DIELS-ALDER REACTIONS OF A CYCLOPENTADIENONE DERIVATIVE

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The undersigned, appointed by the dean of the Graduate School, have examined the dissertation entitled

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A CYCLOPENTADIENONE DERIVATVE

presented by Maria Goretti Gomes,

a candidate for the degree of doctor of philosophy,

and hereby certify that, in their opinion, it is worthy of acceptance.

Professor Michael Harmata

Professor Kent Gates

Professor Timothy Glass

Professor Peter A. Tipton

Professor Paul Sharp

Dedicated to My Parents

For their endless inspiration and love

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ABSTRACT

An ester derivative of cyclopentadienone, a very reactive species, was generated from methyl-2-bromo-3-oxocyclopent-1-enecarboxylate (**96**) which dimerized instantaneously and decarbonylated to generate an indanone (**97**). Diels-Alder reactions were performed by trapping this fleeting cyclopentadienone derivative with electron rich dienes to generate [4+2] Diels-Alder adducts. The cycloadducts were diastereo- and regioselective. The yields of these reactions were moderate to high. A wide range of dienes were used to show the versatility and scope of these reactions. Using the developed methodology, at attempt was taken to synthesize steroidal drug desogestrel (**218**).

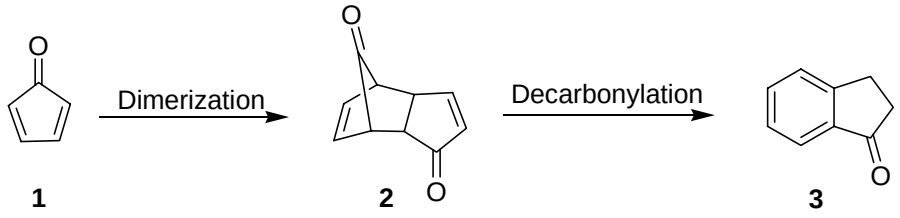
CHAPTER ONE

INTRODUCTION

1-1 Cyclopentadienone and Its Reactivity

1-1.1 Transient Species Cyclopentadienone

Cyclopentadienone (CPD) **1**, also known as cyclone, is a classic example of a fleeting intermediate. Every attempt to isolate **1** has failed since it is prone to dimerize as quickly as it forms and an endo dimer is preferentially formed.[1] Allen and VanAllan[2] observed that any CPD having fewer than three substituents will dimerize as non-dissociating dimers. However, if two of the three substituents are aromatic and next to carbonyl, it will exist as a monomer. Furthermore, if all the four substituents are aromatic, CPDs will sustain as a monomer except when the 2- and 5-positions are methyl or alkyl substituted. Upon heating, the dimer (**2**) undergoes decarbonylation and aromatization to produce indanone (**3**).



Scheme 1. Dimerization of CPD and Decarbonylation

Although isolation of **1** is not known in the literature, instrumental detection of it was first claimed by Chapman and McIntosh.[3] They performed pyrolysis of *o*-phenylene carbonate (**4**) and also *o*-phenylene sulfite (**5**) (Figure 1), deposited the product on NaCl salt plate at -196 °C and recorded the IR spectrum. The product showed a stretching band at 1709 cm^{-1} which was close to the estimated value for carbonyl stretching of **1**, disappeared upon warming. A few years later, Koenig and co-workers[4] performed another type of instrumental detection of CPD **1** using helium I photoelectron spectroscopy. They performed pyrolysis of orthoquinone (**6**), trapped the product in liquid nitrogen, and collected the helium I photoelectron spectrum on it. They believed the spectrum to be of **1**.

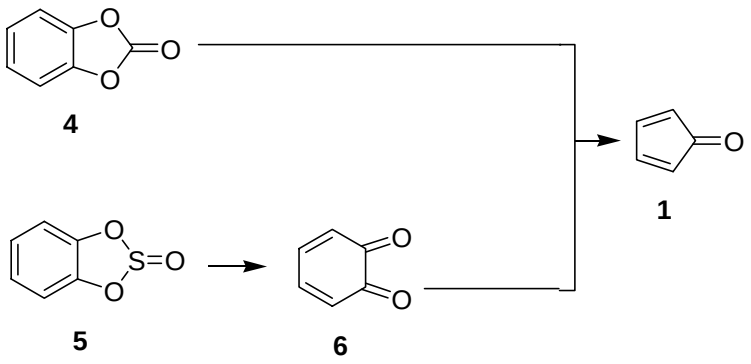


Figure 1. Generation of CPD from Pyrolysis Reaction

1-1.2 Explanations for the Enhanced Reactivity of CPD

Even though CPD (**1**) is similar to fulvene (**10**) structurally, these two compounds behave remarkably differently from each other with respect to chemical reactivity. Fulvene (**10**) can be isolated by distillation and stored in a dilute solution.[5, 6] In contrast,

CPD (**1**), because of its enhanced reactivity, exists as a dimer and therefore can not be isolated.

Garbisch and Sprecher[6] synthesized three different *tert*-butyl substituted cyclopentadienones (Figure 2) in an attempt to explain the enhanced reactivity of CPD **1.** They assumed the bulky substituents would slow the dimerization process, facilitating spectral data collection on these CPD derivatives. The spectral data then would ultimately help them to explain the reactivity in CPD moiety. They found that 2,4-*tert*-butyl and 3-*tert*-butylcyclopentadienones (**7** and **8**) were isolable. However, 2-*tert*-butylcyclopentadienone (**9**) dimerized as soon as it was generated from 4-bromo-2-*tert*-butylcyclopentenone. They determined the rate of dimerization of **7-9** at 30 °C and the relative rates were found to be 1, 5 x 10^6, and >10^8 for **7**, **8**, and **9** respectively (Figure 2). This result reflected the steric influence on retardation of this dimerization process rather than that of bonding interactions.

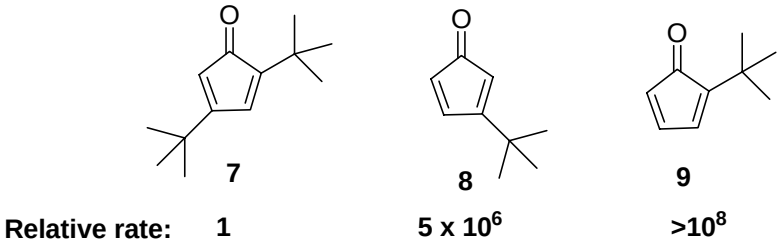


Figure 2. Dimerization Rate of *tert*-Butyl Substituted CPD

From the ^{1}H-NMR spectrum, Garbisch and co-workers found that the chemical shifts of α and β protons in compound **7** were 5.07 and 3.50 ppm and were higher

compared to the corresponding estimated values (3.35 and 1.96 ppm). This observation reflected an increased π-electron density on these α, β carbon atoms in **7**. Consequently the enhanced reactivity of CPD could be from this enhanced electron density centered at C2-C3 bond.

Moreover, the UV spectra of both the compounds **7** and **8** showed two absorption bands around 210 and 385 mμ suggesting a negligible effect of *t*-butyl substitution on the CPD ring. When the solvent was switched from hydrocarbon (isooctane) to alcohol (methanol), a blue shift in the absorption band was observed which was assigned as a π to π^* transition. Fulvene (**10**) had a comparable spectrum in ethanol showing two bands at 241.5 and 360 mμ. These transitions were assigned as $^1A_1 \longrightarrow {}^1A_1$ and $^1A_1 \longrightarrow {}^1B_1$ for these two bands respectively (Figure 3) and a comparison was made with CPD.

From the comparison of the UV spectrum of cyclopentedienone (**1**) with fulvene (**10**) and *HMO* calculation, Garbish and co-workers concluded that the energy gap between *HOMO* and *LUMO* was less in CPD (**1**) compared to that in fulvene (**10**) and was the reason behind the high reactivity of cyclopentadienone (**1**) (Figure 3). Maier *et al.*[7] agreed with Garbish and Sprecher's assumption and also showed that the enhanced reactivity of **1** was due to the reduced energy gap of *HOMO-LUMO* in cylopentadienone (**1**). They explained that *LUMO* of CPD was lowered due to the mixing of low lying π^*_{CO} orbital with the *LUMO* of C=C of the ring.

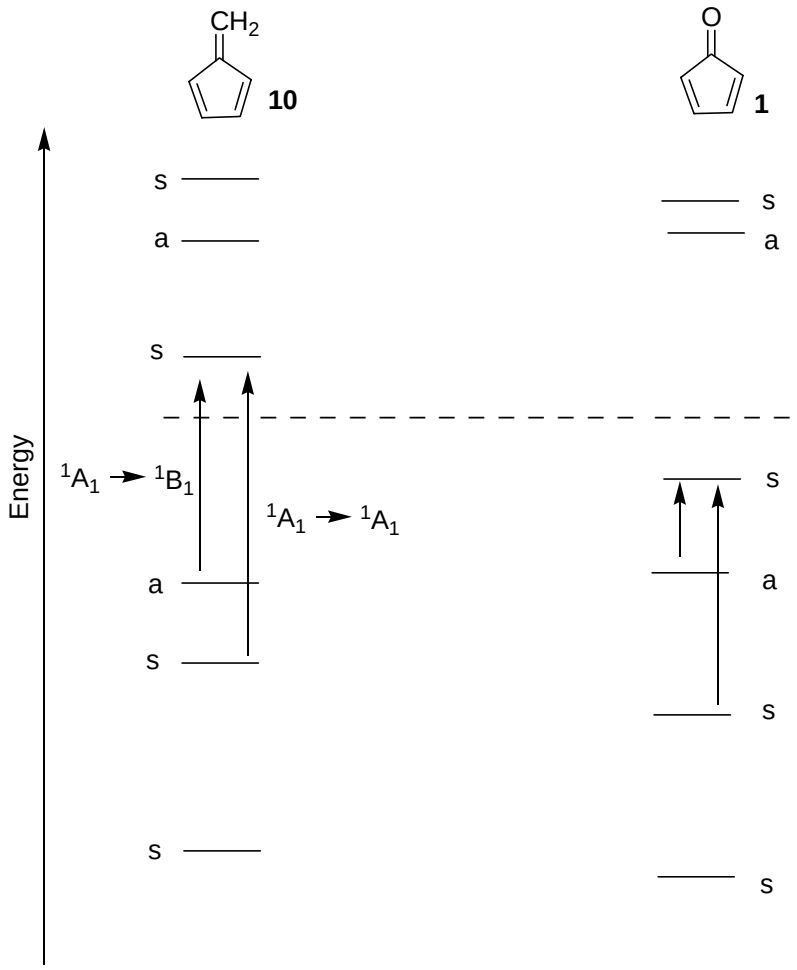


Figure 3. Comparison of HMO Energy between Fulvene (**10**) and CPD (**1**)

In contrast, it is also known in the literature that the inductive effect of carbonyl functionality would lower the *HOMO* of cylopentadienone.[4, 8, 9] Therefore, the enhanced reactivity in cyclopentadienone cannot be due to the reduced energy gap between the frontier molecular orbitals. Quadrelli and Romano *et al.*[10] performed B3LYP/6-31G* calculations on transition states of the cyclopentadieone dimerization process. The results of the caculations showed that the secondary orbital interactions stabilized the *endo* transition state and favored the formation of endo dimer. Electrostatic effects were

responsible for the stereoselectivity, however, the enhanced reactivity in the dimerization process was due to the relief of anti-aromaticity.

According to B3LYP frontier orbital energies of cyclopentadiene and cyclopentadienone, the *HOMO-LUMO* gap in CPD **1** actually was found to be larger than cyclopentadiene, Figure 4. In essence, the energy gap between the *HOMO-LUMO* was not the reason behind the enhanced reactivity of **1**.

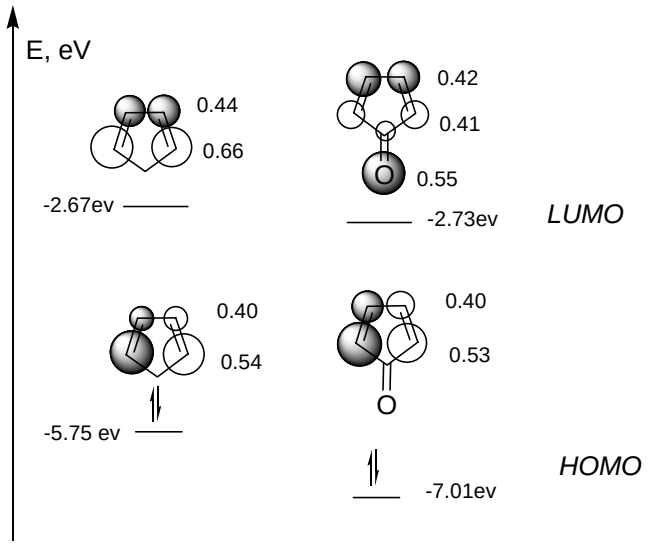


Figure 4. Comparison of Frontier Molecular Orbital Energies between Cyclopentadiene and CPD by B3LYP Method

Furthermore, transition state energy calculations by Quadrelli group showed that the *exo* TS (**11**) lost the antiaromatic property partially, however, the *endo* TS (**12**) lost antiaromaticity completely and the electron delocalization was more pronounced (Figure 5). Besides this, they calculated nucleus-independent chemical shift (NICS)[11] values for the transition states. Negative NICS value refers to an aromatic system and a positive

value indicates an antiaromatic system. CPD showed +11.8 ppm NICS value indicating an antiaromatic system.

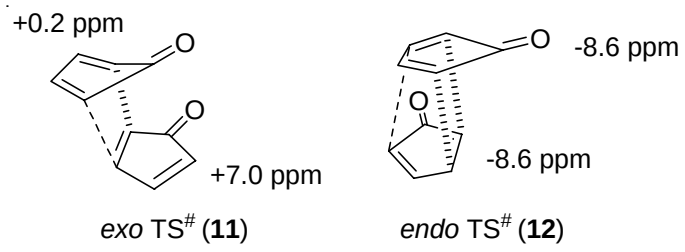


Figure 5. Transition States in Dimerization of CPD and NICS Values

The *exo* TS (**11**) had +0.2 and +7.0 ppm NICS values for 4π and 2π units respectively, reflecting a decrease in antiaromaticity from +11.8ppm. In *endo* TS (**12**), both the units had -8.6 ppm values indicating an aromatic system was generated and an efficient overlapping between both the CPD units occurred. The results of these calculations indicated that relief of antiaromaticity was the reason behind the high reactivity of CPD.

Mitchell and coworkers[12] demonstrated the antiaromatic property of cyclopentadienone from the analysis of ring current and coupling constant changes in cyclopentadienone-fused dihydropyrene system (**13**, **15**). They compared the chemical shifts of both methyl groups on compounds **13-18** (Figure 6) and found that the chemical shifts of methyl groups changed from the cyclopentanone-fused dihydropyrene ring (**14**: -3.74, -3.71 ppm; **16**: -3.50, -3.50ppm) to cyclopentadienone-fused dihydropyrene (**13**: -1.91, -1.87 ppm; **15**: -1.86, -1.83ppm) systems. From the chemical shifts it was obvious that the introduction of the chlorine group on the system did not have much effect as **14**

and **16** as well as **13** and **15** have similar chemical shift values. They assumed the magnitude of the ring current to be proportional to the chemical shift difference between

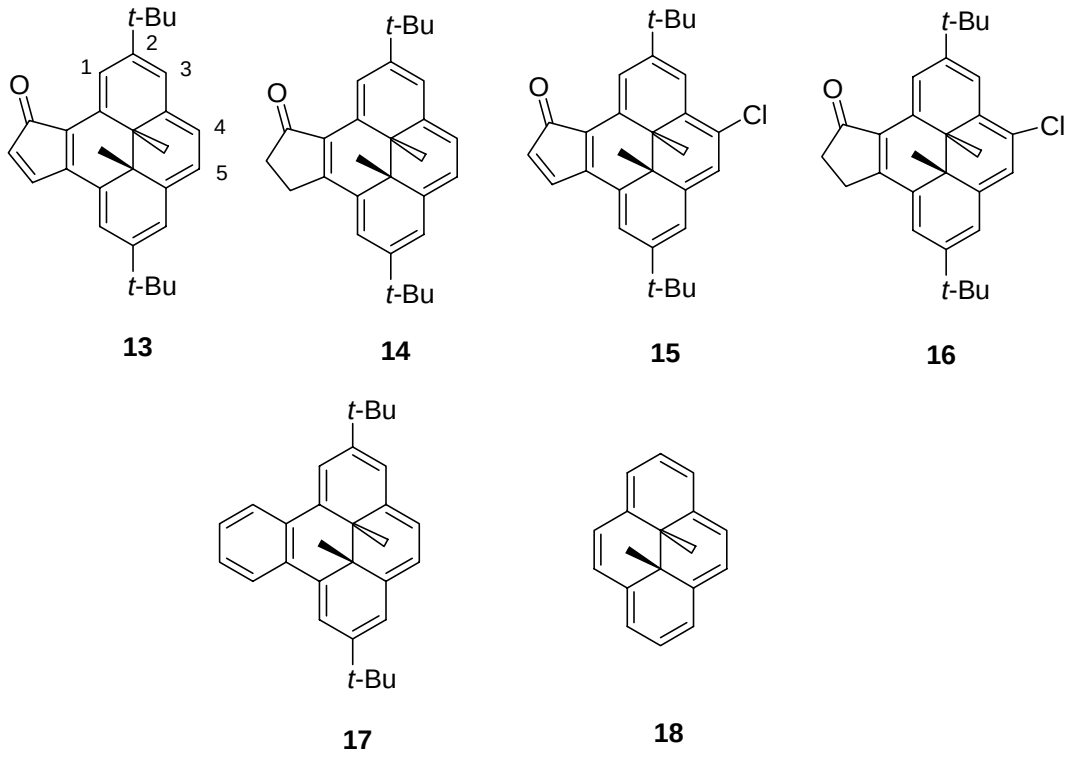


Figure 6. Dihydropyrenes

the internal methyl protons of selected annulene and a nonconjugated system such as **18**. They calculated the ring current effect due to the cyclopentadienone fusion to the dihydropyrenes for **13** as Δδ (**13-14**)/ Δδ (**18-14**) = 39%. Similarly, they found 37% for **15** and 49% for **17** which was due to fused-benzene on **17**. These values indicated that cyclopentadienone has (39/49=) 80% of the ability of benzene to reduce the ring current of dihydropyrene. Additionally, an antiaromatic fusion to the parent ring would shorten

the C4-C5 bond causing an increase in the coupling constant value. They found an increase in $J_{4,5}$ values for compounds **14** to **13** as 6.9 to 8.7 Hz due to the antiaromaticity of cyclopentadienone.

1-1.3 Influence of the Position of Nitrogen Atom(s) in the CPD Molecule

Cyclopentadienones containing a nitrogen atom are known as azaannulenones and they behaved like CPD in chemical reactivity. Gavina and co-workers[13] synthesized different aza- and diazaannulenones (Figure 7) and showed an interesting comparison of the reactivity of these compounds as dienes and dienophiles in the Diels-Alder reaction. 2-Aza-2,4-cyclopentadienone (**19**) could exist freely in the solution and could behave both as a dienophile and a diene.[14] However the C=N bond found to be more reactive than C=C bond as **19** would form adduct only at 2,3 position with a diene. The lifetime of this compound was 2.0 ± 0.5 s, which indicated **19** to be even more reactive than CPD molecule (13.0 s).[14]

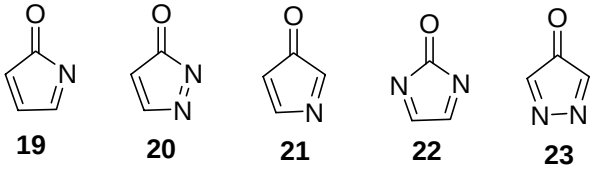


Figure 7. Aza and Diazaannulenones

2,3-Diaza-2,4-cyclopentadienone (**20**) behaved only as a dienophile under the reaction conditions they applied and consequently the probability for dimerization of **20**

was reduced. The lifetime of **20** was found to be 63.5 ± 0.5 s.[15] When all these azaannulenones (**19**-**23**) were generated in the absence of any trapping agent, complex mixtures were formed. Lifetimes of all these reactive intermediates were detected by 'Polyphasic Dynamic Reactor' and are included in Table 1. They found that the position of the nitrogen atom in these molecules was responsible for the reactivity of these species. Compounds **19** and **22** were very short lived indicating the *N*-acylimine group was responsible for their reactivity. Compounds **21** and **23** showed a little longer life span, which Gavina and co-workers explained to be due to the presence of *β*-nitrogen atom in the molecule.

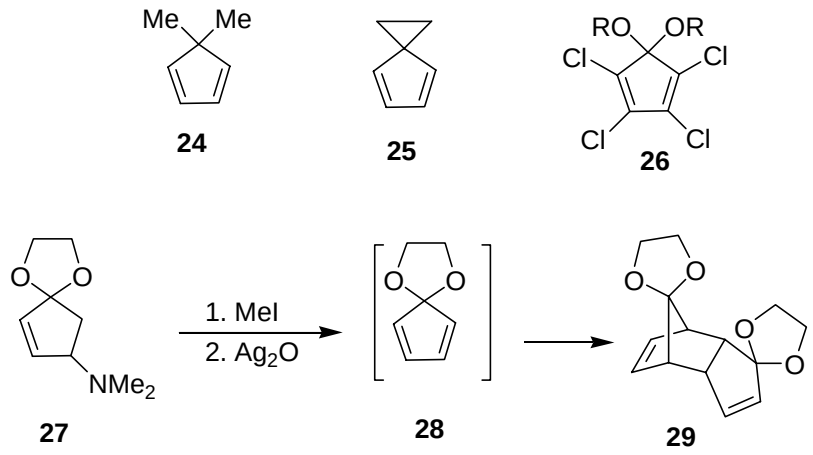
Table 1. Lifetimes of Aza and Diazaannulenones[13]

Annulenones	Lifetimes, s
19	2.0 ± 0.5
20	63.5 ± 0.5
21	11.5 ± 0.5
22	<1
23	16.0 ± 0.5

1-1.4 Reactions of Cyclopentadienone Acetal (CPDA) with Pyrrole and Indole

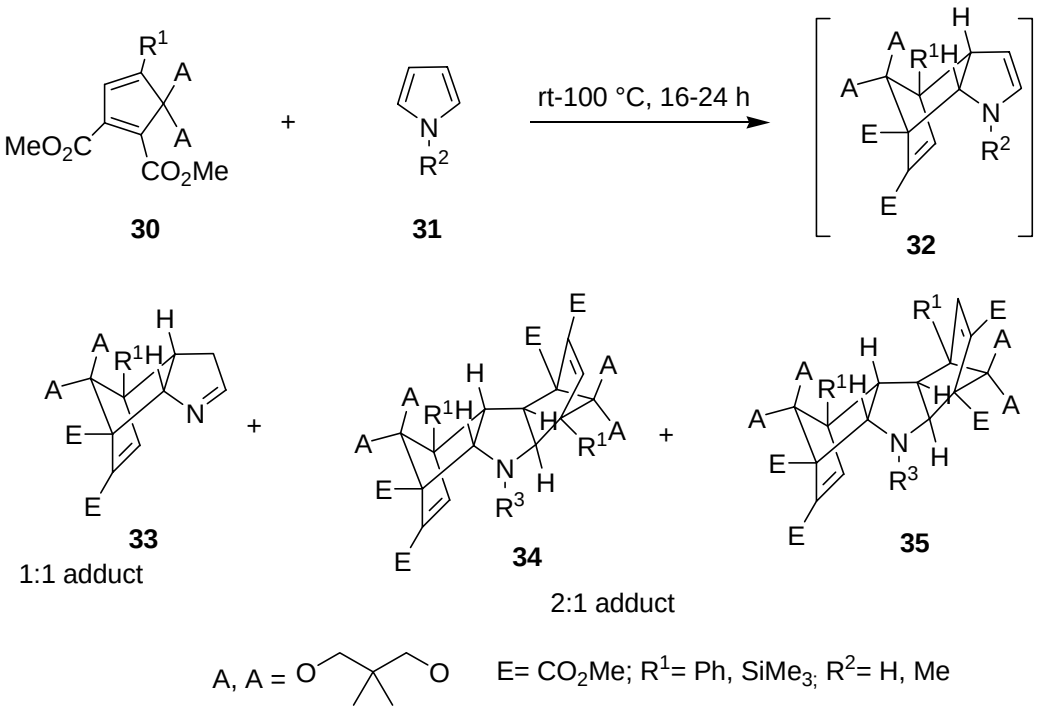
DePuy and co-workers[16, 17] assumed that acetal of CPD would be more stable than CPD as both 1,1-dimethylcyclopentadiene (**24**) and 1,1-dimethylenecyclopentadiene (**25**) were quite stable in the monomeric form and also ketal of tetrachlorocyclopentadineone (**26**) was isolable in its monomer form. They performed Hofmann elimination on 4-dimethylaminocyclopentenone ketal (**27)** in an attempt to isolate CPDA **28**. However, they failed and isolated only dimer **29**. Later Eaton and Hudson[18] experimentally

determined the dimerization rate of ethylene ketal of CPD and found this ketal dimerized 5 x 10^5 times faster than CPD **1**. (Scheme 2)



Scheme 2. Dimerization of CPDA

Recently, Nakamura *et al.*[19] reported Diels-Alder reactions between a methylcarboxy- substituted cyclopentadienone acetal (**30**) and heterocyclic pyrrole (**31**) or indole. They showed for the first time that 1*H*-pyrrole acted as a dienophile. Depending on the substituents on **30**, two different types of adducts (1:1 and/ or 2:1 adducts) were obtained. The cycloadducts were all *endo* selective. They assumed adduct **33** formed via intermediate enamine **32** and a spontaneous isomerization to imine **33** (Scheme 3).



Scheme 3. Diels-Alder Reaction with Pyrroles

Even though **30** had two electron-withdrawing groups (CO_2Me) attached to it, this compound still performed as a diene and pyrroles (**31**) as dienophiles. Computational calculations using HF/6-31G* supported this observation as the *LUMO* of CPD **30** overlapped with *HOMO* of pyrrole **31** (Figure 8).

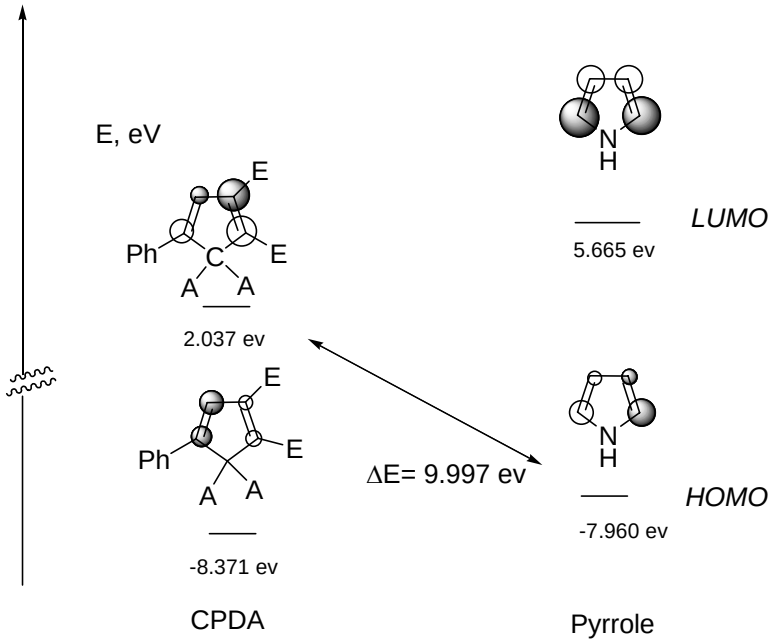
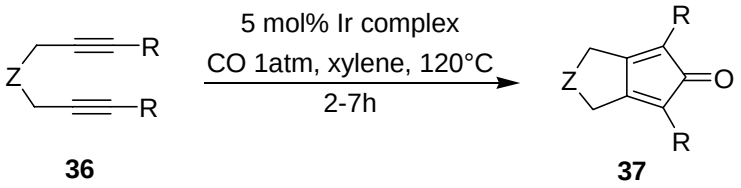


Figure 8. FMOs of CPDA and 1*H*-Pyrrole

1-2 Synthesis of cyclopentadienones

Tetra-substituted cyclopentadienones are stable and easily isolable and can be synthesized by various methods. Transition metal mediated alkyne-alkyne-CO coupling is one of the well known methods to directly synthesize these compounds. In the literature $CpCo(PPh_3)_2$,[20] $RhCl(PPh_3)_3$[21] and iridium- catalyzed [22] synthesis of alkyl and aryl substituted cyclopentadienones are known. Shibata and co-workers[22] showed an efficient way to use catalytic amounts of different iridium catalysts to synthesize these cyclopentadienones (**37**) in high yields. Several examples are included in Table 2.

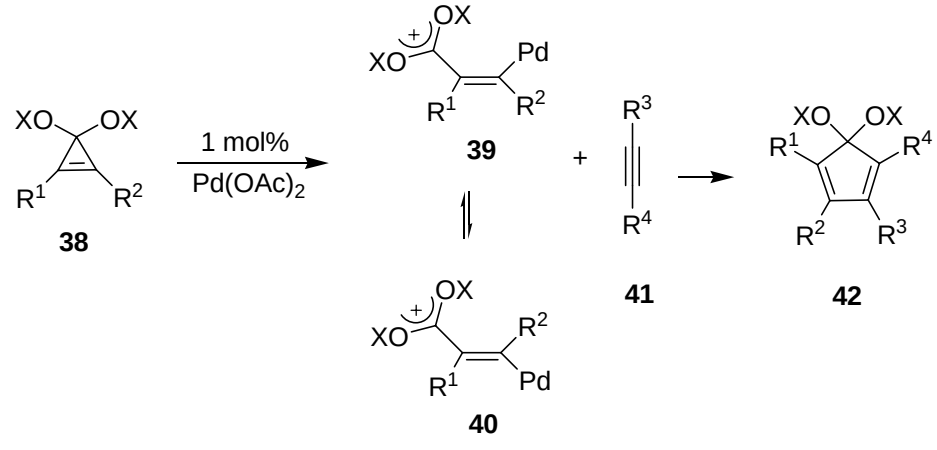
Table 2. Iridium Complex Catalyzed Cyclopentadienone Formation



R	Z	Yield (%)[a]
Ph	$C(CO_2Bn)_2$	85
Ph	$C(CO_2Et)_2$	99
Ph	$C(CO_2t\text{-}Bu)_2$	92
4-MeO-Ph	$C(CO_2Bn)_2$	94
4-Cl-Ph	$C(CO_2Bn)_2$	79
4-MeO_2CPh	$C(CO_2Bn)_2$	89
Ph	CH_2	79
Ph	O	65

[a] Catalyst $IrCl(CO)(PPh_3)_2$ was used in these reactions

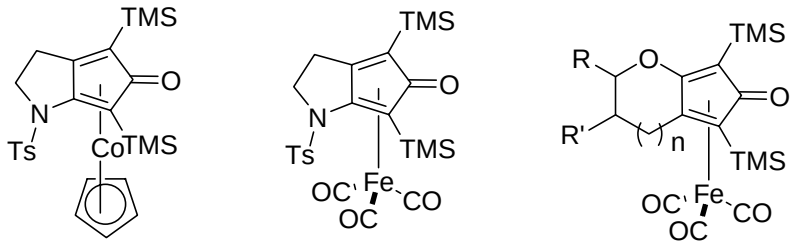
Nakamura *et al.*[23] performed $Pd(OAc)_2$ catalyzed [3+2] synthesis of cyclopentadienone acetals (**42**) from substituted cyclopropenone acetals (**38**) and electron-deficient acetylenes (**41**). Further Diels-Alder reactions of these acetals with dienophiles were performed as well. The proposed mechanism is shown in Scheme 4.



Scheme 4. Pd-catalyzed Synthesis of CPDAs

Recently, Wender and co-workers[24] performed a versatile synthesis of a wide range of substituted cyclopentadienones from $[RhCl(CO)_2]_2$ catalyzed [3+2] cycloaddition of cyclopropenones with aryl-alkyl substituted acetylenes. They used only 1-5 mol% of the catalyst and even benzyne was used as the alkyne to produce 69% of cyclopentadienone derivative.

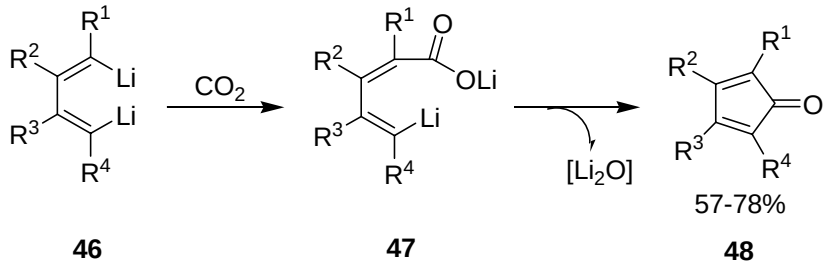
To have more control on reactive cyclopentadienone, Rainier and Imbriglio[25-27] made cyclopentadienone metal complexes. They performed the synthesis of cobalt[25] and iron[26] complexes of 3-amiocyclopentadienones from [2+2+1] cycloadditions of nitrogen acetylenes and pendant alkynes. Later they synthesized iron complexes of 3-alkoxycyclopentadienones from ynol ether alkyne [2+2+1] cycloaddition reactions (Figure 9).[27] Oxidative demasking of these metal complexes followed by trapping the CPDs chemo- and regioselectively with dienes and dienophiles made this process synthetically useful.



43 **44** **45**

Figure 9. Metal Complexes of Cyclopentadienone Derivatives

A simple and convenient synthesis of tetra substituted cyclopentadienones (**48**) was reported by Xi *et al*.[28] They showed that 1,4-dilithio-1,3-dienes (**46**) could be trapped with carbon dioxide and generate cyclopentadienones in single step in high yield (Scheme 5).



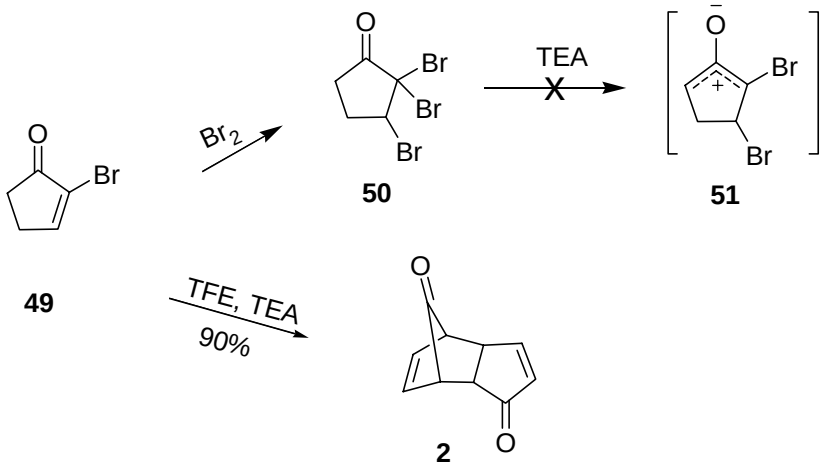
Scheme 5. Synthesis of cyclopentadienones from Dilithiobutadienes

Another versatile way to synthesize cyclopentadienones is choosing a suitable precursor to generate this reactive species *in situ* before trapping it with an appropriate reagent. Among different precursors to produce this transient species, bromocylopentenone derivatives are well known.

In the literature Hafner[29] first showed that 5-bromocyclopentenone could be used as a precursor to generate CPD (**1**). However, soon after this report, DePuy *et al.*[30, 31] proved that CPD was actually generated from 4-bromocyclopentenone rather than 5-bromocyclopetenone. Harmata *et al*.[32] demonstrated for the first time that 2-bromocyclopentenone (**49**) could be used as a precursor to slowly generate CPD.

During an exploration of the 4+3 cycloaddition reaction by Harmata and co-workers, an attempt was made to generate an oxyallylic cation from the

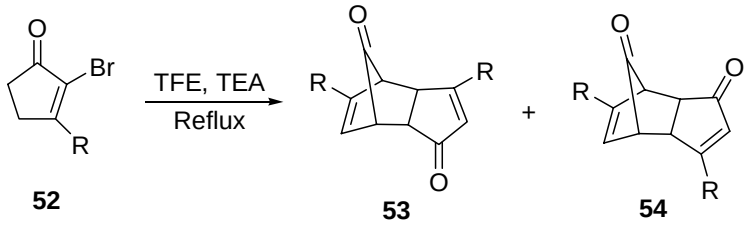
tribromocyclopentanone (**50**), which was derived from 2-bromocyclopentenone (**49**) (Scheme 6). However, CPD dimer (**2**) was isolated in 57% yield when 2-bromocyclopentenone (**49**) was treated with TEA at room temperature in trifluoroethanol (TFE) for a week and later the yield improved to 90% when the reaction was performed at reflux for 1 hour.[32]



Scheme 6. Reaction of 2-bromocyclopentenone with TEA

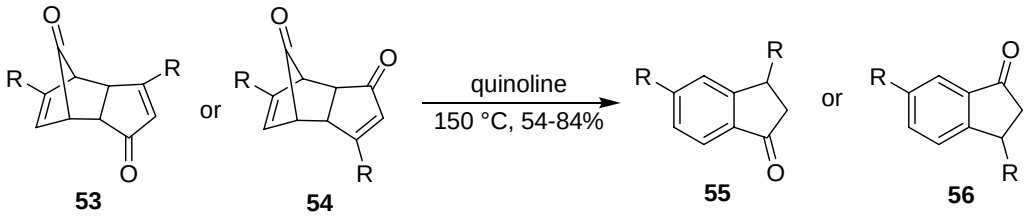
Motivated by this discovery, a series of 3-aryl-2-bromo-cyclopentenones (**52**) was synthesized to explore this reaction under optimized conditions (TEA in refluxing TFE). This reaction generated CPD dimers (**53**, **54**) diastereoselectively and moderately regioselectively. Several results are shown in Table 3.

Table 3. Synthesis of CPD Dimers



R	Yield (%)	Ratio
Ph	72	3:1
3-MeO-Ph	87	4.3:1
4-*t*-Bu-Ph	90	10.2:1
2,5-di-Me-Ph	97	5.6:1

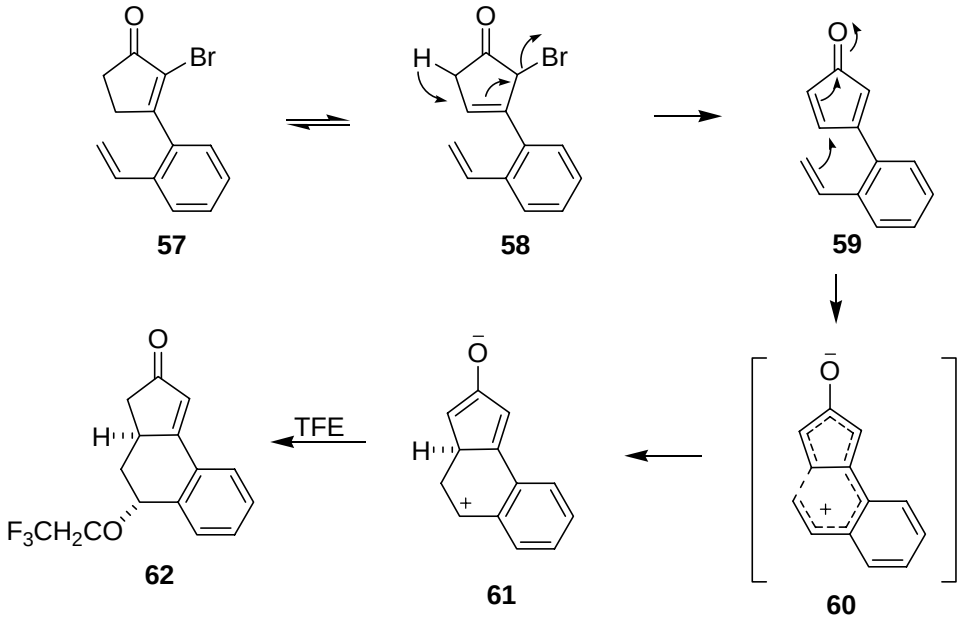
Further heating of these dimers (**53**, **54**) in quinoline generated indanones (**55**, **56**) (Scheme 7). This methodology showed an effective way to slowly generate CPD from a 2-bromocyclopentenone derivative and synthesize substituted indanones.



Scheme 7. Generation of Indanone from CPD Dimer

Recently, Harmata *et al.* showed another interesting way of performing intramolecular cycloaddition involved in cyclopentadienone system.[33] In this reaction, cyclopentadienone (**59**) was generated from 2-bromo-3-(2-vinylphenyl)cyclopent-2-

enone (**57**) and was intramolecularly attacked by the 2π electrons of styrene, generating carbocation (**61**), which was further trapped by the polar solvent trifluoroethanol (TFE) producing product (**62**) (Scheme 8).



Scheme 8. Mechanism of Intramolecular Cyclization Reaction of 2-bromocyclopentenones

This reaction could go through another pathway in what styrene could attack at position C-2 rather than C-4. Density functional theory (DFT) calculations on both the pathways proved that the intermediate involving C-2 attack would generate an antiaromatic intermediate, which had higher nucleus independent chemical (NIC)[34] shift value. On the other hand, attack at C-4 would relieve the antiaromaticity of cyclopentadienone as the calculated NIC value of the intermediate found to be negative.

Thus, the reaction preceded utilizing deantiaromatization as the driving force. Several examples developed by this process are shown in Figure 10.

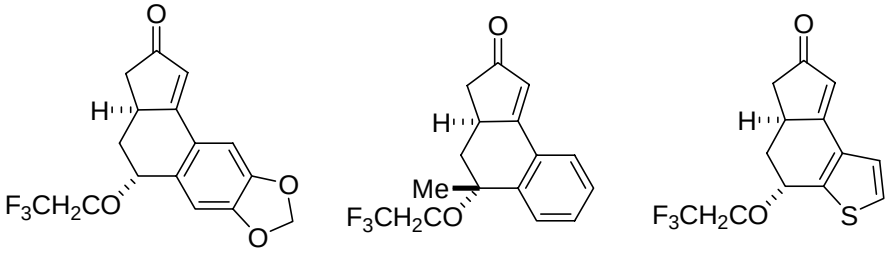
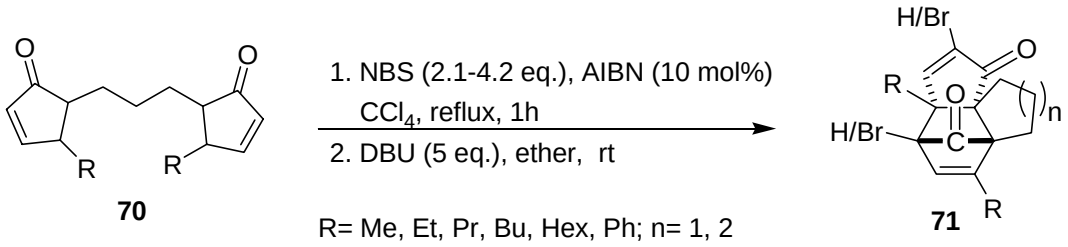


Figure 10. Intramolecular Cycloadducts

Another creative aspect of CPD chemistry was reported by Harmata and Rayanil.[35] They showed that angular triquinane (**71**) units could be generated in a single step from an intramolecular cycloaddition reaction of dicyclopentadienone. Treatment of dicyclopentenones (**70**) with the brominating reagent *N*-bromisuccinamide (NBS) generated 4,4′-dibromocyclopentenones. When these dibromo compounds were subjected to treatment with DBU at room temperature, triquinanes (**71**) were generated in 20-30% yield over three steps (Scheme 9). This reaction was endo selective and only one diastereomer was isolated. Unfortunately, the process suffered from low yield due to the allylic bromination reaction.



Scheme 9. Synthesis of Triquinane from Dicyclopentenone

Fuchs and Nantz[36] synthesized cyclopentenones (**72, 73**) as precursors to benzyl ester substituted cyclopentadienone. When they treated **72** in toluene, isomer **73** was formed in 96% yield. They assumed **73** was formed from a 1,5-sigmatropic rearrangement of the phenylsulfonyl group from the enol of **72**. When they treated **73** with tripropylamine in benzene indanone **78** was formed in 52% yield. However, they found the reaction produced a better yield (75%) when they used **72**. The mechanism for the formation of indanone proposed formation of a cyclopentadienone which reacted with another molecule of itself generating cycloadduct **75**. Further extrusion of CO and aromatization furnished the indanone **78**. They also assumed cycloadduct **79** could form as well and 1,9-sigmatropic rearrangement of **79** would furnish indanone **78** (Figure 11).

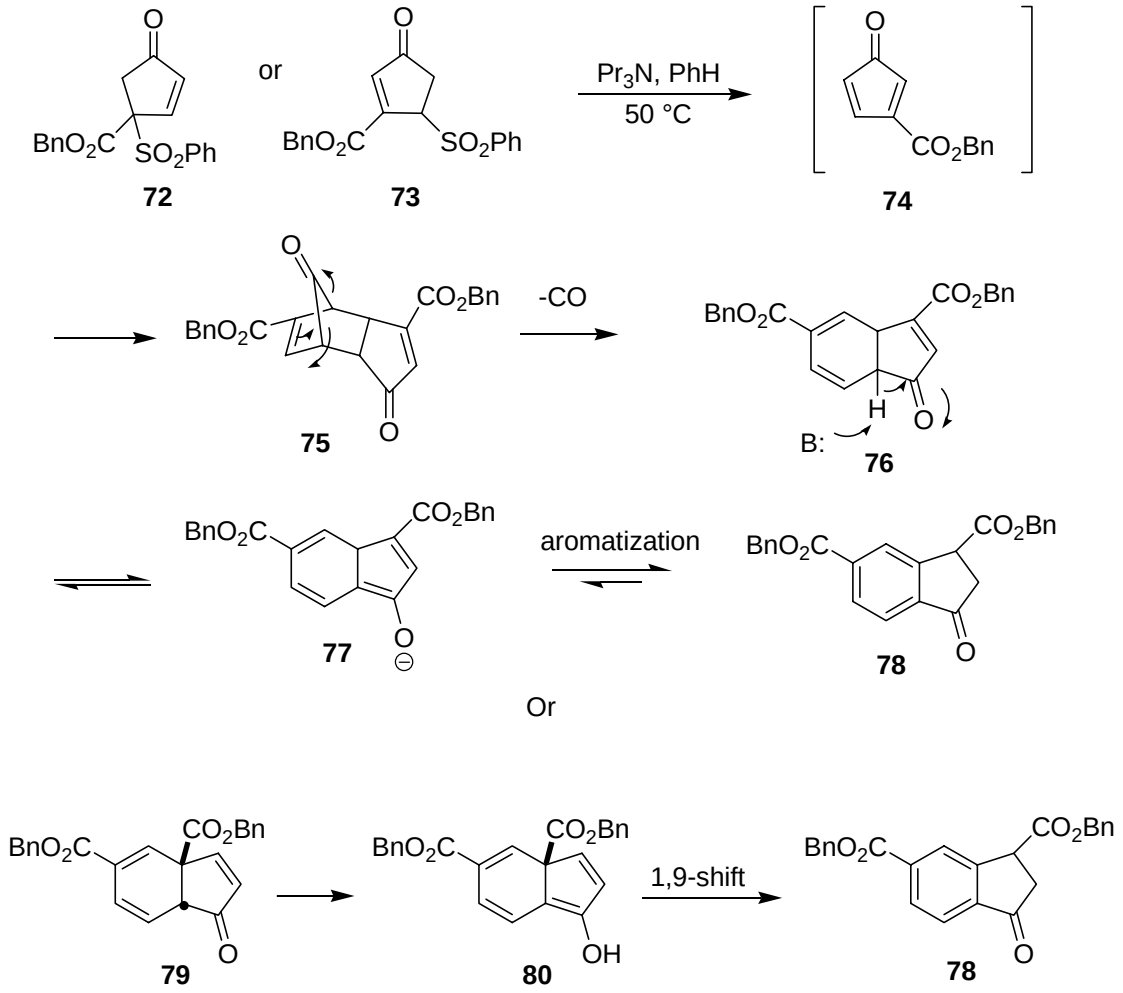


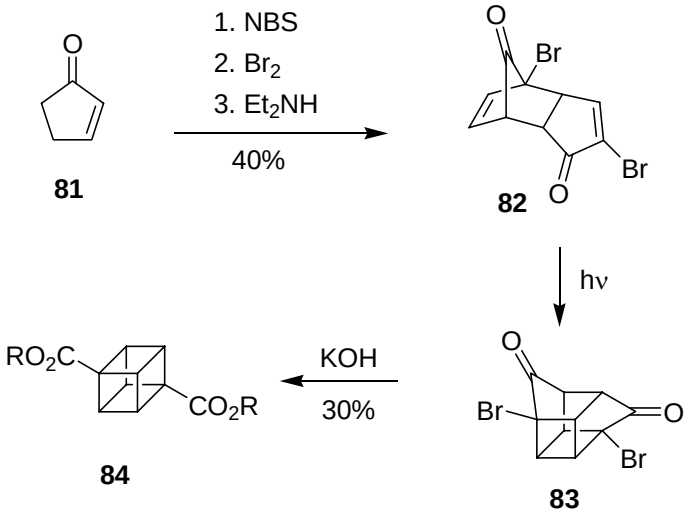
Figure 11. Dimerization of Cyclopentadienone

Fuchs and Nantz also tried to trap cyclopentadienone (**74**) with 2,3-dimethylbutadiene and Danishefsky's diene and successfully obtained the Diels-Alder adducts in 84% and 89% yield, respectively. The results suggested an efficient way of generating cyclopentadienone and using it in stereocontrolled cycloaddition reactions.

1-3 Uses of Cyclopentadienones

Cyclopentadienones are intriguing molecules with a wide variety of synthetic use. These compounds are most widely used in Diels-Alder reactions, organometallic complexes,[37] catalyst synthesis,[38] and precursors to highly substituted aromatic systems used in liquid crystals, nonlinear optical materials and carbon rich polymers.[39]

An interesting cage-like compound cubane was synthesized from a simple cyclopentadieneone molecule by Eaton and Cole.[40] They started with cyclopentenone **81** to generate 2-bromocyclopentadieneone and afforded endo dimer **82** in 40% yield after 3 steps. The dimer was subjected to UV irradiation to generate compound **83** and finally base treatment of **83** furnished the ester substituted cubane **84** in 30% yield from the dimer **82**. (Scheme 10)



Scheme 10. Synthesis of Cubane

Highly functionalized aromatic compounds are synthesized from cyclopentadienone precursors and many examples are known in the literature. Heterosuperbenzenes (**85**), member of graphitic molecules could be used as LED (light emitting diode) material as these molecules have high conjugated π-electron system. Draper and co-workers[39] performed an efficient synthesis of nitrogen substituted superbenzene (**85**) via cyclopentadienone (**86**) in 14% yield after 6 steps starting form *p*-*tert*-butyl-bromobenzene. Hexaethynylbenzenes (**87**), useful as liquid crystals, nonlinear optical materials, precursors to two dimensional carbon network and carbon rich polymeric materials, were produced from cyclopentadienone (**88**) by Tobe *et al.*[41] (Figure 12).

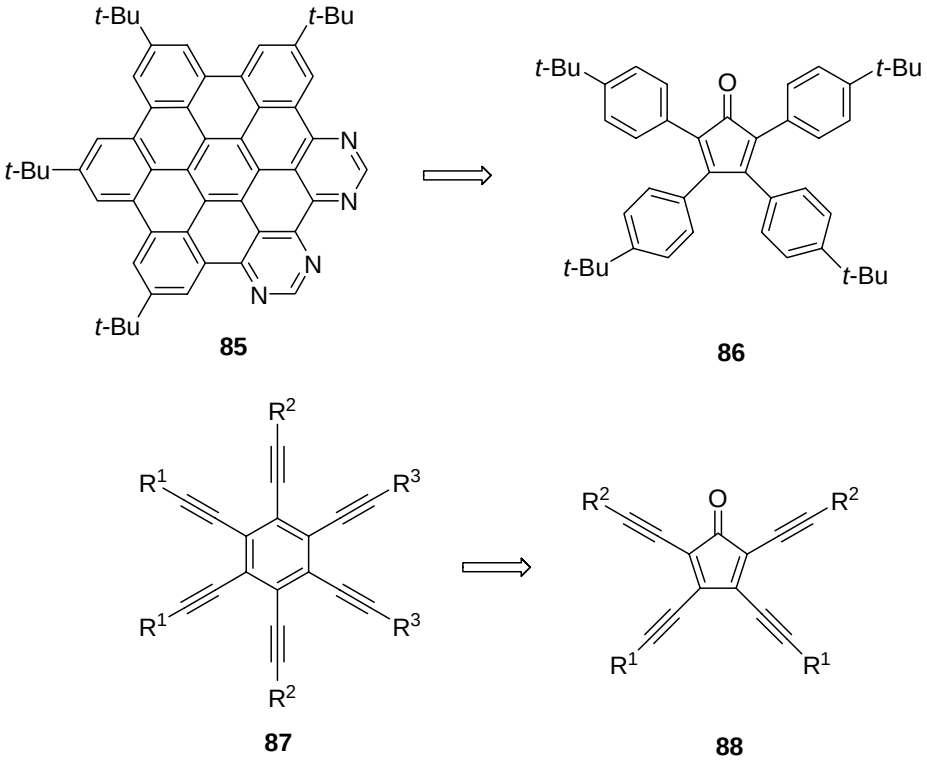


Figure 12. High Functionalized Benzenes from cyclopentadienones

Because of the high reactivity of CPD (**1**), it is not widely used in the synthesis of natural products. Simoni and co-workers[42] showed an elegant way to utilize **1** for the synthesis of (±)-sarkomycin (**92**), Figure 13. Usually **1** performs as a dienophile, a 2π component in a Diels-Alder reaction. When 4-bromocylopentanone (**89**) was treated with TEA, CPD **1** was generated and trapped with ethyl acrylate **90** with 20% yield. From this cycloadduct, they synthesized the natural product **92** in 38% overall yield.

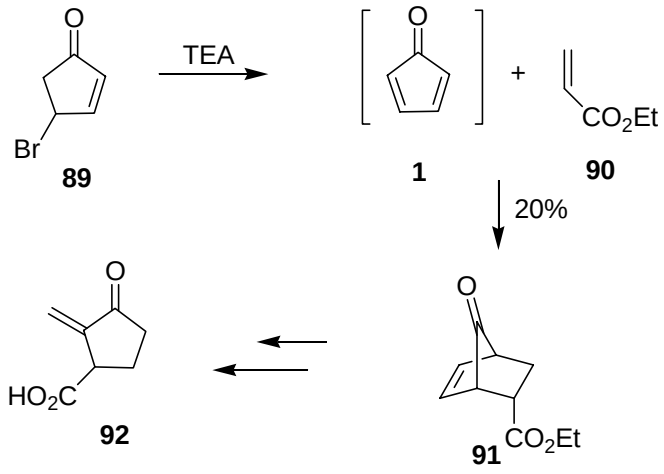


Figure 13. Synthesis of (±) Sarkomycin

The total synthesis of the tricyclopentanoid hirsutic acid (**93**) and complicatic acid (**94**) were performed stereoselectively by Schuda *et al.* from the acetal of cyclopentadienone dimer (**95**).[43]

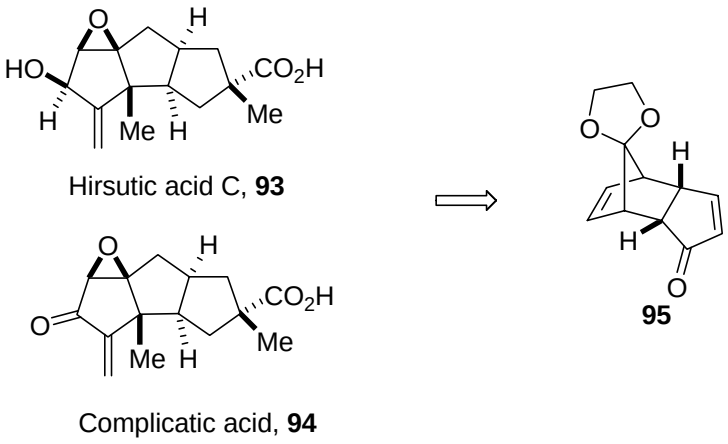


Figure 14. Hirsutic Acid C and Complicatic Acid from CPDA

From the description in previous sections it is clear that cyclopentadienones are synthetically very useful compounds. Because of their high reactivity, these compounds are usually generated *in situ* before utilizing them efficiently in any synthesis. Previously, Harmata and co-workers[32] showed an efficient way to generate 3-aryl substituted cyclopentadienones from 2-bromo-3-phenyl- substituted cyclopentenones **52**. However, an ester-substituted cyclopentadienone was never generated from any 2-bromo-cyclopentenone precursor. Exploration of the chemistry of generation of a 3-carboalkoxy-substituted cyclopentadienone from a 2-bromo-3-carboalkoxy-substituted cyclopentenone and trapping of this transient intermediate with different dienes will be discussed in the following chapter.

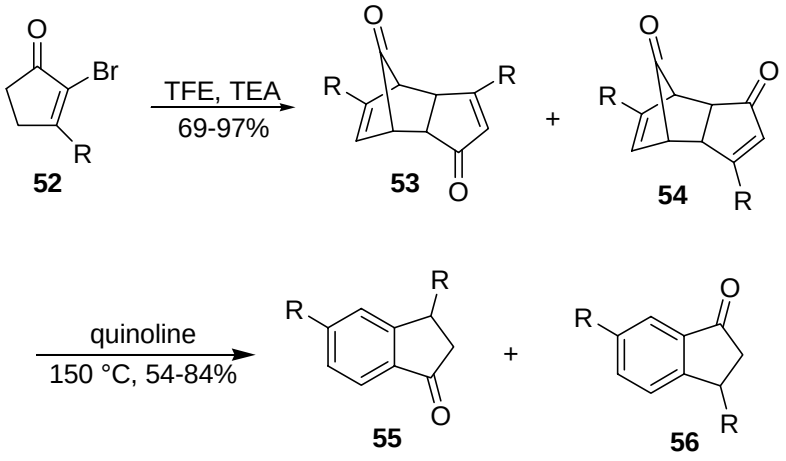
CHAPTER 2

RESULTS AND DISCUSSION

2-1 Cyclopentadienone Formation and Dimerization

2-1.1 Optimization of Dimerization Reaction

In the past our lab demonstrated that 2-bromo-3-aryl substituted cyclopentenones (**52**) could be used as precursors to generate cyclopentadienones that reacted spontaneously to form dimers of cyclopentadienone (**53, 54**), Scheme 11.[32] Further heating of the dimers caused decarbonylation to generate indanones (**55**, **56**).



Scheme 11. Dimerization of Cyclopentadienone Derivatives

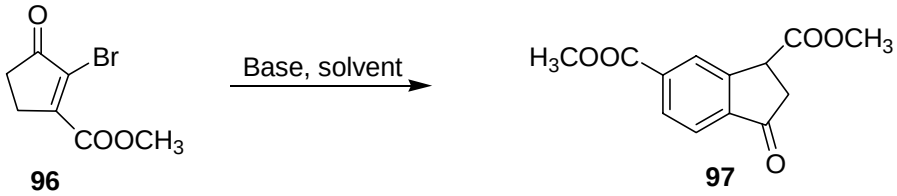
With the precedent of generating cyclopentadienones from 2-bromo-cylopentenone derivatives, methyl-2-bromo-3-oxocyclopent-1-enecarboxylate (**96**) was synthesized to expand the scope of utilizing cyclopentadienones in making synthetically

useful compounds. The synthesis of **96** will be described later in this chapter (Section 2-6).

To explore the chemistry of generation of cyclopentadienone from **96**, it was treated with 2,2,6,6-tetramethylpiperidine (TMP) in acetonitrile at room temperature. However, only starting material **96** was observed by TLC when the reaction was stirred for 48 hours at room temperature and then refluxed for 19 hours. Performing this reaction again in refluxing acetonitrile for two and a half hours resulted only in decomposition of the starting material. With a change in base to triethylamine (TEA), no product was observed. After several attempts, indanone **97** was isolated in 33% yield after 16 hours in refluxing THF. Other solvents such as dichloromethane (DCM), ether, and trifluoroethanol (TFE) were tried, but only decomposition of starting material was observed. A little improvement in the yield (45%) was observed in 1,4-dioxane. Toluene was found to be the best solvent for this reaction. Optimum conditions for indanone formation were found to be 0.1 M refluxing toluene which afforded 71% of indanone in 65 minutes. The results are summarized in Table 4.

The product was found to have two different regioisomers with 10:1 ratio. Therefore, this reaction proceeded with good regioselectively. Recrystallization to obtain good crystals for *X-ray* of this indanone with a variety of solvent systems was unsuccessful.

Table 4. Optimized Results of Dimerization Reaction

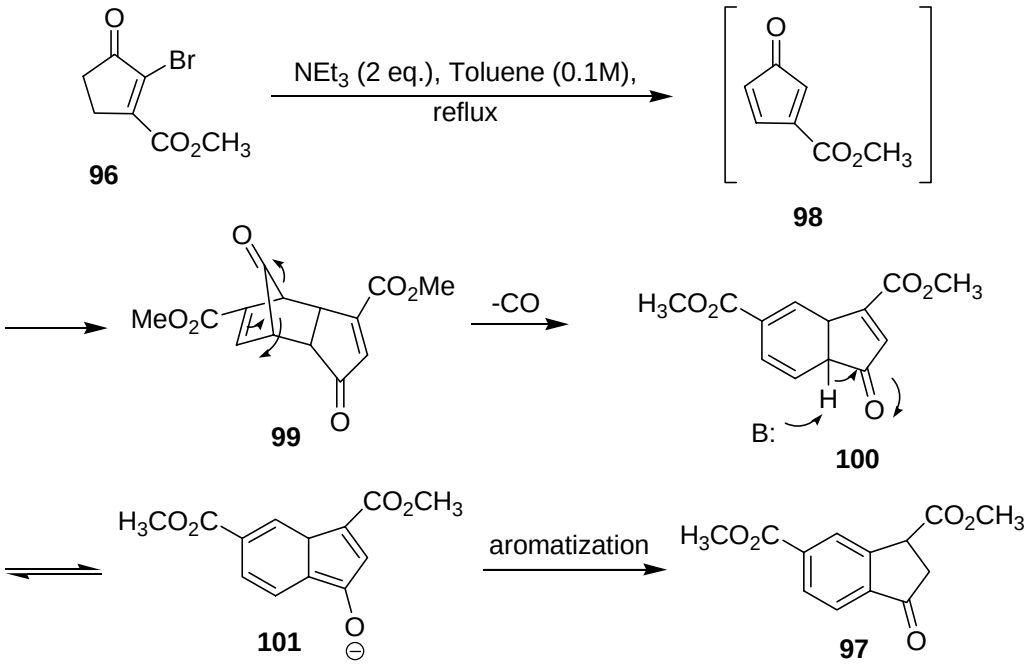


96 **97**

Entry	Base (eq.)	Solvent (conc.)	Reaction condition	Yield (%)
1	TMP (1.5)	CH_3CN (0.03 M)	48h rt, 19h reflux	Decomposed SM
2	TMP (1.5)	CH_3CN (0.03 M)	2.5h reflux	Decomposed SM
3	NEt_3 (1.5)	CH_3CN (0.03 M)	48h rt, 17h reflux	Decomposed SM
4	NEt_3 (3)	CH_2Cl_2 (0.03 M)	9h, reflux	Decomposed SM
5	NEt_3 (3)	Et_2O (0.03 M)	17h, reflux	Decomposed SM
6	NEt_3 (3)	TFE (0.03 M)	3.5h, reflux	Decomposed SM
7	NEt_3 (3)	THF (0.05 M)	16h, reflux	33
8	NEt_3 (3)	1,4-dioxane (0.3 M)	3.5h, reflux	45
9	**NEt_3 (2)**	**Toluene (0.1 M)**	**1h 5min, reflux**	**71**

2-1.2 Proposed Mechanism for Indanone Formation

How did the indanone form? It is known that 2-bromocyclopentenone (**49**) can generate cyclopentadienone when treated with TEA.[32] Based on this work, it is proposed that cyclopentadienone derivative (**98**) was formed as a reactive intermediate when methyl-2-bromo-3-oxocyclopent-1-enecarboxylate (**96**) was treated with TEA. Consequently, it is possible that the reaction followed a pathway illustrated in Scheme 12 where transient cyclopentadienone (**98**) was generated from methyl-2-bromo-3-oxocyclopent-1-enecarboxylate (**96**). The reactive cyclopentadienone (**98**) dimerized to afford **99**. Subsequent decarbonylation of the dimer and tautomerization generated aromatic indanone (**97**). [32, 36]



Scheme 12. Dimerization of Cyclopentadienone and Indanone Formation

2-2 Diels-Alder Reactions with Different Dienes

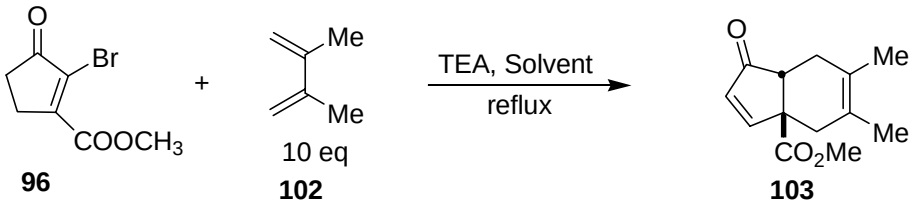
2-2.1 [4+2] Cycloaddition with 2,3-dimethyl-butadiene and Optimization

Previously, Fuchs[36] showed that benzyl 3-oxocyclopenta-1,4-dienecarboxylate (**74**) could be trapped with dienes. Inspired by this precedent, reactions were performed by trapping 3-carbomethoxycyclopentadienone (**98**) with 2,3-dimethyl-butadiene (**102**).

Methyl-2-bromo-3-oxocyclopent-1-enecarboxylate (**96**) was treated with TEA in the presence of 2,3-dimethylbutadiene (10 eq.) in various solvents and the Diels-Alder adduct (DAA) (**103**) was isolated. The results are shown in Table 5. Even though initially the reaction was performed with 5 equivalents of TEA, only 3 equivalents of TEA were necessary for this reaction. Optimizing the reaction in different solvents showed that toluene was again the best solvent, producing 84% of cycloadduct in 90 minutes. Varying the concentration did not have much effect on this cycloaddition reaction (Table 5, entry 8). TMP as base did not improve the yield and DBU led to decomposition of the starting material (**96**).

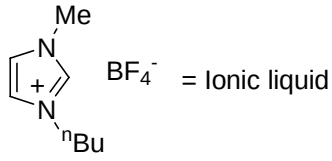
Chemists are currently interested in solvents that can be easily recycled, are 'green', and allow easy isolation of compounds after completion of the reaction. Ionic liquids are a class of compounds that serve as solvents with these properties. An ionic liquid was explored as a solvent for this cycloaddition reaction and 1-*n*-butyl-3-methylimidazolium tetrafluoroborate was chosen. However, the yield was found to be low (Table 5, entry 3).

Table 5. Optimization of the Diels-Alder Reaction with 2,3-dimethylbutadiene



Entry	Base (eq.)	Solvent (0.04M)	Rxn. Time (min)	Yield (%)
1	TEA (5)	MeCN	35	22
2	TEA (5)	2-Butanone	40	61
3	TEA (5)	Ionic liq.[a]	255	22
4	TEA (5)	Acetone	210	22
5	TEA (5)	1,4-Dioxane	70	54
6	**TEA (5)**	**Toluene**	**90**	**84**
7	TEA (3)	THF	160	73
8	TEA (3)	THF(0.10M)	160	71
9	TMP (3)	THF	70	43
10	DBU (3)	Toluene	20	Decomposition
11	DBU (3)	2-Butanone	14	Decomposition

[a] Structure of ionic liquid

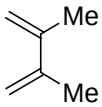
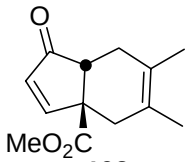
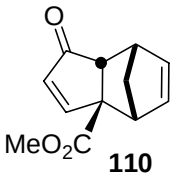


2-2.2 Diels-Alder Reactions with Alkyl Substituted Butadienes

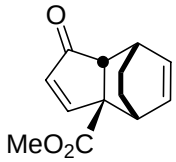
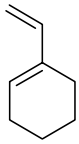
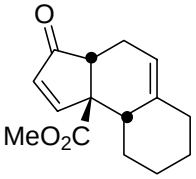
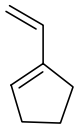
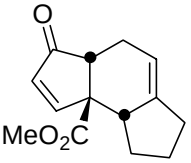
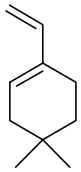
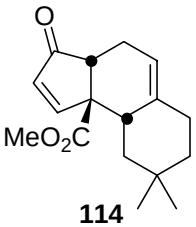
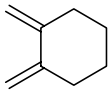
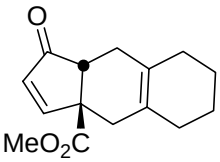
With a successful Diels-Alder reaction of cyclopentadienone derivative (**98**) with diene (**102**), exploration of the scope of this reaction was performed. Various dienes were synthesized and their syntheses will be presented later in this chapter (Section 2-7). The reactions of a number of alkyl-substituted dienes were found to be endo-selective, regiospecific, diastereoselective and high yielding. The reactions were performed in refluxing THF or toluene. Depending on the volatility of the diene, excess stiochiometries of the diene were used in the cycloaddition reaction. The results are shown in Table 6.

Cyclopentadiene gave the best yield of cycloadduct among all the alkyl-substituted dienes. Other dienes showed improved yields when the solvent was switched from THF to toluene. Cyclic dienes (**106-108**) and *exo*-cyclic diene (**109**) exhibited good yields in a range of 57-82%.

Table 6. Diels-Alder Reactions with Different Substituted Dienes

Entry	Diene (eq.)		Time (h), Solvent	Diels-Alder adduct (DAA)	Yield (%)
1	 **102**	(10)	6.0, THF	 **103**	73
		(10)	1.5, Toluene		84
2	 **104**	(10)	2.75, THF	 **110**	89

Continuation of Table 6

Entry	Diene (eq.)	Time (h), Solvent	Diels-Alder adduct (DAA)	Yield (%)
3	 **105**	(3) 4.0, THF (3) 1.5, Toluene	 **111**	17 57
4	 **106**	(3) 4.5, THF (3) 1.5, Toluene	 **112**	63 77
5	 **107**	(3) 3.0, THF (3) 1.5, Toluene	 **113**	33 56
6	 **108**	(3) 1.75, Toluene	 **114**	80
7	 **109**	(5) 1.25, Toluene	 **115**	82

The structures of the products were derived from the 2-D NMR, such as, COSY, NOESY, HMBC, and HMQC. In the DAA-**114**, proton H_e (2.83 ppm, multiplet) showed nOe interaction with the proton H_h (2.2 ppm, a multiplet) which in turn showed correlation with proton H_f (2.7 ppm, a doublet of doublet). These interactions suggested that all these protons are cis to each other. Also a weak correlation was observed between protons H_f and H_e. A chemdraw minimized energy model of **114** is shown in Figure 15. The other regioisomer of **114** was eliminated because this regioisomer is supposed to show a strong correlation between protons H_e and H_f in the COSY spectrum since these protons are next to each other. But no correlation was observed in the COSY spectrum of **114** (See in the attached spectrum in the NMR section). The nOe interactions in Diels-Alder adducts **112** and **113** interpreted from the corresponding 2-D NMR spectra were also supportive of the regioselectivity of these adducts.

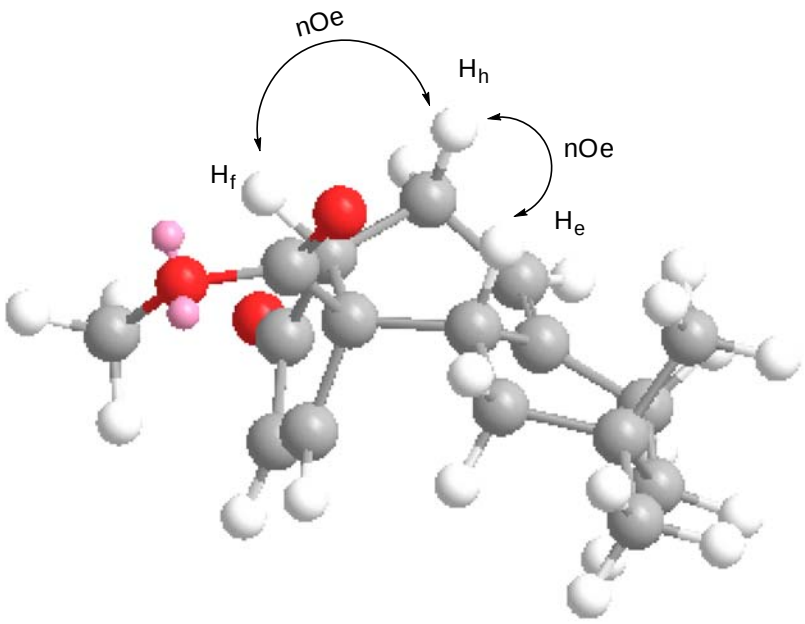
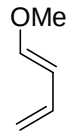
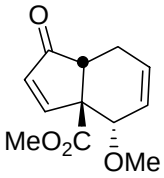
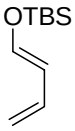
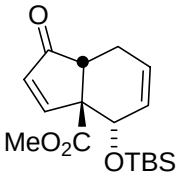
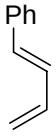
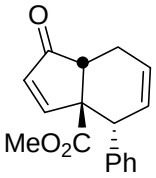


Figure 15. nOe Effect in DAA **114**

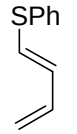
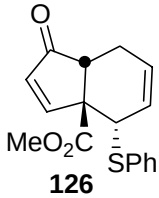
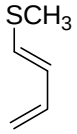
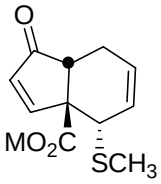
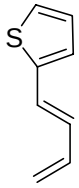
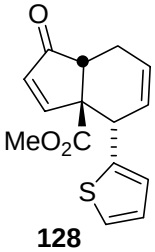
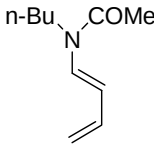
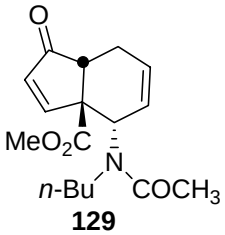
2-2.3 Diels-Alder Reactions with 1-substituted Dienes

Electron-rich 1-substituted dienes were also used to trap the cyclopentadienone derivative. Moderate to high yields (66-84%) of *endo*-selective adducts were formed. Regiospecificity, functional group compatibility under the reaction conditions made the methodology very versatile. Even 2-thienyl (**121**), tertiary-amide (**122**) substituted dienes produced very high yields of cycloadducts showing similar regio- and sterioselectivity. The results are incorporated in Table 7.

Table 7. Results of Diels-Alder Reactions with Different 1-substituted Dienes

Entry	Diene (eq.)	Time, Solvent	Diels-Alder adduct, DAA	Yield (%)
1	 **116**	(2) 6.0, THF	 **123**	52
		(2) 2.25, Toluene		84
2	 **117**	(5) 1.25, THF	 **124**	79
3	 **118**	(3) 1.25, Toluene	 **125**	66

Continuation of Table 7

Entry	Diene (eq.)	Time, Solvent	Diels-Alder adduct, DAA	Yield (%)
4	 **119** (5)	1.25, Toluene	 **126**	84
5	 **120** (3)	1.25, Toluene	 **127**	67
6	 **121** (2)	1.25, Toluene	 **128**	78
7	 **122** (3)	1.5, Toluene	 **129**	84

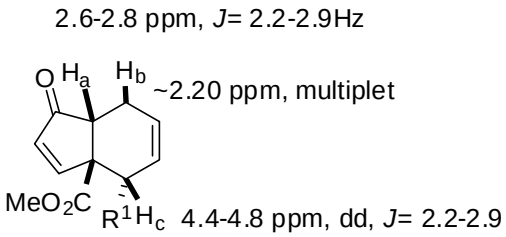


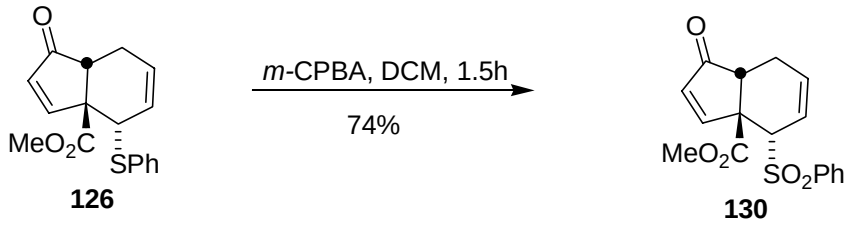
Figure 16. Correlation of protons in DAAs from 1-substituted dienes

The regiochemistry of these adducts were determined from the 2-D NMR spectra. The ^{1}H-NMR spectra of these DAAs showed peaks usually at 2.6-2.8 ppm (doublet of doublets), 2.20 ppm (multiplet), and 4.4-4.8 ppm (doublet of doublet) for protons H_a, H_b, and H_c respectively (Figure 16). One of the coupling constants of protons H_a and H_c were found to be 2.2-2.9 Hz, indicating a long range coupling involved between these protons. The NOESY-NMR spectra of compounds **123** and **124** showed that protons H_a and H_b showed nOe correlation with each other as well as protons H_b and H_c. The nOe correlation of these protons suggested that these protons were all cis to each other. These interactions among protons H_a, H_b, and H_c indicated that the ester group and the substituent on the diene are in 1,2 position and trans to each other in these Diels-Alder adducts.

