



Development of rhodium and cobalt catalyzed cycloadditions
by David B Belanger

A thesis submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy in Chemistry

Montana State University

© Copyright by David B Belanger (1999)

Abstract:

Initial studies on the asymmetric Rh-catalyzed [4+2] cycloaddition using cationic rhodium complexes have shown that the nature of the counterion can dramatically affect the rate of cyclization. This discovery is expected to lead to catalyst systems with improved selectivity and efficiency. The first examples of a $\text{Co}_2(\text{CO})_8$ -catalyzed carbonylative cyclization of allenynes have been discovered. In most cases, product selectivities and yields can be improved by altering alkyne substitution. A novel rhodium-catalyzed carbonylative cyclization of allenynes at 1 atm of CO has been discovered. A novel rhodium-catalyzed cycloisomerization of allenynes has been discovered. An improved method for the catalytic photopromoted intramolecular Pauson-Khand reaction has been developed. It was discovered that careful control of the internal reaction temperature allows for efficient catalysis without photochemical activation. Additional studies on the substrate-based control of diastereoselectivity in the catalytic Pauson-Khand reaction have also been described. The development of an alternative precatalyst for the Pauson-Khand reaction has been described. This novel catalyst offers several advantages over traditional catalyst for the Pauson-Khand reaction as it is easily prepared and is stable in air.

DEVELOPMENT OF RHODIUM AND COBALT CATALYZED CYCLOADDITIONS

by

David B. Belanger

A thesis submitted in partial fulfillment
of the requirements for the degree

of

Doctor of Philosophy

in

Chemistry

MONTANA STATE UNIVERSITY
Bozeman, Montana

November 1999

APPROVAL

D378
B4124

of a thesis submitted by

David B. Belanger

This thesis has been read by each member of the thesis committee and has been found to be satisfactory regarding content, English usage, format, citations, bibliographic style and consistency, and is ready for submission to the College of Graduate Studies.

11/8/99
DateTom V. H.
Chairperson, Graduate Committee

Approved for the Major Department

11/8/99
DatePaul S. S.
Head, Major Department

Approved for the College of Graduate Studies

11-22-99
DateBruce R. McLeod
Graduate Dean

STATEMENT OF PERMISSION TO USE

In presenting this thesis in partial fulfillment of the requirements for a doctoral degree at Montana State University-Bozeman, I agree that the Library shall make it available to borrowers under the rules of the Library. I further agree that copying of this thesis is allowable only for scholarly purposes, consistent with "fair use" as prescribed in the U.S. Copyright Law. Requests for extensive copying or reproduction of this thesis should be referred to University Microfilms International, 300 North Zeeb Road, Ann Arbor, Michigan 48106, to whom I have granted "the exclusive right to reproduce and distribute my dissertation in and from microform along with the non-exclusive right to reproduce and distribute my abstract in any format in whole or in part."

Signature Dwight B. Bulger

Date 11/8/99

ACKNOWLEDGMENTS

I would like to thank Professor Tom Livinghouse for the opportunity to develop my skills under his advisement. I also thank Tom for his enthusiastic support of this work and for the occasional use of the "Iron Fist". I thank the Chemistry Department office staff, particularly Mary McLaughlin and Carol Thurston, for their help during my stay at MSU. I acknowledge Drs. Joe Seárs and Scott Busse for their work obtaining relevant analytical data. I would like to thank the talented individuals in the Livinghouse group that have positively affected this work. Special thanks to Brad Wolfe for reviewing the main chapters of this thesis. I thank the "truckdrivin' neighbor downstairs", Todd Meyer, for his invaluable assistance in the late stages of this endeavor. I thank Drs. Brian Pagenkopf and Donogh O'Mahony for their contribution to the science that is described in this dissertation. Special thanks to Dr. Donogh O'Mahony for his guidance and for teaching me how to find (and remove) the "yellow band of misery". Lastly, I thank my family for their boundless generosity and love. I dedicate this accomplishment to them.

TABLE OF CONTENTS

	Page
1. INTRODUCTION	1
2. BACKGROUND	2
2.1 Rhodium-Catalyzed [4+1] Cycloadditions	2
2.2 Transition Metal-Catalyzed [2+2+1] Cycloadditions	7
a. Stoichiometric Pauson-Khand Reaction	7
b. Catalytic Pauson-Khand Reaction	12
c. Ruthenium-Catalyzed [2+2+1] Cycloaddition	22
d. Rhodium-Catalyzed [2+2+1] Cycloaddition	24
e. Nickel-Catalyzed [2+2+1] Cycloaddition	26
f. Titanium-Catalyzed [2+2+1] Cycloaddition	26
2.3 Transition Metal-Catalyzed [4+2] Cycloadditions	31
a. Nickel-Catalyzed [4+2] Cycloaddition	31
b. Palladium-Catalyzed [4+2] Cycloadditions	34
c. Intermolecular Rhodium-Catalyzed [4+2] Cycloadditions	36
d. Intramolecular Rhodium-Catalyzed [4+2] Cycloaddition	37
e. Enantioselective Rhodium-Catalyzed [4+2] Cycloaddition	43
2.4 Rhodium-Catalyzed [5+2] Cycloadditions	46
a. Intramolecular Rhodium-Catalyzed [5+2] Cycloaddition	46
b. Intermolecular Rhodium-Catalyzed [5+2] Cycloaddition	49
3. RESULTS AND DISCUSSION	51
3.1 Rhodium-Catalyzed [4+2] Cycloaddition	51
a. Introduction	51

b. Asymmetric Catalysis with Cationic Rhodium Complexes	53
c. Studies Towards the Synthesis of Conformationally-Restricted Chiral Phosphine Ligands.....	61
3.2 Catalytic Pauson-Khand Reaction	70
a. Introduction.....	70
b. $\text{Co}_2(\text{CO})_8$ -Catalyzed Carbonylative Allenyne Cyclizations	74
c. Rhodium-Catalyzed Carbonylative Allenyne Cyclization	87
d. Thermally-Promoted Catalytic Pauson-Khand Reaction	94
3.3 Development of More Stable Alternatives to $\text{Co}_2(\text{CO})_8$ for the Catalytic Pauson-Khand Reaction	108
a. Introduction.....	108
b. Alkyne-Cobalt Complexes as Precatalysts for the Pauson-Khand Reaction.....	110
4. SUMMARY.....	127
5. EXPERIMENTAL.....	128
5.1 General Experimental Details.....	128
5.2 Chiral Phosphines and Related Precursors	130
5.3 Rhodium-Catalyzed [4+2] Cycloaddition.....	141
5.4 Catalytic Carbonylative Cyclization of Allenynes.....	157
5.5 Rhodium-Catalyzed Cycloisomerization of Allenynes	196
5.6 Catalytic Pauson-Khand Reaction of Enynes	202
REFERENCES	237
APPENDICES	249
APPENDIX A List of Abbreviations.....	250
APPENDIX B ^1H and ^{13}C Spectra of Compounds.....	255

LIST OF TABLES

Table	Page
2.1 Catalytic Photopromoted Pauson-Khand Reaction	17
3.1 Counterion Effects on the Enantioselective Rh-Catalyzed [4+2] Cycloaddition.....	59
3.2 Preparation of Allenynes via the Mitsunobu Reaction.....	76
3.3 Rh-Catalyzed Cycloisomerization of Allenynes.....	90
3.4 Photochemical versus Thermal Promotion of the Catalytic Pauson-Khand Reaction	95
3.5 Thermal Catalytic Pauson-Khand Reaction of Malonate-Derived Enynes with $\text{Co}_2(\text{CO})_8$	98
3.6 Thermal Catalytic Pauson-Khand Reaction of Tosamide-Derived Enynes with $\text{Co}_2(\text{CO})_8$	99
3.7 Thermal Catalytic Pauson-Khand Reaction of Stereogenic Enynes with $\text{Co}_2(\text{CO})_8$	101
3.8 Thermal Catalytic Pauson-Khand Reaction of Stereogenic Thiomethyl- Enynes with $\text{Co}_2(\text{CO})_8$	105
3.9 Thermal Catalytic Pauson-Khand Reaction of Stereogenic Thio(<i>t</i> -butyl)- Enynes with $\text{Co}_2(\text{CO})_8$	106
3.10 Catalytic Pauson-Khand Reaction with Alkyne-Cobalt Complexes:.....	112
3.11 Effect of Additives on the PKR with Catalytic 2-Methyl-3-butyn-2-ol· $\text{Co}_2(\text{CO})_6$	116
3.12 Effect of Additives on the PKR with Catalytic Phenylethyne· $\text{Co}_2(\text{CO})_6$	117
3.13 Catalytic PKR with Catalytic Alkyne-Cobalt Complexes and	

Et ₃ SiH as Additive.....	119
3.14 Effect of Various Heating Protocols on the PKR with Catalytic 2-Methyl-3-butyn-2-ol•Co ₂ (CO) ₆	121
3.15 Pauson-Khand Reaction of Malonate-Derived Enynes with Catalytic 2-Methyl-3-butyn-2-ol•Co ₂ (CO) ₆	122
3.16 Pauson-Khand Reaction of Tosamide-Derived Enynes with Catalytic 2-Methyl-3-butyn-2-ol•Co ₂ (CO) ₆	123
3.17 Pauson-Khand Reaction of Stereogenic Enynes with Catalytic 2-Methyl-3-butyn-2-ol•Co ₂ (CO) ₆	125

ABSTRACT

Initial studies on the asymmetric Rh-catalyzed [4+2] cycloaddition using *cationic* rhodium complexes have shown that the nature of the counterion can dramatically affect the rate of cyclization. This discovery is expected to lead to catalyst systems with improved selectivity and efficiency. The first examples of a $\text{Co}_2(\text{CO})_8$ -catalyzed carbonylative cyclization of allenyne have been discovered. In most cases, product selectivities and yields can be improved by altering alkyne substitution. A novel rhodium-catalyzed carbonylative cyclization of allenyne at 1 atm of CO has been discovered. A novel rhodium-catalyzed cycloisomerization of allenyne has been discovered. An improved method for the catalytic photopromoted intramolecular Pauson-Khand reaction has been developed. It was discovered that careful control of the internal reaction temperature allows for efficient catalysis without photochemical activation. Additional studies on the substrate-based control of diastereoselectivity in the catalytic Pauson-Khand reaction have also been described. The development of an alternative precatalyst for the Pauson-Khand reaction has been described. This novel catalyst offers several advantages over traditional catalyst for the Pauson-Khand reaction as it is easily prepared and is stable in air.

1. INTRODUCTION

This dissertation describes the development of metal catalyzed syntheses of hetero- and carbocyclic molecules. Though the rhodium-catalyzed cycloisomerization, catalytic Pauson-Khand reaction and other related Co- and Rh-catalyzed carbonylative cyclization reactions are believed to proceed through discreet intermediates, the reactions are regarded as cycloaddition reactions.¹ The use of the word cycloaddition is not meant to imply a concerted reaction mechanism, but is merely used as a description of the product bond connectivity.

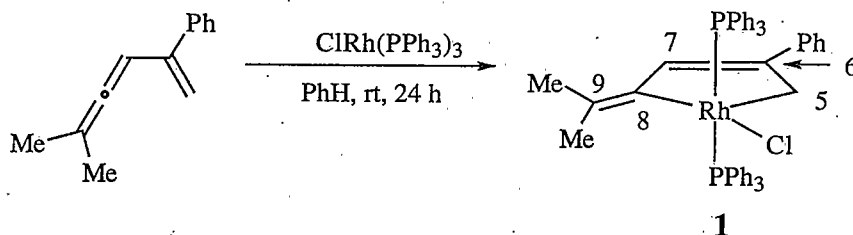
The Background Section contains a brief survey of other metal-catalyzed cycloaddition reactions that are related to the research detailed in this dissertation. The increased interest in metal-catalyzed cycloadditions is evident if one observes that most of the research described in this section has occurred within the last five years. While significant effort has been made to include all relevant chemistry, the rate of new discoveries in this area will almost surely make the review obsolete in a short time.

The Results and Discussion Section describes the original discoveries that have been made. In some cases, the contributions of others are presented to more clearly demonstrate the current scope and limitations of the described chemistry.

2. BACKGROUND

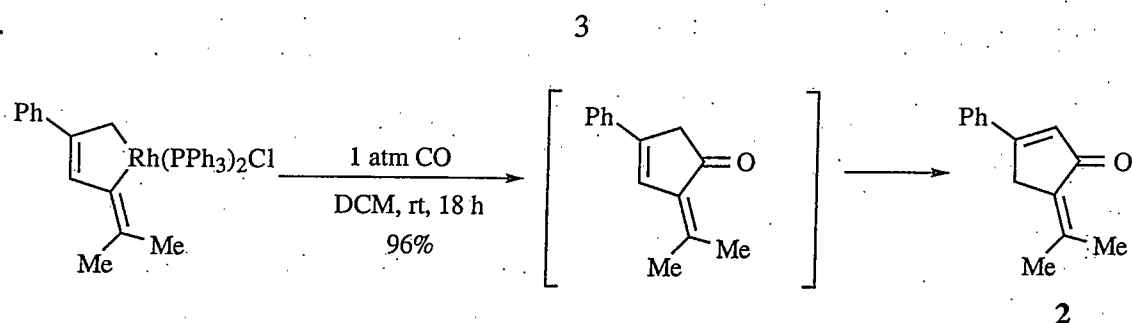
2.1 Rhodium-Catalyzed [4+1] Cycloadditions

Few methods for the formal [4+1] cycloaddition exist despite its potential for the construction of cyclopentenones.¹ Ito has shown that $\text{ClRh}(\text{PPh}_3)_3$ oxidatively adds to vinylallenes. The *pentacoordinate*, distorted octahedral Rh complex **1**, characterized by X-ray crystallography, has a unique structure as the rhodacyclopentene ring is almost planar (Scheme 2.1).^{2b,d} Bond lengths for C6-C7 and C8-C9 were determined to be 1.33 Å



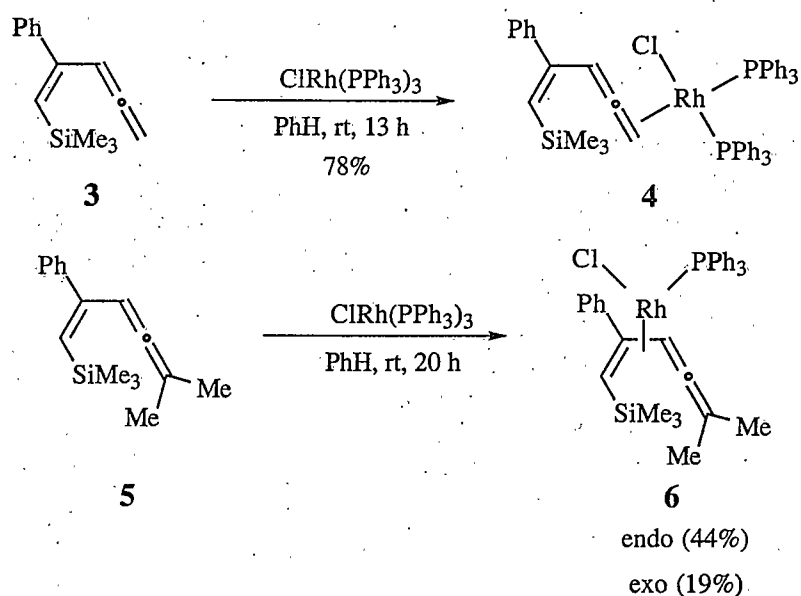
Scheme 2.1

and 1.36 Å, respectively. This suggests that no bonding is occurring between either olefin π -orbital and the Rh center (average bond length for a non-ligated olefin = 1.34 Å). Most notably, the C5-Rh and C8-Rh bond lengths were determined to be identical (2.05 Å), and similar to an sp^3 carbon-rhodium bond (2.02 Å). The bonding characteristics of the two carbon-rhodium bonds suggest that subsequent reactions are possible. Indeed, treatment of the novel rhodium complex with CO formed the α -isopropylidene cyclopentenone **2** after isomerization (Scheme 2.2).



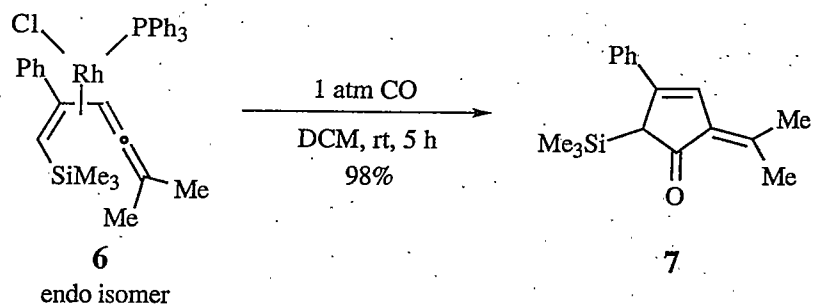
Scheme 2.2

It is also observed that sterically dissimilar vinylallenes ligate to $\text{ClRh}(\text{PPh}_3)_3$ differently. While the terminally unsubstituted allene **3** ligated rhodium via η^2 -



Scheme 2.3

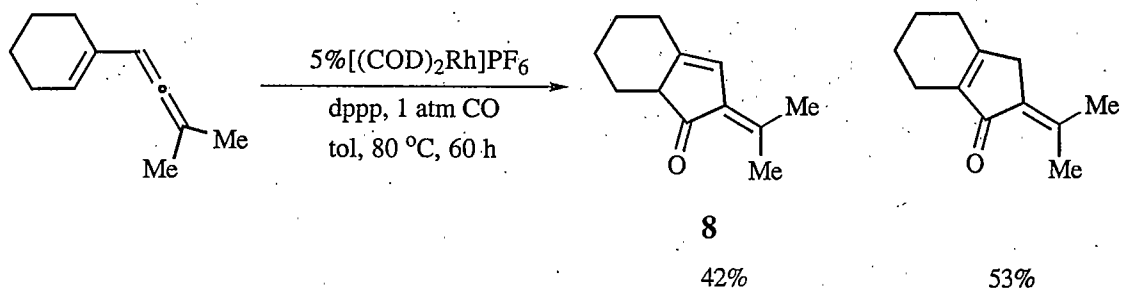
coordination, a related allene **5** bearing dimethyl-substitution ligated in an η^4 fashion (Scheme 2.3).^{2a} Presumably, the sterically encumbered vinyl silane moiety inhibits formation of the rhodacyclopentene. Treatment of the η^4 -bound vinylallene rhodium complex **6** with CO led to the α -isopropylidene cyclopentenone **7** in nearly quantitative



Scheme 2.4

yield (Scheme 2.4). In contrast, the η^2 -ligated vinylallene rhodium complex **4** was unreactive under analogous conditions.

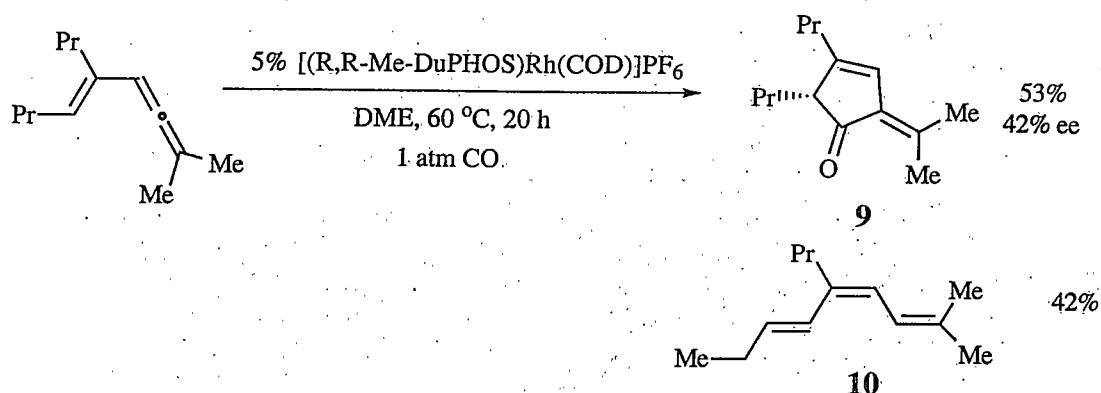
Through the elegant structural studies of vinylallene rhodium complexes, a novel catalytic [4+1] cycloaddition was discovered. Treatment of vinylallenes with Wilkinson's catalyst under 1 atm of CO afforded bicyclopentenones in good yields, though the primary



Scheme 2.5

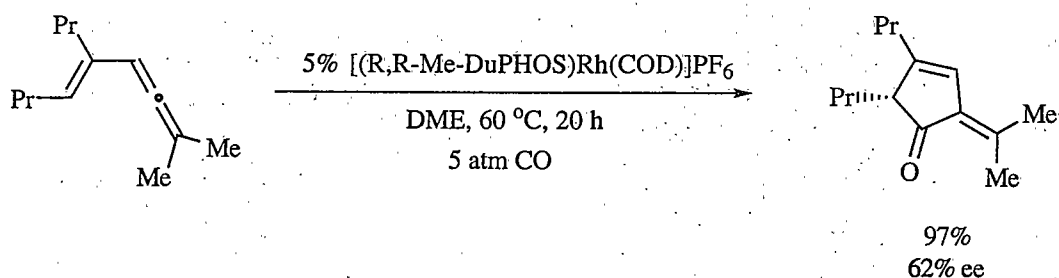
product **8** underwent significant isomerization using these reaction conditions (Scheme 2.5).^{2a}

The enantioselective Rh-catalyzed [4+1] cycloaddition was recently described by Ito. Treatment of vinylallene with 5 mol % [(COD)Rh(R,R-Me-DuPHOS)]PF₆ under 1 atm CO afforded α -isopropylidene cyclopentenone **9** in 53% yield and 42% ee (Scheme 2.6).^{2c} The modest yield resulted from formation of an undesired triene **10**, presumably



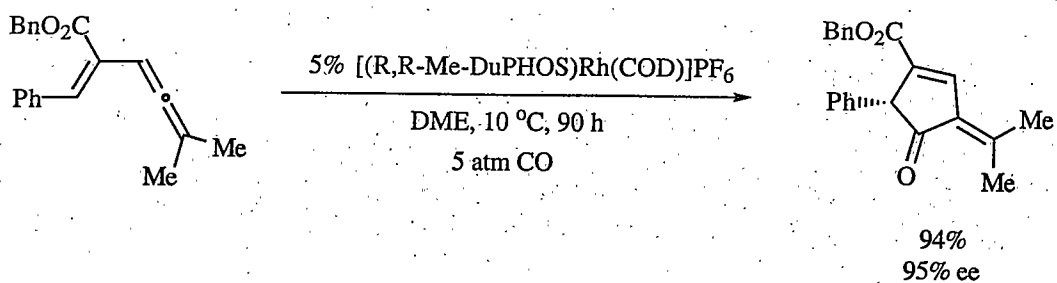
Scheme 2.6

arising through a competing β -hydride elimination/reductive elimination pathway. At higher CO pressures (5 atm), the yield of the expected cyclopentenone **9** was significantly improved. Interestingly, a modest improvement in asymmetric induction was observed at 5



Scheme 2.7

atm of CO (65% ee) (Scheme 2.7).^{2c} Further increases in the CO pressure did not have a notable effect on the level of enantioselection. Carbonylative cyclization of several vinylallene substrates was performed using these conditions affording products with good



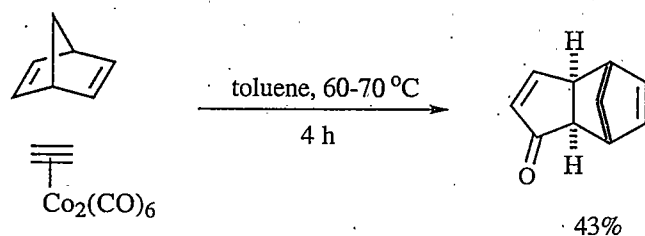
Scheme 2.8

enantiomeric excess. The level of asymmetric induction was dramatically enhanced by judicious placement of an ester functional group (**Scheme 2.8**).^{2c} These ester-modified vinylallenes appear to be more reactive demonstrated by efficient [4+1] cycloaddition at temperatures as low as 10 °C.

2.2 Transition Metal-Catalyzed [2+2+1] Cycloadditions

2.2.a Stoichiometric Pauson-Khand Reaction

Arguably, the most impressive aspect of transition-metal chemistry is the ability to promote C-C bond forming reactions which would otherwise be virtually impossible. The cobalt-mediated [2+2+1] cycloaddition of an alkyne, an alkene and carbon monoxide, introduced by Khand and Pauson in 1973, is representative of the power of such metal-mediated reactions. The method introduced by Pauson required heating alkyne-cobalt

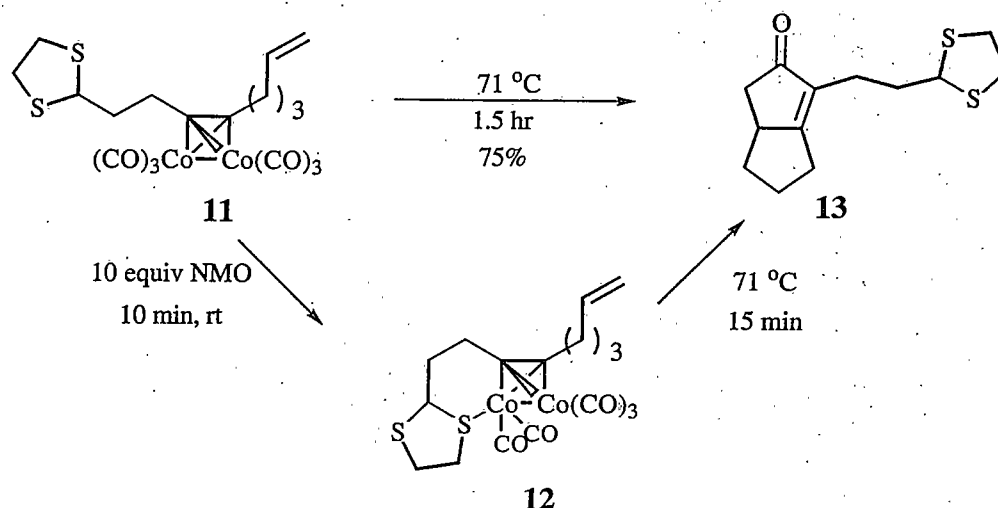


Scheme 2.9

complexes with reactive olefins under an atmosphere of dinitrogen (**Scheme 2.9**).^{3a} Toluene-tetracobaltnonacarbonyl was the only other product isolated from this reaction (22%). Since this seminal discovery, the stoichiometric Pauson-Khand reaction has been well-defined in scope and both the inter- and intramolecular variations are known. The long-standing interest in the PKR has led to several comprehensive reviews.⁴

Despite the intensive study of the Pauson-Khand reaction, very little is known about the reaction mechanism.^{4e} Aside from the initial formation of the alkyne-Co₂(CO)₆ complex, few of the intermediate complexes have either been isolated or observed experimentally. In 1993, Krafft found that treatment of certain enyne-cobalt complexes **11**

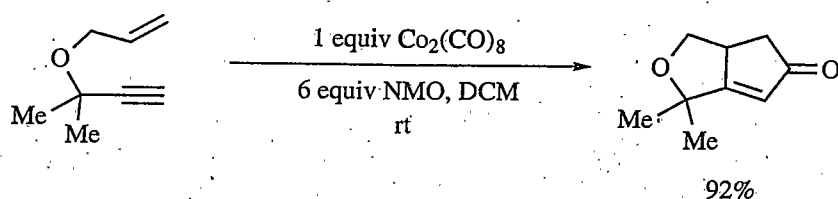
with excess *N*-methyl morpholine *N*-oxide (*vide infra*) afforded isolable complexes **12** in which one of the CO ligands was replaced by a sulfur-cobalt bond (Scheme 2.10).⁵



Scheme 2.10

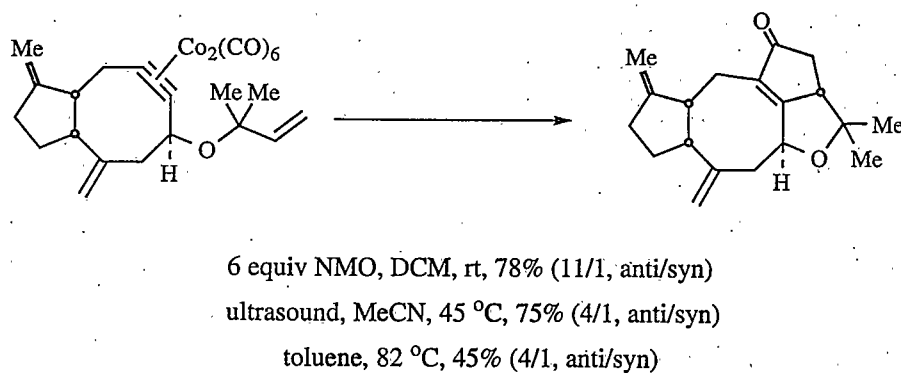
Warming a solution of complex **12** produced the desired pentalenone **13** in only 15 minutes (yield was not reported). In comparison, the corresponding enyne cobalt complex **11** required heating for 1.5 hours to form the same pentalenone **13** (75% yield) (Scheme 2.10). This result suggests that initial loss of carbon monoxide from the enyne-hexacarbonylcobalt complex **11** and subsequent coordination of the pendant olefin provides an intermediate structure that may lie on the mechanistic pathway that leads to product formation.

Though details of the reaction mechanism remain unclear, several groups have introduced procedural modifications that facilitate the stoichiometric Pauson-Khand reaction. In 1990, Schreiber disclosed that excess *N*-methyl morpholine *N*-oxide had a



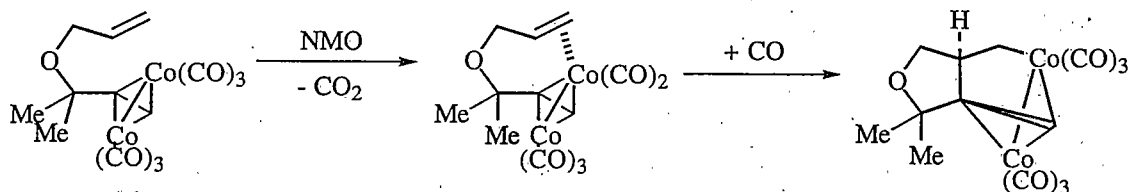
Scheme 2.11

significant rate-accelerating effect on the reaction.⁶ Good yields of bicyclopentenones were isolated using this room temperature procedure (Scheme 2.11). These considerably milder conditions offered improved selectivities when compared to other known methods of that time (Scheme 2.12). It had been known since 1959⁷ that pyridine-*N*-oxide



Scheme 2.12

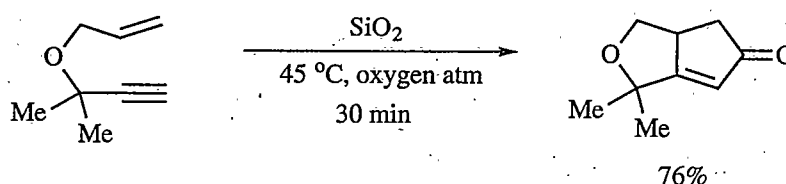
facilitated the removal of CO from metal carbonyl complexes (e.g., $\text{Fe}(\text{CO})_5$), but Schreiber's method is the first example applied to the formation of C-C bonds. Presumably, oxidative decomplexation of CO from the enyne cobalt complex 14 allows



Scheme 2.13

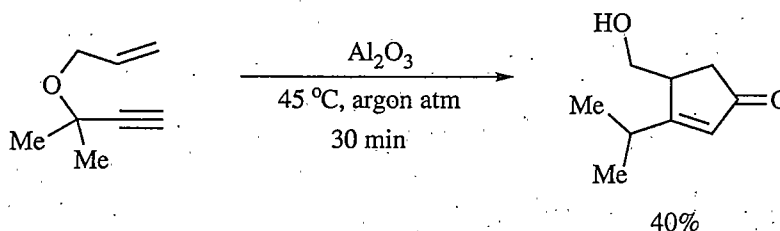
olefin coordination and subsequent oxidative cyclization (**Scheme 2.13**). It is not clear, however, whether NMO has a rate accelerating effect on bond forming events subsequent to olefin coordination.

Another effective method for the promotion of the stoichiometric Pauson-Khand reaction was introduced by Smit and Caple. It was found that adsorption of ether-linked enynes onto silica gel, followed by evaporation of solvent and heating the dry silica gel



Scheme 2.14

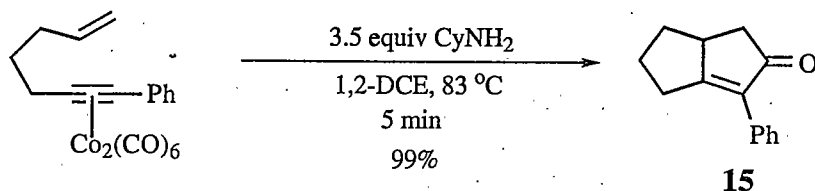
under a slow stream of air led to bicyclopentenones in modest to good yields (**Scheme 2.14**).⁸ While the reason for the improved yields using this method is not entirely evident, one possible explanation is that the conformation of the enyne substrate bound to silica gel is positioned so that the reactive ends are in closer proximity. This manifestation of the reactive rotamer effect appears to be limited to ether-derived enyne substrates. Interestingly, a similar protocol performed on alumina under an argon atmosphere afforded hydroxymethyl cyclopentenones (**Scheme 2.15**).⁸ While the mechanistic origin of these



Scheme 2.15

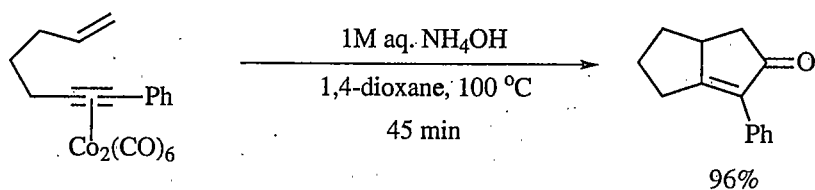
compounds is uncertain, the ease with which the propargyl C-O bond is ruptured is notable as this substrate class often gives reduced yields in the PKR relative to structurally related analogs.⁸²

Recently, certain amines have been used to facilitate the stoichiometric Pauson-Khand reaction. Sugihara discovered that heating enyne cobalt complexes with cyclohexylamine (3.5 to 6 equiv) rapidly afforded bicyclopentenones in excellent yield (Scheme 2.16).⁹ Without the amine additive, the reaction required 10 hours for complete



Scheme 2.16

consumption of starting material and afforded the pentalenone **15** in reduced yield (62%). Sugihara also found that 2M aqueous NH₄OH in 1,4-dioxane (1:3 v/v; dioxane/aq NH₄OH) had a similar rate-accelerating effect though a slightly higher reaction temperature was required (Scheme 2.17).⁹ This is the first example of a Pauson-Khand reaction using water as co-solvent.¹⁰ Several intra- and intermolecular Pauson-Khand reactions



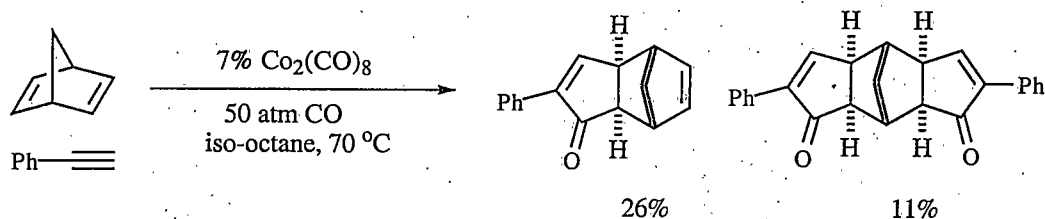
Scheme 2.17

were successfully performed using the procedures developed by Sugihara. While the exact role of the amine remains to be determined, Sugihara suggests that coordinated

cyclohexylamine may facilitate the dissociation of CO and, in turn, promote subsequent ligand substitution reactions. A similar amine-induced rate-accelerating effect has been observed in the ligand substitution chemistry of $\text{Mo}(\text{CO})_5(\text{amine})$ complexes.¹¹

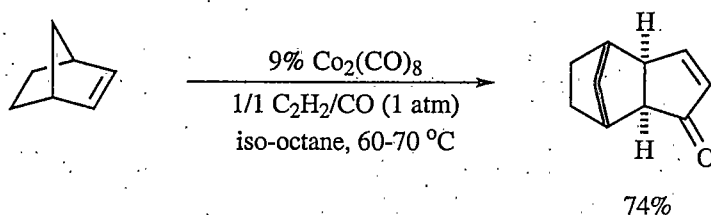
2.2.b Catalytic Pauson-Khand Reaction

Since the discovery of the Pauson-Khand reaction over 25 years ago, only scattered reports of a catalytic variation of the reaction have appeared. This is quite surprising considering that Pauson initially disclosed that catalytic $\text{Co}_2(\text{CO})_8$ was able to achieve



Scheme 2.18

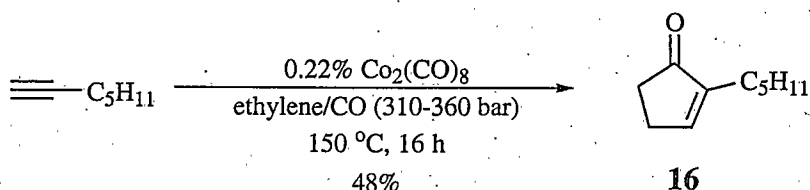
cyclopentenone formation (Scheme 2.18).^{3b} While the intermolecular PKR involving a monosubstituted alkyne required elevated CO pressure (50 atm), the use of a gaseous



Scheme 2.19

alkyne, such as acetylene, allowed for product formation in good yield at *only 1 atm of CO* (Scheme 2.19).^{3b} The inherent instability of $\text{Co}_2(\text{CO})_8$ may reflect, in part, why general catalytic methods have remained elusive until very recently.

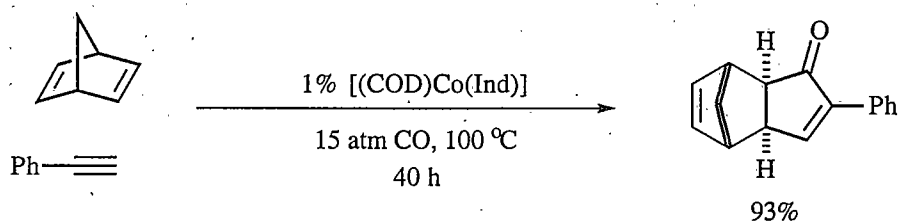
In 1990, Rautenstrauch demonstrated that catalytic $\text{Co}_2(\text{CO})_8$ was effective for the formal [2+2+1] cycloaddition of *n*-heptyne, ethylene and CO under very high pressures of CO and ethylene (initial partial pressures of ethylene and CO at rt were 40 and 100 bar, respectively; total pressure at 150 °C was ca. 310-360 bar) (Scheme 2.20).¹² Although



Scheme 2.20

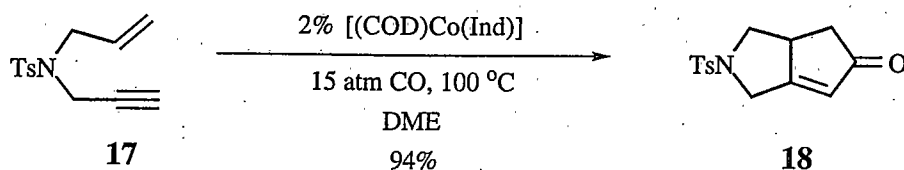
the desired cyclopentenone **16** was obtained in modest yield, this example demonstrates that only catalytic $\text{Co}_2(\text{CO})_8$ could be used for the Pauson-Khand reaction of alkynes and *unstrained* alkenes. Unfortunately, Rautenstrauch found that the method was somewhat irreproducible.¹²

Subsequently, Jeong reported that $(\text{COD})\text{Co}(\text{Ind})$ was a very effective catalyst for the intermolecular Pauson-Khand reaction of strained olefins and terminal alkynes (Scheme 2.21).¹³ The intermolecular PKR of norbornadiene with nonterminal alkynes



Scheme 2.21

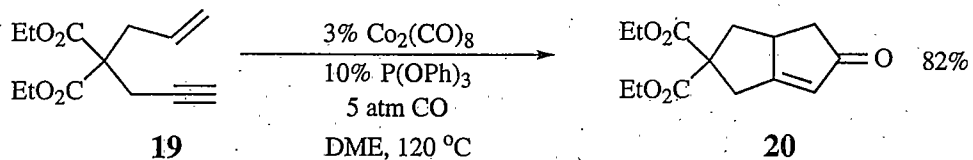
led to markedly reduced yields. In contrast, the enyne **17** bearing a terminal alkyne afforded excellent yield of bicyclopentenone **18** using (COD)Co(Ind) as catalyst precursor (Scheme 2.22).¹³ Interestingly, complexes CpCo(CO)₂ and CpCo(COD) failed to



Scheme 2.22

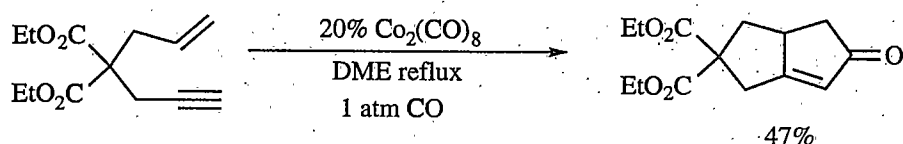
promote bicyclopentenone formation suggesting that η^5 to η^3 ring slippage of the indenyl ligand in [(COD)Co(Ind)] may be necessary for catalytic activity. It is not clear whether Co₂(CO)₈ is formed under the reaction conditions or if a mononuclear cobalt species is the active catalyst. Nevertheless, the development of the first reasonably general catalytic PKR is an important milestone in the long history of this reaction. Though [(COD)Co(Ind)] is described as moderately air-stable, its synthesis requires several steps and is low yielding.¹⁴ In addition, this method may not be attractive to practicing synthetic chemists as it is effective only at very high CO pressures (15 atm).

A more practical method using Co₂(CO)₈ for the catalytic Pauson-Khand reaction was subsequently developed by Jeong. It was discovered that the addition of a coligand, (P(OPh)₃), increased the catalytic turnover to acceptable levels. Specifically, treatment of substrate **19** with Co₂(CO)₈, followed by addition of triphenyl phosphite, then heating allowed for the formation of bicyclopentenone **20** in good yield (Scheme 2.23).¹⁵ Jeong



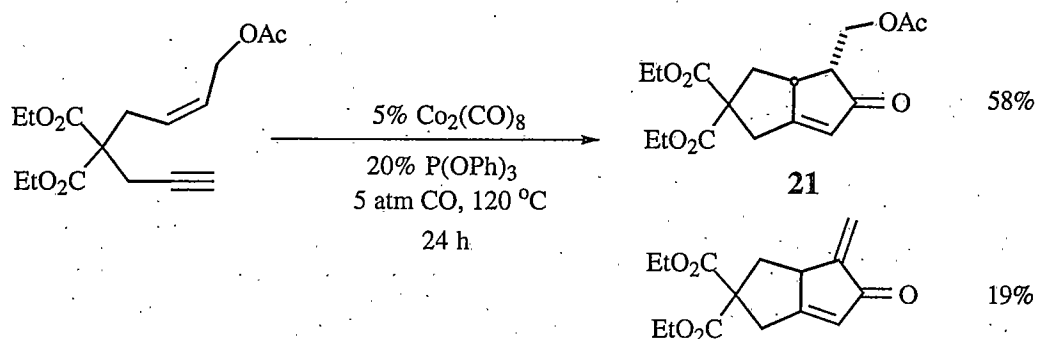
Scheme 2.23

suggested that P(OPh)_3 stabilized the coordinatively unsaturated cobalt species, inhibiting the formation of $\text{Co}_4(\text{CO})_{12}$.¹⁵ The complex $\text{Co}_4(\text{CO})_{12}$ is believed to be catalytically inactive (*vide infra*).^{16,81} Notably, Jeong demonstrated that $\text{Co}_2(\text{CO})_8$ was a poor catalyst precursor without P(OPh)_3 (Scheme 2.24). This finding is consistent with our results on the temperature dependence for successful carbonylative cyclization using catalytic $\text{Co}_2(\text{CO})_8$ at 1 atm CO (*vide infra*). Although moderate CO pressure (4-5 atm) was



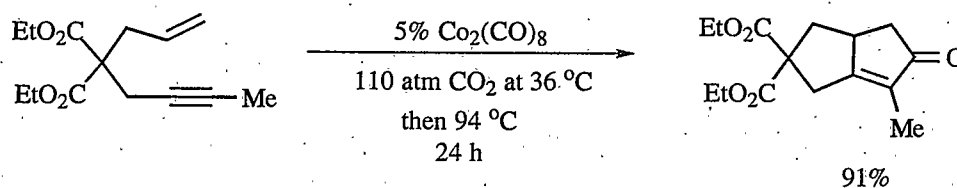
Scheme 2.24

required for effective carbonylative cyclization, the method of Jeong is significant as it only requires the inexpensive, commercially available $\text{Co}_2(\text{CO})_8$ and P(OPh)_3 . One drawback of the method is that the high reaction temperatures may prohibit the synthesis of thermally sensitive cyclopentenones. For example, a low yield of the following carbonylative cyclization was observed due to the β -elimination of acetate from the primary product **21** (Scheme 2.25).¹⁵



Scheme 2.25

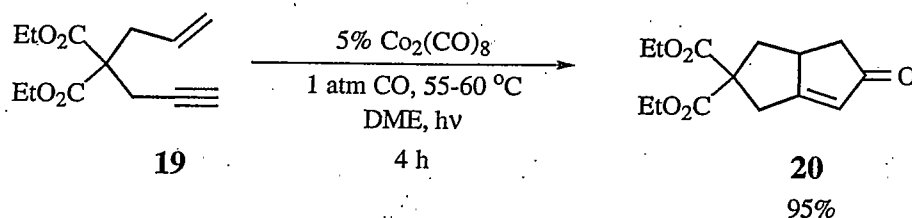
Jeong has recently reported that supercritical CO₂ (Sc CO₂) is a useful medium for the catalytic Pauson-Khand reaction. The perceived advantages of Sc CO₂ are the ease of product isolation, catalyst separation and recovery, the ability to remove and recycle the solvent (CO₂) and the increased solubility of carbon monoxide. Optimal conditions required initial pressurization with carbon monoxide (30 atm at room temperature), subsequent pressurization with CO₂ (110-120 atm at ca. 38 °C) and then heating at 90 °C for 24 hours. A homogeneous supercritical phase was achieved at 40 °C. Modest to



Scheme 2.26

excellent yields of bicyclopentenones were achieved using this procedure (**Scheme 2.26**).¹⁷ One shortcoming of this method is the potential solubility problems of certain substrates in neat Sc CO₂. Jeong noted that several substrates were found to be unreactive towards carbonylative cyclization due to this limitation.¹⁷

In 1996, Pagenkopf and Livinghouse reported an improved procedure for the catalytic Pauson-Khand reaction. It was discovered that efficient cyclization could be achieved using high-purity Co₂(CO)₈ in the presence of high-intensity visible light (Q-Beam irradiation) at *only 1 atmosphere of CO*. Irradiation of a solution of enyne **19** and 5 mol % Co₂(CO)₈ with a 10⁶ candlepower spotlight rapidly formed the desired pentalenone **20** in high yield (**Scheme 2.27**).¹⁸ While the photo-induced dissociation of CO from



Scheme 2.27

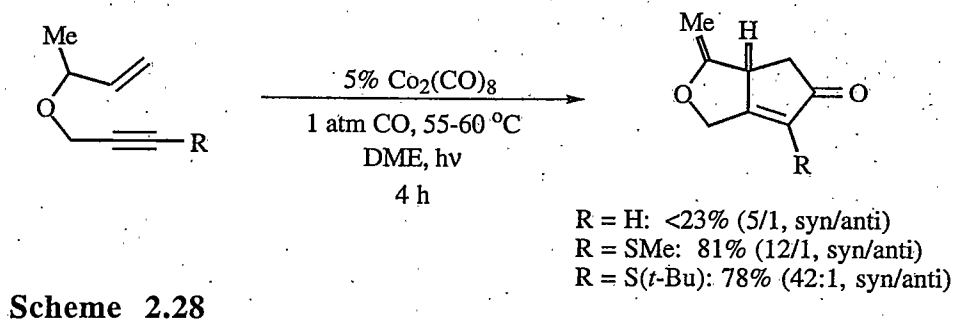
metal carbonyl complexes has been used to facilitate substitution reactions in other metal carbonyl complexes¹⁹, this is the first example that has been applied to the Pauson-Khand reaction. The method has proven to be general as seen in the following examples (Table 2.1).¹⁸

Table 2.1. Catalytic Photopromoted Pauson-Khand Reaction^a

Entry	Substrate	Product	Yield
1			74
2			81
3			91
4			67

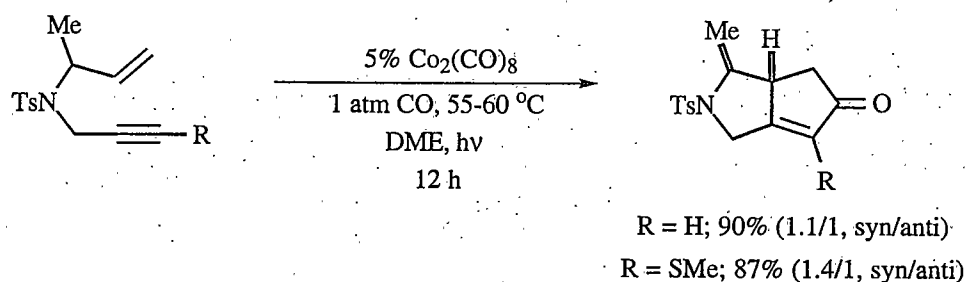
a. All reactions were performed in DME at 55 °C with 5% $\text{Co}_2(\text{CO})_8$, unless otherwise noted. b. 10% $\text{Co}_2(\text{CO})_8$.

Despite these advances, some substrates, such as 1,6-enynes bearing trimethylsilyl-substituted alkynes, failed to undergo carbonylative cyclization using the photopromoted conditions. In addition, it was found that several ether-linked substrates failed to give good yields of bicyclopentenones (Scheme 2.28).²⁰ Modification of substrates bearing terminal alkynes with a thioalkyl moiety allowed for efficient



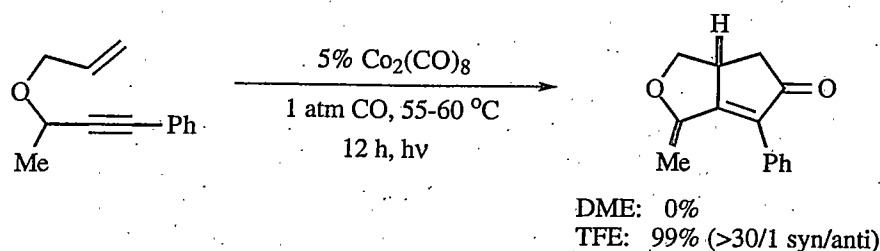
Scheme 2.28

carbonylative cyclization with increased diastereoselectivity. Increasing the steric size of the thioalkyl unit also had a positive effect on the diastereoselectivity (Scheme 2.28).²⁰ Interestingly, the "thiomethyl effect" did not lead to significant increases in the diastereoselectivity of all substrates tested (Scheme 2.29).²⁰ Alternatively, the use of



Scheme 2.29

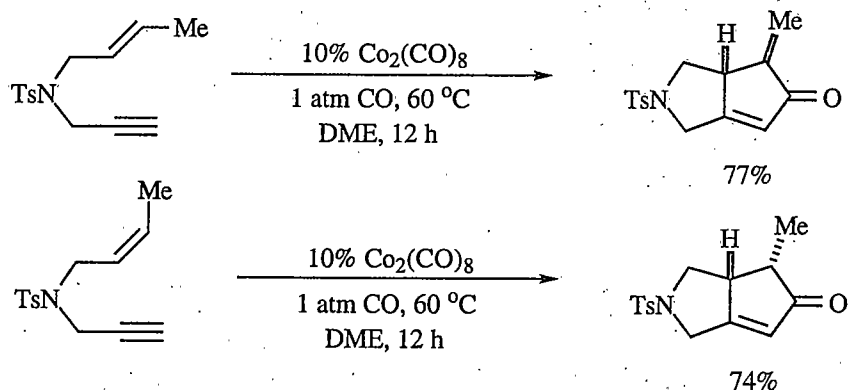
trifluoroethanol as co-solvent was shown to positively affect the cyclization efficiency of ether-linked enynes containing nonterminal alkynes (Scheme 2.30).^{20, 22} This solvent



Scheme 2.30

effect may originate from the increased solubility of CO in the highly polar, fluorinated solvent. In addition, hydrogen bonding of the ether-linked enyne to the protic solvent may be of importance.

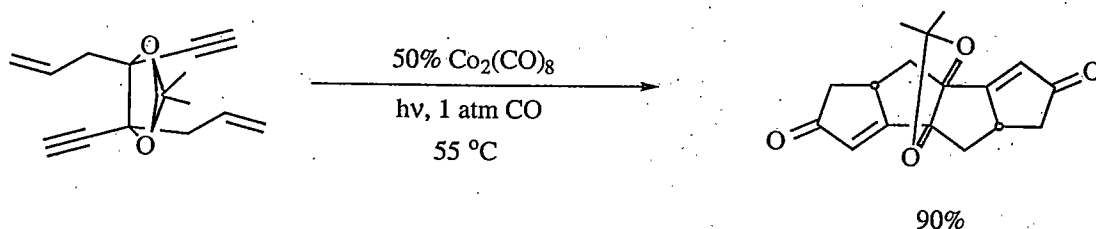
In a study concurrent with the investigations described in this dissertation, O'Mahony and Livinghouse have found that 1,6-enynes bearing substituted alkenes undergo catalytic carbonylative cyclization with complete control of initial olefin geometry (Scheme 2.31).²³ This important discovery may allow for the synthesis of complex



Scheme 2.31

molecules using the catalytic Pauson-Khand reaction. These findings are in direct contrast to the Ru- and Ti-catalyzed [2+2+1] cycloaddition where the stereointegrity of the alkene in the precyclization substrate was compromised in the product (*vide infra*).

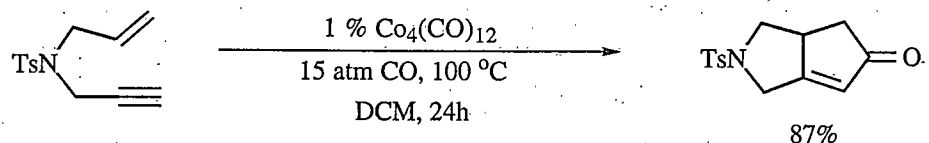
A recent example of the photopromoted catalytic Pauson-Khand reaction has been used by Cook to assemble the tetracyclic core of dicyclopenta[*a,f*]pentalene and dicyclopenta[*a,e*]pentalene (Scheme 2.32).²⁴ While the catalyst loading in each case was



Scheme 2.32

quite high (50 mol %), excellent yields were obtained in the synthesis of these complex ring systems. Interestingly, poor yields were obtained when the PKR was performed using a modification of Schreiber's NMO protocol. Cook noted that the use of substoichiometric amounts of $\text{Co}_2(\text{CO})_8$ simplified purification and may account for the improved yields. The often overlooked challenge of product isolation from reactions employing stoichiometric $\text{Co}_2(\text{CO})_8$ further demonstrates the synthetic importance of the catalytic Pauson-Khand reaction.

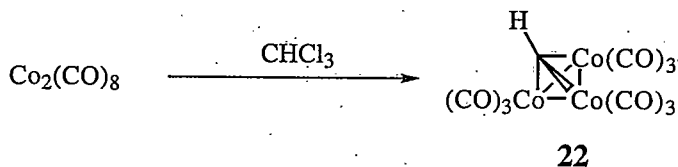
The catalytic Pauson-Khand reaction of enynes using $\text{Co}_4(\text{CO})_{12}$ has very recently been introduced by Chung. Chung found that $\text{Co}_2(\text{CO})_8$ could be generated *in situ* from $\text{Co}_4(\text{CO})_{12}$ at 15 atm CO. Carbonylative annulation of several substrates was achieved in



Scheme 2.33

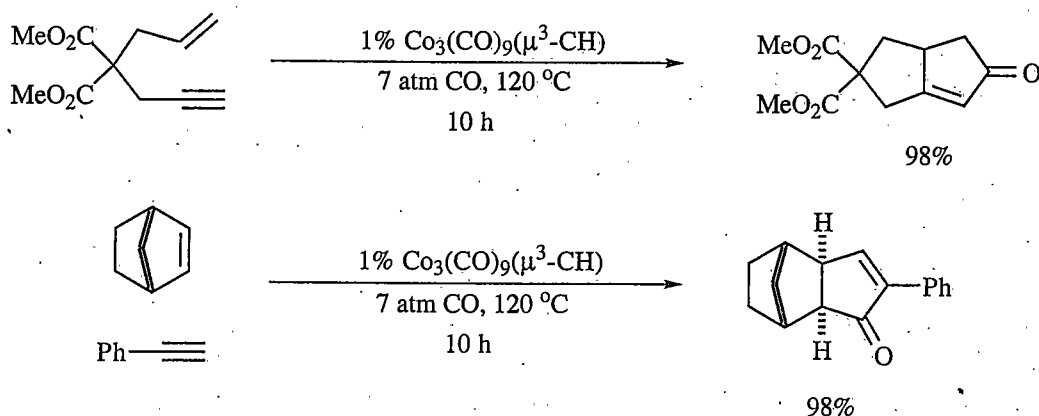
good yield using this procedure (Scheme 2.33).²⁵ There are no apparent advantages to this method as $\text{Co}_4(\text{CO})_{12}$ is more expensive than $\text{Co}_2(\text{CO})_8$ and displays similar stability problems.

In 1999, Sugihara has discovered that methylidenetricobalt nonacarbonyl **22** was a highly effective catalyst for the inter- and intramolecular PKR.²⁶ Alkylidenetricobalt nonacarbonyl complexes are easily prepared from $\text{Co}_2(\text{CO})_8$ and trihaloalkanes (Scheme 2.34).²⁷ Most importantly, these complexes, which are structurally-similar to alkyne-



Scheme 2.34

cobalt complexes, are air stable. Optimal reaction conditions required modest CO pressure and elevated temperatures, but provided excellent yields of product in both the inter- and intramolecular PKR (Scheme 2.35).²⁶ Importantly, with $\text{Co}_2(\text{CO})_8$ as catalyst under

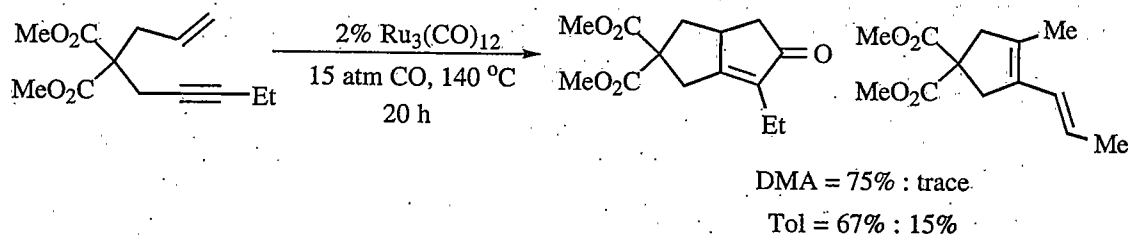


Scheme 2.35

identical reaction conditions (120 °C, 7 atm CO) very poor conversion to product was observed (12%). That $\text{Co}_2(\text{CO})_8$ failed to exhibit similar catalytic activity as $\text{Co}_2(\text{CO})_9(\mu^3\text{-CH})$ suggests it is not being formed *in situ*.

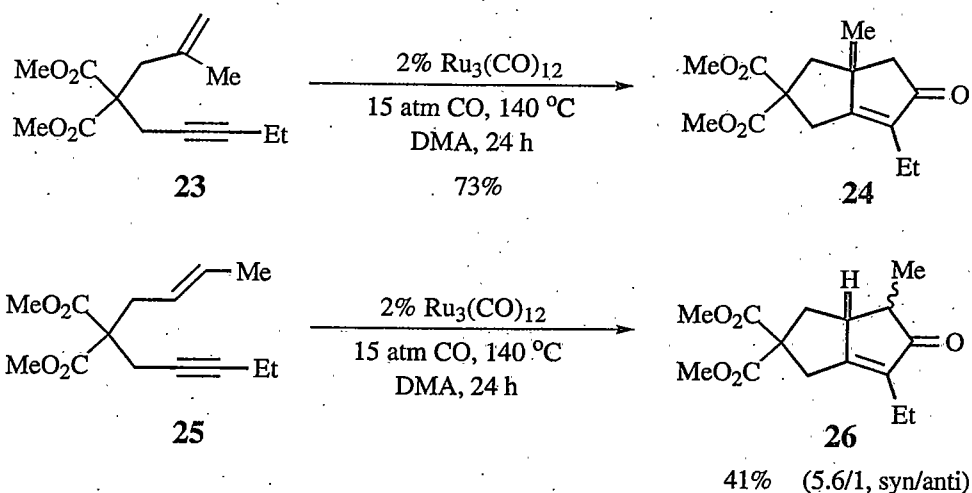
2.2.c Ruthenium-Catalyzed [2+2+1] Cycloaddition

Mitsudo has developed the first example of a ruthenium-catalyzed [2+2+1] cycloaddition. Good yields of bicyclopentenones were obtained using only 2 mol % $\text{Ru}_3(\text{CO})_{12}$ under 15 atm CO at 140 °C. The use of dimethyl acetamide was found to suppress the formation of an undesired diene side product (Scheme 2.36).²⁸ The PKR



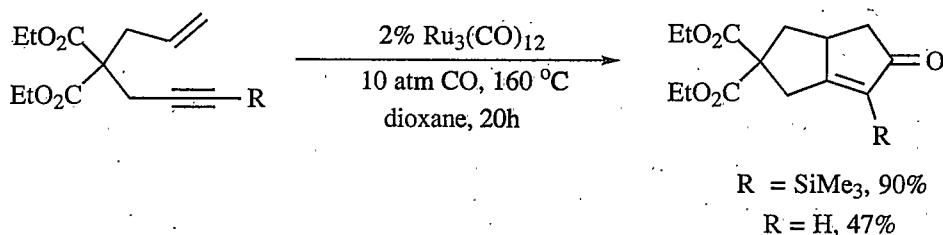
Scheme 2.36

of a 1,6-enyne **23** bearing a 2-substituted alkene led to a good yield of the angularly-substituted pentalenone **24**, while a similar substrate **25** with a *trans*-crotyl moiety resulted in product **26** with significant epimerization (Scheme 2.37).²⁸



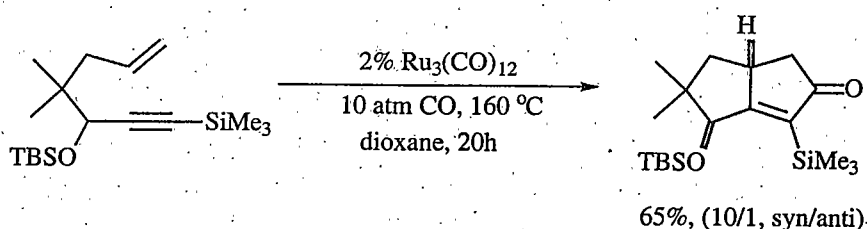
Scheme 2.37

A similar catalyst system was developed by Murai except that dioxane was used as solvent under 10 atm of CO. While the catalytic [2+2+1] cycloaddition of enynes bearing substituted alkynes proceeded in good yields, a substrate bearing a terminal alkyne resulted in low yield of the desired pentalenone (Scheme 2.38).²⁹ In addition, 1,6-enynes bearing substituted alkenes, as well as 1,7-enynes, were unreactive under these conditions.



Scheme 2.38

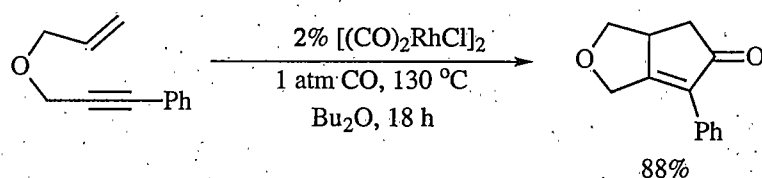
Useful levels of relative stereocontrol were achieved in the carbonylative cyclization of some chiral substrates (Scheme 2.39).²⁹ The origin of the stereoinduction was rationalized according to that originally described by Magnus in the stoichiometric PKR.^{30b,c}



Scheme 2.39

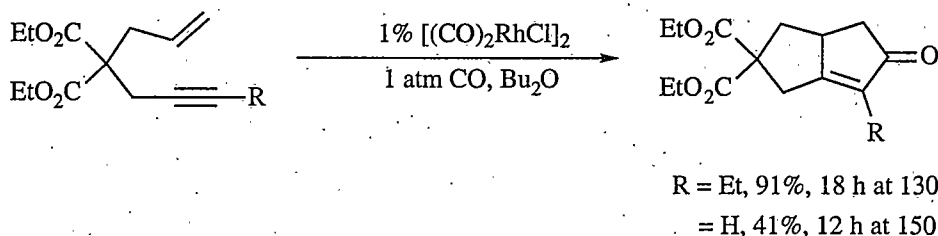
2.2.d Rhodium-Catalyzed [2+2+1] Cycloaddition

The first example of a Rh-catalyzed carbonylative enyne cyclization has been reported by Narasaka. [(CO)₂RhCl]₂ was found to be an effective precatalyst in dibutyl ether or *p*-xylene under 1 atm CO at 90-160 °C (Scheme 2.40).³¹ While 1,6-enynes



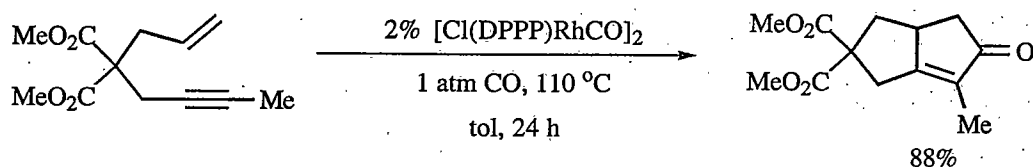
Scheme 2.40

bearing nonterminal alkynes underwent successful carbonylative cyclization, substrates with terminal alkynes afforded only modest yields (Scheme 2.41).³¹



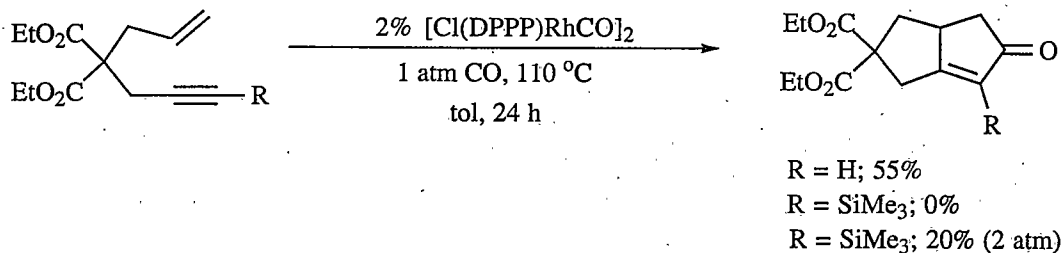
Scheme 2.41

Another example of a Rh-catalyzed [2+2+1] cycloaddition has very recently been reported by Jeong. Cationic rhodium complexes modified with either mono- or bidentate phosphines were found to be effective catalysts for the PKR of 1,6-enynes. The optimized experimental protocol involved heating an enyne with 5 mol % $[\text{ClRh}(\text{DPPP})\text{CO}]_2$ under 1 atm CO.³² Excellent conversion to bicyclopentenones was observed for 1,6-enyne



Scheme 2.42

substrates containing *nonterminal* alkynes (Scheme 2.42). It was determined that 1,6-enynes containing terminal or trimethylsilyl-substituted alkynes were poor substrates using these conditions (Scheme 2.43).³² In addition, all substrates examined only contained

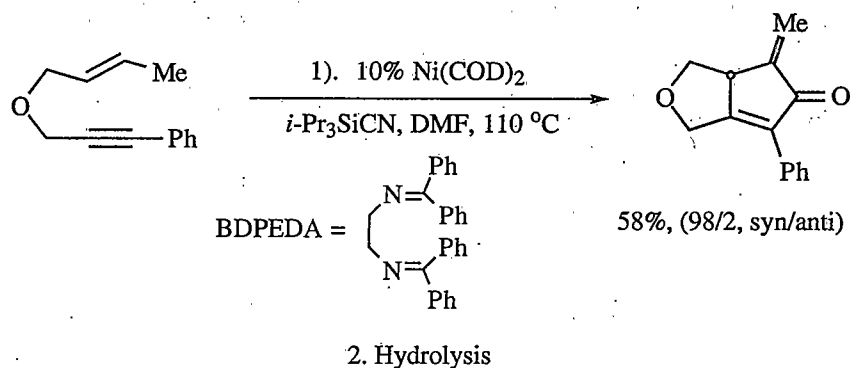


Scheme 2.43

unsubstituted alkenes. Despite these limitations, the disclosure of rhodium catalysts with potentially tunable phosphine ligands may allow for asymmetric catalysis. The Rh-catalyzed methods independently developed by Jeong³² and Narasaka³¹, and Pagenkopf's photopromoted PKR¹⁸, represent the only carbonylative enyne cyclizations that are performed under 1 atm CO.

2.2.e Nickel-Catalyzed [2+2+1] Cycloaddition

Buchwald has recently shown that low-valent nickel complexes are suitable catalysts for the [2+2+1] cycloaddition. The use of *N,N'*-bis(diphenylmethylene)-ethylenediamine (BDPEDA) in combination with $\text{Ni}(\text{COD})_2$ and *i*- Pr_3SiCN as a CO

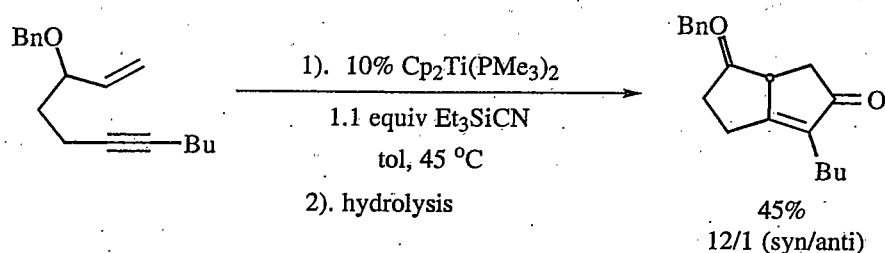


Scheme 2.44

surrogate afforded modest yields of bicyclopentenones after hydrolysis (**Scheme 2.44**).³³ Though this method can potentially be made into an asymmetric process, the reactions are performed at relatively high dilution (0.02 M) and are only useful with enynes bearing substituted alkynes.

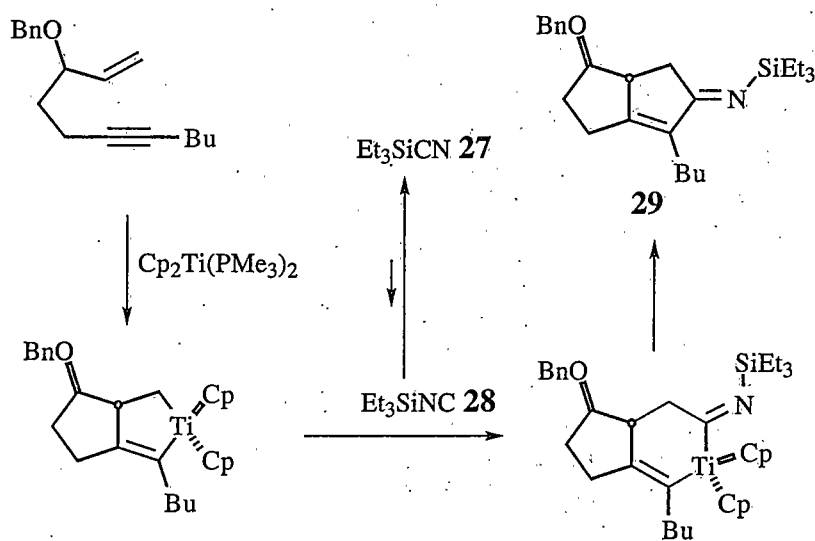
2.2.f Titanium-Catalyzed [2+2+1] Cycloaddition

The two-step conversion of enynes into bicyclopentenones can be accomplished using catalytic $\text{Cp}_2\text{Ti}(\text{PMe}_3)_2$ with stoichiometric triethylsilylcyanide as a CO surrogate. Hydrolysis of the resulting iminosilane afforded bicyclopentenones in modest to good yield (**Scheme 2.45**).³⁴ The catalytic sequence is believed to proceed via ligand exchange and



Scheme 2.45

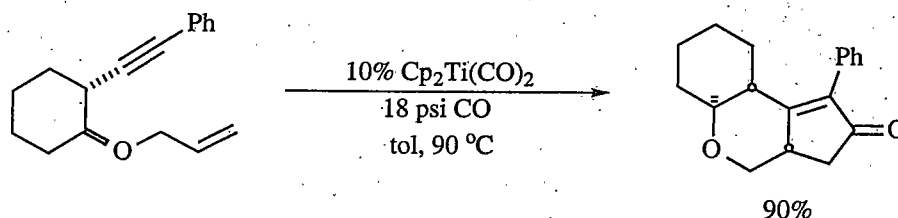
oxidative cyclization. Insertion of the isomeric form of the trialkylcyanide **27**, the isocyanide **28**, into the carbon titanium bond followed by reductive elimination affords the iminosilane **29** (Scheme 2.46).³⁴ Though good levels of relative stereocontrol were



Scheme 2.46

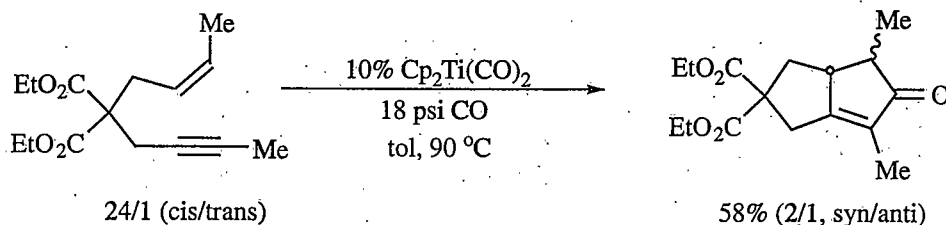
achieved in some cases, this methodology has two drawbacks. Firstly, the precatalyst, $\text{Cp}_2\text{Ti}(\text{PMe}_3)_2$, is highly sensitive to moisture and oxygen and requires manipulation in a glove box. Secondly, the hydrolysis of the iminosilane **29** is somewhat capricious and the yields do not truly reflect the reaction efficiency.

Subsequently, Buchwald has shown that $\text{Cp}_2\text{Ti}(\text{CO})_2$ is a more effective catalyst for cyclopentenone formation under a CO atmosphere. Excellent levels of relative stereoinduction were observed with some enyne substrates (Scheme 2.47).³⁵ One



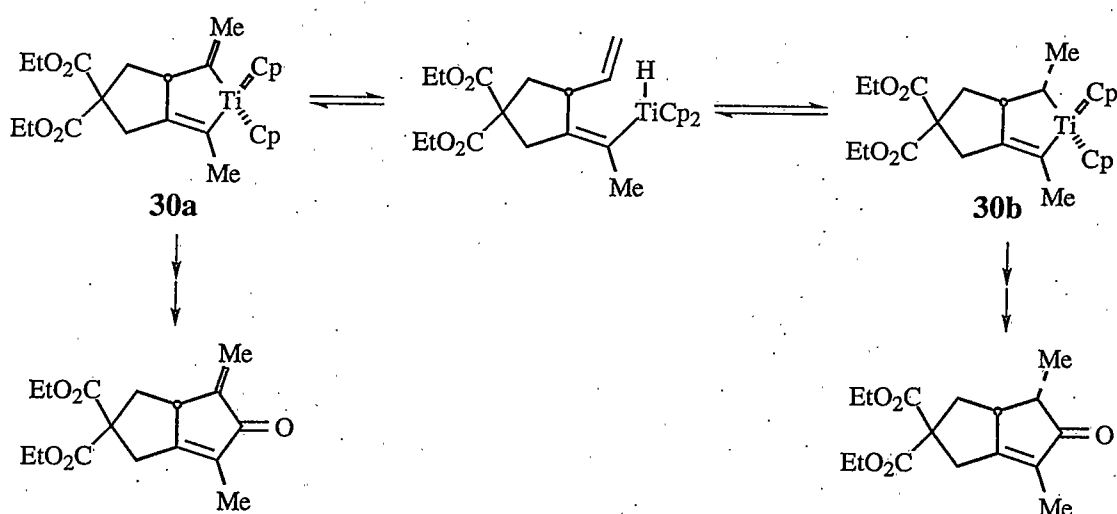
Scheme 2.47

apparent limitation of the $\text{Cp}_2\text{Ti}(\text{CO})_2$ method is the inability to transform substrates bearing substituted olefins into stereochemically pure bicyclopentenones. For example, almost complete scrambling of the *cis*-butenyl moiety was observed using the standard conditions (Scheme 2.48).^{35a} A possible mechanism that explains the erosion of stereochemistry



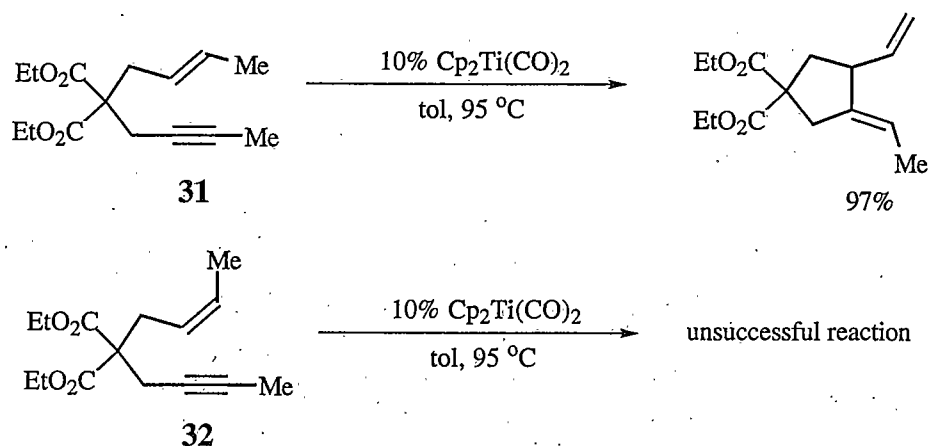
Scheme 2.48

of the olefin involves the putative titanacyclopentenenes **30a,b**. A reversible β -hydride elimination/insertion sequence may lead to scrambling of the initial olefin geometry (Scheme 2.49). Apparently, this competitive pathway is faster than the rate of CO



Scheme 2.49

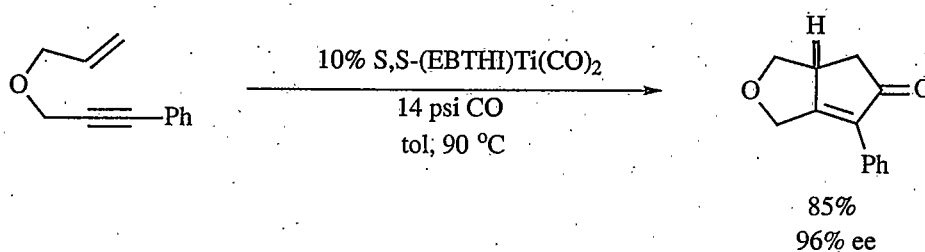
insertion and reductive elimination of the intermediate titanium hydride. Interestingly, Buchwald has shown that the cycloisomerization of enynes can be achieved with catalytic $\text{Cp}_2\text{Ti}(\text{CO})_2$ using a CO deficient atmosphere.³⁶ Cycloisomerization of an enyne **31** bearing a *trans*-crotyl moiety proceeds in high yield while a similar substrate **32** containing a



Scheme 2.50

cis-crotyl unit slowly decomposed under the reaction conditions (Scheme 2.50). Buchwald suggests that the titanocycle derived from the *cis*-enynne does not have a geometrically favored pathway for β -hydride elimination.³⁶

A highly enantioselective variant of the Ti-catalyzed [2+2+1] cycloaddition has been introduced by Buchwald using S,S-(EBTHI)Ti(CO)₂ as catalyst.^{35b} Despite this important advance in asymmetric catalysis, the method may not gain widespread acceptance as the

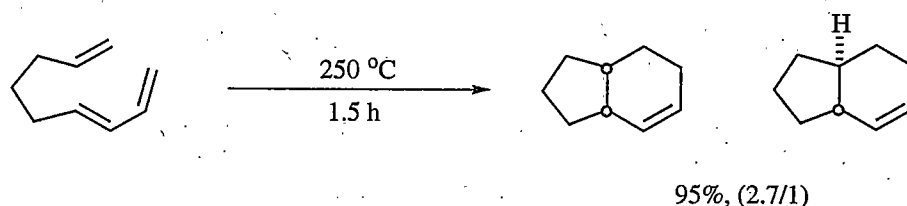


Scheme 2.51

titanium complex is tedious to prepare and is very sensitive to oxygen and water (Scheme 2.51). In addition, the steric requirements of the chiral ligand, S,S-(EBTHI), may limit the substrate types that are useful for this enantioselective reaction.^{35b}

2.3 Transition Metal-Catalyzed [4+2] Cycloadditions

The Diels-Alder reaction has been used quite extensively in the synthesis of complex organic structures.^{37a} While many permutations of the reaction exist, most synthetically useful Diels-Alder reactions take advantage of the favorable electronic characteristics of the diene and dienophile units.^{37b} In contrast, electronically similar dienes and dienophiles will react under more vigorous conditions, but often do so with reduced selectivity (Scheme 2.52).^{37b}

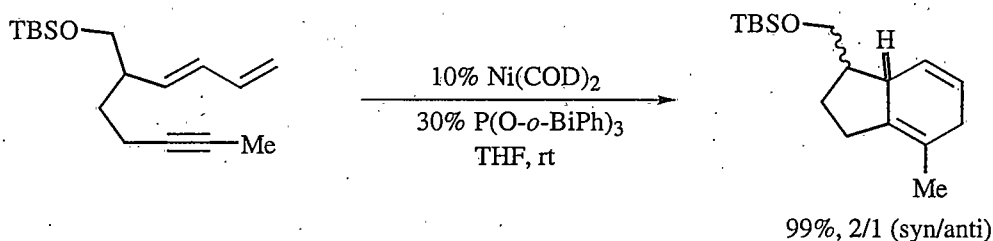


Scheme 2.52

Recently, a number of transition metal complexes have been shown to effect the formal [4+2] cycloaddition of unactivated dienes and dienophiles.

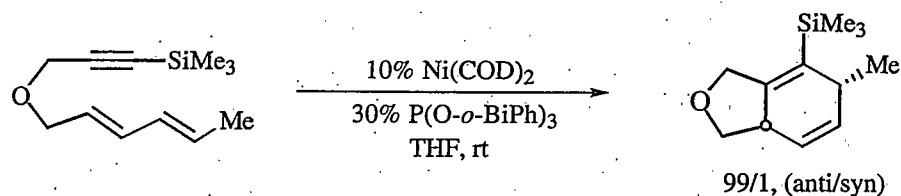
2.3.a Nickel-Catalyzed [4+2] Cycloaddition

In 1989, Wender disclosed an intramolecular nickel-catalyzed [4+2] cycloaddition of dienyynes. $\text{Ni}(\text{COD})_2$, modified with $\text{P}(\text{O}-o\text{-BiPh})_3$, was found to effect cyclization in excellent yield, but with poor relative stereocontrol (Scheme 2.53).^{38a} In addition, this



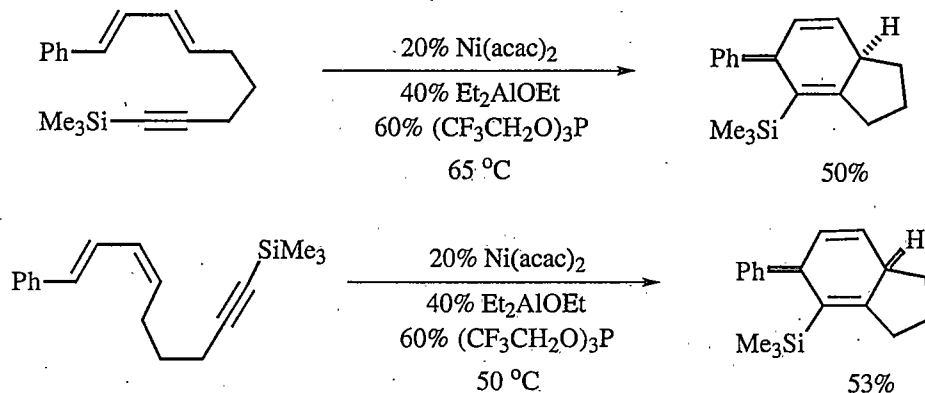
Scheme 2.53

method is only useful for substrates bearing *non-terminal* alkynes under high dilution conditions. It was shown, however, that the cyclization of certain substrates proceeded with almost complete control of the initial diene geometry (**Scheme 2.54**).^{38a}



Scheme 2.54

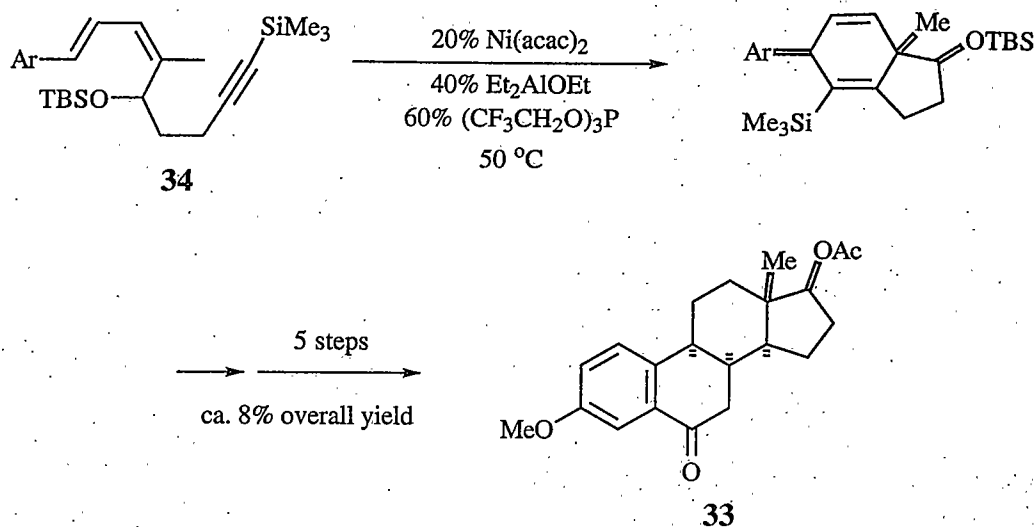
In a continuation of the nickel-catalyzed [4+2] cycloaddition studies, Wender found that cyclization of dienynes bearing both *E,E*- and *E,Z*-dienes proceeded with complete



Scheme 2.55

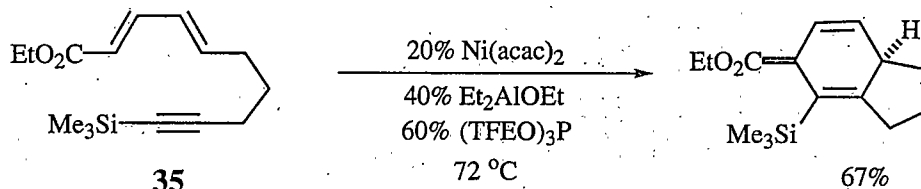
retention of the initial diene geometry, albeit in poor yield (**Scheme 2.55**).^{38b} The cyclization worked best with the electron deficient phosphite, P(OCH₂CF₃)₃.^{22c} Most notably, dienynes with pendant methyl-substituted *E,Z*-dienes underwent cyclization giving angularly-substituted bicycloadducts (**Scheme 2.55**).^{38b} That the angularly-substituted indane core can be prepared is quite significant as it allows for the synthesis of several

classes of naturally occurring compounds, such as steroids and vitamin D. To that end, Wender has shown that protected ($\pm$)-8 α -isoestradiol **33** can be assembled rather



Scheme 2.56

efficiently from an easily prepared dienyne **34** (Scheme 2.56).^{38b,c,d} The generation of the low-valent nickel complex *in situ* from air stable Ni(acac)₂ is a noteworthy, practical discovery as it obviates the use of the unstable Ni(COD)₂.^{38b,c} Wender has also shown that the Ni-catalyzed [4+2] cycloaddition is tolerant of an electron-withdrawing group on

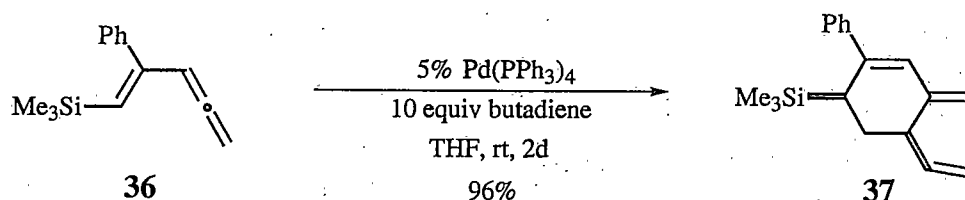


Scheme 2.57

the terminus of the diene unit (Scheme 2.57).^{38c} The attempted thermal cyclization of dienyne **35** only led to its decomposition. Further elucidation of the scope of this reaction is expected.

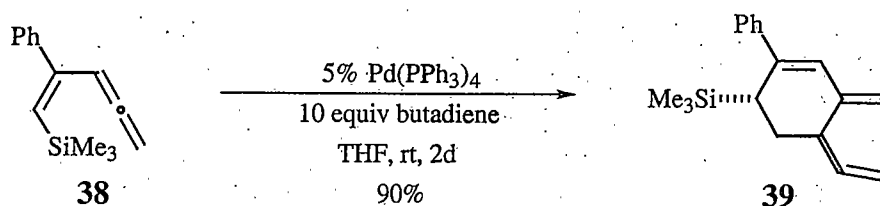
2.3.b Palladium-Catalyzed [4+2] Cycloadditions

The intermolecular Pd-catalyzed [4+2] cycloaddition of electronically similar olefins with vinylallenes has been reported by Ito. Treatment of vinylallene **36** with an excess of 1,3-butadiene and 5 mol % $\text{Pd}(\text{PPh}_3)_4$ led to the diastereomerically pure cycloadduct **37** in



Scheme 2.58

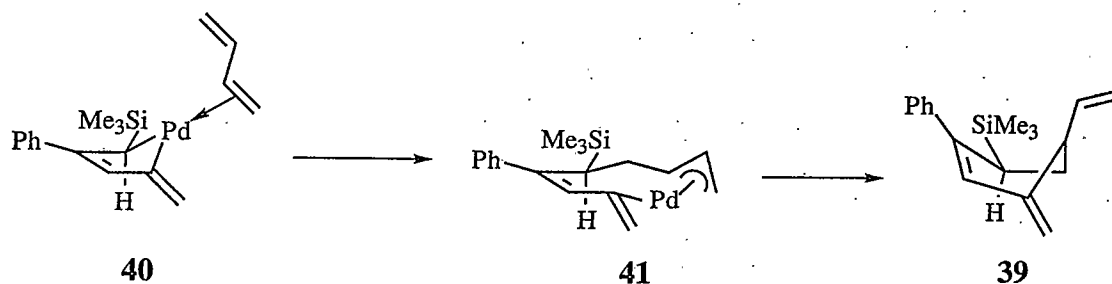
excellent yield (Scheme 2.58).³⁹ Interestingly, subjection of a substrate **38** containing a geometrically opposite vinylsilane moiety to analogous conditions led to the epimeric



Scheme 2.59

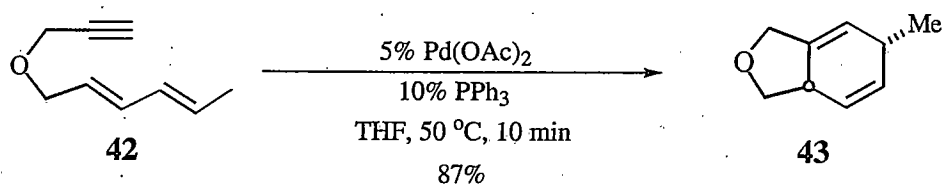
product **39** in 90% yield (Scheme 2.59).³⁹ Presumably, formation of the transient palladacycle **40** followed by insertion of butadiene affords an allyl palladium intermediate **41**. Ito suggested that reductive elimination from the allyl palladium intermediate **41** with

minimization of 1,3-allylic strain may account for the high diastereoselection (Scheme 2.60).³⁹



Scheme 2.60

More recently, Jolly has disclosed a palladium-catalyzed method for the intramolecular [4+2] cycloaddition. Treatment of dienyne **42** with catalytic $\text{Pd}(\text{OAc})_2$ and PPh_3 afforded bicycloadduct **43** in only 15 min at 50 °C (Scheme 2.61).⁴⁰ Importantly,

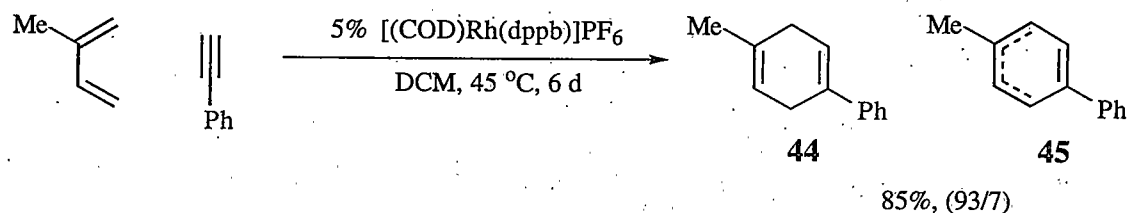


Scheme 2.61

this novel palladium-catalyzed process proceeded at room temperature *and* at 0 °C in good yields (81% and 73% yield, respectively). These conditions, using neutral palladium complexes, were determined to be unsuitable for the cyclization of trienes.⁴⁰

2.3.c Intermolecular Rhodium-Catalyzed [4+2] Cycloadditions

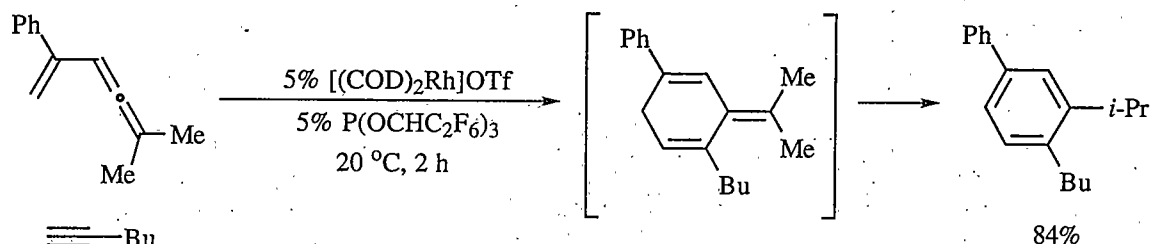
In 1986, Tsuji reported that cationic rhodium complexes effected the intermolecular [4+2] cycloaddition of terminal alkynes and dienes. Under the reaction conditions, the primary 1,4-cyclohexadiene product **44** underwent isomerization to the conjugated 1,3-cyclohexadiene **45** to varying degree depending on the substitution pattern (**Scheme 2.62**).⁴¹ In addition, the reaction was only useful with terminal alkynes and with dienes



Scheme 2.62

that were structurally biased towards an *s-cis* configuration. Nevertheless, the seminal discovery of Tsuji has provided ample precedent for future work in this area.

Most recently, Ito has shown that vinylallenes formed substituted arenes when heated in the presence of alkynes and catalytic rhodium phosphite complexes. This formal [4+2] cycloaddition afforded modest to very good yields of arenes with 5 mol %

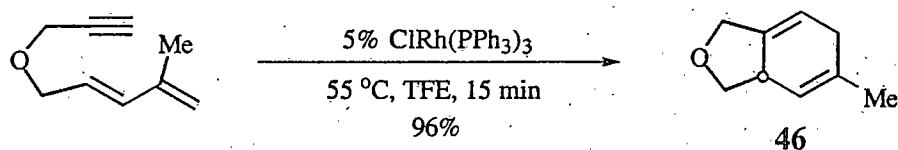


Scheme 2.63

$[(\text{COD})_2\text{Rh}]\text{OTf}$ and 5 mol % $\text{P}(\text{OCHC}_2\text{F}_6)_3$ as catalyst system (Scheme 2.63).⁴² Ito claims that the use of alkenes instead of alkynes afforded substituted cyclohexenes only in low yields for this intermolecular process.

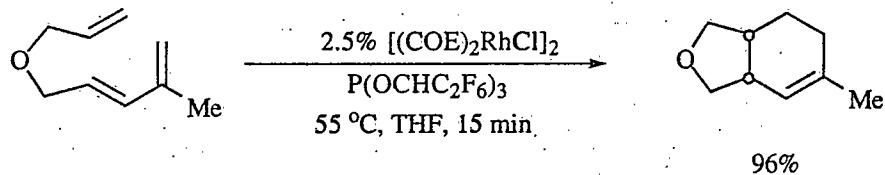
2.3.d Intramolecular Rhodium-Catalyzed [4+2] Cycloaddition

In 1990, the Livinghouse group disclosed the first intramolecular Rh-catalyzed [4+2] cycloaddition. While the use of $\text{ClRh}(\text{PPh}_3)_3$ in THF led to slow formation of product **46**, the use of the highly polar solvent, trifluoroethanol, produced the desired



Scheme 2.64

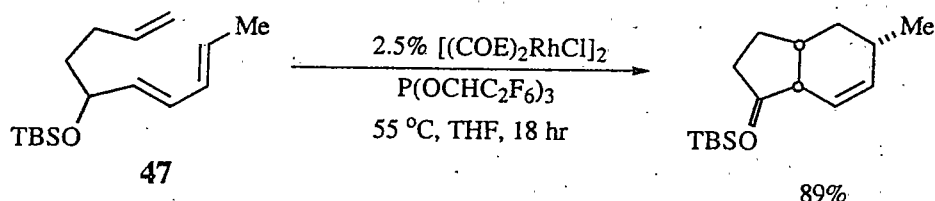
bicycloadduct **46** in 96% yield at 55 °C (Scheme 2.64).^{22a} Though cyclization of dienynes was accomplished using Wilkinson's catalyst, a catalyst system derived from



Scheme 2.65

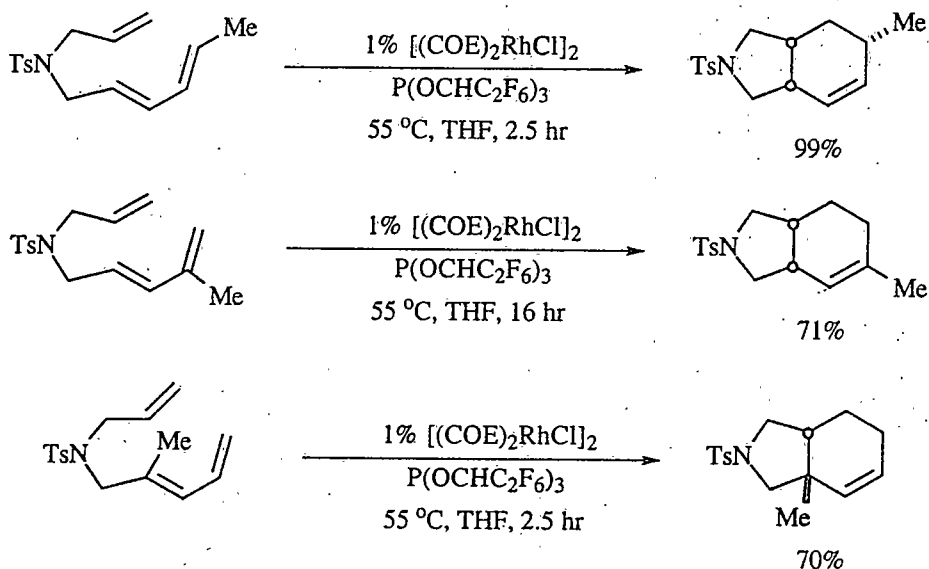
$[(\text{COE})_2\text{RhCl}]_2$ and $\text{P}(\text{OC}_3\text{HF}_6)_3$ proved most useful with triene substrates (Scheme 2.65).^{22a} In contrast to the Ni-catalyzed [4+2] cycloaddition³⁸, this reaction was determined to be useful with dienynes bearing non-terminal *and* terminal alkynes, as well as with trienes. The stereochemistry at the ring junction was determined to be *syn* in all

cases. Most importantly, the cyclization of the stereogenic triene **47** produced a single diastereomer (Scheme 2.66).^{22a}



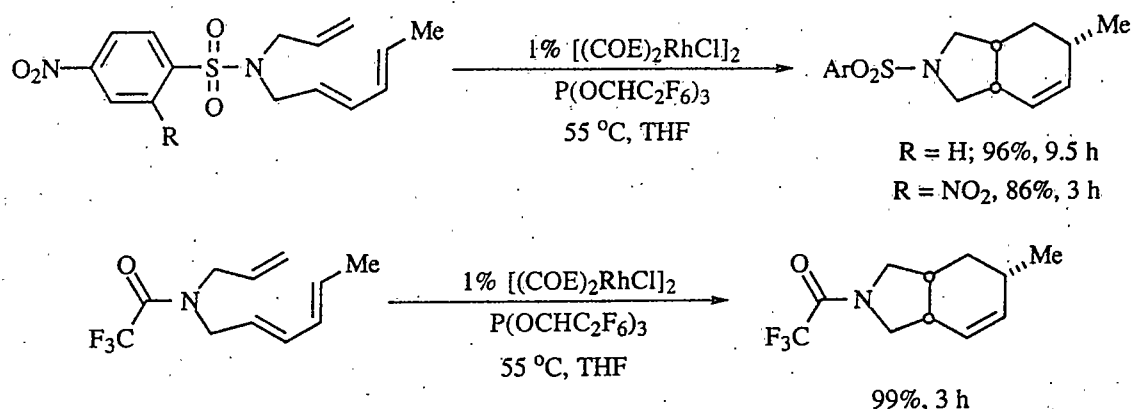
Scheme 2.66

Using the original conditions developed by Livinghouse, O'Mahony has shown that tosyl protected azatrienes bearing a methyl group at various positions on the pendant diene are useful (Scheme 2.67).²³ Additionally, O'Mahony discovered that significantly



Scheme 2.67

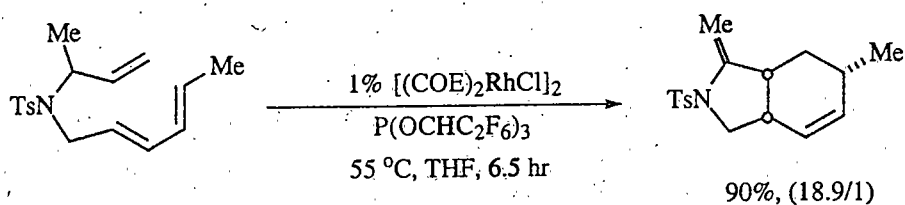
lower catalyst loading was sufficient to achieve good yields of bicycloadduct. A number of protecting groups for nitrogen have been used to evaluate the compatibility with this Rh-catalyzed reaction. In all cases explored, the efficiency and yields of the reaction compare



Scheme 2.68

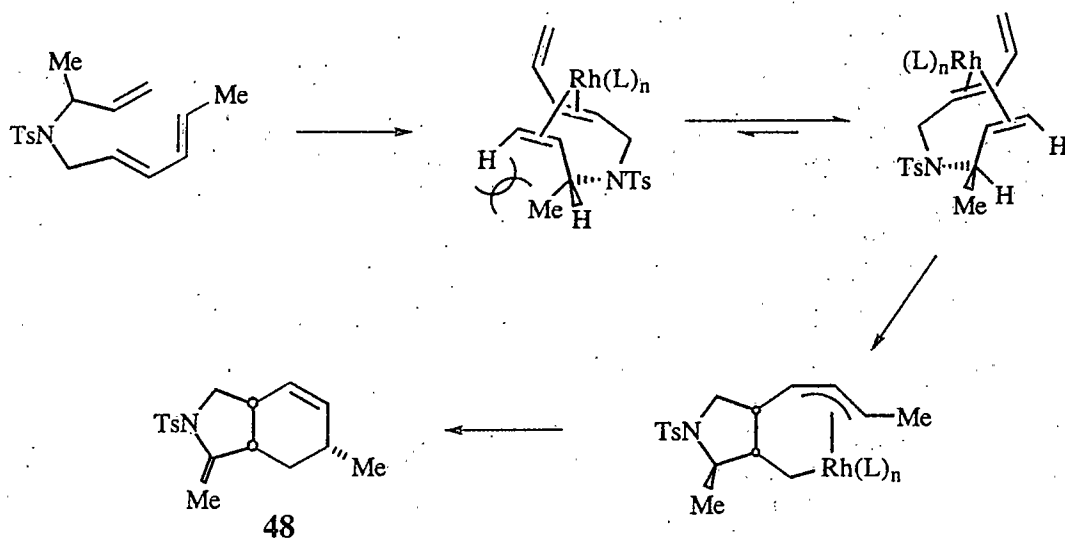
quite favorably with the tosyl-protected azatrienes (Scheme 2.68).²³ In principle, these protecting groups for nitrogen would be more easily removed than the tosyl protecting group for nitrogen.

In a study designed to further define the scope of the Rh-catalyzed [4+2] cycloaddition, O'Mahony and Livinghouse have found that triene substrates bearing a stereogenic group proximal to the allyl moiety can be transformed into hexahydroisindolines with very high levels of relative stereocontrol (Scheme 2.69).⁴³



Scheme 2.69

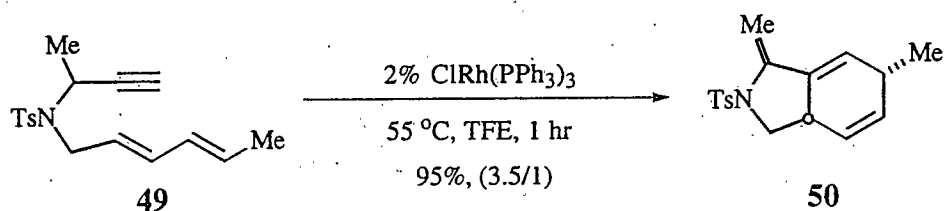
The high stereoselection observed with trienes of this type is presumed to arise from the selective ligation of the substrate with minimization of allylic 1,3-strain.⁴⁴ Selective formation of rhodacycle, followed by isomerization and reductive elimination forms the



Scheme 2.70

observed bicycloadduct **48** (Scheme 2.70). This highly selective catalytic method is quite remarkable considering that thermolysis of this triene (at 100 °C) gave a mixture of all four of the possible diastereomers.²³

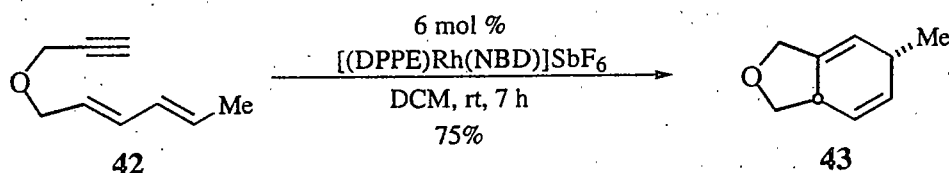
In contrast to the highly selective Rh-catalyzed [4+2] cycloaddition of stereogenic trienes, O'Mahony observed that diyne **49** bearing a methyl group at the propargyl



Scheme 2.71

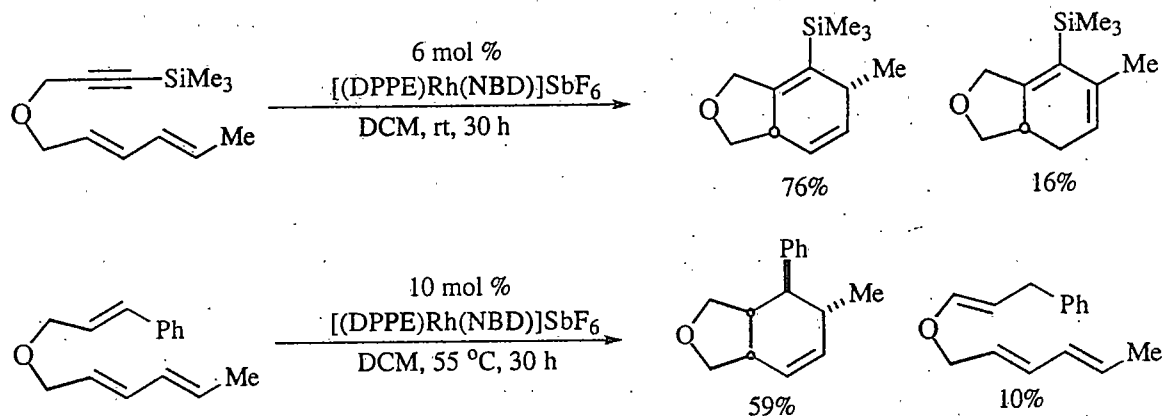
position afforded bicycloadduct **50** with poor selectivity (Scheme 2.71).²³ The decreased level of relative stereocontrol is consistent with the reduced allylic 1,3-strain inherent to substituted alkynes.

Concurrent with investigations described in this dissertation, Gilbertson reported that $[(\text{DPPE})\text{Rh}(\text{NBD})]\text{SbF}_6$ was an efficient catalyst precursor for the Rh-catalyzed [4+2] cycloaddition developed by Livinghouse. Cyclization of a dienyne **42** with 6 mol % precatalyst at room temperature led to bicycloadduct **43** in good yield (Scheme 2.72).⁴⁵



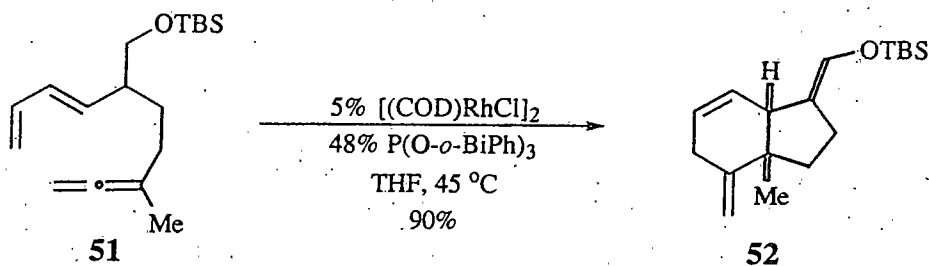
Scheme 2.72

In several examples, significant isomerization of the primary product was observed. In addition, cyclization of trienes proceeded only slowly at room temperature with concomitant isomerization of starting material (Scheme 2.73).⁴⁵



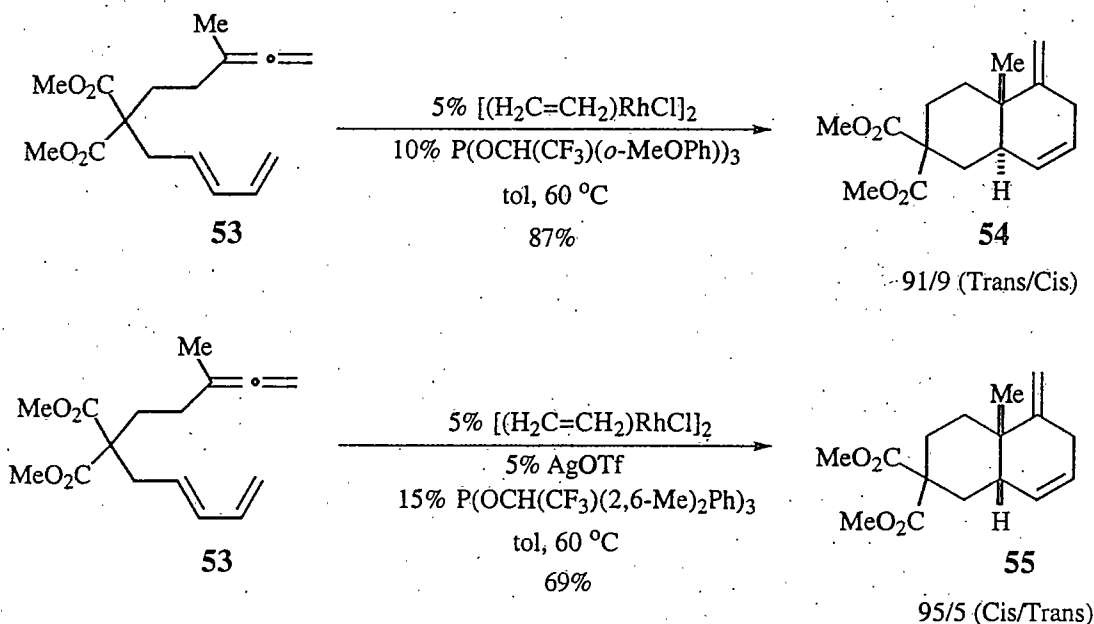
Scheme 2.73

In 1995, Wender extended the Rh-catalyzed [4+2] cycloaddition to include substrate bearing allenes. Treatment of allene-diene **51** with 5 mol % $[(\text{COD})\text{RhCl}]_2$ and 48 mol % $\text{P}(\text{O}-o\text{-BiPh})_3$ in THF produced the hydrinane **52** in excellent yield with high



Scheme 2.74

diastereoselectivity (Scheme 2.74).⁴⁶ Using a variety of different reaction conditions, 5,6-bicycloadducts were prepared with good selectivity, while 6,6-bicycloadducts were formed with some erosion of stereocontrol. For example, cyclization of the allene-diene **53** using a neutral rhodium catalyst produced the *trans*-fused hydrinane **54** as the major product. Interestingly, a cationic rhodium catalyst produced the *cis*-fused hydrinane **55**

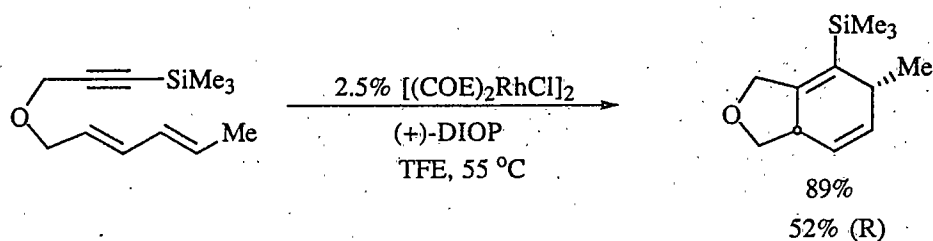


Scheme 2.75

as the dominant isomer (Scheme 2.75).⁴⁶ The discovery that allenes are suitable alkene surrogates has led to the synthesis of angularly-substituted carbocycles.

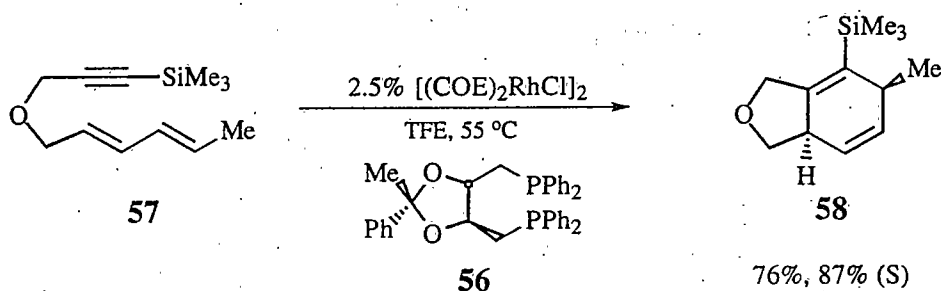
2.3.e Enantioselective Rh-Catalyzed [4+2] Cycloaddition

The highly diastereoselective Rh-catalyzed [4+2] cycloaddition of trienes suggested that an enantioselective variant of the reaction may proceed with similar selectivity. McKinstry and Livinghouse reported that (+)-DIOP-modified rhodium complexes led to the enantioselective formation of bicycloadducts (Scheme 2.76).⁴⁷ Interestingly, a slight



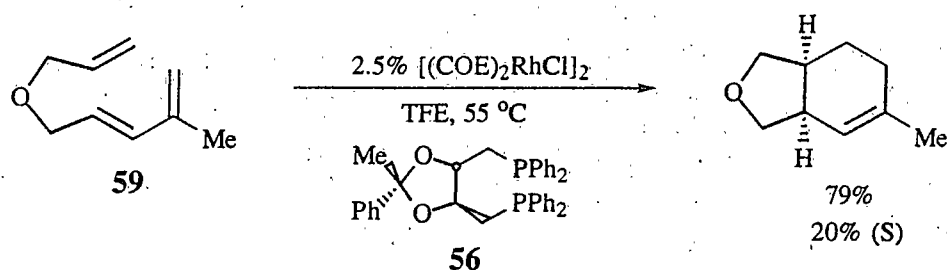
Scheme 2.76

modification of the natural bite angle of the phosphine ligand affects both the absolute sense and the level of asymmetric induction. With bisphosphine **56** as the chiral controller, the cyclization of dienyne **57** afforded bicycloadduct **58** in 87% ee (S) (Scheme 2.77).⁴⁷



Scheme 2.77

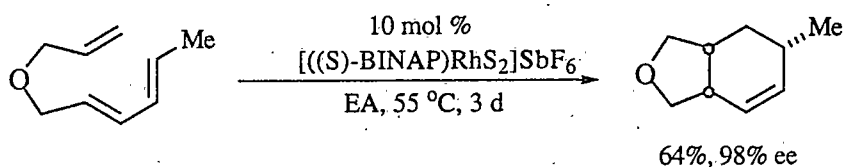
Use of this novel chiral bisphosphine **56** in a reaction with triene **59**, however, led to only low enantiomeric excess (Scheme 2.78).⁴⁷ The dramatic decrease in the level of



Scheme 2.78

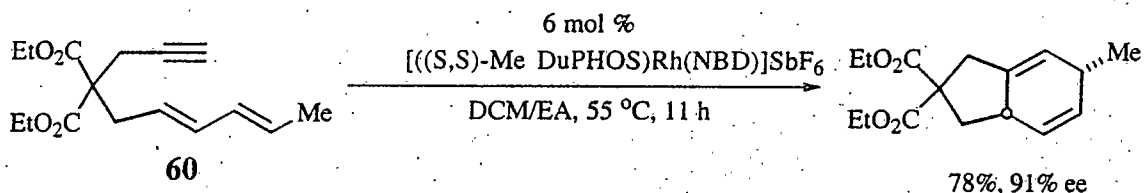
asymmetric induction with the identical ligand when using trienes and dienynes shows that the reaction is quite subtle. The study of McKinsty demonstrated that each substrate class may require a specially designed ligand/catalyst system.

Most recently, Gilbertson has discovered a significant solvent effect on the enantioselective Rh-catalyzed [4+2] cycloaddition. While the cationic (S)-BINAP-Rh complex fails to promote the [4+2] cycloaddition in DCM, the use of ethyl acetate as solvent gave a modest yield of product in 98% ee (Scheme 2.79).⁴⁸ The observed rate



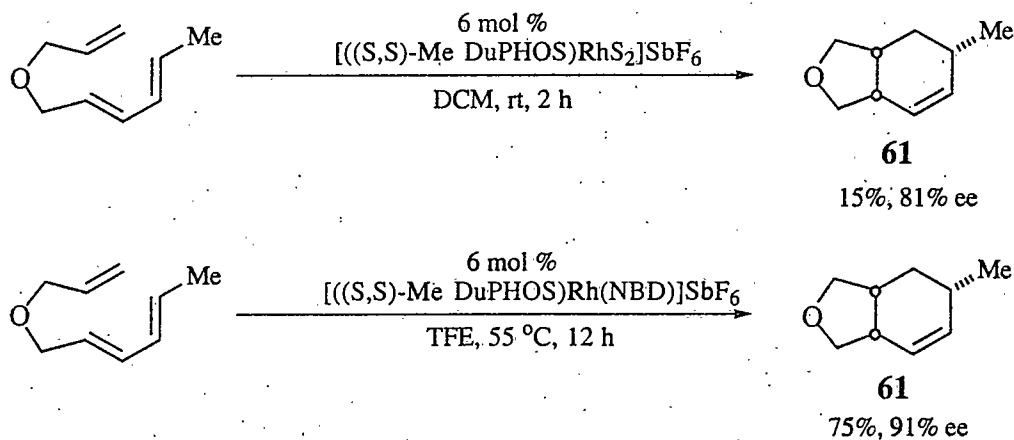
Scheme 2.79

of the reaction with ethyl acetate as solvent is markedly reduced and required high catalyst loading even for this simple substrate. Preliminary experiments suggest that this solvent effect can be extended to dienyne substrates as well. For instance, cyclization of the malonate-derived dienyne **60** proceeded with a high level of enantioselection with DCM/ethyl acetate as solvent (6/1) (Scheme 2.80).⁴⁸ Another interesting discovery



Scheme 2.80

reported by Gilbertson was on the use of different Rh precatalysts. In situ formation of $[(S,S)\text{-Me DuPHOS}]\text{RhS}_2]\text{SbF}_6$ by hydrogenation of $[(S,S)\text{-Me DuPHOS}]\text{Rh(NBD)}]\text{SbF}_6$ afforded a significant amount of undesired by-product giving the bicycloadduct **61** in only 15% yield. In contrast, direct use of $[(S,S)\text{-Me DuPHOS}]\text{Rh(NBD)}]\text{SbF}_6$ produced the bicycloadduct **61** in good yield, though somewhat more forcing conditions were required (Scheme 2.81).⁴⁸

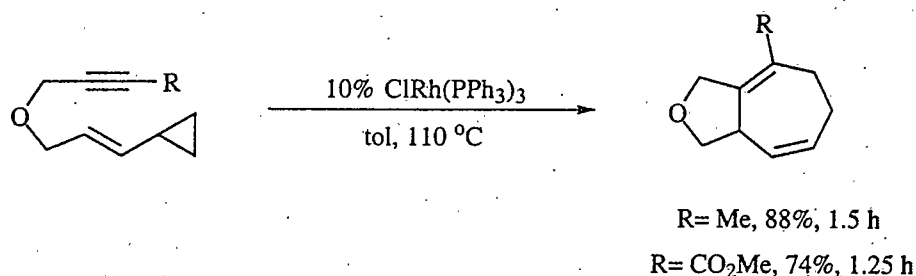


Scheme 2.81

2.4 Rhodium-Catalyzed [5+2] Cycloadditions

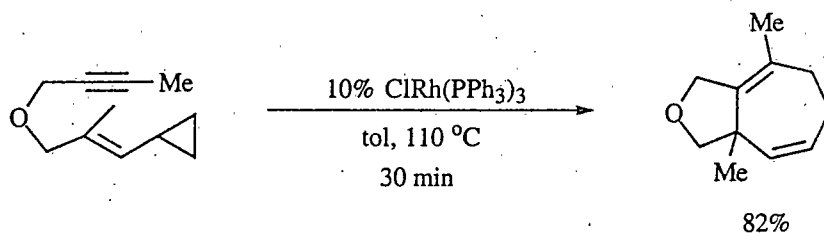
2.4.a Intramolecular Rhodium-Catalyzed [5+2] Cycloaddition

In 1995, Wender discovered that the vinyl-cyclopropyl moiety was a useful diene equivalent in the intramolecular Rh-catalyzed [5+2] cycloaddition. The reaction was tolerant of electronically diverse substituents on the alkyne terminus (**Scheme 2.82**).^{49a}



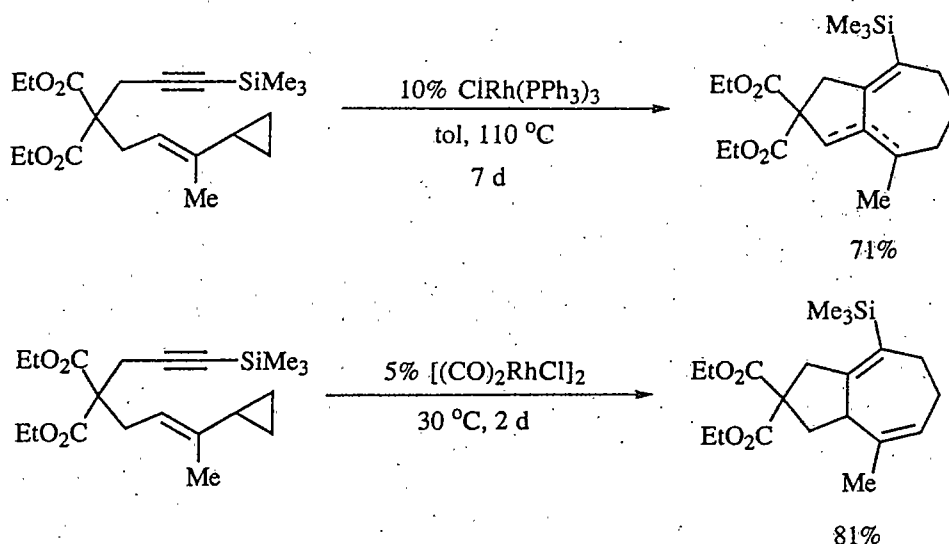
Scheme 2.82

Substitution on the vinyl-cyclopropyl moiety was also tolerated affording the angularly-substituted bicycloadduct (**Scheme 2.83**).^{49a} Certain substitution patterns on the vinyl-



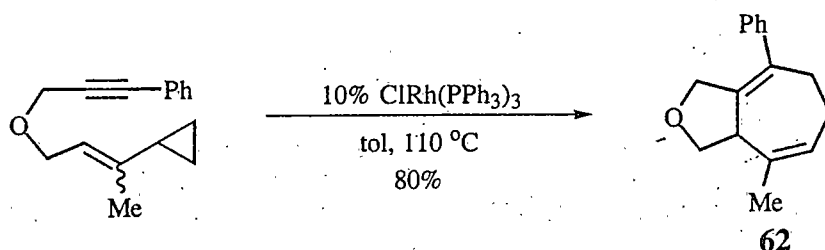
Scheme 2.83

cyclopropyl moiety dramatically slowed the reaction leading to significant isomerization of the initially formed product.^{49a} Subsequently, Wender has shown that $[(\text{CO})_2\text{RhCl}]_2$ is a more active catalyst giving the desired product in good yield (**Scheme 2.84**).^{49c}



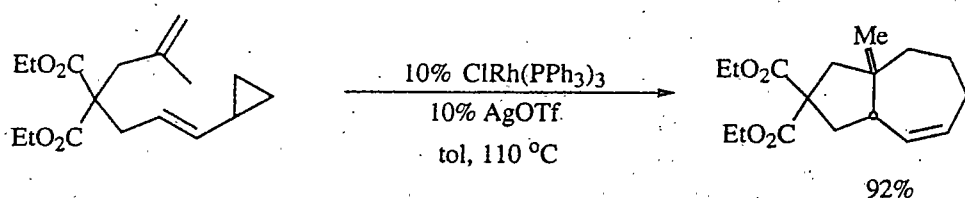
Scheme 2.84

$[(\text{CO})_2\text{RhCl}]_2$ was also used in the synthesis of bicycloadduct **62** where even cationic Wilkinson's catalyst was unreactive (Scheme 2.85).^{49c}



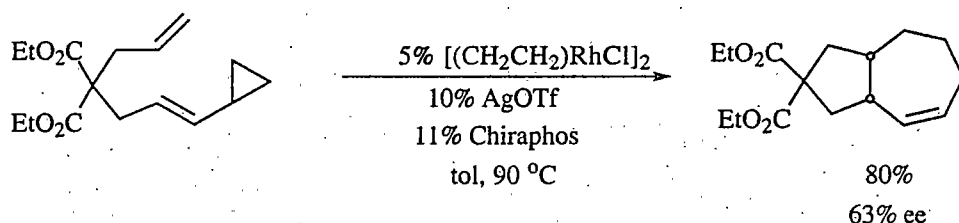
Scheme 2.85

Wender also showed that cationic rhodium complexes are effective catalysts for the [5+2] cycloaddition of cyclopropyl-dienes. Wender claims that substrates bearing 2-substituted olefins undergo cyclization, while substrates bearing *cis*- or *trans*-crotyl units



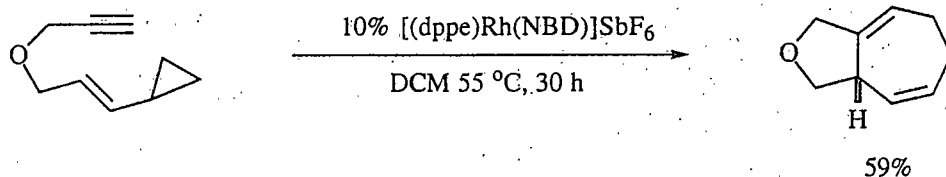
Scheme 2.86

gave undesired products. (Scheme 2.86).^{49b} Initial results have shown that (-)-Chiraphos-modified rhodium complexes afforded enantioenriched products (Scheme 2.87)^{49b}



Scheme 2.87

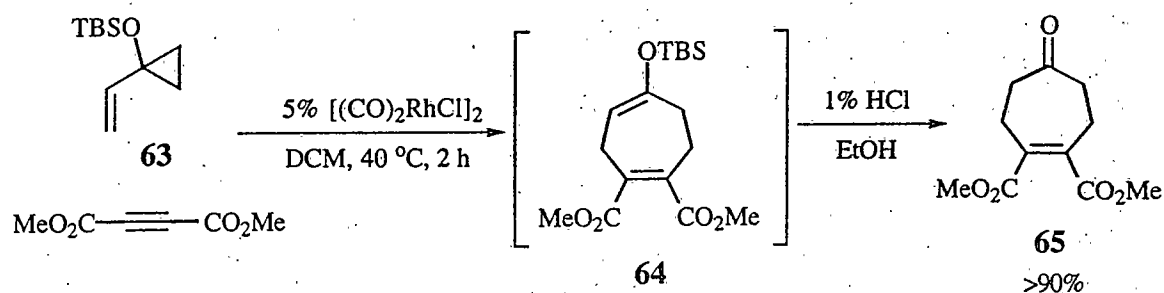
Gilbertson has shown that $[(\text{DPPE})\text{Rh}(\text{NBD})]\text{SbF}_6$ was a suitable precatalyst for the Rh-catalyzed [5+2] cycloaddition developed by Wender. The special reactivity of this catalyst allows for the cyclization to proceed at much lower temperature than in the original work of Wender (Scheme 2.88).⁴⁵



Scheme 2.88

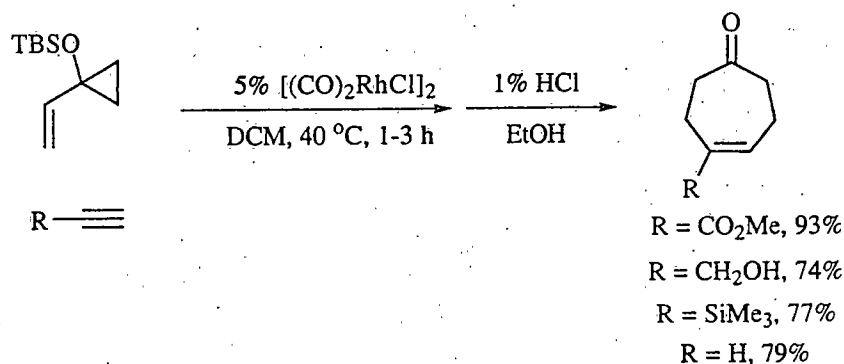
2.4.b Intermolecular Rhodium-Catalyzed [5+2] Cycloaddition

Wender recently has reported that $[(\text{CO})_2\text{RhCl}]_2$ was an effective catalyst for the intermolecular [5+2] cycloaddition. While unactivated vinyl cyclopropanes failed to give clean reactions, the more reactive vinyl silyloxycyclopropane **63** afforded cycloheptanones



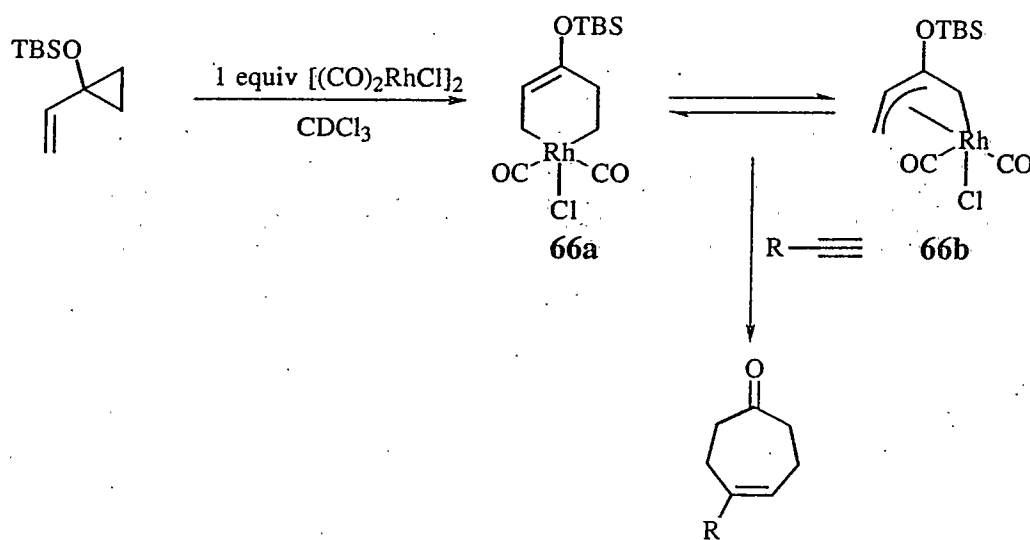
Scheme 2.89

65 after hydrolysis when heated in the presence of DMAD and catalytic $[(\text{CO})_2\text{RhCl}]_2$ (Scheme 2.89).⁵⁰ The initially formed silyl enol ether **64** was observed by ^1H NMR. This novel reaction proved to be quite general as a number of different alkynes led to cycloheptanones in good yield (Scheme 2.90).⁵⁰ Although the reaction mechanism has



Scheme 2.90

not been determined, preliminary ^1H NMR experiments show that a dynamic mixture of rhodium complexes **66a,b** is formed when $[(\text{CO})_2\text{RhCl}]_2$ was treated with the vinyl silyloxycyclopropane. Subsequent addition of an alkyne to this mixture gave the observed silyl enol ether (Scheme 2.91).⁵⁰



Scheme 2.91

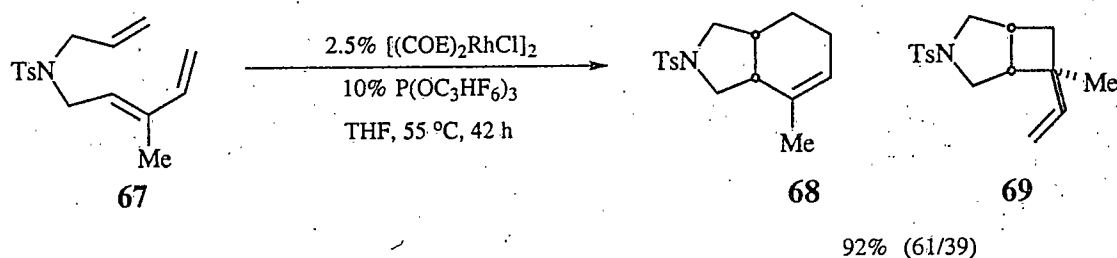
3. RESULTS AND DISCUSSION

3.1 Rhodium-Catalyzed [4+2] Cycloaddition

3.1.a Introduction

The rhodium-catalyzed [4+2] cycloaddition has the potential to become a powerful synthetic tool for the construction of complex molecules. Initial work from the Livinghouse laboratory suggested that certain structural types underwent efficient cyclization.^{22a,23,51a} In addition, promising results were obtained in the area of enantioselective catalysis.^{47,51b} Despite these advances, the scope of the reaction remained to be more fully defined. The studies were directed to provide clues to improving the level of asymmetric induction and at increasing the overall knowledge of the controlling elements of this process.

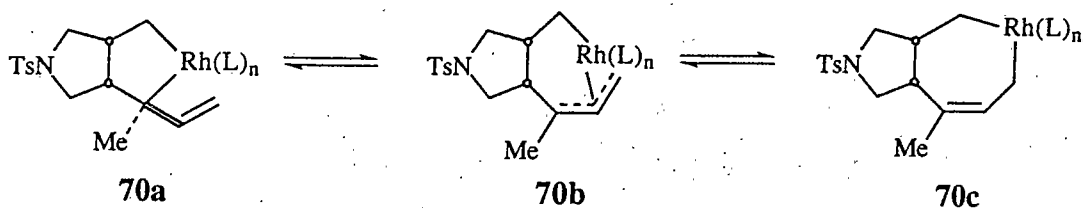
O'Mahony discovered that the Rh-catalyzed [4+2] cycloaddition of the tosyl protected azatriene **67** led to the desired isoindoline **68** admixed with an unexpected



Scheme 3.1

azabicyclo[3.2.0]heptane **69** (Scheme 3.1).⁴³ The interesting vinyl-cyclobutane **69** may arise from one of the intermediate rhodacycles **70a-c** depicted in Scheme 3.2.

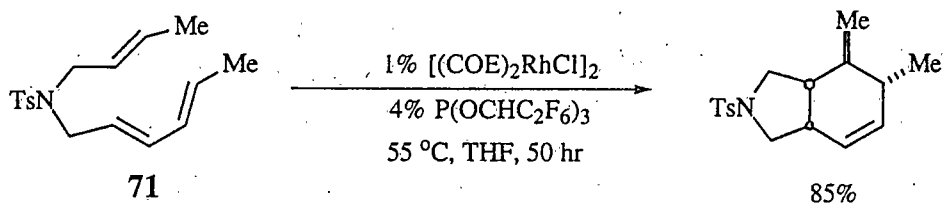
Presumably, initial triene complexation with subsequent oxidative cyclization produced the rhodacyclopentane **70a**. Reductive elimination from intermediate **70a** affords the observed



Scheme 3.2

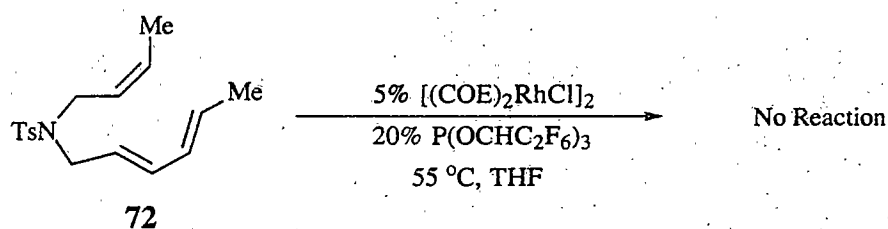
cyclobutane **69**. Alternatively, the sterically-congested nature of the rhodacyclopentane **70a** may favor isomerization to the rhodacycloheptane **70c**. Subsequent reductive elimination with allylic inversion would account for the formation of the vinyl-cyclobutane side-product **69**. Interestingly, this is the only example in which the cyclobutane product is observed in significant quantities.

