDPRG[2          waltz16
PCPD2              80.00 usec
PLW2          18.00000000 W
PLW12          0.37195000 W
PLW13          0.23805000 W

F2 - Processing parameters
SI                 32768
SF            125.7653099 MHz
WDW                   EM
SSB       0
LB                 1.00 Hz
GB        0
PC                 1.40
```

p.252-4

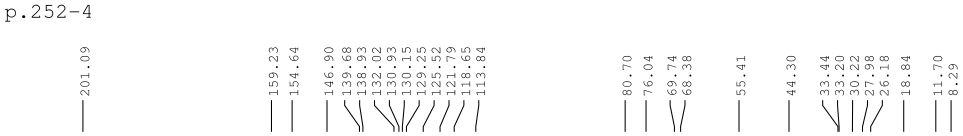


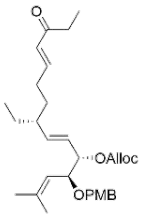


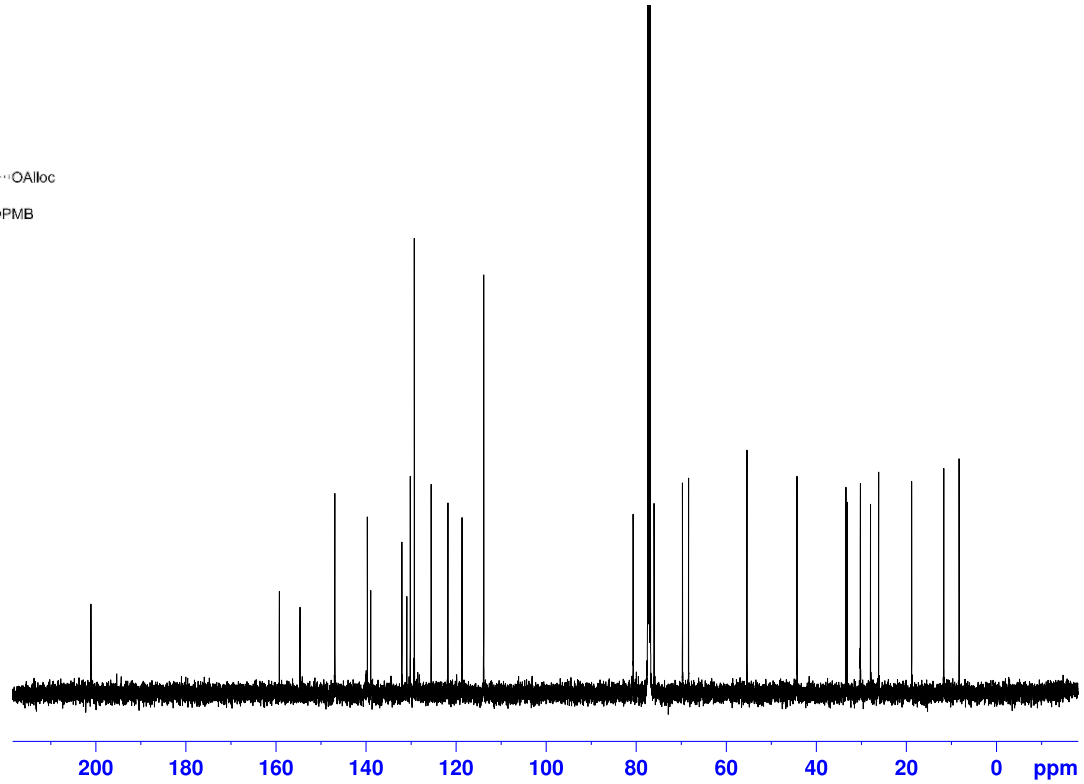



```
Current Data Parameters
NAME            Scott HWE
EXPNO                  20
PROCNO                  1

F2 - Acquisition Parameters
Date_           20180414
Time                1.28
INSTRUM            spect
PROBHD   5 mm PABBO BB/
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH            10000.000 Hz
FIDRES         0.152588 Hz
AQ             3.2767999 sec
RG                  90.5
DW                50.000 usec
DE                 6.50 usec
TE                302.2 K
D1             1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         500.1630887 MHz
NUC1                   1H
P1                 11.50 usec
PLW1         18.00000000 W

F2 - Processing parameters
SI                 65536
SF            500.1600118 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

p.252-4

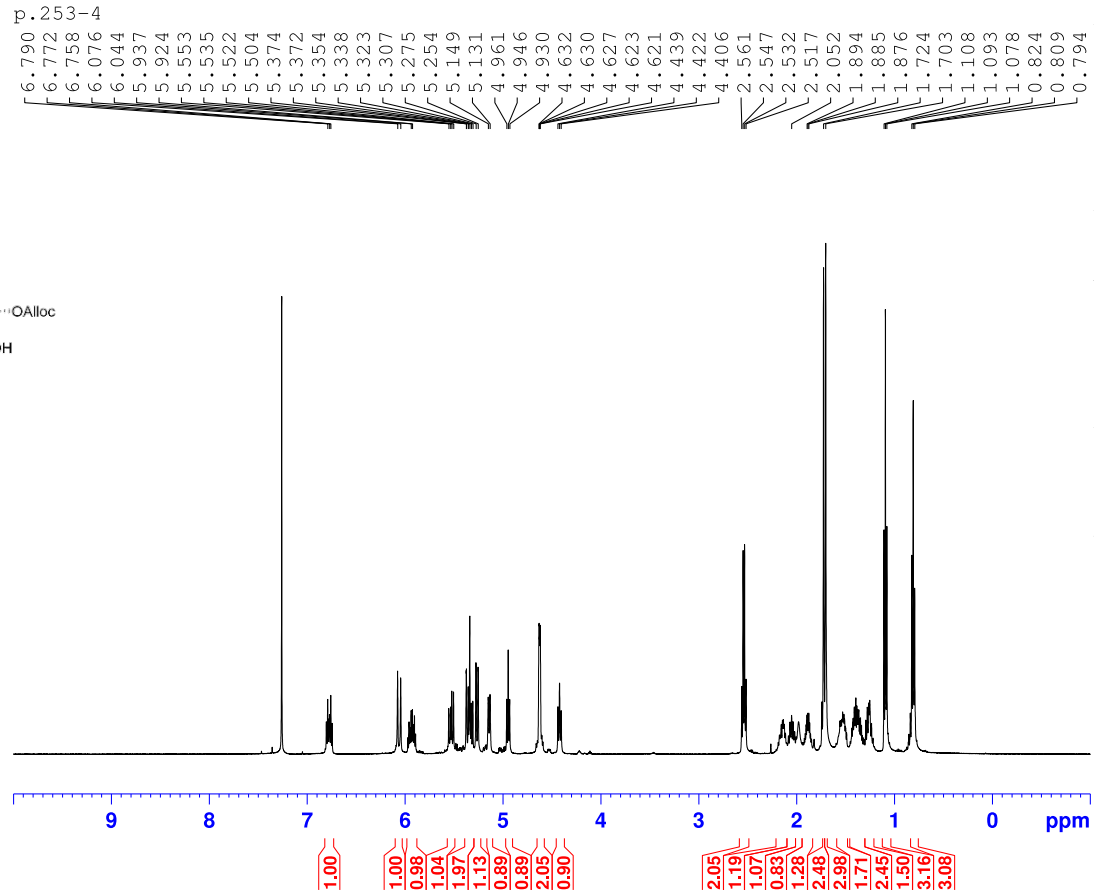






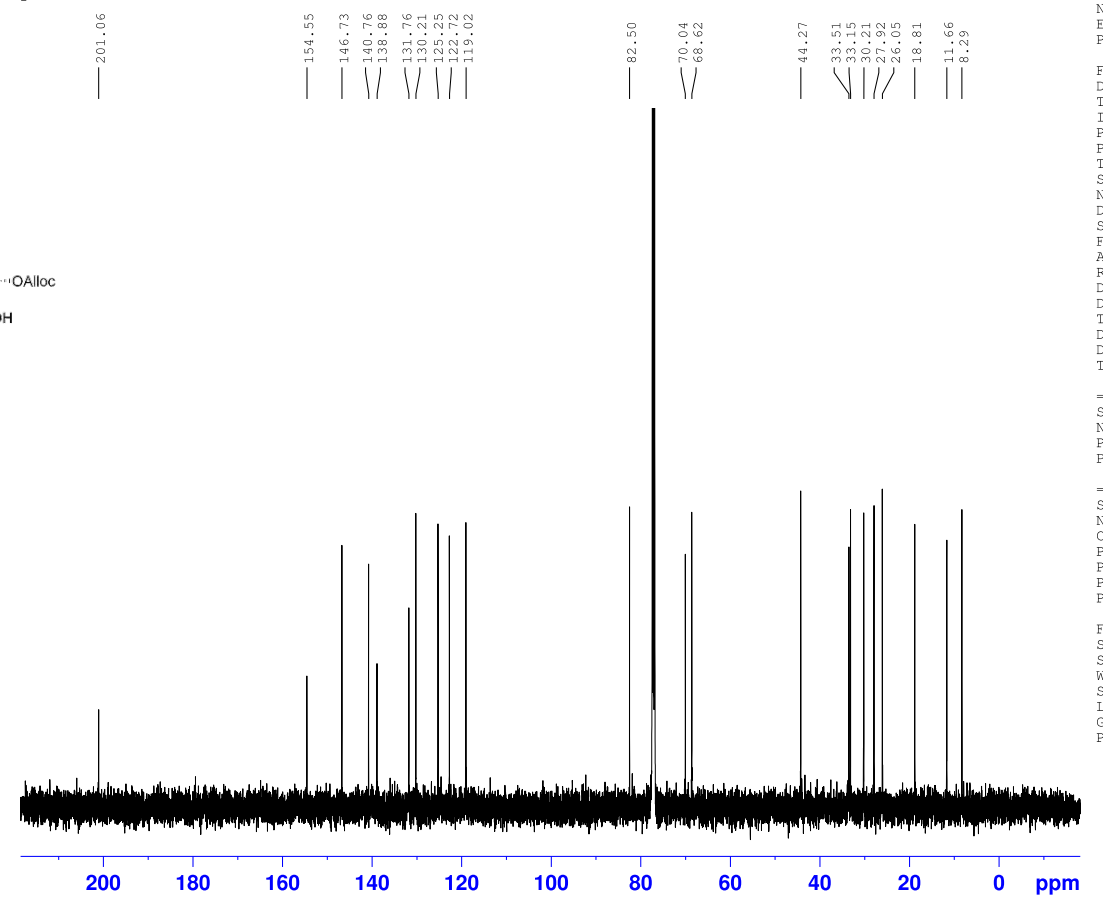

```
Current Data Parameters
NAME            Scott HWE
EXPNO                  21
PROCNO                  1

F2 - Acquisition Parameters
Date_           20180414
Time                2.48
INSTRUM            spect
PROBHD   5 mm PABBO BB/
PULPROG           zgpg30
TD                 65536
SOLVENT            CDCl3
NS                  1500
DS                     2
SWH            29761.904 Hz
FIDRES         0.454131 Hz
AQ             1.1010048 sec
RG                   203
DW                16.800 usec
DE                 6.50 usec
TE                303.2 K
D1             2.00000000 sec
D11            0.03000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         125.7779086 MHz
NUC1                   13C
P1                 10.50 usec
PLW1        110.00000000 W

======== CHANNEL f2 ========
SFO2         500.1620006 MHz
NUC2                   1H
CPDPRG[2          waltz16
PCPD2              80.00 usec
PLW2         18.00000000 W
PLW12         0.37195000 W
PLW13         0.23805000 W

F2 - Processing parameters
SI                 32768
SF           125.7653101 MHz
WDW                   EM
SSB       0
LB                 1.00 Hz
GB        0
PC                 1.40
```

p.253-4



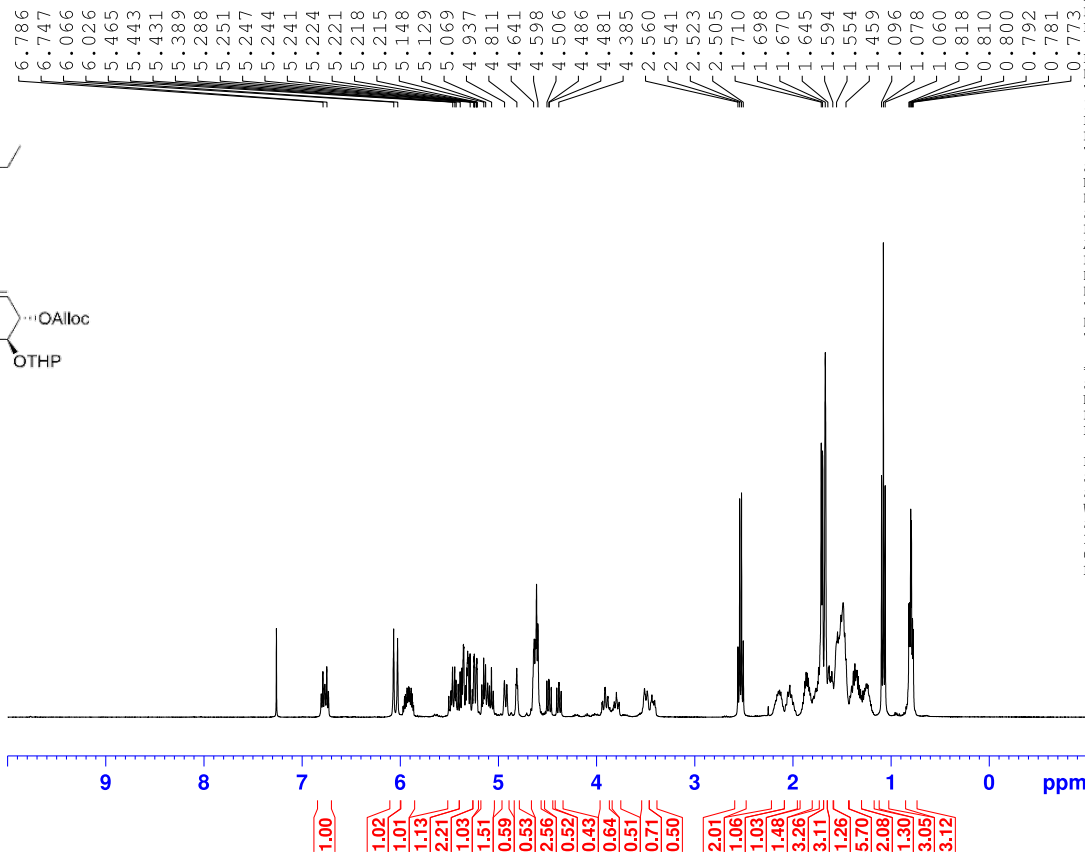

```
Current Data Parameters
NAME            Scott DDQ
EXPNO                  40
PROCNO                  1

F2 - Acquisition Parameters
Date_           20180413
Time                7.04
INSTRUM            spect
PROBHD    5 mm PABBO BB/
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH            10000.000 Hz
FIDRES             0.152588 Hz
AQ              3.2767999 sec
RG                   101
DW                50.000 usec
DE                 6.50 usec
TE                302.5 K
D1             1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1          500.1630887 MHz
NUC1                  1H
P1                 11.50 usec
PLW1          18.00000000 W

F2 - Processing parameters
SI                 65536
SF            500.1600123 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

p.253-4



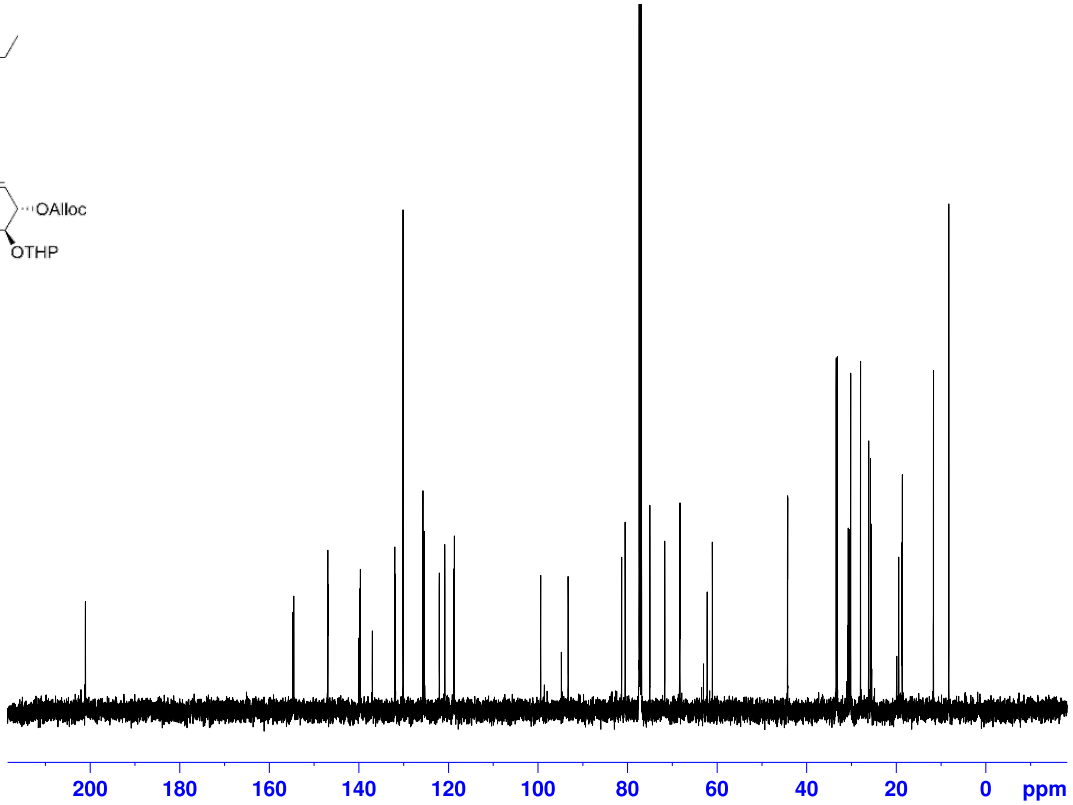

```
Current Data Parameters
NAME            Scott DDQ
EXPNO                  41
PROCNO                  1

F2 - Acquisition Parameters
Date_           20180413
Time                8.24
INSTRUM            spect
PROBHD    5 mm PABBO BB/
PULPROG          zgpg30
TD                 65536
SOLVENT            CDCl3
NS                  1500
DS                     2
SWH            29761.904 Hz
FIDRES             0.454131 Hz
AQ              1.1010048 sec
RG                   203
DW                16.800 usec
DE                 6.50 usec
TE                303.7 K
D1             2.00000000 sec
D11            0.03000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1          125.7779086 MHz
NUC1                  13C
P1                 10.50 usec
PLW1          110.00000000 W

======== CHANNEL f2 ========
SFO2          500.1620006 MHz
NUC2                  1H
CPDPRG[2          waltz16
PCPD2              80.00 usec
PLW2          18.00000000 W
PLW12          0.37195000 W
PLW13          0.23805000 W

F2 - Processing parameters
SI                 32768
SF            125.7653091 MHz
WDW                   EM
SSB       0
LB                 1.00 Hz
GB        0
PC                 1.40
```

p.255-4



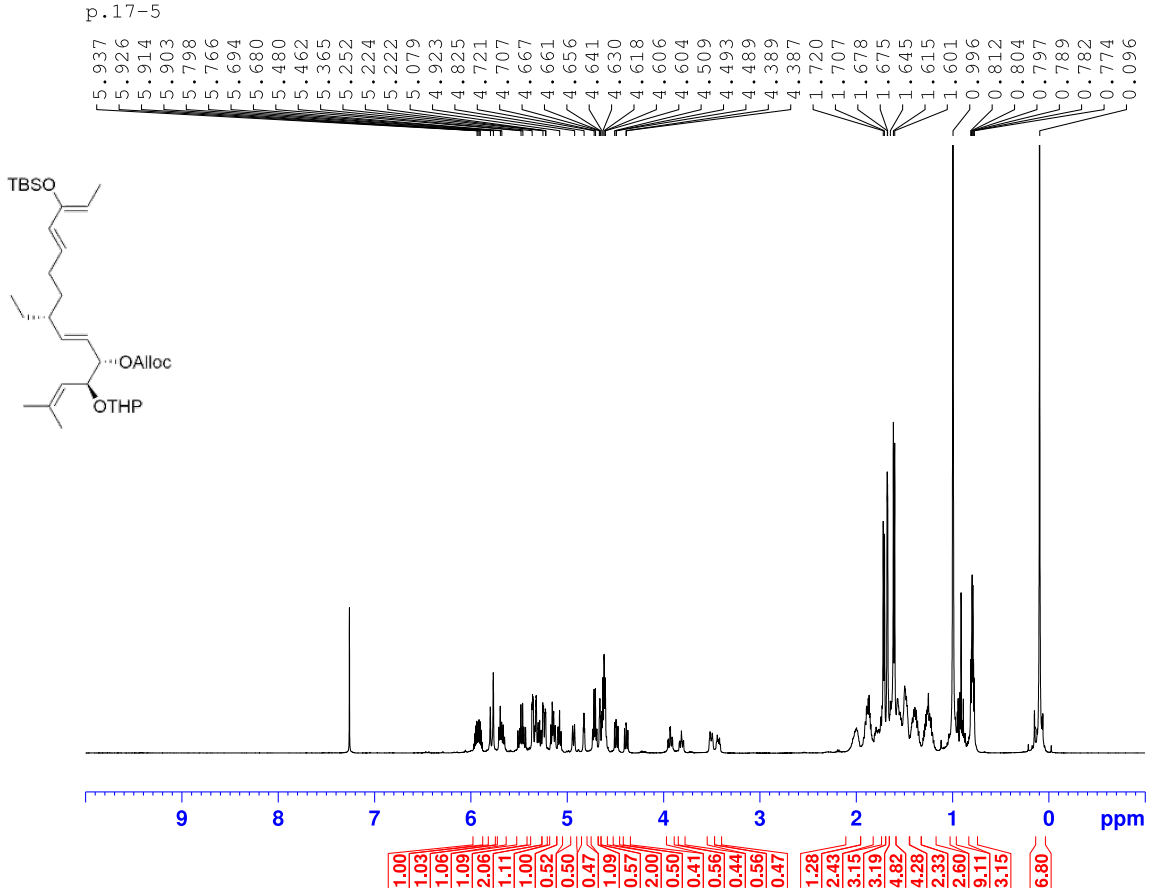

```
Current Data Parameters
NAME            Scott HWE
EXPNO                  10
PROCNO                  1

F2 - Acquisition Parameters
Date_            20180316
Time                8.32
INSTRUM            spect
PROBHD    5 mm PABBO BB-
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8012.820 Hz
FIDRES          0.122266 Hz
AQ              4.0894465 sec
RG                    32
DW                62.400 usec
DE                 6.50 usec
TE                2227.9 K
D1             1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1          400.1324710 MHz
NUC1                  1H
P1                 14.50 usec
PLW1          12.01700020 W

F2 - Processing parameters
SI                 65536
SF            400.1300099 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

p.255-4



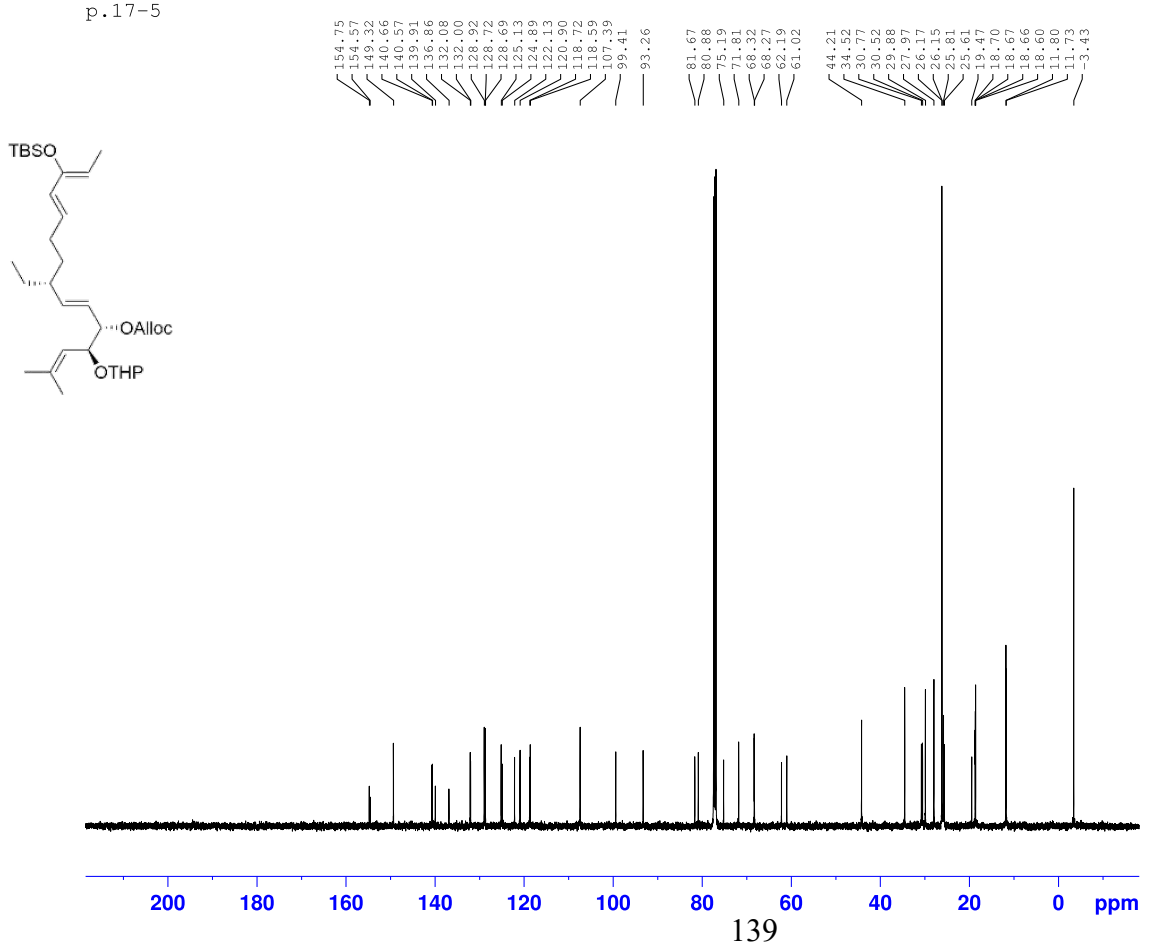

```
Current Data Parameters
NAME            Scott HWE
EXPNO                  10
PROCNO                  1

F2 - Acquisition Parameters
Date_            20180316
Time               11.42
INSTRUM            spect
PROBHD    5 mm PABBO BB/
PULPROG           zgpg30
TD                 65536
SOLVENT            CDCl3
NS                   300
DS                     2
SWH            29761.904 Hz
FIDRES          0.454131 Hz
AQ              1.1010048 sec
RG                   203
DW                16.800 usec
DE                 6.50 usec
TE                298.9 K
D1             2.00000000 sec
D11            0.03000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1          125.7779086 MHz
NUC1                  13C
P1                 10.50 usec
PLW1          110.00000000 W

======== CHANNEL f2 ========
SFO2          500.1620006 MHz
NUC2                  1H
CPDPRG[2          waltz16
PCPD2              80.00 usec
PLW2          18.00000000 W
PLW12          0.37195000 W
PLW13          0.23805000 W

F2 - Processing parameters
SI                 32768
SF            125.7653154 MHz
WDW                   EM
SSB       0
LB                 1.00 Hz
GB        0
PC                 1.40
```

p.17-5

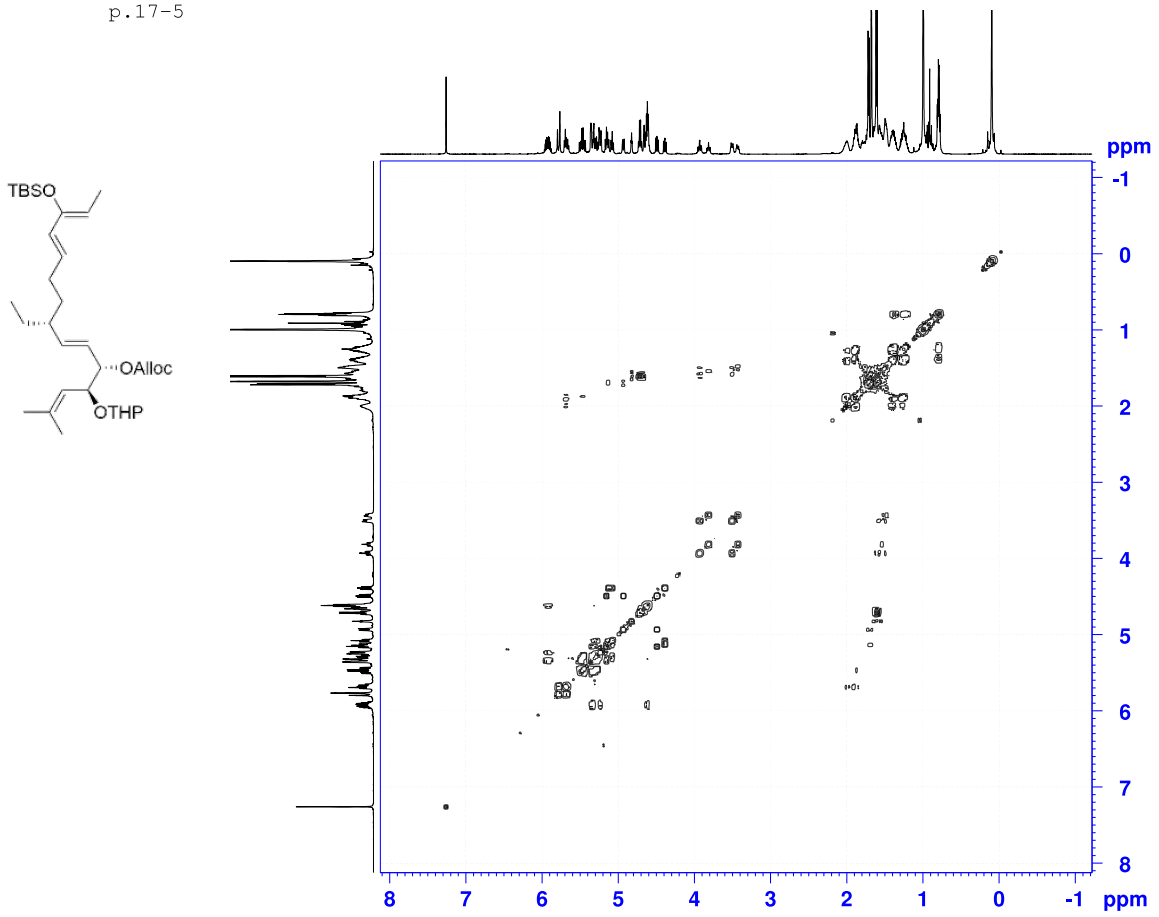



```
Current Data Parameters
NAME      Scott Silyl Enol Ether
EXPNO                 10
PROCNO                 1

F2 - Acquisition Parameters
Date_           20180425
Time                8.42
INSTRUM            spect
PROBHD   5 mm PABBO BB/
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH            10000.000 Hz
FIDRES          0.152588 Hz
AQ              3.2767999 sec
RG                    32
DW                50.000 usec
DE                 6.50 usec
TE                301.3 K
D1             1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         500.1630887 MHz
NUC1                  1H
P1                 11.50 usec
PLW1         18.00000000 W

F2 - Processing parameters
SI                 65536
SF           500.1600122 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

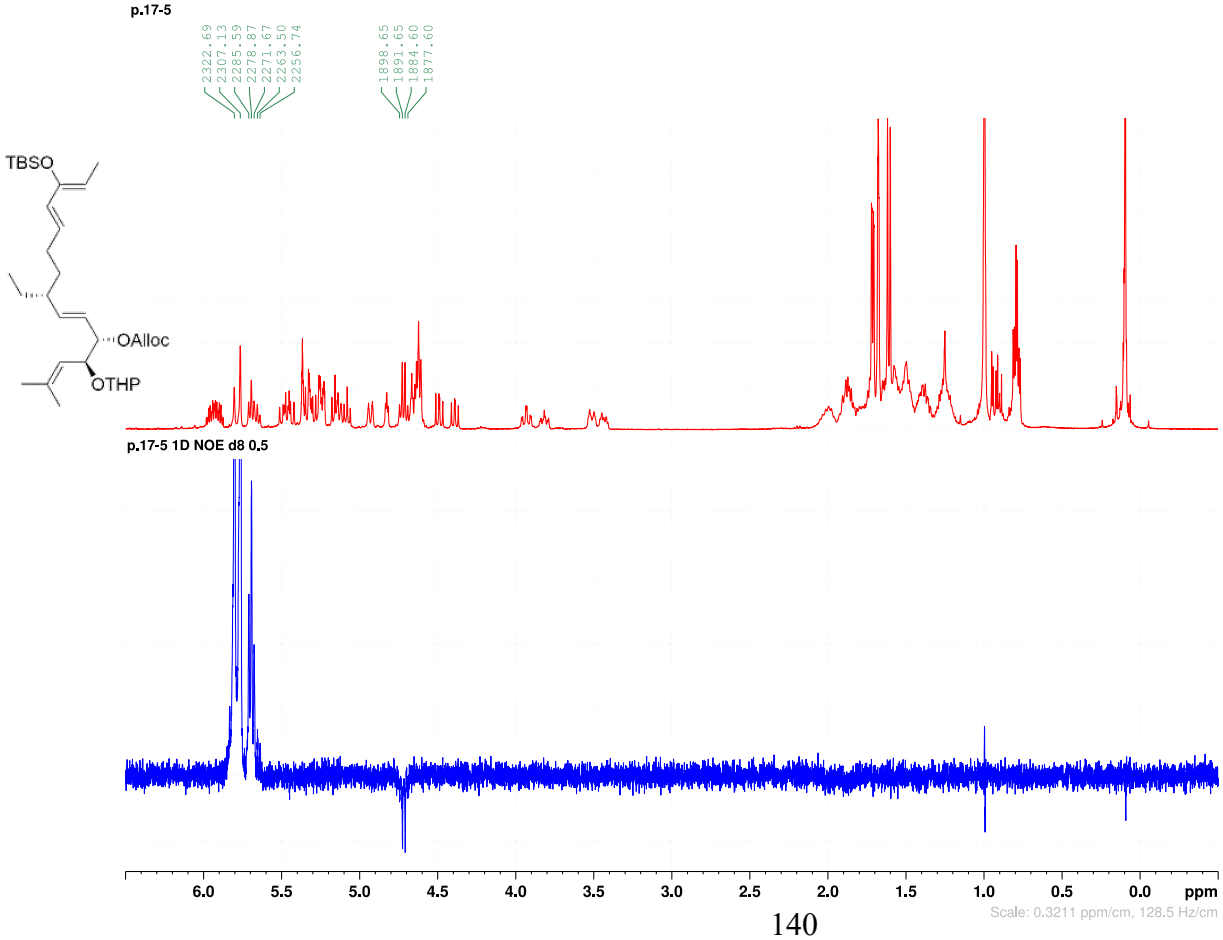
p.17-5




```
Current Data Parameters
NAME      Scott Silyl Enol Ether
EXPNO                 17
PROCNO                 1

F2 - Acquisition Parameters
Date_           20180426
Time                0.55
INSTRUM            spect
PROBHD   5 mm PABBO BB/
PULPROG           zgpg30
TD                 65536
SOLVENT            CDCl3
NS                  1000
DS                     2
SWH            29761.904 Hz
FIDRES          0.454131 Hz
AQ              1.1010048 sec
RG                   203
DW                16.800 usec
DE                 6.50 usec
TE                303.1 K
D1             2.00000000 sec
D11            0.03000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         125.7779086 MHz
NUC1                  13C
P1                 10.50 usec
PLW1        110.00000000 W

======== CHANNEL f2 ========
SFO2         500.1620006 MHz
NUC2                  1H
CPDPRG[2          waltz16
PCPD2              80.00 usec
PLW2         18.00000000 W
PLW12         0.37195000 W
PLW13         0.23805000 W

F2 - Processing parameters
SI                 32768
SF           125.7653108 MHz
WDW                   EM
SSB       0
LB                 1.00 Hz
GB        0
PC                 1.40
```

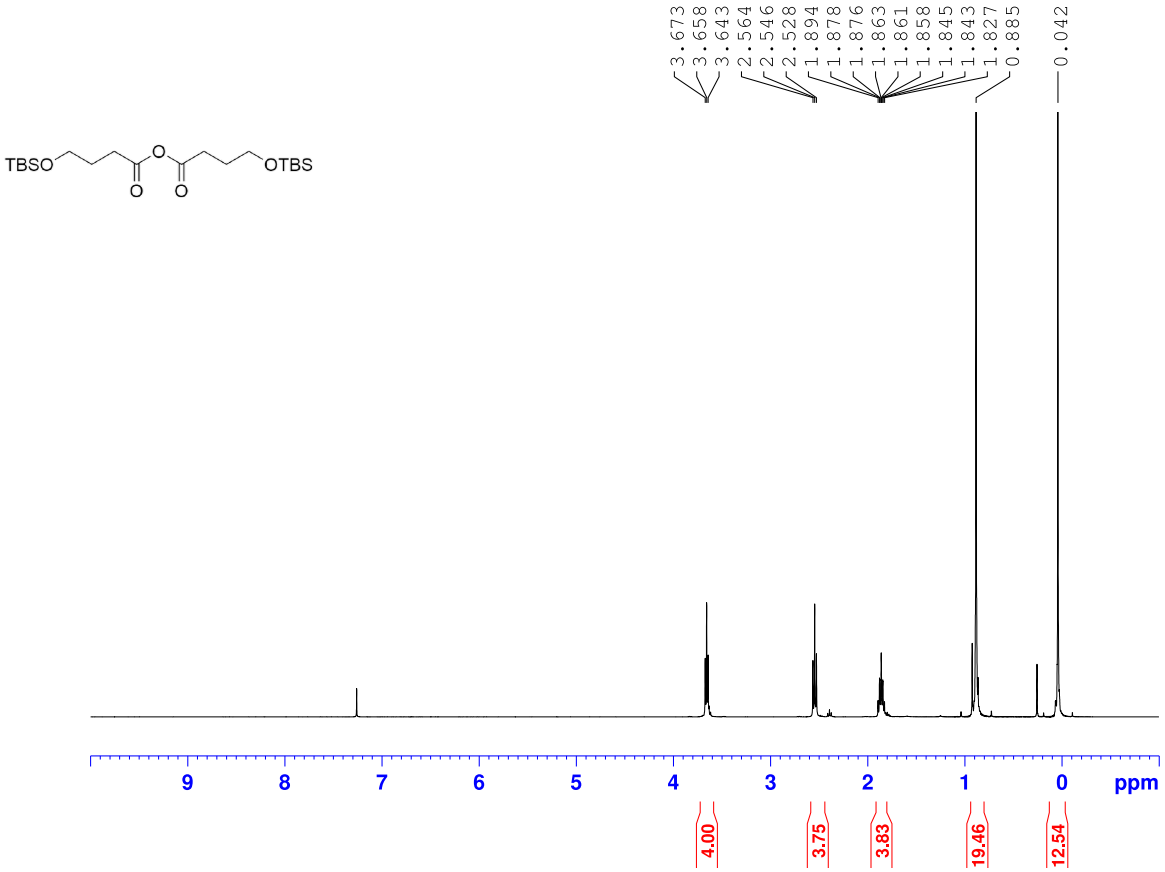



```
Current Data Parameters
NAME      Scott Silyl Enol Ether
EXPNO                 15
PROCNO                 1

F2 - Acquisition Parameters
Date_           20180425
Time               9.39
INSTRUM           spect
PROBHD    5 mm PABBO BB/
PULPROG       cosygpppqf
TD                 2048
SOLVENT           CDCl3
NS                    2
DS                    8
SWH            4672.897 Hz
FIDRES         2.281688 Hz
AQ             0.2191360 sec
RG                 28.5
DW               107.000 usec
DE                 6.50 usec
TE                301.3 K
D0             0.00000300 sec
D1             1.93405402 sec
D11            0.03000000 sec
D12            0.00002000 sec
D13            0.00000400 sec
D16            0.00020000 sec
IN0            0.00021400 sec

======== CHANNEL f1 ========
SFO1         500.1617382 MHz
NUC1               1H
P0                11.50 usec
P1                11.50 usec
P17             2500.00 usec
PLW1        18.00000000 W
PLW10        3.52139997 W

====== GRADIENT CHANNEL =====
GPNAM[1]      SMSQ10.100
GPZ1              10.00 %
P16             1000.00 usec

F1 - Acquisition parameters
TD                 128
SFO1          500.1617 MHz
FIDRES         73.014015 Hz
SW                9.343 ppm
FnMODE             QF

F2 - Processing parameters
SI                1024
SF           500.1600115 MHz
WDW               QSINE
SSB       0
LB        0 Hz
GB        0
PC                1.40

F1 - Processing parameters
SI                1024
MC2                QF
SF           500.1600108 MHz
WDW               QSINE
SSB       0
LB        0 Hz
GB        0
```



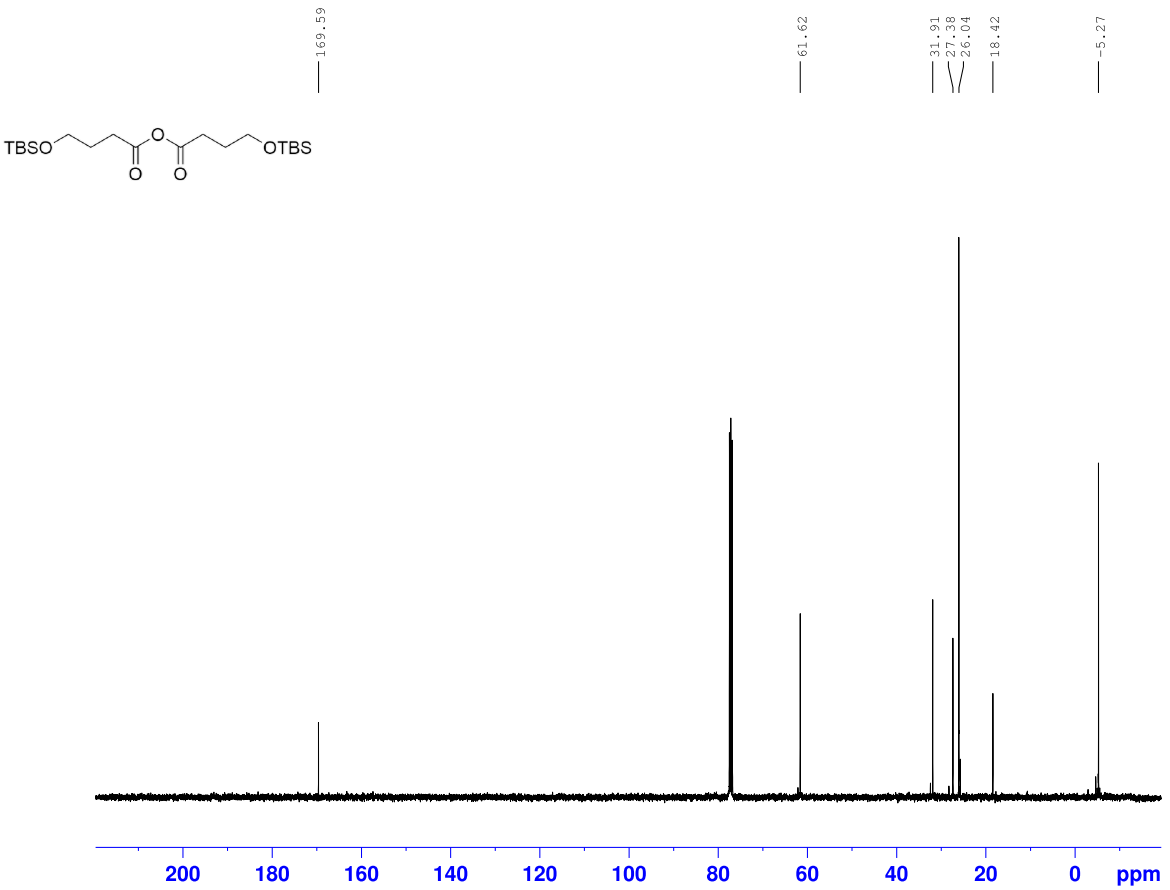

```
Current Data Parameters
NAME      Scott Silyl Enol Ether
EXPNO                 1
PROCNO                1

F2 - Acquisition Parameters
Date_           20180823
Time               8.56
INSTRUM           spect
PROBHD    5 mm PADUL 13C
PULPROG           zg30
TD               65536
SOLVENT           CDCl3
NS                   16
DS                    2
SWH            8223.685 Hz
FIDRES         0.125483 Hz
AQ             3.9845889 sec
RG                  114
DW               60.800 usec
DE                 6.50 usec
TE                294.7 K
D1             2.00000000 sec
TD0                   1

======== CHANNEL f1 ========
NUC1               1H
P1                9.31 usec
PL1              -3.90 dB
PLW1        21.64248466 W
SFO1       400.2324716 MHz