2-2.4 Confirmation of the Regio- and Stereochemistry of the Diels-Alder Adducts

Even though 2D-NMR spectra were collected for most of the DAAs (Diels-Alder adducts) for determining the stereochemistry of these adducts, more concrete evidence was necessary to confirm the stereochemistry of these cycloadducts. The DAA (**126**) from 1-thiophenyl-1,3-butadiene (**119**) (entry 4, Table 6) was oxidized to sulfone (**130**)

by *meta*-chloroperbenzoic acid (*m*-CPBA) in dichloromethane in 74% yield (Scheme 13).[44] *X-ray* crystallographic data was obtained on this sulfone and the structure is shown in Figure 17**.** The *X-ray* of **130** showed that the product was endo; the substituent on the diene was vicinal and trans to the ester, which was consistent with the regiochemistry of the DAAs determined from the 2-D NMR spectra.



Scheme 13. Oxidation of Sulfide to Sulfone

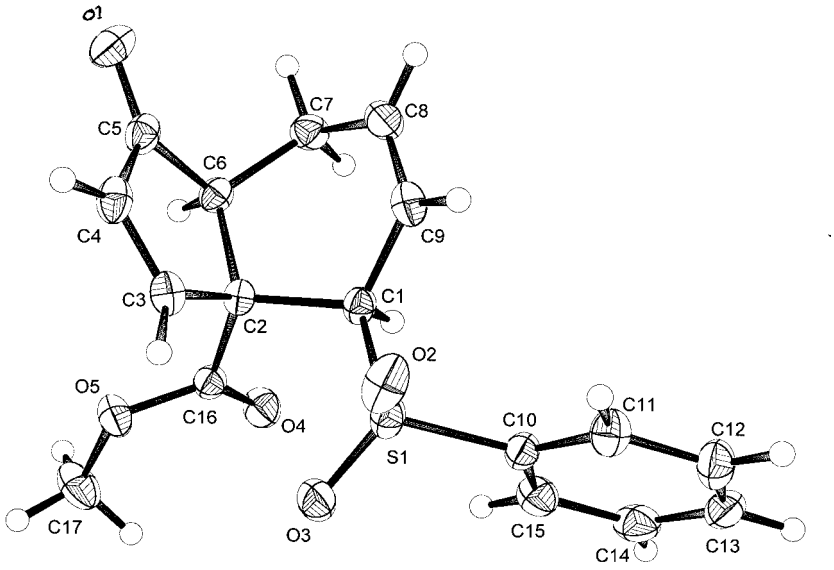


Figure 17. *X-ray* structure of sulfone **(130)**

2-2.5 Diels-Alder Reaction with Methyl sorbate and Styrene

Reactions with an electron-poor diene, such as methyl sorbate (**131**) generated no Diels-Alder adduct; rather decarbonylated dimer (DCD) (**97**) was obtained in 75% yield in 0.04 M refluxing toluene after 3h 20m. Since cyclopentadienone itself is an electron poor system, it was unable to form a cycloadduct with an electron poor diene.

When styrene was used as the trapping agent, cyclopentadienone acted as the 4π component and cycloadduct (**132**) was isolated in 10% yield (Figure 18).

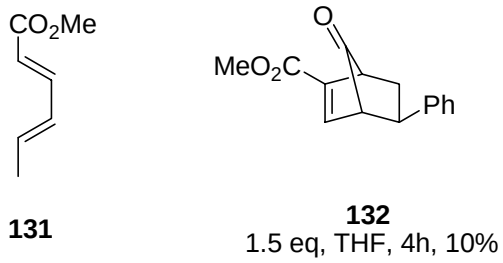


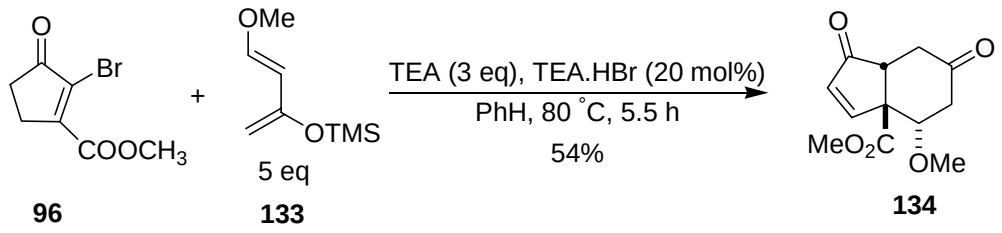
Figure 18. Methyl sorbate and DDA from styrene

2-2.6 Diels Alder Reaction with Danishefsky's Diene

Diene **133**, an equivalent of $^{+}CH{=}CH\text{-}CO\text{-}CH_2{}^{-}$, also known as Danishefsky's diene, is one of the most versatile dienes as it gives accessibility to functional groups in organic molecules which are tough to synthesize otherwise. A reaction was performed with this diene to expand the diversity of this developed methodology.

When the reaction was performed following the standard reaction conditions, no Diels-Alder adduct was isolated. However, performing the reaction in benzene in the presence of 20 mol% triethylamine hydrobromide salt in a sealed tube proceeded in 54%

yield (Scheme 14). Most probably hydrogen bonding of this salt with cyclopentadienone helped the reaction.



Scheme 14. Diels-Alder Reaction with Danishefsky's Diene

2-2.7 Competition between Dimerization and Cycloaddition Reaction

Cyclopentadienone (**98**) acted as a reactive intermediate in both the dimerization and Diels-Alder reaction. Competition between these two pathways was observed with the dienes **135-137** (Figure 19).

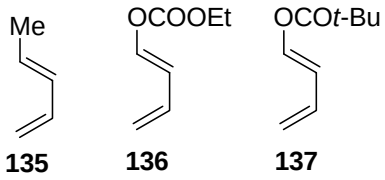


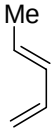
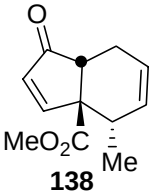
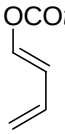
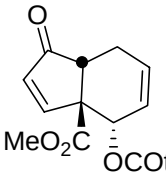
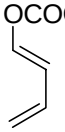
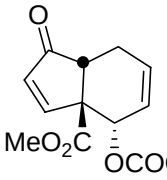
Figure 19. Cycloaddition Reaction with Dienes Produced DCD

Reaction with piperylene (**135**) was sluggish yielding DAA **138** in only 13% yield compared to 26% yield DCD **97**. Since **135** is a volatile diene, the probability of a collision between cyclopentadienone **98** and **135** was less between two molecules of cyclopentadienone **98** in refluxing toluene. Therefore, the reaction conditions were modified to increase the collision probability by performing the reaction in a sealed tube rather than in a flask equipped with a condenser, using excess **135** and increasing the concentration of toluene from 0.04 M to 0.1 M. Under this modified reaction conditions the yield of DAA **138** increased from 13% to 71% with isolation of no DCD **97**, Table 8.

Diels-Alder reaction with dienes **136** and **137**, which have ethylcarbonate and pivaloyloxy substituents attached to the dienes respectively, generated DCD **97** in 40% and 35% yield in addition to the DAAs (**139, 140**). The competition reaction was overcome by using excess diene (Table 8) under the normal reaction conditions. The yields improved from 30% to 72% for pivaloyloxy-1,3-butadiene and 31% to 61% for ethylcarbonate-butadiene respectively and also reducing DCD (**97**) from 40% to none in case of **136** and 35% to 10% for diene **137**.

The *X-ray* crystallographic structure of DAA **139** is shown in Figure 20. This structure also provides the evidence of the regio- and stereoselectivity of the Diels-Alder reaction where the substituent on the diene is '*ortho*' and *trans* to the ester functional group of the dienophile.

Table 8. Results of Overcoming Dimerization Reaction in Diels-Alder Reaction

Diene (eq.)	Time (min)	DAA	Yield (%) [a]
 5	115		13 & 26 DCD
10	75		71 [b]
135		**138**	
 2	75		30 & 40 DCD
5	115		72
136		**139**	
 2	75		31 & 35 DCD
5	75		61 & 10 DCD
137		**140**	

[a] The reactions were conducted in refluxing 0.04M toluene
[b] The reaction was performed in 0.1M toluene in a sealed tube

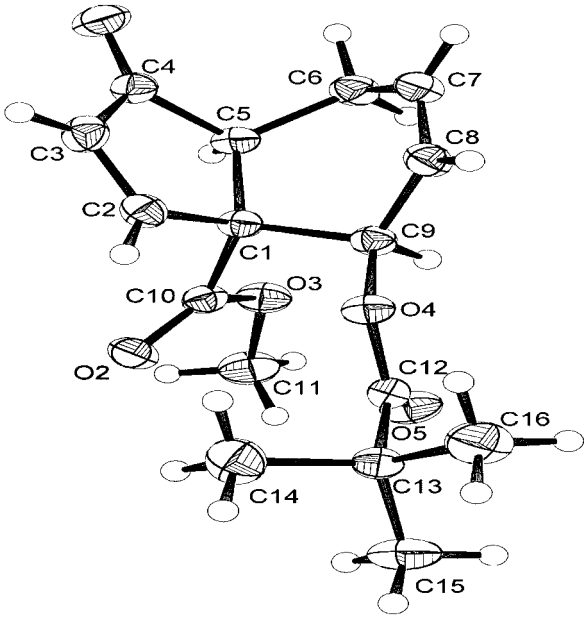


Figure 20. *X-ray* Structure of DAA **139**

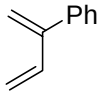
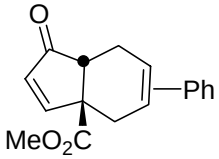
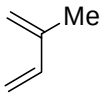
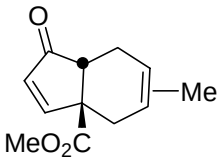
2-2.8 Reaction with 2-substituted Electron Rich Butadienes

The developed Diels-Alder reaction showed high regio- and stereoselectivity with 1-substituted, electron-rich butadienes. However, reactions with 2-substituted, electron rich butadienes showed no consistency in regioselectivity.

When the reaction was performed with 2-phenyl-1,3-butadiene (**141**), the yield of DAA **143** was high (80%). However, a 1:1 mixture of two regioisomers was formed. Another 2-substituted butadiene, isoprene, generated a 48% yield of DAA **144** with two regioisomers in 1.5:1 ratio. In this reaction, a 20% yield of DCD (**97**) and 3% yield of starting material **96** was also obtained. However, when the reaction was performed in a sealed tube using 0.1M toluene and excess diene, 87% DAA **144** was obtained in 1.5:1 ratio. The results are compiled in Table 9. Reactions were also performed with 2-methoxy-1,3-butadiene and 2-phenylsulfide-1,3-butadiene. However, more than two

inseparable isomers were formed and they could not be separated. Conversion of this mixture to their respective derivative might have helped to separate them.

Table 9. Diels Alder Reactions with 2-substituted Butadienes

Diene (eq.)	Time, h		Product	Yield (%) [a]
 **141**	2	1.25	 **143**	80 (1:1)
 **142**	5	1.20	 **144**	48 (1.5:1)
	10	1.15		87 (1.5: 1)[b]

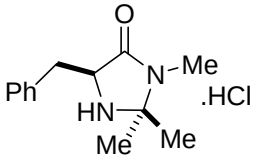
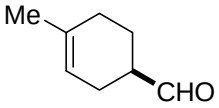
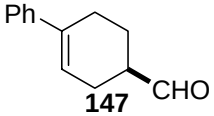
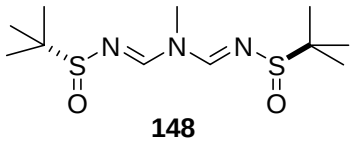
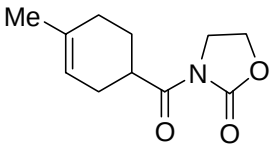
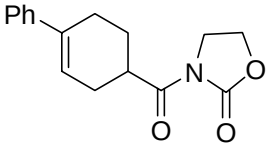
[a] Reactions were done in 0.04 M toluene with 3 eq. of TEA
[b] Reaction was performed in a sealed tube

In the literature, it is known that 2-substituted electron rich dienes such as **141** and **142** form both 1,4 and 1,3- regioisomers.[45-52] However, because of the directing influence of the carbonyl functional group of the dienophile, 1,4-isomer is usually formed predominantly.[53]

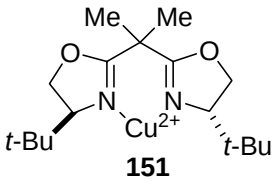
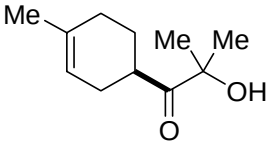
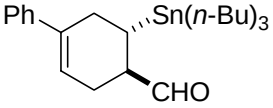
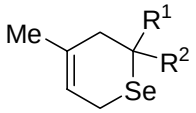
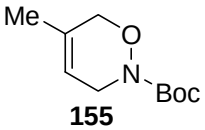
Use of a chiral ligand with a metal catalyst[54-56] or an organocatalyst[57, 58] sometimes can help to generate one isomer almost complete regioselectively in the Diels-Alder reactions with a 2-substituted diene. MacMillan *et al.*[57] performed an amine catalyzed (**145**) complete regioselective reaction between crotonaldehyde and dienes **141** and **142** (Table 10, entry 1). When Owens and co-workers [56] performed Diels-Alder reactions with both **141** and **152** in the presence of $Cu(SbF_6)_2$ and

bis(sulfinyl)imidoamidine (**148**), they obtained DAAs **150** and **149**, 1,4-isomers, in 87 % and 83% respectively (Table 10, entry 2). Also, Arceo *et al*.[55] obtained 99% of 1,4-isomer (**152**) when they used chiral Lewis acid catalyst (**151**) (Table 10, entry 3). Johnson and Kadow[59] found that use of aluminum chloride improved the regioselectivity of the reaction between **141** and trans-β-stannyl enone from 5:1 to 106:1 in favor of 1,4-isomer (**153**). But in Hetero Diels-Alder reactions, isoprene did not react regioselectively (Table 10, entry 5 & 6)).[60, 61] From this discussion it was obvious that 2-phenyl-1,3-butadiene (**141**) and isoprene (**142**) usually generate two different regioisomers which was also observed in the Diels-Alder reactions with cyclopentadienone derivative (**98**).

Table 10. Isoprene and 2-phenyl-1,3-butadiene in Diels-Alder reactions

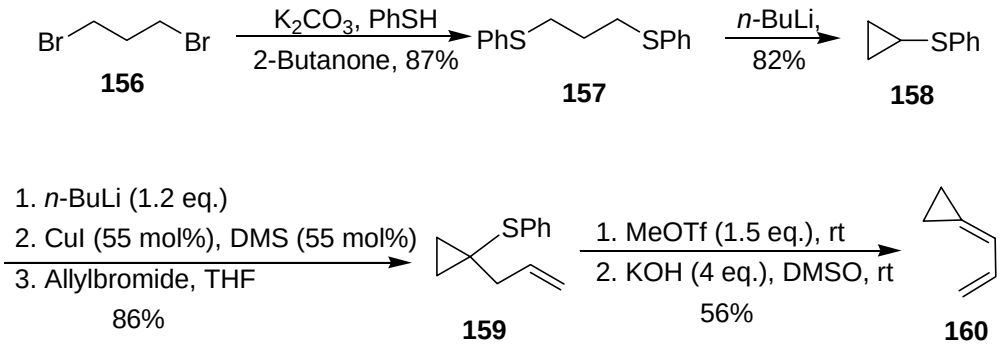
Entry	Rxn conditions, Catalyst	DAA	Yield (%)	Regioselectivity
1	MeOH-H_2O, rt  **145**	 **146**	84	One isomer
		 **147**	90	One isomer
2	DCM, rt  **148**	 **149**	83	19:1
	and $Cu(SbF_6)_2$	 **150**	87	19:1

Continuation of Table 10

Entry	Rxn condition, Catalyst	DAA	Yield (%)	Regioselectivity
3	DCM, -20 °C  **151**	 **152**	87	>99:1
4	Reflux in toluene	 **153**	87	5:1
	-78 °C, DCM, $AlCl_3$		72	106:1
5	DCM:THF (1:1), none	 **154**	93	3:7
6	DCM, rt a. Fe^{III}/ $H_2NCH_2CH_2NH_2$	 **155**	64	
	b. Cu^{I}/ $H_2NCH_2CH_2NH_2$		58	1:1
	c. Cu^{II}/ $H_2NCH_2CH_2NH_2$		65	

2-2.9 Reaction with Allylidenecyclopropane

Allylidinecyclopropane **160** could be used as a precursor to synthesize spiro-[2.5]octane system and also could serve as a precursor to 2,2-dimethyl-cyclohexane system.[62] The presence of cyclopropane ring in this diene made this compound very reactive toward an electrophile.



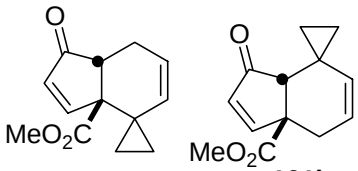
Scheme 15. Synthesis of Allylidenecyclopropane **160**

Allylidinecyclopropane (**160**) was synthesized according to Scheme 15.[63] Treatment of 1,3-dibromopropane (**156**) with K_2CO_3 and thiophenol in 2-butanone generated 1,3-(bisphenylthio)propane (**157**) in 87% yield.[64, 65] When **157** was subjected to treatment with *n*-BuLi, cyclopropylphenyl sulfide (**158**) was generated in 82% yield.[66] A cyclopropyl carbanion from **158** was generated with *n*-BuLi and electrophilic substitution on allyl bromide in the presence of 55 mol% of CuI-DMS generated compound **159** in 86% yield after distillation.[67] Conversion of the sulfide into a better leaving group by methyl triflate and a consecutive treatment with base (KOH) generated 58% yield of allylidenecyclopropane (**160**).[67]

When the Diels-Alder reaction was performed between a slight excess of allylidenecyclopropane (**160**) and 2-bromocyclopentenone derivative **96**, 74% of DAA was isolated. However, two inseparable regioisomers (**161a** & **161b**) were formed in 2.4:1 ratios as well as 8% of DCD (**97**). Again, when the reaction was performed with a large excess of diene (5 eq.), DAAs were formed with little improvement than the previous experiment (78%) and a trace amount of DCD (**97**) was also formed (Table 11). The regiochemistry of these adducts were not determined, however **161a** could be predicted as the predominant regioisomer as cyclopropyl is vicinal to the ester which is the expected regioisomer of this DAA.

The results are included in Table 11. From this result, it was obvious that Diels-Alder reaction with allylidenecyclopropane (**160**) was not regioselective. Krief and Zutterman[68] performed Diels-Alder reactions with **160** and found that it was not regioselective with unsymmetrical dienophiles.

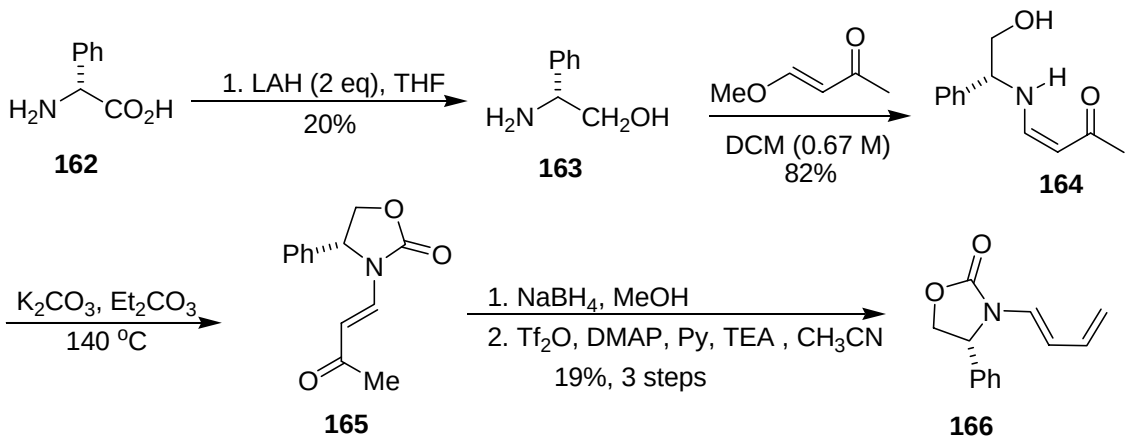
Table 11. Results of DA Reaction with Allylidenecyclopropane **160**

Diene (eq.); Time, [conc.]	**Products**	**Yield (%)**[a], [b]
1.2; 1.25h; 0.1M	 **161a** **161b**	DAA: 74 (2.4:1); DCD: 8.2
5.0; 1.25h; 0.04M		DAA: 78 (2.3:1) DCD: trace

[a] Reactions were performed in refluxing toluene
[b] The structures are not assigned yet

2-2.10 Facial Selectivity in Developed Diels-Alder Reaction

To study facial selectivity in the reaction, a chiral diene, oxazolidinone butadiene (**166**), was synthesized according to Scheme 16. Reduction of *R*-phenylglycine (**162**) with LAH produced 20% of alcohol-amine (**163**).[69] The literature reported yield is higher for this reduction. Use of bad LAH caused the yield to be low. Reaction of this amine (**163**) with 4-methoxy-3-buten-2-one in DCM generated compound **164** in 82% yield, which was subjected to react with diethylcarbonate to generate the oxazolidinone **165**.[70] Carbonyl group of **165** was reduced by $NaBH_4$ and treatment of this generated alcohol with triflic anhydride and a consecutive treatment with base generated the chiral butadiene **166** in 19% yield after 3 steps.[70]



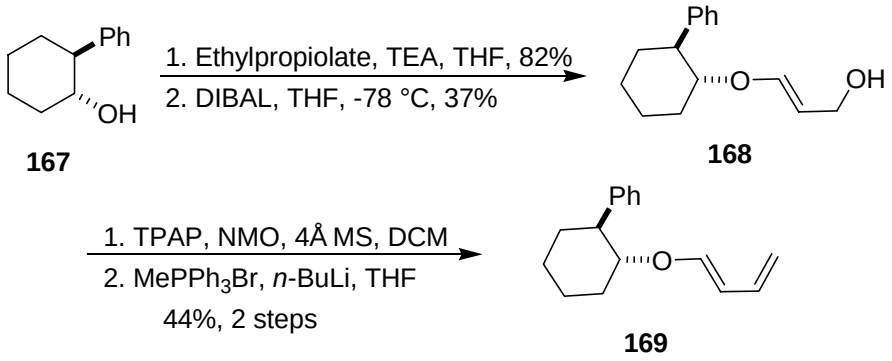
162 **163** **164** **165** **166**

Scheme 16. Synthesis of Chiral Oxazolidinone Butadiene **166**

With 1.1 equivalents of diene **166**, cycloadduct (**171**) was formed in 80% yield in a ratio of 1.6:1 of two stereoisomers. In order to observe whether low temperature would help increase the stereoselectivity, the reaction was performed at room temperature

instead of refluxing toluene. Nevertheless, no improvement was observed in the stereoselectivity except slight improvement in reaction yield (96%). The results of this reaction with cyclopentadienone **98** are presented in the Table 12.

With this outcome, an attempt was made to synthesize another diene (**169**). With the availability of racemic mixture of *trans-2*-phenylcyclohexanol (**167**) in our lab, synthesis of butadiene (**169**) was performed. The synthesis of this diene is shown in Scheme 17. The alcohol **167** was treated with ethylpropiolate in the presence of TEA generating 82% of α,β-unsaturated ester which was reduced by diisobutylaluminum hydride (DIBAL) generating the allylic alcohol **168** in 37% yield.[71] The alcohol **168** was oxidized to aldehyde by tetrapropylammonium perruthenate (TPAP) in the presence of *N*-methylmorpholine *N*-oxide (NMO) and a subsequent Wittig reaction accomplished the diene **169** in 44% after two steps.[71, 72]

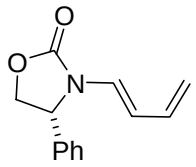
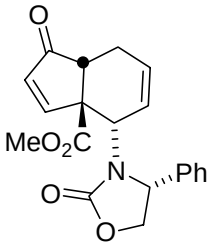
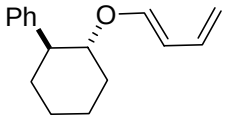
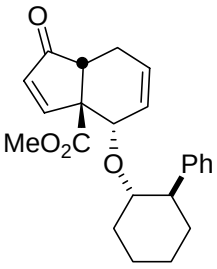
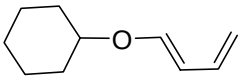
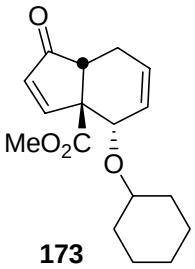


167 **168** **169**

Scheme 17. Synthesis of Chiral Diene **169**

When this diene (**169**) was subjected to Diels-Alder reaction with **96**, 67% DAA (**172**) was formed (Table 12). This diene also showed no facial selectivity just like the oxazolidinone diene **166**. Two inseparable stereoisomers in ratios of 2.2:1 were formed.

Table 12. Diels-Alder Reaction with Chiral Dienes

Diene (eq.)	Time, h	Product	Yield (%)[a]
 **166**	1.1 1.1	1.25 6.0[b]	 **171**	80 (1.6: 1.00) 96 (1.6 : 1.00)
 **169**	1.06	1.20	 **172**	67 (2.2 : 1.00)
 **170**	1.2 1.2	1.75 1.20	 **173**	47 [c] 63 [d]

[a] Reaction was performed under reflux conditions in 0.1M toluene with 3 eq. of TEA except mentioned. [b] Reaction was done at rt over 6 days. [c] Reaction was done at 0.04M toluene. [d] 20% DCD dimer was isolated.

In order to confirm the non facial selectivity of these chiral dienes, an achiral diene **170** was synthesized by removing the phenyl functional group from the diene **169**. Starting from cyclohexanol (**174**), diene **170** was synthesized by following the same route presented in Scheme 17.

Reaction of cyclohexanol (**174**) with ethyl propiolate in the presence of TEA formed 85% of the corresponding α,β-unsaturated ester; which was reduced by DIBAL to generate the allylic alcohol (**175**). Oxidation of **175** with TPAP and NMO furnished an aldehyde, which was converted to butadiene **170** by Wittig reaction in 11% yield over three steps (Scheme 18).

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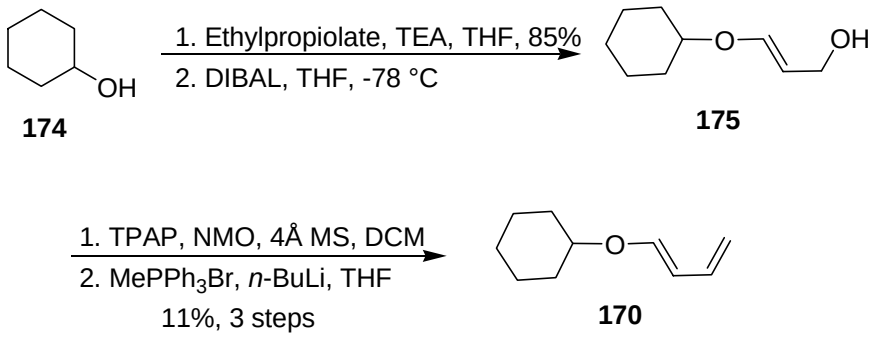


174 **175** **170**

Scheme 18. Synthesis of Cyclohexyloxy Butadiene **170**

When the Diels-Alder reaction was performed with this achiral butadiene **170**, 63% of DAA **173** was formed and only one isomer was obtained regio- and stereoselectively (Table 12). This result implied that the chiral dienes generated DAA regioselectively but not facial selectively. The result could be seen more clearly when ^{1}H-NMR of DDAs **172** and **173** were overlapped on each other (Figure 21). The top ^{1}H-NMR was of DAA-**172** having two sets of peaks showing two different diastereomers were generated. On the other hand, the bottom ^{1}H-NMR represented DAA-**173**, showed only one set of peaks confirming the regioselectivity of this product.

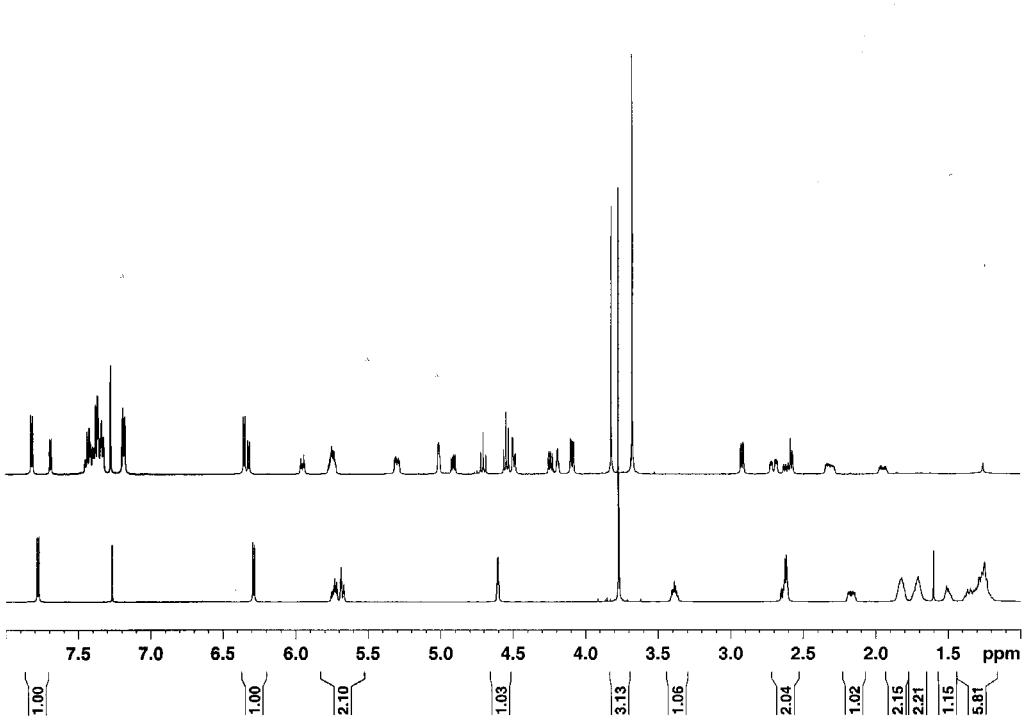
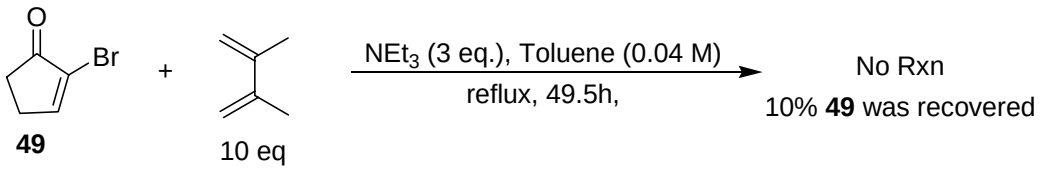


Figure 21. Overlapped ^{1}H-NMR of DAAs **172** and **173**

2-3 Understanding the Mechanism of the Diels-Alder Reaction

2-3.1 Effect of the Ester Group on Cyclopentadienone 98

When a Diels-Alder reaction was performed with 2-bromo-cyclopentenone (**49**) and 2,3-dimethylbutadiene (**102**) in refluxing toluene in the presence of TEA, only **49** was recovered in 10% yield after 49.5 hours. The reaction was performed longer than the optimized Diels-Alder reaction to observe whether prolonged reaction time would help the formation of any DAA.

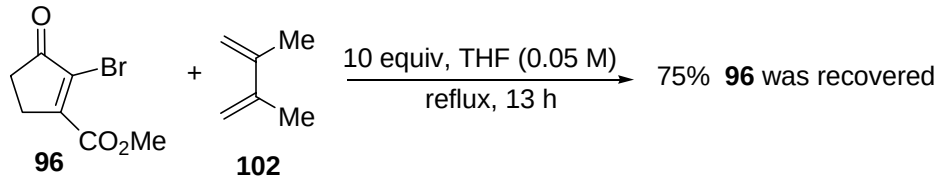


Scheme 19. Reaction Between 2-bromocyclopentenone and 2,3-dimethylbutadiene

The reaction proved that cyclopentadienone was not generated in refluxing toluene even though cyclopentadienone was generated in trifluoroethanol from 2-bromocyclopentenone (**49**).[32] This result suggested that, the presence of the ester group in **96** actually lowered the activation energy to generate cyclopentadienone in toluene.

2-3.2 Evidence of Cyclopentadienone Formation

Another reaction was performed without triethylamine to see whether any reaction occurred between methyl-2-bromo-3-oxocyclopent-1-enecarboxylate (**96**) and 2,3-dimethylbutadiene (**102**). However, only **96** was isolated in 75% yield after 13 hours in refluxing THF, Scheme 20. Consequently, it was obvious that the reaction could not proceed without formation of antiaromatic cyclopentadienone and a base was necessary to generate this reactive species from **96**.

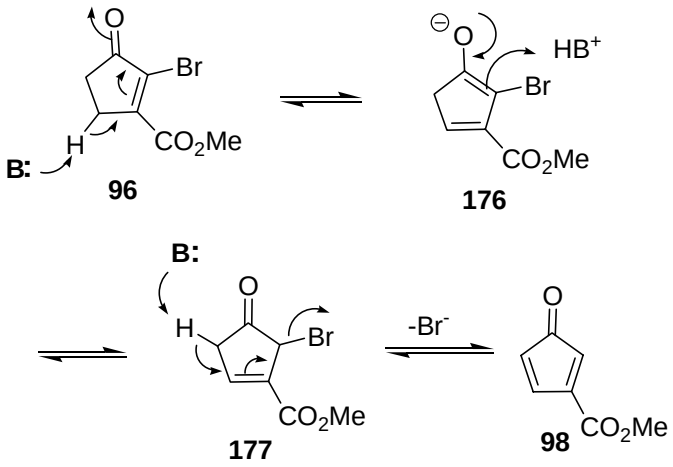


Scheme 20. Diels-Alder Reaction without TEA

2-3.3 Proposed Mechanism for Cyclopentadienone Formation

The developed methodology showed that indanone **97** formed when **96** was treated with TEA and again a DAA was formed when a diene was present in the reaction. In essence, the reaction result showed that a common intermediate was involved in these reactions. A closer look at indanone **97** suggested that it was derived from decarbonylation of cyclopentadienone dimer **99** (Scheme 12). This suggested cyclopentadienone **98** was involved in the reaction. So how did cyclopentadienone generate from **96**?

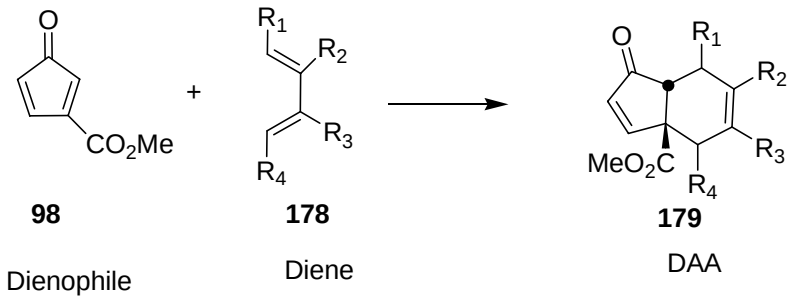
A mechanism for the formation of cyclopentadienone could be proposed as in Scheme 21. Deconjugation of α,β-unsaturated ketone **96** by the base followed by extrusion of hydrobromic acid generated cyclopentadienone **98**.[32] As soon as cyclopentadienone was generated, it dimerized (Scheme 12) or was trapped with a diene to form a Diels-Alder adduct (Section 2.2).



Scheme 21. Mechanism for the Generation of Cyclopentadienone

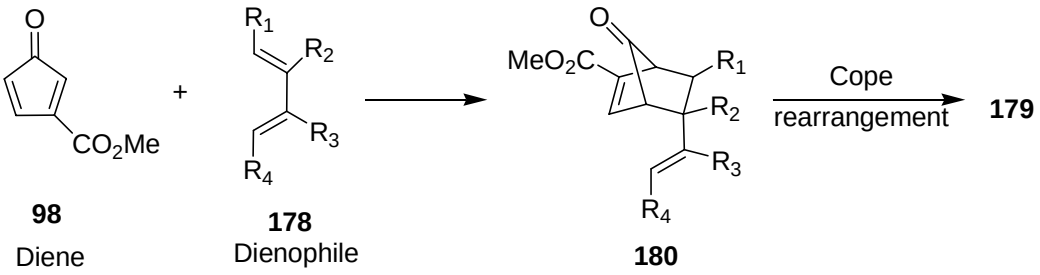
2-3.4 A Plausible Pathway for Diels-Alder Reaction

Diels-Alder reactions described in the previous section involved a reaction between cyclopentadienone derivative and a diene and both of them are 4π electron components. It is known that the Diels-Alder reaction involves a reaction between a 4π component and a 2π component. Therefore, in this reaction one of these two compounds was acting as a 2π component and one as a 4π component. Recent theoretical calculations on cyclopentadienone systems suggested that both cyclopentadienone and diene could act as 2π and 4π components simultaneously.[10, 73, 74] In one pathway cyclopentadienone could act as a dienophile (2π) and the diene as a 4π species and form the expected Diels-Alder adduct **179** (Scheme 22)**.**[75]



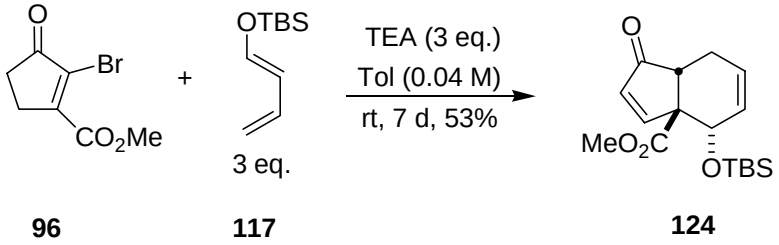
Scheme 22. Pathway A for the [4+2] Cycloadduct Formation

The other pathway could involve the diene behaving as a 2π system to generate **180**, which could undergo a Cope rearrangement to produce the same compound **179** (Scheme 23).[75]



Scheme 23. Pathway B for the [4+2] Cycloadduct Formation

An experiment was designed to trap any intermediate supportive of the mechanism postulated here. A reaction was performed with TBSO-butadiene (**117**) at room temperature to isolate cycloadduct **180**. However, only DAA **124** was isolated in 53% yield after 7 days at room temperature (Scheme 24).



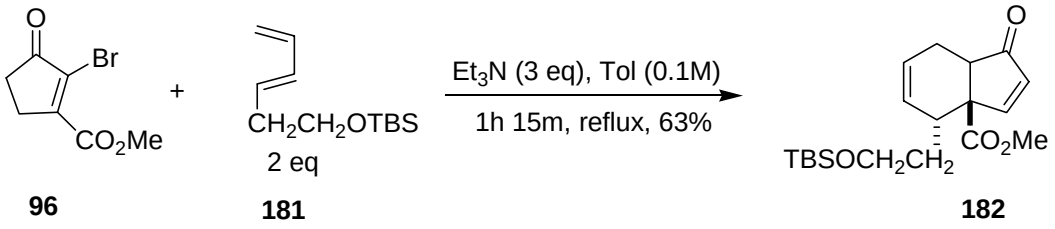
Scheme 24. Diels-Alder Reaction at Room Temperature

A separate synthesis of an adduct like **180** might help to confirm the mechanistic pathway involved in this reaction.

2-4 Reactions with More Dienes

2-4.1 Diels Alder Reaction with (*E*)-*tert*-butyl(hexa-3,5-dienyloxy)dimethylsilane

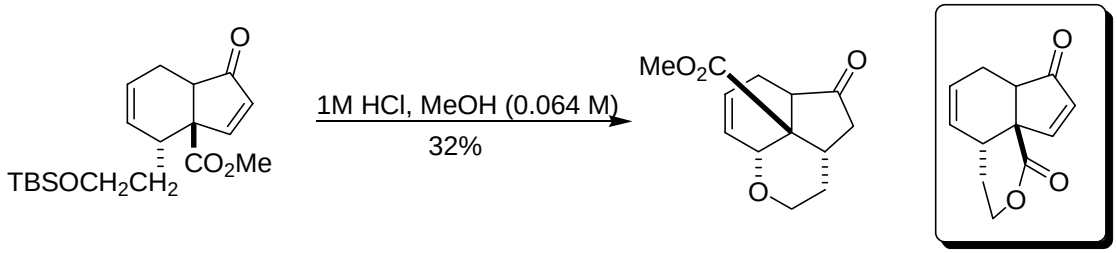
A Diels-Alder reaction was performed with (*E*)-*tert*-butyl(hexa-3,5-dienyloxy)-dimethylsilane (**181**) under the standard reaction conditions. DAA **182** was formed with 63% yield, Scheme 25**.**



96 **181** **182**

Scheme 25. Diels-Alder Reaction with a TBSO-diene **181**

When the silyl group was cleaved by acid hydrolysis in methanol, the alkoxide did nucleophilic attack on β-position of α,β-unsaturated ketone forming ether **183** in 32% yield (Scheme 26). The expected product, lactone **184**, could have formed if the alkoxide ion attacked the ester group.



182 **183** **184**

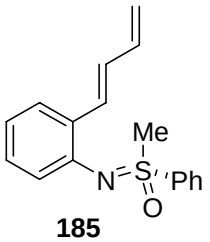
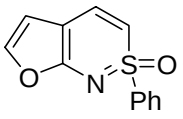
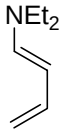
Scheme 26. Intramolecular Cyclization of DAA **182**

2-4.2 Dienes Failed to Form Diels-Alder Adducts

Diels-Alder reactions were performed with sulfoximine butadiene **185** and benzathiazine diene **186**. No Diels-Alder reaction occurred with these dienes, instead, only DCD dimmer was formed (44% DCD **97** was isolated with **185**), Table 13.

An amine-substituted diene **187** was synthesized, which could act both as a diene and a base. But this diene caused the cyclopentadienone precursor **96** to decompose in both the presence and absence of TEA, Table 13.

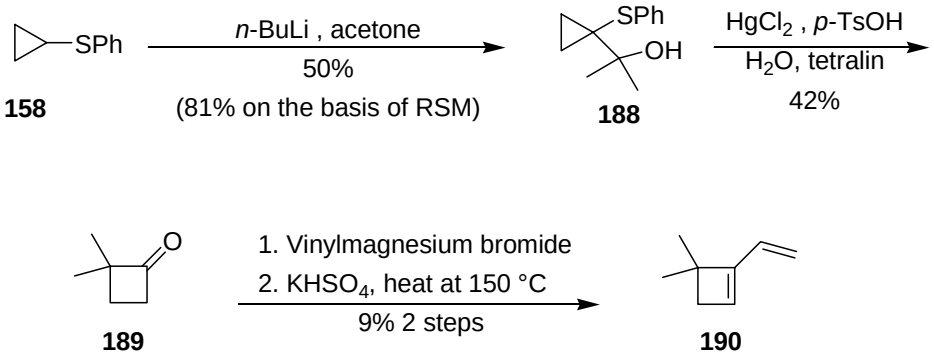
Table 13. Diels-Alder Reaction with Dienes

Entry	Diene	Result
1.	 **185**	44% DCD
2.	 **186**	Only DCD
3	 **187**	Decomposition of SM

2-4.3 Diels Alder Reaction with 2,2-dimethyl-1-vinyl-cyclobutene

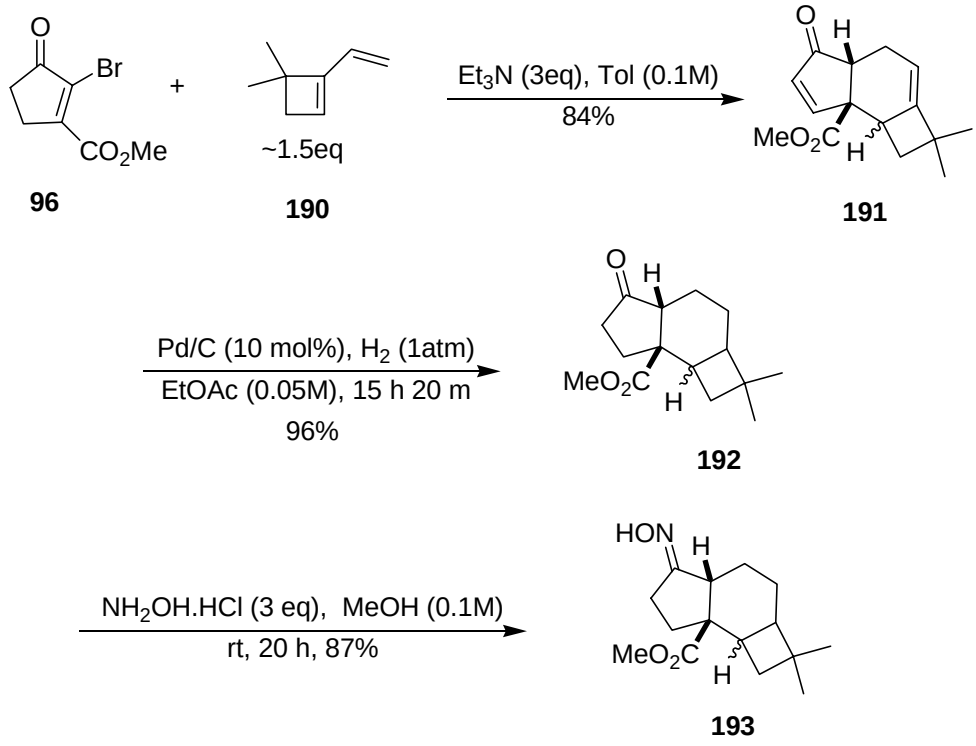
The Diels-Alder reaction with 1-substituted dienes was found to be regioselective in most cases. The ester group in the cycloadduct was always *trans* to the substituent on the 1-substituted diene. In an effort to examine whether the ester group and the substituent of diene could be *cis* to each other, diene 2,2-dimethyl-1-vinyl-cyclobutene (**190**) was synthesized, Scheme 27.

The synthesis initiated with the synthesis of cyclopropylphenyl sulfide (**158**) from 1,3-dibromopropane as described in Scheme 15. When **158** was treated with *n*-BuLi and the anion was trapped with dry acetone, alcohol **188** was formed in 50% yield.[76] The alcohol **188** was subjected to treatment with mercury (II) chloride in the presence of catalytic amount of *p*-TsOH in water and 2,2-dimethylcyclobutaone (**189**) was isolated in 42% yield.[77] The ketone was reacted with vinylmagnesium bromide to generate tertiary alcohol, which was heated with $KHSO_4$ to produce the desired butadiene **190**.[78] Even though the alcohol from ketone **189** was generated in good yield, the dehydration step produced a low yield of diene resulting in only a 9% yield of **190** after two steps. (Scheme 27)



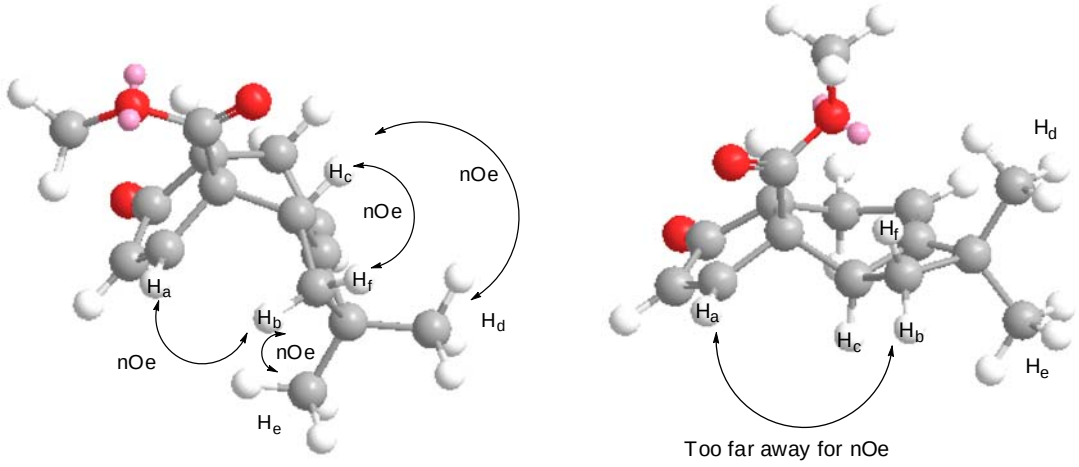
Scheme 27. Synthesis of 2,2-dimethyl-1-vinylcylobutene (**190**)

The Diels-Alder reaction of methyl-2-bromo-3-oxocyclopent-1-enecarboxylate (**96**) with diene **190** produced 84% of the Diels-Alder adduct **191** (Scheme 28). Since this adduct was an oil and *X-ray* structure could not be obtained on **191**, a hydroxylimine derivative was synthesized. Hydrogenation on **191** generated unsaturated compound **192** in 96% yield which was converted to hydroxylamine **193** in 87% yield (Scheme 28). Unfortunately **193** was a liquid compound. In order to figure out the structure of DAA **191**, 2-D NMR data were obtained on it. All the 2-D NMR spectra are attached in the NMR-data section.



Scheme 28. Synthesis of DAA **191** and its derivative **193**

The NOESY spectrum of DAA **191** shows a correlation between protons H_a (7.59 ppm, d, *J*= 5.5 Hz) and H_b (1.76 ppm, dd, *J*= 11.5, 8.0 Hz) which is only possible if the ester group and the proton H_c (3.36-3.30, bm) are cis to each other (Figure 22, **191-A**). On the other hand, the other stereoisomer **191-B** where ester group and proton H_c are *trans* to each other, no nOe correlation could be observed between the protons H_a and H_b as they are too far away from each other. In addition, the proton H_c shows nOe interactions with both the proton H_f (2.06, dd, *J*=11.00, 9.50 Hz) and the protons H_d of the methyl group (1.20 ppm) (**191-A**). Moreover, the proton H_b shows nOe correlation with the protons (H_e) of the other methyl group (0.97 ppm) in this molecule (**191-A**, Figure 22). If **191-B** was the stereochemistry of this compound then the proton H_c should have nOe correlation with H_b instead of H_f and as well as with the protons H_e of the methyl group rather than the protons H_d of the methyl group.



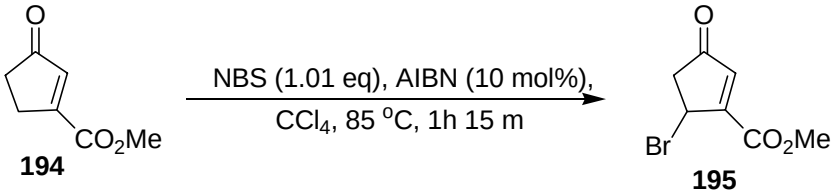
191-A **191-B**

Figure 22. Minimized energy model of DAA **191**

Even though this investigation initiated with the expectation to synthesize DAA **191-B**, however, NMR data suggested compound **191-A** was formed instead, following the standard regio- and stereoselectivity of the developed methodology.

2-5 Diels-Alder Reaction with Cyclopentadienone Generated from 4-bromo Cyclopentene Derivative

It is known that cyclopentadienone can be generated from treating 4-bromo-cyclopentenone with a base.[29-31] Utilizing this idea, cyclopentenone-ester **194** was treated with *N*-bromosuccinamide (NBS) in the presence of radical initiator azaisobutyronitrile (AIBN) in refluxing carbon tetrachloride for an hour (Scheme 29). This reaction generated allylic bromide compound **195**, which was used directly in the cycloaddition step without any purification.

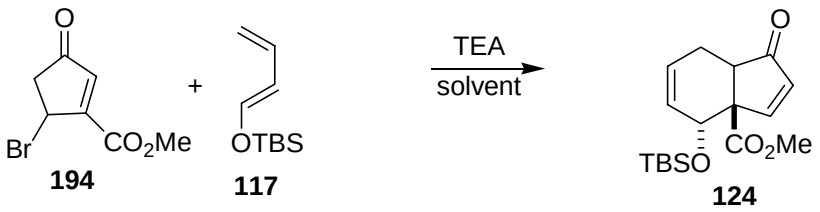


Scheme 29. Allylic Bromination with NBS

When **195** was treated with the diene **117** in the presence of TEA in THF at room temperature, it generated only 7% of DAA **124** after 2 steps. However, when the reaction was performed in refluxing THF by slow addition of a mixture of TEA and the diene **117** to the 4-bromo derivative **195**, the yield improved to 32% and in refluxing toluene the

yield was 20%. Diels-Alder reaction at room temperature in toluene produced 28% of the cycloadduct **124**. The results are tabulated in the Table 14 and the yields are after 2 steps.

Table 14. Diels -Alder Reactions with Allylic Bromide Precursor

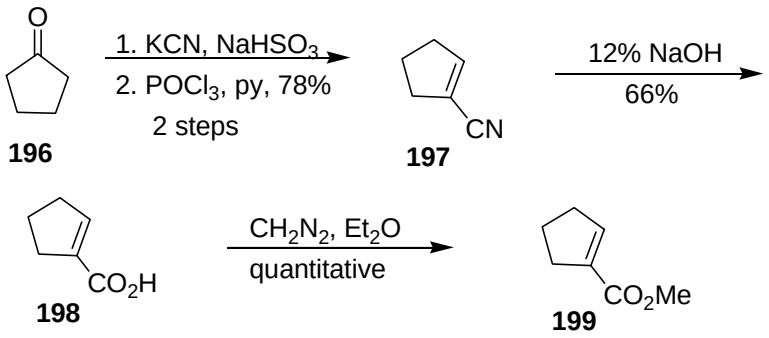


Entry	Diene (eq.)	TEA (eq.)	Solvent	Rxn time, and Temp.	Yield (%)
1	2	2	THF	30m, rt	11
2	1.5	2	THF	1h, reflux	32
3	1.5	2	Toluene	1h 45m, reflux	20

2-6 Synthesis of Methyl-2-bromo-3-oxocyclopent-1-enecarboxylate (96)

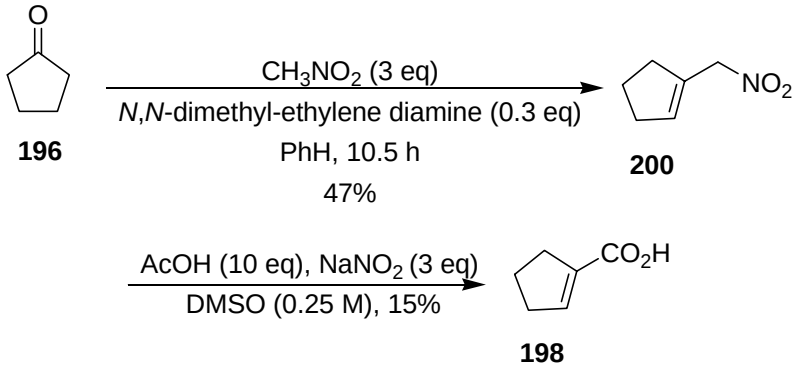
2-6.1 Synthesis of methyl cyclopent-1-enecarboxylate (199)

The synthesis of **96** started with the synthesis of ester **199**. Nucleophilic addition of cyanide to cyclopentanone (**196**) generated cyanohydrin which was dehydrated with $POCl_3$ and pyridine to afford a 78% of 1-cyanocyclopentene **197** in two steps.[79] Base hydrolysis[80] of cyanide **197** gave the carboxylic acid **198** in 66% yield. This acid was esterified with diazomethane producing the ester **199** quantitatively (Scheme 30). Allylic oxidation on **199** was performed by different oxidizing agents to synthesize ester **194** and is discussed in the following section.



Scheme 30. Synthesis of Methyl cyclopent-1-enecarboxylate (**199**)

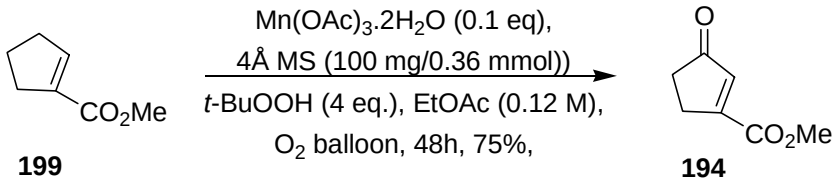
In order to avoid the use of poisonous potassium cyanide, an alternative pathway to synthesize carboxylic acid **198** was tried (Scheme 31). 1-(Nitromethyl)cyclopent-1-ene (**200**) was synthesized in 47% yield by azeotropic removal of water with benzene from a mixture of cyclopentanone (**196**), nitromethane, and catalytic amount of *N*,*N*-dimethyl-ethylene-diamine. Nef reaction on nitro compound **200** with acetic acid and sodium nitrite in dimethyl sulfoxide (DMSO) generated carboxylic acid **198** in 15% yield. Since the yield of acid was low via this route, Scheme 30 was used as the standard procedure to make the carboxylic acid **198**.



Scheme 31. Synthesis of Carboxylic Acid **198** by Nef Reaction

2-6.2 Allylic Oxidation

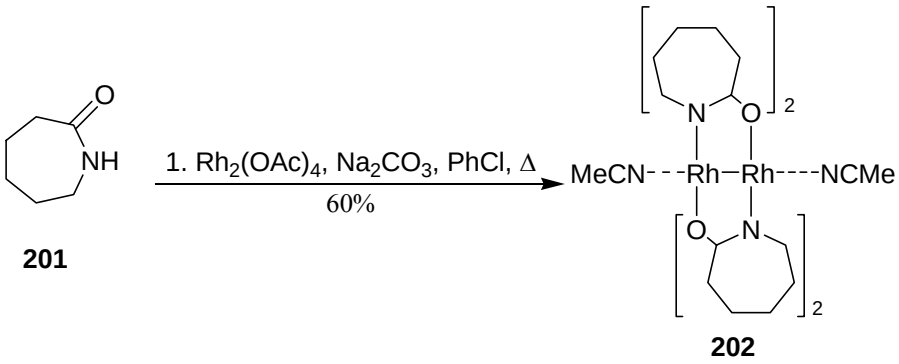
Allylic oxidation on ester **199** was performed with different oxidizing reagents and the results are tabulated in Table 15. The best result was obtained when the oxidation was performed on ester **199** (567 mg scale) by mild oxidizing agent manganese acetate[81] with *tert*-butylhydroperoxide (TBHP) in ethyl acetate over 48 hours under an oxygen atmosphere (Scheme 32). However, when the reaction was performed in large scale (3 g) the yield dropped to 43%.



199 **194**

Scheme 32. Allylic Oxidation with Manganese Acetate

Rhodium caprolactamate catalyst ($Rh_2(cap)_4.2CH_3CN$) (**202**) was another catalyst used for allylic oxidation introduced by Doyle.[82] The catalyst was synthesized from rhodium acetate and caprolactum (**201**) in 60% by following Doyle's[83] protocol (Scheme 33).



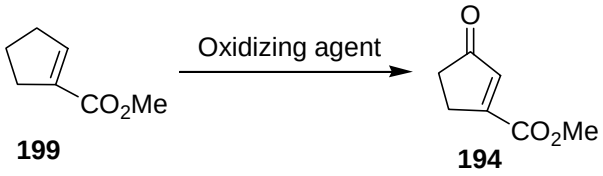
201 **202**

Scheme 33. Synthesis of $Rh_2(cap)_4.2CH_3CN$ (**202**)

Implementing Doyle's[82] protocol on allylic oxidation with TBHP gave cyclopentenone **194** in 47% yield with 0.2 mol % of rhodium catalyst loading. The literature reported yield was 79% with 0.1% catalyst loading.

Another important allylic oxidizing reagent was reported by Corey and co-workers.[84] They showed that palladium hydroxide was an effective catalyst to oxidize an enone to a 1,4-endione using TBHP as the oxidant. When this protocol was used for the oxidation of **199**, however, the yield was moderate (41%).

Table 15. Results of Allylic Oxidation of **199**



199 **194**

Entry	Catalyst (eq.) Oxidizing agent (eq.)	Other reagent (eq.)	Solvent [M] Rxn time	Yield (%)
1.	$Mn(OAc)_3$, 1 0mol % TBHP, 4 eq	4A MS 100 mg/0.36 mmol	EtOAc [0.12] 48h	75[a]
2.	$Rh_2(cap)_4.2CH_3CN$, 0.2 mol % TBHP, 10 eq	K_2CO_3 50 mol %	DCM [0.27] 9.5h	47[b]
3.	$Pd(OH)_2/C$ (20 wt%), 5 mol % TBHP, 5 eq	K_2CO_3 50 mol %	DCM [0.32]	41[[c]
4.	CrO_3, 2.6 eq.	Ac_2O	HOAc 1h	39[d]
5.	$BiCl_3$, 1 mol % TBHP, 10 eq	None	CH_3CN [0/15] 35h	10[a]

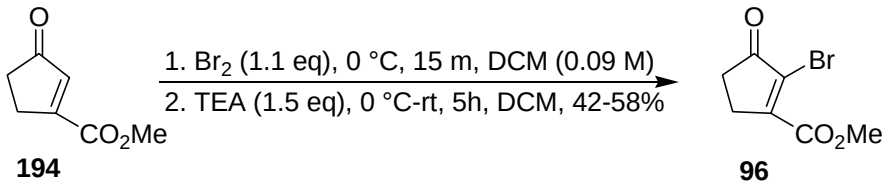
[a] 5-6M TBHP sol^n in decane was used. [b] 5-6M TBHP sol^n in DCM was prepared from 70% aqu. sol of TBHP. [c] 1M sol^n of TBHP was made from in DCM from 70% aqu. sol^n of TBHP. [d] CrO_3 was dissolved in Ac_2O /HOAc (1:2).

Other oxidizing agents such as chromium(VI) oxide[85] in acetic anhydride and acetic acid generated **194** in 39% yield. When a catalytic amount of $BiCl_3$[86] was used with 10 equivalents of TBHP, only 10% conversion was observed after 35 hours of reaction at room temperature. The results of oxidation reaction with various allylic oxidation reagents are presented in Table 15.

To improve the yield of this reaction few things need to be taken care of. The alkyl group of ester could be replaced with a heavier alkyl functional group to make this compound less volatile. Good catalyst and dry TBHP would help to improve the yield.

2-6.3 Bromination of 194

With ester **194** in hand, the desired product **96** was only one step away. Bromination with Br_2 and a consecutive dehydrobromination with triethylamine generated the desired product **96** in 42-58% yield (Scheme 34). In order to improve the yield, 2,6-lutidine was used as a base, however, the yield dropped to 10%. Different brominating reagents, such as, tetramethylammonium tribromide (Me_4NBr_3), tetrabutylammonium tribromide (nBu_4NBr_3), pyridinium hydrobromide perbromide ($PyHBr_3$) were also tried to improve the yield of this reaction. However, many methyl peaks were observed in the crude ^{1}H-NMR indicating more than one product was generated.

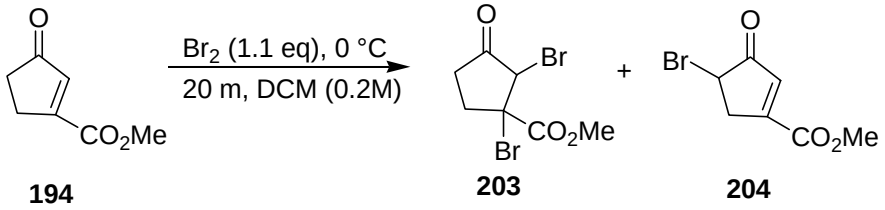


194 **96**

Scheme 34. Bromination Reaction

To examine the dibrominated product after reaction with molecular bromine, 3-oxocyclopent-1-enecarboxylate (**194**) was treated with 1.1 equivalents of bromine in DCM at 0 °C and stirred for 20 minutes at room temperature. Four methyl peaks

appeared in the ^{1}H-NMR of the crude product. In addition to extra methyl peaks, the α-proton from the α,β-unsaturated ketone was also present, indicating the other α -brominated product **204** might have formed in addition to the dibrominated product **203** (Scheme 35)**.**



194 **203** **204**

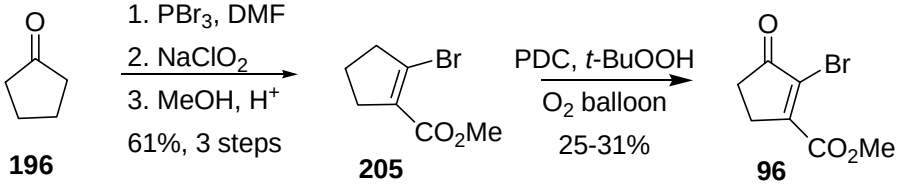
Scheme 35. Reaction with Bromine

As an alternative of bromination, iodination of 3-oxocyclopent-1-enecarboxylate (**194**) was also performed. But when the ester **194** was treated with 2 equivalents of I_2 followed by pyridine generated 23% yield of α-iodinated product in addition to 23% recovered starting material **194**. Since two electron withdrawing groups were attached to cyclopentenone, the double bond was very electron deficient causing low yield of iodinated product.

2-6.4 An Alternative Route to Make Methyl-2-bromo-3-oxocyclopenten-1-enecarboxylate (96)

With difficulties in the allylic oxidation and bromination steps, different alternative routes were explored to make methyl-2-bromo-3-oxocyclopenten-1-enecarboxylate (**96**). Vilsmeier-Haack reaction on cyclopentanone (**196**) generated 2-

bromo-1-carbaldehyde-cyclopentene in good yield.[87] Without any purification, the aldehyde was oxidized[88, 89] to carboxylic acid by sodium chlorite followed by acid catalyzed Fisher esterification in methanol generated the ester **205** in 72% yield over 3 steps. Although the major functional groups were introduced easily, allylic oxidation was still a challenge. Pyridinium dichromate (PDC) was found to be the best oxidizing agent when it was combined with TBHP in an oxygen environment.[90] This reaction generated 25-31% of the desired compound **96** (Scheme 36).

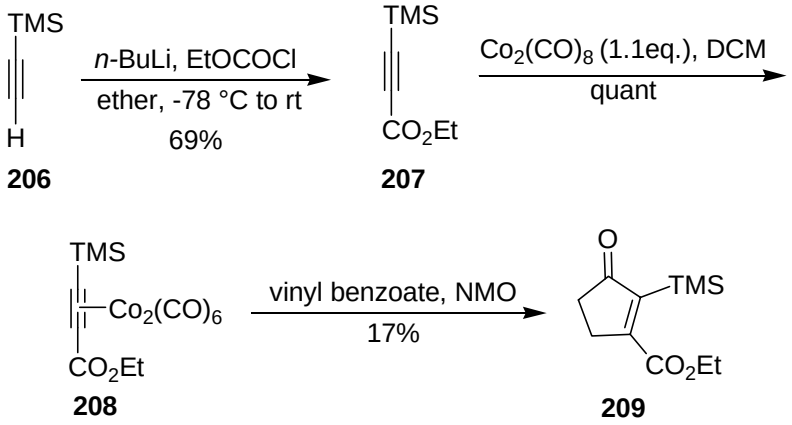


Scheme 36. Synthesis of **96**

Other oxidizing agents were tried to improve the yield of this allylic oxidation step. Among these were rhodium catalyst $Rh_2(cap)_4.2CH_3CN$,[82] palladium on carbon (Pd/C),[91] palladium hydroxide on carbon,[84] chromium(VI) oxide,[85] $Mn(OAc)_3$,[81] and $BiCl_3$[86]. They generated **96** in yields of 24%, 11%, 6%, 19%, 25%, and <10% yield respectively. Even the most common reagent for allylic oxidation SeO_2[92] did not perform well on this reaction as SM: product ratio was 7.1:1 after 6 days of reaction at rt in DCM. Even though the allylic oxidation produced low yield of **96**, this synthetic route (Scheme 35) was used most of the time as it generated 19% over all yield of **96** after four steps.

2-6.5 Synthesis of Ethyl-3-oxo-2-(trimethylsilyl)cyclopent-1-enecarboxylate

Ethyl-3-oxo-2-(trimethylsilyl)cyclopent-enecarboxylate (**209**) was selected as another precursor to synthesize Methyl-2-bromo-3-oxocyclopenten-1- enecarboxylate (**96**), since it is known in the literature that a 2-trimethylsillyl cyclopentenone could be converted to a 2-bromocyclopenteone by NBS[93]. The synthesis of **209** is presented in Scheme 37.



Scheme 37. Synthesis of **209** by Pauson-Khand Reaction

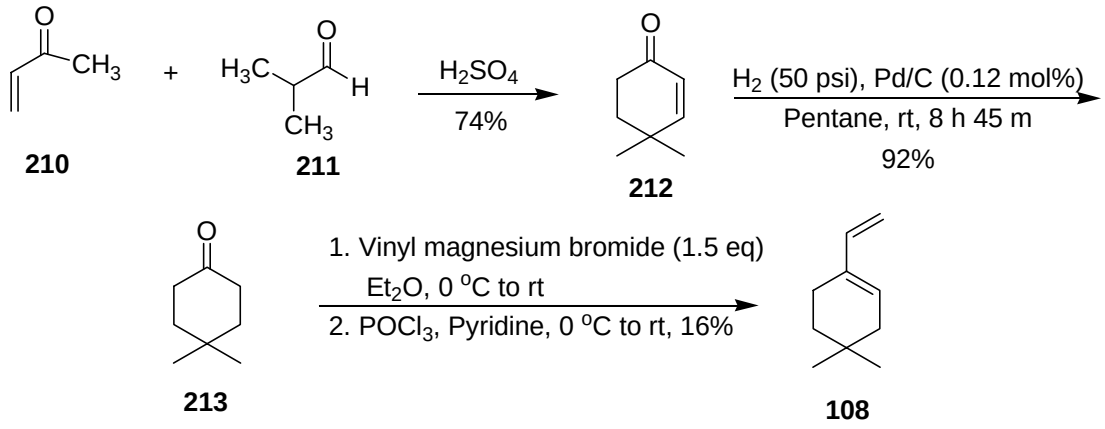
Trimethylsilyl acetelyne (**206**) was treated with *n*-BuLi and trapped with ethyl chloroformate to generate **207** in 69% yield. Cobalt complex **208** was made quantitatively by treating **207** with cobaltoctacarbonyl. Subsequently, the Pauson-Khand[94] reaction was performed between **208** and vinyl benzoate to produce the TMS cyclopentenone derivative **209** in 17% yield. Since the yield was not as high as expected, Scheme 36 was used as the standard procedure to make **96**.

2-7 Synthesis of Dienes

Synthesis of different dienes will be discussed in this section. Synthesis of dienes **108** and **136** were not previously reported in the literature and diene **181** was synthesized by modifying the route reported in the literature.

2-7.1 Synthesis of Alkyl Substituted Diene 108

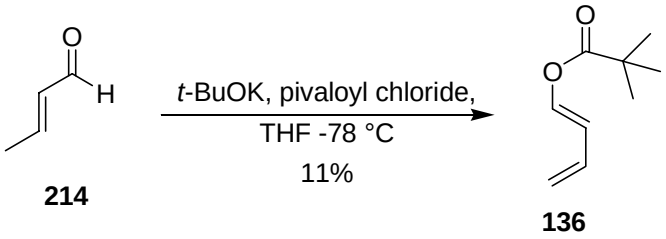
Robinson annulation between isobutyraldehyde (**210**) and methyl vinyl ketone (**211**) generated dimethyl substituted α,β-unsaturated ketone **212** in 74% yield.[95] Saturated cyclohexanone **213** was obtained in 92% yield by hydrogenation of unsaturated ketone **212**.[96] When freshly prepared vinyl magnesium bromide was added to the ketone **213**, tertiary alcohol was generated which was subjected to dehydration without any purification to provide the desired alkene **108** in 16% yield after two steps, Scheme 38.



Scheme 38. Synthesis of 4,4-dimethyl-1-vinylcyclohexene (**108**)

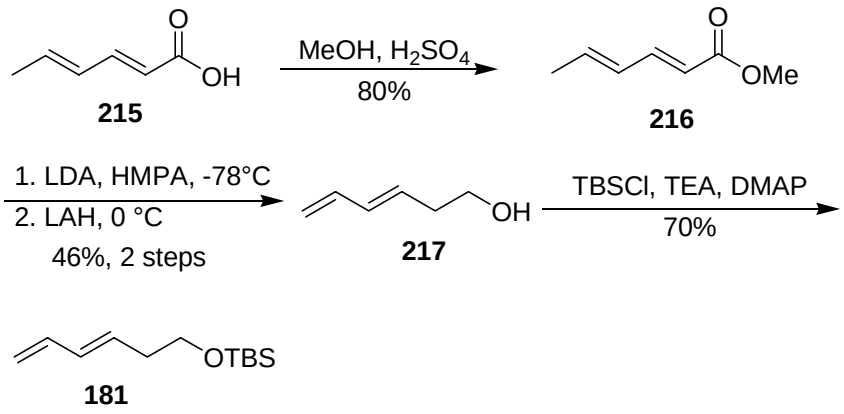
2-7.2 Synthesis of 1-substituted Butadienes 136 and 181

When croton aldehyde (**214**) was treated with KO*t*-Bu and pivaloyl chloride in THF, pivaloyloxy-1,3-butadiene (**136**) was synthesized in only 11% yield (Scheme 39)[97, 98].



Scheme 39: Syntheses of diene **136** from croton aldehyde

Diene **181** was synthesized according to the synthetic route presented in Scheme 40. Methyl sorbate (**216**) was synthesized from sorbic acid (**215**) by Fisher esterification in 80% yield. Transposition of the double bond was performed by treating the ester **216** with LDA in the presence of HMPA followed by LAH reduction at low temperature furnished alcohol **217** in 46% yield in 2 steps. Treatment of alcohol **217** with TBSCl and TEA in DMF furnished the desired diene **181** in 70% yield.



Scheme 40. Synthesis of diene **181**

2-8 Towards the synthesis of Desogestrel

2-8.1 Retrosynthesis

Desogestrel (**218**) is a steroid, one of the most commonly used contraceptive drugs. The word steroid came from 'sterol', which originated from the Greek word 'steros' meaning solid. Sterols originally referred to solid alcohols obtained from the non-saponifiable part of lipid extracts of tissues. Later, all sterol-like compounds came to be known as steroids. Steroids are available from a wide variety of natural sources. They comprise many families of compounds mainly bile acids, sex hormones, adrenocortical hormones, cardiac glycosides, sapogenins, and some alkaloids.

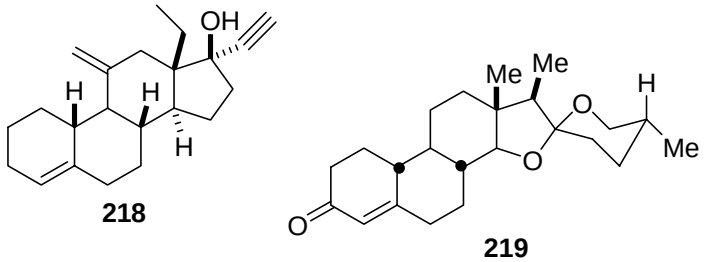
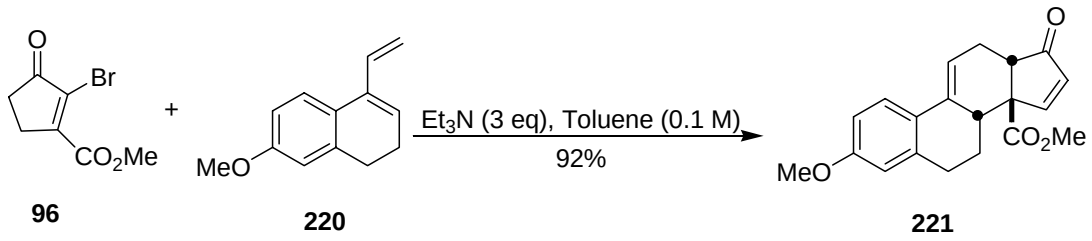


Figure 23. Desogestrel (**218**) and Diosgenin (**219**)

Industrially, desogestrel (**218**) is synthesized from diosgenin (**219**), which is isolated from a type of wild yam. In the literature the enantioselective total synthesis of this compound was reported by Quinkert *et al*. [99, 100] and Corey *et al*.[101, 102]

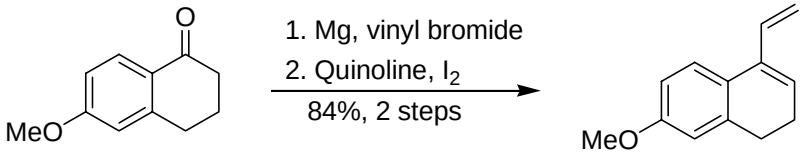
A Diels-Alder reaction was performed with Dane's diene (**220**) and Diels-Alder adduct (**221**) was obtained in 92% yield after 1h 15min in refluxing toluene. The steroidal skeleton was generated in one step stereoselectively as shown in Scheme 41.