The Rh-catalyzed [4+2] cycloaddition is quite sluggish with certain trienes when neutral rhodium complexes are used as catalyst. Most notably, trienes bearing substituted olefins are particularly unreactive or completely unreactive. For example, O'Mahony found that cyclization of an azatriene **71** bearing a *trans*-crotyl moiety required a long reaction



Scheme 3.3

time (Scheme 3.3).²³ Furthermore, the isomeric azatriene **72** was inert to cyclization under the same reaction conditions (Scheme 3.4).²³ The examples depicted in Schemes

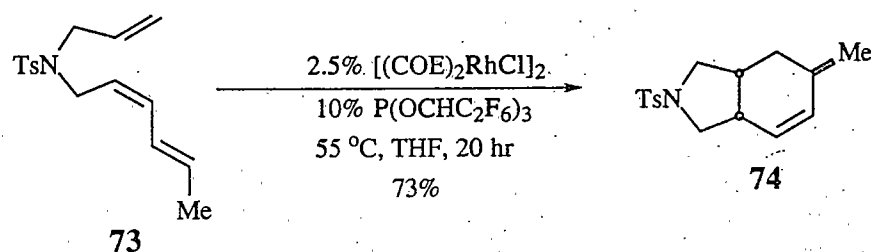


Scheme 3.4

3.3 and 3.4 demonstrate that it is difficult to predict which structural variations will be tolerated in this reaction.

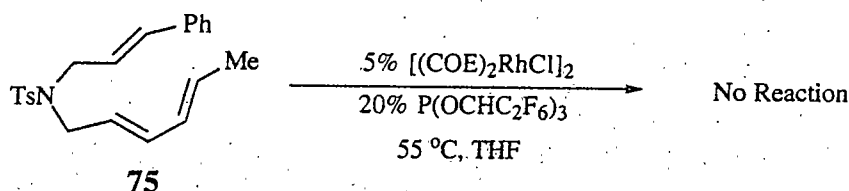
3.1.b Asymmetric Catalysis with Cationic Rhodium Complexes

In a continuation of the ongoing studies in the Livinghouse group, an azatriene **73** bearing a *Z,E*-diene unit was subjected to the standard conditions. Cyclization proceeded



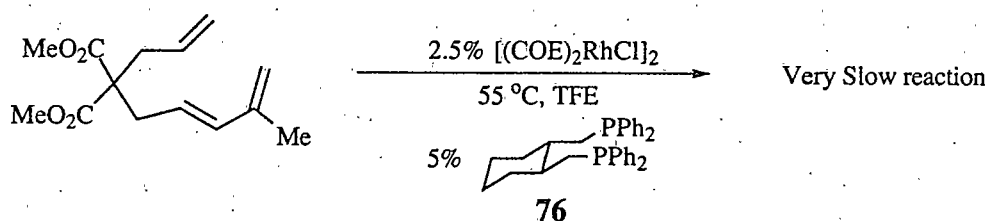
Scheme 3.5

to give the hexahydroindoline **74** with complete retention of initial diene geometry (Scheme 3.5). Further demonstration of the substitution effects of the triene is shown by the *trans*-cinnamyl bearing substrate **75**. No reaction was observed using neutral rhodium catalysts (Scheme 3.6).



Scheme 3.6

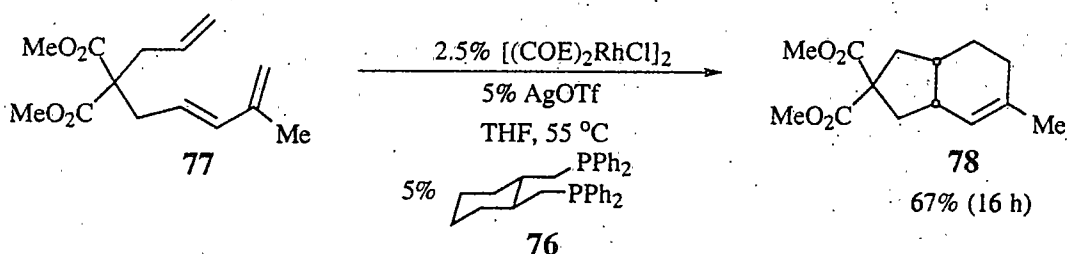
Besides the lack of reactivity with specific trienes, some chelating bis-phosphines completely inhibit useful catalysis. For example, bis-phosphine ligands, such as dppe or BINAP, in combination with $[(\text{COE})_2\text{RhCl}]_2$, provide unreactive catalyst systems. Likewise, a catalyst system derived from (+)-1,2-bis-(diphenylphosphinomethyl)-cyclohexane **76** afforded only trace amount of the desired hexahydroindane **78** even after



Scheme 3.7

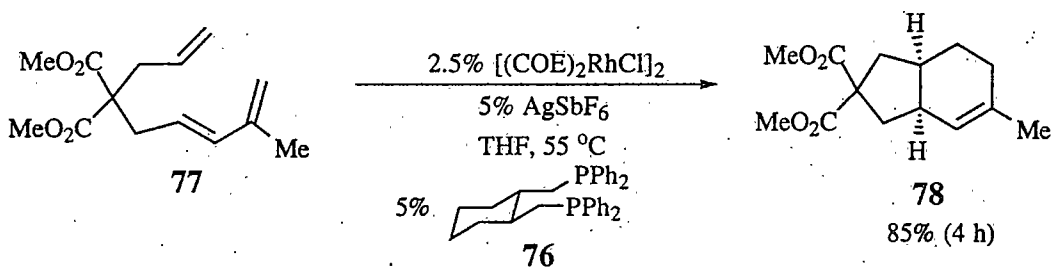
long reaction times (Scheme 3.7). Clearly, the reactivity of the catalyst system must be increased to expand the synthetic utility of this reaction.

A common solution to providing a more reactive catalyst system is to change the nature of the counterion. Most notably, the development of improved polymerization reactions has come with the realization that weakly-coordinating counterions can provide more reactive, efficient catalysts.⁵² To that end, addition of AgOTf to a solution of (+)-1,2-bis(diphenylphosphinomethyl)cyclohexane **76** and $[(\text{COE})_2\text{RhCl}]_2$ provided a more reactive catalyst relative to the corresponding neutral rhodium catalyst affording the desired



Scheme 3.8

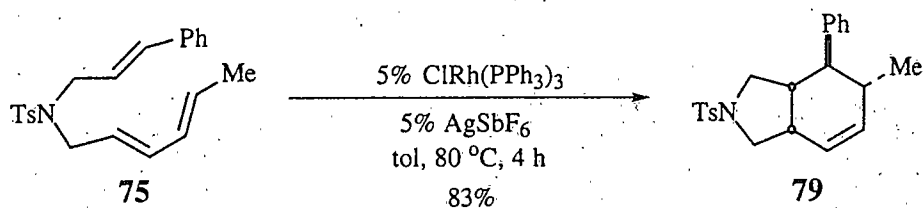
bicycloadduct **78** in 67% yield (Scheme 3.8). Under identical conditions with AgSbF_6 as additive, the bicycloadduct **78** was isolated in 85% yield in only 4 hours (Scheme 3.9). The dramatic difference in the reaction rate clearly shows that the nature of the



Scheme 3.9

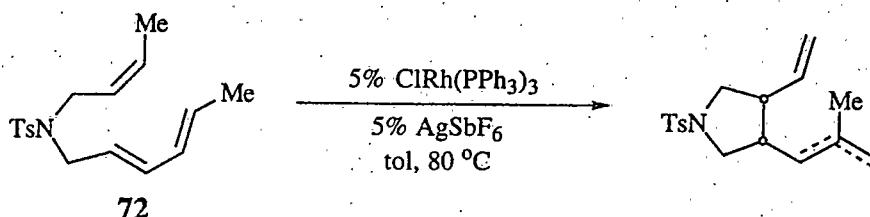
counterion can have a marked consequence on the effectiveness of a metal-catalyzed reaction.⁵³

The dramatic counterion effect observed in Rh-catalyzed [4+2] cycloaddition reaction has led to the re-examination of some of the substrates that were unreactive when using the neutral rhodium catalyst. The use of the more reactive catalyst system allowed



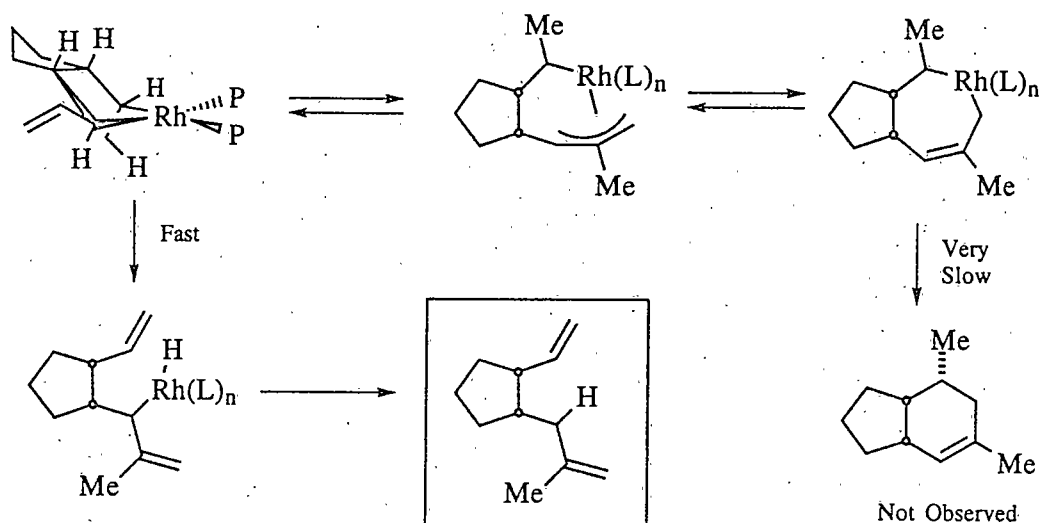
Scheme 3.10

for cyclization of the cinnamyl-derived triene **75** (Scheme 3.10). Unfortunately, some isomerization of the initially formed isoindoline **79** was observed (ca. 10%). In addition, it has been shown that cyclization of a triene **72** bearing a *cis*-crotyl unit affords a diene



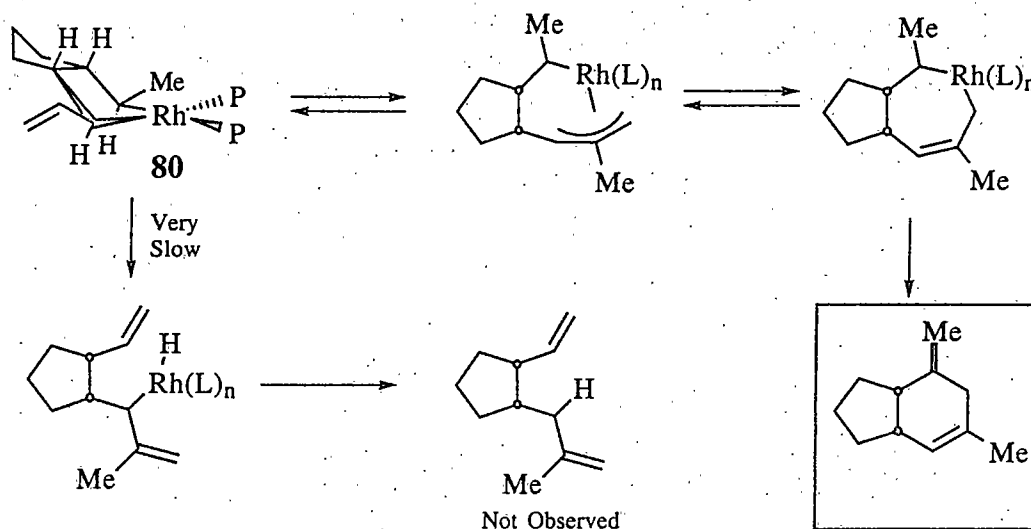
Scheme 3.11

(Scheme 3.11).²³ Presumably, this product arises from a competitive β -hydride elimination/reductive elimination sequence as depicted in Scheme 3.12. Some isomerization of the initially formed diene was observed.²³ The suggested mechanism also explains why substrates bearing *trans*-crotyl moieties lead to the desired bicycloadduct.



Scheme 3.12

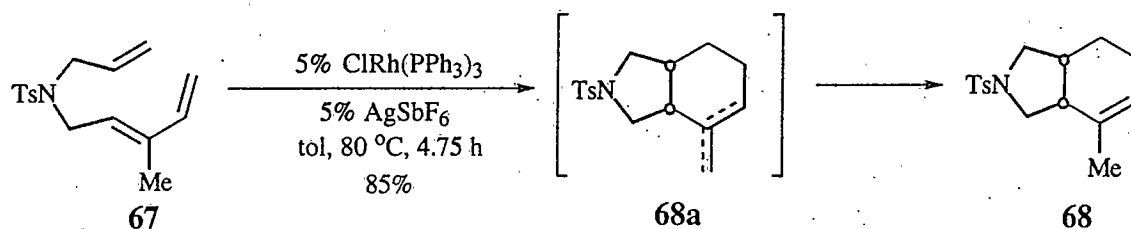
Examination of the putative rhodacyclopentane **80** shows that the required *syn*, co-planar orientation for β -hydride elimination is geometrically disfavored (Scheme 3.13).



Scheme 3.13

Presumably, inversion of the rhodacyclopentane **80** is energetically disfavored due to a pseudo-1,3-diaxial interaction between the methyl and vinyl groups.

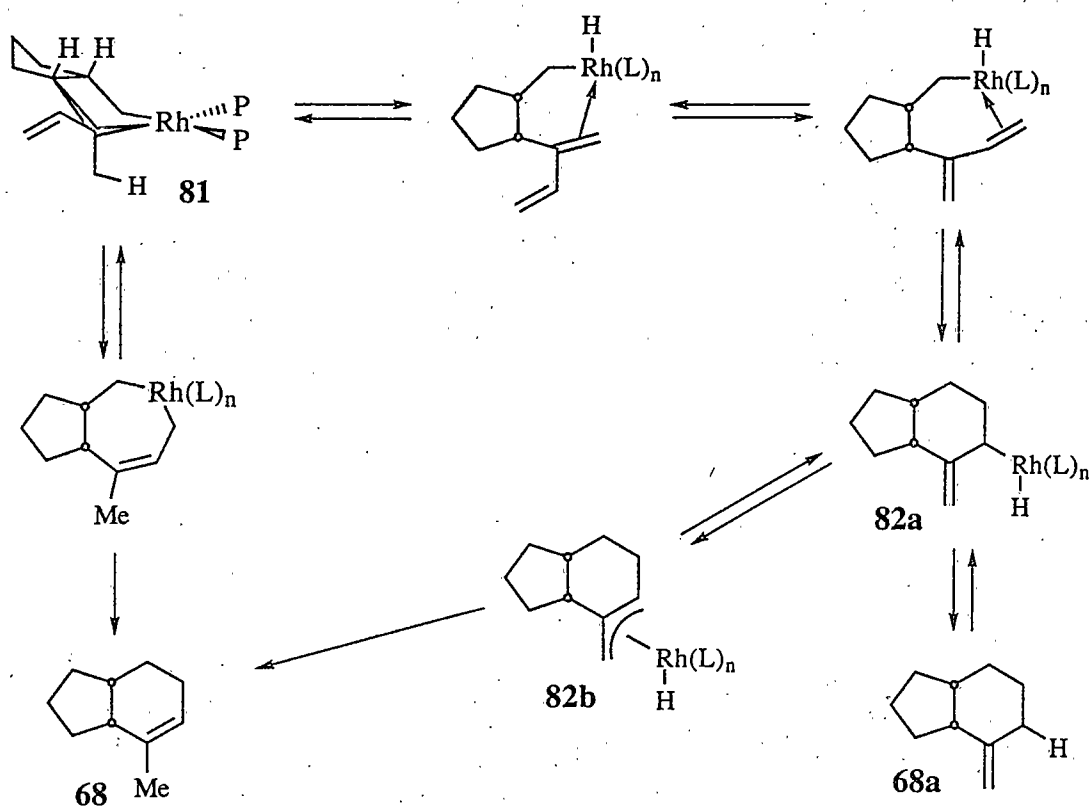
It has been shown that addition of AgSbF_6 to a solution of Wilkinson's catalyst allowed for the cyclization the 3-methyl substituted azatriene **67** (Scheme 3.14).⁴³



Scheme 3.14

While the overall reaction time is 4.75 hours, it was observed that the starting triene is consumed quite rapidly.^{23,43} The primary products of the reaction are the desired

isoidoline **68** and an exo-methylene isoidoline **68a**. Under the reaction conditions, isomerization of the exo-methylene unit of isoidoline **68a** afforded the desired hexahydroisoidoline **68**. The formation of the exo-methylene isoidoline **68a** can be rationalized upon examination of the putative intermediates of the reaction. Initial oxidative cyclization affords an intermediate rhodacycle **81** that possesses a hydrogen that is suitably

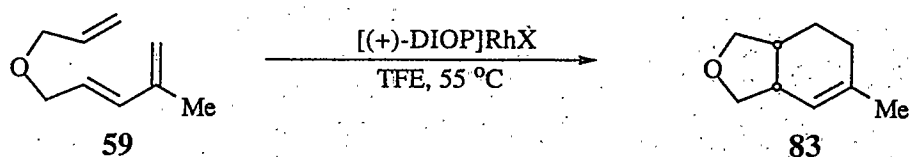


Scheme 3.15

aligned for a β -hydride elimination. Ligand exchange and a carbometallation/reductive elimination sequence provides the observed product **68a** (Scheme 3.15). Under the reaction conditions, isomerization of the exo-methylene isoidoline **68a** to the more stable trisubstituted olefin **68** occurs through the allyl rhodium hydride complex **82a,b**.

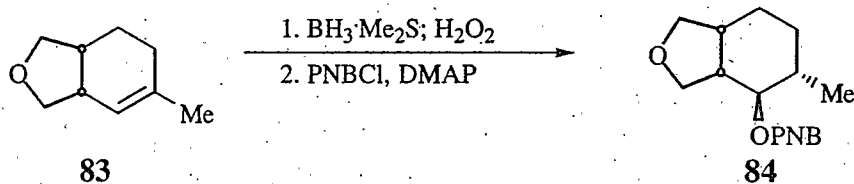
The development of a more active catalyst was hoped to lead to improved selectivity in the enantioselective Rh-catalyzed [4+2] cycloaddition. While the cationic rhodium complexes provided increased reactivity, the level of asymmetric induction remained similar as shown in **Table 3.1**. The yields in **Table 3.1** represent the overall yield for the three-

Table 3.1. Counterion Effects on the Enantioselective Rh-Catalyzed [4+2] Cycloaddition



Counterion	Yield (%)	ee (%)
Cl	57	18
OTf	64	17
SbF ₆	56	17

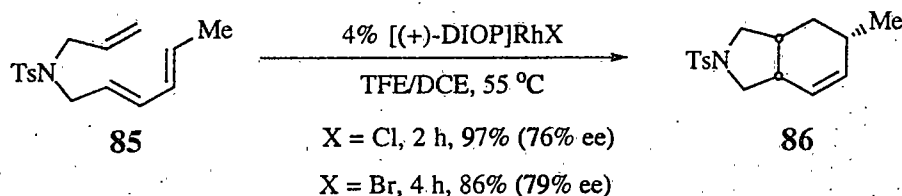
step process to obtain a substrate **84** that was easily resolved by HPLC on a Chiralpak AD. This process involved a hydroboration/oxidation sequence followed by acylation with *p*-nitrobenzoyl chloride (**Scheme 3.16**).



Scheme 3.16

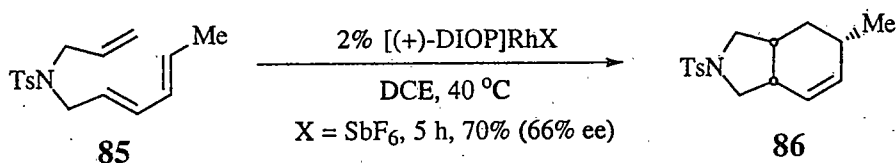
Further exploration of the counterion effect on the enantioselective Rh-catalyzed [4+2] cycloaddition was accomplished with the tosyl-protected azatriene **85**. Reactions

performed with chloride, bromide and triflate as counterions required the use of TFE as co-solvent. The level of asymmetric induction with chloride and bromide as counterion was similar (Scheme 3.17). The use of triflate as counterion led to bicycloadduct **86** with



Scheme 3.17

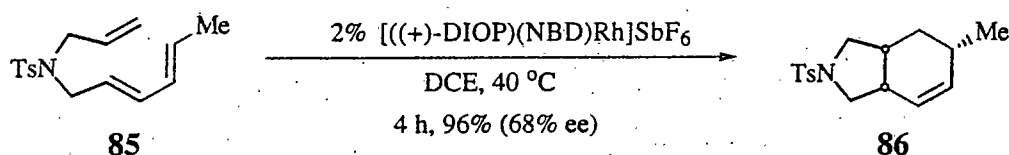
reduced enantioselectivity (61% ee) relative to the inner sphere chloride and bromide counterions. Using the same reaction conditions with hexafluoroantimonate as counterion, almost complete isomerization of the isoindoline **86** was observed. It was found that this highly reactive catalyst system provided the desired product **86**, without isomerization, if



Scheme 3.18

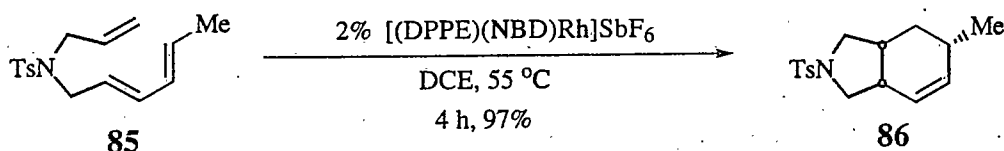
only 1,2-dichloroethane was used as solvent at 40 °C (Scheme 3.18). The level of asymmetric induction was similar to the reaction with triflate as counterion.

A similar, but somewhat more reactive catalyst system, could be generated from [((+)-DIOP)Rh(NBD)]SbF₆. Simply treating a solution of from [((+)-DIOP)Rh(NBD)]SbF₆ with dihydrogen for 15 minutes (followed a by freeze-pump-thaw protocol to remove adventitious H₂), followed by addition of azatriene **85** led to



Scheme 3.19

bicycloadduct **86** in excellent yield (Scheme 3.19). A catalyst system prepared in an analogous fashion using [(DPPE)Rh(NBD)]SbF₆ provided the isoindoline **86** in 97% yield (Scheme 3.20). Interestingly, the catalyst system derived from DPPE, [(COE)₂RhCl]₂



Scheme 3.20

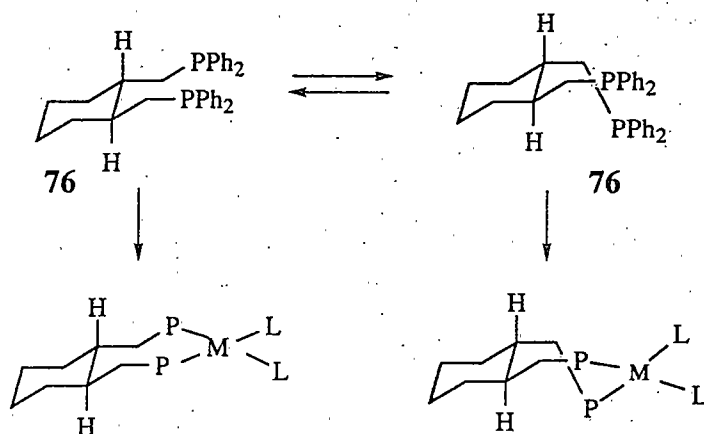
and AgSbF₆ does not lead to any bicycloadduct formation. Catalyst generation from [(NBD)₂Rh]SbF₆ is currently the preferred method for screening chiral bis-phosphines.

3.1.c Studies Toward the Synthesis of Conformationally-Restricted Chiral Phosphine Ligands

Previous studies in the Livinghouse laboratory have shown that bis-phosphine rhodium complexes that form 7-membered chelates are the most active for the Rh-catalyzed [4+2] cycloaddition.⁵¹ Studies described in the previous section have shown that (+)-1,2-bis(diphenylphosphinomethyl)cyclohexane **76** is a poor chiral controller for the Rh-catalyzed [4+2] cycloaddition. In addition, bis-phosphine **76**, structurally related to (+)-DIOP, has been shown to function poorly as a chiral controller for the Rh-catalyzed

hydrogenation of dehydroaminoacid derivatives⁵⁴ and in the intramolecular Rh-catalyzed hydroacylation reaction.⁵⁵

While a rationale for lower stereocontrol in these reactions is speculative and may differ depending on the specific reaction, one explanation may be the ability of bis-phosphine **76** to ligate the transition metal in two diastereomeric modes as depicted in Scheme 3.21 (phenyl groups omitted for clarity). Indeed, low temperature ³¹P NMR

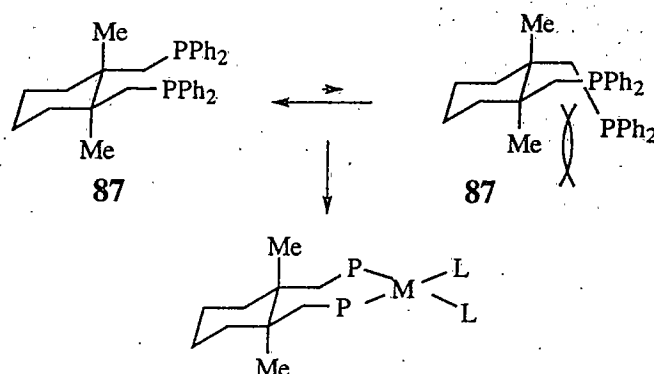


Scheme 3.21

studies of structurally related complexes, [(DIOP)Rh(COD)]BF₄ and [(DIOP)Ir(COD)]BF₄, have shown that each exists as a mixture of diastereomeric complexes.⁵⁶ Though several factors control stereogenesis in metal-catalyzed reactions, poor stereinduction in reactions using structurally flexible ligands may be a result of diastereomeric complexes derived from two energetically similar modes of ligation.

The goal was to prepare novel bis-phosphine ligand **87** that was related to bis-phosphine **76**, but possesses structural features that should favor the formation of only one active metal complex (Scheme 3.22). Introduction of methyl groups into the cyclohexane skeleton should limit the number of available conformations due to a sterically unfavorable pseudo-1,3-diaxial interaction, and should favor a conformation in which both

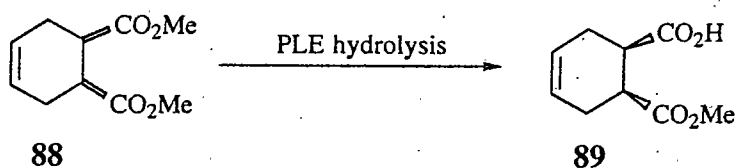
diarylphosphinomethyl units are equatorially disposed. As the constraining effect of the methyl groups is expected to limit the rotational freedom of the phosphinomethyl groups, one would expect the number of energetically favorable metal ligation modes to be reduced (Scheme 3.22). Furthermore, the "edge-face" presentation⁵⁷ of the aryl groups bound



Scheme 3.22

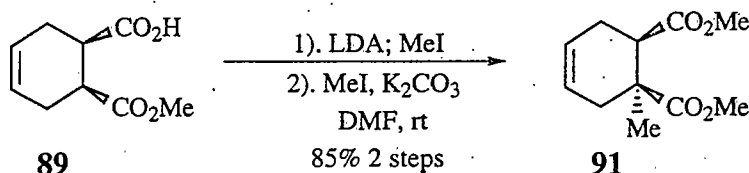
to phosphorus may be enhanced due to the minimization of van der Waals interactions with the methyl groups. On the other hand, a very rigid carbon skeleton may provide an unsuitable natural bite angle⁵⁸ or may limit the number of energetically available bite angles so that catalysis may be impeded. For example, X-RAY data for some sterically demanding chiral ligand-metal complexes have shown that the expected C_2 symmetry is not always observed, and C_1 symmetry is preferred.⁵⁹

The strategy chosen to obtain the chiral carbon backbone of the novel phosphine ligand relies on enzymatic desymmetrization. Ohno has shown that PLE hydrolysis of *cis*-dimethyl cyclohex-3-ene-dicarboxylate **88** is amenable to the large scale preparation of optically pure half ester **89** in high chemical yield (Scheme 3.23).^{60c} In addition, Ohno has reported the conversion of the half ester **89** into the opposite antipode, making our route to the chiral phosphine cost effective and practical as access to both enantiomerically pure bis-phosphines is possible.^{60a}



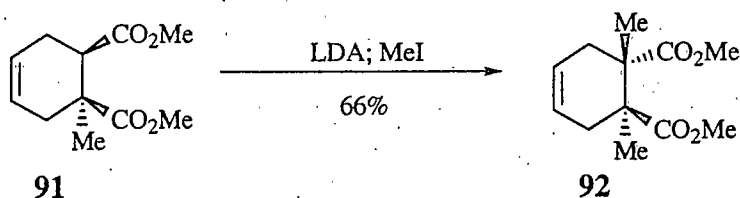
Scheme 3.23

PLE hydrolysis of the *cis*-diester **88** afforded the half ester **89** in 90% yield. Selective methylation of the half ester **89** (LDA, MeI, -78°C) occurred in 88% yield (Scheme 3.24). Methylation was reported to occur *anti* to the carboxylic acid moiety.^{60b} It is important to note that erosion of the facial selectivity in the methylation would seriously compromise the enantiomeric purity of the dimethyl diester **92** as subsequent methylation of a mixture of diastereomers would provide a mixture of enantiomers. Esterification with K_2CO_3 and MeI provided diester **91** (97% yield) as a single diastereomer (Scheme 3.24).



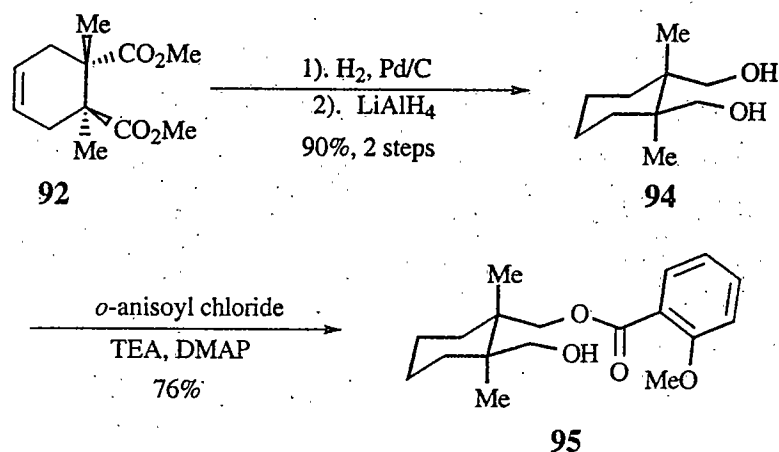
Scheme 3.24

Methylation of the diester **91** provided a mixture of (R,S)-diester **92** and meso-diester **92** (7.5/1 ratio by GC analysis) that were separated by recrystallization (MeOH, 0°C) affording the (R,S)-diester⁶¹ **92** in 66% isolated yield (Scheme 3.25). The meso-



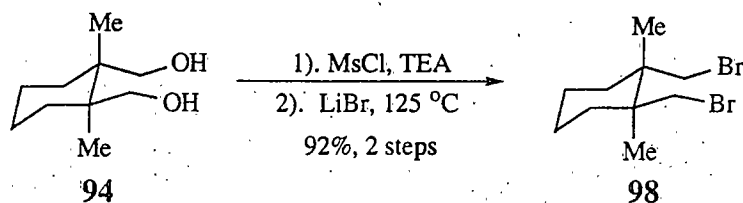
Scheme 3.25

diester **92** could not be recovered in pure form. Olefin reduction followed by lithium aluminum hydride reduction afforded the diol **94** in excellent overall yield. The diol **94** was converted to the mono *o*-anisoate **95** and the optical purity was determined to be >99% ee (HPLC, Chiralpak AD) (Scheme 3.26).



Scheme 3.26

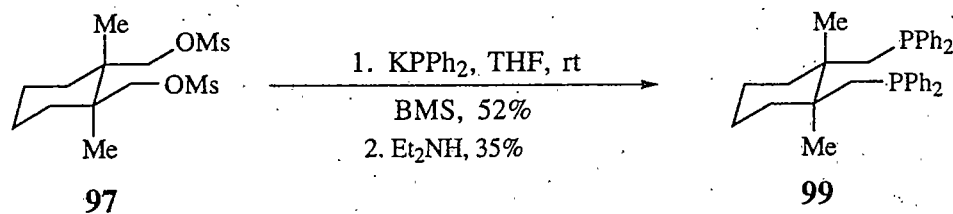
Treatment of the diol **94** with MsCl and triethylamine provided the dimesylate **97** that was transformed into the dibromide **98** with LiBr in HMPA at 125°C (Scheme 3.27). Interestingly, analysis of the crude reaction mixture suggested that the dimesylate **97** was converted to the bromo mesylate within 2.5 hours, but formation of the dibromide **98** required 15 hours.



Scheme 3.27

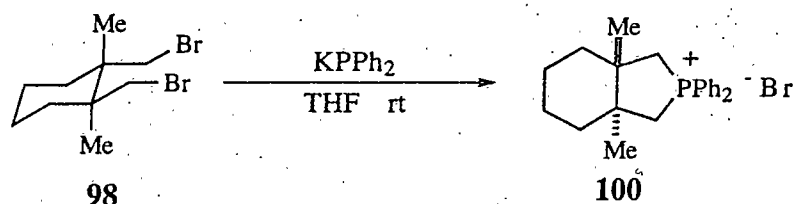
The synthesis of the phosphine ligand precursor **97** has been accomplished in seven steps in 43% overall yield from the commercially available *cis*-dimethyl cyclohex-3-ene-dicarboxylate **88**. The availability of the enantiomerically pure (R,S)-diester **92** presents an opportunity to prepare a variety of novel, conformationally-restricted ligands for asymmetric catalysis.

Early efforts towards the formation of the two carbon phosphorus bonds focused on displacement of a number of different leaving groups by metal phosphides or phosphide-boranes. Phosphide-boranes⁶² were found to be unreactive towards the sterically hindered electrophile. It was discovered that only the most reactive electrophile (mesylate and bromide) and the most potent nucleophile (MPPh₂; M = K) combinations led to the formation of any desired products. Using the optimal conditions, addition of the potassium diphenyl phosphide to the dimesylate **97** at room temperature afforded the desired phosphine in 52% yield after four days at room temperature (Scheme 3.28). The crude reaction mixture was treated with BH₃·THF to facilitate isolation of the desired bis-phosphine. (Scheme 3.28). Deprotection was accomplished by heating with Et₂NH.



Scheme 3.28

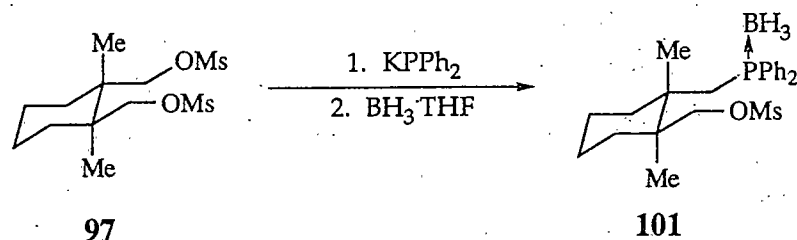
Using similar reaction conditions with the dibromide **98** led to the formation of the diphenylphosphonium bromide **100** as the only isolable product as suggested by ³¹P NMR spectroscopy (61 ppm) (Scheme 3.29). Modifying the temperature at which the



Scheme 3.29

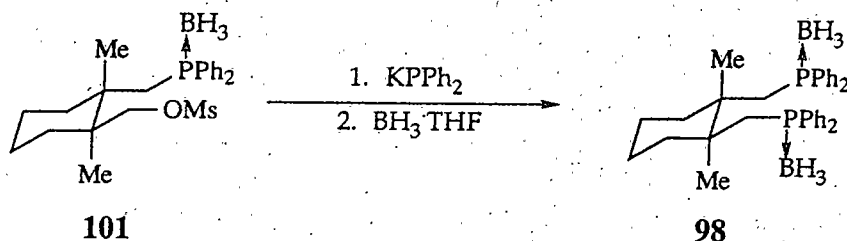
dibromide **98** was added had no effect as the phosphonium salt **100** was the only significant product. The observation that a single substitution on the sterically congested backbone is quite facile, while the second displacement is extraordinarily slow, is consistent with the substitution chemistry of the dimesylate **97** with lithium bromide.

Considering the reactivity profile of this hindered bis-electrophile, an alternative approach involving the stepwise addition of phosphorus nucleophiles could be explored. Specifically, addition of *one* equivalent of potassium diphenylphosphide to the dimesylate **97** followed by treatment with $\text{BH}_3 \cdot \text{THF}$ should selectively form the monophosphine-borane **101** (Scheme 3.30). Purification of the phosphine-borane **101** and subsequent



Scheme 3.30

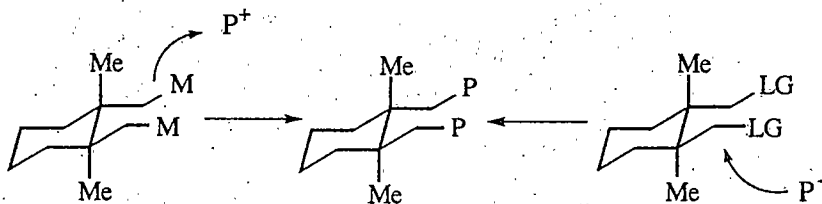
treatment with another equivalent of potassium diphenylphosphide followed by heating should lead to the desired bis-phosphine-borane **98** (Scheme 3.31). Protection of



Scheme 3.31

the phosphine with borane should inhibit the formation of the undesired phosphonium salt, allowing for more vigorous reaction conditions to be used. Clearly, for this approach to succeed, substitution must be faster than any other competitive processes, such as trans-boronation.

While extensive effort had been directed towards the displacement of various leaving groups, the method may ultimately be limited to the synthesis of sterically similar (diaryl)phosphines. For example, nucleophilic attack of more sterically-hindered phosphides, such as an ortho substituted aryl phosphine, may be much slower than just the simple diphenyl phosphide. A potentially more general approach uses the chiral carbon backbone as a nucleophile so that sterically and electronically different phosphine moieties could be introduced using the common procedure. (Scheme 3.32). In addition, the formation of phosphonium salts will be avoided by this reversal of polarity. Whitesides



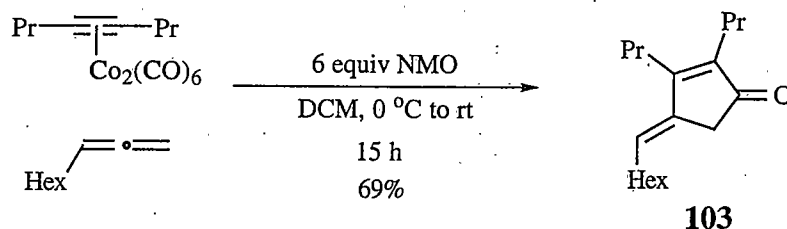
Scheme 3.32

has shown that bis(Grignard) reagents of similar structure can be prepared, albeit in very modest yield.⁶³ Likewise, Knochel has used bis(zinc) reagents for the synthesis of assorted phosphines and phosphine-boranes in reasonable yields.⁶⁴ Unfortunately, all attempts to form the carbon-phosphorus bonds using either the bis(Grignard) or the bis(organozinc) reagents have not produced satisfactory results.

3.2 Catalytic Pauson-Khand Reaction

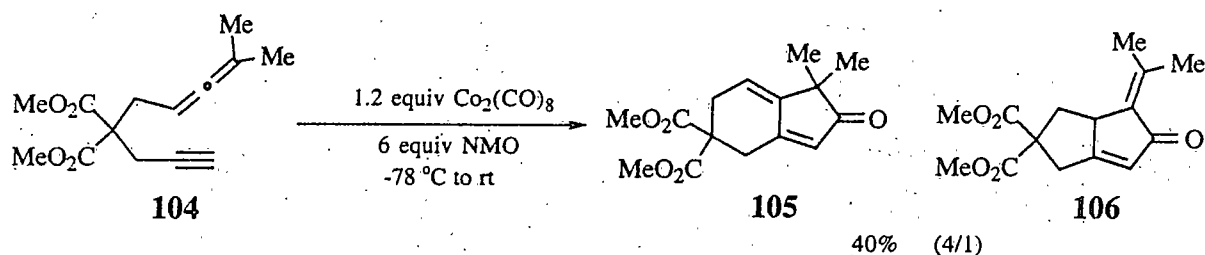
3.2.a Introduction

The initial goal in the area of the catalytic Pauson-Khand reaction was the carbonylative cyclization of allenynes. At the outset of this research, limited examples of this transformation, either with stoichiometric or catalytic transition metal complexes, had appeared in the literature. Cazes was the first to show that isolated cobalt-alkyne complexes formed β -alkylidene cyclopentenones when treated with NMO and allenes (Scheme 3.33).^{65a,b} Interestingly, Cazes noted that the simply heating alkyne cobalt



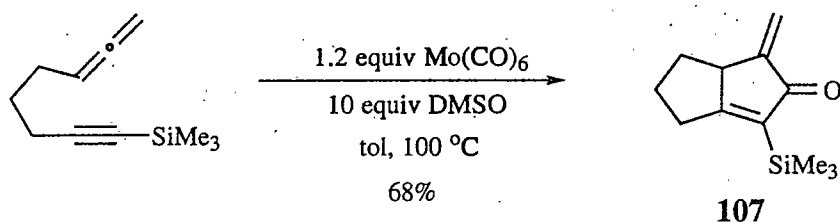
Scheme 3.33

complexes with allenes (toluene, 110 °C) failed to produce a significant quantity of bicyclopentenone **103** (6%).^{65a} Cazes subsequently showed that a similar NMO-promoted protocol provided modest yields of α -alkylidene bicyclopentenones in the intramolecular PKR.^{65c} Initial complexation of the allenyne with $\text{Co}_2(\text{CO})_8$ was performed at 0 °C. The crude allenyne-cobalt complexes were then treated with NMO at -78 °C followed by warming to room temperature. A typical result is shown in Scheme 3.34.



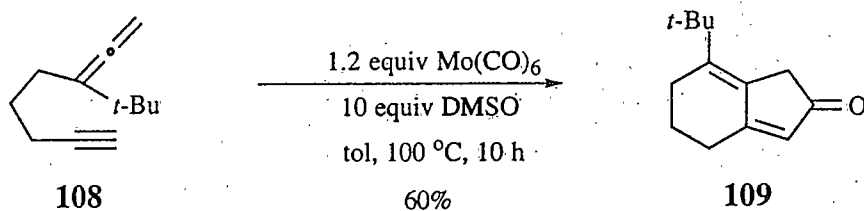
Scheme 3.34

A more selective method for bicyclopentenone formation has been devised by Brummond who found that $\text{Mo}(\text{CO})_6$ was a suitable promoter of the formal [2+2+1] cycloaddition (Scheme 3.35).^{66a} Despite the rather forcing reaction conditions, excellent



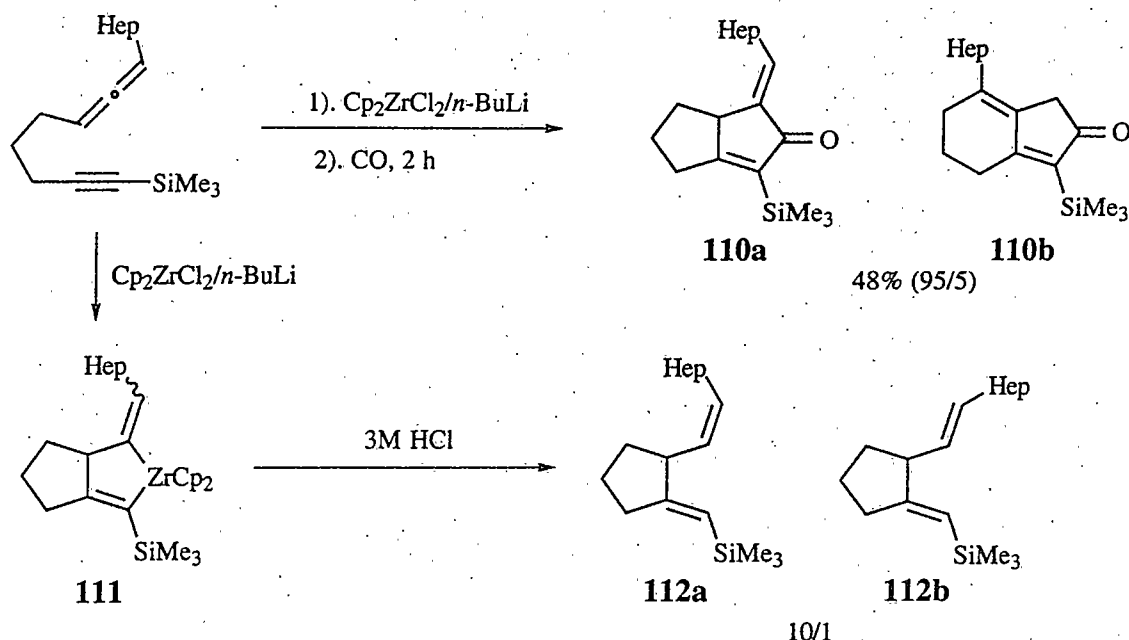
Scheme 3.35

selectivity for the α -methylidene pentalenone **107** was achieved in modest yield. The product formed in the reaction was found to be dependent on the steric nature of the allene moiety. For instance, a substrate **108** bearing a *t*-butyl-substituted allene led to the indenone **109** when subjected to the Mo-promoted reaction conditions (Scheme 3.36).^{66b} Brummond also reported that the Negishi bicyclization/carbonylation protocol⁶⁷



Scheme 3.36

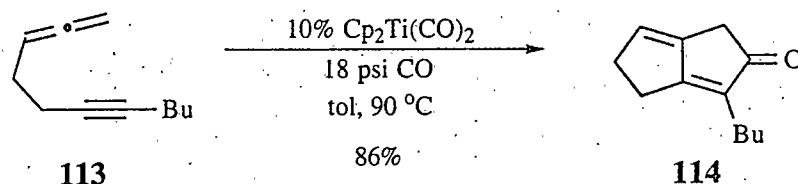
allowed for a modest yield of bicyclopentenones **110a,b** as a 95/5 mixture of pentalenone and indenone (**Scheme 3.37**).^{66c} Hydrolysis of the intermediate zirconacyclopentene



Scheme 3.37

111 showed that the π -bond facial selectivity is not stereospecific as it gave a mixture of (10/1) dienes **112a,b** (yield not determined). It is not clear if the initial oxidative cyclization or the subsequent CO insertion accounted for the reduced yield.

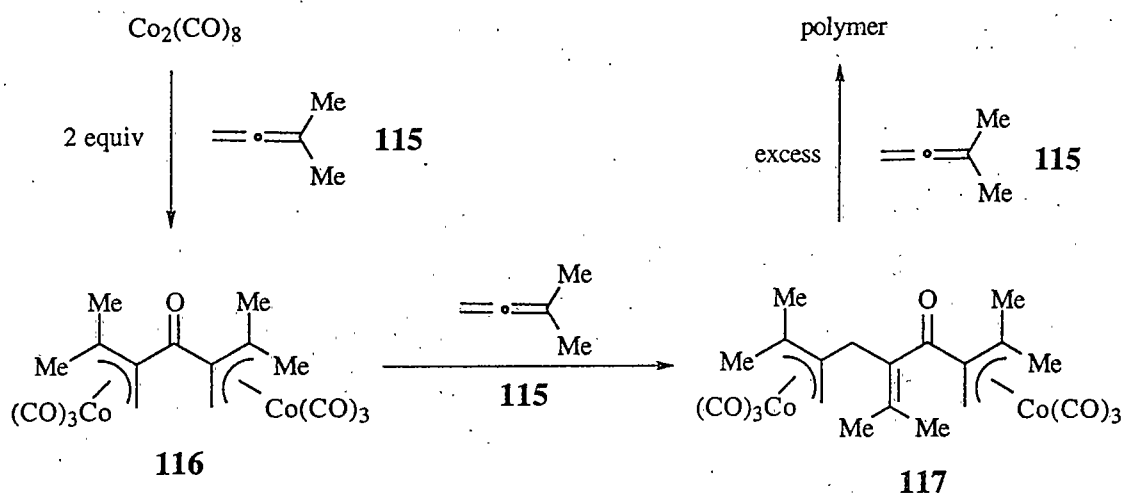
Buchwald has recently disclosed that Cp₂Ti(CO)₂ was an effective catalyst for the [2+2+1] cycloaddition. In addition, a single example of a carbonylative allenyne cyclization was described (**Scheme 3.38**).^{35a} It is significant that this single example



Scheme 3.38

represents the only catalytic carbonylative allenyne cyclization reported in the literature at the time of this writing.

The scarce number of successful examples of the Pauson-Khand reaction involving allenynes may reflect the presumption that allenes are unstable in the presence of $\text{Co}_2(\text{CO})_8$. In 1957, it was reported that certain allenes rapidly reacted with $\text{Co}_2(\text{CO})_8$ at room temperature.⁶⁸ In 1996, Ungváry showed that treatment of $\text{Co}_2(\text{CO})_8$ with excess 3-methyl-1,2-butadiene **115** afforded polymer.⁶⁹ Under more carefully controlled conditions, treatment of $\text{Co}_2(\text{CO})_8$ with 2 equivalents of 3-methyl-1,2-butadiene **115** gave a new cobalt complex **116**. Addition of another equivalent of 3-methyl-1,2-butadiene **115** produced the novel cobalt complex **117** (Scheme 3.39). The X-ray structures of cobalt



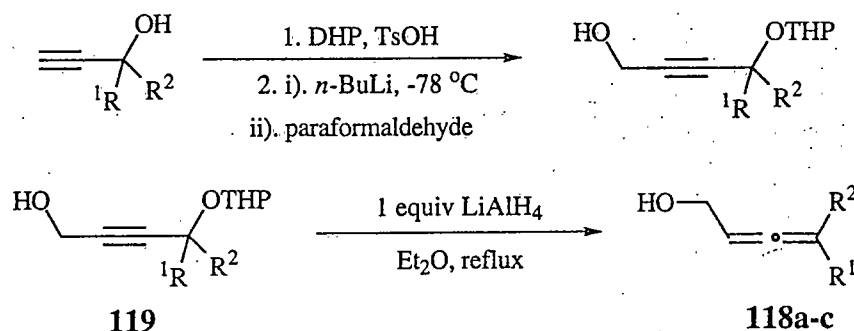
Scheme 3.39

complexes **116** and **117** have been determined.⁶⁹ Further addition of 3-methyl-1,2-butadiene **115** led to its complete consumption. The ability to successfully catalyze the carbonylative cyclization of allenynes may depend on the relative rate of alkyne complexation versus allene complexation.

3.2.b $\text{Co}_2(\text{CO})_8$ -Catalyzed Carbonylative Allenyne Cyclizations

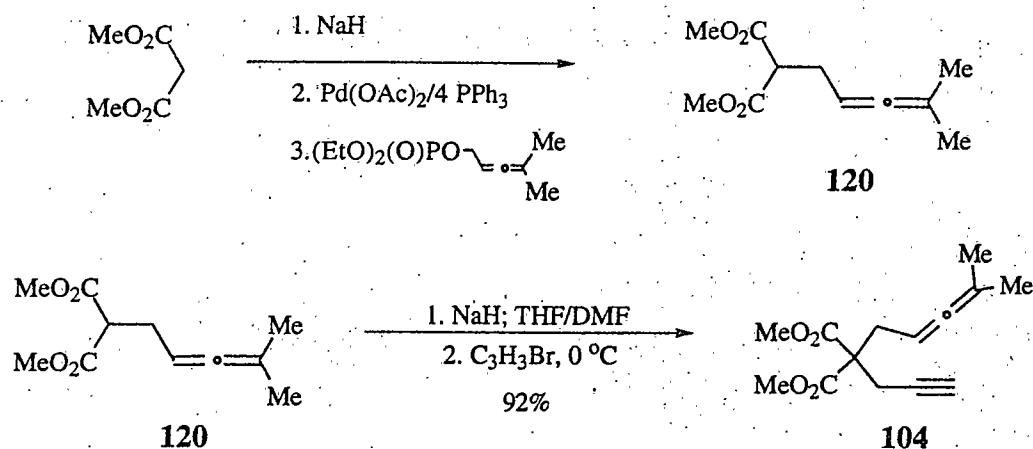
At the outset of this research and at the time of this writing, the $\text{Co}_2(\text{CO})_8$ -catalyzed carbonylative allenyne cyclization has not been reported in the literature. The initial goals in this area were 1). to establish that the reaction could indeed be performed with catalytic $\text{Co}_2(\text{CO})_8$, and 2). to explore the scope of the reaction regarding substrate structure.

In principle, a variety of α -allenic alcohols **118** can be prepared from the corresponding mono-tetrahydropyranyl derivatives of butyne-1,4-diols **119** using known methods (Scheme 3.40).⁷⁰ Three structurally different α -allenic alcohols (**118a**, $\text{R}_1 = \text{R}_2 = \text{H}$, **118b**, $\text{R}_1 = \text{R}_2 = \text{Me}$, **118c**, $\text{R}_1 = \text{Me}$, $\text{R}_2 = \text{H}$) were prepared with the assumption that these simple subunits would provide acceptable models for more complex allene moieties.



Scheme 3.40

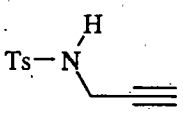
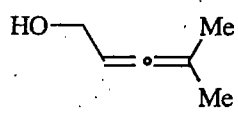
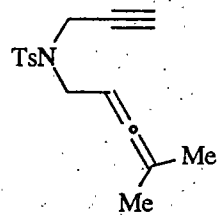
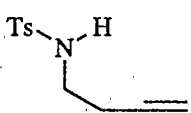
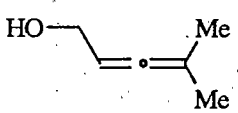
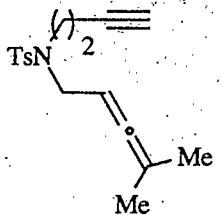
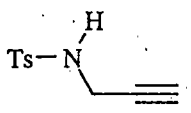
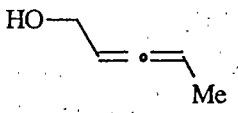
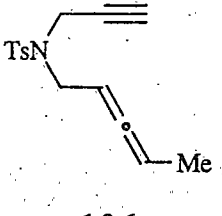
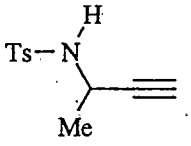
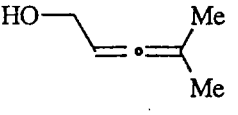
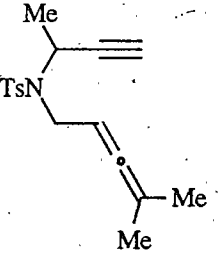
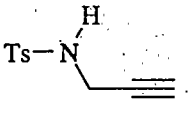
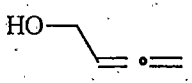
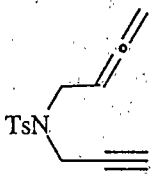
Using a slightly modified procedure developed by Cazes, the following malonate-derived allene **120** was prepared in modest yield.⁷¹ The reaction proved to be somewhat capricious, giving reduced yields upon scale-up. Subsequent alkylation with propargyl bromide afforded the desired allenyne **104** in excellent yield (Scheme 3.41).



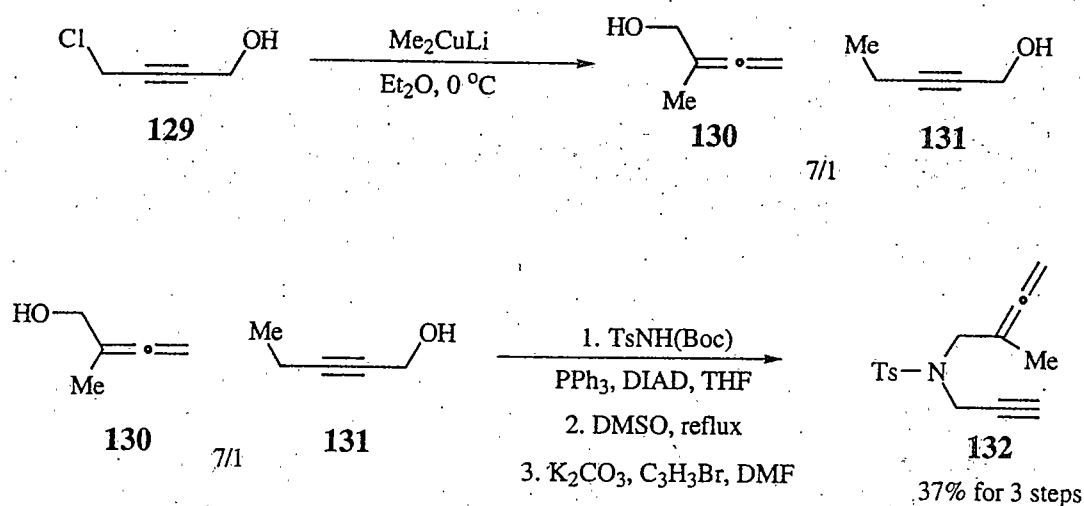
Scheme 3.41

A more convenient route to allenynes was subsequently developed. Subjection of the α -allenic alcohols **118a-c** and alkynyl tosamides to Mitsunobu alkylation⁷² conditions provided good to excellent yield of the desired allenynes. Representative Mitsunobu reactions are depicted in Table 3.2. Besides the improved yields and the higher degree of convergence when using the Mitsunobu reaction, the ability to use α -allenic alcohols **118** directly obviates the need for conversion to volatile, electrophilic reagents.

Table 3.2. Preparation of Allenynes via the Mitsunobu Reaction

Entry	Tosamide	Alcohol	Allenyne	Yield (%)
1	 121	 118b	 124	80
2	 122	 118b	 125	91
3	 121	 118c	 126	91
4	 123	 118b	 127	93
5	 121	 118a	 128	80

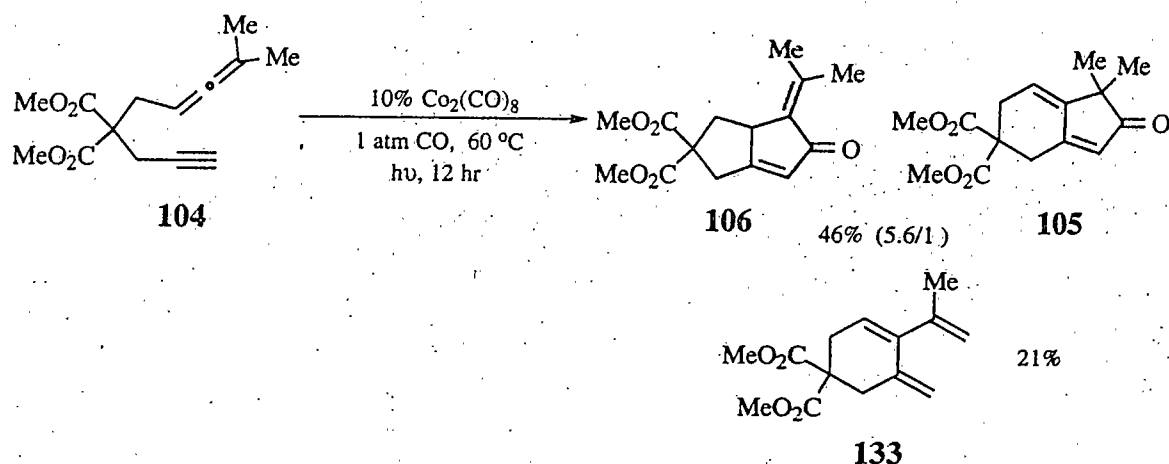
Treatment of the propargyl chloride⁷³ **129** with dimethyl cuprate afforded the 2-methyl-substituted allenol **130** admixed with 2-pentyn-1-ol **131**.⁷¹ Subsequent deprotection, Mitsunobu coupling and alkylation afforded the desired allenyne **132** after recrystallization (Scheme 3.42). It is quite remarkable, considering the high yields



Scheme 3.42

achieved in these reactions, that few Mitsunobu reactions involving α -allenic alcohols have been reported in the literature.⁷²

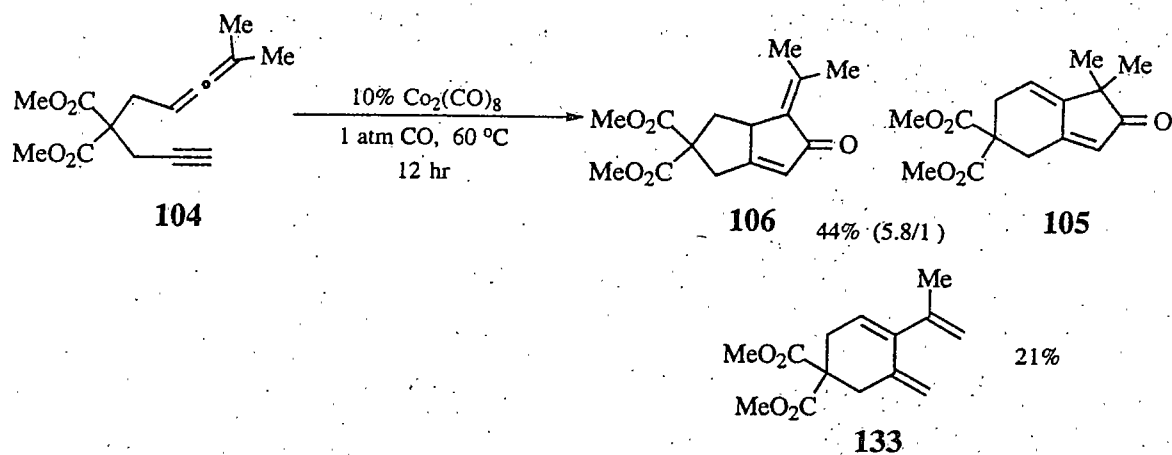
The investigation initially involved allenyne **104**. Treatment of a solution of Co₂(CO)₈ (10 mol % in 1,2-DME at 0 °C) with allenyne **104**, followed by Q-Beam



Scheme 3.43

irradiation^{18,20} afforded a mixture of bicyclopentenones **105** and **106** in poor yield (Scheme 3.43). Interestingly, the major isomer **106** formed in this catalytic photopromoted Pauson-Khand reaction was the minor product observed in the stoichiometric NMO-promoted reaction reported by Cazes (*vide supra*).^{65c} Along with the bicyclopentenone products **105** and **106**, an unexpected triene **133** was isolated in 21% yield.

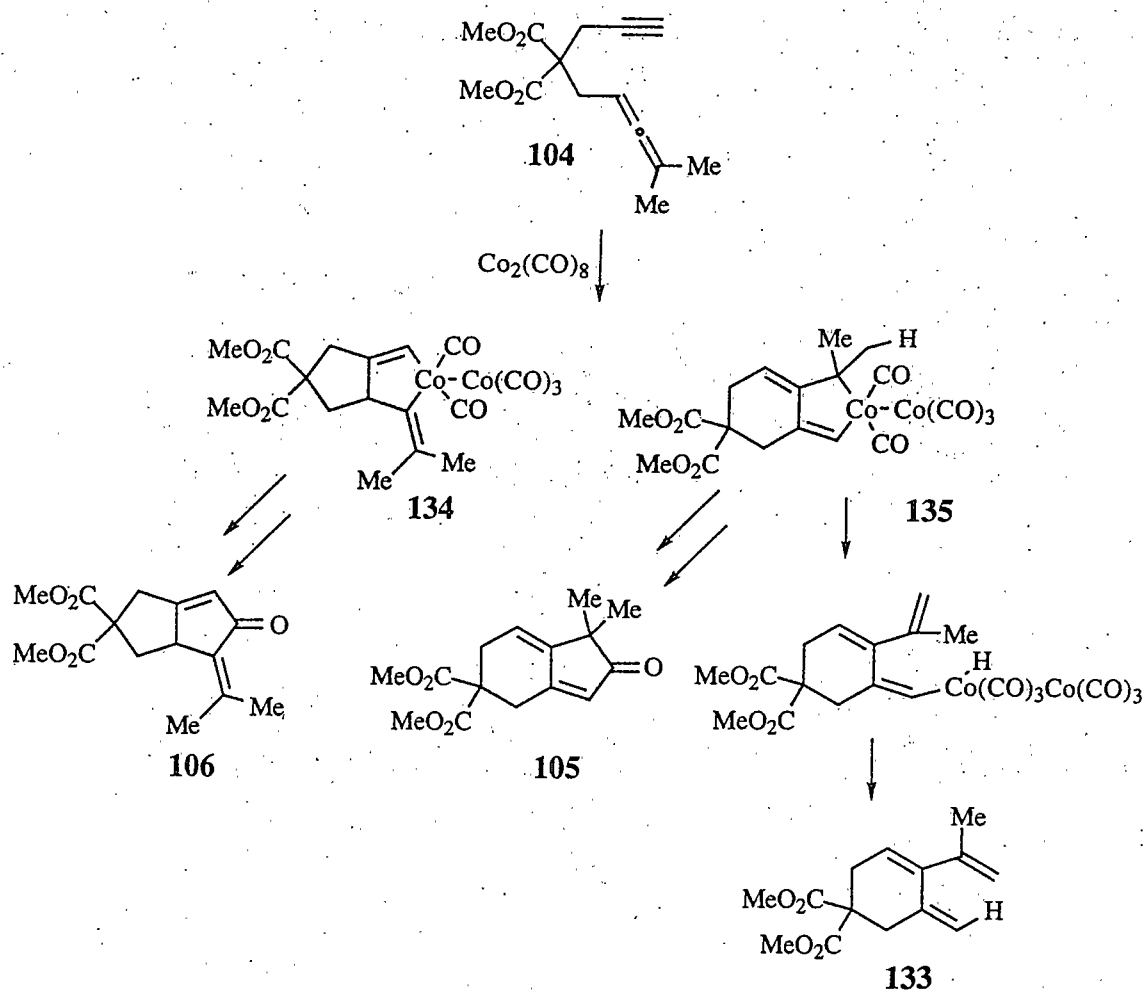
In an attempt to determine whether triene **133** formation was a thermally promoted reaction, an identical experiment was performed at 60 °C *with the exclusion of visible light*. Surprisingly, the thermal reaction afforded a similar yield and isomeric ratio of α -isopropylidene pentalenone **106** and indenone **105** products. In addition, the triene side-product **133** was isolated in the same yield as in reaction using Q-Beam irradiation



Scheme 3.44

(Scheme 3.44). This observation led to a more careful study of the temperature effect on the catalytic photopromoted Pauson-Khand reaction and is described in Section 3.2.c.

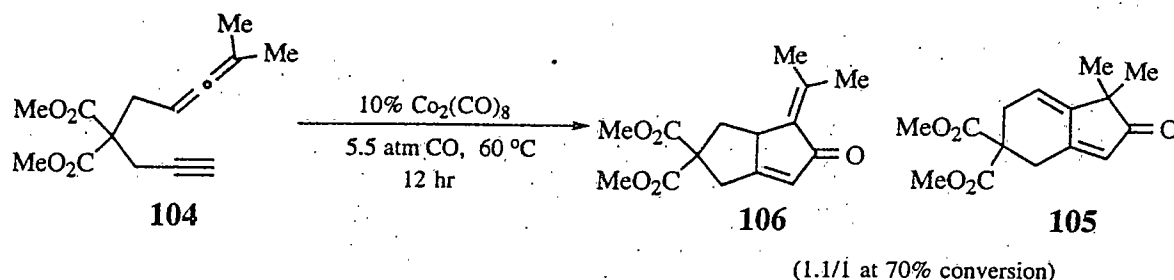
Two limiting mechanisms can be suggested for the triene side-product formation. In the first mechanism, initial complexation and oxidative cyclization can lead to two isomeric cobaltocycles **134** and **135** (Scheme 3.45). A β -hydride/reductive elimination



Scheme 3.45

sequence from the putative cobaltobicyclo[4.3.0]nonadiene **135** gives the observed triene. In principle, the formation of this triene side-product could be minimized at higher CO pressures.

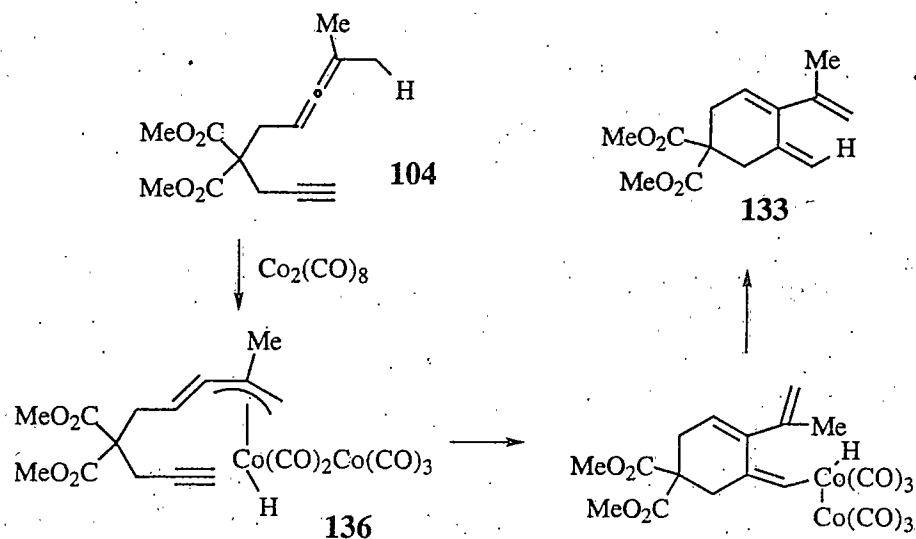
To that end, an identical reaction performed at 5.5 atm CO (estimated internal pressure at 60 °C) afforded a 1.1/1 mixture of bicyclopentenones **106** and **105**, in addition to the undesired triene (Scheme 3.46). At 5.5 atm of CO, the triene **133** was produced in approximately the same amount as in the reaction performed at 1 atm CO. This



Scheme 3.46

interesting experiment reveals the complex nature of this catalytic process. Clearly, the observed pentalenone vs. indenone selectivity is dependent on both the migratory aptitudes of each cobaltocycle, as well as the preference for initial cobaltocycle formation.

A second possible mechanism for triene formation proceeds through a cobalt allyl hydride. Coordination of the allene by a coordinatively unsaturated cobalt species followed by C-H insertion and η^1 to η^3 isomerization gives the putative dicobalt intermediate **136**

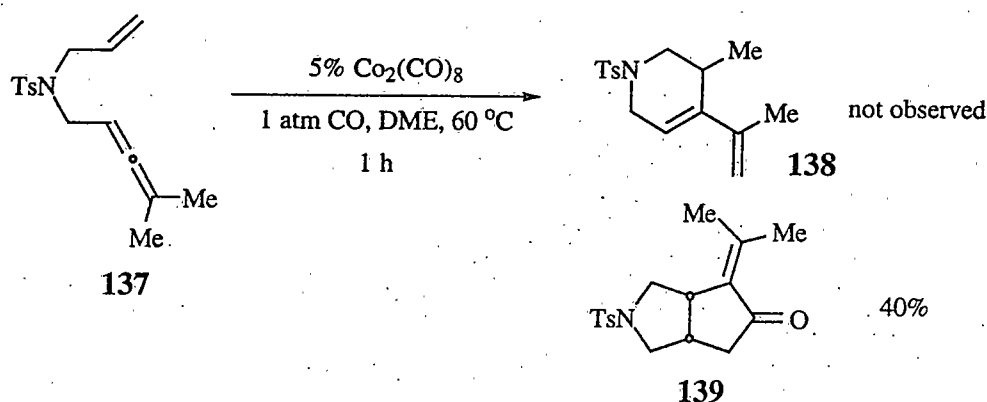


Scheme 3.47

(Scheme 3.47). Subsequent insertion of the pendant alkyne into the cobalt carbon bond followed by reductive elimination gives the observed triene **133**. Malacria has recently

suggested a similar mechanism in the $\text{CpCo}(\text{CO})_2$ -catalyzed formal Alder-ene reaction of a related allenyne.⁷⁴

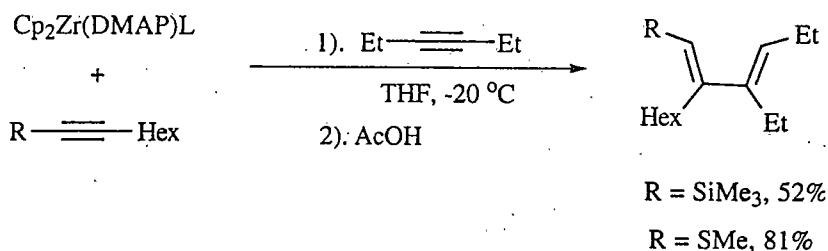
In order to provide support for the a cobalt allyl hydride mechanism, a related ene-allene **137** was prepared and subjected to PKR conditions. Presumably, the pendant olefin would provide a reasonable surrogate for an alkyne (Scheme 3.48). While the desired



Scheme 3.48

diene **138** was not detected, an α -isopropylidene bicyclopentanone **139** was isolated in 40% yield (starting material was recovered in 50% yield). Further optimization of this reaction (15% thiophene as additive)²⁰, allowed for 60% isolated yield of the bicyclopentenone **139** along with unreacted ene-allene **137**.

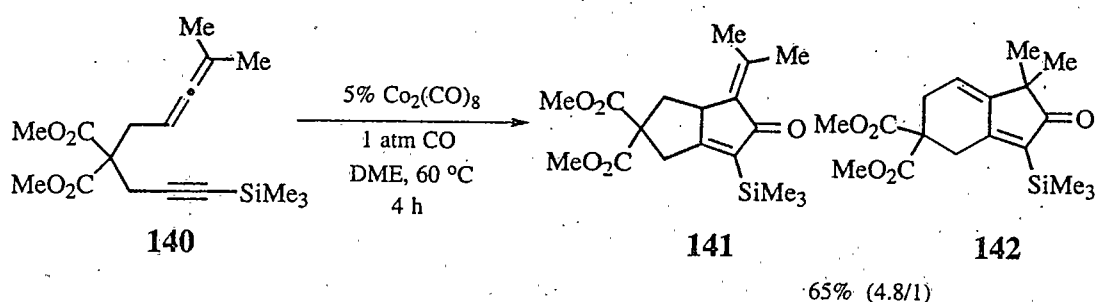
Previous studies in the Livinghouse laboratories have shown that the use of a thioalkyl group on the terminus of an alkyne can affect the efficiency of metal catalyzed reactions. Van Wagenen and Livinghouse were the first to demonstrate this substitution



Scheme 3.49

effect in the Zr-promoted reductive cross-coupling of thiomethyl alkynes with alkynes (Scheme 3.49).²¹ Subsequent to the work of Van Wagenen, similar reactivity trends were observed in the catalytic photopromoted PKR.²⁰

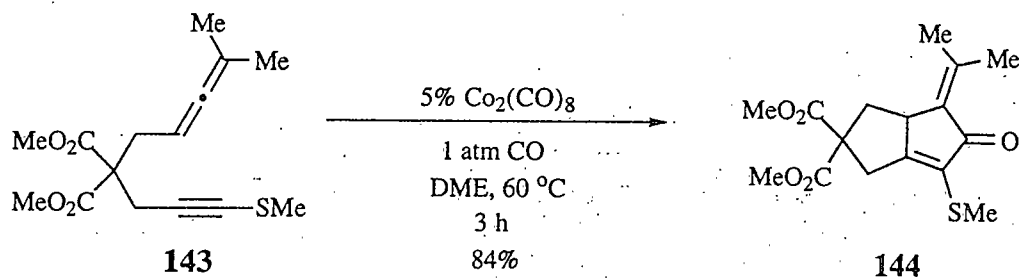
A study of the substituent effect on the catalytic carbonylative allenyne cyclization was initiated in an attempt to improve the selectivity of the reaction. The PKR of the trimethylsilyl-substituted allenyne **140** afforded product with improved yield and similar selectivity for the α -isopropylidene pentalenone **141** (Scheme 3.50). This reaction is



Scheme 3.50

notable as it represents the first substrate bearing a trimethylsilyl-substituted alkyne **140** that undergoes successful carbonylative annulation using the catalytic PKR procedure.

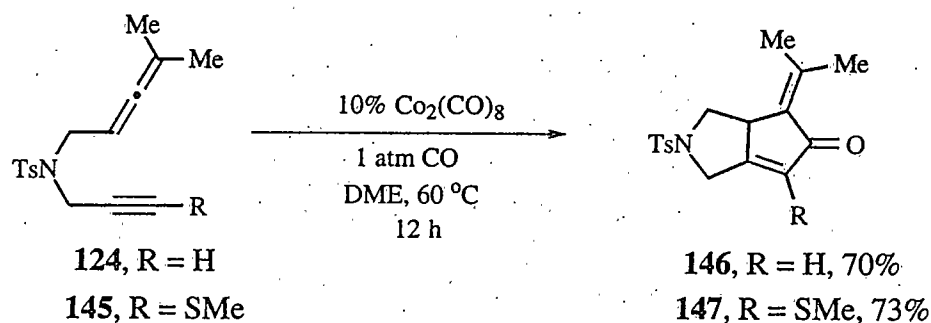
The corresponding thiomethyl-substituted allenyne **143** was found to be an exceptional substrate for the catalytic PKR. Carbonylative cyclization proceeded to give good yield of α -isopropylidene pentalenone **144** as a single isomer (Scheme 3.51). The



Scheme 3.51

formation of the α -isopropylidene pentalenone **144** as the major product clearly indicates a kinetic preference for its formation and suggests that the last irreversible step occurs early in the catalytic sequence.

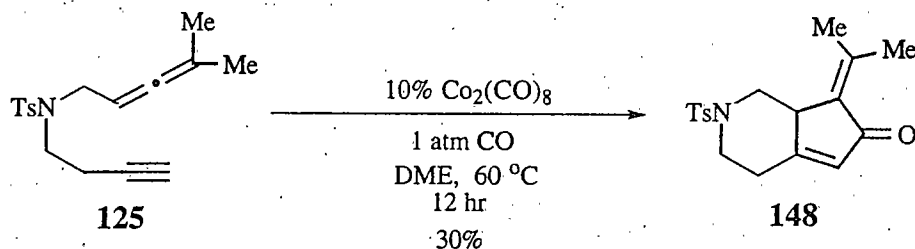
Carbonylative cyclization of structurally related tosamides **124** and **145** using the thermally promoted catalytic protocol provided good yield of the α -isopropylidene pentalenones **146** and **147**, respectively (Scheme 3.52). Interestingly, only the α -



Scheme 3.52

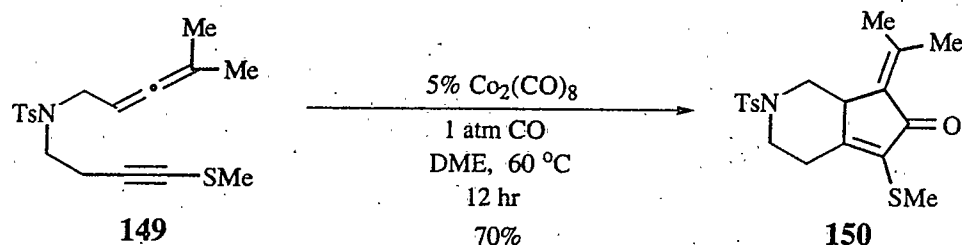
isopropylidene bicyclopentenones **146** and **147** were observed in these examples. This product selectivity may simply be a result of the shorter carbon-nitrogen bonds (1.45 Å for sp^2 nitrogen) in these tosamide-linked allenynes.

Extension of the catalytic method to a more challenging substrate afforded only low yield of product **148** despite 100% conversion of starting allenyne **125** (Scheme 3.53).



Scheme 3.53

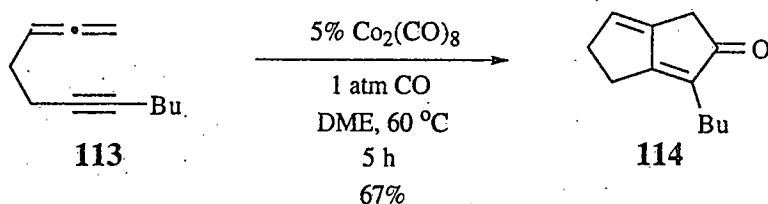
A considerably improved yield was achieved using the thiomethyl-modified tosamide **149** (Scheme 3.54). The improved yield observed with allenynes bearing thiomethyl groups



Scheme 3.54

may be due, in part, to the facility with which these substrates form complexes with $\text{Co}_2(\text{CO})_8$. While solutions of $\text{Co}_2(\text{CO})_8$ and allenynes (or enynes) require 15-30 minutes before a noticeable color change (from brown to deep red) occurs, mixtures of $\text{Co}_2(\text{CO})_8$ and thiomethyl-allenynes (or enynes) form deep black solutions within a few minutes. Presumably, rapid coordination of $\text{Co}_2(\text{CO})_8$ with the alkyne moiety prevents degradation of the substrate via polymerization processes.

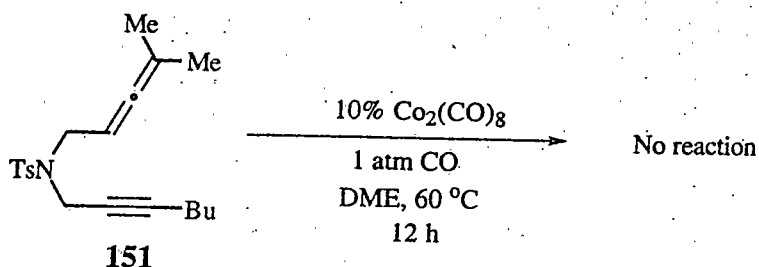
Carbonylative cyclization of a substrate bearing a terminal allene **113** gave the desired pentalenone **114** in moderate yield (Scheme 3.55). While the yield obtained



Scheme 3.55

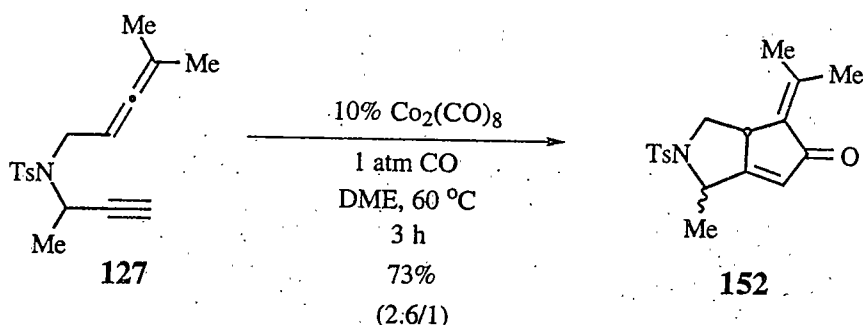
with this substrate is rather modest, it is acceptable considering that this type of structure should be more prone to competing polymerization. In comparison, a tosamide-linked

allenyne **151** containing an alkyl substituted alkyne failed to react under similar conditions (Scheme 3.56).



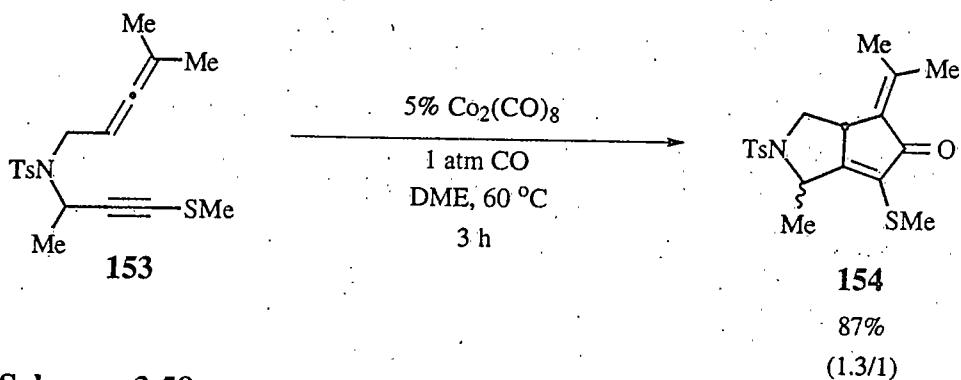
Scheme 3.56

Carbonylative cyclizations of allenynes with a stereogenic group at the propargylic position were explored. The level of relative diastereoselectivity was poor affording a 2.6/1 mixture of exo and endo isomers **152** (Scheme 3.57). Carbonylative cyclization



Scheme 3.57

of the corresponding thiomethyl-modified tosamide **153** provided an increased yield of



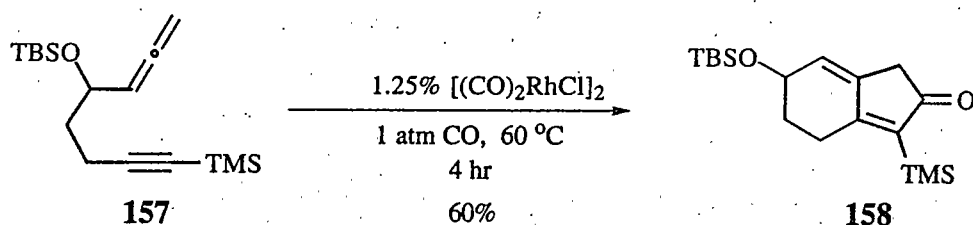
Scheme 3.58

•



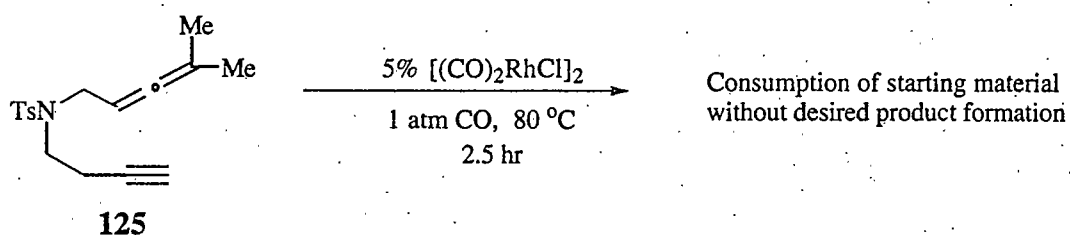
Rh cat. = $[(\text{CO})_2\text{Rh}(\text{dppp})\text{Cl}]_2$, 100°C, 15h, 93%

$[(\text{CO})\text{Rh}(\text{dppp})\text{Cl}]_2$ as precatalyst, though a longer reaction time and a higher temperature were required (Scheme 3.60). Likewise, carbonylative cyclization of a stereogenic allenyne **157** gave the indenone **158** (Scheme 3.61). The low yield observed with substrate **157** is believed to be due to the instability of the product **158**. Analysis of the



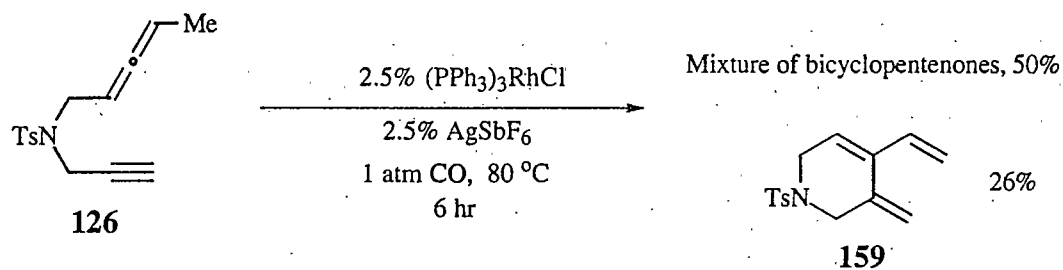
Scheme 3.61

crude reaction (GC and tlc) suggested only one product formed. Extension of this protocol to a more challenging substrate **125** was unsuccessful as depicted in Scheme 3.62.



Scheme 3.62

Rh-catalyzed carbonylative cyclization of allenyne **126** afforded a mixture of isomeric bicyclopentenones and the dihydropyridine **159** (Scheme 3.63).



Scheme 3.63

In principle, formation of the undesired triene side-product **159** could be minimized by increasing the CO pressure. Ito has observed a similar pressure dependence in the Rh-catalyzed [2+2+1] cycloaddition of vinylallenes.² Alternatively, the yield of triene **159** could be maximized at lower CO pressure. Indeed, treatment of allenynes with a cationic rhodium catalyst under an argon atmosphere led efficient cycloisomerization. The results are listed in Table 3.3.

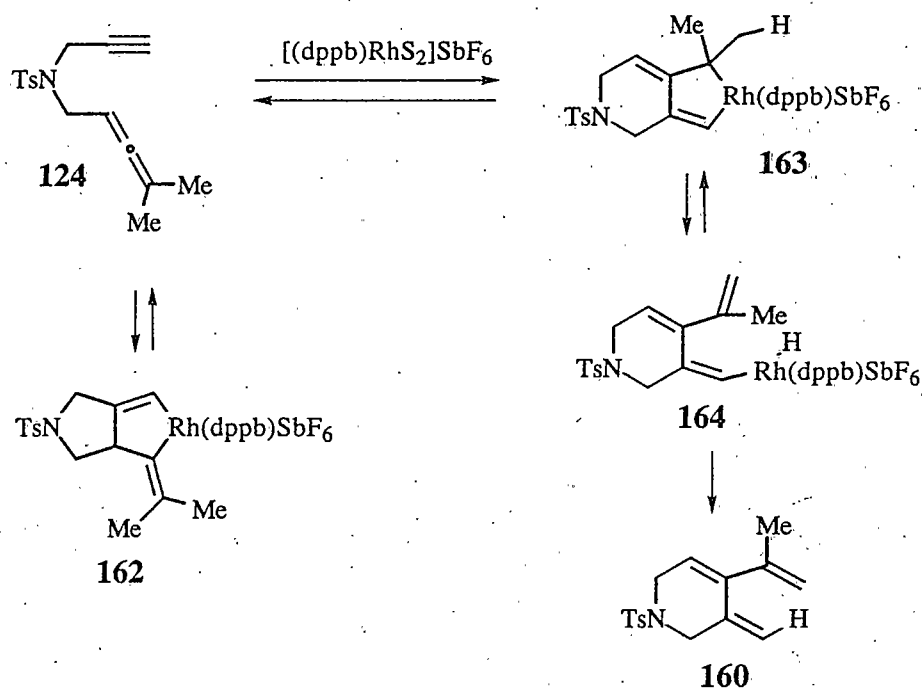
Table 3.3. Rh-Catalyzed Cycloisomerization of Allenynes^a

Entry	Allenyne	Product	Yield (%)
1	 104	 133	82
2	 124	 160	74
3	 127	 159	86 ^b
4	 125	 161	84

a. All reaction were performed using 2 mol % [(NBD)₂Rh]SbF₆ and dppb as precatalyst in 1,2-DCE. The precatalyst was treated with H₂ for 15 minutes, and then freeze-pump-thaw degassed before the addition of substrate.

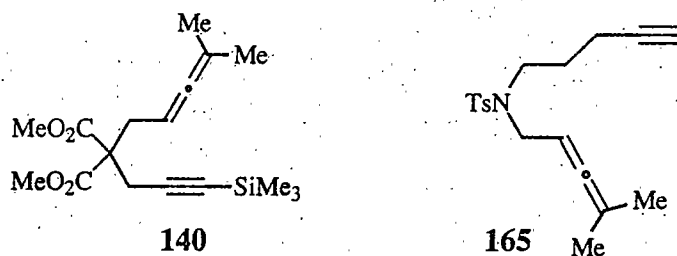
b. A different catalyst system was used, see Experimental Section for details.

In the absence of detailed studies of this reaction, the following mechanism is proposed as a working model to explain product formation (**Scheme 3.64**). Initial complexation and subsequent oxidative cyclization affords a mixture of bicyclorhodacycles **162** and **163**. In the absence of CO, β -hydride elimination of complex **163** and reductive elimination of the resulting rhodium hydride complex **164** is observed. Considering that high turnover is observed in these reactions (35-40 catalytic cycles), initial rhodacycle formation may be reversible and the observed triene **160** is a consequence of a low energy β -hydride elimination/reductive elimination sequence that regenerates the active catalyst.



Scheme 3.64

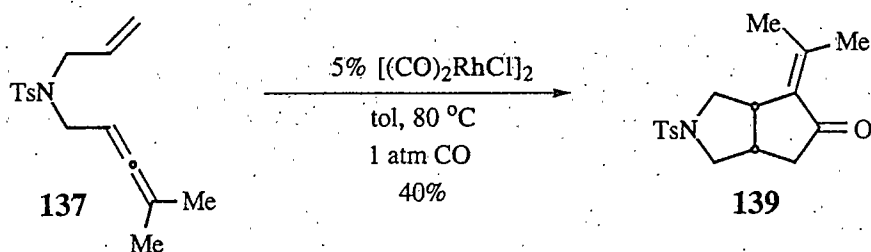
Several substrates proved resistant to cycloisomerization using these conditions. For example, allenyne **140** bearing a trimethylsilyl-substituted alkyne and 1,8-allenyne **165** were unreactive under these conditions (**Scheme 3.65**). The highly convergent



Scheme 3.65

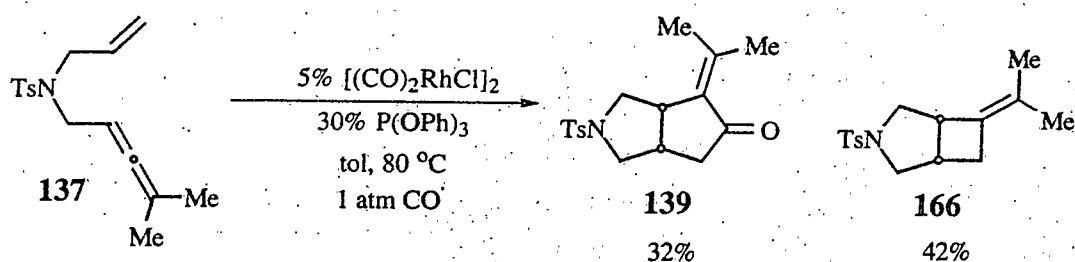
synthesis of these interesting cross-conjugated trienes may allow for the rapid construction of a wide variety of polycyclic organic molecules using a diene-transmissive Diels-Alder strategy.⁷⁵

The Rh-catalyzed [2+2+1] cycloaddition of ene-allenes was explored very briefly. Treatment of the following ene-allene **137** with 5 mol % $[(\text{CO})_2\text{RhCl}]_2$ under 1 atm CO afforded the bicyclopentanone **139** in 40% yield. The starting ene-allene **137** was completely consumed during the reaction (Scheme 3.66). Using a similar catalyst



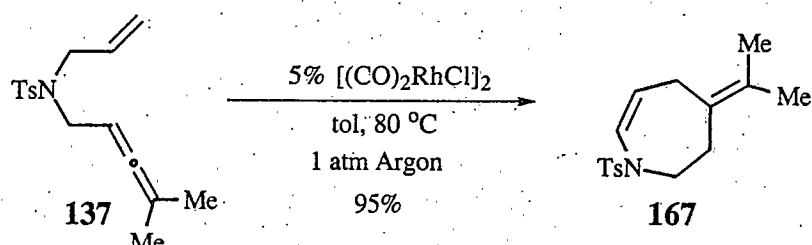
Scheme 3.66

system, with $\text{P}(\text{OPh})_3$ as additive, the desired α -isopropylidene bicyclopentanone **139** was isolated in only 32% yield. Interestingly, an isopropylidene azabicyclo[3.2.0]heptane **166** was isolated in 42% yield (Scheme 3.67).



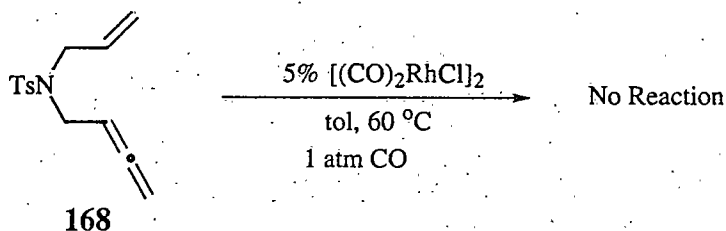
Scheme 3.67

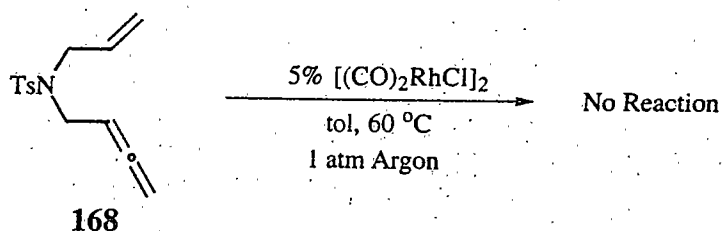
It was initially presumed that azabicyclo[3.2.0]heptane **166** formation, via an intermediate rhodacyclopentane, could be optimized by performing the reaction in a carbon monoxide deficient environment. To explore this possibility, an identical experiment was performed under an argon atmosphere. After three hours at 60 °C, the dehydro azapiene **167** was isolated in nearly quantitative yield (Scheme 3.68).



Scheme 3.68

Under either set of conditions, an ene-allene **168** containing an unsubstituted allene unit failed to give the desired bicyclopentanone and was recovered unchanged (Scheme 3.69). The lack of reactivity with ene-allene **168** may be a consequence of the propensity



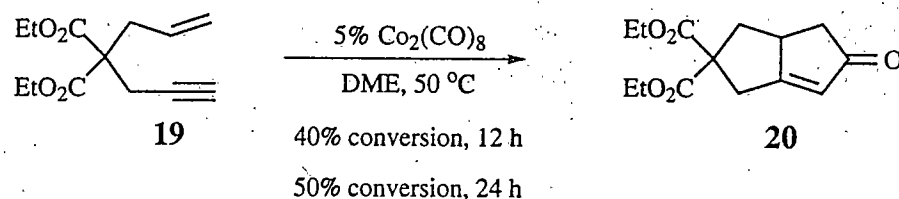


Scheme 3.69

of unsubstituted allenes to coordinate rhodium complexes in an η^2 fashion.² No further attempts were made to optimize these novel, catalytic transformations.

3.2.d Thermally-Promoted Catalytic Pauson-Khand Reaction

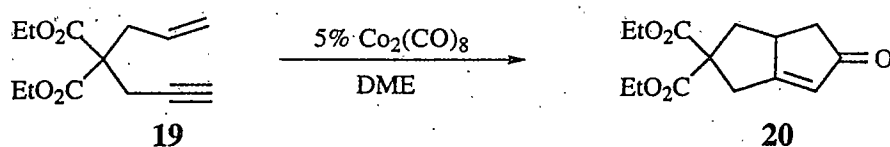
In Section 3.2.b, it was discovered that efficient $\text{Co}_2(\text{CO})_8$ -catalyzed carbonylative cyclization of allenynes could be achieved without Q-Beam irradiation. A study was initiated to determine if this method could be extended to enynes. In consonance with the previous findings²⁰, it was determined that the thermally promoted catalytic Pauson-Khand reaction of enyne **19** was quite slow at 50 °C as only 40% conversion was observed.⁷⁶ Extending the reaction time at 50 °C only led to a modest



Scheme 3.70

improvement in reaction efficiency (Scheme 3.70).⁷⁶ Direct comparison of the reaction efficiency at 55 and 60 °C showed that the photopromoted catalytic protocol was similar to reactions performed without light (Table 3.4).⁷⁶

Table 3.4. Photochemical versus Thermal Promotion of the Catalytic Pauson-Khand Reaction^{a,b}



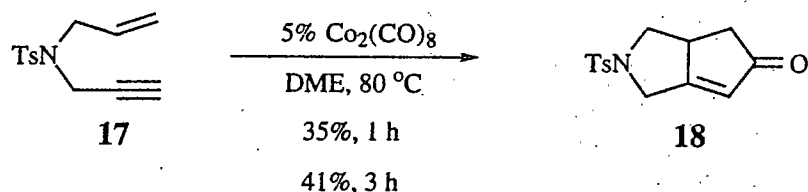
Temperature °C	Light Source	% Conversion	Time (h)
55	Q-Beam	92	14
55	none	85	14
60	Q-Beam	52	4
60	none	42	4

a. Reaction temperatures were monitored internally.

b. From ref. 76.

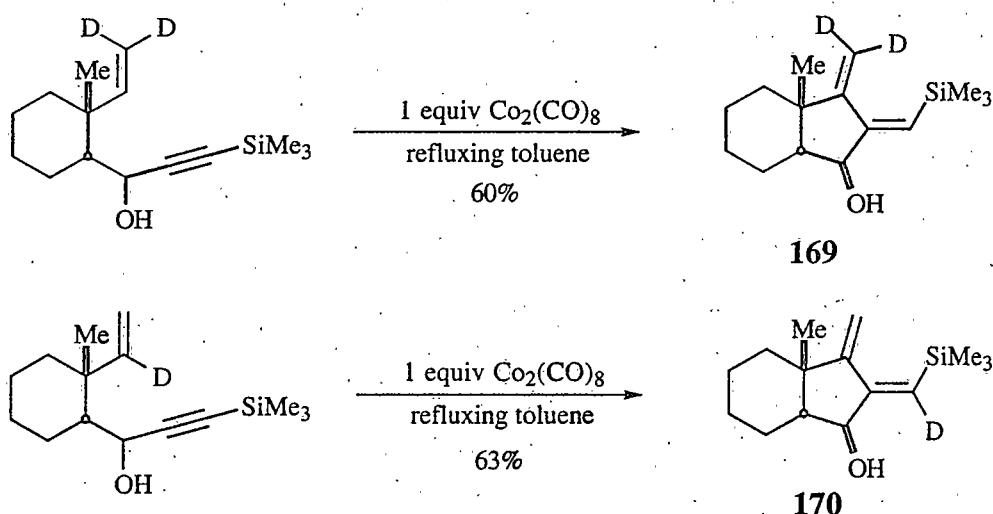
The reported result with enyne **19** (4 h, 95% yield) was unable to be reproduced and may reflect the difficulty of accurately measuring the *internal* reaction temperature when using the photopromoted catalytic protocol (on a small scale). It now seems more reasonable that the internal reaction temperature, in the reported example²⁰, may have been closer to 65 °C, rather than 50-55 °C. For example, the thermally promoted catalytic Pauson-Khand reaction of enyne **19** at 65 °C proceeded to completion in only 4 hours (78% yield), similar to the reaction time reported.²⁰

The upper temperature limit for effective catalysis was explored very briefly. At 80 °C, the tosamide-linked enyne **17** was rapidly consumed, but only a poor yield was



Scheme 3.71

observed (Scheme 3.71). The thermal instability of $\text{Co}_2(\text{CO})_8$ is well documented^{16,77} and may account for the decreased yield. Additionally, the decreased solubility of carbon monoxide in 1,2-DME (bp = 84°C) as it approaches its boiling point may be of importance. Krafft has recently shown that the thermolysis of enyne cobalt complexes in refluxing toluene produces 1,3-dienes **169** and **170** (Scheme 3.72).⁷⁸ Krafft suggests

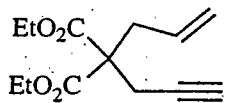
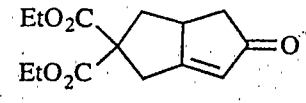
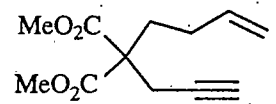
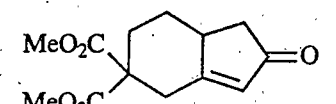
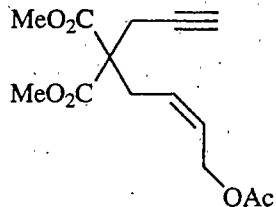
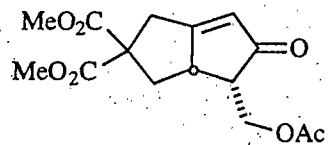
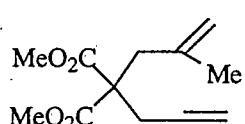
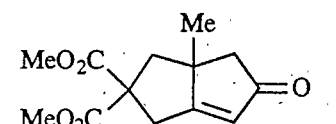
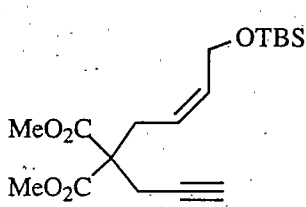
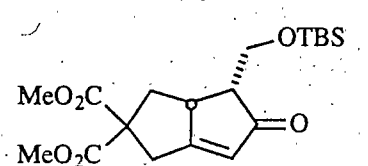


Scheme 3.72

that deuterium labeling studies exclude an α -elimination mechanism for the formation of the observed dienes, and either a β -hydride elimination or an allylic CH insertion mechanism is involved.

A series of thermal carbonylative enyne cyclizations was performed to evaluate the effectiveness of this operationally simple method. All experiments were done without any special precaution to exclude visible light, as control experiments showed that visible light had no effect on the efficiency of the reaction. Results collected in **Table 3.5** show that the thermally promoted catalytic Pauson-Khand reaction is an effective method for the synthesis of a variety of structurally diverse bicyclopentenones.

Table 3.5. Thermal Catalytic Pauson-Khand Reaction of Malonate-Derived Enynes with $\text{Co}_2(\text{CO})_8$ ^a

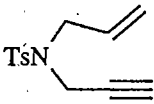
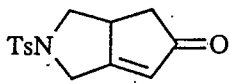
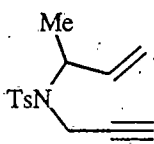
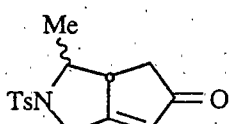
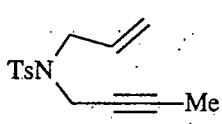
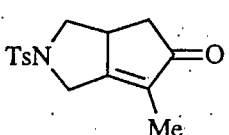
Entry	Substrate	Time (h)	Product	Yield (%)
1	 19	12 4	 20	83 78 ^b
2	 171	12	 172	77 ^c
3	 173	12	 174	78 ^d
4	 175	12	 176	85
5	 177	12	 178	84 ^{c,e}

a. All reactions were performed with 5 mol % $\text{Co}_2(\text{CO})_8$ at 60 °C, unless stated otherwise. b. 65 °C. c. 10 mol % $\text{Co}_2(\text{CO})_8$.

d. 7.5 mol % $\text{Co}_2(\text{CO})_8$. e. >20/1 cis/trans by ¹H NMR spectroscopy.

The reaction rate can be increased three-fold with only a 5 °C increase in reaction temperature with only a minor decrease in reaction yield (Table 3.5, Entry 1). Further definition of the scope of the thermally promoted catalytic PKR is given in Table 3.6.

Table 3.6. Thermal Catalytic Pauson-Khand Reaction of Tosamide-Derived Enynes with $\text{Co}_2(\text{CO})_8$ ^a

Entry	Substrate	Time (h)	Product	Yield (%)
1	 17	12	 18	86 ^c
2	 179	12	 180	78 ^d
3	 181	15	 182	78 ^b

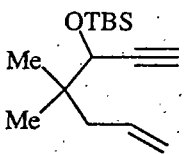
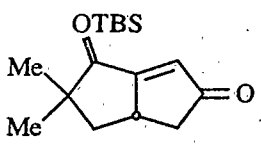
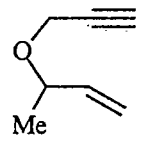
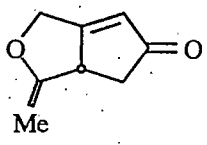
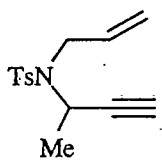
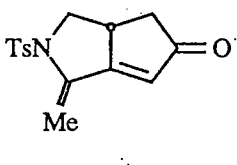
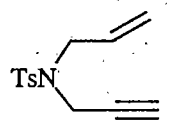
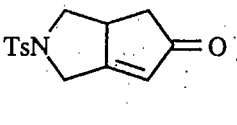
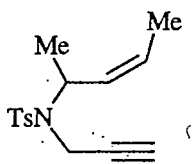
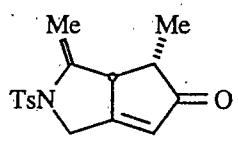
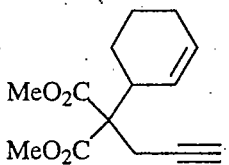
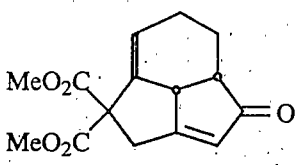
a. All reactions were performed with 5 mol % $\text{Co}_2(\text{CO})_8$ at 60 °C, unless stated otherwise. b. 10 mol % $\text{Co}_2(\text{CO})_8$.

c. 7.5 mol % $\text{Co}_2(\text{CO})_8$ d. 1.3/1.0 ratio of diastereomers.

In continuation of the ongoing studies in the Livinghouse laboratory^{20,23}, a series of enynes was prepared to more fully elucidate the effect of a thioalkyl moiety on the efficiency and diastereoselectivity of the catalytic Pauson-Khand reaction. Table 3.7 shows that modest to good levels of relative stereocontrol can be achieved using the catalytic PKR for substrates bearing allylic substitution (Table 3.7, Entry 2,5 and 6). By

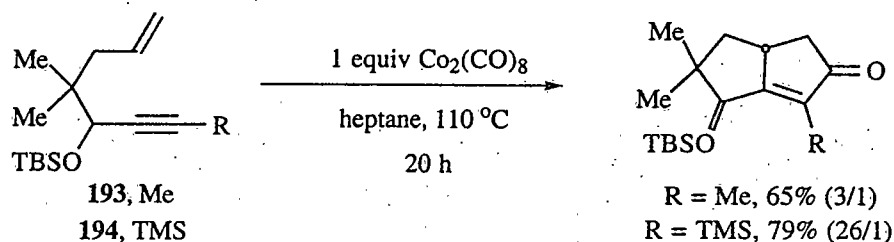
way of contrast, substrates bearing substitution at the propargylic position underwent carbonylative cyclization with poor relative stereocontrol (Table 3.7, Entry 1 and 2).

Table 3.7. Thermal Catalytic Pauson-Khand Reaction of Stereogenic Enynes with $\text{Co}_2(\text{CO})_8$ ^a

Entry	Substrate	Product	Syn/Anti	Yield (%)
1	 183	 184	1.3/1	75 ^b
2	 185	 186	5/1	23 ^c
3	 187	 188	1.5/1	92
4	 17	 18	-	86
5	 189	 190	13.0/1	79 ^{b,d}
6	 191	 192	6.0/1	39 ^{b,d}

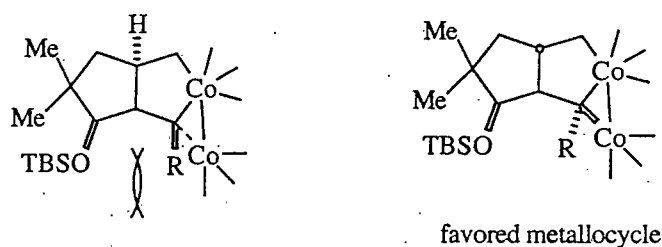
a. All reactions were performed with 5 mol % $\text{Co}_2(\text{CO})_8$ at 60 °C, unless stated otherwise. b. 10 mol % $\text{Co}_2(\text{CO})_8$. c. From ref. 20. d. From ref. 23.

Magnus was the first to recognize the dramatic effect that alkyne substituents can have on the stereoselectivity of the stoichiometric PKR. For example, carbonylative cyclization of an enyne **193** bearing a methyl substituted enyne proceeded with quite modest selectivity (Scheme 3.73).^{30a-c} In contrast, the corresponding trimethylsilyl-



Scheme 3.73

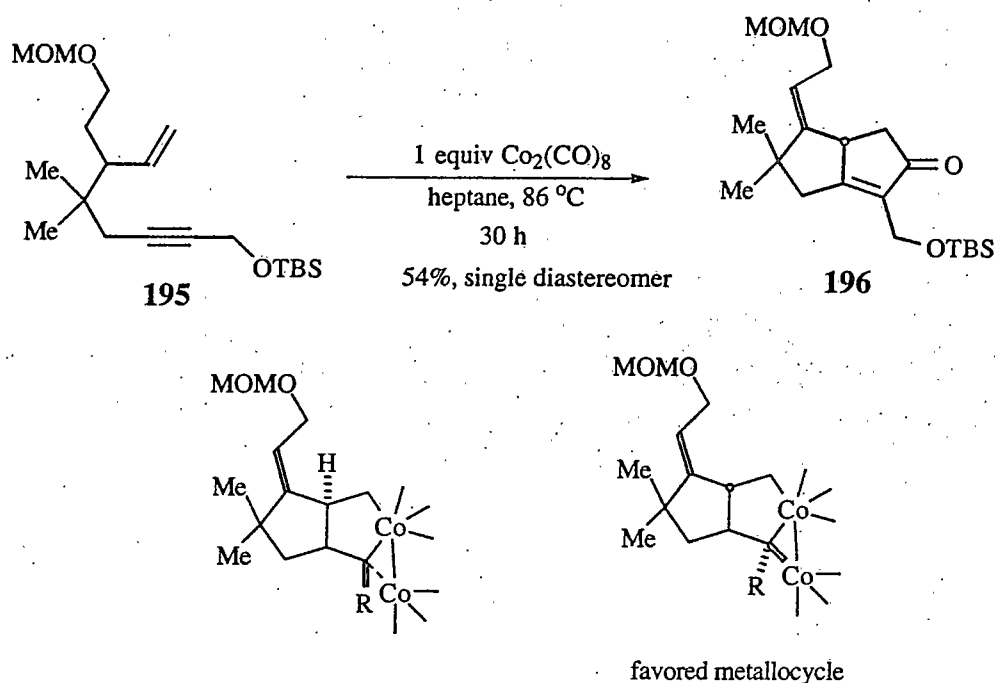
substituted enyne **194** affords a 26/1 ratio of epimeric bicyclopentenones (Scheme 3.73). Magnus reasoned that metallocycle generation, and ultimately product formation, is governed by minimization of a developing pseudo-1,3-diaxial interaction between the trimethylsilyl group and the propargylic silyl ether in the transition state (Scheme 3.74).^{30b,c}



Scheme 3.74

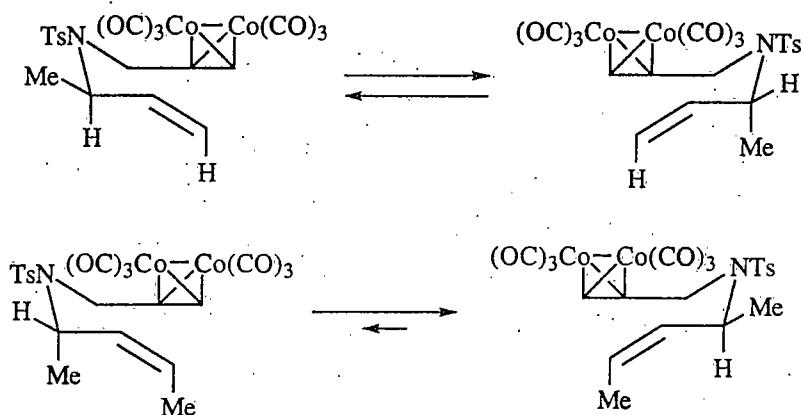
Likewise, Magnus suggested that certain allylically-substituted enynes undergo carbonylative cyclization with selectivity that is consistent with minimization of a pseudo-

1,4-diaxial interaction in the transition state. The PKR of enyne **195** afforded 54% of the desired pentalenone **196** (Scheme 3.75).^{30b,d,e}



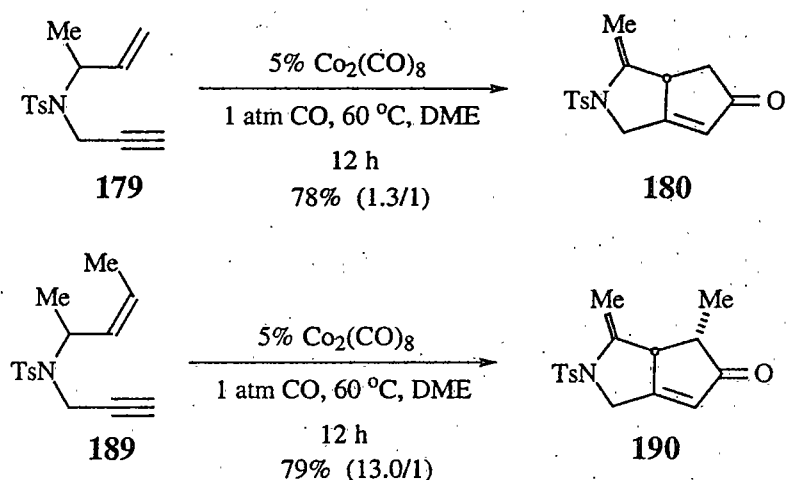
Scheme 3.75

In the absence of alkyne substitution, it has been recognized that Magnus' rationale³⁰ for the stereoselectivity observed with allylicly substituted enynes is not entirely satisfactory.²⁰ The reduction of allylic 1,3-strain in dicobalt-enyne conformers



Scheme 3.76

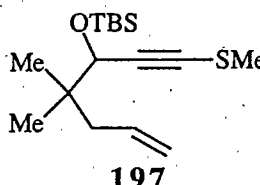
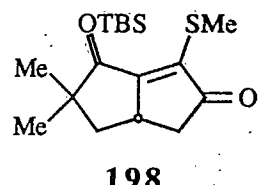
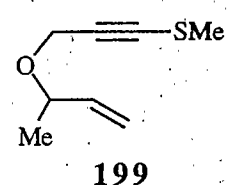
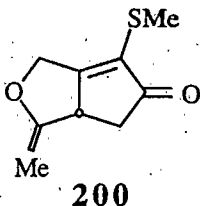
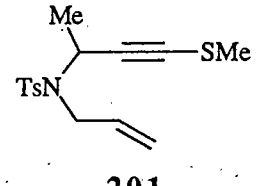
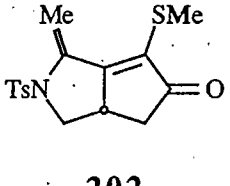
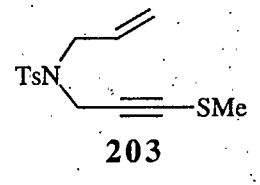
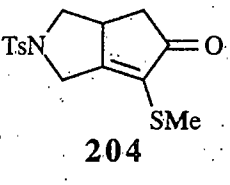
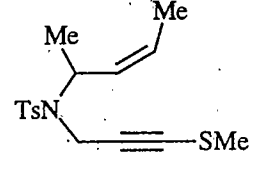
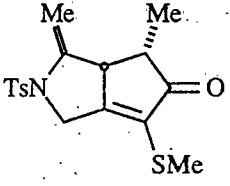
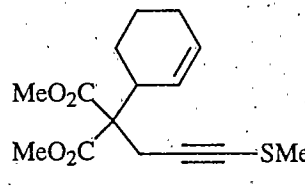
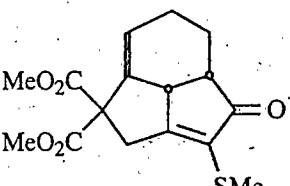
may explain the origin of stereoselectivity (Scheme 3.76).²⁰ This postulate is supported upon comparison of the PKR of two structurally-related tosamides **179** and **189** (Table 3.6, Entry 2 with Table 3.7, Entry 5) (Scheme 3.77).



Scheme 3.77

It has been determined that enynes bearing trimethylsilyl groups failed to react using the photopromoted catalytic PKR.²⁰ To overcome this reactivity problem, it was found that thiomethyl-enynes were exceptional substrates for the catalytic PKR concerning both yield and stereoselectivity (Table 3.8, Entry 2).²⁰ Comparison of Entry 2 (Table 3.8) with Entry 2 (Table 3.7) shows that the enyne containing the thiomethyl group undergoes carbonylative cyclization with increased yield *and* relative stereocontrol. The improved level of relative stereocontrol is consistent with an increased pseudo-1,3-diaxial interaction in the transition state.

Table 3.8. Thermal Catalytic Pauson-Khand Reaction of Stereogenic Thiomethyl-Enynes with $\text{Co}_2(\text{CO})_8$ ^a

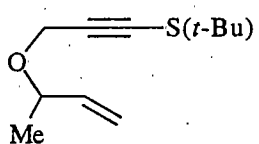
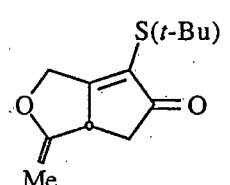
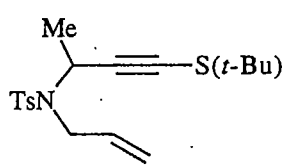
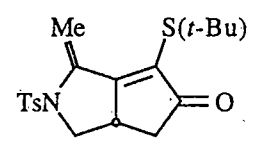
Entry	Substrate	Product	Syn/Anti	Yield (%)
1	 197	 198	3.9/1	99 ^{b,c}
2	 199	 200	12/1	81 ^c
3	 201	 202	2.7/1	93
4	 203	 204	-	88 ^d
5	 205	 206	13.0/1	92 ^b
6	 207	 208	12.3/1	75 ^{b,d}

a. All reactions were performed with 5 mol % $\text{Co}_2(\text{CO})_8$ at 60 °C, unless stated otherwise. b. 10 mol % $\text{Co}_2(\text{CO})_8$. c. From ref. 20. d. From ref. 23.

A similar improvement was observed with Entry 6 (Table 3.8) where the thiomethyl-modified enyne underwent carbonylative cyclization with 12.3/1 selectivity.²³ Less dramatic increases in selectivity was observed with substrates listed in Table 3.8 (Entries 1 and 5). In most cases, yield improvements were observed. The use of thiomethyl-modified enyne has been shown to lead to useful selectivity and yield increases and, presumably, should be an easily removable functional group.⁷⁹ Interestingly, the use of thiomethyl-enynes has seen little use in the intramolecular Pauson-Khand reaction.⁸⁰

Two examples of thio(*t*-butyl)-modified enynes show that even higher levels of stereoselectivity can be achieved in the catalytic PKR (Table 3.9). The improved level of stereoselection is consistent with the increased size of the *t*-butyl moiety.

Table 3.9. Thermal Catalytic Pauson-Khand Reaction of Stereogenic Thio(*t*-butyl)-Enynes with $\text{Co}_2(\text{CO})_8$ ^a

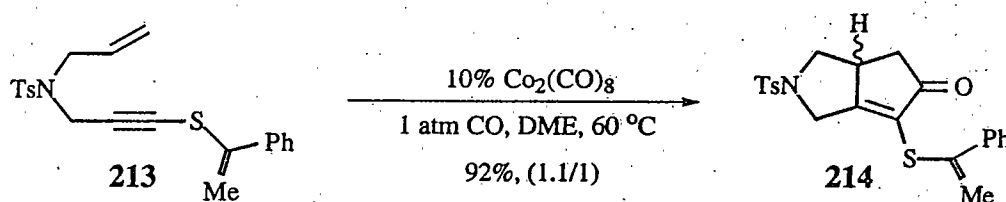
Entry	Substrate	Product	Syn/Anti	Yield (%)
1	 209	 210	42/1	81 ^b
2	 211	 212	5/1	70

a. All reactions were performed with 10 mol % $\text{Co}_2(\text{CO})_8$ at 60 °C.

b. From ref. 20.

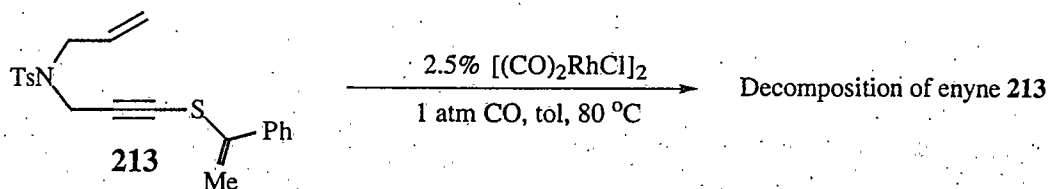
The rather significant thioalkyl effect on the stereoselectivity of the catalytic PKR suggested that a stereogenic thioalkyl moiety may offer a route to diastereo-enriched

bicyclopentenones. Enyne **213** was prepared with the expectation that the thioalkyl group would exert some influence on the selectivity of the newly formed ring junction. Carbonylative cyclization of enyne **213** using $\text{Co}_2(\text{CO})_8$ at 60 °C afforded bicyclopentenone **214** in good yield, but with poor selectivity. (Scheme 3.77). The



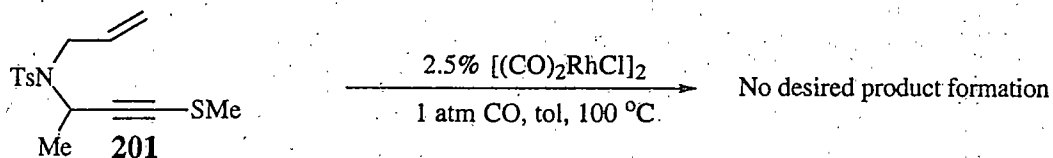
Scheme 3.77

attempted carbonylative cyclization of enyne **213** with $[(\text{CO})_2\text{RhCl}]_2$ as catalyst only led to its complete consumption without product formation (Scheme 3.78). Likewise, enyne



Scheme 3.78

201 was observed to decompose somewhat when subjected to similar conditions at 100 °C (Scheme 3.79). After 12 hours, starting material was observed in addition to some new



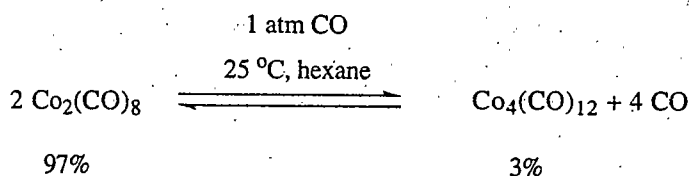
Scheme 3.79

products though analysis of the crude reaction mixture (¹H NMR and IR) suggested that the desired bicyclopentenone had not formed in significant quantity.

3.3 DEVELOPMENT OF MORE STABLE ALTERNATIVES TO $\text{Co}_2(\text{CO})_8$ FOR THE CATALYTIC PAUSON-KHAND REACTION

3.3.a Introduction

While the development of a catalytic Pauson-Khand reaction is an important discovery, *all* current methods require manipulation and storage of $\text{Co}_2(\text{CO})_8$ in a strictly anaerobic environment. Indeed, it was found that the use of high-purity $\text{Co}_2(\text{CO})_8$ was essential for useful catalytic activity in the PKR at 1 atm of CO.²⁰ The inherent instability of $\text{Co}_2(\text{CO})_8$ is well documented.^{16,77} In the absence of a CO atmosphere, the complex is thermodynamically unstable even at temperatures below 0 °C, although at these temperatures, the conversion to $\text{Co}_4(\text{CO})_{12}$ is kinetically quite slow. At 25 °C, the quantitative conversion of $\text{Co}_2(\text{CO})_8$ into $\text{Co}_4(\text{CO})_{12}$ can be achieved under reduced pressure (0.02-0.05 Torr, half-life = 1.25 h).⁷⁷ At 1 atm of CO, $\text{Co}_2(\text{CO})_8$ is considerably

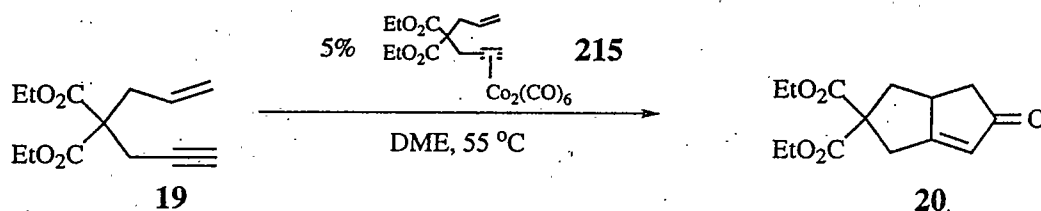


Scheme 3.80

more stable, though a small amount of $\text{Co}_4(\text{CO})_{12}$ is present in hexane solution (Scheme 3.80).⁷⁷ Also, the conversion of $\text{Co}_4(\text{CO})_{12}$ into $\text{Co}_2(\text{CO})_8$ is extremely slow (half-life = 12 years at 1 atm CO and 25 °C). Using our catalytic methods at 1 atm of CO, $\text{Co}_4(\text{CO})_{12}$ is presumed to be a catalytically inactive.⁸¹ In addition to the thermal sensitivity of $\text{Co}_2(\text{CO})_8$, the complex is sensitive to oxidation to Co(II) species.¹⁶ The physical

properties of $\text{Co}_2(\text{CO})_8$ that require glove box manipulation may limit the acceptance of our catalytic method by the scientific community.

Several approaches can be envisioned for the development of a more stable alternative to $\text{Co}_2(\text{CO})_8$. It has been shown that an isolated enyne-cobalt complex **215** provided reaction rates similar to $\text{Co}_2(\text{CO})_8$ when used as catalyst precursor (Scheme 3.81).²⁰ Unfortunately, the stability of the enyne-cobalt complex **215** used as catalyst



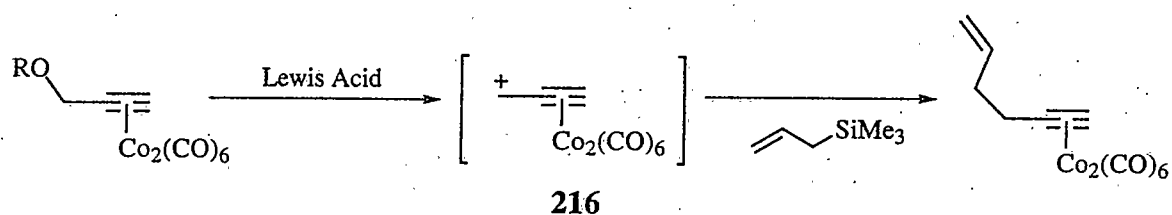
Scheme 3.81

precursor in this example was only a modest improvement relative to $\text{Co}_2(\text{CO})_8$ as it needed to be purified immediately before use to retain sufficient catalytic activity.²⁰

Another approach described in the literature²⁰ involved the use of alkyne-cobalt complexes as catalyst precursor. It is known that cobalt complexes derived from electron-rich alkynes, such as *N,N*-diethyl propargyl amine, are readily displaced by more electron deficient alkynes.^{81b} Presumably, electron deficient alkynes provide for more effective back-bonding stabilizing the low-valent Co metal centers. It was shown that certain alkyne-cobalt complexes were active catalysts, but the activity was directly related to the instability of the complex.²⁰

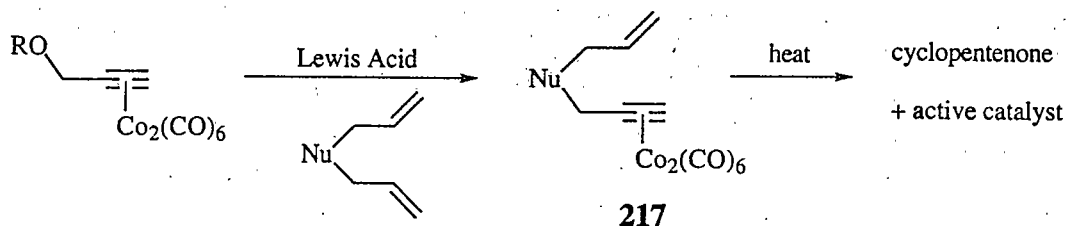
3.3.b Alkyne-Cobalt complexes as Precatalysts for the Pauson-Khand Reaction

Preliminary investigations into the search for an alternative to $\text{Co}_2(\text{CO})_8$ began with air-stable alkyne cobalt complexes. Nicholas has shown that cobalt-complexed propargyl cations **216** (commonly referred to as a Nicholas complex) are easily prepared electrophiles.⁸² Though these *isolated* cobalt complexes may not exhibit the increased stability that we desire, Schreiber has shown that similar complexes **216** can be generated *in situ* with various Lewis acids (Scheme 3.82).⁸³ In principle, under the appropriate



Scheme 3.82

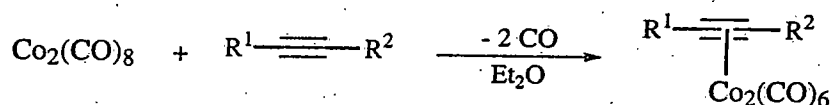
conditions, a Nicholas complex **216** could be generated and subsequently trapped with a nucleophile bearing an olefin. The resulting enyne-cobalt complex **217** may undergo a Pauson-Khand reaction initiating the catalytic cycle (Scheme 3.83). While this approach



Scheme 3.83

may have some merit, control reactions showed that simply heating alkyne-cobalt complexes without additives led to some catalytic activity.

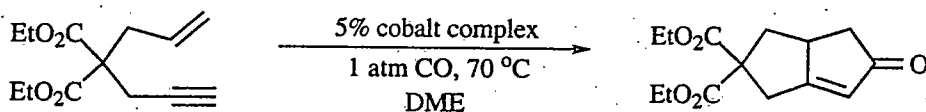
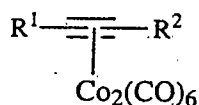
The initial studies in this area required the preparation of a series of electronically and sterically different alkyne- $\text{Co}_2(\text{CO})_6$ complexes using known methods (Scheme 3.84).^{81b} Screening reactions were performed with alkyne-cobalt complexes (5 mol %)



Scheme 3.84

shown in Table 3.10 and enyne **19** at 70 °C. It was discovered that cobalt complexes derived from disubstituted alkynes were unsuitable as catalysts, while the use of cobalt complexes prepared from monosubstituted alkynes displayed some catalytic activity.

Table 3.10. Catalytic Pauson-Khand Reaction with Alkyne-Cobalt Complexes^a



Entry	R ¹	R ²	Time (h)	Yield (%)
1	Me ₃ Si	Me ₃ Si	12	No reaction
2	Ph	Ph	12	No reaction
3	CO ₂ Me	CO ₂ Me	12	No reaction
4	HOCH ₂	HOCH ₂	12	No reaction
5	HOC(Me) ₂	H	8	59 ^b
6 ^d	HOC(Me) ₂	H	12	25 ^c
7	Ph	H	8	61 ^b
8	HOCH ₂	H	2.5	14 ^c

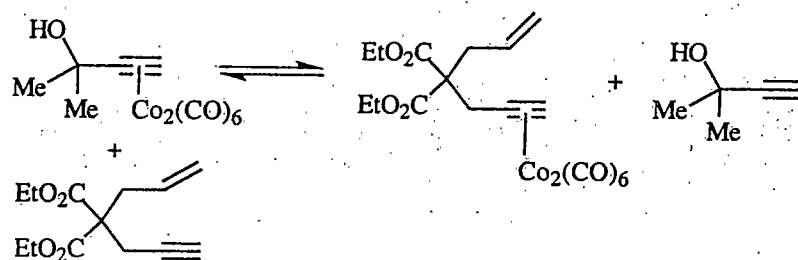
a. All reactions were performed in 1,2-DME (0.1 M).

b. Isolated yield. c. % Conversion, as determined by GC.

d. Reaction temperature was 60 °C.

Though the yields of the successful reactions (Table 3.10, Entries 5 and 7) were quite modest, these preliminary results led to further optimization studies. Lowering the reaction temperature to 60 °C in an attempt to increase the yield led to very slow conversion to the pentalenone 20 (Table 3.10, Entry 6).

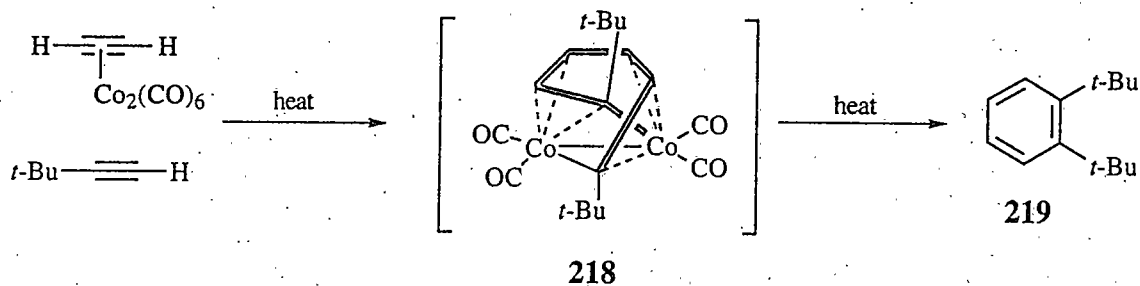
One mechanism for the generation of an active catalyst is an *intermolecular* PKR. Considering that examples of the intermolecular catalytic PKR have not been observed²⁰ using any of our methods at 60 °C and 1 atm CO, it is highly unlikely that it is involved in the generation of an active catalyst in this case. Another mechanism that may allow for



Scheme 3.85

modest success using this approach is simple ligand exchange as depicted in Scheme 3.85).

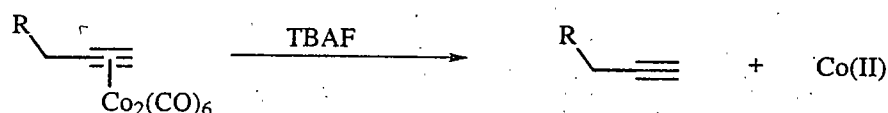
Another conceivable mechanism that could be described for the generation of the enyne cobalt complex is through cyclotrimerization. It has been shown that alkyne-cobalt complexes form arenes when heated in the presence alkynes. This process remains somewhat obscure, but was proposed to occur via coordination and subsequent insertion of 2 equivalents of alkyne (Scheme 3.86).^{4a,h} The so-called “fly-over” complex **218**



Scheme 3.86

would then decompose through a reductive elimination process to afford a substituted arene **219** and a coordinatively unsaturated cobalt species. In principle, the low yield observed in the catalytic reactions listed in **Table 3.10** may be a result of the formation of substituted aromatics via this mechanism. On the other hand, the low yield may simply be a temperature effect.^{76,78}

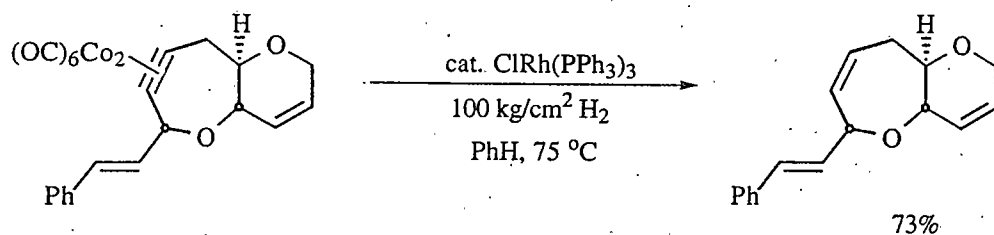
With the modest success using alkyne-cobalt complexes as precatalyst, it was suspected that additives could be used to enhance reactivity. Many mild oxidative methods (*n*-Bu₄NF⁸⁴, NMO⁶, and ceric (IV) ammonium nitrate⁸⁴) are known to effect the decomplexation of alkynes from alkyne-cobalt complexes (**Scheme 3.87**). While the fate



Scheme 3.87

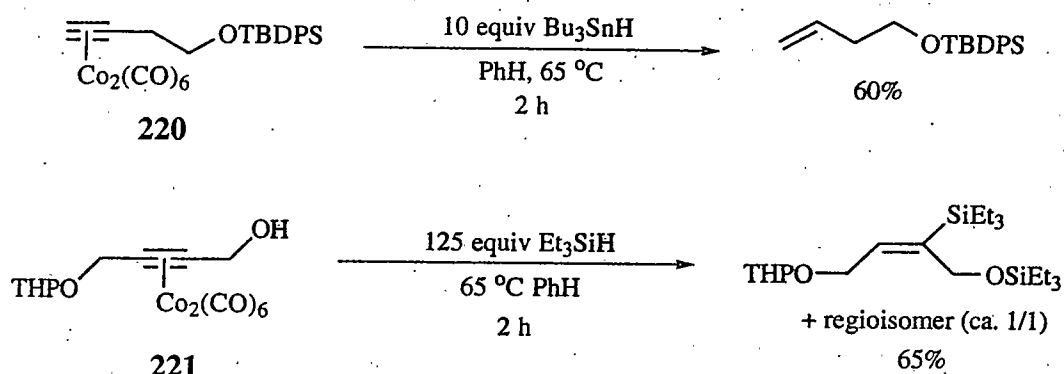
of the cobalt fragment in these reactions has not been precisely determined, it is generally assumed that the oxidation state of the cobalt species had been altered and, therefore, would not provide a suitable method of catalyst generation.

