AN ABSTRACT OF THE DISSERTATION OF

Liang Lu for the degree of Doctor of Philosophy in Chemistry presented on August 24, 2009.

Title: Part I: Synthetic Studies Toward the Southern Portion of Azaspiracid-1; Part II: Total Synthesis of Amphidinolide B_1 and the Proposed Structure of Amphidinolide B_2

Abstract approved :_____

Rich G. Carter

The structural architecture present in marine toxin azaspiracid - 20 stereocenters, 9 rings, 3 separated spirocenters - has attracted considerable synthetic attention. Our efforts toward the synthesis of azaspiracid have led to the completion of both C_1-C_{26} northern and C_{27}-C_{40} southern halves. Herein, the synthesis of southern FGHI ring system is described. The key steps included an Andrus anti-aldol coupling to furnish the C_{32}, C_{33} stereocenters, an acid-catalyzed ketalization to furnish FG rings, and a $Yb(OTf)_3$-mediated spiroaminal formation to generate I ring.

The first total synthesis of cytotoxic macrolides amphidinolide B_1 and the

proposed structure of amphidinolide B_2 have been accomplished. The key developed protocols include a metal catalyst-free sequence for the synthesis of the diene subunit, a non-chelation-controlled aldol coupling to install the C_{18} stereocenter, an efficient macrocyclization of the 26-membered lactone ring, and the incorporation of the labile allylic epoxide moiety.

The unique structure of the highly substituted diene functionality represents significant synthetic challenges. A Wittig / HWE reaction sequence yielded the C_{13}-C_{15} diene moiety in good yield in excellent diastereoselectivity. Subsequent Sharpless epoxidation and Red-Al-mediated regionselective epoxide opening gave the C_{16} tertiary alcohol.

The protecting groups on C_{21} were discovered to have significant effects on the aldol reaction between C_9-C_{18} aldehyde and C_{19}-C_{25} methyl ketone. Although chelating groups such as PMB, Bn afforded 18*S* isomer as a single diastereomer, the removal of these groups has proven problematic. Non-chelating silyl group generated 18*R* isomer in 8:1 dr at -100ºC, while the 18*S* stereomer was obtained at -40ºC in 1.2:1 dr.

A spontaneous intramolecular Wadsworth−Emmons olefination established the 26-membered macrocycle. The oxidation and *in situ* elimination of a selenide moiety proceeded smoothly in the presence of free alcohols using TMSOOTMS. The first total synthesis of amphidinolide B_1 and the proposed structure of amphidinolide B_2 were accomplished in 29 linear steps. Additionally, We

discovered that the initially proposed structure of amphidinolide B_2 was incorrect.

Part I: Synthetic Studies Toward the Southern Portion of Azaspiracid-1; Part II: Total Synthesis of Amphidinolide B_1 and the Proposed Structure of Amphidinolide B_2

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APPROVED:

Major Professor, representing Chemistry

Chair of the Department of Chemistry

Dean of the Graduate School

I understand that my dissertation will become part of the permanent collection of Oregon State University libraries. My signature below authorizes release of my dissertation to any reader upon request.

Liang Lu, Author

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TABLE OF CONTENTS

TABLE OF CONTENTS (Continued)

TABLE OF CONTENTS (Continued)

TABLE OF CONTENTS (Continued)

TABLE OF CONTENTS (Continued)

TABLE OF CONTENTS (Continued)

TABLE OF CONTENTS (Continued)

LIST OF FIGURES

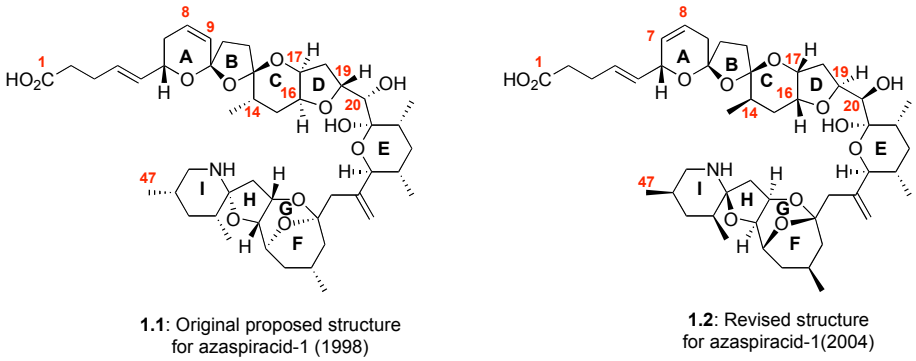
LIST OF TABLES

PART I: SYNTHETIC STUDIES TOWARD THE SOUTHERN PORTION OF AZASPIRACID-1

CHAPTER 1. BACKGROUND OF AZASPIRACID

1.1 Discovery and Bioactivities of Azaspiracid-1

Azaspiracid poisoning is a recent toxic syndrome first reported in 1995, when several individuals became ill after consuming mussels harvested from Killary Harbor in Ireland.[1] An active search for the causative toxin led to the isolation of azaspiracid-1 by the Satake group in 1998.[2] The initial structure of azaspiracid-1 was proposed based on extensive 2D NMR studies;[2] however, this original structure has been recently discredited and was revised by Nicolaou and co-workers in 2004.[3] Independently and concurrently, our laboratory had converged on the same stereochemical conclusion.[4] The major stereochemical errors were believed to be in the ABCDE northern portion of the molecule. In addition to the inverted stereochemical configurations of C_{14}, C_{16}, C_{17}, C_{19} and C_{20}, the southern FGHI ring system was found to be enantiomeric to the proposed structure and the $C_{8,9}$ olefin in the A ring proved to be actually in $C_{7,8}$ position. After structure elucidation of azaspiracid-1, a total of more than 30 azaspiracid analogues differing slightly in their methylation and hydroxylation patterns have subsequently been described and their structure was determined using tandem mass spectrometry and NMR spectroscopy.[5]



1.1: Original proposed structure for azaspiracid-1 (1998)

1.2: Revised structure for azaspiracid-1(2004)

Figure 1.1. Originally Proposed and Revised Structures of Azaspiracid-1

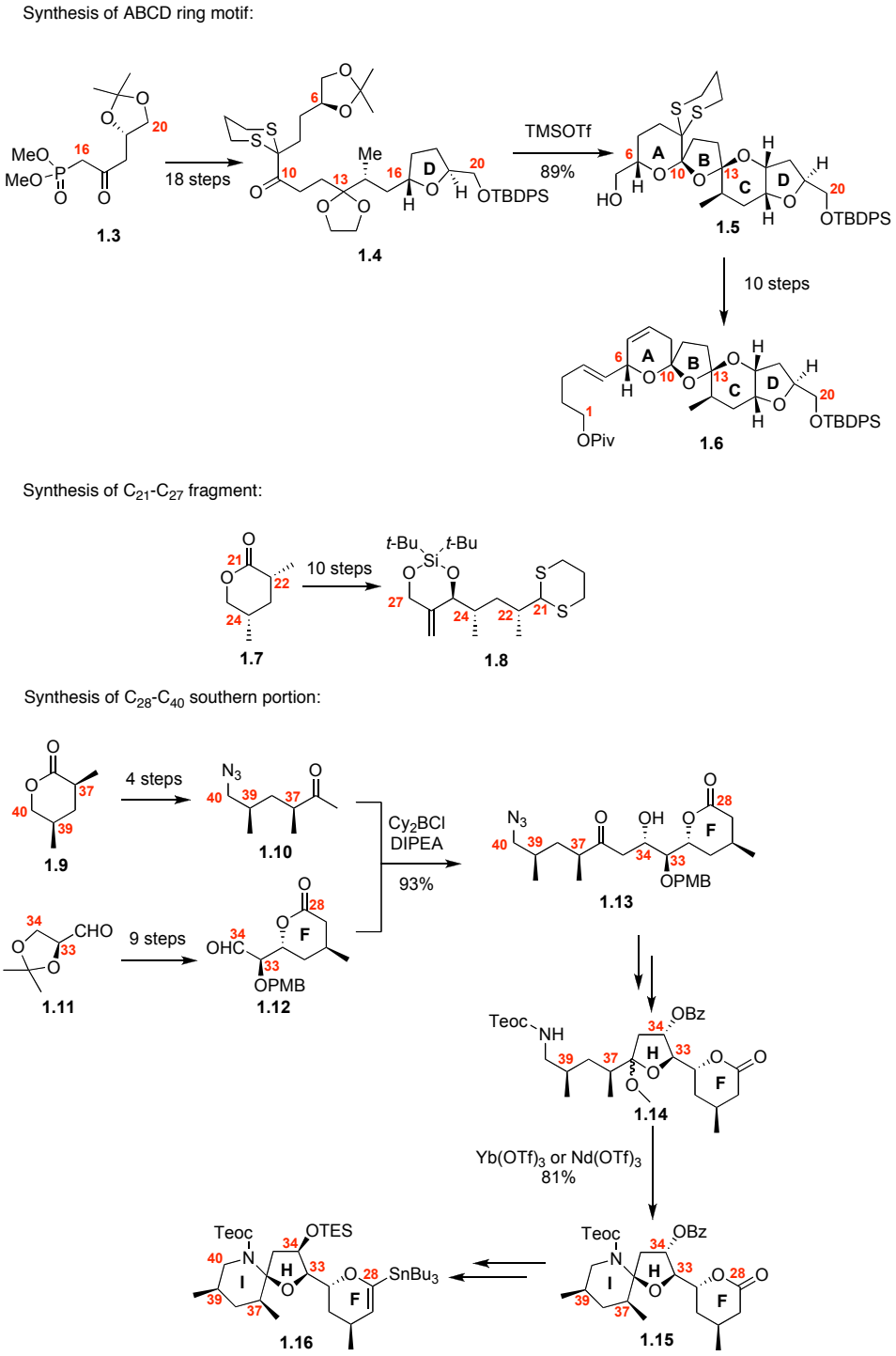
A marine dinoflagellate was proposed to be the origin of azaspiracids[6] and they have been discovered in multiple shellfish species including mussels, oysters, scallops, clams, *etc.*[7] Human consumption of azaspiracid-contaminated shellfish can result in severe acute symptoms such as nausea, vomiting, diarrhea, and stomach cramps.[1] Although there is no information about toxicity of these analogues to humans, azaspiracid-1 is known to possess toxicity *in vitro* with a lethal dose in mice of 0.2 mg / kg.[2] The mechanism by which azaspiracids induce their toxic effects and their biological target/s is still unknown;[8] however, several effects on *in vitro* cell cultures have been revealed for azaspiracid-1 including cytoskeletal alterations,[9] caspase activation,[10] cytotoxicity,[11] cytosolic calcium levels modulation,[12] and alteration of neuronal network.[13] The considerable toxicity and the mechanistic elusiveness have made azaspiracids a significant threat to the shellfish industry and human health. This situation is further complicated by the scarce amount of azaspiracids obtained from natural sources.[6]

1.2 Synthetic Efforts Toward Azaspiracid-1

The intriguing structural architecture (20 stereocenters, 9 rings, 3 spirocenters) of azaspiracid-1 has attracted considerable attention from the synthetic community, in particular by the research groups of Carter,[4, 14] Nicolaou,[3,15] Evans,[16] Forsyth,[17] Sasaki,[18a, 18e] and Mootoo.[18h] The extensive efforts led to the first total synthesis of (-)-azaspiracid-1 and the correction of its structural assignment by the Nicolaou group in 2004.[3] In 2006, Nicolaou and co-workers reported an improved synthesis of (-)-azaspiracid-1.[15g] Besides Nicolaou's landmark work, several partial synthetic studies[4, 14, 17, 18] and Evans' total synthesis of (+)-azaspiracid-1 have also been communicated.[16]

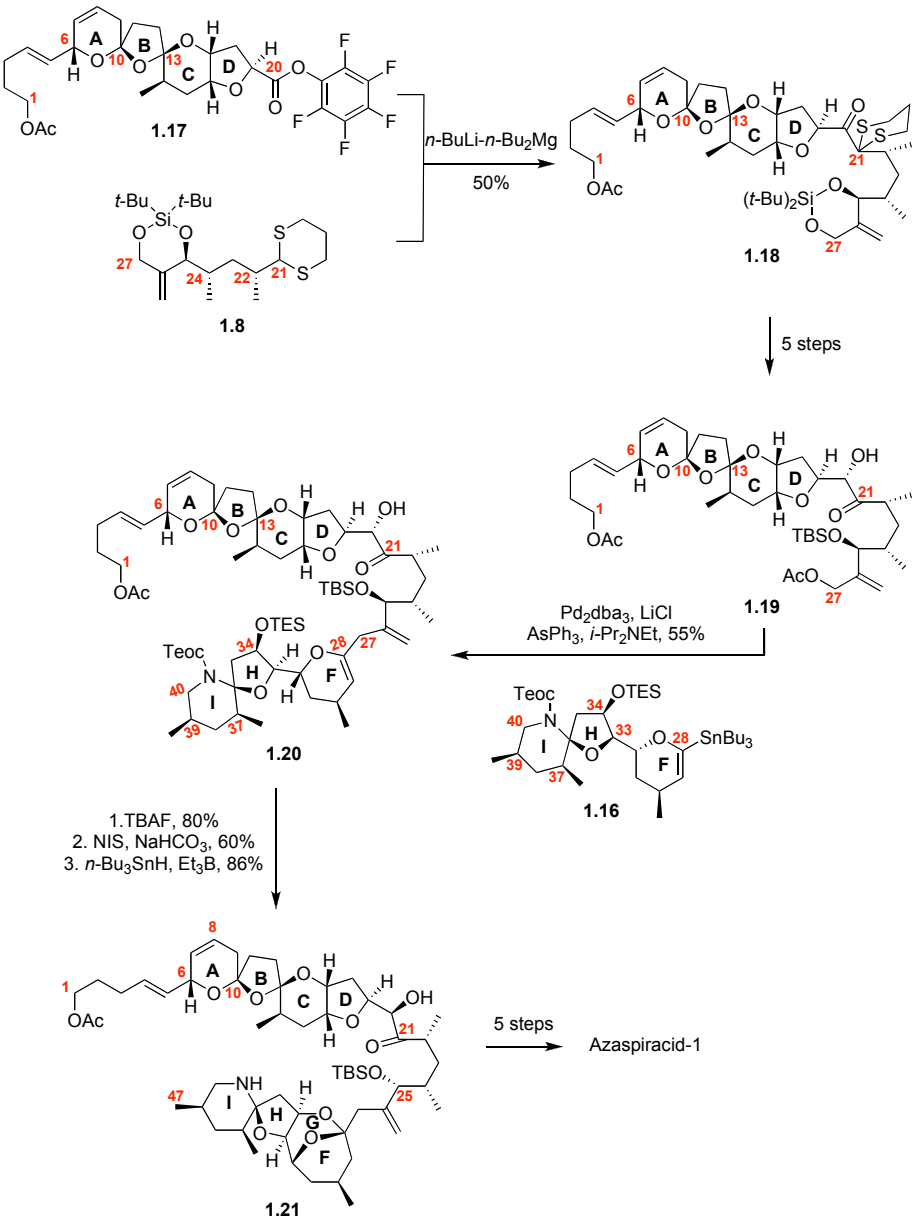
1.2.1 Nicolaou's First-Generation Total Synthesis of (-)-azaspiracid-1

In 2004, Nicolaou and co-workers reported the conquest of (-)-azaspiracid-1 as well as the correction of its originally proposed structure (Scheme 1.1).[3] Nicolaou's approach disconnected the complex molecule into three key building blocks: C_1-C_{20} ABCD ring domain, C_{21}-C_{27} E ring fragment and C_{28}-C_{40} FGHI ring system. The ABCD ring system found in compound **1.5** was accessed via TMSOTf catalyzed polycyclization, whereas the the C_{22} and C_{24} stereocenters in C_{21}-C_{27} fragment **1.8** were obtained from the known lactone **1.7**.[19] The key steps in the synthesis of FGHI ring system included a $Yb(OTf)_3$- or $Nd(OTf)_3$-mediated highly stereoselective spiroaminal formation to afford compound **1.15**.



Scheme 1.1. Nicolaou's Strategy for the Synthesis of Three Major Fragments

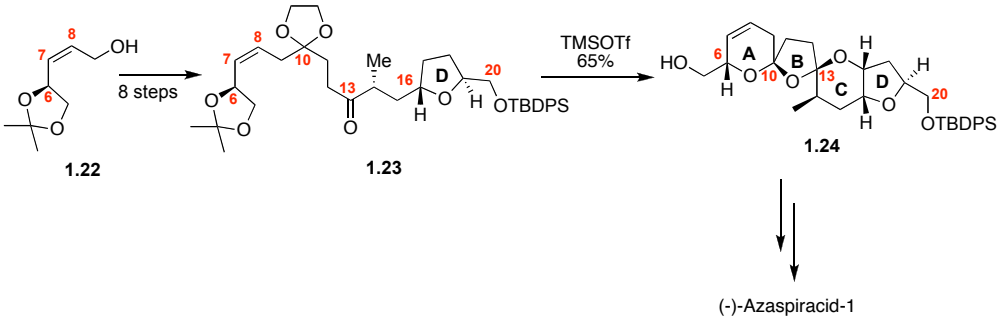
The coupling of these fragments and the completion of the synthesis is shown in Scheme 1.2. The addition of the stabilized dithiane anion to pentafluorophenol ester **1.17** formed C_{21}-C_{20} bond. The following Stille coupling between allylic acetate **1.19** and stannane **1.16** furnished compound **1.20**, which contains all carbon atoms needed for the azaspiracid-1 structure. In the presence of NIS, G ring was produced via an intramolecular iodoetherification. After the spontaneous formation of E ring during the global desilylation, (-)-azapsiracid-1 was obtained in sequence of 50 longest linear steps.



Scheme 1.2. Nicolaou's First-Generation Total Synthesis of (-)-Azaspiracid-1

1.2.2 Nicolaou's Second-Generation Total Synthesis of (-)-Azaspiracid-1

In 2006, the Nicolaou group reported their second-generation total synthesis of (-)-azaspiracid-1.[15g] The major improvement of the modified synthesis rest on the construction of ABCD ring fragment. Instead of a dithiane functionality at C_9, the key TMSOTf-mediated ring-closing cascade was conducted with $C_{7,8}$ alkene in place. After obtaining ABCD ring fragment **1.23**, (-)-azaspiracid-1 was synthesized via the analogous sequence used in Nicolaou's first-generation synthesis. The new strategy afforded the natural product in 39 linear steps.

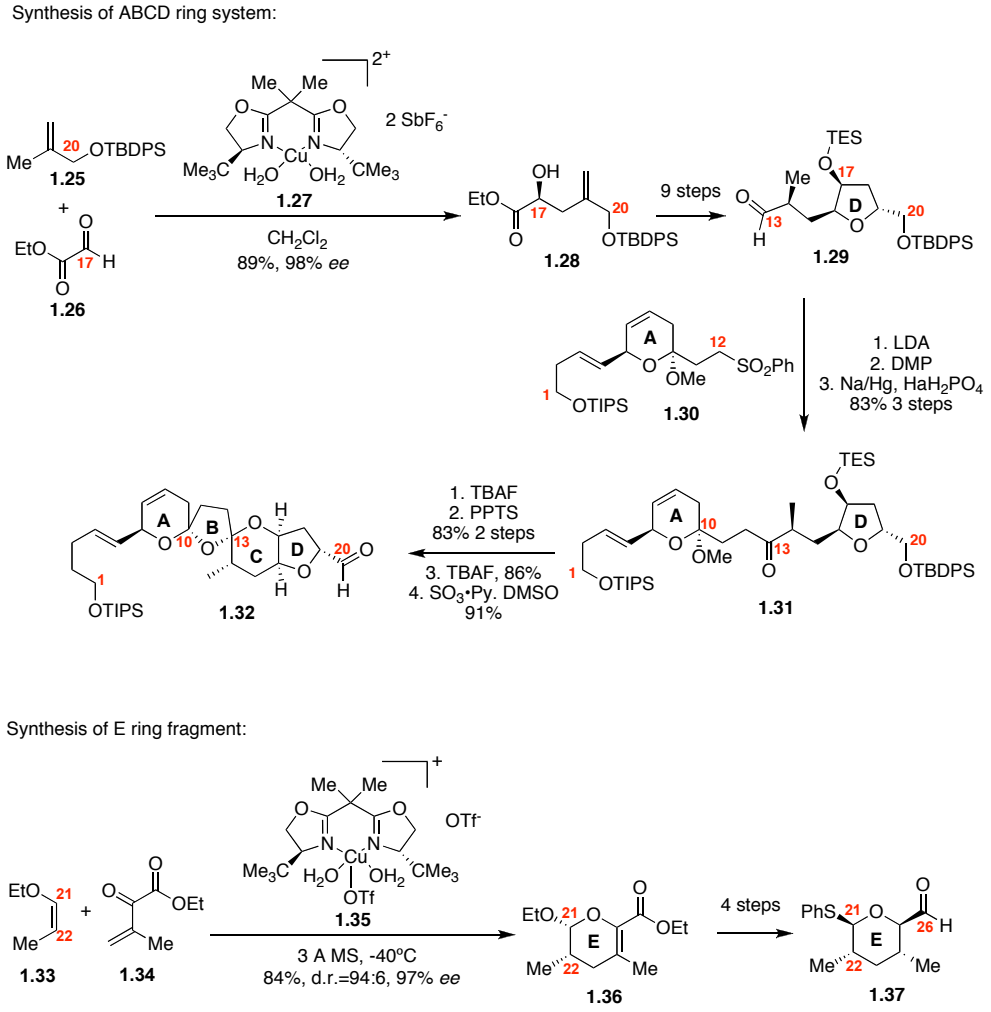


Scheme 1.3. Nicolaou's Second-Generation Total Synthesis of (-)-Azaspiracid-1

1.2.3 Evans' Total Synthesis of (+)-Azaspiracid-1

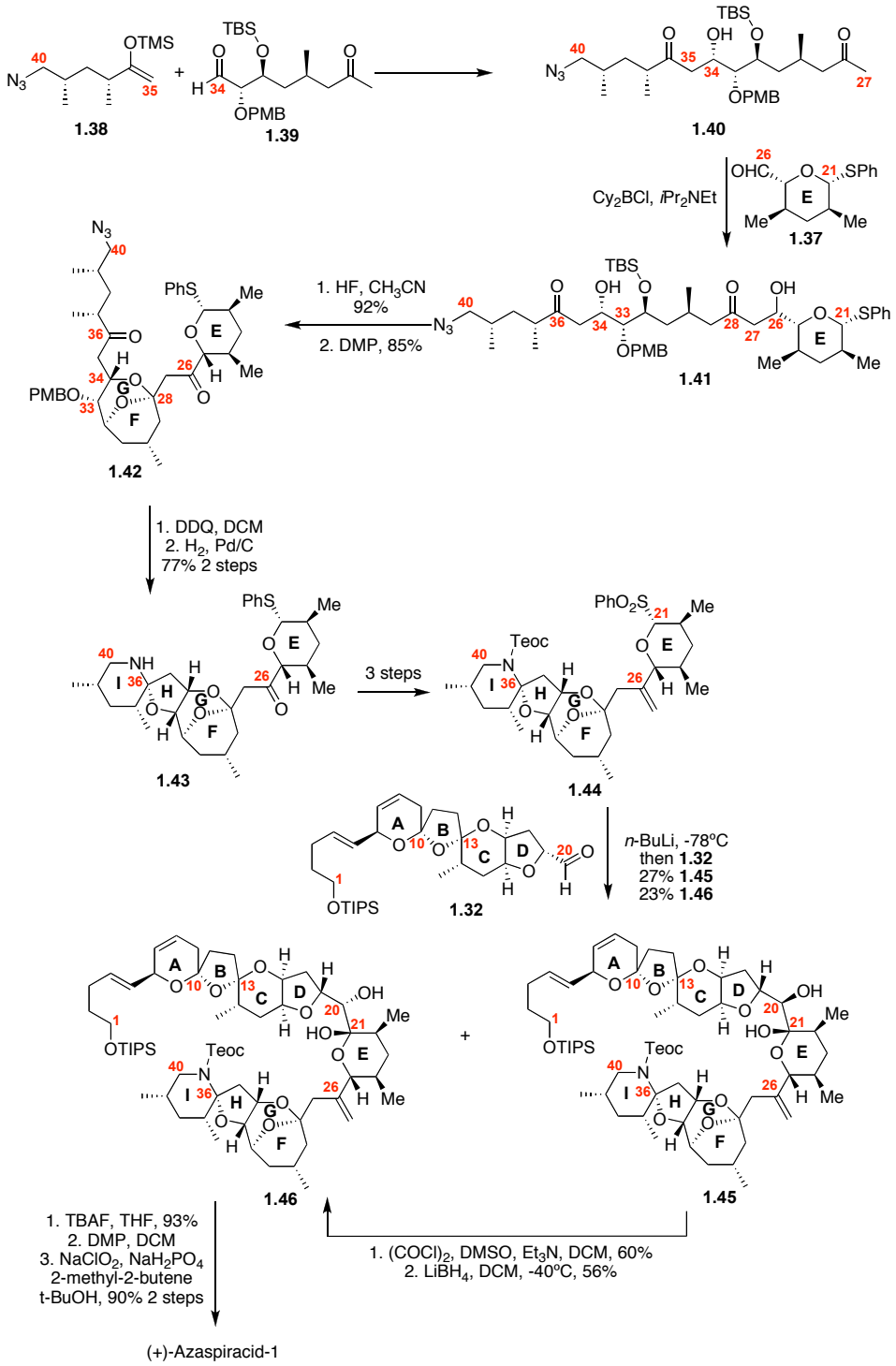
In 2007, the Evans group accomplished the total synthesis of (+)-azaspiracid-1.[16] Sharing the similar disconnection with Nicolaou's approach, Evans' strategy disassembled (+)-azaspiracid-1 into three portions: C_1-C_{20} ABCD ring moiety, C_{21}-C_{26} E ring fragment and C_{27}-C_{40} linear motif. The stereocenter at C_{17} existed in compound **1.28** was generated from a highly

enantioselective Cu^{2+}-catalyzed glyoxylate-ene reaction, whereas the similar catalyst was also found effective in the Diels-Alder cycloaddition to construct E ring fragment **1.37**. Treatment of ketone **1.31** with TBAF then PPTS in nonpolar solvent initiated a stereoselective polycyclization cascade to yield the desired ABCD ring system.



Scheme 1.3. Evans' Synthesis of ABCD Ring and E Ring Fragments

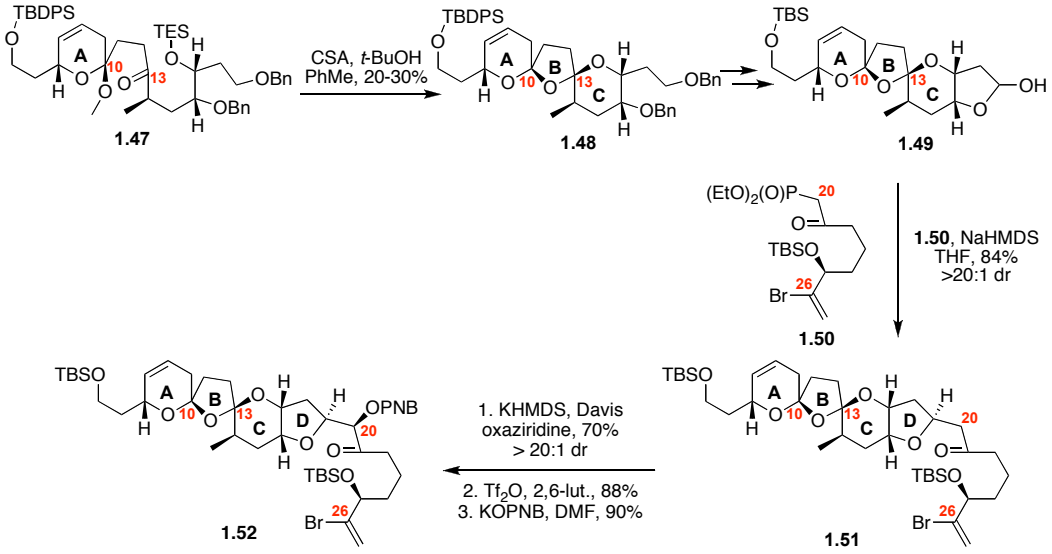
Unlike Nicolaou's synthesis, Evans' approach combined E ring fragment with C_{27}-C_{40} motif prior to the formation of FGHI ring system (Scheme 1.4). A chelate-controlled Mukaiyama aldol reaction was used to build C_{34} stereocenter, while a boron-mediated aldol coupling between methyl ketone **1.40** and aldehyde **1.37** constructed C_{26}-C_{27} bond. The FGHI ring system **1.43** was constructed via spontaneous ketalization and a spiroaminal formation. Addition of sulfone **1.44** to aldehyde **1.32** followed by a quench at -78ºC with pH5 buffer afforded two diastereomers. The undesired alcohol **1.45** was then converted to the desired C_{20}-diastereomer **1.46** via a Swern oxidation / $LiBH_4$ reduction sequence. Further elaboration including the desilylation and a Lindgren-Kraus oxidation (Pinnick oxidation)[20] yielded (+)-azaspiracid-1 in only 26 linear steps.



Scheme 1.4. Evans' Total Synthesis of (+)-Azaspiracid-1

1.2.4 The Carter Group

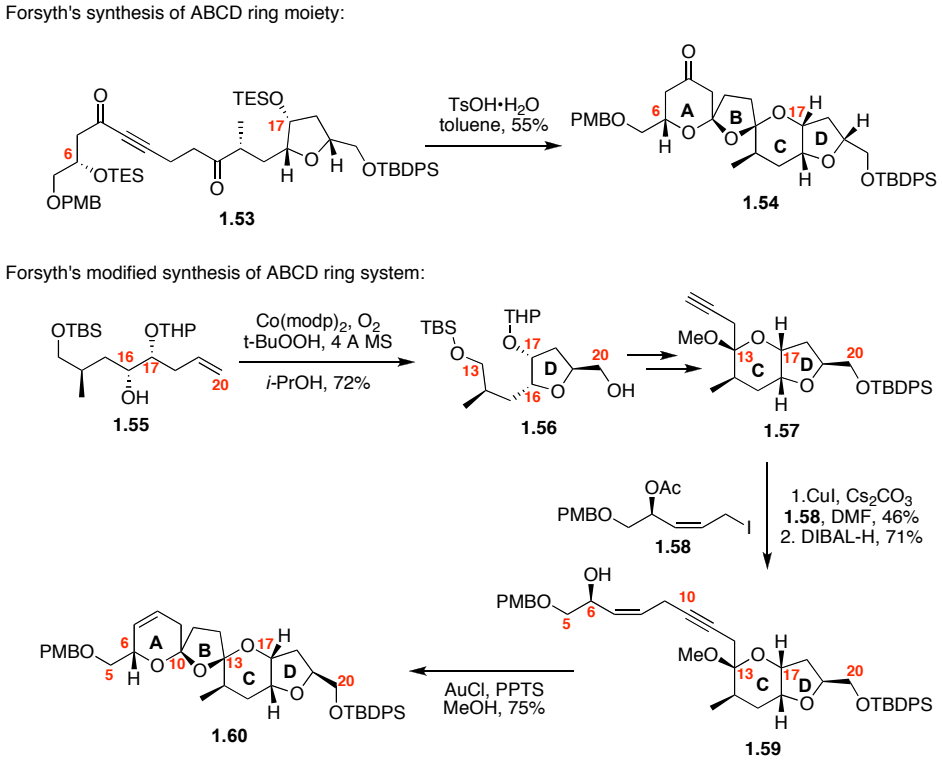
Since our first publication in 2000,[14a] our group have made significant contribution to the synthesis of azaspiracid-1.[4, 14] Our conclusion that the correct structure contained the epimeric stereochemistries at C_{14}, C_{16}, C_{17} and C_{20} was reported in 2004[4] – independently and concurrently to Nicolaou's efforts.[3] In 2006, we completed the C_1-C_{26} northern half of azaspiracid-1 (Scheme 1.5).[14f] When compound **1.47** was treated with CSA, *t*-BuOH / PhMe, the de-silylation and ketalization proceeded smoothly to give the transoidal bisspiroketal **1.48**. Two other highlights of our work are the highly diastereoselective tandem HWE reaction / intramolecular heteratom Michael addition to give compound **1.51** and the highly diastereoselective hydroxylation at C_{20} of ketone **1.51**. Our synthesis of C_{27}-C_{40} southern portion will be discussed in the following chapter.



Scheme 1.5. Carter's Synthesis of ABCD Ring Fragment

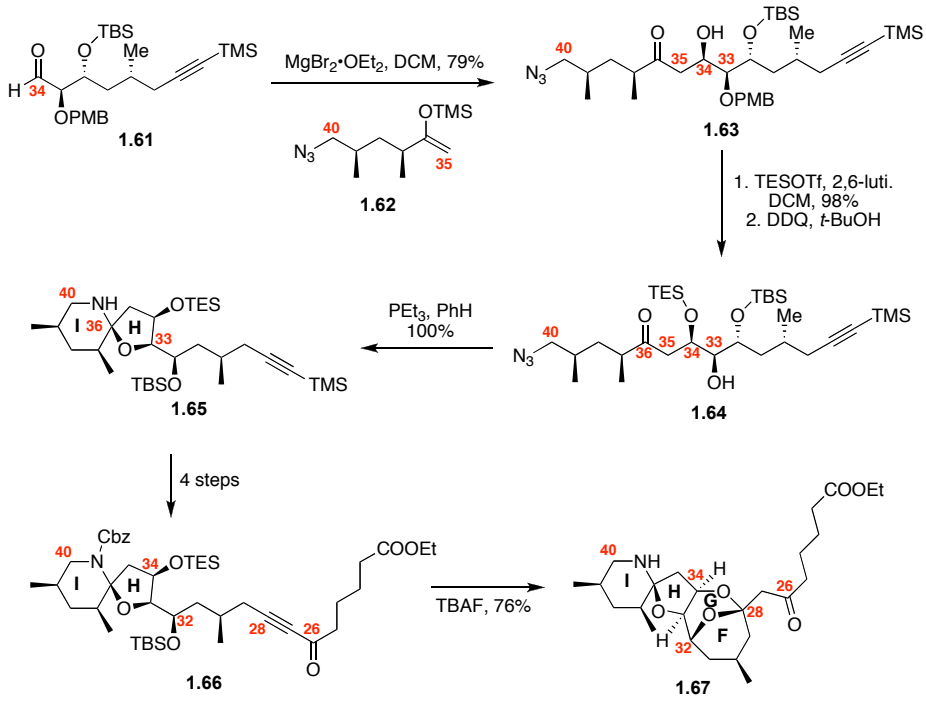
1.2.5. The Forsyth Group

Shortly after the elucidation of the structure of azaspiracid-1, Forsyth and co-workers reported a strategy for the synthesis of the ABCD ring trioxadisprioketal (Scheme 1.5).[17f] When ynedione **1.53** was treated with TsOH, selective cleavage of the C_6 and C_{17} TES group and the following trioxadispiroketal formation afforded the desired ABCD ring system in a highly diastereoselective manner. Later, a modified synthesis of C_5-C_{20} ABCD ring motif was developed.[17i] In the new strategy, the D ring was obtained from a cobalt-catalyzed oxyetherification. Exposure of enyne **1.59** to Au(I) catalyst led to the bis-spiroketal formation to yield the AB ring moiety.



Scheme 1.6. Forsyth's Strategy for the Synthesis of ABCD ring

In 2006, the Forsyth group reported the synthesis of C_{26}-C_{40} FGHI ring system (Scheme 1.7). The C_{34}-C_{35} bond was built from a Mukiyama type aldol coupling between **1.61** and **1.62**. PEt_3 mediated azide reduction also induced the spontaneous spiroaminal formation to afford HI ring. Finally, FG ring was installed via a fluoride initiated bis-conjugate addition of C_{32} and C_{34} hydroxyl groups upon the C_{28} Michael acceptor.[17h]

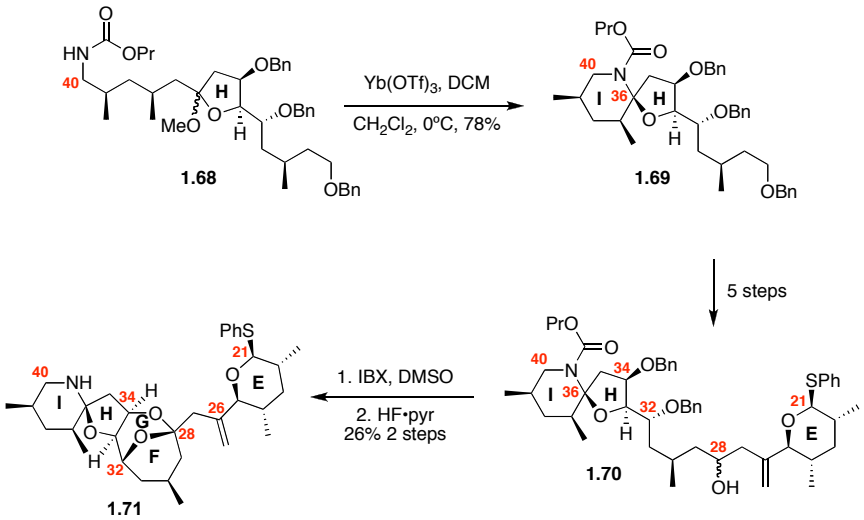


Scheme 1.7. Forsyth's Synthesis of C_{26}-C_{40} FGHI Ring Fragment

1.2.6 The Sasaki Group

In 2006, the Sasaki group published the synthesis of C_{21}-C_{40} EFGHI ring fragment (Scheme 1.8).[18e] The key steps included a $Yb(OTf)_3$-catalyzed

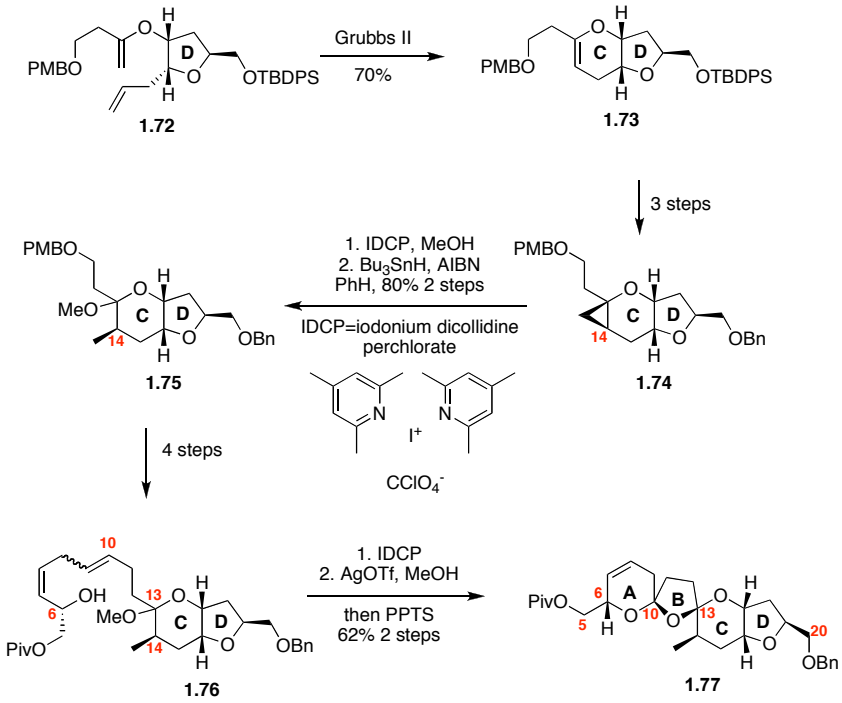
spiroaminal formation to give HI ring and a HF•Pyridine-mediated intramolecular ketalization to afford FG ring. Unfortunately, the C_{21}-C_{40} portion **1.71** was synthesized in only 0.025% overall yield.



Scheme 1.8. Sasaki's Approach for the Synthesis of C_{21}-C_{40} Portion

1.2.7 The Mootoo Group

More recently, the Mootoo group reported their approach for the synthesis of C_5-C_{20} ABCD ring motif (Scheme 1.9).[18h] After the formation of C ring via RCM, subsequent diastereoselective cyclopropanation and opening of the cyclopropane ring afforded C_{14} stereocenter. The ketalization initiated by iodonium dicollidine perchlorate (IDCP) and AgOTf gave the desired trioxadispiroketal **1.77**.



Scheme 1.9. Mootoo's Synthesis of ABCD Ring System

1.3 Conclusion

In summary, the intriguing structure and the unique bioactivity of marine toxin azaspiracid-1 have spurred considerable interests from the synthetic community. These efforts led to the correction of the originally proposed structure in 2004.[3] Subsequent studies resulted in Nicolaou's first-generation and second-generation total syntheses of (-)-azapisracid-1 with longest linear sequence of 50 and 39 steps, respectively. The enantiomer of (-)-azaspiracid-1, (+)-azaspriacid-1, was later synthesized by Evans and co-workers in only 26 linear steps. Several partial syntheses from the research groups including Carter, Forsyth, Sasaki,

Mootoo, *etc*. have also been reported. Despite all these achievements, there are still several problems such as understanding the controlling features in the formation of the polycyclic systems, more efficient combination of the northern and southern halves, *etc.* deserving more attention from the synthetic chemists. Herein, our endeavors toward the southern portion of azaspiracid-1 are described in the following chapter.

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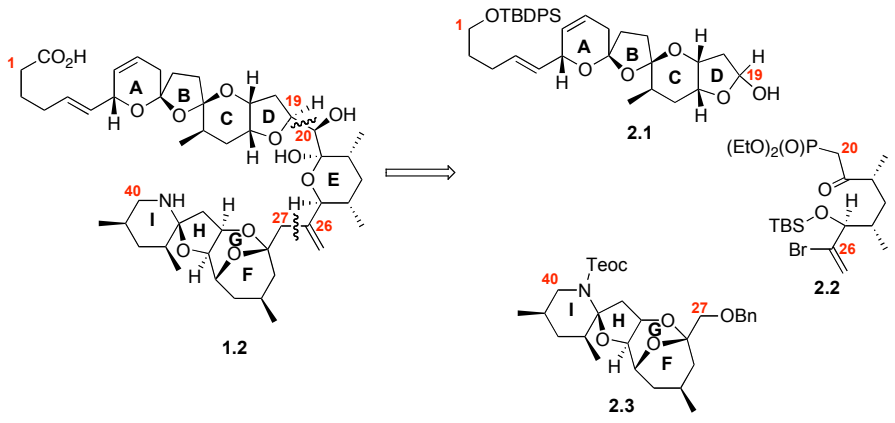
CHAPTER 2. STUDIES TOWARD THE SYNTHESIS OF C_{27}-C_{40} SOUTHERN PORTION OF AZASPIRACID-1

2.1 Retrosynthesis of Azaspiracid-1

As was shown in the previous chapter, the unique structural architecture present in azaspiracid-1 (20 stereocenters, 9 rings, 3 spirocenters) has attracted considerable synthetic attention. Our group were particularly drawn to this molecule by the unusual bisspiroketal ABCD ring moiety as well as the FGHI ring system containing the spiroaminal and ketal. Our retrosynthesis disconnected azaspiracid-1 into C_1-C_{19} ABCD ring northern fragment **2.1**, C_{20}-C_{26} motif **2.2**, and C_{27}-C_{40} FGHI ring southern portion **2.3** (Scheme 2.1). Our endeavors have led to the completion of both C_1-C_{19} and C_{20}-C_{26} subunits.[1] We also coupled these two substrates successfully to afford the C_1-C_{26} northern halves.[1g] Herein, the studies toward the synthesis of C_{27}-C_{40} southern portion will be discussed.[2]

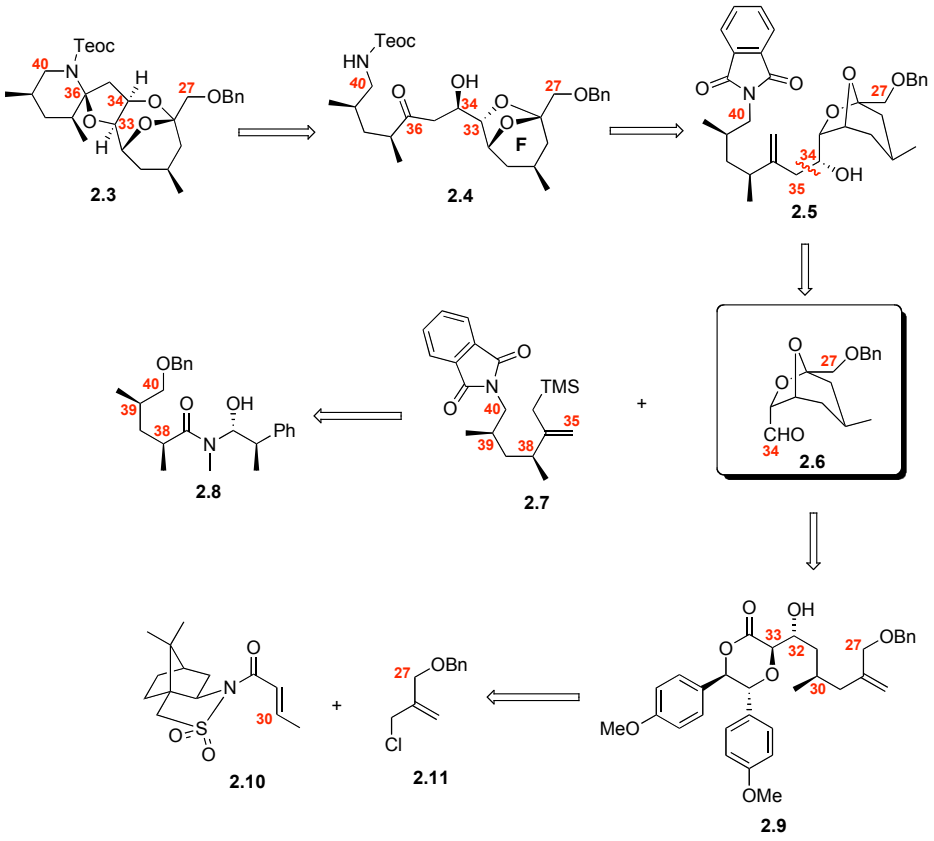


Scheme 2.1. Retrosynthetic Analysis of Azaspiracid-1

2.2 First-Generation Synthesis of Southern Portion

2.2.1 Retrosynthetic Analysis of C_{27}-C_{40} Southern Portion

Our initial retrosynthetic strategy for the C_{27}-C_{40} southern portion of azaspiracid-1 cleaved the FGHI ring system via a tandem ring arrangement and spiroaminal formation cascade (Scheme 2.2). Further disconnection at C_{34}–C_{35} linkage yielded allyl silane **2.7** and aldehyde **2.6.** To establish the correct C_{34} stereochemistry, this key coupling would need to proceed via a Cram-chelated intermediate.[3] The allyl silane portion would be available from the known Myers alkylation product **2.8**.[4] The aldehyde **2.6** could be accessible from the Andrus anti-aldol adduct **2.9**,[5] which in turn could be constructed from the known sultam **2.10**[6] and the chloride **2.11**.

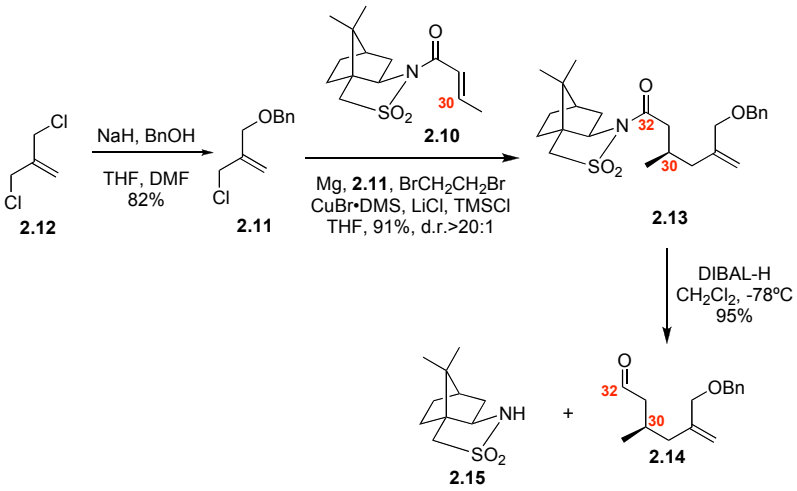


Scheme 2.2. Retrosynthesis of Southern Portion **2.3**

2.2.2 Synthesis of Aldehyde 2.14

Synthesis of the aldehyde **2.14**, the requisite precusor for the anti-aldol coupling, was accomplished in three steps (Scheme 2.3). Monobenzylation of dichloride **2.12**, followed by the cuprate addition on sultam **2.10** under similar conditions described by Paquette and Boulet,[7] generated the stereocenter at C_{30} with excellent diastereoselectivity (dr>20:1). It is noteworthy that the preparation of Grignard reagent from allylic chloride **2.11** has extremely low yield (0-10%) due to the undesired Wurtz-type coupling.[8] The side reaction was suppressed by

using activated Mg metal (Dry-stirring under inert atmosphere for 120 hours) and the yield was improved to 50%. When compound **2.13** was treated with DIBAL-H, aldehyde **2.14** was produced with the recovery of the sultam auxiliary **2.15**.

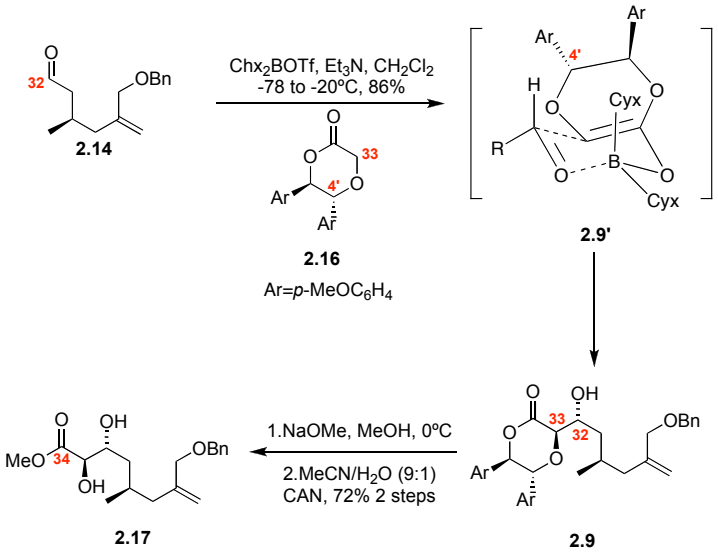


Scheme 2.3. Synthesis of Aldehyde **2.14**

2.2.3 Anti-aldol Coupling between Aldehyde 2.14 and Dioxane 2.16

With aldehyde **2.14** and the known dioxane **2.16**[5] in hand, we investigated the anti-aldol coupling (Scheme 2.4). Using the conditions described by Andrus and co-workers,[5] the reaction did not proceed to completion (40-50% conversion). Fortunately, we found that increasing the concentration of the reaction mixture to 0.5 M facilitated complete conversion. A proposed model for the observed stereochemical outcome is shown in transition-state **2.9'**. With the enolate locked in the *E*-configuration, the Zimmerman-Traxler aldol transition state[9] **2.9'** led to the *anti*-aldol adduct. The facial attack on the aldehyde is controlled by the

stereochemistry at $C_{4'}$. The attack at the less hindered face of the enolate generated the corresponding 32*R*, 33*R* stereocenters. Subsequent lactone ring opening and cleavage of the auxiliary with CAN yielded diol **2.17**.

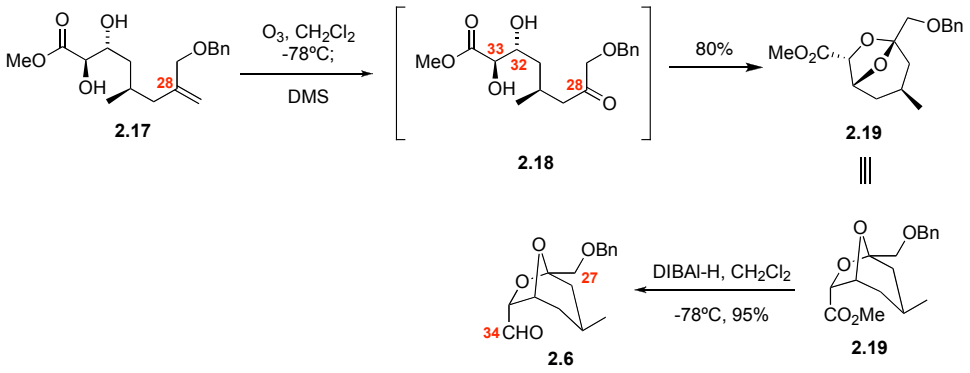


Scheme 2.4. Synthesis of Diol **2.17**

2.2.4 Synthesis of Bicyclic Aldehyde 2.6

After obtaining diol **2.17**, we shifted our focus to the key ketalization (Scheme 2.5). The [3.2.1] bicyclic ketal moiety was constructed through ozonolysis of **2.17** with DMS workup, which induced spontaneous C_{28}-ketal formation (Scheme 2.5). This ketalization process could be driven to completion by the addition of Amberlyst-15. Finally, reduction with DIBAL-H proceeded cleanly to give the aldehyde **2.6**. The stereochemistry of aldehyde **2.6** was

conclusively established through X-ray crystal structure assignment of the 2,4-dinitrohydrazone derivative **2.20** (Figure 2.1).



Scheme 2.5. Synthesis of Aldehyde **2.6**

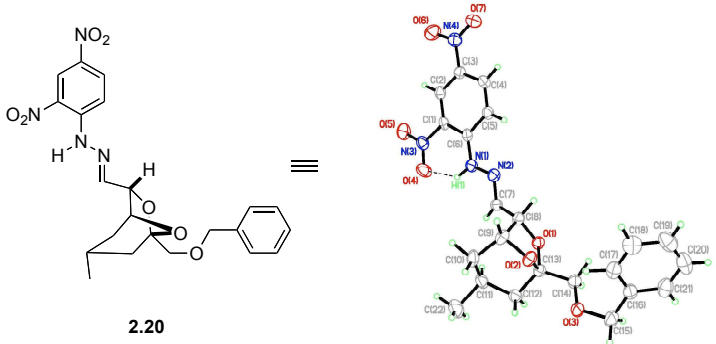
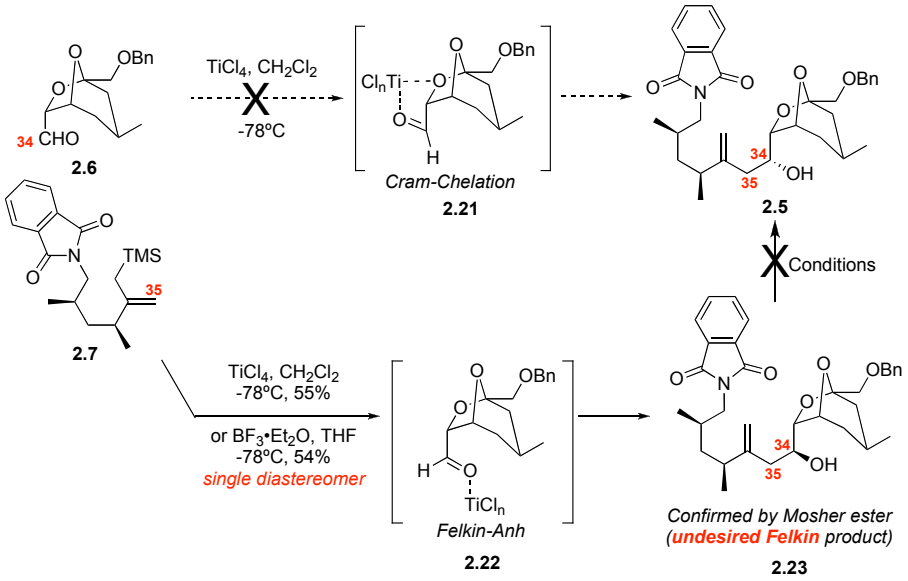


Figure 2.1. ORTEP Representation of 2,4-Dinitrohydrazone **2.20**

2.2.5 Aldol Coupling between Aldehyde 2.6 and Allyl Silane 2.7

Further investigation from our group[2] showed that Lewis acids ($TiCl_4$ or $SnCl_4$) promoted aldol reaction between aldehyde **2.6** and allyl silane **2.7** provided

the coupled material as a single diastereomer at C_{34} (Scheme 2.6). We had hypothesized that chelating Lewis acids such as titanium or tin[10] would proceed via the intermediate **2.21** to give the desired alcohol **2.5**. We were surprised to find, upon conversion of the intermediate into its Mosher ester,[11] that the C_{34} stereochemistry was in fact that of the undesired isomer. Further support for this assignment can be found in the fact that treatment of **2.7** with $BF_3{\cdot}Et_2O$ (a Lewis acid incapable of proceeding via intermediate **2.21**)[10] also gave alcohol **2.23**, again as a single diastereomer. Despite our considerable efforts to invert the C_{34} stereochemistry by Mitsunobu reaction or by oxidation-reduction sequence, we were unable to devise a viable route to invert the stereochemistry at C_{34}.



Scheme 2.6. Aldol Reaction between Allyl Silane **2.7** and Aldehyde **2.6**

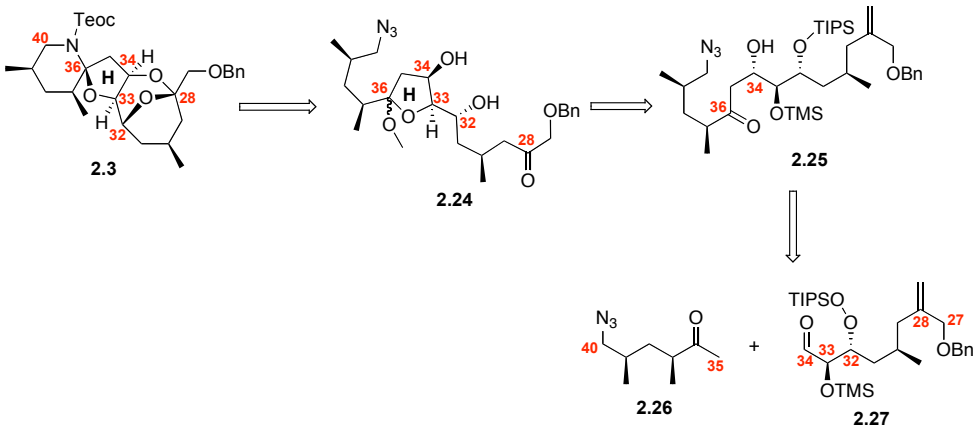
Although still under investigation, one possible explanation for the incapability to chelate might be the highly oxygenated area found in the bicyclic

aldehyde **2.6**. The three O atoms could trap the metal ion and the formation of the desired 5-membered chelation intermediate **2.21** would be prevented. The bulky bicyclic moiety also contributed to the steric congestion at C_{34}, which led to the inability to invert the C_{34} stereochemisty.

2.3 Second-Generation Synthesis of C_{27}-C_{40} Southern Portion

2.3.1 Modified Retrosynthesis of Southern Portion

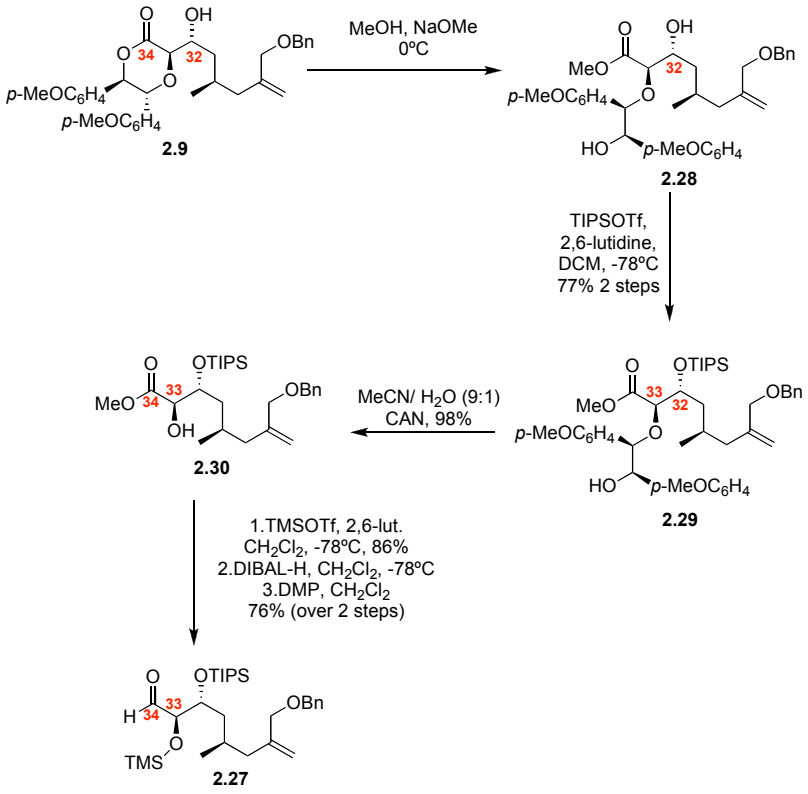
It would appear from our efforts that the encumbered nature of bicyclic moiety made it impossible to properly install the C_{34} stereogenic center. On the basis of this setback, we chose to revise our approach and the modified retrosynthesis was shown in Scheme 2.7. Subsequent ketalization and aminial formation were employed to build FGHI ring system. The C_{27}-C_{40} linear carbon backbone and the C_{34} stereochemistry would be constructed prior to the formation of polycyclic ring system. Using the new strategy, we could avoid the complexity caused by the bicyclic structure. Further cleavage at C_{34}-C_{35} linkage generated two key subunits, methyl ketone **2.26** and aldehyde **2.27**.



Scheme 2.7. Modified Retrosynthesis of C_{27}-C_{40} Southern Portion

2.3.2 Synthesis of Aldehyde 2.27

The synthesis of the aldehyde component **2.27** commenced from the previously made anti-aldol adduct **2.9**. Triisopropylsilylation of compound **2.9** did yield the corresponding silyl ether; however, methanolysis of the lactone proved unsuccessful. The TIPS ether decomposed upon treatment with NaH / MeOH. Fortunately, exposure of **2.9** to TIPSOTf and 2,6-lutidine at low temperature gave selectively the C_{32}-OTIPS product **2.28**. None of the corresponding benzyl OTIPS ether was observed, presumably due to the decreased electronic reactivity of the hydroxyl group. Finally, removal of auxiliary with CAN, C_{33} TMS protection, and subsequent conversion of methyl ester to aldehyde yielded the desired fragment **2.27**.

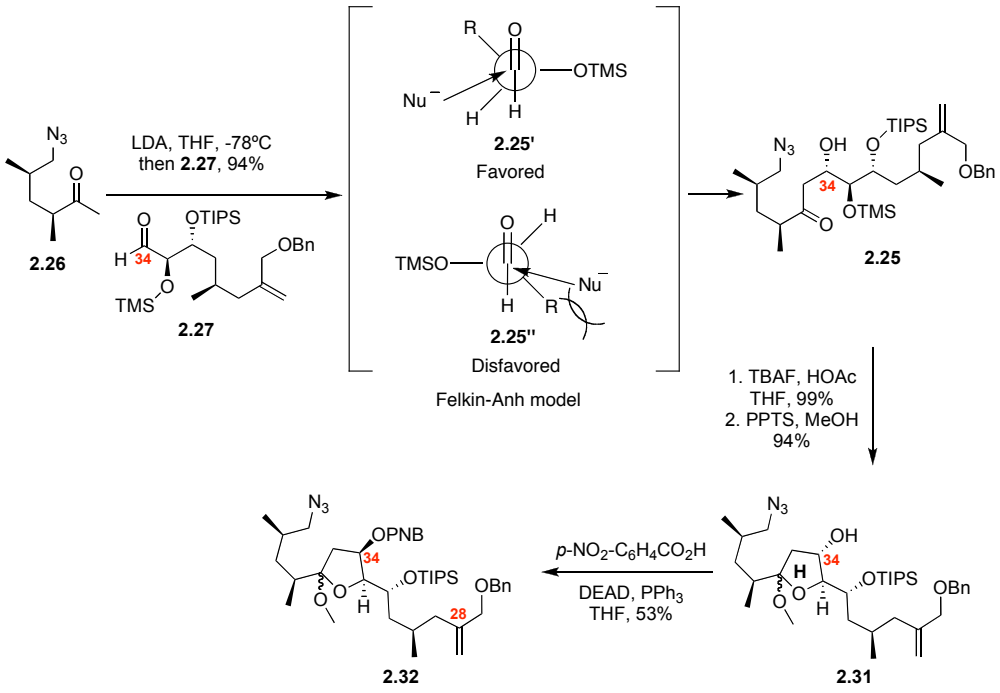


Scheme 2.8. Synthesis of Aldehyde **2.27**

2.3.3 Completion of C_{27}-C_{40} Southern Fragment

With the key intermediate aldehyde **2.27** in hands, we explored the aldol reaction to install C_{34} stereochemistry (Scheme 2.9).[2] The LDA-mediated aldol coupling between aldehyde **2.27** and the previously made methyl ketone **2.26**[2] generated undesired C_{34} stereocenter as a single diastereomer. The stereochemical outcome of the aldol reaction could be explained via Felkin-Anh model in which the α OTMS group is perpendicular to the carbonyl bond.[12] In this way, the $\sigma^*_{C\text{-}O}$ orbital is aligned parallel with the π orbital of the carbonyl group, allowing the

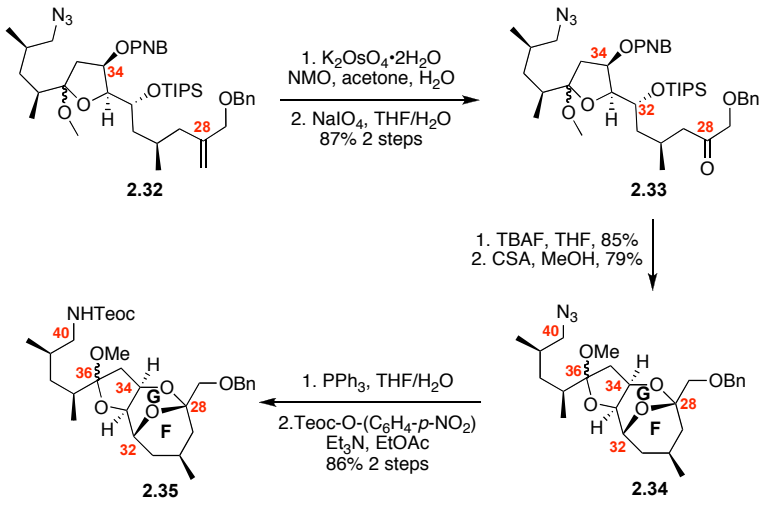
stabilization of the substrate through hyperconjugation. An attack by the enolate on the carbonyl center, in a Bürgi-Dunitz angle (*ca.* 107º relative to the oxygen-carbon double bond[13]) from the side of H (**2.25'**), resulted in the expected 34*S* stereocenter. In contrast, the nucleophilic addition from the side of the more bulky R (**2.25''**) is disfavored due to the increased steric interaction between the enolate and R. After the acid-catalyzed formation of H ring, we were gratified to find that C_{34} stereochemistry was inverted successfully using Martin's modified Mitsunobu conditions.[14]



Scheme 2.9. Installation of the C_{34} Stereocenter

With the setting of the correct C_{34} stereochemistry, we were able to construct the FG rings (Scheme 2.10). Since the PNB group is base labile, the basicity of TBAF was harnessed to simultaneously remove the TIPS at C_{32} and the

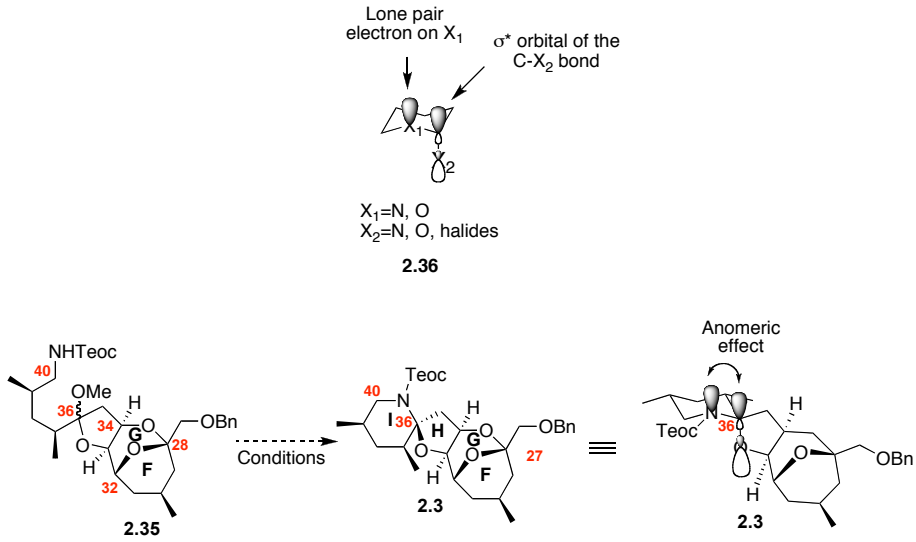
PNB group at C_{34}. The following acid-catalyzed ketalization afforded the desired FG rings. Subsequent azide reduction and Teoc protection yielded Teoc protected amine **2.35**.



Scheme 2.10. Formation of FG Rings

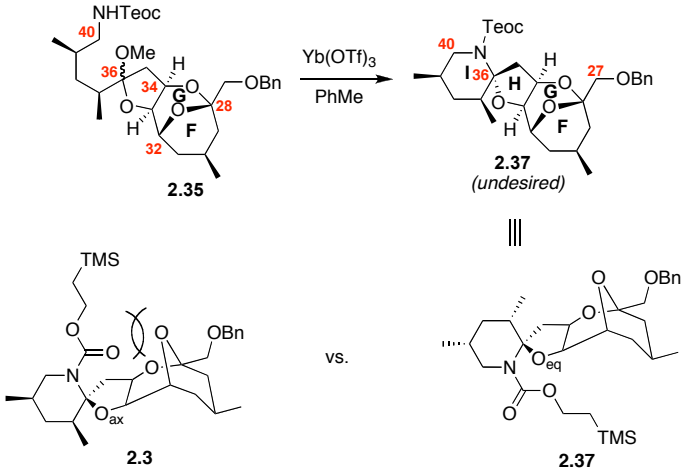
With the FGH rings now in place the next challenge was the formation of the spiroaminal functionality. We had envisioned the desired spiroaminal **2.3** to be the favored product (Scheme 2.11). Our postulation was primarily based on the anomeric effect,[15] a stereoelectronic effect that describes the tendency of heteroatomic substituents adjacent to a heteratom within a cyclohexane ring to prefer the *axial* orientation instead of the less hindered *equatorial* orientation that would be expected from steric considerations. The origins of the anomeric effect are proposed to be the hyperconjugation effects. When the C-X_2 bond is axial, an interaction between the axial lone pair electron on the heteratom and the σ^* orbital of the C-X_2 bond is possible. This interaction leads to

the delocalization of the unshared electrons and would help stabilizing the substrate. In spiroaminal **2.3**, the axial orientation of the C-O bond would be stabilized by the overlap between the axial lone pair electron on the N atom and the σ* orbital of the C-O bond.



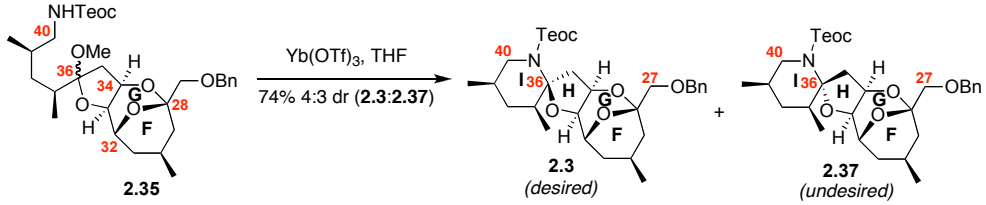
Scheme 2.11. Proposed Spiroaminal Formation

Interestingly, treatment of **2.35** with $Yb(OTf)_3$ in PhMe led to the rapid formation (30 min, room temperature) of a kinetic product **2.37** (Scheme 2.12). Careful analysis by 2D NMR spectroscopy revealed that **2.37** possessed the undesired stereochemistry at C_{36}. We did find that the formation of the non-anomeric **2.37** as the kinetic product to be surprising, as the anomerically stabilized axial orientation is typically kinetically favored as a result of a presumed lower transition-state energy. We attribute this unusual behavior to a severe steric interaction between the NTeoc group and the fused GH ring system.



Scheme 2.12. Formation of the Undesired Kinetic Product **2.37**

We next investigated the conditions that would lead to the thermodynamic product **2.3** (Scheme 2.13). Use of extended reaction times in PhMe resulted in the formation of a second compound, the desired anomeric diastereomer; however, decomposition was a competitive pathway under these conditions. Fortunately, use of an alternate solvent (THF) led to spiroaminal **2.3** as the major product (74% yield, **2.3**/**2.37** 4:3 ratio). The minor undesired compound could be recycled by resubmission to the $Yb(OTf)_3$ / THF conditions to generate the diastereomers in the same thermodynamic 4:3 ratio.



Scheme 2.13. Completion of the Synthesis of FGHI Ring System

2.4 Conclusion

In summary, we have successfully synthesized C_{27}-C_{40} FGHI ring fragment with a longest linear sequence of 21 steps. Although our 1st generation strategy led to the key [3.2.1] bicyclic ketal moiety via a spontaneous ketalization, the encumbered nature of bicyclic structure made it impossible to properly install the C_{34} stereogenic center. Our modified approach solved this problem by generating C_{34} stereocenter prior to the formation of polycyclic system and resulted in the completion of C_{27}-C_{40} southern half of azaspiracid. The key steps included a highly regioselective C_{32} TIPS protection, a Mitsunobu reaction to install the desired C_{34} stereocenter, and a $Yb(OTf)_3$-catalyzed spiroaminal formation.

2.5 References

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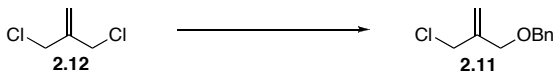
2.6 Experimental

General. Infrared spectra were recorded neat, unless otherwise indicated and are reported in cm^{-1}. ^{1}H NMR spectra were recorded in deuterated solvents and are reported in ppm relative to tetramethylsilane and referenced internally to the residually protonated solvent. ^{13}C NMR spectra were recorded in deuterated solvents and are reported in ppm relative to tetramethylsilane and referenced internally to the residually protonated solvent.

Routine monitoring of reactions was performed using EM Science DC-Alufolien silica gel, aluminum-backed TLC plates. Flash chromatography was performed with the indicated eluents on EM Science Gedurian 230-400 mesh silica gel.

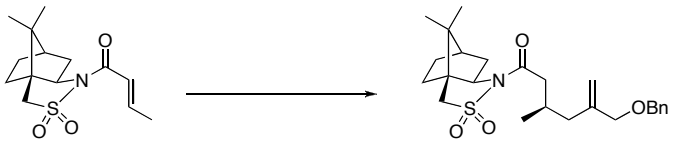
Air and / or moisture sensitive reactions were performed under usual inert atmosphere conditions. Reactions requiring anhydrous conditions were performed under a blanket of argon, in glassware dried in an oven at 120°C or by a Bunsen flame, then cooled under argon. Solvents and commercial reagents were purified in accord with Perrin and Armarego[1] or used without further purification.



2.12 **2.11**

Allyl chloride 2.11: To a stirred slurry of pentane-washed NaH (2.05 g, 51.3 mmol, 60% in mineral oil) in THF (70 mL) was added BnOH (5.64 g, 5.4

mL, 52.5 mmol). After 30 min, DMF (15 mL) was added and the reaction mixture was warmed up to reflux. After 30 min, the reaction was allowed to cool to rt. The resulted mixture was then added dropwise to a solution of 3-chloro-2-chloromethyl-1-propene (3.77 g, 3.5 mL, 30.2 mmol) in THF (20 mL) over 1 h at rt. After another 16 h, the reaction mixture was quenched with H_2O (50 mL) and extracted with ether-pentane (1:1, 3 X 50 mL). The organic phase was washed with water (50 mL) and sat. aq. NaCl (50 mL). The dried extract ($MgSO_4$) was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 2-5% Et_2O / Pentane, to give the known allyl chloride **2.11**[2] (4.86 g, 24.8 mmol, 82%) as a colorless oil: IR (neat) 3087, 3064, 3031, 2924, 2855, 1496, 1453, 1097, 1075, 1028, 924, 736, 697 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.28-7.36 (m, 5H), 5.33 (d, J = 0.7 Hz, 1H), 5.28 (d, J = 1.2 Hz, 1H), 4.53 (s, 2H), 4.14 (d, J = 0.7 Hz, 2H), 4.13 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.4, 138.4, 128.8, 128.1(2), 117.3, 72.8, 70.7, 45.6.



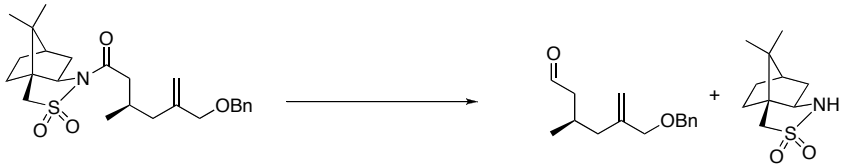
2.10 **2.13**

Sultam 2.13: Following the similar procedure described by Paquette,[3] Mg (8.0 g, 333 mmol) was stirred vigorously at rt in a dry flask under Ar. After 120 h, when black coating formed inside the flask, THF (100 mL) and 1,2-dibromoethane (1.30 g, 0.6 mL, 6.9 mmol) were added sequentially. After 30 min, a solution of allyl chloride **2.11** (6.5 g, 33.2 mmol) in THF (25 mL) was added slowly to the Mg

slurry over 5 h. The resulted mixture was stirred overnight at rt to give 130 mL Grignard reagent (0.126 M, 50%) as gray solution. The concentration of the Grignard reagent was determined by the titration using menthol in the presence of 1,10-phenonthroline.[4]

Separately, CuBr•SMe_2 (3.39 g, 16.5 mmol) and LiCl (0.75 g, 17.7 mmol) were dissolved in THF (25 mL) and added to the Grignard solution at -78°C *via* syringe. TMSCl (1.81 g, 2.1 mL, 16.7 mmol) was then added followed by a solution of sultam **2.10**[5] (3.2 g, 11.3 mmol) in THF (25 mL). After another 90 min, the reaction was quenched with aq. NH_4Cl-NH_4OH (9:1, pH 9, 20 mL), warmed to rt and partitioned between ether (200 mL) and water (100 mL). The aqueous layer was extracted with EtOAc (3 X 100 mL). The organic phase was washed with sat. aq. NaCl (100 mL). The dried extract ($MgSO_4$) was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 20% EtOAc / Hexanes, to give the sultam **2.13** (4.57 g, 10.3 mmol, 91%) as a colorless oil: $[\alpha]_D^{23}$ = -29.7 (*c* 1.2, $CHCl_3$); IR (neat) 2959, 2881, 1695, 1455, 1330, 1217, 1134, 1116, 1058 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.33-7.44 (m, 5H), 5.15 (s, 1H), 4.99 (s, 1H), 4.53 (dd, *J* = 13.4, 12.1 Hz, 2H), 4.00 (dd, *J* = 17.1, 12.9 Hz, 2H), 3.90 (t, *J* = 6.3 Hz, 1H), 3.48 (dd, *J* = 26.0, 13.9 Hz, 2H), 2.79 (dd, *J* = 16.1, 5.8 Hz, 1H), 2.53 (dd, *J* = 16.1, 7.6 Hz, 1H), 2.30-2.40 (m, 1H), 2.02-2.17 (m, 4H), 1.86-1.98 (m, 3H), 1.35-1.46 (m, 2H), 1.00 (d, *J* = 6.3 Hz, 3H), 0.99 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.8, 144.4, 138.9, 128.7, 128.0, 127.9, 114.1, 73.1, 72.4, 65.6, 53.4,

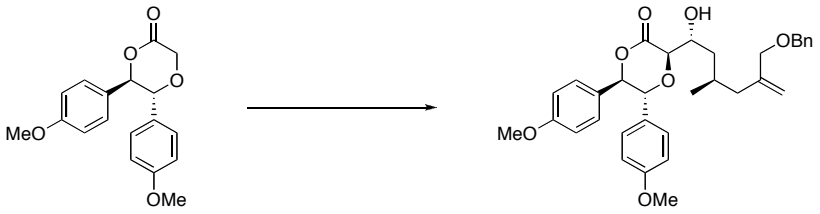
48.7, 48.1, 45.0, 42.9, 41.2, 39.0, 33.3, 28.4, 26.9, 21.2, 20.3; HRMS (ES^+) calcd. for $C_{25}H_{36}NO_4S$ (M+H) 446.2365, found 446.2337.



2.13 **2.14** **2.15**

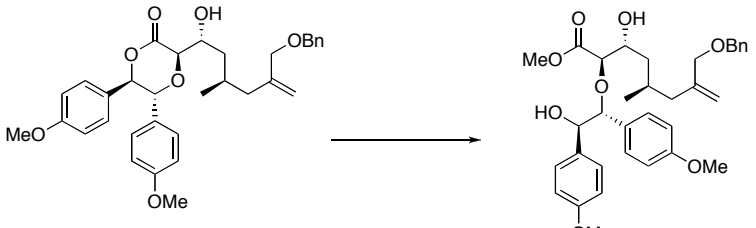
Aldehyde 2.14: To a stirred solution of sultam **2.13** (12.50 g, 28.1 mmol) in CH_2Cl_2 (146 mL) at -78°C was added DIBAL-H (58 mL, 58.0 mmol, 1.0 M in CH_2Cl_2) dropwise over 25 min. After 2 h, the reaction was carefully quenched with methanol (2.0 mL) and poured into aq. sodium potassium tartrate (250 mL, 10%) at rt. The reaction flask was rinsed with an addition portion of CH_2Cl_2 (150 mL). After 3.5 h, the aqueous layer was extracted with CH_2Cl_2 (3 X 100 mL). The dried extract ($MgSO_4$) was concentrated *in vacuo*. The oil was dissolved in a solution of 10% EtOAc / Hexanes solution (40 mL) and placed in the refrigerator to induce crystallization. After 16 h, the crystals were filtered (5% EtOAc / Hexanes rinse) to yield the recovered auxiliary **2.15** (4.38 g, 20.4 mmol) and the mother liquor was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 10-30% EtOAc / Hexanes, to give the aldehyde **2.14** (5.81 g, 26.7 mmol, 95%). Further elution with 75% EtOAc / Hexanes gave additional auxiliary **2.15** (1.00 g, 4.65 mmol, 89% combined yield). **2.14**: $[\alpha]_D^{23}$ = +3.9 (*c* 1.0, $CHCl_3$); IR (neat) 2956, 2926, 2851, 2719, 1723, 1455, 1095, 1073 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.74 (dd, *J* = 2.4, 1.6 Hz, 1H), 7.28-7.40 (m, 5H), 5.14 (s, 1H), 4.94 (s, 1H), 4.50 (s, 2H), 3.95 (s, 2H), 2.53 (ddd, *J* = 15.3, 4.0 and 1.7

Hz, 1H), 2.16-2.32 (m, 2H), 2.00-2.13 (m, 2H), 0.96 (d, J = 6.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 203.0, 144.2, 138.7, 128.8, 128.1, 128.0, 114.5, 73.1, 72.5, 51.0, 41.4, 26.7, 20.5; HRMS (ES^+) calcd. for $C_{15}H_{20}O_2Na$ (M+Na) 255.1361, found 255.1366.



Andrus aldol adduct 2.9: To a solution of dioxalone **2.16**[6] (6.25 g, 19.90 mmol) in CH_2Cl_2 (20 mL) at -78°C was added Et_3N (3.19 g, 4.4 mL, 31.58 mmol). After 3 min, a solution of Chx_2BOTf[7] (28.0 mL, 28.00 mmol, 1.0 M in Hexanes) was added dropwise over 15 min. After 140 min, a solution of the aldehyde **2.14** (5.04 g, 23.10 mmol) in CH_2Cl_2 (5 mL, precooled) was added *via* cannula. The aldehyde flask was rinsed with an additional portion of CH_2Cl_2 (2 X 0.75 mL, precooled). After 10 min, the reaction flask was transferred to the freezer (approximately -30°C). After 14 h, the reaction was quenched by the addition of MeOH (15 mL). The solution was then poured into a stirring solution of aq. pH 7 phosphate buffer (100 mL) at rt. The reaction flask was rinsed with an additional portion of CH_2Cl_2 (75 mL). To the stirring solution was then added H_2O_2 (20 mL, 30% aqueous). After 90 min, the reaction mixture was diluted with sat. aq. NaCl (100 mL) and CH_2Cl_2 (100 mL) and extracted with CH_2Cl_2 (3 X 100 mL). The organic layer was then washed with NaCl (200 mL) and the aqueous layer was

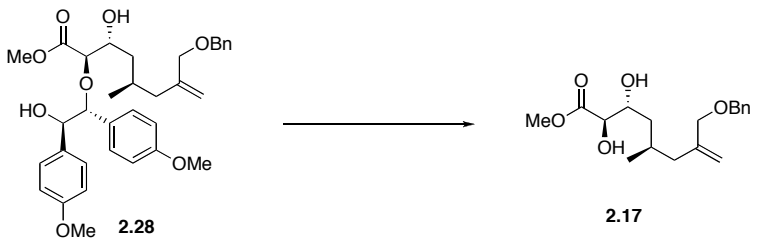
back extracted with CH_2Cl_2 (2 X 100 mL). The dried extract ($MgSO_4$) was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 25-50% EtOAc / Hexanes to give **2.9** (9.10 g, 17.11 mmol, 86%) as a colorless oil: $[\alpha]_D^{23}$ = +28.4 (*c* 1.0, CH_3CN); IR (neat) 3426, 2956, 2930, 2838, 1740, 1614, 1515, 1455, 1249, 1177, 1029 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.27-7.36 (m, 5H), 6.96 (dd, *J* = 8.7, 6.9 Hz, 4H), 6.75 (d, *J* = 8.1 Hz, 4H), 5.35 (d, *J* = 9.3 Hz, 1H), 5.07 (s, 1H), 4.96 (d, *J* = 9.3 Hz, 1H), 4.93, (s, 1H), 4.47 (m, 3H), 4.26 (br s, 1H), 3.94 (dd, *J* = 22.0, 12.6 Hz, 2H), 3.75 (s, 3H), 3.74 (s, 3H), 3.54-3.62 (m, 1H), 3.26 (br s, 1H), 2.30 (dd, *J* = 13.6, 4.6 Hz, 1H), 1.66-1.98 (m, 6H), 1.49-1.58 (m, 1H), 1.21-1.31 (m, 2H), 0.94 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.3, 160.4, 160.2, 145.0, 138.7, 129.2, 129.0, 128.8, 128.4, 128.1, 128.0, 127.1, 114.2, 114.1, 113.8. 85.6, 78.2, 76.9, 73.3, 72.5, 72.0, 55.6, 41.4, 40.7, 27.8, 21.1; HRMS (FAB^+) calcd. for $C_{33}H_{38}O_7$ (M+) 546.2618, found 546.2641.



2.9 **2.28**

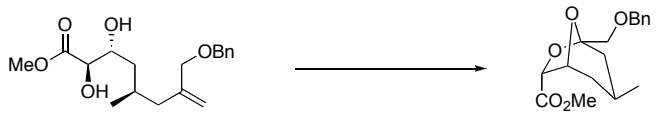
Methyl ester 2.28: To a stirred solution of aldol product **2.9** (9.10 g, 17.1 mmol) in dry MeOH (160 mL) at 0°C was added NaH (72 mg, 1.80 mmol, 60% in mineral oil). After 25 min, the reaction was quenched with sat. aq. NH_4Cl (10 mL). The MeOH was then removed *in vacuo* and the residue was diluted with sat. aq. NaCl (200 mL) and extracted with EtOAc (3 X 150 mL). The dried extract

($MgSO_4$) was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 20-66% EtOAc / Hexanes to give **2.28** (17.1 mmol) as a glassy semi-solid. The highly glassy nature of **2.28** made effective removal of all residual solvent impossible on large scale. A small amount of **2.28** (50 mg) was placed under high vacuum overnight to provide an analytically pure sample for characterization, but the glassy semi-solid was used in the subsequent step without complete removal of solvents. **2.28**: $[\alpha]_D^{23}$ = +55.7 (*c* 1.5, $CHCl_3$); IR (neat) 3423, 2954, 2927, 2837, 1734, 1613, 1514, 1455, 1250, 1176, 1031 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.40-7.30(m, 5H), 7.01-6.96 (m, 4H), 6.80-6.76 (m, 4H), 5.10 (s, 1H), 4.95 (s, 1H), 4.94 (d, *J* = 9.3 Hz, 1H), 4.50-4.48 (m, 3H), 4.30-4.26 (m, 1H), 3.96 (dd, *J* = 19.2, 12.6 Hz, 2H), 3.79 (s, 3H), 3.78 (s, 3H), 3.66 (d, *J* = 1.7 Hz, 1H), 3.52 (s, 3H), 3.01 (d, *J* = 4.8 Hz, 1H), 2.32 (dd, *J* = 13.8, 4.8 Hz, 1H), 2.05-1.65 (m, 4H), 0.97 (d, *J* = 6.6 Hz, 3H); ^{13}C (75 MHz, $CDCl_3$): δ 171.3, 159.7, 159.5, 145.0, 138.6, 132.0, 129.7, 129.6, 128.8, 128.7, 128.2, 128.1, 114.0, 113.8, 113.7, 89.7, 82.2, 78.7, 73.3, 72.5, 70.8, 55.6, 52.1, 40.9, 40.0, 28.0, 21.3; HRMS (FAB^+) calcd. for $C_{34}H_{42}O_8Na$ (M+Na) 601.2777, found 601.2801.



Diol 2.17: To a vigorously stirred solution of methyl ester **2.28** (0.82 g, 1.42 mmol) in MeCN-H_2O (10:1, 40 mL) at 0°C was added CAN (1.00 g, 1.82

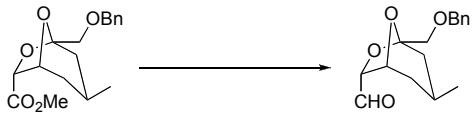
mmol) portionwise over 90 min. After a further 30 min, the reaction mixture was diluted with EtOAc (100 mL), the organic phase washed with sat. aq. NaCl (100 mL), and the aqueous layer re-extracted with EtOAc (3 X 100 mL). The dried extract ($MgSO_4$) was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 25-50% EtOAc / Hexanes, to give diol **2.17** (330 mg, 1.02 mmol, 72% 2 steps) as a colorless oil: $[\alpha]_D^{23}$ = -3.6 (*c* 1.7, $CHCl_3$); IR (neat) 3419, 2923, 2852, 1738, 1454, 1199, 1096 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.29-7.41 (m, 5H), 5.13 (s, 1H), 4.97 (s, 1H), 4.53 (d, *J* =1.8 Hz, 2H), 4.23 (dd, *J* = 5.6, 3.6 Hz, 1H), 3.94-4.05 (m, 3H), 3.82 (s, 3H), 2.40 (d, *J* = 6.5 Hz, 1H), 2.20-2.28 (m, 1H), 1.83-1.94 (m, 2H), 1.50 (ddd, *J* = 14.7, 9.3 and 5.5 Hz, 1H), 1.40 (ddd, *J* = 13.0, 7.3 and 4.2 Hz, 1H), 0.97 (d, *J* = 6.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.5, 144.9, 138.7, 128.8, 128.2, 128.1, 114.0, 74.5, 73.3, 72.4, 71.8, 53.0, 41.0, 39.4, 28.1, 21.1; HRMS (FAB^+) calcd. for $C_{18}H_{27}O_5$ (M+H) 323.1856, found 323.1854.



2.17 **2.19**

Bicyclic ester 2.19: To a stirred solution of methyl ester **2.17** (78 mg, 0.24 mmol) in CH_2Cl_2-MeOH (1:1, 4 mL) at –78°C was bubbled ozone until a faint blue color was observed (4 min). At this point, the reaction mixture was briefly degassed with argon. Next, DMS (0.34 g, 0.40 mL, 5.4 mmol) was added. After 10 min, the cold bath was removed and the solution was allowed to warm to rt. The

solvents were removed *in vacuo* followed by the addition of CH_2Cl_2 (4 mL). The resulted solution was stirred with amberlyst-15 resin (*ca*. 100 mg) until the reaction was complete by TLC (1-3 h). The reaction mixture was filtered through Celite, concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 25-50% EtOAc / Hexanes, to give the bicyclic ketal **2.19** (59 mg, 0.193 mmol, 80%) as a colorless oil: $[\alpha]_D^{23}$ = +47.2 (*c* 0.25, $CHCl_3$); IR (neat) 2954, 2922, 2870, 2851, 1762, 1732, 1454, 1438, 1206, 1110, 1073 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.27-7.38 (m, 5H), 4.73-4.77 (m, 1H), 4.63 (dd, *J* = 20.6, 12.2 Hz, 2H) overlaps with 4.63 (d, *J* = 6.0 Hz, 1H), 3.81 (s, 3H), 3.58 (dd, $J_1 = J_2$ = 10.3 Hz, 2H), 2.08-2.21 (m, 1H), 1.90 (dd, *J* = 13.6, 5.7 Hz, 1H), 1.71 (dd, *J* = 14.1, 5.5 Hz, 1H), 1.45 (dd, *J* = 13.4, 11.4 Hz, 1H) overlaps with 1.43-1.55 (m, 1H), 0.90 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.0, 138.3, 128.8, 128.2, 128.1, 109.8, 78.4, 74.1, 72.9, 52.6, 39.7, 34.5, 23.5, 22.1; HRMS (FAB^+) calcd. for $C_{17}H_{25}O_5$ (M+H) 307.1545, found 307.1541.



2.19 **2.6**

Aldehyde 2.6: To a stirred solution of methyl ester **2.19** (59 mg, 0.18 mmol) in CH_2Cl_2 (1.3 mL) was added DIBAL-H (0.27 mL, 0.27 mmol, 1.0 M in CH_2Cl_2) at –78°C. After 75 min, the reaction was quenched by the addition of methanol (0.1 mL) at and poured into aq. sodium potassium tartrate (10 mL, 10%) at rt. The reaction flask was rinsed with an additional portion of CH_2Cl_2 (2 mL).

After 2 h, the reaction mixture was extracted with ether (3 X 25 mL) and the organic phase washed with water (25 mL) and sat. aq. NaCl (25 mL). The dried extract ($MgSO_4$) was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 25-50% EtOAc / Hexanes, to give aldehyde **2.6** (47.5 mg, 0.172 mmol, 95%) as a colorless oil: $[\alpha]_D^{23}$ = +23.3 (*c* 1.6, $CHCl_3$); IR (neat) 2957, 2922, 2851, 1731, 1455, 1260, 1104, 1070, 1027 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 10.03 (d, *J* = 1.1 Hz, 1H), 7.27-7.37 (m, 5H), 4.74-4.78 (m, 1H), 4.65 (s, 2H), 4.42 (d, *J* = 5.5 Hz, 1H), 3.59 (dd, *J* = 13.2, 10.6 Hz, 2H), 1.90 (dd, *J* = 13.3, 5.5 Hz, 1H), 1.73-1.86 (m, 1H), 1.66 (dd, *J* = 14.3, 5.7 Hz, 1H), 1.45 (dd, *J* = 13.5, 10.4 Hz, 1H) overlaps with 1.52 (dd, *J* = 12.2, 3.0 Hz, 1H), 0.94 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 200.9, 138.2, 128.8, 128.2(2), 109.7, 84.4, 74.2, 73.0, 39.6, 33.9, 25.1, 21.9; HRMS (CI^+) calcd. for $C_{16}H_{21}O_4$ (M+H) 277.1440, found 277.1437.

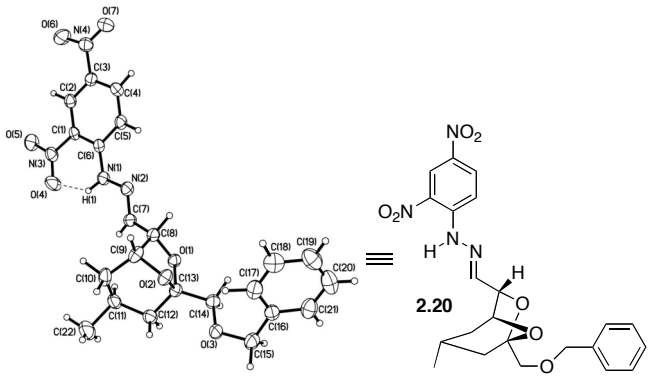
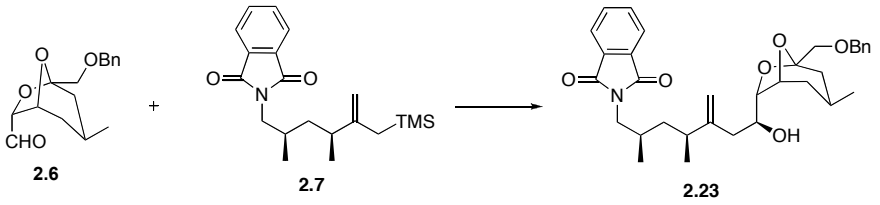
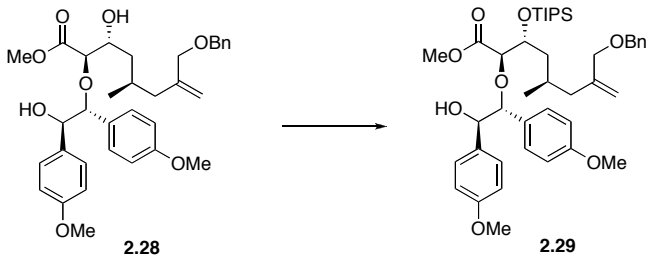


Figure 1. ORTEP Representation of 2,4-Dinitrohydrazone **2.20**[8]



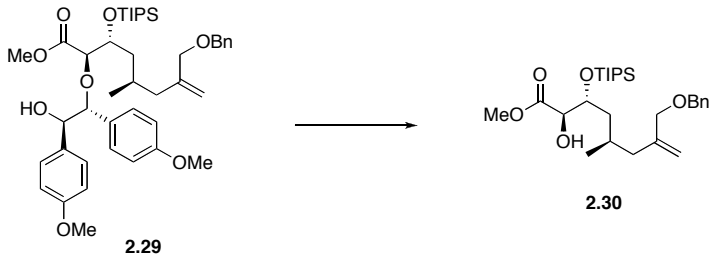
Coupled product 2.23: To a stirred solution of aldehyde **2.6** (42.6 mg, 0.154 mmol) in CH_2Cl_2 (3.0 mL) at -78°C was added BF_3•Et_2O (23.8 mL, 0.184 mmol). The resulted faintly pink solution was stirred for 5 min before the addition of allyl silane **2.7** (163 mg, 0.475 mmol) in CH_2Cl_2 (0.5 mL). After 10 min, the reaction was quenched with aq. pH 7 buffer (3 mL) and extracted with ether (3 x 5 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 10 - 30% EtOAc / Hexanes, to give product **2.23** (45.6 mg, 0.083 mmol, 54%) as colorless oil: $[\alpha]_D^{23}$ = + 37.3 (*c* 4.2, $CHCl_3$); IR (neat) 3488, 2963, 2933, 2860, 1767, 1711, 1449, 1393, 1109, 1066, 1015, 911, 756, 722 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.84 – 7.87 (m, 2H), 7.72 – 7.75 (m, 2H), 7.30 – 7.39 (m, 5H), 4.94 (s, 1H), 4.93 (s, 1H), 4.68 (d, *J* = 12.0 Hz, 1H), 4.64 (d, *J* = 12.4 Hz, 1H), 4.55 (m, 1H), 3.99 (t, *J* = 10.0 Hz, 1H), 3.79 (dd, *J* = 9.2, 4.0 Hz, 1H), 3.48 – 3.59 (m, 4H), 2.71 (d, *J* = 14.4 Hz, 1H), 2.37 – 2.43 (m, 1H), 1.97 – 2.20 (m, 5H), 1.84 (dd, *J* = 13.2, 6.0 Hz, 1H), 1.42 – 1.59 (m, 3H), 1.19 – 1.25 (m, 1H), 1.13 (d, *J* = 6.8 Hz, 3H), 0.96 (d, *J* = 6.8 Hz, 3H), 0.93 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.7, 150.1, 138.1, 133.9, 131.9, 128.3, 127.7, 127.5, 123.2, 112.0, 107.6, 82.7, 76.6, 73.6, 73.3, 67.8, 44.0, 40.9, 40.6, 39.4, 37.7, 33.1, 30.4, 24.4, 22.1, 20.8, 18.0; HRMS (FAB^+) calcd. for $C_{33}H_{42}NO_6$ (M+H) 548.3012, found 548.3027.

MTPA esters: To a solution of **2.23** (20 mg, 0.058 mmol) in CH_2Cl_2 (1 mL) was sequentially added DMAP (71.2 mg, 0.58 mmol) and (*R*) or (*S*)-(+)-α-methoxy-α-trifluoromethylphenylacetyl chloride (73.2 mg, 54.3 µL, 0.29 mmol). After 10 min, the solution was evaporated and the residue was loaded directly onto silica gel and purified by chromatography, eluting with 2 - 10% EtOAc / Hexanes, to give product **(*S*)-** or **(*R*)- MTPA esters** (68-72%) as colorless oils. ^{1}H NMR Difference in ppm [(*S*)-Mosher Ester – (*R*)-Mosher ester, $CDCl_3$, $CDCl_3$, 300 MHz NMR] H_{32}: 4.030 – 3.910 = +0.120, H_{33}: 4.031 – 4.210 = +0.179, H_{35}: 2.7215 – 2.7655 = -0.044, $H_{36'}$: 4.792 – 4.877 = -0.085, $H_{36'}$: 4.779 – 4.877 = -0.098.



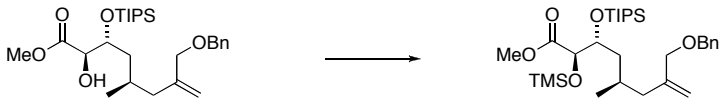
TIPS ether 2.29: To a stirred solution of methyl ester **2.28** (9.87 g, 17.1 mmol) in CH_2Cl_2 (150 mL) at -78ºC was sequentially added 2,6-lutidine (4.06 g, 4.4 mL, 37.9 mmol) and TIPSOTf (5.93 g, 5.2 mL, 19.3 mmol). An additional portion of TIPSOTf (343 mg, 0.3 mL, 1.11 mmol) was added after 25 min. After an additional l0 min, the reaction was quenched with MeOH (1 mL) followed by the addition of sat. aq. $NaHCO_3$ (200 mL) and extracted with CH_2Cl_2 (3 X 100 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 10-25% EtOAc / Hexanes, to give

2.29 (9.68 g, 13.2 mmol, 77%) as a colorless oil: $[\alpha]_D^{23}$ = +15.7 (*c* 0.88, $CHCl_3$); IR (neat) 3567, 2946, 2866, 1757, 1733, 1612, 1514, 1249, 1173 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.37-7.35 (m, 5H), 6.95-6.91 (dd, *J* = 2.1, 8.7 Hz, 4H), 6.71-6.67 (dd, *J* = 2.1, 8.7 Hz, 4H), 5.17 (s, 1H), 4.98 (s, 1H), 4.71 (d, *J* = 8.4 Hz, 1H), 4.52 (s, 2H), 4.45 (d, *J* = 8.7 Hz, 2H), 4.17 (d, *J* = 1.8 Hz, 1H), 3.97 (s, 2H), 3.92 (s, 1H), 3.75 (s, 3H), 3.74 (s, 3H), 3.50 (s, 3H), 2.15-2.05 (m, 2H), 1.97-1.90 (m, 1H), 1.70-1.60(m, 1H), 1.44-1.37 (m, 1H), 1.13 (s, 21H), 0.90 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 159.2, 158.9, 144.3, 138.5, 131.5, 129.5, 129.4, 128.5, 128.4, 127.6, 127.5, 113.3, 113.2, 113.1, 89.6, 81.7, 78.5, 73.0, 72.9, 71.9, 55.2, 55.1, 51.5, 42.1, 41.1, 27.1, 19.8, 18.2, 12.6; HRMS (ES^+) calcd. for $C_{43}H_{61}O_7Si$ (M-OH) 717.4187, found 717.4198.



Alcohol 2.30: To a stirred solution of **2.29** (612 mg, 0.83 mmol) in CH_3CN / H_2O (27.7 mL, 10 : 1) at 0°C was added CAN (1.14 g, 2.08 mmol). After 1 h, the reaction was quenched with H_2O (50 mL) and extracted with Et_2O (3 x 50 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 10-20% EtOAc / Hexanes, to give product **2.30** (391 mg, 0.818 mmol, 98%) as a colorless oil: $[\alpha]_D^{23}$ = -15.6 (*c* 0.63, $CHCl_3$); IR (neat) 2946, 2864, 1737, 1651, 1458, 1247, 1109, 838 cm^{-1}; ^1H NMR

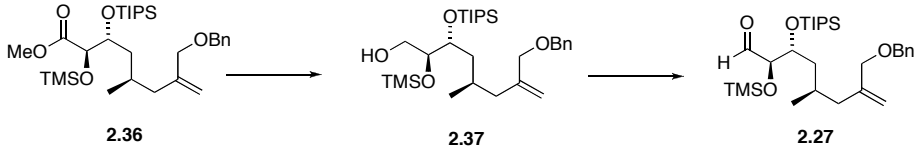
(300 MHz, $CDCl_3$) δ 7.28-7.38 (m 5H), 5.14 (s, 1H), 4.97 (s, 1H), 4.52 (s, 2H), 4.24-4.26 (m, 2H), 3.97-3.99 (m, 2H), 3.70 (s, 3H), 1.74-2.05 (m, 4H), 1.27-1.31 (m, 1H), 1.09 (m, 21H), 0.91 (d, J = 6.6 Hz, 3H), 0.14 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.3, 144.2, 138.5, 128.3, 127.6, 127.4, 113.0, 76.0, 73.7, 72.9, 71.9, 51.5, 42.1, 41.5, 27.4, 19.7, 18.1, 12.6, -0.11; HRMS (CI^+) calcd. for $C_{27}H_{47}O_5Si$ (M+H) 479.3192, found 479.3224.



2.30 **2.36**

TMS ether 2.36: To a stirred solution of **2.30** (260 mg, 0.54 mmol) in CH_2Cl_2 (5.4 mL) at –78°C was sequentially added 2,6-lutidine (0.23 g, 0.25 mL, 2.16 mmol) and TMSOTf (0.24 g, 0.20 mL, 1.08 mmol). After 30 min, the reaction was quenched with sat. aq. NH_4Cl (5 mL) and extracted with Et_2O (3 x 10 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 10-20% EtOAc / Hexanes, to give product **2.36** (256 mg, 0.465 mmol, 86%) as a colorless oil: $[\alpha]_D^{23}$ = -15.6 (*c* 0.63, $CHCl_3$); IR (neat) 2946, 2864, 1737, 1651, 1458, 1247, 1109, 838 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.28-7.38 (m, 5H), 5.14 (s, 1H), 4.97 (s, 1H), 4.52 (s, 2H), 4.24-4.26 (m, 2H), 3.97-3.99 (m, 2H), 3.70 (s, 3H), 1.74-2.05 (m, 4H), 1.27-1.31 (m, 1H), 1.09 (m, 21H), 0.91 (d, J = 6.6 Hz, 3H), 0.14 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.3, 144.2, 138.5, 128.3, 127.6, 127.4, 113.0, 76.0, 73.7, 72.9, 71.9,

51.5, 42.1, 41.5, 27.4, 19.7, 18.1, 12.6, -0.11; HRMS (ES^+) calcd. for $C_{30}H_{54}O_5Si_2Na$ (M + Na) 573.3408, found 573.3403.



Aldehyde 2.27: To a stirred solution of **2.36** (250 mg, 0.45 mmol) in CH_2Cl_2 (4.5 mL) at -78°C was added DIBAL-H (1.08 mL, 1.08 mmol, 1.0 M in CH_2Cl_2). After 1 h, the reaction was allowed to warm to 0°C, quenched with methanol (0.2 mL) and poured into aq. sodium potassium tartrate (10 mL, 10%) at rt. The reaction flask was rinsed with an additional portion of CH_2Cl_2 (5 mL). After another 3 h, the reaction mixture was extracted with EtOAc (3 x 10 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 10-40% EtOAc / Hexanes, to give alcohol **2.37** (138 mg, 0.26 mmol, 59%) and partial aldehyde **2.27** (69 mg, 0.13 mmol, 29%) as colorless oils. Data for **2.37**: $[\alpha]_D^{23}$ = -23.8 (*c* 1.20, $CHCl_3$); IR (neat) 3557, 2956, 2863, 1646, 1463, 1390, 1252, 1106, 842, 675 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.29-7.38 (m, 5H), 5.16 (s, 1H), 4.96 (s, 1H), 4.54 (d, *J* = 11.6 Hz, 1H), 4.51 (d, *J* = 12.0 Hz, 1H), 4.07-4.09 (m, 1H), 3.95 (s, 2H), 3.81-3.86 (m, 1H), 3.61-3.66 (m, 2H), 2.56-2.58 (m, 1H), 2.08 (dd, *J* = 13.6, 6.0 Hz, 1H), 1.98 (dd, *J* = 13.6, 6.0 Hz, 1H), 1.68-1.75 (m, 2H), 1.31-1.38 (m, 1H), 1.11-1.16 (m, 21H), 0.95 (d, *J* = 6.4 Hz, 3H), 0.17 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.0, 138.3, 128.4, 127.7,

127.6, 113.6, 75.1, 73.8, 72.9, 71.9, 63.4, 42.6, 42.1, 27.8, 19.5, 18.2, 12.6, 0.27; HRMS (FAB^+) calcd. for $C_{29}H_{55}O_4Si_2$ (M+H) 523.3639, found 523.3641.

To a stirred solution of **2.37** (138 mg, 0.26 mmol) in CH_2Cl_2 (2.6 mL) at room temperature was added DMP (330 mg, 0.78 mmol) and solid $NaHCO_3$ (*ca*. 50 mg). After 1 h, the reaction was quenched with sat. aq. $NaHCO_3$ (10 mL) and extracted with CH_2Cl_2 (3 x 10 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 10-40% EtOAc / Hexanes, to give product **2.27** (108 mg, 0.21 mmol, 80%) as colorless oil: $[\alpha]_D^{23}$ = -28.2 (*c* 0.68, $CHCl_3$); IR (neat) 2954, 2864, 1733, 1251, 1088, 873, 838, 679 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.64 (s 1H), 7.29-7.39 (m, 5H), 5.16 (s, 1H), 4.98 (s, 1H), 4.54 (d, *J* = 12.0 Hz, 1H), 4.51 (d, *J* = 12.0 Hz, 1H), 4.22 (dd, *J* = 10.4, 3.2 Hz, 1H), 3.95-4.06 (m, 3H), 2.06, (d, *J* = 7.2 Hz, 2H), 1.84-1.91 (1H), 1.62-1.66 (m, 1H), 1.23-1.30 (m, 1H), 1.13-1.23 (m, 21H), 0.90 (d, *J* = 6.8 Hz, 3H), 0.17 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.0, 144.0, 138.4, 128.3, 127.6, 127.5, 80.4, 74.9, 72.8, 71.9, 42.1, 41.0, 27.1, 19.5, 18.1, 12.5, 0.06; HRMS (FAB^+) calcd. for $C_{29}H_{51}O_4Si_2$ (M–H) 519.3326, found 519.3319.

References

1. Perrin, D. D.; Armarego, W. L. F. *Purification of Laboratory Chemicals: Third Edition*; Pergamon Press: New York, 1993.

2. Kelly, D. R.; Mahdi, J. G. *Tetrahedron Lett.* **2002**, *43*, 511.

3. Boulet, S. L.; Paquette, L. A. *Synthesis* **2002**, 895.

4. Titration of Grignard reagent: To a stirred solution of menthol (15.6 mg, 0.1 mmol) and 1,10-phenoanthroline (2 mg) in THF (0.5 mL) was added prepared Grignard reagent solution until a burgundy color persists. The concentration was calculated using the formula:

[RMgX] = 0.1 mmol / volume of added RMgX in mL

For the references, see: (a) Lin, H, -S; Paquette, L. A. *Synth. Comm.* **1994**, *24*, 2503. (b) Watson, S. C.; Eastham, J. F. *J. Organomet. Chem.* **1967**, *9*, 165.

5. Vanderwalle, M.; Van der Eychen, J.; Oppolzer, W.; Vullioud, C. *Tetrahedron* **1986**, *42*, 4035.

6. Dioxalone **2.16** was prepared via a modified procedure to originally described by Andrus (*J. Org. Chem*. **2003**, *68*, 8162-69). To a vigorously stirred heterogeneous solution of 4,4-dimethoxy-stilbene (9.525 g, 39.6 mmol) in *t*-BuOH (16 mL) and NMO (12 mL, 51.2 mmol, 50% w/v in H_2O) was added $(DHQD)_2PHAL$ (86.2 mg, 0.11 mmol, 0.3 mol%) and $K_2OsO_4 \cdot 2H_2O$ (28.7 mg, 0.078 mmol, 0.2 mol%). After 16 h, sat. aq. $Na_2S_2O_3$ (75 ml) was added. After 20 min, the mixture was filtered to isolate (1*R*,2*R*)-Bis-(4-methoxy-phenyl)-ethane-1,2-diol (washed sequentially with H_2O and Hexanes). The diol was dried on paper then under high vacuum to give the product (9.095 g, 33.2 mmol, 84%). To a stirred solution of the diol (9.095 g, 33.2 mmol) in PhMe (500 mL) was added Bu_2SnO (9.00 g, 36.2 mmol) and equipped with a Dean-Stark apparatus. The solution was heated to reflux. After 18 h, the solution was allowed to cool. Next,

TBAI (19.28 g, 52.2 mmol) and *t*-butylbromoacetate (12.95 g, 9.8 mL, 66.4 mmol) were sequentially added. The reaction was again heated to reflux. After 4 h, the reaction was cooled to rt, quenched with aq. $Na_2S_2O_3$ (300 mL, 10%), diluted with Et_2O (200 mL) and sat. aq. NaCl (75 mL) and extracted with Et_2O (3 X 250 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 20-75% EtOAc / Hexanes, followed by recrystallization from EtOAc / Hexanes to give the dioxalone **2.16** (6.60 g, 21.0 mmol, 63%).

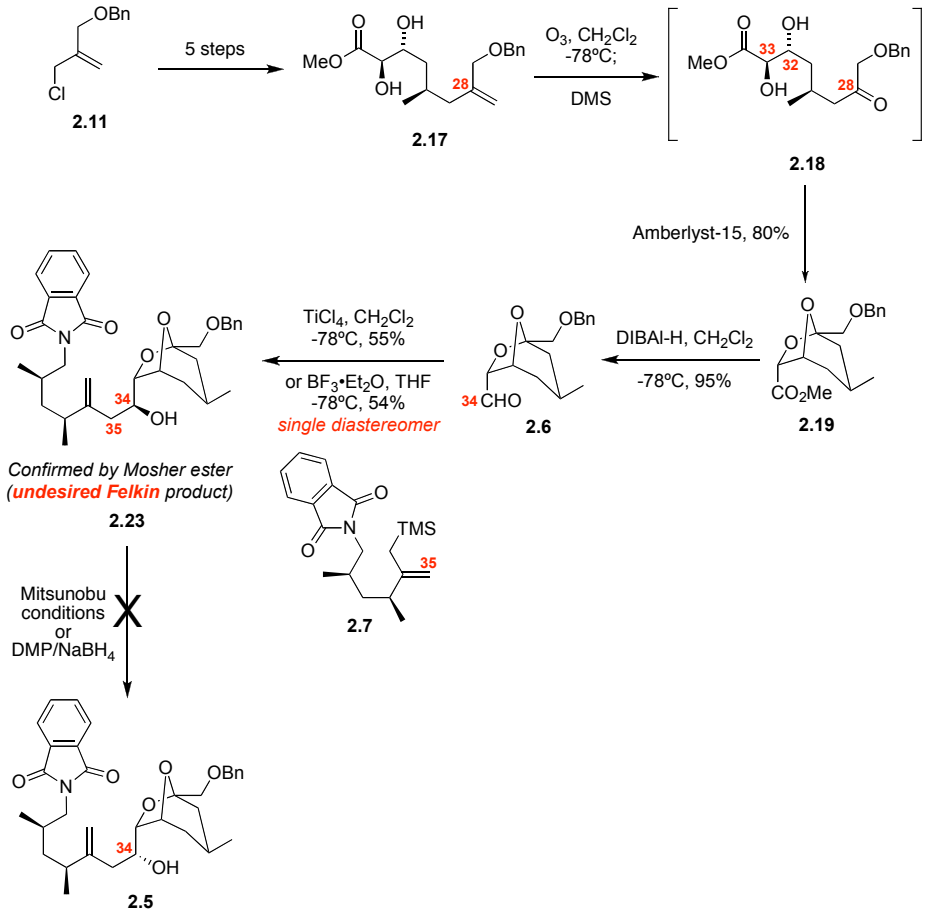
7. Brown, H. C.; Ganesan, K.; Dhar, R. K. *J. Org. Chem.* **1993**, *58*, 147.

8. CCDC-605,862 contains the supplementary crystallographic data of compound **2.20** from this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/ data_request/cif.

CHAPTER 3. CONCLUSION AND PROPOSED FUTURE WORK

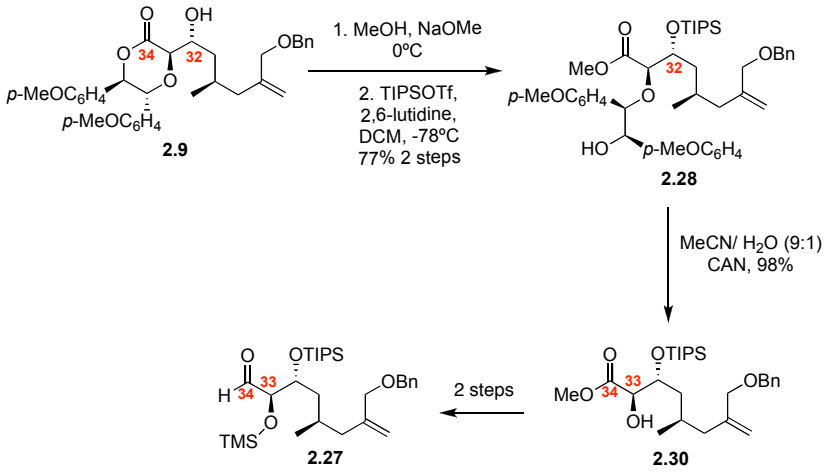
3.1 Conclusion

In summary, we have successfully synthesized C_{27}-C_{40} FGHI ring fragment with a longest linear sequence of 22 steps. Our 1st generation strategy features a spontaneous ketalization to afford the key [3.2.1] bicyclic ketal moiety. Unfortunately, we were unable to install the desired C_{34} stereocenter through the chelation-controlled aldol coupling and our attempts to invert the C_{34} stereochemistry also proved problematic.



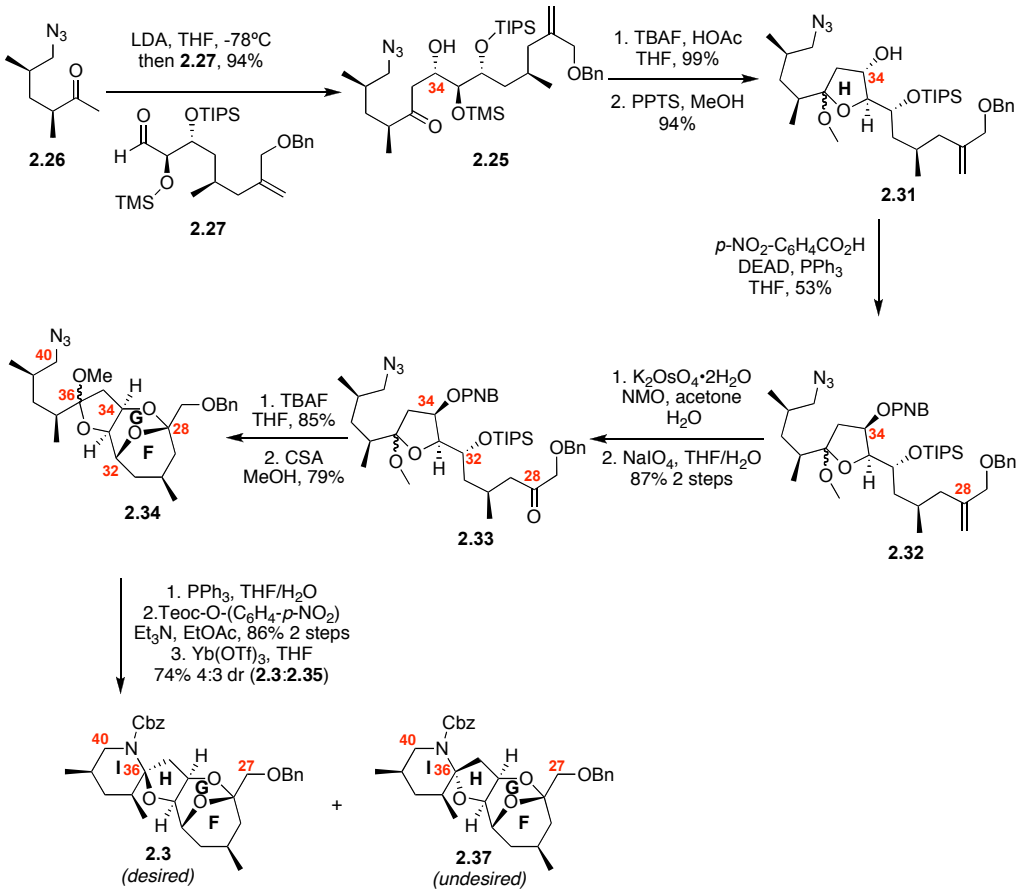
Scheme 3.1. Our 1st Generation Approach for the Synthesis of Southern Portion

Faced with these roadblocks, we were forced to revise the synthetic strategy. Our 2nd generation strategy required the synthesis of aldehyde **2.27** (Scheme 3.2). Commenced from the anti-aldol adduct **2.9**, aldehyde **2.27** was prepared in 5 steps. Key steps include a highly regioselective C_{32} TIPS protection.



Scheme 3.2. Synthesis of Aldehyde **2.27**

The parallel research from our group led to the other fragment, methyl ketone **2.26**. With both fragments in hand, we were finally able to complete the synthesis of C_{27}-C_{40} southern portion (Scheme 3.3). The key steps include a highly stereoselective aldol coupling between aldehyde **2.26** and methyl ketone **2.27**, a Mitsunobu reaction to install the desired C_{34} stereocenter, and a $Yb(OTf)_3$-catalyzed spiroaminal formation.

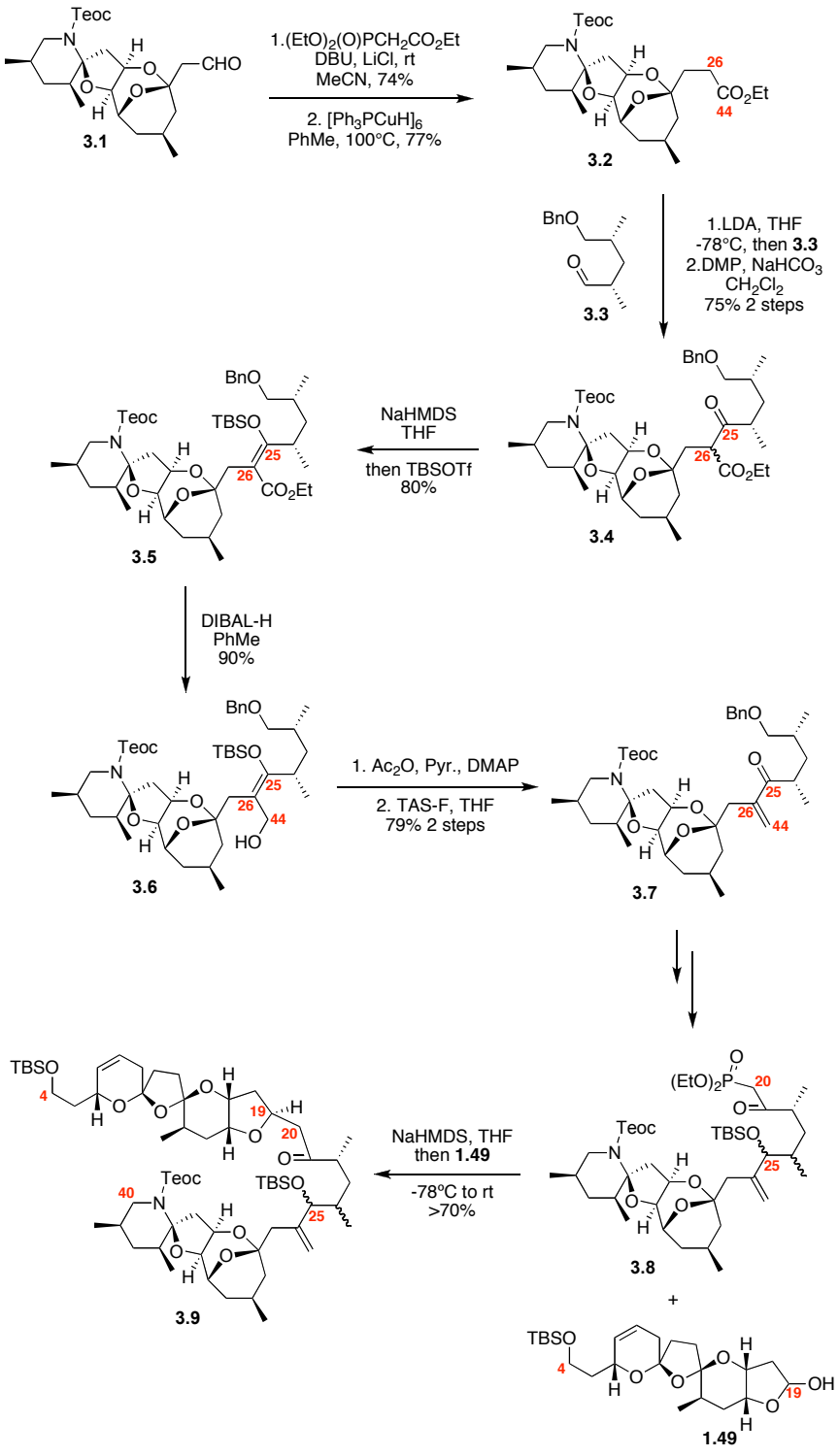


Scheme 3.3. Completion of the Synthesis of C_{27}-C_{40} Southern Portion **2.3**

3.2 Proposed Future Work

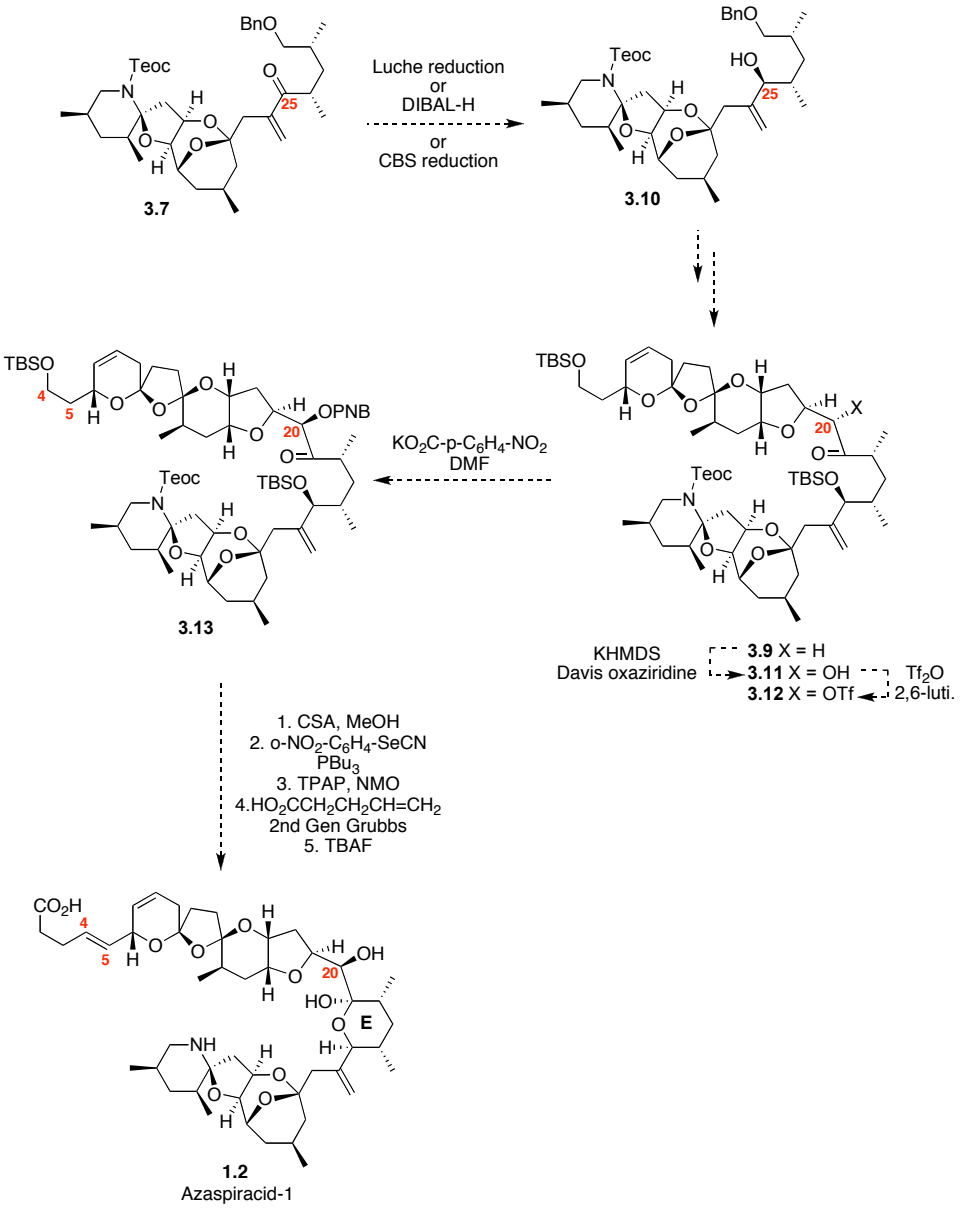
With efficient routes to both southern and northern portions, we are in excellent position to complete the total synthesis of azaspiracid-1. Our group have recently advanced to the key intermediate enone **3.7** using the sequence shown in Scheme 3.4. Ester **3.2** was obtained from aldehyde **3.1** via HWE reaction and reduction of the double bond with Stryker's reagent. LDA-mediated aldol coupling

proceeded smoothly to give an inconsequential mixture of diastereomers. The following Dess-Martin oxidation afforded the ketone **3.4** as tautomers. Treatment of compound **3.4** with NaHMDS and TBSOTf led to enol ether **3.5**. Sequential DIBAL-H reduction, C_{44} acylation, and TASF-induceded desilylation / elimination finally yielded the key intermediate, enone **3.7**. More recently, our preliminary results showed that enone **3.7** was converted to phosphonate **3.8** in moderate diastereoselectivity via an un-optimized protocol. We next investigated the key combination of southern and northern halves. Gratifyingly, the HWE reaction between phosphonate **3.8** and the previously made lactol **1.49**[1], followed by the *in situ* Michael addition, afforded the desired coupling product **3.9** in greater than 70% yield.



Scheme 3.4. Our Recent Progress on the Synthesis of Azaspiracid-1

With the encouraging results obtained from our recent research, the next target would be the development of a distereoselective route to phospohnate **3.8** and accomplish the total synthesis of azaspiracid-1 (Scheme 3.5). Luche reduction, DIBAL-H reduction, or CBS reduction are the potential options for the diastereoselective installation of C_{25} stereocenter. After the combination of southern and northern halves, the remaining steps will follow closely our previously reported procedure.[1] Diastereoselective incorporation of the C_{20} hydroxyl functionality using Davis oxiziridine followed by triflation and inversion with KOPNB will afford **3.13**. Removal of the primary TBS group under acidic conditions followed by selenation, elimination and cross metathesis will yield the protected version of azaspiracid-1. Finally, removal of the secondary TBS group should led to the spontaneous ketalization to give azaspiracid-1 in approximately 40 linear steps.



Scheme 3.5. Proposed Route to the Total Synthesis of Azaspiracid-1

3.3 References

1. Zhou, X.-T.; Carter, R. G. *Angew. Chem., Int. Ed.* **2006**, *45,* 1787.

PART II: TOTAL SYNTHESIS OF AMPHIDINOLIDE B_1 AND THE PROPOSED STRUCTURE OF AMPHIDINOLIDE B_2

CHAPTER 4: BACKGROUND OF AMPHIDINOLIDE B

4.1 Introduction of Amphidinolide Family

As the producers of substances with novel structures and appealing bioactivities, dinoflagellates have been investigated worldwide by natural product chemists.[1] Since Kobayashi and co-workers discovered the first amphidinolide, amphidinolide A, from the cultures of the dinoflagellates *Amphidinium sp.* in 1986,[2] amphidinolides have extended to a family of more than 30 macrolides consisting 12–29 membered macrocycles.[3] Most amphidinolides exhibit potent cytotoxicity against a series of human cancer cell lines.[3] Intrigued by their structural features and significant bioactivity, the synthetic community has devoted much attention to the synthesis of amphidinolides in the past two decades. Total syntheses of many amphidinolides including amphidinolide A[4], E[5], G and H[6], J[7], K[8], P[9], T[10], V[11], W[12], X[13] and Y[14] have been accomplished, with several resulting in stereochemistry reassignment.

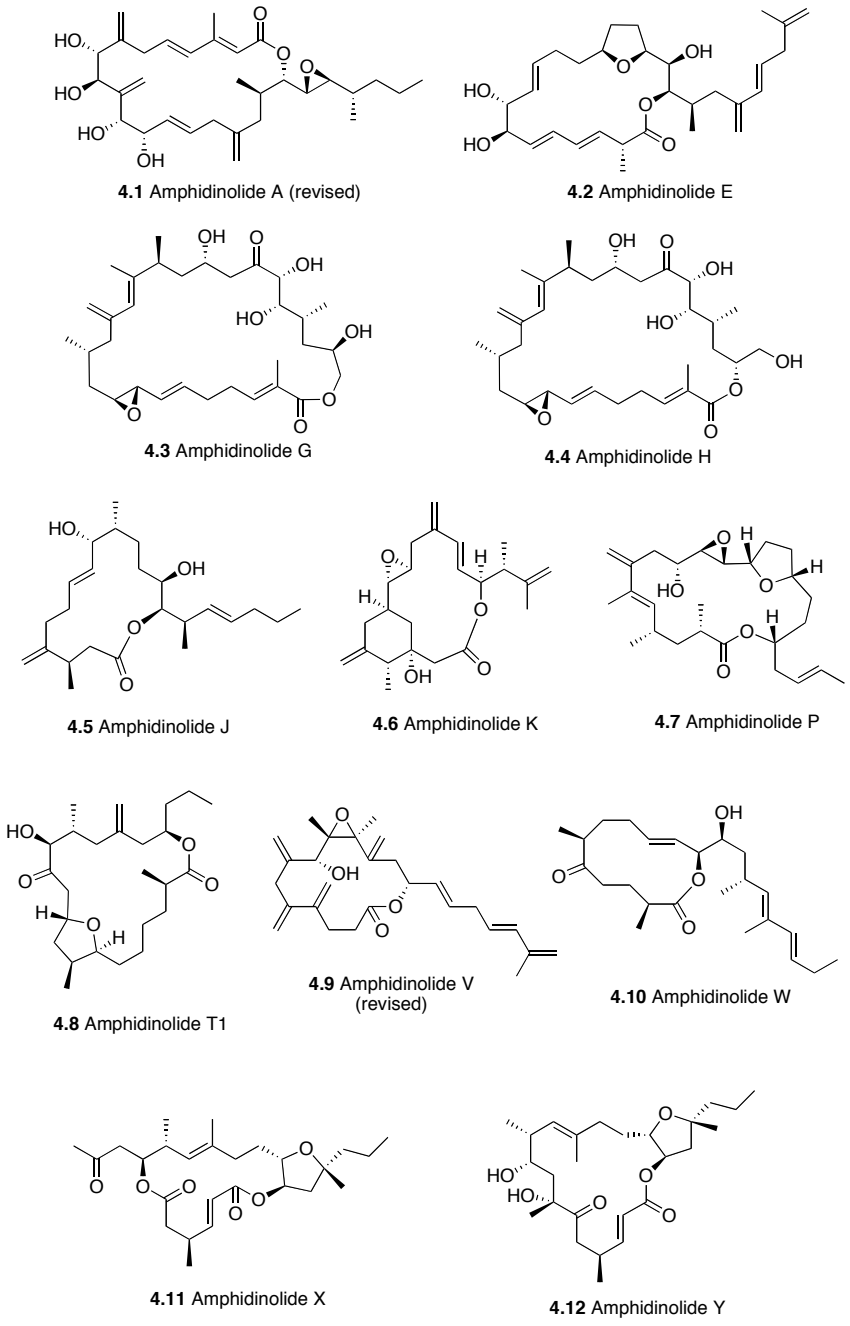


Figure 4.1. Synthesized Amphidinolides

4.2 Isolation and Bioactivity of Amphidinolide B

In 1987, the Kobayashi group discovered Amphidinolide B from the dinoflagellate *Amphidinium* sp., which was isolated from the Okinawan flatworm *Amphiscolops* sp..[15] Later, three amphidinolide B congeners, namely amphidinolides B_1 (**4.13**), B_2 (**4.14**) and B_3 (**4.15**), were isolated by Shimizu and co-workers from a free-swimming dinoflagellate *Amphidinium operculatum* ver nov *Gibbosum*.[16] In accord with the isolation of amphidinolide B, structural investigations by both the Kobayashi and Shimizu groups led to the determination of the relative stereochemistry of amphidinolide B_1 with the use of X-ray crystallography.[15, 16] Subsequently, the absolute stereochemistry was established via chemical degradation.[17] NMR spectra data analysis indicated that amphidinolide B_2 was the C_{18} epimer of amphidinolide B_1 and the structure of amphidinolide B_3 was 22-*epi*-amphidinolide B_1.[16]

4.13 Amphidinolide B_1: $R_1 = R_3 = OH$, $R_2 = R_4 = H$
4.14 Amphidinolide B_2: $R_2 = R_3 = OH$, $R_1 = R_4 = H$
4.15 Amphidinolide B_3: $R_1 = R_4 = OH$, $R_2 = R_3 = H$

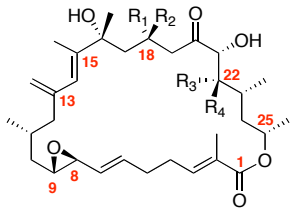


Figure 4.2. Structure of Amphidinolide B_1, B_2 and B_3

Amphidinolide B is among the most cytotoxic molecules in the family of amphidinolides. Amphidinilide B_1 displays significant IC_{50} values against a series of human cancer cell lines: the L1210 murine leukemia cell line (0.14 ng/mL); the

human colon tumor HCT 116 cell line (0.122 μg/mL); and the KB cancer cell line (4.2 ng/mL).[18] In addition to its potent cytotoxicity, amphidinolide B_1 was also used as a powerful activator of actomyosin ATPase to enhance skeletal muscle contraction.[19]

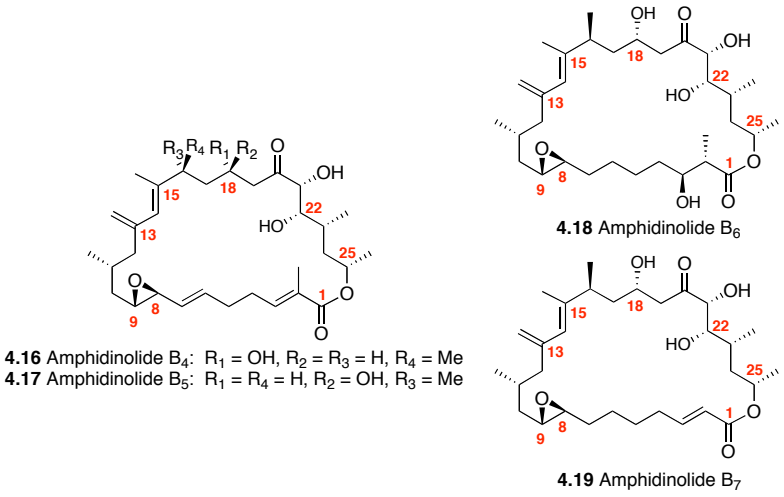


Figure 4.3. Structures of Amphidinolide B_4, B_5, B_6 and B_7

More recently, several other amphidinolide B macrolides, namely amphidinolide B_4, B_5, B_6 and B_7, were isolated from the marine acoel flatworms of the genus *Amphiscolops*.[20] Sharing similar structural features with amphidinolide B_1, amphidinolide B_4 and B_5 showed potent cytoxicity against the L1210 murine leukemia cell line (IC_{50}: 0.12 ng/mL and 1.4 ng/mL, respectively) and the KB cancer cell line (IC_{50}: 1.0 ng/mL and 4.0 μg/mL, respectively), whereas amphidinolide B_6 and B_7 exhibited cytoxicity against human B lymphocyte DG-75 cells (IC_{50}: 0.02 μg/mL and 0.4 μg/mL, respectively).

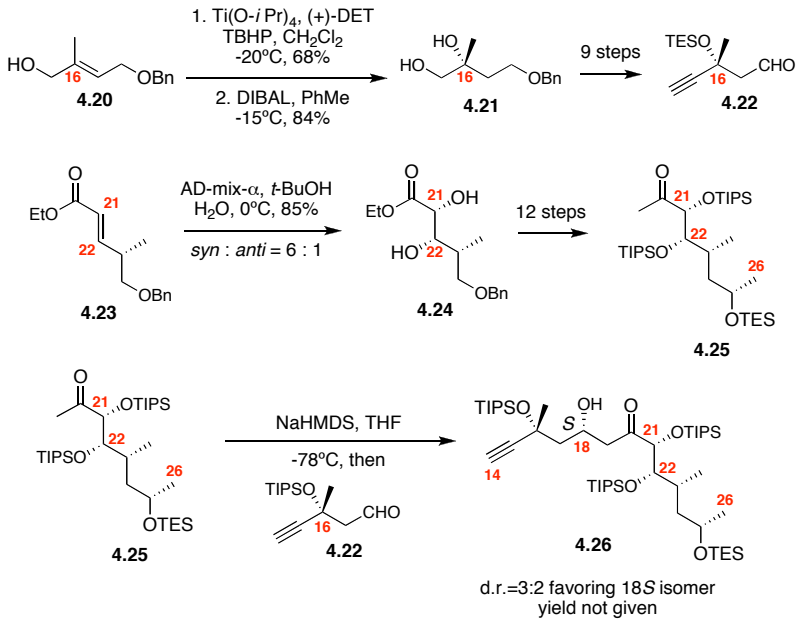
4.3 Synthetic Efforts toward Amphidinolide B_1

Amphidinolide B_1 possesses unique structural features including a highly substituted C_{13}-C_{15} diene, the C_{21}-C_{25} domain with dense area of stereocenters, an unusual vinyl epoxide motif and a 26-membered macrolactone. In addition to the intriguing structure of amphidinolide B_1, the highly potent cytotoxicity and the sparse amounts available from natural sources have made it an attractive synthetic target. Since the first synthetic efforts reported by Chakraborty and co-workers in 1997,[21] numerous research groups have been working on the synthesis of amphidinolide B_1.[21-26, 28, 29] Despite all these efforts, no total synthesis had been accomplished prior to our efforts.

4.3.1 The Chakraborty Group

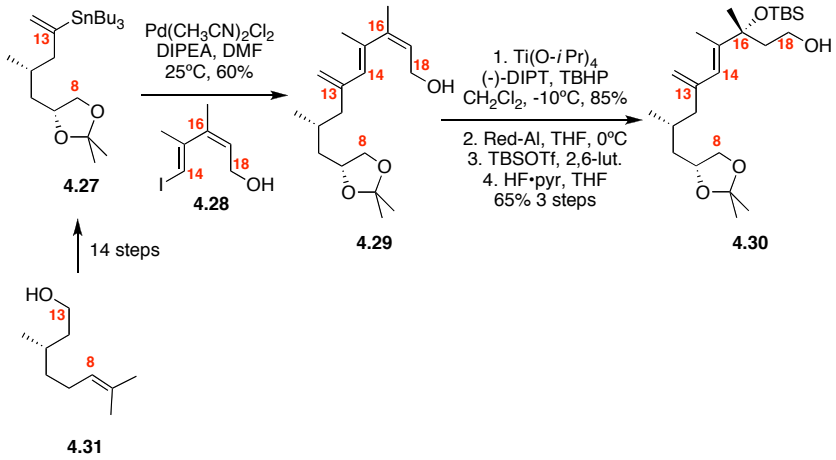
In 1997, Chakraborty and co-workers reported the first approach towards amphidinolide B_1.[21a-b] In the synthesis of C_{14}-C_{26} moiety **4.26**, the C_{16} tertiary alcohol was accessed from allylic alcohol **4.20** via Sharpless asymmetric epoxidation and a regioselective epoxide opening (Scheme 4.1). To set the *cis*-diol relationship across the C_{21}–C_{22} bond, the Sharpless dihydroxylation of unsaturated ester **4.23** (*cis:trans* = 6:1) was utilized. An aldol reaction between aldehyde **4.22** and methyl ketone **4.25** was employed to construct the C_{18} stereochemistry in 3:2

dr, favoring the 18*S* isomer. The lengthy sequences and the poor diastereoselectivity of the aldol coupling made this method not practical.



Scheme 4.1. Chakraborty's Synthesis of C_{14}-C_{26} Portion

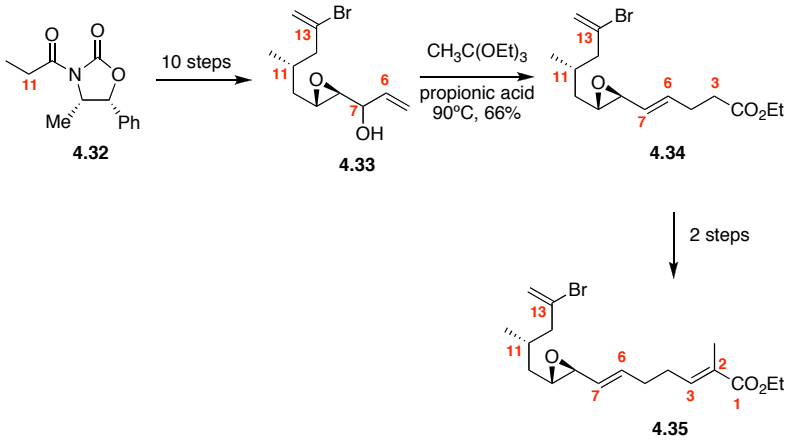
Later, the Chakraborty group published their revised approach to the synthesis of the C_8-C_{18} fragment (Scheme 4.2).[21c] A palladium-catalyzed Stille coupling was used to construct C_{13}-C_{14} bond. Subsequent Sharpless asymmetric epoxidation and a regioselective epoxide opening afforded the desired compound **4.30.** Although **4.30** was successfully made, the number of steps (14 steps from commercially available material **4.31**) required for synthesis of coupling precursor **4.27** diminished the efficiency of this approach.



Scheme 4.2. Chakraborty's Revised Synthesis of C_8-C_{18} Motif.

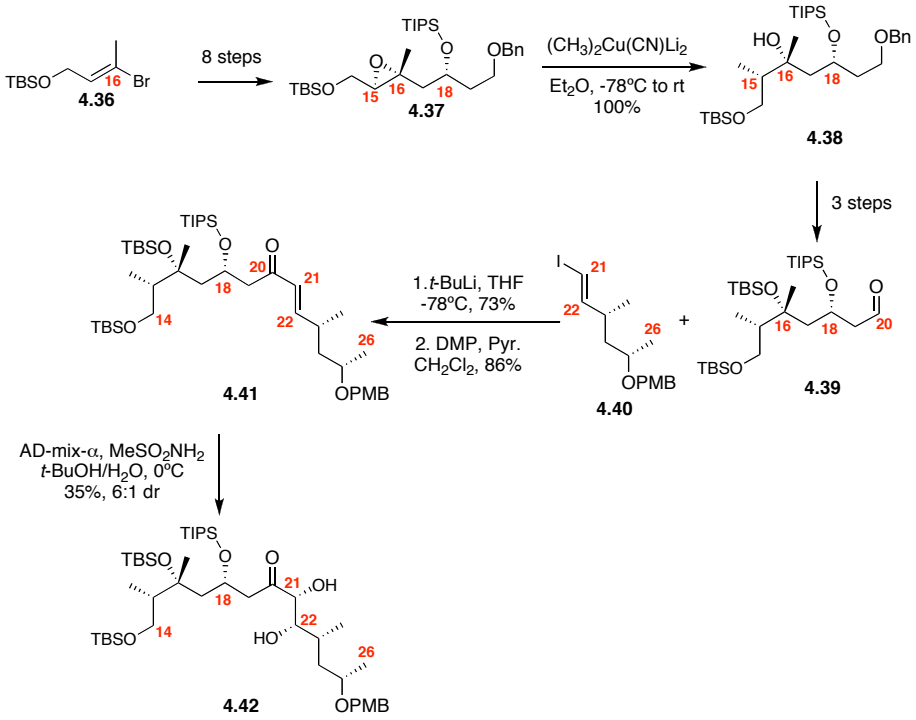
4.3.2 The Lee Group

In 1997, the Lee group synthesized C_1-C_{13} portion **4.35** of amphidinolide B_1 via a 13-step sequence, starting from propionyl oxazolidinone **4.32** (Scheme 4.3).[22a] The orthoester Claisen rearrangement reaction was employed to form the C_6-C_7 *trans* double bond. Further elaboration produced compound **4.35** in only 3.5% overall yield.



Schmem 4.3. Lee's Approach For the Synthesis of C_1-C_{13} Fragment

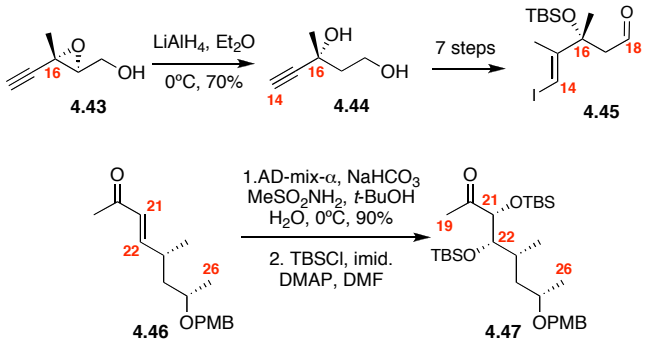
In a later 2000 publication, Lee and co-workers revealed their approach to the synthesis of the C_{14}-C_{25} fragment **4.42** (Scheme 4.4).[22b] A Sharpless asymmetric epoxidation, followed by the regioselective epoxide opening with methyl cuprate, yielded C_{16} tertiary alcohol. The C_{21} and C_{22} stereocenters were produced via Sharpless dihydroxylation in 35% yield in 6:1 dr.



Scheme 4.4. Lee's Efforts to the Synthesis of C_{14}-C_{26} Portion

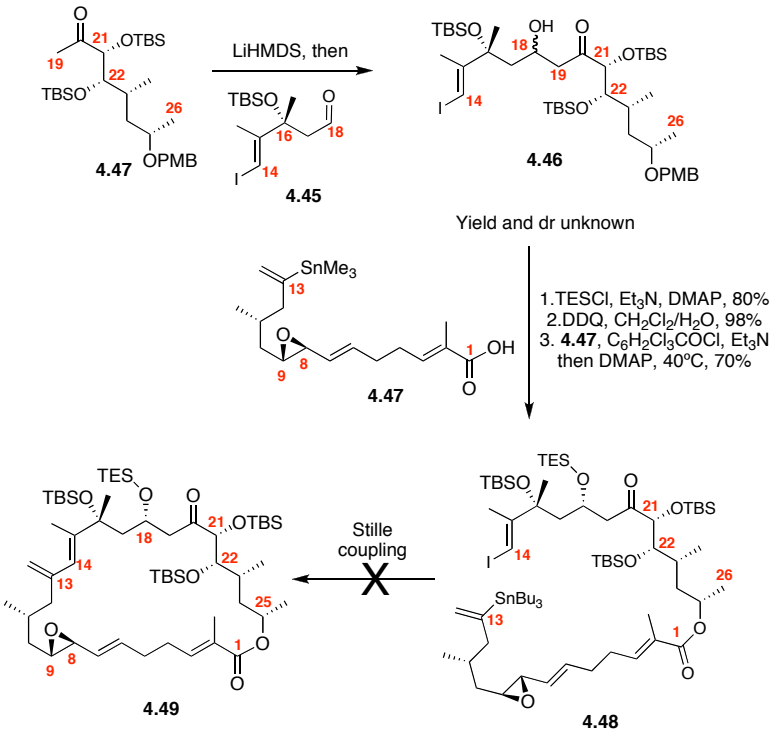
4.3.3 The Pattenden Group

In 1998, the Pattenden group synthesized the aldehyde **4.45** and methyl ketone **4.47**, the precursors required for the synthesis of C_{14}-C_{26} portion of amphidinolide B (Scheme 4.5).[23a] Similarly, the regioselective epoxide opening generated C_{16} tertiary alcohol while a Sharpless dihydroxylation was used to construct the C_{21} and C_{22} stereocenters. The conversion of alkyne **4.44** to the corresponding *E*-trisubstituted vinyl iodide **4.45** required seven steps.