96 **220** **221**

Scheme 41. Diels-Alder Reaction with Dane's Diene

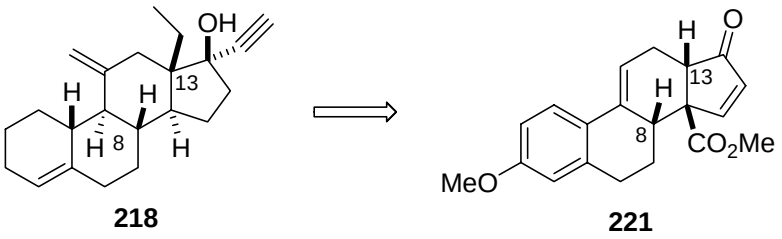
Dane's diene was prepared from tetralone (**222**). Tetralone was treated with freshly prepared vinyl magnesium bromide to generate tertiary alcohol. The crude alcohol was treated with quinoline in the presence of catalytic iodine and water was azeotropically removed with benzene yielding 84% of diene **220** in two steps (Scheme 42).[103]



222 **220**

Scheme 42. Synthesis of Dane's diene (**220**)

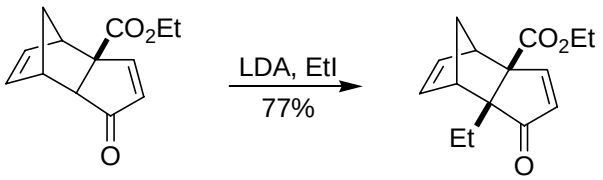
When the structure of DAA **221** was compared with desogestrel (**218**), it was found that the main ring structure of **218** was already established in **221** and the stereocenters at position C-8 were the same (Figure 23). Also an ethyl group needed to be



218 **221**

Figure 24. Desogestrel and DAA **229**

introduced at C-13. A similar α-ethylation was performed by Lange *et al.*[104] in which the *α,β*-unsaturated ketone **223** was treated with lithium diisopropylamine (LDA) and trapped the enolate with ethyl iodide to generate **224** in 77% yield (Scheme 43).



223 **224**

Scheme 43. Ethylation of *α,β*-unsaturated Ketone

With this precedent in mind, the total synthesis of **218** was pursued. A retrosynthesis is shown in Figure 25. Desogestrel (**218**) could be synthesized from protected alcohol **225**, which in turn could be synthesized from the oxidation of alcohol

226 and a subsequent olefination reaction. Alcohol **226** could be generated from borane hydroxylation of alkene **227**, which could be synthesized from DAA **221** by introduction of ethyl group at C-13, reduction of α,β-unsaturated ketone and removal of ester group by reduction with introduction of the proper stereochemistry at C-8.

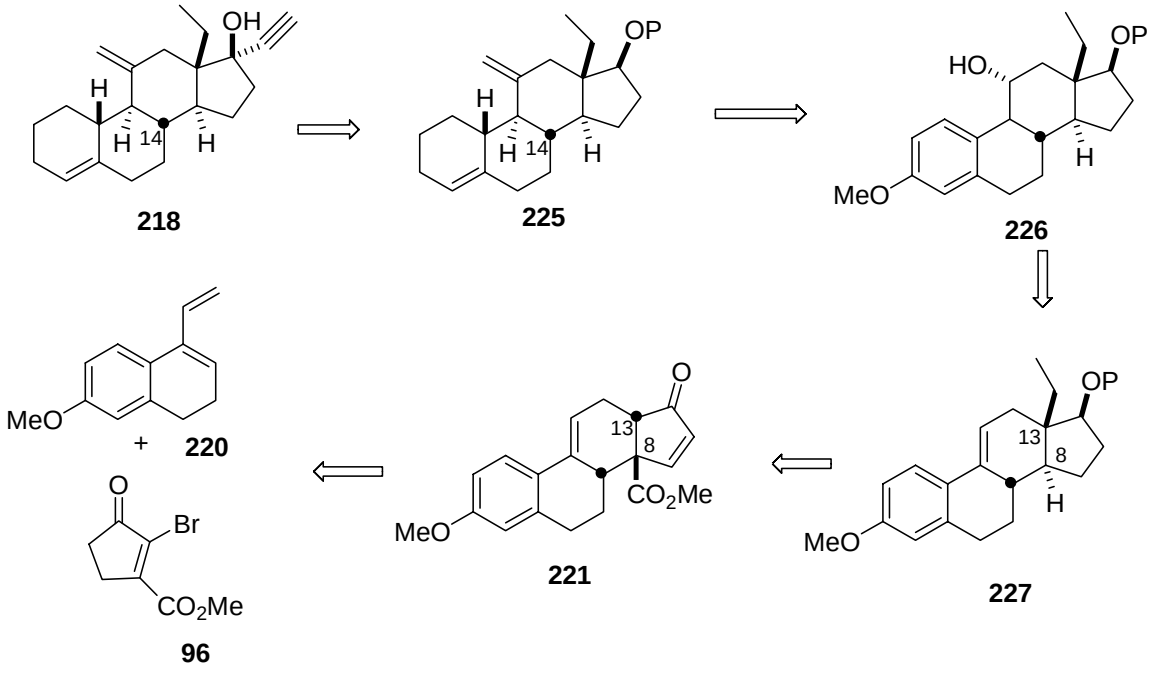
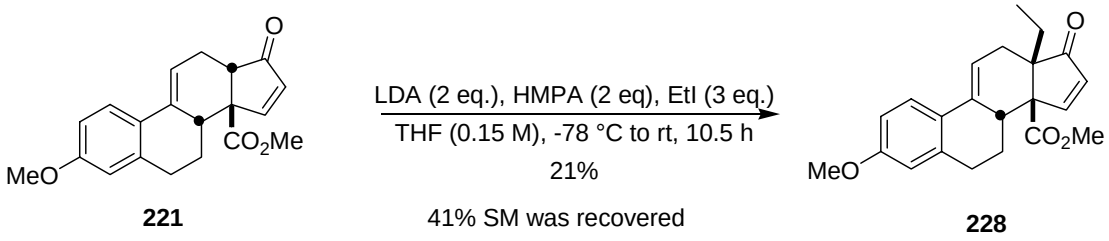


Figure 25. Retrosynthesis of Desogestrel (**218**)

2-8.2 Ethylation of 221

Ethylation of Diels-Alder adduct **221** was attempted with LDA and trapping the enolate with ethyl iodide generated **228**. However, the yield was only 21% with 41% recovered starting material (Scheme 44).



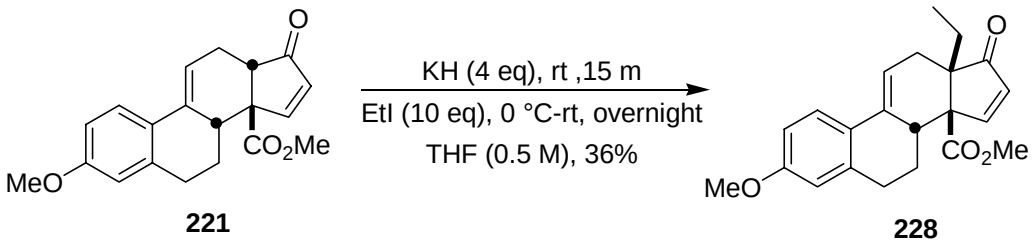
221 **228**

Scheme 44. Ethylation of **221** with LDA and EtI

Bases, such as potassium hexamethyldisilylazide (KHMDS), sodium hexamethyldisilylazide (NaHMDS), potassium *tert*-butoxide (KO*t*-Bu), sodium hydride (NaH), and potassium hydride (KH) were tried. In all cases, the yield of ethylation was low.

To examine whether enolate formation encountered problems, the ketone **221** was treated with bases such as LDA and also NHMDS separately followed by quenching the reaction mixture with D_2O. The result of deuteration illustrated that enolate was deuterated almost completely (See the ^{1}H-NMR attached in the NMR section). This observation confirmed that enolate formation was not a problem, but trapping the enolate with EtI was. Most likely, the presence of the ester group in the molecule hindered the approach of the electrophile.

The best yield for the ethylation reaction was obtained when the ketone **221** was treated with 4 equivalents of KH at room temperature overnight in THF (Scheme 45). The reaction yield was 36%. Although a reaction was performed starting at -78^o C with KH and slowly warmed to room temperature, the yield didn't improve and starting material was isolated as well.



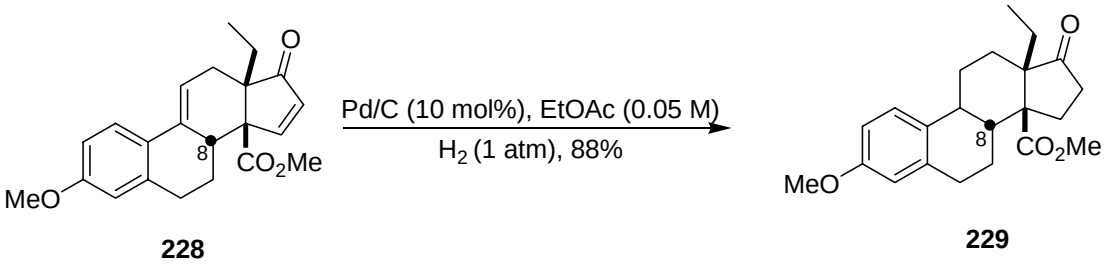
221 **228**

Scheme 45. Ethylation with KH

Although additives like HMPA, $ZnEt_2$, BEt_3 were used to increase the reactivity of enolate, no improvement in ethylation was observed. A reaction was also performed with MeI as an electrophile; however, the reaction was incomplete and the yield was 30%.

2-8.3 Reduction Reaction

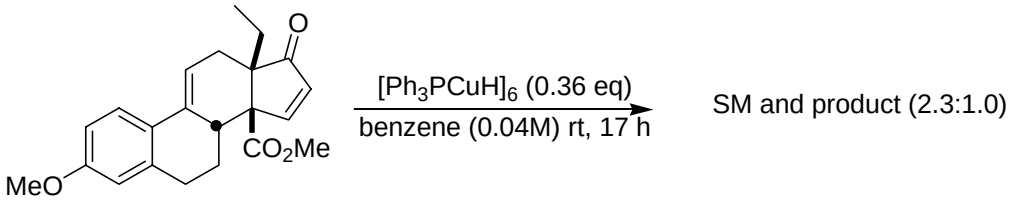
Even though problems were encountered in the ethylation step of the total synthesis of desogestrel (**218**), the synthesis was moved forward by performing the reduction of the double bond of α,β-unsaturated ketone **228**. Although there was a benzylic double bond in the molecule, palladium catalyzed reduction of α,β-unsaturated double bond by hydrogenation was performed. Unexpectedly, both the double bonds present in the compound were reduced and saturated compound **229** was isolated in 88% yield (Scheme 46). An *X-ray* of this compound was obtained (See in Appendix), which showed both the ethyl group and the hydrogen at position C-8 were cis to each other as it was found in the natural product desogestrel (**218**).



228 **229**

Scheme 46. Reduction by Hydrogenation

Copper hydride sources for reduction of of α,β-unsaturated ketones is well known in the literature.[105, 106] Triphenylphosphine copper hydride hexamer was used to accomplish the reduction of **228**. However, an incomplete conversion with a ratio of 2.3:1 of starting material to product was found, Scheme 47. Unfortunately, the product was inseparable from the starting material.



228

Scheme 47. Reduction of α,β-unsaturated Double Bond with Copper hydride

Making enough cyclopentadienone precursor **96** was the toughest hurdle for producing enough DAA **221.** A large scale synthesis of **96** and finding a proper condition for ethylation would facilitate the completion of the synthesis of desogestrel (**218**).

2-9 Conclusions

An efficient methodology was developed to slowly generate an ester derivative of cyclopentadienone **98** from 2-bromo-3-methylcarboxycyclopentenone (**96**). When **96** was treated with TEA in refluxing toluene, transient intermediate cyclopentadienone **98** was formed, which dimerized instantly to furnish cyclopentadienone dimer. However, the dimer was not isolable. Under the reaction conditions the dimer decarbonylated to generate indanone **97**. The indanone was a mixture of two regioisomers with one major isomer (10:1).

Diels-Alder reactions were performed by trapping this transient cyclopentadienone derivative with a wide variety of dienes generating [4+2] cycloadducts. Electron rich dienes preferably participated in these reactions effectively as cyclopentadienone was relatively electron poor species. Different alkyl-substituted, 1-substituted dienes produced high yields of regio- and diastereoselective cycloadducts. The structures of these cycloadducts were confirmed by comparing 2-D NMR spectra with the NMR spectra of two cycloadducts **130** and **139** of which *X-ray* structures were obtained.

Even though the reaction was stereoselective with 1-substituted dienes, it was not regioselective when 2-substituted butadienes were used as well as with allylidenecyclopropane (**160**). Additionally, no facial selectivity was observed when reactions were performed with chiral dienes **166** and **169.**

A high yield of cycloadduct **221** was obtained with Dane's diene (**220**). Similarity in structure with desogestrel (**218**) and with an established core structure, an attempt was

made to pursue the total synthesis of this steroidal compound. However, ethylation of cycloadduct **221** suffered from low reaction yield. Finding proper conditions for ethylation step, the total synthesis of **218** could be accomplished.

CHAPTER 3

EXPERIMENTAL

3-1 General Information

All the reactions were performed in an oven dried flask cooled under nitrogen or in a flame-dried flask for lithium reagent reactions under a nitrogen or argon atmosphere. Lithium reagents such as n-BuLi, tert-BuLi, LHMDS, DIBAL-H were measured and transferred by gas tight syringes under argon. Moisture sensitive reagents were transferred in a glove bag under a nitrogen atmosphere. Tetrahydrofuran (THF), and toluene were freshly distilled over benzophenone, and sodium. Dichloromethane (CH_2Cl_2), triethylamine (NEt_3), diisopropylamine (*iso*-Pr_2NH) were freshly distilled over calcium hydride. Solvent was removed by rotary evaporator under vacuum (water aspirator). Residual solvent was removed under reduced pressure using a vacuum pump usually at 3 mm Hg. Chromatographic separation was performed on Silicycle ultra pure silica gel (230-400 mesh) and also on 60 mesh from Aldrich with ACS grade solvents. Analytical thin layer chromatography was done on glass-back silica gel plates with F-254 indicator. Compounds were visualized under UV light or by vanillin, phosphomolybdic acid solution and heating the TLC plate on a hot plate heated to 350 °C or potassium permanganate solution. Melting points were determined with a Fisher-Johns melting point apparatus and are uncorrected. Infrared spectra were recorded on a Perkin Elmer 1600 series FT-IR spectrometer as neat liquids on NaCl cells or as a solution in chloroform (passed through neutral alumina right before using) liquid IR cell. Gas

chromatography was performed on a Hewlett-Packard 5890 instrument equipped with a SE-30 Alltech econocap column and a flame ionization detector. Chromatograms were recorded on a Hewlett-packard series II integrator.

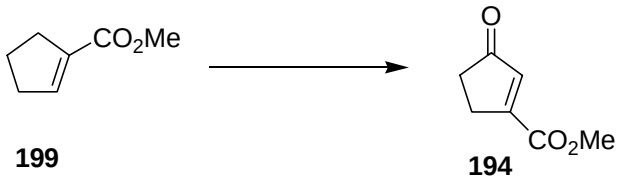
^{1}H-NMR were recorded on a Bruker ARS-250 (250 MHz), DRX-300 (300 MHz), and DRX-500 (500 MHz) spectrometer and are reported in ppm (δ) from tetramehtylsilane (TMS: δ= 0.0ppm). Data are reported according to the following sequence: chemical shift, multiplicity (s =singlet, d =doublet, t =triplet, q= quartet, m= multiplet, dd= doublet of doublet, ddd= doublet of doublet of doublet, bm= broad multiplet), coupling constants in Hz, and integration. ^{13}C-NMR spectra were performed on a Bruker ARS-250 (62.5 MHz), DRX-300 (75 MHz), and DRX-500 (125 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in ppm from tetramethylsilane with solvent resonance as the internal standard ($CDCl_3$: δ 77 ppm).

Elemental analyses were performed by MHW Laboratories, Phoenix Arizona. High-resolution mass spectra were performed by the Department of Chemistry, Ohio State University, Columbus, OH; College of Sciences Major Instrumentation Cluster, Old Dominion University, 4600 Elkhorn Ave, Norfolk, VA 23529 with a Bruker 12 Tesla FTICR-MS with an Apollo II ion source. X-Ray diffraction data were collected by Dr. Charles Barnes at Department of Chemistry, University of Missouri-Columbia.

3-2 Synthesis of compound 96

3-2.1 Allylic oxidation

The following oxidation reaction was performed with different oxidizing agents and is elaborated in the following section.



199 **194**

3-2.1.1 Allylic oxidation with $Mn(OAc)_3.2H_2O$

A solution of cyclopentene ester **199** (567.4 mg, 4.5 mmol) was prepared in freshly distilled (over CaH_2) EtOAc (0.12M, 37.5 mL) in an oven dried 100mL round bottom flask equipped with a magnetic stir bar. 5-6M *tert*-butylhydroperoxide* solution in decane (18 mmol, 3.3 mL) and 4A^o MS (100 mg/0.36 mmol; 508.8 mg) were added to this solution an stirred for 30m. $Mn(OAc)_3.2H_2O$ (0.45 mmol, 120.6 mg) was transferred in a nitrogen glove bag in a vial and added quickly to the reaction mixture. The reaction mixture was degassed for 3m with nitrogen gas and stirred the reaction mixture under oxygen balloon at rt for 48h. The reaction mixture was filtered through a small silica gel packing under vacuum and washed with EtOAC. Solvent was removed and purified with 10% to 50% Et_2O/pentanes on silica gel using flash chromatography. 472mg enone ester **194** isolated with 75% yield.

***** 5-6M *tert*-butylhydroperoxide solution in decane saved over 4A^o MS was bought from Aldrich.

3-2.1.2 Allylic oxidation with $Rh_2cap_4.2CH_3CN$

A 50 mL oven dried flask was equipped with a magnetic stir bar was charged with enester **199** (764.8 mg, 6.06 mmol), $Rh_2cap_4.2CH_3CN$ (4.5 mg, 0.1 mol%, 0.006 mmol), K_2CO_3** (419 mg, 50 mol%, 3.03 mmol), and DCM (0.27 M, 22 mL). The flask was sealed with a rubber septum and *tert*-butylhydroperoxide solution* (5 equiv, 30.3 mmol, 6 mL, 5-6 M sol^n in DCM) was added. The reaction mixture turned magenta color and bubble was generated. An empty balloon was placed to capture oxygen gas that was generated from the peroxide. After one hour $Rh_2cap_4.2CH_3CN$ (4.5 mg, 0.1 mol%, 0.006 mmol) and *tert*-butylhydroperoxide solution (5 equiv, 30.3 mmol, 6 mL) were added and stirred for another hour. The reaction mixture was filtered over silica gel under vacuum and solvent was removed. The crude product was purified by flash chromatography with 20% Et_2O/pentanes over silica gel and 403.5 mg enone-ester **194** was isolated.

* The 5-6 M TBHP solution was prepared by taking 17 mL 70% aqueous solution of TBHP and extracting it with 14 mL DCM. The aqueous layer was drained in a separatory funnel and the organic layer was dried over $MgSO_4$ three times for 10 minutes before using it in the reaction.

** K_2CO_3 was activated overnight by heating at 140 °C it under vacuum.

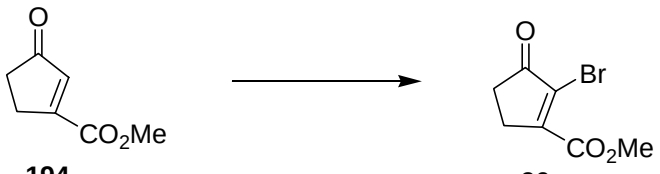
3-2.1.3 Allylic oxidation with $Pd(OH)_2/C$

Cyclopentene-ester **199** (290 mg, 2.35 mmol) was weighed in a 25mL oven dried round bottom flask equipped with a magnetic stir bar. $Pd(OH)_2/C$ (20 wt%, 66.2 mg, 5 mol%) and K_2CO_3 (50 mol%, 163 mg), and DCM (0.32 M) were added to the flask. 1 M *tert*-butylhydroperoxide solution* in DMC (11.77 mmol., 11.8 mL) was added drop wise

to the prepared reaction mixture at ice bath temp. The flask was then sealed with a rubber septum and a nitrogen balloon was placed in the flask through the septum. Oxygen gas was generated. Then it was stirred for 48 hrs at room temperature. The reaction was monitored by thin layer chromatography (TLC). Three spots were observed on the TLC from the cyclopentene ester (SM), side product and product. The reaction mixture was filtered through a short silica layer and washed with enough DCM. The solvent was removed with a rotary evaporator. Crude product was purified with 5%, 10%, and 20% Et_2O/pentane consecutively on silica gel by flash chromatography and 129.7 mg of the desired product **194** was isolated in 41% yield. The ^{1}H-NMR was compared with the literature reported ^{1}H-NMR and it matched with the literature reported one.

* 1M *tert*-butylhydroperoxide solution was prepared following the procedure reported in 'Purification of Laboratory Chemicals' Fifth Edition, by Armarego and Chai.

3-2.2 Bromination reaction



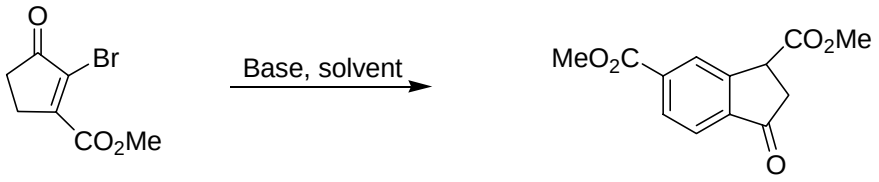
194 **96**

A solution of 3-oxocyclopent-1-enecarboxylate **194** (190 mg, 1.356 mmol) was made in DCM (15 mL, 0.09 M) in a 100 mL round bottom flask equipped with a magnetic stir bar. A solution of bromine (1.5e q, 77 μL) in DCM (0.15 M) was added from an additional funnel to the previous reaction mixture at 0 °C drop wise. The other

end of the addition funnel was connected to a drying tube. After complete addition of the bromine solution the reaction mixture was stirred at rt for 15 m. The reaction was again cooled to 0C with an ice bath and a solution of TEA (2.03 mmol, 0.385 mL) in DCM (0.20 M) was added to the reaction mixture drop wise. After complete addition the reaction mixture was again warmed to rt and stirred for 5 hr at rt. The reaction was monitored with TLC. The reaction mixture was diluted with DCM and washed with 1M HCl, sat $NaHCO_3$ sol^n, dried over $MgSO_4$. Solvent was removed under reduced pressure. Crude product was purified by 10% EtOAc/hexanes by flash chromatography over silica gel and 172.8 mg of **96** was isolated in 58% yield.

White solid, mp 66-67 °C, IR (neat): 3000, 2970, 2361, 2333, 1718 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 2.63-2.66 (m, 2H), 2.88-2.91 (m, 2H), 3.92 (s, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 28.3, 32.6, 52.4, 130.9, 157.5, 163.8, 201.3; HRMS calculated for $C_7H_7BrO_3^+$ 217.957307 amu, found 217.9597 amu.

3-3 Dimerization Reaction



96 **97**

A solution of bromo-enone ester **96** (46.2 mg, 0.211 mmol) was prepared in a 10 mL round bottom flask in toluene (0.1 M, 2.1 mL) equipped with a stir bar. TEA (59 μL, 0.422 mmol) was added to this solution and a condenser was placed on the flask and

refluxed for 65 minutes at 120 °C as the TLC showed all SM was consumed. The reaction mixture had a light dark color. Toluene was removed by rotavap and a flash column was performed on the crude product with 20% EtOAc/hexanes to produce 18.5 mg of DCD **97** in 71% yield. It was colorless solid, mp 98-99 °C, IR (neat): 3020, 2400, 1724, 1615, 1523, 1437, 1301, 1255, 1210 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$): δ 2.96 (dd, *J*= 19.1, 8.2 Hz, 1H), 3.23 (dd, *J*= 19.2, 3.7 Hz, 1H), 3.82 (s, 3H), 3.97 (s, 3H), 4.38 (dd, *J*= 8.1, 3.6, 1H), 7.80 (d, *J*=8.1 Hz, 1H), 8.32 (dd, *J*= 8.1, 1.6, 1H), 8.44 (d, *J*=1.5Hz, 1H); ^{13}C-NMR (125 MHz, $CDCl_3$): δ 39.7, 43.5, 52.5, 52.9, 125.4, 126.8, 131.2, 135.7, 136.6, 155.0, 165.9, 171.5, 202.9; HRMS calculated for $C_{13}H_{12}O_5Na^+$ 271.057693 amu, found 271.05614 amu.

3-4 Diels-Alder Reactions with Different Dienes

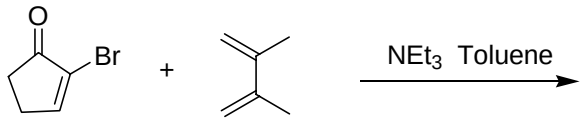
3-4.1 General Procedure of Diels-Alder Reactions in THF

Methyl-2-bromo-3-oxocyclopent-1-enecarboxylate **96** was taken into a 10 mL flask equipped with a stir bar and a condenser. A solution of this compound was made in THF in 0.10-0.04 M concentration. Desired amount of diene and triethylamine were added into this solution and heated to gentle reflux under nitrogen atmosphere. Reaction was monitored by TLC. Usually a pale yellow color reaction mixture was obtained when the reaction was complete. After completion of the reaction, THF was removed under vacuum. The crude product was dissolved in dichloromethane, washed with 1×5 mL 1M HCl, 1×5 mL water, 1×5 mL brine, dried over $MgSO_4$ and concentrated. Purification of this crude product by flash chromatography on silica gel with 15-25% EtOAC/hexanes gave the desired Diels-Alder adduct.

3-4.2 General Procedure of Diels-Alder Reactions in Toluene

Reactions were usually carried out in 20-40 mg scale of compound **96** and reproducible**.** Into a 10 mL flask enone ester **96** was taken and a solution of this was made in toluene in 0.04 M concentration. Desired amount of diene and triethylamine were added into this solution and heated to reflux under nitrogen atmosphere at bath temperature 120-130 °C. Reaction was monitored by TLC. A nice light yellow color was an indicative of a successful reaction. After completion of the reaction, toluene was removed under vacuum. Purification of this crude product by flash chromatography on silica gel with 15-20% EtOAC/hexanes provided the desired product.

3-4.3 Diels-Alder reaction with 2-bromocyclopenteneone

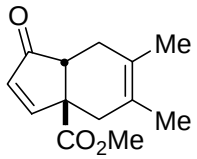


49 **102**

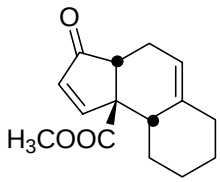
A 0.04 M solution of 2-bromocyclopentenone **49** (0.166 mmol) was prepared in toluene in a 25 mL round bottom flask and 2,3-dimethyl-butadiene **102** (10 eq, 1.66 mmol, 0.188 mL) and triethylamine (3 eq, 0.499 mmol, 70 μL) were added to this solution. A condenser sealed with a rubber septum was placed on the flask and a nitrogen balloon was placed on the condenser. The reaction mixture was refluxed for 49.5 hours and solvent was removed by rotary evaporator. ^{1}H-NMR of the crude compound was

checked and a flash column chromatography was done with 20% EtOAc/Hexanes. Only 2-bromocyclopentenone (**49**) was recovered with 10% yield.

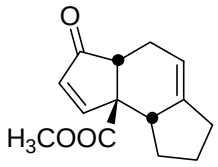
3-4.4 Diels-Alder Adducts from Alkyl Substituted Dienes



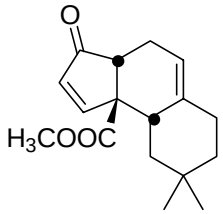
(**103**) White solid, mp 60-61 °C, 73% yield, IR (neat): 2987, 2952, 2858, 1715, 1437, 1294, 1220, 1132 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$): δ 1.59 (s, 3H), 1.64 (s, 3H), 2.18 (d, *J*= 14.7 Hz, 1H), 2.25 (bm, 1H), 2.37 (dd, *J*= 14.7, 3.1 Hz, 1H), 2.4 (bd, J= 14.7 Hz, 1H), 2.87 (dd, *J*= 6.1, 3.1, 1H), 3.75 (s, 3H), 6.14 (d, *J*=5.6 Hz, 1H), 7.44 (d, *J*= 5.6 Hz, 1H); ^{13}C-NMR (125 MHz, $CDCl_3$): δ 19.18, 19.22, 31.0, 37.5, 48.3, 52.6, 56.9, 124.0, 128.2, 134.4, 163.4, 174.2, 210.1; HRMS calculated for $C_{13}H_{16}O_3Na^+$ 234.099163 amu, observed mass 243.09964 amu.



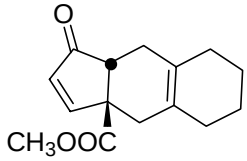
(112) Oil, 77% yield in Toluene, 63% in THF, IR (neat): 2936, 2867, 1717, 1435, 1236, cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$): δ 1.35-1.27 (m, 1H), 1.50-1.40 (m, 2H), 1.61-1.53 (m, 1H), 1.83-1.71(m, 2H), 2.15-2.02 (m, 2H), 2.29-2.22 (m, 1H), 2.63 (ddd, *J*= 17.0, 6.5, 2.0 Hz, 1H), 2.73-2.68 (m, 1H), 2.74 (dd, *J*= 7.2, 2.1 Hz, 1H), 3.79 (s, 3H), 5.51-5.47 (m, 1H), 6.25 (d, *J*= 5.8Hz, 1H), 7.70 (d, *J*= 5.8Hz, 1H); ^{13}C-NMR (62.5 MHz, $CDCl_3$): δ 23.0, 23.1, 26.1, 30.9, 42.1, 49.3, 52.6, 58.6, 118.8, 134.2, 138.8, 162.1, 174.6, 209.0; HRMS calculated for $C_{15}H_{18}O_3Na^+$ 301.104643 amu, found 301.10412 amu.



(**113**) Oil, 56% yield in Toluene, 33% yield in THF, IR (neat): 2952, 1715, 1434, 1233 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$): δ 1.63-1.55 (m, 2H), 1.81-1.63 (m, 1H), 2.02-1.96 (m, 1H), 2.24-2.08 (m, 3H), 2.66 (ddd, 14.7, 7.3, 1.9Hz, 1H), 2.83 (dd, *J*= 6.2, 2.0 Hz, 1H), 2.87-2.84 (m, 1H), 3.77 (s, 3H), 6.00-5.78 (m, 1H), 6.22 (d, *J*= 5.8Hz, 1H), 7.60 (d, *J*= 5.8Hz, 1H); ^{13}C-NMR (62.5 MHz, $CDCl_3$): δ 25.1, 26.2, 28.1, 31.6, 45.3, 50.0, 52.6, 59.4, 116.5, 135.6, 144.7, 161.6, 174.5, 209.9; HRMS calculated for ($C_{14}H_{16}O_3Na^+ + O_2 + Na^+$) 287.088993 amu, found 287.08989 amu.



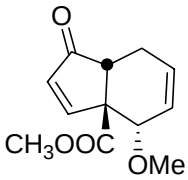
(**114**) Oil, 80% yield, IR (neat): 2953, 2927, 2863, 1717, 1237 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$): δ 0.96 (s, 3H), 0.97 (s, 3H), 1.28-1.16 (m, 2H), 1.43-1.32 (m, 2H), 2.10-1.98 (m, 2H), 2.25-2.16 (m, 1H), 2.63 (ddd, *J*= 15.7, 7.9, 1.9 Hz, 1H), 2.72 (dd, *J*=6.8, 2.0 Hz, 1H), 2.86-2.80 (bm, 1H), 3.77 (s, 3H), 5.50-5.49 (b, 1H), 6.24-6.23 (d, J= 5.8 Hz, 1H), 7.66-7.64 (d, *J*= 5.9 Hz, 1H); ^{13}C –NMR (75 MHz, $CDCl_3$): δ 23.5, 27.5, 28.5, 30.1, 37.3, 38.4, 38.9, 49.7, 52.6, 58.8, 118.8, 134.7, 138.9, 162.1, 174.6, 209.3; HRMS calculated for $C_{17}H_{22}O_3Na^+$ 297.146113 amu, found 297.14694 amu.



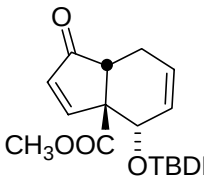
(115) Oil, 82% yield, IR (neat) 2930, 715, 1436, 1252 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$): δ 1.45-1.55 (m, 4H), 1.67-2.50 (m, 4H), 2.25-2.35 (m, 2H), 2.88 (dd, *J*= 12, 6.6Hz, 1H), 3.75 (s, 3H), 6.14

(d, *J*= 5.6 Hz, 1H), 7.45 (d, *J*= 5.6 Hz, 1H) ; ^{13}C-NMR (125 MHz, $CDCl_3$): δ 22.8, 22.9, 29.63, 30.3, 30.2, 36.4, 48.2, 52.6, 56.8, 126.6, 130.7, 134.1, 163.5, 174.2, 210.1; HRMS calculated for ($C_{15}H_{18}O_3 + O_2 + Na^+$) 301.104643 amu, found 301.10599 amu.

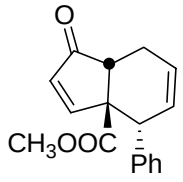
3-4.5 Diels-Alder Adducts with 1-Substituted Dienes



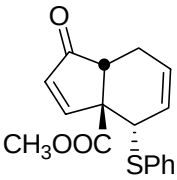
(**123**) Oil, 84 % yield in Toluene, 52% yield in THF, IR (neat): 3046, 2952, 2829, 1716, 1593, 1437, 1256 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 2.22-2.17 (m, 1H), 2.69-2.63 (m, 2H), 3.47 (s, 3H), 3.81 (s, 3H), 4.48 (dd, *J*= 4.3, 2.2 Hz, 1H), 5.84-5.76 (m, 2H), 6.33 (d, *J*= 5.8 Hz, 1H), 7.73 (d, *J*=5.8 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 24.3, 48.4, 52.8, 58.1, 61.1, 80.0, 126.8, 129.6, 135.9, 162.4, 173.9, 208.8; HRMS (EI) calculated for $C_{12}H_{14}O_4^+$ 222.08921 amu, found 222.0779 amu.



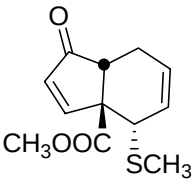
(**124**) Oil, 79% Yield, IR (neat): 2953, 2856, 1718, 1254, 1119 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$): δ 0.08 (s, 3H), 0.10 (s, 3H), 0.92 (s, 9H), 2.23-2.18 (m, 1H), 2.67-2.62 (m, 2H), 3.77 (s, 3H), 4.85 (q, *J*= 4.72, 2.32 Hz, 1H), 5.61-5.58 (m, 1H), 5.76-5.71(m, 1H), 6.32 (d, *J*= 5.8 Hz, 1H), 7.80 (d, *J*= 5.8 Hz 1H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ 5.4, -4.6, 17.9, 24.3, 25.6, 30.9, 48.1, 52.6, 62.5, 72.3, 125.9, 133.1, 135.8, 162.9, 174.0, 207.0; HRMS calculated for $C_{17}H_{26}O_4SiNa^+$ 345.149255 amu, found 345.14820 amu.



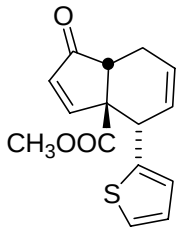
(**125)** Oil, 66% yield; IR (neat): 3032, 2952, 2847, 1717, 1598, 1454, 1254, 1230 cm^{-1}; ^{1}H-NMR (250 MHz, $CDCl_3$): δ 2.10-2.40 (m, 1H), 2.75-2.87 (m, 2H), 3.68 (s, 3H), 4.07 (q, *J*= 2.9Hz, 1H), 5.87-5.93 (m, 1H), 5.99-6.04 (m, 1H), 6.21 (d, *J*= 5.9 Hz, 1H), 7.09-7.15 (m, 2H), 7.19 (d, *J*= 5.9 Hz, 1H), 7.29-7.40 (m, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 24.2, 47.0, 49.5, 52.4, 61.5, 127.4, 128.5, 129.0, 129.1, 130.7, 134.8, 139.1, 162.2, 174.0, 209.0; Elemental analysis: Expt C, 75.97%; H, 6.23% Calculated C 76.10%, H, 6.01%.



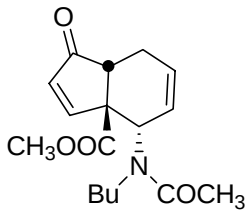
(**126**) Oil, 84% yield; IR (neat): 3053, 2952, 2847, 1717, 1585, 1479, 1438, 1300, 1233 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 2.42-2.27 (m, 1H) , 2.73-2.63 (m, 1H), 2.79 (dd, =5.3, 2.9, 1H), 3.63 (s, 3H), 4.47-4.44 (m, 1H), 5.83-5.77 (m, 1H), 5.94-5.88 (m, 1H), 6.33 (d, *J*= 5.8 Hz, 1H), 7.46-7.25 (m, 5H), 7.76 (d, *J*= 5.8 Hz, 1H); ^{13}C-NMR (125 MHz, $CDCl_3$): δ 23.8, 49.7, 49.9, 52.8, 60.6, 127.5, 129.3, 129.9, 130.2, 131.9, 134.4, 135.9, 139.1, 161.5, 173.2, 208.2; HRMS calculated for ($C_{17}H_{16}O_3S$ + O + Na^+) 339.066148 amu, observed 339.06514 amu.



(**127)** Oil 67% yield; IR (neat): 30.42, 2953, 2920, 2847, 1716, 1594, 1435, 1232 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$): δ 2.16 (s, 3H), 2.26-2.33 (m, 1H), 2.64 (ddd, *J*= 19.2, 6.5, 3.0 Hz, 1H) 2.77 (dd, *J* =7.5, 3.0 Hz, 1H), 3.79 (s, 3H), 3.92-3.94 (m, 1H), 5.74-5.77 (m, 1H), 5.89-5.92 (m, 1H), 6.30 (d, *J*= 5.5Hz, 1H), 7.72 (d, *J*= 5.5 Hz, 1H) ; ^{13}C-NMR (125 MHz, $CDCl_3$): δ 16.1, 23.8, 47.6, 49.8, 52.9, 60.8, 129.0, 130.1, 135.5, 161.7, 173.55, 208.3; Elemental analysis: Expt C, 60.27%; H, 5.76% Calculated C 60.48%, H, 5.92%.

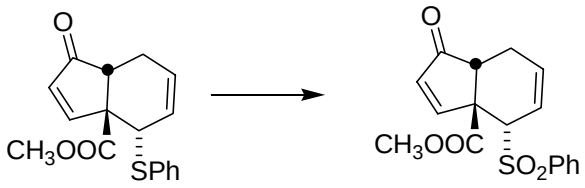


(**128**) Oil, 78% yield; IR (neat): 3044, 2952, 2902, 2361, 2329, 1716, 1435, 1297, 1231 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 2.98-2.40 (m, 1H), 2.74-2.85 (m, 2H), 3.75 (s, 3H), 4.46 (dd, *J*= 5.7, 3.0 Hz, 1H), 5.89-6.06 (m, 2H), 6.25 (d, *J*= 5.6Hz, 1H), 6.84 (d, *J*= 3.6, 1H), 7.01 (q, *J*= 3.6Hz, 1H), 7.24 (dd, *J*= 5.1, 1.2 Hz, 1H), 7.32-7.29 (d, *J*= 5.6 Hz, 1H) ; ^{13}C-NMR (75 MHz, $CDCl_3$): δ 24.5, 42.0, 49.6, 52.7, 61.8, 124.8, 126.1, 127.1, 129.1, 130.7, 135.47, 142.06, 162.0, 173.9, 208.8; Elemental analysis: Expt C, 65.72%; H, 4.99% Calculated C 65.67%, H, 5.14%.



(**129**) Oil, 84% yield, IR (neat liq): 2957, 2874, 2362, 1718, 1653, 1413, 1239 cm^{-1}; ^{1}H-NMR (250 MHz, $CDCl_3$): δ 0.93 (t, *J*= 7.3Hz, 3H), 1.33-1.24 (m, 2H), 1.68-1.40 (m, 2H), 2.14 (s, 3H), 2.38-2.34 (m, 1H), 2.91-2.72 (m, 3H), 3.17-3.11 (m, 1H), 3.78 (s, 3H), 5.42 (q, *J*=2.7 Hz, 1H), 5.68 (dt, *J*= 9.8, 3.0 Hz, 1H), 6.03-5.96 (m, 1H), 6.23 (d, *J*= 5.9Hz, 1H), 7.55 (d, *J*=5.9 Hz, 1H); ^{13}C-NMR (62.5 MHz, $CDCl_3$): δ 13.6, 20.2, 21.9, 22.4, 33.4, 48.26, 48.35, 52.9, 56.6, 60.0, 125.6, 129.5, 133.5, 162.0, 171.6, 173.5, 207.9; HRMS calculated for ($C_{17}H_{23}NO_4^-$ Na^+) 328.151927amu, found 328.15191 amu.

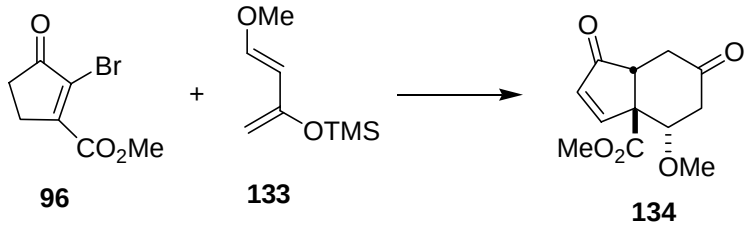
3-4.6 Oxidation of Sulfide to Sulfone



126 **130**

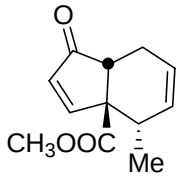
A solution of DAA **126** (32.1 mg, 0.107 mmol) was prepared in DCM (0.05 M, 2 mL) and the temperature was lowered to -30 °C. A solution *m*-CPBA (55.4 mg, 0.16 mol) in DCM (1 mL) was added to the reaction mixture drop wise under nitrogen atmosphere and stirred for 1.5 h. The solvent was removed and purification of the crude was done on silicagel column providing 26.2 mg, 74% yield of the desired sulfone **130**. It was a white solid with a mp of 160-161 °C ; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 2.15-2.05 (m, 1H), 2.81-2.67 (m, 2H), 5.82 (dt, *J*= 3.1 Hz, 1H), 6.09-6.00 (m, 1H), 6.41 (d, *J*= 5.8 Hz, 1H), 7.73-7.56 (m, 3H), 7.96-7.92 (m, 2H), 7.96-7.92 (m, 2H), 8.07 (d, *J*= 5.8 Hz, 1H); ^{13}C-NMR (62.5 MHz, $CDCl_3$): δ 23.9, 50.1, 53.6, 57.6, 65.5, 121.4, 128.4, 129.5, 131.9, 134.2, 135.9, 139.0, 160.6, 173.1, 206.7; HRMS calculated for ($C_{17}H_{16}O_5SNa^+$) 355.061065 amu, found 355.060844 amu. X-Ray crystallography data on this compound was obtained.

3-4.7 Diels-Alder Reaction with Danishefsky's Diene

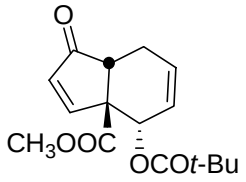


A solution of Bromo-enone-ester **96** (8.1 mg, 0.037 mmol) and $Et_3N.HBr$ (0.007 mmol, 20 mol%) was made in d_6-benzene under nitrogen atmosphere. Denishefsky diene **133** (0.185 mmol) and Et_3N (0.111 mmol) were added to the reaction mixture and transferred to an NMR tube. The reaction was monitored by ^{1}H-NMR at 80 °C. After 5.5 hours all the SM (**96**) was consumed. The reaction mixture was cooled down to room tempreture and poured into 5% HCl. The aqueous medium was extracted with EtOAc (3 × 10 mL). The combined organic layers was washed with $NaHCO_3$ solution, brine, dried over Na_2SO_4 and concentrated. Purification by flash chromatography on silica gel with Hexanes/Et_2O (1: 2) provided 53% of the DA adduct **134.** Oil, 53% yield, IR (neat): 3076, 2955, 2836, 1792, 1718, 1457, 1437, 1232, 1100 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$): δ 2.18 (dd, J= 18, 10 Hz, 1H), 2.55-2.67 (m 2H), 2.78-2.95 (m, 2H), 3.42 (s, 3H), 3.83 (s, 3H), 4.31 (dd, J= 8.0, 3.4 Hz, 1H), 6.43 (d, *J*=5.8 Hz, 1H), 7.75 (d, *J*= 5.8 Hz, 1H); ^{13}C-NMR (125 MHz, $CDCl_3$): δ 37.8, 39.8, 45.7, 53.2, 57.7, 59.0, 77.8, 134.6, 161.0, 173.0, 205.8, 206.5; HRMS calculated for ($C_{12}H_{14}O_5Na^+$) 261.073345 amu, found 261.07297 amu.

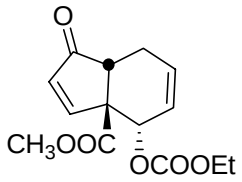
3-4.8 More Diels-Alder Adducts



Reaction in a sealed tube: In a sealed tube 37.2 mg (0.17 mmol) of 2-bromo-enone-ester (**96**) was dissolved in 1.7mL toluene (0.1M). Piperylene (1.7 mmol, 0.17 mL) and TEA (0.51 mmol, 122 μL) were added to this solution and the tube was sealed. The reaction was heated at 115 °C for 1h 15 m. Solvent as removed and a flash column was performed on this crude product with 15% EtOAc/Hexanes. 71% DAA **138** and 14% DCD **97** were isolated. Oil, IR (neat): 3036, 2954, 2879, 2848, 1715, 1595, 1457, 1436, 1254, 1231 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$): δ 1.18 (d, J =9.0 Hz, 3H), 2.19-2.25 (m, 1H), 2.66 (ddd, J= 15.0, 7.5, 2.2 Hz, 1H), 2.76 (dd, J= 7.5, 2.0 Hz, 1H), 2.80-2.85 (m, 1H), 3.77 (s, 3H), 5.42-5.45 (m, 1H), 5.81-5.86 (m, 1H), 6.25 (d, J= 5.5 Hz, 1H), 7.64 (d, J= 5.5 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 15.9, 24.4, 35.5, 50.1, 52.6, 60.3, 128.0, 132.5, 135.7, 161.5, 174.4, 209.4; Elemental analysis: Expt C, 69.83%; H, 6.59% Calculated C 69.88%, H, 6.84%.

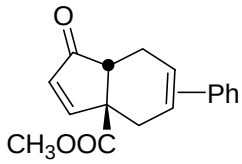


(**139**) White Solid, mp 62-63 °C, 61% yield; IR (neat): 2974, 1736, 1716, 1480, 1485, 1437, 1255, 1279, 1234, 1147 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$): δ 1.23 (s, 9H), 2.36-2.28 (m, 1H), 2.69 (ddd, J= 15.6, 7.5, 2.5Hz, 1H), 2.90 (dd, J= 7.0, 2.5Hz, 1H), 3.76 (s, 3H), 5.58 (dt, J= 10.0, 2.5Hz, 1H), 5.77 (q, J= 2.5Hz, 1H), 5.91-5.86 (m, 1H), 6.34 (d, J=6.0Hz, 1H), 7.66 (d, J= 6.0Hz, 1H); ^{13}C-NMR (125 MHz, $CDCl_3$): δ 23.9, 27.0, 38.9, 47.1, 53.0, 60.2, 71.4, 128.0, 128.4, 136.1, 160.6, 172.4, 177.2, 208.1; Elemental analysis: Expt C, 65.57%; H, 6.85% Calculated C 65.74%, H, 6.90%. X-ray crystallographic data as obtained on this compound.

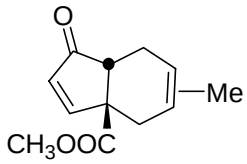


(**140**) Oil, 72% yield; IR (neat): 2956, 2361, 1750, 1718, 1437, 1472, 1257cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 1.33 (t, *J*= 7.2Hz, 3H), 2.20-2.34 (m, 1H), 2.70 (ddd, *J*= 16.7, 6.9, 2.1Hz, 1H), 2.81 (dd, *J*= 6.9, 2.1Hz, 1H), 3.78 (s, 3H), 4.24 (q, *J*= 7.2 Hz, 2H), 5.66 (dt, *J*= 9.6, 2.7 Hz, 1H), 5.83-5.92 (m, 1H), 6.34 (d, *J*= 5.7Hz, 1H), 7.72 (d, *J*= 5.7 Hz, 1H) ; ^{13}C-NMR (125 MHz, $CDCl_3$): δ 14.2, 23.9, 47.4, 53.1, 60.0, 64.6, 75.4, 127.8, 128.1, 136.4, 154.4, 160.6, 172.4, 208.0; Elemental analysis: Expt C, 60.16%; H, 5.57% Calculated C 59.99%, H, 5.75%.

3-4.9 Diels-Alder adducts with 2-substituted dienes

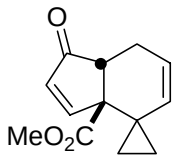


(**143**) Oil, 80% yield, 1:1 mixture of two regeoisomers; IR (neat): 3032, 2952, 2900, 2844, 1714, 1593, 1495, 1436, 1249, 1220 cm^{-1}; ^{1}H-NMR (250 MHz, $CDCl_3$): δ 2.35-3.15 (m, 5H, from each regeoisomers), 3.79 (s, 3H, from each regeoisomers), 5.9-5.97 (m, 1H from one regioisomer), 6.15-6.23 (m, 3H, from both isomers), 7.17-7.37 (m, 5H, from each regeoisomers), 7.50 (d, 2H, *J*= 5.6Hz, from each regeoisomers) ; ^{13}C-NMR (62.5 MHz, $CDCl_3$): δ 25.4, 27.8, 31.7, 33.7, 47.5, 48.4, 52.78, 52.83, 56.4, 56.97, 120.6, 124.3, 125.2, 125.5, 127.26, 127.3, 128.35, 128.40, 134.63, 134.9, 140.18, 140.54, 163.4, 163.9, 173.9, 173.9, 209.28, 209.8, from both the regeoisomers; HRMS calculated for $C_{17}H_{16}O_3Na^+$ to be 291.099163 amu, found 291.09932 amu.

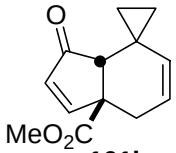


(**144**) Oil, 48% yield, 1.5: 1.0 mixture of two regioisomers; IR (neat): 2954, 2848, 1713, 1593, 1436, 1250, 1222 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$): δ 1.66 (s, 3H, major isomer), 1.69 (s, 3H, minor isomer), 2.6-2.17 (m, 8H, both isomers 4 x CH_2), 2.88 (dd, 1H, *J*= 11.00, 4.5 Hz, major isomer), 2.99 (dd, 1H, *J*= 11.00, 5.00 Hz, , minor isomer), 3.77 (s, 6H, both isomers CH_3), 5.37 (bm, 1H, minor isomer), 5.55 (m, 1H, major isomer), 6.15 (d, 1H, *J*= 5.65Hz, minor isomer), 6.16 (d, 1H, *J*= 5.66 Hz, major isomer), 7.45 (d, 1H, *J*= 5.68 Hz, major isomer), 7.46 (d, 1H, *J*= 5.68 Hz, minor isomer); ^{13}C-NMR (62.5 MHz, $CDCl_3$): δ major isomer: 23.2, 29.3, 35.7, 47.8, 52.7, 56.5, 121.2, 134.1, 134.3, 163.5, 174.0, 210.2 ; minor isomer: 24.4, 31.1, 35.7, 48.1, 52.63 56.0, 117.5, 133.5, 137.7, 164.0, 174.2, 209.6; HRMS calculated for $C_{12}H_{14}O_3Na^+$ to be 229.0835151 amu, found 229.083348 amu.

3-4.10 Diels-Alder adduct with allylidenecyclopropane



161a

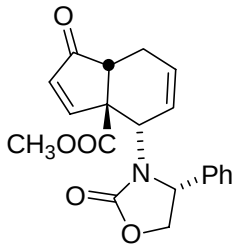


161b

Oil, IR 3034, 3004, 2954, 2847, 2361, 2337, 1717, 1456, 1436, 1255, 1212 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$): δ 0.42-0.39 (m, 1H, major isomer), 0.57-0.53 (m, 1H, minor isomer), 0.67-0.63 (m, 1H, minor isomer), 0.89-0.81 (m, 1H, major isomer), 1.03-0.98 (m, 1H, minor isomer), 1.37-1.32 (m, 1H, major isomer), 1.64 (s, 1H, minor isomer), 2.22 (s, 1H, major isomer), 2.46 (dd, 1H, *J*= 15.5, 8.5 Hz, major isomer), 2.53-2.49 (m, 1H, minor isomer), 2.61-2.55 (m, 1H, minor isomer), 2.67 (dt, 1H, *J*= 15, 3.0 Hz, major isomer), 3.09 (dd, 1H, *J*= 8, 4 Hz, minor isomer), 3.73 (s, 3H, minor

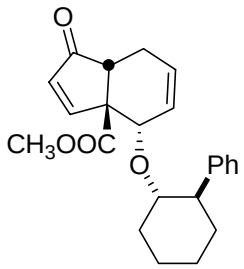
isomer), 3.76 (s, 3H, major isomer), 5.16 (dd, 1H, *J*= 9.0, 2.00 Hz., minor isomer), 5.56 (dd, 1H, *J*= 9.0, 3.0 Hz, major isomer), 5.73-5.69 (m, 1H, major isomer), 5.87-5.82 (m, 1H, minor isomer), 6.17 (d, 1H, *J*= 5.5 Hz, major isomer), 6.19 (d, 1H, *J*= 6.0Hz, minor isomer), 7.40 (d, 1H, J= 6.00 Hz, major isomer), 7.50 (d, 1H, *J*= 5.5 Hz, minor isomer) ; ^{13}C-NMR (125 MHz, $CDCl_3$): δ 10.8, 11.8, 12.2, 12.4, 19.7, 22.8, 23.0, 31.1, 50.0, 52.4, 52.8, 55.1, 57.9, 58.7, 125.4, 127.3, 132.8, 133.4, 134.4, 135.7, 163.1, 172.6, 174.0, 208.6, 209.1; Elemental analysis: Expt C, 71.55%; H, 6.33% Calculated C, 71.54%, H, 6.47%.

3-4.11 Diels-Alder reactions with chiral dienes

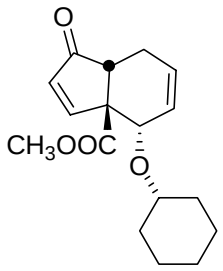


(**171**) Oil, IR (neat): 3034, 2954, 2909, 2848, 2361, 2252, 1751, 1594, 1477, 1458, 1409, 1358, 1237 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$): δ 1.99-1.90 (m, 1H, minor isomer), 2.36-2.27 (m, 1H, major isomer), 2.64-2.5 (m, 2H, minor), 2.74-2.66 (m, 1H, major), 2.92 (dd, 1H, *J*= 8.0, 2.50 Hz, major), 3.67 (s, 3H, major), 3.82 (s, 3H, minor), 4.09 (dd, 1H, *J*= 8.00, 3.00 Hz, major), 4.20 (q, 1H, minor), 4.24 (dd, 1H, J= 8.5, 5.5 Hz, minor), 4.54 (t, 1H, *J*= 8.00 Hz, major), 4.58 (dd, 1H, *J*= 8.00, 3.00 Hz, major), 4.70 (t, 1H, *J*= 8.5 Hz, minor), 4.90 (dd, 1H, *J*= 9.0, 5.5 Hz, minor), 5.02-4.99 (m, 1H, major), 5.32-5.27 (m, 1H, major), 5.80-5.70 (m, 2H, both), 5.98-5.92 (m, 1H, minor), 6.32 (d, 1H, *J*= 6.00 Hz, minor), 6.35 (d, 1H, *J*= 6.00 Hz, major), 7.46-7.17 (m, 10H, both), 7.69 (d, 1H, *J*= 5.5 Hz, minor), 7.82 (d, 1H, *J*= 6.0 Hz, major) ;^{13}C-NMR (125 MHz, $CDCl_3$): δ 22.5, 23.9, 48.0, 49.4, 53.1, 53.1, 54.6, 54.6, 60.1, 60.8, 61.9, 62.2, 70.0, 70.7, 124.0, 126.0, 126.98,

127.1, 127.5, 128.8, 130.0, 129.4, 129.5, 130.6, 134.5, 135.2, 138.20, 140.4, 157.5, 158.3, 160.8, 161.7, 172.4, 174.0, 207.4, 208.0 ; Elemental analysis: Expt C, 68.11%; H, 5.67% Calculated C, 67.98%, H, 5.42%.

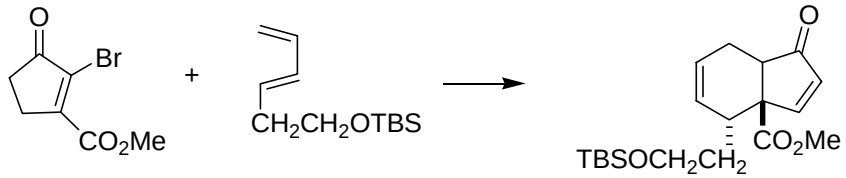


(**172**) Oil, IR (neat): 2928, 2857, 2361, 1734, 1718, 1254, 1098 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$): δ 0.90-0.83 (m, 2H both), 0.97 (d, H, *J*= 7.00 Hz), 1.44-1.15 (m, 7H), 1.64-1.50 (m, 2H), 1.80-1.70 (m, 2H), 1.93-1.83 (m, 4H), 2.4- 1.97 (m, 2H), 2.24-2.15 (m 2H), 2.30 (dd, 1H, *J*= 6.5, 2.0 Hz, minor), 2.42 (ddd, 2H, *J*= 30.00, 7.50, 2.00 Hz), 2.58-2.48 (m, 3H), 3.32 (td, 1H, *J*= 10.00, 4.00 Hz), 3.52 (s, 3H, minor), 3.62 (td, 1H, *J*= 7.8, 4.7Hz, minor), 3.76 (s, 3H, major), 4.42 (q, 1H, major), 4.65-4.62 (m, 1H, minor), 4.70 (dt, 1H, *J*= 10.00, 2.5 Hz, major), 5.48-5.38 (m, 1H, major), 5.68-5.58 (m, 2H, minor isomer), 6.09 (d, 1H, *J*=6.0Hz, minor), 6.14 (d, 1H, *J*= 6.0 Hz, major), 6.80 (d, 1H, *J*= 6.0 Hz, minor), 7.34-7.15 (m, 10H, both), 7.53 (d, 1H, *J*=6.00 Hz, major); ^{13}C-NMR (125 MHz, $CDCl_3$): δ 23.7, 24.3, 24.7, 25.0, 25.8, 25.9, 31.8, 32.8, 33.1, 33.4, 48.2, 48.4, 50.9, 51.1, 52.56, 52.63, 61.3, 61.6, 75.7, 76.2, 81.8, 84.0, 125.3, 125.7, 126.0, 126.2, 126.8, 127.8, 127.9, 128.0, 128.7, 130.6, 133.2, 135.1, 135.5, 144.3, 144.8, 162.9, 163.7, 173.5, 174.0, 208.91, 208.93 ; Elemental analysis: Expt C, 75.20%; H, 6.92% Calculated C, 75.38%, H, 7.15%.



(**173**) Oil, IR(neat): 2932, 2856, 1734, 1717, 1437, 1254, 1233, 1097 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$): δ 1.34-1.23 (m, 5H), 1.51 (m, 1H), 1.73-1.70 (m, 2H), 1.85-1.81 (m, 2H), 2.21-2.14 (m, 1H), 2.65-2.60 (m, 2H), 3.42-3.35 (m, 1H), 3.77 (s, 3H), 4.60 (dd, 1H, *J*= 4.5, 2.0 Hz), 5.77-5.66 (m, 2H), 6.29 (d, 1H, *J*= 5.5 Hz), 7.78 (d, 1H, J= 5.5 Hz); ^{13}C-NMR (125 MHz, $CDCl_3$): δ 23.79, 23.85, 24.40, 25.66, 31.65, 33.14, 48.21, 52.63, 61.62, 76.45, 77.64, 126.14, 131.92, 135.70, 163.20, 174.13, 208.99; Elemental analysis: Experimental C, 70.40%, H 7.58%; Theoretical C 70.31%, H 7.64%.

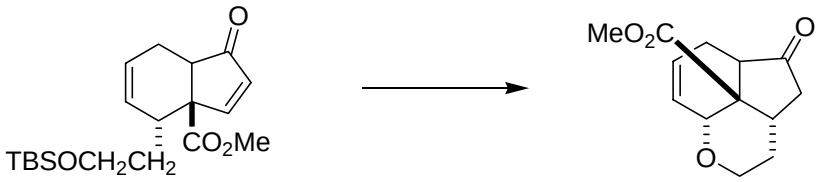
3-4.12 Diels-Alder reaction with Diene 181 and formation of 183



96 **181** **182**

The reaction was performed following the general procedure of Diels-Alder reactions in toluene described in **3-3.2**. This compound **182** is an oil. IR (neat): 2954, 2929, 2856, 1734, 1718, 1253, 1228, 1095, 836, 777 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$): δ 0.056 (s, 3H), 0.059 (s, 3H), 0.90 (s, 9H), 1.59-1.50 (m, 1H), 1.88-1.82 (m, 1H), 2.27-2.20 (m, 1H), 2.68 (ddd, J= 14.5, 7.00, 2.00 Hz, 1H), 2.75 (dd, *J*= 6.00, 2.00, 1H), 2.88-2.81 (m, 1H), 3.70-3.60 (m, 1H), 3.77-3.73(m, 1H), 3.77 (s, 3H), 5.71-5.54 (m, 1H), 5.91-5.86 (m, 1H), 6.25 (d, *J*=6.0 Hz, 1H), 7.60 (d, *J*= 5.5 Hz, 1H) ; ^{13}C-NMR (125

MHz, $CDCl_3$): δ -5.5. -5.4, 18.3, 24.5, 25.9, 33.8, 37.6, 50.2, 52.6, 60.2, 61.2, 128.4, 130.9, 135.8, 161.8, 174.3, 209.3.

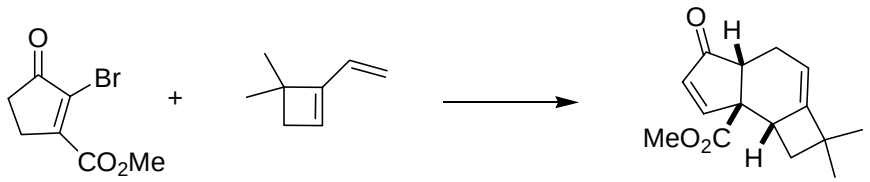


182 **183**

Diels-Alder adduct **182** (22.6 mg) was dissolved in methanol (0.064 M), and 100 μL of 1M HCl was added to this solution at 0°C and warmed to rt. After stirring overnight the solvent was removed and a column was done on the crude product with 20% EtOAc/Hexanes producing **183** in 32% yield.

White solid, IR (neat): 2954, 2924, 2845, 2361, 2333, 1750, 1718, 1082 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$): δ 1.56-1.47 (m, 1H), 1.87 (dt,, 1H, *J*= 32.0, 2.0 Hz), 2.31-2.23 (m, 2H), 2.42 (dt, 1H, *J*= 18.0, 4.0 Hz), 2.58 (dd, 1H, *J*= 19.5, 6.0 Hz), 2.81 (ddd, 1H, *J*= 11.0, 6.0, 1.5 Hz), 3.19-3.12 (m, 1H), 3.50 (td, 1H, *J*= 11.0, 1.5 Hz), 3.67 (s, 3H), 3.96 (ddd, 1H, *J*= 11.7, 5.0, 2.0 Hz), 4.18 (d, 1H, *J*=6.0 Hz), 5.74-6.65 (m, 2H) ; ^{13}C-NMR (125 MHz, $CDCl_3$): δ 23.2, 28.0, 37.2, 43.50, 43.52, 52.06, 52.4, 66.4, 75.7, 126.2, 130.4, 173.7, 212.7; HRMS calculated for $C_{13}H_{16}O_4Na^+$ to be 259.094080 amu, found 259.093638 amu.

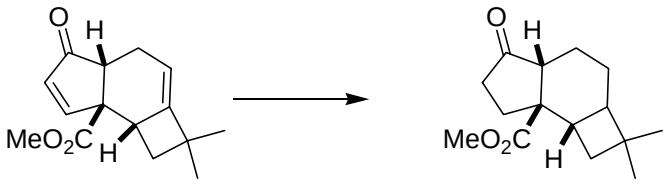
3-4.13 Formation of DAA 190 and its hydroxylamine derivative 193



96 **190** **191**

A solution of **96** (40.5 mg, 0.185 mmol) and diene **190** (excess) was prepared in toluene (0.1M) and TEA (78 μL, 0.55 mmol) was added to it and refluxed for 1hour 20 min. Toluene was removed, and the crude compound was purified by flash chromatography on silica gel with 15% EtOAc/ Hexanes producing 38.4mg of DAA **191** in 84% yield.

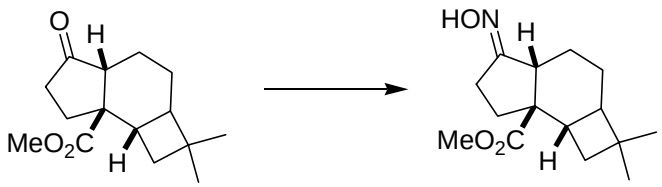
Oil, IR (neat):2954, 1737, 1713,1720, 1435, 1272, 1251, 1230 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$): δ 0.97 (s, 3H), 1.20 (s, 3H), 1.76 (dd, *J*= 11.5, 8.00 Hz, 1H), 2.06 (dd, *J*= 11.00, 9.50 Hz, 1H), 2.17-2.11 (m, 2H), 2.64 (ddd, *J*= 20.56, 7.50, 2.00 Hz, 1H), 2.87 (dd, *J*= 6.00, 1.50 Hz, 1H), 3.36-3.30 (m, 1H), 3.77 (s, 3H), 5.42-5.38 (dt, *J*= 7.5, 3.0 Hz, 1H), 6.24 (d, *J*= 5.50 Hz, 1H), 7.58 (d, *J*= 5.50 Hz, 1H); ^{13}C-NMR (125 MHz, $CDCl_3$): δ 22.6, 26.6, 27.3, 37.2, 39.1, 44.3, 50.1, 52.7, 56.9, 112.3, 133.7, 151.4, 162.7, 174.6, 209.9; HRMS calculated for $C_{15}H_{18}O_3Na^+$ to be 269.114816 amu, found 269.114326 amu.



191 **192**

DAA **191** (36 mg, 0.146 mmol) was dissolved in EtOAc (2.9mL, 0.05M) and a hydrogen balloon was placed on the flask through a rubber septum. The reaction was stirred for 15 hour 20 min. The reaction mixture was filtered through a short silica gel pad under vacuum and washed with chough DCM. Solvent was removed and a clean product **192** (35.3mg) was obtained in 96% yield.

Oil, IR (neat): 2951, 2866, 1730, 1460, 1434, 1269, 1237, 1204, 1164 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 0.91 (s, 3H), 1.18 (s, 3H), 1.57-1.40 (m, 3H), 2.00-1.65 (m, 5H), 2.31-2.11 (m, 2H), 2.49-2.35 (m, 1H), 2.82 (t, *J*= 6.3 Hz, 1H), 3.01 (dt, *J*= 10.8, 8.4 H), 3.74 (s, 3H) ; ^{13}C-NMR (75 MHz, $CDCl_3$): δ 19.7, 20.2, 24.0, 28.5, 29.0, 32.8, 34.3, 36.3, 36.5, 40.5, 49.3, 49.5, 52.4, 177.8, 220.0; HRMS calculated for $C_{15}H_{22}O_3Na^+$ to be 273.146116 amu, found 273.145743 amu.



192 **193**

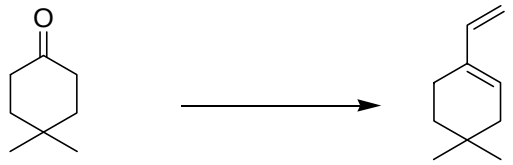
A solution of ketone **192** (27.8 mg, 0.111 mmol) in MeOH (0.3 M, 0.4 mL) was prepared and K_2CO_3 (23 mg, 0.166 mmol) and $NH_2OH.HCl$ (11.6 mg, 0.166 mmol) were

added to this solution. The reaction mixture was stirred for 20 hours at room temperature. After completion of the reaction, it was filtered through a short silica gel pad under vacuum and washed with enough DCM. The solvent was removed and 25.6 mg of compound **193** was obtained in 87% yield.

Oil, ^{1}H-NMR (300 MHz, $CDCl_3$): δ 0.93 (s, 3H), 1.17 (s, 3H), 2.13-1.4 (m, 8H), 2.62-2.55 (m, 2H), 2.91 (dt, *J*= 11.1, 8.1 Hz, 1H), 3.14 (t, *J*= 6.0Hz, 1H), 3.70 (s, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 19.2, 22.4, 24.2, 26.2, 28.9, 31.1, 32.7, 34.3, 36.4, 40.9, 43.4, 51.0, 52.2, 168.1, 178.0.

3-5 Synthesis of some selected Dienes

3-5.1 Synthesis of 108



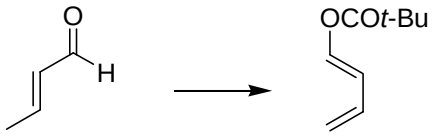
211 **108**

Synthesis of Ketone **213** is known in the literature and the references are given in section **2-7.3**. A solution of ketone **213** (3.15 g, 20.5 mmol) solution in Et_2O was added to freshly prepared vinylmagnesium bromide solution (1.5 eq) at 0 °C in 15 min. It was warmed to rt and refluxed for 3 hrs. The rxn mixture was cooled down to rt, quenched with sat. NH_4Cl solution, extracted with Et_2O. The organic layer was washed with brine once, dried over $MgSO_4$, and concentrated. To this crude alcohol (3.85 g, 25 mmol) was added 20 mL pyridine and $POCl_3$ was added to this solution and stirred for 12 hrs. After

the reaction, solvent was removed and the product was purified by biotage collecting 4 fractions. The first fraction produced 16% of **108**.

^{1}H-NMR (250 MHz, $CDCl_3$): δ 0.91 (s, 6H), 1.38 (t, 2H, J= 7.0 Hz), 1.92 (bs, 2H), 2.18-2.12 (m, 2H), 4.90 (dd, 2H, *J*= 28.4, 17.5 Hz), 5.65 (bm, 1H), 6.36 (dd, 1H, *J*= 17.5, 10.7 Hz); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 21.6, 28.2, 29.0, 35.2, 39.8, 109.7, 128.9, 139.9.

3-5.2 Synthesis of 136

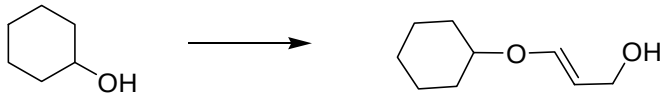


214 **136**

KO*t*-Bu (3.80 g, 33.9 mmol) was transferred in a flask in a glove bag under nitrogen atmosphere. To this was added 40 mL THF and cooled to -78 °C. A solution of crotonaldehyde **214** (1.87 mmL, 22.6 mmol) in 5 mL THF was prepared and added to the solution of KO*t*-Bu at -78 °C. A solution of pivallyl chloride (3.47 mmL, 28.25 mmol) in THF (5mL) was then added to the reaction mixture at -78 °C and let it stir for 10 minutes. Since there was no color change, the reaction was warmed to 0 °C and let it stir for 0.5 hour. The reaction was quenched with water and extracted 3 x with Et_2O. The combined organic layer was washed with brine, dried over Na_2SO_4, and concentrated. Khogelrohr distillation at 60 °C @ 3 mm Hg was performed but it was still contaminated with some pivallyl-side product. A column was done on silica gel with 25% Et_2O/ pentanes producing 309 mg of diene **136** in 9% yield.

Oil, ^{1}H-NMR (250 MHz, $CDCl_3$): δ 1.25 (s, 9H), 5.06 (d, *J*= 16.3 Hz, 1H), 5.20 (d, *J*= 16.3 Hz, 1H), 6.09 (d, *J*= 12.0 Hz, 1H), 6.29 (dt, *J*= 17.0, 10.7 Hz, 1H), 7.39 (d, *J*= 12.3 Hz, 1H); ^{13}C-NMR (62.5 MHz, $CDCl_3$): δ 26.9, 38.7, 115.9, 116.9, 131.8, 139.2, 175.4.

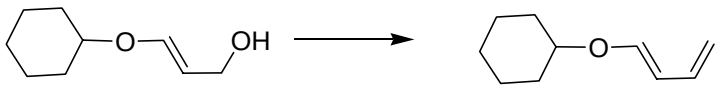
3-5.3 Synthesis of 170



174 **175**

Cyclohexanol **174** was freshly distilled from CaH_2 under vacuum. A solution of **174** (2.36 g, 23.6 mmol) and ethylpropiolate (2.4 mL, 23.8 mmol) was made in THF (0.6 M, 40 mL) and TEA (3.3 mL, 23.8 mmol) was added to this solution at rt and stirred at rt over night (20h). Solvent was removed and the product was purified by Khogelrohr distillation at 140 °C, 3 mm (Hg) pressure with 85% yield of α,β-unsaturated ester.

The ester (1.47 g, 7.41 mmol) was dissolved in THF (0.2 M, 37 mL) and cooled to -78 °C. DIBAL (1 M, 7.48 mL) was added to this cooled solution drop wise stirred for 12 h. It was then stirred at 0 °C for 15 min. Into this rxn mixture were added 0.3 mL (= 7.48 mmol DIBAL x 0.04) water, 0.3 mL (= 7.48 mmol DIBAL x 0.04) 15% NaOH, 0.75 mL (=7.48 x 0.1) water consecutively at 0 °C. After stirring at rt for 15 min anhydrous $MgSO_4$ was added and stirred extra 15 min before filtering. Solvent was removed and the alcohol **175** was used in the next step without any purification.

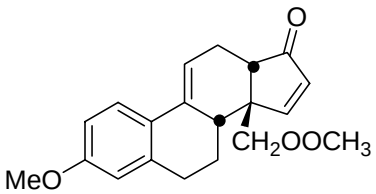


175 **170**

Alcohol **175** (1.29 g, 8.26 mmol) was dissolved in DCM (16.5 mL, 2 M). 4 A^o MS (200 mg/ mmol), and NMO (1.18g, 8.67 mmol) were added to this under argon. After stirring 15 min at rt, TPAP (0.145g, 0.413 mmol) was added to this rxn mixture and stirred for 1h at rt. In another flask, *n*-BuLi (2.2 M, 5.63 mL, 12.4 mmol) was added drop wise to CH_3PPh_3 (4.42g, 12.4 mmol) at 0 °C and stirred for 1h 15 min. An orange color solution was produced. Into this mixture was added aldehyde solution by a syringe drop wise. The rxn mixture was warmed to rt over 6 hrs. Saturated NH_4Cl solution was added to the rxn mixture and stirred for 15 min. Then it was extracted with Et_2O 3x 15 mL. The combined organic layer was dried over $MgSO_4$, filtered and concentrated. Clean diene **170** (0.222 g) was formed in 11% yield from the α,β-unsaturated ester.