F2 - Processing parameters
SI                32768
SF           400.2300000 MHz
WDW                  EM
SSB       0
LB                0.30 Hz
GB        0
PC                1.00

Current Data Parameters
NAME      Scott Silyl Enol Ether
EXPNO                 2
PROCNO                1

F2 - Acquisition Parameters
Date_           20180823
Time               9.01
INSTRUM           spect
PROBHD    5 mm PADUL 13C
PULPROG         selnogp
TD                32768
SOLVENT           CDCl3
NS                   16
DS                    4
SWH            8223.685 Hz
FIDRES         8.250967 Hz
AQ             1.9922944 sec
RG                  203
DW               60.800 usec
DE                 6.50 usec
TE                294.7 K
D1             2.00000000 sec
D8             0.50000000 sec
D16            0.00020000 sec
D20            0.24879999 sec
TD0                   1

======== CHANNEL f1 ========
NUC1               1H
P1               10.95 usec
P2               21.90 usec
P12           80000.00 usec
PL0             120.00 dB
PL1              -3.90 dB
PLW0     0 W
PLW1        21.64248466 W
SFO1       400.2323295 MHz
SP2               58.64 dB
SPNAM[2] Gaus1_180r.1000
SPOAL2            0.500
SPOFFS2  0 Hz

====== GRADIENT CHANNEL =====
GPNAM[1]      SMSQ10.100
GPNAM[2]      SMSQ10.100
GPZ1              15.00 %
GPZ2              40.00 %
P16             1000.00 usec

F2 - Processing parameters
SI                65536
SF           400.2300136 MHz
WDW                  EM
SSB       0
LB                0.10 Hz
GB        0
PC                1.00
```

p.258-4 recovered sm 2



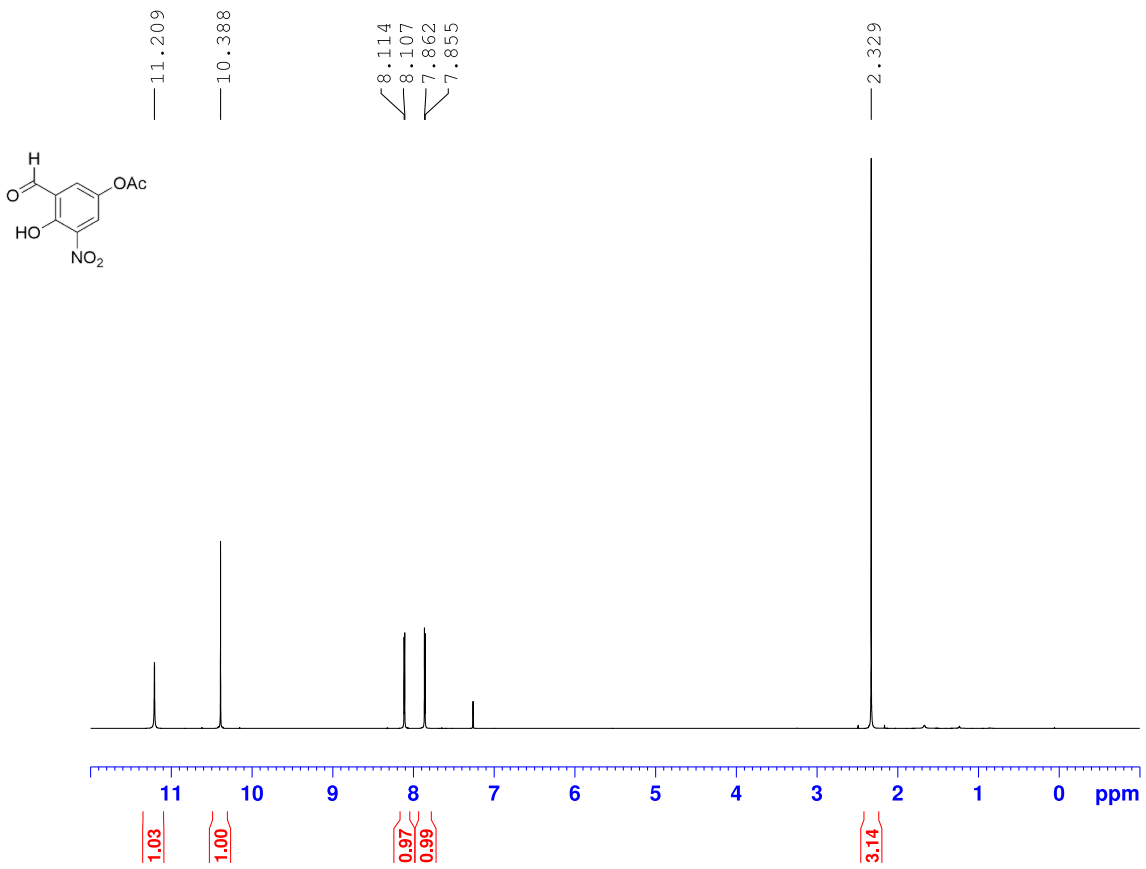

```
Current Data Parameters
NAME      Scott Anhydride
EXPNO                  10
PROCNO                  1

F2 - Acquisition Parameters
Date_           20180418
Time                8.52
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8012.820 Hz
FIDRES          0.122266 Hz
AQ              4.0894465 sec
RG                    32
DW                62.400 usec
DE                 6.50 usec
TE                2405.6 K
D1           1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         400.1324710 MHz
NUC1                   1H
P1                 14.50 usec
PLW1         12.01700020 W

F2 - Processing parameters
SI                 65536
SF           400.1300109 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

p.258-4 recovered sm 2



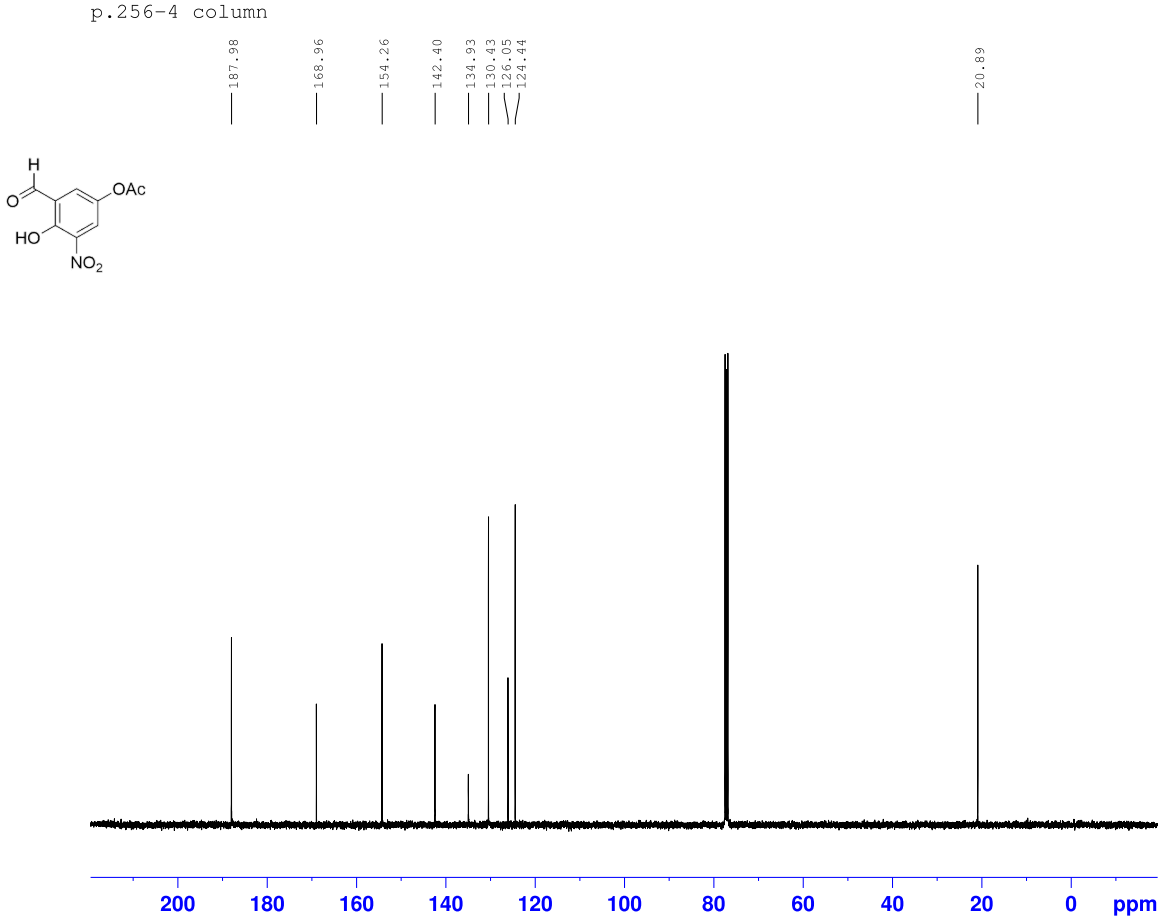

```
Current Data Parameters
NAME      Scott Anhydride
EXPNO                  11
PROCNO                  1

F2 - Acquisition Parameters
Date_           20180418
Time                9.08
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG           zgpg30
TD                 65536
SOLVENT            CDCl3
NS                   250
DS                     4
SWH            24038.461 Hz
FIDRES          0.366798 Hz
AQ              1.3631488 sec
RG                   203
DW                20.800 usec
DE                 6.50 usec
TE                2390.0 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         100.6228293 MHz
NUC1                   13C
P1                 10.00 usec
PLW1         56.13299942 W

======== CHANNEL f2 ========
SFO2         400.1316005 MHz
NUC2                   1H
CPDPRG[2         waltz16
PCPD2              90.00 usec
PLW2         12.01700020 W
PLW12         0.31191999 W
PLW13         0.25266001 W

F2 - Processing parameters
SI                 32768
SF           100.6127540 MHz
WDW                   EM
SSB       0
LB                 1.00 Hz
GB        0
PC                 1.40
```

p.256-4 column



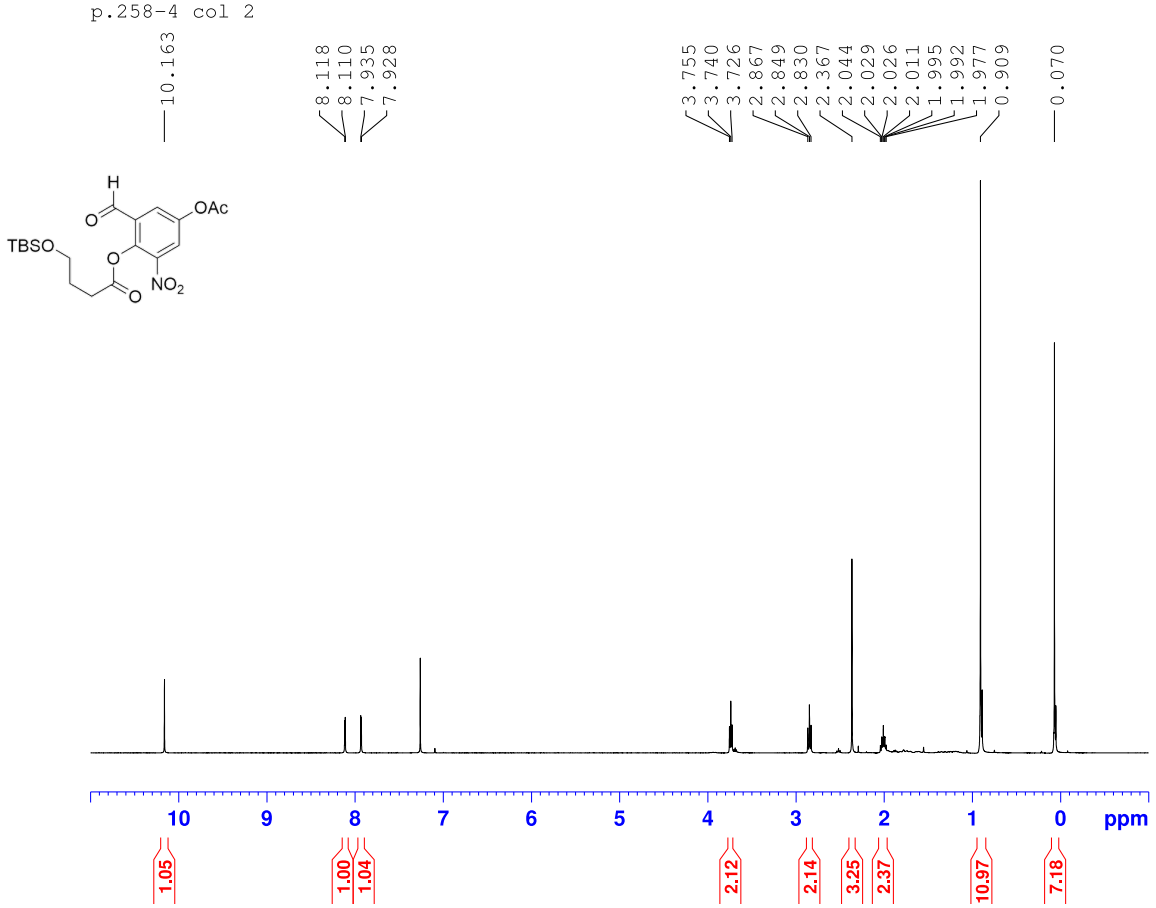

```
Current Data Parameters
NAME                  Scott
EXPNO                    10
PROCNO                    1

F2 - Acquisition Parameters
Date_              20180801
Time                  9.04
INSTRUM              spect
PROBHD    5 mm PABBO BB-
PULPROG               zg30
TD                   65536
SOLVENT              CDC13
NS                      16
DS                       2
SWH               8012.820 Hz
FIDRES               0.122266 Hz
AQ                4.0894465 sec
RG                      64
DW                  62.400 usec
DE                   6.50 usec
TE                  21736.0 K
D1               1.00000000 sec
TD0                      1

======== CHANNEL f1 ========
SFO1            400.1324710 MHz
NUC1                    1H
P1                   14.50 usec
PLW1            12.01700020 W

F2 - Processing parameters
SI                   65536
SF              400.1300098 MHz
WDW                     EM
SSB          0
LB                    0.30 Hz
GB           0
PC                    1.00
```

p.256-4 column



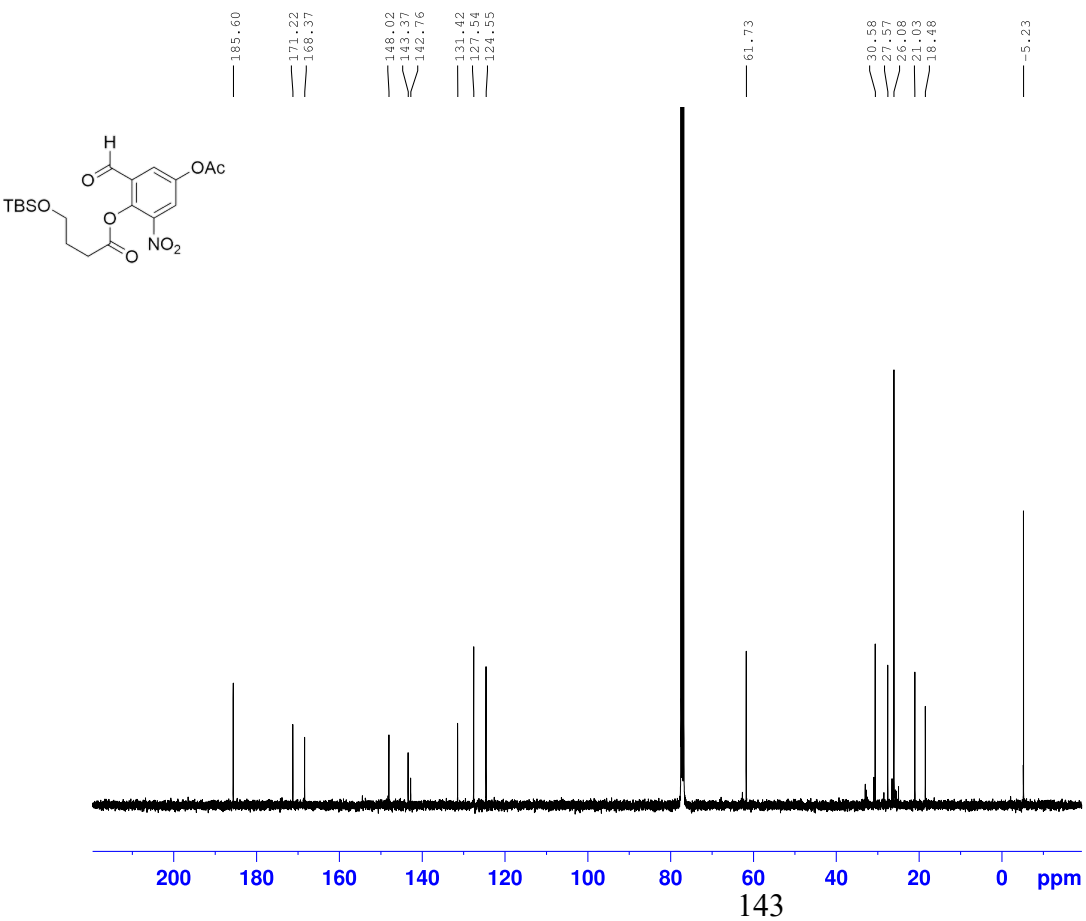

```
Current Data Parameters
NAME      Scott Deacetylation
EXPNO                    11
PROCNO                    1

F2 - Acquisition Parameters
Date_              20180801
Time                  9.21
INSTRUM              spect
PROBHD    5 mm PABBO BB-
PULPROG             zgpg30
TD                   65536
SOLVENT              CDC13
NS                     256
DS                       4
SWH              24038.461 Hz
FIDRES               0.366798 Hz
AQ                1.3631488 sec
RG                     203
DW                  20.800 usec
DE                   6.50 usec
TE                  21548.0 K
D1               2.00000000 sec
D11              0.03000000 sec
TD0                      1

======== CHANNEL f1 ========
SFO1            100.6228293 MHz
NUC1                    13C
P1                   10.00 usec
PLW1            56.13299942 W

======== CHANNEL f2 ========
SFO2            400.1316005 MHz
NUC2                    1H
CPDPRG[2            waltz16
PCPD2                90.00 usec
PLW2            12.01700020 W
PLW12            0.31191999 W
PLW13            0.25266001 W

F2 - Processing parameters
SI                   32768
SF              100.6127594 MHz
WDW                     EM
SSB          0
LB                    1.00 Hz
GB           0
PC                    1.40
```

p.258-4 col 2



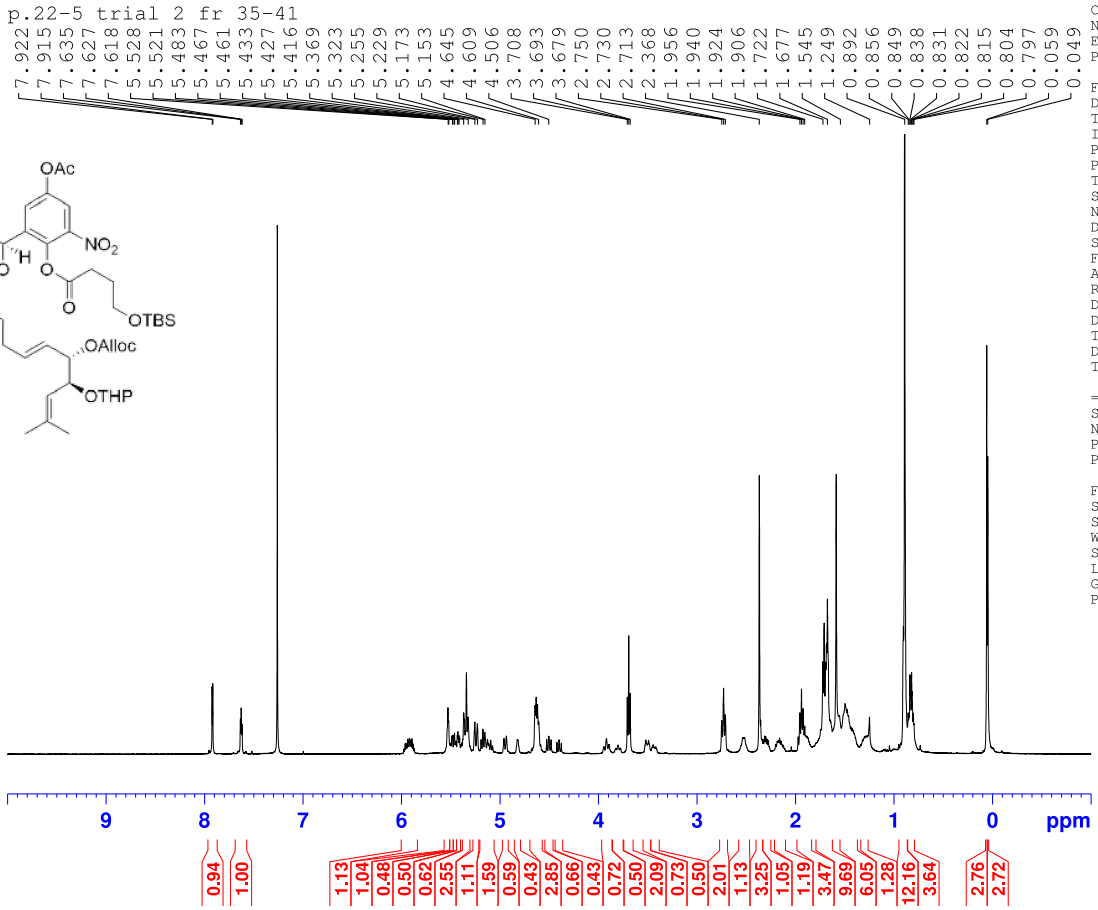

```
Current Data Parameters
NAME      Scott Acylation
EXPNO                  40
PROCNO                  1

F2 - Acquisition Parameters
Date_           20180418
Time              11.06
INSTRUM           spect
PROBHD    5 mm PABBO BB-
PULPROG            zg30
TD                65536
SOLVENT           CDCl3
NS                   16
DS                    2
SWH            8012.820 Hz
FIDRES            0.122266 Hz
AQ              4.0894465 sec
RG                  101
DW                62.400 usec
DE                 6.50 usec
TE               2457.1 K
D1            1.00000000 sec
TD0                   1

======== CHANNEL f1 ========
SFO1         400.1324710 MHz
NUC1               1H
P1                14.50 usec
PLW1         12.01700020 W

F2 - Processing parameters
SI                65536
SF           400.1300100 MHz
WDW                EM
SSB       0
LB                0.30 Hz
GB        0
PC                1.00
```

p.258-4 col 2



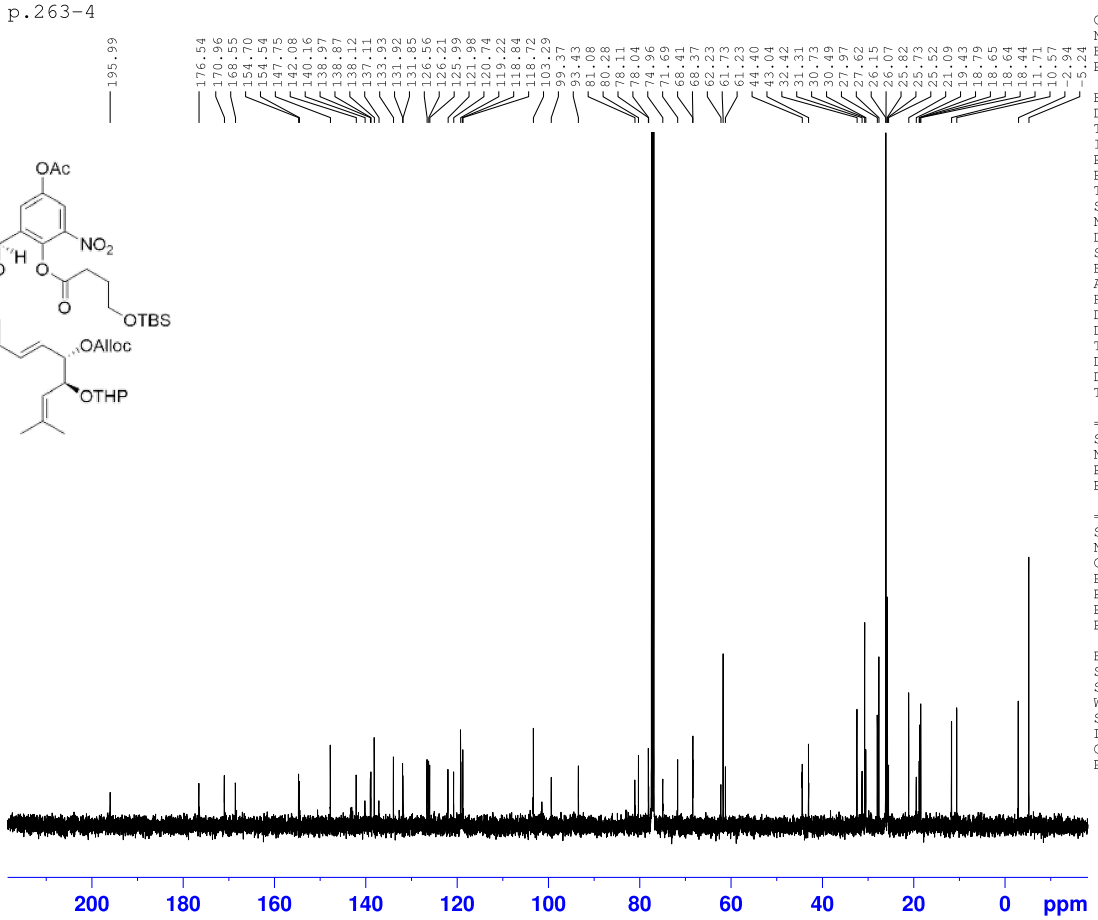

```
Current Data Parameters
NAME      Scott Acylation
EXPNO                  50
PROCNO                  1

F2 - Acquisition Parameters
Date_           20180418
Time              22.56
INSTRUM           spect
PROBHD    5 mm PABBO BB-
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                 3000
DS                    4
SWH           24038.461 Hz
FIDRES            0.366798 Hz
AQ              1.3631488 sec
RG                  203
DW                20.800 usec
DE                 6.50 usec
TE               2189.8 K
D1            2.00000000 sec
D11           0.03000000 sec
TD0                   1

======== CHANNEL f1 ========
SFO1         100.6228293 MHz
NUC1               13C
P1                10.00 usec
PLW1         56.13299942 W

======== CHANNEL f2 ========
SFO2         400.1316005 MHz
NUC2               1H
CPDPRG[2         waltz16
PCPD2             90.00 usec
PLW2         12.01700020 W
PLW12         0.31191999 W
PLW13         0.25266001 W

F2 - Processing parameters
SI                32768
SF           100.6127532 MHz
WDW                EM
SSB       0
LB                1.00 Hz
GB        0
PC                1.40
```

p.22-5 trial 2 fr 35-41



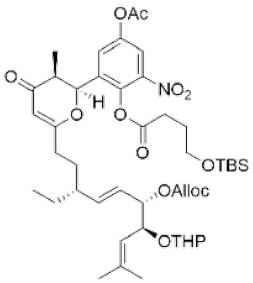

```
Current Data Parameters
NAME            Scott DDQ
EXPNO                  40
PROCNO                  1

F2 - Acquisition Parameters
Date_            20180504
Time                16.02
INSTRUM             spect
PROBHD    5 mm PABBO BB-
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8012.820 Hz
FIDRES          0.122266 Hz
AQ              4.0894465 sec
RG                  90.5
DW                62.400 usec
DE                 6.50 usec
TE                 89.2 K
D1              1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         400.1324710 MHz
NUC1                   1H
P1                  14.50 usec
PLW1         12.01700020 W

F2 - Processing parameters
SI                 65536
SF            400.1300097 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

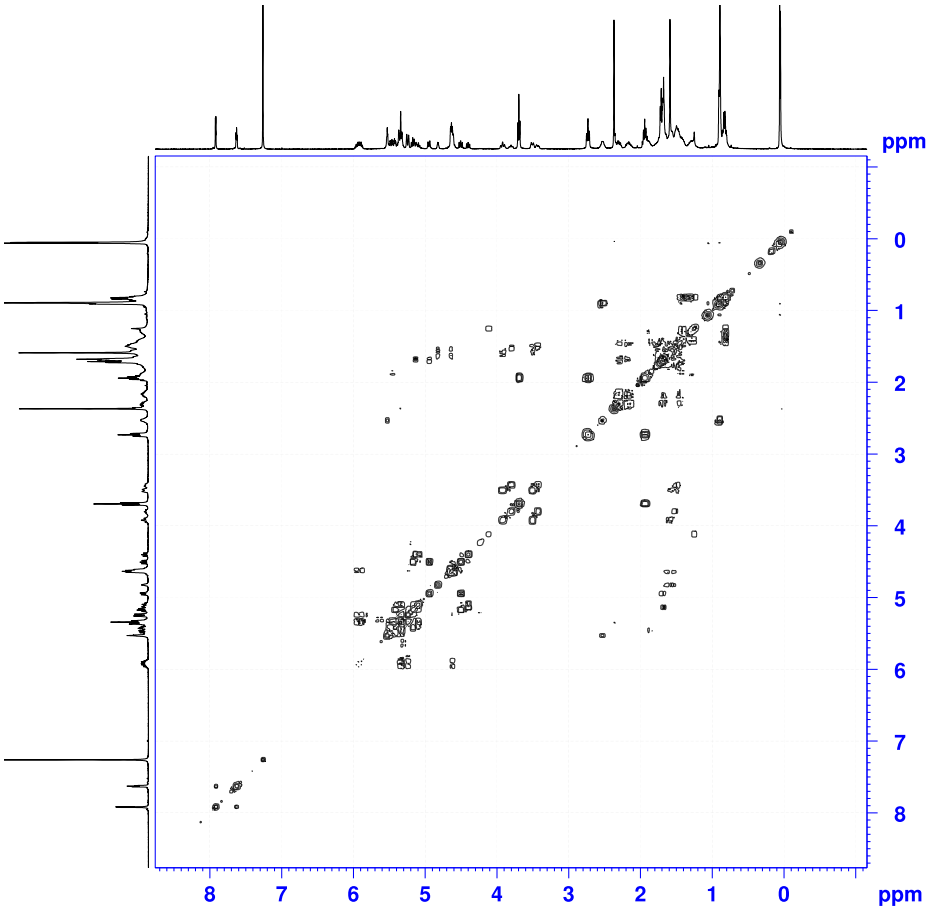
p.263-4




```
Current Data Parameters
NAME            Scott DDQ
EXPNO                  30
PROCNO                  1

F2 - Acquisition Parameters
Date_            20180316
Time                12.03
INSTRUM             spect
PROBHD    5 mm PABBO BB/
PULPROG           zgpg30
TD                 65536
SOLVENT            CDCl3
NS                   300
DS                     2
SWH            29761.904 Hz
FIDRES          0.454131 Hz
AQ              1.1010048 sec
RG                  203
DW                16.800 usec
DE                 6.50 usec
TE                299.0 K
D1              2.00000000 sec
D11             0.03000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1        125.7779086 MHz
NUC1                   13C
P1                 10.50 usec
PLW1        110.00000000 W

======== CHANNEL f2 ========
SFO2         500.1620006 MHz
NUC2                   1H
CPDPRG[2          waltz16
PCPD2              80.00 usec
PLW2         18.00000000 W
PLW12         0.37195000 W
PLW13         0.23805000 W

F2 - Processing parameters
SI                 32768
SF           125.7653145 MHz
WDW                   EM
SSB       0
LB                 1.00 Hz
GB        0
PC                 1.40
```

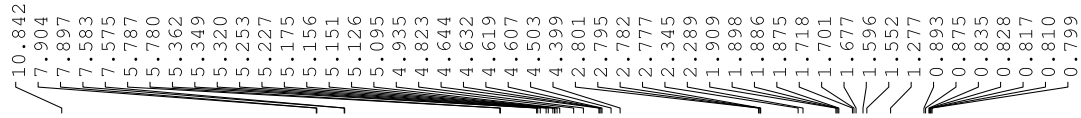
p.263-4

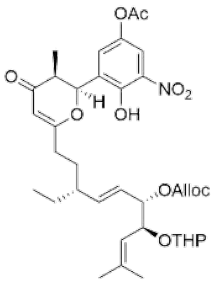





```
Current Data Parameters
NAME            Scott DDQ
EXPNO                  31
PROCNO                  1

F2 - Acquisition Parameters
Date_           20180316
Time                8.51
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG       cosygpppqf
TD                  2048
SOLVENT            CDC13
NS                     1
DS                     8
SWH             3968.254 Hz
FIDRES          1.937624 Hz
AQ              0.2580480 sec
RG                  28.5
DW                126.000 usec
DE                  6.50 usec
TE                221.0 K
D0              0.00000300 sec
D1              1.93364501 sec
D11             0.03000000 sec
D12             0.00002000 sec
D13             0.00000400 sec
D16             0.00020000 sec
IN0             0.00025200 sec

======== CHANNEL f1 ========
SFO1          400.1315325 MHz
NUC1                    1H
P0                  14.50 usec
P1                  14.50 usec
P17               2500.00 usec
PLW1         12.01700020 W
PLW10         3.73749995 W

====== GRADIENT CHANNEL =====
GPNAM[1]       SMSQ10.100
GPZ1                10.00 %
P16               1000.00 usec

F1 - Acquisition parameters
TD                   128
SFO1            400.1315 MHz
FIDRES          62.003967 Hz
SW                9.917 ppm
FnMODE                QF

F2 - Processing parameters
SI                   1024
SF            400.1300110 MHz
WDW                 QSINE
SSB       0
LB        0 Hz
GB        0
PC                  1.40

F1 - Processing parameters
SI                   1024
MC2                    QF
SF            400.1300098 MHz
WDW                 QSINE
SSB       0
LB        0 Hz
GB        0
```

p.293-4



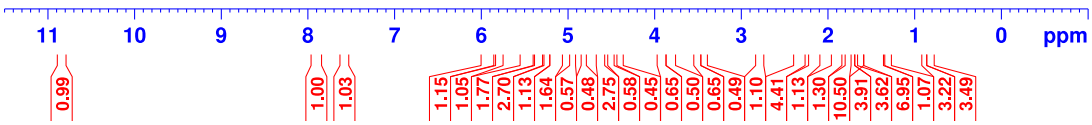


Current Data Parameters
NAME Scott HF-Pyr
EXPNO 20
PROCNO 1

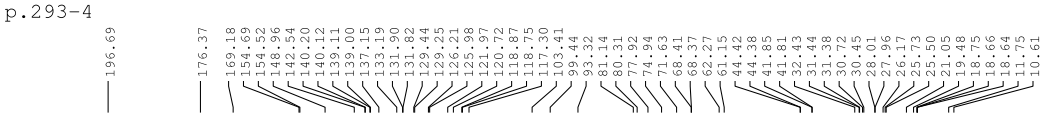
F2 - Acquisition Parameters
Date_ 20180323
Time 9.30
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.122266 Hz
AQ 4.0894465 sec
RG 64
DW 62.400 usec
DE 6.50 usec
TE 1924.7 K
D1 1.00000000 sec
TD0 1

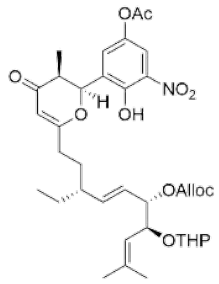
======== CHANNEL f1 ========
SFO1 400.1324710 MHz
NUC1 1H
P1 14.50 usec
PLW1 12.01700020 W

F2 - Processing parameters
SI 65536
SF 400.1300099 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00



p.293-4





Current Data Parameters
NAME Scott HF-Pyr
EXPNO 1
PROCNO 1

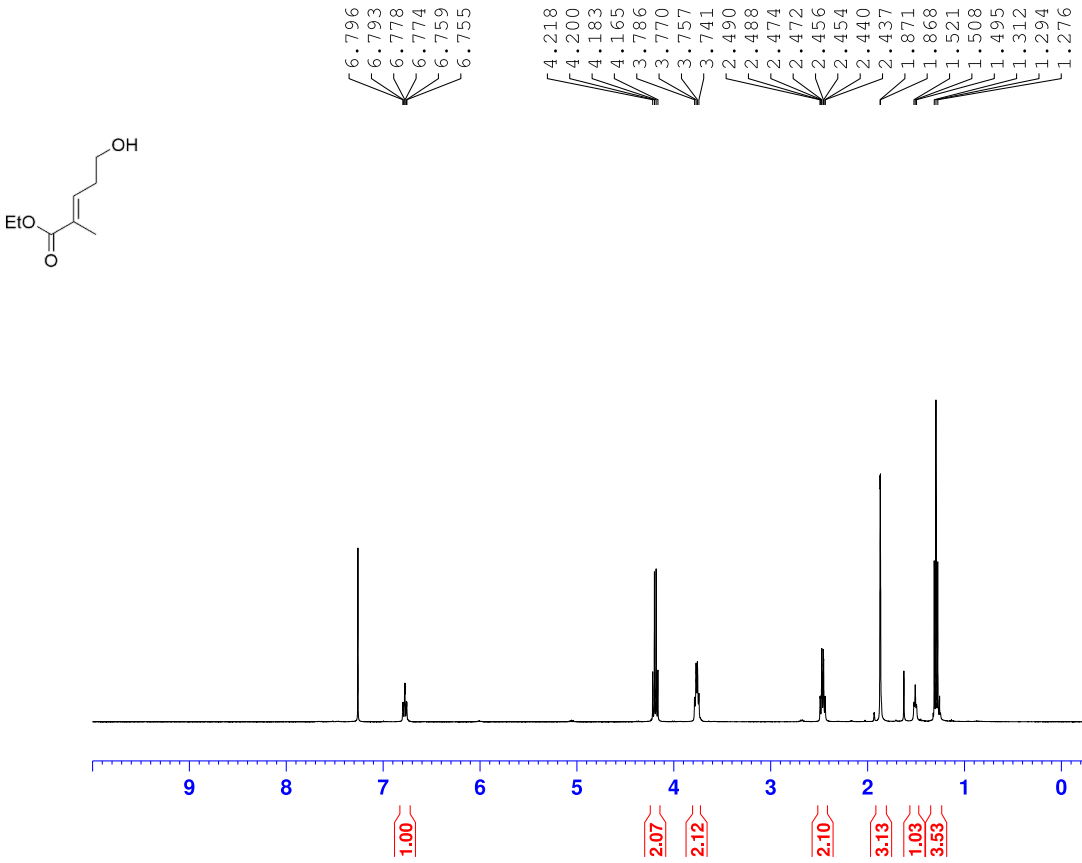
F2 - Acquisition Parameters
Date_ 20180323
Time 12.26
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 3100
DS 4
SWH 36057.691 Hz
FIDRES 0.550197 Hz
AQ 0.9087659 sec
RG 203
DW 13.867 usec
DE 6.50 usec
TE 297.2 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1

======== CHANNEL f1 ========
NUC1 13C
P1 11.50 usec
PL1 0 dB
PL1W 97.46119690 W
SFO1 151.0637542 MHz

======== CHANNEL f2 ========
CPDPRG[2 waltz16
NUC2 1H
PCPD2 70.00 usec
PL2 -2.00 dB
PL12 14.19 dB
PL13 120.00 dB
PL2W 19.70630455 W
PL12W 0.47381112 W
PL13W 0 W
SFO2 600.7124028 MHz

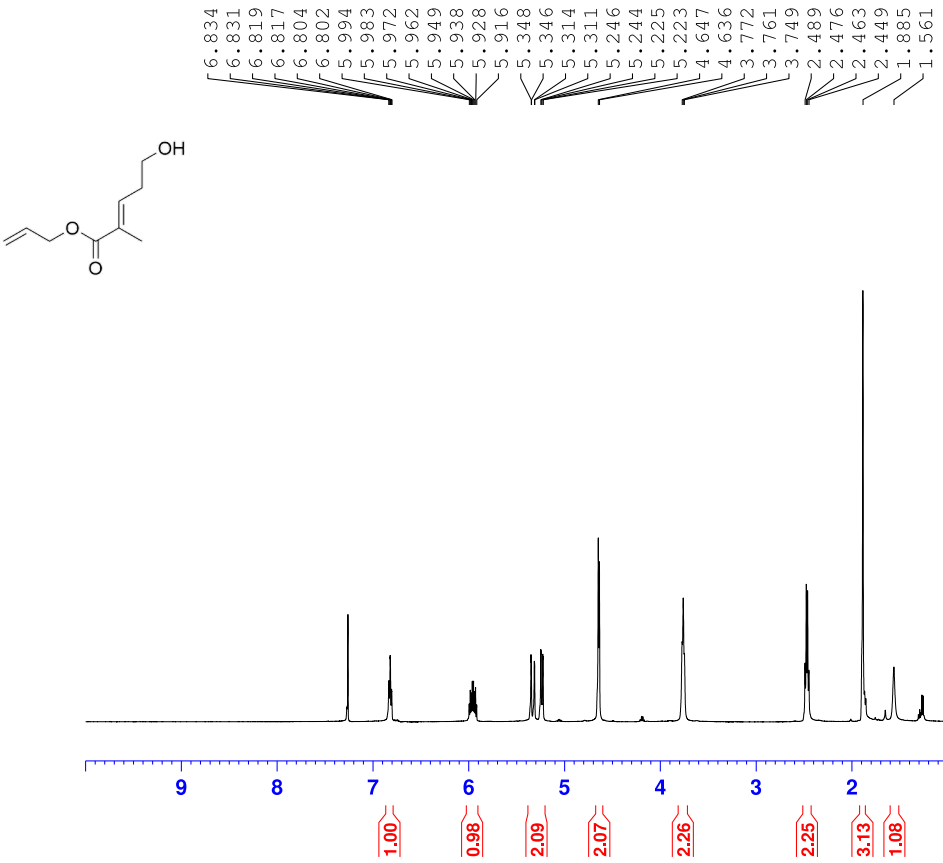
F2 - Processing parameters
SI 32768
SF 151.0486305 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

p.55-5



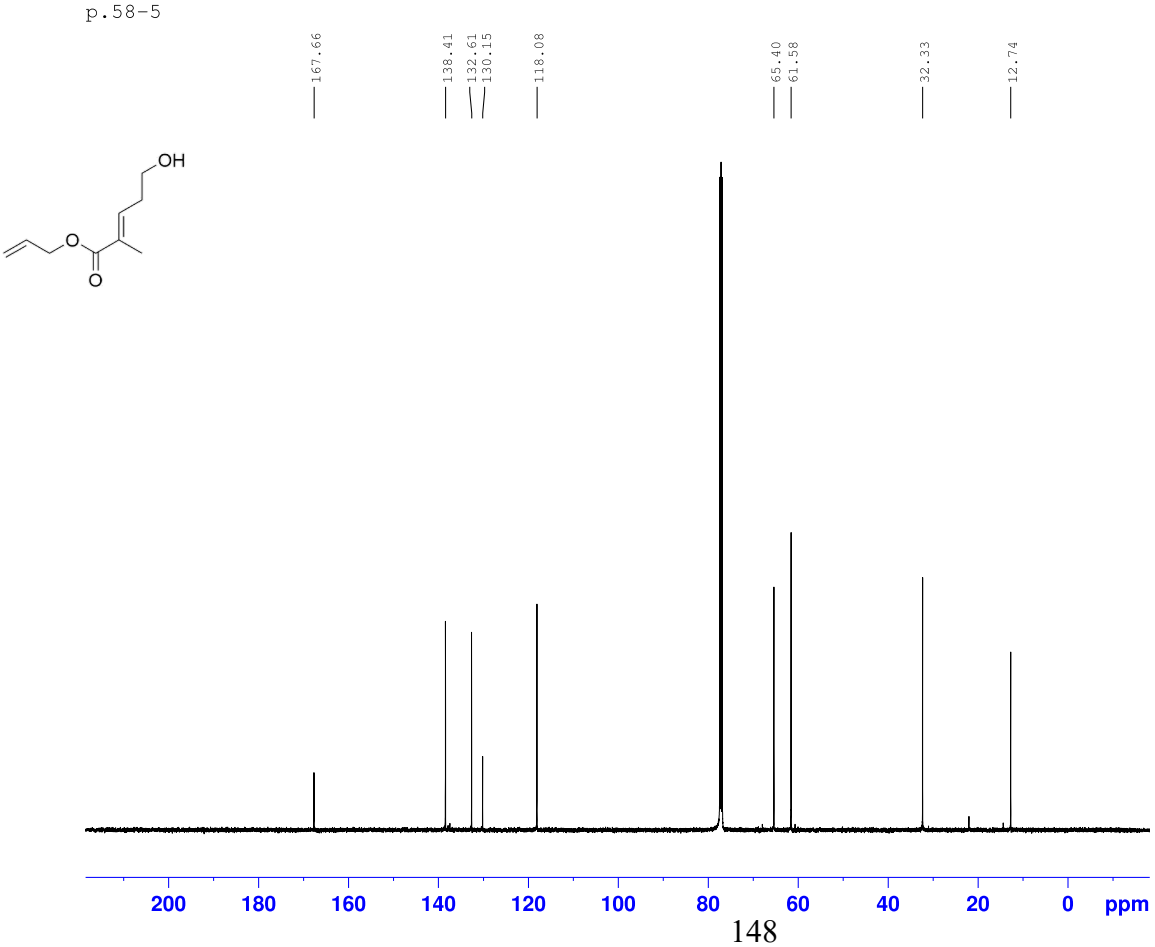