Scheme 4.5. Pattenden's Synthesis of C_{14}-C_{18} and C_{19}-C_{26} Fragments

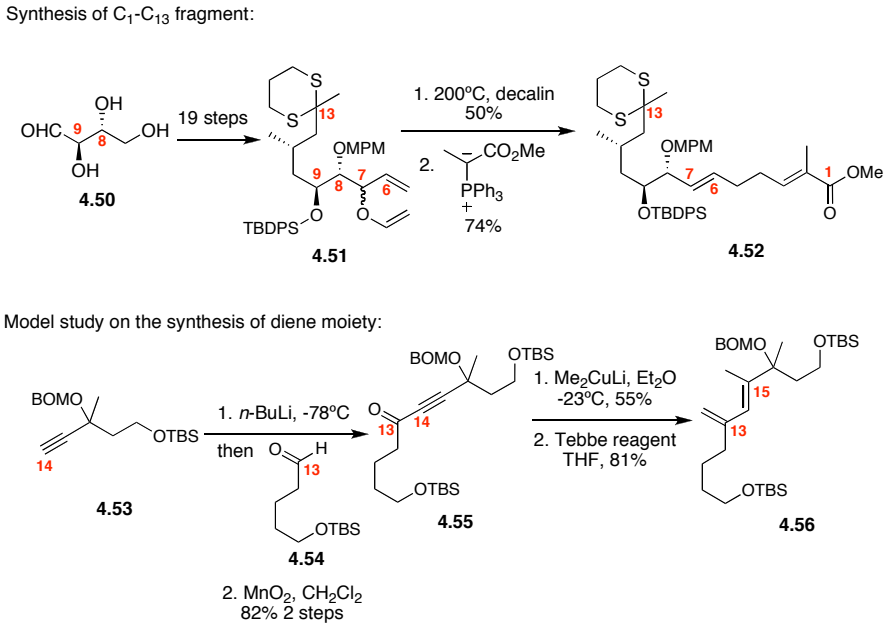
In Pattenden's sebsequent research, the aldol reaction between **4.47** and **4.48** yielded the C_{18} stereocenter; however, the yield and the dr were not specified by the authors (Scheme 4.6).[23b] An intermolecular Yamaguchi esterification linked the C_1–C_{13} intermediate to the C_{14}–C_{26} fragment. Unfortunately, efforts to affect an intramolecular Stille reaction for the construction of the C_{13}–C_{14} bond in the sterically demanding system were unsuccessful. Only a dimer species and a destannylated compound were formed.



Scheme 4.6. Pattenden's Attempts on the Intramolecular Stille Reaction

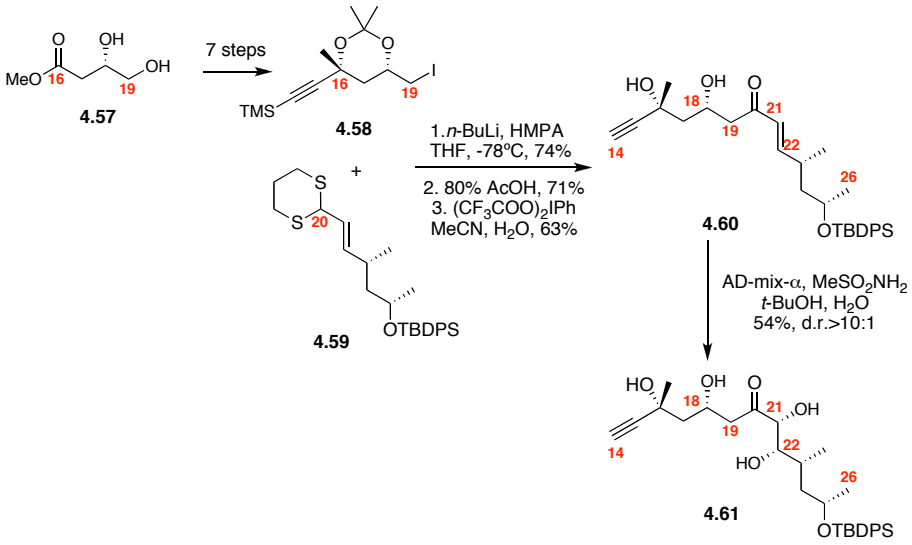
4.3.4 The Nishiyama Group

At about the same time as Pattenden's research was published, the Nishiyama group reported their synthesis of the C_1-C_{13} subunit **4.52** (Scheme 4.7).[24a] A Claisen rearrangement was used to generate the C_6-C_7 alkene, whereas a (*D*)-erythrose-derived diol **4.50** served as the source for the C_8 and C_9 stereocenters. In a following model study, the same group successfully synthesized the racemic form of diene **4.56** via a Michael addition of methyl group to compound **4.55** and the subsequent methylenation of the resulted enone with Tebbe reagent.[24b]



Scheme 4.7. Nishiyama's Strategy for the Synthesis of C_1-C_{13} Fragment and the Model Study on the Synthesis of C_{13}-C_{15} diene

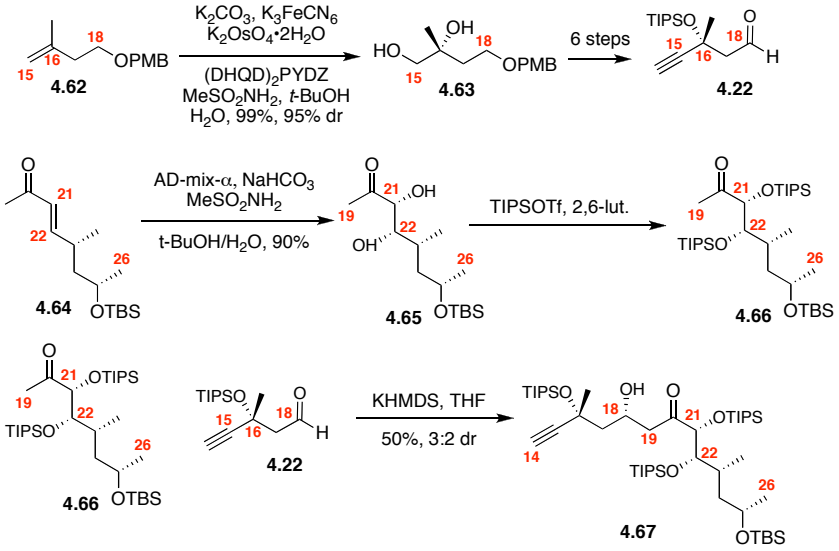
Encouraged by the results obtained from the model study, Nishiyama and co-workers then reported their strategy for the synthesis of the C_{14}-C_{26} fragment (Scheme 4.8).[24c] The key steps included the addition of the anion of dithiane **4.59** to iodide **4.58** and the Sharpless dihydroxylation of enone **4.60** to yield the C_{21} and C_{22} stereocenters in good diastereoselectivity. To date, the chemistry from the model study has not been applied to the real substrates.



Scheme 4.8. Nishiyama's Synthesis of C_{14}-C_{26} Motif

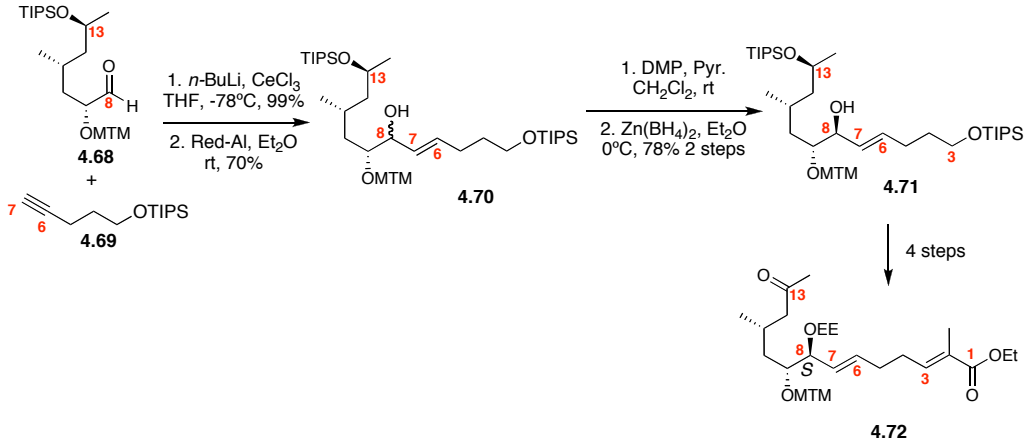
4.3.5 The Kobayashi Group

Similar to Chakraborty's and Pattenden's syntheses, Kobayashi's approach to the synthesis of the C_{14}-C_{26} fragment **4.67** involves an aldol disconnection (Scheme 4.9).[25a] The C_{16} tertiary alcohol stereocenter in aldehyde **4.22** was set using Sharpless' asymmetric dihyroxylation, as was the stereochemistry at C_{21} and C_{22}. The diastereoselectivity of the aldol coupling was poor, only 3:2 favoring the desired 18*S* diastereomer.



Scheme 4.9. Kobayashi's Synthesis of C_{14}-C_{26} Portion

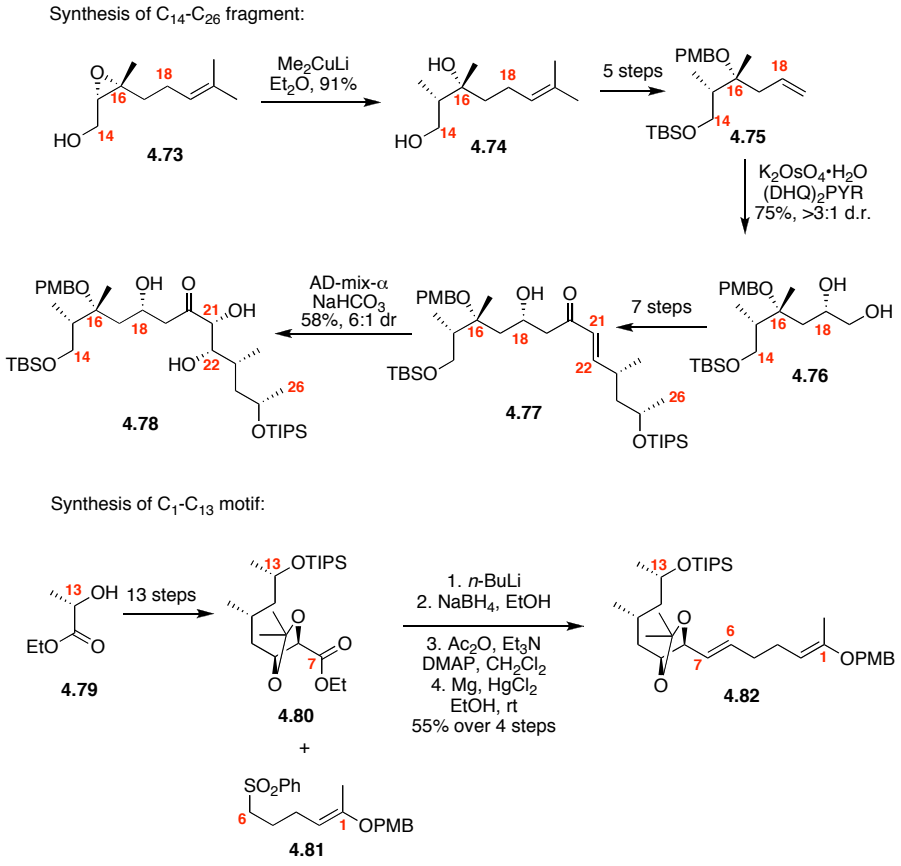
After the preparation of C_{14}-C_{26} fragment, Kobayashi and co-workers reported the synthesis of the lower C_1-C_{13} fragment **4.72** (Scheme 4.10). The addition of acetylene **4.69** to aldehyde **4.68**, followed by the Red-Al-mediated reduction, generated the C_6-C_7 double bond.[25b] A consecutive oxidation / reduction sequence produced the C_8 stereocenter. Further elaboration afforded the desired C_3-C_{13} fragment.



Scheme 4.10. Kobayashi's Approach to the Synthesis of C_1-C_{13} Intermediate

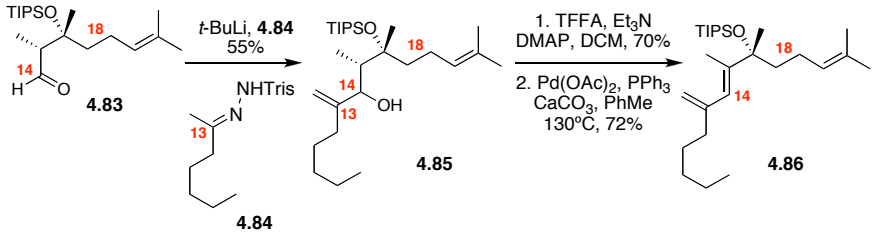
4.3.6 The Myles Group

In 1999, the Myles group reported the synthesis of the C_1-C_{13} and the C_{14}-C_{26} fragments (Scheme 4.11).[26a] The C_6-C_7 alkene found in C_1-C_{13} subunit was furnished through a Julia coupling. The strategy to C_{14}-C_{26} fragment featured an epoxide opening to build C_{16} tertiary alcohol, and a Sharpless dihydroxylation to generate the C_{21} and C_{22} stereocenters.



Scheme 4.11. Myles' Strategy for the Synthesis of C_1-C_{13} and C_{14}-C_{26} Fragments

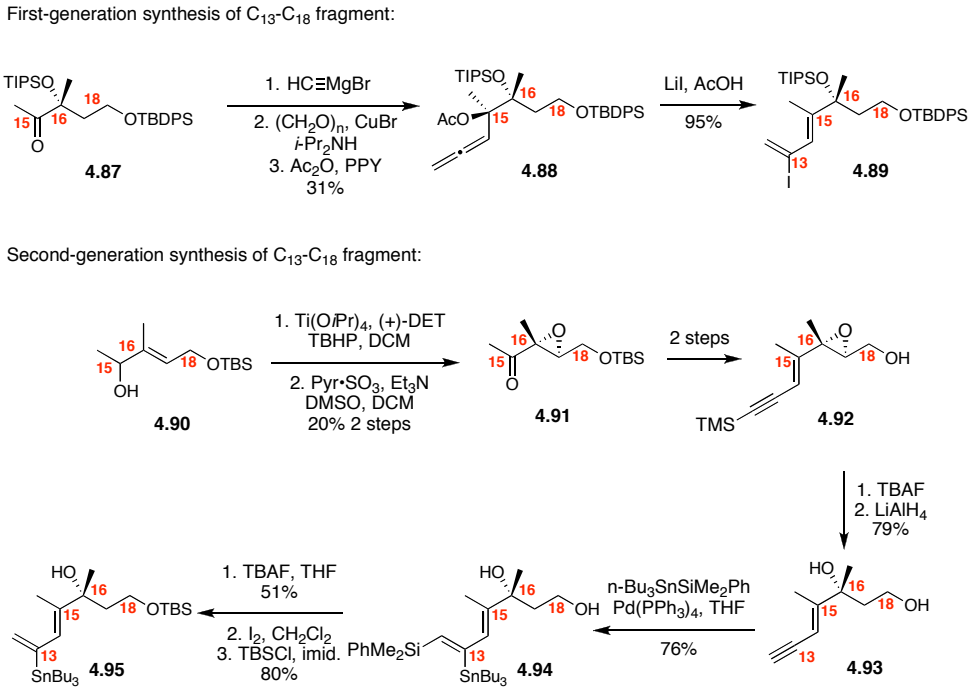
In Myles' model study,[26b] a Shapiro reaction between aldehyde **4.83** and trisylhydrazone **4.84** was utilized to form the C_{13}-C_{14} bond. The diene motif **4.86** was successfully synthesized through a sequence involving the conversion of alcohol **4.85** to the corresponding trifluoroacetate ester and the Pd-mediated Hauser-type elimination (Scheme 4.12).[27] To date, there have been no reports that discuss applying the developed approach on the authentic substrates.



Scheme 4.12. Myles' Model Study on the Synthesis of the Diene Motif

4.3.7 The Crews Group

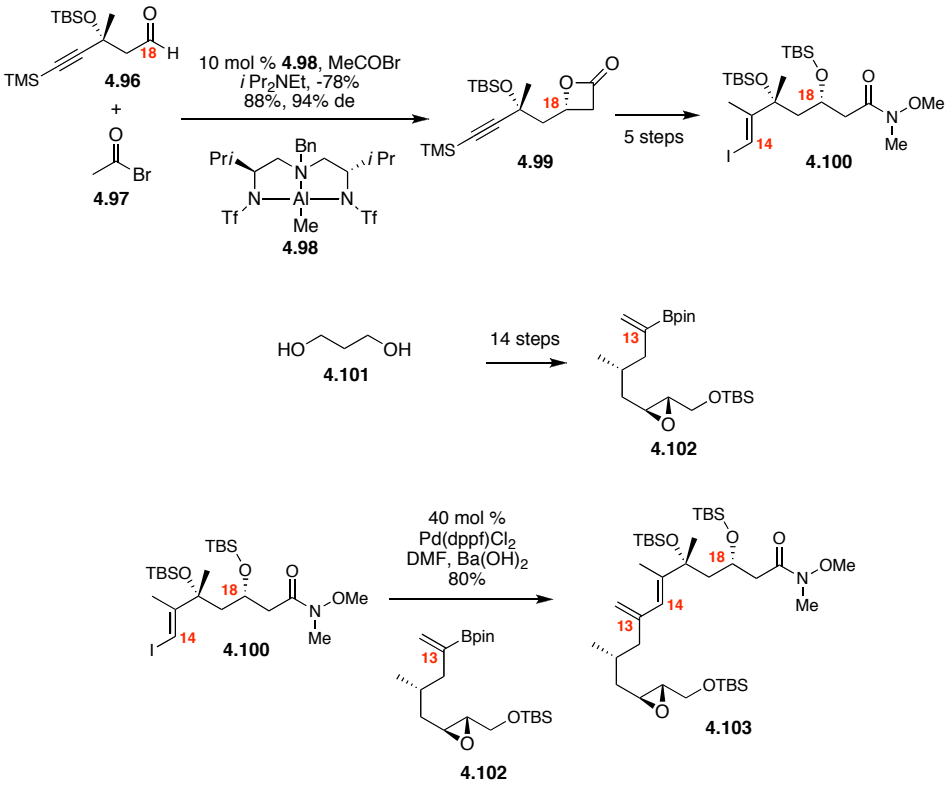
In their 2005 publication, Crews and co-workers revealed their first-generation strategy for the synthesis of the C_1-C_{12}, C_{13}-C_{18} and C_{19}-C_{25} fragments (Scheme 4.13).[28a] Notable steps included an iodide-mediated S_N2' reaction on the allenic acetate **4.88** to generate the diene motif **4.89**; however, the yield of the synthesis of the allenic acetate **4.88** was moderate. One year later, the second-generation approach for the synthesis of the three fragments was reported (Scheme 4.13).[28b] Stereochemistry at C_{16} was installed via Sharpless asymmetric epoxidation / regioselective epoxide opening. The triple bond of enyne **4.93** was silylstannylated regio- and stereoselectively employing *n*-$Bu_3SnSiMe_2Ph$/ $Pd(PPh_3)_4$ to ultimately furnishthe functionalized diene **4.94**. After the removal of $PhMe_2Si$ group with TBAF, sequential iodization and selective TBS protection gave the C_{13}-C_{18} fragment **4.95.**



Scheme 4.13. Crews' Efforts on the Synthesis of Amphidinolide B_1

4.3.8 The Nelson Group

In 2006, Nelson and co-workers reported a successful synthesis of the C_7-C_{20} fragment (Scheme 4.14).[29] Nelson's approach featured with an asymmetric acyl halide-aldehyde cyclocondensation to furnish the C_{18} stereochemistry and a Pd-catalyzed Suzuki coupling between iodide **4.100** and boronic ester **4.102** to yield diene motif **4.103**. Unfortunately, the synthesis of Suzuki coupling precursor **4.102** required 14 steps from the commercially available starting material and 40 mol % palladium catalyst was used in the key Suzuki coupling.

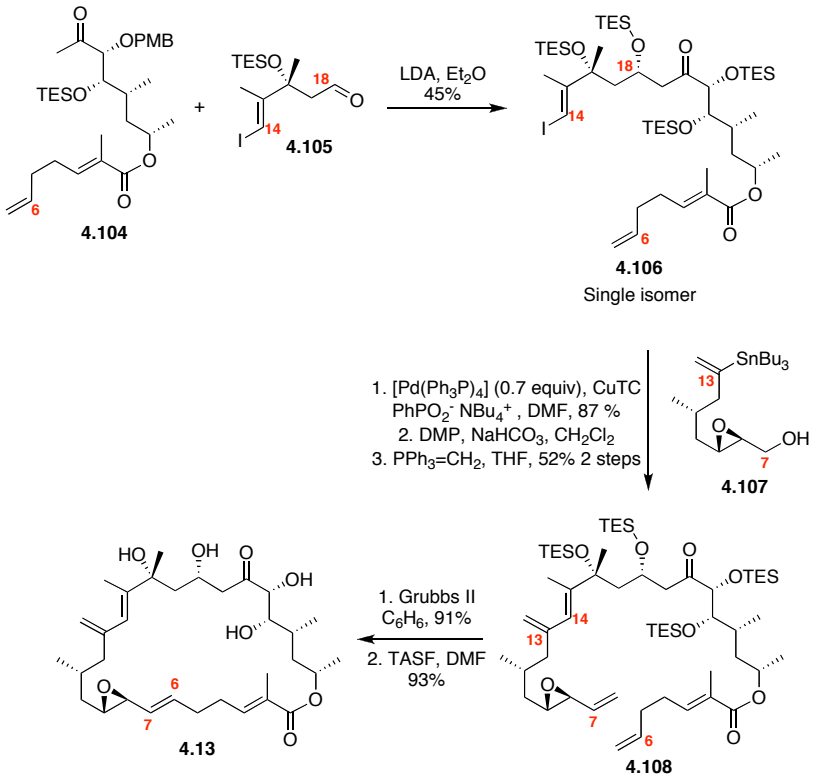


Scheme 4.14. Nelson's Synthesis of C_7-C_{20} Fragment

4.3.9 Fürstner's Total Synthesis of Amphidinolide B_1

In 2008, our group reported the first conquest of amphidinolide B_1 and the proposed structure of amphidinolide B_2.[30] More recently, the second total synthesis of amphidinolide B_1 by Fürstner and co-workers has followed.[31] The C_{18} stereocenter was established via a chelation controlled aldol coupling developed by our group.[32] The successful route hinged upon a highly productive Stille–Migita cross-coupling reaction to construct C_{13}-C_{15} diene motif, which required 70 mol % palladium catalyst and the development of a chloride- and fluoride-free

protocol. The macrocycle was furnished via ring-closing metathesis engaging a vinyl epoxide unit as one of the reaction partners.



Scheme 4.15. Füerstner's Total Synthesis of Amphidinolide B_1

4.4 Conclusion

Although extensive efforts have been made toward the synthesis of amphidinolide B_1 since 1997, questions still arise as to how to efficiently prepare the C_{13}-C_{15} diene motif, cyclize the 26-membered macrocycle, and incorporate the labile allylic epoxide moiety by the date we initiated our synthetic study. In 2008, our group accomplished the first total synthesis of amphidinolide B_1 and the

proposed structure of amphidinolide B_2.[30] One year later, another total synthesis of amphidinolide B_1 was reported by Fürstner and co-workers.[31] Herein, our synthetic studies toward amphidinolide B will be detailed in the next several chapters.

4.5 References

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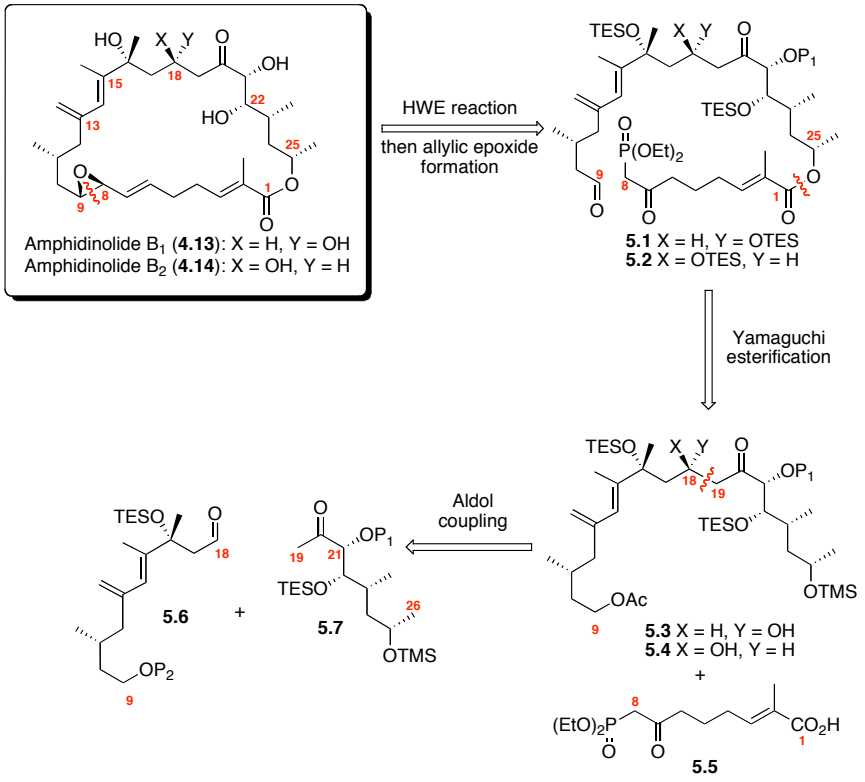
CHAPTER 5. STNTHESIS OF DIENE SUBUNITS

5.1 Retrosynthesis

As discussed in the previous chapter, amphidinolide B has shown potent cytotoxicity against several cancer cell lines and its structural architecture contains an unusual highly substituted diene, a dense area of stereocenters, a 26-membered marcocycle and a labile allyl epoxide moiety. After more than ten years of extensive efforts toward the synthesis of amphidinolide B, most synthetic problems were still not successfully addressed. Attracted by the unique structure and the potent cytotoxicity of amphidinolide B, we initiated our synthetic research with the intension of synthesizing the key motifs and ultimately complete the total synthesis of amphidinolide B. Our retrosynthesis commences with a disconnection at $C_{8,9}$ via intramolecular HWE reaction to reveal aldehyde **5.1** and **5.2** (Scheme 2.1). Further cleavage at $C_{18,19}$ via aldol coupling and C_1 C-O bond via Yamaguchi esterification resulted in three key intermediates: aldehyde **5.6**, methyl ketone **5.7** and phosphonate **5.5**. Our idea was to control the stereoselectivity of the aldol reaction between aldehyde **5.6** and methyl ketone **5.7** by employing different protecting group for the C_{21} hydroxyl group.

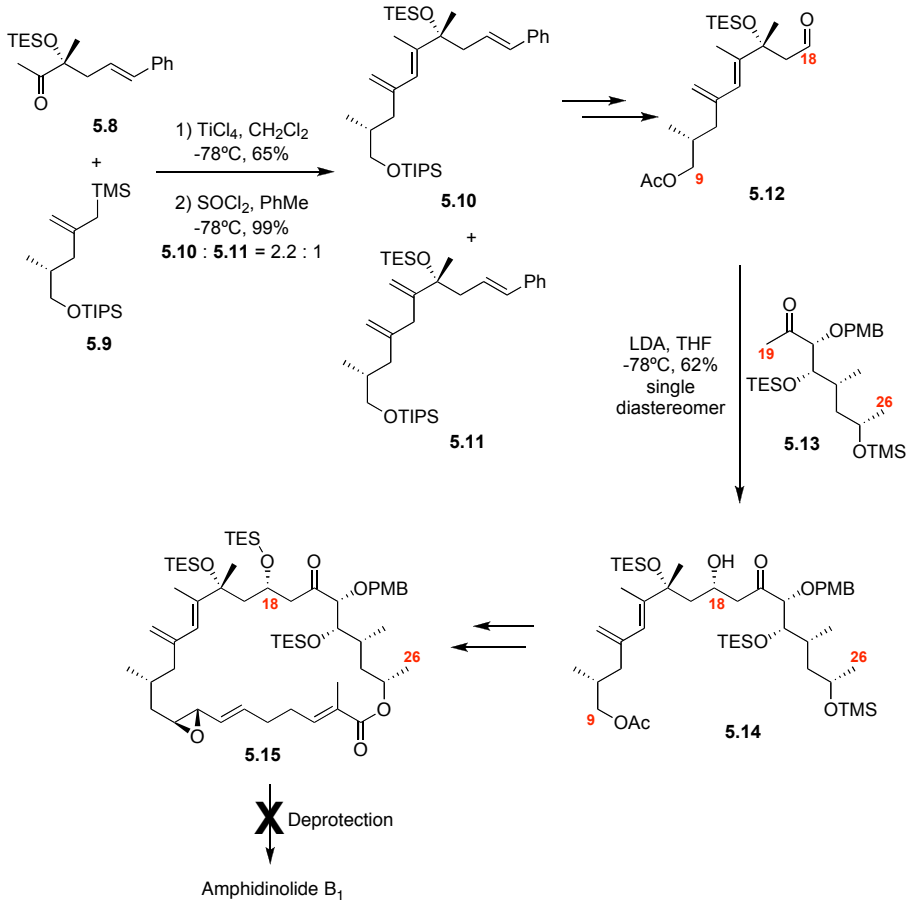


Scheme 5.1. Retrosynthetic Study of Amphidinolide B_1 and B_2

5.2 Our Previous Progress toward the Synthesis of Amphidinolide B_1

After several years of extensive efforts, our group had made significant progress toward the total synthesis of amphidinolide B_1 (Scheme 5.2).[1] We have previously reported the 1st generation synthesis of C_9-C_{26} fragment of amphidinolide B_1, which featured a chelation controlled aldol reaction between aldehyde **5.12** and methyl ketone **5.13** to build the C_{18} stereocenter. The other key steps included the Fleming-type coupling of two readily available subunits, methyl ketone **5.8** and allyl silane **5.9**, and the following $SOCl_2$ dehydration to furnish the

highly substituted C_{13}-C_{15} diene.. Further elaboration afforded the fully functionalized amphidinolide B_1 **5.15** with the hydroxyl groups protected with TES groups and a PMB group. Unfortunately, all the attempts to remove protecting groups resulted in decomposition of the substrate. Similar results have been reported by Fürstner in his recent synthesis of amphidinolide G and H.[2] Besides the difficulties associated with the deprotection step, the inability to scale up the coupling between methyl ketone **5.8** and allyl silane **5.9**, as well as the tedious separation of diene **5.10** and its isomer **5.11** presented additional obstacles in our efforts to finish the total synthesis of amphidinolide B_1.



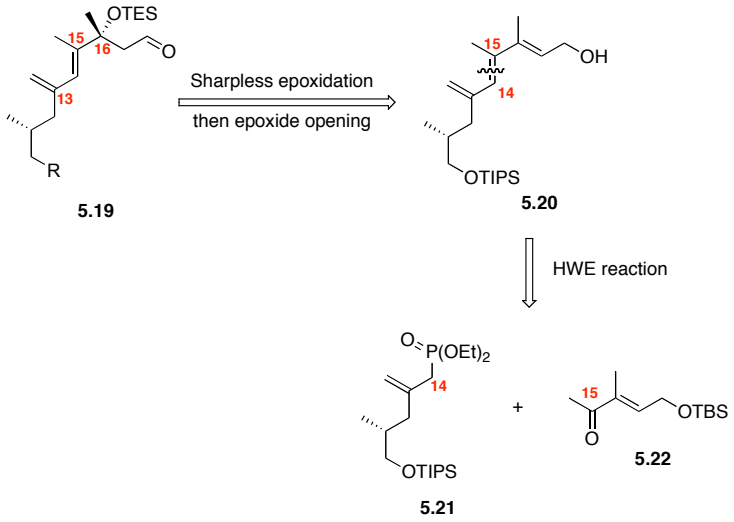
Scheme 5.2. Our Previous Progress toward the Synthesis of Amphidinolide B_1

5.3 Modified Strategy for the Synthesis of C_{13}-C_{15} Diene Motif

5.3.1 Retrosynthetic Analysis

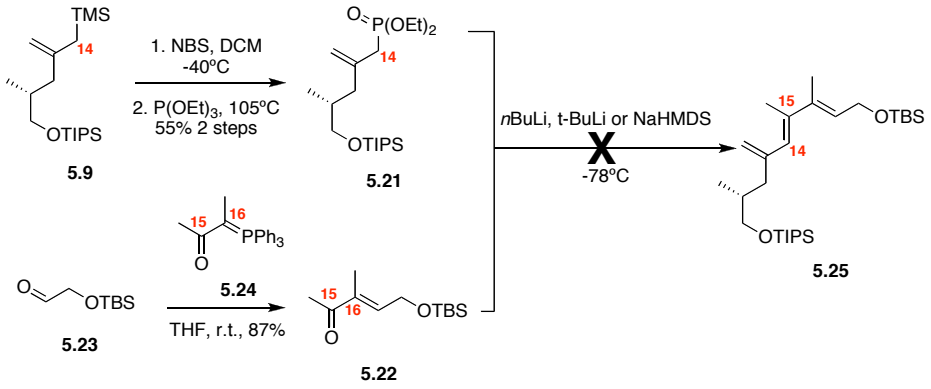
Faced with the roadblocks mentioned previously, we were forced to reconsider the strategy for the synthesis of the C_{13}-C_{15} diene moiety. As is discussed in the previous chapter, this diene functionality has frustrated numerous synthetic laboratories during their endeavors toward amphidinolide B. In the prior

syntheses, the disconnection between C_{13}-C_{14} linkage typically involves a palladium-mediated coupling between a suitably functionalized and stereodefined vinyl halide and its corresponding 1,1-disubstituted coupling partner. As has been demonstrated by Pattenden,[3] this coupling in sterically challenging systems does not perform well. More recently, Nelson and co-workers[4] did demonstrate a successful metal-mediated coupling process; however, it required extremely high catalyst loadings (40 mol%) – a requirement not amendable to total synthesis. The previously reported research and our own experience made us mindful in selecting the approaches for the synthesis of the diene subunit **5.19**. In our modified retrosynthesis, to avoid the steric bulk introduced by the C_{16} tertiary alcohol, the subsequent Sharpless epoxidation and the regioselective epoxide opening were employed to install the C_{16} stereocenter after the formation of the diene motif. Instead of the C_{13}-C_{14} cleavage, we chose to disconnect the molecule at the C_{14}-C_{15} double bond. Using this method, we could envision the formation of two subunits as coming from the methyl ketone **5.22** and an allyl phosphonate **5.21**.[5]



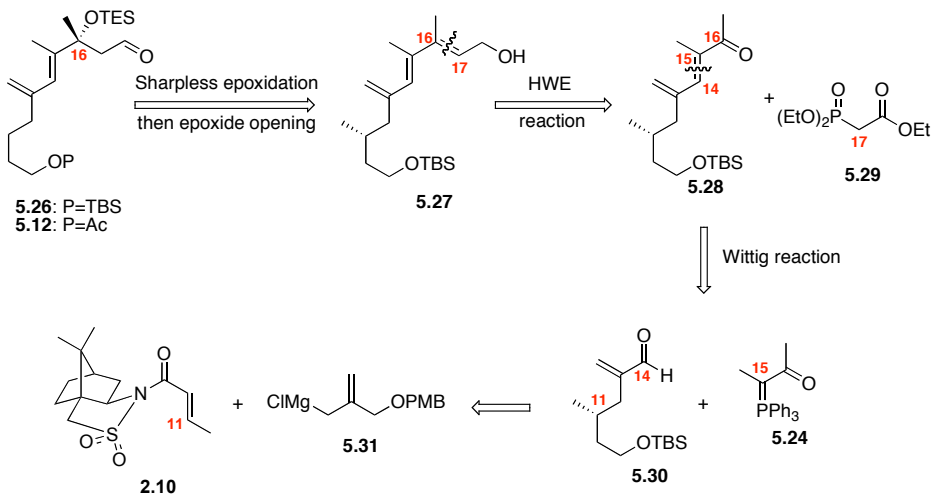
Scheme 5.4. Retrosynthesis of Diene **5.19**.

Commenced from previously synthesized allyl silane **5.9**,[1] phosphonate **5.21** was produced in moderate yield after a bromation and subsequent Arbuzov reaction (Scheme 5.5). The Wittig reaction between the known ylide **5.24**[6] and aldehyde **5.23**[7] furnished methyl ketone **5.22**. With these two intermediates in hand, we investigated the Horner-Wadsworth-Emmons olefination. Unfortunately, our repeated attempts proved unsuccessful as phosphonate **5.21** decomposed when treated with strong base (e.g. *n*BuLi, *t*-BuLi, KHMDS) at -78ºC.



Scheme 5.5. HWE Reaction between Phosphoante **5.21** and Methyl Ketone **5.22**

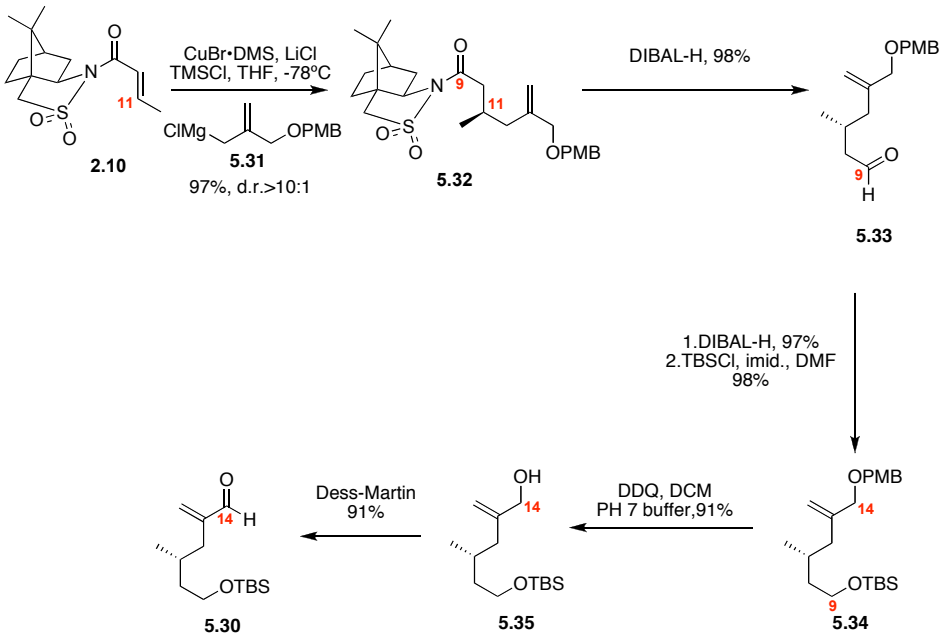
After the unsuccessful attempts of using HWE olefination, we sought a Wittig reaction[5] as a reasonable substitute to construct the C_{14}-C_{15} alkene (Scheme 5.6). As similar method was used to produce the C_{16} tertiary alcohol from triene alcohol **5.27**, the C_{16}-C_{17} double bond could be obtained from a HWE reaction. Further disconnection at C_{14}-C_{15} led to the known ylide **5.24**[6] and the aldehyde **5.30**. The C_{11} stereocenter of aldehyde **5.30** could be generated through the cuprate addition to the commercially available Oppolzer sultam derivative **2.10**.[8] Our synthetic plan required the selective removal of C_9 protecting group in the presence of secondary TES and PMB groups. The use of TBS group would be the first option based on our strategy for the synthesis of diene subunit. If the deprotection proved problematic, the previously employed acetate group[1] would be an alternative. Next, our focus shifted to the synthesis of C_9 TBS protected and C_9 acetate protected diene fragments.



Scheme 5.6. Modified Retrosynthesis of Diene Subunit

5.3.2 Preparation of Aldehyde 5.30

The required aldehyde **5.30** was prepared in six steps from the known sultam **2.10** (Scheme 5.6).[9] Cuprate addition of Grinard reagent **5.31**[9] to sultam **2.10**, under similar conditions described by Paquette,[9] afforded the stereocenter at C_{11} with excellent diastereoselectivity (dr>20:1). The following reductive cleavage of the auxiliary and C_9 TBS protection produced TBS ether **5.34**. The PMB group was then removed using DDQ to yield alcohol **5.35**. Finally, Dess-Martin oxidation[10] revealed the coupling precursor **5.30**.



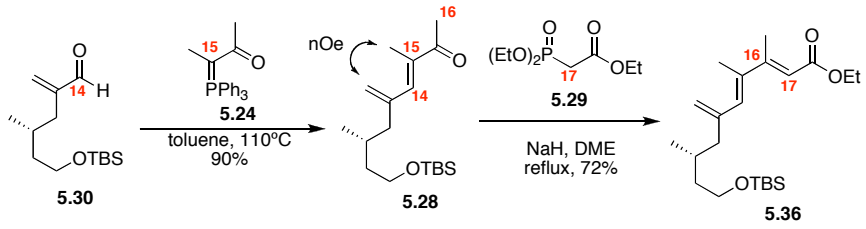
2.10 **5.31** **5.32** **5.33** **5.34** **5.35** **5.30**

Scheme 5.7. Synthesis of Aldehyde **5.30**

5.3.3 Wittig / HWE Reaction Sequence

With aldehyde **5.30** in hand, we next explored the key Wittig / HWE reaction sequence (Scheme 5.8). In general, "stabilized" ylides with strongly conjugating substituents (e.g., COOMe,CN, or $COCH_3$) on the ylidic carbon are known to favor the production of *E* alkenes.[5] We were pleased to find that the Wittig reaction between aldehyde **5.30** and the known ylide **5.24**[6] performed smoothly in good yield and great *E/Z* selectivity. The geometry of C_{14}-C_{15} double bond was confirmed via nOe analysis. Due to the low reactivity of ketone **5.28** with phosphonate **5.29**,[5] the Horner-Wadsworth-Emmons olefination was sluggish

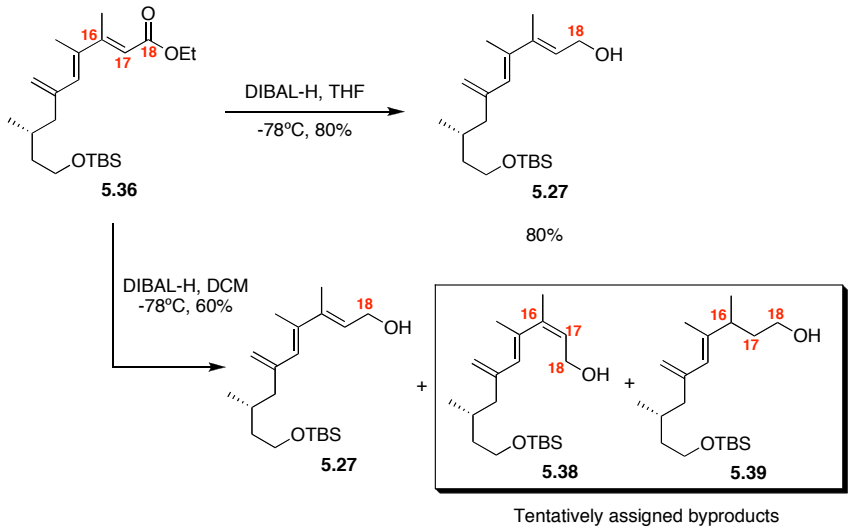
at room temperature. Fortunately, upon refluxing the reaction mixture in DME, we observed significant rate acceleration and the reaction was completed in 4 hours to give C_{16}-C_{17} alkene.



Scheme 5.8. Wittig / HWE Reaction Sequence

5.3.4 Reduction of α,β-Unsaturated Ester 5.36

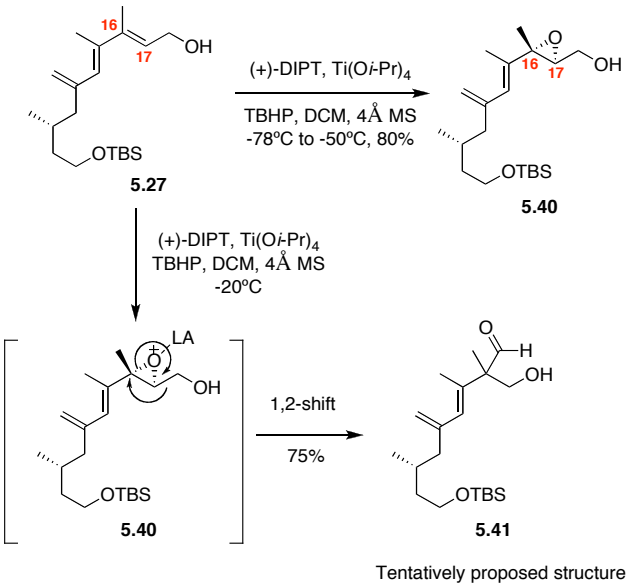
The Wittig / HWE reaction sequence generated the highly substituted C_{13}-C_{15} diene moiety successfully. The remained challenges were the installation of C_{16} tertiary alcohol via sequential epoxidation and regioselective opening of the epoxide. The required reduction of ester **5.36** is shown in Scheme 5.9. Under typical DIBAL-H reduction conditions (DIBAL-H / DCM), moderate yield was obtained with the occurrence of the several undesired compounds. The unidentified by-products appeared to arise from the double bond *E/Z* isomerization and 1,4-reduction of α,β-unsaturated ester **5.36**. Interestingly, using THF as solvent[11] suppressed the formation of the by-products and the yield was improved to 80%.



Scheme 5.9. Reduction of Ester **5.36**

5.3.5 Epoxidation of C_{16}-C_{17} Alkene

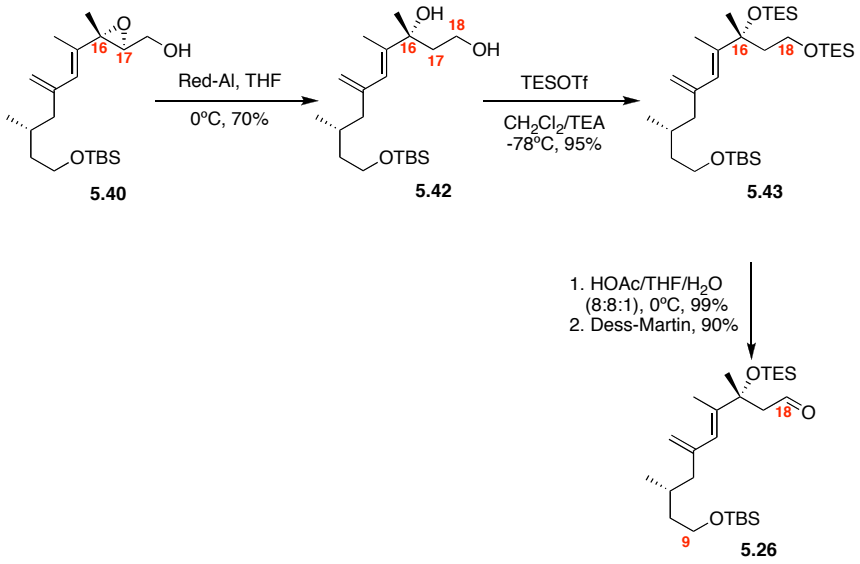
After obtaining triene alcohol **5.27**, we investigated the epoxidation on this highly reactive system. When the epoxidation was conducted at -20ºC, we were surprised that the major product was an aldehyde most likely resulting from Yamamoto-type epoxide rearrangement of substrate **5.40**.[12] Lower temperature (-78ºC to -50ºC) and freshly distilled Ti(O-*i*Pr)$_4$ suppressed this 1,2-alkyl shift and the desired epoxide **5.40** was obtained in 80% yield.



Scheme 5.10. Epoxidation of C_{16}-C_{17} Alkene

5.3.6 Regioselective Opening of the Epoxide

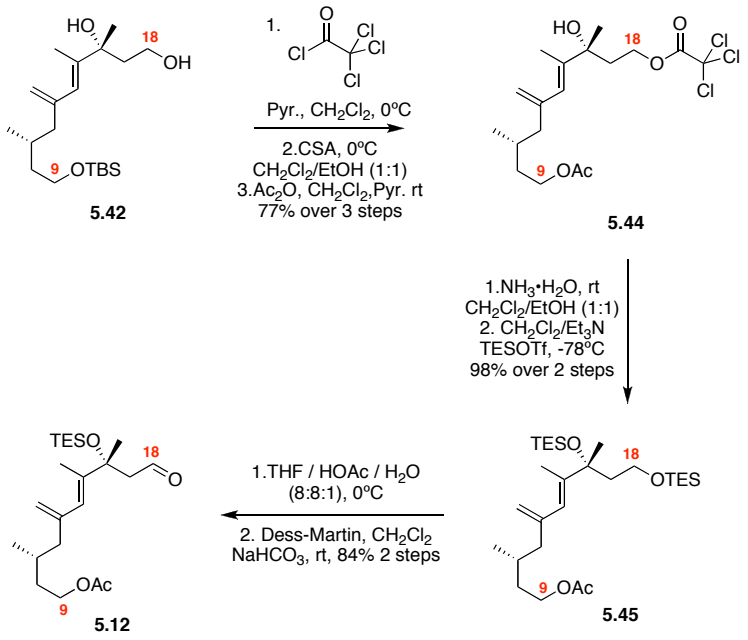
With the epoxidation of C_{16}-C_{17} alkene, the last challenge was the regioselective epoxide opening (Scheme 5.11). Base-catalyzed epoxide opening in which nucleophile provides the driving force generally involves the break of the C-O bond at the less substituted position.[13] Gratifyingly, treatment of epoxide **5.42** with Red-Al[14] yielded the desired diene diol **5.43**. Subsequent TES protection, selective removal of primary TES group[15] and Dess-Martin oxidation[11] finally afforded diene aldehyde **5.26**.



Scheme 5.12. Synthesis of Diene Aldehyde **5.26**

5.3.7 Synthesis of C_9 Acetate Protected Diene Motif 5.12

Synthesis of C_9 acetate-protected diene aldehyde **5.12** required protecting group manipulations on diene diol **5.42**, which was realized by using a trichloroacetate group[16] (Scheme 5.13). Commenced from diene diol **5.42**, protecting group manipulation afforded ester **5.44**. Next, selective removal of the trichloroacetate group in the presence of acetate group,[16] followed by the TES protection, yielded TES ether **5.48**. Finally, consecutive deprotection of the C_{18} primary TES and Dess-Martin oxidation give the desired C_9 acetate protected diene aldehyde **5.12**.



Scheme 5.13. Synthesis of Diene Aldehyde **5.12**

5.4 Conclusion

In summary, C_9 TBS-protected and acetate-protected C_9-C_{18} diene subunits have been synthesized diastereoselectively from commercially available Oppolzer sultam derivative **2.10** in 13 steps in 20% overall yield and in 17 steps in 14% overall yield respectively. The key steps included a Wittig / HWE sequence to yield C_{13}-C_{15} diene moiety and a regioselective epoxide opening to generate the C_{16} stereocenter. The new strategy has proven to be much more conducive to scale up than our 1st generation synthesis. Both diene aldehydes have been prepared on grams scale, which provided a solid base for the completion of the total syntheses of amphidinolide B_1 and B_2.

5.5 References

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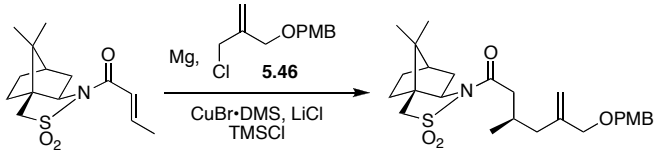
5.6 Experimental

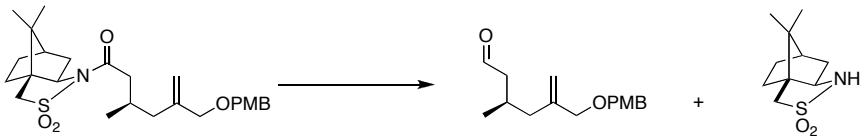


2.10 **5.32**

Sultam 5.32: Following the similar procedure described by Paquette,[1] Mg (36.0 g, 1.5 mol) was stirred vigorously at rt in a dry flask under Ar. After 120 h, when black coating formed inside the flask, THF (200 mL) and 1,2-dibromoethane (2.60 g, 1.2 mL, 13.9 mmol) were added sequentially. After 30 min, a solution of allyl chloride **5.46** (17.0 g, 75.0 mmol) in THF (80 mL) was added slowly to the Mg slurry over 5 h. The resulted mixture was stirred overnight at rt to give 300 mL Grignard reagent (0.12 M, 47%) as gray solution. The concentration of the Grignard reagent was determined by the titration using menthol in the presence of 1,10-phenonthroline.[2]

Separately, $CuBr•SMe_2$ (7.29 g, 35.5 mmol) and LiCl (1.61 g, 37.9 mmol) were dissolved in THF (80 mL) and added to the solution of Grinard reagent (263 mL, 31.5 mmol) at -78°C *via* syringe. TMSCl (3.96 g, 4.5 mL, 36.5 mmol) was then added followed by a solution of known sultam **2.10**[3] (6.9 g, 24.3 mmol) in THF (60 mL). After another 90 min, the reaction was quenched with NH_4Cl-NH_4OH (9:1, pH 9, 60 mL), warmed to rt. The aqueous layer was extracted with EtOAc (3 X 200 mL). The organic phase was washed with sat. aq. NaCl (100 mL). The dried extract ($MgSO_4$) was concentrated *in vacuo* and purified by

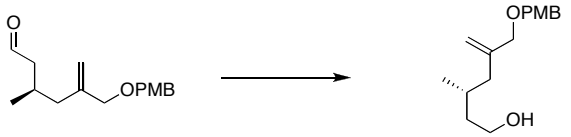
chromatography over silica gel, eluting with 8-15% EtOAc / Hexanes, to give the product **5.32** (11.2 g, 34.4 mmol, 97%) as a colorless oil: $[\alpha]_D^{23}$ = -68.0 (*c* 0.51, $CHCl_3$); IR (neat) 2959, 2927, 2851, 1693, 1512, 1454, 1328, 1246, 1032 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.28 (d, *J* = 8.7 Hz, 2H), 6.88 (d, *J* = 8.7 Hz, 2H), 5.12 (s, 1H), 4.96 (s, 1H), 4.44 (t, *J* = 11.8 Hz, 2H), 3.94 (t, *J* = 11.8 Hz, 2H), 4.00 (dd, *J* = 14.0 Hz, 2H), 3.88 (t, *J* = 6.2 Hz, 1H), 3.82 (s, 3H), 3.46 (dd, *J* = 23.0, 13.8 Hz, 2H), 2.78 (dd, *J* = 16.1, 5.7 Hz, 1H), 2.51 (dd, *J* = 16.1, 7.6 Hz, 1H), 2.30-2.40 (m, 1H), 2.02-2.15 (m, 4H), 1.82-1.96 (m, 3H), 1.28-1.45 (m, 3H), 1.15 (s, 3H), 0.99 (d, *J* = 6.4 Hz, 3H), 0.98 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.4, 159.1, 144.1, 130.6, 129.3, 113.7, 113.6, 72.4, 71.7, 65.2, 55.3, 53.0, 48.3, 47.7, 44.7, 42.5, 40.8, 38.6, 32.9, 28.0, 26.5, 20.8, 19.9; HRMS (ES^+) calcd. for $C_{26}H_{37}NO_5SNa$ (M+Na) 498.2290, found 498.2271.



5.32 **5.33** **2.15**

Aldehyde 5.33: To a stirred solution of sultam **5.32** (11.0 g, 23.1 mmol) in CH_2Cl_2 (115 mL) at -78°C was added DIBAL-H (50.8 mL, 50.8 mmol, 1.0 M in CH_2Cl_2). After 2 h, the reaction was carefully quenched with methanol (2.0 mL) and poured into aq. sodium potassium tartrate (250 mL, 10% aq.) at rt. The reaction flask was rinsed with an additional portion of CH_2Cl_2 (150 mL). After 3 h,

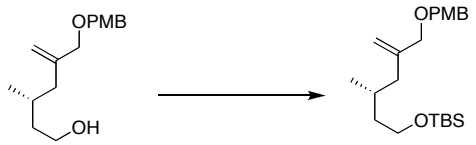
the aqueous layer was extracted with CH_2Cl_2 (3 X 150 mL). The dried extract ($MgSO_4$) was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 10% EtOAc / Hexanes, to give the aldehyde **5.33** (5.9 g, 22.6 mmol, 98%) as colorless oil. Further elution with 5% MeOH / EtOAc gave recovered auxiliary **2.15** (4.9 g, 22.4 mmol, 97%). **5.33**: $[\alpha]_D^{23}$ = +5.93 (*c* 0.91, $CHCl_3$); IR (neat) 2956, 2929, 2837, 1723, 1612, 1513, 1247, 1077, 1034 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.75 (t, *J* = 1.5 Hz, 1H), 7.29 (d, *J* = 8.7 Hz, 2H), 6.90 (d, *J* = 8.7 Hz, 2H), 5.14 (d, *J* = 1.2 Hz, 1H), 4.95 (s, 1H), 4.44 (s, 2H), 3.93 (s, 2H), 3.83 (s, 3H), 2.47 (ddd, *J* = 14.0, 4.0 and 1.3 Hz, 1H), 2.17-2.34 (m, 2H), 2.01-2.11 (m, 2H), 0.98 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 202.6, 159.2, 143.9, 130.3, 129.3, 114.1, 113.8, 72.4, 71.7, 55.3, 50.6, 41.0, 26.3, 20.1; HRMS (ES^+) calcd. for $C_{16}H_{22}O_3Na$ (M+Na) 285.1467, found 285.1494.



5.33 **5.47**

Aldohol 5.47: To a stirred solution of aldehyde **5.33** (5.6 g, 21.4 mmol) in CH_2Cl_2 (110 mL) at -78°C was added DIBAL-H (28.3 mL, 28.3 mmol, 1.0 M in CH_2Cl_2). After 1 h, the reaction was carefully quenched with methanol (2.0 mL) and poured into aq. sodium potassium tartrate (250 mL, 10% aq.) at rt. The reaction flask was rinsed with an additional portion of CH_2Cl_2 (150 mL). After 3 h, the aqueous layer was extracted with CH_2Cl_2 (3 X 150 mL). The dried extract

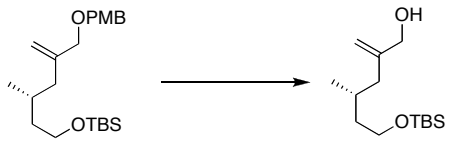
($MgSO_4$) was concentrated *in vacuo* to give the alcohol **5.47** (5.6 g, 20.8 mmol, 97%) as a colorless oil: $[\alpha]_D^{23}$ = -2.94 (*c* 0.51, $CHCl_3$); IR (neat) 3407, 2926, 2868, 1612, 1513, 1461, 1248, 1059, 1036 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.29 (d, *J* = 8.7 Hz, 2H), 6.90 (d, *J* = 8.7 Hz, 2H), 5.10 (s, 1H), 4.94 (s, 1H), 4.44 (t, *J* = 12.2 Hz, 2H), 3.91 (t, *J* = 13.4 Hz, 2H), 3.82 (s, 3H), 3.61-3.78 (m, 2H), 2.15 (dd, *J* = 13.8, 6.0 Hz, 1H), 1.89-1.96 (m, 1H), 1.89-1.96 (m, 1H), 1.72-1.86 (m, 1H), 1.57-1.69 (m, 1H), 1.23-1.45 (m, 1H), 0.91 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.2, 144.6, 130.4, 129.3, 113.8, 113.4, 72.6, 71.6, 61.0, 55.3, 41.3, 39.7, 27.5, 19.7, 18.8; HRMS (ES^+) calcd. for $C_{16}H_{24}O_3Na$ (M+Na) 287.1623, found 285.1649.



5.47 **5.34**

TBS ether 5.34: To a stirred solution of alcohol **5.47** (5.5 g, 20.8 mmol) in DMF (50 mL) at rt was sequentially added imidazole (3.4 g, 50.0 mmol) and TBSCl (3.8 g, 25.2 mmol). After 1 h, the reaction was quenched with sat. aq. NH_4Cl (50 mL) and extracted with Et_2O (3 x 150 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 5% EtOAc / Hexanes, to give TBS ether **5.34** (7.7 g, 20.3 mmol, 97%) as a colorless oil: $[\alpha]_D^{23}$ = -3.27 (*c* 1.31, $CHCl_3$); IR (neat) 2954, 2928, 2856, 1513, 1249, 1094, 835 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.29 (d, *J* = 8.7 Hz, 2H),

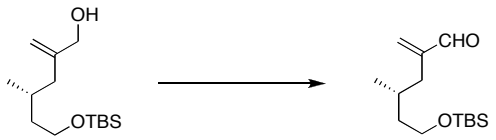
6.90 (d, J = 8.7 Hz, 2H), 5.11 (s, 1H), 4.93 (s, 1H), 4.44 (s, 2H), 3.92 (s, 2H), 3.83 (s, 3H), 3.63-3.70 (m, 2H), 2.13 (dd, J = 13.8, 6.3 Hz, 1H), 1.88-1.96 (m, 1H), 1.76-1.86 (m, 1H), 1.57-1.69 (m, 1H), 1.28-1.35 (m, 1H), 0.91 (s, 9H), 0.89 (d, J = 6.6 Hz, 3H), 0.06 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.1, 144.7, 130.6, 129.3, 113.8, 112.8, 72.6, 71.6, 61.3, 55.3, 41.4, 39.8, 27.5, 26.0, 19.6, 18.3, -5.3; HRMS (ES^+) calcd. for $C_{22}H_{38}O_3Na$ (M+Na) 401.2488, found 401.2489.



5.34 **5.35**

Alcohol 5.35: To a stirred solution of TBS ether **5.34** (3.85 g, 10.2 mmol) in CH_2Cl_2/PH 7 buffer (10 : 1, 110 mL) was added DDQ (2.77 g, 12.2 mmol) at rt. After 1 h, the reaction was quenched with sat. aq. $NaHCO_3$ (50 mL) and extracted with Et_2O (3 x 100 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 8% EtOAc / Hexanes, to give a mixture of product **5.35** and 4-methoxybenzaldehyde (3.90 g, 1:1 mole/mole, 9.9 mmol, 97%) as colorless oil. An analytically pure sample was prepared by chromatography over silica gel, eluting with 3%-5% EtOAc / Hexanes, for characterization, but the product mixture was used in the subsequent step without complete removal of 4-methoxybenzaldehyde. **5.35**: $[\alpha]_D^{23}$ = -6.09 (*c* 1.21, $CHCl_3$); IR (neat) 3338, 2955, 2929, 2858, 1471, 1463, 1255, 1098, 835 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.09 (d, J = 1.5 Hz, 1H), 4.89 (s, 1H), 4.07 (d, J =

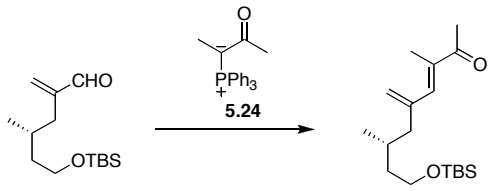
6.3 Hz, 2H), 3.61-3.75 (m, 2H), 2.13 (dd, *J* = 13.5, 6.0 Hz, 1H), 1.75-1.95 (m, 2H), 1.55-1.66 (m, 1H), 1.41-1.50 (m, 1H), 1.27-1.38 (m, 1H), 0.91 (s, 9H), 0.89 (d, *J* = 6.6 Hz, 3H), 0.07 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.6, 110.7, 65.8, 61.2, 41.2, 39.6, 27.6, 26.0, 19.7, 18.3, -5.3; HRMS (EI^+) calcd. for $C_{14}H_{31}O_2Si$ (M+H) 259.2093, found 259.2091.



5.35 **5.30**

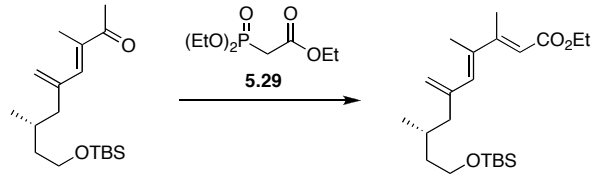
Aldehyde 5.30: To a stirred solution of alcohol **5.35** and 4-methoxybenzaldehyde (7.8 g, 1:1 mole/mole, 19.7 mmol) in CH_2Cl_2 (200 mL) was sequentially added $NaHCO_3$ (3.0 g, 35.7 mmol) and DMP (10.0 g, 23.7 mmol) at rt. After 1 h, the reaction was quenched with sat. aq. $NaHCO_3$ (50 mL) and extracted with Et_2O (3 x 150 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 3% EtOAc / Hexanes, to give aldehyde **5.30** (4.6 g, 17.7 mmol, 90%) as a colorless oil: $[\alpha]_D^{23}$ = -8.20 (*c* 1.21, $CHCl_3$); IR (neat) 2956, 2929, 2857, 1698, 1255, 1099, 835 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.56 (s, 1H), 6.28 (s, 1H), 6.07 (s, 1H), 3.60-3.73 (m, 2H), 2.28 (dd, *J* = 14.1, 6.9 Hz, 1H), 2.12 (dd, *J* = 13.8, 8.1 Hz, 1H),1.77-1.86 (m, 1H), 1.53-1.64 (m, 1H), 1.29-1.39 (m, 1H), 0.91 (s, 9H), 0.89 (d, *J* = 6.6 Hz, 3H), 0.07 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 194.7, 149.0, 135.2, 61.1, 39.5, 35.2,

28.4, 25.9, 25.5, 19.4, -5.4; HRMS (EI^+) calcd. for $C_{14}H_{28}O_2Si$ (M) 256.1859, found 256.1861.



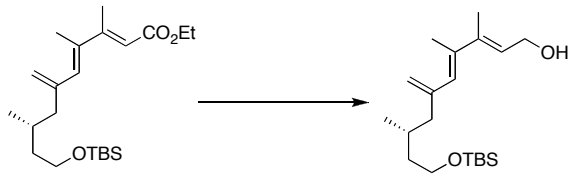
5.30 **5.28**

Methyl ketone 5.28: A solution of aldehyde **5.30** (4.5 g, 17.5 mmol) and ylide **5.24**[4] (10.2 g, 30.7 mmol) in toluene (60 mL) was refluxed in a sealed tube (oil bath 112ºC). After 16 h, the reaction mixture was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 5% EtOAc / Hexanes (1% Et_3N added), to give diene **5.28** (5.0 g, 16.1 mmol, 92%) as a slightly yellow oil: $[\alpha]_D^{23}$ = -41.1 (*c* 0.53, $CHCl_3$); IR (neat) 2955, 2928, 2857, 1671, 1255, 1100, 836, 775 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.90 (s, 1H), 5.29 (s, 1H), 5.14 (s, 1H), 3.62-3.73 (m, 2H), 2.37 (s, 3H), 2.30 (dd, *J* = 10.2, 4.8 Hz, 1H), 2.05 (dd, *J* = 10.5, 6.3 Hz, 1H), 1.97 (d, *J* = 10.2 Hz, 3H), 1.71-1.78 (m, 1H), 1.59-1.64 (m, 1H), 1.34-1.38 (m, 1H), 0.91 (s, 9H), 0.89 (d, *J* = 6.6 Hz, 3H), 0.07 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.3, 143.7, 140.9, 137.8, 118.9, 61.0, 45.1, 39.6, 28.4, 25.9, 25.7, 19.3, 18.3, 13.1, -5.3; HRMS (FAB^+) calcd. for $C_{18}H_{35}O_2Si$ (M+H) 311.2406, found 311.2400.



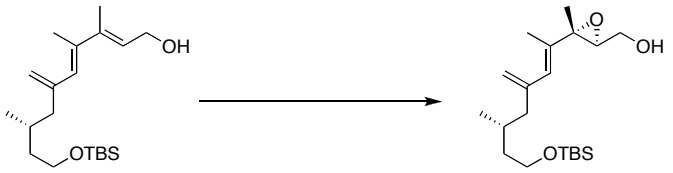
5.28 **5.36**

Triene ester 5.36: To a stirred slurry of NaH (1.29 g, 32.2 mmol) in DME (50 mL) was added phosphonate **5.29** (6.48 g, 5.74 mL, 28.9 mmol) at rt. After 1 h, a solution of methyl ketone **5.28** (5.00 g, 16.1 mmol) in DME (25 mL) was added. The resulted solution was refluxed for 3 h then quenched with H_2O (15 mL) and extracted with Et_2O (3 x 150 mL). The dried extract ($MgSO_4$) was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 2% EtOAc / Hexanes (1% Et_3N added), to give triene ester **5.36** (4.42 g, 11.6 mmol, 70%) as a colorless oil: $[\alpha]_D^{23}$ = -34.7 (*c* 1.66, $CHCl_3$); IR (neat) 2955, 2928, 2857, 1716, 1610, 1255, 1163, 1098, 836, 775 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.24 (s, 1H), 5.92 (s, 1H), 5.13 (s, 1H), 4.93 (s, 1H), 4.19 (q, *J* = 7.1 Hz, 2H), 3.61-3.68 (m, 2H), 2.36 (s, 3H), 2.20 (dd, *J* = 13.3, 5.9 Hz, 1H), 1.93-2.00 (m, 4H), 1.53-1.71 (m, 2H), 1.31 (t, *J* = 7.2 Hz, 3H), 0.89 (s, 9H), 0.87 (d, *J* = 6.9 Hz, 3H), 0.05 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.4, 156.4, 144.7, 137.8, 132.4, 116.4, 115.9, 61.2, 59.7, 45.7, 39.7, 28.3, 25.9, 19.5, 18.3, 15.8, 15.5, 14.4, -5.3; HRMS (EI^+) calcd. for $C_{22}H_{40}O_3Si$ (M+H) 380.2747, found 380.2732.



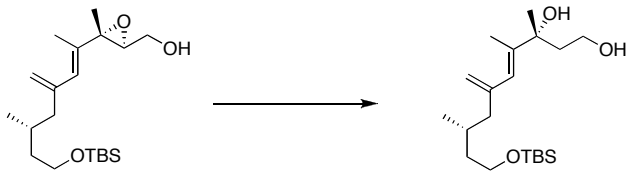
5.36 5.27

Allyl alcohol 5.27: To a stirred solution of triene ester **5.36** (8.61 g, 22.6 mmol) in THF (200 mL) was added DIBAL-H (46 mL, 46.0 mmol, 1 M in toluene) at -78ºC. After 1.5 h, the reaction was quenched with MeOH (1.0 mL) and poured into aq. sodium potassium tartrate (350 mL, 10% aq.) at rt. The reaction flask was rinsed with an additional portion of Et_2O (50 mL). After 3 h, the aqueous layer was extracted with Et_2O (3 X 200 mL). The dried extract ($MgSO_4$) was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 8% EtOAc / Hexanes, to give allyl alcohol **5.27** (6.20 g, 18.3 mmol, 81%) as a colorless oil: $[\alpha]_D^{23}$ = -36.6 (*c* 1.66, $CHCl_3$); IR (neat) 3327, 2954, 2928, 2857, 1471, 1462, 1376, 1255, 1098, 1006, 835, 775 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.97 (s, 1H), 5.80 (t, *J* = 6.3 Hz, 1H), 5.08 (s, 1H), 4.87 (s, 1H), 4.34 (d, *J* = 6.4 Hz, 2H), 3.46-3.72 (m, 2H), 2.18 (dd, *J* = 13.6, 6.0 Hz, 1H), 1.99 (d, *J* = 0.8 Hz, 3H), 1.93 (dd, *J* = 13.5, 5.2 Hz, 1H), 1.86 (s, 3H), 1.54-1.73 (m, 2H), 1.28-1.37 (m, 1H), 0.90 (s, 9H), 0.87 (d, *J* = 6.6 Hz, 3H), 0.05 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.2, 139.3, 137.6, 128.1, 125.9, 115.4, 61.3, 60.1, 46.0, 39.7, 28.3, 25.9, 19.5, 18.3, 15.6, 14.2, -5.3; HRMS (EI^+) calcd. for $C_{20}H_{38}O_2Si$ (M) 338.2641, found 338.2612.



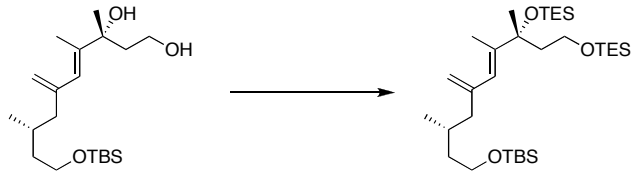
5.27 5.40

Epoxide 5.40: To a stirred solution of (+)-DIPT (41.5 mg, 0.18 mmol) and 4 Å mol sieves (about 200 mg) in CH_2Cl_2 (4.0 mL) was sequentially added Ti(O-*i*Pr)$_4$ (34 mg, 34.6 μL, 0.12 mmol) and TBHP (236 μL, 1.30 mmol, 5.0-6.0 M in decane) at -20ºC. After 20 min, the reaction mixture was cooled to -78ºC and a pre-cooled solution (-78ºC) of allyl alcohol **5.27** (200 mg, 0.59 mmol) in CH_2Cl_2 (4.0 mL) was added *via* cannula. The resulted solution was warmed up to -50ºC. After another 60 min, the reaction was quenched with pH7 phosphate buffer (0.5 mL), filtered over Celite, and extracted with Et_2O (3 x 20 mL). The dried organic layers ($MgSO_4$) was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 10% EtOAc / Hexanes, to give epoxide **5.40** (167 mg, 0.47 mmol, 80%) as colorless oil: $[\alpha]_D^{23}$ = -17.3 (*c* 1.66, $CHCl_3$); IR (neat) 3430, 2954, 2927, 2856, 1471, 1463, 1378, 1255, 1097, 836, 775 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.89 (s, 1H), 5.03 (s, 1H), 4.86 (s, 1H), 3.86-3.92 (m, 1H), 3.73-3.81 (m, 1H), 3.62-3.71 (m, 2H), 3.02 (dd, *J* = 10.5, 6.3 Hz, 1H), 2.14 (dd, *J* = 13.5, 5.6 Hz, 1H), 1.91 (dd, *J* = 13.5, 8.4 Hz, 1H), 1.84 (d, *J* = 1.1 Hz, 3H), 1.54-1.66 (m, 2H), 1.45 (s, 3H), 1.27-1.34 (m, 1H), 0.91 (s, 9H), 0.83 (d, *J* = 6.4 Hz, 3H), 0.06 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.0, 137.5, 126.2, 115.2, 63.7, 61.3, 45.6, 39.8, 28.2, 26.0, 19.3, 18.3, 16.7, 14.8, -5.3; HRMS (CI^+) calcd. for $C_{20}H_{39}O_3Si$ (M+H) 355.2669, found 355.2666.



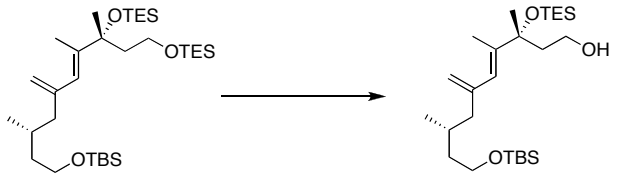
5.40 **5.42**

Diol 5.42: To a stirred solution of epoxide **5.40** (1.5 g, 4.23 mmol) in THF (30 mL) was added Red-Al (1.5 mL, 9.91 mmol, 65% W/V in toluene) at 0ºC. After 1 h, another portion of Red-Al (1.5 mL, 9.91 mmol, 65% W/V in toluene) was added. After another 1.5 h, the reaction was quenched with H_2O (0.10 mL), and extracted with CH_2Cl_2 (3 X 150 mL). The dried organic layers ($MgSO_4$) was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 6-12% EtOAc / Hexanes (1% Et_3N added), to give diol **5.42** (1.05 g, 2.96 mmol, 70%) as a colorless oil: $[\alpha]_D^{23}$ = -29.4 (*c* 0.81, $CHCl_3$); IR (neat) 3389, 2955, 2928, 2858, 1471, 1462, 1382, 1255, 1097, 836, 775 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.10 (s, 1H), 5.04 (d, *J* = 0.9 Hz, 1H), 4.84 (s, 1H), 3.62-3.77 (m, 4H), 3.04 (s, br, 1H), 2.60 (s, br, 1H), 2.16 (dd, *J* = 13.2, 5.1 Hz, 1H), 1.88-1.96 (m, 3H), 1.79 (d, *J* = 0.9 Hz, 3H), 1.55-1.70 (m, 2H), 1.37 (s, 1H), 1.27-1.34 (m, 1H), 0.91 (s, 9H), 0.86 (d, *J* = 6.5 Hz, 3H), 0.07 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.1, 141.7, 125.1, 114.4, 77.1, 61.6, 60.4, 46.1, 40.1, 39.7, 28.6, 28.2, 26.0, 19.6, 18.4, 15.1, -5.2; HRMS (ES^+) calcd. for $C_{20}H_{40}O_3SiNa$ (M+Na) 379.2644, found 379.2643



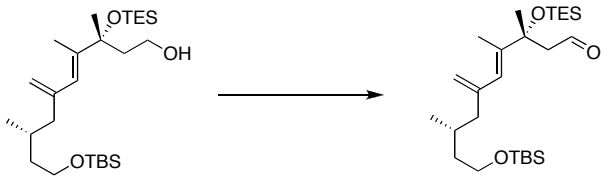
5.42 **5.43**

TES ether 5.43: To a stirred solution of diol **5.42** (470 mg, 1.32 mmol) in DCM / TEA (6 mL, 1:1) was added freshly distilled TESOTf (1.05 g, 0.89 mL, 3.96 mmol) at -78ºC. After 30 min, the reaction was quenched with sat. aq. $NaHCO_3$ (1 mL) and extracted with ether (3 X 20 mL). The dried extract ($MgSO_4$) was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 2-5% EtOAc / Hexanes, to give **5.43** (732 mg, 1.25 mmol, 95%) as a colorless oil: $[\alpha]_D^{23}$ = -21.3 (*c* 1.37, $CHCl_3$); IR (neat) 2954, 2929, 2876, 1460, 1254, 1093, 1007, 835, 741 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.88 (s, 1H), 4.99 (s, 1H), 4.80 (s, 1H), 3.61-3.71 (m, 3H), 3.47 (dt, *J* = 15.6, 5.4 Hz, 1H), 2.15 (dd, *J* = 13.5, 5.4 Hz, 1H), 1.80-1.99 (m, 5H), 1.77 (d, *J* = 0.9 Hz, 3H), 1.54-1.66 (m, 1H), 0.88-1.00 (m, 27H), 0.84 (d, *J* = 6.3 Hz, 3H), 0.55-0.66 (m, 12H), 0.063 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.2, 142.0, 124.6, 114.1, 77.2, 61.7, 59.3, 46.2, 44.5, 40.0, 28.7, 26, 19.6, 18.4, 14.7, 7.2, 7.0, 6.9, 6.8, 4.4, -5.3; HRMS (EI^+) calcd. for $C_{32}H_{68}O_3Si_3$ (M+) 584.4476, found 584.4500.



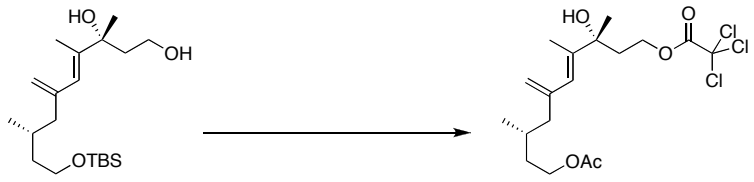
5.43 **5.48**

Aldohol 5.48: TES ether **5.43** (300 mg, 0.51 mmol) was dissolved in a stirred solution of HOAc / THF / H_2O (8 mL, 8:8:1) at 0ºC. After 1.5 h, the reaction was then quenched with solid $NaHCO_3$ and extracted with ether (3 X 20 mL). The dried extract ($MgSO_4$) was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 10% EtOAc / Hexanes, to give alcohol **5.48** (241 mg, 0.51 mmol, 99%) as a colorless oil: $[\alpha]_D^{23}$ = -15.5 (*c* 0.64, $CHCl_3$); IR (neat) 3437, 2954, 2928, 2876, 1461, 1254, 1099, 1008, 835 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.02 (s, 1H), 5.04 (s, 1H), 4.85 (s, 1H), 3.63-3.73(m, 4H), 2.79 (t, *J* = 5.6 Hz, 1H), 2.17 (dd, *J* = 13.6, 5.6 Hz, 1H), 1.88-1.97 (m, 3H), 1.74-1.83 (m, 1H), 1.79 (d, *J* = 1.2 Hz, 3H), 1.59-1.68 (m, 1H), 1.47 (s, 3H), 1.28-1.40 (m, 1H), 0.99-1.03 (t, *J* = 7.6 Hz, 9H), 0.92 (s, 9H), 0.88 (d, *J* = 6.4 Hz, 3H), 0.69 (q, *J* = 7.2 Hz, 6H), 0.078 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.0, 141.4, 125.6, 114.6, 80.0, 61.6, 60.1, 46.1, 42.8, 39.9, 29.7, 28.6, 27.6, 26.0, 19.5, 18.4, 14.9, 7.2, 6.9, 6.8, -5.3; HRMS (EI^+) calcd. for $C_{26}H_{54}O_3Si_2$ (M+) 470.3611, found 470.3604.



5.48 **5.26**

Aldehyde 5.26: To a stirred solution of alcohol **5.48** (1.29 g, 2.73 mmol) in DCM (40 mL, 1:1) was sequentially added DMP (2.17 g, 5.12 mmol) and $NaHCO_3$ (1.68 g, 20.0 mmol) at rt. After 30 min, the reaction was quenched with sat. aq. $NaHCO_3$ (10 mL) and extracted with ether (3 X 40 mL). The dried extract ($MgSO_4$) was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 5% EtOAc / Hexanes, to give aldehyde **5.46** (1.17 g, 2.49 mmol, 91%) as a colorless oil: $[\alpha]_D^{23}$ = -12.5 (*c* 0.56, $CHCl_3$); IR (neat) 2955, 2929, 2877, 1725, 1255, 1099, 1007, 836, 726 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.69 (t, *J* = 3.3 Hz, 1H), 6.03 (s, 1H), 5.03 (s, 1H), 4.83 (s, 1H), 3.61-3.68(m, 2H), 2.64 (dd, *J* = 15.0, 3.0 Hz, 1H), 2.45 (dd, *J* = 15.0, 3.0 Hz, 1H), 2.15 (dd, *J* = 13.5, 6.0 Hz, 1H), 1.85-1.92 (m, 1H), 1.83 (d, *J* = 1.2 Hz, 3H), 1.54-1.64 (m, 1H), 1.49 (s, 3H), 1.25-1.35 (m, 2H), 0.95-1.00 (t, *J* = 7.7 Hz, 9H), 0.91 (s, 9H), 0.85 (d, *J* = 6.5 Hz, 3H), 0.65 (q, *J* = 7.8 Hz, 6H), 0.061 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.1, 144.7, 141.0, 126.0, 114.9, 76.9, 61.5, 54.2, 46.0, 39.9, 28.5, 27.8, 26.0, 19.5, 18.3, 14.7, 7.1, 6.7, -5.3; HRMS (EI^+) calcd. for $C_{26}H_{52}O_3Si_3$ (M+) 468.3455, found 468.3448



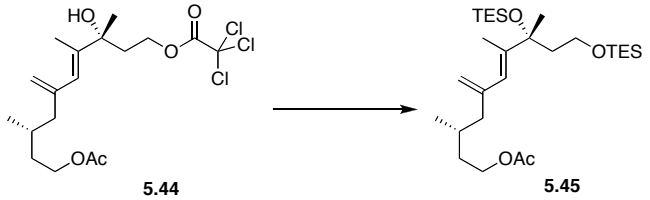
5.42 **5.44**

Ester 5.44:To a stirred solution of diol **5.42** (2.10 g, 5.89 mmol) in CH_2Cl_2 (50 mL) was sequentially added pyridine (1.37 g, 1.40 mL, 17.7 mmol) and trichloroacetyl chloride (1.29 g, 0.79 mL, 7.09 mmol). After 3 h, the reaction was quenched with sat. aq. NH_4Cl (10 mL) and extracted with ether (3 X 30 mL). The dried extract ($MgSO_4$) was concentrated *in vacuo* to give crude ester (3.30 g) as a colorless oil, which was used in the next step without further purification.

To a stirred solution of crude ester (3.30 g) in CH_2Cl_2 / EtOH (1:1, 50 mL) was added CSA (2.31 g, 9.88 mmol) at 0ºC. After 1.5 h, the reaction was quenched with sat. aq. $NaHCO_3$ (10 mL) and extracted with ether (3 X 40 mL). The dried extract ($MgSO_4$) was concentrated *in vacuo* to give crude diol (2.02 g), which was used in the next step without further purification.

To a stirred solution of crude diol (2.02 g) in CH_2Cl_2 (50 mL) was sequentially added pyridine (1.53 g, 1.57 mL, 19.5 mmol) and Ac_2O (0.99 g, 0.92 mL, 9.73 mmol). After 1.5 h, the reaction was quenched with sat. aq. NH_4Cl (10 mL) and extracted with ether (3 X 40 mL). The dried extract ($MgSO_4$) was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 10% EtOAc / Hexanes, to give **5.44** (1.90 g, 4.42 mmol, 75% over 3 steps) as a colorless oil: $[\alpha]_D^{23}$ = -14.1 (*c* 1.16, $CHCl_3$); IR (neat) 3481, 2962, 2928, 1766, 1739, 1720, 1458, 1368, 1247, 828, 682 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.01

(s, 1H), 5.04 (s, 1H), 4.85 (s, 1H), 4.47-4.36 (m, 2H), 4.15-4.06 (m, 2H), 2.12-2.02 (m, 3H), 2.03 (s, 3H), 1.97-1.89 (m, 3H), 1.83 (s, 3H), 1.70-1.60 (m, 2H), 1.50-1.38 (m, 1H), 1.41 (s, 3H), 0.89 (d, J = 6.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.2, 161.9, 144.1, 141.4, 124.9, 115.3, 74.6, 66.5, 62.3, 45.6, 37.8, 35.2, 28.7, 28.3, 21.0, 19.4, 14.9; HRMS (EI^+) calcd. for $C_{18}H_{27}O_5Cl_3$ (M+) 428.0924, found 428.0932.



5.44 5.45

TES ether 5.45: To a stirred solution of alcohol **5.44** (1.90 g, 4.4 mmol) in CH_2Cl_2 / EtOH (1:1, 50 mL) was added NH_3•H_2O (15 mL) at rt. After 1 h, the reaction was quenched with sat. aq. NH_4Cl (15 mL) and extracted with ether (3 X 40 mL). The dried extract ($MgSO_4$) was concentrated *in vacuo* to afford crude diol (1.55 g), which which was used in the next step without further purification.

To a stirred solution of crude diol (1.55 g) in CH_2Cl_2 / Et_3N (1:1, 30 mL) was added freshly distilled TESOTf (3.52 g, 3.01 mL, 13.1 mmol) at -78ºC. After 20 min, the reaction was quenched with sat. aq. $NaHCO_3$ (10 mL) and extracted with ether (3 X 40 mL). The dried extract ($MgSO_4$) was concentrated *in vacuo* andpurified by chromatography over silica gel, eluting with 2% EtOAc / Hexanes, to give TES ether **5.45** (2.12 g, 4.09 mmol, 93% over 2 steps) as a colorless oil: $[\alpha]_D^{23}$ = -18.4 (*c* 1.11, $CHCl_3$); IR (neat) 29554, 2912, 2876, 1748, 1458, 1238,

1086, 1016, 741 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.89 (s, 1H), 5.00 (d, *J* = 1.2 Hz, 1H), 4.81 (d, *J* = 1.2 Hz, 1H), 4.18-4.05 (m, 2H), 3.72-3.63 (m, 1H), 3.54-3.41 (m, 1H), 2.15 (dd, *J* = 13.5, 5.4 Hz, 1H), 2.05 (s, 3H), 1.95-1.89 (m, 2H), 1.87-1.78 (m, 1H), 1.77 (d, *J* = 1.2 Hz, 3H), 1.71-1.58 (m, 2H), 1.49-1.39 (m, 1H), 1.42 (s, 3H), 1.12-0.91 (m, 18H), 0.87 (d, *J* = 6.6 Hz, 3H), 0.74-0.50 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 144.8, 142.3, 124.3, 114.4, 77.2, 62.3, 59.5, 46.0, 44.4, 35.3, 28.8, 27.8, 21.0, 19.3, 14.6, 7.2, 6.9, 6.8, 6.4, 5.8, 4.4; HRMS (EI^+) calcd. for $C_{28}H_{56}O_4Si_2Na$ (M+Na) 535.3615, found 535.3637.

5.45 **5.12**

Aldehyde 5.12: TES ether **5.45** (2.1 mg, 4.09 mmol) was dissolved in a stirred solution of HOAc / THF / H_2O (34 mL, 8:8:1) at 0ºC. After 1.5 h, the reaction was then quenched with solid $NaHCO_3$ and extracted with ether (4 X 50 mL). The dried extract ($MgSO_4$) was concentrated *in vacuo* to afford crude alcohol (2.0 g), which was used in the next step without further purification.

To a stirred solution of crude alcohol (2.0 g) in CH_2Cl_2 (20 mL) was added sequentially solid $NaHCO_3$ (1.0 g, 11.9 mmol) and DMP (2.16 g, 5.09 mmol) at rt. After 1 h, the reaction was quenched with sat. aq. $NaHCO_3$ (15 mL) and extracted with ether (3 X 40 mL). The dried extract ($MgSO_4$) was concentrated *in vacuo* andpurified by chromatography over silica gel, eluting with 5% EtOAc / Hexanes,

to give aldehyde **5.12** (1.36 g, 3.43 mmol, 74% over 2 steps) as a colorless oil: $[\alpha]_D^{23}$ = -11.6 (*c* 1.83, $CHCl_3$); IR (neat) 2957, 2877, 1741, 1724, 1458, 1368, 1239, 1050, 1017, 743 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.66 (t, *J* = 3.0 Hz, 1H), 6.02 (s, 1H), 5.03 (s, 1H), 4.83 (s, 1H), 4.14-4.04 (m, 2H), 2.65 (dd, *J* = 15.1, 2.9 Hz, 1H), 2.46 (dd, *J* = 15.1, 3.1 Hz, 1H), 2.14 (dd, *J* = 13.6, 5.8 Hz, 1H), 2.04 (s, 3H), 1.92 (dd, *J* = 13.5, 7.8 Hz, 1H), 1.82 (s, 3H), 1.70 -1.60 (m, 2H), 1.48 (s, 3H), 1.45-1.39 (m, 1H), 1.00-0.94 (m, 9H), 0.87 (d, *J* = 6.5 Hz, 3H), 0.68-0.56 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 203.0, 171.2, 144.3, 141.2, 125.7, 115.1, 62.8, 54.0, 45.8, 35.3, 28.7, 27.9, 20.9, 19.2, 14.7, 7.1, 6.7, 6.6, 5.8; HRMS (EI^+) calcd. for $C_{22}H_{40}O_4Si$ (M+) 396.2696, found 396.2678.

---

1. Boulet, S. L.; Paquette, L. A. *Synthesis* **2002**, 895.

2. Titration of Grignard reagent: To a stirred solution of menthol (15.6 mg, 0.1 mmol) and 1,10-phenoanthroline (2 mg) in THF (0.5 mL) was added prepared Grignard reagent solution until a burgundy color persists. The concentration was calculated using the formula:

[RMgX] = 0.1 mmol / volume of added RMgX in mL

For the references, see: (a) Lin, H, -S; Paquette, L. A. *Synth. Comm.* **1994**, *24*, 2503. (b) Watson, S. C.; Eastham, J. F. *J. Organomet. Chem.* **1967**, *9*, 165.

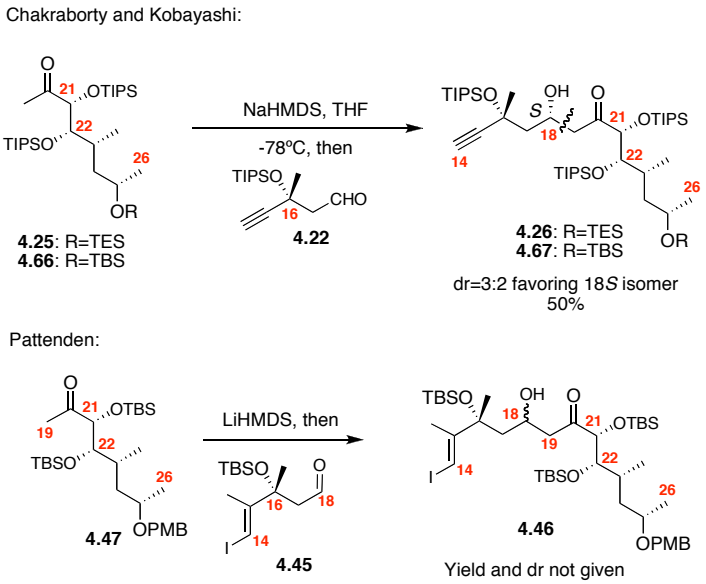
3. Vanderwalle, M.; Van der Eychen, J.; Oppolzer, W.; Vullioud, C. *Tetrahedron* **1986**, *42*, 4035.

4. Aitken, R. A.; Atherton, J. I. *J. Chem. Soc., Perkin Trans. 1* **1994**, 1281.

CHAPTER 6. GAME OF PROTECTING GROUPS AND THE STUDIES OF THE KEY ALDOL COUPLING

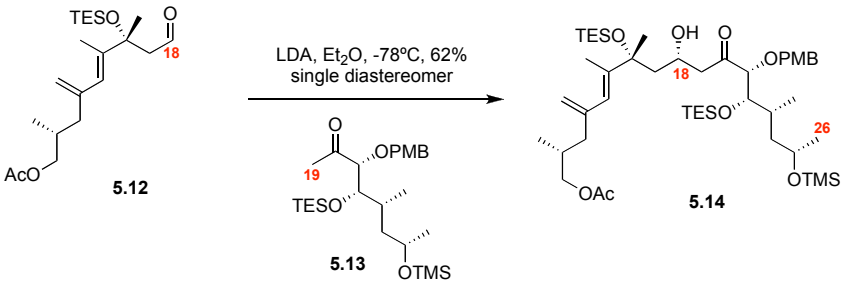
6.1 The Chelation-Controlled Aldol Reaction

After the success in the synthesis of the key diene subunits, our priority shifted to the aldol reaction to install the C_{18} stereocenter. There have been several attempts from Chakraborty,[1a] Pattenden,[1b] and Kobayashi[1c] to furnish the C_{18} stereochemistry utilizing the aldol coupling (Scheme 6.1). Unfortunately, the aldol reaction between an aldehyde and the C_{21} TBS- or TIPS-protected methyl ketone led to low yield and poor diastereoselectivity.



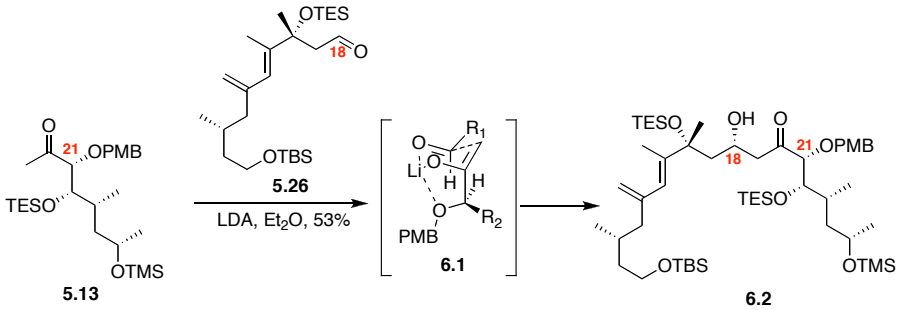
Scheme 6.1. Precedents of Aldol Coupling

Our group have reported the first chelation-controlled aldol reaction to give C_{18} stereocenter diastereoselectively (Scheme 6.2).[2] The aldol coupling between aldehyde **5.12** and C_{21} PMB-protected methyl ketone **5.13** afforded 18*S* aldol adduct as a single diastereomer. This strategy has been used in Fürstner's recent synthesis of amphidinolide G, H and B.[3]



Scheme 6.2. Carter's Chelation-Controlled Aldol Coupling

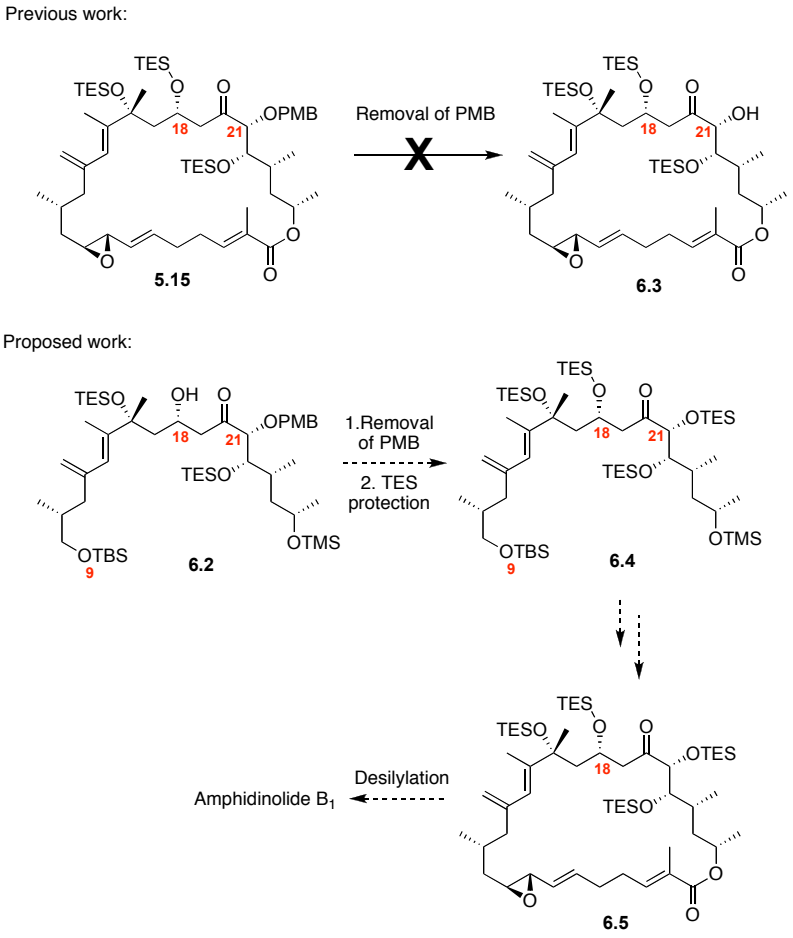
Equipped with the knowledge gained from our successful experience, we next investigated the key aldol reaction between the diene motif and the C_{21} PMB-protected methyl ketone **5.13**[2] (Scheme 6.3). We initially chose to explore our proposed chemistry on the C_9 TBS protected diene aldehyde **5.26**. Under our typical conditions (LDA / Et_2O, -78ºC), the adol coupling proceeded smoothly to yield 18*S* adduct **6.2** in 53% yield as a single diastereomer. Since the PMB protected hydroxyl group is known for its ability to participate in chelation-controlled processes,[4] one possible explanation for the excellent stereoselectivity is depicted in transition state **6.1**. The chelation effect of the PMB protected C_{21} hydroxyl group would result in a transition state like **6.1**, which in turn should lead to the 18*S* isomer **6.2** in good diastereoselectivity.



Scheme 6.3. Aldol Reaction Between Methyl Ketone **5.13** and Aldehyde **5.26**

6.2 Attempts to Remove the PMB Protecting Group

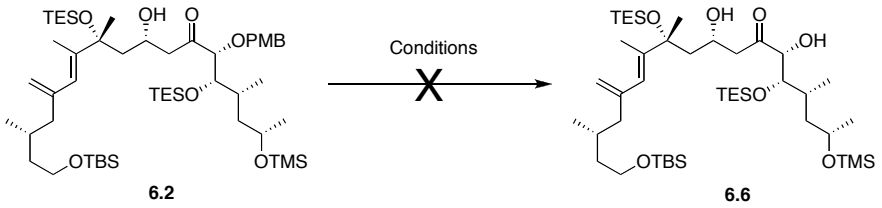
With adol adduct **6.2** in hand, we next focused on the deprotection of PMB group. Our previous work[2b] indicated that general PMB deprotection conditions (DDQ, CAN, *etc.*) would lead to the decomposition of macrocycle **5.15**. Under the suspicion that the presence of an allylic epoxide moiety might be problematic, we decided to investigate the removal of the PMB group found in coupound **6.2**. Cleavage of the PMB protecting group followed by C_{21} TES protection should afford TES ether **6.4**. After converting **6.4** to the TES protected version of amphidinolide B, the TES groups could be deprotected under mild conditions in the presence of the labile allylic epoxide moiety.



Scheme 6.4. Modified Deprotection Strategy

Our previous difficulties with deprotection [2b] made us mindful in selecting the deprotection conditions we would employ for this transformation. Generally, PMB protecting groups can be removed under oxidative conditions (DDQ, CAN, NBS, *etc.*);[5] reductive conditions ($NaBH_3(CN)$ / $BF_3•OEt_2$);[6] acidic conditions (TFA, HCl, *etc.)*;[7] or Lewis acidic conditions (TMSI, $MgBr_2•Et_2O$, *etc.*).[8] Due to the diene motif and the carbonyl group found in adol adduct **6.2**, only oxidative conditions would be reasonable for this substrate. Consequently, we chose to

explore the deprotection using the most widely used oxidizing reagents, DDQ and CAN. Unfortunately, all attempts to remove PMB group failed (Table 6.1). The diene motif of adol adduct **6.2** decomposed upon treatment with DDQ in CH_2Cl_2 / H_2O at room temperature. Addition of pH buffer solution to the reaction or switching the oxidizing reagent to CAN led to similar results. Conducting the experiments at a lower temperature (0ºC) resulted in no reaction. Exposure of adol adduct **6.2** to Lewis acid,[7] even the mild $MgBr_2 \bullet Et_2O$, led to decomposition of the diene.



6.2 **6.6**

Entry	Conditions	Results
1	DDQ, pH 7 buffer, CH_2Cl_2, rt	Decomposition
2	DDQ, pH 9 buffer, CH_2Cl_2, rt	Decomposition
3	CAN, pH 7 buffer, rt	Decomposition
4	DDQ, aq $NaHCO_3$, CH_2Cl_2, 0ºC	No Reaction
5	$MgBr_2 \bullet Et_2O$, THF, 0ºC	Decomposition

Table 6.1. Attempts to Remove PMB Group

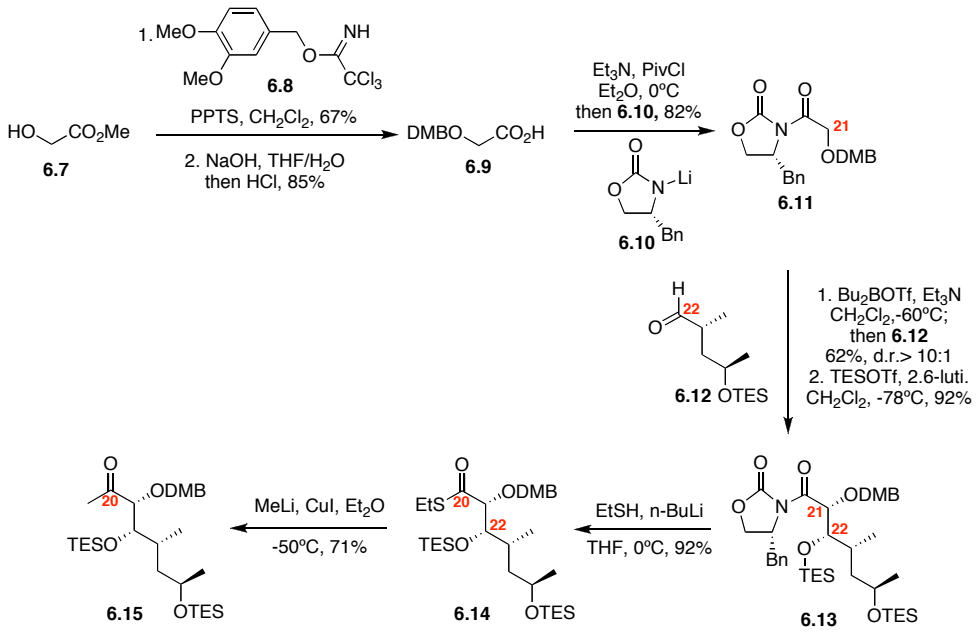
6.3 Studies of DMB Group as Protecting Group

6.3.1 Synthesis of C_{21} DMB Protected Methyl Ketone 6.13

Given that PMB group could not be removed without the decomposition of the aldol adduct **6.2**, an alternate plan would involve implementing different protecting groups on the C_{21} hydroxyl group. First, we investigated the 3,4-dimethoxybenzyl (DMB) group, a moiety that is a structurally similar to the PMB group.[9] Utilization of the DMB group would provide the desired chelation control in the aldol coupling. More importantly, the DMB group is much more reactive toward the oxidizing reagents due to its lower oxidation potential than that of PMB group ($E_{1/2}$=1.45 V and 1.78 V, respectively).[10] DMB groups have been reported to be successfully removed from an alcohol with DDQ in the presence of PMB group with 98% selectivity.[11] Due to its greater reactivity, we could potentially cleave the DMB group at lower temperature allowing the diene moiety to remain intact.

Our next goal was focused on the synthesis of C_{21} DMB-protected methyl ketone (Scheme 6.5). Oxazolidinone **6.11** was prepared via the known procedure described by Roush and co-workers.[12] Boron-mediated aldol reaction[13] between the previously made aldehyde **6.12** and compound **6.11** gave the C_{21}-C_{23} *syn*, *syn* adduct in 80% yield with good diastereoselectivity (d.r.>10:1). Subsequent silylation at the C_{22} hydroxyl group, the conversion of oxazolidinone **6.13** to the

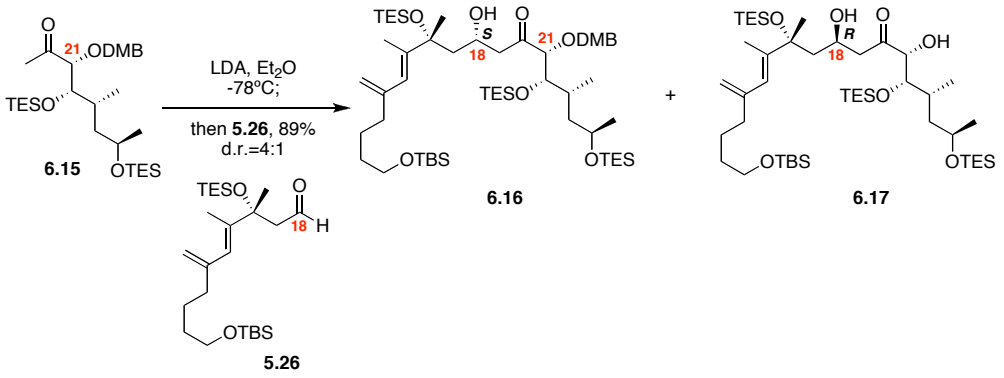
corresponding thioester **6.14** and cuprate addition of the desired methyl group gave the requisite methyl ketone **6.15**.[14]



Scheme 6.5. Synthesis of Methyl Ketone **6.15**

6.3.2 Aldol Coupling Between Methyl ketone 6.15 and Aldehyde 5.26

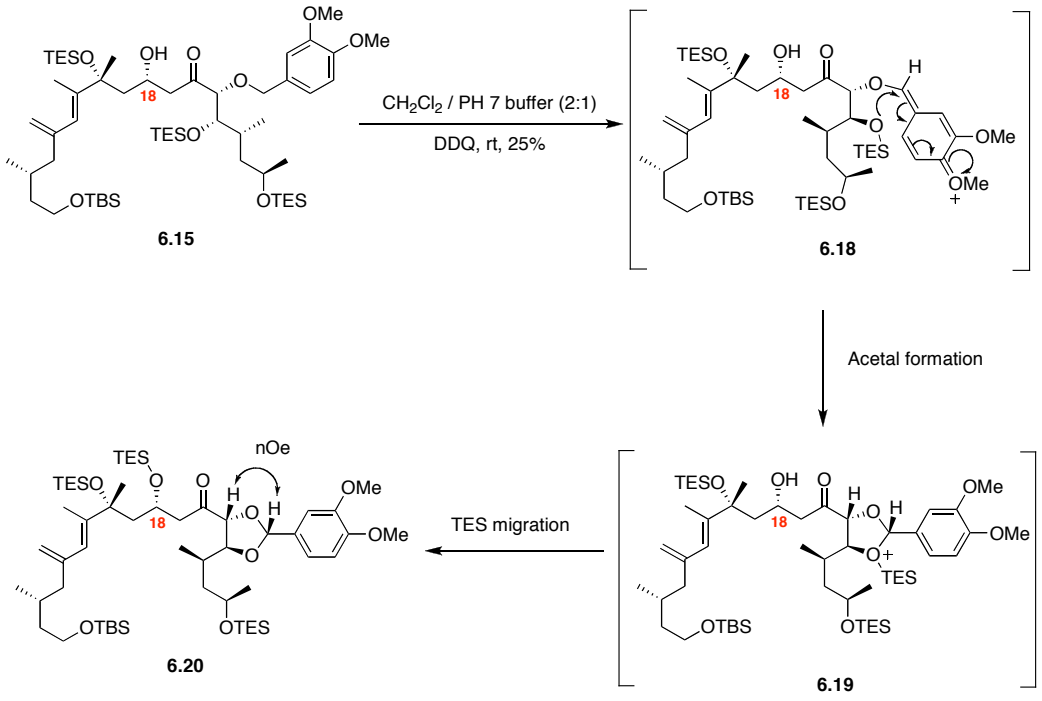
With both aldol precursors in hand, the next target became the coupling between aldehyde **5.26** and methyl ketone **6.15** (Scheme 6.6). Using our typical protocol (LDA / Et_2O, -78ºC),[2] the use of DMB-protected methyl ketone led to better overall yield, albeit in moderate diastereoselectivity (4:1, favoring the 18*S* isomer). Fortunately, the two isomers were easily separated via conventional silica gel chromatography.



Scheme 6.6. Aldol Coupling Between Methyl Ketone **6.15** and Aldehyde **5.26**

6.3.3 Attempts to Remove DMB Group

After obtaining the adol adduct **6.16**, our next priority became the deprotection of the DMB group (Scheme 6.7). When DMB ether **6.16** was treated with DDQ in DCM / pH 7 buffer at 0ºC or room temperature, an unexpected compound was isolated as a single isomer in 25% yield. The undesired product appeared to be acetal **6.20**, which would arise from the formation of an acetal and the migration of the TES group. The stereochemistry was determined by nOe analysis. Attempts to improve the yield by using anhydrous CH_2Cl_2 as solvent, lowing the reaction temperature, or utilizing alternative oxidizing reagents (CAN or 2,3,5,6-tetrachlorobenzoquinone[15]) resulted in comparable yields or no reaction.



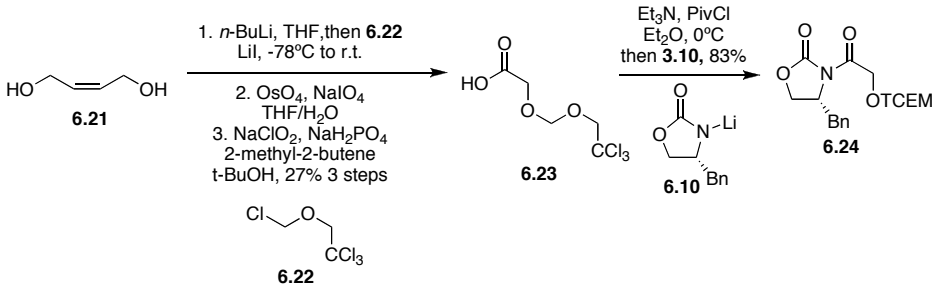
Scheme 6.7. Attempt to Remove DMB Group

6.4 Studies of Other Chelation Protecting Groups

Our synthetic efforts demonstrated that a PMB-type protecting group provided satisfactory chelation control during the aldol coupling. Unfortunately, conditions required to remove these groups were not amendable to the diene substrate. A reasonable solution to this problem would be to use another C_{21} chelation protecting group, the removal of which would not require harsh conditions. First, we studied 2,2,2-trichloroethoxymethyl (TCEM) group.[16] This MEM group derivative should generate the desired chelation control and could be removed under much milder conditions.[16]

6.4.1 Synthesis of Oxazolidinone 6.20

Our new strategy required the synthesis of oxazolidinone **6.24** (Scheme 6.8). Starting from diol **6.21**, acid **6.23** was produced in three steps in moderate yield. After converting acid **6.23** to the corresponding *t*-butyl ester, the addition of anion **6.10** yielded the desired oxazolidinone **6.24**.

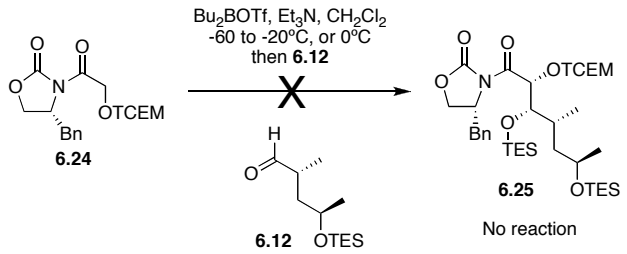


Scheme 6.8. Synthesis of Oxazolidinone **6.24**

6.4.2 Aldol Coupling Between Oxazolidinone 6.24 and Aldehyde 6.12

With oxazolidinone **6.24** in hand, we explored the aldol coupling between compound **6.24** and aldehyde **6.12** (Scheme 6.9). Unfortunately, the aldol coupling was unsuccessful due to the steric hindrance introduced by the TCEM group. Attempts to accelerate the reaction by raising the temperature and increasing the concentration of the reaction mixture proved unsuccessful. Once we realized the inefficiency of the TCEM group, we investigated several other chelation protecting groups including benzyl group,[17] THP group,[18] acetonide[19] and DMB acetal groups. Again, our efforts were thwarted either by poor diastereoselectivity and

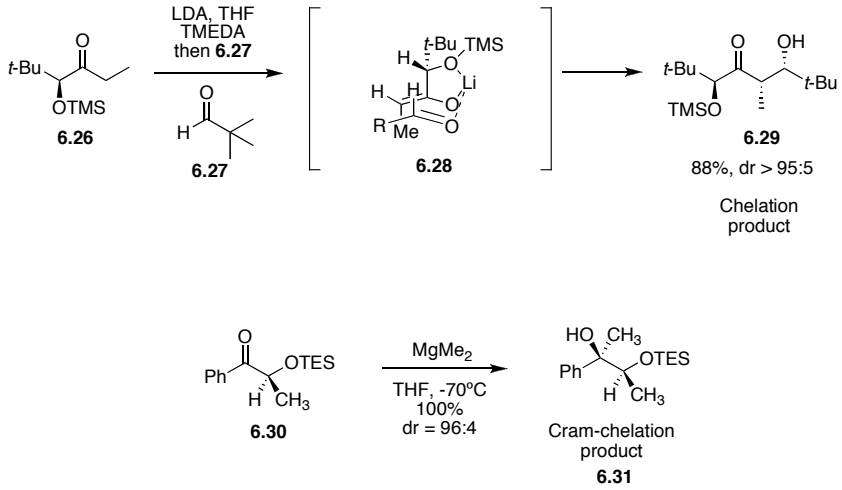
low conversion during the aldol coupling, or by the inability to remove the protecting groups.



Scheme 6.9. Aldol Coupling between Oxazolidinone **6.24** and Aldehyde **6.12**

6.5 Studies of Silyl Groups as C_{21} Protecting Group

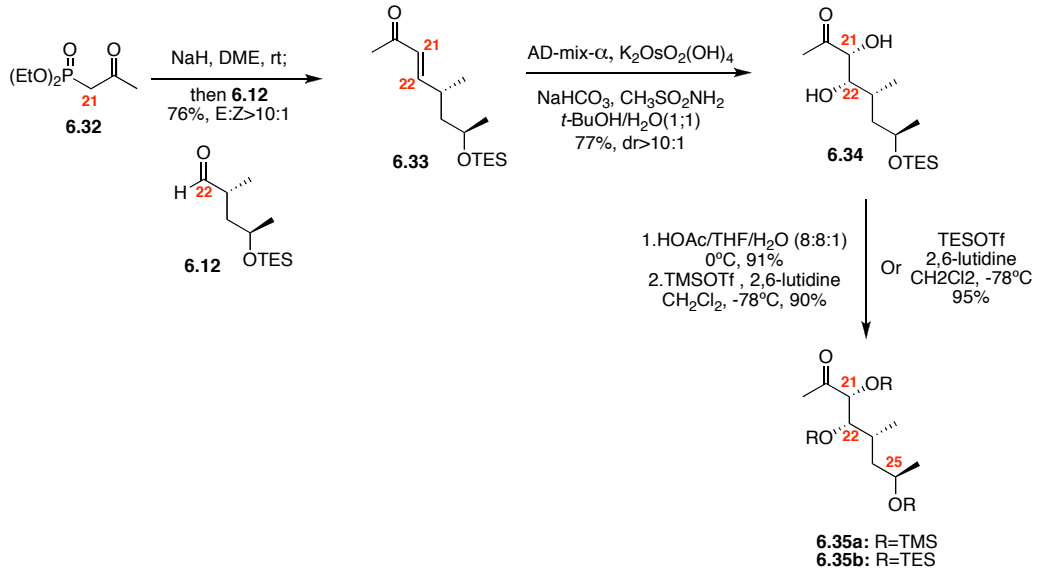
Our strategies employing alkoxyl groups proved problematic due to the incompatibility of the diene moiety with the deprotection conditions. In order to circumvent this problem, we shifted our focus on the silyl protecting groups. Conventional wisdom states that hindered silyl protecting groups prevent chelation with most metal ions[20] due to the decreased basicity of O atom;[21] however, the research from Heathcock and Frye groups demonstrated that chelation control is possible for small silyl groups such as TMS or TES (Scheme 6.10).[22] More evidence to support this concept was obtained when a X-ray structure of a dimeric lithium ketone enolate-lithium diisopropylamide complex, where the coordination between TBS ether oxygen and lithium ion was observed.[23] Based on this information, we decided to investigate the use of relatively small silyl groups (TMS and TES) as possible C_{21} protecting groups.



Scheme 6.10. Examples of Chelation Control of Silyl Groups

6.5.1 Synthesis of Methyl Ketone 6.35a/b

With a modified strategy in hand, we sought to synthesize the C_{21} TMS and TES protected methyl ketones (Scheme 6.11). Starting with previously synthesized aldehyde **6.12**,[2a] a Horner−Wadsworth−Emmons olefination and Sharpless dihydroxylation yielded the diol **6.34**. Consecutive de-silylation and the tri-silylation yielded the TMS-protected methyl ketone **6.35a**. Alternatively, TES-protected methyl ketone **6.35b** was generated via the di-silylation of diol **6.34**.

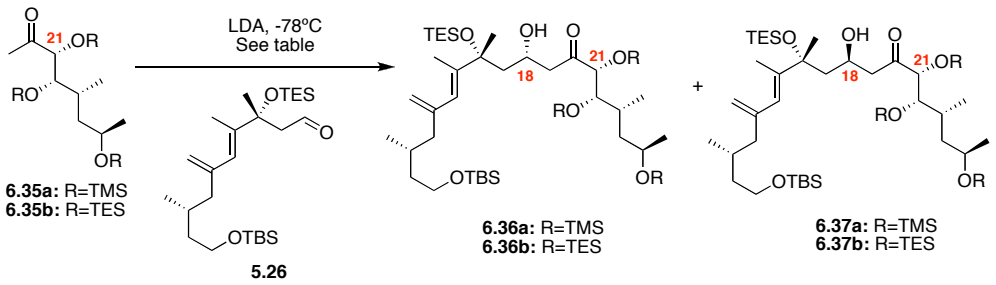


Scheme 6.11. Synthesis of Methyl Ketone **6.35a/b**

6.5.2 Aldol Coupling between Methyl ketone 6.35a/b and Aldehyde 5.26

After obtaining both methyl ketones with the undesired stereochemistry at C_{25}, we studied the key aldol reaction on the model system (Table 6.2). Treatment of ketone **6.35a** under our standard LDA / THF conditions resulted in low conversion (~15%) and poor diastereoselectivity favoring the 18*S* stereochemistry [approximately 1.1:1 dr (**6.36a**:**6.37a**)]. Suspecting that aggregation of lithium enolate decreased its reactivity, we added TMEDA to the reaction mixture with the intension the break the aggregation.[24] We were pleased to find that the addition of TMEDA led to dramatic rate acceleration and complete conversion, although the diastereoselectivity was still poor [1.1:1 dr (**6.36a**:**6.37a**)]. Fortunately, the two

diastereomers were easily separable by conventional silica chromatography. When the TES protected methyl ketone was treated under the same conditions, almost identical results were obtained. Switching the solvent to ether resulted in poor conversion with similar diastereoselectivity. The desired chelation-control was not observed under all the conditions we investigated.



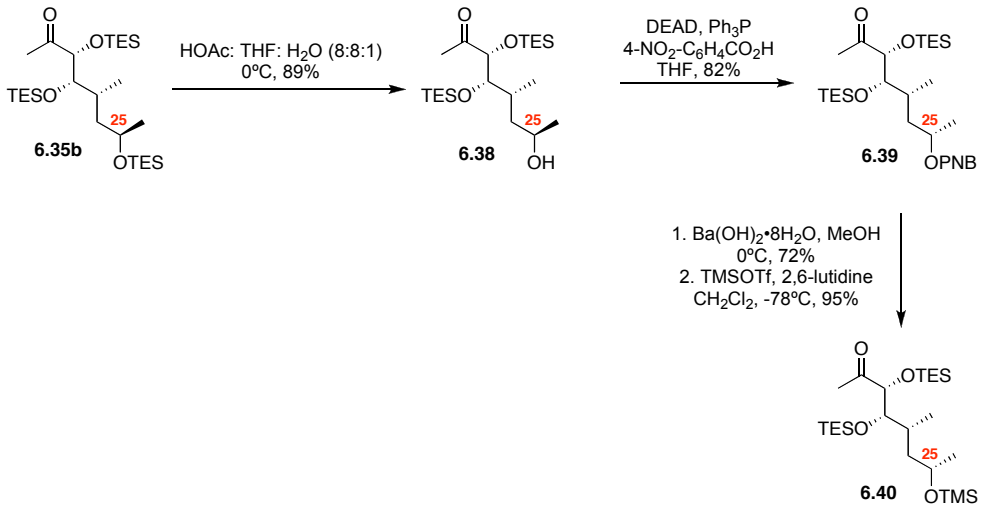
R	Conditions	Yield	dr (6.36:6.37)
R = TMS	THF	~10% (15% conversion)	1.1:1
	TMEDA, THF	65% (100% conversion)	1.1:1
R = TES	TMEDA, THF	64% (100% conversion)	1.1:1
	TMEDA, ether	<10% (30% conversion)	1.5:1

Table 6.2. Aldol Coupling between Methyl ketone **6.35a/b** and Aldehyde **5.26**

6.5.3 Synthesis of Methyl Ketone 6.40

Equipped with the knowledge gained from our previous study, we shifted our focus to the authentic substrate. To avoid the potential problems associated with the lability of TMS group, we chose to use TES to protect the C_{21} hydroxyl group. The desired C_{25} stereocenter was generated through the sequence shown in

Scheme 6.12. Selective C_{25} TES deprotection yielded the free alcohol **6.38**. Subsequent Mitsunobu inversion of the alcohol, followed by saponification of PNB ester and C_{25} TMS protection revealed the desired methyl ketone **6.40**.

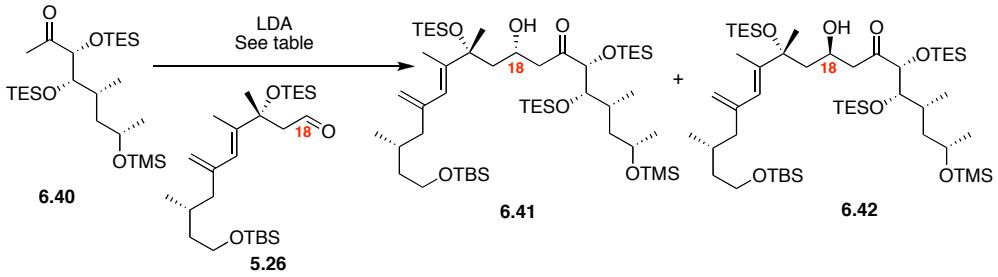


Scheme 6.12. Synthesis of Methyl Ketone **6.40**

6.5.4 Aldol Coupling between Methyl Ketone 6.40 and Aldehyde 5.26

With the ability to efficiently prepare methyl ketone **6.40**, our next target was the key aldol coupling (Table 6.3). Warming of the reaction to -40°C led to improved diastereoselectivity toward 18*S* diastereomer [1.8:1 dr (**6.41**:**6.42**)] in reasonable yield (67% overall). We were gratified to find that when the reaction was cooled to -85ºC, the diastereoselectivity of the 18*R* diastereomer was improved significantly to 1:5 (**6.41**:**6.42**). It should be noted that the addition of other ligands such as HMPA[25] or PMDTA[26] to the aldol reaction resulted in

complex mixtures or poor conversions. The absolute stereochemistry at C_{18} of the 18*S* isomer was confirmed by Mosher ester analysis (Figure 6.1).



Entry	Conditions	Yield	dr (6.41:6.42)
1	TMEDA, THF, -78ºC	64%	1.1:1
2	HMPA, THF, -78ºC	Complex mixture	N/A
3	PMDTA, Et_2O, -78ºC	10% (~15% conversion)	1.4:1
4	TMEDA, THF, -40ºC	67%	1.8:1
5	TMEDA, THF, -85ºC	68%	1:5

Table 6.3. Aldol Coupling Between Methyl Ketone **6.40** and Aldehyde **5.26**

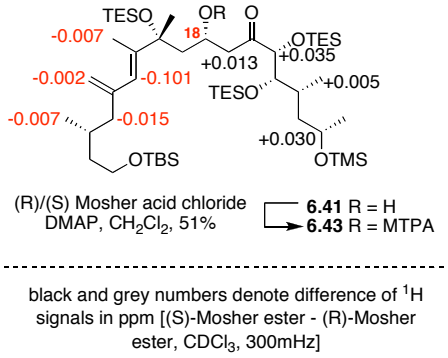
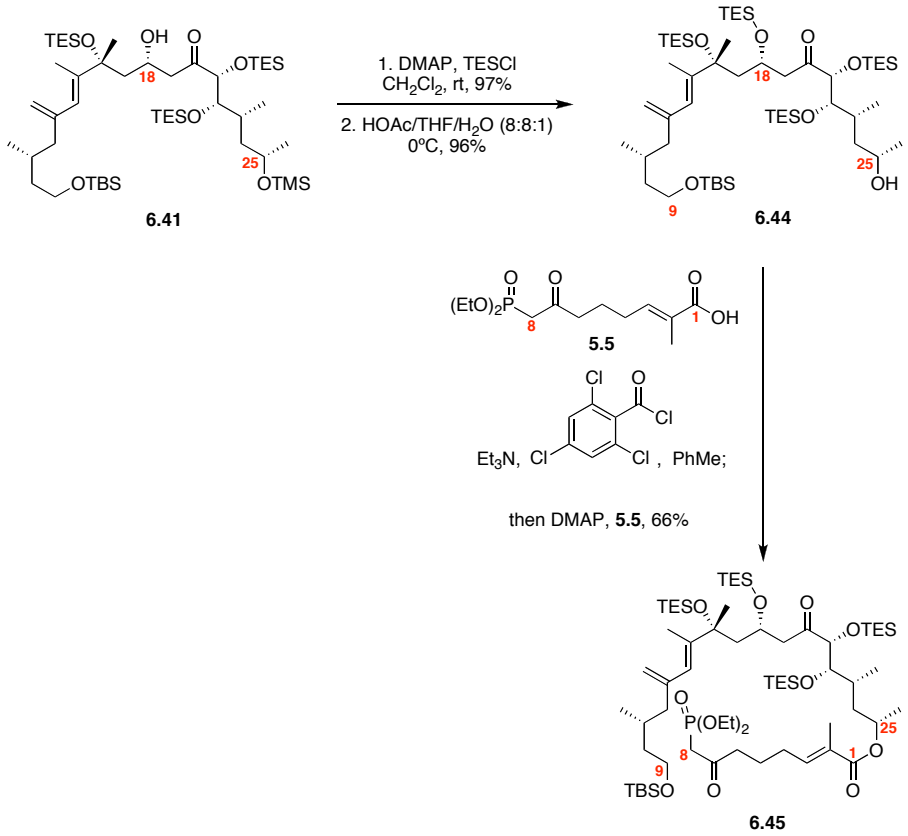


Figure 6.1. Mosher Ester Analysis of Adol Adduct **6.41**

6.5.5 Synthesis of Phosphonate 6.45

After successful synthesis of the key aldol adducts, the next priority became the coupling of the C_1-C_8 phosphonate acid **5.5**[1] with the C_9-C_{25} fragment (Scheme 6.13). We initially used 18*S* isomer **6.41** to explore our proposed chemistry. Our attempts to silylate C_{18} hydroxyl group with TES were not successful. When alcohol **6.41** was treated with Et_3N / DCM / TESOTf at -78ºC, a complex mixture was obtained due to the decomposition of the diene moiety. There was no reaction when TESCl / imid. / DMF conditions were employed, presumably because of the steric congestion at C_{18} hydroxyl group. After extensive investigation, we discovered that the silylation proceeded smoothly to give TES ether **6.44** when excess DMAP (15 eq.) and TESCl (10 eq.) were used. Next, selective deprotection of the C_{25} TMS group, followed by the intermolecular Yamaguchi esterfication,[27] revealed the desired phosphonate **6.45**. It should be noted that compound **6.45** containes all the carbon atoms required to complete the synthesis of amphidinolide B.

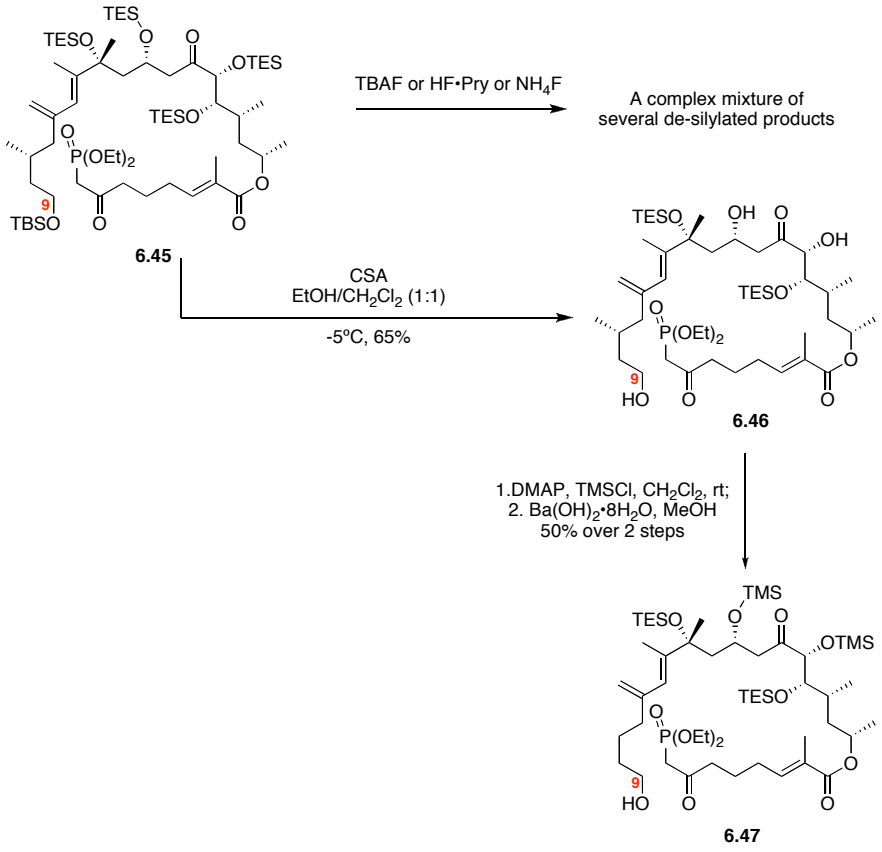


Scheme 6.13. Synthesis of Phosphonate **6.45**

6.5.6 Attempts to Selectively Remove C_9 TBS Group

With the synthesis of phosphonate **6.45**, the next goal was the selective removal of the C_9 TBS group in the presence of several secondary TES groups (Scheme 6.14). Unfortunately, our efforts were thwarted by the poor selectivity. Under fluoride based conditions, a complex mixture of several de-silylated products were observed. The exposure of TBS ether **6.45** to acidic conditions generated triol **6.46** with the deprotection of TBS group and relatively less hindered C_{18}, C_{21} TES groups in moderate yield (65%). The desired alcohol **6.47**

was prepared through a sequence involving the silylation of triol **6.46** and the selective deprotection of C_9 primary TMS group. Unfortunately, the low overall yield (32% from phosphonate **6.45**) limited our ability to move forward.

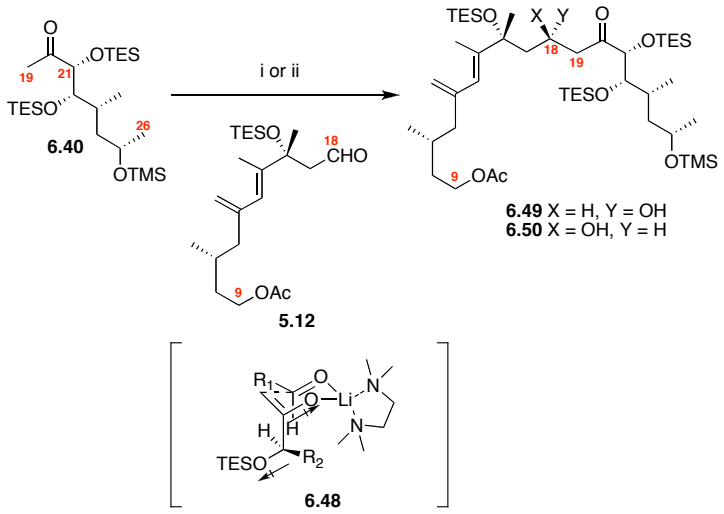


Scheme 6.14. Attempts to Selectively Remove TBS Group

6.5.7 Aldol Coupling between Methyl Ketone 6.40 and Aldehyde 5.12

Faced with these synthetic hurdles, we were forced to use the C_9 acetate protected diene aldehyde **5.12** (Scheme 6.15). After conducting more investigation on the key aldol coupling, we were pleased to find the excellent

diastereoselectivity (1:8 dr, favoring 18*R* diastereomer) was obtained at -100ºC. The alternate 18*S* diastereomer can be afforded by performing the reaction at higher temperature (-40°C, 1.2:1 dr) and elongation of the reaction time resulted in no ratio change. Although still under investigation, a transition state **6.48** which minimizes the dipoles of the C_{21} C−O σ bond and the enolate might lead to the good diastereoselectivity at -100ºC.



(i) LDA, TMEDA, THF, -100°C then add **5.12**, 65% (1:8 dr, **6.49**:**6.50**); (ii) LDA, TMEDA, THF, -40°C then add **5.12**, 66% (1.2:1 dr, **6.49**:**6.50**)

Scheme 6.15. Aldol Coupling Between Methyl Ketone **6.40** and Aldehyde **5.12**

One possible explanation for the observed stereochemical outcome could be a dueling kinetic vs. thermodynamic controlled process, which has been widely reported by the others.[28] The proposed energy diagram of the aldol coupling is depicted in Figure 6.2. This argument would pose that 18*R* diastereomer **6.50** would be the kinetic product as it is generated at low temperature (-100ºC) and

would require lower activation energy. In contrast, the diastereomeric mixture (18*S*:18*R*=1.2:1) observed at a higher temperature (-40ºC) would support the presumed energetic similarity between 18*S* & 18*R* diastereomers under reversible (thermodynamic) conditions.

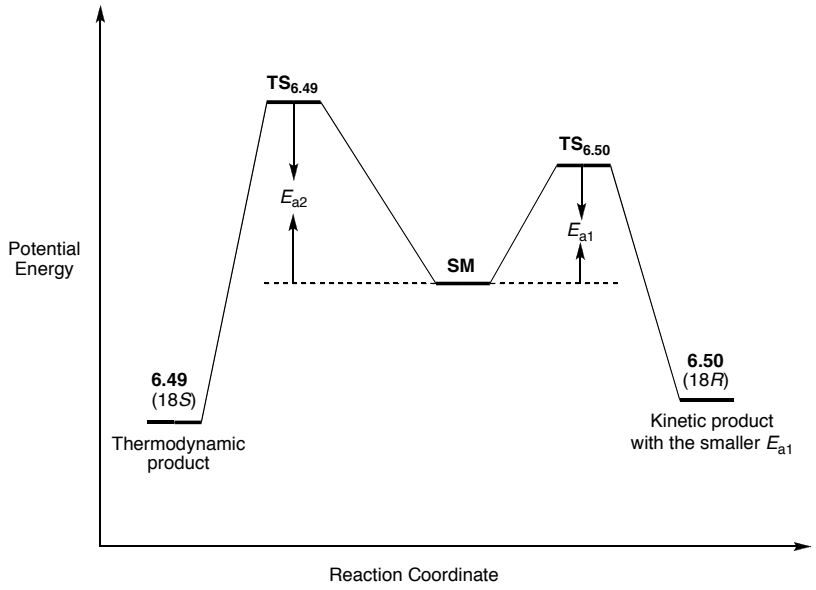
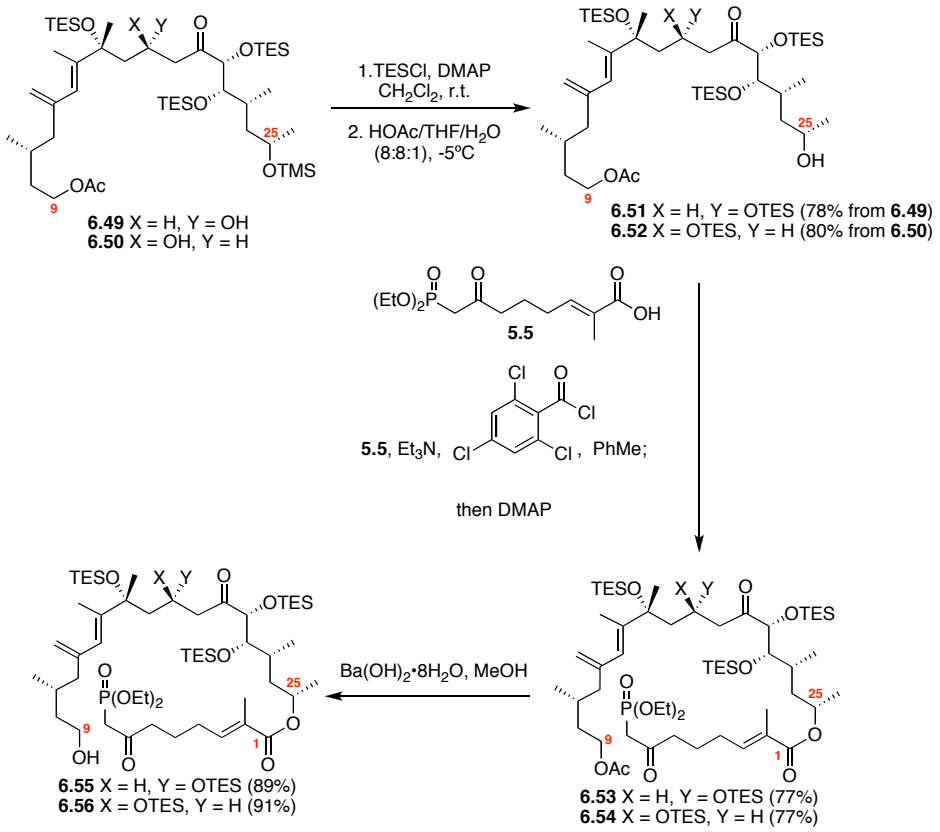


Figure 6.2. Proposed Energy Diagram of the Aldol Coupling

6.5.8 Synthesis of Phosphonate Alcohol 6.55 and 6.56

The conversion of aldol adducts to phosphonate alcohol **6.55**/**6.56** was displayed in Scheme 6.16. Silylation, followed by selective removal of C_{25} TMS group and Yamaguchi esterfication produced phosphonate **6.53**/**6.54**. When **6.53**/**6.54** was treated with $Ba(OH)_2 \cdot 8H_2O$ in MeOH, the selective deprotection of acetate group proceeded cleanly to yield phosphonate alcohols **6.55**/**6.56** in high yield.



Scheme 6.16: Synthesis of phosphonate alcohol **6.55**/**6.56**

6.6 Conclusion

The key aldol coupling between the C_9-C_{18} diene moiety and C_{19}-C_{26} methyl ketone fragment was investigated. The protecting groups on C_{21} were discovered to have significant effects on the aldol reaction. Although the PMB and Bn groups provided chelation-control to give great diastereoselectivity, favoring the 18*S* isomer, the attempts to remove these groups proved unseccessful. The C_{21} TES-protected methyl ketone led to the production of the 18*R* isomer in 1:8 dr at -100°C, while the 18*S* isomer was yielded at -40°C in 1.2:1 dr. Both C_9-C_{26} adol

adducts were successfully coupled with C_1-C_8 fragment and were converted to the corresponding phosphonate alcohols. With compounds **6.55** and **6.56** in hand, the challenges that remained were the macrocyclization, incorporation of the allylic epoxide moiety and the global de-silylation. Our methods to effect these transformations will be discussed in the next chapter.

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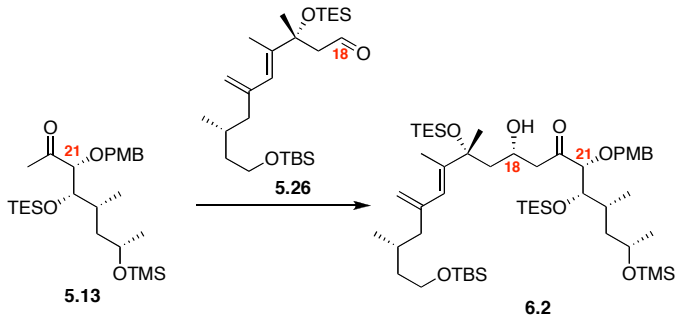
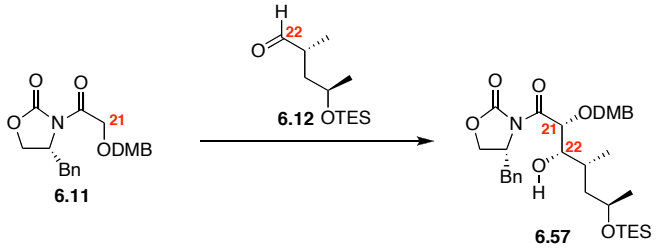
6.8 Experimental



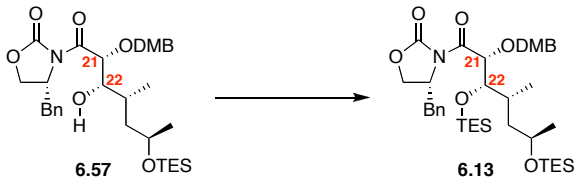
Aldol adduct 6.2: To a stirred solution of methyl ketone **5.13**[1] (136 mg, 0.27 mmol) in THF (1.5 mL) at -78ºC was added LDA[2] (0.32 mL, 1 M in THF) was added. After 30 min, a pre-cooled (-78ºC) solution of aldehyde **5.26** (117 mg, 0.25 mmol) in THF (0.5 mL) was added via *cannula* in one portion. After another 0.5 h, the reaction was quenched with sat. aq. NH_4Cl (2 mL) at -78ºC , warmed up to rt and extracted with ether (3 X 15 mL). The dried extract ($MgSO_4$) was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 3-5% EtOAc / Hexanes, to give aldol adduct **6.2** (128 mg, 0.13 mmol, 53%) as a colorless oil: $[\alpha]_D^{23}$ = +11.8 (*c* 0.61, $CHCl_3$); IR (neat) 3513, 2955, 2929, 2877, 1715, 1614, 1515, 1462, 1250, 1091, 1038, 1007, 838, 742 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.30 (d, *J* = 8.7 Hz, 2H), 6.87 (d, *J* = 8.7 Hz, 2H), 5.89 (s, 1H), 5.03 (s, 1H), 4.84 (s, 1H), 4.55 (d, *J* = 11.1 Hz, 1H), 4.42 (br, 1H), 4.37(d, *J* = 11.4 Hz, 1H), 3.82 (s, 3H), 3.72-3.82 (m, 3H), 3.62-3.69 (m, 2H), 3.10 (dd, *J* = 17.7, 7.2 Hz, 1H), 2.31 (dd, *J* = 17.7, 4.8 Hz, 1H), 2.19 (dd, *J* = 13.5, 5.1 Hz, 1H), 1.80-1.91 (m, 1H), 1.83 (s, 3H), 1.42-1.70 (m, 4H), 1.54 (s, 3H), 1.20-1.37 (m, 4H), 1.13 (d, *J*=6.0 Hz, 3H), 0.89-1.00 (m, 27H), 0.82-0.87 (m, 6H), 0.54-0.67 (m,

12H), 0.08 (s, 9H), 0.06 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 211.2, 159.2, 144.6, 143.1, 129.9, 129.7, 125.1, 114.9, 113.6, 88.1, 79.5, 77.1, 72.4, 65.9, 64.8, 61.4, 55.2, 48.1, 46.3, 46.0, 44.4, 39.9, 32.1, 29.7, 28.4, 26.0, 24.8, 19.5, 18.3, 14.7, 12.9, 7.2, 7.1, 6.6, 5.3, 0.4, -5.2; HRMS (ES^+) calcd. for $C_{52}H_{100}O_8Si_4Na$ (M+Na) 987.6393, found 987.6396.



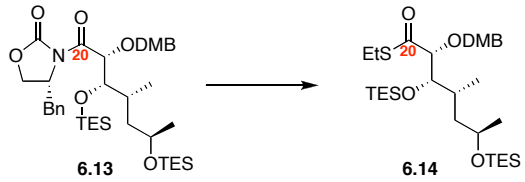
Aldol adduct 6.57: To a stirred solution of **6.11** (1.60 g, 0.15 mmol) in CH_2Cl_2 (11.2 mL) at -60°C was sequentially added Et_3N (0.44 g, 0.60 mL, 4.33 mmol) and Bu_2BOTf (1.19 g, 1.08 mL, 4.33 mmol). After 3 h, the resulted solution was warmed up 0°C for 30 min and then cooled back to -60°C. A solution of aldehyde **6.12**[3] (1.12 g, 4.86 mmol) in DCM (4.8 mL) was transferred to the reaction mixture via *cannula*. After 2 h, the reaction was allowed to warm up to 0°C. After another 20 min, the reaction was quenched by adding pH 7 phosphate buffer (20 mL) followed by MeOH (15 mL) and 30% H_2O_2 (4 mL). After 1 h, the reaction mixture was extracted with EtOAc (4 X 35 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 15-20% EtOAc / Hexanes, to give **6.57** (1.58 g, 2.57 mmol, 62%) as a colorless oil: $[\alpha]_D^{23}$ = -9.2 (*c* 0.77, $CHCl_3$); IR (neat) 3493, 2957, 2876, 1781, 1709, 1593, 1517, 1455, 1390, 1265, 1240, 1159, 1052, 1028, 746 cm^{-1}; ^{1}H NMR

(400 MHz) δ 7.23-7.38 (m, 5H), 6.83-7.03 (m, 3H), 5.36 (d, J = 2.0 Hz, 1H), 4.63-4.71 (m, 2H), 4.51 (d, J = 10.8 Hz, 1H), 4.21-4.29 (m, 2H), 3.93 (s, 3H), 3.84-3.90 (m, 1H), 3.88 (s, 3H), 3.62-3.66 (m, 1H), 3.32 (dd, J = 13.6, 3.6 Hz, 1H), 2.77 (dd, J = 13.6, 10.0 Hz, 1H), 2.32 (d, J = 10.0 Hz, 1H), 1.78-1.80 (m, 1H), 1.58-1.64 (m, 1H), 1.15 (d, J = 6.0 Hz, 3H), 1.03 (d, J = 6.8 Hz, 3H), 0.98 (t, J = 8.0 Hz, 9H), 0.62 (q, J = 8.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.2, 153.2, 149.1, 149.0, 135.2, 129.5, 129.4, 129.0, 127.4, 121.4, 112.1, 110.9, 78.1, 76.1, 66.9, 55.9, 55.7, 42.8, 37.7, 34.1, 23.2, 15.7, 6.9, 4.9; HRMS (ES$^+$) calcd. for $C_{33}H_{49}NO_8SiNa$ (M+Na) 638.3125, found 638.3155.



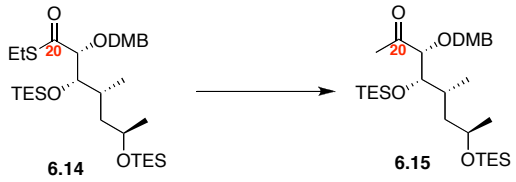
TES ether 6.13: To a stirred solution of adol adduct **6.57** (500 mg, 0.81 mmol) in DCM (3.32 mL) at 0°C was sequentially added 2,6-lutidine (184 mg, 0.20 mL, 1.72 mmol) and TESOTf (287 mg, 0.25 mL, 1.09 mmol). After 1 h, the reaction was quenched with sat. aq. NH_4Cl (10 mL) and extract with Et_2O (3 X 30 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 15% EtOAc / Hexanes, to give **6.13** (570 mg, 0.78 mmol, 96%) as a colorless oil: $[\alpha]_D^{23}$ = -40.7 (*c* 0.42, $CHCl_3$); IR (neat) 2955, 2911, 2876, 1784, 1702, 1517, 1456, 1239, 1084, 740 cm^{-1}; ^{1}H NMR (300 MHz) δ 7.17-7.32 (m,H), 6.80-7.00 (m, 3H), 5.28 (d, J = 6.0 Hz, 1H), 4.71

(d, J = 11.7 Hz, 1H), 4.54 (d, J = 11.7 Hz, 2H), 4.47-4.49 (m, 1H), 4.00-4.12 (m, 3H), 3.90 (s, 3H), 3.84 (s, 3H), 3.78-3.82 (m, 1H), 3.14 (dd, J = 3.0, 13.2 Hz, 1H), 2.40 (dd, J = 10.5, 13.5 Hz, 1H), 1.42-1.56 (m, 3H), 1.11 (d, J = 5.7 Hz, 3H), 0.89-0.97 (m, 21H), 0.55-0.63 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.9, 152.9, 148.7, 148.8, 135.3, 130.3, 129.3, 129.0, 127.3, 121.1, 111.9, 110.7, 73.4, 67.2, 66.4, 56.0, 55.9, 55.8, 44.4, 37.4, 33.5, 23.7, 14.8, 7.1, 6.9, 5.4, 5.3, 5.2, 5.0; HRMS (ES^+) calcd. for $C_{39}H_{63}NO_8Si_2Na$ (M+Na) 752.3990, found 752.3992.



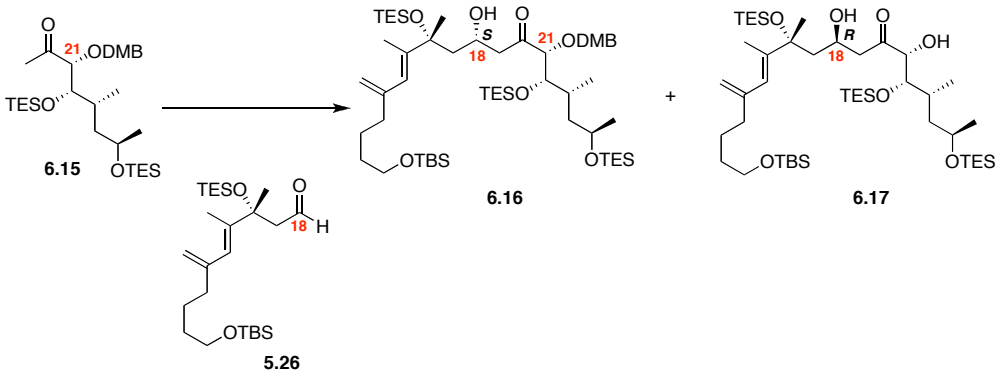
Thiol ester 6.14: To a stirred solution of EtSH (90 mg, 0.107 mL, 1.45 mmol) in THF (12.6 mL) at 0°C was added *n*-BuLi (0.51 mL, 1.27 mmol, 2.5 M in Hexanes). After 1 h, a solution of **6.13** (610 mg, 0.83 mmol) in THF (2.7 mL) was added dropwise via *cannula*. After another 1 h, the reaction was quenched with sat. aq. NH_4Cl (10 mL) and extract with Et_2O (3 X 30 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 5-8% EtOAc / Hexanes, to give **6.14** (470 mg, 0.76 mmol, 92%) as a colorless oil: $[\alpha]_D^{23}$ = +42.0 (*c* 0.39, $CHCl_3$); IR (neat) 2955, 2911, 2876, 1683, 1517, 1458, 1419, 1378, 1266, 1240, 1161, 1079, 1032, 811, 740 cm^{-1}; ^{1}H NMR (400 MHz) δ 7.04 (dd, J = 1.6 Hz, 1H), 6.94 (dd, J = 1.6, 8.0 Hz, 1H), 6.86 (d, J = 8.4 Hz, 1H), 4.63 (d, J = 10.8 Hz, 1H), 4.43 (d, J = 10.8 Hz, 1H), 3.94 (s, 3H),

3.92-3.93 (m, 4H), 3.81-3.86 (m, 2H), 2.91 (q, J = 7.6 Hz, 2H), 1.45-1.57 (m, 3H), 1.30 (t, J = 7.2 Hz, 3H), 1.14 (d, J = 6.0 Hz, 3H), 0.90-0.98 (m, 21H), 0.53-0.62 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.2, 148.8, 148.6, 129.9, 120.6, 110.6, 110.7, 88.2, 72.9, 66.9, 55.9, 55.8, 44.9, 32.7, 23.4, 22.5, 14.6, 13.6, 7.0, 6.9, 5.3, 5.2, 5.0; HRMS (ES^+) calcd. for $C_{31}H_{58}O_6Si_2SNa$ (M+Na) 637.3390, found 637.3407.