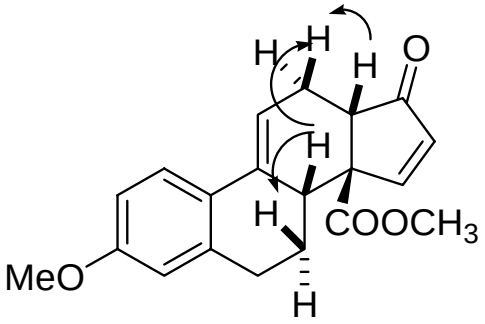
3-6 Towards the Synthesis of Desogestrel 218

3-6.1 Diels-Alder adduct 221



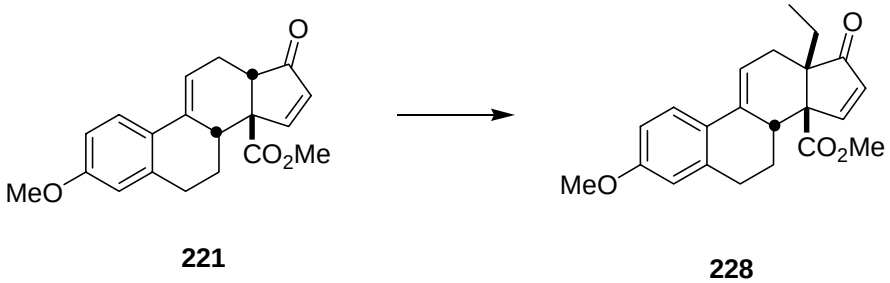
Diels-Alder adduct **221** was synthesized following the general standard reaction procedure described in section 3-4.2. It is a white semi solid, 92% yield, IR (neat): 3020, 2949, 2839, 1713, 1607, 1572, 1496, 1435, 1248 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$): δ 1.64-1.56 (m, 1H), 2.07-2.02 (m, 1H), 2.41-2.36 (m, 1H), 2.73-2.62 (m 2H), 2.85-2.80 (m, 2H), 3.14-3.09 (m, 1H), 3.77 (s, 3H), 3.81(s, 3H), 6.18-6.16 (m, 1H), 6.21 (d, *J*=5.8

Hz, 1H), 6.61 (dd, *J*= 2.61 Hz, 1H), 6.69 (dd, *J*= 8.6, 2.7 Hz, 1H), 7.40 (d, *J*= 5.7 Hz, 1H), 7.62S (d, *J*= 5.8 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 23.8, 25.0, 30.0, 41.5, 50.7, 52.7, 55.2, 60.0, 112.66, 112.72, 119.0, 125.0, 126.9, 135.1, 136.0, 138.7, 158.7, 161.5, 174.3, 209.6; HRMS calculated 347.125378 amu, found 347.12457 amu.



The nOe effect in Diels-Alder Adduct 221

3-6.2 Ethylation of DAA 221 with LDA



221 **228**

In a flame dried flask, 1M LDA was prepared at 0 °C by adding *n*-BuLi (2.3 M, 0.47 mL, 1.07 mmol) to a solution of diisopropyl amine (190 µL, 1.34 mmol) in THF (1.0 mL). Prepared LDA solution was cooled to -78 °C and HMPA (186 µL, 1.61 mmol) was added to it. A solution of **221** (174 mg, 0.536 mmol) in THF (0.2M, 2.7 mL) was

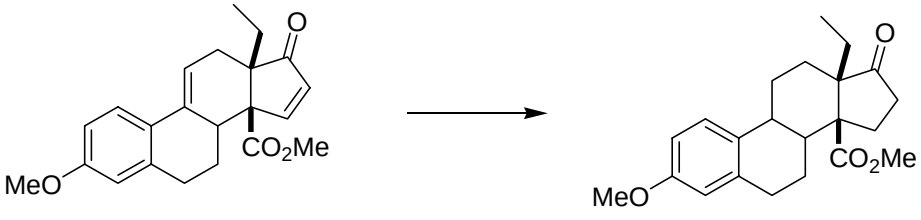
transferred via a cannula to this mixture at -78 °C. An orange color solution was formed. After stirring for 20 min, neat EtI (130 μL, 01.61 mmol) was added to the reaction mixture at -78 °C and stirred for 10.5 hrs. TLC showed SM **221** was still present. Flash column purification on this crude mixture produced 21% of ethylated product **228** with 41% of **221**.

3-6.3 Ethylation of DAA 221 with KH

In a flame dried flask 0.211 g of KH (30% wt, 0.608 mmol) was transferred and washed with THF twice, purged with Argon until all THF was evaporated. Into KH was added 0.8 mL of THF and a solution of **221** (98.7 mg, 0.304 mmol) in THF (10 mL) was transferred with a syringe to this KH mixture at rt and stirred for 10 min. Neat EtI (123 μL, 1.52 mmol) was added to the reaction mixture at rt and stirred for 10.5 hrs. Solvent was removed and crude product was removed with 15% EtOAc/hexanes to produce 34.8 mg of oil **228**.

Oil, IR (neat): 2942, 2836, 1711, 1607, 1496, 1457, 1437, 1270, 1237, 1043, 819, 731 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$): δ 0.72 (t, 3H, *J*= 7.5 Hz), 1.56 (ddd, 1H, *J*= 27.5, 12.5, 3.5 Hz), 1.77-1.65 (m, 2H), 1.97-1.90 (m, 1H), 2.09 (dt, 1H, *J*= 15, 2.5), 2.72-2.57 (m, 3H), 3.25-3.19 (m, 1H), 3.77 (s, 3H), 3.82 (s, 3H), 6.16-6.12 (m, 1H), 6.19 (d, 1H. *J*= 6.00Hz), 6.60 (d, 1H, *J*= 2.5Hz), 6.69 (dd, 1H, *J*= 8.5, 2.50Hz), 7.33 (d, 1H, *J*= 9.0 Hz), 7.63 (d, 1H, *J*= 6.00 Hz) ;^{13}C-NMR (125 MHz, $CDCl_3$): δ 8.6, 24.1, 28.1, 30.1, 32.7, 43.6, 52.2, 55.2, 57.7, 64.0, 112.60, 112.65, 119.7, 125.0, 127.1, 135.1, 135.2, 138.7, 158.7, 161.6, 173.6, 211.8.

3-6.3 Hydrogenation

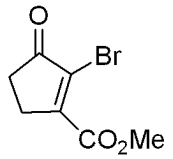


228 **229**

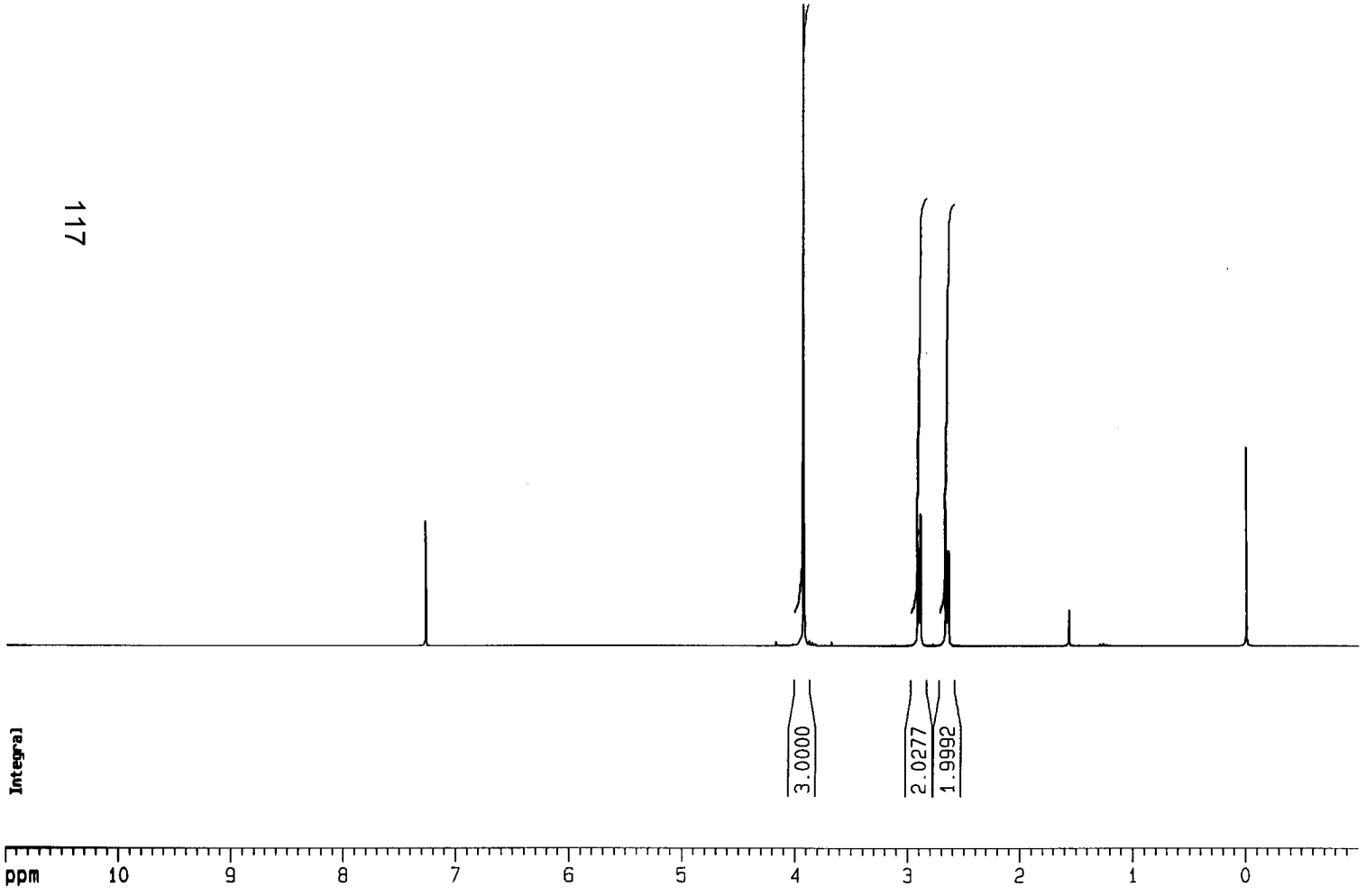
In a flask 36.6 mg of **228** was dissolved in EtOAc (0.05 M) and sealed with a rubber septum. The solution was purged with hydrogen gas for 5 min and let it stir at rt for 8 hrs. The reaction mixture was filtered through a celite pad under vacuum and solvent was removed. Column with 15% EtOAc/ Hexanes produced 88% of reduced product **229**. White solid, mp 127-128 °C; ^{1}H-NMR (500 MHz, $CDCl_3$): δ 0.74 (t, *J*= 7.5Hz, 3H), 1.64-1.48 (m, 5H), 1.76-1.69 (m, 2H), 2.46-2.38 (m, 1H), 2.61-2.51 (m, 1H), 2.84-2.68 (m, 2H), 3.09 (dt, *J*= 12.5, 3.7 Hz, 1H), 3.71 (s, 3H), 3.75 (s, 3H), 6.54 (d, *J*= 2.5 Hz, 1H), 6.69 (dd, *J*= 8.50, 2.50 Hz, 1H), 6.99 (d, *J*= 8.50 Hz, 1H); ^{13}C-NMR (125 MHz, $CDCl_3$): δ 7.5, 14.1, 20.7, 22.6, 25.0, 25.4, 27.9, 28.3, 30.6, 34.6, 36.1, 41.6, 51.7, 53.4, 55.2, 56.3, 112.3, 112.7, 129.9, 133.6, 136.0, 157.6, 175.5, 217.2; HRMS calculated for $C_{22}H_{28}O_4Na^+$ to be 379.187980 amu, found 379.187872 amu.

APPENDIX

^{1}H, ^{13}C-NMR and COSY, NOESY, Dept135, HMBC, HMQC spectrum



96



Current Data Parameters
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EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20040824
Time 23.46
INSTRUM drx300
PROBHD 5 mm Multinucl
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 16
DS 2
SWH 6172.839 Hz
FIDRES 0.188380 Hz
AQ 2.6542580 sec
RG 1024
DW 81.000 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec
D31 0.00000000 sec

======== CHANNEL f1 ========
NUC1 1H
P1 7.05 usec
PL1 0.00 dB
SFO1 300.1318534 MHz

F2 - Processing parameters
SI 32768
SF 300.1300047 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.30

1D NMR plot parameters
CX 20.00 cm
CY 12.50 cm
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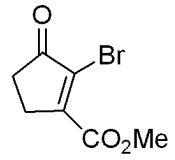
F1 3301.43 Hz
F2P -1.000 ppm
F2 -300.13 Hz
PPMCM 0.60000 ppm/cm
HZCM 180.07799 Hz/cm



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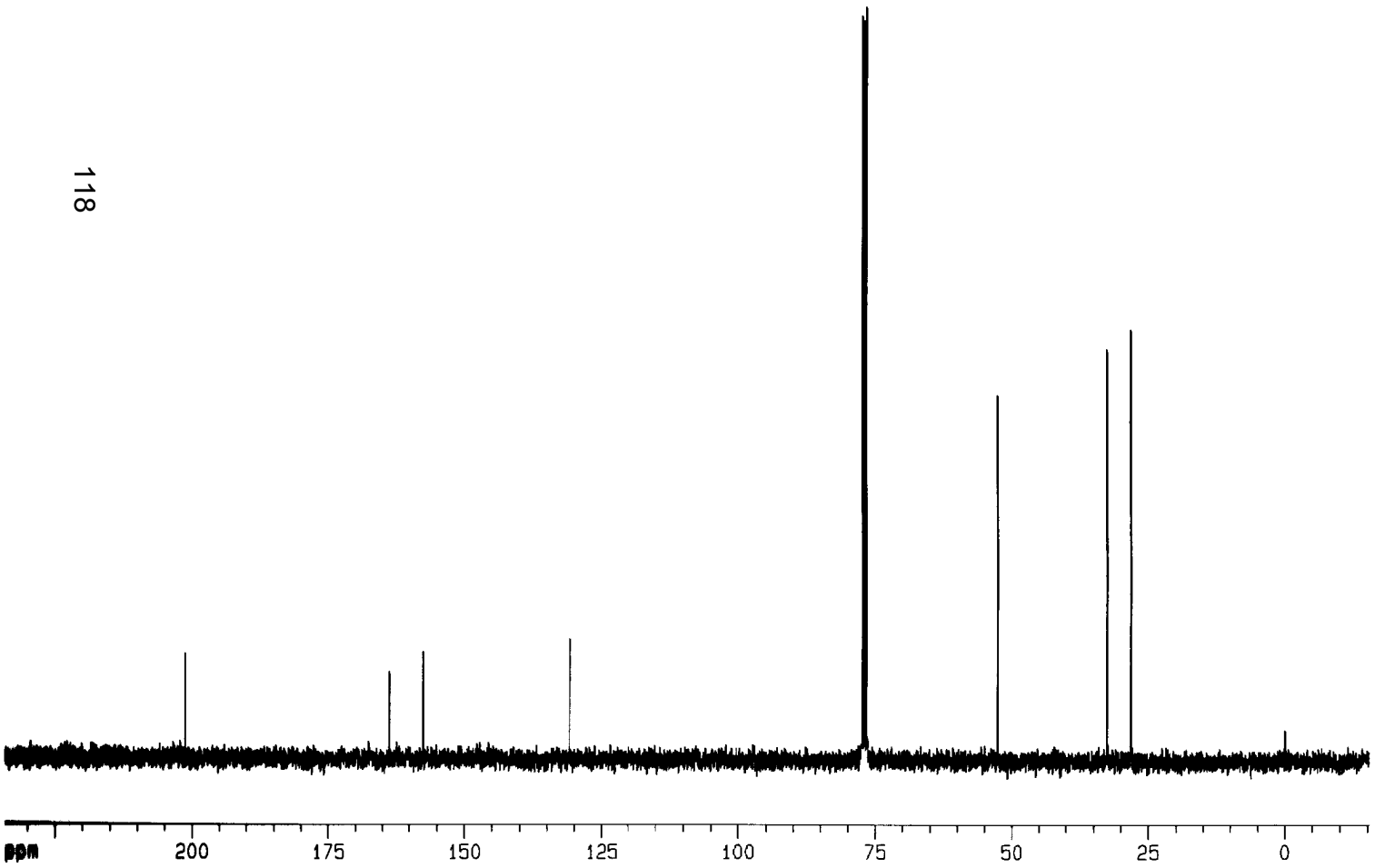


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PROCNO                 1

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Time               11.06
INSTRUM          drx300
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PULPROG          zgdc30
TD                65536
SOLVENT           CDCl3
NS                  572
DS                    4
SWH           18832.393 Hz
FIDRES         0.287360 Hz
AQ             1.7400308 sec
RG                22528
DW               26.550 usec
DE                6.00 usec
TE               297.1 K
D1           1.29999995 sec
d11          0.03000000 sec
D31          0.00000000 sec

======== CHANNEL f1 ========
NUC1                13C
P1                8.50 usec
PL1               5.00 dB
SFO1         75.4760107 MHz

======== CHANNEL f2 ========
CPDPRG2         waltz16
NUC2                1H
PCPD2           100.00 usec
PL2             120.00 dB
PL12             25.60 dB
SFO2        300.1312005 MHz

F2 - Processing parameters
SI                32768
SF           75.4677514 MHz
WDW                  EM
SSB                   0
LB                 1.00 Hz
GB                    0
PC                 1.40

1D NMR plot parameters
CX                20.00 cm
CY                11.00 cm
F1P              234.213 ppm
F1             17675.51 Hz
F2P              -15.329 ppm
F2             -1156.88 Hz
PPMCM          12.47711 ppm/cm
HZCM          941.61957 Hz/cm
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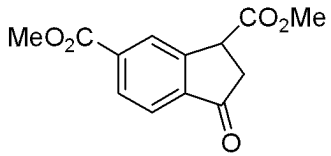

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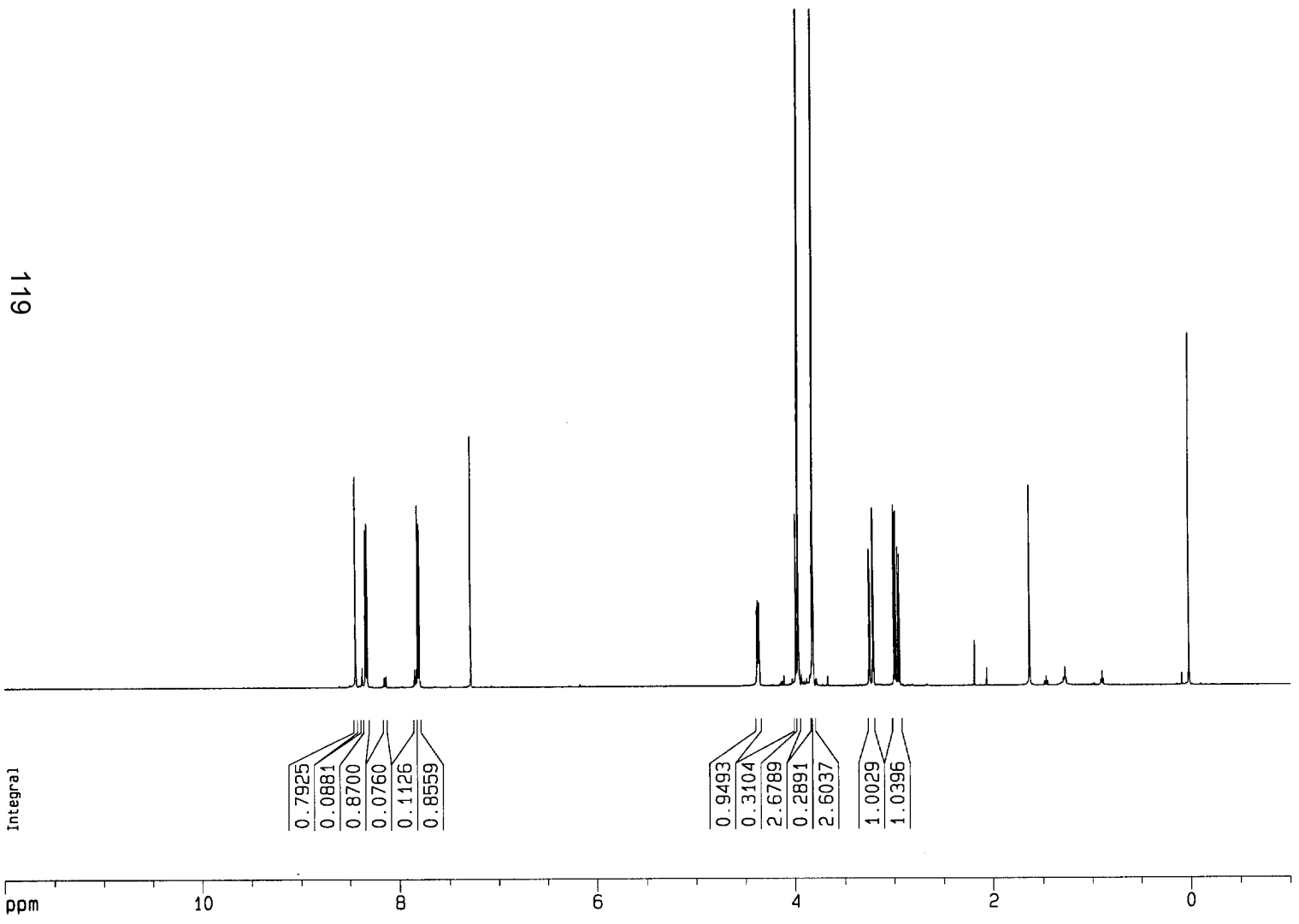

Current Data Parameters

NAME	MG-IV-048b-500
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20050506
Time	17.09
INSTRUM	DRX500
PROBHD	5 mm Multinucl
PULPROG	zg30
TD	57344
SOLVENT	CDCl3
NS	16
DS	2
SWH	10330.578 Hz
FIDRES	0.180151 Hz
AQ	2.7754996 sec
RG	161.3
DW	48.400 usec
DE	6.00 usec
TE	296.7 K
D1	1.00000000 sec

======== CHANNEL f1 ========

NUC1	1H
P1	13.25 usec
PL1	-3.00 dB
SFO1	500.1330885 MHz

F2 - Processing parameters

SI	32768
SF	500.1300000 MHz
WDW	EM
SSB	0
LB	0.20 Hz
GB	0
PC	1.40

1D NMR plot parameters

CX	20.00 cm
CY	30.00 cm
F1P	12.000 ppm
F1	6001.56 Hz
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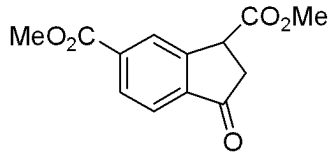
F2	-500.13 Hz
PPMCM	0.65000 ppm/cr
HZCM	325.08450 Hz/cm



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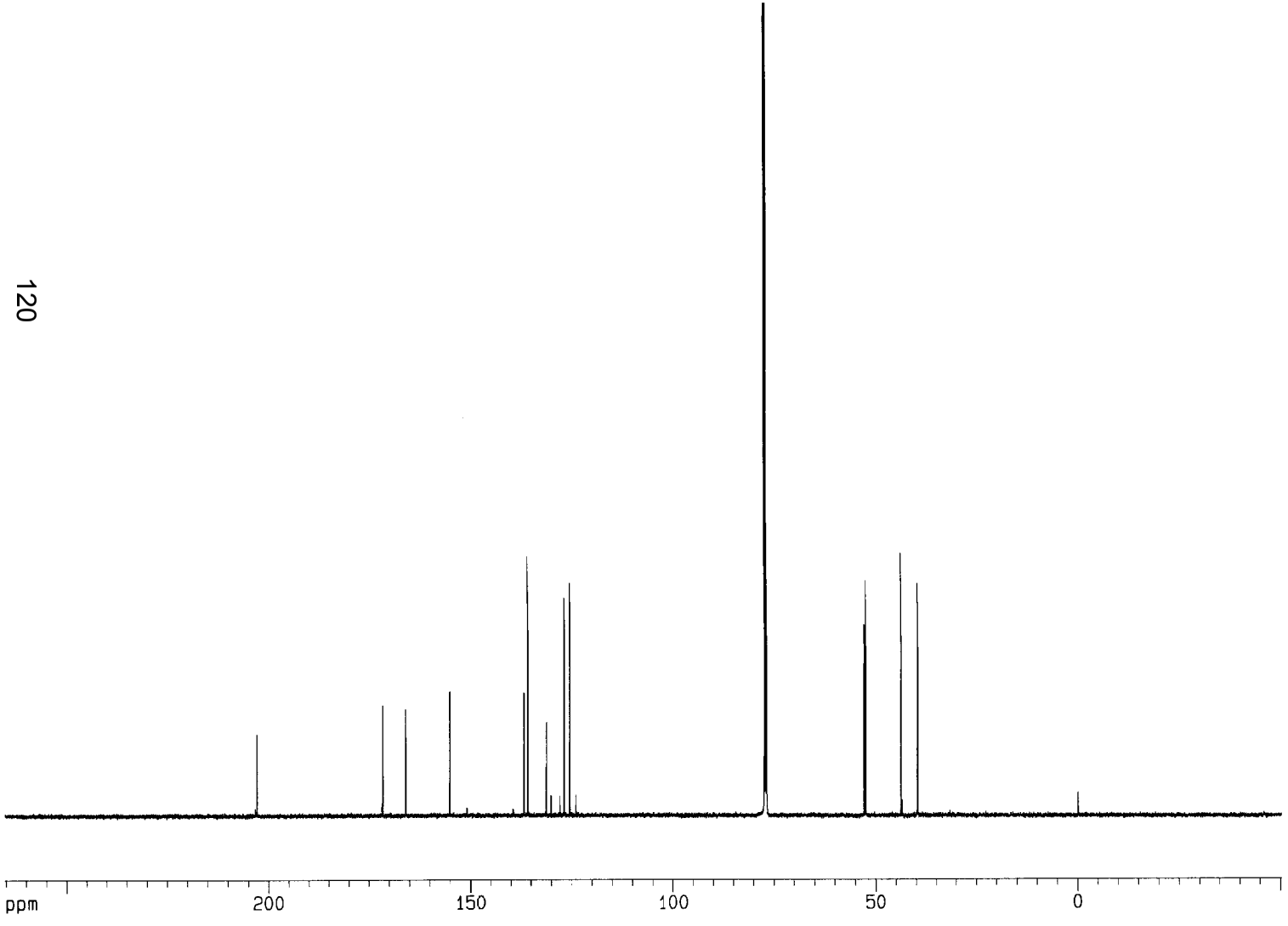

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NAME	MG-IV-048b-500
EXPNO	2
PROCNO	1

F2 - Acquisition Parameters

Date_	20050506
Time	17.12
INSTRUM	DRX500
PROBHD	5 mm Multinucl
PULPROG	zgdc30
TD	65536
SOLVENT	CDCl3
NS	8310
DS	4
SWH	39681.812 Hz
FIDRES	0.605496 Hz
AQ	0.8258188 sec
RG	16384
DW	12.600 usec
DE	6.00 usec
TE	298.0 K
D1	2.00000000 sec
d11	0.03000000 sec

======== CHANNEL f1 ========

NUC1	13C
P1	8.10 usec
PL1	3.00 dB
SFO1	125.7713108 MHz

======== CHANNEL f2 ========

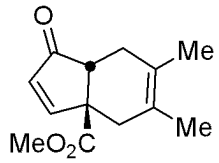
CPDPRG2	waltz16
NUC2	1H
PCPD2	88.00 usec
PL2	0.00 dB
PL12	21.00 dB
SFO2	500.1320005 MHz

F2 - Processing parameters

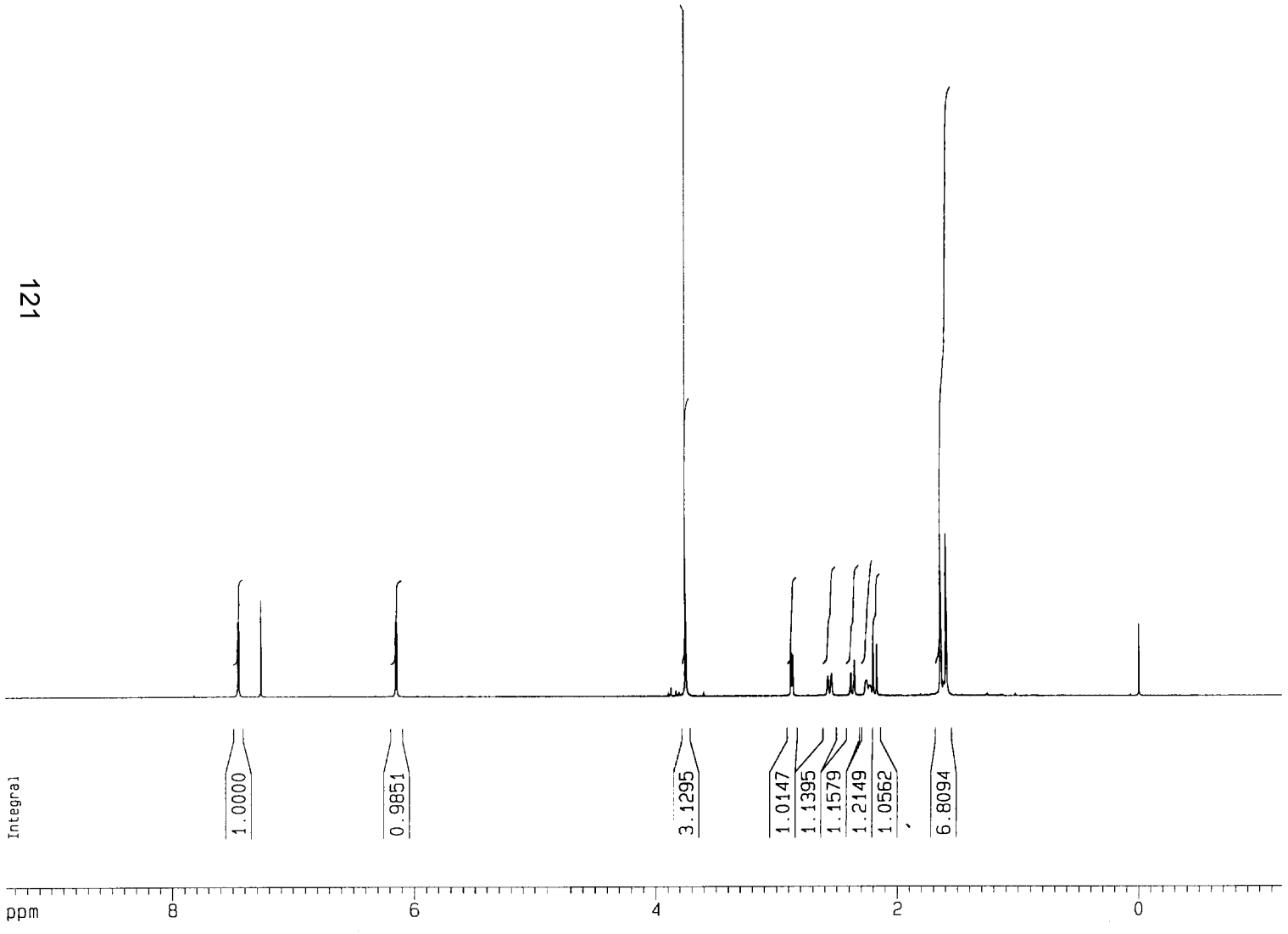
SI	32768
SF	125.7577935 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

1D NMR plot parameters

CX	20.00 cm
CY	24.00 cm
F1P	265.258 ppm
F1	33358.26 Hz
F2P	-50.284 ppm
F2	-6323.55 Hz
PPMCM	15.77708 ppm/cm
HZCM	1984.09045 Hz/cm



103



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EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
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Time 12.05
INSTRUM DRX500
PROBHD 5 mm Multinucl
PULPROG zg30
TD 57344
SOLVENT CDCl3
NS 16
DS 2
SWH 10330.578 Hz
FIDRES 0.180151 Hz
AQ 2.7754996 sec
RG 114
DW 48.400 usec
DE 6.00 usec
TE 296.7 K
D1 1.00000000 sec

======== CHANNEL f1 ========
NUC1 1H
P1 13.25 usec
PL1 -3.00 dB
SFO1 500.1330885 MHz

F2 - Processing parameters
SI 32768
SF 500.1300093 MHz
WDW EM
SSB 0
LB 0.20 Hz
GB 0
PC 1.40

1D NMR plot parameters
CX 20.00 cm
CY 12.50 cm
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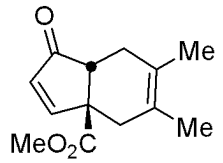
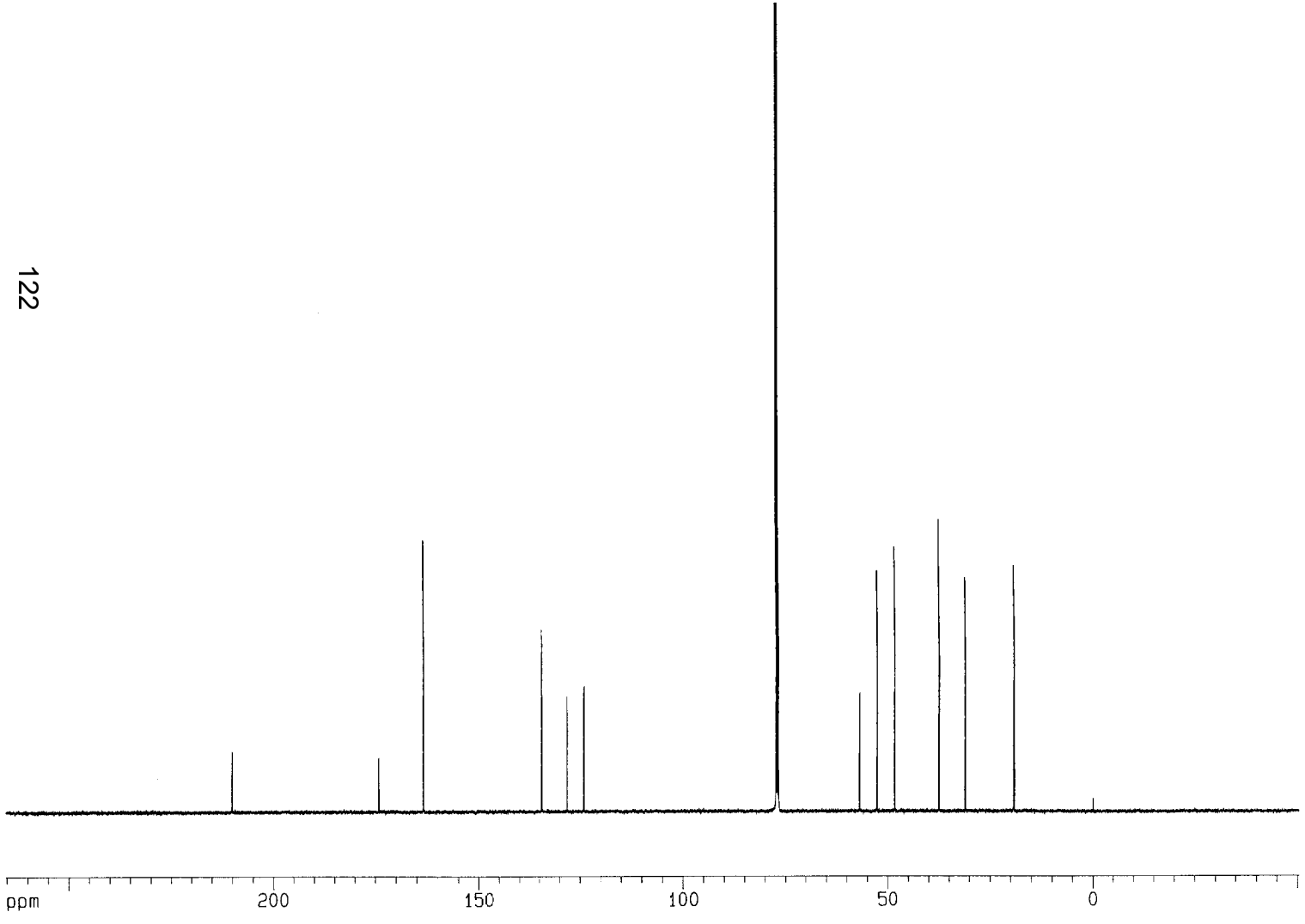
F1 4690.87 Hz
F2P -1.182 ppm
F2 -590.93 Hz
PPMCM 0.52804 ppm/cr
HZCM 264.08994 Hz/cm



103

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Current Data Parameters
NAME       MG-2-034a-500
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
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Time               12.07
INSTRUM          DRX500
PROBHD   5 mm Multinucl
PULPROG          zgdc30
TD                65536
SOLVENT           CDCl3
NS                 4994
DS                    4
SWH           39681.812 Hz
FIDRES         0.605496 Hz
AQ             0.8258188 sec
RG                16384
DW               12.600 usec
DE                6.00 usec
TE                298.0 K
D1           2.00000000 sec
d11          0.03000000 sec

======== CHANNEL f1 ========
NUC1                 13C
P1                 8.10 usec
PL1                3.00 dB
SFO1        125.7713108 MHz

======== CHANNEL f2 ========
CPDPRG2          waltz16
NUC2                 1H
PCPD2             88.00 usec
PL2                0.00 dB
PL12               21.00 dB
SFO2        500.1320005 MHz

F2 - Processing parameters
SI                 32768
SF          125.7577935 MHz
WDW                   EM
SSB                    0
LB                 1.00 Hz
GB                     0
PC                  1.40

1D NMR plot parameters
CX                20.00 cm
CY                15.00 cm
F1P              265.258 ppm
F1              33358.26 Hz
F2P              -50.284 ppm
F2             -6323.55 Hz
PPMCM           15.77708 ppm/cm
HZCM          1984.09045 Hz/cm
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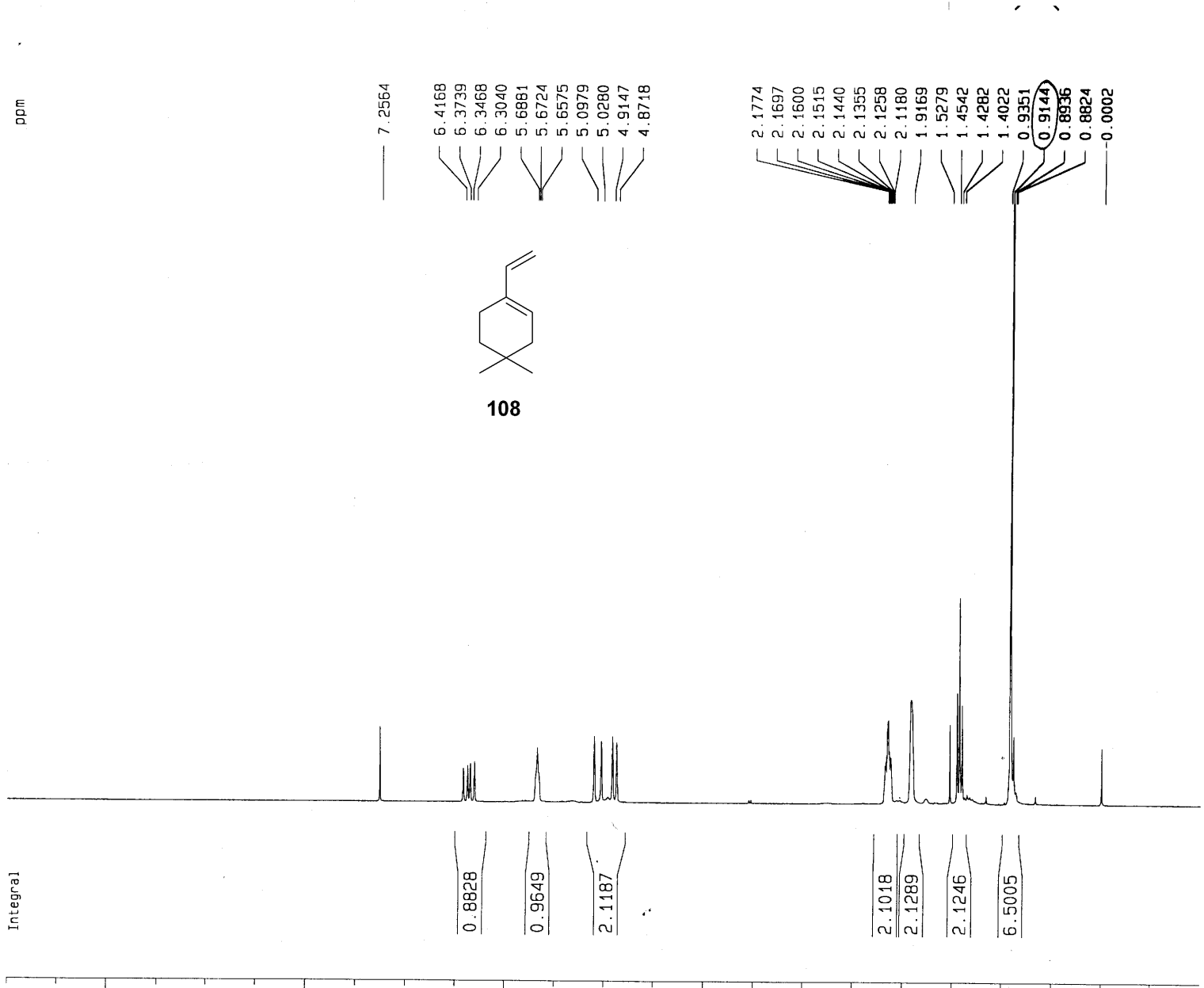

108

Current Data Parameters

NAME	MG-3-069a-250
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20050114
Time	12.59
INSTRUM	arx250
PROBHD	5 mm QNP 1H
PULPROG	zg30
TD	32768
SOLVENT	CDCl3
NS	16
DS	2
SWH	5208.333 Hz
FIDRES	0.158946 Hz
AQ	3.1457779 sec
RG	1024
DW	96.000 use
DE	137.14 use
TE	300.0 K
D1	1.00000000 sec
P1	8.70 use
SF01	250.1315321 MHz
NUCLEUS	1H

F2 - Processing parameters

SI	16384
SF	250.1300084 MHz
WDW	EM
SSB	0
LB	0.20 Hz
GB	0
PC	1.50

1D NMR plot parameters

CX	20.00 cm
CY	30.00 cm
F1P	11.000 ppm
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F2P	-1.000 ppm
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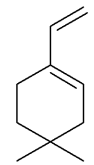
PPMCM	0.60000 ppm
HZCM	150.07800 Hz/



108

Current Data Parameters

NAME	MG-3-069a-250
EXPNO	2
PROCNO	1

F2 - Acquisition Parameters

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Time	13.04
INSTRUM	arx250
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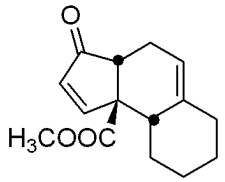
PULPROG	zgdc30
TD	36864
SOLVENT	CDCl3
NS	89
DS	4
SWH	17241.379 Hz
FIDRES	0.467702 Hz
AQ	1.0691060 sec
RG	22800
DW	29.000 use
DE	41.43 use
TE	300.0 K
D12	0.00002000 sec
DL5	23.00 dB
CPDPRG	waltz16
P31	103.00 use
D1	1.00000000 sec
P1	6.00 use
SF01	62.9023694 MHz
NUCLEUS	13C
D11	0.03000000 sec

F2 - Processing parameters

SI	32768
SF	62.8952398 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

1D NMR plot parameters

CX	20.00 cm
CY	10.00 cm
F1P	250.422 ppm
F1	15750.34 Hz
F2P	-23.707 ppm
F2	-1491.04 Hz
PPMCM	13.70643 ppm
HZCM	862.06891 Hz/



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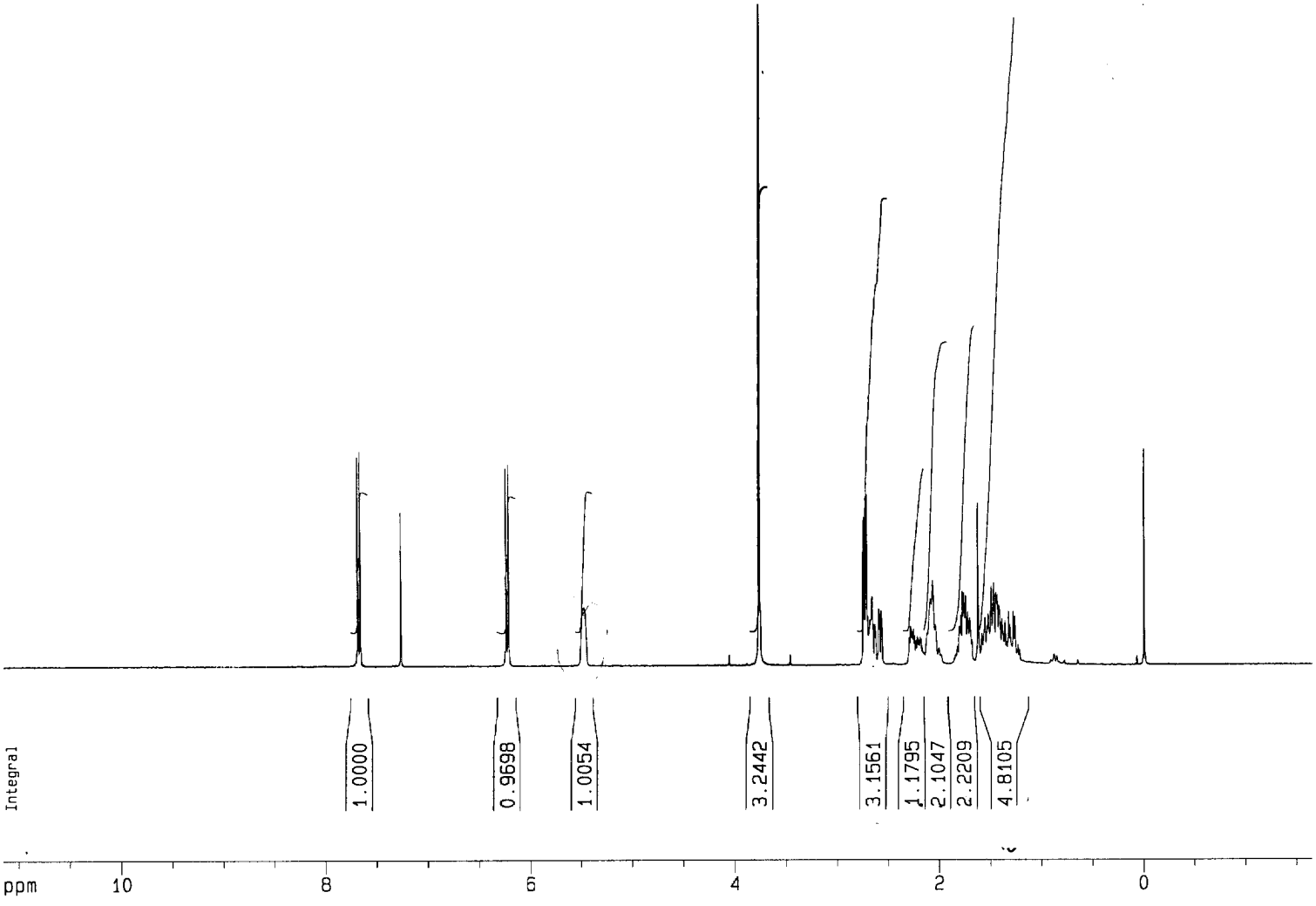


Current Data Parameters

NAME	MG-2-110a-250
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

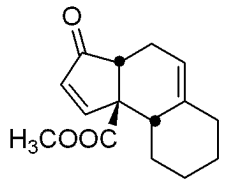
Date_	20040528
Time	17.18
INSTRUM	arx250
PROBHD	5 mm QNP 1H
PULPROG	zg30
TD	32768
SOLVENT	CDCl3
NS	16
DS	2
SWH	5208.333 Hz
FIDRES	0.158946 Hz
AQ	3.1457779 sec
RG	1430
DW	96.000 use
DE	137.14 use
TE	300.0 K
D1	1.00000000 sec
P1	8.70 use
SFO1	250.1315321 MHz
NUCLEUS	1H

F2 - Processing parameters

SI	16384
SF	250.1300055 MHz
WDW	EM
SSB	0
LB	0.20 Hz
GB	0
PC	1.50

1D NMR plot parameters

CX	20.00 cm
CY	30.00 cm
F1P	11.155 ppm
F1	2790.11 Hz
F2P	-1.647 ppm
F2	-412.05 Hz
PPMCM	0.64010 ppm
HZCM	160.10803 Hz/



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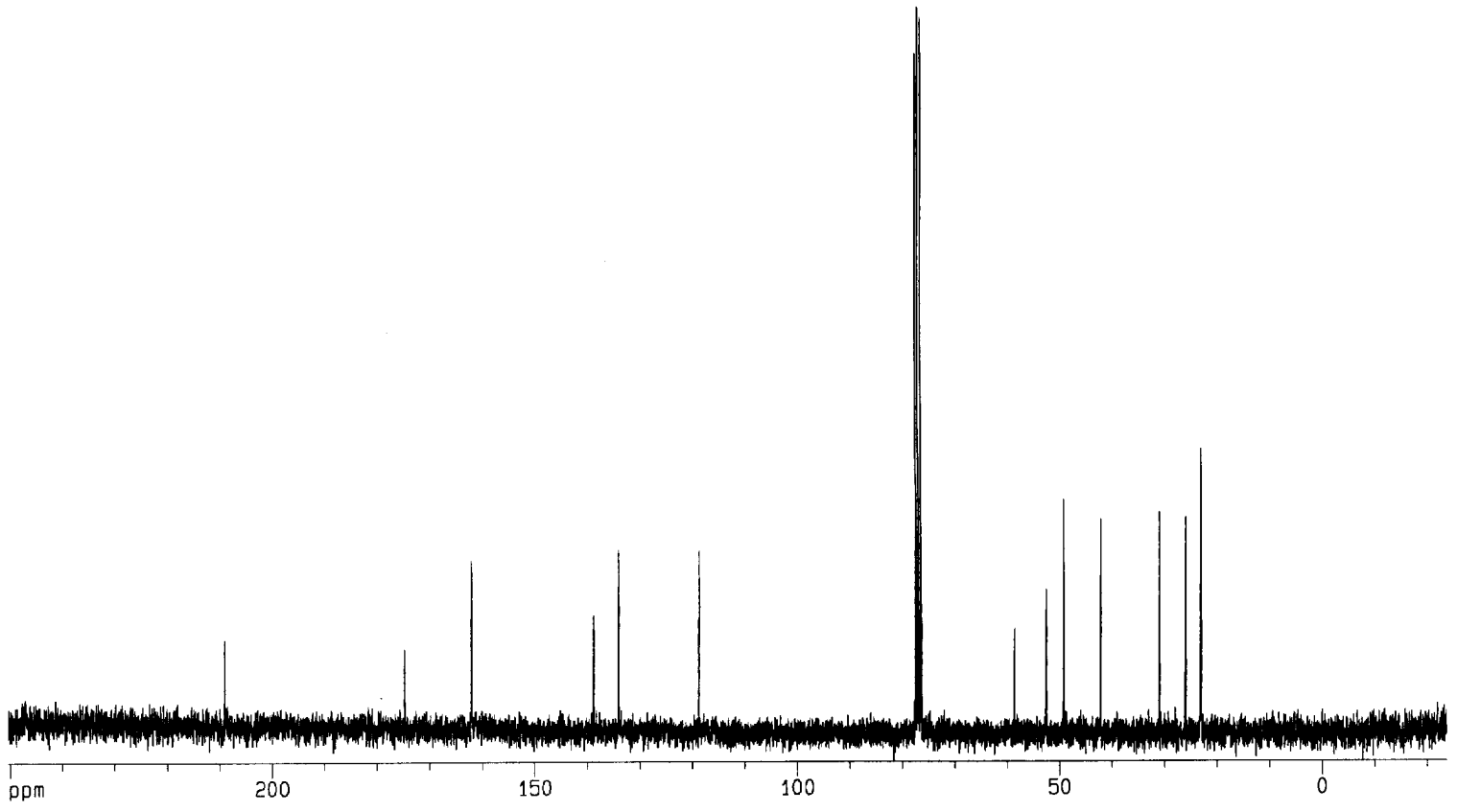


Current Data Parameters

NAME	MG-2-110a-250
EXPNO	2
PROCNO	1

F2 - Acquisition Parameters

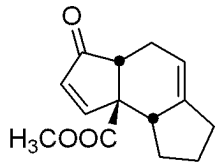
Date_	20040528
Time	17.22
INSTRUM	arx250
PROBHD	5 mm QNP 1H
PULPROG	zgdc30
TD	36864
SOLVENT	CDCl3
NS	722
DS	4
SWH	17241.379 Hz
FIDRES	0.467702 Hz
AQ	1.0691060 sec
RG	22800
DW	29.000 use
DE	41.43 use
TE	300.0 K
D12	0.00002000 sec
DL5	23.00 dB
CPDPRG	waltz16
P31	103.00 use
D1	1.00000000 sec
P1	5.35 use
SFO1	62.9023694 MHz
NUCLEUS	13C
D11	0.03000000 sec

F2 - Processing parameters

SI	32768
SF	62.8952408 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

1D NMR plot parameters

CX	20.00 cm
CY	10.00 cm
F1P	250.405 ppm
F1	15749.28 Hz
F2P	-23.724 ppm
F2	-1492.10 Hz
PPMCM	13.70643 ppm
HZCM	862.06891 Hz/



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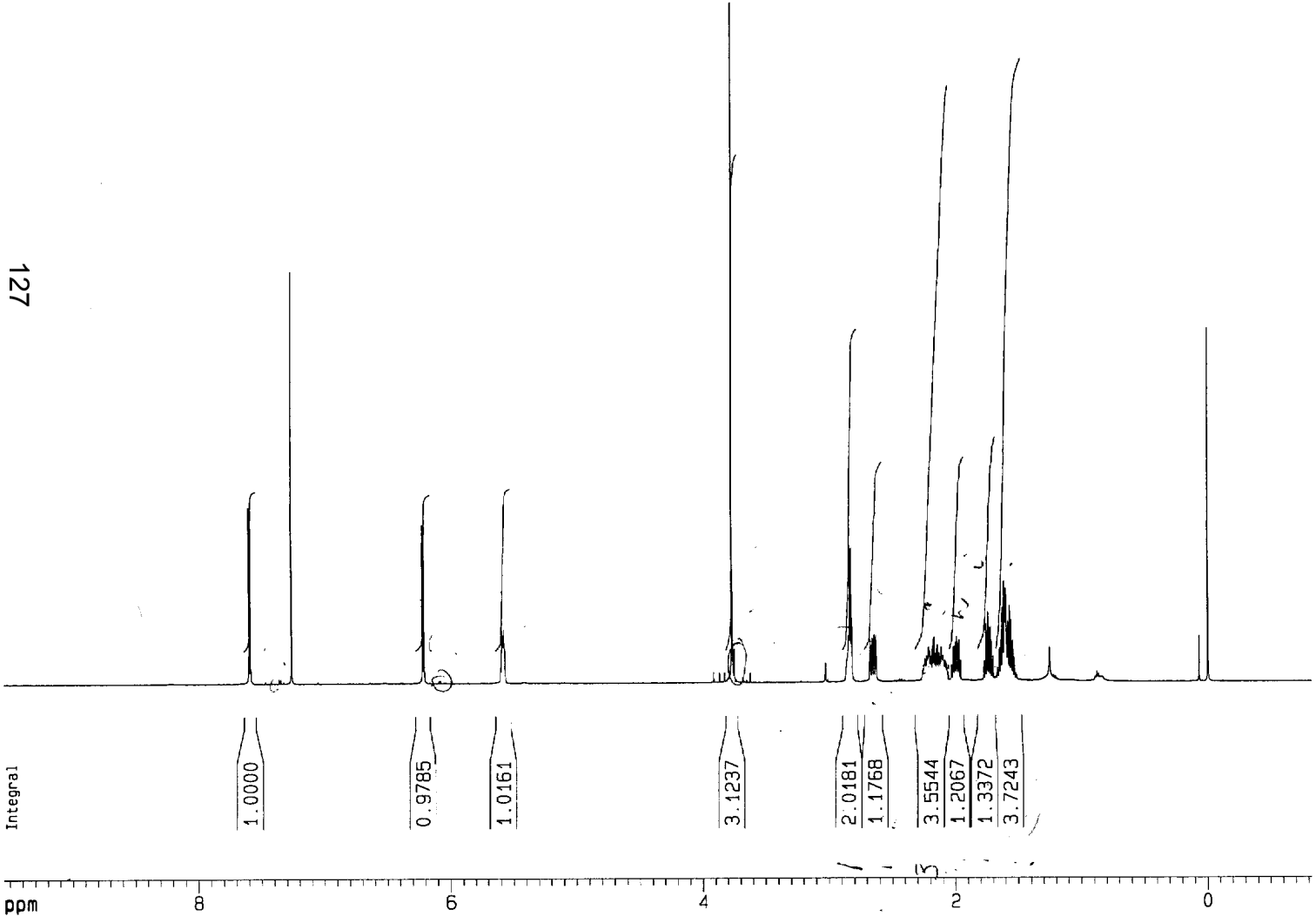

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Current Data Parameters

NAME	MG-2-111a-500
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20040606
Time	12.51
INSTRUM	DRX500
PROBHD	5 mm Multinucl
PULPROG	zg30
TD	57344
SOLVENT	CDCl3
NS	16
DS	2
SWH	10330.578 Hz
FIDRES	0.180151 Hz
AQ	2.7754996 sec
RG	161.3
DW	48.400 usec
DE	6.00 usec
TE	296.7 K
D1	1.00000000 sec

======== CHANNEL f1 ========

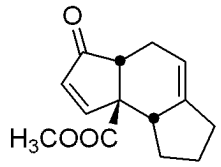
NUC1	1H
P1	13.25 usec
PL1	-3.00 dB
SFO1	500.1330885 MHz

F2 - Processing parameters

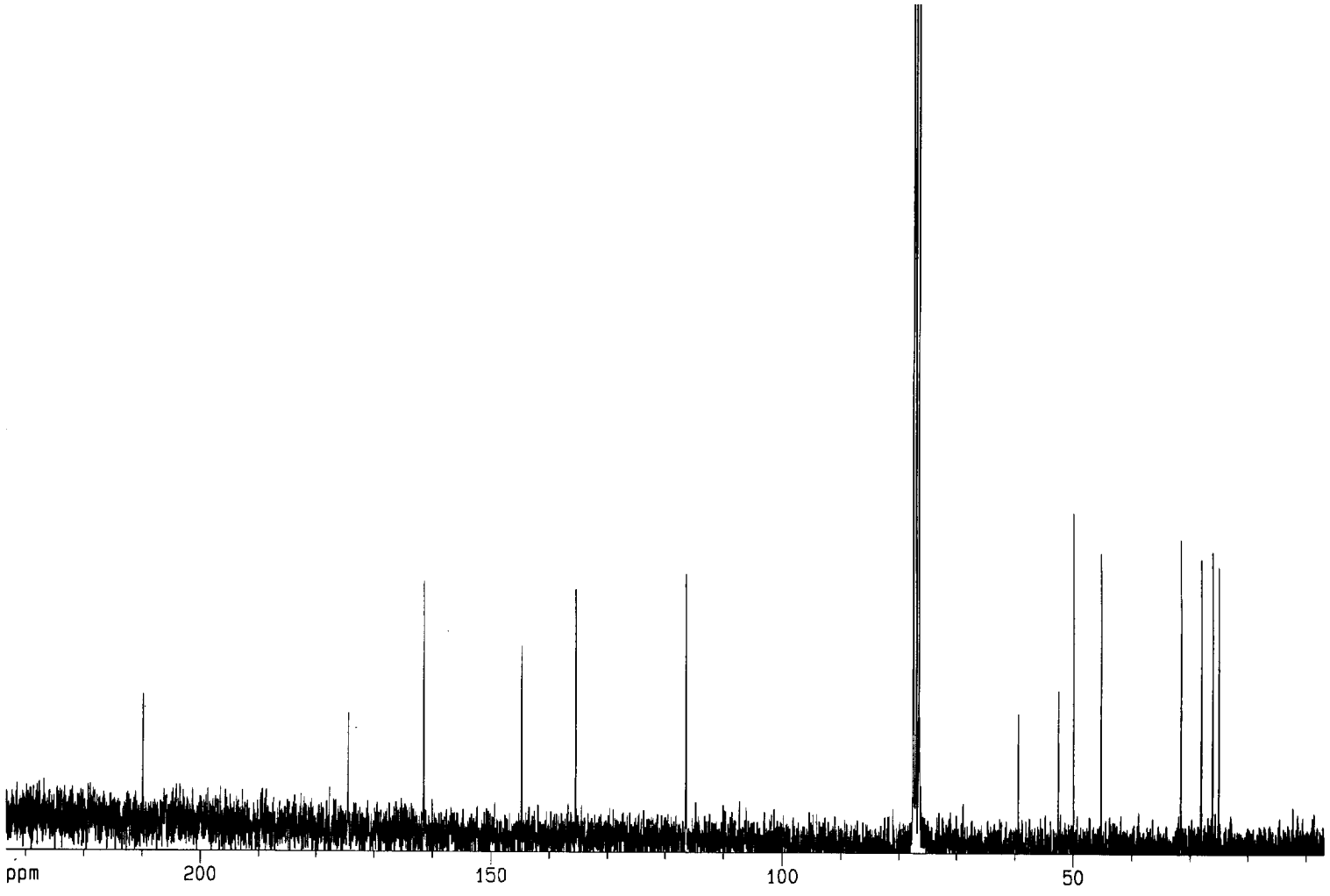
SI	32768
SF	500.1300109 MHz
WDW	EM
SSB	0
LB	0.20 Hz
GB	0
PC	1.40

1D NMR plot parameters

CX	20.00 cm
CY	30.00 cm
F1P	9.549 ppm
F1	4775.63 Hz
F2P	-0.820 ppm
F2	-410.00 Hz
PPMCM	0.51843 ppm/cr
HZCM	259.28125 Hz/cm



113



3

Current Data Parameters

NAME	MG-2-111a-250
EXPNO	2
PROCNO	1

F2 - Acquisition Parameters

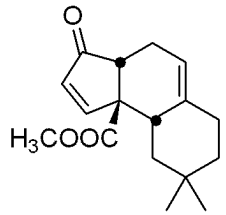
Date_	20040601
Time	13.19
INSTRUM	arx250
PROBHD	5 mm QNP 1H
PULPROG	zgdc30
TD	36864
SOLVENT	CDCl3
NS	2007
DS	4
SWH	17241.379 Hz
FIDRES	0.467702 Hz
AQ	1.0691060 sec
RG	22800
DW	29.000 usec
DE	41.43 usec
TE	300.0 K
D12	0.00002000 sec
DL5	23.00 dB
CPDPRG	waltz16
P31	103.00 usec
D1	1.00000000 sec
P1	5.35 usec
SFO1	62.9023694 MHz
NUCLEUS	13C
D11	0.03000000 sec

F2 - Processing parameters

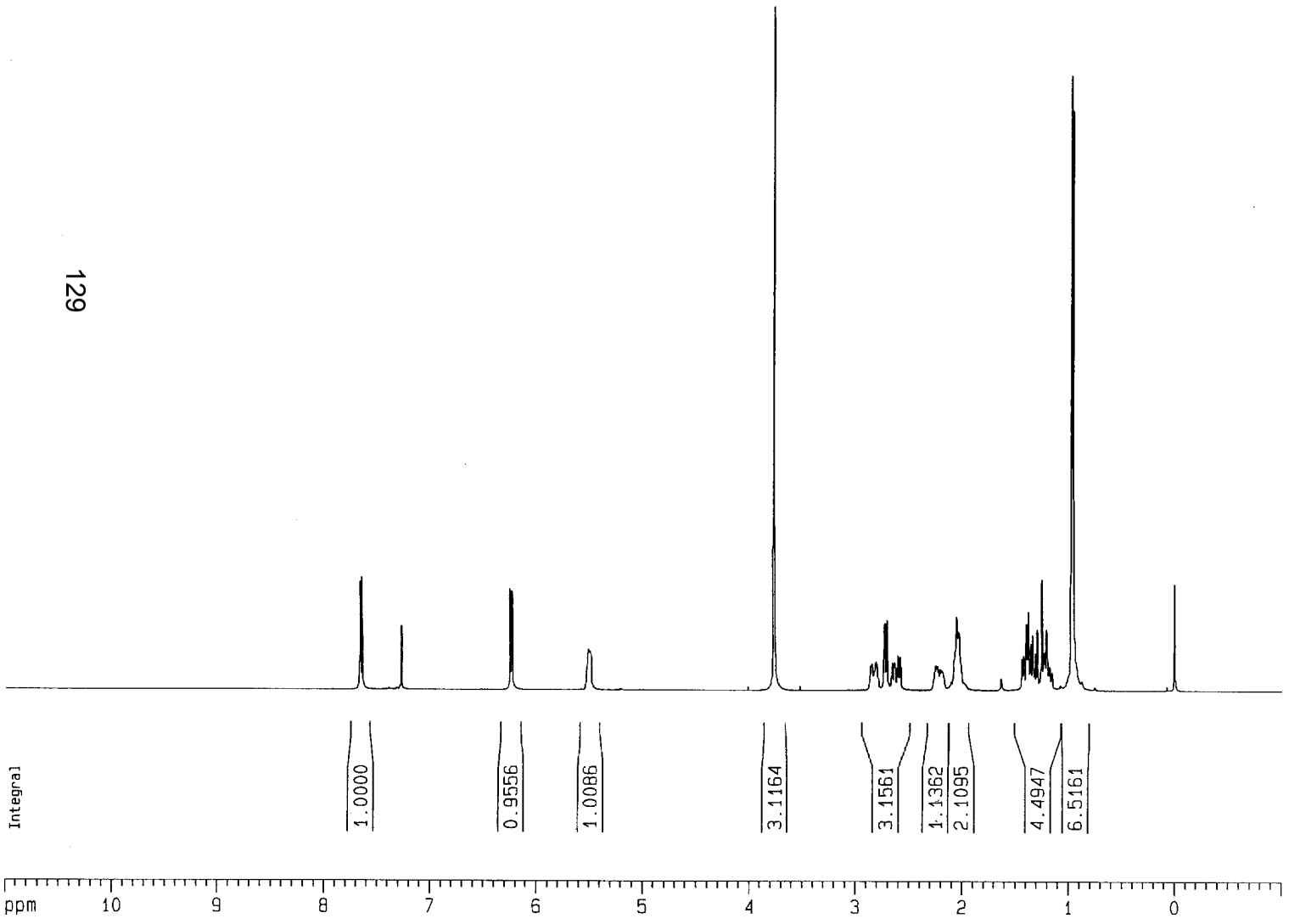
SI	32768
SF	62.8952403 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

1D NMR plot parameters

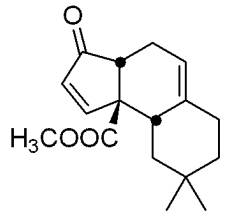
CX	20.00 cm
CY	30.00 cm
F1P	233.411 ppm
F1	14680.45 Hz
F2P	6.889 ppm
F2	433.28 Hz
PPMCM	11.32611 ppm
HZCM	712.35852 Hz/



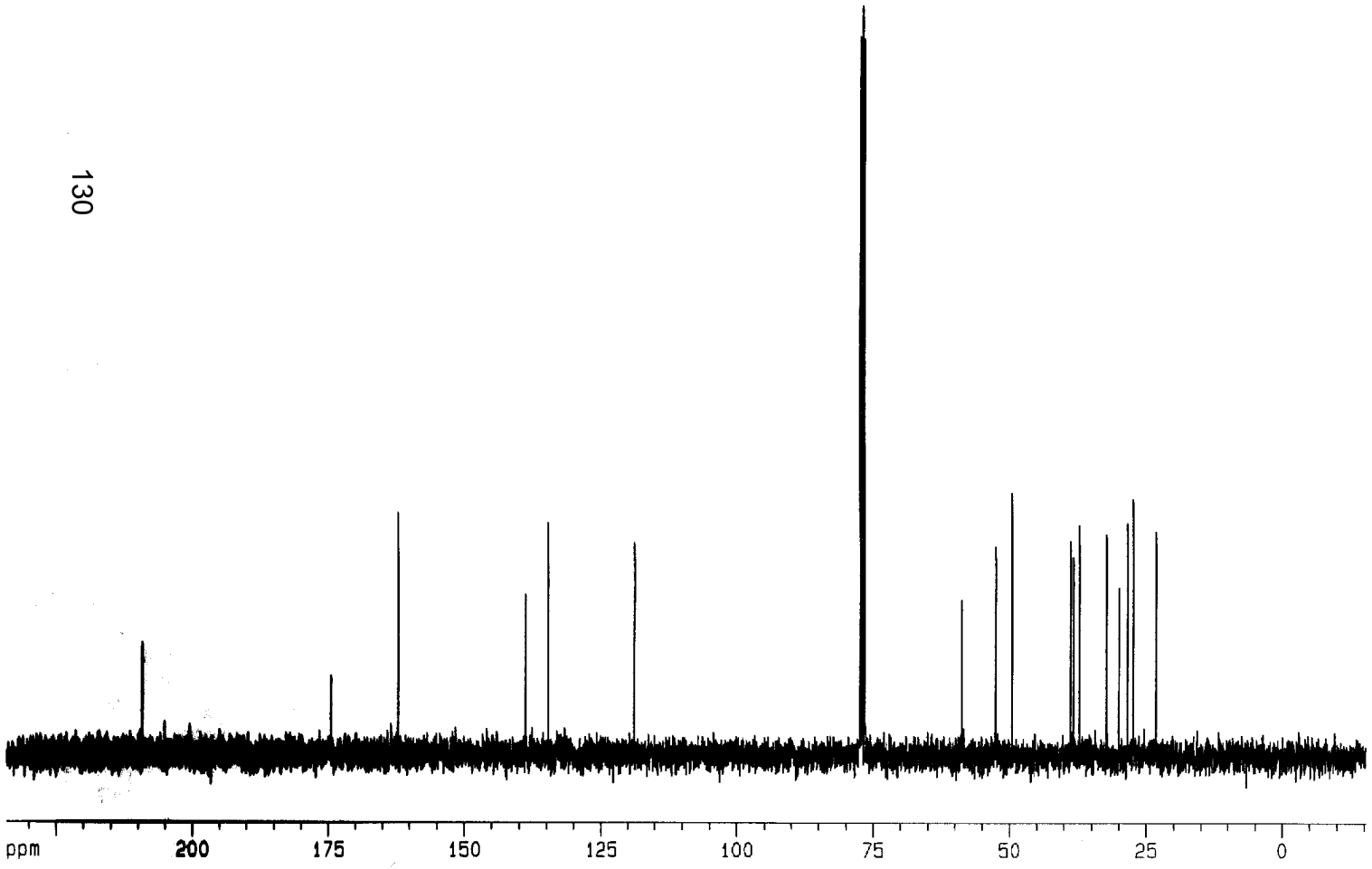
114




```
Current Data Parameters
NAME        MG-3-073a-300
EXPNO                   1
PROCNO                  1

F2 - Acquisition Parameters
Date_            20050124
Time                15.56
INSTRUM           drx300
PROBHD   5 mm Multinucl
PULPROG             zg30
TD                 32768
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             6172.839 Hz
FIDRES          0.188380 Hz
AQ              2.6542580 sec
RG                 228.1
DW                81.000 usec
DE                 6.00 usec
TE                300.0 K
D1             1.00000000 sec
D31            0.00000000 sec

======== CHANNEL f1 ========
NUC1                   1H
P1                  7.05 usec
PL1                 0.00 dB
SFO1         300.1318534 MHz

F2 - Processing parameters
SI                 32768
SF          300.1300022 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.30

1D NMR plot parameters
CX                 20.00 cm
CY                 12.50 cm
F1P               11.000 ppm
F1               3301.43 Hz
F2P               -1.000 ppm
F2               -300.13 Hz
PPMCM            0.60000 ppm/cm
HZCM           180.07800 Hz/cm
```



114



Current Data Parameters
NAME MG-3-073a-300
EXPNO 2
PROCNO 1

F2 - Acquisition Parameters

Date_	20050124
Time	15.58
INSTRUM	drx300
PROBHD	5 mm Multinucl
PULPROG	zgdc30
TD	65536
SOLVENT	CDCl3
NS	158
DS	4
SWH	18832.393 Hz
FIDRES	0.287360 Hz
AQ	1.7400308 sec
RG	22528
DW	26.550 usec
DE	6.00 usec
TE	297.1 K
D1	1.29999995 sec
d11	0.03000000 sec
D31	0.00000000 sec

======== CHANNEL f1 ========

NUC1	13C
P1	8.50 usec
PL1	5.00 dB
SFO1	75.4760107 MHz

======== CHANNEL f2 ========

CPDPRG2	waltz16
NUC2	1H
PCPD2	100.00 usec
PL2	120.00 dB
PL12	25.60 dB
SFO2	300.1312005 MHz

F2 - Processing parameters

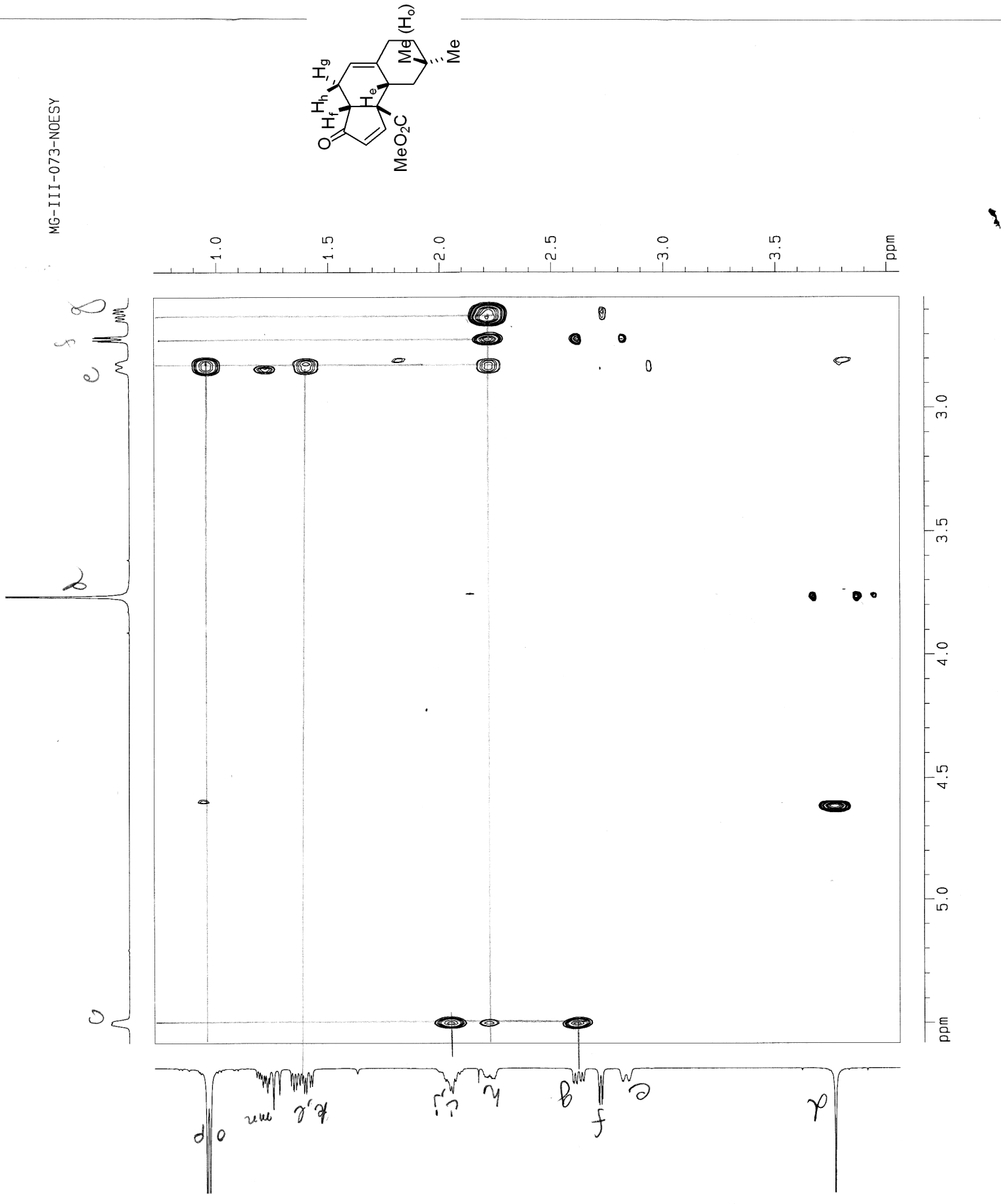
SI	32768
SF	75.4677508 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