```
Current Data Parameters
NAME        Scott Wittig
EXPNO                 20
PROCNO                 1

F2 - Acquisition Parameters
Date_           20180807
Time               14.30
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8012.820 Hz
FIDRES          0.122266 Hz
AQ            4.0894465 sec
RG                   101
DW                62.400 usec
DE                 6.50 usec
TE              -25658.0 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         400.1324710 MHz
NUC1                   1H
P1                 14.50 usec
PLW1        12.01700020 W

F2 - Processing parameters
SI                 65536
SF           400.1300104 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

p.58-5



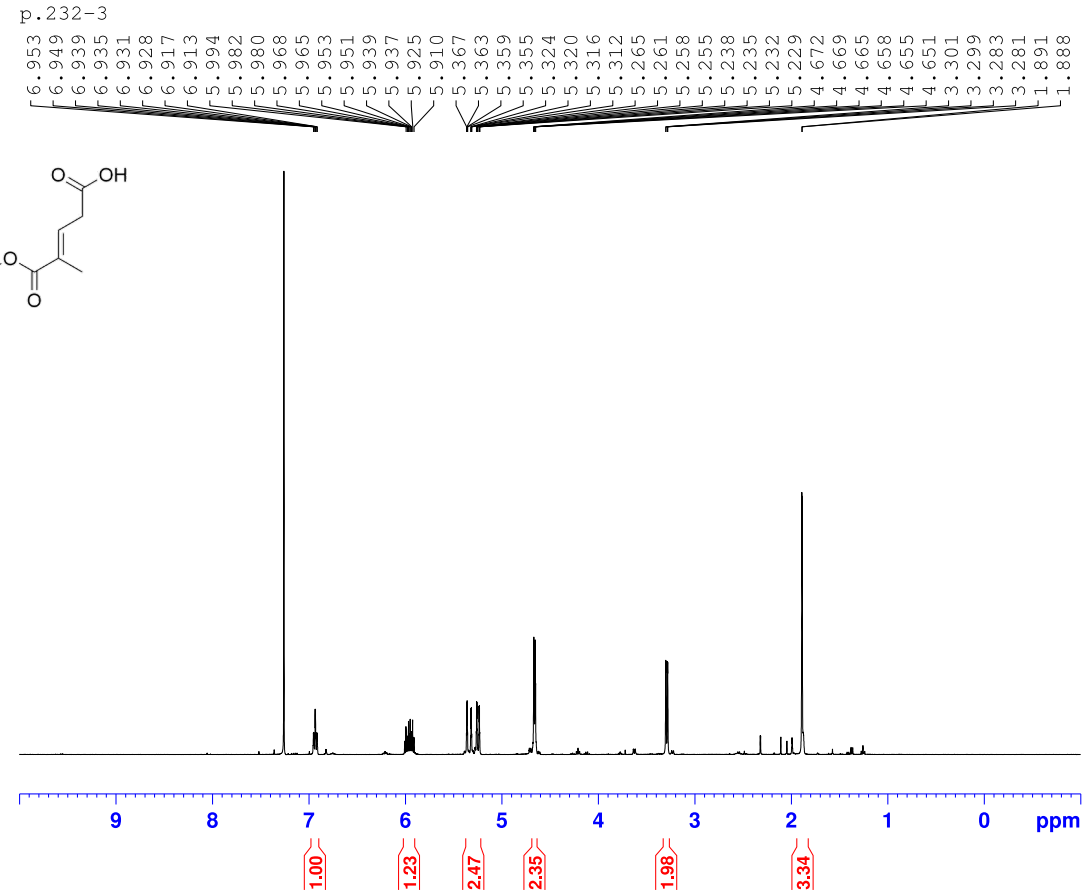

```
Current Data Parameters
NAME      Scott Transesterification
EXPNO                10
PROCNO                1

F2 - Acquisition Parameters
Date_            20180808
Time                12.31
INSTRUM             spect
PROBHD    5 mm PABBO BB/
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH            10000.000 Hz
FIDRES          0.152588 Hz
AQ             3.2767999 sec
RG                  90.5
DW                50.000 usec
DE                 6.50 usec
TE                296.1 K
D1             1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1          500.1630887 MHz
NUC1                  1H
P1                 11.50 usec
PLW1          18.00000000 W

F2 - Processing parameters
SI                 65536
SF            500.1600131 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

p.58-5



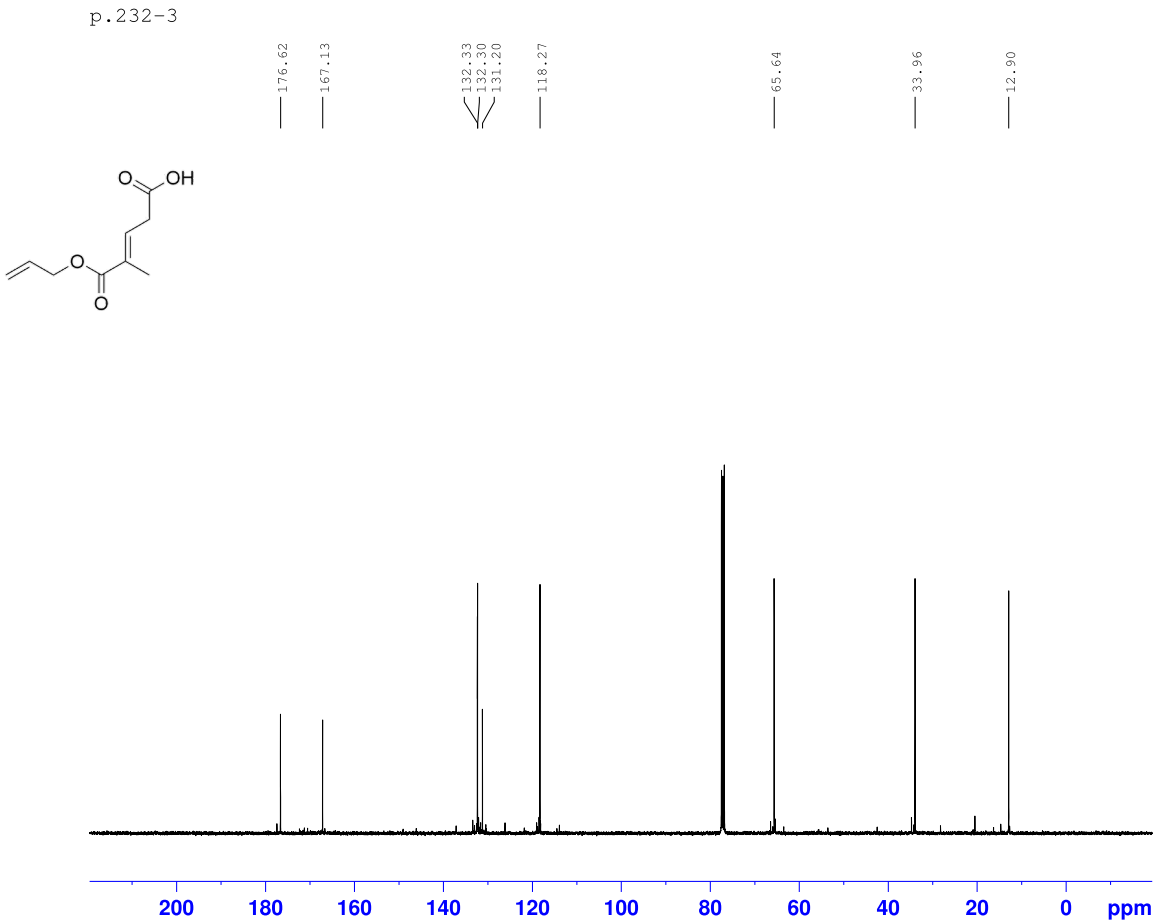

```
Current Data Parameters
NAME      Scott Transesterification
EXPNO                11
PROCNO                1

F2 - Acquisition Parameters
Date_            20180809
Time                5.28
INSTRUM             spect
PROBHD    5 mm PABBO BB/
PULPROG          zgpg30
TD                 65536
SOLVENT            CDCl3
NS                  4000
DS                     2
SWH            29761.904 Hz
FIDRES          0.454131 Hz
AQ             1.1010048 sec
RG                   203
DW                16.800 usec
DE                 6.50 usec
TE                299.9 K
D1             2.00000000 sec
D11            0.03000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1          125.7779086 MHz
NUC1                 13C
P1                 10.50 usec
PLW1          110.00000000 W

======== CHANNEL f2 ========
SFO2          500.1620006 MHz
NUC2                  1H
CPDPRG[2          waltz16
PCPD2              80.00 usec
PLW2          18.00000000 W
PLW12          0.37195000 W
PLW13          0.23805000 W

F2 - Processing parameters
SI                 32768
SF            125.7653127 MHz
WDW                   EM
SSB       0
LB                 1.00 Hz
GB        0
PC                 1.40
```

p.232-3



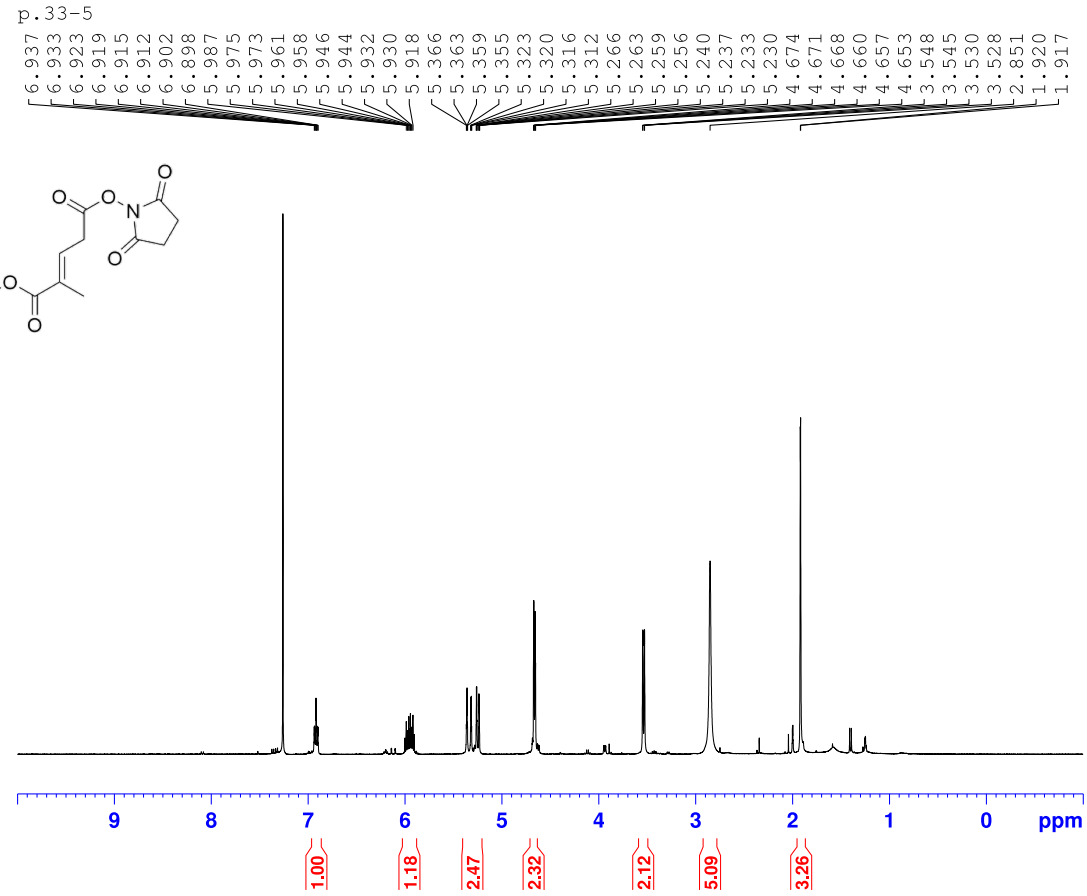

```
Current Data Parameters
NAME         Scott Jones
EXPNO                 30
PROCNO                 1

F2 - Acquisition Parameters
Date_           20161121
Time               19.10
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8012.820 Hz
FIDRES             0.122266 Hz
AQ              4.0894465 sec
RG                   128
DW                62.400 usec
DE                 6.50 usec
TE                 481.4 K
D1              1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1          400.1324710 MHz
NUC1                  1H
P1                 13.75 usec
PLW1          12.01700020 W

F2 - Processing parameters
SI                 65536
SF            400.1300105 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

p.232-3



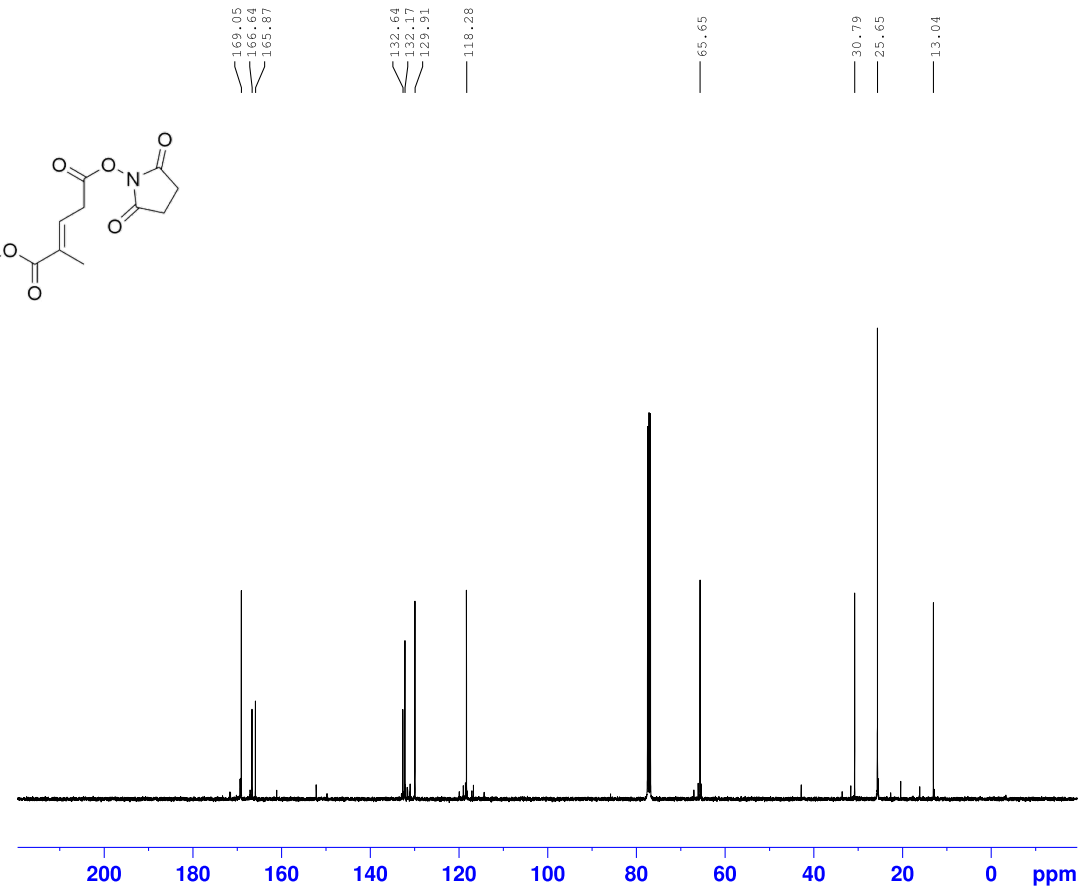

```
Current Data Parameters
NAME         Scott Jones
EXPNO                 11
PROCNO                 1

F2 - Acquisition Parameters
Date_           20180809
Time                3.30
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG           zgpg30
TD                 65536
SOLVENT            CDCl3
NS                  1024
DS                     4
SWH            24038.461 Hz
FIDRES             0.366798 Hz
AQ              1.3631488 sec
RG                   203
DW                20.800 usec
DE                 6.50 usec
TE              -30194.0 K
D1              2.00000000 sec
D11             0.03000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1          100.6228293 MHz
NUC1                  13C
P1                 10.00 usec
PLW1          56.13299942 W

======== CHANNEL f2 ========
SFO2          400.1316005 MHz
NUC2                  1H
CPDPRG[2          waltz16
PCPD2              90.00 usec
PLW2          12.01700020 W
PLW12          0.31191999 W
PLW13          0.25266001 W

F2 - Processing parameters
SI                 32768
SF            100.6127580 MHz
WDW                   EM
SSB       0
LB                 1.00 Hz
GB        0
PC                 1.40
```

p.33-5



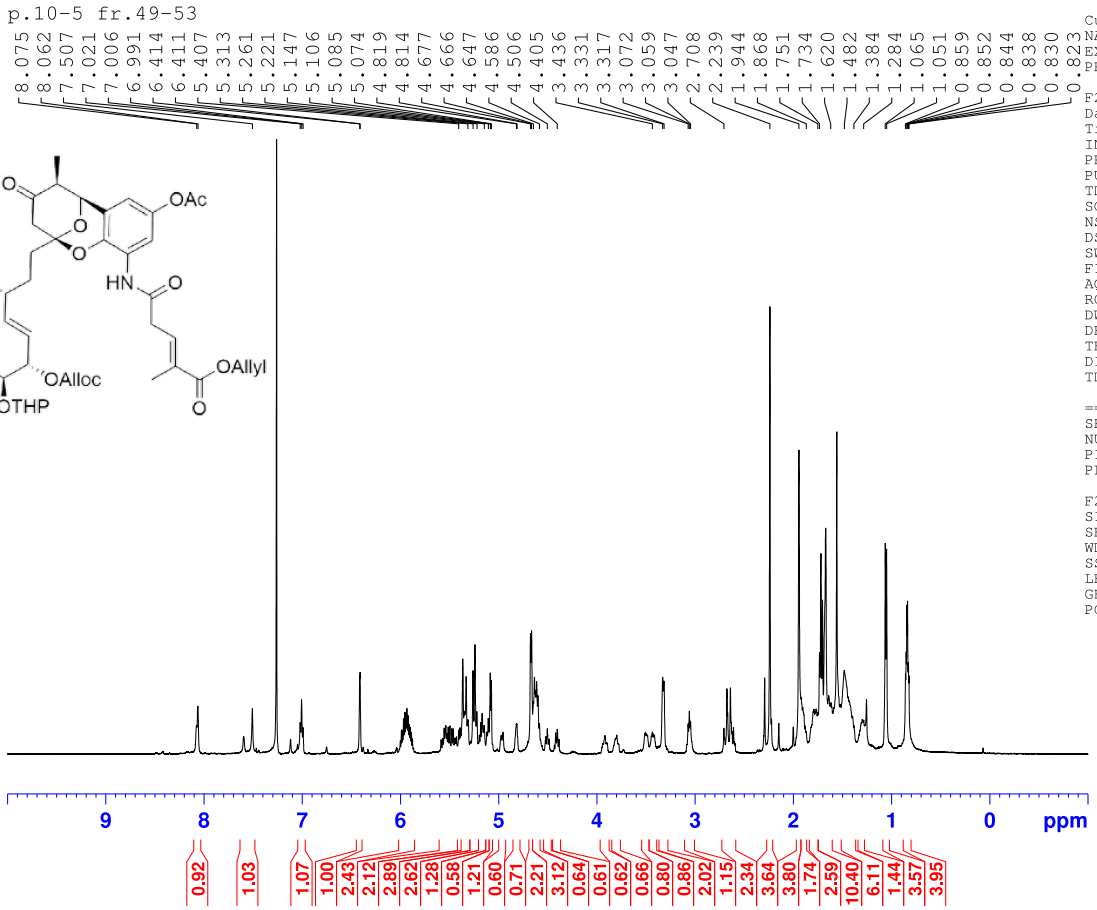

```
Current Data Parameters
NAME      Scott Succinimidyl
EXPNO                   30
PROCNO                   1

F2 - Acquisition Parameters
Date_           20180530
Time                11.05
INSTRUM             spect
PROBHD   5 mm PABBO BB-
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH              8012.820 Hz
FIDRES           0.122266 Hz
AQ               4.0894465 sec
RG                   128
DW                62.400 usec
DE                 6.50 usec
TE               -1837.0 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         400.1324710 MHz
NUC1                   1H
P1                  14.50 usec
PLW1         12.01700020 W

F2 - Processing parameters
SI                 65536
SF           400.1300103 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

p.33-5



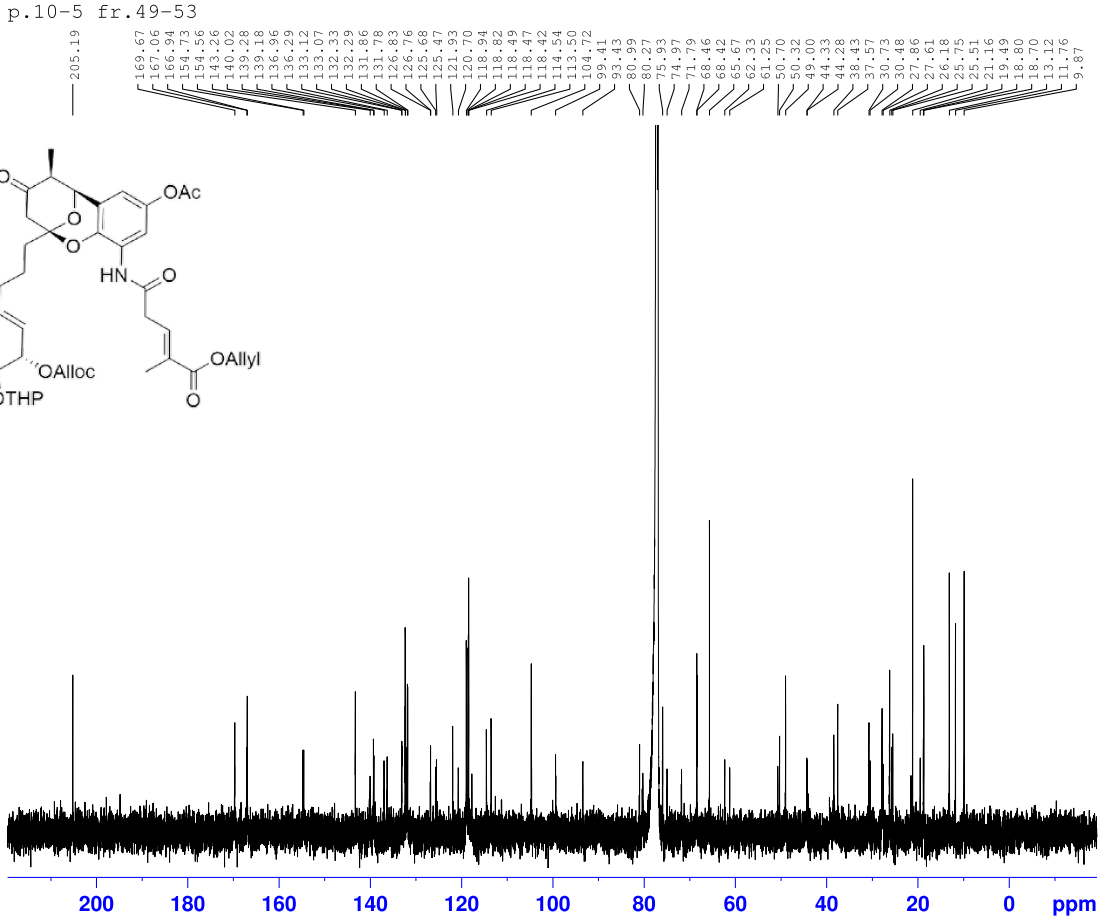

```
Current Data Parameters
NAME      Scott Succinimidyl
EXPNO                   41
PROCNO                   1

F2 - Acquisition Parameters
Date_           20180809
Time                4.34
INSTRUM             spect
PROBHD   5 mm PABBO BB-
PULPROG           zgpg30
TD                 65536
SOLVENT            CDCl3
NS                  1024
DS                     4
SWH             24038.461 Hz
FIDRES           0.366798 Hz
AQ               1.3631488 sec
RG                   203
DW                20.800 usec
DE                 6.50 usec
TE               -29950.0 K
D1            2.00000000 sec
D11           0.03000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         100.6228293 MHz
NUC1                  13C
P1                 10.00 usec
PLW1         56.13299942 W

======== CHANNEL f2 ========
SFO2         400.1316005 MHz
NUC2                   1H
CPDPRG[2          waltz16
PCPD2              90.00 usec
PLW2         12.01700020 W
PLW12         0.31191999 W
PLW13         0.25266001 W

F2 - Processing parameters
SI                 32768
SF           100.6127615 MHz
WDW                   EM
SSB       0
LB                 1.00 Hz
GB        0
PC                 1.40
```

p.10-5 fr.49-53



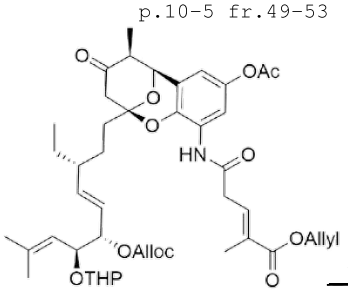

```
Current Data Parameters
NAME      Scott Cyclization
EXPNO                   20
PROCNO                   1

F2 - Acquisition Parameters
Date_               20180416
Time                   10.18
INSTRUM                spect
PROBHD    5 mm PABBO BB/
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH               10000.000 Hz
FIDRES                0.152588 Hz
AQ                3.2767999 sec
RG                      101
DW                   50.000 usec
DE                    6.50 usec
TE                   301.0 K
D1              1.00000000 sec
TD0                      1

======== CHANNEL f1 ========
SFO1            500.1630887 MHz
NUC1                       1H
P1                     11.50 usec
PLW1           18.00000000 W

F2 - Processing parameters
SI                    65536
SF              500.1600122 MHz
WDW                      EM
SSB          0
LB                    0.30 Hz
GB           0
PC                    1.00
```

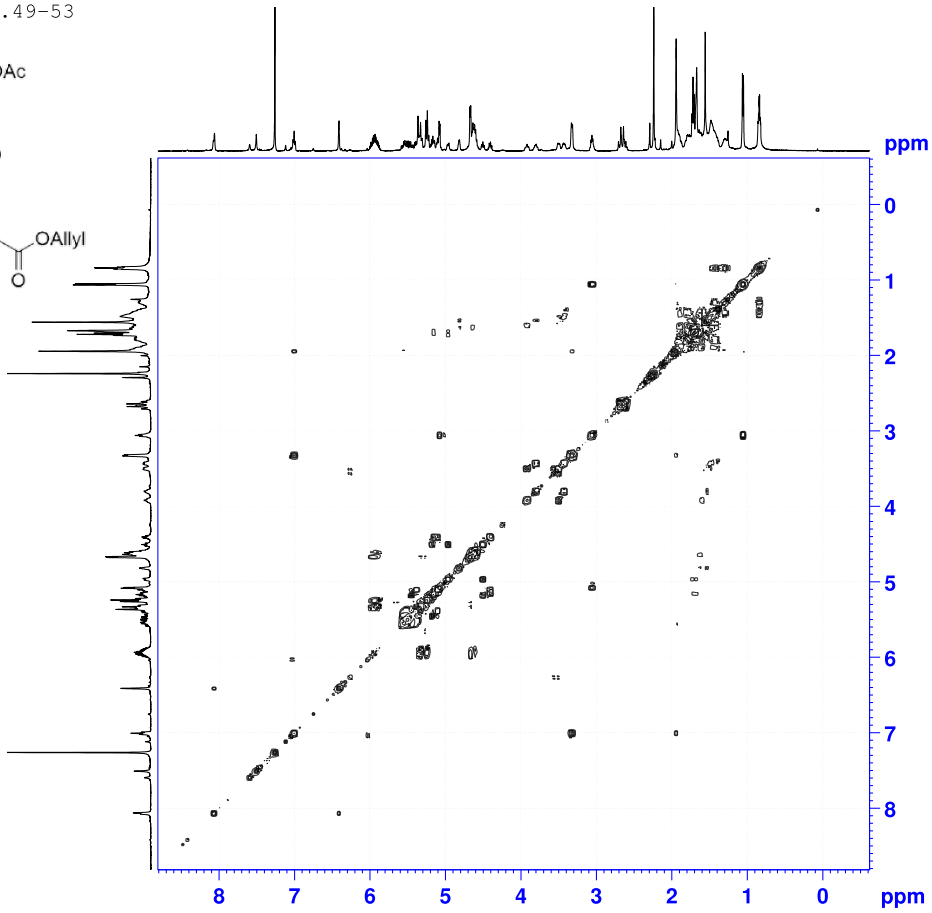
p.10-5 fr.49-53




```
Current Data Parameters
NAME      Scott Cyclization
EXPNO                    6
PROCNO                   1

F2 - Acquisition Parameters
Date_               20180419
Time                   12.00
INSTRUM                spect
PROBHD    5 mm PABBO BB-
PULPROG             zgpg30
TD                    65536
SOLVENT               CDCl3
NS                    26500
DS                        4
SWH              36057.691 Hz
FIDRES                0.550197 Hz
AQ                0.9087659 sec
RG                      203
DW                   13.867 usec
DE                    6.50 usec
TE                   295.4 K
D1              2.00000000 sec
D11             0.03000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                      13C
P1                     11.50 usec
PL1          0 dB
PL1W           97.46119690 W
SFO1          151.0637542 MHz

======== CHANNEL f2 ========
CPDPRG[2           waltz16
NUC2                      1H
PCPD2                 70.00 usec
PL2                   -2.00 dB
PL12                  14.19 dB
PL13                 120.00 dB
PL2W           19.70630455 W
PL12W           0.47381112 W
PL13W     0 W
SFO2          600.7124028 MHz

F2 - Processing parameters
SI                    32768
SF              151.0486295 MHz
WDW                      EM
SSB          0
LB                    1.00 Hz
GB           0
PC                    1.40
```

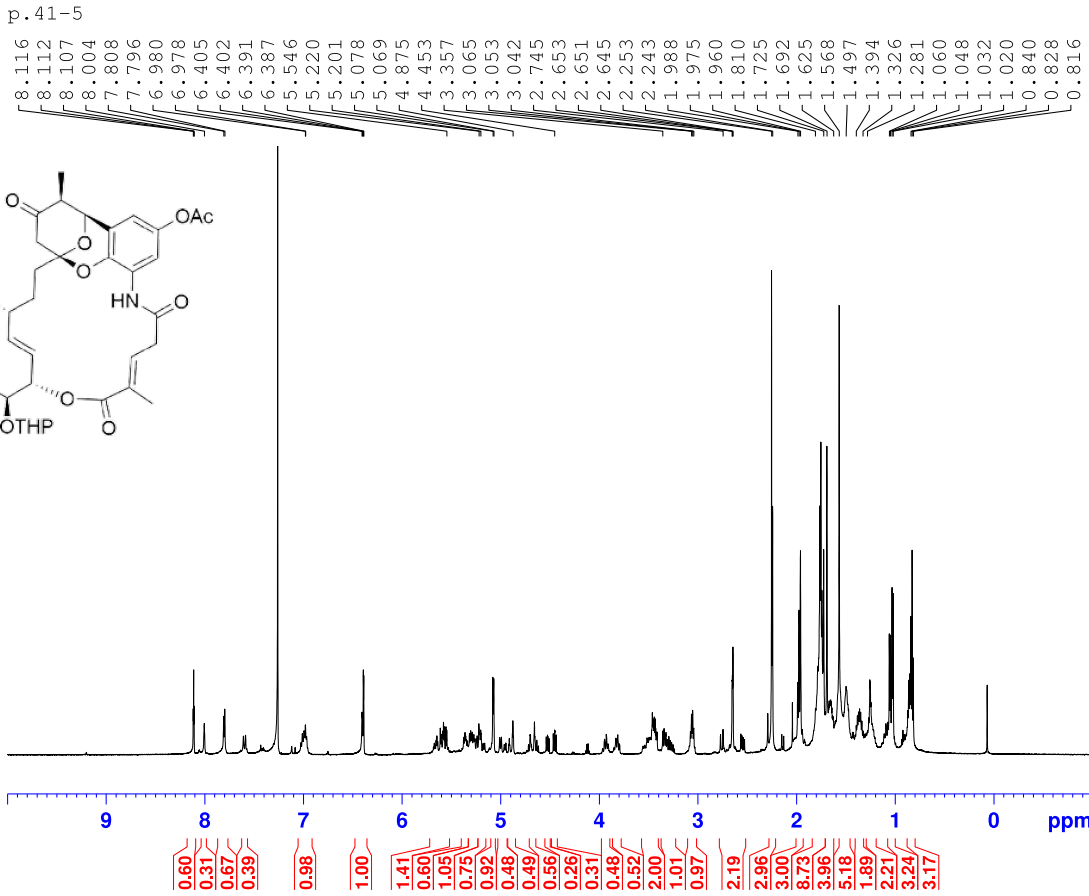
p.10-5 fr.49-53





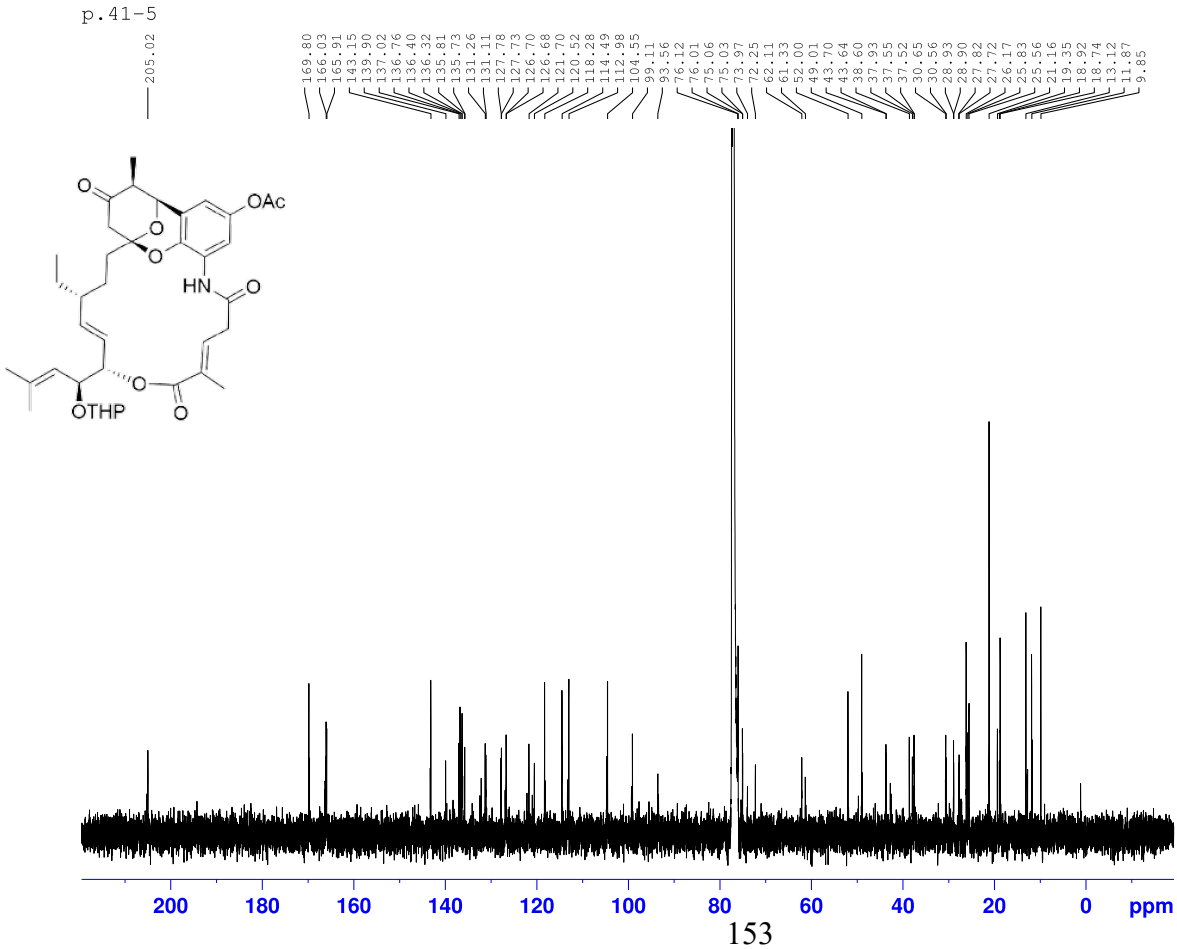

```
Current Data Parameters
NAME      Scott Cyclization
EXPNO                   21
PROCNO                   1

F2 - Acquisition Parameters
Date_              20180416
Time                 10.19
INSTRUM              spect
PROBHD    5 mm PABBO BB/
PULPROG       cosygpppqf
TD                    2048
SOLVENT            CDCl3
NS                       2
DS                       8
SWH               4716.981 Hz
FIDRES            2.303213 Hz
AQ                0.2170880 sec
RG                      64
DW                106.000 usec
DE                  6.50 usec
TE                 301.0 K
D0              0.00000300 sec
D1              1.93610203 sec
D11             0.03000000 sec
D12             0.00002000 sec
D13             0.00000400 sec
D16             0.00020000 sec
IN0             0.00021200 sec

======== CHANNEL f1 ========
SFO1          500.1620617 MHz
NUC1                     1H
P0                   11.50 usec
P1                   11.50 usec
P17                2500.00 usec
PLW1          18.00000000 W
PLW10          3.52139997 W

====== GRADIENT CHANNEL =====
GPNAM[1]       SMSQ10.100
GPZ1                10.00 %
P16               1000.00 usec

F1 - Acquisition parameters
TD                       128
SFO1              500.1621 MHz
FIDRES           73.702827 Hz
SW                   9.431 ppm
FnMODE                   QF

F2 - Processing parameters
SI                       1024
SF              500.1600127 MHz
WDW                    QSINE
SSB         0
LB          0 Hz
GB          0
PC                     1.40

F1 - Processing parameters
SI                       1024
MC2                      QF
SF              500.1600114 MHz
WDW                    QSINE
SSB         0
LB          0 Hz
GB          0
```

p.41-5



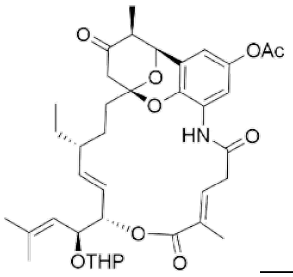

```
Current Data Parameters
NAME          Scott MNBA
EXPNO                 12
PROCNO                 1

F2 - Acquisition Parameters
Date_           20180613
Time               12.46
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH           12335.526 Hz
FIDRES         0.188225 Hz
AQ            2.6563926 sec
RG                   144
DW                40.533 usec
DE                 6.50 usec
TE                298.0 K
D1           1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                10.86 usec
PL1               -2.00 dB
PL1W         19.70630455 W
SFO1         600.7137096 MHz

F2 - Processing parameters
SI                 32768
SF           600.7100157 MHz
WDW                   EM
SSB       0
LB                0.30 Hz
GB        0
PC                1.00
```

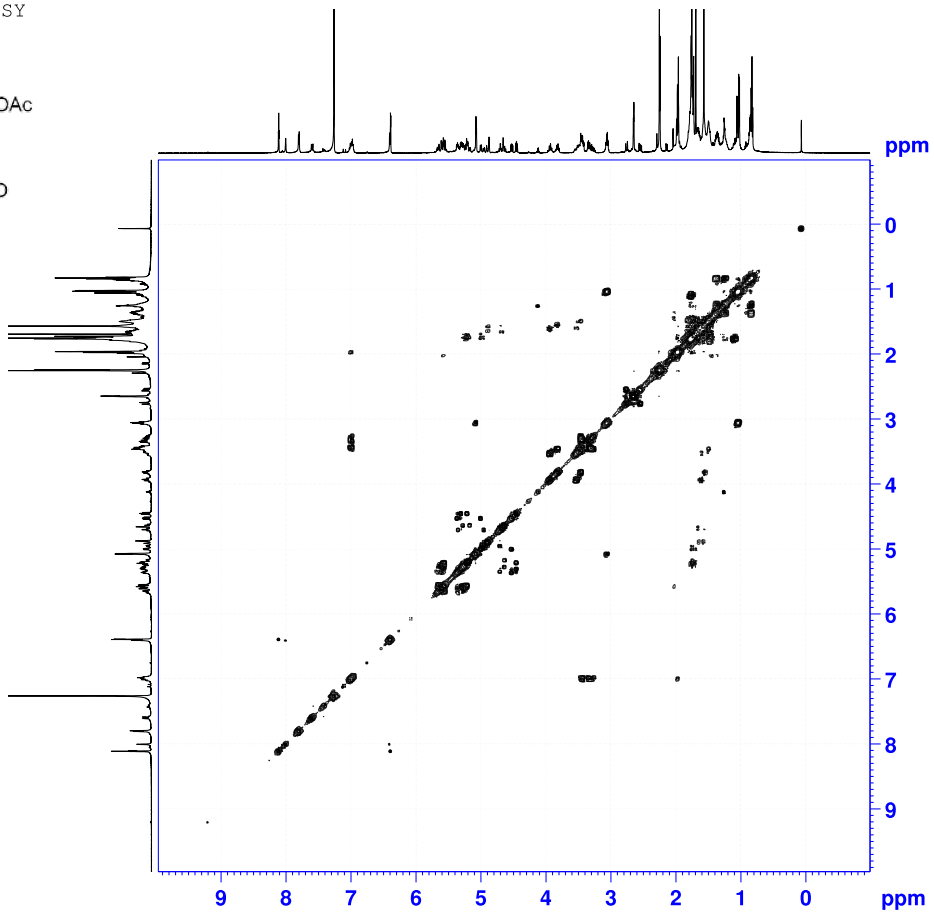
p.41-5




```
Current Data Parameters
NAME          Scott MNBA
EXPNO                 14
PROCNO                 1

F2 - Acquisition Parameters
Date_           20180614
Time               12.07
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG          zgpg30
TD                 65536
SOLVENT            CDCl3
NS                 27750
DS                     4
SWH           36057.691 Hz
FIDRES         0.550197 Hz
AQ            0.9087659 sec
RG                   203
DW                13.867 usec
DE                 6.50 usec
TE                298.0 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                 13C
P1                11.50 usec
PL1       0 dB
PL1W         97.46119690 W
SFO1         151.0637542 MHz

======== CHANNEL f2 ========
CPDPRG[2          waltz16
NUC2                  1H
PCPD2             70.00 usec
PL2               -2.00 dB
PL12              14.19 dB
PL13             120.00 dB
PL2W         19.70630455 W
PL12W         0.47381112 W
PL13W     0 W
SFO2         600.7124028 MHz