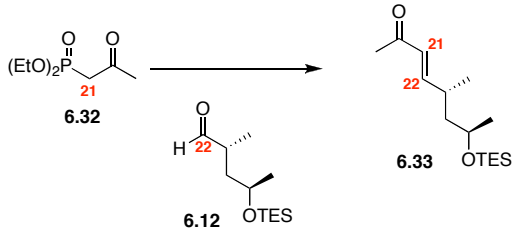
Methyl ketone 6.15: To a stirred slurry of CuI (859 mg, 4.51 mmol) in Et_2O (8.3 mL) at 0°C was added MeLi (5.6 mL, 9.6 mmol, 1.6 M in Et_2O). After 15 min, the colorless solution was cooled to -50°C and a solution of **6.14** (450 mg, 0.75 mmol) in Et_2O (4.2 mL) was transferred into the reaction mixture dropwise via *cannula*. After 2 h, the reaction was quenched with sat. aq. NH_4Cl (10 mL) at -50°C, warmed to rt and extracted with Et_2O (3 X 30 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 2-4% EtOAc / Hexanes, to give **6.15** (296 mg, 0.52 mmol, 71%) as a colorless oil: $[\alpha]_D^{23}$ = +22.6 (*c* 0.23, $CHCl_3$); IR (neat) 2955, 2911, 2876, 1716, 1517, 1457, 1267, 1240, 1082, 1031, 1007, 741 cm^{-1}; ^{1}H NMR (400 MHz) δ 6.82-6.90 (m, 3H), 4.50 (dd, J = 11.4, 15.0 Hz, 2H), 3.90 (s, 6H), 3.80-3.85 (m, 2H), 3.76 (d, J = 6.3 Hz, 1H), 2.13 (s, 3H), 1.50-1.52 (m, 3H), 1.13 (d, J = 6.0 Hz, 3H),

0.88-1.00 (m, 21H), 0.57-0.64 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 210.6, 148.8, 129.9, 120.7, 111.4, 110.8, 88.5, 72.9, 67.0, 55.9, 55.8, 44.5, 33.1, 27.0, 23.5, 14.0, 7.0, 6.9, 5.3, 5.0; HRMS (ES^+) calcd. for $C_{30}H_{56}O_6Si_2Na$ (M+Na) 591.3513, found 591.3527.



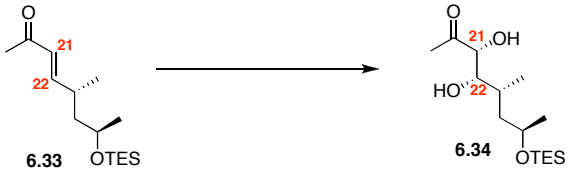
Aldol adduct 6.16: To a stirred solution of methyl ketone **6.15** (30 mg, 0.0527 mmol) in Et_2O (0.5 mL) at -78ºC was added LDA[2] (64 µL, 0.064 mmol, 1 M in THF). After 15 min, a pre-cooled (-78ºC) solution of aldehyde **5.26** (50 mg, 0.105 mmol) in THF (0.5 mL) was added via *cannula* in one portion. After another 0.5 h, the reaction was quenched with sat. aq. NH_4Cl (2 mL) at -78ºC, warmed up to rt and extracted with ether (3 X 10 mL). The dried extract ($MgSO_4$) was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 6-8% EtOAc / Hexanes, to sequentially give aldol adduct **6.17** (10 mg, 0.0096 mmol, 18%) and **6.16** (39 mg, 0.0375 mmol, 71%) and as colorless oils. **6.16**: $[\alpha]_D^{23}$ = +9.1 (*c* 0.58, $CHCl_3$); IR (neat) 3503, 2955, 2934, 2876, 1715, 1517, 1463, 1265, 1240, 1095, 1007, 741 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.83-6.97 (m, 3H), 5.90 (s, 1H), 5.05 (s, 1H), 4.85 (s, 1H), 4.53 (d, *J* = 11.2 Hz, 1H), 4.44-

4.50 (m, 1H), 4.39(d, *J* = 10.8 Hz, 1H), 3.91 (s, 6H), 3.76-3.83 (m, 3H), 3.66-3.70 (m, 2H), 3.05 (dd, *J* = 17.6, 6.8 Hz, 1H), 2.38 (dd, *J* = 17.6, 5.6 Hz, 1H), 2.19 (dd, *J* = 13.5, 4.8 Hz, 1H), 1.80-1.91 (m, 1H), 1.84 (s, 3H), 1.48-1.68 (m, 4H), 1.57 (s, 3H), 1.20-1.42 (m, 4H), 1.10 (d, *J*=6.0 Hz, 3H), 0.86-1.00 (m, 42H), 0.57-0.66 (m, 18H), 0.08 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 211.0, 148.8, 148.6, 144.6, 142.9, 130.1, 125.2, 120.7, 114.9, 111.5, 110.7, 88.3, 79.5, 72.6, 66.9, 64.8, 61.4, 55.9, 55.8, 48.0, 46.7, 46.0, 44.8, 39.9, 33.1, 28.4, 23.3, 19.5, 14.7, 13.5, 7.1, 7.0, 6.9, 6.5, 5.3, 5.0, -5.2; HRMS (ES^+) calcd. for $C_{56}H_{107}O_9Si_4$ (M+H) 1035.6992, found 1035.7047.



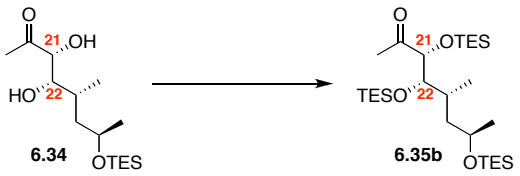
Enone 36: To a stirred slurry of NaH (36 mg, 0.90 mmol, 60% W / W in mineral oil) in DME (2 mL) was added phosphonate **6.32** (138 mg, 0.83 mmol) at rt. After 1 h, a solution of aldehyde **6.12** (160 mg, 0.69 mmol) in DME (2 mL) was added via *cannula*. After another 6 h, the reaction was quenched with sat. aq. NH_4Cl (2 mL) and extracted with Et_2O (4 X 10 mL). The dried extract ($MgSO_4$) was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 5% EtOAc / Hexanes, to give enone **6.33** (142 mg, 0.52 mmol, 76%) as a colorless oil: $[\alpha]_D^{23}$ = -46.0 (*c* 1.47, $CHCl_3$); IR (neat) 2958, 2877, 1700, 1678, 1627, 1458, 1360, 1252, 1139, 1055, 984, 745 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ

6.76 (dd, J = 15.9, 7.8 Hz, 1H), 6.09 (d, J = 15.9 Hz, 1H), 3.86-3.79 (m, 1H), 2.58-2.53 (m, 1H), 2.26 (s, 3H), 1.41-1.55 (m, 2H), 1.18 (d, J = 6.0 Hz, 3H), 1.09 (d, J = 6.9 Hz, 3H), 0.97 (t, J = 7.8 Hz, 9H), 0.64 (q, J = 7.5 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.8, 153.5, 129.6, 66.4, 46.3, 33.4, 27.0, 24.3, 20.3, 6.9, 5.2, 5.0; HRMS (EI^+) calcd. for $C_{15}H_{30}O_2Si$ (M+) 270.2015, found 270.2008.

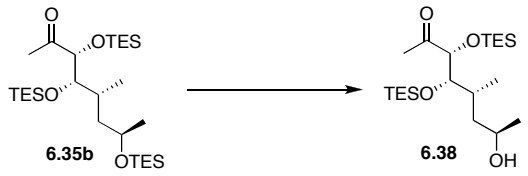


Diol 6.34: To a stirred solution of enone **6.33** (142 mg, 0.52 mmol) in *t*BuOH/H_2O (5 mL, 1:1) at 0ºC was sequentially added AD-mix-α (0.735 g), $NaHCO_3$ (132 mg, 1.57mmol), $MeSO_2NH_2$ (50.6 mg, 0.53 mmol), and $K_2OsO_2(OH)_4$ (1.9 mg, 0.005 mmol). After 8 h, the reaction was quenched with sat. aq. Na_2SO_3 (8 mL) and extracted with EtOAc (4 X 10 mL). The dried extract ($MgSO_4$) was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 15-40% EtOAc / Hexanes, to give diol **6.34** (122 mg, 0.40 mmol, 77%) as a colorless oil: $[\alpha]_D^{23}$ = -29.2 (*c* 1.5, $CHCl_3$); IR (neat) 3456, 2957, 2877, 1717, 1380, 1238, 1132, 1048, 1011, 744 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.28 (d, J = 3.6 Hz, 1H), 4.04-3.99 (m, 1H), 3.72-3.78 (m, 1H & OH), 2.41 (d, J = 10.4 Hz, 1H), 2.30 (s, 3H), 1.89-1.96 (m, 1H), 1.71-1.77 (m, 1H), 1.40-1.47 (m, 1H), 1.22 (d, J = 6.0 Hz, 3H), 1.10 (d, J = 6.8 Hz, 3H), 1.00 (t, J = 7.8 Hz, 9H), 0.68 (q, J = 7.9 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.9, 77.7, 75.2, 66.9, 42.8, 34.0,

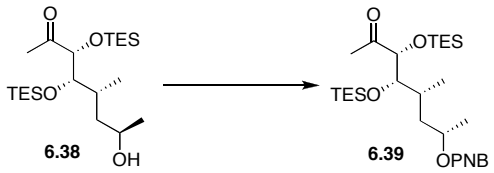
25.3, 23.1, 16.4, 6.9, 4.9; HRMS (ES^+) calcd. for $C_{15}H_{32}O_4SiNa$ (M+Na) 327.1968, found 327.1950.



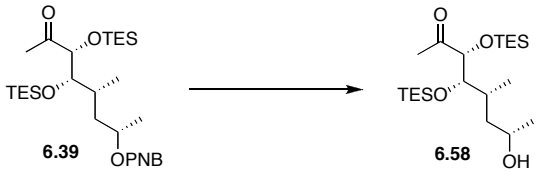
TES ether 6.35b: To a stirred solution of diol **6.34** (800 mg, 2.63 mmol) in CH_2Cl_2 (10 mL) at -78ºC was sequentially added 2,6-lutidine (1.41 g, 1.53 mL, 13.1 mmol) and TESOTf (1.74 g, 1.49 mL, 6.58 mmol). After 30 min, the reaction was quenched with sat. aq. NH_4Cl (10 mL) and extracted with Et_2O (4 X 25 mL). The dried extract ($MgSO_4$) was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 10% EtOAc / Hexanes, to give TES ether **6.35b** (1.29 g, 2.42 mmol, 92%) as a colorless oil: $[\alpha]_D^{23}$ = -0.83 (*c* 1.2, $CHCl_3$); IR (neat) 2957, 2878, 1716, 1458, 1238, 1005 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.07 (d, *J* = 6.0 Hz, 1H), 3.78-3.85 (m, 1H), 3.70 (dd, *J* = 5.9, 2.6 Hz, 1H), 2.20 (s, 3H), 1.60-1.64 (m, 1H), 1.45-1.51 (m, 2H), 1.13 (d, *J* = 6.0 Hz, 3H), 0.94-1.00 (m, 27H), 0.83 (d, *J* = 6.6 Hz, 3H), 0.55-0.70 (m, 18H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 210.0, 81.5, 78.6, 67.1, 45.4, 32.2, 27.3, 23.1, 14.0, 7.0, 6.84, 6.79, 5.2, 4.9, 4.8; HRMS (ES^+) calcd. for $C_{27}H_{60}O_4Si_3Na$ (M+Na) 555.3697, found 555.3683.



Alcohol 6.38: TES ether **6.35b** (5.60 g, 10.5 mmol) was dissolved in a stirred solution of HOAc / THF / H_2O (107 mL, 8:8:1) at 0ºC. After 12 h, the reaction was quenched with solid $NaHCO_3$, filtered over Celite and extracted with ether (4 X 100 mL). The dried extract ($MgSO_4$) was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 10% EtOAc / Hexanes, to give alcohol **6.38** (3.90 g, 9.31 mmol, 89%) as a colorless oil: $[\alpha]_D^{23}$ = -30.5 (*c* 1.45, $CHCl_3$); IR (neat) 3446, 2958, 2878, 1716, 1458, 1239, 1005, 739 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.18 (d, *J* = 5.6 Hz, 1H), 3.86-3.88 (m, 2H), 2.24 (s, 3H), 1.90 (d, *J* = 4.0 Hz, 1H), 1.82 (m, 1H), 1.41-1.55 (m, 2H), 1.20 (d, *J* = 6.0 Hz, 3H), 0.97-1.05 (m, 18H), 0.87 (d, *J* = 6.8 Hz, 3H), 0.61-0.73 (m, 12H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 209.3, 81.4, 76.4, 65.6, 43.7, 31.6, 27.8, 23.6, 15.4, 7.0, 6.8, 5.2, 4.8, 4.7; HRMS (ES^+) calcd. for $C_{21}H_{46}O_4Si_2Na$ (M+Na) 441.2832, found 441.2836.

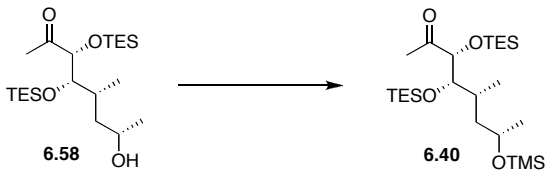


PNB ester 6.39: To a stirred solution of alcohol **6.38** (600 mg, 1.43 mmol) in THF (15 mL) at 0ºC was sequentially added PPh_3 (1.50 g, 5.72 mmol), 4-nitrobenzoic acid (0.96 g, 5.74 mmol), and DEAD (0.99 g, 0.90 mL, 5.70 mmol). After 1 h, the reaction mixture was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 1-3% EtOAc / Hexanes, to give ester **6.39** (670 mg, 1.18 mmol, 82%) as a colorless oil: $[\alpha]_D^{23}$ = +13.6 (*c* 1.08, $CHCl_3$); IR (neat) 2956, 2878, 1723, 1530, 1319, 1275, 1014, 721 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.31 (d, *J*=9.0 Hz, 2H), 8.23 (d, *J*=9.0 Hz, 2H), 5.26 (m, 1H), 4.17 (d, *J* = 4.8 Hz, 1H), 3.69 (t, *J* = 4.8 Hz, 1H), 2.18 (s, 3H), 2.02-2.12 (m, 1H), 1.76 (m, 1H), 1.45-1.49 (m, 1H), 1.38 (d, *J* = 6.1 Hz, 3H), 0.93-1.02 (m, 18H), 0.90 (d, *J* = 6.6 Hz, 3H), 0.56-0.70 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 209.3, 164.3, 150.4, 136.1, 130.7, 123.4, 81.5, 78.2, 70.8, 40.2, 32.4, 27.9, 20.9, 14.8, 7.0, 6.8, 5.1, 4.8; HRMS (ES^+) calcd. for $C_{28}H_{49}NO_7Si_2Na$ (M+Na) 590.2945, found 590.2926.



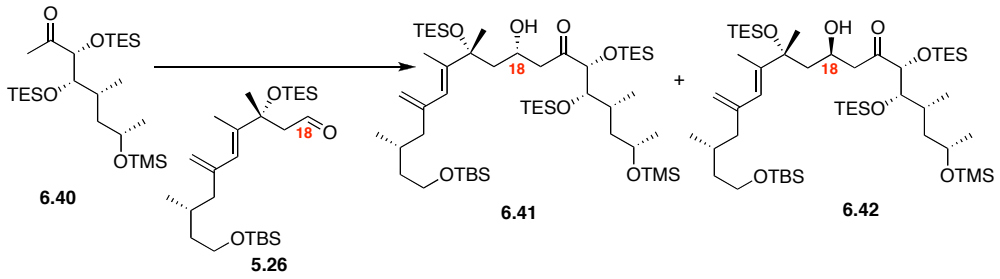
Alcohol 6.58: To a stirred solution of ester **6.39** (700 mg, 1.23 mmol) in MeOH (20 mL) at 0ºC was added $Ba(OH)_2 \cdot 8H_2O$ (390 mg, 1.24 mmol). After 4 h,

the reaction was quenched with sat. aq. NH_4Cl (10 mL) and extracted with EtOAc (4 X 20 mL). The dried extract ($MgSO_4$) was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 15% EtOAc / Hexanes, to give alcohol **6.58** (369 mg, 0.88 mmol, 72%) as a colorless oil: $[\alpha]_D^{23}$ = -7.6 (*c* 1.2, $CHCl_3$); IR (neat) 3434, 2957, 2878, 1716, 1459, 1415, 1239, 1005, 739 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.17 (d, *J* = 5.4 Hz, 1H), 3.81 (m, 1H), 3.69 (dd, *J* = 5.4, 3.9 Hz, 1H), 2.22 (s, 3H), 1.83 (m, 1H), 1.61-1.69 (m, 1H), 1.24-1.30 (m, 1H), 1.20 (d, *J* = 6.0 Hz, 3H), 0.94-1.04 (m, 18H), 0.87 (d, *J* = 6.6 Hz, 3H), 0.58-0.71 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 210.1, 81.5, 78.1, 66.2, 43.8, 32.9, 27.6, 24.4, 15.2, 7.0, 6.8, 5.2, 4.8; HRMS (ES^+) calcd. for $C_{21}H_{47}O_4Si_2$ (M+H) 419.3013, found 419.2993.



TMS ether 6.40: To a stirred solution of alcohol **6.58** (1.90 g, 4.54 mmol) in CH_2Cl_2 (25 mL) at -78ºC was sequentially added 2,6-lutidine (1.45 g, 1.58 mL, 13.5 mmol) and TMSOTf (1.51 g, 1.23 mL, 6.81 mmol). After 30 min, the reaction was quenched with sat. aq. NH_4Cl (10 mL) and extracted with Et_2O (4 X 20 mL). The dried extract ($MgSO_4$) was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 10% EtOAc / Hexanes, to give TMS ether **6.40** (2.12 g, 4.32 mmol, 95%) as a colorless oil: $[\alpha]_D^{23}$ = +14.4(*c* 2.2, $CHCl_3$); IR (neat) 2957, 2878, 1716, 1459, 1415, 1124, 1006, 841, 741 cm^{-1}; ^1H

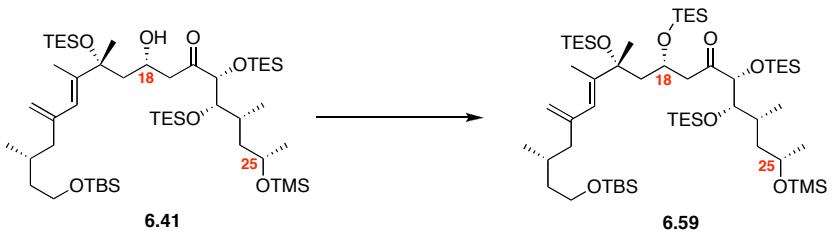
NMR (300 MHz, $CDCl_3$) δ 4.03 (d, *J* = 6.3 Hz, 1H), 3.79-3.85 (m, 1H), 3.71 (dd, *J* = 6.3, 2.4 Hz, 1H), 2.19 (s, 3H), 1.73-1.79 (m, 1H), 1.45-1.54 (m, 1H), 1.23-1.32 (m, 1H), 1.16 (d, *J* = 6.0 Hz, 3H), 0.95-1.03 (m, 18H), 0.83 (d, *J* = 6.6 Hz, 3H), 0.58-0.70 (m, 12H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 210.2, 81.8, 78.6, 65.9, 45.3, 31.3, 26.8, 24.7, 13.2, 7.0, 6.8, 5.3, 4.8, 0.3; HRMS (ES^+) calcd. for $C_{24}H_{54}O_4Si_3Na$ (M+Na) 513.3224, found 513.3204.



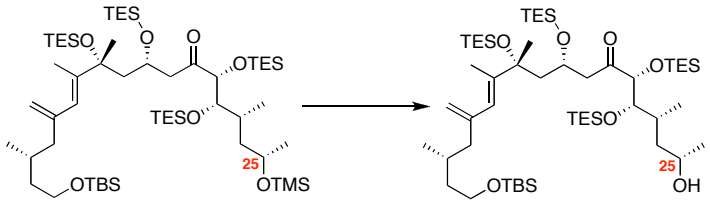
Aldol adduct 6.41&6.42: To a stirred solution of methyl ketone **6.40** (312 mg, 0.64 mmol) in THF (5 mL) at -78ºC was added LDA[2] (0.765 mL, 1 M in THF). After 15 min, TMEDA (133 mg, 0.172 mL, 1.14 mmol) was added. After 5 min, the reaction was warmed up to -40ºC, followed by the addition of a pre-cooled (-40ºC) solution of aldehyde **5.26** (200 mg, 0.43 mmol) in THF (5 mL) via *cannula* in one portion. After another 0.5 h, the reaction was quenched with sat. aq. NH_4Cl (10 mL) -78ºC, warmed up to rt and extracted with ether (4 X 20 mL). The dried extract ($MgSO_4$) was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 1-1.5% EtOAc / Hexanes, to give aldol adduct **6.41** (142 mg, 0.15 mmol, 35%) and **6.42** (114 mg, 0.12 mmol, 28%) as colorless oil. **6.41**: $[\alpha]_D^{23}$ = -12.0 (*c* 1.3, $CHCl_3$); IR (neat) 3511, 2955, 2929, 2877, 1715, 1460, 1413, 1250, 1092, 1006, 838, 742 cm^{-1}; ^1H NMR (300 MHz,

$CDCl_3$) δ 5.89 (s, 1H), 5.02 (s, 1H), 4.83 (s, 1H), 4.33 (m, 1H), 4.10 (d, *J* = 5.7 Hz, 1H), 3.82 (m, 1H), 3.74 (s, 1H), 3.64-3.72 (m, 3H), 2.96 (dd, *J* = 17.7, 6.2 Hz, 1H), 2.60 (dd, *J* = 18.1, 6.4 Hz, 1H), 2.18 (dd, *J* = 12.8, 4.0 Hz, 1H), 1.81-1.90 (m, 2H), 1.84 (s, 3H), 1.47-1.67 (m, 4H), 1.56 (s, 3H), 1.22-1.38 (m, 3H), 1.15 (d, *J*=6.0 Hz, 3H), 0.92-1.03 (m, 36H), 0.87 (d, *J*=6.4 Hz, 3H), 0.80 (d, *J*=6.7 Hz, 3H), 0.58-0.70 (m, 18H), 0.10 (s, 9H), 0.06 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 210.7, 144.7, 125.1, 114.7, 81.1, 79.4, 78.4, 65.9, 65.1, 61.5, 48.2, 47.2, 46.0, 45.0, 39.9, 31.1, 28.5,26.2, 26.0, 24.7, 19.5, 18.3, 14.7, 13.8, 7.2, 7.1, 6.9, 6.6, 5.3, 4.9, 0.4, -5.2; HRMS (ES^+) calcd. for $C_{50}H_{106}O_7Si_5Na$ (M+Na) 981.6683, found 981.6646.

MTPA esters: To a solution of **6.41** (5 mg, 0.005 mmol) in CH_2Cl_2 (0.5 mL) was sequentially added DMAP (6.4 mg, 0.052 mmol) and (*R*) or (*S*)-(+)-α-methoxy-α-trifluoromethylphenylacetyl chloride (6.6 mg, 4.9 μL, 0.026 mmol). After 10 min, the solution was evaporated and the residue was loaded directly onto silica gel and purified by chromatography, eluting with 2 - 10% EtOAc / Hexanes, to give product **(*S*)-** or **(*R*)- MTPA esters** (52-61%) as colorless oils. ^1H NMR Difference in ppm [(*S*)-Mosher Ester – (*R*)-Mosher ester, $CDCl_3$, $CDCl_3$, 300 MHz NMR] H_{19} = 2.847 – 2.834 = +0.013, H_{21}: 3.996 – 3.961 = +0.035, H_{22}: 3.686 – 3.678 = +0.008, H_{25}: 3.848 – 3.818 = +0.030, $H_{31'}$: 0.881 – 0.876 = +0.005, H_{29}: 1.888 – 1.895 = -0.007, H_{14}: 5.723 – 5.824 = -0.101, H_{28}: 4.905 – 4.925 = -0.020, H_{12}: 2.319 – 2.334 = -0.015, H_{279}: 1.130 – 1.137 = -0.007.

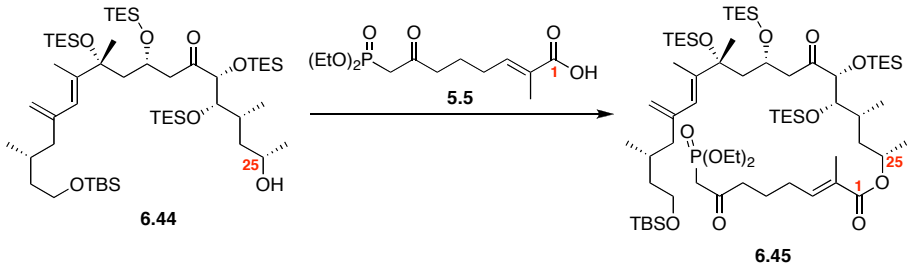


TES ether 6.59: To a stirred solution of aldol adduct **6.41** (247 mg, 0.26 mmol) in DCM (5 mL) at rt was sequentially added DMAP (471 mg, 3.86 mmol) and TESCl (194 mg, 0.216 mL, 1.29 mmol). After 1 h, the reaction mixture was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 3% EtOAc / Hexanes, to give TES ether **6.59** (271 mg, 0.25 mmol, 97%) as a colorless oil: $[\alpha]_D^{23}$ = -30.6 (*c* 0.32, $CHCl_3$); IR (neat) 2955, 2929, 2877, 1717, 1459, 1414, 1250, 1093, 1006, 838, 741 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.78 (s, 1H), 5.02 (s, 1H), 4.91 (s, 1H), 4.19 (m, 1H), 4.04 (d, *J* = 5.7 Hz, 1H), 3.80-3.86 (m, 1H), 3.63-3.72 (m, 3H), 2.93 (dd, *J* = 18.0, 5.7 Hz, 1H), 2.73 (dd, *J* = 18.0, 6.3 Hz, 1H), 2.17 (dd, *J* = 12.8, 5.40 Hz, 1H), 1.79-1.89 (m, 2H), 1.85 (s, 3H), 1.46-1.73 (m, 4H), 1.45 (s, 3H), 1.23-1.39 (m, 3H), 1.15 (d, *J*=5.7 Hz, 3H), 0.91-1.04 (m, 45H), 0.87 (d, *J*=6.3 Hz, 3H), 0.78 (d, *J*=6.9 Hz, 3H), 0.56-0.68 (m, 24H), 0.11 (s, 9H), 0.07 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.6, 144.7, 142.7, 125.2, 114.7, 81.0, 78.3, 77.7, 66.1, 65.7, 61.6, 49.9, 48.5, 46.1, 44.9, 40.0, 31.0, 29.7, 28.4, 27.9, 26.0, 24.6, 19.4, 18.3, 14.5, 14.2, 7.2, 7.1, 7.0, 6.9, 6.8, 5.3, 4.9, 0.4, -5.3; HRMS (ES^+) calcd. for $C_{56}H_{120}O_7Si_6Na$ (M+Na) 1095.7547, found 1095.7495.



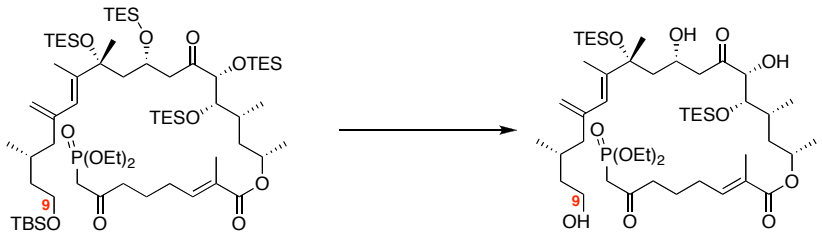
6.59 **6.44**

Alcohol 6.44: TMS ether **6.59** (543 mg, 0.51 mmol) was dissolved in a stirred solution of HOAc / THF / H_2O (28 mL, 8:8:1) at 0ºC. After 4 h, the reaction was quenched with solid $NaHCO_3$, filtered over Celite and extracted with ether (4 X 20 mL). The dried extract ($MgSO_4$) was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 10-20% EtOAc / Hexanes, to give alcohol **6.44** (490 mg, 0.49 mmol, 96%) as a colorless oil: $[\alpha]_D^{23}$ = -35.6 (*c* 0.39, $CHCl_3$); IR (neat) 3481, 2955, 2877, 1717, 1459, 1414, 1240, 1098, 1005, 836, 740 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.78 (s, 1H), 5.02 (s, 1H), 4.90 (s, 1H), 4.21 (m, 1H), 4.13 (d, *J* = 5.7 Hz, 1H), 3.80 (m, 1H), 3.65-3.69 (m, 3H), 2.92 (dd, *J* = 18.3, 6.0 Hz, 1H), 2.78 (dd, *J* = 18.3, 6.3 Hz, 1H), 2.17 (dd, *J* = 13.2, 5.1 Hz, 1H), 1.56-1.89 (m, 6H), 1.84 (s, 3H), 1.44 (s, 3H), 1.28 (m, 3H), 1.19 (d, *J*=6.1 Hz, 3H), 0.91-1.05 (m, 45H), 0.81-0.86 (m, 6H), 0.59-0.73 (m, 24H), 0.06 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 208.9, 144.7, 142.3, 125.4, 114.7, 81.4, 78.1, 77.7, 66.3, 65.4, 61.6, 49.7, 49.0, 46.0, 44.1, 40.0, 32.6, 28.4, 28.0, 26.0, 24.4, 19.5, 18.3, 15.6, 14.5, 7.2, 7.0, 6.9, 6.8, 5.3, 5.2, 4.8, -5.3; HRMS (ES^+) calcd. for $C_{53}H_{112}O_7Si_5Na$ (M+Na) 1023.7152, found 1023.7132.



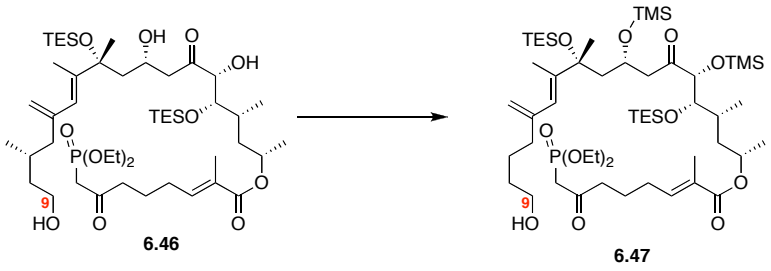
Phosphonate 6.45: To a stirred solution of acid **5.5** (421 mg, 1.37 mmol) in PhMe (5.2 mL) at rt was sequentially added Et_3N (139 mg, 0.191 mL, 1.37 mmol) and 2,4,6-trichlorobenzoyl chloride (323 mg, 0.207 mL, 1.37 mmol). After 12 h, the resulted solution was concentrated *in vacuo*. DMAP (168 mg, 1.37 mmol) was added, followed by the addition of a solution of alcohol **6.44** (260 mg, 0.26 mmol) in PhMe (5.2 mL). After another 12 h, the reaction was quenched with sat. aq. $NaHCO_3$ (10 mL) and extracted with EtOAc (4 X 20 mL). The dried extract ($MgSO_4$) was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 20-60% EtOAc / Hexanes, to give ester **6.45** (220 mg, 0.17 mmol, 66%) as a colorless oil: $[\alpha]_D^{23}$ = -23.8 (*c* 1.1, $CHCl_3$); IR (neat) 2955, 2877, 1715, 1459, 1255, 1096, 1019, 836, 741 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.70 (t, *J* = 8.3 Hz, 1H), 5.79 (s, 1H), 5.05 (m, 1H), 5.03 (s, 1H), 4.90 (s, 1H), 4.21 (m, 1H), 4.14-4.22 (m, 5H), 4.10 (d, *J* = 5.3 Hz, 1H), 3.61-3.73 (m, 3H), 3.12 (d, *J* = 22.8 Hz, 2H), 2.89 (dd, *J* = 18.1, 6.0 Hz, 1H), 2.77 (dd, *J* = 18.3, 6.2 Hz, 1H), 2.68 (t, *J* = 7.3 Hz, 2H), 2.13-2.22 (m, 3H), 1.58-1.89 (m, 8H), 1.84 (s, 3H), 1.83 (s, 3H), 1.46 (s, 3H), 1.36 (t, *J* = 7.1 Hz, 6H), 1.32-1.40 (m, 1H), 1.25 (d, *J* = 6.0 Hz, 3H), 0.92-1.03 (m, 45H), 0.87 (d, *J*=6.5 Hz, 3H), 0.81 (d, *J*=6.8 Hz, 3H), 0.56-0.71 (m, 24H), 0.07 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 208.4, 201.5, 167.6, 144.7,

142.5, 140.5, 129.0, 125.3, 114.7, 80.9, 77.8, 77.6, 68.8, 65.6, 62.6, 62.5, 61.6, 49.8, 49.0, 46.1, 43.4, 43.1, 41.9, 40.6, 40.0, 31.4, 28.4, 27.9, 27.7, 26.3, 26.0, 22.3, 20.7, 19.5, 18.3, 16.4, 16.3, 14.7, 14.5, 7.2, 7.0, 6.9, 6.8, 5.2, 5.1, 4.9, -5.3; HRMS (ES^+) calcd. for $C_{66}H_{133}O_{12}Si_5PNa$ (M+Na) 1311.8279, found 1311.8269.



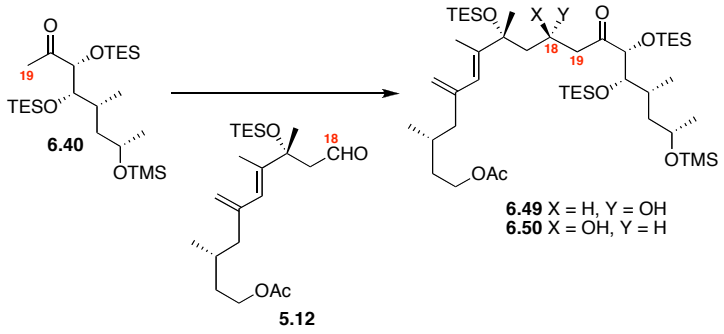
Triol 6.46: To a stirred solution of TBS ether **6.45** (129 mg, 0.10 mmol) in DCM / EtOH (6 mL, 1:1) at -5ºC was added CSA (35 mg, 0.15 mmol). After 12 h, the reaction was quenched with sat. aq. $NaHCO_3$ (8 mL) and extracted with EtOAc (4 X 15 mL). The dried extract ($MgSO_4$) was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 20-40-80% EtOAc / Hexanes, to give triol **6.46** (62 mg, 0.065 mmol, 65%) as a colorless oil: $[\alpha]_D^{23}$ = -1.64 (*c* 0.61, $CHCl_3$); IR (neat) 3420, 2955, 2877, 1715, 1458, 1253, 1022, 969, 742 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.71 (t, *J* = 6.4 Hz, 1H), 6.05 (s, 1H), 5.05 (m, 1H), 5.02 (s, 1H), 4.84 (s, 1H), 4.46 (m, 1H), 4.13-4.19 (m, 5H), 3.62-3.74 (m, 3H), 3.13 (d, *J*=22.8 Hz, 1H), 2.91 (dd, *J*=18.4, 8.6 Hz, 1H), 2.59-2.75 (m, 3H), 2.11-2.23 (m, 3H), 1.98 (dd, *J*=12.0, 8.0 Hz, 1H), 1.59-1.91 (m, 13H), 1.43 (s, 3H), 1.31-1.39 (m, 1H), 1.36 (t, *J* =7.1 Hz, 6H), 1.25 (d, *J* =6.2 Hz, 3H), 0.96-1.03 (m, 18H), 0.89 (d, *J* =6.6 Hz, 3H), 0.85 (d, *J* =6.7 Hz, 3H), 0.59-0.70 (m, 12H); ^{13}C

NMR (75 MHz, $CDCl_3$) δ 212.2, 201.6, 167.7, 145.0, 143.3, 140.8, 128.9, 124.0, 114.5, 81.2, 78.3, 75.4, 68.7, 65.5, 62.7, 62.6, 61.0, 47.7, 45.9, 45.0, 43.5, 43.4, 43.1, 41.8, 40.5, 39.7, 32.1, 29.7, 28.3, 27.8, 26.3, 26.0, 22.3, 20.9, 19.6, 18.3, 16.4, 16.3, 14.7, 12.4, 7.0, 6.8, 5.4, 5.2, 4.8; HRMS (ES^+) calcd. for $C_{48}H_{91}O_{12}Si_2PNa$ (M+Na) 969.5784, found 969.5720.



TMS ether 6.47: To a stirred solution of triol **6.46** (62 mg, 0.065 mmol) in DCM (2 mL) at rt was sequentially added DMAP (155 mg, 1.27 mmol) and TMSCl (66 mg, 80 µL, 0.63 mmol). After 1 h, the reaction mixture was concentrated *in vacuo* and then diluted with MeOH (2 mL), followed by the addition of $Ba(OH)_2•8H_2O$ (19 mg, 0.062 mmol). After another 10 min, the reaction was quenched with sat. aq. NH_4Cl (3 mL) and extracted with Et_2O (3 X 10 mL). The dried extract ($MgSO_4$) was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 40-60% EtOAc / Hexanes, to give ester **6.47** (37 mg, 0.034 mmol, 52% over 2 steps) as a colorless oil: $[\alpha]_D^{23}$ = -29.7 (*c* 0.31, $CHCl_3$); IR (neat) 3447, 2955, 2877, 1716, 1458, 1250, 1021, 841, 744 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.69 (t, *J* = 7.4 Hz, 1H), 5.79 (s, 1H), 5.05 (m,

1H), 5.03 (s, 1H), 4.87 (s, 1H), 4.14-4.21 (m, 5H), 4.07 (d, *J* = 5.4 Hz, 1H), 3.66-3.74 (m, 3H), 3.12 (d, *J* = 22.8 Hz, 2H), 3.01 (dd, *J* = 18.5, 6.9 Hz, 1H), 2.80 (dd, *J* = 18.3, 4.9 Hz, 1H), 2.68 (t, *J* = 7.2 Hz, 2H), 2.09-2.22 (m, 3H), 1.64-1.90 (m, 15H), 1.44 (s, 3H), 1.36 (t, *J* = 7.01 Hz, 6H), 1.32-1.39 (m, 1H), 1.25 (d, *J* = 6.0 Hz, 3H), 0.92-1.03 (m, 18H), 0.87 (d, *J*=6.4 Hz, 3H), 0.81 (d, *J*=6.8 Hz, 3H), 0.56-0.71 (m, 12H), 0.13 (s, 9H), 0.08 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 209.1, 201.5, 167.7, 144.9, 142.0, 140.5, 129.0, 125.5, 114.9, 80.7, 78.2, 77.9, 68.9, 65.2, 62.6, 62.5, 61.0, 49.2, 49.0, 46.2, 43.5, 43.4, 41.9, 40.7, 40.0, 31.2, 28.4, 27.8, 22.3, 20.7, 19.4, 16.4, 16.3, 14.9, 14.7, 7.1, 6.9, 5.2, 4.9, 2.4, 0.6; HRMS (ES$^+$) calcd. for $C_{54}H_{107}O_{12}Si_4PNa$ (M+Na) 1113.6475, found 1113.6493

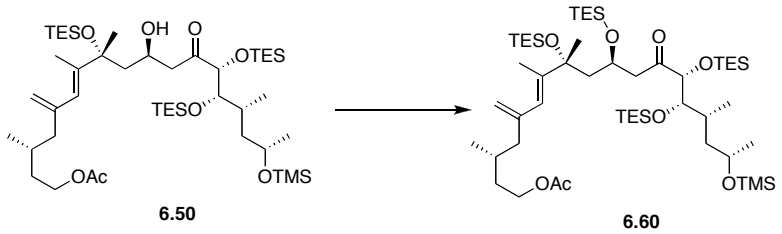


Aldol adducts 6.49 & 6.50: *Method A (-100°C Conditions)* – To a stirred solution of methyl ketone **6.40** (574 mg, 1.17 mmol) in THF (6 mL) at -78ºC was added LDA[2] (1.38 mL, 1 M in THF). After 15 min, TMEDA (400 mg, 0.310 mL, 3.44 mmol) was added. After 5 min, the reaction was cooled to -100ºC, followed by the addition of a pre-cooled (-100ºC) solution of aldehyde **5.12** (310 mg, 0.78 mmol) in THF (6 mL) via *cannula* in one portion. After another 0.5 h, the reaction

was quenched with 1 M AcOH in THF (1.5 mL) at -100ºC. The reaction mixture was then warmed up to rt, diluted with sat. aq. NH_4Cl (10 mL) and extracted with ether (4 X 25 mL). The dried extract ($MgSO_4$) was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 50% CH_2Cl_2 / Hexanes - 2% EtOAc / Hexanes, to give aldol adduct **6.50** (405 mg, 0.45 mmol, 58%) and **6.49** (50 mg, 0.056 mmol, 7%) as colorless oils.

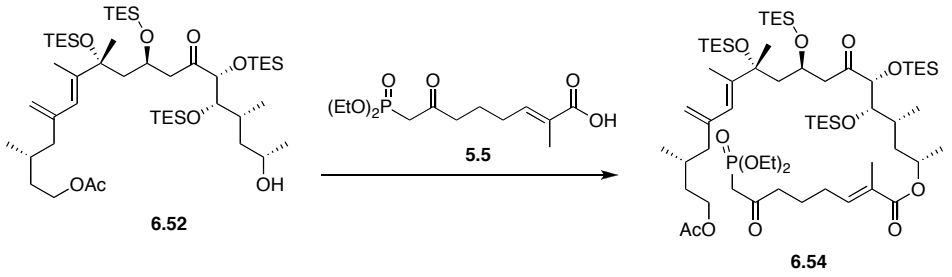
Method B (-40°C Conditions) – To a stirred solution of methyl ketone **6.40** (37.2 mg, 0.0758 mmol) in THF (0.4 mL) at -78ºC was added LDA[2] (90 μL, 0.09 mmol, 1 M in THF). After 15 min, TMEDA (15.5 mg, 20 μL, 0.133 mmol) was added. After 5 min, the reaction was warmed up to -40ºC, followed by the addition of a pre-cooled (-40ºC) solution of aldehyde **5.12** (20 mg, 0.0504 mmol) in THF (0.4 mL) via *cannula* in one portion. After another 0.5 h, the reaction was quenched with sat. aq. NH_4Cl (2 mL) and extracted with ether (4 X 5 mL). The dried extract ($MgSO_4$) was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 50% CH_2Cl_2 / Hexanes -2% EtOAc / Hexanes, to give aldol adduct **6.49** (16.1 mg, 0.0181 mmol, 36%) and **6.50** (13.4 mg, 0.0151 mmol, 30%) as colorless oils. **6.49**: $[\alpha]_D^{23}$ = -9.42 (*c* 1.21, $CHCl_3$); IR (neat) 3516, 2956, 2913, 2877, 1743, 1719, 1458, 1414, 1370, 1249, 1116, 1088, 1008, 841, 742 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.89 (s, 1H), 5.02 (s, 1H), 4.83 (s, 1H), 4.38-4.27 (m, 1H), 4.06-4.10 (m, 3H), 3.86-3.75 (m, 1H), 3.72-3.68 (m, 1H), 3.66 (s, 1H, OH), 2.96 (dd, *J* = 17.9, 6.2 Hz, 1H), 2.59 (dd, *J* = 18.0, 6.1 Hz, 1H), 2.15 (dd, *J* = 13.2, 5.7 Hz, 1H), 2.04 (s, 3H), 1.94-1.76 (m, 4H), 1.81 (s, 3H), 1.70-1.63 (m,

2H), 1.54 (s, 3H), 1.48-1.38 (m, 2H), 1.27-1.22 (m, 1H), 1.13 (d, *J* = 5.9 Hz, 3H), 1.02-0.93 (m, 27H), 0.89 (d, *J* = 6.3 Hz, 3H), 0.79 (d, *J* = 6.6 Hz, 3H), 0.59-0.69 (m, 18H), 0.09 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 210.8, 171.1, 144.3, 143.3, 124.8, 115.0, 81.0, 79.3, 78.4, 65.9, 65.0, 62.9, 48.2, 47.2, 45.8, 45.0, 35.3, 31.0, 28.7, 26.3, 24.6, 21.0, 19.3, 14.7, 13.8, 7.1, 7.0, 6.8, 6.6, 5.2, 4.9, 0.3; HRMS (ES^+) calcd. for $C_{46}H_{94}O_8Si_4Na$ (M+Na) 909.5924, found 909.5895. **6.50**: $[\alpha]_D^{23}$ = +1.76 (*c* 1.25, $CHCl_3$); IR (neat) 3511, 2956, 2913, 2877, 1743, 1718, 1458, 1369, 1249, 1119, 1088, 1011, 841, 742 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.06 (s, 1H), 5.03 (s, 1H), 4.88 (s, 1H), 4.17-4.06 (m, 4H), 3.88 (s, 1H, OH), 3.88-3.81 (m, 1H), 3.73-3.69 (m, 1H), 2.66-2.78 (m, 2H), 2.17 (dd, *J* = 13.5, 6.0 Hz, 1H), 2.05 (s, 3H), 1.97-1.93 (m, 1H), 1.85-1.78 (m, 1H), 1.82(s, 3H), 1.74-1.70 (m, 1H), 1.62-1.14 (m, 4H), 1.44 (s, 3H), 1.28-1.20 (m, 2H), 1.14 (d, *J* = 5.8 Hz, 3H), 1.02-0.94 (m, 27H), 0.91 (d, *J* = 6.2 Hz, 3H), 0.78 (d, *J* = 6.6 Hz, 3H), 0.72-0.57 (m, 18H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 210.5, 171.1, 144.5, 140.8, 125.4, 114.8, 81.3, 80.7, 78.4, 66.0, 65.7, 63.0, 47.1, 45.9, 45.0, 35.2, 31.0, 29.7, 28.7, 28.2, 24.6, 21.0, 19.4, 14.9, 13.6, 7.1, 7.0, 6.9, 6.8, 6.6, 5.2, 4.8, 0.3; HRMS (ES^+) calcd. for $C_{46}H_{94}O_8Si_4Na$ (M+Na) 909.5924, found 909.5948.



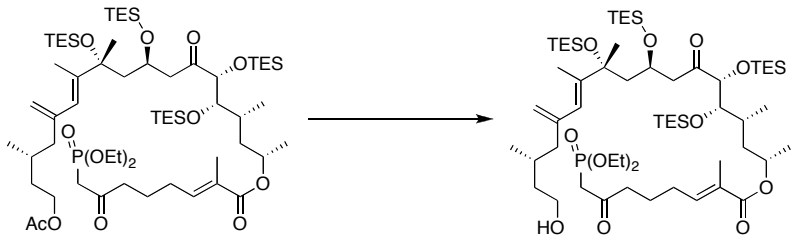
TES ether 6.60: To a stirred solution of aldol adduct **6.50** (440 mg, 0.496 mmol) in CH_2Cl_2 (20 mL) at rt was sequentially added DMAP (910 mg, 7.44 mmol) and TESCl (557 mg, 0.620 mL, 3.72 mmol). After 3 h, the reaction mixture was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 2% EtOAc / Hexanes, to give TES ether **6.60** (445 mg, 0.444 mmol, 90%) as a colorless oil: $[\alpha]_D^{23}$ = -20.0 (*c* 0.24, $CHCl_3$); IR (neat) 2955, 2912, 2877, 1744, 1717, 1458, 1249, 1127, 1069, 1008, 840, 742 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.81 (s, 1H), 5.00 (s, 1H), 4.85 (s, 1H), 4.43-4.30 (m, 1H), 4.16-4.03 (m, 3H), 3.88-3.78 (m, 1H), 3.69-3.72 (m, 1H), 2.88 (dd, *J* = 17.4, 4.8 Hz, 1H), 2.73 (dd, *J* = 17.4, 7.2 Hz, 1H), 2.13 (dd, *J* = 13.8, 6.0 Hz, 1H), 2.04 (s, 3H), 1.82-1.94 (m, 3H), 1.79 (s, 3H), 1.64-1.75 (m, 3H), 1.46 (s, 3H), 1.39-1.51 (m, 2H), 1.20-1.28 (m, 1H), 1.14 (d, *J* = 6.0 Hz, 3H), 0.84-1.03 (m, 39H), 0.77 (d, *J* = 6.6 Hz, 3H), 0.56-0.71 (m, 24H), 0.11 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 208.4, 171.1, 144.3, 143.8, 124.3, 114.8, 81.1, 78.4, 77.3, 66.1 (2C), 62.9, 50.3, 48.7, 45.9, 45.2, 35.2, 30.7, 28.7, 26.9, 24.7, 21.0, 19.3, 14.8, 13.8, 7.2, 7.0, 6.9, 6.7, 5.4, 5.3, 5.0, 0.3; HRMS (ES^+) calcd. for $C_{52}H_{108}O_8Si_5Na$ (M+Na) 1023.6788, found 1023.6737.

Alcohol 6.52: To a stirred solution of TMS ether **6.60** (432 mg, 0.43 mmol) in THF / H_2O (9 mL, 8:1) at -20ºC was added HOAc (8 mL). After 5 h, the reaction was quenched with solid $NaHCO_3$, filtered over Celite and extracted with ether (4 X 20 mL). The dried extract ($MgSO_4$) was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 5-10-20% EtOAc / Hexanes, to give alcohol **6.52** (338 mg, 0.36 mmol, 85%) as a colorless oil: $[\alpha]_D^{23}$ = -20.8 (*c* 1.01, $CHCl_3$); IR (neat) 3503, 2955, 2912, 2877, 1744, 1720, 1458, 1414, 1367, 1239, 1007, 741 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.85 (s, 1H), 5.02 (s, 1H), 4.86 (s, 1H), 4.50-4.40 (m, 1H), 4.18-4.03 (m, 3H), 3.85-3.77 (m, 1H), 3.67 (t, *J* = 5.0 Hz, 1H), 2.74-2.86 (m, 2H), 2.19 (br, OH), 2.14 (dd, *J* = 13.6, 6.3 Hz, 1H), 2.06 (s, 3H), 1.89-1.96 (m, 2H), 1.80 (s, 3H), 1.66-1.85 (m, 5H), 1.45 (s, 3H), 1.39-1.42 (m, 1H), 1.19 (d, *J* = 6.0 Hz, 3H), 1.10-1.22 (m, 1H), 0.95-1.05 (m, 36H), 0.90 (d, *J* = 6.4 Hz, 3H), 0.85 (d, *J* = 6.4 Hz, 3H), 0.59-0.72 (m, 24H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.4, 171.2, 144.3, 143.5, 124.4, 115.0, 82.1, 78.5, 77.3, 66.0, 65.9, 63.0, 50.0, 48.0, 45.9, 44.4, 35.2, 32.3, 28.7, 27.3, 24.2, 21.0, 19.3, 15.4, 15.0, 7.3, 7.1, 7.0, 6.9, 6.8, 5.3, 5.2, 4.9; HRMS (ES^+) calcd. for $C_{49}H_{100}O_8Si_4Na$ (M+Na) 951.6393, found 951.6418.



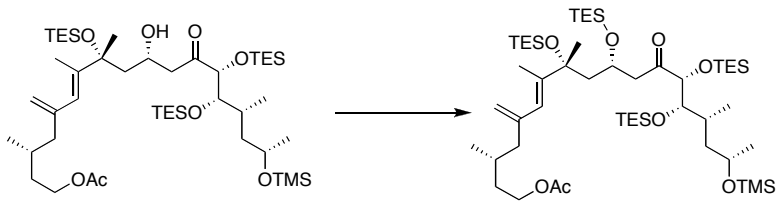
Phosphonate 6.54: To a stirred solution of acid **5.5** (837 mg, 2.73 mmol) in PhMe (6 mL) at rt was sequentially added Et_3N (276 mg, 0.379 mL, 2.73 mmol) and 2, 4, 6-trichlorobenzoyl chloride (641 mg, 0.411 mL, 2.73 mmol). After 12 h, the resulted solution was concentrated *in vacuo*. DMAP (333 mg, 2.73 mmol) was added, followed by the addition of a solution of alcohol **6.52** (445 mg, 0.479 mmol) in PhMe (10.5 mL). After another 19 h, the reaction was quenched with sat. aq. NH_4Cl (15 mL) and extracted with EtOAc (4 X 50 mL). The dried extract ($MgSO_4$) was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 20-60% EtOAc / Hexanes, to give phosphonate **6.54** (450 mg, 0.100 mmol, 77%) as a colorless oil: $[\alpha]_D^{23}$ = -20.3 (*c* 1.23, $CHCl_3$); IR (neat) 2955, 2913, 2877, 1740, 1716, 1458, 1368, 1243, 1056, 1019, 968, 742 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.69 (t, *J* = 6.4 Hz, 1H), 5.82 (s, 1H), 5.10-5.02 (m, 1H), 5.01 (s, 1H), 4.84 (s, 1H), 4.42-4.32 (m, 1H), 4.21-4.02 (m, 7H), 3.76-3.68 (m, 1H), 3.12 (d, *J* = 22.8 Hz, 2H), 2.85 (dd, *J* = 17.4, 4.1 Hz, 1H), 2.65-2.76 (m, 3H), 2.12-2.22 (m, 2H), 2.10-2.04 (m, 1H), 2.05 (s, 3H), 1.58-1.93 (m, 10H), 1.82 (s, 3H), 1.79 (s, 3H), 1.45 (s, 3H), 1.43-1.39 (m, 1H), 1.35 (t, *J* = 7.1 Hz, 6H), 1.24 (d, *J* = 5.9 Hz, 3H), 0.87-1.03 (m, 39H), 0.79 (d, *J* = 6.6 Hz, 3H), 0.55-0.68 (m, 24H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 208.3, 201.4, 171.1, 167.6, 144.3, 143.7,

140.5, 129.0, 124.4, 114.9, 81.1, 77.9, 77.34, 68.8, 66.2, 62.9, 62.6, 62.5, 50.3, 49.0, 45.9, 43.3, 41.6, 40.8, 35.2, 31.1, 28.7, 27.7, 26.9, 22.3, 21.0, 20.7, 19.3, 16.3, 16.2, 14.8, 14.3, 12.4, 7.2, 7.1, 7.0, 6.9, 6.7, 5.3, 5.2, 5.0; HRMS (ES^+) calcd. for $C_{62}H_{121}O_{13}Si_4PNa$ (M+Na) 1239.7520, found 1239.7563.



Alcohol 6.56: To a stirred solution of ester **6.54** (170 mg, 0.140 mmol) in MeOH (0.5 mL) at rt was added a saturated solution of $Ba(OH)_2 \bullet 8H_2O$ in MeOH (6.0 mL). After 20 min, the reaction mixture was purified directly by chromatography over silica gel, eluting with 20-60% EtOAc / Hexanes, to give alcohol **6.56** (150 mg, 0.127 mmol, 91%) as a colorless oil: $[\alpha]_D^{23}$ = -20.3 (*c* 0.60, $CHCl_3$); IR (neat) 3440, 2955, 2877, 1716, 1458, 1242, 1019, 969, 742 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 6.69 (t, *J* = 6.2 Hz, 1H), 5.82 (s, 1H), 5.10-5.03 (m, 1H), 5.00 (s, 1H), 4.83 (s, 1H), 4.42-4.31 (m, 1H), 4.20-4.08 (m, 5H), 3.63-3.74 (m, 3H), 3.12 (d, *J* = 22.8 Hz, 2H), 2.78-2.72 (m, 2H), 2.66 (t, *J* = 7.1 Hz, 2H), 2.04-2.19 (m, 3H), 1.89-1.61 (m, 10H), 1.81 (s, 3H), 1.78 (s, 3H), 1.44 (s, 3H), 1.43-1.38 (m, 1H), 1.35 (t, *J* = 7.1 Hz, 6H), 1.24 (d, *J* = 5.9 Hz, 3H), 1.03-0.92 (m, 36H), 0.87 (d, *J* = 6.4 Hz, 3H), 0.79 (d, *J* = 6.6 Hz, 3H), 0.55-0.71 (m, 24H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.5, 201.5, 167.7, 144.6, 143.5, 140.6, 129.0, 124.7,

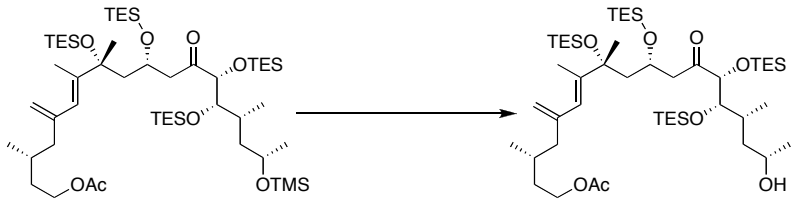
114.7, 81.2, 78.0, 68.8, 66.1, 62.6, 62.5, 61.1, 50.3, 49.1, 46.1, 43.5, 43.4, 41.8, 40.9, 39.8, 31.1, 28.5, 27.8, 27.1, 22.3, 20.8, 19.5, 16.4, 16.3, 14.9, 14.2, 12.4, 7.3, 7.1, 7.0, 6.9, 6.8, 5.3, 5.2, 5.0; HRMS (ES^+) calcd. for $C_{60}H_{119}O_{12}Si_4PNa$ (M+Na) 1197.7414, found 1197.7423.



6.49 **6.51**

TES ether 6.51: To a stirred solution of aldol adduct **6.49** (295 mg, 0.332 mmol) in CH_2Cl_2 (10 mL) at rt was sequentially added DMAP (608 mg, 4.98 mmol) and TESCl (375 mg, 0.418 mL, 2.49 mmol). After 3 h, the reaction mixture was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 2% EtOAc / Hexanes, to give TES ether **6.51** (290 mg, 0.289 mmol, 87%) as a colorless oil: $[\alpha]_D^{23}$ = -31.4 (*c* 0.85, $CHCl_3$); IR (neat) 2955, 2913, 2877, 1745, 1718, 1459, 1368, 1249, 1127, 1086, 1007, 841, 742 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.78 (s, 1H), 5.03 (s, 1H), 4.92 (s, 1H), 4.20-4.08 (m, 3H), 4.04 (d, *J* = 5.7 Hz, 1H), 3.84-3.81 (m, 1H), 3.72-3.68 (m, 1H), 2.86 (dd, *J* = 18.0, 5.8 Hz, 1H), 2.72 (dd, *J* = 17.4, 7.2 Hz, 1H), 2.17 (dd, *J* = 13.8, 6.0 Hz, 1H), 2.05 (s, 3H), 1.93-1.64 (m, 5H), 1.84 (s, 3H), 1.54-1.39 (m, 3H), 1.45 (s, 3H), 1.27-1.21 (m 1H), 1.14 (d, *J* = 6.0 Hz, 3H), 1.03-0.87 (m, 39H), 0.78 (d, *J* = 6.7 Hz, 3H), 0.71-0.55 (m, 24H), 0.11 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 208.6, 171.1, 144.3, 143.0, 125.0, 115.1, 81.0, 78.3, 77.7, 66.1, 65.7, 63.0, 49.8, 48.5, 46.0, 44.9, 35.4, 31.0,

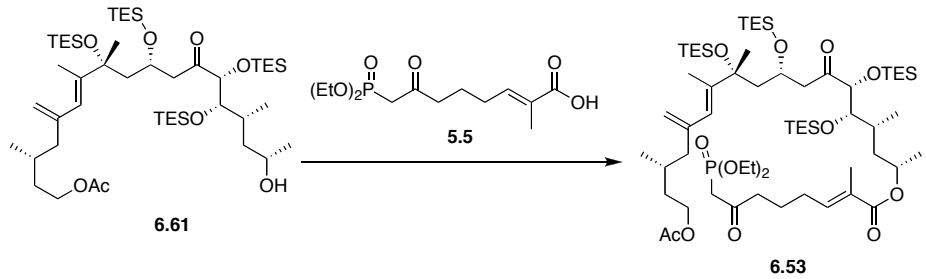
28.6, 27.9, 24.6, 21.0, 19.2, 14.5, 14.2, 7.2, 7.0, 6.9, 6.8, 5.2, 4.9, 0.4; HRMS (ES^+) calcd. for $C_{52}H_{108}O_8Si_5Na$ (M+Na) 1023.6788, found 1023.6785.



6.51 **6.61**

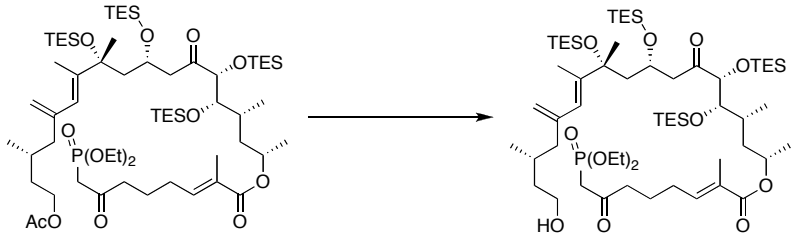
Alcohol 6.61: To a stirred solution of TMS ether **6.51** (290 mg, 0.289 mmol) in THF / H_2O (6.52 mL, 8:1) at -20ºC was added HOAc (4 X 1.45 mL) in 4 portions every 60 min. After 5 h, the reaction was quenched with solid $NaHCO_3$, filtered over Celite and extracted with ether (4 X 15 mL). The dried extract ($MgSO_4$) was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 5-10% EtOAc / Hexanes, to give alcohol **6.61** (220 mg, 0.237 mmol, 82%) as a colorless oil: $[\alpha]_D^{23}$ = -31.6 (*c* 1.01, $CHCl_3$); IR (neat) 3510, 2956, 2912, 2877, 1744, 1720, 1458, 1414, 1368, 1239, 1062, 1006, 741 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.78 (s, 1H), 5.02 (s, 1H), 4.90 (s, 1H), 4.22-4.08 (m, 4H), 3.81-3.77 (m, 1H), 3.69-3.66(m, 1H), 2.94 (dd, *J* = 18.3, 6.1 Hz, 1H), 2.78 (dd, *J* = 18.3, 5.7 Hz, 1H), 2.15 (dd, *J* = 13.1, 5.7 Hz, 1H), 2.04 (s, 3H), 1.93-1.60 (m, 6H), 1.83 (s, 3H), 1.45-1.34 (m, 2H), 1.44 (s, 3H), 1.30-1.20 (m, 1H), 1.17 (d, *J* = 6.0 Hz, 3H), 1.04-0.87 (m, 39H), 0.82 (d, *J* = 6.0 Hz, 3H), 0.72-0.56 (m, 24H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 208.8, 171.2, 144.4, 142.6, 125.2, 115.1, 81.4, 78.1, 77.7, 66.2, 65.4, 63.1, 49.7, 49.0, 45.9, 44.2, 35.3, 32.5, 28.6, 28.0, 24.3, 21.0,

19.2, 15.5, 14.6, 7.2, 7.0, 6.8, 5.3, 5.2, 4.8; HRMS (ES^+) calcd. for $C_{49}H_{100}O_8Si_4Na$ (M+Na) 951.6393, found 951.6398.



Phosphonate 6.53: To a stirred solution of acid **5.5** (450 mg, 1.47 mmol) in PhMe (3.2 mL) at rt was sequentially added Et_3N (149 mg, 0.204 mL, 1.47 mmol) and 2, 4, 6-trichlorobenzoyl chloride (346 mg, 0.222 mL, 1.47 mmol). After 12 h, the resulted solution was concentrated *in vacuo*. DMAP (180 mg, 1.47 mmol) was added, followed by the addition of a solution of alcohol **6.61** (240 mg, 0.258 mmol) in PhMe (5.7mL). After another 19 h, the reaction was quenched with sat. aq. NH_4Cl (8 mL) and extracted with EtOAc (4 X 50 mL). The dried extract ($MgSO_4$) was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 20-60% EtOAc / Hexanes, to give phosponate **6.53** (235 mg, 0.193 mmol, 78%) as a colorless oil: $[\alpha]_D^{23}$ = -23.6 (*c* 0.83, $CHCl_3$); IR (neat) 2955, 2912, 2877, 1734, 1716, 1458, 1369, 1241, 1056, 1019, 970, 741 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.69 (t, *J* = 6.3 Hz, 1H), 5.79 (s, 1H), 5.10-5.00 (m, 1H), 5.03 (s, 1H), 4.92 (s, 1H), 4.22-4.08 (m, 8H), 3.72 (dd, *J* = 5.1, 3.6 Hz, 1H), 3.13 (d, *J* = 27.8 Hz, 2H), 2.90 (dd, *J* = 18.0, 5.9 Hz, 1H), 2.77 (dd, *J* = 17.8, 6.0

Hz, 1H), 2.68 (t, *J* = 7.2 Hz, 2H), 2.18-2.07 (m, 3H), 2.06 (s, 3H), 1.94-1.68 (m, 9H), 1.842 (s, 3H), 1.82 (s, 3H), 1.46 (s, 3H), 1.43-1.39 (m, 2H), 1.36 (t, *J* = 7.0 Hz, 6H), 1.25 (d, *J* = 6.0 Hz, 3H), 1.03-0.92 (m, 36H), 0.90 (d, *J* = 6.4 Hz, 3H), 0.80 (d, *J* = 6.7 Hz, 3H), 0.70-0.55 (m, 24H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 208.4, 201.3, 171.1, 167.6, 144.3, 142.7, 140.5, 127.9, 125.1, 115.1, 80.9, 77.8, 77.6, 68.8, 65.6, 63.0, 62.9, 62.8, 48.7, 49.0, 45.9, 43.4, 41.7, 40.6, 35.3, 31.4, 28.6, 28.0, 27.7, 22.3, 21.0, 20.7, 19.2, 16.3, 16.2, 14.7, 14.5, 12.4, 7.2, 7.0, 6.9, 6.8, 5.3, 5.2, 4.9; HRMS (ES^+) calcd. for $C_{62}H_{121}O_{13}Si_4PNa$ (M+Na) 1239.7520, found 1239.7458.



Alcohol 6.55: To a stirred solution of ester **6.53** (230 mg, 0.189 mmol) in MeOH (10 mL) at rt was added $Ba(OH)_2$•$8H_2O$ (66.4 mg, 0.189 mmol). After 1 h, the reaction mixture was purified directly by chromatography over silica gel, eluting with 20-60% EtOAc / Hexanes, to give alcohol **6.55** (204 mg, 0.168 mmol, 89%) as a colorless oil: $[\alpha]_D^{23}$ = -27.0 (*c* 0.80, $CHCl_3$); IR (neat) 3434, 2955, 2877, 1716, 1458, 1376, 1242, 1019, 742 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.68 (t, *J* = 6.8 Hz, 1H), 5.78 (s, 1H), 5.11-5.00 (m, 1H), 5.00 (s, 1H), 4.86 (s, 1H),

4.19-4.05 (m, 6H), 3.73-3.66 (m, 3H), 3.07 (d, *J* = 27.8 Hz, 2H), 2.93 (dd, *J* = 18.0, 6.1 Hz, 1H), 2.78 (dd, *J* = 18.3, 5.7 Hz, 1H), 2.65 (t, *J* = 7.1 Hz, 2H), 2.22-2.11 (m, 3H), 1.92-1.59 (m, 8H), 1.81 (s, 6H), 1.43 (s, 3H), 1.42-1.39 (m, 3H), 1.33 (t, *J* = 7.0 Hz, 6H), 1.23 (d, *J* = 6.3 Hz, 3H), 1.02-0.85 (m, 39H), 0.78 (d, *J* = 6.5 Hz, 3H), 0.69-0.52 (m, 24H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 209.0, 201.4, 167.6, 144.8, 142.3, 140.5, 129.0, 125.5, 114.9, 80.8, 77.8, 77.7, 68.8, 65.6, 62.6, 62.5, 61.0, 49.5, 49.0, 46.2, 43.3, 41.6, 40.6, 40.0, 31.4, 28.3, 28.1, 27.7, 22.3, 20.7, 19.3, 16.3, 16.2, 14.7 (2C), 12.4, 7.2, 7.0, 6.9, 6.8, 5.2, 5.1, 4.9; HRMS (ES^+) calcd. for $C_{60}H_{119}O_{12}Si_4PNa$(M+Na) 1197.7414, found 1197.7422.

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1. (a) Zhang, W.; Carter, R. G. *Org. Lett.* **2005**, *7*, 4209. (b) Zhang, W. Ph.D. Dissertation, Oregon State University, 2006.

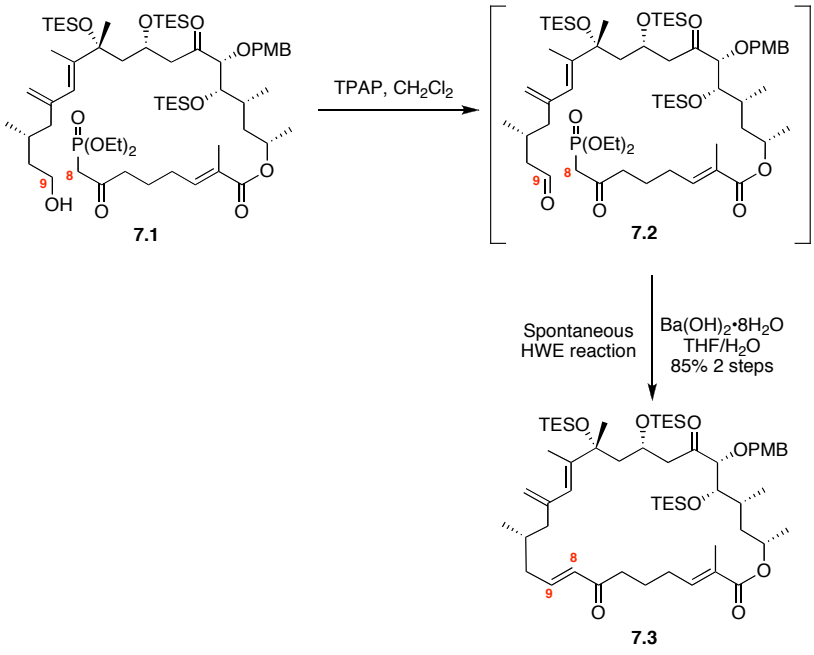
2. Preparation of LDA Solution: To a solution of diisopropylamine (101.9 mg, 0.14 mL, 1.0 mmol) in THF (0.46 mL) at –78°C was added *n*-BuLi (0.4 mL, 1.0 mmol, 2.5 M in THF). After 5 min, the white slurry was warmed to –10°C and stirred for an additional 15 min.

3. Zhang, W.; Carter, R. G.; Yokochi, A. F. T. *J. Org. Chem.* **2004**, *69,* 2569.

CHAPTER 7. COMPLETION OF THE SYNTHESIS

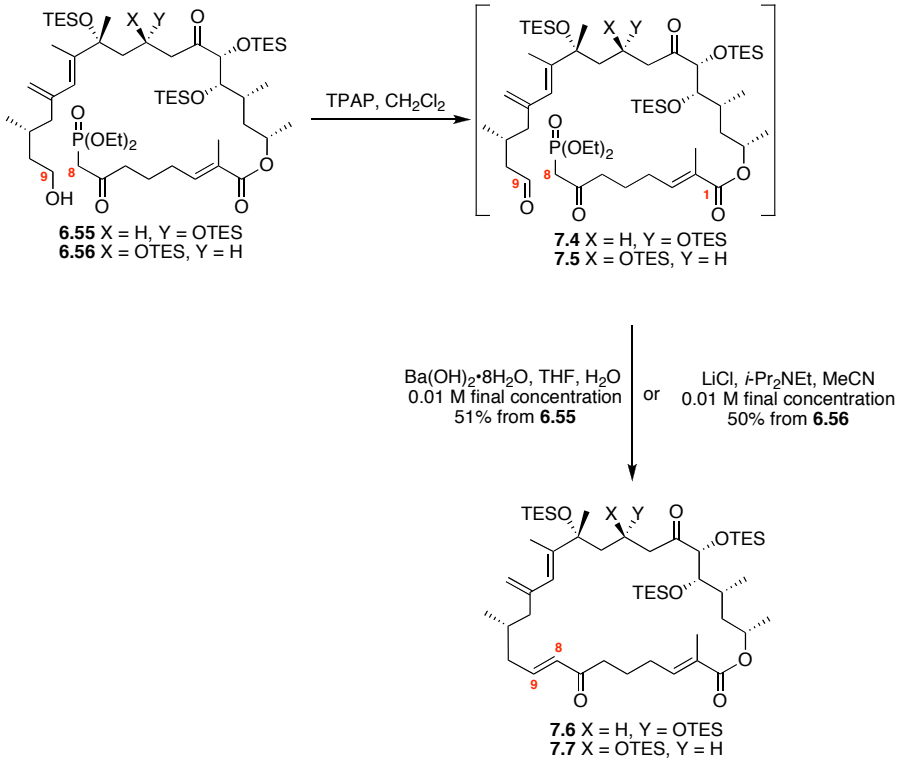
7.1 Macrocyclization

Once the synthesis of the phosphonate alcohol was accomplished, our sights were focused on the key macrocyclization. In our 1st generation synthesis of amphidinolide B,[1] we had developed the first successful macrocyclization of this natural product via a spontaneous intramolecular Horner-Wadsworth-Emmons olefination. The cyclization was driven to completion by the addition of $Ba(OH)_2 \cdot 8H_2O$ to give macrocylce **7.3** in good yield.



Scheme 7.1. Our Developed Strategy for the Macrocyclization

Equipped with the knowledge gained from our previous research, we applied the similar conditions on phosphonate alcohol **6.56**. Gratifyingly, significant amounts of the macrocycle **7.7** formed during the TPAP oxidation, appeared to undergo spontaneous intramolecular Horner-Wadsworth-Emmons olefination to provide the desired macrocycle. The conversion could be driven to completion by the addition of LiCl and Hunig's base.[2] A similar sequence was followed for construction of the 18*S* macrocycle **7.6**. In this case, $Ba(OH)_2$ proved more effective for driving the macrocyclization to completion. Additionally, we were pleased to observe that macrocycle **7.6** crystallized upon standing - allowing us to confirm the stereochemistry in the 26-membered macrocycle (Figure 7.1).



Scheme 7.2. Synthesis of Macrocycle **7.6** and **7.7**

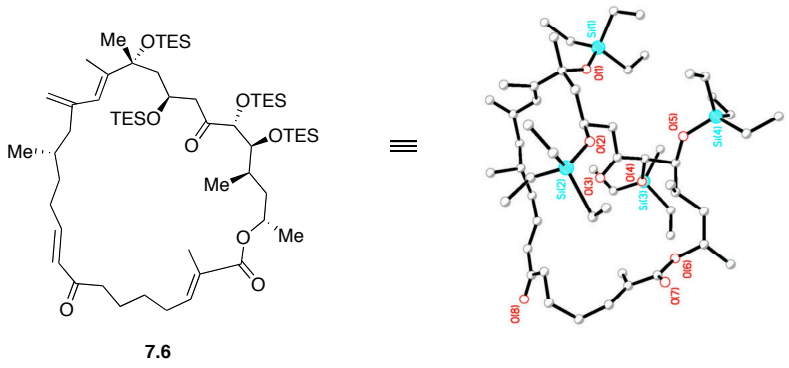
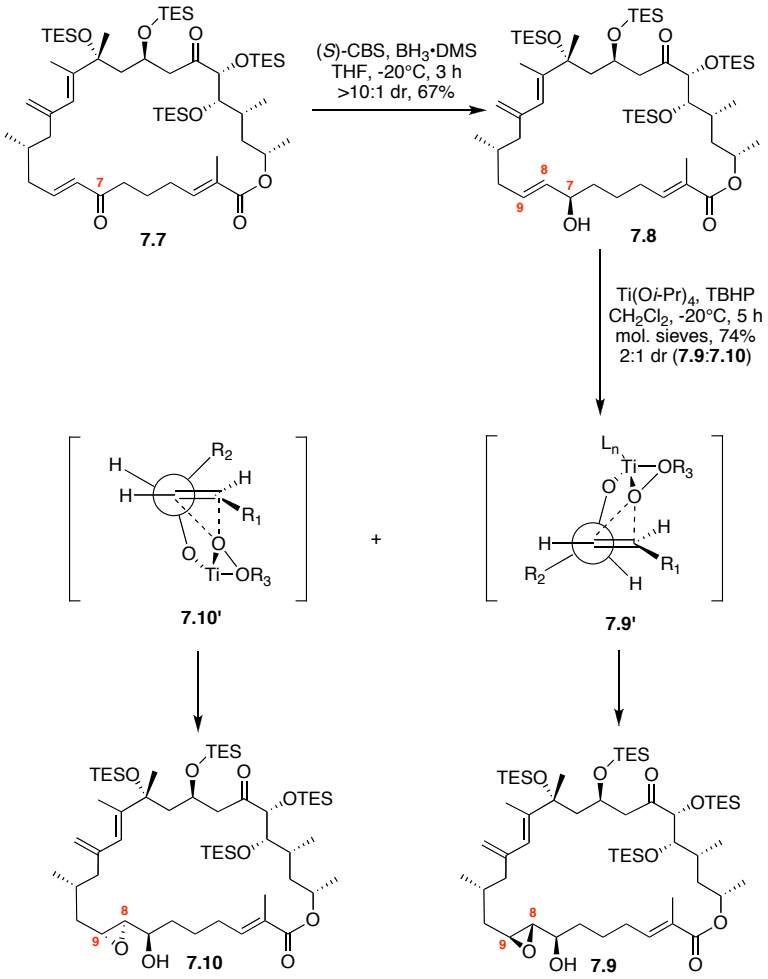


Figure 7.1. ORTEP Representation of Macrocycle **7.6**

7.2 Epoxidation of $C_{8,9}$ Alkene

With an efficient route into macrocycles **7.6** and **7.7**, the final challenges that remained were the incorporation of the C_6-C_9 allylic epoxide moiety and deprotection of silyl groups. We performed our initial explorations on the more readily available 18*R* macrolactone **7.7** (Scheme 7.3). Regio- and stereoselective reduction of the C_7 carbonyl functionality could be accomplished with the (*S*)-CBS reagent.[3] The possible reduction at the C_{20} ketone was not observed, presumably due to the increased steric congestion caused by the C_{21} stereocenter. We had next intended to epoxidize the alkene using Sharpless conditions;[4] however, the presumed steric congestion of the C_7 alcohol thwarted this approach. Walsh and co-workers have recently shown that the *threo (syn)* epoxy alcohol can be obtained from a Ti(O*i*-Pr)$_4$ / TBHP system.[5] As proposed by Adam and co-workers,[6] the binding of the allylic alkoxide to the titanium peroxy complex favors a dihedral angle of 70-90º. In Walsh's work, this dihedral angle led to a modest (~2:1) preference for the *syn* diastereomer in the epoxidation of a chiral *E*-disubstituted allylic alcohol.[5] In contrast, a 40-50º dihedral angle for VO(acac)$_2$ / TBHP system resulted in a moderate diastereoselectivity (~1.8:1) favoring the *anti* epoxy alcohol.[5] We were gratified to find that a similar reactivity profile appeared to take place with our system. The epoxidation led to the formation of both the *syn* (from transition-state **7.9'**) and *anti* (from transition-state **7.10'**) diastereomers - favoring the *syn* stereochemistry (2:1 dr). It is worth noting that the relative stereochemical

assignments are based on literature precedent.[5] We cannot at this time rigorously establish the relative stereochemistries of these two epoxy alcohols

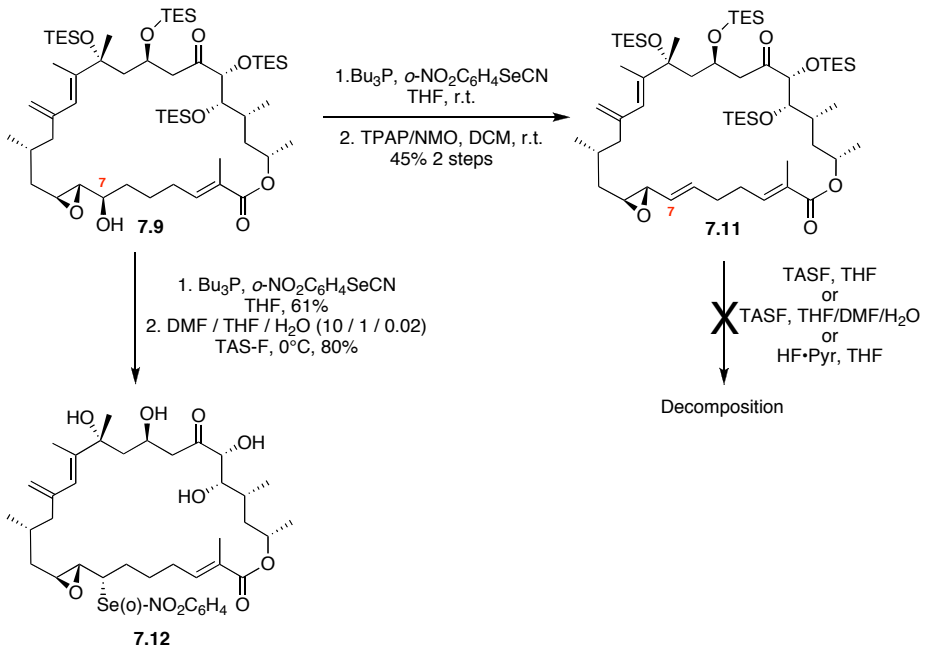


Scheme 7.3. Synthesis of Epoxy Alcohol **7.9** and **7.10**

7.3 Formation of $C_{6,7}$ Alkene and the Attempts to Remove TES Groups

As the *syn* diastereomer **7.9** contained the stereochemistry proposed for amphidinolide B_2, we initially proceeded forward with that diastereomer (Scheme 7.4). Selenide incorporation using a large excess of *o*-nitrophenylselenium nitrile

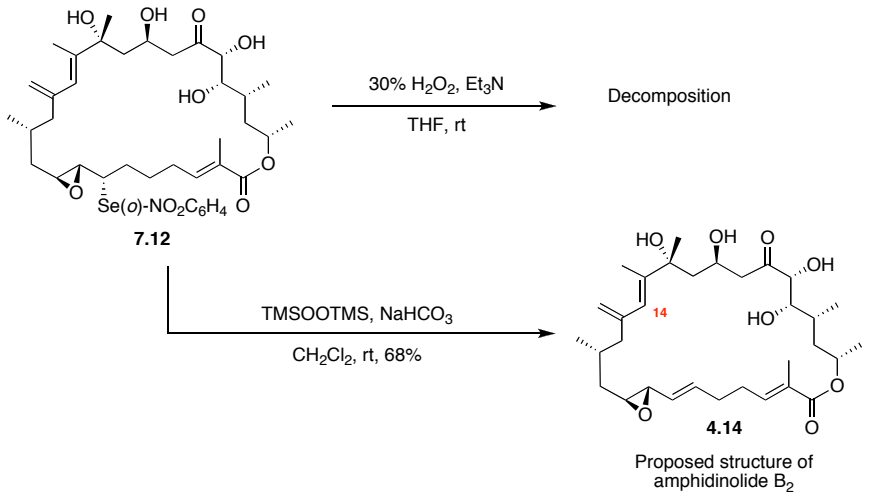
and PBu_3 (30 equivalent)[7] and subsequent elimination under our recently developed TPAP / NMO conditions[8] yielded the fully functionalized macrocycle **7.11**. Unfortunately, all attempts to remove the silyl protecting groups under fluoride or acidic conditions led to decomposition. We were surprised by these unexpected results since Fürstner and co-workers reported a successful de-silylation using TAS-F[9] on a similar system in their recent synthesis of amphidinolide G and H.[10] Suspecting that the allylic epoxide might be the culpable functionality, we next explored global deprotection on the epoxy selenide. We were quite pleased to find that treatment of the expoxy selenide with TAS-F cleanly removed all silyl protecting groups to provide the polyol **7.12**.



Scheme 7.4. Global Deprotection of TES Groups.

7.4 Completion of the Proposed Structure of Amphidinolide B_2

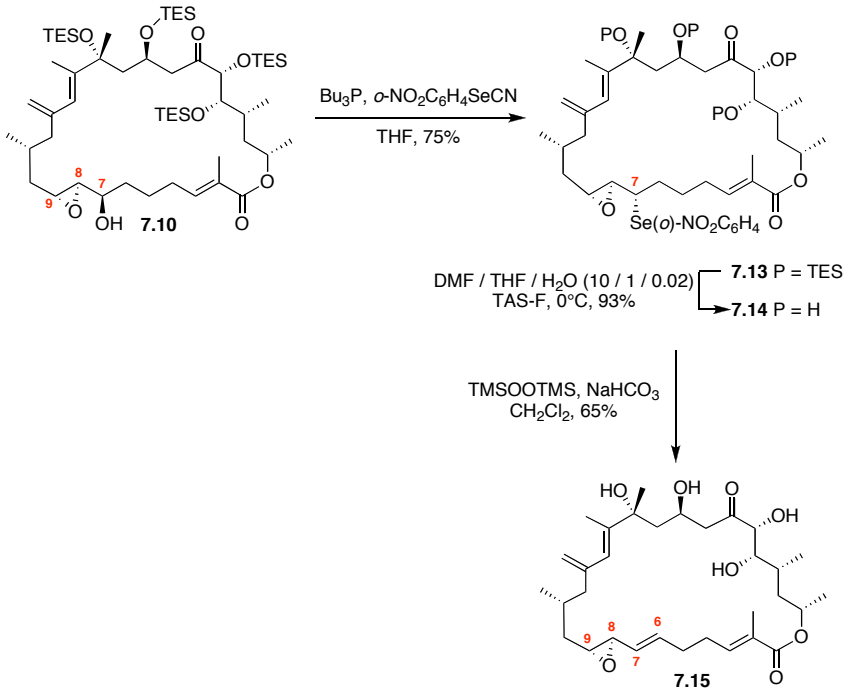
With the polyol in hand, the only challenge that remained was the oxidation and elimination of the selenide. The standard (H_2O_2) conditions[11] led to the decomposition of compound **7.12**. This issue was not completely surprising as we have previously encountered this problem in our azaspiracid work[12] as well as in an earlier generation approach to amphidinolide B.[1] We have attributed this deleterious reactivity to the α-hydroxy ketone moiety or the $C_{21,22}$ diol structure. A H_2O_2-induced Baeyer-Villiger oxidation of the α-hydroxy ketone or the oxidative cleavage of 1,2-diol to carboxylic acids might lead to the decomposition.[13] Our previously employed TPAP / NMO conditions are not compatible with the polyol functionality of **7.12**. A logical solution to this problem would be an alternative reagent that would not affect the α-hydroxy ketone and 1,2-diol functionality. Bistrimethylsilylperoxide has been used as a replacement of H_2O_2 in the metal catalyzed epoxidation of alkenes, [14] also has been employed to oxidize phosphonates to phosphates;[15] however, no precedents for the oxidation of a selenide have been reported. We were gratified to find that bistrimethylsilyl-peroxide (TMSOOTMS) cleanly facilitated the desired transformation to reveal compound **4.14**, the proposed structure of amphidinolide B_2. Surprisingly, this synthetic product (**4.14**) *did not match* with the spectra data provided for the natural product amphidinolide B_2.[16]



Scheme 7.7. Synthesis of The Proposed Structure of Amphidinolide B_2.

7.5 Synthesis of $C_{8,9}$ Epoxide Diastereomer of Amphidinolide B_2

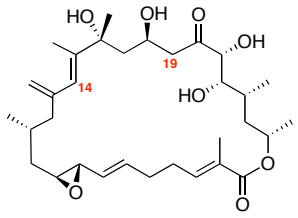
We followed a similar sequence on *anti*-epoxy alcohol **7.10** to afford $C_{8,9}$ epoxide diastereomer of amphidinolide B_2 (Scheme 7.5). Interestingly, the selenation had better yield (75% vs. 61%) and significantly shorter reaction time (30 min vs. 4 hours) compared to that of the *syn*-epoxy alcohol **7.9**. This observation was in agreement with our stereochemical assignments on epoxy alcohol **7.9** and **7.10**. In the formation of compound **7.13**, the nucleophilic attack from the selenide would not be hindered by the epoxide ring, while this effect would appear on substrate **7.9** due to the *syn*-epoxy alcohol relationship. Unfortunately, compound **7.15** also did not correlate with the reported data for amphidinolide B_2.[16]



Scheme 7.5. Synthesis of $C_{8,9}$ Epoxide Diastereomer of Amphidinolide B_2

7.6 Proposed Structure of Amphidinolide B_2

Comparison of the ^1H NMR data is shown in Table 7.1. The most significant differences are in the chemical shifts and coupling constants of H_{14} and H_{19}. In both cases, the ^1H NMR shift for the H_{14} alkene was shifted significantly downfield and the ^1H NMR shift for H_{19b} moved upfield as compared to the natural product data.



4.14
Originally proposed structure of amphidinolide B_2

Position	Natural amphidinolide B_2	Synthesized amphidinolide B_2	7.15
H_{14}	5.93 ppm, br, s	6.06 ppm, s	6.08 ppm, s
H_{19a}	3.09 ppm, dd	3.05 ppm, m	2.90 ppm, dd
	J = 2.3, 8.8 Hz		J = 9.9, 17.1 Hz
H_{19b}	2.63 ppm, dd	2.48 ppm, dd	2.45 ppm, m
	J = 8.6, 17.7 Hz	J = 8.0, 17.0 Hz	

Table 7.1. Comparison of the ^{1}H NMR Data

Careful inspection of the isolation paper revealed that the stereochemical analysis of amphidinolide B_2 was based primarily on the differences in the ^{1}H NMR in the C_{17}-C_{19} region of the natural product as compared to amphidinolide B_1 (**4.13**). It is important to note that Shimizu and Clardy[16] obtained X-ray crystallographic structure of natural product **4.13**. It is clear from our work that the structural differences between amphidinolide B_1 and B_2 are more complicated than initially expected. On the basis of this information, we have concluded that the proposed structure of amphidinolide B_2 is incorrect. Based on our tentative ^{1}H NMR data analysis, we suspect that the culprit stereochemistry is in fact the C_{16} tertiary alcohol. We speculate that a common *syn* relationship is present between C_{16} and C_{18} in amphidinolide B_2 (Figure 7.2).

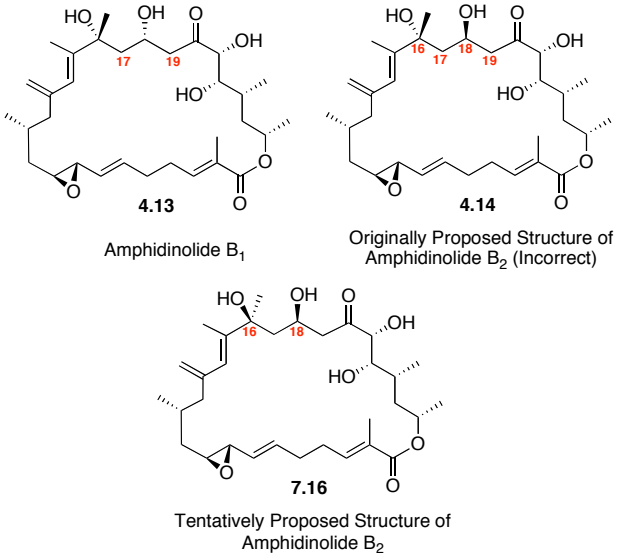
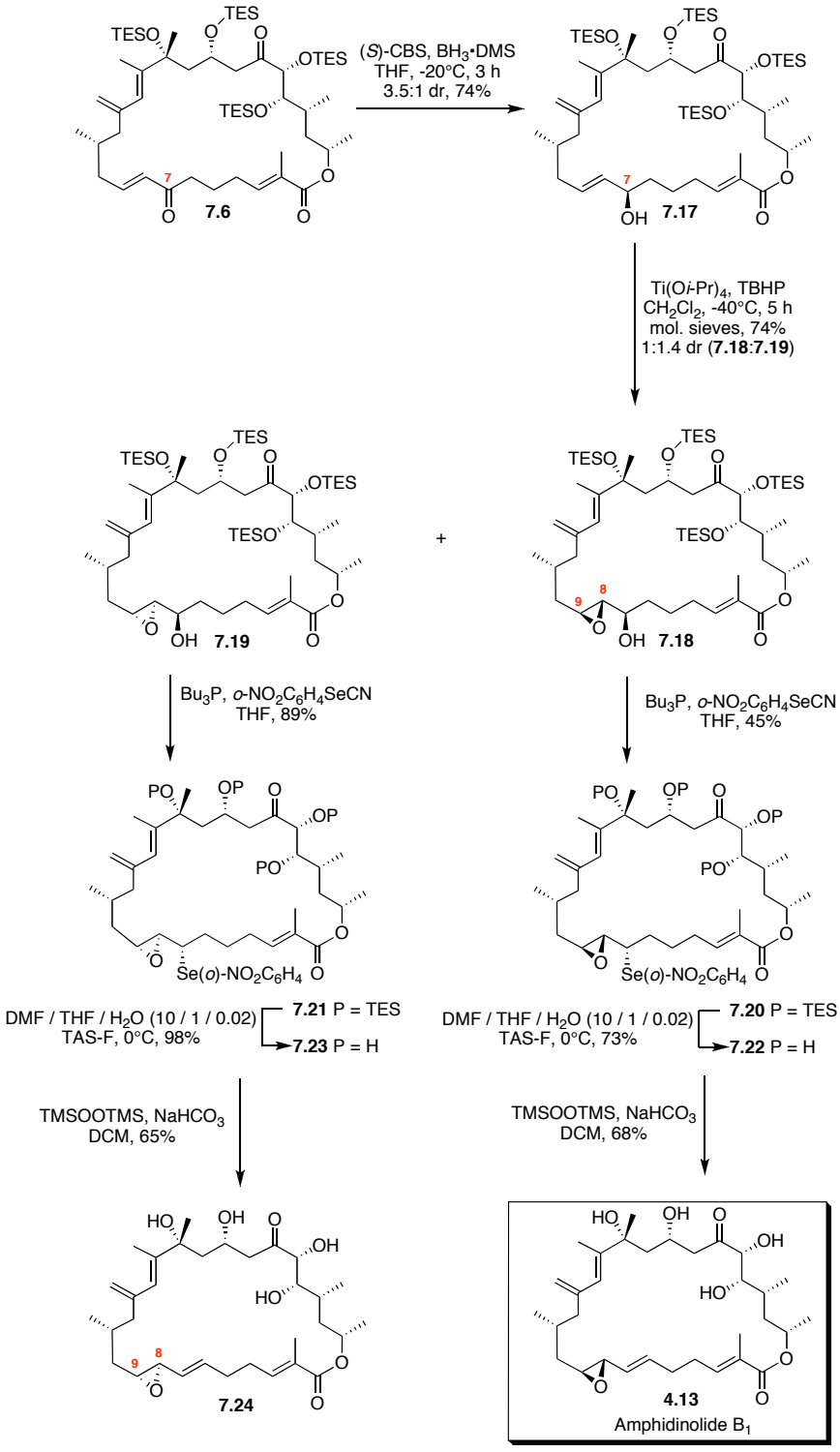


Figure 7.2. Tentatively Proposed Structure of Amphidinolide B_2

7.7 Completion of the Synthesis of Amphidinolide B_1

Next, we shifted our focus to the total synthesis of amphidinolide B_1 (**4.13**) (Scheme 7.6). We applied an analogous strategy for the synthesis of **4.13** as was described for the 18*R* series. It appears that a slight reversal in selectivity in the epoxidation occurs with the 18*S* stereochemistry - now with a modest preference for the undesired $C_{8,9}$ epoxide, probably due to the geometry change of the macrocycle caused by the 18*S* stereocenter. This is supported spectroscopically by the downfield shift for C_8 & C_9 proton (5.52 & 5.65 ppm, respectively) in the ^{1}H NMR of the 18*S* allylic alcohol **7.17** compared to that (5.43 & 5.55 ppm, respectively) of its C_{18} epimer **7.8**. Again, assignment of the relative

stereochemistries were based on literature precedent.[5] Fortunately, these diastereomers are chromatographically separable. Conversion of both epoxides to the selenides, followed by TAS-F deprotection yielded the penultimate intermediates. Finally, we were grateful to find that tandem selenide oxidation / elimination using our bis-TMS peroxide conditions yielded the natural product amphidinolide B_1 (**4.13**) and its $C_{8,9}$ epoxide diastereomer **7.27.** The synthesized material **4.13** matched with the spectra data reported by Kobayashi and co-workers for amphidinolide B_1 (Figure 7.3).[17]



Scheme 7.6. Synthesis of Amphidinolide B_1 and its $C_{8,9}$ Epoxide Isomer

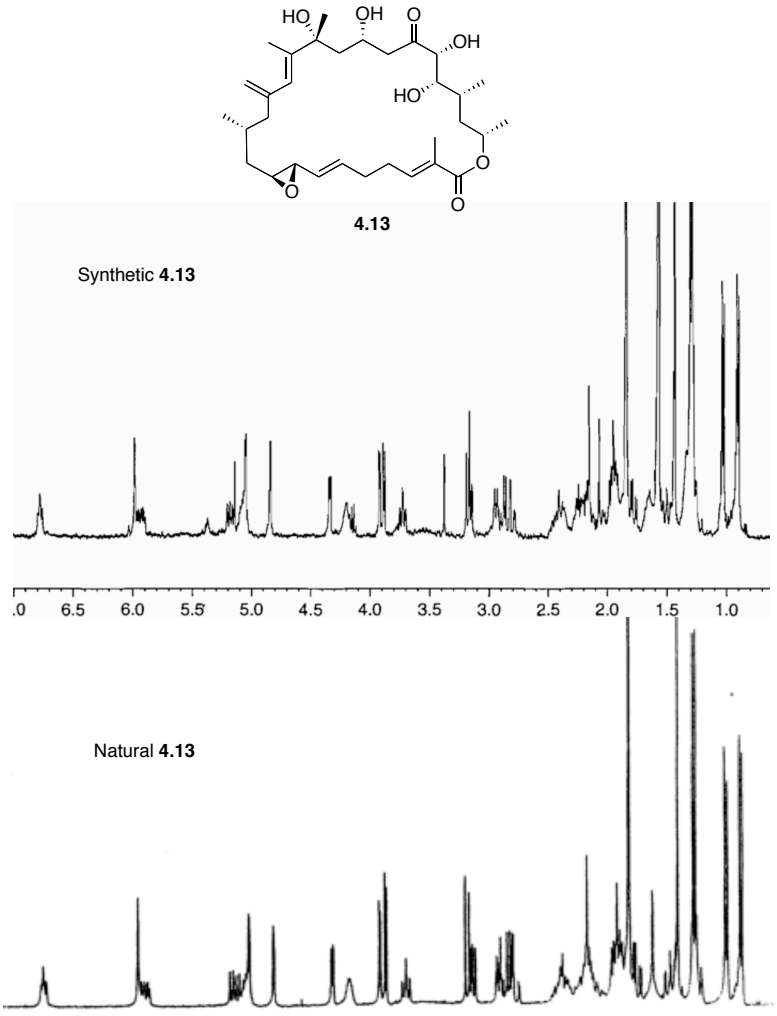


Figure 7.3. Comparsion of the ^{1}H NMR Data For the Synthetic and Natural Amphidinolide B_1 (**4.13**)

7.8 Conclusion

In summary, we have successfully cyclized the 26-membered macrocycle via an intramolecular Horner-Wadsworth−Emmons olefination and removed the TES protecting groups on the selenide moiety with TAS-F. We also developed the

mild conditions for the oxidation and elimination of selenide using TMSOOTMS. The total syntheses of amphodinolide B_1 and the proposed structure of amphidinolide B_2 were finally accomplished with a longest linear sequence of 29 steps. The originally proposed structure of amphidinolide B_2 was found to be incorrect based on our careful analysis of the structural data.

7.9 References

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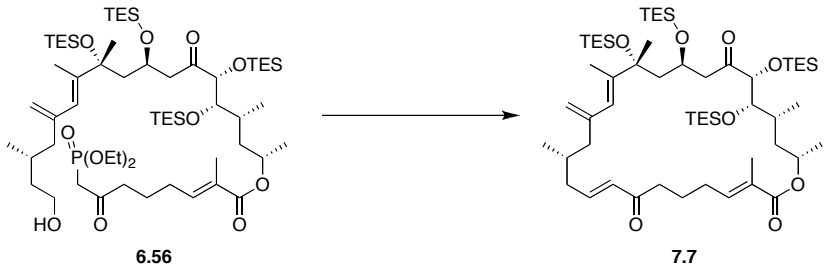
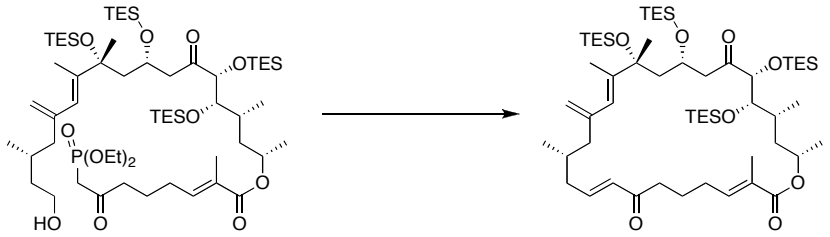
7.10 Experimental



Macrocycle 7.7: To a stirred solution of alcohol **6.56** (170 mg, 0.144 mmol) in CH_2Cl_2 (4 mL) at rt was added TPAP (61 mg, 0.173 mmol). After 0.5 h, the reaction mixture was diluted with CH_2Cl_2 (3 mL) / CH_3CN (7 mL) and Hunig's base (297 mg, 0.4 mL, 2.29 mmol) was added, followed by the addition of LiCl (20 mg, 0.476 mmol). After 24 h, the reaction mixture was purified directly by chromatography over silica gel, eluting with 5% EtOAc / Hexanes, to give macrocycle **7.7** (75 mg, 0.073 mmol, 51% over 2 steps) as a colorless oil: $[\alpha]_D^{23}$ = -10.0 (*c* 0.62, $CHCl_3$); IR (neat) 2955, 2913, 2876, 1708, 1674, 1457, 1417, 1375, 1240, 1124, 1072, 1008, 742 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.88 (dt, *J* = 16.2, 7.4 Hz, 1H), 6.72 (t, *J* = 8.0 Hz, 1H), 6.10 (d, *J* = 16.0 Hz, 1H), 5.82 (s, 1H), 5.08-4.99 (m, 1H), 5.02 (s, 1H), 4.87 (s, 1H), 4.30-4.22 (m, 1H), 4.01 (d, *J* = 6.4 Hz, 1H), 3.58 (dd, *J* = 6.4, 2.7 Hz, 1H), 2.86 (dd, *J* = 17.4, 8.6 Hz, 1H), 2.77 (dd, *J* = 15.4, 6.0 Hz, 1H), 2.62-2.54 (m, 2H), 2.36-2.19 (m, 4H), 2.14 (dd, *J* = 17.4, 8.6

Hz, 1H), 2.05-1.76 (m, 7H), 1.80 (s, 3H), 1.79 (s, 3H), 1.70-1.60 (m, 1H), 1.57-1.51 (m, 1H), 1.41 (s, 3H), 1.25 (d, J = 6.2 Hz, 3H), 1.05-0.93 (m, 36H), 0.84 (d, J = 6.6 Hz, 3H), 0.76 (d, J = 6.6 Hz, 3H), 0.73-0.58 (m, 24H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.1. 201.0, 167.6, 147.3, 147.1, 144.0, 142.8, 140.8, 132.4, 129.3, 124.7, 115.1, 80.6, 77.4 (2C), 68.5, 65.1, 50.6, 49.0, 46.1, 41.7, 40.2, 37.2, 31.3, 30.8, 27.8, 27.4, 23.1, 21.0, 19.7, 15.3, 12.8, 12.5, 7.3, 7.1, 7.0, 6.9, 5.3, 5.2, 4.9; HRMS (ES^+) calcd. for $C_{56}H_{106}O_8Si_4Na$ (M+Na) 1041.6863, found 1041.6824.



Macrocycle 7.6: To a stirred solution of alcohol **6.55** (125 mg, 0.106 mmol) in CH_2Cl_2 (4 mL) at rt was added TPAP (45 mg, 0.127 mmol). After 0.5 h, the reaction mixture was diluted with THF (6.5 mL) / H_2O (16 μL) and $Ba(OH)_2•8H_2O$ (3 x 74 mg, 0.636 mmol) was added in 3 portions every 30 min. After another 2 h, the reaction mixture was purified directly by chromatography over silica gel, eluting with 5% EtOAc / Hexanes, to give macrocycle **7.6** (54 mg,

0.053 mmol, 50% over 2 steps) as colorless crystals: $[\alpha]_D^{23}$ = -27.0 (*c* 0.40, $CHCl_3$); IR (neat) 2955, 2925, 2876, 1727, 1708, 1675, 1458, 1417, 1260, 1127, 1064, 1009, 741 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.15-7.03 (m, 1H), 6.73 (t, *J* = 6.9 Hz, 1H), 6.19 (d, *J* = 16.3 Hz, 1H), 5.78 (s, 1H), 5.00 (s, 1H), 5.05-4.97 (m, 1H), 4.82 (s, 1H), 4.18-4.09 (m, 1H), 4.11 (d, *J* = 5.1 Hz, 1H), 3.62-3.58 (m, 1H), 3.00-2.93 (m, 2H), 2.85-2.70 (m, 1H), 2.62-2.50 (m, 1H), 2.37-2.21 (m, 3H), 2.15-2.00 (m, 2H), 1.91-1.63 (m, 7H), 1.80 (s, 6H), 1.45-1.35 (m, 2H), 1.41 (s, 3H), 1.25 (d, *J* = 6.1 Hz, 3H), 1.08-0.83 (m, 39H), 0.75-0.47 (m, 27H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.2, 201.0, 167.6, 147.2, 144.7, 141.8, 140.6, 132.4, 129.2, 125.8, 115.4, 80.5, 79.6, 77.9, 68.3, 64.9, 49.7, 48.6, 46.7, 43.2, 41.1, 37.5, 31.0, 29.2, 28.9, 27.8, 22.6, 21.0, 18.8, 15.6, 13.3, 12.5, 7.3, 7.1, 7.0, 5.2, 4.8; HRMS (ES^+) calcd. for $C_{56}H_{106}O_8Si_4Na$ (M+Na) 1041.6863, found 1041.6812.

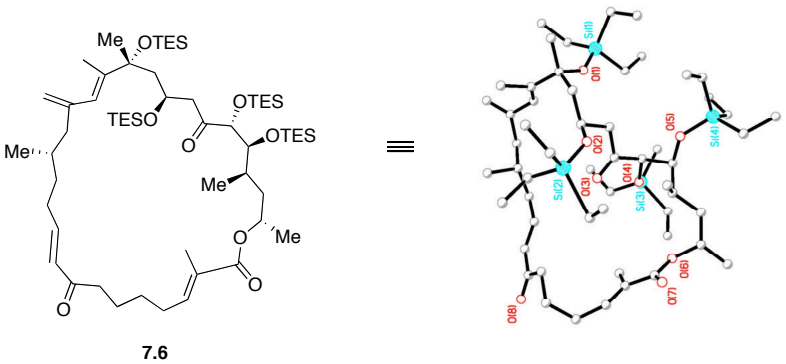
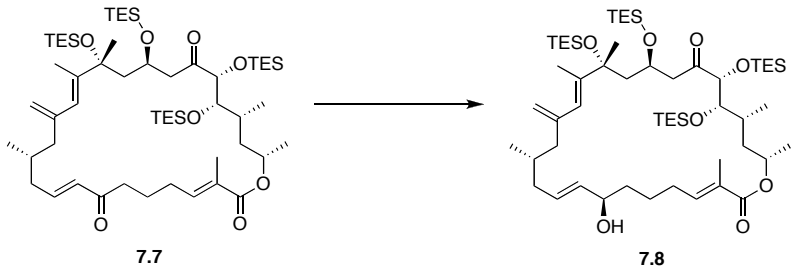
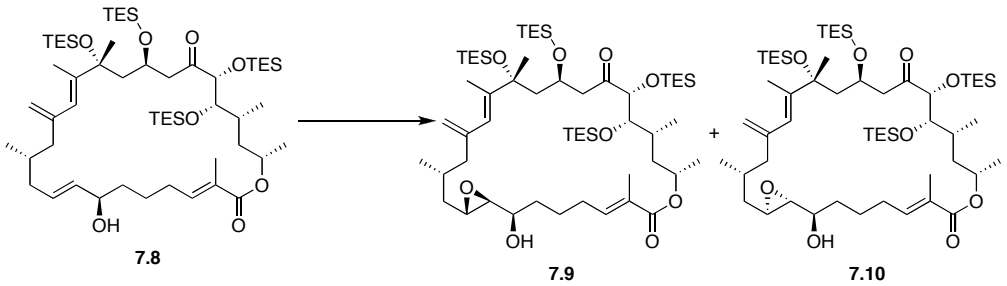


Figure 1. ORTEP Representation of macrocycle **7.6**



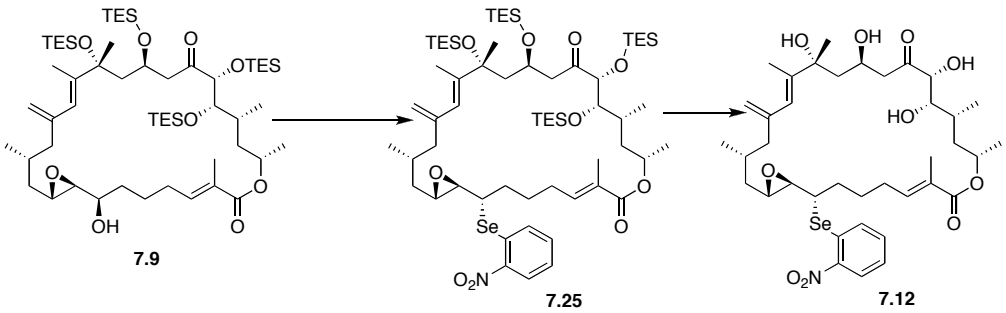
Allylic alcohol 7.8: To a stirred solution of macrocycle **7.7** (107 mg, 0.105 mmol) in CH_2Cl_2 (5.4 mL) at -20ºC was sequentially added (*S*)-CBS (0.42 mL, 0.42 mmol, 1 M in PhMe) and BH_3•DMS (0.84 mL, 0.84 mmol, 1 M in THF). After 45 min, the reaction was quenched with MeOH (0.3 mL), diluted with aq. $NaHCO_3$ (5 mL) and extracted with Et_2O (3 x 8 mL). The dried extract ($MgSO_4$) was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 3-6% EtOAc / Hexanes, to give allylic alcohol **7.8** (72 mg, 0.0704 mmol, 67%) as a colorless oil: $[\alpha]_D^{23}$ = -16.3 (*c* 0.30, $CHCl_3$); IR (neat) 3431, 2954, 2913, 2876, 1708, 1674, 1458, 1414, 1376, 1241, 1128, 1073, 1009, 742 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.80 (t, *J* = 8.0 Hz, 1H), 5.89 (s, 1H), 5.63-5.52 (m, 1H), 5.45 (dd, *J* = 15.4, 7.5 Hz, 1H), 5.10-5.00 (m, 1H), 4.98 (s, 1H), 4.82 (s, 1H), 4.32-4.20 (m, 1H), 4.19-4.09 (m, 1H), 4.04 (d, *J* = 6.2 Hz, 1H), 3.57 (dd, *J* = 6.2, 2.5 Hz, 1H), 2.87 (dd, *J* = 17.0, 9.0 Hz, 1H), 2.49 (d, *J* = 16.8 Hz, 1H), 2.28-2.20 (m, 2H), 2.13-1.98 (m, 3H), 1.90-1.61 (m, 9H), 1.86 (s, 3H), 1.75 (s, 3H), 1.55-1.46 (m, 2H), 1.39 (s, 3H), 1.26 (d, *J* = 6.0 Hz, 3H), 1.06-0.94 (m, 36H), 0.82 (d, *J* = 6.4 Hz, 3H), 0.73-0.60 (m, 27H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.5,

167.8, 144.6, 142.0, 141.3, 134.6, 130.8, 128.2, 125.4, 114.4, 80.6, 78.0, 72.9, 68.4, 65.2, 50.3, 49.2, 45.4, 41.8, 39.7, 36.8, 31.3, 30.4, 28.8, 28.2, 24.0, 20.9, 19.6, 15.4, 12.5, 12.4, 7.3, 7.1, 7.0, 5.3, 5.2, 4.9; HRMS (ES^+) calcd. for $C_{56}H_{108}O_8Si_4Na$ (M+Na) 1043.7019, found 1043.7052



Epoxide 7.9 & 7.10: To a stirred solution of allylic alcohol **7.8** (70 mg, 0.0685 mmol) in CH_2Cl_2 (6 mL) at -20ºC was sequentially added 4Å MS (50 mg), TBHP (37 μL, 0.206 mmol, 5.5 M in decane) and Ti(O-*i*Pr)$_4$ (23.3 mg, 24 μL, 0.082 mmol). After 5 h, the reaction was quenched with aq. $NaHCO_3$ (3 mL) and extracted with Et_2O (3 x 7 mL). The dried extract ($MgSO_4$) was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 6-10% EtOAc / Hexanes, to give epoxide **7.9** (35 mg, 0.0342 mmol, 50%) and epoxide **7.10** (17 mg, 0.0166 mmol, 24%) as colorless oils. **7.9**: $[\alpha]_D^{23}$ = -29.0 (*c* 0.42, $CHCl_3$); IR (neat) 3431, 2954, 2923, 2876, 1708, 1647, 1458, 1414, 1377, 1242, 1128, 1073, 1009, 742 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.78 (t, *J* = 8.0 Hz, 1H), 5.88 (s, 1H), 5.05-4.98 (m, 1H), 5.01 (s, 1H), 4.86 (s, 1H), 4.30-4.20 (m, 1H), 4.05 (d, *J* = 6.1 Hz, 1H), 3.59 (dd, *J* = 6.1, 2.0 Hz, 1H), 3.52-3.43 (m, 1H), 3.22-3.15 (m, 1H),

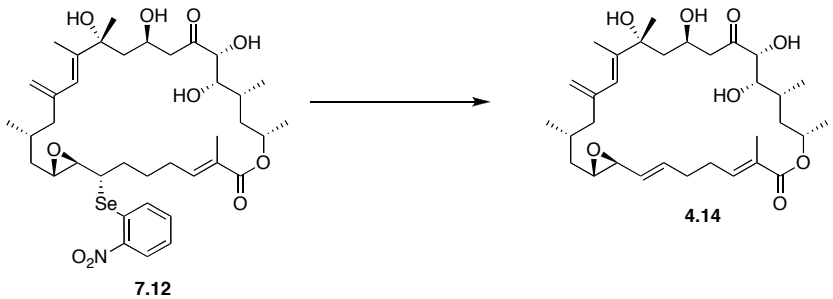
2.91 (dd, *J* =16.3, 9.1 Hz, 1H), 2.70 (dd, *J* =6.0, 2.0 Hz, 1H), 2.44-2.25 (m, 3H), 2.18 (dd, *J* =13.0, 5.6 Hz, 1H), 2.10-1.63 (m, 12H), 1.87 (s, 3H), 1.78 (s, 3H), 1.41 (s, 3H), 1.26 (d, *J* = 6.0 Hz, 3H), 1.15-1.09 (m, 1H), 1.07-0.89 (m, 36H), 0.80 (d, *J* = 6.4 Hz, 3H), 0.76-0.59 (m, 27H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.4, 167.7, 144.0, 142.1, 141.4, 128.6, 125.0, 114.9, 80.8, 78.2, 77.5, 71.8, 68.3, 65.6, 62.8, 56.4, 50.6, 49.1, 46.6, 42.1, 38.9, 33.1, 30.1, 29.4, 28.8, 28.3, 23.7, 21.0, 19.8, 15.5, 12.5, 12.4, 7.3, 7.1, 7.0, 5.3, 5.2, 5.0; HRMS (ES^+) calcd. for $C_{56}H_{108}O_9Si_4Na$ (M+Na) 1059.6968, found 1059.7009. **7.10**: $[\alpha]_D$ = -26.2 (*c* 0.60, $CHCl_3$); IR (neat) 3482, 2954, 2923, 2876, 1708, 1458, 1414, 1377, 1240, 1128, 1008, 742 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.79 (t, *J* = 7.7 Hz, 1H), 5.87 (s, 1H), 5.05-4.98 (m, 1H), 4.99 (s, 1H), 4.84 (s, 1H), 4.30-4.20 (m, 1H), 4.09 (d, *J* = 5.9 Hz, 1H), 3.75-3.69 (m, 1H), 3.57 (dd, *J* = 5.6, 3.2 Hz, 1H), 2.91-2.78 (m, 3H), 2.68-2.60 (m, 2H), 2.38-2.20 (m, 3H), 2.07 (dd, *J* =12.9, 6.2 Hz, 1H), 1.93-1.62 (m, 10H), 1.85 (s, 3H), 1.76 (s, 3H), 1.50-1.44 (m, 2H), 1.40 (s, 3H), 1.25 (d, *J* = 6.0 Hz, 3H), 1.05-0.93 (m, 39H), 0.74-0.59 (m, 27H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.6, 167.8, 144.1, 142.5, 141.5, 128.4, 124.9, 114.9, 81.0, 78.2, 77.4, 69.0, 68.4, 65.5, 60.7, 54.9, 50.3, 49.2, 46.3, 41.7, 38.4, 33.3, 30.7, 30.3, 29.0, 27.9, 23.7, 21.0, 20.0, 15.3, 13.2, 12.4, 7.3, 7.1, 7.0, 6.9, 5.3, 5.2, 4.9; HRMS (ES^+) calcd. for $C_{56}H_{108}O_9Si_4Na$ (M+Na) 1059.6968, found 1059.7009.



Selenide 7.25: To a stirred solution of epoxide **7.9** (42 mg, 0.0405 mmol) in THF (2 mL) at rt was sequentially added *o*-$NO_2C_6H_4SeCN$ (184 mg, 0.809 mmol) and PBu_3 (164 mg, 202 μL, 0.809 mmol). After 5 h, the reaction mixture was concentrated *in vacuo* purified by chromatography over silica gel, eluting with Hexanes then with 4% EtOAc / Hexanes, to give crude selenide **7.25** (30 mg) as yellow oils which was used directly in next step without further purification.

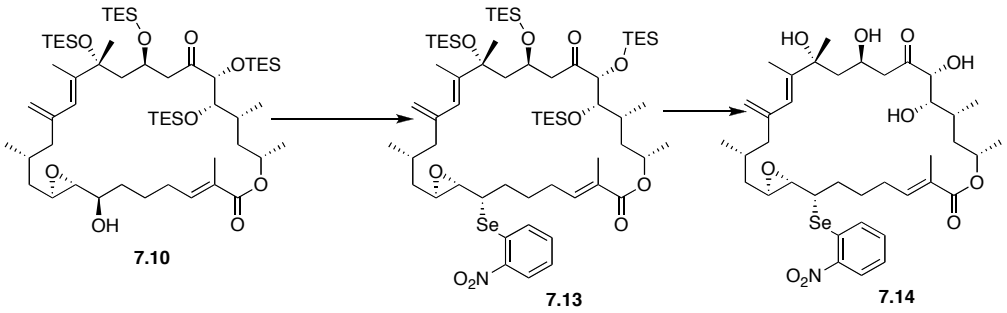
Polyol 7.12: To a stirred solution of selenide **7.25** (30 mg) in THF /DMF / H_2O (10:1:0.02, 1.8 mL / 180 μL / 3.6 μL) at 0ºC was added TAS-F (33.7 mg, 0.123 mmol). The reaction mixture was then warmed up to rt. After 2 h, the reaction mixture was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 10-65% EtOAc / Hexanes, to give polyol **7.12** (15 mg, 0.0196 mmol, 48% over 2 steps) as a yellow solid: $[\alpha]_D^{23}$ = -20.1 (*c* 0.12, $CHCl_3$); IR (neat) 3447, 2925, 2854, 1701, 1520, 1456, 1334, 1273, 759, 732 cm^{-1}; ^1H

NMR (400 MHz, $CDCl_3$) δ 8.28 (d, *J* = 8.3 Hz, 1H), 7.66 (d, *J* = 7.8 Hz, 1H), 7.56 (t, *J* = 8.1 Hz, 1H), 7.38 (t, *J* = 8.1 Hz, 1H), 6.81 (t, *J* = 6.4 Hz, 1H), 6.05 (s, 1H), 5.10-5.00 (m, 1H), 5.02 (s, 1H), 4.80 (s, 1H), 4.38 (d, *J* = 3.6 Hz, 1H), 4.18 (s, 1H), 4.17-4.11 (m, 1H), 4.07 (t, *J* = 9.6 Hz, 1H), 3.58 (t, *J* = 8.6 Hz, 1H), 3.18-3.10 (m, 1H), 2.97 (d, *J* = 8.1 Hz, 1H), 2.79 (dd, *J* = 12.8, 10.1 Hz, 1H), 2.37-2.28 (m, 1H), 2.40-2.30 (m, 1H), 2.22-2.04 (m, 3H), 1.94-1.76 (m, 7H), 1.83 (s, 3H), 1.79 (s, 3H), 1.72-1.62 (m, 3H), 1.38 (s, 3H), 1.31 (d, *J* = 6.1 Hz, 3H), 1.25-1.19 (m, 2H), 1.07 (d, *J* = 6.4 Hz, 3H), 0.83 (d, *J* = 6.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 211.1, 167.6, 149.6, 144.4, 141.0 (2C), 133.1, 132.5, 128.9, 128.3, 127.0, 126.0, 125.1, 115.0, 78.3, 77.5, 75.3, 68.7, 68.3, 62.3, 59.3, 46.7, 45.7, 45.5, 43.8, 40.4, 40.0, 32.8, 31.6, 29.1, 29.0, 28.1, 26.1, 21.2, 17.7, 16.2, 15.3, 12.5; HRMS (ES^+) calcd. for $C_{38}H_{55}NO_{10}NaSe$ (M+Na) 788.2889, found 788.2859.



Proposed structure of Amphidinolide B_2 (4.14): To a stirred solution of selenide **7.12** (6.0 mg, 0.00784 mmol) in CH_2Cl_2 (1.2 mL) at rt was sequentially

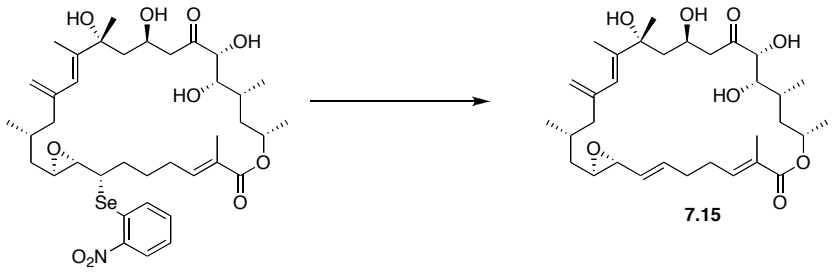
added $NaHCO_3$ (60 mg, 0.714 mmol) and TMSOOTMS (41.7 mg, 50 μL, 0.233 mmol). After 1.5 h, the yellow color vanished and the reaction mixture was purified by preparative TLC, eluting with 60% EtOAc / Hexanes, to give allylic epoxide **4.14** (3.0 mg, 0.00533 mmol, 68%): $[\alpha]_D^{23}$ = -52.3 (*c* 0.21, $CHCl_3$); IR (neat) 3446, 2923, 2853, 1701, 1457, 1273, 1120 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.74 (t, *J* = 6.4 Hz, 1H), 6.06 (s, 1H), 5.92 (ddd, *J* = 15.0, 8.9, 4.4 Hz, 1H), 5.20 (dd, *J* = 15.5, 8.8 Hz, 1H), 5.11-5.07 (m, 1H), 5.07 (s, 1H), 4.86 (s, 1H), 4.28 (d, *J* =5.4, 1H), 4.14 (s, OH), 4.14-4.09 (m, 1H), 3.73 (d, *J* = 5.6 Hz, OH), 3.69 (t, *J* = 9.5 Hz, 1H), 3.50 (d, *J* = 6.8 Hz, 1H), 3.23 (dd, *J* = 8.7, 2.2 Hz, 1H), 3.08-3.03 (m, 2H), 2.95 (d, *J* = 9.2 Hz, OH), 2.53-2.45 (m, 1H), 2.45-2.36 (m, 1H), 2.28 (dd, *J* = 13.2, 1.8 Hz, 1H), 2.17-2.12 (m, 3H), 1.97-1.93 (m, 4H), 1.85 (s, 3H), 1.82-1.79 (m, 1H), 1.80 (s, 3H), 1.78-1.75 (m, 1H), 1.64-1.60 (m, 1H), 1.34 (s, 3H), 1.31 (d, *J* = 6.1 Hz, 3H), 1.17-1.12 (m, 1H), 1.03 (d, *J* = 6.7 Hz, 3H), 0.98 (d, *J* = 5.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 212.53, 167.68, 144.65, 141.59, 139.52, 136.29, 128.41, 128.34, 124.88, 114.59, 78.14, 75.58, 69.28, 68.23, 61.45, 59.5, 47.14, 46.41, 44.14, 39.98, 39.36, 33.25, 31.04, 29.32, 28.27, 26.69, 21.19, 17.52, 15.91, 15.17, 12.60; HRMS (ES^+) calcd. for $C_{32}H_{50}O_8Na$ (M+Na) 585.3403, found 585.3390.



Selenide 7.13: To a stirred solution of epoxide **7.10** (12 mg, 0.0116 mmol) in THF (0.7 mL) at rt was sequentially added *o*-$NO_2C_6H_4SeCN$ (53 mg, 0.232 mmol) and PBu_3 (47 mg, 58 μL, 0.232 mmol). After 0.5 h, the reaction mixture was concentrated *in vacuo* purified by chromatography over silica gel, eluting with Hexanes then with 4% EtOAc / Hexanes, to give crude selenide **7.13** (10.6 mg) as a yellow oil which was used directly in next step without further purification.

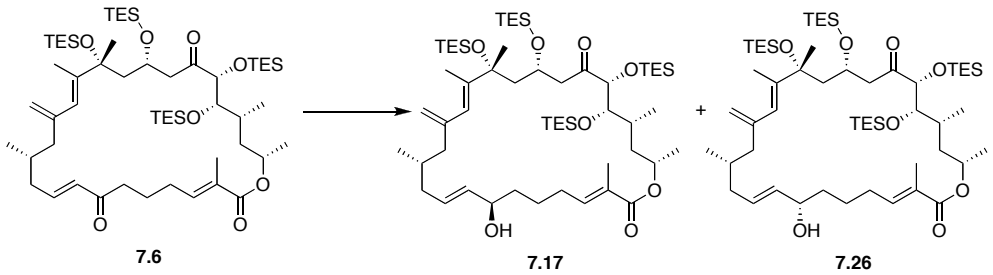
Polyol 7.14: To a stirred solution of selenide **7.13** (10.6 mg) in THF / DMF / H_2O (10:1:0.02, 1.0 mL / 100 μL / 2.0 μL) at 0ºC was added TAS-F (12 mg, 0.0434 mmol). The reaction mixture was then warmed up to rt. After 2 h, the reaction mixture was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 10-65% EtOAc / Hexanes, to give polyol **7.14** (6.2 mg, 0.00811 mmol, 70% over 2 steps) as a yellow oil: $[\alpha]_D$ = -47.0 (*c* 0.30, $CHCl_3$); IR (neat) 3446, 2925, 2854, 1701, 1515, 1456, 1332, 1271, 757, 731 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, *J* = 8.1 Hz, 1H), 7.70 (d, *J* = 8.0 Hz, 1H), 7.55 (t, *J* = 7.4 Hz, 1H), 7.42 (t, *J* = 7.8 Hz, 1H), 6.85 (t, *J* = 6.3 Hz, 1H), 6.02 (s, 1H),

5.11-5.05 (m, 1H), 5.04 (s, 1H), 4.81 (s, 1H), 4.38 (d, *J* = 3.6 Hz, 1H), 4.32-4.25 (m, 1H), 4.17-4.12 (m, 1H), 3.89 (d, *J* = 4.6 Hz, 1H), 3.72-3.65 (m, 1H), 3.62-3.55 (m, 1H), 3.10-3.05 (m, 2H), 2.84 (dd, *J* = 14.8, 9.2 Hz, 1H), 2.52 (dd, *J* = 14.8, 2.5 Hz, 1H), 2.38 (d, *J* = 9.5 Hz, 1H), 2.40-2.20 (m, 3h), 1.97-1.74 (m, 8H), 1.83 (s, 3H), 1.76 (s, 3H), 1.70-1.60 (m, 3H), 1.36 (s, 3H), 1.33 (d, *J* = 6.1 Hz, 3H), 1.06 (d, *J* = 6.7 Hz, 3H), 0.87 (d, *J* = 6.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 212.0, 167.7, 147.7, 144.6, 141.3, 140.9, 133.7, 132.3, 130.1, 128.6, 126.5, 126.1, 125.6, 115.1, 78.0, 77.0, 75.5, 69.1, 67.7, 60.6, 58.4, 45.7, 45.6, 43.7, 43.1, 40.4, 39.2, 33.8, 30.3, 29.5, 28.9, 28.0, 27.0, 21.2, 19.7, 16.3, 15.2, 12.5; HRMS (ES^+) calcd. for $C_{38}H_{55}NO_{10}NaSe$(M+Na) 788.2889, found 788.2897.



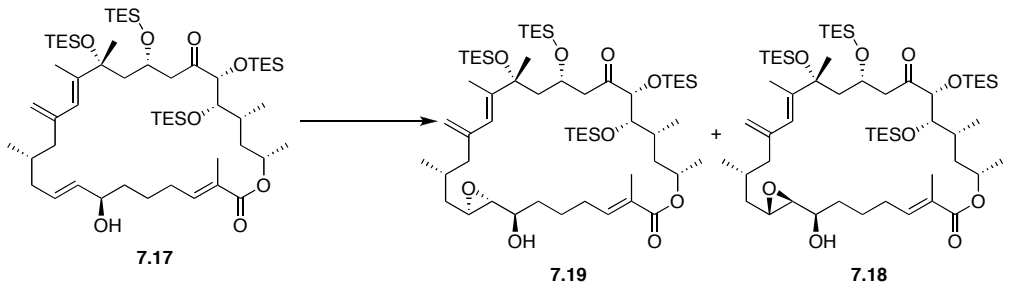
Allylic epoxide 7.15: To a stirred solution of selenide **7.14** (2.5 mg, 0.00327 mmol) in CH_2Cl_2 (0.5 mL) at rt was sequentially added $NaHCO_3$ (20 mg, 0.238 mmol) and TMSO-OTMS (19.1 mg, 23 μL, 0.107 mmol). After 1.5 h, the yellow color vanished and the reaction mixture was purified by preparative TLC,

eluting with 60% EtOAc / Hexanes, to give allylic epoxide **7.15** (1.2 mg, 0.00213 mmol, 65%): $[\alpha]_D$ = -27.5 (*c* 0.12, $CHCl_3$); IR (neat) 3443, 2924, 2852, 1703, 1457, 1379, 1272, 1118 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.71-6.63 (m, 1H), 6.08 (s, 1H), 5.88-5.78 (m, 1H), 5.26 (dd, *J* = 15.1, 8.4 Hz, 1H), 5.12-5.05 (m, 1H), 5.05 (s, 1H), 4.84 (s, 1H), 4.29 (dd, *J* =5.7, 1.5 Hz, 1H), 4.30-4.20 (m, 1H), 3.71 (t, *J* = 7.9 Hz, 1H), 3.66 (d, *J* = 5.7 Hz, 1H), 3.19 (d, *J* = 9.6 Hz, 1H), 3.12 (dd, *J* = 8.6, 2.2 Hz, 1H), 3.01-2.87 (m, 2H), 2.46 (dd, *J* = 14.4, 2.1 Hz, 1H), 2.36-2.20 (m, 5H), 2.00-1.74 (m, 6H), 1.83 (s, 3H), 1.77 (s, 3H), 1.60-1.55 (m, 1H), 1.35 (s, 3H), 1.33-1.28 (m, 1H), 1.30 (d, *J* = 6.1 Hz, 3H), 1.18-1.11 (m, 1H), 1.03 (d, *J* = 6.6 Hz, 3H), 0.88 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 212.90, 167.45, 144.94, 141.56, 140.29, 136.40, 128.71, 128.60, 125.65, 114.95, 78.20, 76.56, 75.86, 68.49, 68.18, 60.18, 60.01, 45.84, 45.13, 43.77, 39.43, 39.29, 33.62, 30.96, 30.26, 28.54, 27.02, 21.22, 20.02, 15.82, 15.22, 12.74; HRMS (ES^+) calcd. for $C_{32}H_{50}O_8Na$ (M+Na) 585.3403, found 585.3394.



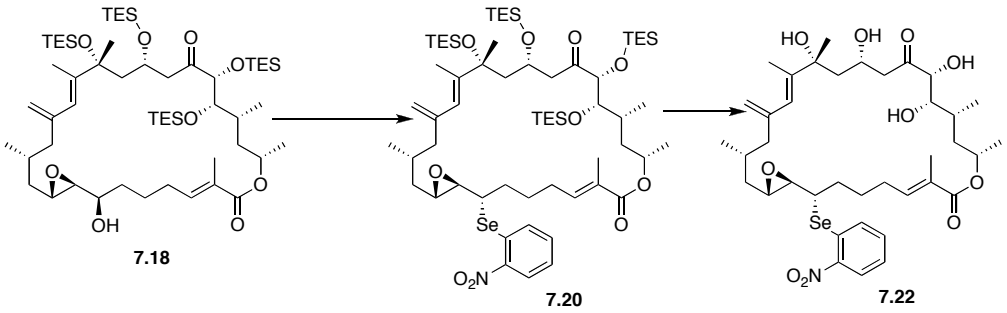
Allylic alcohol 7.17: To a stirred solution of macrocycle **7.6** (50 mg, 0.049 mmol) in CH_2Cl_2 (2.3 mL) at -30ºC was sequentially added (*S*)-CBS (0.196 mL, 0.196 mmol, 1 M in PhMe) and BH_3•DMS (0.3934 mL, 0.393 mmol, 1 M in THF). After 45 min, the reaction was quenched with MeOH (0.3 mL), diluted with aq. $NaHCO_3$ (3 mL) and extracted with Et_2O (4 x 6 mL). The dried extract ($MgSO_4$) was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 3-6% EtOAc / Hexanes, to give allylic alcohol **7.17** (29 mg, 0.028 mmol, 58%) and **7.26** (8 mg, 0.0078 mmol, 16%) as colorless oils. **7.17**: $[\alpha]_D^{23}$ = -23.6 (*c* 0.25, $CHCl_3$); IR (neat) 3503, 2954, 2911, 2876, 1707, 1458, 1376, 1240, 1128, 1007, 742 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.81 (t, *J* = 6.9 Hz, 1H), 5.76 (s, 1H), 5.70-5.62 (m, 1H), 5.53 (dd, *J* = 13.2, 6.3 Hz, 1H), 5.00-4.95 (m, 1H), 4.98 (s, 1H), 4.84 (s, 1H), 4.15-4.04 (m, 3H), 3.58 (dd, *J* = 5.7, 2.4 Hz, 1H), 2.93 (dd, *J* = 18.4, 6.2 Hz, 1H), 2.78 (dd, *J* = 18.4, 6.0 Hz, 1H), 2.28-2.22 (m, 2H), 2.18-2.10 (m, 2H), 2.08-1.99 (m, 1H), 1.89-1.57 (m, 9H), 1.84 (s, 3H), 1.81 (s, 3H), 1.48-1.40 (m, 2H), 1.45 (s, 3H), 1.26 (d, *J* = 6.1 Hz, 3H), 1.07-0.91 (m, 36H), 0.88 (d, *J* = 6.6 Hz, 3H), 0.74-0.53 (m, 27H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.8, 167.8, 145.5,

142.5 (2C), 134.9, 129.7, 127.9, 125.7, 114.9, 80.6, 79.2, 77.9, 71.9, 68.2, 65.3, 49.6, 49.2, 45.6, 42.2, 39.4, 37.0, 31.8, 29.8, 29.0, 28.1, 23.6, 21.0, 19.9, 14.7, 12.7, 12.4, 7.2, 7.1, 7.0, 6.9, 6.8, 5.3, 5.2, 4.7; HRMS (ES^+) calcd. for $C_{56}H_{108}O_8Si_4Na$ (M+Na) 1043.7019, found 1043.7072. **7.26**: $[\alpha]_D$ = -29.1 (*c* 0.80, $CHCl_3$); IR (neat) 3481, 2954, 2876, 1707, 1458, 1241, 1130, 1008, 742 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.74 (t, *J* = 7.4 Hz, 1H), 5.77 (s, 1H), 5.75-5.70 (m, 1H), 5.55 (dd, *J* = 15.5, 7.0 Hz, 1H), 5.00-4.96 (m, 1H), 4.99 (s, 1H), 4.83 (s, 1H), 4.22-4.15 (m, 1H), 4.11-4.06 (m, 1H), 4.07 (d, *J* = 5.8 Hz, 1H), 3.57 (dd, *J* = 5.6, 2.3 Hz, 1H), 2.96 (dd, *J* = 18.4, 7.4 Hz, 1H), 2.78 (dd, *J* = 18.3, 4.2 Hz, 1H), 2.23-2.08 (m, 4H), 1.95-1.52 (m, 11H), 1.834 (s, 3H), 1.80 (s, 3H), 1.48-1.40 (m, 1H), 1.43 (s, 3H), 1.25 (d, *J* = 6.1 Hz, 3H), 1.06-0.87 (m, 39H), 0.73-0.55 (m, 27H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.4, 167.9, 145.3, 142.2, 141.7, 134.2, 130.9, 128.3, 125.9, 114.9, 80.9, 79.0, 77.7, 73.2, 68.4, 65.1, 49.2, 48.8, 45.5, 42.1, 39.8, 36.8, 31.7, 30.1, 28.5, 28.3, 24.5, 21.0, 19.4, 15.0, 13.1, 12.4, 7.3, 7.1, 7.0, 6.9, 6.8, 5.2, 5.1, 4.8; HRMS (ES^+) calcd. for $C_{56}H_{108}O_8Si_4Na$ (M+Na) 1043.7019, found 1043.6984.



Epoxide 7.18 & 7.19: To a stirred solution of allylic alcohol **7.17** (29 mg, 0.0284 mmol) in CH_2Cl_2 (2.2 mL) at -40ºC was sequentially added 4Å MS (20 mg), TBHP (15.5 µL, 0.0852 mmol, 5.5 M in decane) and Ti(O-*i*Pr)$_4$ (16.1 mg, 16.6 µL, 0.0567 mmol). After 5 h, the reaction was quenched with aq. $NaHCO_3$ (3 mL) and extracted with Et_2O (4 x 4 mL). The dried extract ($MgSO_4$) was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 6-10% EtOAc / Hexanes, to give epoxide **7.19** (13.6 mg, 0.0131 mmol, 46%) and epoxide **7.18** (9.1 mg, 0.00867 mmol, 31%) as colorless oils. **7.19**: $[\alpha]_D^{23}$ = -32.3 (*c* 0.73, $CHCl_3$); IR (neat) 3482, 2954, 2911, 2876, 1706, 1458, 1380, 1239, 1131, 1073, 1009, 742 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.83 (t, *J* = 7.0 Hz, 1H), 5.76 (s, 1H), 5.00-4.92 (m, 1H),4.98 (s, 1H), 4.83 (s, 1H), 4.20-4.10 (m, 1H), 4.10(d, *J* = 5.5 Hz, 1H), 3.58 (dd, *J* = 5.4, 1.7 Hz, 1H), 3.60-3.50 (m, 1H), 3.12-3.05 (m, 1H), 2.98-2.92 (m, 2H), 2.90-2.82 (m, 1H), 2.77 (dd, *J* = 5.0, 2.0 Hz, 1H), 2.40-2.30 (m, 2H), 2.17 (dd, *J* = 12.7, 4.3 Hz, 1H), 2.12-2.00 (m, 1H), 1.91-1.61 (m, 8H), 1.82 (s, 3H), 1.79 (s, 3H), 1.50-1.40 (m, 3H), 1.42 (s, 3H), 1.30-1.20 (m, 1H), 1.26 (d, *J* = 6.0 Hz, 3H), 1.08-0.87 (m, 39H), 0.75-0.50 (m, 27H); ^{13}C NMR

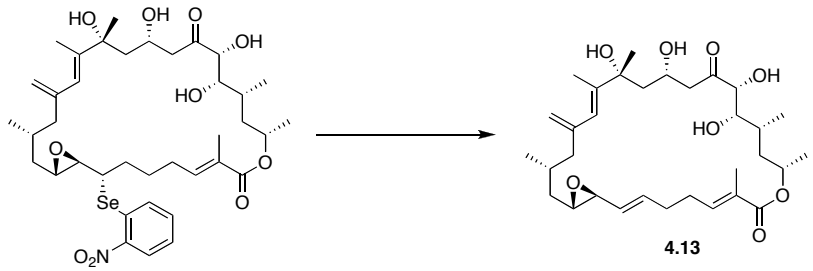
(75 MHz, $CDCl_3$) δ 208.1, 167.8, 144.7, 141.8, 141.7, 128.2, 125.9, 115.0, 80.5, 79.4, 77.9, 70.4, 68.2, 65.1, 60.8, 55.8, 49.8, 48.9, 45.9, 42.9, 39.3, 33.6, 30.2, 29.2, 28.6, 28.5 24.0, 21.1, 19.5, 15.1, 12.9, 12.4, 7.3, 7.1, 6.9, 5.2, 4.7; HRMS (ES^+) calcd. for $C_{56}H_{108}O_9Si_4Na$ (M+Na) 1059.6968, found 1059.7001. **7.18**: $[\alpha]_D^{23}$ = -25.7 (*c* 0.42, $CHCl_3$); IR (neat) 3482, 2954, 2876, 1708, 1458, 1378, 1240, 1130, 1008, 742 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.76 (t, *J* = 6.1 Hz, 1H), 5.83 (s, 1H), 5.05-4.90 (m, 1H), 5.01 (s, 1H), 4.86 (s, 1H), 4.15-4.10 (m, 1H), 4.08 (d, *J* = 5.8 Hz, 1H), 3.58 (dd, *J* = 5.5, 2.6 Hz, 1H), 3.59-3.49 (m, 1H), 3.11-3.03 (m, 1H), 2.95-2.91 (m, 2H), 2.77 (dd, *J* = 5.5, 2.0 Hz, 1H), 2.35-2.20 (m, 3H), 2.02-1.59 (m, 10H), 1.83 (s, 3H), 1.81 (s, 3H), 1.44 (s, 3H), 1.50-1.40 (m, 3H), 1.25 (d, *J* = 6.0 Hz, 3H), 1.06-0.89 (m, 39H), 0.74-0.52 (m, 27H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.7, 167.8, 144.8, 142.3, 141.5, 128.4, 125.4, 115.3, 80.8, 78.9, 77.8, 71.5, 68.4, 65.3, 61.8, 55.5, 49.2 (2C), 45.4, 41.7, 38.8, 33.3, 30.4, 29.6, 28.5, 28.3, 23.9, 21.0, 20.0, 15.0, 13.2, 12.5, 7.2, 7.1, 7.0, 6.9, 5.2, 4.8; HRMS (ES^+) calcd. for $C_{56}H_{108}O_9Si_4Na$ (M+Na) 1059.6968, found 1059.6982.



Selenide 7.20: To a stirred solution of epoxide **7.18** (8.5 mg, 0.00819 mmol) in THF (0.5 mL) at rt was sequentially added *o*-$NO_2C_6H_4SeCN$ (37 mg, 0.164 mmol) and PBu_3 (33.2 mg, 41μL, 0.164 mmol). After 5 h, the reaction mixture was concentrated *in vacuo* purified by chromatography over silica gel, eluting with Hexanes then with 4% EtOAc / Hexanes, to give crude selenide **7.20** (4.5 mg) as a yellow oil which was used directly in next step without further purification.

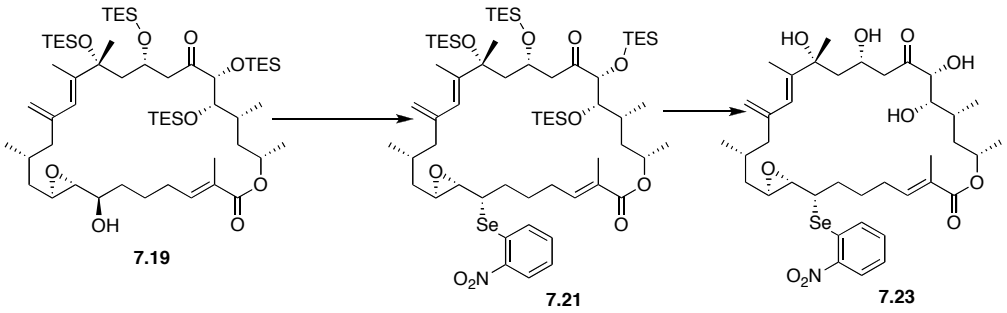
Polyol 7.22: To a stirred solution of selenide **7.20** (4.5 mg) in THF / DMF / H_2O (10:1:0.02, 0.50 mL / 50 μL / 1 μL) at 0ºC was added TAS-F (5 mg, 0.0180 mmol). The reaction mixture was then warmed up to rt. After 2 h, the reaction mixture was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 10-65% EtOAc / Hexanes, to give polyol **7.22** (2.0 mg, 0.00261 mmol, 32% over 2 steps) as a yellow oil: $[\alpha]_D^{23}$ = -41.7 (*c* 0.12, $CHCl_3$); IR (neat) 3446, 2924, 2854, 1701, 1519, 1457, 1378, 1334, 1121, 759, 732 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.17 (d, *J* = 8.0 Hz, 1H), 7.70 (d, *J* = 8.0 Hz, 1H), 7.55 (t, *J* = 7.4

Hz, 1H), 7.42 (t, *J* = 7.5 Hz, 1H), 6.88 (t, *J* = 6.3 Hz, 1H), 5.87 (s, 1H), 5.15-5.08 (m, 1H), 5.03 (s, 1H), 4.82 (s, 1H), 4.50 (s, 1H), 4.20-4.10 (m, 2H), 3.78-3.69 (m, 1H), 3.20-3.10 (m, 1H), 2.94-2.77 (m, 3H), 2.39-2.33 (m, 1H), 2.30-2.13 (m, 2H), 2.07-1.50 (m, 11H), 1.84 (s, 6H), 1.41 (s, 3H), 1.40-1.28 (m, 5H), 1.07 (d, *J* = 6.5 Hz, 3H), 0.77 (t, *J* = 6.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 211.4, 167.7, 149.7, 144.0, 143.0, 141.1, 133.1, 132.6, 128.8, 128.4, 127.1, 125.9, 123.9, 115.2, 77.6, 76.0, 75.3, 68.3, 66.0, 62.1, 59.0, 46.8, 46.1, 45.3, 44.7, 40.3, 40.2, 32.7, 31.9, 29.2, 28.9, 28.0, 26.3, 21.2, 17.8, 15.9, 15.4, 12.5; HRMS (ES^+) calcd. for $C_{38}H_{55}NO_{10}NaSe$(M+Na) 788.2889, found 788.2891.



Amphidinolide B_1 (4.13): To a stirred solution of selenide **7.22** (2.0 mg, 0.00261 mmol) in CH_2Cl_2 (0.4 mL) at rt was sequentially added $NaHCO_3$ (20 mg, 0.238 mmol) and TMSO-OTMS (16.6 mg, 20 μL, 0.0929 mmol). After 1.5 h, the yellow color vanished and the reaction mixture was purified by preparative TLC, eluting with 60% EtOAc / Hexanes, to give amphidinilide B_1 (**4.13**) (1.0 mg,

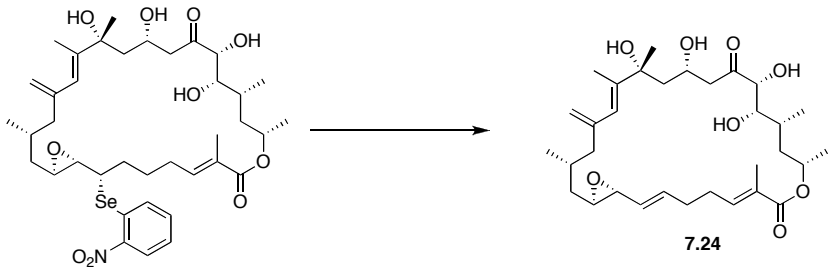
0.00178 mmol, 68%): $[\alpha]_D^{23}$ = -63.7 (*c* 0.08, $CHCl_3$), Literature Value:[1] -62.5 (*c* 0.39, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.78 (t, *J* = 7.8 Hz, 1H), 5.99 (s, 1H), 5.93 (ddd, *J* = 15.2, 8.5, 4.8 Hz, 1H), 5.18 (dd, *J* = 15.8, 8.6 Hz, 1H), 5.06 (m, 1H), 5.05(s, 1H), 4.84 (s, 1H), 4.34 (dd, *J* =4.8, 1.4 Hz, 1H), 4.20 (m, 1H), 3.92 (d, *J* = 3.3 Hz, 1H), 3.88 (d, *J* = 5.0 Hz, 1H), 3.73 (ddd, *J* = 10.3, 8.8, 1.5 Hz, 1H), 3.19 (d, *J* = 10.0 Hz, 1H), 3.16 (dd, *J* = 8.3, 2.0 Hz, 1H), 2.94 (ddd, *J* = 8.9, 2.6, 2.2 Hz, 1H), 2.86 (d, *J* = 7.3 Hz, 1H), 2.80 (dd, *J* = 15.9, 3.2 Hz, 1H), 2.43 (m, 1H), 2.38 (m, 1H), 2.25 (m, 1H), 2.20 (m, 1H), 2.17 (m, 1H), 2.16 (s, 1H), 1.98-1.91 (m, 4H), 1.80 (s, 6H), 1.76 (dd, *J* =14.5, 5.2 Hz, 1H), 1.64 (m, 1H), 1.49 (ddd, *J* = 13.6, 10.9, 3.0 Hz, 1H), 1.44 (s, 3H), 1.31 (m, 1H), 1.30 (d, *J* = 6.1 Hz, 3H), 1.26 (m, 1H), 1.03 (d, *J* = 6.6 Hz, 3H), 0.90 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 212.51, 167.77, 144.47, 143.17, 140.02, 135.52, 128.58, 128.45, 124.40, 114.92, 77.86, 76.07, 75.69, 68.44, 66.70, 60.19, 46.99, 45.98, 45.35, 39.52, 39.39, 33.31, 30.95, 29.35, 28.44, 26.88, 21.07, 18.27, 15.71, 15.15, 12.50; HRMS (ES^+) calcd. for $C_{32}H_{50}O_8Na$ (M+Na) 585.3403, found 585.3411.



Selenide 7.21: To a stirred solution of epoxide **7.19** (14.5 mg, 0.0139 mmol) in THF (0.8 mL) at rt was sequentially added *o*-$NO_2C_6H_4SeCN$ (63 mg, 0.279 mmol) and PBu_3 (56.7 mg, 70 µL, 0.279 mmol). After 1 h, the reaction mixture was concentrated *in vacuo* purified by chromatography over silica gel, eluting with Hexanes then with 4% EtOAc / Hexanes, to give crude selenide **7.21** (15.2 mg) as a yellow oil which was used directly in next step without further purification.

Polyol 7.23: To a stirred solution of selenide **7.21** (15.2 mg, 0.0122 mmol) in THF / DMF / H_2O (10:1:0.02, 1.6 mL / 0.16 mL / 3.2 µL) at 0ºC was added TAS-F (16.8 mg, 0.0610 mmol). The reaction mixture was then warmed up to rt. After 2 h, the reaction mixture was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 10-65% EtOAc / Hexanes, to give polyol **7.23** (9.1 mg, 0.0119 mmol, 86% over 2 steps) as yellow oils: $[\alpha]_D^{23}$ = -51.8 (*c* 0.44, $CHCl_3$); IR (neat) 3447, 2926, 2855, 1701, 1514, 1456, 1332, 1271, 1037, 902, 756, 731 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.26 (d, *J* = 8.3 Hz, 1H), 7.73

(d, *J* = 8.0 Hz, 1H), 7.55 (t, *J* = 7.3 Hz, 1H), 7.36 (t, *J* = 7.9 Hz, 1H), 6.81 (t, *J* = 7.0 Hz, 1H), 5.97 (s, 1H), 5.10-5.03 (m, 1H), 5.03 (s, 1H), 4.83 (s, 1H), 4.47 (s, OH), 4.40-4.32 (m, 1H), 4.14 (dd, *J* = 14.2, 7.2 Hz, 1H), 3.88-3.78 (m, 1H), 3.42-3.35 (m, 1H), 3.05-2.97 (m, 1H & OH), 2.85 (d, *J* = 4.8 Hz, 2H), 2.50-2.38 (br, 1H), 2.30-2.20 (m, 2H), 2.07 (s, OH), 2.11-2.02 (m, 1H), 1.96-1.65 (m, 11H), 1.83 (s, 6H), 1.44 (s, 3H), 1.40-1.32 (m, 2H), 1.33 (d, *J* = 5.8 Hz, 3H), 1.08 (d, *J* = 6.3 Hz, 3H), 0.90 (d, *J* = 4.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 211.6, 167.9, 147.6, 144.0, 143.5, 141.2, 133.6, 132.3, 130.6, 128.7, 126.4, 126.0, 124.0, 115.5, 78.0, 76.1, 75.0, 69.5, 66.3, 60.7, 58.7, 46.1, 45.8, 44.8, 43.8, 40.5, 39.5, 33.5, 30.4 (2C), 28.2, 27.7, 27.1, 20.8, 19.6, 16.5, 15.2, 12.5; HRMS (ES^+) calcd. for $C_{38}H_{55}NO_{10}NaSe$ (M+Na) 788.2889, found 788.2934.