In contrast to the numerous oxidative decomplexation methods, few protocols exist that remove alkynes in a reductive fashion. Isobe has shown that olefins can be prepared directly from alkyne-cobalt complexes when subjected to dihydrogen and catalytic $\text{ClRh}(\text{PPh}_3)_3$ (**Scheme 3.88**).⁸⁵ More recently, Isobe shown that treatment of alkyne-



Scheme 3.88

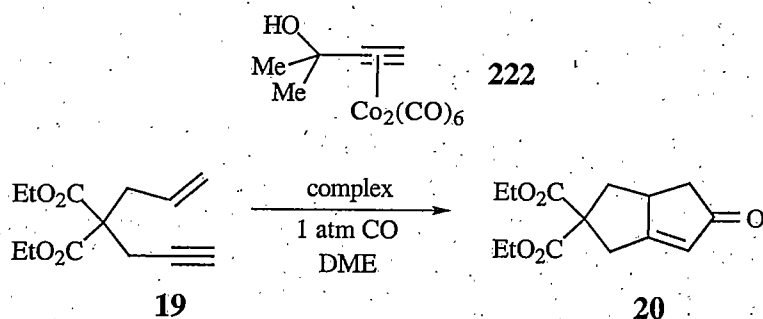
cobalt complexes **220** and **221** with excess $n\text{-Bu}_3\text{SnH}$ or Et_3SiH , respectively, allows for reductive functionalization (Scheme 3.89).⁸⁶ While the exact mechanism of these



Scheme 3.89

reactions is not known, the relatively mild, reducing conditions may allow for decomplexation to occur without concomitant rupture of the relatively weak cobalt-cobalt bond. Indeed, treatment of 2-Methyl-3-butyne-2-ol- $\cdot\text{Co}_2(\text{CO})_6$ **222** with triethylsilane (1 equiv per alkyne-cobalt complex **222**) followed by warming to 60°C slowly produced the desired pentalenone **20** (Table 3.11). Using 10 mol % 2-methyl-3-butyne-2-ol- $\cdot\text{Co}_2(\text{CO})_6$ **222** as precatalyst with 10 mol % Et_3SiH , the desired bicyclopentenone **20** was formed in 81% yield (Table 3.11, Entry 3). At 5 mol % however, the reaction was very slow giving only 80% conversion after 17 hours at 60°C (Table 3.11, Entry 4). At 70°C under identical conditions, pentalenone **20** was obtained in 69% after 5 hours (Table 3.11, Entry 5). Interestingly, the addition of cyclohexylamine had a positive effect on the rate of the cyclization without Et_3SiH (Table 3.11, Entry 2).

Table 3.11. Effect of Additives on the PKR with Catalytic 2-Methyl-3-butyn-2-ol·Co₂(CO)₆^a



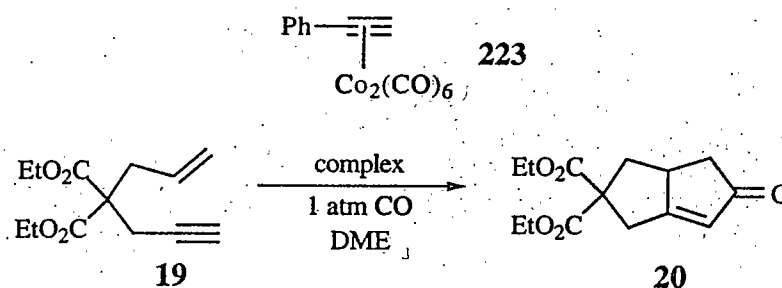
Entry	Additive ^d	Temperature (°C)	Time (h)	Conversion (%)
1	none	60	12	25 ^b
2	35% CyNH ₂	60	12	60 ^b
3	Et ₃ SiH	60	12	81 ^{b,e}
4	Et ₃ SiH	60	17	80 ^c
5	Et ₃ SiH	70	5	69 ^{c,e}

a. All reactions were performed in 1,2-DME (0.1 M) with 5 mol % 2-methyl-3-butyn-2-ol·Co₂(CO)₆, unless noted otherwise. b. 10 mol % 2-methyl-3-butyn-2-ol·Co₂(CO)₆. c. 5 mol % 2-methyl-3-butyn-2-ol·Co₂(CO)₆. d. 1 equiv/complex. e. isolated yield.

A variety of different additives were evaluated using phenylethyne·Co₂(CO)₆ **223** as precatalyst (**Table 3.12**). Of the additives tested, Et₃SiH and (EtO)₃SiH proved effective giving the pentalenone **20** in 69 and 68% yield, respectively (**Table 3.12**, Entry

7 and 8). It is important to note that even a slight excess of Et_3SiH (2 equiv/cobalt complex)

Table 3.12. Effect of Additives on the PKR with Catalytic Phenylethyne· $\text{Co}_2(\text{CO})_6$



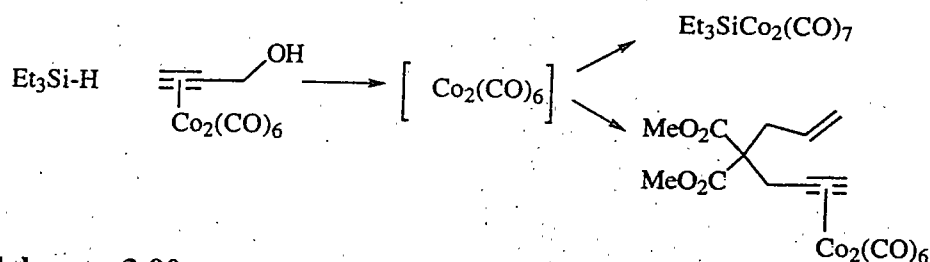
Entry	Additive ^a	Time (h)	Conversion (%)
1	HBpin	1	6
2	10% Et_3SiH	3.5	56
3	PMHS	1.5	18
4	$\text{Et}_3\text{SiH}/125\%$ DMSO	1.5	No Reaction
5	Et_3SiH	1.5	21 ^b
6	Et_3SiH	1.5	33 ^c
7	Et_3SiH	4	69 ^d
8	$(\text{EtO})_3\text{SiH}$	4	68 ^d
9	<i>n</i> - Bu_3SnH	2	18

a. 1 Equiv/phenylethyne· $\text{Co}_2(\text{CO})_6$, unless noted otherwise.

b. 1,2-DCE as solvent (0.1M) at 70 °C. c. Toluene as solvent.

d. Isolated yield

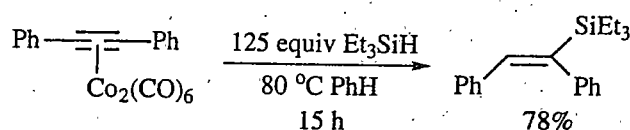
had a negative effect on the overall rate of cyclization even though the initial rate was faster (**Entry 2**). This may be a result competitive reaction of Et_3SiH with solvated $\text{Co}_2(\text{CO})_8$ as depicted in **Scheme 3.90**. While it is known that $\text{Co}_2(\text{CO})_8$ forms $\text{Me}_3\text{SiCo}(\text{CO})_7$ and



Scheme 3.90

dihydrogen when treated with trimethylsilane¹⁶, it is not clear that this would be a catalytically active species.

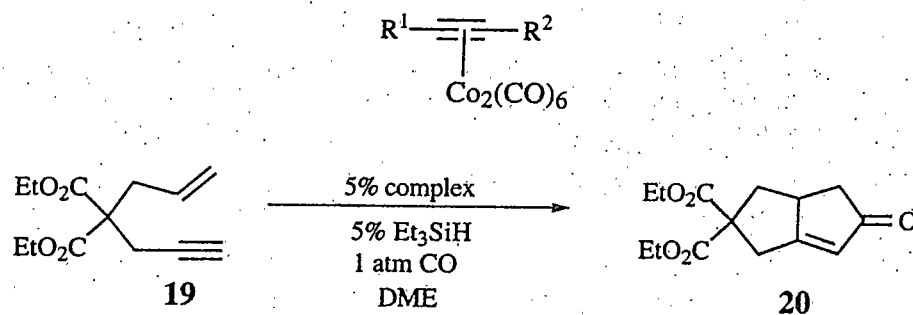
Several alkyne-cobalt complexes were evaluated as precatalysts with Et_3SiH as additive. Most complexes derived from disubstituted alkynes were found to be catalytically inactive (**Table 3.13**). This observation is in consonance with the findings of Isobe⁸⁶, who found that long reaction times at elevated temperatures were required for complete



Scheme 3.91

reduction of cobalt complexes derived from disubstituted alkynes (**Scheme 3.91**). In contrast, cobalt complexes derived from terminal alkynes were effective precatalysts (**Table 3.13**). Alkyne cobalt complexes **222** and **223** exhibited similar catalytic activity.

Table 3.13. Catalytic PKR with Catalytic Alkyne-Cobalt Complexes and Et_3SiH as Additive



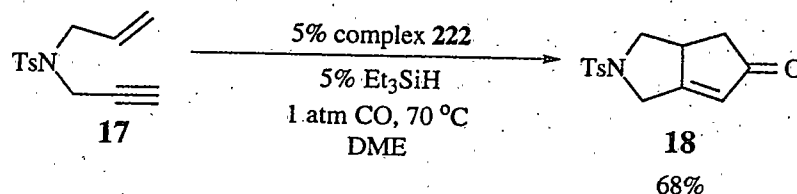
Entry	R^1	R^2	Time (h)	Yield (%)
1	Me_3Si	Me_3Si	6	No reaction
2	Ph	Ph	6	No reaction
3	CO_2Me	CO_2Me	6	trace
4	Ph	H	4	68
5	$\text{HOC}(\text{Me})_2$	H	5	70 ^a
6	$\text{HOC}(\text{Me})_2$	H	5	69 ^b
7	HOCH_2	HOCH_2	6	100% conv ^c
8	HOCH_2	H	8	100% conv ^c

a. Average of 3 runs. b. $\text{TMANO} \cdot 2\text{H}_2\text{O}$ work-up.

c. Yield not determined.

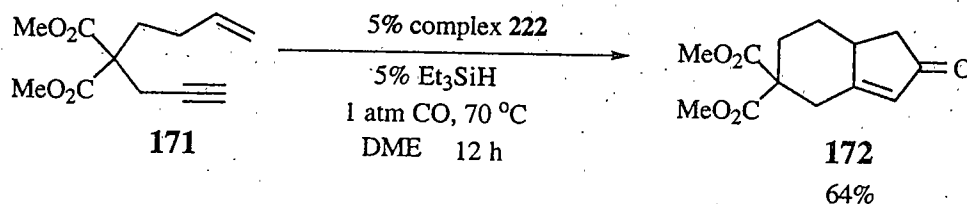
when using Et_3SiH as additive (Entry 4 and 5). The cobalt complex **222** derived from 2-methyl-3-butyne-2-ol offers significant advantages when compared to the phenylacetylene hexacarbonyldicobalt complex **223** as it is a microcrystalline solid. Presumably, the crystalline precatalyst **222** would be less prone to oxidation than the liquid complex derived from phenylacetylene.

Extension of the new catalytic PKR protocol to other enyne substrates led to somewhat disappointing results. Carbonylative cyclization of a tosyl protected enyne **17** afforded a 68% isolated yield of bicyclopentenone **18** (Scheme 3.92). In addition, the



Scheme 3.92

Pauson-Khand reaction of a more challenging 1,7-enyne substrate **171** afforded only a 64% yield of the indenone **172** using these conditions (Scheme 3.93). While the

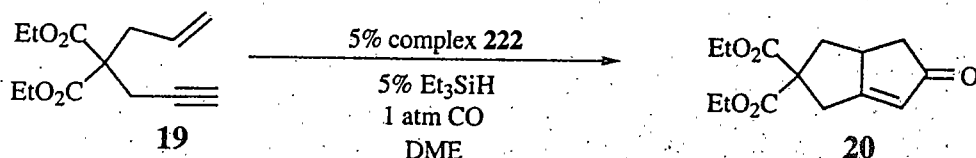


Scheme 3.93

method was modestly successful, the yields do not compare favorably with reactions that used $\text{Co}_2(\text{CO})_8$ as precatalyst, so further optimization studies were initiated.

Without Et_3SiH , slow product formation was observed when the alkyne-cobalt precatalyst **222** was heated with the enyne **19** (Table 3.11, Entry 1). On the presumption that a reductive decomplexation process with Et_3SiH was competitive with unproductive side reactions involving the enyne **19**, a number of different activation protocols were studied. It was believed that if the reductive decomplexation of the alkyne-cobalt complex **222** could be achieved before the addition of the enyne **19**, a higher yield may result. These results are recorded in Table 3.14. All reactions were performed by

Table 3.14. Effect of Various Heating Protocols on the PKR with Catalytic 2-Methyl-3-butyn-2-ol·Co₂(CO)₆^c



Entry	Heating time ^a	Temperature (°C)	Time (h)	Yield ^b (%)
1	15 min	60	12	83 ^b
2	1 h	60	12	70 ^b
3	15 min	65	10	72
4	30 min	65	10	75
5	15 min with 15% CyNH ₂	65	6	92 ^c
6	15 min, Co ₂ (CO) ₈	65	4	71

a. Heating time represents the time that the cobalt-alkyne complex and Et₃SiH were

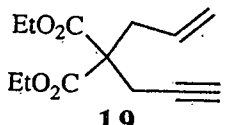
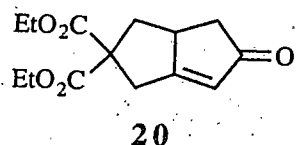
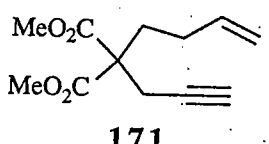
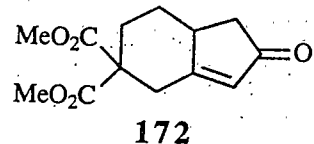
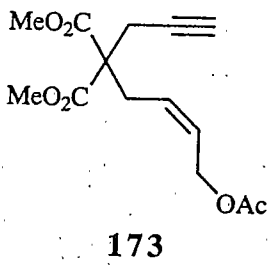
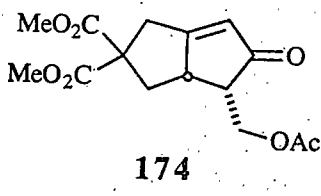
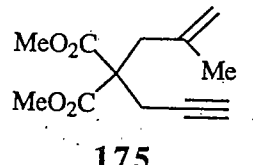
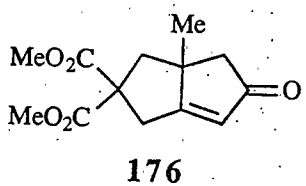
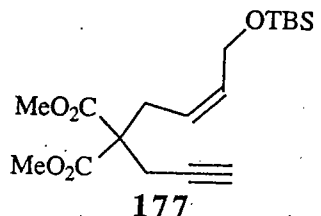
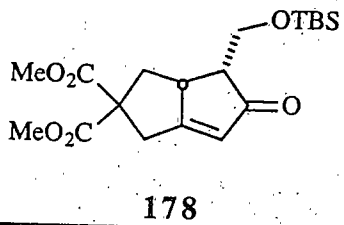
heated before the addition of substrate. b. % conversion.

c. 2-Methyl-3-butyn-2-ol·Co₂(CO)₆ was used as precatalyst.

heating precatalyst 2-Methyl-3-butyn-2-ol·Co₂(CO)₆ **222** with Et₃SiH in 1,2-DME for the specified time, followed by the addition of substrate **19**. Activation in this manner at 60 °C (15 min or 1 h, Entry 1 and 2, Table 3.14) led to moderate conversion to product, while activation at 65 °C allowed for complete conversion (Entries 3 and 4, Table 3.14). The yield using this method at 65 °C was almost the same as the yields obtained using the other method at 70 °C (Entry 4 and 5, Table 3.13). The reductive decomplexation was then performed in the presence of cyclohexylamine⁹ for 15 min, followed by the addition of

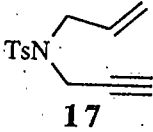
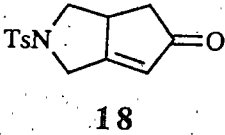
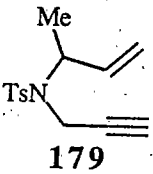
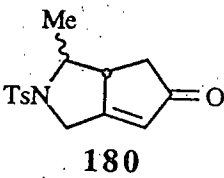
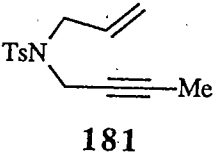
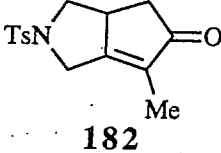
substrate **19**. This modification led to a greatly improved yield (Entry 5, Table 3.14). Initial results on the scope of the new method are shown in Tables 3.15 and 3.16.^{87a}

Table 3.15. Pauson-Khand Reaction of Malonate-Derived Enynes with Catalytic 2-Methyl-3-butyn-2-ol•Co₂(CO)₆^a

Entry	Substrate	Time (h)	Product	Yield (%)
1	 19	12	 20	92 ^b
2	 171	12	 172	86 ^{b,c}
3	 173	12	 174	81 ^{d,e,f}
4	 175	12	 176	95
5	 177	12	 178	90 ^{d,f}

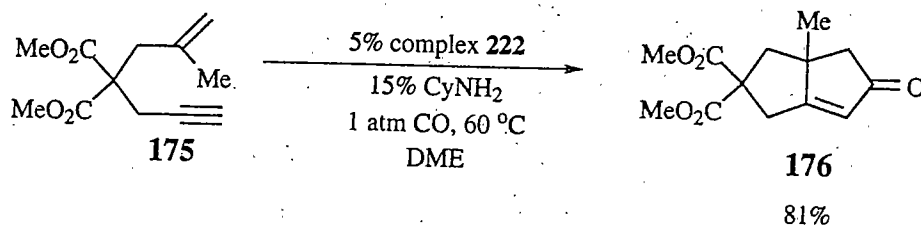
a. All reactions were performed using substrate concentrations of 0.1M with 5 mol % Et₃SiH, 15 mol % CyNH₂ and 5 mol % alkyne-cobalt complex at 65 °C, unless stated otherwise. b. Average of two experiments. c. 7.5 mol % alkyne-cobalt complex. d. 10 mol % alkyne-cobalt complex e. Thiophene was used (30 mol %) instead of CyNH₂. f. >20/1 cis/trans by ¹H NMR spectroscopy.

Table 3.16. Pauson-Khand Reaction of Tosamide-Derived Enynes with Catalytic 2-Methyl-3-butyn-2-ol• Co₂(CO)₈^a

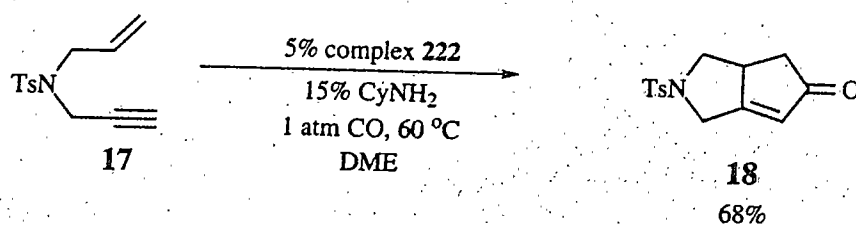
Entry	Substrate	Time (h)	Product	Yield (%)
1	 17	12	 18	77 ^{b,c}
2	 179	12	 180	85 ^e
3	 181	15	 182	92 ^d

a. All reactions were performed using substrate concentrations of 0.1M with 5 mol % Et₃SiH, 15 mol % CyNH₂ and 5 mol % alkyne-cobalt complex at 65 °C, unless stated otherwise.
 b. average of two experiments. c. 7.5 mol% alkyne-cobalt complex. d. 10 mol % alkyne-cobalt complex e. 1.3/1.0 ratio of diastereomers.

Control reactions show that, without Et₃SiH, reduced yields of bicyclopentenones 176 and 18 are obtained (Scheme 3.94 and Scheme 3.95).



Scheme 3.94

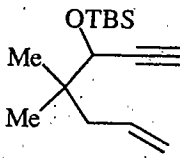
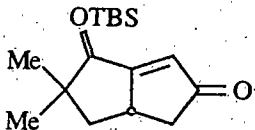
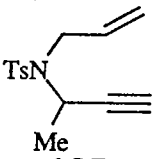
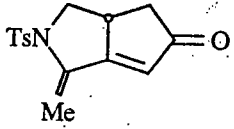
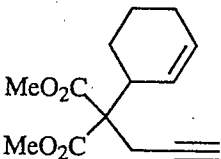
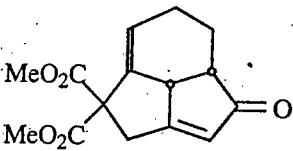
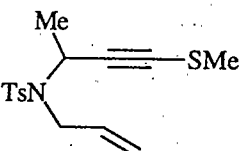
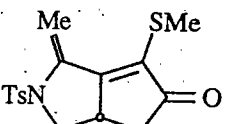
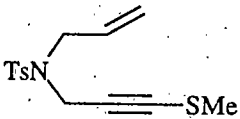
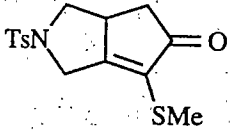
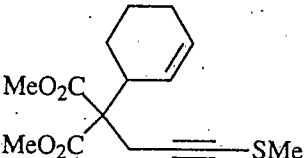
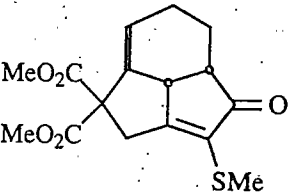


Scheme 3.95

Clearly, the combination of Et₃SiH, cyclohexylamine and 2-methyl-3-butyn-2-ol·Co₂(CO)₆ **222** is required to achieve high yields using this method.^{87b}

Further definition of the scope of novel catalyst **222** for the PKR is shown in Table 3.17.

Table 3.17. Pauson-Khand Reaction of Stereogenic Enynes with Catalytic 2-Methyl-3-butyn-2-ol•Co₂(CO)₆^{a,c}

Entry	Substrate	Product	Syn/Anti	Yield (%)
1	 183	 184	not determined	30% conversion
2	 187	 188	1.7/1	90
3	 191	 192	7.2/1	65 ^{b,c}
4	 201	 202	2.6/1	90
5	 203	 204	-	78 ^c
6	 207	 208	4.7/1	86 ^{b,c}

a. All reactions were performed using substrate concentrations of 0.1M with 5 mol % Et₃SiH, 15% CyNH₂ and 5 mol % alkyne-cobalt complex at 65 °C, unless stated otherwise. b. 10 mol % alkyne-cobalt complex c. From reference 23.

The goal of developing a more stable catalyst for the Pauson-Khand reaction has been realized. The complex, 2-methyl-3-butyn-2-ol·Co₂(CO)₆ **222**, is easily prepared from the inexpensive, commercially available 2-methyl-3-butyn-2-ol and Co₂(CO)₈. 2-Methyl-3-butyn-2-ol·Co₂(CO)₆ **222** is microcrystalline at room temperature and does not require handling in an inert atmosphere. Exposure of complex **222** to air for 24 hours does not reduce its ability to be an effective catalyst for the intramolecular Pauson-Khand reaction.⁸⁸

4. SUMMARY

Initial studies on the asymmetric Rh-catalyzed [4+2] cycloaddition using *cationic* rhodium complexes have shown that the nature of the counterion can dramatically effect the rate of cyclization. This discovery is expected to lead to catalyst systems with improved selectivity and efficiency.

The first examples of a $\text{Co}_2(\text{CO})_8$ -catalyzed carbonylative cyclization of allenynes have been discovered. In most cases, product selectivities and yields can be improved by altering alkyne substitution. A novel rhodium-catalyzed carbonylative cyclization of allenynes at 1 atm of CO has been discovered. Preliminary results suggest that this reaction offers complementary selectivities when compared to the $\text{Co}_2(\text{CO})_8$ -catalyzed protocols, though further studies are required to more fully elucidate the scope of this reaction. A novel rhodium-catalyzed cycloisomerization of allenynes has been discovered.

Further modifications have been made to the catalytic photopromoted intramolecular Pauson-Khand reaction, originally discovered in these laboratories. It was discovered that careful control of the internal reaction temperature allows for efficient catalysis without photochemical activation. Additional studies on the substrate-based control of diastereoselectivity in the catalytic Pauson-Khand reaction have also described. The development of an alternative precatalyst for the Pauson-Khand reaction has been described. This novel catalyst offers several advantages over the traditional catalyst for the Pauson-Khand reaction as it is easily prepared and is stable in air.

5. EXPERIMENTAL

5.1 General Experimental Details

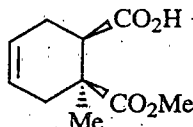
^1H NMR and ^{13}C NMR spectra were recorded on a Bruker AC-300 or Bruker DPX300 (300 MHz ^1H , 75.5 ^{13}C) spectrometer in deuteriochloroform (CDCl_3) with chloroform as an internal reference (7.24 ppm ^1H , 77.00 ppm ^{13}C), unless otherwise noted. Phosphorus NMR spectra (^{31}P NMR) were measured at 121 MHz with a Bruker DPX300 spectrometer and are referenced externally to PPh_3 (-6.0 ppm). Data are reported in the following order: chemical shifts are given (δ); apparent multiplicities are indicated (br (broadened), s (singlet), d (doublet), t (triplet), q (quartet), hex (hextet), m (multiplet), exch (exchangeable), app (apparent)). ^1H NMR coupling constants, J , are reported (Hz). Infrared spectra were recorded on a Bruker ISF 25 spectrometer. Peaks are reported (cm^{-1}) with the following relative intensities: s (strong, 67-100%), m (medium, 40-67%), w (weak, 20-40%) and br (broad). Electron impact mass spectra (70-eV) were recorded with a Hewlett Packard 5970 series mass selective detector. High resolution mass spectra were recorded on a VG Instruments 70E-HF spectrometer. Analytical gas chromatograms were obtained on a Varian Model 3700 gas chromatograph or a Hewlett Packard 5890 equipped with flame ionization detection, and either an Alltech Econocap SE-54 bonded phase column (15 m length, 0.54 mm id, and 1.2 mm film thickness) or a Heliflex (Alltech) RSL 150BP bonded phase column (15 m length, 0.32 mm id, and 0.25 mm film thickness). Optical rotation measurements were performed at approximately 25 $^\circ\text{C}$ with a Perkin-Elmer 241 MC Polarimeter and are reported as follows: $[\alpha]_{\lambda}^{25}$ (c g / 100 mL of solvent). Enantiomeric excesses were determined using an IBM HPLC on a Chiralpak AD analytical

column. Melting points were obtained using a Mel-Temps apparatus and are reported uncorrected.

All reactions were performed in oven- and/or flame-dried glassware under a static argon atmosphere, except those reactions utilizing water as a solvent, which were run under air. Analytical thin-layer chromatography (TLC) was performed on plates supplied by Alltech and Associates. Visualization was accomplished by UV-light, KMnO_4 , phosphomolybdenic acid, ammonium molybdate, or iodine. Bulk solvents for chromatography were reagent grade. Flash column chromatography was performed with Merck silica gel 60, unless otherwise noted. Solvents used as reaction media were distilled immediately before use: tetrahydrofuran, diethyl ether and 1,2-dimethoxyethane, toluene, *p*-xylene, benzene and *t*-butyl methyl ether were distilled from sodium-benzophenone ketyl. Acetonitrile, dichloromethane, 1,2-dichloroethane, 2,2,2-trifluoroethanol and 2-butanol were distilled from calcium hydride at atmospheric pressure under argon. Dimethyl formamide, dimethyl acetamide, and hexamethylphosphoramide were distilled from calcium hydride at reduced pressure. After distillation, dichloromethane, 1,2-dichloroethane, toluene, benzene and 2,2,2-trifluoroethanol were transferred to a Schlenk flask and freeze-pump-thaw degassed before use in reactions involving transition metal catalysis. Hydrocarbon solvents were purified by repeated stirring over concentrated H_2SO_4 until no discoloration was observed, washed with water, dried (MgSO_4), and distilled from sodium or potassium. "Brine" refers to a saturated aqueous solution of NaCl . Unless otherwise specified, solutions of NH_4Cl , NaHCO_3 , KOH , NaOH , etc. refer to aqueous solutions. Titration of *n*-BuLi was accomplished using the method of Suffert.⁸⁹

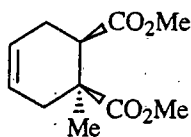
5.2 Chiral Phosphines and Related Precursors

(+)-(1*R*, 2*S*)-Methyl 2-methylcyclohex-4-ene-2-carboxylate-1-carboxylic acid (90)



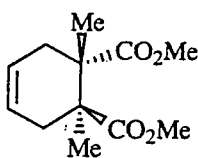
In a one liter round-bottomed flask, a solution of diisopropylamine (32.0 mL, 0.23 mol, 2.3 equiv) in THF (400 mL) was cooled to $-78\text{ }^{\circ}\text{C}$ (CO_2/IPA). To this solution was added *n*-BuLi (84.0 mL of a 2.5 M solution in hexanes, 0.21 mol, 2.1 equiv) over 25 min. The resulting light yellow solution was allowed to stir for 30 min at $-78\text{ }^{\circ}\text{C}$, then a 1.0 M solution of (1*R*, 2*S*)-methyl 2-methylcyclohex-4-ene-2-carboxylate-1-carboxylic acid (89)⁶⁰ (18.4 g, 0.10 mol, 1.00 equiv) in THF was added dropwise via cannula over 35 min. After an additional 35 min at $-78\text{ }^{\circ}\text{C}$, MeI (12.5 mL, 0.300 mol, 2.00 equiv) was added over 25 min and the resulting mixture was allowed to warm to room temperature very slowly. After 18 h, the reaction mixture was cooled to $0\text{ }^{\circ}\text{C}$ (ice/water) and 1.0 M H_2SO_4 (250 mL) was added. The reaction mixture was extracted twice with ethyl acetate (450 and 150 mL) and the combined organic layers were washed with brine (350 mL) and dried (Na_2SO_4). Evaporation of most of the solvent followed by addition of pentane (250 mL) afforded 17.4 g (88 %) of the title compound as a colorless solid. Data for the title compound 90 ($[\alpha]_{\text{D}}^{25} = +13.0^{\circ}$ ($c = 1.00$ in 2-propanol) were consistent that described in the literature.⁹⁰

(+)-(1*S*, 2*R*)-Dimethyl 1-methylcyclohex-4-ene-1,2-dicarboxylate (**91**)



In a 250 mL round-bottomed flask, a solution of (+)-(1*R*, 2*S*)-methyl 2-methylcyclohex-4-ene-2-carboxylate-1-carboxylic acid (**90**) (17.4 g, 88.0 mmol, 1.00 equiv) and K_2CO_3 (18.2 g, 132.0 mmol, 1.50 equiv) in DMF (90 mL) was allowed to stir for 30 min at rt at which time MeI (8.2 mL, 132.0 mmol, 1.5 equiv) was added rapidly. After a brief induction period (ca. 2-3 min), a mildly exothermic reaction occurred and the suspension was allowed to stir for 2.5 h at which time tlc analysis (30% ethyl acetate in hexane, $KMnO_4$ stain) showed consumption of starting material ($R_f = 0.36$) and formation of one product ($R_f = 0.66$). The mixture was partitioned between diethyl ether (300 mL) and water (250 mL). The aqueous phase was washed with diethyl ether (2 x 100 mL) and the combined organic layers were washed with water (200 mL), brine (250 mL) and dried (Na_2SO_4). Evaporation of solvent afforded a yellow oil which was purified by Kugelrohr distillation (80 °C, 0.025 Torr) to give 18.0 g (97%) of the title compound as a colorless oil. Data for the title compound **91** were consistent with that reported in the literature⁹⁰: 1H NMR (300 MHz, $CDCl_3$) δ 5.50 (br m, 2H), 3.58 (s, 3H), 3.53 (s, 3H), 2.87 (dd, $J = 6.6, 2.3$ Hz, 1H), 2.65 (d with fine structure, $J = 18.0$ Hz, 1H), 2.26 (m, 1H), 1.92 (m, 1H), 1.12 (s, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 177.2 (C), 173.7 (C), 124.9 (CH), 122.7 (CH), 51.6 (CH_3), 51.5 (CH_3), 44.2 (CH), 41.3 (C), 31.0 (CH_2), 24.5 (CH_2), 23.7 (CH_3); IR (thin film, NaCl) 3029 (s), 2952 (s), 2850 (s), 1734 (br s), 1435 (s), 1198 (br s), 1109 (s); high resolution (EI) mass spectrum calculated for $C_{11}H_{16}O_4$ (M^+) 213.1127, found 213.1122.

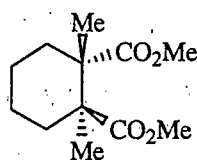
(+)-(1*S*, 2*R*)-Dimethyl 1,2-dimethylcyclohex-4-ene-1,2-dicarboxylate (92)



In a one liter round-bottomed flask, a THF (422 mL) solution of diisopropylamine (14.3 mL, 101.8 mmol, 1.2 equiv) was cooled to -78°C . To this solution was added *n*-BuLi (37.3 mL, 93.3 mmol, 1.1 equiv) over 10 min. The resulting light yellow solution was allowed to stir for 30 min at -78°C . After 30 min, a 1.0 M solution of the (+)-(1*S*, 2*R*)-dimethyl 1-methylcyclohex-4-ene-1,2-dicarboxylate (91) (18.0 g, 84.8 mmol, 1.00 equiv) in THF was added over 50 min at -78°C . The resulting bright yellow solution was allowed to stir at -78°C for 2 h then MeI (7.90 mL, 127.2 mmol, 1.50 equiv) was added over 50 min. The resulting homogeneous solution was stirred overnight as the cold bath was allowed to slowly warm to room temperature. After 12 h, the reaction mixture was cooled to 0°C (ice/water) and quenched by the addition of 33% (v/v) acetic acid in THF (130 mL). The mixture was extracted twice with diethyl ether (350 mL) and the combined organic phases were washed with half-saturated NaHCO_3 (300 mL), saturated NaHCO_3 (2 x 300 mL), water (200 mL), brine (2 x 250 mL), and dried (Na_2SO_4). Evaporation of solvent afforded a yellow-orange solid which contained a mixture of diastereomers (GC analysis revealed a 8/1 mixture (trans/cis)). The solid was purified by dissolving in hot MeOH (ca. 40 mL) and allowing the mixture to cool to room temperature at which time crystals had formed. Cooling to -20°C for 5 h followed by filtration through a pre-cooled coarse frit afforded a mixture of (+)-(1*S*, 2*R*)-dimethyl 1,2-dimethylcyclohex-4-ene-1,2-dicarboxylate (92) and *meso*-dimethyl 1,2-dimethylcyclohex-4-ene-1,2-dicarboxylate (92) (18/1). A second recrystallization in the identical manner described above affords

9.82 g (50%) of (+)-diester **92** as a colorless solid (>99/1 ratio of diastereomers by GC analysis). A second crop of (+)-diester **92** could be obtained by recrystallization (3.06 g, 16%) that was of the same level of purity. Data for the title compound (+)-**92**: ($[\alpha]_D^{25} = +19.5^\circ$ ($c = 1.02$ in 2-propanol); mp = 60-61 °C; ^1H NMR (300 MHz, CDCl_3) δ 5.58 (app s with fine structure, 2H), 3.64 (s, 6H), 2.68 (d, $J = 16.5$ Hz, 2H), 1.90 (dd, $J = 16.5$, 2.7 Hz, 2H), 1.24 (s, 6H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 176.0 (2 x C), 123.5 (2 x CH), 51.7 (2 x CH_3), 46.2 (2 x C), 33.2 (2 x CH_2), 19.7 (2 x CH_3); IR (thin film, NaCl) 3036 (m), 2978 (m), 2957 (m), 2923 (m), 2851 (m), 1725 (br s), 1429 (m), 1278 (s), 1234 (s); High resolution mass spectrum calculated for $\text{C}_{12}\text{H}_{18}\text{O}_4$ (M^+) 226.1205, found 226.1209.

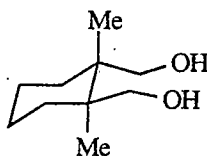
(+)-(1S, 2R)-Dimethyl 1,2-dimethylcyclohexane-1,2-dicarboxylate (93)



In a 250 mL round-bottomed flask, a 0.4 M suspension of (+)-(1S, 2R)-dimethyl 1,2-dimethylcyclohex-4-ene-1,2-dicarboxylate (**92**) (8.96 g, 39.6 mmol, 1.00 equiv) and 5% Pd/C (2.4 g) in EtOH was allowed to stir under Ar. A dihydrogen filled balloon was added and allowed to purge the system for one minute, after which time the exit needle was removed and the suspension was stirred for 3 h at rt. The reaction vessel was purged with Ar for 5 min and then filtered through a piece of filter paper covered with celite (5.5 x 2 cm). The pad of celite was rinsed with EtOH (5 x 30 mL). Evaporation of solvent afforded a colorless solid. The solid was dissolved in CCl_4 and then evaporated to give 8.69 g (96 %) of (+)-(1S, 2R)-dimethyl 1,2-dimethylcyclohexane-1,2-dicarboxylate (**93**)

as a colorless solid which was sufficiently pure for the next step. Data for (+)-(1*S*, 2*R*)-dimethyl 1,2-dimethylcyclohexane-1,2-dicarboxylate (**93**): ($[\alpha]_D^{25} = +44.7^\circ$ ($c = 1.02$ in 2-propanol); mp = 54-55 °C; ^1H NMR (300 MHz, CDCl_3) δ 3.62 (s, 6H), 2.03 (m, 2H), 1.50 (m, 6H), 1.27 (s, 6H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 176.4 (2 x C), 51.5 (2 x CH_3), 47.3 (2 x C), 31.4 (2 x CH_2), 20.5 (2 x CH_2), 19.8 (2 x CH_3); IR (thin film, NaCl) 2992 (m), 2958 (m), 2872 (m), 1725 (s), 1247 (s); High resolution mass spectrum calculated for $\text{C}_{11}\text{H}_{16}\text{O}_3$ ($\text{M} + \text{CH}_3\text{OH}$) $^+$ 196.1099, found 196.1100.

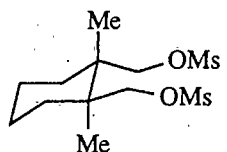
(-)-(1*S*, 2*R*)-1,2-Dimethyl-1,2-di(hydroxymethyl)cyclohexane (94**)**



A solution of (+)-(1*S*, 2*R*)-dimethyl 1,2-dimethylcyclohexane-1,2-dicarboxylate (**93**) (8.64 g, 37.8 mmol, 1.00 equiv) in THF (40 mL) was added dropwise to a suspension of LiAlH_4 (2.20 g, 56.8 mmol, 1.50 equiv) in THF (100 mL) at 0 °C (ice/water) over a period of 20 min. The resulting suspension was heated to reflux for 4 h. After 4 h, the suspension was cooled to 0 °C (ice/water) and quenched by the sequential addition of ethyl acetate (10 mL) and water (10 mL). The resulting mixture was then poured into 1.0 M H_2SO_4 (275 mL) and extracted with ethyl acetate (250 mL). The layers were separated and the aqueous layer was washed with ethyl acetate (2 x 100 mL). The combined organic layers were washed with water (300 mL), brine (250 mL) and dried (Na_2SO_4). Filtration and evaporation of solvent afforded a colorless solid which was recrystallized from hot methylcyclohexane (50 mL) to afford 6.11g (94 %) of (-)-(1*S*, 2*R*)-1,2-dimethyl-1,2-di(hydroxymethyl)cyclohexane (**94**) as colorless crystals. Data for the title compound **94**:

($[\alpha]_D^{25} = -5.93^\circ$ ($c = 1.03$ in THF); mp = 215-218 °C; ^1H NMR (300 MHz, CDCl_3) δ 3.78 (s, 2H), 3.60 (d, $J = 11.3$ Hz, 2H), 2.96 (d, $J = 11.3$ Hz, 2H), 1.40 (m, 6H), 1.05 (s, 6H), 1.10-0.92 (m, 2H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 69.8 (2 x CH_2), 40.2 (2 x C), 32.7 (2 x CH_2), 21.5 (2 x CH_2), 17.3 (2 x CH_3); IR (thin film, NaCl) 3122 (br s), 2970 (s), 2915 (s), 2859 (s), 1046 (s); High resolution mass spectrum calculated for $\text{C}_{10}\text{H}_{16}(\text{M} - 2\text{H}_2\text{O})^+$ 136.1252, found 136.1257.

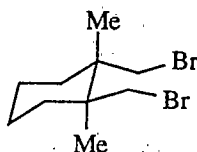
(-)-(1S, 2R)-1,2-Dimethyl-1,2-di(methanesulfonylmethyl)cyclohexane (97)



In a 100 mL round-bottomed flask, a suspension of (-)-(1S, 2R)-1,2-dimethyl-1,2-di(hydroxymethyl)cyclohexane (**94**) (1.72 g, 10.0 mmol, 1.00 equiv) and methanesulfonyl chloride (1.7 mL, 22.0, 2.2 equiv) in DCM (35 mL) was cooled to ca. -5 °C (ice/salt/water) for 15 min. Dropwise addition of triethylamine (4.2 mL, 30.0 mL, 3.0 equiv) over 15 min caused dissolution of the partially insoluble diol **94** followed by formation of triethylamine hydrochloride as a colorless ppt. The reaction mixture was allowed to stir for 13 h at 0 °C. At this time the reaction mixture was partitioned between DCM (50 mL) and 1.0 M H_2SO_4 (50 mL). The organic layer was washed with half-saturated NaHCO_3 (50 mL), water (50 mL), and dried (Na_2SO_4). Filtration and evaporation of solvent affords 3.3 g of a light tan solid which was purified by recrystallization from hot absolute EtOH (50 mL) to give 3.08 g (94%) of (-)-(1S, 2R)-1,2-Dimethyl-1,2-di(methanesulfonylmethyl)cyclohexane (**97**) as colorless crystals. Data for the title compound: ($[\alpha]_D^{25} = -5.05^\circ$ ($c = 1.01$ in THF); mp = 129-132 °C; ^1H NMR (300

MHz, CDCl_3) δ 4.16 (d, $J = 9.6$ Hz, 2H), 4.00 (d, $J = 9.6$ Hz, 2H), 2.99 (s, 6H), 1.4 (m, 8H), 1.04 (s, 6H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 75.0 (2 x CH_2), 38.5 (2 x C), 37.1 (2 x CH_3), 31.5 (2 x CH_2), 20.9 (2 x CH_2), 18.1 (2 x CH_3); IR (thin film, NaCl) 2941 (m), 2867 (w), 1367 (s), 1349 (s), 1179 (s), 954 (s); High resolution (CI, NH_3) mass spectrum calculated for $\text{C}_{12}\text{H}_{28}\text{NO}_6\text{S}$ ($\text{M} + \text{NH}_4$) $^+$ 346.1358, found 346.1348.

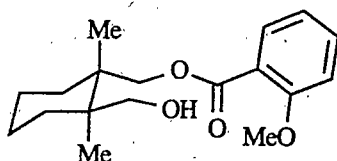
(-)-(1*S*, 2*R*)-1,2-Dimethyl-1,2-di(bromomethyl)cyclohexane (98)



In a 25 mL round-bottomed flask equipped with a reflux condenser, a suspension of (-)-(1*S*, 2*R*)-1,2-dimethyl-1,2-di(methanesulfonylmethyl)cyclohexane (**97**) (1.23 g, 3.73 mmol, 1.00 equiv) and LiBr (0.84 g, 9.7 mmol, 2.6 equiv) in HMPA (7.5 mL) was heated at 125 °C for 15 h. The reaction mixture was allowed to cool to rt and then partitioned between pentane (20 mL) and water (20 mL). The aqueous phase was washed with pentane (2 x 10 mL) and the combined organic layers were washed with water (3 x 10 mL), brine (15 mL) and dried (Na_2SO_4). Evaporation of solvent followed by flash chromatography (basic alumina, 100 % pentane) afforded 0.852 g (94%) of (-)-(1*S*, 2*R*)-1,2-dimethyl-1,2-di(bromomethyl)cyclohexane (**98**) as a colorless oil which solidified upon standing at room temperature. Data for (-)-(1*S*, 2*R*)-1,2-dimethyl-1,2-di(bromomethyl)cyclohexane (**98**): ($[\alpha]_{\text{D}}^{25} = -6.51^\circ$ ($c = 1.00$ in THF); mp = 59-60 °C; ^1H NMR (300 MHz, CDCl_3) δ 3.66 (d, $J = 10.1$ Hz, 2H), 3.54 (d, $J = 10.1$ Hz, 2H), 1.64-1.53 (m, 2H), 1.46-1.37 (m, 6H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 43.9 (2 x CH_2), 39.3 (2 x C), 32.7 (2 x CH_2), 21.4 (2 x CH_2), 19.9 (2 x CH_3); IR (thin film, NaCl) 2969

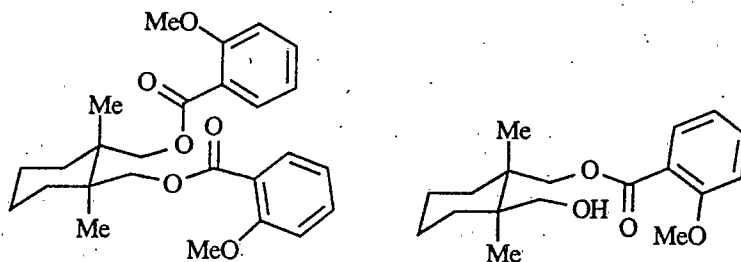
(m), 2934 (s), 2862 (s), 1465 (m), 1254 (m); High resolution mass spectrum calculated for $C_9H_{16}Br$ ($M - CH_2Br$)⁺ 203.0435, found 203.0431.

(1*S*, 2*R*)-1-Methyl-1-(2-methoxybenzoylmethyl)-2-(hydroxymethyl)-2-methylcyclohexane (95)



A solution of (-)-(1*S*, 2*R*)-1,2-dimethyl-1,2-di(hydroxymethyl)cyclohexane (**94**) (43 mg, 0.25 mmol, 1.00 equiv), triethylamine (0.42 mL, 0.30 mmol, 1.2 equiv), and 4-dimethylaminopyridine (3 mg, 0.03 mmol, 0.1 equiv) in DCM (1 mL) was cooled to 0 °C for 10 min. To the colorless solution at 0 °C was added *o*-anisoyl chloride (0.37 mL, 0.25 mmol, 1.0 equiv). After 30 min at 0 °C, the volatiles were evaporated at reduced pressure and the residue was partitioned between diethyl ether (15 mL) and water (15 mL). The organic layer was washed with brine (15 mL) and dried (Na_2SO_4). Evaporation of solvent followed by flash chromatography (SiO_2 , 30% ethyl acetate in hexane) afforded 0.56 g (76%) of the title compound **95** as a colorless oil. HPLC analysis (Chiralpak AD, 90/10 Hexane/IPA at 1.0 mL/min; 245 nm; minor at 18.1 min, major at 19.9 min) of the chromatographically pure monoester revealed 99.4% ee.

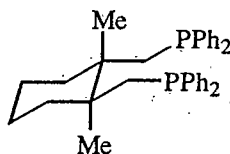
($\pm$)-1,2-Dimethyl-1,2-di(2-methoxybenzoylmethyl-2-(hydroxymethyl))-cyclohexane (96) and ($\pm$)-1-methyl-1-(2-methoxybenzoylmethyl)-2-(hydroxymethyl)-2-methylcyclohexane (95)



In a 5 mL round-bottomed flask, triethylamine (0.84 mL, 6.0 mmol, 3.0 equiv) was added dropwise to a suspension of ($\pm$)-1,2-dimethyl-1,2-di(hydroxymethyl)cyclohexane (94) (344 mg, 2.0 mmol, 1.00 equiv), and DMAP (24 mg, 0.20 mmol, 0.1 equiv) in DCM (2 mL) at rt. To the colorless solution at rt was added *o*-anisoyl chloride (387 μ L, 2.60 mmol, 1.30 equiv) rapidly and an exothermic reaction ensued. After stirring for 18 h, the DCM was evaporated at reduced pressure and the residue was partitioned between diethyl ether (15 mL) and water (15 mL). The organic layer was washed with brine (15 mL) and dried (Na_2SO_4). Evaporation of solvent followed by flash chromatography (SiO_2 , 15% ethyl acetate in hexane to 30% ethyl acetate in hexane gradient for elution) afforded 0.21 g (24%) of the diester as a colorless, viscous oil which solidified on standing and 0.246 g (40%) of the monoester as a colorless, viscous oil. Data for ($\pm$)-diester 96: ^1H NMR (300 MHz, CDCl_3) δ 7.79 (m, 2H), 7.44 (m, 2H), 6.96 (m, 4H), 4.32 (d, J = 11.2 Hz, 2H), 4.30 (d, J = 11.2 Hz, 2H), 3.87 (s, 6H), 1.61 (m, 2H), 1.44 (m, 6H) 1.08 (s, 6H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 166.4 (2 x C), 159.0 (2 x C), 133.3 (2 x CH), 131.5 (2 x CH), 120.0 (2 x C), 199.9 (2 x CH), 111.7 (2 x CH), 70.1 (2 x CH_2), 55.6 (2 x CH_3), 38.1 (2 x C), 31.7 (2 x CH_2), 21.3 (2 x CH_2), 18.7 (2 x CH_3); IR (thin film, NaCl) 2937 (s), 2863 (m), 2838 (m), 1727 (br s), 1700 (br s), 1303 (s), 1253 (s). High resolution (EI)

mass spectrum calculated for $C_{26}H_{32}O_6$ (M^+) 440.2199, found 440.2210. Data for ($\pm$)-monoester **95**: 1H NMR (300 MHz, $CDCl_3$) δ 7.76 (m, 1H), 7.41 (m, 1H), 6.94 (m, 2H), 4.24 (d, $J = 11.2$ Hz, 1H), 4.18 (d, $J = 11.2$ Hz, 1H), 3.84 (s, 3H), 3.62 (dd, $J = 11.2$, 5.3 Hz, 1H), 3.36 (dd, $J = 11.2$, 5.3 Hz, 1H), 2.27 (t, $J = 5.3$ Hz, 1H), 1.38 (m, 8H), 1.01 (s, 3H), 0.99 (s, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 166.5 (C), 158.7 (C), 133.4 (CH), 131.7 (CH), 120.0 (C), 111.7 (CH), 70.6 (CH_2), 68.5 (CH_2), 55.6 (CH_3), 39.3 (C), 38.2 (C), 32.1 (CH_2), 31.5 (CH_2), 21.45 (CH_2), 21.4 (CH_2), 18.1 (CH_3), 17.9 (CH_3); IR (thin film, NaCl) 2937 (s), 2863 (m), 2838 (m), 1727 (br s), 1700 (br s), 1303 (s), 1253 (s). High resolution (CI, NH_3) mass spectrum calculated for $C_{18}H_{27}O_4$ ($M + H$)⁺ 307.1909, found 307.1895. The ($\pm$)-diester was resolved by HPLC (Chiralpak AD, 90/10 hexane/isopropanol, 1.0 mL/min, 254 nm, 17.1 min, 19.0 min).

($\pm$)-1,2-Dimethyl-1,2-bis(diphenylphosphinomethyl)cyclohexane (99**)**



To a suspension of ($\pm$)-phosphine-borane **98** (0.078 g, 0.145 mmol, 1.00 equiv) in toluene (1 mL) was added morpholine (51 μ L, 0.582 mmol, 4.0 equiv). The resulting suspension became a colorless solution upon heating to 70 $^{\circ}C$. After 6 h at 70 $^{\circ}C$, the solution was allowed to cool to rt and the solvent was removed by rotary evaporation. The resulting solid was triturated with methylcyclohexane and the combined portions were concentrated affording a colorless solid. Recrystallization from ethanol afforded 0.026 g (35%) phosphine **99** as a colorless solid. Data for ($\pm$)-1,2-dimethyl-1,2-bis(diphenylphosphinomethyl)cyclohexane (**99**): mp = 155-158 $^{\circ}C$; 1H NMR (300 MHz,

CDCl_3) δ 7.30-7.47 (aromatic envelope, 20H), 2.36 (dd, $J = 14.1, 4.5$ Hz, 2H), 2.24 (d with fine structure, $J = 14.1$ Hz, 2H), 1.61 (br s, 4H), 1.30 (br s, 4H), 1.07 (s, 6H); ^{13}C NMR (75.5, CDCl_3) δ 140.6 (C), 133.1 (d, $J = 3.8$ Hz, CH), 132.8 (d, $J = 3.5$ Hz, CH), 128.40 (d, $J = 2.5$ Hz, CH), 128.31 (d, $J = 2.6$ Hz, CH), 128.25 (d, $J = 1.9$ Hz, CH), 39.9 (d, $J = 9.0$ Hz, CH_2), 37.6 (d, $J = 16.0$ Hz, CH_2), 34.8 (d, $J = 12.8$ Hz, CH_2), 21.9 (d, $J = 13.4$ Hz, CH_2), 21.5 (CH_3); ^{31}P NMR (202 MHz, CDCl_3) -23.5; IR (NaCl, thin film) 2924 (s), 1433 (s), 1372 (m), 1181 (m), 1115 (m), 912 (m), 741 (s), 695 (s); high resolution (EI) mass spectrum calculated for $\text{C}_{34}\text{H}_{38}\text{P}_2$ (M^+) 508.2449, found 508.2449.

5.3 Rh-Catalyzed [4+2] Cycloaddition

Cycloisomerization Procedure A (Neutral; solid phosphine)

An oven-dried test tube was charged with $[(\text{COE})_2\text{RhCl}]_2$ and phosphine. The test tube was carefully flushed with argon, solvent was introduced, and the resulting solution was allowed to stir at least five minutes. Triene (neat) was added to the solution via a gastight syringe and then the reaction was heated at the described temperature for the specified length of time.

Cycloisomerization Procedure B (Neutral; liquid phosphine)

A oven-dried test tube was charged with $[(\text{COE})_2\text{RhCl}]_2$. The test tube was carefully flushed with argon, solvent was introduced followed by the addition of phosphine. The resulting solution was allowed to stir at least five minutes. Triene (neat) was added to the solution via a gastight syringe and then the reaction was heated at the described temperature for the specified length of time.

Cycloisomerization Procedure C (Silver Salt)

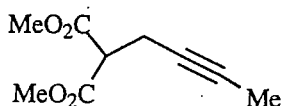
An oven-dried test tube was charged with $[(\text{COE})_2\text{RhCl}]_2$ and a phosphine or $\text{ClRh}(\text{PPh}_3)_3$. The test tube was carefully flushed with argon, solvent was introduced and the resulting solution was allowed to stir for 5 min. A 0.05 M solution of silver salt in 1,2-DCE was added dropwise and the resulting suspension was allowed to stir for an additional 15 min. Triene (neat) was added solution via a gastight syringe and the reaction was heated at the described temperature for the specified length of time. At the completion of the

reaction, the mixture was diluted with diethyl ether and filtered through a plug of neutral alumina to remove silver salts.

Cycloisomerization Procedure D (Diene/H₂)

A dry 10 mL Schlenk flask was charged with the desired rhodium complex and the vessel was subjected to three evacuation/argon backfill cycles. Solvent was introduced and the resulting solution was stirred for 2 min. A dihydrogen-filled balloon was introduced and the system was allowed to stir 15 min. After 15 min, the hydrogen balloon is replaced with an argon-filled balloon and the solution is frozen in a liquid nitrogen bath. The reaction solution is subjected to a freeze-pump-thaw-degas cycle (two cycles). Triene (neat) is added to the solution via a gastight syringe and the resulting solution is heated at the desired temperature for the specified time.

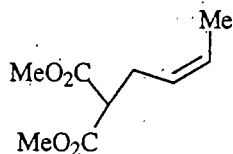
2-(2-Butynyl)malonic acid dimethyl ester



In a 250 mL round-bottomed flask, a solution of diisopropylamine (3.20 mL, 22.5 mmol, 2.25 equiv) in THF (80 mL) was cooled to -78 °C. To this solution was added *n*-BuLi (8.3 mL, 20.5 mmol; 2.05 equiv) and the resulting light yellow solution was allowed to stir for 20 min at -78 °C. To the solution of LDA at -78 °C was added hexamethylphosphoramide (3.6 mL, 20.5 mmol, 2.05 equiv) dropwise. The resulting suspension was allowed to stir at -78 °C until homogeneous (ca. 10 min) at which time 2-(2-propynyl)malonic acid dimethyl ester (1.70 g, 10.0 mmol, 1.00 equiv) was added over

a period of 1-2 min. Near the end of the addition, a colorless precipitate formed and the reaction mixture was stirred for 30 min. After 30 min, MeI (0.70 mL, 11.0 mmol, 1.1 equiv) was added dropwise and the resulting suspension is allowed to stir at -78 °C for 1 h. After 1 h, the reaction vessel was transferred to a -20 °C bath (cold room) and allowed to stir at this temperature for an additional 30 min at which time a light yellow solution formed. The reaction solution was quenched at -20 °C by the addition of saturated NH₄Cl (12 mL). The resulting biphasic mixture was extracted with diethyl ether (100 mL, 2 x 50 mL) and the combined organic phases were washed with saturated NH₄Cl (2 x 100 mL), 2.0 M HCl (50 mL), water (2 x 100 mL), brine (100 mL), and dried (Na₂SO₄). Evaporation of volatiles followed by purification by flash chromatography (SiO₂, 5% ethyl acetate in hexanes to 15% ethyl acetate in hexanes gradient for elution) afforded 1.60 g (87%) of 2-(2-butyryl)malonic acid dimethyl ester as a colorless oil. Data for 2-(2-butyryl)malonic acid dimethyl ester: ¹H NMR (300 MHz, CDCl₃) δ 3.63 (s, 6H), 3.43 (t, *J* = 7.6 Hz, 1H), 2.58 (dq, *J* = 7.6, 2.6 Hz, 2H), 1.62 (t, *J* = 2.6 Hz, 3H); ¹³C NMR (75.5 MHz, CDCl₃) δ 168.4 (2 x C), 77.7 (C), 74.4 (C), 52.5 (2 x CH₃), 51.2 (CH), 18.7 (CH₃), 3.2 (CH₃); IR (thin film, NaCl) 3474 (w), 3005 (m), 2956 (s), 2924 (m), 2848 (m), 2244 (w), 1734 (s br), 1437 (s br), 1344 (s br), 1239 (s), 1032 (s); high resolution (EI) mass spectrum calculated for C₉H₁₂O₄ (M⁺) 184.0736, found 184.0737.

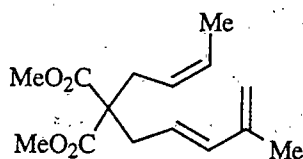
2-(2Z-Butenyl)malonic acid dimethyl ester



In a 25 mL round-bottomed flask, a 1.0 M solution of NaBH₄ (0.30 mL, 0.30 mmol, 0.05 equiv) in ethanol was added to a solution of Ni(OAc)₂ (0.074 g, 0.30 mmol, 0.05 equiv) in

ethanol (12 mL). The resulting black suspension was allowed to stir for five min at which time dihydrogen was introduced and purged through the system for one min. To the black suspension was added ethylene diamine (0.060 mL, 0.90 mmol, 0.15 equiv) followed by the dropwise addition of 2-(2-butyryl)malonic acid dimethyl ester (1.10 g, 5.97, 1.00 equiv). The reaction suspension was allowed to stir for 6 h and then argon was purged through the system for 5 min. Filtration of the crude reaction mixture through neutral alumina followed by evaporation of volatiles afforded 1.06 g (95%) of 2-(2Z-butenyl)malonic acid dimethyl ester as a colorless oil. Data for 2-(2Z-butenyl)malonic acid dimethyl ester: ^1H NMR (300 MHz, CDCl_3) δ 5.52 (dtq, $J = 11.3, 6.8, 1.5$ Hz, 1H), 5.26 (dtq, $J = 11.3, 7.4, 1.8$ Hz, 1H), 3.67 (s, 3H), 3.34 (t, $J = 7.4$ Hz, 1H), 2.59 (app dd, $J = 7.4$ Hz, 2H), 1.57 (dd with fine structure, $J = 6.8, 1.8$ Hz, 3H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 169.4, 127.2, 125.4, 61.3, 52.3, 51.6, 51.5, 26.3, 13.9, 12.6; IR (thin film, NaCl) 3019 (m), 2956 (m), 1738 (s), 1436 (m), 1340 (m), 1234 (s), 1156 (s), 1029 (m); high resolution (EI) mass spectrum calculated for $\text{C}_9\text{H}_{14}\text{O}_4$ (M^+) 186.0892, found 186.0892.

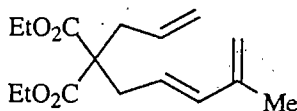
2-(2Z-Butenyl)-2-(4-methylpenta-2E,4-dienyl)malonic acid dimethyl ester



To a suspension of NaH (150 mg (deoled), 6.3 mmol, 1.1 equiv) in THF (5 mL) at 0°C was added a solution of 2-(2Z-butenyl)malonic acid dimethyl ester (1.06 g, 5.69 mmol, 1.00 equiv) in THF (2 mL) over 15 min. The resulting suspension was allowed to stir at rt for 1 h and then was recooled to 0°C . A solution of 1-chloro-4-methyl-penta-2,4-diene

(0.73 g, 6.3 mmol, 1.1 equiv) in THF (3 mL) was added to the sodium malonate at 0 °C dropwise over 15 min. The resulting mixture was allowed to stir 4 h at 0 °C, then an additional 15 h at rt. The resulting mixture was diluted with ethyl acetate (3 mL) and quenched by the addition of saturated NH_4Cl (3 mL) at 0 °C. The mixture was partitioned between diethyl ether/1M H_2SO_4 (30/10 mL), the organic phase was washed with water (25 mL), brine (25 mL) and dried (Na_2SO_4). Concentration and purification by flash chromatography (SiO_2 , 5% ethyl acetate in hexanes) afforded 1.29 g (79%) of the title compound as a colorless oil. Data for 2-(2Z-butenyl)-2-(4-methylpenta-2E,4-dienyl)malonic acid dimethyl ester: ^1H NMR (300 MHz, CDCl_3) δ 6.10 (d, J = 15.5 Hz, 1H), 5.56 (m, 1H), 5.40 (dt, J = 15.5, 7.4 Hz, 1H), 5.19 (m, 1H), 4.84 (app br d, J = 5.2 Hz, 2H), 3.66 (s, 6H), 2.61 (app br t, J = 7.4 Hz, 4H), 1.74 (s, 3H), 1.55 (d, J = 6.9 Hz, 3H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 171.3 (2 x C), 141.5 (C), 136.9 (CH), 127.9 (CH), 123.5 (CH), 123.4 (CH), 115.6 (CH_2), 57.8 (C), 52.2 (CH_3), 35.9 (CH_2), 29.9 (CH_2), 18.4 (CH_3), 12.8 (CH_3); IR (thin film, NaCl) 3474 (w), 3081 (m), 3021 (m), 2953 (s), 2860 (m), 1734 (br s), 1610 (m), 1436 (s), 1206 (br s), 969 (m), 889 (m), 710 (m); high resolution (EI) mass spectrum calculated for $\text{C}_{15}\text{H}_{22}\text{O}_4$ (M^+) 266.1518, found 266.1508.

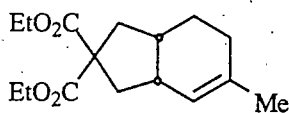
2-(3-Propenyl)-2-(4-methyl-2E,4-pentadienyl)malonic acid diethyl ester (77)



In a 500 mL round-bottomed flask, a suspension of NaH (1.10 g, 27.4 mmol, 1.30 equiv) in THF (25 mL) was cooled to 0 °C (ice/water). To the cooled suspension, diethyl

allylmalonate (4.20 mL, 21.1 mmol, 1.00 equiv) was added dropwise over 20 min and the resulting mixture was allowed to warm to rt and stir an additional 30 min. After 30 min, the resulting solution was cooled to 0 °C and a solution of 1-chloro-4-methyl-2,4-pentadiene (2.58 g, 22.1 mmol, 1.05 equiv) in THF (10 mL) was added dropwise via cannula over 15 min. The reaction mixture was allowed to warm to rt over a period of 6 h and then allowed to stir at rt for 20 h. The reaction was quenched at 0 °C by the addition of pH 7.0 phosphate buffer (10 mL) and then water (10 mL). Flash chromatography (SiO₂, 100% hexanes to 2% ethyl acetate in hexanes to 5% ethyl acetate in hexanes gradient for elution) to afford 2.61 g (44%) triene **77** as a colorless oil and 1.88 g of impure triene **77** (light yellow oil) which required repurification. Data for 2-(3-propenyl)-2-(4-methyl-2E,4-pentadienyl)malonic acid diethyl ester (**77**): ¹H NMR (300 MHz, CDCl₃) δ 6.15 (d, *J* = 15.4 Hz, 1H), 5.65 (m, 1H), 5.44 (dt, *J* = 15.4, 7.5 Hz, 1H), 5.12-5.06 (m, 2H), 4.87 (app br d, *J* = 6.4 Hz, 2H), 4.16 (q, *J* = 7.1 Hz, 4H), 2.66 (d, *J* = 7.5 Hz, 2H), 2.62 (d, *J* = 7.5 Hz, 2H), 1.78 (s, 3H), 1.22 (t, *J* = 7.1 Hz, 6H); ¹³C NMR (75.5 MHz, CDCl₃) δ 171.2 (2 x C), 142.0 (C), 137.4 (CH), 132.8 (CH), 124.0 (CH), 119.5 (CH₂), 116.1 (CH₂), 61.6 (2 x CH₂), 58.0 (C), 37.4 (CH₂), 36.3 (CH₂), 18.9 (CH₃), 14.5 (2 x CH₃); IR (thin film, NaCl) 3081 (m), 2981 (s), 2939 (m), 1734 (br s), 1444 (s), 1209 (s); High resolution (EI) mass spectrum calculated for C₁₆H₂₄O₄ (M⁺) 280.1675, found 280.1661.

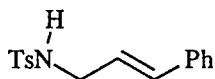
6-Methyl-1,3,3a,4,5,7a-hexahydro-indene-2,2-dicarboxylic acid diethyl ester (78)



The title compound was prepared in 90% yield using Procedure B (1 mol % [(COE)₂RhCl]₂, 2 mol % (*i*-C₃F₆HO)₃P, 0.1M in THF, 55 °C, 9 h). The title compound

was prepared in 67% yield using Procedure C (2.5 mol % $[(\text{COE})_2\text{RhCl}]_2$, 5 mol % diphosphine **76**, 5 % AgOTf , 0.1M in THF, 55 °C, 16 h). The title compound was prepared in 85% yield using Procedure C (2.5 mol % $[(\text{COE})_2\text{RhCl}]_2$, 5 mol % diphosphine **76**, 5 % AgSBF_6 , 0.1M in THF, 55 °C, 4 h). Data for the title compound **78**: ^1H NMR (300 MHz, CDCl_3) δ 5.29 (m, 1H), 3.98 (q, $J = 7.0$ Hz, 2H), 3.96 (q, $J = 7.0$ Hz, 2H), 2.75 (dd, $J = 13.4, 7.6$ Hz, 1H), 2.66 (dd, $J = 13.4, 7.6$ Hz, 1H), 2.64-2.54 (m, 1H), 2.33-2.23 (m, 2H), 2.11 (m, 1H), 1.74-1.66 (m, 2H), 1.53 (s, 3H), 1.50-1.42 (m, 2H), 0.97 (t, $J = 7.0$ Hz, 3H), 0.95 (t, $J = 7.0$ Hz, 3H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 172.9 (C), 172.4 (C), 134.2 (C), 123.1 (CH), 61.3 (CH_2), 61.1 (CH_2), 59.7 (C), 40.2 (CH_2), 39.0 (CH), 38.2 (CH_2), 35.9 (CH), 28.0 (CH_2), 25.5 (CH_2), 23.7 (CH_3), 14.0 (2 x CH_3); IR (thin film, NaCl) 3464 (w), 2980 (s), 2926 (s), 2835 (m), 1734 (s br), 1446 (s), 1366 (s), 1246 (s br), 1180 (s br), 1067 (s), 861 (m); High resolution mass spectrum calculated for $\text{C}_{16}\text{H}_{24}\text{O}_4$ (M^+) 280.1675, found 280.1670.

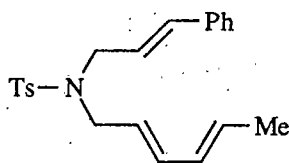
***N*-(3-Phenyl-2-propenyl)-4-methylbenzenesulfonamide**



To a solution of *N*-*t*-butoxycarbonyl-4-methylbenzenesulfonamide (4.07 g, 15.0 mmol, 1.00 equiv), *trans*-cinnamyl alcohol (3.02 g, 22.5 mmol, 1.50 equiv), and triphenylphosphine (5.90 g, 22.5 mmol, 1.50 equiv) in THF (50 mL) at 0 °C was added diethyl azodicarboxylate (3.50 mL, 22.5 mmol, 1.50 equiv) over 20 min. The resulting solution was allowed to warm to rt over a period of 35 min and then was quenched with the addition of methanol (1 mL). The volatiles were removed in vacuo and the residue was treated with diethyl ether (25 mL). To the vigorously stirred ether solution was added hexane (65 mL) and the resulting ppt was filtered through a coarse frit with the aid of

diethyl ether (200 mL). Evaporation of solvent followed by flash chromatography (SiO₂; 2% ethyl acetate in hexanes to 8% ethyl acetate in hexanes for gradient elution) produced 4.75 g (82%) of a colorless solid. To a cloudy solution of trifluoromethanesulfonic acid (0.16 mL, 1.8 mmol, 0.15 equiv) in DCM (30 mL) at 0 °C was added *N*-*t*-(butoxycarbonyl)-*N*-(3-phenyl-2-propenyl)-4-methylbenzenesulfonamide (4.75 g, 12.3 mmol, 1.00 equiv) in one portion. The transfer was quantitated with the use of DCM (2 x 5 mL). The resulting solution was allowed to stir at 0 °C for 1.2 h and then was quenched at 0 °C with the addition of water (25 mL). The resulting biphasic mixture was poured into DCM/water (100/50 mL). The aqueous layer was rinsed with an additional portion of DCM (50 mL) and then the combined organic layers were washed with saturated NaHCO₃ (100 mL), brine (100 mL) and then dried (Na₂SO₄). Evaporation of solvent followed by flash chromatography (SiO₂, 5% ethyl acetate in hexane to 40% ethyl acetate in hexane gradient for elution) afforded 2.95 g (83%) of the title compound as a colorless solid. Spectral data for the title compound were consistent with that reported in the literature.⁹¹

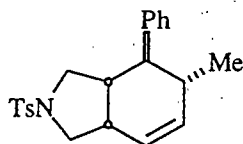
***N*-(3-Phenyl-prop-2-enyl)-*N*-(hexa-2*E*,4*E*-dienyl)-4-methylbenzenesulfonamide (75)**



To a solution of *N*-(3-phenyl-2-propenyl)-4-methylbenzenesulfonamide (1.15 g, 4.00 mmol, 1.00 equiv), tributylphosphine (1.5 mL, 6.0 mmol, 1.5 equiv), and *E,E*,-hexa-3,5-dien-1-ol (0.59 g, 6.0 mmol, 1.5 equiv) in THF (10 mL) at 0 °C was added diethyl azodicarboxylate (0.94 mL, 6.0 mmol, 1.5 equiv) over 15 min. After stirring the

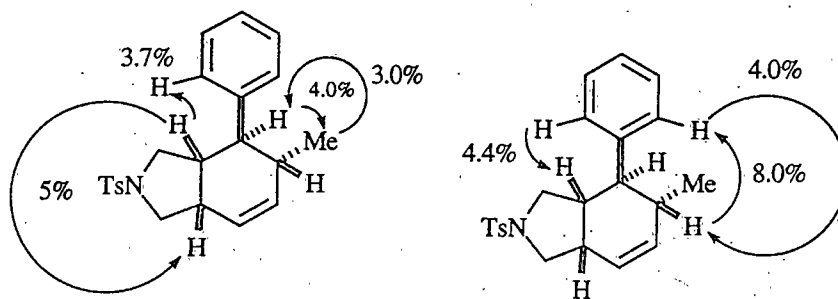
resulting solution an additional 2 h at 0 °C, the reaction mixture was quenched by the addition of water (12 drops). The volatiles were removed in vacuo and the resulting oil was dissolved in diethyl ether (10 mL). To this solution was added hexane (10 mL) with stirring and the resulting ppt was filtered through a coarse frit with the aid of diethyl ether/hexane (1/1). Evaporation of volatiles and purification by flash chromatography (SiO₂; 100% hexanes to 5% ethyl acetate in hexanes gradient for elution) afforded 1.26 g (86%) of the title compound as a colorless, viscous oil. Data for the title compound **75**: ¹H NMR (300 MHz, CDCl₃) δ 7.72 (d with fine structure, *J* = 8.4 Hz, 2H), 7.32-7.19 (m, 7H), 6.4 (d, *J* = 15.9 Hz, 1H), 6.09-5.88 (m, 3H), 5.64 (dq, *J* = 14.4, 6.7 Hz, 1H), 5.32 (dt, *J* = 14.4, 6.7 Hz, 1H), 3.94 (d, *J* = 6.7 Hz, 2H), 3.85 (d, *J* = 6.7 Hz, 2H), 2.41 (s, 3H), 1.73 (d, *J* = 6.7 Hz, 3H); ¹³C NMR (75.5 MHz, CDCl₃) δ 143.1 (C), 137.4 (C), 136.2 (C), 134.6 (CH), 133.7 (CH), 130.33 (CH), 130.28 (CH), 129.6 (2 x CH), 129.5 (CH), 128.4 (CH), 127.7 (CH), 127.1 (2 x CH), 127.0 (CH), 126.3 (2 x CH), 124.1 (CH), 123.8 (CH), 48.6 (CH₂), 21.3 (CH₃), 17.9 (CH₃); IR (thin film, NaCl) 3023 (m), 2918 (m), 1597 (m), 1494 (m), 1448 (m), 1340 (s), 1158 (s), 1091 (s), 990 (m), 969 (m), 908 (m), 815 (m), 730 (m); high resolution (Ei) mass spectrum calculated for C₂₂H₂₃NO₂S (M⁺) 367.1606, found 367.1607.

2-[(4-Methylbenzene)sulfonyl]-5β-methyl-6α-phenyl-2,3,3a,4,5,7a-hexahydro-1*H*-isoindole (79)



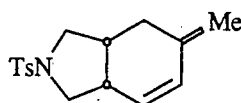
The title compound was prepared in 75% yield (16% isomerization of the primary product) using Procedure C (5 mol % ClRh(PPh₃)₃, 5 % AgOTf, 0.1M in toluene, 80 °C, 24 h).

The title compound was prepared in 83% yield (10% isomerization of the primary product) using Procedure C (5 mol % $\text{ClRh}(\text{PPh}_3)_3$, 5 % AgSbF_6 , 0.1M in toluene, 80 °C, 2.5 h). Resubjection of bicycloadduct **79** (84/16 mixture) to the following conditions (5 mol % $\text{ClRh}(\text{PPh}_3)_3$, 5 % AgSbF_6 , 0.1M in toluene, 80 °C, 18 h) afforded a (40/60) mixture of bicycloadduct/isomer(s) (40/60). An analytical sample was obtained by preparatory gas chromatography. Data for the title compound **79**: ^1H NMR (300 MHz, CDCl_3) δ 7.64 (d with fine structure, $J = 8.4$ Hz, 2H), 7.32 (d with fine structure, $J = 8.4$ Hz, 2H), 7.26-7.18 (m, 3H), 6.85-6.81 (m, 2H), 5.69-5.59 (m, 2H), 3.62 (dd, $J = 9.3, 8.3$ Hz, 1H), 3.11 (dd, $J = 10.4, 6.6$ Hz, 1H), 2.94 (dd, $J = 10.4, 9.3$ Hz, 1H), 2.87 (dd, $J = 10.4, 1.4$ Hz, 1H), 2.71 (m, 1H), 2.46 (s, 3H), 2.44 (m, 1H), 2.24 (m, 1H), 1.81 (dd, $J = 12.3, 10.4$ Hz, 1H), 0.69 (d, $J = 7.1$ Hz, 3H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 143.3 (C), 142.6 (C), 135.5 (CH), 134.0 (C), 129.6 (2 x CH), 128.50 (2 x CH), 128.43 (2 x CH), 127.7 (2 x CH), 126.6 (CH), 123.9 (CH), 52.7 (CH_2), 51.4 (CH_2), 48.9 (CH), 42.8 (CH), 39.2 (CH), 36.7 (CH), 21.6 (CH_3), 19.6 (CH_3); IR (thin film, NaCl) 3024 (w), 2955 (w), 2876 (w), 1597 (w), 1343 (m), 1156 (m), 666 (m); high resolution (EI) mass spectrum calculated for $\text{C}_{22}\text{H}_{23}\text{NO}_2\text{S}$ (M^+) 367.1606, found 367.1607. The stereochemical assignment was based on the following NOE data determined at 250 MHz.



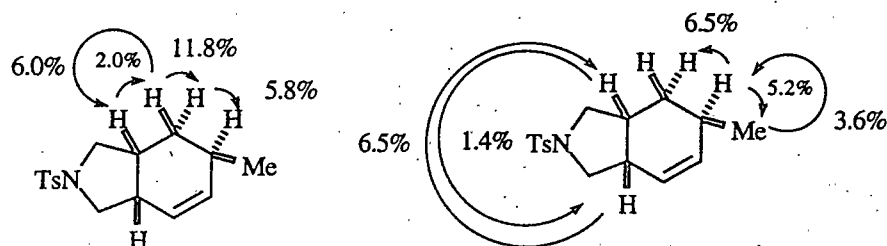
Hexa-2Z,4E-dien-1-ol

To a suspension of LiAlH_4 (0.650 g, 17.0 mmol, 1.05 equiv) at -35°C (external temperature) in diethyl ether (25 mL) was added a solution of ethyl hexa-2Z,4E-dienoate (2.27 g, 16.2 mmol, 1.00 equiv) in diethyl ether (14 mL) over a period of 40 min while maintaining the internal temperature below -15°C . The resulting suspension was allowed to remain at that temperature for 1 h and then was stirred overnight (13 h) at rt. Workup in the usual way followed by Kugelrohr distillation afforded 1.39 g (87%) of the title compound as a 42/1 mixture (as determined by GC analysis) of isomers (colorless oil). Spectral data for hexa-2Z,4E-dien-1-ol were consistent with that reported in the literature.⁹²

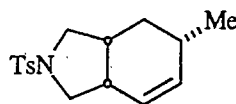
2-[(4-Methylbenzene)sulfonyl]-5 β -methyl-2,3,3a,4,5,7a-hexahydro-1H-isoindole (74)


The title compound was cyclized according to cycloisomerization procedure B (2.5 mol % $[(\text{COE})_2\text{RhCl}]_2$ and 15 mol % $(i\text{-C}_3\text{F}_6\text{HO})_3\text{P}$, THF) in 73% yield. Data for the title compound **74**: ^1H NMR (250 MHz, CDCl_3) δ 7.67 (d, $J = 8.1$ Hz, 2H), 7.28 (d, $J = 8.1$ Hz, 2H), 5.47 (m, 1H), 5.29 (m, 1H), 3.41 (dd, $J = 9.7, 7.7$ Hz, 1H), 3.38 (dd, $J = 9.7, 7.7$ Hz, 1H), 3.06-2.97 (m, 2H), 2.40 (s, 3H), 2.34 (m, 1H), 2.08 (m, 1H), 1.51 (m, 1H), 1.22 (m, 1H), 0.91 (d, $J = 7.1$ Hz, 3H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 143.1 (C), 134.2 (CH), 134.0 (C), 129.4 (2 x CH), 127.4 (2 x CH), 125.4 (CH), 52.9 (CH_2), 51.1

(CH₂), 37.5 (CH), 34.2 (CH), 30.4 (CH₂), 26.2 (CH), 21.4 (CH₃), 20.8 (CH₃); IR (thin film, NaCl) 3014 (w), 2954 (m), 2954 (m), 2924 (m), 1597 (m), 1344 (s), 1161 (s), 1092 (m), 816 (m), 666 (m); high resolution (EI) mass spectrum calculated for C₁₆H₂₁NO₂S (M⁺) 291.1293, found 291.1292. The stereochemical assignment was based on the following NOE data determined at 250 MHz (C₆D₆):



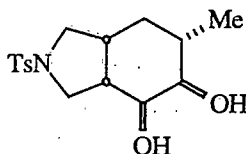
2-[(4-Methylbenzene)sulfonyl]-5 α -methyl-2,3,3a,4,5,7a-hexahydro-1*H*-isoindole (86)



The title compound was prepared in 69% yield (27% ee) using Procedure A (2.5 mol % [(COE)₂RhCl]₂, 5 mol % diphosphine **76**, 0.1M in TFE/DCE(1.5/0.5 mL), 55 °C, 24 h). The title compound was prepared in 70% yield (66% ee) using cycloisomerization procedure C (1 mol % [(COE)₂RhCl]₂, 2 mol % (+)-DIOP, 2 mol % AgSbF₆, 0.1M in 1,2-DCE, 40 °C, 5 h). The title compound was prepared in 96% yield (68% ee) using cycloisomerization procedure D (2 mol % [(NBD)Rh((+)-DIOP)]SbF₆, 0.1M in 1,2-DCE, 40 °C, 4 h). The title compound was prepared in 84% yield (61% ee) using cycloisomerization procedure C (2 mol % [(COE)₂RhCl]₂, 4 mol % (+)-DIOP, 4 mol % AgOTf, 0.1M in 1,2-DCE/TFE (1/1), 55 °C, 2 h). The title compound was prepared in

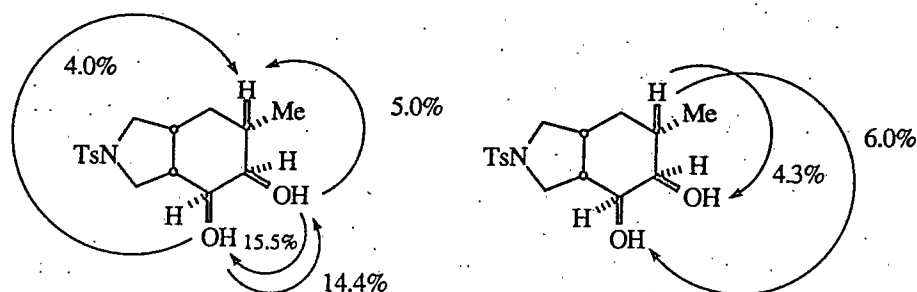
97% yield (76% ee) using cycloisomerization procedure A (2 mol % $[(\text{COE})_2\text{RhCl}]_2$ and 4 mol % (+)-DIOP, 0.1M in 1,2-DCE/TFE (1/1), 55 °C, 1.8 h). The title compound was prepared in 76% yield (77% ee) using cycloisomerization procedure A (2 mol % $[(\text{COE})_2\text{RhBr}]_2$ and 4 mol % (+)-DIOP, 0.1M in 1,2-DCE/TFE (1/1), 55 °C, 4 h). The title compound was prepared in 86% yield (79% ee) using cycloisomerization procedure A (2 mol % $[(\text{COE})_2\text{RhCl}]_2$ and 4 mol % (+)-DIOP, 0.1M in 1,2-DCE/TFE (1/3), 55 °C, 4 h). The title compound was prepared in 98% yield using cycloisomerization procedure D (2 mol % $[(\text{NBD})\text{Rh}(\text{dppe})]\text{SbF}_6$, 0.1M in 1,2-DCE, 55 °C, 2.5 h). Spectral data for the title compound were consistent with that reported in the literature.²³

2-[(4-Methylbenzene)sulfonyl]-6 α -methyl-octahydro-isoindole-4 β ,5 β -diol

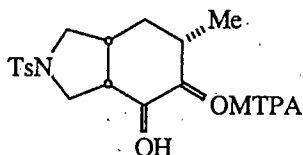


To a solution of 2-[(4-methylbenzene)sulfonyl]-5 α -methyl-2,3,3a,4,5,7a-hexahydro-1*H*-isoindole (58 mg, 0.20 mmol, 1.00 equiv) in ethyl acetate (1 mL) was added water (1 mL). To the resulting solution at 0 °C was sequentially added NMO (62 μL , 0.60 mmol, 3.0 equiv) and a solution of OsO_4 (200 μL of a 0.05 M solution in toluene, 0.01 mmol, 5 mol %). The resulting suspension was allowed to warm to rt and was stirred an additional 20 h. Data for the title compound: ^1H NMR (300 MHz, $\text{DMSO}-d_6$) δ 7.68 (d, J = 7.9 Hz, 2H), 7.42 (d, J = 7.9 Hz, 2H), 4.37 (d, J = 3.5 Hz, 1H), 4.20 (d, J = 7.0 Hz, 1H), 3.56 (m, 1H), 3.38-3.27 (m, 2H), 3.14 (dd, J = 10.3, 5.0 Hz, 1H), 2.98-2.81 (m, 3H), 2.48 (s, 3H), 2.30-2.17 (m, 2H), 1.26 (m, 1H), 0.76 (d, J = 6.5 Hz, 3H), 0.20 (m, 1H); ^{13}C NMR (75.5 MHz, $\text{DMSO}-d_6$) δ 143.9 (C), 134.9 (C), 130.2 (2 x CH), 128.0 (2 x CH),

73.8 (CH), 68.8 (CH), 54.6 (CH₂), 47.9 (CH), 45.7 (CH), 34.8 (CH), 34.5 (CH₂), 31.6 (CH), 21.1 (CH₃), 18.3 (CH₃); IR (thin film, NaCl) 3416 (br m), 2923 (m), 1337 (m), 1541 (m), 1092 (m), 1049 (m); high resolution (EI) mass spectrum calculated for C₁₆H₂₃NO₄S (M⁺) 325.1348, found 325.1343. The stereochemical assignment was based on the following NOE data determined at 250 MHz (DMSO-*d*₆):



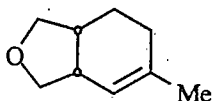
(±)-Mosher's ester of 2-[(4-methylbenzene)sulfonyl]-6α-methyl-octahydro-isoindole-4β,5β-diol



To a solution of (±)-2-[(4-methylbenzene)sulfonyl]-6α-methyl-octahydro-isoindole-4β,5β-diol (0.20 mmol, 1.00 equiv) and DMAP (43 mg, 0.35 mmol, 1.8 equiv) in DCM (1 mL) was added (+)-*S*-MTPACl (56 μL, 0.30 mmol, 1.5 equiv). The resulting solution was allowed to stir at rt for 15 h, the solvent was evaporated and the residue was purified by flash chromatography (SiO₂, 30% ethyl acetate in hexanes) affording 70 mg (65%) of a viscous, colorless oil. Data for the title compound: ¹H NMR (300 MHz, CDCl₃) δ 7.72 (d, *J* = 8.2 Hz, 4H), 7.75-7.47 (m, 4H), 7.45-7.37 (m, 6H), 7.34 (d, *J* = 8.2 Hz, 4H), 4.78 (dd, *J* = 10.7, 2.6 Hz, 1H), 4.73 (dd, *J* = 10.7, 2.6 Hz, 1H), 3.96 (br s, 2H), 3.89 (br s,

2H), 3.55 (s with fine structure, 3H), 3.50 (s with fine structure, 3H), 3.42 (app t, $J = 9.8$ Hz, 2H), 3.27-3.09 (m, 6H), 2.43 (s, 6H), 2.40-2.30 (m, 4H), 2.10-1.97 (m, 2H), 1.78 (br s, 2H), 1.59-1.48 (m, 4H), 0.83 (d, $J = 6.6$ Hz, 3H), 0.72 (d, $J = 6.6$ Hz, 3H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 166.1, 166.0, 143.6, 133.8, 132.1, 131.8, 129.90, 129.86, 129.7, 128.7, 128.6, 127.4, 127.3, 126.9, 125.2, 121.4, 79.7, 79.4, 66.74, 66.36, 55.7, 55.3, 53.6, 47.1, 46.9, 44.4, 33.9, 33.8, 33.6, 29.7, 28.94, 28.51, 17.95, 17.61; high resolution (EI) mass spectrum calculated for $\text{C}_{26}\text{H}_{29}\text{NO}_6\text{SF}_3$ ($M - \text{H}$) $^+$ 540.1668, found 540.1657.

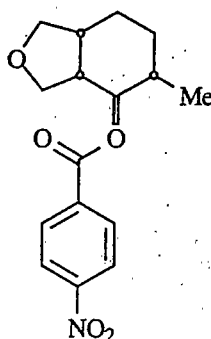
1,3,3ab,6,7,7ab-Hexahydro-5-methylisobenzofuran (83)



The title compound was prepared according to cycloisomerization procedure A (1 mol % $[(\text{COE})_2\text{RhCl}]_2$, 2 mol % (+)-DIOP, 2 mol % AgSbF_6 , 0.1M in 1,2-DCE, 55 °C, 2 h). The solution was concentrated and dissolved in THF (2 mL). To the solution at 0 °C was added $\text{BH}_3 \cdot \text{Me}_2\text{S}$ (25 μL , 0.25 mmol). The resulting solution was allowed to stir for 1 h at 0 °C and then for an additional 15 h at rt. To the solution at 0 °C was sequentially added ethanol/*t*-butyl methyl ether (2 mL, 1/1), 2M NaOH (2 mL) and 30% H_2O_2 (1 mL). The resulting mixture was allowed to warm to rt over 1 h and was stirred an additional 3 h at rt. After extraction, drying (MgSO_4) and concentration, the crude residue was dissolved in DCM (2 mL) and treated with DMAP (0.25 mmol) and *p*-nitrobenzoyl chloride (0.25 mmol) at rt. After 2 h at rt, the volatiles were evaporated and the residue was partitioned between ethyl acetate/water (10/10 mL). The organic phase was washed with brine and

dried (MgSO_4). Concentration and purification by flash chromatography (SiO_2 , 5% ethyl acetate in hexanes) afforded 39 mg (64%) of the title as a colorless oil (17% ee).

1,3,3ab,6,7,7ab-Hexahydro-6-(4-nitrobenzoyl)-5-methylisobenzofuran
(84)

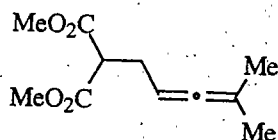


To a solution of alcohol (0.010 g, 0.64 mmol, 1.00 equiv) and DMAP (10 mg, 0.08 mmol, 1.3 equiv) in DCM (1 mL) at rt was added PNB Cl (14 mg, 0.077 mmol, 1.2 equiv) in one portion. After stirring at rt for 30 min, the resulting solution was passed through a short column (SiO_2 , 20% ethyl acetate in hexanes) and concentrated. Data for PNB ester: ^1H NMR (300 MHz, CDCl_3) δ 8.29-8.26 (m, 2H), 8.22-8.19 (m, 2H), 4.95 (app t, J = 10.6 Hz, 1H), 3.88 (app t, J = 8.5 Hz, 1H), 3.78 (app br d, J = 8.5 Hz, 1H), 3.71 (app br d, J = 8.5 Hz, 1H), 3.63 (dd, J = 10.6, 8.5 Hz, 1H), 2.66 (m, 1H), 2.27 (m, 1H), 1.80-1.62 (m, 4H), 1.35 (m, 1H), 0.91 (d, J = 6.4 Hz, 3H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 164.6 (C), 150.6 (C), 137.7 (C), 130.8 (2 x CH), 123.5 (2 x CH), 78.9 (CH), 71.5 (CH_2), 69.3 (CH_2), 45.3 (CH), 39.1 (CH), 36.9 (CH), 28.4 (CH_2), 22.7 (CH_2), 18.3 (CH_3); IR (thin film, NaCl) 2927 (m), 2868 (m), 1721 (s), 1526 (s), 1347 (m), 1273 (s), 1115 (m), 1103 (m), 719 (m); high resolution (PCI/ NH_3) mass spectrum calculated for $\text{C}_{16}\text{H}_{20}\text{NO}_5$ ($\text{M} + \text{H}$) $^+$ 306.1341, found 306.1335.

5.4 Catalytic Carbonylative Cyclization of Allenynes

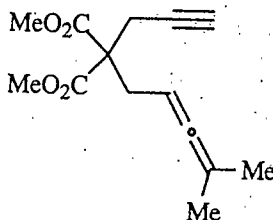
The following compounds were prepared by literature methods: 4-methyl-penta-2,3-dien-1-ol⁷⁰, penta-2,3-dien-1-ol⁷⁰, buta-2,3-dien-1-ol⁷⁰, *N*-*t*-butoxycarbonyl-4-methylbenzenesulfonamide⁹³, 5-(trimethylsilyl)pent-4-yn-1-ol⁹⁴, 5-(trimethylsilyl)pent-4-yn-1-al⁹⁴, (1-thiocyanato-ethyl)-benzene⁹⁵, undeca-1,2-dien-6-yne⁹⁶ and *N*-(prop-2-ynyl)-4-methylbenzenesulfonamide⁹⁸.

2-(4-Methyl-penta-2,3-dienyl)malonic acid dimethyl ester (120)



The title compound was prepared according to the literature procedure and the spectral data were consistent with that reported.⁷¹ Data for 2-(4-methyl-penta-2,3-dienyl)malonic acid dimethyl ester (120): ¹H NMR (300 MHz, CDCl₃) δ 4.98 (m, 1H), 3.72 (s, 6H), 3.48 (t, *J* = 7.5 Hz, 1H), 2.54 (dd, *J* = 7.5, 5.8 Hz, 2H), 1.63 (s, 3H), 1.62 (s, 3H).

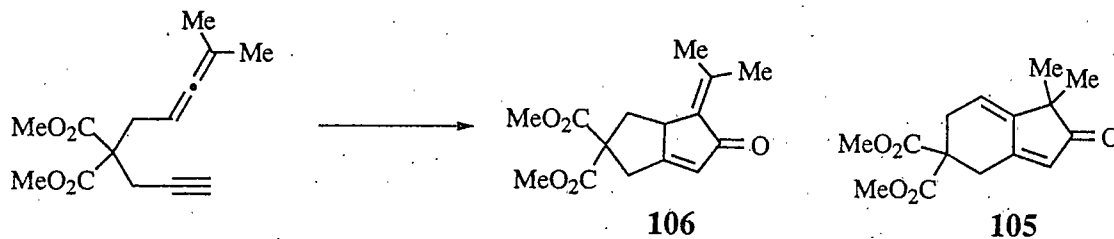
2-(4-Methyl-2,3-pentadienyl)-2-(2-propynyl)malonic acid dimethyl ester (104)



To a suspension of NaH (0.187 g (decoiled), 7.80 mmol, 1.10 equiv) in DMF/THF (7/3 mL) at 0 °C was added 2-(4-methyl-penta-2,3-dienyl)malonic acid dimethyl ester (120)

(1.50 g, 7.07 mmol, 1.00 equiv) dropwise. The reaction mixture was allowed to stir at rt 1 h then the reaction vessel was cooled to 0 °C and propargyl bromide (0.70 mL, 8.5 mmol, 1.2 equiv) was added dropwise. The resulting suspension was allowed to warm to rt and was stirred overnight. The reaction mixture was quenched with the addition of saturated NH_4Cl (5 mL) and then poured into ethyl acetate/water (50/25 mL). The organic phase was washed with water (20 mL), brine (20 mL) and dried (Na_2SO_4). Evaporation of solvent and purification by flash chromatography (SiO_2 , 5% ethyl acetate in hexanes) afforded 1.65 g (92%) of 2-(4-methyl-2,3-pentadienyl)-2-(2-propynyl)malonic acid dimethyl ester (**104**) as a slightly yellow oil. Data for 2-(4-Methyl-2,3-pentadienyl)-2-(2-propynyl)malonic acid dimethyl ester (**104**): ^1H NMR (300 MHz, CDCl_3) δ 4.74 (m, 1H), 3.71 (s, 6H), 2.95 (s, 2H), 2.68 (d, $J = 7.6$ Hz, 2H), 2.30 (s, 1H), 1.63 (s, 6H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 203.7 (C), 169.8 (2 x C), 95.2 (C), 82.0 (CH), 78.5 (C), 71.1 (CH), 56.9 (C), 52.5 (2 x CH_3), 32.2 (CH_2), 22.2 (CH_2), 20.2 (2 x CH_3); IR (NaCl, thin film) 3292 (s br), 2981 (s), 2954 (s), 2910 (s), 2854 (s), 2123 (m), 1969 (m), 1735 (s br), 1438 (s), 1210 (s br); high resolution (EI) mass spectrum calculated for $\text{C}_{14}\text{H}_{18}\text{O}_4$ (M^+) 250.1205, found 250.1203.

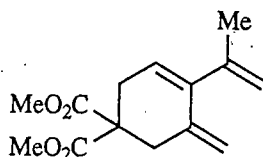
1-Isopropylidene-2-oxo-4,5,6,6a-tetrahydro-1H-pentalene-5,5-dicarboxylic acid dimethyl ester (106) and 5,5-dimethyl-2-oxo-1,2,4,6-tetrahydroindene-5,5-dicarboxylic acid dimethyl ester (105)



The title compound was prepared as a mixture of isomers (5.8/1) in 47% yield using Procedure C except that 10 mol % $\text{Co}_2(\text{CO})_8$ was used (12 h). Purification by flash

chromatography (SiO₂, 15% ethyl acetate in hexanes to 30% ethyl acetate in hexanes gradient for elution) afforded 33 mg (47%) of 1-isopropylidene-2-oxo-4,5,6,6a-tetrahydro-1*H*-pentalene-5,5-dicarboxylic acid dimethyl ester (**106**) and 5,5-dimethyl-2-oxo-1,2,4,6-tetrahydro-indene-5,5-dicarboxylic acid dimethyl ester (**105**) as a slightly yellow oil. An authentic sample of the major isomer **106** was prepared according to a literature procedure.⁶⁶ Data for 1-isopropylidene-2-oxo-4,5,6,6a-tetrahydro-1*H*-pentalene-5,5-dicarboxylic acid dimethyl ester (**106**) (major isomer): mp = 80-81 °C; ¹H NMR (300 MHz, C₆D₆) δ 5.88 (br s, 1H), 3.36-3.25 (obscured peak, 1H), 3.33 (s, 3H), 3.29 (s, 3H), 3.11 (m, 1H), 2.98 (m, 1H), 2.90 (dd, *J* = 12.6, 7.8 Hz, 1H), 2.27 (s, 3H), 1.53 (app t, *J* = 12.6 Hz, 1H), 1.46 (s, 3H); ¹³C NMR (75.5 MHz, C₆D₆) δ 196.2 (C), 174.2 (C), 172.0 (C), 171.0 (C), 145.1 (C), 133.3 (C), 128.7 (CH), 61.2 (C), 52.66 (CH₃), 52.48 (CH₃), 48.9 (CH), 38.0 (CH₂), 34.4 (CH₂), 24.1 (CH₃), 19.5 (CH₃); IR (NaCl, thin film) 2993 (m), 2955 (m), 2848 (m), 1734 (br s), 1690 (s), 1651 (s), 1632 (s), 1435 (s), 1264 (br s); high resolution (EI) mass spectrum calculated for C₁₅H₁₈O₅ (M⁺) 278.1156, found 278.1154. The minor isomer **105** was not fully characterized. Data for 5,5-dimethyl-2-oxo-1,2,4,6-tetrahydro-indene-5,5-dicarboxylic acid dimethyl ester (**105**): high resolution (EI) mass spectrum calculated for C₁₅H₁₈O₅ (M⁺) 278.1166, found 278.1154.

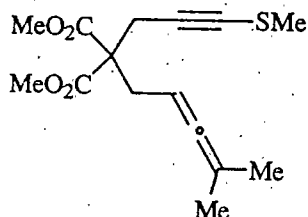
5-Methylene-4-(propen-2-yl)-cyclohex-3-ene-1,1-dicarboxylic acid dimethyl ester (133)



The title compound was isolated from a Co₂(CO)₈-catalyzed carbonylative cyclization reaction of 2-(4-methyl-2,3-pentadienyl)-2-(2-propynyl)malonic acid dimethyl ester (**104**)

using Procedure C. Purification by flash chromatography (SiO_2 , 15% ethyl acetate in hexanes to 30% ethyl acetate in hexanes gradient for elution) afforded crude triene **133**. Further purification by flash chromatography (neutral Al_2O_3 , 5% ethyl acetate in hexanes to 15% ethyl acetate in hexanes gradient for elution) afforded 13 mg (21%) of the title compound as a colorless oil. Data for 5-methylene-4-(propen-2-yl)-cyclohex-3-ene-1,1-dicarboxylic acid dimethyl ester (**133**): ^1H NMR (300 MHz, CDCl_3) δ 5.59 (dt, $J = 4.1$, 1.0 Hz, 1H), 4.99-4.93 (m, 3H), 4.81 (m, 1H), 3.69 (s, 6H), 2.86 (s, 2H), 2.70 (d, $J = 4.1$ Hz, 2H), 1.82 (d, $J = 1.0$ Hz, 3H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 171.3 (2 x C), 144.1 (C), 141.7 (C), 137.8 (C), 123.0 (CH), 114.5 (CH_2), 114.0 (CH_2), 54.3 (2 x C), 52.7 (CH_3), 37.4 (CH_2), 31.5 (CH_2), 22.9 (CH_3); IR (NaCl, thin film) 3091 (w), 2955 (m), 2918 (m), 2849 (m), 1735 (s) 1436 (m); high resolution (EI) mass spectrum calculated for $\text{C}_{14}\text{H}_{18}\text{O}_4$ (M^+) 250.1205, found 250.1202.

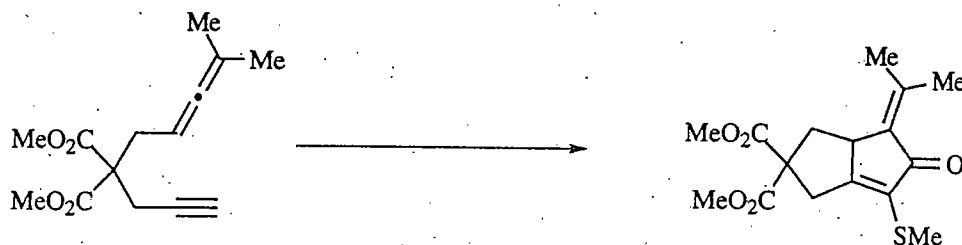
2-(4-Methyl-2,3-pentadienyl)-2-(3-methylthio-2-propynyl)malonic acid dimethyl ester (143)



To a suspension of NaH (98 mg (60% dispersion in oil), 2.44 mol, 1.08 equiv) in DMF/THF (2/1 mL) at 0 °C was added 2-(4-methyl-penta-2,3-dienyl) malonic acid dimethyl ester (**120**) (0.479 g, 2.26 mmol, 1.00 equiv). The resulting mixture was allowed to stir for 30 min at which time 1-chloro-3-thiomethylpropyne (341 mg, 2.83

mmol, 1.25 equiv) was added dropwise. The resulting solution was stirred 4 h at rt and then was quenched with the addition of saturated NH_4Cl (1 mL). The suspension was partitioned between diethyl ether/water (25/10 mL). The organic phase was washed with water (10 mL) and dried (MgSO_4). Evaporation of solvent and purification by flash chromatography (SiO_2 , hexanes to 5% ethyl acetate in hexanes gradient for elution) afforded 400 mg (60%) of 2-(4-methyl-2,3-pentadienyl)-2-(3-methylthio-2-propynyl)malonic acid dimethyl ester (**143**) as a yellow oil. Data for 2-(4-methyl-2,3-pentadienyl)-2-(3-methylthio-2-propynyl)malonic acid dimethyl ester (**143**): ^1H NMR (300 MHz, CDCl_3) δ 4.72 (m, 1H), 3.69 (s, 6H), 2.93 (s, 2H), 2.66 (d, $J = 7.5$ Hz, 2H), 2.28 (s, 3H), 1.62 (s, 3H), 1.61 (s, 3H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 203.9 (C), 170.2 (2 x C), 95.3 (C), 87.4 (C), 82.3 (CH), 73.7 (C), 57.4 (C), 52.6 (2 x CH_3), 32.6 (CH_2), 24.1 (CH_2), 20.4 (2 x CH_3), 19.2 (CH_3); IR (NaCl, thin film) 2980 (m), 2952 (s), 2930 (s), 2853 (m), 2194 (w), 1696 (m), 1234 (s br), 1436 (s), 1288 (s), 1208 (s br); high resolution (EI) mass spectrum calculated for $\text{C}_{15}\text{H}_{20}\text{O}_4\text{S}$ (M^+) 296.1076, found 296.1082.

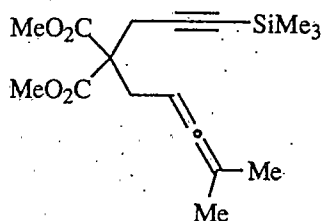
1-Isopropylidene-2-oxo-4,5,6,6a-tetrahydro-3-methylthio-1H-pentalene-5,5-dicarboxylic acid dimethyl ester (144**)**



The title compound was prepared in 84% yield using Procedure A. Purification by flash chromatography (SiO_2 , 15% ethyl acetate in hexanes to 30% ethyl acetate in hexanes

gradient for elution) afforded 69 mg (84%) of 1-isopropylidene-2-oxo-4,5,6,6a-tetrahydro-3-methylthio-1*H*-pentalene-5,5-dicarboxylic acid dimethyl ester (**144**): mp = 90-91 °C; ^1H NMR (300 MHz, CDCl_3) δ 3.80 (s, 3H), 3.73 (s, 3H), 3.51 (dd with fine structure, $J = 12.5, 7.3$ Hz, 1H), 3.33 (d, $J = 19.4$ Hz, 1H), 3.26 (d, $J = 19.4$ Hz, 1H), 2.91 (dd, $J = 12.5, 7.3$ Hz, 1H), 2.42 (s, 3H), 2.27 (s, 3H), 1.91 (s, 3H), 1.67 (app t, $J = 12.5$ Hz, 1H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 193.3 (C), 172.0 (C), 171.1 (C), 168.6 (C), 147.7 (C), 135.0 (C), 131.5 (C), 61.1 (C), 53.3 (CH_3), 53.1 (CH_3), 47.9 (CH), 37.7 (CH_2), 34.3 (CH_2), 24.6 (CH_3), 19.9 (CH_3), 14.6 (CH_3); IR (NaCl, thin film) 2995 (m), 2954 (m), 1733 (s), 1682 (s), 1651 (m), 1622 (m), 1435 (m br), 1260 (m br), 1063 (m); high resolution (EI) mass spectrum calculated for $\text{C}_{16}\text{H}_{20}\text{O}_5\text{S}$ (M^+) 324.1026, found 324.1031.

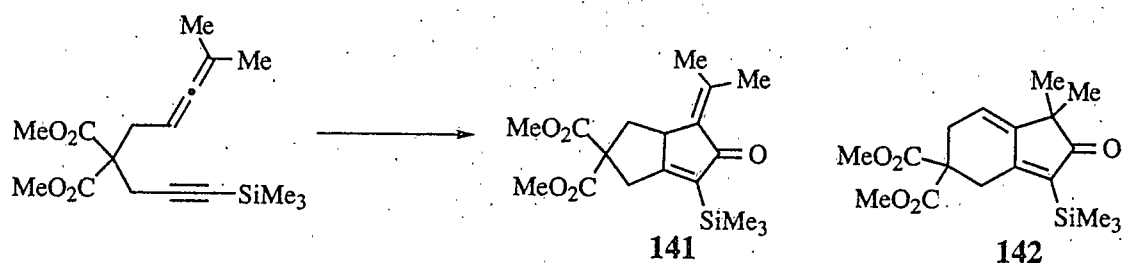
2-(4-Methyl-2,3-pentadienyl)-2-(3-trimethylsilyl-2-propynyl)malonic acid dimethyl ester (140**)**



To a suspension of NaH (0.197 g of a 60% dispersion in oil, 4.93 mmol, 1.10 equiv) in DMF/THF (8/4 mL) at 0 °C was added 2-(4-methyl-penta-2,3-dienyl)malonic acid dimethyl ester (**120**) (0.952 g, 4.48 mmol, 1.00 equiv) dropwise. The reaction mixture was allowed to stir at rt 1 h then the reaction vessel was cooled to 0 °C and 3-trimethylsilyl-1-bromo-2-propyne (1.07 g, 5.60 mmol, 1.25 equiv) was added dropwise. The resulting suspension was allowed to warm to rt and was stirred overnight. The reaction mixture was quenched with the addition of saturated NH_4Cl (5 mL) and then poured into ethyl

acetate/water (30/15 mL). The organic phase was washed with water (10 mL), brine (10 mL) and dried (Na_2SO_4). Evaporation of solvent and purification by flash chromatography (SiO_2 , hexanes to 5% ethyl acetate in hexanes) afforded 0.84 g (58%) of the title compound as a slightly yellow oil. Data for 2-(4-methyl-2,3-pentadienyl)-2-(3-trimethylsilyl-propynyl)malonic acid dimethyl ester (**140**): ^1H NMR (300 MHz, CDCl_3) 4.77 (m, 1H), 3.71 (s, 6H), 2.86 (s, 2H), 2.69 (d, $J = 7.6$ Hz, 2H), 1.64 (s, 3H), 1.63 (s, 3H), 0.10 (s, 9H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 203.9 (C), 170.1 (2 x C), 101.3 (CH), 95.2 (C), 87.9 (C), 82.3 (CH), 57.4 (C), 52.6 (2 x CH_3), 32.5 (CH_2), 23.8 (CH_2), 20.4 (2 x CH_3), -0.11 (3 x CH_3); IR (NaCl, thin film) 2956 (m), 2909 (m), 2855 (m), 2180 (m), 1969 (w), 1741 (br s), 1437 (s), 1207 (br s), 845 (s); high resolution (EI) mass spectrum calculated for $\text{C}_{17}\text{H}_{27}\text{O}_4\text{Si}$ ($\text{M} + \text{H}$) $^+$ 323.1679, found 323.1669.

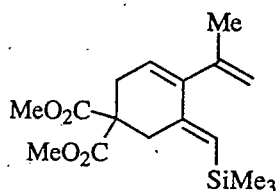
1-Isopropylidene-2-oxo-3-trimethylsilyl-4,5,6,6a-tetrahydro-1H-pentalene-5,5-dicarboxylic acid dimethyl ester (141) and 1,1-dimethyl-2-oxo-1,2,4,6-tetrahydro-3-trimethylsilyl-indene-5,5-dicarboxylic acid dimethyl ester (142)



The title compound was prepared as a mixture of isomers (4.8/1) in 66% yield using Procedure C except that 10 mol % $\text{Co}_2(\text{CO})_8$ was used (12 h). Data for 1-isopropylidene-2-oxo-3-trimethylsilyl-4,5,6,6a-tetrahydro-1H-pentalene-5,5-dicarboxylic acid dimethyl ester (**141**) (major isomer): ^1H NMR (300 MHz, CDCl_3) δ 3.77 (s, 3H), 3.70 (s, 3H),

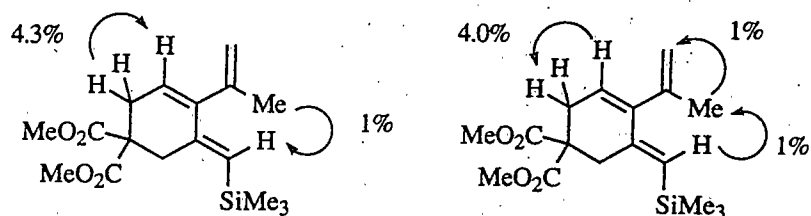
3.48 (dd, $J = 12.3, 7.8$ Hz, 1H), 3.28 (d, $J = 18.3$ Hz, 1H), 3.20 (d, $J = 18.3$ Hz, 1H), 2.93 (dd, $J = 12.3, 7.8$ Hz, 1H), 2.21 (s, 3H), 1.87 (s, 3H), 0.19 (s, 9H); High resolution mass spectrum calculated for $C_{18}H_{26}O_5Si$ (M^+) 350.1156, found 350.1150. Data for minor isomer: High resolution (EI) mass spectrum calculated for $C_{18}H_{26}O_5Si$ (M^+) 350.1154, found 350.1150.

5-(*E*-Trimethylsilylmethylene)-4-(propen-2-yl)-cyclohex-3-ene-1,1-dicarboxylic acid dimethyl ester



The title compound was isolated from a $Co_2(CO)_8$ -catalyzed carbonylative cyclization reaction of 2-(4-methyl-2,3-pentadienyl)-2-(3-trimethylsilyl-2-propynyl) malonic acid dimethyl ester (**140**) using Procedure C except that 10 mol % $Co_2(CO)_8$ was used (12h). Purification by flash chromatography (SiO_2 , 15% ethyl acetate in hexanes to 30% ethyl acetate in hexanes gradient for elution) afforded crude triene. Further purification by flash chromatography (neutral Al_2O_3 , 5% ethyl acetate in hexanes to 15% ethyl acetate in hexanes gradient for elution) afforded 30 mg of the title compound as a colorless oil (30%). Data for the title compound: 1H NMR (300 MHz, C_6D_6) δ 5.95 (br s, 1H), 5.72 (app t, $J = 4.2$ Hz, 1H), 5.09-5.06 (m, 2H), 3.40 (s, 6H), 3.31 (d, $J = 1.2$ Hz, 2H), 2.83 (d, $J = 4.2$ Hz, 2H), 1.94 (s, 3H), 0.31 (s, 9H), ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 171.0 (2 x C), 145.95 (C), 145.62 (C), 144.5 (C), 127.9 (CH), 124.0 (CH), 115.0 (CH_2), 54.6 (C), 52.2 (2 x CH_3), 36.5 (CH_2), 31.8 (CH_2), 23.4 (CH_3), 0.11 (3 x CH_3), IR (thin film, NaCl) 3479 (w), 3079 (m), 2953 (s), 2917 (m), 2848 (m), 1743 (br s), 1578 (m), 1310 (m), 1251 (br s), 1197 (s), 1086 (s), 1061 (s), 894 (s), 861 (s), 838 (m), 754 (m), 692

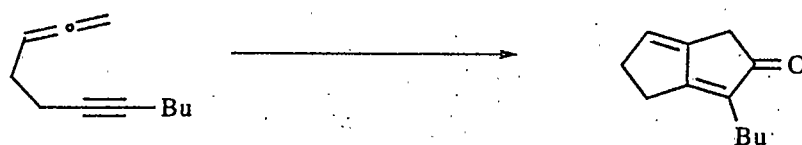
(m); high resolution (EI) mass spectrum calculated for $C_{17}H_{26}O_4Si$ (M^+) 322.1596, found 322.1600. The stereochemical assignment was based on the following GOESY data determined at 250 MHz in C_6D_6 :



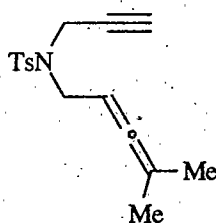
Undeca-1,2-dien-6-yne (113)



The title compound was prepared using a slight modification of the literature procedure. A suspension of paraformaldehyde (0.96 g, 32.0 mmol, 3.2 equiv), diisopropylamine (1.7 mL, 12.0 mmol, 1.2 equiv), 1,5-dodecadiyne (1.34 g, 10.0 mmol, 1.00 equiv) and CuBr·SMe₂ (0.68 g, 3.3 mmol, 0.33 equiv) in dioxane (25 mL) were heated at reflux for 2 h. The mixture was partitioned between pentane and water (30 mL each). The organic phase was washed with brine (3 x 20 mL) and dried (Na₂SO₄). Evaporation of volatiles and purification by flash chromatography (SiO₂, hexane) afforded 0.98 g (66%) of Undeca-1,2-dien-6-yne (113) as a colorless, volatile oil. Data for Undeca-1,2-dien-6-yne (113): ¹H NMR (300 MHz, CDCl₃) δ 5.15 (app dt, *J* = 13.2, 6.6 Hz, 1H), 4.67 (m, 2H), 2.18 (m, 6H), 1.42 (m, 4H), 1.95 (t, *J* = 7.3 Hz, 3H); ¹³C NMR (75.5 MHz, CDCl₃) δ 208.5, 88.9, 80.8, 79.2, 75.2, 31.2, 28.2, 21.9, 18.79, 18.41, 13.6.

3-Butyl-4,5-dihydro-1H-pentalene-2-one (114)

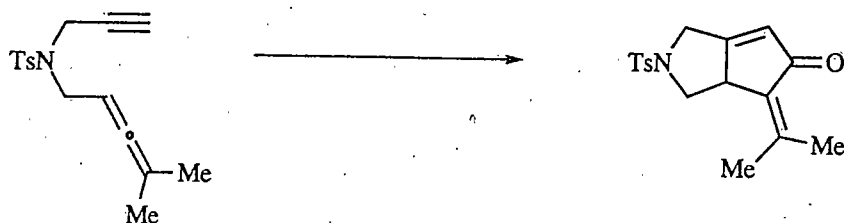
The title compound was prepared in 67% yield using Procedure C. Data for 3-butyl-4,5-dihydro-1H-pentalene-2-one (**114**) were consistent with that described in the literature.^{35a} Data for 3-butyl-4,5-dihydro-1H-pentalene-2-one (**114**): ^1H NMR (300 MHz, C_6D_6) δ 5.35 (s, 1H), 2.62 (s with fine structure, 2H), 2.33 (m, 4H), 2.19-2.16 (m, 2H), 1.53-1.40 (m, 2H), 1.32-1.19 (m, 2H), 0.87 (t, $J = 7.3$ Hz, 3H); ^{13}C NMR (75.5 MHz, C_6D_6) δ 205.6 (C), 179.3 (C), 144.5 (C), 134.2 (C), 128.3 (CH), 35.7 (CH_2), 35.5 (CH_2), 30.2 (CH_2), 24.6 (CH_2), 24.1 (CH_2), 23.0 (CH_2), 14.1 (CH_3).

***N*-(Prop-2-ynyl)-*N*-(4-methyl-penta-2,3-dienyl)-4-methylbenzenesulfonamide (124)**

To a solution of *N*-(prop-2-ynyl)-4-methylbenzenesulfonamide (**121**) (2.09 g, 9.99 mmol, 1.00 equiv), PPh_3 (3.14 g, 12.0 mmol, 1.20 equiv) and 4-methyl-penta-2,3-dien-1-ol (1.18 g, 12.0 mmol, 1.20 equiv) in THF (25 mL) at 0°C was added DIAD (2.40 mL, 12.0 mmol, 1.20 equiv) over 10 min. The resulting solution was allowed to stir for 1 h at 0°C and then was stirred an additional h at rt. Evaporation of solvent at reduced pressure

afforded a viscous oil. To the oil was added 20% ethyl acetate/hexanes (100 mL). After stirring at rt, a colorless ppt formed and was removed by filtration with the aid of 5% ethyl acetate/hexanes (30 mL). Concentration and purification by flash chromatography (SiO_2 , 2% ethyl acetate in hexanes to 7.5% ethyl acetate in hexanes gradient for elution) afforded 1.43 g (83%) of the title compound as a colorless oil that solidified at rt. Recrystallization from ethyl acetate/hexanes afforded colorless prisms. Data for *N*-(prop-2-ynyl)-*N*-(4-methyl-penta-2,3-dienyl)-4-methylbenzenesulfonamide (**124**): mp = 58-59 °C; ^1H NMR (300 MHz, CDCl_3) δ 7.71 (d, J = 8.2 Hz, 2H), 7.26 (d, J = 8.2 Hz, 2H), 4.82 (m, 1H), 4.14 (d, J = 2.4 Hz, 2H), 3.77 (d, J = 7.0 Hz, 2H), 2.40 (s, 3H), 1.97 (t, J = 2.4 Hz, 1H), 1.65 (s, 3H), 1.64 (s, 3H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 203.9 (C), 143.4 (C), 136.2 (C), 129.4 (2 x CH), 127.7 (2 x CH), 97.1 (C), 83.6 (CH), 76.6 (CH), 73.3 (C), 46.6 (CH_2), 35.5 (CH_2), 21.5 (CH_3), 20.3 (2 x CH_3); IR (NaCl, thin film) 3279 (br m), 2981 (m), 2911 (m), 2955 (m), 2119 (w), 1969 (w), 1598 (m), 1348 (m), 1162 (s); high resolution (EI) mass spectrum calculated for $\text{C}_{16}\text{H}_{19}\text{NO}_2\text{S}$ (M^+) 289.1128, found 289.1136.

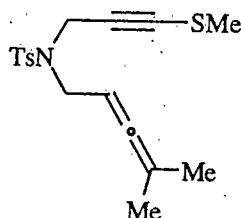
4-Isopropylidene-6-methylthio-2-[(4-methylbenzene)sulfonyl]-1,3-dihydro-1*H*-cyclopenta<c>pyrrol-5-one (146**)**



The title compound was prepared in 65% yield using Procedure C except that 10 mol % $\text{Co}_2(\text{CO})_8$ was used (10 h). Data for 4-isopropylidene-6-methylthio-2-[(4-

methylbenzene)sulfonyl]-1,3-dihydro-1*H*-cyclopenta<c>pyrrol-5-one (**146**): ^1H NMR (300 MHz, CDCl_3) δ 7.69 (d, $J = 8.1$ Hz, 2H), 6.81 (d, $J = 8.1$ Hz, 2H), 5.60 (br s, 1H), 3.98 (app t, $J = 8.9$ Hz, 1H), 3.88 (m, 1H), 3.54 (d, $J = 15.5$ Hz, 1H), 2.94 (br app t, $J = 8.9$ Hz, 1H), 2.34 (dd, $J = 11.0, 8.9$ Hz, 1H), 2.12 (s, 3H), 1.88 (s, 3H), 1.23 (s, 3H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 194.9 (C), 168.3 (C), 147.1 (C), 143.4 (C), 135.1 (C), 130.5 (C), 129.9 (2 x CH), 129.0 (CH), 127.7 (2 x CH), 51.4 (CH_2), 47.6 (CH), 47.0 (CH_2), 24.0 (CH_3), 21.1 (CH_3), 19.3 (CH_3); IR (NaCl, thin film) 2923 (w), 2860 (w), 1693 (s), 1657 (s), 1368 (s), 1162 (s), 674 (m); high resolution (EI) mass spectrum calculated for $\text{C}_{17}\text{H}_{19}\text{NO}_3\text{S}$ (M^+) 319.1238, found 319.1238.

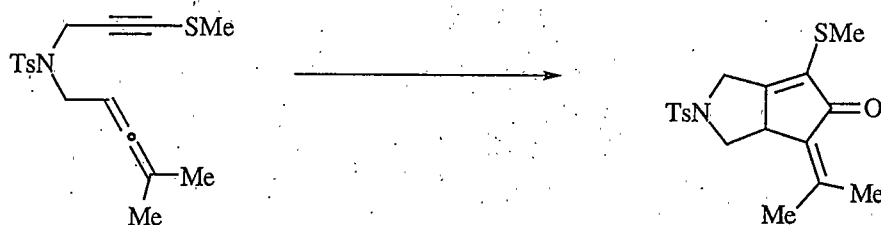
***N*-(3-Methylthio-prop-2-ynyl)-*N*-(4-methyl-penta-2,3-dienyl)-4-methylbenzenesulfonamide (**145**)**



To a solution of *N*-(prop-2-ynyl)-*N*-(4-methyl-penta-2,3-dienyl)-4-methylbenzenesulfonamide (**124**) (0.589 g, 2.04 mmol, 1.00 equiv) in THF (7 mL) at -78°C was added *n*-BuLi (1.34 mL of a 1.6 M solution in hexanes, 2.14 mmol, 1.05 equiv) dropwise. The resulting solution was stirred an additional 10 min then methyl thiocyanate (161 μL , 2.35 mmol, 1.15 equiv) was added dropwise. The resulting solution was allowed to warm to rt over 2 h and stirred an additional 2 h at rt. The reaction mixture was quenched with the addition of water (10 mL). The biphasic mixture was partitioned between ethyl acetate/water (75/25 mL). The organic phase was washed with water (50 mL), brine (75

mL) and dried (MgSO_4). Concentration and final purification by flash chromatography (SiO_2 , hexanes to 7% ethyl acetate in hexanes gradient for elution) afforded the title compound **145** as a yellow oil. A second column (SiO_2 , hexanes to 10% ethyl acetate in hexanes gradient for elution) afforded 0.38 g (58%) of the title compound **145** as a yellow oil. Data for *N*-(3-methylthio-prop-2-ynyl)-*N*-(4-methyl-penta-2,3-dienyl)-4-methylbenzenesulfonamide (**145**): ^1H NMR (300 MHz, CDCl_3) δ 7.68 (d, $J = 8.2$ Hz, 2H), 7.27 (d with fine structure, $J = 8.2$ Hz, 2H), 4.80 (m, 1H), 4.21 (s, 2H), 3.74 (d, $J = 7.0$ Hz, 2H), 2.39 (s, 3H), 2.11 (s, 3H), 1.64 (s, 3H), 1.63 (s, 3H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 203.9 (C), 143.3 (C), 136.0 (C), 129.4 (2 x CH), 127.7 (2 x CH), 96.9 (C), 85.4 (C), 83.7 (CH), 77.1 (C), 46.6 (CH_2), 36.9 (CH_2), 21.5 (CH_3), 20.2 (2 x CH_3), 18.7 (CH_3); IR (NaCl, thin film) 2980 (w), 2927 (w), 2186 (w), 1964 (w), 1348 (m), 1162 (m), 1093 (m), 894 (m), 666 (m); high resolution (EI) mass spectrum calculated for $\text{C}_{17}\text{H}_{21}\text{NO}_2\text{S}_2$ (M^+) 335.1014, found 335.1014.

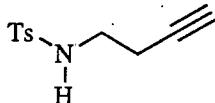
4-Isopropylidene-6-methylthio-2-[(4-methylbenzene)sulfonyl]-1,3-dihydro-1*H*-cyclopenta< c >pyrrol-5-one (147**)**



The title compound was prepared in 75% yield using Procedure B (12h). Data for 4-isopropylidene-6-methylthio-2-[(4-methylbenzene)sulfonyl]-1,3-dihydro-1*H*-cyclopenta< c >pyrrol-5-one (**147**): ^1H NMR (300 MHz, CDCl_3) δ 7.70 (d, $J = 8.1$ Hz, 2H), 7.32 (d, $J = 8.1$ Hz, 2H), 4.30 (d with fine structure, $J = 15.8$ Hz, 1H), 4.08 (app t,

$J = 8.4$ Hz, 1H), 3.98 (d, $J = 15.8$ Hz, 1H), 3.54 (br app t, $J = 9.2$ Hz, 1H), 2.49 (dd, $J = 10.8, 9.2$ Hz, 1H), 2.41 (s, 3H), 2.35 (s, 3H), 2.22 (s, 3H), 1.86 (s, 3H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 192.1 (C), 160.6 (C), 150.0 (C), 144.1 (C), 137.0 (C), 133.5 (C), 130.0 (2 x CH), 129.1 (C), 127.4 (2 x CH), 51.1 (CH), 47.0 (2 x CH), 24.7 (CH_3), 21.5 (CH_3), 19.9 (CH_3), 14.2 (CH_3); IR (NaCl, thin film) 2925 (m), 2854 (m), 1687 (s), 1651 (s), 1626 (s), 1597 (m), 1439 (br m), 1346 (s), 1162 (s), 1094 (s), 816 (m), 686 (s), 655 (s), 561 (s), 548 (s); high resolution (EI) mass spectrum calculated for $\text{C}_{18}\text{H}_{21}\text{NO}_3\text{S}_2$ (M^+) 363.0963, found 363.0963

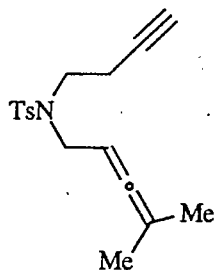
***N*-(But-3-ynyl)-4-methylbenzenesulfonamide (122)**



To a solution of *N*-*t*-butoxycarbonyl-4-methylbenzenesulfonamide (3.60 g, 13.3 mmol, 1.00 equiv), PPh_3 (4.19 g, 16.0 mmol, 1.20 equiv) and 3-butyne-1-ol (1.10 g, 16.0 mmol, 1.20 equiv) in THF (40 mL) at 0°C was added DIAD (3.30 mL, 16.6 mmol, 1.25 equiv) dropwise over 10 min. After 5 min at 0°C , the reaction solution was allowed to warm to rt and was stirred 1 h. The solvent was removed under reduced pressure and the resulting oil was purified by flash chromatography (SiO_2 , 100% hexanes to 15% ethyl acetate in hexanes gradient for elution). The purified oil was dissolved in DMSO (50 mL) and heated at reflux for 10 min. The resulting solution was partitioned between ethyl acetate/water (100/50 mL). The aqueous layer was washed with ethyl acetate (25 mL) and the combined organic phases were washed with water (2 x 50 mL), brine (3 x 50 mL) and dried (Na_2SO_4). Evaporation of solvent and purification by flash chromatography afforded the title compound as an off-white solid. Recrystallization from ethyl acetate/hexanes

afforded 1.89 g (64%, 1st crop) of *N*-(but-3-ynyl)-4-methylbenzenesulfonamide as a colorless, microcrystalline solid. A second crop was obtained by similar recrystallization. Data for the title compound were consistent with that reported in the literature.⁹⁷ Data for *N*-(but-3-ynyl)-4-methylbenzenesulfonamide (**122**): ¹H NMR (300 MHz, CDCl₃) δ 7.74 (d, *J* = 8.2 Hz, 2H), 7.29 (d, *J* = 8.2 Hz, 2H), 4.84 (br t, *J* = 6.0 Hz, 1H), 3.08 (dt, *J* = 6.6, 6.0 Hz, 2H), 2.41 (s, 3H), 2.35 (dt, *J* = 6.6, 2.6 Hz, 2H), 1.98 (t, *J* = 2.6, 1H); ¹³C NMR (75.5 MHz, CDCl₃) δ 143.6 (C), 136.9 (C), 129.8 (2 x CH), 127.1 (2 x CH), 80.3 (C), 70.9 (CH), 41.6 (CH₂), 21.5 (CH₃), 19.8 (CH₂).

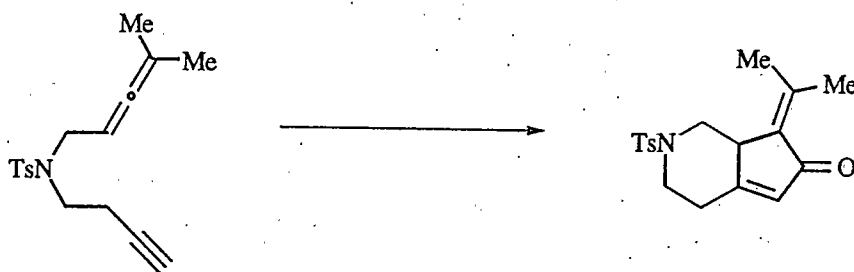
***N*-(But-3-ynyl)-*N*-(4-methyl-penta-2,3-dienyl)-4-methylbenzenesulfonamide (**125**)**



To solution of *N*-(but-3-ynyl)-4-methylbenzenesulfonamide (**122**) (1.72 g, 6.74 mmol, 1.00 equiv), PPh₃ (2.73 g, 10.4 mmol, 1.35 equiv) and 4-methyl-2,3-pentadien-1-ol (0.985 g, 10.0 mmol, 1.30 equiv) in THF (23 mL) at 0 °C was added DIAD (2.05 mL, 10.4 mmol, 1.35 equiv) over 10 min. The resulting solution was allowed to slowly warm to rt and stirred overnight (12 h). Evaporation of solvent and purification by flash chromatography (SiO₂, hexanes to 5% ethyl acetate in hexanes gradient for elution) afforded 2.05 g (91%) of *N*-(but-3-ynyl)-*N*-(4-methyl-penta-2,3-dienyl)-4-methylbenzenesulfonamide (**125**) as a colorless solid. Recrystallization from ethyl acetate/hexanes afforded colorless prisms. Data for the title compound: mp = 67-68 °C; ¹H

NMR (300 MHz, CDCl_3) δ 7.64 (d, $J = 8.2$ Hz, 2H), 7.24 (d, $J = 8.2$ Hz, 2H), 4.70 (m, 1H), 3.73 (d, $J = 7.1$ Hz, 2H), 3.28 (app t, $J = 7.6$ Hz, 2H), 2.42 (dt, $J = 7.6, 2.5$ Hz, 2H), 2.36 (s, 3H), 1.93 (t, $J = 2.5$ Hz, 1H), 1.61 (s, 3H), 1.60 (s, 3H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 203.4 (C), 143.2 (C), 136.7 (C), 129.6 (2 x CH), 126.9 (2 x CH), 96.9 (C), 84.1 (CH), 80.7 (C), 70.0 (CH), 48.2 (CH_2), 45.5 (CH_2), 21.3 (CH_3), 20.1 (2 x CH_3), 18.9 (CH_2); IR (NaCl, thin film) 3292 (m br), 2980 (m), 2912 (m), 2869 (m), 2120 (w), 1968 (w), 1598 (m), 1344 (s br); high resolution (EI) mass spectrum calculated for $\text{C}_{17}\text{H}_{21}\text{NO}_2\text{S}$ (M^+) 303.1292, found 303.1293.

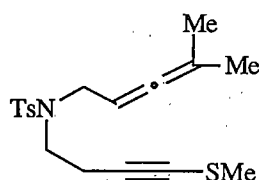
2-[(4-Methylbenzene)sulfonyl]-5-isopropylidene-1,2,3,4,4a,5-hexahydro-[2]-pyridin-6-one (148)



The title compound was prepared in 30% yield using Procedure C except that 10 mol % $\text{Co}_2(\text{CO})_8$ was used. Data for 2-[(4-methylbenzene)sulfonyl]-5-isopropylidene-1,2,3,4,4a,5-hexahydro-[2]-pyridin-6-one (148): ^1H NMR (300 MHz, CDCl_3) δ 7.62 (d, $J = 8.2$ Hz, 2H), 7.29 (d, $J = 8.2$ Hz, 2H), 5.96 (s, 1H), 4.36 (ddd, $J = 7.5, 5.6, 1.8$ Hz, 1H), 4.10 (m, 1H), 3.36 (dd, $J = 10.8, 5.6$ Hz, 1H), 2.72-2.57 (m, 2H), 2.40 (s, 3H), 2.40-2.27 (m, 2H), 2.25 (s, 3H), 1.96 (s, 3H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 195.4 (C), 168.4 (C), 148.7 (C), 143.9 (C), 134.1 (C), 130.8 (CH), 129.9 (2 x CH), 129.7 (C), 127.3 (2 x CH), 51.7 (CH_2), 46.8 (CH_2), 44.8 (CH), 29.89 (CH_2), 24.2 (CH_3), 21.5 (CH_3), 20.1 (CH_3); IR (thin film, NaCl) 2922 (m), 2850 (m), 1688 (s), 1645 (m),

1627 (s), 1361 (m), 1340 (m), 1163 (s), 1097 (m), 720 (m); high resolution (EI) mass spectrum calculated for $C_{18}H_{21}NO_3S$ (M^+) 331.1798, found 331.1804.

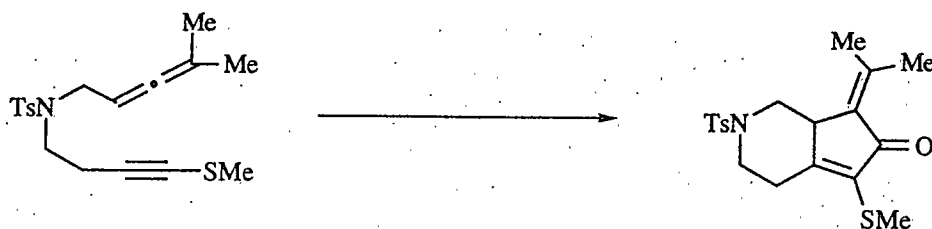
***N*-(4-Methylthio-but-3-ynyl)-*N*-(4-methyl-penta-2,3-dienyl)-4-methylbenzenesulfonamide (149)**



To a solution of *N*-(but-3-ynyl)-*N*-(4-methyl-penta-2,3-dienyl)-4-methylbenzenesulfonamide (**125**) (1.57 g, 4.69 mmol, 1.00 equiv) in THF (16 mL) at -78°C was added *n*-BuLi (3.4 mL of a 1.6 M solution in hexanes, 5.4 mmol, 1.2 equiv) dropwise. After stirring 15 min at -78°C , MeSCN (0.40 mL, 5.9 mmol, 1.3 equiv) was added dropwise. The solution was stirred 30 min at -78°C , and then placed in a 0°C bath for 15 min, at which time water (5 mL) was added. The mixture was partitioned between ethyl acetate/water (50/50 mL), washed with water (2 x 25 mL), brine (50 mL) and dried (Na_2SO_4). Evaporation of solvent and purification by flash chromatography (SiO_2 , 5 x 2 cm, 5% ethyl acetate in hexanes) afforded 2.05 g (91 %) of the title compound as an orange-yellow oil. Data for *N*-(4-methylthio-but-3-ynyl)-*N*-(4-methyl-penta-2,3-dienyl)-4-methylbenzenesulfonamide (**149**): ^1H NMR (300 MHz, CDCl_3) δ 7.64 (d, $J = 8.2$ Hz, 2H), 7.24 (d, $J = 8.2$ Hz, 2H), 4.70 (m, 1H), 3.72 (d, $J = 7.1$ Hz, 2H), 3.26 (app t with fine structure, $J = 7.6$ Hz, 2H), 2.52 (app t with fine structure, $J = 7.6$ Hz, 2H), 2.36 (s, 3H), 2.25 (s, 3H), 1.60 (s, 3H), 1.59 (s, 3H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 203.4 (C), 143.1 (C), 136.8 (C), 129.6 (2 x CH), 126.9 (2 x CH), 96.9 (C), 89.3 (C), 84.1 (CH), 72.2 (C), 48.2 (CH_2), 45.6 (CH_2), 21.3 (CH_3), 20.5 (CH_2), 20.1 (2 x CH_3), 18.9

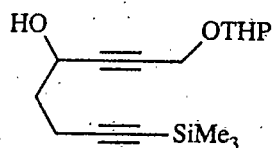
(CH₃); IR (NaCl, thin film) 2979 (w), 2927 (m), 1967 (w), 1598 (w), 1344 (m), 1160 (s); high resolution (EI) mass spectrum calculated for C₁₈H₂₃NO₂S₂ (M⁺) 349.1167, found 349.1170.