F2 - Processing parameters
SI                 32768
SF           151.0486277 MHz
WDW                   EM
SSB       0
LB                1.00 Hz
GB        0
PC                1.40
```

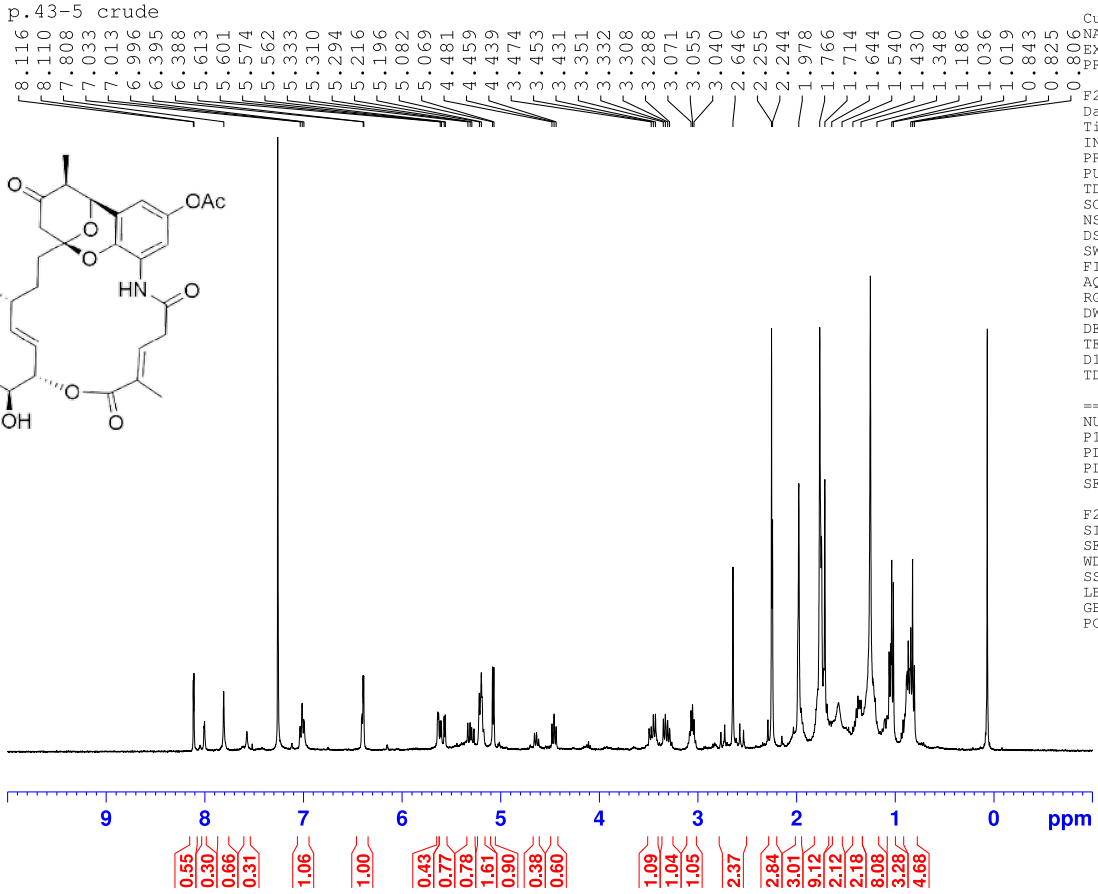
p.41-5 COSY





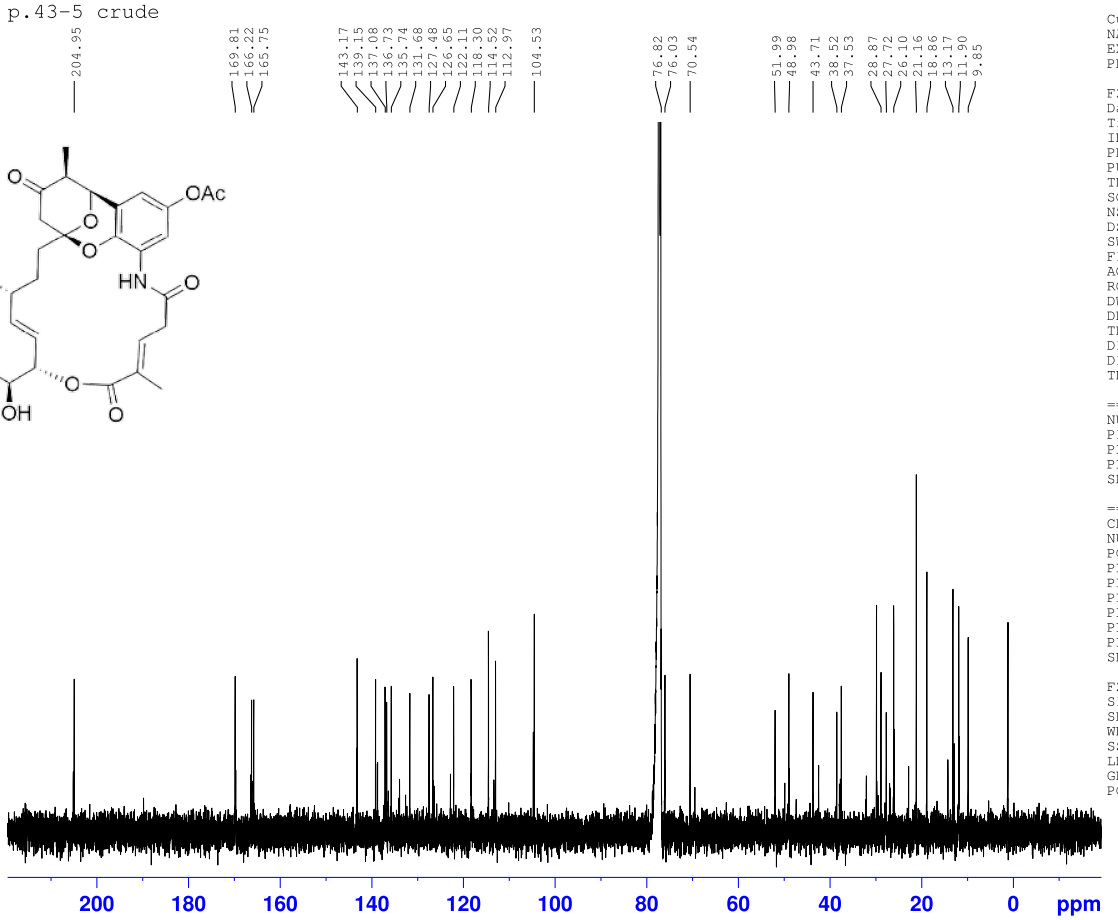

```
Current Data Parameters
NAME          Scott MNBA
EXPNO                 13
PROCNO                 1

F2 - Acquisition Parameters
Date_           20180613
Time              12.56
INSTRUM           spect
PROBHD   5 mm PABBO BB-
PULPROG        cosygpqf
TD                2048
SOLVENT           CDCl3
NS                   3
DS                   8
SWH            6578.947 Hz
FIDRES         3.212377 Hz
AQ             0.1556480 sec
RG                 203
DW               76.000 usec
DE                6.50 usec
TE               298.0 K
D0            0.00000300 sec
D1            1.48689198 sec
D13           0.00000400 sec
D16           0.00020000 sec
IN0           0.00015200 sec

======== CHANNEL f1 ========
NUC1                1H
P0                10.86 usec
P1                10.86 usec
PL1               -2.00 dB
PL1W        19.70630455 W
SFO1        600.7127075 MHz

====== GRADIENT CHANNEL =====
GPNAM[1]        SINE.100
GPZ1              10.00 %
P16             1000.00 usec

F1 - Acquisition parameters
TD                  128
SFO1          600.7127 MHz
FIDRES        102.796021 Hz
SW              10.952 ppm
FnMODE                QF

F2 - Processing parameters
SI                 1024
SF          600.7100106 MHz
WDW                SINE
SSB       0
LB        0 Hz
GB        0
PC                 1.40

F1 - Processing parameters
SI                 1024
MC2                  QF
SF          600.7100105 MHz
WDW                SINE
SSB       0
LB        0 Hz
GB        0
```

p.43-5 crude



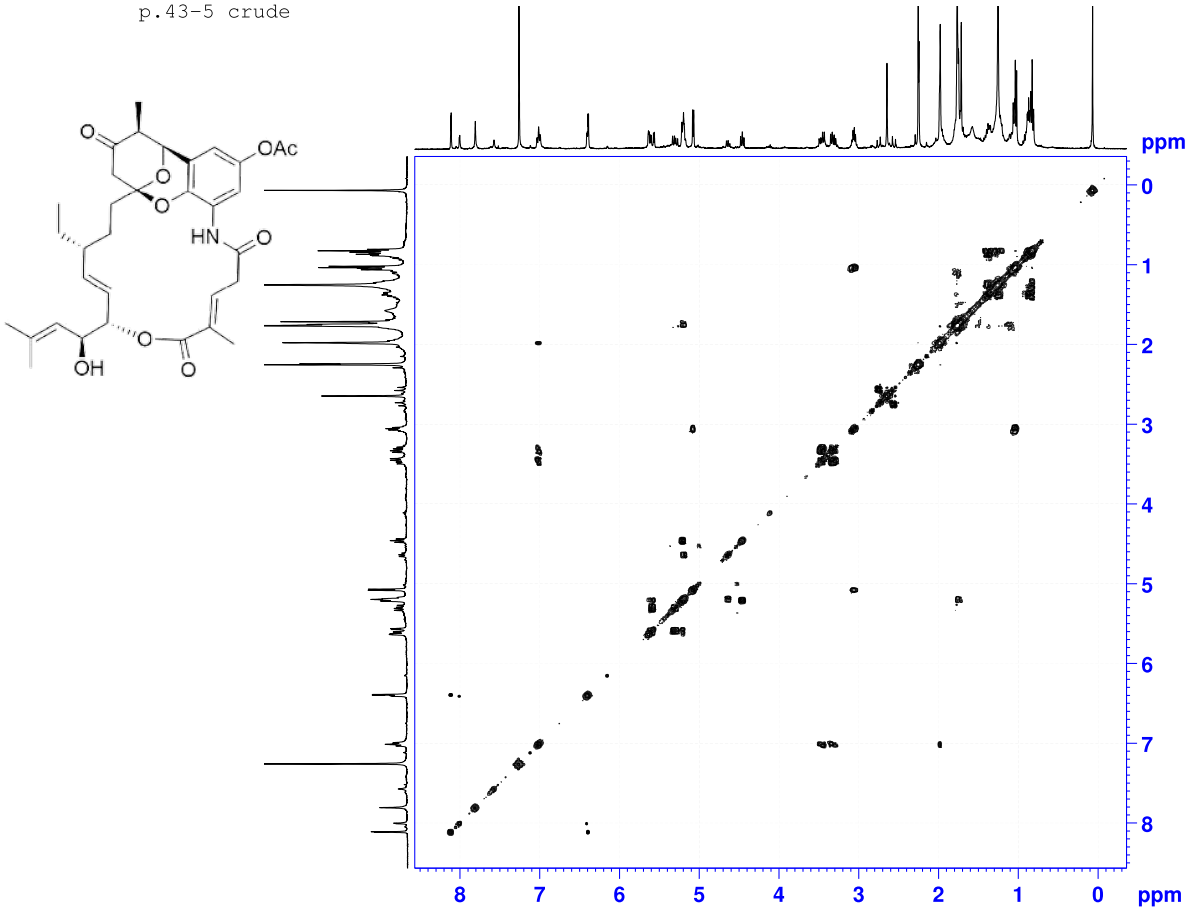

```
Current Data Parameters
NAME            Scott THP
EXPNO                   2
PROCNO                  1

F2 - Acquisition Parameters
Date_            20180620
Time                9.42
INSTRUM            spect
PROBHD    5 mm PADUL 13C
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8223.685 Hz
FIDRES          0.125483 Hz
AQ              3.9845889 sec
RG                   114
DW                60.800 usec
DE                 6.50 usec
TE                298.2 K
D1             2.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                  9.31 usec
PL1                -3.90 dB
PL1W         21.64248466 W
SFO1         400.2324716 MHz

F2 - Processing parameters
SI                 32768
SF           400.2300125 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

p.43-5 crude



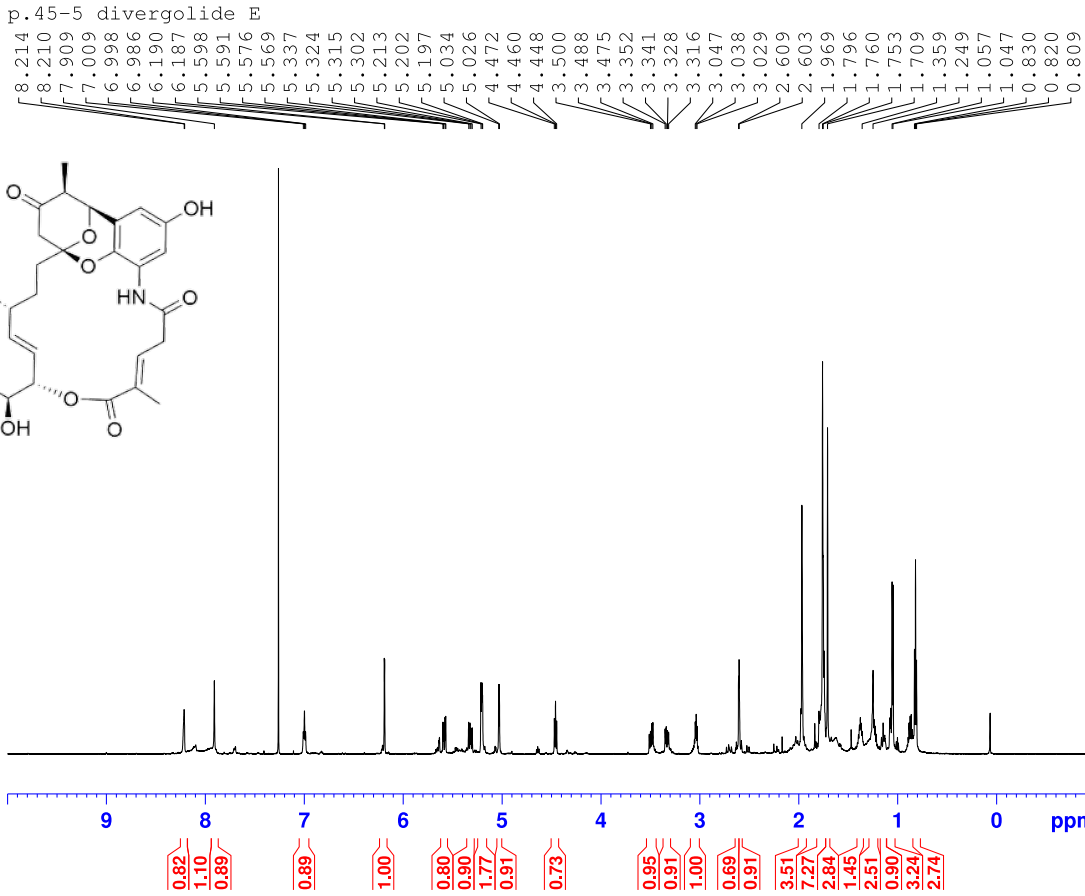

```
Current Data Parameters
NAME            Scott THP
EXPNO                   2
PROCNO                  1

F2 - Acquisition Parameters
Date_            20180622
Time                8.58
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG          zgpg30
TD                 65536
SOLVENT            CDCl3
NS                 28000
DS                     4
SWH            36057.691 Hz
FIDRES          0.550197 Hz
AQ              0.9087659 sec
RG                   203
DW                13.867 usec
DE                 6.50 usec
TE                298.0 K
D1             2.00000000 sec
D11            0.03000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                 13C
P1                 11.50 usec
PL1       0 dB
PL1W         97.46119690 W
SFO1        151.0637542 MHz

======== CHANNEL f2 ========
CPDPRG[2         waltz16
NUC2                  1H
PCPD2              70.00 usec
PL2                -2.00 dB
PL12               14.19 dB
PL13              120.00 dB
PL2W         19.70630455 W
PL12W         0.47381112 W
PL13W     0 W
SFO2         600.7124028 MHz

F2 - Processing parameters
SI                 32768
SF           151.0486287 MHz
WDW                   EM
SSB       0
LB                 1.00 Hz
GB        0
PC                 1.40
```

p.43-5 crude




```
Current Data Parameters
NAME            Scott THP
EXPNO                   7
PROCNO                  1

F2 - Acquisition Parameters
Date_            20180620
Time                10.21
INSTRUM             spect
PROBHD   5 mm PADUL 13C
PULPROG          cosygpqf
TD                  2048
SOLVENT             CDCl3
NS                     4
DS                     8
SWH              3571.428 Hz
FIDRES           1.743862 Hz
AQ               0.2867200 sec
RG                   203
DW                140.000 usec
DE                  6.50 usec
TE                298.2 K
D0            0.00000300 sec
D1            1.48689198 sec
D13           0.00000400 sec
D16           0.00020000 sec
IN0           0.00028000 sec

======== CHANNEL f1 ========
NUC1                 1H
P0                9.31 usec
P1                9.31 usec
PL1              -3.90 dB
PL1W         21.64248466 W
SFO1         400.2316531 MHz

====== GRADIENT CHANNEL =====
GPNAM[1]         SINE.100
GPZ1                10.00 %
P16               1000.00 usec

F1 - Acquisition parameters
TD                   128
SFO1            400.2317 MHz
FIDRES          55.803551 Hz
SW                8.923 ppm
FnMODE                QF

F2 - Processing parameters
SI                   1024
SF           400.2300101 MHz
WDW                  SINE
SSB       0
LB        0 Hz
GB        0
PC                  1.40

F1 - Processing parameters
SI                   1024
MC2                    QF
SF           400.2300101 MHz
WDW                  SINE
SSB       0
LB        0 Hz
GB        0
```

p.45-5 divergolide E



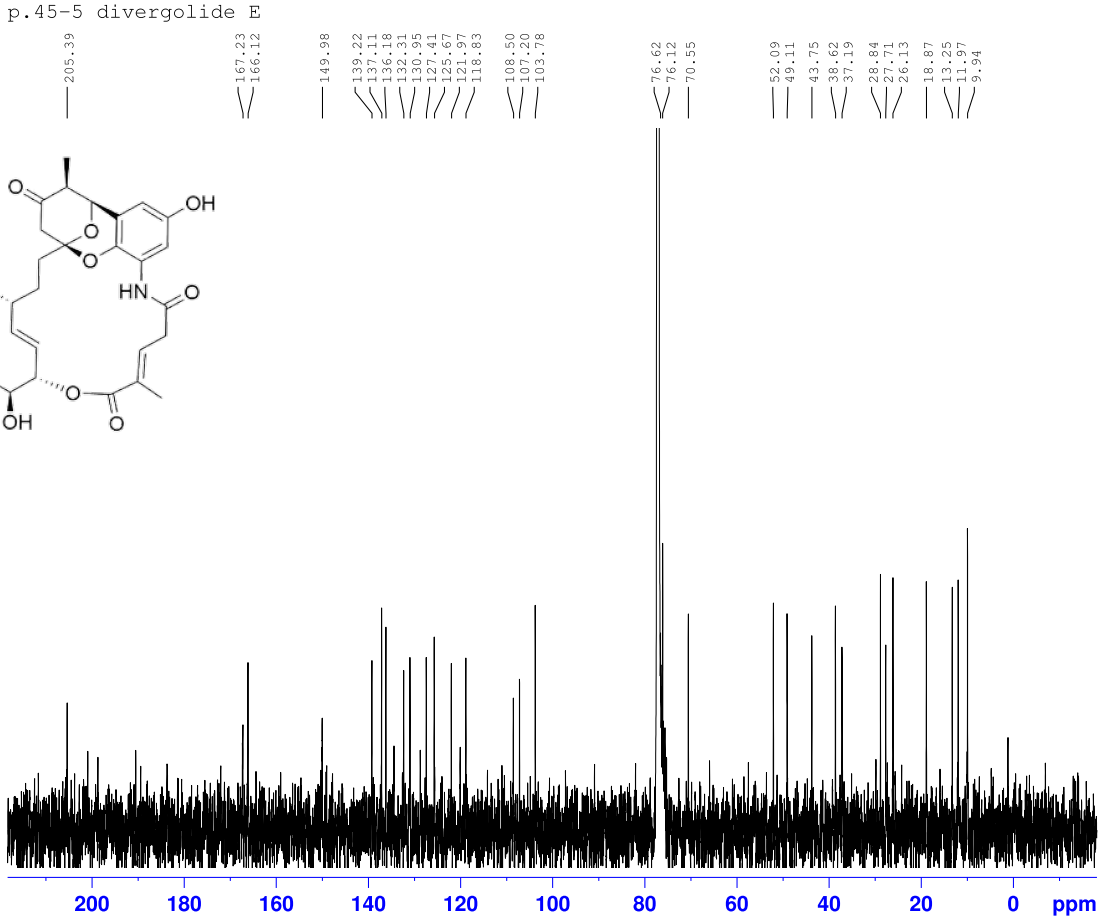
Current Data Parameters
NAME Scott Deacylation
EXPNO 2
PROCNO 1

F2 - Acquisition Parameters
Date_ 20180703
Time 11.15
INSTRUM spect
PROBHD 1.7 mm PATXI 1
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 14423.077 Hz
FIDRES 0.220079 Hz
AQ 2.2719147 sec
RG 575
DW 34.667 usec
DE 6.50 usec
TE 297.3 K
D1 1.00000000 sec
TD0 1

======== CHANNEL f1 ========
NUC1 1H
P1 7.73 usec
PL1 7.50 dB
PL1W 4.03355265 W
SFO1 700.7043271 MHz

F2 - Processing parameters
SI 32768
SF 700.7000180 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

p.45-5 divergolide E



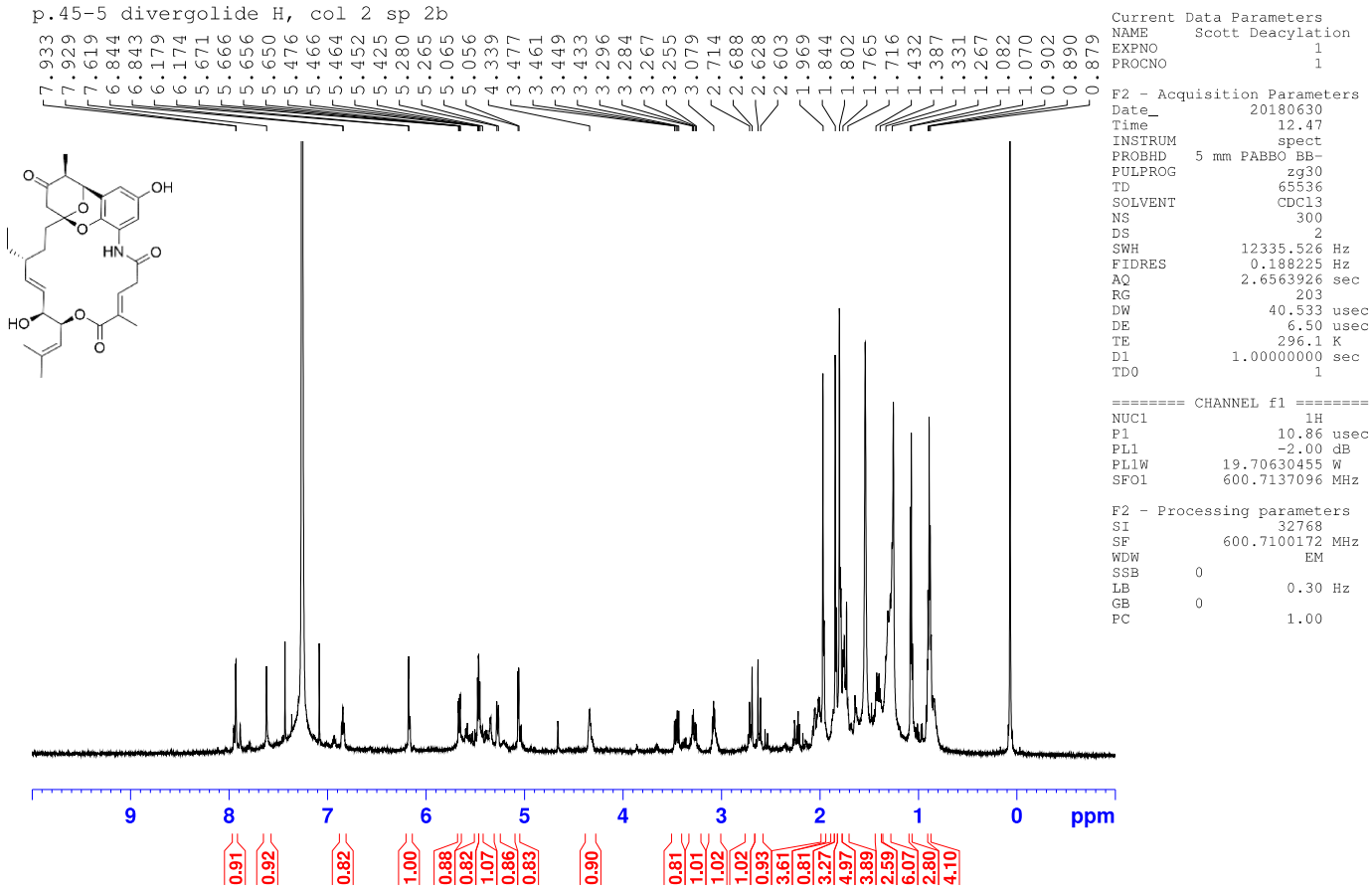
Current Data Parameters
NAME Scott Deacylation
EXPNO 6
PROCNO 1

F2 - Acquisition Parameters
Date_ 20180719
Time 9.24
INSTRUM spect
PROBHD 1.7 mm PATXI 1
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 33000
DS 4
SWH 41666.668 Hz
FIDRES 0.635783 Hz
AQ 0.7864320 sec
RG 2050
DW 12.000 usec
DE 6.50 usec
TE 288.2 K
D1 3.00000000 sec
D11 0.03000000 sec
TD0 1

======== CHANNEL f1 ========
NUC1 13C
P1 8.65 usec
PL1 3.00 dB
PL1W 60.93199158 W
SFO1 176.2087739 MHz

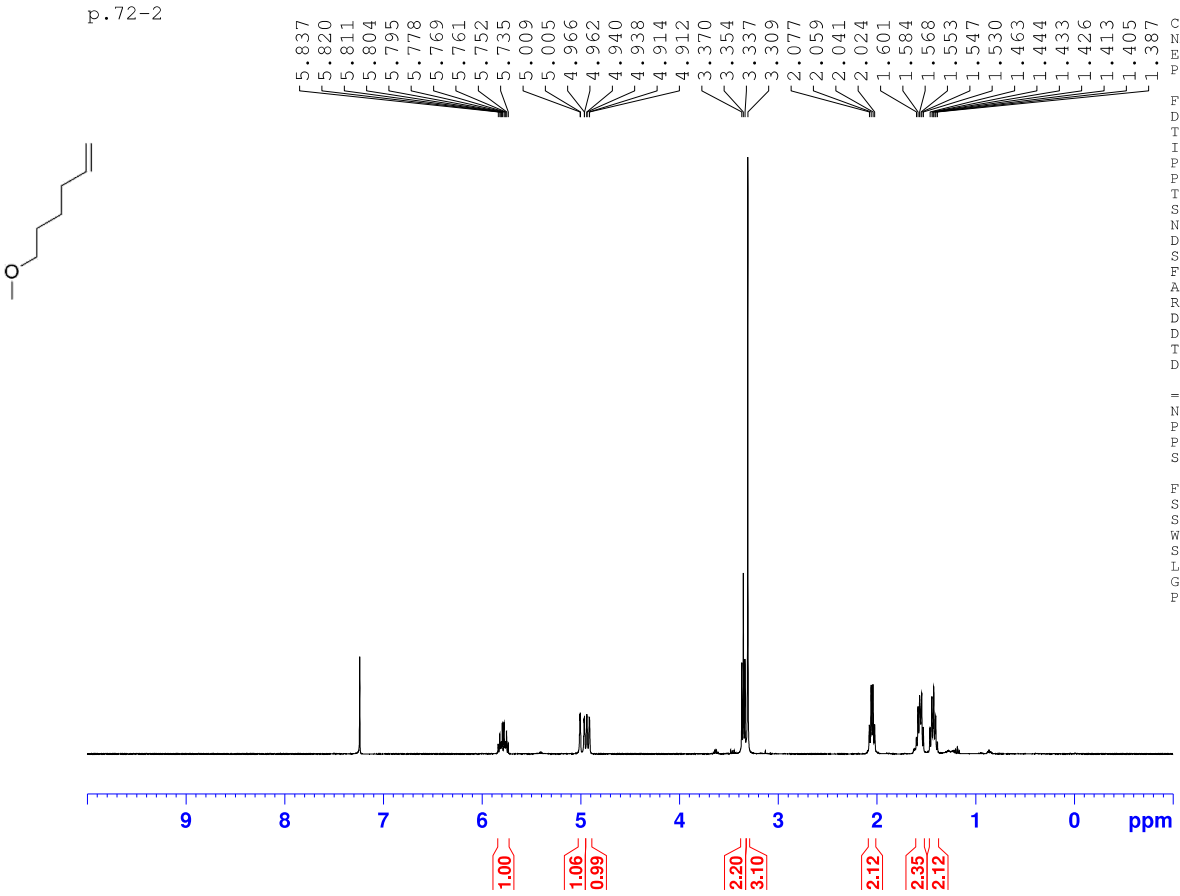
======== CHANNEL f2 ========
CPDPRG[2 waltz16
NUC2 1H
PCPD2 60.00 usec
PL2 7.50 dB
PL12 25.30 dB
PL13 120.00 dB
PL2W 4.03355265 W
PL12W 0.06694033 W
PL13W 0 W
SFO2 700.7028028 MHz

F2 - Processing parameters
SI 32768
SF 176.1911374 MHz
WDW EM
SSB 0
LB 5.00 Hz
GB 0
PC 1.40



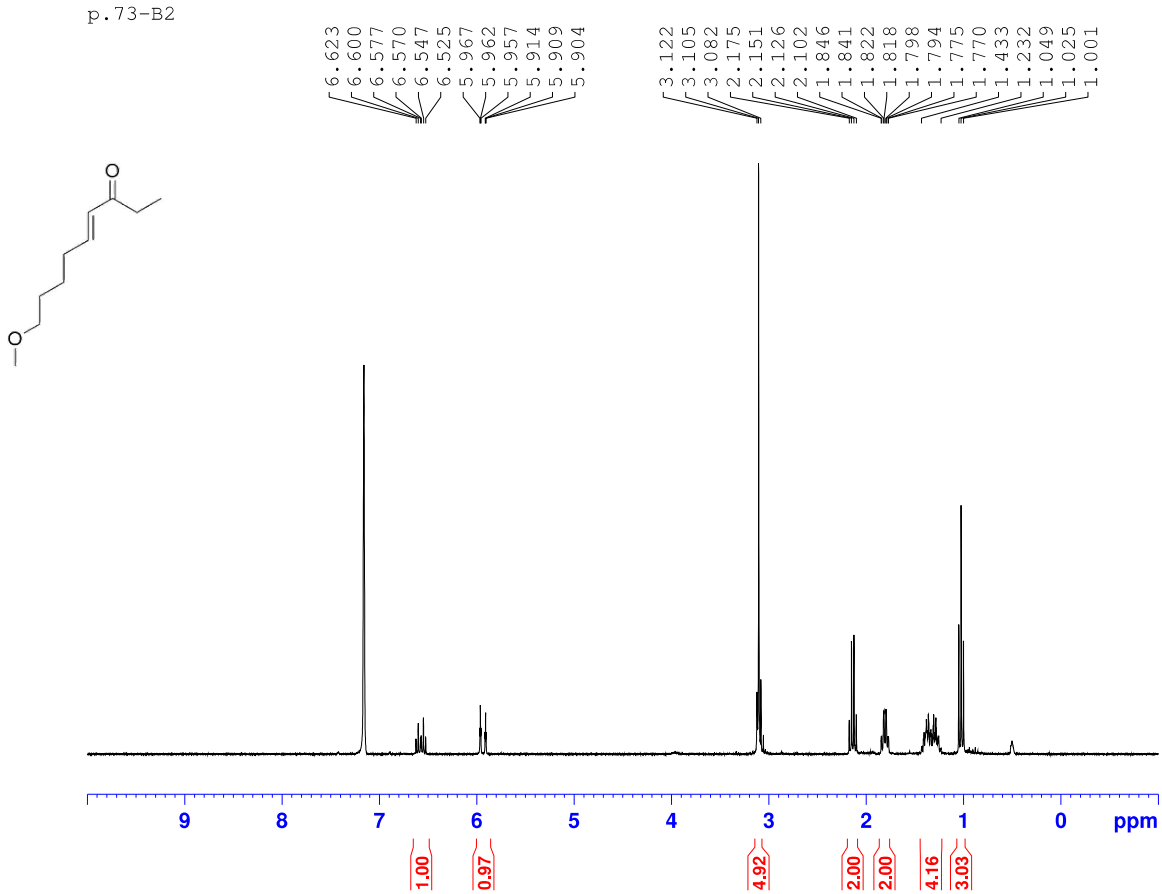

```
Current Data Parameters
NAME      Scott Deacylation
EXPNO                   1
PROCNO                  1

F2 - Acquisition Parameters
Date_           20180630
Time                12.47
INSTRUM             spect
PROBHD   5 mm PABBO BB-
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                   300
DS                     2
SWH            12335.526 Hz
FIDRES          0.188225 Hz
AQ             2.6563926 sec
RG                   203
DW                40.533 usec
DE                 6.50 usec
TE                296.1 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                 10.86 usec
PL1                -2.00 dB
PL1W         19.70630455 W
SFO1         600.7137096 MHz

F2 - Processing parameters
SI                 32768
SF           600.7100172 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

p.72-2



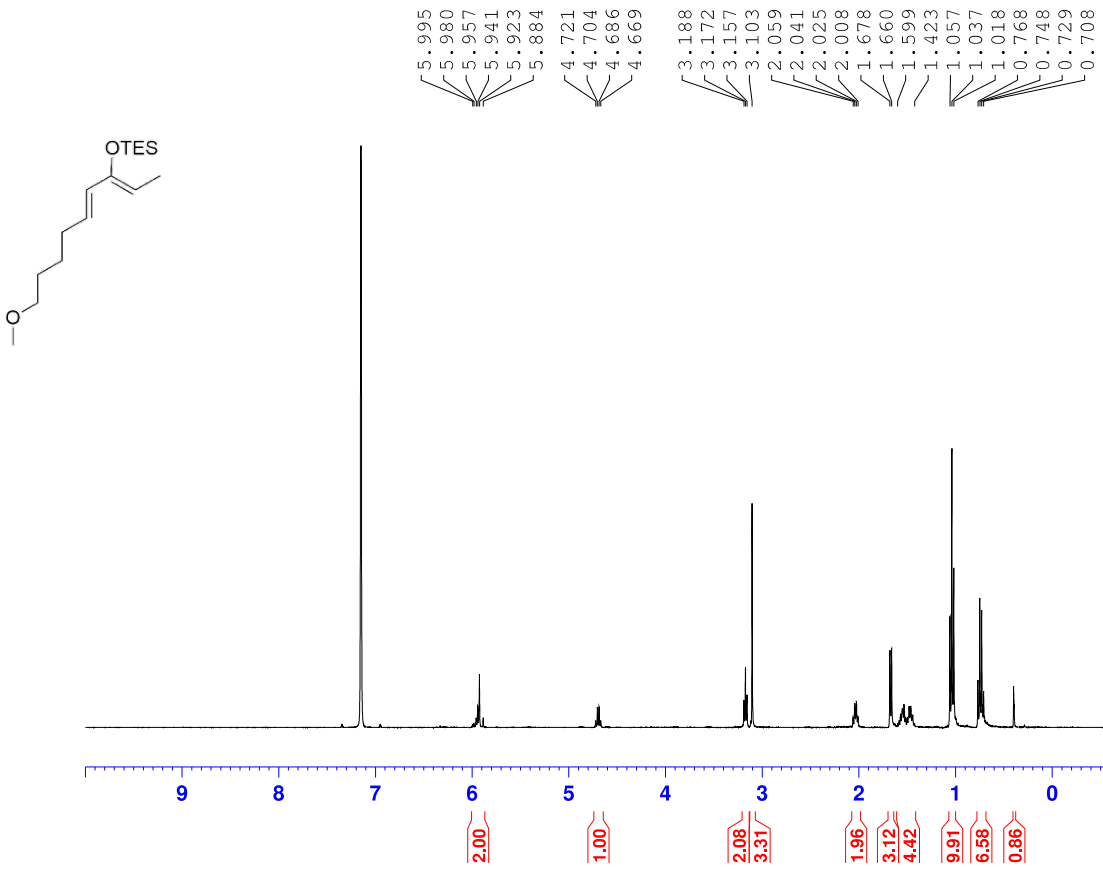

```
Current Data Parameters
NAME       Scott diene 2
EXPNO                20
PROCNO                1

F2 - Acquisition Parameters
Date_          20130712
Time              10.29
INSTRUM           spect
PROBHD   5 mm PABBO BB-
PULPROG            zg30
TD                65536
SOLVENT           CDCl3
NS                   16
DS                    2
SWH            8223.685 Hz
FIDRES        0.125483 Hz
AQ           3.9845889 sec
RG                  101
DW             60.800 usec
DE              6.50 usec
TE              295.5 K
D1          1.00000000 sec

======== CHANNEL f1 ========
NUC1                1H
P1              13.75 usec
PLW1        12.01700020 W
SFO1       400.1324710 MHz

F2 - Processing parameters
SI                65536
SF         400.1300187 MHz
WDW                  EM
SSB       0
LB              0.30 Hz
GB        0
PC                1.00
```

p.73-B2



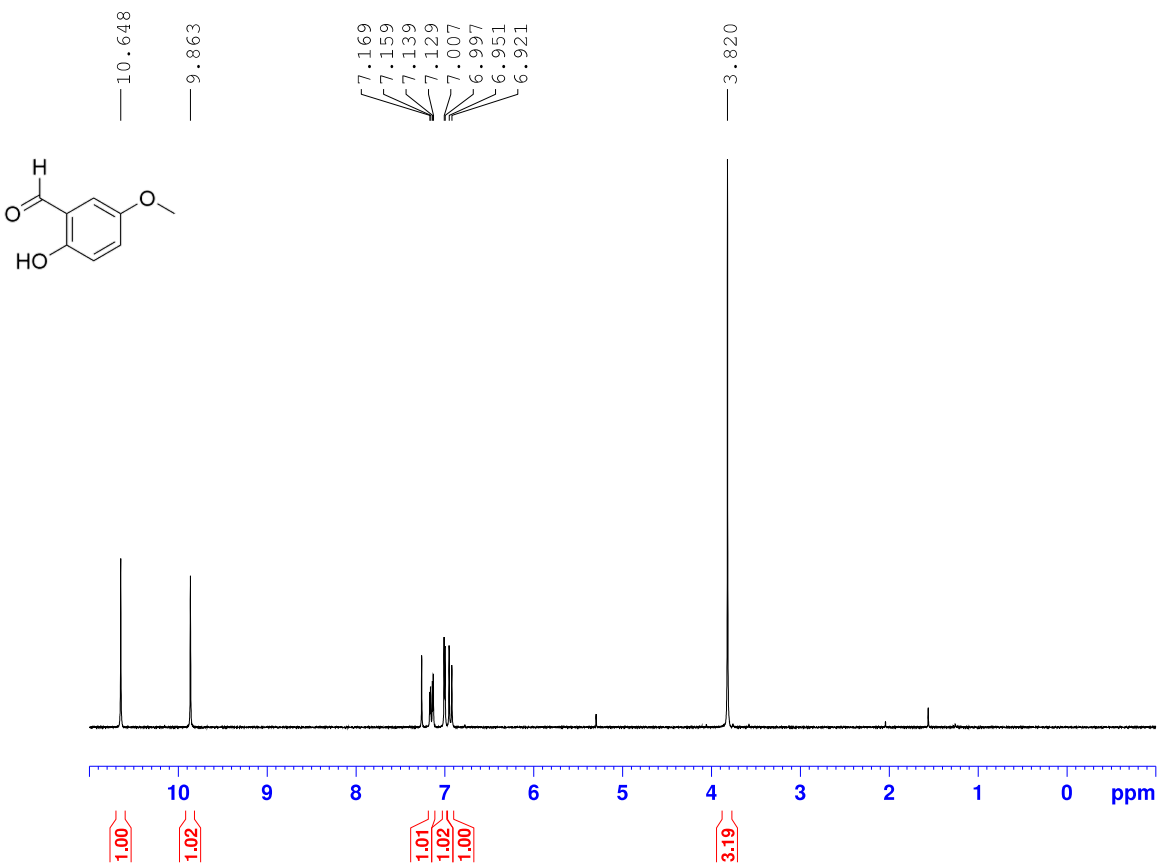

```
Current Data Parameters
NAME       Scott diene 3
EXPNO                11
PROCNO                1

F2 - Acquisition Parameters
Date_          20130806
Time              11.20
INSTRUM           spect
PROBHD   5 mm QNP  1H/1
PULPROG            zg30
TD                32768
SOLVENT            C6D6
NS                   16
DS                    2
SWH            6188.119 Hz
FIDRES        0.188846 Hz
AQ           2.6476543 sec
RG                  322
DW             80.800 usec
DE              6.50 usec
TE             -925.6 K
D1          1.00000000 sec

======== CHANNEL f1 ========
NUC1                1H
P1              12.71 usec
PLW1        18.19700050 W
SFO1       300.2318540 MHz

F2 - Processing parameters
SI                32768
SF         300.2300000 MHz
WDW                  EM
SSB       0
LB              0.10 Hz
GB        0
PC                1.00
```

p.83 fr 14,15



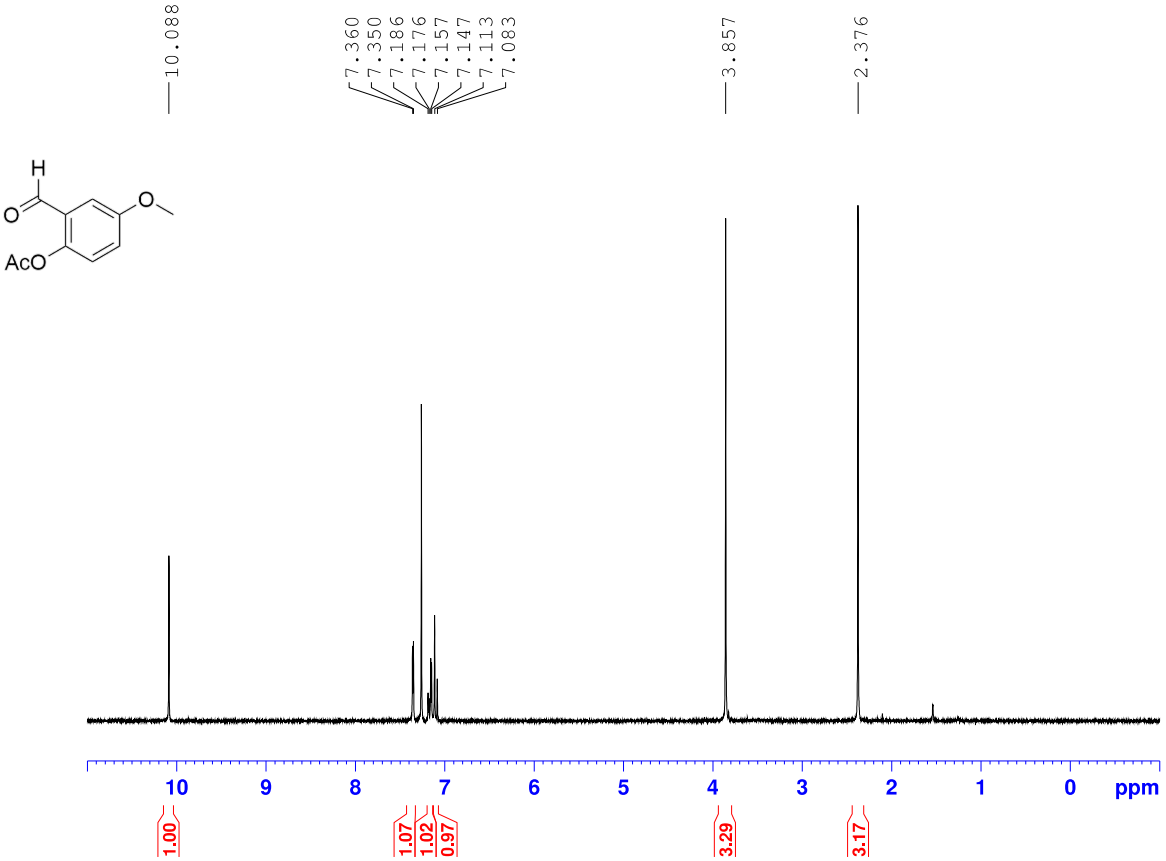

```
Current Data Parameters
NAME       Scott diene 3
EXPNO                 12
PROCNO                 1

F2 - Acquisition Parameters
Date_           20130806
Time               19.25
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG             zg30
TD                 65536
SOLVENT             C6D6
NS                    16
DS                     2
SWH             8223.685 Hz
FIDRES          0.125483 Hz
AQ              3.9845889 sec
RG                   101
DW                60.800 usec
DE                 6.50 usec
TE                296.1 K
D1             1.00000000 sec

======== CHANNEL f1 ========
NUC1                  1H
P1                13.75 usec
PLW1         12.01700020 W
SFO1         400.1324710 MHz

F2 - Processing parameters
SI                 65536
SF          400.1300018 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