Allylic epoxide 7.24: To a stirred solution of selenide **7.23** (2.7 mg, 0.00353 mmol) in CH_2Cl_2 (0.5 mL) at rt was sequentially added $NaHCO_3$ (30 mg, 0.357 mmol) and TMSO-OTMS (22.5 mg, 27 μL, 0.126 mmol). After 1.5 h, the

yellow color vanished and the reaction mixture was purified by preparative TLC, eluting with 60% EtOAc / Hexanes, to give allylic epoxide **7.24** (1.3 mg, 0.00231 mmol, 65%): $[\alpha]_D^{23}$ = +10.0 (*c* 0.13, $CHCl_3$); IR (neat) 3422, 2923, 2853, 1701, 1457, 1377, 1261, 1103; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.72 (t, *J* = 4.9 Hz, 1H), 6.04 (s, 1H), 5.88-5.80 (m, 1H), 5.28 (dd, *J* = 15.4, 8.4 Hz, 1H), 5.10-5.05 (m, 1H), 5.06 (s, 1H), 4.84 (s, 1H), 4.35 (dd, *J* =4.2, 1.5 Hz, 1H), 4.30-4.20 (m, 1H), 4.13 (s, 1H), 3.79 (t, *J* = 9.8 Hz, 1H), 3.77 (d, *J* = 4.6 Hz, 1H), 3.40 (d, *J* = 10.2 Hz, 1H), 3.09 (dd, *J* = 8.5, 2.1 Hz, 1H), 2.98-2.93 (m, 2H), 2.76 (dd, *J* = 15.4, 2.4 Hz, 1H), 2.38-2.23 (m, 5H), 2.35 (s, 1H), 1.98 (m, 1H), 1.95 (m, 1H), 1.88 (m, 1H), 1.85 (m, 1H), 1.84 (s, 6H), 1.78 (dd, *J* =14.6, 4.7 Hz, 1H), 1.70 (m, 1H), 1.64 (m, 1H), 1.32 (m, 1H), 1.30 (d, *J* = 6.1 Hz, 3H), 1.13 (m, 1H), 1.03 (d, *J* = 6.6 Hz, 3H), 0.83 (d, *J* = 6.4 Hz, 3H) ^{13}C NMR (100 MHz, $CDCl_3$) δ 212.64, 167.52, 144.58, 143.16, 140.79, 135.90, 128.87, 128.68, 124.34, 114.91, 78.27, 76.07, 75.46, 68.31, 66.79, 60.29, 59.18, 46.45, 46.10, 45.60, 39.55, 33.25, 31.24, 30.45, 29.71, 28.55, 27.08, 21.04, 19.90, 15.74, 15.41, 12.69; HRMS (ES^+) calcd. for $C_{32}H_{50}O_8Na$ (M+Na) 585.3403, found 585.3409.

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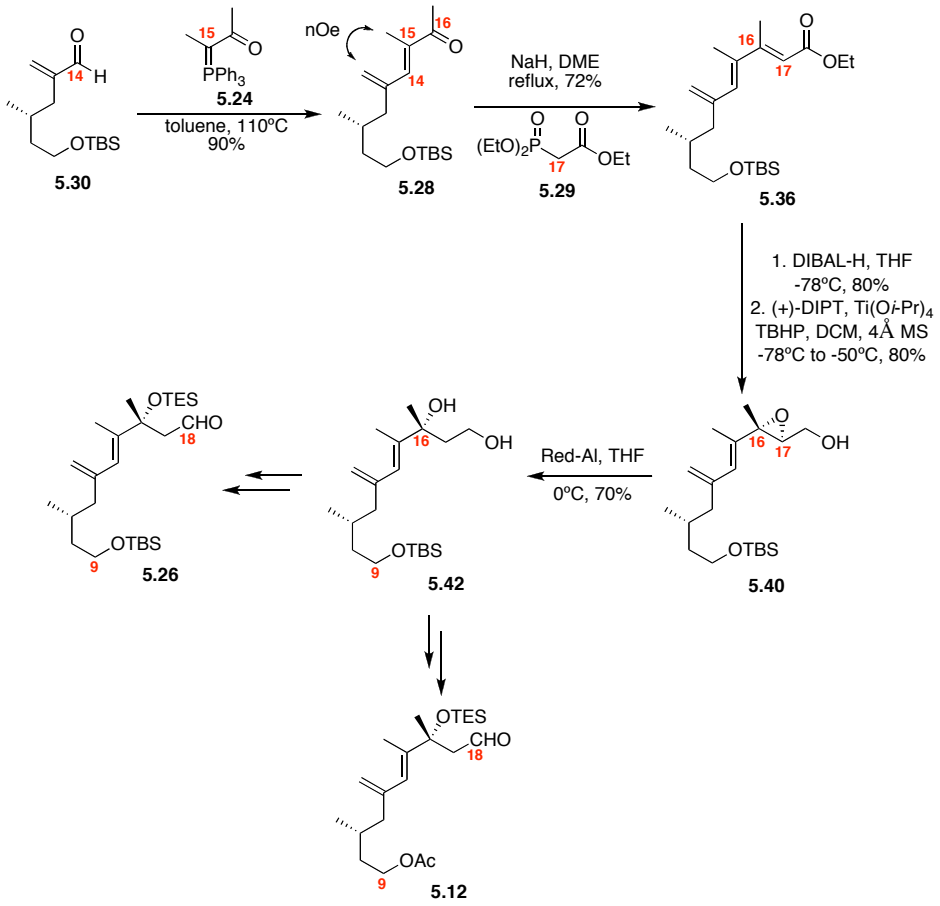
CHAPTER 8. CONCLUSION AND FUTURE WORK

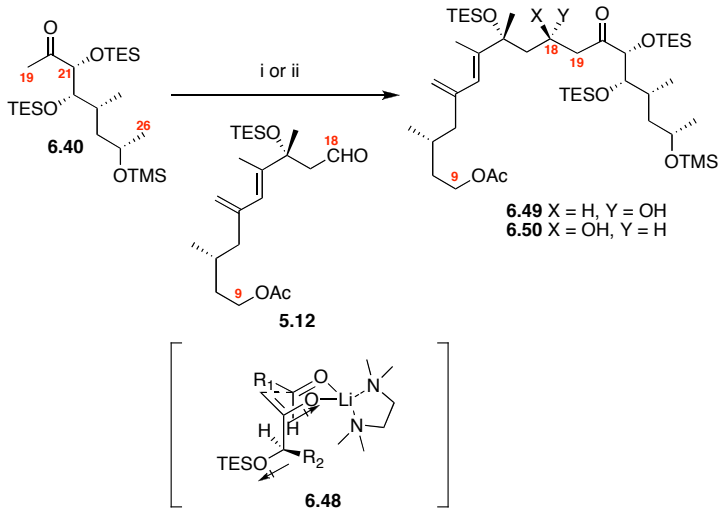
8.1 General Conclusion

During our endeavors toward amphidinolide B_1 and B_2, we developed several important protocols. Our metal catalyst-free strategy yielded the unusual highly substituted C_{13}-C_{15} diene efficiently (Scheme 8.1). Utilizing a Wittig reaction between aldehyde **5.30** and ylide **5.24**, we could synthesize this difficult C_{13}-C_{15} diene moiety in good yield and excellent *E/Z* selectivity. Two other highlights of our approach are a HWE reaction to build C_{16}-C_{17} alkene and a Sharpless epoxidation / regioselective epoxide opening sequence to yield C_{16} tertiary alcohol.



Scheme 8.1. Synthesis of Diene Subunits

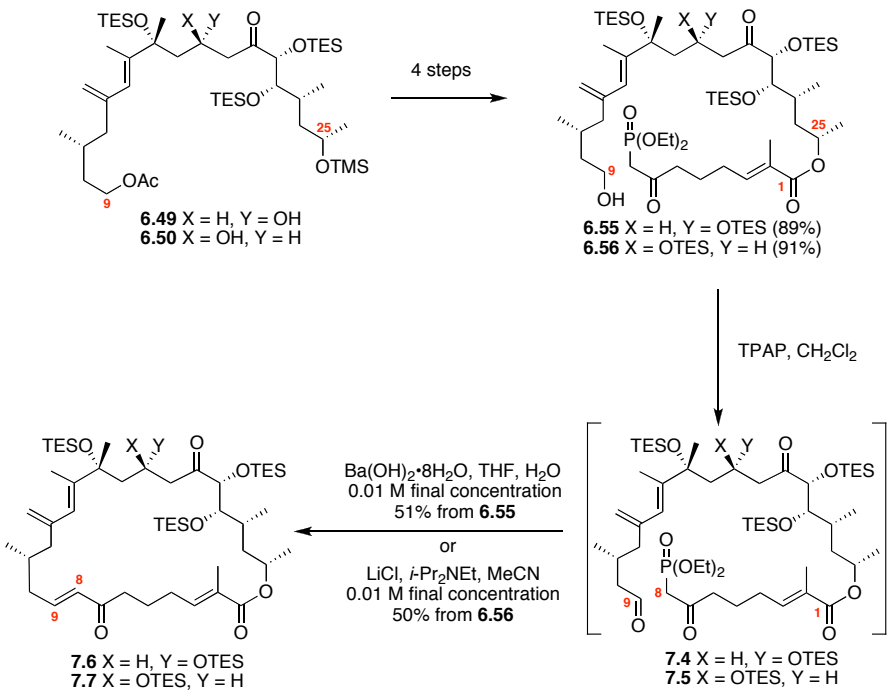
Using C_{21} TES-protected methyl ketone **6.40**, the non-chelation-controlled aldol reaction led to 18*R* isomer **6.50** in 1:8 dr (**6.49**:**6.50**) at -100ºC (Scheme 8.2). Alternatively, the 18*S* stereisomer **6.49** was generated in 1.2:1 dr (**6.49**:**6.50**) at -40ºC. While we are still exploring the nature of the diastereoselectivity, one possible explanation could be that a transition state **6.48**, which minimizes the dipoles of the C_{21} C−O σ bond and the enolate, determines the stereochemical outcome of the reaction.



(i) LDA, TMEDA, THF, -100°C then add **5.12**, 65% (1:8 dr, **6.49**:**6.50**); (ii) LDA, TMEDA, THF, -40°C then add **5.12**, 66% (1.2:1 dr, **6.49**:**6.50**)

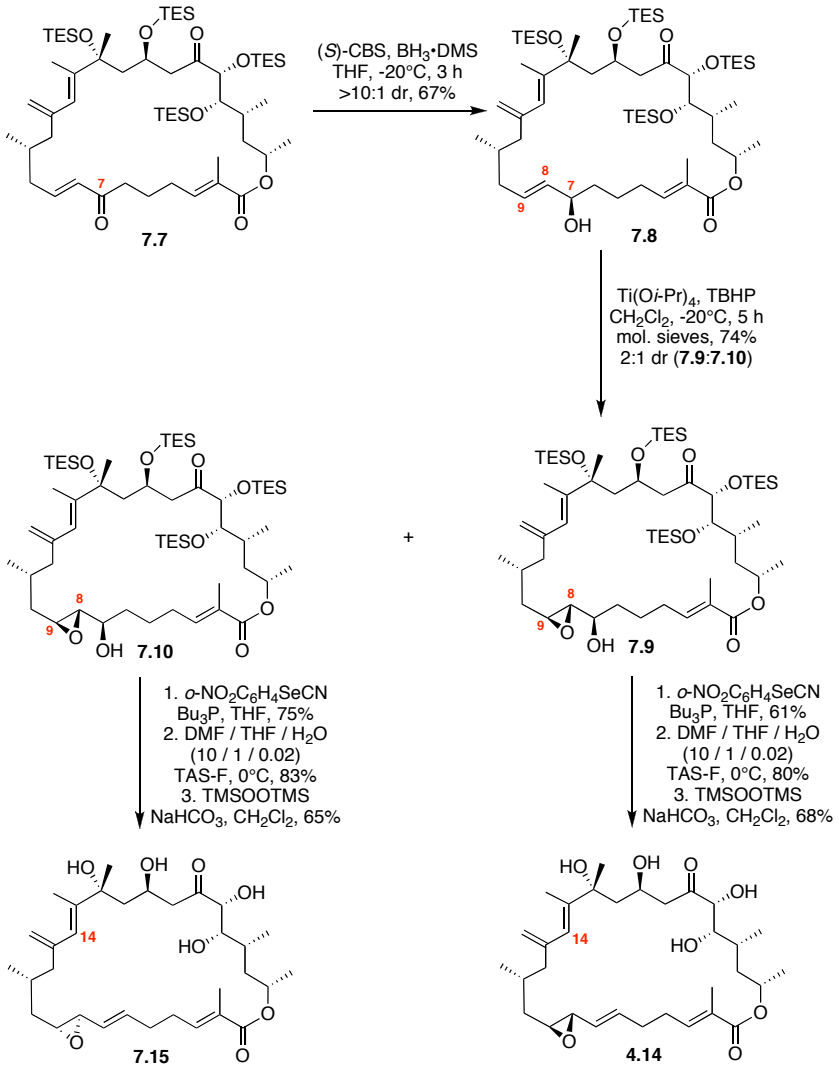
Scheme 8.2. Aldol Coupling between Methyl Ketone **6.40** and Aldehyde **5.12**

Another highlight of our work is the macrocyclization of the 26-membered lactone ring (Scheme 8.3) Further chemical elaboration of aldol adducts **6.49**/**6.50** gave rise to phosphonate alcohol **6.55**/**6.56.** When phosphonate **6.55/6.56** was exposed to TPAP / CH_2Cl_2, significant amounts of the macrocycle **7.6/7.7** formed via a spontaneous intramolecular Horner-Wadsworth−Emmons olefination. The conversion could be driven to completion by the addition of LiCl and Hunig's base or $Ba(OH)_2 \bullet 8H_2O$, respectively.



Scheme 8.3. Macrocyclization of 26-Membered Ring

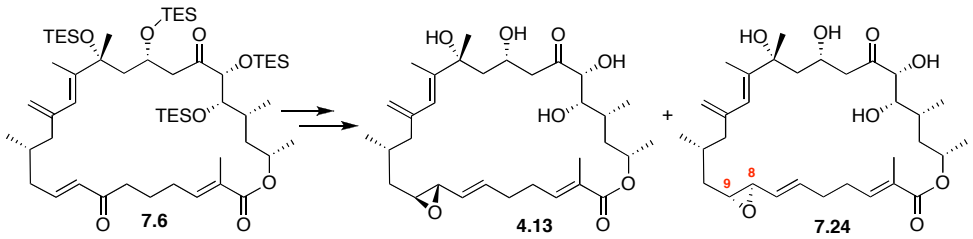
The key steps of the incorporation of the allylic epoxide moiety include a region- and stereoselective reduction of the C_7 carbonyl functionality with the (*S*)-CBS reagent, a Ti(O*i*-Pr)$_4$ / TBHP-mediated epoxidation, and a TMSOOTMS induced oxidation and *in situ* elimination of a selenide (Scheme 8.4). The proposed structure of amphidinolide B_2 (**4.14**) and its $C_{8,9}$ epoxide diastereomer **7.15** were finally synthesized with a longest linear of 29 steps. To our surprise, these synthesized compounds **4.14** and **7.15** *did not match* with the spectra data provided for amphidinolide B_2. In both cases, the ^{1}H NMR shift for the H_{14} alkene was shifted significantly downfield as compared to the natural product data.



Scheme 8.4. Synthesis of Proposed Structure of Amphidinolide B_2 and its C8,9 Epoxide Diastereomer

Careful inspection of the isolation paper revealed that the stereochemical analysis of amphidinolide B_2 was based primarily on the differences in the ^1H NMR in the C_{17}–C_{19} region of the natural product as compared to amphidinolide

B_1 (**4.13**). It is important to note that Shimizu and Clardy obtained X-ray crystallographic structure of natural product **4.13**. It is clear from our work that the structural differences between amphidinolide B_1 and B_2 are more complicated than initially expected. On the basis of this information, we have concluded that the proposed structure of amphidinolide B_2 is incorrect. We applied an analogous strategy for the synthesis of **4.13** as was described for the 18*R* series (Scheme 8.5). The synthesized material **4.13** matched with the spectra data reported by Kobayashi and co-workers for amphidinolide B_1.



Scheme 8.5. Synthesis of Amphidinolide B_1 and its $C_{8,9}$ Epoxide Diastereomer

8.2 Proposed Future Work

We have developed a synthetic route for amphidinolide B and its analogs. First syntheses of amphidinolide B_1 and the proposed structure of amphidinolide B_2 have been accomplished based on this strategy; however the originally proposed structure of amphidinolide B_2 was found to be incorrect. Consequently, our next target would be the correction of the proposed structure of amphidinolide B_2. We intend to do extensive 2D NMR on coumpound **4.14** to firmly assign each

H and C for the compound. Based on our tentative assignments of the data we have already collected, we suspect that the culprit stereochemistry is in fact the C_{16} tertiary alcohol. We speculate that a common *syn* relationship is present between C_{16} and C_{18} in amphidinolide B_2 (Figure 8.1).

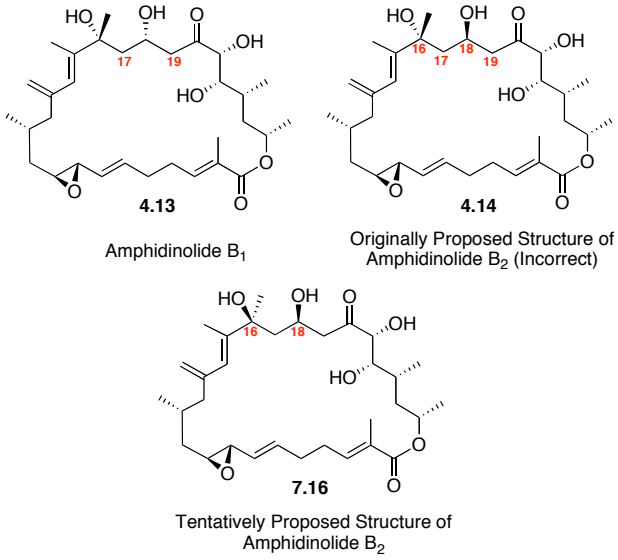
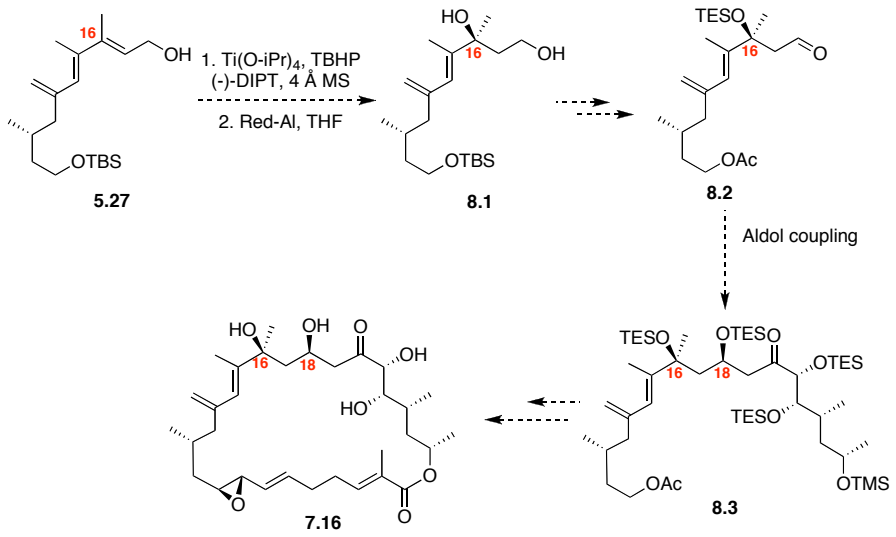


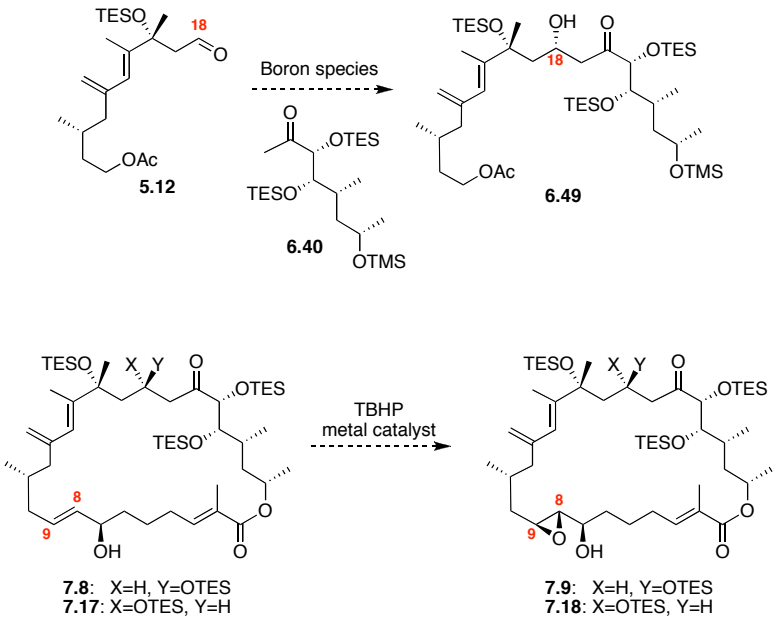
Figure 8.1. Tentatively Proposed Structure of Amphidinolide B_2

The first compound we would like to synthesize will be epimeric at C_{16}-compound **7.16** (Scheme 8.6). The epimer stereochemistry can be readily available from the Sharpless epoxidation and the following transformation could be accomplished using analogous strategy for the synthesis of the proposed structure of amphidinolide B_2.



Scheme 8.6. Proposed Synthesis of Compound **7.16**

Besides the correction of the proposed structure of amphidinolide B_2, we also intend to investigate other options to improve the diastereoselectivity of several steps including the aldol coupling to afford 18*S* isomer and the epoxidation to install C_8-C_9 epoxide (Scheme 8.7). Boron enolate based asymmetric aldol reactions[1] would be a potential option for the aldol coupling. We have already shown that $Ti(O\text{-}iPr)_4$ can be used to access both diastereomers of the C_8-C_9 epoxide. We would like to explore other transition metal oxidants (e.g. $VO(acac)_2$) to see if an improved diastereoselectivy can be obtained.



Scheme 8.7. Proposed Optimization of Current Work

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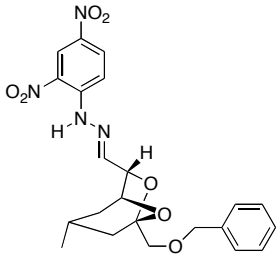
APPENDIX: X-RAY CRYSTALLOGRAPHIC DATA

X-ray Crystal Structure Determination. X-ray diffraction intensity data were collected with a Bruker Smart Apex CCD diffractometer using MoKa – radiation (0.71073 Å). Crystallographic data and some details of data collections and refinements for the investigated structures are given in Tables A1-A16. The structures were solved using direct methods, completed by subsequent difference Fourier syntheses, and refined by full matrix least-squares procedures on F^2. The non-hydrogen atoms in all structures were refined with anisotropic thermal parameters. Highly disordered solvent molecules were treated by SQUEEZE (Van der Sluis, P. & Spek, A. L. (1990) Acta Cryst. Sect. A, A46, 194-201). All software and scattering factor sources are contained in the SHELXTL (5.10) program package (G. Sheldrick, Bruker XRD, Madison, WI).

2,4-Dinitrohydrazone 2.20:



2.20

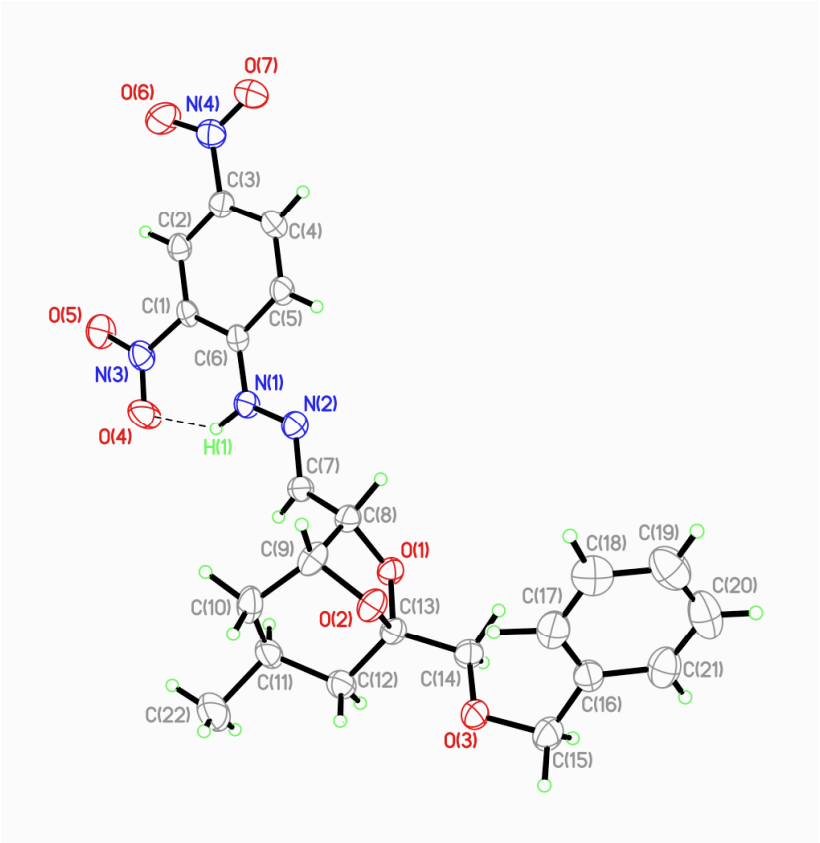
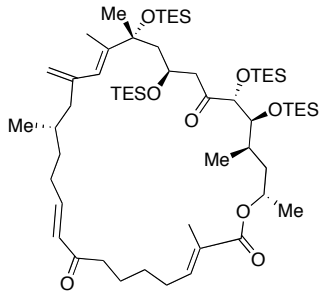


Table 1. Crystal data and structure refinement for rc4.

Identification code	rc4	
Empirical formula	C22 H24 N4 O7	
Formula weight	456.45	
Temperature	293(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	C2	
Unit cell dimensions	a = 24.757(4) Å	a= 90°.
	b = 6.6425(10) Å	b= 131.966(2)°.
	c = 18.281(3) Å	g = 90°.
Volume	2235.3(6) $Å^3$	
Z	4	
Density (calculated)	1.356 Mg/m^3	
Absorption coefficient	0.103 mm^{-1}	
F(000)	960	
Crystal size	0.48 x 0.05 x 0.02 mm^3	
Theta range for data collection	1.50 to 25.00°.	
Index ranges	-29<=h<=29, -7<=k<=7, -21<=l<=21	
Reflections collected	8138	

Independent reflections	3905 [R(int) = 0.0334]
Completeness to theta = 25.00°	100.0 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	1.000 and 0.837
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3905 / 1 / 394
Goodness-of-fit on F^2	0.986
Final R indices [I>2sigma(I)]	R1 = 0.0477, wR2 = 0.0561
R indices (all data)	R1 = 0.0965, wR2 = 0.0675
Absolute structure parameter	-0.5(11)
Largest diff. peak and hole	0.122 and -0.118 e.$Å^{-3}$

Macrocycle 7.6:



7.6

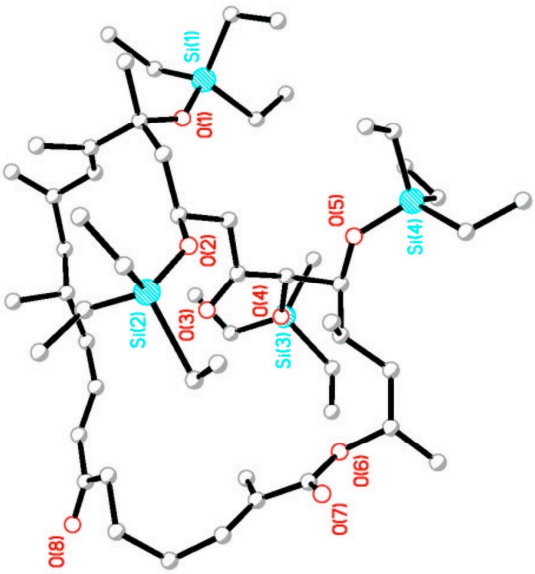
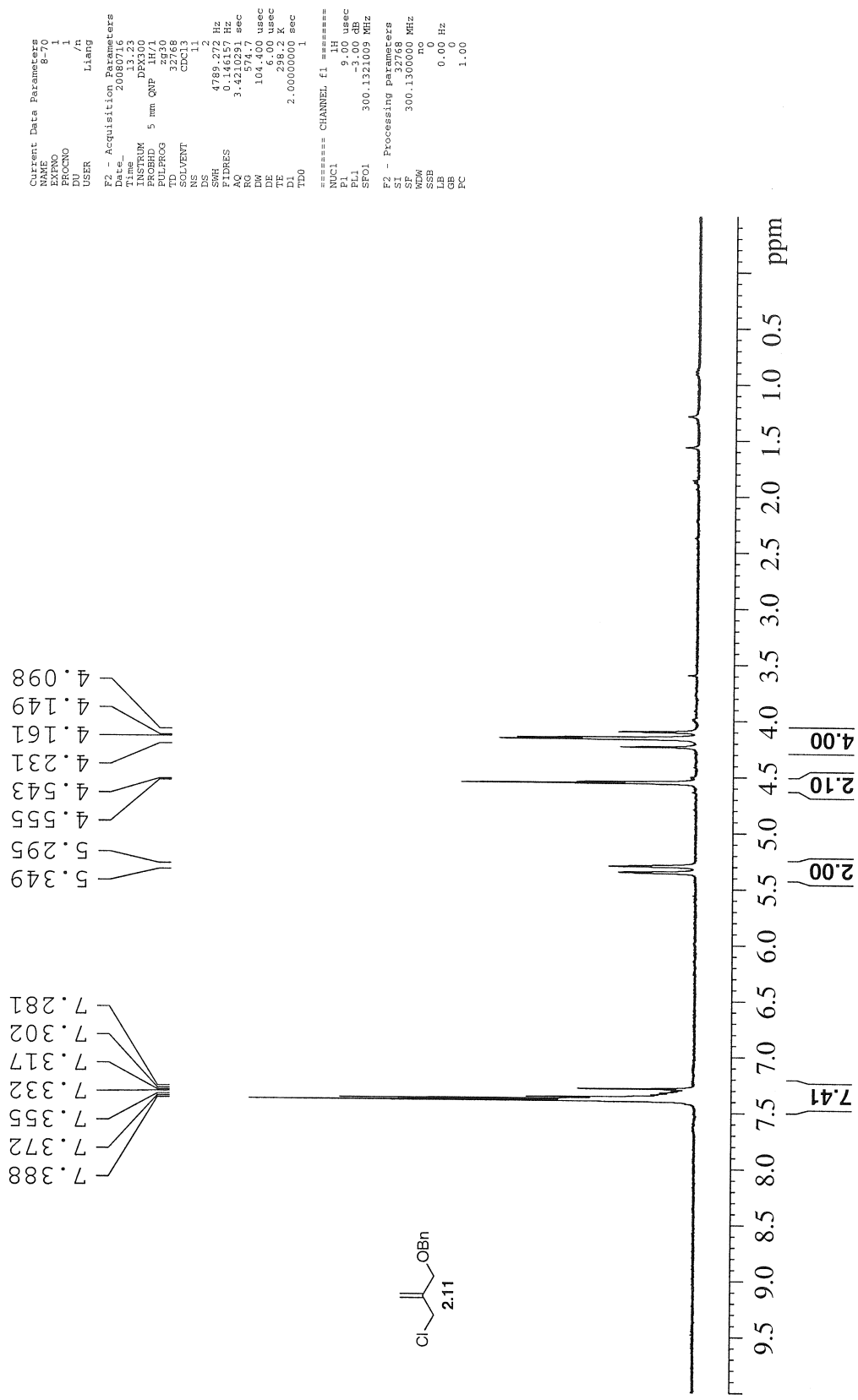


Table 1. Crystal data and structure refinement for rcrr34.

Identification code	rcrr34	
Empirical formula	C56 H106 O8 Si4	
Formula weight	1019.77	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2(1)	
Unit cell dimensions	a = 11.5018(14) Å	a= 90°.
	b = 22.813(3) Å	b= 107.376(2)°.
	c = 12.7063(15) Å	g = 90°.
Volume	3181.9(7) $Å^3$	
Z	2	
Density (calculated)	1.064 Mg/m^3	
Absorption coefficient	0.139 mm^{-1}	
F(000)	1124	
Crystal size	0.38 x 0.36 x 0.09 mm^3	
Theta range for data collection	1.68 to 25.00°.	
Index ranges	-13<=h<=13, -27<=k<=27, -15<=l<=15	
Reflections collected	30468	

Independent reflections	11188 [R(int) = 0.0335]
Completeness to theta = 25.00°	100.0 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9876 and 0.9491
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	11188 / 13 / 809
Goodness-of-fit on F^2	1.043
Final R indices [I>2sigma(I)]	R1 = 0.0600, wR2 = 0.1442
R indices (all data)	R1 = 0.0769, wR2 = 0.1563
Absolute structure parameter	0.00(12)
Largest diff. peak and hole	0.420 and -0.367 e.$Å^{-3}$

APPENDIX: NMR DATA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EXPNO 1
PROCNO 1
DU /n
USER Liang
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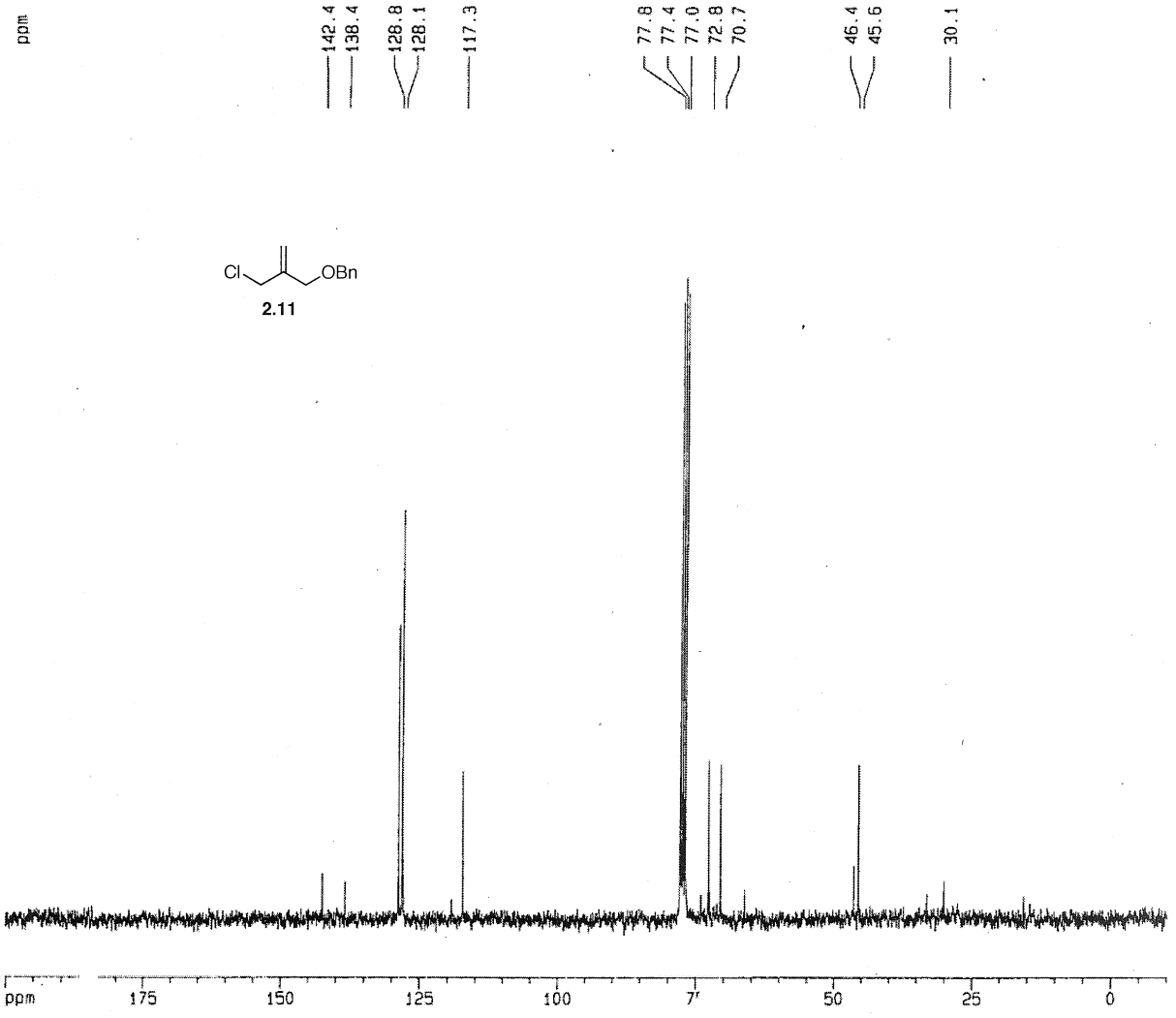
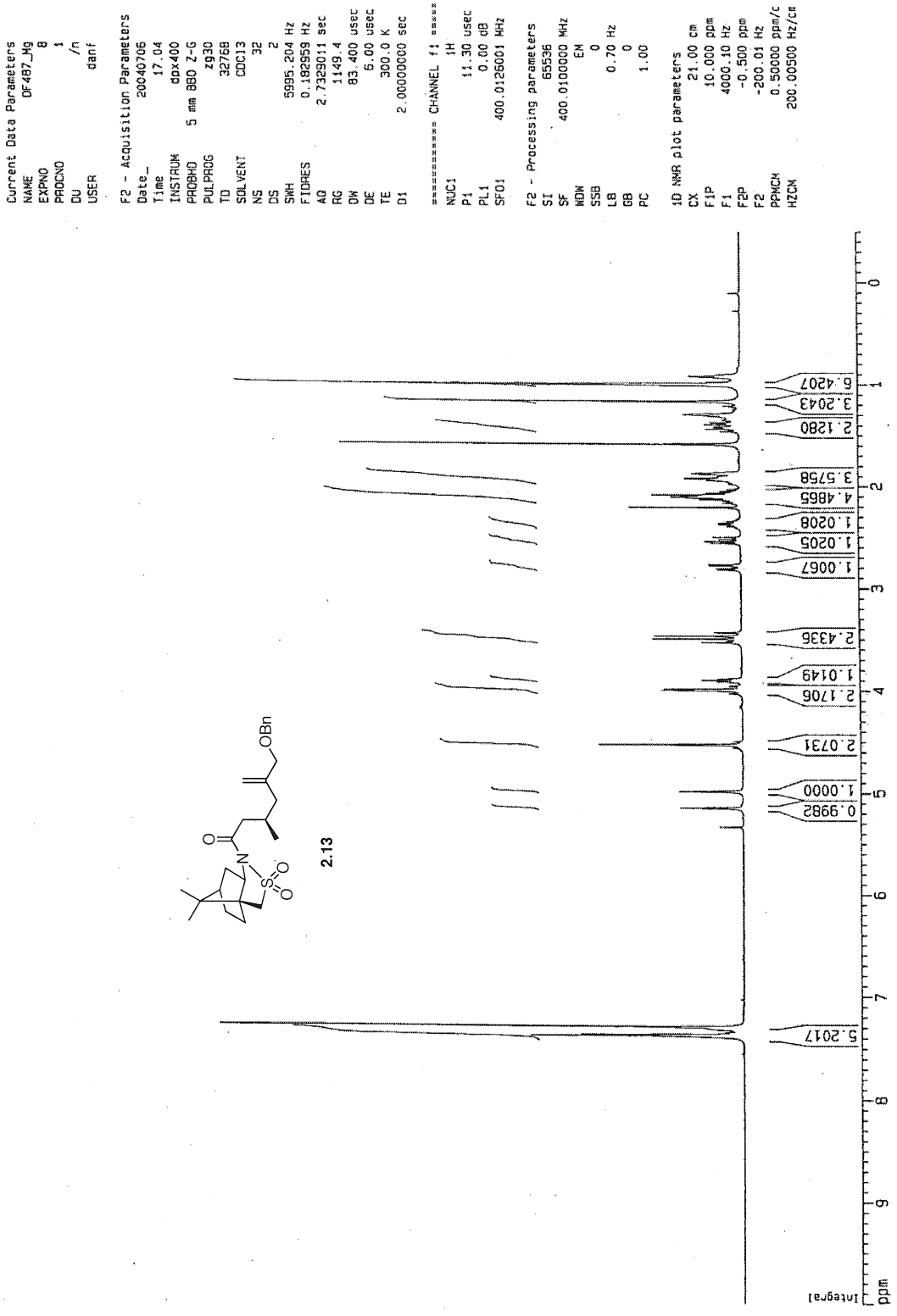
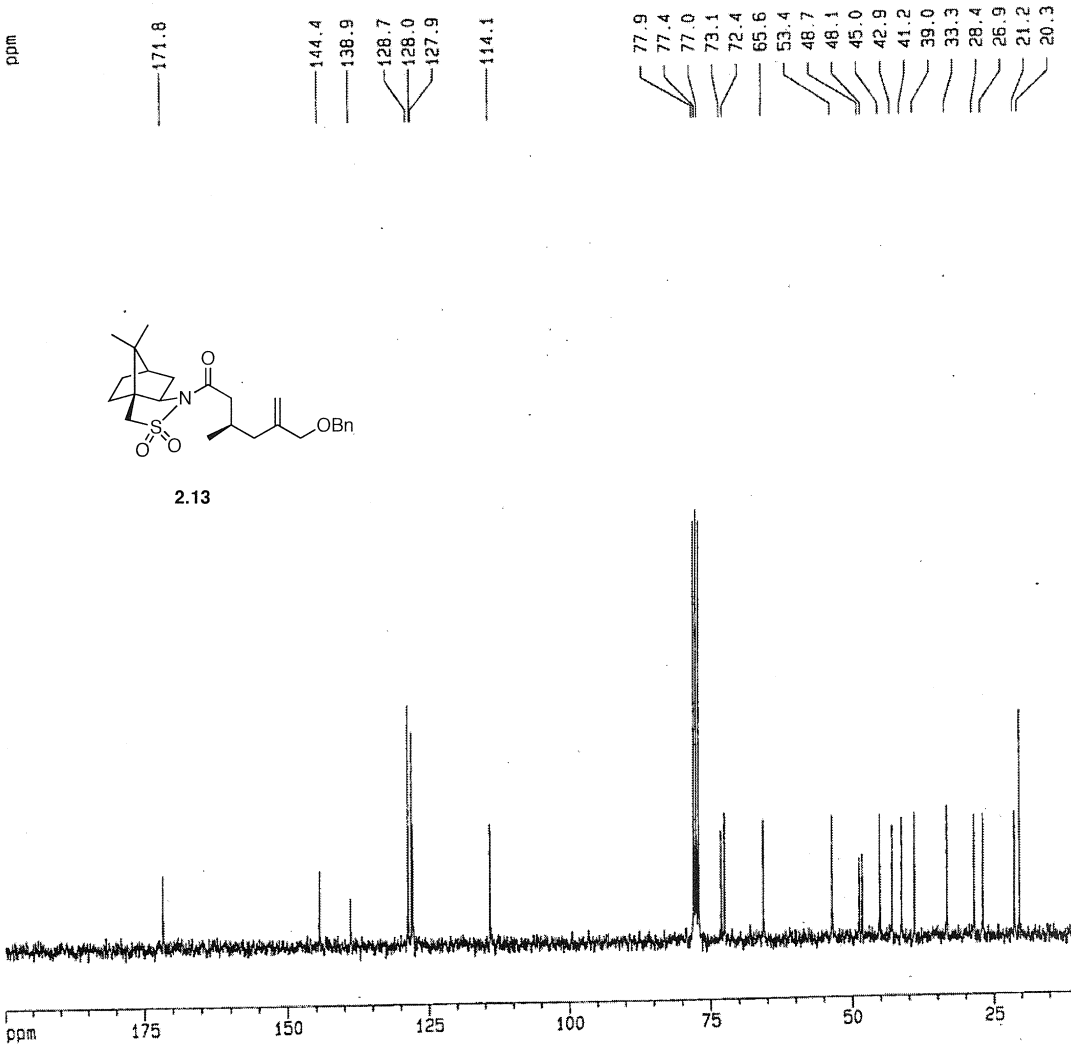
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 11
DS 2
SWH 4789.272 Hz
FIDRES 0.146157 Hz
AQ 3.4210291 sec
RG 574.7
DW 104.400 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.00 usec
PL1 3.00 dB
SFO1 300.1321009 MHz
F2 - Processing parameters
SI 32768
SF 300.1300000 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
7.388
7.372
7.355
7.332
7.317
7.302
7.281
5.349
5.295
4.555
4.543
4.231
4.161
4.149
4.098
OBn
Cl
2.11
7.41
2.00
2.10
4.00
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
ppm



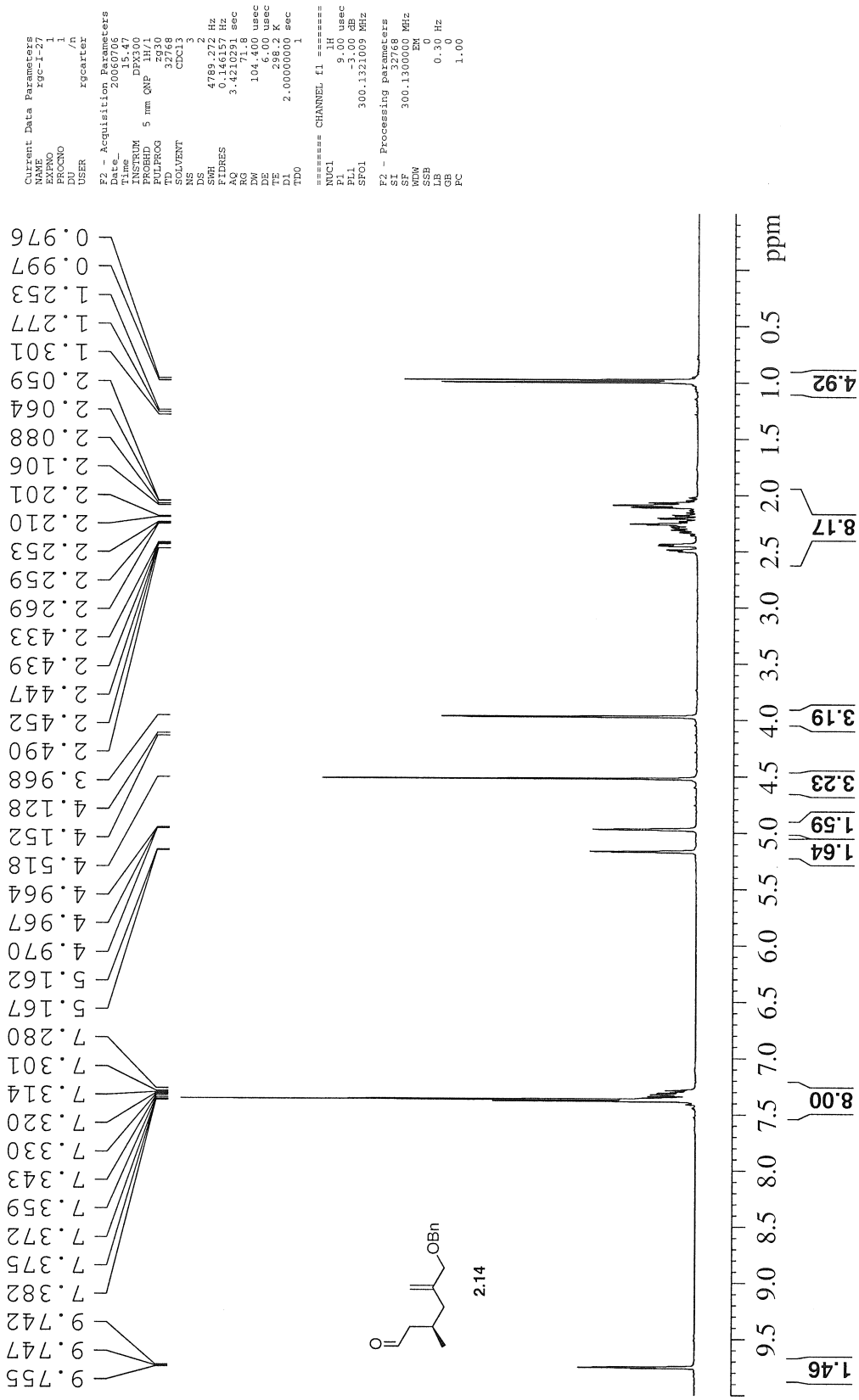

```
Current Data Parameters
NAME                  DF485_OBn
EXPNO                         7
PROCNO                        1
OU                           /n
USER                      danf

F2 - Acquisition Parameters
Date_                  20040826
Time                      12.40
INSTRUM                  dpx300
PROBHD     5 mm QNP  1H
PULPROG                 zgpg30
TD                       65536
SOLVENT
NS                         953
DS                           2
SWH                  18832.393 Hz
FIDRES                0.287360 Hz
AQ                    1.7400308 sec
RG                       16384
DW                      26.550 usec
DE                       6.00 usec
TE                      300.0 K
D1                    0.00300000 sec
D11                   0.03000000 sec
D12                   0.00002000 sec

============ CHANNEL f1 ========
NUC1                       13C
P1                        7.60 usec
PL1                      -3.00 dB
SFO1                75.4756431 MHz

============ CHANNEL f2 ========
CPDPRG2                waltz16
NUC2                       1H
PCPD2                    80.00 usec
PL2                       2.00 dB
PL12                     17.55 dB
PL13                     19.00 dB
SFO2               300.1315007 MHz

F2 - Processing parameters
SI                       131072
SF                  75.4677190 MHz
WDW                         EM
SSB                          0
LB                        3.00 Hz
GB                           0
PC                        1.40

1D NMR plot parameters
CX                       20.00 cm
F1P                     200.000 ppm
F1                     15093.54 Hz
F2P                     -10.000 ppm
F2                      -754.68 Hz
PPMCM                 10.50000 ppm/cm
HZCM                    107 Hz/cm
```

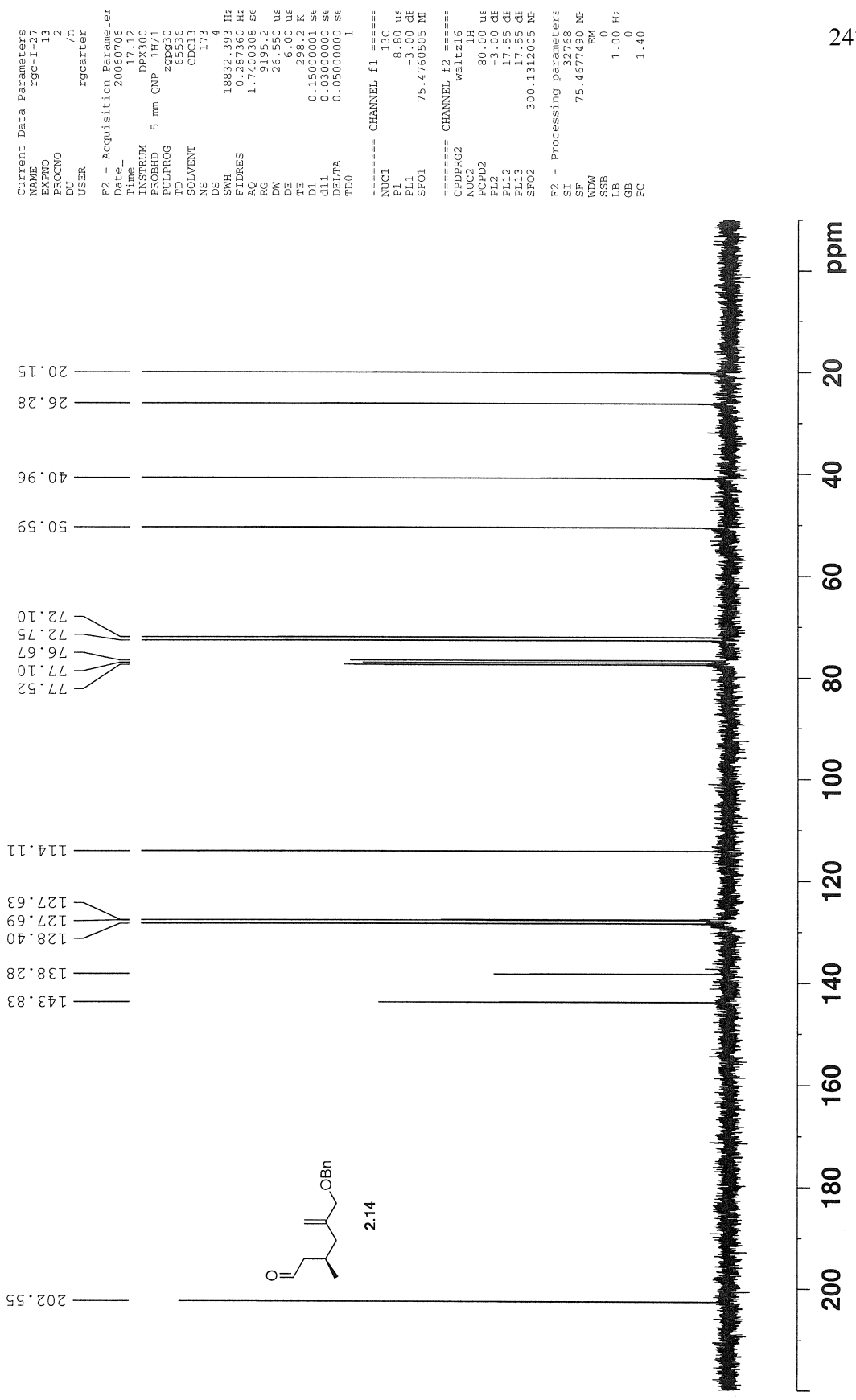

Current Data Parameters
NAME DF487_Mg
EXPNO 8
PROCNO 1
DU /n
USER danf
F2 - Acquisition Parameters
Date_ 20040706
Time 17.04
INSTRUM dpx400
PROBHD 5 mm BBO Z-G
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 5995.204 Hz
FIDRES 0.182959 Hz
AQ 2.7329011 sec
RG 1149.4
DW 83.400 usec
DE 6.00 usec
TE 300.0 K
D1 2.00000000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 11.30 usec
PL1 0.00 dB
SFO1 400.0126001 MHz
F2 - Processing parameters
SI 65536
SF 400.0100000 MHz
WDW EM
SSB 0
LB 0.70 Hz
GB 0
PC 1.00
1D NMR plot parameters
CX 21.00 cm
F1P 10.000 ppm
F1 4000.10 Hz
F2P -0.500 ppm
F2 -200.01 Hz
PPMCM 0.50000 ppm/c
HZCM 200.00500 Hz/cm
OBn
O
N
S
O
O
2.13
5.2017
0.9982
1.0000
2.0731
2.1706
1.0149
2.4336
1.0067
1.0205
1.0208
4.4865
3.5758
2.1280
3.2043
6.4207
Integral
ppm

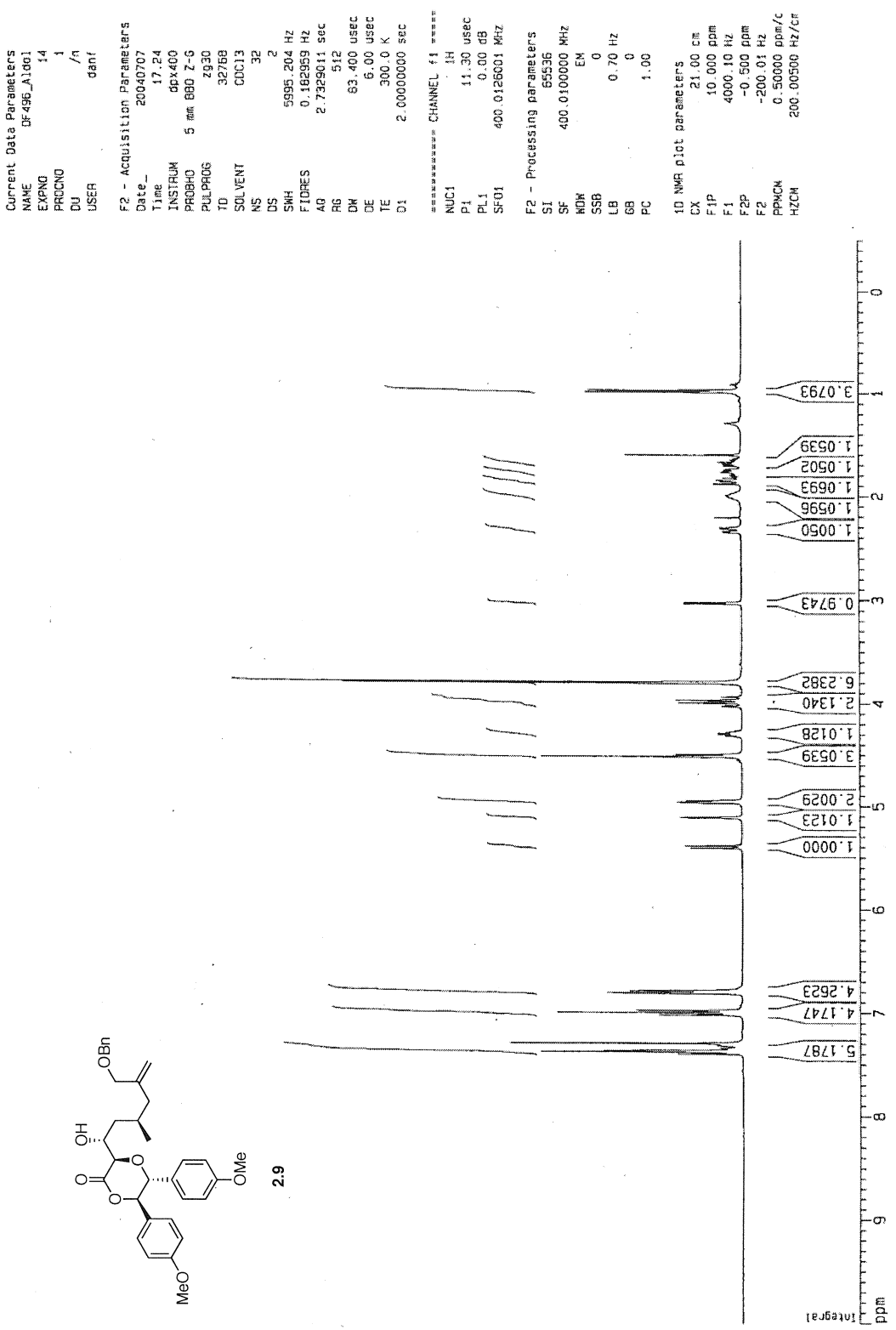


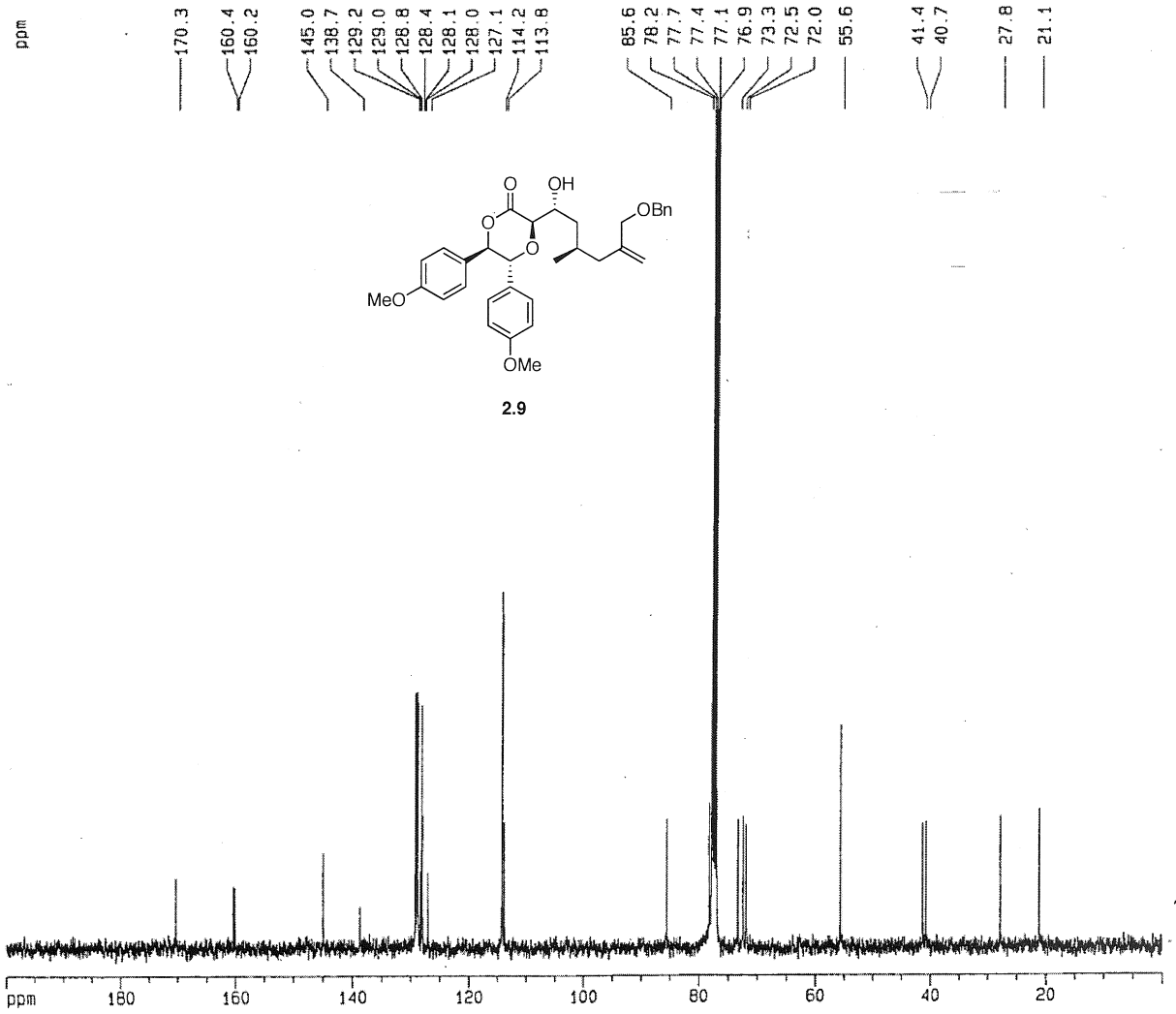
2.13

```
Current Data Parameters
NAME                  DF487_Mg
EXPNO                        6
PROCNO                       1
DU                          /n
USER                     danf

F2 - Acquisition Parameters
Date_                 20040705
Time                     11.42
INSTRUM                  dpx300
PROBHD     5 mm QNP  1H
PULPROG                 zgpg30
TD                       65536
SOLVENT
NS                         778
DS                           2
SWH                  18832.393 Hz
FIDRES               0.287360 Hz
AQ                   1.7400308 sec
RG                       16384
DW                      26.550 usec
DE                       6.00 usec
TE                      300.0 K
D1                   0.00300000 sec
D11                  0.03000000 sec
D12                  0.00002000 sec

========== CHANNEL f1 =========
NUC1                       13C
P1                        7.60 usec
PL1                      -3.00 dB
SFO1                75.4756431 MHz

========== CHANNEL f2 =========
CPDPRG2                waltz16
NUC2                        1H
PCPD2                    80.00 usec
PL2                       2.00 dB
PL12                     17.55 dB
PL13                     19.00 dB
SFO2               300.1315007 MHz

F2 - Processing parameters
SI                       131072
SF                  75.4677190 MHz
WDW                          EM
SSB                           0
LB                        3.00 Hz
GB                            0
PC                         1.40

1D NMR plot parameters
CX                       20.00 cm
F1P                     200.000 ppm
F1                    15093.54 Hz
F2P                     -10.000 ppm
F2                     -754.68 Hz
PPMCM                  10.50000 ppm/cm
HZCM                  792.41107 Hz/cm
```

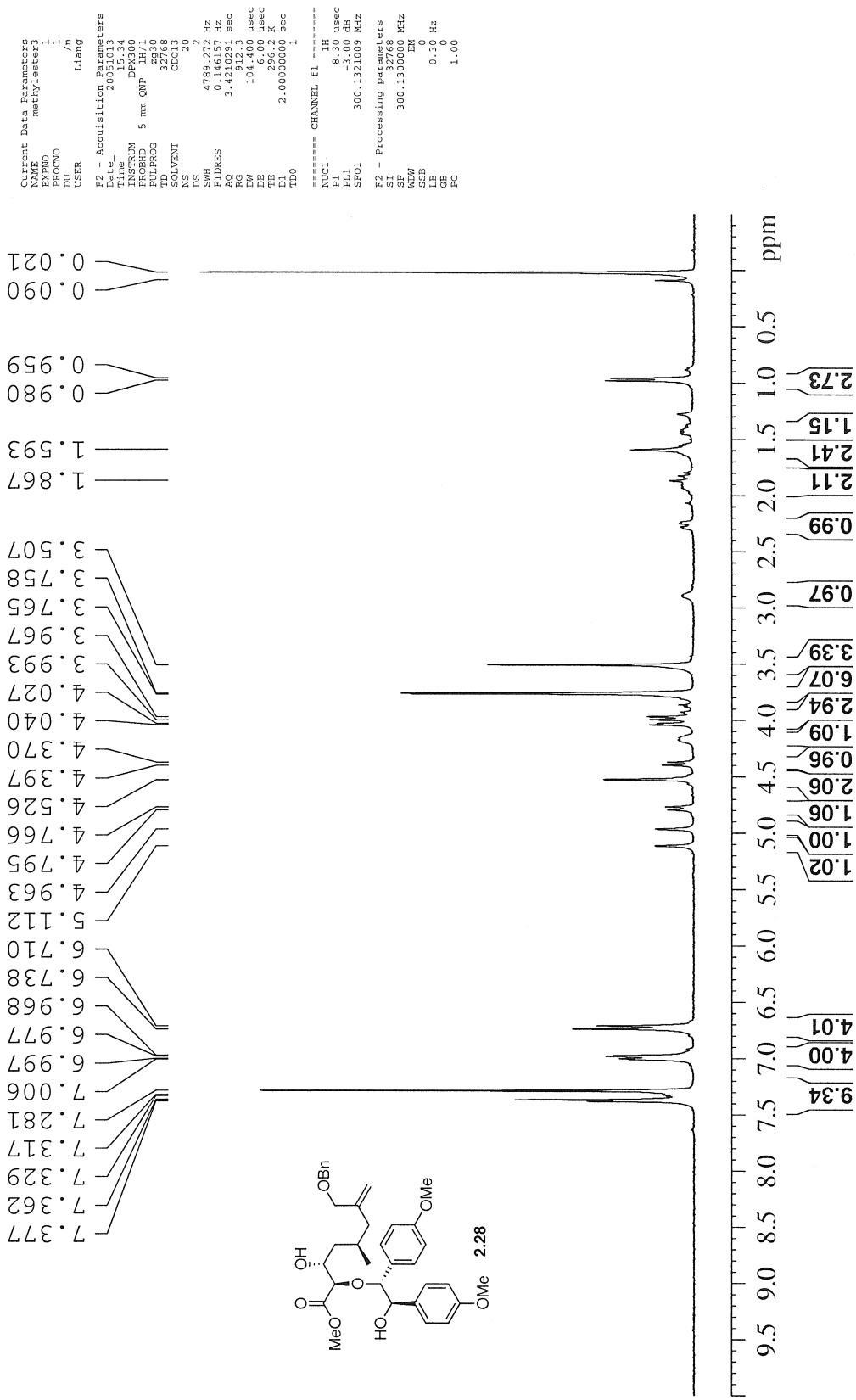

Current Data Parameters
NAME rgc-1-27
EXPNO 1
PROCNO 1
DU /n
USER rgcarter
F2 - Acquisition Parameters
Date_ 20060706
Time 15.47
INSTRUM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 3
DS 2
SWH 4789.272 Hz
FIDRES 0.146157 Hz
AQ 3.4210291 sec
RG 71.8
DW 104.400 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.00 usec
PL1 -3.00 dB
SFO1 300.1321009 MHz
F2 - Processing parameters
SI 32768
SF 300.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
9.755
9.747
9.742
7.382
7.375
7.372
7.359
7.343
7.330
7.320
7.314
7.301
7.280
5.167
5.162
4.970
4.967
4.964
4.518
4.152
4.128
3.968
2.490
2.452
2.447
2.439
2.433
2.269
2.259
2.253
2.210
2.201
2.106
2.088
2.064
2.059
1.301
1.277
1.253
0.997
0.976
OBn
O
2.14
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
1.46
8.00
1.64
1.59
3.23
3.19
8.17
4.92

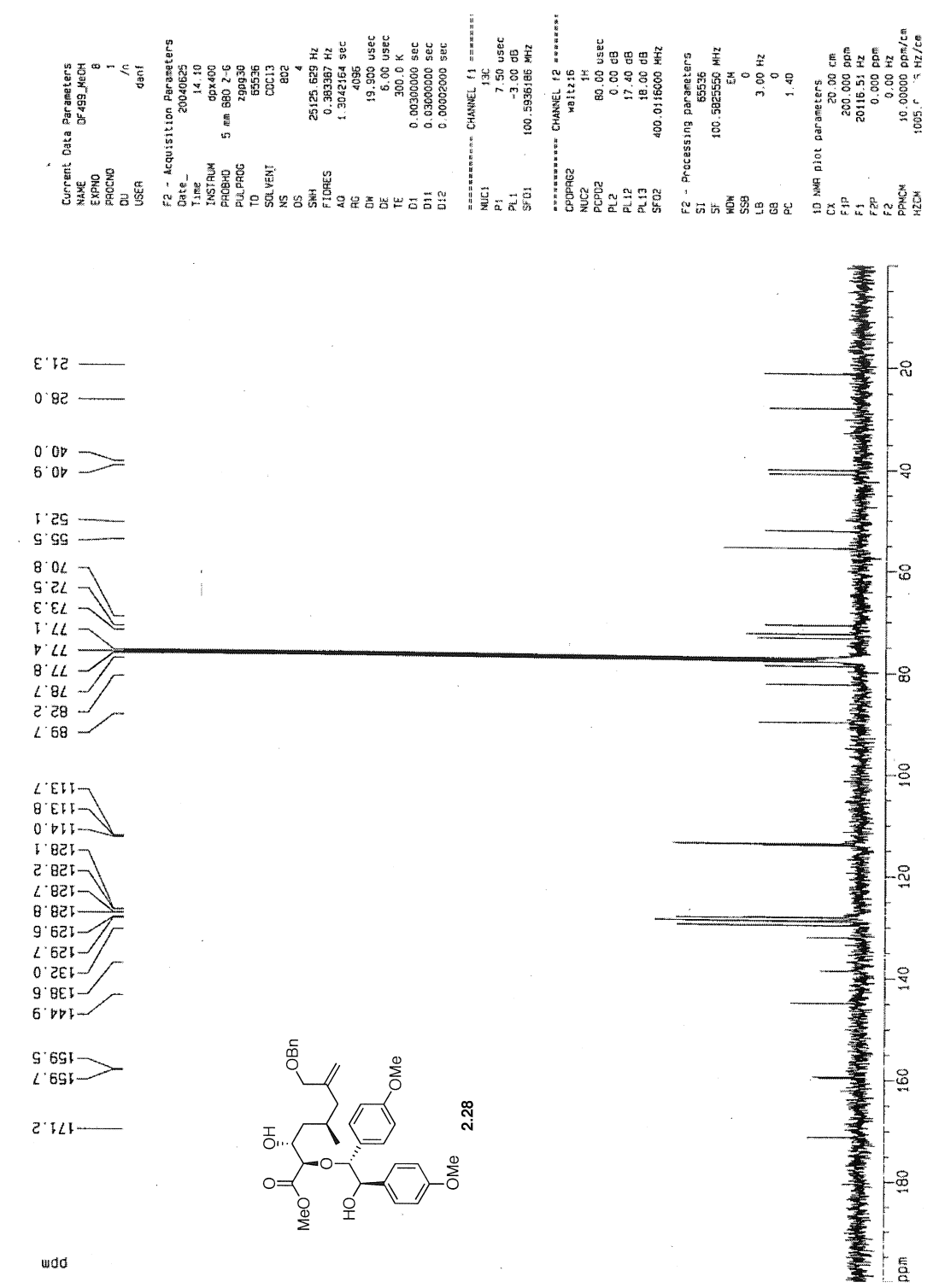

Current Data Parameters
NAME rgc-I-27
EXPNO 13
PROCNO 2
DU /n
USER rgcarter
F2 - Acquisition Parameter
Date_ 20060706
Time 17.12
INSTRUM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 173
DS 4
SWH 18832.393 Hz
FIDRES 0.287360 Hz
AQ 1.7400308 sec
RG 9195.2
DW 26.550 usec
DE 6.00 usec
TE 298.2 K
D1 0.15000001 sec
d11 0.03000000 sec
DELTA 0.05000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 8.80 usec
PL1 -3.00 dB
SFO1 75.4760505 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 -3.00 dB
PL12 17.55 dB
PL13 17.55 dB
SFO2 300.1312005 MHz
F2 - Processing parameters
SI 32768
SF 75.4677490 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
20.15
26.28
40.96
50.59
72.10
72.75
76.67
77.10
77.52
114.11
127.63
127.69
128.40
138.28
143.83
202.55
OBn
O
2.14
ppm
200
180
160
140
120
100
80
60
40
20

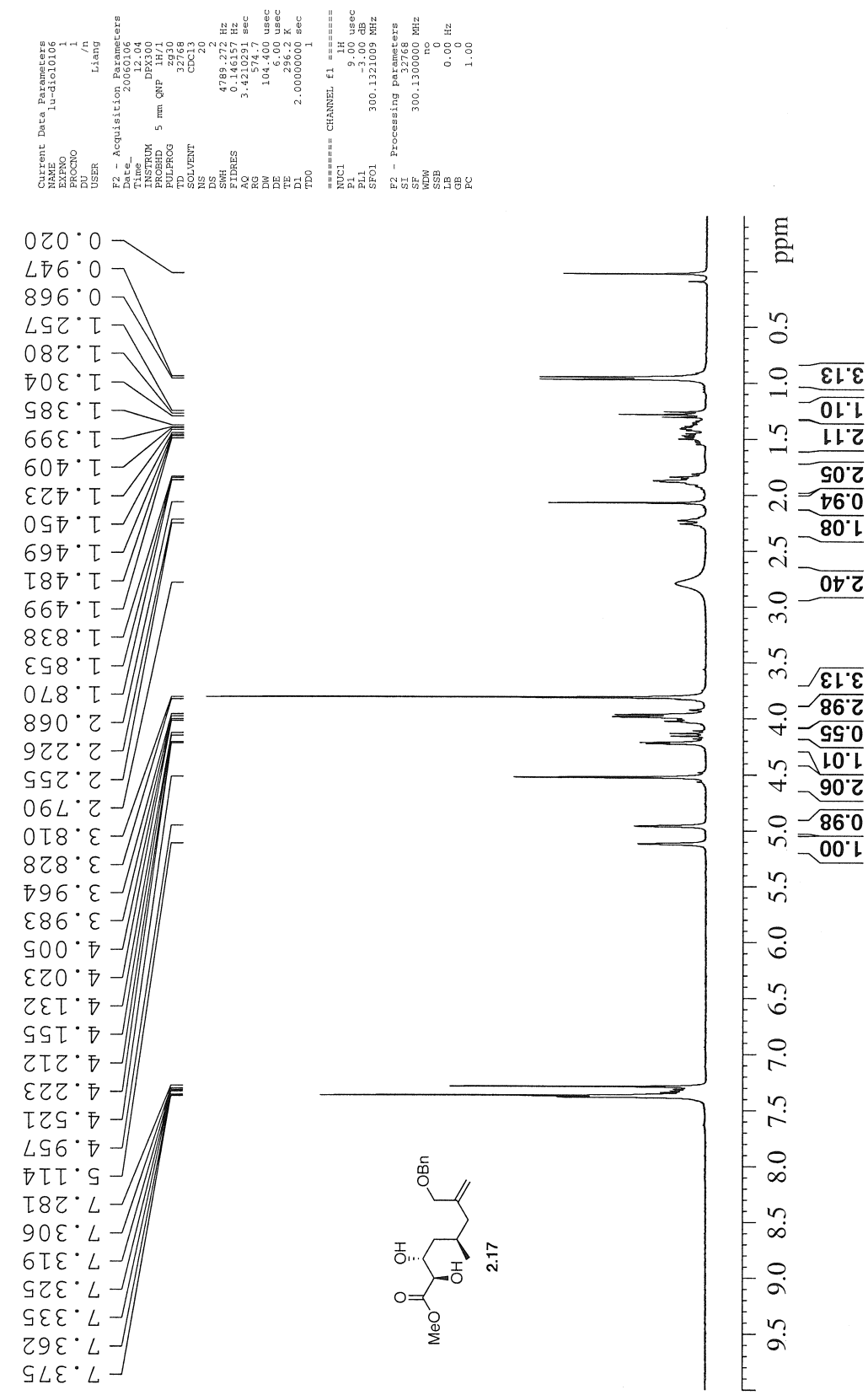

Current Data Parameters
NAME DF496_Aldol
EXPNO 14
PROCNO 1
DU /n
USER danf
F2 - Acquisition Parameters
Date_ 20040707
Time 17.24
INSTRUM dpx400
PROBHD 5 mm BBO Z-G
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 5995.204 Hz
FIDRES 0.182959 Hz
AQ 2.7329011 sec
RG 512
DW 83.400 usec
DE 6.00 usec
TE 300.0 K
D1 2.00000000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 11.30 usec
PL1 0.00 dB
SFO1 400.0126001 MHz
F2 - Processing parameters
SI 65536
SF 400.0100000 MHz
WDW EM
SSB 0
LB 0.70 Hz
GB 0
PC 1.00
1D NMR plot parameters
CX 21.00 cm
F1P 10.000 ppm
F1 4000.10 Hz
F2P -0.500 ppm
F2 -200.01 Hz
PPMCM 0.50000 ppm/c
HZCM 200.00500 Hz/cm
3.0793
1.0539
1.0502
1.0693
1.0596
1.0050
0.9743
6.2382
2.1340
1.0128
3.0539
1.0123
2.0029
1.0000
4.2623
4.1747
5.1787
integral
ppm
OBn
OH
O
O
O
OMe
MeO
2.9

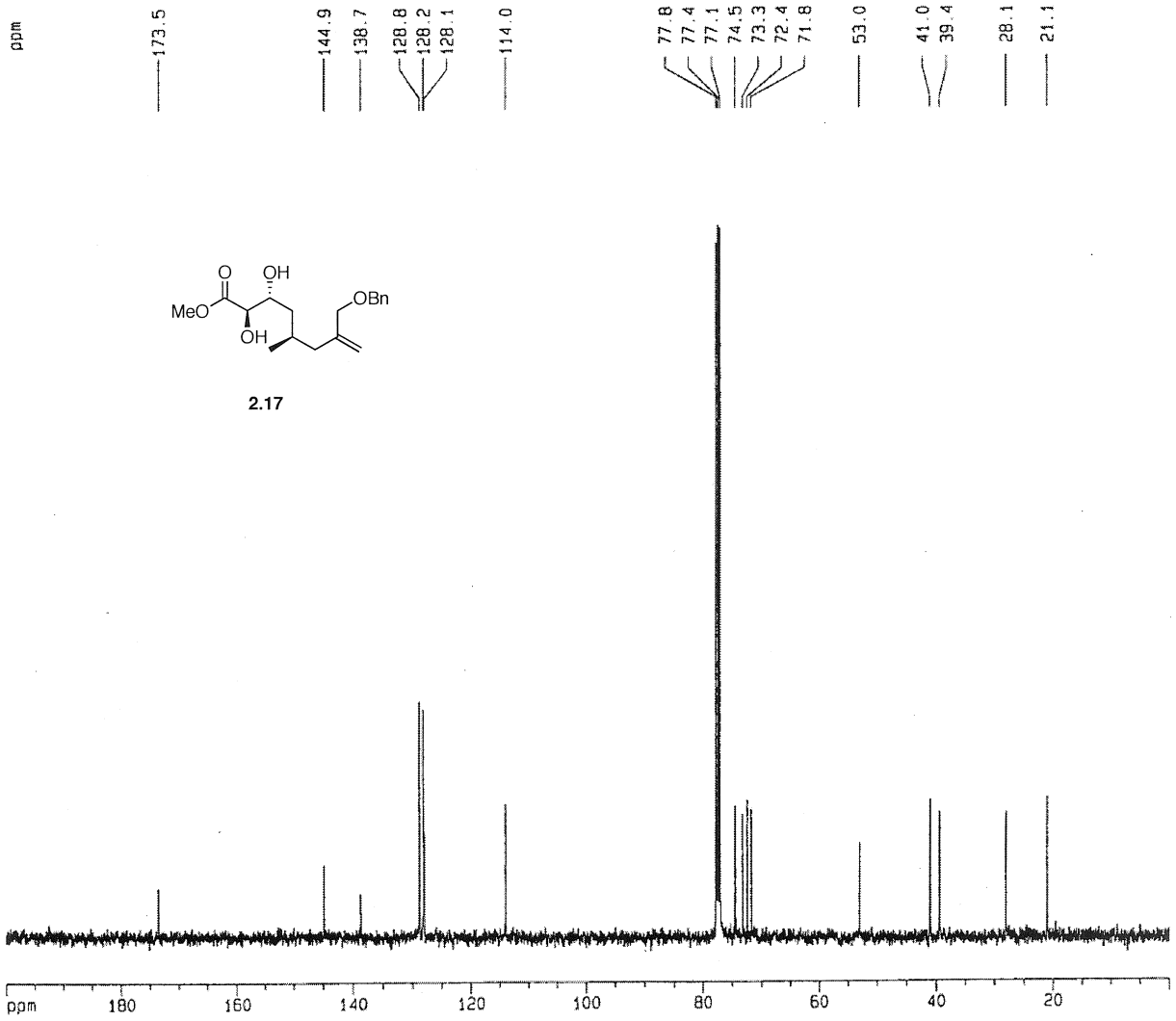



```
Current Data Parameters
NAME          DF49G_Aldol
EXPNO                  15
PROCNO                  1
OU                     /n
USER                 danf

F2 - Acquisition Parameters
Date_              20040707
Time                  17.47
INSTRUM              dpx400
PROBHD     5 mm BBO Z-G
PULPROG            zgpg30
TD                  65536
SOLVENT              CDCl3
NS                    4404
DS                       4
SWH              25125.629 Hz
FIDRES           0.383387 Hz
AQ               1.3042164 sec
RG                  2298.8
DW                19.900 usec
DE                   6.00 usec
TE                  300.0 K
D1               0.00300000 sec
D11              0.03000000 sec
D12              0.00002000 sec

********** CHANNEL f1 *******
NUC1                   13C
P1                    7.50 usec
PL1                  -3.00 dB
SFO1           100.5936186 MHz

********** CHANNEL f2 *******
CPDPRG2             waltz16
NUC2                    1H
PCPD2                80.00 usec
PL2                   0.00 dB
PL12                 17.40 dB
PL13                 18.00 dB
SFO2           400.0116000 MHz

F2 - Processing parameters
SI                    65536
SF             100.5825550 MHz
WDW                      EM
SSB                       0
LB                    3.00 Hz
GB                        0
PC                     1.40

1D NMR plot parameters
CX                   20.00 cm
F1P                200.000 ppm
F1                 20116.51 Hz
F2P                  0.000 ppm
F2                    0.00 Hz
PPMCM             10.00000 ppm/cm
HZCM              1005 [illegible]6 Hz/cm
```


Current Data Parameters
NAME methylester3
EXPNO 1
PROCNO 1
DU /n
USER Liang
F2 - Acquisition Parameters
Date_ 20051013
Time 15.34
INSTRUM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 20
DS 2
SWH 4789.272 Hz
FIDRES 0.146157 Hz
AQ 3.42102911 sec
RG 912.3
DW 104.400 usec
DE 6.00 usec
TE 296.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 8.30 usec
PL1 -3.00 dB
SFO1 300.1321009 MHz
F2 - Processing parameters
SI 32768
SF 300.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
7.377
7.362
7.329
7.317
7.281
7.006
6.997
6.977
6.968
6.738
6.710
5.112
4.963
4.795
4.766
4.526
4.397
4.370
4.040
4.027
3.993
3.967
3.765
3.758
3.507
1.867
1.593
0.980
0.959
0.090
0.021
9.34
4.00
4.01
1.02
1.00
1.06
2.06
0.96
1.09
2.94
6.07
3.39
0.97
0.99
2.11
2.41
1.15
2.73
ppm
OBn
OMe
OH
O
MeO
HO
OMe
2.28

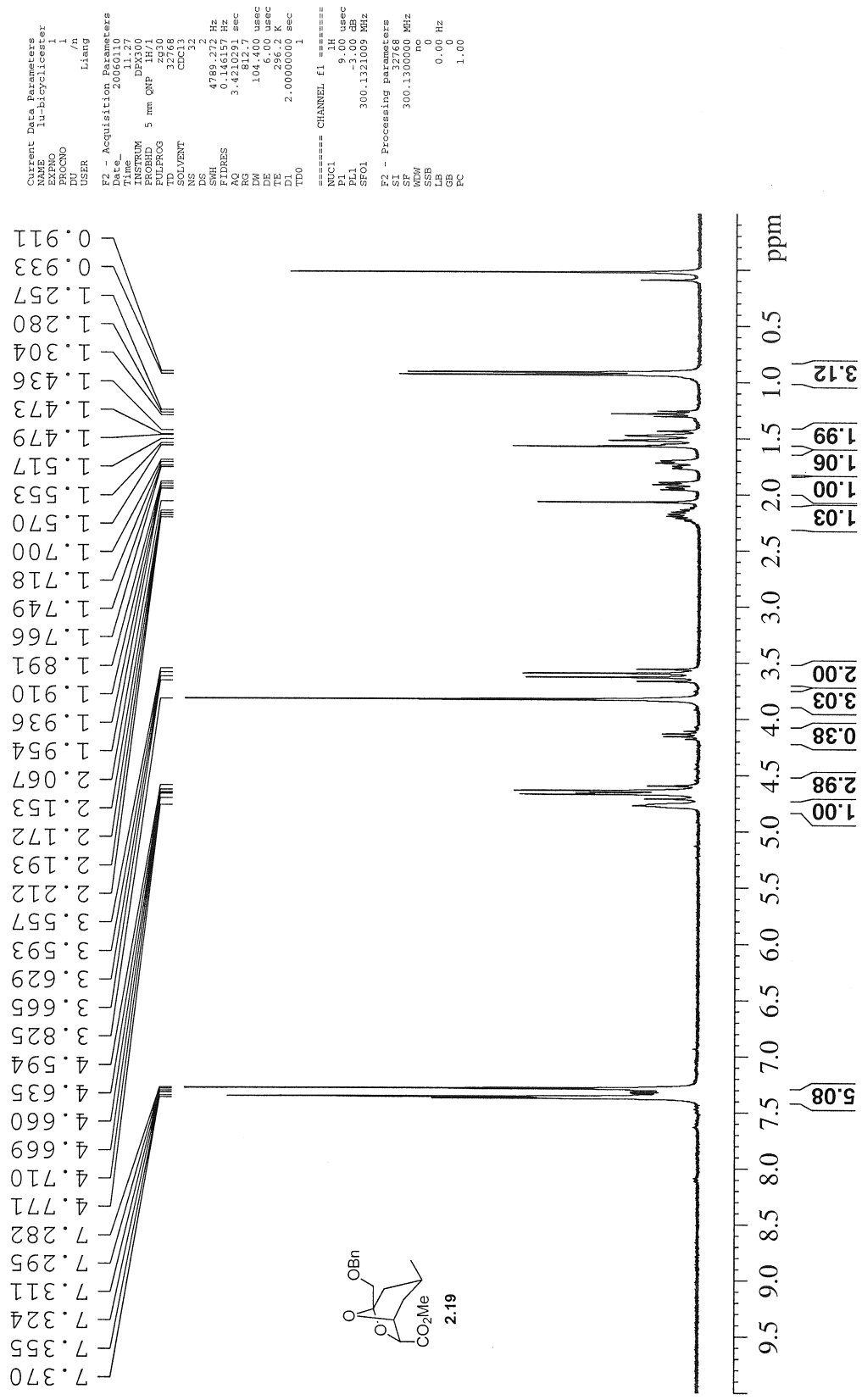

Current Data Parameters
NAME DF499_MeOH
EXPNO 8
PROCNO 1
DU /n
USER danf
F2 - Acquisition Parameters
Date_ 20040625
Time 14.10
INSTRUM dpx400
PROBHD 5 mm BBO 2-G
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 802
DS 4
SWH 25125.629 Hz
FIDRES 0.383387 Hz
AQ 1.3042164 sec
RG 4096
DW 19.900 usec
DE 6.00 usec
TE 300.0 K
D1 0.00300000 sec
D11 0.03600000 sec
D12 0.00002000 sec
CHANNEL f1
NUC1 13C
P1 7.50 usec
PL1 -3.00 dB
SFO1 100.5936186 MHz
CHANNEL f2
CPDPRG2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 0.00 dB
PL12 17.40 dB
PL13 18.00 dB
SFO2 400.0116000 MHz
F2 - Processing parameters
SI 65536
SF 100.5925550 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
1D NMR plot parameters
CX 20.00 cm
F1P 200.000 ppm
F1 20116.51 Hz
F2P 0.000 ppm
F2 0.00 Hz
PPMCM 10.00000 ppm/cm
HZCM 1005.[illegible] Hz/cm
21.3
28.0
40.0
40.9
52.1
55.5
70.8
72.5
73.3
77.1
77.4
77.8
78.7
82.2
89.7
113.7
113.8
114.0
128.1
128.2
128.7
128.8
129.6
129.7
132.0
138.6
144.9
159.5
159.7
171.2
OBn
OMe
OMe
OH
O
MeO
HO
2.28
ppm
20
40
60
80
100
120
140
160
180
ppm

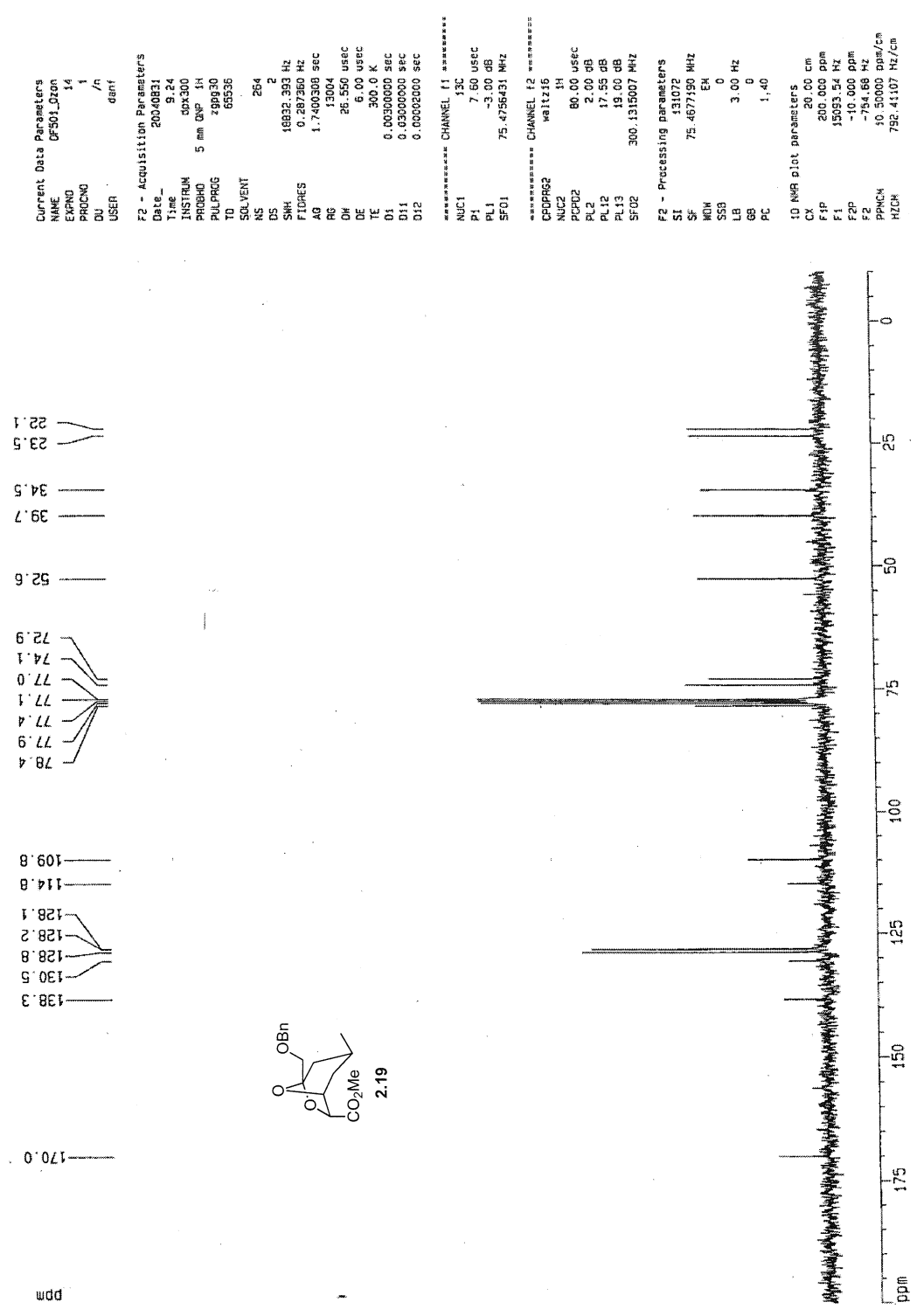

Current Data Parameters
NAME lu-diol0106
EXPNO 1
PROCNO /n
DU
USER Liang
F2 - Acquisition Parameters
Date_ 20060106
Time 12.04
INSTRUM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 20
DS 2
SWH 4789.272 Hz
FIDRES 0.146157 Hz
AQ 3.4210291 sec
RG 574.7
DW 104.400 usec
DE 6.00 usec
TE 296.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.00 usec
PL1 -3.00 dB
SFO1 300.1321009 MHz
F2 - Processing parameters
SI 32768
SF 300.1300000 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
7.375
7.362
7.335
7.325
7.319
7.306
7.281
5.114
4.957
4.521
4.223
4.212
4.155
4.132
4.023
4.005
3.983
3.964
3.828
3.810
2.790
2.255
2.226
2.068
1.870
1.853
1.838
1.499
1.481
1.469
1.450
1.423
1.409
1.399
1.385
1.304
1.280
1.257
0.968
0.947
0.020
OBn
OH
OH
O
MeO
2.17
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
ppm
1.00
0.98
2.06
1.01
0.55
2.98
3.13
2.40
1.08
0.94
2.05
2.11
1.10
3.13

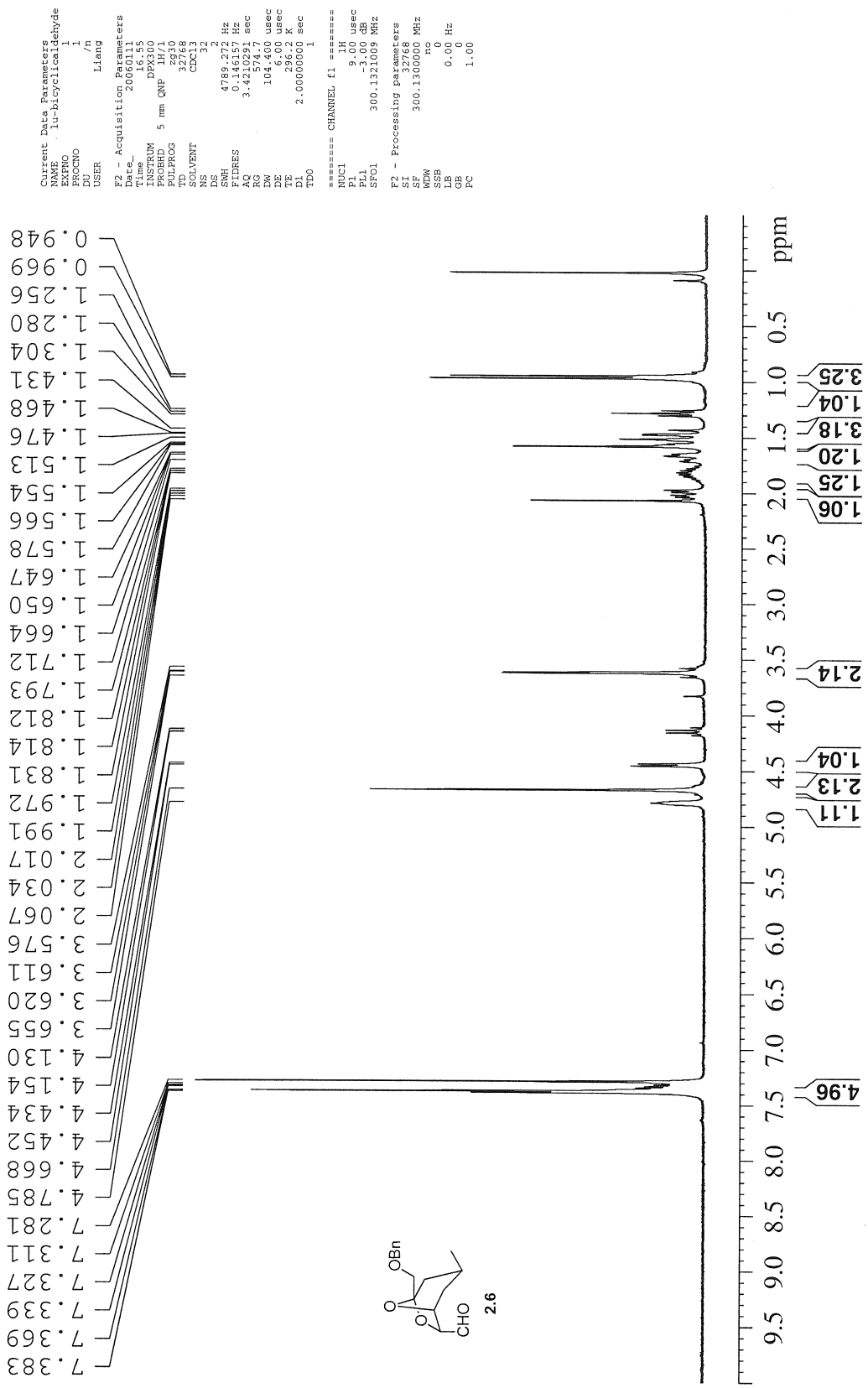


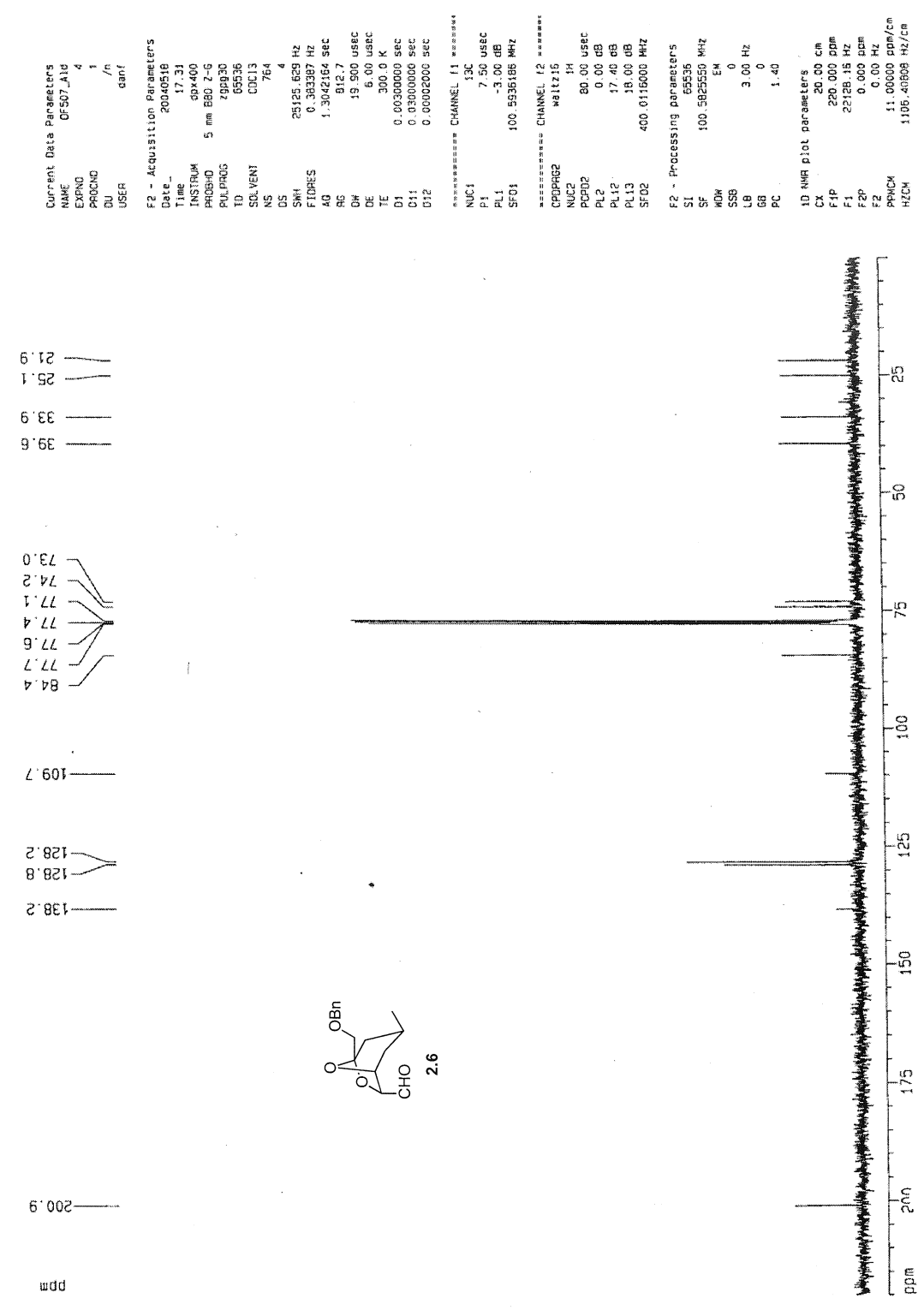
2.17

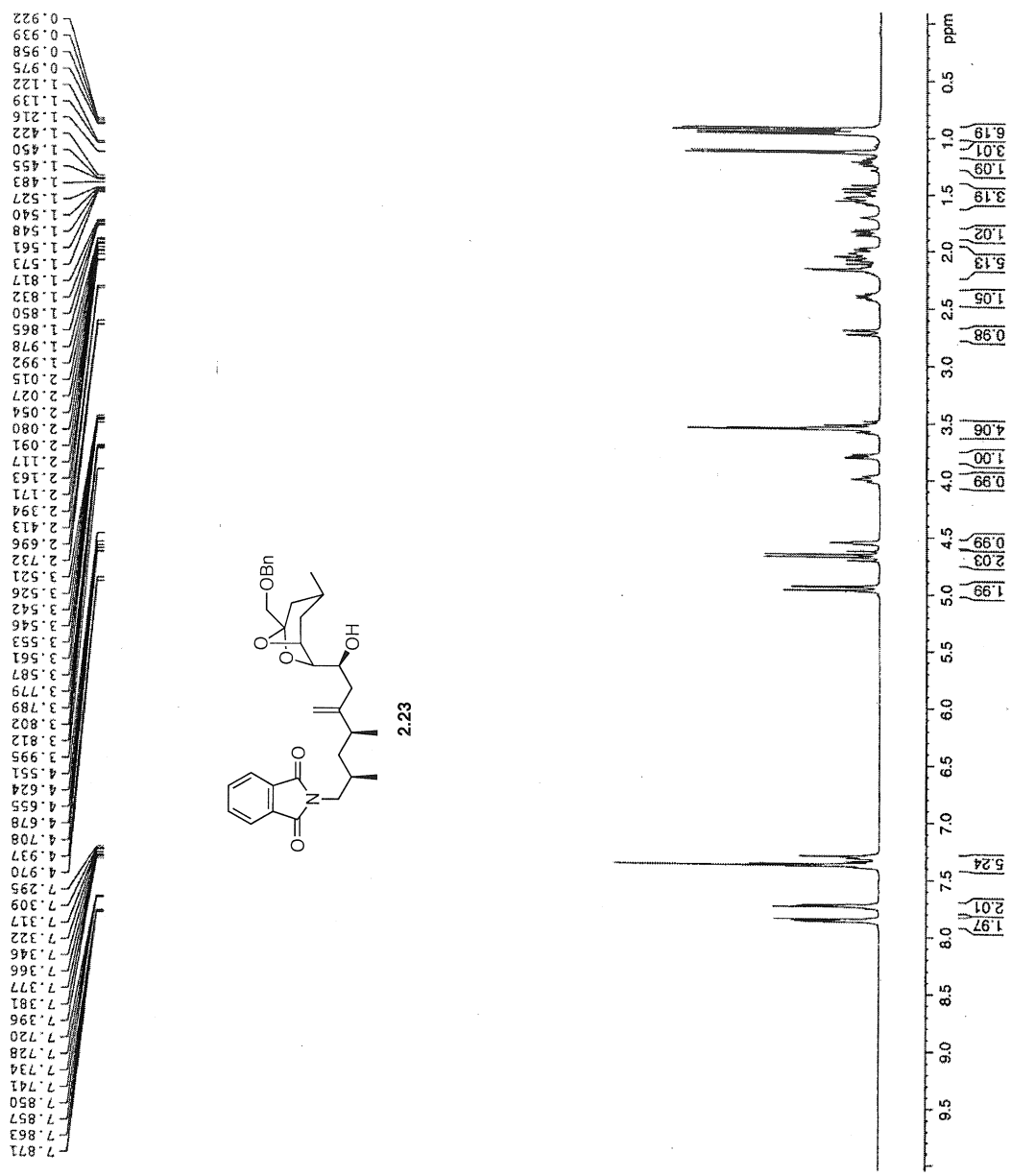
```
Current Data Parameters
NAME            DF500_CAN
EXPNO                   7
PROCNO                  1
DU                     /n
USER                danf

F2 - Acquisition Parameters
Date_           20040423
Time                16.02
INSTRUM           dpx400
PROBHD     5 mm BBO Z-G
PULPROG          zgpg30
TD                 65536
SOLVENT            CDCl3
NS                  1034
DS                     4
SWH            25125.629 Hz
FIDRES         0.383387 Hz
AQ             1.3042164 sec
RG                  1024
DW                19.900 usec
DE                 6.00 usec
TE                300.0 K
D1             0.00300000 sec
D11            0.03000000 sec
D12            0.00002000 sec

============ CHANNEL f1 ========
NUC1                  13C
P1                   7.50 usec
PL1                 -3.00 dB
SFO1          100.5936186 MHz

============ CHANNEL f2 ========
CPDPRG2           waltz16
NUC2                  1H
PCPD2               80.00 usec
PL2                  0.00 dB
PL12                17.40 dB
PL13                18.00 dB
SFO2          400.0116000 MHz

F2 - Processing parameters
SI                 65536
SF            100.5825550 MHz
WDW                   EM
SSB                    0
LB                  3.00 Hz
GB                     0
PC                  1.40

1D NMR plot parameters
CX                 20.00 cm
F1P               200.000 ppm
F1              20116.51 Hz
F2P                0.000 ppm
F2                 0.00 Hz
PPMCM             10.00000 ppm/cm
HZCM            1005.82556 Hz/cm
```

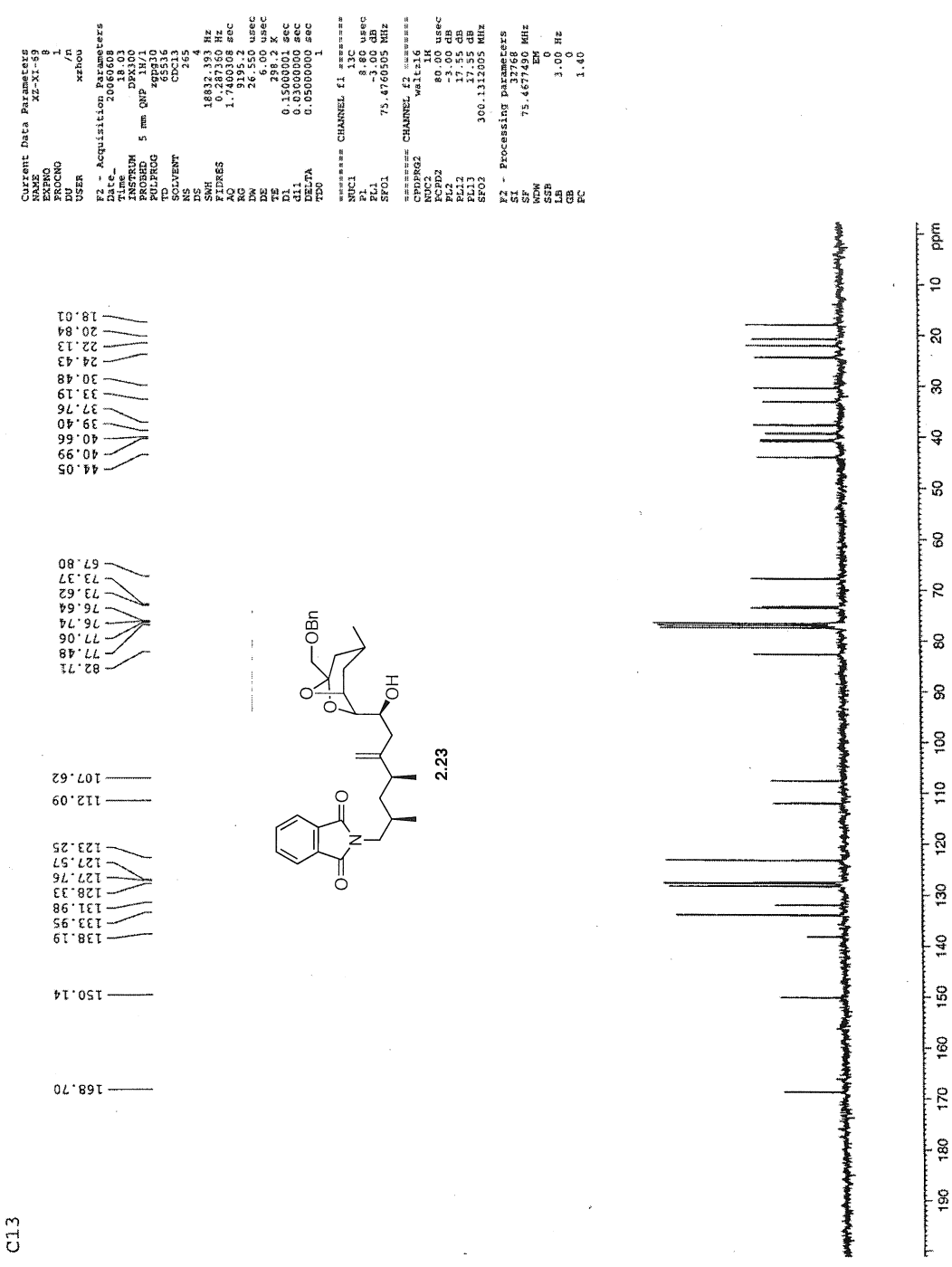

Current Data Parameters
NAME lu-bicyclicester
EXPNO 1
PROCNO 1
DU /n
USER Liang
F2 - Acquisition Parameters
Date_ 20060110
Time 11.27
INSTRUM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 4789.272 Hz
FIDRES 0.146157 Hz
AQ 3.4211091 sec
RG 8127
DW 104.400 usec
DE 6.00 usec
TE 296.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.00 usec
PL1 3.00 dB
SFO1 300.1321009 MHz
F2 - Processing parameters
SI 32768
SF 300.1300000 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
OBn
O
O
CO2Me
2.19
ppm
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
5.08
1.00
2.98
0.38
3.03
2.00
1.03
1.00
1.06
1.99
3.12
7.370
7.355
7.324
7.311
7.295
7.282
4.771
4.710
4.669
4.660
4.635
4.594
3.825
3.665
3.629
3.593
3.557
2.212
2.193
2.172
2.153
2.067
1.954
1.936
1.910
1.891
1.766
1.749
1.718
1.700
1.570
1.553
1.517
1.479
1.473
1.436
1.304
1.280
1.257
0.933
0.911

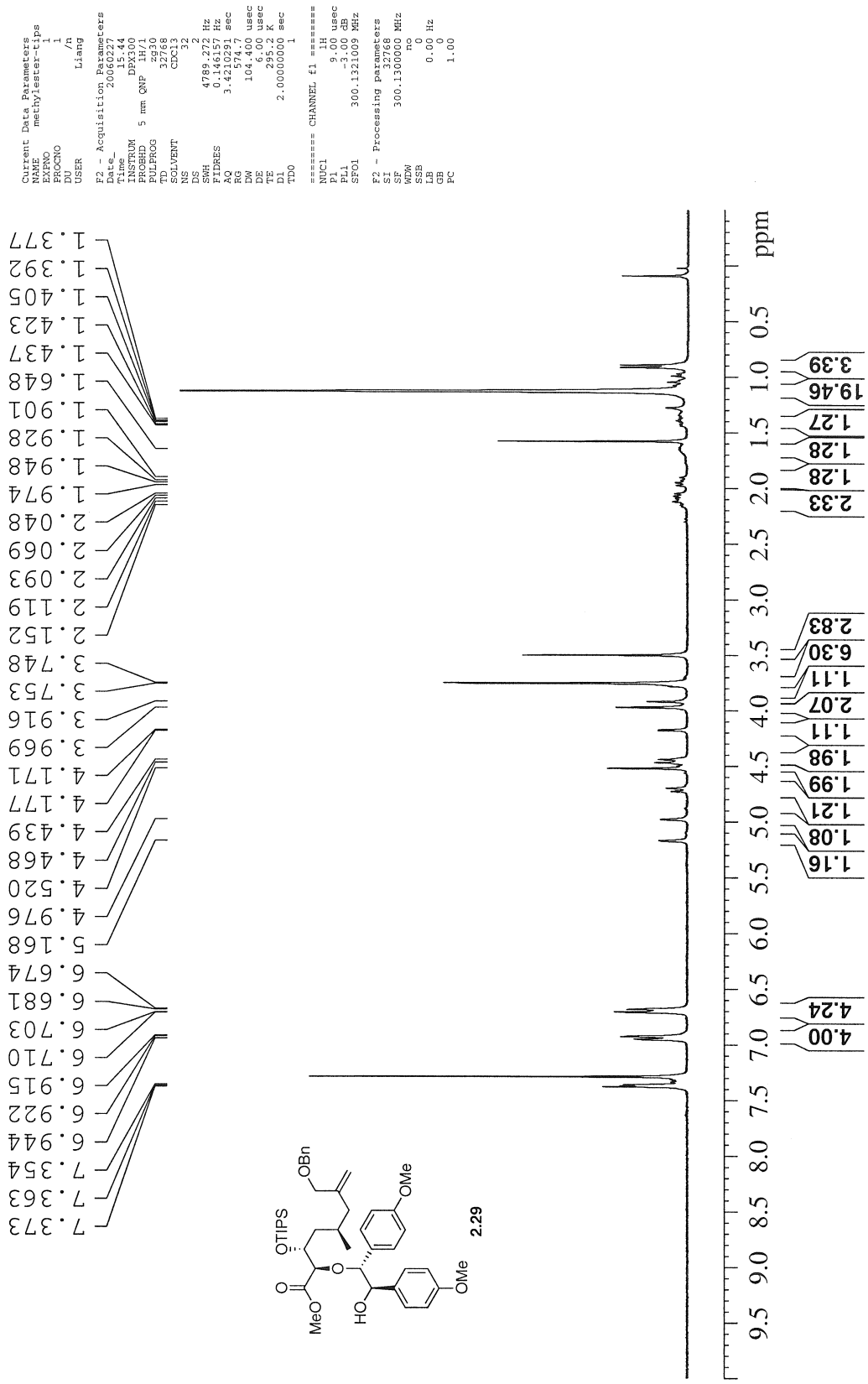

Current Data Parameters
NAME DP501_Ozon
EXPNO 14
PROCNO 1
DU /n
USER danf
F2 - Acquisition Parameters
Date_ 20040831
Time 9.24
INSTRUM dpx300
PROBHD 5 mm QNP 1H
PULPROG zgpg30
TD 65536
SOLVENT
NS 256
DS 2
SWH 10832.393 Hz
FIDRES 0.287360 Hz
AQ 1.7400308 sec
RG 13004
DW 26.550 usec
DE 6.00 usec
TE 300.0 K
D1 0.00300000 sec
D11 0.03000000 sec
D12 0.00002000 sec
CHANNEL f1
NUC1 13C
P1 7.60 usec
PL1 -3.00 dB
SFO1 75.4756431 MHz
CHANNEL f2
CPDPRG2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 2.00 dB
PL12 17.55 dB
PL13 19.00 dB
SFO2 300.1315007 MHz
F2 - Processing parameters
SI 131072
SF 75.4677190 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
1D NMR plot parameters
CX 20.00 cm
F1P 200.000 ppm
F1 15093.54 Hz
F2P -10.000 ppm
F2 -754.68 Hz
PPMCM 10.50000 ppm/cm
HZCM 792.41107 Hz/cm
170.0
138.3
130.5
128.8
128.2
128.1
114.8
109.8
78.4
77.9
77.4
77.1
77.0
74.1
72.9
52.6
39.7
34.5
23.5
22.1
OBn
O
O
CO2Me
2.19
ppm
0
25
50
75
100
125
150
175
ppm

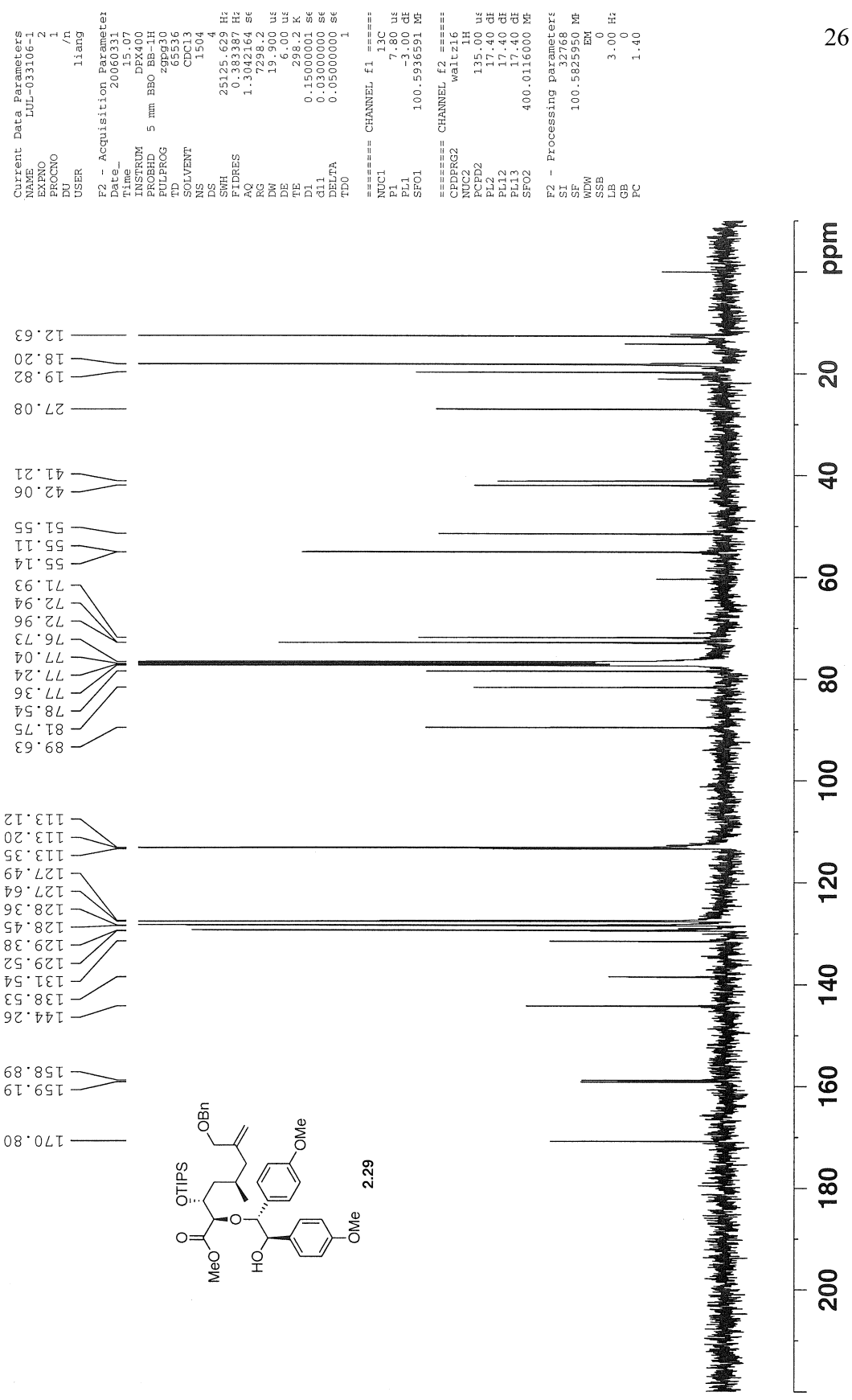

Current Data Parameters
NAME lu-bicyclicaldehyde
EXPNO 1
PROCNO /n
DU Liang
F2 - Acquisition Parameters
Date_ 20060111
Time 16.55
INSTRUM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 4789.272 Hz
FIDRES 0.146157 Hz
AQ 3.4210291 sec
RG 574.7
DW 104.400 usec
DE 6.00 usec
TE 296.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.00 usec
PL1 -3.00 dB
SFO1 300.1321009 MHz
F2 - Processing parameters
SI 32768
SF 300.1300000 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
7.383
7.369
7.339
7.327
7.311
7.281
4.785
4.668
4.452
4.434
4.154
4.130
3.655
3.620
3.611
3.576
2.067
2.034
2.017
1.991
1.972
1.831
1.814
1.812
1.793
1.712
1.664
1.650
1.647
1.578
1.566
1.554
1.513
1.476
1.468
1.431
1.304
1.280
1.256
0.969
0.948
OBn
O
O
CHO
2.6
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
4.96
1.11
2.13
1.04
2.14
1.06
1.25
1.20
3.18
1.04
3.25

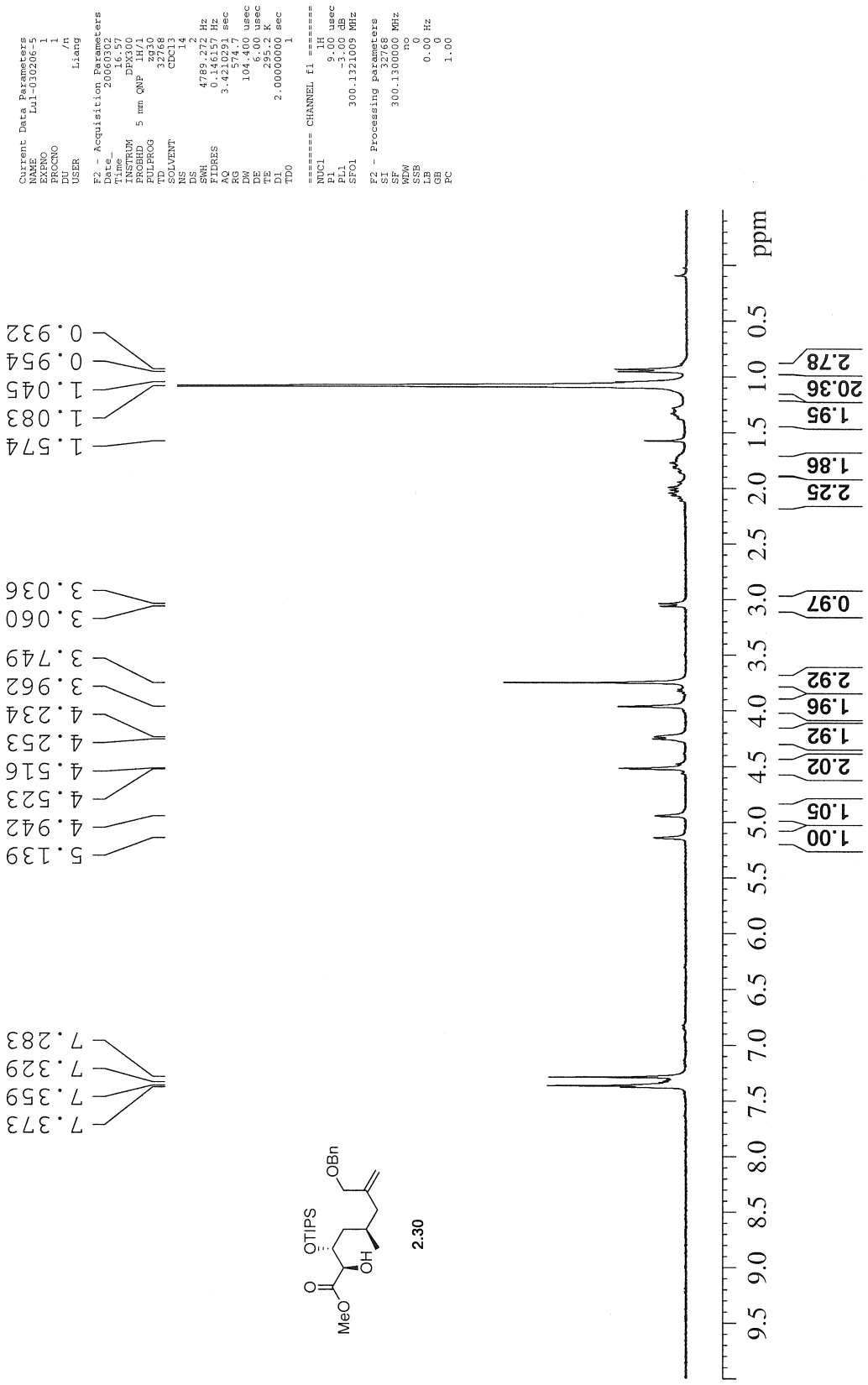

Current Data Parameters
NAME QF507_Ald
EXPNO 4
PROCNO 1
DU /n
USER conf
F2 - Acquisition Parameters
Date_ 20040518
Time 17.31
INSTRUM dpx400
PROBHD 5 mm BBO 2-G
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 764
DS 4
SWH 25125.629 Hz
FIDRES 0.383387 Hz
AQ 1.3042164 sec
RG 912.7
DW 19.900 usec
DE 6.00 usec
TE 300.0 K
D1 0.00300000 sec
D11 0.03000000 sec
D12 0.00002000 sec
========== CHANNEL f1 ========
NUC1 13C
P1 7.50 usec
PL1 -3.00 dB
SFO1 100.5936185 MHz
========== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 0.00 dB
PL12 17.40 dB
PL13 18.00 dB
SFO2 400.0116000 MHz
F2 - Processing parameters
SI 65536
SF 100.5925550 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
1D NMR plot parameters
CX 20.00 cm
F1P 220.000 ppm
F1 22128.15 Hz
F2P 0.000 ppm
F2 0.00 Hz
PPMCM 11.00000 ppm/cm
HZCM 1105.40808 Hz/cm
200.9
138.2
128.8
128.2
109.7
84.4
77.7
77.6
77.4
77.1
74.2
73.0
39.6
33.9
25.1
21.9
OBn
O
O
CHO
2.6
ppm
200
175
150
125
100
75
50
25

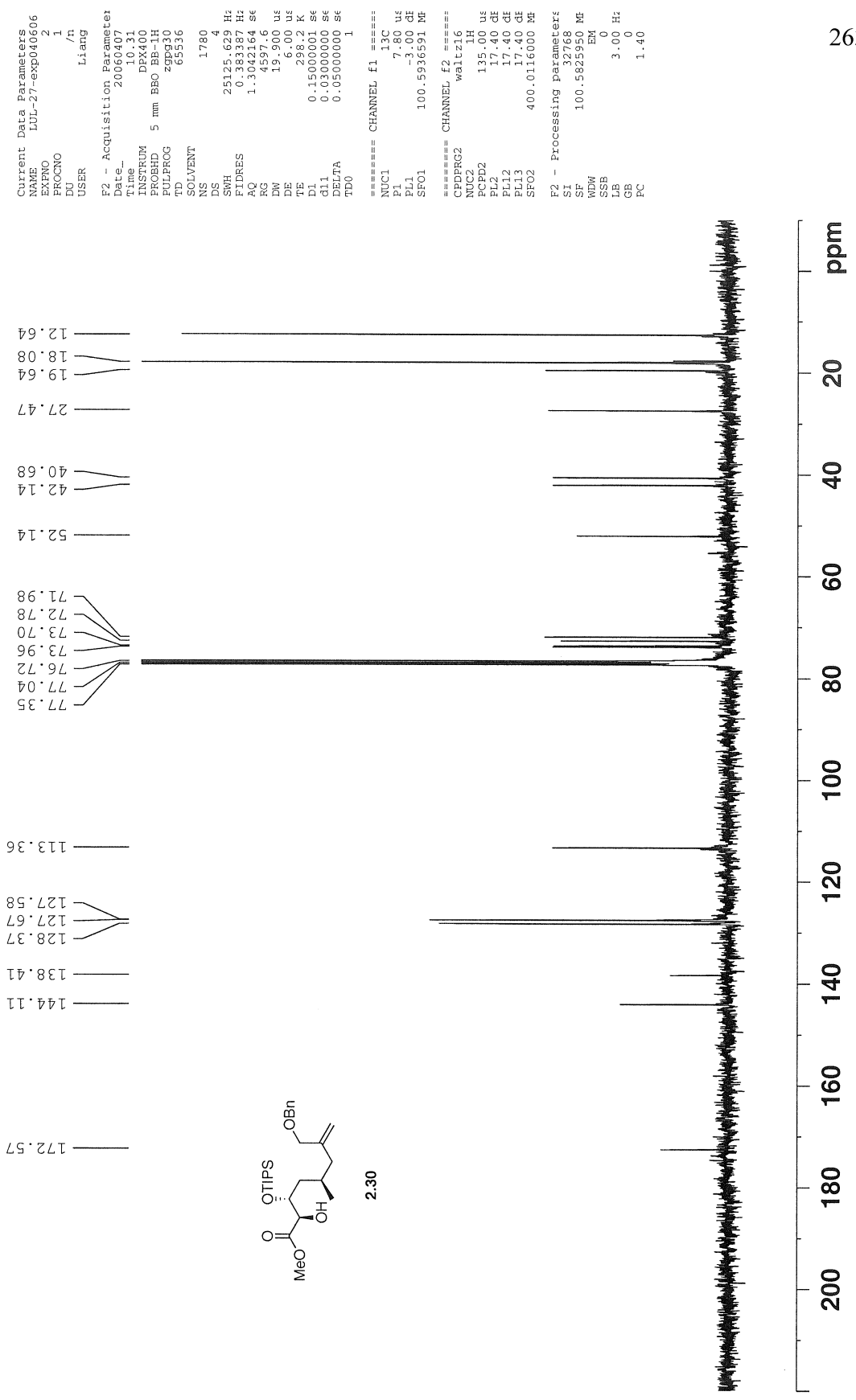

Current Data Parameters
NAME XZ-XI-72
EXPNO 3
PROCNO 1
DU /m
USER xzhou
F2 - Acquisition Parameters
Date_ 20060608
Time 19.47
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5559540 sec
RG 143.7
DW 78.000 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
NUC1 1H
P1 14.70 usec
PL1 0.00 dB
SFO1 400.0128001 MHz
F2 - Processing parameters
SI 32768
SF 400.0100000 MHz
WDW EM
SSB 0
LB 0.70 Hz
GB 0
PC 1.00
OBn
OH
2.23
ppm
6.19
3.01
1.09
3.19
1.02
5.13
1.05
0.98
4.06
1.00
0.99
0.99
2.03
1.99
5.24
2.01
1.97

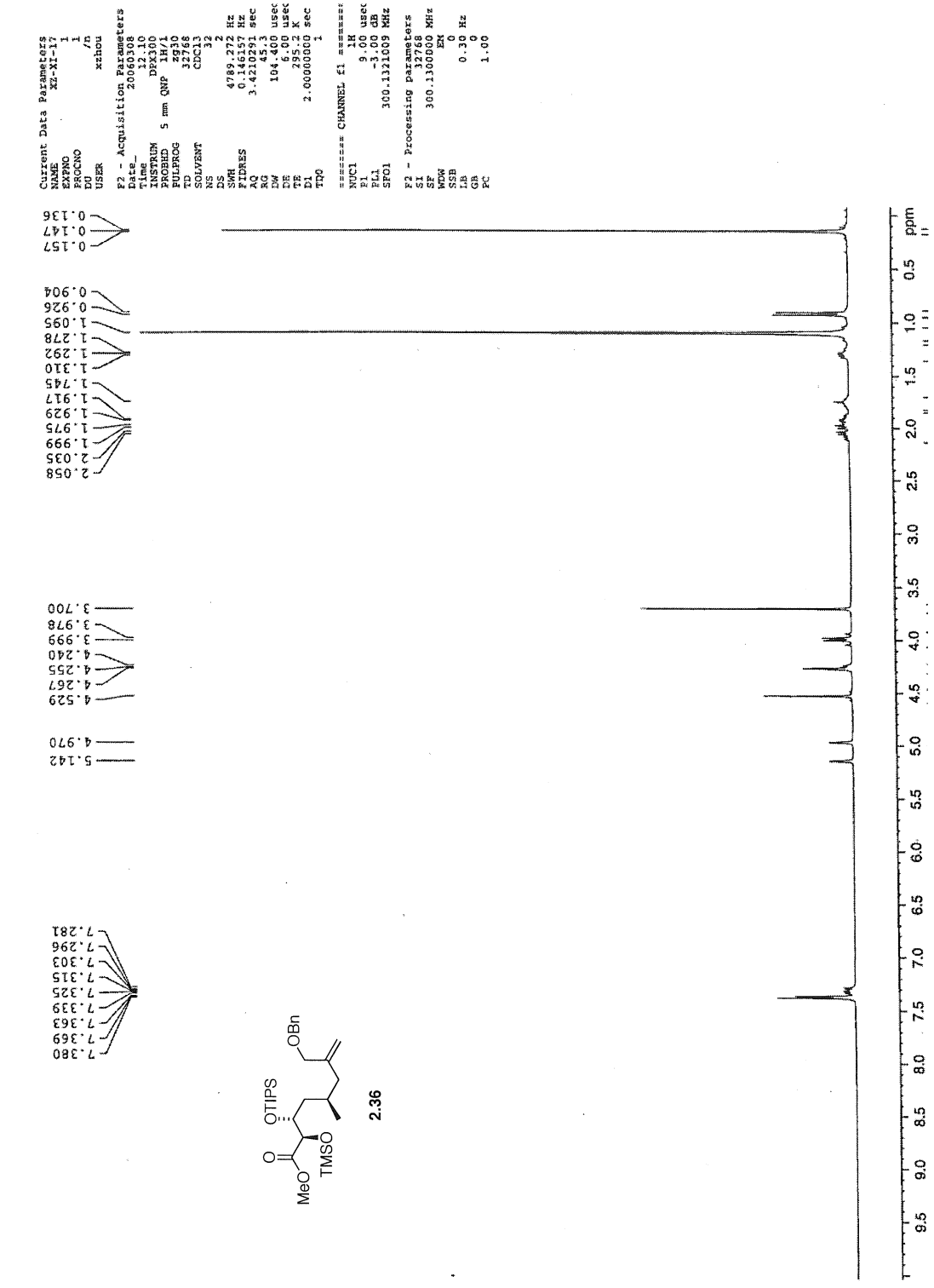

C13
Current data Parameters
NAME XZ-XI-69
EXPNO 8
PROCNO 1
DU /n
USER xzhou
F2 - Acquisition Parameters
Date_ 20060608
Time_ 18.03
INSTRUM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 265
DS 4
SWH 18832.393 Hz
FIDRES 0.2873360 Hz
AQ 1.7400308 sec
RG 9195.2
DW 26.550 usec
DE 6.00 usec
TE 298.2 K
D1 0.15000001 sec
d11 0.03000000 sec
DELTA 0.05000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 8.80 usec
PL1 -3.00 dB
SFO1 75.4760505 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 -3.00 dB
PL12 17.55 dB
PL13 17.55 dB
SFO2 300.1312005 MHz
F2 - Processing parameters
SI 32768
SF 75.4677490 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
168.70
150.14
138.19
133.95
131.98
128.33
127.76
127.57
123.25
112.09
107.62
82.71
77.48
77.06
76.74
76.64
73.62
73.37
67.80
44.05
40.99
40.66
39.40
37.76
33.19
30.48
24.43
22.13
20.84
18.01
OBn
OH
2.23
ppm

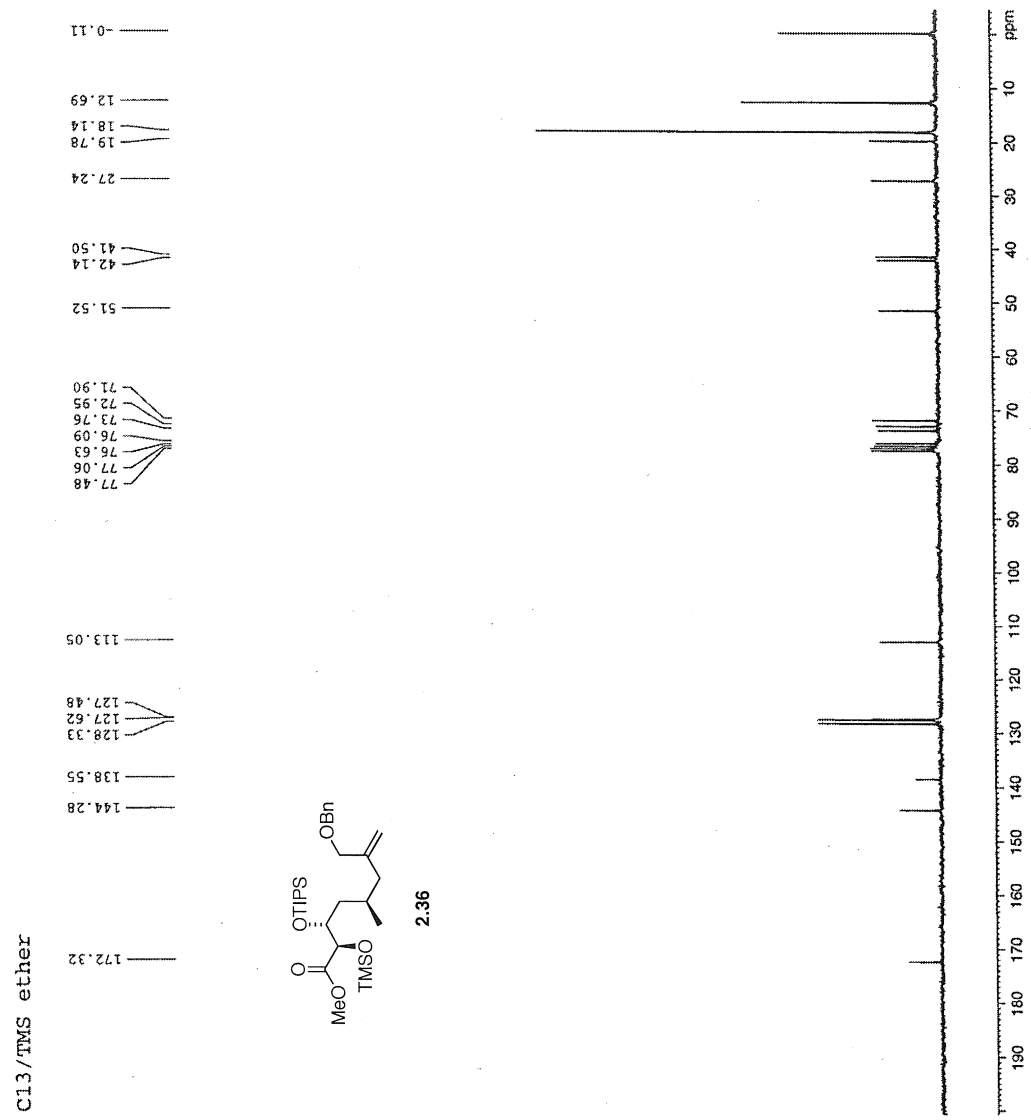

Current Data Parameters
NAME methylester-tips
EXPNO 1
PROCNO 1
DU /n
USER Liang
F2 - Acquisition Parameters
Date_ 20060227
Time 15.44
INSTRUM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 4789.272 Hz
FIDRES 0.146157 Hz
AQ 3.4210291 sec
RG 574.7
DW 104.400 usec
DE 6.00 usec
TE 295.7 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.00 usec
PL1 -3.00 dB
SFO1 300.1321009 MHz
F2 - Processing parameters
SI 32768
SF 300.1300000 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
7.373
7.363
7.354
6.944
6.922
6.915
6.710
6.703
6.681
6.674
5.168
4.976
4.520
4.468
4.439
4.177
4.171
3.969
3.916
3.753
3.748
2.152
2.119
2.093
2.069
2.048
1.974
1.948
1.928
1.901
1.648
1.437
1.423
1.405
1.392
1.377
OTIPS
OBn
OMe
OMe
MeO
HO
O
O
2.29
4.00
4.24
1.16
1.08
1.21
1.99
1.98
1.11
2.07
1.11
6.30
2.83
2.33
1.28
1.28
1.27
19.46
3.39
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
ppm

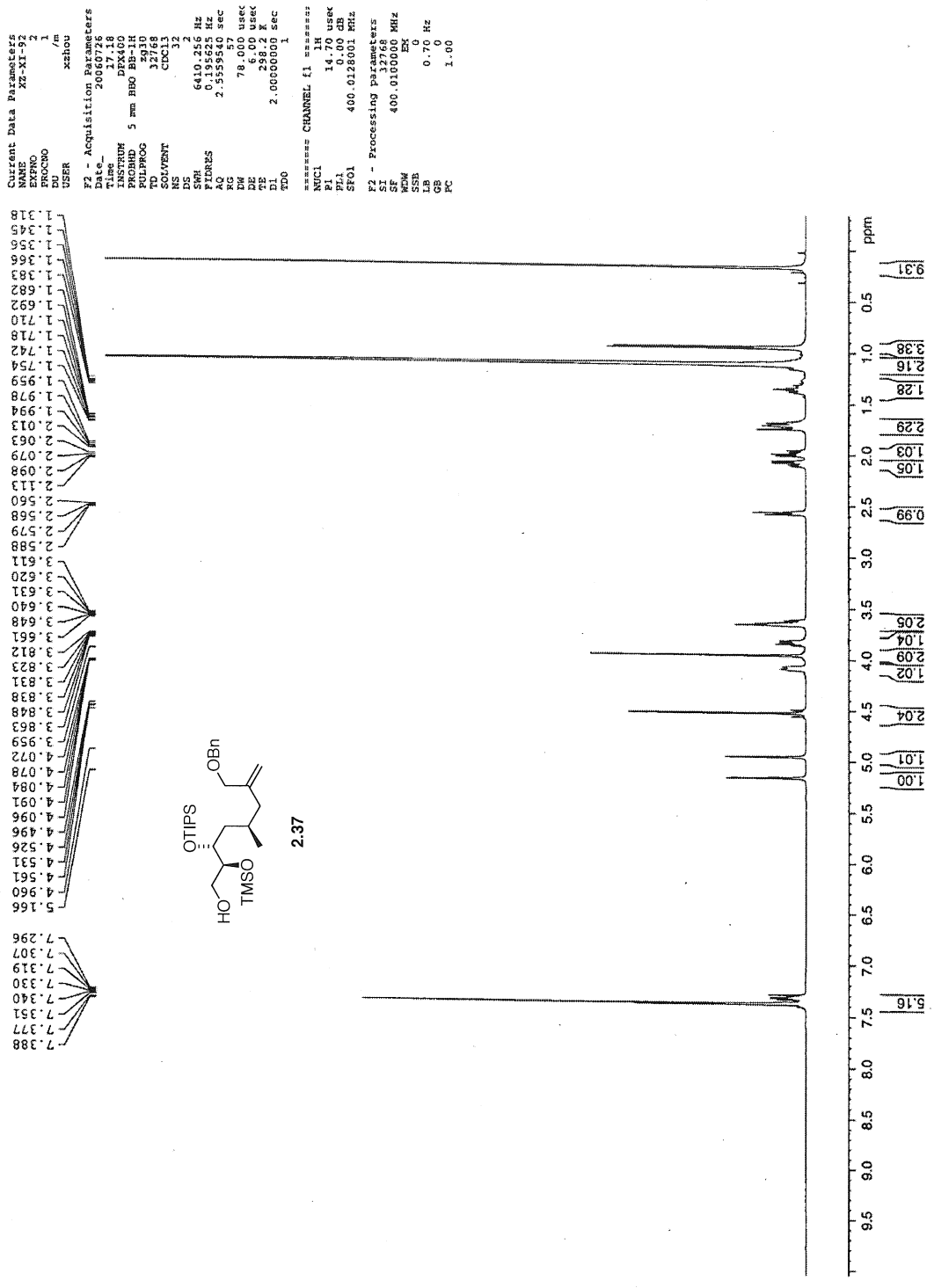

Current Data Parameters
NAME LUL-033106-1
EXPNO 2
PROCNO 1
DU /n
USER liang
F2 - Acquisition Parameter
Date_ 20060331
Time 15.07
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 1504
DS 4
SWH 25125.629 Hz
FIDRES 0.383387 Hz
AQ 1.3042164 se
RG 7298.2
DW 19.900 us
DE 6.00 us
TE 298.2 K
D1 0.15000001 se
d11 0.03000000 se
DELTA 0.05000000 se
TD0 1
======== CHANNEL f1 ======
NUC1 13C
P1 7.80 us
PL1 -3.00 dB
SFO1 100.5936591 MH
======== CHANNEL f2 ======
CPDPRG2 waltz16
NUC2 1H
PCPD2 135.00 us
PL2 17.40 dB
PL12 17.40 dB
PL13 17.40 dB
SFO2 400.0116000 MH
F2 - Processing parameters
SI 32768
SF 100.5825950 MH
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
170.80
159.19
158.89
144.26
138.53
131.54
129.52
129.38
128.45
128.36
127.64
127.49
113.35
113.20
113.12
89.63
81.75
78.54
77.36
77.24
77.04
76.73
72.96
72.94
71.93
55.14
55.11
51.55
42.06
41.21
27.08
19.82
18.20
12.63
OTIPS
OBn
OMe
OMe
MeO
HO
O
2.29
200
180
160
140
120
100
80
60
40
20
ppm

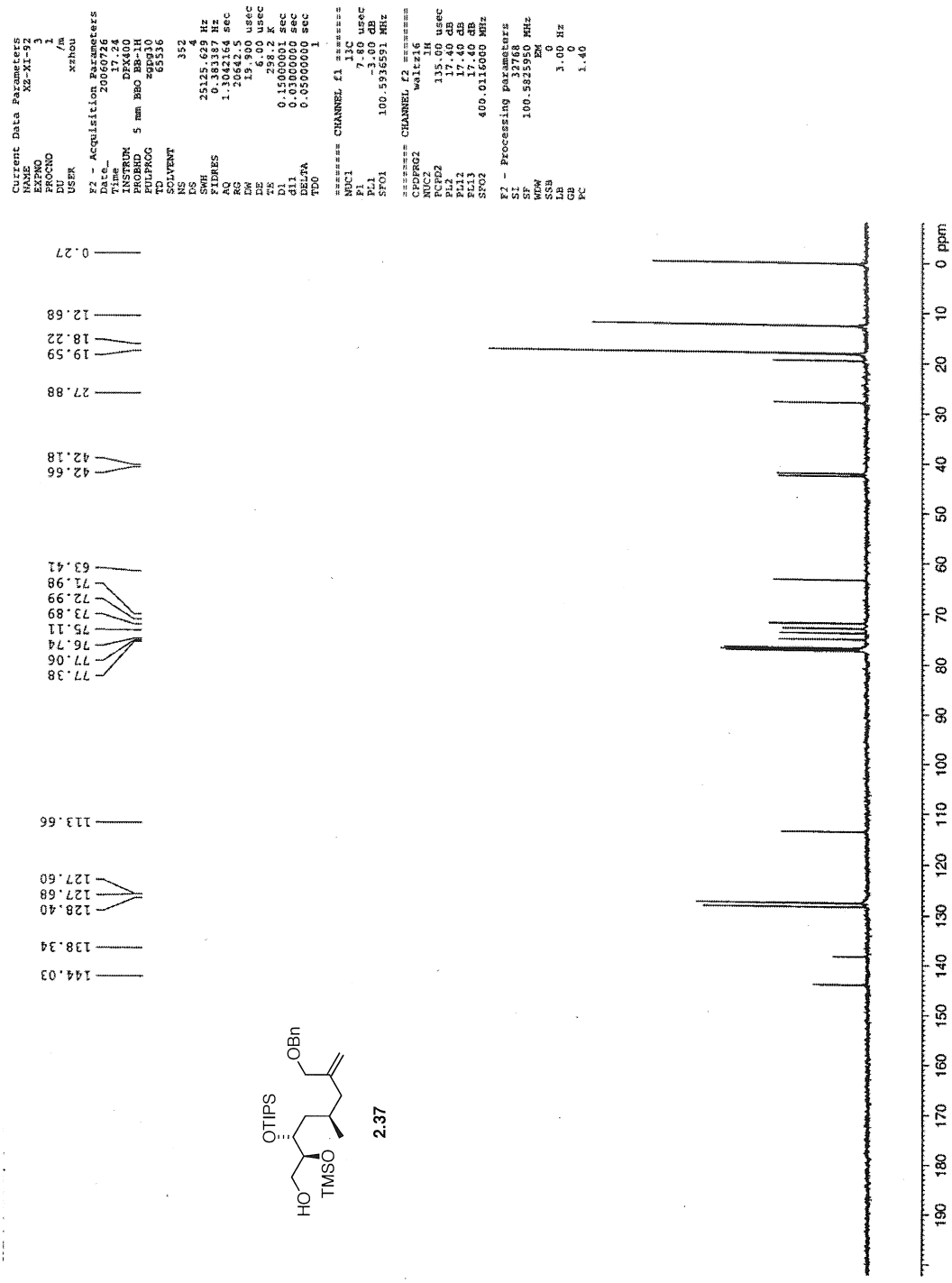

Current Data Parameters
NAME Lu1-030206-5
EXPNO 1
PROCNO 1
DU /n
USER Liang
F2 - Acquisition Parameters
Date_ 20060302
Time 16.57
INSTRUM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 14
DS 2
SWH 4789.272 Hz
FIDRES 0.146157 Hz
AQ 3.42102291 sec
RG 574.7
DW 104.400 usec
DE 6.00 usec
TE 285.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.00 usec
PL1 -3.00 dB
SFO1 300.1321009 MHz
F2 - Processing parameters
SI 32768
SF 300.1300000 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
7.373
7.359
7.329
7.283
5.139
4.942
4.523
4.516
4.253
4.234
3.962
3.749
3.060
3.036
1.574
1.083
1.045
0.954
0.932
1.00
1.05
2.02
1.92
1.96
2.92
0.97
2.25
1.86
1.95
20.36
2.78
OTIPS
OBn
MeO
OH
O
2.30
ppm