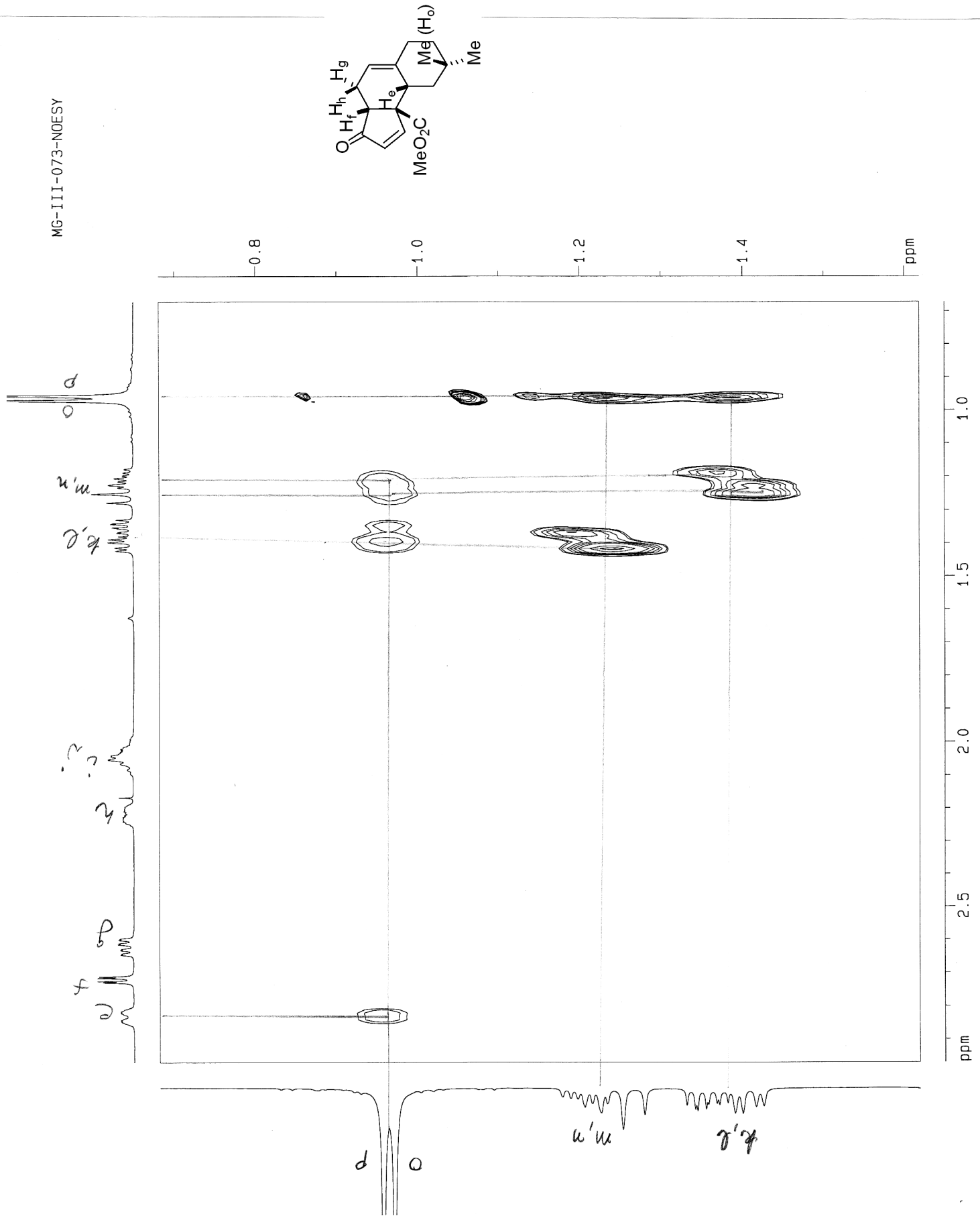
1D NMR plot parameters

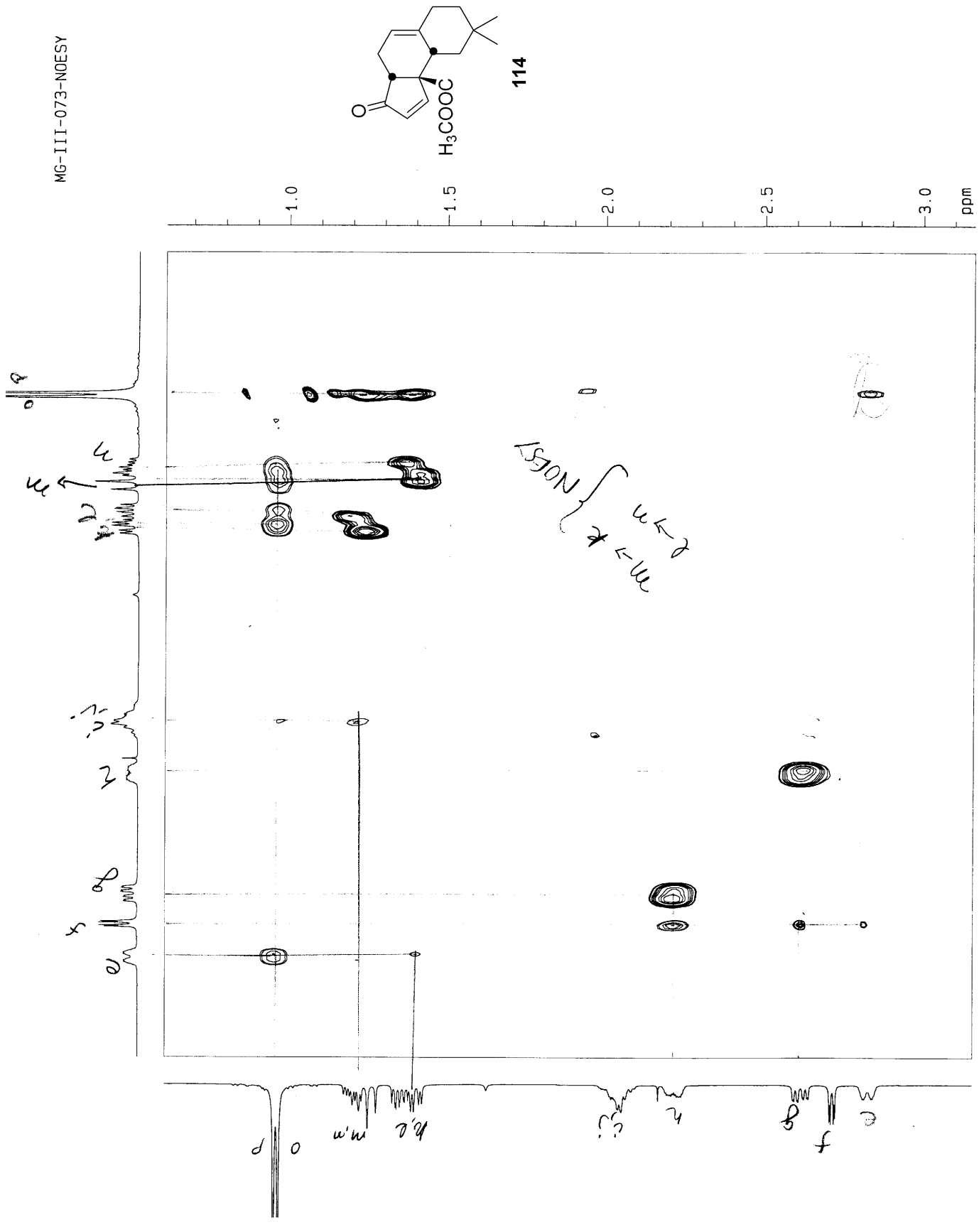
CX	20.00 cm
CY	11.00 cm
F1P	234.220 ppm
F1	17676.09 Hz
F2P	-15.322 ppm
F2	-1156.30 Hz
PPMCM	12.47711 ppm/cm
HZCM	941.61957 Hz/cm

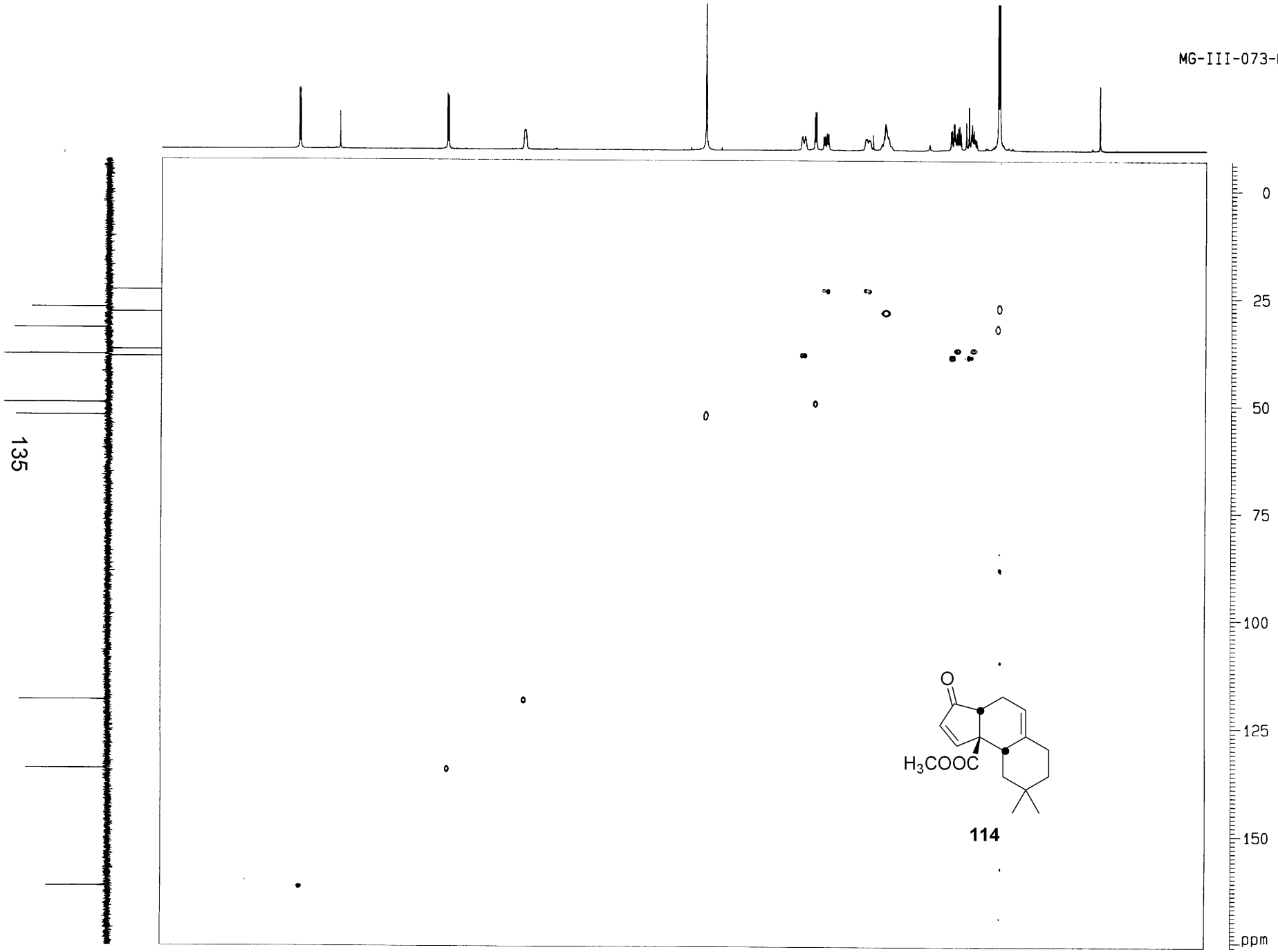
MG-III-073-COSY

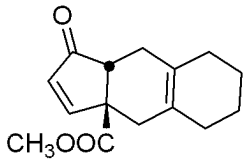
114


MG-III-073-NOESY
Me (Ho)
Me
Hg
Hh
Hf
He
O
MeO2C
1.0
1.5
2.0
2.5
3.0
3.5
ppm
3.0
3.5
4.0
4.5
5.0
ppm

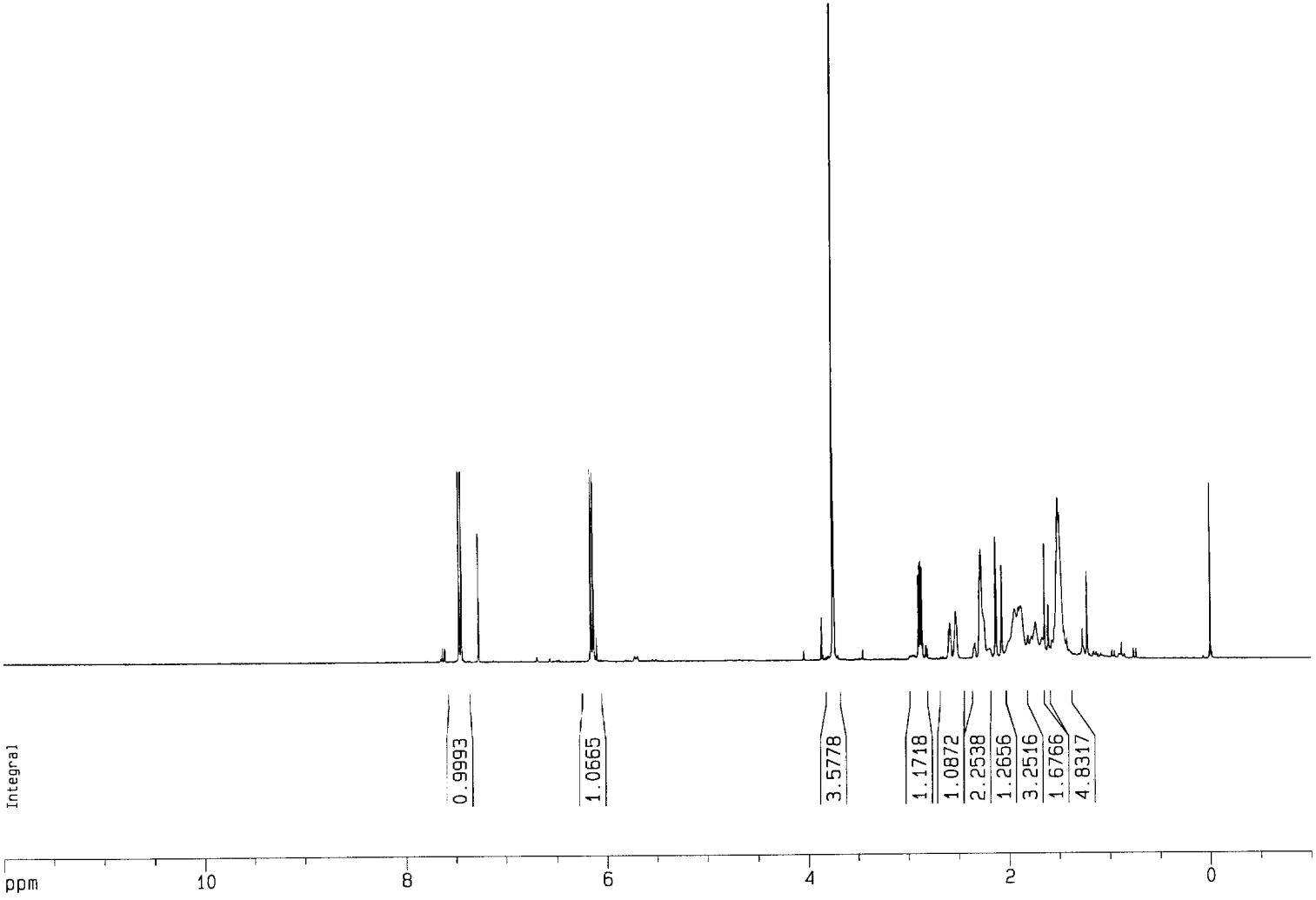

MG-III-073-NOESY
Me (Ho)
Me
Hh
Hg
He
Hf
O
MeO2C
0.8
1.0
1.2
1.4
ppm
1.0
1.5
2.0
2.5
ppm


MG-III-073-NOESY
O
H3COOC
114
1.0
1.5
2.0
2.5
3.0
ppm


MG-III-073-hmqc
135
0
25
50
75
100
125
150
ppm
O
H3COOC
114



115



Current Data Parameters

NAME	MG-4-018a-250
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

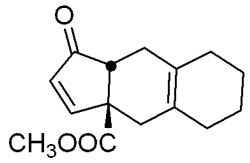
Date_	20050401
Time	0.52
INSTRUM	arx250
PROBHD	5 mm QNP 1H
PULPROG	zg30
TD	32768
SOLVENT	CDCl3
NS	16
DS	2
SWH	5208.333 Hz
FIDRES	0.158946 Hz
AQ	3.1457779 sec
RG	715
DW	96.000 use
DE	137.14 use
TE	300.0 K
D1	1.00000000 sec
P1	8.70 use
SFO1	250.1315321 MHz
NUCLEUS	1H

F2 - Processing parameters

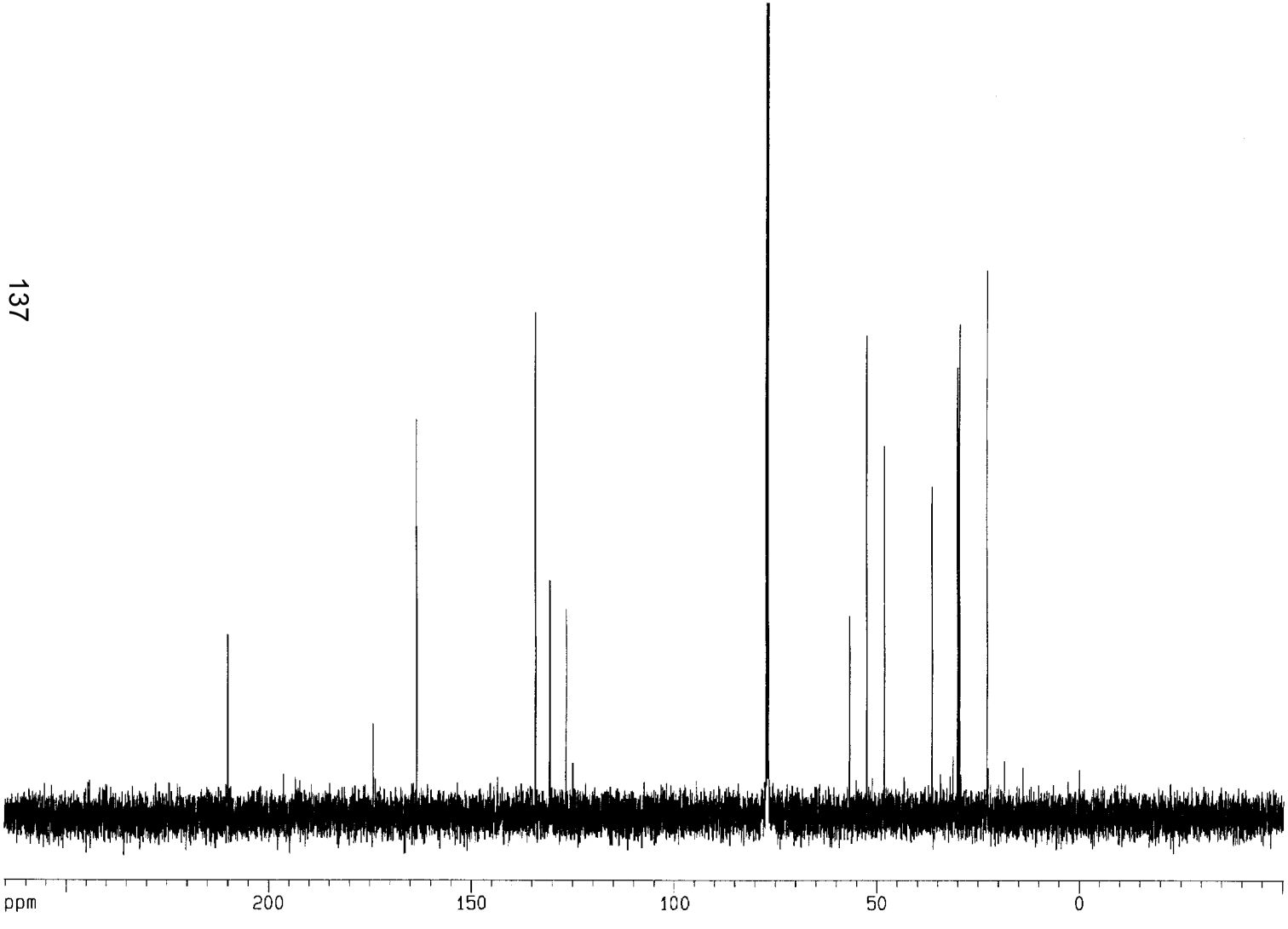
SI	16384
SF	250.1300043 MHz
WDW	EM
SSB	0
LB	0.20 Hz
GB	0
PC	1.50

1D NMR plot parameters

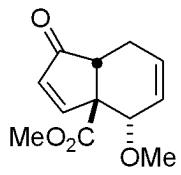
CX	20.00 cm
CY	30.00 cm
F1P	12.000 ppm
F1	3001.56 Hz
F2P	-1.000 ppm
F2	-250.13 Hz
PPMCM	0.65000 ppm
HZCM	162.58450 Hz/



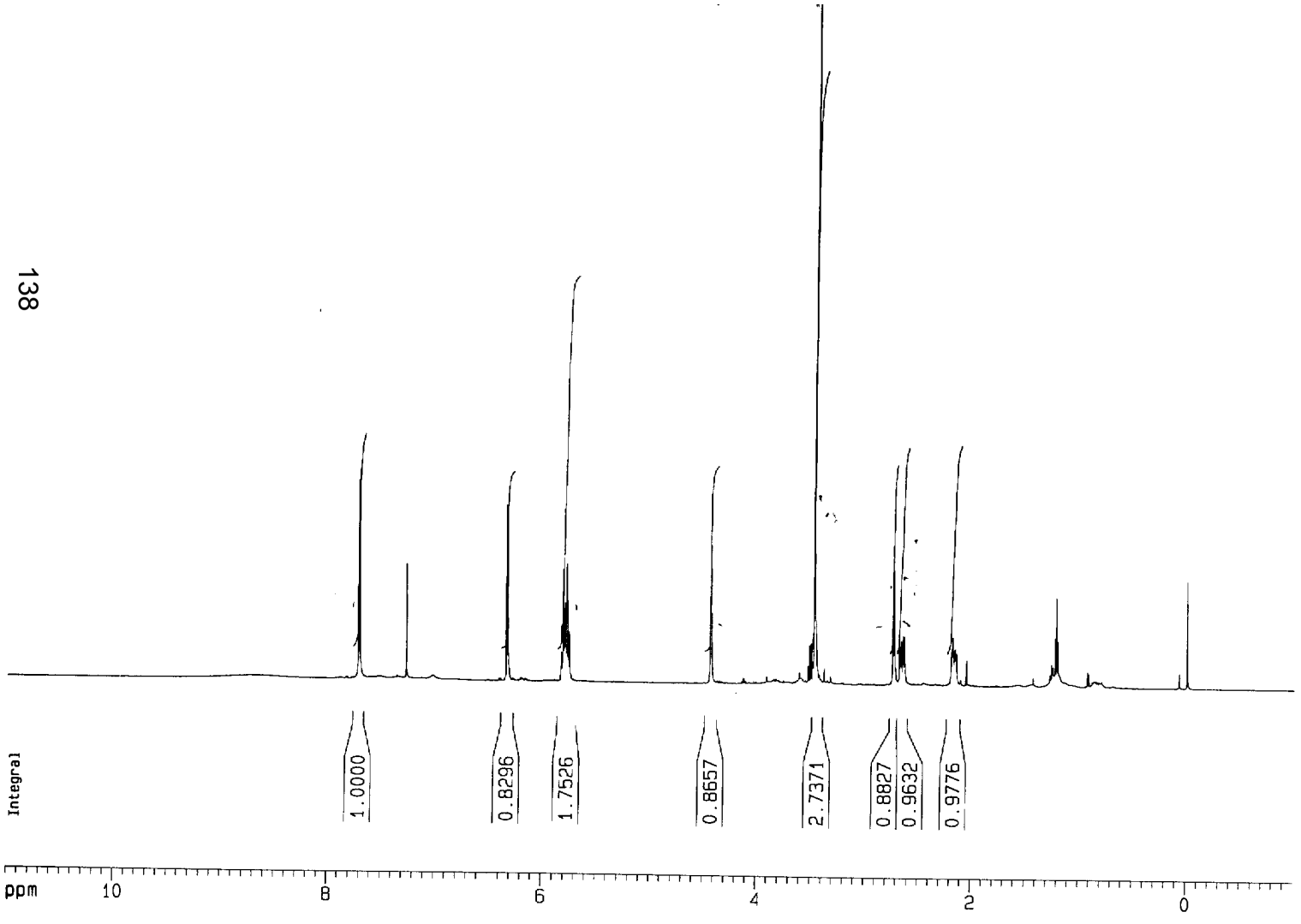
115



Current Data Parameters	
NAME	MG-4-015a-500
EXPNO	2
PROCNO	1
F2 - Acquisition Parameters	
Date_	20050329
Time	1.25
INSTRUM	DRX500
PROBHD	5 mm Multinucl
PULPROG	zgdc30
TD	65536
SOLVENT	CDCl3
NS	182
DS	4
SWH	39681.812 Hz
FIDRES	0.605496 Hz
AQ	0.8258188 sec
RG	16384
DW	12.600 usec
DE	6.00 usec
TE	298.0 K
D1	2.00000000 sec
d11	0.03000000 sec
======== CHANNEL f1 ========	
NUC1	13C
P1	8.10 usec
PL1	3.00 dB
SFO1	125.7713108 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	88.00 usec
PL2	0.00 dB
PL12	21.00 dB
SFO2	500.1320005 MHz
F2 - Processing parameters	
SI	32768
SF	125.7577922 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40
1D NMR plot parameters	
CX	20.00 cm
CY	35.00 cm
F1P	265.268 ppm
F1	33359.46 Hz
F2P	-50.274 ppm
F2	-6322.34 Hz
PPMCM	15.77708 ppm/cm
HZCM	1984.09033 Hz/cm



123



Current Data Parameters

NAME	MG-3-025a-500
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20040902
Time	22.56
INSTRUM	DRX500
PROBHD	5 mm Multinucl
PULPROG	zg30
TD	57344
SOLVENT	CDCl3
NS	16
DS	2
SWH	10330.578 Hz
FIDRES	0.180151 Hz
AQ	2.7754996 sec
RG	128
DW	48.400 usec
DE	6.00 usec
TE	296.7 K
D1	1.00000000 sec

======== CHANNEL f1 ========

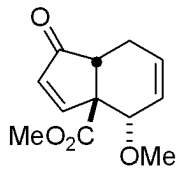
NUC1	1H
P1	13.25 usec
PL1	-3.00 dB
SFO1	500.1330885 MHz

F2 - Processing parameters

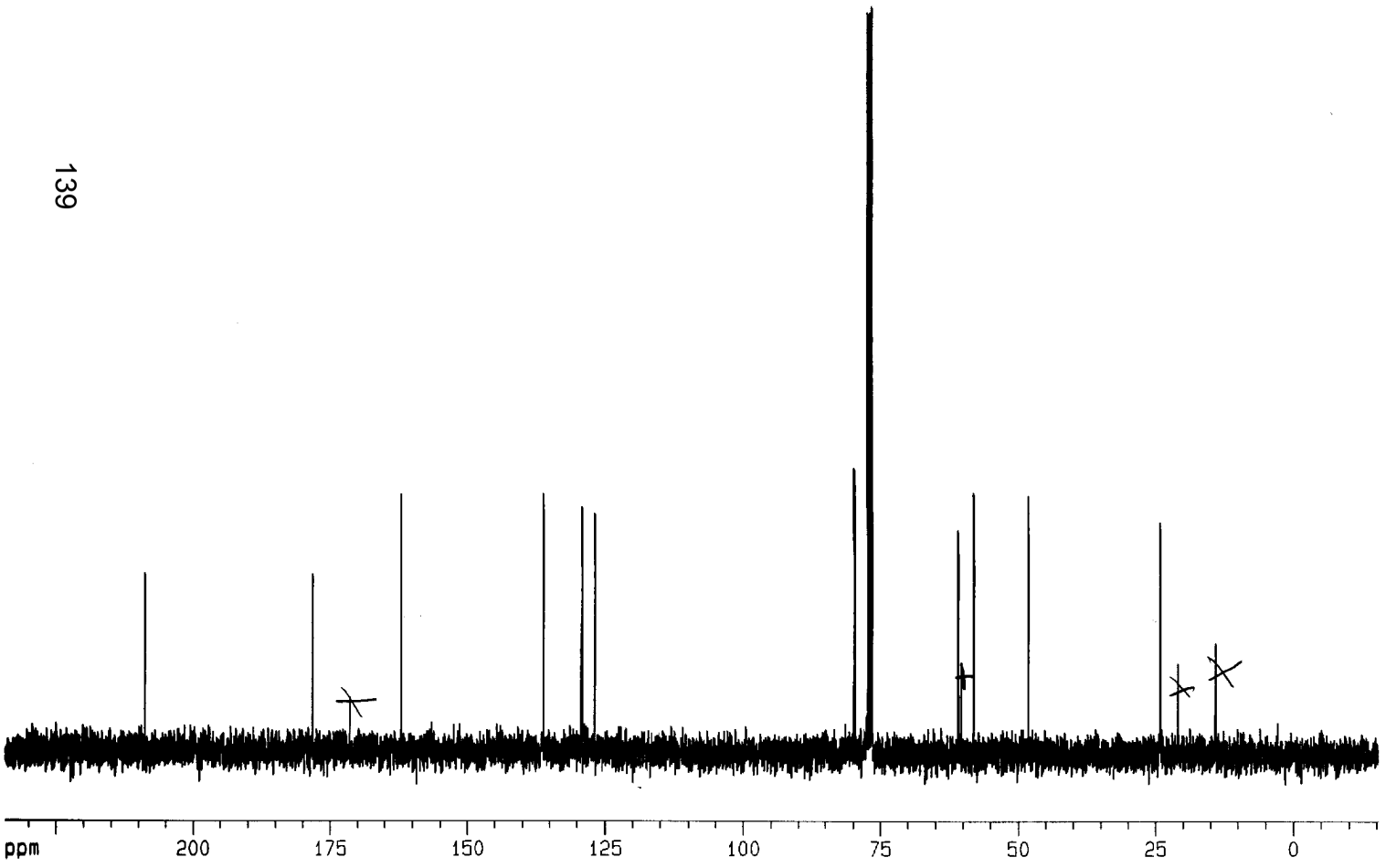
SI	32768
SF	500.1300081 MHz
WDW	EM
SSB	0
LB	0.20 Hz
GB	0
PC	1.40

1D NMR plot parameters

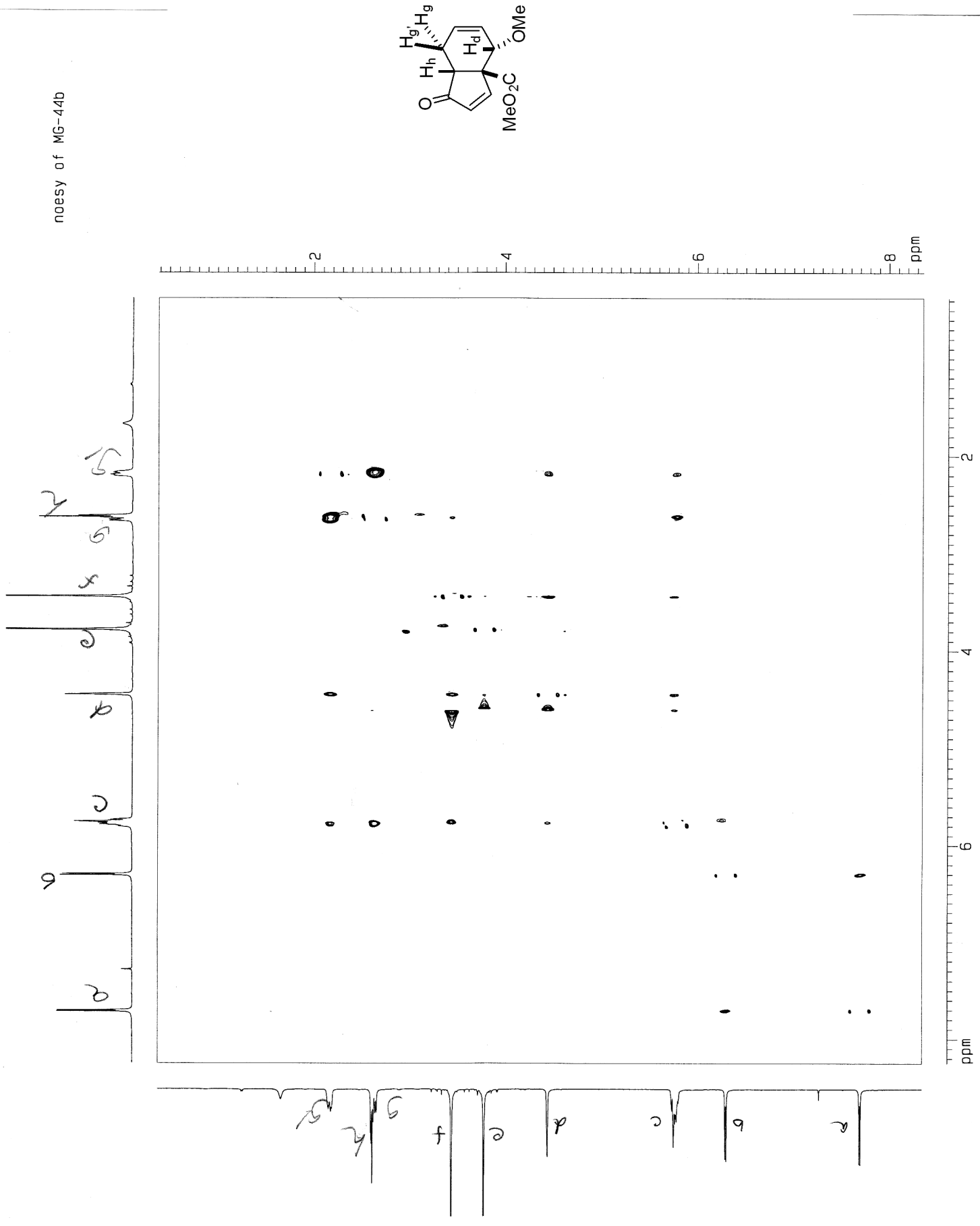
CX	20.00 cm
CY	20.00 cm
F1P	11.000 ppm
F1	5501.43 Hz
F2P	-1.000 ppm
F2	-500.13 Hz
PPMCM	0.60000 ppm/cr
HZCM	300.07800 Hz/cm

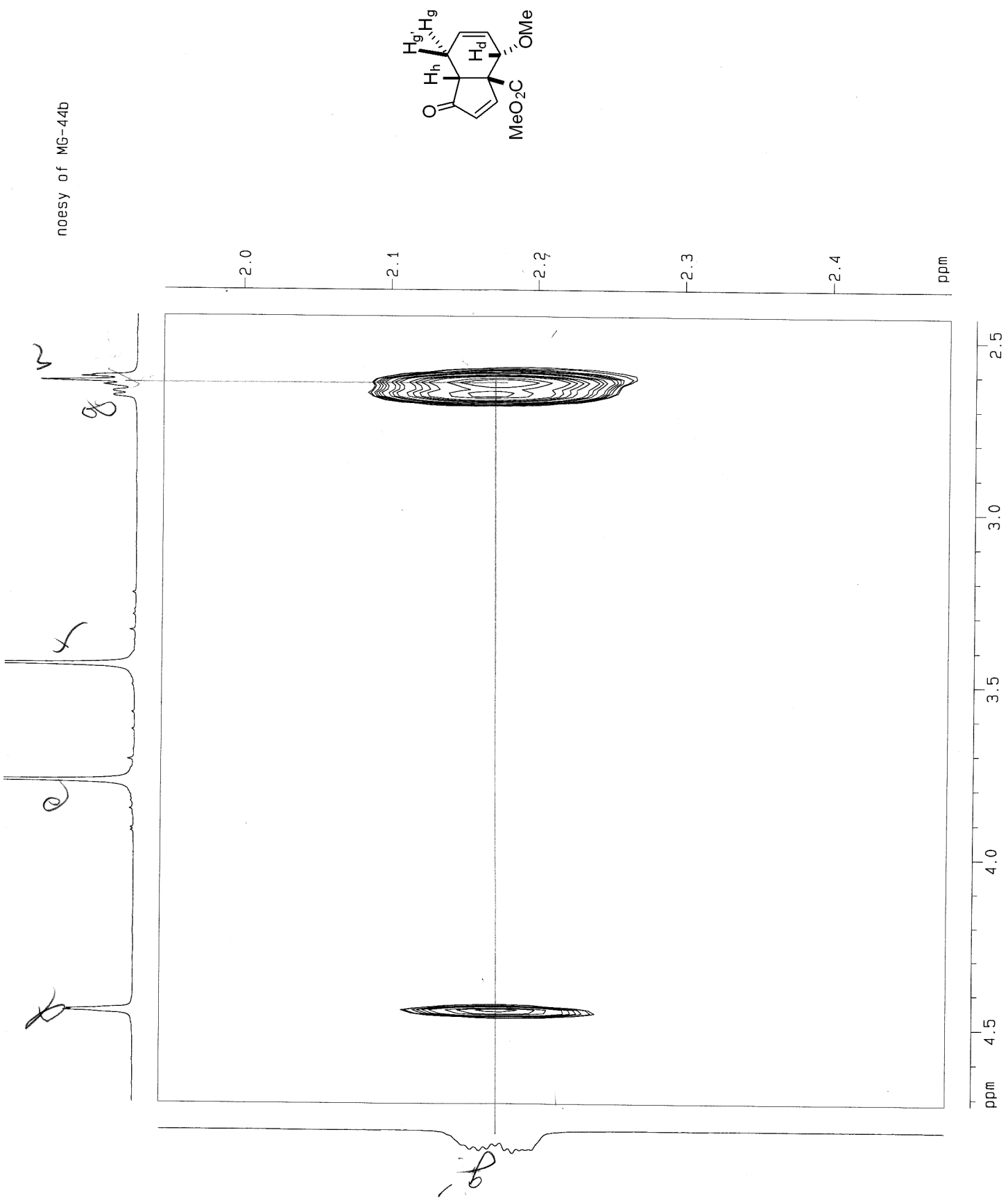


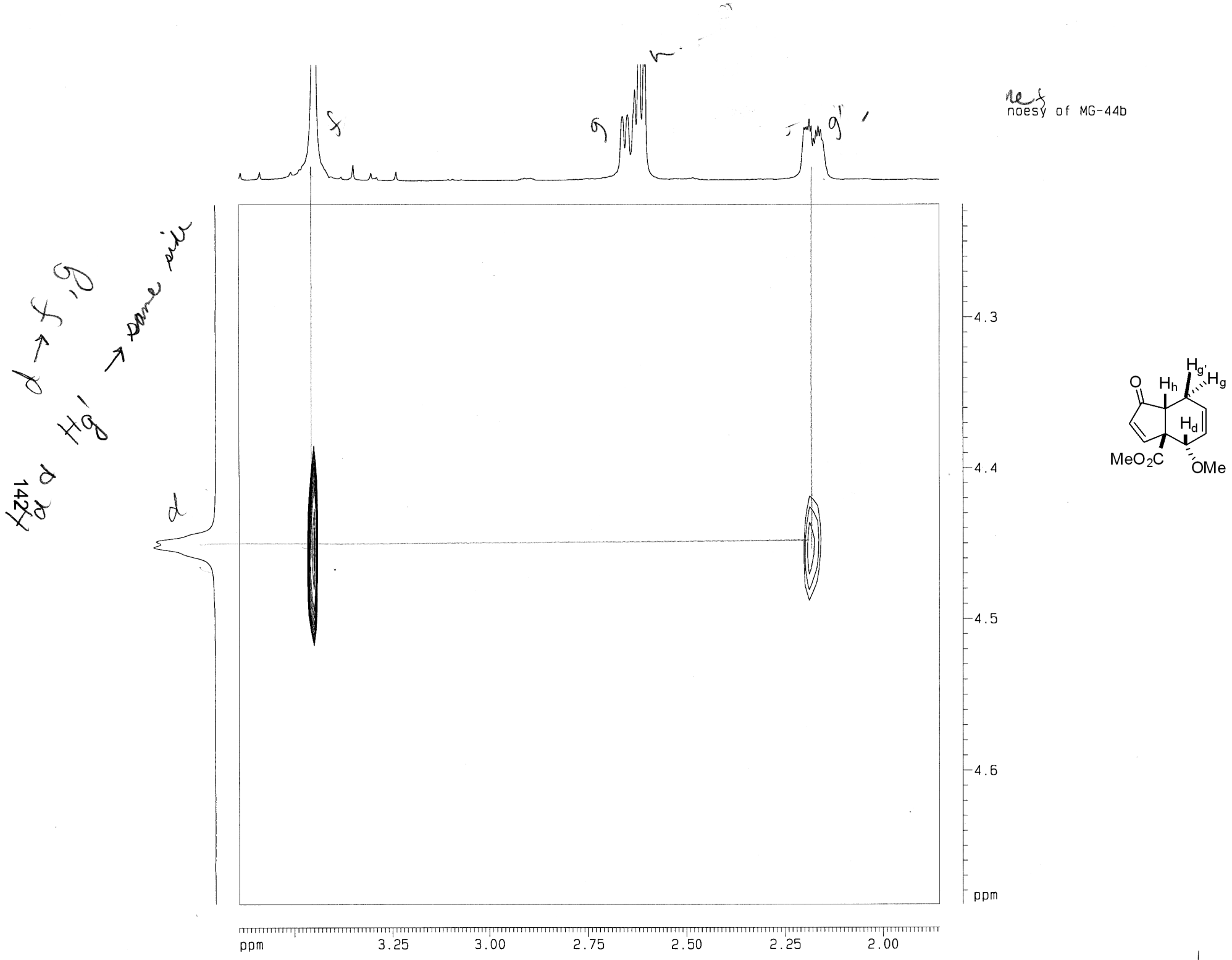
123

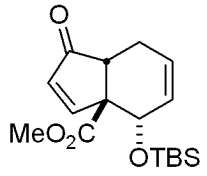


Current Data Parameters		
NAME	MG-3-025-300	
EXPNO	2	
PROCNO	1	
F2 - Acquisition Parameters		
Date_	20040902	
Time	13.20	
INSTRUM	drx300	
PROBHD	5 mm Multinucl	
PULPROG	zgdc30	
TD	65536	
SOLVENT	CDCl3	
NS	121	
DS	4	
SWH	18832.393	Hz
FIDRES	0.287360	Hz
AQ	1.7400308	sec
RG	22528	
DW	26.550	usec
DE	6.00	usec
TE	297.1	K
D1	1.29999995	sec
d11	0.03000000	sec
D31	0.00000000	sec
======== CHANNEL f1 ========		
NUC1	13C	
P1	8.50	usec
PL1	5.00	dB
SFO1	75.4760107	MHz
======== CHANNEL f2 ========		
CPDPRG2	waltz16	
NUC2	1H	
PCPD2	100.00	usec
PL2	120.00	dB
PL12	25.60	dB
SFO2	300.1312005	MHz
F2 - Processing parameters		
SI	32768	
SF	75.4677520	MHz
WDW	EM	
SSB	0	
LB	1.00	Hz
GB	0	
PC	1.40	
1D NMR plot parameters		
CX	20.00	cm
CY	11.00	cm
F1P	234.205	ppm
F1	17674.94	Hz
F2P	-15.337	ppm
F2	-1157.45	Hz
PPMCM	12.47711	ppm/cm
HZCM	941.61957	Hz/cm

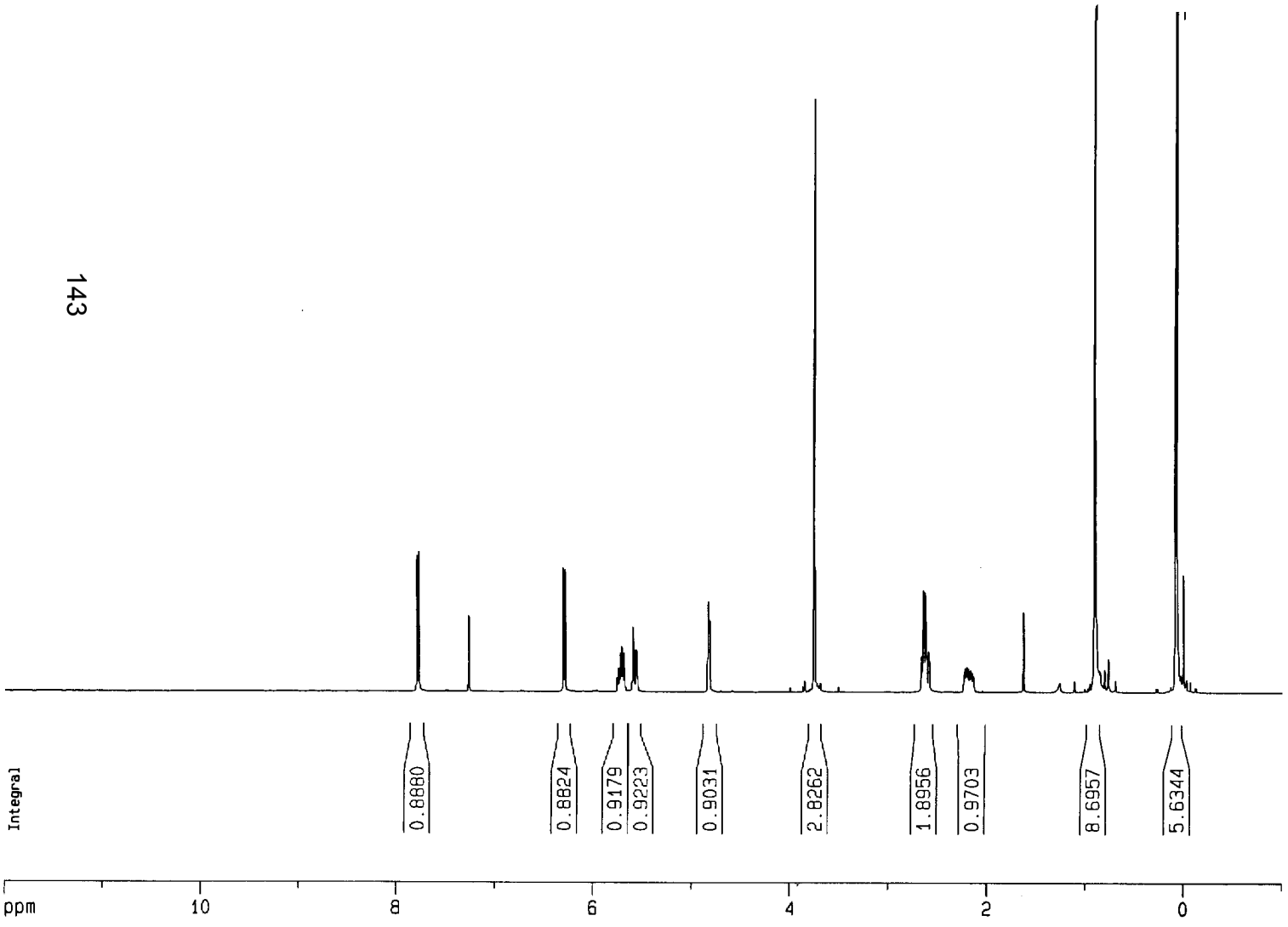

noesy of MG-44b
$H_{g'}H_g$
H_h
H_d
OMe
O
MeO_2C
2
4
6
8
ppm


noesy of MG-44b
$H_{g'}$ H_g
H_d
OMe
H_h
O
MeO_2C
2.0
2.1
2.2
2.3
2.4
ppm
2.5
3.0
3.5
4.0
4.5
ppm


noesy of MG-44b
d → f, g
d → Hg' → same pair
d
f
g
g'
h
4.3
4.4
4.5
4.6
ppm
3.25
3.00
2.75
2.50
2.25
2.00
O
Hh
Hg'
Hg
Hd
MeO2C
OMe



124



Current Data Parameters
NAME MG-4-024a-300
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters

Date_	20050406
Time	12.38
INSTRUM	drx300
PROBHD	5 mm Multinucl
PULPROG	zg30
TD	32768
SOLVENT	CDCl3
NS	16
DS	2
SWH	6172.839 Hz
FIDRES	0.188380 Hz
AQ	2.6542580 sec
RG	203.2
DW	81.000 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec
D31	0.00000000 sec

======== CHANNEL f1 ========

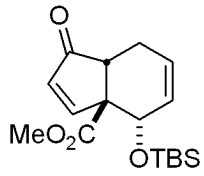
NUC1	1H
P1	7.05 usec
PL1	0.00 dB
SFO1	300.1318534 MHz

F2 - Processing parameters

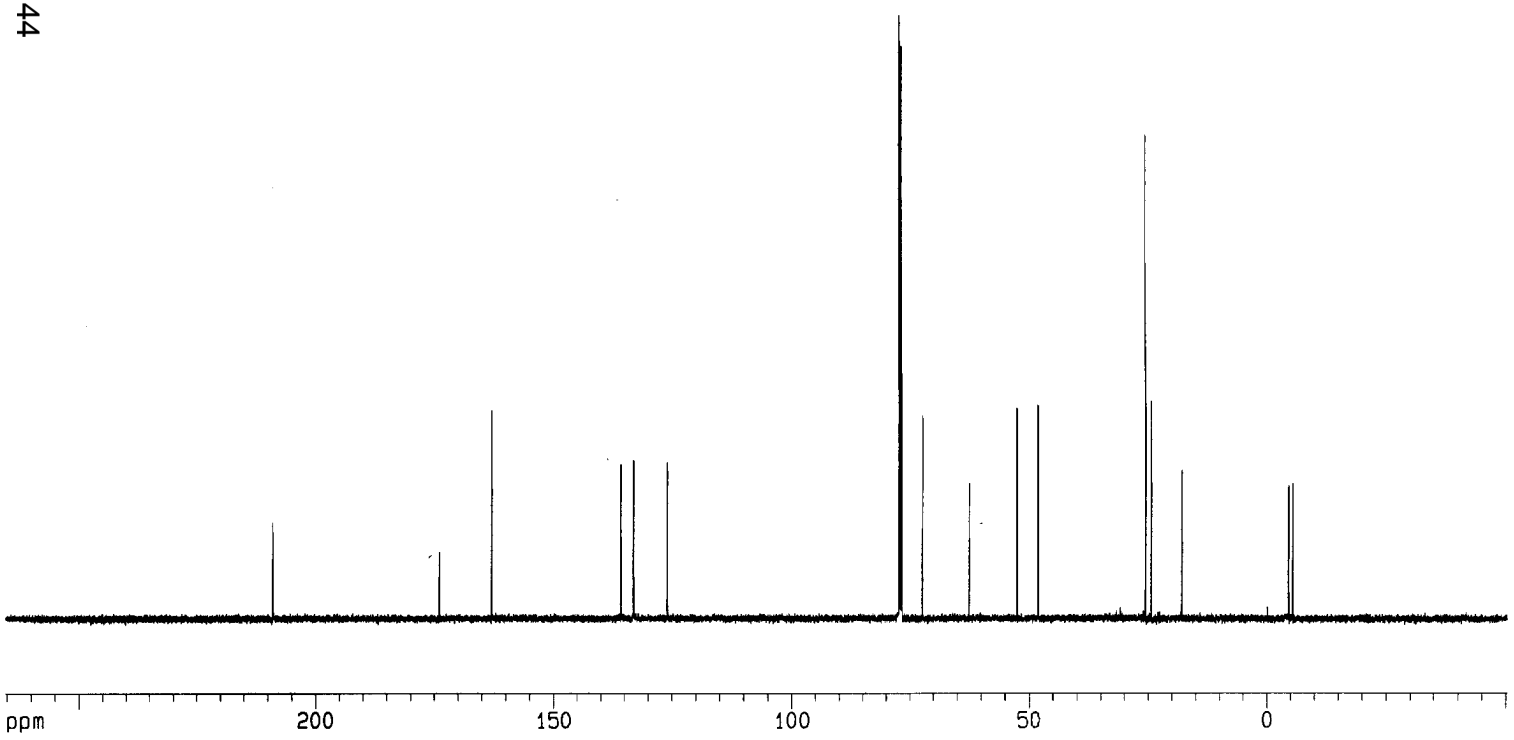
SI	32768
SF	300.1300037 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.30

1D NMR plot parameters

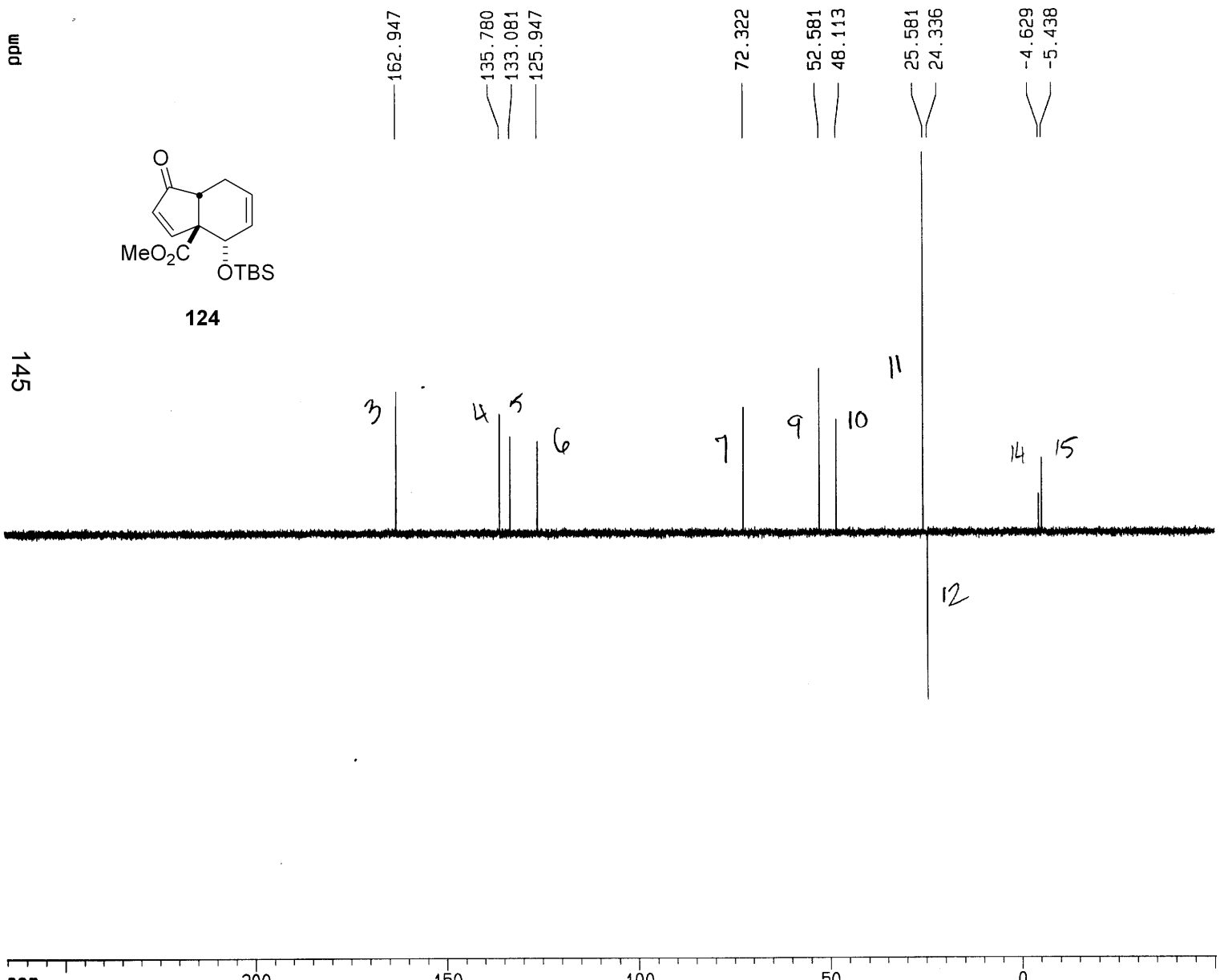
CX	20.00 cm
CY	40.00 cm
F1P	12.000 ppm
F1	3601.56 Hz
F2P	-1.000 ppm
F2	-300.13 Hz
PPMCM	0.65000 ppm/cm
HZCM	195.08450 Hz/cm



124



Current Data Parameters	
NAME	MG-4-024a-500
EXPNO	2
PROCNO	1
F2 - Acquisition Parameters	
Date_	20050407
Time	20.41
INSTRUM	DRX500
PROBHD	5 mm Multinucl
PULPROG	zgdc30
TD	65536
SOLVENT	CDCl3
NS	495
DS	4
SWH	39681.812 Hz
FIDRES	0.605496 Hz
AQ	0.8258188 sec
RG	16384
DW	12.600 usec
DE	6.00 usec
TE	298.0 K
D1	2.00000000 sec
d11	0.03000000 sec
======== CHANNEL f1 ========	
NUC1	13C
P1	8.10 usec
PL1	3.00 dB
SFO1	125.7713108 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	88.00 usec
PL2	0.00 dB
PL12	21.00 dB
SFO2	500.1320005 MHz
F2 - Processing parameters	
SI	32768
SF	125.7577935 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40
1D NMR plot parameters	
CX	20.00 cm
CY	8.00 cm
F1P	265.258 ppm
F1	33358.26 Hz
F2P	-50.284 ppm
F2	-6323.55 Hz
PPMCM	15.77708 ppm/cm
HZCM	1984.09045 Hz/cm



Current Data Parameters

NAME	MG-4-024a-500
EXPNO	3
PROCNO	1

F2 - Acquisition Parameters

Date_	20050407
Time	21.06
INSTRUM	DRX500
PROBHD	5 mm Multinucl
PULPROG	dept135
TD	65536
SOLVENT	CDCl3
NS	83
DS	4
SWH	39682.539 Hz
FIDRES	0.605507 Hz
AQ	0.8258036 sec
RG	16384
DW	12.600 usec
DE	6.00 usec
TE	300.0 K
CNST2	145.0000000
D1	2.00000000 sec
d2	0.00344828 sec
d12	0.00002000 sec
DELTA	0.00001031 sec

======== CHANNEL f1 ========

NUC1	13C
P1	8.10 usec
p2	16.20 usec
PL1	3.00 dB
SFO1	125.7713108 MHz

======== CHANNEL f2 ========

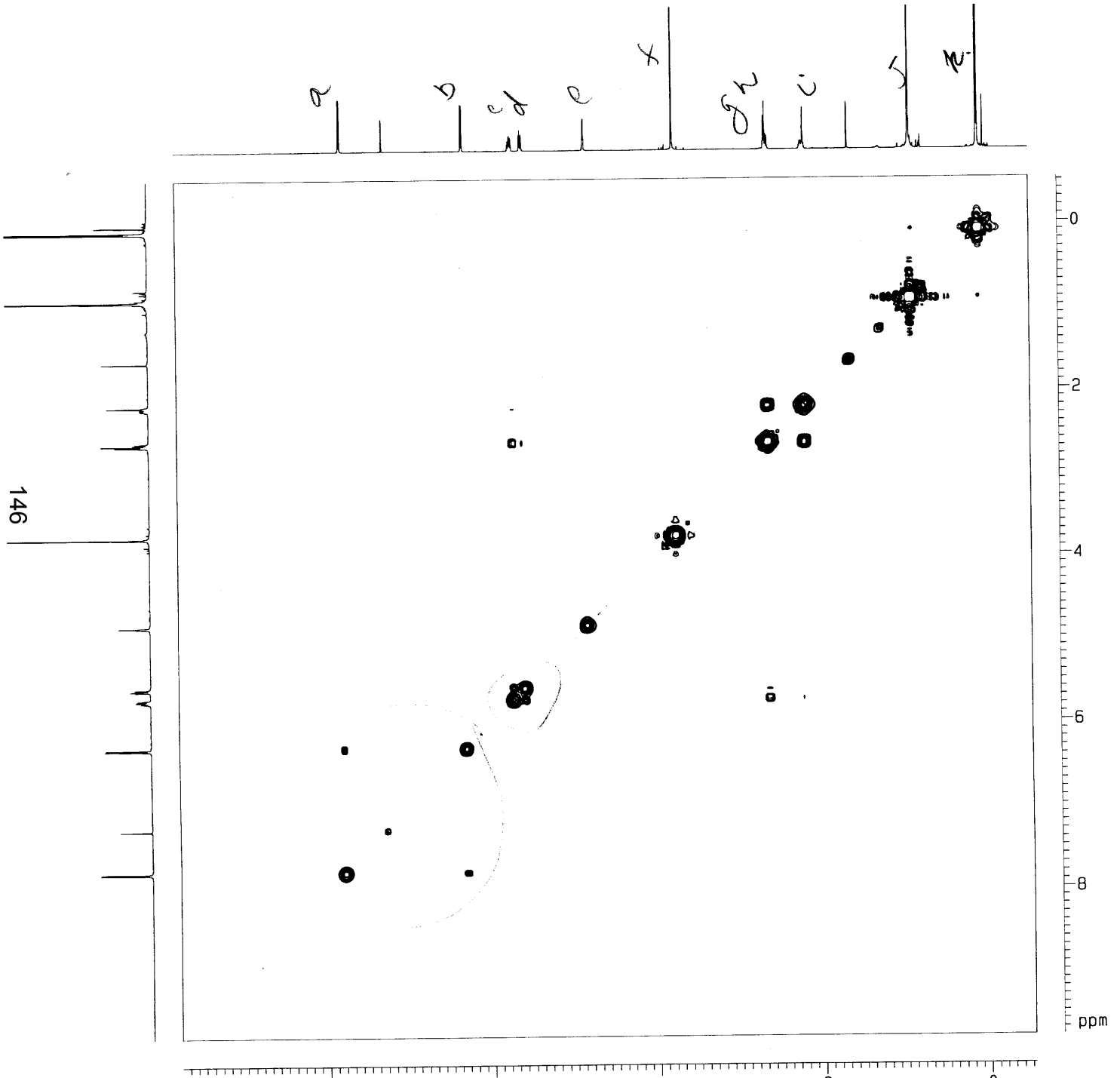
CPDPRG2	waltz16
NUC2	1H
P3	10.40 usec
p4	20.80 usec
PCPD2	88.00 usec
PL2	0.00 dB
PL12	21.00 dB
SFO2	500.1320005 MHz

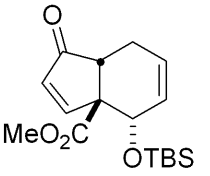
F2 - Processing parameters

SI	32768
SF	125.7577932 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

1D NMR plot parameters

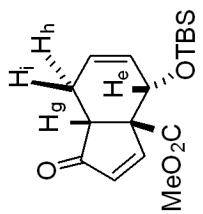
CX	20.00 cm
CY	6.50 cm
F1P	265.263 ppm
F1	33358.83 Hz
F2P	-50.285 ppm
F2	-6323.71 Hz
PPMCM	15.77737 ppm/cm

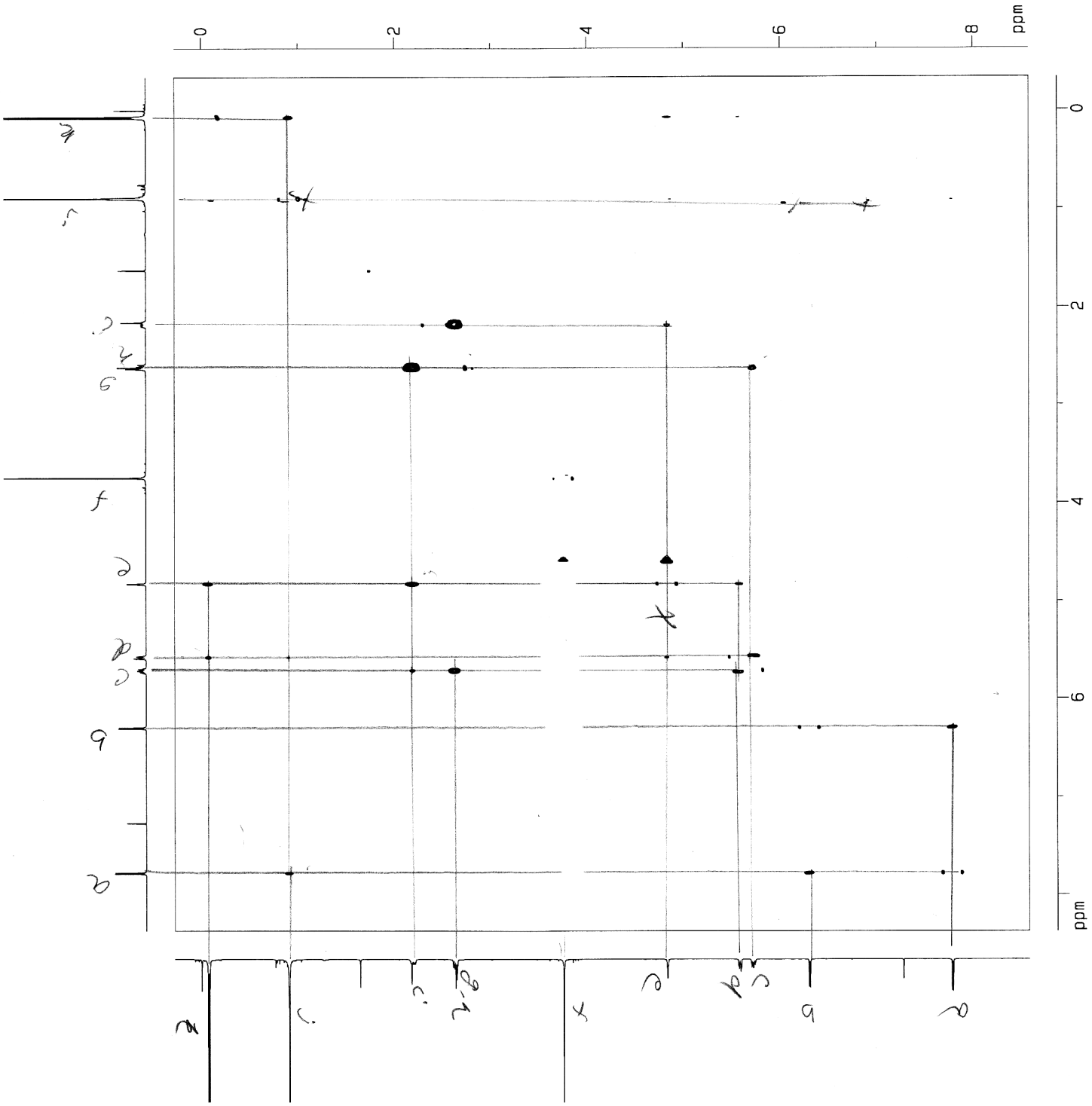




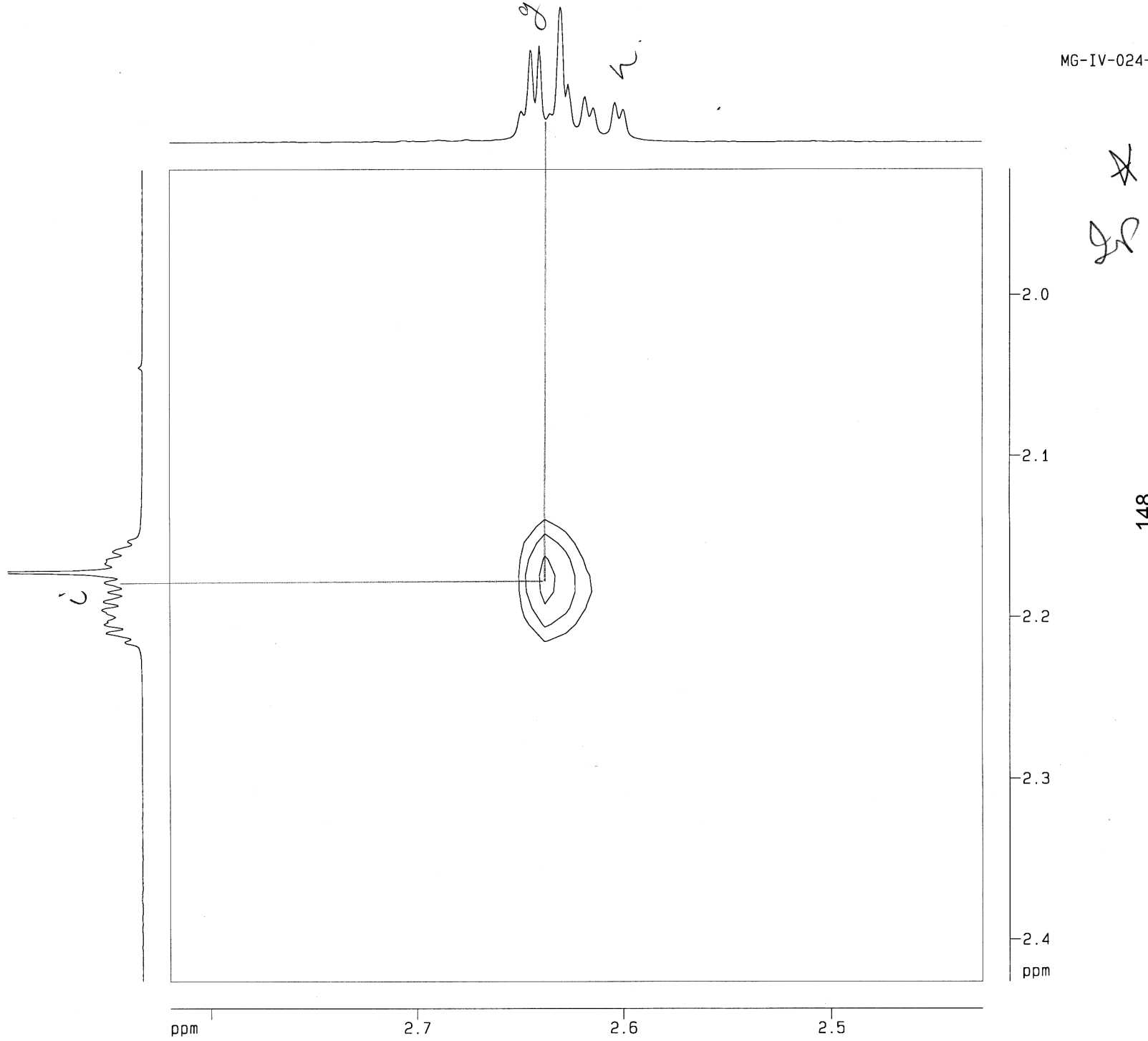
124

MG-IV-024-NOESY



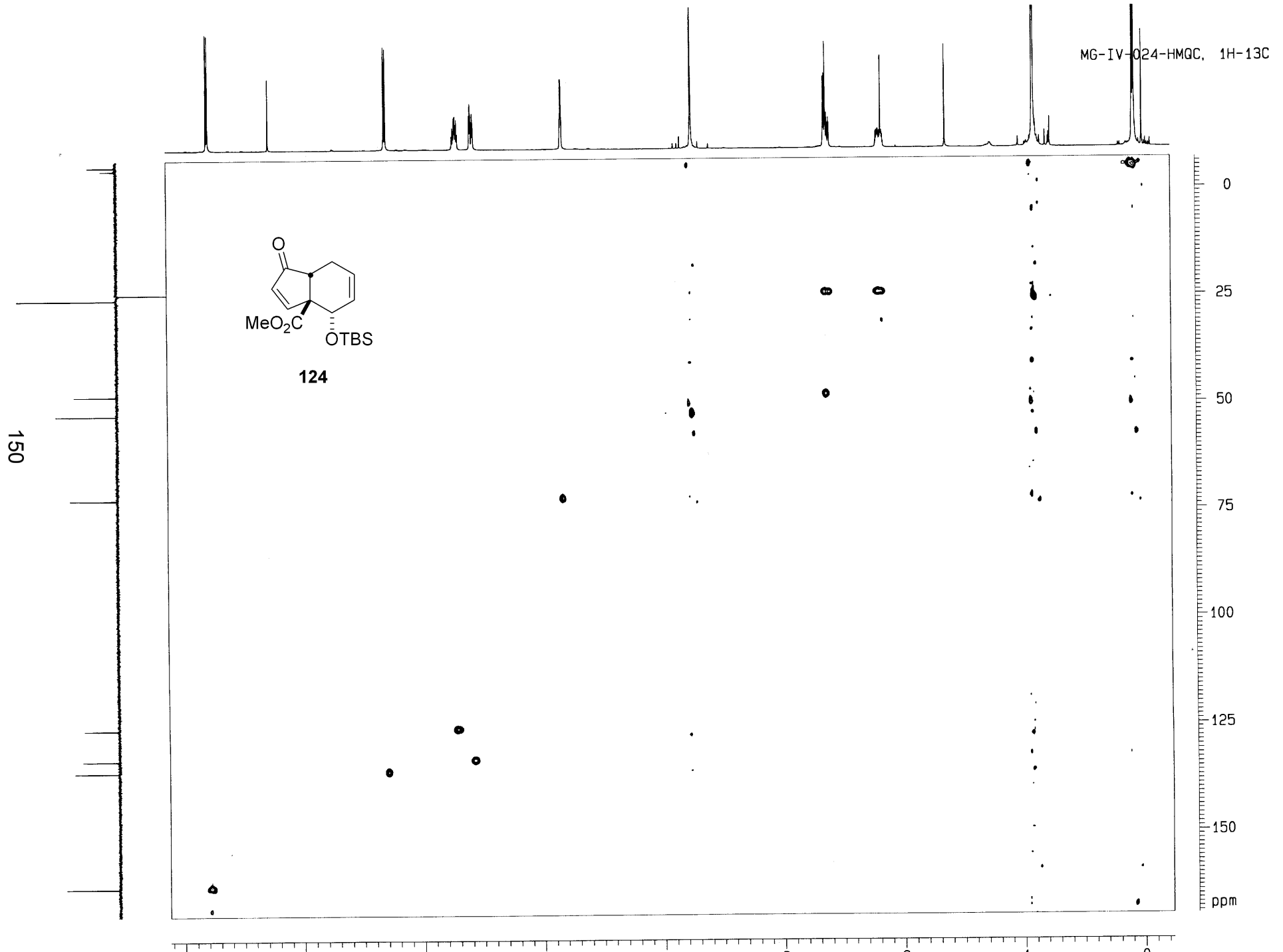


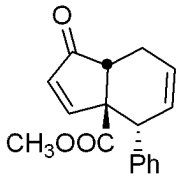
MG-IV-024-NOESY



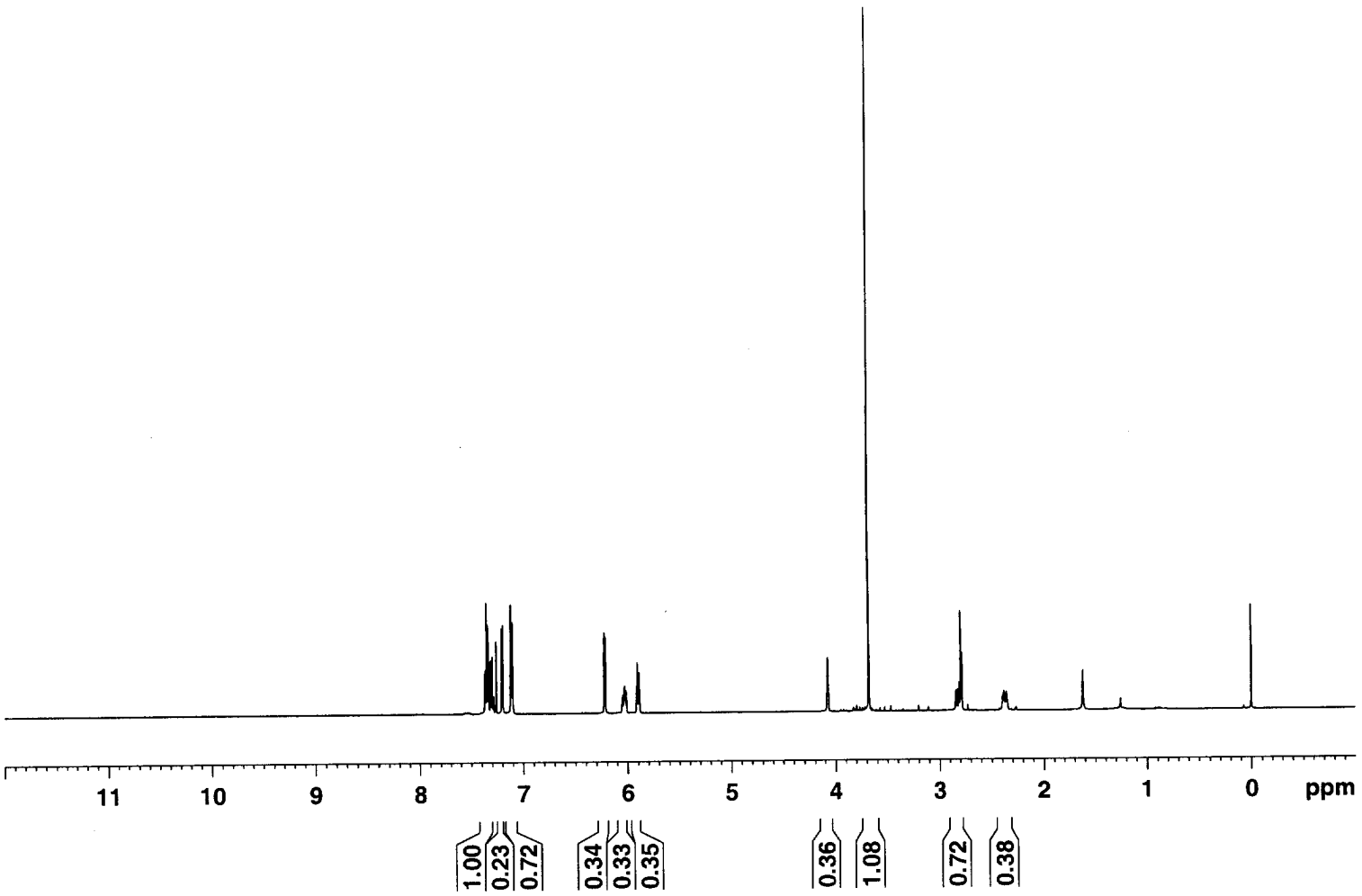
148

MG-IV-024-NOESY

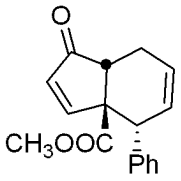

MG-IV-024-HMQC, 1H-13C
O
MeO2C
OTBS
124
150
0
25
50
75
100
125
150
ppm



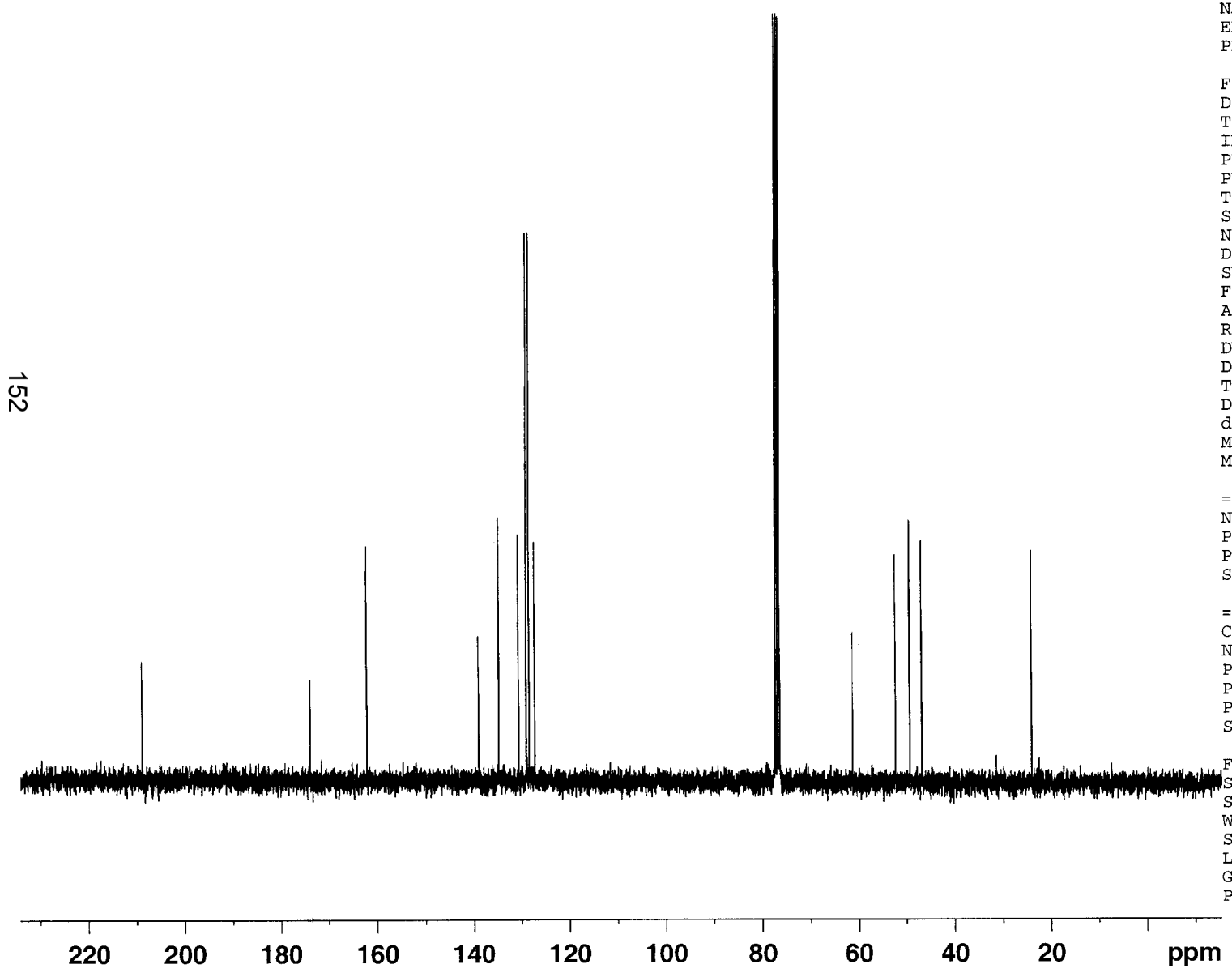
125



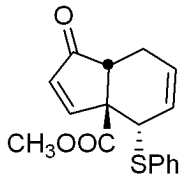

```
Current Data Parameters
NAME          MG-IV-77a-A3
EXPNO                    1
PROCNO                   1

F2 - Acquisition Parameters
Date_             20060208
Time                 14.38
INSTRUM             DRX500
PROBHD    5 mm Multinucl
PULPROG           zg30pad
TD                   65536
SOLVENT              CDCl3
NS                      16
DS                       2
SWH           10330.578 Hz
FIDRES         0.157632 Hz
AQ            3.1719923 sec
RG                     128
DW                48.400 use
DE                 6.00 use
TE                300.0 K
D1           1.00000000 sec
D31          0.00000000 sec

======== CHANNEL f1 =======
NUC1                   1H
P1                 11.50 use
PL1                 0.00 dB
SFO1        500.1330885 MHz

F2 - Processing parameters
SI                     32768
SF          500.1300115 MHz
WDW                       EM
SSB                        0
LB                  0.30 Hz
GB                         0
PC                      1.40
```