2-[(4-Methylbenzene)sulfonyl]-5-isopropylidene-7-methylthio-1,2,3,4,4a,5-hexahydro-[2]-pyridin-6-one (150)



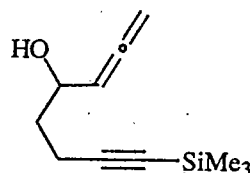
The title compound was prepared in 70% yield using Procedure C. Data for 2-[(4-methylbenzene)sulfonyl]-5-isopropylidene-7-methylthio-1,2,3,4,4a,5-hexahydro-[2]-pyridin-6-one (150): ¹H NMR (300 MHz, C₆D₆) δ 7.58 (d, *J* = 8.1 Hz, 2H), 6.78 (d, *J* = 8.1 Hz, 2H), 4.38 (ddd, *J* = 11.2, 5.5, 1.8 Hz, 1H), 3.89 (m, 1H), 2.96 (dd with fine structure, *J* = 11.2, 5.5 Hz, 1H), 2.77 (m, 1H), 2.28 (s, 3H), 2.19 (s, 3H), 2.16 (m, 1H), 1.90 (s, 3H), 1.84 (m, 1H), 1.61 (app t, *J* = 11.2 Hz, 1H), 1.48 (s, 3H); ¹³C NMR (75.5 MHz, CDCl₃) δ 191.9 (C), 165.4 (C), 149.7 (C), 143.8 (C), 135.8 (C), 133.9 (C), 129.8 (2 x CH), 128.2 (C), 127.2 (2 x CH), 51.5 (CH₂), 46.4 (CH₂), 43.9 (CH), 28.3 (CH₂), 24.1 (CH₃), 21.4 (CH₃), 20.2 (CH₃), 15.0 (CH₃); IR (NaCl, thin film) 2925 (w), 1685 (m), 1643 (m), 1607 (m), 1336 (m), 1165 (s), 1098 (m), 749 (m), 651 (m); high resolution (EI) mass spectrum calculated for C₁₉H₂₃NO₃S₂ (M⁺) 377.1123, found 377.1119.

1-Tetrahydropyranyl-8-(trimethylsilyl)-octa-2,7-diyne-4-ol

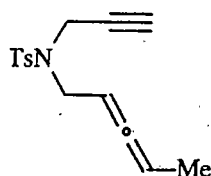


To a solution of 1-tetrahydropyranyl-2-propynyl ether (2.05 g, 14.6 mmol, 1.00 equiv) in THF (20 mL) at -78°C was added *n*-BuLi (8.2 mL of a 1.6M solution in hexanes, 13.2 mmol, 0.90 equiv) dropwise. The solution was allowed to stir an additional 5 min at -78°C and then was added dropwise to 5-(trimethylsilyl)pent-4-yn-1-al (2.26 g, 14.6 mmol, 1.00 equiv) in THF (10 mL) at -78°C . The resulting solution was allowed to warm to 0°C over 2 h at which time saturated NH_4Cl (10 mL) was added dropwise. The resulting mixture was partitioned between ethyl acetate and saturated NH_4Cl (50/50 mL). The organic layer was washed with water (2 x 75 mL), brine (75 mL) and dried (Na_2SO_4). Evaporation of solvent and purification by flash chromatography (SiO_2 , hexanes to 10% ethyl acetate in hexanes gradient for elution) afforded 3.43 g (88%) of the title compound as a viscous, pale yellow oil as a mixture of anomers. For analytical measurements, a pure sample of the major anomer was collected. Data for 1-tetrahydropyranyl-8-(trimethylsilyl)-octa-2,7-diyne-4-ol: ^1H NMR (300 MHz, CDCl_3) δ 4.77 (t, $J = 3.0$ Hz, 1H), 4.54 (s with fine structure, 1H), 4.27 (app dt, $J = 15.6, 10.5$ Hz, 2H), 3.78 (m, 1H), 3.51 (m, 1H), 2.49-2.30 (m, 2H), 2.22 (br s, 1H), 1.89 (app q, $J = 6.8$ Hz, 2H), 1.84-1.45 (CH_2 envelope, 6H), 0.12 (s, 9H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 106.0 (C), 96.9 (CH), 86.2 (C), 85.6 (C), 81.3 (C), 62.0 (CH_2), 61.4 (CH), 54.2 (CH_2), 36.2 (CH_2), 30.2 (CH_2), 25.3 (CH_2), 19.0 (CH_2), 15.9 (CH_2), 0.1 (3 x CH_3); IR (NaCl, thin film) 3420 (m br), 2955 (s br), 2871 (m), 2174 (m), 1250 (m), 1024 (s); high resolution (EI) mass spectrum calculated for $\text{C}_{16}\text{H}_{26}\text{O}_3\text{Si}$ ($\text{M} + \text{H}$) $^+$ 295.1729, found 295.1732.

8-Trimethylsilyl-octa-1,2-dien-7-yn-4-ol



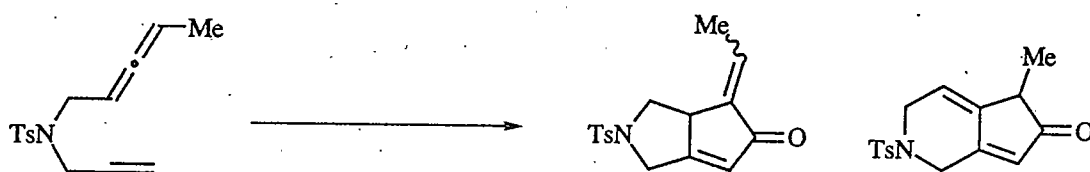
To a suspension of LiAlH_4 (0.464 g, 12.2 mmol, 1.05 equiv) in diethyl ether (25 mL) at rt was added a solution of 1-tetrahydropyranyl-8-(trimethylsilyl)-octa-2,7-diyne-4-ol (3.43 g, 11.6 mmol, 1.00 equiv) in diethyl ether (10 mL) over 1 h. The resulting suspension was heated at reflux for 2 h, allowed to cool to rt, and then quenched by the addition of water (2.5 mL). The resulting suspension was filtered through celite with the aid of ethyl acetate (7 x 25 mL), the solvent was evaporated and the residue was purified by flash chromatography (SiO_2 , 5 x 6 cm, 5% ethyl acetate in hexanes to 10% ethyl acetate in hexanes gradient for elution) affording 1.99 g (88%) of 8-trimethylsilyl-octa-1,2-dien-7-yn-4-ol as a colorless oil. Data for 8-trimethylsilyl-octa-1,2-dien-7-yn-4-ol: ^1H NMR (300 MHz, CDCl_3) δ 5.16 (app dd with fine structure, $J = 12.8, 6.5$ Hz, 1H), 4.83-4.77, (m, 2H), 4.29-4.18 (br m, 1H), 2.30 (br t, $J = 7.2$ Hz, 2H), 2.30 (br s, 1H), 1.72 (dt, $J = 13.4, 6.7$ Hz, 2H), 0.080 (s, 9H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 207.0 (C), 106.6 (C), 94.1 (CH), 85.1 (C), 77.5 (CH_2), 68.4 (CH), 35.8 (CH_2), 16.1 (CH_2), 0.0 (3 x CH_3); IR (NaCl, thin film) 3400 (m vbr), 3309 (m br), 2959 (m), 2175 (m), 1250 (m), 1061 (m), 843 (s); high resolution (EI) mass spectrum calculated for $\text{C}_{11}\text{H}_{17}\text{OSi}$ ($\text{M} - \text{H}$) $^+$ 193.1049, found 194.1049.

***N*-(Prop-2-ynyl)-*N*-(penta-2,3-dienyl)-4-methylbenzenesulfonamide (126)**

To a solution of *N*-prop-2-ynyl-4-methylbenzenesulfonamide (**121**) (1.75 g, 8.36 mmol, 1.00 equiv), PPh_3 (2.62 g, 10.0 mmol, 1.20 equiv) and 2,3-pentadien-1-ol (0.84 mmol, 10.0 mmol, 1.2 equiv) in THF (20 mL) at 0 °C was added DIAD (1.97 mL, 10.0 mmol, 1.20 equiv) dropwise. The resulting solution was allowed to stir 1 h at 0 °C then 2 drops of water were added. The solvent was removed under reduced pressure and the residue was treated with diethyl ether (30 mL). The resulting suspension was treated with hexanes (30 mL) and filtered with the aid of 10% ethyl acetate in hexanes (100 mL). Evaporation of solvent and purification by flash chromatography (SiO_2 , 5 x 10 cm, 2% ethyl acetate in hexanes to 10% ethyl acetate in hexanes gradient for elution) afforded 2.1 g (91%) of *N*-(prop-2-ynyl)-*N*-(penta-2,3-dienyl)-4-methylbenzenesulfonamide as a pale yellow, viscous oil. After prolonged storage at 0 °C, the title compound formed a colorless semi-solid. Data for *N*-(prop-2-ynyl)-*N*-(penta-2,3-dienyl)-4-methylbenzenesulfonamide (**126**): ^1H NMR (300 MHz, CDCl_3) δ 7.68 (d, J = 8.4 Hz, 2H), 7.24 (d, J = 8.4 Hz, 2H), 5.10 (m, 1H), 4.90 (m, 1H), 4.14 (dd, J = 18.4, 2.3 Hz, 1H), 4.06 (dd, J = 18.3, 2.3 Hz, 1H), 3.82 (ddd, J = 14.1, 6.9, 2.2 Hz, 1H), 3.74 (ddd, J = 14.1, 6.9, 2.2 Hz, 1H), 2.36 (s, 3H), 1.98 (app t with fine structure, J = 2.3 Hz, 1H), 1.58 (dd, J = 7.1, 3.1 Hz, 3H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 206.4 (C), 143.4 (C), 135.9 (C), 129.4 (2 x CH), 127.5 (2 x CH), 87.3 (CH), 85.1 (CH), 76.3 (CH), 73.4 (C), 46.0 (CH_2), 35.5 (CH_2), 21.4 (CH_3), 13.8 (CH_3); IR (thin film, NaCl) 3288 (m br), 2925 (m), 2858 (m), 2120 (w), 1967 (m),

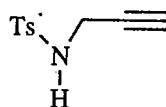
1348 (s), 1162 (s); high resolution (EI) mass spectrum calculated for $C_{15}H_{17}NO_2S$ (M^+) 275.0980, found 275.0989.

4-Ethylidene-2-[(4-methylbenzene)sulfonyl]-2,3,3a,4-tetrahydro-1H-cyclopenta[c]pyrrol-5-one and 2-[(4-methylbenzene)sulfonyl]-5-methyl-1,2,3,5-tetrahydro-[2]-pyridin-6-one



The title compound was prepared as a mixture of 3 isomers in 66% yield using Procedure C except that 10 mol % $Co_2(CO)_8$ was used. Data for 4-Ethylidene-2-[(4-methylbenzene)sulfonyl]-2,3,3a,4-tetrahydro-1H-cyclopenta[c]pyrrol-5-one and 2-[(4-methylbenzene)sulfonyl]-5-methyl-1,2,3,5-tetrahydro-[2]-pyridin-6-one: High resolution (EI) mass spectrum calculated for $C_{16}H_{17}NO_3S$ (M^+) 321.0856, found 321.0857.

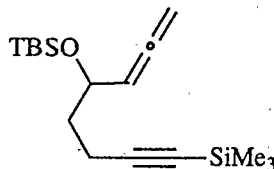
N-(Prop-2-ynyl)-4-methylbenzenesulfonamide (121)



To a suspension of *N*-*t*-butoxycarbonyl-4-methylbenzenesulfonamide (5.69 g, 21.0 mmol, 1.00 equiv) and K_2CO_3 (4.25 g, 31.5 mmol, 1.50 equiv) in DMF (25 mL) at rt was added propargyl bromide (2.40 mL, 32.0 mmol, 2.00 equiv). The resulting suspension was allowed to stir 15 h at rt and then was partitioned between ethyl acetate and water (200/150

mL). The organic phase was washed with brine (2 x 150 mL) and dried (Na_2SO_4). Evaporation of solvent afforded a viscous oil that was dissolved in DMSO (65 mL). The solution was heated at reflux for 10 min and allowed to cool to rt. Workup in the usual way afforded a yellow solid which was recrystallized with ethyl acetate/hexanes. First crop afforded 1.84 g (42%) of *N*-(prop-2-ynyl)-4-methylbenzenesulfonamide (**121**). Second crop afforded 1.73 g (39%) of *N*-(prop-2-ynyl)-4-methylbenzenesulfonamide (**121**). Spectral data of the title compound were consistent with that reported in the literature.⁹⁸

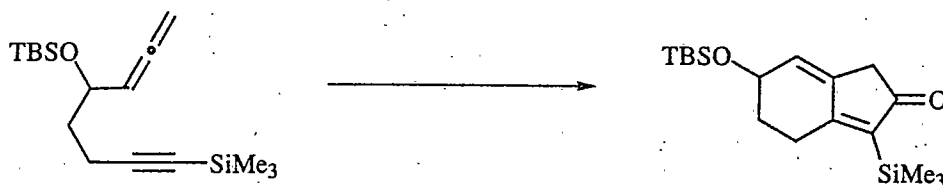
4-[[[(1,1-Dimethylethyl)dimethylsilyl]oxy]-8-trimethylsilyl-octa-1,2-dien-7-yn-4-ol (157**)**



To a solution of 8-trimethylsilyl-octa-1,2-dien-7-yn-4-ol (1.52 g, 7.82 mmol, 1.00 equiv) and imidazole (1.06 g, 15.6 mmol, 2.00 equiv) in DMF (4 mL) was added TBSCl (1.30 g, 8.60 mmol, 1.20 equiv) at rt in one portion. The resulting mixture was allowed to stir 1 h at rt and then was poured into hexane/water (100/50 mL). The organic layer was washed with water (50 mL), brine (3 x 50 mL) and dried (MgSO_4). Evaporation of solvent and purification by flash chromatography (SiO_2 , 5% ethyl acetate in hexanes) afforded 1.71 g (93%) of 4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-8-trimethylsilyl-octa-1,2-dien-7-yn-4-ol (**157**) as a colorless oil. Data for 4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-8-trimethylsilyl-octa-1,2-dien-7-yn-4-ol (**157**): ^1H NMR (300 MHz, C_6D_6) δ 5.01 (dt, $J = 7.2, 6.8$ Hz, 1H), 4.63-4.49 (m, 2H), 4.32 (m, 1H), 2.31-2.10 (m, 2H), 1.75-1.60 (m, 2H), 0.91 (s, 9H), 0.18 (s, 9H), 0.094 (s, 3H), 0.085 (s, 3H); ^{13}C NMR (75.5 MHz,

C_6D_6) δ 207.8 (C), 107.3 (C), 94.8 (CH), 85.0 (C), 76.2 (CH₂), 70.2 (CH), 37.5 (CH₂), 26.1 (3 x CH₃), 18.3 (C), 16.4 (CH₂), 0.33 (3 x CH₃), -4.1 (CH₃), -4.8 (CH₃); IR (thin film, NaCl) 2957 (m), 2933 (m), 2860 (m), 2176 (m), 1958 (m), 1250 (m), 1089 (m), 838 (s), 776 (m); high resolution (EI) mass spectrum calculated for $C_{17}H_{32}OSi_2$ (M^+) 308.1992, found 308.1995.

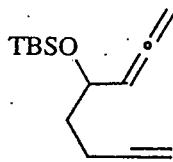
4-[[[(1,1-Dimethylethyl)dimethylsilyl]oxy]-7-trimethylsilyl-1,4,5,6-tetrahydro-inden-2-one (158)



To a solution of $[(CO)_2RhCl]_2$ (1.0 mg, 2 mol %) in toluene (2.5 mL) under CO (1 atm) was added 4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-8-trimethylsilanyl-octa-1,2-dien-7-yn-4-ol (**160**) (77 mg, 0.25 mmol, 1.00 equiv). After stirring 5 min at rt, the solution was heated to 60 °C for 5 h. Evaporation of solvent and purification by flash chromatography (basic Al_2O_3 , 5% ethyl acetate in hexanes) afforded 50 mg (60%) of the title compound as a pale yellow oil. Data for 4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-7-trimethylsilyl-1,4,5,6-tetrahydro-inden-2-one (**158**): 1H NMR (300 MHz, $CDCl_3$) δ 5.57 (s with fine structure, 1H), 4.12 (m, 1H), 2.68 (m, 1H), 2.61 (s with fine structure, 2H), 2.16 (ddd, J = 15.3 Hz, 10.4, 4.8 Hz, 1H), 1.72-1.51 (m, 2H), 0.98 (s, 9H), 0.33 (s, 9H), 0.07 (s, 6H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 207.3 (C), 174.3 (C), 140.3 (C), 138.8 (C), 128.0 (CH), 66.9 (CH), 39.2 (CH₂), 32.6 (CH₂), 25.8 (3 x CH₃), 24.4 (CH₂), 18.3 (C), -0.4 (3 x CH₃), -4.5 (2 x CH₃); IR (NaCl, thin film) 2954 (m), 2896

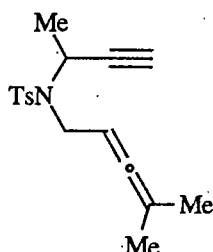
(m), 2856 (m), 1693 (m), 1557 (m), 1249 (m), 1069 (m), 836 (s); high resolution (EI) mass spectrum calculated for $C_{18}H_{32}O_2Si_2$ (M^+) 336.1941, found 336.1947.

4-[[[(1,1-Dimethylethyl)dimethylsilyl]oxy]-octa-1,2-dien-7-yn-4-ol



To a solution of 4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-8-trimethylsilanyl-octa-1,2-dien-7-yn-4-ol (**160**) (77 mg, 0.25 mmol, 1.00 equiv) in MeOH (1 mL) at rt was added K_2CO_3 (36 mg, 0.26 mmol, 1.05 equiv) in one portion. After 1.5 h, the reaction was partitioned between diethyl ether and water (10/5 mL). The organic phase was washed with water (5 mL), brine (5 mL) and dried ($MgSO_4$). Evaporation of solvent and purification by flash chromatography (SiO_2 , 5% ethyl acetate in hexanes) afforded 56 mg (95%) of 4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-octa-1,2-dien-7-yn-4-ol as a light yellow liquid. Data for 4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-octa-1,2-dien-7-yn-4-ol: 1H NMR (300 MHz, $CDCl_3$) δ 5.08 (app dt, $J = 13.7, 6.8$ Hz, 1H), 4.80-4.69 (m, 2H), 4.27 (m, 1H), 2.24 (dt, $J = 7.1, 2.6$ Hz, 2H), 1.92 (t, $J = 2.6$ Hz, 1H), 1.80-1.65 (m, 2H), 0.87 (s, 9H), 0.062 (s, 3H), 0.051 (s, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 207.4 (C), 94.3 (CH), 84.2 (C), 76.3 (CH_2), 69.8 (CH), 68.4 (C), 37.1 (CH_2), 29.7 (C), 25.8 (3 x CH_3), 18.1 (C), 14.6 (CH_2), -4.3 (CH_3), -5.0 (CH_3); IR (thin film, NaCl) 3312 (m), 2956 (m), 2929 (m), 2857 (m), 2120 (w), 1956 (m), 1252 (m), 1089 (m), 838 (m), 776 (m); high resolution (EI) mass spectrum calculated for $C_{11}H_{21}OSi$ ($M - C_3H_3$) $^+$ 197.1362, found 197.1372.

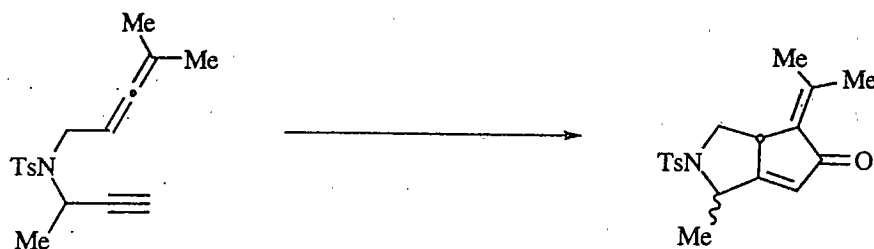
***N*-(1-Methyl-prop-2-ynyl)-*N*-(4-methyl-penta-2,3-dienyl)-4-methylbenzenesulfonamide (127)**



To a solution of *N*-(2-methyl-prop-2-ynyl)-4-methylbenzenesulfonamide²³ (1.45 g, 6.50 mmol, 1.00 equiv), PPh₃ (2.20 g, 8.45 mmol, 1.30 equiv) and 4-methyl-2,3-pentadien-1-ol (0.831 g, 8.45 mmol, 1.30 equiv) in THF (20 mL) at 0 °C was added DIAD (1.7 mL, 8.5 mmol, 1.3 equiv) dropwise over 10 min. After 30 min at 0 °C, the reaction solution was allowed to warm to rt and was stirred 1.5 h. The solvent was removed under reduced pressure and the resulting oil was purified by flash chromatography (SiO₂, 100% hexanes to 5% ethyl acetate in hexanes gradient for elution). Evaporation of solvent and purification by flash chromatography afforded 1.83 g (93%) of *N*-(2-methyl-prop-2-ynyl)-*N*-(4-methyl-penta-2,3-dienyl)-4-methylbenzenesulfonamide (127) as a colorless solid. Recrystallization from ethyl acetate/hexanes afforded colorless prisms. Data for *N*-(2-methyl-*N*-prop-2-ynyl)-*N*-(4-methyl-penta-2,3-dienyl)-4-methyl-benzenesulfonamide (127): mp = 68-69 °C; ¹H NMR (300 MHz, CDCl₃) δ 7.70 (d, *J* = 8.0 Hz, 2H), 7.25 (d, *J* = 8.0 Hz, 2H), 5.05 (m, 1H), 4.86 (dq, *J* = 7.1, 2.4 Hz, 1H), 3.89 (dd, *J* = 15.7, 5.4 Hz, 1H), 3.66 (dd, *J* = 15.7, 7.8 Hz, 1H), 2.38 (s, 3H), 2.10 (d, *J* = 2.4 Hz, 1H), 1.656 (s, 3H), 1.647 (s, 3H), 1.46 (d, *J* = 7.1 Hz, 3H); ¹³C NMR (75.5 MHz, CDCl₃) δ 202.1 (C), 143.2 (C), 136.6 (C), 129.4 (2 x CH), 127.5 (2 x CH), 97.0 (C), 87.8 (CH), 81.5 (CH), 73.0 (C), 45.9 (CH), 44.8 (CH₂), 22.8 (CH₃), 21.5 (CH₃), 20.2 (CH₃), 19.8 (CH₃); IR (thin film, NaCl) 3276 (br s), 2983 (m), 2936 (m), 2869 (m), 2112 (w), 1970

(w), 1598 (m), 1450 (m), 1343 (s), 1166 (s), 1153 (s), 1108 (m), 991 (m), 660 (s); high resolution (EI) mass spectrum calculated for $C_{17}H_{21}NO_2S$ (M^+) 303.1295, found 303.1293.

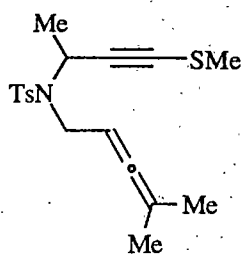
2-[(4-Methylbenzene)sulfonyl]-1-methyl-4-isopropylidene-2,3,3a,4-tetrahydro-1*H*-cyclopenta[*c*]pyrrol-5-one (152)



The title compound was prepared as a mixture of isomers (2.6/1) in 73% yield using Procedure C except that 10 mol % $Co_2(CO)_8$ was used (15 h). Purification by flash chromatography (SiO_2 , 30% ethyl acetate in hexanes to 50% ethyl acetate in hexanes gradient for elution) afforded 61 mg (73%) of 2-[(4-methylbenzene)sulfonyl]-1-methyl-4-isopropylidene-2,3,3a,4-tetrahydro-1*H*-cyclopenta[*c*]pyrrol-5-one (**152**) as a colorless solid. Data for the title compound: 1H NMR (300 MHz, $CDCl_3$) δ 7.78 (d, $J = 8.2$ Hz, 2H), 7.65 (d, $J = 8.4$, 2H), 7.34-7.28 (m, 4H), 6.05 (s with fine structure, 1H), 5.88 (s, 1H), 4.52 (q, $J = 6.6$ Hz, 1H), 4.20 (q, $J = 6.6$ Hz, 1H), 4.14-4.01 (m, 2H), 3.84 (br app t, $J = 9.5$ Hz, 1H), 2.99 (br app t, $J = 9.8$ Hz, 1H), 2.87 (app t, $J = 11.2$ Hz, 1H), 2.42 (s, 3H), 2.40 (s, 3H), 2.21 (s, 3H), 2.20 (s, 3H), 1.87 (s, 3H), 1.78 (s, 3H), 1.58 (d, $J = 6.6$ Hz, 3H), 1.52 (d, $J = 6.6$ Hz, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 175.9, 172.7, 149.21, 148.8, 144.1, 135.8, 130.0, 129.9, 128.5, 127.6, 127.2, 127.1, 55.0, 54.9, 52.0, 50.7, 47.3, 45.2, 29.6, 24.8, 22.5, 20.2, 19.73, 19.67; IR (NaCl, thin film) 2926 (m), 1692 (s), 1344 (s), 1160 (s), 1002 (s); major diastereomer: High resolution (EI)

mass spectrum calculated for $C_{17}H_{21}NO_3S_2$ (M^+) 331.1242, found 331.1242. minor diastereomer: High resolution (EI) mass spectrum calculated for $C_{17}H_{21}NO_3S_2$ (M^+) 331.1227, found 331.1242.

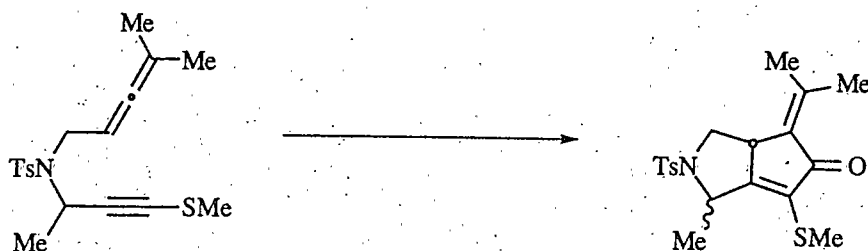
***N*-(1-Methyl-3-methylthio-prop-2-ynyl)-*N*-(4-methyl-penta-2,3-dienyl)-4-methylbenzenesulfonamide (153)**



To a solution *N*-(1-methyl-prop-2-ynyl)-*N*-(4-methyl-penta-2,3-dienyl)-4-methylbenzenesulfonamide (**127**) (0.404 g, 1.31 mmol, 1.00 equiv) in THF (4 mL) at -78°C was added *n*-BuLi (0.90 mL of a 1.6 M solution in hexanes, 1.4 mmol, 1.1 equiv) dropwise. After 15 min, MeSCN (112 μL , 1.64 mmol, 1.25 equiv) was added dropwise and the resulting solution was allowed to warm to rt over a few hours and then was stirred at rt (3 h). The reaction was quenched by the addition of water (2 mL) at rt and then was partitioned between ethyl acetate and water (15/10 mL). The organic layer was washed with water (10 mL), brine (2 x 10 mL) and dried (MgSO_4). Evaporation of solvent and purification by flash chromatography (SiO_2 , hexanes to 5% ethyl acetate in hexanes gradient for elution) afforded 0.295 g (46%) *N*-(1-methyl-3-thiomethyl-prop-2-ynyl)-*N*-(4-methyl-penta-2,3-dienyl)-4-methylbenzenesulfonamide (**153**) as a slightly yellow oil. Data for the title compound: ^1H NMR (300 MHz, CDCl_3) δ 7.64 (d, $J = 8.2$ Hz, 2H), 7.21 (d, $J = 8.2$ Hz, 2H), 5.00 (m, 1H); 4.86 (q, $J = 7.1$ Hz, 1H), 3.81 (dd, $J = 15.6, 5.5$, 1H), 3.58 (dd, $J = 15.6, 7.7$ Hz, 1H), 2.33 (s, 3H), 2.05 (s, 3H), 2.04 (s, 3H), 1.61 (s, 3H), 1.60 (s, 3H);

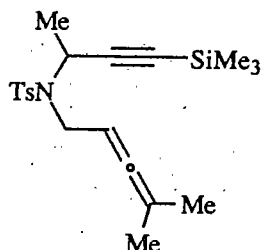
^{13}C NMR (75.5 MHz, CDCl_3) δ 201.8 (C), 143.0 (C), 136.2 (C), 129.2 (2 x CH), 127.3 (2 x CH), 96.7 (C), 89.8 (C), 87.7 (C), 76.4 (C), 46.9 (CH), 44.7 (CH_2), 22.2 (CH_3), 21.2 (CH_3), 20.0 (CH_3), 19.6 (CH_3), 18.5 (CH_3); IR (NaCl, thin film) 2981 (m), 2932 (m), 2867 (m), 2172 (w), 1968 (w), 1918 (w), 1598 (m), 1494 (m), 1448 (m), 1344 (br s), 1166 (s), 1103 (s), 1001 (m), 978 (m), 878 (s), 814 (s), 666 (s); high resolution (EI) mass spectrum calculated for $\text{C}_{18}\text{H}_{23}\text{NO}_2\text{S}_2$ (M^+) 349.1176, found 349.1170.

2-[(4-Methylbenzene)sulfonyl]-1-methyl-4-isopropylidene-7-methylthio-2,3,3a,4-tetrahydro-1*H*-cyclopenta[*c*]pyrol-5-one (154)



The title compound was prepared as a 1.3/1 mixture of isomers in 87% yield using Procedure C. Purification by flash chromatography (SiO_2 , 15% ethyl acetate in hexanes to 50% ethyl acetate in hexanes gradient for elution) afforded 83 mg of 2-[(4-methylbenzene)sulfonyl]-1-methyl-4-isopropylidene-7-methylthio-2,3,3a,4-tetrahydro-1*H*-cyclopenta[*c*]pyrol-5-one (**154**) as a colorless solid. Data for 2-[(4-methylbenzene)sulfonyl]-1-methyl-4-isopropylidene-7-methylthio-2,3,3a,4-tetrahydro-1*H*-cyclopenta[*c*]pyrol-5-one (**154**): IR (NaCl, thin film) 2923 (m), 1683 (s), 1619 (s), 1346 (s), 1250 (m), 1162 (s), 1002 (s); high resolution (EI) mass spectrum calculated for $\text{C}_{19}\text{H}_{23}\text{NO}_3\text{S}_2$ (M^+) 377.1119, found 377.1118.

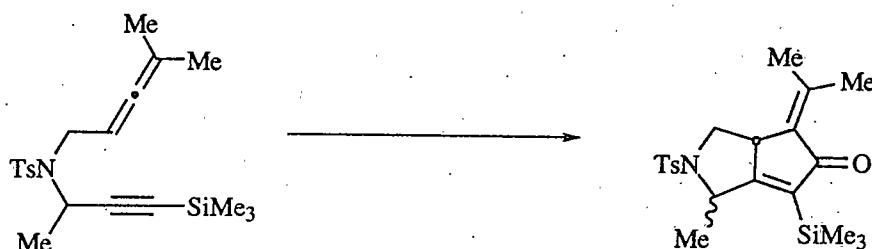
***N*-(1-Methyl-3-trimethylsilyl-prop-2-ynyl)-*N*-(4-methyl-penta-2,3-dienyl)-4-methylbenzenesulfonamide (155)**



To a solution *N*-(1-methyl-prop-2-ynyl)-*N*-(4-methyl-penta-2,3-dienyl)-4-methylbenzenesulfonamide (**127**) (0.322 g, 1.05 mmol, 1.00 equiv) in THF (5 mL) at -78 °C was added *n*-BuLi (0.69 mL of a 1.6 M solution in hexanes, 1.10 mmol, 1.05 equiv) dropwise. After 10 min, Me₃SiCl (156 µL, 6.20 mmol, 1.30 equiv) was added dropwise and the resulting solution was allowed to warm to rt over 2 h and then was stirred at rt (3 h). The reaction suspension was quenched at rt by the addition of saturated NH₄Cl (1 mL) and then was partitioned between ethyl acetate (25 mL) and half-saturated NH₄Cl (20 mL). The organic layer was washed with water (20 mL), brine (2 x 20 mL) and dried (MgSO₄). Evaporation of solvent and purification by flash chromatography (SiO₂, hexanes to 10% ethyl acetate in hexanes gradient for elution) afforded 0.358 g (90%) of *N*-(1-methyl-3-trimethylsilyl-prop-2-ynyl)-*N*-(4-methyl-penta-2,3-dienyl)-4-methylbenzenesulfonamide (**155**) as a viscous, colorless oil. Recrystallization with ethyl acetate/hexanes afforded colorless prisms. Data *N*-(1-methyl-3-trimethylsilyl-prop-2-ynyl)-*N*-(4-methyl-penta-2,3-dienyl)-4-methylbenzenesulfonamide (**155**): mp = 51-53 °C; ¹H NMR (300 MHz, CDCl₃) δ 7.71 (d, *J* = 8.2 Hz, 2H), 7.24 (d with fine structure, *J* = 8.2 Hz, 2H), 5.04 (m, 1H), 4.84 (q, *J* = 7.1 Hz, 1H), 3.86 (dd, *J* = 15.6, 5.4 Hz, 1H), 3.64 (dd, *J* = 15.6, 7.8 Hz, 1H), 2.39 (s, 3H), 1.671 (s, 3H), 1.661 (s, 3H), 1.44 (d, *J* = 7.1 Hz, 3H), -0.03 (s, 9H); ¹³C NMR (75.5 MHz, CDCl₃) δ 202.0 (C), 143.0 (C), 136.4 (C), 129.3 (2 x CH), 127.5 (2 x CH),

103.0 (C), 96.8 (CH), 89.4 (C), 87.9 (CH), 46.6 (CH), 44.8 (CH₂), 22.5 (CH₃), 21.4 (CH₃), 20.2 (CH₃), 19.7 (CH₃), -0.4 (3 x CH₃); IR (thin film, NaCl) 2982 (m), 2959 (m), 2937 (m), 2870 (m), 2169 (w), 1970 (w), 1599 (m), 1345 (s), 1167 (s), 845 (s), 665 (s); high resolution (EI) mass spectrum calculated for C₂₀H₂₉NO₂SSi (M⁺) 375.1865, found 375.1668.

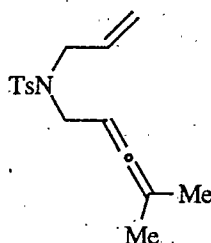
2-[(4-Methylbenzene)sulfonyl]-1-methyl-4-isopropylidene-7-trimethylsilyl-2,3,3a,4-tetrahydro-1*H*-cyclopenta[*c*]pyrol-5-one (156)



The title compound was prepared as a 1.1/1 mixture of isomers in 59% yield using Procedure C. Data for the title compound **156**: ¹H NMR (300 MHz, CDCl₃) δ 7.77 (d, *J* = 8.1 Hz, 2H), 7.65 (d, *J* = 8.1 Hz, 2H), 7.35-7.31 (m, 2H), 7.29 (d, *J* = 8.1 Hz, 2H), 4.76 (q, *J* = 6.7 Hz, 1H), 4.27 (q, *J* = 6.5 Hz, 1H), 4.09 (dd, *J* = 10.7, 7.1 Hz, 1H), 4.02 (app t, *J* = 8.2 Hz, 1H), 3.80 (br app t, *J* = 9.5 Hz, 1H), 3.03-2.85 (m, 2H), 2.42 (s, 3H), 2.39 (s, 3H), 2.34 (dd, *J* = 10.7, 8.4 Hz, 1H), 2.20 (br s, 6H), 1.86 (s, 3H), 1.77 (s, 3H), 1.56 (d, *J* = 6.5 Hz, 3H), 1.48 (d, *J* = 6.7 Hz, 3H), 0.22 (s, 9H), 0.07 (s, 9H); ¹³C NMR (300 MHz, CDCl₃) δ 199.9 (C), 185.9 (C), 179.1 (C), 147.9 (C), 146.8 (C), 143.9 (C), 143.8 (C), 141.2 (C), 139.0 (C), 136.5 (C), 132.9 (C), 130.6 (C), 130.5 (C), 130.0 (2 x CH), 129.7 (2 x CH), 127.5 (2 x CH), 127.0 (C), 126.9 (2 x CH), 56.0 (CH), 55.2 (CH), 51.61 (CH₂), 51.20 (CH₂), 48.9 (CH), 46.2 (CH), 25.0 (CH₃), 24.8 (CH₃), 22.8 (CH₃), 22.7 (CH₃), 21.5 (CH₃), 21.4 (CH₃), 19.7 (CH₃), 19.5 (CH₃), -0.6

(3 x CH₃), -1.3 (3 x CH₃); high resolution (EI) mass spectrum calculated for C₂₁H₂₉NO₃SSi (M⁺) 403.1642, found 403.1637.

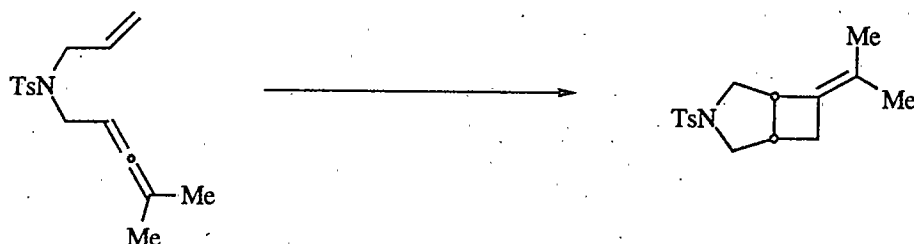
***N*-(2-Propenyl)-*N*-(4-methyl-penta-2,3-dienyl)-4-methylbenzenesulfonamide (137)**



To a solution of *N*-(2-propenyl)-4-methylbenzenesulfonamide (0.528 g, 2.50 mmol, 1.00 equiv), PPh₃ (0.852 g, 3.25 mmol, 1.30 equiv) and 4-methyl-2,3-pentadien-1-ol (0.319 g, 3.25 mmol, 1.30 equiv) in THF (6 mL) at 0 °C was added DIAD (0.64 mL, 3.2 mmol, 1.3 equiv) dropwise over 10 min. After 5 min at 0 °C, the solution was allowed to warm to rt and was stirred an additional 1 h. The solvent was removed under reduced pressure and the resulting oil was purified by flash chromatography (SiO₂, 100% hexanes to 5% ethyl acetate in hexanes gradient for elution) affording 0.556 g (76%) of *N*-(2-propenyl)-*N*-(4-methyl-penta-2,3-dienyl)-4-methylbenzenesulfonamide (**137**) as colorless oil. Data for *N*-(2-propenyl)-*N*-(4-methyl-penta-2,3-dienyl)-4-methylbenzenesulfonamide (**137**): ¹H NMR (300 MHz, CDCl₃) δ 7.67 (d, *J* = 8.2 Hz, 2H), 7.26 (d, *J* = 8.2 Hz, 2H), (ddt, *J* = 16.4, 10.1, 6.5 Hz, 1H), 5.16-5.08 (m, 2H), 4.68 (m, 1H), 3.82 (d, *J* = 6.5 Hz, 2H), 3.74 (d, *J* = 6.5 Hz, 2H), 2.38 (s, 3H), 1.61 (s, 3H), 1.60 (s, 3H); ¹³C NMR (75.5 MHz, CDCl₃) δ 203.3 (C), 143.0 (C), 137.6 (C), 132.7 (CH), 129.6 (2 x CH), 127.1 (2 x CH), 118.7 (CH₂), 96.6 (C), 84.1 (CH), 48.8 (CH₂), 46.5 (CH₂), 21.4 (CH₃), 20.2 (2 x CH₃); IR (thin film, NaCl) 2981 (m), 2936 (m), 2911 (m), 2855 (m), 1968 (w), 1598 (m), 1340

(s), 1160 (s); high resolution (EI) mass spectrum calculated for $C_{16}H_{21}NO_2S$ (M^+) 291.1293, found 291.1286.

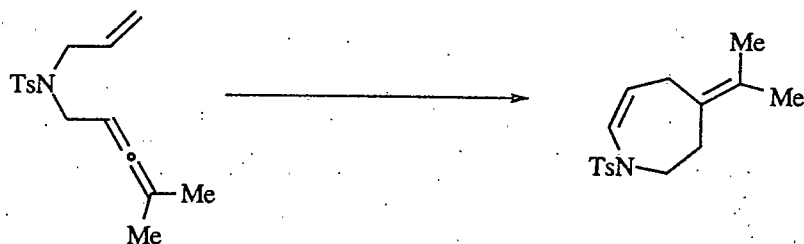
***cis*-6-Isopropylidene-3-*N*-[(4-methylbenzene)sulfonyl]-azabicyclo[3.2.0]heptane (166)**



To a solution of $[(CO)_2RhCl]_2$ (1 mg, 0.0025 mmol, 1 mol %) and $P(OPh)_3$ (2.6 μ L, 0.01 mmol, 4 mol %) in toluene (2.5 mL) was added *N*-(2-propenyl)-*N*-(4-methyl-penta-2,3-dienyl)-4-methylbenzenesulfonamide (**137**) (73 mg, 0.25 mmol, 1.00 equiv). The resulting solution was heated at 80 °C for 5 h. After cooling to rt, the solution was concentrated and purified by flash chromatography (SiO_2 , 5% ethyl acetate in hexanes to 15% ethyl acetate in hexanes gradient for elution) affording 30 mg (42%) of the title compound as a colorless solid and 26 mg (32%) of *cis*-2-[(4-methylbenzene)sulfonyl]-4-isopropylidene-5-oxo-hexahydro-cyclopenta[c]pyrrole (**139**) as a pale yellow oil. Data for *cis*-6-Isopropylidene-3-*N*-[(4-methylbenzene)sulfonyl]-azabicyclo[3.2.0]heptane (**166**): mp = 131-133 °C (dec), 1H NMR (300 MHz, $CDCl_3$) δ 7.66 (d, J = 8.0 Hz, 2H), 7.29 (d, J = 8.0 Hz, 2H), 3.53 (d, J = 9.4 Hz, 1H), 3.42 (d, J = 9.4 Hz, 1H), 3.25 (m, 1H), 2.75-2.58 (m, 4H), 2.35 (m, 1H), 2.40 (s, 3H), 1.47 (s, 3H), 1.43 (s, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 143.4 (C), 131.9 (C), 129.7 (C), 129.4 (2 x CH), 128.0 (2 x CH), 125.6 (C), 54.2 (CH_2), 53.1 (CH_2), 44.8 (CH), 33.1 (CH_2), 32.8 (CH), 21.5 (CH_3), 18.4 (CH_3), 18.0 (CH_3); IR (NaCl, thin film) 2965 (m), 2973 (m), 2850 (m), 1717 (w),

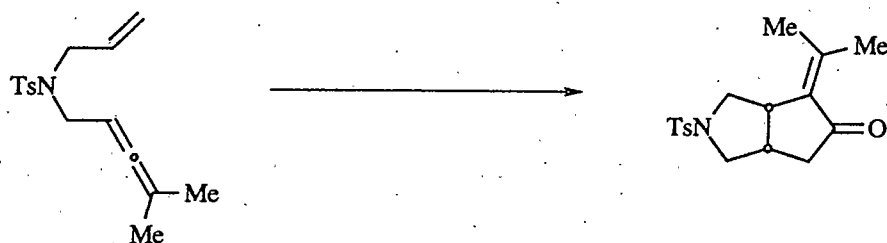
1597 (w), 1345 (m), 1169 (s), 1090 (m), 1063 (m), 812 (m), 664 (m); high resolution (EI) mass spectrum calculated for $C_{16}H_{21}NO_2S$ (M^+) 291.1298, found 291.1293.

***N*-[(4-Methylbenzene)sulfonyl]-4-isopropylidene-2,3,4,5-1*H*-azepine (167)**

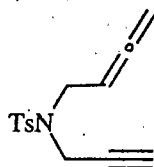


To a solution of $[(CO)_2RhCl]_2$ (1 mg, 1 mol %) in toluene (2 mL) under an argon atmosphere was added *N*-(2-propenyl)-*N*-(4-methyl-penta-2,3-dienyl)-4-methylbenzenesulfonamide (137) (58 mg, 0.25 mmol, 1.00 equiv). The resulting solution was heated at 60 °C for 3.25 h. The solution was allowed to cool to rt, the solvent was evaporated and the residue was passed through a short plug of neutral Al_2O_3 (diethyl ether) affording 55 mg of the title compound (95%) as a pale yellow oil. Data for *N*-[(4-methylbenzene)sulfonyl]-4-isopropylidene-2,3,4,5-1*H*-azepine (167): 1H NMR (300 MHz, $CDCl_3$) δ 7.60 (d, J = 8.4 Hz, 2H), 7.21 (d, J = 8.4 Hz, 2H), 6.35 (d, J = 9.0 Hz, 1H), 4.94 (dt, J = 9.0, 5.7 Hz, 1H), 3.65 (app t, J = 5.7 Hz, 2H), 2.76 (d, J = 5.7 Hz, 2H), 2.36 (obscured peak, 2H), 2.34 (s, 3H), 1.49 (s, 3H), 1.30 (s, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 143.2 (C), 137.1 (C), 129.5 (2 x CH), 127.9 (CH), 127.5 (C), 126.7 (2 x CH), 125.8 (C), 111.7 (CH), 47.1 (CH_2), 32.2 (CH_2), 28.2 (CH_2), 21.4 (CH_3), 20.3 (CH_3), 19.8 (CH_3); IR (NaCl, thin film) 3442 (br w), 3047 (w), 2922 (m), 2861 (m), 1647 (m), 1597 (m), 1339 (s), 1164 (s), 1092 (s), 669 (s); high resolution (EI) mass spectrum calculated for $C_{16}H_{21}NO_2S$ (M^+) 291.1292, found 291.1293.

***cis*-2-[(4-Methylbenzene)sulfonyl]-4-isopropylidene-5-oxo-hexahydro-cyclopenta[*c*]pyrrole (139)**

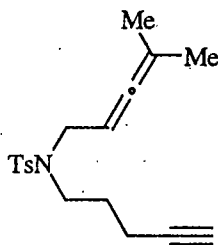


The title compound was prepared in 60% yield using Procedure C except that 15 mol % thiophene was used as additive (4 h). Purification of the crude residue by flash chromatography (SiO₂, 15% ethyl acetate in hexanes gradient for elution) afforded 54 mg (68%) of the title compound as a colorless oil. Data for *cis*-2-[(4-methylbenzene)sulfonyl]-4-isopropylidene-5-oxo-hexahydro-cyclopenta[*c*]pyrrole (139): ¹H NMR (250 MHz, CDCl₃) δ 7.53 (d, *J* = 8.1 Hz, 2H), 7.26 (d, *J* = 8.1 Hz, 2H), 3.41-3.28 (m, 2H), 3.12 (dd, *J* = 10.1, 6.8 Hz, 1H), 2.89 (dd, *J* = 10.1, 6.8 Hz, 1H), 2.76 (m, 1H), 2.61 (m, 1H), 2.30 (dd, *J* = 10.4, 9.4 Hz, 1H), 2.25 (s, 3H), 1.95 (s, 3H), 1.86 (dd, *J* = 4.4, 2.2, 1H), 1.66 (s, 3H); ¹³C NMR (62.9 MHz C₆D₆) δ 203.4 (C), 148.9 (C), 143.2 (C), 134.1 (C), 133.4 (C), 129.6 (2 x CH), 128.1 (2 x CH), 54.0 (CH₂), 53.5 (CH₂), 44.3 (CH₂), 43.9 (CH₂), 35.3 (CH₂), 24.0 (CH₃), 21.1 (CH₃), 20.2 (CH₃); IR (NaCl, thin film) 3391 (w), 3061 (m), 2926 (m), 2854 (m), 1705 (s), 1627 (s), 1597 (s), 1345 (br s), 1263 (s), 1186 (br s), 1163 (br s), 1092 (s), 815 (s), 735 (s), 709 (s); high resolution (EI) mass spectrum calculated for C₁₇H₂₁NO₃S (M⁺) 319.1249, found 319.1242.

***N*-(2,3-Butadienyl)-*N*-(2-propynyl)-4-methylbenzenesulfonamide (128)**

To a solution of *N*-(prop-2-ynyl)-4-methylbenzenesulfonamide (**121**) (0.760 g, 3.65 mmol, 1.00 equiv), PPh_3 (1.20 g, 4.74 mmol, 1.3 equiv), buta-2,3-dien-1-ol (0.330 g, 4.74 mmol, 1.30 equiv) in THF (9 mL) at 0 °C was added DIAD (0.93 mL, 4.7 mmol, 1.3 equiv) dropwise. The resulting solution was allowed to warm to rt and stirred an additional 30 min. The volatiles were removed under reduced pressure and the residue was purified by flash chromatography (SiO_2 , 2% ethyl acetate in hexanes to 10% ethyl acetate in hexanes gradient for elution) to afford a colorless oil that solidified in the freezer. The colorless solid was recrystallized from ethyl acetate/hexanes to give 0.76 g (80%) of the title compound as colorless flakes. Data for *N*-(2,3-butadienyl)-*N*-(2-propynyl)-4-methylbenzenesulfonamide (**128**): mp = 62–63 °C; ^1H NMR (300 MHz, CDCl_3) δ 7.70 (d, J = 8.4 Hz, 2H), 7.26 (d with fine structure, J = 8.4 Hz, 2H), 5.00 (dt, J = 6.8, 6.8 Hz, 1H), 4.74 (dt, J = 6.8, 2.4 Hz, 2H), 4.12 (d, J = 2.4 Hz, 2H), 3.84 (dt, J = 6.8, 2.4 Hz, 2H), 2.39 (s, 3H), 2.00 (t, J = 2.4 Hz, 1H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 209.7 (C), 143.5 (C), 136.0 (C), 129.4 (2 x CH), 127.6 (2 x CH), 85.3 (CH), 76.4 (CH_2), 73.6 (CH), 45.5 (CH_2), 35.8 (CH_2), 21.4 (CH_3); IR (thin film, NaCl) 3289 (m br), 2924 (m), 2120 (w), 1956 (m), 1598 (m), 1348 (s), 1162 (s); high resolution mass spectrum calculated for $\text{C}_{14}\text{H}_{15}\text{NO}_2\text{S}$ (M^+) 261.0824, found 261.0831.

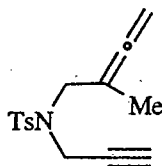
***N*-(Pent-4-ynyl)-*N*-(4-methyl-penta-2,3-dienyl)-4-methylbenzene-sulfonamide (165)**



To a solution of *N*-(pent-4-ynyl)-*N*-(4-methyl-penta-2,3-dienyl)-4-methylbenzene-sulfonamide²³ (0.560 g, 2.23 mmol, 1.00 equiv), PPh₃ (0.760 g, 2.90 mmol, 1.3 equiv), 5-(trimethylsilyl)pent-4-yn-1-ol (0.450 g, 2.90 mmol, 1.30 equiv) in THF (6 mL) at 0 °C was added DIAD (0.57 mL, 2.9 mmol, 1.3 equiv) dropwise. The resulting solution was allowed to warm to rt and stirred an additional 12 h. The volatiles were removed under reduced pressure and the residue was dissolved in MeOH (15 mL). To the resulting solution was added K₂CO₃ (0.42 g, 3.0 mmol) and the suspension was allowed to stir for 5 h at rt. The suspension was partitioned between ethyl acetate and water (50/50 mL). The organic layer was washed with water (50 mL), brine (50 mL) and dried (MgSO₄). Evaporation of solvent and purification by flash chromatography (SiO₂, hexanes to 5% ethyl acetate in hexanes gradient for elution) afforded 0.57 g (80%) of a colorless oil. Data for *N*-(pent-4-ynyl)-*N*-(4-methyl-penta-2,3-dienyl)-4-methylbenzenesulfonamide (**165**): ¹H NMR (300 MHz, CDCl₃) δ 7.64 (d, *J* = 8.3 Hz, 2H), 7.23 (d, *J* = 8.3 Hz, 2H), 4.66 (m, 1H), 3.70 (d, *J* = 7.1 Hz, 2H), 3.20 (t, *J* = 7.2 Hz, 2H), 2.34 (s, 3H), 2.16 (dt, *J* = 7.2, 2.6 Hz, 2H), 1.89 (t, *J* = 2.6 Hz, 1H), 1.73 (tt, *J* = 7.2, 7.2 Hz, 2H), 1.58 (s, 3H), 1.57 (s, 3H); ¹³C NMR (75.5 MHz, CDCl₃) δ 203.1 (C), 143.0 (C), 137.0 (C), 129.5 (2 x CH), 126.9 (2 x CH), 96.6 (C), 84.2 (CH), 83.1 (C), 68.8 (CH), 47.9 (CH₂), 45.8 (CH₂), 26.9 (CH₂), 21.3 (CH₃), 20.1 (2 x CH₃), 15.6 (CH₂); IR (thin film, NaCl) 3289

(m br), 2924 (m), 2120 (w), 1956 (m), 1598 (m), 1348 (s), 1162 (s); high resolution (EI) mass spectrum calculated for $C_{18}H_{23}NO_2S$ (M^+) 317.1450, found 317.1449.

***N*-(2-Methyl-buta-2,3-dienyl)-*N*-(prop-2-ynyl)-4-methylbenzenesulfonamide (132)**



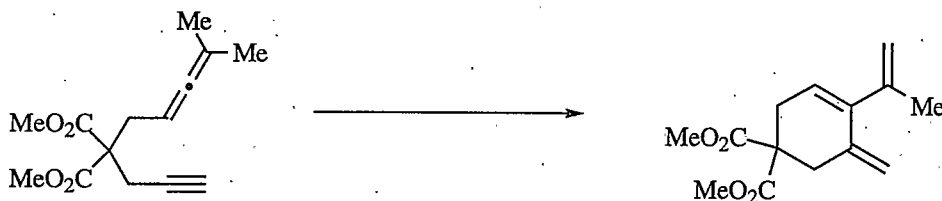
To a solution of *N*-*t*-butoxycarbonyl-4-methylbenzenesulfonamide⁹³ (5.32 g, 19.6 mmol, 1.00 equiv), PPh_3 (6.20 g, 23.5 mmol, 1.20 equiv), and a mixture of 2-methyl-buta-2,3-dien-1-ol and 2-pentyn-1ol (7/1 mixture, 1.98 g, 23.5 mmol, 1.00 equiv) at 0 °C was added DIAD (4.60 mL, 23.5 mmol, 1.20 equiv) dropwise. The resulting solution was allowed to stir for 1 h at rt. The solution was concentrated and partially purified by flash chromatography (SiO_2 , 10% ethyl acetate in hexanes). The residue was dissolved in DMSO (120 mL) and heated at reflux for 10 min. Workup in the usual manner and purification by flash chromatography (SiO_2 , 15% ethyl acetate in hexanes) afforded 4.43 g (79%) of the desired products as a 3/1 mixture. To a suspension of the mixture (3/1, 3.06 g, 12.9 mmol, 1.00 equiv) and K_2CO_3 (2.67 g, 19.3 mmol, 1.50 equiv) in DMF (10 mL) was added propargyl bromide (1.90 mL, 25.8 mmol, 2.00 equiv). The resulting suspension was allowed to stir 3 h at rt. The suspension was partitioned between ethyl acetate/water (50/50 mL). The aqueous phase was washed with ethyl acetate (25 mL) and the combined organic layers were washed with water (2 x 50 mL), brine (50 mL) and dried ($MgSO_4$). The solution was concentrated and purified by flash chromatography (SiO_2 , hexanes to 5% ethyl acetate in hexanes gradient for elution) affording 3.2 g (91%) of

material as a white solid. Recrystallization of the solid from ethyl acetate/hexanes afforded 1.5 g (47%) of the title compound as colorless crystals. Data for *N*-(2-methyl-buta-2,3-dienyl)-*N*-(prop-2-ynyl)-4-methylbenzenesulfonamide (**132**): mp = 74-76 °C; ¹H NMR (300 MHz, CDCl₃) δ 7.71 (d, *J* = 8.2 Hz, 2H), 7.26 (d, *J* = 8.2 Hz, 2H), 4.68-4.51 (m, 2H), 4.08 (d, *J* = 2.4 Hz, 2H), 3.76 (app t, *J* = 2.7 Hz, 2H), 2.40 (s, 3H), 1.94 (t, *J* = 2.4 Hz, 1H), 1.69 (app t, *J* = 2.7 Hz, 3H); ¹³C NMR (75.5 MHz, CDCl₃) δ 207.6 (C), 143.5 (C), 136.1 (C), 129.4 (2 x CH), 127.7 (2 x CH), 93.3 (C), 76.3 (C), 75.1 (CH₂), 73.5 (CH), 49.9 (CH₂), 35.6 (CH₂), 21.5 (CH₃), 15.8 (CH₃); IR (thin film, NaCl) 3277 (m), 2983 (w), 2921 (w), 2118 (w), 1961 (w), 1347 (m); high resolution (EI) mass spectrum calculated for C₁₅H₁₇NO₂S (M⁺) 275.0980, found 275.0980.

5.5 Rhodium-Catalyzed Cycloisomerization of Allenynes

The following compounds were prepared according to the literature procedures: 4-(tetrahydropyran-2-yloxy)hex-2-yn-1-ol⁷⁰ and hexa-2,3-dien-1-ol.⁷⁰

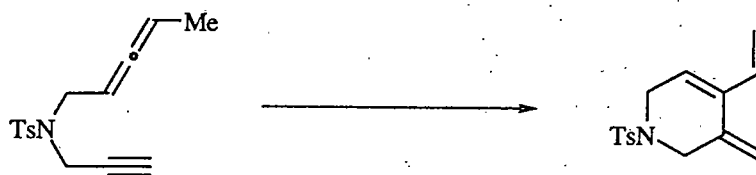
5-Methylene-4-(propen-2-yl)-cyclohex-3-ene-1,1-dicarboxylic acid dimethyl ester (133)



A solution of [(NBD)₂Rh]SbF₆ (2.1 mg, 0.0040 mmol, 2 mol %) and bis(diphenylphosphino)propane (1.7 mg, 0.0042 mmol, 2.1 mol%) in 1,2-DCE (2 mL) was stirred under dihydrogen (1 atm) for 15 min. The resulting solution was then freeze-pump-thaw-degassed (2 cycles) to remove adventitious dihydrogen. After stirring the solution under argon for 1 min, 2-(4-methyl-2,3-pentadienyl)-2-(2-propynyl) malonic acid dimethyl ester (**104**) (50 mg, 0.2 mmol) was added via a gastight syringe. The resulting solution was heated at 60 °C for 3 h, allowed to cool to rt and concentrated under reduced pressure. Purification of the crude residue by flash chromatography (SiO₂, 10% ethyl acetate in hexanes) afforded 41 mg (82%) of the title compound as a colorless oil. Data for 5-methylene-4-(propen-2-yl)-cyclohex-3-ene-1,1-dicarboxylic acid dimethyl ester (**133**): ¹H NMR (300 MHz, CDCl₃) δ 5.59 (dt, *J* = 4.1, 1.0 Hz, 1H), 4.99-4.93 (m, 3H), 4.81 (m, 1H), 3.69 (s, 6H), 2.86 (s, 2H), 2.70 (d, *J* = 4.1 Hz, 2H), 1.82 (d, *J* = 1.0 Hz, 3H); ¹³C NMR (75.5 MHz, CDCl₃) δ 171.3 (2 x C), 144.1 (C), 141.7 (C), 137.8 (C), 123.0 (CH), 114.5 (CH₂), 114.0 (CH₂), 54.3 (2 x C), 52.7 (CH₃), 37.4 (CH₂), 31.5 (CH₂),

22.9 (CH₃); IR (NaCl, thin film) 3091 (w), 2955 (m), 2918 (m), 2849 (m), 1735 (s) 1436 (m); high resolution (EI) mass spectrum calculated for C₁₄H₁₈O₄ (M⁺) 250.1205, found 250.1202.

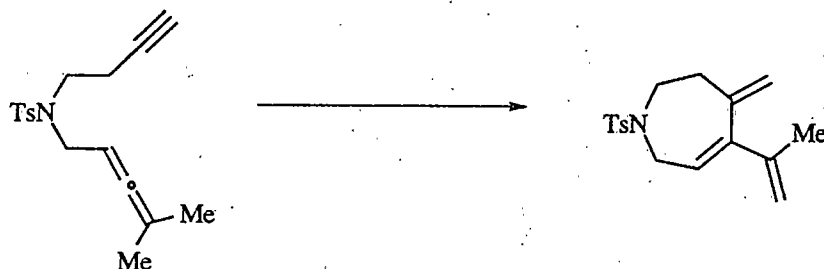
1-[(4-Methylbenzene)sulfonyl]-3-methylene-4-vinyl-1,2,3,6-tetrahydro-pyridine (159)



To a yellow solution of [(COE)₂RhCl]₂ (1.8 mg, 1 mol %) and dppp (2.1 mg, 2 mol %) in toluene (2.5 mL) under CO (1 atm) was added AgSbF₆ (100 µL of a 0.05M solution in 1,2-DCE, 2 mol %). The resulting suspension was allowed to stir 15 min and then *N*-prop-2-ynyl-*N*-(penta-2,3-dienyl)-4-methyl-benzenesulfonamide (**124**) (69 mg, 0.25 mmol) was added. The reaction mixture was heated at 60 °C for 5 h. Evaporation of solvent and purification by flash chromatography (SiO₂, hexanes to 5% ethyl acetate in hexanes gradient for elution) afforded 59 mg (86%) of **159** as a colorless oil that solidified at room temperature upon standing. Data for 1-[(4-methylbenzene)sulfonyl]-3-methylene-4-vinyl-1,2,3,6-tetrahydro-pyridine (**159**): mp = 69-71 °C; ¹H NMR (300 MHz, CDCl₃) δ 7.63 (d, *J* = 8.2 Hz, 2H), 7.26 (d, *J* = 8.2 Hz, 2H), 6.26 (dd, *J* = 17.2, 10.8 Hz, 1H), 5.72 (br s, 1H), 5.25 (d, *J* = 17.2 Hz, 1H), 5.08-4.97 (m, 3H), 3.77 (s with fine structure, 4H), 2.37 (s, 3H); ¹³C NMR (75.5 MHz, CDCl₃) δ 143.6 (C), 136.5 (C), 135.4 (C), 133.6 (CH), 133.3 (C), 129.5 (2 x CH), 127.7 (2 x CH), 121.5 (CH), 116.6 (CH₂), 112.0 (CH₂), 49.3 (CH₂), 45.7 (CH₂), 21.4 (CH₃); IR (NaCl, thin film) 3089 (m), 3037

(m), 2921 (m), 1596 (m), 1345 (s), 1161 (s), 860 (m), 815 (m), 671 (m); high resolution (EI) mass spectrum calculated for $C_{15}H_{17}NO_2S$ (M^+) 275.0980, found 275.0985.

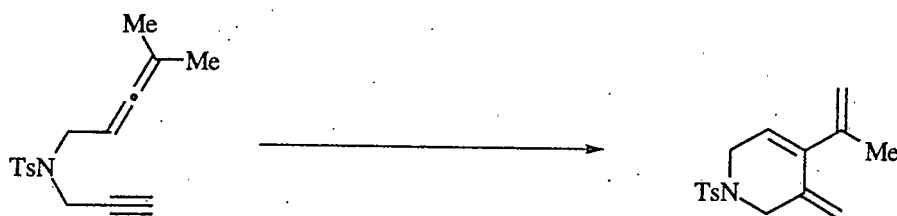
5-Isopropenyl-4-methylene-2,3,4,7-tetrahydro-1*H*-[(4-methylbenzene)sulfonyl]azepine (161)



A solution of $[(NBD)_2Rh]SbF_6$ (2.1 mg, 0.0040 mmol, 2 mol %) and bis(diphenylphosphino)butane (1.7 mg, 0.0042 mmol, 2.1 mol %) in 1,2-DCE (1 mL) was stirred under dihydrogen (1 atm) for 15 min. The resulting solution was then freeze-pump-thaw-degassed (2 cycles) to remove adventitious dihydrogen. After stirring the solution under argon for 1 min, a solution of *N*-But-3-ynyl-*N*-(4-methyl-penta-2,3-dienyl)-4-methyl-benzenesulfonamide (**125**) (50 mg, 0.2 mmol) in 1,2-DCE (1 mL) was added dropwise. The resulting solution was heated at 60 °C for 3.5 h, allowed to cool to rt and concentrated at reduced pressure. Purification of the crude residue by flash chromatography (SiO_2 , 10% ethyl acetate in hexanes) afforded 50 mg (82%) of the title compound as a colorless oil. Data for 5-isopropenyl-4-methylene-2,3,4,7-tetrahydro-1*H*-[(4-methylbenzene)sulfonyl]azepine (**161**): 1H NMR (300 MHz, $CDCl_3$) δ 7.64 (d, J = 8.2 Hz, 2H), 7.25 (d, J = 8.2 Hz, 2H), 5.66 (t, J = 6.0 Hz, 1H), 5.12 (s, 1H), 4.93 (d, J = 12.8 Hz, 2H), 4.78 (d, J = 1.6 Hz, 1H), 3.86 (d, J = 6.0 Hz, 2H), 3.42 (t, J = 6.1 Hz, 2H), 2.39 (s, 3H), 2.36 (t, J = 6.1 Hz, 2H), 1.77 (s, 3H); ^{13}C NMR (75.5 MHz, C_6D_6) δ 148.2 (C), 144.0 (C), 143.7 (C), 142.5 (C), 137.8 (C), 129.4 (2 x CH), 127.7 (2 x CH),

121.7 (CH), 117.4 (CH₂), 115.5 (CH₂), 50.3 (CH₂), 46.2 (CH₂), 35.9 (CH₂), 21.0 (CH₃), 20.9 (CH₃); IR (NaCl, thin film) 3081 (w), 3029 (w), 2921 (w), 1598 (m), 1334 (m), 1160 (s), 1098 (m), 897 (m); high resolution (EI) mass spectrum calculated for C₁₇H₂₁NO₂S (M⁺) 303.1278, found 303.1293.

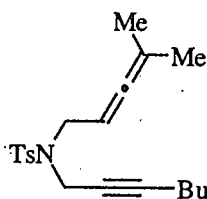
1-[(4-Methylbenzene)sulfonyl]-3-methylene-4-(propen-2-yl)-1,2,3,6-tetrahydro-pyridine (160)



A solution of [(NBD)₂Rh]SbF₆ (3.1 mg, 0.006 mmol, 2 mol %) and bis(diphenylphosphino)butane (2.6 mg, 0.063 mmol, 2.1 mol %) in 1,2-DCE (1.5 mL) was stirred under dihydrogen (1 atm) for 15 min. The resulting solution was then freeze-pump-thaw-degassed (2 cycles) to remove adventitious dihydrogen. After stirring the solution under argon for 1 min, a solution of *N*-prop-2-ynyl-*N*-(4-methyl-penta-2,3-dienyl)-4-methyl-benzenesulfonamide (**124**) (87 mg, 0.3 mmol) in 1,2-DCE (1.5 mL) was added dropwise. The resulting solution was heated at 60 °C for 3.5 h, allowed to cool to rt and concentrated under reduced pressure. Purification of the crude residue by flash chromatography (SiO₂, 10% ethyl acetate in hexanes) afforded 64 mg (74%) of the title compound as a colorless oil. Data for the title compound **160**: ¹H NMR (300 MHz, C₆D₆) δ 7.65 (d, *J* = 8.1 Hz, 2H), 6.84 (d, *J* = 8.1 Hz, 2H), 5.14 (br s with fine structure, 1H), 4.89 (br d, *J* = 13.0 Hz, 2H), 4.73 (br d, *J* = 13.6 Hz, 2H), 3.72 (s, 2H), 3.57 (d, *J* = 3.6 Hz, 2H), 1.96 (s, 3H), 1.62 (s, 3H); ¹³C NMR (300 MHz, CDCl₃) δ 143.2 (C),

143.1 (C), 140.4 (C), 136.3 (C), 134.7 (C), 129.6 (2 x CH), 128.2 (2 x CH), 121.8 (CH), 115.2 (CH₂), 113.2 (CH₂), 49.7 (CH₂), 45.6 (CH₂), 22.7 (CH₃), 21.1 (CH₃); IR (NaCl, thin film) 3086 (w), 2966 (w), 2921 (w), 1348 (m), 1167 (m), 667 (m); high resolution (EI) mass spectrum calculated for C₁₆H₁₉NO₂S (M⁺) 289.1139, found 289.1136.

***N*-(Hept-2-ynyl)-*N*-(4-methyl-penta-2,3-dienyl)-4-methylbenzenesulfonamide (151)**



To a solution of *N*-(4-methyl-penta-2,3-dienyl)-4-methyl-benzenesulfonamide (1.33 g, 5.00 mmol, 1.00 equiv), PPh₃ (1.44 g, 5.50 mmol, 1.1 equiv) and 2-butyne-1-ol (0.54 g, 5.5 mmol, 1.1 equiv) in THF (13 mL) at 0 °C was added DIAD (1.08 mL, 5.5 mmol, 1.1 equiv) dropwise over 5 min. After stirring the resulting solution for 60 min at 0 °C, the volatiles were removed under reduced pressure and the crude residue was purified by flash chromatography (SiO₂, 5% ethyl acetate in hexanes to 10% ethyl acetate in hexanes gradient for elution) affording 1.43 g (83%) of the title compound **151** as a pale yellow oil. Data for the title compound **151**: ¹H NMR (300 MHz, CDCl₃) δ 7.68 (d, *J* = 8.2 Hz, 2H), 7.23 (d with fine structure, *J* = 8.2 Hz, 2H), 4.80 (m, 1H), 4.08 (br t, *J* = 2.1 Hz, 2H), 3.72 (d, *J* = 7.0 Hz, 2H), 2.36 (s, 3H), 1.89-1.80 (m, 2H), 1.625 (s, 3H), 1.615 (s, 3H), 1.24-1.11 (m, 4H), 0.78 (t with fine structure, *J* = 7.1 Hz, 3H); ¹³C NMR (75.5 MHz, CDCl₃) δ 203.7 (C), 143.0 (C), 136.2 (C), 129.2 (2 x CH), 127.7 (2 x CH), 96.7 (C), 85.8 (C), 83.8 (CH), 72.1 (C), 46.3 (CH₂), 36.0 (CH₂), 30.3 (CH₂), 21.6 (CH₂),

21.4 (CH₃), 20.1 (2 x CH₃), 18.0 (CH₂), 13.4 (CH₃); IR (NaCl, thin film) 3029 (w), 2957 (s), 2932 (s), 2871 (s), 2287 (w), 2225 (w), 1970 (w), 1717 (br w), 1598 (m); high resolution (EI) mass spectrum calculated for C₂₀H₂₇NO₂S (M⁺) 345.1762, found 345.1760.

5.6 Catalytic Pauson-Khand Reaction of Enynes

The following compounds were prepared by literature methods: 2-methyl-3-butyn-2-ol hexacarbonyldicobalt^{81b}, phenylacetylene hexacarbonyldicobalt^{81b}, but-2-yne-1,4-diol hexacarbonyldicobalt^{81b}, dimethyl acetylenedicarboxylate hexacarbonyldicobalt^{81b}, bis(trimethylsilyl)acetylene hexacarbonyldicobalt^{81b} and prop-2-yn-1-ol hexacarbonyldicobalt.^{81b} GOESY data was obtained using the method of Shaka.¹⁰⁰

General Procedures for the Catalytic Pauson-Khand Reaction

Representative Catalytic Pauson-Khand Reaction with $\text{Co}_2(\text{CO})_8$,

Procedure A: To a solution of dicobalt octacarbonyl (8.5 mg, 0.025 mmol, 5 mol %) in 1,2-DME (5 mL) under a CO atmosphere was added 2-allyl-2-prop-2-ynyl malonic acid diethyl ester (119 mg, 0.500 mmol) via a gastight syringe. After 30 min, the resulting solution was heated to 60 °C in a constant temperature bath for 6 h. After cooling to room temperature, brine and ethyl acetate were added (1 mL each) and the biphasic mixture was stirred open to the atmosphere for 30 min. Workup with EtOAc/brine (50/25 mL) and drying (Na_2SO_4) followed by evaporation of solvent and subsequent purification by flash chromatography (SiO_2 , 15% ethyl acetate in hexanes to 30% ethyl acetate in hexanes gradient for elution) afforded 125 mg (83%) of 5-oxo-3,3a,4,5-tetrahydro-1*H*-pentalene-2,2-dicarboxylic acid diethyl ester as a colorless oil.

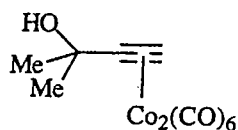
Representative Catalytic Pauson-Khand Reaction with alkyne-

$\text{Co}_2(\text{CO})_6$, **Procedure B:** To a solution of 2-methyl-3-butyn-2-ol hexacarbonyldicobalt (9.2 mg, 0.025 mmol, 5 mol %) in 1,2-DME (5 mL) under a CO atmosphere was sequentially added Et_3SiH (50 μL of a 0.5 M solution in *p*-xylene, 0.025 mmol) and

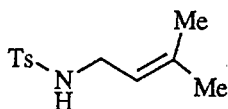
cyclohexylamine (9 μ L, 0.075 mmol). The resulting solution was heated at 65 °C for 15 min at which time 2-allyl-2-prop-2-ynyl malonic acid diethyl ester (119 mg, 0.500 mmol) was added via a gastight syringe. The resulting solution was maintained at 65 °C for 6 h. After cooling to room temperature, brine and ethyl acetate were added (1 mL each) and the biphasic mixture was stirred open to the atmosphere for 30 min. Workup with EtOAc/brine (50/25 mL) and drying (Na_2SO_4) followed by evaporation of solvent and subsequent purification by flash chromatography (SiO_2 , 15% ethyl acetate in hexanes to 30% ethyl acetate in hexanes gradient for elution) afforded 125 mg (93%) of 5-oxo-3,3a,4,5-tetrahydro-1*H*-pentalene-2,2-dicarboxylic acid diethyl ester as a colorless oil.

Representative Catalytic Pauson-Khand Reaction with $\text{Co}_2(\text{CO})_8$,

Procedure C: To a solution of dicobalt octacarbonyl (8.5 mg, 0.025 mmol, 5 mol %) in 1,2-DME (5 mL) under a CO atmosphere was added substrate (0.5 mmol) via a gastight syringe. After 15-20 min, the resulting solution was heated to 60 °C in a constant temperature bath until consumption of starting substrate was observed by tlc. After cooling to room temperature, evaporation of volatiles and subsequent purification by flash chromatography (SiO_2 , 15% ethyl acetate in hexanes to 30% ethyl acetate in hexanes gradient for elution) afforded the desired product. In some instances, further purification was required and was accomplished by passing a DCM solution of substrate through a plug of neutral Al_2O_3 .

2-Methyl-3-butyn-2-ol hexacarbonyldicobalt (222)

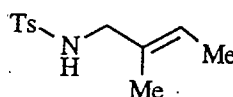
To a solution of $\text{Co}_2(\text{CO})_8$ (1.8 g, 5.3 mmol, 1.00 equiv) in diethyl ether (25 mL) at room temperature under CO (1 atm) was added 2-methyl-3-butyn-2-ol (0.49 mL, 5.0 mmol, 0.95 equiv) in portions via a gastight syringe. The resulting solution was allowed to stir at room temperature under an argon atmosphere for 5 h. The solvent was evaporated and the residue was purified by flash chromatography (SiO_2 , 5 x 9 cm, hexanes to 15% diethyl ether in hexanes gradient for elution). Evaporation of solvent afforded 1.57 g (85%) of the title compound **222** as a red oil which solidified upon storage in the refrigerator. Data were consistent with that reported in the literature.^{81b}

***N*-(3-Methyl-but-2-enyl)-4-methylbenzenesulfonamide**

To a solution of *N*-*t*-butoxycarbonyl-4-methylbenzenesulfonamide (1.36 g, 5.00 mmol, 1.00 equiv), PPh_3 (2.62 g, 10.0 mmol, 2.00 equiv), and 3-methyl-2-buten-1-ol (0.76 mL, 1.5 mmol, 1.5 equiv) in THF (13 mL) at 0 °C was added DEAD (1.6 mL, 10.0 mmol, 2.0 equiv) dropwise. The solution was allowed to warm to rt and stirred overnight (14 h). The solvent was evaporated under reduced pressure and the residue was purified by flash chromatography (SiO_2 , hexanes to 10% ethyl acetate in hexanes gradient for elution). The resulting colorless, viscous oil was dissolved in DMSO (15 mL) and heated at reflux for 10 min. After cooling to rt, the solution was diluted with ethyl acetate (25 mL) and washed

with water (2 x 25 mL). The aqueous layer was extracted with ethyl acetate (20 mL) and the combined organic fractions were washed with brine (3 x 50 mL) and dried (MgSO_4). Evaporation of solvent and flash chromatography (SiO_2 , 5% ethyl acetate in hexanes to 15% ethyl acetate in hexanes gradient for elution) afforded *N*-(3-methyl-but-2-enyl)-4-methylbenzenesulfonamide as a viscous oil which solidified on standing at rt (1.13 g, 94% for the two steps). Data for the title compound: mp = 61-62 °C; ^1H NMR (300 MHz, CDCl_3) δ 7.72 (d, J = 8.1 Hz, 2H), 7.24 (d, J = 8.1 Hz, 2H), 4.98 (t with fine structure, J = 7.1 Hz, 2H), 3.45 (br s with fine structure, 2H), 2.36 (s, 3H), 1.54 (s with fine structure, 3H), 1.46 (s with fine structure, 3H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 143.1 (C), 137.0 (C), 136.9 (C), 129.4 (2 x CH), 127.0 (2 x CH), 118.8 (CH), 40.8 (CH_2), 25.3 (CH_3), 21.3 (CH_3), 17.6 (CH_3); IR (NaCl, thin film) 3282 (s br), 2972 (s), 2924 (s), 2860 (m), 1675 (w), 1599 (s), 1423 (s br), 1327 (s br), 1159 (s br), 1094 (s), 1052 (s), 815 (s), 663 (s br); high resolution (EI) mass spectrum calculated for $\text{C}_{12}\text{H}_{17}\text{NO}_2\text{S}$ (M^+) 239.0980, found 239.0974.

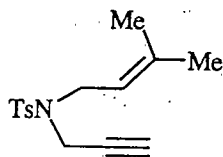
***N*-(2-Methyl-but-2-enyl)-4-methylbenzenesulfonamide**



To a solution of *N*-*t*-butoxycarbonyl-4-methylbenzenesulfonamide (2.70 g, 10.0 mmol, 1.00 equiv), PPh_3 (5.20 g, 20.0 mmol, 2.00 equiv), and 2-methyl-2-buten-1-ol (1.08 g, 12.5 mmol, 1.25 equiv) in THF (25 mL) at 0 °C was added DEAD (3.2 mL, 20.0 mmol, 2.0 equiv) dropwise. The solution was allowed to warm to rt and stirred 2 h. The solvent was evaporated and the residue was dissolved in diethyl ether (50 mL) and treated with hexanes (20 mL). The resulting suspension was filtered and washed with diethyl

ether/hexanes (50/50 mL). Evaporation of solvent and purification by flash chromatography (SiO₂, 5% ethyl acetate in hexanes to 20% ethyl acetate in hexanes gradient for elution) afforded a colorless, viscous oil. The resulting colorless, viscous oil was dissolved in DMSO (30 mL) and heated at reflux for 10 min. After cooling to rt, the solution was diluted with ethyl acetate (50 mL) and washed with water (2 x 50 mL). The aqueous layer was extracted with ethyl acetate (40 mL) and the combined organic fractions were washed with brine (3 x 100 mL) and dried (MgSO₄). Evaporation of solvent and flash chromatography (SiO₂, 5% ethyl acetate in hexanes to 20% ethyl acetate in hexanes gradient for elution) afforded *N*-(2-methyl-but-2-enyl)-4-methylbenzenesulfonamide as a viscous oil which solidified on standing at rt (2.21 g, 93% for the two steps). Data for the title compound: mp = 54-55 °C; ¹H NMR (300 MHz, CDCl₃) δ 7.72 (d, *J* = 8.2 Hz, 2H), 7.27 (d, *J* = 8.2 Hz, 2H), 5.32 (m, 1H), 4.60 (br t, *J* = 6.0 Hz, 1H), 3.40 (d, *J* = 6.0 Hz, 2H), 2.40 (s, 3H), 1.50 (s, 3H), 1.48 (s, 3H); ¹³C NMR (75.5 MHz, CDCl₃) δ 143.2 (C), 137.1 (C), 130.8 (C), 129.5 (2 x CH), 127.1 (2 x CH), 123.0 (CH), 51.1 (CH₂), 21.5 (CH₃), 13.8 (CH₃), 13.2 (CH₃); IR (NaCl, thin film) 3284 (m br), 2920 (m), 1160 (m) 814 (m), 663 (m); high resolution (EI) mass spectrum calculated for C₁₂H₁₇NO₂S (M⁺) 239.0980, found 239.0978.

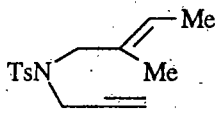
***N*-(3-Methyl-but-2-enyl)-*N*-(prop-2-ynyl)-4-methylbenzenesulfonamide**



To a suspension of K₂CO₃ (0.97 g, 7.0 mmol, 1.5 equiv) and *N*-(3-methyl-but-2-enyl)-4-methylbenzenesulfonamide (1.12 g, 4.67 mmol, 1.00 equiv) in DMF (8 mL) at rt was

added propargyl bromide (0.74 mL, 9.3 mmol, 2.0 equiv) in one portion. The resulting suspension was allowed to stir overnight (13 h) and then ethyl acetate (20 mL) and water (10 mL) were added. The resulting biphasic mixture was poured into ethyl acetate (20 mL) and water (20 mL). The organic layer was washed with water (20 mL) and the combined organic fractions were extracted with ethyl acetate (2 x 20 mL), washed with brine (3 x 30 mL) and dried (MgSO₄). Evaporation of solvent and flash chromatography (SiO₂, 2% ethyl acetate in hexanes to 12.5% ethyl acetate in hexanes gradient for elution) afforded the title compound as a pale yellow oil which solidified on standing (1.26 g, 97%). Data for *N*-(3-methyl-but-2-enyl)-*N*-(prop-2-ynyl)-4-methylbenzenesulfonamide: mp = 68-69 °C; ¹H NMR (300 MHz, CDCl₃) δ 7.68 (d, *J* = 8.2 Hz, 2H), 7.24 (d, *J* = 8.2 Hz, 2H), 5.04 (m, 1H), 4.00 (d, *J* = 2.4 Hz, 2H), 3.76 (d, *J* = 7.2 Hz, 2H), 2.36 (s, 3H), 1.95 (t, *J* = 2.4 Hz, 1H), 1.66 (s, 3H), 1.61 (s, 3H); ¹³C NMR (75.5 MHz, CDCl₃) δ 143.2 (C), 138.8 (C), 135.9 (C), 129.2 (2 x CH), 127.6 (2 x CH), 117.7 (CH), 76.8 (C), 73.3 (CH), 43.7 (CH₂), 35.2 (CH₂), 25.7 (CH₃), 21.3 (CH₃), 17.6 (CH₃); IR (NaCl, thin film) 3260 (m), 2978 (m), 2115 (w), 1344 (s), 1158 (s); high resolution (EI) mass spectrum calculated for C₁₅H₁₈NO₂S (M - H)⁺ 276.1058, found 276.1049.

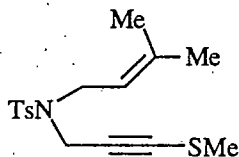
***N*-(2-Methyl-but-2-enyl)-*N*-(prop-2-ynyl)-4-methylbenzenesulfonamide**



To a suspension of K₂CO₃ (0.829 g, 6.00 mmol, 1.50 equiv) and *N*-(2-methyl-but-2-enyl)-4-methylbenzenesulfonamide (0.957 g, 4.00 mmol, 1.00 equiv) in DMF (7 mL) at rt was added propargyl bromide (0.64 mL, 8.0 mmol, 2.0 equiv) in one portion. The suspension was allowed to stir 4 h and then ethyl acetate (20 mL) and water (10 mL) were

added. The resulting biphasic mixture was poured into ethyl acetate (20 mL) and water (20 mL). The organic layer was washed with water (20 mL) and the combined organic fractions were extracted with ethyl acetate (2 x 20 mL), washed with brine (3 x 30 mL) and dried (MgSO₄). Evaporation of solvent and flash chromatography (SiO₂, 2% ethyl acetate in hexanes to 10% ethyl acetate in hexanes gradient for elution) afforded the title compound as a colorless oil which solidified on standing at rt (0.99 g, 89%). Data for *N*-(2-methyl-but-2-enyl)-*N*-(prop-2-ynyl)-4-methylbenzenesulfonamide: mp = 86-88 °C; ¹H NMR (300 MHz, CDCl₃) δ 7.63 (d, *J* = 8.1 Hz, 2H), 7.18 (d, *J* = 8.1 Hz, 2H), 5.37 (app q, *J* = 6.2 Hz, 1H), 3.90 (d, *J* = 2.3 Hz, 2H), 3.58 (s, 2H), 2.31 (s, 3H), 1.84 (app t, *J* = 2.3 Hz, 1H), 1.53 (s, 3H), 1.50 (obscured d, *J* = 6.2 Hz, 3H); ¹³C NMR (75.5 MHz, CDCl₃) δ 143.3 (C), 136.0 (C), 129.5 (C), 129.3 (2 x CH), 127.7 (2 x CH), 125.1 (CH), 76.6 (C), 73.5 (CH), 54.1 (CH₂), 35.0 (CH₂), 21.4 (CH₃), 13.45 (CH₃), 13.39 (CH₃); IR (thin film, NaCl) 3258 (br m), 2919 (m), 2860 (m), 2116 (w), 1598 (m), 1350 (s), 1162 (s), 1065 (s), 898 (m), 661 (s); high resolution (EI) mass spectrum calculated for C₁₅H₁₈NO₂S (M - H)⁺ 276.1058, found 276.1057.

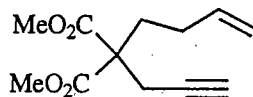
***N*-(3-Methyl-but-2-enyl)-*N*-(3-thiomethyl-prop-2-ynyl)-4-methylbenzenesulfonamide**



To a solution of *N*-(3-methyl-but-2-enyl)-*N*-(prop-2-ynyl)-4-methylbenzenesulfonamide (0.277 g, 1.00 mmol, 1.00 equiv) in THF (2.5 mL) at -78 °C was added *n*-BuLi (0.44 mL of a 2.5M solution in hexanes, 1.1 mmol, 1.1 equiv) dropwise. The resulting brown

solution was allowed to stir 10 min at -78°C and then MeSCN ($82\ \mu\text{L}$, $1.3\ \text{mmol}$, 1.2 equiv) was added dropwise. The reaction mixture was allowed to warm to rt over 1 h. After 1 h at rt, the reaction mixture was quenched by the addition of saturated NH_4Cl ($1.5\ \text{mL}$). The mixture was partitioned between ethyl acetate/water ($10/10\ \text{mL}$), washed with water ($2 \times 5\ \text{mL}$), brine ($10\ \text{mL}$) and dried (Na_2SO_4). Evaporation of solvent and purification by flash chromatography (SiO_2 , $5 \times 2\ \text{cm}$, 5% ethyl acetate in hexanes) afforded $0.242\ \text{g}$ (75%) of the title compound as an tan solid. Recrystallization from ethyl acetate/hexanes afforded colorless prisms. Data for *N*-(3-methyl-but-2-enyl)-*N*-(3-thiomethyl-prop-2-ynyl)-4-methylbenzenesulfonamide: mp = $64\text{--}65^{\circ}\text{C}$; ^1H NMR ($300\ \text{MHz}$, CDCl_3) δ 7.70 (d, $J = 8.2\ \text{Hz}$, 2H), 7.28 (d, $J = 8.2\ \text{Hz}$, 2H), 5.08 (app tq, $J = 7.3, 1.4\ \text{Hz}$, 1H), 4.11 (s, 2H), 3.77 (d, $J = 7.3\ \text{Hz}$, 2H), 2.40 (s, 3H), 2.11 (s, 3H), 1.70 (s, 3H), 1.64 (s, 3H); ^{13}C NMR ($75.5\ \text{MHz}$, CDCl_3) δ 143.3 (C), 138.9 (C), 136.1 (C), 129.4 (2 $\times$ CH), 127.8 (2 $\times$ CH), 118.0 (CH), 86.0 (C), 44.0 (CH_2), 36.8 (CH_2), 25.8 (CH_3), 21.5 (CH_3), 18.6 (CH_3), 17.8 (CH_3); IR (NaCl, thin film) 2971 (m), 2186 (m), 1346 (s), 1162 (s), 899 (s), 666 (s); high resolution (EI) mass spectrum calculated for $\text{C}_{16}\text{H}_{20}\text{NO}_2\text{S}_2$ (M^+) 323.1014, found 323.1006.

2-(But-3-enyl)-2-(prop-2-ynyl)malonic acid dimethyl ester (171)



The title compound was prepared according to a literature method.²⁰ Data for 2-(but-3-enyl)-2-(prop-2-ynyl)malonic acid dimethyl ester (171): ^1H NMR ($300\ \text{MHz}$, CDCl_3) δ 5.75 (ddt, $J = 17.1, 10.3, 6.3\ \text{Hz}$, 1H), 5.04–4.93 (m, 2H), 3.70 (s, 6H), 2.8 (d, $J = 2.6\ \text{Hz}$, 2H), 2.15–2.10 (m, 2H), 1.99–1.00 (m, 3H); ^{13}C NMR ($75.5\ \text{MHz}$, CDCl_3) δ 170.5

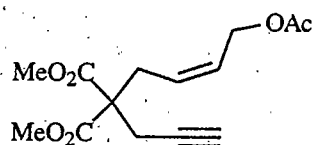
(2 x C), 137.1 (CH), 115.2 (CH₂), 77.4 (C), 71.4 (CH), 56.5 (C), 52.7 (2 x CH₃), 31.2 (CH₂), 28.2 (CH₂), 22.9 (CH₂); IR (thin film, NaCl) 3478 (w), 3294 (s br), 3079 (m), 3002 (s), 2955 (s), 2845 (m), 2123 (w), 1734 (s br), 1642 (s), 1436 (s br), 1273 (s br), 648 (s br); high resolution (PCI/NH₃) mass spectrum calculated for C₁₂H₁₇O₄ (M + H)⁺ 225.1127, found 225.1118.

2-Oxo-1,2,4,6,7,7a-hexahydro-indene-5,5-dicarboxylic acid dimethyl ester (172)



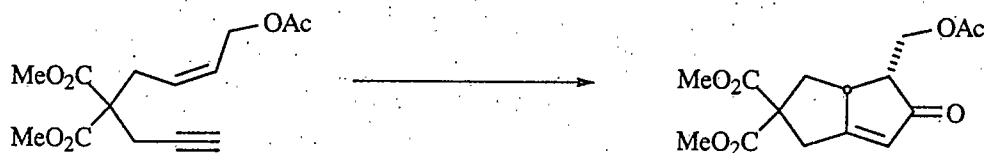
The title compound was prepared in 77% yield using Procedure A except that 10 mol % Co₂(CO)₈ was used (12 h). The title compound was prepared in 86% yield using Procedure B except 10 mol % 2-methyl-3-butyn-2-ol hexacarbonyldicobalt, 10 mol % Et₃SiH and 30 mol % cyclohexylamine were used (12 h). Data for 2-oxo-1,2,4,6,7,7a-hexahydro-indene-5,5-dicarboxylic acid dimethyl ester (172): ¹H NMR (300 MHz, CDCl₃) δ 5.88 (s, 1H), 3.68 (s, 3H), 3.63 (s, 3H), 3.40 (d with fine structure, *J* = 12.5 Hz, 1H), 2.66-2.38 (m, 4H), 2.09 (m, 1H), 1.92-1.81 (m, 2H), 1.19 (m, 1H); ¹³C NMR (75.5 MHz, CDCl₃) δ 208.0 (C), 178.4 (C), 171.1 (C), 169.8 (C), 129.6 (CH), 56.4 (C), 53.0 (CH₃), 52.6 (CH₃), 41.7 (CH₂), 40.4 (CH), 35.2 (CH₂), 30.55 (CH₂), 30.51 (CH₂); IR (thin film, NaCl) 3469 (m), 2955 (s), 2868 (m), 1734 (br s), 1628 (s), 1435 (s), 1251 (s); high resolution (EI) mass spectrum calculated for C₁₃H₁₆O₅ (M⁺) 252.0998, found 252.0998.

2-(4-Acetoxy-but-2-enyl)-2-(prop-2-ynyl)malonic acid dimethyl ester (173)



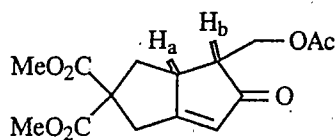
The title compound was prepared according to a literature method.²⁰ Data for 2-(4-acetoxy-but-2-enyl)-2-(prop-2-ynyl)malonic acid dimethyl ester (**173**): ¹H NMR (300 MHz, CDCl₃) δ 5.67 (m, 1H), 5.38 (m, 1H), 4.60 (d, *J* = 6.8 Hz, 2H), 3.69 (s, 6H), 2.82 (d, *J* = 7.9 Hz, 2H), 2.74 (d, *J* = 2.6 Hz, 2H), 2.00 (s with shoulder, 4H); ¹³C NMR (75.5 MHz, CDCl₃) δ 170.7 (C), 169.8 (2 x C), 128.4 (CH), 127.1 (CH), 78.4 (C), 71.7 (CH), 60.0 (CH₂), 56.5 (C), 52.8 (2 x CH₃), 30.1 (CH₂), 22.6 (CH₂), 20.8 (CH₃); IR (thin film, NaCl) 3284 (br s), 3004 (m), 2956 (s), 2122 (w), 1733 (br s), 1436 (s), 1212 (br s); high resolution (PCI/NH₃) mass spectrum calculated for C₁₄H₁₉NO₂S (M + H)⁺ 283.1182, found 283.1176.

***cis*-1-[(Acetoxy)methyl]-1,4,6,6a-tetrahydro-1*H*-pentalen-2-one 5,5-dicarboxylic acid dimethyl ester (174)**



The title compound was prepared in 78% yield using Procedure A except that 7.5 mol % Co₂(CO)₈ was used (12 h). The title compound was prepared in 81% yield using Procedure B except 10 mol % 2-Methyl-3-butyn-2-ol hexacarbonyldicobalt, 10 mol % Et₃SiH and 30 mol % thiophene were used. Data for *cis*-1-[(acetoxy)methyl]-1,4,6,6a-

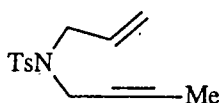
tetrahydro-1*H*-pentalen-2-one 5,5-dicarboxylic acid dimethyl ester (**174**): mp = 77-79 °C; ¹H NMR (300 MHz, CDCl₃) δ 5.89 (d, *J* = 1.5 Hz, 1H), 4.22 (dd, *J* = 11.3, 4.6 Hz, 1H), 4.00 (dd, *J* = 11.3, 9.0 Hz, 1H), 3.74 (s, 3H), 3.70 (s, 3H), 3.39-3.26 (m, 2H), 3.21 (m, 1H), 2.87 (ddd, *J* = 9.0, 6.9, 4.6 Hz, 1H), 2.60 (dd, *J* = 12.8, 7.8 Hz, 1H), 1.98 (s, 3H), 1.86 (app t, *J* = 12.8 Hz, 1H); ¹³C NMR (75.5 MHz, CDCl₃) δ 207.4 (C), 185.0 (C), 171.6 (C), 171.0 (C), 170.4 (C), 124.6 (CH), 62.2 (C), 60.2 (CH₂), 53.2 (CH₃), 53.1 (CH₃), 48.3 (CH), 47.7 (CH), 35.2 (CH₂), 34.0 (CH₂), 20.7 (CH₃); IR (NaCl, thin film) ; high resolution (PCI/NH₃) mass spectrum calculated for C₁₅H₁₉O₇ (M + H)⁺ 311.1131, found 311.1122. The stereochemical assignment was based on the following NOE data determined at 500 MHz (C₆D₆):



A 3% NOE of H_b was observed upon irradiation of H_a

A 5% NOE of H_a was observed upon irradiation of H_b

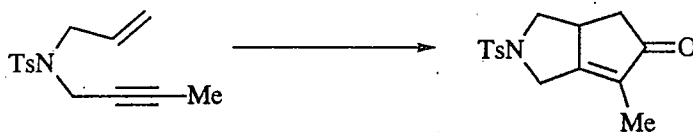
N-(2-propenyl)-*N*-(but-2-ynyl)-4-methylbenzenesulfonamide (**181**)



To a solution of *N*-(2-propenyl)-4-methylbenzenesulfonamide (2.50 g, 10.0 mmol, 1.00 equiv) in THF (25 mL) at -78 °C was added *n*-BuLi (7.4 mL of a 1.55 M solution in hexanes, 11.5 mmol, 1.15 equiv) dropwise. The solution was allowed to stir 20 min at -78 °C and then MeI (0.75 mL, 12.0 mmol, 1.2 equiv) was added. The reaction was allowed to warm to rt slowly and then stirred overnight (13 h). The suspension was

quenched with saturated NH_4Cl (20 mL) and extracted with ethyl acetate (100 mL). The organic fraction was washed with water (50 mL), brine (50 mL) and dried (MgSO_4). Evaporation of solvent and purification by flash chromatography (SiO_2 , 5% ethyl acetate in hexanes to 10% ethyl acetate in hexanes gradient for elution) afforded 2.32 g (88%) of the title compound as a slightly yellow oil which solidified in the freezer. Recrystallization from ethyl acetate/hexanes afforded colorless prisms. Data for *N*-(2-propenyl)-*N*-(but-2-ynyl)-4-methylbenzenesulfonamide (**181**): mp = 34-35 °C; ^1H NMR (300 MHz, CDCl_3) δ 7.70 (d, J = 8.2 Hz, 2H), 7.26 (d, J = 8.2 Hz, 2H), 5.70 (ddt, J = 17.1, 10.1, 6.4 Hz, 1H), 5.22 (m, 2H), 3.98 (app q, J = 2.4 Hz, 2H), 3.76 (d, J = 6.4 Hz, 2H), 2.38 (s, 3H), 1.50 (t, J = 2.4 Hz, 3H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 143.2 (C), 136.1 (C), 132.1 (CH), 129.2 (2 x CH), 127.8 (2 x CH), 119.4 (CH_2), 81.5 (C), 71.5 (C), 48.9 (CH_2), 36.2 (CH_2), 21.4 (CH_3), 3.13 (CH_3), IR (thin film, NaCl) 2920 (w), 1348 (s), 1163 (s), 754 (m), 663 (m); high resolution (PCI/ NH_3) mass spectrum calculated for $\text{C}_{14}\text{H}_{18}\text{NO}_2\text{S}$ ($\text{M} + \text{H}$) $^+$ 262.0902, found 262.0906.

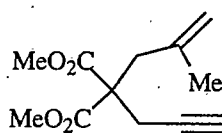
6-Methyl-2-[(4-methylbenzene)sulfonyl]-1,3,3a,4-tetrahydro-1*H*-cyclopenta<c>pyrrol-5-one (182**)**



The title compound was prepared in 78% yield using Procedure A except that 10 mol% $\text{Co}_2(\text{CO})_8$ was used (15 h). The title compound was prepared in 92% yield using Procedure B except 10 mol % 2-methyl-3-butyn-2-ol hexacarbonyldicobalt, 10 mol % Et_3SiH and 30 mol % cyclohexylamine were used (15 h). Data for 6-methyl-2-[(4-methylbenzene)sulfonyl]-1,3,3a,4-tetrahydro-1*H*-cyclopenta<c>pyrrol-5-one (**182**): mp =

95-97 °C; ^1H NMR (300 MHz, CDCl_3) δ 7.70 (d, $J = 8.2$ Hz, 2H), 7.31 (d, $J = 8.2$ Hz, 2H), 4.2 (d, $J = 16.0$ Hz, 1H), 3.98-3.92 (m, 2H), 2.97 (m, 1H), 2.61-2.50 (m, 2H), 2.40 (s, 3H), 1.99 (dd, $J = 18.1, 3.2$ Hz, 1H), 1.64 (s, 3H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 207.6 (C), 171.0 (C), 144.0 (C), 134.0 (C), 133.6 (C), 129.9 (2 x CH), 127.4 (2 x CH), 52.6 (CH_2), 46.7 (CH_2), 41.6 (CH), 39.1 (CH_2), 21.5 (CH_3), 8.74 (CH_3); IR (thin film, NaCl) 2922 (w), 1716 (m br), 1683 (m br), 1343 (m br), 1162 (m), 1094 (m), 659 (m); high resolution (PCI/ NH_3) mass spectrum calculated for $\text{C}_{15}\text{H}_{18}\text{NO}_3\text{S}$ ($\text{M} + \text{H}$) $^+$ 291.0929, found 291.0920.

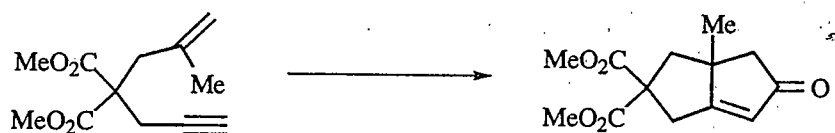
2-(But-3-enyl)-2-(prop-2-ynyl)malonic acid dimethyl ester (175)



To a suspension of NaH (0.35 g of a 60% dispersion in oil, 8.8 mmol, 1.1 equiv) in DMF/THF (14/4 mL) at 0 °C was added 2-(prop-2-ynyl)malonic acid dimethyl ester (1.1 g, 8.0 mmol, 1.00 equiv) dropwise over 15 min. The transfer was quantitated with THF (2 mL). The suspension was allowed to warm to rt and stirred 6 h. To the reaction mixture was added methallyl chloride (0.94 mL, 9.6 mmol, 1.2 equiv) dropwise and the resulting mixture was allowed to stir 6 h whereupon another portion of methallyl chloride (0.94 mL, 9.6 mmol, 1.2 equiv) was added and the mixture was allowed to stir overnight (13 h). The reaction mixture was quenched with the addition of satd NH_4Cl (5 mL) and then poured into ethyl acetate/water (50/25 mL). The organic phase was washed with water (20 mL), brine (20 mL) and dried (Na_2SO_4). Evaporation of solvent and purification by flash chromatography (SiO_2 , 5% ethyl acetate in hexanes) afforded 1.65 g (92 %) of the title compound as a slightly yellow oil. Kugelrohr distillation at 20 mTorr afforded the title

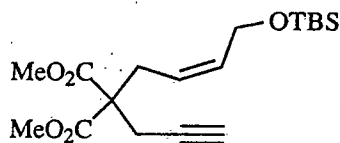
compound as a colorless oil. Data for 2-(but-3-enyl)-2-(prop-2-ynyl)malonic acid dimethyl ester (**175**): ^1H NMR (300 MHz, CDCl_3) δ 4.88-4.81 (m, 2H), 3.70 (s, 6H), 2.80 (s, 2H), 2.80 (obscured d, $J = 2.6$ Hz, 2H), 2.00 (t, $J = 2.6$ Hz, 1H), 1.61 (s, 3H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 170.5 (2 x C), 139.7 (C), 116.3 (CH_2), 79.0 (C), 71.6 (CH), 56.4 (C), 52.7 (2 x CH_3), 39.5 (CH_2), 23.1 (CH_3), 22.6 (CH_2); IR (thin film, NaCl) 3289 (m br), 2954 (m), 1739 (s br), 1436 (s), 1296 (s), 1210 (s br), 1061 (m), 978 (m), 904 (m); high resolution (EI) mass spectrum calculated for $\text{C}_{12}\text{H}_{16}\text{O}_4$ (M^+) 224.1049, found 224.1052.

3a-Methyl-5-oxo-3,3a,4,5-tetrahydro-1H-pentalene-2,2-dicarboxylic acid dimethyl ester (176)



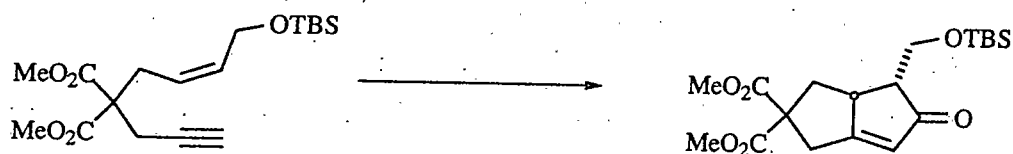
The title compound was prepared in 85% yield using Procedure A. The title compound was prepared in 95% yield using Procedure B. Recrystallization from ethyl acetate/hexanes gives colorless needles. Data for 3a-methyl-5-oxo-3,3a,4,5-tetrahydro-1H-pentalene-2,2-dicarboxylic acid dimethyl ester (**176**): mp = 63-64 °C; ^1H NMR (300 MHz, CDCl_3) δ 5.80 (d, $J = 1.8$ Hz, 1H), 3.77 (s, 3H), 3.70 (s, 3H), 3.48 (dd, $J = 17.7, 1.8$ Hz, 1H), 3.19 (d, $J = 17.7$ Hz, 1H), 2.57 (d, $J = 13.7$ Hz, 1H), 2.36 (s, 2H), 2.20 (d, $J = 13.7$ Hz, 1H), 1.12 (s, 3H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 209.0 (C), 188.1 (C), 172.0 (C), 171.7 (C), 124.3 (CH), 59.9 (C), 53.31 (CH_3), 53.26 (CH_3), 51.7 (CH_2), 49.8 (C), 44.5 (CH_2), 34.3 (CH_2), 26.5 (CH_3); IR (thin film, NaCl) 2958 (w), 1735 (s), 1711 (s), 1637 (m), 1437 (w), 1262 (br m), 1166 (m); high resolution (EI) mass spectrum calculated for $\text{C}_{13}\text{H}_{16}\text{O}_5$ (M^+) 252.0998, found 252.1001.

2-(4-[(1,1-Dimethylethyl)dimethylsilyl]oxy]-but-2-enyl)-2-(prop-2-ynyl)malonic acid dimethyl ester (177)

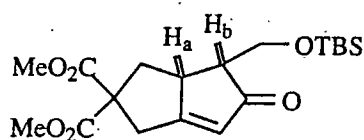


To a suspension of NaH (0.350 g of a 60% dispersion in oil, 4.76 mmol, 1.10 equiv) in DMF (5 mL) at 0 °C was added malonate (0.658 g, 4.76 mmol, 1.00 equiv) dropwise. The mixture was allowed to warm to rt and then was stirred 2 h. After 1 h, the reaction mixture was cooled to 0 °C and then *cis*-4-chloro-but-2-ol-trimethylsilyl ether (1.10 g, 5.00 mmol, 1.05 equiv) was added dropwise. The resulting mixture was allowed to warm to rt slowly and then was stirred overnight. The reaction mixture was quenched with the addition of saturated NH₄Cl (5 mL) and then poured into ethyl acetate/water (50/25 mL). The organic phase was washed with water (20 mL), brine (20 mL) and dried (Na₂SO₄). Evaporation of solvent and purification by flash chromatography (SiO₂, 5% ethyl acetate in hexanes) afforded 1.27 g (75%, >20/1 *cis*/*trans*) of the title compound as a colorless oil. Data for 2-(4-[(1,1-dimethylethyl)dimethylsilyl]oxy]-but-2-enyl)-2-(prop-2-ynyl)malonic acid dimethyl ester (177): ¹H NMR (300 MHz, C₆D₆) δ 5.76 (m, 1H), 5.26 (m, 1H), 4.31-4.29 (m, 2H), 3.30 (s, 6H), 3.08 (d, *J* = 7.8 Hz, 2H), 2.96 (d, *J* = 2.6 Hz, 2H), 1.74 (t, *J* = 2.6 Hz, 1H), 0.96 (s, 9H), 0.06 (s, 6H); ¹³C NMR (75.5 MHz, C₆D₆) δ 169.9 (2 x C), 135.3 (CH), 128.3 (CH), 79.2 (C), 71.9 (CH₃), 59.6 (CH₂), 57.1 (C), 52.4 (2 x CH₃), 30.8 (CH₂), 26.1 (3 x CH₃), 23.0 (CH₂), 18.4 (C), -5.1 (2 x CH₃); IR (thin film, NaCl) 3287 (m br), 3067 (w), 2954 (s), 1739 (s br); high resolution (EI) mass spectrum calculated for C₁₈H₃₁O₅Si (M + H)⁺ 355.1941, found 355.1951.

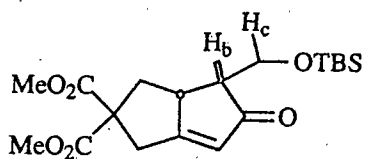
***cis*-1-[(1,1-Dimethylethyl)dimethylsilyl]oxy]-1,4,6,6a-tetrahydro-1*H*-pentalen-2-one 5,5-dicarboxylic acid dimethyl ester (178)**



The title compound was prepared in 84% yield using Procedure A except that 10 mol % $\text{Co}_2(\text{CO})_8$ was used (12 h). The title compound was prepared in 90% yield using Procedure B except 10 mol % 2-methyl-3-butyne-2-ol hexacarbonyldicobalt, 10 mol % Et_3SiH and 30 mol % cyclohexylamine were used (12 h). Recrystallization from diethyl ether/hexanes afforded colorless prisms. Data for *cis*-1-[(1,1-dimethylethyl)dimethylsilyl]oxy]-1,4,6,6a-tetrahydro-1*H*-pentalen-2-one 5,5-dicarboxylic acid dimethyl ester (178): mp = 61–63 °C; ^1H NMR (500 MHz, C_6D_6) δ 5.71 (d, J = 1.6 Hz, 1H), 3.78 (dd, J = 10.2, 6.5 Hz, 1H), 3.66 (dd, J = 10.2, 3.1 Hz, 1H), 3.31 (s, 3H), 3.29 (s, 3H), 3.16–3.05 (m, 2H), 2.92 (m, 1H), 2.69 (dd, J = 12.8, 7.7 Hz, 1H), 2.42 (app t, J = 12.8 Hz, 1H), 2.36 (ddd, J = 6.5, 6.5, 3.1 Hz, 1H), 0.88 (s, 9H), 0.01 (s, 3H), -0.02 (s, 3H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 208.0 (C), 184.5 (C), 172.1 (C), 171.2 (C), 125.4 (CH), 61.8 (CH_2), 60.7 (C), 52.6 (CH_3), 52.4 (CH_3), 52.0 (CH), 48.4 (CH_3), 35.2 (CH_2), 34.3 (CH_2), 25.9 (3 x CH_3), 18.1 (C), -5.6 (CH_3), -5.7 (CH_3); IR (NaCl, thin film) 2954 (s), 2857 (s), 1740 (s br), 1709 (s br), 1638 (s); high resolution (PCI/ NH_3) mass spectrum calculated for $\text{C}_{19}\text{H}_{31}\text{O}_6\text{Si}$ ($\text{M} + \text{H}$) $^+$ 383.1890, found 383.1873. The stereochemical assignment was based on the following NOE data determined at 500 MHz (C_6D_6):

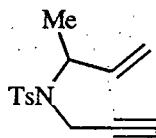


A 5% reciprocal NOE was observed between H_a and H_b



A 5% NOE of H_c was observed upon irradiation of H_b
A 3% NOE of H_b was observed upon irradiation of H_c

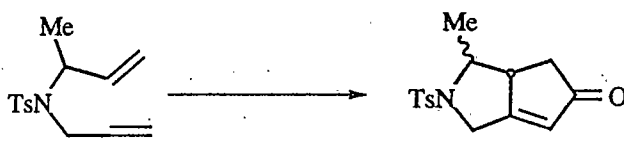
***N*-(1-Methyl-2-propenyl)-*N*-(prop-2-ynyl)-4-methylbenzenesulfonamide (179)**



To a suspension of *N*-(1-methyl-2-propenyl)-4-methylbenzenesulfonamide (1.02 g, 4.30 mmol, 1.00 equiv) and K_2CO_3 (0.890 g, 6.45 mmol, 1.50 equiv) in DMF (8 mL) was added propargyl bromide (0.68 mL, 8.6 mmol, 2.0 equiv) at rt. The resulting suspension was allowed to stir at rt overnight (15 h). The reaction mixture was partitioned between ethyl acetate/water (100/100 mL). The aqueous phase was extracted with ethyl acetate (50 mL) and the combined organic phases were washed with water (100 mL), brine (2 x 100 mL) and dried (Na_2SO_4). Evaporation of solvent and purification by flash chromatography (SiO_2 , 2% ethyl acetate in hexanes to 15% ethyl acetate in hexanes gradient for elution) afforded 1.13 g (95 %) of the title compound as a tan solid. Recrystallization from ethyl acetate/hexanes afforded a colorless, microcrystalline solid. Data for *N*-(1-methyl-2-propenyl)-*N*-(prop-2-ynyl)-4-methylbenzenesulfonamide (179) were consistent with that reported in the literature²⁰: 1H NMR (300 MHz, $CDCl_3$) δ 7.77 (d, J = 8.0 Hz, 2H), 7.25 (d, J = 8.0 Hz, 2H), 5.71 (m, 1H), 5.14-5.08 (m, 2H), 4.51 (m, 1H), 4.10 (dd, J = 18.5, 2.3 Hz, 1H), 3.84 (dd, J = 18.5, 2.3 Hz, 1H), 2.39 (s, 3H), 2.12 (t, J = 2.3 Hz, 1H),

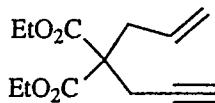
1.24 (d, $J = 7.0$ Hz, 3H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 143.3 (C), 137.7 (C), 137.3 (CH), 129.4 (2 x CH), 127.4 (2 x CH), 117.1 (CH_2), 80.1 (C), 72.3 (CH), 54.7 (CH), 32.2 (CH_2), 21.5 (CH_3), 17.0 (CH_3).

3-Methyl-2-[(4-methylbenzene)sulfonyl]-2,3,3a,4-tetrahydro-1H-cyclopenta< c >pyrrol-5-one (180)



The title compound was prepared in 84% yield using Procedure A (12 h). The title compound was prepared in 85% yield using Procedure B (12 h). The diastereomeric ratio using either procedure was identical (1.3/1.0, as determined by GC analysis). Data for 3-methyl-2-[(4-methylbenzene)sulfonyl]-2,3,3a,4-tetrahydro-1H-cyclopenta< c >pyrrol-5-one (180) were consistent with that reported in the literature.²⁰

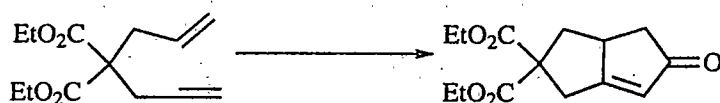
2-(2-Propenyl)-2-(prop-2-ynyl)malonic acid diethyl ester (19)



The title compound was prepared according to a literature method.²⁰ Data for 2-(2-Propenyl)-2-(prop-2-ynyl)malonic acid diethyl ester (19): ^1H NMR (300 MHz, CDCl_3) δ 5.62 (m, 1H), 5.15 (m, 2H), 4.14 (app q, $J = 7.1$ Hz, 4H), 2.73 (m, 4H), 1.96 (t with fine structure, $J = 2.5$ Hz, 1H), 1.19 (app t, $J = 7.1$ Hz, 6H); ^{13}C NMR (75.5 MHz,

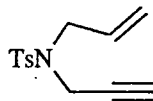
CDCl_3) δ 169.5 (2 x C), 131.6 (CH), 119.7 (CH_2), 78.7 (C), 71.3 (CH), 61.5 (2 x CH_2), 56.5 (C), 36.2 (CH_2), 22.4 (CH_2), 13.9 (2 x CH_3).

5-Oxo-3,3a,4,5-tetrahydro-1*H*-pentalene-2,2-dicarboxylic acid diethyl ester (20)



The title compound was prepared in 83% yield using Procedure A. The title compound was prepared in 92% yield using Procedure B (12 h). Data for 5-oxo-3,3a,4,5-tetrahydro-1*H*-pentalene-2,2-dicarboxylic acid diethyl ester (**20**) were consistent with that reported in the literature²⁰: ^1H NMR (300 MHz, CDCl_3) δ 5.84 (s with fine structure, 1H), 4.16 (q, J = 7.2 Hz, 2H), 4.12 (q, J = 7.2 Hz, 2H), 3.27 (br d, J = 19.0 Hz, 1H), 3.16 (br d, J = 19.0 Hz, 1H), 3.02 (m, 1H), 2.72 (dd, J = 12.8, 7.7 Hz, 1H), 2.54 (dd, J = 17.9, 6.4 Hz, 1H), 2.02 (dd, J = 17.9, 3.3 Hz, 1H), 1.66 (app t, J = 12.8 Hz, 1H), 1.20 (t, J = 7.2 Hz, 3H), 1.17 (t, J = 7.2 Hz, 3H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 209.2 (C), 185.4 (C), 171.2 (C), 170.5 (C), 125.3 (CH), 61.9 (CH_2), 61.8 (CH_2), 60.6 (C), 44.8 (CH), 41.9 (CH_2), 38.7 (CH_2), 34.9 (CH_2), 13.8 (2 x CH_3).

***N*-(2-propenyl)-*N*-(prop-2-ynyl)-4-methylbenzenesulfonamide (17)**



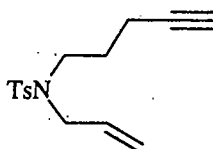
The title compound was prepared according to a literature method.²⁰ Data for *N*-(2-propenyl)-*N*-(prop-2-ynyl)-4-methylbenzenesulfonamide (**17**): ^1H NMR (300 MHz,

CDCl₃) δ 7.70 (d, J = 8.2 Hz, 2H), 7.26 (d, J = 8.2 Hz, 2H), 5.69 (ddt, J = 16.9, 6.6, 6.5 Hz, 1H), 5.29-5.18 (m, 2H), 4.06 (d, J = 2.4 Hz, 2H), 3.79 (d, J = 6.6 Hz, 2H), 2.39 (s, 3H), 1.98 (t, J = 2.4 Hz, 1H); ¹³C NMR (75.5 MHz, CDCl₃) δ 143.5 (C), 135.9 (C), 131.8 (CH), 129.4 (2 x CH), 127.6 (2 x CH), 119.9 (CH₂), 76.4 (C), 73.7 (CH), 48.9 (CH₂), 35.7 (CH₂), 21.5 (CH₃).

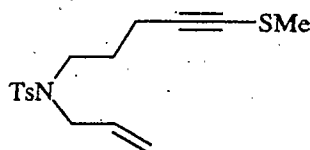
2-[(4-Methylbenzene)sulfonyl]-2,3,3a,4-tetrahydro-1*H*-cyclopenta<c>pyrrol-5-one (18)



The title compound was prepared in 86% yield using Procedure A except that 7.5 mol % Co₂(CO)₈ was used (12 h). The title compound was prepared in 77% yield using Procedure B except 7.5 mol % 2-methyl-3-butyn-2-ol hexacarbonyldicobalt, 7.5 mol % Et₃SiH and 22.5 mol % cyclohexylamine were used (12 h). Data for 2-[(4-methylbenzene)sulfonyl]-2,3,3a,4-tetrahydro-1*H*-cyclopenta<c>pyrrol-5-one (**18**) were consistent with that reported in the literature²⁰: ¹H NMR (300 MHz, CDCl₃) δ 7.70 (d, J = 8.2 Hz, 2H), 7.32 (d, J = 8.2 Hz, 2H), 5.96 (s, 1H), 4.30 (d, J = 16.6 Hz, 1H), 4.02-3.96 (m, 2H), 3.13 (m, 1H), 2.60 (m, 1H), 2.55 (dd, J = 11.4, 6.6 Hz, 1H), 2.41 (s, 3H), 2.02 (dd, J = 17.9, 3.6 Hz, 1H); ¹³C NMR (75.5 MHz, CDCl₃) δ 207.4 (C), 178.7 (C), 144.1 (C), 133.4 (C), 130.0 (2 x CH), 127.4 (2 x CH), 126.2 (CH), 52.4 (CH₂), 47.6 (CH₂), 43.9 (CH), 39.8 (CH₂), 21.5 (CH₃).

***N*-(2-propenyl)-*N*-(pent-4-ynyl)-4-methylbenzenesulfonamide**

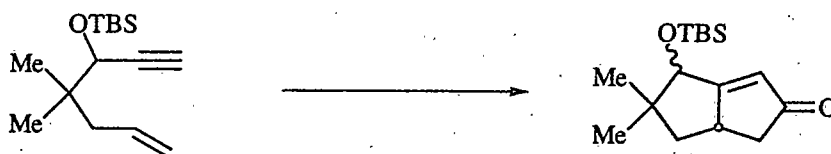
To a solution of *N*-(2-propenyl)-4-methylbenzenesulfonamide (1.06 g, 5.00 mmol, 1.00 equiv), PPh_3 (1.51 g, 5.75 mmol, 1.15 equiv) and 5-trimethylsilyl-pent-4-yn-1-ol (0.899 g, 5.75 mmol, 1.15 equiv) in THF (12 mL) at 0°C was added DIAD (1.1 mL, 5.75 mmol, 1.15 equiv) dropwise over 10 min. The resulting solution was allowed to stir for 15 min at 0°C and then was allowed to warm to room temperature and stirred overnight. The solvent was removed in vacuo and the residue was dissolved in MeOH (5 mL). To the solution at rt was added K_2CO_3 (0.83 g, 6.00 mmol, 1.04 equiv) in one portion. The resulting suspension was allowed to stir 2 h and then was partitioned between ethyl acetate and water (30/30 mL). The organic phase was washed with water (30 mL) and brine (30 mL). Evaporation of solvent and purification of the residue by flash chromatography (SiO_2 , hexanes to 5% ethyl acetate in hexanes gradient for elution) afforded 1.18 g (85%) of *N*-(2-propenyl)-*N*-(pent-4-ynyl)-4-methylbenzenesulfonamide as a viscous colorless oil. Spectral data for the title compound were consistent with that reported in the literature²⁰: ^1H NMR (300 MHz, CDCl_3) δ 7.68 (d, $J = 8.2$ Hz, 2H), 7.28 (d, $J = 8.2$ Hz, 2H), 5.62 (ddt, $J = 16.6, 10.0, 6.6$ Hz, 1H), 5.28-5.10 (m, 2H), 3.78 (d, $J = 6.4$ Hz, 2H), 3.19 (t, $J = 7.2$ Hz, 2H), 2.41 (s, 3H), 2.18 (dt, $J = 7.2, 2.6$ Hz, 2H), 1.92 (t, $J = 2.6$ Hz, 1H), 1.75 (tt, $J = 7.2, 7.2$ Hz, 2H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 143.1 (C), 136.7 (C), 132.9 (CH), 129.6 (2 x CH), 127.0 (2 x CH), 118.9 (CH_2), 83.1 (C), 68.9 (CH), 50.9 (CH_2), 46.3 (CH_2), 27.2 (CH_2), 21.3 (CH_3), 15.6 (CH_2).

***N*-(2-propenyl)-*N*-(5-methylthio-pent-4-ynyl)-4-methylbenzenesulfonamide**

To a solution of for *N*-(2-propenyl)-*N*-(pent-4-ynyl)-4-methylbenzenesulfonamide (0.832 g, 3.00 mmol, 1.00 equiv) in THF (7.5 mL) at -78°C was added *n*-BuLi (2.0 mL, 3.15 mmol, 1.05 equiv) over 5 min. The resulting solution was allowed to stir 5 min at -78°C at which time MeSCN (0.24 mL, 3.4 mmol, 1.2 equiv) was added dropwise. The resulting suspension was allowed to stir 1 h at -78°C and then was quenched by the addition of saturated NH_4Cl (3 mL) and allowed to warm to room temperature. The reaction mixture was poured into ethyl acetate and water (30/25 mL). The organic phase was washed with water (25 mL), brine (25 mL), and dried (MgSO_4). Evaporation of solvent and purification of the residue by flash chromatography (SiO_2 , 5% ethyl acetate in hexanes to 10% ethyl acetate in hexanes gradient for elution) afforded 0.79 g (81%) of the title compound as a pale yellow oil. Data for *N*-(2-propenyl)-*N*-(5-methylthio-pent-4-ynyl)-4-methylbenzenesulfonamide: ^1H NMR (300 MHz, CDCl_3) δ 7.67 (d, $J = 8.4$ Hz, 2H), 7.27 (d, $J = 8.4$ Hz, 2H), 5.68-5.54 (ddt, $J = 16.8, 10.0, 6.5$ Hz, 1H), 5.19-5.10 (m, 2H), 3.77 (d, $J = 6.5$ Hz, 2H), 3.16 (t, $J = 7.2$ Hz, 2H), 2.40 (s, 3H), 2.31 (s, 3H), 2.26 (t, $J = 7.2$ Hz, 2H), 1.71 (tt, $J = 7.2, 7.2$ Hz, 2H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 143.2 (C), 136.8 (C), 133.1 (CH), 129.6 (2 x CH), 127.1 (2 x CH), 119.0 (CH_2), 91.7 (C), 70.9 (C), 51.0 (CH_2), 46.3 (CH_2), 27.5 (CH_2), 21.4 (CH_3), 19.1 (CH_3), 17.4 (CH_2); IR (thin film, NaCl) 3081 (m), 2927 (m), 2870 (m), 2189 (w), 1921 (w), 1598 (m), 1345 (s), 1152 (s), 1093 (s), 924 (s), 816 (s), 747 (s), 661 (s), 545 (s); high

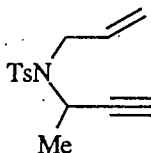
resolution (PCI/NH₃) mass spectrum calculated for C₁₆H₂₁NO₂S₂ (M⁺) 323.1032, found 323.1014.

5,5-dimethyl-4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-4,5,6,6a-tetrahydro-2(1*H*)-pentalenone (184)



The title compound was prepared as a mixture of diastereomers (1.3/1) in 75% yield using Procedure A except that 10 mol % Co₂(CO)₈ was used (12h). Data for 5,5-dimethyl-4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-4,5,6,6a-tetrahydro-2(1*H*)-pentalenone (184) were consistent with that reported in the literature.²⁰

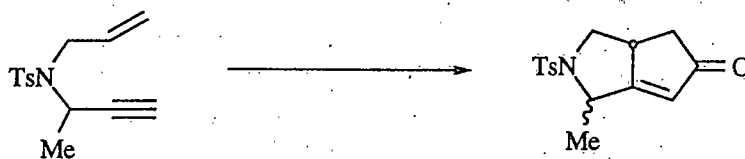
***N*-(1-Methyl-prop-2-ynyl)-*N*-(2-propenyl)-4-methylbenzenesulfonamide (187)**



To a suspension of *N*-(1-methyl-prop-2-ynyl)-4-methylbenzenesulfonamide (0.89 g, 4.0 mmol, 1.00 equiv) and K₂CO₃ (1.1 g, 8.0 mmol, 2.0 equiv) in DMF (8 mL) at room temperature was added allyl bromide (0.52 mL, 6.0 mmol, 1.5 equiv). The resulting suspension was allowed to stir for 3 h and then was partitioned between ethyl acetate and water (30/30 mL). The organic phase was washed with water (2 x 30 mL), brine (2 x 30

mL) and dried (MgSO_4). Evaporation of solvent and purification by flash chromatography (chromatography (SiO_2 , hexanes to 5% ethyl acetate in hexanes gradient for elution) afforded 1.02 g (97%) of *N*-(1-methyl-prop-2-ynyl)-*N*-(2-propenyl)-4-methylbenzenesulfonamide (**187**) as a pale yellow oil. Spectral data for the title compound were consistent with that reported in the literature.⁹⁹ ^1H NMR (300 MHz, CDCl_3) δ 7.68 (d with fine structure, $J = 8.2$ Hz, 2H), 7.25 (d, $J = 8.2$ Hz, 2H), 5.88 (m, 1H), 5.22 (m, 1H), 5.09 (m, 1H), 4.87 (m, 1H), 3.90 (m, 1H), 3.70 (m, 1H), 2.38 (s, 3H), 2.10 (d, $J = 2.3$ Hz, 1H), 1.41 (d, $J = 7.1$ Hz, 3H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 143.3 (C), 136.2 (C), 135.8 (CH), 129.4 (2 x CH), 127.5 (2 x CH), 117.1 (CH_2), 81.2 (C), 73.3 (CH), 47.2 (CH_2), 46.1 (CH), 22.6 (CH_3), 21.4 (CH_3).

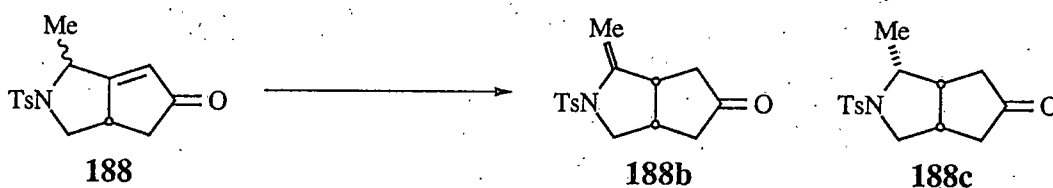
1-Methyl-2-[(4-methylbenzene)sulfonyl]-2,3,3a,4-tetrahydro-1*H*-cyclopentacpyrrol-5-one (188**)**



The title compound was prepared as a mixture of diastereomers (2.1/1) in 92% yield using Procedure A (12 h). The title compound was prepared as a mixture of diastereomers (1.9/1) in 77% yield using Procedure B (12 h). Purification by flash chromatography (SiO_2 , 15% ethyl acetate in hexanes to 40% ethyl acetate gradient for elution) afforded the title compound as a colorless, viscous oil. Data for syn- and anti-1-methyl-2-[(4-methylbenzene)sulfonyl]-2,3,3a,4-tetrahydro-1*H*-cyclopentacpyrrol-5-one (**188**): ^1H NMR (300 MHz, CDCl_3) δ 7.68 (d, $J = 7.7$ Hz, 2H), 7.61 (d, $J = 7.7$ Hz, 2H), 7.25 (app d, $J = 7.7$ Hz, 4H), 5.88 (s, 1H), 5.76 (s, 1H), 4.46 (q, $J = 6.7$ Hz, 1H), 4.22 (q, $J =$

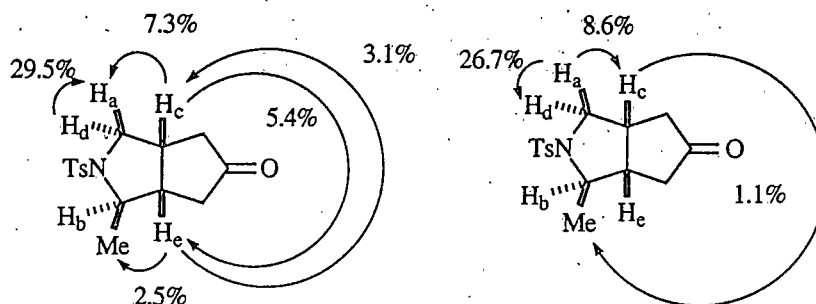
6.7 Hz, 1H), 3.94 (app t, $J = 10.2$ Hz, 1H), 3.87 (app t, $J = 8.4$ Hz, 1H), 3.32 (m, 1H), 2.87 (app t, $J = 11.6$ Hz, 1H), 2.51 (dd, $J = 17.9, 6.5$ Hz, 1H), 2.42-2.38 (m, 2H), 2.34 (br s, 6H), 1.96 (m, 1H), 1.95 (m, 2H), 1.52 (d, $J = 6.7$ Hz, 3H), 1.48 (d, $J = 6.7$ Hz, 3H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 207.4 (2 x C), 185.5 (C), 182.8 (C), 143.94 (C), 143.81 (C), 135.3 (C), 132.7 (C), 129.90 (2 x CH), 129.73 (2 x CH), 127.4 (2 x CH), 126.9 (2 x CH), 125.5 (CH), 124.1 (CH), 55.3 (CH), 55.2 (CH), 53.2 (CH_2), 51.7 (CH_2), 42.9 (CH), 41.1 (CH), 40.0 (CH_2), 39.5 (CH_2), 22.0 (CH_3), 21.3 (2 x CH_3), 20.3 (CH_3); IR (thin film) 3409 (m), 2978 (m), 2930 (m), 1716 (s br), 1652 (s), 1343 (s br), 1163 (s br), 1093 (s), 819 (s), 667 (s); major diastereomer: high resolution (EI) mass spectrum calculated for $\text{C}_{15}\text{H}_{17}\text{NO}_3\text{S}$ (291.0930), found 291.0929; minor diastereomer: high resolution (EI) mass spectrum calculated for $\text{C}_{15}\text{H}_{17}\text{NO}_3\text{S}$ (M^+) 291.0933, found 291.0929.

Syn-1-Methyl-2-[(4-methylbenzene)sulfonyl]-hexahydro-1*H*-cyclopentacpyrrol-5-one (188b) and anti-1-methyl-2-[(4-methylbenzene)sulfonyl]-hexahydro-1*H*-cyclopentacpyrrol-5-one (188c)

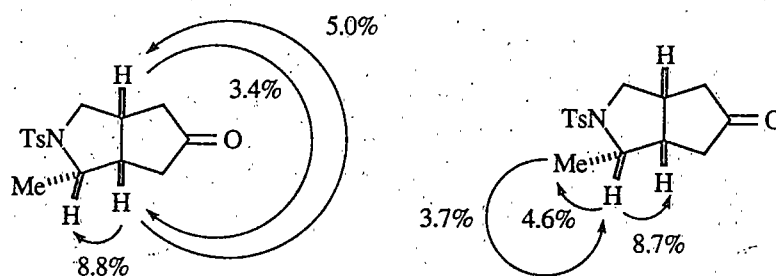


A solution of syn- and anti-1-methyl-2-[(4-methylbenzene)sulfonyl]-2,3,3a,4-tetrahydro-1*H*-cyclopentacpyrrol-5-one (188) (0.129 g, 0.443 mmol, 1.00 equiv, 1.5/1 mixture of diastereomers) and $\text{Pd}(\text{OH})_2$ (13 mg of 20% $\text{Pd}(\text{OH})_2$ on carbon) in ethyl acetate (1.5 mL) under an atmosphere of dihydrogen was allowed to stir 2 h. Filtration of the suspension through celite and concentration afforded 0.126 g of the title compounds.

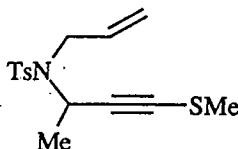
Analysis of the crude residue by ^1H NMR revealed a 1.5/1 mixture of diastereomers. Purification by flash chromatography (basic Al_2O_3 , 13 x 2 cm, 5% ethyl acetate in hexanes to 25% ethyl acetate in hexanes gradient for elution) afforded syn-1-methyl-2-[(4-methylbenzene)sulfonyl]-2,3,3a,4-tetrahydro-1*H*-cyclopenta$\langle c \rangle$pyrrol-5-one (**188b**) and anti-1-methyl-2-[(4-methylbenzene)sulfonyl]-2,3,3a,4-tetrahydro-1*H*-cyclopenta$\langle c \rangle$pyrrol-5-one (**188c**). Data for syn-1-methyl-2-[(4-methylbenzene)sulfonyl]-2,3,3a,4-tetrahydro-1*H*-cyclopenta$\langle c \rangle$-pyrrol-5-one (**188b**) (major diastereomer, less polar): ^1H NMR (300 MHz, CDCl_3) δ 7.68 (d, $J = 8.2$ Hz, 2H), 7.29 (d, $J = 8.2$ Hz, 2H), 3.76 (dd, $J = 10.0, 7.2$ Hz, 1H), 3.50 (dq, $J = 6.4, 3.4$ Hz, 1H), 3.00 (m, 1H), 2.90 (dd, $J = 10.0, 7.2$ Hz, 1H), 2.47 (m, 1H), 2.41 (s, 3H), 2.28 (app d, $J = 8.5$ Hz, 1H), 2.21 (app d, $J = 8.5$ Hz, 1H), 1.79 (dd, $J = 19.1, 3.4$ Hz, 1H), 1.40-1.23 (obscured peak, 1H), 1.39 (d, $J = 6.4$ Hz, 3H); ^{13}C NMR (62.9 MHz, CDCl_3) δ 216.5 (C), 143.8 (C), 134.2 (C), 129.8 (2 x CH), 127.3 (2 x CH), 61.3 (CH), 52.9 (CH_2), 47.6 (CH), 41.5 (CH_2), 41.1 (CH_2), 37.6 (CH), 22.3 (CH_3), 21.6 (CH_3); IR (NaCl, thin film) 2966 (w), 2928 (w), 2851 (w), 1742 (s), 1341 (m), 1091 (s); major diastereomer: high resolution (EI) mass spectrum calculated for $\text{C}_{14}\text{H}_{16}\text{NO}_3\text{S}$ ($\text{M} - \text{CH}_3$) $^+$ 293.1086, found 293.1084. The stereochemical assignment was based on the following NOE data determined at 500 MHz (CDCl_3):



Data for anti-1-methyl-2-[(4-methylbenzene)sulfonyl]-2,3,3a,4-tetrahydro-1*H*-cyclopenta<c>pyrrol-5-one (**188c**) (minor diastereomer, more polar): ^1H NMR (300 MHz, CDCl_3) δ 7.70 (d, $J = 8.1$ Hz, 2H), 7.32 (d, $J = 8.1$ Hz, 2H), 3.67 (q, $J = 6.6$ Hz, 1H), 3.58 (dd, $J = 11.4, 8.7$ Hz, 1H), 3.16 (dd, $J = 11.4, 8.7$ Hz, 1H), 2.74 (m, 1H), 2.52 (m, 1H), 2.42 (s, 3H), 2.31-2.23 (m, 2H), 2.14 (dd, $J = 19.0, 3.4$ Hz, 1H), 1.41-1.35 (obscured peak, 1H), 1.34 (d, $J = 6.6$ Hz, 3H); ^{13}C NMR (62.9 MHz, CDCl_3) δ 216.0 (C), 143.7 (C), 134.2 (C), 129.8 (2 x CH), 127.5 (2 x CH), 58.3 (CH_2), 53.6 (CH_2), 45.0 (CH), 42.0 (CH_2), 38.3 (CH_2), 37.5 (CH), 21.5 (CH_3), 18.4 (CH_3); IR (NaCl, thin film) 2929 (w), 1742 (s), 1338 (s), 1161 (s), 1090 (m); high resolution (EI) mass spectrum calculated for $\text{C}_{14}\text{H}_{16}\text{NO}_3\text{S}$ ($\text{M} - \text{CH}_3$) $^+$ 293.1086, found 293.1084. The stereochemical assignment was based on the following NOE data determined at 500 MHz (CDCl_3):



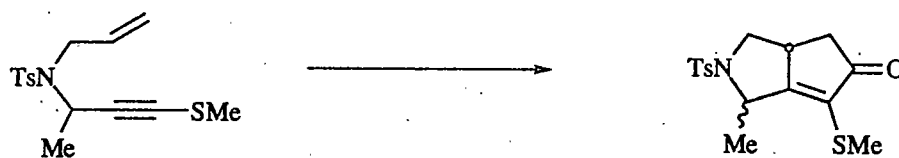
***N*-(1-Methyl-3-methylthio-prop-2-ynyl)-*N*-(2-propenyl)-4-methylbenzenesulfonamide (201)**



To a solution of *N*-(1-methyl-prop-2-ynyl)-*N*-(2-propenyl)-4-methylbenzenesulfonamide (187) (0.631 g, 2.40 mmol, 1.00 equiv) in THF (6 mL) at -78°C was added *n*-BuLi (1.6 mL of a 1.6 M solution in hexanes, 2.52 mmol, 1.05 equiv) over 5 min. The resulting solution was allowed to stir 5 min at -78°C at which time MeSCN (189 μL , 2.76 mmol, 1.15 equiv) was added dropwise. The resulting suspension was allowed to stir 1 h at -78°C and then was quenched by the addition of saturated NH_4Cl (3 mL) and allowed to warm to room temperature. The reaction mixture was poured into ethyl acetate and water (30/25 mL). The organic phase was washed with water (25 mL), brine (25 mL), and dried (MgSO_4). Evaporation of solvent and purification by flash chromatography (SiO_2 , hexanes to 10% ethyl acetate in hexanes gradient for elution) afforded 1.0 g (85%) of the title compound as a pale yellow semi-solid. Data for *N*-(1-methyl-3-methylthio-prop-2-ynyl)-*N*-(2-propenyl)-4-methylbenzenesulfonamide (201): ^1H NMR (300 MHz, CDCl_3) δ 7.64 (d, $J = 8.2$ Hz, 2H), 7.22 (d, $J = 8.2$ Hz, 2H), 5.84 (m, 1H), 5.41 (app dt, $J = 17.1, 1.4$ Hz, 1H), 5.04 (app dt, $J = 10.2, 1.4$ Hz, 1H), 4.87 (app q, $J = 7.1$ Hz, 1H), 3.84 (m, 1H), 3.62 (m, 1H), 2.33 (s, 3H), 2.05 (s with fine structure, 3H), 1.33 (d with fine structure, $J = 7.1$ Hz, 3H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 143.1 (C), 135.95 (CH), 135.68 (C), 129.2 (2 x CH), 127.4 (2 x CH), 116.7 (CH_2), 89.6 (C), 76.6 (C), 47.17 (CH), 47.14 (CH_2), 22.3 (CH_3), 21.2 (CH_3), 18.5 (CH_3); IR (thin film, NaCl) 3081 (w), 2985 (m), 2930 (m), 2870 (w), 2173 (m), 1344 (s), 1167 (s), 1008 (m br), 668 (s), 566

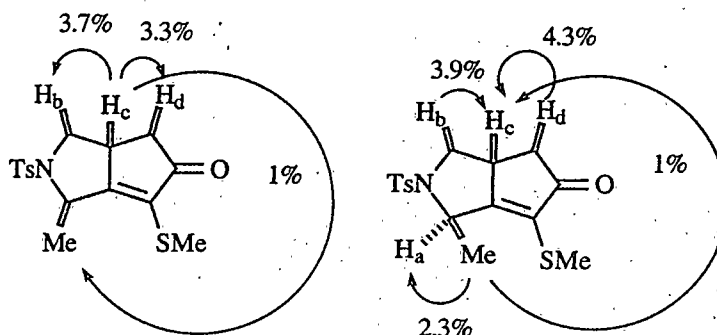
(s); high resolution (EI) mass spectrum calculated for $C_{15}H_{19}NO_2S_2$ (M^+) 309.0855, found 309.0857.