2-hydroxy-5-methoxybenzaldehyde



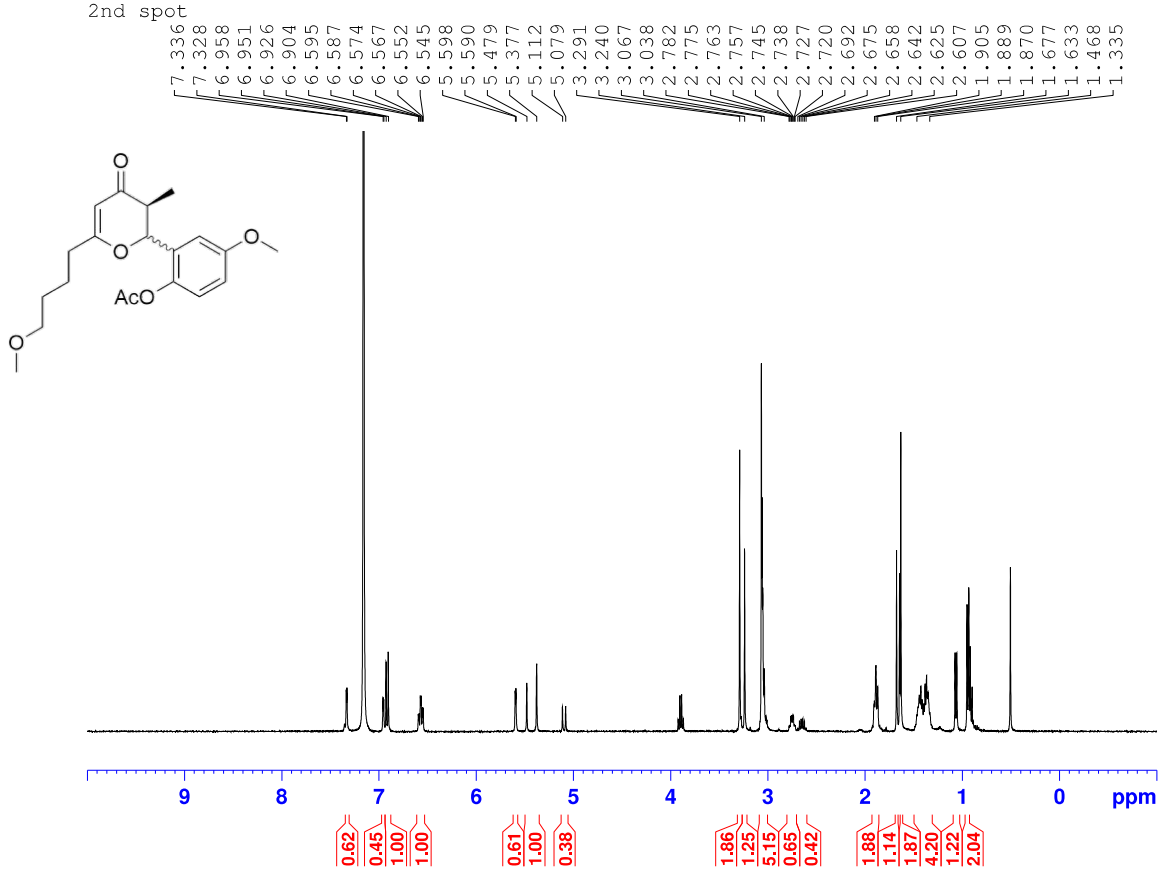

```
Current Data Parameters
NAME        Scott Caplan
EXPNO                 30
PROCNO                 1

F2 - Acquisition Parameters
Date_           20130729
Time               15.33
INSTRUM            spect
PROBHD   5 mm QNP  1H/1
PULPROG             zg30
TD                 32768
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             6188.119 Hz
FIDRES          0.188846 Hz
AQ              2.6476543 sec
RG                   575
DW                80.800 usec
DE                 6.50 usec
TE                -924.0 K
D1             1.00000000 sec

======== CHANNEL f1 ========
NUC1                  1H
P1                12.71 usec
PLW1         18.19700050 W
SFO1         300.2318540 MHz

F2 - Processing parameters
SI                 32768
SF          300.2300105 MHz
WDW                   EM
SSB       0
LB                 0.10 Hz
GB        0
PC                 1.00
```

p.79 crude



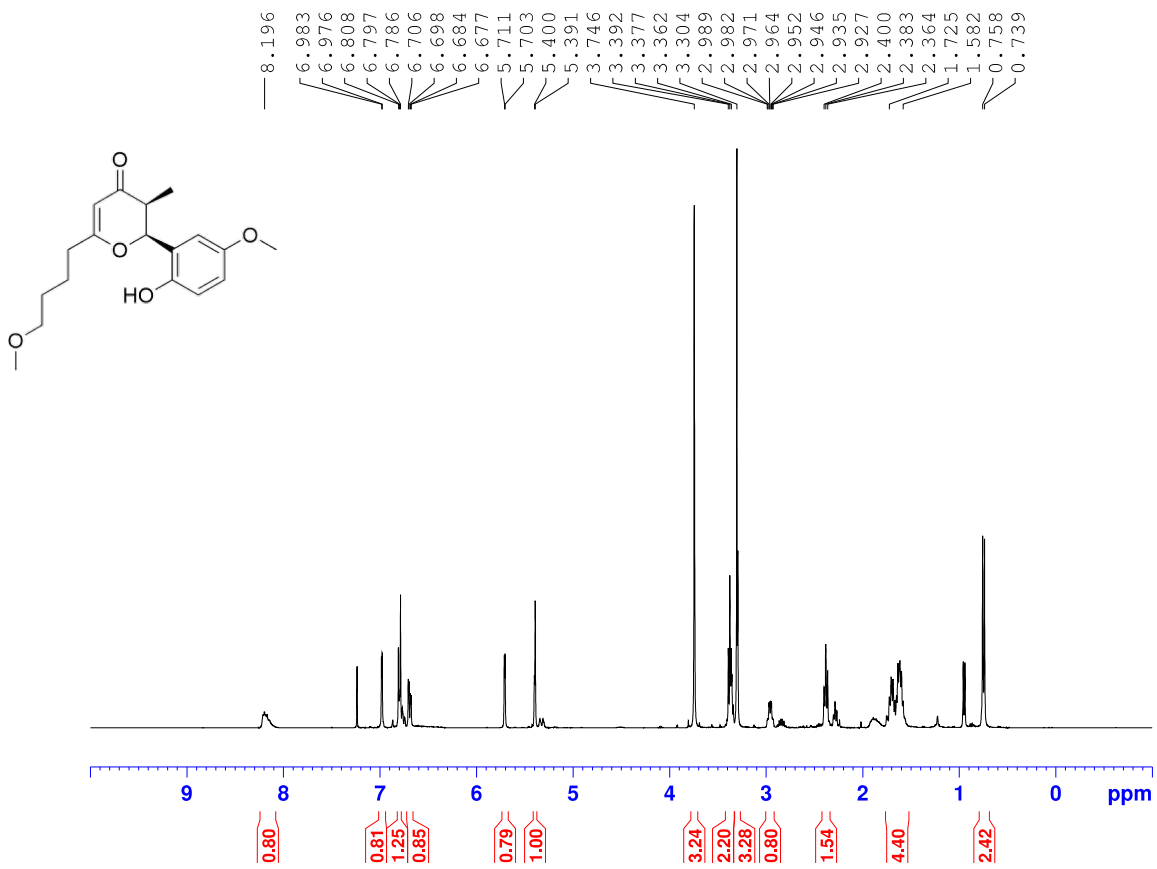

```
Current Data Parameters
NAME      Scott Acetylation
EXPNO                    20
PROCNO                    1

F2 - Acquisition Parameters
Date_              20130802
Time                 11.04
INSTRUM              spect
PROBHD    5 mm QNP  1H/1
PULPROG              zg30
TD                  32768
SOLVENT             CDCl3
NS                     32
DS                      2
SWH              6188.119 Hz
FIDRES           0.188846 Hz
AQ              2.6476543 sec
RG                    812
DW                80.800 usec
DE                 6.50 usec
TE                -924.4 K
D1             1.00000000 sec

======== CHANNEL f1 ========
NUC1                   1H
P1                  12.71 usec
PLW1         18.19700050 W
SFO1         300.2318540 MHz

F2 - Processing parameters
SI                  32768
SF           300.2300093 MHz
WDW                    EM
SSB       0
LB                  0.10 Hz
GB        0
PC                  1.00
```

p.84 after DDQ, column 2, benz.
2nd spot



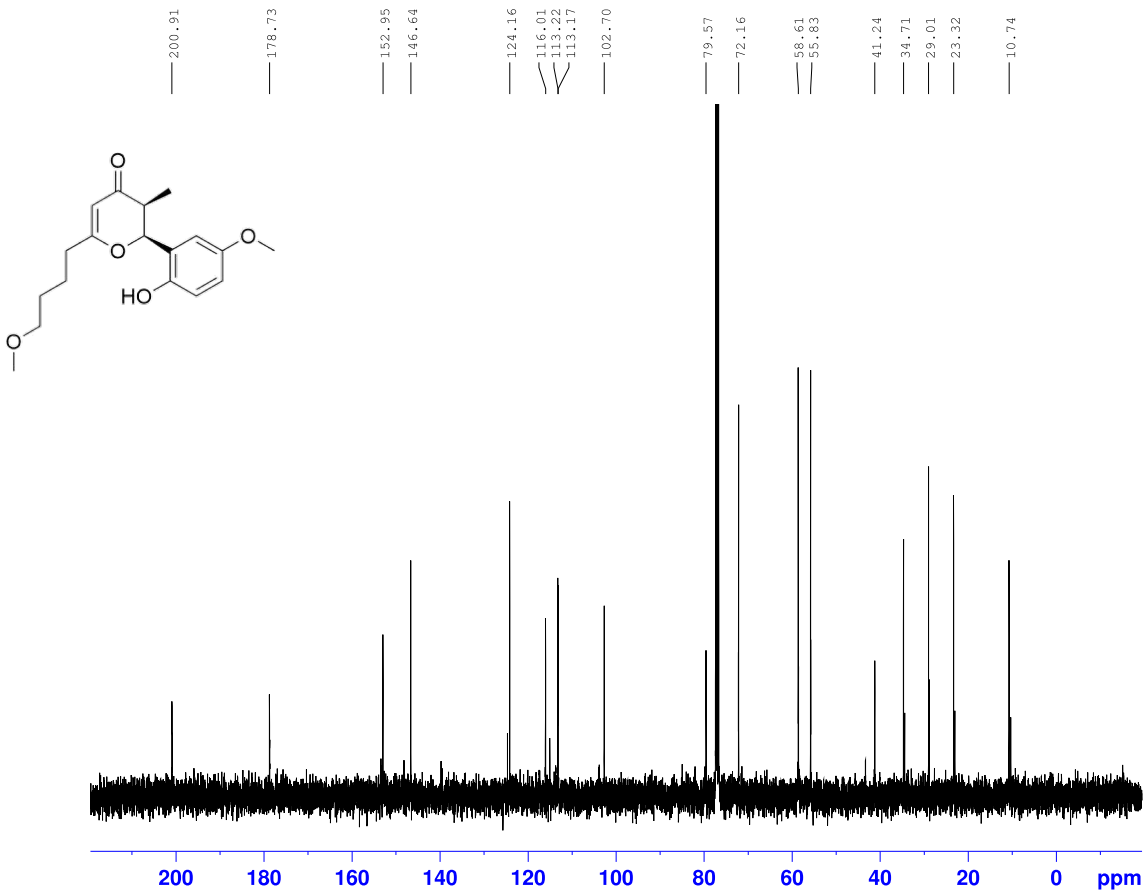

```
Current Data Parameters
NAME           Scott DDQ
EXPNO                 42
PROCNO                 1

F2 - Acquisition Parameters
Date_           20130809
Time              15.29
INSTRUM           spect
PROBHD    5 mm PABBO BB-
PULPROG           zg30
TD               65536
SOLVENT           C6D6
NS                  16
DS                   2
SWH           8223.685 Hz
FIDRES        0.125483 Hz
AQ            3.9845889 sec
RG                 101
DW              60.800 usec
DE               6.50 usec
TE              294.9 K
D1          1.00000000 sec

======== CHANNEL f1 ========
NUC1                1H
P1               13.75 usec
PLW1        12.01700020 W
SFO1        400.1324710 MHz

F2 - Processing parameters
SI               65536
SF          400.1299977 MHz
WDW                 EM
SSB       0
LB               0.30 Hz
GB        0
PC               1.00
```

p.86 spot 2



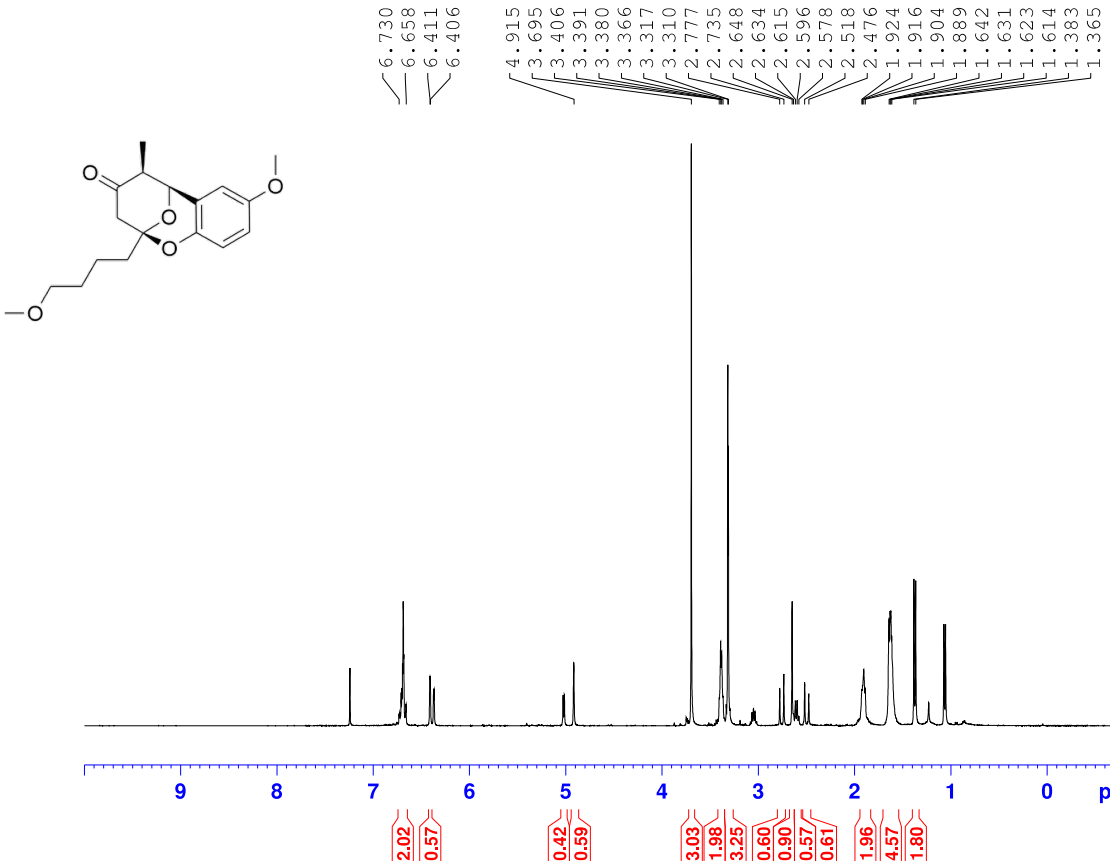

```
Current Data Parameters
NAME      Scott Deacetylation
EXPNO                  10
PROCNO                  1

F2 - Acquisition Parameters
Date_           20130810
Time               16.45
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8223.685 Hz
FIDRES          0.125483 Hz
AQ              3.9845889 sec
RG                    32
DW                60.800 usec
DE                 6.50 usec
TE                296.1 K
D1           1.00000000 sec

======== CHANNEL f1 ========
NUC1                  1H
P1                13.75 usec
PLW1         12.01700020 W
SFO1        400.1324710 MHz

F2 - Processing parameters
SI                 65536
SF          400.1300186 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

p.86 spot 2



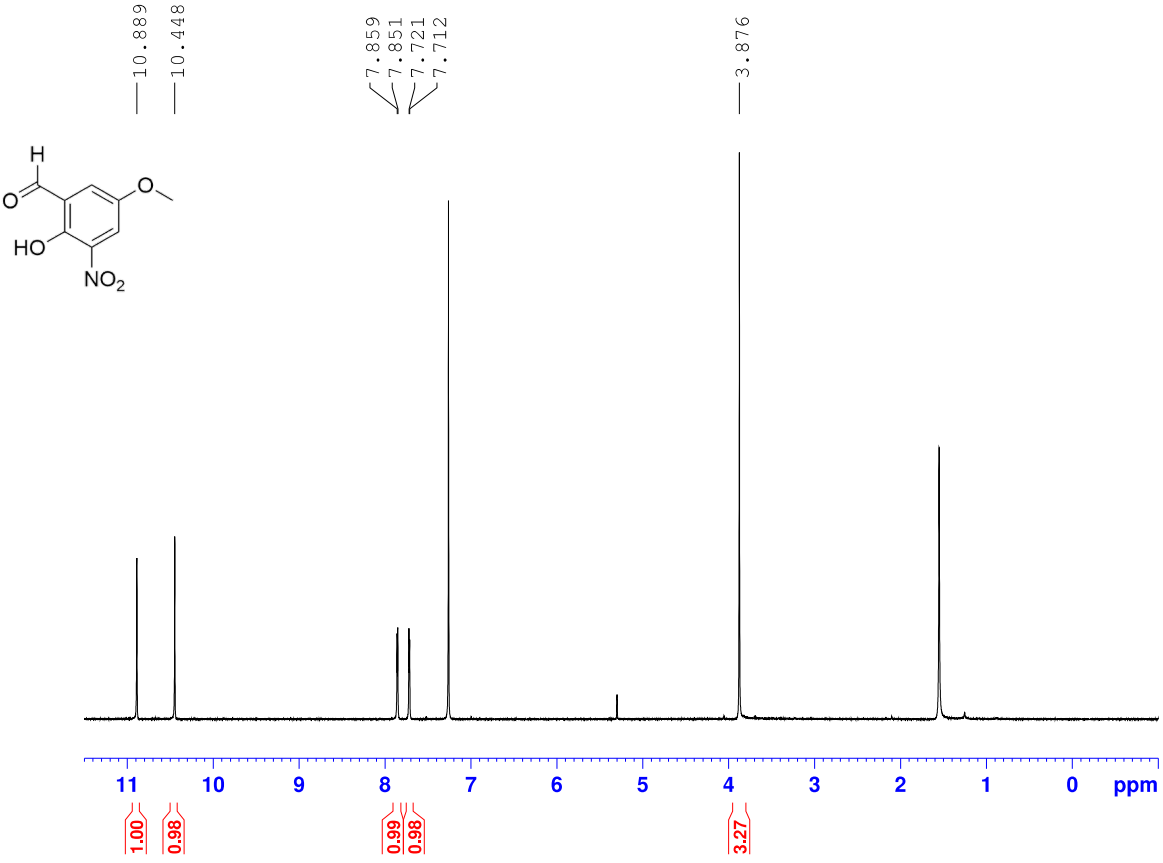

```
Current Data Parameters
NAME      Scott Deacetylation
EXPNO                  12
PROCNO                  1

F2 - Acquisition Parameters
Date_           20130810
Time               17.16
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG           zgpg30
TD                 65536
SOLVENT            CDCl3
NS                   250
DS                     4
SWH            24038.461 Hz
FIDRES          0.366798 Hz
AQ              1.3631488 sec
RG                   203
DW                20.800 usec
DE                 6.50 usec
TE                296.6 K
D1           2.00000000 sec
D11          0.03000000 sec

======== CHANNEL f1 ========
NUC1                 13C
P1                10.00 usec
PLW1         56.13299942 W
SFO1        100.6228293 MHz

======== CHANNEL f2 ========
CPDPRG[2         waltz16
NUC2                  1H
PCPD2             90.00 usec
PLW2         12.01700020 W
PLW12         0.29076999 W
PLW13     0 W
SFO2         400.1316005 MHz

F2 - Processing parameters
SI                 32768
SF          100.6127690 MHz
WDW                   EM
SSB       0
LB                 1.00 Hz
GB        0
PC                 1.40
```

p.86 spot 1



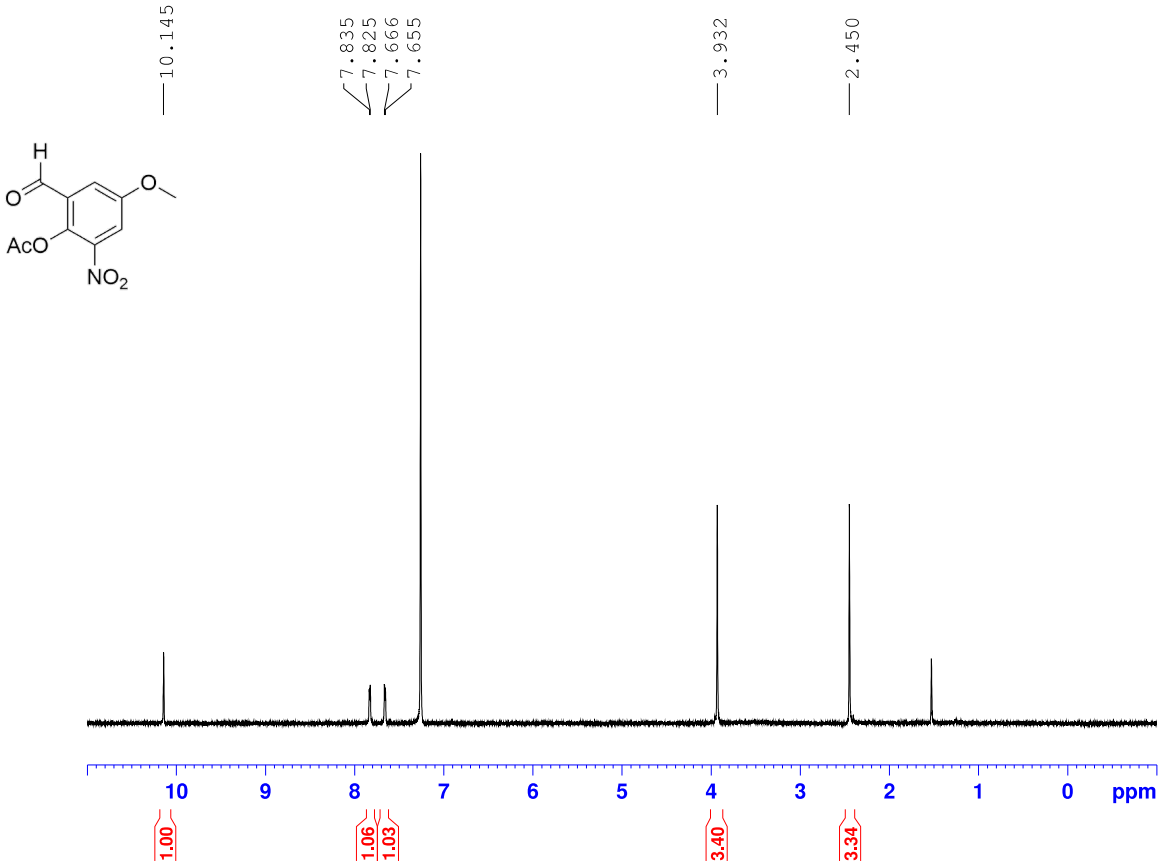

```
Current Data Parameters
NAME      Scott Deacetylation
EXPNO                      20
PROCNO                      1

F2 - Acquisition Parameters
Date_              20130810
Time                  17.23
INSTRUM               spect
PROBHD    5 mm PABBO BB-
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH                8223.685 Hz
FIDRES             0.125483 Hz
AQ                 3.9845889 sec
RG                      50.8
DW                    60.800 usec
DE                     6.50 usec
TE                    296.2 K
D1              1.00000000 sec

======== CHANNEL f1 ========
NUC1                      1H
P1                     13.75 usec
PLW1           12.01700020 W
SFO1           400.1324710 MHz

F2 - Processing parameters
SI                    65536
SF             400.1300175 MHz
WDW                      EM
SSB       0
LB                     0.30 Hz
GB        0
PC                     1.00
```

2-hydroxy-5-methoxy-3-nitrobenzaldehyde



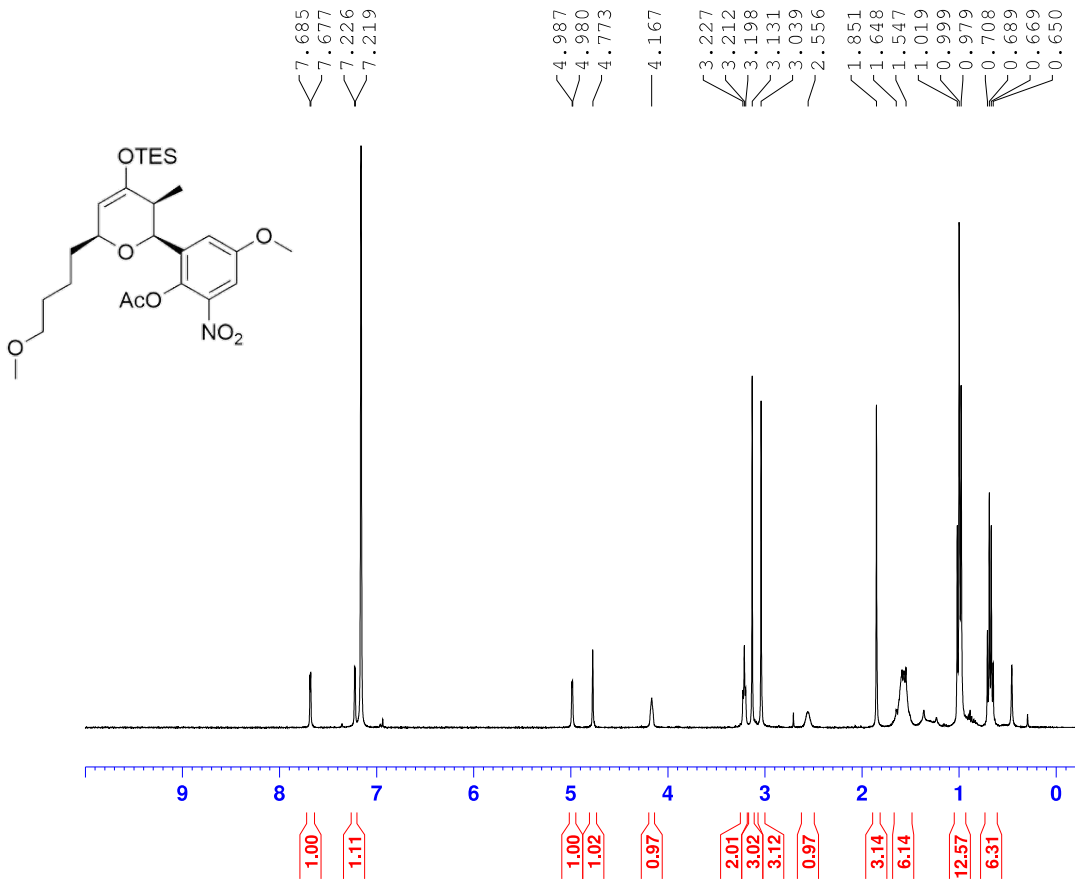

```
Current Data Parameters
NAME        Scott Caplan
EXPNO                  20
PROCNO                  1

F2 - Acquisition Parameters
Date_              20130510
Time                  16.19
INSTRUM               spect
PROBHD    5 mm PABBO BB-
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       32
DS                        2
SWH                8223.685 Hz
FIDRES             0.125483 Hz
AQ                 3.9845889 sec
RG                      161
DW                    60.800 usec
DE                     6.50 usec
TE                    296.4 K
D1              1.00000000 sec

======== CHANNEL f1 ========
NUC1                      1H
P1                     13.75 usec
PLW1           12.01700020 W
SFO1           400.1324710 MHz

F2 - Processing parameters
SI                    65536
SF             400.1300086 MHz
WDW                      EM
SSB       0
LB                     0.30 Hz
GB        0
PC                     1.00
```

p.97 trial 2



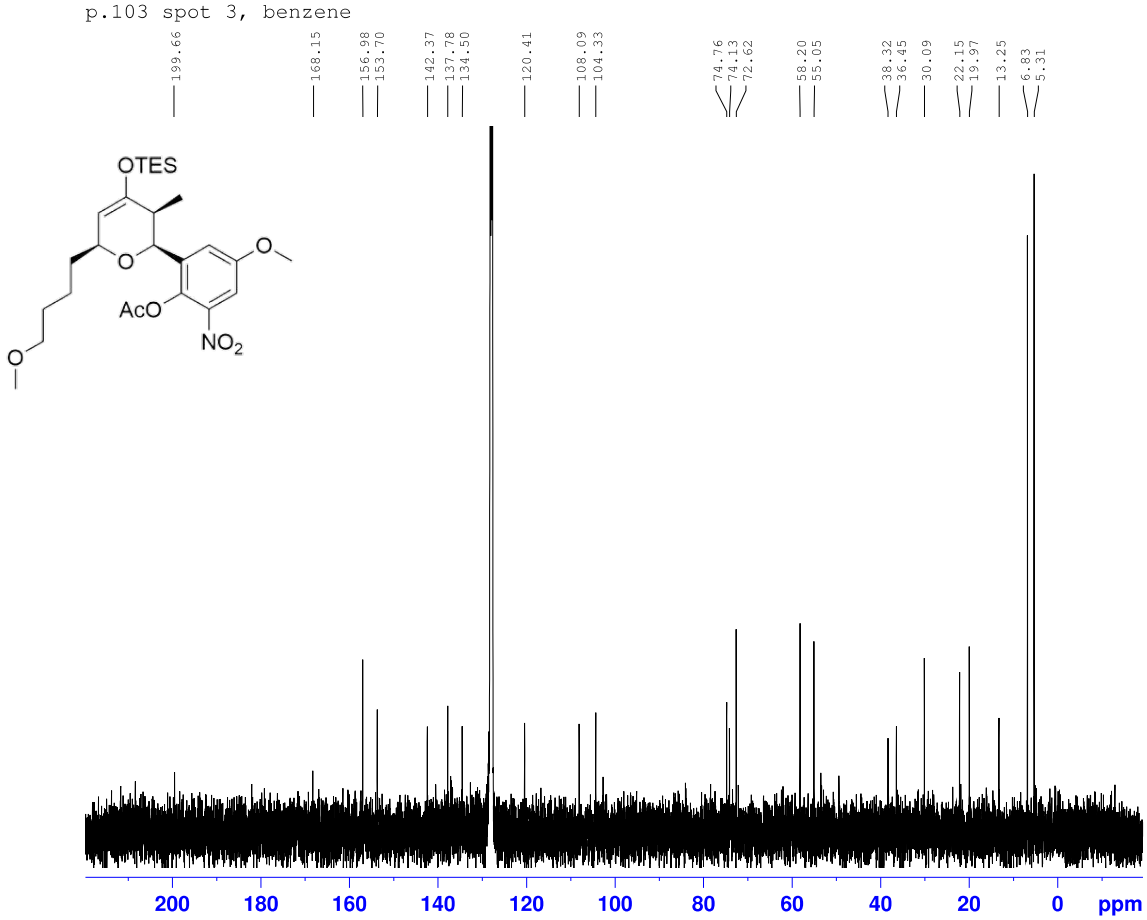

```
Current Data Parameters
NAME      Scott Acetylation
EXPNO                   70
PROCNO                   1

F2 - Acquisition Parameters
Date_           20130923
Time               14.28
INSTRUM            spect
PROBHD    5 mm QNP  1H/1
PULPROG             zg30
TD                 32768
SOLVENT            CDCl3
NS                    32
DS                     2
SWH             6188.119 Hz
FIDRES          0.188846 Hz
AQ             2.6476543 sec
RG                   724
DW                80.800 usec
DE                 6.50 usec
TE                -924.1 K
D1            1.00000000 sec

======== CHANNEL f1 ========
NUC1                  1H
P1                 12.71 usec
PLW1         18.19700050 W
SFO1         300.2318540 MHz

F2 - Processing parameters
SI                 32768
SF           300.2300106 MHz
WDW                   EM
SSB       0
LB                 0.10 Hz
GB        0
PC                 1.00
```

p.103 spot 3



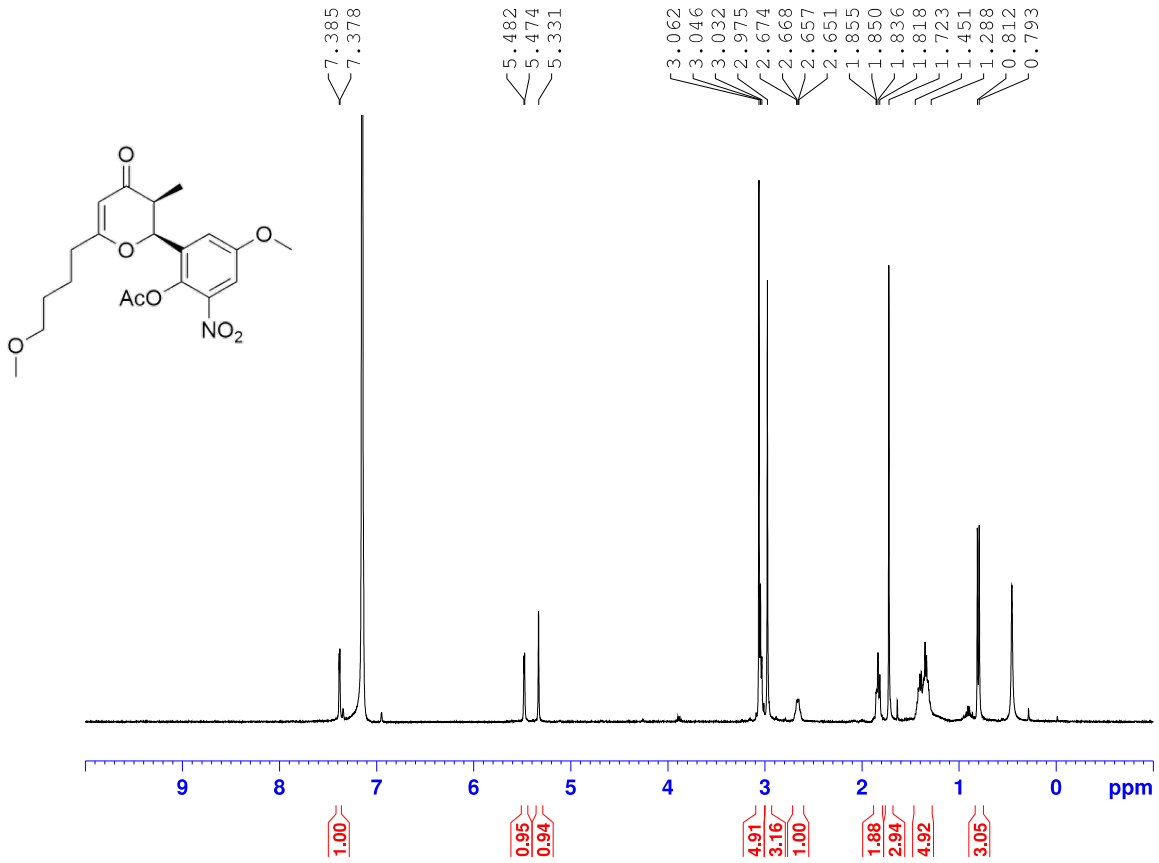

```
Current Data Parameters
NAME            Scott HDA
EXPNO                 100
PROCNO                  1

F2 - Acquisition Parameters
Date_           20131002
Time                21.20
INSTRUM             spect
PROBHD    5 mm PABBO BB-
PULPROG              zg30
TD                  65536
SOLVENT              C6D6
NS                     16
DS                      2
SWH              8223.685 Hz
FIDRES           0.125483 Hz
AQ               3.9845889 sec
RG                   80.6
DW                60.800 usec
DE                 6.50 usec
TE                296.6 K
D1             1.00000000 sec

======== CHANNEL f1 ========
NUC1                   1H
P1                  13.75 usec
PLW1         12.01700020 W
SFO1         400.1324710 MHz

F2 - Processing parameters
SI                  65536
SF           400.1299960 MHz
WDW                    EM
SSB       0
LB                  0.30 Hz
GB        0
PC                  1.00
```

p.103 spot 3, benzene



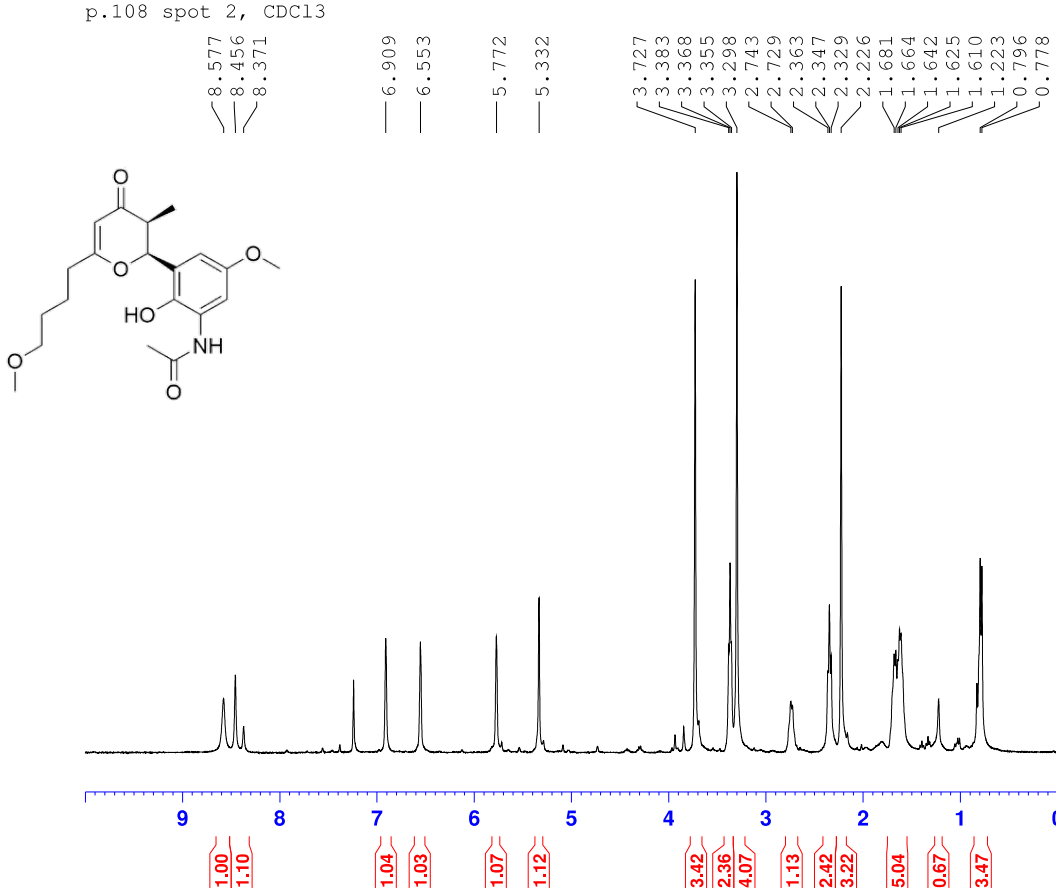

```
Current Data Parameters
NAME            Scott HDA
EXPNO                  95
PROCNO                  1

F2 - Acquisition Parameters
Date_           20131002
Time                10.28
INSTRUM             spect
PROBHD    5 mm PABBO BB-
PULPROG           zgpg30
TD                  65536
SOLVENT              C6D6
NS                    250
DS                      4
SWH             24038.461 Hz
FIDRES           0.366798 Hz
AQ               1.3631488 sec
RG                    203
DW                20.800 usec
DE                 6.50 usec
TE                297.0 K
D1             2.00000000 sec
D11            0.03000000 sec

======== CHANNEL f1 ========
NUC1                  13C
P1                  10.00 usec
PLW1         56.13299942 W
SFO1         100.6228293 MHz

======== CHANNEL f2 ========
CPDPRG[2          waltz16
NUC2                   1H
PCPD2               90.00 usec
PLW2         12.01700020 W
PLW12         0.29076999 W
PLW13     0 W
SFO2         400.1316005 MHz

F2 - Processing parameters
SI                  32768
SF           100.6127469 MHz
WDW                    EM
SSB       0
LB                  1.00 Hz
GB        0
PC                  1.40
```

p.105 product



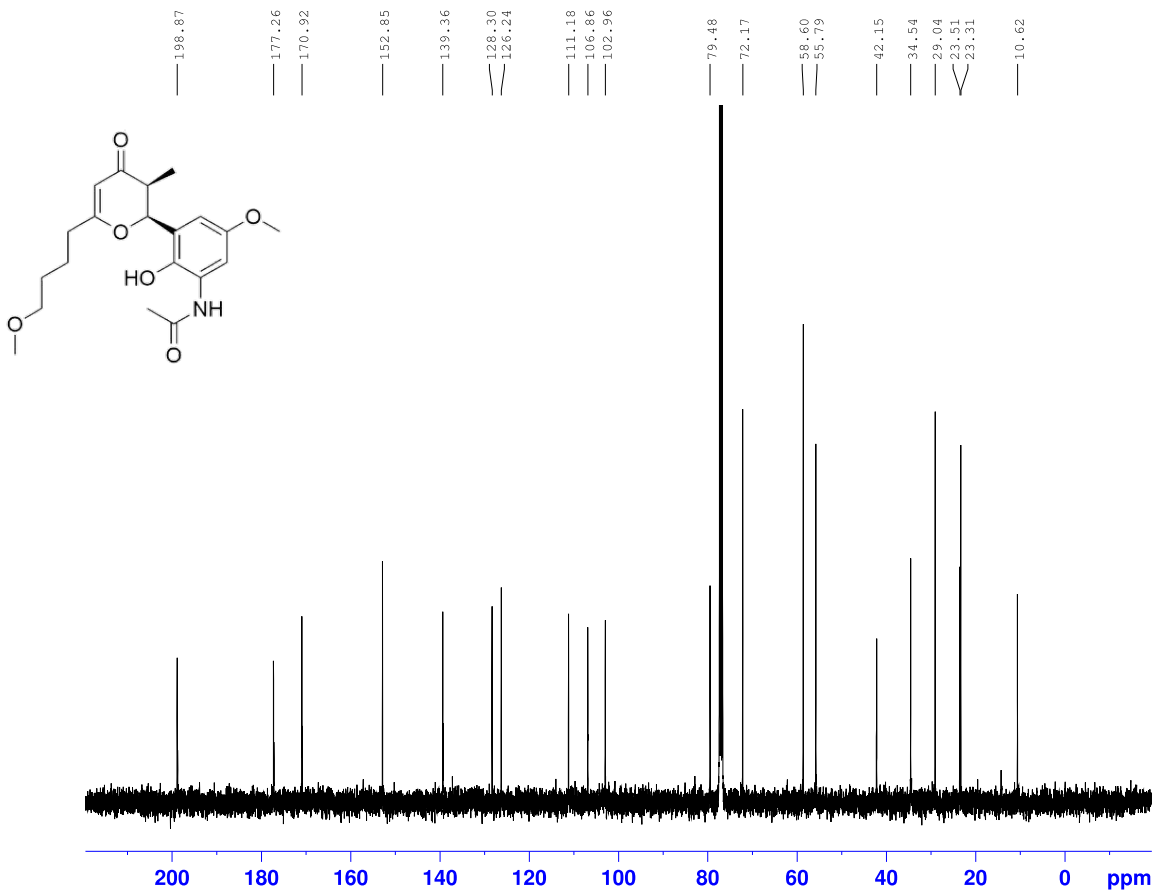

```
Current Data Parameters
NAME            Scott DDQ
EXPNO                  50
PROCNO                  1

F2 - Acquisition Parameters
Date_           20131003
Time                18.03
INSTRUM             spect
PROBHD    5 mm PABBO BB-
PULPROG              zg30
TD                  65536
SOLVENT              C6D6
NS                     25
DS                      2
SWH              8223.685 Hz
FIDRES           0.125483 Hz
AQ               3.9845889 sec
RG                    114
DW                 60.800 usec
DE                  6.50 usec
TE                 296.3 K
D1              1.00000000 sec

======== CHANNEL f1 ========
NUC1                   1H
P1                  13.75 usec
PLW1         12.01700020 W
SFO1         400.1324710 MHz

F2 - Processing parameters
SI                  65536
SF           400.1300016 MHz
WDW                    EM
SSB       0
LB                  0.30 Hz
GB        0
PC                  1.00
```

p.108 spot 2, CDCl3

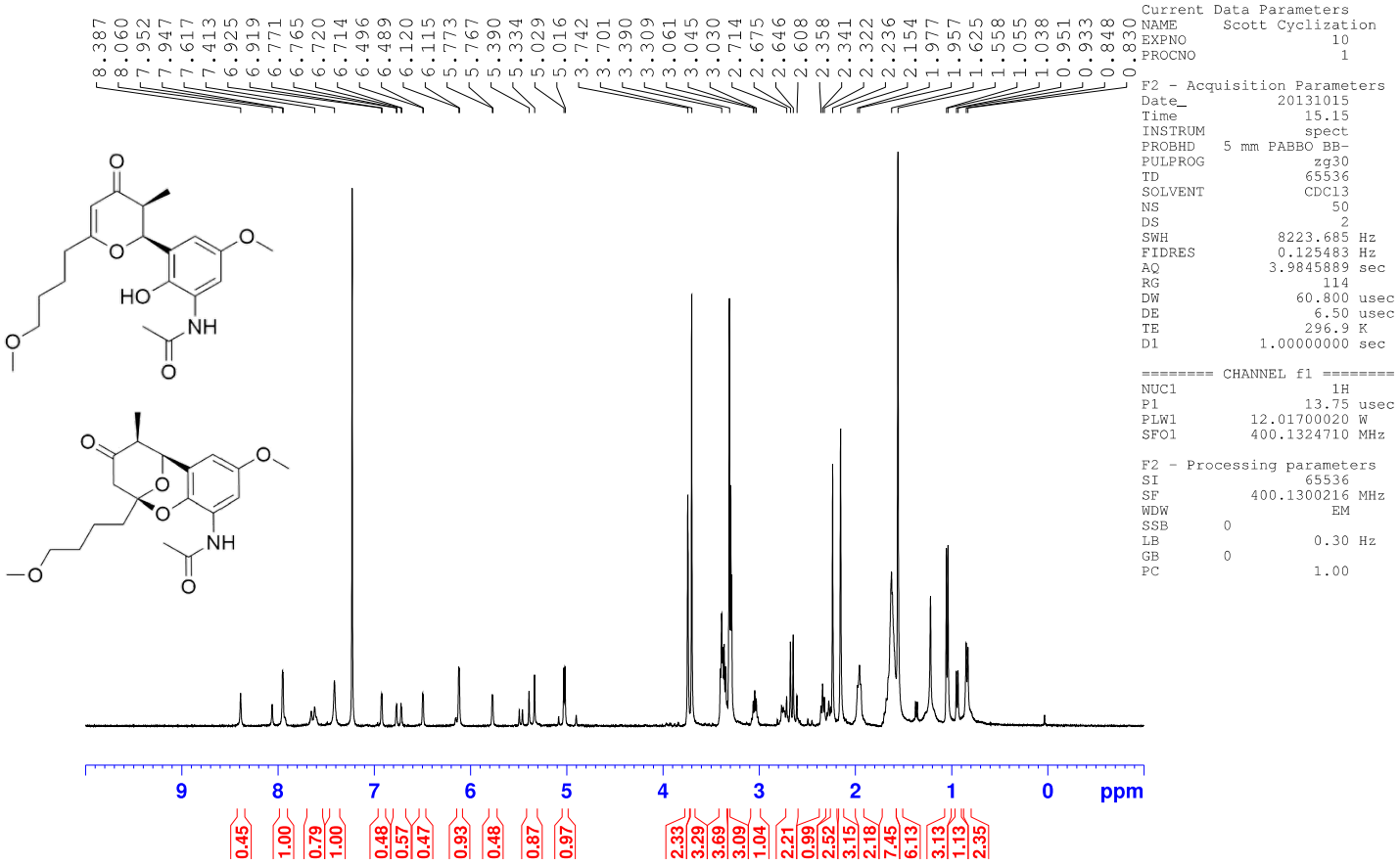