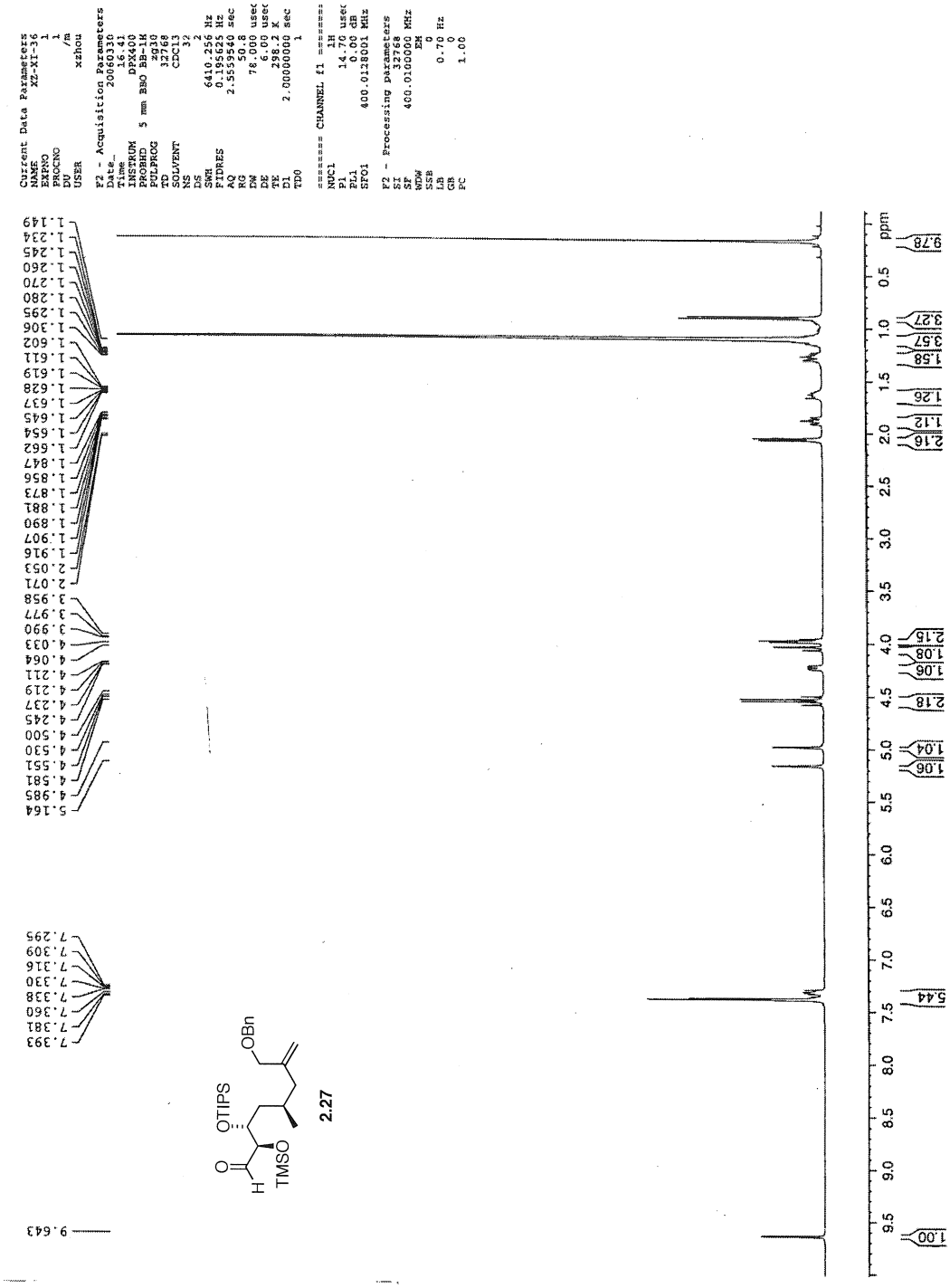

Current Data Parameters
NAME LUL-27-exp0406
EXPNO 2
PROCNO 1
DU /n
USER Liang
F2 - Acquisition Parameter
Date_ 20060407
Time 10.31
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT
NS 1780
DS 4
SWH 25125.629 Hz
FIDRES 0.383387 Hz
AQ 1.3042164 se
RG 4597.6
DW 19.900 us
DE 6.00 us
TE 298.2 K
D1 0.15000001 se
d11 0.03000000 se
DELTA 0.05000000 se
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 7.80 us
PL1 -3.00 dB
SFO1 100.5936591 MH
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 135.00 us
PL2 17.40 dB
PL12 17.40 dB
PL13 17.40 dB
SFO2 400.0116000 MH
F2 - Processing parameters
SI 32768
SF 100.5825950 MH
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
172.57
144.11
138.41
128.37
127.67
127.58
113.36
77.35
77.04
76.72
73.96
73.70
72.78
71.98
52.14
42.14
40.68
27.47
19.64
18.08
12.64
OTIPS
OBn
OH
MeO
O
2.30
ppm
200
180
160
140
120
100
80
60
40
20

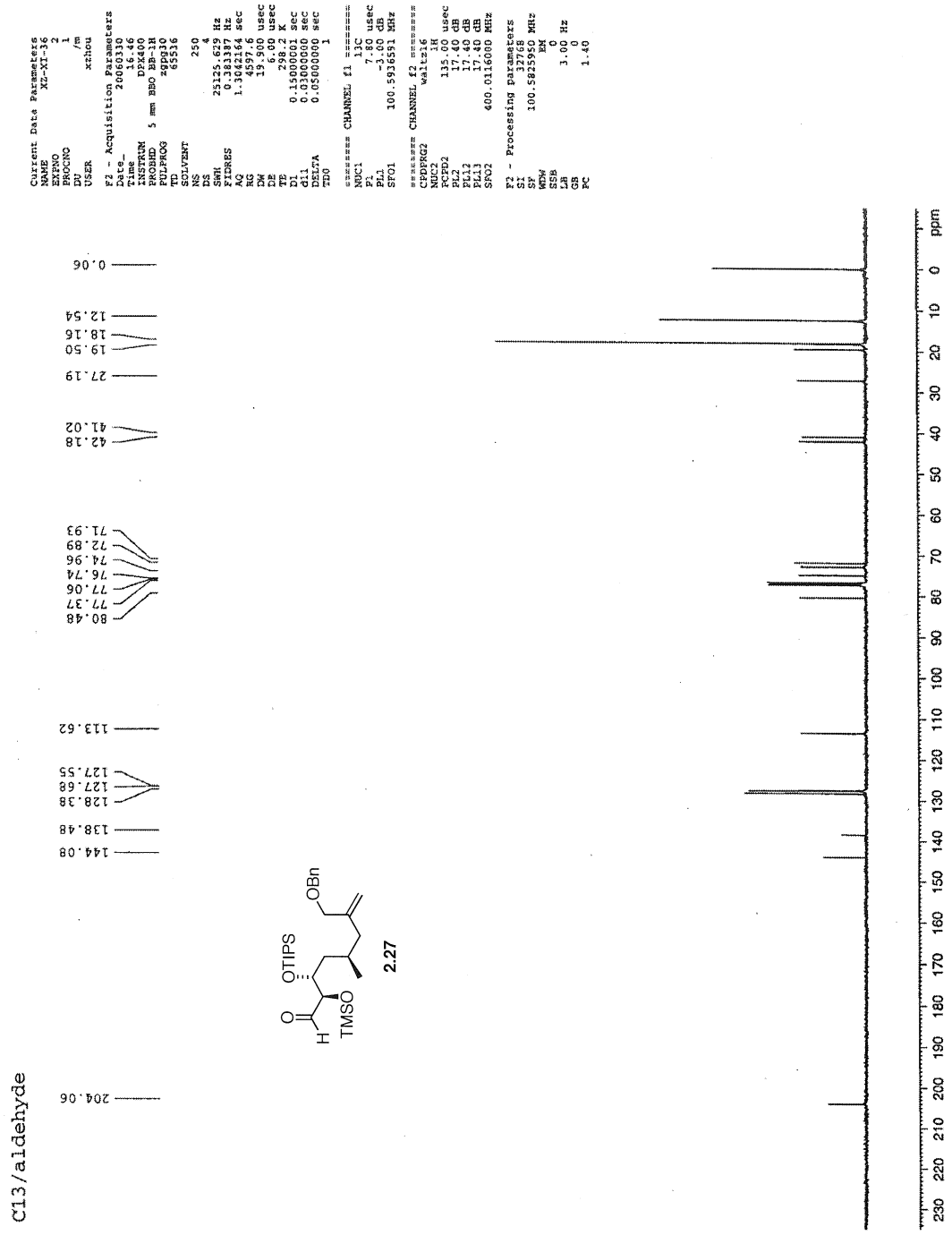

Current Data Parameters
NAME XZ-XI-17
EXPNO 1
PROCNO 1
DU /n
USER xzhou
F2 - Acquisition Parameters
Date_ 20060308
Time 21.10
INSTRUM DPX300
PROBHD 5 mm QNP
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 4789.272 Hz
FIDRES 0.146157 Hz
AQ 3.4210291 sec
RG 45.3
DW 104.400 usec
DE 6.00 usec
TE 295.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.00 usec
PL1 -3.00 dB
SFO1 300.1321009 MHz
F2 - Processing parameters
SI 32768
SF 300.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
0.136
0.147
0.157
0.904
0.926
1.095
1.278
1.292
1.310
1.745
1.917
1.929
1.975
1.999
2.035
2.058
3.700
3.978
3.999
4.240
4.255
4.267
4.529
4.970
5.142
7.281
7.296
7.303
7.315
7.325
7.339
7.363
7.369
7.380
OTIPS
OBn
O
MeO
TMSO
2.36
ppm

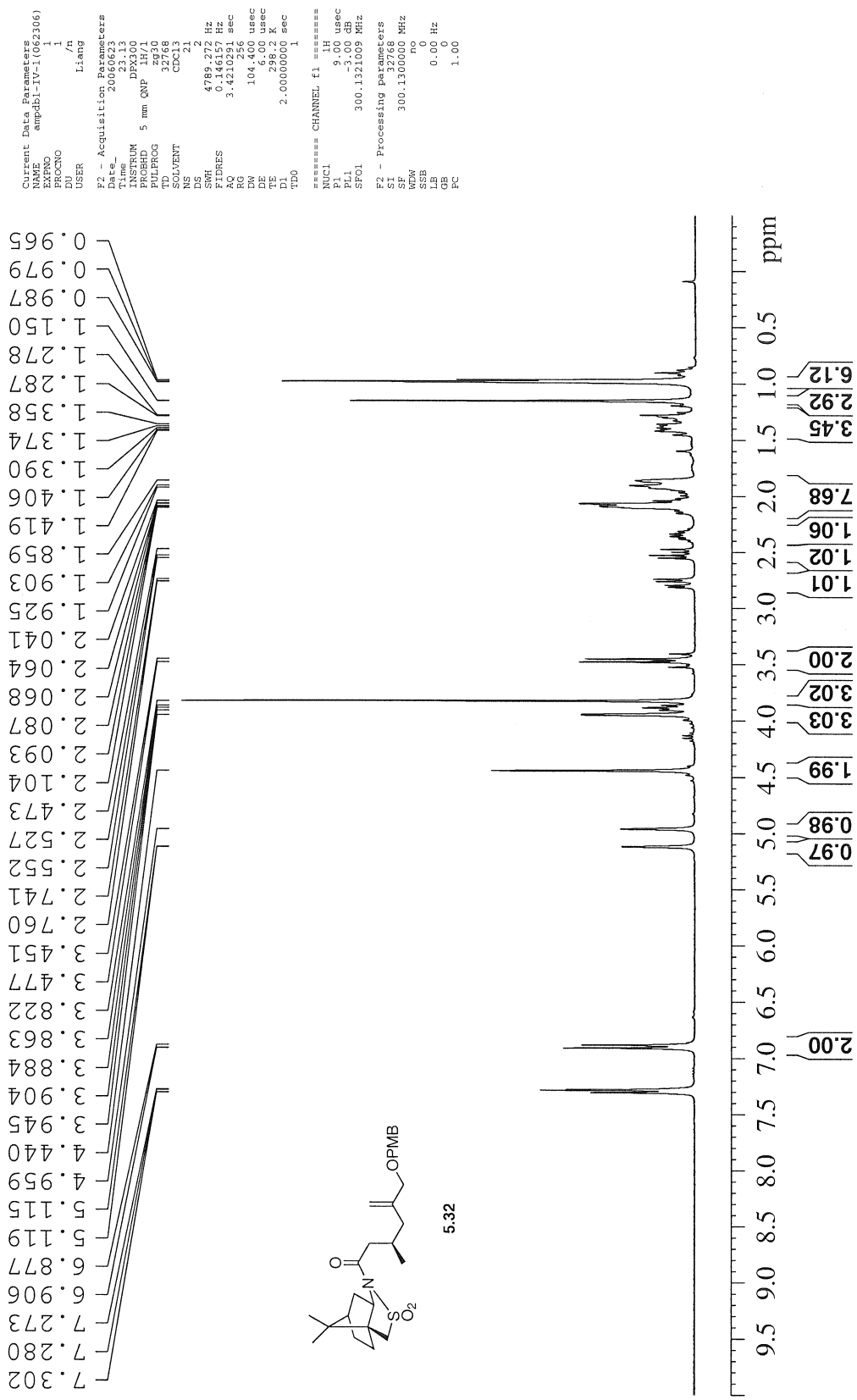

C13/TMS ether
Current Data Parameters
NAME XZ-XI-17
EXPNO 2
PROCNO 1
DU /n
USER xzhou
F2 - Acquisition Parameters
Date_ 20060308
Time 12.15
INSTRUM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 170
DS 4
SWH 18832.393 Hz
FIDRES 0.2871360 Hz
AQ 1.7400308 sec
RG 13004
DW 26.550 usec
DE 6.00 usec
TE 296.2 K
D1 0.15000001 sec
d11 0.03000000 sec
DELTA 0.05000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 8.80 usec
PL1 -3.00 dB
SFO1 75.4760505 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 -3.00 dB
PL12 17.55 dB
PL13 17.55 dB
SFO2 300.1312005 MHz
F2 - Processing parameters
SI 32768
SF 75.4677490 MHz
WDW EM
SSB 3.00 Hz
LB 0
GB 0
PC 1.40
-0.11
12.69
18.14
19.78
27.24
41.50
42.14
51.52
71.90
72.95
73.76
76.09
76.63
77.06
77.48
113.05
127.48
127.62
128.33
138.55
144.28
172.32
OTIPS
OBn
MeO
TMSO
O
2.36
ppm

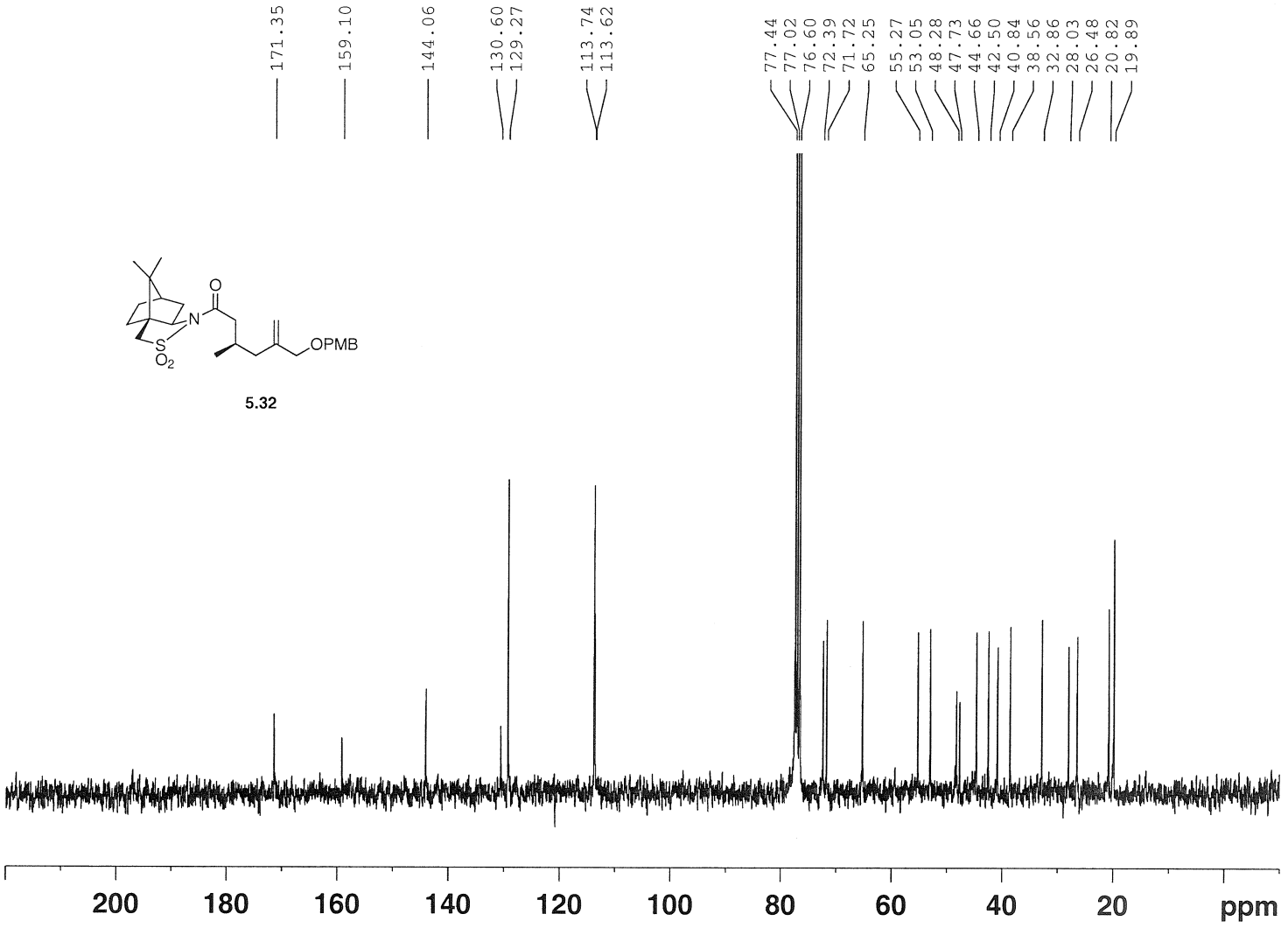

Current Data Parameters
NAME XZ-XI-92
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20060726
Time 17.18
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5559540 sec
RG 57
DW 78.000 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
F2 - Processing parameters
SI 32768
SF 400.0100000 MHz
WDW EM
SSB 0
LB 0.70 Hz
GB 0
PC 1.00
OTIPS
OBn
HO
TMSO
2.37
ppm


Current Data Parameters
NAME X2-XI-92
EXPNO 3
PROCNO 1
F2 - Acquisition Parameters
Date_ 20060726
Time 17.24
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT
NS 352
DS 4
SWH 25125.629 Hz
FIDRES 0.383387 Hz
AQ 1.3042164 sec
RG 20642.5
DW 19.900 usec
DE 6.00 usec
TE 298.2 K
D1 0.15000001 sec
d11 0.03000000 sec
DELTA 0.05000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 7.60 usec
PL1 -3.00 dB
SFO1 100.5936591 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 135.60 usec
PL2 17.40 dB
PL12 17.40 dB
PL13 17.40 dB
SFO2 400.0116000 MHz
F2 - Processing parameters
SI 32768
SF 100.5825950 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
0.27
12.68
18.22
19.59
27.88
42.18
42.66
63.41
71.98
72.99
73.89
75.11
76.74
77.06
77.38
113.66
127.60
127.68
128.40
138.34
144.03
OTIPS
OBn
HO
TMSO
2.37
0 ppm


Current Data Parameters
NAME XZ-XI-36
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20060330
Time 16.41
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195645 Hz
AQ 2.555648 sec
RG 50.8
DW 78.000 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.70 usec
PL1 0.00 dB
SFO1 400.0128001 MHz
F2 - Processing parameters
SI 32768
SF 400.0100000 MHz
WDW EM
SSB 0
LB 0.70 Hz
GB 0
PC 1.00
OTIPS
OBn
TMSO
2.27
ppm

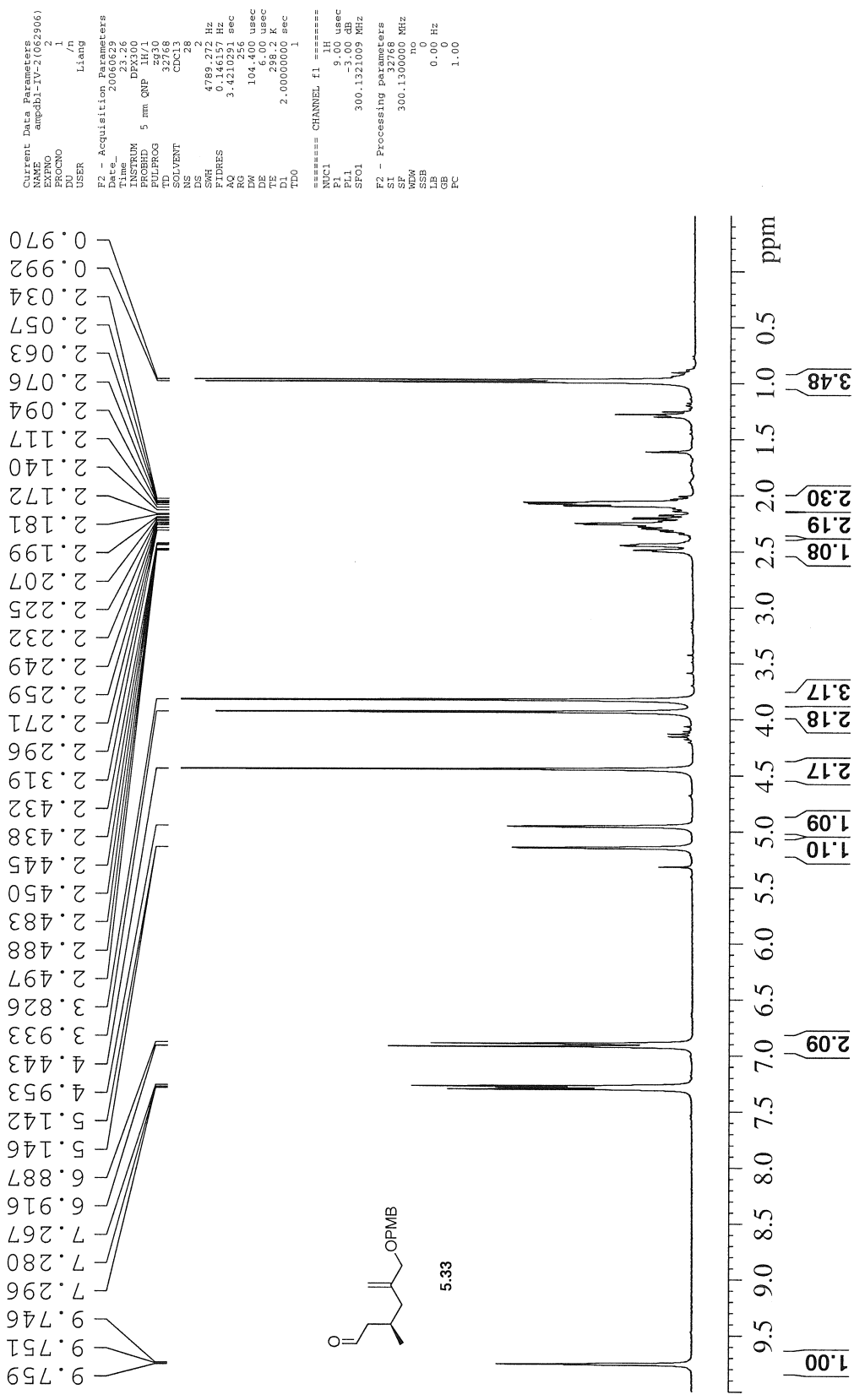

C13/aldehyde
Current Data Parameters
NAME Xz-XI-36
EXPNO 2
PROCNO 1
DU /m
USER xzhou
F2 - Acquisition Parameters
Date_ 20060330
Time 16.46
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT
NS 250
DS 4
SWH 25125.629 Hz
FIDRES 0.383387 Hz
AQ 1.3042164 sec
RG 4597.6
DW 19.900 usec
DE 6.00 usec
TE 298.1 K
D1 0.15000001 sec
d11 0.03000000 sec
DELTA 0.05000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 7.80 usec
PL1 -3.00 dB
SFO1 100.5936591 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 135.00 usec
PL2 17.40 dB
PL12 17.40 dB
PL13 17.40 dB
SFO2 400.0116080 MHz
F2 - Processing parameters
SI 32768
SF 100.5825950 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
204.06
144.08
138.48
128.38
127.68
127.55
113.62
80.48
77.37
77.06
76.74
74.96
72.89
71.93
42.18
41.02
27.19
19.50
18.16
12.54
0.06
OTIPS
OBn
TMSO
O
H
2.27
ppm

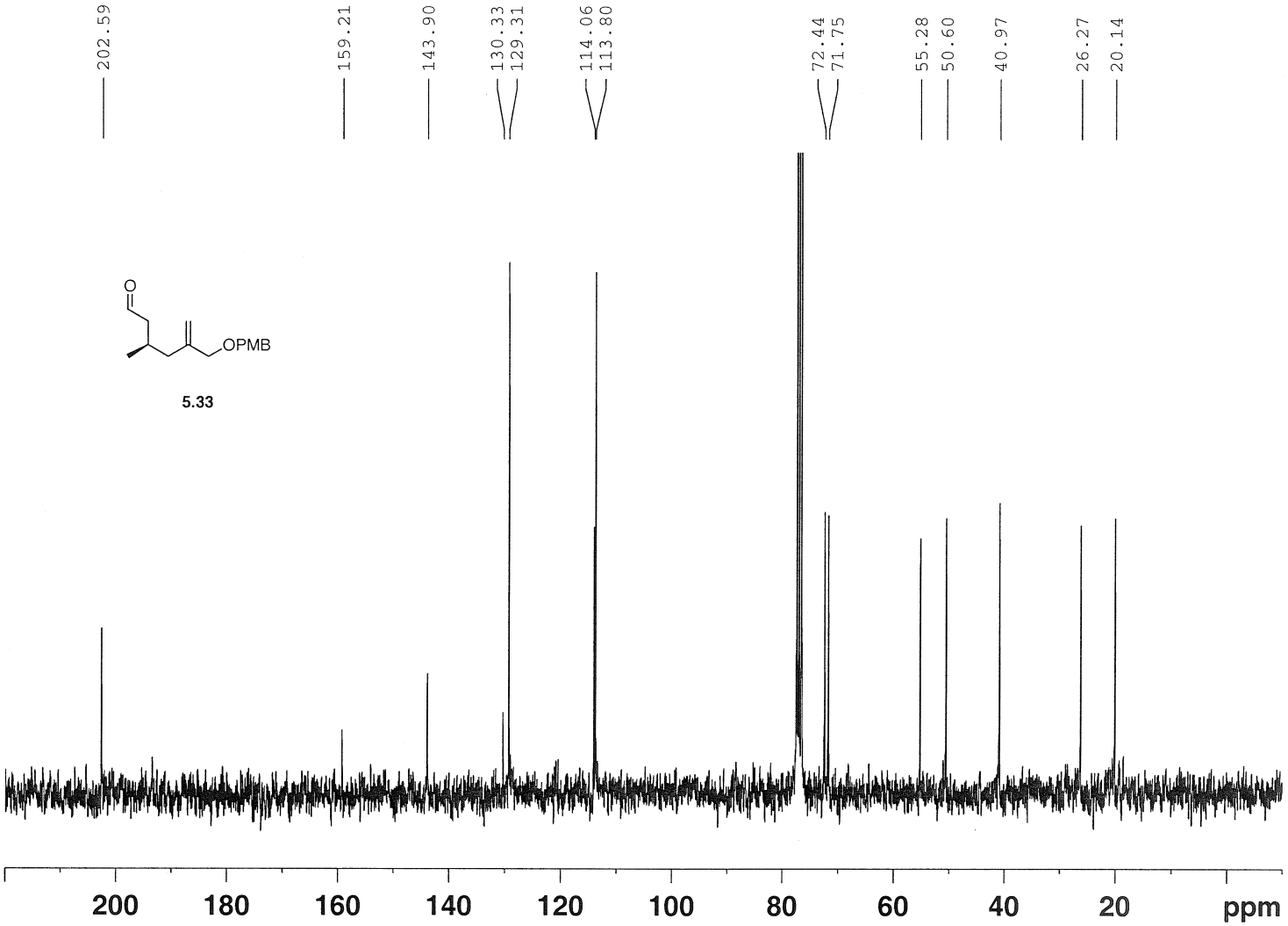

Current Data Parameters
NAME ampdbl-IV-1(0623106)
EXPNO 1
PROCNO 1
DU /n
USER Liang
F2 - Acquisition Parameters
Date_ 20060623
Time 23.13
INSTRUM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 21
DS 2
SWH 4789.272 Hz
FIDRES 0.146157 Hz
AQ 3.42102291 sec
RG 256
DW 104.400 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.00 usec
PL1 -3.00 dB
SFO1 300.1321009 MHz
F2 - Processing parameters
SI 32768
SF 300.1300000 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
7.302
7.280
7.273
6.906
6.877
5.119
5.115
4.959
4.440
3.945
3.904
3.884
3.863
3.822
3.477
3.451
2.760
2.741
2.552
2.527
2.473
2.104
2.093
2.087
2.068
2.064
2.041
1.925
1.903
1.859
1.419
1.406
1.390
1.374
1.358
1.287
1.278
1.150
0.987
0.979
0.965
OPMB
5.32
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
2.00
0.97
0.98
1.99
3.03
3.02
2.00
1.01
1.02
1.06
7.68
3.45
2.92
6.12



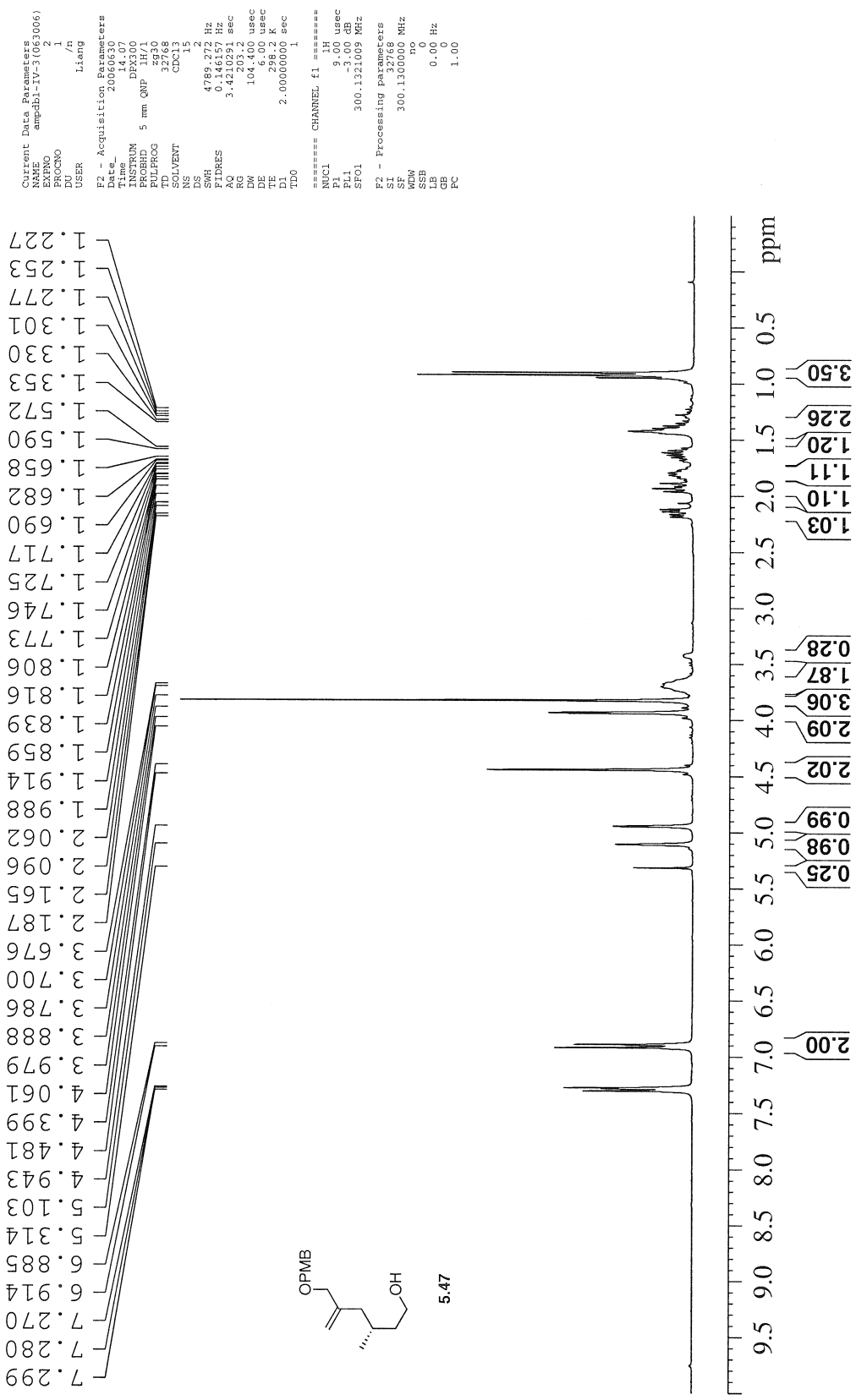
5.32

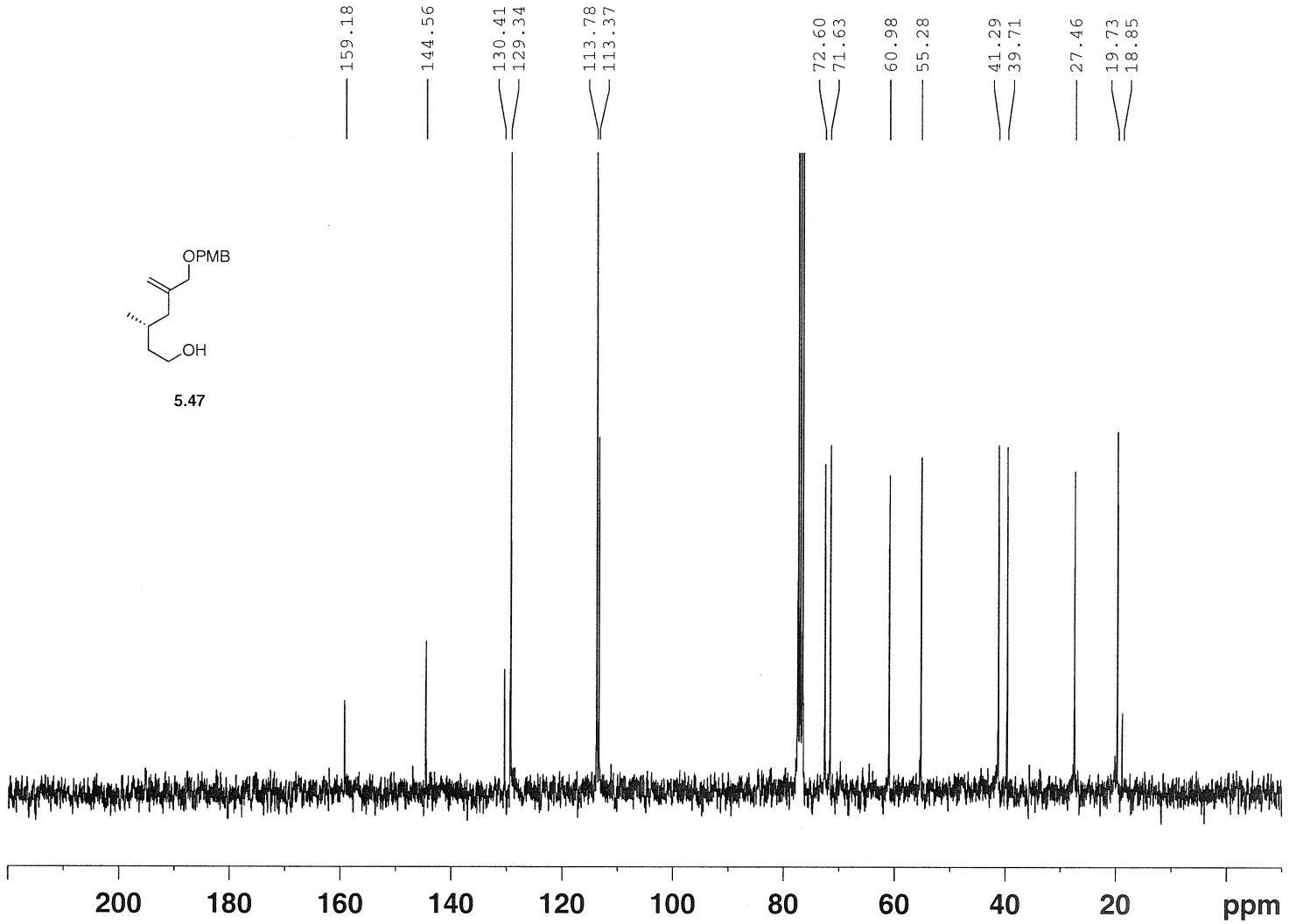
```
Current Data Parameters
NAME      ampdb1-IV-1(0623(
EXPNO                    2
PROCNO                   1
DU                      /n
USER                Liang

F2 - Acquisition Parameter
Date_             20060623
Time                 23.38
INSTRUM            DPX300
PROBHD   5 mm QNP  1H/1
PULPROG            zgpg30
TD                  65536
SOLVENT             CDCl3
NS                    694
DS                      4
SWH           18832.393 Hz
FIDRES         0.287360 Hz
AQ             1.7400308 se
RG                9195.2
DW                26.550 us
DE                 6.00 us
TE                298.2 K
D1            0.15000001 se
d11           0.03000000 se
DELTA         0.05000000 se
TD0                     1

======== CHANNEL f1 ======
NUC1                  13C
P1                   8.80 us
PL1                 -3.00 dB
SFO1          75.4760505 MH

======== CHANNEL f2 ======
CPDPRG2           waltz16
NUC2                  1H
PCPD2              80.00 us
PL2                -3.00 dB
PL12               17.55 dB
PL13               17.55 dB
SFO2         300.1312005 MH

F2 - Processing parameters
SI                  32768
SF           75.4677490 MH
WDW                    EM
SSB                     0
LB                   3.00 Hz
GB                      0
PC                   1.40
```


Current Data Parameters
NAME amgcb1-1V-2(0622906)
EXPNO 2
PROCNO 1
DU /n
USER Liang
F2 - Acquisition Parameters
Date_ 20060629
Time 23.26
INSTRUM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 28
DS 2
SWH 4789.272 Hz
FIDRES 0.146157 Hz
AQ 3.42102291 sec
RG 256
DW 104.400 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.00 usec
PL1 -3.00 dB
SFO1 300.1321009 MHz
F2 - Processing parameters
SI 32768
SF 300.1300000 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
9.759
9.751
9.746
7.296
7.280
7.267
6.916
6.887
5.146
5.142
4.953
4.443
3.933
3.826
2.497
2.488
2.483
2.450
2.445
2.438
2.432
2.319
2.296
2.271
2.259
2.249
2.232
2.225
2.207
2.199
2.181
2.172
2.140
2.117
2.094
2.076
2.063
2.057
2.034
0.992
0.970
OPMB
5.33
O
ppm
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
1.00
2.09
1.10
1.09
2.17
2.18
3.17
1.08
2.19
2.30
3.48

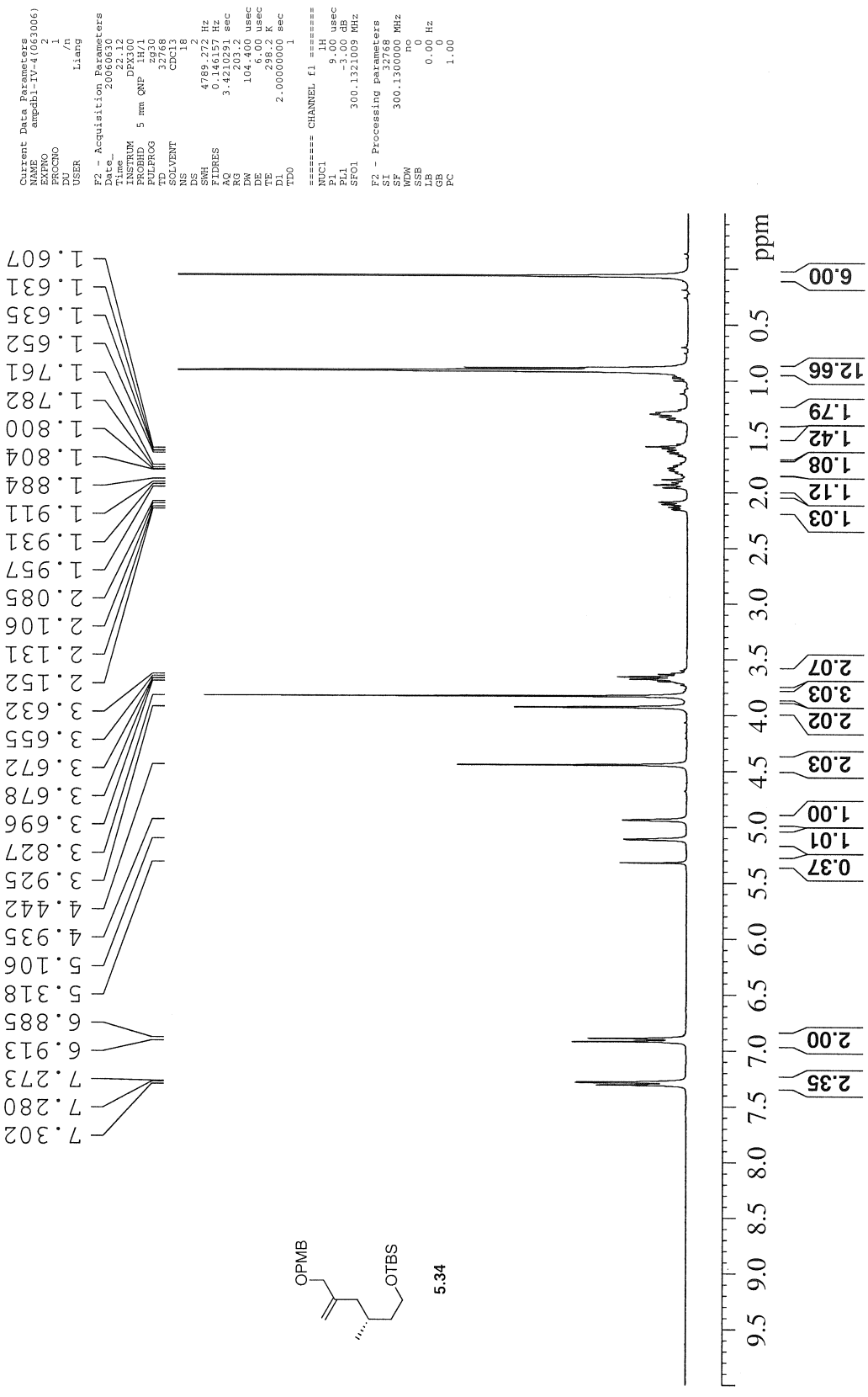


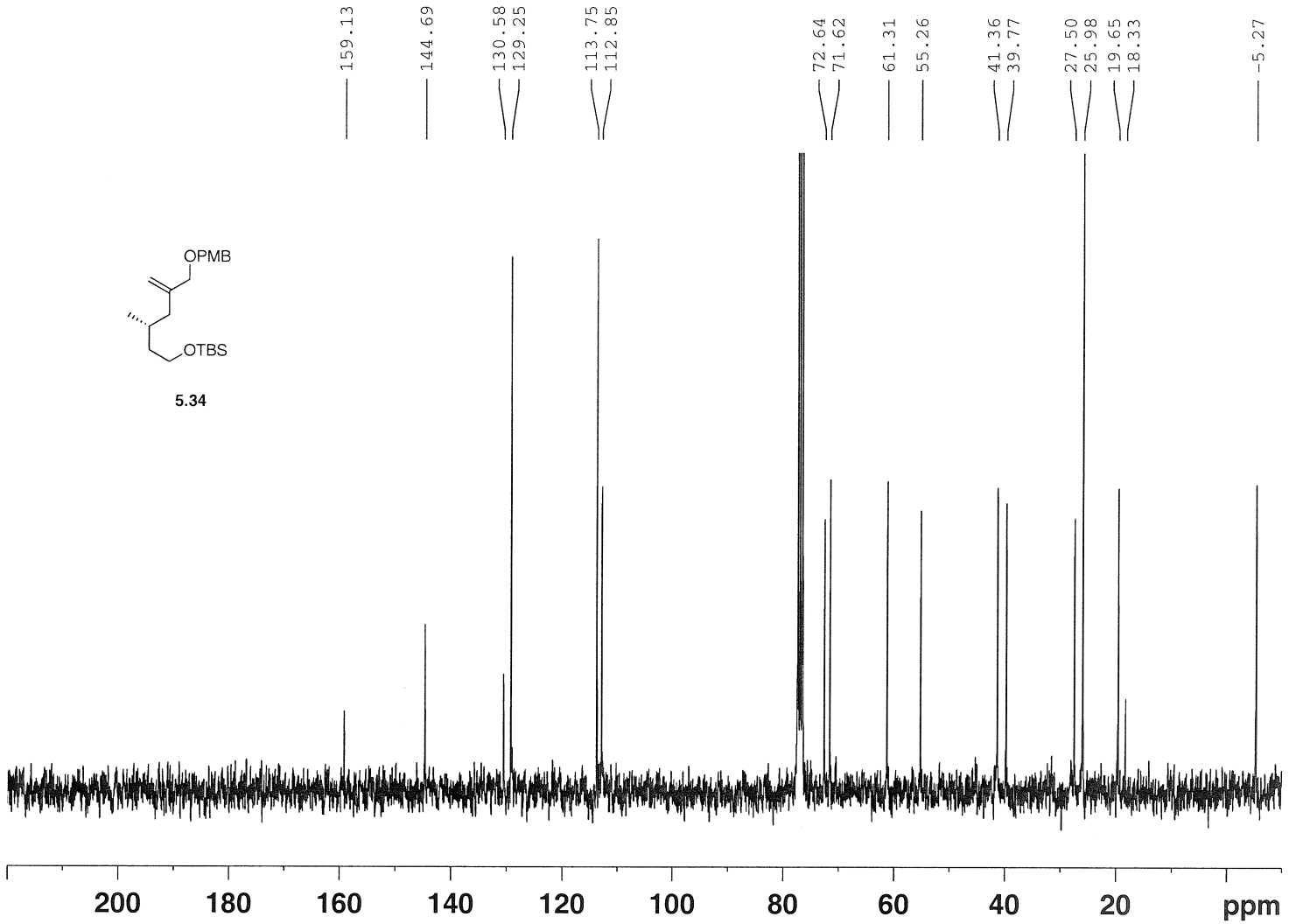

```
Current Data Parameters
NAME      ampdb1-IV-2(0629(
EXPNO                    4
PROCNO                   1
DU                      /n
USER                Liang

F2 - Acquisition Parameter
Date_             20060712
Time                 9.56
INSTRUM           DPX300
PROBHD   5 mm QNP  1H/1
PULPROG           zgpg30
TD                65536
SOLVENT           CDCl3
NS                  375
DS                    4
SWH           18832.393 Hz
FIDRES         0.287360 Hz
AQ             1.7400308 se
RG                9195.2
DW                26.550 us
DE                 6.00 us
TE                298.2 K
D1            0.15000001 se
d11           0.03000000 se
DELTA         0.05000000 se
TD0                   1

======== CHANNEL f1 ======
NUC1                 13C
P1                  8.80 us
PL1                -3.00 dB
SFO1         75.4760505 MH

======== CHANNEL f2 ======
CPDPRG2          waltz16
NUC2                 1H
PCPD2             80.00 us
PL2               -3.00 dB
PL12              17.55 dB
PL13              17.55 dB
SFO2        300.1312005 MH

F2 - Processing parameters
SI                32768
SF           75.4677490 MH
WDW                  EM
SSB                   0
LB                 3.00 Hz
GB                    0
PC                 1.40
```


Current Data Parameters
NAME ampadb1-IV-3(0603006)
EXPNO 2
PROCNO 1
DU /n
USER Liang
F2 - Acquisition Parameters
Date_ 20060630
Time 14.07
INSTRUM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 15
DS 2
SWH 4789.272 Hz
FIDRES 0.146157 Hz
AQ 3.4210291 sec
RG 203.2
DW 104.400 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.00 usec
PL1 -3.00 dB
SFO1 300.1321009 MHz
F2 - Processing parameters
SI 32768
SF 300.1300000 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
OPMB
OH
5.47
7.299
7.280
7.270
6.914
6.885
5.314
5.103
4.943
4.481
4.399
4.061
3.979
3.888
3.786
3.700
3.676
2.187
2.165
2.096
2.062
1.988
1.914
1.859
1.839
1.816
1.806
1.773
1.746
1.725
1.717
1.690
1.682
1.658
1.590
1.572
1.353
1.330
1.301
1.277
1.253
1.227
2.00
0.25
0.98
0.99
2.02
2.09
3.06
1.87
0.28
1.03
1.10
1.11
1.20
2.26
3.50
ppm



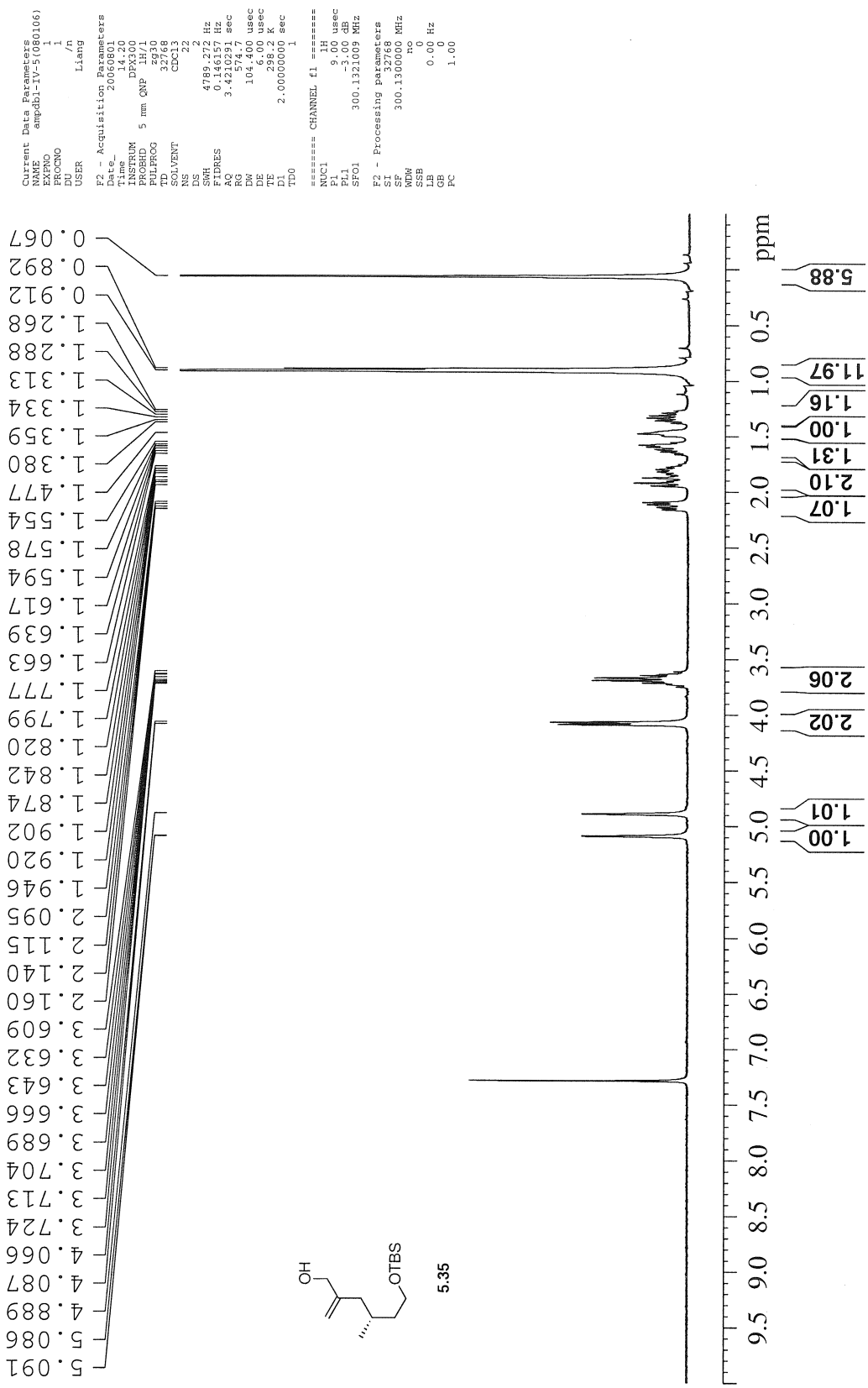

```
Current Data Parameters
NAME        ampdb1-IV-3(0630(
EXPNO                    1
PROCNO                   1
DU                      /n
USER                 Liang

F2 - Acquisition Parameter
Date_             20060630
Time                 23.00
INSTRUM            DPX300
PROBHD   5 mm QNP  1H/1
PULPROG            zgpg30
TD                  65536
SOLVENT             CDCl3
NS                    602
DS                      4
SWH             18832.393 Hz
FIDRES          0.287360 Hz
AQ              1.7400308 se
RG                11585.2
DW                26.550 us
DE                 6.00 us
TE                298.2 K
D1           0.15000001 se
d11          0.03000000 se
DELTA        0.05000000 se
TD0                     1

======== CHANNEL f1 ======
NUC1                  13C
P1                   8.80 us
PL1                 -3.00 dB
SFO1          75.4760505 MH

======== CHANNEL f2 ======
CPDPRG2          waltz16
NUC2                  1H
PCPD2              80.00 us
PL2                -3.00 dB
PL12               17.55 dB
PL13               17.55 dB
SFO2         300.1312005 MH

F2 - Processing parameters
SI                  32768
SF           75.4677490 MH
WDW                   EM
SSB                    0
LB                  3.00 Hz
GB                     0
PC                  1.40
```

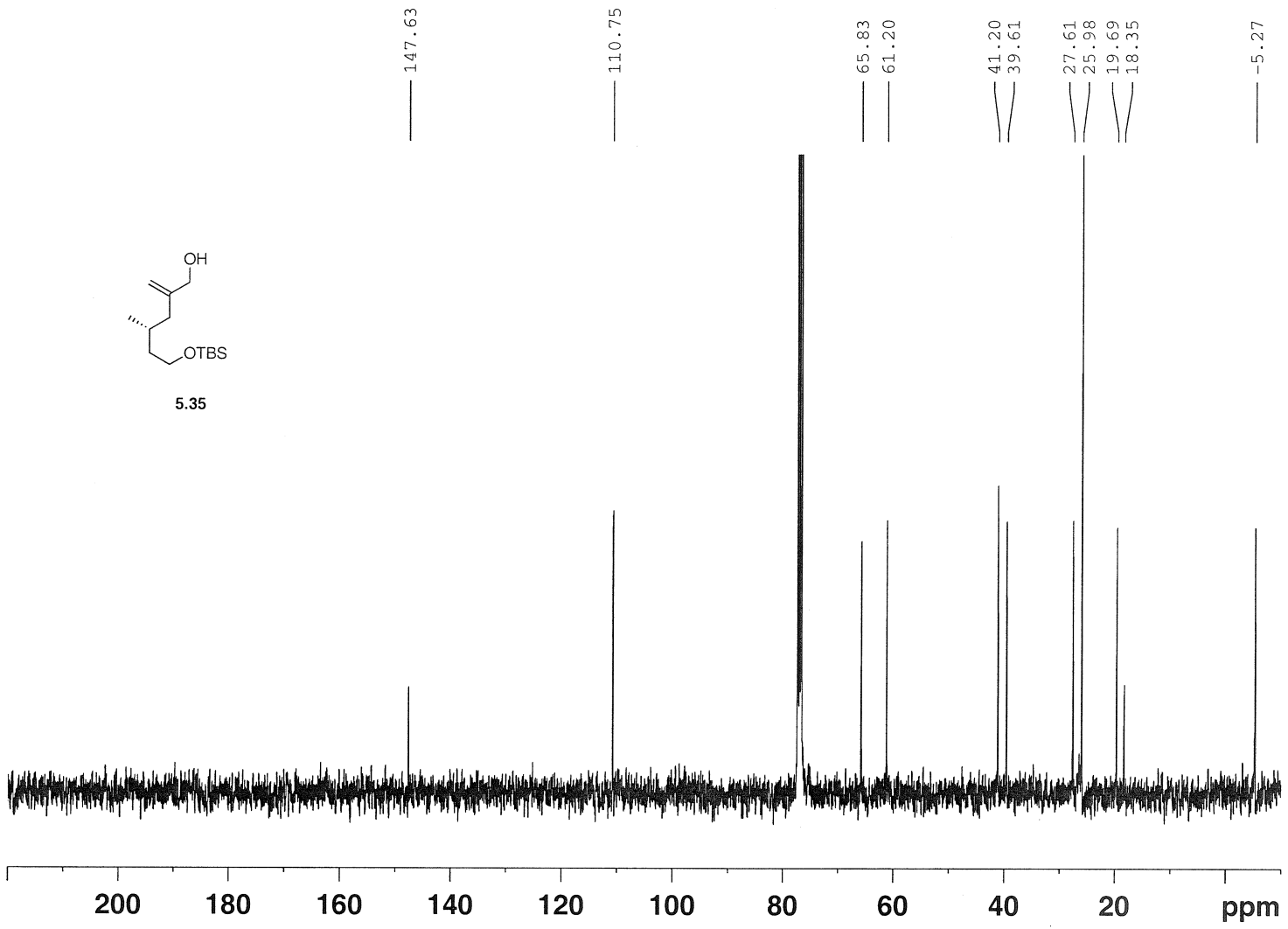

Current Data Parameters
NAME ampdbl-IV-4(063006)
EXPNO 2
PROCNO 1
DU /n
USER Liang
F2 - Acquisition Parameters
Date_ 20060630
Time 22.12
INSTRUM DPX300
PROBHD 5 mm QNP 1H/
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 18
DS 2
SWH 4789.272 Hz
FIDRES 0.146157 Hz
AQ 3.4210291 sec
RG 203.2
DW 104.400 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.00 usec
PL1 -3.00 dB
SFO1 300.1321009 MHz
F2 - Processing parameters
SI 32768
SF 300.1300000 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
7.302
7.280
7.273
6.913
6.885
5.318
5.106
4.935
4.442
3.925
3.827
3.696
3.678
3.672
3.655
3.632
2.152
2.131
2.106
2.085
1.957
1.931
1.911
1.884
1.804
1.800
1.782
1.761
1.652
1.635
1.631
1.607
OPMB
OTBS
5.34
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
ppm
2.35
2.00
0.37
1.01
1.00
2.03
2.02
3.03
2.07
1.03
1.12
1.08
1.42
1.79
12.66
6.00



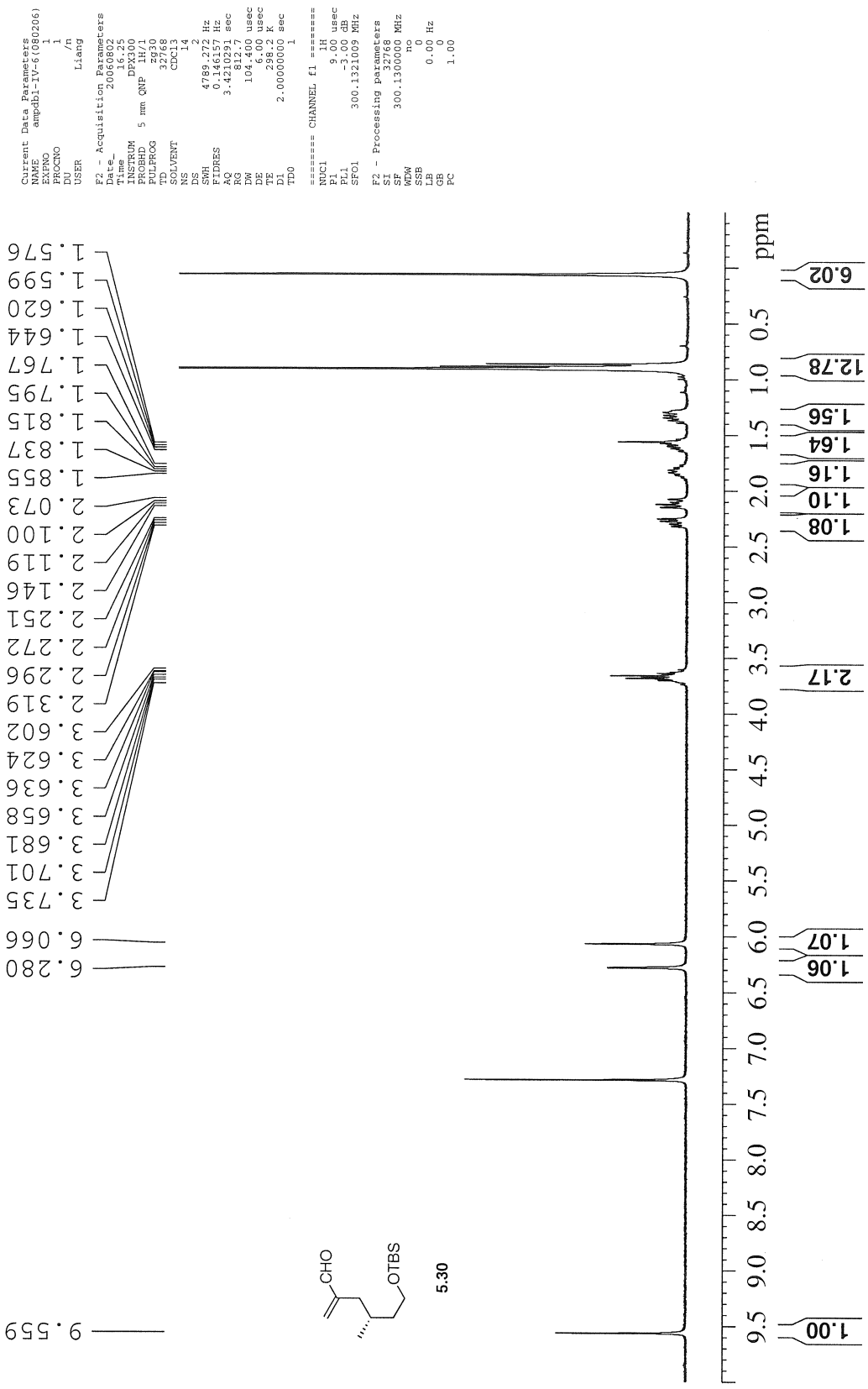
5.34

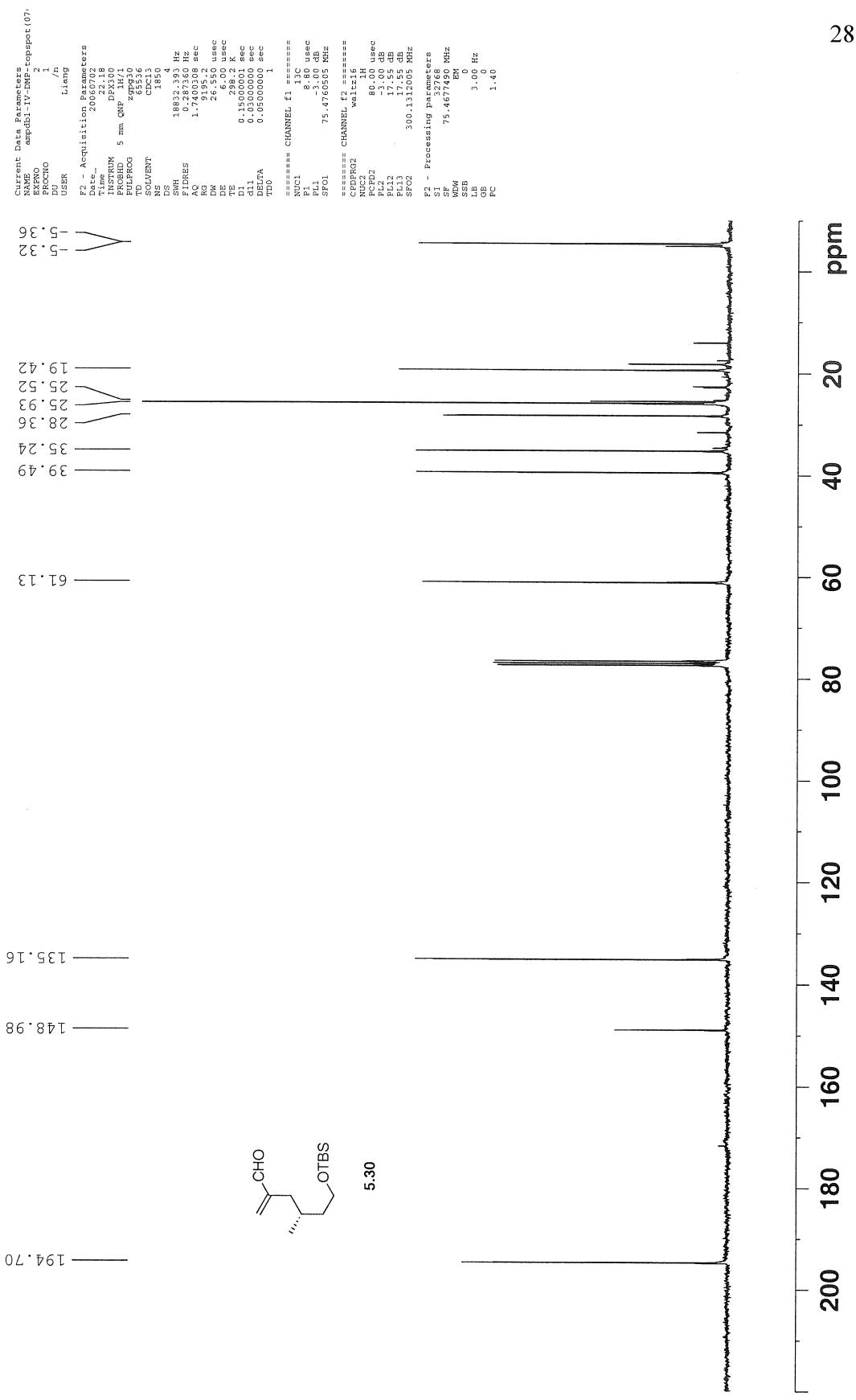
```
Current Data Parameters
NAME        ampdb1-IV-4(0630(
EXPNO                      1
PROCNO                     1
DU                        /n
USER                   Liang

F2 - Acquisition Parameter
Date_               20060630
Time                   22.31
INSTRUM              DPX300
PROBHD    5 mm QNP  1H/1
PULPROG              zgpg30
TD                    65536
SOLVENT               CDCl3
NS                      528
DS                        4
SWH               18832.393 Hz
FIDRES             0.287360 Hz
AQ                 1.7400308 se
RG                    9195.2
DW                    26.550 us
DE                     6.00 us
TE                    298.2 K
D1              0.15000001 se
d11             0.03000000 se
DELTA           0.05000000 se
TD0                       1

======== CHANNEL f1 ======
NUC1                    13C
P1                     8.80 us
PL1                   -3.00 dB
SFO1           75.4760505 MH

======== CHANNEL f2 ======
CPDPRG2             waltz16
NUC2                    1H
PCPD2                80.00 us
PL2                  -3.00 dB
PL12                 17.55 dB
PL13                 17.55 dB
SFO2          300.1312005 MH

F2 - Processing parameters
SI                     32768
SF            75.4677490 MH
WDW                       EM
SSB                        0
LB                    3.00 Hz
GB                         0
PC                     1.40
```

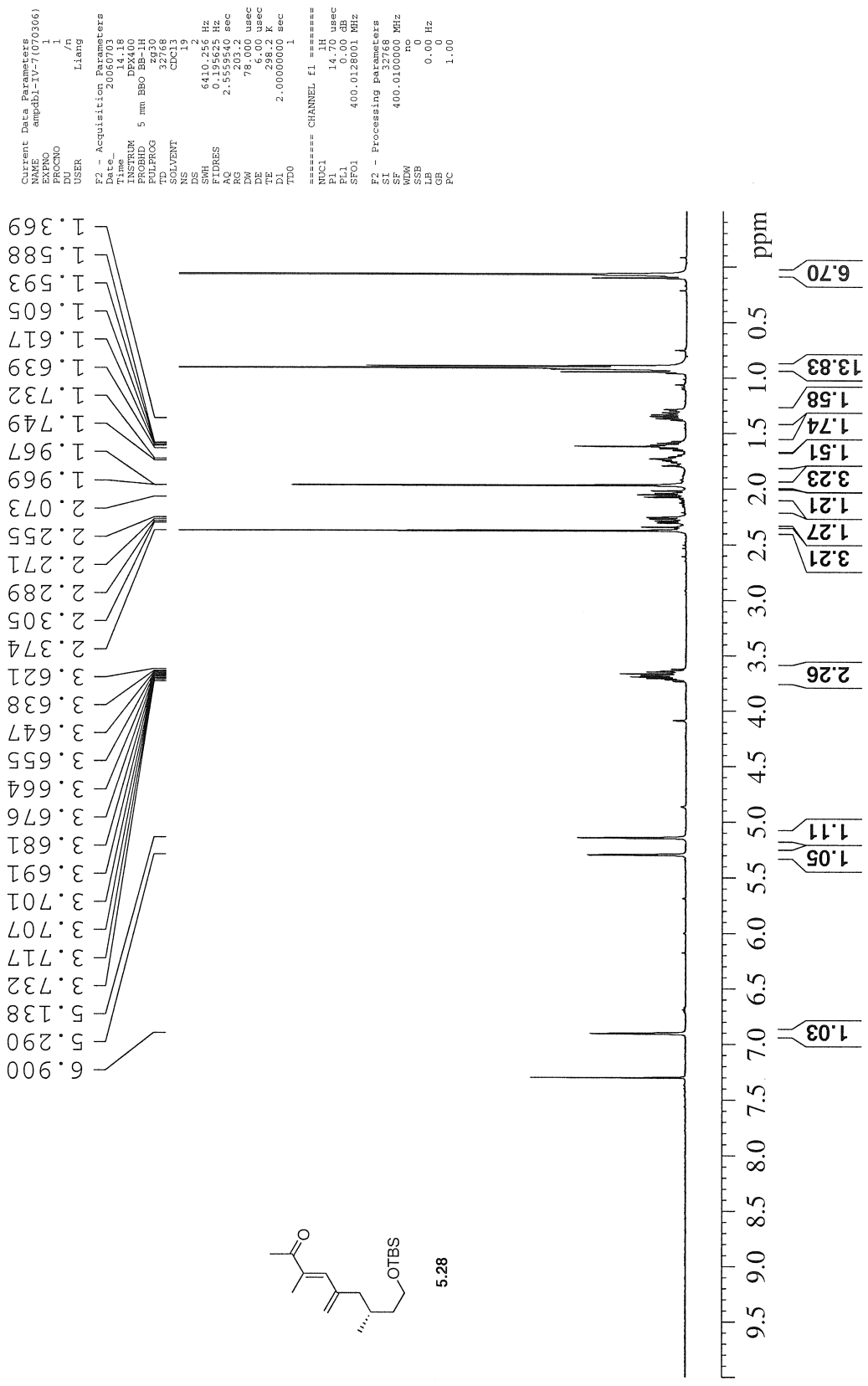

Current Data Parameters
NAME ampdb1-IV-5(0801
EXPNO 1
PROCNO 1
DU /n
USER Liang
F2 - Acquisition Parameters
Date_ 20060801
Time 14.20
INSTRUM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 22
DS 2
SWH 4789.272 Hz
FIDRES 0.146157 Hz
AQ 3.4210291 sec
RG 574.7
DW 104.400 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.00 usec
PL1 -3.00 dB
SFO1 300.1321009 MHz
F2 - Processing parameters
SI 32768
SF 300.1300000 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
OH
OTBS
5.35
ppm
5.88
11.97
1.16
1.00
1.31
2.10
1.07
2.06
2.02
1.00
1.01

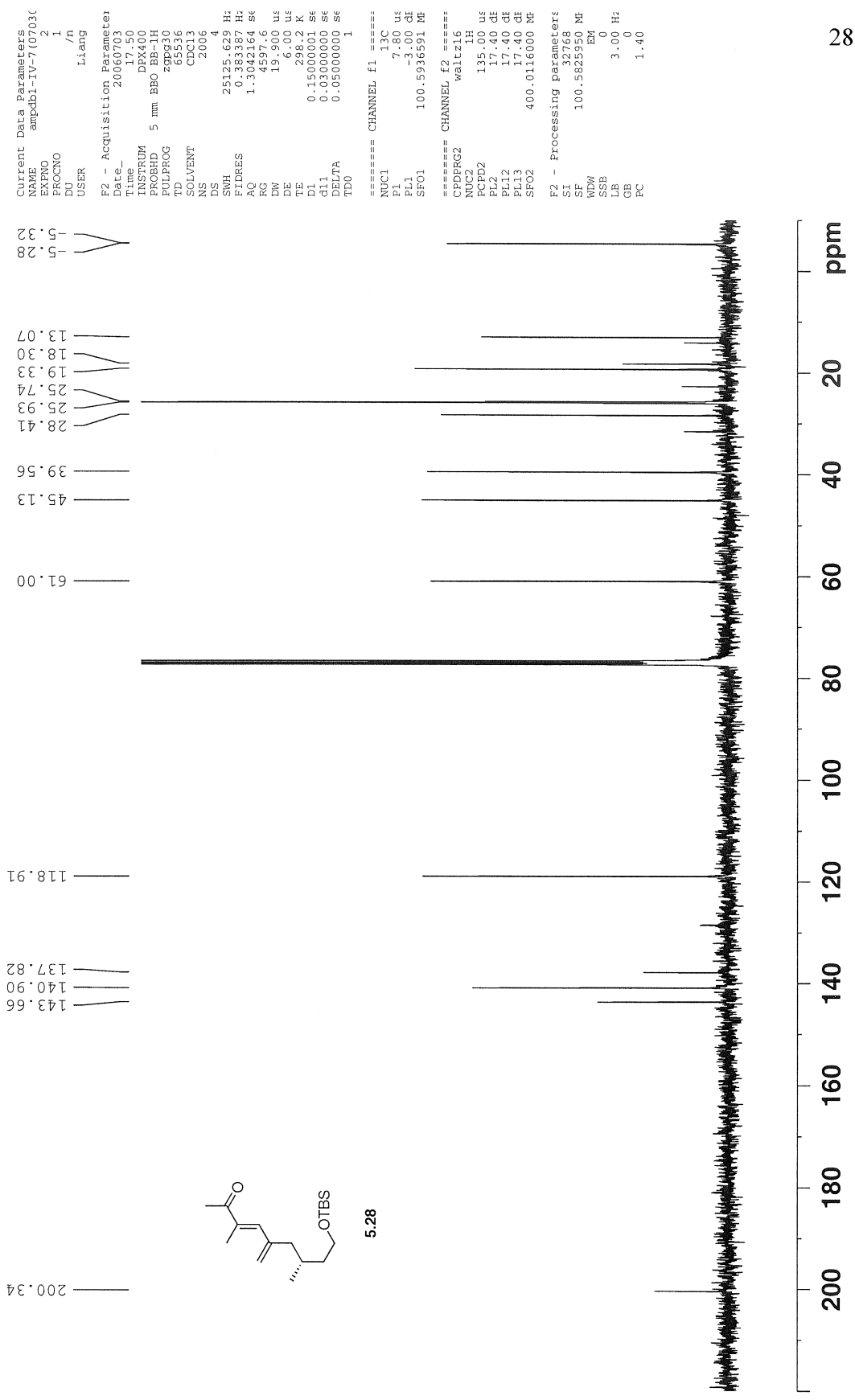


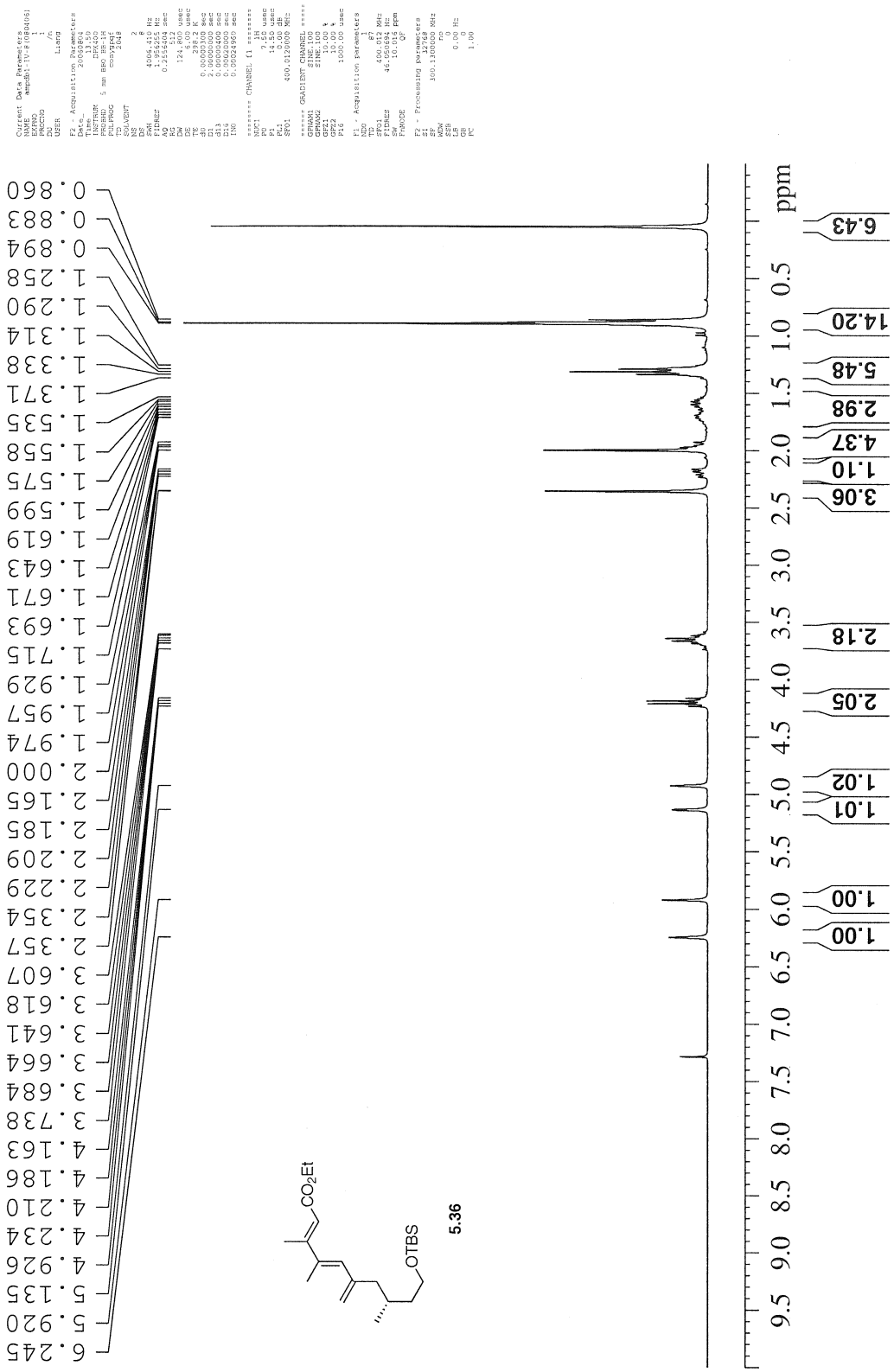

```
Current Data Parameters
NAME      ampdb1-IV-5(0801(
EXPNO                    3
PROCNO                   1
DU                      /n
USER                Liang

F2 - Acquisition Parameter
Date_             20060801
Time                 16.39
INSTRUM            DPX400
PROBHD   5 mm BBO BB-1H
PULPROG           zgpg30
TD                 65536
SOLVENT            CDCl3
NS                  1143
DS                     4
SWH           25125.629 Hz
FIDRES         0.383387 Hz
AQ             1.3042164 se
RG                9195.2
DW                19.900 us
DE                 6.00 us
TE                298.2 K
D1            0.15000001 se
d11           0.03000000 se
DELTA         0.05000000 se
TD0                    1

======== CHANNEL f1 ======
NUC1                 13C
P1                  7.80 us
PL1                -3.00 dB
SFO1        100.5936591 MH

======== CHANNEL f2 ======
CPDPRG2          waltz16
NUC2                 1H
PCPD2            135.00 us
PL2               17.40 dB
PL12              17.40 dB
PL13              17.40 dB
SFO2        400.0116000 MH

F2 - Processing parameters
SI                 32768
SF          100.5825950 MH
WDW                 EM
SSB                  0
LB                3.00 Hz
GB                   0
PC                1.40
```


Current Data Parameters
NAME ampdbl-1V-6(0802O6)
EXPNO 1
PROCNO 1
DU /n
USER Liang
F2 - Acquisition Parameters
Date_ 20060802
Time 16.25
INSTRUM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 14
DS 2
SWH 4789.272 Hz
FIDRES 0.146157 Hz
AQ 3.4210291 sec
RG 812.7
DW 104.400 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.00 usec
PL1 -3.00 dB
SFO1 300.1321009 MHz
F2 - Processing parameters
SI 32768
SF 300.1300000 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
9.559
6.280
6.066
3.735
3.701
3.681
3.658
3.636
3.624
3.602
2.319
2.296
2.272
2.251
2.146
2.119
2.100
2.073
1.855
1.837
1.815
1.795
1.767
1.644
1.620
1.599
1.576
CHO
OTBS
5.30
ppm
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
1.00
1.07
1.06
2.17
1.08
1.10
1.16
1.64
1.56
12.78
6.02


Current Data Parameters
NAME ampdbl-IV-DMP-topspot(07
EXPNO 2
PROCNO 1
DU /n
USER Liang
F2 - Acquisition Parameters
Date_ 20060702
Time 22.18
INSTRUM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 180
DS 4
SWH 18832.393 Hz
FIDRES 0.287360 Hz
AQ 1.7400308 sec
RG 2565.2
DW 26.550 usec
DE 6.00 usec
TE 298.2 K
D1 0.15000001 sec
d11 0.03000000 sec
DELTA 0.05000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 8.80 usec
PL1 -3.00 dB
SFO1 75.4760505 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 -3.00 dB
PL12 17.55 dB
PL13 17.55 dB
SFO2 300.1312005 MHz
F2 - Processing parameters
SI 32768
SF 75.4677490 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
-5.36
-5.32
19.42
25.52
25.93
28.36
35.24
39.49
61.13
135.16
148.98
194.70
CHO
OTBS
5.30
ppm
200
180
160
140
120
100
80
60
40
20


Current Data Parameters
NAME ampdb1-1V-7(0703066)
EXPNO 1
PROCNO 1
DU /n
USER Liang
F2 - Acquisition Parameters
Date_ 20060703
Time 14.18
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 19
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.55559540 sec
RG 203.2
DW 78.000 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.70 usec
PL1 0.00 dB
SFO1 400.0128001 MHz
F2 - Processing parameters
SI 32768
SF 400.0100000 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
6.900
5.290
5.138
3.732
3.717
3.707
3.701
3.691
3.681
3.676
3.664
3.655
3.647
3.638
3.621
2.374
2.305
2.289
2.271
2.255
2.073
1.969
1.967
1.749
1.732
1.639
1.617
1.605
1.593
1.588
1.369
OTBS
5.28
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
ppm
1.03
1.05
1.11
2.26
3.21
1.27
1.21
3.23
1.51
1.74
1.58
13.83
6.70


Current Data Parameters
NAME ampdbl-IV-7(07030
EXPNO 2
PROCNO 1
DU /n
USER Liang
F2 - Acquisition Parameter
Date_ 20060703
Time 17.50
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 2006
DS 4
SWH 25125.629 Hz
FIDRES 0.383387 Hz
AQ 1.3042164 se
RG 4597.6
DW 19.900 us
DE 6.00 us
TE 298.2 K
D1 0.15000001 se
d11 0.03000000 se
DELTA 0.05000000 se
TD0 1
======== CHANNEL f1 ======
NUC1 13C
P1 7.80 us
PL1 -3.00 dB
SFO1 100.5936591 MH
======== CHANNEL f2 ======
CPDPRG2 waltz16
NUC2 1H
PCPD2 135.00 us
PL2 17.40 dB
PL12 17.40 dB
PL13 17.40 dB
SFO2 400.0116000 MH
F2 - Processing parameters
SI 32768
SF 100.5825950 MH
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
200.34
143.66
140.90
137.82
118.91
61.00
45.13
39.56
28.41
25.93
25.74
19.33
18.30
13.07
5.32
5.28
OTBS
5.28
200
180
160
140
120
100
80
60
40
20
ppm

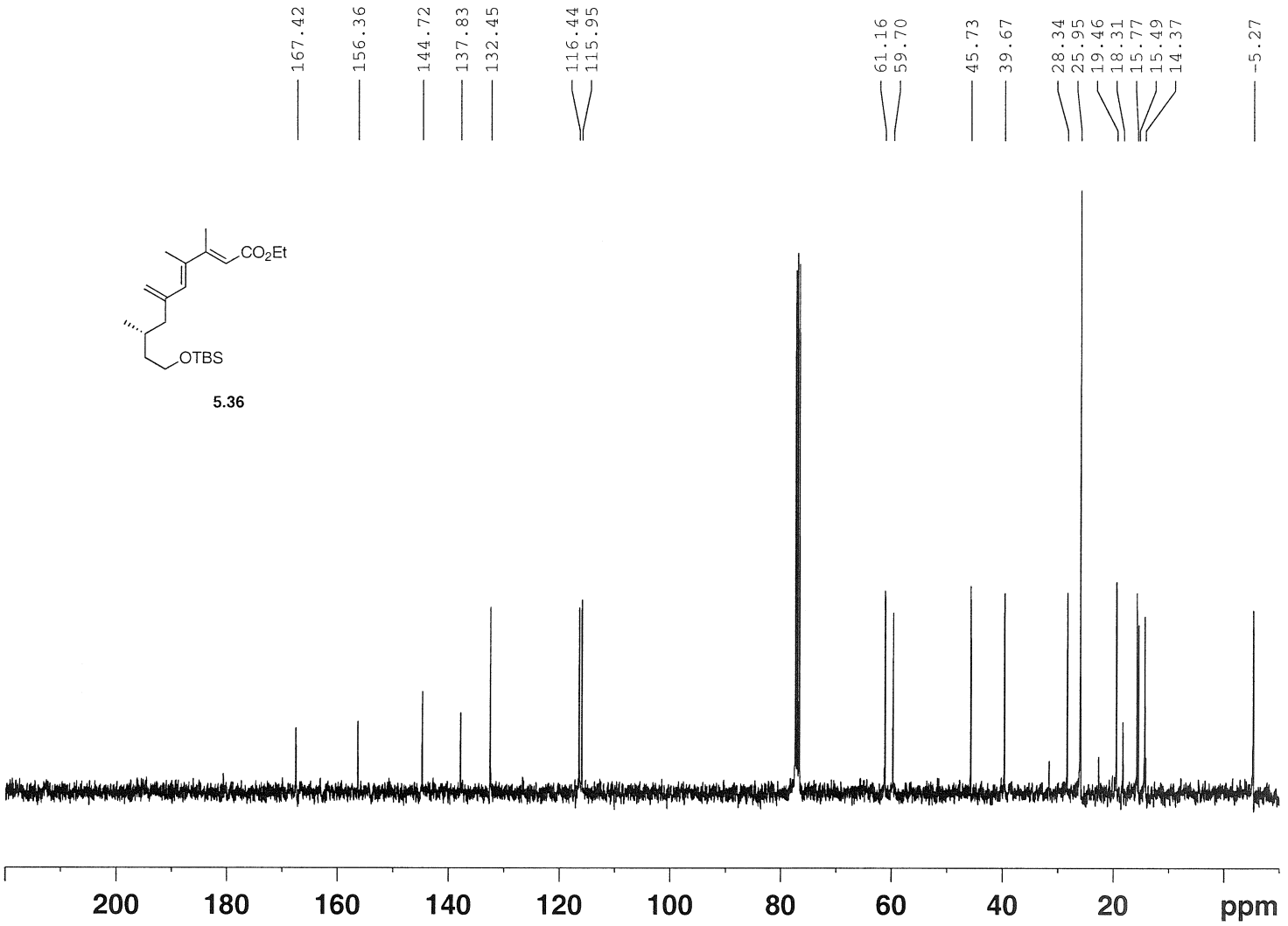

Current Data Parameters
NAME ampbi-TU-F(0804061
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20060804
Time 13.50
INSTRUM DRX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 8
DS 2
SWH 4006.410 Hz
FIDRES 0.122254 Hz
AQ 4.0894404 sec
RG 512
DW 124.800 usec
DE 6.00 usec
TE 298.0 K
D0 0.00000300 sec
D1 2.00000000 sec
D11 0.03000000 sec
D13 0.00002000 sec
IN0 0.00024960 sec
======== CHANNEL f1 ========
NUC1 1H
P1 7.45 usec
PL1 14.50 usec
PL1W 49.40 W
SFO1 400.0120000 MHz
===== GRADIENT CHANNEL =====
GPNAM1 SINE.100
GPNAM2 SINE.100
GPZ1 10.00 %
GPZ2 10.00 %
P16 1000.00 usec
F1 - Acquisition parameters
TD0 1
TD 64
SFO1 400.0132 MHz
FIDRES 46.156064 Hz
SW 10.014 ppm
FnMODE QF
F2 - Processing parameters
SI 32768
SF 400.1300000 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00

6.245
5.920
5.135
4.926
4.234
4.210
4.186
4.163
3.738
3.684
3.664
3.641
3.618
3.607
2.357
2.354
2.229
2.209
2.185
2.165
2.000
1.974
1.957
1.929
1.715
1.693
1.671
1.643
1.619
1.599
1.575
1.558
1.535
1.371
1.338
1.314
1.290
1.258
0.894
0.883
0.860

9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
1.00
1.00
1.01
1.02
2.05
2.18
3.06
1.10
4.37
2.98
5.48
14.20
6.43

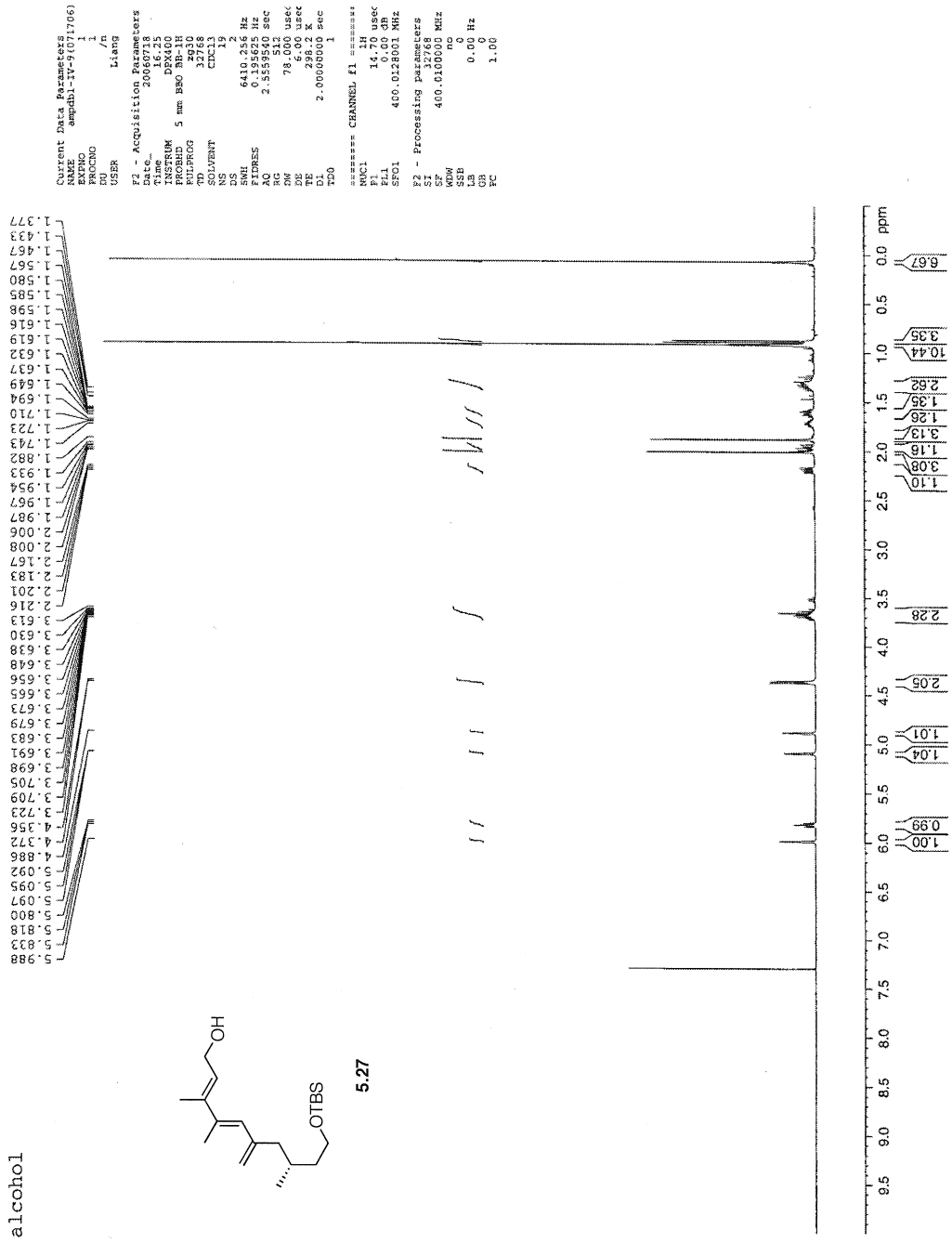
CO2Et
OTBS

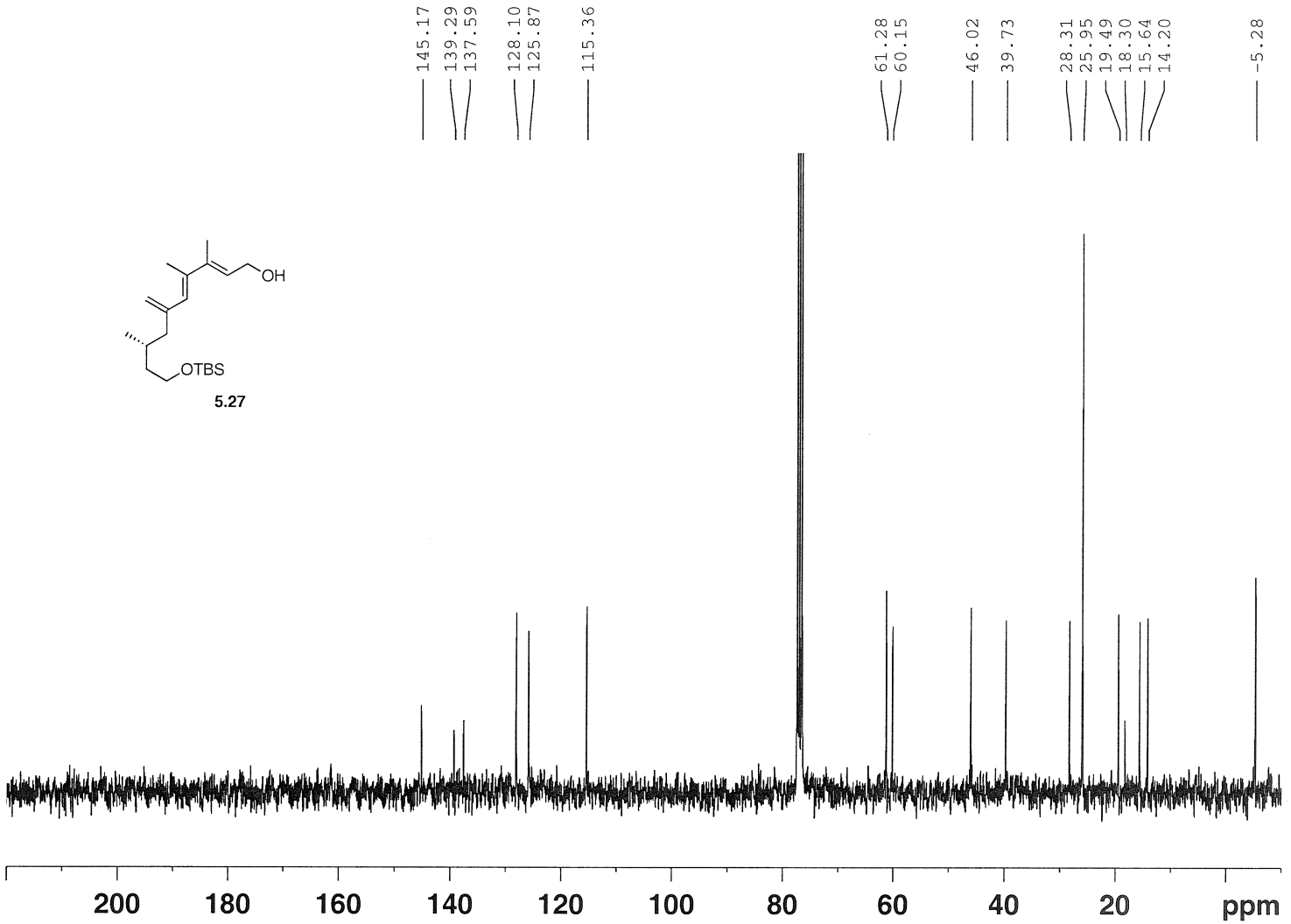
5.36



5.36

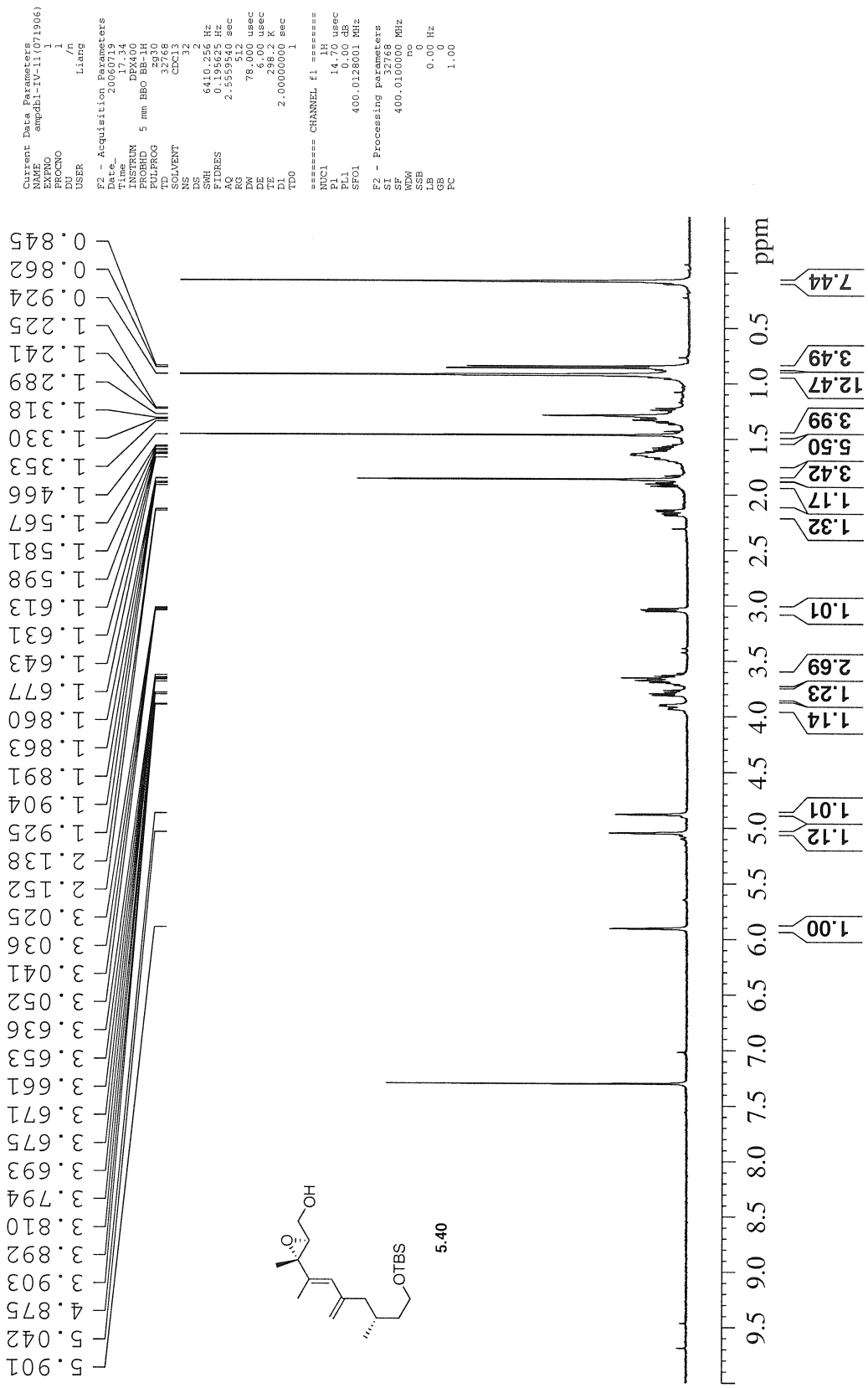
```
Current Data Parameters
NAME      ampdb1-IV-8(080406)
EXPNO                       1
PROCNO                      3
DU                         /n
USER                    Liang

F2 - Acquisition Parameters
Date_                20060804
Time                    13.50
INSTRUM                DPX400
PROBHD   5 mm BBO BB-1H
PULPROG           cosygpqf
TD                      2048
SOLVENT
NS                         2
DS                         8
SWH                 4006.410 Hz
FIDRES              1.956255 Hz
AQ                  0.2556404 sec
RG                        512
DW                    124.800 usec
DE                      6.00 usec
TE                     298.2 K
d0                0.00000300 sec
D1                2.00000000 sec
d13               0.00000400 sec
D16               0.00020000 sec
IN0               0.00024960 sec

======== CHANNEL f1 ========
NUC1                       1H
P0                      7.50 usec
P1                     14.50 usec
PL1                     0.00 dB
SFO1           400.0120000 MHz

====== GRADIENT CHANNEL =====
GPNAM1            SINE.100
GPNAM2            SINE.100
GPZ1                 10.00 %
GPZ2                 10.00 %
P16                1000.00 usec

F1 - Acquisition parameters
ND0                        1
TD                        87
SFO1                400.012 MHz
FIDRES            46.050694 Hz
SW                   10.016 ppm
FnMODE                   QF

F2 - Processing parameters
SI                     32768
SF              100.5825950 MHz
WDW                       EM
SSB                        0
LB                      3.00 Hz
GB                         0
PC                      1.40
```

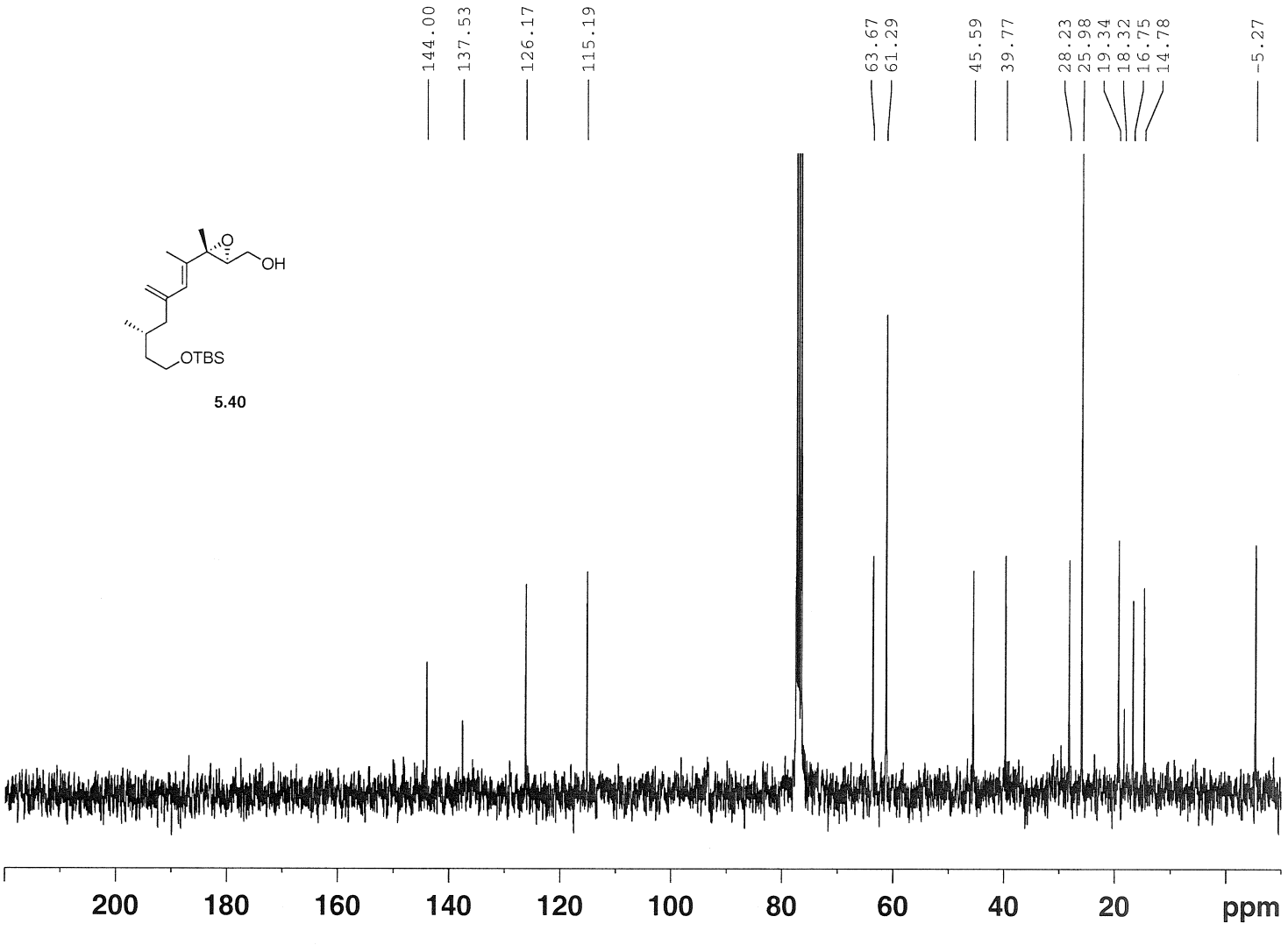

alcohol
5.27
OH
OTBS
Current Data Parameters
NAME ampdbl-IV-9(071706)
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20060718
Time 16.25
INSTRUM DRX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 16
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5559540 sec
RG 512
DW 78.000 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.70 usec
PL1 0.00 dB
SFO1 400.0128001 MHz
F2 - Processing parameters
SI 32768
SF 400.0100000 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
6.67
3.35
10.44
2.82
1.35
1.26
3.13
1.16
3.08
1.10
2.28
2.05
1.04
1.01
1.00
0.99
ppm



5.27

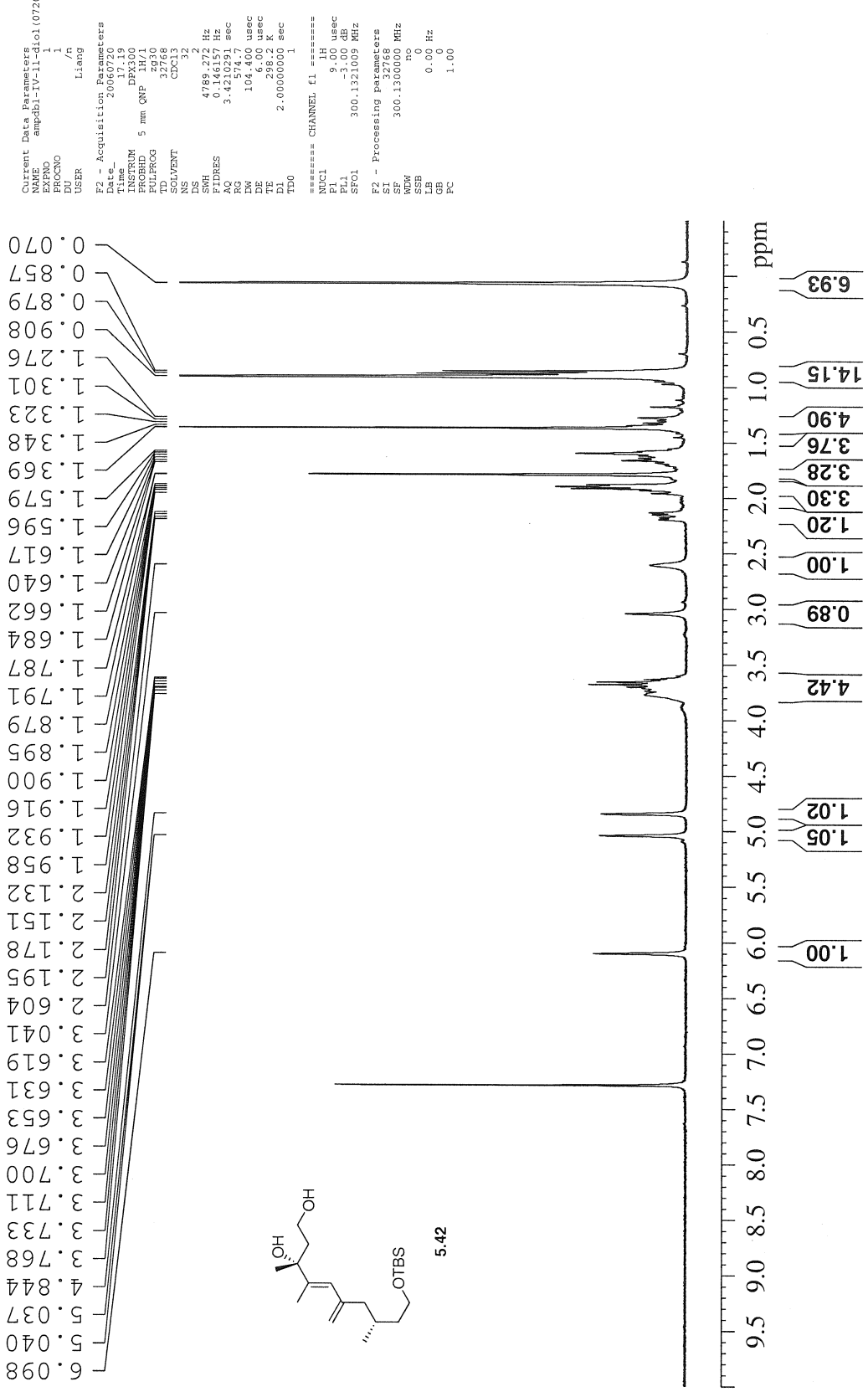
```
Current Data Parameters
NAME      ampdb1-IV-9(0808(
EXPNO                    2
PROCNO                   1
DU                      /n
USER                Liang

F2 - Acquisition Parameter
Date_             20060808
Time                 12.31
INSTRUM             DPX300
PROBHD   5 mm QNP  1H/1
PULPROG             zgpg30
TD                   65536
SOLVENT              CDCl3
NS                     495
DS                       4
SWH              18832.393 Hz
FIDRES           0.287360 Hz
AQ               1.7400308 se
RG                 10321.3
DW                 26.550 us
DE                  6.00 us
TE                 298.2 K
D1            0.15000001 se
d11           0.03000000 se
DELTA         0.05000000 se
TD0                      1

======== CHANNEL f1 ======
NUC1                   13C
P1                    8.80 us
PL1                  -3.00 dB
SFO1          75.4760505 MH

======== CHANNEL f2 ======
CPDPRG2           waltz16
NUC2                   1H
PCPD2                80.00 us
PL2                  -3.00 dB
PL12                 17.55 dB
PL13                 17.55 dB
SFO2         300.1312005 MH

F2 - Processing parameters
SI                   32768
SF            75.4677490 MH
WDW                    EM
SSB                     0
LB                   3.00 Hz
GB                      0
PC                   1.40
```

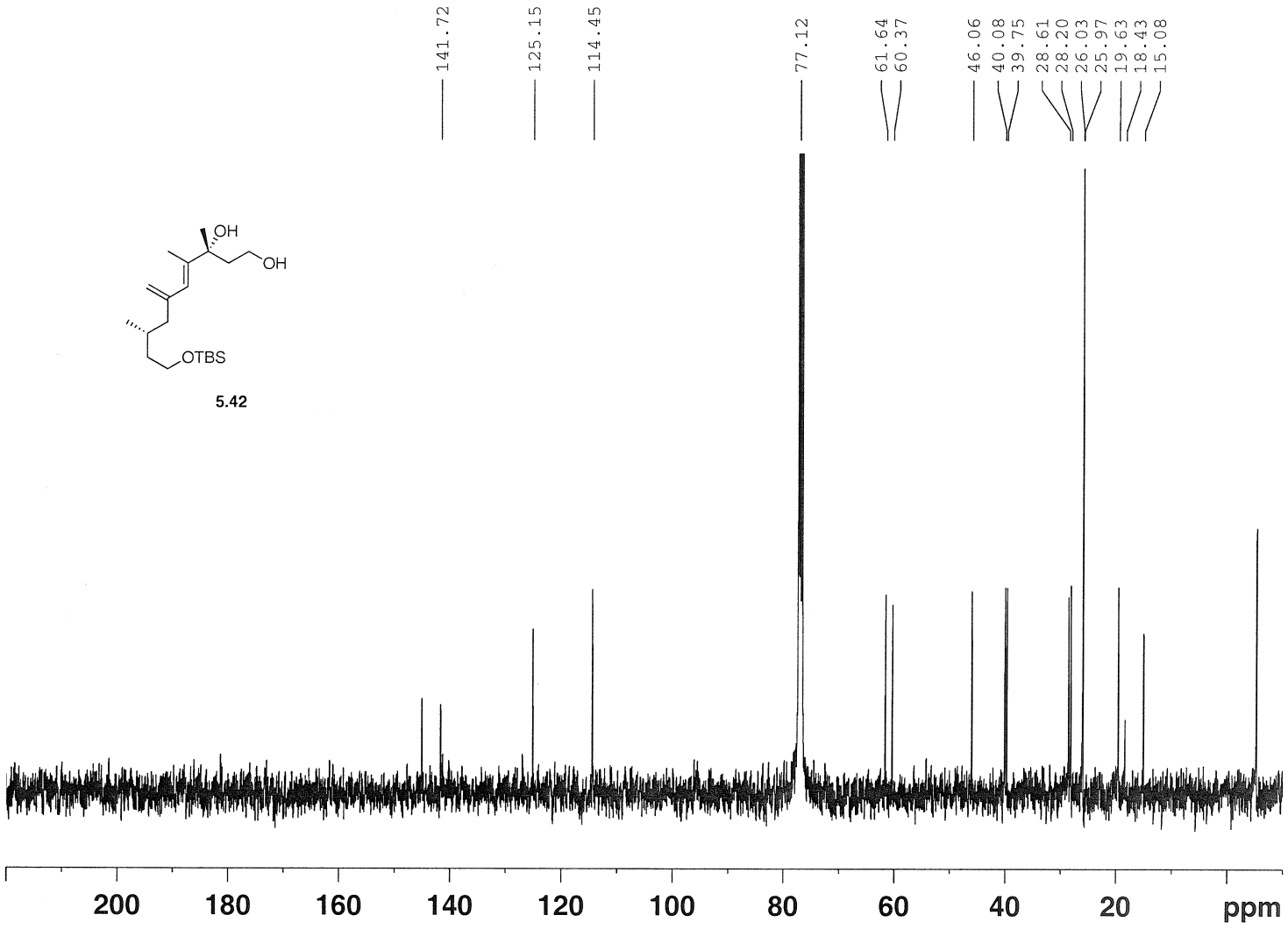

Current Data Parameters
NAME ampddb1-IV-11(071906)
EXPNO 1
PROCNO 1
DIR /n
USER Liang
F2 - Acquisition Parameters
Date_ 20060719
Time 17.34
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.55559540 sec
RG 512
DW 78.000 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.70 usec
PL1 0.00 dB
SFO1 400.0128001 MHz
F2 - Processing parameters
SI 32768
SF 400.0100000 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
5.901
5.042
4.875
3.903
3.892
3.810
3.794
3.693
3.675
3.671
3.661
3.653
3.636
3.052
3.041
3.036
3.025
2.152
2.138
1.925
1.904
1.891
1.863
1.860
1.677
1.643
1.631
1.613
1.598
1.581
1.567
1.466
1.353
1.330
1.318
1.289
1.241
1.225
0.924
0.862
0.845
OH
O
OTBS
5.40
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
1.00
1.12
1.01
1.14
1.23
2.69
1.01
1.32
1.17
3.42
5.50
3.99
12.47
3.49
7.44



5.40

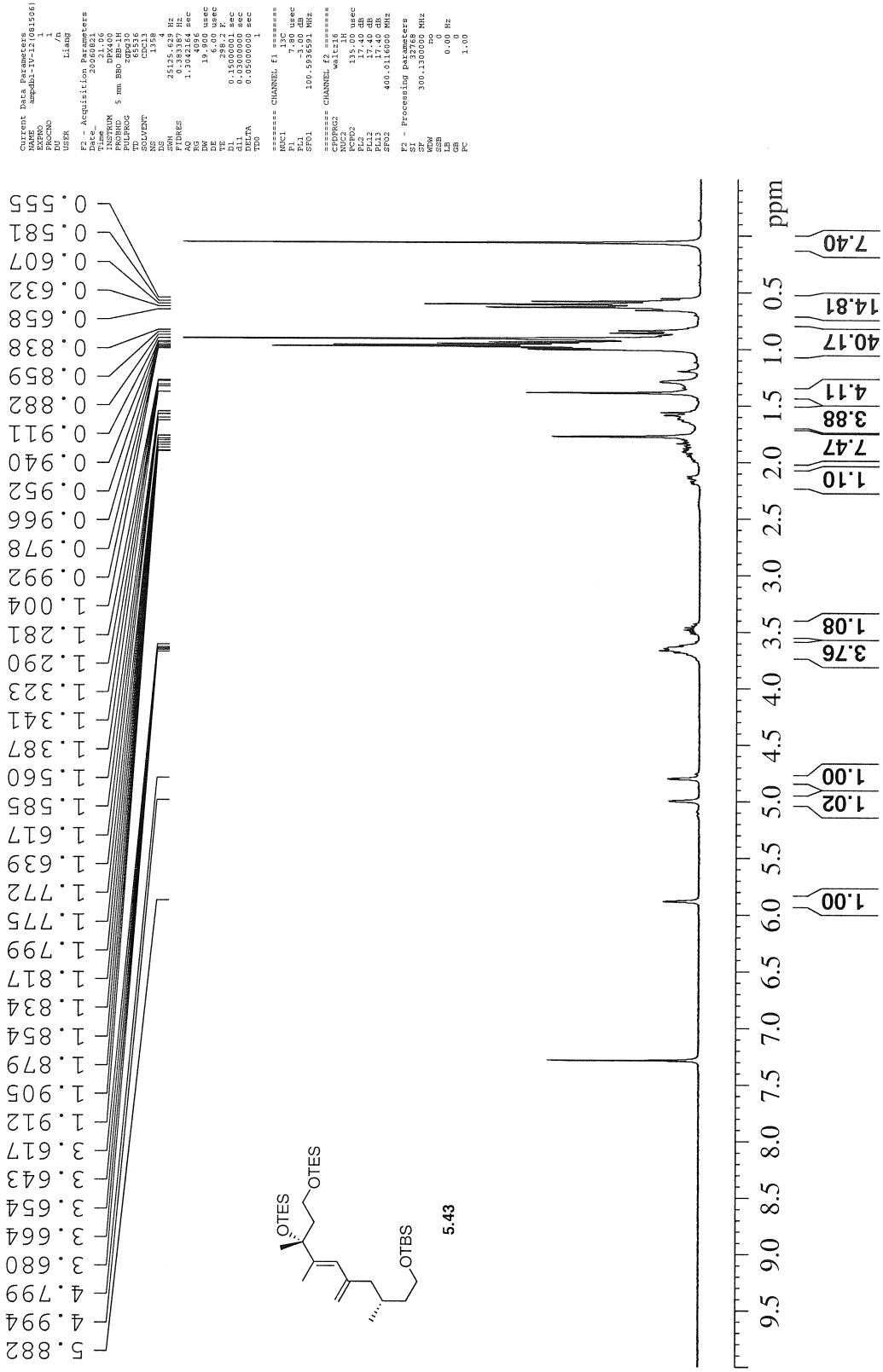
```
Current Data Parameters
NAME      ampdbl-IV-11-2(071
EXPNO                     2
PROCNO                    1
DU                       /n
USER                 Liang

F2 - Acquisition Parameters
Date_              20060719
Time                  17.50
INSTRUM              DPX300
PROBHD   5 mm QNP  1H/1
PULPROG              zgpg30
TD                    65536
SOLVENT               CDCl3
NS                     1074
DS                        4
SWH              18832.393 Hz
FIDRES            0.287360 Hz
AQ                1.7400308 sec
RG                   9195.2
DW                   26.550 use
DE                    6.00 use
TE                   298.2 K
D1             0.15000001 sec
d11            0.03000000 sec
DELTA          0.05000000 sec
TD0                       1

======== CHANNEL f1 =======
NUC1                    13C
P1                    8.80 use
PL1                  -3.00 dB
SFO1          75.4760505 MHz

======== CHANNEL f2 =======
CPDPRG2             waltz16
NUC2                    1H
PCPD2                80.00 use
PL2                  -3.00 dB
PL12                 17.55 dB
PL13                 17.55 dB
SFO2         300.1312005 MHz

F2 - Processing parameters
SI                     32768
SF            75.4677490 MHz
WDW                       EM
SSB                        0
LB                    3.00 Hz
GB                         0
PC                     1.40
```

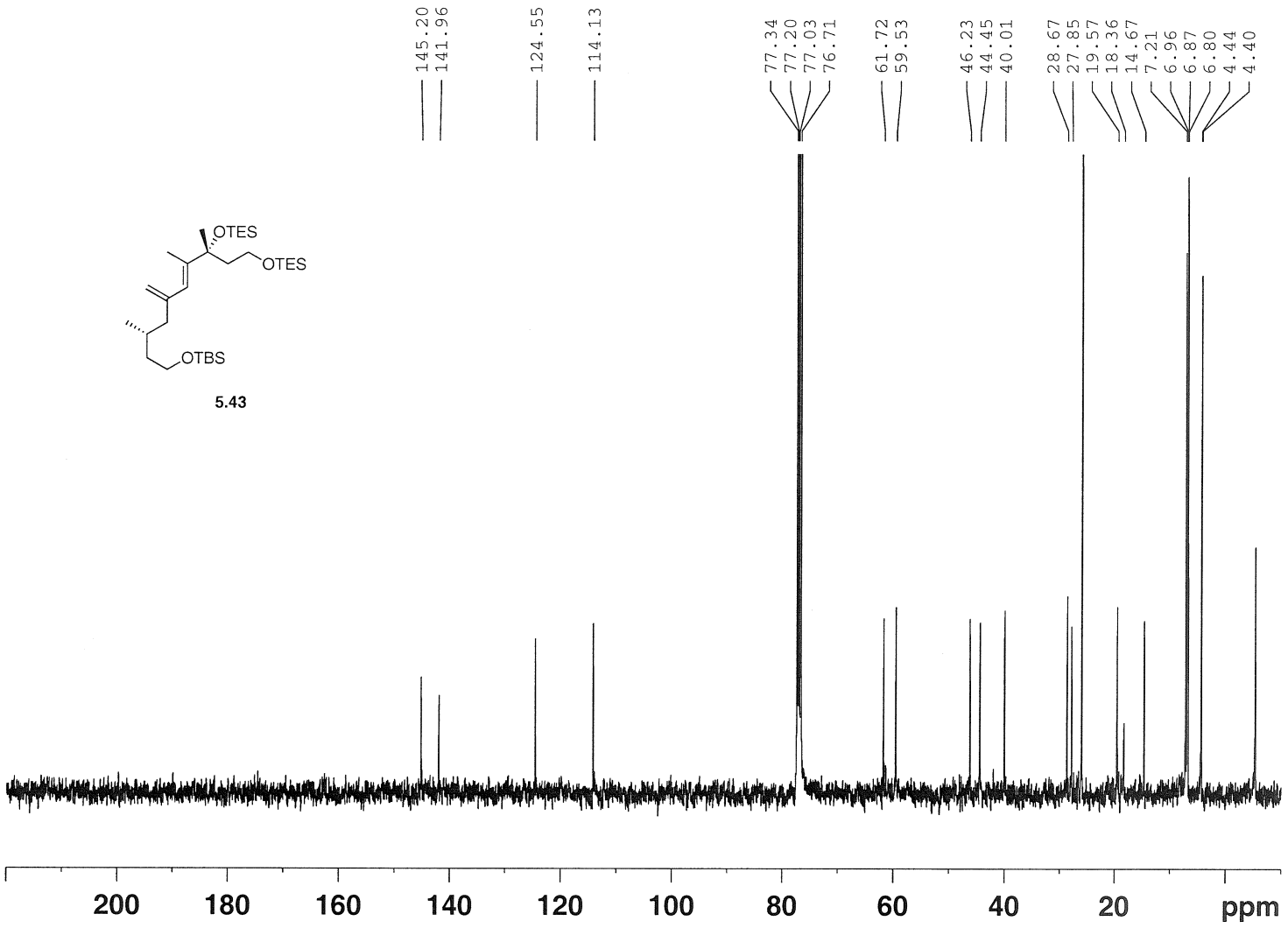

Current Data Parameters
NAME amp4b1-iV-11-diol(072006)
EXPNO 1
PROCNO 1
DU /n
USER Liang
F2 - Acquisition Parameters
Date_ 20060720
Time 17.19
INSTRUM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 4789.272 Hz
FIDRES 0.146157 Hz
AQ 3.4210291 sec
RG 574.7
DW 104.400 usec
DE 6.00 usec
TE 283.2 K
D1 2.00000001 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.00 usec
PL1 -3.00 dB
SFO1 300.1321009 MHz
F2 - Processing parameters
SI 32768
SF 300.1300000 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
OH
OH
OTBS
5.42
6.098
5.040
5.037
4.844
3.768
3.733
3.711
3.700
3.676
3.653
3.631
3.619
3.041
2.604
2.195
2.178
2.151
2.132
1.958
1.932
1.916
1.900
1.895
1.879
1.791
1.787
1.684
1.662
1.640
1.617
1.596
1.579
1.369
1.348
1.323
1.301
1.276
0.908
0.879
0.857
0.070
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
1.00
1.05
1.02
4.42
0.89
1.00
1.20
3.30
3.28
3.76
4.90
14.15
6.93



5.42

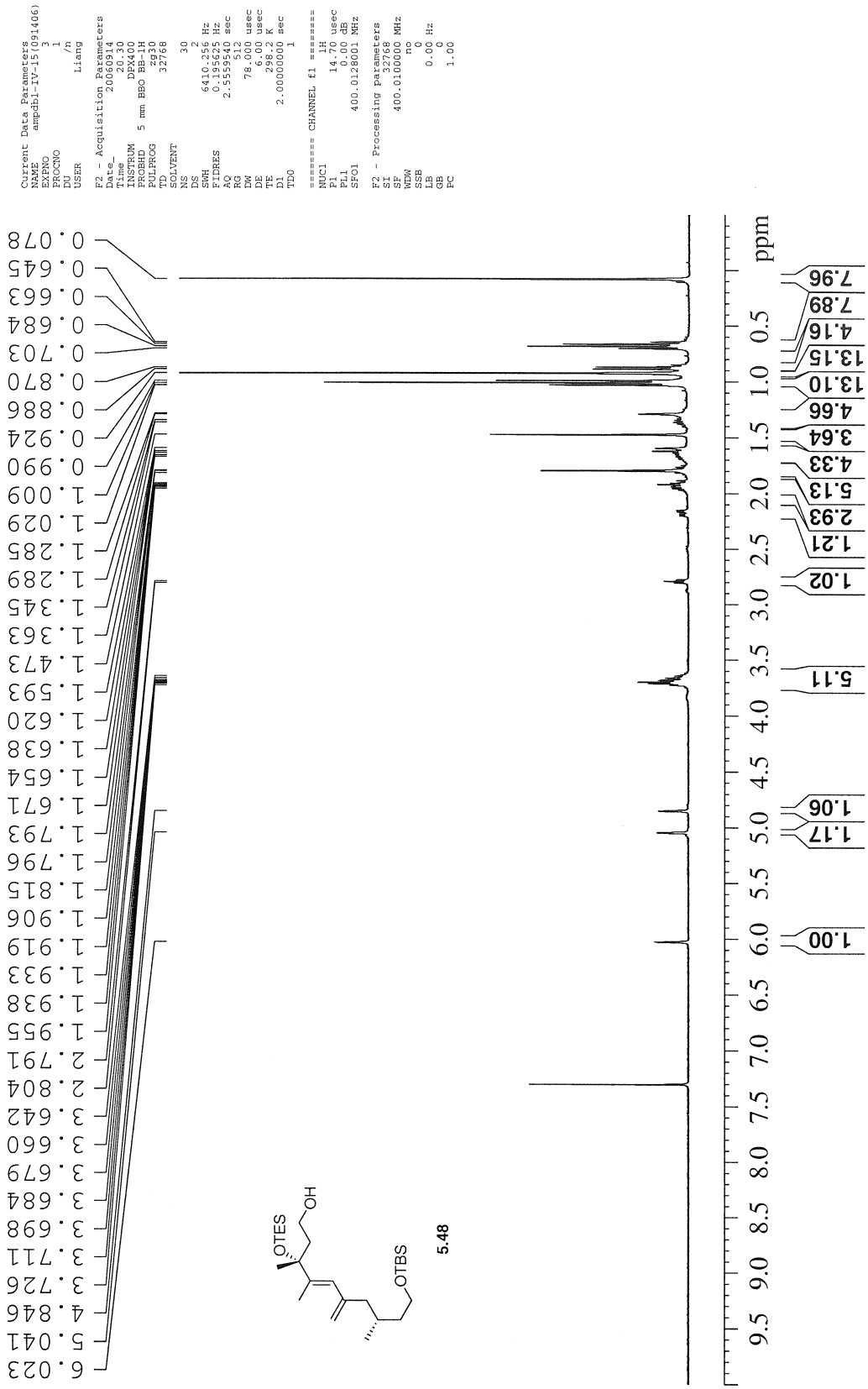
```
Current Data Parameters
NAME      ampdb1-IV-11-diol(072
EXPNO                         4
PROCNO                        1
DU                           /n
USER                      Liang

F2 - Acquisition Parameters
Date_                  20060720
Time                      23.00
INSTRUM                 DPX400
PROBHD   5 mm BBO BB-1H
PULPROG                zgpg30
TD                        65536
SOLVENT
NS                         1943
DS                            4
SWH                25125.629 Hz
FIDRES              0.383387 Hz
AQ                  1.3042164 sec
RG                     4597.6
DW                    19.900 usec
DE                     6.00 usec
TE                     298.2 K
D1                 0.15000001 sec
d11                0.03000000 sec
DELTA              0.05000000 sec
TD0                           1

======== CHANNEL f1 ========
NUC1                        13C
P1                        7.80 usec
PL1                      -3.00 dB
SFO1               100.5936591 MHz

======== CHANNEL f2 ========
CPDPRG2                waltz16
NUC2                        1H
PCPD2                   135.00 usec
PL2                      17.40 dB
PL12                     17.40 dB
PL13                     17.40 dB
SFO2               400.0116000 MHz

F2 - Processing parameters
SI                         32768
SF                 100.5825950 MHz
WDW                           EM
SSB                            0
LB                        3.00 Hz
GB                             0
PC                         1.40
```

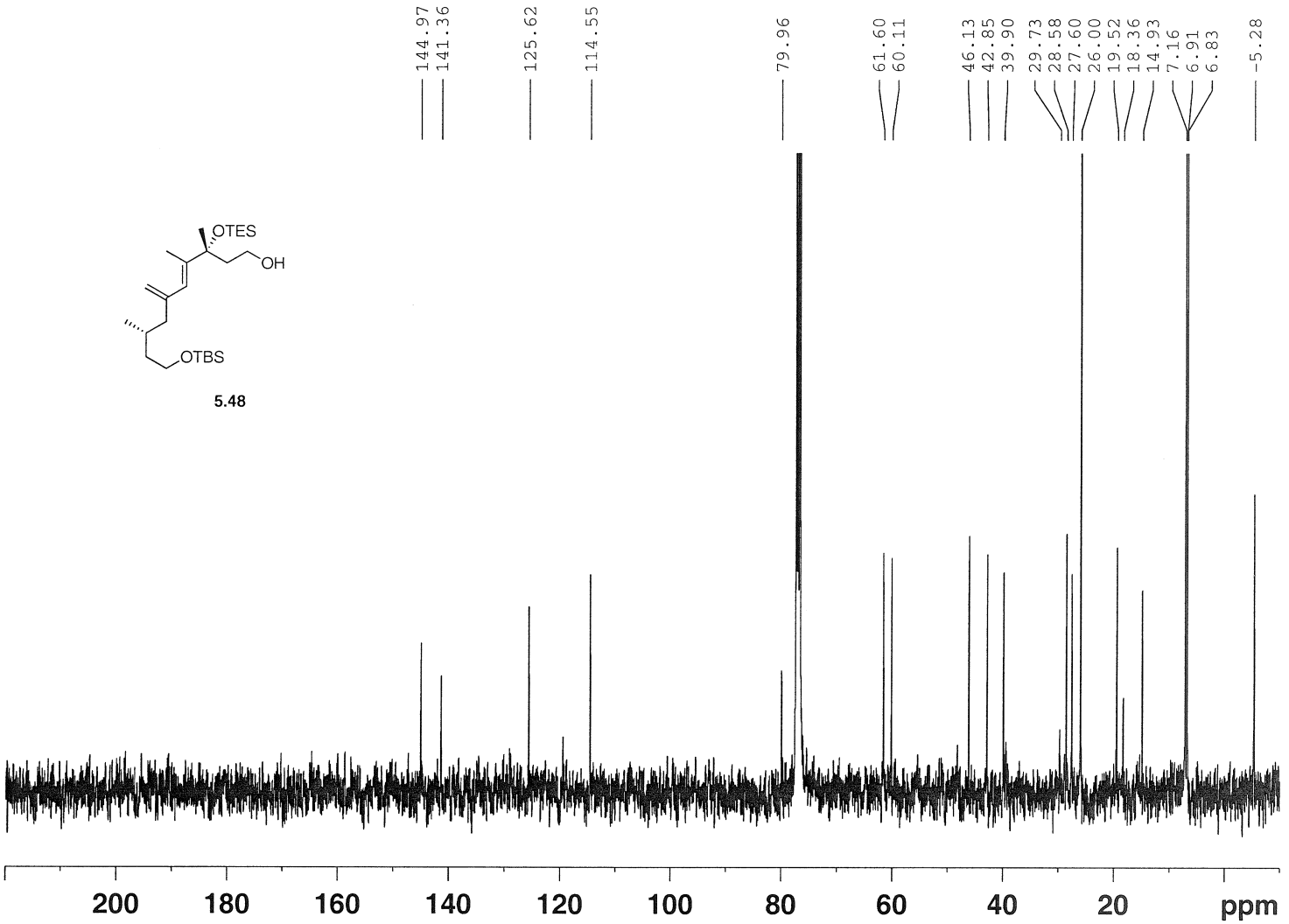

Current Data Parameters
NAME amgdbi-IV-12(081506)
EXPNO 1
PROCNO /1
PD /1
USER Liang
F2 - Acquisition Parameters
Date_ 20060821
Time 21.06
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 128
DS 4
SWH 25125.629 Hz
FIDRES 0.383524 Hz
AQ 1.3042164 sec
RG 4096
DW 19.900 usec
DE 6.00 usec
TE 298.2 K
D1 0.15000001 sec
d11 0.03000000 sec
DELTA 0.05000001 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 7.80 usec
PL1 7.00 dB
SFO1 100.5936892 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 135.00 usec
PL2 17.40 dB
PL12 17.40 dB
PL13 17.40 dB
SFO2 400.0116000 MHz
F2 - Processing parameters
SI 32768
SF 300.1300000 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
OTES
OTES
OTBS
5.43
ppm
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
1.00
1.02
1.00
3.76
1.08
1.10
7.47
3.88
4.11
40.17
14.81
7.40
5.882
4.994
4.799
3.680
3.664
3.654
3.643
3.617
1.912
1.905
1.879
1.854
1.834
1.817
1.799
1.775
1.772
1.639
1.617
1.585
1.560
1.387
1.341
1.323
1.290
1.281
1.004
0.992
0.978
0.966
0.952
0.940
0.911
0.882
0.859
0.838
0.658
0.632
0.607
0.581
0.555



5.43

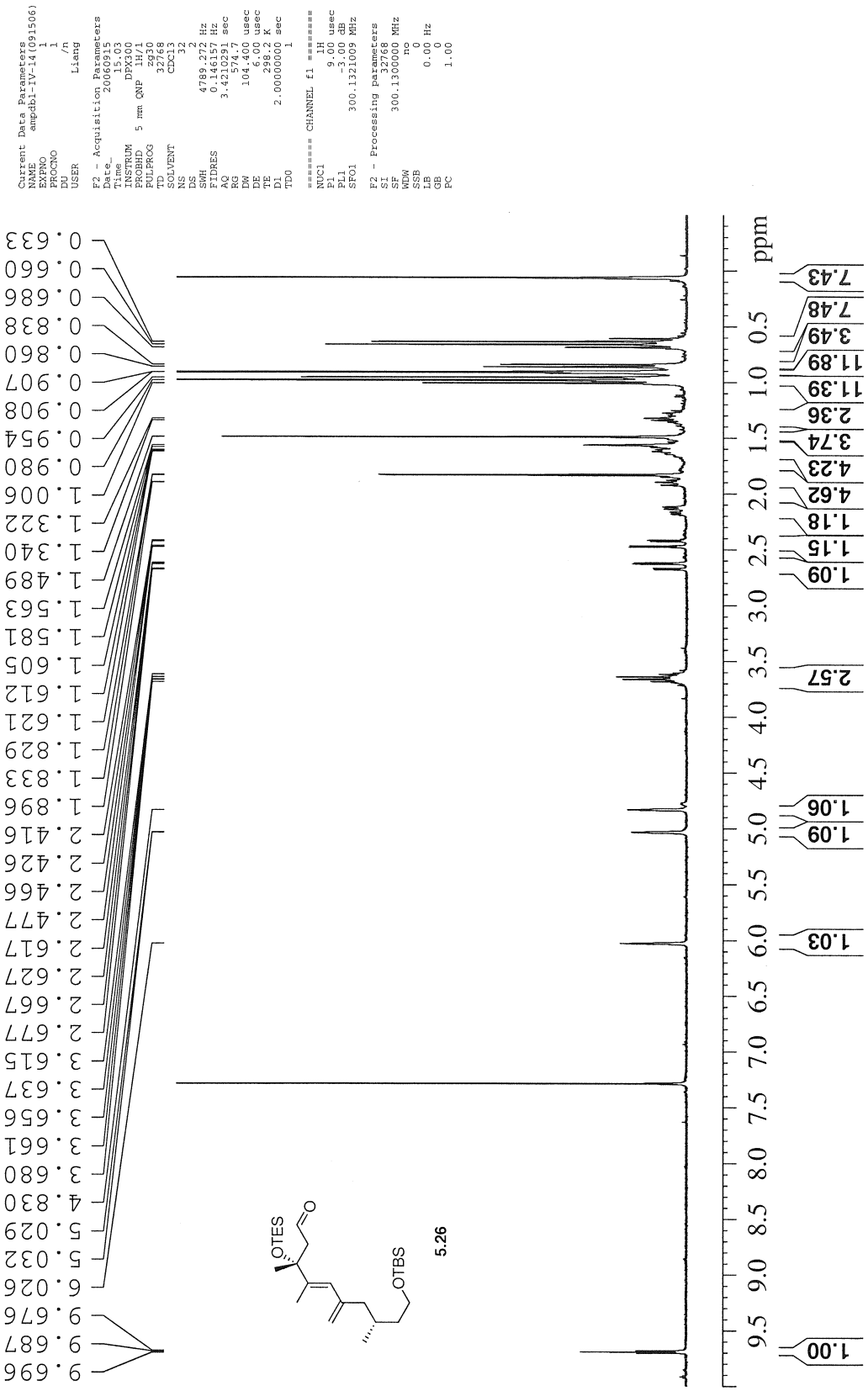
```
Current Data Parameters
NAME        ampdb1-IV-12(081
EXPNO                      1
PROCNO                     3
DU                        /n
USER                   Liang

F2 - Acquisition Parameter
Date_               20060821
Time                   21.06
INSTRUM              DPX400
PROBHD    5 mm BBO BB-1H
PULPROG             zgpg30
TD                     65536
SOLVENT              CDCl3
NS                      1358
DS                         4
SWH                25125.629 Hz
FIDRES             0.383387 Hz
AQ                 1.3042164 se
RG                      4096
DW                   19.900 us
DE                    6.00 us
TE                   298.2 K
D1              0.15000001 se
d11             0.03000000 se
DELTA           0.05000000 se
TD0                        1

======== CHANNEL f1 ======
NUC1                     13C
P1                    7.80 us
PL1                  -3.00 dB
SFO1          100.5936591 MH

======== CHANNEL f2 ======
CPDPRG2             waltz16
NUC2                     1H
PCPD2               135.00 us
PL2                  17.40 dB
PL12                 17.40 dB
PL13                 17.40 dB
SFO2          400.0116000 MH

F2 - Processing parameters
SI                     32768
SF            100.5825950 MH
WDW                       EM
SSB                        0
LB                    3.00 Hz
GB                         0
PC                     1.40
```

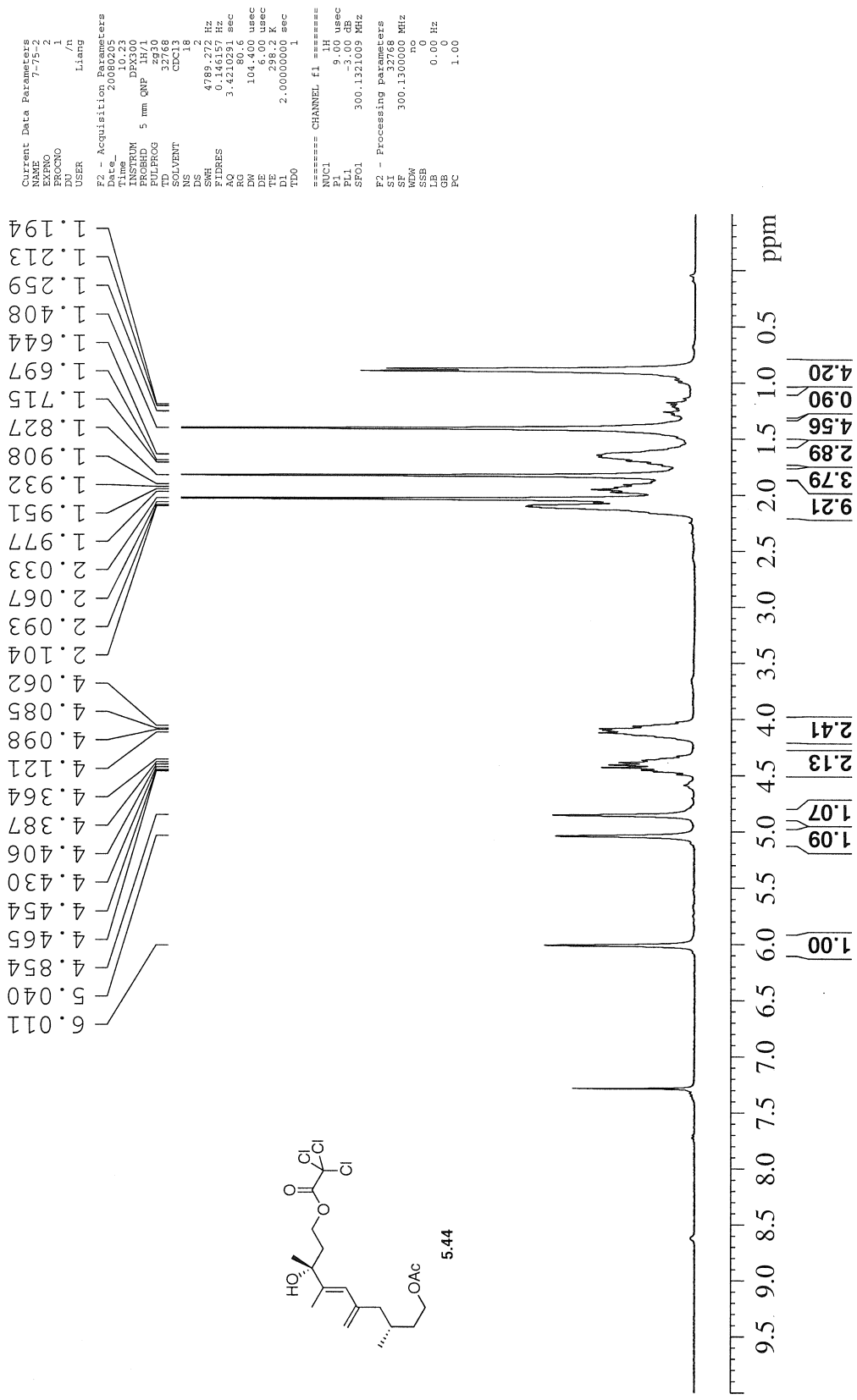

Current Data Parameters
NAME ampdb1-IV-157(091406)
EXPNO 3
PROCNO 1
DU /n
USER Liang
F2 - Acquisition Parameters
Date_ 20060914
Time 20.30
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT
NS 30
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.55559540 sec
RG 512
DW 78.000 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.70 usec
PL1 0.00 dB
SFO1 400.0128001 MHz
F2 - Processing parameters
SI 32768
SF 400.0100000 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
OTES
OH
OTBS
5.48
ppm
1.00
1.17
1.06
5.11
1.02
1.21
2.93
5.13
4.33
3.64
4.66
13.10
13.15
4.16
7.89
7.96

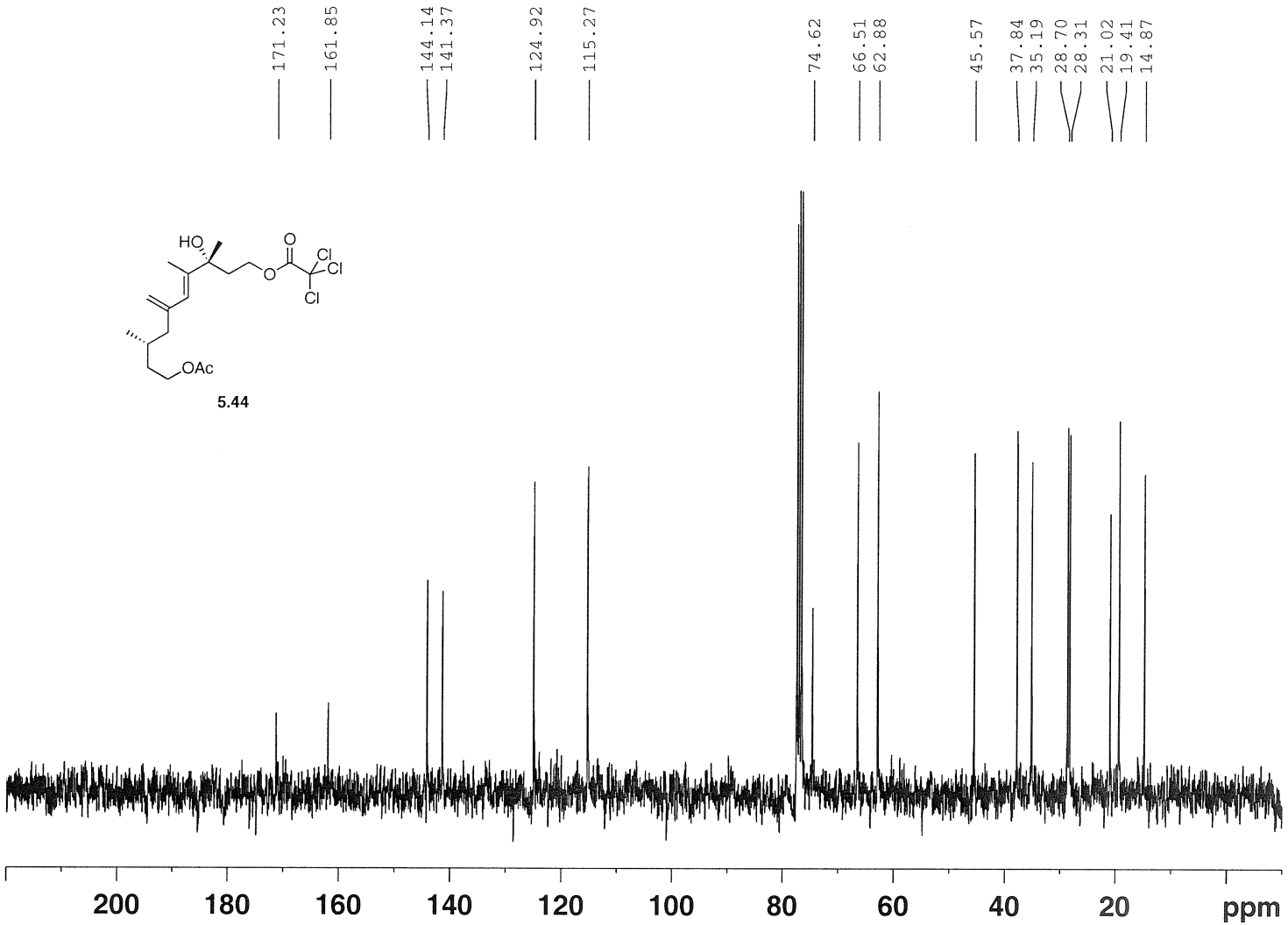


5.48

```
Current Data Parameters
NAME      ampdbl-IV-15(0914
EXPNO                    5
PROCNO                   1
DU                      /n
USER                 Liang

F2 - Acquisition Parameter
Date_             20060914
Time                 21.48
INSTRUM            DPX400
PROBHD   5 mm BBO BB-1H
PULPROG            zgpg30
TD                  65536
SOLVENT
NS                   2450
DS                      4
SWH              25125.629 Hz
FIDRES           0.383387 Hz
AQ               1.3042164 se
RG                   6502
DW                 19.900 us
DE                  6.00 us
TE                 298.2 K
D1             0.15000001 se
d11            0.03000000 se
DELTA          0.05000000 se
TD0                     1

======== CHANNEL f1 ======
NUC1                  13C
P1                   7.80 us
PL1                 -3.00 dB
SFO1         100.5936591 MH

======== CHANNEL f2 ======
CPDPRG2          waltz16
NUC2                  1H
PCPD2             135.00 us
PL2                17.40 dB
PL12               17.40 dB
PL13               17.40 dB
SFO2         400.0116000 MH

F2 - Processing parameters
SI                  32768
SF           100.5825950 MH
WDW                   EM
SSB                    0
LB                  3.00 Hz
GB                     0
PC                  1.40
```

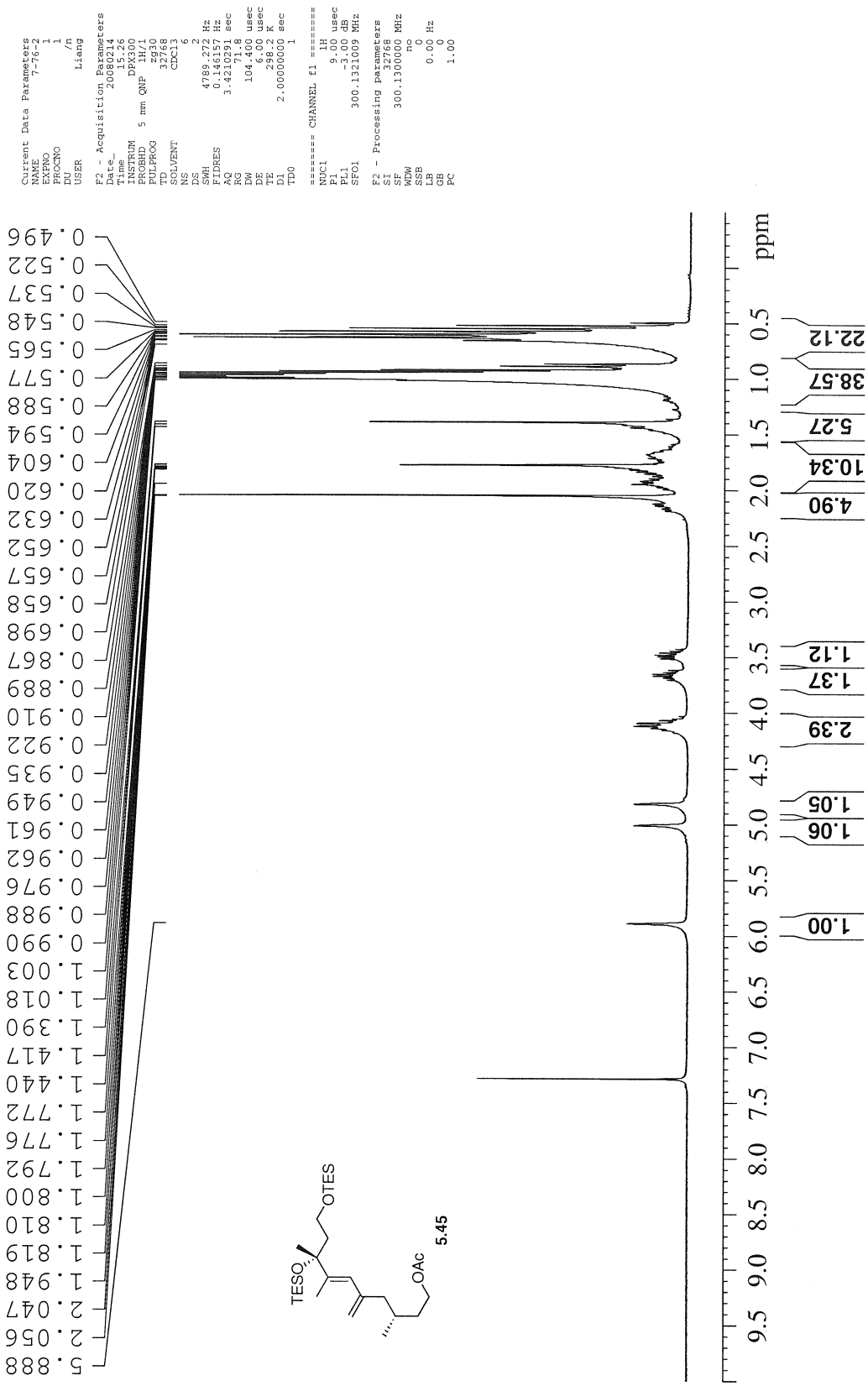

Current Data Parameters
NAME amgabi-1V-141(0911506)
EXPNO 1
PROCNO 1
DU /n
USER Liang
F2 - Acquisition Parameters
Date_ 20060915
Time 15.03
INSTRUM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 4789.272 Hz
FIDRES 0.146157 Hz
AQ 3.4210291 sec
RG 574.7
DW 104.400 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.00 usec
PL1 -3.00 dB
SFO1 300.1321009 MHz
F2 - Processing parameters
SI 32768
SF 300.1300000 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
OTES
OTBS
5.26
ppm
9.696
9.687
9.676
6.026
5.032
5.029
4.830
3.680
3.661
3.656
3.637
3.615
2.677
2.667
2.627
2.617
2.477
2.466
2.426
2.416
1.896
1.833
1.829
1.621
1.612
1.605
1.581
1.563
1.489
1.340
1.322
1.006
0.980
0.954
0.908
0.907
0.860
0.838
0.686
0.660
0.633
1.00
1.03
1.09
1.06
2.57
1.09
1.15
1.18
4.62
4.23
3.74
2.36
11.39
11.89
3.49
7.48
7.43