1-Methyl-2-[(4-methylbenzene)sulfonyl]-7-methylthio-2,3,3a,4-tetrahydro-1*H*-cyclopenta<c>pyrrol-5-one (206)

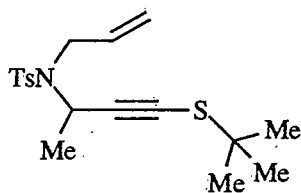


The title compound was prepared as a mixture of diastereomers (2.7/1) in 93% yield using Procedure A (12 h). The title compound was prepared as a mixture of diastereomers (2.6/1) in 90 % yield using Procedure B (12 h). Purification by flash chromatography (SiO_2 , 15% ethyl acetate in hexanes to 40% ethyl acetate gradient for elution) afforded the title compound as a colorless, viscous oil. Further purification by flash chromatography (SiO_2 , 5% ethyl acetate to 25% ethyl acetate in hexanes gradient for elution) afforded syn-1-methyl-2-[(4-methylbenzene)sulfonyl]-7-methylthio-2,3,3a,4-tetrahydro-1*H*-cyclopenta<c>pyrrol-5-one (**206**) (major diastereomer, less polar): Data for the major isomer **206**: 1H NMR (300 MHz, $CDCl_3$) δ 7.70 (d, $J = 8.1$ Hz, 2H), 7.32 (d, $J = 8.1$ Hz, 2H), 4.38 (q, $J = 6.5$ Hz, 1H), 3.90 (app t, $J = 8.2$ Hz, 1H), 3.28 (m, 1H), 2.65 (dd, $J = 17.8, 6.5$ Hz, 1H), 2.46-2.38 (obscured peak, 1H), 2.42 (s, 3H), 2.30 (s, 3H), 2.04 (dd, $J = 17.8, 3.4$ Hz, 1H), 1.56 (d, $J = 6.5$ Hz, 3H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 203.9 (C), 176.0 (C), 144.1 (C), 133.2 (C), 130.9 (C), 129.9 (2 x CH), 127.7 (2 x CH), 55.5 (CH_2), 53.3 (CH_2), 39.766 (CH), 39.700 (CH), 21.6 (2 x CH_3), 13.8 (CH_3); IR (NaCl, thin film) 2977 (w), 2927 (w), 1714 (br m), 1343 (br m), 1162 (s); high resolution (EI) mass spectrum calculated for $C_{16}H_{19}NO_3S_2$ (337.0800), found 337.0806. minor

diastereomer: high resolution (EI) mass spectrum calculated for $C_{16}H_{19}NO_3S_2$ (M^+) 337.0803, found 337.0806. The stereochemical assignment of the major diastereomer was based on the following GOESY data (mixing time = 800 msec) determined at 250 MHz ($CDCl_3$):



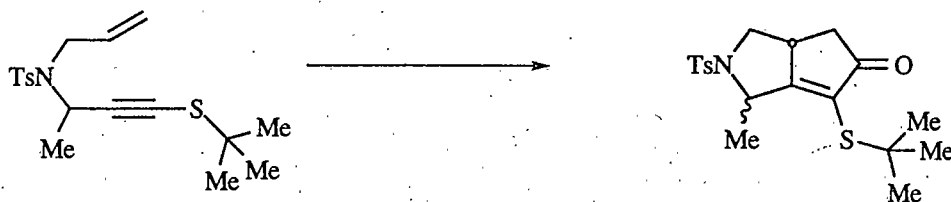
***N*-(1-Methyl-3-[(1,1-dimethylethyl)thio]-prop-2-ynyl)-*N*-(2-propenyl)-4-methylbenzenesulfonamide (212)**



To a solution of *N*-(1-methyl-prop-2-ynyl)-*N*-(2-propenyl)-4-methylbenzenesulfonamide (287) (0.750 g, 2.85 mmol, 1.00 equiv) in THF (7 mL) at $-78^\circ C$ was added *n*-BuLi (1.9 mL of a 1.6 M solution in hexanes, 3.08 mmol, 1.08 equiv) dropwise. The resulting solution was allowed to stir 10 min at that temperature and then a solution of *t*-butylsulfenylsulfonate (0.836 g, 3.42 mmol, 1.2 equiv) was added dropwise. The resulting solution was allowed to warm to rt over 2 h and then was quenched by the addition of half saturated NH_4Cl (10 mL). The mixture was partitioned between ethyl acetate/water (75/10 mL). The organic phase was washed with water (20 mL), brine (25

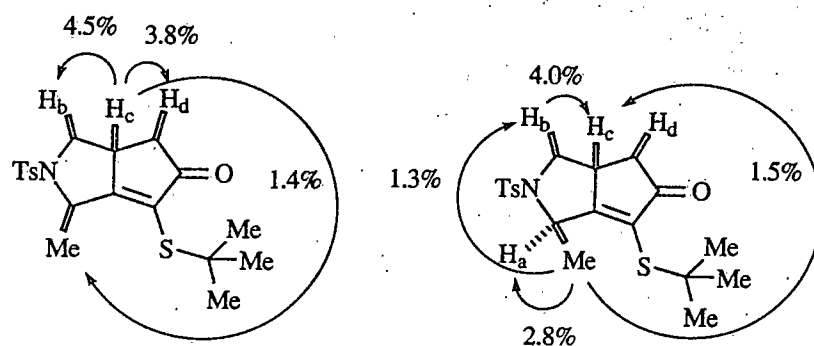
mL) and dried (MgSO_4). Concentration and purification by flash chromatography afforded 0.65 g (65%) of the title compound as a colorless oil. Data for the title compound **212**: ^1H NMR (300 MHz, CDCl_3) δ 7.70 (d, $J = 8.2$ Hz, 2H), 7.26 (d, $J = 8.2$ Hz, 2H), 5.91 (dddd, $J = 17.2, 10.2, 7.0, 5.0$ Hz, 1H), 5.24 (m, 1H), 5.10 (m, 1H), 5.00 (app q, $J = 7.1$ Hz, 1H), 3.92 (m, 1H), 3.73 (dd with fine structure, $J = 17.4, 7.0$ Hz, 1H), 2.39 (s, 3H), 1.45 (d, $J = 7.1$ Hz, 3H), 1.23 (s, 9H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 143.2 (C), 136.4 (C), 135.9 (CH), 129.5 (2 x CH), 127.4 (2 x CH), 117.0 (CH_2), 94.1 (C), 75.0 (C), 30.8 (C), 47.55 (CH), 47.38 (CH_2), 30.0 (3 x CH_3), 23.1 (CH_3), 21.4 (CH_3); IR (thin film, NaCl) 2964 (w), 2924 (w), 2867 (w), 2168 (w), 1335 (br m), 1166 (m), 669 (m); high resolution (EI) mass spectrum calculated for $\text{C}_{18}\text{H}_{25}\text{NO}_2\text{S}_2$ ($\text{M} - \text{C}_4\text{H}_9$) $^+$ 294.0622, found 294.0616.

1-Methyl-2-[(4-methylbenzene)sulfonyl]-7-[(1,1-dimethylethyl)thio]-2,3,3a,4-tetrahydro-1*H*-cyclopenta< c >pyrrol-5-one (206)

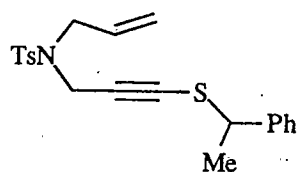


The title compound was prepared as a mixture of diastereomers (5/1) in 70% yield using Procedure C (9 h) expect that 10 mol % $\text{Co}_2(\text{CO})_8$ was used. Recrystallization from ethyl acetate/hexanes afforded the major diastereomer. Data for major diastereomer: mp = 162–163 °C; ^1H NMR (300 MHz, CDCl_3) δ 7.68 (d, $J = 8.4$ Hz, 2H), 7.28 (d, $J = 8.4$ Hz, 2H), 4.33 (q, $J = 6.5$ Hz, 1H), 4.00 (app t, $J = 8.6$ Hz, 1H), 3.36 (m, 1H), 2.71 (dd, $J = 18.0, 6.7$ Hz, 1H), 2.44 (dd, $J = 10.8, 8.6$ Hz, 1H), 2.38 (s, 3H), 2.07 (dd, $J = 18.0, 3.5$ Hz, 1H), 1.58 (d, $J = 6.5$ Hz, 3H), 1.10 (s, 9H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 205.1 (C), 187.1 (C), 144.1 (C), 132.6 (C), 129.8 (2 x CH), 129.5 (C), 127.7 (2 x CH),

56.0 (CH), 53.8 (CH₂), 48.0 (C), 39.72 (CH), 39.44 (CH₂), 31.8 (3 x CH₃), 22.0 (CH₃), 21.5 (CH₃); IR (thin film, NaCl) 2965 (w), 2923 (w), 2897 (w), 2864 (w), 1720 (br m), 1637 (w), 1598 (w), 1457 (w), 1345 (m), 1167 (s), 1093 (m), 1038 (m), 817 (w), 755 (w), 673 (w); high resolution (EI) mass spectrum calculated for C₁₉H₂₅NO₃S₂ (M⁺) 379.1276, found 379.1265. The stereochemical assignment of the major diastereomer was based on the following GOESY data (mixing time = 800 msec) determined at 250 MHz (CDCl₃):



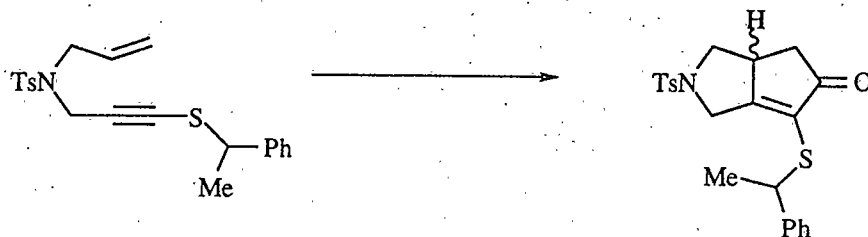
***N*-(2-Propenyl)-*N*-[3-(1-phenyl-ethylthio)-prop-2-ynyl]-4-methylbenzenesulfonamide (213)**



To a solution of *N*-(2-propenyl)-*N*-(prop-2-ynyl)-4-methylbenzenesulfonamide (17) (0.748 g, 3.00 mmol, 1.00 equiv) in THF (10 mL) at -78 °C was added *n*-BuLi (2.0 mL of a 1.6 M solution in hexanes, 3.24 mmol, 1.08 equiv) dropwise. After 5 min at -78 °C, phenethyl thiocyanate (0.560 g, 3.45 mmol, 1.15 equiv) was added dropwise and the resulting solution was allowed to warm to rt slowly over 2 h. The reaction mixture was

quenched by the addition of saturated NH_4Cl (5 mL). The mixture was extracted with ethyl acetate and water (40/30 mL). The organic phase was washed with water (2 x 30 mL), brine (30 mL) and dried (MgSO_4). Evaporation of the solvents and purification by flash chromatography (SiO_2 , 10% ethyl acetate in hexanes to 15% ethyl acetate in hexanes gradient for elution) afforded 0.81 g (70%) of the title compound as an viscous orange oil. Data for *N*-(2-propenyl)-*N*-[3-(1-phenyl-ethylthio)-prop-2-ynyl]-4-methylbenzenesulfonamide (213): ^1H NMR (300 MHz, CDCl_3) δ 7.66 (d, J = 8.3 Hz, 2H), 7.31-7.17 (m, 7H), 5.66 (dddd, J = 16.8, 10.3, 6.4, 6.4 Hz, 1H), 5.18-5.10 (m, 2H), 4.14 (s, 2H), 4.00 (q, J = 7.0 Hz, 1H), 3.73-3.59 (m, 2H), 2.39 (s, 3H), 1.55 (d, J = 7.0 Hz, 3H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 143.3 (C), 141.0 (C), 135.7 (C), 131.8 (CH), 129.3 (2 x CH), 128.3 (2 x CH), 127.6 (CH), 127.5 (2 x CH), 126.9 (2 x CH), 119.5 (CH_2), 88.7 (C), 75.3 (C), 48.8 (CH_2), 47.6 (CH), 37.0 (CH_2), 21.4 (CH_3), 21.1 (CH_3); IR (thin film, NaCl) 3029 (w), 2976 (w), 2924 (w), 2181 (w), 1348 (m br), 1162 (m), 1092 (m), 666 (m); high resolution (EI) mass spectrum calculated for $\text{C}_{21}\text{H}_{23}\text{NO}_2\text{S}_2$ (M^+) 385.1168, found 385.1175.

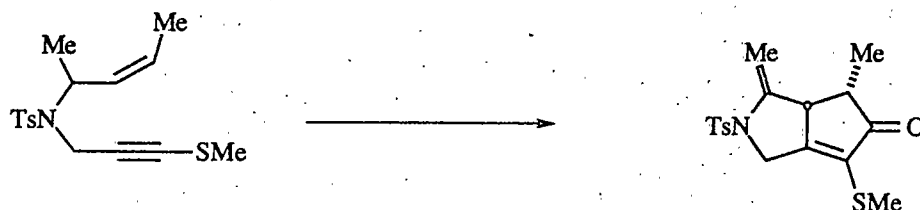
1-Methyl-2-[(4-methylbenzene)sulfonyl]-7-(1-phenyl-ethylthio)-2,3,3a,4-tetrahydro-1*H*-cyclopentacpyrrol-5-one (214)



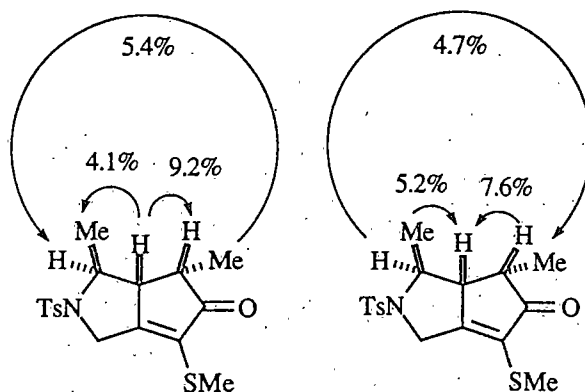
The title compound was prepared as a 1.1/1 mixture of diastereomers in 92% yield using Procedure A except that 10 mol % $\text{Co}_2(\text{CO})_8$ was used (12 h). Purification by flash

chromatography (SiO₂, 15% ethyl acetate in hexanes to 30% ethyl acetate in hexanes gradient for elution) afforded the title compound as a pale yellow, foul oil. Further purification (SiO₂, 15% ethyl acetate in hexanes) allowed for separation of the diastereomers. The relative stereochemistry of each diastereomer was not determined. Data for the less polar diastereomer **214**: ¹H NMR (300 MHz, CDCl₃) δ 7.66 (d, *J* = 8.2 Hz, 2H), 7.36 (d, *J* = 8.2 Hz, 2H), 7.04-6.97 (m, 2H), 6.93-6.86 (m, 3H), 4.66 (q, *J* = 7.0 Hz, 1H), 4.36 (dd, *J* = 17.0, 1.4 Hz, 1H), 3.80 (app t, *J* = 9.0 Hz, 1H), 3.60 (br d, *J* = 16.9 Hz, 1H), 2.84 (m, 1H), 2.54-2.45 (obscured peak, 1H), 2.47 (s, 3H), 1.94 (dd, *J* = 11.0, 9.0 Hz, 1H), 1.63-1.50 (obscured peak, 1H), 1.53 (d, *J* = 7.1 Hz, 3H); ¹³C NMR (75.5 MHz, CDCl₃) δ 204.0 (C), 177.5 (C), 143.9 (C), 143.3 (C), 134.1 (C), 132.2 (C), 130.0 (2 x CH), 128.0 (2 x CH), 127.4 (2 x CH), 127.13 (2 x CH), 126.96 (CH), 52.0 (CH₂), 47.4 (CH₂), 44.0 (CH), 42.2 (CH₂), 39.7 (CH₂), 21.6 (CH₃), 21.4 (CH₃); IR (thin film, NaCl) 2923 (m), 1713.8 (s), 1644 (m), 1598 (m), 1454 (m), 1347 (m), 1101 (s), 1093 (s), 1050 (m); high resolution (EI) mass spectrum calculated for C₂₂H₂₃NO₃S₂ (M⁺) 413.1112, found 413.1119. Data for the more polar diastereomer **214**: ¹H NMR (300 MHz, CDCl₃) δ 7.66 (d, *J* = 8.2 Hz, 2H), 7.32 (d, *J* = 8.2 Hz, 2H), 7.32-7.18 (m, 5H), 4.50 (q, *J* = 7.0 Hz, 1H), 3.94 (dd, *J* = 9.3, 8.3 Hz, 1H), 3.86-3.72 (m, 2H), 2.94 (m, 1H), 2.63 (dd, *J* = 17.9, 6.5 Hz, 1H), 2.46 (dd, *J* = 11.0, 9.3 Hz, 1H), 2.41 (s, 3H), 2.01 (dd, *J* = 17.9, 3.6 Hz, 1H), 1.46 (d, *J* = 7.0 Hz, 3H); ¹³C NMR (75.5 MHz, CDCl₃) δ 204.2 (C), 178.3 (C), 144.1 (C), 142.3 (C), 133.3 (C), 131.7 (C), 130.0 (2 x CH), 128.5 (2 x CH), 127.6 (CH), 127.5 (2 x CH), 127.4 (2 x CH), 52.5 (CH₂), 47.6 (CH₂), 42.2 (CH), 39.5 (CH₂), 22.2 (CH₃), 21.5 (CH₃); IR (thin film, NaCl) 3028 (w), 2966 (m), 2922 (m), 1714.0 (s), 1643 (m), 1597 (m), 1453 (m), 1346 (s), 1162 (s), 1092 (m), 1045 (m), 700 (m), 658 (m); high resolution (EI) mass spectrum calculated for C₂₂H₂₃NO₃S₂ (M⁺) 413.1112, found 413.1119.

3-Methyl-4-methyl-2-[(4-methylbenzene)sulfonyl]-6-methylthio-2,3,3a,4-tetrahydro-1*H*-cyclopenta<c>pyrrol-5-one (206)



The title compound was prepared as a mixture of diastereomers (13.0/1) in 92% yield using Procedure C (12 h) expect that 10 mol % $\text{Co}_2(\text{CO})_8$ was used. Data for the title compound 206: ^1H NMR (300 MHz, CDCl_3) δ 7.68 (d, $J = 8.1$ Hz, 2H), 7.30 (d, $J = 8.1$ Hz, 2H), 4.35-4.21 (m, 2H), 3.10 (m, 1H), 2.93 (m, 1H), 2.62 (dq, $J = 14.6, 7.6$ Hz, 1H), 2.39 (s, 3H), 2.24 (s, 3H), 1.53 (d, $J = 6.0$ Hz, 3H), 0.84 (d, $J = 7.6$ Hz, 3H); ^{13}C NMR (62.9 MHz, CDCl_3) δ 207.1 (C), 167.8 (C), 144.0 (C), 133.8 (C), 129.8 (2 x CH), 127.48 (2 x CH), 127.42 (C), 56.7 (CH), 54.1 (CH), 49.7 (CH_2), 42.2 (CH), 21.5 (2 x CH_3), 14.2 (CH_3), 13.0 (CH_3); IR (thin film, NaCl) 2968 (m), 2928 (m), 1711 (s), 1643 (m), 1597 (m), 1454 (m), 1346 (s), 1160 (br s), 1090 (s), 1040 (m), 817 (m), 716 (m), 655 (s); high resolution (EI) mass spectrum calculated for $\text{C}_{17}\text{H}_{21}\text{NO}_3\text{S}_2$ (M^+) 351.0963, 351.0963.



REFERENCES

1. (a) Lautens, M.; Klute, W.; Tam, W. *Chem. Rev.* **1996**, *96*, 49-92. (b) Tröst, B.M. *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 259-281.
- 2 (a) Murakami, M.; Itami, K.; Ito, Y. *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 2691-2694. (b) Murakami, M.; Itami, K.; Ito, Y. *J. Am. Chem. Soc.* **1996**, *118*, 11672-11673. (c) Murakami, M.; Itami, K.; Ito, Y. *J. Am. Chem. Soc.* **1997**, *119*, 2950-2951. (d) Murakami, M.; Itami, K.; Ito, Y. *Organometallics* **1999**, *18*, 1326-1336.
3. (a) Khand, I.U.; Knox, G.R.; Pauson, P.L.; Watts, W.E. *J. Chem. Soc., Perkin 1* **1973**, 975-977. (b) Khand, I.U.; Knox, G.R.; Pauson, P.L.; Watts, W.E.; Foreman, M.I. *J. Chem. Soc., Perkin 1* **1973**, 977-981. (c) An early account of the thermolysis of alkyne-dicobalt complexes in the presence of nobornadiene suggested that "ketonic products" were formed, see Khand, I.U.; Knox, G.R.; Pauson, P.L.; Watts, W.E. *J. Chem. Soc., Chem. Commun.* **1971**, 36.
4. (a) Pauson, P.L. *Tetrahedron* **1985**, *41*, 5855. (b) Schore N.E. *Chem. Rev.* **1988**, *88*, 1081. (c) *Org. React. (NY)* **1991**, *41*, 1. (d) Schore, N.E. In *Comprehensive Organometallic Chemistry* Trost, B.M., Ed.: Pergamon: Oxford, 1991; Vol. 5, p 1037. (e) Schore, N.E. In *Comprehensive Organometallic Chemistry II*: Hegedus, L.S., Ed.: Elsevier: Oxford, 1995; Vol. 12, p 703. (f) Geis, O.; Schmalz, H-G. *Angew. Chem. Int. Ed. Engl.* **1998**, *37*, 911-914. (g) For a review of the asymmetric Pauson-Khand reaction, see: Ingate, S.T.; Marco-Contelles, J. *Organic Preparations and Procedures Int.* **1998**, *30*, 121-143. (h) Mills, O.S.; Robinson, G. *Proc. Chem. Soc.* **1974**, 379.
5. Krafft, M.E.; Scott, I.L.; Romero, R.H.; Feibelman, S.; Van Pelt, C.E. *J. Am. Chem. Soc.* **1993**, *115*, 7199-7207.
6. Shambayati, S.; Crowe, W.E.; Schreiber, S.L. *Tetrahedron Lett.* **1990**, *31*, 5289-5292. Subsequent to Schreiber's disclosure that NMO promoted the stoichiometric PKR, Jeong reported a similar observation with trimethylamine *N*-oxide: Jeong, N.; Chung, Y.K.; Lee, B.Y.; Lee, H.L. *Synlett* **1991**, 204.
7. Hieber, W.; Lipp, A. *Chem. Ber.* **1959**, *92*, 2085.

8. Smit, W.A.; Simonyan, S.O.; Tarasov, V.A.; Mikeelian, G.S.; Gybin, A.S.; Ibragimov, I.I.; Caple, R.; Froen, D.; Kraeger, A. *Synthesis* **1989**, 472-476.
9. Sugihara, T.; Yamada, M.; Ban, H.; Yamaguchi, M.; Kanedo, C. *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 2801-2804.
10. More recently, Sugihara has reported that water promoted the catalytic Pauson-Khand reaction of enynes using $\text{Co}_2(\text{CO})_8$ at 7 atm and 120 °C: Sugihara, T.; Yamaguchi, M. *Synlett* **1998**, 1384-1386. Sugihara has also shown that alkyl methyl sulfides promote the stoichiometric inter- and intramolecular Pauson-Khand reaction of enynes, see Sugihara, T.; Yamada, M.; Yamaguchi, M.; Nishizawa, M. *Synlett*, **1999**, 771-773.
11. (a) Darensbourg, D.J.; Kump, R.L. *Inorg. Chem.* **1978**, *17*, 2680-2682. (b) Darensbourg, R.J.; Darensbourg, D.J. *Inorg. Chem.* **1972**, *11*, 72-77.
12. Rautenstrauch, V.; Megard, P.; Conesa, J.; Kuster, W. *Angew. Chem. Int. Ed. Engl.* **1990**, *29*, 1413.
13. Lee, B.Y.; Chung, Y.K.; Jeong, N.; Lee, Y.; Hwang, S.H. *J. Am. Chem. Soc.* **1994**, *116*, 8793-8794.
14. Yamazaki, H.; Wakazuki, Y. *Organometallic Synthesis* 1988; Vol 14, p 278.
15. Jeong, N.; Hwang, S.H.; Lee, Y.; Chung, Y.K. *J. Am. Chem. Soc.* **1994**, *116*, 3159-3160.
16. Kemmitt, R.D.W.; Russel, D.R. In *Comprehensive Organometallic Chemistry*, Wilkinson, G., Ed.: Oxford, Pergamon Press, 1982; pp. 1-276.
17. Jeong, N.; Hwang, S.H.; Lee, Y.W.; Lim, J.S. *J. Am. Chem. Soc.* **1997**, *119*, 10549-10550.
18. Pagenkopf, B.L.; Livinghouse, T. *J. Am. Chem. Soc.* **1996**, *118*, 2285-2286.

19. For leading references on organometallic photochemistry, see: (a) Rigby, J.H.; Ateeq, H.S.; Charles, N.R.; Cuisat, S.V.; Ferguson, M.D.; Henshilwood, J.A.; Krueger, A.C.; Ogbu, C.O.; Short, K.M.; Heeg, M.J. *J. Am. Chem. Soc.* **1993**, *115*, 1382. (b) Hegedus, L.S.; de Weck, G.; D'Andrea, S. *J. Am. Chem. Soc.* **1988**, *110*, 2122.
20. Pagenkopf, B.L., *Substrate and Reagent Control of Diastereoselectivity in Transition Metal Mediated Processes: Development of a Catalytic Photopromoted Pauson-Khand Reaction*, Ph.D. dissertation, Montana State University, 1996.
21. For an example of this substrated based effect in a zirconium-mediated process, see: Van Wagenen, B.C.; Livinghouse, T. *Tetrahedron Lett.* **1989**, *30*, 3495.
22. Further examples of the rate and efficiency enhancements of metal-catalyzed reactions with trifluoroethanol as solvent, see (a) Jolly, R.S.; Luedtke, G.; Sheehan, D.; Livinghouse, T. *J. Am. Chem. Soc.* **1990**, *112*, 4965. (b) Takacs, M.; Lawson, E.C. *Organometallics* **1994**, *13*, 4787-4793. (c) Livinghouse was the first to demonstrate that $\text{P}(\text{OCH}_2\text{CF}_3)_3$ was an effective ligand in metal catalyzed cycloadditions, see reference 22a.
23. O'Mahony, D.J.R., Montana State University, Post-doctoral fellow, unpublished results.
24. (a) Van Ornum, S.G.; Cook, J.M. *Tetrahedron Lett.* **1997**, *38*, 3657. (b) Van Ornum, S.G.; Cook, J.M. *Tetrahedron Lett.* **1996**, *37*, 7185. (c) Van Ornum, S.G.; Bruendl, M.M.; Cook, J.M. *Tetrahedron Lett.* **1998**, *39*, 6649-6650. (d) Bruendl, M.M.; Van Ornum, S.G.; Chan, T-M.; Cook, J.M. *Tetrahedron Lett.* **1999**, *40*, 1113-1116.
25. Kim, J.W.; Chung, Y.K. *Synthesis* **1998**, *2*, 142-144.
26. Sugihara, T.; Yamaguchi, M. *J. Am. Chem. Soc.* **1998**, *120*, 2635-2636
27. Seyferth, D.; Hallgren, J.E.; Hung, P.L.K. *J. Organomet. Chem.* **1973**, *50*, 265.
28. Kondo, T.; Suzuki, N.; Okada, T.; Mitsudo, T-a. *J. Am. Chem. Soc.* **1997**, *119*, 6187-6188.

29. Morimoto, T.; Chantani, N.; Fukumoto, Y.; Murai, S. *J. Org. Chem.* **1997**, *62*, 3762-3765.
30. (a) Magnus, P.; Exon, C. *J. Am. Chem. Soc.* **1983**, *105*, 2477-2478. (b) Magnus, P.; Principe, L.M. *Tetrahedron Lett.* **1985**, *26*, 4851-4854. (c) Magnus, P.; Exon, C.; Albaugh-Robertson, P. *Tetrahedron* **1985**, *41*, 5861-5869. (d) Magnus, P.; Becker, D.P. *J. Am. Chem. Soc.* **1987**, *109*, 7495-7498. (e) Magnus, P.; Principe, L.M.; Slater, M.J. *J. Am. Chem. Soc.* **1987**, *52*, 1483-1486.
31. Koga, Y.; Kobayashi, T.; Narasaka, K. *Chem. Lett.* **1998**, 249-250.
32. Jeong, N.; Lee, S.; Sung, B.K. *Organometallics* **1998**, *17*, 3642-3644.
33. Zhang, M.; Buchwald, S.L. *J. Org. Chem.* **1996**, *61*, 4498-4499.
34. (a) Grossman, R.B.; Buchwald, S.L. *J. Am. Chem. Soc.* **1992**, *114*, 5802-5803. (b) Berk, S.C.; Grossman, R.B.; Buchwald, S.L. *J. Am. Chem. Soc.* **1994**, *116*, 8593-8601.
35. (a) Hicks, F.A.; Kablaoui, N.M.; Buchwald, S.L. *J. Am. Chem. Soc.* **1996**, *118*, 9450-9451. (b) Hicks, F.A.; Buchwald, S.L. *J. Am. Chem. Soc.* **1996**, *118*, 11688-11689.
36. Sturla, S.J.; Kablaoui, N.M.; Buchwald, S.L. *J. Am. Chem. Soc.* **1999**, *121*, 1976-1977.
37. For recent examples of the inter- and intramolecular Diels-Alder reaction in the synthesis of natural products, see (a) May, S.A.; Grieco, P.A.; Lee, H.-H. *Synlett*, **1997**, 493-494. (b) Grieco, P.A.; Collins, J.L.; Moher, E.D.; Fleck, T.J.; Gross, R.S. *J. Am. Chem. Soc.* **1993**, *115*, 6078-6093. For reviews of the intramolecular Diels-Alder reaction, see (c) Fallis, A.G. *Can. J. Chem.* **1984**, *62*, 183-234. (f) Roush, W.R. In *Comprehensive Organic Synthesis*; Trost, B.M., Ed.: Vol. 5, Pergamon Press, Oxford, 1991, Ch. 4.4; pp. 513-550. (g) Craig, D. *Chem. Soc. Rev.* **1987**, *16*, 187-238.

38. (a) Wender, P.A.; Jenkins, T.E. *J. Am. Chem. Soc.* **1989**, *111*, 6432-6434. (b) Wender, P.A.; Smith, T.E. *J. Org. Chem.* **1995**, *60*, 2962-2963. (c) Wender, P.A.; Smith, T.E. *Tetrahedron* **1998**, *54*, 1255-1275. (d) Wender, P.A.; Husfeld, C.O.; Langkopf, E.; Love, J.A.; Pleuss, N. *Tetrahedron* **1998**, *54*, 7203-7220.
39. Murakami, M.; Ubukata, M.; Itami, K.; Ito, Y. *Angew. Chem. Int. Ed. Engl.* **1998**, *37*, 2248-2249.
40. Kumar, K.; Jolly, R.S. *Tetrahedron Lett.* **1998**, *39*, 3047-3048.
41. Matsuda, I.; Shibata, M.; Sato, S.; Izumi, Y. *Tetrahedron Lett.* **1987**, 3361-3362.
42. Murakami, M.; Ubukata, M.; Itami, K.; Ito, Y. *Angew. Chem. Int. Ed. Engl.* **1998**, *37*, 2248-2250.
43. O'Mahony, D.J.R.; Belanger, D.B.; Livinghouse, T. *Synlett* **1998**, *4*, 443-445.
44. For a review of allylic 1,3 strain, see: Hoffman, R.W. *Chem. Rev.* **1989**, *89*, 1841-1860.
45. Gilbertson, S.R.; Hoge, G.S. *Tetrahedron Lett.* **1998**, *39*, 2075-2078.3361-
46. Wender, P.A.; Jenkins, T.E.; Suzuki, S. *J. Am. Chem. Soc.* **1995**, *117*, 1843-1844.
47. McKinstry, L.; Livinghouse, T. *Tetrahedron* **1994**, *50*, 6145.
48. Gilbertson, S.R.; Hoge, G.S.; Genov, D.G. *J. Org. Chem.* **1998**, *63*, 10077-10080.
49. (a) Wender, P.A.; Takahashi, H.; Witulski, B. *J. Am. Chem. Soc.* **1995**, *117*, 4720-4721. (b) Wender, P.A.; Husfeld, C.O.; Langkopf, E.; Love, J.A. *J. Am. Chem. Soc.* **1998**, *120*, 1940-1941. (c) Wender, P.A.; Sperandio, D. *J. Org. Chem.* **1998**, *63*, 4164-4165.

50. Wender, P.A.; Rieck, H.; Fuji, M. *J. Am. Chem. Soc.* **1998**, *120*, 10976-10977.
51. (a) Sheehan, D., Montana State University, unpublished results. (b) McKinstry, L, *The Asymmetric Rh (I) Catalyzed [4 + 2] Cycloisomerization reaction: New Homochiral Bisphosphine Ligands*, Ph.D. dissertation, Montana State University, 1994.
52. Bochmann, M. *Top. Catal.* **1999**, *7*, 9-22.
53. Recent studies show that the OTf ion behaves as a moderately strong ligand and should not be classified as a weakly-coordinating anion, see: Svetlanova-Larsen, A.; Hubbard, J.L. *Inorg. Chem.* **1996**, *35*, 3073-3076. For a review of the trifluoromethanesulfonate ligand, see: Lawrance, G.A. *Chem. Rev.* **1986**, *86*, 17-33. For reviews on weakly-coordinating counterions, see: (a) Strauss, S.H. *Chem. Rev.* **1993**, *93*, 927-942. (b) Beck, W.; Sunkel, K. *Chem. Rev.* **1988**, *88*, 1405-1421. For a review of carboranes, see: Reed, C.A. *Acc. Chem. Res.* **1998**, *31*, 133-139.
54. (a) Glaser, R.; Twaik, M.; Geresh, S.; Blumenfeld, J. *Tetrahedron Lett.* **1977**, *52*, 4635-4638. (b) Glaser, R.; S.; Blumenfeld, J.; Twaik, M. *Tetrahedron Lett.* **1977**, *52*, 4639-4642. (c) Glaser, R.; Geresh, S.; Blumenfeld, J.; Twaik, M. *Tetrahedron* **1978**, *34*, 2405-2408. (d) Glaser, R.; Geresh, S.; Twaik, M.; Benoiton, N. L. *Tetrahedron* **1978**, *34*, 3617-3621.
55. (a) Taura, Y.; Tanaka, M.; Wu, X-M.; Funakoshi, K.; Sakai, K. *Tetrahedron* **1991**, *47*, 4879-4888. (b) Wu, X-M.; Funakoshi, K.; Sakai, K. *Tetrahedron Lett.* **1993**, *34*, 5927-5930.
56. Chaloner, P. A. *J. Organomet. Chem.* **1984** *266*, 191-201.
57. Knowles, W.S. *Acc. Chem. Res.* **1983**, *16*, 106-112.
58. For the effect of natural bite angle on the Rh-catalyzed hydroformylation of olefins, see: (a) Casey, C.P.; Paulsen, E.L.; Beuttenmueller, E.W.; Proft, B.R.; Petrovich, L.M.; Matter, B.A.; Powell, D.R. *J. Am. Chem. Soc.* **1997**, *119*, 11817-11825. (b) Casey, C.P.; Petrovich, L.M. *J. Am. Chem. Soc.* **1995**, *117*, 6007-6014. (c) Kranenburg, M.;

- van der Burgt, Y.E.M.; Kamer, P.C.J.; van Leuwen, P.W.N.M. *Organometallics* **1995**, *14*, 3081-3089. (d) Casey, C.P.; Whiteker, G.T.; Melville, M.G.; Petrovich, L.M.; Gavney, J.A.; Powell, D.R. *J. Am. Chem. Soc.* **1992**, *114*, 5535-5543.
59. Burk, M.J.; Colletti, S.L.; Halterman, R.L. *Organometallics* **1991**, *10*, 2998-3000.
60. (a) Shimada, M.; Kobayashi, S.; Ohno, M. *Tetrahedron Lett.* **1988** *29*, 52, 6961-6964. (b) Kobayashi, S.; Kamiyama, K.; Iimori, T.; Ohno, M. *Tetrahedron Lett.* **1984**, *25*, 2557-2560. (c) Kobayashi, S.; Kamiyama, K.; Ohno, M. *Chem. Pharm. Bull.* **1990**, *38*, 350-354.
61. The ($\pm$)-diester **92** has been prepared by a similar route, see: (a) Rae, I.D.; Serelis, A.K. *Aust. J. Chem.* **1990**, *43*, 1941-1948. (b) Bilyard, K. G.; Garret, P.J.; Hunter, R.; Lete, E. *J. Org. Chem.* **1982**, *47*, 4731-4736.
62. (a) Imamoto, T.; Oshiki, T.; Onozawa, T.; Kusumoto, T.; Sato, K. *J. Am. Chem. Soc.* **1990**, *112*, 5244. (b) McKinsty, L.; Livinghouse, T. *Tetrahedron Lett.* **1994**, *35*, 9319. (c) Reference 51b.
63. Whitesides, G.M.; Hackett, M.; Brainard, R.L.; Lavalleye, J-P.P.M.; Sowinski, A.F.; Izumi, A.N.; Moore, S.S.; Brown, D.W.; Staudt, E.M. *Organometallics* **1985**, *4*, 1819-1830.
64. (a) Longeau, A.; Durand, S.; Spiegel, A.; Knochel, P. *Tetrahedron: Asymmetry* **1997**, *8*, 987-990. (b) Longeau, A.; Langer, F.; Knochel, P. *Tetrahedron Lett.* **1996**, *37*, 2209-2212. (c) Langer, F.; Knochel, P. *Tetrahedron Lett.* **1995**, *36*, 4591-4594.
65. (a) Ahmar, M.; Antras, F.; Cazes, B. *Tetrahedron Lett.* **1995**, *36*, 4417-4420. (b) Ahmar, M.; Chabanis, O.; Gauthier, J.; Cazes, B. *Tetrahedron Lett.* **1997**, *38*, 5277-5280. (c) Ahmar, M.; Locatelli, C.; Colombier, D.; Cazes, B. *Tetrahedron Lett.* **1997**, *38*, 5281-5284.

66. (a) Kent, J.L.; Wan, H.; Brummond, K.M. *Tetrahedron Lett.* **1995**, *36*, 2407-2410.
(b) Brummond, K.M.; Wan, H. *Tetrahedron Lett.* **1998**, *39*, 931-934. (c) Brummond, K.M.; Wan, H.; Kent, J.L. *J. Org. Chem.* **1998**, *63*, 6535-6545.
67. For a leading reference on the Zirconium-mediated bicyclization/carbonylation method, see: Negishi, E.I.; Holmes, S.J.; Tour, J.M.; Miller, J.A. *J. Am. Chem. Soc.* **1985**, *107*, 2568-2569.
68. Greenfield, H.; Wender, I.; Wotiz, J.H. *J. Am. Chem. Soc.* **1957**, *21*, 875-878.
69. Sóvágó, J.; Newton, Gary, M.G.; Mushina, E.A.; Ungváry, F. *J. Am. Chem. Soc.* **1996**, *118*, 9589-9596.
70. Cowie, J.S.; Landor, P.D.; Landor, S.R. *J. Chem. Soc. Perkin 1* **1973**, 720-724.
71. Djahanbini, D.; Cazes, B.; Gore, J. *Tetrahedron* **1987**, *43*, 3441-3452.
72. For a review of the Mitsunobu reaction, see: Mitsunobu, O. *Synthesis* **1981**, 1.
73. Gerson, F.; Hopf, H.; Merstetter, P.; Mlynek, C.; Fischer, D. *J. Am. Chem. Soc.* **1998**, *120*, 4815-4824.
74. For an example of a cobalt-mediated Alder ene reaction, see: Lierena, D.; Aubert, C., Malacria, M. *Tetrahedron Lett.* **1996**, *37*, 7027.
75. For leading references on the diene-transmissive Diels-Alder strategy, see: (a) Spino, C.; Liu, G.; Tu, N.; Girard, S. *J. Org. Chem.* **1994**, *59*, 5596-5608. (b) Tsuge, O.; Kanemasa, S.; Wada, E.; Sakoh, H. *J. Synth. Org. Chem. Jpn.* **1986**, *44*, 756-766.
76. Belanger, D.B.; O'Mahony, D.J.R.; Livinghouse, T. *Tetrahedron Lett.* **1998**, *39*, 7637-7640.
77. Bor, G.; Dietler, U.K. *J. Organomet. Chem.* **1980**, *191*, 295-302.

78. Krafft, M.E.; Wilson, A.M.; Dasse, O.A.; Bonaga, L.V.R.; Cheung, Y.Y.; Fu, Z.; Shao, B.; Scott, I.L. *Tetrahedron Lett.* **1998**, 39, 5911-5914.
79. Very recently, desulfurization of an α -thiomethylcyclopentenone has been accomplished using lithium thiophenolate, followed by aqueous NaOH, see: Mizuno, H.; Domon, K.; Masuya, K.; Yanino, K.; Kuwajima, I. *J. Org. Chem.* **1999**, 64, 2648-2656.
80. For an example of an intramolecular PKR involving a thiomethyl-enyne, see: Montenegro, E.; Poch, M.; Moyano, A.; Pericas, M.A.; Riera, A. *Tetrahedron Lett.* **1998**, 39, 335-338. For scattered reports on the intermolecular PKR involving aryl- or alkylthio alkynes, see: reference 4e.
81. Several authors suggest that $\text{Co}_4(\text{CO})_{12}$ is unreactive towards enynes and, therefore, is unable to mediate the Pauson-Khand reaction, see: references 13 and 30e. Contrary reports exist and state that isolable alkyne- $\text{Co}_4(\text{CO})_{10}$ can be prepared simply by mixing $\text{Co}_4(\text{CO})_{12}$ with alkynes and stirring at room temperature, see: (a) Dickson, R.S.; Tailby, G.R. *Aust. J. Chem.* **1970**, 23, 229-41. (b) Dickson, R.S.; Fraser, P. *Adv. Organomet. Chem.* **1974**, 12, 323. In addition, Chung has reported that $\text{Co}_4(\text{CO})_{12}$ is a useful catalyst for the inter- and intramolecular PKR under elevated pressure of CO, see: reference 25. The ability of $\text{Co}_4(\text{CO})_{12}$ to act as a catalyst using the photo-promoted or thermal protocol at 1 atm of CO has not been explored. Likewise, the use of alkyne- $\text{Co}_2(\text{CO})_6$ complexes as precatalysts for the PKR may involve the formation of enyne- $\text{Co}_2(\text{CO})_6$, $\text{Co}_2(\text{CO})_8$ and $\text{Co}_4(\text{CO})_{12}$.
82. For a review of cobalt-complexed propargyl cations, see: Nicholas, K.M. *Acc. Chem. Res.* **1987**, 20, 207-214.
83. (a) Schreiber, S.L.; Sammakia, T.; Crowe, W.E. *J. Am. Chem. Soc.* **1986**, 108, 3128. (b) Jamison, T.F.; Shambayati, S.; Crowe, W.E.; Schreiber, S.L. *J. Am. Chem. Soc.* **1997**, 119, 4353.
84. Jones, G.B.; Wright, J.M.; Rush, T.M.; Plourde, G.W.; Kelton, T.F.; Mathews, J.E.; Huber, R.S.; Davidson, J.P. *J. Org. Chem.* **1997**, 62, 9379-9381.

85. (a) Shibuya, S.; Isobe, M. *Synlett* **1998**, 373-374. (b) Hosokawa, S.; Isobe, M. *Synlett* **1996**, 351-352. (c) Isobe, M.; Hosokawa, S.; Kira, K. *Chem. Lett.* **1996**, 473-474.
86. Hosokawa, S.; Isobe, M. *Tetrahedron Lett.* **1998**, 39, 2609.
87. (a) Belanger, D.B.; Livinghouse, T. *Tetrahedron Lett.* **1998**, 39, 7641-7644. (b) It was reported in reference 87a that, without Et_3SiH , only 15% conversion was observed for the enyne depicted in Entry 1, Table 3.15. Subsequent studies show that 100% conversion of the starting enyne to product is observed, though the isolated yield of product is compromised (as shown in Scheme 3.96).
88. Exposure of the precatalyst to air for 24 hours followed by use in a catalytic PKR (with Entry 4, Table 3.15) afforded a 95% isolated yield in 12 hours. Very recently, the complex 222 has been shown to be a very effective, air-stable catalyst for the hydrosilylation of alkynes, see: Isobe, M.; Nishizawa, T.; Yoza, K. *Tetrahedron Lett.* **1999**, 40, 6927-6932.
89. Suffert, J. *J. Org. Chem.* **1989**, 54, 509-510.
90. Shimada, M.; Kobayashi, S.; Ohno, M. *Tetrahedron Lett.* **1988**, 29, 6961-6964
91. (a). Nishibayashi, Y.; Chiba, T.; Ohe, K.; Uemura, S. *J. Chem. Soc., Chem. Commun.* **1995**, 12, 1243-1244. (b). Schweizer, L.D.; E.E.; Smucker, L.D.; Votral, R.J. *J. Org. Chem.* **1966**, 31, 467.
92. Paquette, L.A.; Crouse, G.D.; Sharma, A.K. *J. Am. Chem. Soc.* **1982**, 104, 4411-4423.
93. Henry, J.R.; Marcin, L.R.; McIntosh, M.C.; Scola, P.M.; Harris Jr., G.D.; Weinreb, S.M. *Tetrahedron Lett.* **1989**, 30, 5709-5712.

94. Cruciani, P.; Stammler, R.; Aubert, C.; Malacria, M. *J. Org. Chem.* **1996**, *61*, 2699-2708.
95. Smith, P.A.S.; Emerson, D.W. *J. Am. Chem. Soc.* **1960**, *82*, 3076-3082.
96. Crabbé, P.; Fillon, H.; Andre, D.; Luche, J-L. *J. Chem Soc., Chem. Commun.* **1979**, 859.
97. Bonfand, E.; Motherwell, W.B.; Pennel, A.M.K.; Uddin, M.K.; Ujjainwalla, F. *Heterocycles* **1997**, *46*, 523-534.
98. Masquelin, T.; Obrecht, D. *Synthesis* **1995**, *3*, 276-284.
99. Kataoka, T.; Yoshimatsu, M.; Noda, Y.; Sato, T.; Shimizu, H.; Hori, M. *J. Chem. Soc., Perkin Trans. 1* **1993**, *1*, 121-130.
100. GOESY is a 1-dimensional NOESY that uses selective refocussing with two shaped pulses. For leading references, see: (a) Stott, K.; Stonehouse, J.; Keeler, J.; Hwang, T.L.; Shaka, A.J. *J. Am. Chem. Soc.* **1995**, *117*, 4199-4200. (b) Stonehouse, J.; Adell, J.; Keeler, J.; Shaka, A.J. *J. Am. Chem. Soc.* **1994**, *116*, 6037.

APPENDICES

APPENDIX A

List of Abbreviations

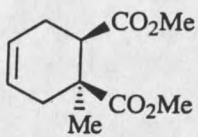
Ac	Acetyl
Ar	Aryl
atm	Atmophere(s)
BINAP	2,2'-Bis(diphenylphosphino)-1,1'binaphthyl
BMS	Borane-dimethyl sulfide
Bn	Benzyl
Boc	<i>t</i> -Butoxycarbonyl
Bu	<i>n</i> -Butyl
Chiraphos	2,3-Bis(diphenylphosphino)butane
CO	Carbon monoxide, carbonyl
COD	1,5-Cyclooctadiene
COE	Cyclooctene
Cp	Cyclopentadienyl
Cy	Cyclohexyl
d	Day(s)
D	Deuterium
DCE	1,2-Dichloroethane
DCM	Dichloromethane
DEAD	Diethyl azodicarboxylate
DHP	3,4-Dihydro-2 <i>H</i> -pyran
DIAD	Diisopropyl azodicarboxylate
DIOP	2,3- <i>O</i> -Isopropylidene-2,3-dihydroxy-1,4-
dppb	bis(diphenylphosphino)butane
diphos	bis(diphenylphosphino)ethane
DMA	Dimethylacetamide
DMAD	Dimethyl acetylenedicarboxylate

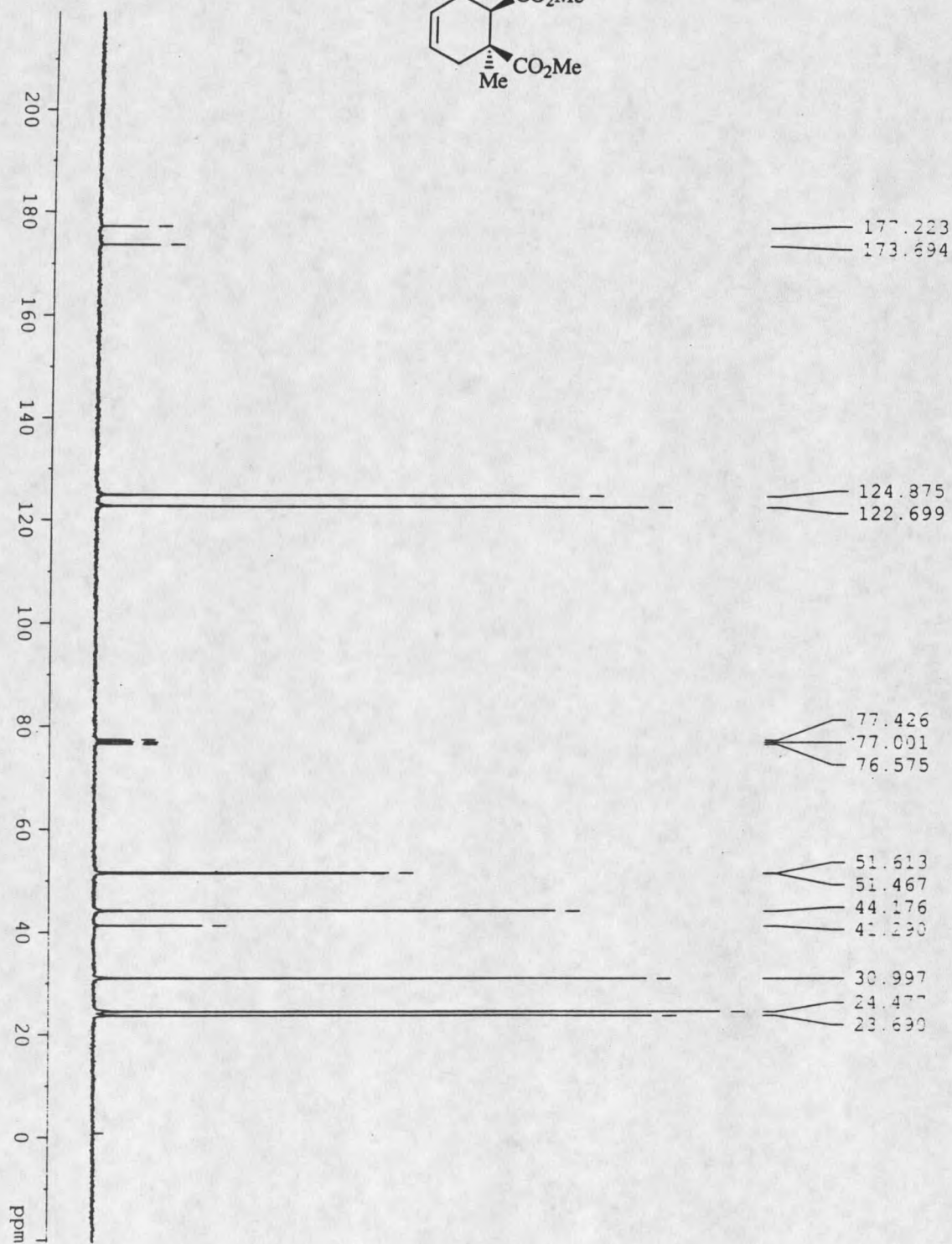
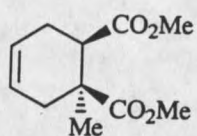
DMAP	4- <i>N,N</i> -Dimethylaminopyridine
DME	1,2-dimethoxyethane
DMF	Dimethylformamide
DMSO	Dimethylsulfoxide
dppe	1,3-Bis(diphenylphosphino)ethane
dppb	1,3-Bis(diphenylphosphino)butane
dppp	1,3-Bis(diphenylphosphino)propane
EA	Ethyl acetate
EBTHI	1,1'-Ethylenebis(tetrahydroindenyl)
ee	Enantiomeric excess
equiv	Equivalent(s)
Et	Ethyl
GC	Gas chromatography
HBpin	Pinacolborane
Hex	<i>n</i> -Hexyl
HMPA	Hexamethylphosphoramide
HPLC	High performance liquid chromatography
hr	Hour(s)
h ν	Light, Q-BEAM irradiation
Ind	Indenyl
IPA	Isopropanol
(L) _n	Unspecified ligand
LDA	Lithium diisopropylamide
M	Molarity, mol/L
Me	Methyl
MeCN	Acetonitrile

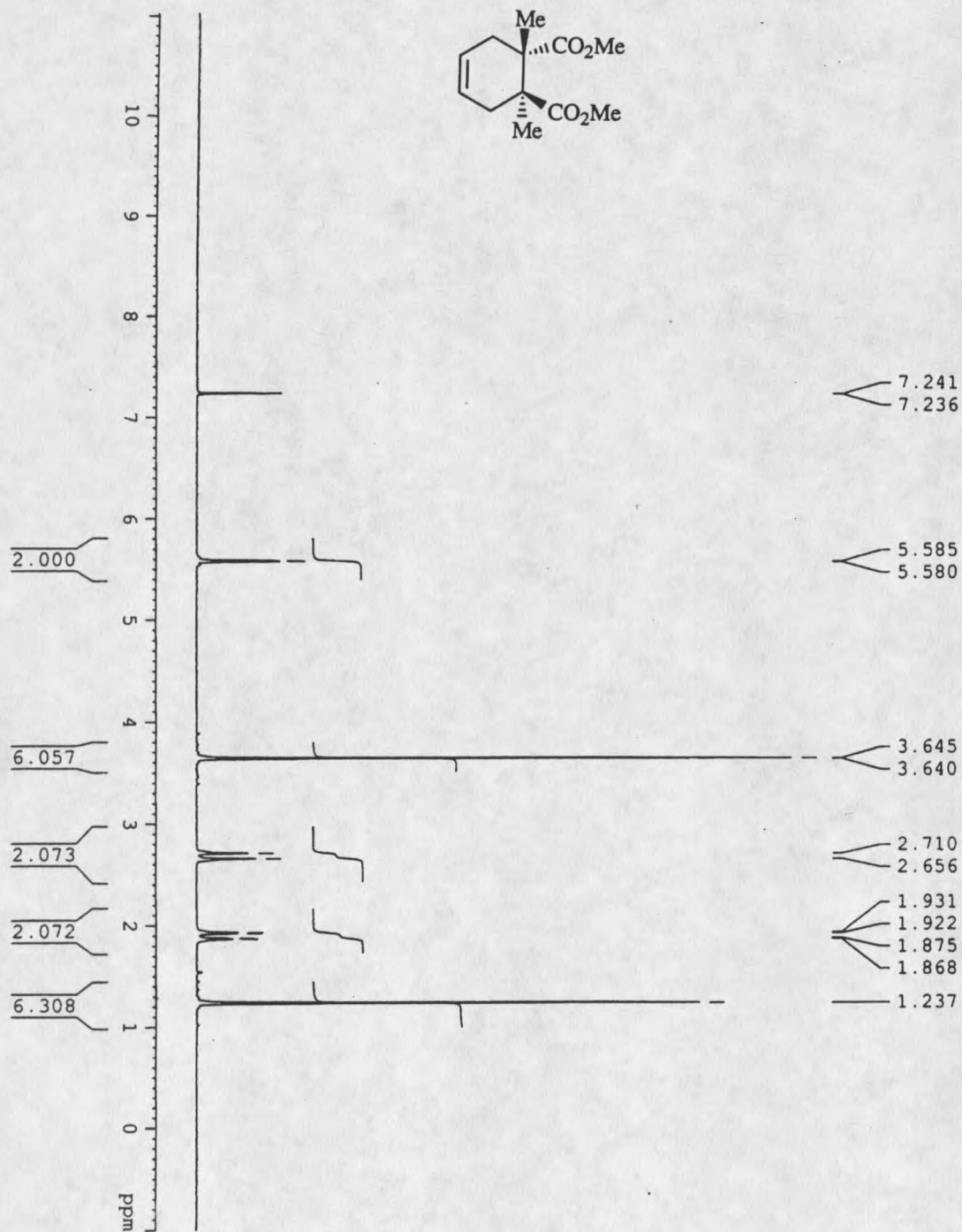
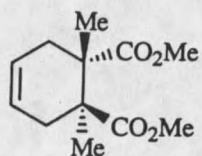
min	Minute(s)
Ms	Methanesulfonyl
NBD	Norbornadiene
NMO	<i>N</i> -Methyl morpholine <i>N</i> -oxide
NMR	Nuclear magnetic resonance
NOE	Nuclear Overhauser enhancement
Nu	Unspecified nucleophile
Ph	Phenyl
PhH	Benzene
PKR	Pauson-Khand reaction
PLE	Pig liver esterase
PMHS	Polymethylhydrosiloxane
PNB	<i>p</i> -nitrobenzoyl
P(O- <i>o</i> -BiPh) ₃	tris(2-phenyl phenol)phosphite
ppt	Precipitate
Pr	<i>n</i> -Propyl
psi	Pounds/square inch
rt	Room temperature
S	Solvent
Sc CO ₂	Supercritical CO ₂
TBAF	tetrabutylammonium fluoride
TBDPS	<i>t</i> -Butyldiphenylsilyl
TBS	<i>t</i> -Butyldimethylsilyl
TEA	Triethylamine
Tf	Trifluoromethanesulfonyl
TFE	2,2,2-Trifluoroethanol

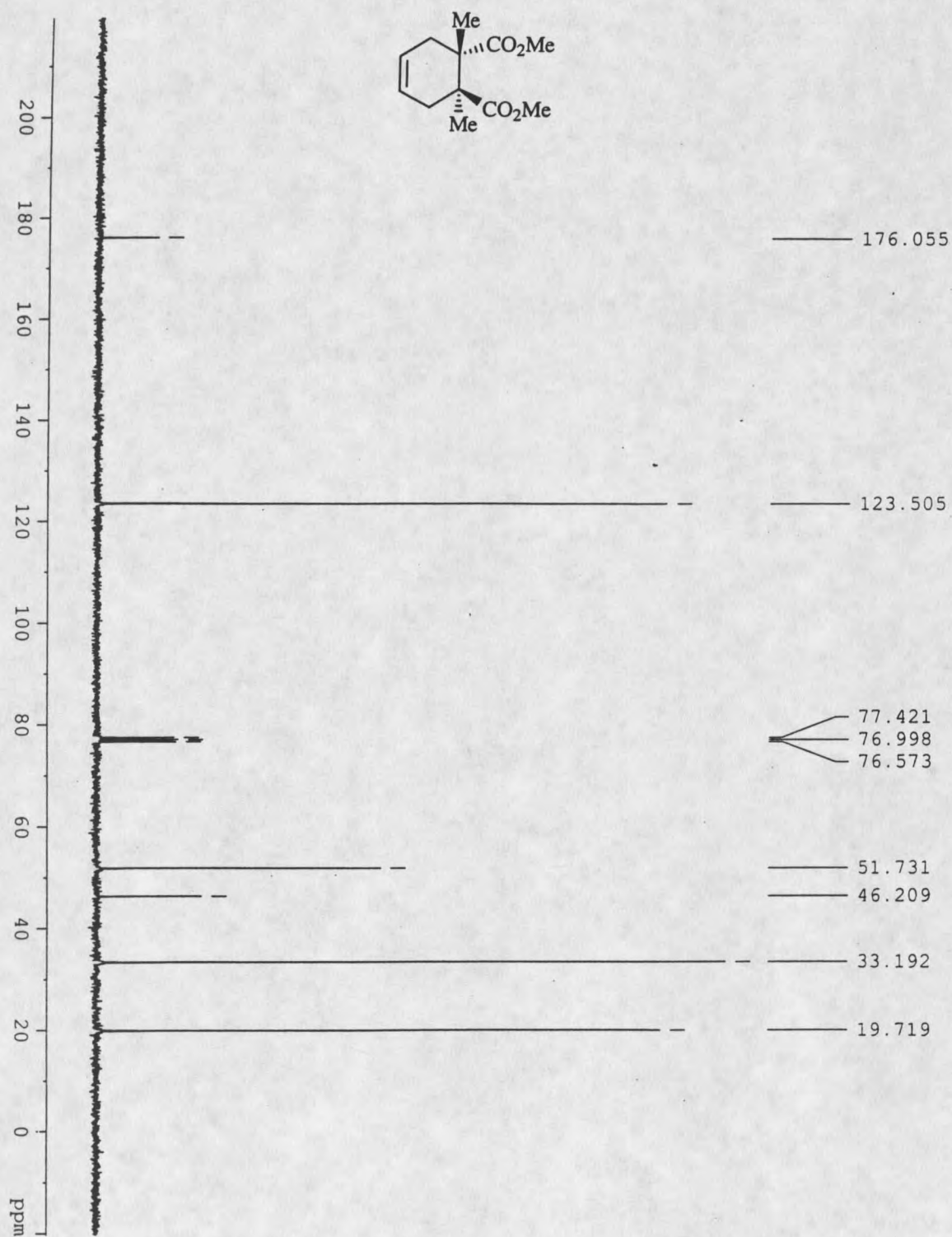
THF	Tetrahydrofuran
THP	Tetrahydropyranyl
TLC	Thin layer chromatography
TMANO	Trimethylamine- <i>N</i> -oxide
TMS	Trimethylsilyl
tol	Toluene
Ts	<i>p</i> -Toluenesulfonyl
TsNH(Boc)	<i>N</i> - <i>t</i> -butoxycarbonyl-4-methyl-benzenesulfonamide

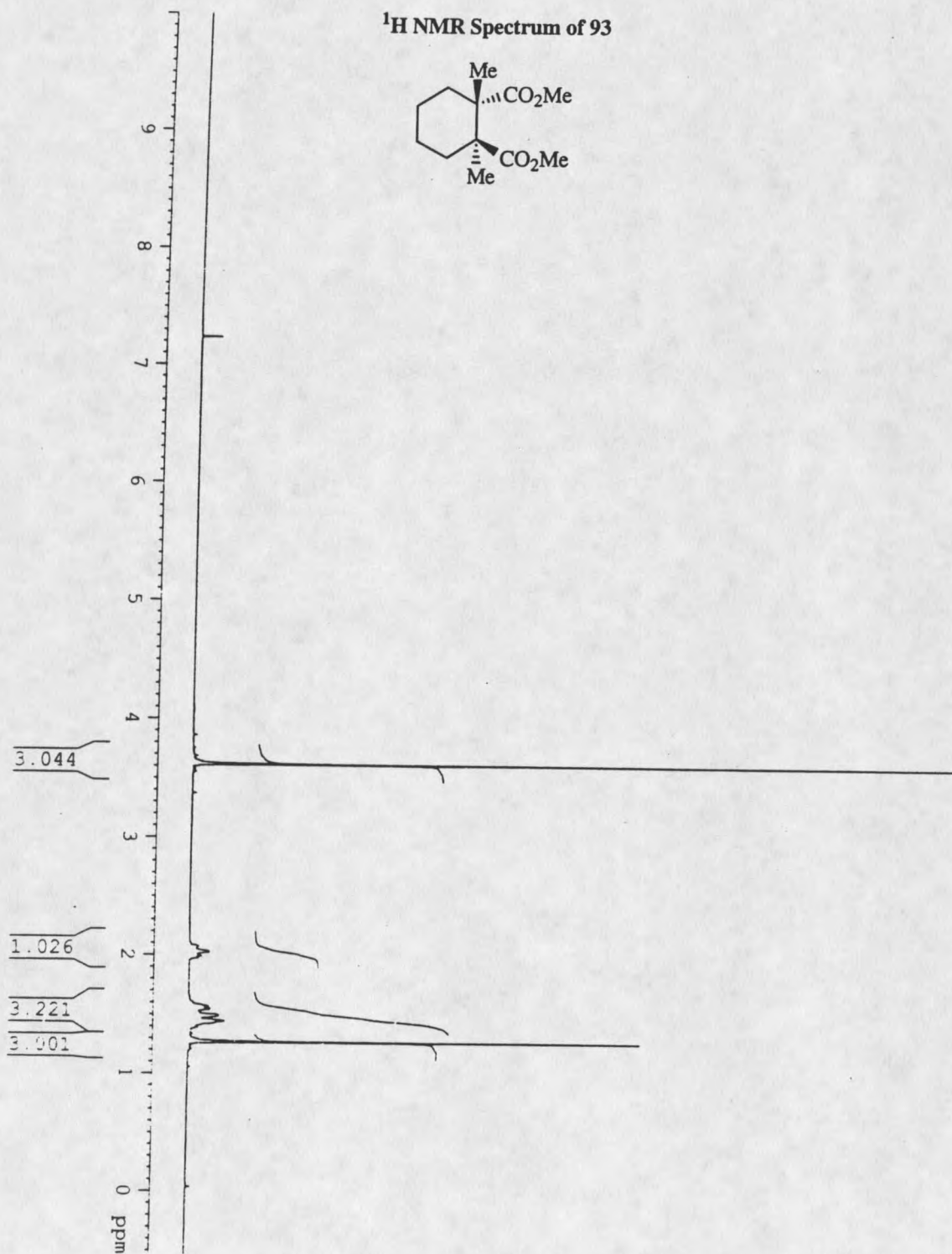
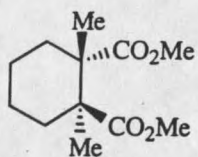
APPENDIX B **^1H and ^{13}C NMR Spectral Data**

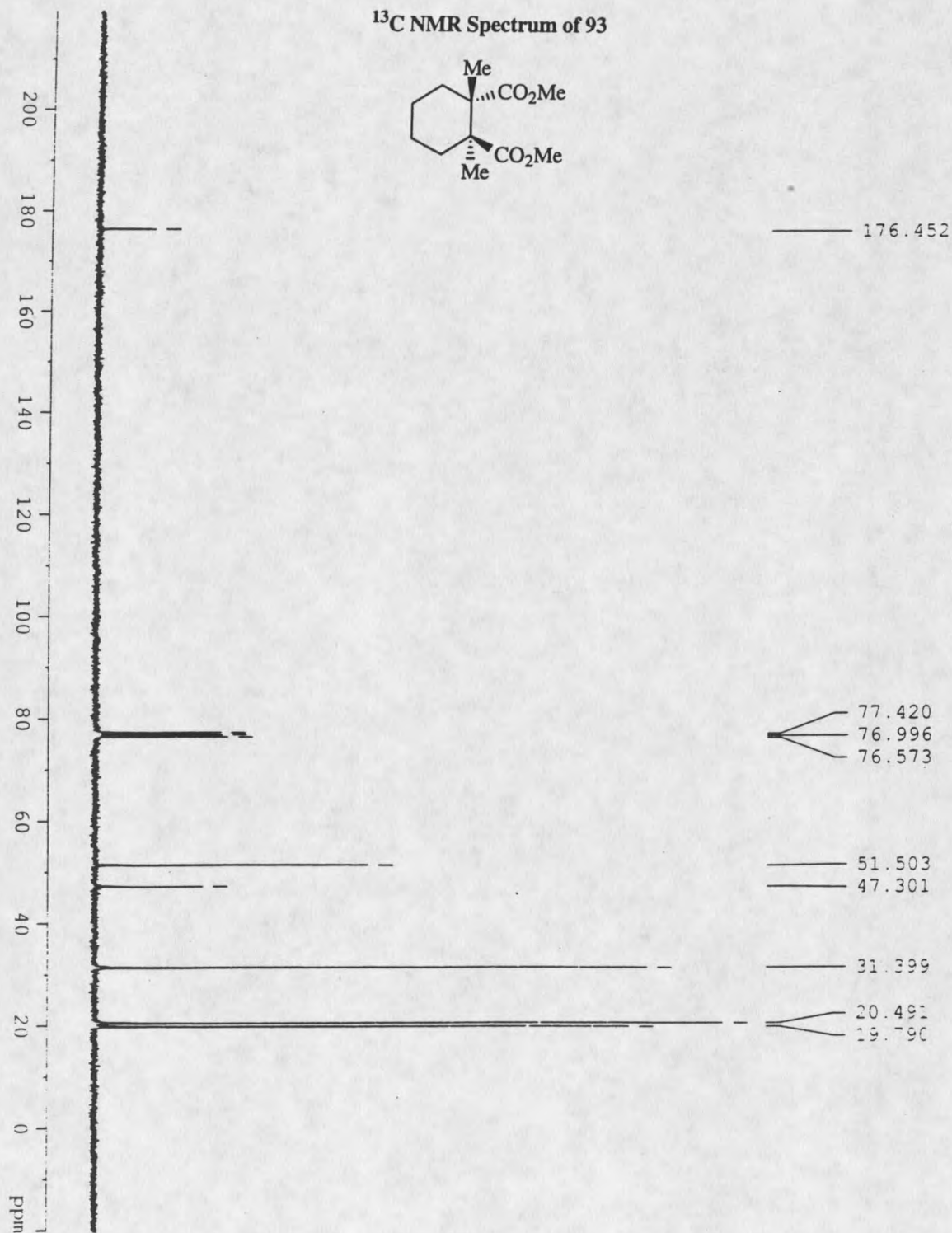
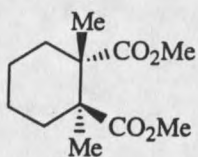
¹H NMR Spectrum of 91

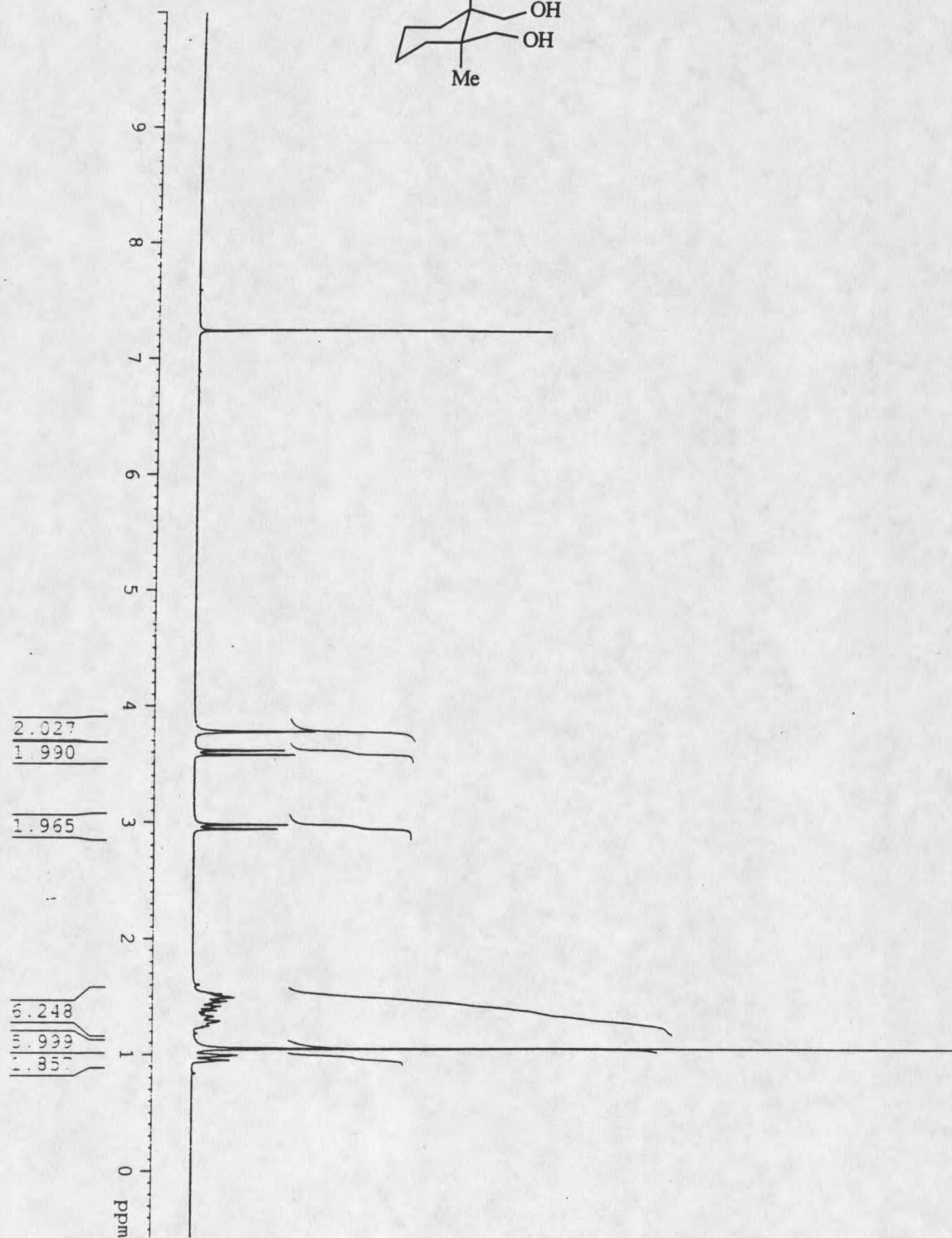
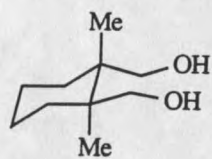
¹³C NMR Spectrum of 91

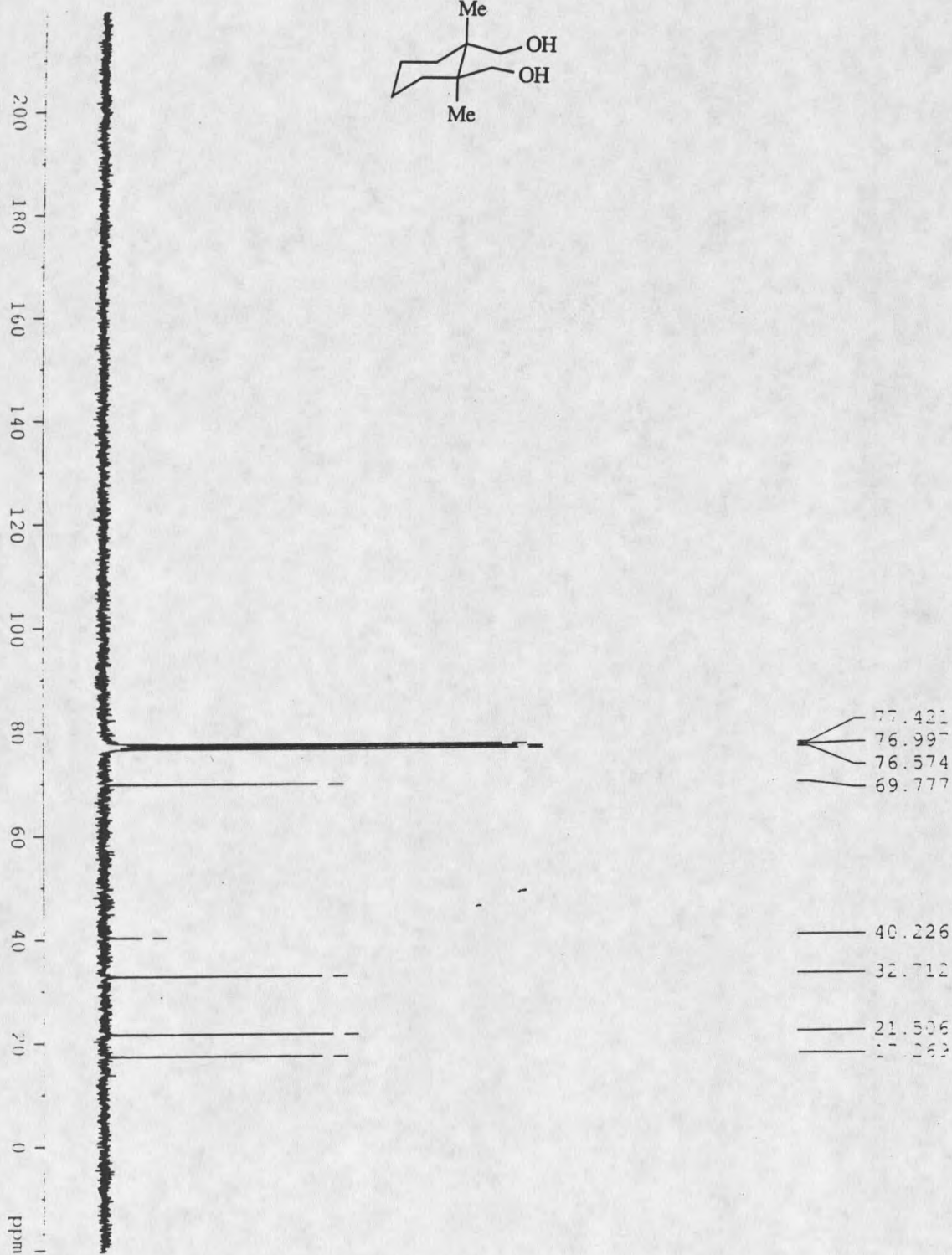
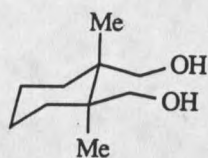
¹H NMR Spectrum of 92

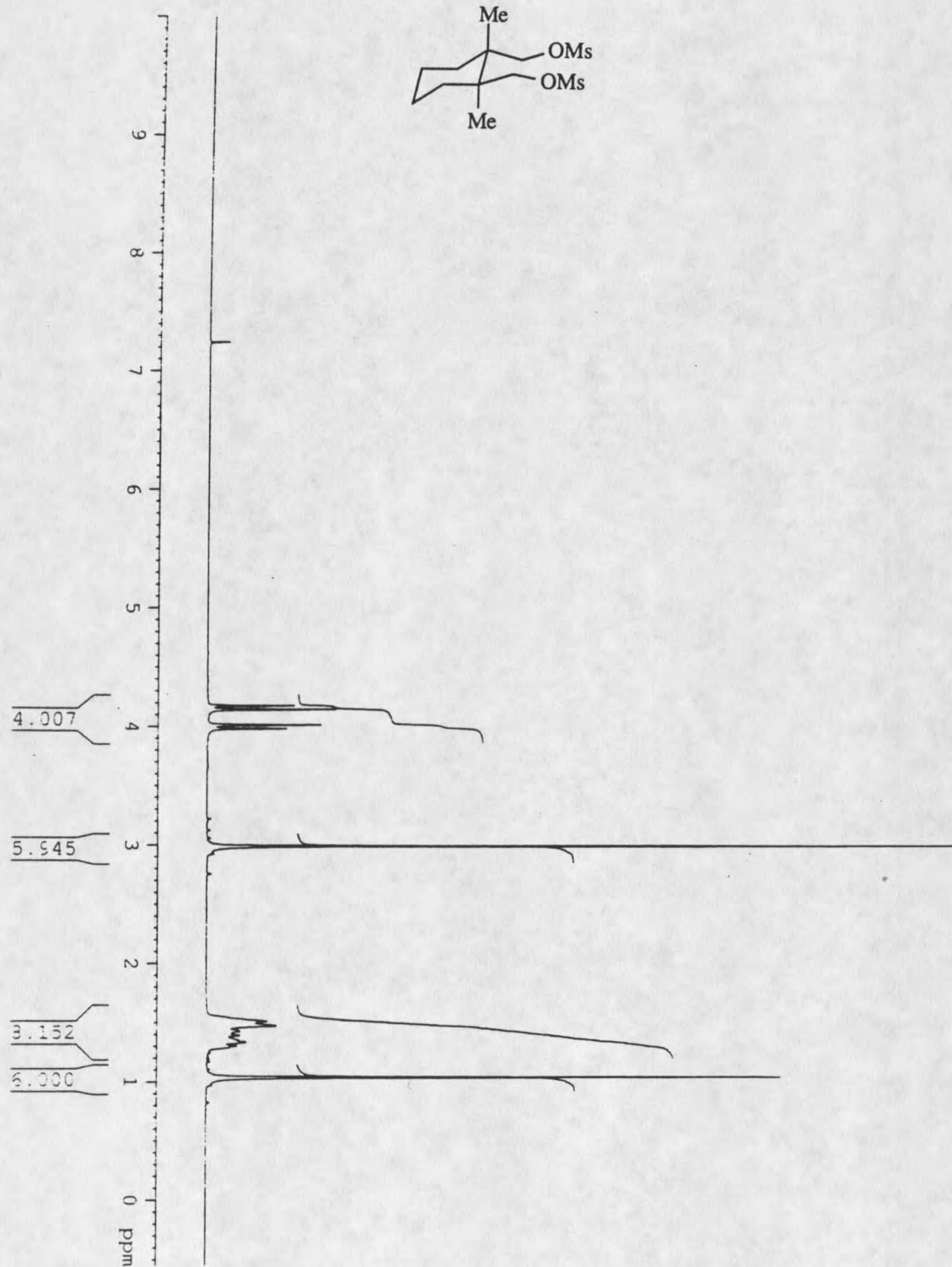
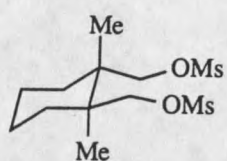
¹³C NMR Spectrum of 92

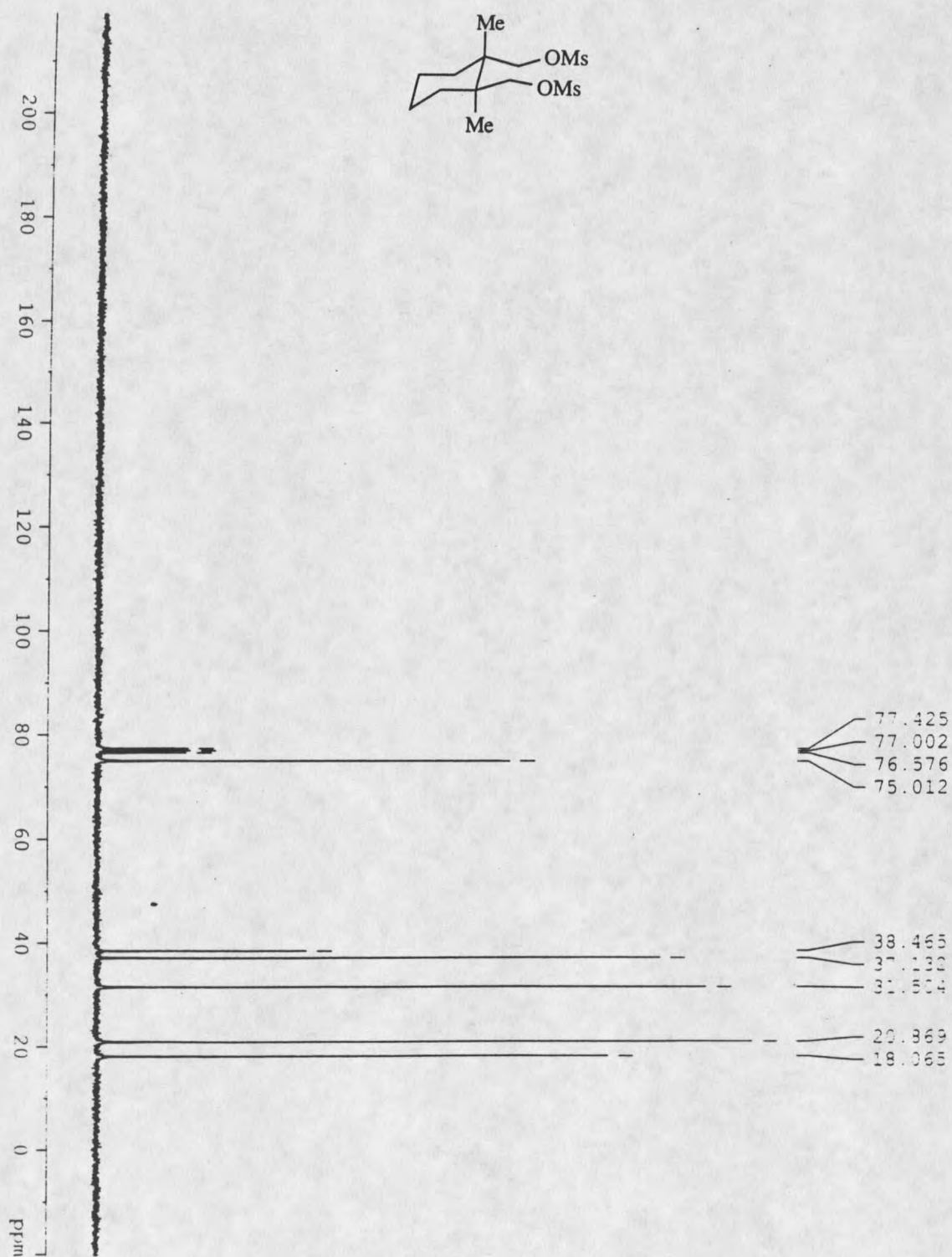
¹H NMR Spectrum of 93

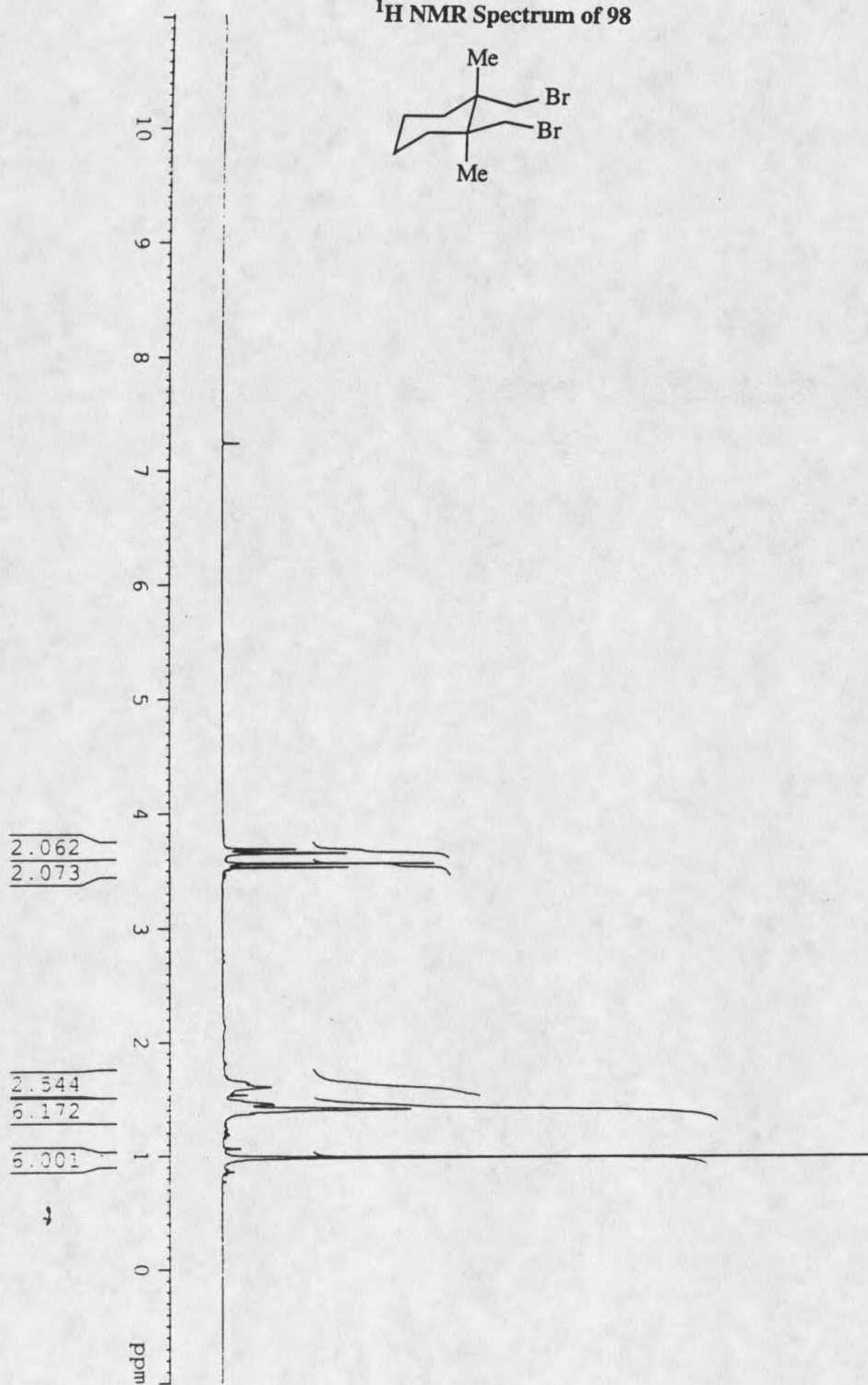
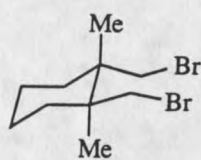
^{13}C NMR Spectrum of 93

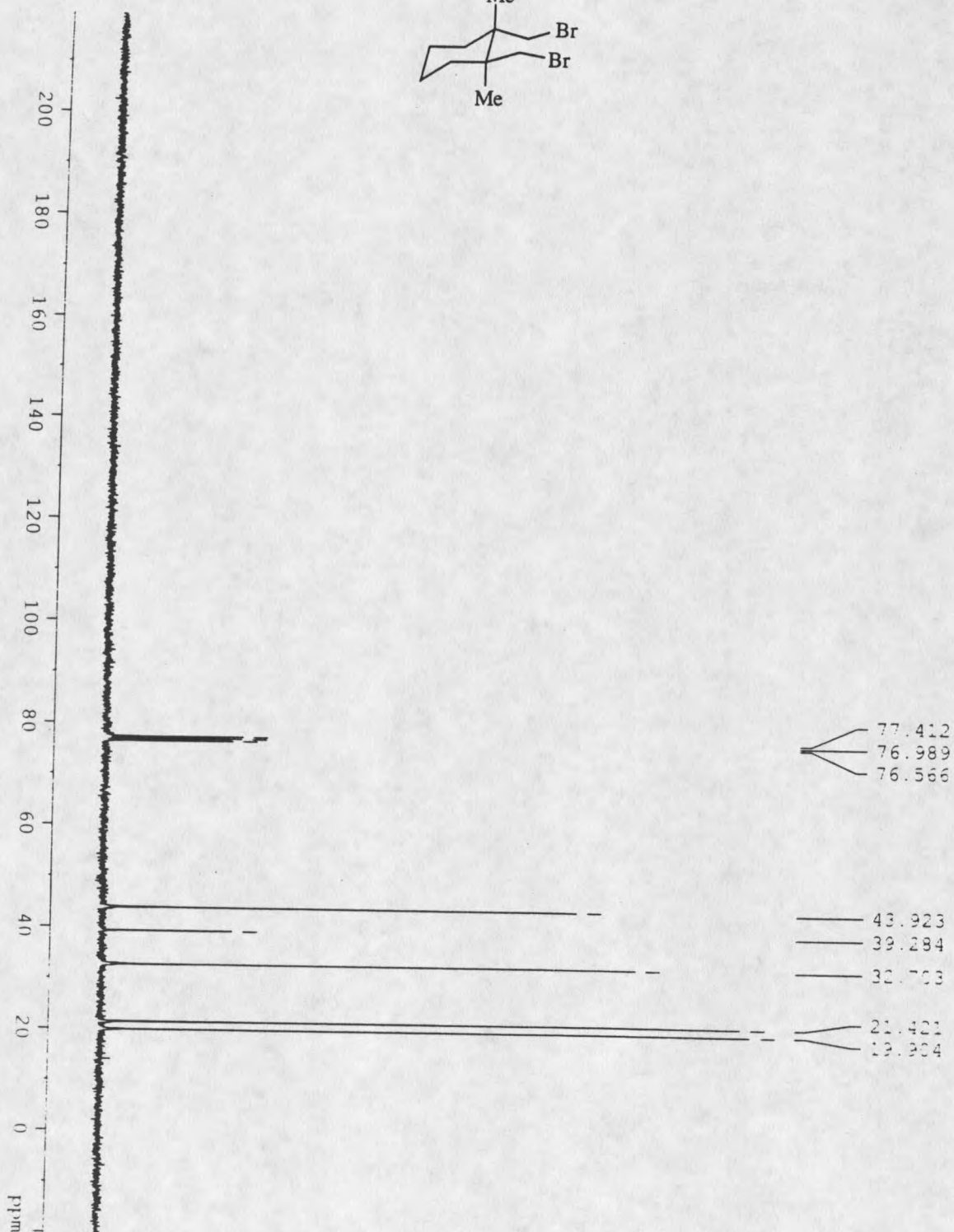
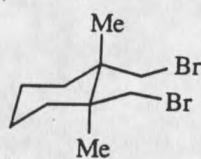
¹H NMR Spectrum of 94

¹³C NMR Spectrum of 94

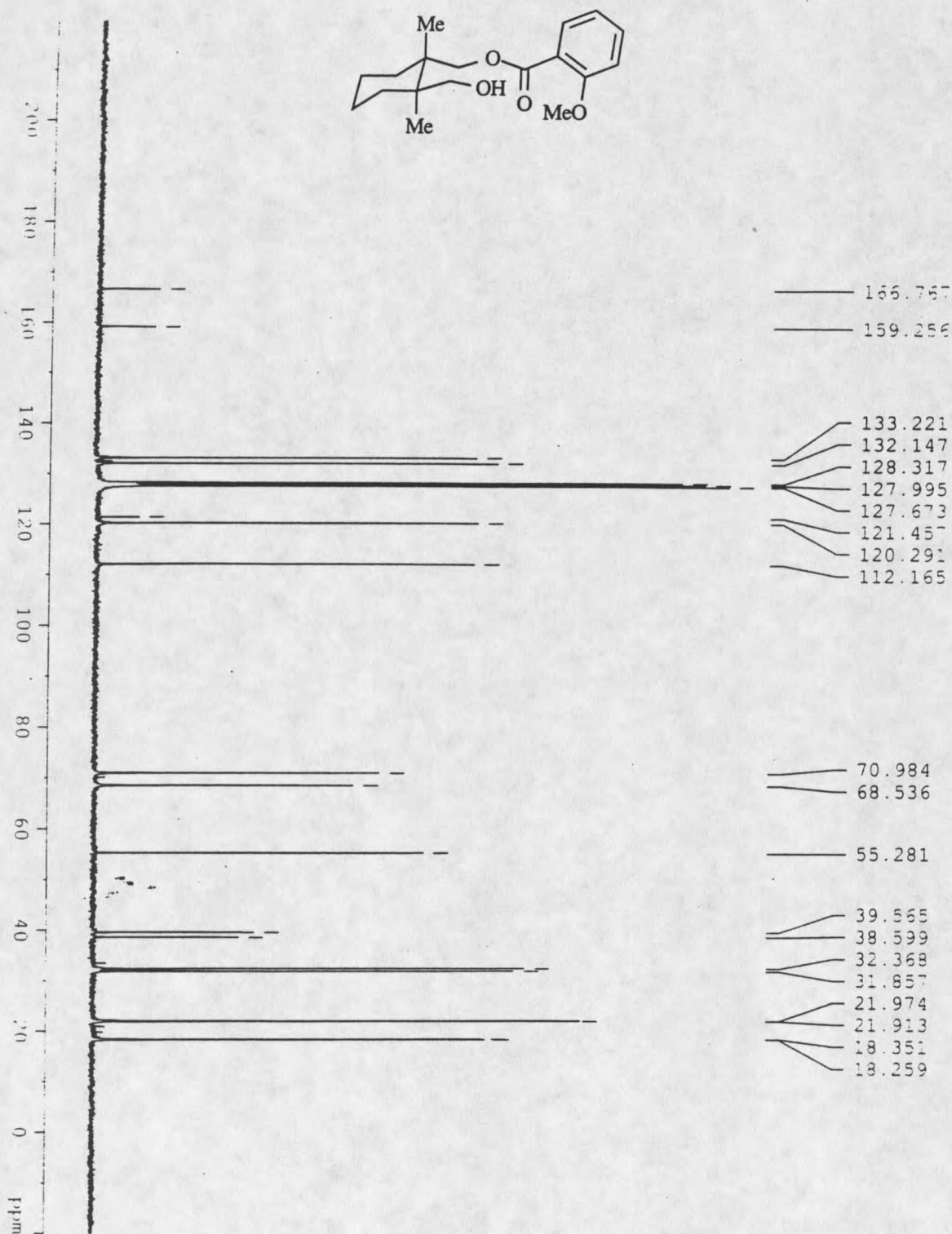
¹H NMR Spectrum of 97

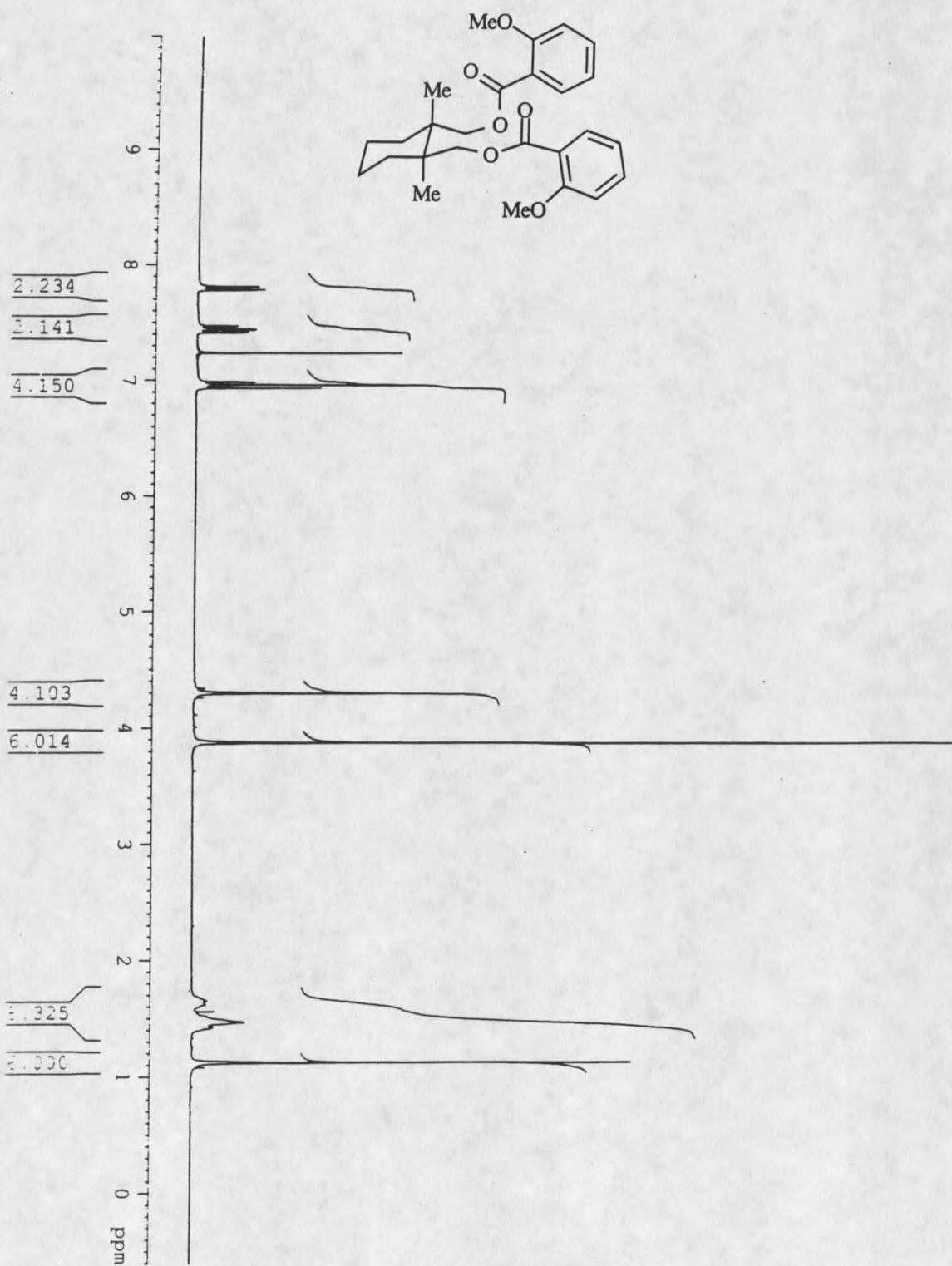
^{13}C NMR Spectrum of 97

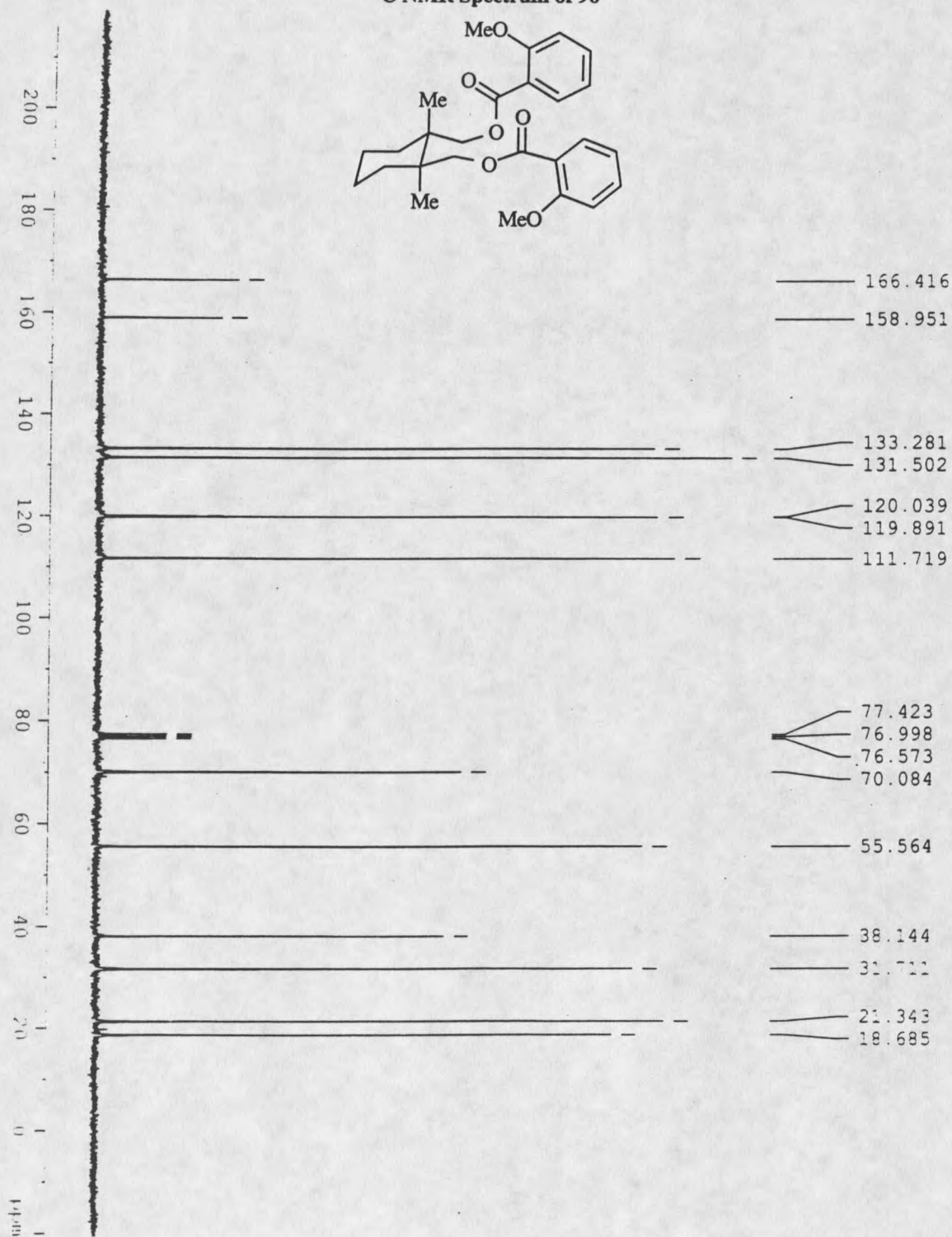
¹H NMR Spectrum of 98

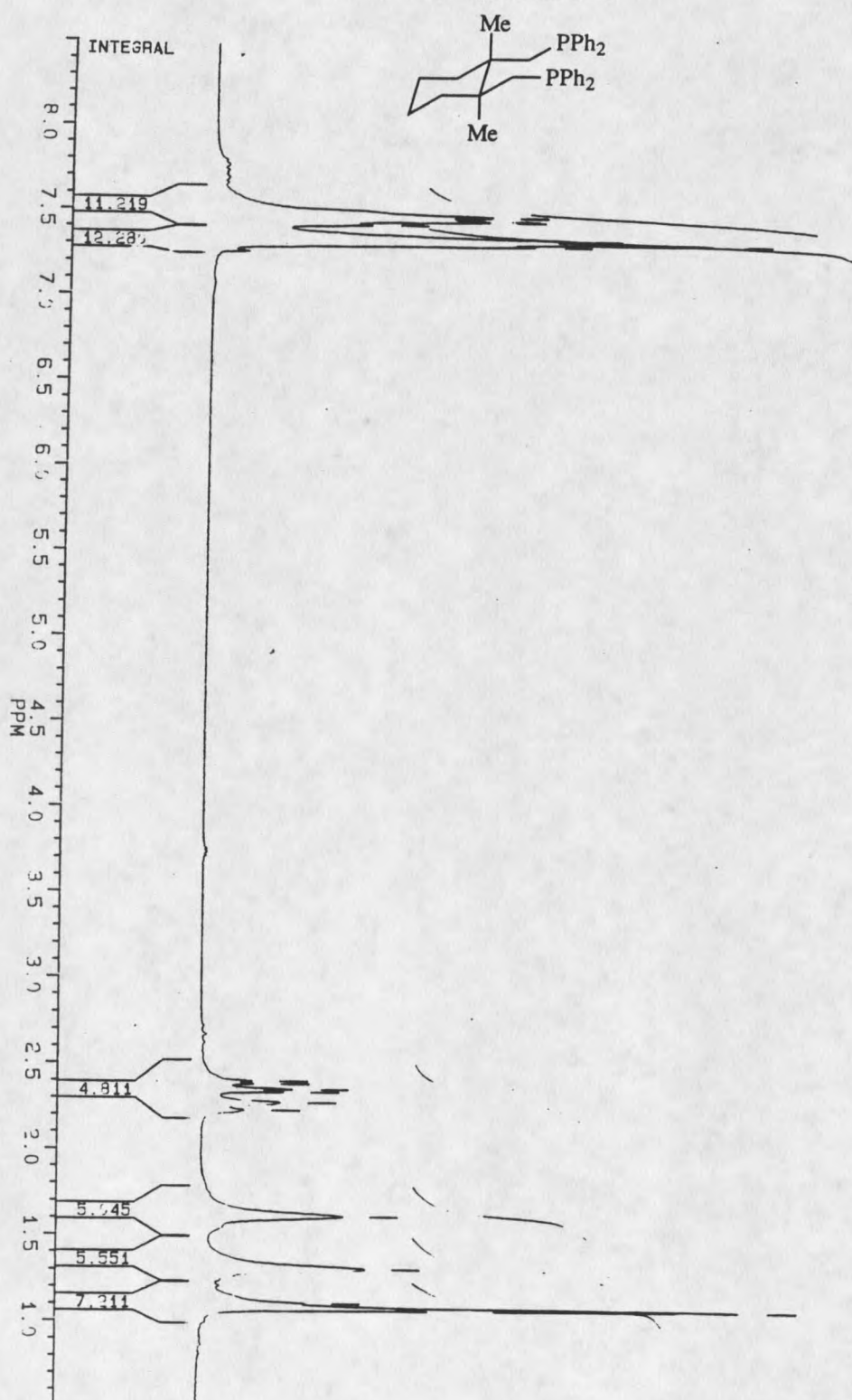
^{13}C NMR Spectrum of 98

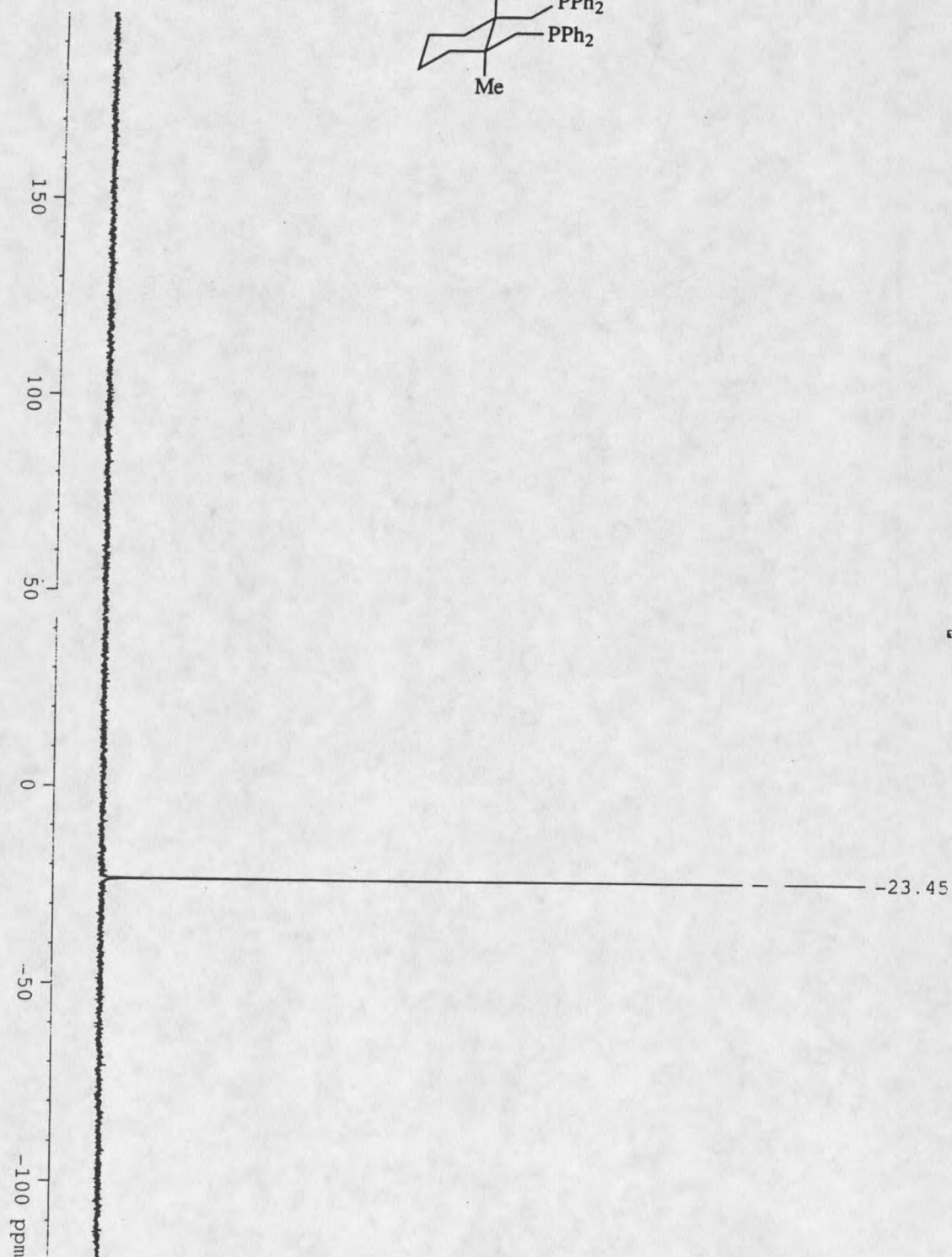
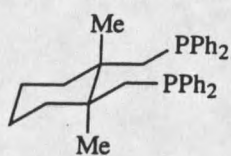
¹H NMR Spectrum of 95

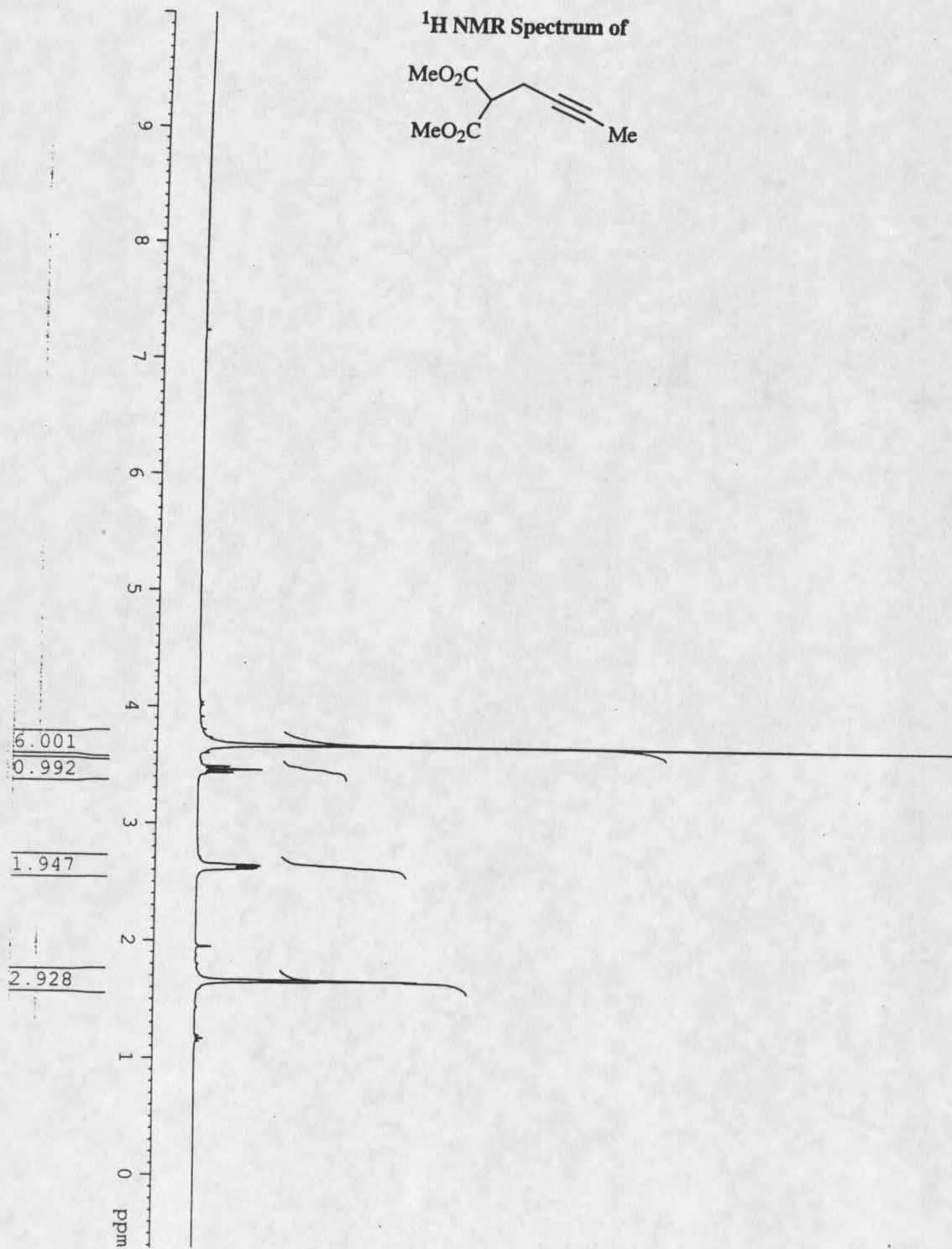
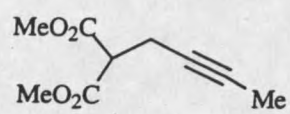
¹³C NMR Spectrum of 95

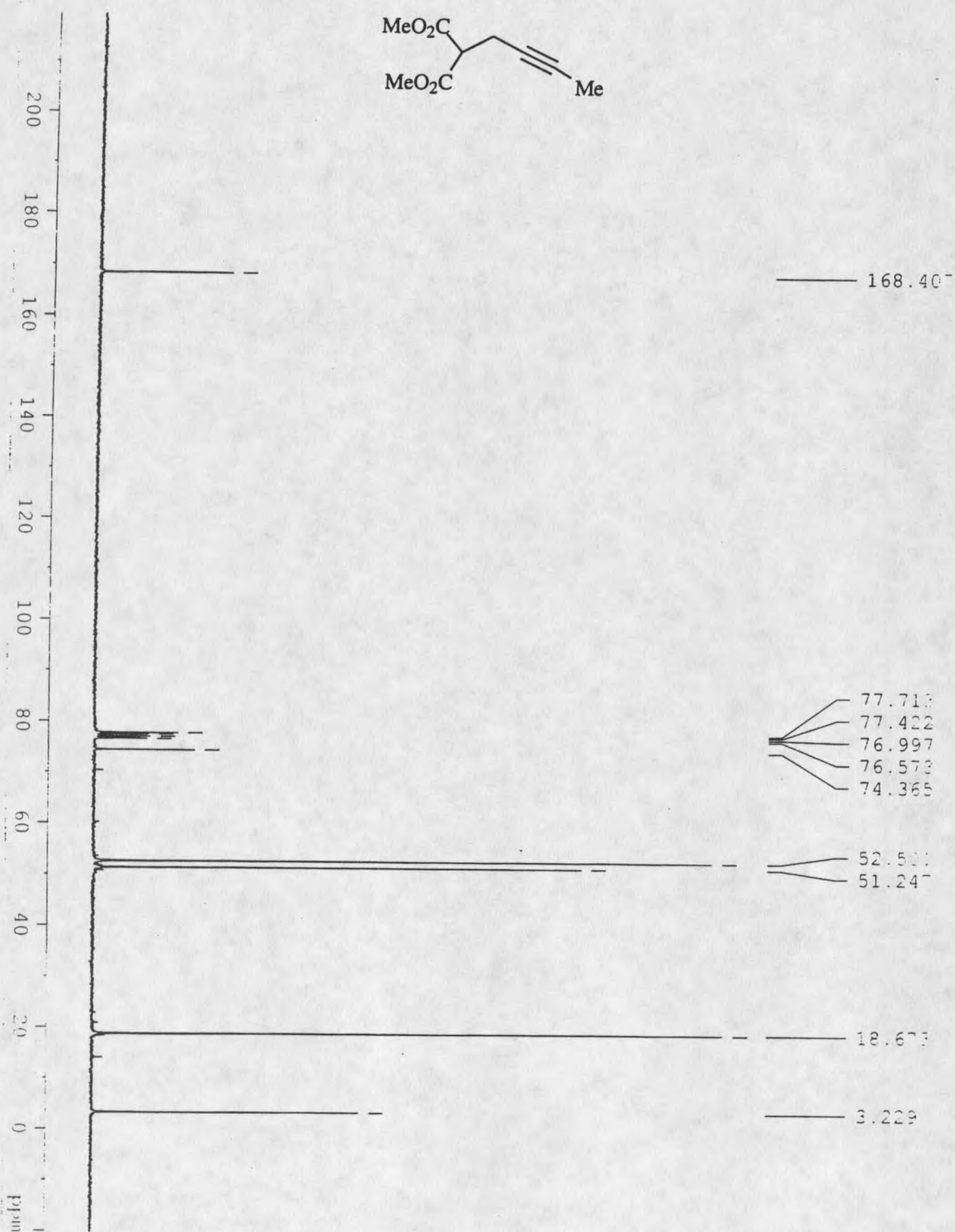
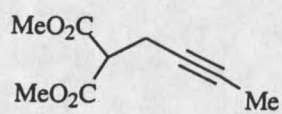
¹H NMR Spectrum of 96

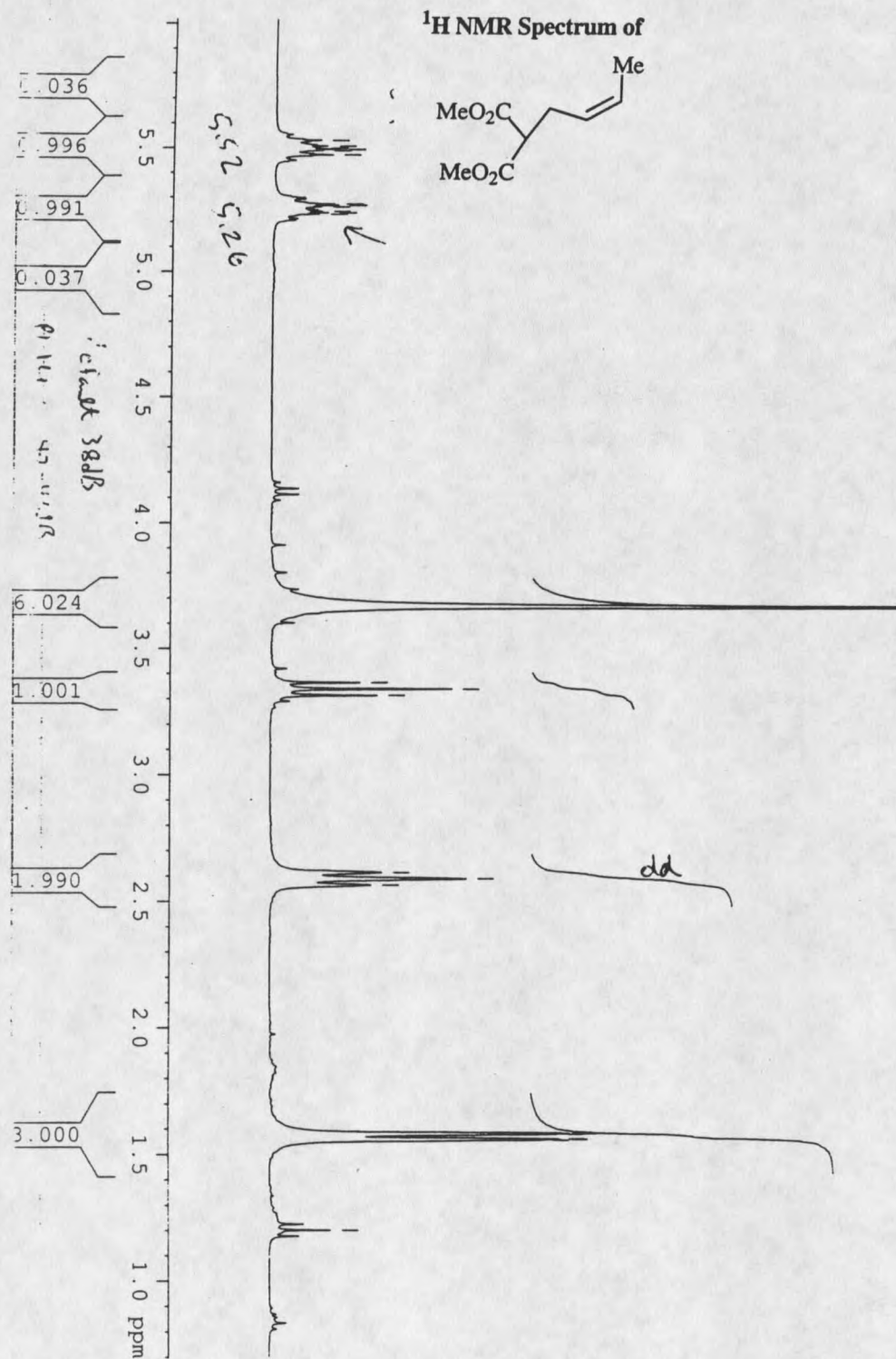
¹³C NMR Spectrum of 96

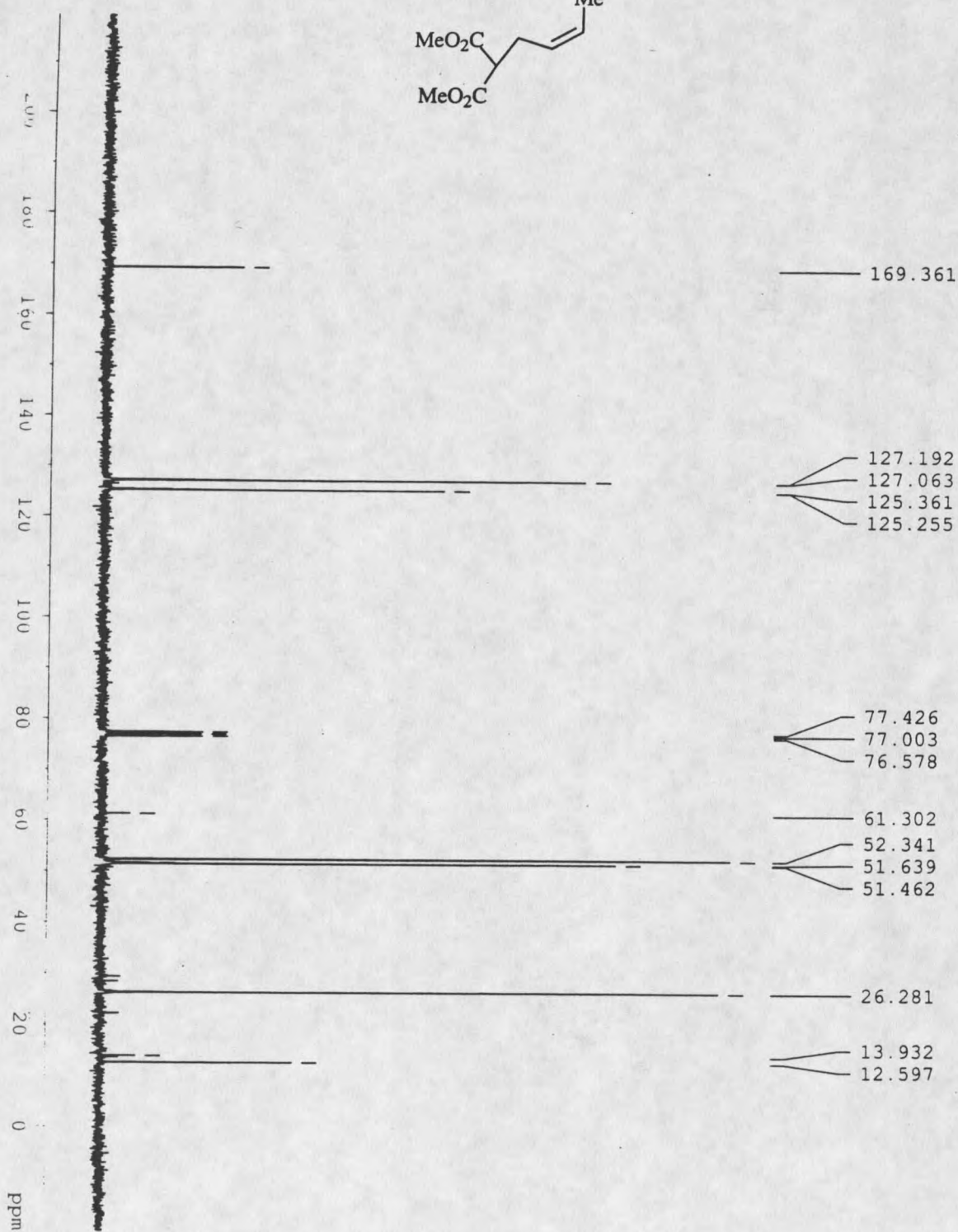
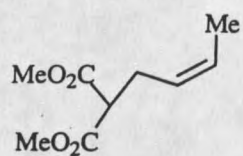
¹H NMR Spectrum of 99

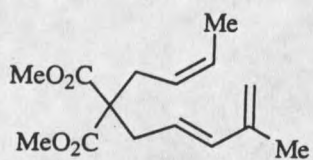
^{31}P NMR Spectrum of 99

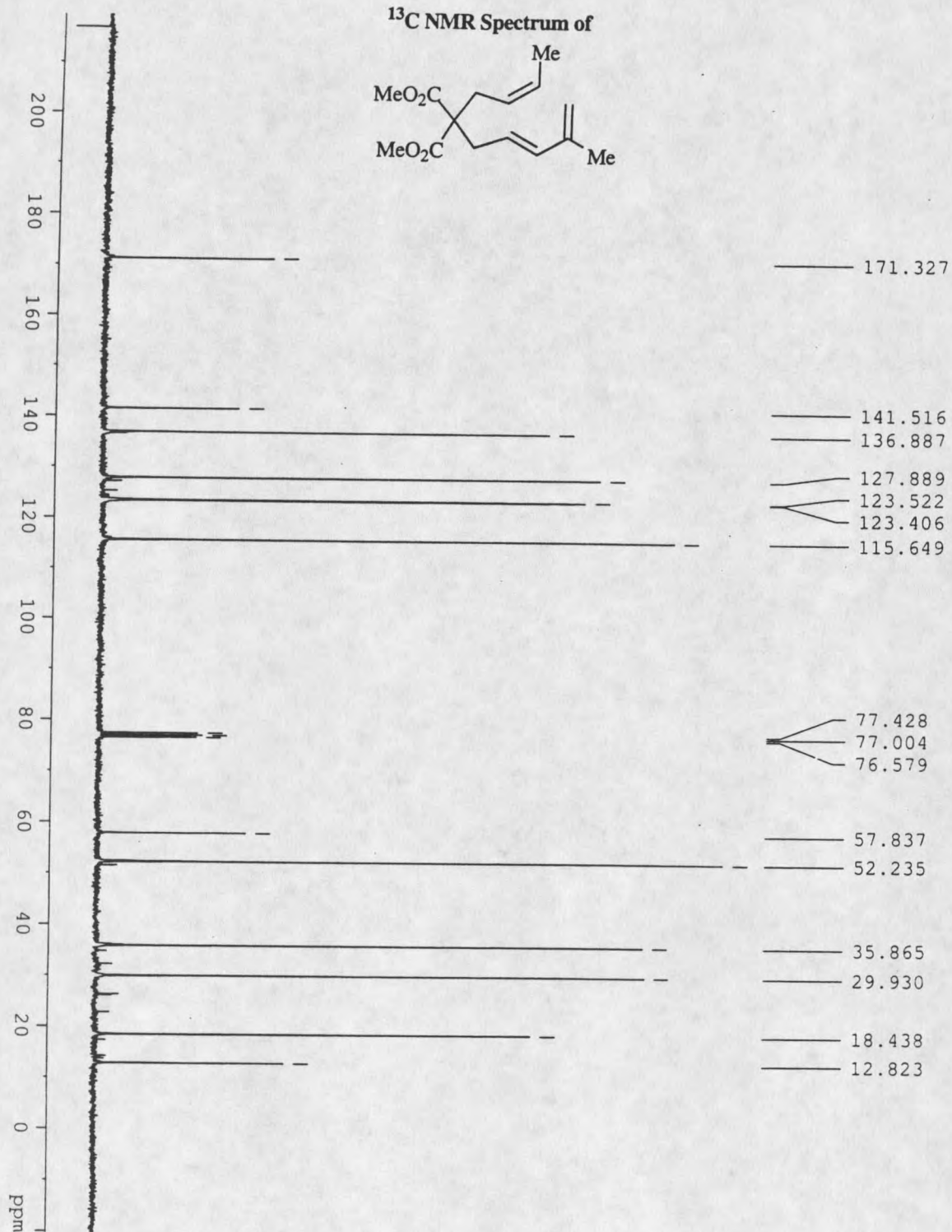
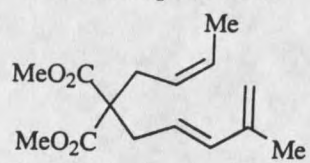
¹H NMR Spectrum of

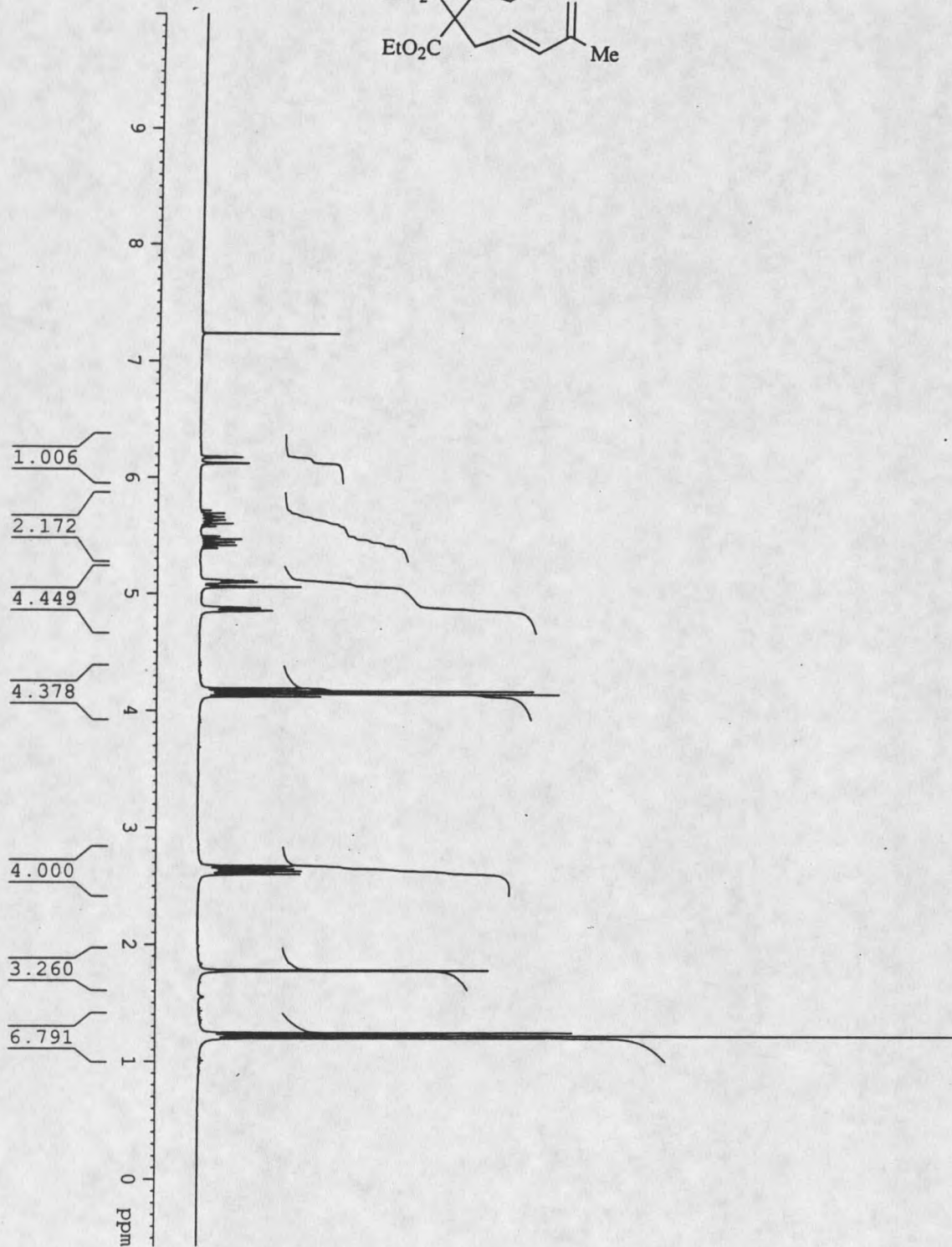
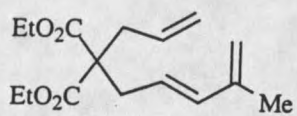
¹³C NMR Spectrum of