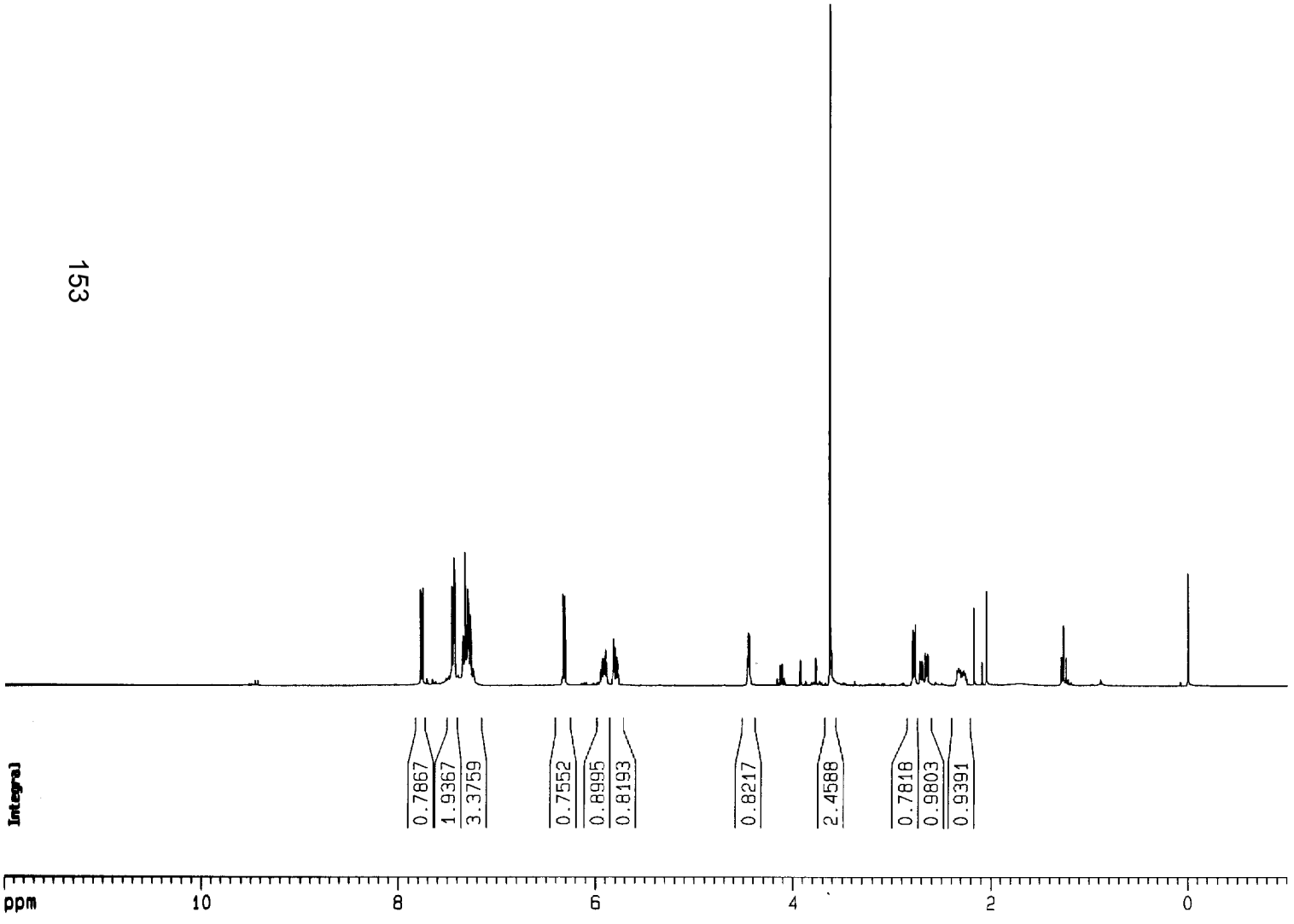
125



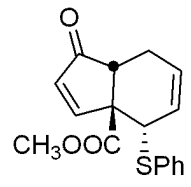

```
Current Data Parameters
NAME      MG-IV-077b-300
EXPNO                   2
PROCNO                  1

F2 - Acquisition Parameters
Date_            20050628
Time                22.26
INSTRUM           DRX300
PROBHD   5 mm Multinucl
PULPROG           zgdc30
TD                65536
SOLVENT           CDCl3
NS                   13
DS                    4
SWH           18832.393 Hz
FIDRES         0.287360 Hz
AQ             1.7400308 sec
RG                22528
DW               26.550 usec
DE                6.00 usec
TE               300.0 K
D1            2.00000000 sec
d11           0.03000000 sec
MCREST        0.00000000 sec
MCWRK         0.01500000 sec

======== CHANNEL f1 ========
NUC1                 13C
P1                 9.00 usec
PL1                5.00 dB
SFO1         75.4760107 MHz

======== CHANNEL f2 ========
CPDPRG2          waltz16
NUC2                 1H
PCPD2            100.00 usec
PL2              120.00 dB
PL12              25.60 dB
SFO2        300.1312005 MHz

F2 - Processing parameters
SI                32768
SF           75.4677514 MHz
WDW                  EM
SSB                   0
LB                 1.00 Hz
GB                    0
PC                 1.40
```



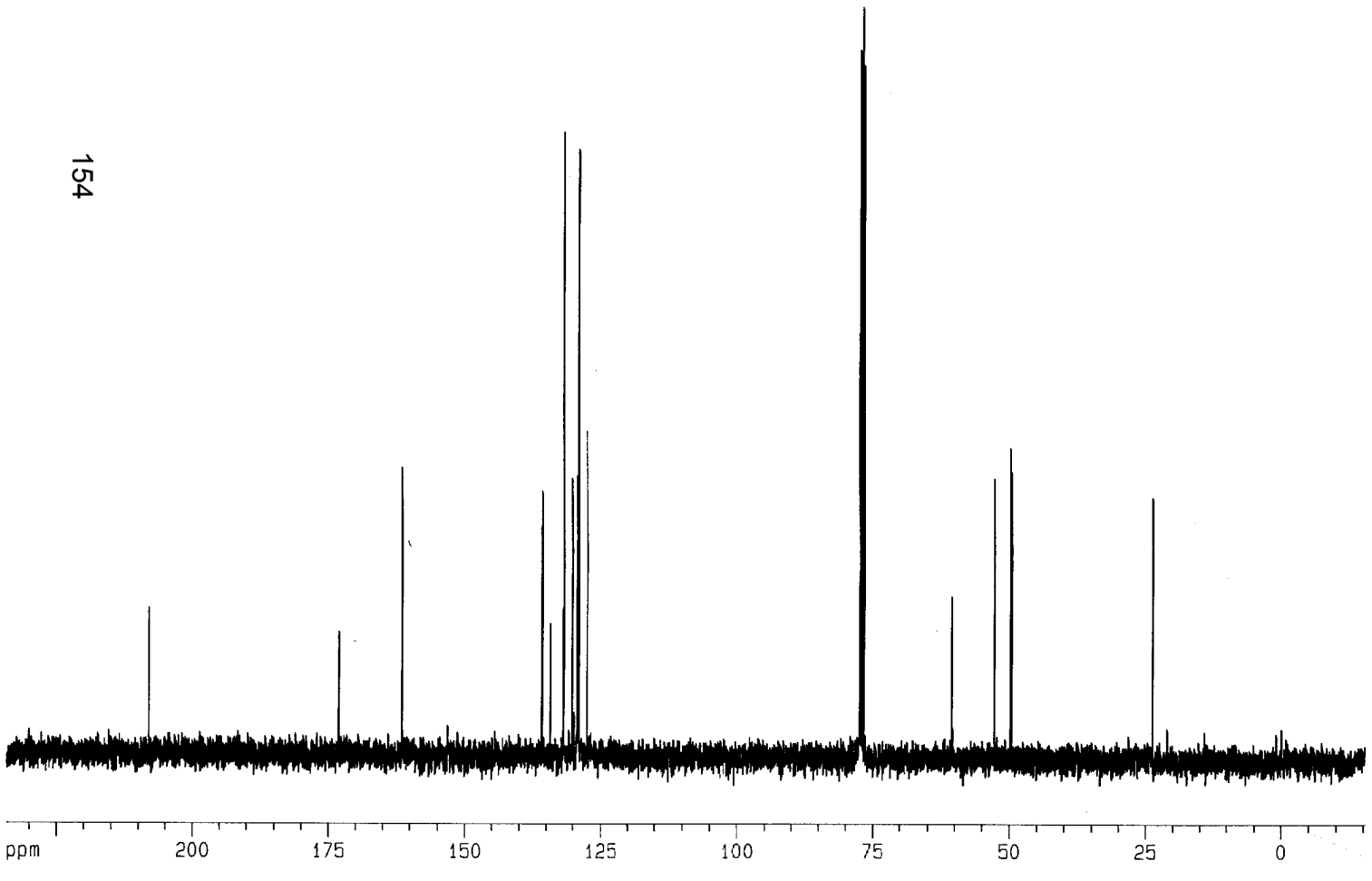
126



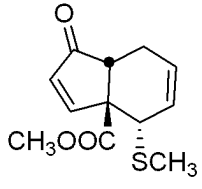

```
Current Data Parameters
NAME       MG-4-035a-300
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20050429
Time               14.42
INSTRUM          drx300
PROBHD   5 mm Multinucl
PULPROG            zg30
TD                32768
SOLVENT           CDCl3
NS                   16
DS                    2
SWH           6172.839 Hz
FIDRES        0.188380 Hz
AQ            2.6542580 sec
RG                  256
DW               81.000 usec
DE                6.00 usec
TE               300.0 K
D1            1.00000000 sec
D31           0.00000000 sec

======== CHANNEL f1 ========
NUC1                 1H
P1                7.05 usec
PL1               0.00 dB
SFO1        300.1318534 MHz

F2 - Processing parameters
SI                32768
SF          300.1300022 MHz
WDW                  EM
SSB                   0
LB                0.30 Hz
GB                    0
PC                1.30

1D NMR plot parameters
CX               20.00 cm
CY               12.50 cm
F1P              12.000 ppm
F1             3601.56 Hz
F2P              -1.000 ppm
F2             -300.13 Hz
PPMCM          0.65000 ppm/cm
HZCM         195.08450 Hz/cm
```



126



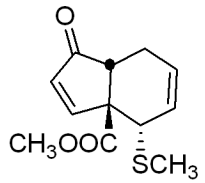

```
Current Data Parameters
NAME        MG-4-35a-300
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20050422
Time               22.49
INSTRUM          drx300
PROBHD   5 mm Multinucl
PULPROG          zgdc30
TD                65536
SOLVENT           CDCl3
NS                  321
DS                    4
SWH           18832.393 Hz
FIDRES         0.287360 Hz
AQ             1.7400308 sec
RG                22528
DW               26.550 usec
DE                6.00 usec
TE               297.1 K
D1            1.79999995 sec
d11           0.03000000 sec
D31           0.00000000 sec

======== CHANNEL f1 ========
NUC1                 13C
P1                  8.50 usec
PL1                 5.00 dB
SFO1          75.4760107 MHz

======== CHANNEL f2 ========
CPDPRG2          waltz16
NUC2                 1H
PCPD2             100.00 usec
PL2               120.00 dB
PL12               25.60 dB
SFO2         300.1312005 MHz

F2 - Processing parameters
SI                  32768
SF           75.4677508 MHz
WDW                  EM
SSB                   0
LB                 1.00 Hz
GB                    0
PC                 1.40

1D NMR plot parameters
CX                20.00 cm
CY                11.00 cm
F1P              234.220 ppm
F1             17676.09 Hz
F2P              -15.322 ppm
F2             -1156.30 Hz
PPMCM           12.47711 ppm/cm
HZCM           941.61957 Hz/cm
```



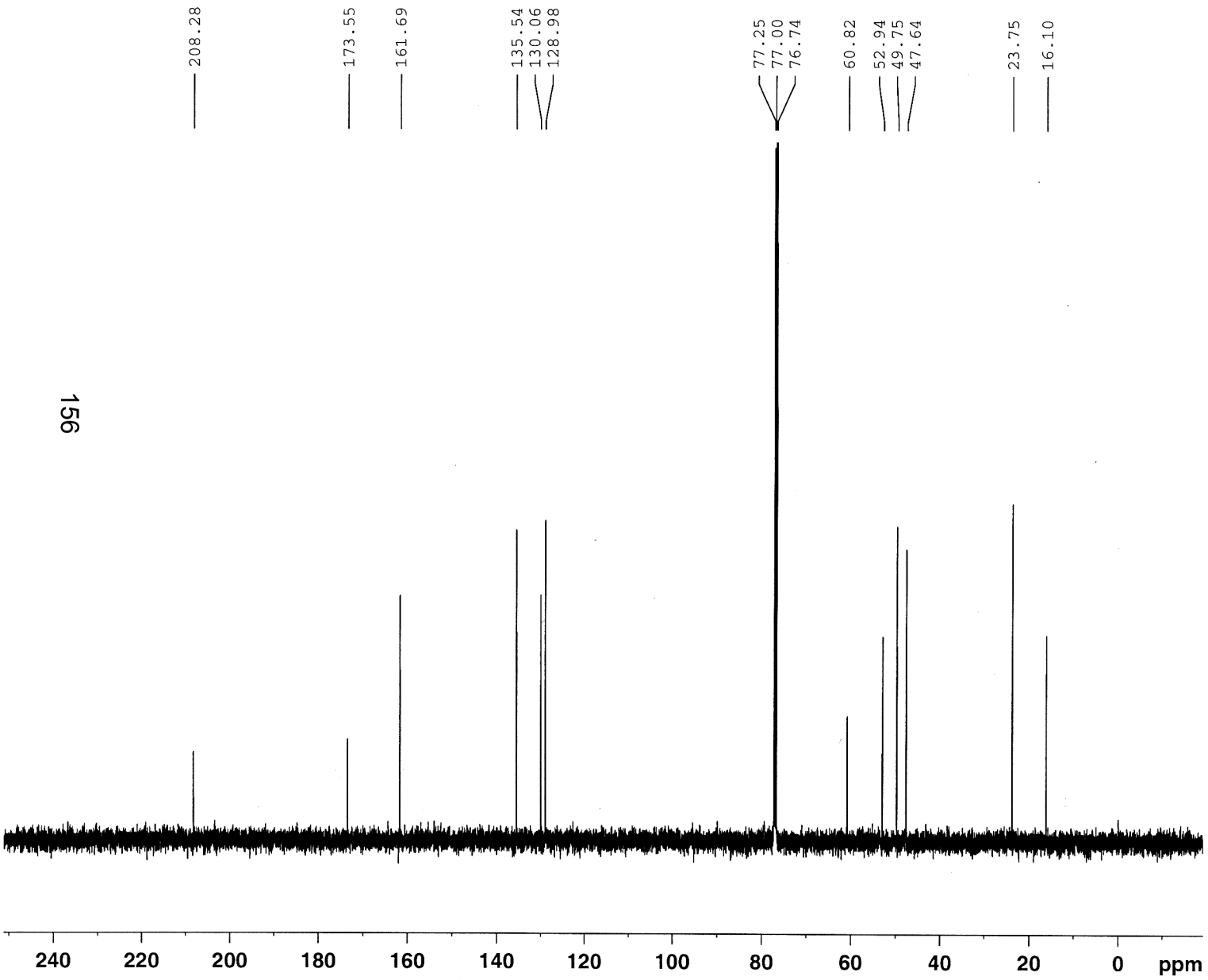
127


```
Current Data Parameters
NAME         MG-V-83a-A3
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20060210
Time               14.09
INSTRUM           DRX500
PROBHD   5 mm Multinucl
PULPROG         zg30pad
TD                65536
SOLVENT           CDCl3
NS                   16
DS                    2
SWH           10330.578 Hz
FIDRES         0.157632 Hz
AQ            3.1719923 sec
RG                  114
DW                48.400 use
DE                 6.00 use
TE                300.0 K
D1           1.00000000 sec
D31          0.00000000 sec

======== CHANNEL f1 =======
NUC1                1H
P1                11.50 use
PL1                0.00 dB
SFO1        500.1330885 MHz

F2 - Processing parameters
SI                 32768
SF          500.1300068 MHz
WDW                   EM
SSB                    0
LB                0.30 Hz
GB                     0
PC                 1.40
```

MG-V-83

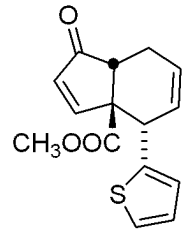


127

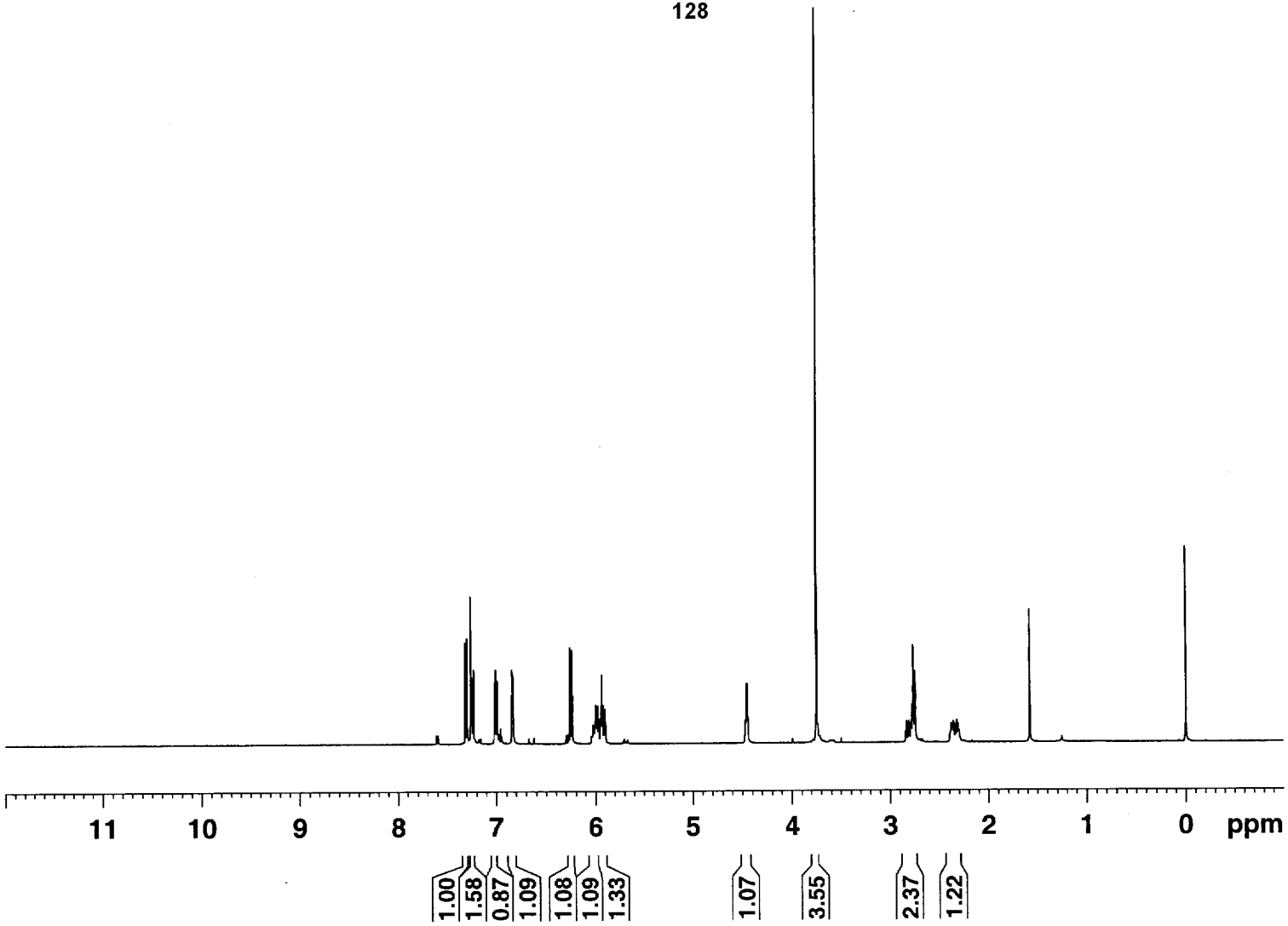


156

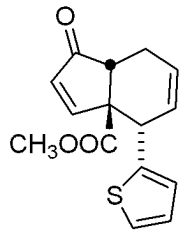
```
Current Data Parameters
NAME          MG-V-83a-A3
EXPNO                   2
PROCNO                  1

F2 - Acquisition Parameters
Date_          20060210
Time              14.14
INSTRUM          DRX500
PROBHD   5 mm Multinucl
PULPROG          zgdc30
TD                65536
SOLVENT           CDCl3
NS                   64
DS                    4
SWH           34013.605 Hz
FIDRES         0.519006 Hz
AQ             0.9634292 sec
RG                32768
DW               14.700 usec
DE                6.00 usec
TE                300.0 K
D1           2.00000000 sec
d11          0.03000000 sec
D31          0.00000000 sec

======== CHANNEL f1 ========
NUC1                 13C
P1                 8.10 usec
PL1                3.00 dB
SFO1        125.7723786 MHz

======== CHANNEL f2 ========
CPDPRG2          waltz16
NUC2                 1H
PCPD2             88.00 usec
PL2                0.00 dB
PL12              21.00 dB
SFO2        500.1320005 MHz

F2 - Processing parameters
SI                32768
SF          125.7577948 MHz
WDW                  EM
SSB                   0
LB                 1.00 Hz
GB                    0
PC                 1.40
```



128

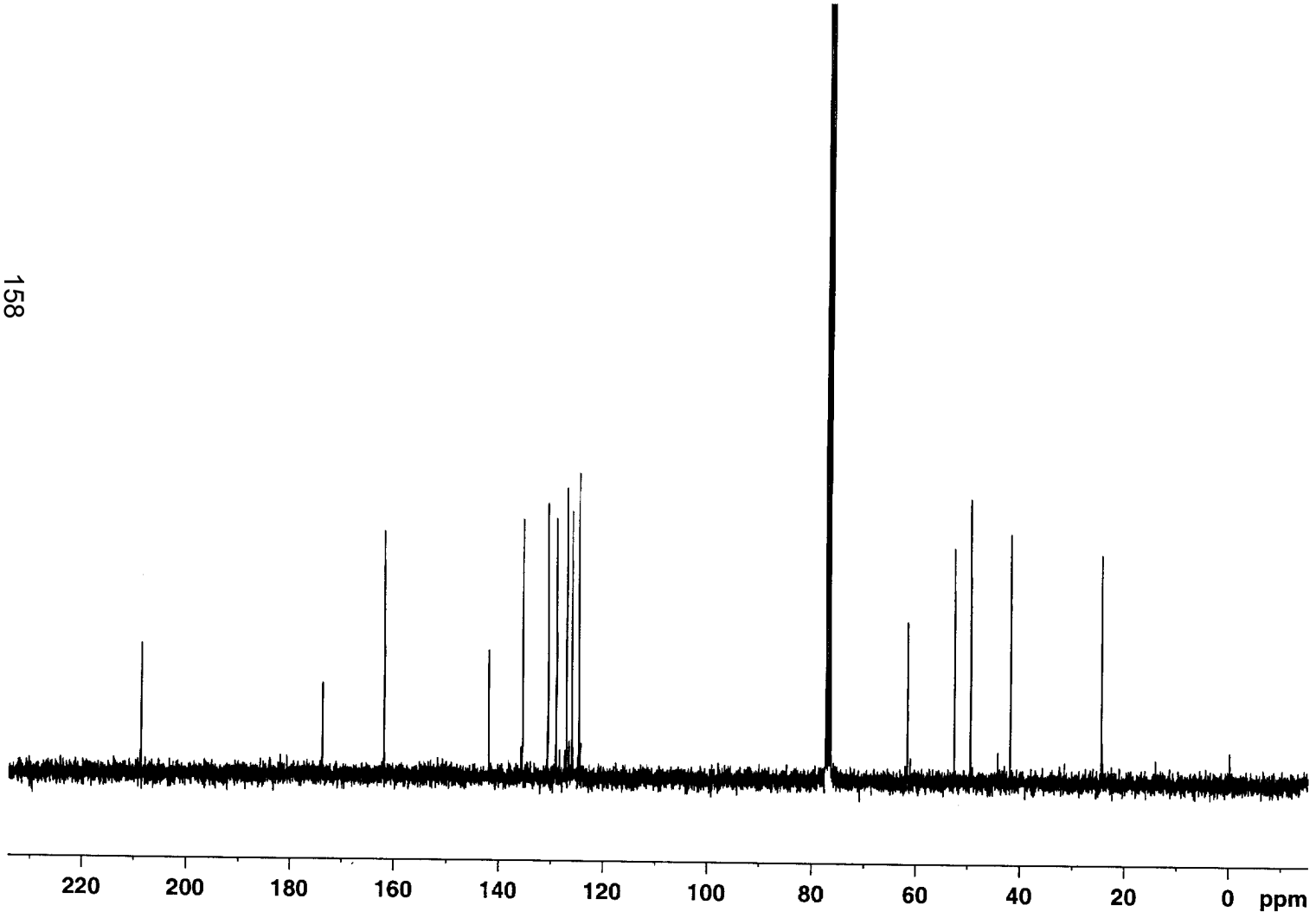



```
Current Data Parameters
NAME      MG-IV-142ba-A2
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20050908
Time               10.58
INSTRUM          DRX300
PROBHD   5 mm Multinucl
PULPROG          zg30pad
TD                 32768
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             6172.839 Hz
FIDRES          0.188380 Hz
AQ              2.6542580 sec
RG                 645.1
DW                81.000 use
DE                 6.00 use
TE                300.0 K
D1           1.00000000 sec
D31          0.00000000 sec

======== CHANNEL f1 =======
NUC1                   1H
P1                 7.05 use
PL1                0.00 dB
SFO1        300.1318534 MHz

F2 - Processing parameters
SI                 32768
SF          300.1300054 MHz
WDW                   EM
SSB                    0
LB                 0.30 Hz
GB                     0
PC                  1.30
```

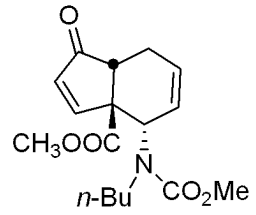


128

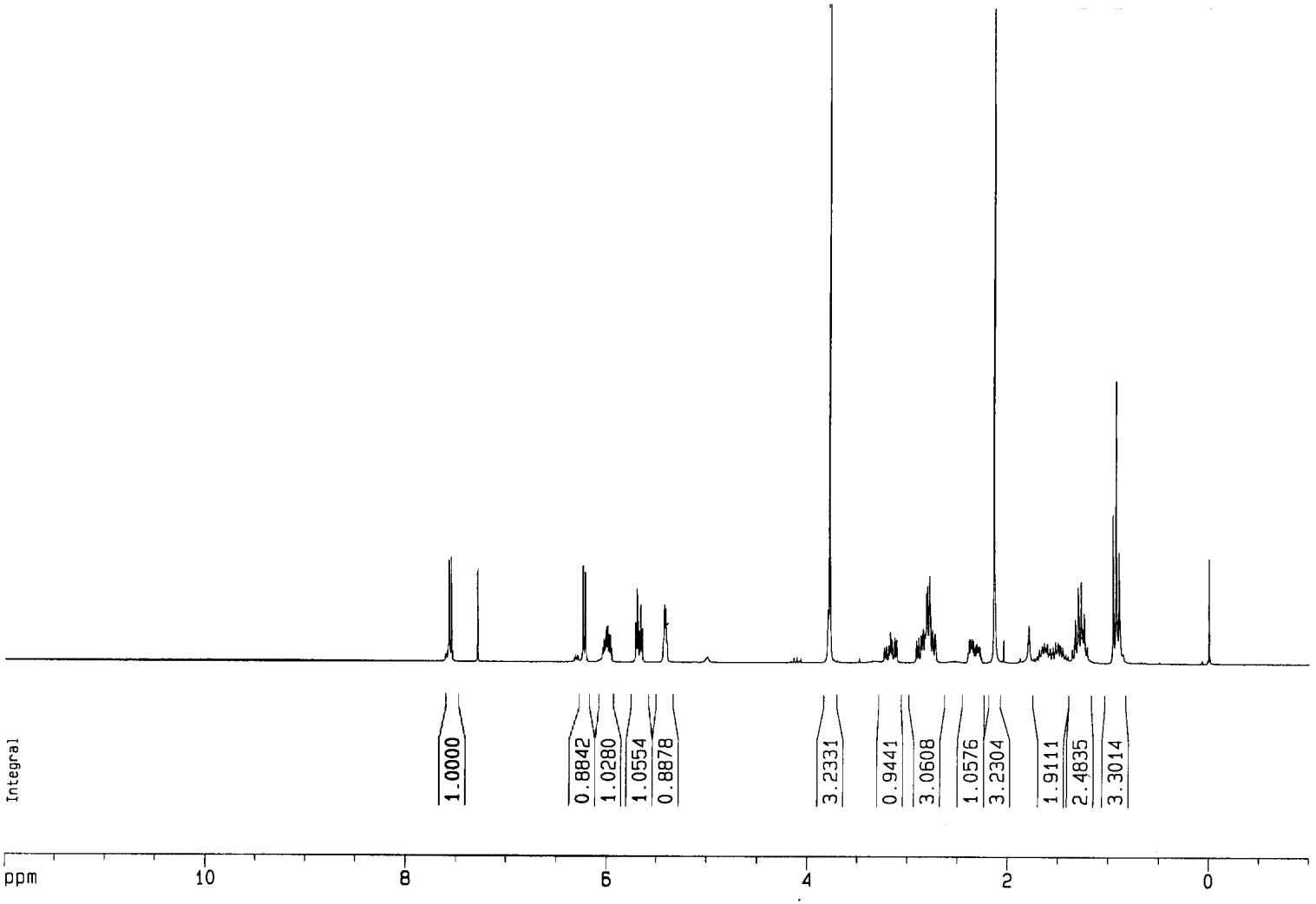
158




```
Current Data Parameters
NAME       MG-IV-142b-A2
EXPNO                 2
PROCNO                1

F2 - Acquisition Parameters
Date_          20050907
Time              12.11
INSTRUM          DRX300
PROBHD   5 mm Multinucl
PULPROG       zgdc30pad
TD                65536
SOLVENT           CDCl3
NS                  561
DS                    4
SWH           18832.393 Hz
FIDRES         0.287360 Hz
AQ             1.7400308 sec
RG                22528
DW               26.550 usec
DE                6.00 usec
TE               300.0 K
D1            2.00000000 sec
D11           0.03000000 sec
D31           0.00000000 sec

======== CHANNEL f1 ========
NUC1                 13C
P1                 9.00 usec
PL1                5.00 dB
SFO1          75.4760107 MHz

======== CHANNEL f2 ========
CPDPRG2          waltz16
NUC2                 1H
PCPD2            100.00 usec
PL2              120.00 dB
PL12              25.60 dB
SFO2         300.1312005 MHz

F2 - Processing parameters
SI                32768
SF          75.4677508 MHz
WDW                  EM
SSB                   0
LB                 1.00 Hz
GB                    0
PC                 1.40
```



129



Current Data Parameters

NAME	MG-4-066b-250
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

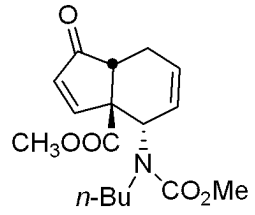
Date_	20050530
Time	23.03
INSTRUM	arx250
PROBHD	5 mm QNP 1H
PULPROG	zg30
TD	32768
SOLVENT	CDCl3
NS	16
DS	2
SWH	5208.333 Hz
FIDRES	0.158946 Hz
AQ	3.1457779 sec
RG	715
DW	96.000 use
DE	137.14 use
TE	300.0 K
D1	1.00000000 sec
P1	8.70 use
SFO1	250.1315321 MHz
NUCLEUS	1H

F2 - Processing parameters

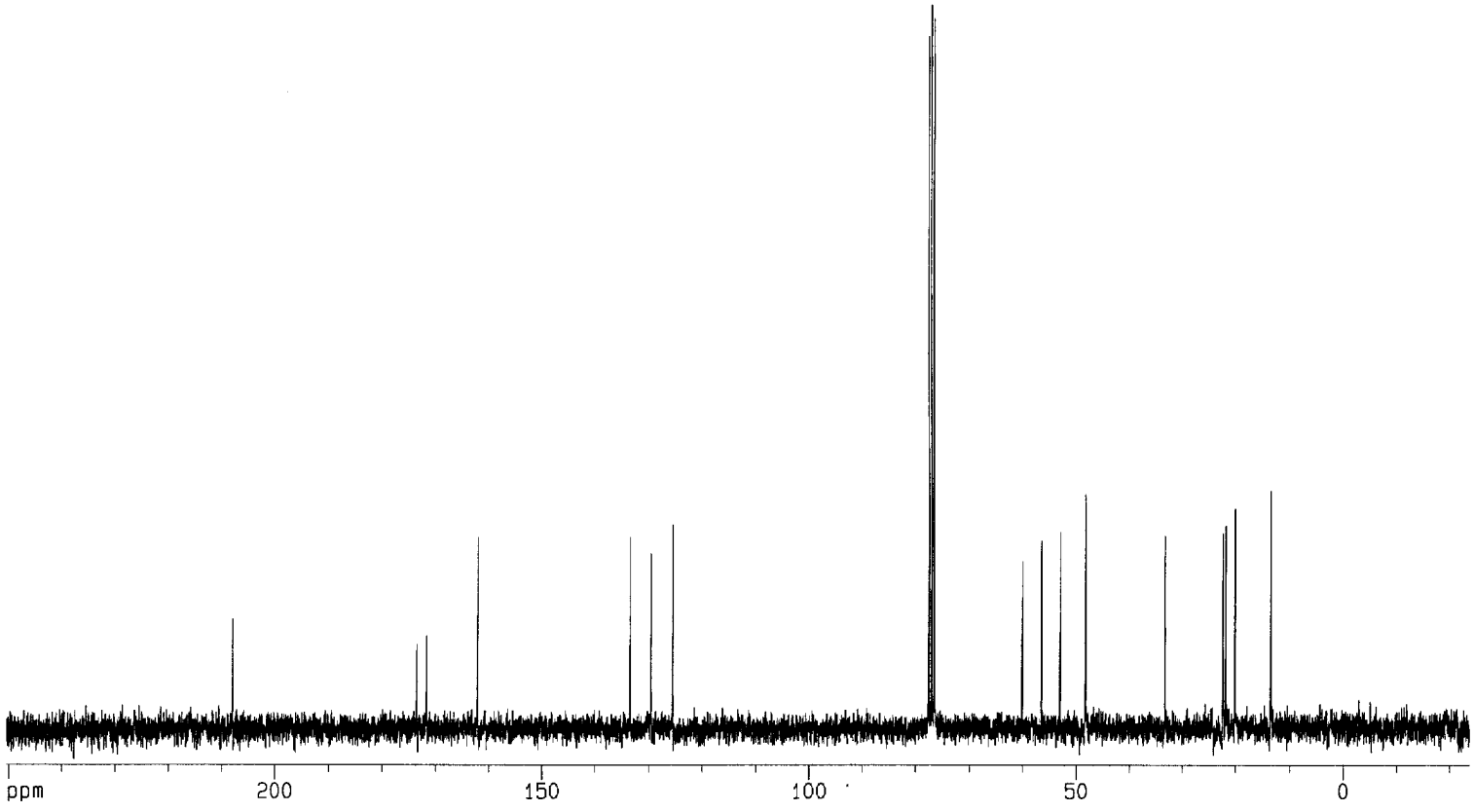
SI	16384
SF	250.1300024 MHz
WDW	EM
SSB	0
LB	0.20 Hz
GB	0
PC	1.50

1D NMR plot parameters

CX	20.00 cm
CY	12.50 cm
F1P	12.000 ppm
F1	3001.56 Hz
F2P	-1.000 ppm
F2	-250.13 Hz
PPMCM	0.65000 ppm
HZCM	162.58450 Hz/



129



Current Data Parameters

NAME	MG-4-066b-250
EXPNO	2
PROCNO	1

F2 - Acquisition Parameters

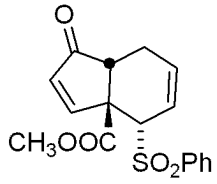
Date_	20050530
Time	23.07
INSTRUM	arx250
PROBHD	5 mm QNP 1H
PULPROG	zgdc30
TD	36864
SOLVENT	CDCl3
NS	450
DS	4
SWH	17241.379 Hz
FIDRES	0.467702 Hz
AQ	1.0691060 sec
RG	22800
DW	29.000 use
DE	41.43 use
TE	300.0 K
D12	0.00002000 sec
DL5	23.00 dB
CPDPRG	waltz16
P31	103.00 use
D1	2.00000000 sec
P1	6.00 use
SF01	62.9023694 MHz
NUCLEUS	13C
D11	0.03000000 sec

F2 - Processing parameters

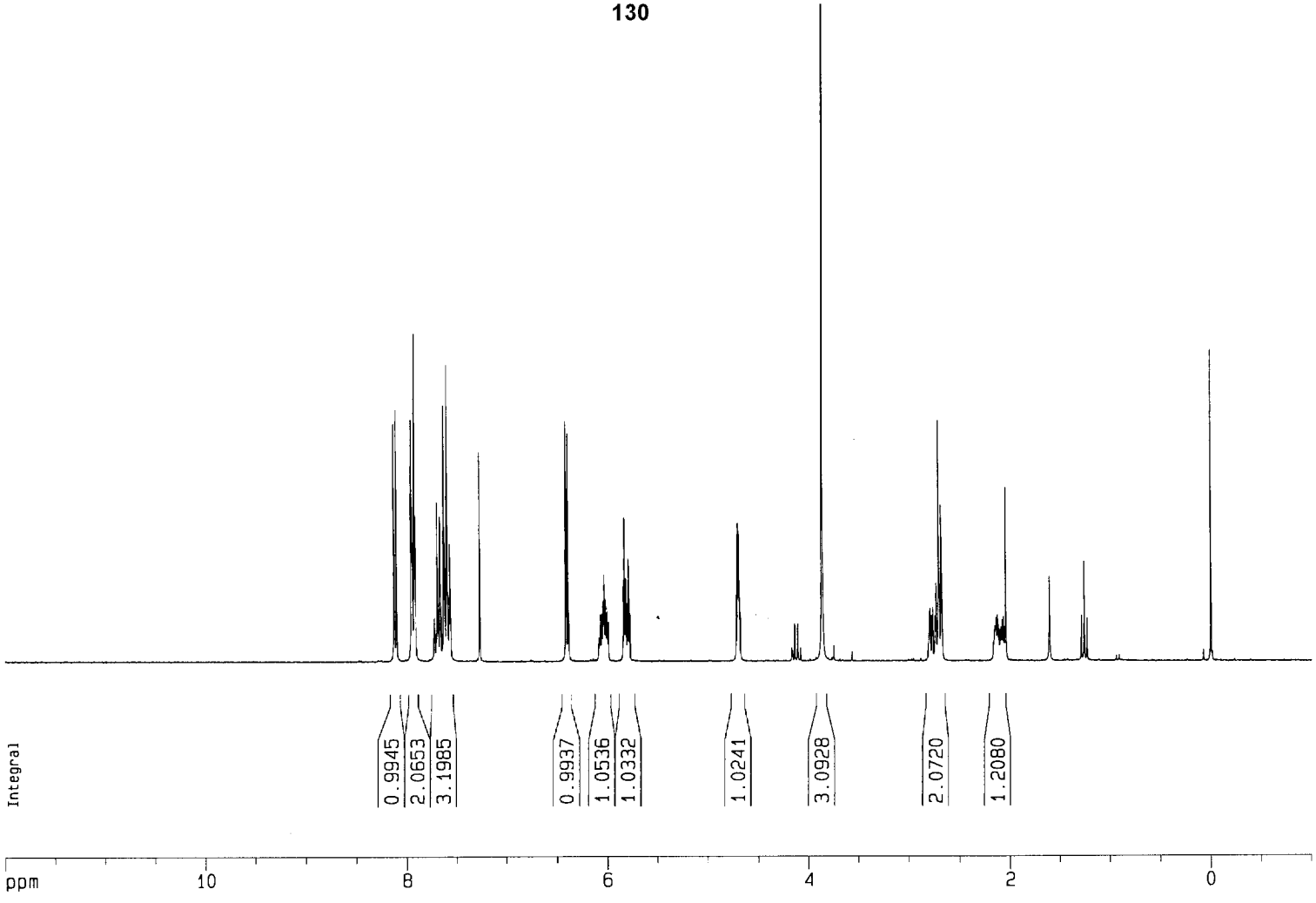
SI	32768
SF	62.8952419 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

1D NMR plot parameters

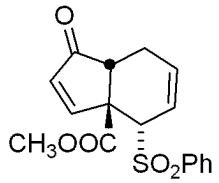
CX	20.00 cm
CY	10.00 cm
F1P	250.388 ppm
F1	15748.23 Hz
F2P	-23.740 ppm
F2	-1493.15 Hz
PPMCM	13.70643 ppm
HZCM	862.06903 Hz/



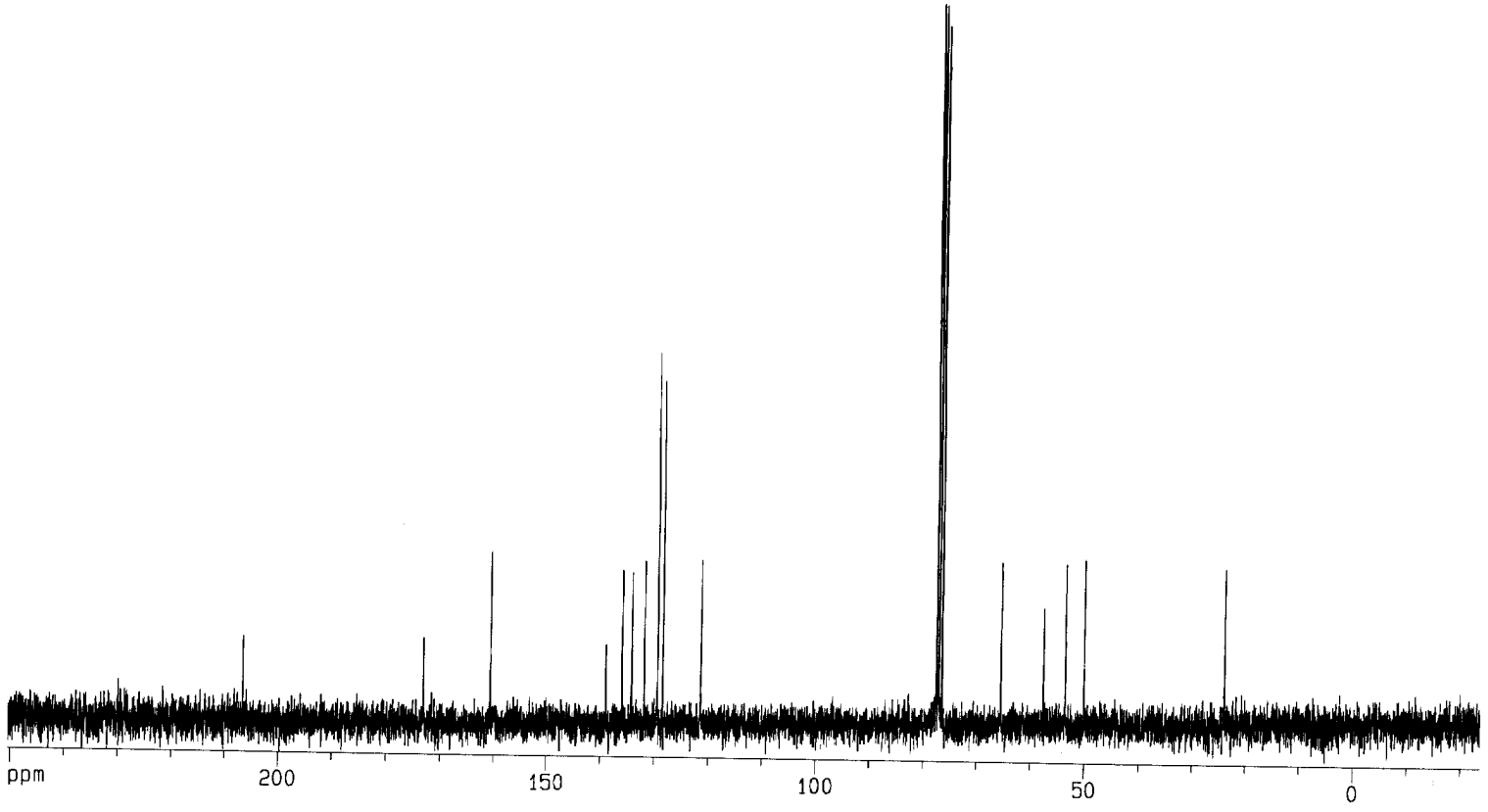
130




```
Current Data Parameters
NAME      MG-IV-046a-250
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20050505
Time                0.35
INSTRUM          arx250
PROBHD     5 mm GNP  1H
PULPROG             zg30
TD                 32768
SOLVENT            CDCl3
NS                    16
DS                     2
SWH           5208.333 Hz
FIDRES        0.158946 Hz
AQ            3.1457779 sec
RG                  2048
DW             96.000 use
DE             137.14 use
TE              300.0 K
D1          1.00000000 sec
P1             8.70 use
SF01        250.1315321 MHz
NUCLEUS               1H

F2 - Processing parameters
SI                 16384
SF          250.1300049 MHz
WDW                   EM
SSB                    0
LB                0.20 Hz
GB                     0
PC                  1.50

1D NMR plot parameters
CX                20.00 cm
CY                30.00 cm
F1P              12.000 ppm
F1              3001.56 Hz
F2P              -1.000 ppm
F2              -250.13 Hz
PPMCM            0.65000 ppm
HZCM          162.58452 Hz/
```



130

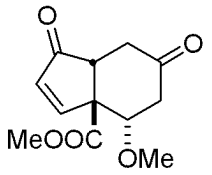


Current Data Parameters	
NAME	MG-IV-046a-250
EXPNO	2
PROCNO	1

F2 - Acquisition Parameters	
Date_	20050505
Time	0.39
INSTRUM	arx250
PROBHD	5 mm QNP 1H
PULPROG	zgdc30
TD	36864
SOLVENT	CDCl3
NS	209
DS	4
SWH	17241.379 Hz
FIDRES	0.467702 Hz
AQ	1.0691060 sec
RG	22800
DW	29.000 use
DE	41.43 use
TE	300.0 K
D12	0.00002000 sec
DL5	23.00 dB
CPDPRG	waltz16
P31	103.00 use
D1	2.00000000 sec
P1	6.00 use
SFO1	62.9023694 MHz
NUCLEUS	13C
D11	0.03000000 sec

F2 - Processing parameters	
SI	32768
SF	62.8952408 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

1D NMR plot parameters	
CX	20.00 cm
CY	10.00 cm
F1P	250.405 ppm
F1	15749.28 Hz
F2P	-23.724 ppm
F2	-1492.10 Hz
PPMCM	13.70643 ppm
HZCM	862.06891 Hz/



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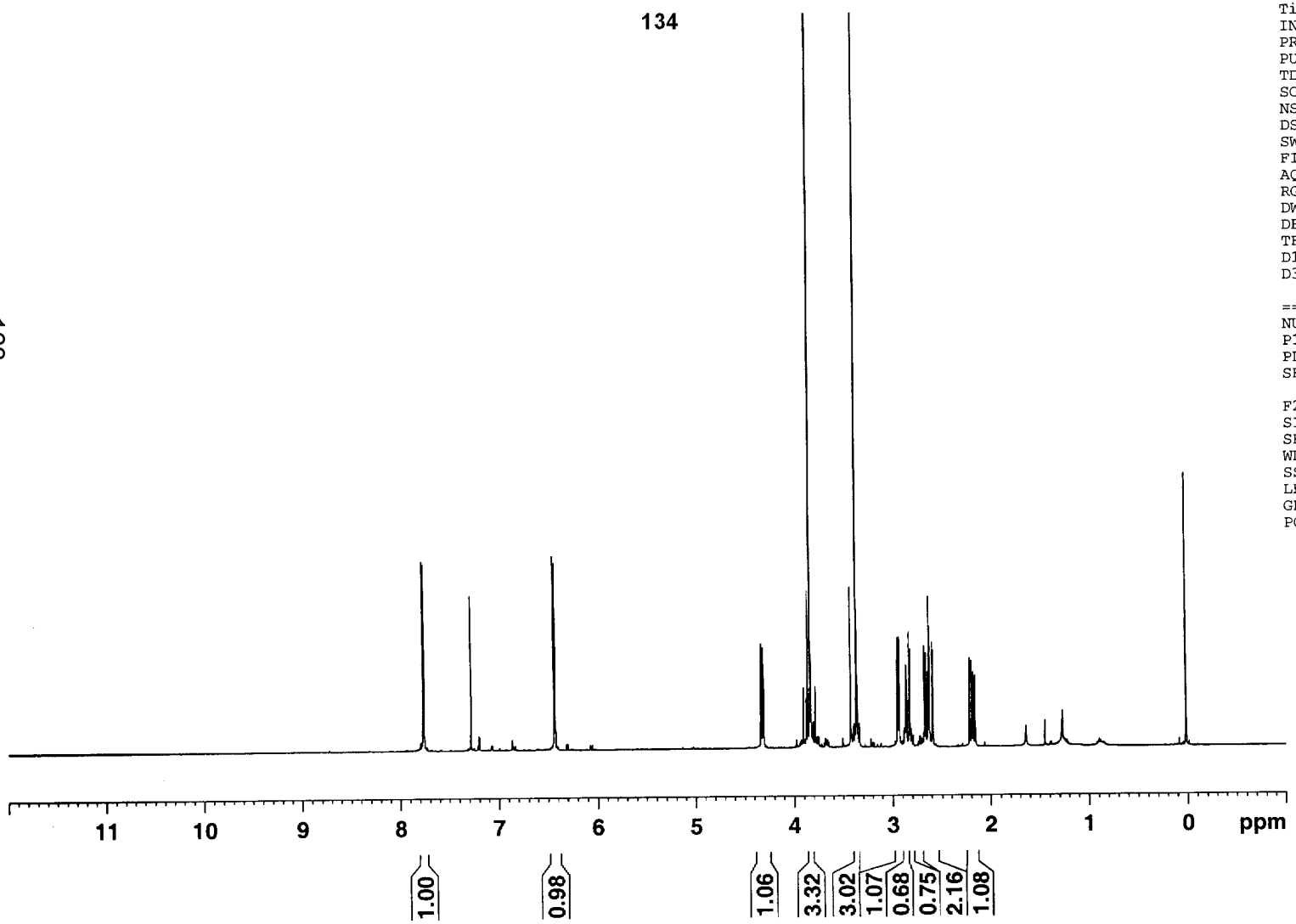
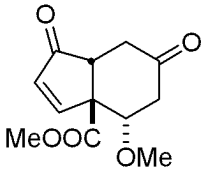



```
Current Data Parameters
NAME          MG-V-93b-A3
EXPNO                   1
PROCNO                  1

F2 - Acquisition Parameters
Date_            20060227
Time                14.51
INSTRUM           DRX500
PROBHD   5 mm Multinucl
PULPROG          zg30pad
TD                 65536
SOLVENT            CDCl3
NS                     6
DS                     2
SWH           10330.578 Hz
FIDRES         0.157632 Hz
AQ            3.1719923 sec
RG                 143.7
DW                48.400 usec
DE                 6.00 usec
TE                300.0 K
D1           1.00000000 sec
D31          0.00000000 sec

======== CHANNEL f1 ========
NUC1                   1H
P1                 11.50 usec
PL1                 0.00 dB
SFO1         500.1330885 MHz

F2 - Processing parameters
SI                 32768
SF         500.1300000 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.40
```



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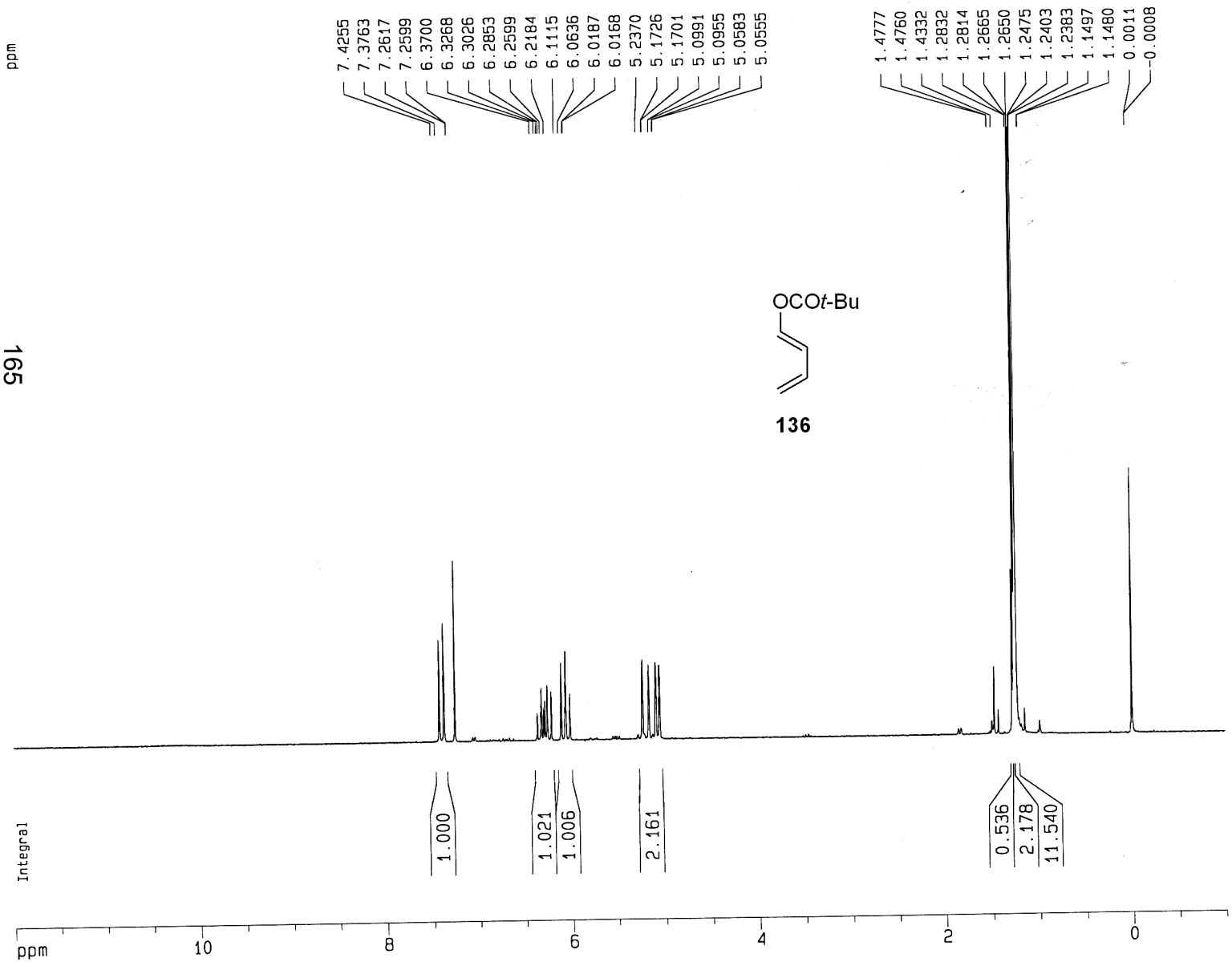
```
Current Data Parameters
NAME         MG-V-93b-A3
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20060227
Time               14.53
INSTRUM           DRX500
PROBHD   5 mm Multinucl
PULPROG           zgdc30
TD                65536
SOLVENT           CDCl3
NS                  669
DS                    4
SWH           34013.605 Hz
FIDRES         0.519006 Hz
AQ            0.9634292 sec
RG                32768
DW               14.700 usec
DE                6.00 usec
TE               300.0 K
D1           2.00000000 sec
d11          0.03000000 sec
D31          0.00000000 sec

======== CHANNEL f1 ========
NUC1                 13C
P1                 8.10 usec
PL1                3.00 dB
SFO1        125.7723786 MHz

======== CHANNEL f2 ========
CPDPRG2          waltz16
NUC2                 1H
PCPD2             88.00 usec
PL2                0.00 dB
PL12              21.00 dB
SFO2        500.1320005 MHz

F2 - Processing parameters
SI                32768
SF          125.7577938 MHz
WDW                  EM
SSB                   0
LB                 1.00 Hz
GB                    0
PC                 1.40
```

MG-IV-134ab-1st frac
Column done with 20% Et20/pentane
1H NMR



165

Current Data Parameters

NAME	MG-IV-134ab-A1
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20050829
Time	18.27
INSTRUM	arx250
PROBHD	5 mm QNP 1H
PULPROG	zg30
TD	32768
SOLVENT	CDCl3
NS	16
DS	2
SWH	5208.333 Hz
FIDRES	0.158946 Hz
AQ	3.1457779 sec
RG	2048
DW	96.000 use
DE	137.14 use
TE	300.0 K
D1	1.00000000 sec
P1	8.70 use
SFO1	250.1315321 MHz
NUCLEUS	1H

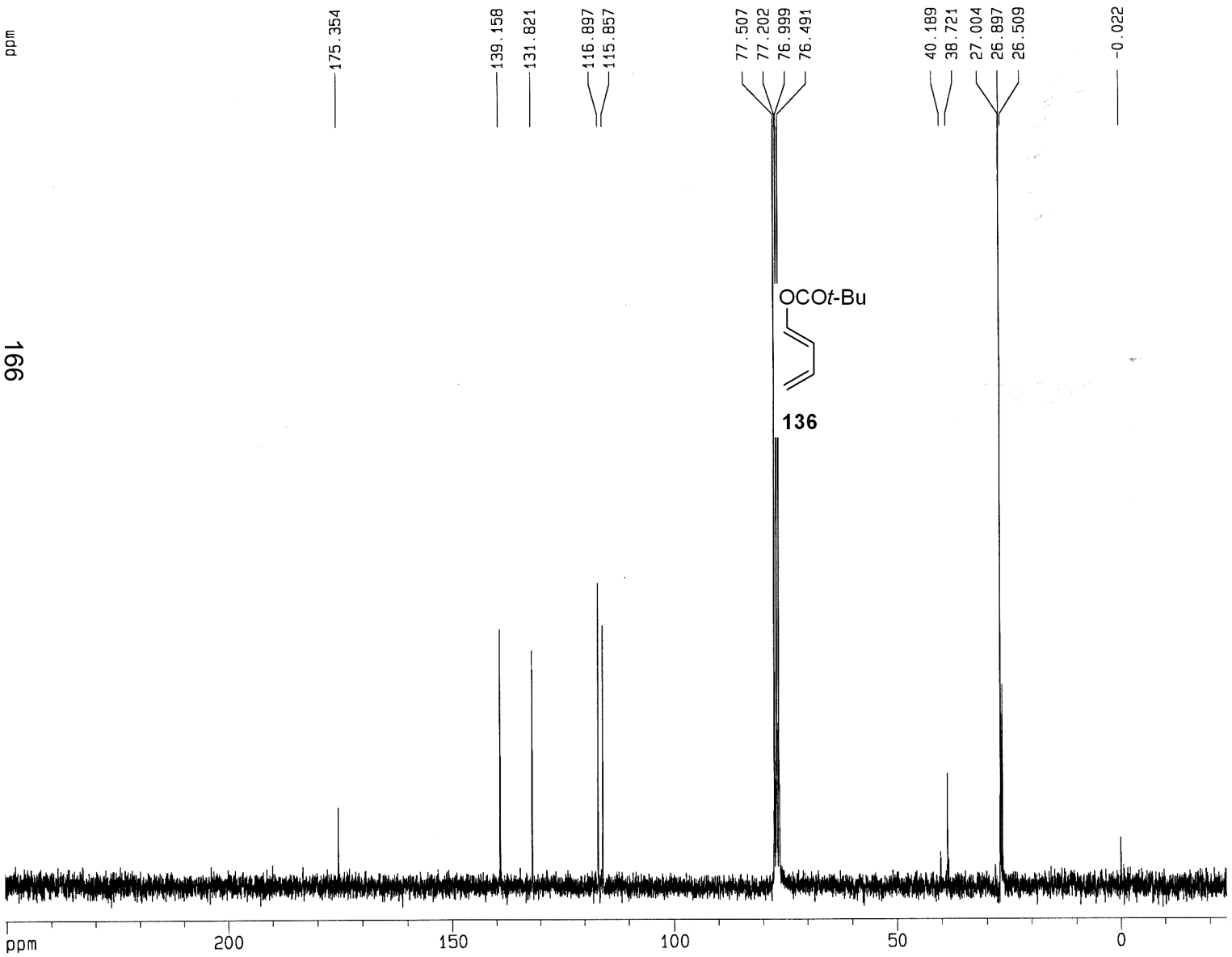
F2 - Processing parameters

SI	16384
SF	250.1300072 MHz
WDW	EM
SSB	0
LB	0.20 Hz
GB	0
PC	1.50

1D NMR plot parameters

CX	20.00 cm
CY	45.00 cm
F1P	12.000 ppm
F1	3001.56 Hz
F2P	-1.000 ppm
F2	-250.13 Hz
PPMCM	0.65000 ppm
HZCM	162.58452 Hz/

13C NMR



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Current Data Parameters

NAME	MG-IV-134ab-A1
EXPNO	2
PROCNO	1

F2 - Acquisition Parameters

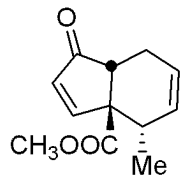
Date_	20050829
Time	18.31
INSTRUM	arx250
PROBHD	5 mm QNP 1H
PULPROG	zgdc30
TD	36864
SOLVENT	CDCl3
NS	3904
DS	4
SWH	17241.379 Hz
FIDRES	0.467702 Hz
AQ	1.0691060 sec
RG	22800
DW	29.000 use
DE	41.43 use
TE	300.0 K
D12	0.00002000 sec
DL5	23.00 dB
CPDPRG	waltz16
P31	103.00 use
D1	2.00000000 sec
P1	6.00 use
SFO1	62.9023694 MHz
NUCLEUS	13C
D11	0.03000000 sec

F2 - Processing parameters

SI	32768
SF	62.8952398 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

1D NMR plot parameters

CX	20.00 cm
CY	30.00 cm
F1P	250.422 ppm
F1	15750.34 Hz
F2P	-23.707 ppm
F2	-1491.04 Hz
PPMCM	13.70643 ppm
HZCM	862.06891 Hz/



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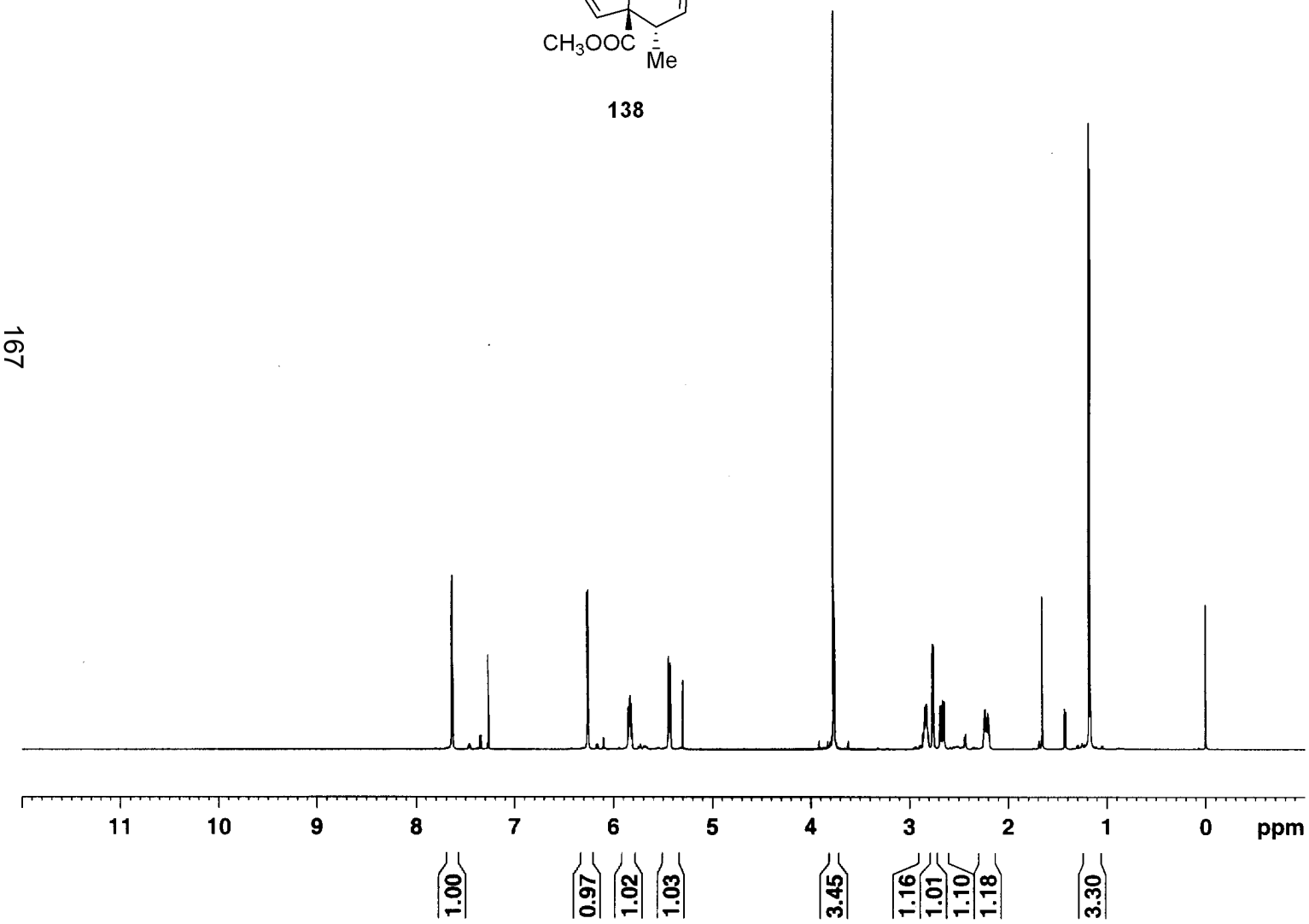
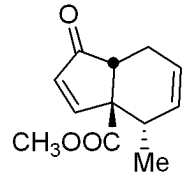



```
Current Data Parameters
NAME          MG-V-84a-A3
EXPNO                   1
PROCNO                  1

F2 - Acquisition Parameters
Date_           20060210
Time               22.43
INSTRUM           DRX500
PROBHD   5 mm Multinucl
PULPROG          zg30pad
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH           10330.578 Hz
FIDRES         0.157632 Hz
AQ            3.1719923 sec
RG                   114
DW                48.400 use
DE                 6.00 use
TE                300.0 K
D1           1.00000000 sec
D31          0.00000000 sec

======== CHANNEL f1 =======
NUC1                   1H
P1                 11.50 use
PL1                 0.00 dB
SFO1         500.1330885 MHz

F2 - Processing parameters
SI                 32768
SF         500.1300071 MHz
WDW                   EM
SSB                    0
LB                 0.30 Hz
GB                     0
PC                 1.40
```