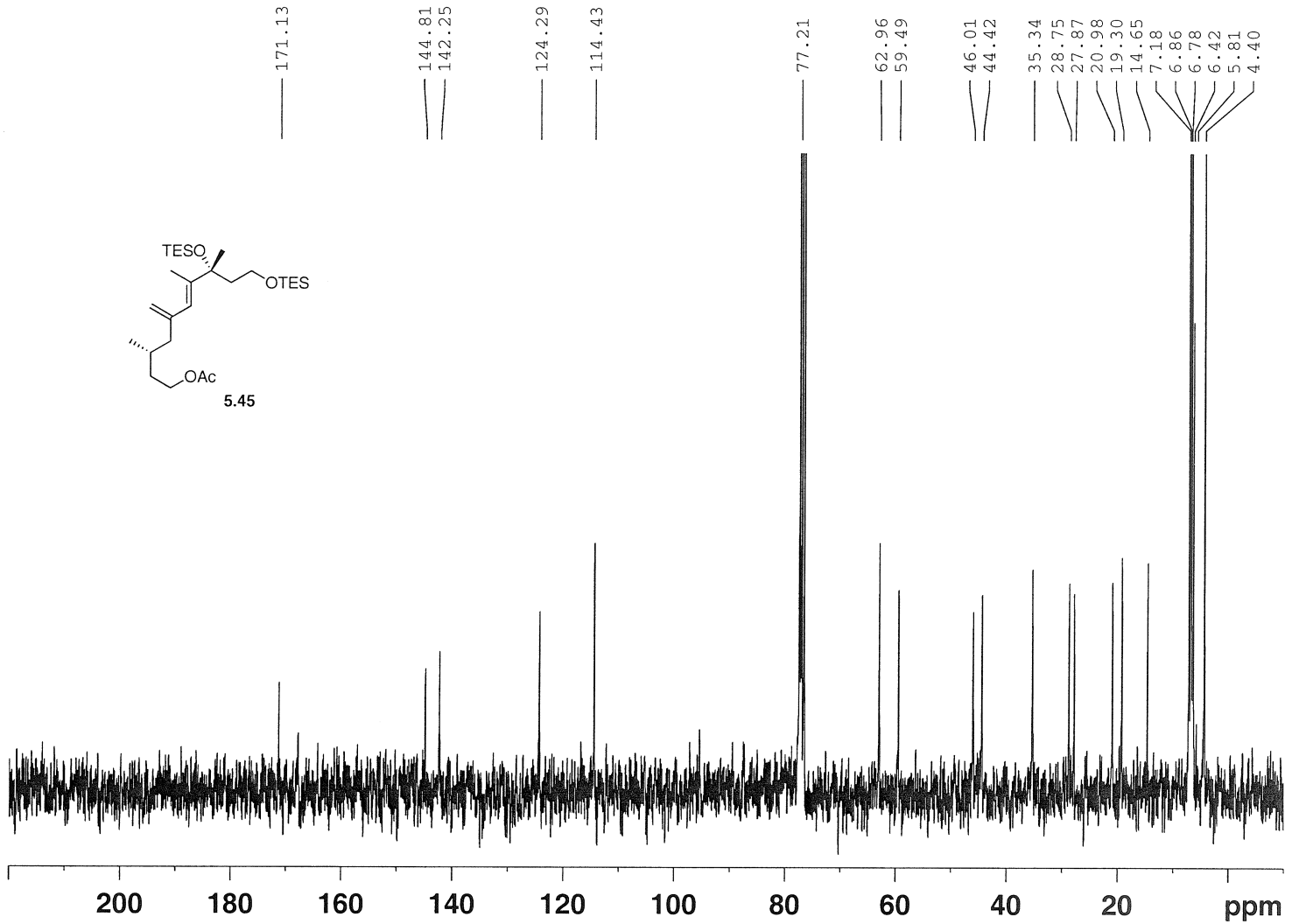

Current Data Parameters
NAME 7-75-2
EXPNO 2
PROCNO 1
DU /n
USER Liang
F2 - Acquisition Parameters
Date_ 20080205
Time 10.23
INSTRUM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 18
DS 2
SWH 4789.272 Hz
FIDRES 0.146157 Hz
AQ 3.4210291 sec
RG 80.6
DW 104.400 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.00 usec
PL1 -3.00 dB
SFO1 300.1321009 MHz
F2 - Processing parameters
SI 32768
SF 300.1300000 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
6.011
5.040
4.854
4.465
4.454
4.430
4.406
4.387
4.364
4.121
4.098
4.085
4.062
2.104
2.093
2.067
2.033
1.977
1.951
1.932
1.908
1.827
1.715
1.697
1.644
1.408
1.259
1.213
1.194
HO
OAc
5.44
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
1.00
1.09
1.07
2.13
2.41
9.21
3.79
2.89
4.56
0.90
4.20



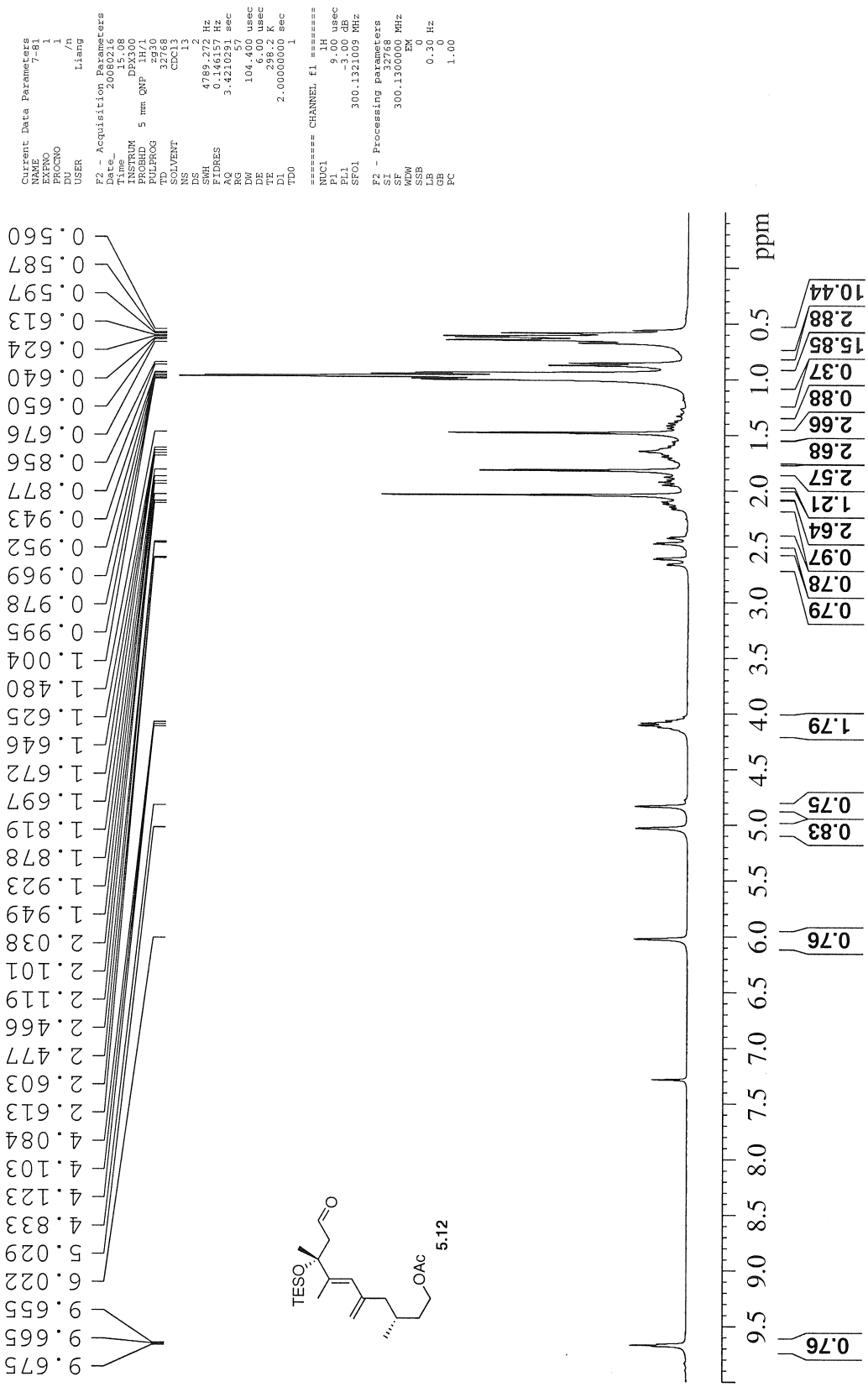
5.44

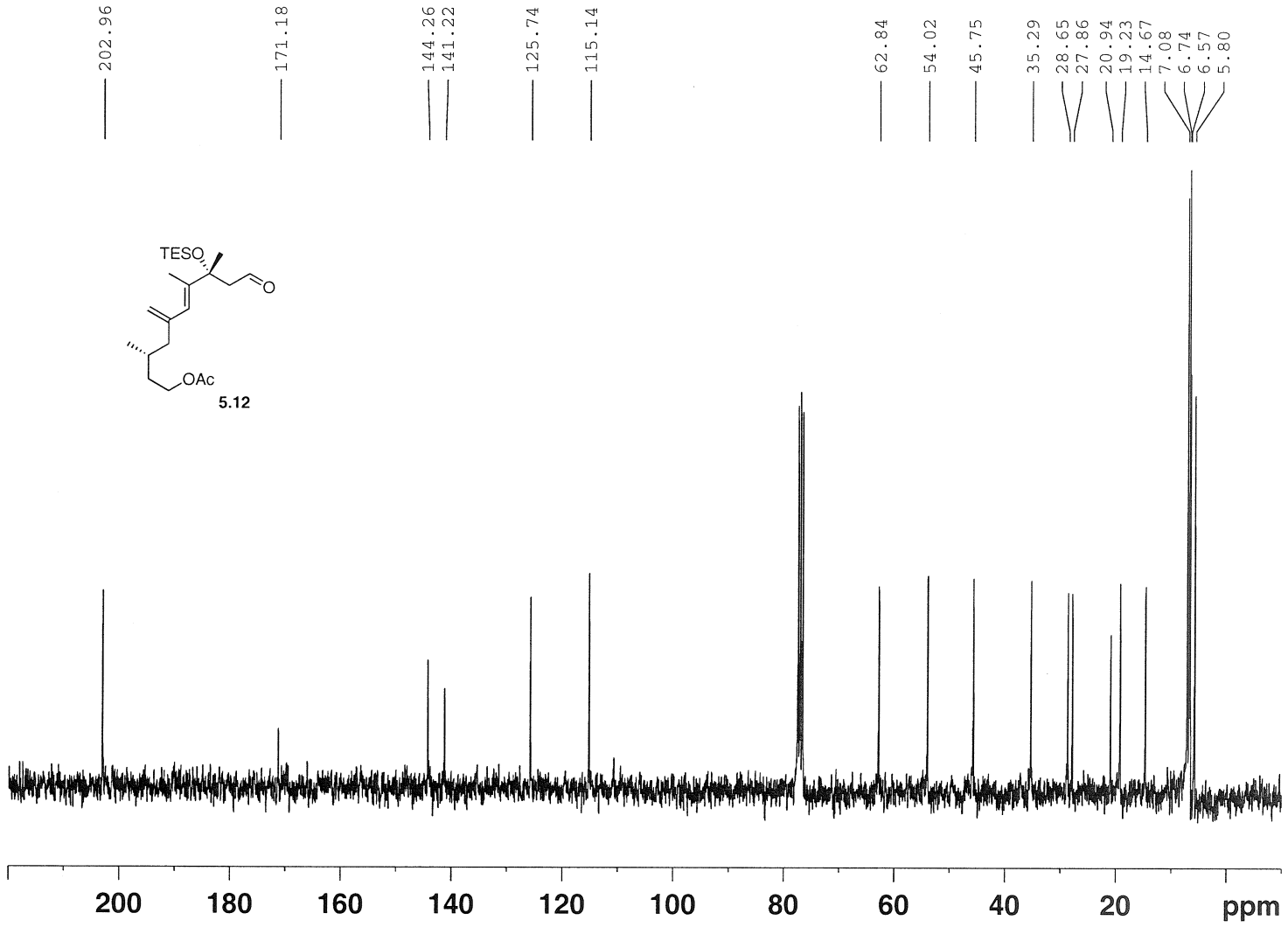
```
Current Data Parameters
NAME                  7-75-2
EXPNO                      3
PROCNO                     1
DU                        /n
USER                   Liang

F2 - Acquisition Parameter
Date_              20080205
Time                  10.26
INSTRUM             DPX300
PROBHD   5 mm QNP  1H/1
PULPROG             zgpg30
TD                   65536
SOLVENT              CDCl3
NS                     156
DS                       4
SWH              18832.393 Hz
FIDRES           0.287360 Hz
AQ               1.7400308 se
RG                  9195.2
DW                  26.550 us
DE                   6.00 us
TE                  298.2 K
D1             0.15000001 se
d11            0.03000000 se
DELTA          0.05000000 se
TD0                      1

======== CHANNEL f1 ======
NUC1                   13C
P1                    8.80 us
PL1                  -3.00 dB
SFO1           75.4760505 MH

======== CHANNEL f2 ======
CPDPRG2            waltz16
NUC2                   1H
PCPD2                80.00 us
PL2                  -3.00 dB
PL12                 17.55 dB
PL13                 17.55 dB
SFO2          300.1312005 MH

F2 - Processing parameters
SI                   32768
SF             75.4677490 MH
WDW                    EM
SSB                     0
LB                   3.00 Hz
GB                      0
PC                   1.40
```


Current Data Parameters
NAME 7-76-2
EXPNO 1
PROCNO 1
DU /n
USER Liang
F2 - Acquisition Parameters
Date_ 20080214
Time 15.26
INSTRUM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 6
DS 2
SWH 4789.272 Hz
FIDRES 0.146157 Hz
AQ 3.4210291 sec
RG 71.8
DW 104.400 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.00 usec
PL1 -3.00 dB
SFO1 300.1321009 MHz
F2 - Processing parameters
SI 32768
SF 300.1300000 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
TESO
OTES
OAc
5.45
ppm
1.00
1.06
1.05
2.39
1.37
1.12
4.90
10.34
5.27
38.57
22.12

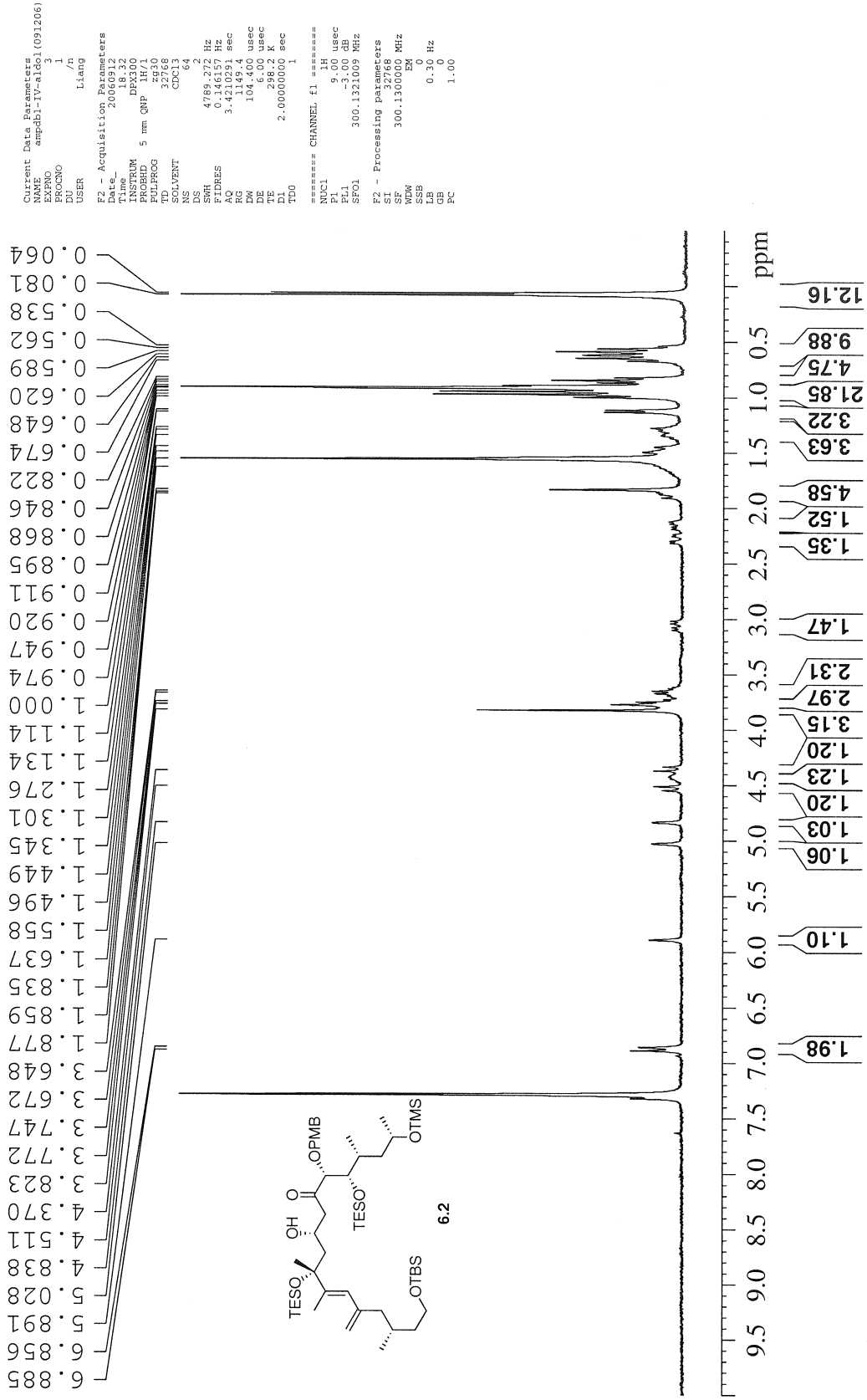


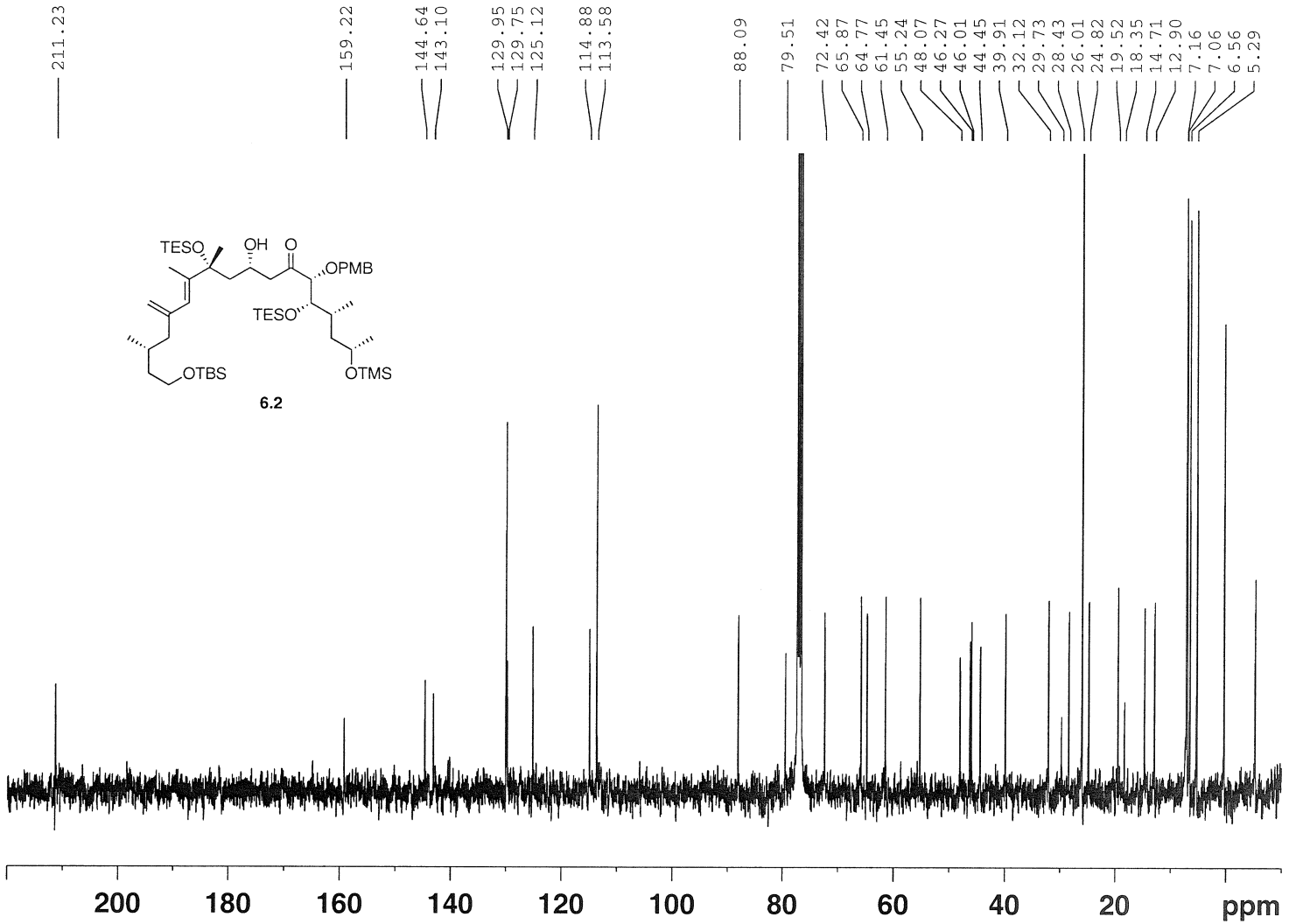

```
Current Data Parameters
NAME                  7-76-2
EXPNO                      2
PROCNO                     1
DU                        /n
USER                  Liang

F2 - Acquisition Parameter
Date_              20080214
Time                  15.30
INSTRUM             DPX300
PROBHD   5 mm QNP  1H/1
PULPROG             zgpg30
TD                    65536
SOLVENT               CDCl3
NS                      189
DS                        4
SWH              18832.393 Hz
FIDRES           0.287360 Hz
AQ               1.7400308 se
RG                  9195.2
DW                  26.550 us
DE                   6.00 us
TE                  298.2 K
D1              0.15000001 se
d11             0.03000000 se
DELTA           0.05000000 se
TD0                       1

======== CHANNEL f1 ======
NUC1                    13C
P1                     8.80 us
PL1                   -3.00 dB
SFO1           75.4760505 MH

======== CHANNEL f2 ======
CPDPRG2            waltz16
NUC2                    1H
PCPD2                80.00 us
PL2                  -3.00 dB
PL12                 17.55 dB
PL13                 17.55 dB
SFO2          300.1312005 MH

F2 - Processing parameters
SI                    32768
SF             75.4677490 MH
WDW                      EM
SSB                       0
LB                    3.00 Hz
GB                        0
PC                     1.40
```


Current Data Parameters
NAME 7-81
EXPNO 1
PROCNO 1
DU /n
USER Liang
F2 - Acquisition Parameters
Date_ 20080216
Time 15.08
INSTRUM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 13
DS 2
SWH 4789.272 Hz
FIDRES 0.146157 Hz
AQ 3.4210291 sec
RG 57
DW 104.400 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.00 usec
PL1 -3.00 dB
SFO1 300.1321009 MHz
F2 - Processing parameters
SI 32768
SF 300.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
9.675
9.665
9.655
6.022
5.029
4.833
4.123
4.103
4.084
2.613
2.603
2.477
2.466
2.119
2.101
2.038
1.949
1.923
1.878
1.819
1.697
1.672
1.646
1.625
1.480
1.004
0.995
0.978
0.969
0.952
0.943
0.877
0.856
0.676
0.650
0.640
0.624
0.613
0.597
0.587
0.560
TESO
OAc
5.12
ppm
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
0.76
0.76
1.79
0.75
0.83
0.79
0.78
0.97
2.64
1.21
2.57
2.68
2.66
0.88
0.37
15.85
2.88
10.44

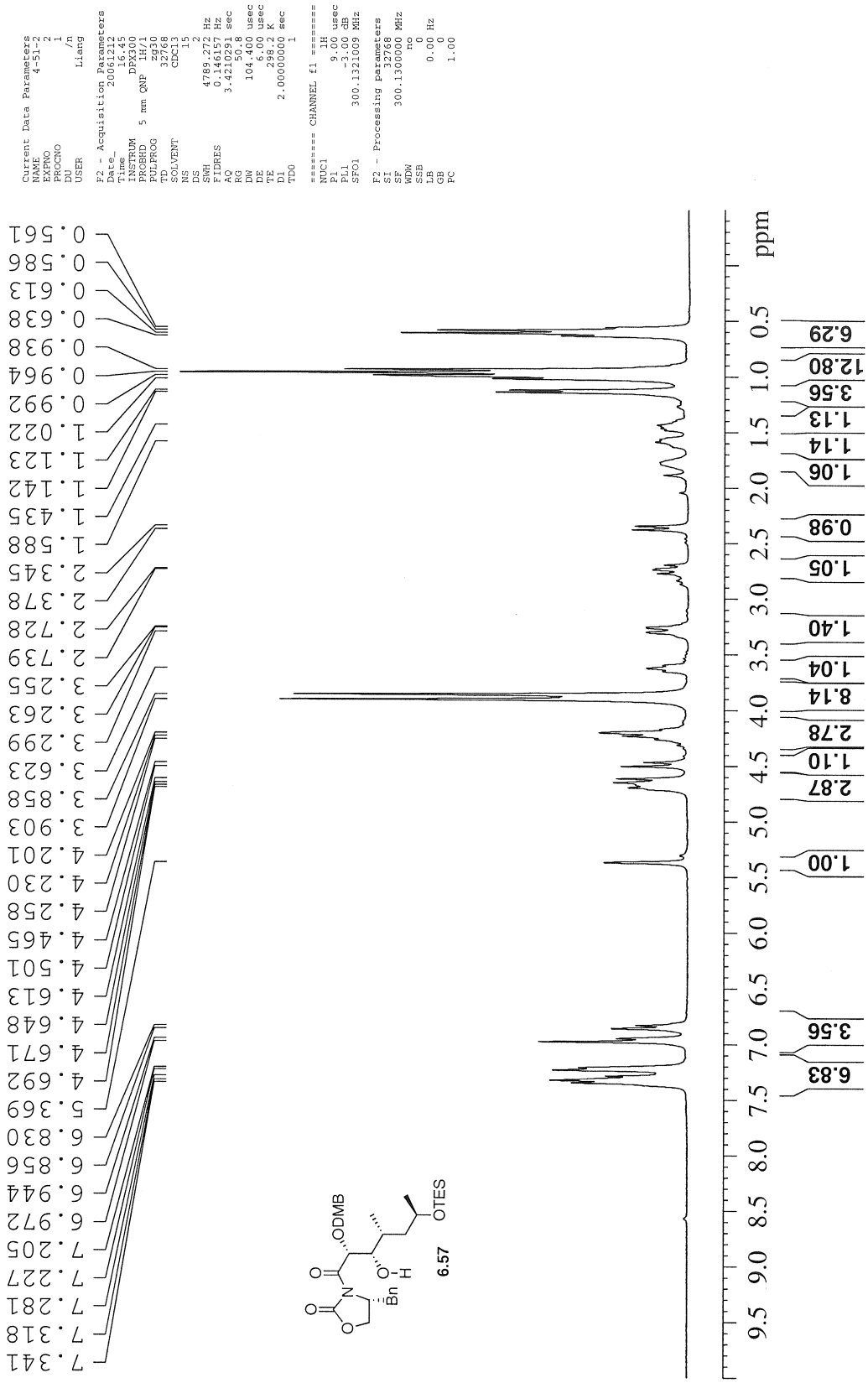


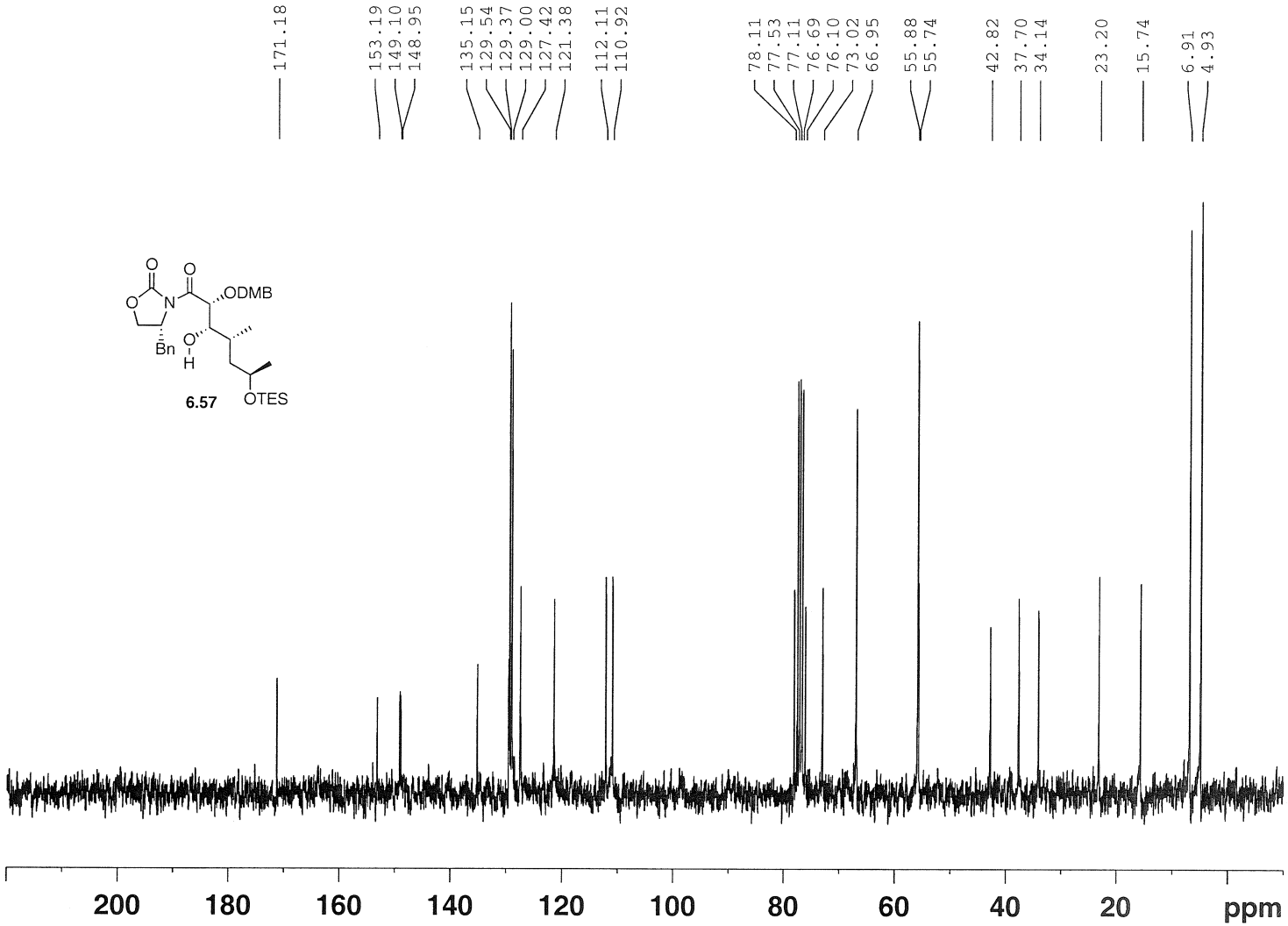

```
Current Data Parameters
NAME                  7-81
EXPNO                    3
PROCNO                   1
DU                      /n
USER                 Liang

F2 - Acquisition Parameter
Date_              20080216
Time                  15.23
INSTRUM             DPX300
PROBHD   5 mm QNP  1H/1
PULPROG             zgpg30
TD                   65536
SOLVENT              CDC13
NS                     188
DS                       4
SWH             18832.393 Hz
FIDRES          0.287360 Hz
AQ              1.7400308 se
RG                 9195.2
DW                 26.550 us
DE                  6.00 us
TE                 298.2 K
D1            0.15000001 se
d11           0.03000000 se
DELTA         0.05000000 se
TD0                      1

======== CHANNEL f1 ======
NUC1                   13C
P1                    8.80 us
PL1                  -3.00 dB
SFO1          75.4760505 MH

======== CHANNEL f2 ======
CPDPRG2           waltz16
NUC2                   1H
PCPD2                80.00 us
PL2                  -3.00 dB
PL12                 17.55 dB
PL13                 17.55 dB
SFO2         300.1312005 MH

F2 - Processing parameters
SI                   32768
SF            75.4677490 MH
WDW                     EM
SSB                      0
LB                    3.00 Hz
GB                       0
PC                    1.40
```


Current Data Parameters
NAME ampdb1-IV-aldol(091206)
EXPNO 3
PROCNO 1
DIR /n
USER Liang
F2 - Acquisition Parameters
Date_ 20060912
Time 18.32
INSTRUM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 64
DS 2
SWH 4789.272 Hz
FIDRES 0.146157 Hz
AQ 3.42110291 sec
RG 1149.4
DW 104.400 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.00 usec
PL1 -3.00 dB
SFO1 300.1321009 MHz
F2 - Processing parameters
SI 32768
SF 300.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
TESO
OH
O
OPMB
TESO
OTMS
OTBS
6.2
ppm
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
1.98
1.10
1.06
1.03
1.20
1.23
1.20
3.15
2.97
2.31
1.47
1.35
1.52
4.58
3.63
3.22
21.85
4.75
9.88
12.16
6.885
6.856
5.891
5.028
4.838
4.511
4.370
3.823
3.772
3.747
3.672
3.648
1.877
1.859
1.835
1.637
1.558
1.496
1.449
1.345
1.301
1.276
1.134
1.114
1.000
0.974
0.947
0.920
0.911
0.895
0.868
0.846
0.822
0.674
0.648
0.620
0.589
0.562
0.538
0.081
0.064

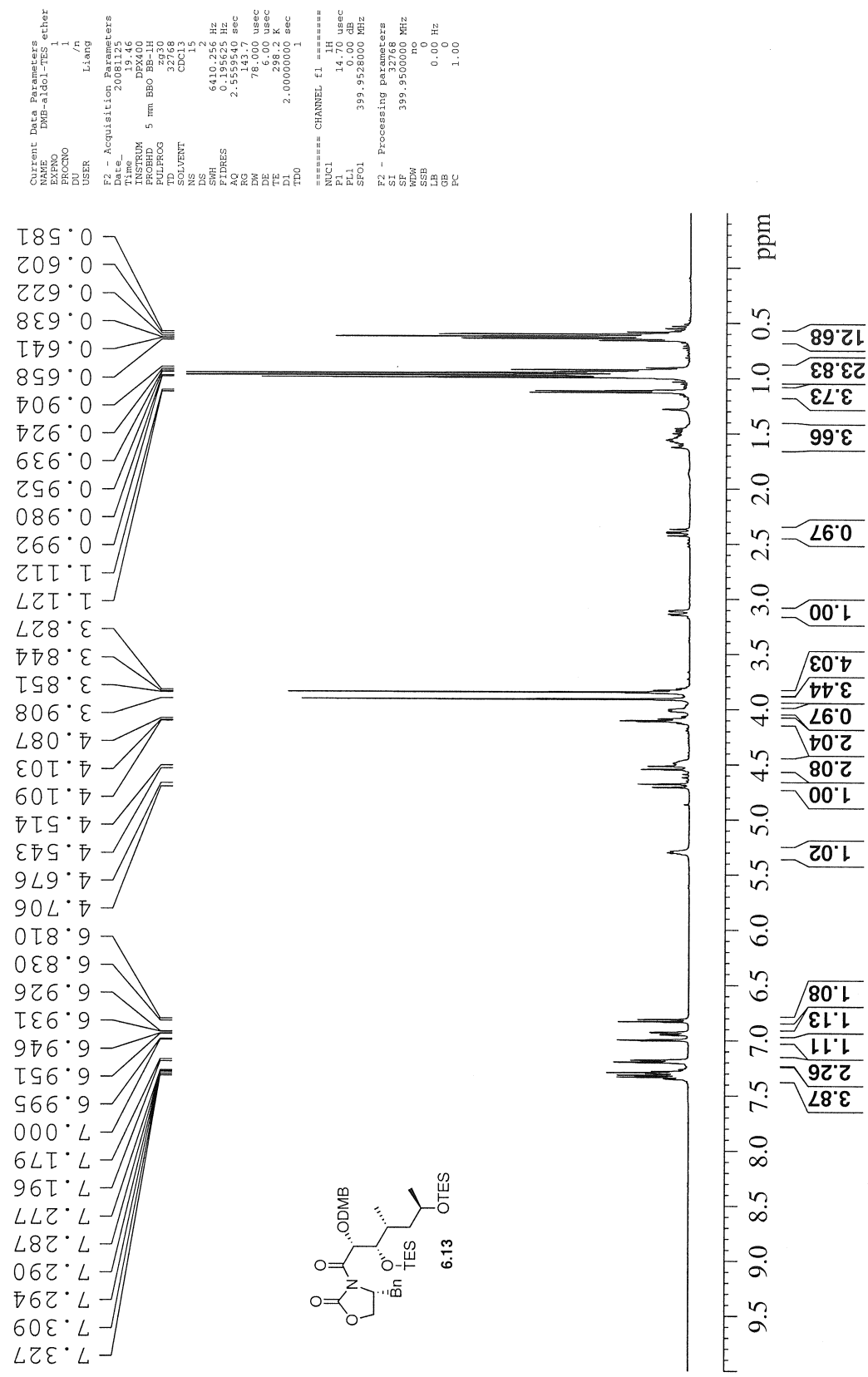


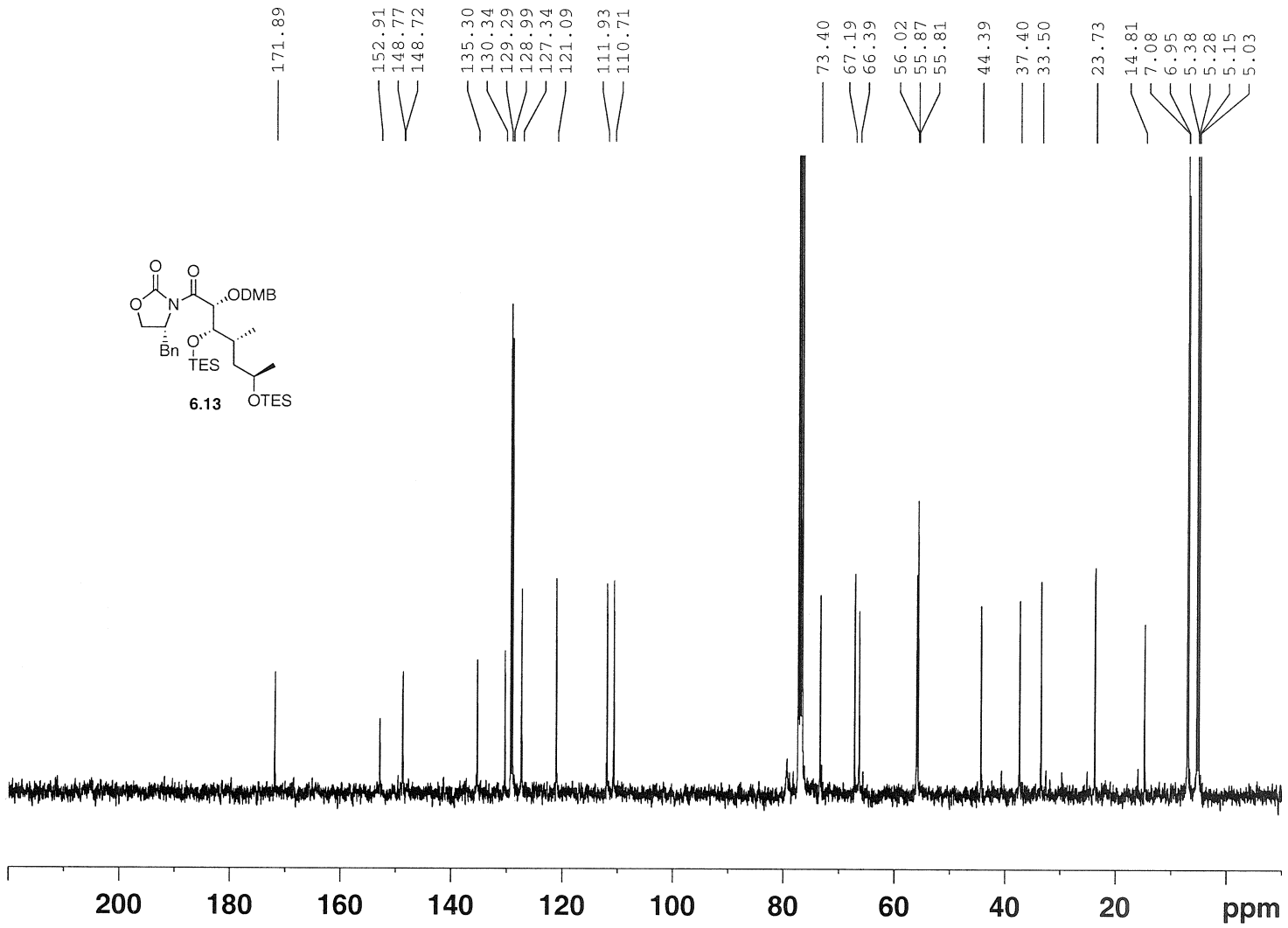

```
Current Data Parameters
NAME                  3-49
EXPNO                    4
PROCNO                   1
DU                      /n
USER                 Liang

F2 - Acquisition Parameter
Date_              20060928
Time                  15.46
INSTRUM             DPX400
PROBHD   5 mm BBO BB-1H
PULPROG             zgpg30
TD                   65536
SOLVENT
NS                    1600
DS                       4
SWH             25125.629 Hz
FIDRES          0.383387 Hz
AQ              1.3042164 se
RG                    2048
DW                19.900 us
DE                 6.00 us
TE                298.2 K
D1            0.15000001 se
d11           0.03000000 se
DELTA         0.05000000 se
TD0                      1

======== CHANNEL f1 ======
NUC1                  13C
P1                 7.80 us
PL1               -3.00 dB
SFO1         100.5936591 MH

======== CHANNEL f2 ======
CPDPRG2           waltz16
NUC2                  1H
PCPD2             135.00 us
PL2                17.40 dB
PL12               17.40 dB
PL13               17.40 dB
SFO2         400.0116000 MH

F2 - Processing parameters
SI                   32768
SF           100.5825950 MH
WDW                    EM
SSB                     0
LB                 3.00 Hz
GB                      0
PC                   1.40
```


Current Data Parameters
NAME 4-51-2
EXPNO 2
PROCNO 1
DU /n
USER Liang
F2 - Acquisition Parameters
Date_ 20061212
Time 16.45
INSTRUM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 15
DS 2
SWH 4789.272 Hz
FIDRES 0.146157 Hz
AQ 3.4210291 sec
RG 50.8
DW 104.400 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.00 usec
PL1 -3.00 dB
SFO1 300.1321009 MHz
F2 - Processing parameters
SI 32768
SF 300.1300000 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
7.341
7.318
7.281
7.227
7.205
6.972
6.944
6.856
6.830
5.369
4.692
4.671
4.648
4.613
4.501
4.465
4.258
4.230
4.201
3.903
3.858
3.623
3.299
3.263
3.255
2.739
2.728
2.378
2.345
1.588
1.435
1.142
1.123
1.022
0.992
0.964
0.938
0.638
0.613
0.586
0.561
ppm
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
6.83
3.56
1.00
2.87
1.10
2.78
8.14
1.04
1.40
1.05
0.98
1.06
1.14
1.13
3.56
12.80
6.29
ODMB
OTES
Bn
6.57

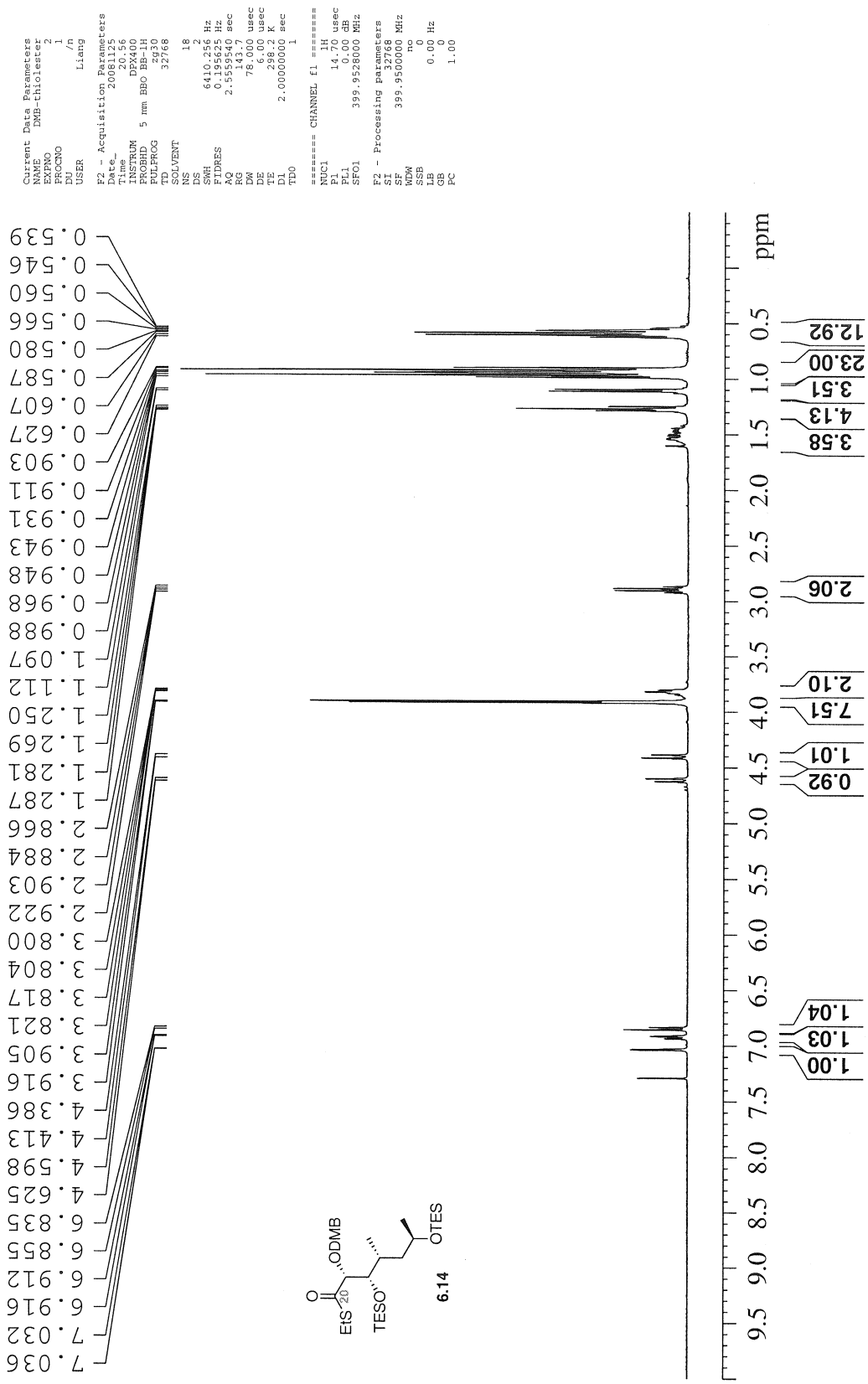


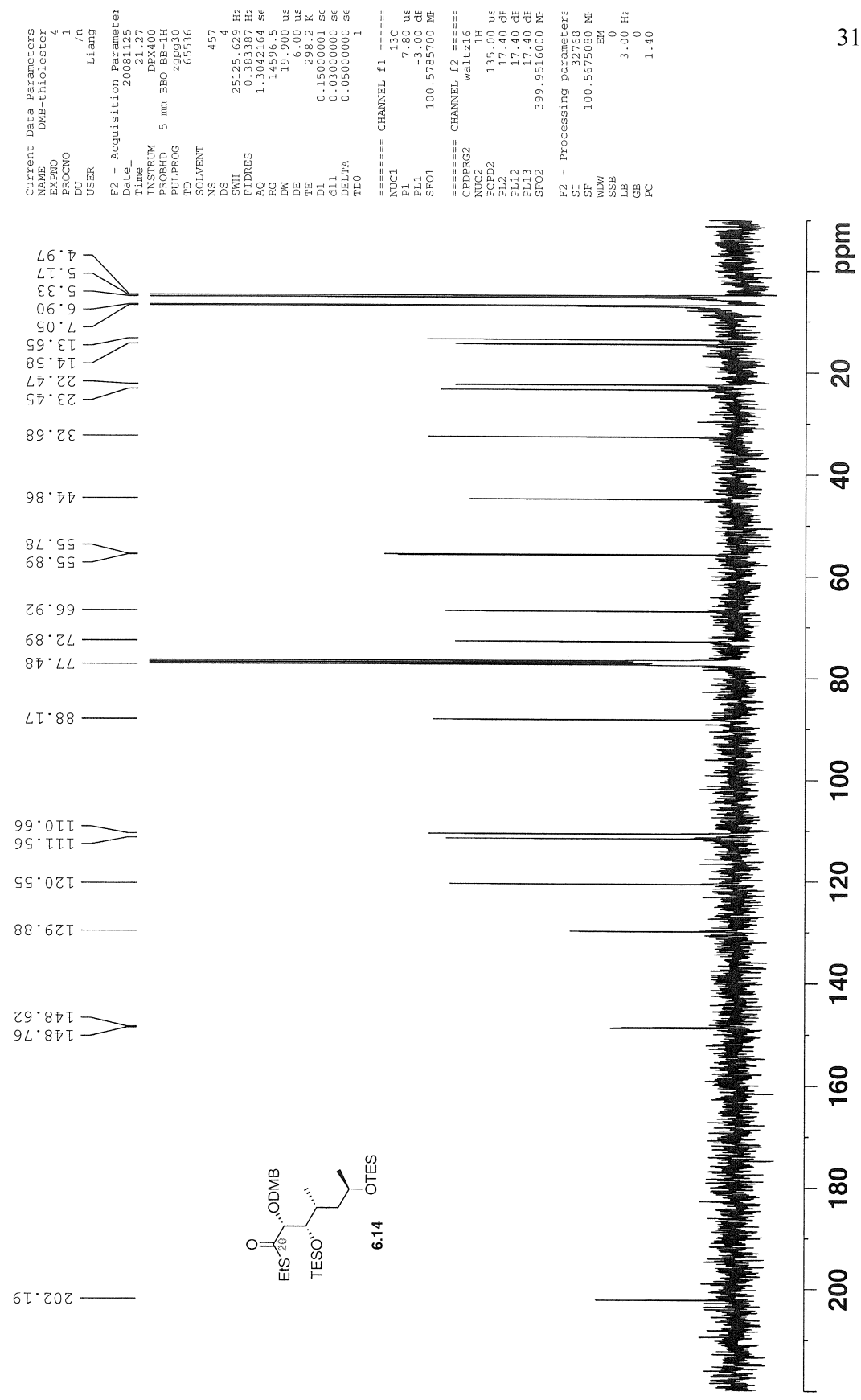

```
Current Data Parameters
NAME                  4-51-2
EXPNO                      4
PROCNO                     1
DU                        /n
USER                   Liang

F2 - Acquisition Parameter
Date_               20061212
Time                   17.03
INSTRUM               DPX300
PROBHD    5 mm QNP  1H/1
PULPROG               zgpg30
TD                     65536
SOLVENT                CDCl3
NS                        58
DS                         4
SWH                18832.393 Hz
FIDRES             0.287360 Hz
AQ                 1.7400308 se
RG                     16384
DW                    26.550 us
DE                     6.00 us
TE                    298.2 K
D1                0.15000001 se
d11               0.03000000 se
DELTA             0.05000000 se
TD0                        1

======== CHANNEL f1 ======
NUC1                     13C
P1                      8.80 us
PL1                    -3.00 dB
SFO1              75.4760505 MH

======== CHANNEL f2 ======
CPDPRG2              waltz16
NUC2                     1H
PCPD2                 80.00 us
PL2                    -3.00 dB
PL12                   17.55 dB
PL13                   17.55 dB
SFO2             300.1312005 MH

F2 - Processing parameters
SI                     32768
SF                75.4677490 MH
WDW                       EM
SSB                        0
LB                     3.00 Hz
GB                         0
PC                      1.40
```

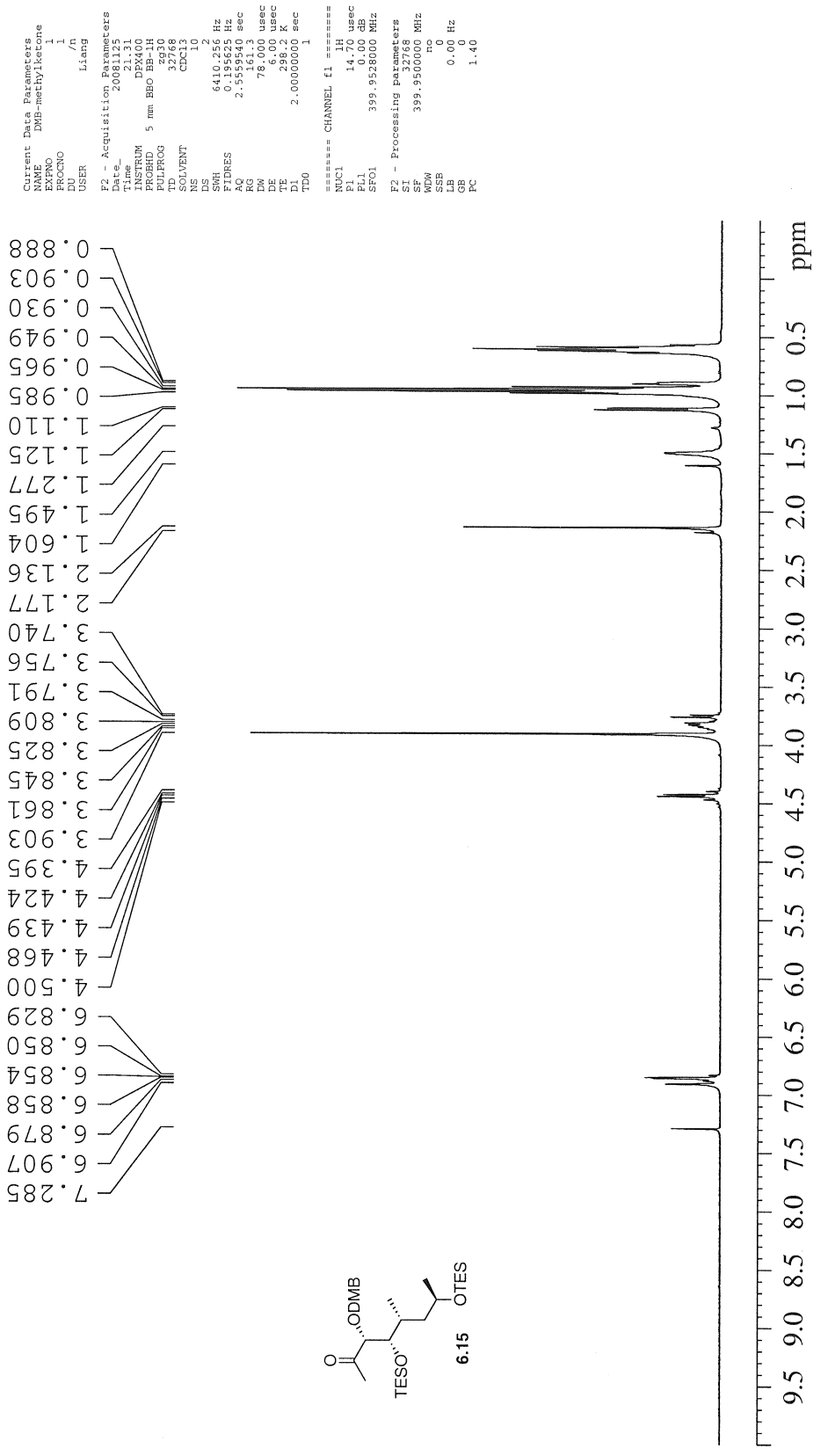

Current Data Parameters
NAME DMB-aldol-TES ether
EXPNO 1
PROCNO 1
DU /n
USER Liang
F2 - Acquisition Parameters
Date_ 20081125
Time 19.46
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 15
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.55595540 sec
RG 143.7
DW 78.000 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.70 usec
PL1 0.00 dB
SFO1 399.9528000 MHz
F2 - Processing parameters
SI 32768
SF 399.9500000 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
ppm
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
3.87
2.26
1.11
1.13
1.08
1.02
1.00
2.08
2.04
0.97
3.44
4.03
1.00
0.97
3.66
3.73
23.83
12.68
7.327
7.309
7.294
7.290
7.287
7.277
7.196
7.179
7.000
6.995
6.951
6.946
6.931
6.926
6.830
6.810
4.706
4.676
4.543
4.514
4.109
4.103
4.087
3.908
3.851
3.844
3.827
1.127
1.112
0.992
0.980
0.952
0.939
0.924
0.904
0.658
0.641
0.638
0.622
0.602
0.581
ODMB
O
O
N
O
Bn
O
TES
OTES
6.13

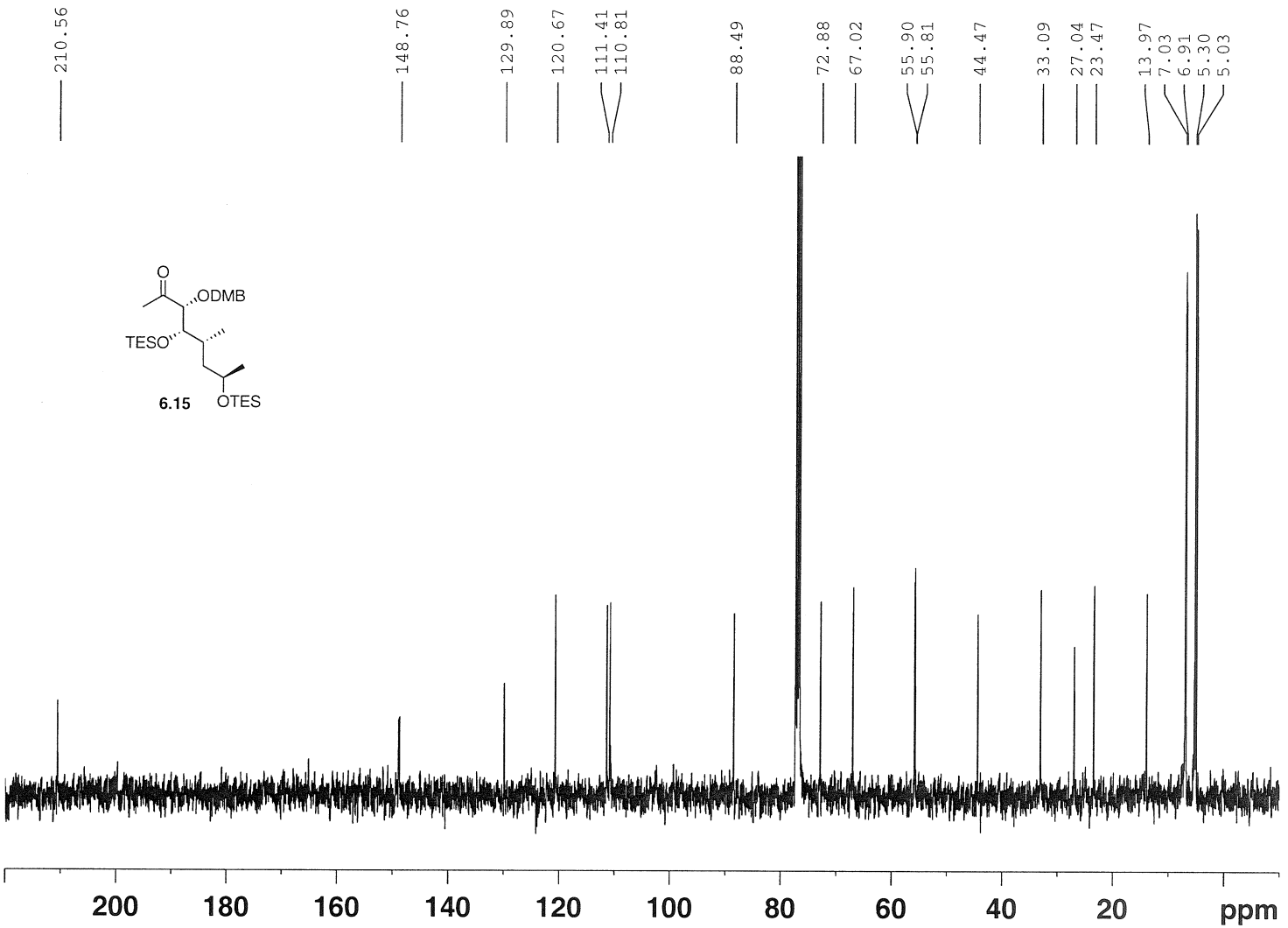



```
Current Data Parameters
NAME      DMB-aldol-TES et
EXPNO                   3
PROCNO                  1
DU                     /n
USER                Liang

F2 - Acquisition Parameter
Date_            20081125
Time                20.41
INSTRUM           DPX400
PROBHD   5 mm BBO BB-1H
PULPROG          zgpg30
TD                65536
SOLVENT
NS                 1641
DS                    4
SWH           25125.629 Hz
FIDRES        0.383387 Hz
AQ            1.3042164 se
RG                16384
DW               19.900 us
DE                6.00 us
TE                298.2 K
D1           0.15000001 se
d11          0.03000000 se
DELTA        0.05000000 se
TD0                   1

======== CHANNEL f1 ======
NUC1                 13C
P1                7.80 us
PL1              -3.00 dB
SFO1        100.5785700 MH

======== CHANNEL f2 ======
CPDPRG2          waltz16
NUC2                 1H
PCPD2            135.00 us
PL2              17.40 dB
PL12             17.40 dB
PL13             17.40 dB
SFO2        399.9516000 MH

F2 - Processing parameters
SI                32768
SF          100.5675080 MH
WDW                  EM
SSB                   0
LB                3.00 Hz
GB                    0
PC                1.40
```

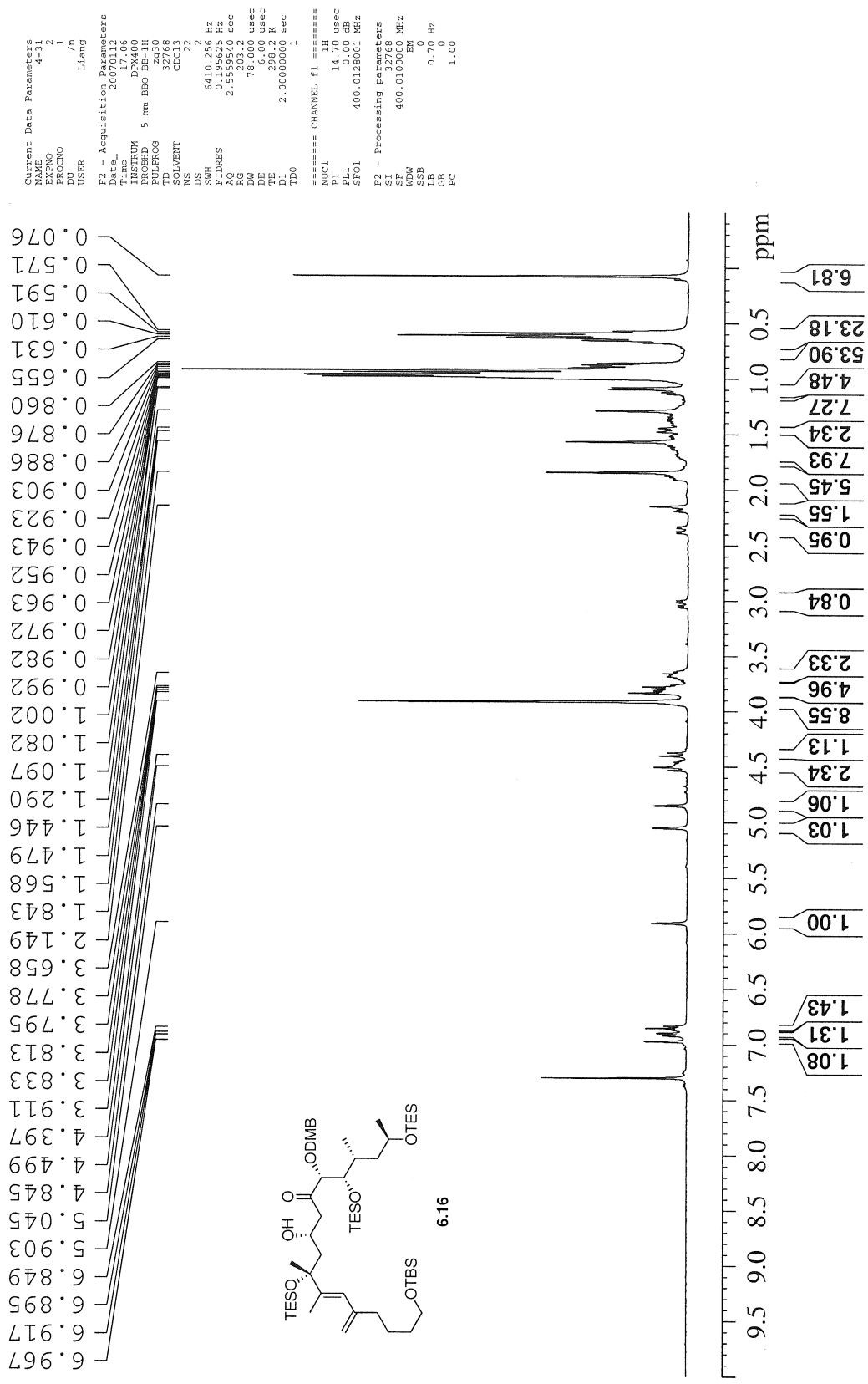

Current Data Parameters
NAME DMB-thioleester
EXPNO 2
PROCNO 1
DU /n
USER Liang
F2 - Acquisition Parameters
Date_ 20081125
Time 20.56
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT
NS 18
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.55599540 sec
RG 143.7
DW 78.000 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.70 usec
PL1 0.00 dB
SFO1 399.9528000 MHz
F2 - Processing parameters
SI 32768
SF 399.9500000 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
7.036
7.032
6.916
6.912
6.855
6.835
4.625
4.598
4.413
4.386
3.916
3.905
3.821
3.817
3.804
3.800
2.922
2.903
2.884
2.866
1.287
1.281
1.269
1.250
1.112
1.097
0.988
0.968
0.948
0.943
0.931
0.911
0.903
0.627
0.607
0.587
0.580
0.566
0.560
0.546
0.539
ppm
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
1.00
1.03
1.04
0.92
1.01
7.51
2.10
2.06
3.58
4.13
3.51
23.00
12.92
EtS
20
O
ODMB
TESO
OTES
6.14

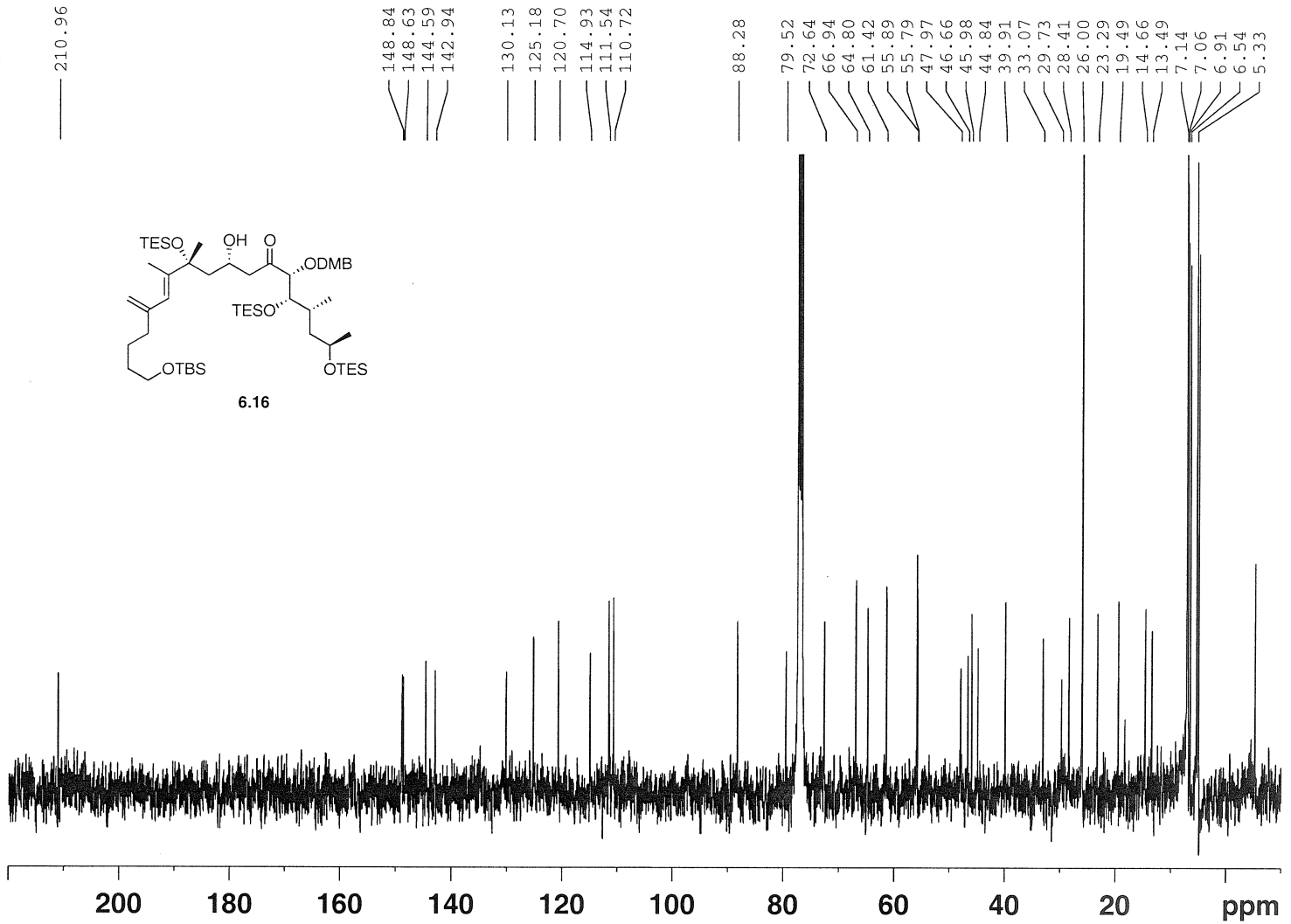

Current Data Parameters
NAME DMB-thiolester
EXPNO 4
PROCNO 1
DU /n
USER Liang
F2 - Acquisition Parameter
Date_ 20081125
Time 21.27
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT
NS 457
DS 4
SWH 25125.629 Hz
FIDRES 0.383387 Hz
AQ 1.3042164 se
RG 14596.5
DW 19.900 us
DE 6.00 us
TE 298.2 K
D1 0.15000001 se
d11 0.03000000 se
DELTA 0.05000000 se
TD0 1
======== CHANNEL f1 ======
NUC1 13C
P1 7.80 us
PL1 -3.00 dB
SFO1 100.5785700 MH
======== CHANNEL f2 ======
CPDPRG2 waltz16
NUC2 1H
PCPD2 135.00 us
PL2 17.40 dB
PL12 17.40 dB
PL13 17.40 dB
SFO2 399.9516000 MH
F2 - Processing parameters
SI 32768
SF 100.5675080 MH
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
4.97
5.17
5.33
6.90
7.05
13.65
14.58
22.47
23.45
32.68
44.86
55.78
55.89
66.92
72.89
77.48
88.17
110.66
111.56
120.55
129.88
148.62
148.76
202.19
ppm
20
40
60
80
100
120
140
160
180
200
EtS
20
ODMB
TESO
OTES
O
6.14


Current Data Parameters
NAME DMB-methylketone
EXPNO 1
PROCNO 1
DU /n
USER Liang
F2 - Acquisition Parameters
Date_ 20081125
Time 21.31
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 10
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5559540 sec
RG 161.3
DW 78.000 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.70 usec
PL1 0.00 dB
SFO1 399.9528000 MHz
F2 - Processing parameters
SI 32768
SF 399.9500000 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.40
7.285
6.907
6.879
6.858
6.854
6.850
6.829
4.500
4.468
4.439
4.424
4.395
3.903
3.861
3.845
3.825
3.809
3.791
3.756
3.740
2.177
2.136
1.604
1.495
1.277
1.125
1.110
0.985
0.965
0.949
0.930
0.903
0.888
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
ppm
TESO
ODMB
OTES
O
6.15



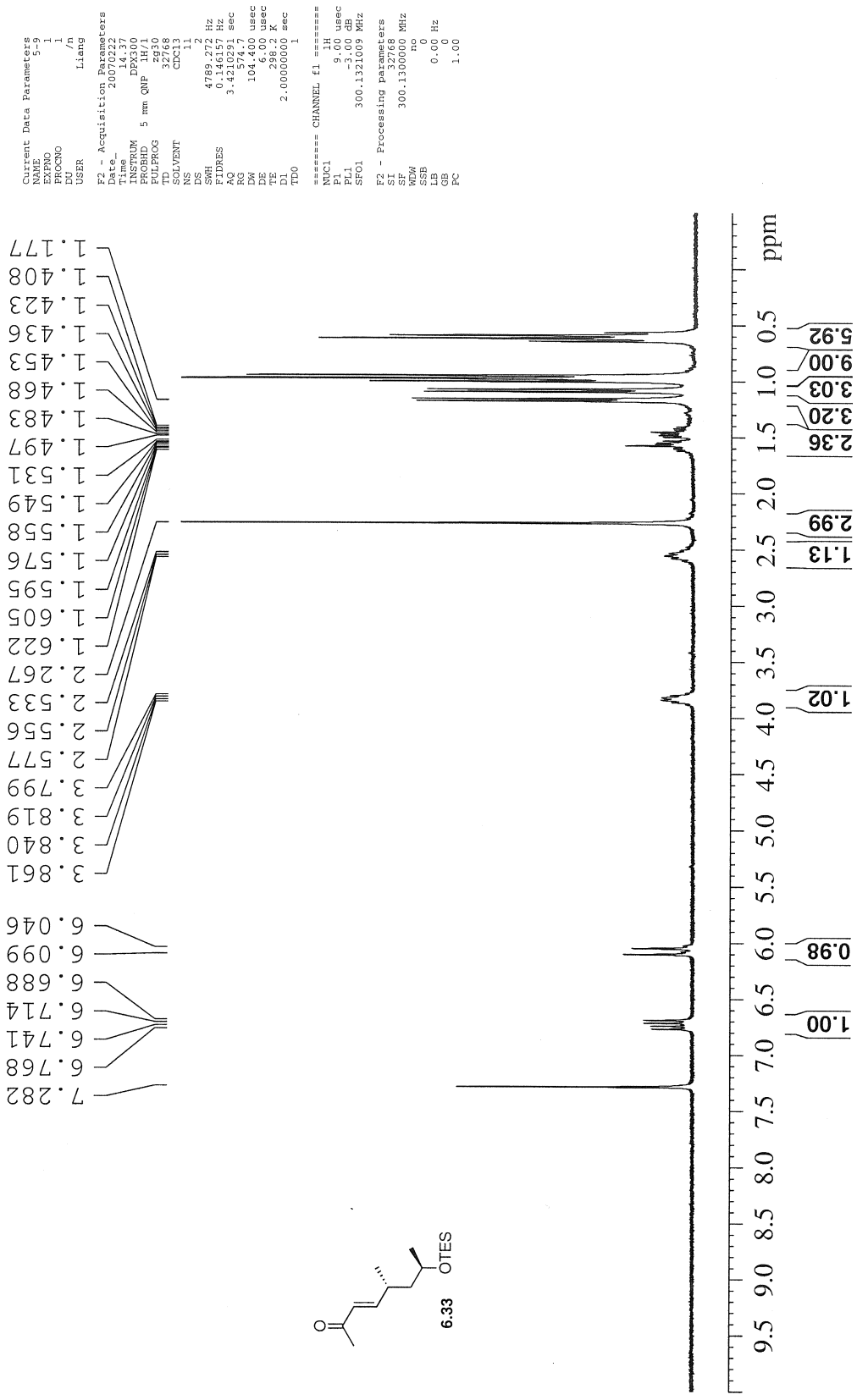

```
Current Data Parameters
NAME      DMB-methylketone
EXPNO                    3
PROCNO                   1
DU                      /n
USER                Liang

F2 - Acquisition Parameter
Date_            20081125
Time                21.45
INSTRUM           DPX400
PROBHD   5 mm BBO BB-1H
PULPROG          zgpg30
TD                65536
SOLVENT
NS                  494
DS                    4
SWH           25125.629 Hz
FIDRES        0.383387 Hz
AQ            1.3042164 se
RG               5792.6
DW               19.900 us
DE                6.00 us
TE               298.2 K
D1           0.15000001 se
d11          0.03000000 se
DELTA        0.05000000 se
TD0                   1

======== CHANNEL f1 ======
NUC1                 13C
P1                7.80 us
PL1              -3.00 dB
SFO1        100.5785700 MH

======== CHANNEL f2 ======
CPDPRG2          waltz16
NUC2                 1H
PCPD2           135.00 us
PL2              17.40 dB
PL12             17.40 dB
PL13             17.40 dB
SFO2        399.9516000 MH

F2 - Processing parameters
SI                32768
SF          100.5675080 MH
WDW                  EM
SSB                   0
LB                3.00 Hz
GB                    0
PC                1.40
```

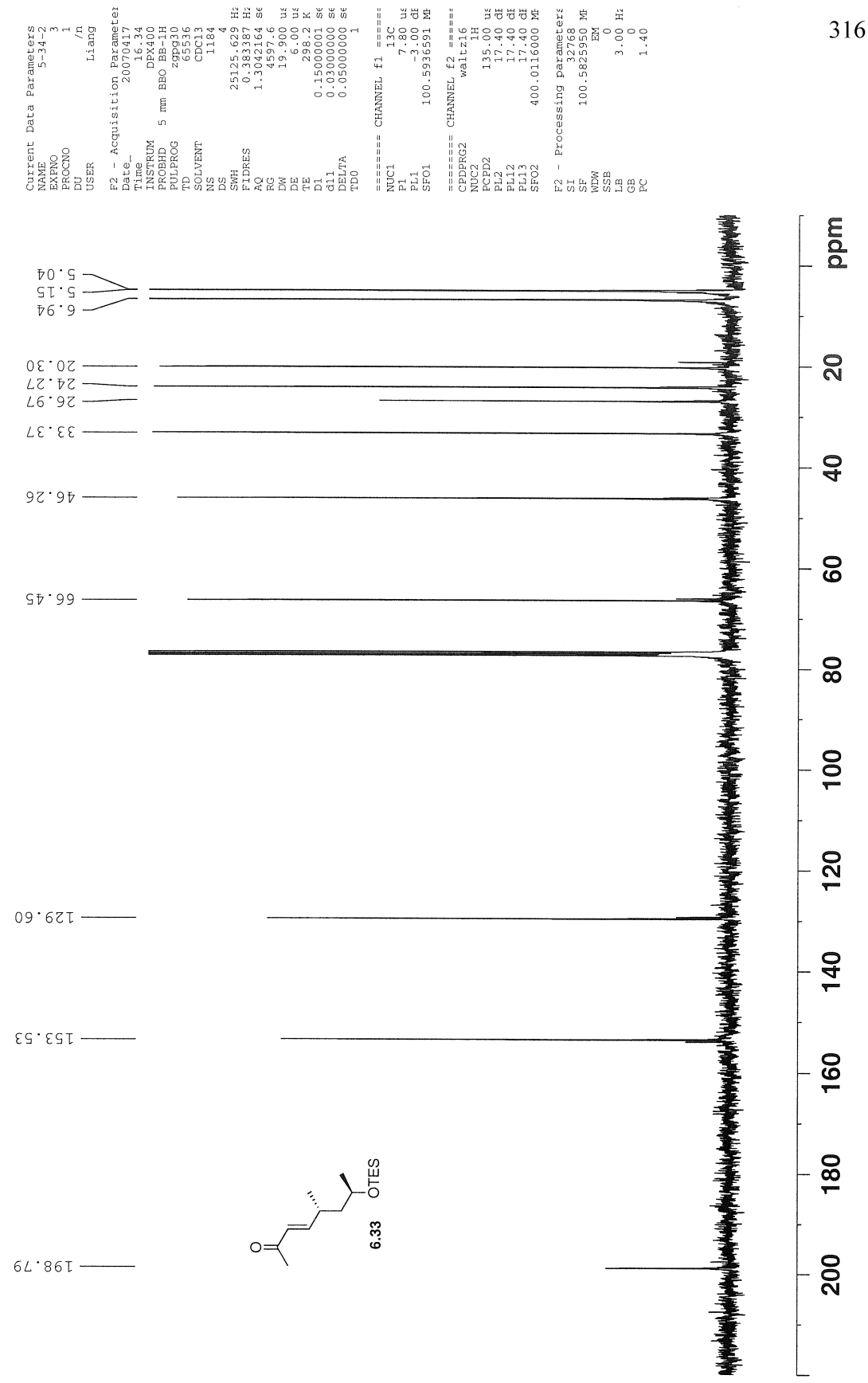

Current Data Parameters
NAME 4-51
EXPNO 2
PROCNO 1
DU /n
USER Liang
F2 - Acquisition Parameters
Date_ 20070112
Time 17.06
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 22
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5559540 sec
RG 203.2
DW 78.000 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.70 usec
PL1 0.00 dB
SFO1 400.0128001 MHz
F2 - Processing parameters
SI 32768
SF 400.0100000 MHz
WDW EM
SSB 0
LB 0.70 Hz
GB 0
PC 1.00
TESO
OH
O
ODMB
TESO
OTES
OTBS
6.16
ppm
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
1.08
1.31
1.43
1.00
1.03
1.06
2.34
1.13
8.55
4.96
2.33
0.84
0.95
1.55
5.45
7.93
2.34
7.27
4.48
53.90
23.18
6.81
6.967
6.917
6.895
6.849
5.903
5.045
4.845
4.499
4.397
3.911
3.833
3.813
3.795
3.778
3.658
2.149
1.843
1.568
1.479
1.446
1.290
1.097
1.082
1.002
0.992
0.982
0.972
0.963
0.952
0.943
0.923
0.903
0.886
0.876
0.860
0.655
0.631
0.610
0.591
0.571
0.076

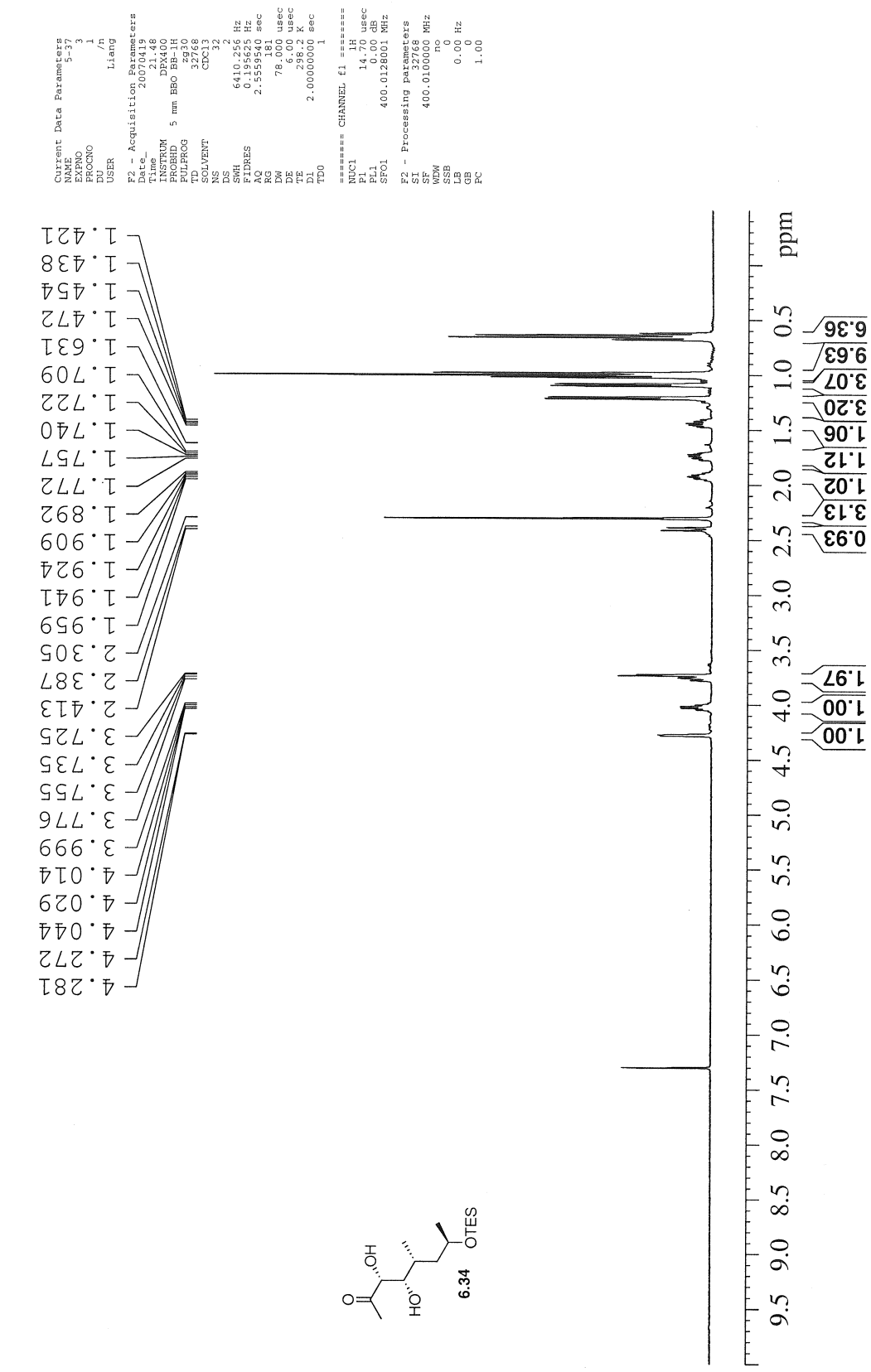


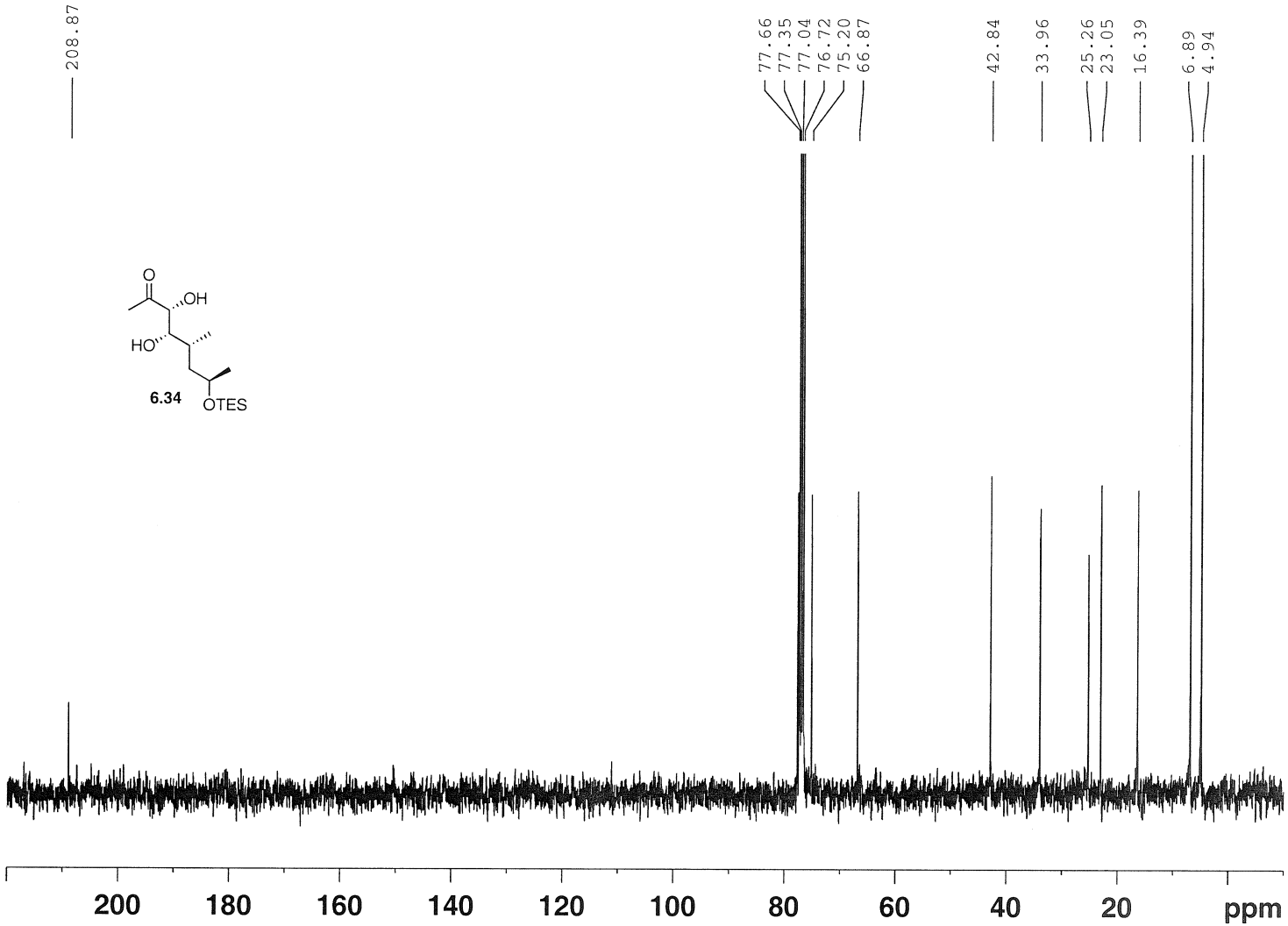
6.16

```
Current Data Parameters
NAME                  4-31
EXPNO                    4
PROCNO                   1
DU                      /n
USER                 Liang

F2 - Acquisition Parameter
Date_              20070112
Time                  17.21
INSTRUM              DPX400
PROBHD   5 mm BBO BB-1H
PULPROG             zgpg30
TD                    65536
SOLVENT
NS                     2442
DS                        4
SWH               25125.629 Hz
FIDRES            0.383387 Hz
AQ                1.3042164 se
RG                  18390.4
DW                   19.900 us
DE                    6.00 us
TE                   298.2 K
D1              0.15000001 se
d11             0.03000000 se
DELTA           0.05000000 se
TD0                       1

======== CHANNEL f1 ======
NUC1                    13C
P1                     7.80 us
PL1                   -3.00 dB
SFO1          100.5936591 MH

======== CHANNEL f2 ======
CPDPRG2            waltz16
NUC2                    1H
PCPD2                135.00 us
PL2                   17.40 dB
PL12                  17.40 dB
PL13                  17.40 dB
SFO2          400.0116000 MH

F2 - Processing parameters
SI                     32768
SF            100.5825950 MH
WDW                       EM
SSB                        0
LB                    3.00 Hz
GB                         0
PC                     1.40
```

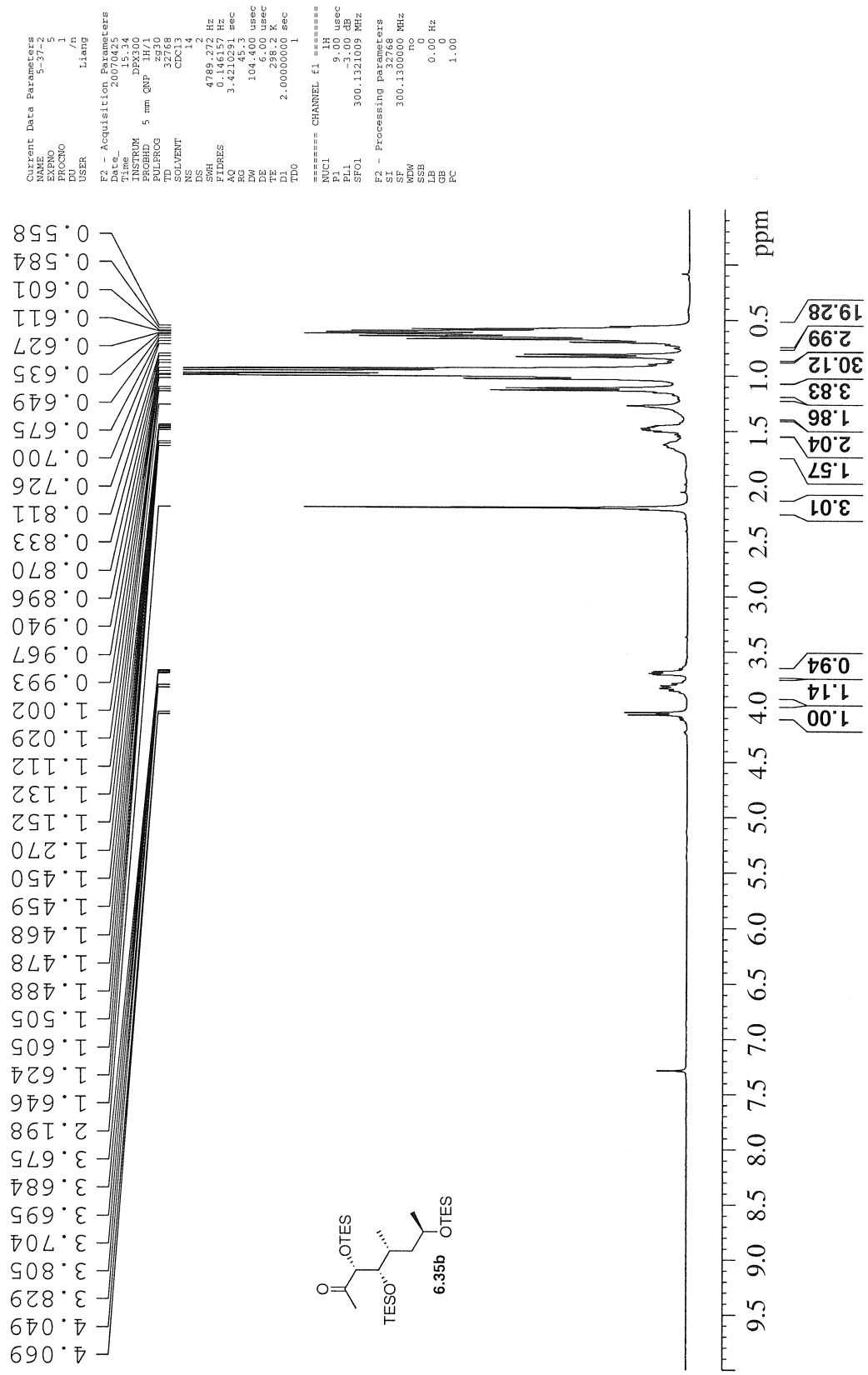

Current Data Parameters
NAME 5-9
EXPNO 1
PROCNO 1
DU /n
USER Liang
F2 - Acquisition Parameters
Date_ 20070222
Time 14.37
INSTRUM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 11
DS 2
SWH 4789.272 Hz
FIDRES 0.146157 Hz
AQ 3.4210291 sec
RG 574.7
DW 104.400 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.00 usec
PL1 -3.00 dB
SFO1 300.1321009 MHz
F2 - Processing parameters
SI 32768
SF 300.1300000 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
7.282
6.768
6.741
6.714
6.688
6.099
6.046
3.861
3.840
3.819
3.799
2.577
2.556
2.533
2.267
1.622
1.605
1.595
1.576
1.558
1.549
1.531
1.497
1.483
1.468
1.453
1.436
1.423
1.408
1.177
1.00
0.98
1.02
1.13
2.99
2.36
3.20
3.03
9.00
5.92
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
ppm
O
OTES
6.33

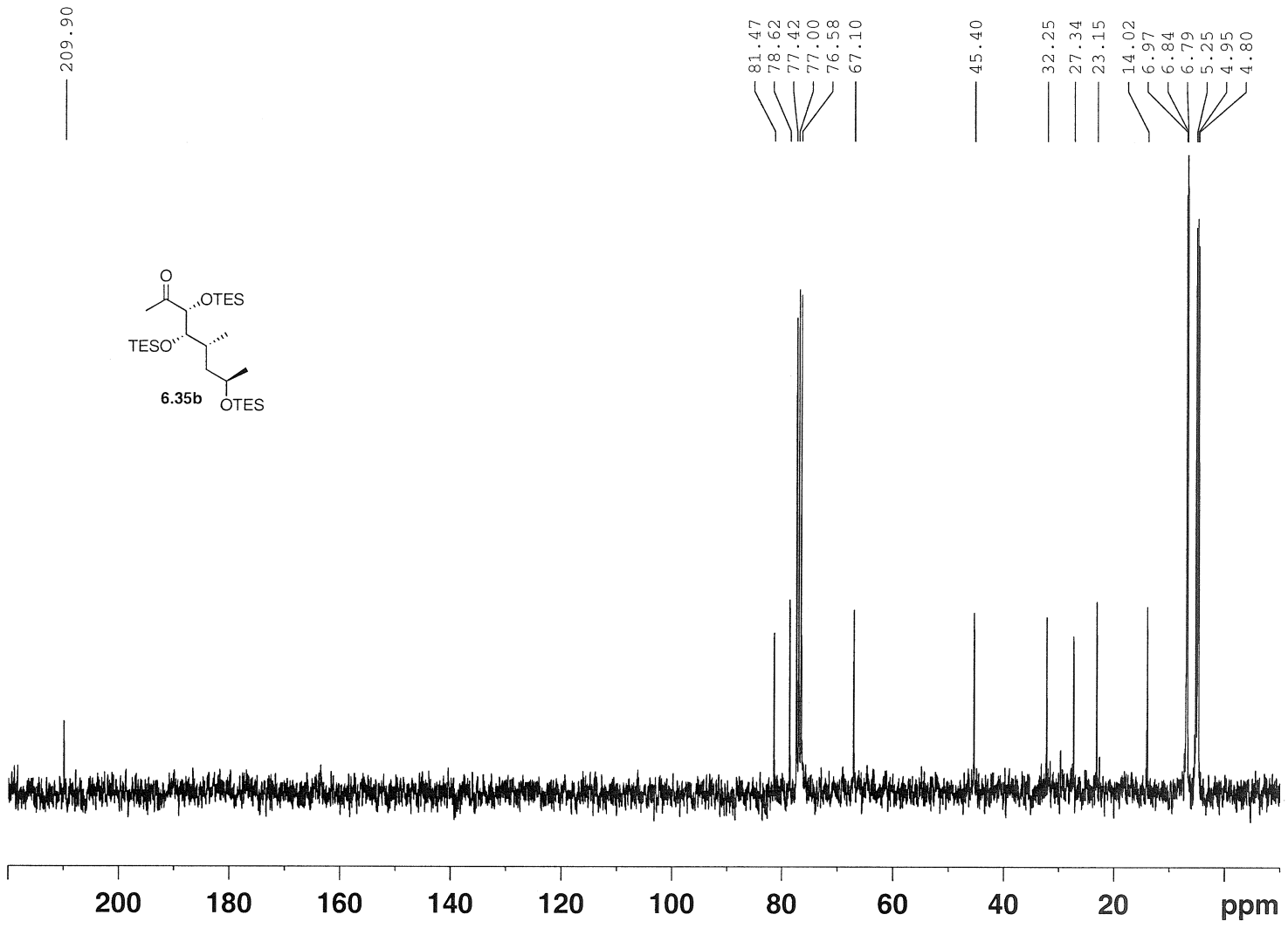

Current Data Parameters
NAME 5-34-2
EXPNO 3
PROCNO 1
DU /n
USER Liang
F2 - Acquisition Parameter
Date_ 20070417
Time 16.34
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 1184
DS 4
SWH 25125.629 Hz
FIDRES 0.383387 Hz
AQ 1.3042164 se
RG 4597.6
DW 19.900 us
DE 6.00 us
TE 298.2 K
D1 0.15000001 se
d11 0.03000000 se
DELTA 0.05000000 se
TD0 1
======== CHANNEL f1 ======
NUC1 13C
P1 7.80 us
PL1 -3.00 dB
SFO1 100.5936591 MH
======== CHANNEL f2 ======
CPDPRG2 waltz16
NUC2 1H
PCPD2 135.00 us
PL2 17.40 dB
PL12 17.40 dB
PL13 17.40 dB
SFO2 400.0116000 MH
F2 - Processing parameter
SI 32768
SF 100.5825950 MH
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
198.79
153.53
129.60
66.45
46.26
33.37
26.97
24.27
20.30
6.94
5.15
5.04
6.33
OTES
O
200
180
160
140
120
100
80
60
40
20
ppm


Current Data Parameters
NAME 5-37
EXPNO 3
PROCNO 1
DU /n
USER Liang
F2 - Acquisition Parameters
Date_ 20070419
Time 21.48
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.55599540 sec
RG 181
DW 78.000 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.70 usec
PL1 0.00 dB
SFO1 400.0128001 MHz
F2 - Processing parameters
SI 32768
SF 400.0100000 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
4.281
4.272
4.044
4.029
4.014
3.999
3.776
3.755
3.735
3.725
2.413
2.387
2.305
1.959
1.941
1.924
1.909
1.892
1.772
1.757
1.740
1.722
1.709
1.631
1.472
1.454
1.438
1.421
1.00
1.00
1.97
0.93
3.13
1.02
1.12
1.06
3.20
3.07
9.63
6.36
OH
HO
O
OTES
6.34
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
ppm

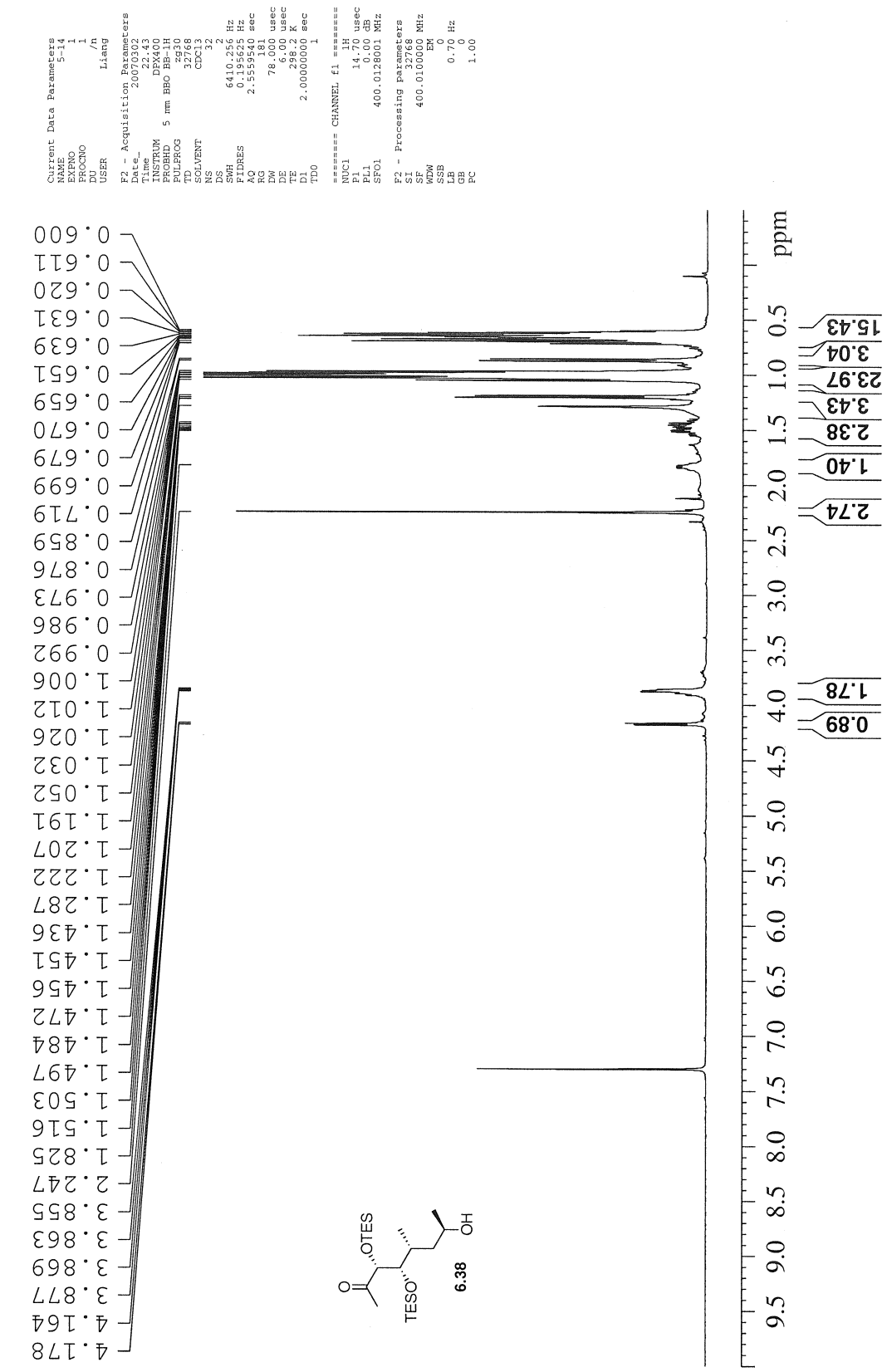


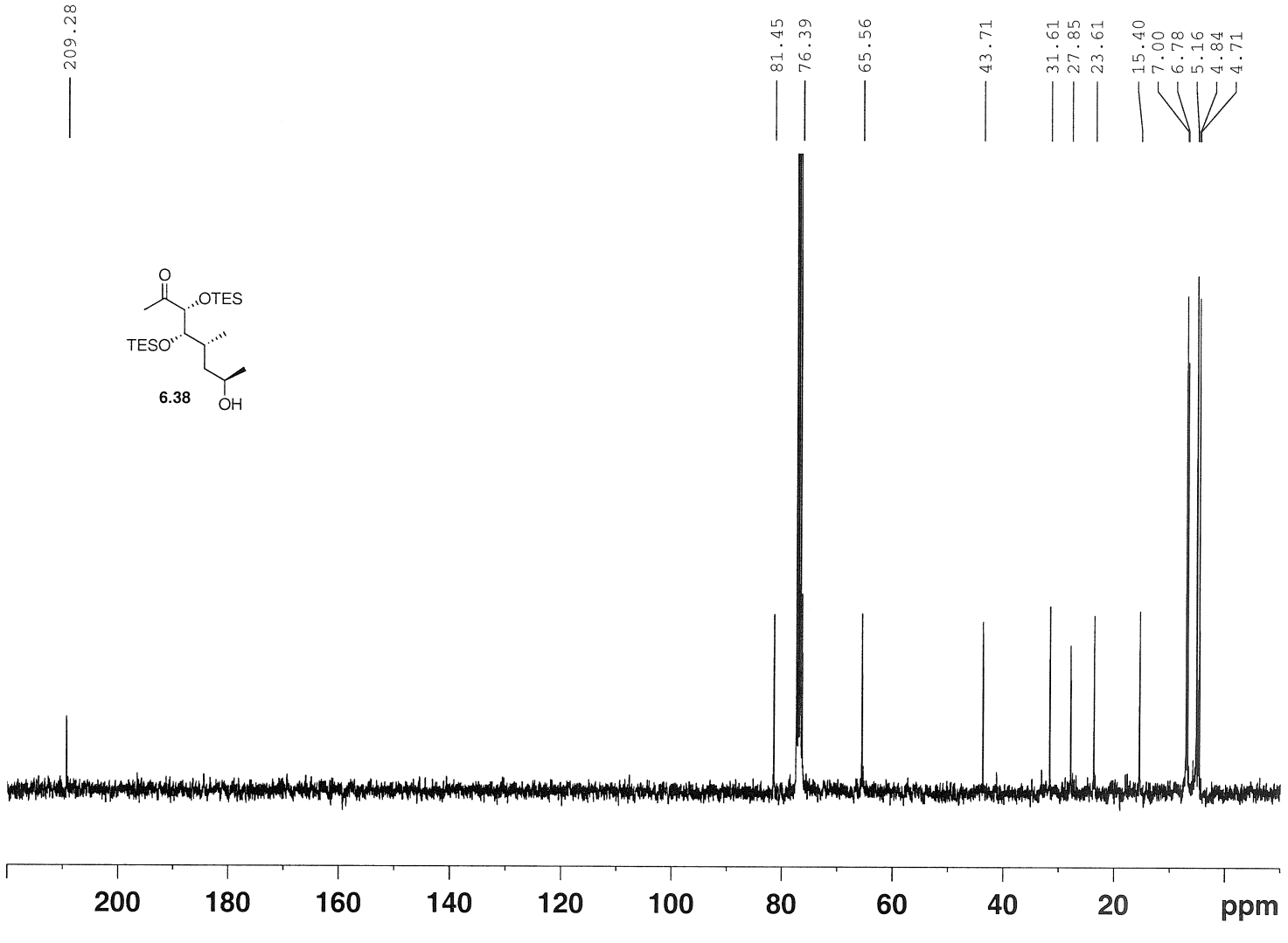

```
Current Data Parameters
NAME                  5-37
EXPNO                    5
PROCNO                   1
DU                      /n
USER                 Liang

F2 - Acquisition Parameter
Date_              20070419
Time                 22.24
INSTRUM            DPX400
PROBHD   5 mm BBO BB-1H
PULPROG           zgpg30
TD                 65536
SOLVENT            CDCl3
NS                   342
DS                     4
SWH            25125.629 Hz
FIDRES         0.383387 Hz
AQ             1.3042164 se
RG               11585.2
DW                19.900 us
DE                 6.00 us
TE                298.2 K
D1            0.15000001 se
d11           0.03000000 se
DELTA         0.05000000 se
TD0                    1

======== CHANNEL f1 ======
NUC1                  13C
P1                 7.80 us
PL1               -3.00 dB
SFO1         100.5936591 MH

======== CHANNEL f2 ======
CPDPRG2          waltz16
NUC2                  1H
PCPD2            135.00 us
PL2               17.40 dB
PL12              17.40 dB
PL13              17.40 dB
SFO2         400.0116000 MH

F2 - Processing parameters
SI                 32768
SF          100.5825950 MH
WDW                   EM
SSB                    0
LB                3.00 Hz
GB                     0
PC                 1.40
```


Current Data Parameters
NAME 5-37-2
EXPNO 5
PROCNO 1
DU /n
USER Liang
F2 - Acquisition Parameters
Date_ 20070425
Time 15:34
INSTRUM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 14
DS 2
SWH 4789.272 Hz
FIDRES 0.146157 Hz
AQ 3.4210291 sec
RG 45.3
DW 104.400 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.00 usec
PL1 -3.00 dB
SFO1 300.1321009 MHz
F2 - Processing parameters
SI 32768
SF 300.1300000 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
OTES
TESO
OTES
6.35b
ppm
1.00
1.14
0.94
3.01
1.57
2.04
1.86
3.83
30.12
2.99
19.28

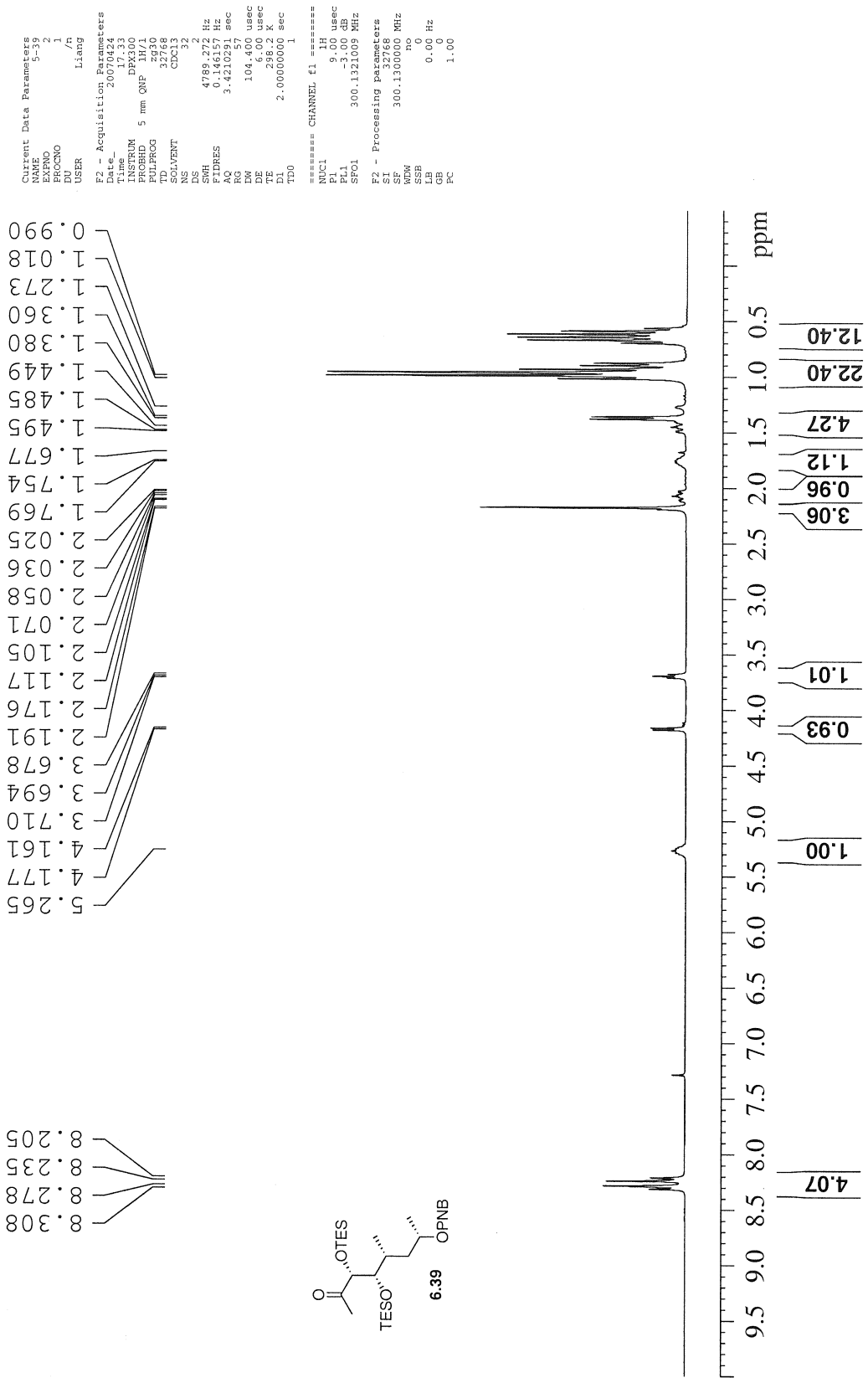


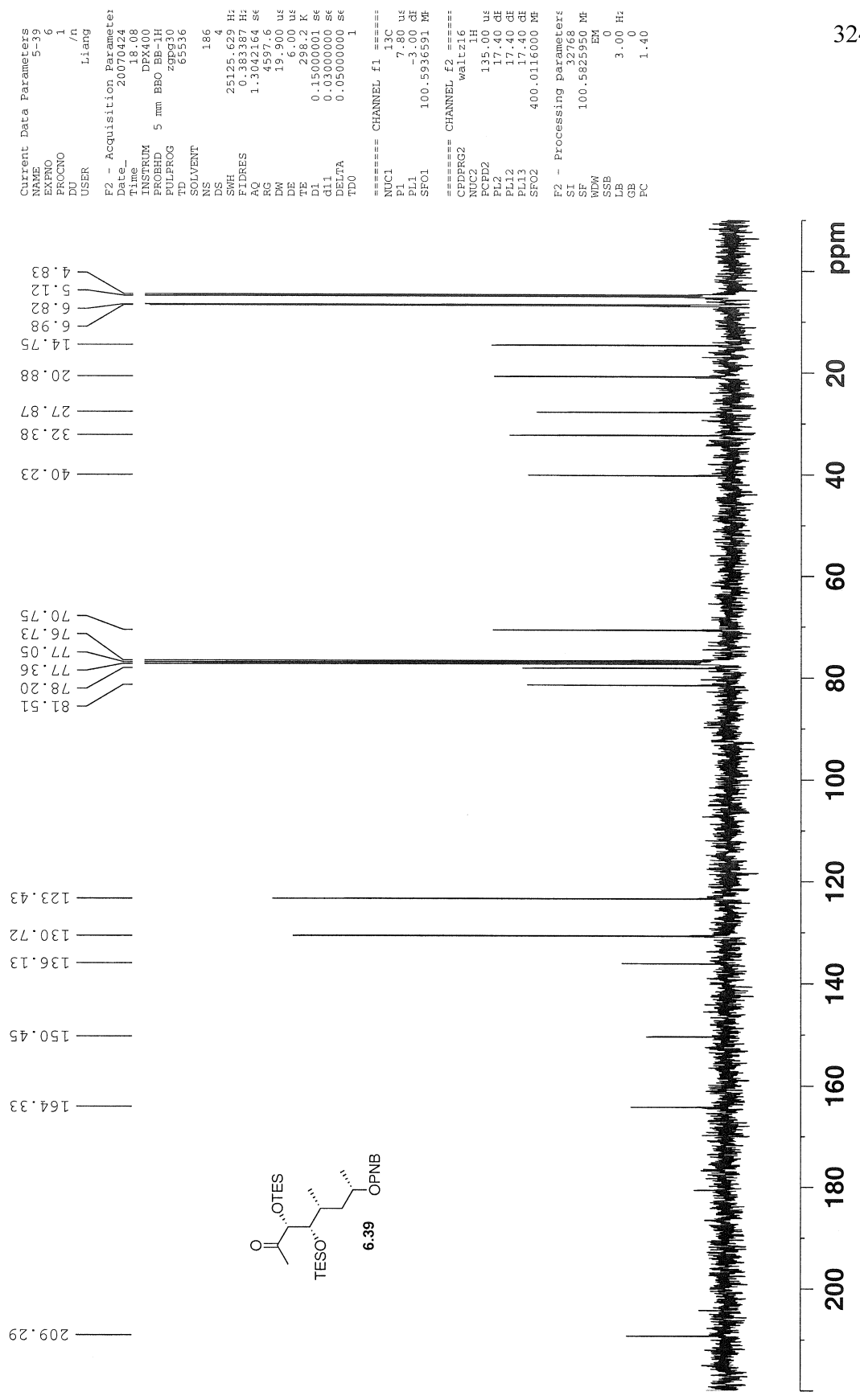

```
Current Data Parameters
NAME                  5-37-2
EXPNO                      8
PROCNO                     1
DU                        /n
USER                  Liang

F2 - Acquisition Parameter
Date_              20070425
Time                  16.46
INSTRUM             DPX300
PROBHD   5 mm QNP  1H/1
PULPROG             zgpg30
TD                    65536
SOLVENT               CDCl3
NS                      116
DS                        4
SWH               18832.393 Hz
FIDRES             0.287360 Hz
AQ                 1.7400308 se
RG                    9195.2
DW                    26.550 us
DE                     6.00 us
TE                    298.2 K
D1              0.15000001 se
d11             0.03000000 se
DELTA           0.05000000 se
TD0                       1

======== CHANNEL f1 ======
NUC1                    13C
P1                     8.80 us
PL1                   -3.00 dB
SFO1           75.4760505 MH

======== CHANNEL f2 ======
CPDPRG2            waltz16
NUC2                    1H
PCPD2                80.00 us
PL2                   -3.00 dB
PL12                  17.55 dB
PL13                  17.55 dB
SFO2          300.1312005 MH

F2 - Processing parameters
SI                     32768
SF            75.4677490 MH
WDW                       EM
SSB                        0
LB                    3.00 Hz
GB                         0
PC                     1.40
```

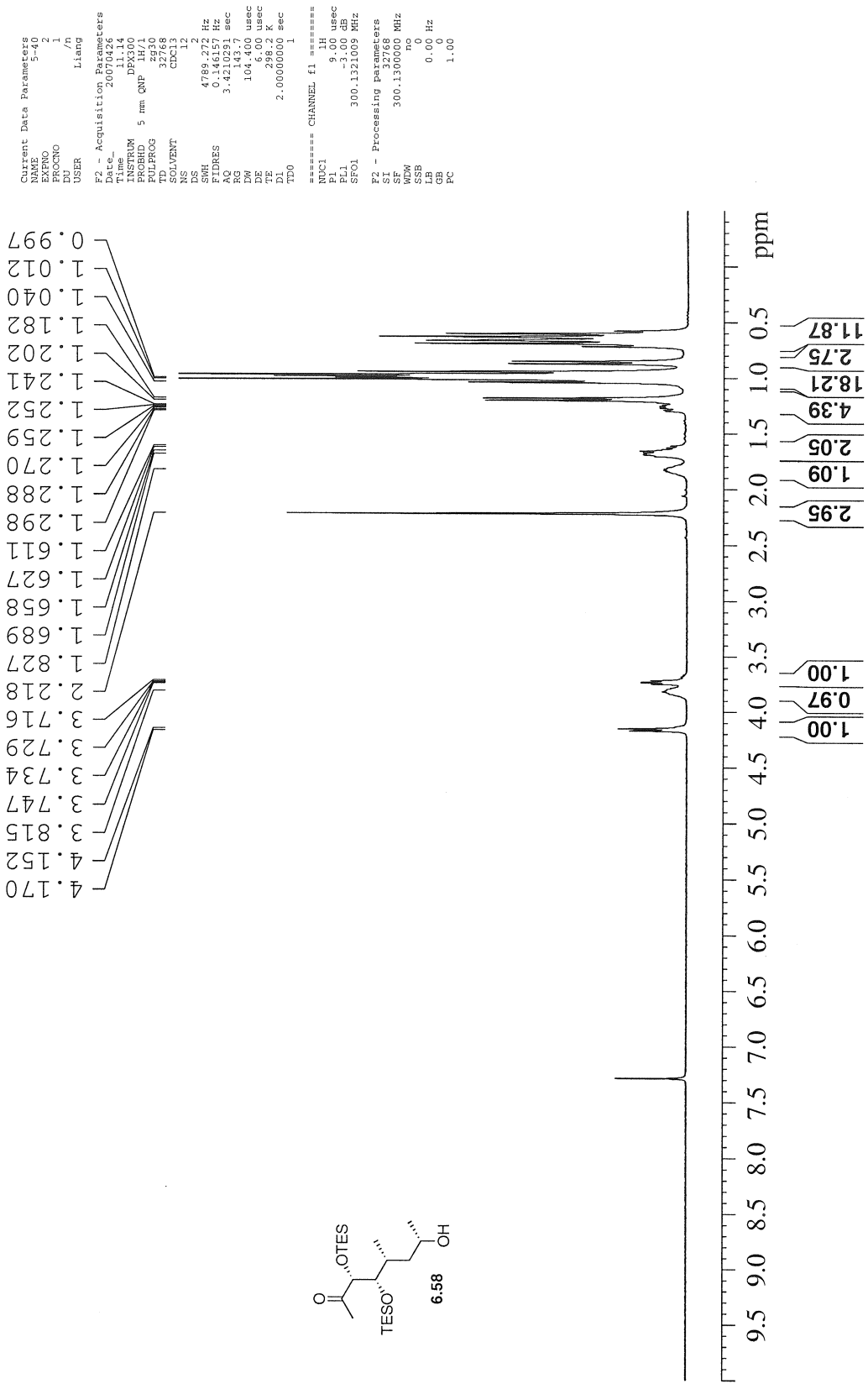

Current Data Parameters
NAME 5-14
EXPNO 1
PROCNO 1
DU /n
USER Liang
F2 - Acquisition Parameters
Date_ 20070302
Time 22.43
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.55599540 sec
RG 181
DW 78.000 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.70 usec
PL1 0.00 dB
SFO1 400.0128001 MHz
F2 - Processing parameters
SI 32768
SF 400.0100000 MHz
WDW EM
SSB 0
LB 0.70 Hz
GB 0
PC 1.00
4.178
4.164
3.877
3.869
3.863
3.855
2.247
1.825
1.516
1.503
1.497
1.484
1.472
1.456
1.451
1.436
1.287
1.222
1.207
1.191
1.052
1.032
1.026
1.012
1.006
0.992
0.986
0.973
0.876
0.859
0.719
0.699
0.679
0.670
0.659
0.651
0.639
0.631
0.620
0.611
0.600
OTES
TESO
O
OH
6.38
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
ppm
0.89
1.78
2.74
1.40
2.38
3.43
23.97
3.04
15.43

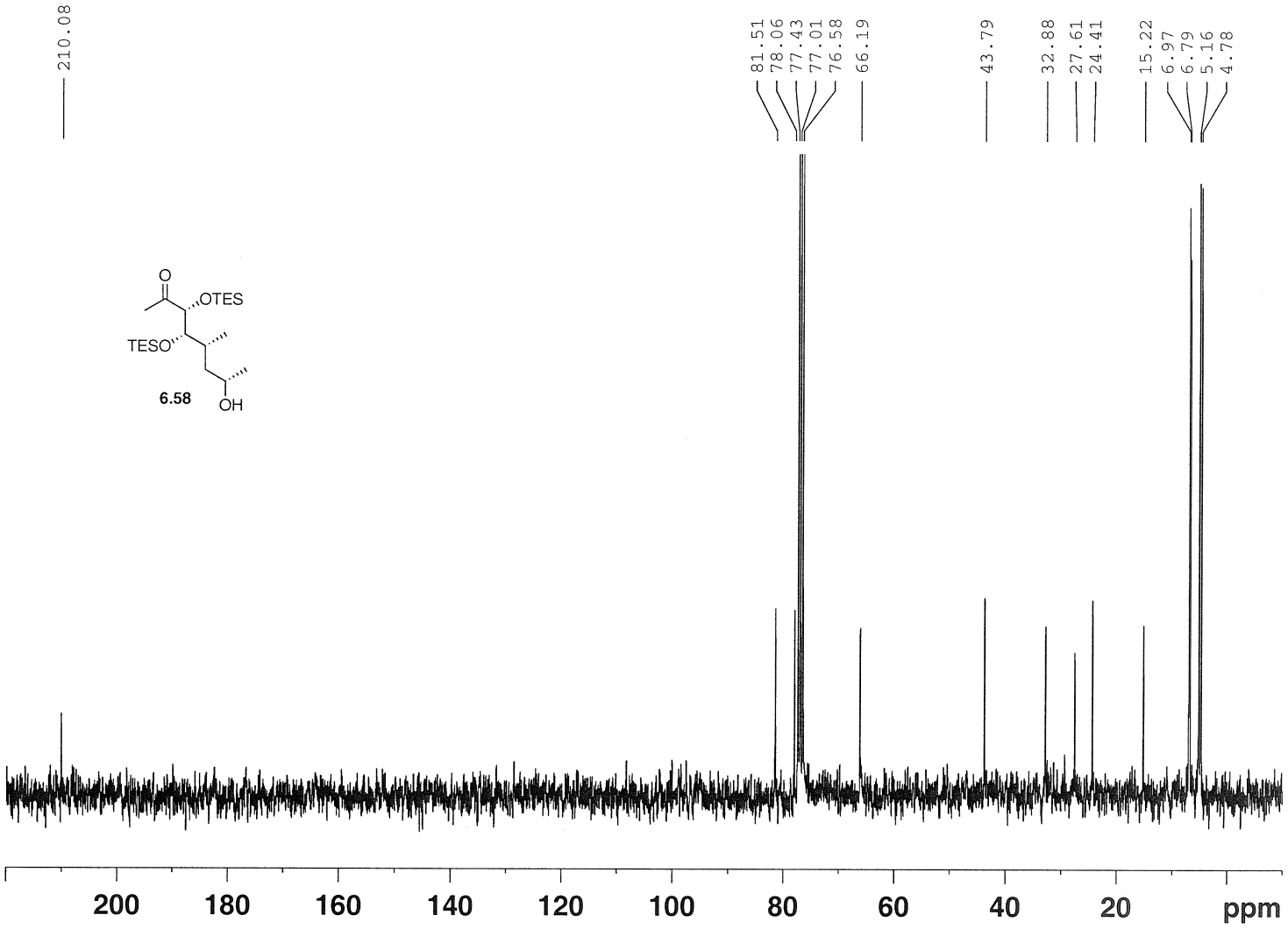



```
Current Data Parameters
NAME                  5-38
EXPNO                    4
PROCNO                   1
DU                      /n
USER                 Liang

F2 - Acquisition Parameter
Date_              20070424
Time                 18.56
INSTRUM             DPX400
PROBHD   5 mm BBO BB-1H
PULPROG            zgpg30
TD                    65536
SOLVENT
NS                      740
DS                        4
SWH               25125.629 Hz
FIDRES            0.383387 Hz
AQ                1.3042164 se
RG                   4597.6
DW                  19.900 us
DE                   6.00 us
TE                  298.2 K
D1              0.15000001 se
d11             0.03000000 se
DELTA           0.05000000 se
TD0                      1

======== CHANNEL f1 ======
NUC1                   13C
P1                    7.80 us
PL1                  -3.00 dB
SFO1          100.5936591 MH

======== CHANNEL f2 ======
CPDPRG2           waltz16
NUC2                   1H
PCPD2               135.00 us
PL2                  17.40 dB
PL12                 17.40 dB
PL13                 17.40 dB
SFO2          400.0116000 MH

F2 - Processing parameters
SI                    32768
SF           100.5825950 MH
WDW                     EM
SSB                      0
LB                   3.00 Hz
GB                       0
PC                    1.40
```

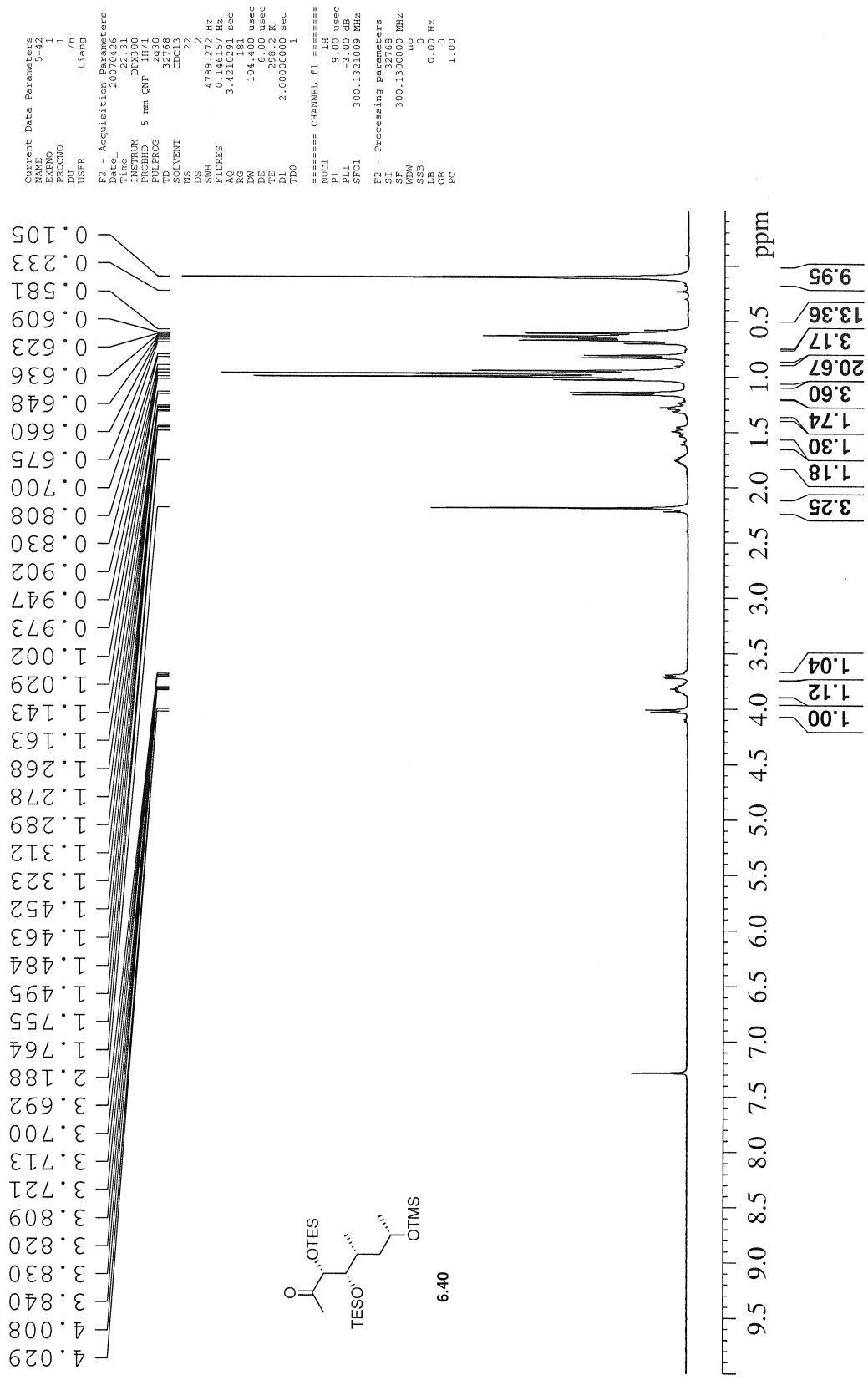

Current Data Parameters
NAME 5-39
EXPNO 2
PROCNO 1
DU /n
USER Liang
F2 - Acquisition Parameters
Date_ 20070424
Time 17.33
INSTRUM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 4789.272 Hz
FIDRES 0.146157 Hz
AQ 3.42102912 sec
RG 57
DW 104.400 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.00 usec
PL1 -3.00 dB
SFO1 300.1321009 MHz
F2 - Processing parameters
SI 32768
SF 300.1300000 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
8.308
8.278
8.235
8.205
5.265
4.177
4.161
3.710
3.694
3.678
2.191
2.176
2.117
2.105
2.071
2.058
2.036
2.025
1.769
1.754
1.677
1.495
1.485
1.449
1.380
1.360
1.273
1.018
0.990
OTES
TESO
OPNB
6.39
ppm
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
4.07
1.00
0.93
1.01
3.06
0.96
1.12
4.27
22.40
12.40

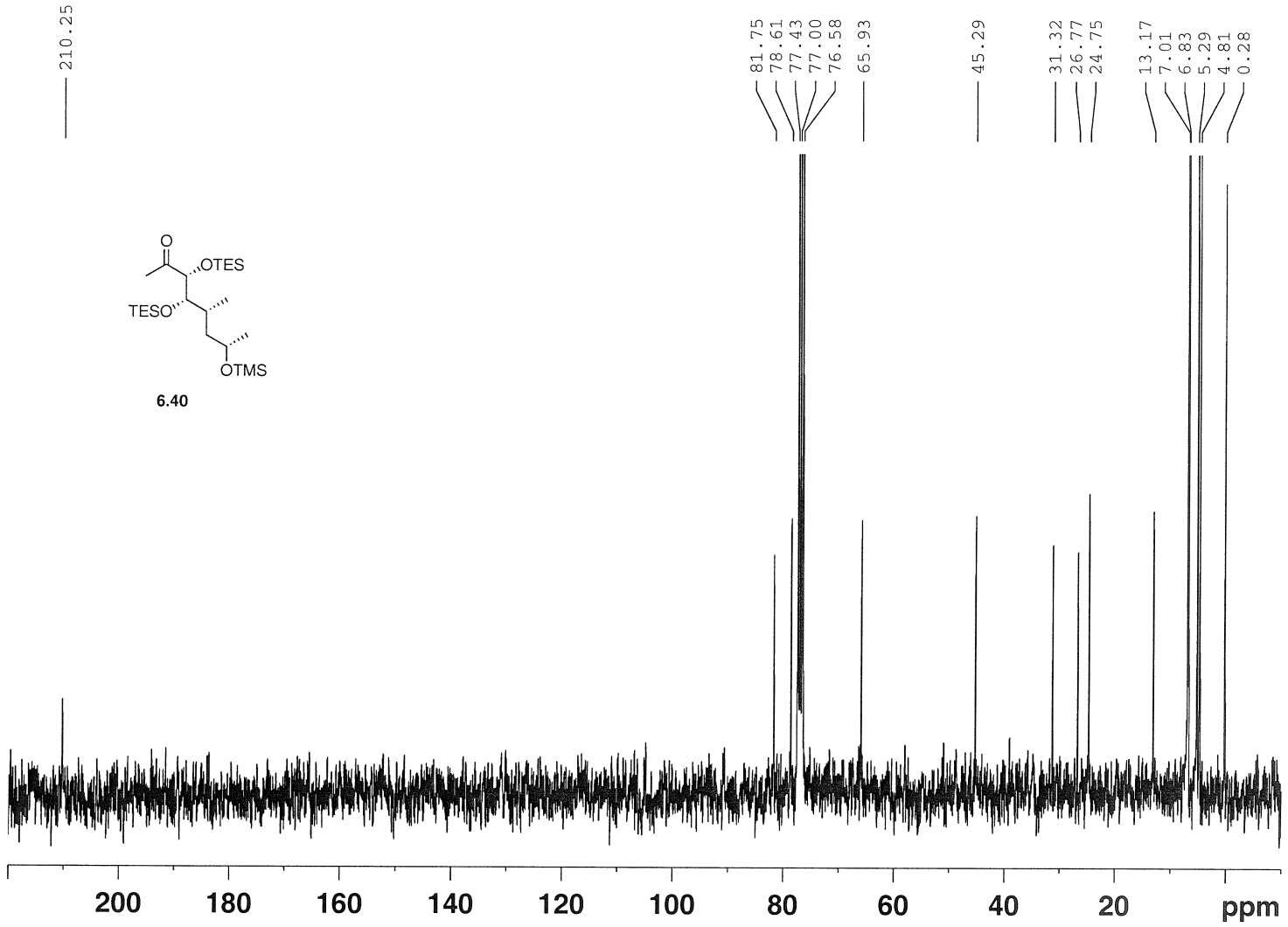

Current Data Parameters
NAME 5-39
EXPNO 6
PROCNO 1
DU /n
USER Liang
F2 - Acquisition Parameter
Date_ 20070424
Time 18.08
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT
NS 186
DS 4
SWH 25125.629 Hz
FIDRES 0.383387 Hz
AQ 1.3042164 se
RG 4597.6
DW 19.900 us
DE 6.00 us
TE 298.2 K
D1 0.15000001 se
d11 0.03000000 se
DELTA 0.05000000 se
TD0 1
======== CHANNEL f1 ======
NUC1 13C
P1 7.80 us
PL1 -3.00 dB
SFO1 100.5936591 MH
======== CHANNEL f2 ======
CPDPRG2 waltz16
NUC2 1H
PCPD2 135.00 us
PL2 17.40 dB
PL12 17.40 dB
PL13 17.40 dB
SFO2 400.0116000 MH
F2 - Processing parameters
SI 32768
SF 100.5825950 MH
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
4.83
5.12
6.82
6.98
14.75
20.88
27.87
32.38
40.23
70.75
76.73
77.05
77.36
78.20
81.51
123.43
130.72
136.13
150.45
164.33
209.29
OTES
TESO
OPNB
O
6.39
ppm
200
180
160
140
120
100
80
60
40
20


Current Data Parameters
NAME 5-40
EXPNO 2
PROCNO 1
DU /n
USER Liang
F2 - Acquisition Parameters
Date_ 20070426
Time 11.14
INSTRUM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 12
DS 2
SWH 4789.272 Hz
FIDRES 0.146157 Hz
AQ 3.42102291 sec
RG 143.7
DW 104.400 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.00 usec
PL1 -3.00 dB
SFO1 300.1321009 MHz
F2 - Processing parameters
SI 32768
SF 300.1300000 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
4.170
4.152
3.815
3.747
3.734
3.729
3.716
2.218
1.827
1.689
1.658
1.627
1.611
1.298
1.288
1.270
1.259
1.252
1.241
1.202
1.182
1.040
1.012
0.997
1.00
0.97
1.00
2.95
1.09
2.05
4.39
18.21
2.75
11.87
ppm
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
OTES
TESO
O
OH
6.58

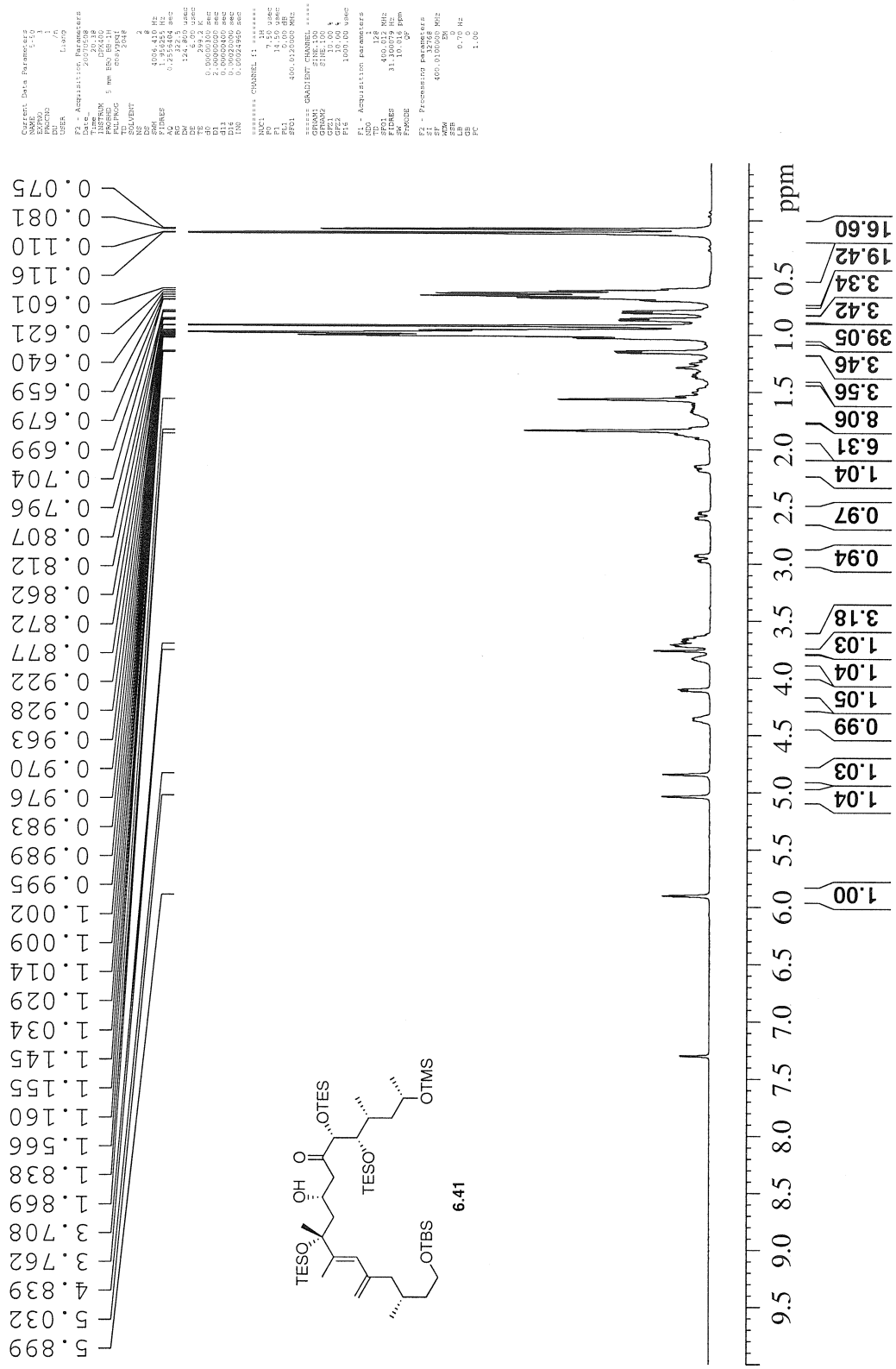


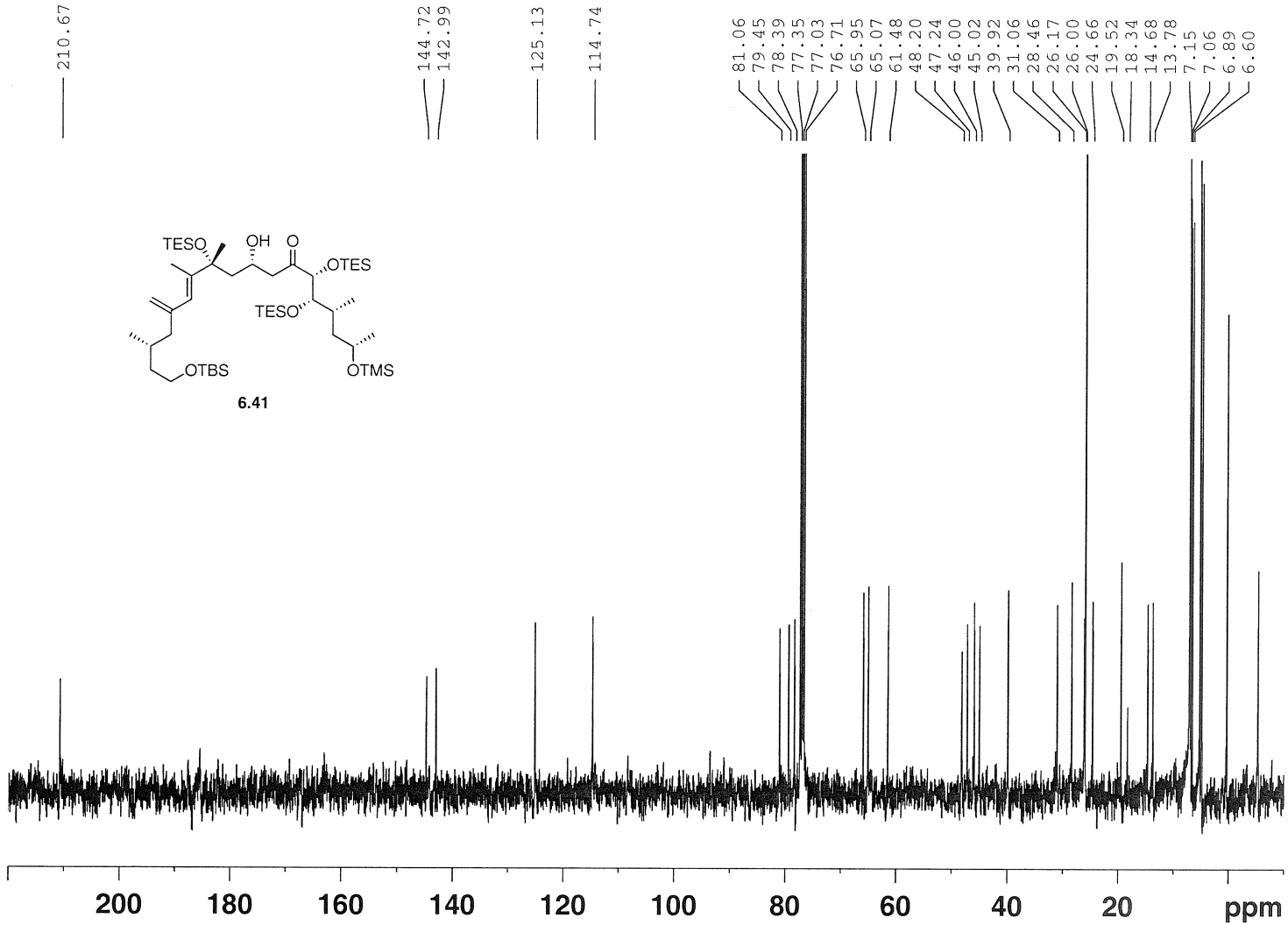

```
Current Data Parameters
NAME                  5-40
EXPNO                    4
PROCNO                   1
DU                      /n
USER                 Liang

F2 - Acquisition Parameter
Date_              20070426
Time                 11.26
INSTRUM             DPX300
PROBHD   5 mm QNP  1H/1
PULPROG             zgpg30
TD                   65536
SOLVENT              CDCl3
NS                     204
DS                       4
SWH              18832.393 Hz
FIDRES           0.287360 Hz
AQ               1.7400308 se
RG                  9195.2
DW                 26.550 us
DE                  6.00 us
TE                 298.2 K
D1            0.15000001 se
d11           0.03000000 se
DELTA         0.05000000 se
TD0                      1

======== CHANNEL f1 ======
NUC1                   13C
P1                  8.80 us
PL1                -3.00 dB
SFO1          75.4760505 MH

======== CHANNEL f2 ======
CPDPRG2            waltz16
NUC2                   1H
PCPD2              80.00 us
PL2                -3.00 dB
PL12               17.55 dB
PL13               17.55 dB
SFO2         300.1312005 MH

F2 - Processing parameters
SI                   32768
SF            75.4677490 MH
WDW                    EM
SSB                     0
LB                 3.00 Hz
GB                      0
PC                   1.40
```


Current Data Parameters
NAME 5-42
EXPNO 1
PROCNO 1
DU /n
USER Liang
F2 - Acquisition Parameters
Date_ 20070426
Time 22.31
INSTRUM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 22
DS 2
SWH 4789.272 Hz
FIDRES 0.146157 Hz
AQ 3.42102291 sec
RG 181
DW 104.400 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.00 usec
PL1 -3.00 dB
SFO1 300.1321009 MHz
F2 - Processing parameters
SI 32768
SF 300.1300000 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
4.029
3.840
3.830
3.820
3.809
3.721
3.713
3.700
3.692
2.188
1.764
1.755
1.495
1.484
1.463
1.452
1.323
1.312
1.289
1.278
1.268
1.163
1.143
1.029
1.002
0.973
0.947
0.902
0.830
0.808
0.700
0.675
0.660
0.648
0.636
0.623
0.609
0.581
0.233
0.105
OTES
TESO
OTMS
O
6.40
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
ppm
9.95
13.36
3.17
20.67
3.60
1.74
1.30
1.18
3.25
1.04
1.12
1.00



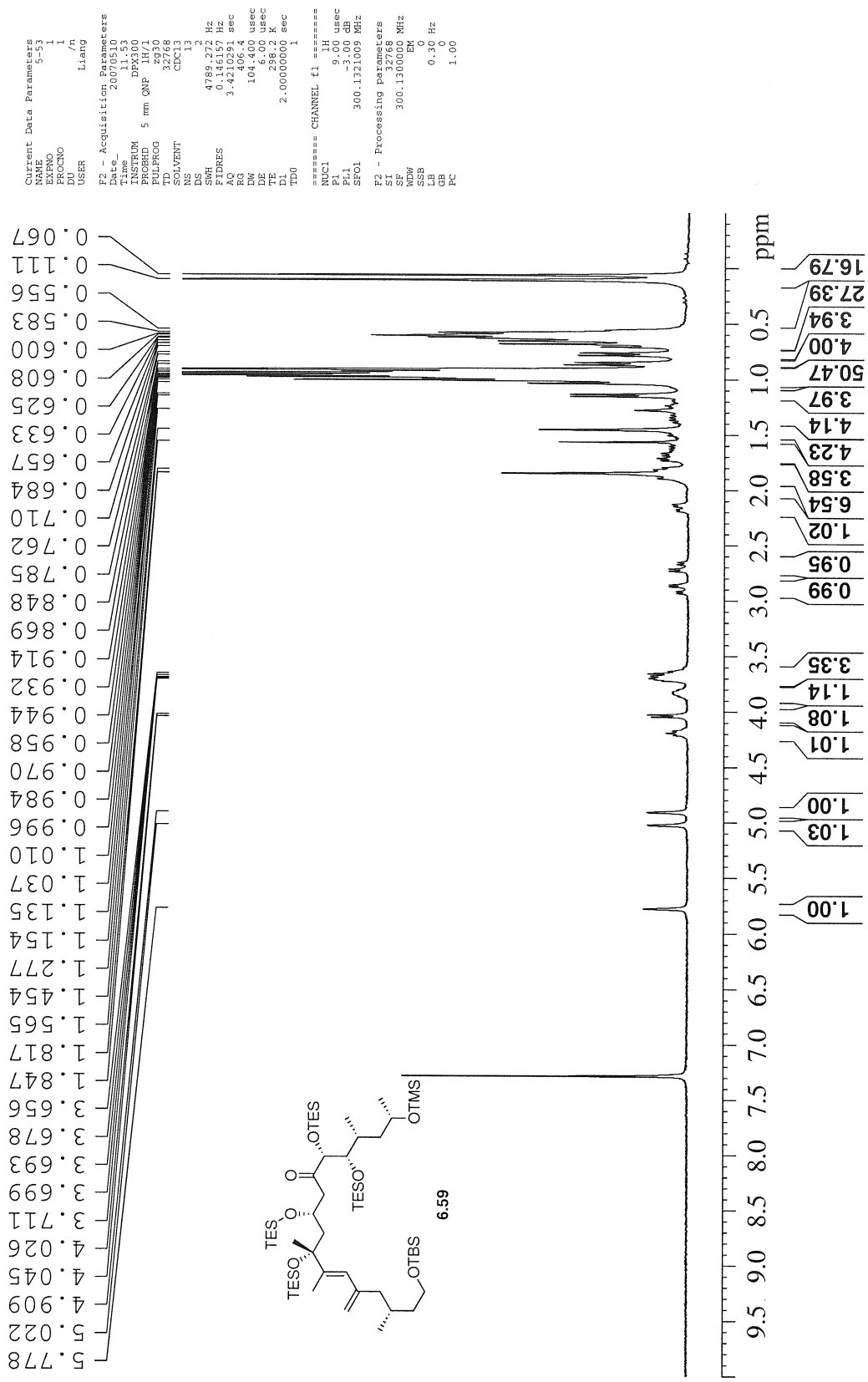

```
Current Data Parameters
NAME                   5-42
EXPNO                     3
PROCNO                    1
DU                       /n
USER                 Liang

F2 - Acquisition Parameter
Date_               20070426
Time                   22.45
INSTRUM              DPX300
PROBHD   5 mm QNP  1H/1
PULPROG              zgpg30
TD                    65536
SOLVENT               CDC13
NS                      407
DS                        4
SWH              18832.393 Hz
FIDRES            0.287360 Hz
AQ                1.7400308 se
RG                   9195.2
DW                  26.550 us
DE                   6.00 us
TE                  298.2 K
D1              0.15000001 se
d11             0.03000000 se
DELTA           0.05000000 se
TD0                       1

======== CHANNEL f1 ======
NUC1                    13C
P1                   8.80 us
PL1                 -3.00 dB
SFO1           75.4760505 MH

======== CHANNEL f2 ======
CPDPRG2            waltz16
NUC2                    1H
PCPD2               80.00 us
PL2                 -3.00 dB
PL12                17.55 dB
PL13                17.55 dB
SFO2          300.1312005 MH

F2 - Processing parameters
SI                    32768
SF             75.4677490 MH
WDW                      EM
SSB                       0
LB                   3.00 Hz
GB                        0
PC                     1.40
```