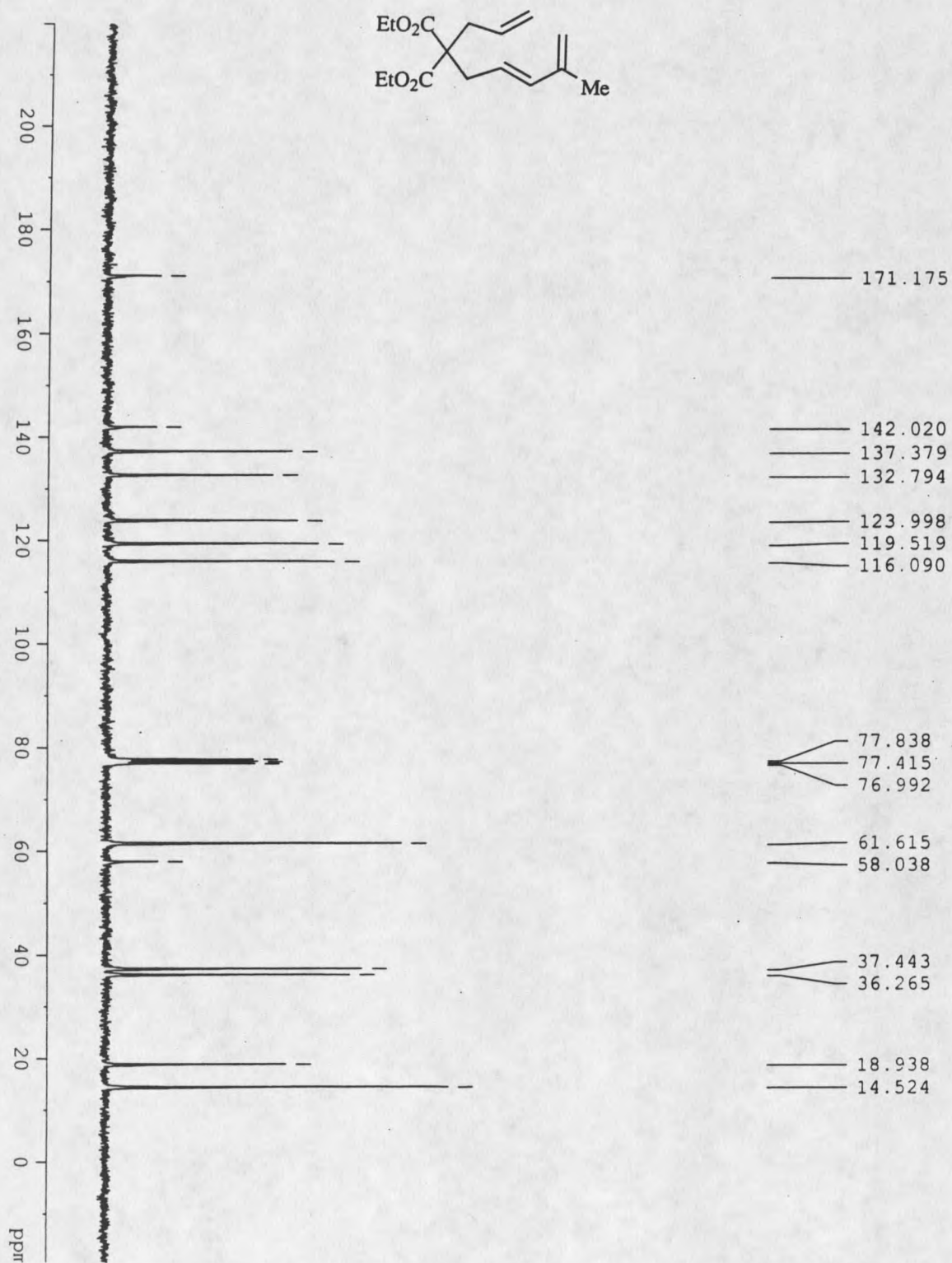


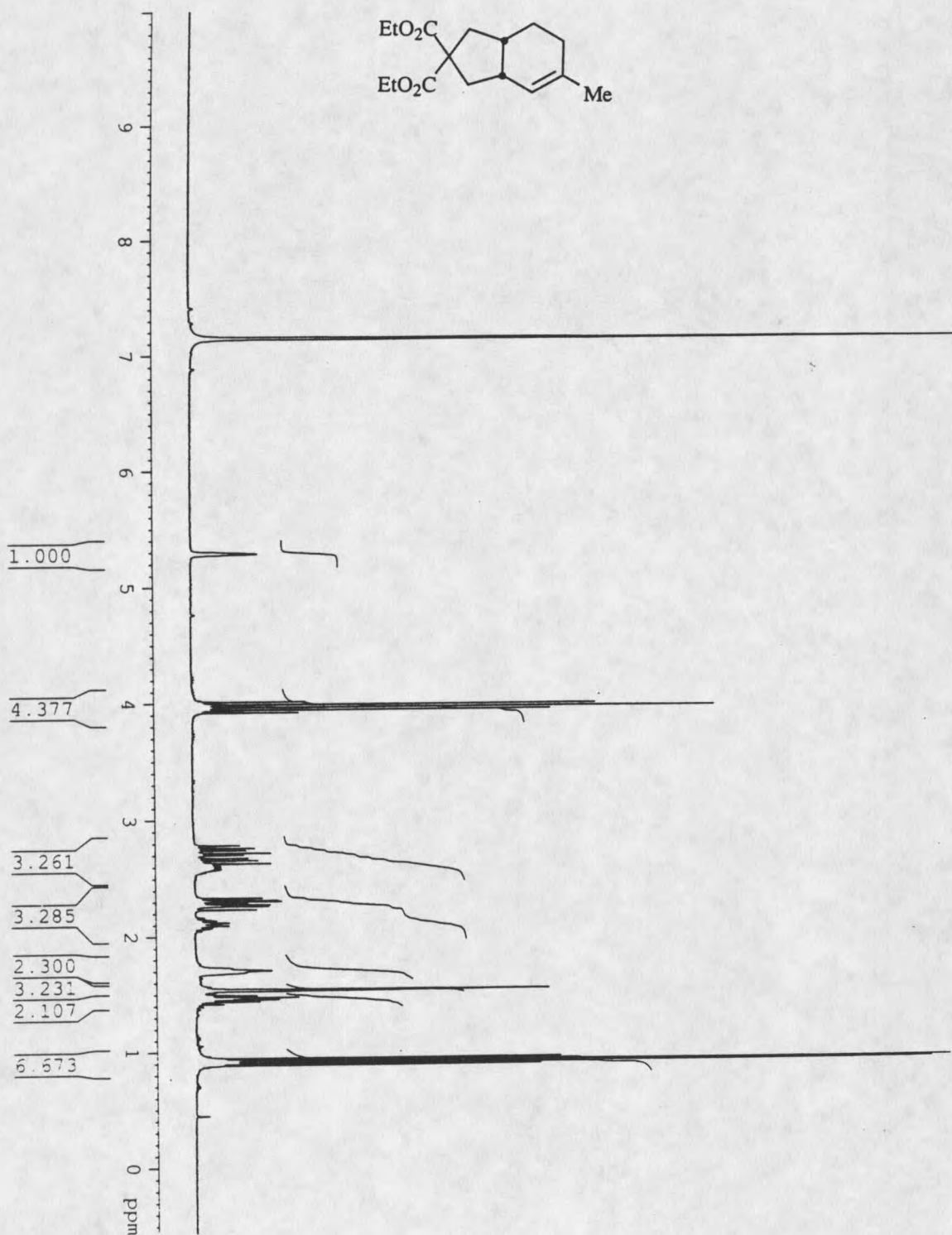
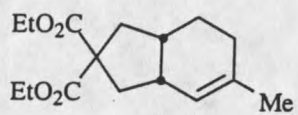
¹³C NMR Spectrum of

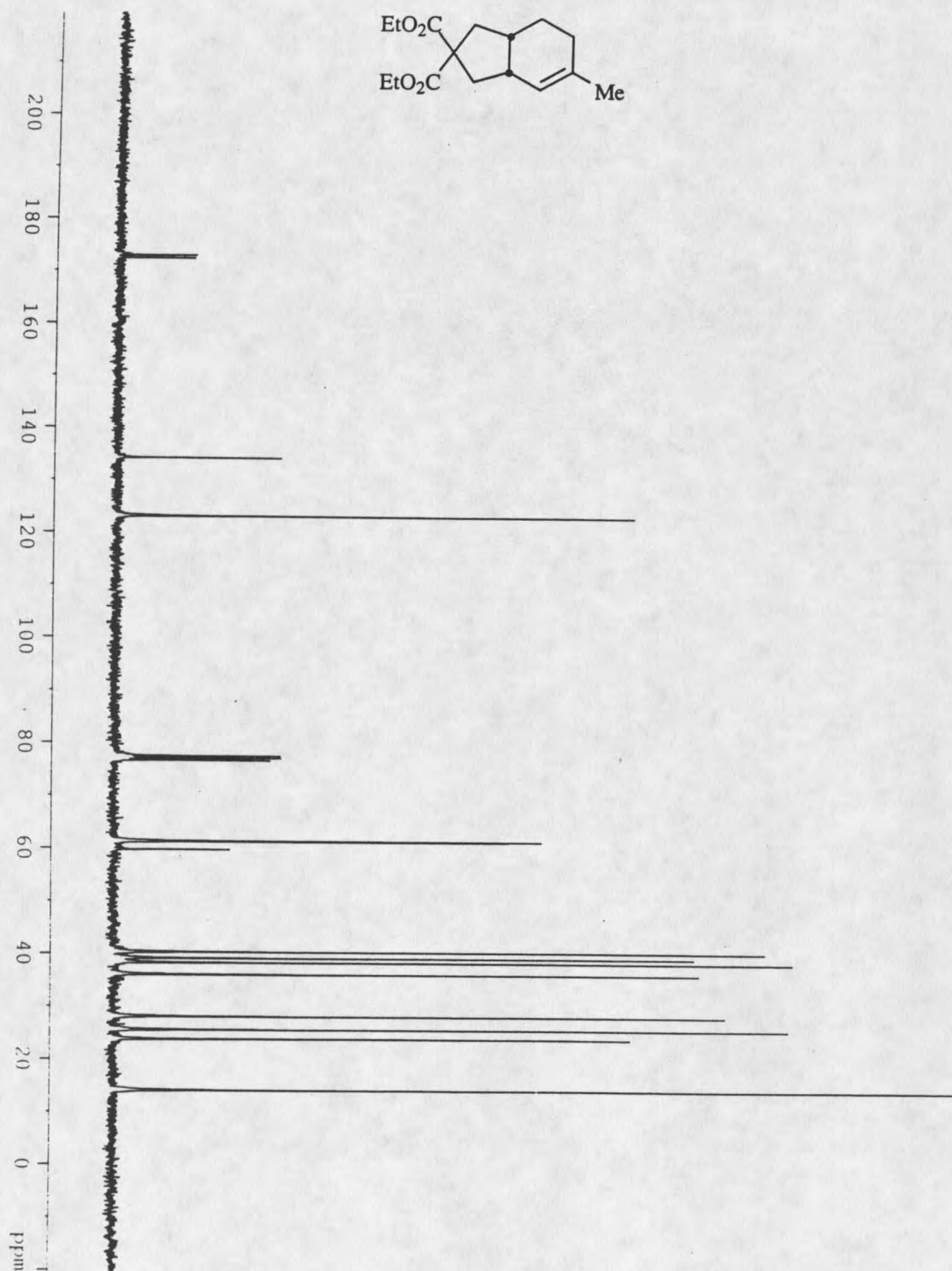
¹H NMR Spectrum of

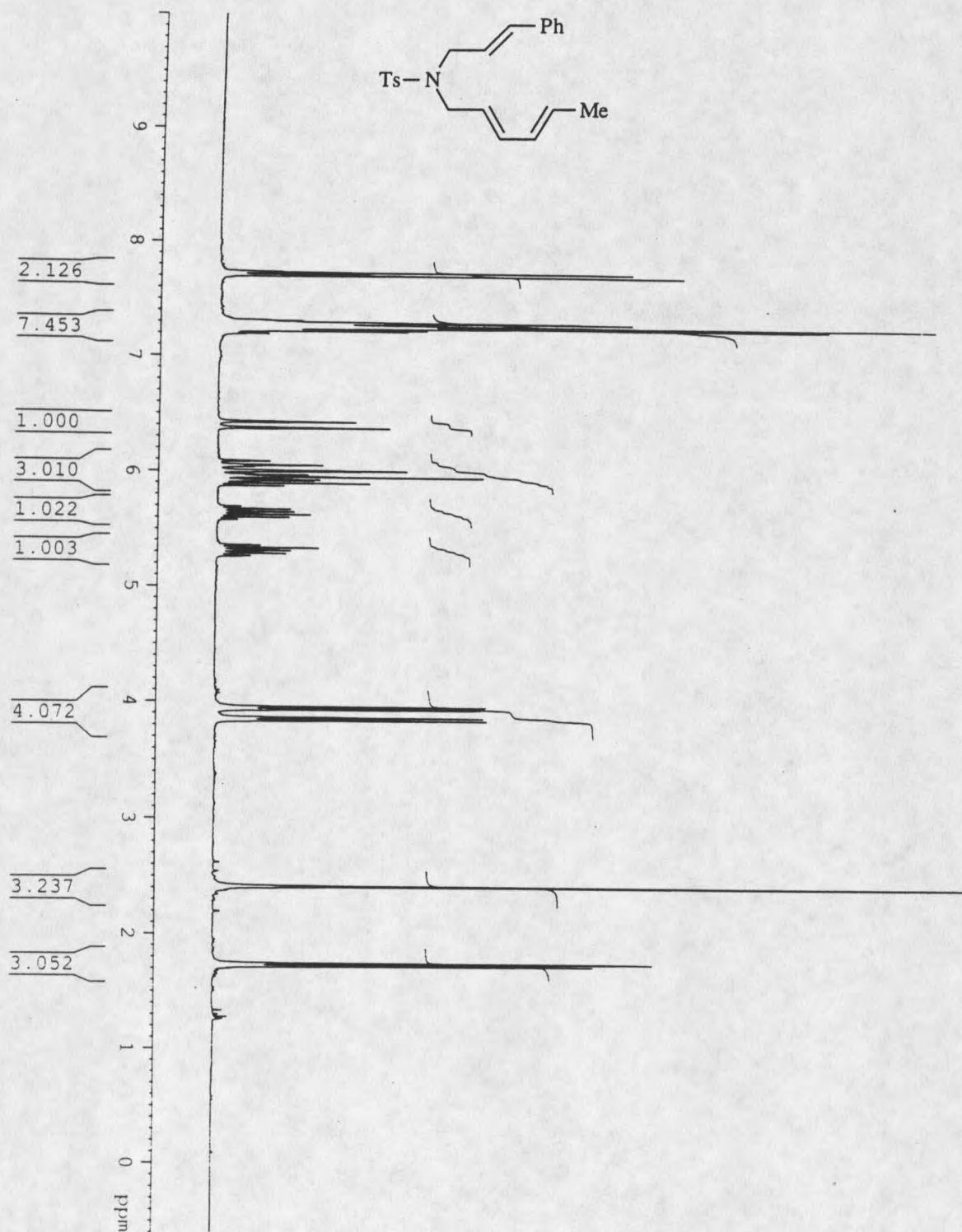
¹³C NMR Spectrum of

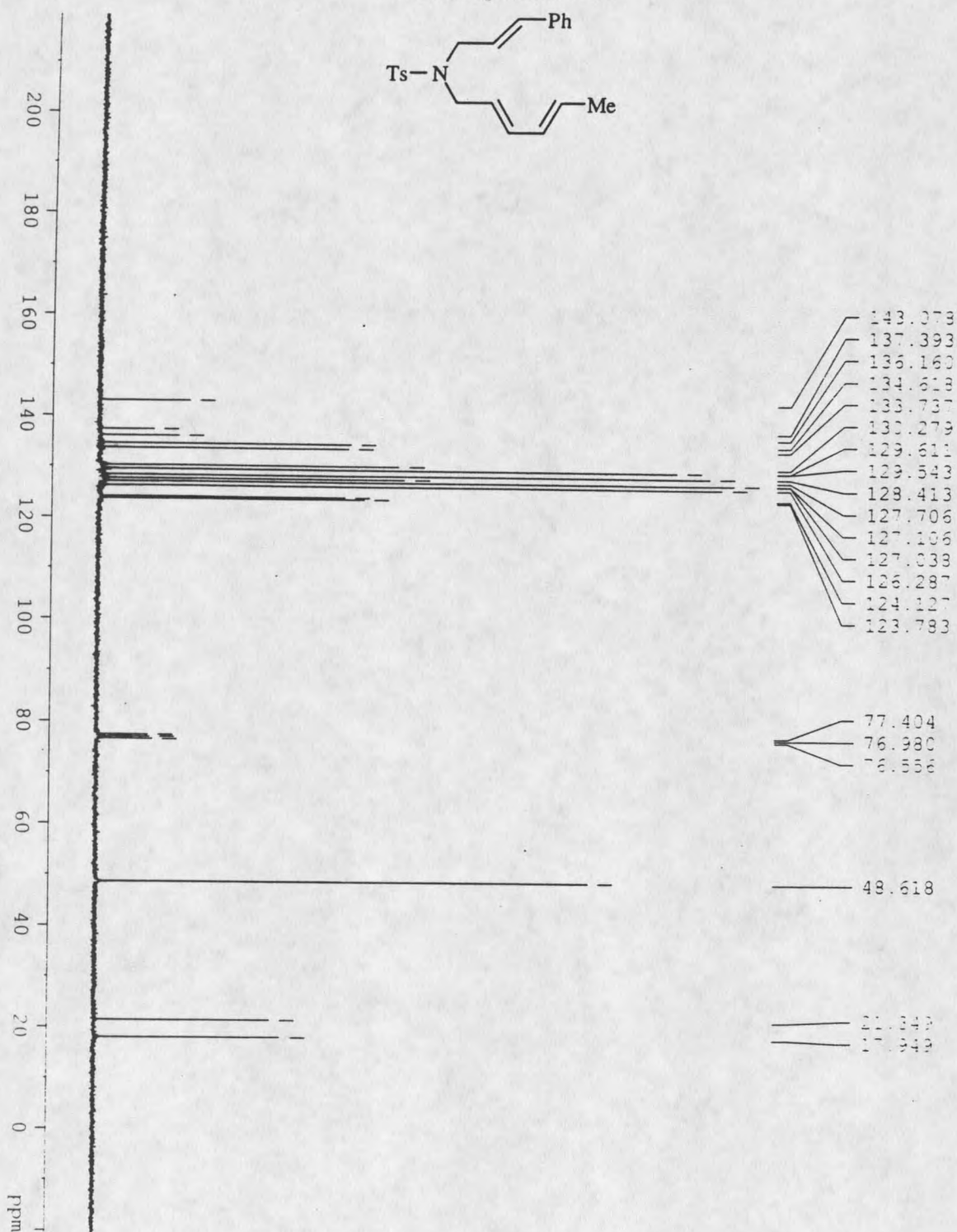
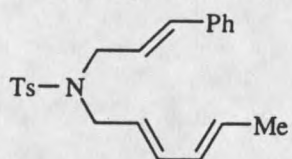
¹H NMR Spectrum of 77

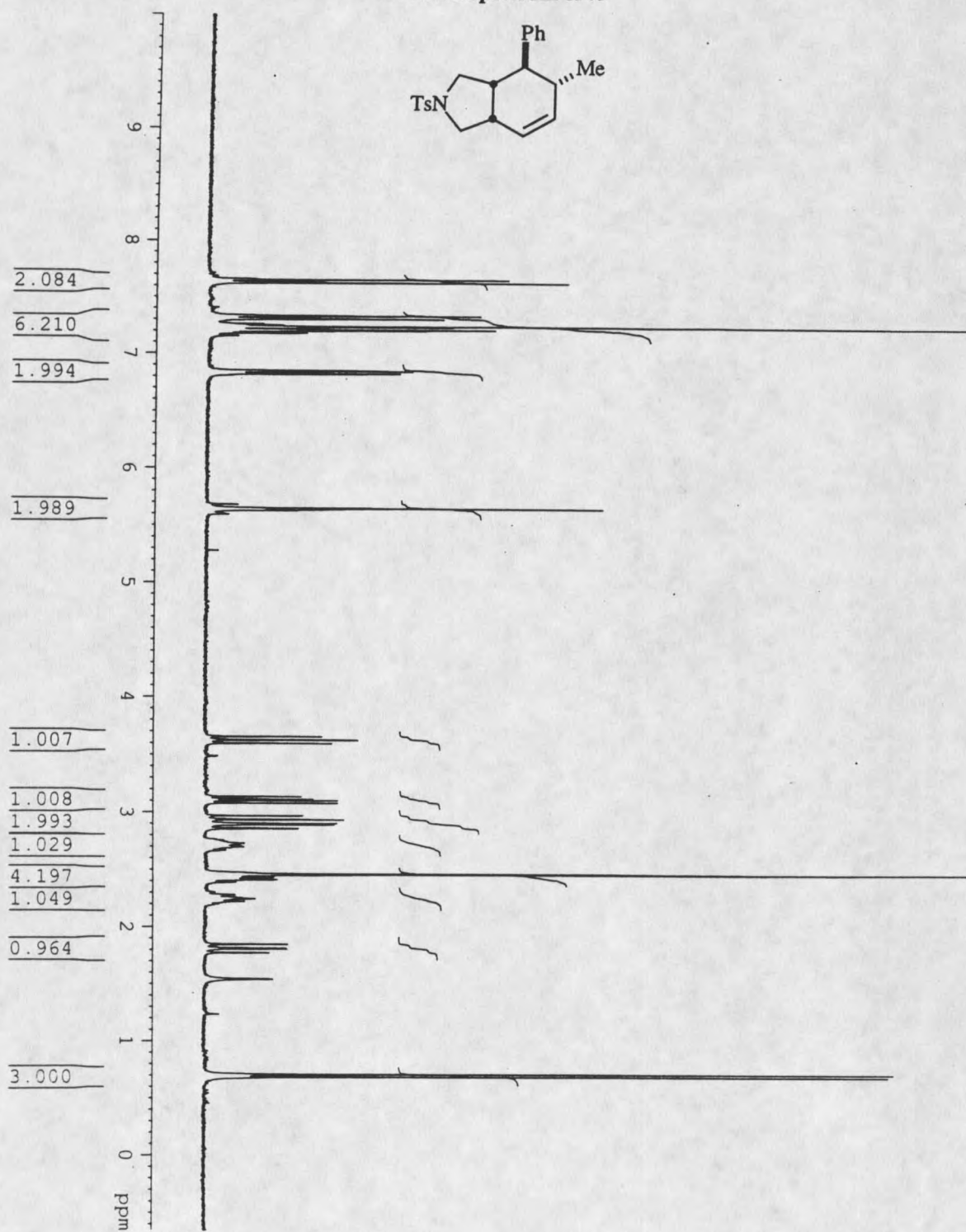
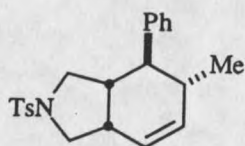
¹³C NMR Spectrum of 77

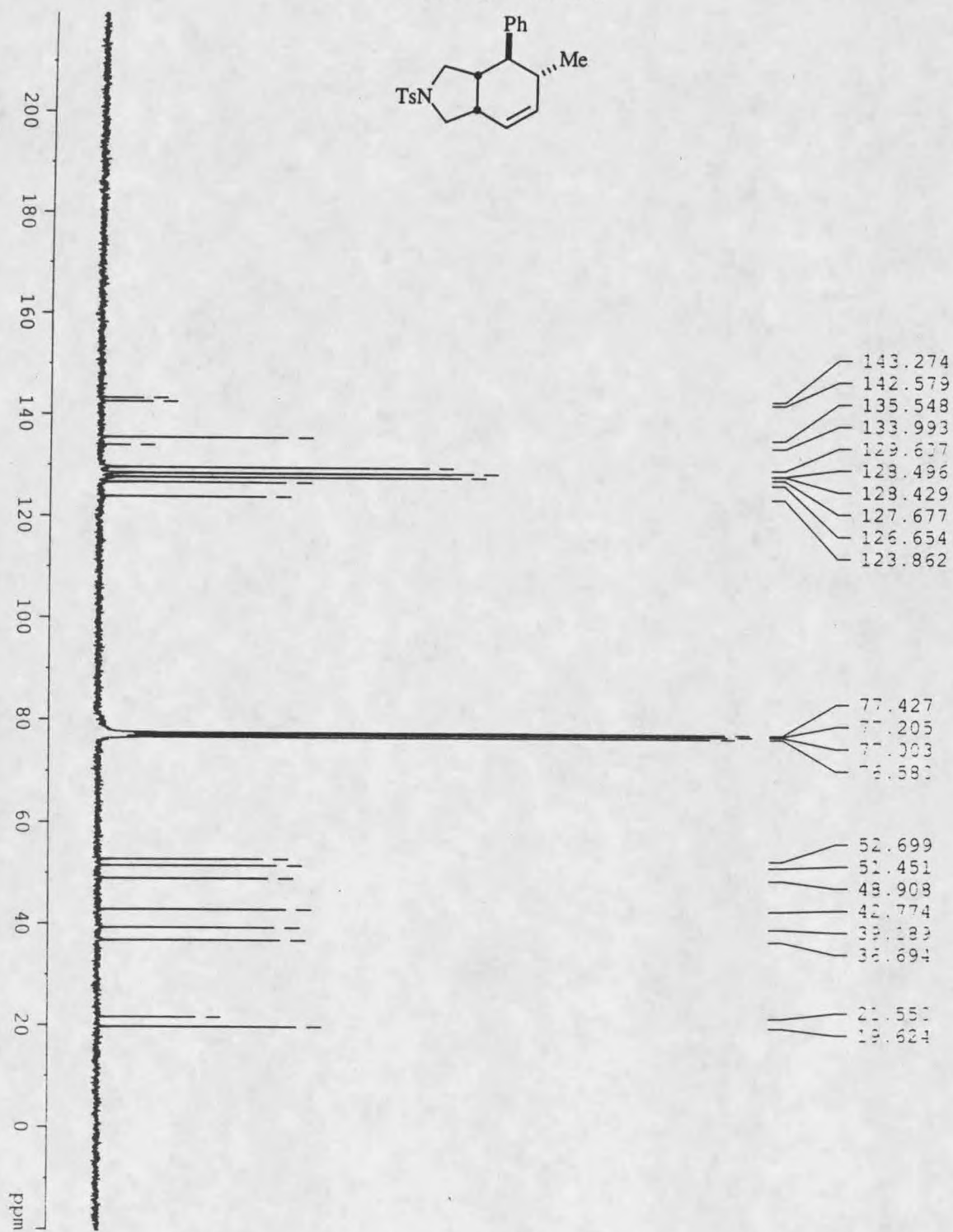
¹H NMR Spectrum of 78

^{13}C NMR Spectrum of 78

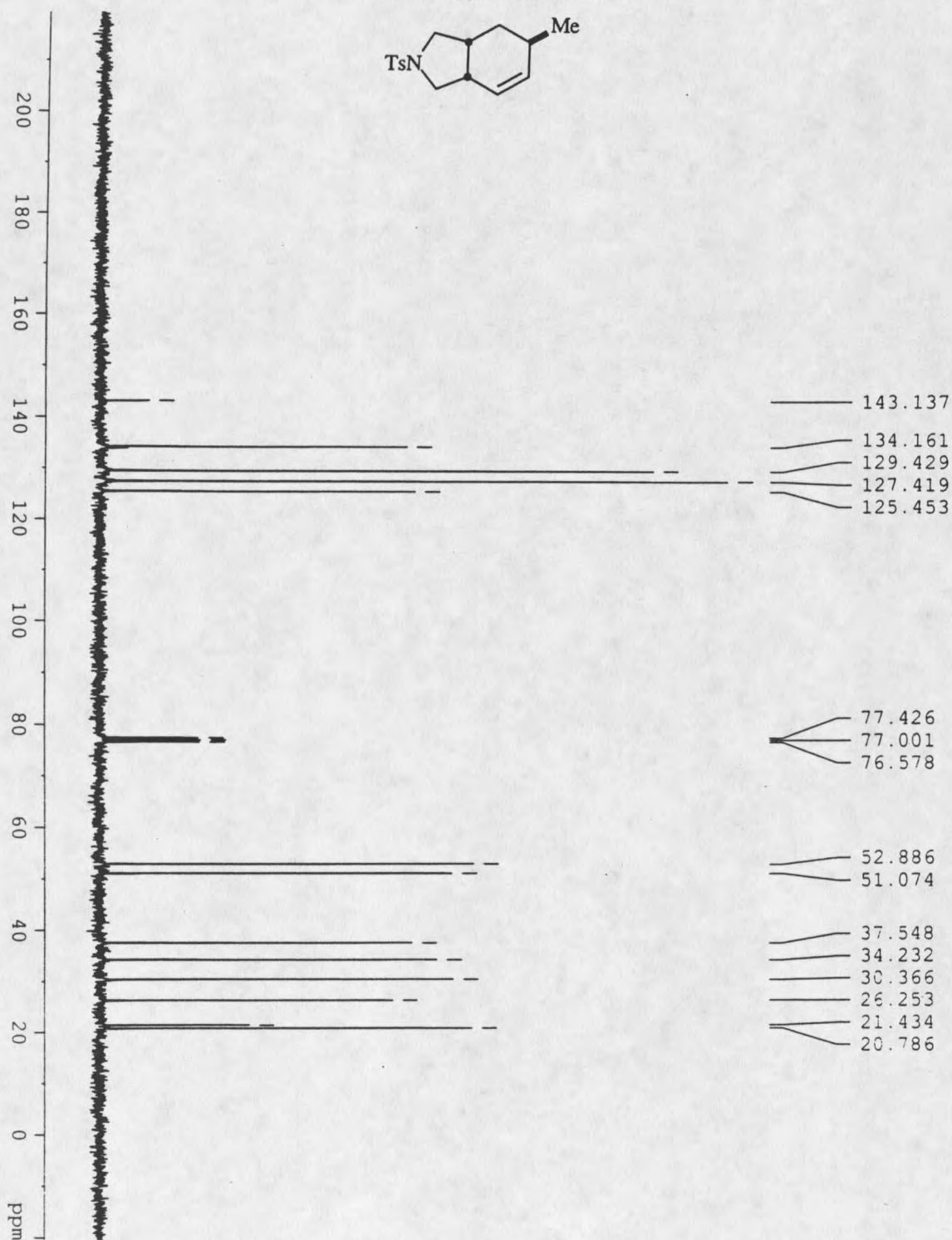
¹H NMR Spectrum of 75

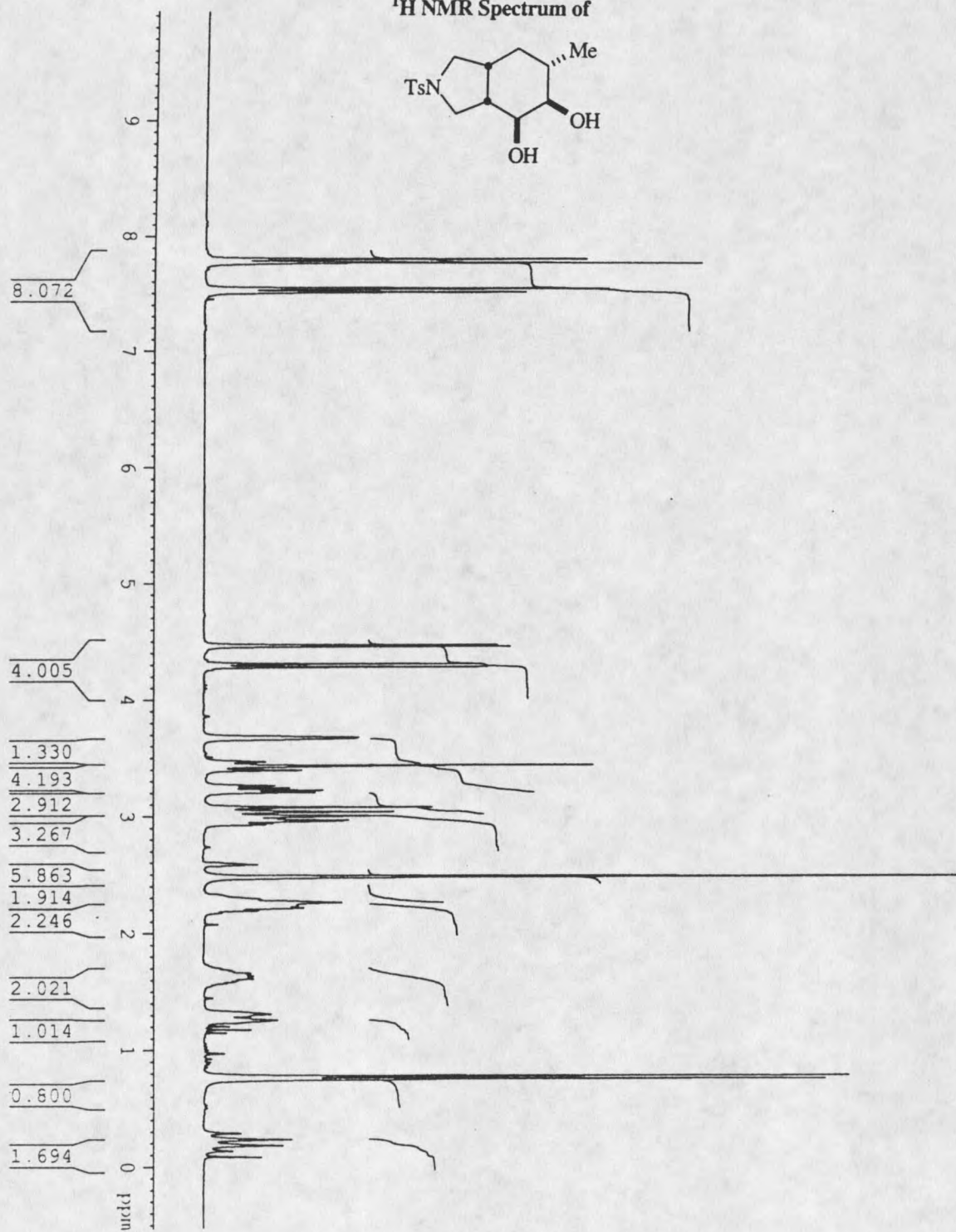
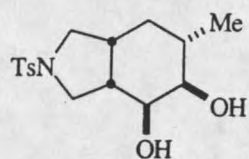
^{13}C NMR Spectrum of 75

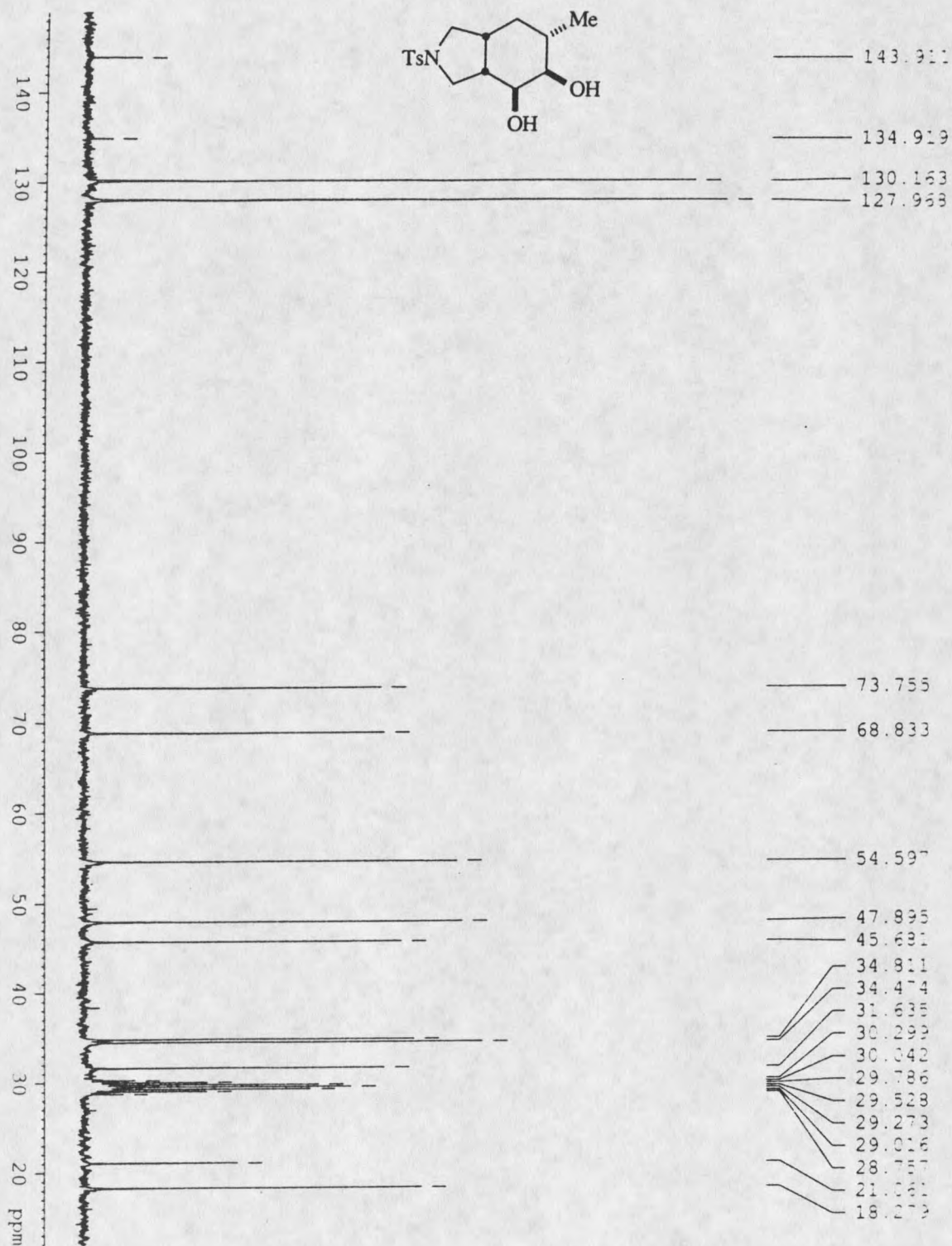
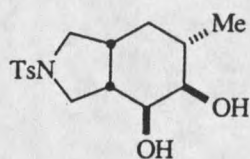
¹H NMR Spectrum of 79

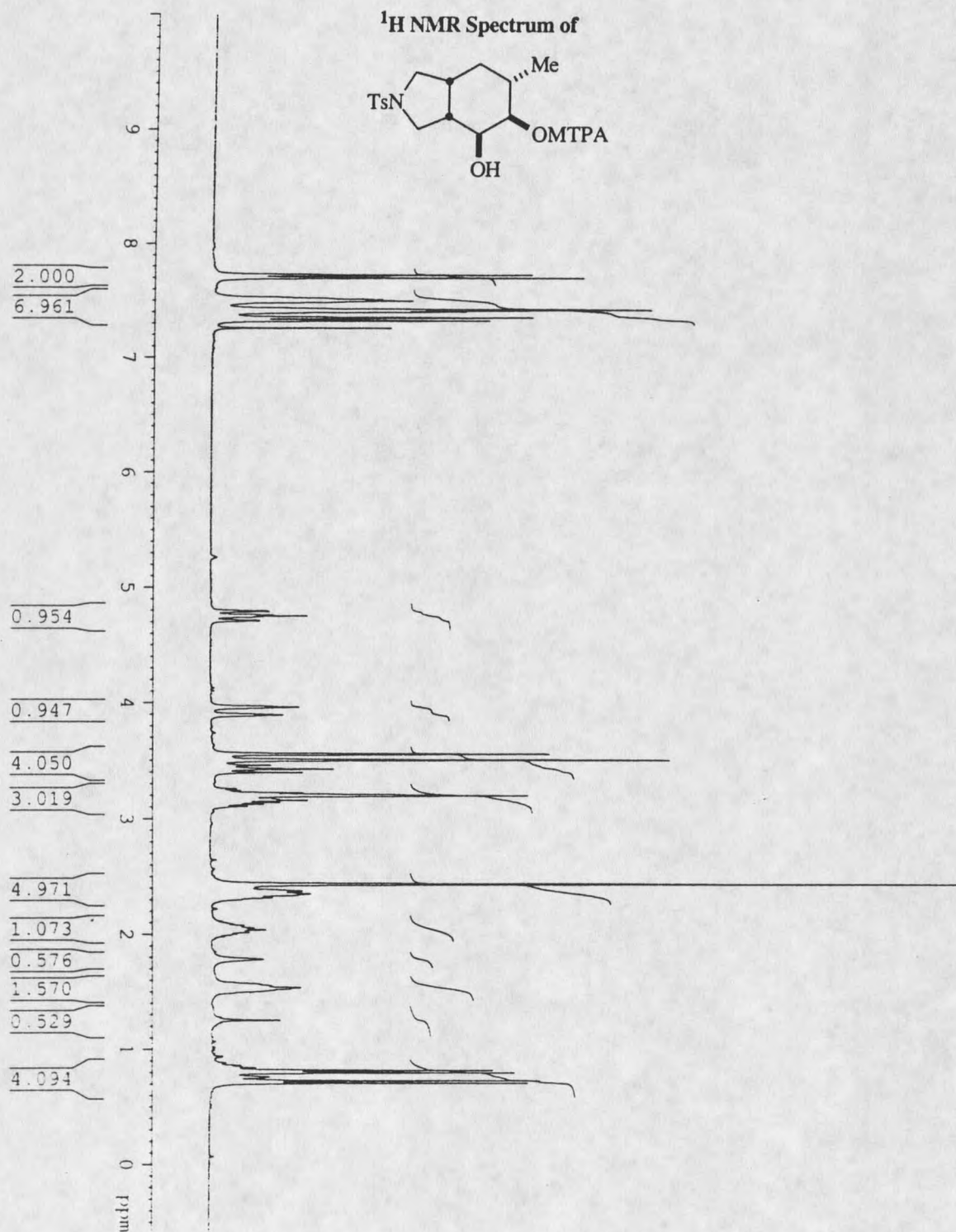
¹³C NMR Spectrum of 79

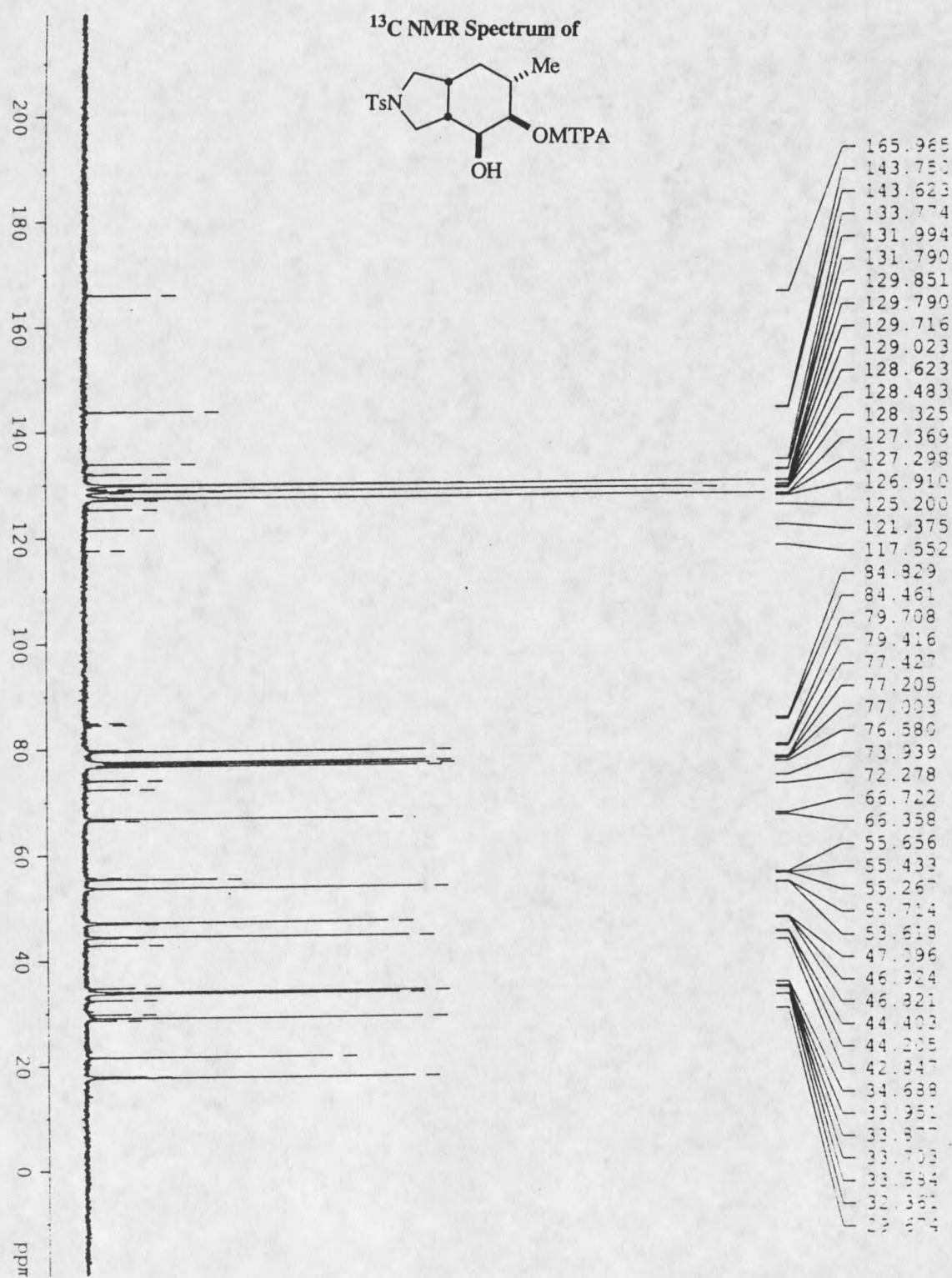
¹H NMR Spectrum of 79

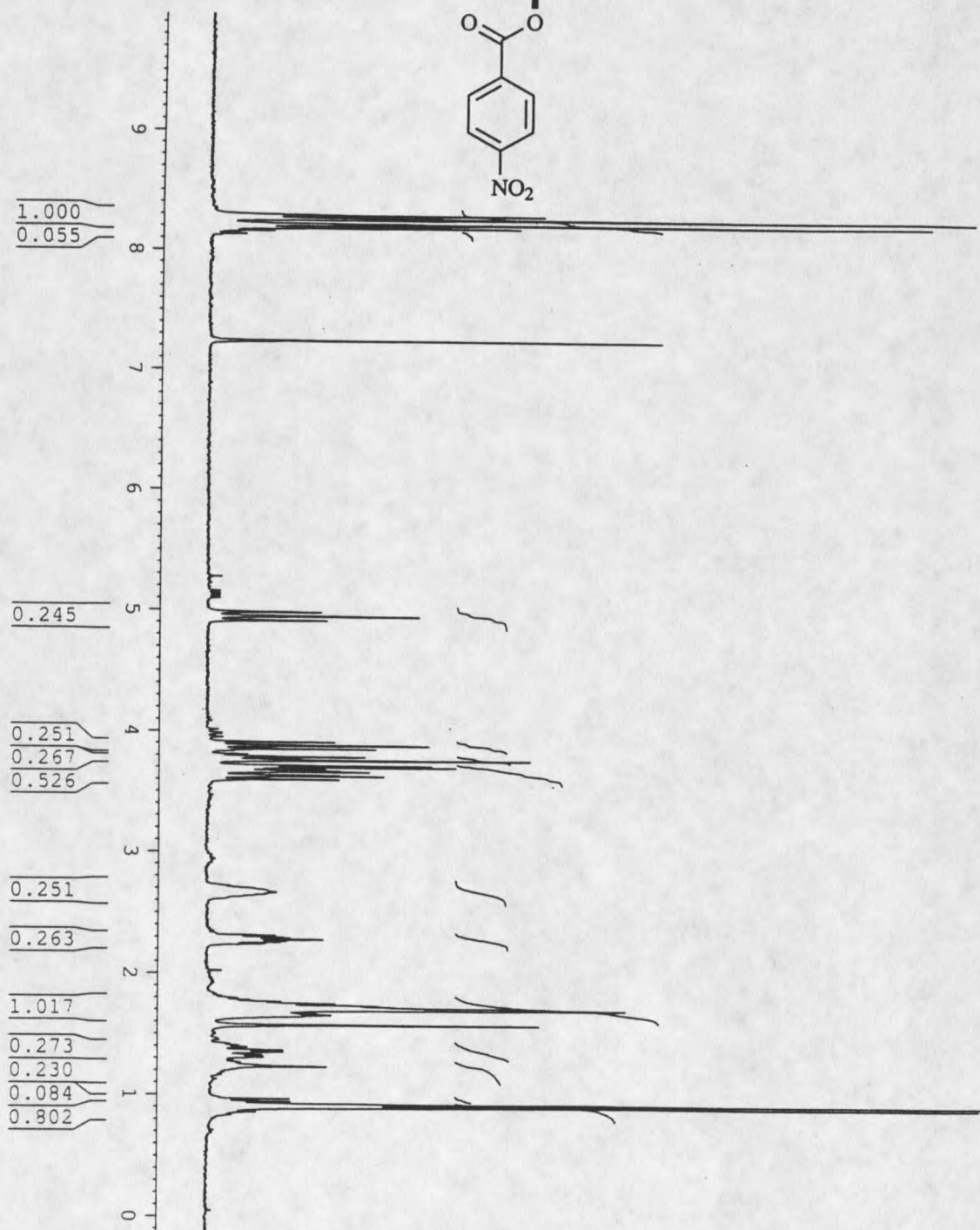
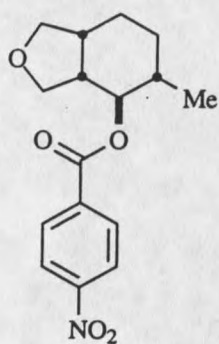
¹³C NMR Spectrum of 79

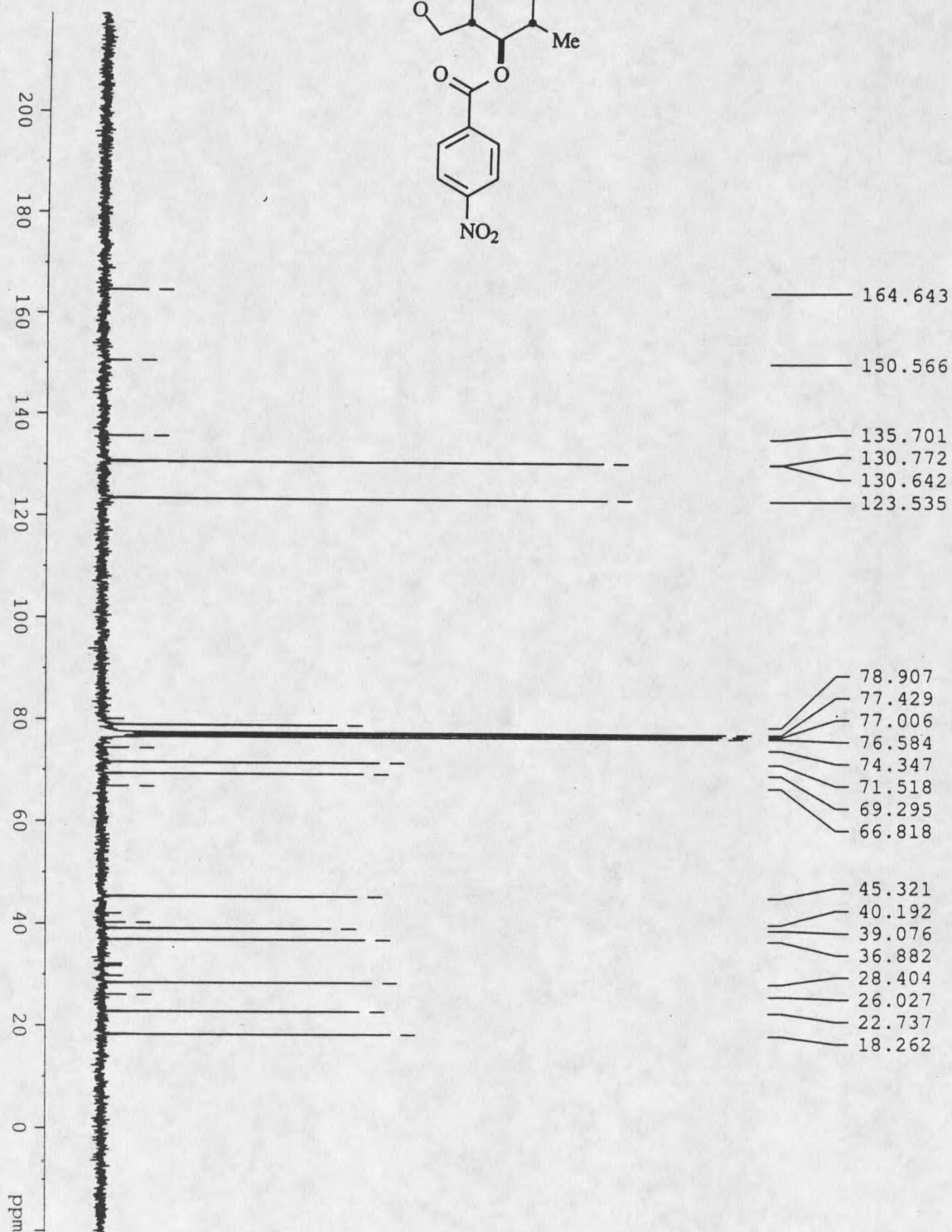
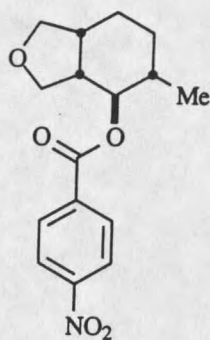
¹H NMR Spectrum of

¹³C NMR Spectrum of

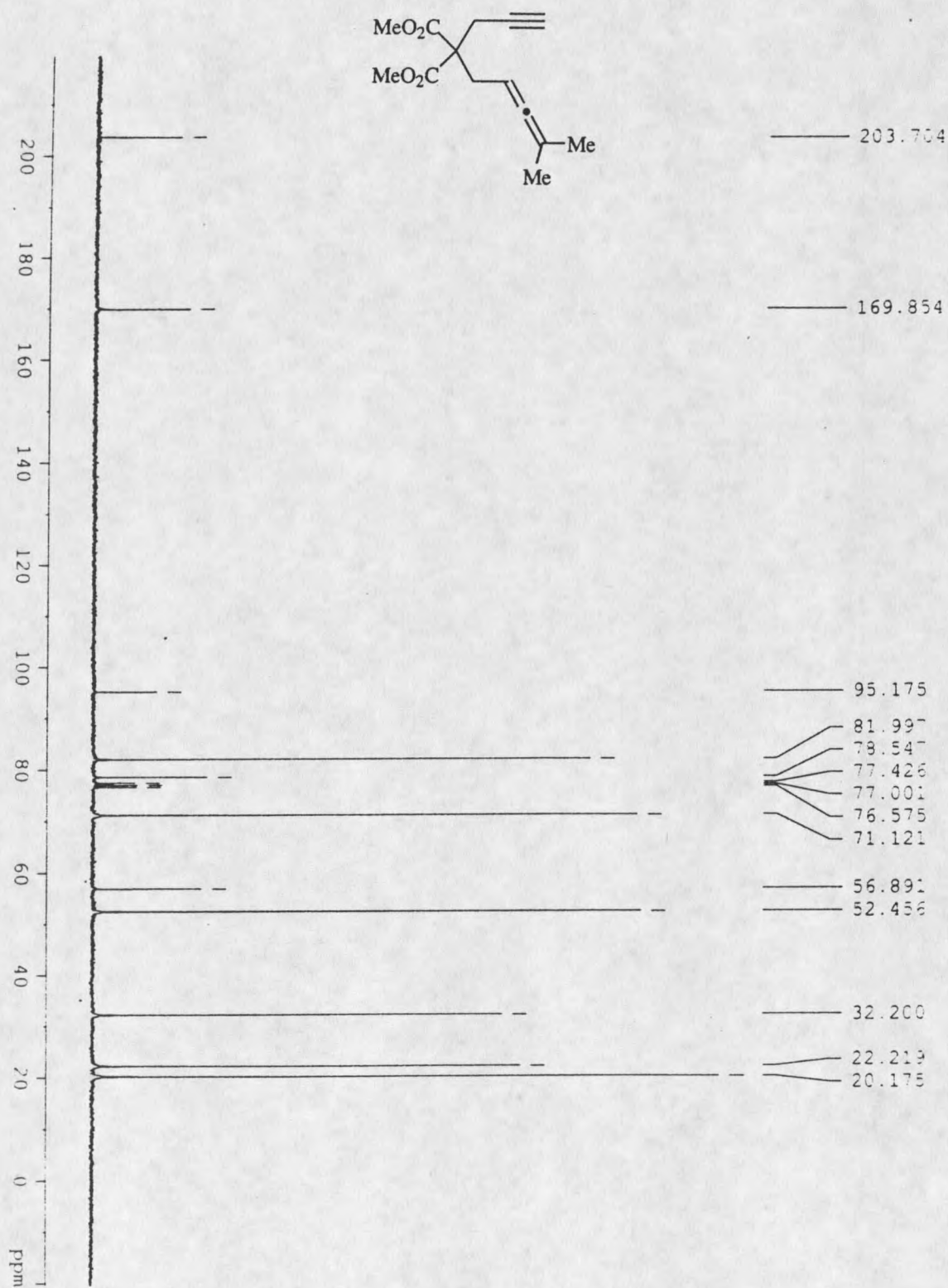


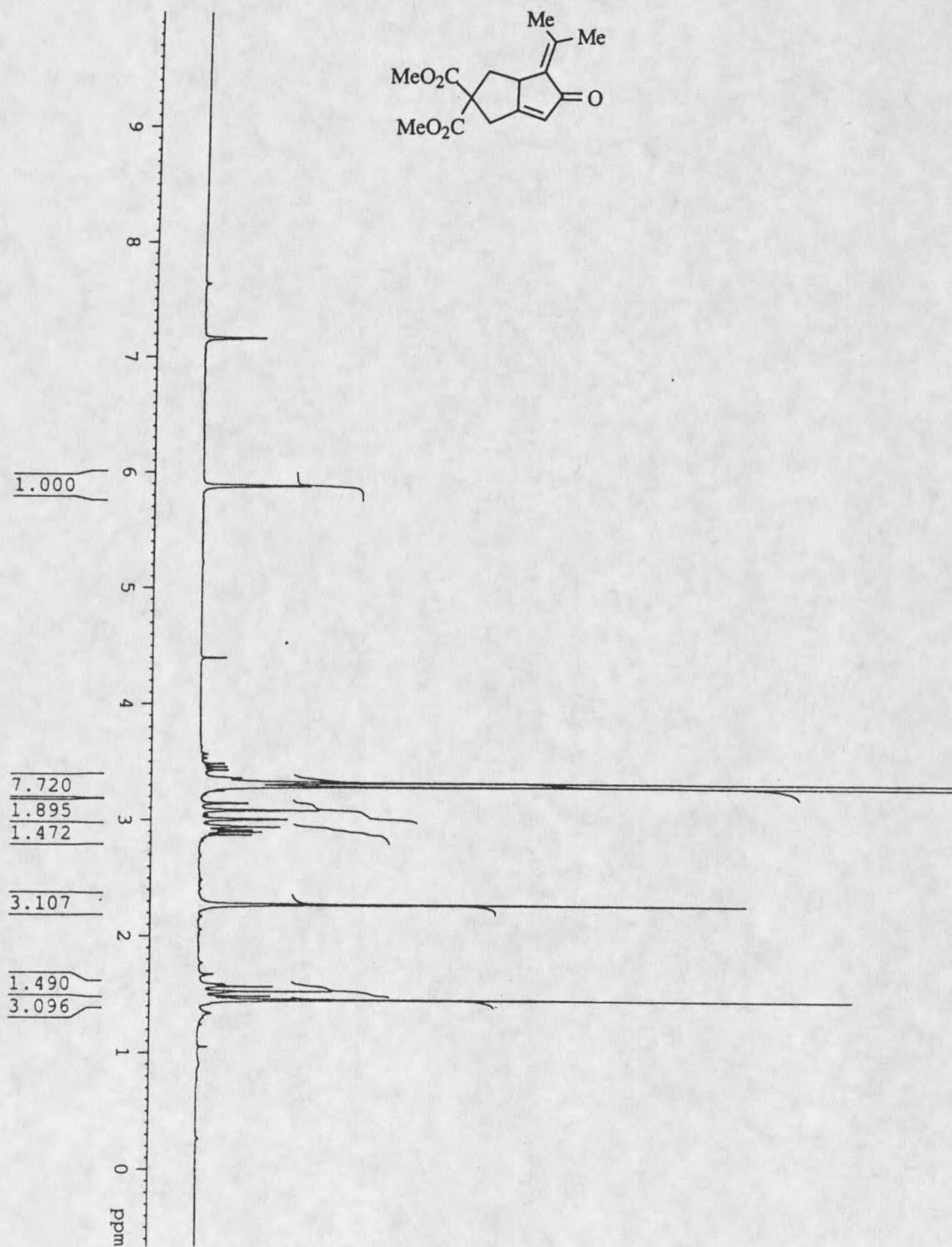


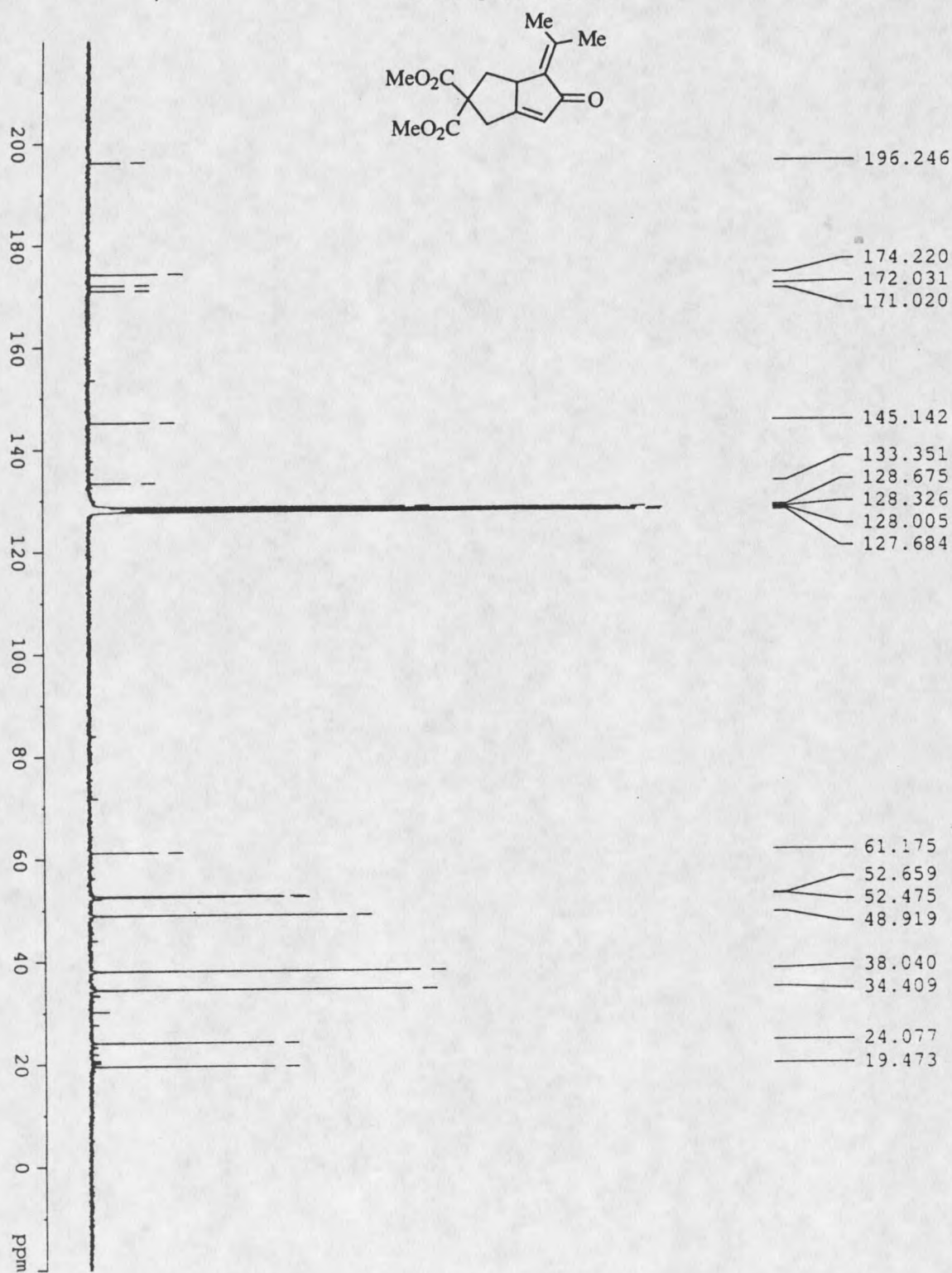
¹H NMR Spectrum of

¹³C NMR Spectrum of

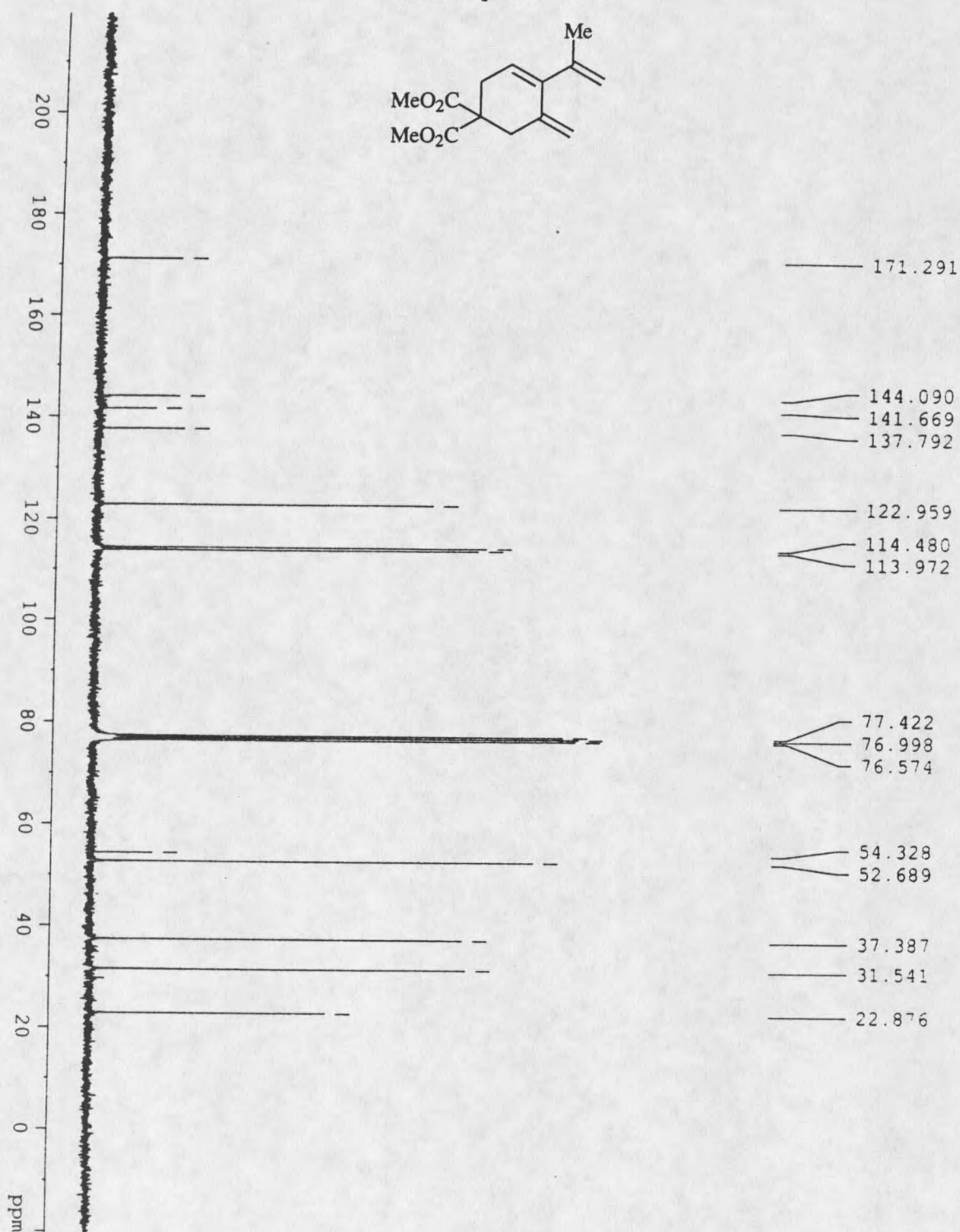
¹H NMR Spectrum of 104

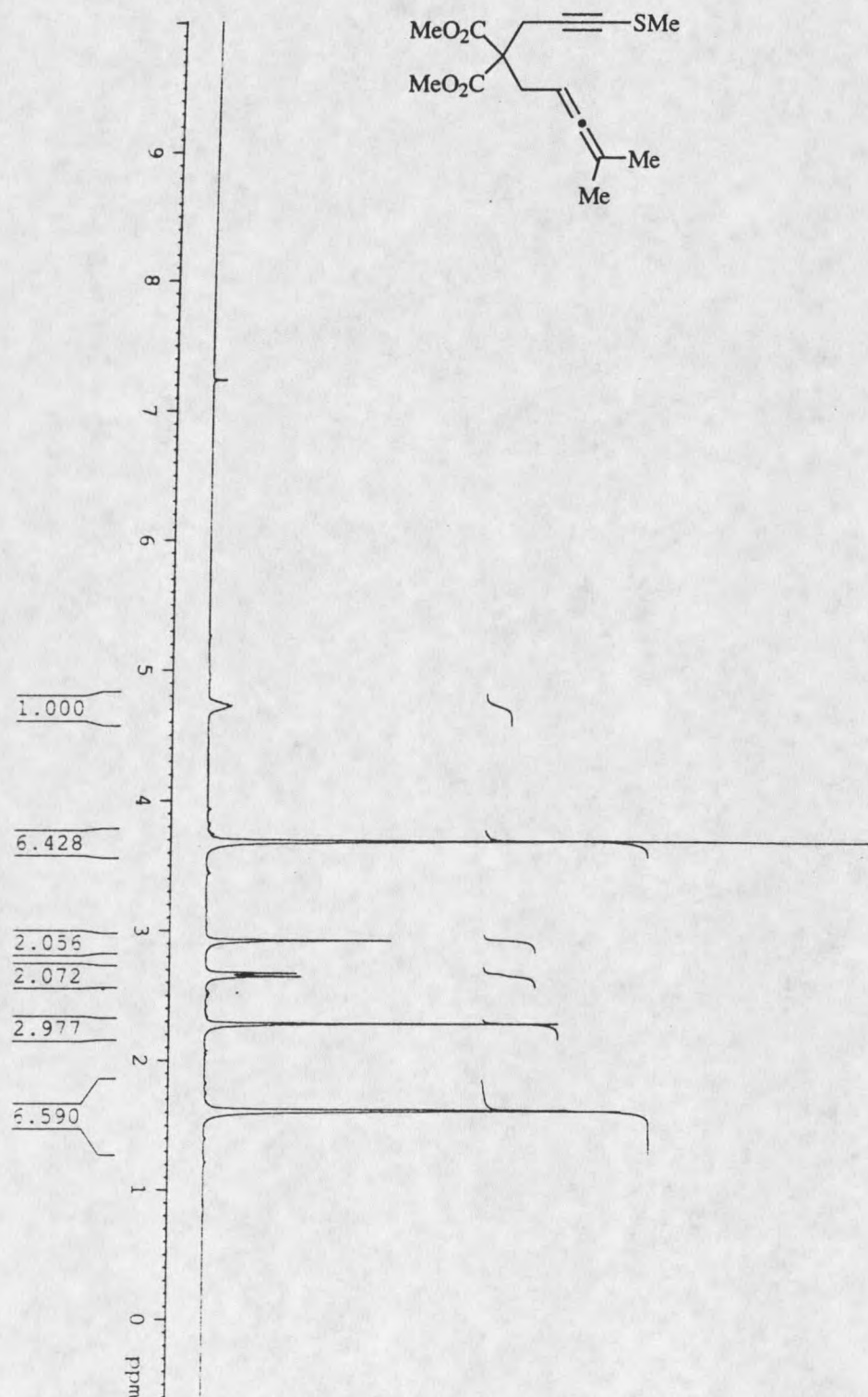
¹³C NMR Spectrum of 104

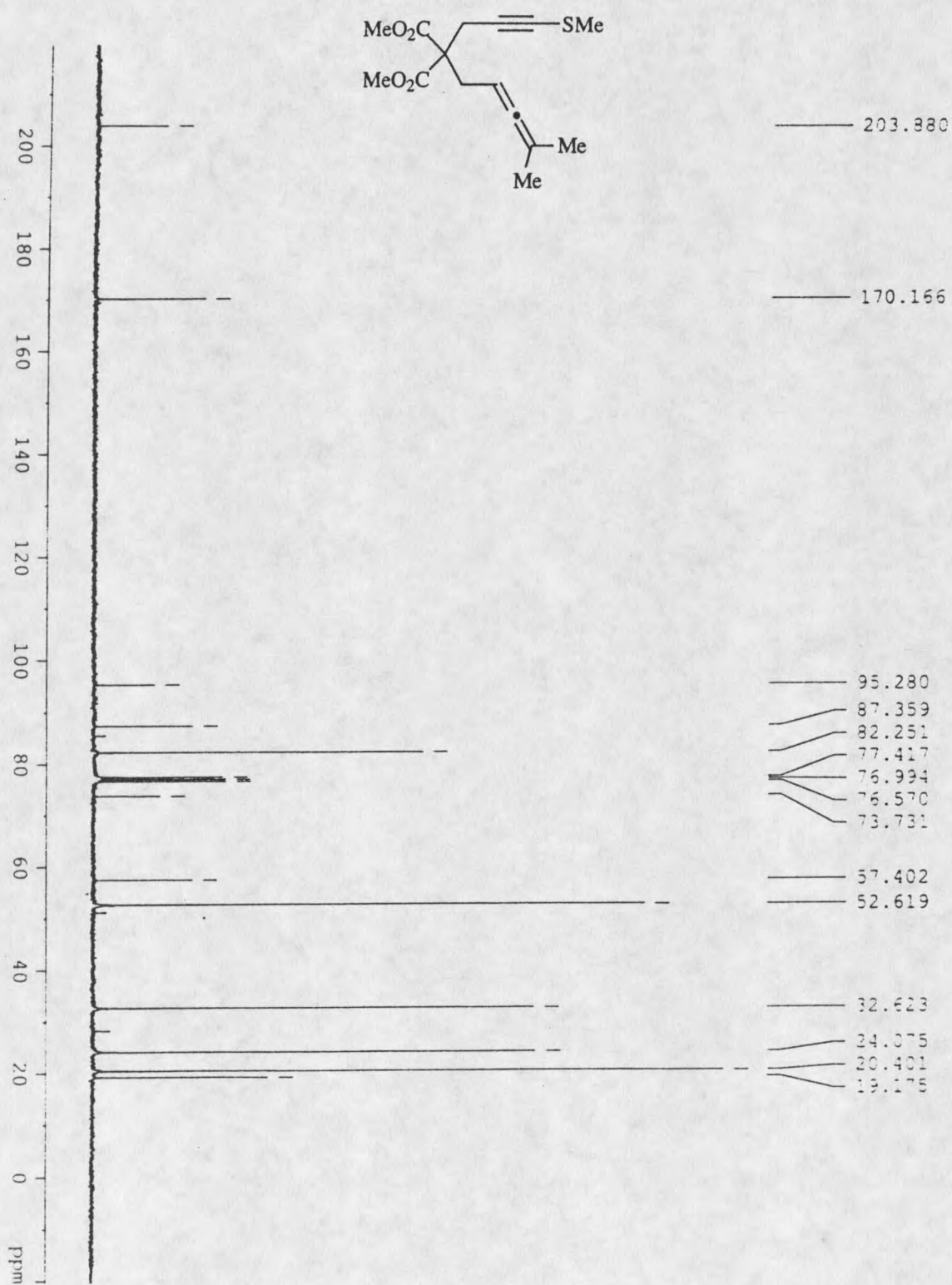
¹H NMR Spectrum of 106

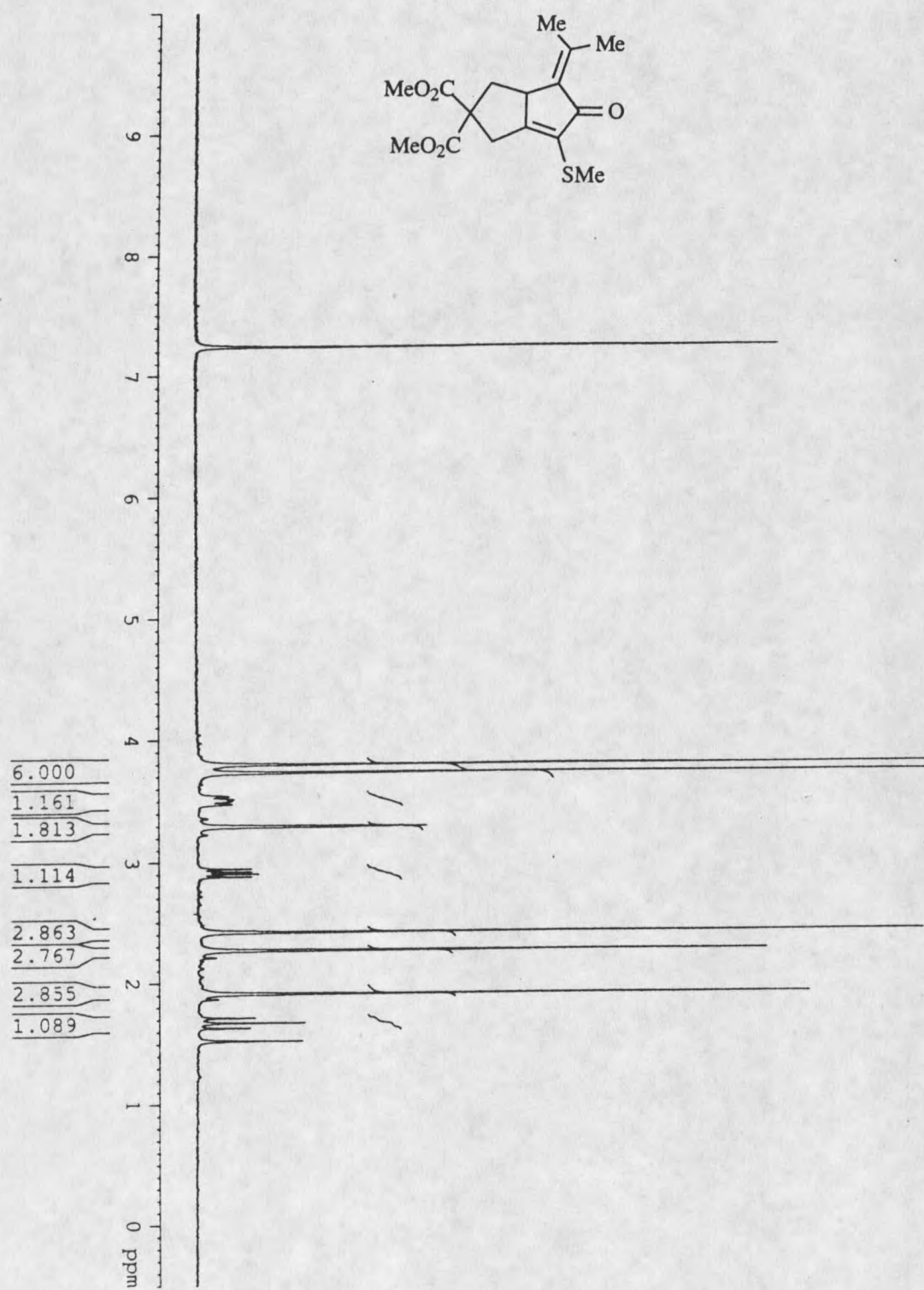
¹³C NMR Spectrum of 106

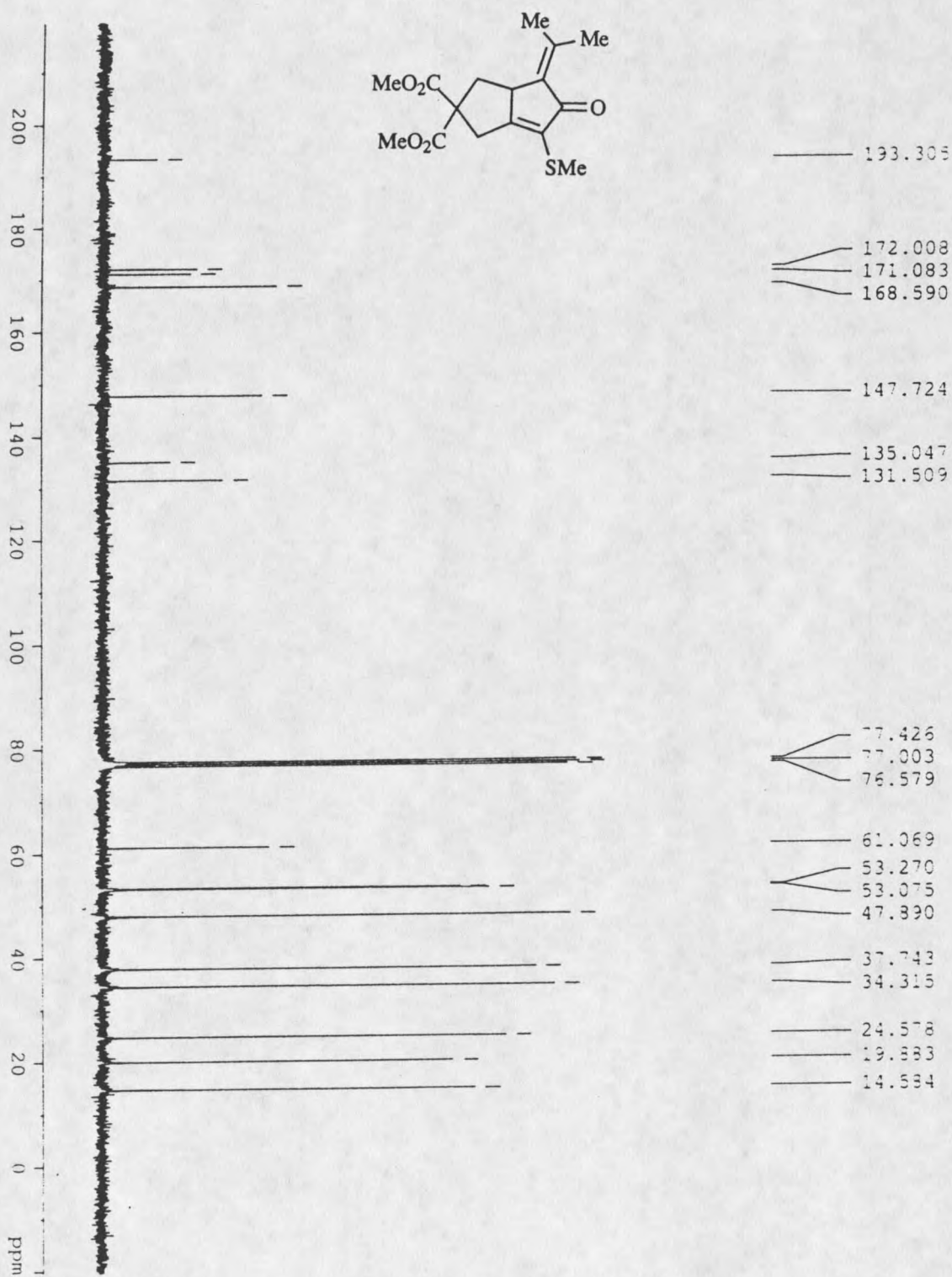
¹H NMR Spectrum of 133

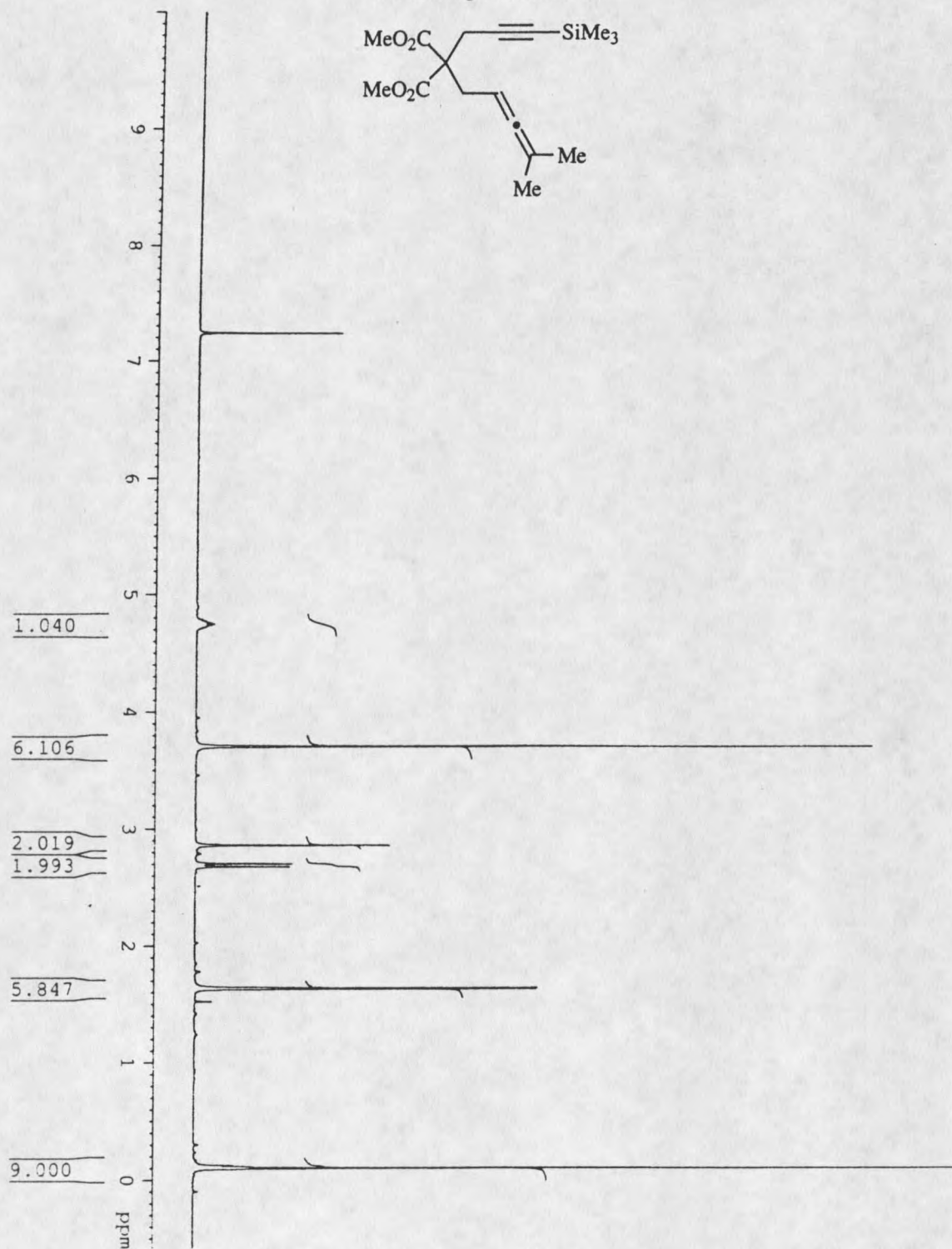
¹³C NMR Spectrum of 133

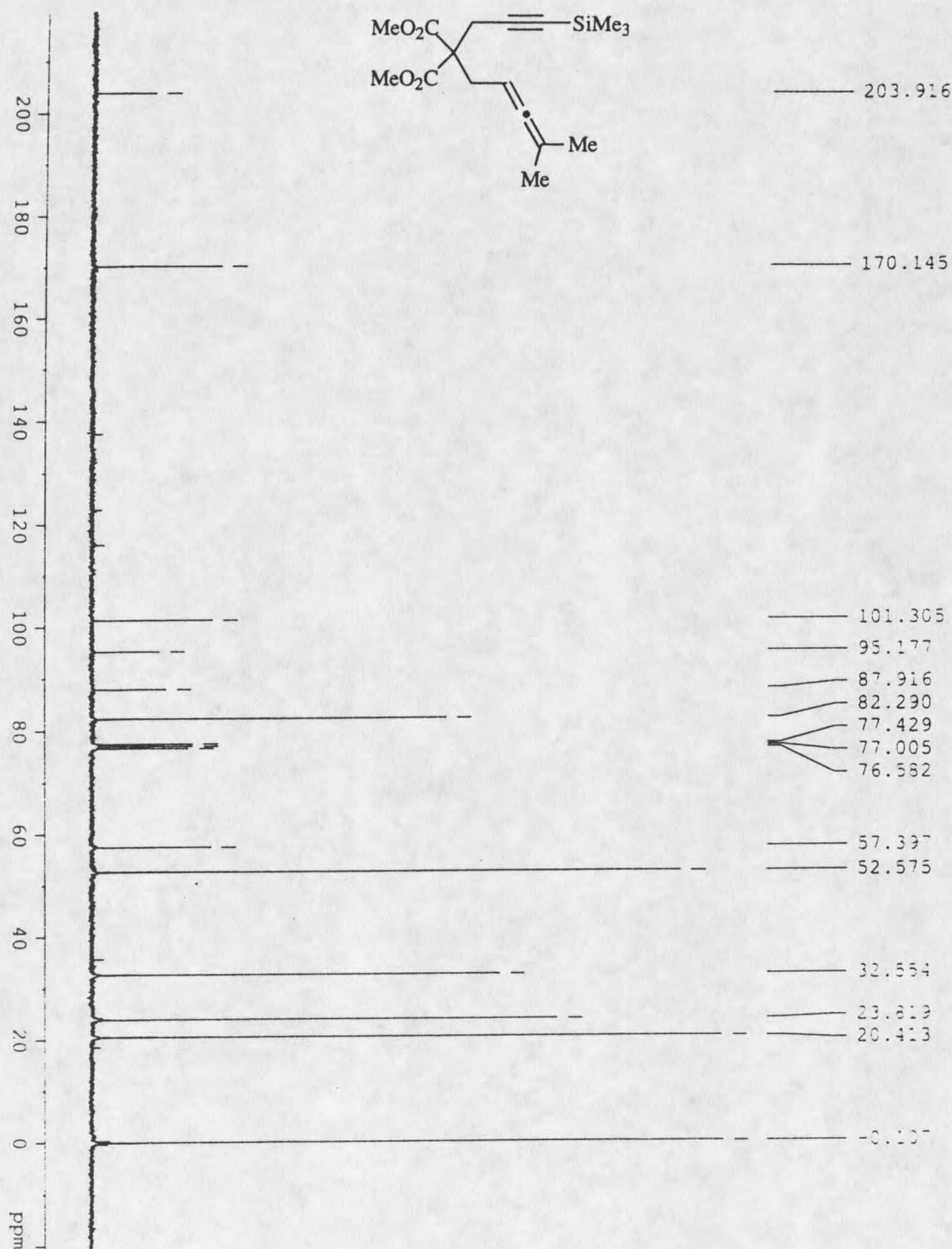
¹H NMR Spectrum of 143

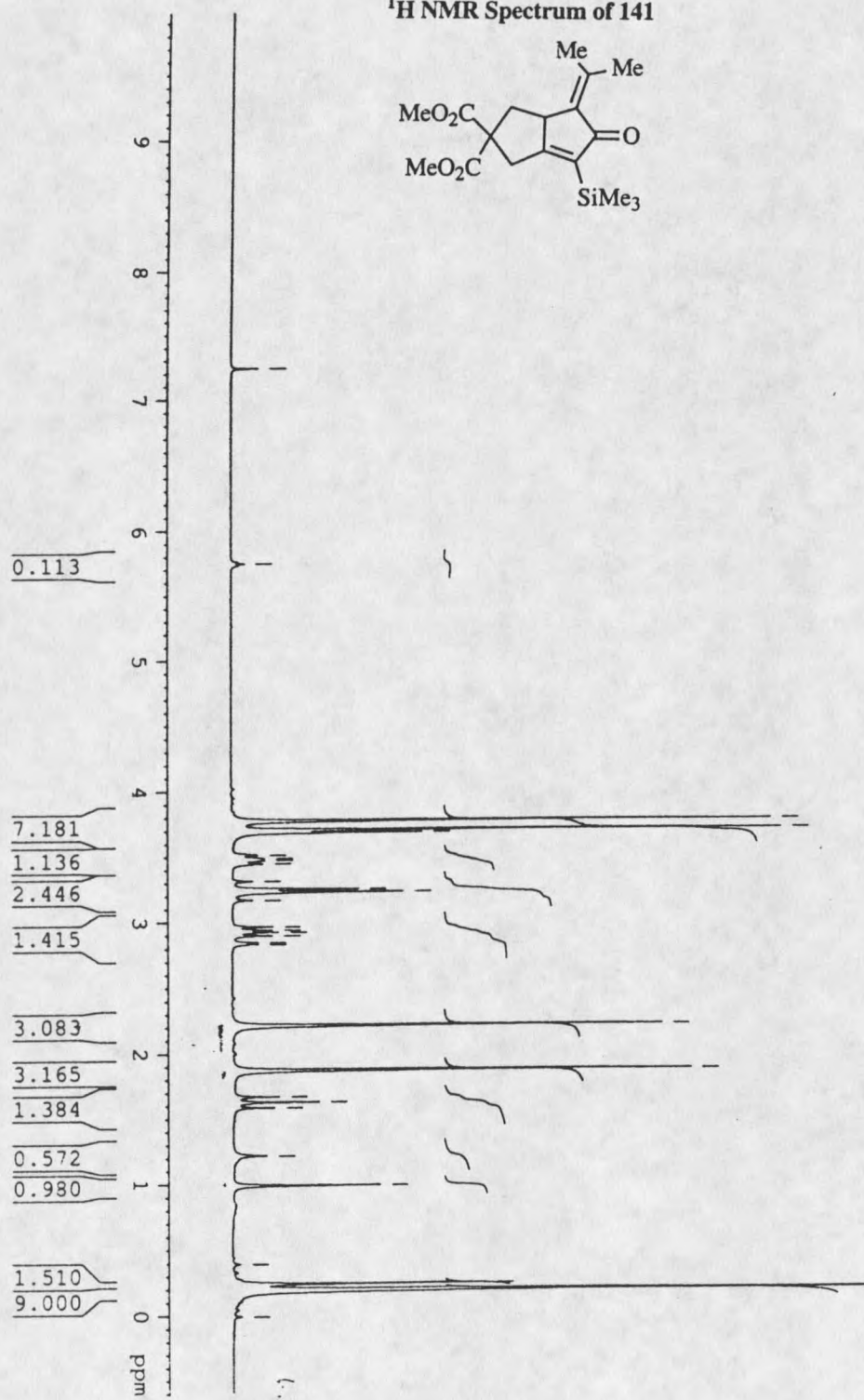
¹³C NMR Spectrum of 143

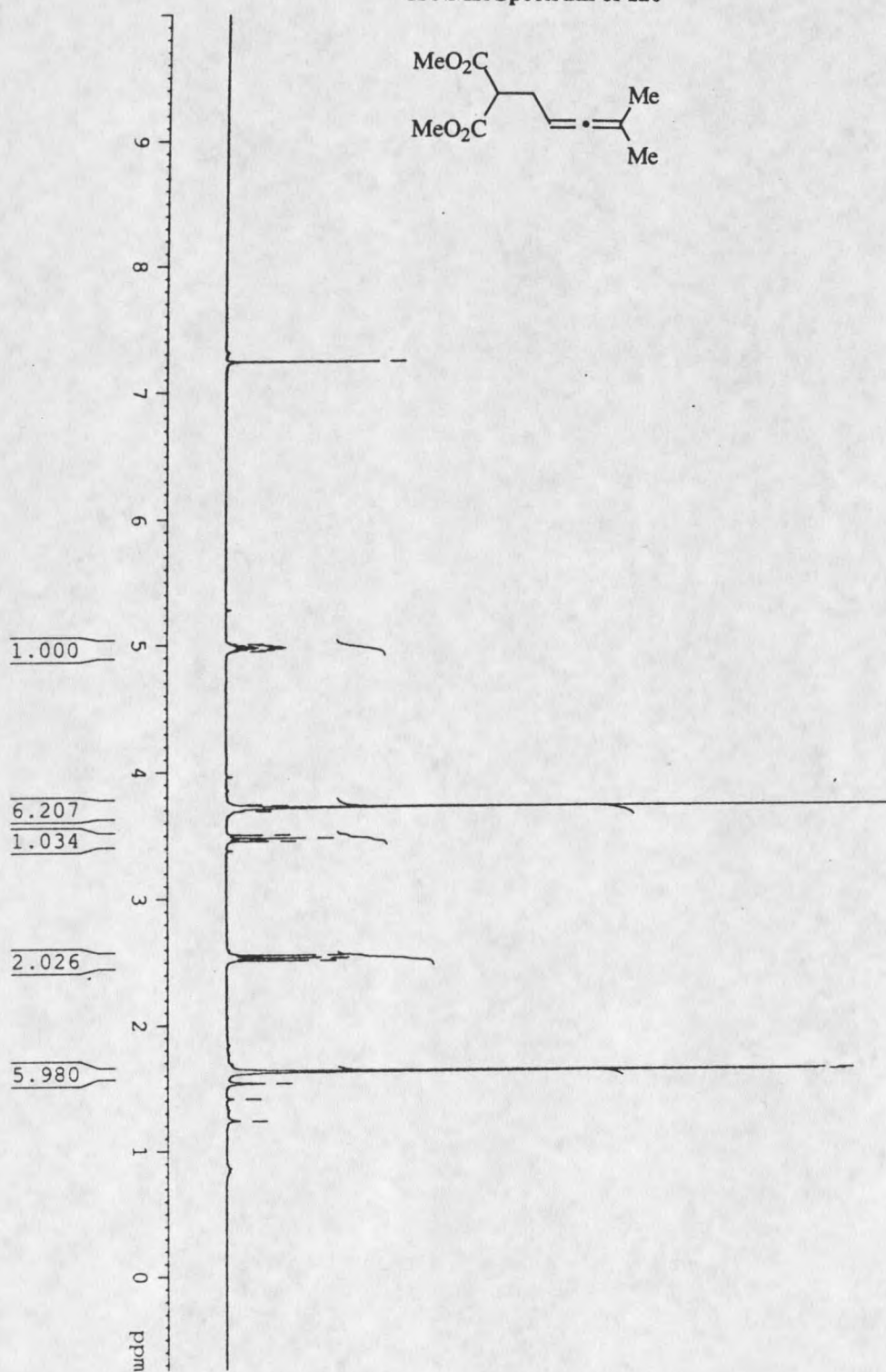
¹H NMR Spectrum of 144

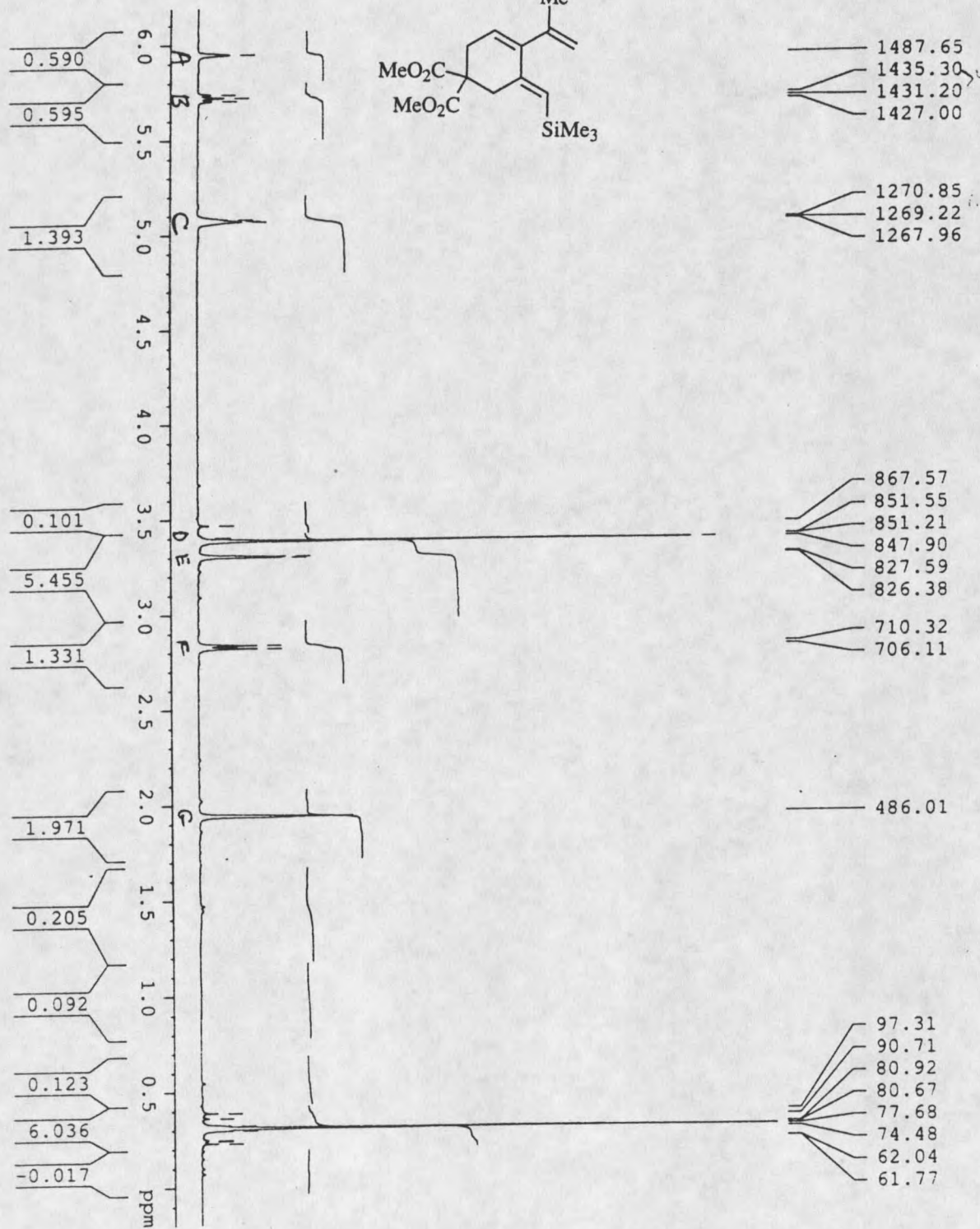
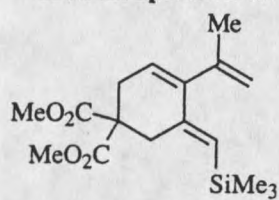
¹³C NMR Spectrum of 144

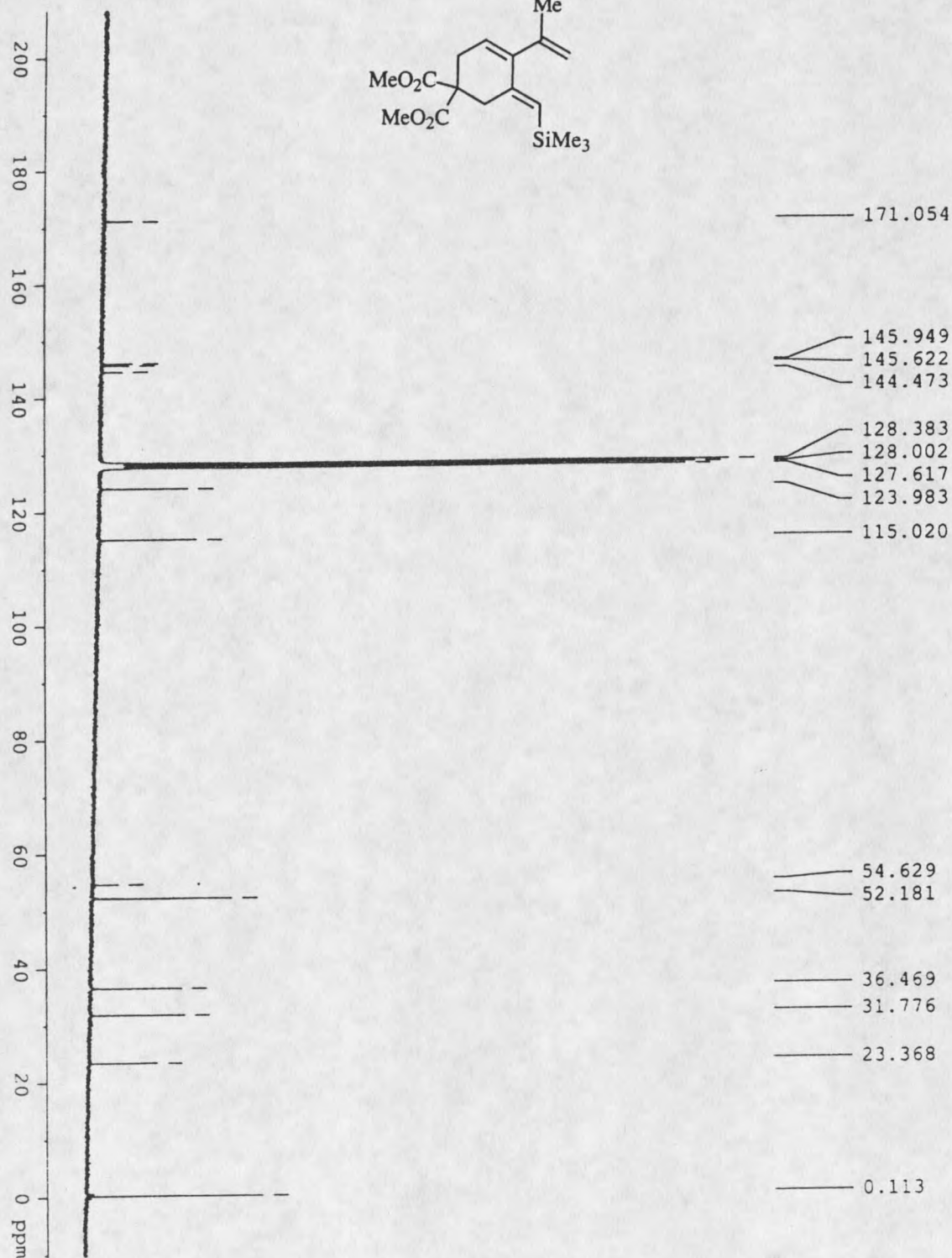
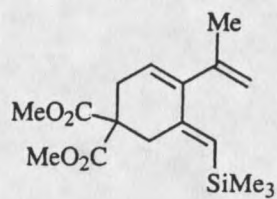
¹H NMR Spectrum of 140

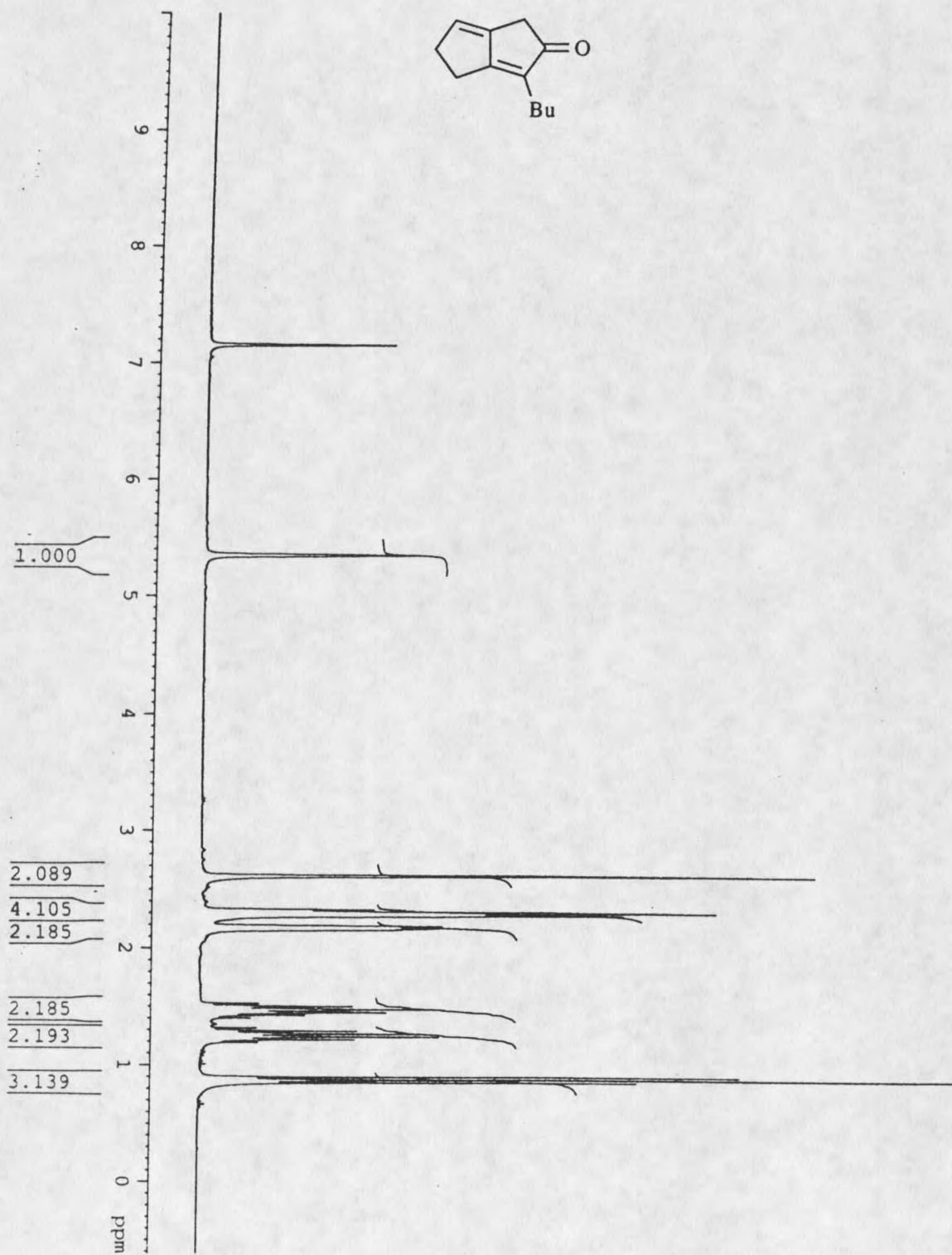
¹³C NMR Spectrum of 140

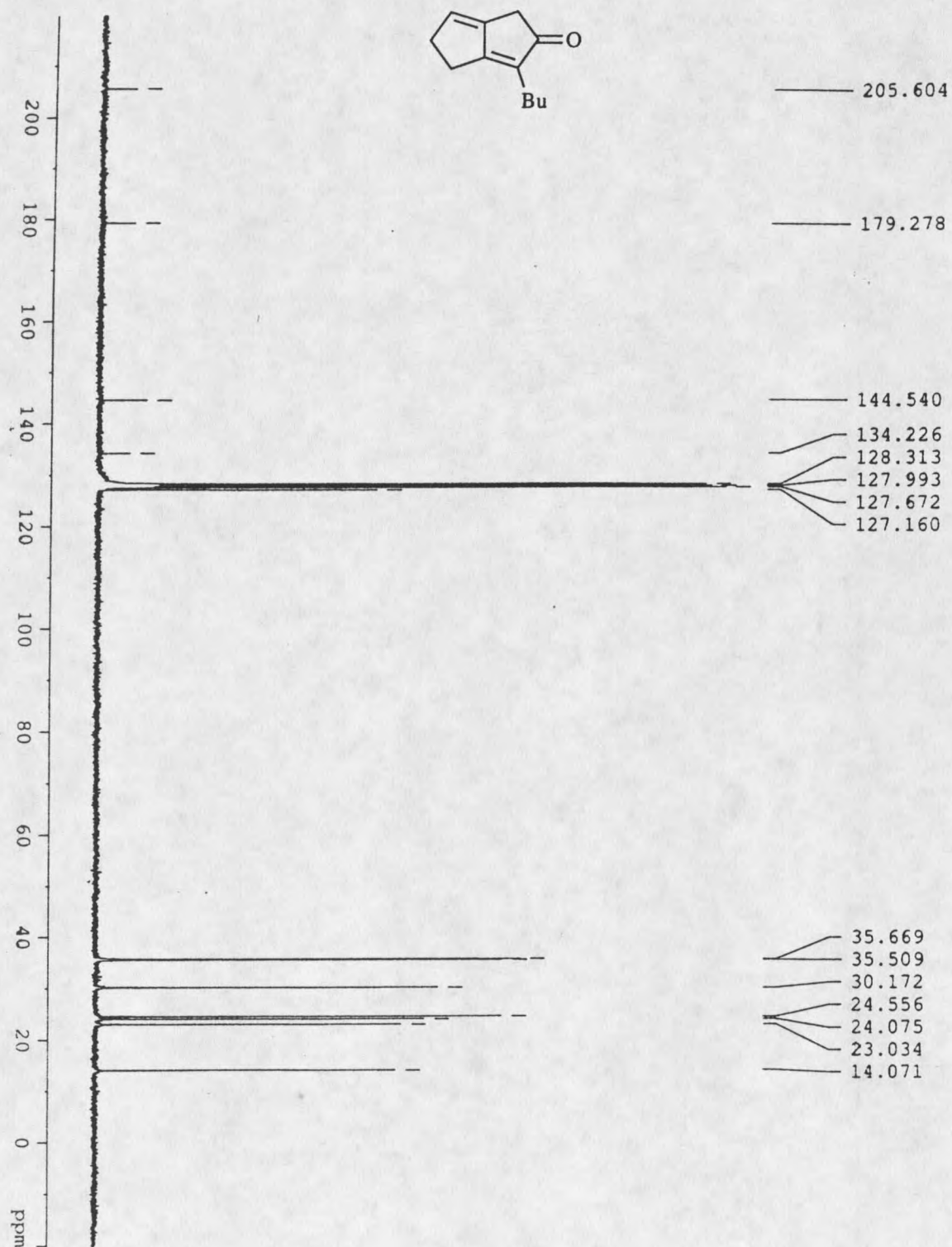
¹H NMR Spectrum of 141

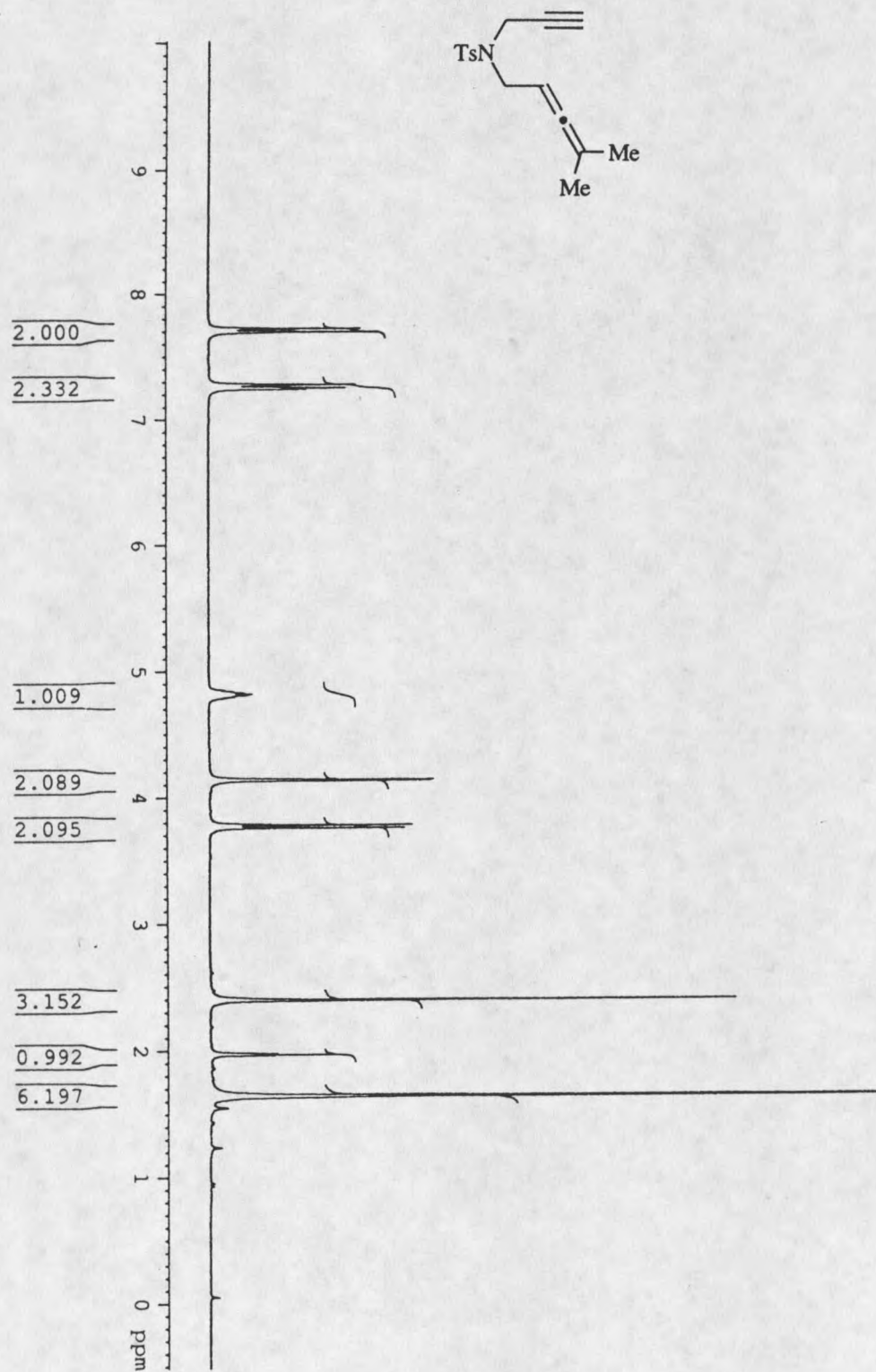
¹H NMR Spectrum of 120

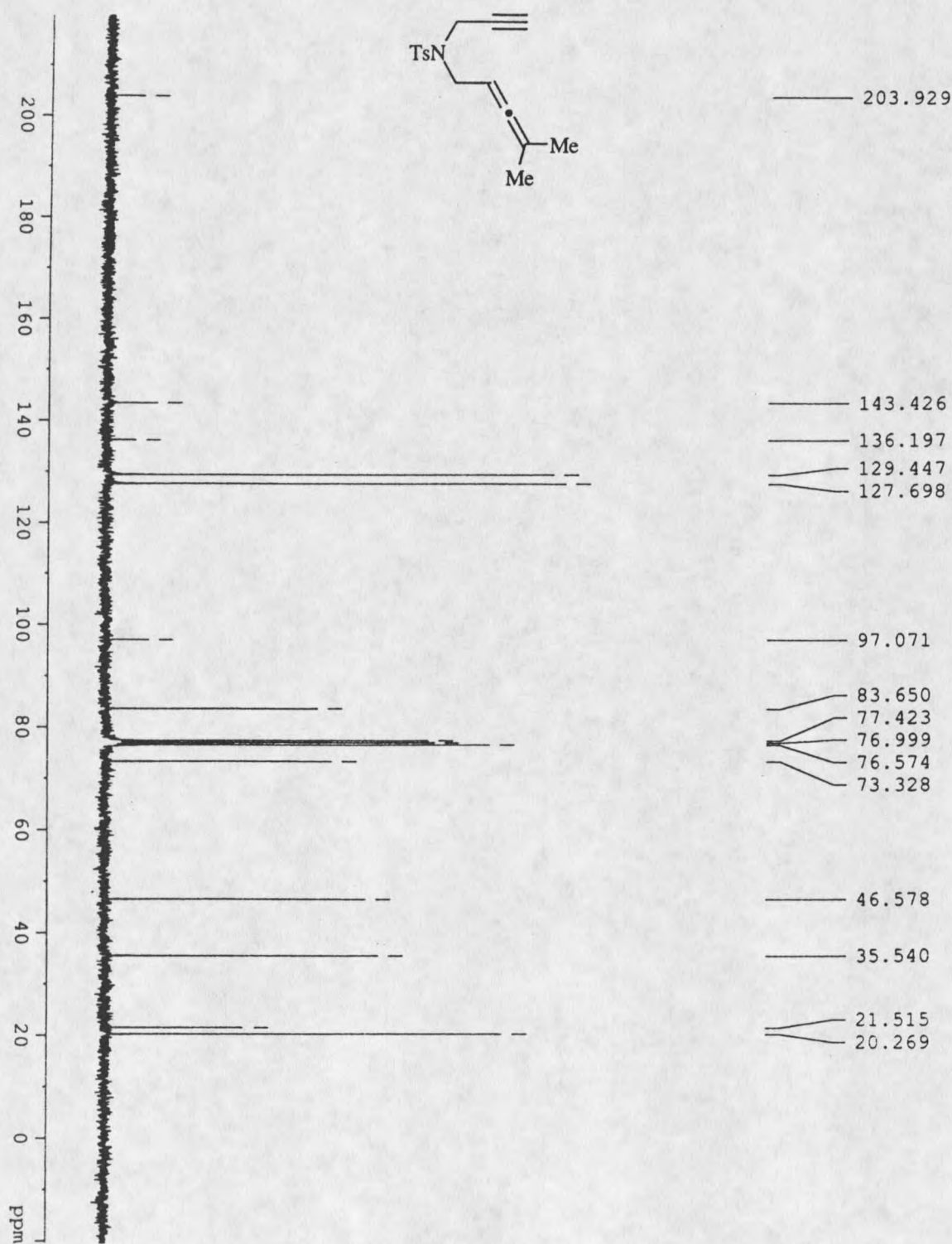
¹H NMR Spectrum of

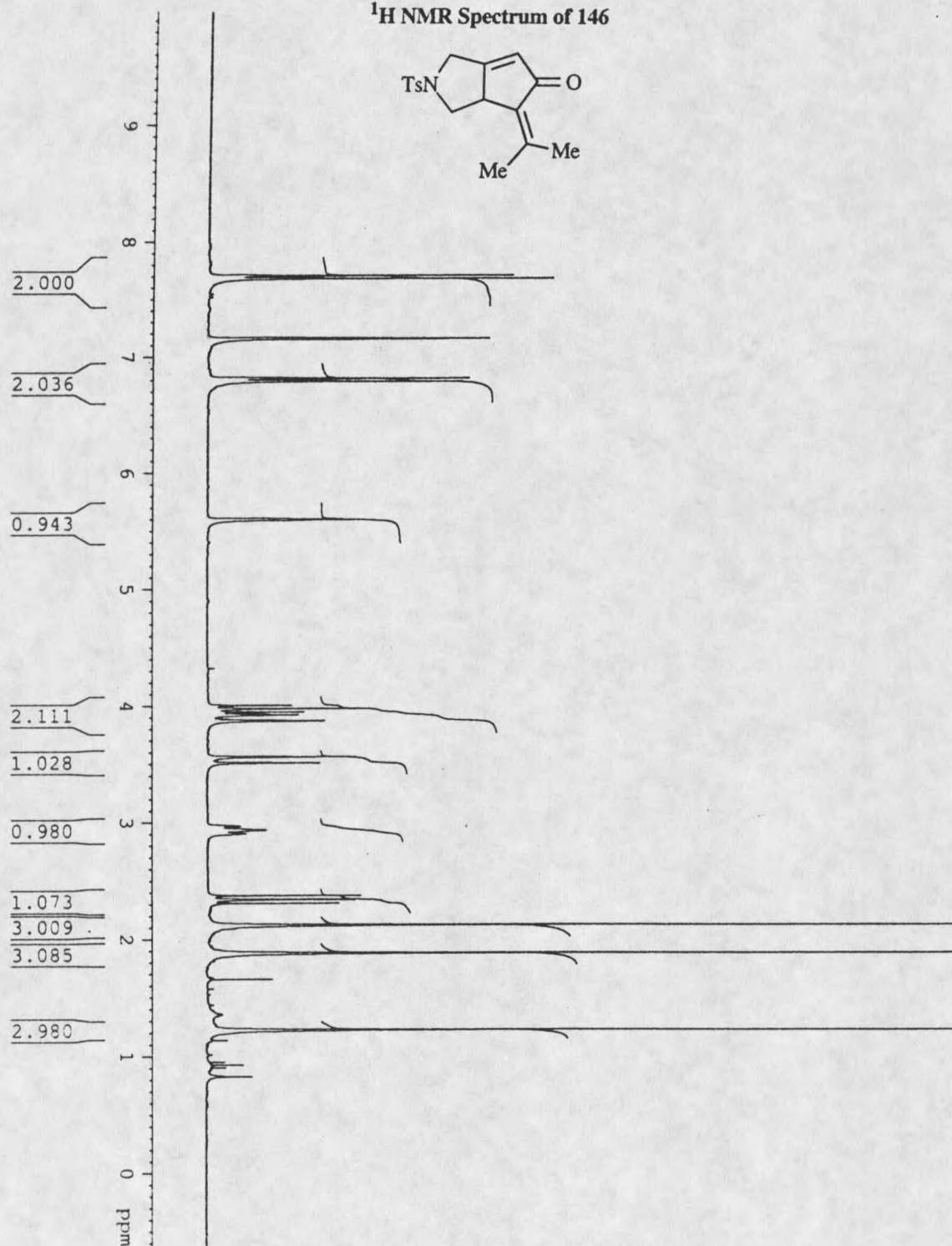
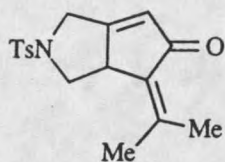
^{13}C NMR Spectrum of

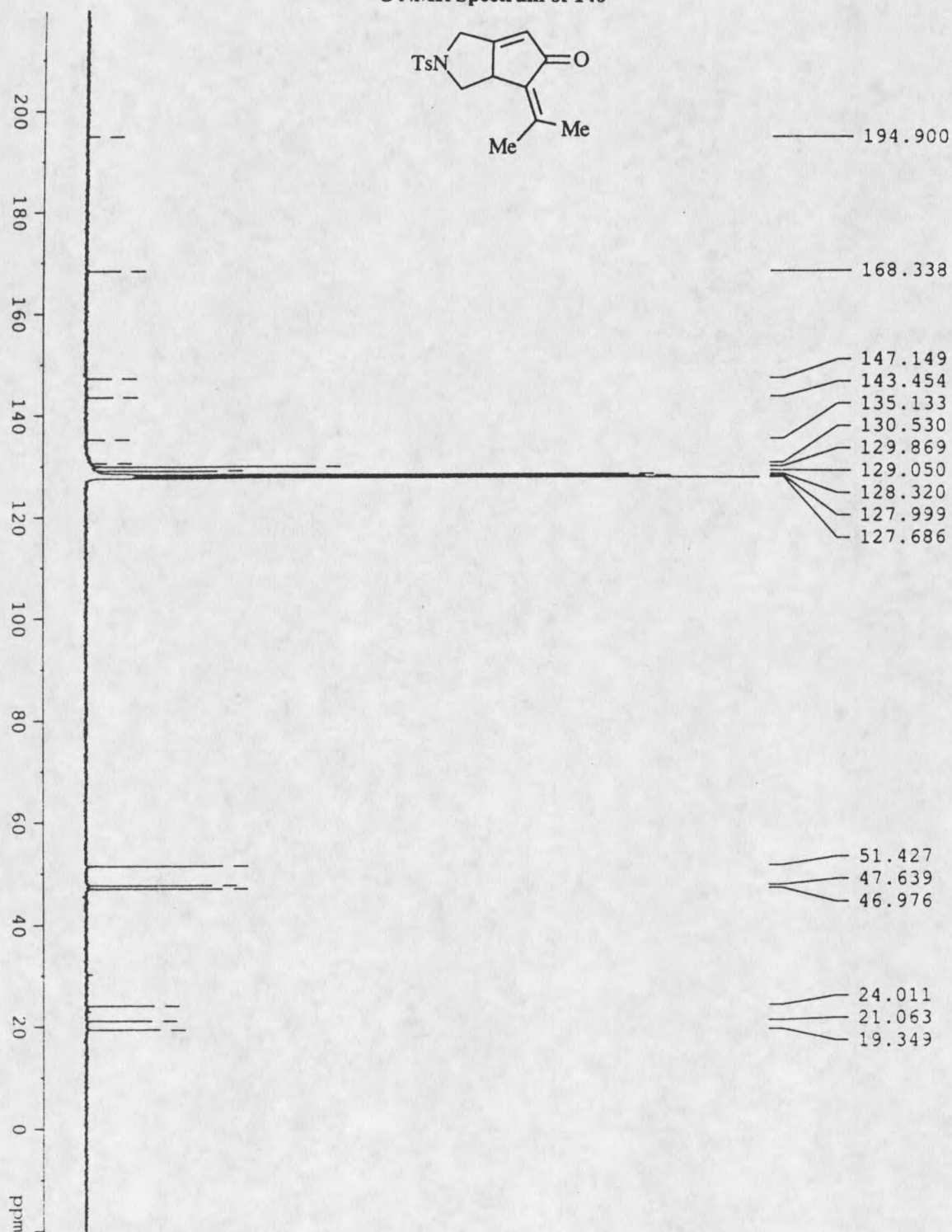
¹H NMR Spectrum of 114

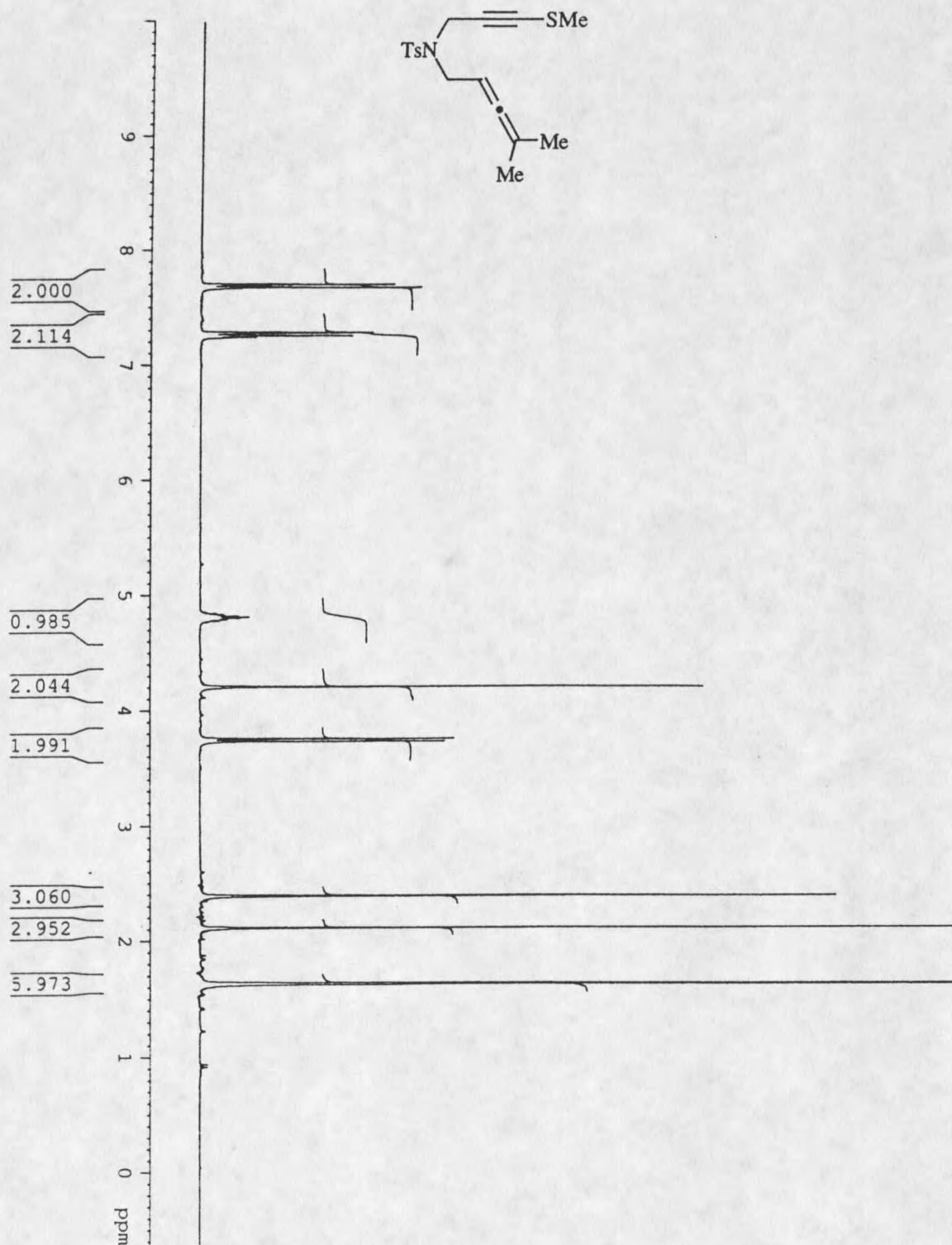
¹³C NMR Spectrum of 114

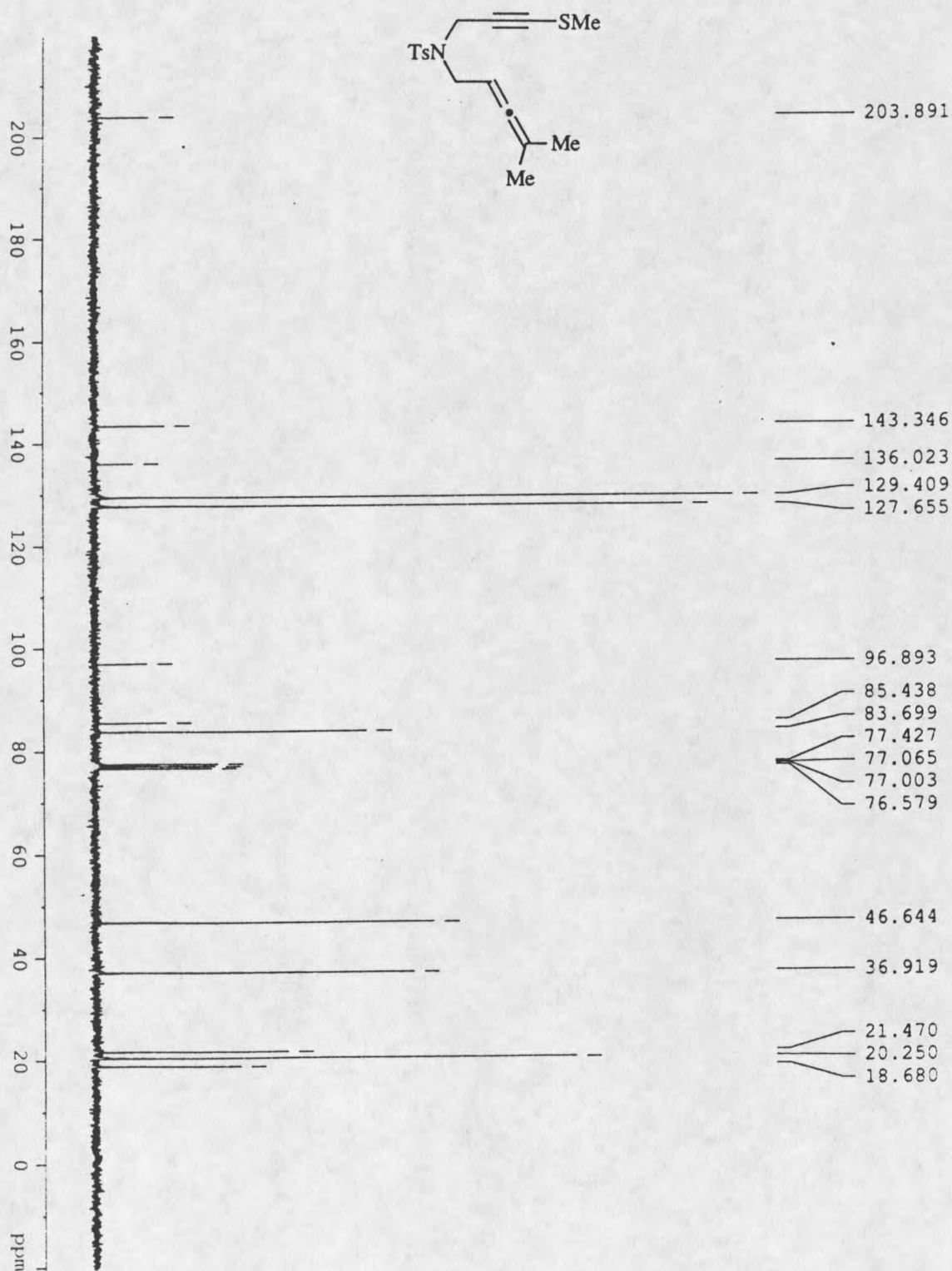
¹H NMR Spectrum of 124

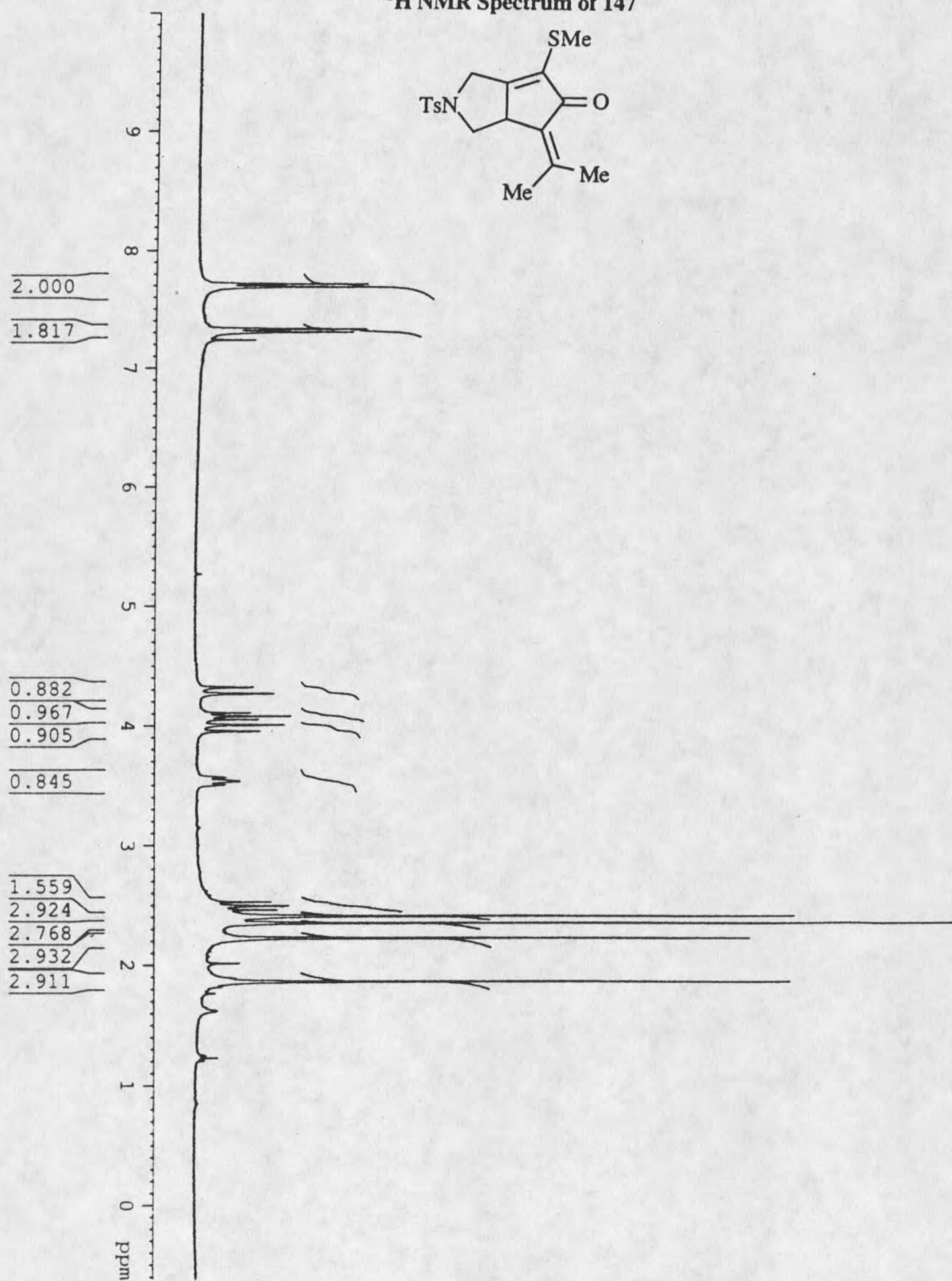
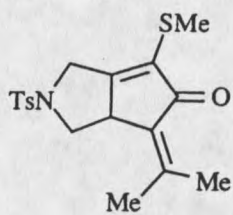
¹³C NMR Spectrum of 124