```
Current Data Parameters
NAME      Scott Nitro Reduction
EXPNO                    20
PROCNO                    1

F2 - Acquisition Parameters
Date_           20131010
Time                18.33
INSTRUM             spect
PROBHD   5 mm PABBO BB-
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8223.685 Hz
FIDRES          0.125483 Hz
AQ              3.9845889 sec
RG                    57
DW                60.800 usec
DE                 6.50 usec
TE                296.7 K
D1           1.00000000 sec

======== CHANNEL f1 ========
NUC1                  1H
P1                 13.75 usec
PLW1         12.01700020 W
SFO1         400.1324710 MHz

F2 - Processing parameters
SI                 65536
SF           400.1300187 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

p.108 spot 2, CDCl3

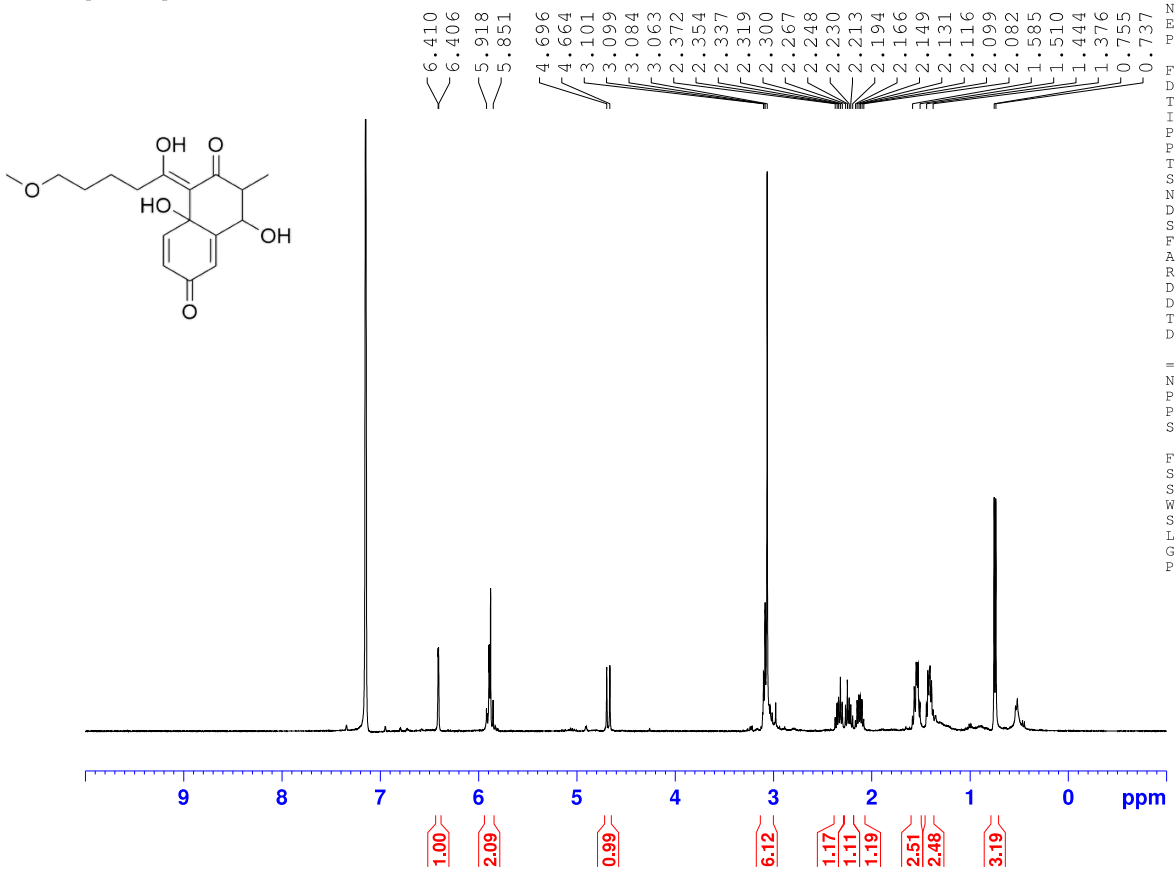



```
Current Data Parameters
NAME      Scott Nitro Reduction
EXPNO                    22
PROCNO                    1

F2 - Acquisition Parameters
Date_           20131011
Time                 3.36
INSTRUM             spect
PROBHD   5 mm PABBO BB-
PULPROG           zgpg30
TD                 65536
SOLVENT            CDCl3
NS                  1024
DS                     4
SWH            24038.461 Hz
FIDRES          0.366798 Hz
AQ              1.3631488 sec
RG                   203
DW                20.800 usec
DE                 6.50 usec
TE                297.3 K
D1           2.00000000 sec
D11          0.03000000 sec

======== CHANNEL f1 ========
NUC1                 13C
P1                10.00 usec
PLW1         56.13299942 W
SFO1         100.6228293 MHz

======== CHANNEL f2 ========
CPDPRG[2         waltz16
NUC2                  1H
PCPD2              90.00 usec
PLW2         12.01700020 W
PLW12         0.29076999 W
PLW13     0 W
SFO2         400.1316005 MHz

F2 - Processing parameters
SI                 32768
SF           100.6127690 MHz
WDW                   EM
SSB       0
LB                 1.00 Hz
GB        0
PC                 1.40
```



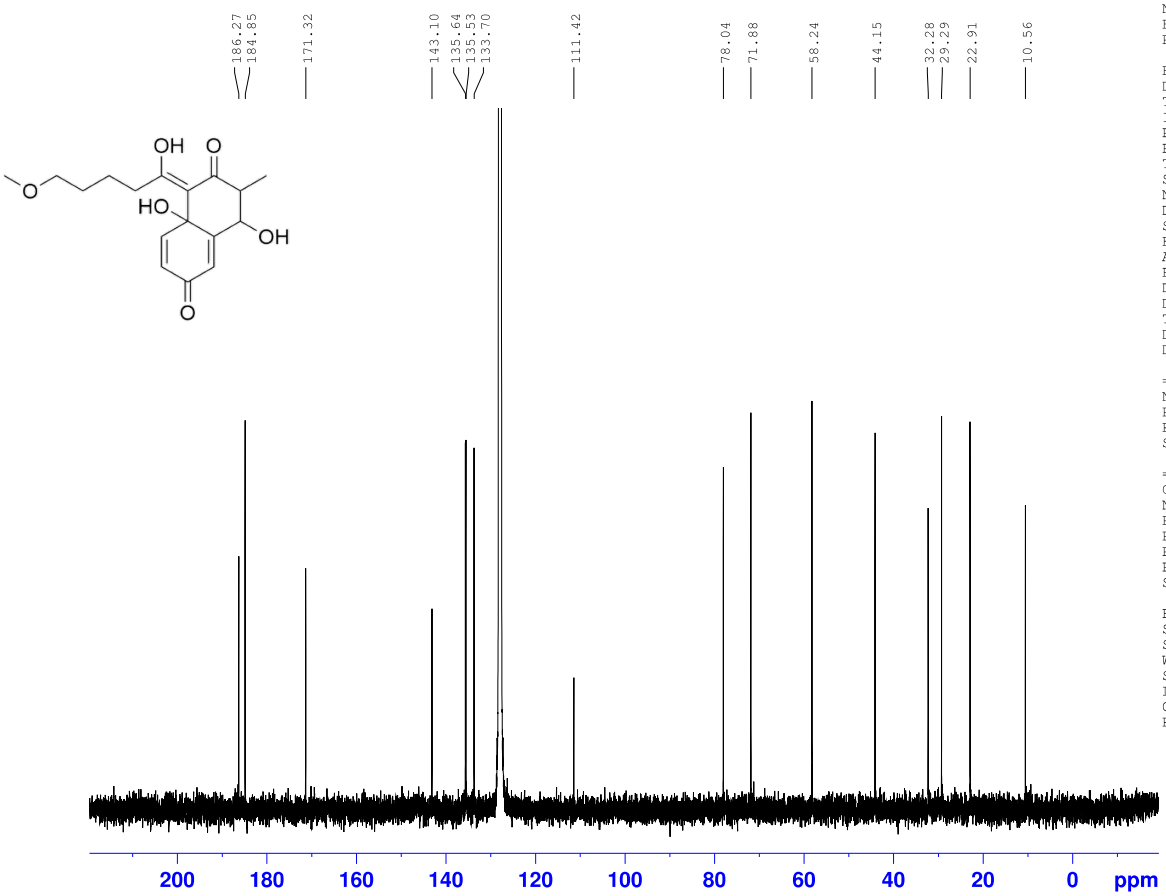

```
Current Data Parameters
NAME      Scott Cyclization
EXPNO                   10
PROCNO                   1

F2 - Acquisition Parameters
Date_             20131015
Time                 15.15
INSTRUM              spect
PROBHD    5 mm PABBO BB-
PULPROG              zg30
TD                  65536
SOLVENT             CDCl3
NS                     50
DS                      2
SWH              8223.685 Hz
FIDRES           0.125483 Hz
AQ               3.9845889 sec
RG                    114
DW                 60.800 usec
DE                  6.50 usec
TE                 296.9 K
D1              1.00000000 sec

======== CHANNEL f1 ========
NUC1                   1H
P1                  13.75 usec
PLW1          12.01700020 W
SFO1          400.1324710 MHz

F2 - Processing parameters
SI                  65536
SF            400.1300216 MHz
WDW                    EM
SSB       0
LB                  0.30 Hz
GB        0
PC                  1.00
```

p.93 spot 2a

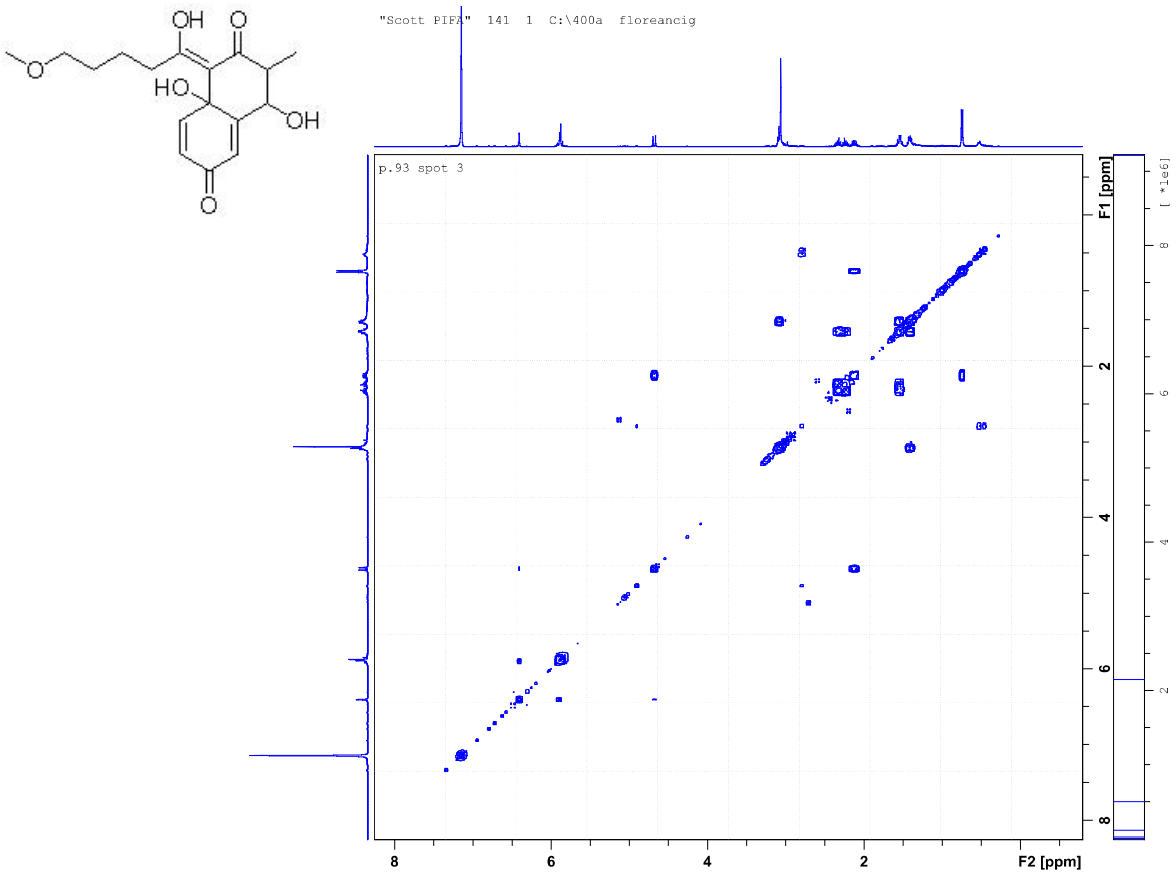


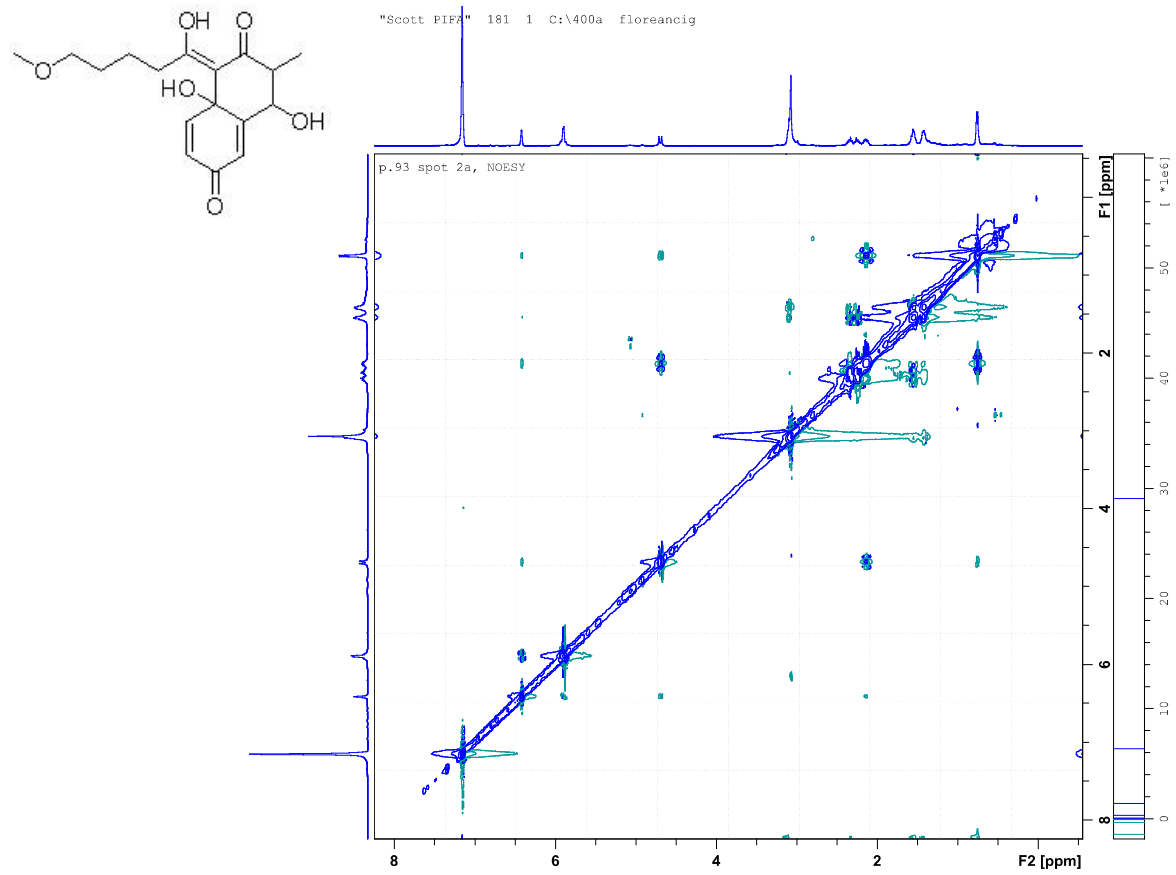

```
Current Data Parameters
NAME          Scott PIFA
EXPNO                140
PROCNO                 1

F2 - Acquisition Parameters
Date_           20130912
Time               17.33
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG            zg30
TD                65536
SOLVENT            C6D6
NS                   32
DS                    2
SWH             8223.685 Hz
FIDRES          0.125483 Hz
AQ              3.9845889 sec
RG                  101
DW                60.800 usec
DE                 6.50 usec
TE                294.9 K
D1             1.00000000 sec

======== CHANNEL f1 ========
NUC1                1H
P1                13.75 usec
PLW1         12.01700020 W
SFO1        400.1324710 MHz

F2 - Processing parameters
SI                 65536
SF          400.1300019 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

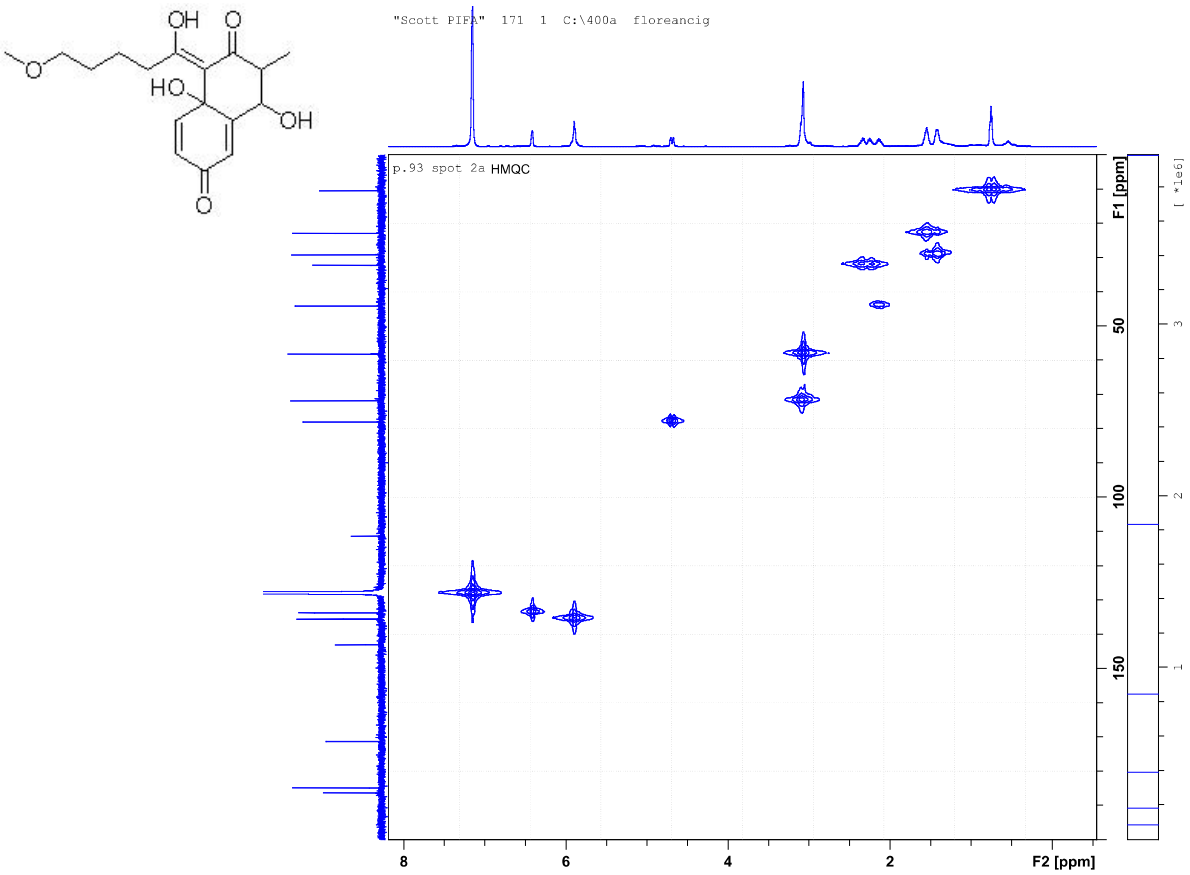
p.93 spot 2a

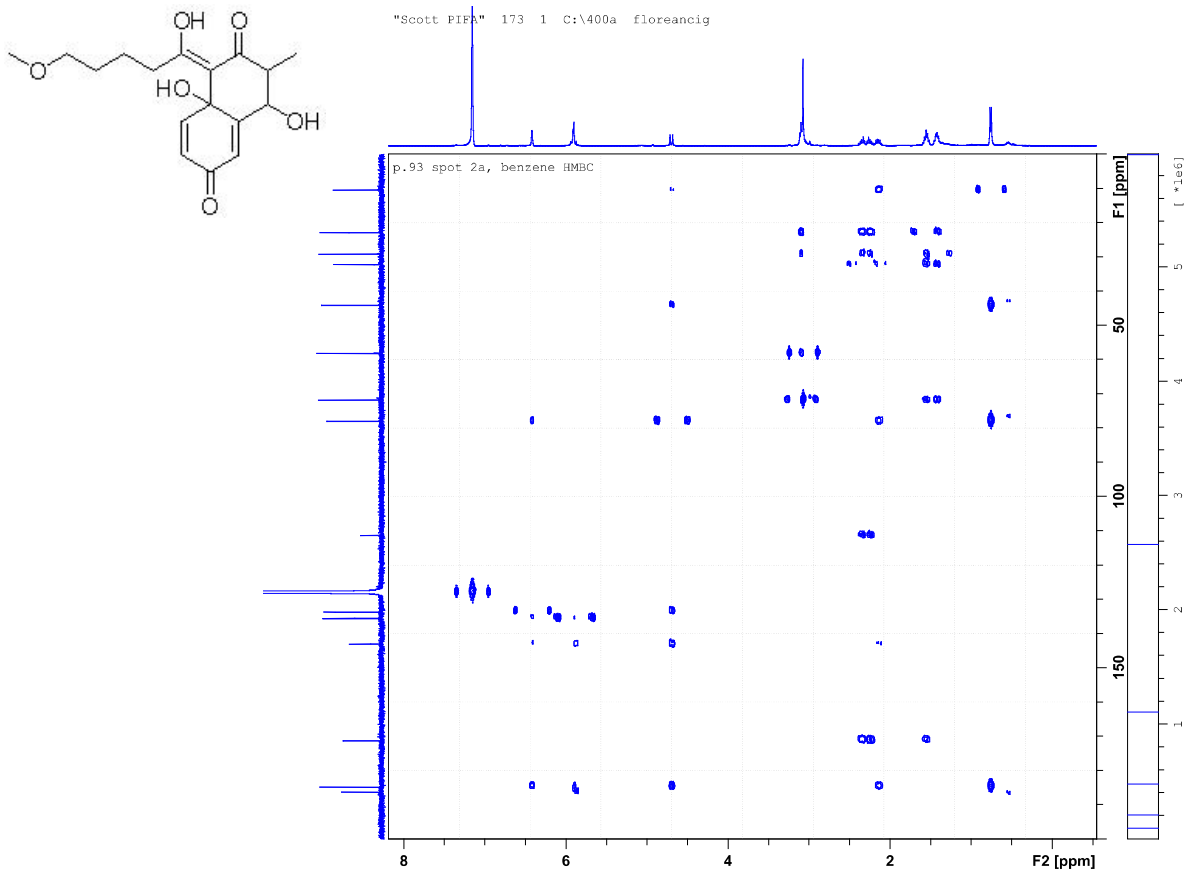



```
Current Data Parameters
NAME          Scott PIFA
EXPNO                160
PROCNO                 1

F2 - Acquisition Parameters
Date_           20130913
Time               23.58
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG          zgpg30
TD                65536
SOLVENT            C6D6
NS                 4000
DS                    4
SWH            24038.461 Hz
FIDRES          0.366798 Hz
AQ              1.3631488 sec
RG                  203
DW                20.800 usec
DE                 6.50 usec
TE                297.1 K
D1             2.00000000 sec
D11            0.03000000 sec

======== CHANNEL f1 ========
NUC1                13C
P1                10.00 usec
PLW1         56.13299942 W
SFO1        100.6228293 MHz

======== CHANNEL f2 ========
CPDPRG[2          waltz16
NUC2                1H
PCPD2             90.00 usec
PLW2         12.01700020 W
PLW12         0.29076999 W
PLW13     0 W
SFO2        400.1316005 MHz

F2 - Processing parameters
SI                 32768
SF          100.6127469 MHz
WDW                   EM
SSB       0
LB                 1.00 Hz
GB        0
PC                 1.40
```

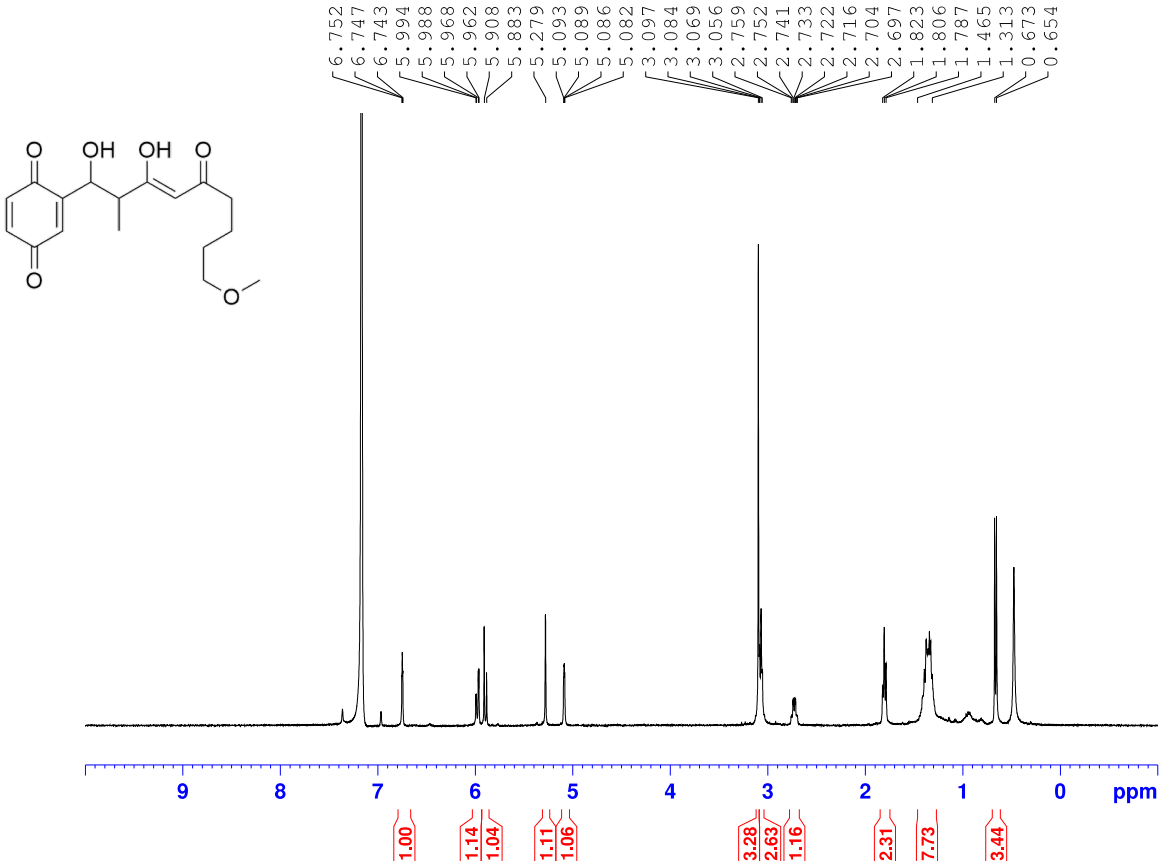

"Scott PIFA" 141 1 C:\400a floreancig
p.93 spot 3
F1 [ppm]
F2 [ppm]
8
6
4
2
[*1e6]


"Scott PIFA" 181 1 C:\400a floreancig
p.93 spot 2a, NOESY
F1 [ppm]
F2 [ppm]
8
6
4
2
[*1e6]

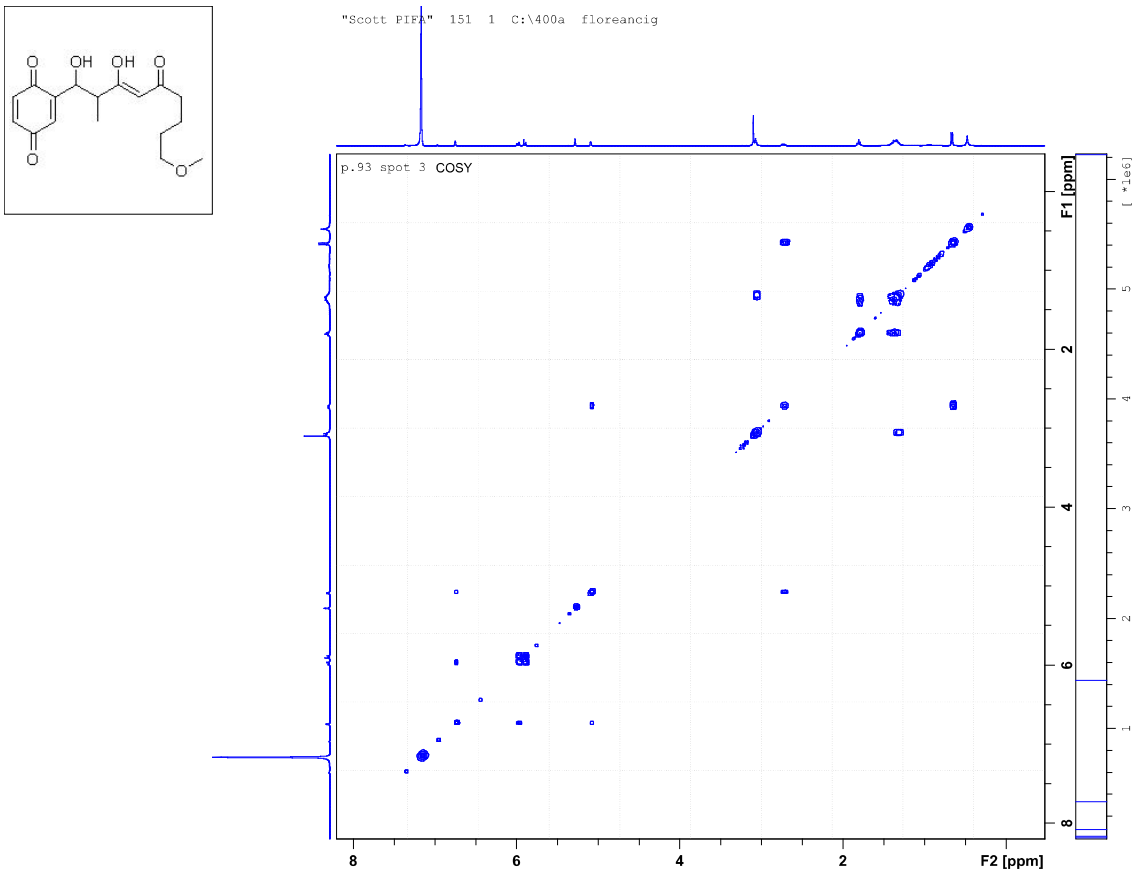

"Scott PIPA" 171 1 C:\400a floreancig
p.93 spot 2a HMQC
F1 [ppm]
F2 [ppm]
8
6
4
2
50
100
150
[*1e6]


"Scott PIPA" 173 1 C:\400a floreancig
p.93 spot 2a, benzene HMBC
F1 [ppm]
F2 [ppm]
8
6
4
2
50
100
150
[*1e6]

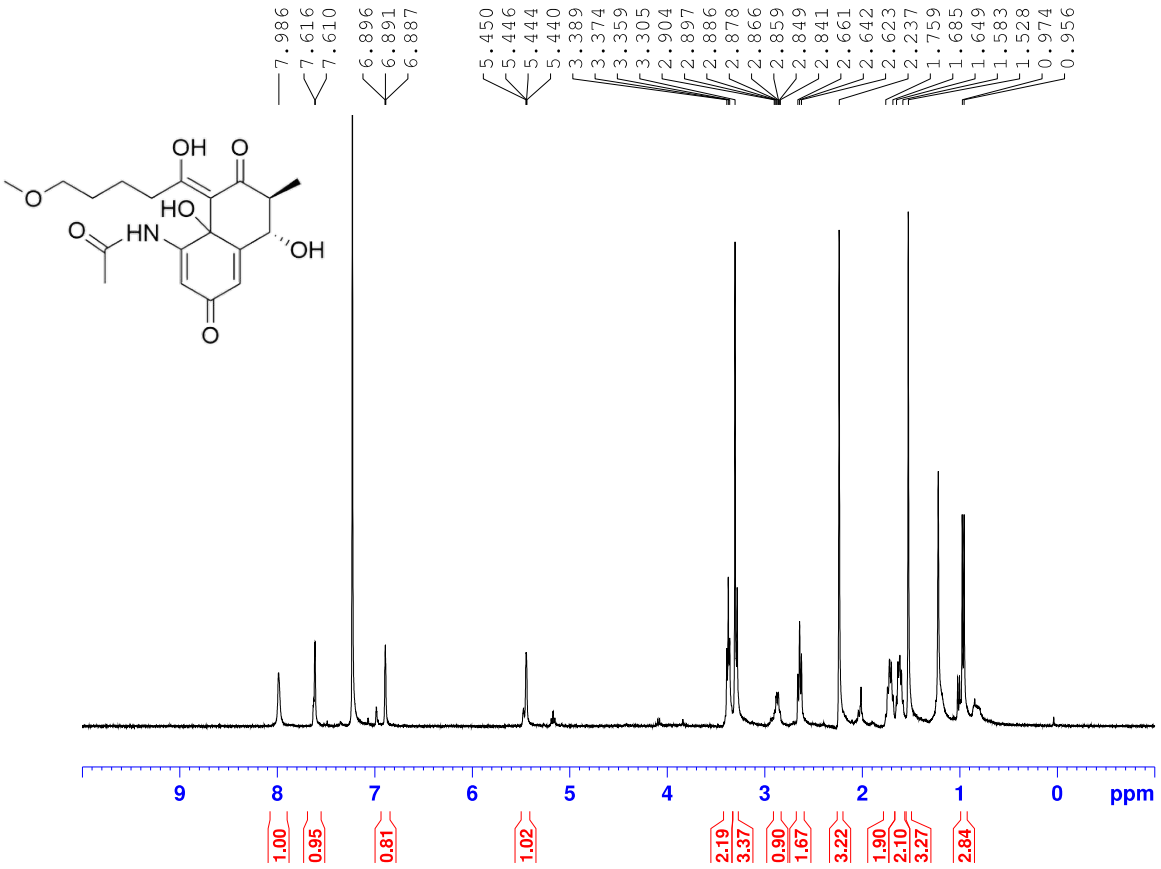
p.93 spot 3




```
Current Data Parameters
NAME          Scott PIFA
EXPNO                150
PROCNO                 1

F2 - Acquisition Parameters
Date_           20130912
Time               17.56
INSTRUM            spect
PROBHD    5 mm PABBO BB-
PULPROG             zg30
TD                 65536
SOLVENT             C6D6
NS                    50
DS                     2
SWH             8223.685 Hz
FIDRES          0.125483 Hz
AQ              3.9845889 sec
RG                   114
DW                60.800 usec
DE                 6.50 usec
TE                294.7 K
D1             1.00000000 sec

======== CHANNEL f1 ========
NUC1                  1H
P1                 13.75 usec
PLW1         12.01700020 W
SFO1         400.1324710 MHz

F2 - Processing parameters
SI                 65536
SF          400.1299953 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```



p.111 spot 2



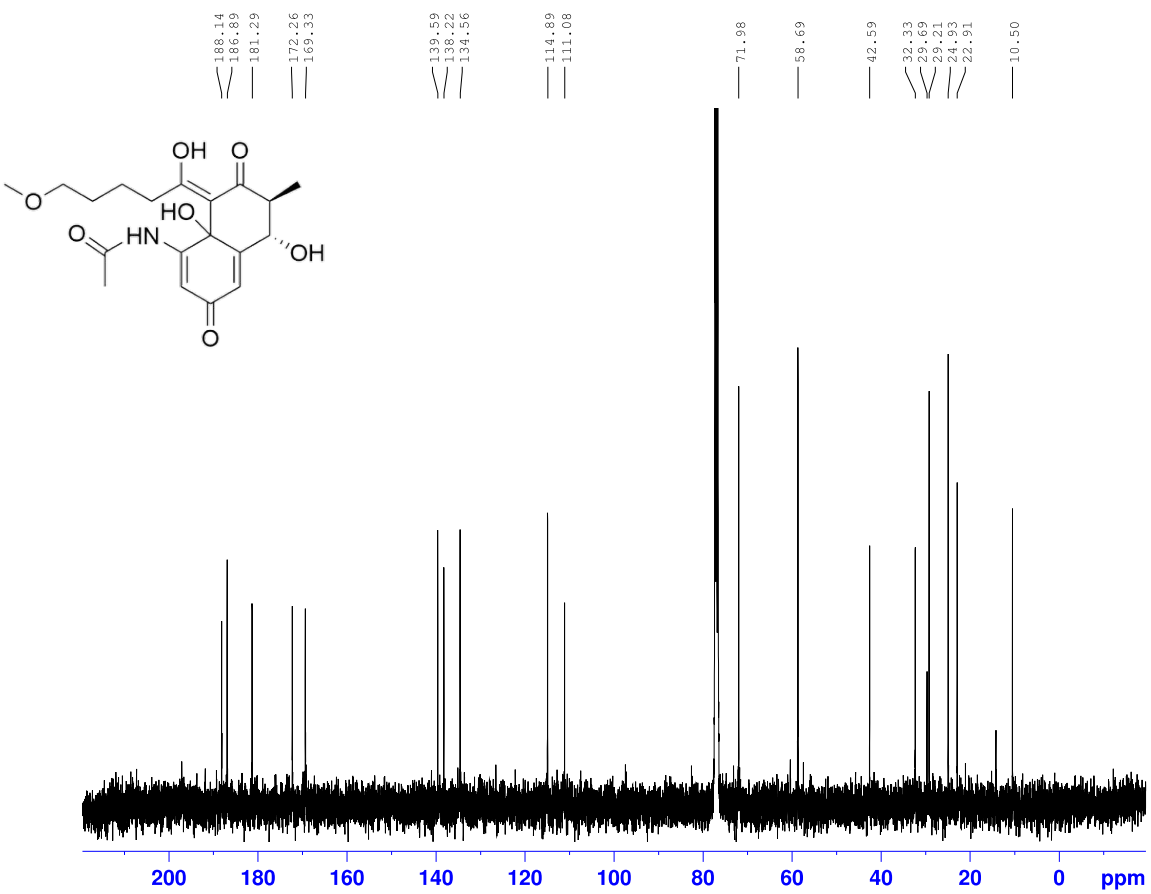
Current Data Parameters
NAME Scott PIFA
EXPNO 190
PROCNO 1

F2 - Acquisition Parameters
Date_ 20131015
Time 18.17
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 40
DS 2
SWH 8223.685 Hz
FIDRES 0.125483 Hz
AQ 3.9845889 sec
RG 144
DW 60.800 usec
DE 6.50 usec
TE 297.2 K
D1 1.00000000 sec

======== CHANNEL f1 ========
NUC1 1H
P1 13.75 usec
PLW1 12.01700020 W
SFO1 400.1324710 MHz

F2 - Processing parameters
SI 65536
SF 400.1300214 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

p.111 spot 1-2



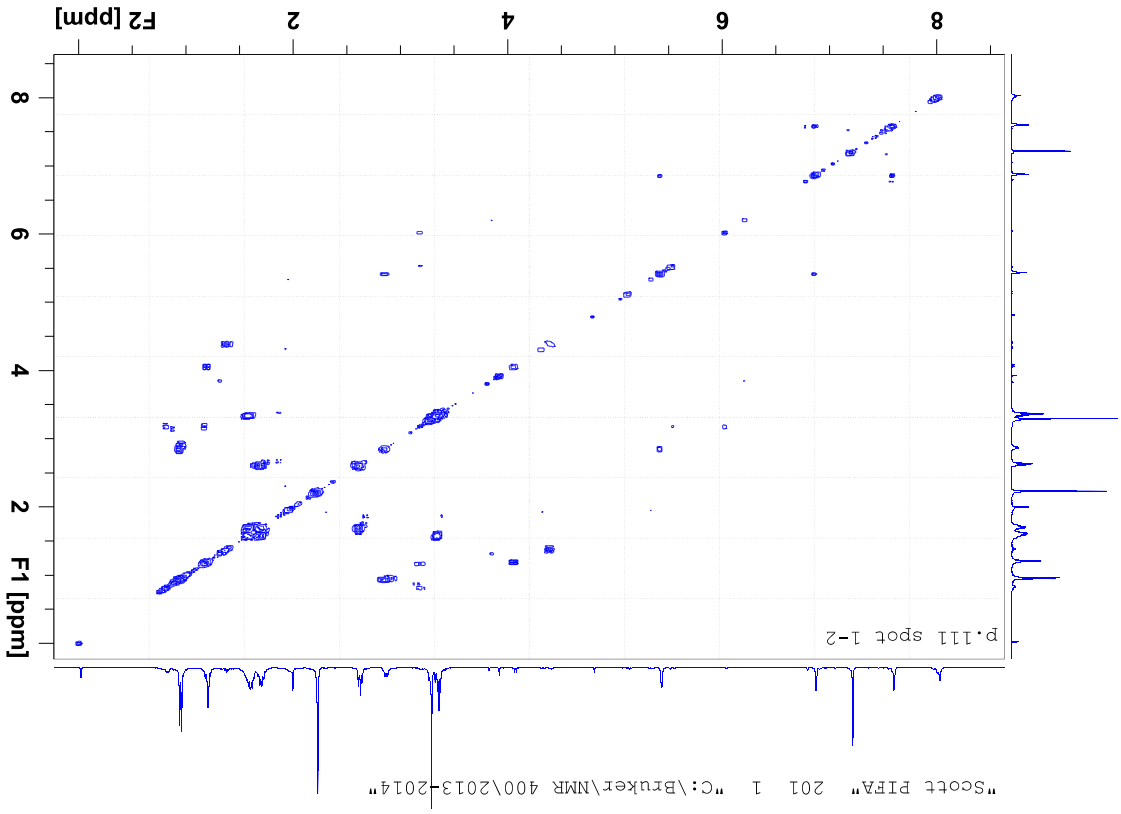
Current Data Parameters
NAME Scott PIFA
EXPNO 202
PROCNO 1