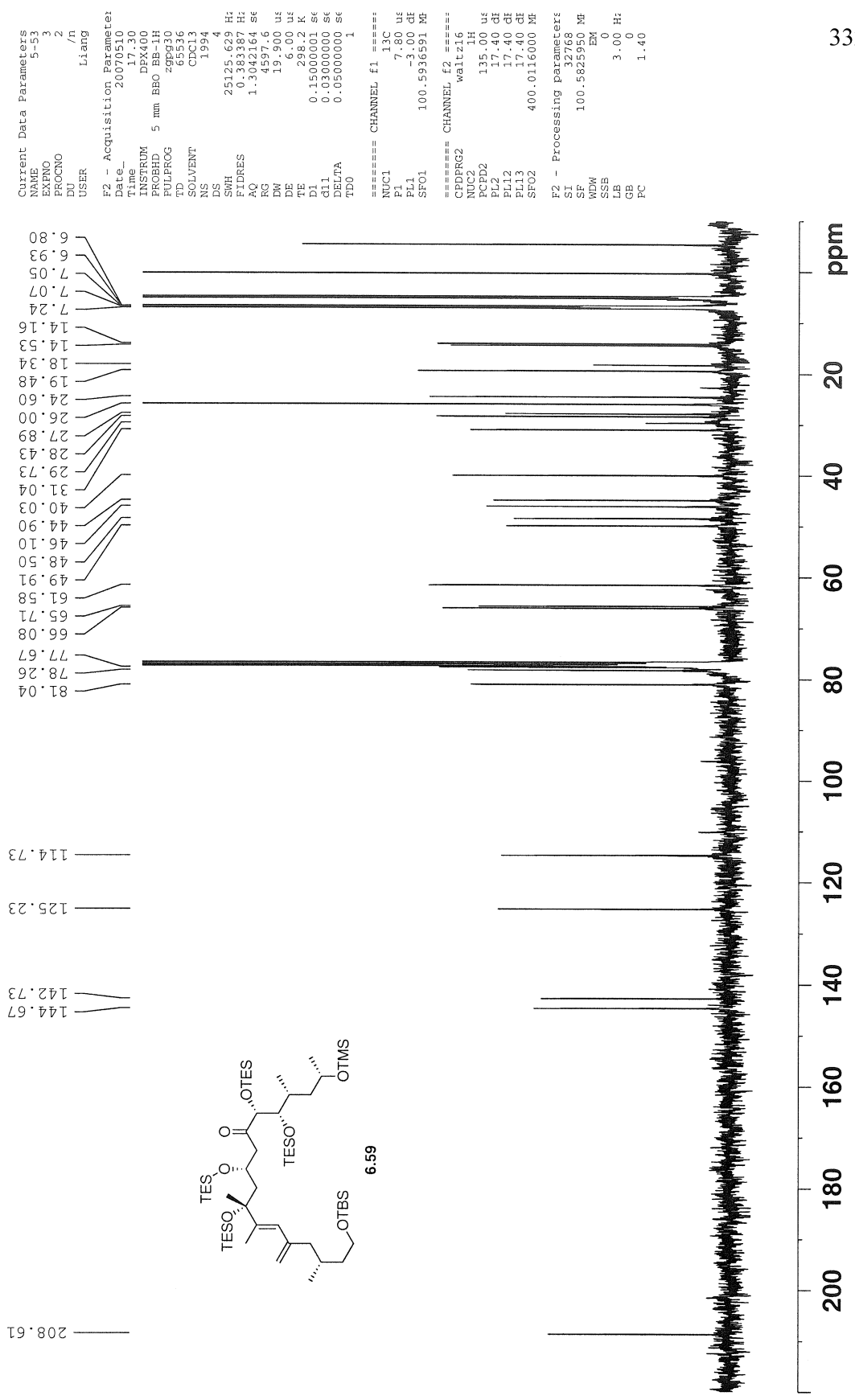

TESO
OH
O
OTES
TESO
OTMS
OTBS
6.41
ppm

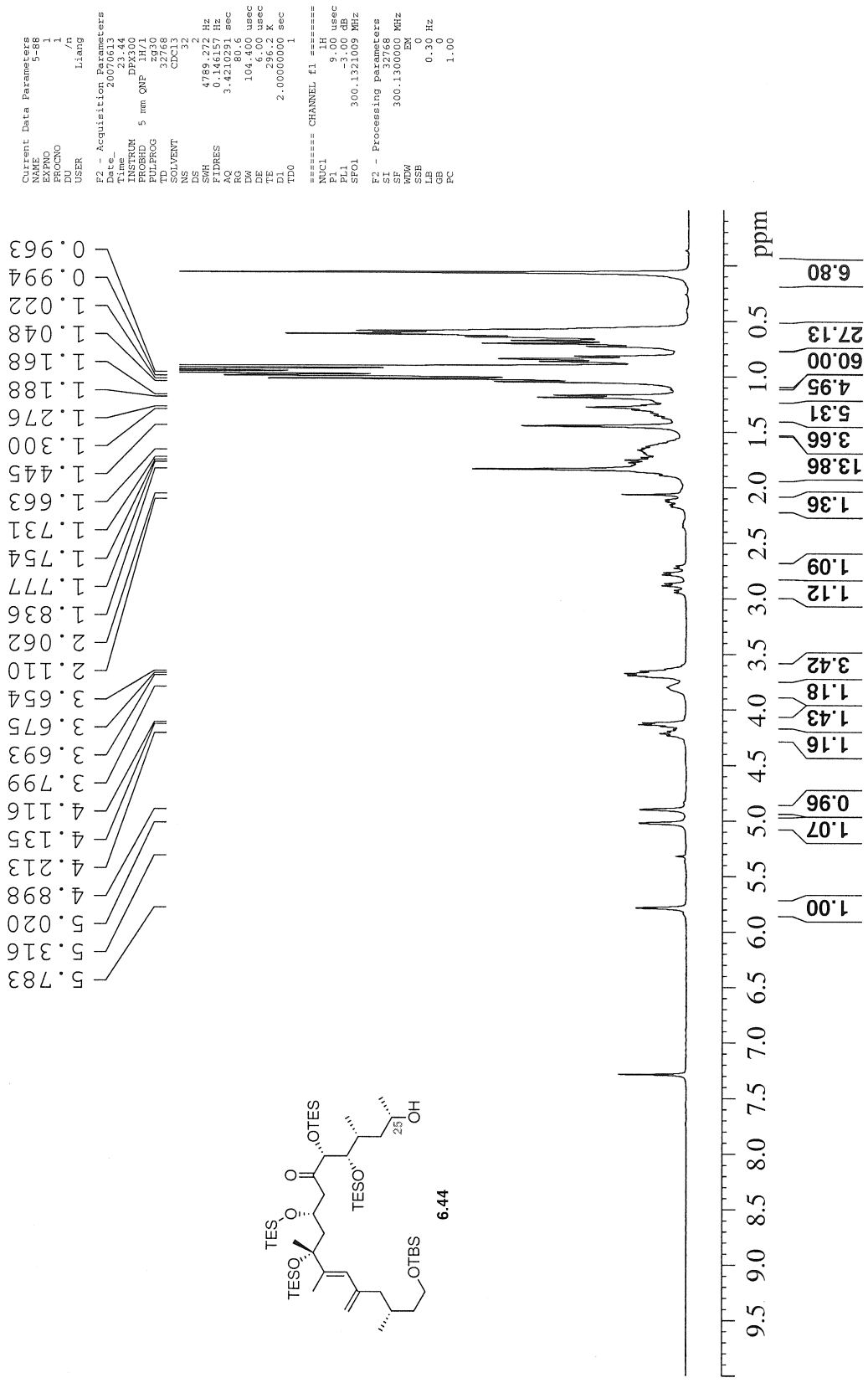


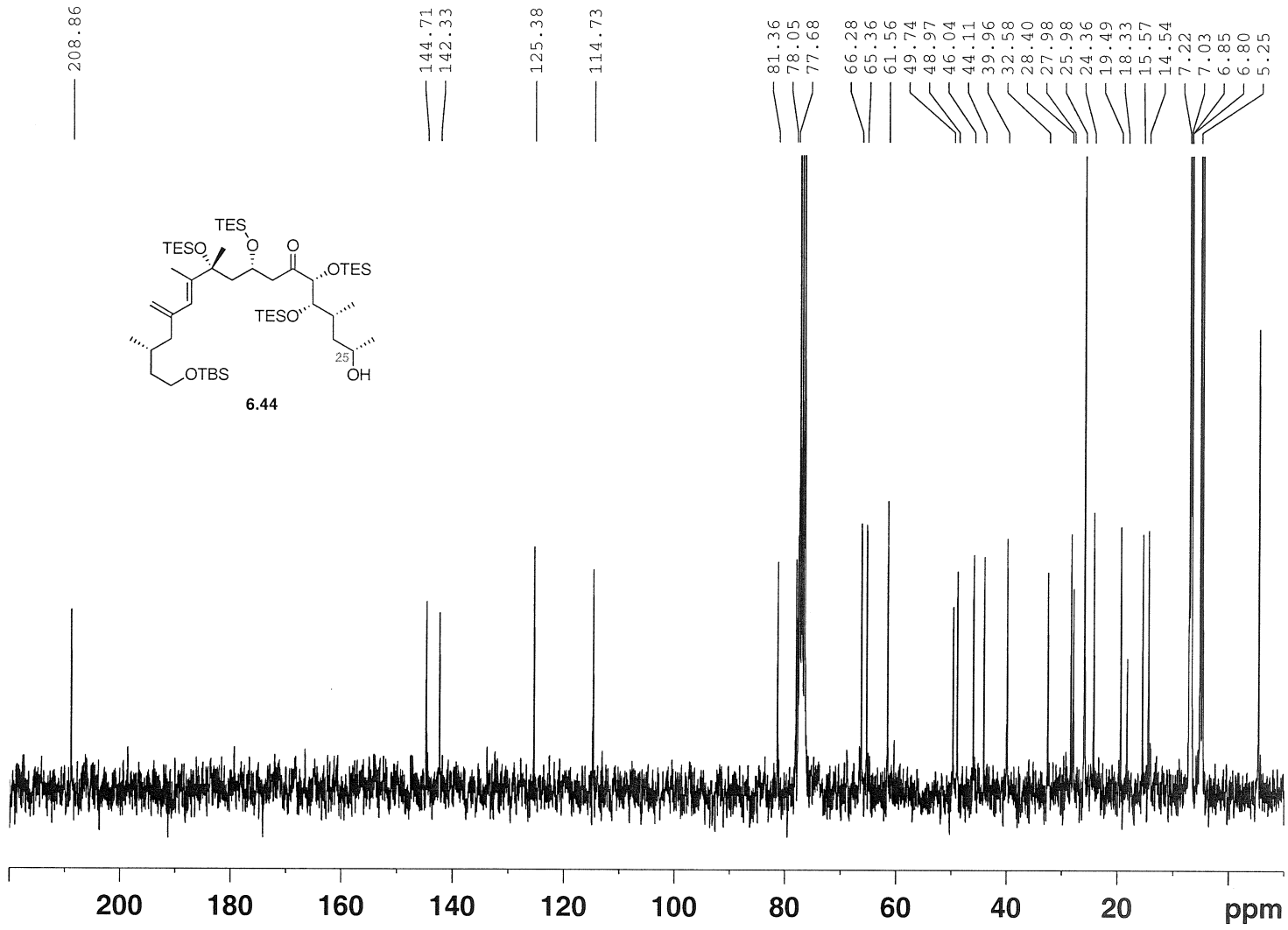
6.41

```
Current Data Parameters
NAME                  5-50
EXPNO                    3
PROCNO                   3
DU                      /n
USER                 Liang

F2 - Acquisition Parameters
Date_              20070508
Time                 20.38
INSTRUM             DPX400
PROBHD   5 mm BBO BB-1H
PULPROG          cosygpqf
TD                   2048
SOLVENT
NS                      2
DS                      8
SWH              4006.410 Hz
FIDRES           1.956255 Hz
AQ               0.2556404 sec
RG                   322.5
DW                 124.800 usec
DE                   6.00 usec
TE                  299.2 K
d0             0.00000300 sec
D1             2.00000000 sec
d13            0.00000400 sec
D16            0.00020000 sec
IN0            0.00024960 sec

======== CHANNEL f1 ========
NUC1                   1H
P0                   7.50 usec
P1                  14.50 usec
PL1                  0.00 dB
SFO1          400.0120000 MHz

====== GRADIENT CHANNEL =====
GPNAM1           SINE.100
GPNAM2           SINE.100
GPZ1                10.00 %
GPZ2                10.00 %
P16               1000.00 usec

F1 - Acquisition parameters
ND0                     1
TD                    128
SFO1              400.012 MHz
FIDRES          31.300079 Hz
SW                 10.016 ppm
FnMODE                 QF

F2 - Processing parameters
SI                  32768
SF            100.5825950 MHz
WDW                    EM
SSB                     0
LB                   3.00 Hz
GB                      0
PC                   1.40
```


Current Data Parameters
NAME 3-53
EXPNO 1
PROCNO 1
DU /n
USER Liang
F2 - Acquisition Parameters
Date_ 20070510
Time 11.53
INSTRUM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 13
DS 2
SWH 4789.272 Hz
FIDRES 0.146157 Hz
AQ 3.42102291 sec
RG 406.4
DW 104.400 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.00 usec
PL1 -3.00 dB
SFO1 300.1321009 MHz
F2 - Processing parameters
SI 32768
SF 300.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
OTES
TESO
O
TES
O
TESO
OTMS
OTBS
6.59
ppm
1.00
1.03
1.00
1.01
1.08
1.14
3.35
0.99
0.95
1.02
6.54
3.58
4.23
4.14
3.97
50.47
4.00
3.94
27.39
16.79

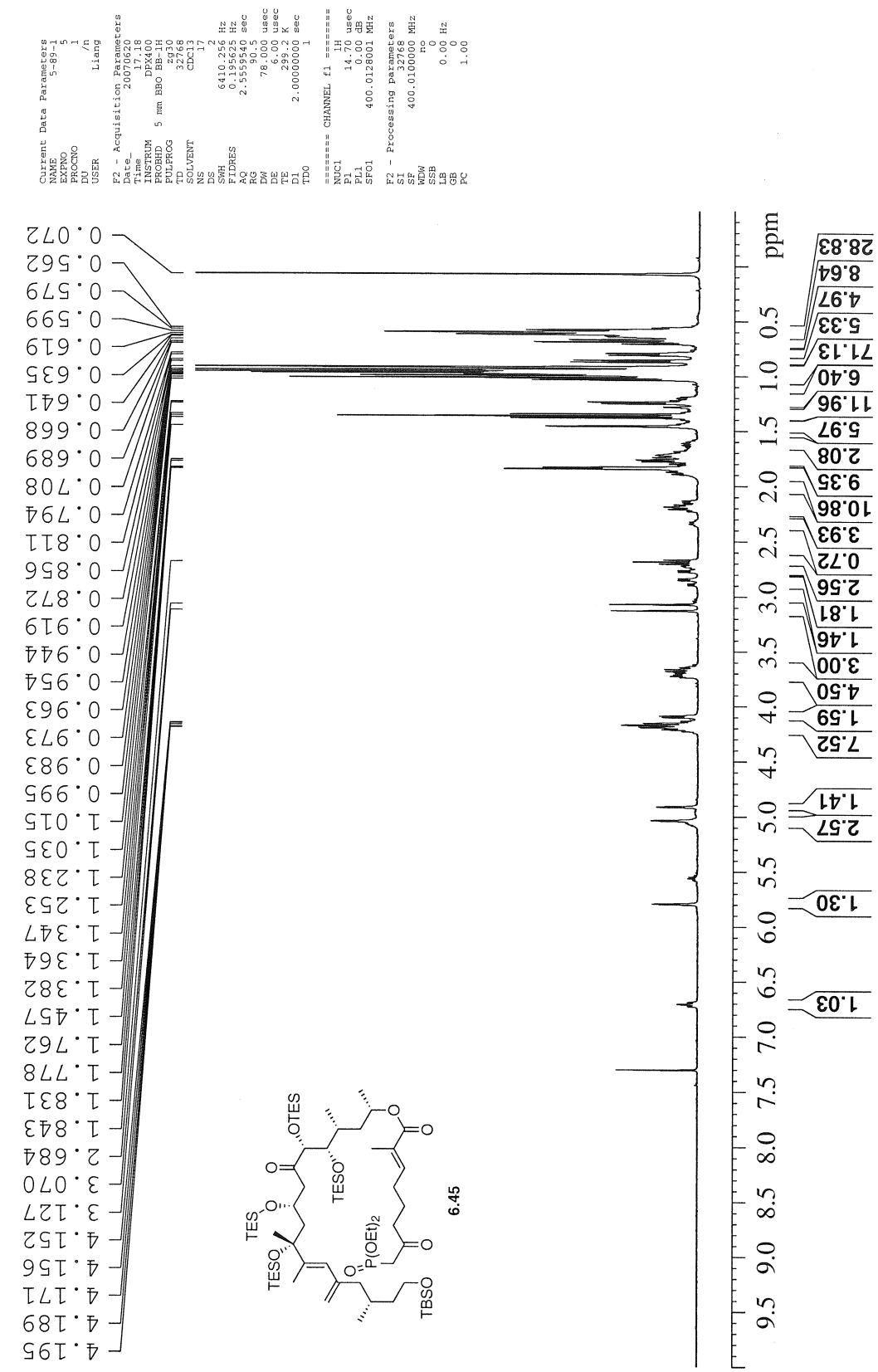

Current Data Parameters
NAME 5-53
EXPNO 3
PROCNO 2
DU /n
USER Liang
F2 - Acquisition Parameter
Date_ 20070510
Time 17.30
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 1994
DS 4
SWH 25125.629 Hz
FIDRES 0.383387 Hz
AQ 1.3042164 sec
RG 4597.6
DW 19.900 usec
DE 6.00 usec
TE 298.2 K
D1 0.15000001 sec
d11 0.03000000 sec
DELTA 0.05000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 7.80 usec
PL1 -3.00 dB
SFO1 100.5936591 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 135.00 usec
PL2 17.40 dB
PL12 17.40 dB
PL13 17.40 dB
SFO2 400.0116000 MHz
F2 - Processing parameters
SI 32768
SF 100.5825950 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
6.80
6.93
7.05
7.07
7.24
14.16
14.53
18.34
19.48
24.60
26.00
27.89
28.43
29.73
31.04
40.03
44.90
46.10
48.50
49.91
61.58
65.71
66.08
77.67
78.26
81.04
114.73
125.23
142.73
144.67
208.61
TES
TESO
O
OTES
TESO
OTMS
OTBS
6.59
ppm
200
180
160
140
120
100
80
60
40
20

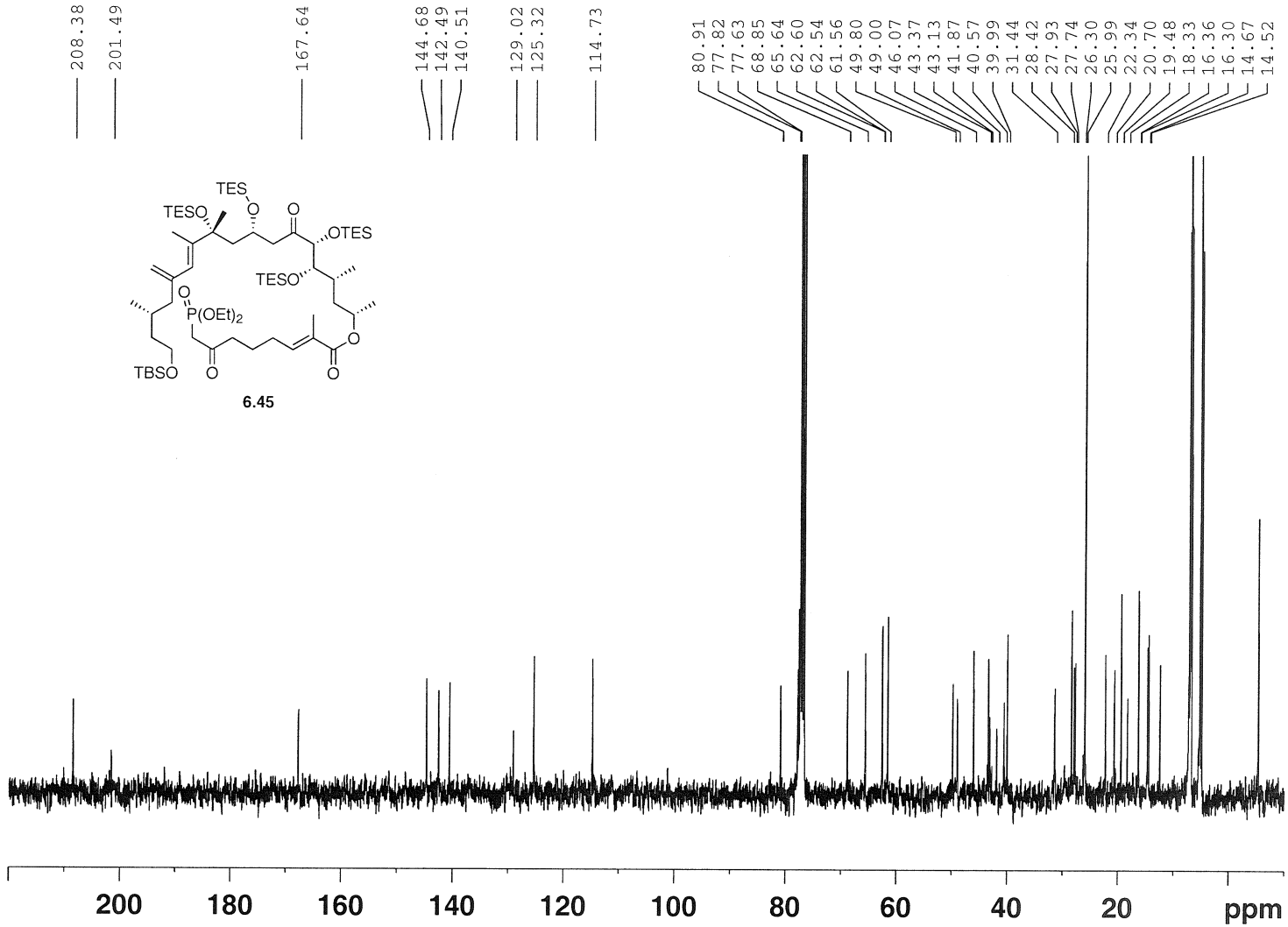

Current Data Parameters
NAME 5-88
EXPNO 1
PROCNO 1
DU /n
USER Liang
F2 - Acquisition Parameters
Date_ 20070613
Time 23.44
INSTRUM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 4789.272 Hz
FIDRES 0.146157 Hz
AQ 3.42102291 sec
RG 80.6
DW 104.400 usec
DE 6.00 usec
TE 296.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.00 usec
PL1 -3.00 dB
SFO1 300.1321009 MHz
F2 - Processing parameters
SI 32768
SF 300.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
5.783
5.316
5.020
4.898
4.213
4.135
4.116
3.799
3.693
3.675
3.654
2.110
2.062
1.836
1.777
1.754
1.731
1.663
1.445
1.300
1.276
1.188
1.168
1.048
1.022
0.994
0.963
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
1.00
1.07
0.96
1.16
1.43
1.18
3.42
1.12
1.09
1.36
13.86
3.66
5.31
4.95
60.00
27.13
6.80
TES
TESO
O
O
TESO
OTES
25
OH
OTBS
6.44



6.44

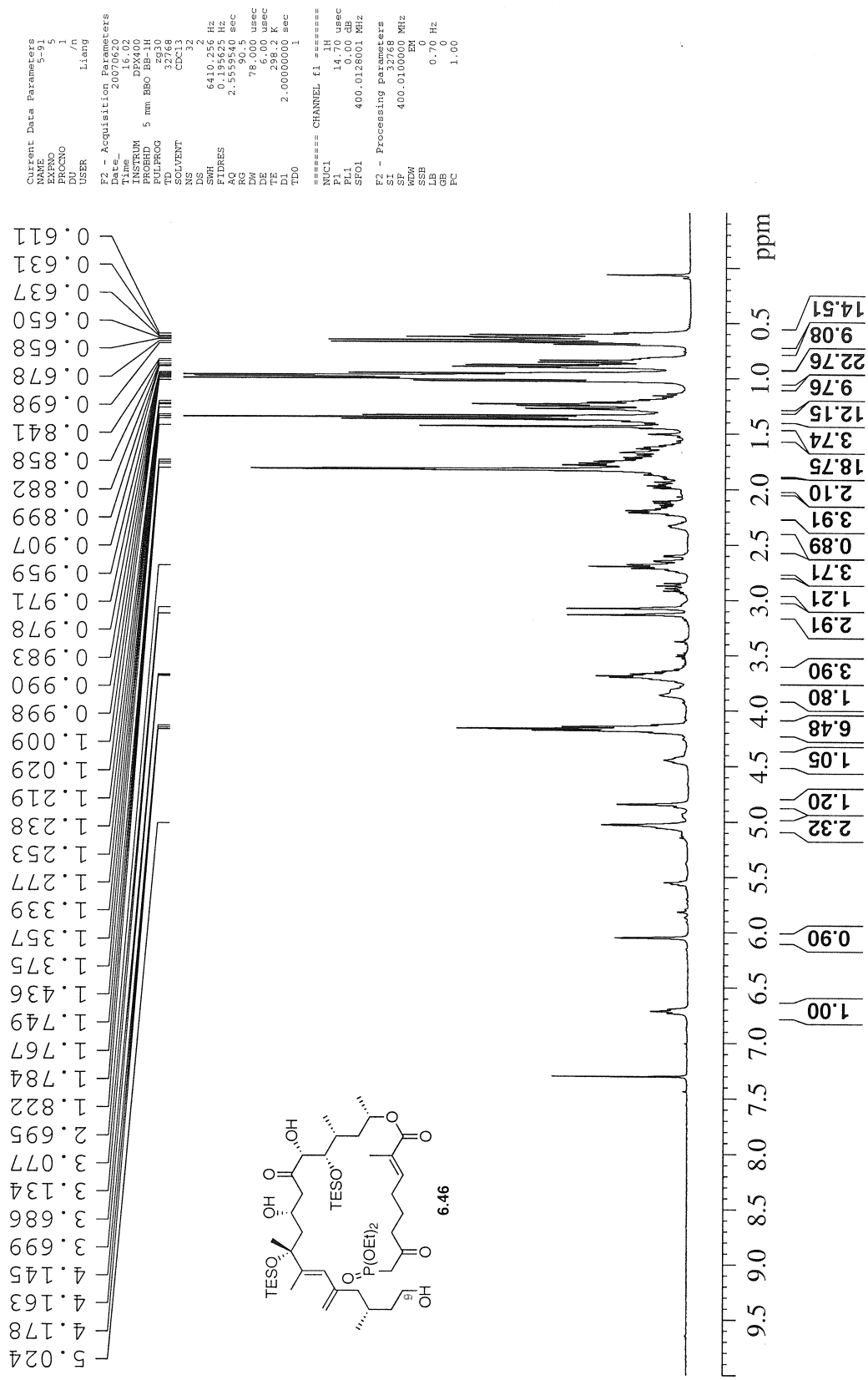
```
Current Data Parameters
NAME                  5-88
EXPNO                    3
PROCNO                   1
DU                      /n
USER                 Liang

F2 - Acquisition Parameter
Date_              20070614
Time                   0.36
INSTRUM              DPX300
PROBHD   5 mm QNP  1H/1
PULPROG             zgpg30
TD                   65536
SOLVENT              CDCl3
NS                    1136
DS                       4
SWH             18832.393 Hz
FIDRES          0.287360 Hz
AQ              1.7400308 se
RG                 9195.2
DW                 26.550 us
DE                  6.00 us
TE                 296.2 K
D1              0.15000001 se
d11             0.03000000 se
DELTA           0.05000000 se
TD0                      1

======== CHANNEL f1 ======
NUC1                   13C
P1                    8.80 us
PL1                  -3.00 dB
SFO1           75.4760505 MH

======== CHANNEL f2 ======
CPDPRG2            waltz16
NUC2                   1H
PCPD2                80.00 us
PL2                  -3.00 dB
PL12                 17.55 dB
PL13                 17.55 dB
SFO2          300.1312005 MH

F2 - Processing parameters
SI                    32768
SF             75.4677490 MH
WDW                      EM
SSB                       0
LB                    3.00 Hz
GB                        0
PC                     1.40
```

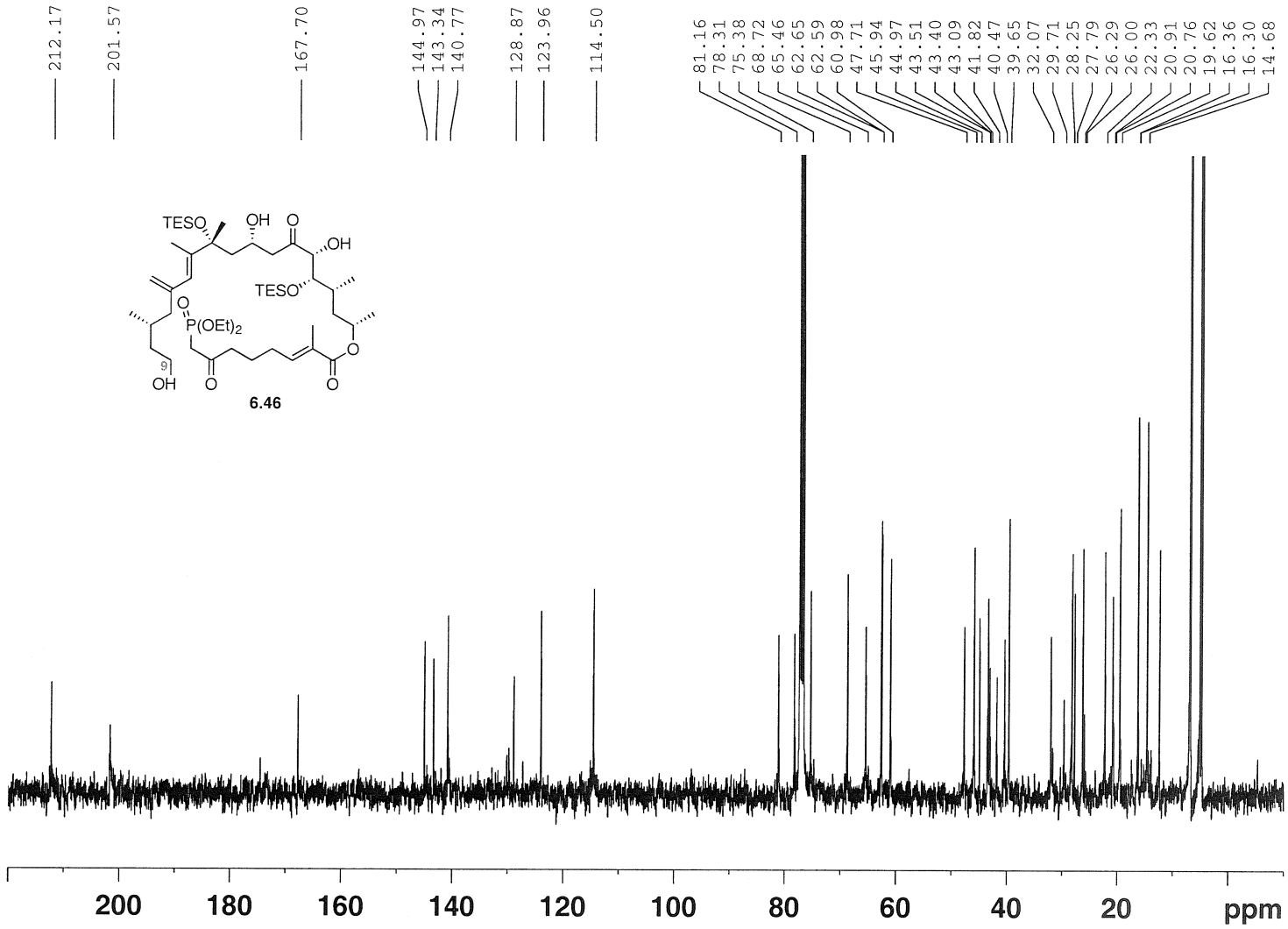

Current Data Parameters
NAME 5-89-1
EXPNO 5
PROCNO 1
DU /n
USER Liang
F2 - Acquisition Parameters
Date_ 20070620
Time 17.18
INSTRUM DPX400
PROBHD 5 mm BBO BH-1H
PULPROG 2g30
TD 32768
SOLVENT CDCl3
NS 17
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5559540 sec
RG 90.5
DW 78.000 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.70 usec
PL1 0.00 dB
SFO1 400.0128001 MHz
F2 - Processing parameters
SI 32768
SF 400.0100000 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
TES
TESO
OTES
TESO
P(OEt)2
TBSO
6.45
ppm
1.03
1.30
2.57
1.41
7.52
1.59
4.50
3.00
1.46
1.81
2.56
0.72
3.93
10.86
9.35
2.08
5.97
11.96
6.40
71.13
5.33
4.97
8.64
28.83



6.45

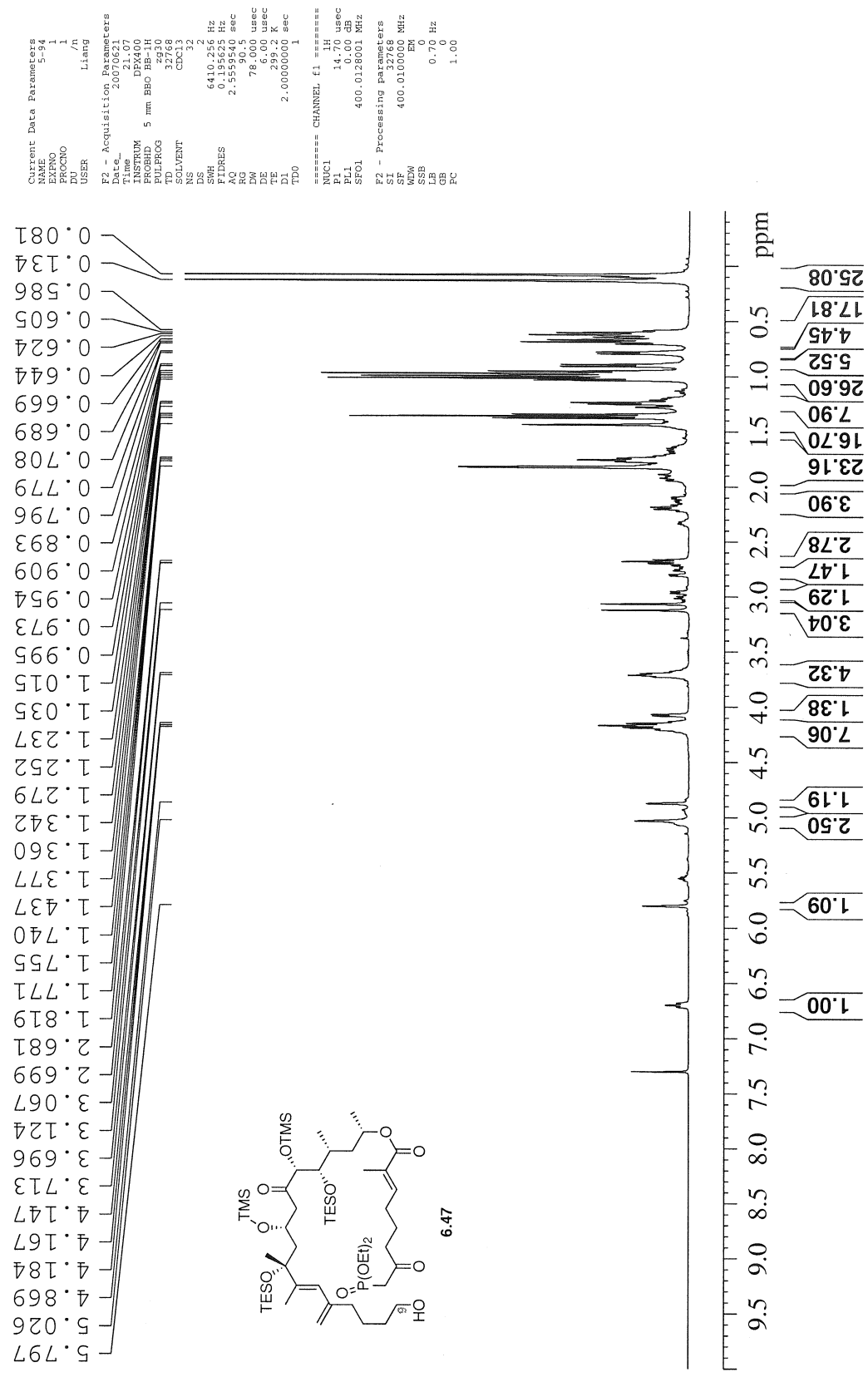
```
Current Data Parameters
NAME                  5-89-1
EXPNO                      7
PROCNO                     1
DU                        /n
USER                  Liang

F2 - Acquisition Parameter
Date_              20070620
Time                  17.40
INSTRUM             DPX400
PROBHD   5 mm BBO BB-1H
PULPROG             zgpg30
TD                    65536
SOLVENT
NS                      894
DS                        4
SWH               25125.629 Hz
FIDRES            0.383387 Hz
AQ                1.3042164 se
RG                   4597.6
DW                   19.900 us
DE                    6.00 us
TE                   299.2 K
D1              0.15000001 se
d11             0.03000000 se
DELTA           0.05000000 se
TD0                       1

======== CHANNEL f1 ======
NUC1                    13C
P1                    7.80 us
PL1                  -3.00 dB
SFO1          100.5936591 MH

======== CHANNEL f2 ======
CPDPRG2             waltz16
NUC2                    1H
PCPD2               135.00 us
PL2                  17.40 dB
PL12                 17.40 dB
PL13                 17.40 dB
SFO2          400.0116000 MH

F2 - Processing parameters
SI                      32768
SF            100.5825950 MH
WDW                      EM
SSB                       0
LB                    3.00 Hz
GB                        0
PC                    1.40
```

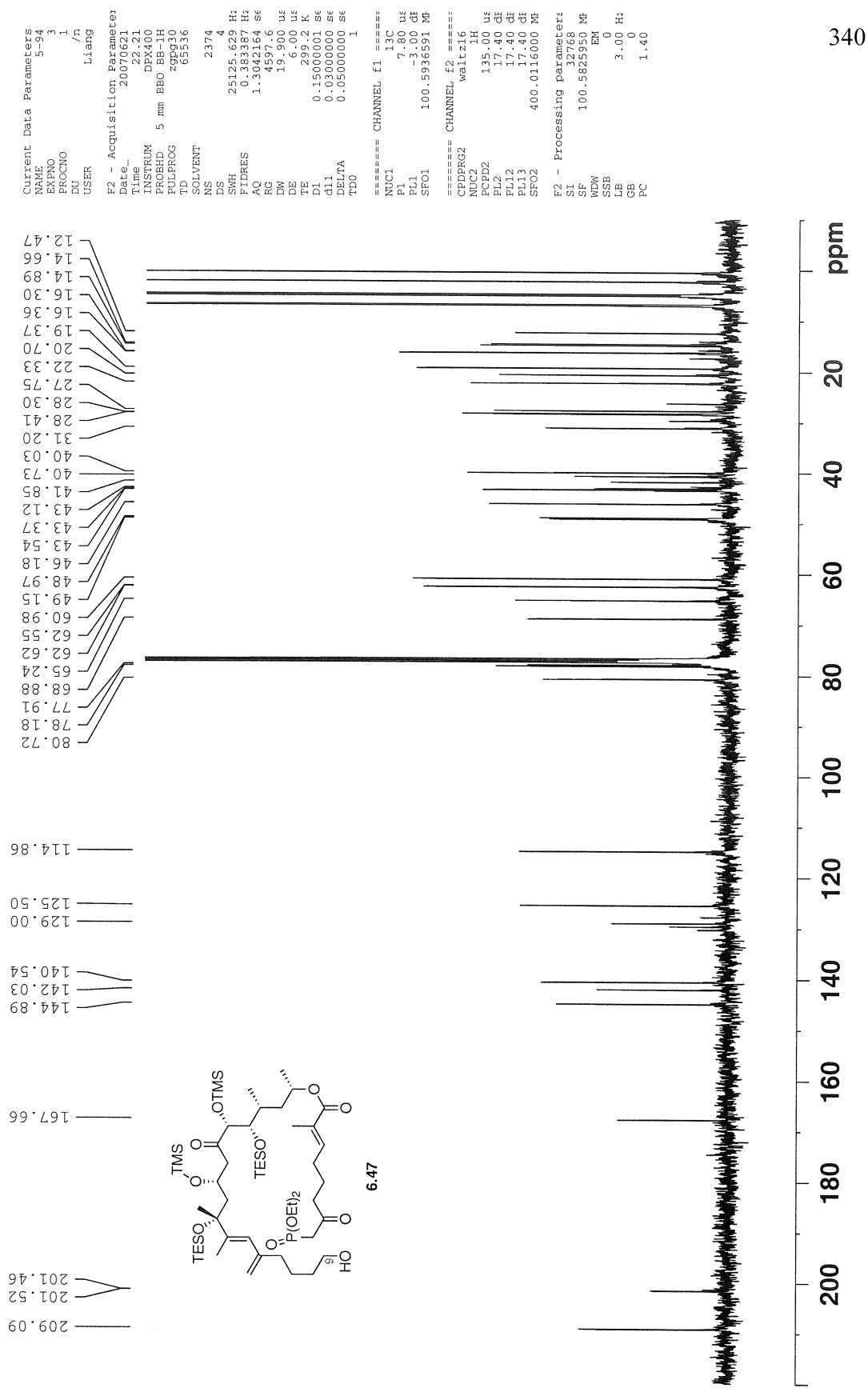

Current Data Parameters
NAME 5-91
EXPNO 5
PROCNO 1
DU /n
USER Liang
F2 - Acquisition Parameters
Date_ 20070620
Time 16.02
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.55595540 sec
RG 90.5
DW 78.000 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.70 usec
PL1 0.00 dB
SFO1 400.0128001 MHz
F2 - Processing parameters
SI 32768
SF 400.0100000 MHz
WDW EM
SSB 0
LB 0.70 Hz
GB 0
PC 1.00
TESO
OH
O
OH
TESO
P(OEt)2
O
O
O
O
OH
6.46
ppm
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
1.00
0.90
2.32
1.20
1.05
6.48
1.80
3.90
2.91
1.21
3.71
0.89
3.91
2.10
18.75
3.74
12.15
9.76
22.76
9.08
14.51
5.024
4.178
4.163
4.145
3.699
3.686
3.134
3.077
2.695
1.822
1.784
1.767
1.749
1.436
1.375
1.357
1.339
1.277
1.253
1.238
1.219
1.029
1.009
0.998
0.990
0.983
0.978
0.971
0.959
0.907
0.899
0.882
0.858
0.841
0.698
0.678
0.658
0.650
0.637
0.631
0.611

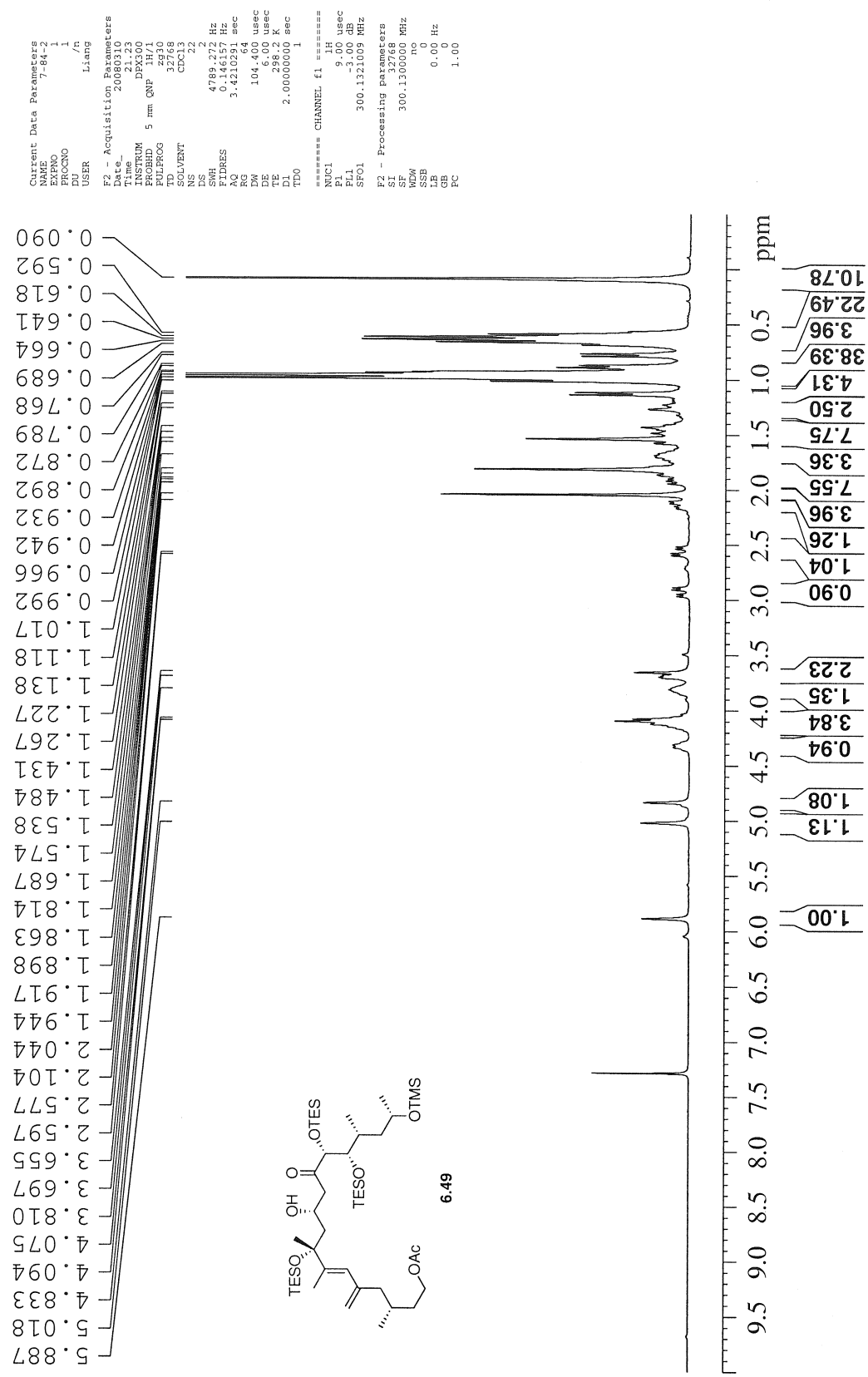


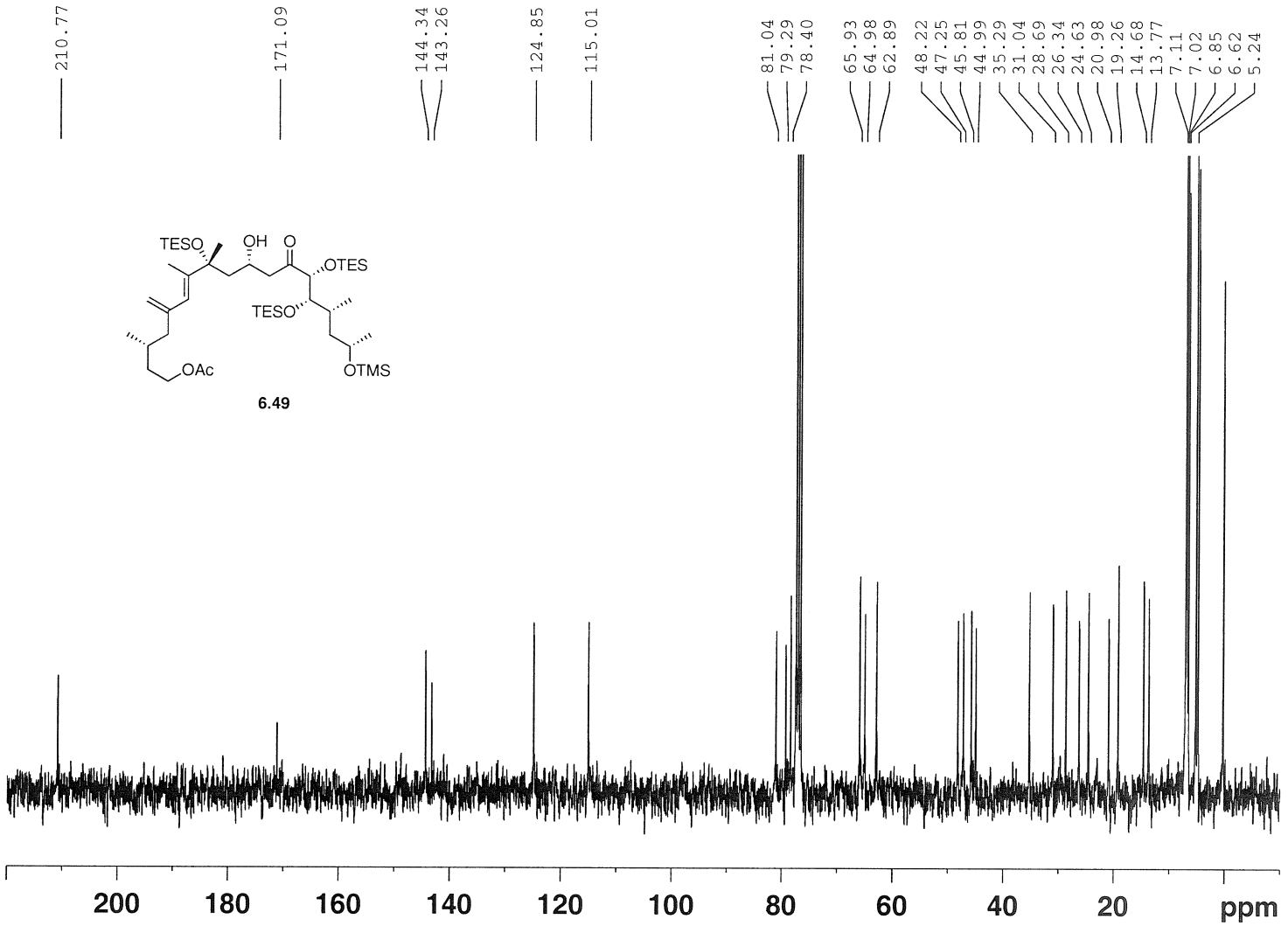
6.46

```
Current Data Parameters
NAME                  5-91
EXPNO                    7
PROCNO                   1
DU                      /n
USER                 Liang

F2 - Acquisition Parameter
Date_              20070620
Time                  16.27
INSTRUM              DPX400
PROBHD   5 mm BBO BB-1H
PULPROG              zgpg30
TD                    65536
SOLVENT
NS                     2130
DS                        4
SWH              25125.629 Hz
FIDRES               0.383387 Hz
AQ                1.3042164 se
RG                   4597.6
DW                  19.900 us
DE                   6.00 us
TE                   299.2 K
D1              0.15000001 se
d11             0.03000000 se
DELTA           0.05000000 se
TD0                       1

======== CHANNEL f1 ======
NUC1                    13C
P1                   7.80 us
PL1                 -3.00 dB
SFO1          100.5936591 MH

======== CHANNEL f2 ======
CPDPRG2             waltz16
NUC2                    1H
PCPD2              135.00 us
PL2                 17.40 dB
PL12                17.40 dB
PL13                17.40 dB
SFO2          400.0116000 MH

F2 - Processing parameters
SI                     32768
SF            100.5825950 MH
WDW                      EM
SSB                       0
LB                   3.00 Hz
GB                        0
PC                     1.40
```


Current Data Parameters
NAME 5-54
EXPNO 1
PROCNO 1
DU /n
USER Liang
F2 - Acquisition Parameters
Date_ 20070621
Time 21.07
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5559540 sec
RG 90.5
DW 78.000 usec
DE 6.00 usec
TE 299.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.70 usec
PL1 0.00 dB
SFO1 400.0128001 MHz
F2 - Processing parameters
SI 32768
SF 400.0100000 MHz
WDW EM
SSB 0
LB 0.70 Hz
GB 0
PC 1.00
TMS
OTMS
TESO
TESO
P(OEt)2
HO
6.47
ppm
1.00
1.09
2.50
1.19
7.06
1.38
4.32
3.04
1.29
1.47
2.78
3.90
23.16
16.70
7.90
26.60
5.52
4.45
17.81
25.08

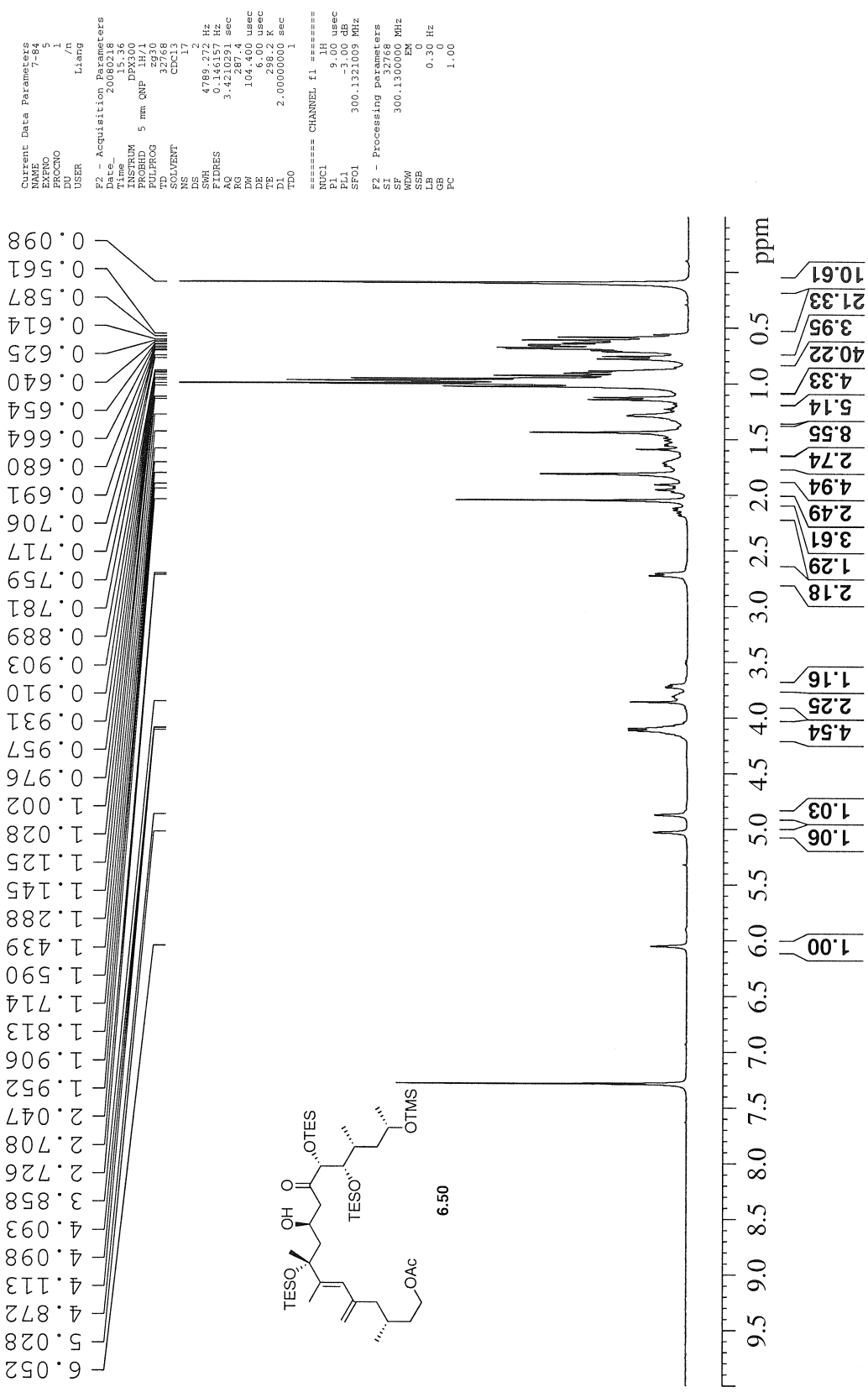

Current Data Parameters
NAME 5-94
EXPNO 3
PROCNO 1
DU /n
USER Liang
F2 - Acquisition Parameter
Date_ 20070621
Time 22.21
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT
NS 2374
DS 4
SWH 25125.629 Hz
FIDRES 0.383387 Hz
AQ 1.3042164 se
RG 4597.6
DW 19.900 us
DE 6.00 us
TE 299.2 K
D1 0.15000001 se
d11 0.03000000 se
DELTA 0.05000000 se
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 7.80 us
PL1 -3.00 dB
SFO1 100.5936591 MH
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 135.00 us
PL2 17.40 dB
PL12 17.40 dB
PL13 17.40 dB
SFO2 400.0116000 MH
F2 - Processing parameters
SI 32768
SF 100.5825950 MH
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
80.72
78.18
77.91
68.88
65.24
62.62
62.55
60.98
49.15
48.97
46.18
43.54
43.37
43.12
41.85
40.73
40.03
31.20
28.41
28.30
27.75
22.33
20.70
19.37
16.36
16.30
14.89
14.66
12.47
114.86
125.50
129.00
140.54
142.03
144.89
167.66
201.46
201.52
209.09
TMS
OTMS
TESO
TESO
P(OEt)2
HO
6
6.47
200
180
160
140
120
100
80
60
40
20
ppm

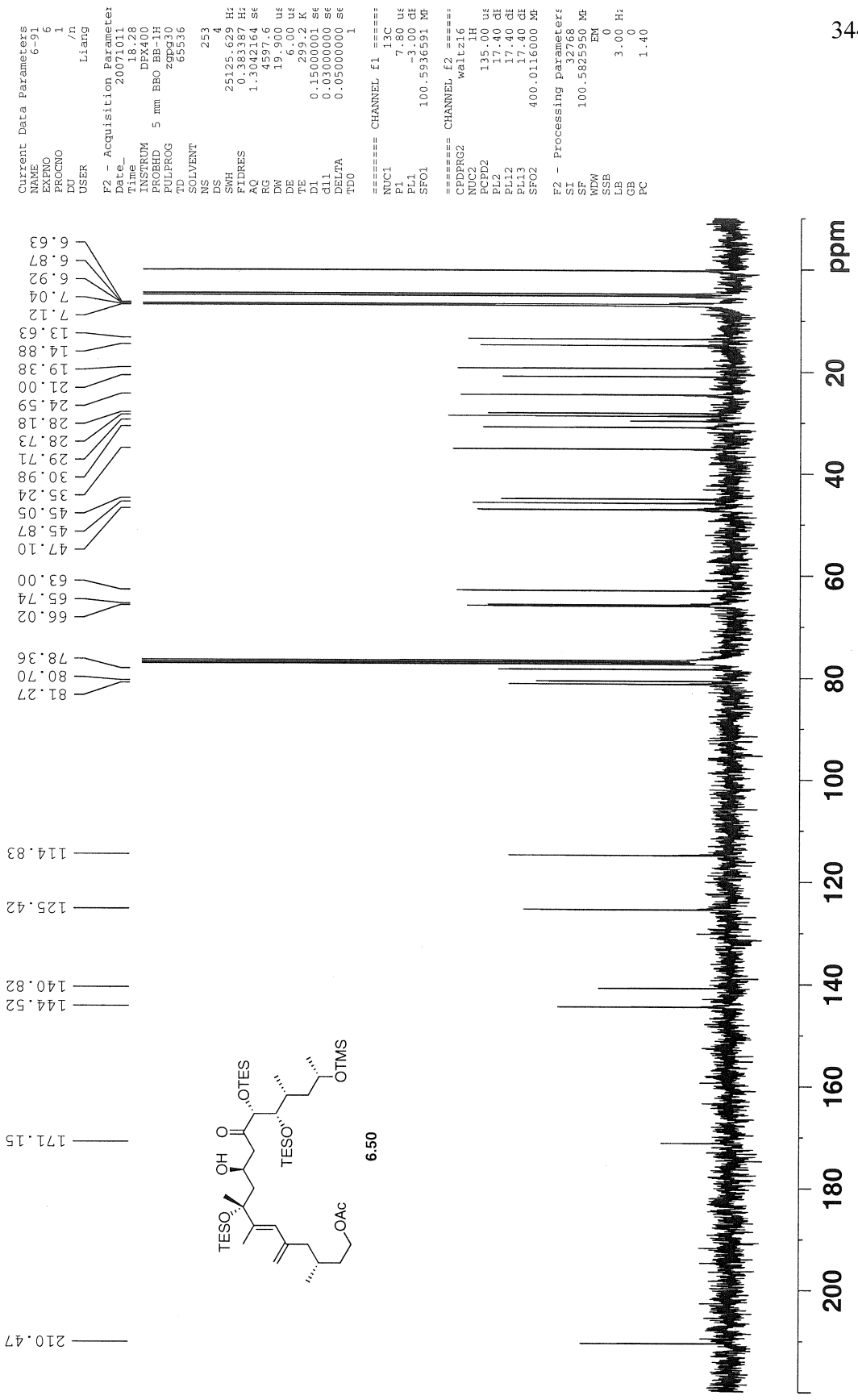

Current Data Parameters
NAME 7-84-2
EXPNO 1
PROCNO 1
DU /n
USER Liang
F2 - Acquisition Parameters
Date_ 20080310
Time 21.23
INSTRUM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 22
DS 2
SWH 4789.272 Hz
FIDRES 0.146157 Hz
AQ 3.42102911 sec
RG 64
DW 104.400 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000001 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.00 usec
PL1 -3.00 dB
SFO1 300.1321009 MHz
F2 - Processing parameters
SI 32768
SF 300.1300000 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
TESO
OH O
OTES
TESO
OTMS
OAc
6.49
ppm
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
1.00
1.13
1.08
0.94
3.84
1.35
2.23
0.90
1.04
1.26
3.96
7.55
3.36
7.75
2.50
4.31
38.39
3.96
22.49
10.78
5.887
5.018
4.833
4.094
4.075
3.810
3.697
3.655
2.597
2.577
2.104
2.044
1.944
1.917
1.898
1.863
1.814
1.687
1.574
1.538
1.484
1.431
1.267
1.227
1.138
1.118
1.017
0.992
0.966
0.942
0.932
0.892
0.872
0.789
0.768
0.689
0.664
0.641
0.618
0.592
0.090

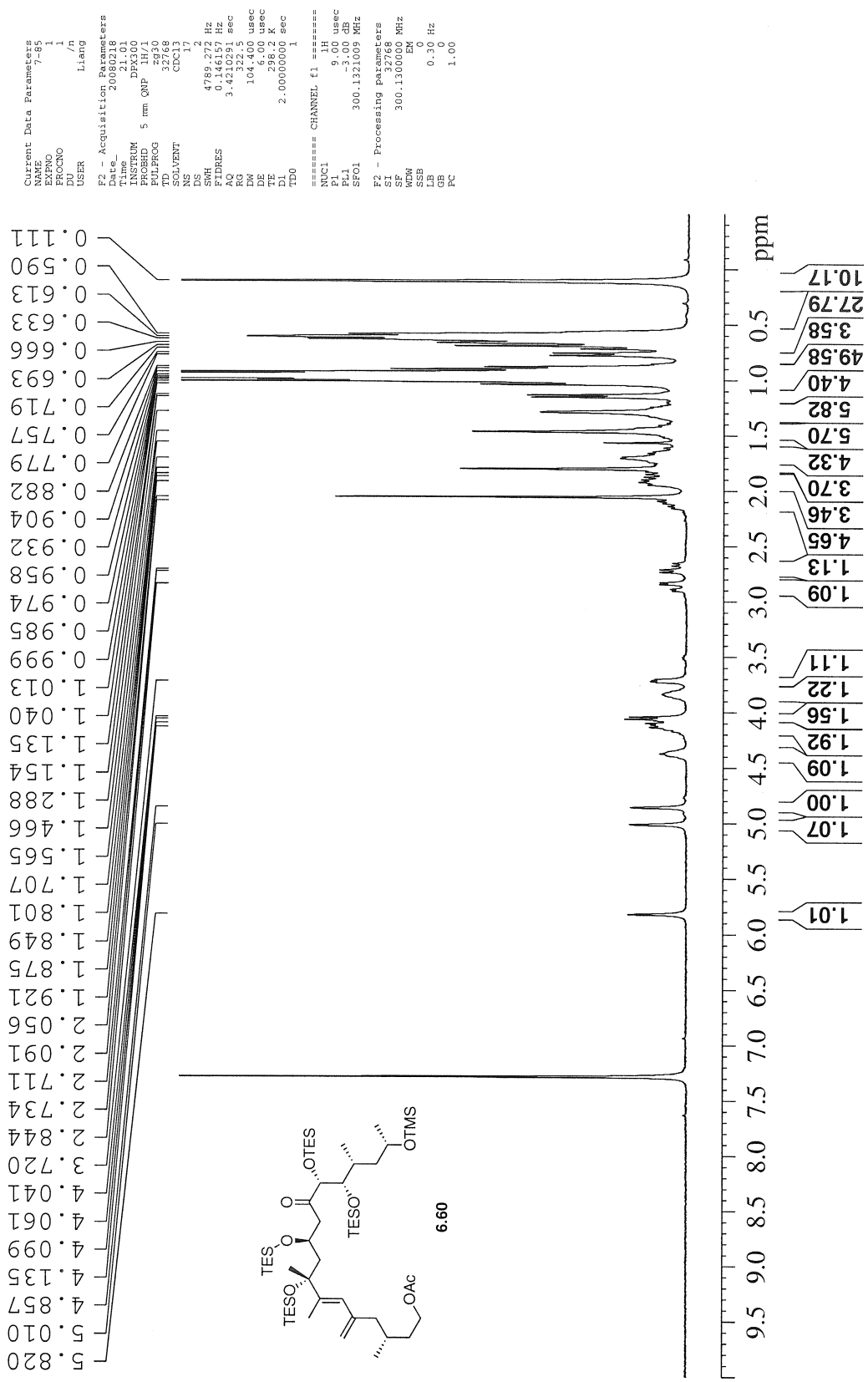


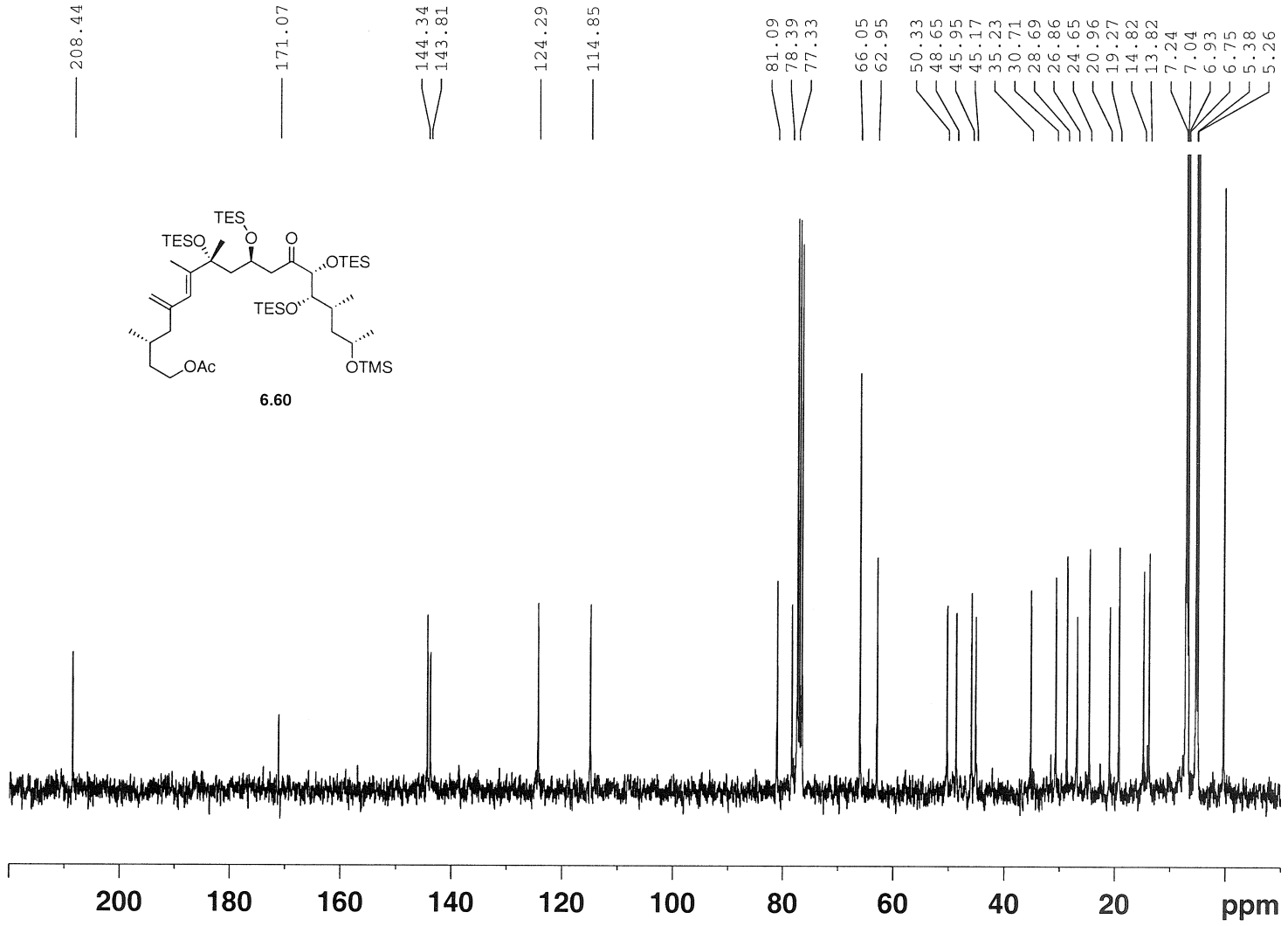
6.49

```
Current Data Parameters
NAME                  7-84-2
EXPNO                      3
PROCNO                     1
DU                        /n
USER                   Liang

F2 - Acquisition Parameter
Date_              20080310
Time                  21.40
INSTRUM              DPX300
PROBHD   5 mm QNP  1H/1
PULPROG             zgpg30
TD                   65536
SOLVENT              CDCl3
NS                     277
DS                       4
SWH              18832.393 Hz
FIDRES           0.287360 Hz
AQ               1.7400308 se
RG                  9195.2
DW                  26.550 us
DE                   6.00 us
TE                  298.2 K
D1             0.15000001 se
d11            0.03000000 se
DELTA          0.05000000 se
TD0                      1

======== CHANNEL f1 ======
NUC1                   13C
P1                    8.80 us
PL1                  -3.00 dB
SFO1          75.4760505 MH

======== CHANNEL f2 ======
CPDPRG2            waltz16
NUC2                   1H
PCPD2                80.00 us
PL2                  -3.00 dB
PL12                 17.55 dB
PL13                 17.55 dB
SFO2         300.1312005 MH

F2 - Processing parameters
SI                   32768
SF            75.4677490 MH
WDW                    EM
SSB                     0
LB                   3.00 Hz
GB                      0
PC                   1.40
```


Current Data Parameters
NAME 7-84
EXPNO 5
PROCNO 1
DU /n
USER Liang
F2 - Acquisition Parameters
Date_ 20080218
Time 15.36
INSTRUM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 17
DS 2
SWH 4789.272 Hz
FIDRES 0.146157 Hz
AQ 3.4210291 sec
RG 287.4
DW 104.400 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000001 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.00 usec
PL1 -3.00 dB
SFO1 300.1321009 MHz
F2 - Processing parameters
SI 32768
SF 300.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
TESO
OH O
OTES
TESO
OTMS
OAc
6.50
ppm
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
1.00
1.06
1.03
4.54
2.25
1.16
2.18
1.29
3.61
2.49
4.94
2.74
8.55
5.14
4.33
40.22
3.95
21.33
10.61
6.052
5.028
4.872
4.113
4.098
4.093
3.858
2.726
2.708
2.047
1.952
1.906
1.813
1.714
1.590
1.439
1.288
1.145
1.125
1.028
1.002
0.976
0.957
0.931
0.910
0.903
0.889
0.781
0.759
0.717
0.706
0.691
0.680
0.664
0.654
0.640
0.625
0.614
0.587
0.561
0.098

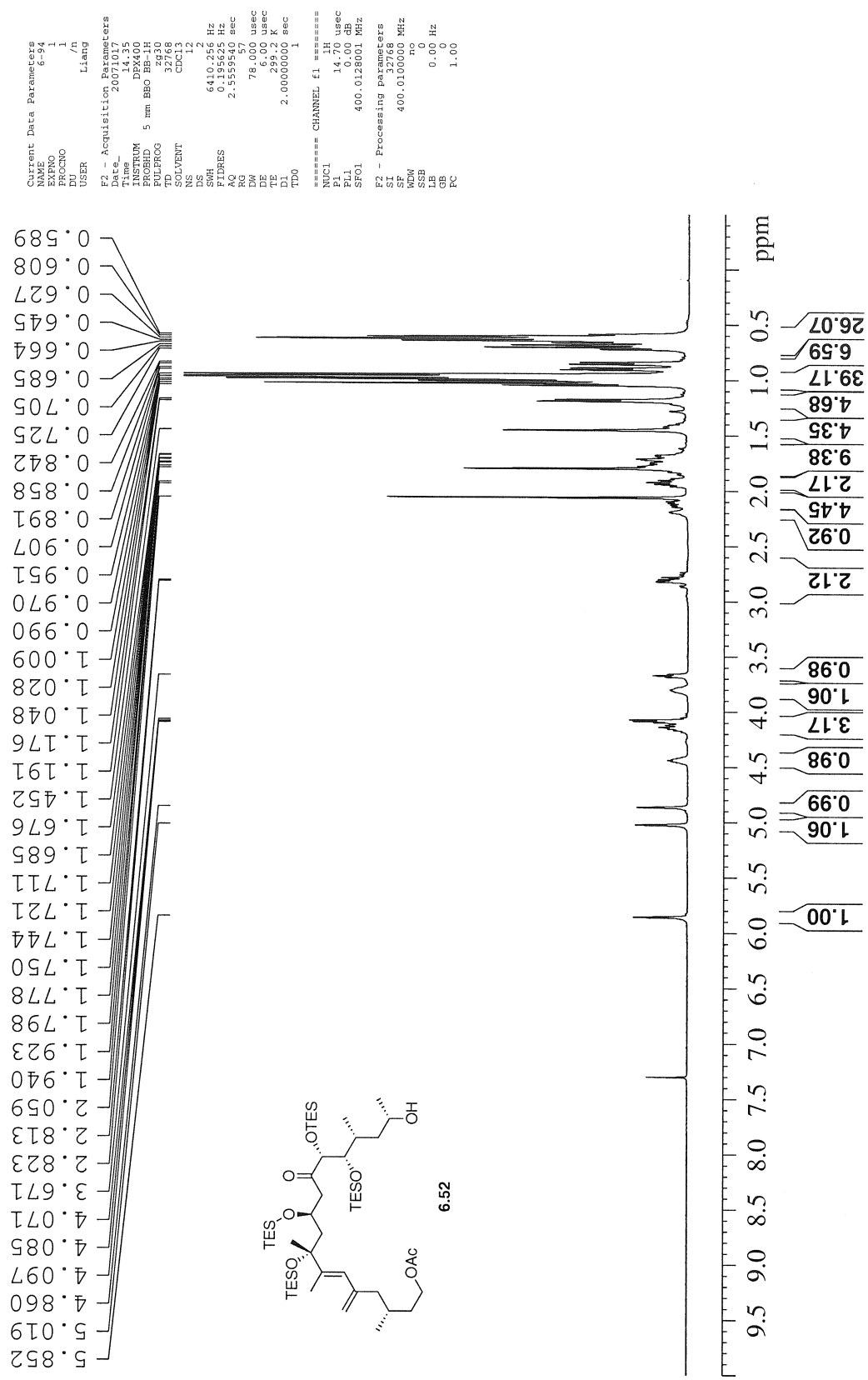

Current Data Parameters
NAME 6-91
EXPNO 6
PROCNO 1
DU /n
USER Liang
F2 - Acquisition Parameter
Date_ 20071011
Time 18.28
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT
NS 253
DS 4
SWH 25125.629 H
FIDRES 0.383387 H
AQ 1.3042164 s
RG 4597.6
DW 19.900 u
DE 6.00 u
TE 299.2 K
D1 0.15000001 s
d11 0.03000000 s
DELTA 0.05000000 s
TD0 1
======== CHANNEL f1 ======
NUC1 13C
P1 7.80 u
PL1 -3.00 d
SFO1 100.5936591 M
======== CHANNEL f2 ======
CPDPRG2 waltz16
NUC2 1H
PCPD2 135.00 u
PL2 17.40 d
PL12 17.40 d
PL13 17.40 d
SFO2 400.0116000 M
F2 - Processing parameter
SI 32768
SF 100.5825950 M
WDW EM
SSB 0
LB 3.00 H
GB 0
PC 1.40
6.63
6.87
6.92
7.04
7.12
13.63
14.88
19.38
21.00
24.59
28.18
28.73
29.71
30.98
35.24
45.05
45.87
47.10
63.00
65.74
66.02
78.36
80.70
81.27
114.83
125.42
140.82
144.52
171.15
210.47
OH
O
OTES
TESO
OTMS
TESO
OAc
6.50
ppm

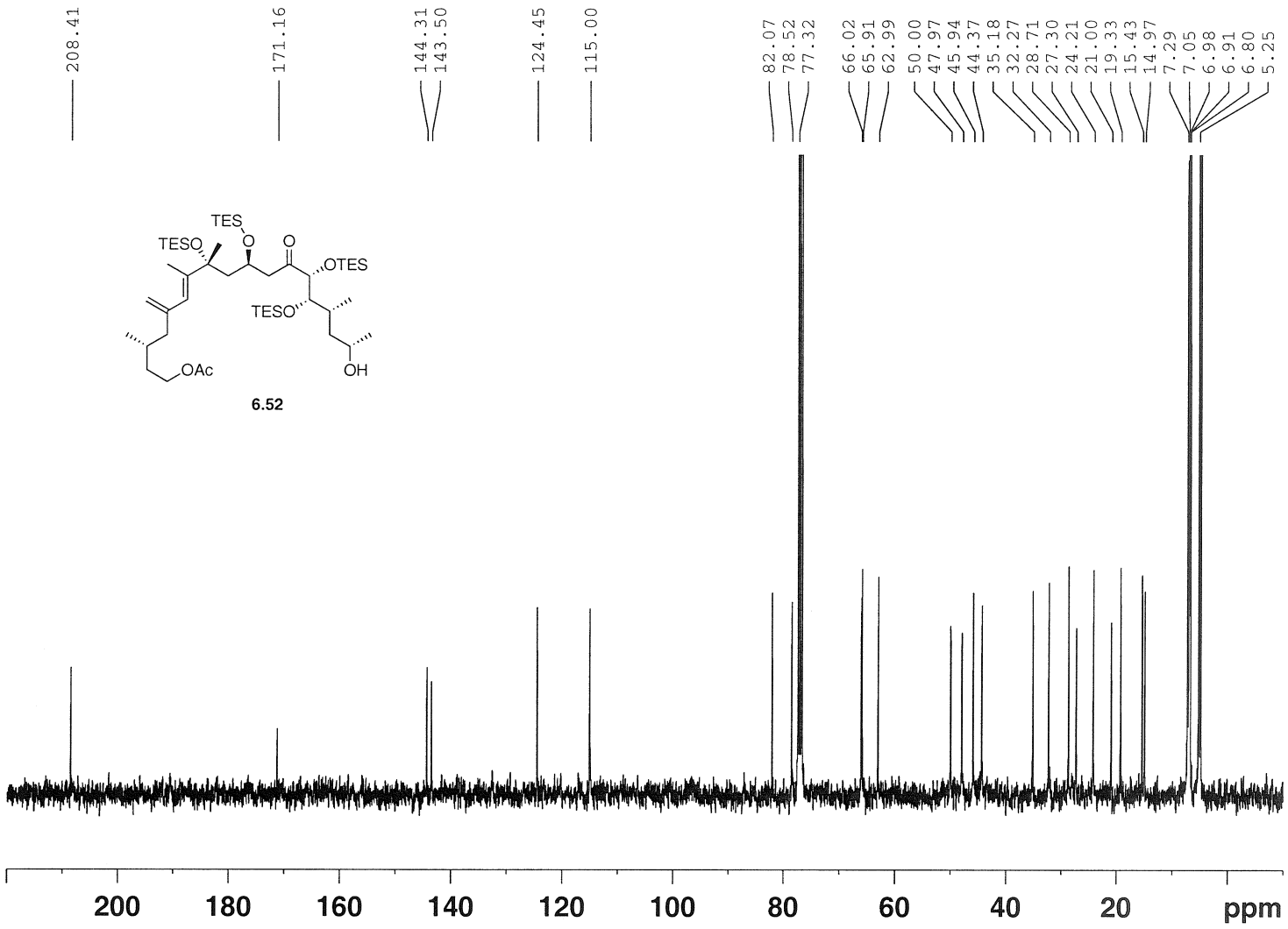

Current Data Parameters
NAME 7-85
EXPNO 1
PROCNO 1
DU /n
USER Liang
F2 - Acquisition Parameters
Date_ 20080218
Time 21.01
INSTRUM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 17
DS 2
SWH 4789.272 Hz
FIDRES 0.146157 Hz
AQ 3.4210291 sec
RG 322.5
DW 104.400 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.00 usec
PL1 -3.00 dB
SFO1 300.1321009 MHz
F2 - Processing parameters
SI 32768
SF 300.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
TESO
TES
O
OTES
TESO
OTMS
OAc
6.60
ppm
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
1.01
1.07
1.00
1.09
1.92
1.56
1.22
1.11
1.09
1.13
4.65
3.46
3.70
4.32
5.70
5.82
4.40
49.58
3.58
27.79
10.17
5.820
5.010
4.857
4.135
4.099
4.061
4.041
3.720
2.844
2.734
2.711
2.091
2.056
1.921
1.875
1.849
1.801
1.707
1.565
1.466
1.288
1.154
1.135
1.040
1.013
0.999
0.985
0.974
0.958
0.932
0.904
0.882
0.779
0.757
0.719
0.693
0.666
0.633
0.613
0.590
0.111



6.60

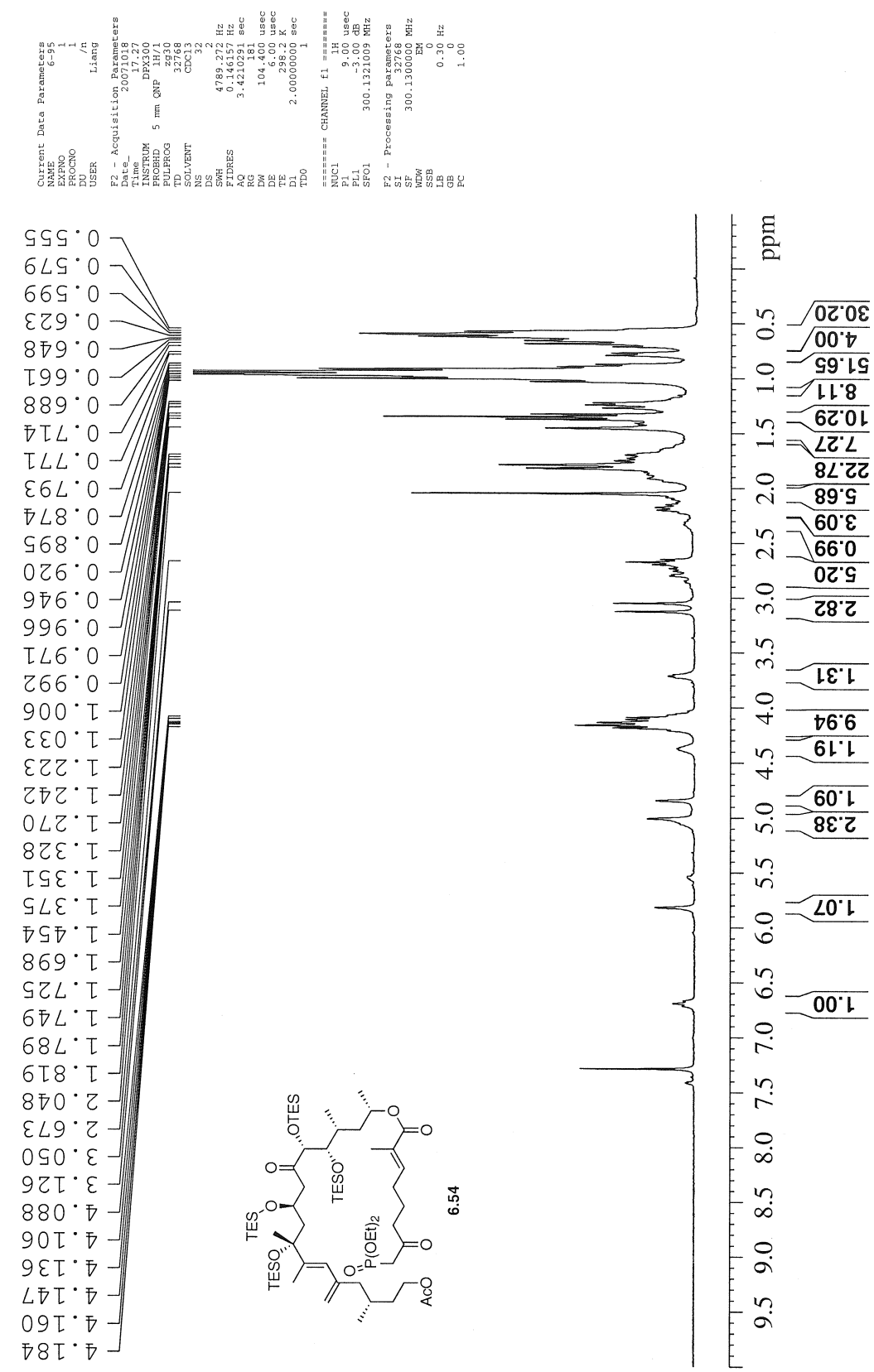
```
Current Data Parameters
NAME                  6-93
EXPNO                    3
PROCNO                   1
DU                      /n
USER                 Liang

F2 - Acquisition Parameter
Date_              20071014
Time                 21.15
INSTRUM              DPX300
PROBHD    5 mm QNP  1H/1
PULPROG             zgpg30
TD                   65536
SOLVENT              CDCl3
NS                     335
DS                       4
SWH              18832.393 Hz
FIDRES           0.287360 Hz
AQ               1.7400308 se
RG                  9195.2
DW                 26.550 us
DE                  6.00 us
TE                 298.2 K
D1              0.15000001 se
d11             0.03000000 se
DELTA           0.05000000 se
TD0                      1

======== CHANNEL f1 ======
NUC1                   13C
P1                  8.80 us
PL1                -3.00 dB
SFO1          75.4760505 MH

======== CHANNEL f2 ======
CPDPRG2            waltz16
NUC2                   1H
PCPD2              80.00 us
PL2                -3.00 dB
PL12               17.55 dB
PL13               17.55 dB
SFO2         300.1312005 MH

F2 - Processing parameters
SI                   32768
SF            75.4677490 MH
WDW                    EM
SSB                     0
LB                 3.00 Hz
GB                      0
PC                   1.40
```

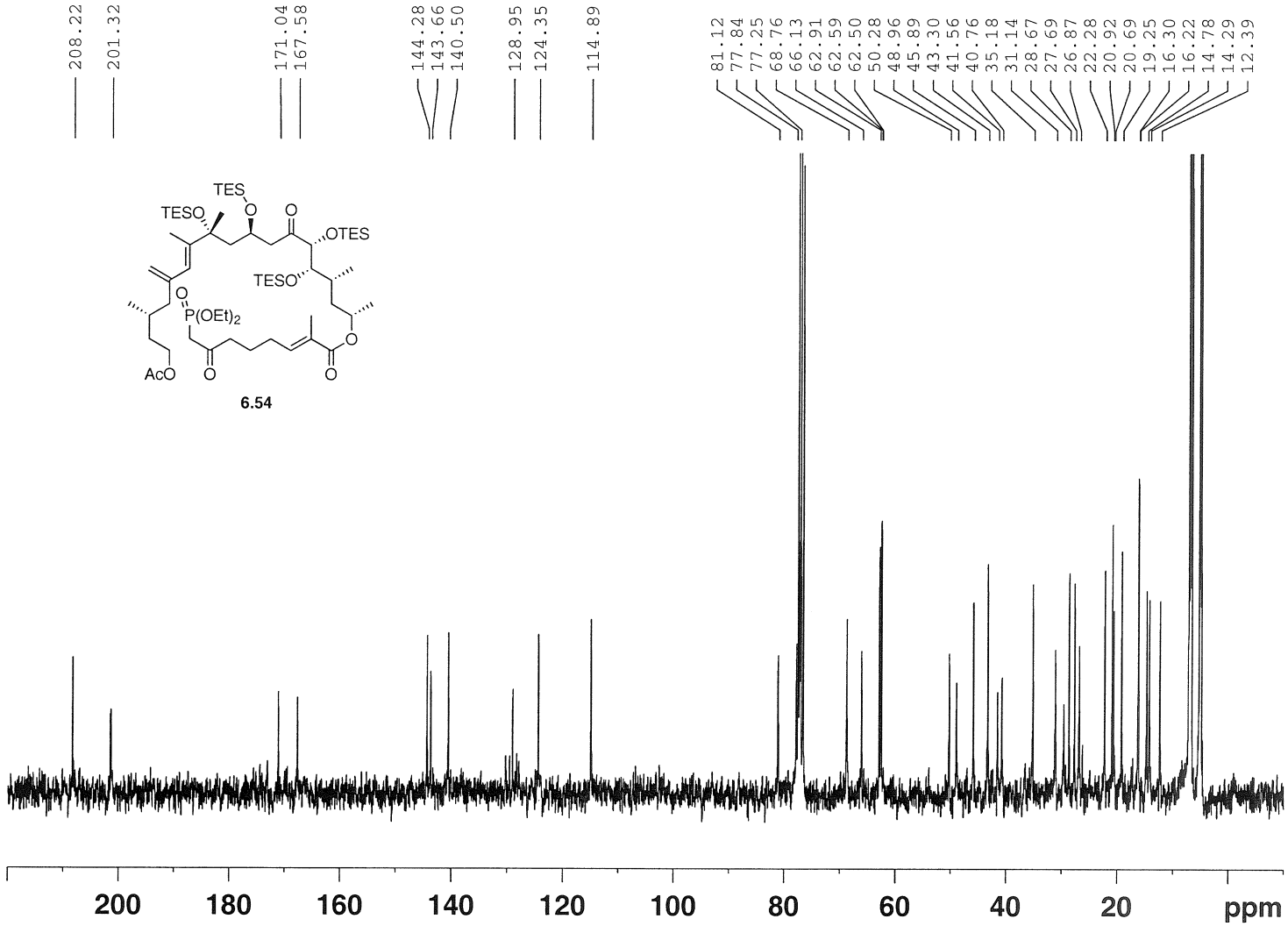

Current Data Parameters
NAME 6-94
EXPNO 1
PROCNO 1
DIR /n
USER Liang
F2 - Acquisition Parameters
Date_ 20071017
Time 14.35
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 12
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5559540 sec
RG 57
DW 78.000 usec
DE 6.00 usec
TE 299.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.70 usec
PL1 0.00 dB
SFO1 400.0128001 MHz
F2 - Processing parameters
SI 32768
SF 400.0100000 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
TES
TESO
O
OTES
TESO
OH
OAc
6.52
ppm
1.00
1.06
0.99
0.98
3.17
1.06
0.98
2.12
0.92
4.45
2.17
9.38
4.35
4.68
39.17
6.59
26.07



6.52

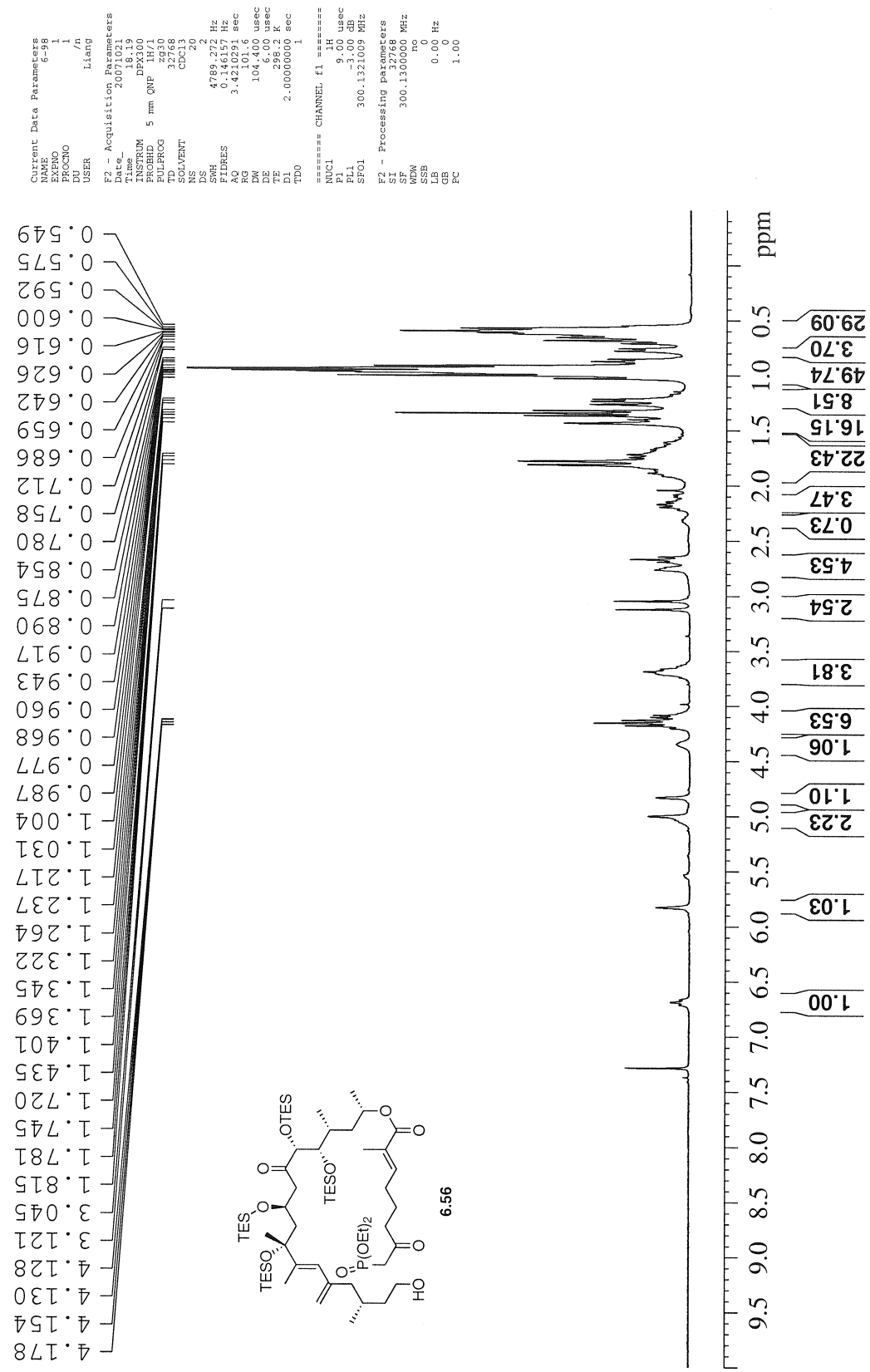
```
Current Data Parameters
NAME                  6-94
EXPNO                    3
PROCNO                   1
DU                      /n
USER                 Liang

F2 - Acquisition Parameter
Date_              20071017
Time                 14.51
INSTRUM             DPX400
PROBHD   5 mm BBO BB-1H
PULPROG            zgpg30
TD                  65536
SOLVENT
NS                    305
DS                      4
SWH             25125.629 Hz
FIDRES          0.383387 Hz
AQ              1.3042164 se
RG                 4597.6
DW                19.900 us
DE                 6.00 us
TE                299.2 K
D1            0.15000001 se
d11           0.03000000 se
DELTA         0.05000000 se
TD0                     1

======== CHANNEL f1 ======
NUC1                  13C
P1                 7.80 us
PL1               -3.00 dB
SFO1         100.5936591 MH

======== CHANNEL f2 ======
CPDPRG2          waltz16
NUC2                  1H
PCPD2            135.00 us
PL2               17.40 dB
PL12              17.40 dB
PL13              17.40 dB
SFO2         400.0116000 MH

F2 - Processing parameters
SI                  32768
SF          100.5825950 MH
WDW                   EM
SSB                    0
LB                3.00 Hz
GB                     0
PC                 1.40
```

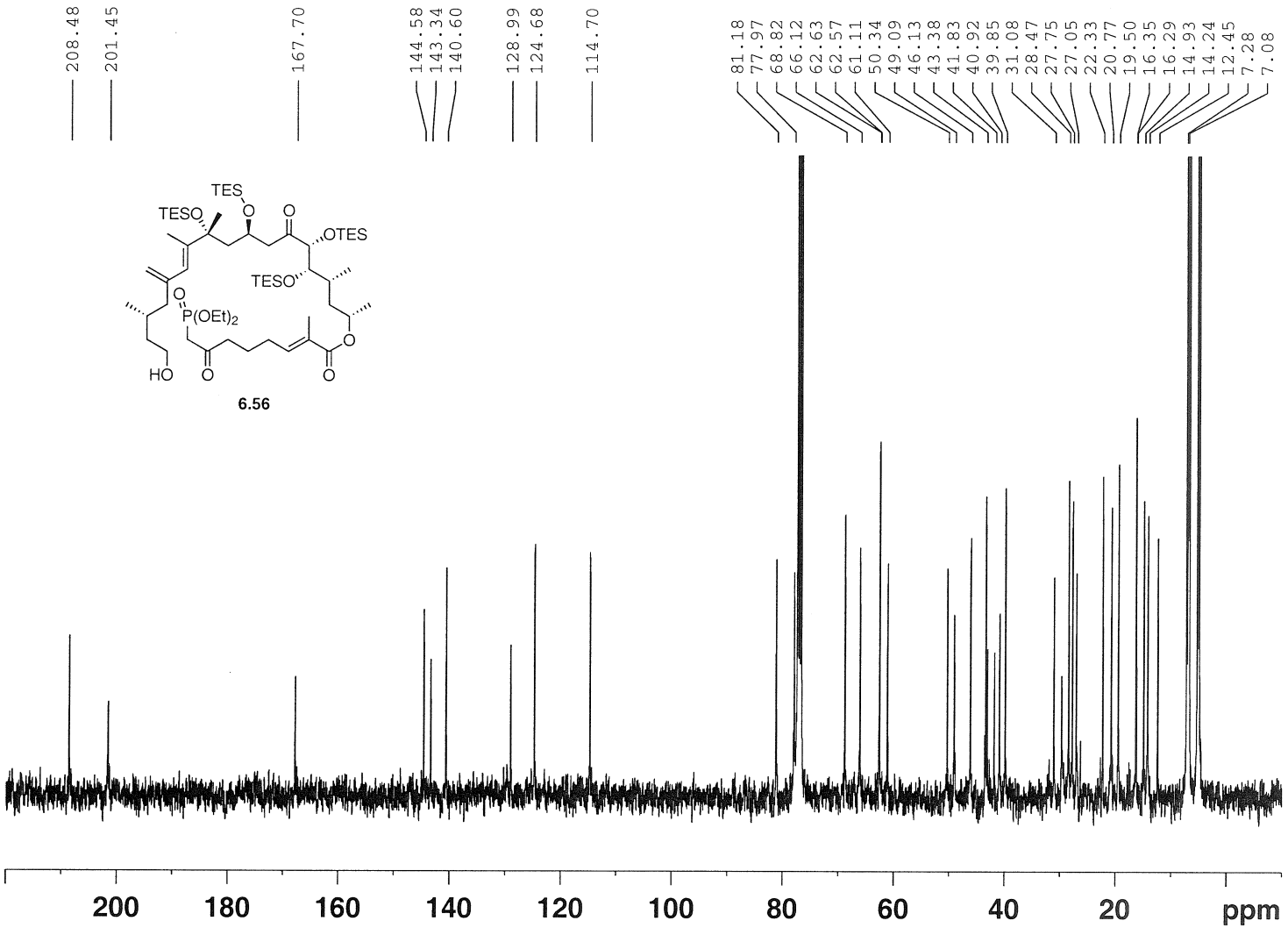

Current Data Parameters
NAME 6-95
EXPNO 1
PROCNO /n
USER Liang
F2 - Acquisition Parameters
Date_ 20071018
Time 17.27
INSTRUM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 4789.272 Hz
FIDRES 0.146157 Hz
AQ 3.42210291 sec
RG 181
DW 104.400 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.00 usec
PL1 -3.00 dB
SFO1 300.1321009 MHz
F2 - Processing parameters
SI 32768
SF 300.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
0.555
0.579
0.599
0.623
0.648
0.661
0.688
0.714
0.771
0.793
0.874
0.895
0.920
0.946
0.966
0.971
0.992
1.006
1.033
1.223
1.242
1.270
1.328
1.351
1.375
1.454
1.698
1.725
1.749
1.789
1.819
2.048
2.673
3.050
3.126
4.088
4.106
4.136
4.147
4.160
4.184
TES
TESO
OTES
TESO
P(OEt)2
AcO
6.54
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
ppm
1.00
1.07
2.38
1.09
1.19
9.94
1.31
2.82
5.20
0.99
3.09
5.68
22.78
7.27
10.29
8.11
51.65
4.00
30.20



6.54

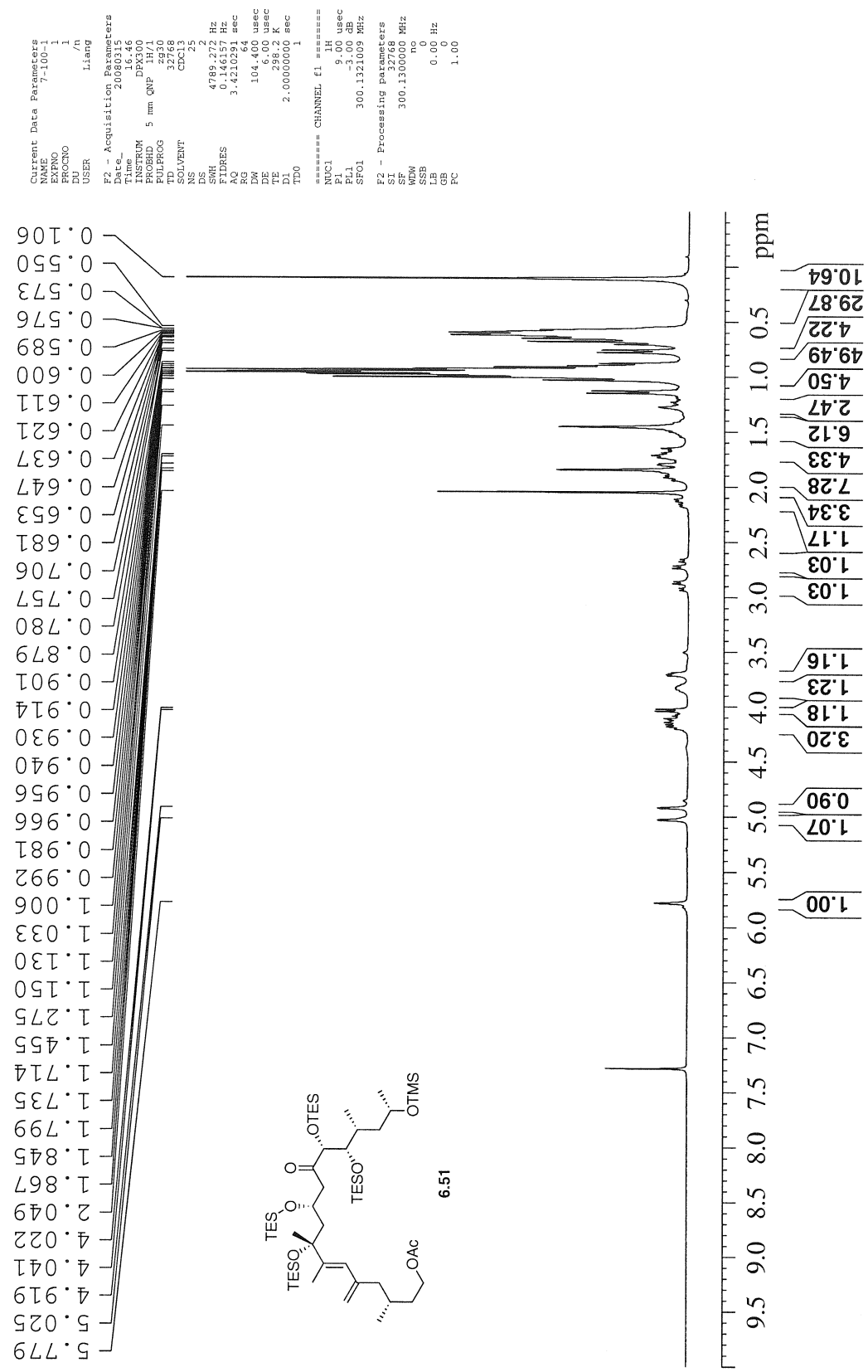
```
Current Data Parameters
NAME                  6-96
EXPNO                    3
PROCNO                   1
DU                      /n
USER                 Liang

F2 - Acquisition Parameter
Date_              20071019
Time                 11.38
INSTRUM             DPX300
PROBHD   5 mm QNP  1H/1
PULPROG            zgpg30
TD                  65536
SOLVENT             CDCl3
NS                    229
DS                      4
SWH             18832.393 Hz
FIDRES          0.287360 Hz
AQ              1.7400308 se
RG                 9195.2
DW                26.550 us
DE                 6.00 us
TE                298.2 K
D1             0.15000001 se
d11            0.03000000 se
DELTA          0.05000000 se
TD0                     1

======== CHANNEL f1 ======
NUC1                  13C
P1                 8.80 us
PL1               -3.00 dB
SFO1          75.4760505 MH

======== CHANNEL f2 ======
CPDPRG2           waltz16
NUC2                  1H
PCPD2             80.00 us
PL2               -3.00 dB
PL12              17.55 dB
PL13              17.55 dB
SFO2         300.1312005 MH

F2 - Processing parameters
SI                  32768
SF            75.4677490 MH
WDW                   EM
SSB                    0
LB                3.00 Hz
GB                     0
PC                 1.40
```

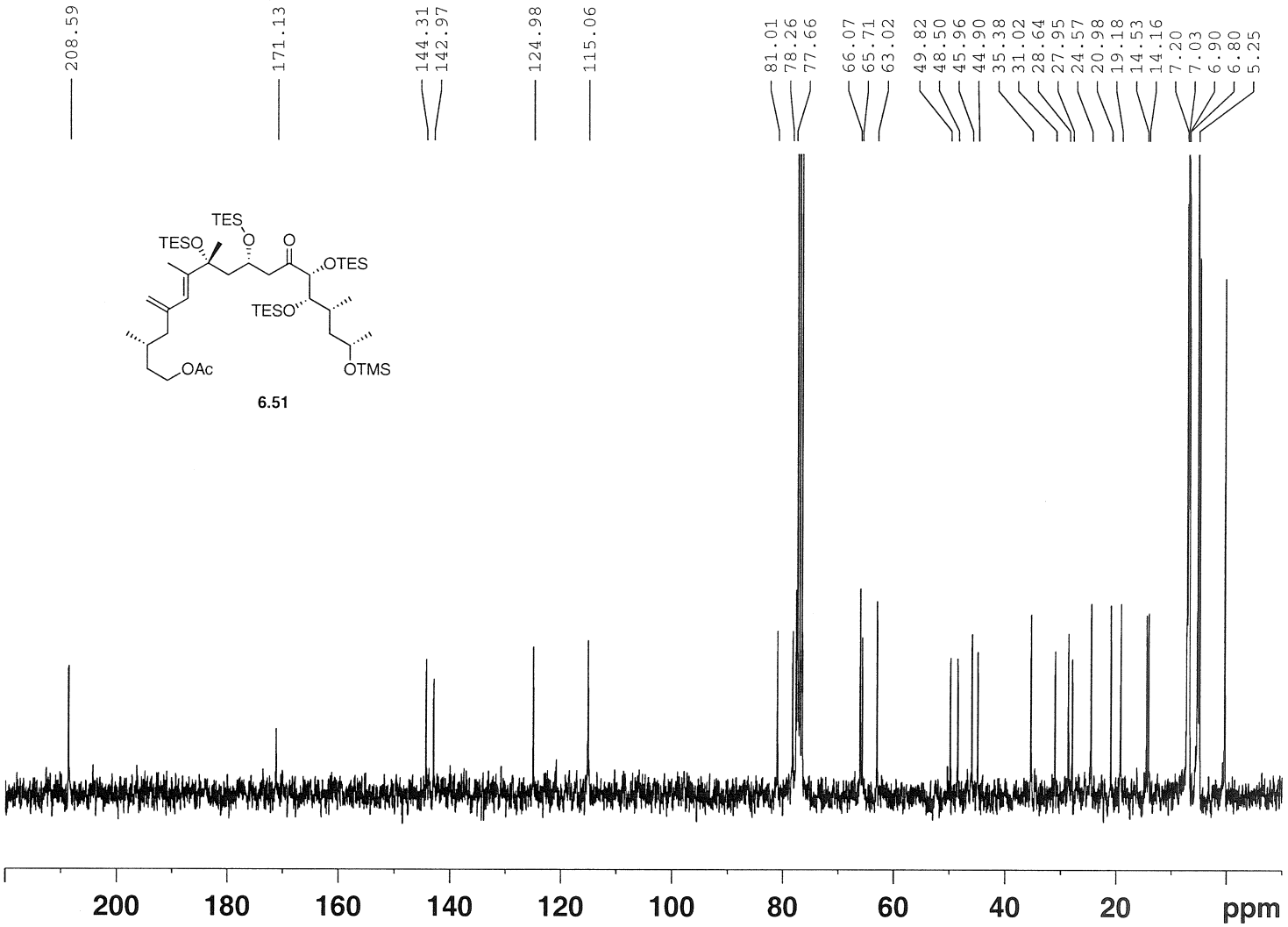

Current Data Parameters
NAME 6-98
EXPNO 1
PROCNO 1
DU /c
USER Liang
F2 - Acquisition Parameters
Date_ 20071021
Time 18.19
INSTRUM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 20
DS 2
SWH 4789.272 Hz
FIDRES 0.146157 Hz
AQ 3.4210291 sec
RG 101.6
DW 104.400 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.00 usec
PL1 -3.00 dB
SFO1 300.1321009 MHz
F2 - Processing parameters
SI 32768
SF 300.1300000 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
4.178
4.154
4.130
4.128
3.121
3.045
1.815
1.781
1.745
1.720
1.435
1.401
1.369
1.345
1.322
1.264
1.237
1.217
1.031
1.004
0.987
0.977
0.968
0.960
0.943
0.917
0.890
0.875
0.854
0.780
0.758
0.712
0.686
0.659
0.642
0.626
0.616
0.600
0.592
0.575
0.549
TES
TESO
OTES
TESO
P(OEt)2
HO
6.56
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
ppm
1.00
1.03
2.23
1.10
1.06
6.53
3.81
2.54
4.53
0.73
3.47
22.43
16.15
8.51
49.74
3.70
29.09



6.56

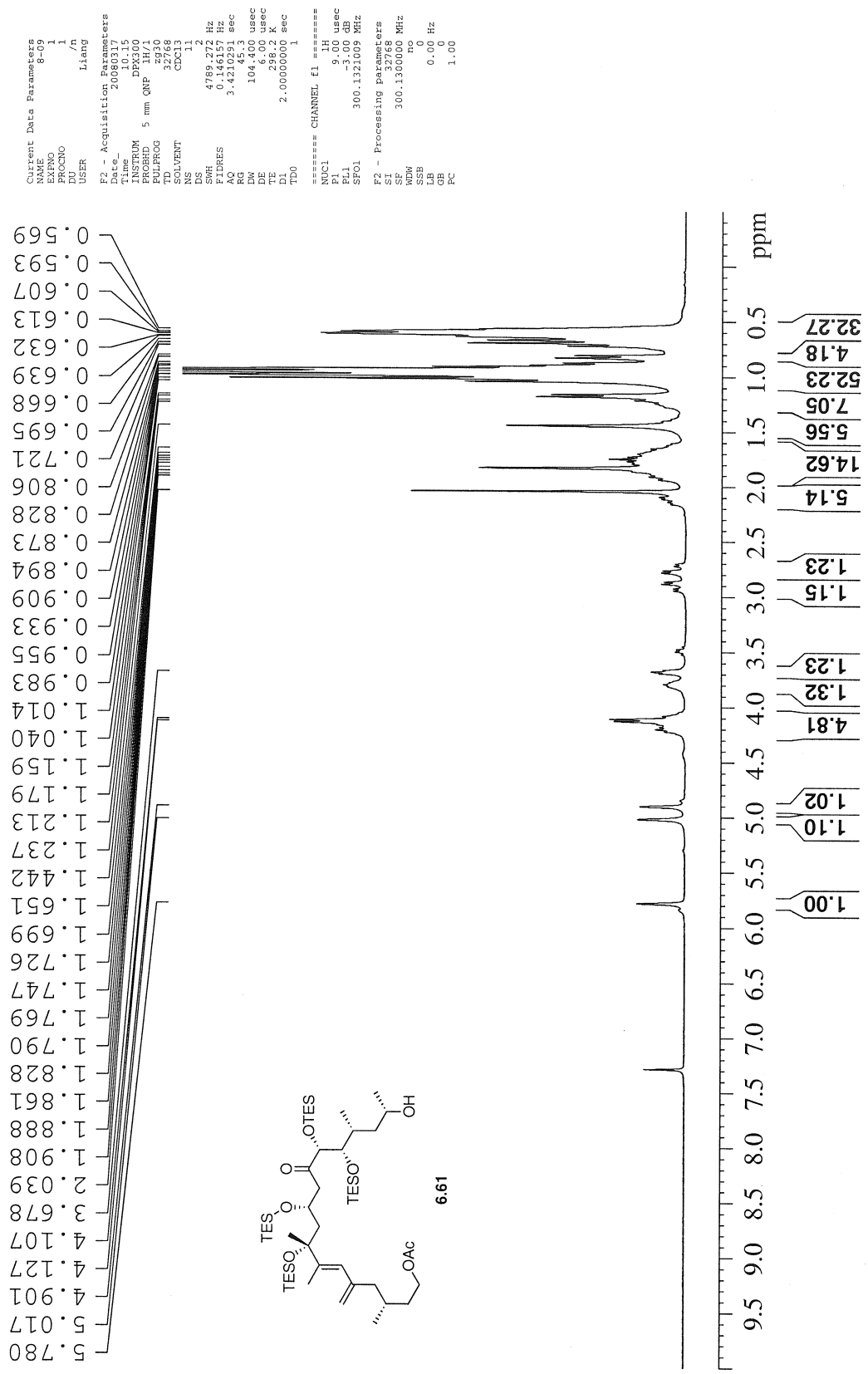
```
Current Data Parameters
NAME                  6-100
EXPNO                     3
PROCNO                    1
DU                       /n
USER                  Liang

F2 - Acquisition Parameter
Date_              20071022
Time                  16.47
INSTRUM             DPX400
PROBHD   5 mm BBO BB-1H
PULPROG             zgpg30
TD                   65536
SOLVENT              CDCl3
NS                    2172
DS                       4
SWH             25125.629 Hz
FIDRES              0.383387 Hz
AQ                1.3042164 se
RG                   4597.6
DW                  19.900 us
DE                   6.00 us
TE                   299.2 K
D1              0.15000001 se
d11             0.03000000 se
DELTA           0.05000000 se
TD0                       1

======== CHANNEL f1 ======
NUC1                    13C
P1                   7.80 us
PL1                 -3.00 dB
SFO1          100.5936591 MH

======== CHANNEL f2 ======
CPDPRG2            waltz16
NUC2                    1H
PCPD2              135.00 us
PL2                 17.40 dB
PL12                17.40 dB
PL13                17.40 dB
SFO2          400.0116000 MH

F2 - Processing parameters
SI                    32768
SF            100.5825950 MH
WDW                      EM
SSB                       0
LB                   3.00 Hz
GB                        0
PC                    1.40
```

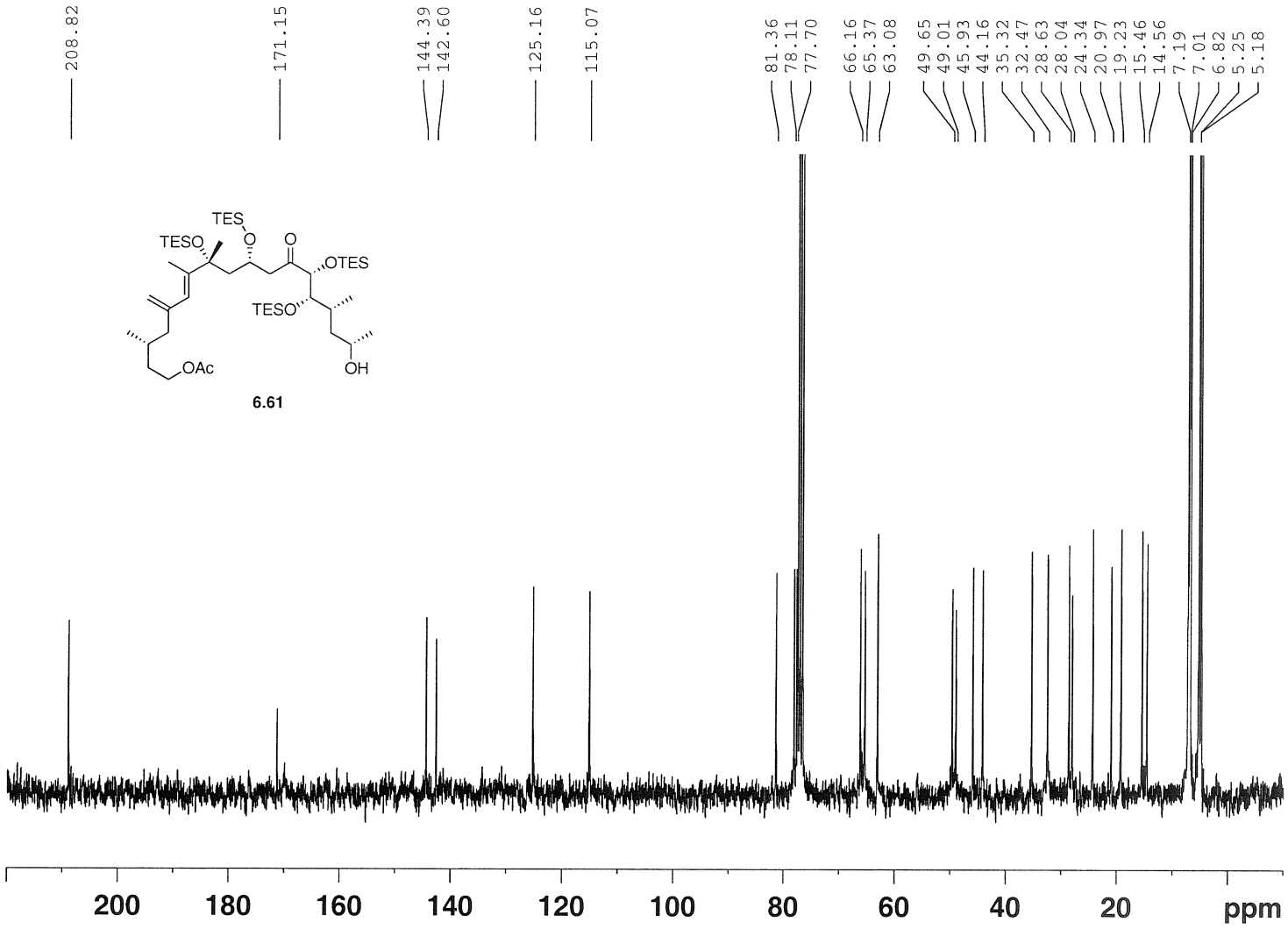

Current Data Parameters
NAME 7-100-1
EXPNO 1
PROCNO 1
DU /n
USER Liang
F2 - Acquisition Parameters
Date_ 20080315
Time 16.46
INSTRUM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG 2930
TD 22768
SOLVENT CDCl3
NS 25
DS 2
SWH 4789.272 Hz
FIDRES 0.146157 Hz
AQ 3.42102912 sec
RG 64
DW 104.400 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.00 usec
PL1 -3.00 dB
SFO1 300.1321009 MHz
F2 - Processing parameters
SI 32768
SF 300.1300000 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
TES
TESO
TESO
OTES
OTMS
OAc
6.51
ppm
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
1.00
1.07
0.90
3.20
1.18
1.23
1.16
1.03
1.03
1.17
3.34
7.28
4.33
6.12
2.47
4.50
49.49
4.22
29.87
10.64
5.779
5.025
4.919
4.041
4.022
2.049
1.867
1.845
1.799
1.735
1.714
1.455
1.275
1.150
1.130
1.033
1.006
0.992
0.981
0.966
0.956
0.940
0.930
0.914
0.901
0.879
0.780
0.757
0.706
0.681
0.653
0.647
0.637
0.621
0.611
0.600
0.589
0.576
0.573
0.550
0.106



6.51

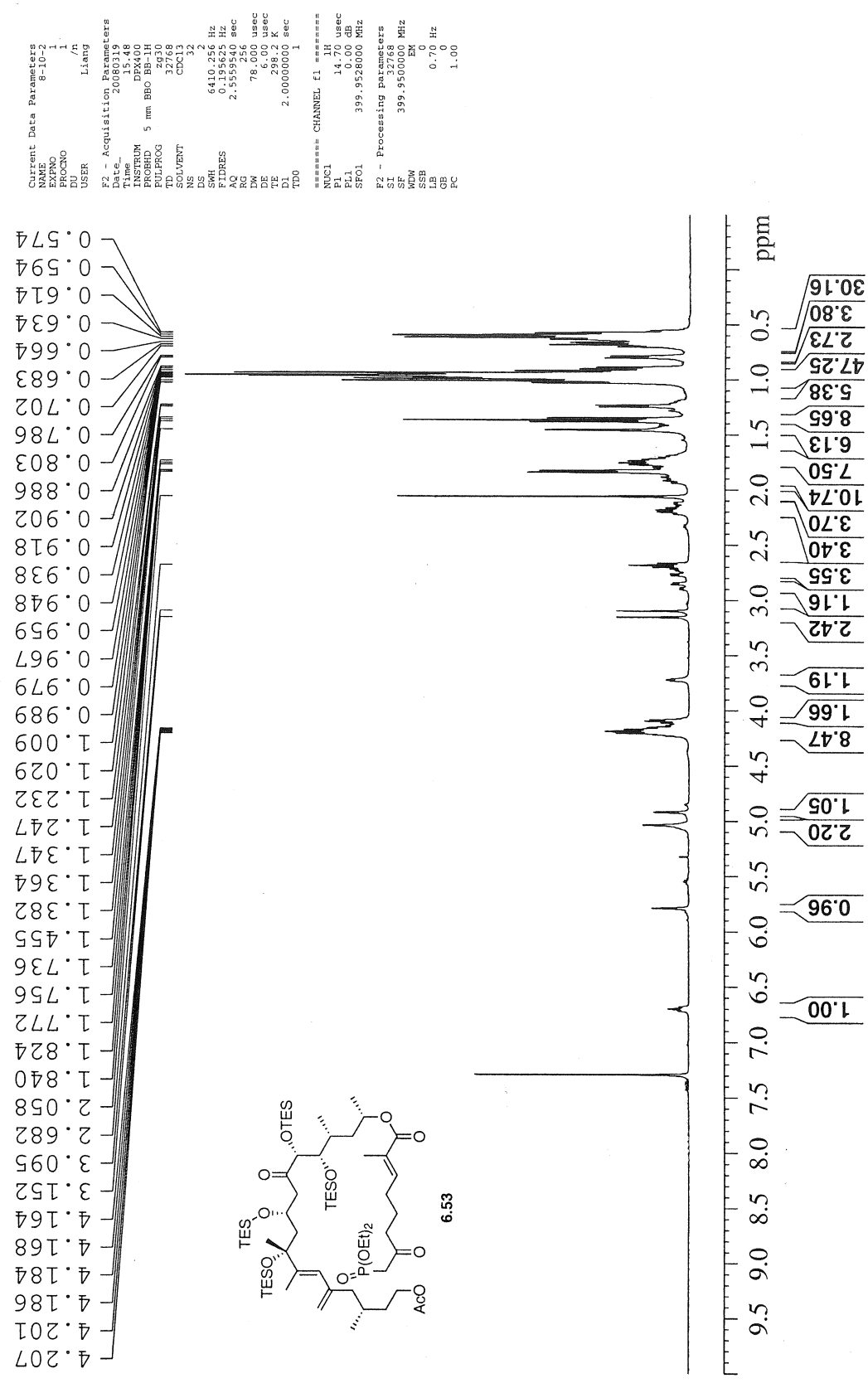
```
Current Data Parameters
NAME                  7-100-1
EXPNO                       3
PROCNO                      1
DU                         /n
USER                    Liang

F2 - Acquisition Parameter
Date_                20080315
Time                    17.04
INSTRUM                DPX300
PROBHD    5 mm QNP  1H/1
PULPROG                zgpg30
TD                      65536
SOLVENT                 CDCl3
NS                        533
DS                          4
SWH                 18832.393 Hz
FIDRES              0.287360 Hz
AQ                  1.7400308 se
RG                     9195.2
DW                    26.550 us
DE                     6.00 us
TE                    298.2 K
D1                0.15000001 se
d11               0.03000000 se
DELTA             0.05000000 se
TD0                         1

======== CHANNEL f1 ======
NUC1                      13C
P1                     8.80 us
PL1                   -3.00 dB
SFO1             75.4760505 MH

======== CHANNEL f2 ======
CPDPRG2              waltz16
NUC2                      1H
PCPD2                 80.00 us
PL2                   -3.00 dB
PL12                  17.55 dB
PL13                  17.55 dB
SFO2            300.1312005 MH

F2 - Processing parameters
SI                        32768
SF               75.4677490 MH
WDW                          EM
SSB                          0
LB                    3.00 Hz
GB                           0
PC                        1.40
```

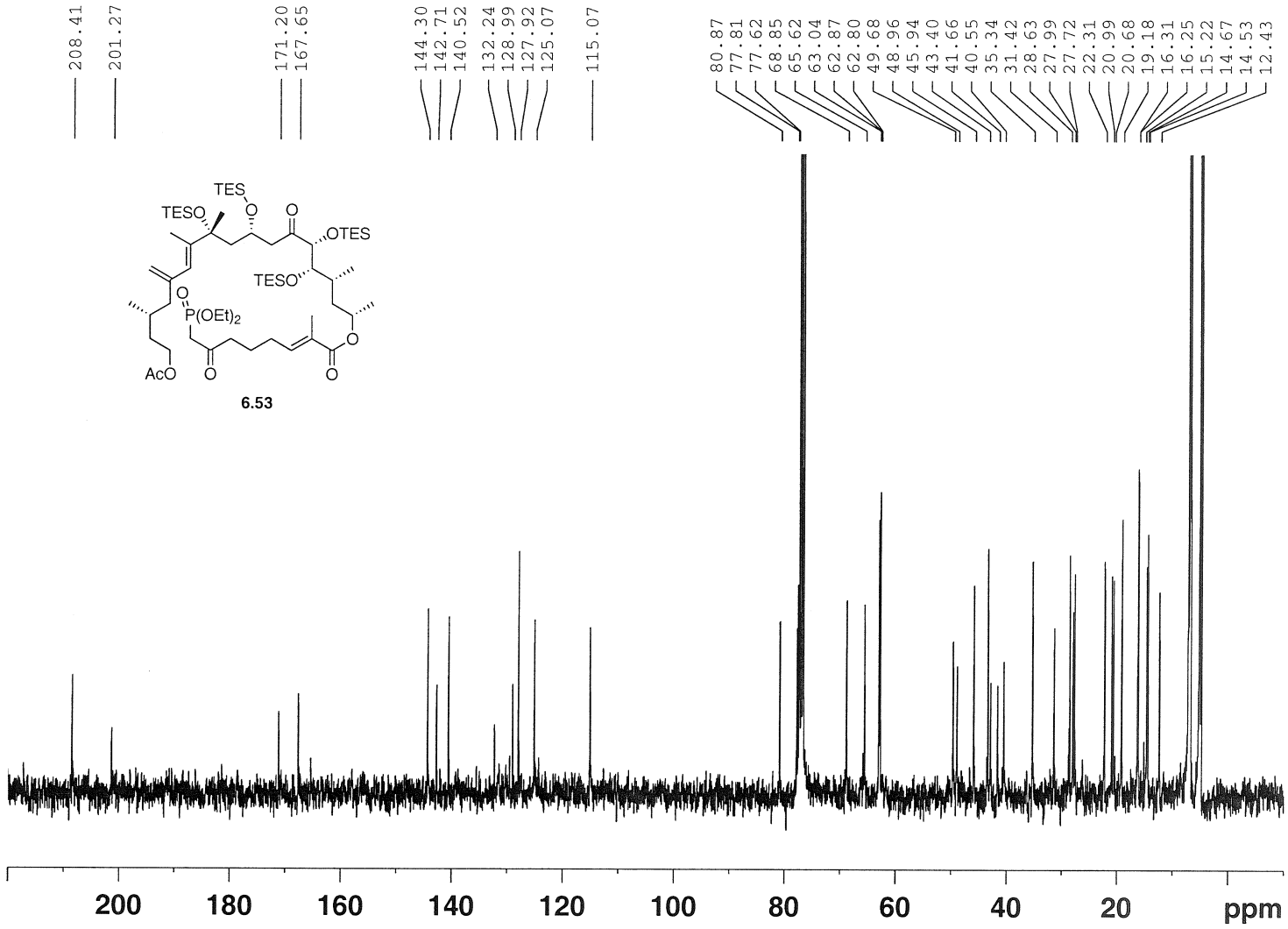

Current Data Parameters
NAME 8-09
EXPNO 1
PROCNO /n
USER Liang
F2 - Acquisition Parameters
Date_ 20080317
Time 10.15
INSTRUM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 11
DS 2
SWH 4789.272 Hz
FIDRES 0.146157 Hz
AQ 3.42102911 sec
RG 45.3
DW 104.400 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.00 usec
PL1 -3.00 dB
SFO1 300.1321009 MHz
F2 - Processing parameters
SI 32768
SF 300.1300000 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
TES
TESO
TESO
OTES
O
O
OAc
OH
6.61
ppm
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
1.00
1.10
1.02
4.81
1.32
1.23
1.15
1.23
5.14
14.62
5.56
7.05
52.23
4.18
32.27
5.780
5.017
4.901
4.127
4.107
3.678
2.039
1.908
1.888
1.861
1.828
1.790
1.769
1.747
1.726
1.699
1.651
1.442
1.237
1.213
1.179
1.159
1.040
1.014
0.983
0.955
0.933
0.909
0.894
0.873
0.828
0.806
0.721
0.695
0.668
0.639
0.632
0.613
0.607
0.593
0.569



6.61

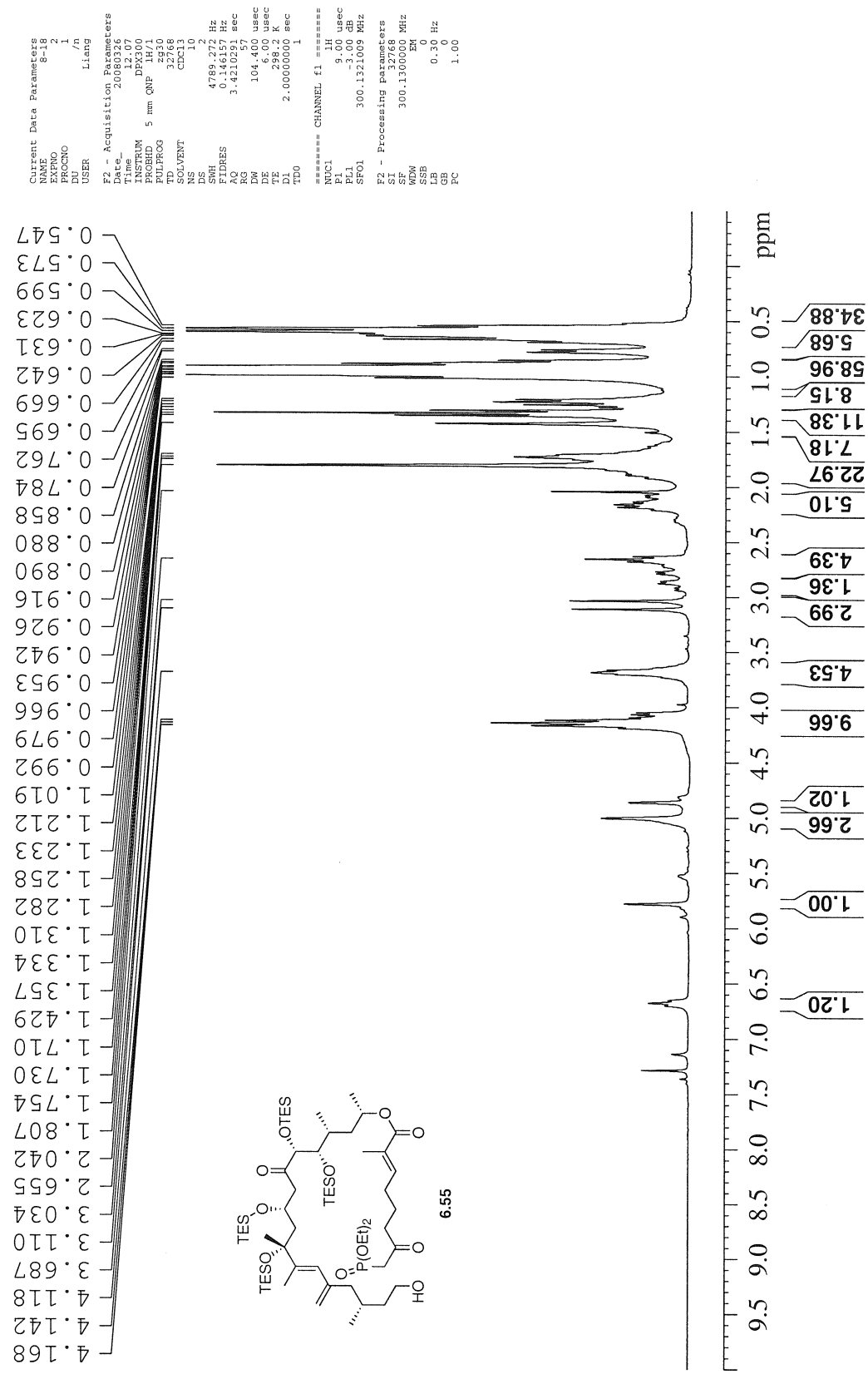
```
Current Data Parameters
NAME                  8-09
EXPNO                    3
PROCNO                   1
DU                      /n
USER                 Liang

F2 - Acquisition Parameter
Date_              20080317
Time                 10.58
INSTRUM             DPX300
PROBHD   5 mm QNP  1H/1
PULPROG            zgpg30
TD                  65536
SOLVENT             CDCl3
NS                    423
DS                      4
SWH             18832.393 Hz
FIDRES          0.287360 Hz
AQ              1.7400308 se
RG                 9195.2
DW                26.550 us
DE                 6.00 us
TE                298.2 K
D1           0.15000001 se
d11          0.03000000 se
DELTA        0.05000000 se
TD0                     1

======== CHANNEL f1 ======
NUC1                  13C
P1                 8.80 us
PL1               -3.00 dB
SFO1         75.4760505 MH

======== CHANNEL f2 ======
CPDPRG2          waltz16
NUC2                  1H
PCPD2             80.00 us
PL2               -3.00 dB
PL12              17.55 dB
PL13              17.55 dB
SFO2        300.1312005 MH

F2 - Processing parameters
SI                 32768
SF          75.4677490 MH
WDW                  EM
SSB                   0
LB                 3.00 Hz
GB                    0
PC                 1.40
```

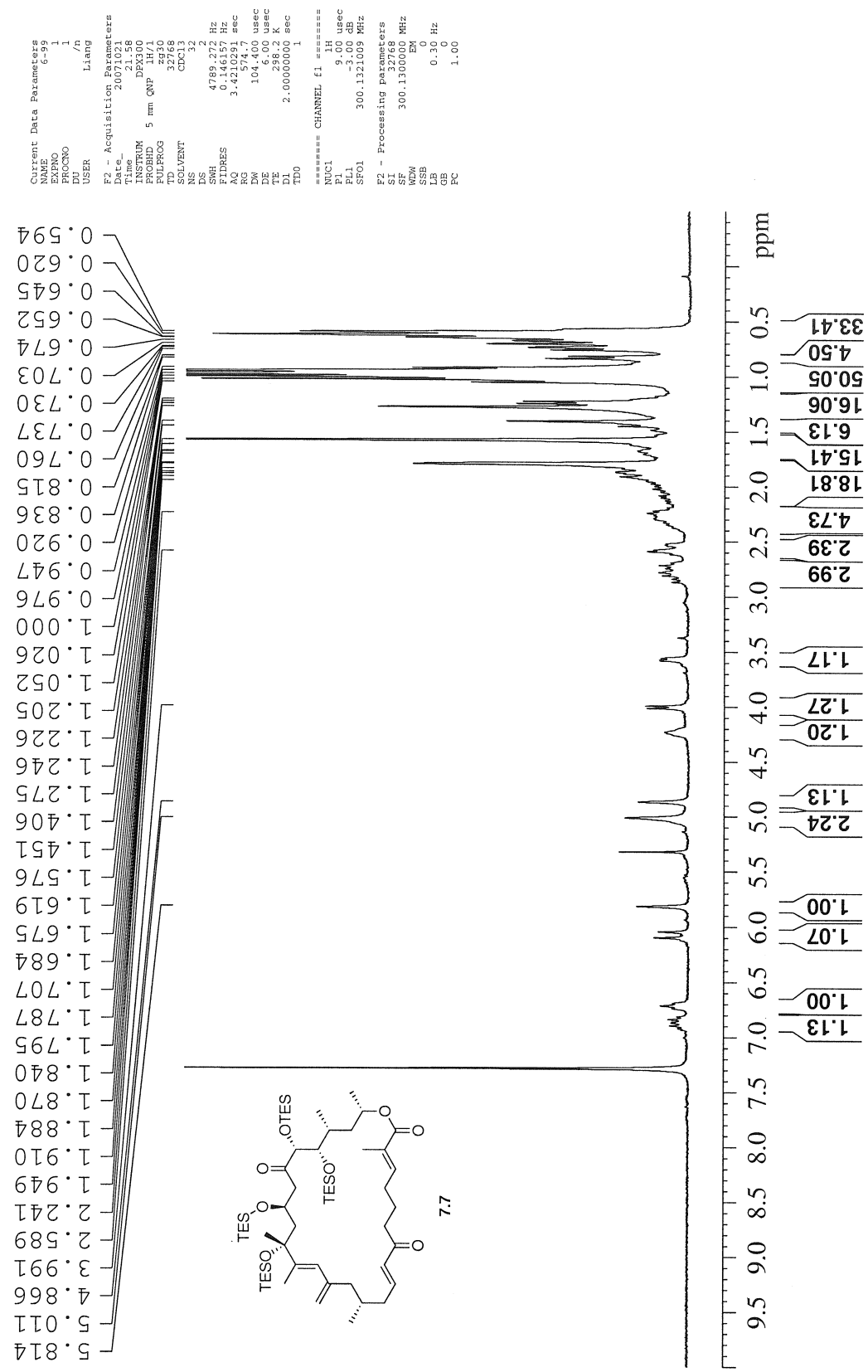

Current Data Parameters
NAME 8-10-2
EXPNO 1
PROCNO 1
DU /n
USER Liang
F2 - Acquisition Parameters
Date_ 20080319
Time 15.48
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.55559540 sec
RG 256
DW 78.000 usec
DE 6.00 usec
TE 298.1 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.70 usec
PL1 0.00 dB
SFO1 399.9528000 MHz
F2 - Processing parameters
SI 32768
SF 399.9500000 MHz
WDW EM
SSB 0
LB 0.70 Hz
GB 0
PC 1.00
TES
TESO
OTES
TESO
P(OEt)2
AcO
6.53
4.207
4.201
4.186
4.184
4.168
4.164
4.152
3.095
2.682
2.058
1.840
1.824
1.772
1.756
1.736
1.455
1.382
1.364
1.347
1.247
1.232
1.029
1.009
0.989
0.979
0.967
0.959
0.948
0.938
0.918
0.902
0.886
0.803
0.786
0.702
0.683
0.664
0.634
0.614
0.594
0.574
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
1.00
0.96
2.20
1.05
8.47
1.66
1.19
2.42
1.16
3.55
3.40
3.70
10.74
7.50
6.13
8.65
5.38
47.25
2.73
3.80
30.16

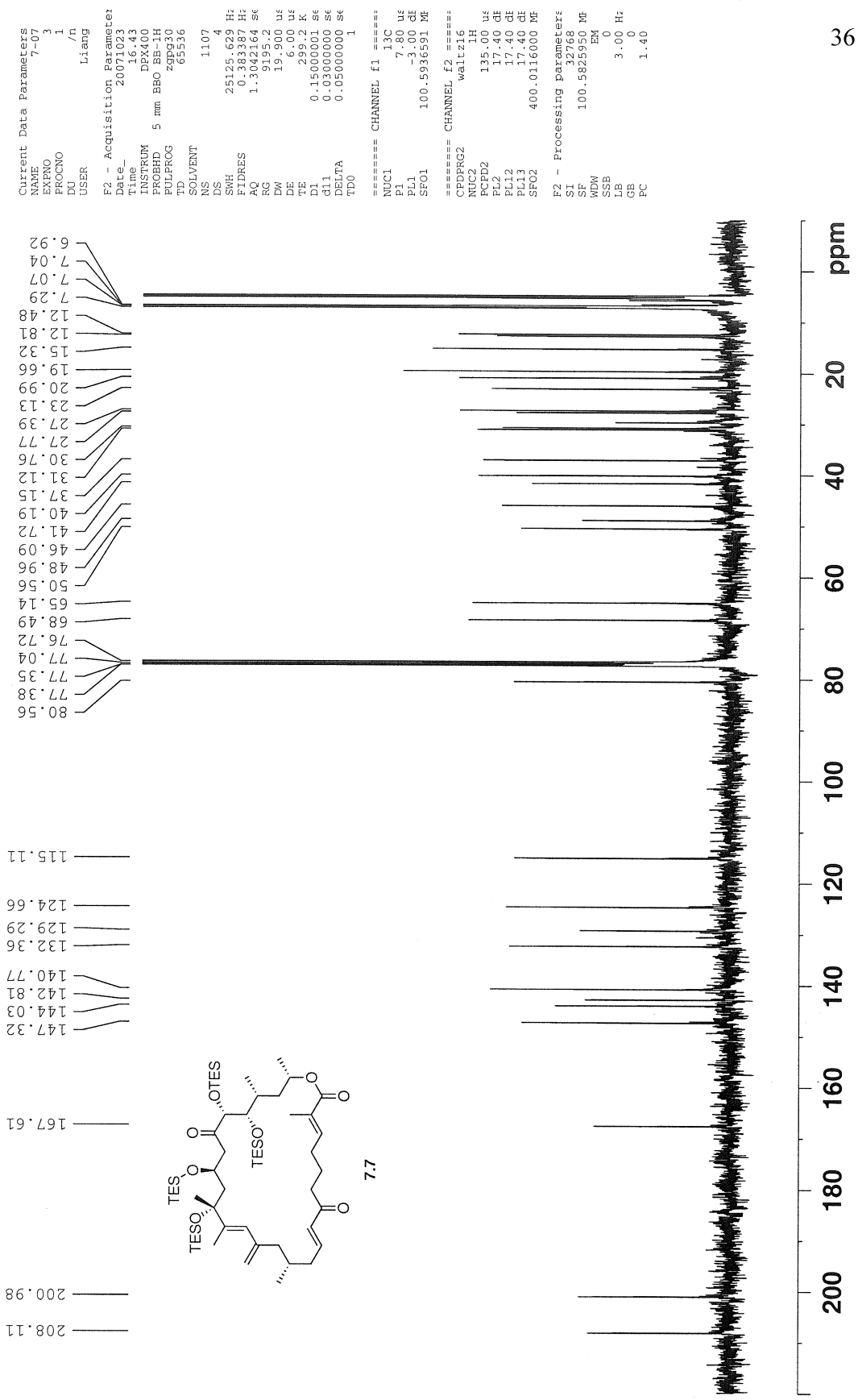


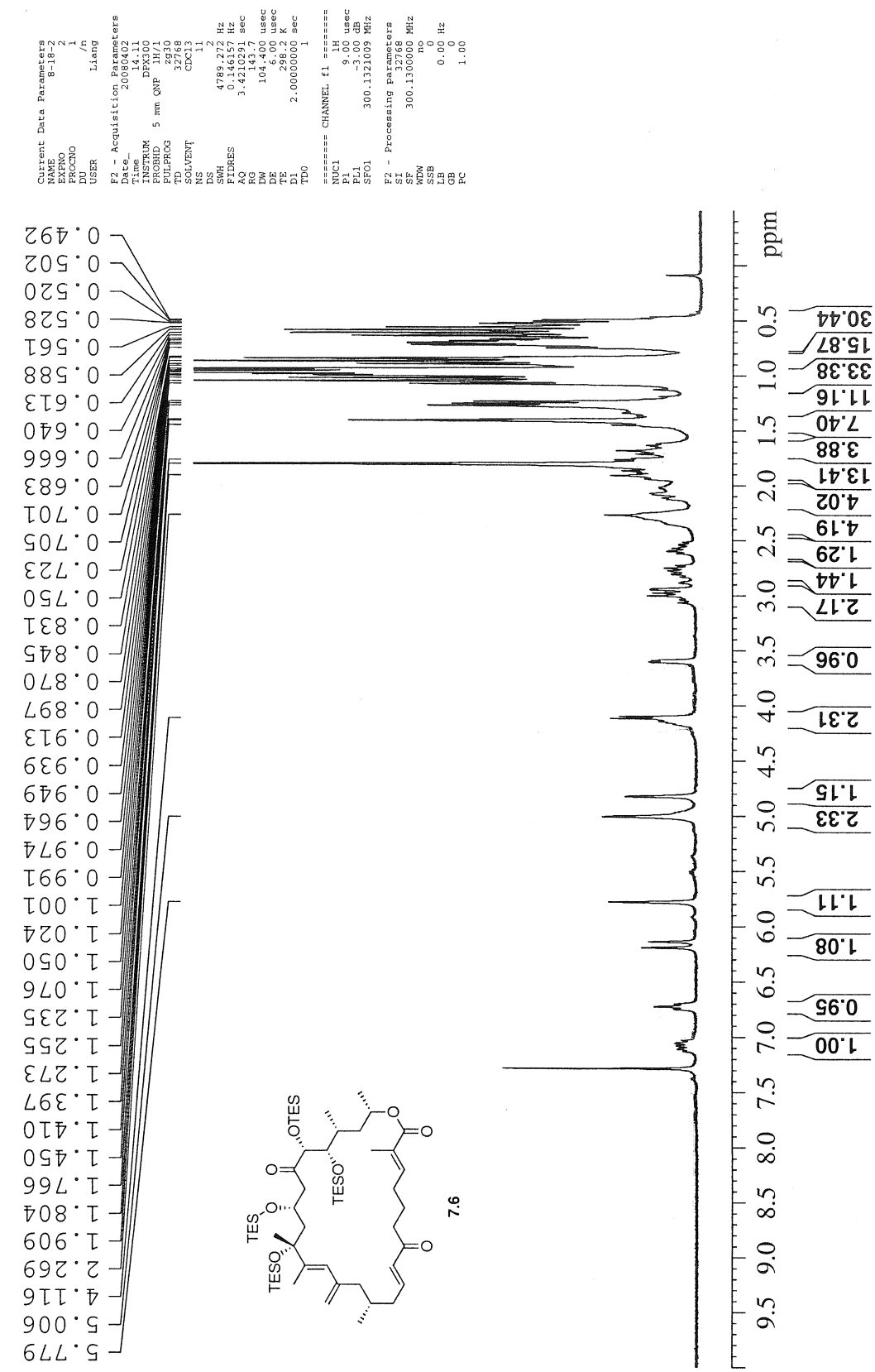
6.53

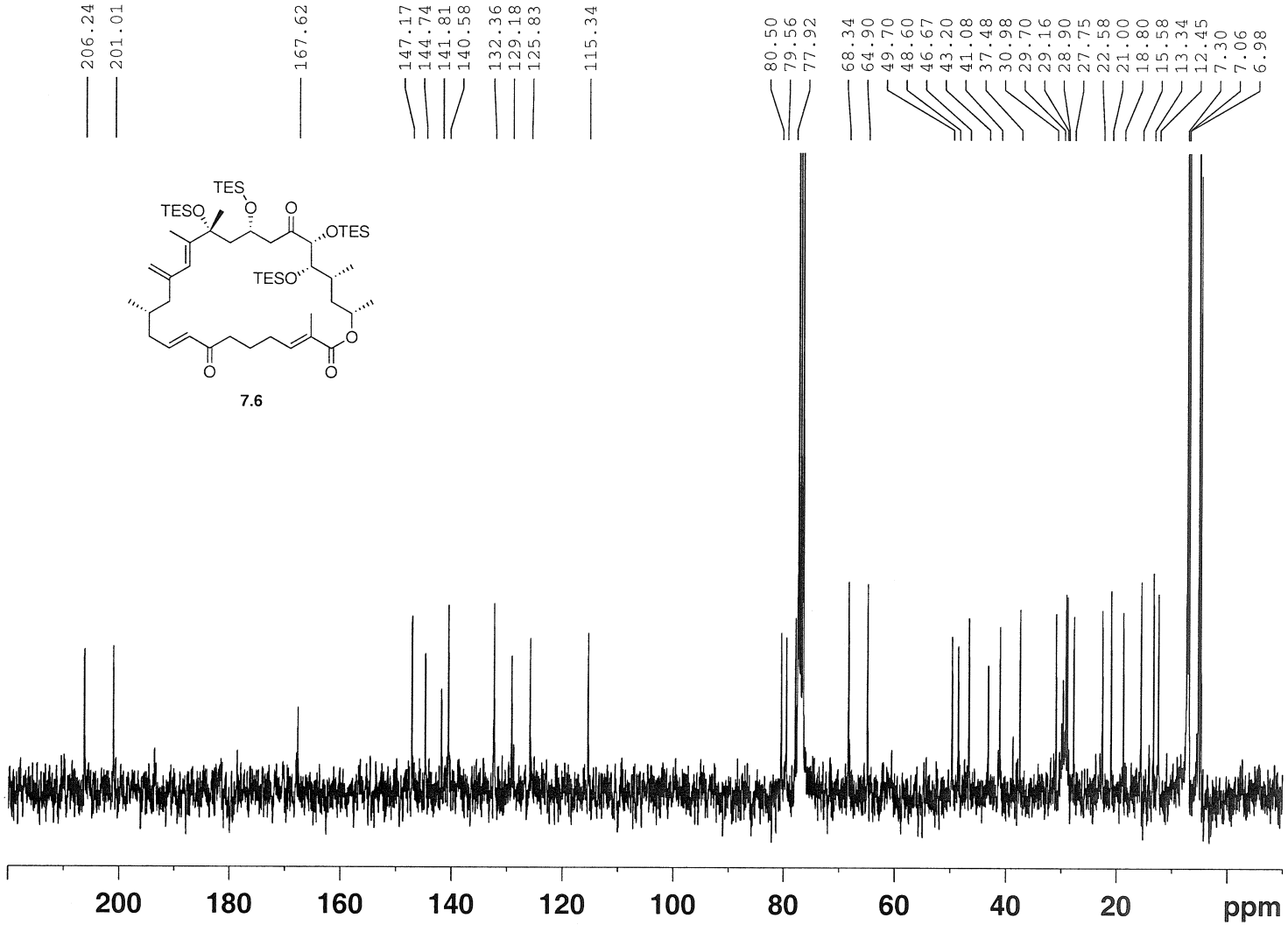
```
Current Data Parameters
NAME                  8-10-2
EXPNO                      4
PROCNO                     1
DU                        /n
USER                  Liang

F2 - Acquisition Parameter
Date_              20080319
Time                  18.56
INSTRUM             DPX400
PROBHD   5 mm BBO BB-1H
PULPROG             zgpg30
TD                    65536
SOLVENT
NS                      710
DS                        4
SWH             25125.629 Hz
FIDRES          0.383387 Hz
AQ              1.3042164 se
RG                    16384
DW                 19.900 us
DE                  6.00 us
TE                  298.2 K
D1             0.15000001 se
D11            0.03000000 se
DELTA          0.05000000 se
TD0                       1

======== CHANNEL f1 ======
NUC1                   13C
P1                  7.80 us
PL1                -3.00 dB
SFO1         100.5785700 MH

======== CHANNEL f2 ======
CPDPRG2           waltz16
NUC2                   1H
PCPD2             135.00 us
PL2                17.40 dB
PL12               17.40 dB
PL13               17.40 dB
SFO2         399.9516000 MH

F2 - Processing parameters
SI                    32768
SF           100.5675080 MH
WDW                     EM
SSB                      0
LB                 3.00 Hz
GB                       0
PC                    1.40
```