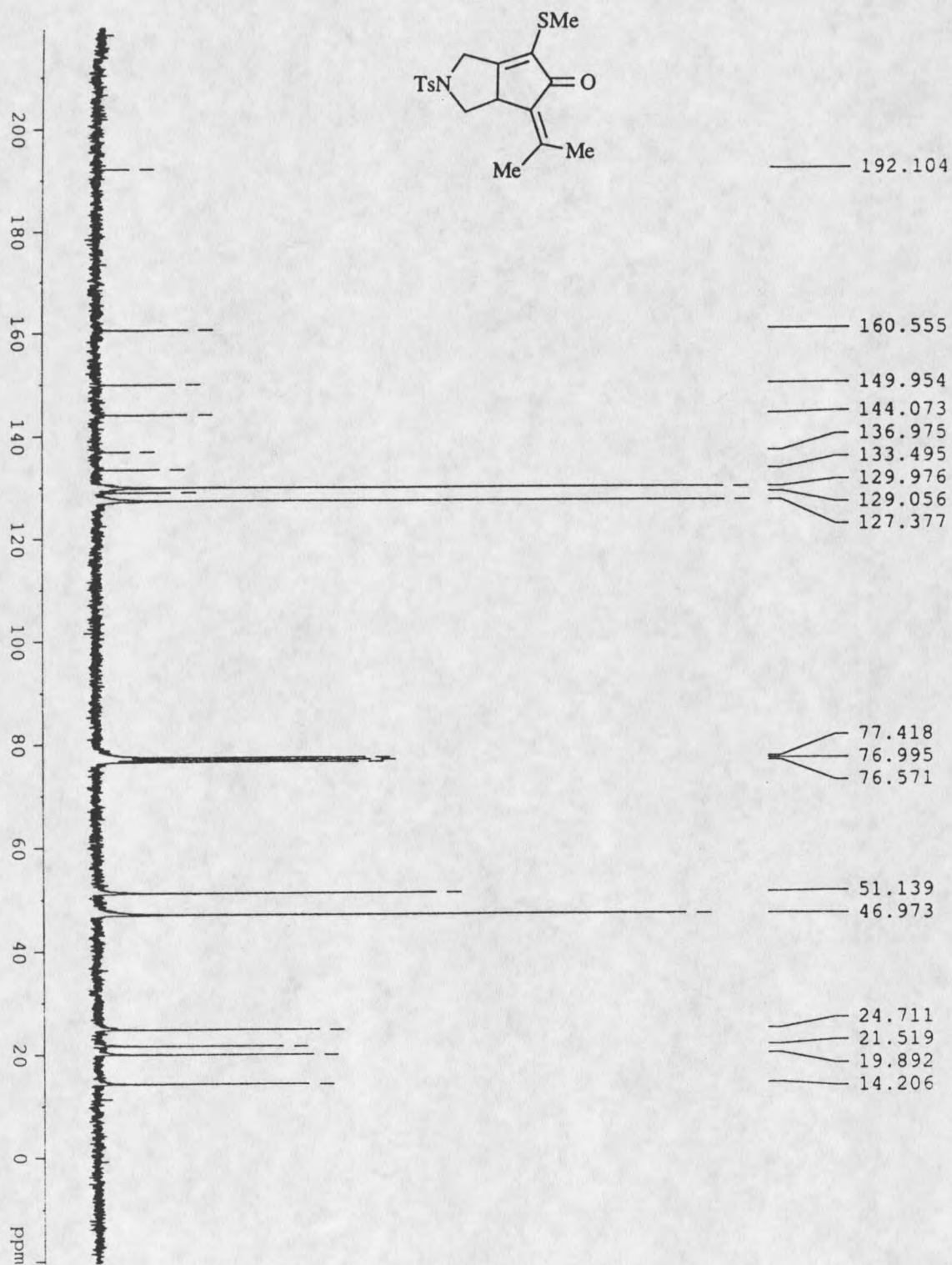
¹H NMR Spectrum of 146

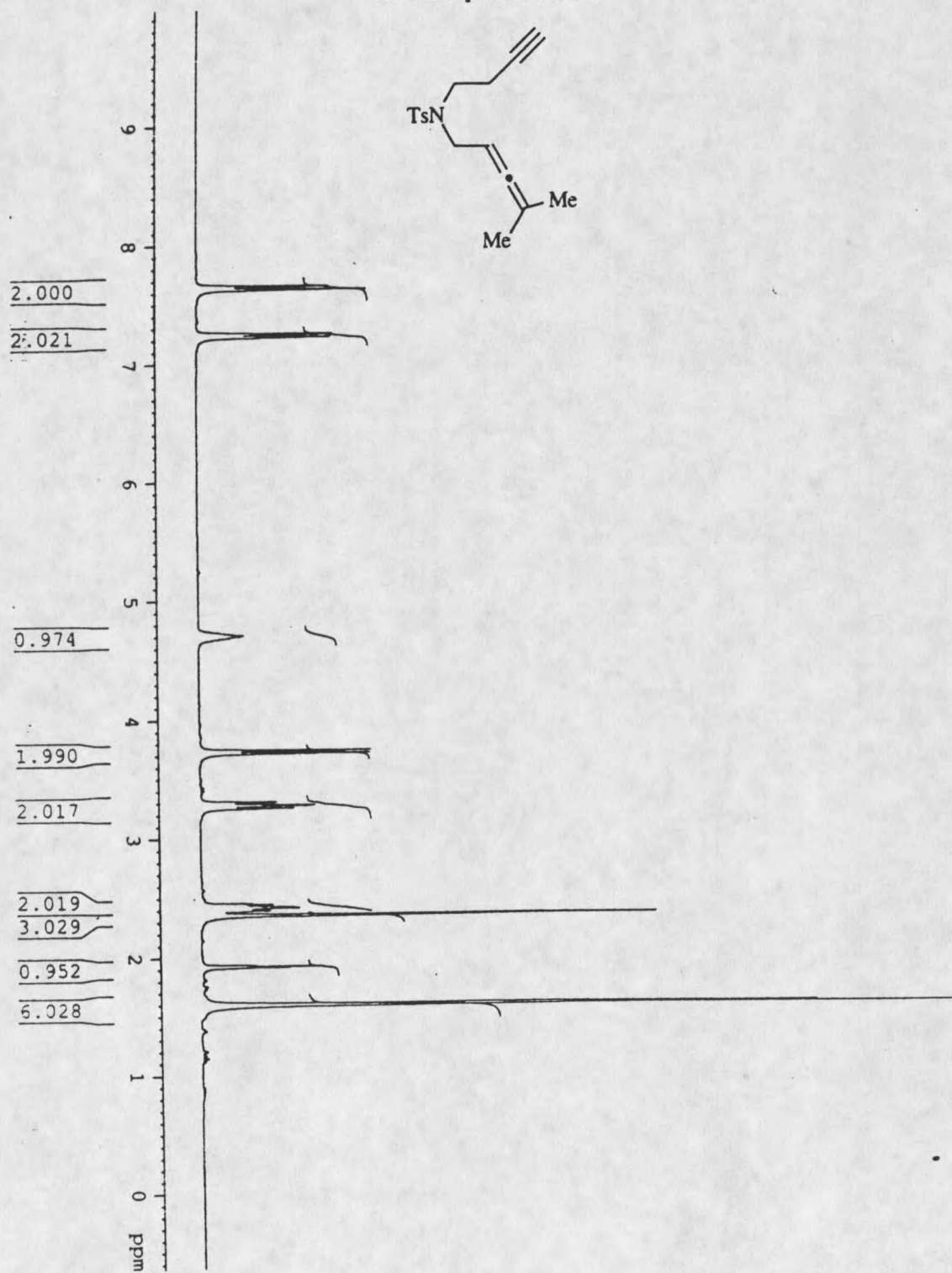
¹³C NMR Spectrum of 146

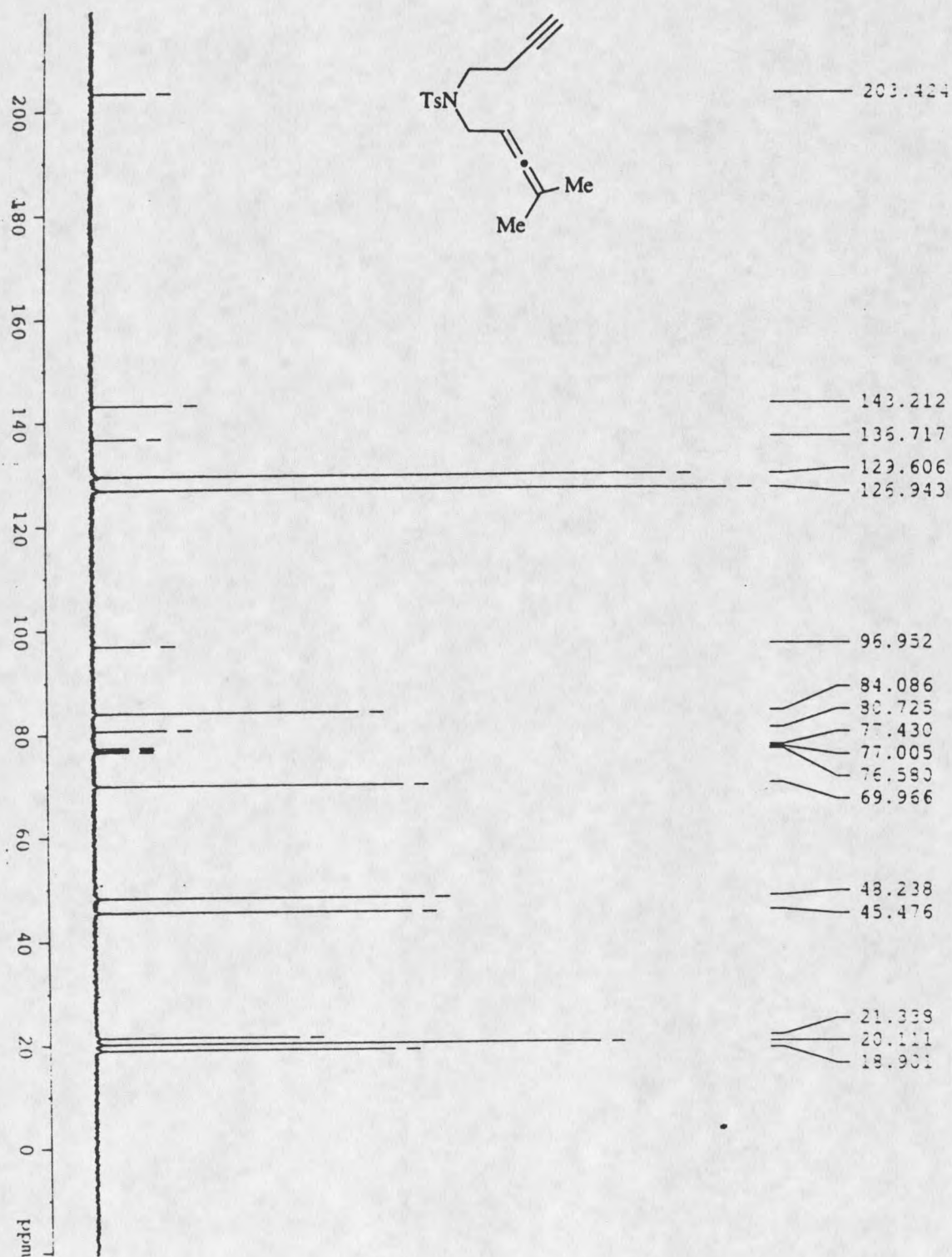
¹H NMR Spectrum of 145

¹³C NMR Spectrum of 145

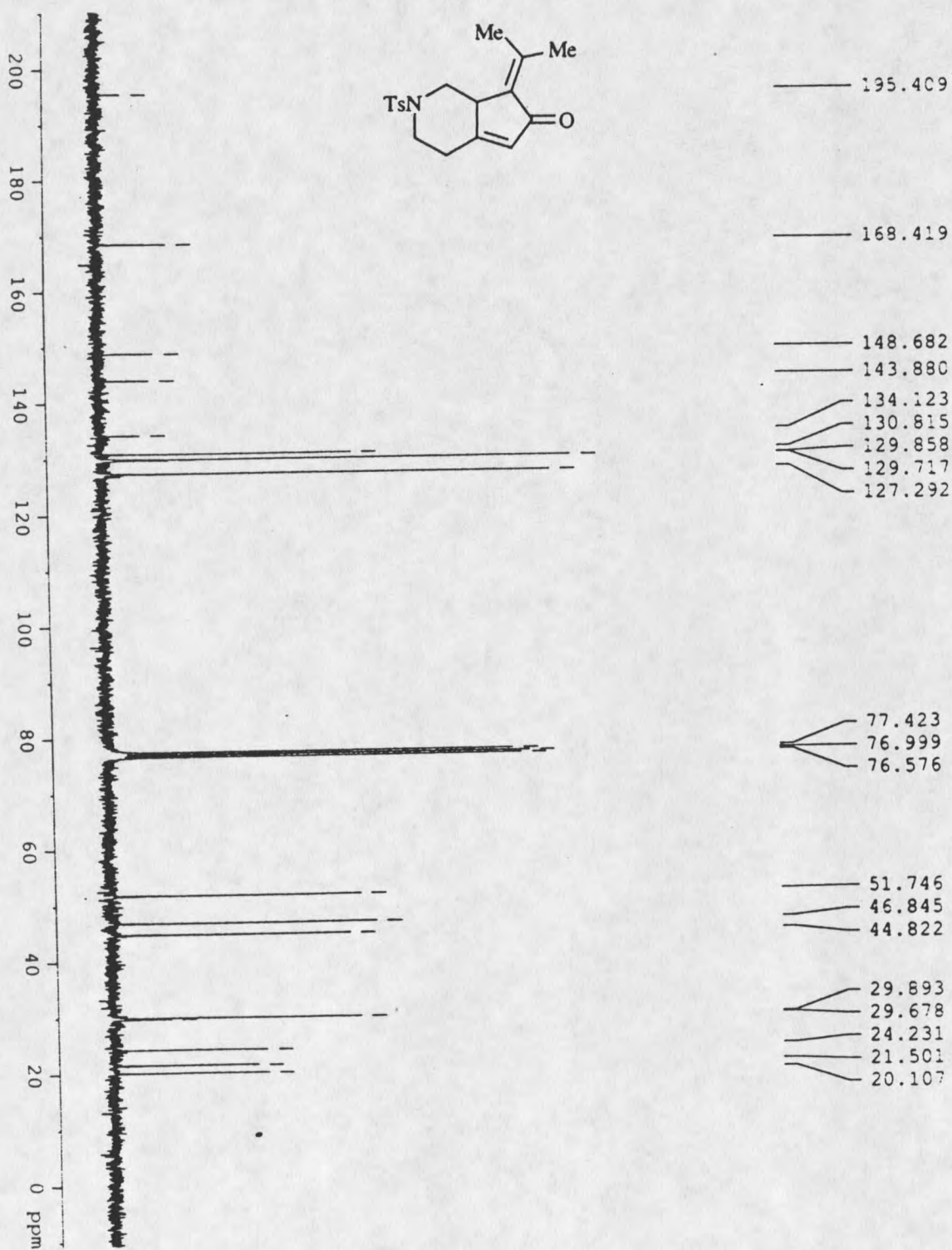
¹H NMR Spectrum of 147

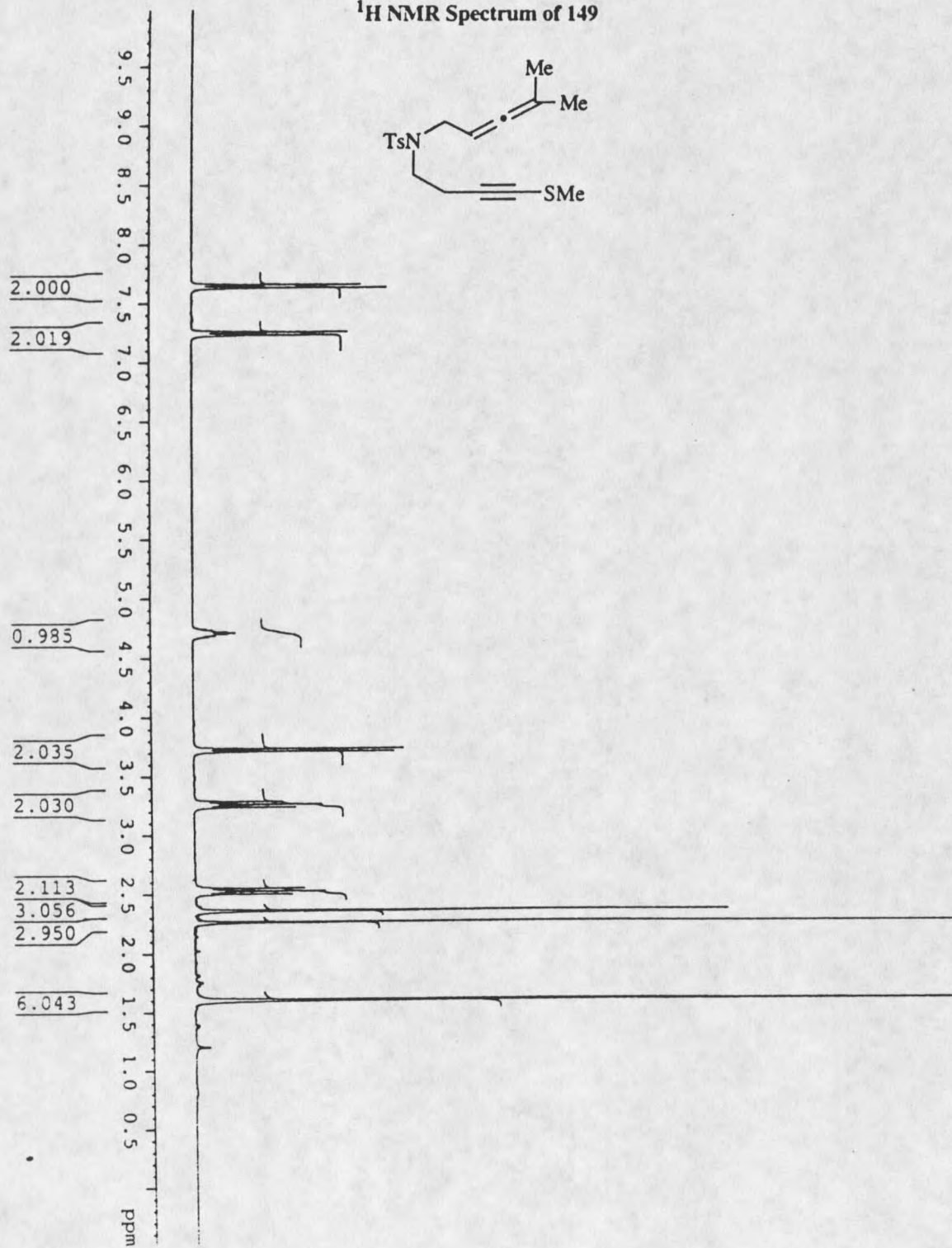
¹³C NMR Spectrum of 147

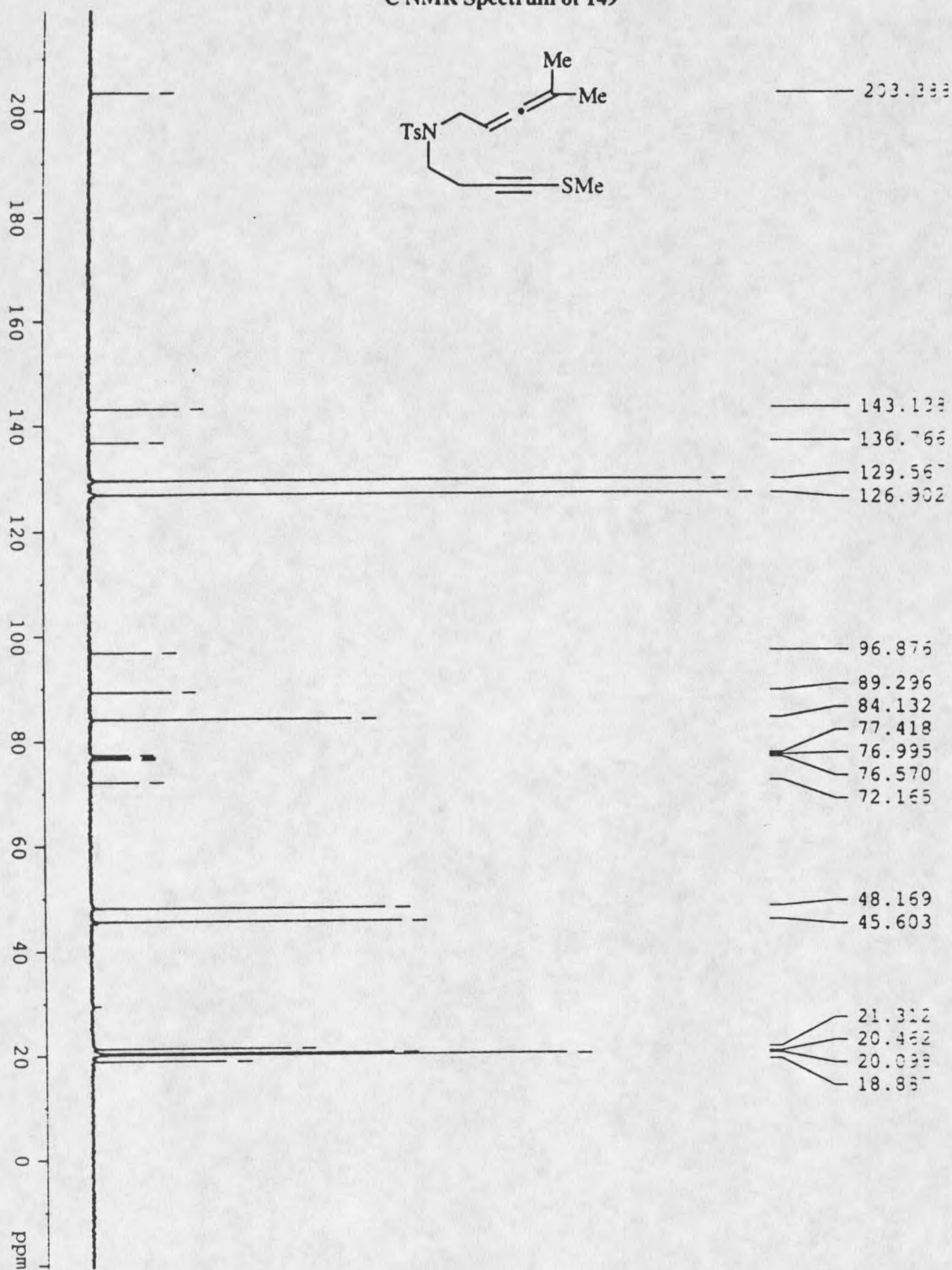
¹H NMR Spectrum of 125

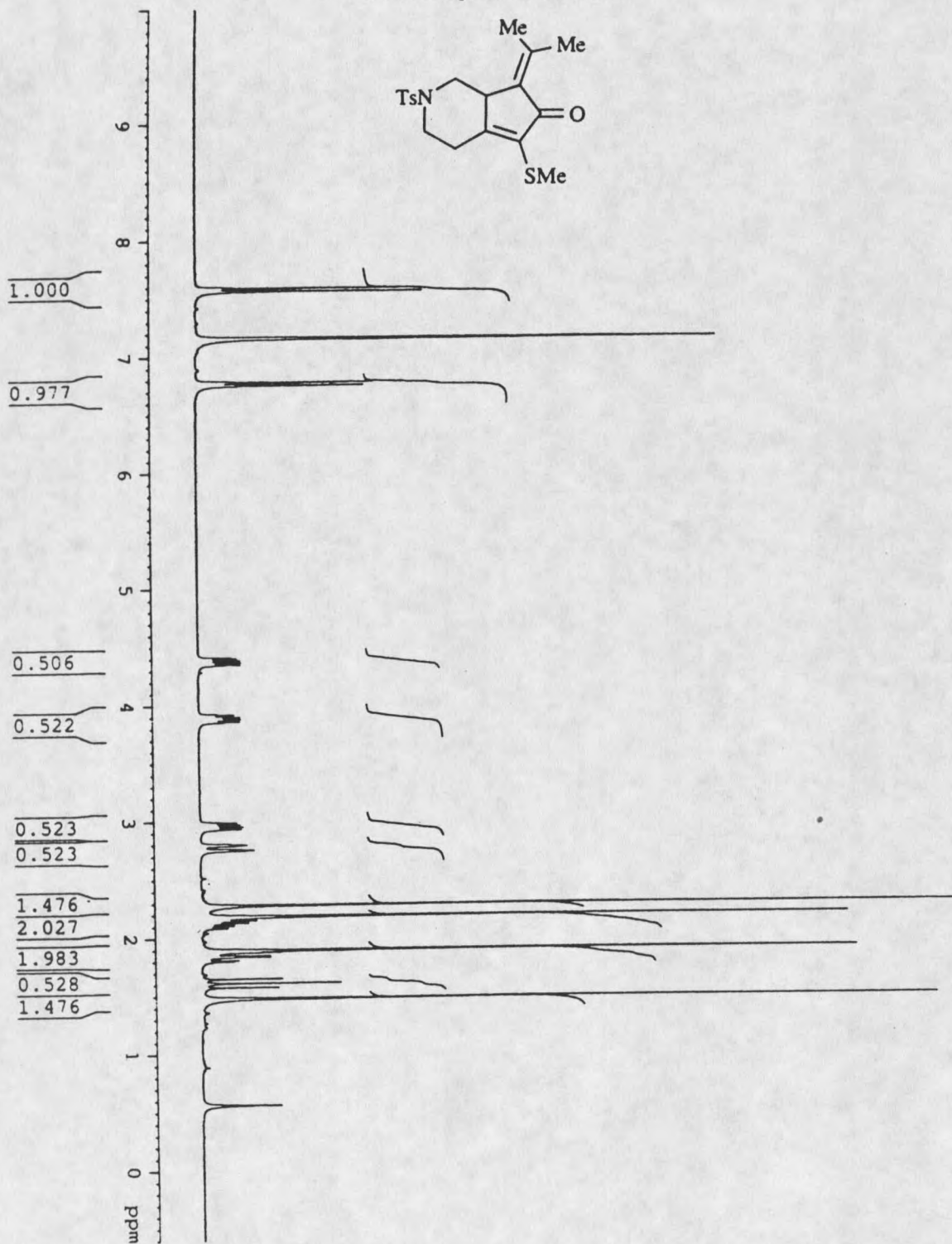
¹³C NMR Spectrum of 125

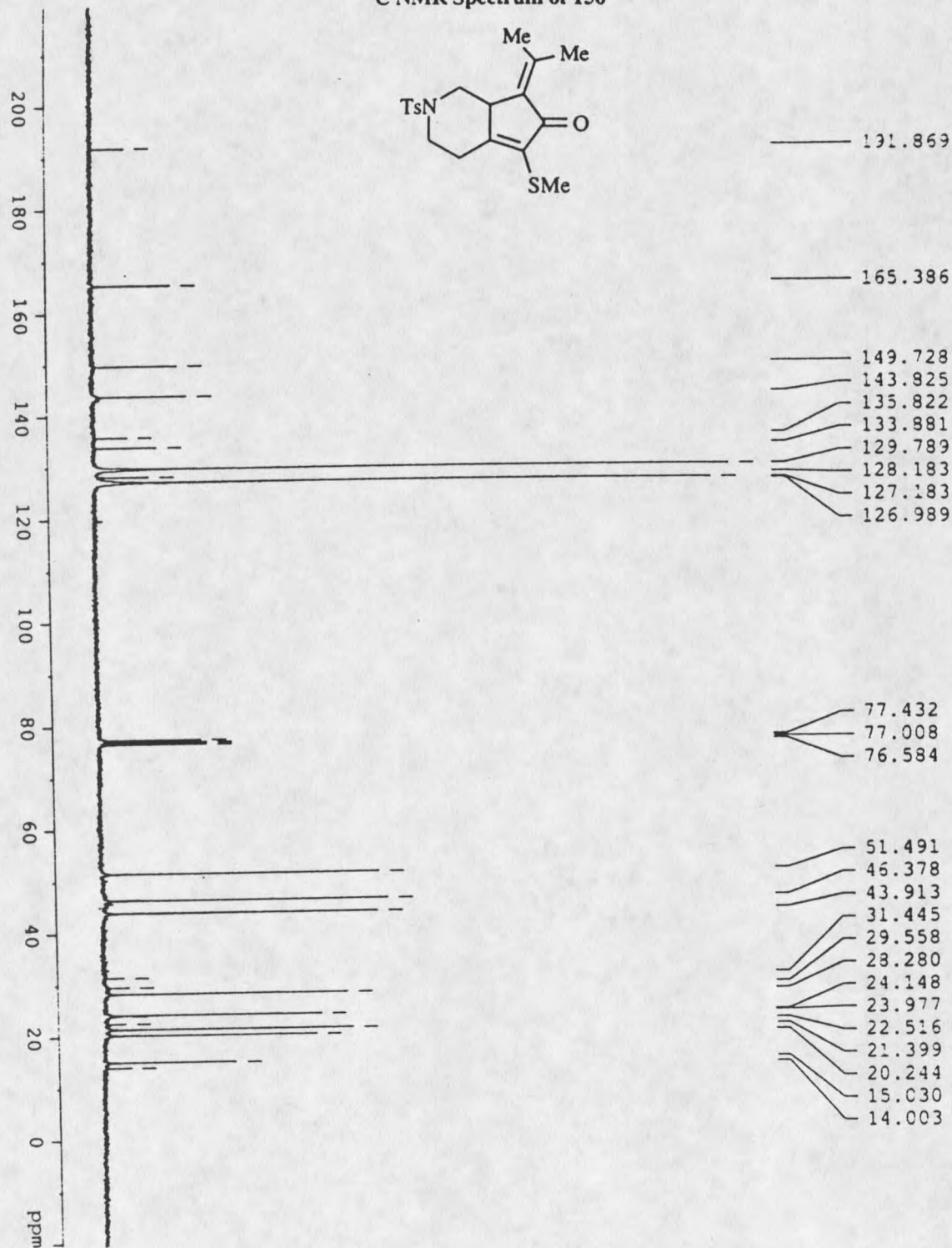
¹H NMR Spectrum of 148

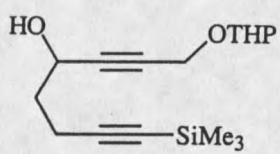
¹³C NMR Spectrum of 148

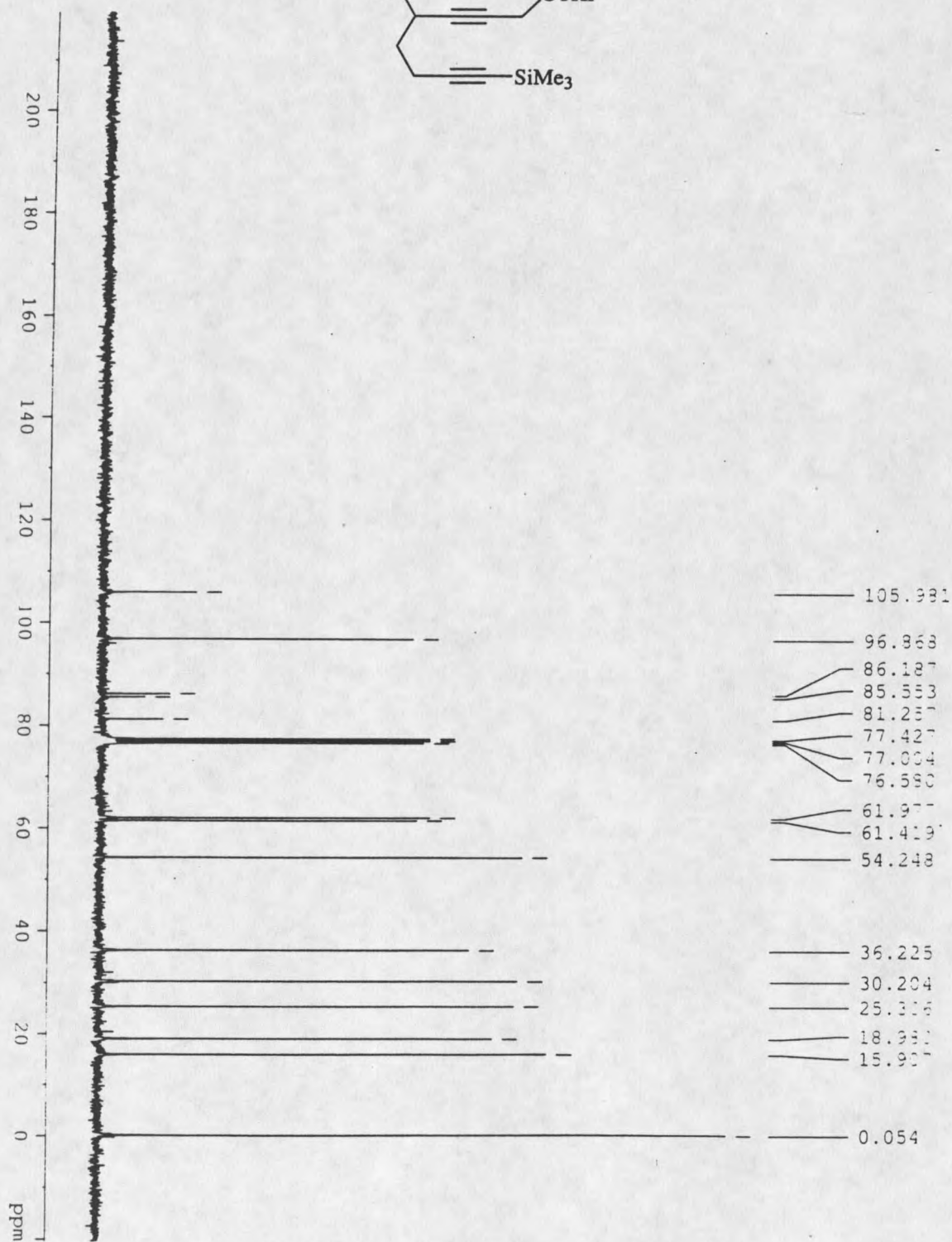
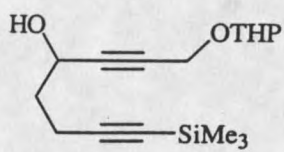
¹H NMR Spectrum of 149

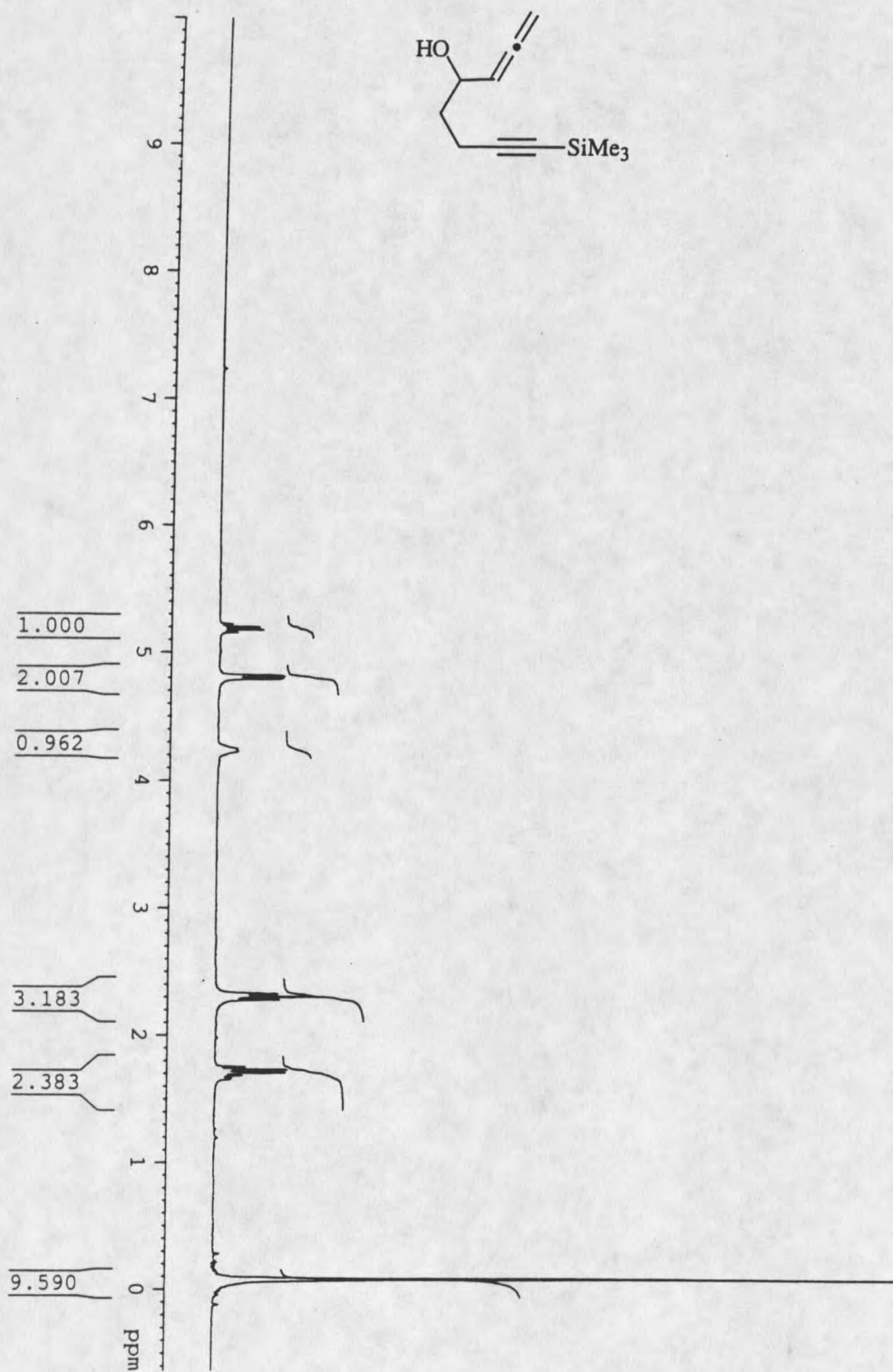
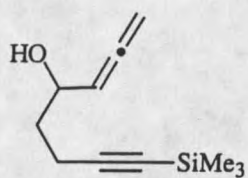
^{13}C NMR Spectrum of 149

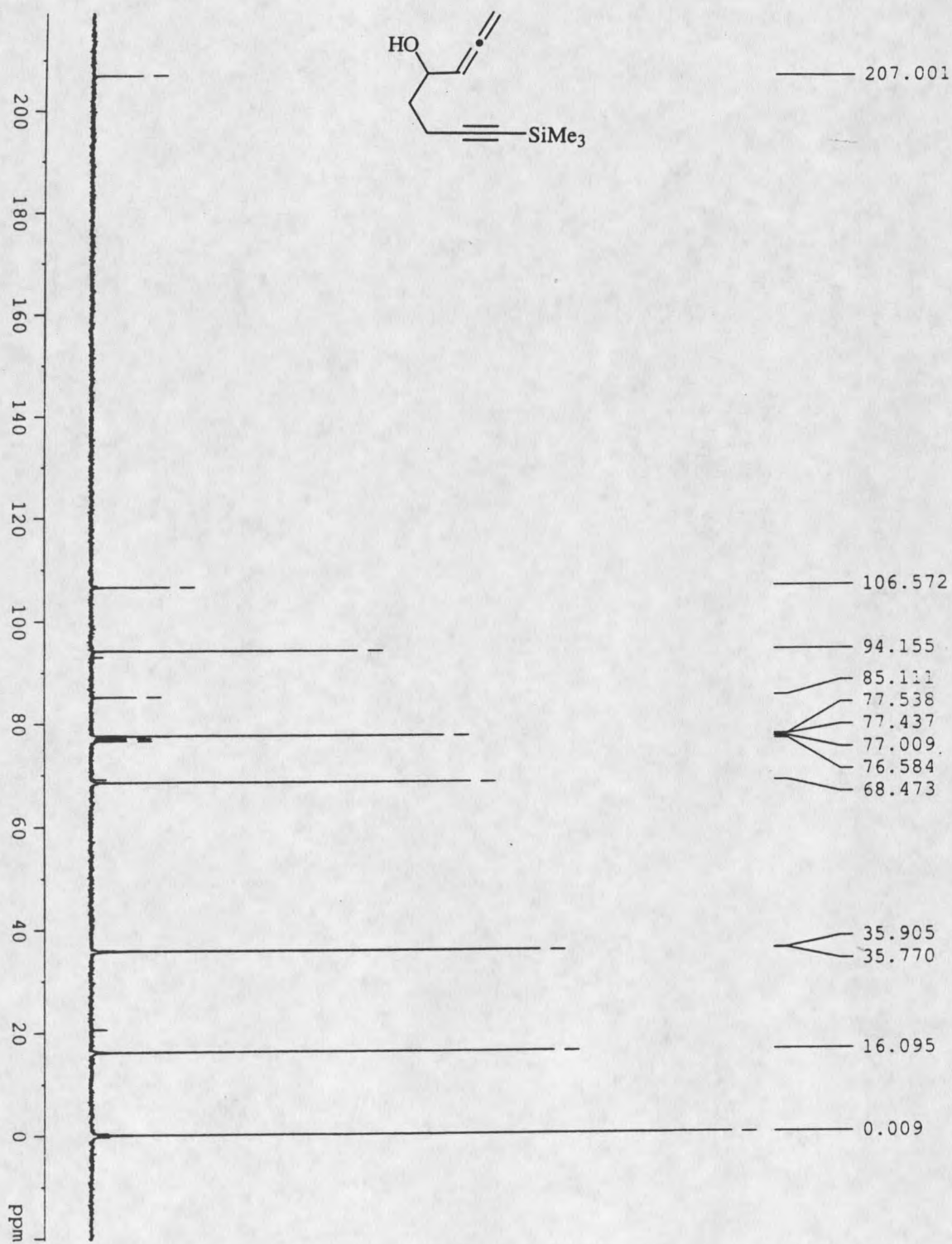
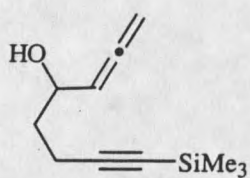
¹H NMR Spectrum of 150

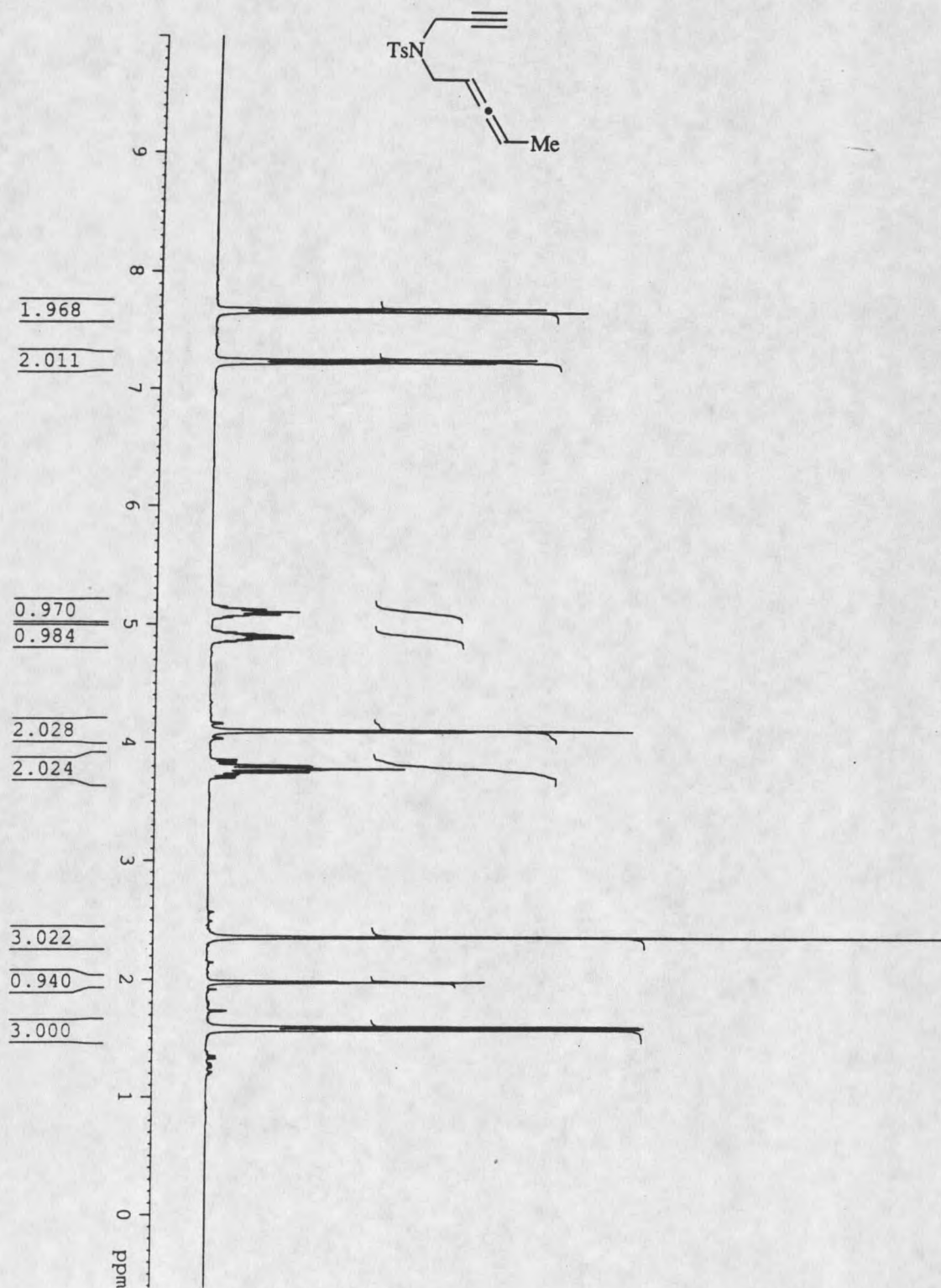
¹³C NMR Spectrum of 150

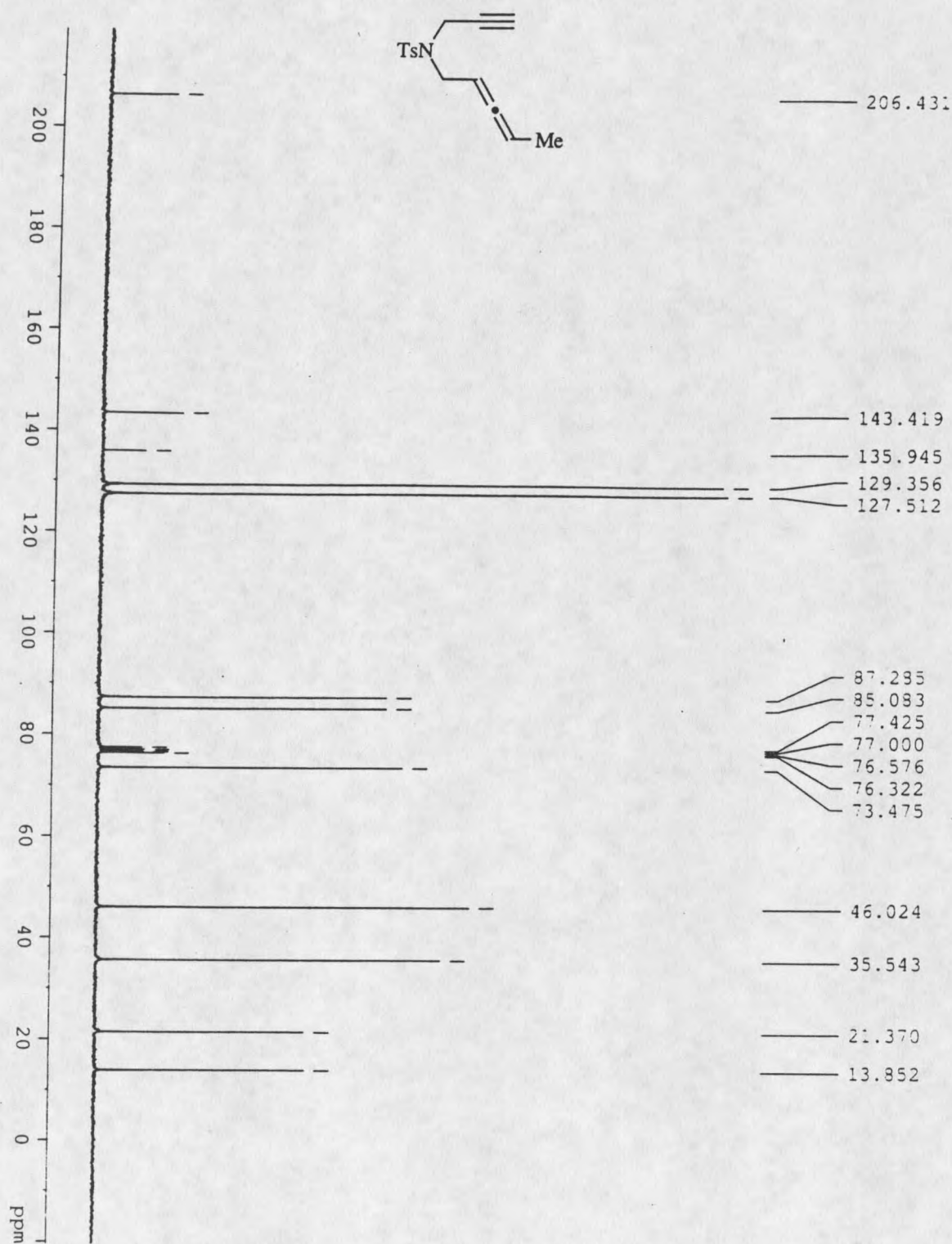
¹H NMR Spectrum of

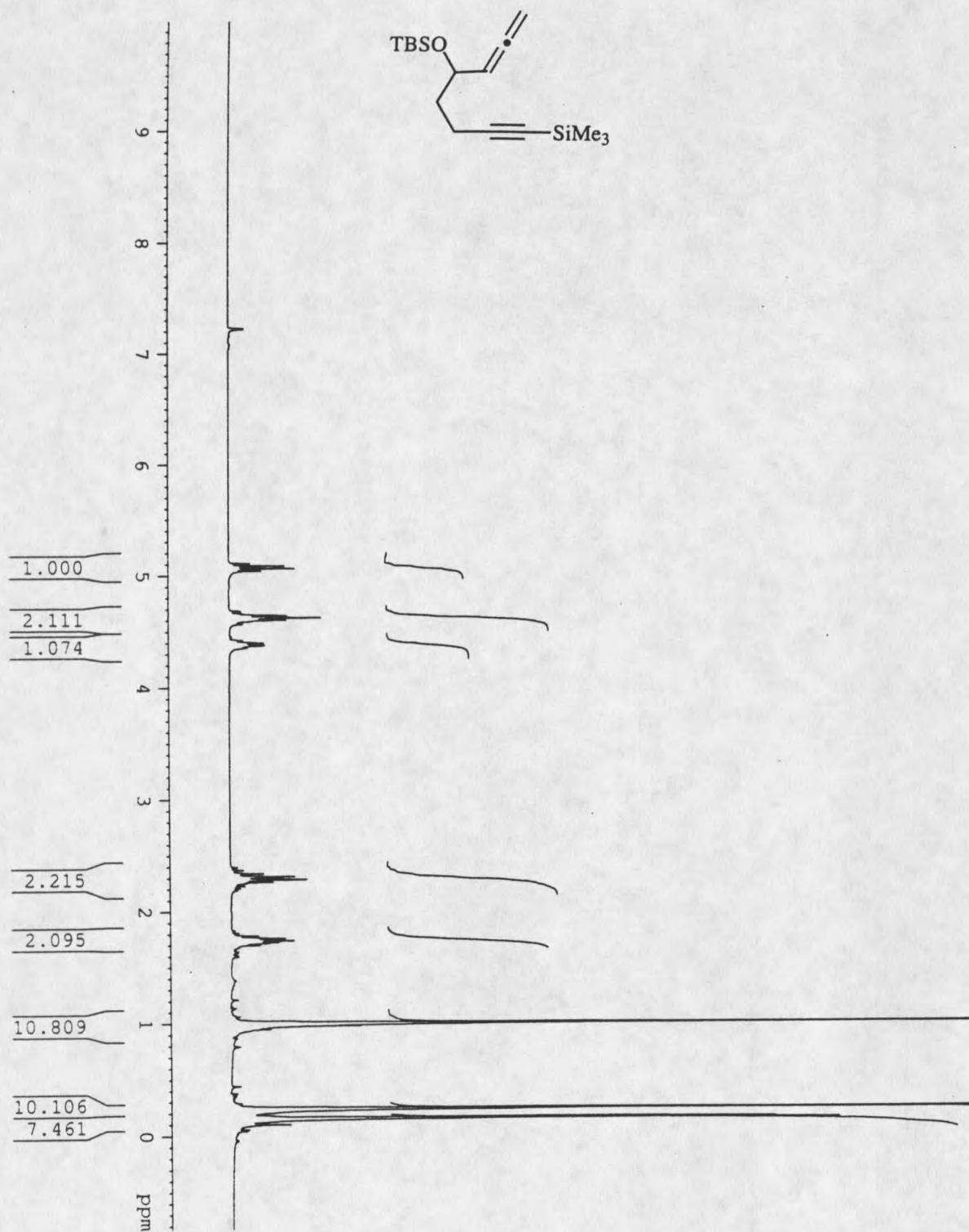
¹³C NMR Spectrum of

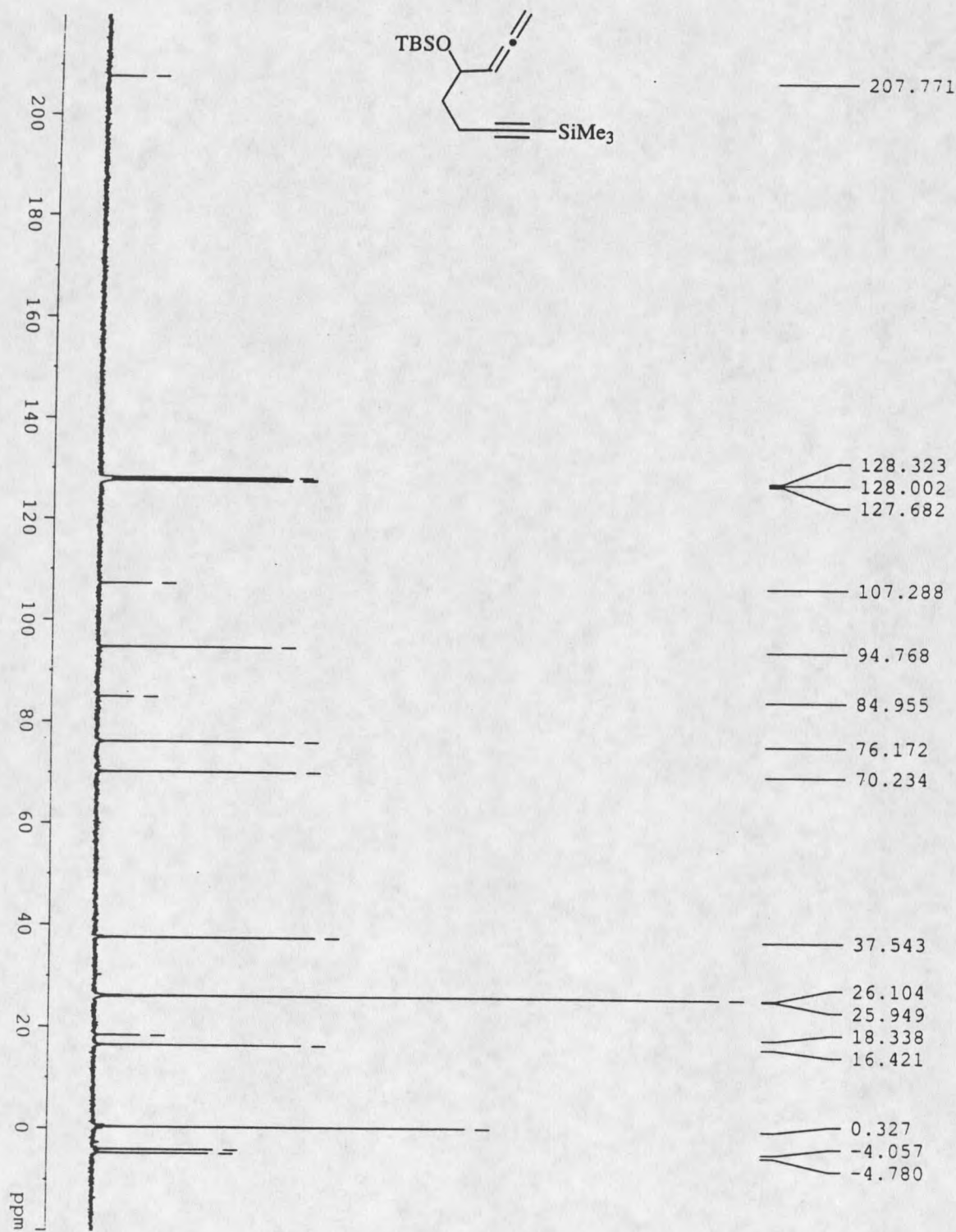
¹H NMR Spectrum of

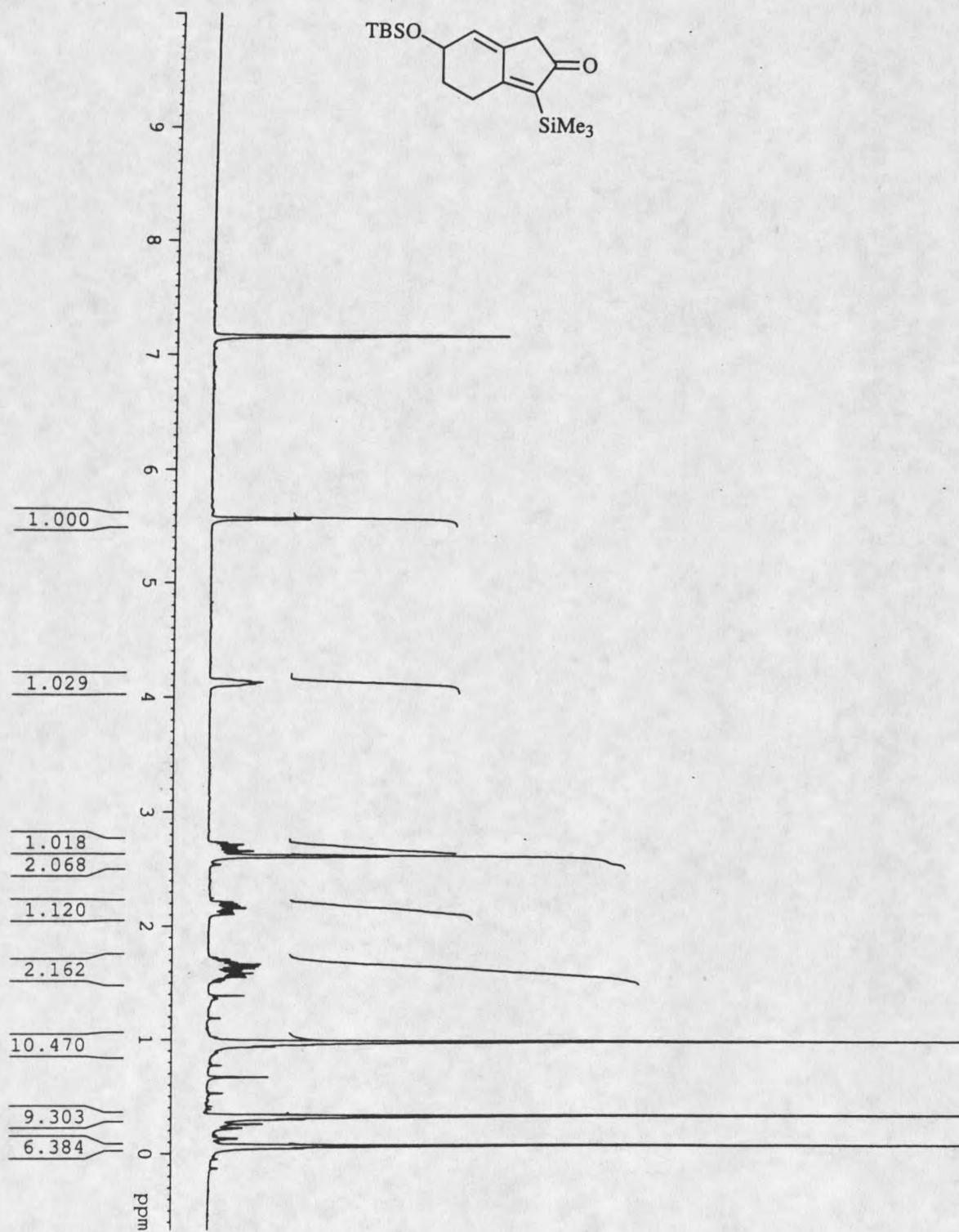
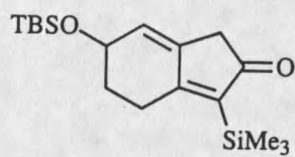
^{13}C NMR Spectrum of

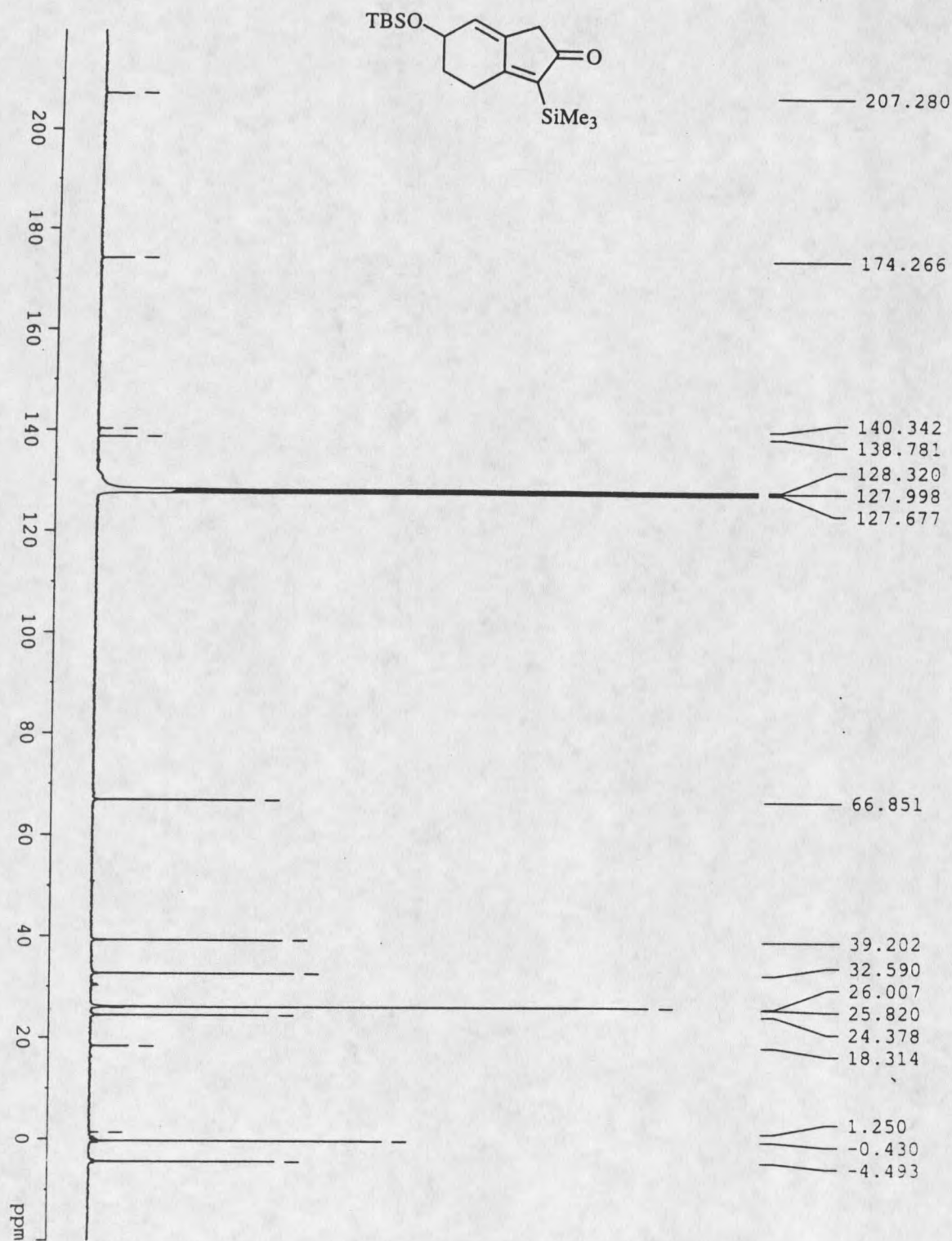
¹H NMR Spectrum of 126

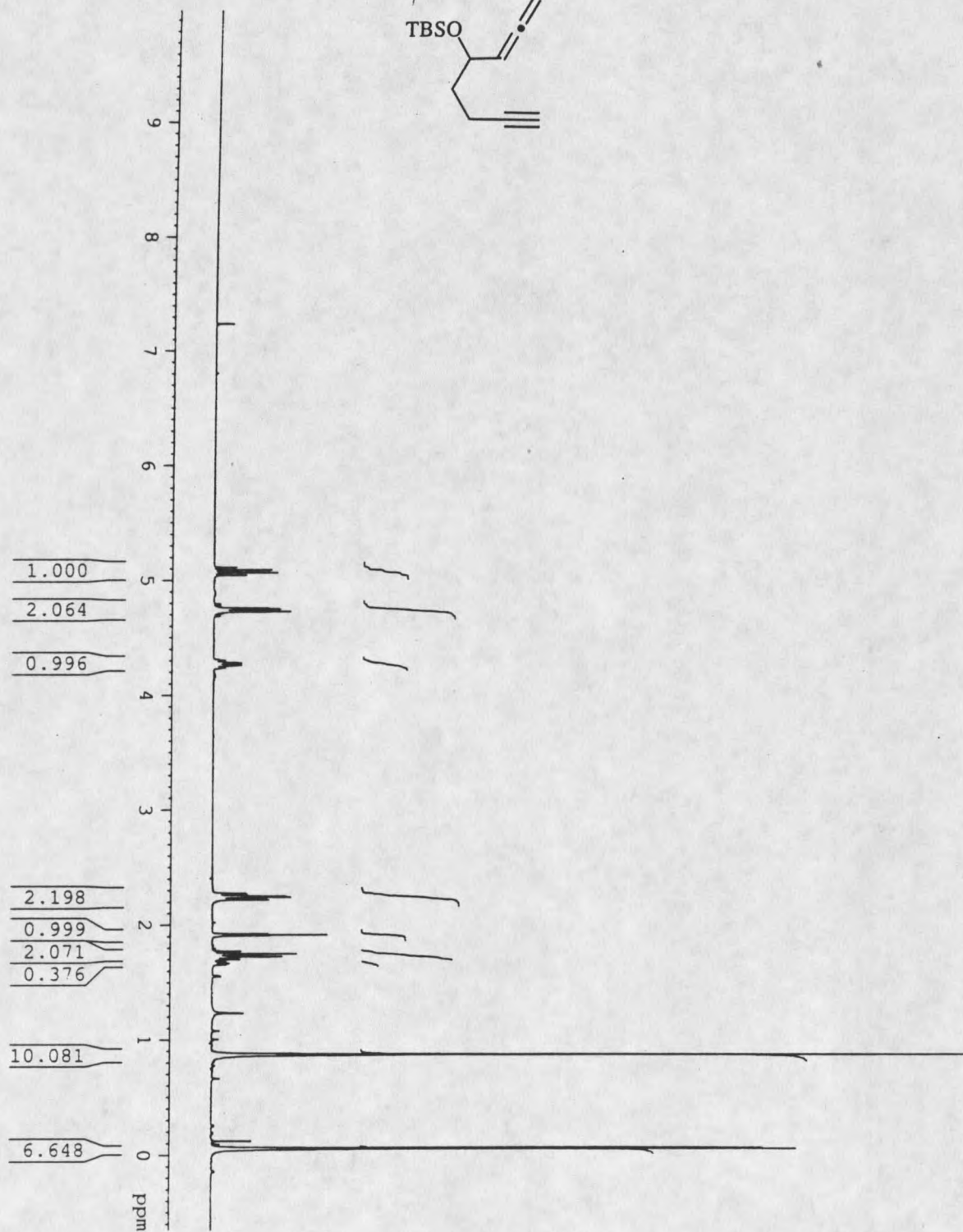
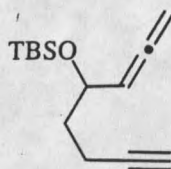
¹³C NMR Spectrum of 126

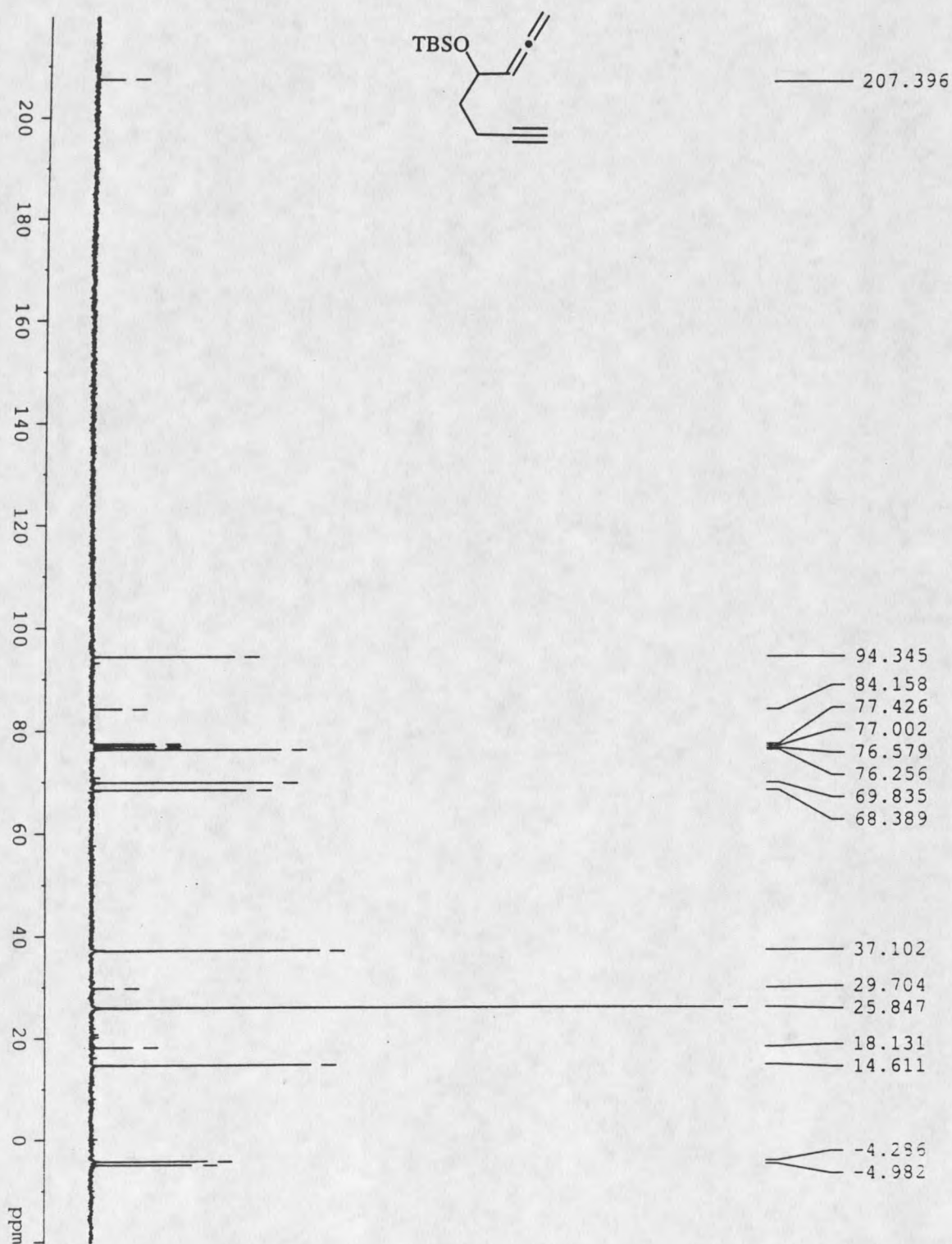
¹H NMR Spectrum of 157

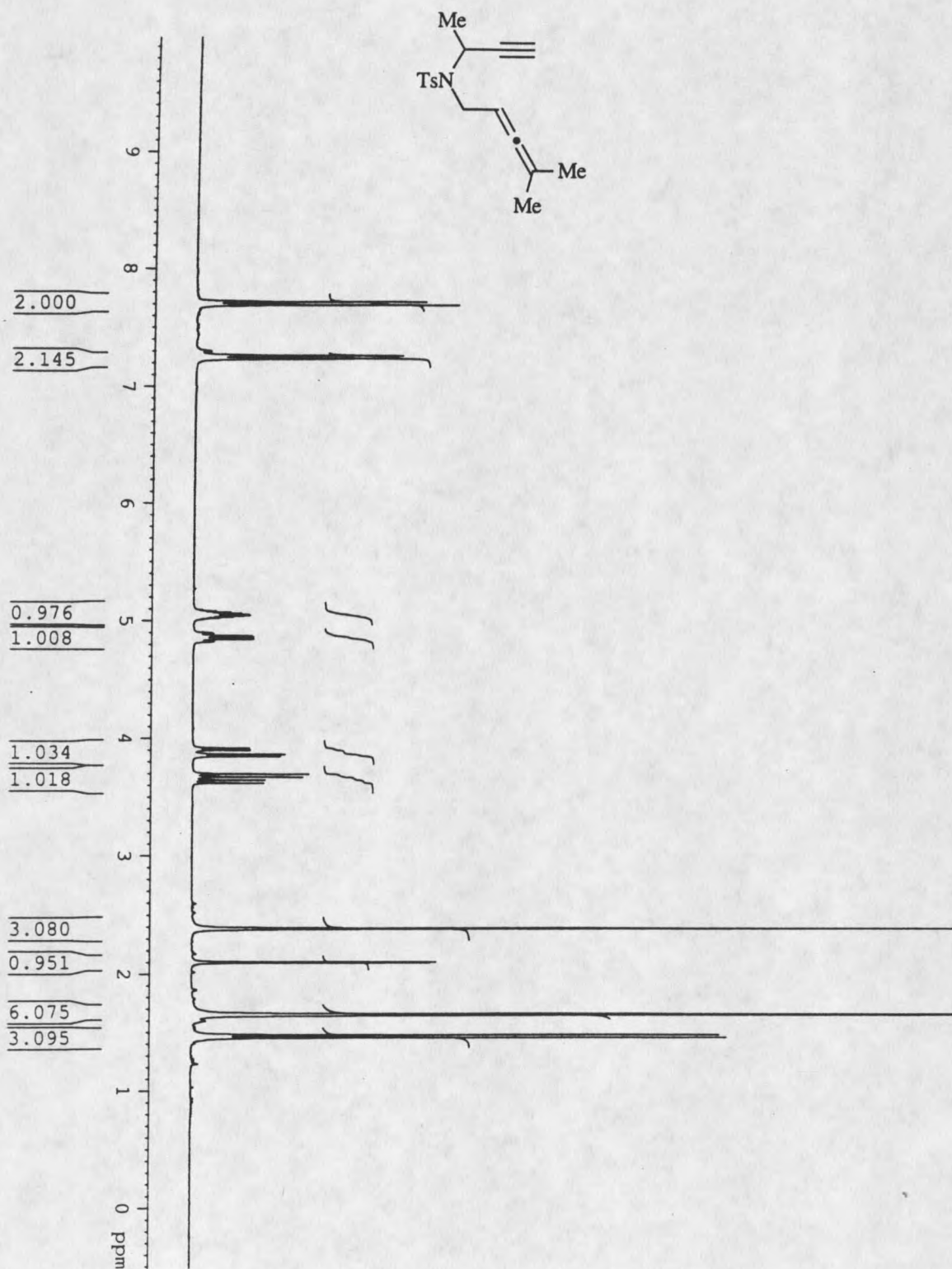
^{13}C NMR Spectrum of 157

¹H NMR Spectrum of 158

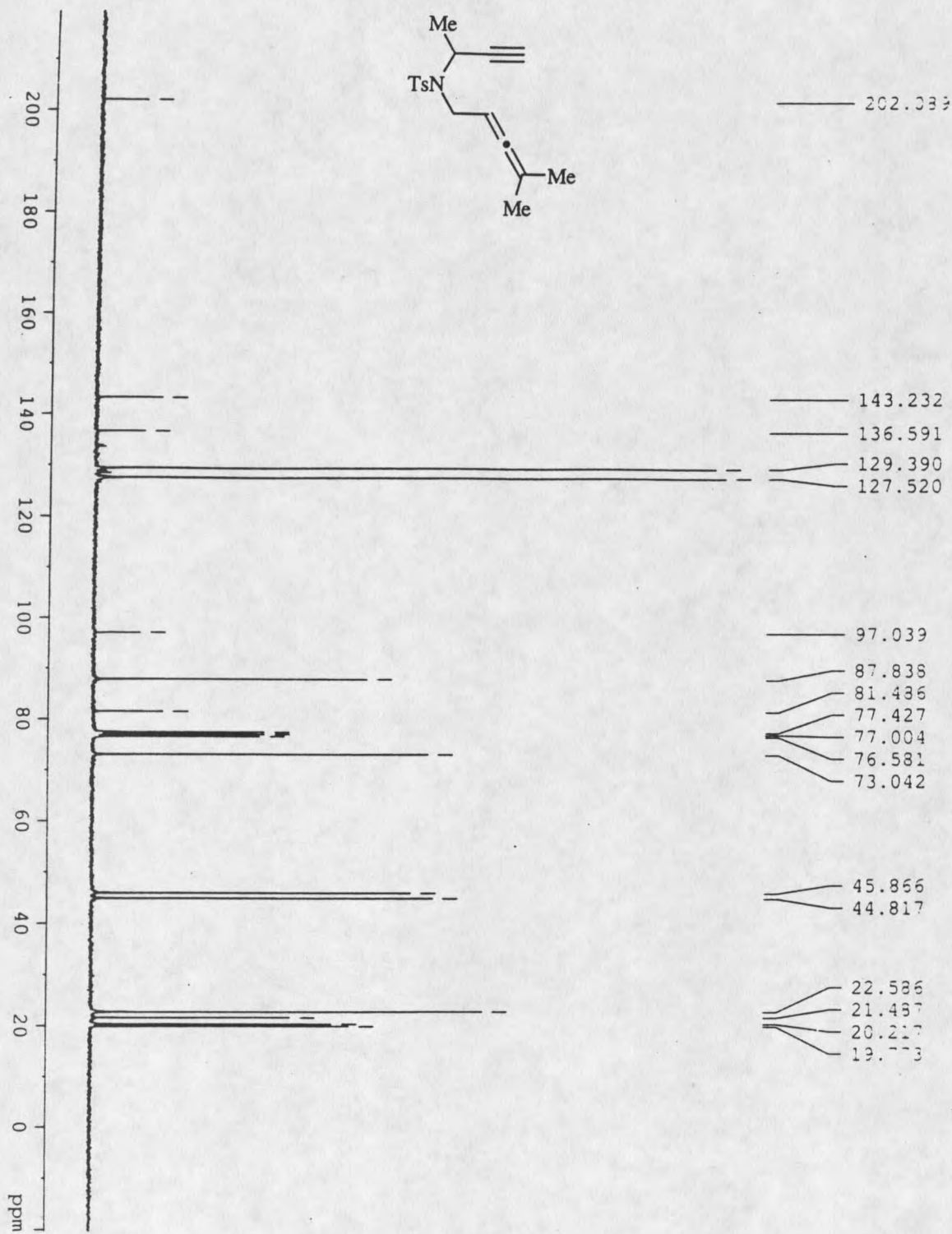
¹³C NMR Spectrum of 158

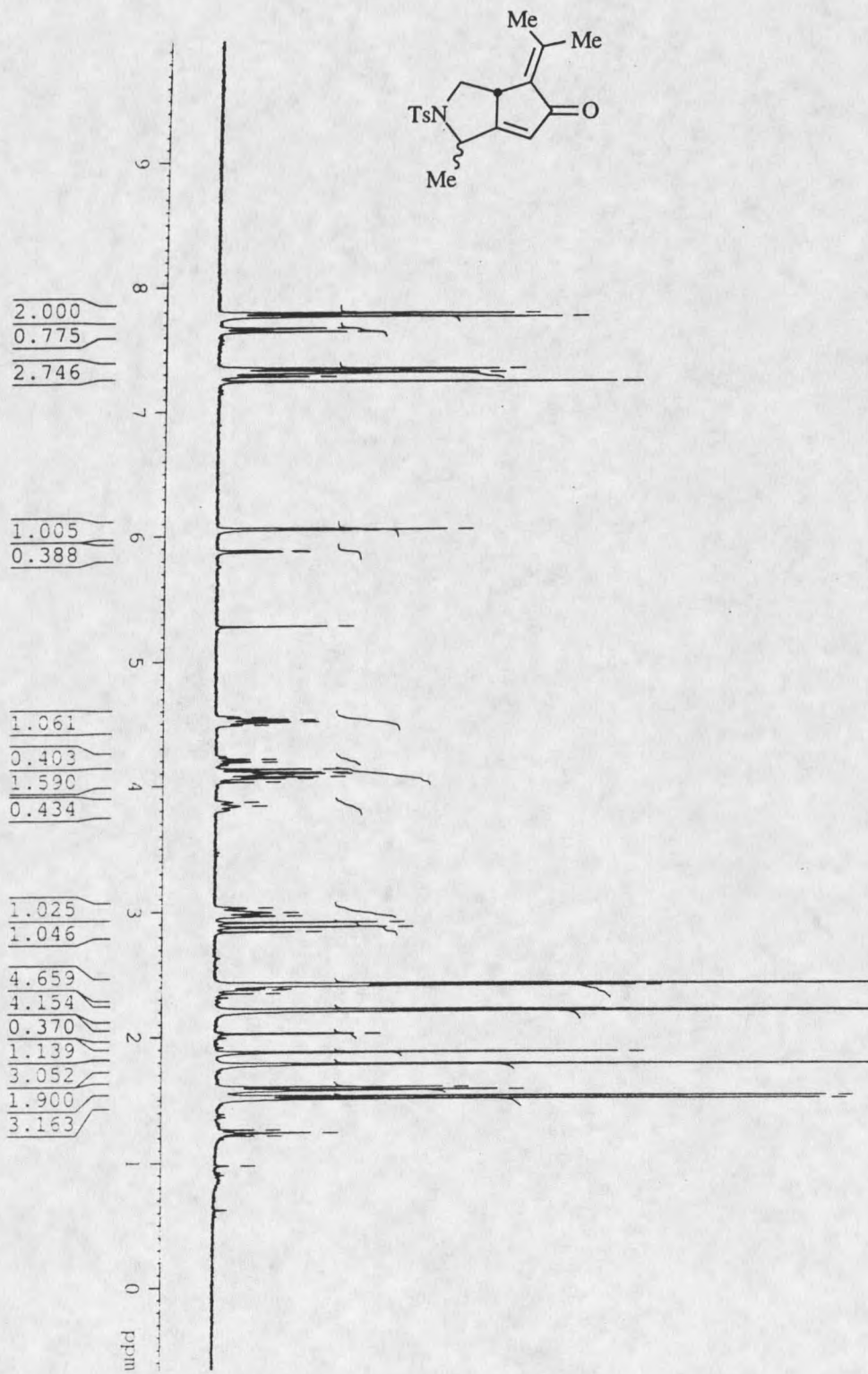
¹H NMR Spectrum of

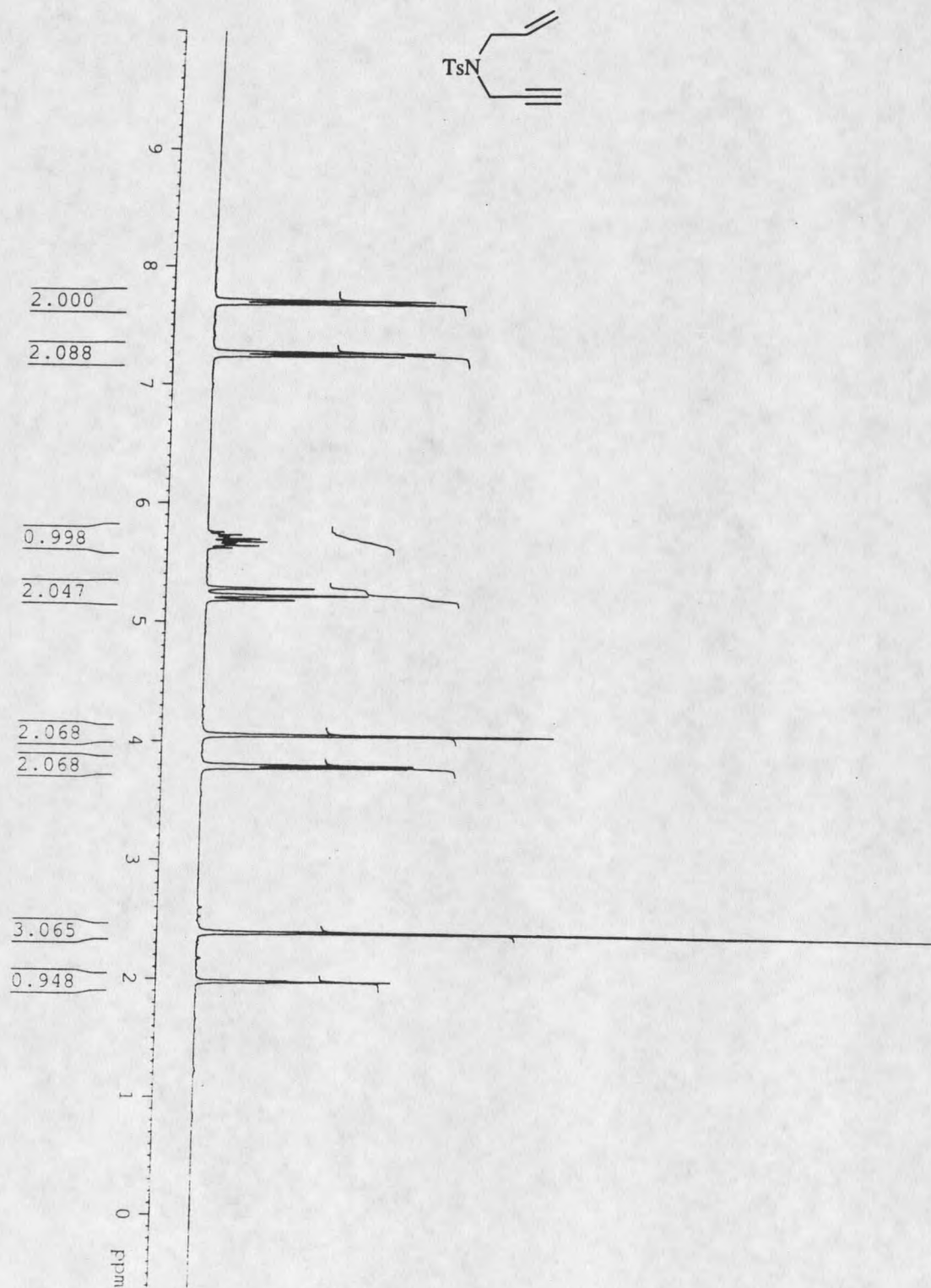
¹³C NMR Spectrum of

¹H NMR Spectrum of 127

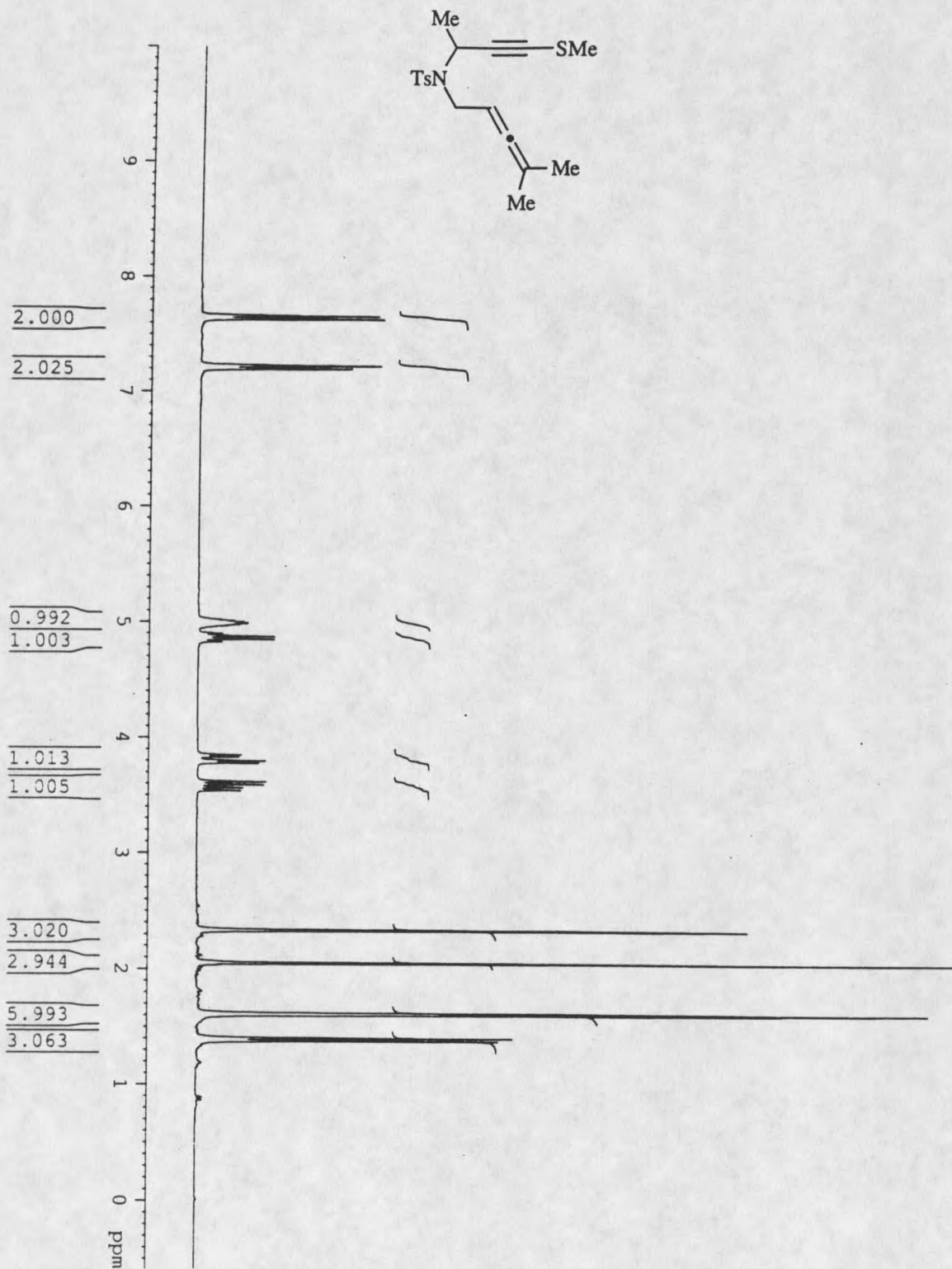
¹³C NMR Spectrum of 127

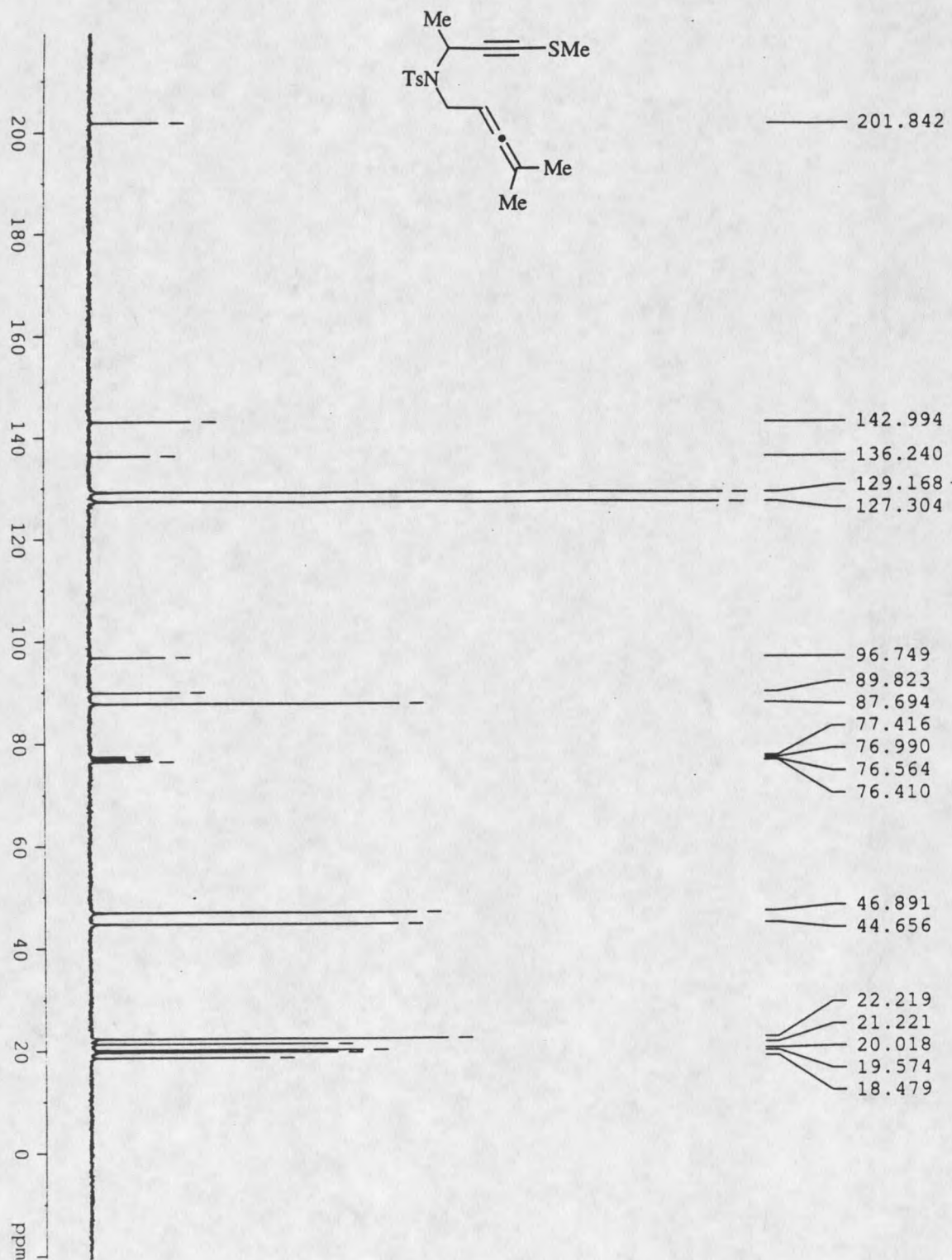


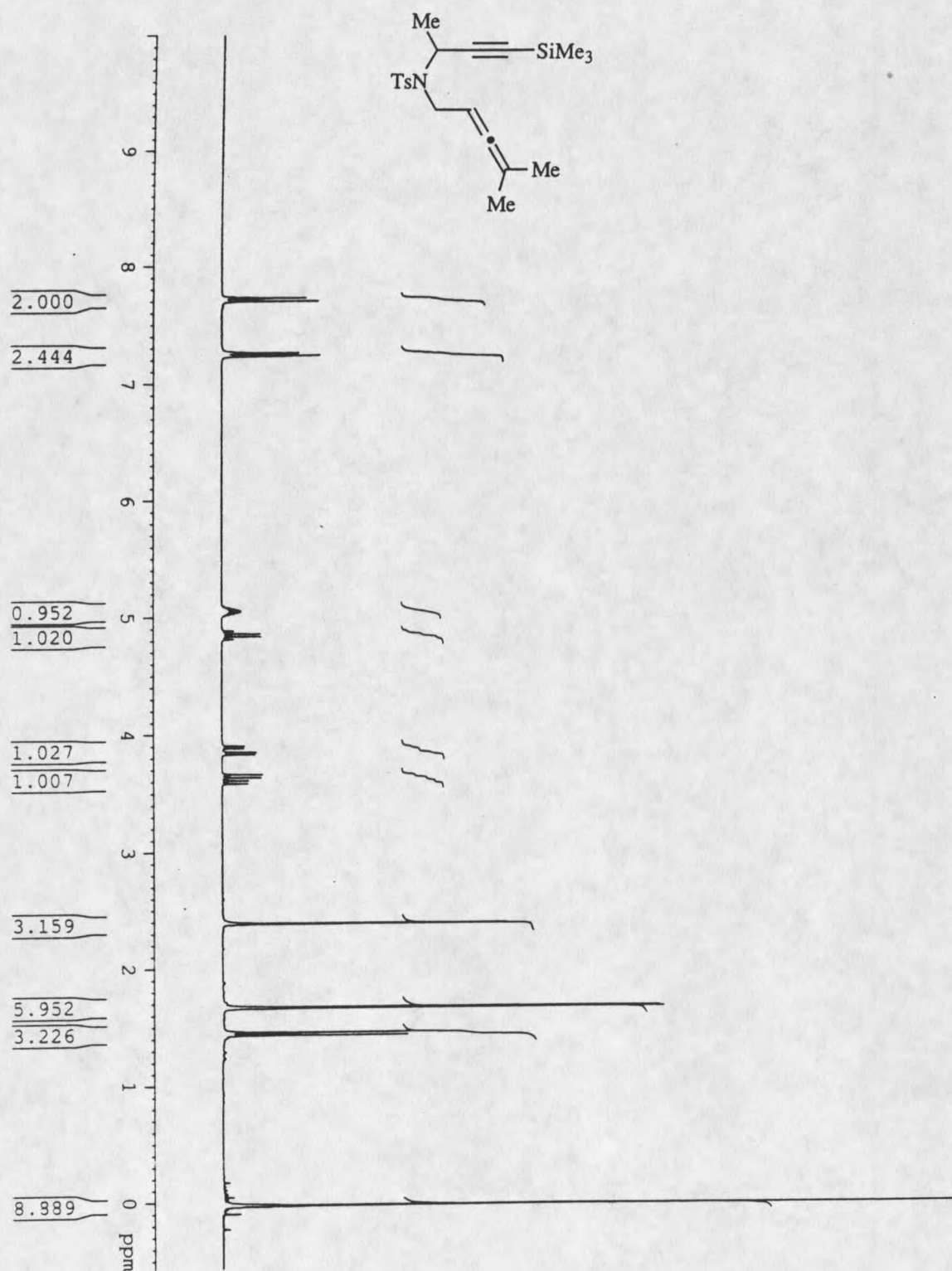
¹H NMR Spectrum of 127

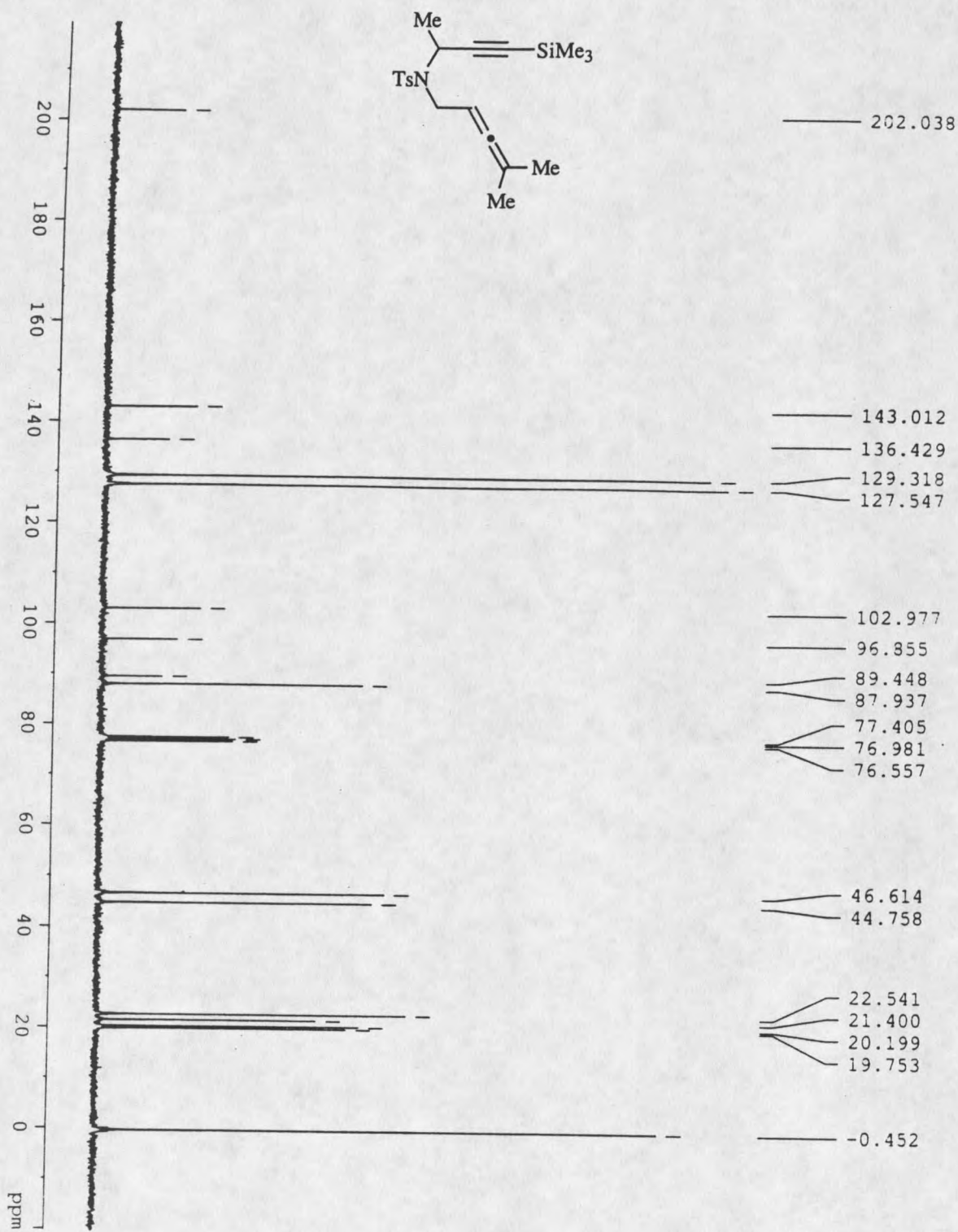
¹H NMR Spectrum of 17

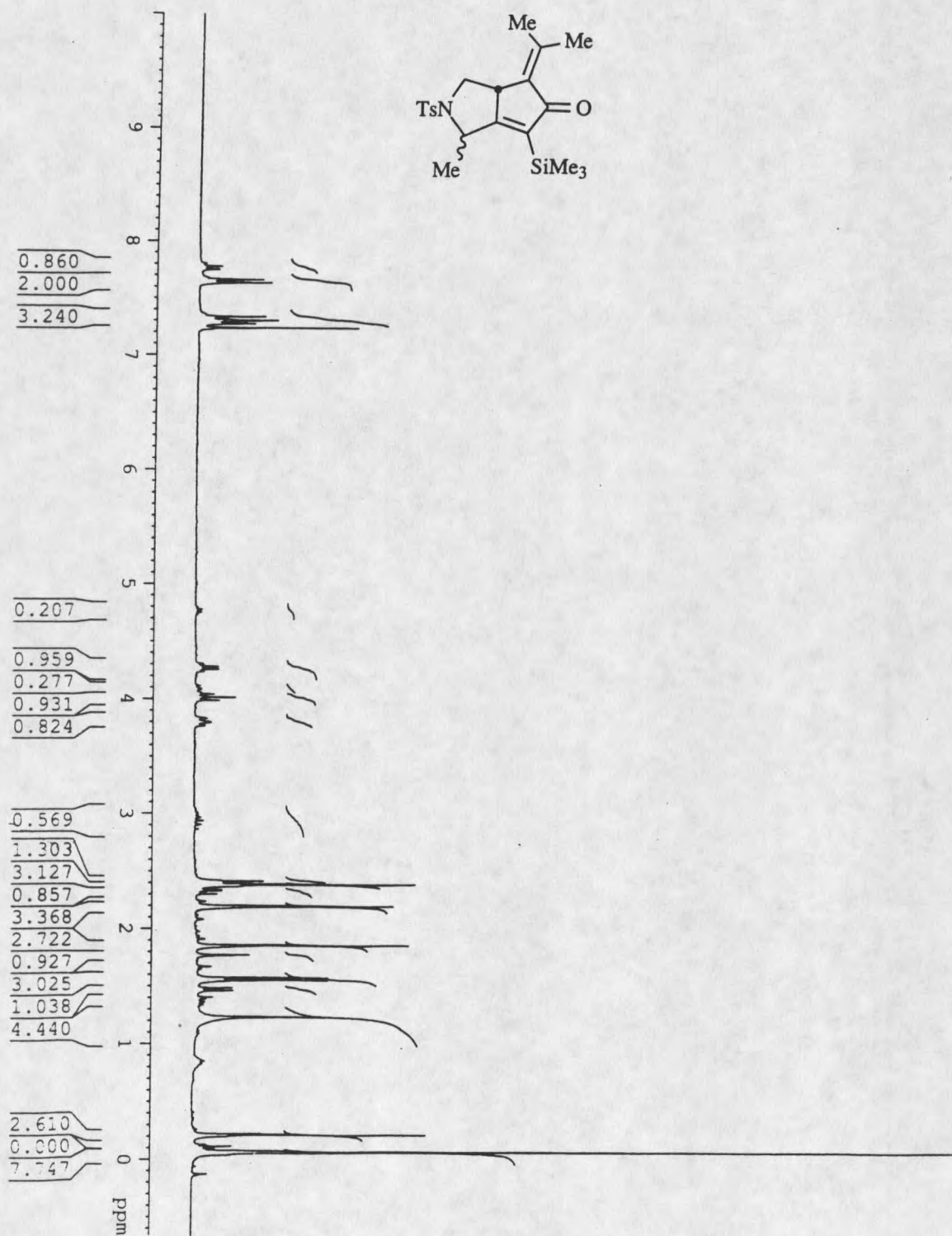
¹H NMR Spectrum of 153



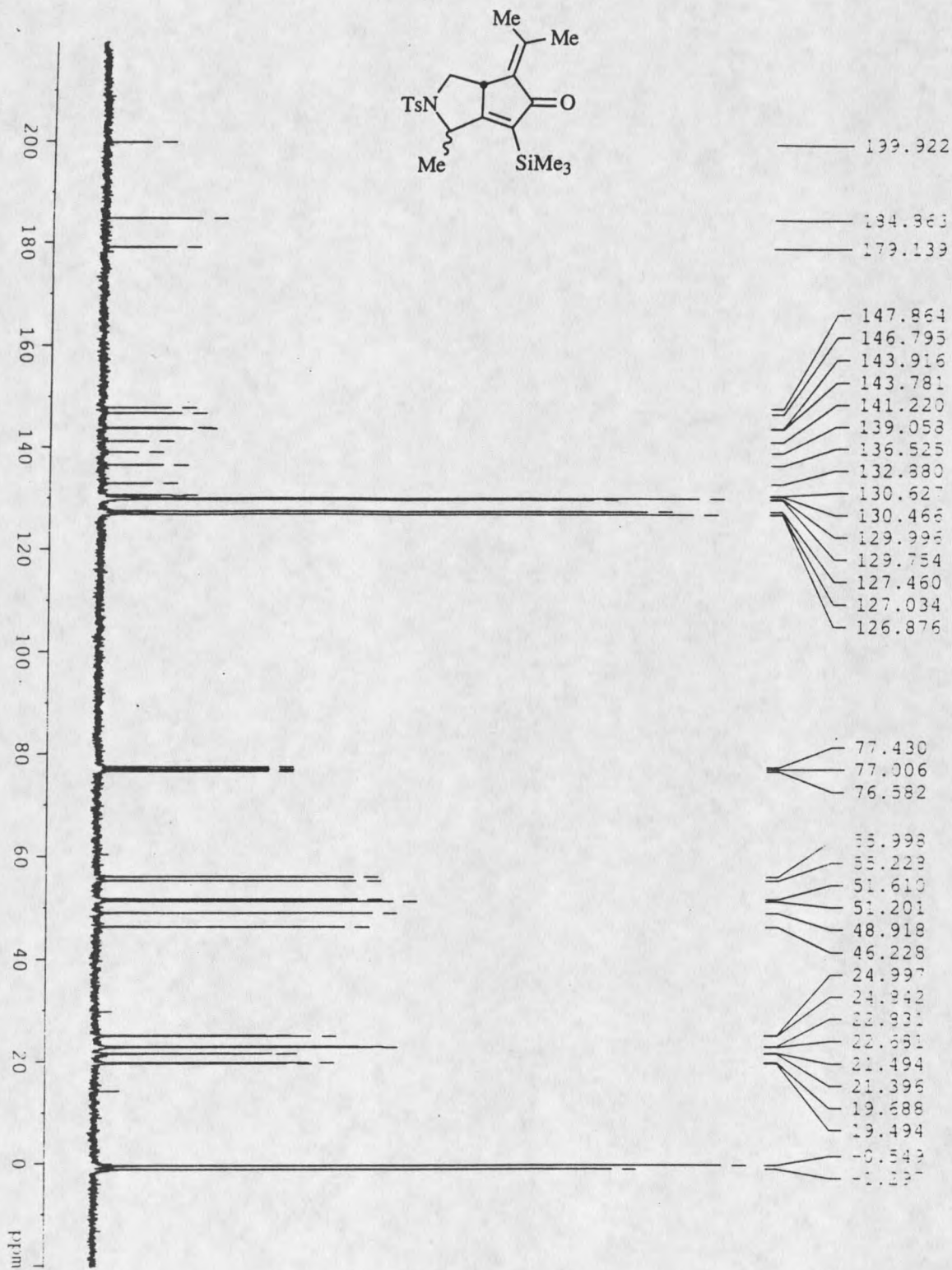
¹³C NMR Spectrum of 153

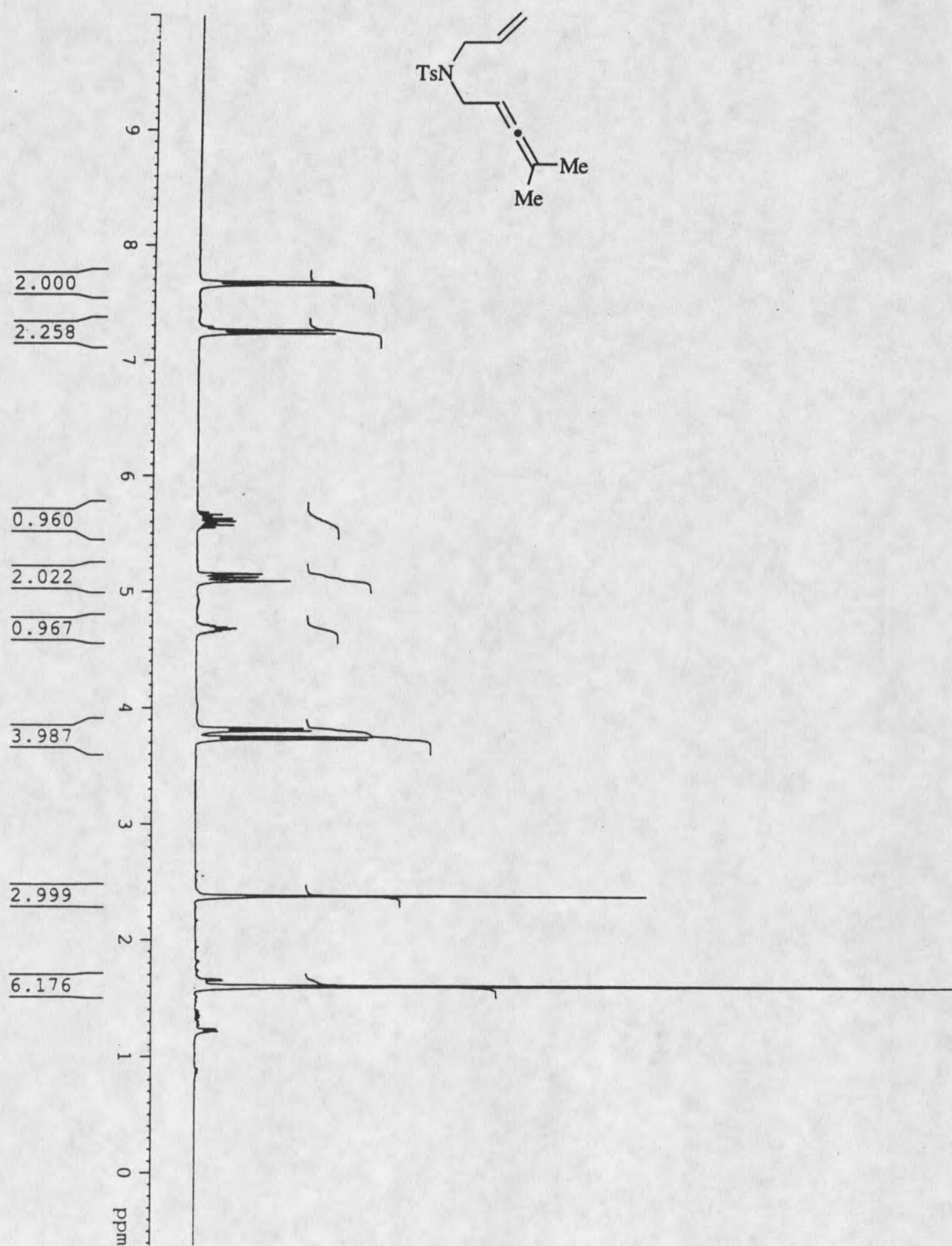
¹H NMR Spectrum of 155

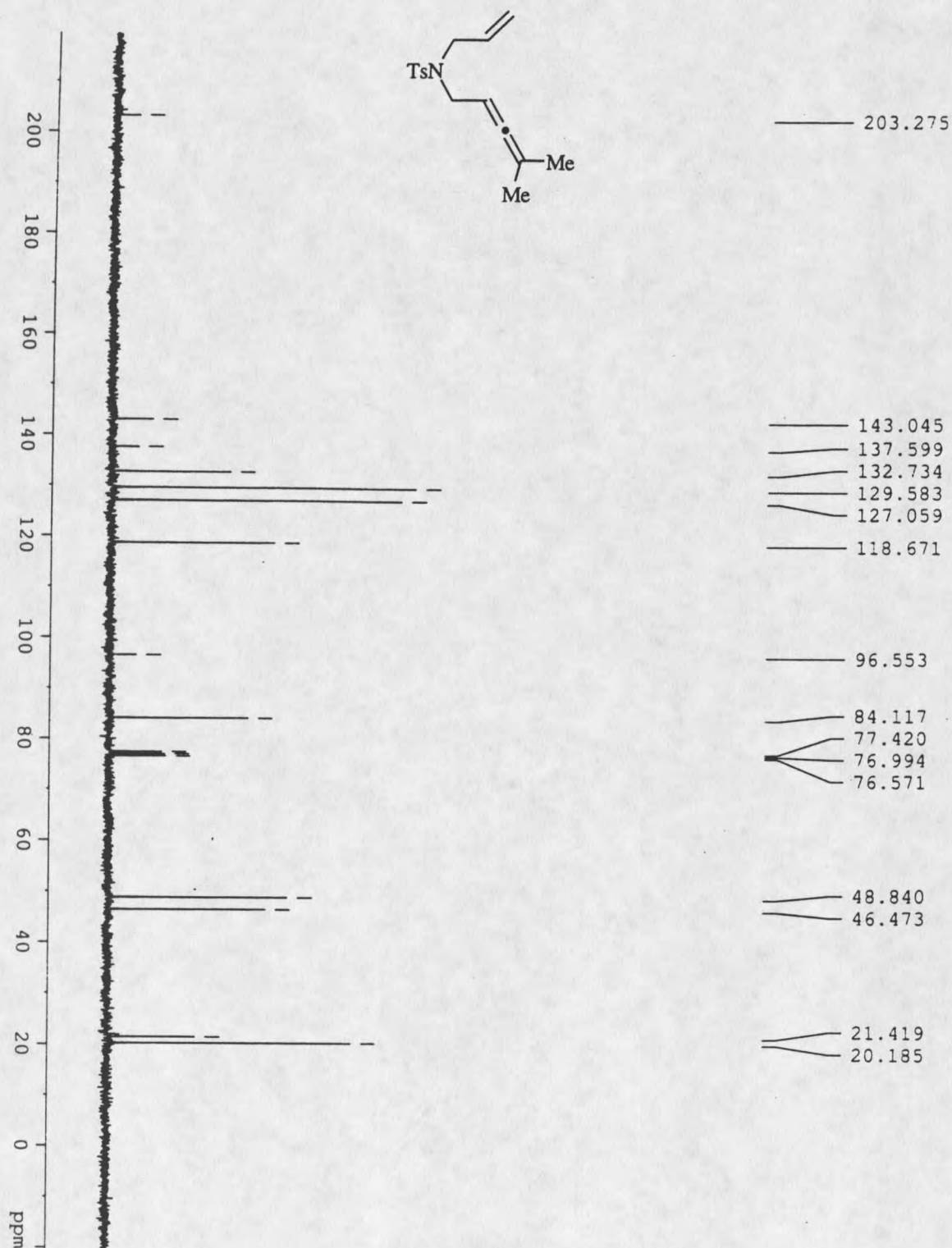
¹³C NMR Spectrum of 155

¹H NMR Spectrum of 156

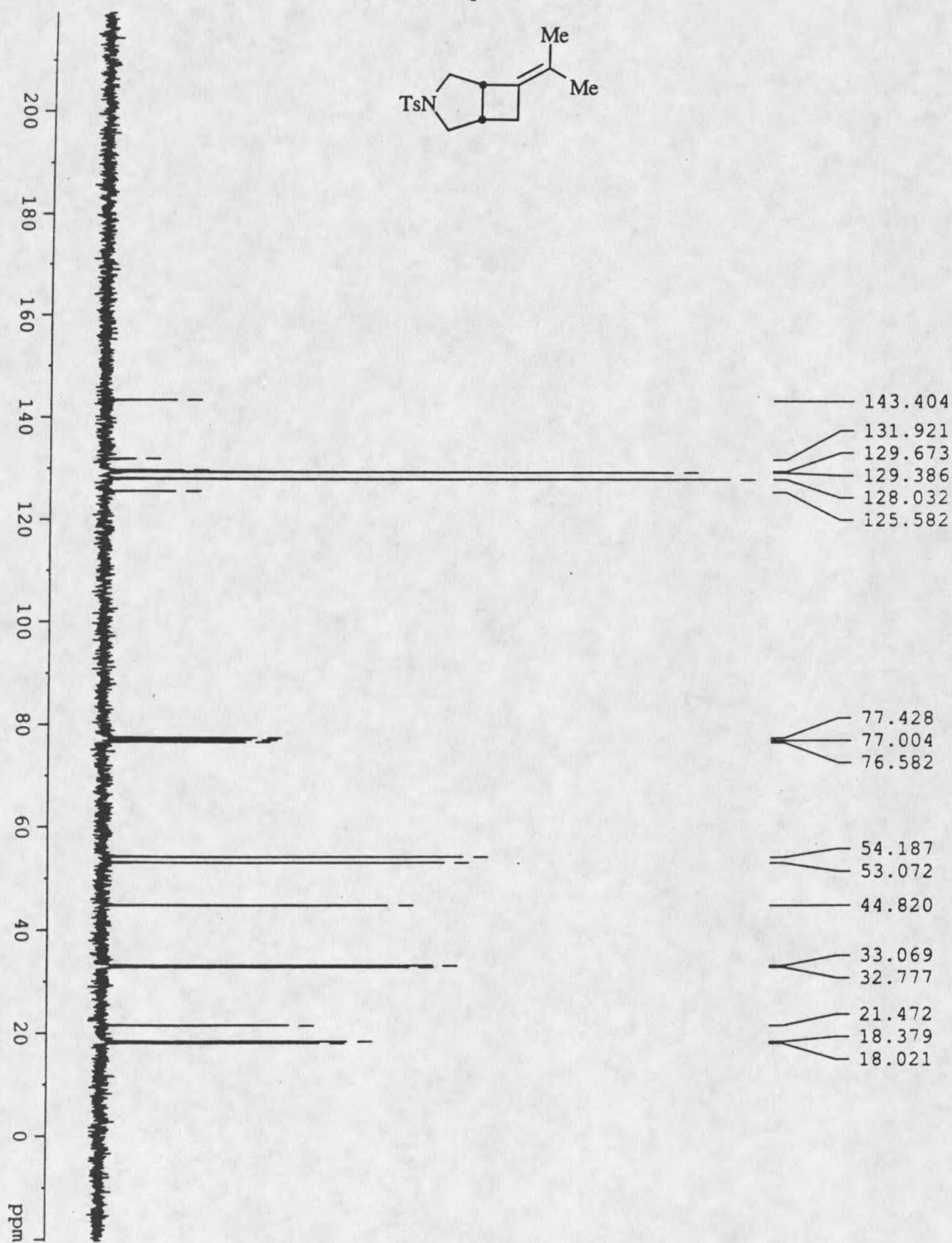
¹³C NMR Spectrum of 156

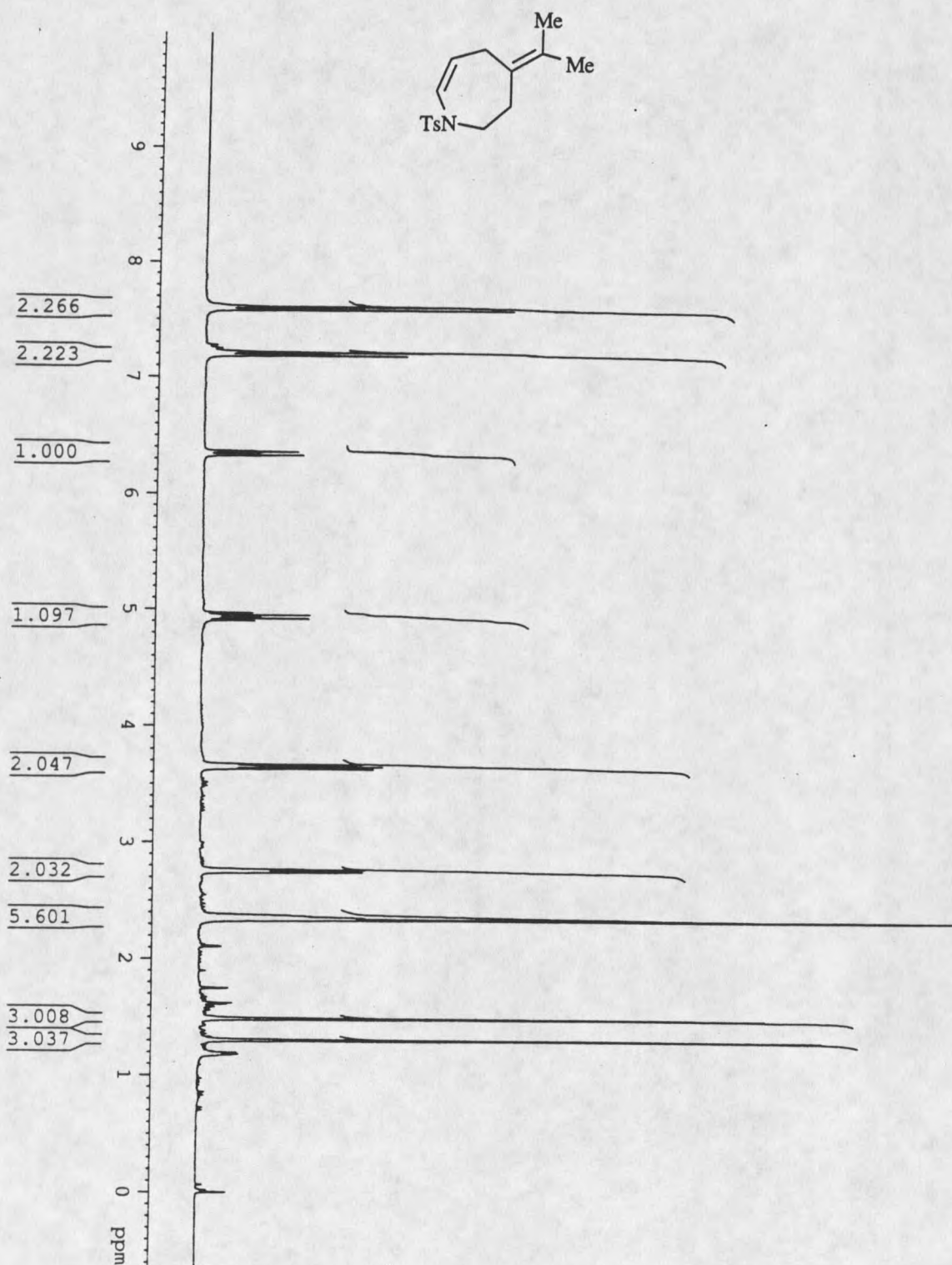


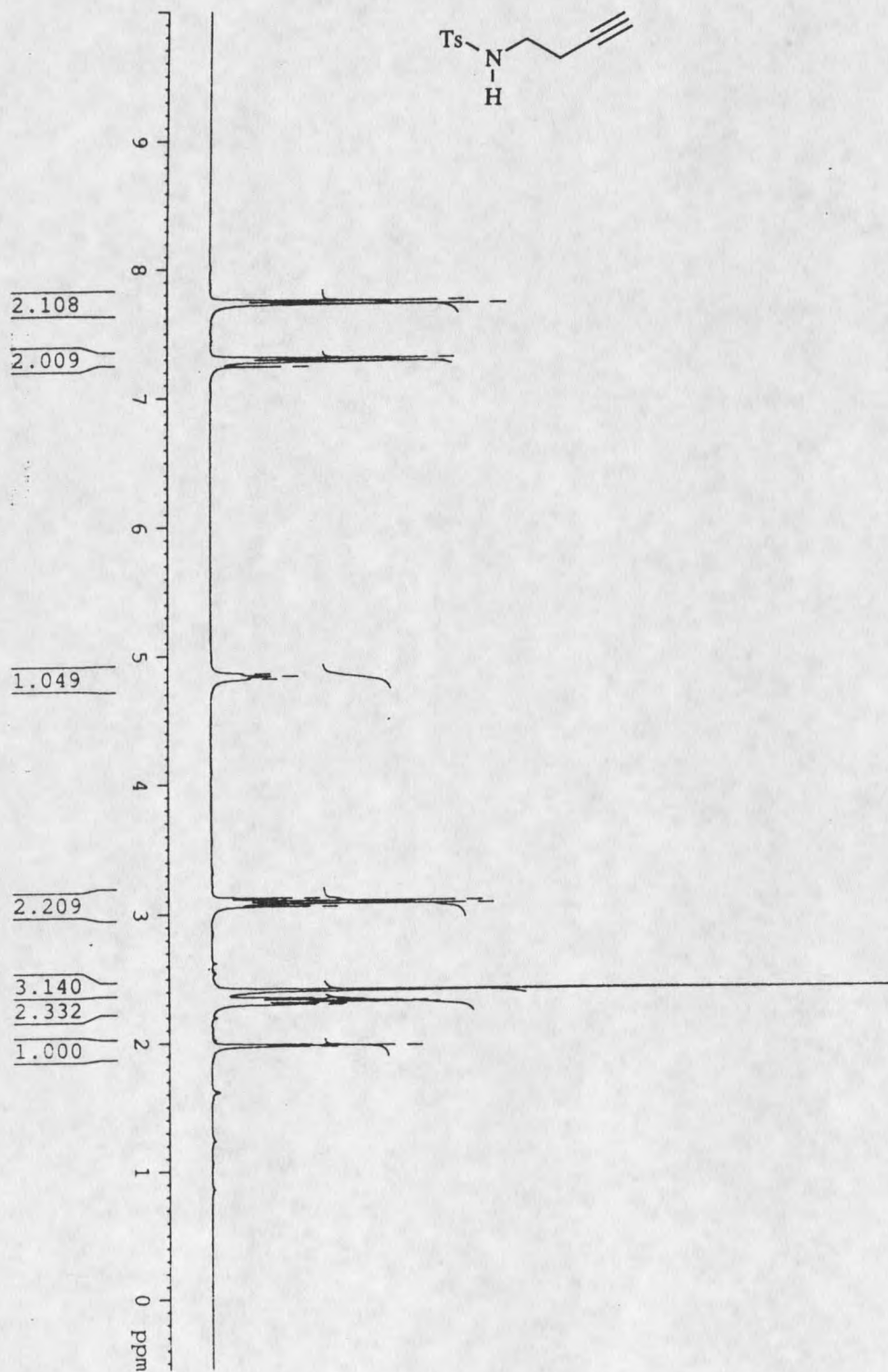
¹H NMR Spectrum of 137

^{13}C NMR Spectrum of 137

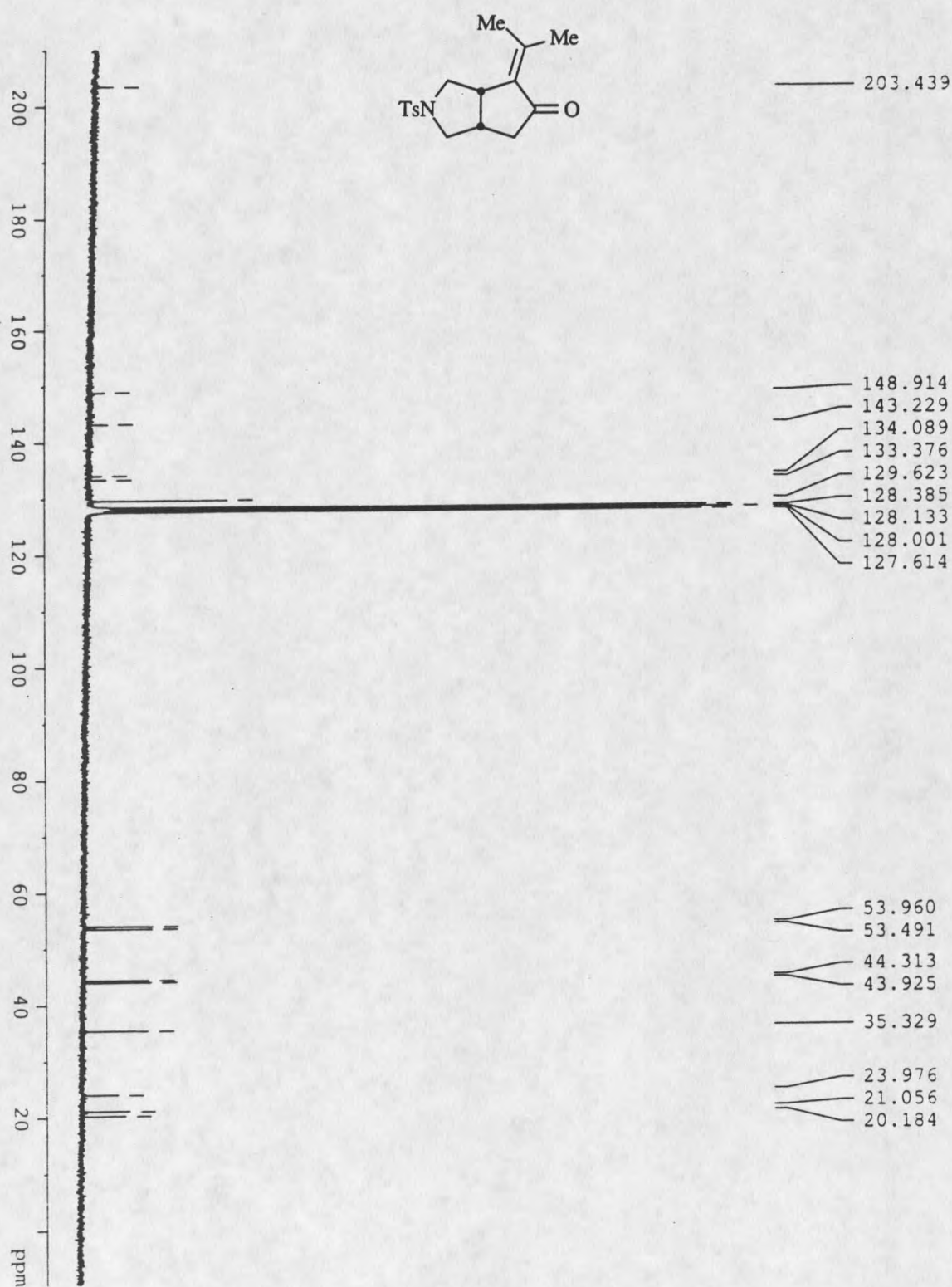
¹H NMR Spectrum of 166

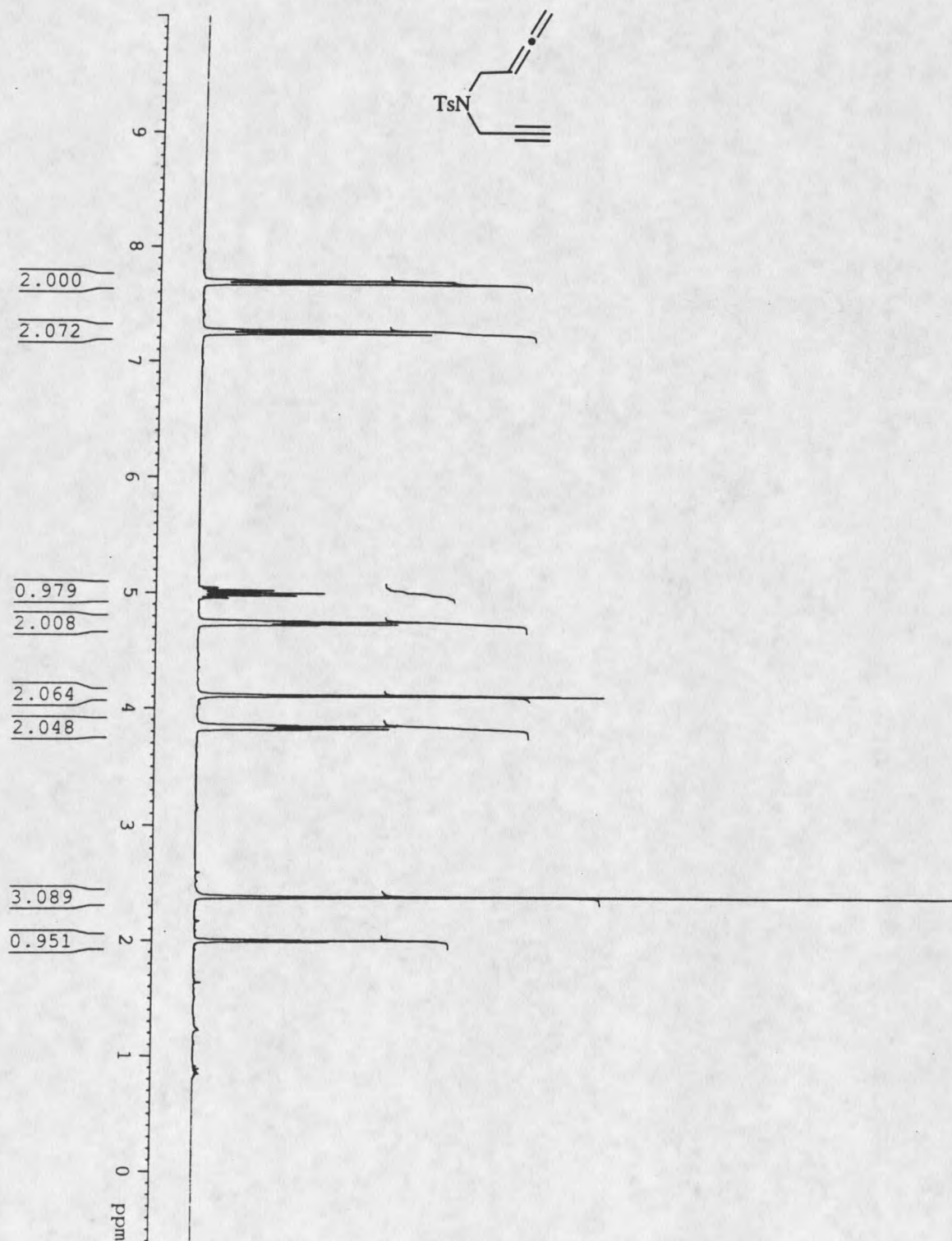
¹³C NMR Spectrum of 166

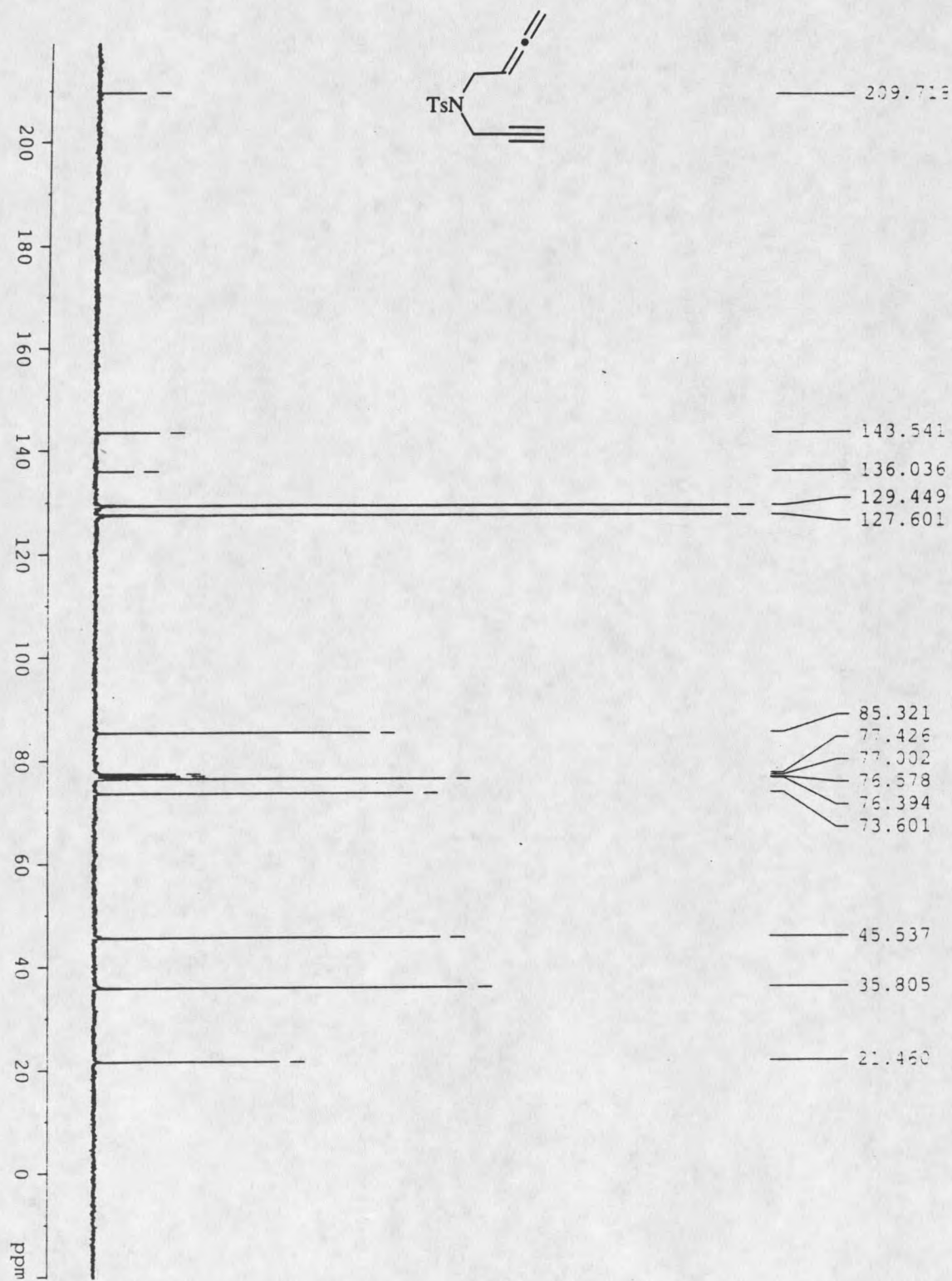
¹H NMR Spectrum of 167

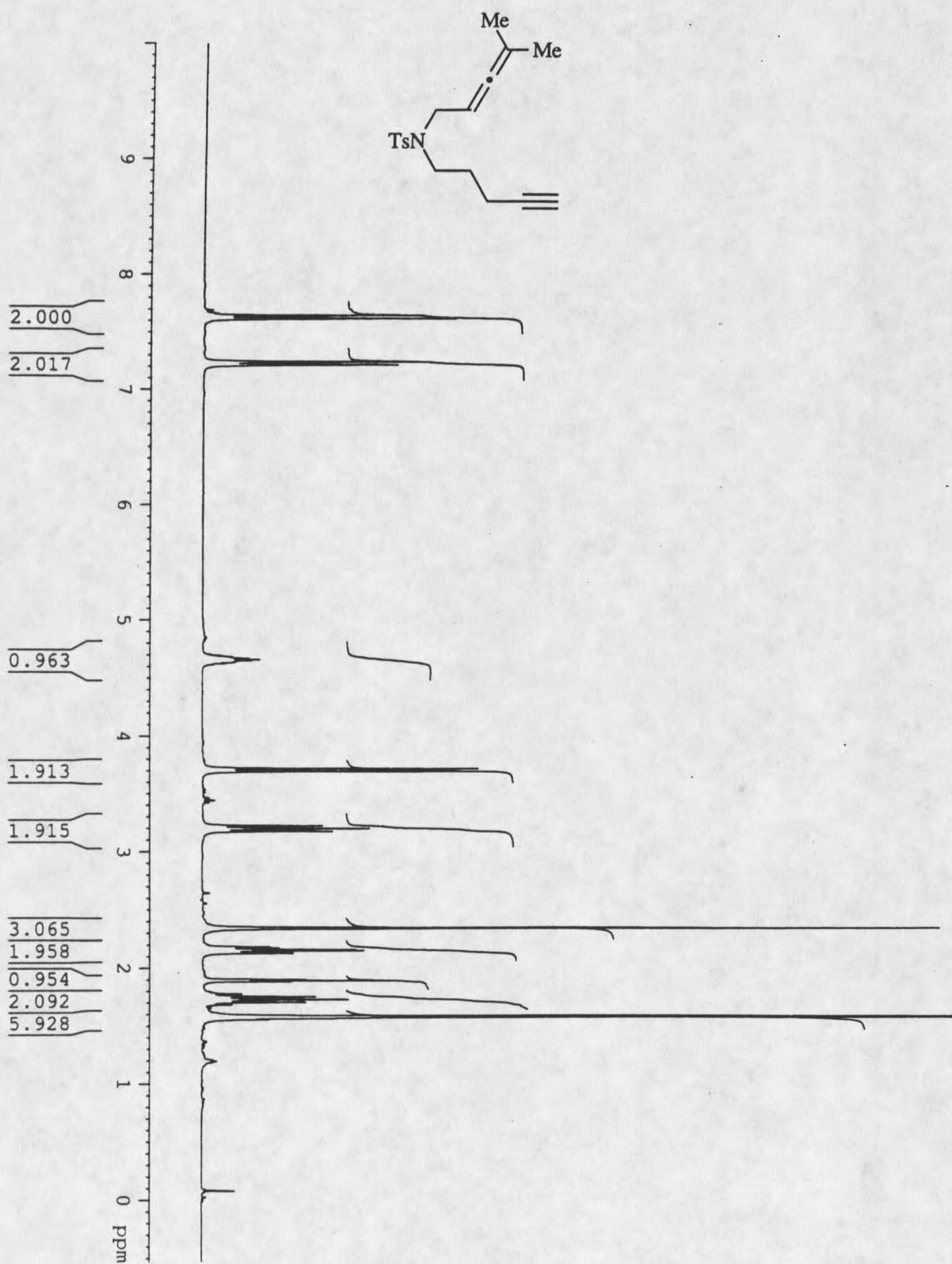
¹H NMR Spectrum of 122

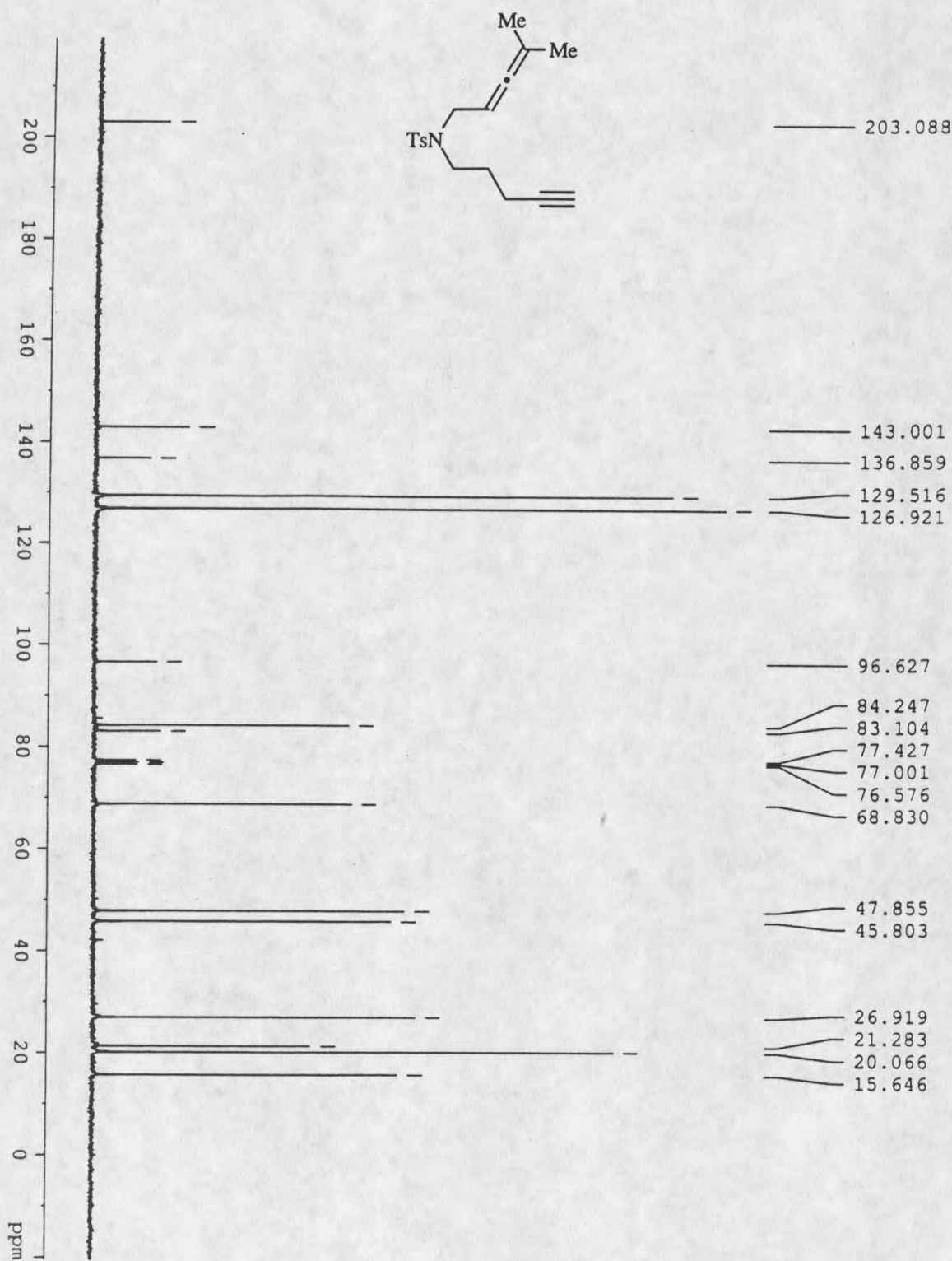
¹H NMR Spectrum of 139

¹³C NMR Spectrum of 139

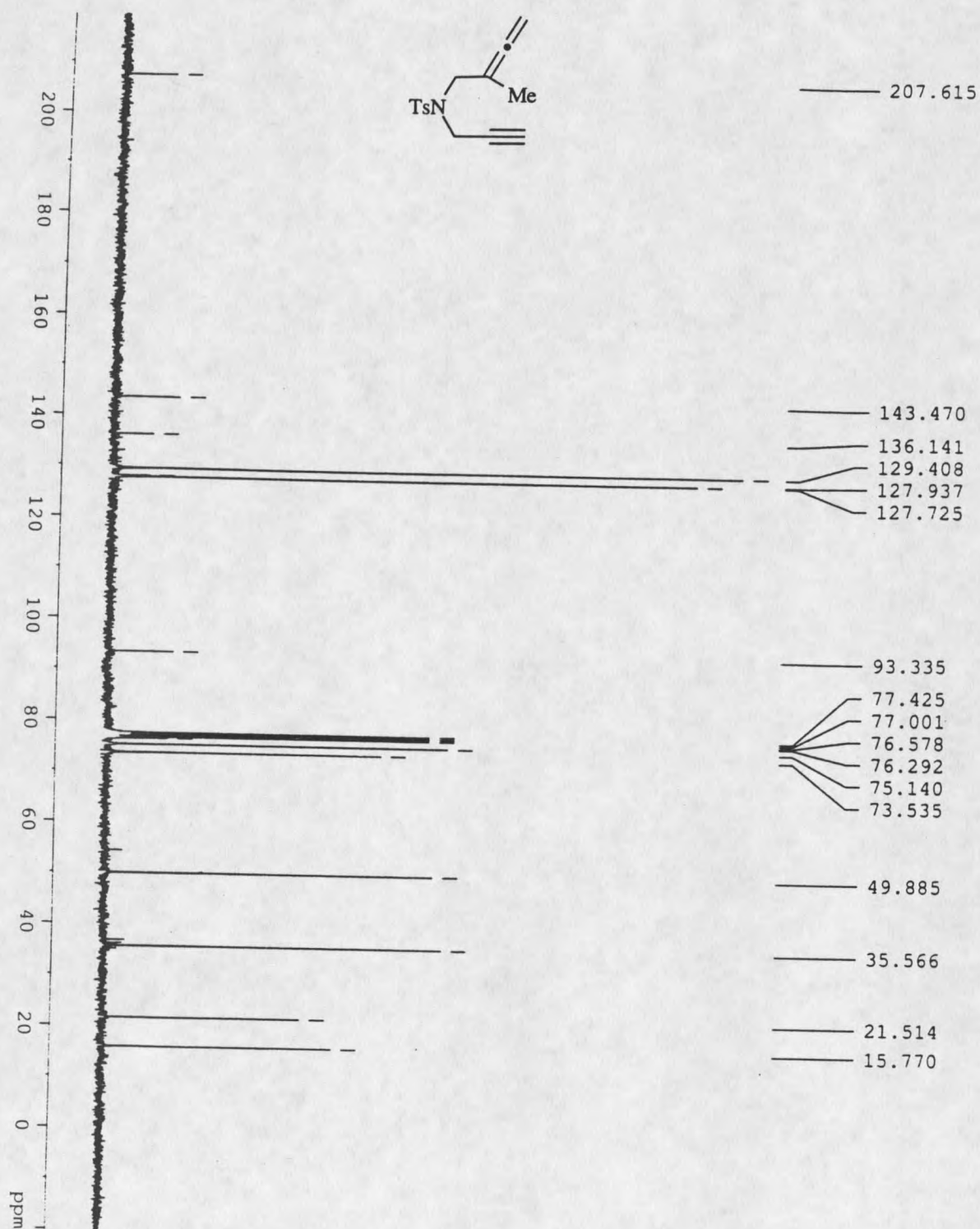
¹H NMR Spectrum of 128

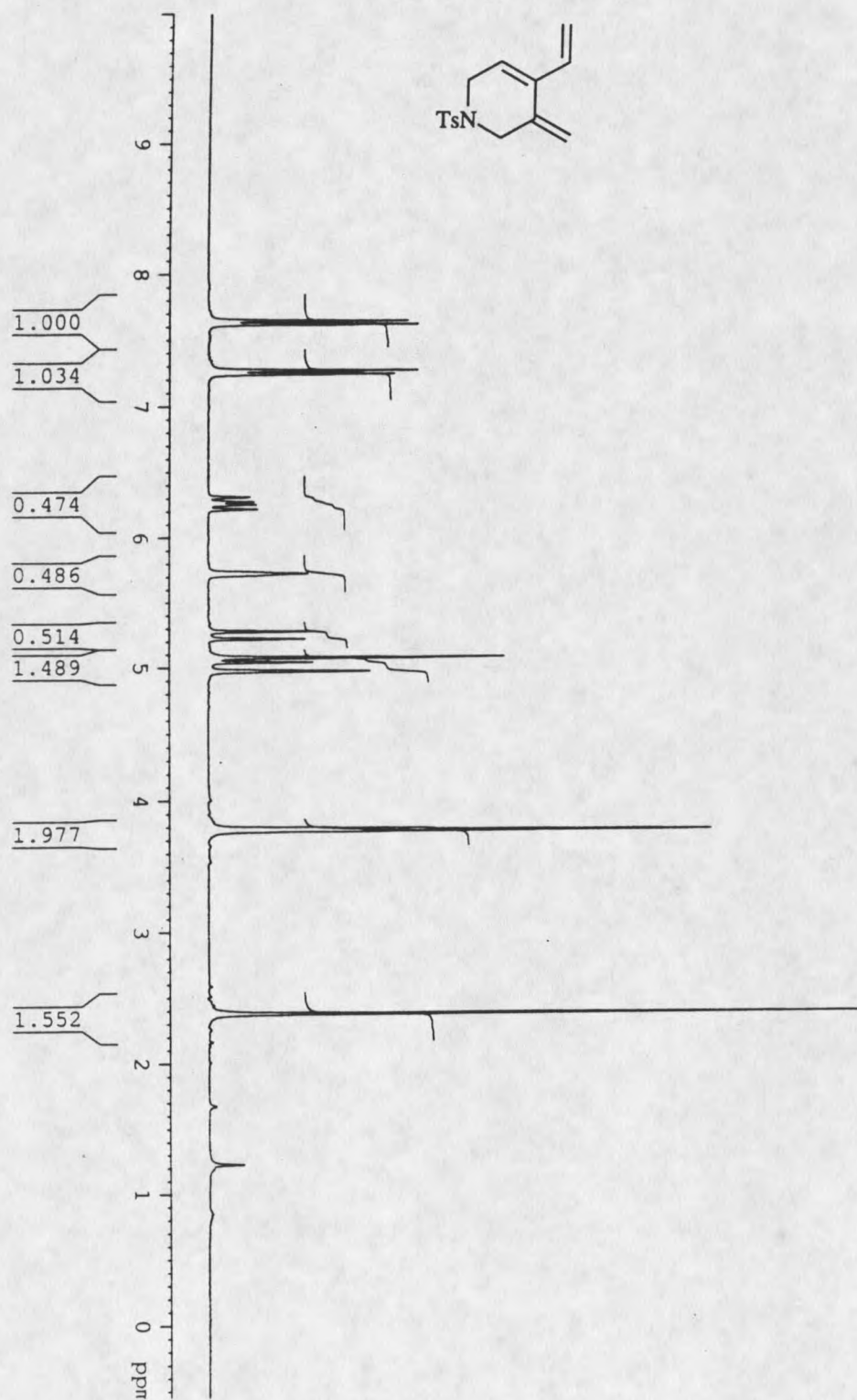
^{13}C NMR Spectrum of 128

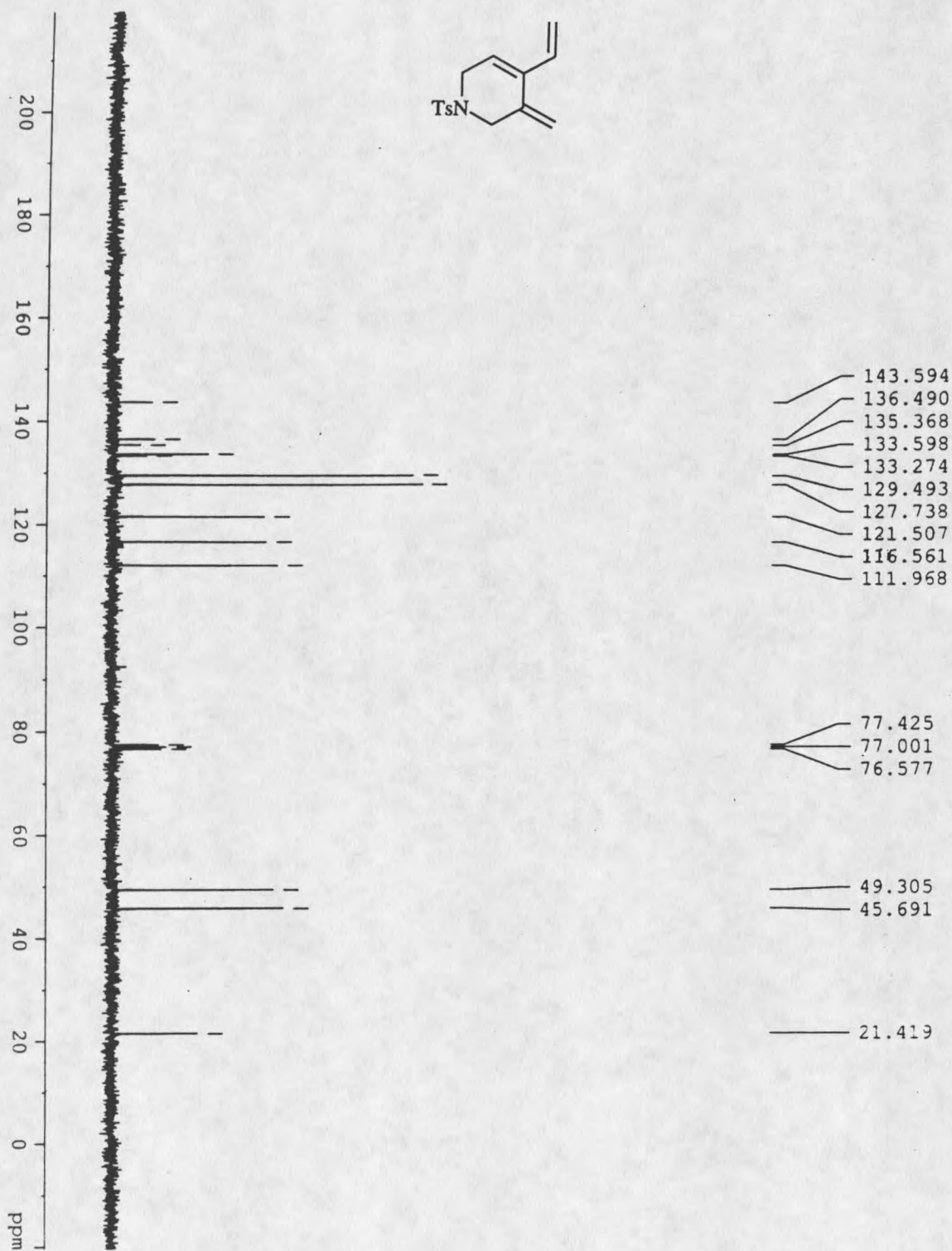
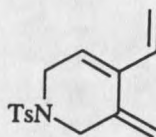
¹H NMR Spectrum of 165