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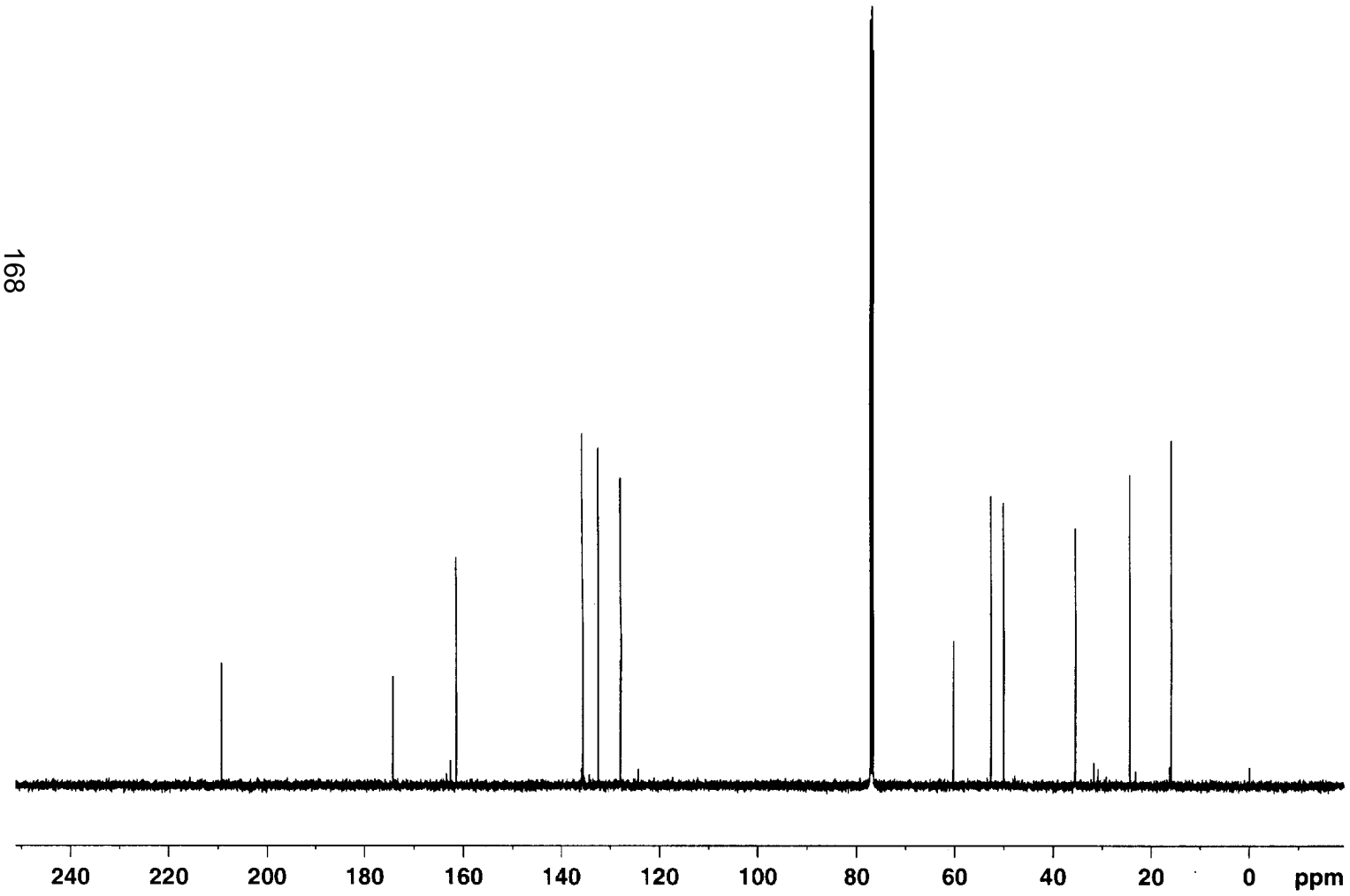
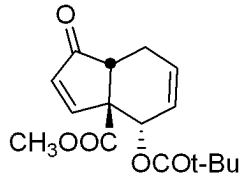
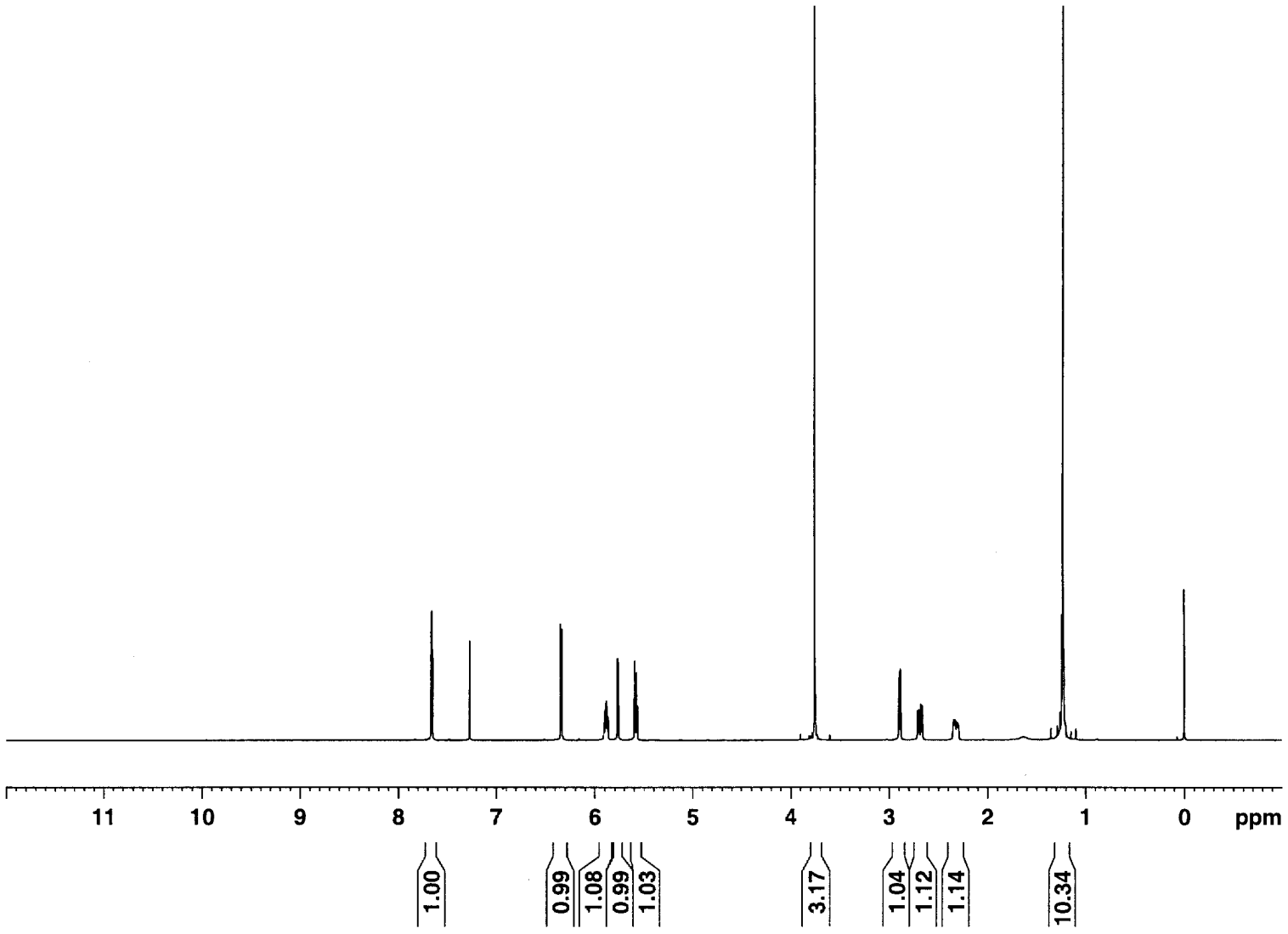


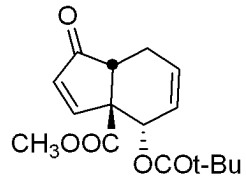

```
Current Data Parameters
NAME          MG-V-84a-A3
EXPNO                   2
PROCNO                  1

F2 - Acquisition Parameters
Date_            20060210
Time                23.07
INSTRUM           DRX500
PROBHD   5 mm Multinucl
PULPROG           zgdc30
TD                 65536
SOLVENT             CDCl3
NS                    428
DS                      4
SWH            34013.605 Hz
FIDRES          0.519006 Hz
AQ              0.9634292 sec
RG                  32768
DW                 14.700 usec
DE                  6.00 usec
TE                 300.0 K
D1            2.00000000 sec
d11           0.03000000 sec
D31           0.00000000 sec

======== CHANNEL f1 ========
NUC1                  13C
P1                  8.10 usec
PL1                 3.00 dB
SFO1         125.7723786 MHz

======== CHANNEL f2 ========
CPDPRG2          waltz16
NUC2                 1H
PCPD2              88.00 usec
PL2                 0.00 dB
PL12               21.00 dB
SFO2         500.1320005 MHz

F2 - Processing parameters
SI                  32768
SF           125.7577938 MHz
WDW                    EM
SSB                     0
LB                  1.00 Hz
GB                      0
PC                   1.40
```



139

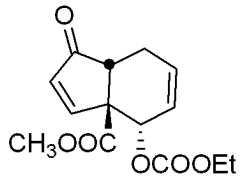

```
Current Data Parameters
NAME       MG-IV-136b-A3
EXPNO                 1
PROCNO                1

F2 - Acquisition Parameters
Date_          20050830
Time              21.33
INSTRUM          DRX500
PROBHD   5 mm Multinucl
PULPROG        zg30pad
TD               65536
SOLVENT          CDCl3
NS                  16
DS                   2
SWH          10330.578 Hz
FIDRES        0.157632 Hz
AQ           3.1719923 sec
RG                71.8
DW              48.400 use
DE               6.00 use
TE              300.0 K
D1          1.00000000 sec
D31         0.00000000 sec

======== CHANNEL f1 ========
NUC1                1H
P1              13.25 use
PL1             -3.00 dB
SFO1       500.1330885 MHz

F2 - Processing parameters
SI               32768
SF         500.1300087 MHz
WDW                 EM
SSB                  0
LB              0.30 Hz
GB                   0
PC              1.40
```



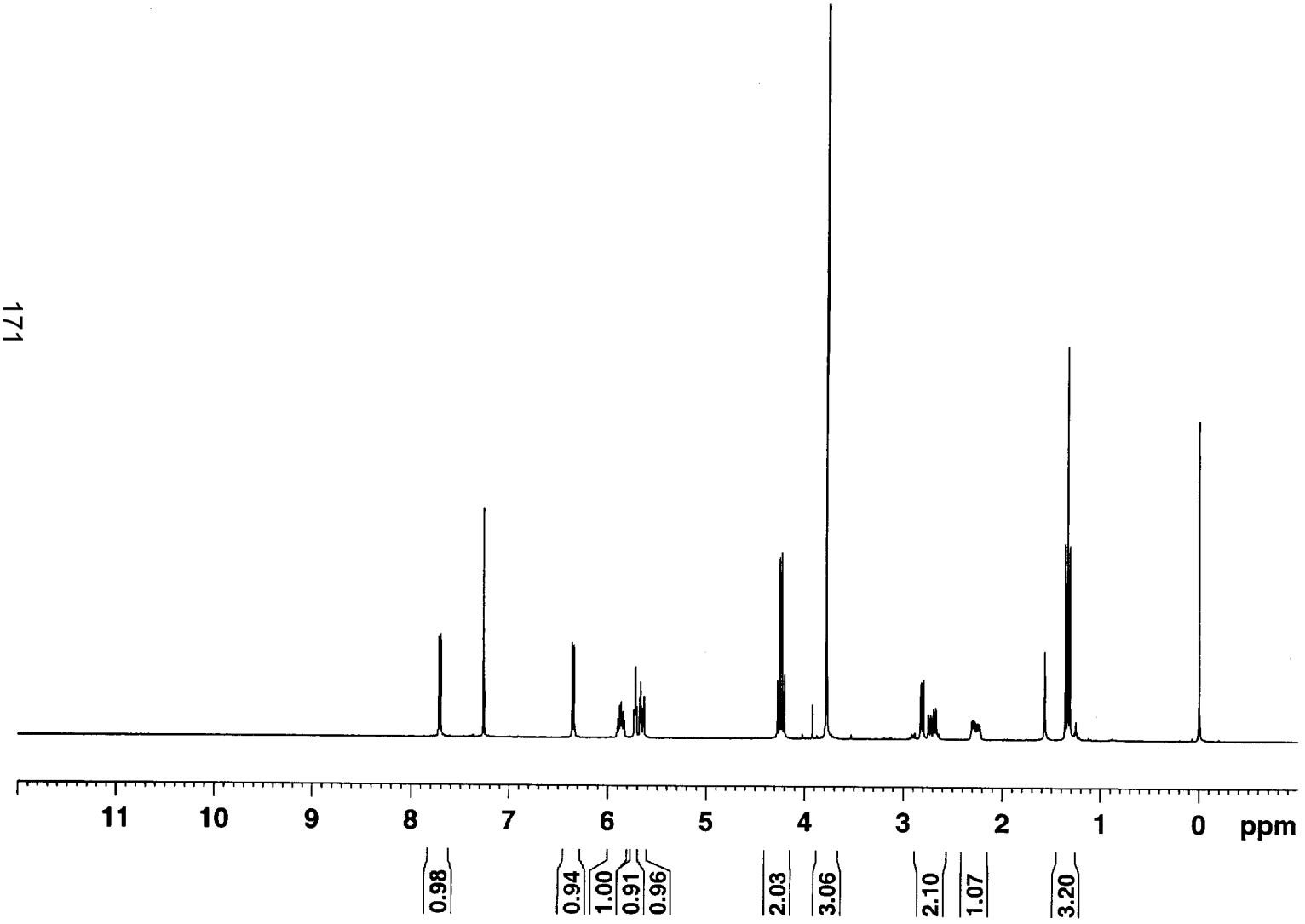


139

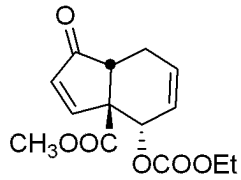

```
Current Data Parameters
NAME       MG-IV-136b-A3
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20050830
Time               21.40
INSTRUM           DRX500
PROBHD   5 mm Multinucl
PULPROG           zgdc30
TD                65536
SOLVENT           CDCl3
NS                  831
DS                    4
SWH           34013.605 Hz
FIDRES         0.519006 Hz
AQ            0.9634292 sec
RG                32768
DW               14.700 usec
DE                6.00 usec
TE               300.0 K
D1           2.00000000 sec
d11          0.03000000 sec
D31          0.00000000 sec

======== CHANNEL f1 ========
NUC1                 13C
P1                 8.10 usec
PL1                3.00 dB
SFO1        125.7723786 MHz

======== CHANNEL f2 ========
CPDPRG2          waltz16
NUC2                 1H
PCPD2             88.00 usec
PL2                0.00 dB
PL12              21.00 dB
SFO2        500.1320005 MHz

F2 - Processing parameters
SI                32768
SF          125.7577938 MHz
WDW                  EM
SSB                   0
LB                 1.00 Hz
GB                    0
PC                 1.40
```



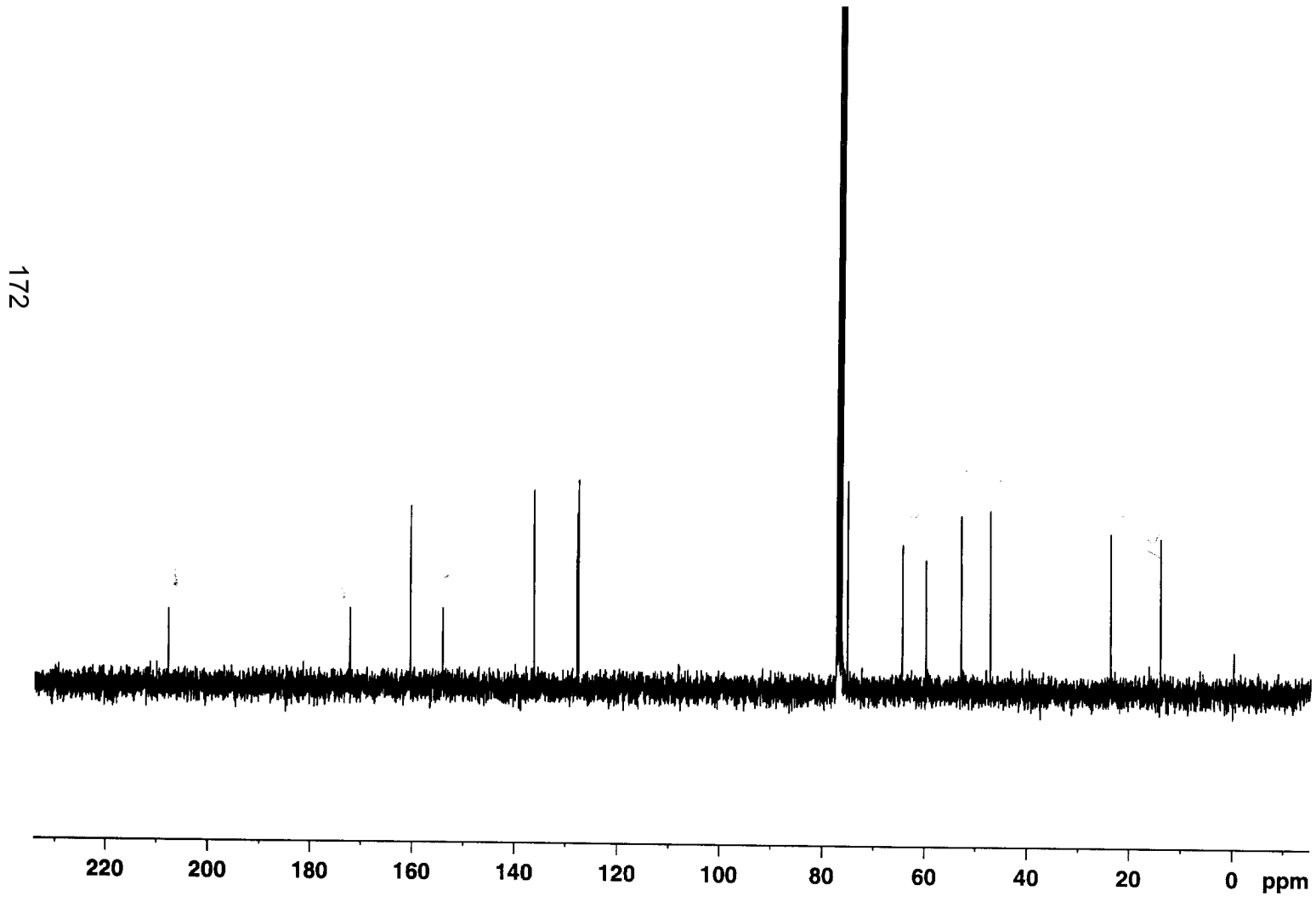
140



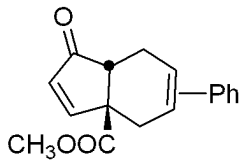

```
Current Data Parameters
NAME       MG-IV-135b-A2
EXPNO                 1
PROCNO                1

F2 - Acquisition Parameters
Date_          20050830
Time              14.24
INSTRUM          DRX300
PROBHD   5 mm Multinucl
PULPROG          zg30pad
TD                32768
SOLVENT           CDCl3
NS                   16
DS                    2
SWH            6172.839 Hz
FIDRES         0.188380 Hz
AQ             2.6542580 sec
RG                812.7
DW                81.000 use
DE                 6.00 use
TE                300.0 K
D1             1.00000000 sec
D31            0.00000000 sec

======== CHANNEL f1 =======
NUC1                  1H
P1                 7.05 use
PL1                0.00 dB
SFO1         300.1318534 MHz

F2 - Processing parameters
SI                 32768
SF           300.1300045 MHz
WDW                   EM
SSB                    0
LB                0.30 Hz
GB                     0
PC                  1.30
```



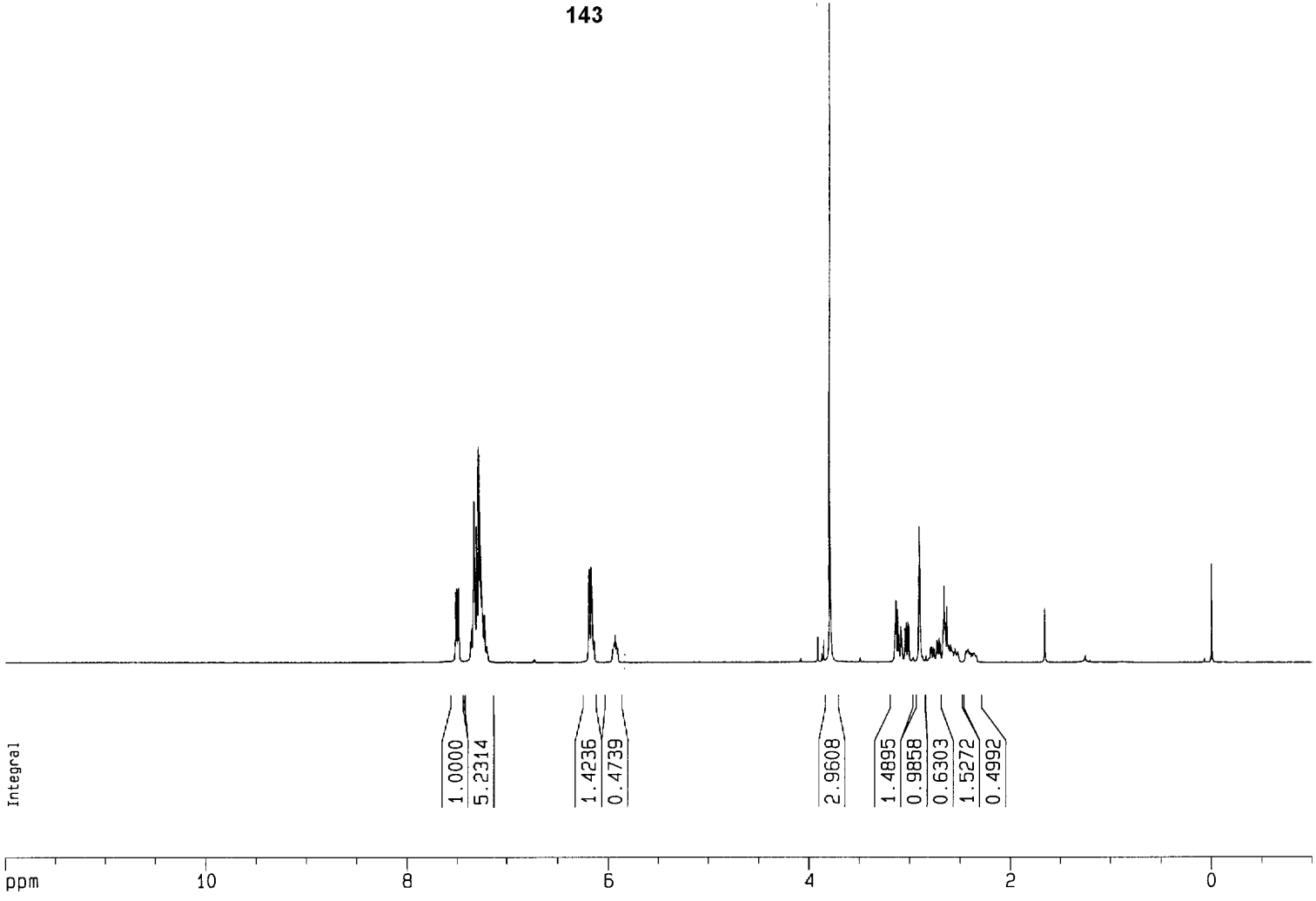
140



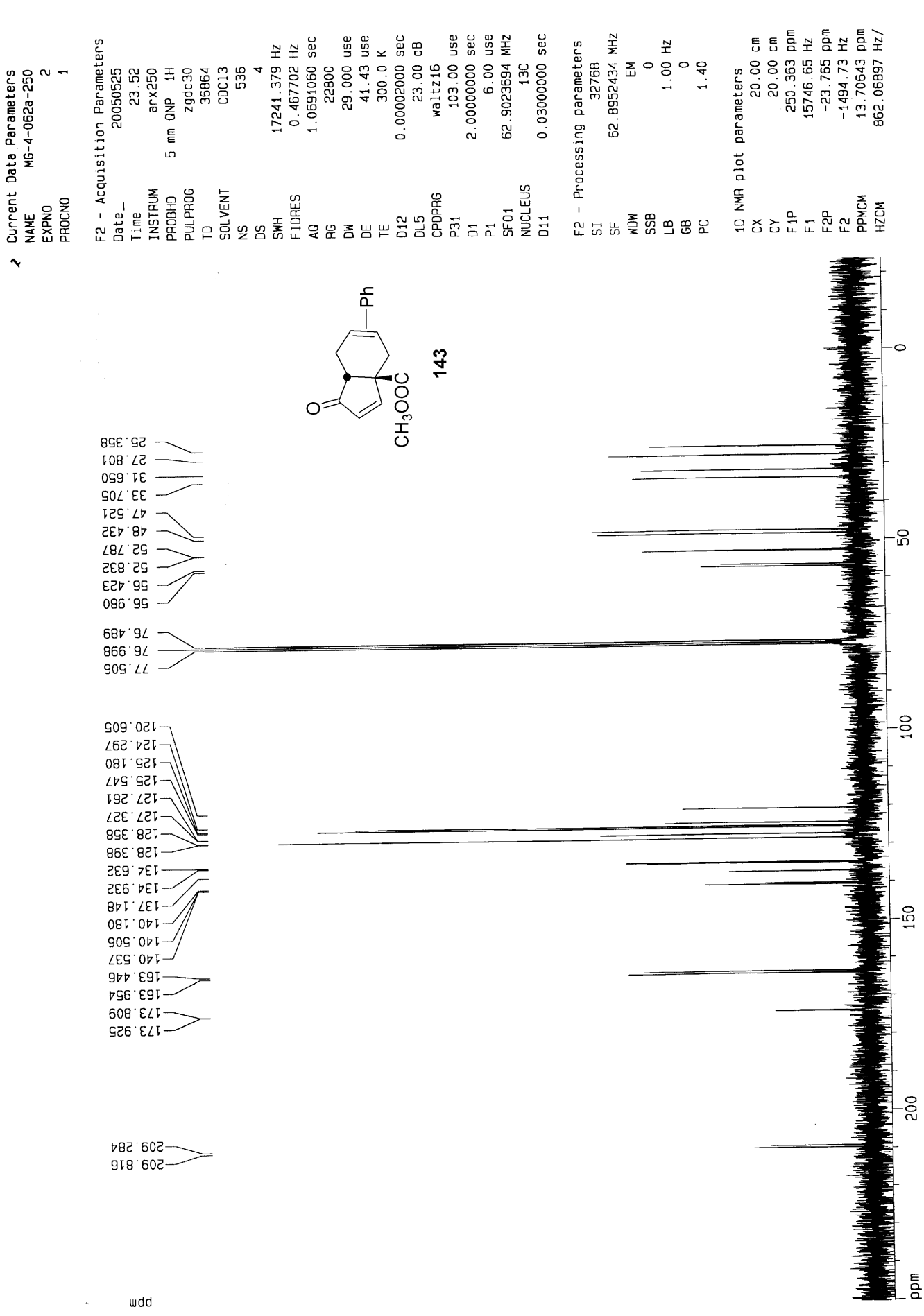

```
Current Data Parameters
NAME       MG-IV-135b-A2
EXPNO                 2
PROCNO                1

F2 - Acquisition Parameters
Date_          20050830
Time              14.29
INSTRUM          DRX300
PROBHD   5 mm Multinucl
PULPROG       zgdc30pad
TD                65536
SOLVENT           CDCl3
NS                  923
DS                    4
SWH           18832.393 Hz
FIDRES         0.287360 Hz
AQ             1.7400308 sec
RG                22528
DW               26.550 usec
DE                6.00 usec
TE               300.0 K
D1            2.00000000 sec
D11           0.03000000 sec
D31           0.00000000 sec

======== CHANNEL f1 ========
NUC1                 13C
P1                 9.00 usec
PL1                5.00 dB
SFO1          75.4760107 MHz

======== CHANNEL f2 ========
CPDPRG2          waltz16
NUC2                 1H
PCPD2            100.00 usec
PL2              120.00 dB
PL12              25.60 dB
SFO2         300.1312005 MHz

F2 - Processing parameters
SI                32768
SF          75.4677497 MHz
WDW                  EM
SSB                   0
LB                 1.00 Hz
GB                    0
PC                 1.40
```

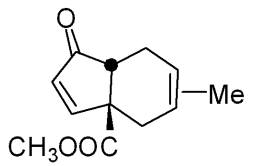


143




```
Current Data Parameters
NAME        MG-4-062a-250
EXPNO                   1
PROCNO                  1

F2 - Acquisition Parameters
Date_            20050525
Time                23.48
INSTRUM           arx250
PROBHD      5 mm GNP  1H
PULPROG             zg30
TD                 32768
SOLVENT            CDCl3
NS                    16
DS                     2
SWH           5208.333 Hz
FIDRES        0.158946 Hz
AQ            3.1457779 sec
RG                  1024
DW             96.000 use
DE             137.14 use
TE              300.0 K
D1          1.00000000 sec
P1             8.70 use
SFO1       250.1315321 MHz
NUCLEUS             1H

F2 - Processing parameters
SI                 16384
SF        250.1300075 MHz
WDW                   EM
SSB                    0
LB              0.20 Hz
GB                     0
PC                  1.50

1D NMR plot parameters
CX              20.00 cm
CY              12.50 cm
F1P            12.000 ppm
F1            3001.56 Hz
F2P            -1.000 ppm
F2            -250.13 Hz
PPMCM         0.65000 ppm
HZCM       162.58450 Hz/
```


Current Data Parameters
NAME MG-4-062a-250
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20050525
Time 23.52
INSTRUM arx250
PROBHD 5 mm QNP 1H
PULPROG zgdc30
TD 36864
SOLVENT CDCl3
NS 536
DS 4
SWH 17241.379 Hz
FIDRES 0.467702 Hz
AQ 1.0691060 sec
RG 22800
DW 29.000 use
DE 41.43 use
TE 300.0 K
D12 0.00002000 sec
DL5 23.00 dB
CPDPRG waltz16
P31 103.00 use
D1 2.00000000 sec
P1 6.00 use
SFO1 62.9023694 MHz
NUCLEUS 13C
D11 0.03000000 sec
F2 - Processing parameters
SI 32768
SF 62.8952434 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
1D NMR plot parameters
CX 20.00 cm
CY 20.00 cm
F1P 250.363 ppm
F1 15746.65 Hz
F2P -23.765 ppm
F2 -1494.73 Hz
PPMCM 13.70643 ppm
HZCM 862.06897 Hz/
Ph
O
CH3OOC
143
25.358
27.801
31.650
33.705
47.521
48.432
52.787
52.832
56.423
56.980
76.489
76.998
77.506
120.605
124.297
125.180
125.547
127.261
127.327
128.358
128.398
134.632
134.932
137.148
140.180
140.506
140.537
163.446
163.954
173.809
173.925
209.816
209.284
ppm
0
50
100
150
200
ppm



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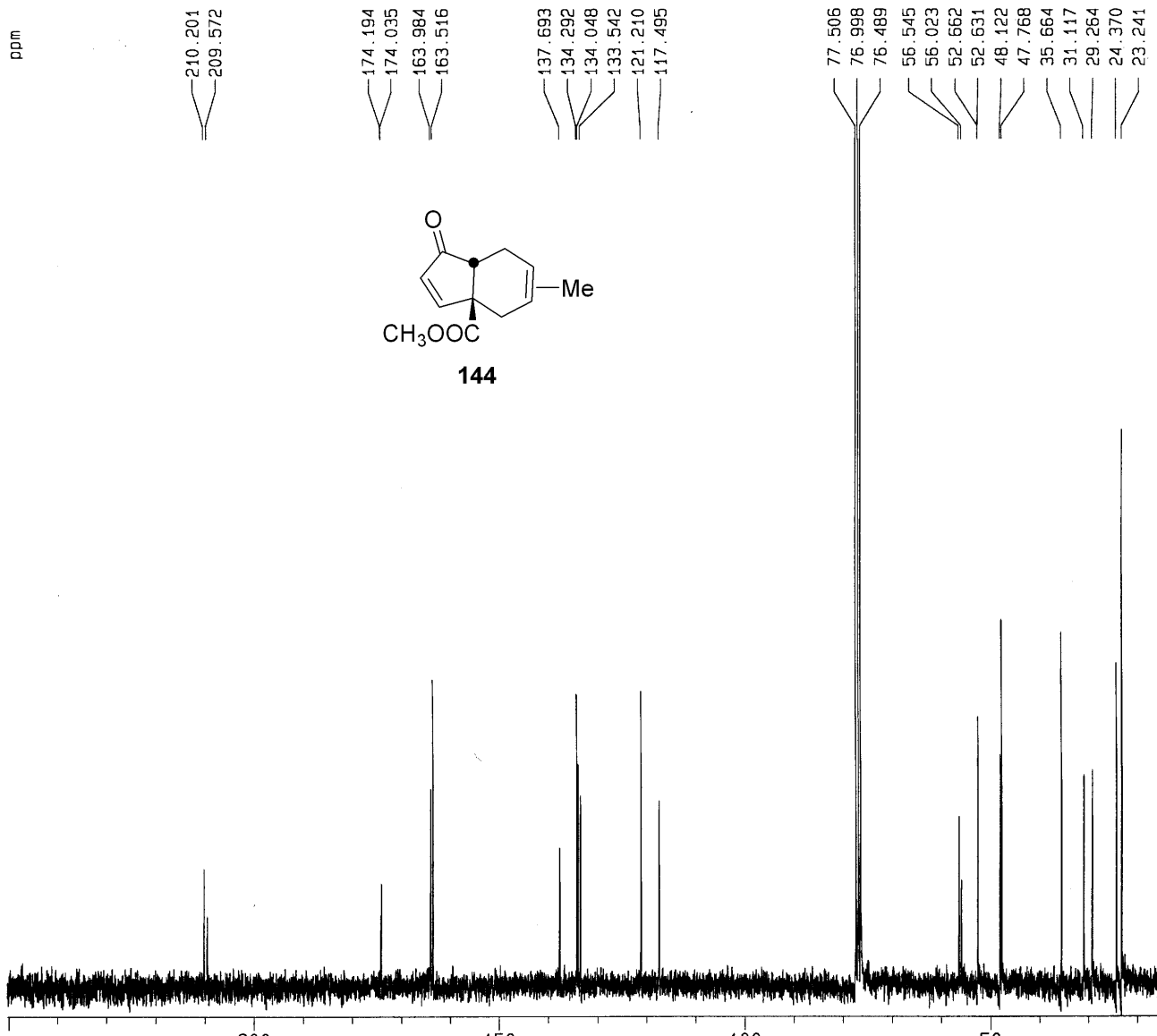
Current Data Parameters
NAME MG-VII-81a
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20070831
Time 23.35
INSTRUM DRX300
PROBHD 5 mm Multinucl
PULPROG zg30pad
TD 32768
SOLVENT CDCl3
NS 16
DS 2
SWH 6172.839 Hz
FIDRES 0.188380 Hz
AQ 2.6542580 sec
RG 256
DW 81.000 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec
D31 0.00000000 sec

======== CHANNEL f1 ========
NUC1 1H
P1 7.05 usec
PL1 0.00 dB
SFO1 300.1318534 MHz

F2 - Processing parameters
SI 32768
SF 300.1300013 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.30



144

Current Data Parameters

NAME	MG-IV-063a-250
EXPNO	2
PROCNO	1

F2 - Acquisition Parameters

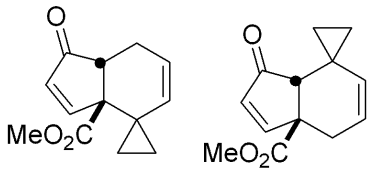
Date_	20050601
Time	22.52
INSTRUM	arx250
PROBHD	5 mm QNP 1H
PULPROG	zgdc30
TD	36864
SOLVENT	CDCl3
NS	929
DS	4
SWH	17241.379 Hz
FIDRES	0.467702 Hz
AQ	1.0691060 sec
RG	22800
DW	29.000 use
DE	41.43 use
TE	300.0 K
D12	0.00002000 sec
DL5	23.00 dB
CPDPRG	waltz16
P31	103.00 use
D1	2.00000000 sec
P1	6.00 use
SF01	62.9023694 MHz
NUCLEUS	13C
D11	0.03000000 sec

F2 - Processing parameters

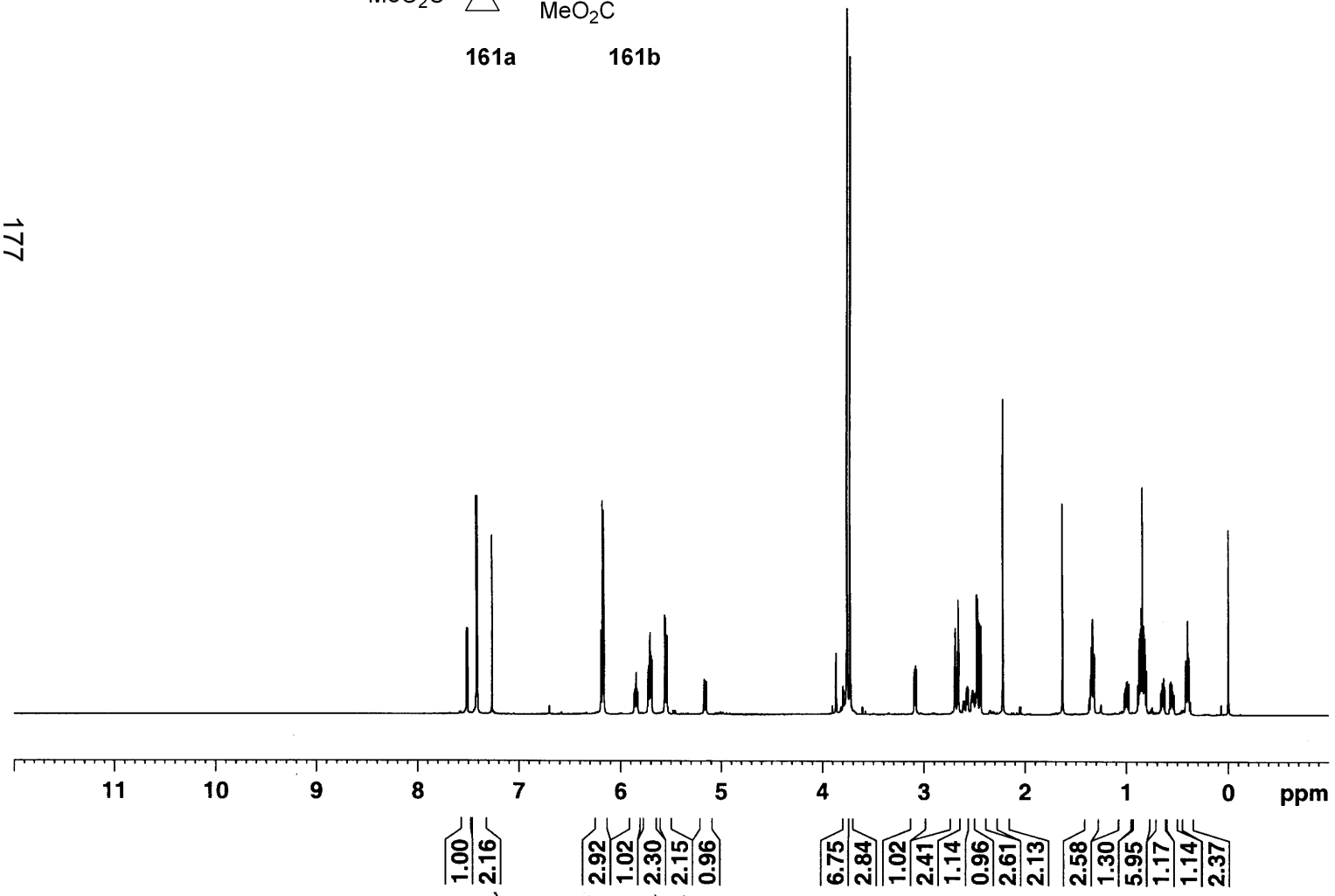
SI	32768
SF	62.8952413 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

1D NMR plot parameters

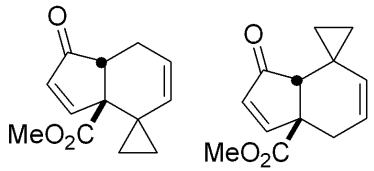
CX	20.00 cm
CY	15.00 cm
F1P	250.397 ppm
F1	15748.76 Hz
F2P	-23.732 ppm
F2	-1492.62 Hz
PPMCM	13.70643 ppm
HZCM	862.06903 Hz/



161a **161b**

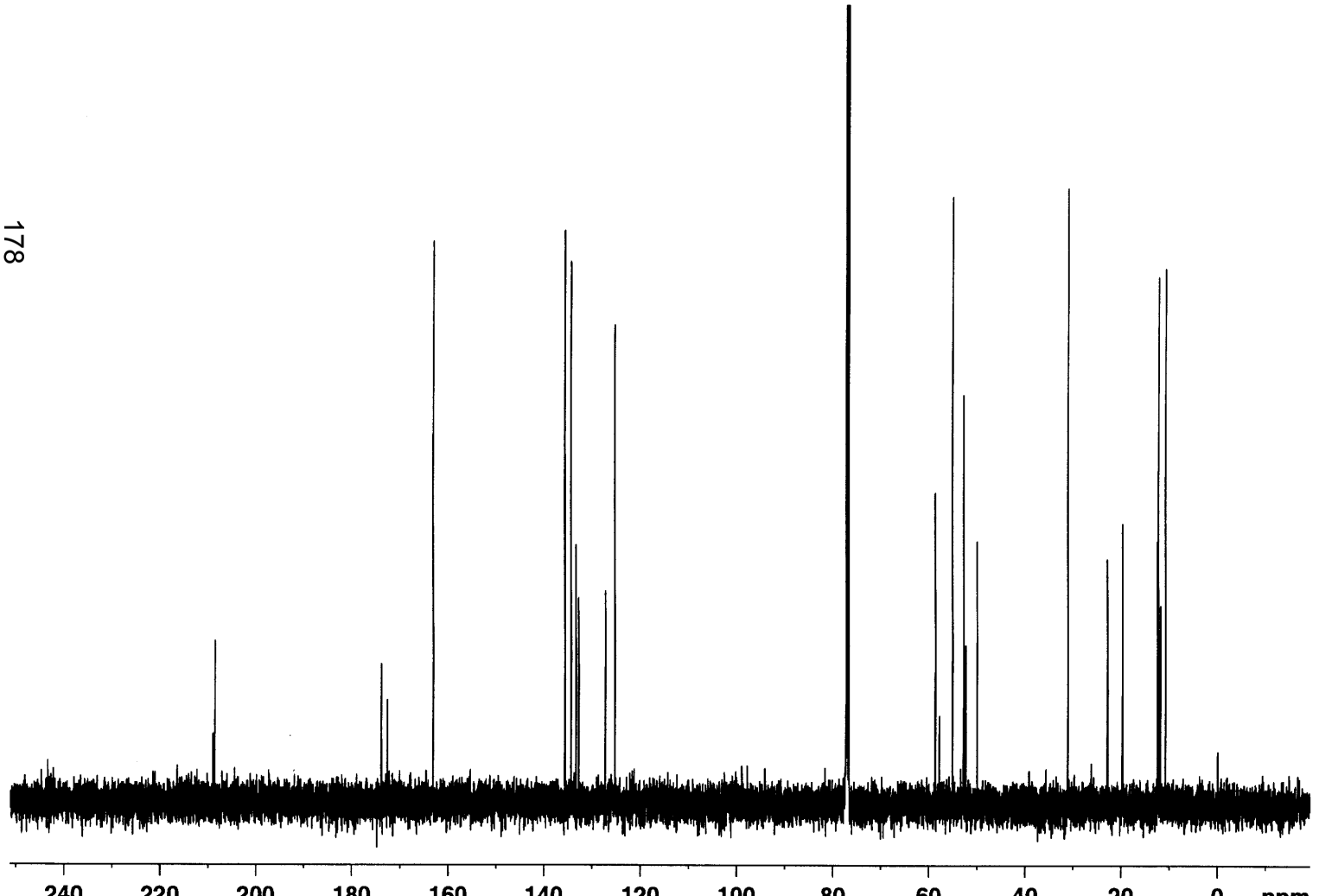



```
Current Data Parameters
NAME      MG-V-48pure-A3
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20051112
Time               12.43
INSTRUM           DRX500
PROBHD   5 mm Multinucl
PULPROG         zg30pad
TD                65536
SOLVENT           CDCl3
NS                   16
DS                    2
SWH           10330.578 Hz
FIDRES         0.157632 Hz
AQ            3.1719923 sec
RG                  114
DW               48.400 use
DE                6.00 use
TE               300.0 K
D1           1.00000000 sec
D31          0.00000000 sec

======== CHANNEL f1 =======
NUC1                1H
P1               13.25 use
PL1              -3.00 dB
SFO1        500.1330885 MHz

F2 - Processing parameters
SI                 32768
SF          500.1300096 MHz
WDW                   EM
SSB                    0
LB                0.30 Hz
GB                     0
PC                1.40
```

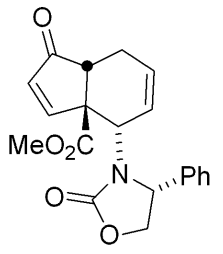


161a **161b**

178

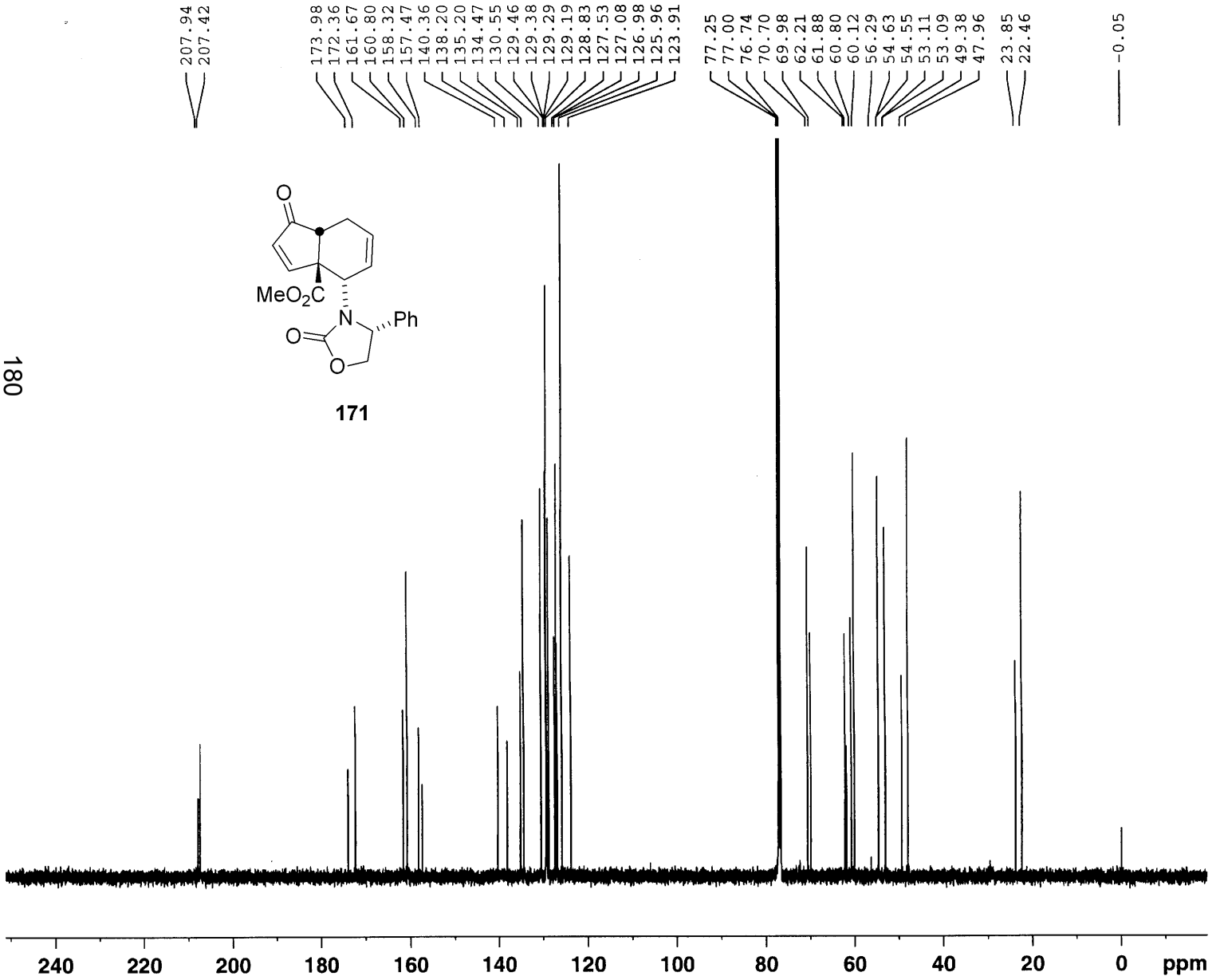



```
Current Data Parameters
NAME      MG-V-48pure-A3
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20051112
Time               12.52
INSTRUM           DRX500
PROBHD   5 mm Multinucl
PULPROG          zgdc30
TD                65536
SOLVENT           CDCl3
NS                  302
DS                    4
SWH           34013.605 Hz
FIDRES         0.519006 Hz
AQ            0.9634292 sec
RG                32768
DW               14.700 usec
DE                6.00 usec
TE               300.0 K
D1           2.00000000 sec
d11          0.03000000 sec
D31          0.00000000 sec

======== CHANNEL f1 ========
NUC1                 13C
P1                8.10 usec
PL1               3.00 dB
SFO1        125.7723786 MHz

======== CHANNEL f2 ========
CPDPRG2         waltz16
NUC2                 1H
PCPD2            88.00 usec
PL2               0.00 dB
PL12             21.00 dB
SFO2        500.1320005 MHz

F2 - Processing parameters
SI                32768
SF          125.7577938 MHz
WDW                  EM
SSB                   0
LB                1.00 Hz
GB                    0
PC                 1.40
```



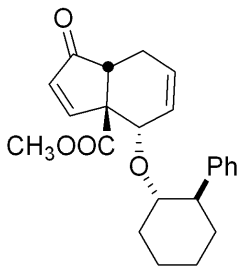
171


```
Current Data Parameters
NAME          MG-V-56a-A3
EXPNO                   1
PROCNO                  1

F2 - Acquisition Parameters
Date_            20051206
Time                12.44
INSTRUM           DRX500
PROBHD    5 mm Multinucl
PULPROG          zg30pad
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH           10330.578 Hz
FIDRES         0.157632 Hz
AQ             3.1719923 sec
RG                  71.8
DW                48.400 use
DE                 6.00 use
TE                300.0 K
D1            1.00000000 sec
D31           0.00000000 sec

======== CHANNEL f1 =======
NUC1                   1H
P1                  13.25 use
PL1                 -3.00 dB
SFO1          500.1330885 MHz

F2 - Processing parameters
SI                 32768
SF          500.1300074 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.40
```



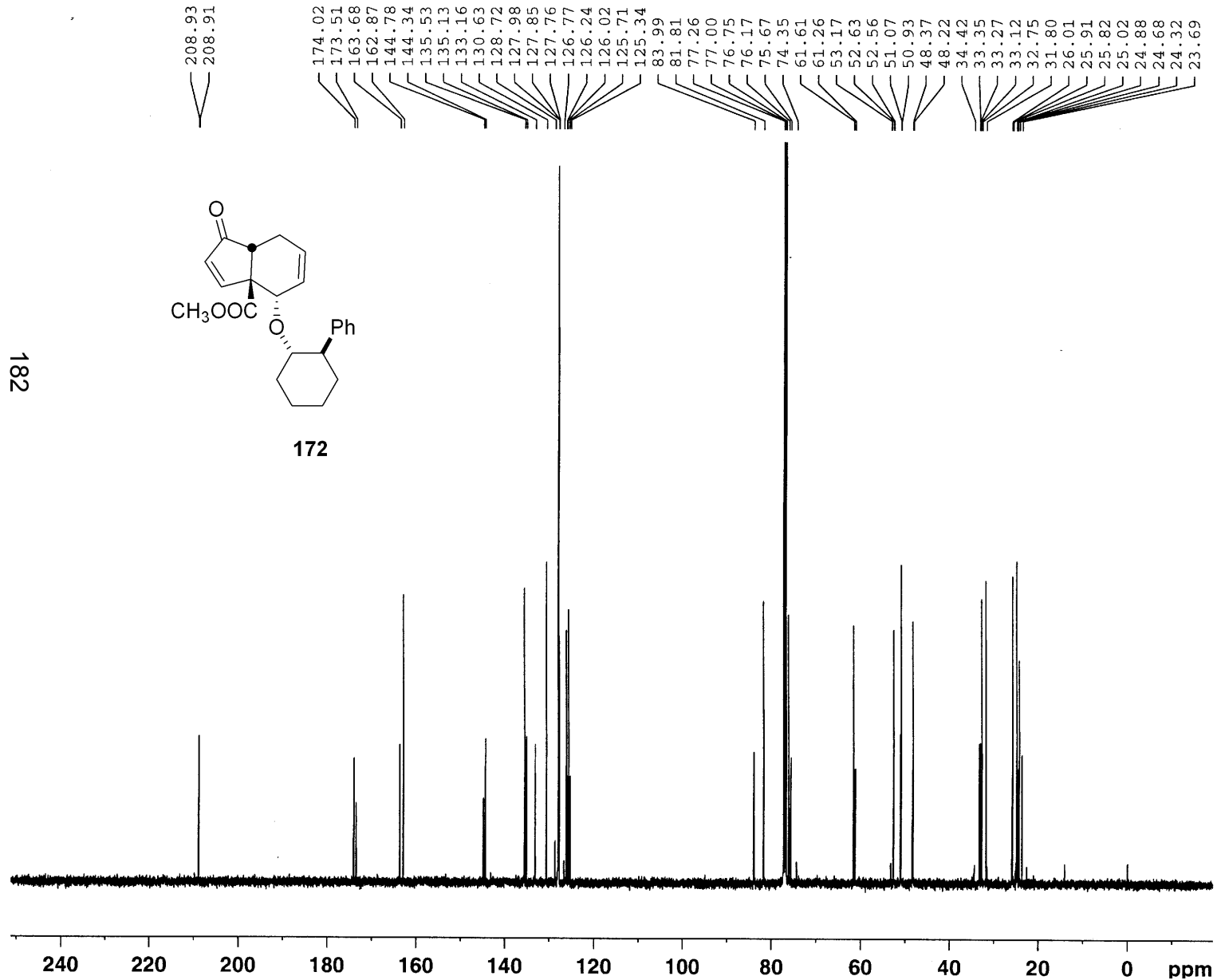

```
Current Data Parameters
NAME          MG-V-56a-A3
EXPNO                   2
PROCNO                  1

F2 - Acquisition Parameters
Date_            20051206
Time                12.50
INSTRUM            DRX500
PROBHD   5 mm Multinucl
PULPROG            zgdc30
TD                  65536
SOLVENT             CDCl3
NS                   1060
DS                      4
SWH           34013.605 Hz
FIDRES         0.519006 Hz
AQ            0.9634292 sec
RG                  32768
DW                14.700 usec
DE                 6.00 usec
TE                300.0 K
D1           2.00000000 sec
d11          0.03000000 sec
D31          0.00000000 sec

======== CHANNEL f1 ========
NUC1                  13C
P1                 8.10 usec
PL1                3.00 dB
SFO1        125.7723786 MHz

======== CHANNEL f2 ========
CPDPRG2          waltz16
NUC2                  1H
PCPD2             88.00 usec
PL2                0.00 dB
PL12              21.00 dB
SFO2        500.1320005 MHz

F2 - Processing parameters
SI                  32768
SF          125.7577969 MHz
WDW                    EM
SSB                     0
LB                 1.00 Hz
GB                      0
PC                   1.40
```

MG-V-68b-2nd frac
DA rxn with R*O-butadiene



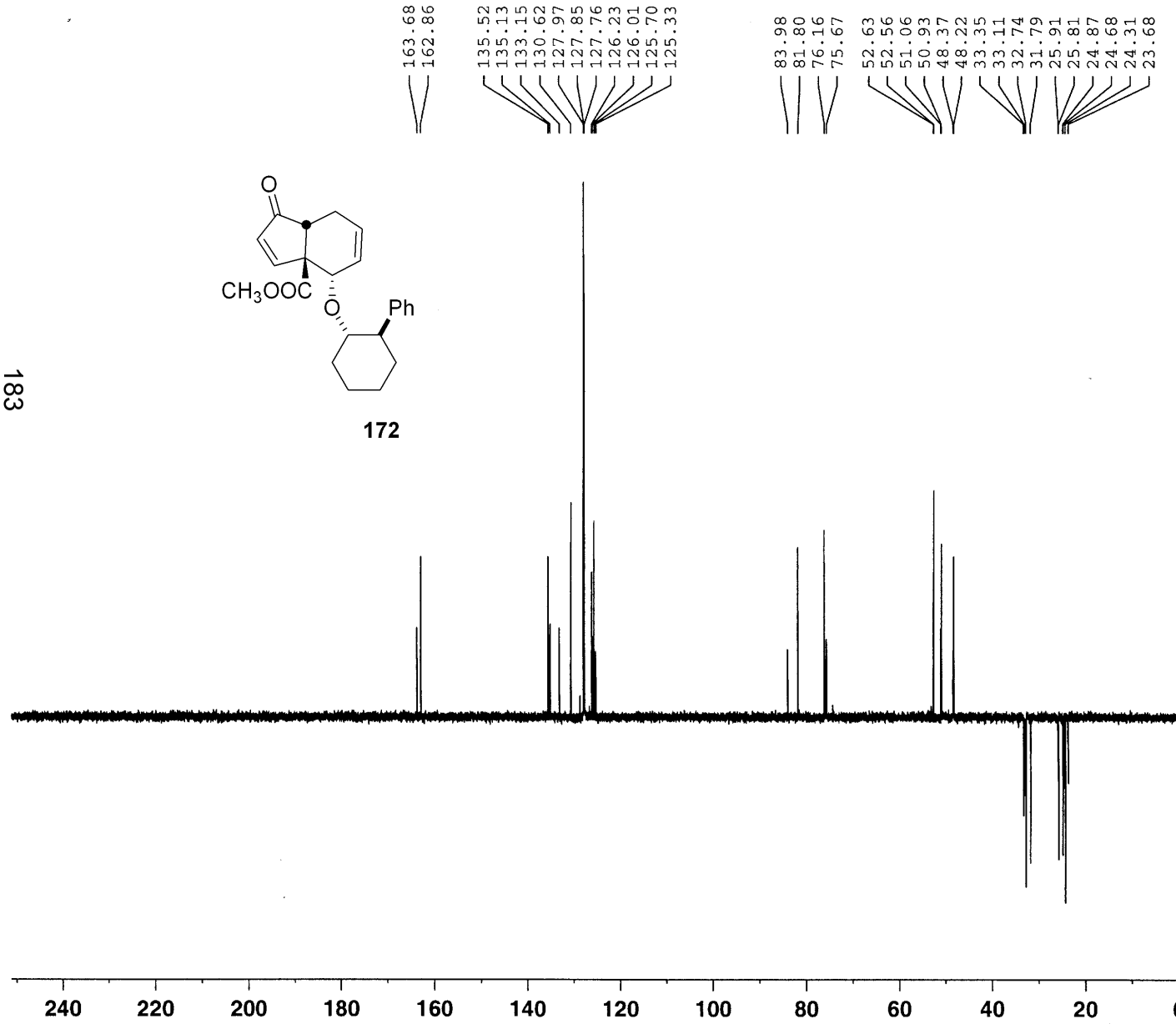
172


```
Current Data Parameters
NAME          MG-V-68b-A3
EXPNO                   1
PROCNO                  1

F2 - Acquisition Parameters
Date_            20051223
Time                17.20
INSTRUM            DRX500
PROBHD   5 mm Multinucl
PULPROG          zg30pad
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH           10330.578 Hz
FIDRES         0.157632 Hz
AQ            3.1719923 sec
RG                  71.8
DW                48.400 use
DE                 6.00 use
TE                300.0 K
D1           1.00000000 sec
D31          0.00000000 sec

======== CHANNEL f1 =======
NUC1                   1H
P1                 13.25 use
PL1                -3.00 dB
SFO1        500.1330885 MHz

F2 - Processing parameters
SI                 32768
SF          500.1300125 MHz
WDW                   EM
SSB                    0
LB                0.30 Hz
GB                     0
PC                 1.40
```



172

```
Current Data Parameters
NAME      MG-V-068b-2-A3
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20060116
Time               11.51
INSTRUM           DRX500
PROBHD   5 mm Multinucl
PULPROG          zgdc30
TD                65536
SOLVENT           CDCl3
NS                  577
DS                    4
SWH           34013.605 Hz
FIDRES         0.519006 Hz
AQ             0.9634292 sec
RG                32768
DW               14.700 usec
DE                6.00 usec
TE                300.0 K
D1            2.00000000 sec
d11           0.03000000 sec
D31           0.00000000 sec

======== CHANNEL f1 ========
NUC1                 13C
P1                8.10 usec
PL1               3.00 dB
SFO1        125.7723786 MHz

======== CHANNEL f2 ========
CPDPRG2          waltz16
NUC2                 1H
PCPD2            88.00 usec
PL2               0.00 dB
PL12             21.00 dB
SFO2        500.1320005 MHz

F2 - Processing parameters
SI                32768
SF          125.7577969 MHz
WDW                  EM
SSB                   0
LB                1.00 Hz
GB                    0
PC                 1.40
```



172

Current Data Parameters

NAME	MG-V-068b-2-A3
EXPNO	3
PROCNO	1

F2 - Acquisition Parameters

Date_	20060116
Time	12.20
INSTRUM	DRX500
PROBHD	5 mm Multinucl
PULPROG	dept135
TD	65536
SOLVENT	CDCl3
NS	99
DS	4
SWH	34013.605 Hz
FIDRES	0.519006 Hz
AQ	0.9634292 sec
RG	16384
DW	14.700 usec
DE	6.00 usec
TE	300.0 K
CNST2	145.0000000
D1	2.00000000 sec
d2	0.00344828 sec
d12	0.00002000 sec
DELTA	0.00001031 sec
MCREST	0.00000000 sec
MCWRK	0.01500000 sec

======== CHANNEL f1 ========

NUC1	13C
P1	8.10 usec
p2	16.20 usec
PL1	3.00 dB
SFO1	125.7723786 MHz

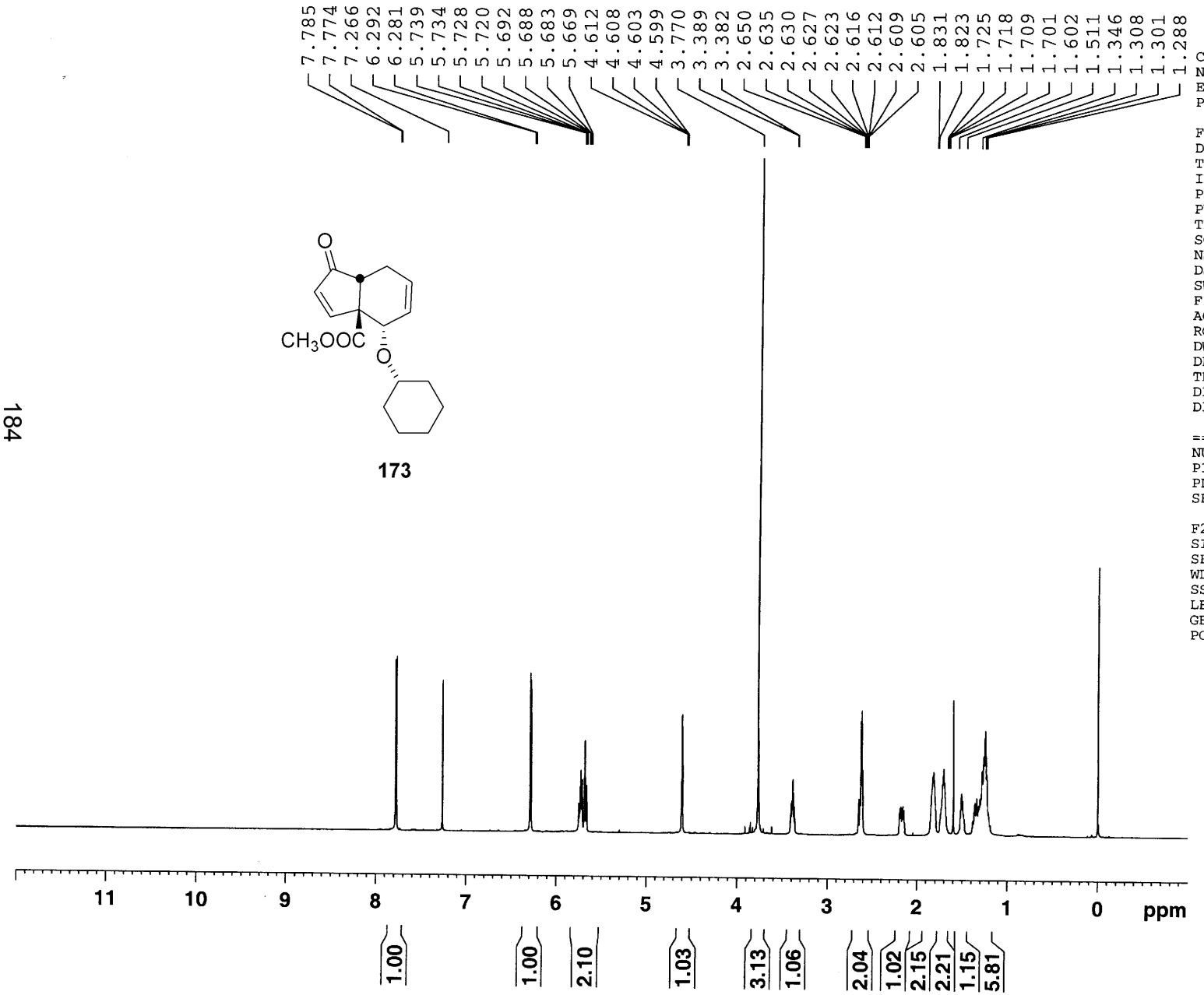
======== CHANNEL f2 ========

CPDPRG2	waltz16
NUC2	1H
P3	10.40 usec
p4	20.80 usec
PCPD2	88.00 usec
PL2	0.00 dB
PL12	21.00 dB
SFO2	500.1320005 MHz

F2 - Processing parameters

SI	32768
SF	125.7577977 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

1H NMR



173

Current Data Parameters

NAME	MG-V-94a-A3
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

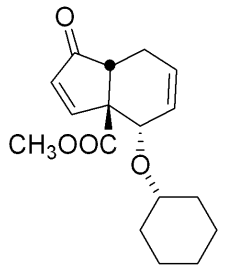
Date_	20060228
Time	22.49
INSTRUM	DRX500
PROBHD	5 mm Multinucl
PULPROG	zg30pad
TD	65536
SOLVENT	CDCl3
NS	16
DS	2
SWH	10330.578 Hz
FIDRES	0.157632 Hz
AQ	3.1719923 sec
RG	143.7
DW	48.400 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec
D31	0.00000000 sec

======== CHANNEL f1 ========

NUC1	1H
P1	11.50 usec
PL1	0.00 dB
SFO1	500.1330885 MHz

F2 - Processing parameters

SI	32768
SF	500.1300103 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.40



173

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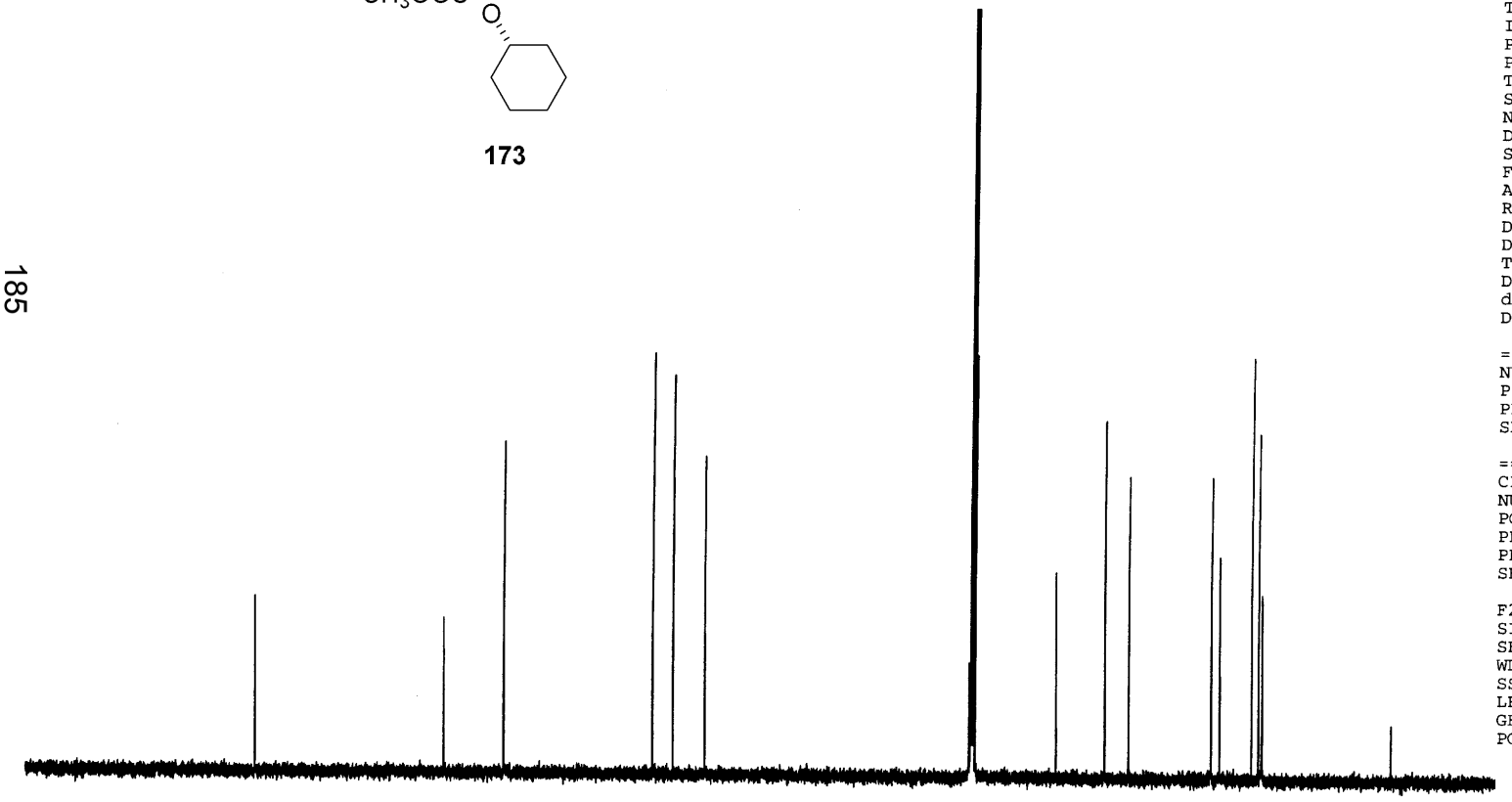


240 220 200 180 160 140 120 100 80 60 40 20 0 ppm

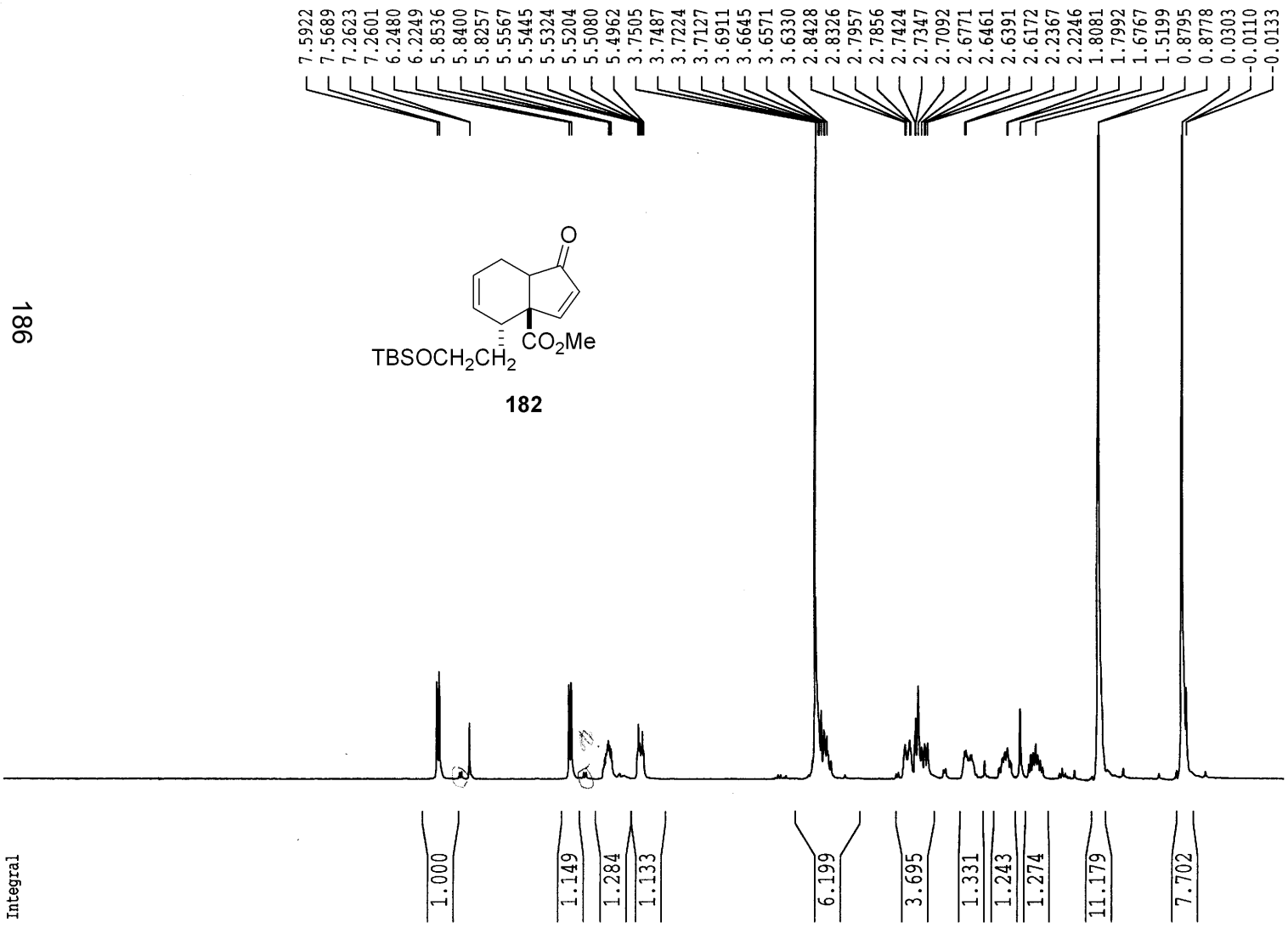
```
Current Data Parameters
NAME                  MG-V-94a-A3
EXPNO                           2
PROCNO                          1

F2 - Acquisition Parameters
Date_                    20060228
Time                        22.53
INSTRUM                    DRX500
PROBHD    5 mm Multinucl
PULPROG                    zgdc30
TD                          65536
SOLVENT                     CDCl3
NS                           1098
DS                              4
SWH                    34013.605 Hz
FIDRES                  0.519006 Hz
AQ                      0.9634292 sec
RG                          32768
DW                         14.700 usec
DE                          6.00 usec
TE                          300.0 K
D1                     2.00000000 sec
d11                    0.03000000 sec
D31                    0.00000000 sec

======== CHANNEL f1 ========
NUC1                          13C
P1                          8.10 usec
PL1                         3.00 dB
SFO1                125.7723786 MHz

======== CHANNEL f2 ========
CPDPRG2                   waltz16
NUC2                          1H
PCPD2                      88.00 usec
PL2                         0.00 dB
PL12                       21.00 dB
SFO2                500.1320005 MHz

F2 - Processing parameters
SI                          32768
SF                 125.7577928 MHz
WDW                            EM
SSB                             0
LB                          1.00 Hz
GB                              0
PC                           1.40
```



182

Current Data Parameters

NAME	MG-VI-35-A1
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

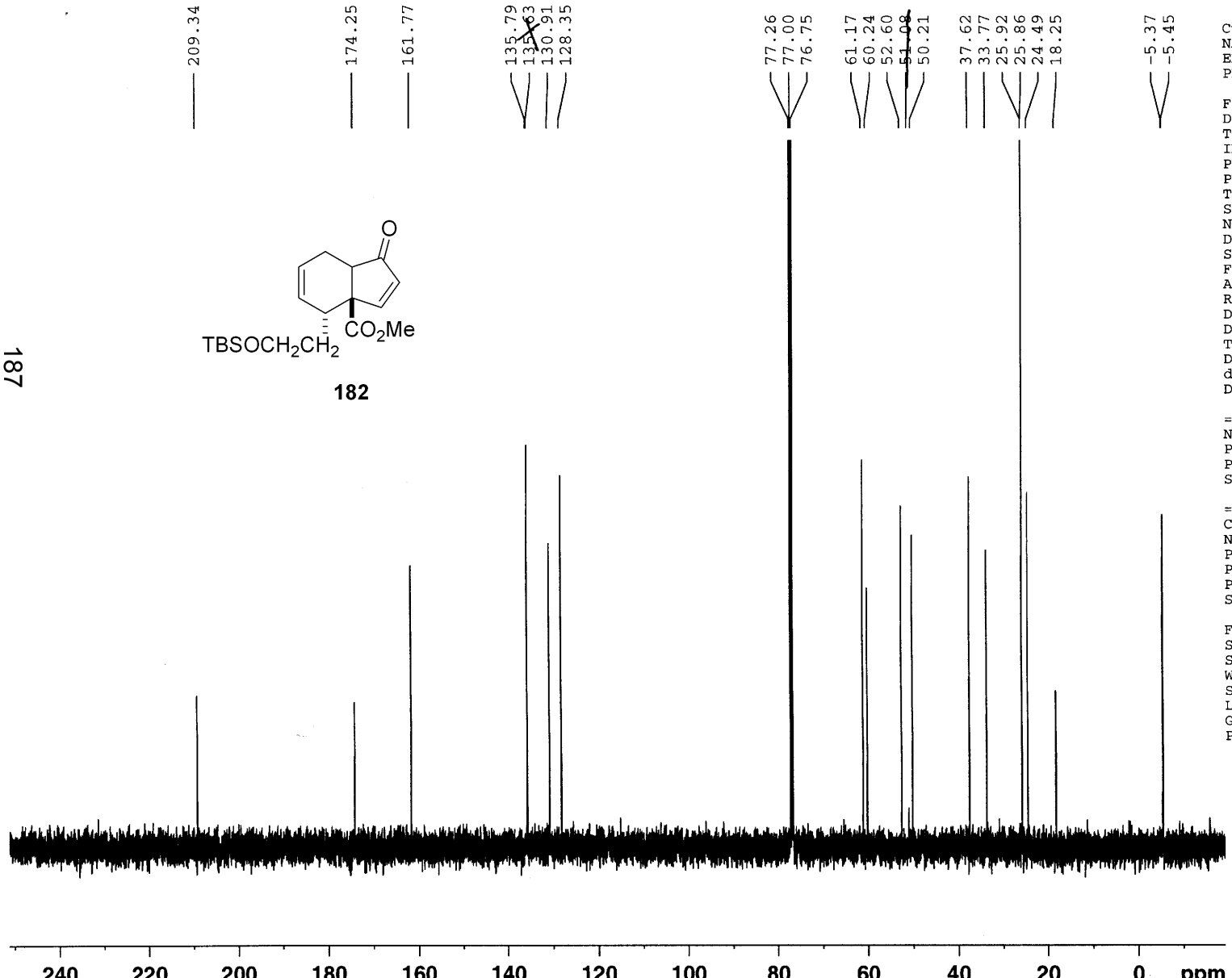
Date_	20060717
Time	15.05
INSTRUM	arx250
PROBHD	5 mm QNP 1H
PULPROG	zg30
TD	32768
SOLVENT	CDCl3
NS	16
DS	2
SWH	5208.333 Hz
FIDRES	0.158946 Hz
AQ	3.1457779 sec
RG	715
DW	96.000 usec
DE	137.14 usec
TE	300.0 K
D1	1.00000000 sec
P1	9.50 usec
SFO1	250.1315321 MHz
NUCLEUS	1H