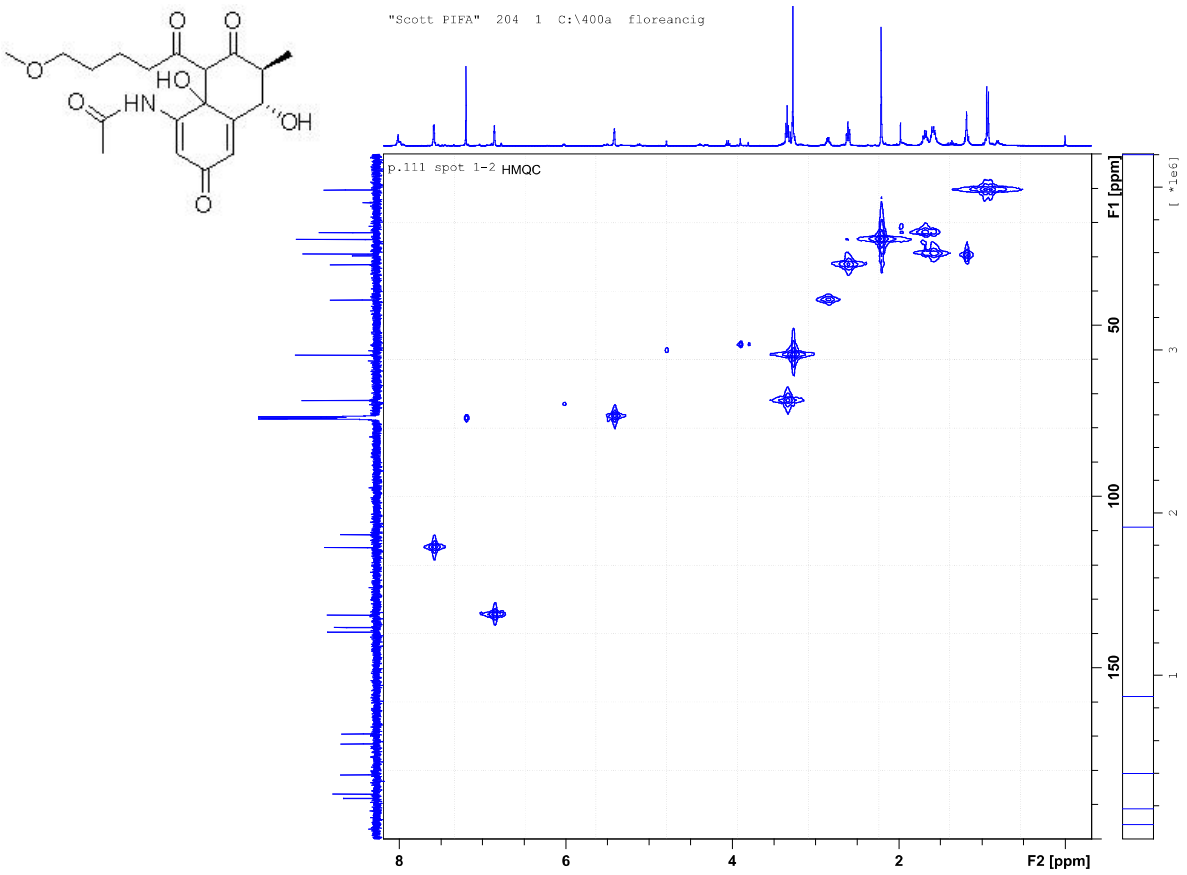
F2 - Acquisition Parameters
Date_ 20131016
Time 6.09
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 4000
DS 4
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3631488 sec
RG 203
DW 20.800 usec
DE 6.50 usec
TE 298.6 K
D1 2.00000000 sec
D11 0.03000000 sec

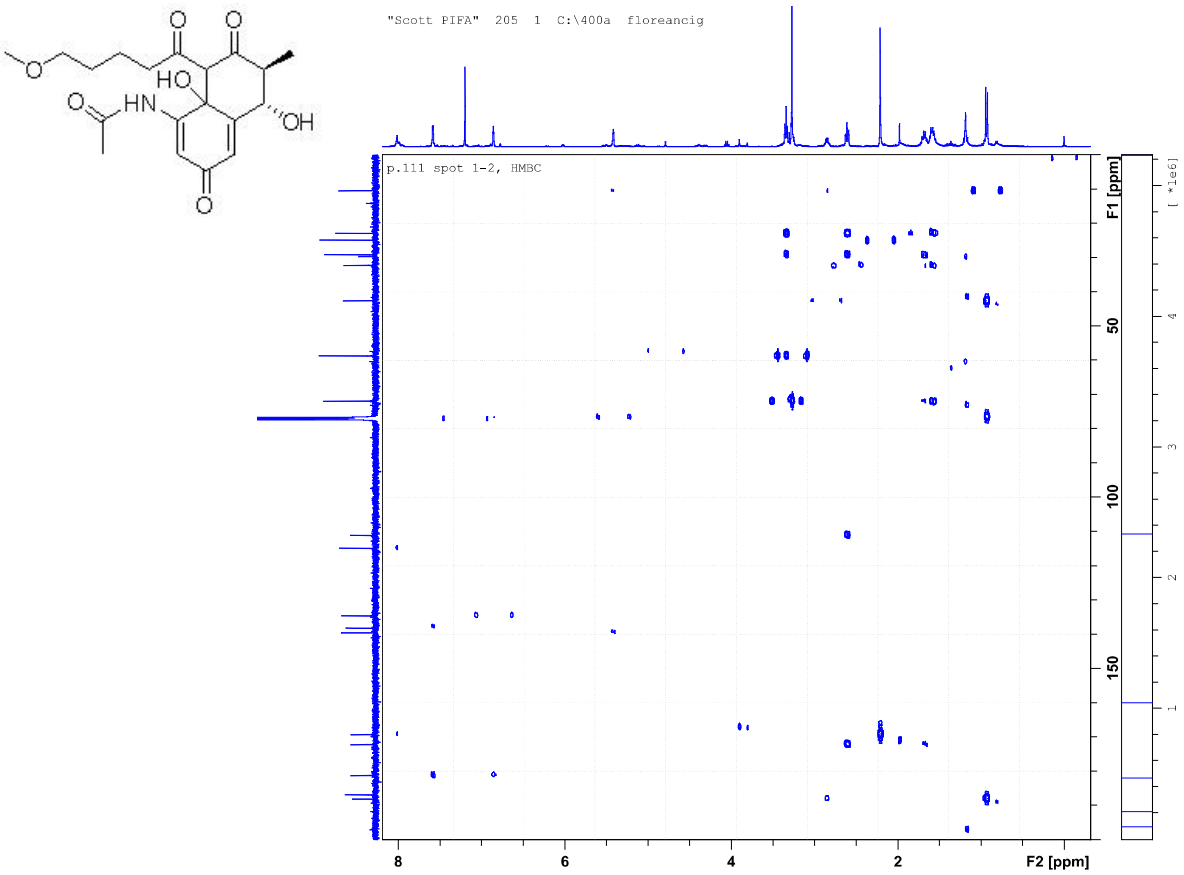
======== CHANNEL f1 ========
NUC1 13C
P1 10.00 usec
PLW1 56.13299942 W
SFO1 100.6228293 MHz

======== CHANNEL f2 ========
CPDPRG[2 waltz16
NUC2 1H
PCPD2 90.00 usec
PLW2 12.01700020 W
PLW12 0.29076999 W
PLW13 0 W
SFO2 400.1316005 MHz

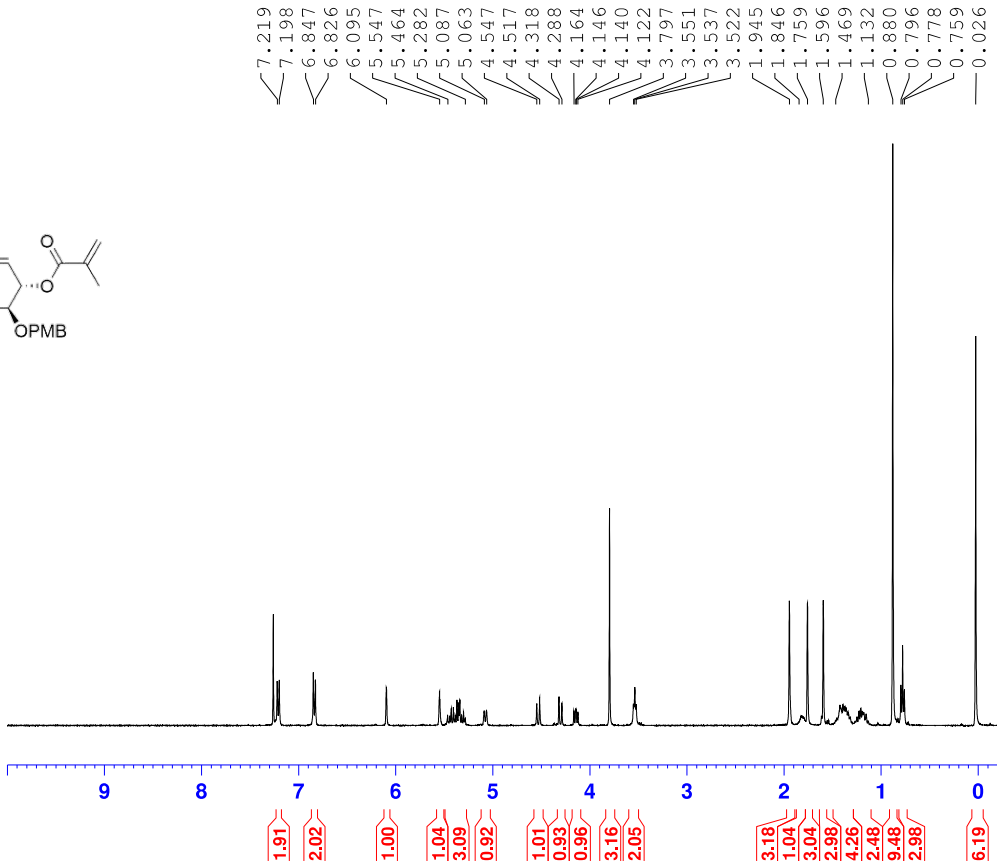
F2 - Processing parameters
SI 32768
SF 100.6127690 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40


F2 [ppm]
F1 [ppm]
p.111 spot 1-2
"Scott PIFA" 201 1 "C:\Bruker\NMR 400\2013-2014"


"Scott PIFA" 204 1 C:\400a floreancig
p.111 spot 1-2 HMQC
F1 [ppm]
F2 [ppm]
HO
HN
OH

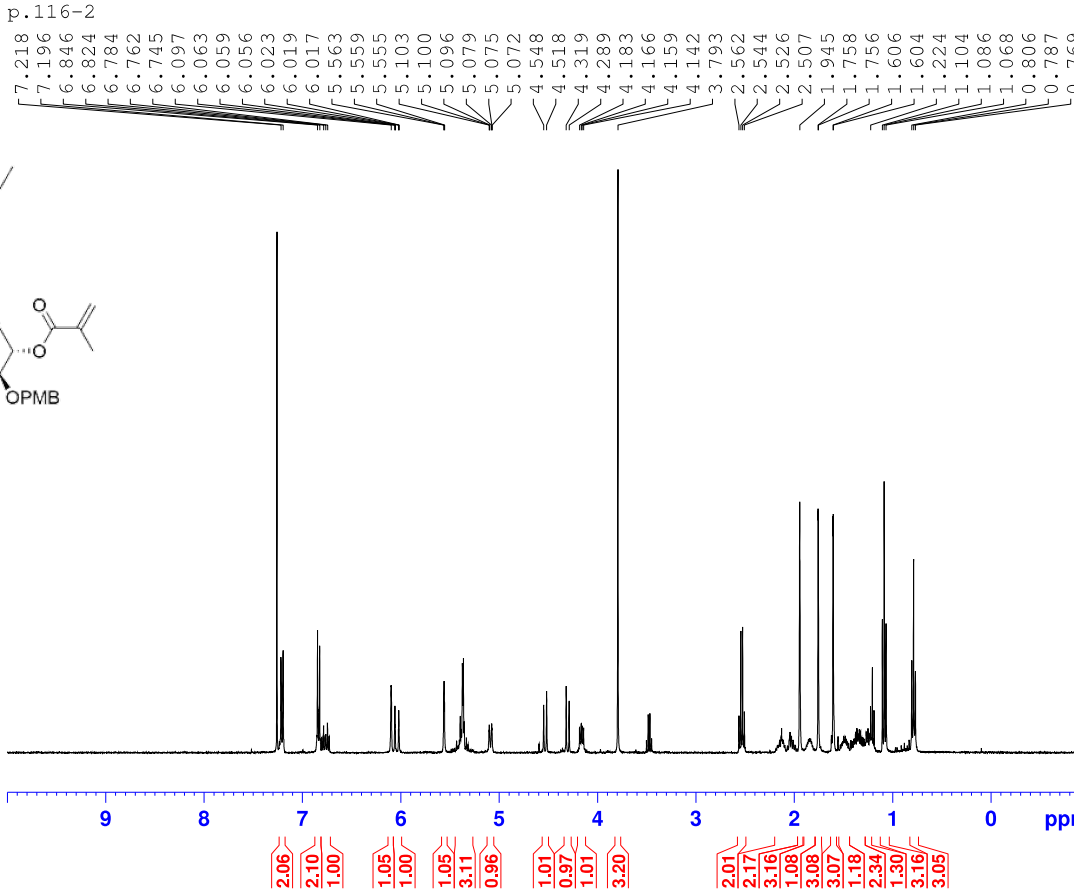

"Scott PIFA" 205 1 C:\400a floreancig
p.111 spot 1-2, HMBC
F1 [ppm]
F2 [ppm]
8
6
4
2
50
100
150
[*1e6]

p.105-2 major diast.



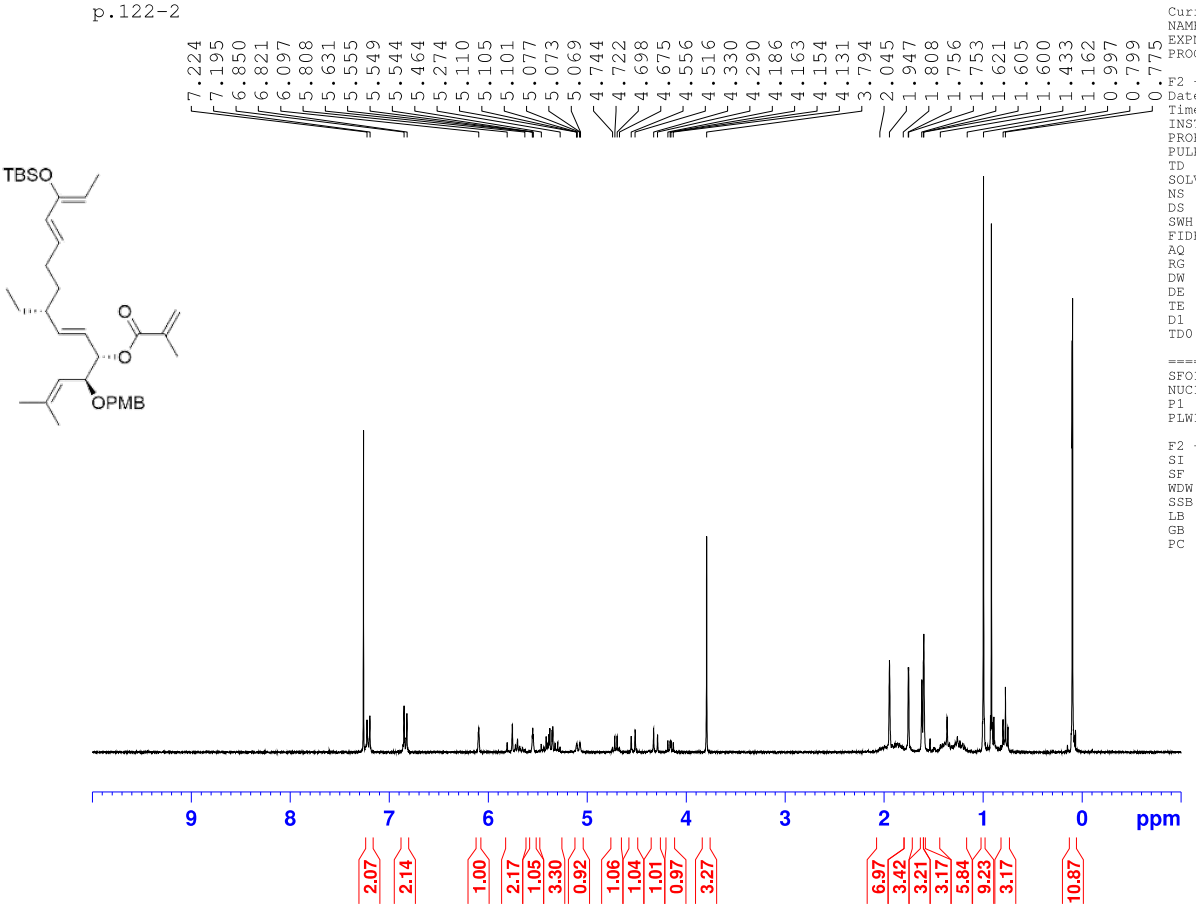

```
Current Data Parameters
NAME      Scott Methacryloyl
EXPNO                     90
PROCNO                     1

F2 - Acquisition Parameters
Date_              20150226
Time                  17.52
INSTRUM               spect
PROBHD    5 mm PABBO BB-
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH                8223.685 Hz
FIDRES            0.125483 Hz
AQ                3.9845889 sec
RG                     90.5
DW                  60.800 usec
DE                   6.50 usec
TE                  695.7 K
D1              1.00000000 sec

======== CHANNEL f1 ========
NUC1                      1H
P1                     13.75 usec
PLW1           12.01700020 W
SFO1           400.1324710 MHz

F2 - Processing parameters
SI                    65536
SF             400.1300101 MHz
WDW                      EM
SSB       0
LB                    0.30 Hz
GB        0
PC                    1.00
```

p.116-2



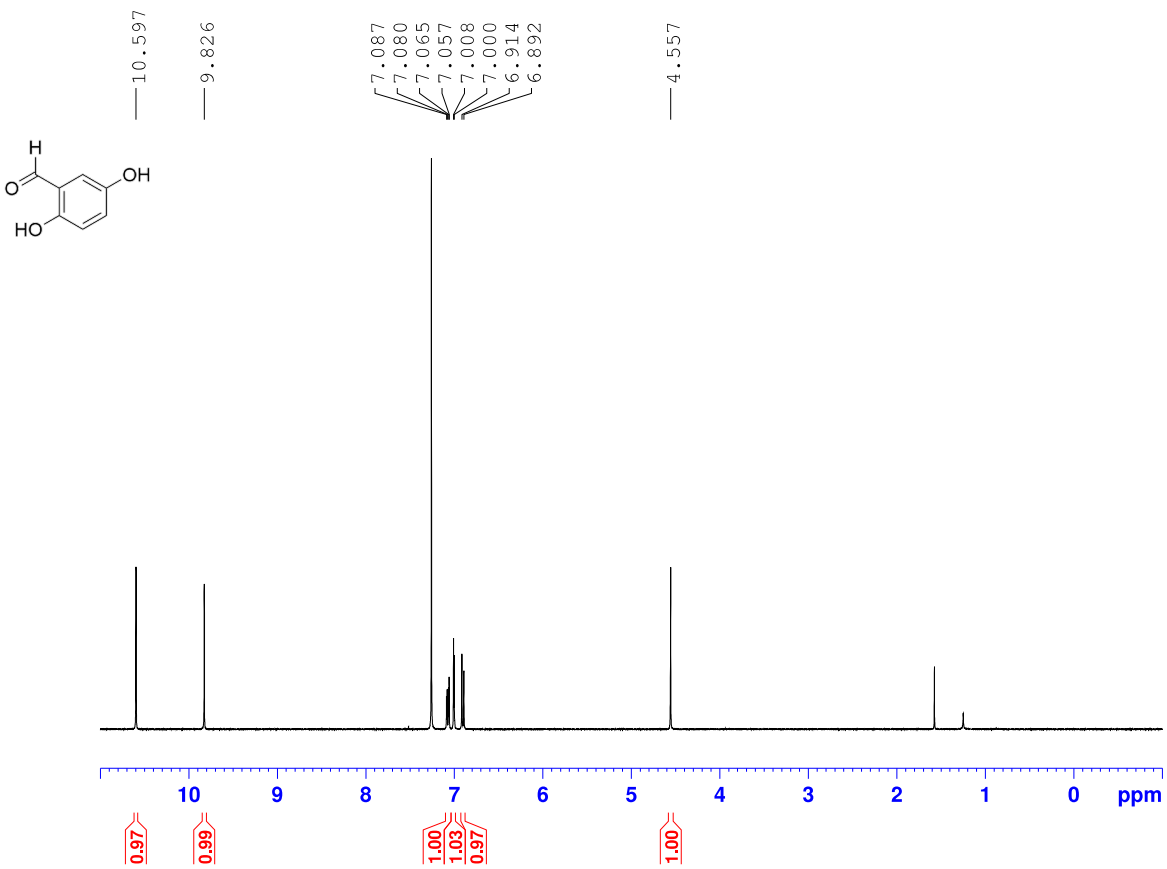

```
Current Data Parameters
NAME           Scott HWE
EXPNO                 20
PROCNO                 1

F2 - Acquisition Parameters
Date_              20150309
Time                  16.13
INSTRUM               spect
PROBHD    5 mm PABBO BB-
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH                8223.685 Hz
FIDRES            0.125483 Hz
AQ                3.9845889 sec
RG                     128
DW                  60.800 usec
DE                   6.50 usec
TE                  91.4 K
D1              1.00000000 sec

======== CHANNEL f1 ========
NUC1                      1H
P1                     13.75 usec
PLW1           12.01700020 W
SFO1           400.1324710 MHz

F2 - Processing parameters
SI                    65536
SF             400.1300111 MHz
WDW                      EM
SSB       0
LB                    0.30 Hz
GB        0
PC                    1.00
```

p.122-2



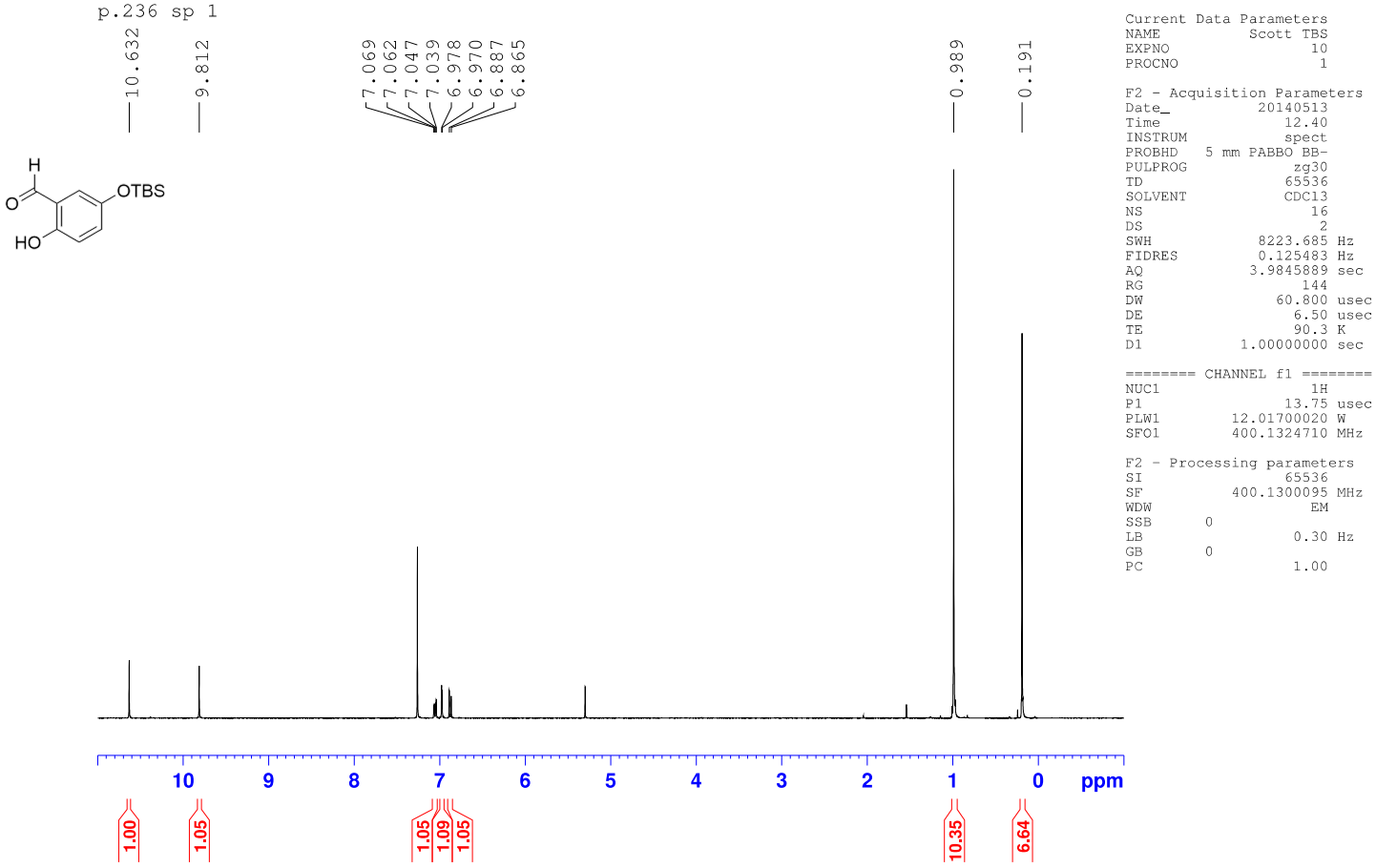

```
Current Data Parameters
NAME      Scott Silyl Enol Ether
EXPNO                 10
PROCNO                 1

F2 - Acquisition Parameters
Date_           20150319
Time              17.39
INSTRUM           spect
PROBHD   5 mm QNP  1H/1
PULPROG           zg30
TD               32768
SOLVENT           CDCl3
NS                   16
DS                    2
SWH           6188.119 Hz
FIDRES        0.188846 Hz
AQ            2.6476543 sec
RG                 322
DW              80.800 usec
DE               6.50 usec
TE              -928.3 K
D1           1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1        300.2318540 MHz
NUC1                  1H
P1                12.71 usec
PLW1        18.19700050 W

F2 - Processing parameters
SI                32768
SF          300.2300090 MHz
WDW                  EM
SSB       0
LB                0.10 Hz
GB        0
PC                1.00
```

p.233



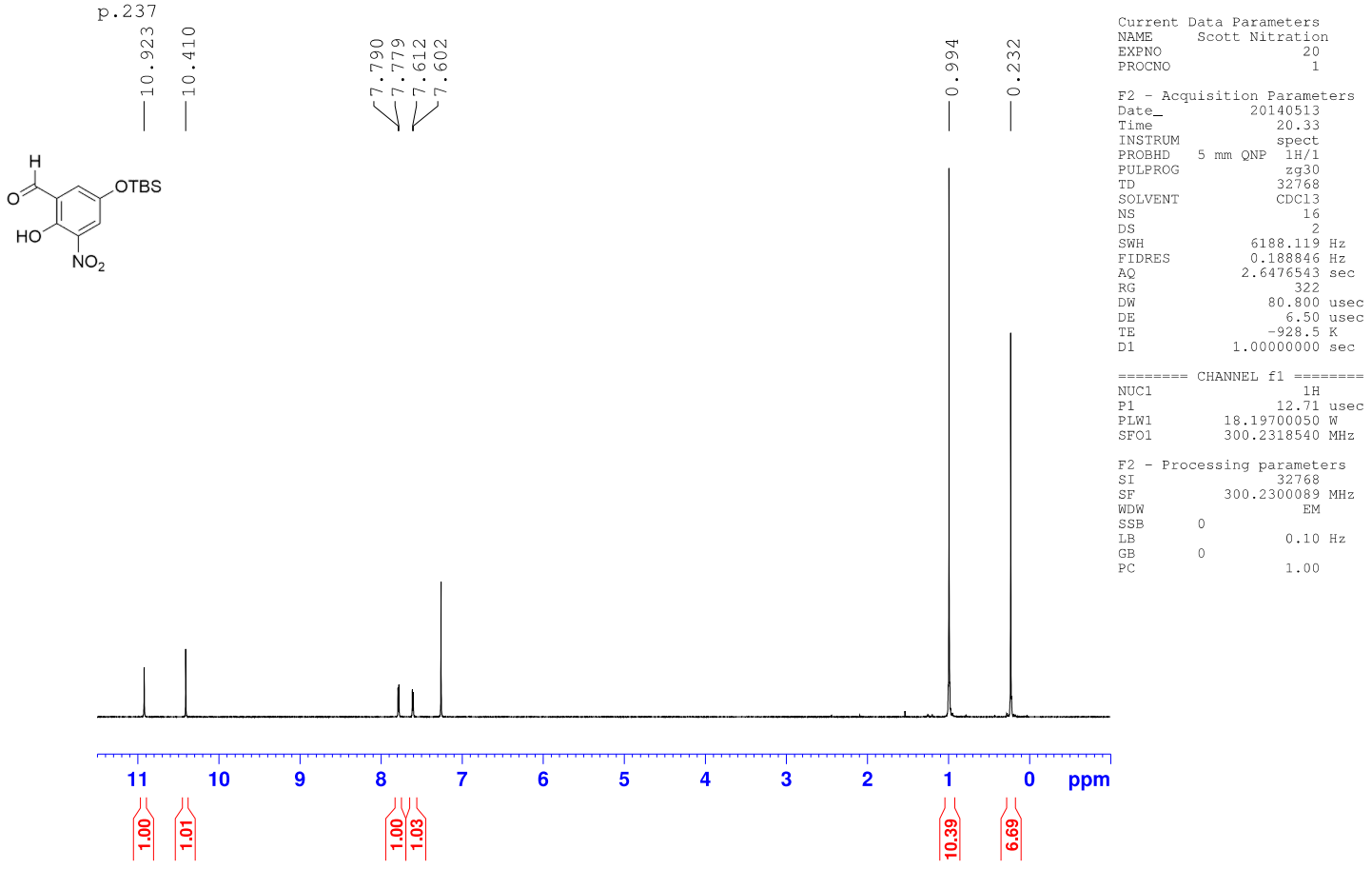

```
Current Data Parameters
NAME          Scott BBr3
EXPNO                 10
PROCNO                 1

F2 - Acquisition Parameters
Date_           20140509
Time              17.22
INSTRUM           spect
PROBHD   5 mm PABBO BB-
PULPROG           zg30
TD               65536
SOLVENT           CDCl3
NS                   16
DS                    2
SWH           8223.685 Hz
FIDRES        0.125483 Hz
AQ            3.9845889 sec
RG                 181
DW              60.800 usec
DE               6.50 usec
TE               88.6 K
D1           1.00000000 sec

======== CHANNEL f1 ========
NUC1                  1H
P1                13.75 usec
PLW1        12.01700020 W
SFO1        400.1324710 MHz

F2 - Processing parameters
SI                65536
SF          400.1300109 MHz
WDW                  EM
SSB       0
LB                0.30 Hz
GB        0
PC                1.00
```

p.236 sp 1



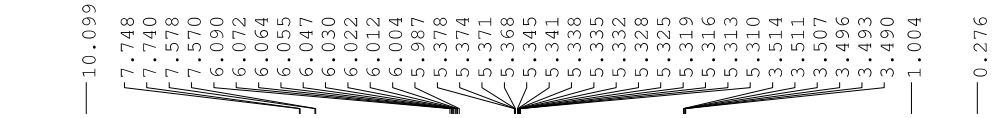

```
Current Data Parameters
NAME            Scott TBS
EXPNO                  10
PROCNO                  1

F2 - Acquisition Parameters
Date_            20140513
Time                12.40
INSTRUM            spect
PROBHD    5 mm PABBO BB-
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8223.685 Hz
FIDRES          0.125483 Hz
AQ              3.9845889 sec
RG                   144
DW                60.800 usec
DE                 6.50 usec
TE                 90.3 K
D1              1.00000000 sec

======== CHANNEL f1 ========
NUC1                  1H
P1                 13.75 usec
PLW1         12.01700020 W
SFO1         400.1324710 MHz

F2 - Processing parameters
SI                 65536
SF           400.1300095 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

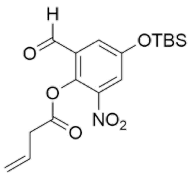
p.237

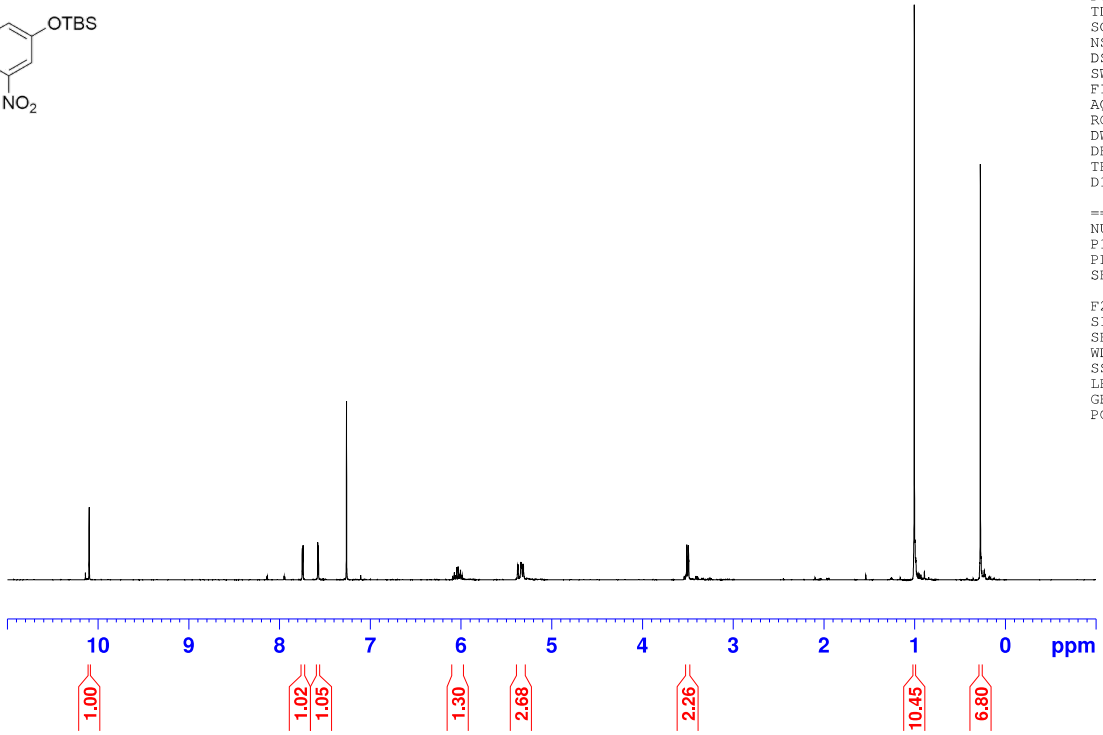



```
Current Data Parameters
NAME      Scott Nitration
EXPNO                  20
PROCNO                  1

F2 - Acquisition Parameters
Date_            20140513
Time                20.33
INSTRUM            spect
PROBHD    5 mm QNP  1H/1
PULPROG             zg30
TD                 32768
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             6188.119 Hz
FIDRES          0.188846 Hz
AQ              2.6476543 sec
RG                   322
DW                80.800 usec
DE                 6.50 usec
TE                -928.5 K
D1              1.00000000 sec

======== CHANNEL f1 ========
NUC1                  1H
P1                 12.71 usec
PLW1         18.19700050 W
SFO1         300.2318540 MHz

F2 - Processing parameters
SI                 32768
SF           300.2300089 MHz
WDW                   EM
SSB       0
LB                 0.10 Hz
GB        0
PC                 1.00
```

p.118-2 after hi-vac 55C

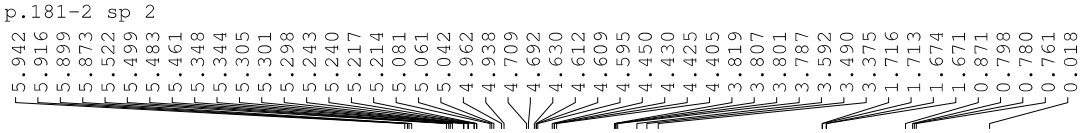


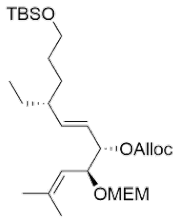


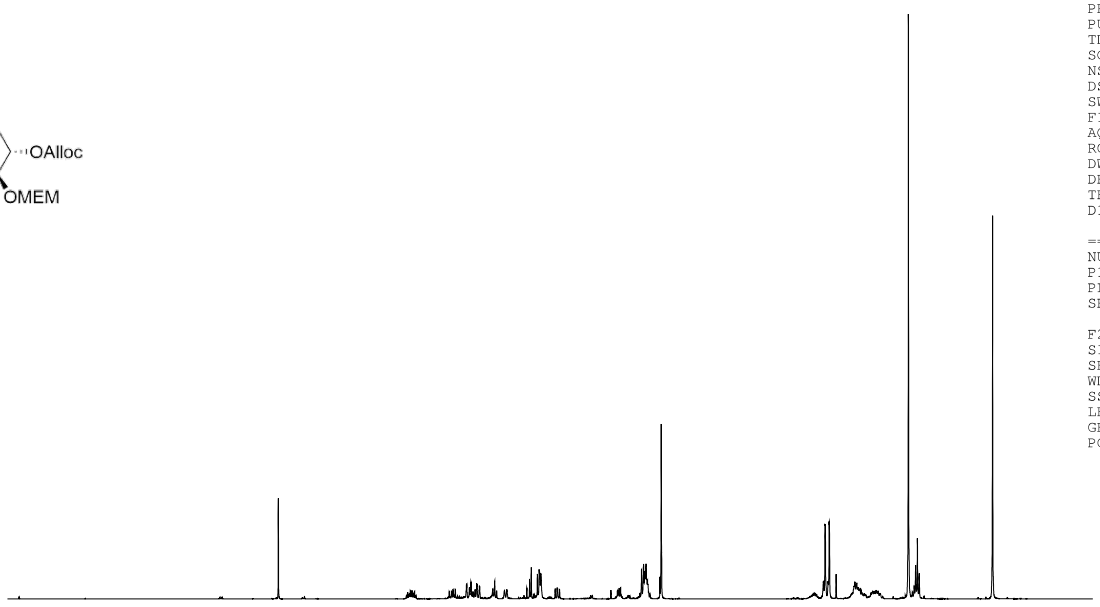


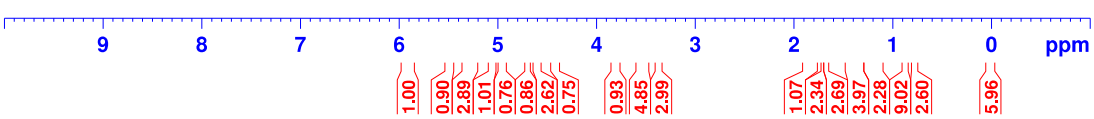

```
Current Data Parameters
NAME      Scott Acetylation
EXPNO                   30
PROCNO                   1

F2 - Acquisition Parameters
Date_           20150318
Time                14.37
INSTRUM             spect
PROBHD    5 mm PABBO BB-
PULPROG              zg30
TD                  65536
SOLVENT             CDCl3
NS                     16
DS                      2
SWH              8223.685 Hz
FIDRES           0.125483 Hz
AQ               3.9845889 sec
RG                    144
DW                60.800 usec
DE                 6.50 usec
TE                298.6 K
D1             1.00000000 sec

======== CHANNEL f1 ========
NUC1                   1H
P1                 13.75 usec
PLW1         12.01700020 W
SFO1         400.1324710 MHz

F2 - Processing parameters
SI                  65536
SF           400.1300103 MHz
WDW                    EM
SSB       0
LB                  0.30 Hz
GB        0
PC                  1.00
```

p.181-2 sp 2



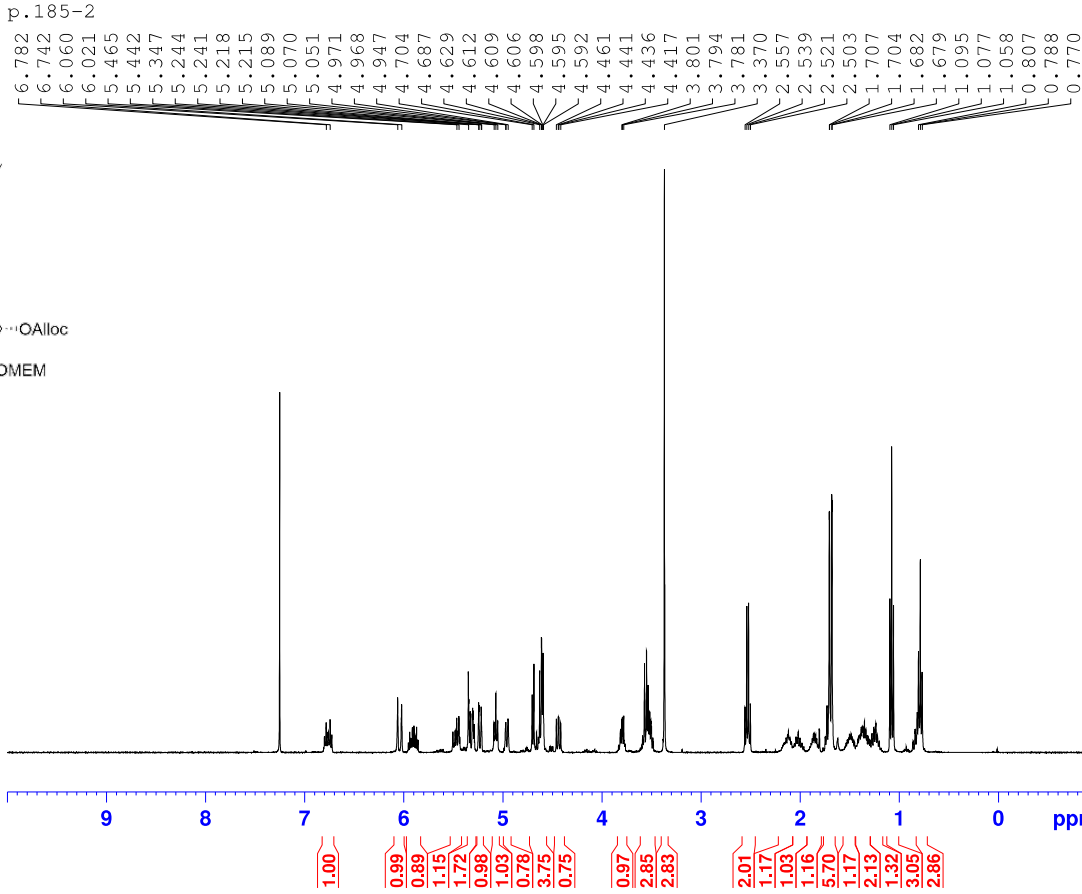


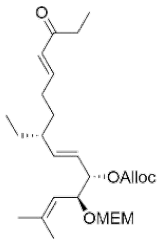





```
Current Data Parameters
NAME           Scott MEM
EXPNO                 30
PROCNO                 1

F2 - Acquisition Parameters
Date_           20150609
Time                19.59
INSTRUM             spect
PROBHD    5 mm PABBO BB-
PULPROG              zg30
TD                  65536
SOLVENT             CDCl3
NS                     16
DS                      2
SWH              8223.685 Hz
FIDRES           0.125483 Hz
AQ               3.9845889 sec
RG                     64
DW                60.800 usec
DE                 6.50 usec
TE                 96.7 K
D1             1.00000000 sec

======== CHANNEL f1 ========
NUC1                   1H
P1                 13.75 usec
PLW1         12.01700020 W
SFO1         400.1324710 MHz

F2 - Processing parameters
SI                  65536
SF           400.1300130 MHz
WDW                    EM
SSB       0
LB                  0.30 Hz
GB        0
PC                  1.00
```

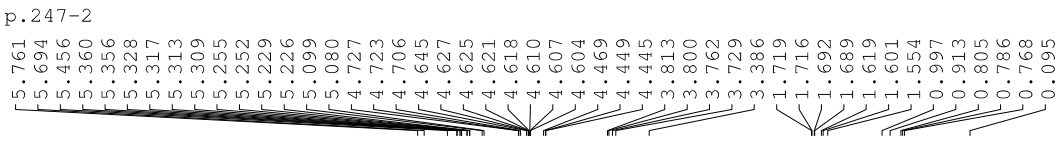
p.185-2

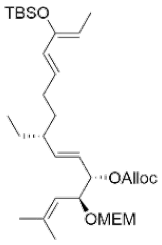


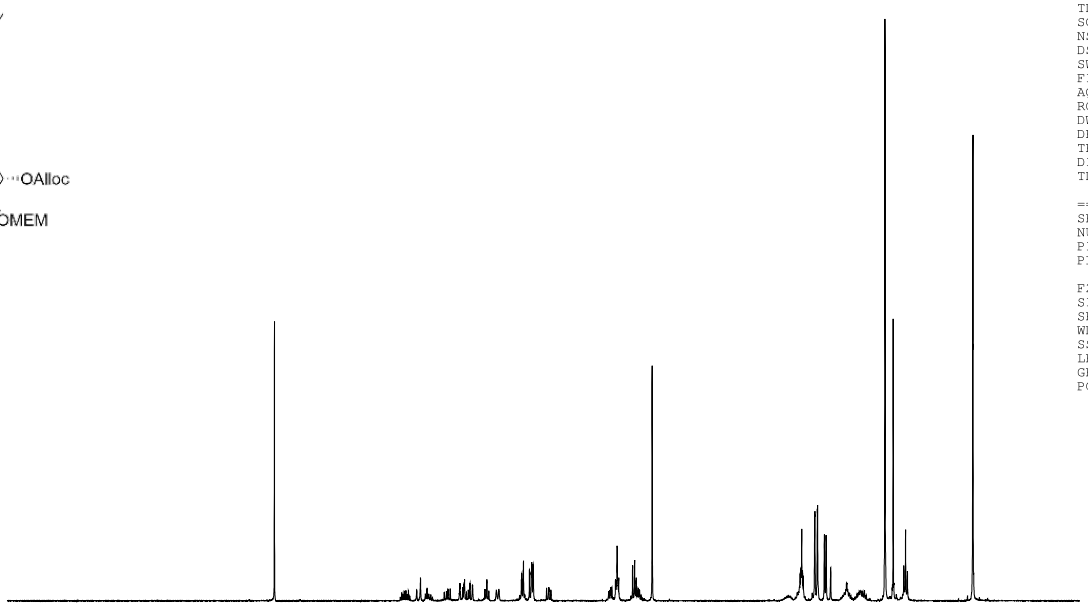


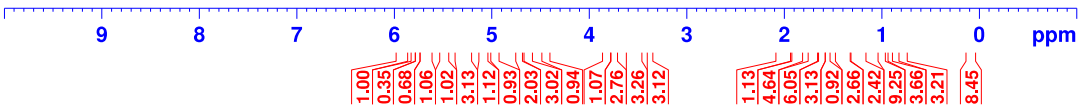