Current Data Parameters
NAME 8-18
EXPNO 2
PROCNO 1
DU /n
USER Liang
F2 - Acquisition Parameters
Date_ 20080326
Time 12.07
INSTRUM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 10
DS 2
SWH 4789.272 Hz
FIDRES 0.146157 Hz
AQ 3.42102991 sec
RG 57
DW 104.400 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.00 usec
PL1 -3.00 dB
SFO1 300.1321009 MHz
F2 - Processing parameters
SI 32768
SF 300.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
4.168
4.142
4.118
3.687
3.110
3.034
2.655
2.042
1.807
1.754
1.730
1.710
1.429
1.357
1.334
1.310
1.282
1.258
1.233
1.212
1.019
0.992
0.979
0.966
0.953
0.942
0.926
0.916
0.890
0.880
0.858
0.784
0.762
0.695
0.669
0.642
0.631
0.623
0.599
0.573
0.547
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
1.20
1.00
2.66
1.02
9.66
4.53
2.99
1.36
4.39
5.10
22.97
7.18
11.38
8.15
58.96
5.68
34.88
TES
TESO
OTES
TESO
O
O
O
O
P(OEt)2
O
HO
6.55


Current Data Parameters
NAME 6-99
EXPNO 1
PROCNO /n
DU Liang
F2 - Acquisition Parameters
Date_ 20071021
Time 21.58
INSTRUM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 4789.272 Hz
FIDRES 0.146157 Hz
AQ 3.42110291 sec
RG 574.7
DW 104.400 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.00 usec
PL1 -3.00 dB
SFO1 300.1321009 MHz
F2 - Processing parameters
SI 32768
SF 300.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
TES
TESO
OTES
TESO
7.7
ppm
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
1.13
1.00
1.00
1.07
2.24
1.13
1.20
1.27
1.17
2.99
2.39
4.73
18.81
15.41
6.13
16.06
50.05
4.50
33.41
5.814
5.011
4.866
3.991
2.589
2.241
1.949
1.910
1.884
1.870
1.840
1.795
1.787
1.707
1.684
1.675
1.619
1.576
1.451
1.406
1.275
1.246
1.226
1.205
1.052
1.026
1.000
0.976
0.947
0.920
0.836
0.815
0.760
0.737
0.730
0.703
0.674
0.652
0.645
0.620
0.594

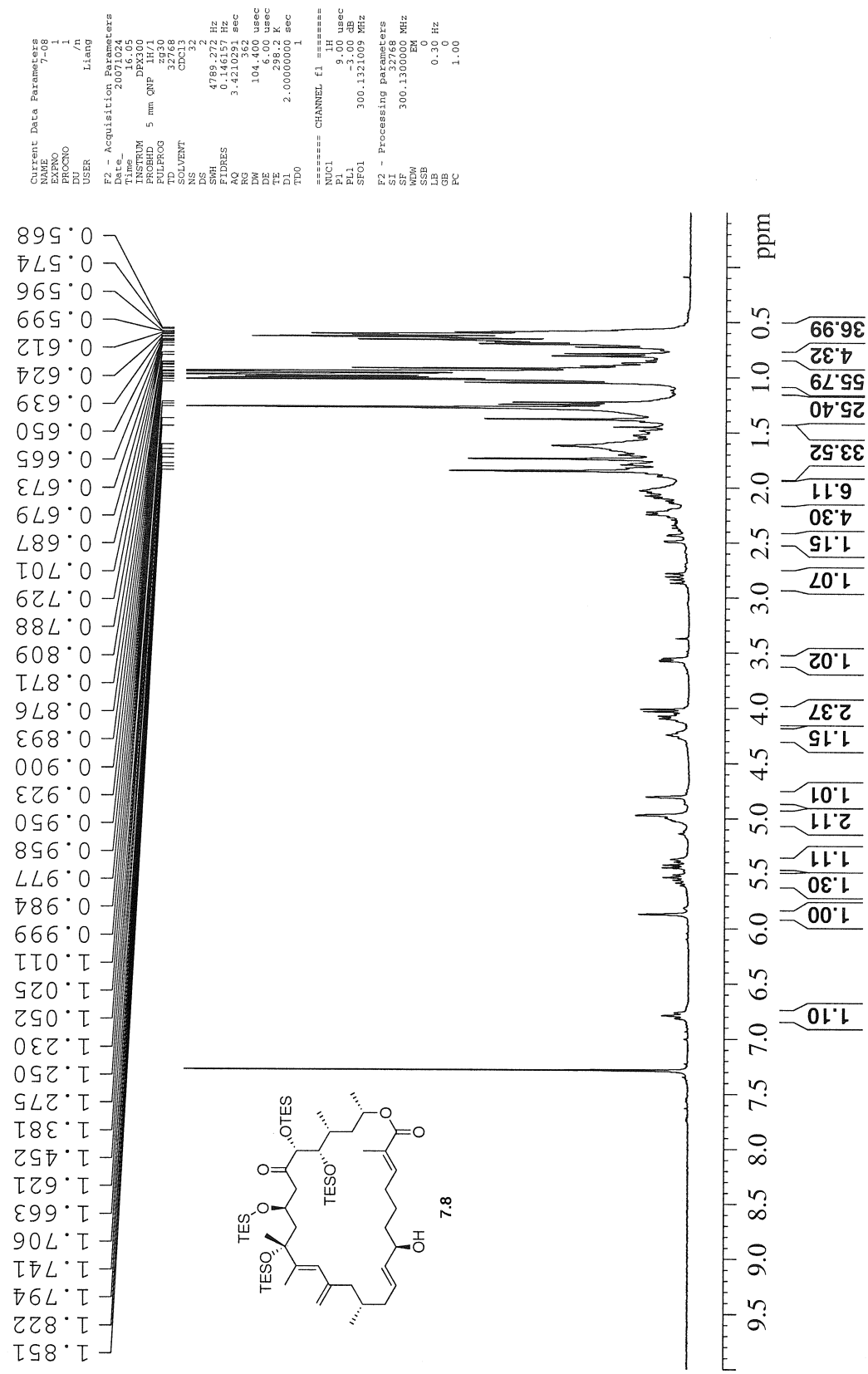

Current Data Parameters
NAME 7-07
EXPNO 3
PROCNO 1
DU /n
USER Liang
F2 - Acquisition Parameter
Date_ 20071023
Time 16.43
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT
NS 1107
DS 4
SWH 25125.629 Hz
FIDRES 0.383387 Hz
AQ 1.3042164 se
RG 9195.2
DW 19.900 us
DE 6.00 us
TE 299.2 K
D1 0.15000001 se
d11 0.03000000 se
DELTA 0.05000000 se
TD0 1
======== CHANNEL f1 ======
NUC1 13C
P1 7.80 us
PL1 -3.00 dB
SFO1 100.5936591 MH
======== CHANNEL f2 ======
CPDPRG2 waltz16
NUC2 1H
PCPD2 135.00 us
PL2 17.40 dB
PL12 17.40 dB
PL13 17.40 dB
SFO2 400.0116000 MH
F2 - Processing parameters
SI 32768
SF 100.5825950 MH
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
6.92
7.04
7.07
7.29
12.48
12.81
15.32
19.66
20.99
23.13
27.39
27.77
30.76
31.12
37.15
40.19
41.72
46.09
48.96
50.56
65.14
68.49
76.72
77.04
77.35
77.38
80.56
115.11
124.66
129.29
132.36
140.77
142.81
144.03
147.32
167.61
200.98
208.11
OTES
TESO
TES
O
TESO
7.7
ppm
200
180
160
140
120
100
80
60
40
20

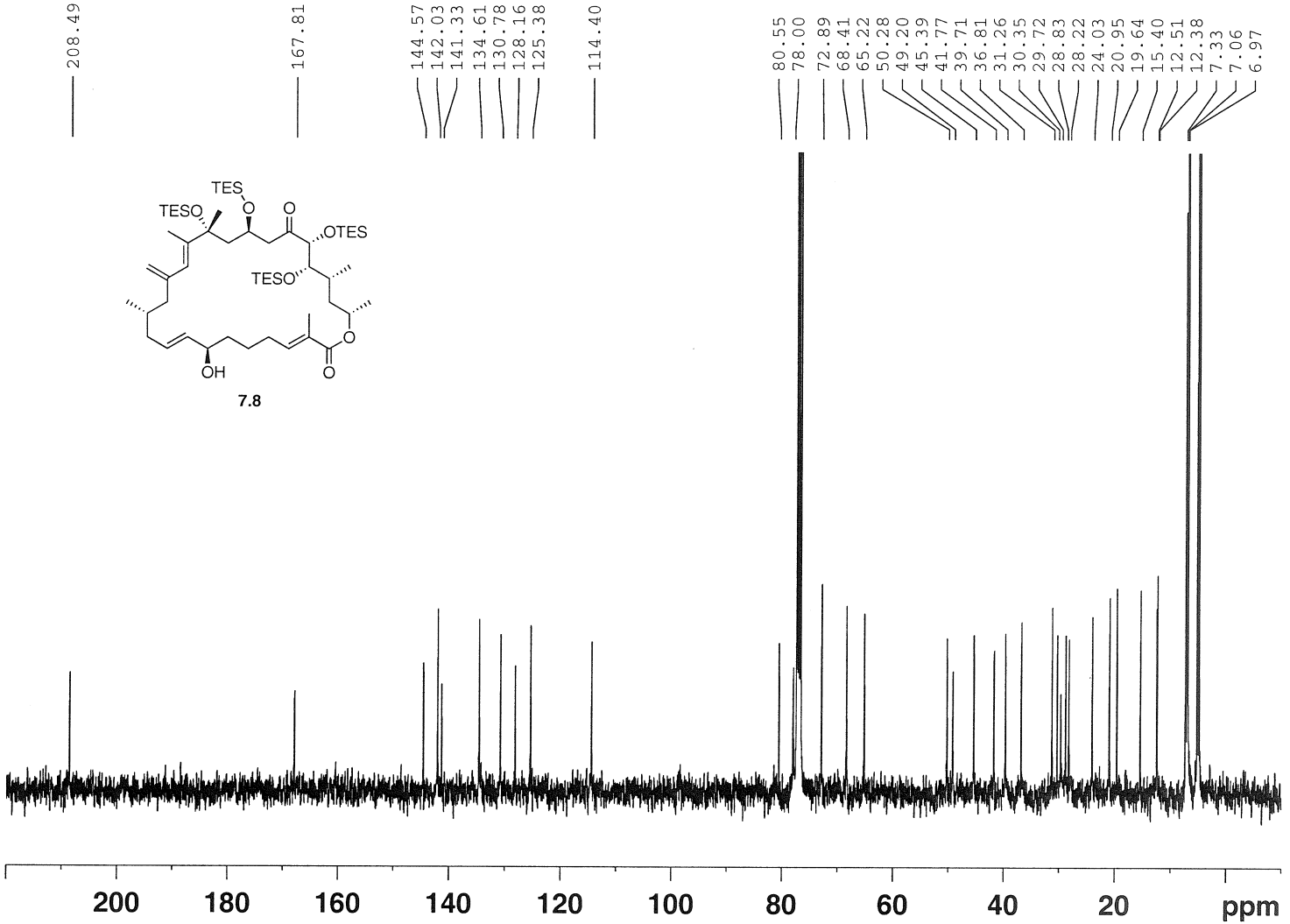

Current Data Parameters
NAME 8-18-2
EXPNO 1
PROCNO 1
DU /n
USER Liang
F2 - Acquisition Parameters
Date_ 20080402
Time 14.11
INSTRUM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 11
DS 2
SWH 4789.272 Hz
FIDRES 0.146157 Hz
AQ 3.4210291 sec
RG 143.7
DW 104.400 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.00 usec
PL1 -3.00 dB
SFO1 300.1321009 MHz
F2 - Processing parameters
SI 32768
SF 300.1300000 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
5.779
5.006
4.116
2.269
1.909
1.804
1.766
1.450
1.410
1.397
1.273
1.255
1.235
1.076
1.050
1.024
1.001
0.991
0.974
0.964
0.949
0.939
0.913
0.897
0.870
0.845
0.831
0.750
0.723
0.705
0.701
0.683
0.666
0.640
0.613
0.588
0.561
0.528
0.520
0.502
0.492
TES
TESO
TESO
OTES
7.6
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
ppm
1.00
0.95
1.08
1.11
2.33
1.15
2.31
0.96
2.17
1.44
1.29
4.19
4.02
13.41
3.88
7.40
11.16
33.38
15.87
30.44



7.6

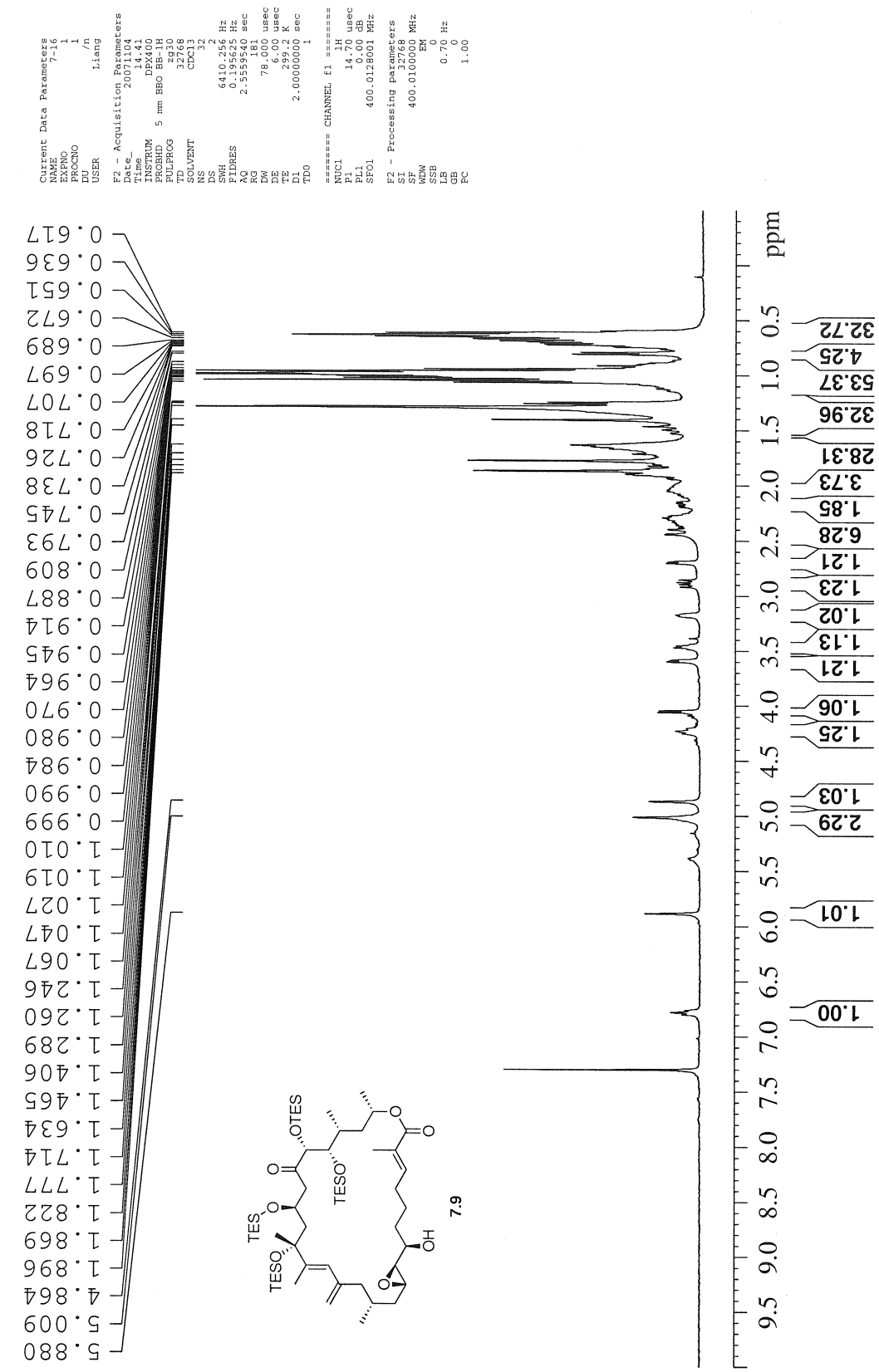
```
Current Data Parameters
NAME                  8-18-2
EXPNO                      5
PROCNO                     1
DU                        /n
USER                   Liang

F2 - Acquisition Parameter
Date_              20080402
Time                  14.59
INSTRUM              DPX300
PROBHD    5 mm QNP  1H/1
PULPROG              zgpg30
TD                    65536
SOLVENT               CDCl3
NS                      556
DS                        4
SWH               18832.393 Hz
FIDRES            0.287360 Hz
AQ                1.7400308 se
RG                     1024
DW                   26.550 us
DE                    6.00 us
TE                   298.2 K
D1              0.15000001 se
d11             0.03000000 se
DELTA           0.05000000 se
TD0                       1

======== CHANNEL f1 ======
NUC1                    13C
P1                     8.80 us
PL1                   -3.00 dB
SFO1           75.4760505 MH

======== CHANNEL f2 ======
CPDPRG2             waltz16
NUC2                    1H
PCPD2                80.00 us
PL2                  -3.00 dB
PL12                 17.55 dB
PL13                 17.55 dB
SFO2          300.1312005 MH

F2 - Processing parameters
SI                     32768
SF            75.4677490 MH
WDW                       EM
SSB                        0
LB                    3.00 Hz
GB                         0
PC                     1.40
```

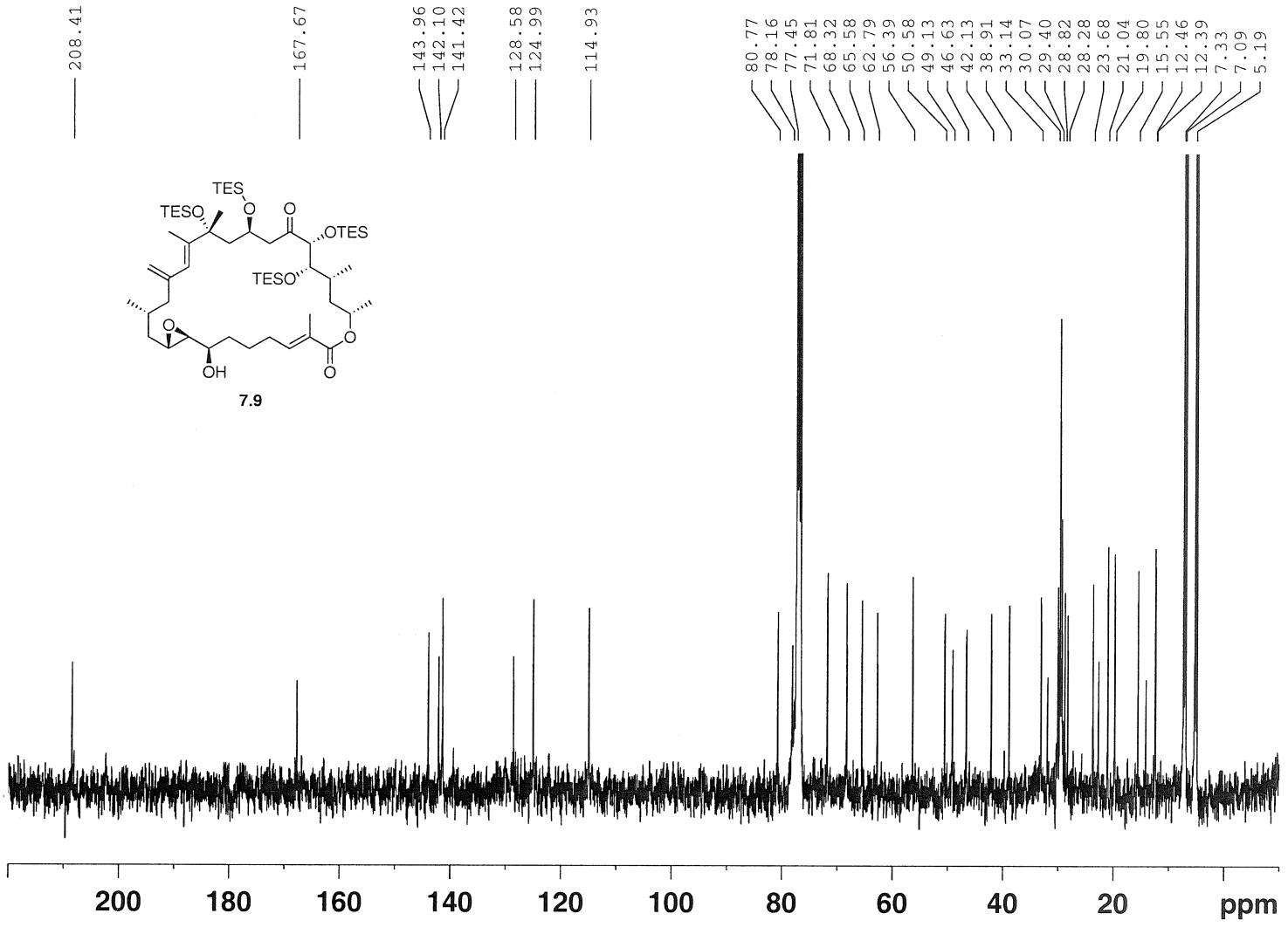

Current Data Parameters
NAME 7-08
EXPNO 1
PROCNO /n
DU Liang
F2 - Acquisition Parameters
Date_ 20071024
Time 16.05
INSTRUM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 4789.272 Hz
FIDRES 0.146157 Hz
AQ 3.42210291 sec
RG 362
DW 104.400 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.00 usec
PL1 -3.00 dB
SFO1 300.1321009 MHz
F2 - Processing parameters
SI 32768
SF 300.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
TES
TESO
TESO
OTES
OH
7.8
ppm
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
1.10
1.00
1.30
1.11
2.11
1.01
1.15
2.37
1.02
1.07
1.15
4.30
6.11
33.52
25.40
55.79
4.32
36.99
1.851 1.822 1.794 1.741 1.706 1.663 1.621 1.452 1.381 1.275 1.250 1.230 1.052 1.025 1.011 0.999 0.984 0.977 0.958 0.950 0.923 0.900 0.893 0.876 0.871 0.809 0.788 0.729 0.701 0.687 0.679 0.673 0.665 0.650 0.639 0.624 0.612 0.599 0.596 0.574 0.568



7.8

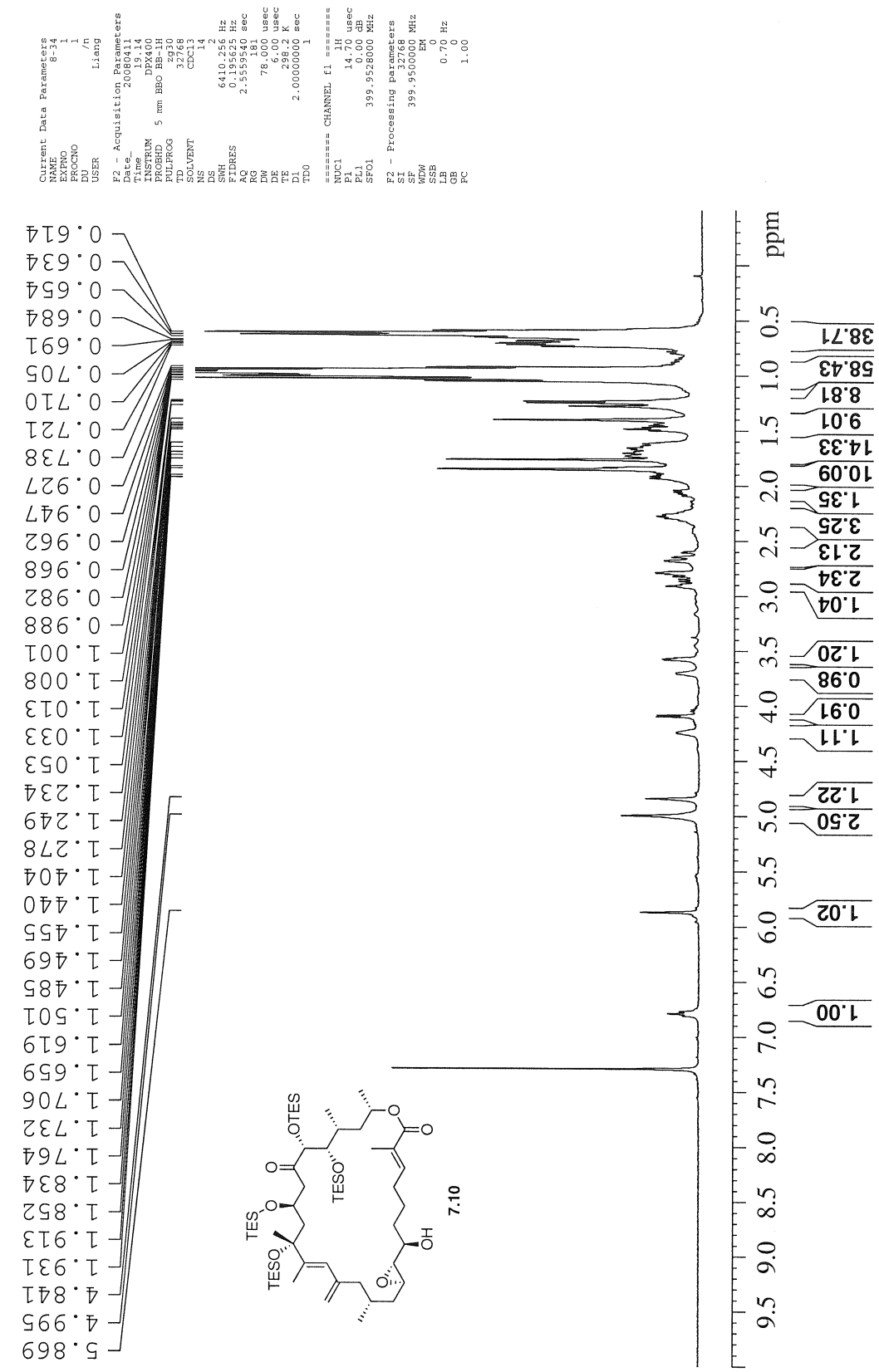
```
Current Data Parameters
NAME                  7-11
EXPNO                    3
PROCNO                   1
DU                      /n
USER                 Liang

F2 - Acquisition Parameter
Date_             20071028
Time                19.33
INSTRUM            DPX400
PROBHD   5 mm BBO BB-1H
PULPROG            zgpg30
TD                  65536
SOLVENT
NS                   1151
DS                      4
SWH             25125.629 Hz
FIDRES          0.383387 Hz
AQ              1.3042164 se
RG                 5792.6
DW                19.900 us
DE                 6.00 us
TE                299.2 K
D1           0.15000001 se
d11          0.03000000 se
DELTA        0.05000000 se
TD0                     1

======== CHANNEL f1 ======
NUC1                  13C
P1                 7.80 us
PL1               -3.00 dB
SFO1        100.5936591 MH

======== CHANNEL f2 ======
CPDPRG2          waltz16
NUC2                  1H
PCPD2            135.00 us
PL2               17.40 dB
PL12              17.40 dB
PL13              17.40 dB
SFO2        400.0116000 MH

F2 - Processing parameters
SI                  32768
SF          100.5825950 MH
WDW                   EM
SSB                    0
LB                3.00 Hz
GB                     0
PC                 1.40
```

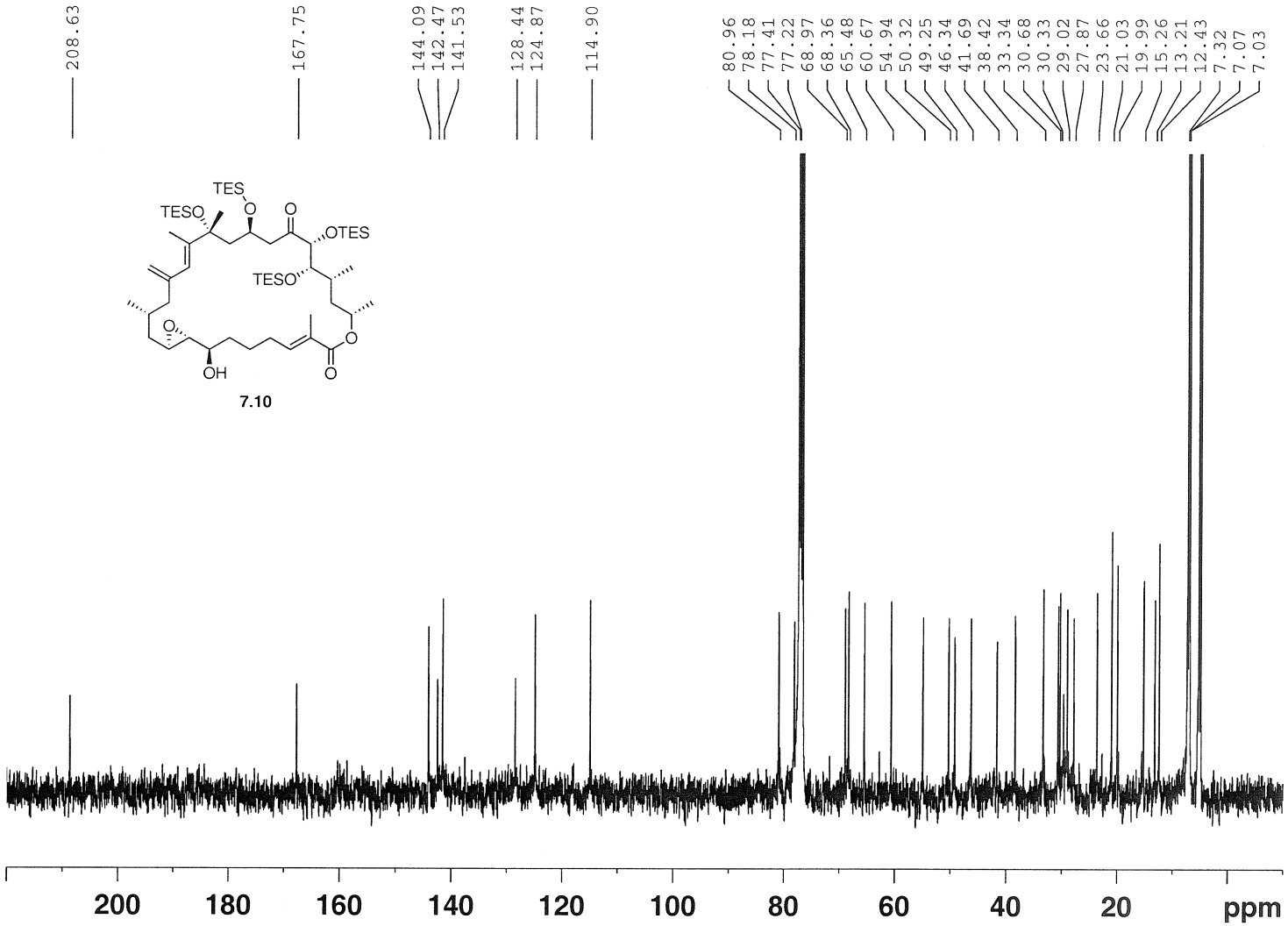

Current Data Parameters
NAME 7-16
EXPNO 1
PROCNO 1
DU /n
USER Liang
F2 - Acquisition Parameters
Date_ 20071104
Time 14.41
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5559540 sec
RG 181
DW 78.000 usec
DE 6.00 usec
TE 299.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.70 usec
PL1 0.00 dB
SFO1 400.0128001 MHz
F2 - Processing parameters
SI 32768
SF 400.0100000 MHz
WDW EM
SSB 0
LB 0.70 Hz
GB 0
PC 1.00
TES
TESO
TESO
OTES
O
O
O
OH
7.9
ppm
1.00
1.01
2.29
1.03
1.25
1.06
1.21
1.13
1.02
1.23
1.21
6.28
1.85
3.73
28.31
32.96
53.37
4.25
32.72



7.9

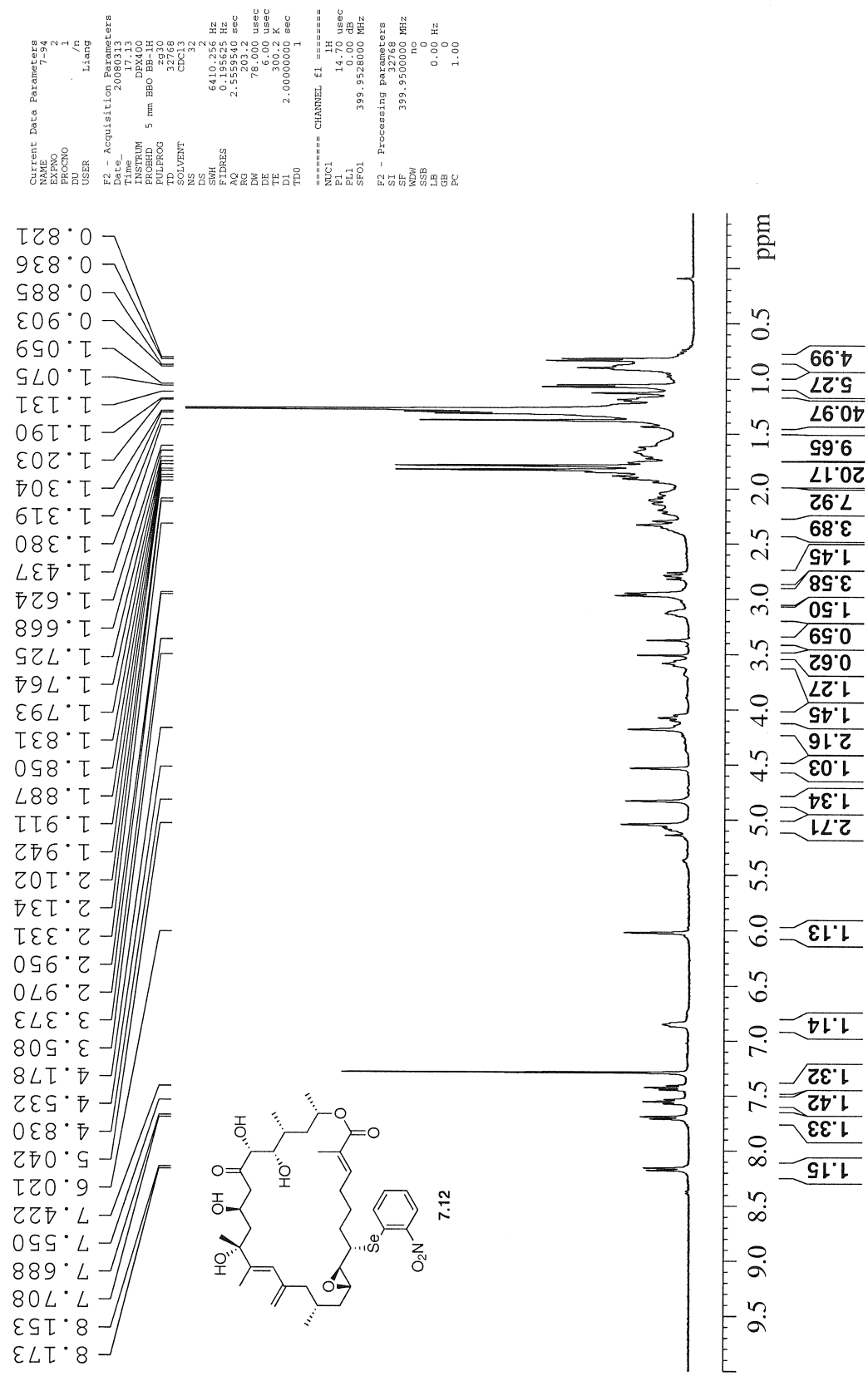
```
Current Data Parameters
NAME                  7-16
EXPNO                    2
PROCNO                   1
DU                      /n
USER                 Liang

F2 - Acquisition Parameter
Date_              20071104
Time                 14.50
INSTRUM              DPX400
PROBHD   5 mm BBO BB-1H
PULPROG             zgpg30
TD                   65536
SOLVENT
NS                    4003
DS                       4
SWH              25125.629 Hz
FIDRES           0.383387 Hz
AQ               1.3042164 se
RG                  4597.6
DW                19.900 us
DE                 6.00 us
TE                299.2 K
D1            0.15000001 se
d11           0.03000000 se
DELTA         0.05000000 se
TD0                      1

======== CHANNEL f1 ======
NUC1                   13C
P1                  7.80 us
PL1                -3.00 dB
SFO1         100.5936591 MH

======== CHANNEL f2 ======
CPDPRG2            waltz16
NUC2                   1H
PCPD2             135.00 us
PL2                17.40 dB
PL12               17.40 dB
PL13               17.40 dB
SFO2         400.0116000 MH

F2 - Processing parameters
SI                   32768
SF           100.5825950 MH
WDW                    EM
SSB                     0
LB                 3.00 Hz
GB                      0
PC                   1.40
```

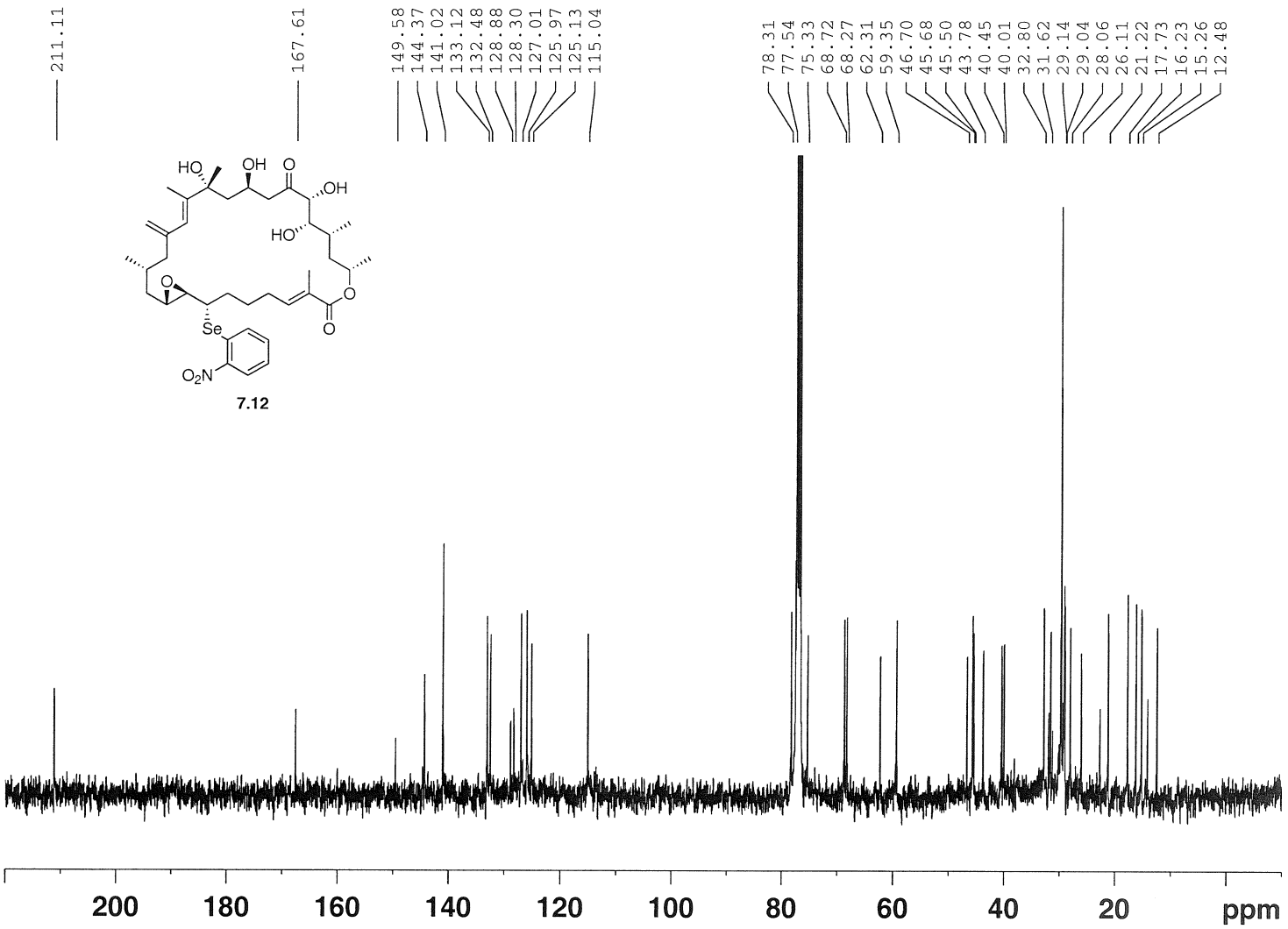

Current Data Parameters
NAME 8-34
EXPNO 1
PROCNO 1
DU /n
USER Liang
F2 - Acquisition Parameters
Date_ 20080411
Time 19.14
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 37768
SOLVENT CDCl3
NS 14
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.55599540 sec
RG 181
DW 78.000 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.70 usec
PL1 0.00 dB
SFO1 399.9528000 MHz
F2 - Processing parameters
SI 32768
SF 399.9500000 MHz
WDW EM
SSB 0
LB 0.70 Hz
GB 0
PC 1.00
TES
TESO
TESO
OTES
O
O
O
OH
7.10
ppm
1.00
1.02
2.50
1.22
1.11
0.91
0.98
1.20
1.04
2.34
2.13
3.25
1.35
10.09
14.33
9.01
8.81
58.43
38.71



7.10

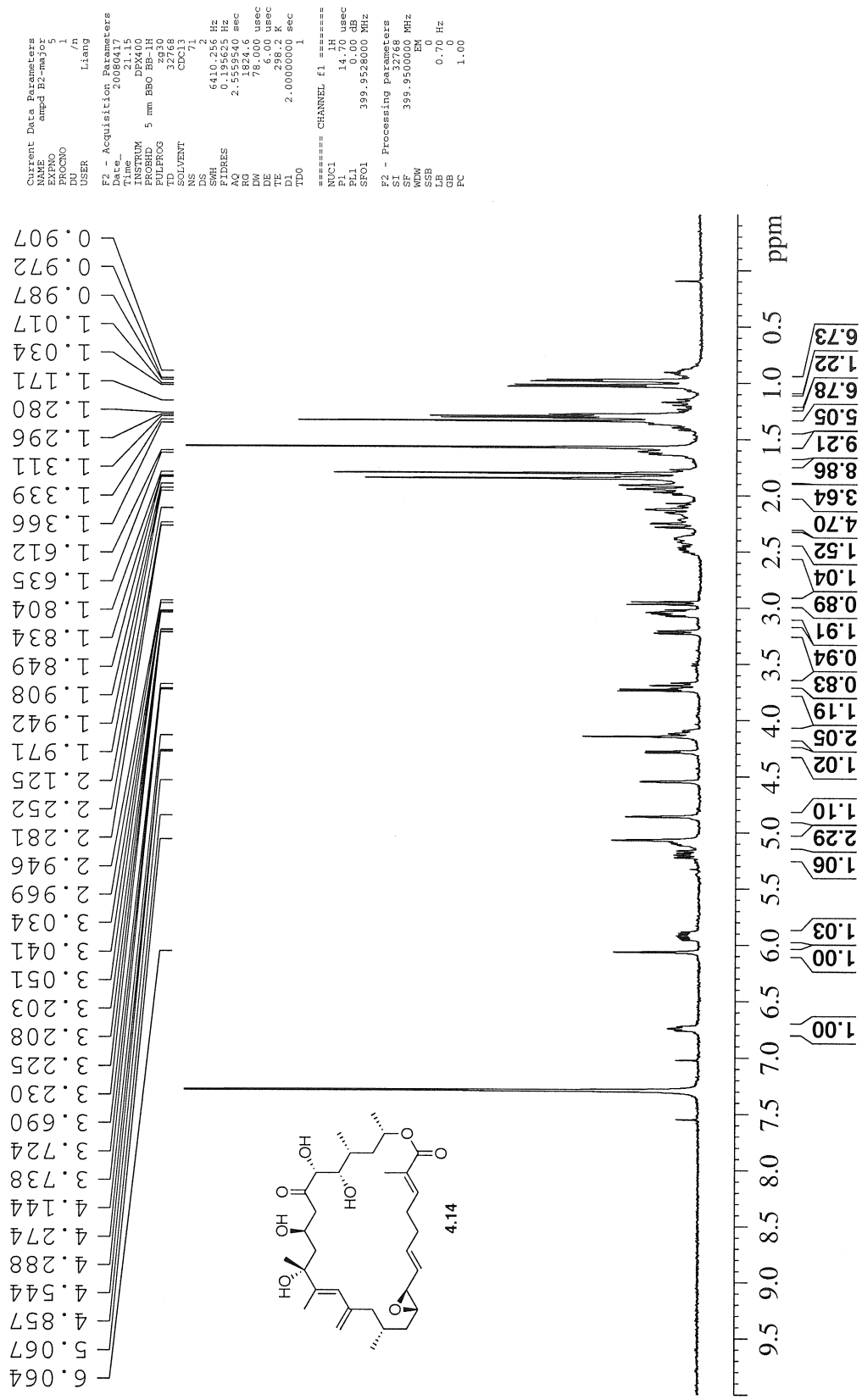
```
Current Data Parameters
NAME                  8-34
EXPNO                    3
PROCNO                   1
DU                      /n
USER                 Liang

F2 - Acquisition Parameter
Date_              20080411
Time                 19.32
INSTRUM             DPX400
PROBHD   5 mm BBO BB-1H
PULPROG             zgpg30
TD                   65536
SOLVENT
NS                    4030
DS                       4
SWH              25125.629 Hz
FIDRES           0.383387 Hz
AQ               1.3042164 se
RG                   16384
DW                19.900 us
DE                 6.00 us
TE                298.2 K
D1            0.15000001 se
D11           0.03000000 se
DELTA         0.05000000 se
TD0                      1

======== CHANNEL f1 ======
NUC1                  13C
P1                 7.80 us
PL1               -3.00 dB
SFO1        100.5785700 MH

======== CHANNEL f2 ======
CPDPRG2           waltz16
NUC2                  1H
PCPD2             135.00 us
PL2                17.40 dB
PL12               17.40 dB
PL13               17.40 dB
SFO2        399.9516000 MH

F2 - Processing parameters
SI                   32768
SF          100.5675080 MH
WDW                    EM
SSB                     0
LB                 3.00 Hz
GB                      0
PC                   1.40
```

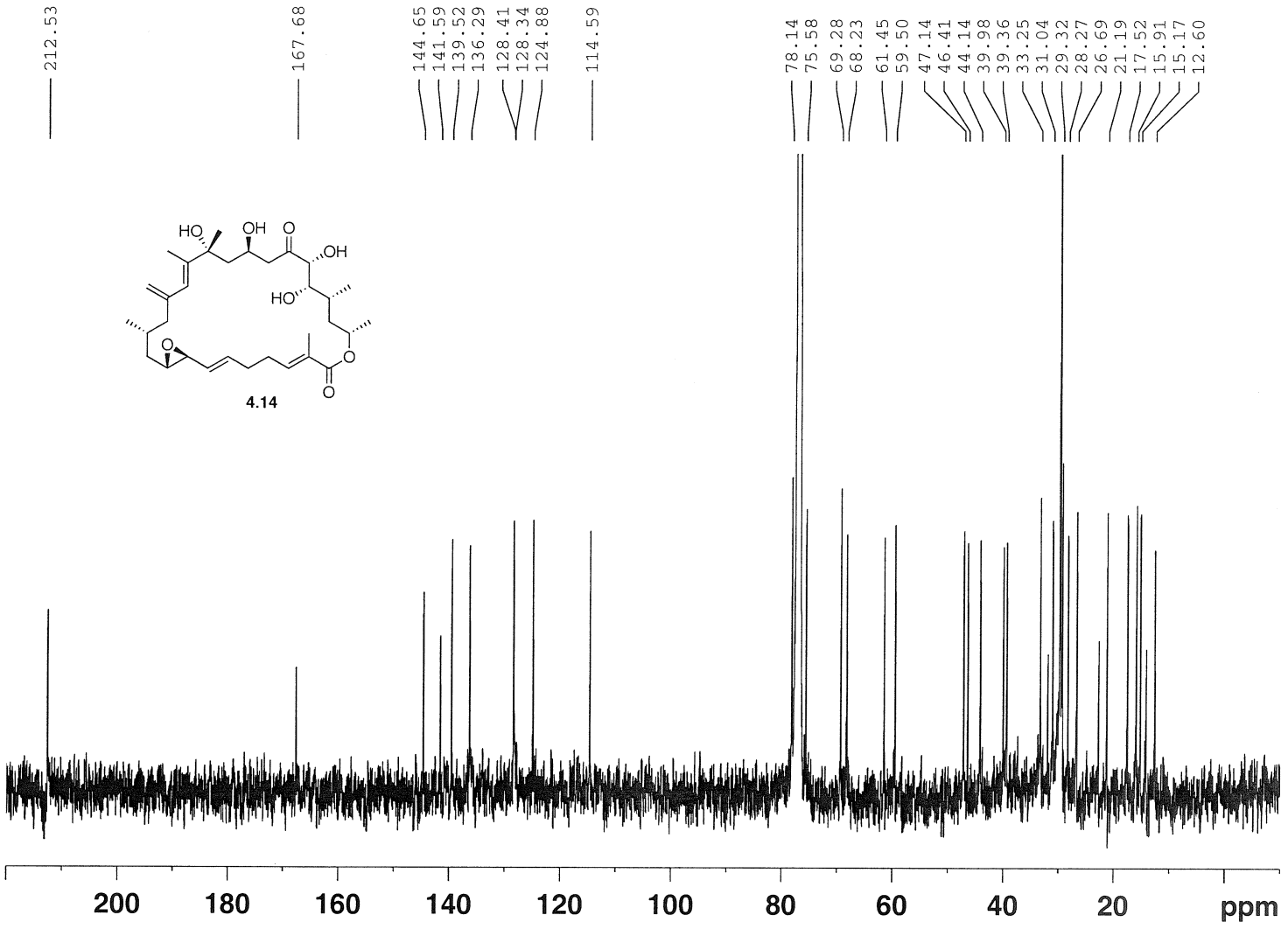

Current Data Parameters
NAME 7-94
EXPNO 2
PROCNO 1
DU /n
USER Liang
F2 - Acquisition Parameters
Date_ 20080313
Time 17.13
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.55599540 sec
RG 203.2
DW 78.000 usec
DE 6.00 usec
TE 300.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.70 usec
PL1 0.00 dB
SFO1 399.9528000 MHz
F2 - Processing parameters
SI 32768
SF 399.9500000 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
8.173
8.153
7.708
7.688
7.550
7.422
6.021
5.042
4.830
4.532
4.178
3.508
3.373
2.970
2.950
2.331
2.134
2.102
1.942
1.911
1.887
1.850
1.831
1.793
1.764
1.725
1.668
1.624
1.437
1.380
1.319
1.304
1.203
1.190
1.131
1.075
1.059
0.903
0.885
0.836
0.821
7.12
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
1.15
1.33
1.42
1.32
1.14
1.13
2.71
1.34
1.03
2.16
1.45
1.27
0.62
0.59
1.50
3.58
1.45
3.89
7.92
20.17
9.65
40.97
5.27
4.99



7.12

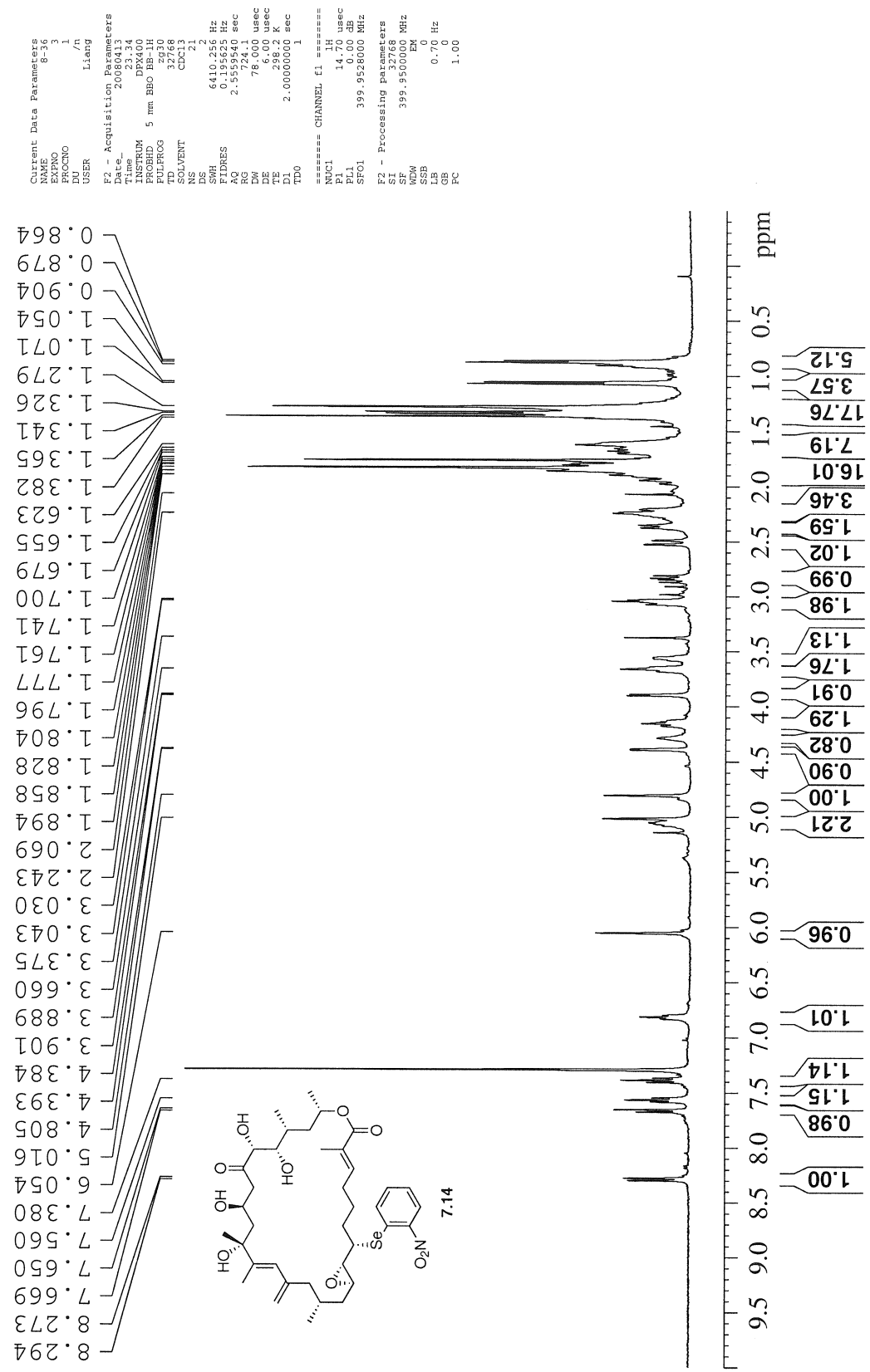
```
Current Data Parameters
NAME                  7-94
EXPNO                    4
PROCNO                   1
DU                      /n
USER                 Liang

F2 - Acquisition Parameter
Date_              20080313
Time                 17.32
INSTRUM              DPX400
PROBHD   5 mm BBO BB-1H
PULPROG              zgpg30
TD                    65536
SOLVENT
NS                     4199
DS                        4
SWH              25125.629 Hz
FIDRES           0.383387 Hz
AQ               1.3042164 se
RG                    16384
DW                19.900 us
DE                 6.00 us
TE                298.2 K
D1            0.15000001 se
D11           0.03000000 se
DELTA         0.05000000 se
TD0                       1

======== CHANNEL f1 ======
NUC1                  13C
P1                 7.80 us
PL1                -3.00 dB
SFO1         100.5785700 MH

======== CHANNEL f2 ======
CPDPRG2           waltz16
NUC2                  1H
PCPD2             135.00 us
PL2                17.40 dB
PL12               17.40 dB
PL13               17.40 dB
SFO2         399.9516000 MH

F2 - Processing parameters
SI                    32768
SF           100.5675080 MH
WDW                     EM
SSB                      0
LB                 3.00 Hz
GB                       0
PC                    1.40
```

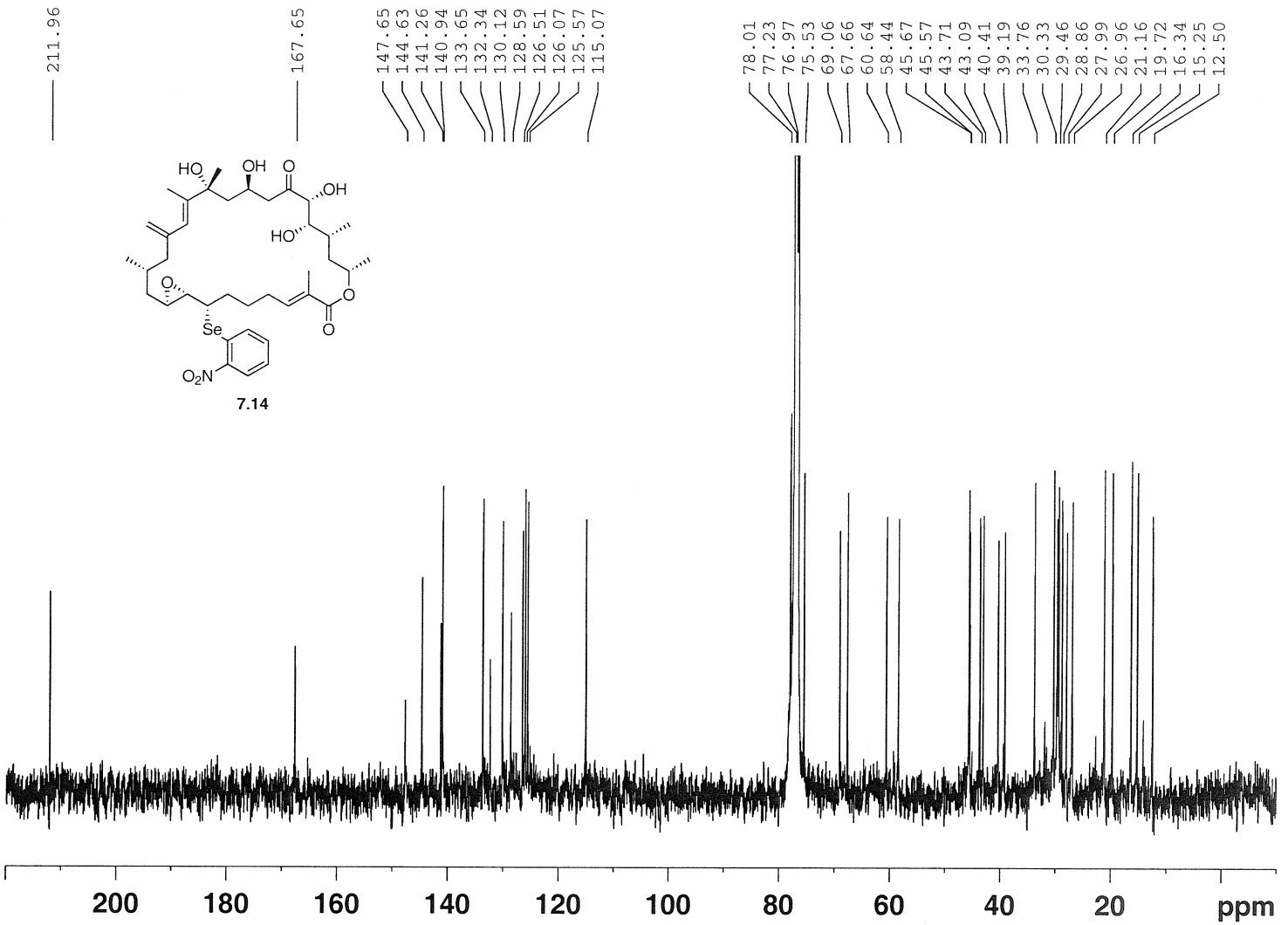

Current Data Parameters
NAME ampd B2-major
EXPNO 5
PROCNO 1
DU /n
USER Liang
F2 - Acquisition Parameters
Date_ 20080417
Time 21.15
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 71
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.55595540 sec
RG 1824.6
DW 78.000 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.70 usec
PL1 0.00 dB
SFO1 399.9528000 MHz
F2 - Processing parameters
SI 32768
SF 399.9500000 MHz
WDW EM
SSB 0
LB 0.70 Hz
GB 0
PC 1.00
4.14
ppm
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
1.00 1.00 1.03 1.06 2.29 1.10 1.02 2.05 1.19 0.83 0.94 1.91 0.89 1.04 1.52 4.70 3.64 8.86 9.21 5.05 6.78 1.22 6.73
6.064 5.067 4.857 4.544 4.288 4.274 4.144 3.738 3.724 3.690 3.230 3.225 3.208 3.203 3.051 3.041 3.034 2.969 2.946 2.281 2.252 2.125 1.971 1.942 1.908 1.849 1.834 1.804 1.635 1.612 1.366 1.339 1.311 1.296 1.280 1.171 1.034 1.017 0.987 0.972 0.907



4.14

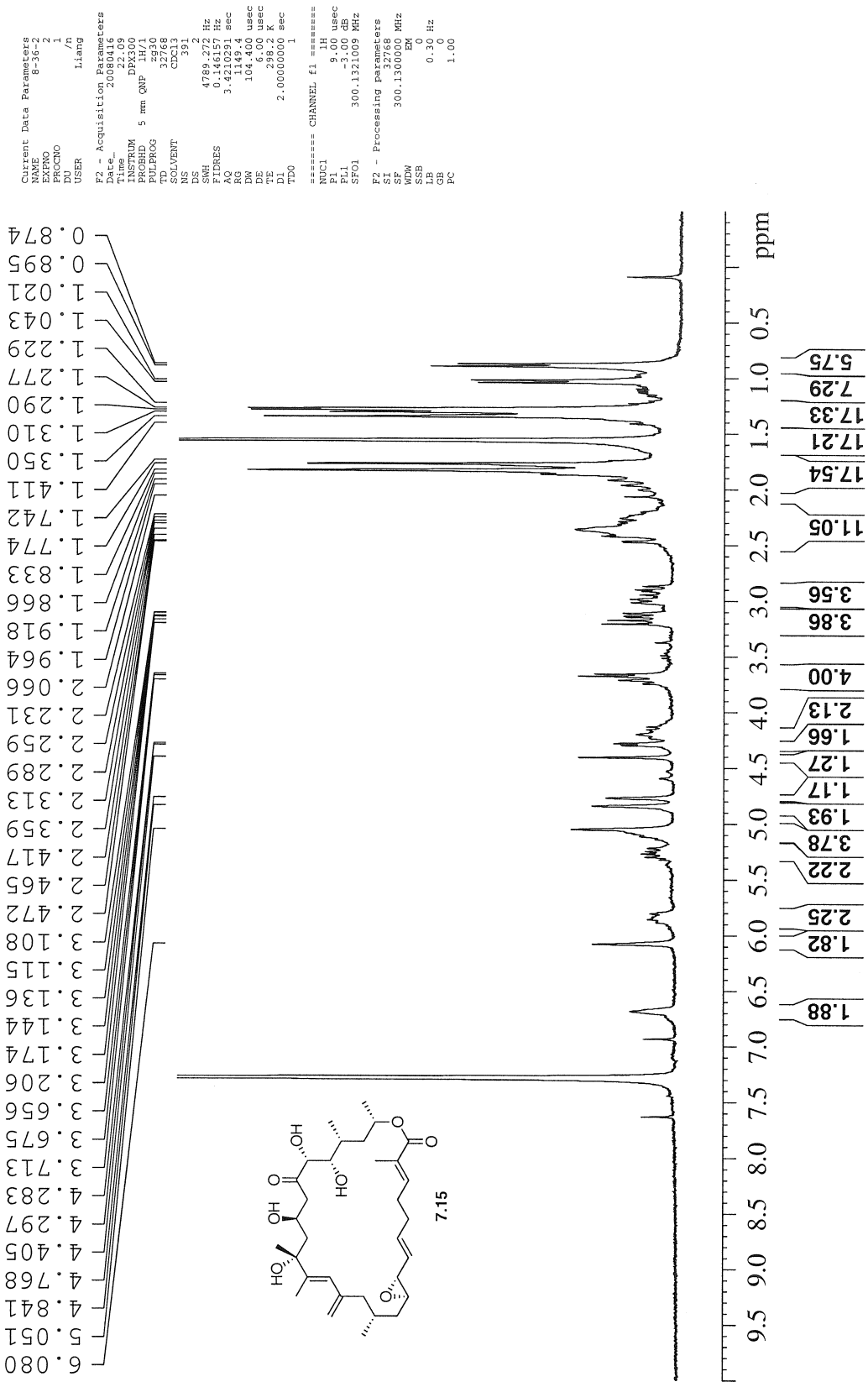
```
Current Data Parameters
NAME                  7-95
EXPNO                    7
PROCNO                   1
DU                      /n
USER                 Liang

F2 - Acquisition Parameter
Date_              20080313
Time                  7.57
INSTRUM             DPX400
PROBHD   5 mm BBO BB-1H
PULPROG             zgpg30
TD                   65536
SOLVENT
NS                   22500
DS                       4
SWH              25125.629 Hz
FIDRES           0.383387 Hz
AQ               1.3042164 se
RG                  5792.6
DW                  19.900 us
DE                   6.00 us
TE                  298.2 K
D1             0.15000001 se
D11            0.03000000 se
DELTA          0.05000000 se
TD0                      1

======== CHANNEL f1 ======
NUC1                   13C
P1                    7.80 us
PL1                  -3.00 dB
SFO1         100.5785700 MH

======== CHANNEL f2 ======
CPDPRG2            waltz16
NUC2                    1H
PCPD2                135.00 us
PL2                  17.40 dB
PL12                 17.40 dB
PL13                 17.40 dB
SFO2         399.9516000 MH

F2 - Processing parameters
SI                   32768
SF           100.5675080 MH
WDW                     EM
SSB                      0
LB                    3.00 Hz
GB                       0
PC                    1.40
```

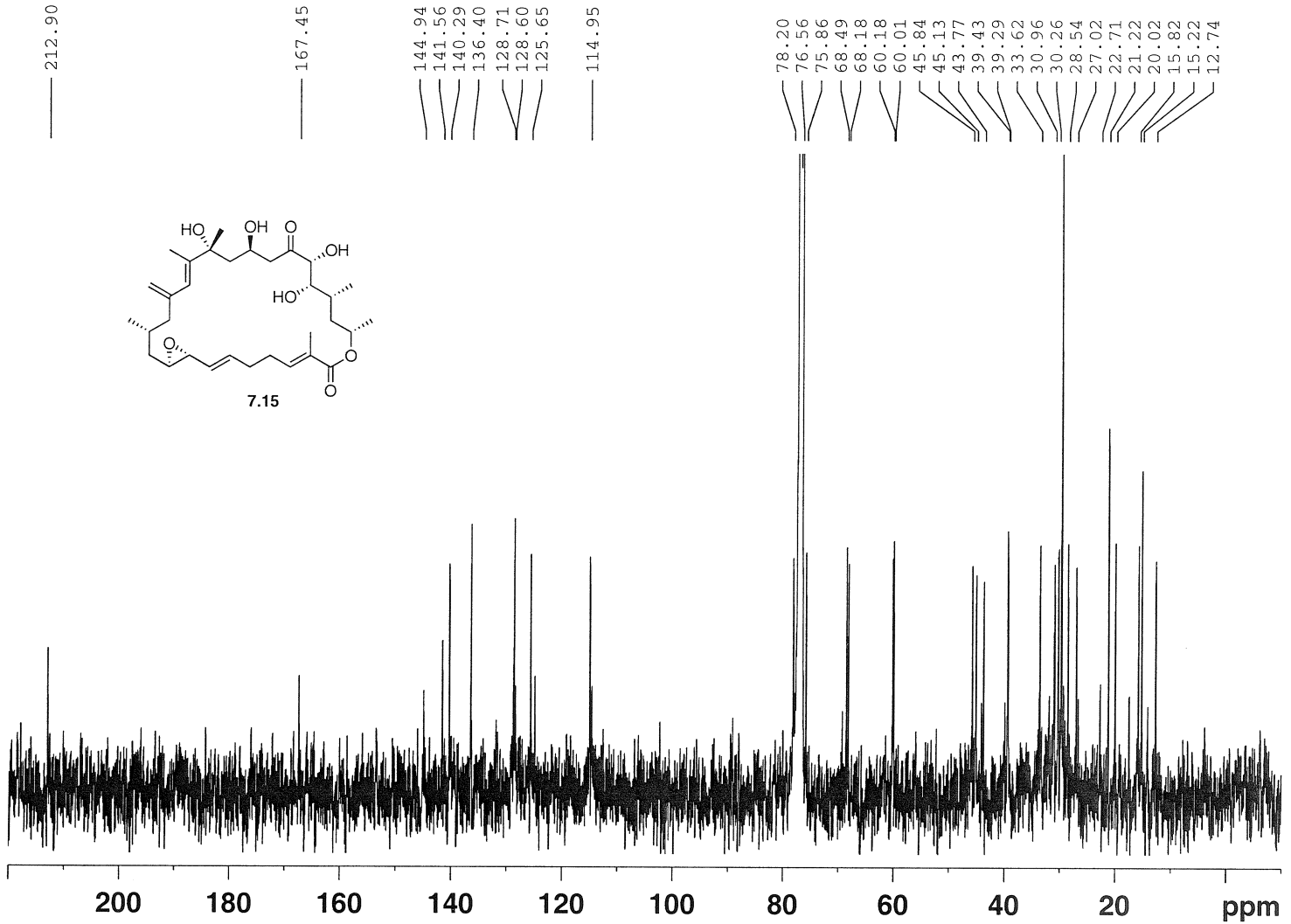

Current Data Parameters
NAME 8-36
EXPNO 3
PROCNO 1
DU /n
USER Liang
F2 - Acquisition Parameters
Date_ 20080413
Time 23.34
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 21
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.55599540 sec
RG 724.1
DW 78.000 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.70 usec
PL1 0.00 dB
SFO1 399.9528000 MHz
F2 - Processing parameters
SI 32768
SF 399.9500000 MHz
WDW EM
SSB 0
LB 0.70 Hz
GB 0
PC 1.00
7.14
ppm
1.00
0.98
1.15
1.14
1.01
0.96
1.00
2.21
1.00
0.90
0.82
1.29
0.91
1.76
1.13
1.98
0.99
1.02
1.59
3.46
16.01
7.19
17.76
3.57
5.12



7.14

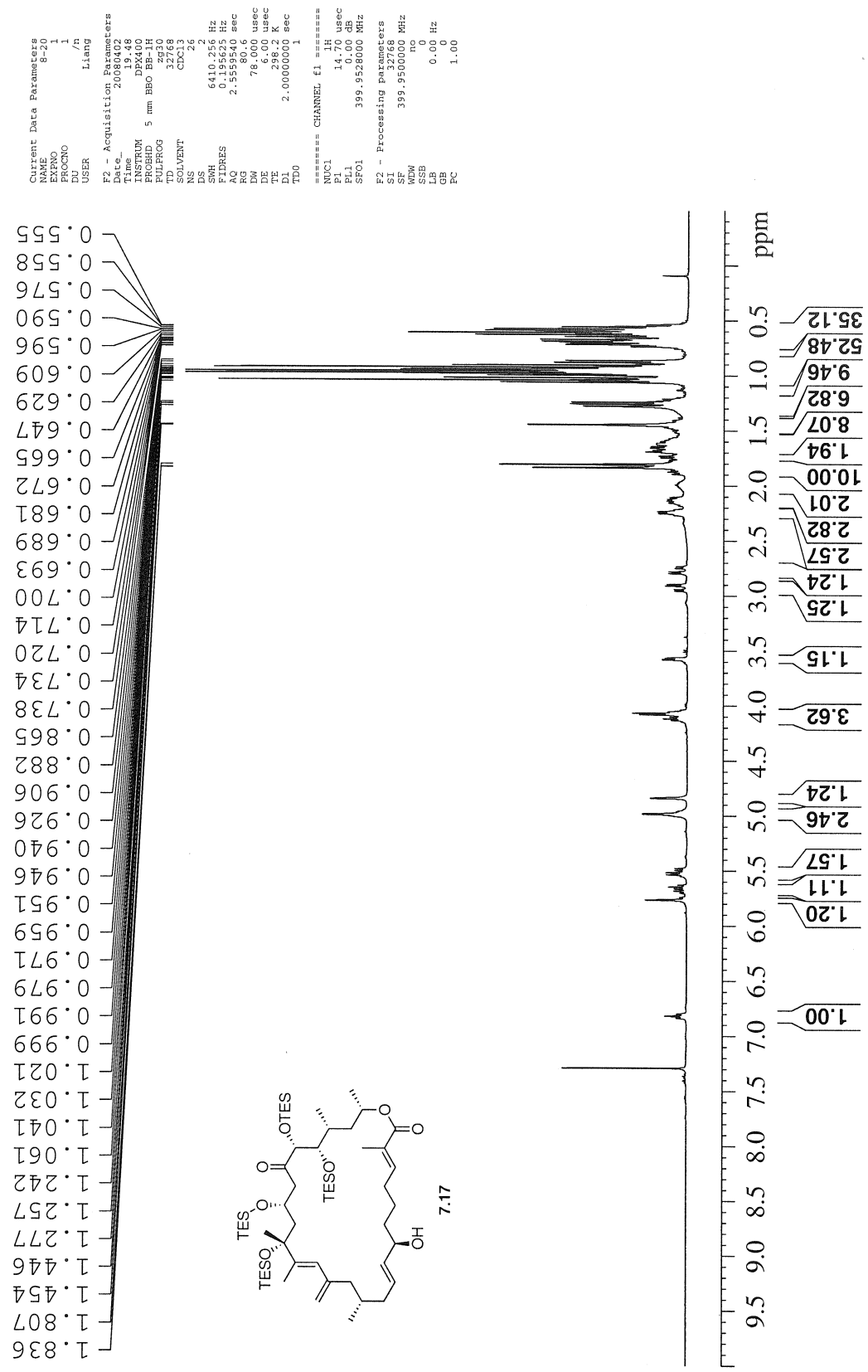
```
Current Data Parameters
NAME                  8-36
EXPNO                    5
PROCNO                   1
DU                      /n
USER                 Liang

F2 - Acquisition Parameter
Date_              20080413
Time                 23.50
INSTRUM             DPX400
PROBHD   5 mm BBO BB-1H
PULPROG             zgpg30
TD                   65536
SOLVENT
NS                   19205
DS                       4
SWH             25125.629 Hz
FIDRES          0.383387 Hz
AQ              1.3042164 se
RG                   16384
DW                19.900 us
DE                 6.00 us
TE                298.2 K
D1            0.15000001 se
D11           0.03000000 se
DELTA         0.05000000 se
TD0                      1

======== CHANNEL f1 ======
NUC1                  13C
P1                 7.80 us
PL1               -3.00 dB
SFO1         100.5785700 MH

======== CHANNEL f2 ======
CPDPRG2           waltz16
NUC2                  1H
PCPD2            135.00 us
PL2                17.40 dB
PL12               17.40 dB
PL13               17.40 dB
SFO2         399.9516000 MH

F2 - Processing parameters
SI                   32768
SF           100.5675080 MH
WDW                    EM
SSB                     0
LB                 3.00 Hz
GB                      0
PC                   1.40
```

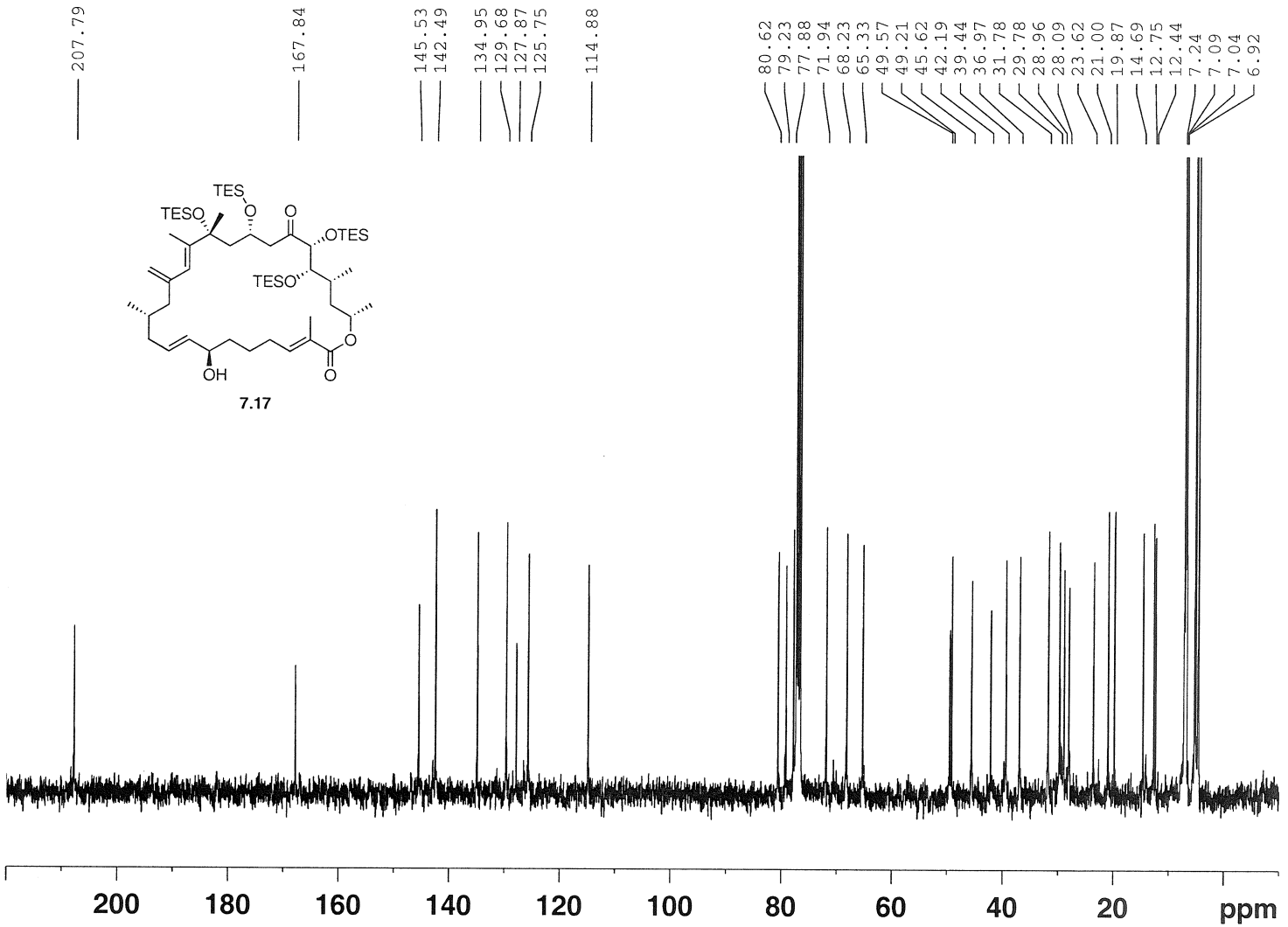

Current Data Parameters
NAME 8-36-2
EXPNO 2
PROCNO 1
DU /n
USER Liang
F2 - Acquisition Parameters
Date_ 20080416
Time 22.09
INSTRUM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 391
DS 2
SWH 4789.272 Hz
FIDRES 0.146157 Hz
AQ 3.4210291 sec
RG 1149.4
DW 104.400 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.00 usec
PL1 -3.00 dB
SFO1 300.1321009 MHz
F2 - Processing parameters
SI 32768
SF 300.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
7.15
ppm
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
1.88
1.82
2.25
2.22
3.78
1.93
1.17
1.27
1.66
2.13
4.00
3.86
3.56
11.05
17.54
17.21
17.33
7.29
5.75
6.080
5.051
4.841
4.768
4.405
4.297
4.283
3.713
3.675
3.656
3.206
3.174
3.144
3.136
3.115
3.108
2.472
2.465
2.417
2.359
2.313
2.289
2.259
2.231
2.066
1.964
1.918
1.866
1.833
1.774
1.742
1.411
1.350
1.310
1.290
1.277
1.229
1.043
1.021
0.895
0.874



7.15

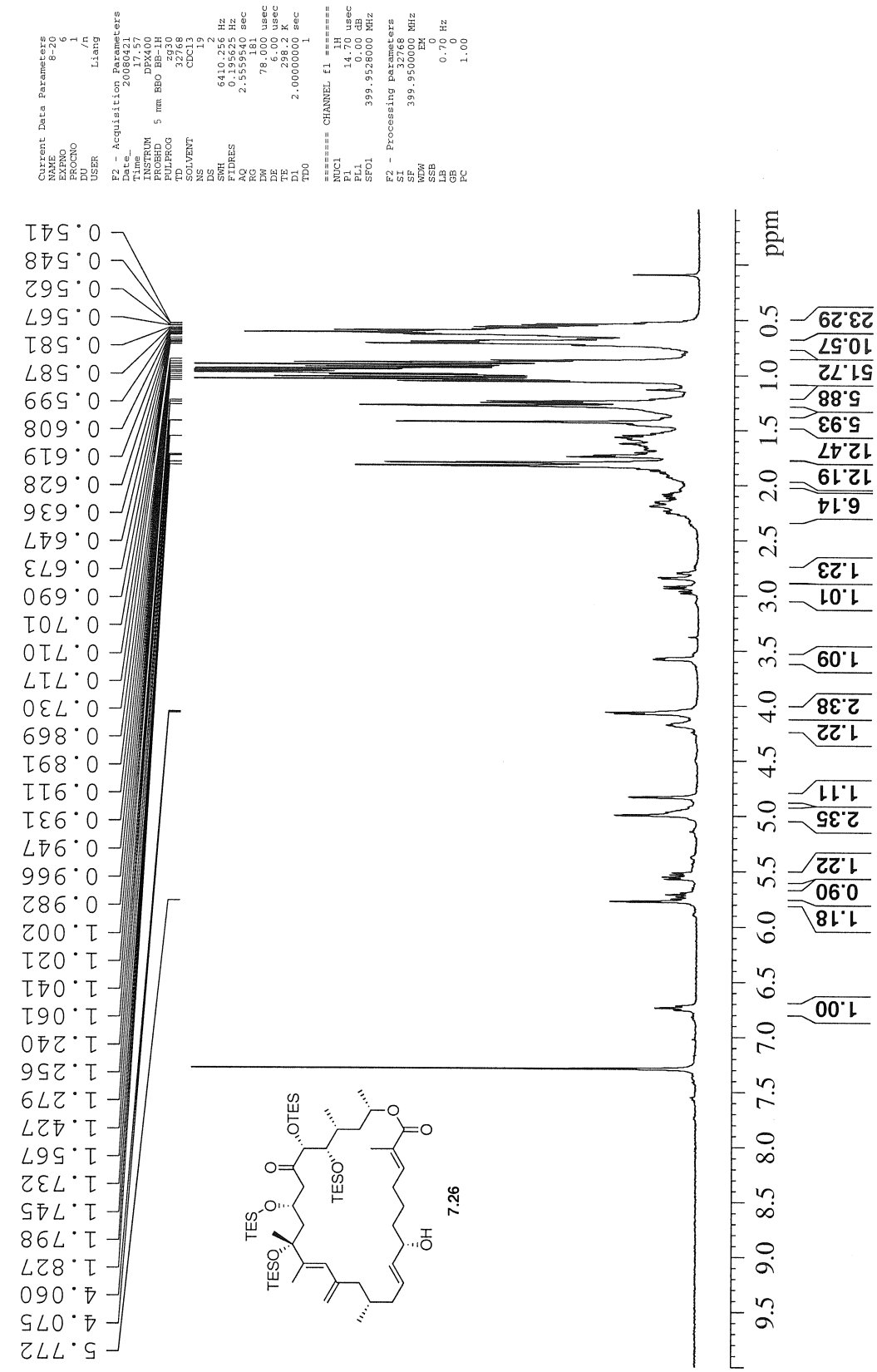
```
Current Data Parameters
NAME                  7-97-2
EXPNO                      3
PROCNO                     1
DU                        /n
USER                  Liang

F2 - Acquisition Parameter
Date_              20080314
Time                   7.52
INSTRUM             DPX400
PROBHD   5 mm BBO BB-1H
PULPROG             zgpg30
TD                   65536
SOLVENT
NS                   19200
DS                       4
SWH              25125.629 Hz
FIDRES           0.383387 Hz
AQ               1.3042164 se
RG                 11585.2
DW                 19.900 us
DE                  6.00 us
TE                  298.2 K
D1             0.15000001 se
D11            0.03000000 se
DELTA          0.05000000 se
TD0                      1

======== CHANNEL f1 ======
NUC1                   13C
P1                    7.80 us
PL1                  -3.00 dB
SFO1         100.5785700 MH

======== CHANNEL f2 ======
CPDPRG2            waltz16
NUC2                   1H
PCPD2              135.00 us
PL2                 17.40 dB
PL12                17.40 dB
PL13                17.40 dB
SFO2         399.9516000 MH

F2 - Processing parameters
SI                   32768
SF           100.5675080 MH
WDW                    EM
SSB                     0
LB                   3.00 Hz
GB                      0
PC                   1.40
```

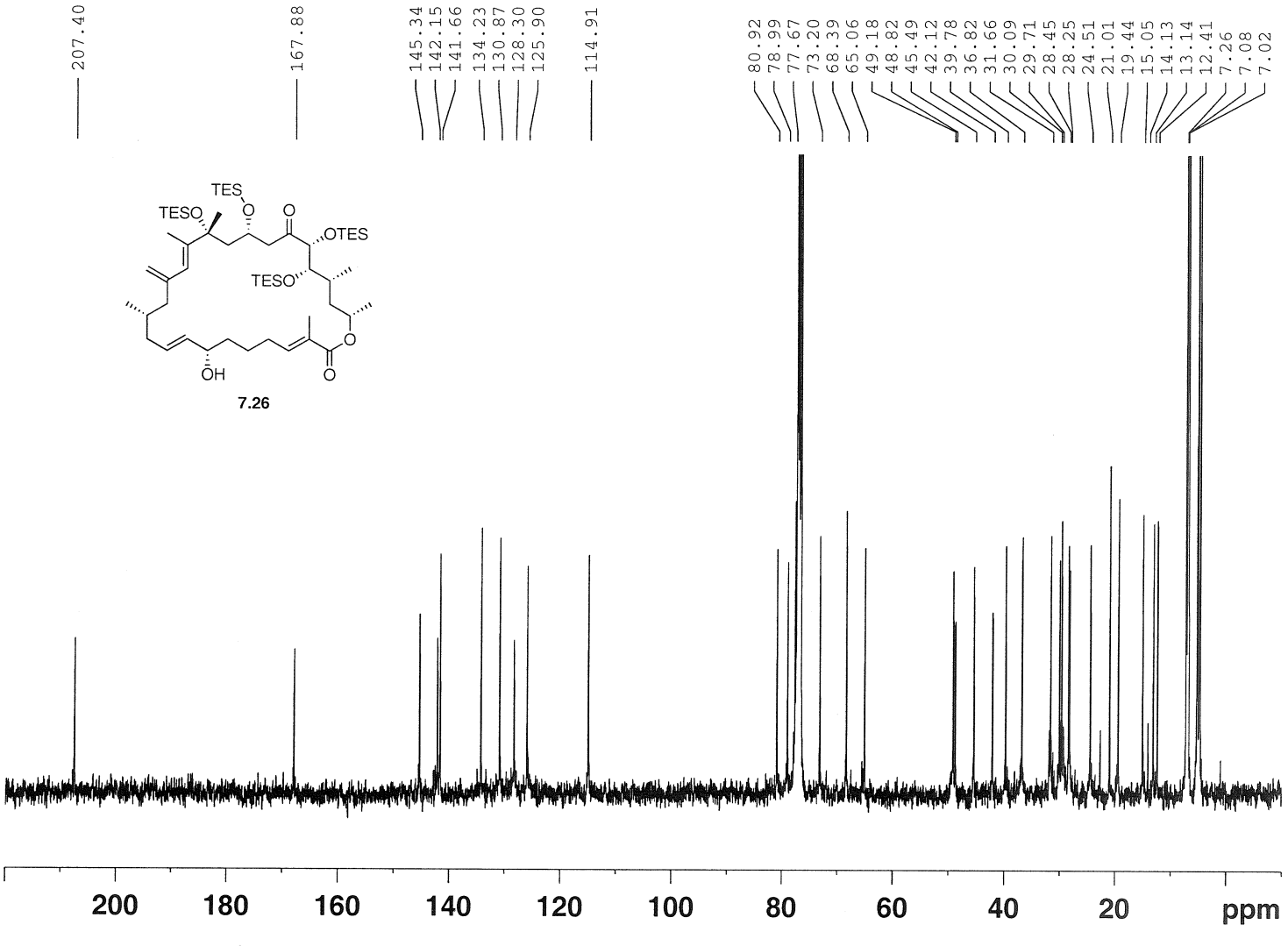

Current Data Parameters
NAME 8-20
EXPNO 1
PROCNO /n
DU Liang
USER
F2 - Acquisition Parameters
Date_ 20080402
Time 19.48
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 26
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5559540 sec
RG 80.6
DW 78.000 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.70 usec
PL1 0.00 dB
SFO1 399.9528000 MHz
F2 - Processing parameters
SI 32768
SF 399.9500000 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
TESO
TES
O
OTES
TESO
O
O
OH
7.17
ppm
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
1.00
1.20
1.11
1.57
2.46
1.24
3.62
1.15
1.25
1.24
2.57
2.82
2.01
10.00
1.94
8.07
6.82
9.46
52.48
35.12
0.555
0.558
0.576
0.590
0.596
0.609
0.629
0.647
0.665
0.672
0.681
0.689
0.693
0.700
0.714
0.720
0.734
0.738
0.865
0.882
0.906
0.926
0.940
0.946
0.951
0.959
0.971
0.979
0.991
0.999
1.021
1.032
1.041
1.061
1.242
1.257
1.277
1.446
1.454
1.807
1.836



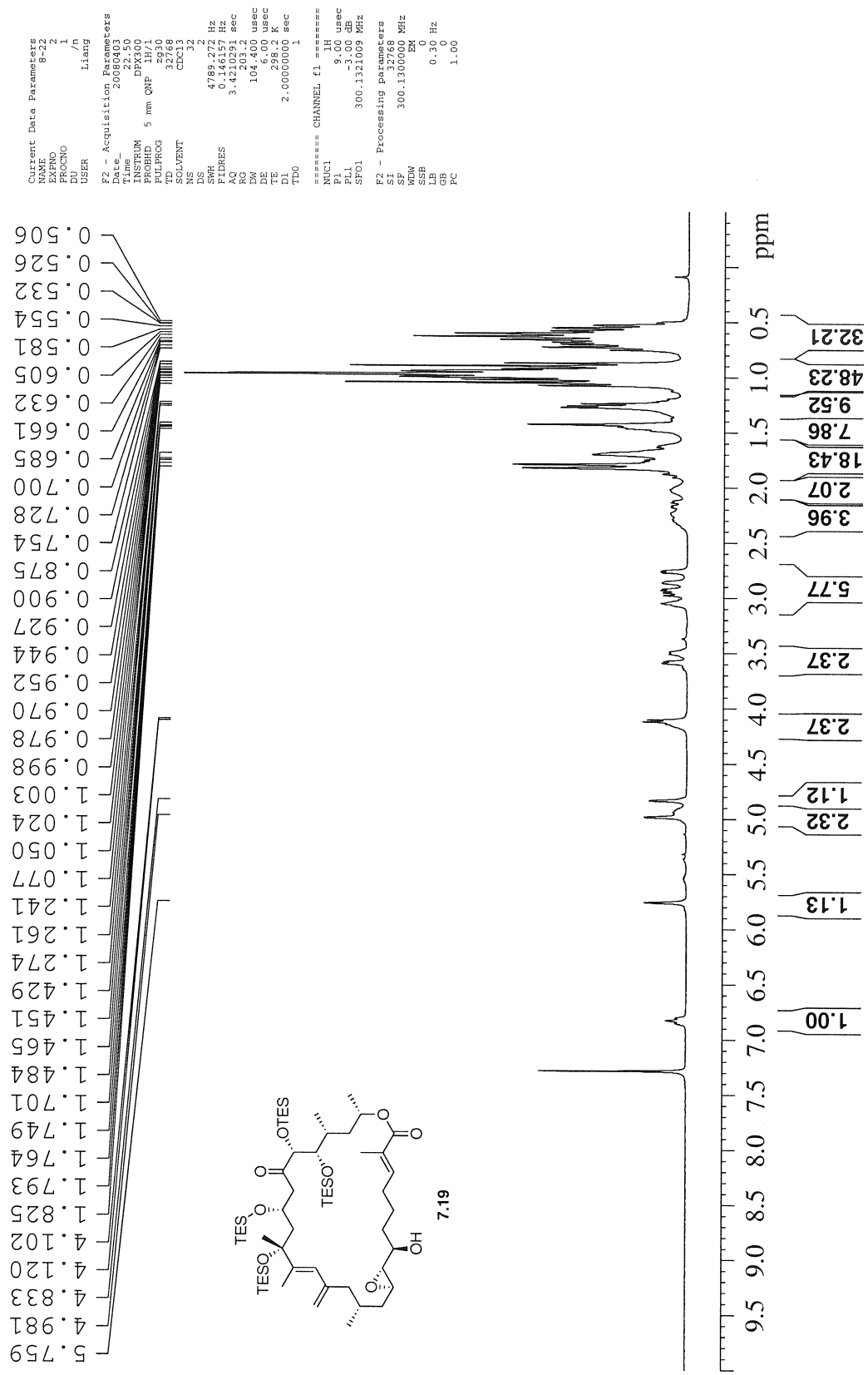
7.17

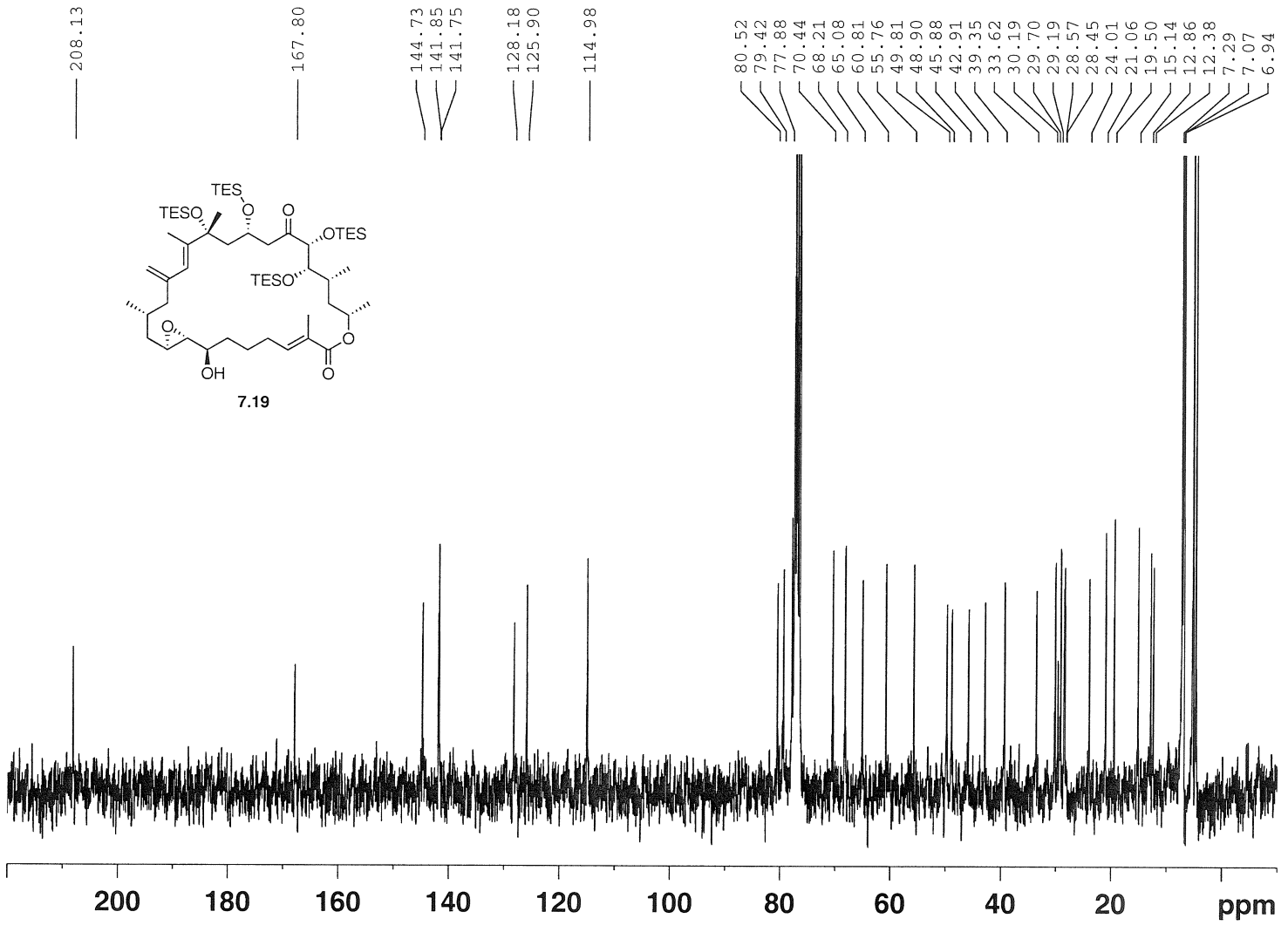
```
Current Data Parameters
NAME                  8-20
EXPNO                    3
PROCNO                   1
DU                      /n
USER                 Liang

F2 - Acquisition Parameter
Date_              20080402
Time                 20.03
INSTRUM             DPX400
PROBHD   5 mm BBO BB-1H
PULPROG             zgpg30
TD                   65536
SOLVENT
NS                    1737
DS                       4
SWH              25125.629 Hz
FIDRES           0.383387 Hz
AQ               1.3042164 se
RG                  4597.6
DW                19.900 us
DE                 6.00 us
TE                298.2 K
D1           0.15000001 se
D11          0.03000000 se
DELTA        0.05000000 se
TD0                      1

======== CHANNEL f1 ======
NUC1                  13C
P1                 7.80 us
PL1               -3.00 dB
SFO1        100.5785700 MH

======== CHANNEL f2 ======
CPDPRG2          waltz16
NUC2                  1H
PCPD2            135.00 us
PL2               17.40 dB
PL12              17.40 dB
PL13              17.40 dB
SFO2        399.9516000 MH

F2 - Processing parameters
SI                32768
SF          100.5675080 MH
WDW                  EM
SSB                   0
LB                3.00 Hz
GB                    0
PC                 1.40
```


Current Data Parameters
NAME 8-20
EXPNO 6
PROCNO 1
F2 - Acquisition Parameters
Date_ 20080421
Time 17.57
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 12
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5559540 sec
RG 181
DW 78.000 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.70 usec
PL1 0.00 dB
SFO1 399.9528000 MHz
F2 - Processing parameters
SI 32768
SF 399.9500000 MHz
WDW EM
SSB 0
LB 0.70 Hz
GB 0
PC 1.00
TES
TESO
TESO
OTES
O
O
O
OH
7.26
ppm
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
1.00
1.18
0.90
1.22
2.35
1.11
1.22
2.38
1.09
1.01
1.23
6.14
12.19
12.47
5.93
5.88
51.72
10.57
23.29
5.772
4.075
4.060
1.827
1.798
1.745
1.732
1.567
1.427
1.279
1.256
1.240
1.061
1.041
1.021
1.002
0.982
0.966
0.947
0.931
0.911
0.891
0.869
0.730
0.717
0.710
0.701
0.690
0.673
0.647
0.636
0.628
0.619
0.608
0.599
0.587
0.581
0.567
0.562
0.548
0.541



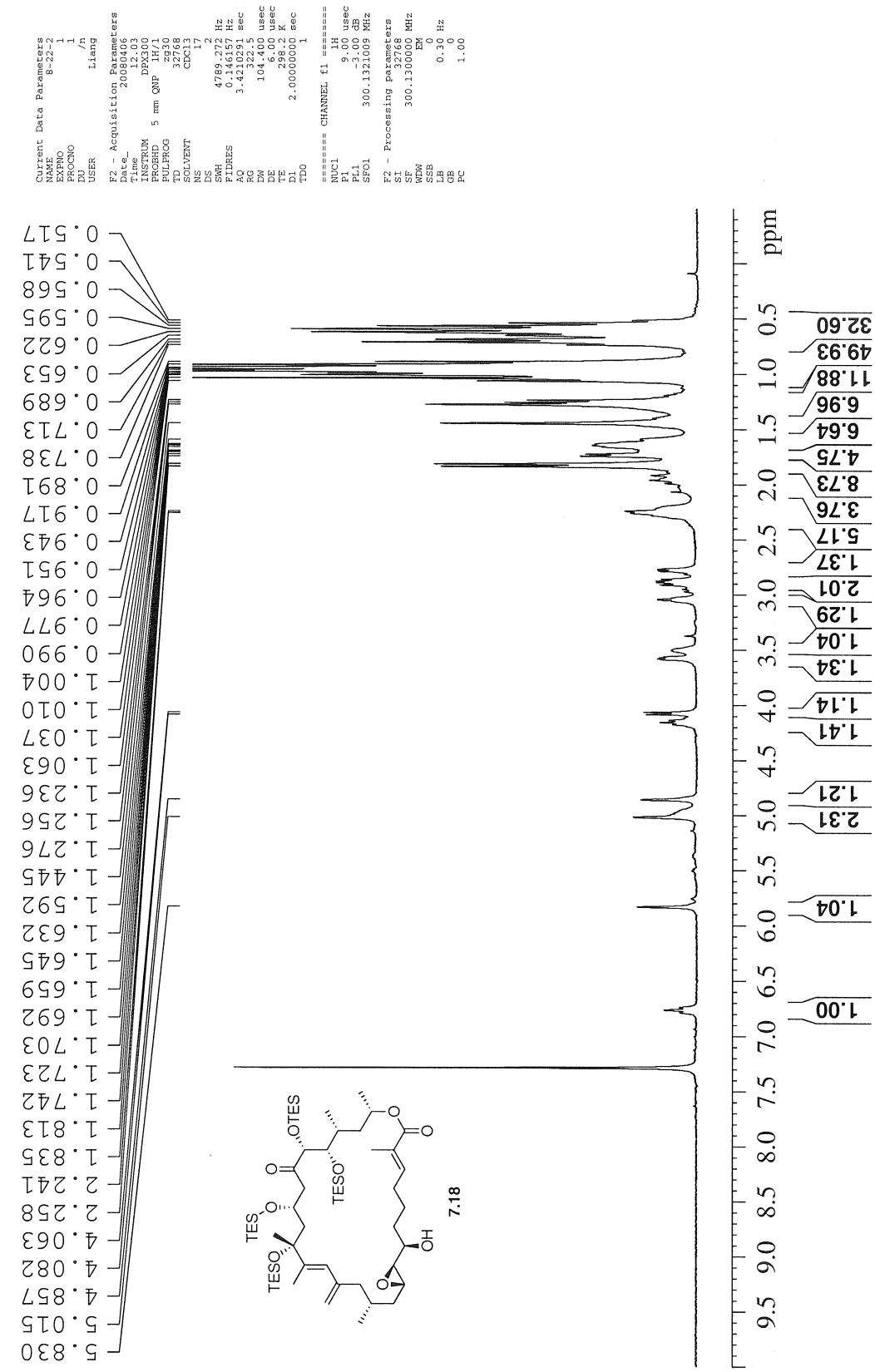

```
Current Data Parameters
NAME                  8-20
EXPNO                    8
PROCNO                   1
DU                      /n
USER                 Liang

F2 - Acquisition Parameter
Date_              20080421
Time                 21.52
INSTRUM              DPX400
PROBHD   5 mm BBO BB-1H
PULPROG              zgpg30
TD                    65536
SOLVENT               CDC13
NS                    24500
DS                        4
SWH              25125.629 Hz
FIDRES           0.383387 Hz
AQ               1.3042164 se
RG                  3649.1
DW                19.900 us
DE                 6.00 us
TE                298.2 K
D1            0.15000001 se
D11           0.03000000 se
DELTA         0.05000000 se
TD0                       1

======== CHANNEL f1 ======
NUC1                   13C
P1                  7.80 us
PL1                -3.00 dB
SFO1         100.5785700 MH

======== CHANNEL f2 ======
CPDPRG2            waltz16
NUC2                   1H
PCPD2             135.00 us
PL2                17.40 dB
PL12               17.40 dB
PL13               17.40 dB
SFO2         399.9516000 MH

F2 - Processing parameters
SI                    32768
SF           100.5675080 MH
WDW                     EM
SSB                      0
LB                3.00 Hz
GB                       0
PC                1.40
```

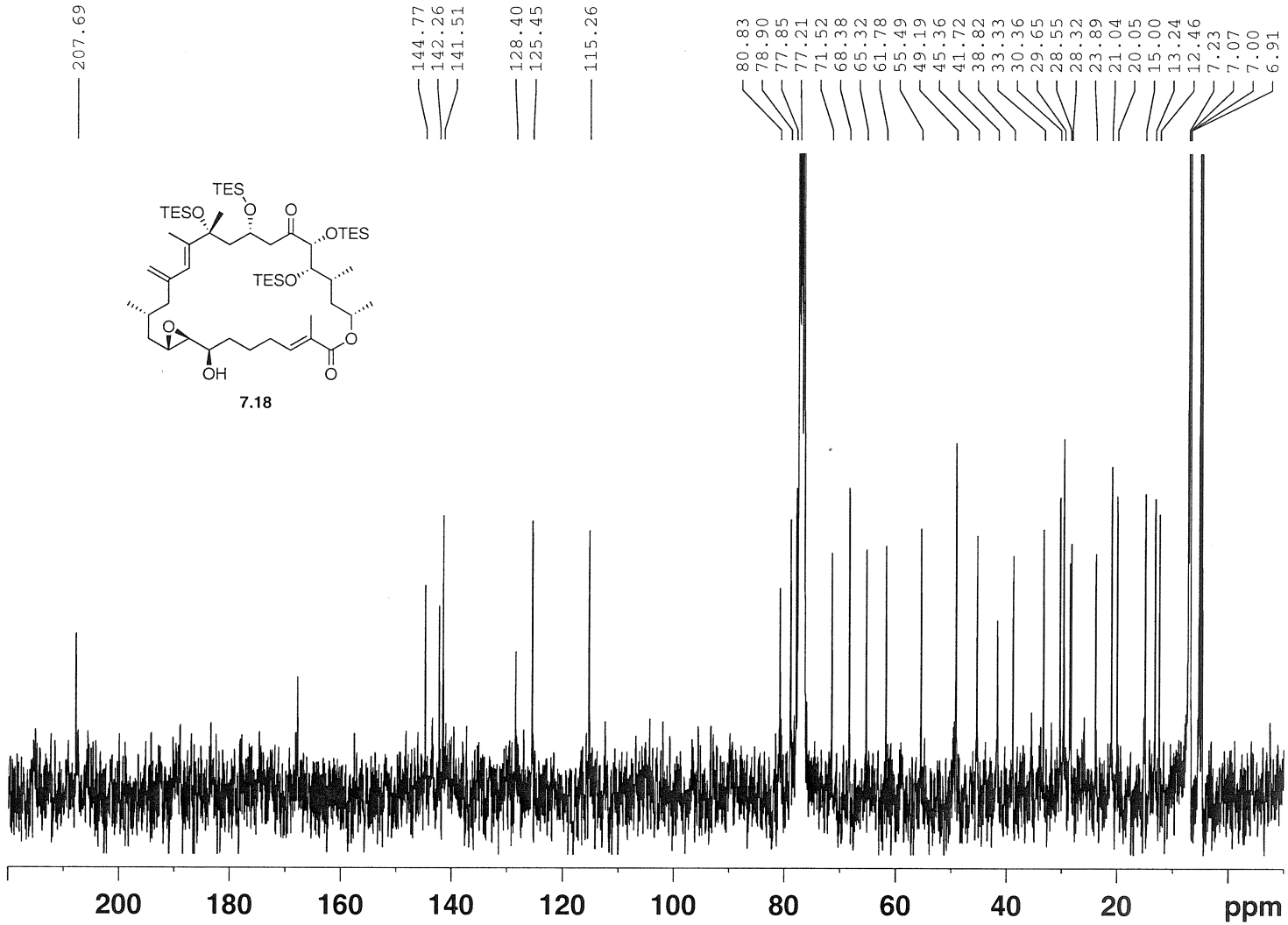

Current Data Parameters
NAME 8-22
EXPNO 2
PROCNO 1
DU /n
USER Liang
F2 - Acquisition Parameters
Date_ 20080403
Time 22.50
INSTRUM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 4789.272 Hz
FIDRES 0.146157 Hz
AQ 3.4210291 sec
RG 203.2
DW 104.400 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.00 usec
PL1 -3.00 dB
SFO1 300.1321009 MHz
F2 - Processing parameters
SI 32768
SF 300.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
5.759
4.981
4.833
4.120
4.102
1.825
1.793
1.764
1.749
1.701
1.484
1.465
1.451
1.429
1.274
1.261
1.241
1.077
1.050
1.024
1.003
0.998
0.978
0.970
0.952
0.944
0.927
0.900
0.875
0.754
0.728
0.700
0.685
0.661
0.632
0.605
0.581
0.554
0.532
0.526
0.506
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
1.00
1.13
2.32
1.12
2.37
2.37
5.77
3.96
2.07
18.43
7.86
9.52
48.23
32.21
TES
TESO
OTES
TESO
O
O
O
O
OH
7.19



7.19

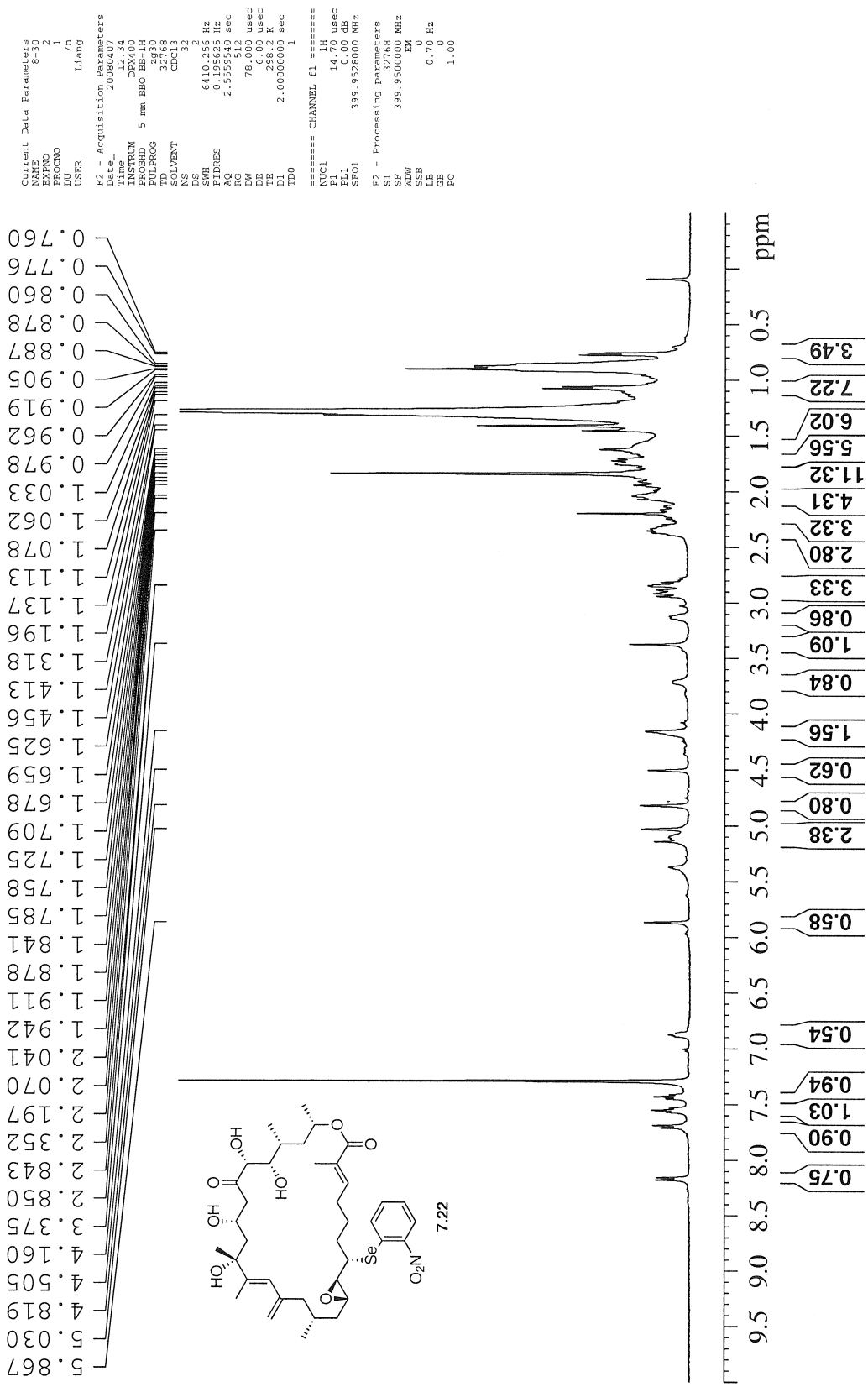
```
Current Data Parameters
NAME                  8-22
EXPNO                    4
PROCNO                   1
DU                      /n
USER                 Liang

F2 - Acquisition Parameter
Date_              20080403
Time                 23.05
INSTRUM             DPX300
PROBHD   5 mm QNP  1H/1
PULPROG             zgpg30
TD                   65536
SOLVENT              CDCl3
NS                    1392
DS                       4
SWH              18832.393 Hz
FIDRES           0.287360 Hz
AQ               1.7400308 se
RG                   812.7
DW                26.550 us
DE                 6.00 us
TE                298.2 K
D1            0.15000001 se
d11           0.03000000 se
DELTA         0.05000000 se
TD0                      1

======== CHANNEL f1 ======
NUC1                  13C
P1                 8.80 us
PL1               -3.00 dB
SFO1          75.4760505 MH

======== CHANNEL f2 ======
CPDPRG2          waltz16
NUC2                  1H
PCPD2             80.00 us
PL2               -3.00 dB
PL12              17.55 dB
PL13              17.55 dB
SFO2         300.1312005 MH

F2 - Processing parameters
SI                32768
SF           75.4677490 MH
WDW                  EM
SSB                   0
LB                 3.00 Hz
GB                    0
PC                 1.40
```

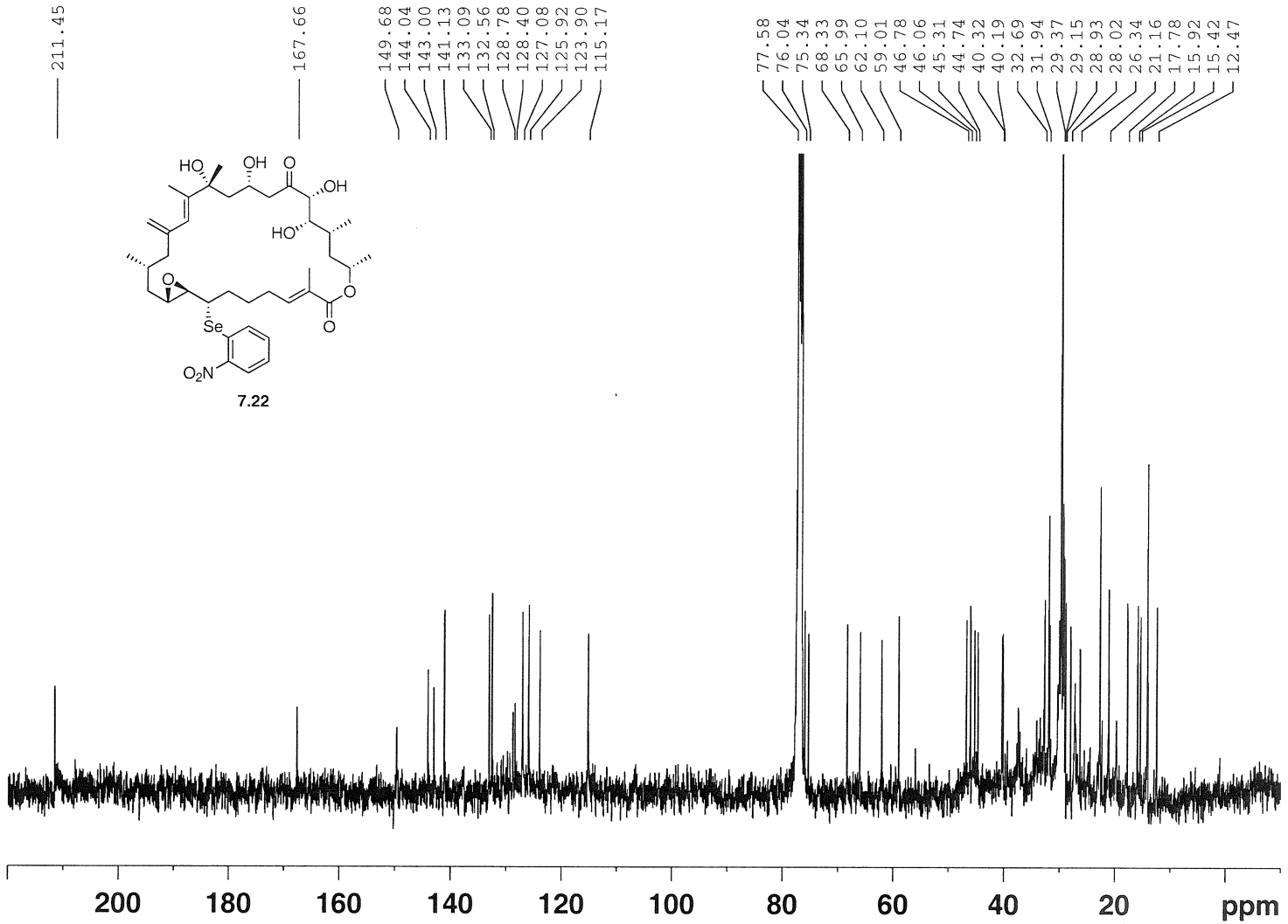

Current Data Parameters
NAME 8-22-2
EXPNO 1
PROCNO 1
DU /n
USER Liang
F2 - Acquisition Parameters
Date_ 20080406
Time 12.03
INSTRUM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 17
DS 2
SWH 4789.272 Hz
FIDRES 0.146157 Hz
AQ 3.4210291 sec
RG 322.5
DW 104.400 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.00 usec
PL1 -3.00 dB
SFO1 300.1321009 MHz
F2 - Processing parameters
SI 32768
SF 300.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
TES
TESO
TESO
OTES
OH
7.18
ppm
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
1.00
1.04
2.31
1.21
1.41
1.14
1.34
1.04
1.29
2.01
1.37
5.17
3.76
8.73
4.75
6.64
6.96
11.88
49.93
32.60
5.830
5.015
4.857
4.082
4.063
2.258
2.241
1.835
1.813
1.742
1.723
1.703
1.692
1.659
1.645
1.632
1.592
1.445
1.276
1.256
1.236
1.063
1.037
1.010
1.004
0.990
0.977
0.964
0.951
0.943
0.917
0.891
0.738
0.713
0.689
0.653
0.622
0.595
0.568
0.541
0.517



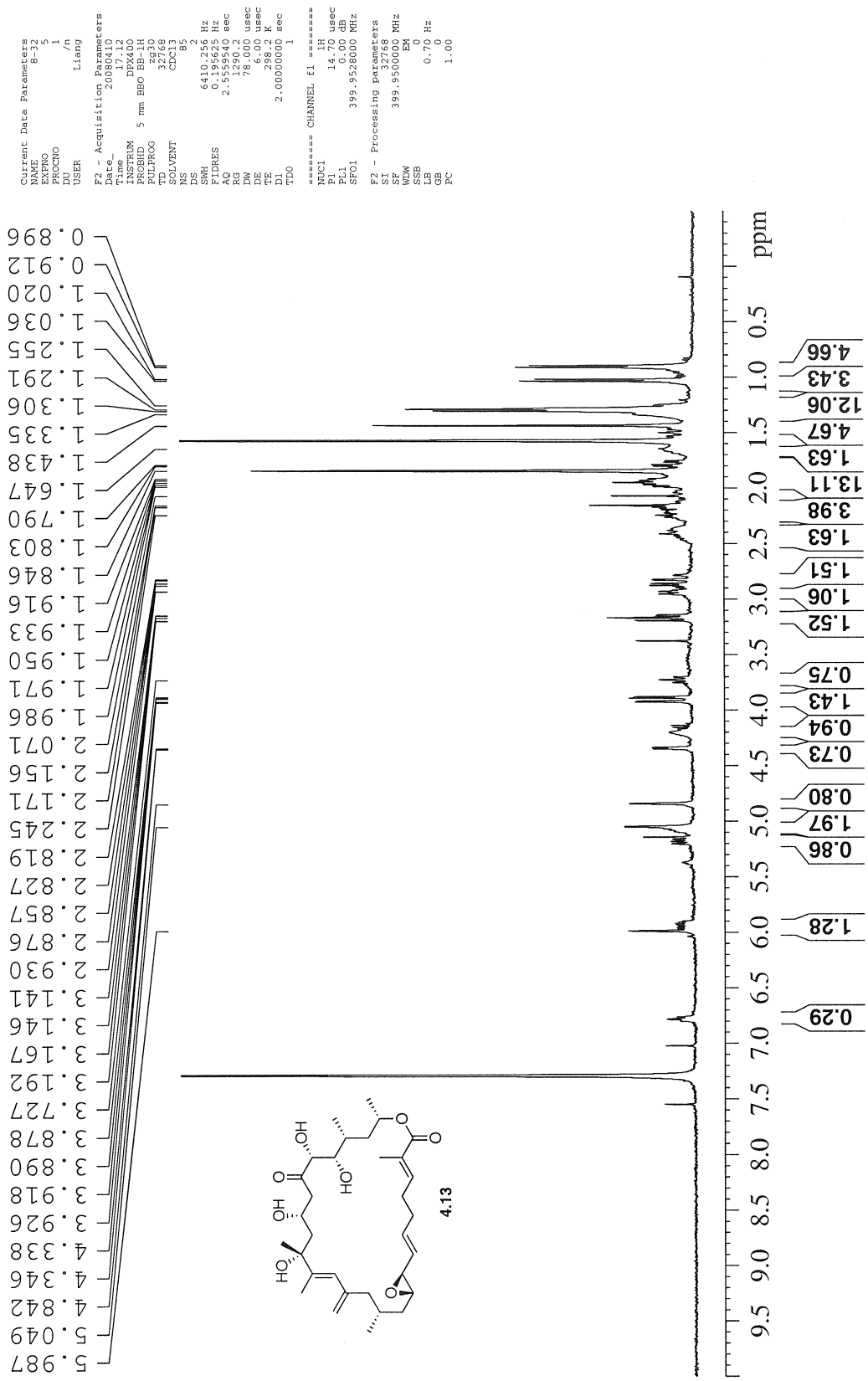
7.18

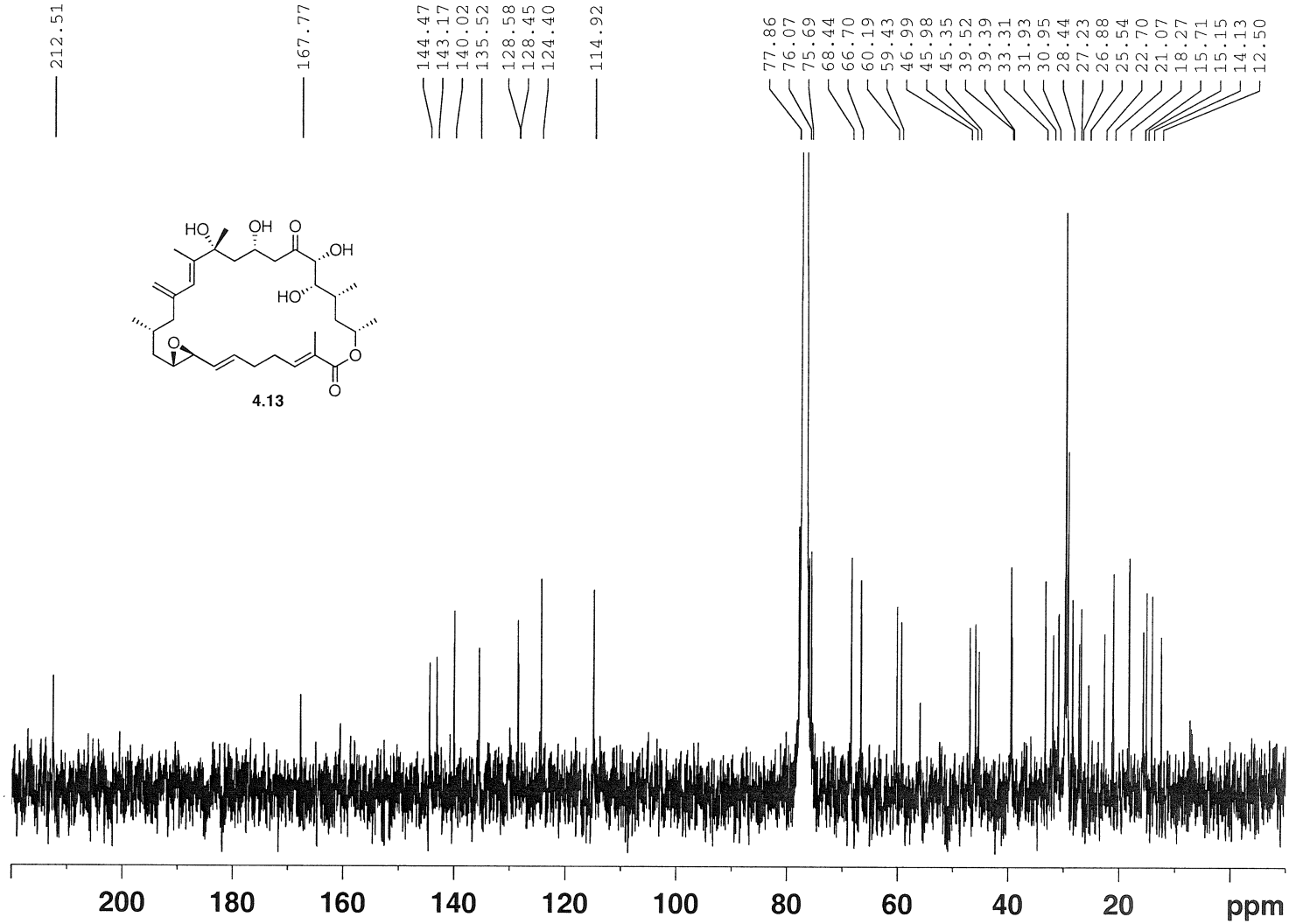
```
Current Data Parameters
NAME                  8-22-2
EXPNO                      3
PROCNO                     1
DU                        /n
USER                  Liang

F2 - Acquisition Parameter
Date_              20080406
Time                  12.20
INSTRUM              DPX300
PROBHD   5 mm QNP  1H/1
PULPROG             zgpg30
TD                   65536
SOLVENT              CDCl3
NS                    3364
DS                       4
SWH             18832.393 Hz
FIDRES          0.287360 Hz
AQ              1.7400308 se
RG                   912.3
DW                26.550 us
DE                 6.00 us
TE                 298.2 K
D1            0.15000001 se
d11           0.03000000 se
DELTA         0.05000000 se
TD0                      1

======== CHANNEL f1 ======
NUC1                  13C
P1                 8.80 us
PL1               -3.00 dB
SFO1          75.4760505 MH

======== CHANNEL f2 ======
CPDPRG2           waltz16
NUC2                  1H
PCPD2             80.00 us
PL2               -3.00 dB
PL12              17.55 dB
PL13              17.55 dB
SFO2         300.1312005 MH

F2 - Processing parameters
SI                   32768
SF            75.4677490 MH
WDW                    EM
SSB                     0
LB                 3.00 Hz
GB                      0
PC                   1.40
```


Current Data Parameters
NAME 8-30
EXPNO 2
PROCNO 1
DU /n
USER Liang
F2 - Acquisition Parameters
Date_ 20080407
Time 12.34
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5599540 sec
RG 512
DW 78.000 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.70 usec
PL1 0.00 dB
SFO1 399.9528000 MHz
F2 - Processing parameters
SI 32768
SF 399.9500000 MHz
WDW EM
SSB 0
LB 0.70 Hz
GB 0
PC 1.00
7.22
ppm
0.75
0.90
1.03
0.94
0.54
0.58
2.38
0.80
0.62
1.56
0.84
1.09
0.86
3.33
2.80
3.32
4.31
11.32
5.56
6.02
7.22
3.49



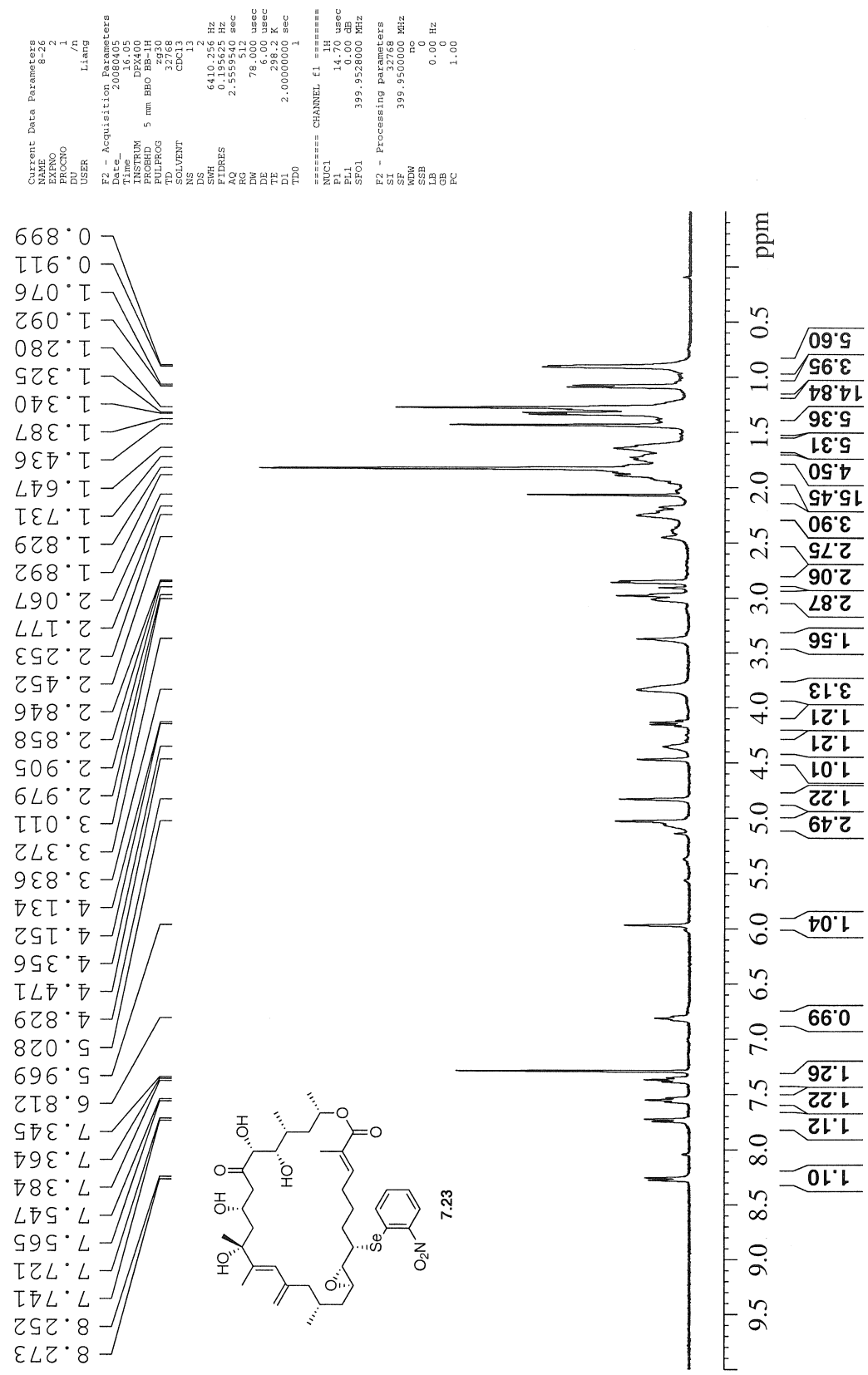

```
Current Data Parameters
NAME                  8-30
EXPNO                    5
PROCNO                   1
DU                      /n
USER                 Liang

F2 - Acquisition Parameter
Date_              20080407
Time                 22.39
INSTRUM             DPX400
PROBHD   5 mm BBO BB-1H
PULPROG            zgpg30
TD                  65536
SOLVENT
NS                  22019
DS                      4
SWH             25125.629 Hz
FIDRES          0.383387 Hz
AQ              1.3042164 se
RG                 2298.8
DW                 19.900 us
DE                  6.00 us
TE                 298.2 K
D1            0.15000001 se
D11           0.03000000 se
DELTA         0.05000000 se
TD0                     1

======== CHANNEL f1 ======
NUC1                  13C
P1                  7.80 us
PL1                -3.00 dB
SFO1         100.5785700 MH

======== CHANNEL f2 ======
CPDPRG2           waltz16
NUC2                  1H
PCPD2             135.00 us
PL2                17.40 dB
PL12               17.40 dB
PL13               17.40 dB
SFO2         399.9516000 MH

F2 - Processing parameters
SI                  32768
SF          100.5675080 MH
WDW                   EM
SSB                    0
LB                 3.00 Hz
GB                     0
PC                  1.40
```

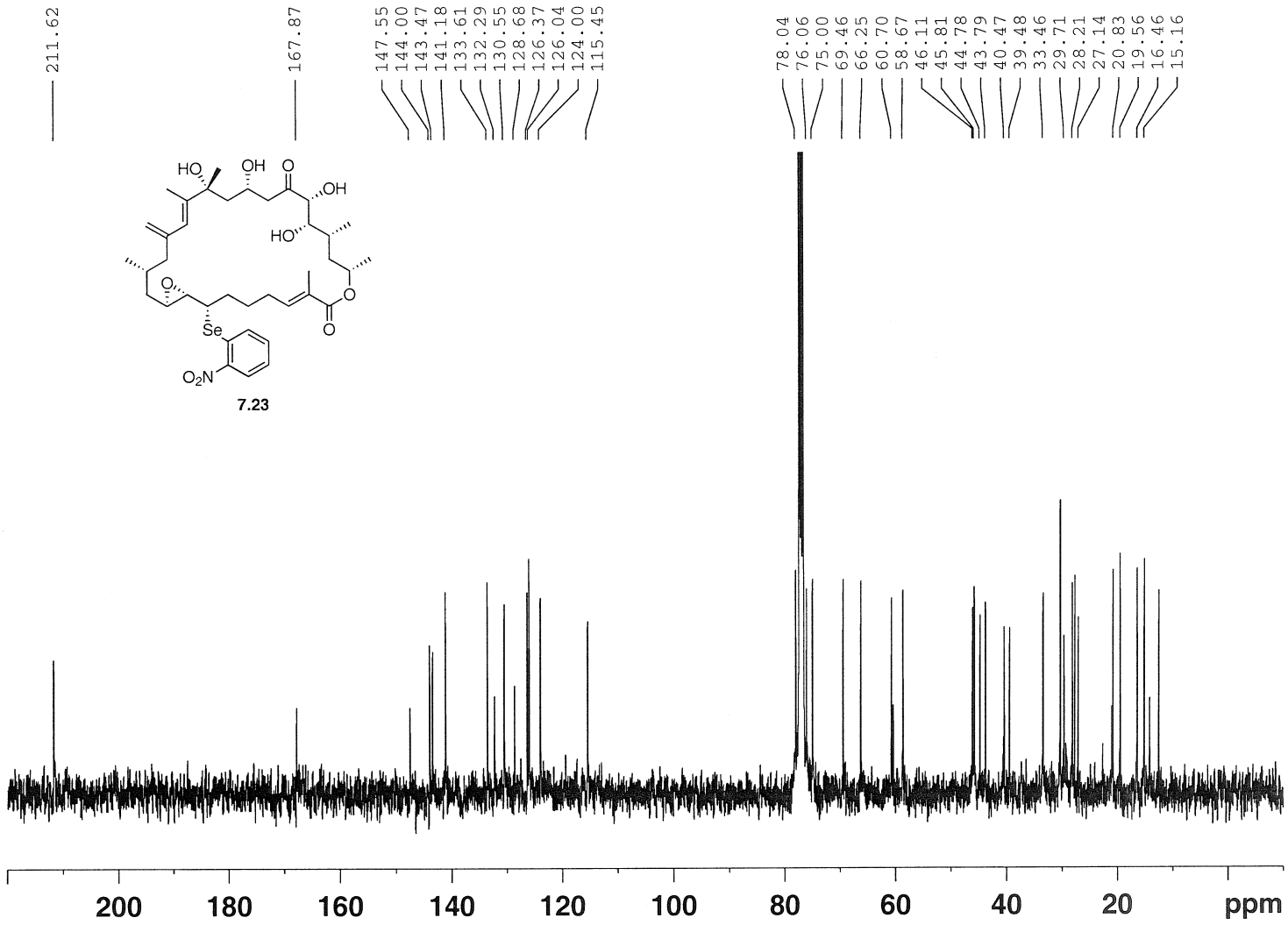

Current Data Parameters
NAME 8-12
EXPNO 5
PROCNO 1
DU /n
USER Liang
F2 - Acquisition Parameters
Date_ 20080410
Time 17.12
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 85
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5559540 sec
RG 1290.2
DW 78.000 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.70 usec
PL1 0.00 dB
SFO1 399.9528000 MHz
F2 - Processing parameters
SI 32768
SF 399.9500000 MHz
WDW EM
SSB 0
LB 0.70 Hz
GB 0
PC 1.00
4.13
ppm
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
0.29
1.28
0.86
1.97
0.80
0.73
0.94
1.43
0.75
1.52
1.06
1.51
1.63
3.98
13.11
1.63
4.67
12.06
3.43
4.66
5.987
5.049
4.842
4.346
4.338
3.926
3.918
3.890
3.878
3.727
3.192
3.167
3.146
3.141
2.930
2.876
2.857
2.827
2.819
2.245
2.171
2.156
2.071
1.986
1.971
1.950
1.933
1.916
1.846
1.803
1.790
1.647
1.438
1.335
1.306
1.291
1.255
1.036
1.020
0.912
0.896



4.13

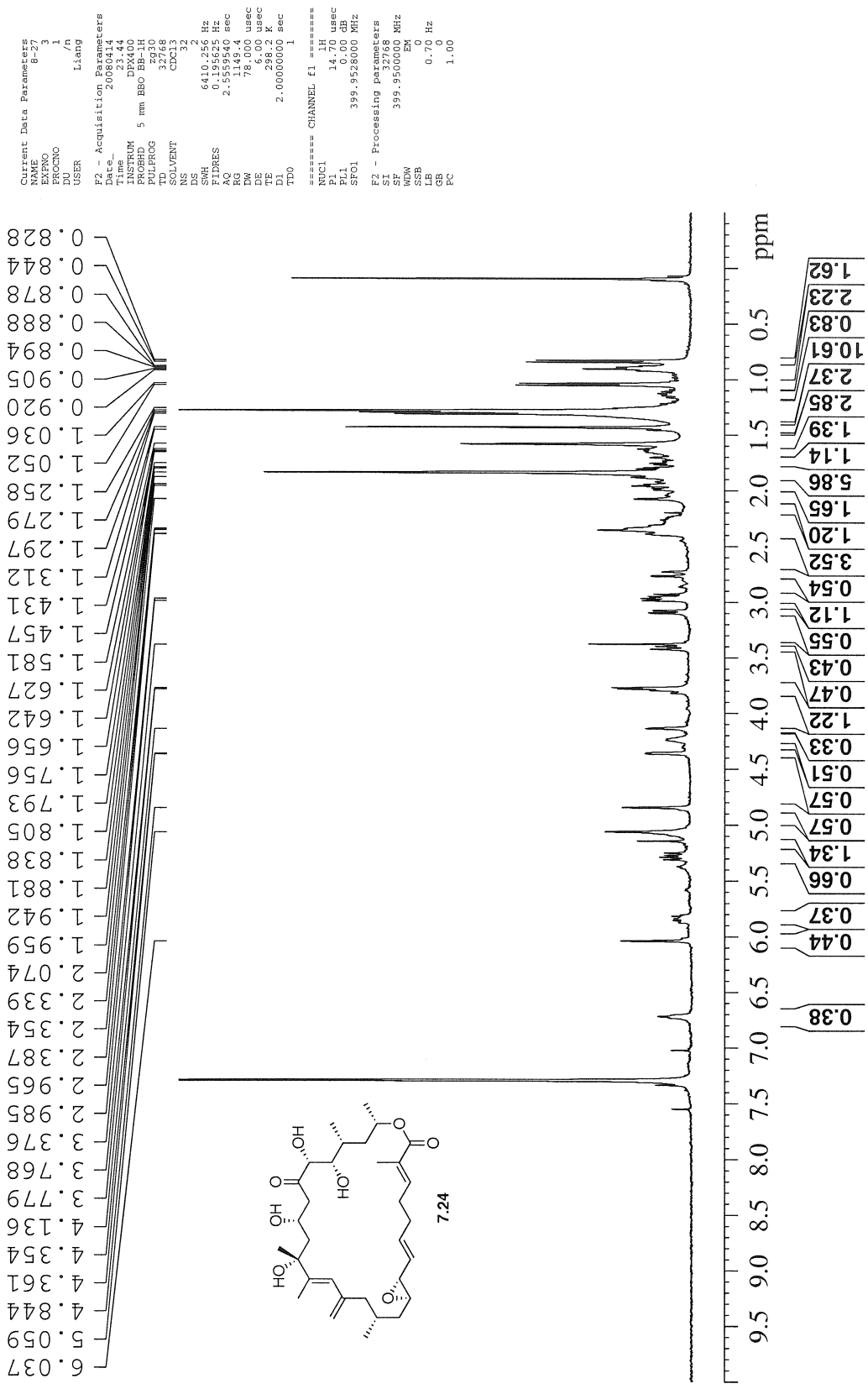
```
Current Data Parameters
NAME                  8-32
EXPNO                   10
PROCNO                   1
DU                      /n
USER                 Liang

F2 - Acquisition Parameter
Date_              20080411
Time                 21.28
INSTRUM            DPX400
PROBHD   5 mm BBO BB-1H
PULPROG             zgpg30
TD                   65536
SOLVENT
NS                   57641
DS                       4
SWH              25125.629 Hz
FIDRES           0.383387 Hz
AQ               1.3042164 se
RG                  3649.1
DW                  19.900 us
DE                   6.00 us
TE                  298.2 K
D1             0.15000001 se
D11            0.03000000 se
DELTA          0.05000000 se
TD0                      1

======== CHANNEL f1 ======
NUC1                   13C
P1                    7.80 us
PL1                  -3.00 dB
SFO1          100.5785700 MH

======== CHANNEL f2 ======
CPDPRG2            waltz16
NUC2                   1H
PCPD2               135.00 us
PL2                  17.40 dB
PL12                 17.40 dB
PL13                 17.40 dB
SFO2          399.9516000 MH

F2 - Processing parameters
SI                   32768
SF            100.5675080 MH
WDW                    EM
SSB                     0
LB                   3.00 Hz
GB                      0
PC                   1.40
```

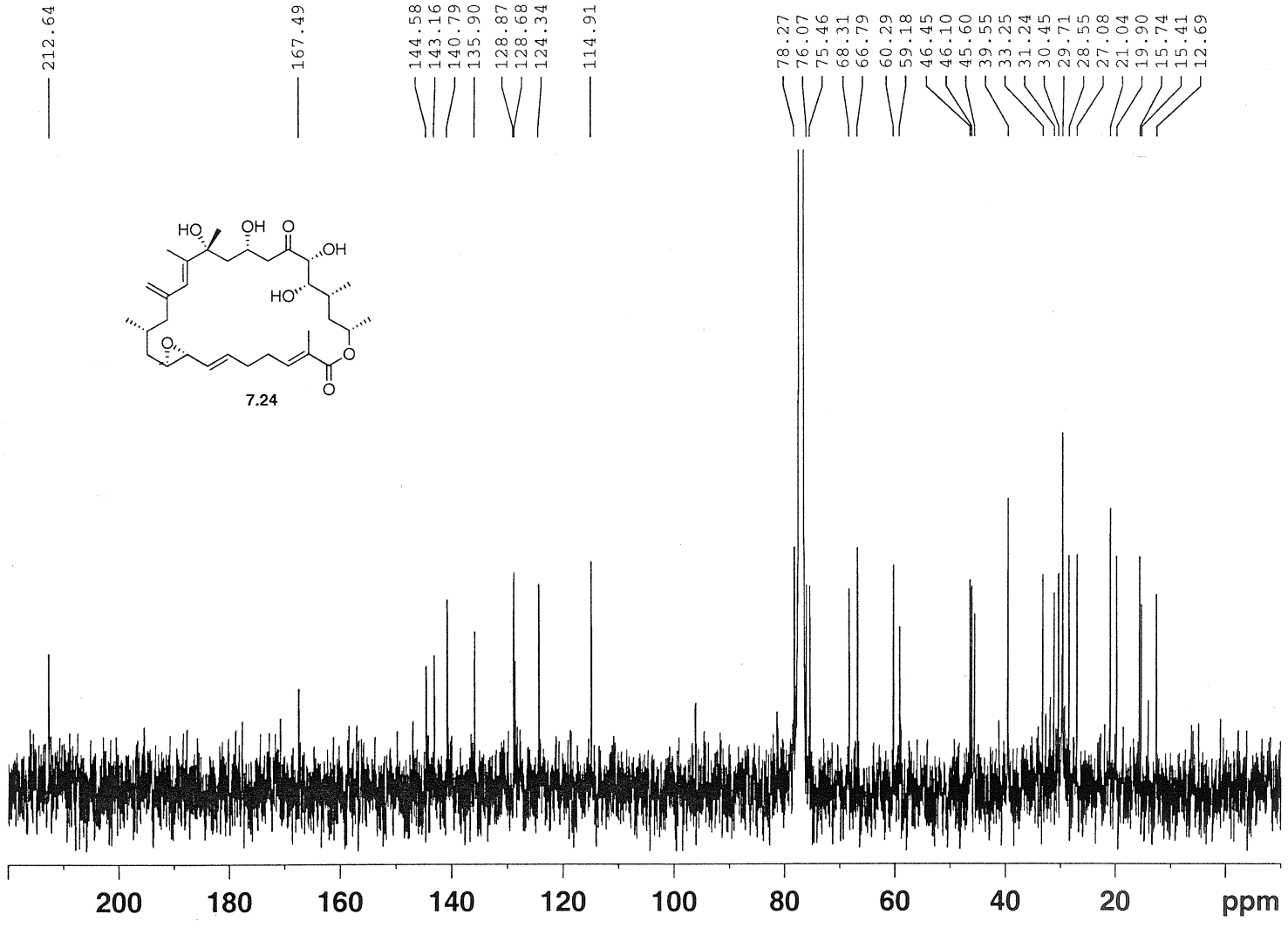

Current Data Parameters
NAME 8-26
EXPNO 2
PROCNO 1
DU /n
USER Liang
F2 - Acquisition Parameters
Date_ 20080405
Time 16.05
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 13
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5559540 sec
RG 512
DW 78.000 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.70 usec
PL1 0.00 dB
SFO1 399.9528000 MHz
F2 - Processing parameters
SI 32768
SF 399.9500000 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
8.273
8.252
7.741
7.721
7.565
7.547
7.384
7.364
7.345
6.812
5.969
5.028
4.829
4.471
4.356
4.152
4.134
3.836
3.372
3.011
2.979
2.905
2.858
2.846
2.452
2.253
2.177
2.067
1.892
1.829
1.731
1.647
1.436
1.387
1.340
1.325
1.280
1.092
1.076
0.911
0.899
7.23
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
1.10
1.12
1.22
1.26
0.99
1.04
2.49
1.22
1.01
1.21
1.21
3.13
1.56
2.87
2.06
2.75
3.90
15.45
4.50
5.31
5.36
14.84
3.95
5.60



7.23

```
Current Data Parameters
NAME                  8-26
EXPNO                    4
PROCNO                   1
DU                      /n
USER                 Liang

F2 - Acquisition Parameter
Date_              20080405
Time                 16.55
INSTRUM             DPX400
PROBHD   5 mm BBO BB-1H
PULPROG             zgpg30
TD                   65536
SOLVENT
NS                    3726
DS                       4
SWH              25125.629 Hz
FIDRES           0.383387 Hz
AQ               1.3042164 se
RG                    4096
DW                19.900 us
DE                 6.00 us
TE                298.2 K
D1            0.15000001 se
D11           0.03000000 se
DELTA         0.05000000 se
TD0                      1

======== CHANNEL f1 ======
NUC1                  13C
P1                 7.80 us
PL1                -3.00 dB
SFO1         100.5785700 MH

======== CHANNEL f2 ======
CPDPRG2           waltz16
NUC2                  1H
PCPD2             135.00 us
PL2                17.40 dB
PL12               17.40 dB
PL13               17.40 dB
SFO2         399.9516000 MH

F2 - Processing parameters
SI                   32768
SF           100.5675080 MH
WDW                    EM
SSB                     0
LB                 3.00 Hz
GB                      0
PC                   1.40
```


Current Data Parameters
NAME 6-27
EXPNO 3
PROCNO 1
DU /n
USER Liang
F2 - Acquisition Parameters
Date_ 20080414
Time 23.44
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.55599540 sec
RG 1149.4
DW 78.000 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.70 usec
PL1 0.00 dB
SFO1 399.9528000 MHz
F2 - Processing parameters
SI 32768
SF 399.9500000 MHz
WDW EM
SSB 0
LB 0.70 Hz
GB 0
PC 1.00
7.24
ppm
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
0.38
0.44
0.37
0.66
1.34
0.57
0.57
0.51
0.33
1.22
0.47
0.43
0.55
1.12
0.54
3.52
1.20
1.65
5.86
1.14
1.39
2.85
2.37
10.61
0.83
2.23
1.62
6.037
5.059
4.844
4.361
4.354
4.136
3.779
3.768
3.376
2.985
2.965
2.387
2.354
2.339
2.074
1.959
1.942
1.881
1.838
1.805
1.793
1.756
1.656
1.642
1.627
1.581
1.457
1.431
1.312
1.297
1.279
1.258
1.052
1.036
0.920
0.905
0.894
0.888
0.878
0.844
0.828



7.24

```
Current Data Parameters
NAME                  8-27
EXPNO                    5
PROCNO                   1
DU                      /n
USER                 Liang

F2 - Acquisition Parameter
Date_              20080414
Time                 23.58
INSTRUM             DPX400
PROBHD   5 mm BBO BB-1H
PULPROG             zgpg30
TD                   65536
SOLVENT
NS                   18937
DS                       4
SWH              25125.629 Hz
FIDRES           0.383387 Hz
AQ               1.3042164 se
RG                    6502
DW                19.900 us
DE                 6.00 us
TE                298.2 K
D1            0.15000001 se
D11           0.03000000 se
DELTA         0.05000000 se
TD0                      1

======== CHANNEL f1 ======
NUC1                  13C
P1                 7.80 us
PL1               -3.00 dB
SFO1        100.5785700 MH

======== CHANNEL f2 ======
CPDPRG2          waltz16
NUC2                  1H
PCPD2             135.00 us
PL2                17.40 dB
PL12               17.40 dB
PL13               17.40 dB
SFO2        399.9516000 MH

F2 - Processing parameters
SI                   32768
SF          100.5675080 MH
WDW                    EM
SSB                     0
LB                 3.00 Hz
GB                      0
PC                   1.40
```