F2 - Processing parameters

SI	16384
SF	250.1300073 MHz
WDW	EM
SSB	0
LB	0.20 Hz
GB	0
PC	1.50

1D NMR plot parameters

CX	20.00 cm
CY	30.00 cm
F1P	12.000 ppm
F1	3001.56 Hz
F2P	-1.000 ppm
F2	-250.13 Hz
PPMCM	0.65000 ppm/cm
HZCM	162.58450 Hz/cm



182

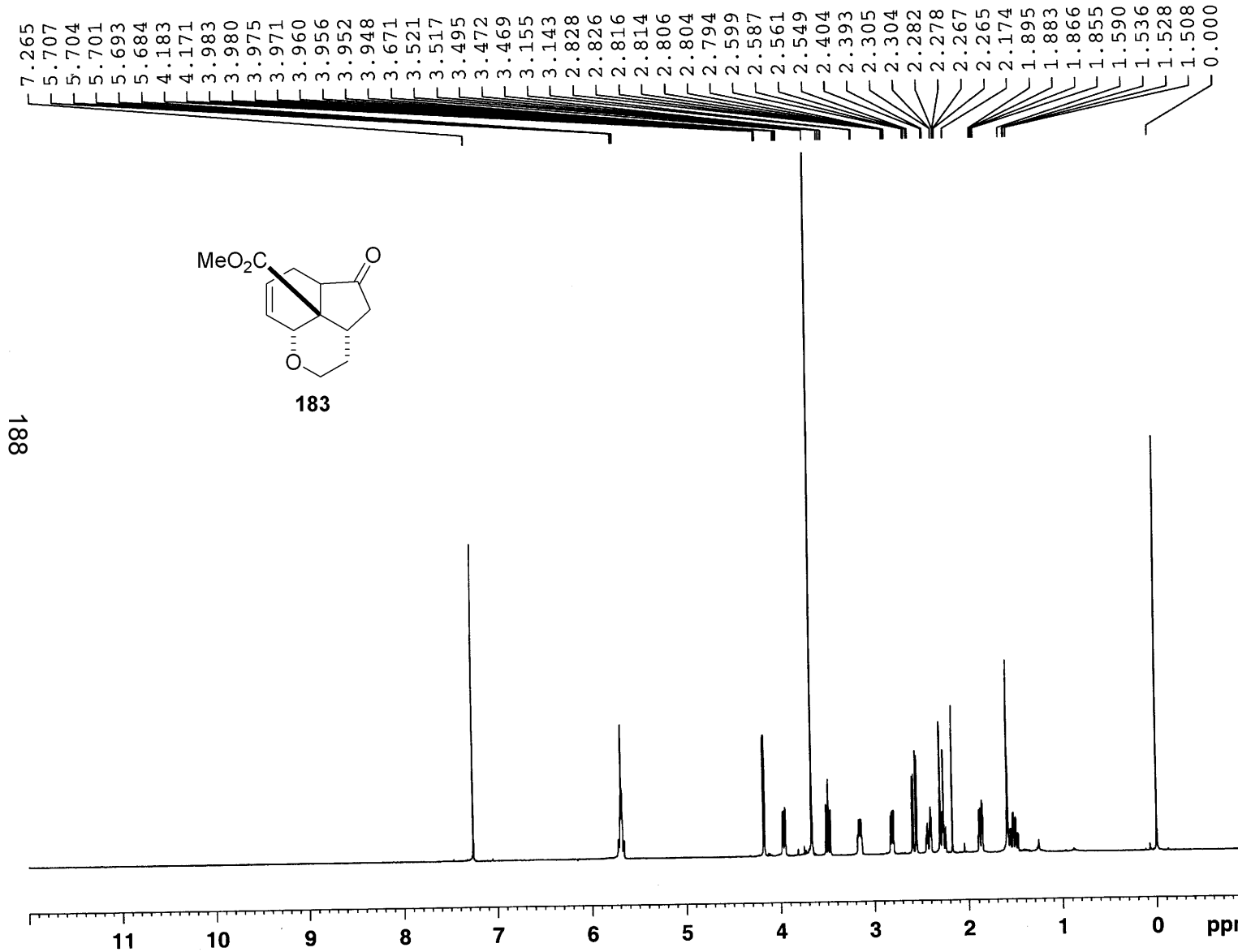
```
Current Data Parameters
NAME          MG-V-100b-A3
EXPNO                    2
PROCNO                   1

F2 - Acquisition Parameters
Date_             20060307
Time                 22.31
INSTRUM              DRX500
PROBHD   5 mm Multinucl
PULPROG              zgdc30
TD                    65536
SOLVENT               CDCl3
NS                       59
DS                        4
SWH              34013.605 Hz
FIDRES           0.519006 Hz
AQ               0.9634292 sec
RG                    32768
DW                14.700 usec
DE                 6.00 usec
TE                 300.0 K
D1            2.00000000 sec
d11           0.03000000 sec
D31           0.00000000 sec

======== CHANNEL f1 ========
NUC1                   13C
P1                  8.10 usec
PL1                 3.00 dB
SFO1         125.7723786 MHz

======== CHANNEL f2 ========
CPDPRG2           waltz16
NUC2                   1H
PCPD2              88.00 usec
PL2                 0.00 dB
PL12               21.00 dB
SFO2         500.1320005 MHz

F2 - Processing parameters
SI                    32768
SF           125.7577928 MHz
WDW                     EM
SSB                      0
LB                  1.00 Hz
GB                       0
PC                    1.40
```



183

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Current Data Parameters

NAME	MG-V-108-109
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

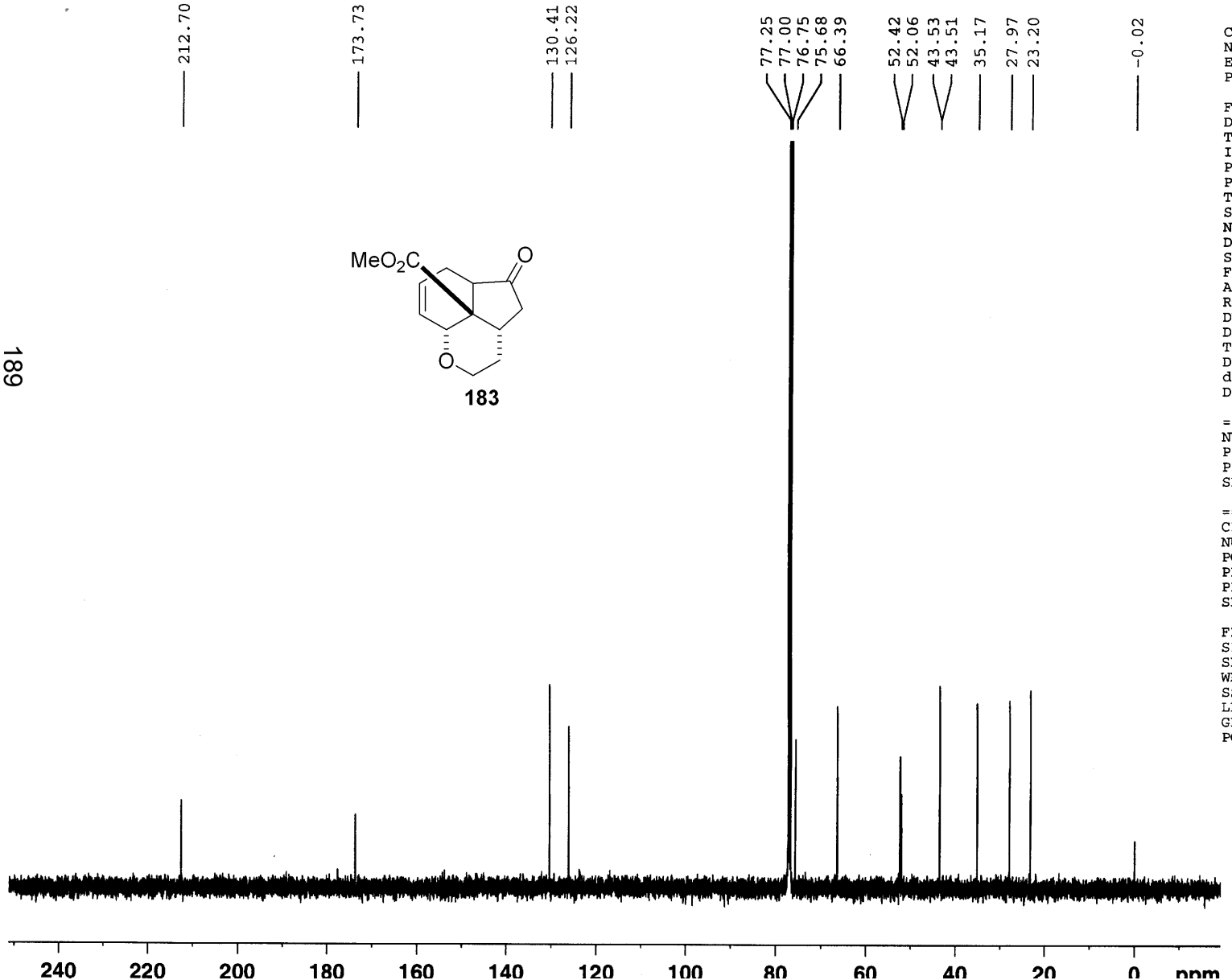
Date_	20060712
Time	20.42
INSTRUM	DRX500
PROBHD	5 mm Multinucl
PULPROG	zg30pad
TD	65536
SOLVENT	CDCl3
NS	16
DS	2
SWH	10330.578 Hz
FIDRES	0.157632 Hz
AQ	3.1719923 sec
RG	161.3
DW	48.400 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec
D31	0.00000000 sec

======== CHANNEL f1 ========

NUC1	1H
P1	11.50 usec
PL1	0.00 dB
SFO1	500.1330885 MHz

F2 - Processing parameters

SI	32768
SF	500.1300109 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.40



183

```
Current Data Parameters
NAME        MG-V-108-109
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20060712
Time               20.47
INSTRUM           DRX500
PROBHD   5 mm Multinucl
PULPROG          zgdc30
TD                65536
SOLVENT           CDC13
NS                  419
DS                    4
SWH           34013.605 Hz
FIDRES         0.519006 Hz
AQ             0.9634292 sec
RG                32768
DW               14.700 usec
DE                6.00 usec
TE                300.0 K
D1           2.00000000 sec
d11          0.03000000 sec
D31          0.00000000 sec

======== CHANNEL f1 ========
NUC1                13C
P1                8.10 usec
PL1               3.00 dB
SFO1        125.7723786 MHz

======== CHANNEL f2 ========
CPDPRG2         waltz16
NUC2                1H
PCPD2            88.00 usec
PL2               0.00 dB
PL12             21.00 dB
SFO2        500.1320005 MHz

F2 - Processing parameters
SI                32768
SF          125.7577928 MHz
WDW                EM
SSB                 0
LB              1.00 Hz
GB                  0
PC                1.40
```

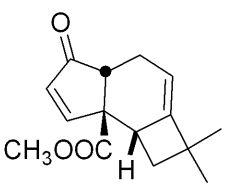
MG-VII-83c
DA rxn with 2,3-di-Me-1-vinyl-butene
1H NMR

Current Data Parameters

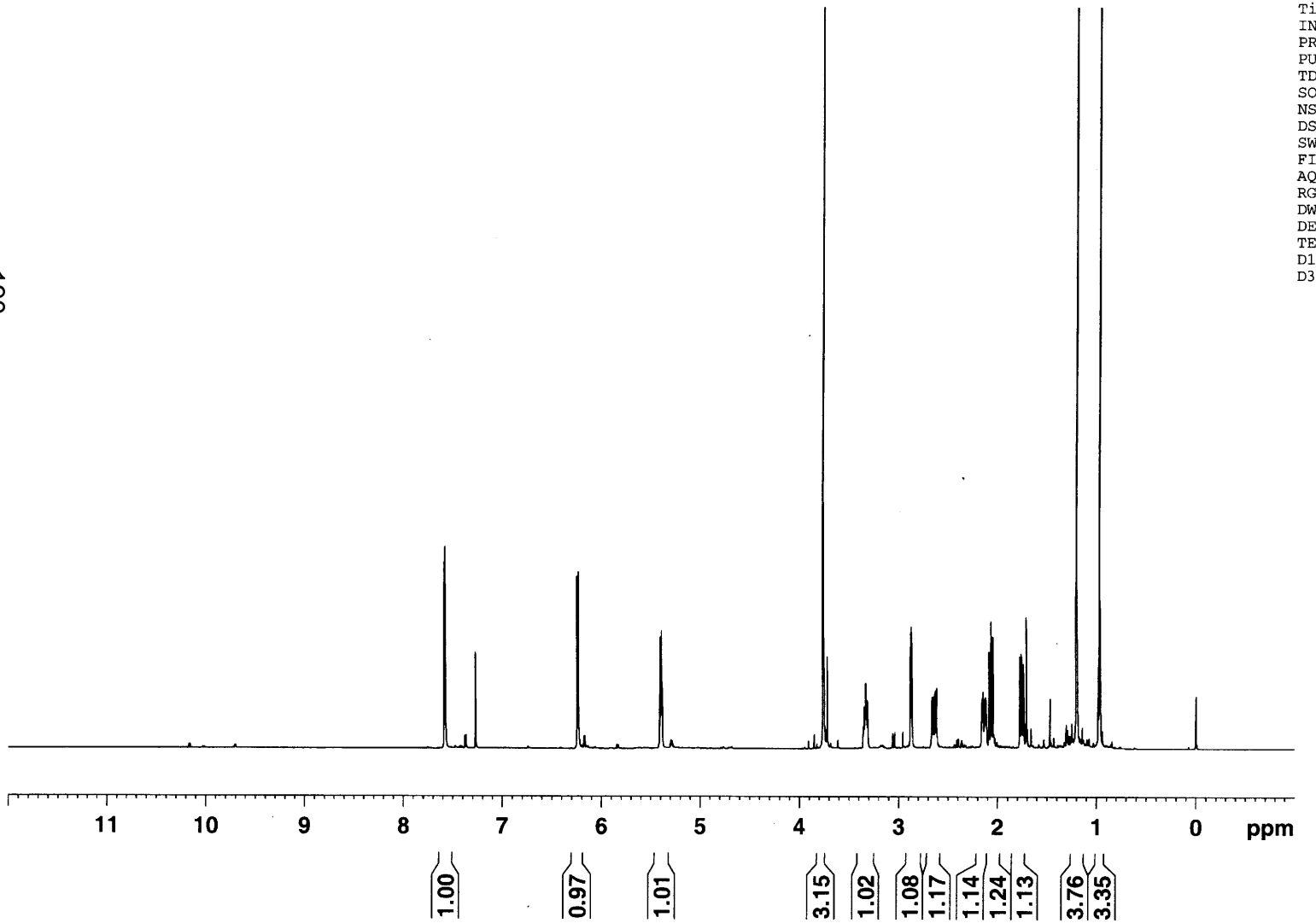
NAME	MG-VII-83c
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

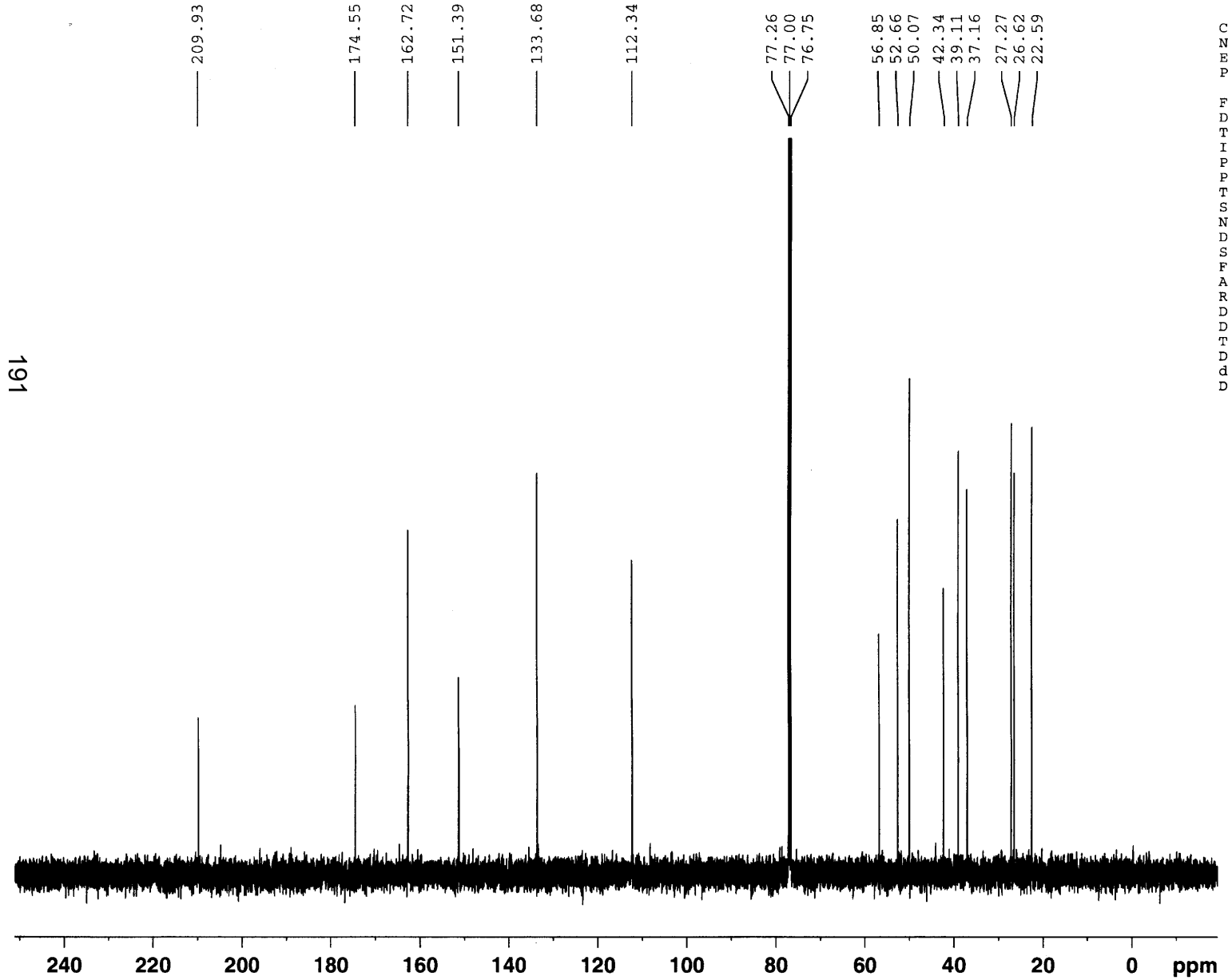
Date_	20070903
Time	18.46
INSTRUM	DRX500
PROBHD	5 mm Multinucl
PULPROG	zg30pad
TD	65536
SOLVENT	CDCl3
NS	16
DS	2
SWH	10330.578 Hz
FIDRES	0.157632 Hz
AQ	3.1719923 sec
RG	71.8
DW	48.400 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec
D31	0.00000000 sec



191



13C NMR



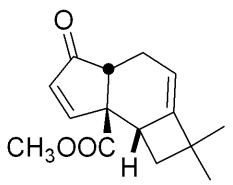
191

Current Data Parameters

NAME	MG-VII-83c
EXPNO	2
PROCNO	1

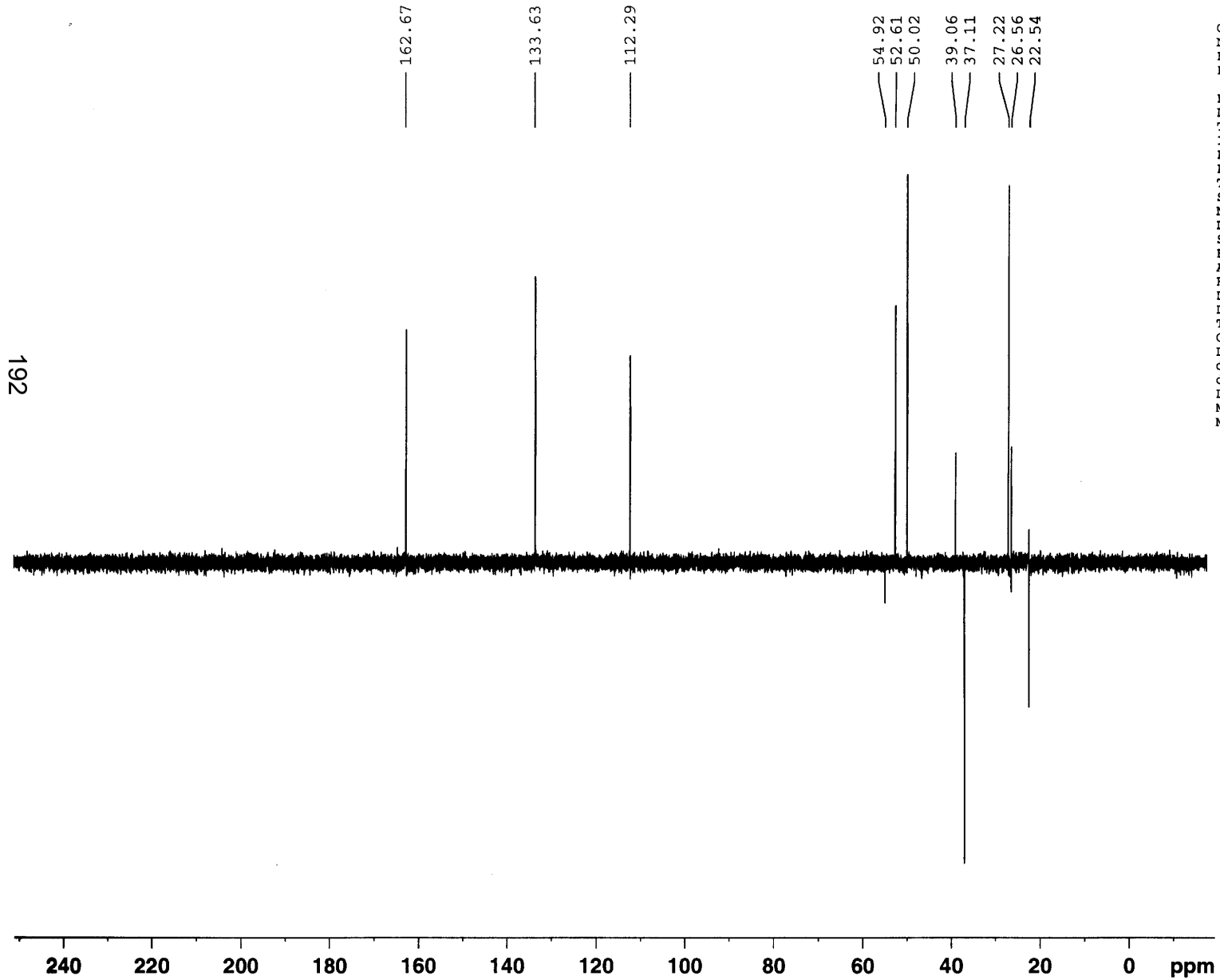
F2 - Acquisition Parameters

Date_	20070903
Time	18.51
INSTRUM	DRX500
PROBHD	5 mm Multinucl
PULPROG	zgdc30
TD	65536
SOLVENT	CDCl3
NS	108
DS	4
SWH	34013.605 Hz
FIDRES	0.519006 Hz
AQ	0.9634292 sec
RG	32768
DW	14.700 usec
DE	6.00 usec
TE	300.0 K
D1	2.00000000 sec
d11	0.03000000 sec
D31	0.00000000 sec



191

13C dept135



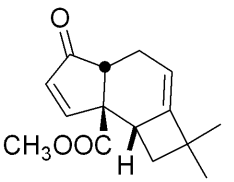
192

Current Data Parameters

NAME	MG-VII-83c
EXPNO	3
PROCNO	1

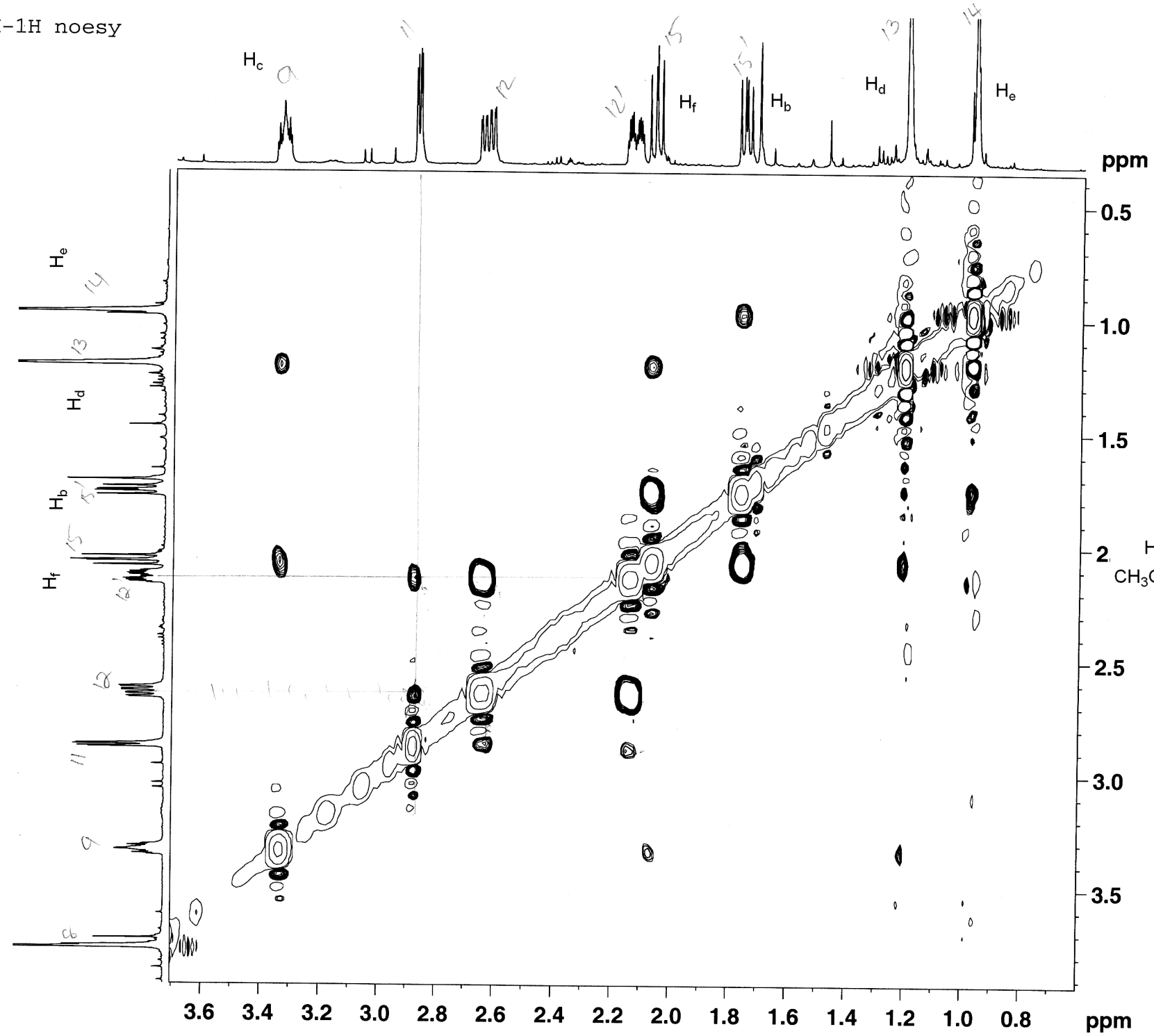
F2 - Acquisition Parameters

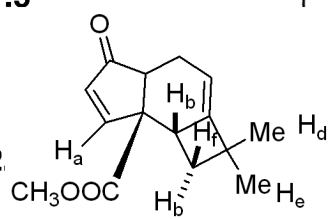
Date_	20070903
Time	18.57
INSTRUM	DRX500
PROBHD	5 mm Multinucl
PULPROG	dept135
TD	65536
SOLVENT	CDCl3
NS	83
DS	4
SWH	34013.605 Hz
FIDRES	0.519006 Hz
AQ	0.9634292 sec
RG	16384
DW	14.700 usec
DE	6.00 usec
TE	300.0 K
CNST2	145.0000000
D1	2.00000000 sec
d2	0.00344828 sec
d12	0.00002000 sec
DELTA	0.00001031 sec
MCREST	0.00000000 sec
MCWRK	0.01500000 sec



191

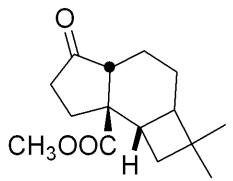
1H-1H noesy





191

MG-VII-85
Hydrogenation of DAA from 2,2-diMe-1-vinyl-butene
1H NMR



192

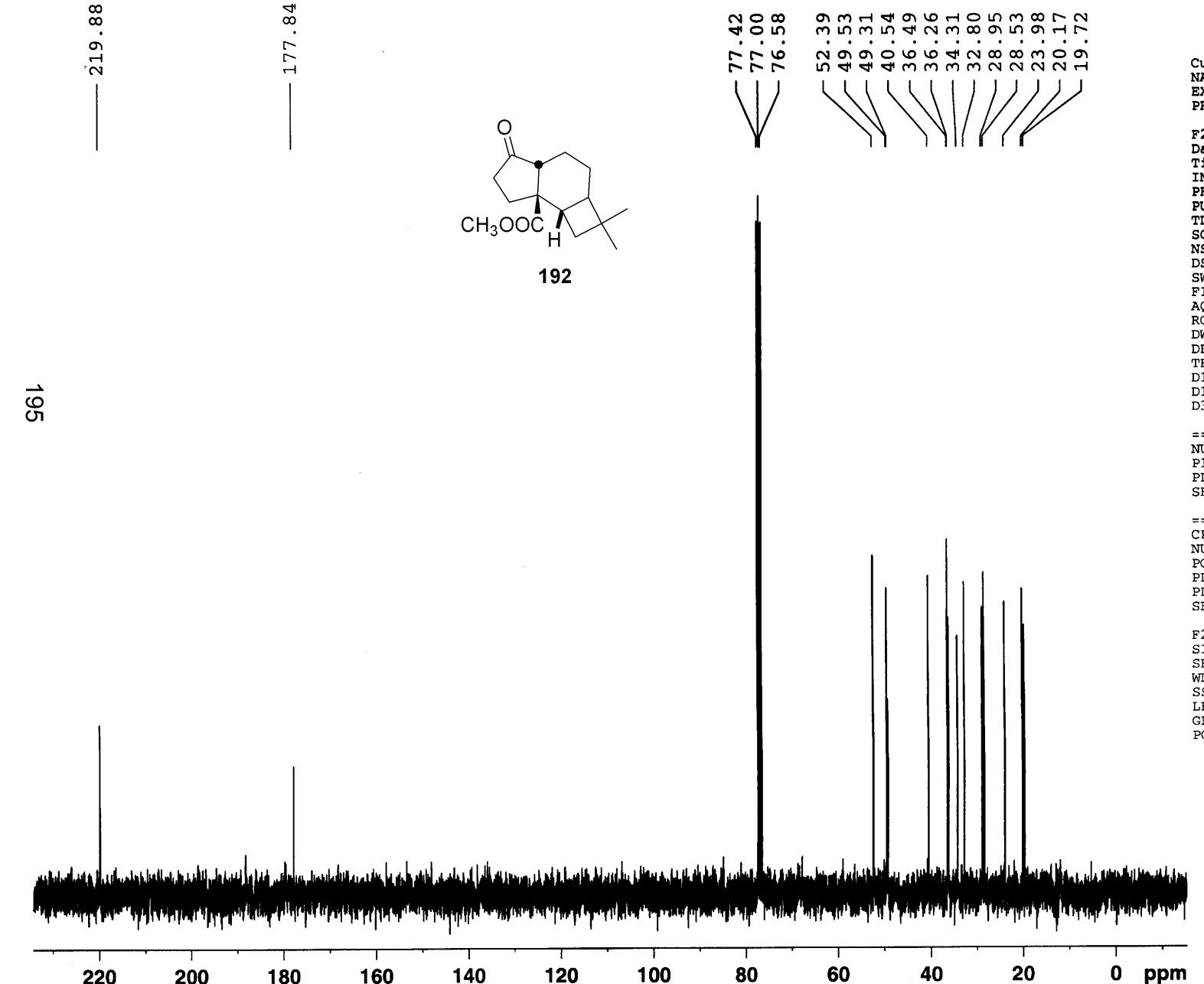
Current Data Parameters
NAME MG-VII-85
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20070911
Time 23.29
INSTRUM DRX300
PROBHD 5 mm Multinucl
PULPROG zg30pad
TD 32768
SOLVENT CDCl3
NS 16
DS 2
SWH 6172.839 Hz
FIDRES 0.188380 Hz
AQ 2.6542580 sec
RG 143.7
DW 81.000 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec
D31 0.00000000 sec

======== CHANNEL f1 ========
NUC1 1H
P1 7.05 usec
PL1 0.00 dB
SFO1 300.1318534 MHz

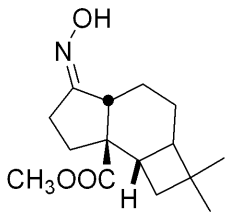
F2 - Processing parameters
SI 32768
SF 300.1300001 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.30

13C NMR




```
Current Data Parameters
NAME                  MG-VII-85
EXPNO                         2
PROCNO                        1

F2 - Acquisition Parameters
Date_                  20070911
Time                      23.32
INSTRUM                  DRX300
PROBHD    5 mm Multinucl
PULPROG               zgdc30pad
TD                        65536
SOLVENT                   CDCl3
NS                           57
DS                            4
SWH                  18832.393 Hz
FIDRES               0.287360 Hz
AQ                   1.7400308 sec
RG                        22528
DW                     26.550 usec
DE                      6.00 usec
TE                      300.0 K
D1                  2.00000000 sec
D11                 0.03000000 sec
D31                 0.00000000 sec

======== CHANNEL f1 ========
NUC1                        13C
P1                       9.00 usec
PL1                      5.00 dB
SFO1                75.4760107 MHz

======== CHANNEL f2 ========
CPDPRG2                waltz16
NUC2                        1H
PCPD2                  100.00 usec
PL2                    120.00 dB
PL12                    21.41 dB
SFO2               300.1312005 MHz

F2 - Processing parameters
SI                        32768
SF                  75.4677514 MHz
WDW                          EM
SSB                           0
LB                       1.00 Hz
GB                            0
PC                         1.30
```

1H NMR



193

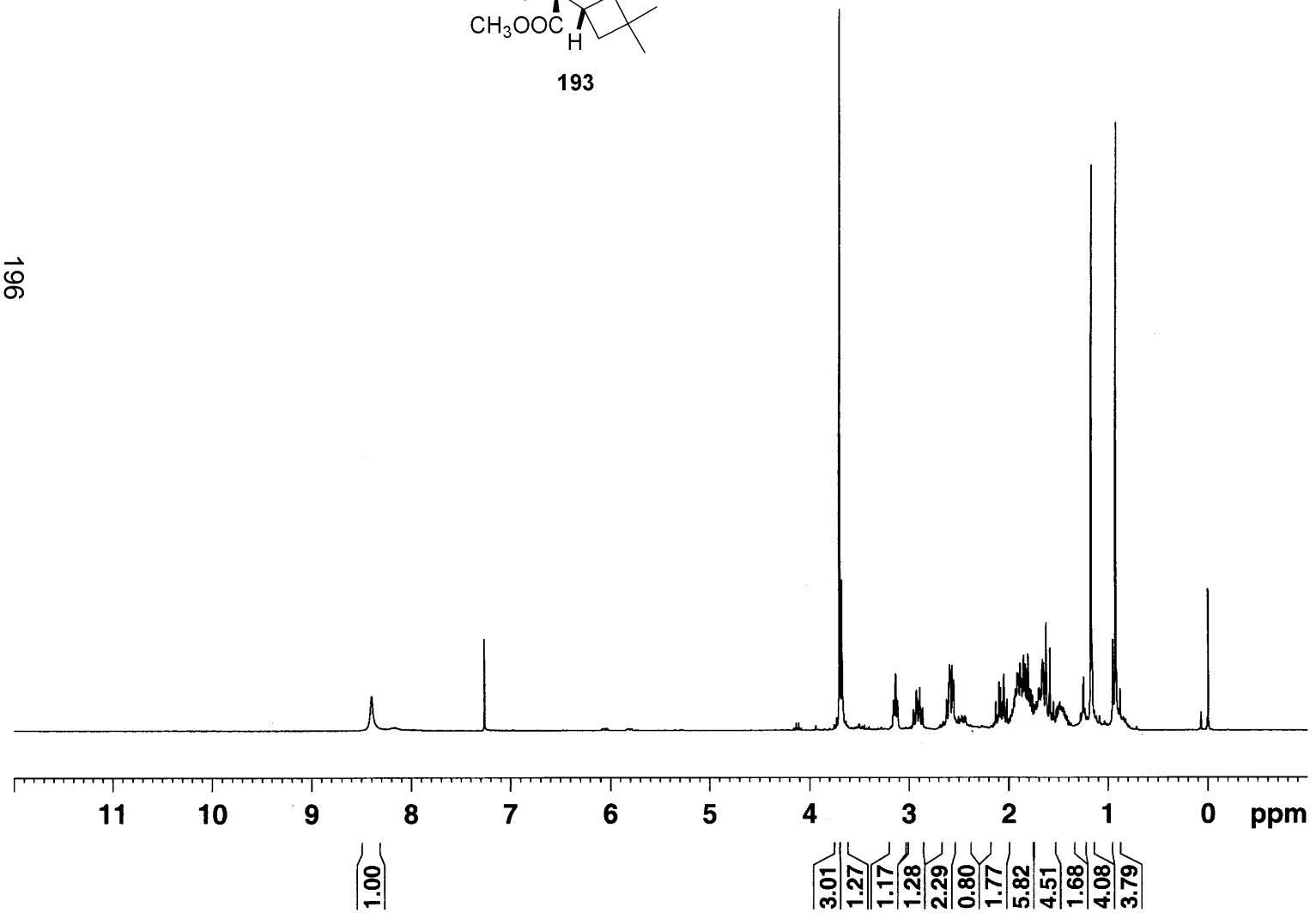
196

Current Data Parameters
NAME MG-VII-86cr
EXPNO 1
PROCNO 1

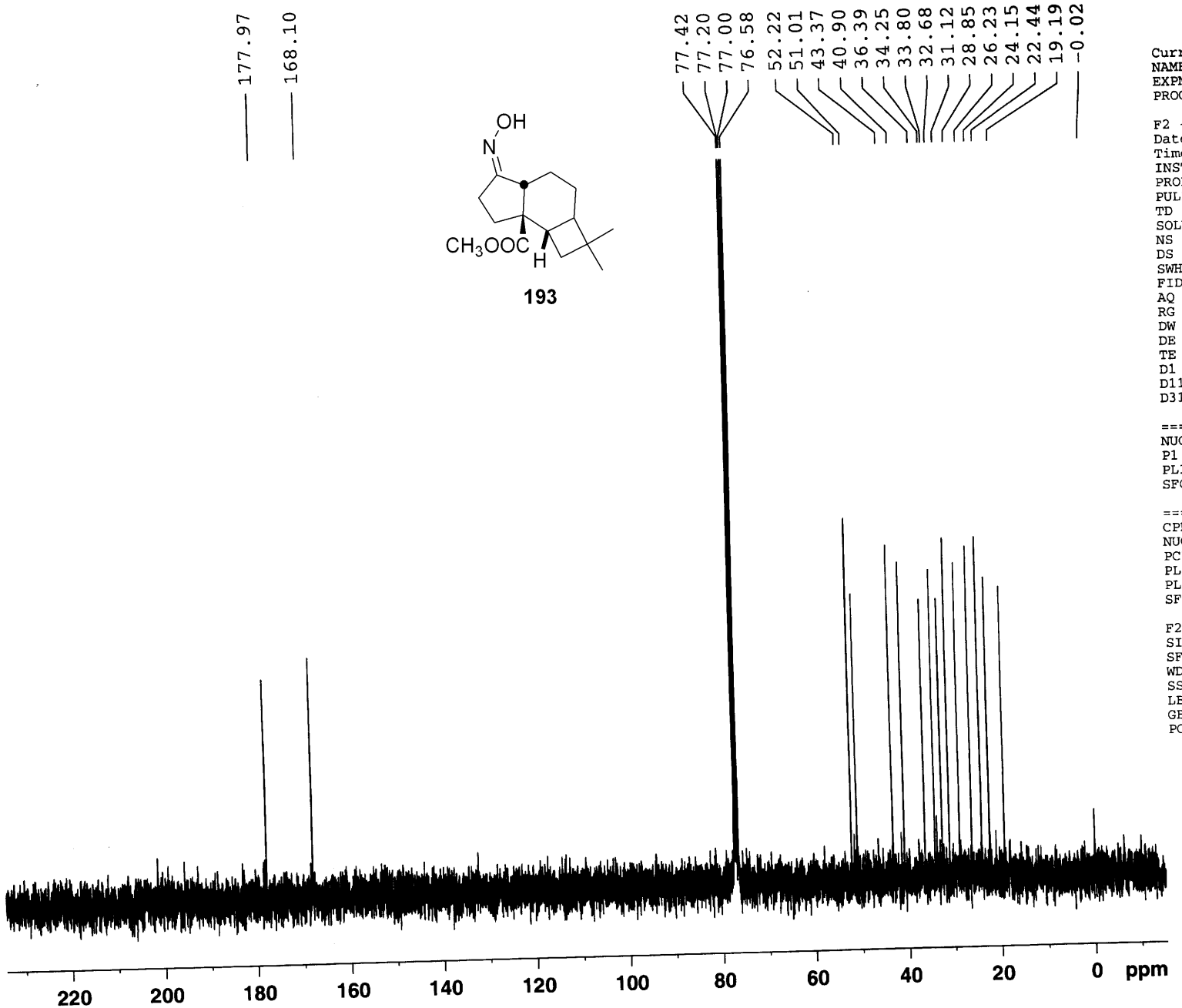
F2 - Acquisition Parameters
Date_ 20070913
Time 12.40
INSTRUM DRX300
PROBHD 5 mm Multinucl
PULPROG zg30pad
TD 32768
SOLVENT CDCl3
NS 16
DS 2
SWH 6172.839 Hz
FIDRES 0.188380 Hz
AQ 2.6542580 sec
RG 228.1
DW 81.000 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec
D31 0.00000000 sec

======== CHANNEL f1 ========
NUC1 1H
P1 7.05 usec
PL1 0.00 dB
SFO1 300.1318534 MHz

F2 - Processing parameters
SI 32768
SF 300.1300039 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.40



13C NMR



Current Data Parameters

NAME	MG-VII-86cr
EXPNO	2
PROCNO	1

F2 - Acquisition Parameters

Date_	20070913
Time	12.44
INSTRUM	DRX300
PROBHD	5 mm Multinucl
PULPROG	zgdc30pad
TD	65536
SOLVENT	CDCl3
NS	267
DS	4
SWH	18832.393 Hz
FIDRES	0.287360 Hz
AQ	1.7400308 sec
RG	22528
DW	26.550 usec
DE	6.00 usec
TE	300.0 K
D1	2.00000000 sec
D11	0.03000000 sec
D31	0.00000000 sec

======== CHANNEL f1 ========

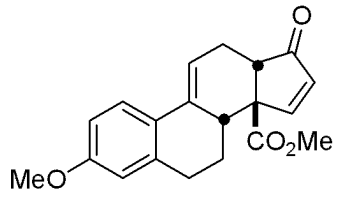
NUC1	13C
P1	9.00 usec
PL1	5.00 dB
SFO1	75.4760107 MHz

======== CHANNEL f2 ========

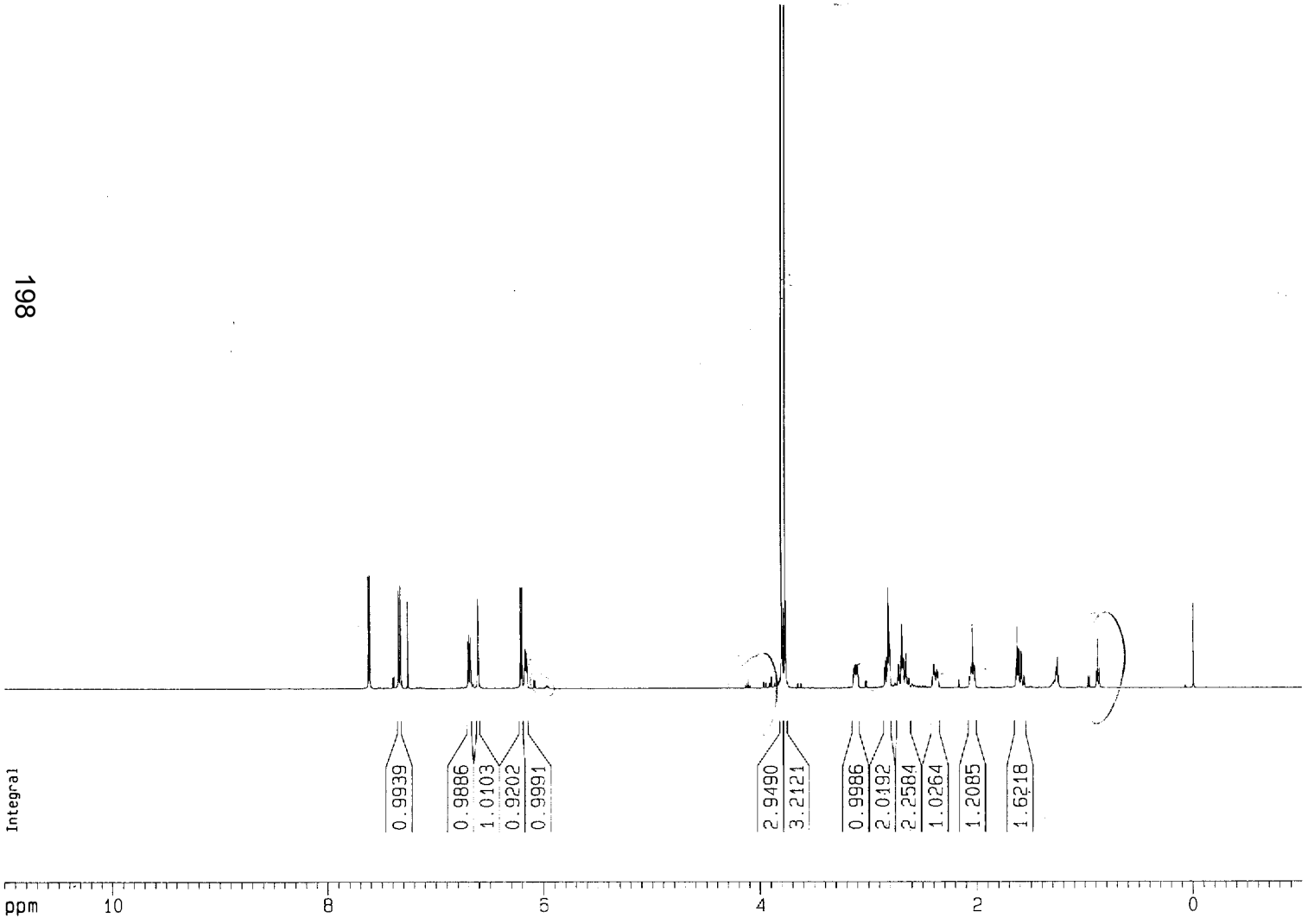
CPDPRG2	waltz16
NUC2	1H
PCPD2	100.00 usec
PL2	120.00 dB
PL12	21.41 dB
SFO2	300.1312005 MHz

F2 - Processing parameters

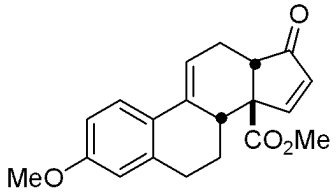
SI	32768
SF	75.4677502 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40



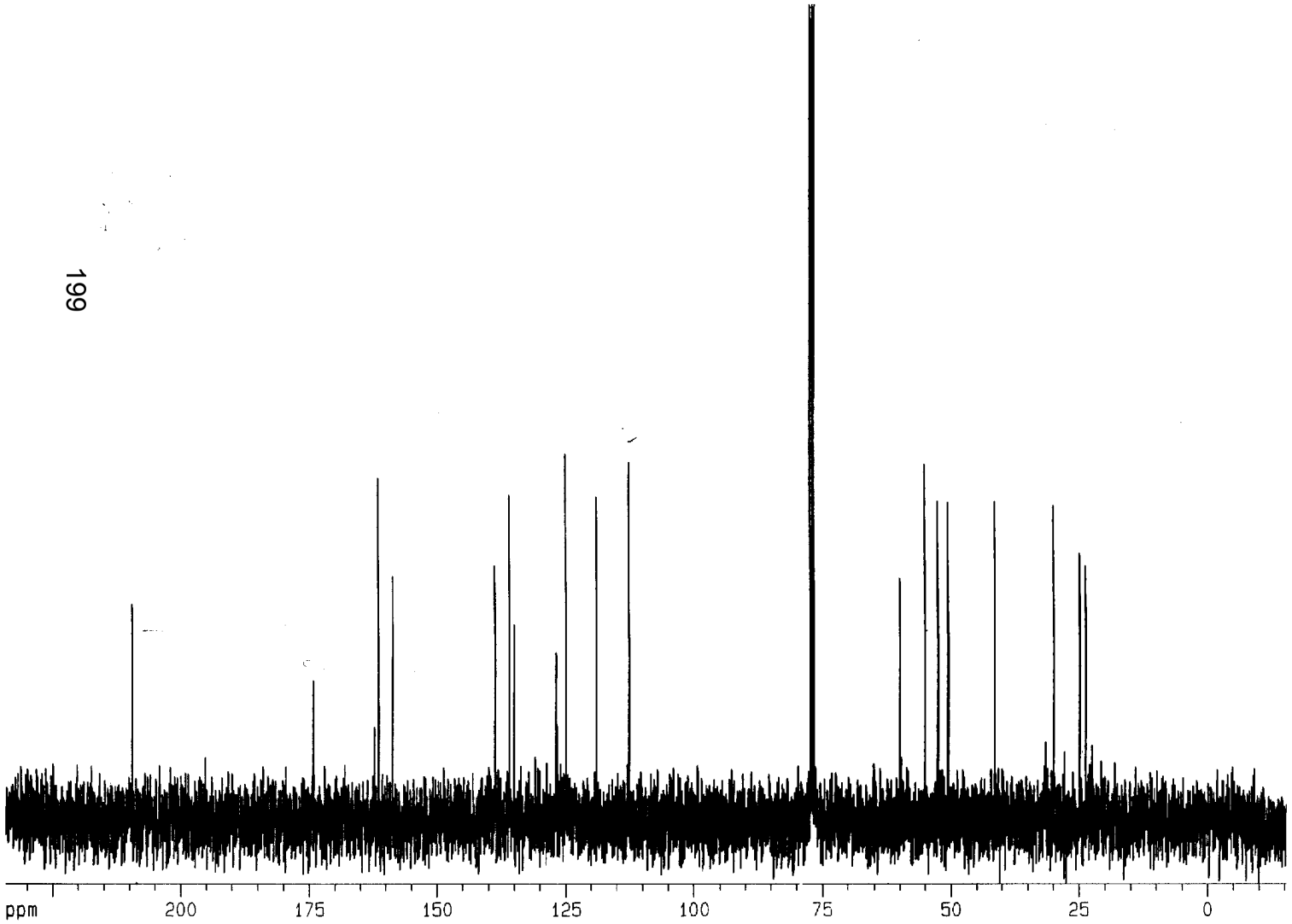
221




```
Current Data Parameters
NAME        MG-3-061a-500
EXPNO               1
PROCNO              1

F2 - Acquisition Parameters
Date_          20041102
Time             20.39
INSTRUM          DRX500
PROBHD   5 mm Multinucl
PULPROG          zg30
TD              57344
SOLVENT          CDCl3
NS                 16
DS                  2
SWH          10330.578 Hz
FIDRES        0.180151 Hz
AQ            2.7754996 sec
RG                101.6
DW             48.400 usec
DE              6.00 usec
TE              296.7 K
D1          1.00000000 sec

======== CHANNEL f1 ========
NUC1                1H
P1             13.25 usec
PL1             -3.00 dB
SFO1       500.1330885 MHz

F2 - Processing parameters
SI                 32768
SF         500.1300125 MHz
WDW                EM
SSB                 0
LB              0.20 Hz
GB                  0
PC                1.40

1D NMR plot parameters
CX              20.00 cm
CY              15.00 cm
F1P             11.000 ppm
F1             5501.43 Hz
F2P             -1.000 ppm
F2             -500.13 Hz
PPMCM          0.60000 ppm/cr
HZCM          300.07800 Hz/cm
```



221



Current Data Parameters
NAME MG-3-050a-300
EXPNO 2
PROCNO 1

F2 - Acquisition Parameters
Date_ 20041101
Time 22.58
INSTRUM drx300
PROBHD 5 mm Multinucl
PULPROG zgdc30
TD 65536
SOLVENT CDCl3
NS 78
DS 4
SWH 18832.393 Hz
FIDRES 0.287360 Hz
AQ 1.7400308 sec
RG 22528
DW 26.550 usec
DE 6.00 usec
TE 297.1 K
D1 1.29999995 sec
d11 0.03000000 sec
D31 0.00000000 sec

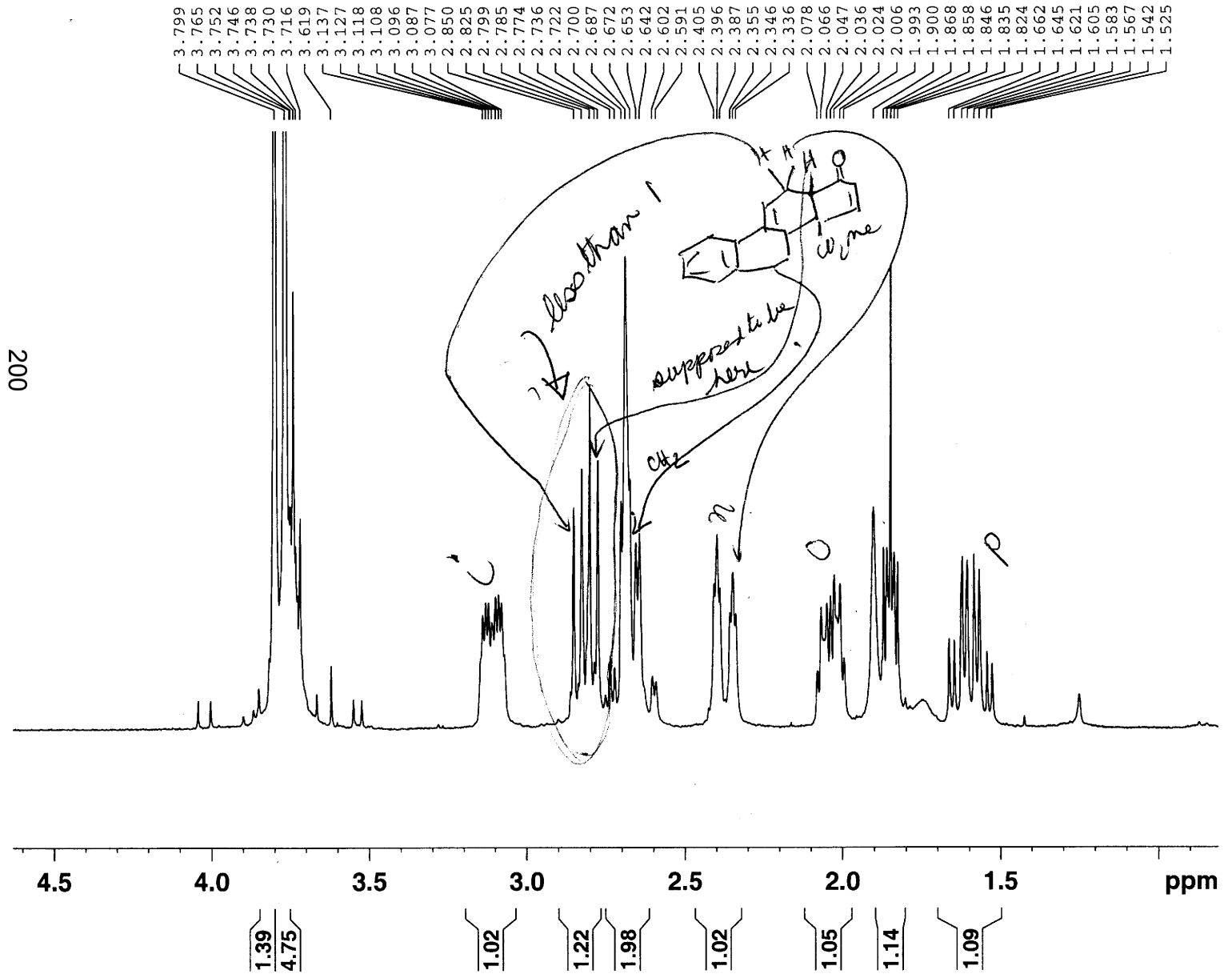
======== CHANNEL f1 ========
NUC1 13C
P1 8.50 usec
PL1 5.00 dB
SFO1 75.4760107 MHz

======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 120.00 dB
PL12 25.60 dB
SFO2 300.1312005 MHz

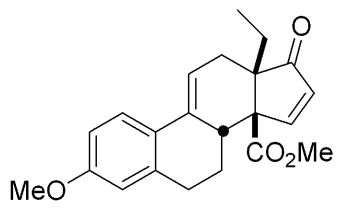
F2 - Processing parameters
SI 32768
SF 75.4677514 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

1D NMR plot parameters
CX 20.00 cm
CY 20.00 cm
F1P 234.213 ppm
F1 17675.51 Hz
F2P -15.329 ppm
F2 -1156.88 Hz
PPMCM 12.47711 ppm/cm
HZCM 941.61957 Hz/cm

MG-VII-17-crude
Enolate formation with NaHMDS and quench with D20

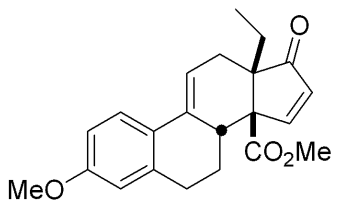



```
Current Data Parameters
NAME                  MG-VII-17-cr
EXPNO                            1
PROCNO                           1

F2 - Acquisition Parameters
Date_                     20070226
Time                         22.07
INSTRUM                     DRX300
PROBHD           5 mm Multinucl
PULPROG                   zg30pad
TD                          32768
SOLVENT                      CDCl3
NS                              16
DS                               2
SWH                       6172.839 Hz
FIDRES                    0.188380 Hz
AQ                        2.6542580 sec
RG                          228.1
DW                         81.000 usec
DE                          6.00 usec
TE                          300.0 K
D1                        1.00000000 sec
D31                       0.00000000 sec

======== CHANNEL f1 ========
NUC1                            1H
P1                           7.05 usec
PL1                          0.00 dB
SFO1                  300.1318534 MHz

F2 - Processing parameters
SI                              32768
SF                    300.1300062 MHz
WDW                             EM
SSB                              0
LB                           0.30 Hz
GB                               0
PC                           1.30
```



228


```
Current Data Parameters
NAME          MG-VI-90a-A3
EXPNO                    1
PROCNO                   1

F2 - Acquisition Parameters
Date_             20060926
Time                 10.03
INSTRUM             DRX500
PROBHD    5 mm Multinucl
PULPROG           zg30pad
TD                  65536
SOLVENT             CDCl3
NS                     16
DS                      2
SWH           10330.578 Hz
FIDRES         0.157632 Hz
AQ            3.1719923 sec
RG                  71.8
DW                48.400 usec
DE                 6.00 usec
TE                300.0 K
D1           1.00000000 sec
D31          0.00000000 sec

======== CHANNEL f1 ========
NUC1                   1H
P1                 11.50 usec
PL1                 0.00 dB
SFO1        500.1330885 MHz

F2 - Processing parameters
SI                  32768
SF          500.1300125 MHz
WDW                    EM
SSB                     0
LB                 0.30 Hz
GB                      0
PC                   1.40
```



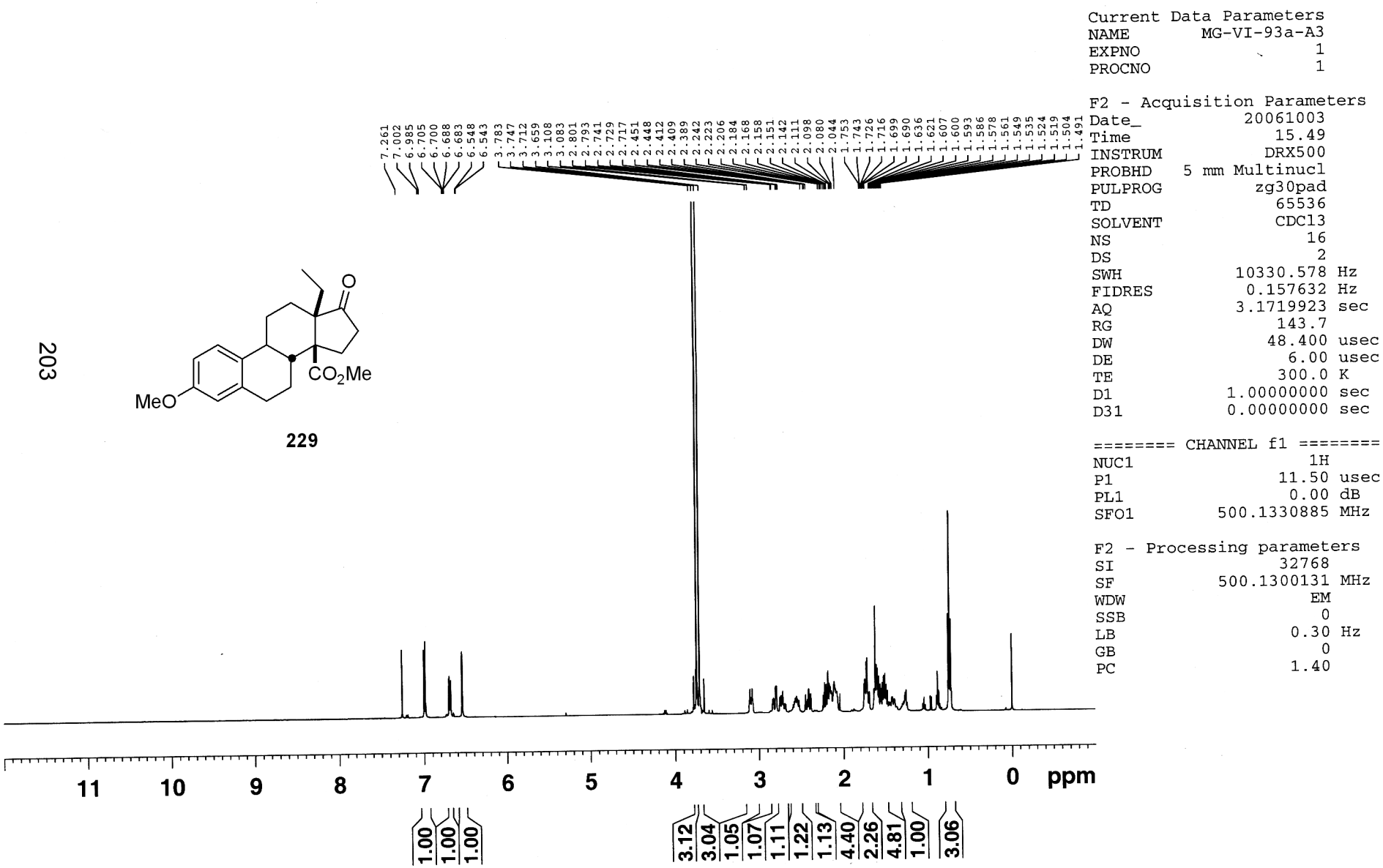
228

211.76
173.60
161.64
158.69
138.68
135.24
135.13
127.09
125.01
119.74
112.65
112.60
77.25
77.00
76.74
64.02
57.67
55.21
52.24
43.59
32.70
30.12
28.09
24.06
8.60

240 220 200 180 160 140 120 100 80 60 40 20 0 ppm

```
Current Data Parameters
NAME          MG-VI-90a-A3
EXPNO                    2
PROCNO                   1

F2 - Acquisition Parameters
Date_             20060926
Time                 10.11
INSTRUM              DRX500
PROBHD    5 mm Multinucl
PULPROG              zgdc30
TD                    65536
SOLVENT               CDCl3
NS                      116
DS                        4
SWH               34013.605 Hz
FIDRES             0.519006 Hz
AQ                 0.9634292 sec
RG                    32768
DW                   14.700 usec
DE                    6.00 usec
TE                   300.0 K
D1                2.00000000 sec
d11               0.03000000 sec
D31               0.00000000 sec

======== CHANNEL f1 ========
NUC1                    13C
P1                    8.10 usec
PL1                   3.00 dB
SFO1          125.7723786 MHz

======== CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                    1H
PCPD2                88.00 usec
PL2                   0.00 dB
PL12                 21.00 dB
SFO2          500.1320005 MHz

F2 - Processing parameters
SI                      32768
SF            125.7577948 MHz
WDW                        EM
SSB                         0
LB                   1.00 Hz
GB                          0
PC                       1.40
```

MG-VI-093a
Reduction of Et-DA adduct, with H2, Pd/C, over reduction
1H NMR



229

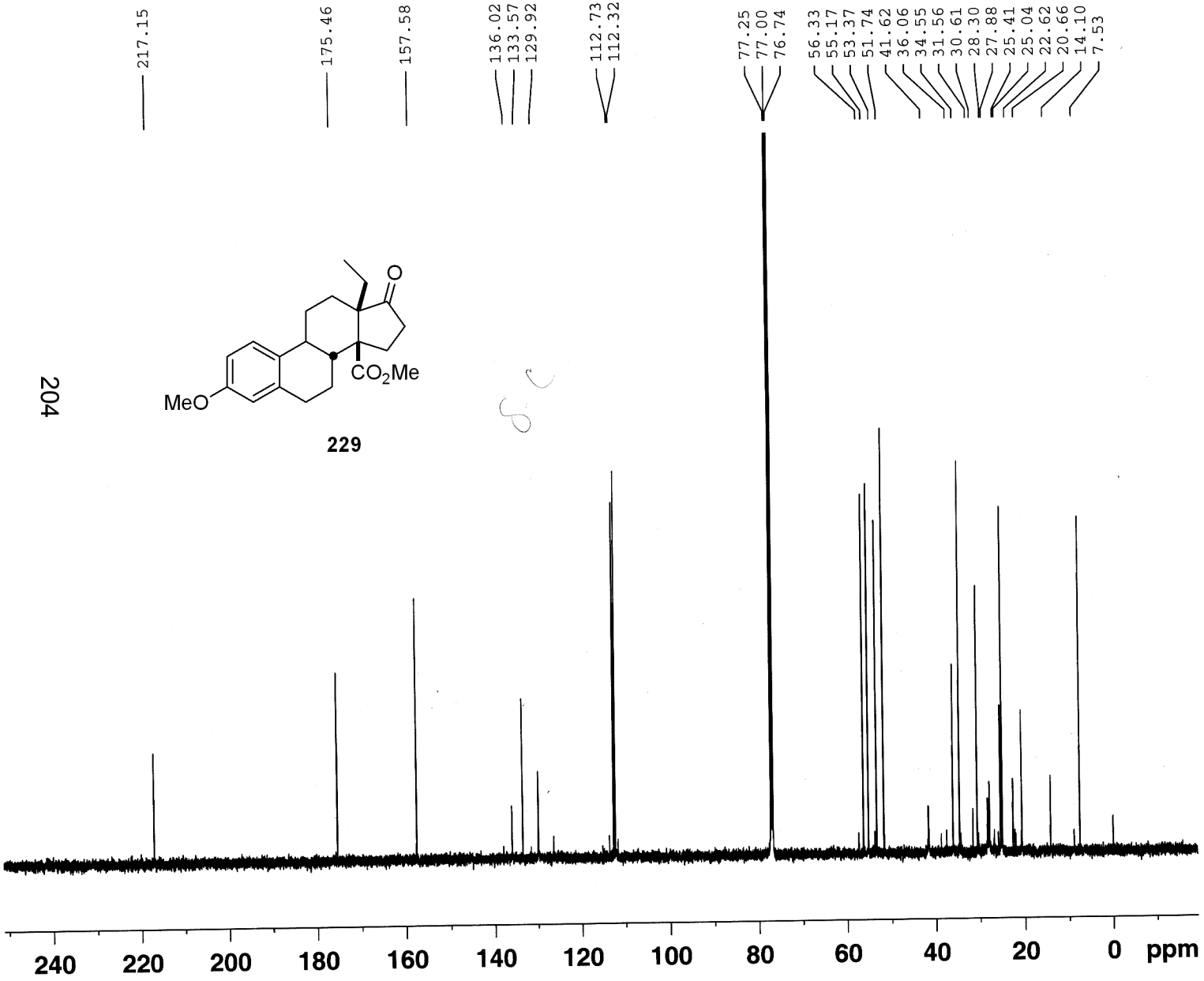
Current Data Parameters
NAME MG-VI-93a-A3
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20061003
Time 15.49
INSTRUM DRX500
PROBHD 5 mm Multinucl
PULPROG zg30pad
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 10330.578 Hz
FIDRES 0.157632 Hz
AQ 3.1719923 sec
RG 143.7
DW 48.400 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec
D31 0.00000000 sec

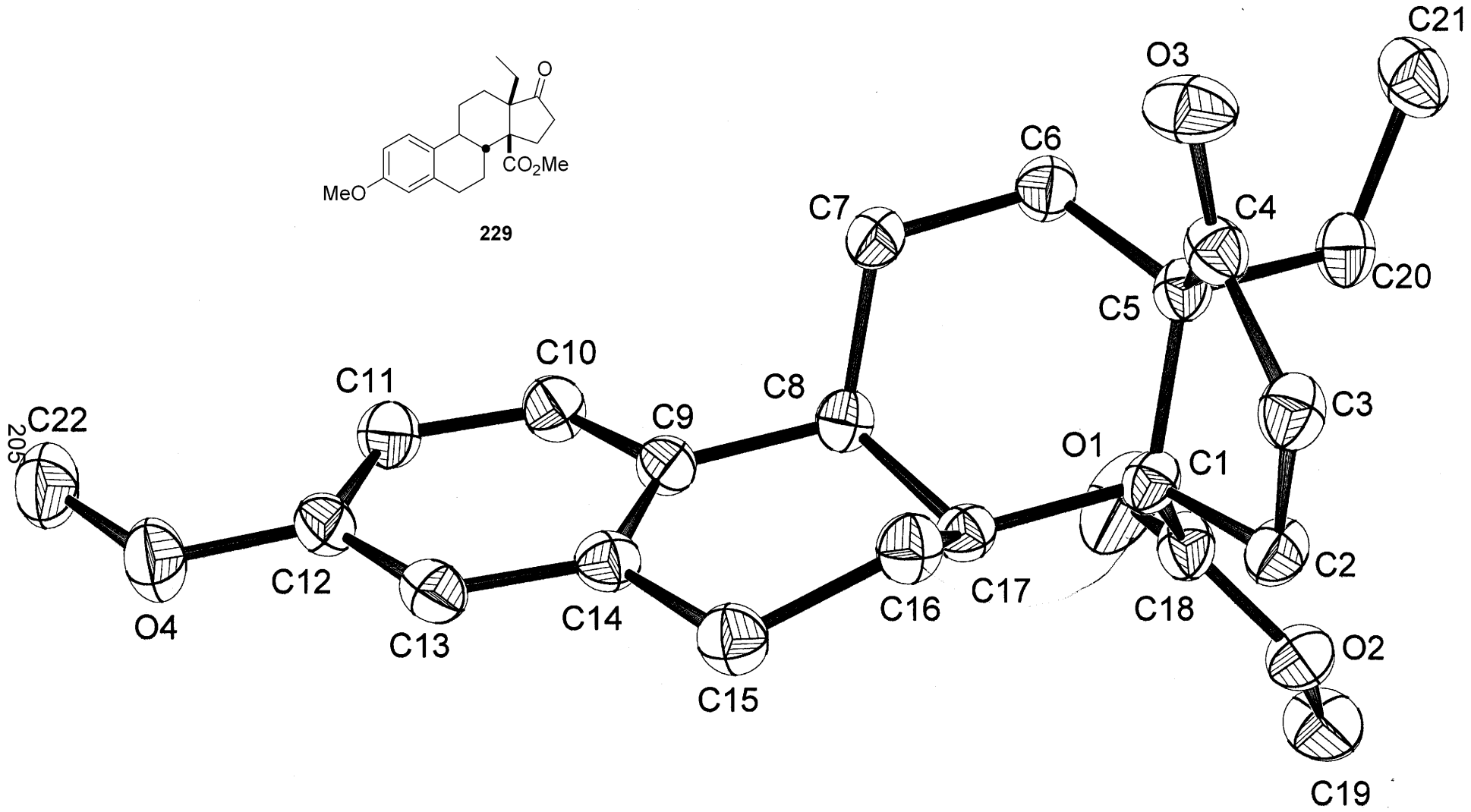
======== CHANNEL f1 ========
NUC1 1H
P1 11.50 usec
PL1 0.00 dB
SFO1 500.1330885 MHz

F2 - Processing parameters
SI 32768
SF 500.1300131 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.40

13C NMR




```
Current Data Parameters
NAME            MG-VI-93a-A3
EXPNO                      2
PROCNO                     1

F2 - Acquisition Parameters
Date_                20061003
Time                    15.53
INSTRUM                DRX500
PROBHD   5 mm Multinucl
PULPROG                zgdc30
TD                      65536
SOLVENT                 CDCl3
NS                       1417
DS                          4
SWH                34013.605 Hz
FIDRES             0.519006 Hz
AQ                 0.9634292 sec
RG                      32768
DW                   14.700 usec
DE                    6.00 usec
TE                    300.0 K
D1                 2.00000000 sec
d11                0.03000000 sec
D31                0.00000000 sec

======== CHANNEL f1 ========
NUC1                      13C
P1                     8.10 usec
PL1                    3.00 dB
SFO1           125.7723786 MHz

======== CHANNEL f2 ========
CPDPRG2               waltz16
NUC2                      1H
PCPD2                 88.00 usec
PL2                    0.00 dB
PL12                  21.00 dB
SFO2           500.1320005 MHz

F2 - Processing parameters
SI                      32768
SF             125.7577948 MHz
WDW                        EM
SSB                         0
LB                     1.00 Hz
GB                          0
PC                     1.40
```


O
CO2Me
MeO
229
C21
O3
C6
C7
C4
C20
C5
C10
C11
C8
C3
C22
205
C9
O1
C1
C12
C2
C17
C16
C18
O4
C13
C14
O2
C15
C19

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