```
Current Data Parameters
NAME            Scott HWE
EXPNO                  30
PROCNO                  1

F2 - Acquisition Parameters
Date_            20150614
Time                12.47
INSTRUM             spect
PROBHD    5 mm PABBO BB-
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8223.685 Hz
FIDRES          0.125483 Hz
AQ              3.9845889 sec
RG                  71.8
DW                60.800 usec
DE                 6.50 usec
TE                 97.8 K
D1             1.00000000 sec

======== CHANNEL f1 ========
NUC1                   1H
P1                 13.75 usec
PLW1          12.01700020 W
SFO1         400.1324710 MHz

F2 - Processing parameters
SI                 65536
SF            400.1300139 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

p.247-2



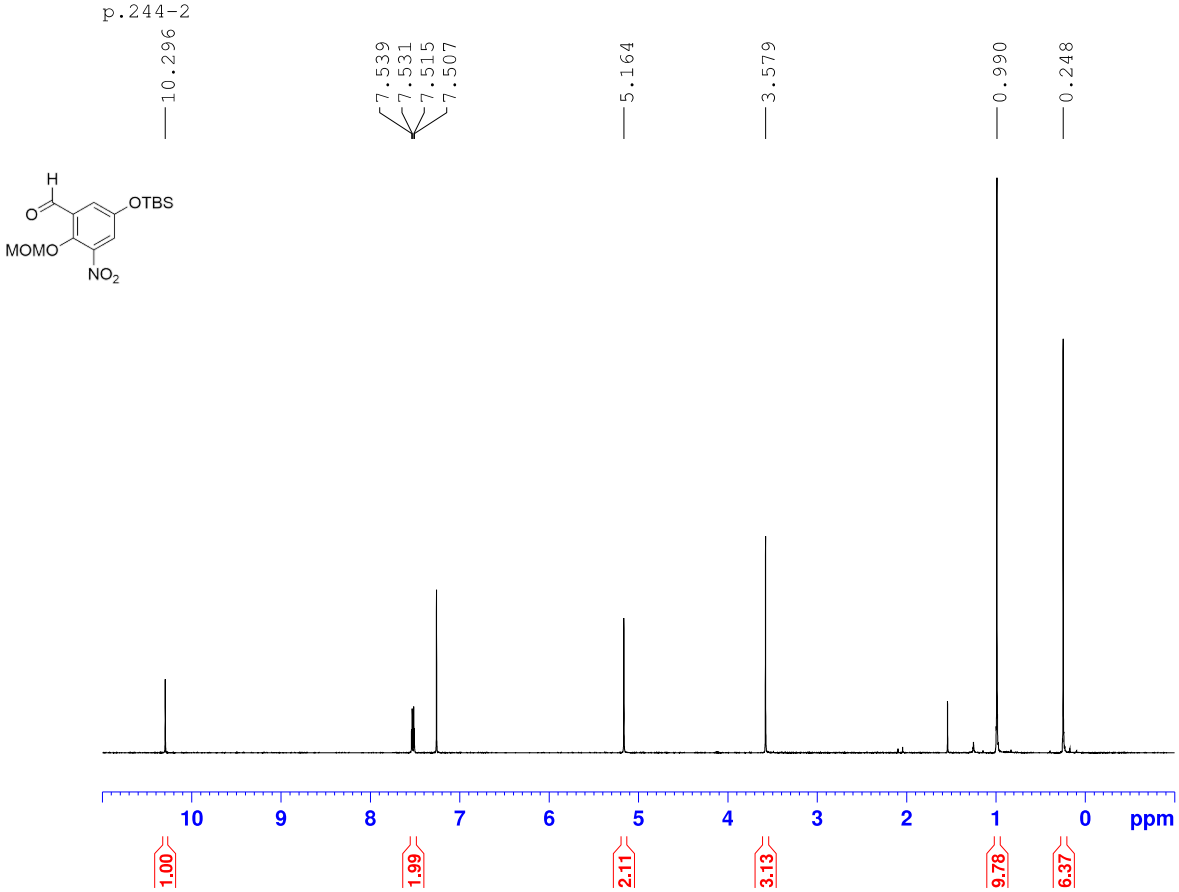






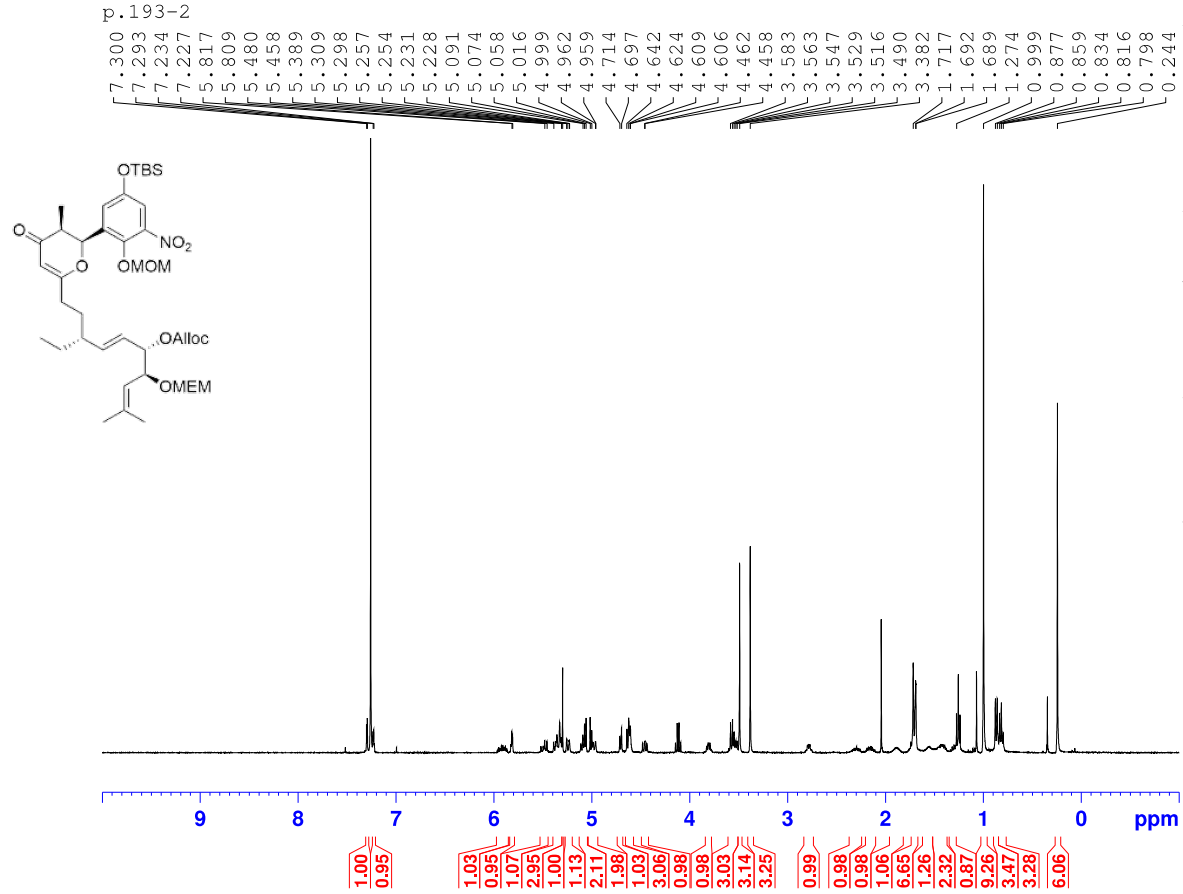

```
Current Data Parameters
NAME      Scott Silyl Enol Ether
EXPNO                  30
PROCNO                  1

F2 - Acquisition Parameters
Date_            20150921
Time                17.36
INSTRUM             spect
PROBHD    5 mm PABBO BB-
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8012.820 Hz
FIDRES          0.122266 Hz
AQ              4.0894465 sec
RG                   128
DW                62.400 usec
DE                 6.50 usec
TE                 95.5 K
D1             1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         400.1324710 MHz
NUC1                   1H
P1                 13.75 usec
PLW1          12.01700020 W

F2 - Processing parameters
SI                 65536
SF            400.1300106 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

p.244-2



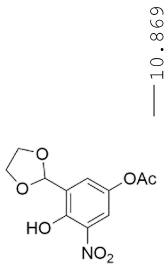

```
Current Data Parameters
NAME            Scott MOM
EXPNO                  40
PROCNO                  1

F2 - Acquisition Parameters
Date_           20150920
Time               14.39
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8012.820 Hz
FIDRES          0.122266 Hz
AQ              4.0894465 sec
RG                   144
DW                62.400 usec
DE                 6.50 usec
TE                 95.2 K
D1             1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1          400.1324710 MHz
NUC1                  1H
P1                 13.75 usec
PLW1          12.01700020 W

F2 - Processing parameters
SI                 65536
SF            400.1300104 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

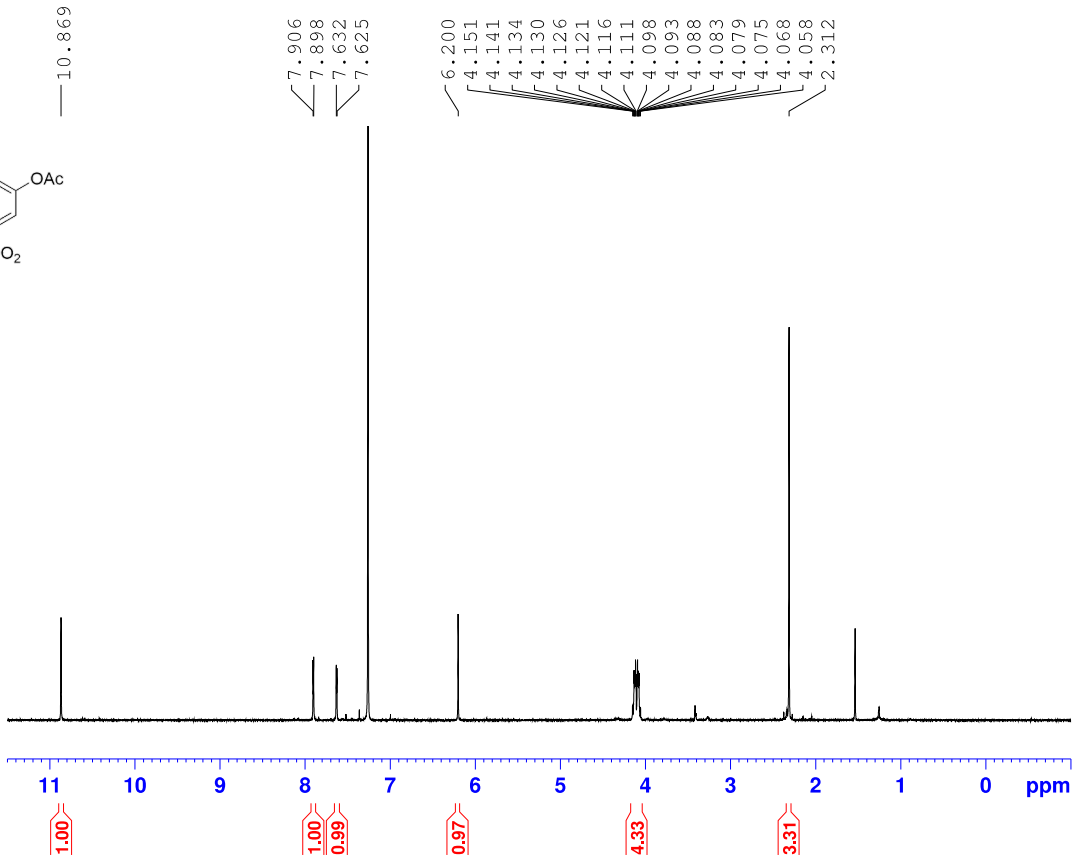
p.193-2




```
Current Data Parameters
NAME       Scott HDA-DDQ
EXPNO                 50
PROCNO                 1

F2 - Acquisition Parameters
Date_           20150702
Time               12.36
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    50
DS                     2
SWH             8223.685 Hz
FIDRES          0.125483 Hz
AQ              3.9845889 sec
RG                   144
DW                60.800 usec
DE                 6.50 usec
TE                 96.0 K
D1             1.00000000 sec

======== CHANNEL f1 ========
NUC1                  1H
P1                 13.75 usec
PLW1          12.01700020 W
SFO1          400.1324710 MHz

F2 - Processing parameters
SI                 65536
SF            400.1300107 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

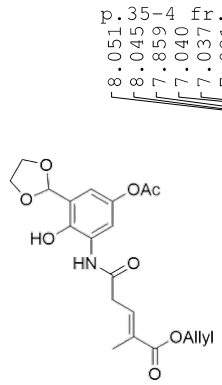
p.210-3





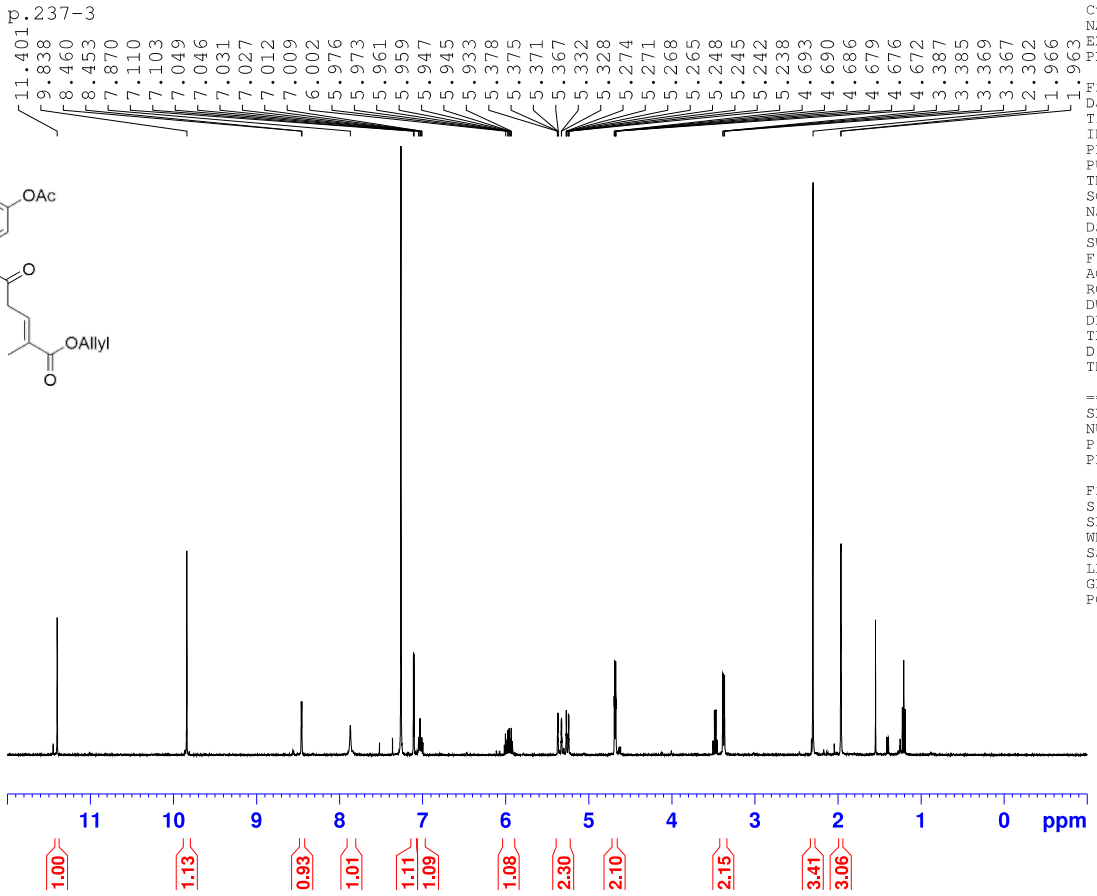

```
Current Data Parameters
NAME       Scott Acetal
EXPNO                80
PROCNO                1

F2 - Acquisition Parameters
Date_          20161101
Time              11.35
INSTRUM           spect
PROBHD   5 mm PABBO BB-
PULPROG           zg30
TD               65536
SOLVENT          CDCl3
NS                  16
DS                   2
SWH           8012.820 Hz
FIDRES        0.122266 Hz
AQ            4.0894465 sec
RG                 181
DW              62.400 usec
DE               6.50 usec
TE               88.8 K
D1          1.00000000 sec
TD0                  1

======== CHANNEL f1 ========
SFO1        400.1324710 MHz
NUC1                1H
P1                13.75 usec
PLW1        12.01700020 W

F2 - Processing parameters
SI               65536
SF          400.1300103 MHz
WDW                 EM
SSB       0
LB              0.30 Hz
GB        0
PC              1.00
```

p.35-4 fr.29-36



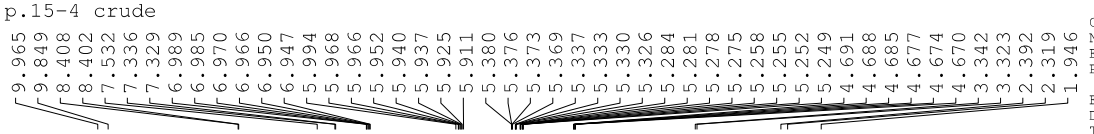

```
Current Data Parameters
NAME     Scott Amidation
EXPNO                 20
PROCNO                 1

F2 - Acquisition Parameters
Date_          20170331
Time              12.51
INSTRUM           spect
PROBHD   5 mm PABBO BB-
PULPROG           zg30
TD               65536
SOLVENT          CDCl3
NS                  16
DS                   2
SWH           8012.820 Hz
FIDRES        0.122266 Hz
AQ            4.0894465 sec
RG                 128
DW              62.400 usec
DE               6.50 usec
TE              -2138.5 K
D1          1.00000000 sec
TD0                  1

======== CHANNEL f1 ========
SFO1        400.1324710 MHz
NUC1                1H
P1                13.75 usec
PLW1        12.01700020 W

F2 - Processing parameters
SI               65536
SF          400.1300106 MHz
WDW                 EM
SSB       0
LB              0.30 Hz
GB        0
PC              1.00
```

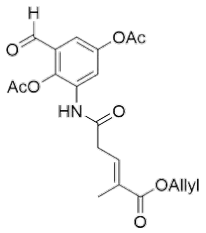
p.237-3

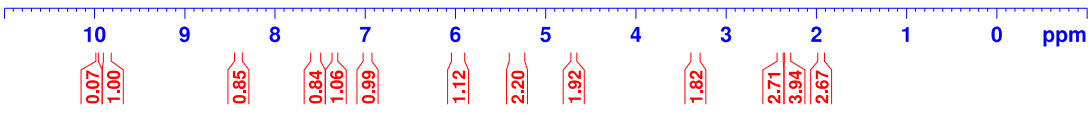



```
Current Data Parameters
NAME        Scott Acetal
EXPNO                130
PROCNO                 1

F2 - Acquisition Parameters
Date_           20161129
Time               16.57
INSTRUM             spect
PROBHD    5 mm PABBO BB-
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8012.820 Hz
FIDRES          0.122266 Hz
AQ              4.0894465 sec
RG                   181
DW                62.400 usec
DE                 6.50 usec
TE                 92.4 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         400.1324710 MHz
NUC1                   1H
P1                 13.75 usec
PLW1         12.01700020 W

F2 - Processing parameters
SI                 65536
SF           400.1300099 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

p.15-4 crude








```
Current Data Parameters
NAME          Scott Acyl
EXPNO                 80
PROCNO                 1

F2 - Acquisition Parameters
Date_           20170310
Time               8.39
INSTRUM             spect
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PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8012.820 Hz
FIDRES          0.122266 Hz
AQ              4.0894465 sec
RG                  90.5
DW                62.400 usec
DE                 6.50 usec
TE                 876.0 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         400.1324710 MHz
NUC1                   1H
P1                 13.75 usec
PLW1         12.01700020 W

F2 - Processing parameters
SI                 65536
SF           400.1300112 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
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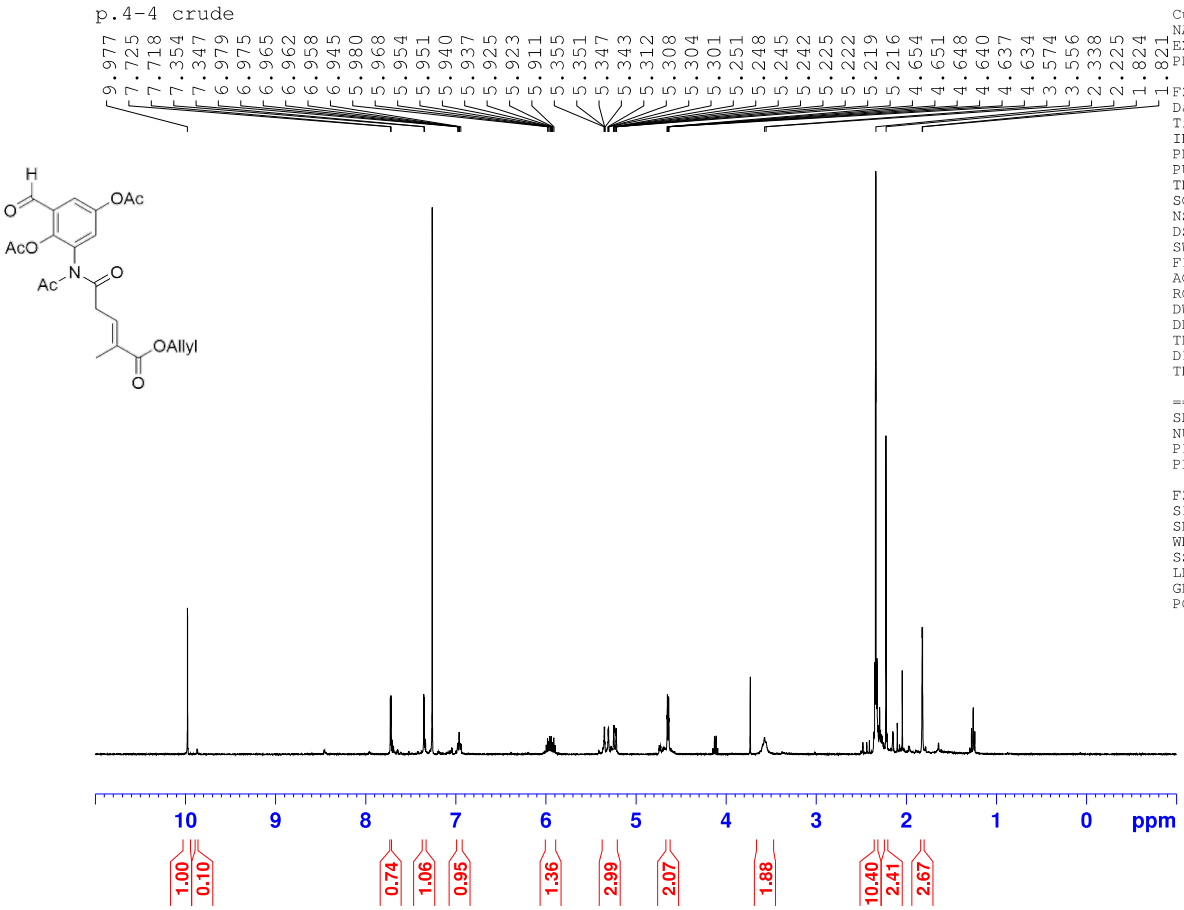
p.4-4 crude

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Current Data Parameters
NAME      Scott Acylation
EXPNO                  10
PROCNO                  1

F2 - Acquisition Parameters
Date_           20170224
Time                9.18
INSTRUM            spect
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PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8012.820 Hz
FIDRES             0.122266 Hz
AQ              4.0894465 sec
RG                   144
DW                62.400 usec
DE                 6.50 usec
TE                 86.3 K
D1              1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         400.1324710 MHz
NUC1                   1H
P1                 13.75 usec
PLW1         12.01700020 W

F2 - Processing parameters
SI                 65536
SF           400.1300100 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```
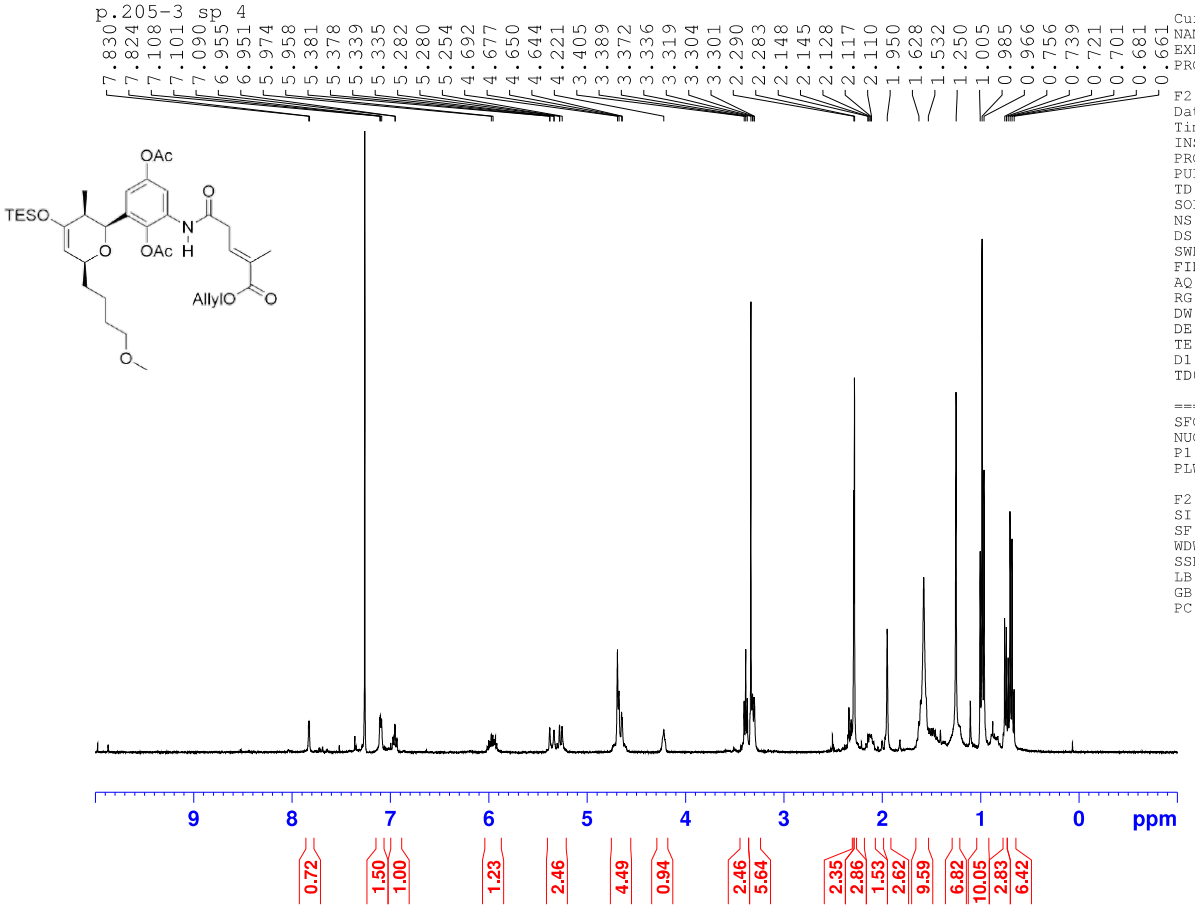

p.205-3 sp 4

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Current Data Parameters
NAME           Scott HDA
EXPNO                 70
PROCNO                 1

F2 - Acquisition Parameters
Date_           20161018
Time               17.46
INSTRUM            spect
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PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8012.820 Hz
FIDRES             0.122266 Hz
AQ              4.0894465 sec
RG                   128
DW                62.400 usec
DE                 6.50 usec
TE                 88.1 K
D1              1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         400.1324710 MHz
NUC1                   1H
P1                 13.75 usec
PLW1         12.01700020 W

F2 - Processing parameters
SI                 65536
SF           400.1300103 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
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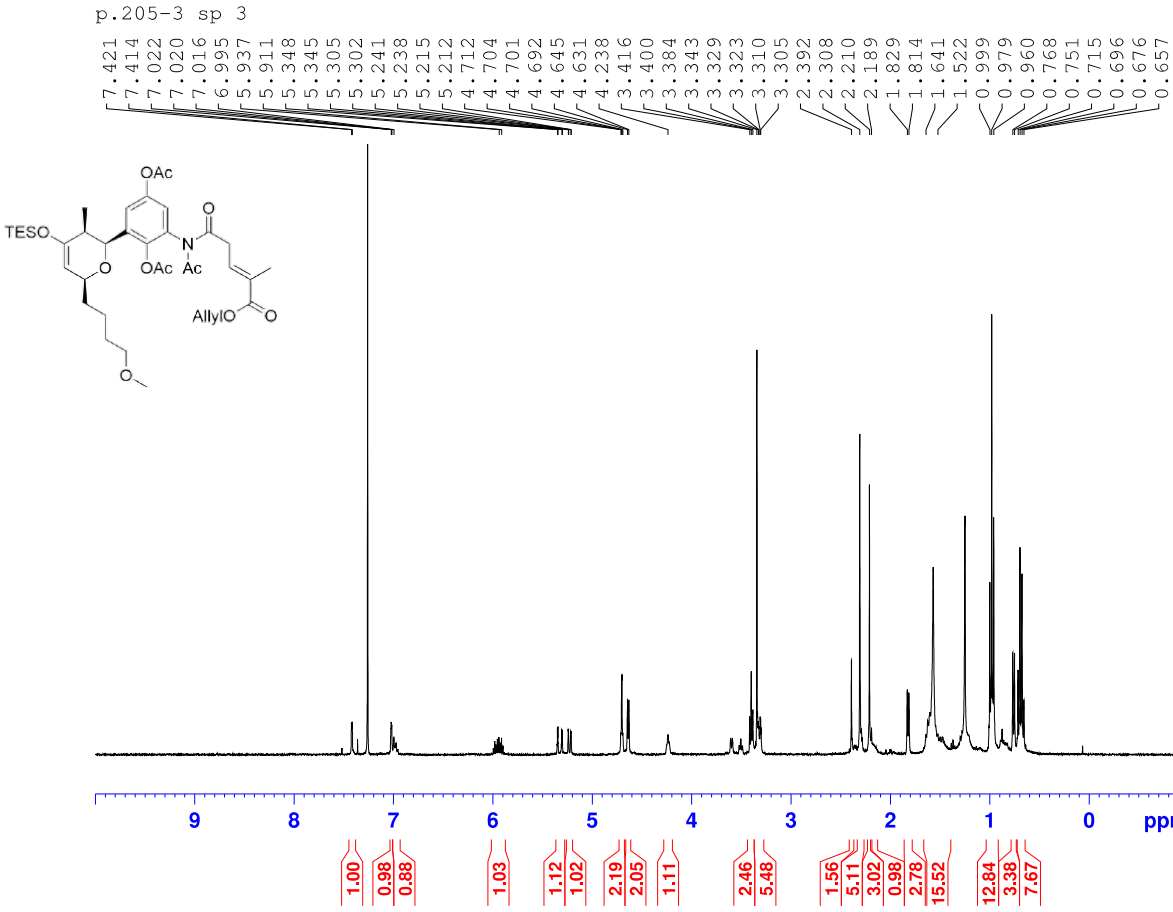
p.205-3 sp 3



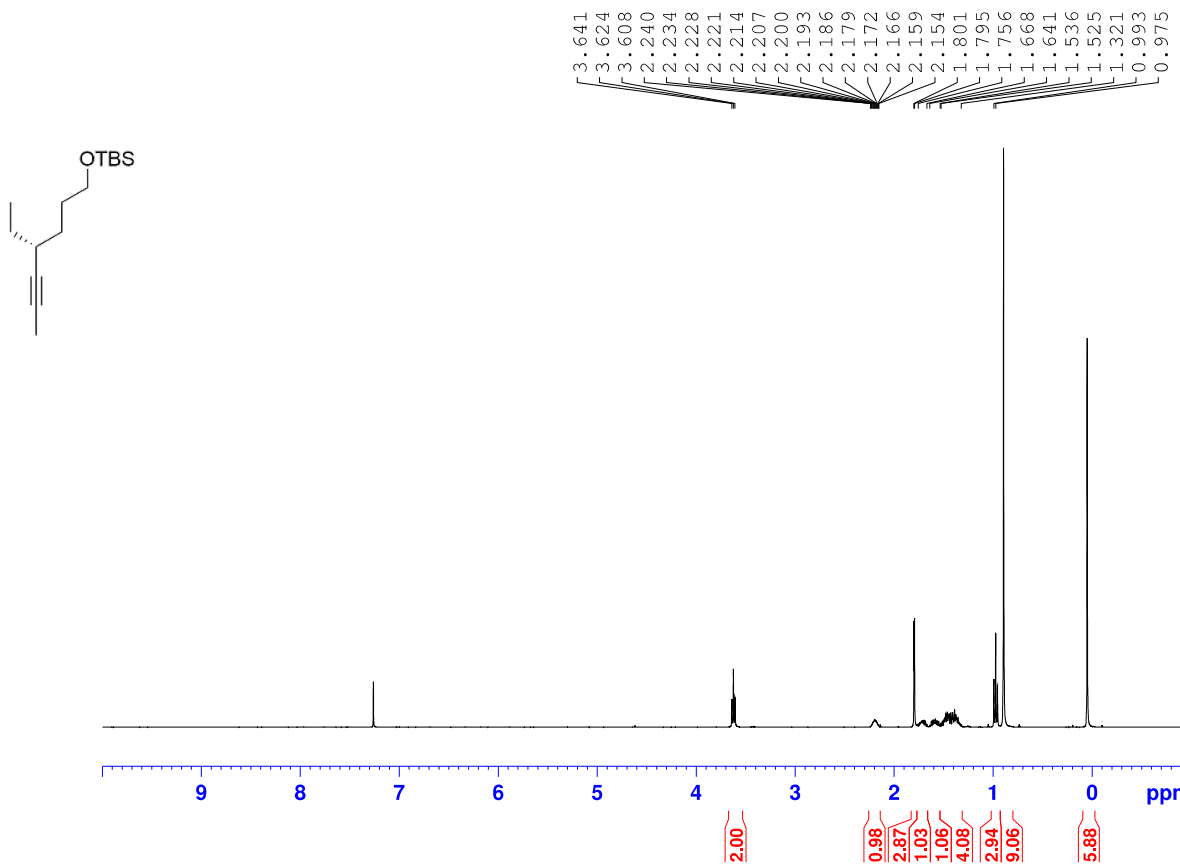
Current Data Parameters
NAME Scott HDA
EXPNO 60
PROCNO 1

F2 - Acquisition Parameters
Date_ 20161018
Time 17.36
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.122266 Hz
AQ 4.0894465 sec
RG 128
DW 62.400 usec
DE 6.50 usec
TE 88.1 K
D1 1.00000000 sec
TD0 1

======== CHANNEL f1 ========
SFO1 400.1324710 MHz
NUC1 1H
P1 13.75 usec
PLW1 12.01700020 W

F2 - Processing parameters
SI 65536
SF 400.1300107 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

p.284-3 fr 9-16



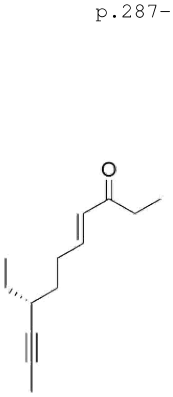
Current Data Parameters
NAME Scott Methylation
EXPNO 10
PROCNO 1

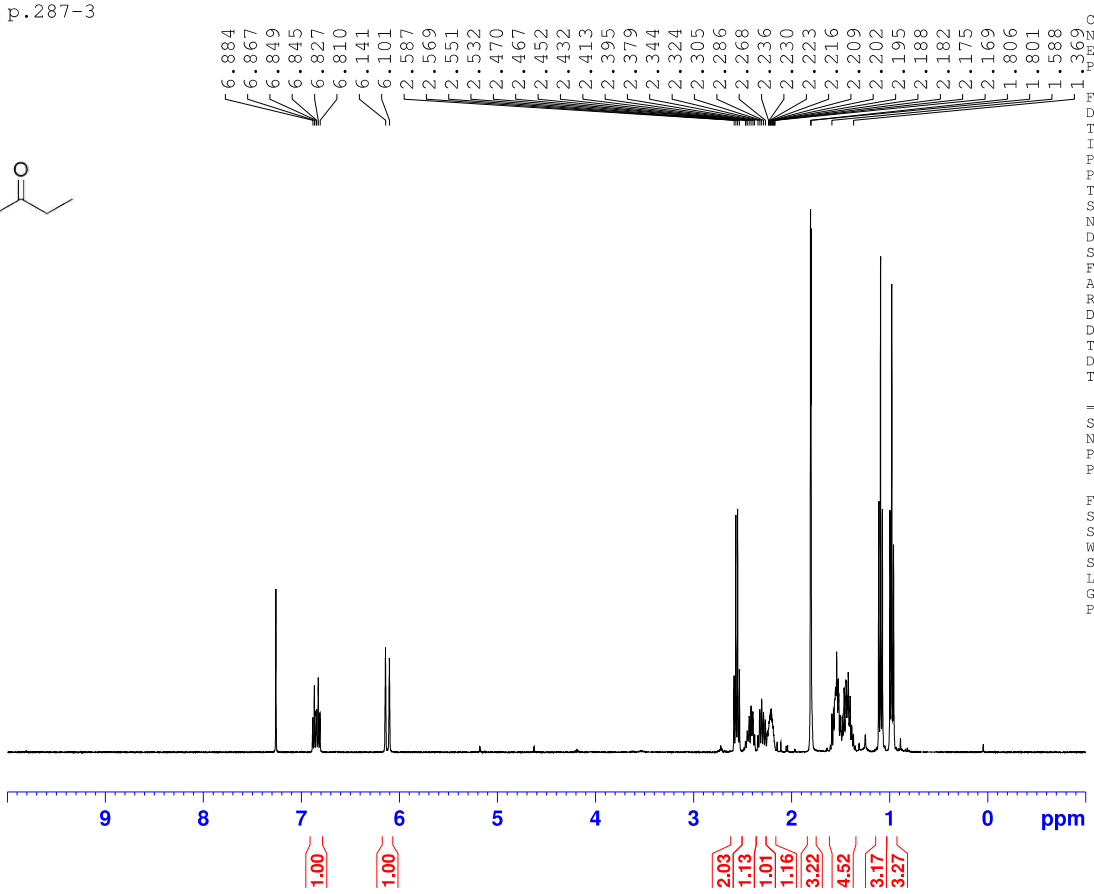
F2 - Acquisition Parameters
Date_ 20170204
Time 11.55
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.122266 Hz
AQ 4.0894465 sec
RG 90.5
DW 62.400 usec
DE 6.50 usec
TE 87.9 K
D1 1.00000000 sec
TD0 1

======== CHANNEL f1 ========
SFO1 400.1324710 MHz
NUC1 1H
P1 13.75 usec
PLW1 12.01700020 W

F2 - Processing parameters
SI 65536
SF 400.1300098 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

p.287-3



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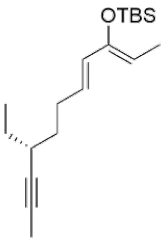
Current Data Parameters
NAME            Scott HWE
EXPNO                  10
PROCNO                  1

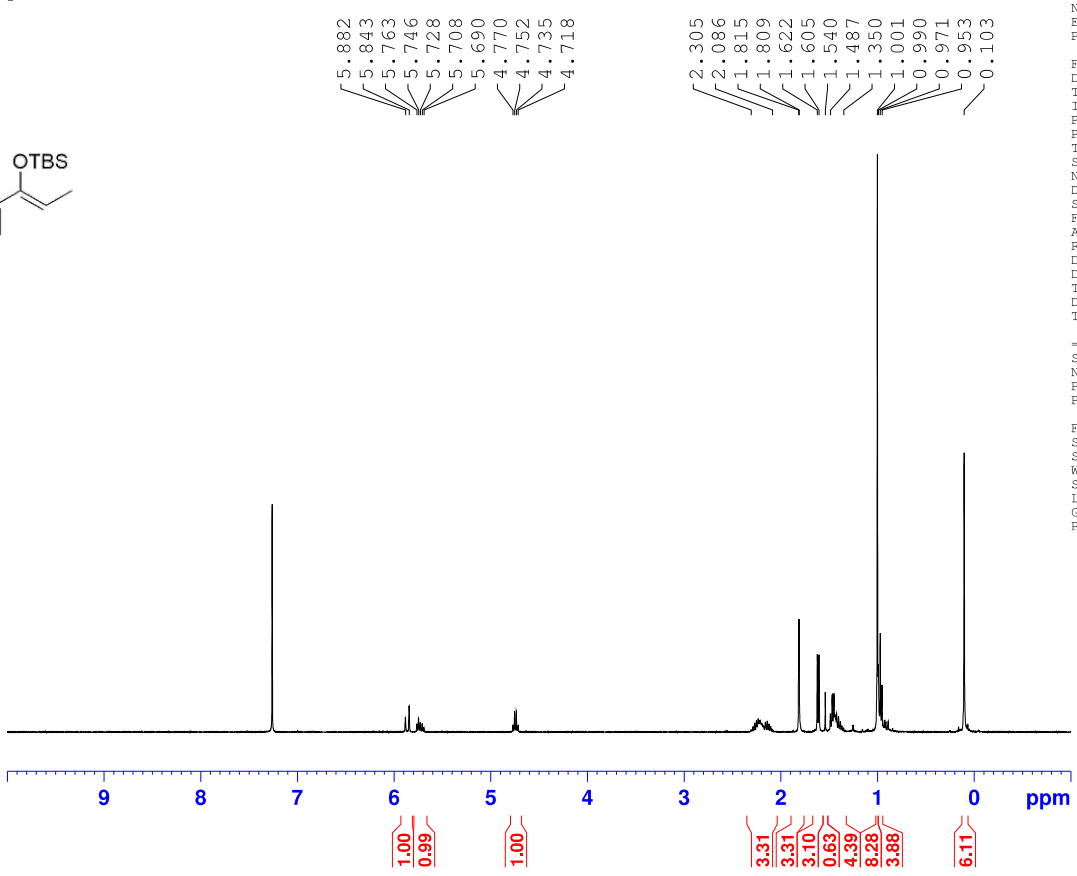
F2 - Acquisition Parameters
Date_            20170208
Time                10.34
INSTRUM             spect
PROBHD    5 mm PABBO BB-
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH              8012.820 Hz
FIDRES           0.122266 Hz
AQ               4.0894465 sec
RG                  90.5
DW                62.400 usec
DE                 6.50 usec
TE                 87.0 K
D1             1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1          400.1324710 MHz
NUC1                  1H
P1                 13.75 usec
PLW1          12.01700020 W

F2 - Processing parameters
SI                 65536
SF            400.1300101 MHz
WDW                   EM
SSB       0
LB                0.30 Hz
GB        0
PC                1.00
```

p.6-4






```
Current Data Parameters
NAME      Scott Silyl Enol Ether
EXPNO                  30
PROCNO                  1

F2 - Acquisition Parameters
Date_            20170225
Time                11.13
INSTRUM             spect
PROBHD    5 mm PABBO BB-
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH              8012.820 Hz
FIDRES           0.122266 Hz
AQ               4.0894465 sec
RG                   144
DW                62.400 usec
DE                 6.50 usec
TE                 85.7 K
D1             1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1          400.1324710 MHz
NUC1                  1H
P1                 13.75 usec
PLW1          12.01700020 W

F2 - Processing parameters
SI                 65536
SF            400.1300106 MHz
WDW                   EM
SSB       0
LB                0.30 Hz
GB        0
PC                1.00
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