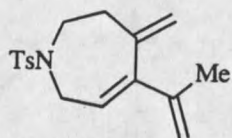
¹³C NMR Spectrum of 165

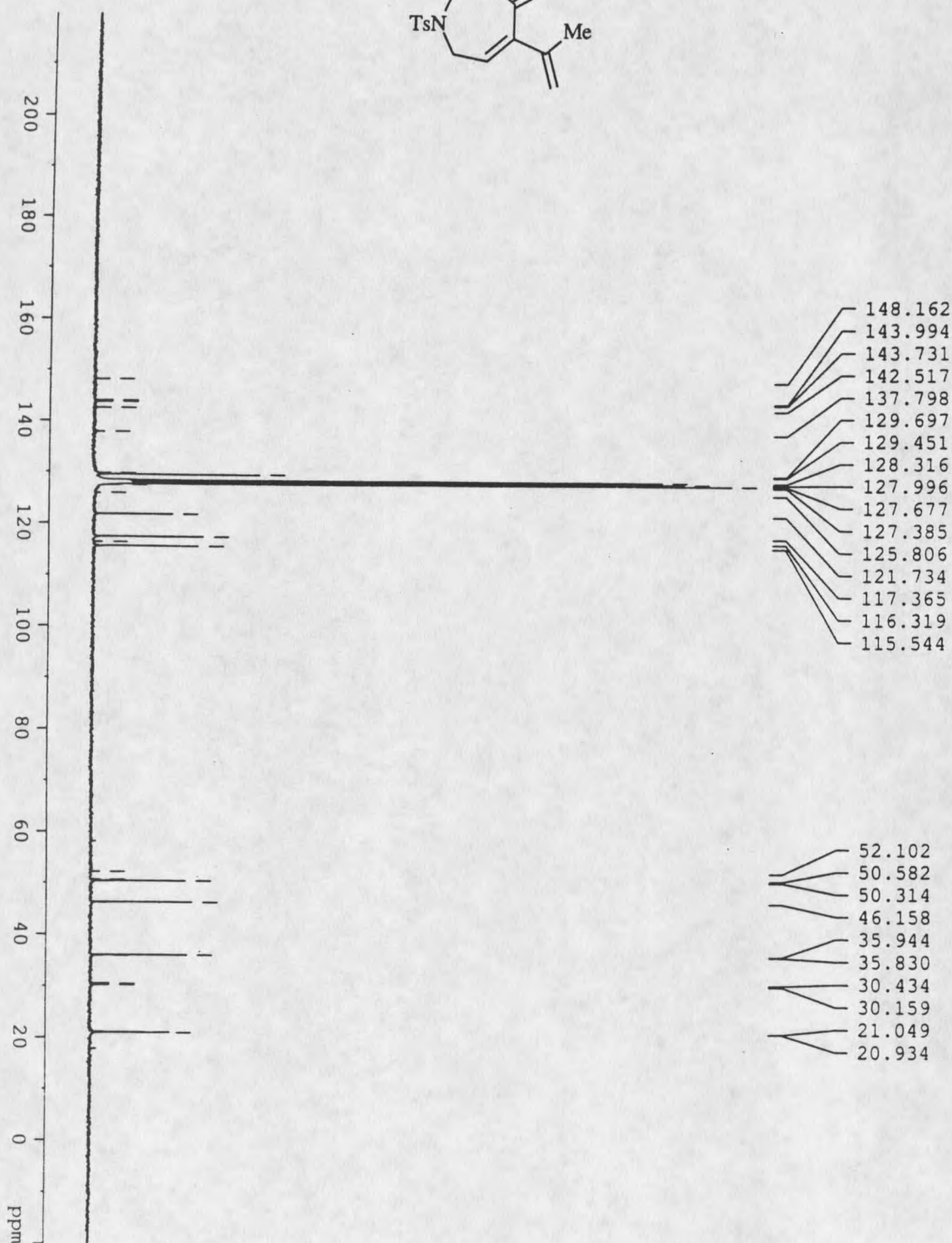
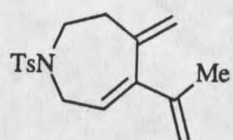
¹H NMR Spectrum of 132

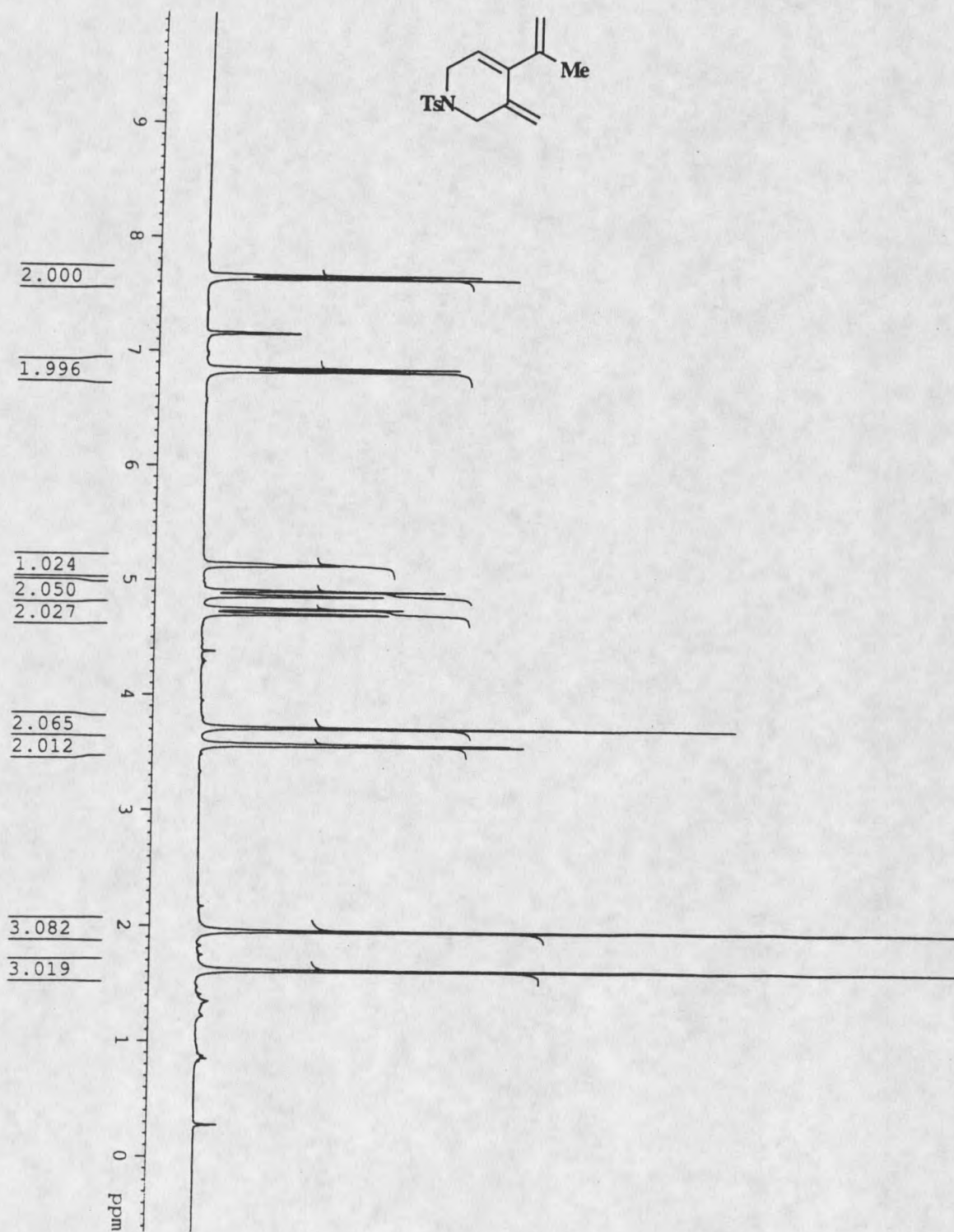
¹³C NMR Spectrum of 132

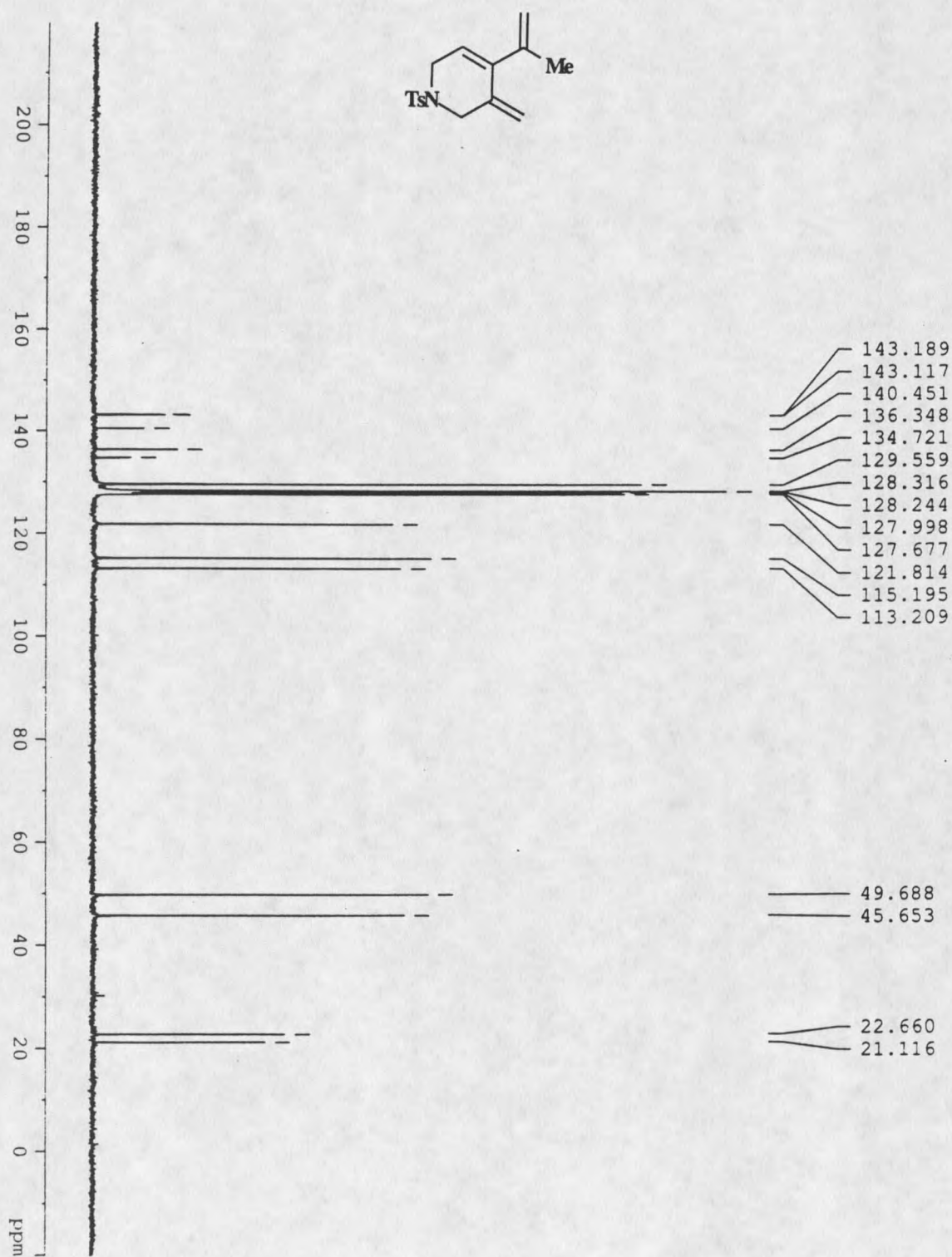
¹H NMR Spectrum of 159

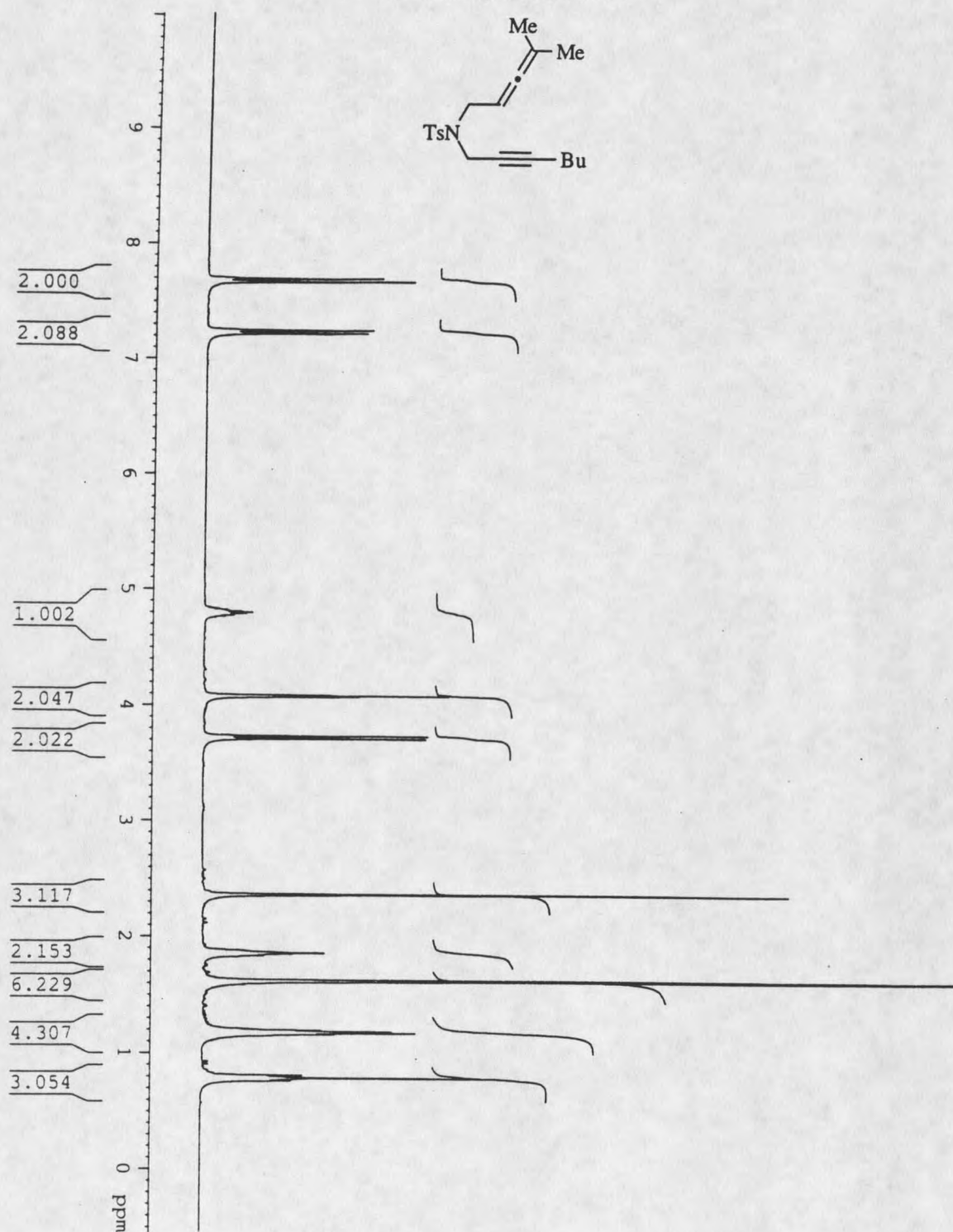
¹³C NMR Spectrum of 159

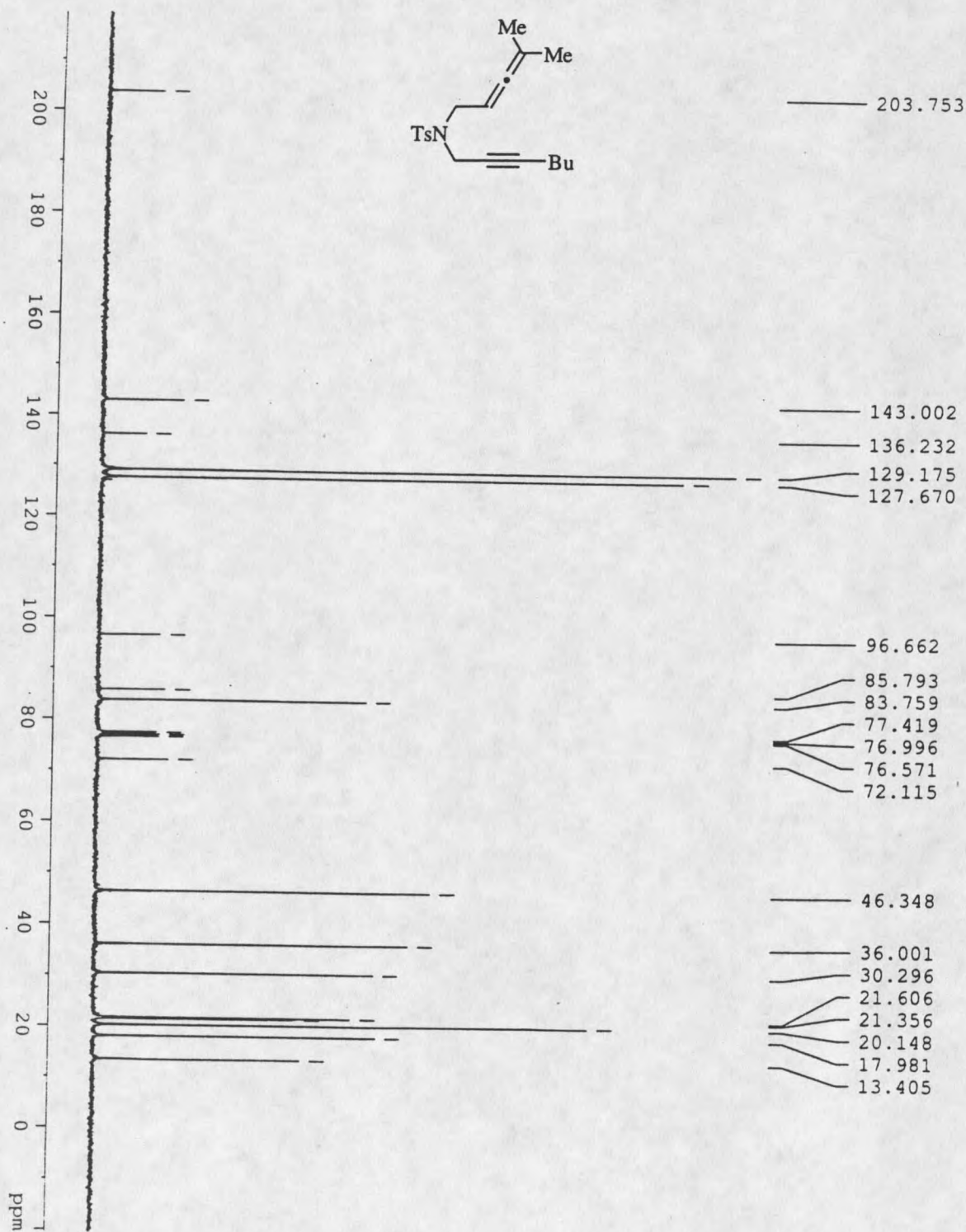
¹H NMR Spectrum of 161

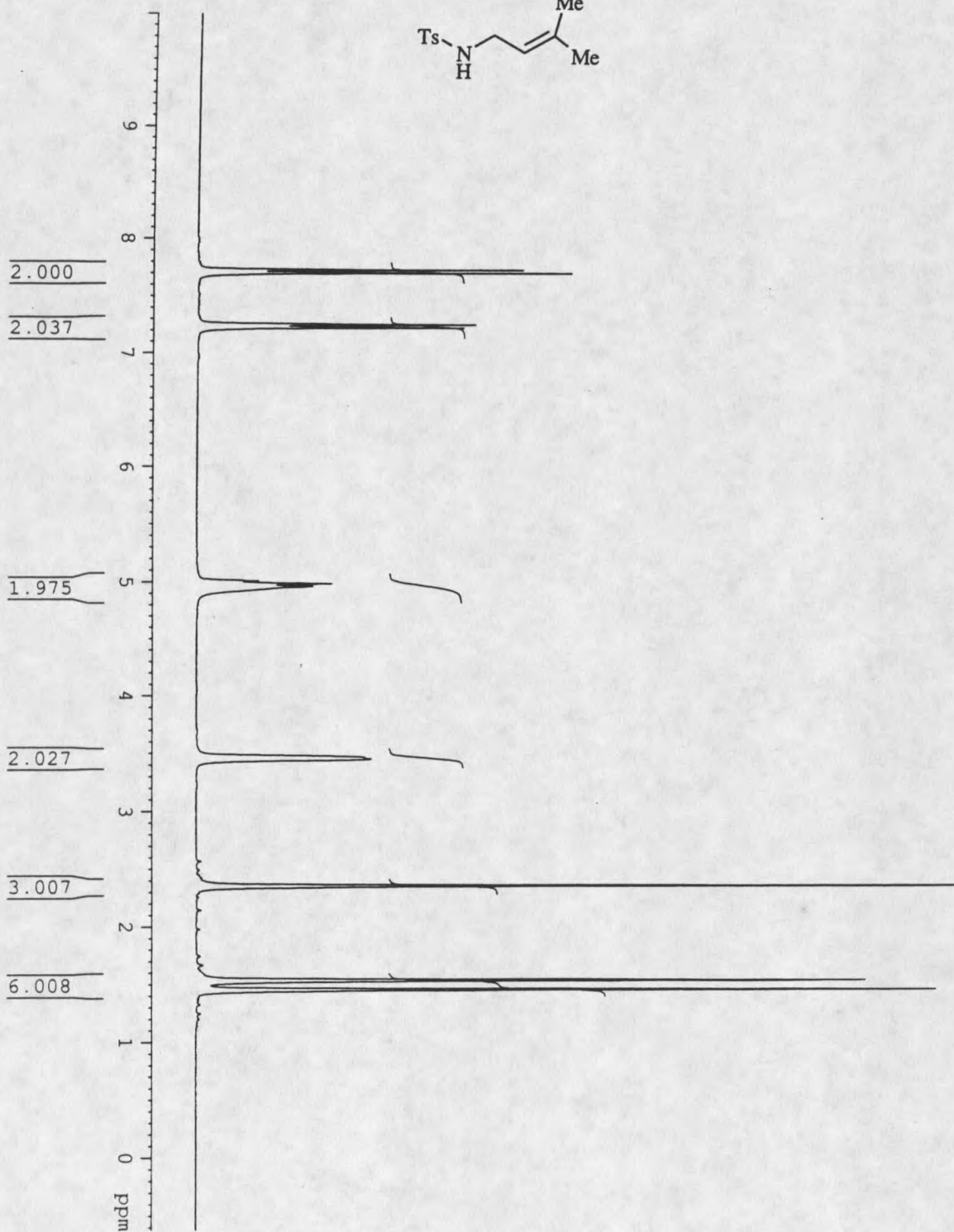
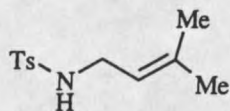
¹³C NMR Spectrum of 161

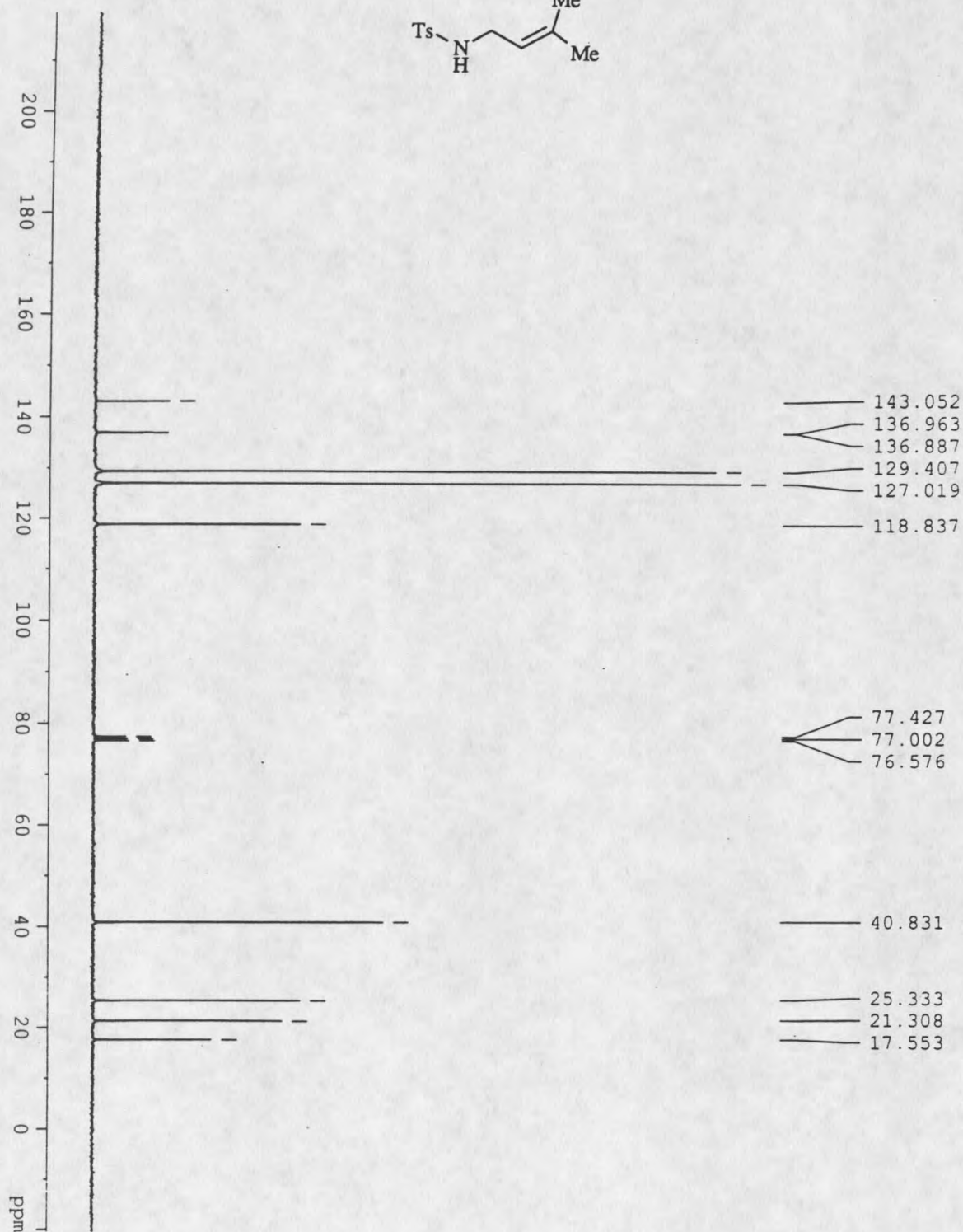
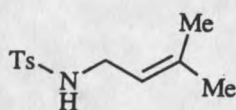
¹H NMR Spectrum of 160

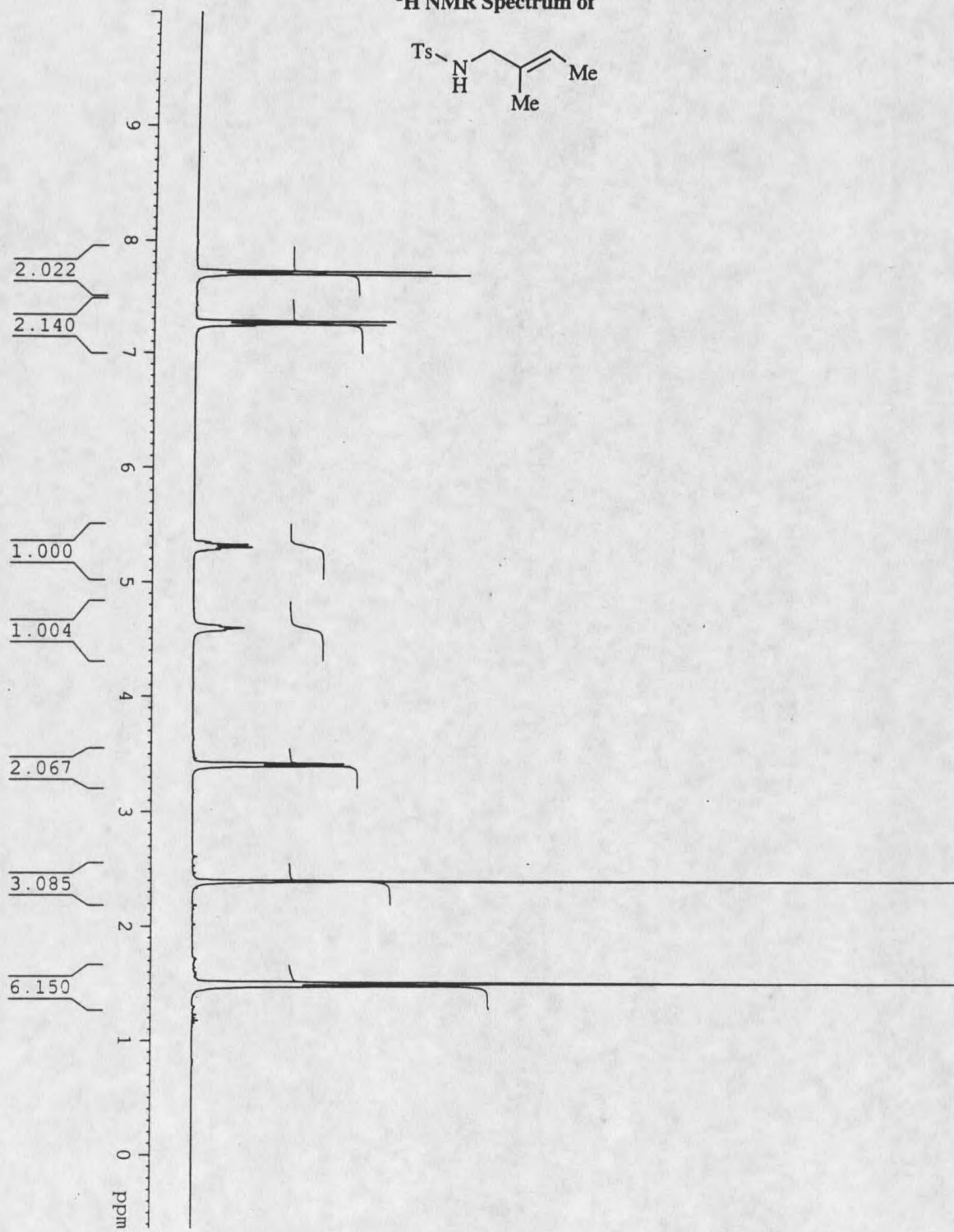
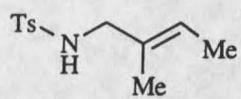
^{13}C NMR Spectrum of 160

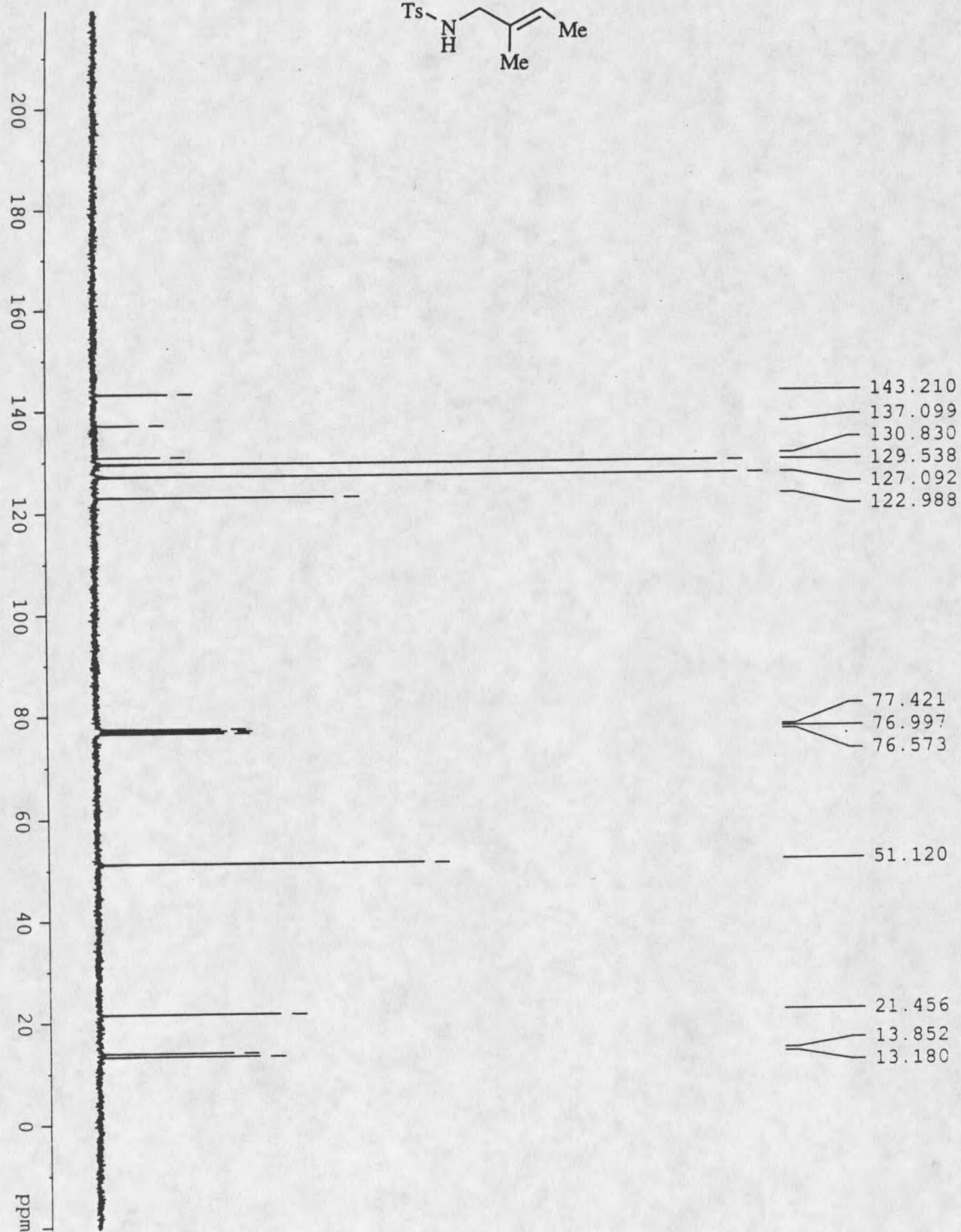
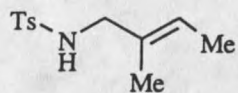
¹H NMR Spectrum of 151

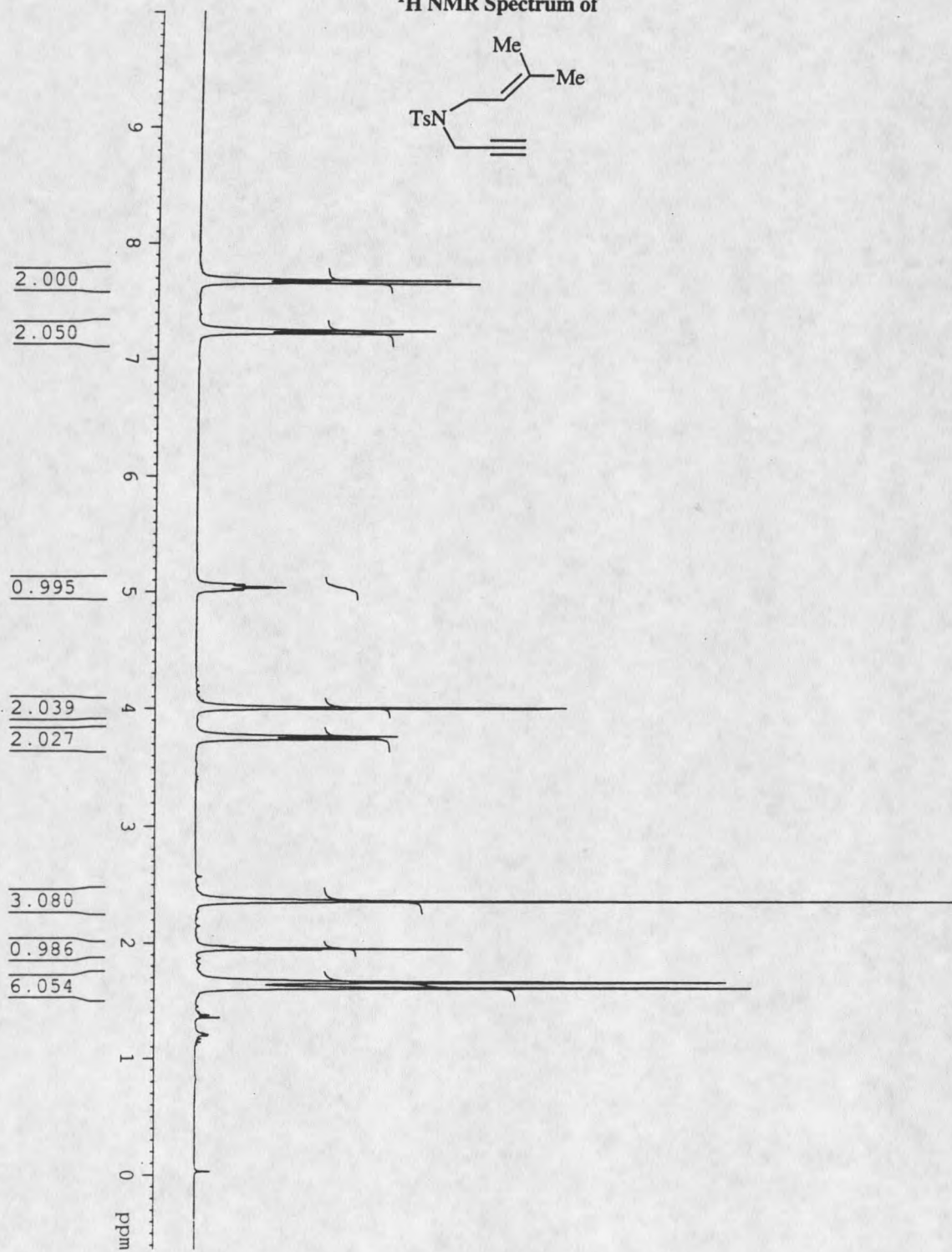
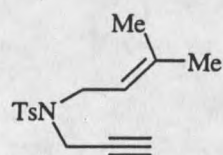
¹³C NMR Spectrum of 151

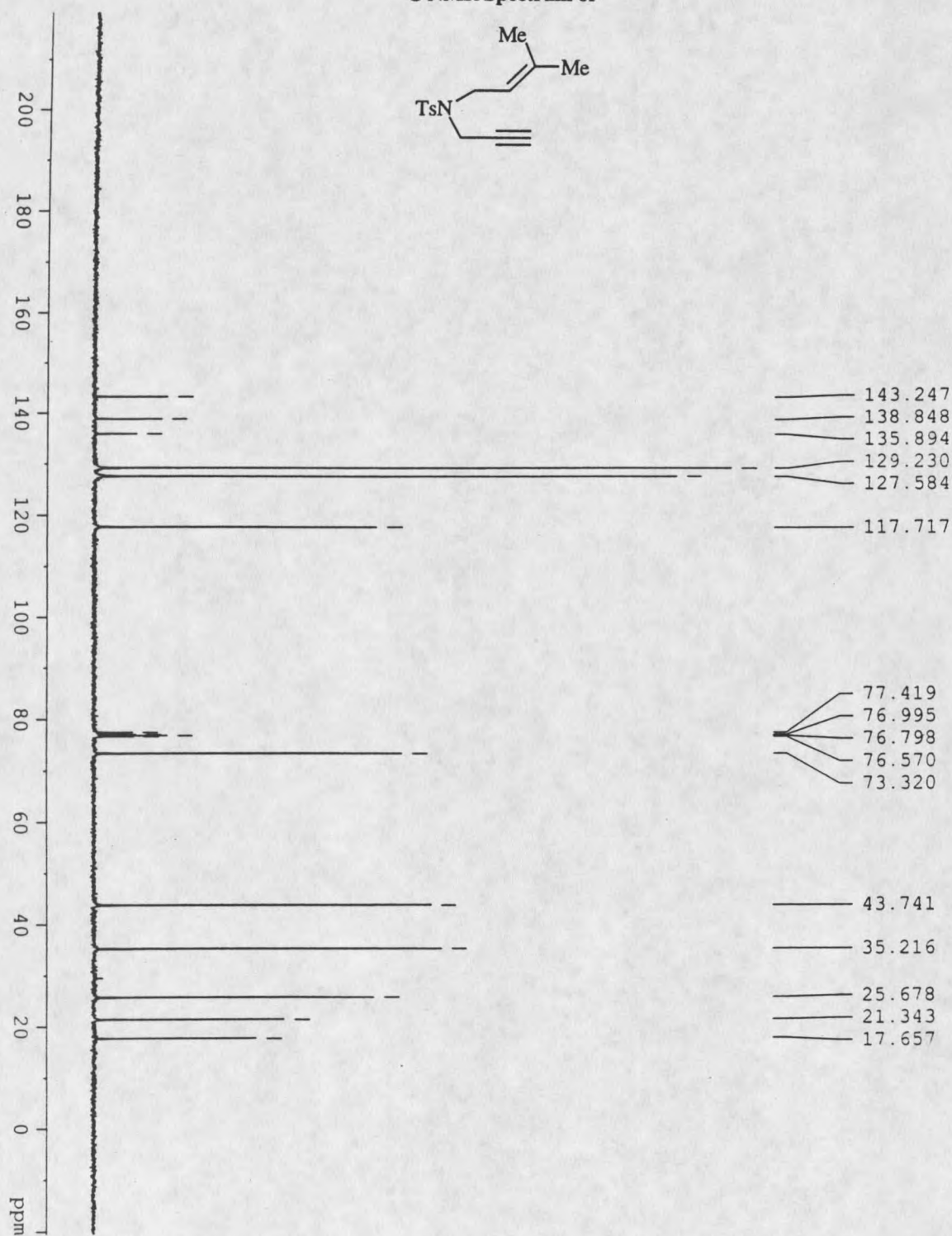
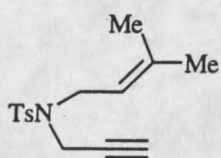
¹H NMR Spectrum of

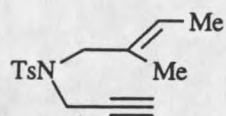
¹³C NMR Spectrum of

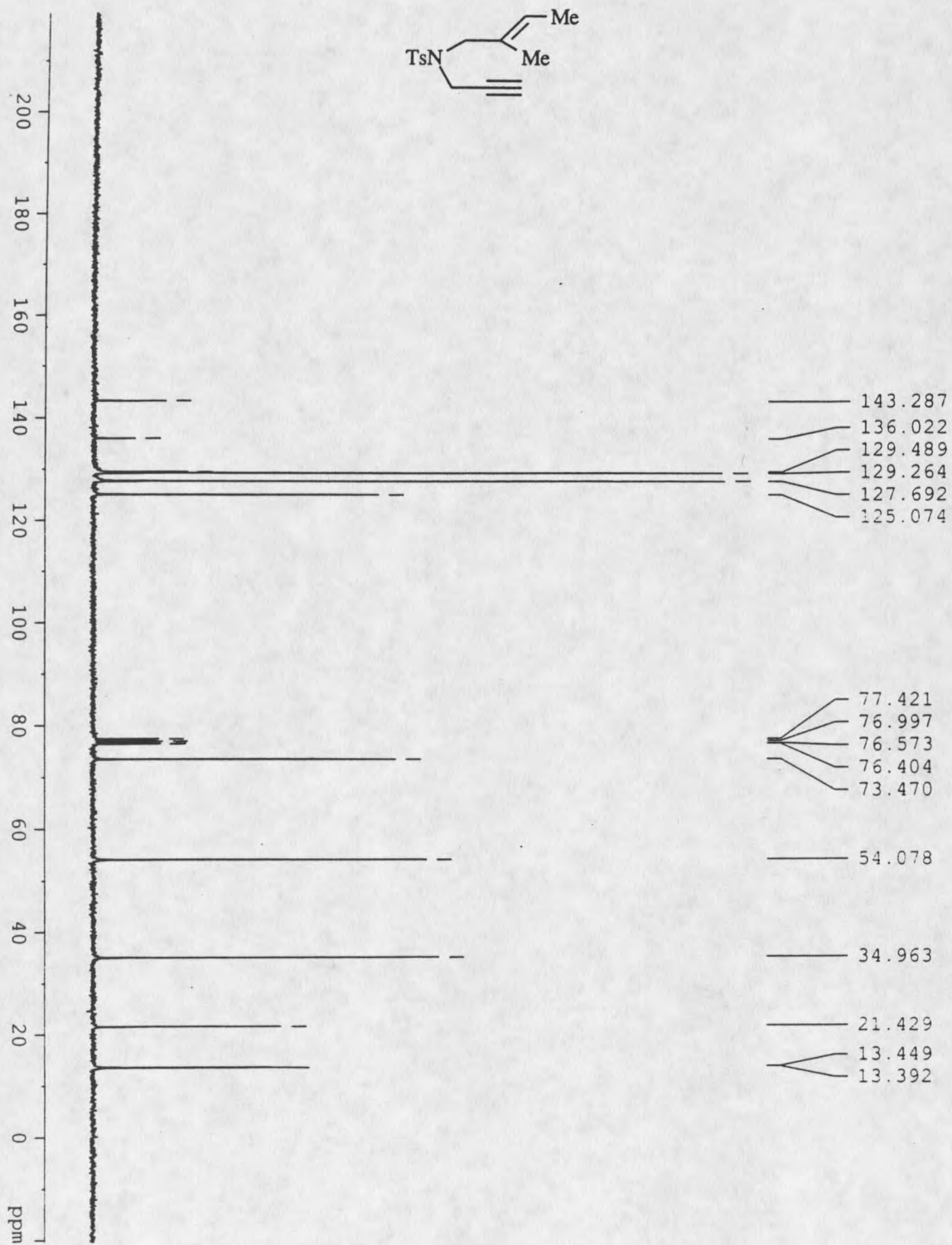
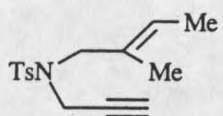
¹H NMR Spectrum of

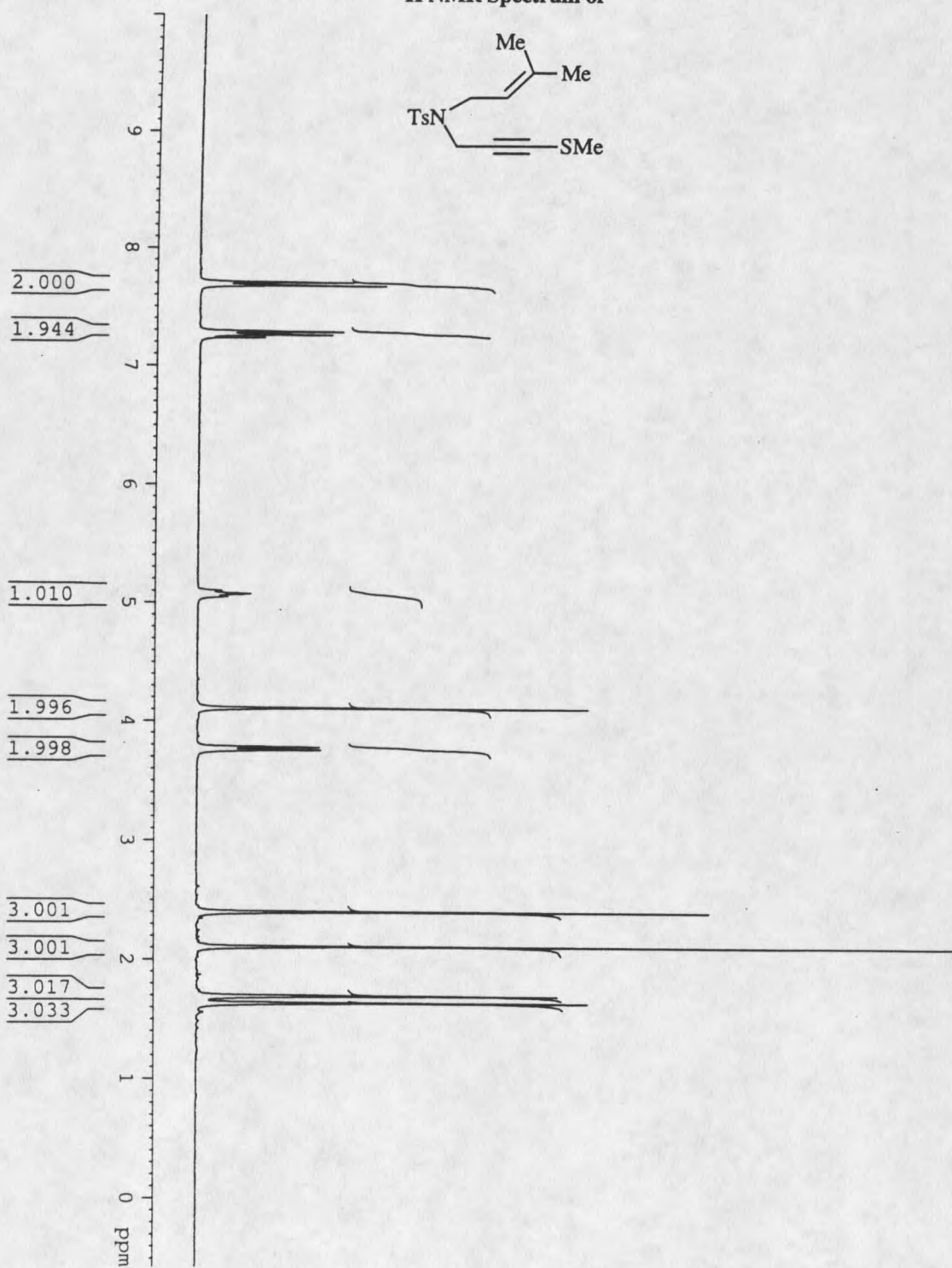
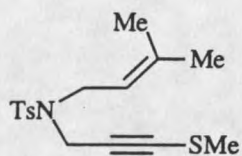
¹³C NMR Spectrum of

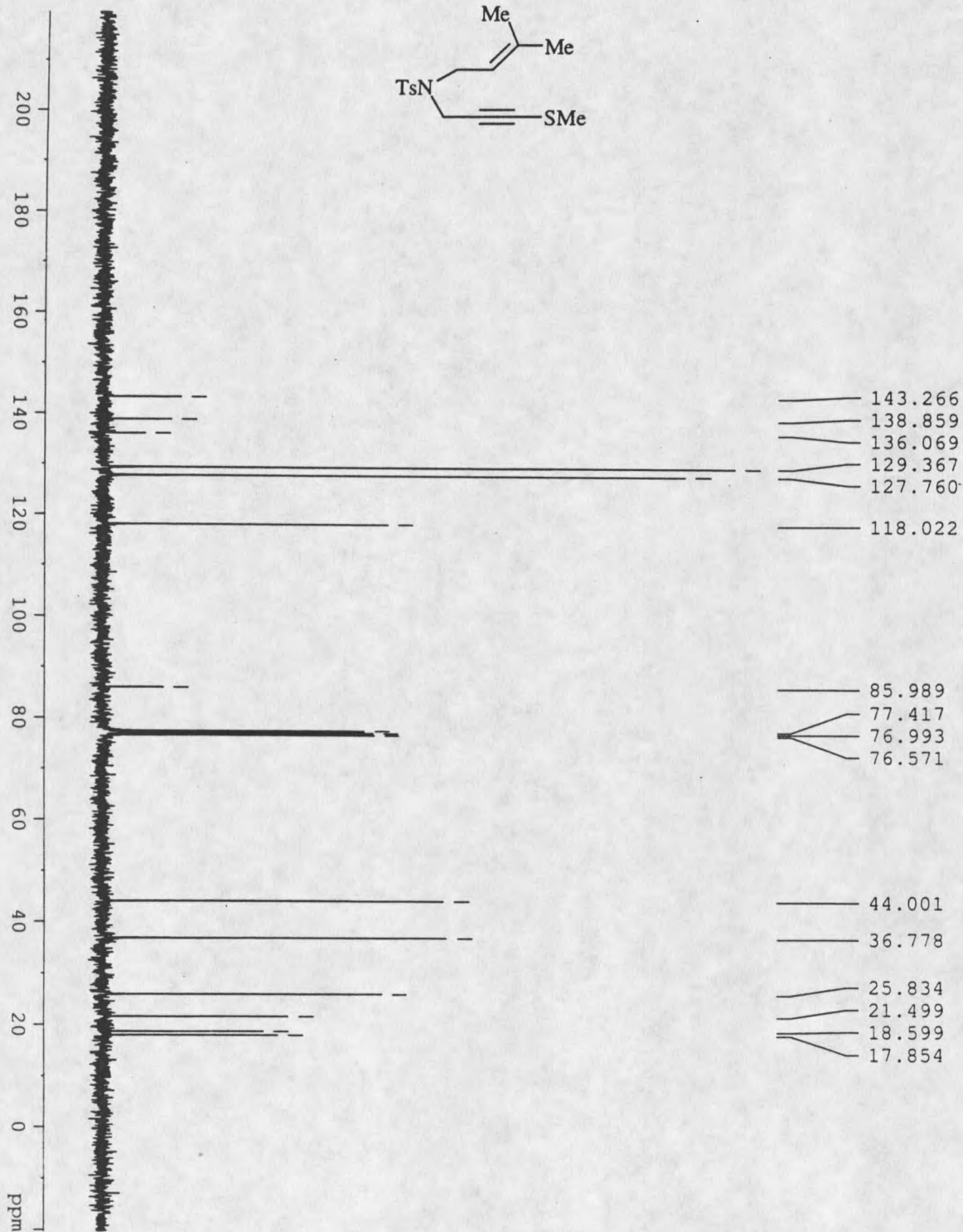
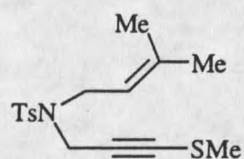
¹H NMR Spectrum of

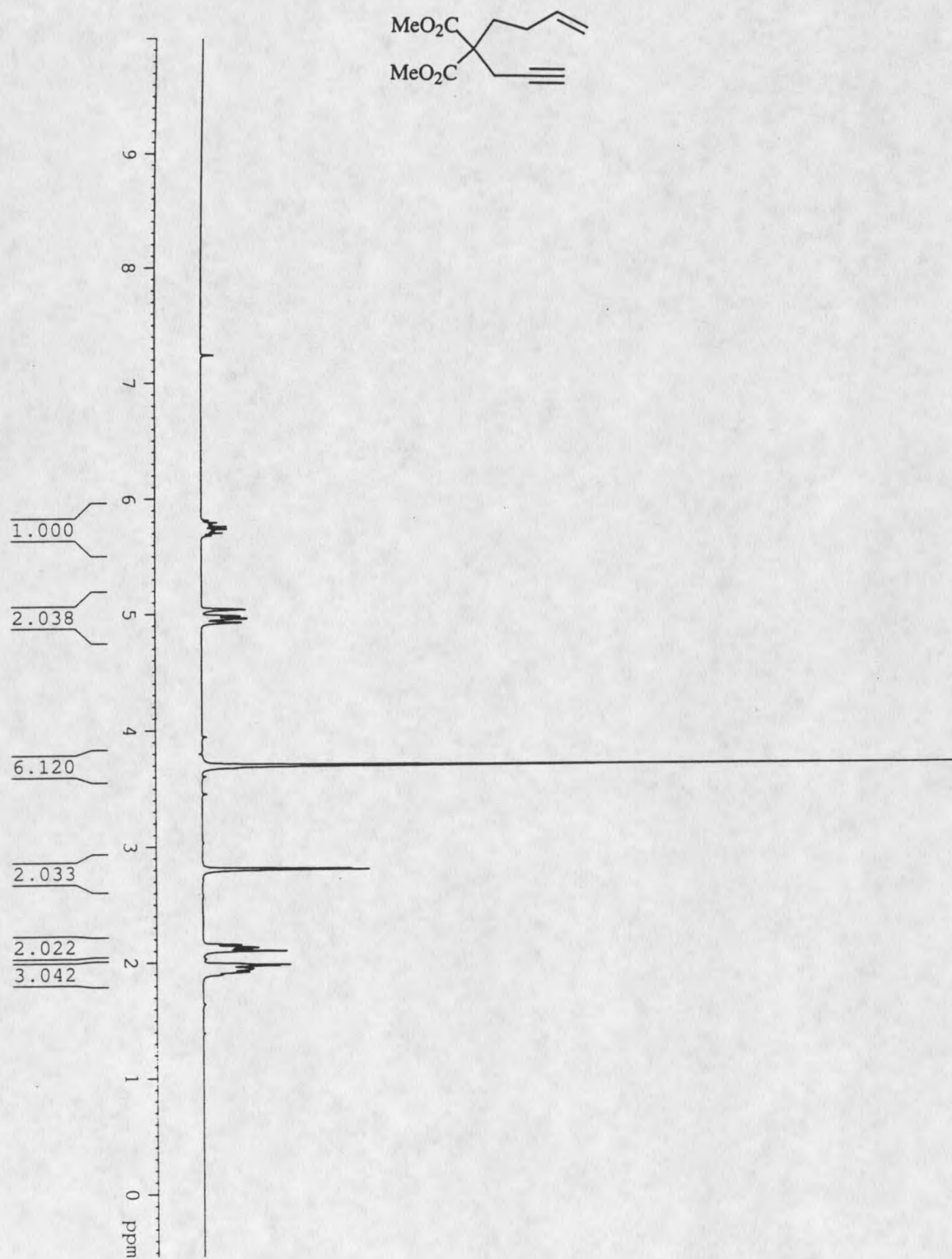
¹³C NMR Spectrum of

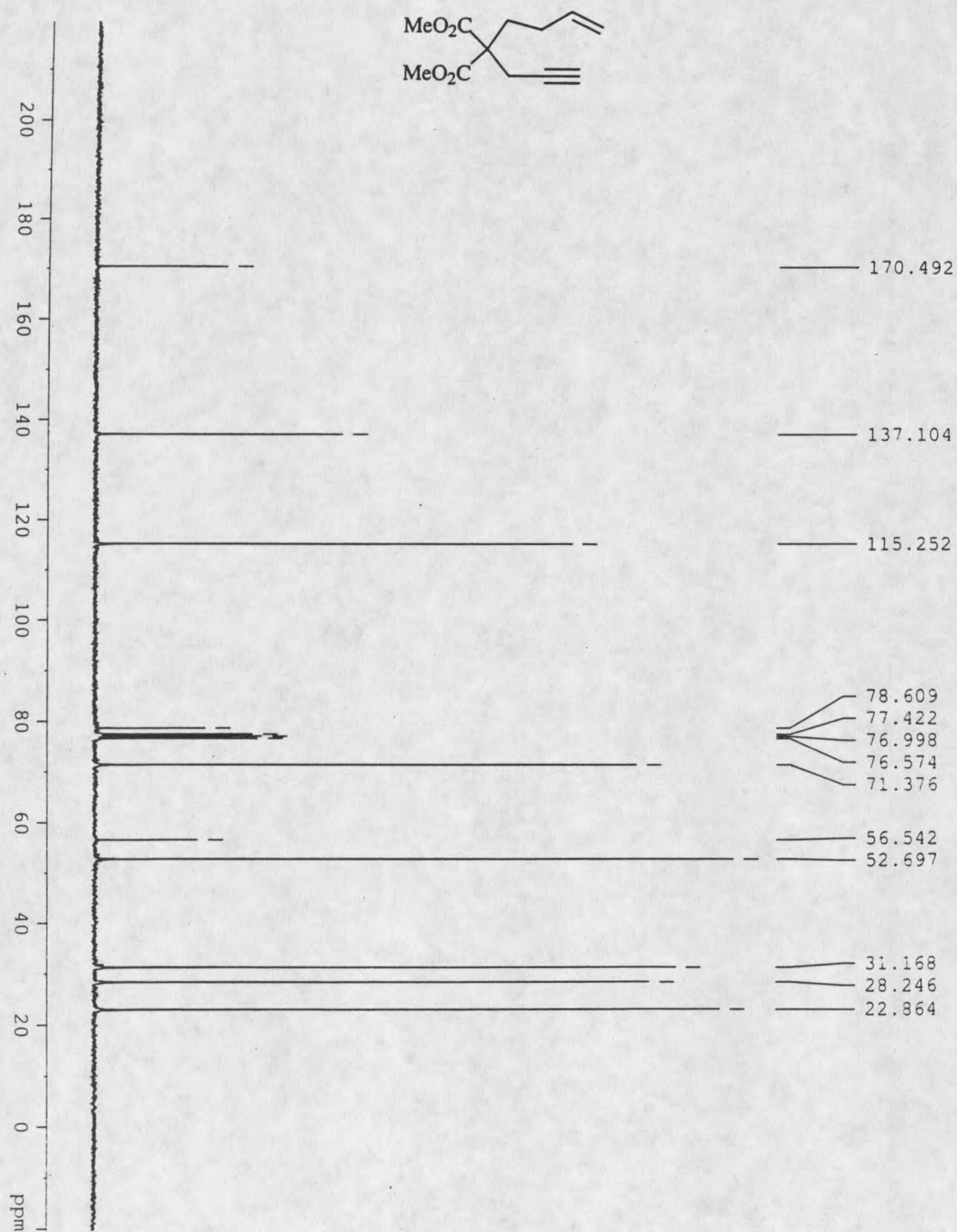
¹H NMR Spectrum of

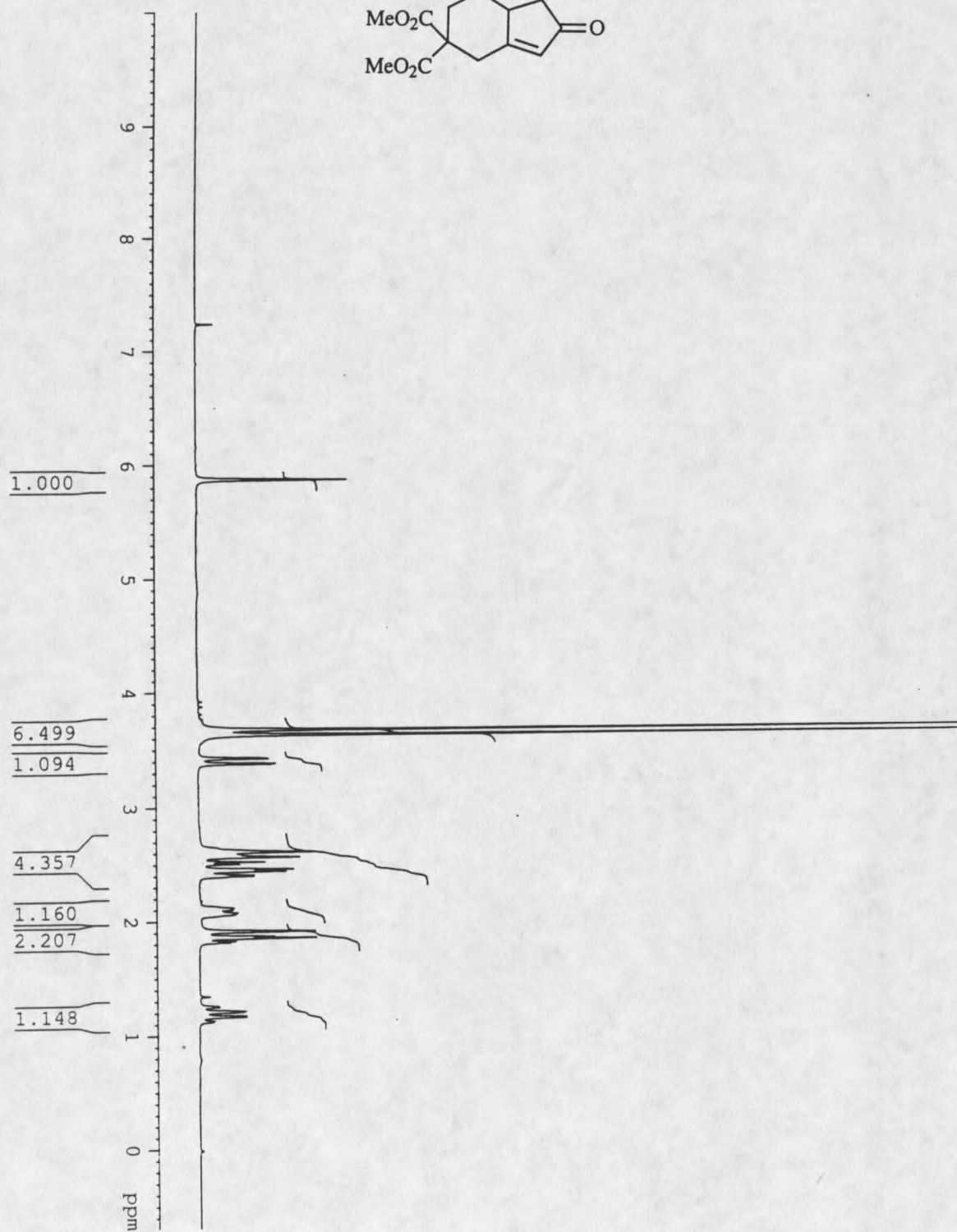
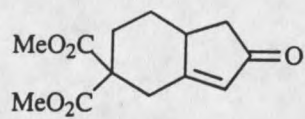
¹³C NMR Spectrum of

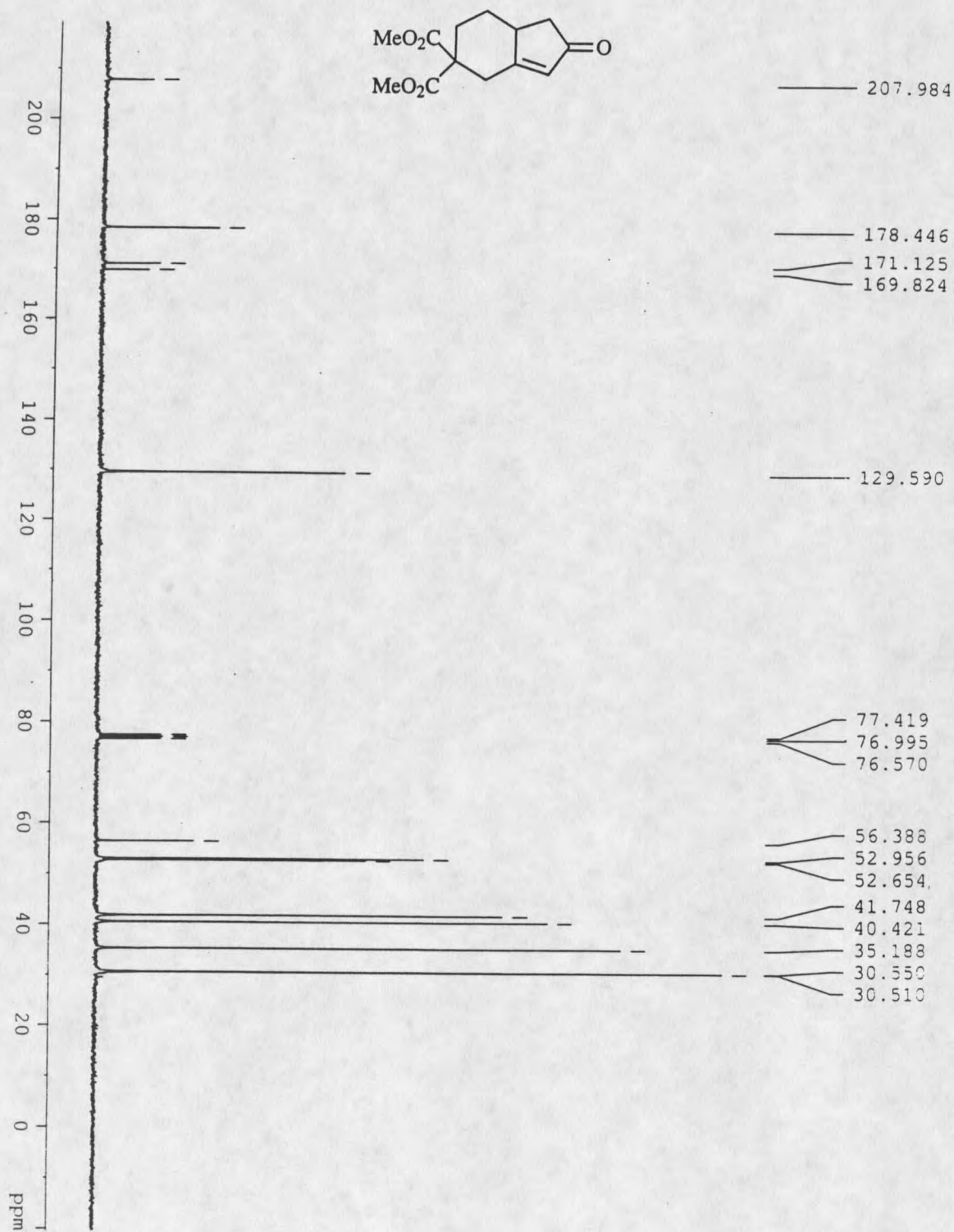
¹H NMR Spectrum of

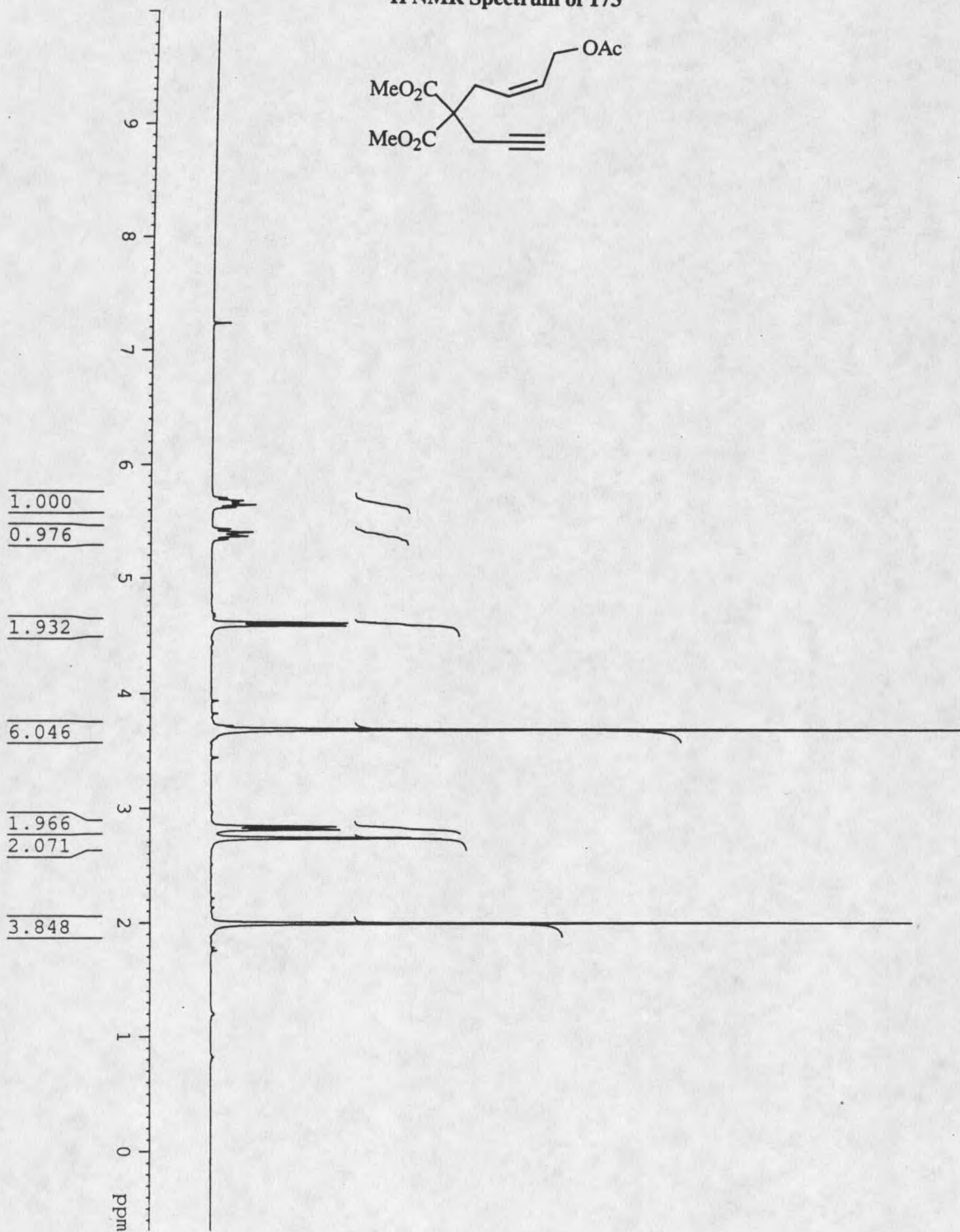
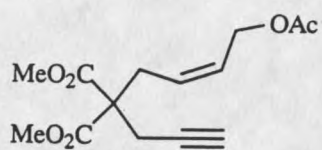
¹³C NMR Spectrum of

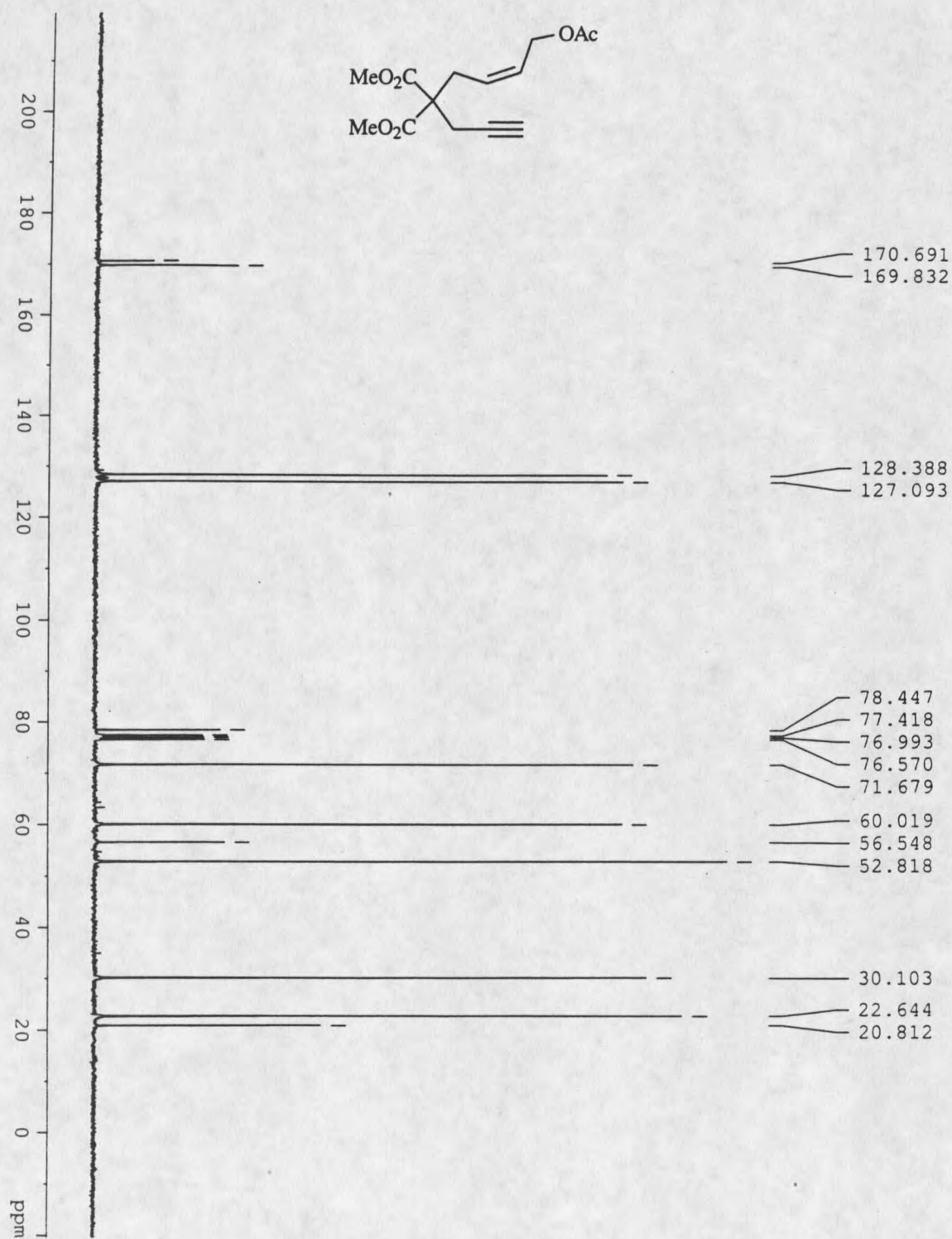
¹H NMR Spectrum of 171

¹³C NMR Spectrum of 171

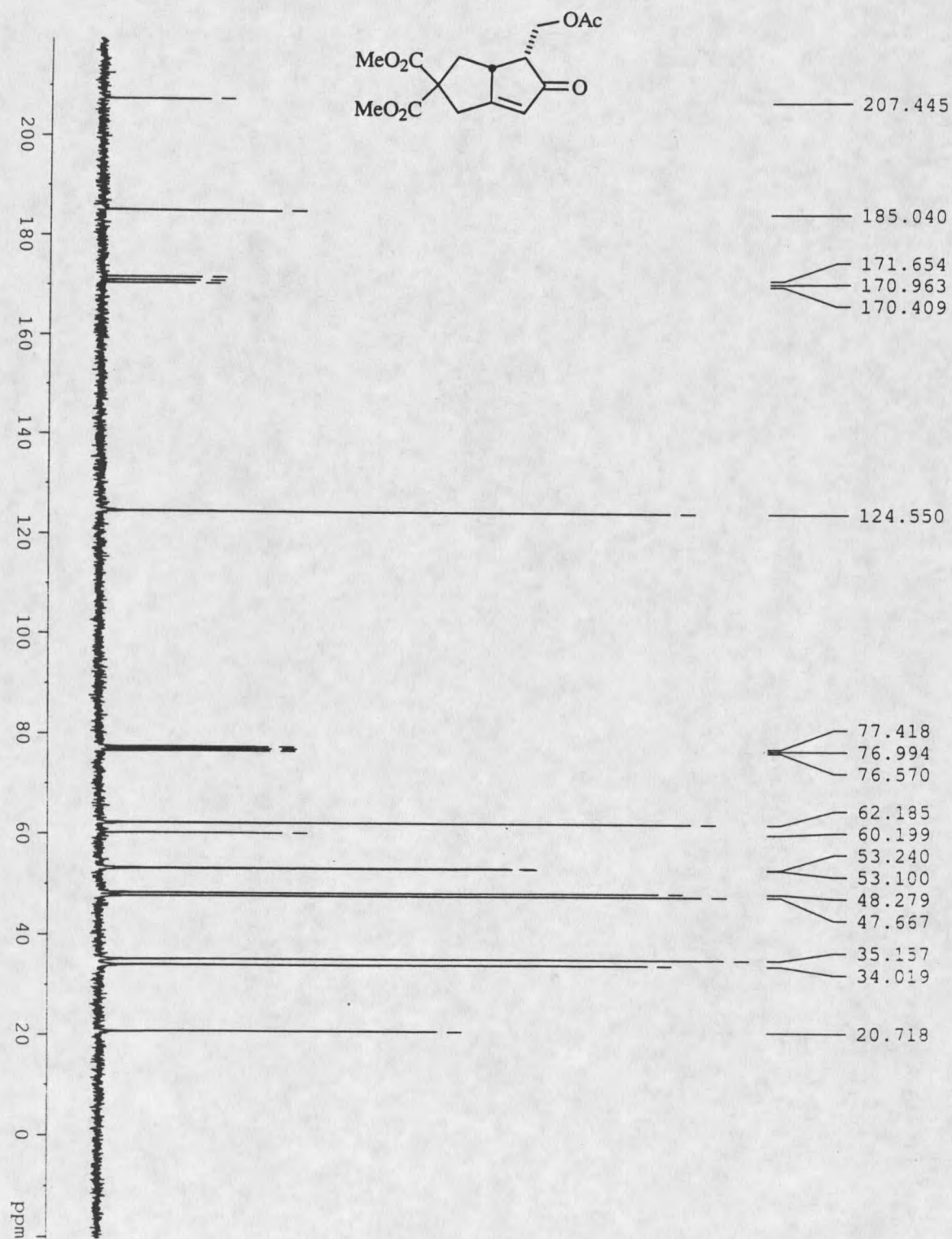
¹H NMR Spectrum of 172

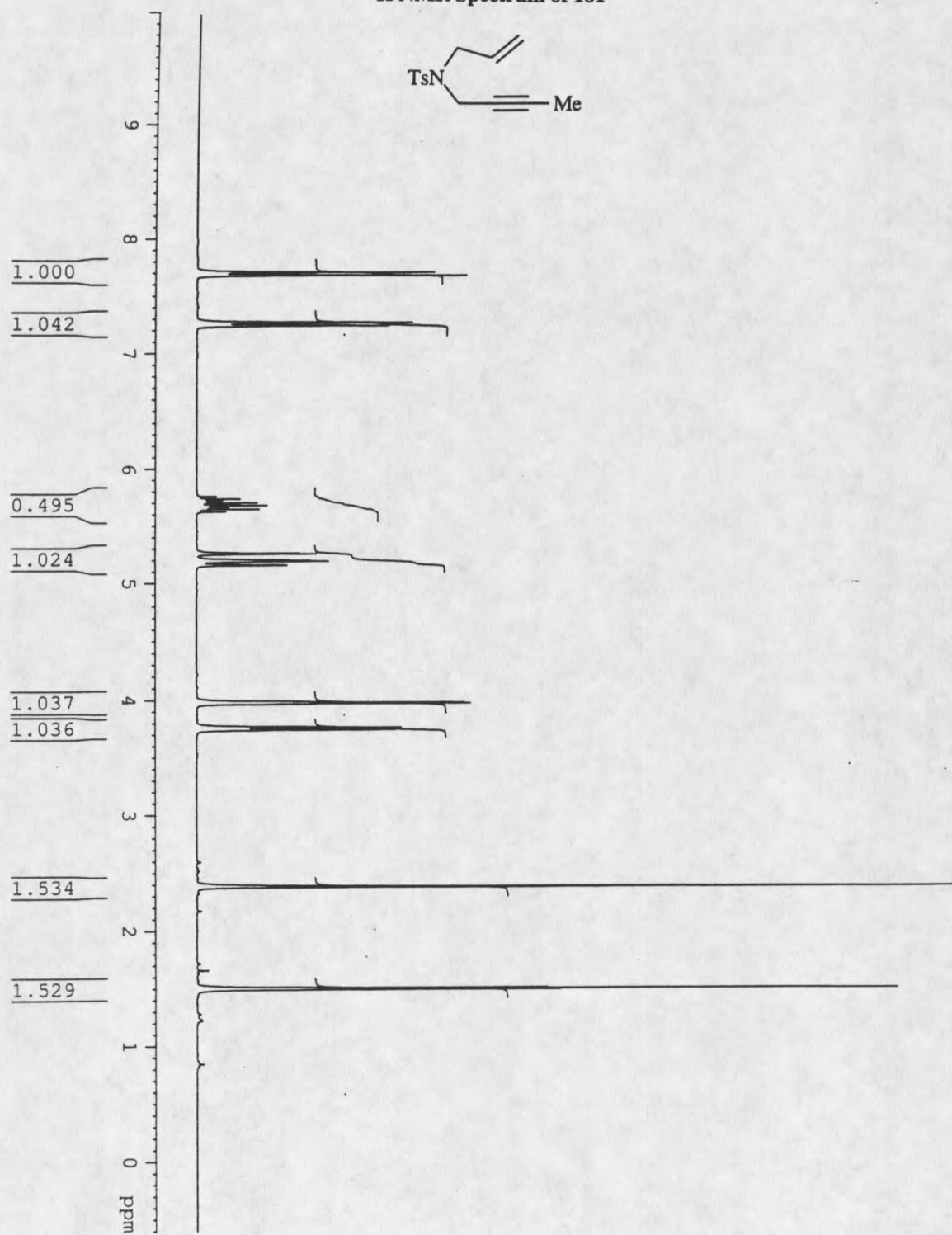
¹³C NMR Spectrum of 172

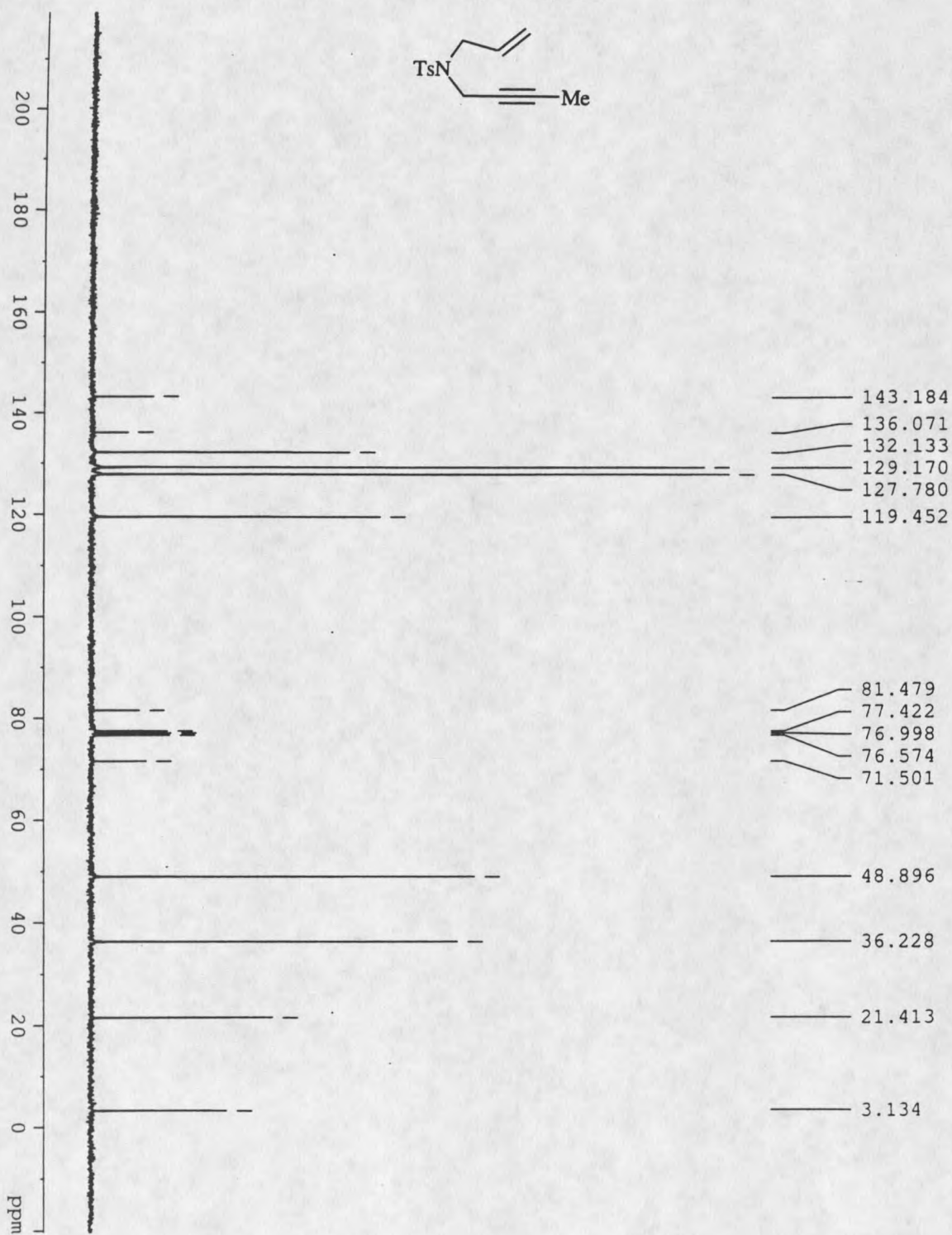
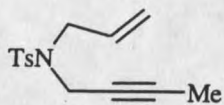
¹H NMR Spectrum of 173

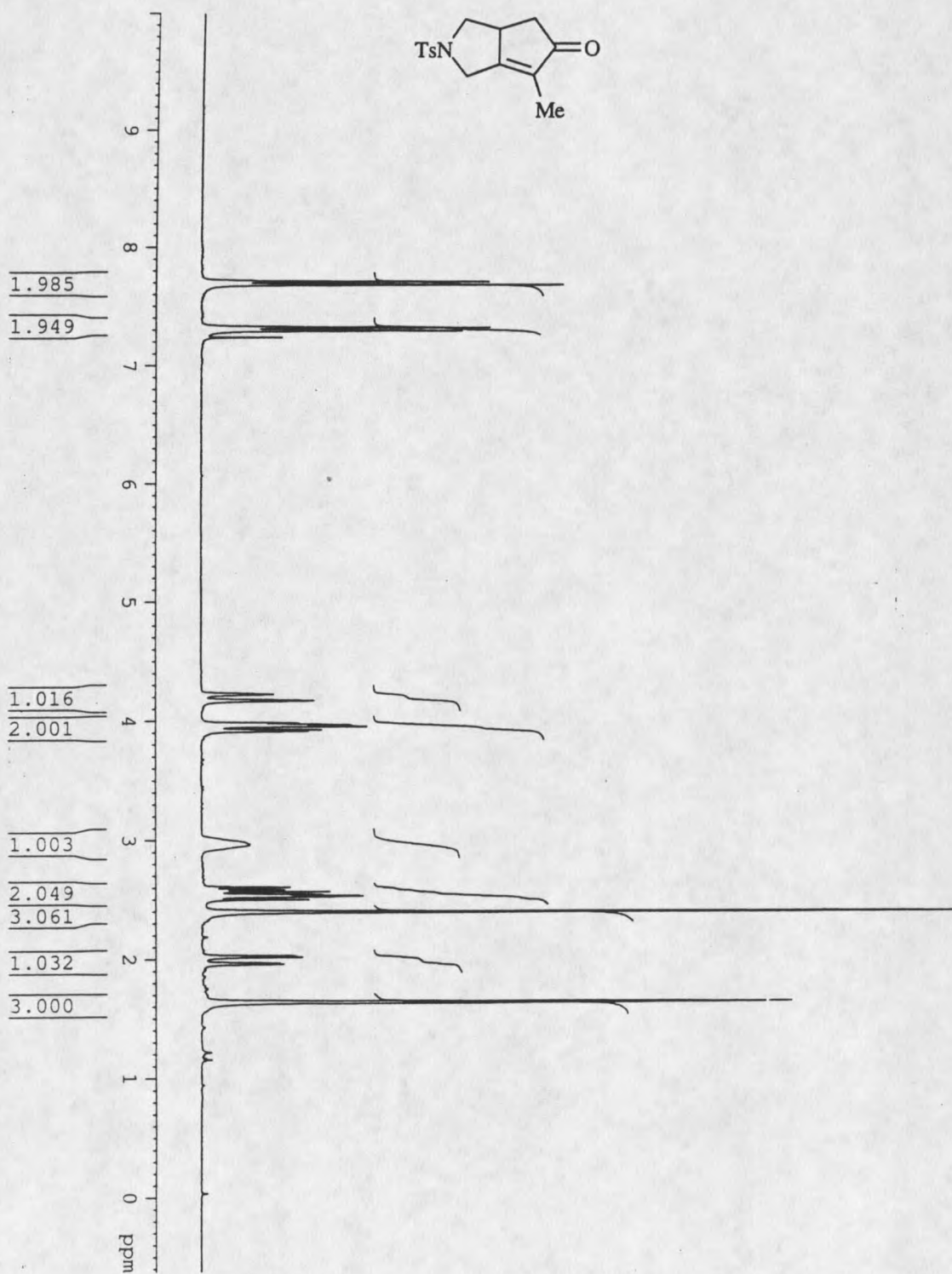
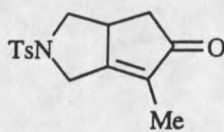
¹³C NMR Spectrum of 173

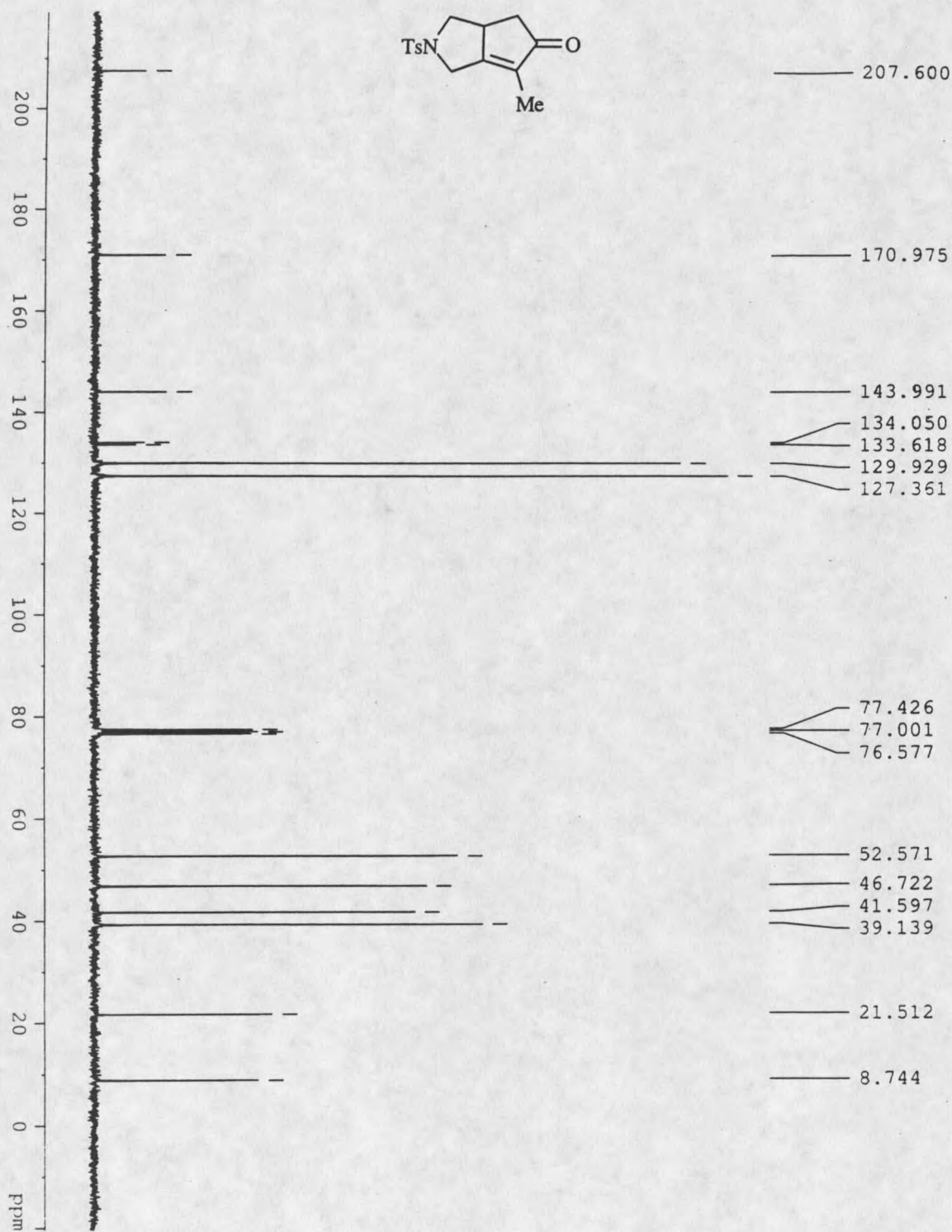
¹H NMR Spectrum of 174

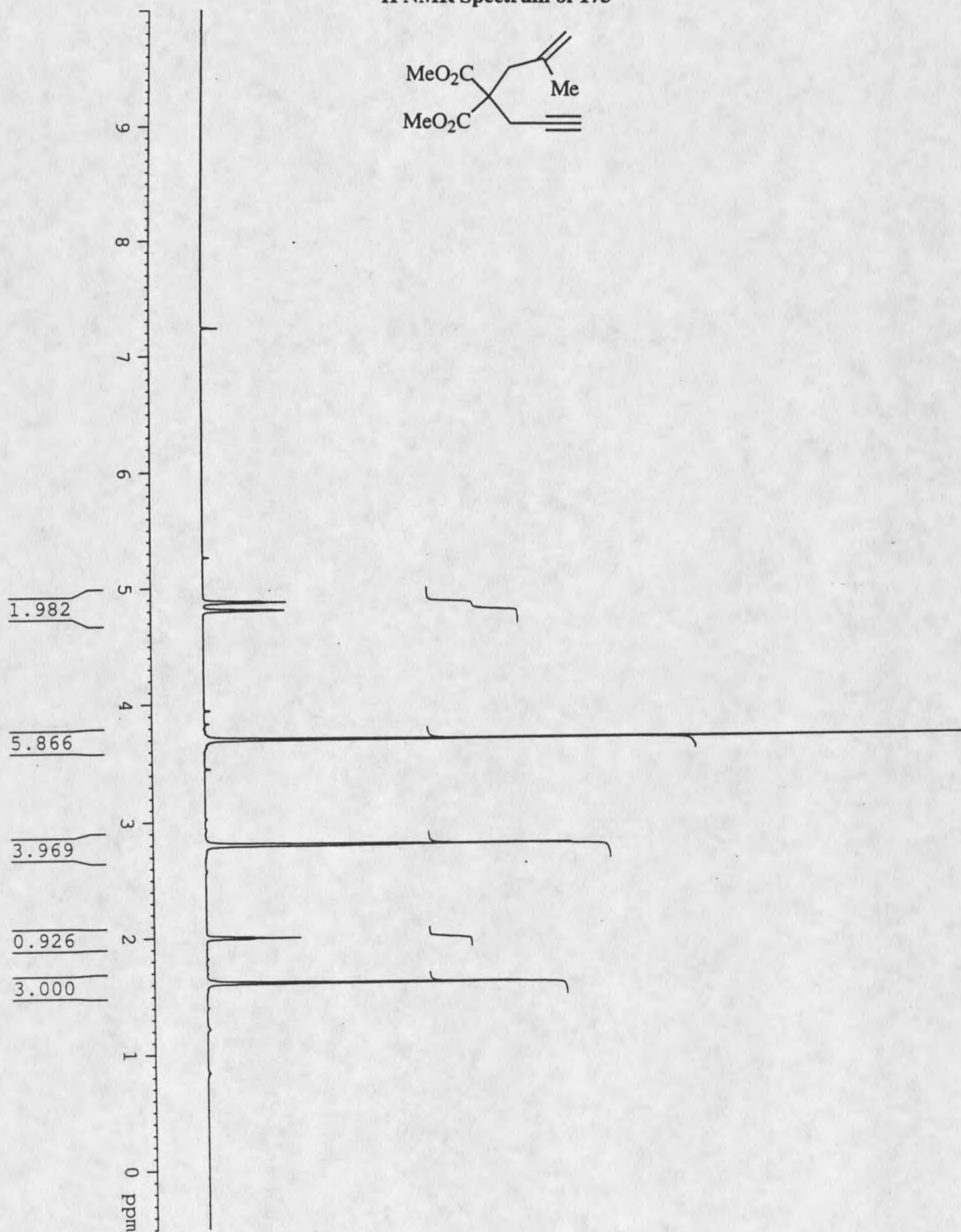
^{13}C NMR Spectrum of 174

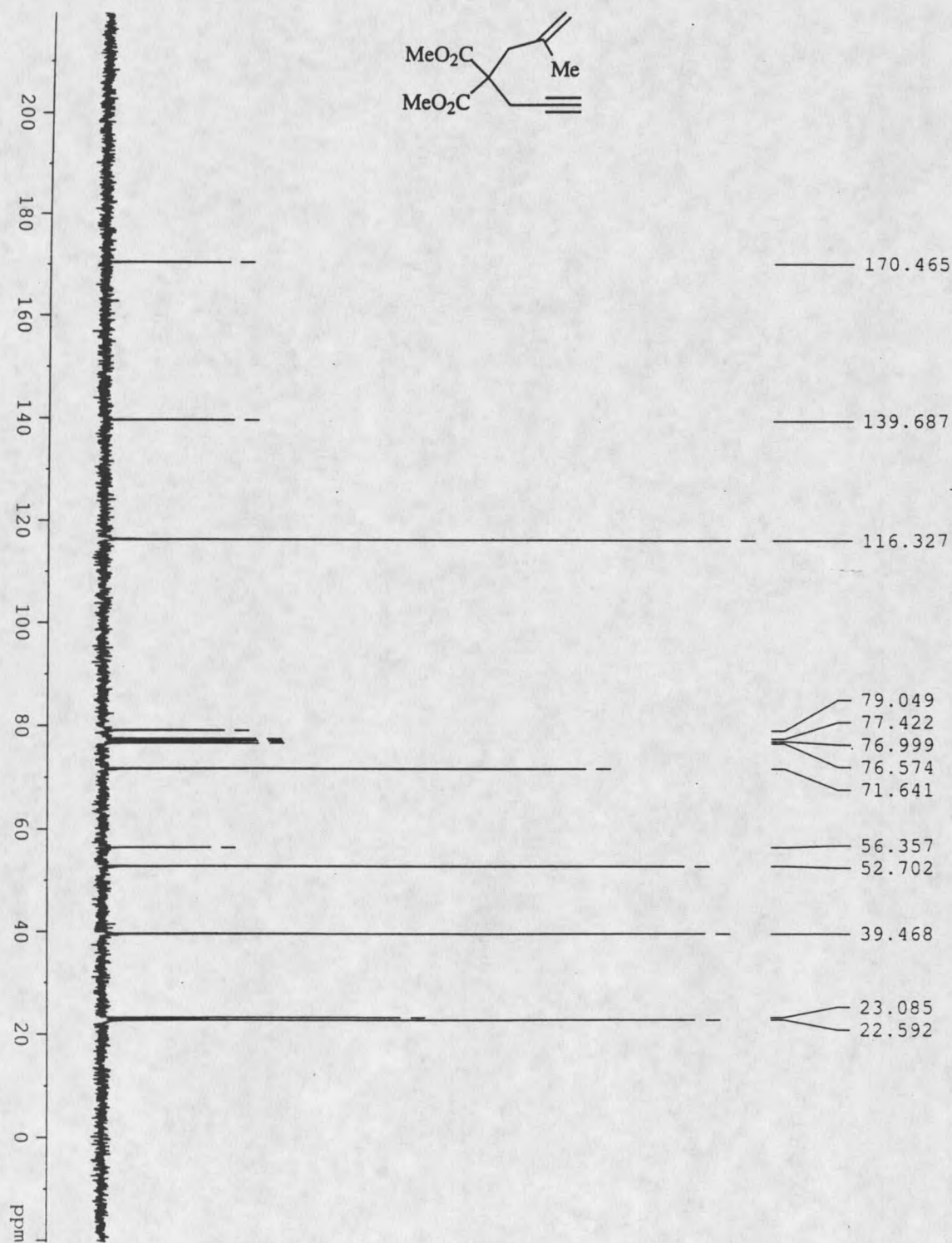
¹H NMR Spectrum of 181

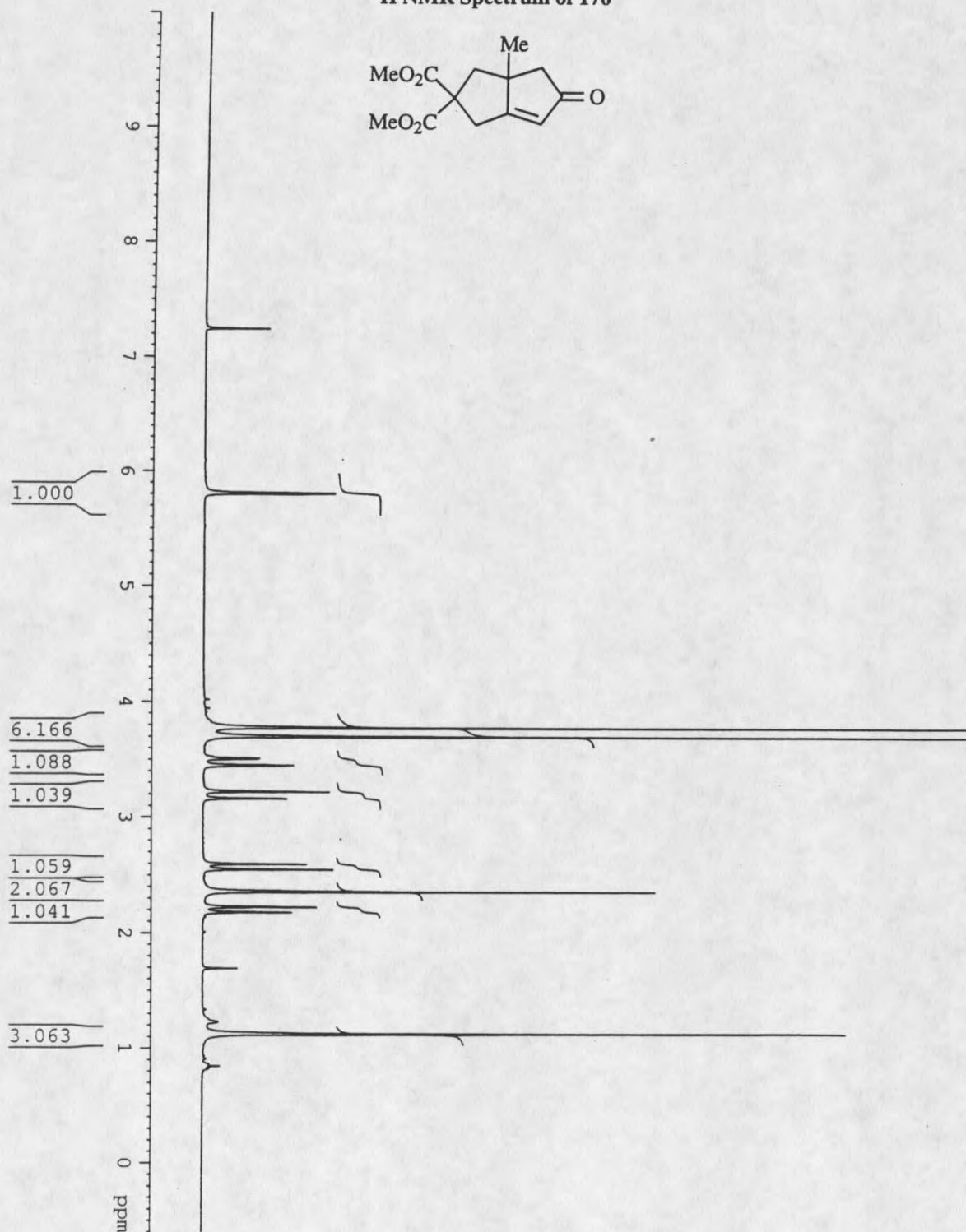
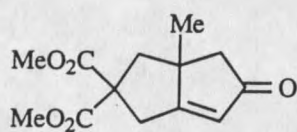
¹³C NMR Spectrum of 181

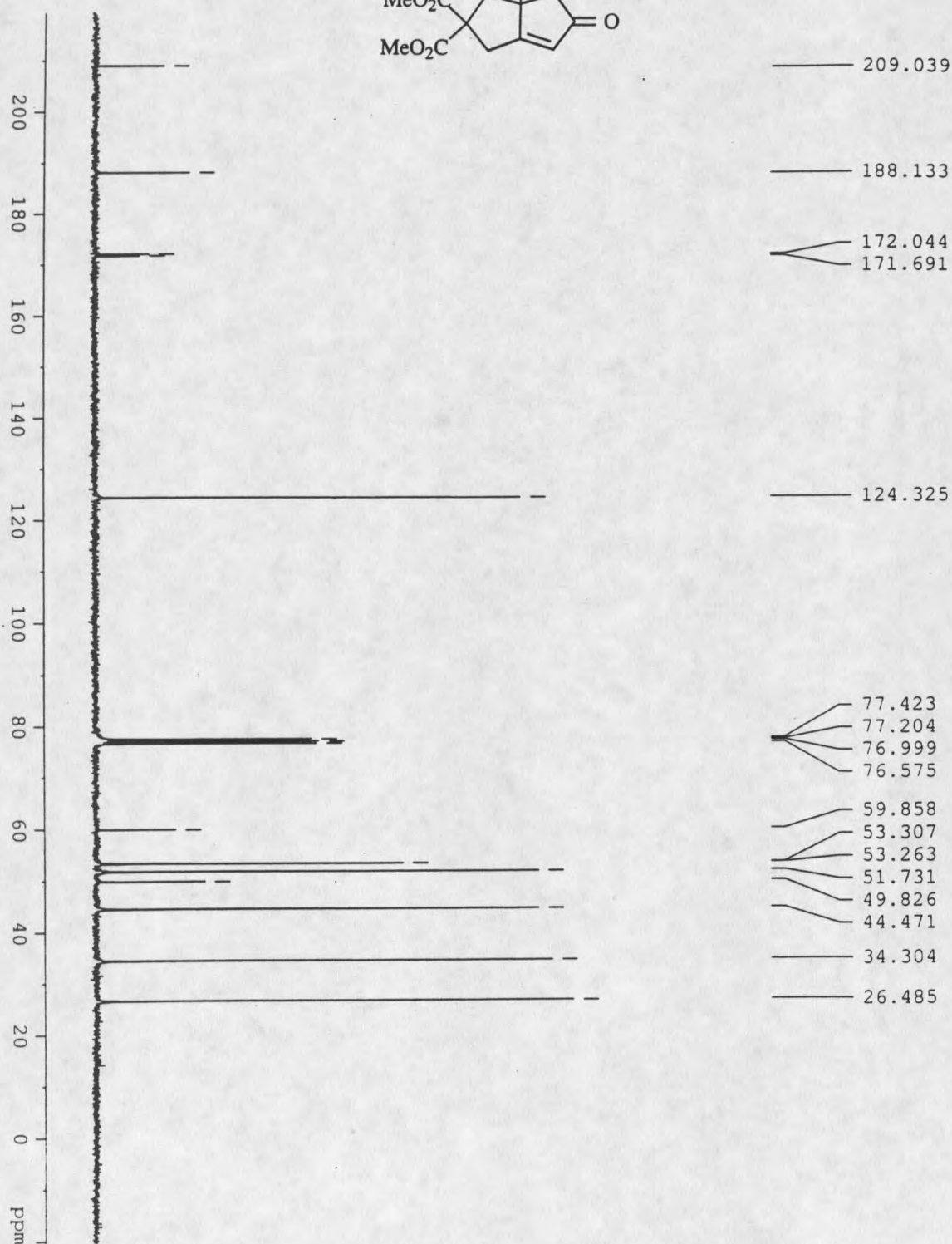
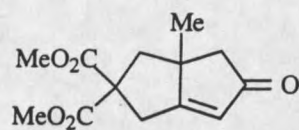
¹H NMR Spectrum of 182

¹³C NMR Spectrum of 182

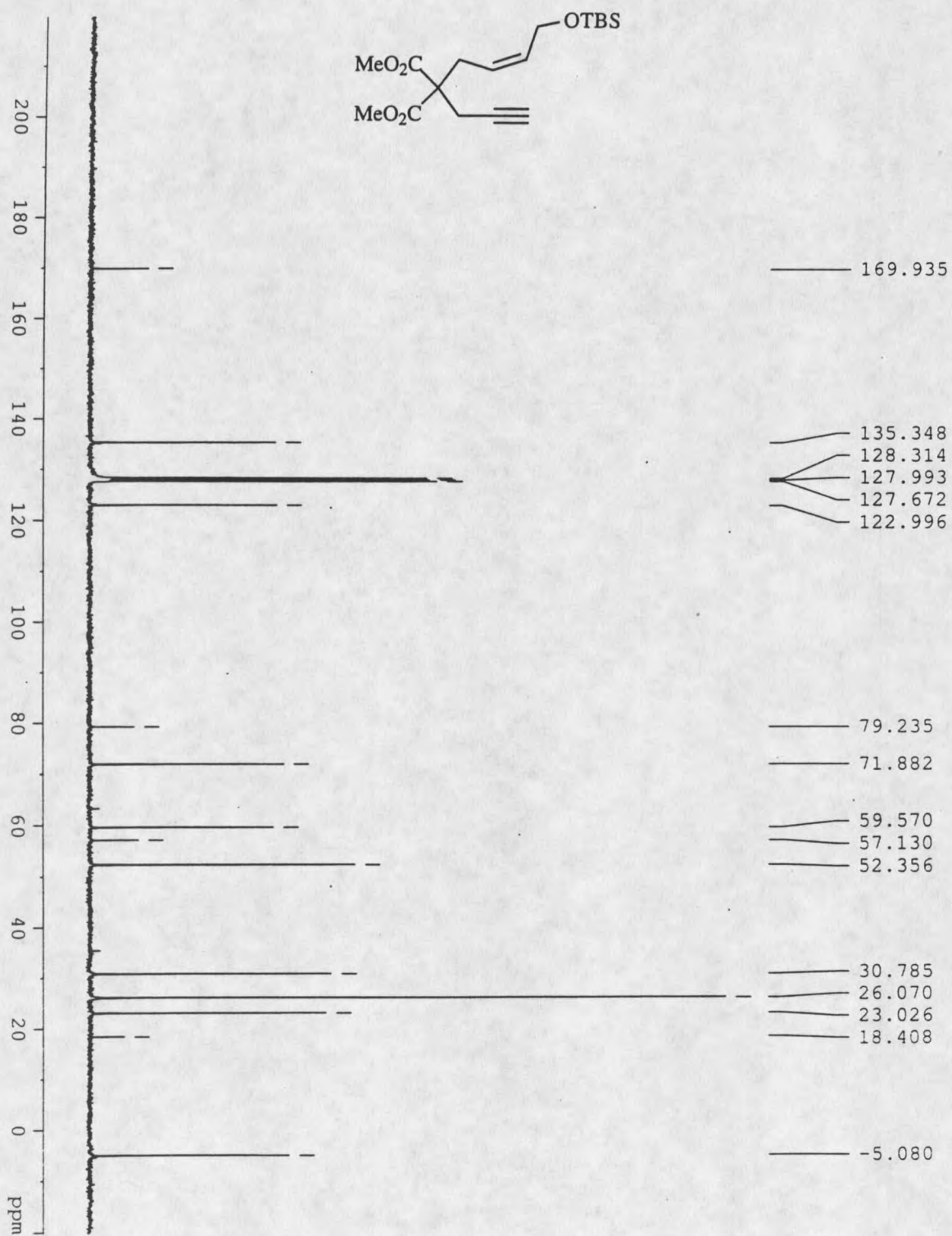
¹H NMR Spectrum of 175

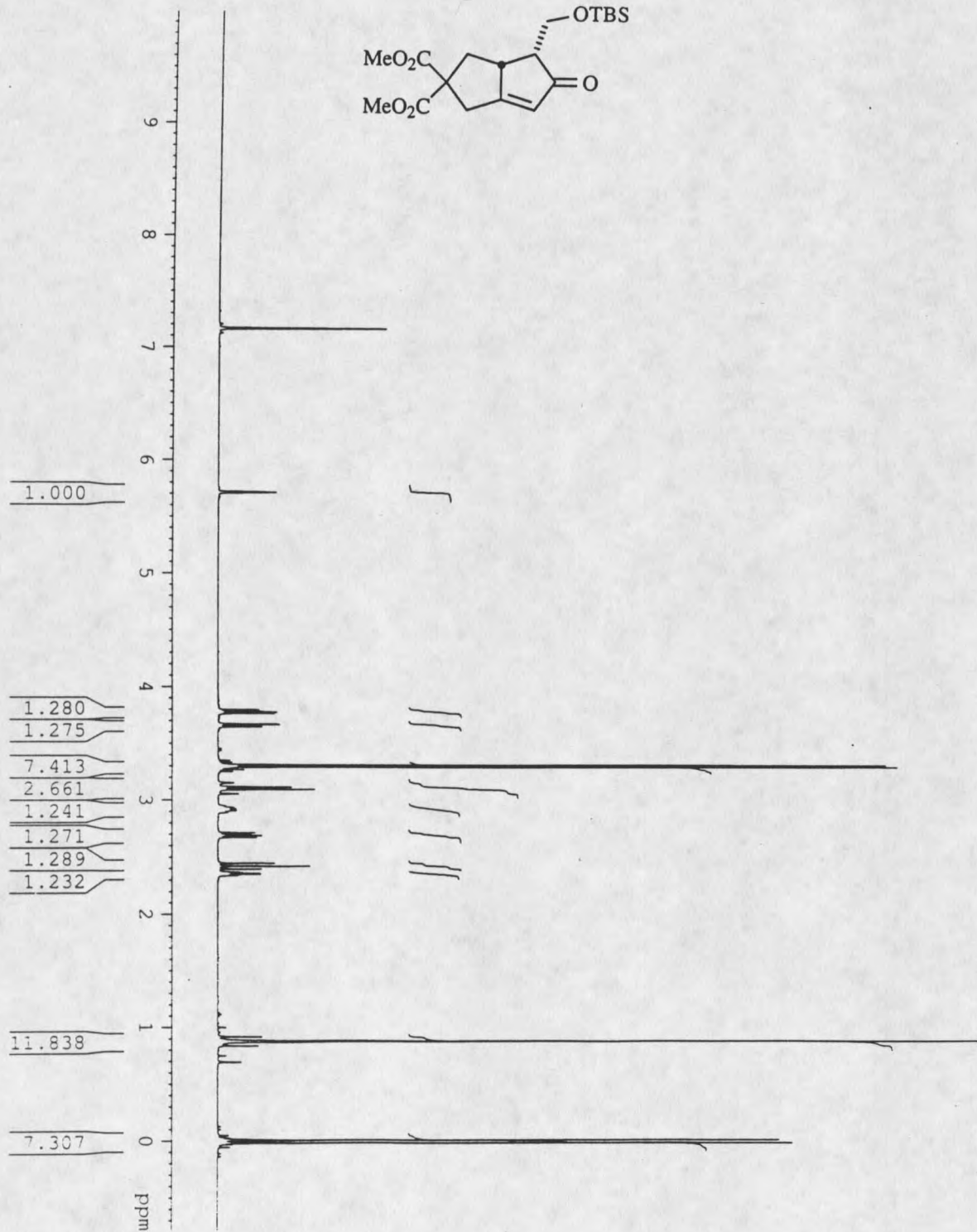
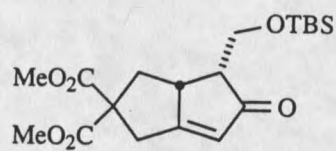
^{13}C NMR Spectrum of 175

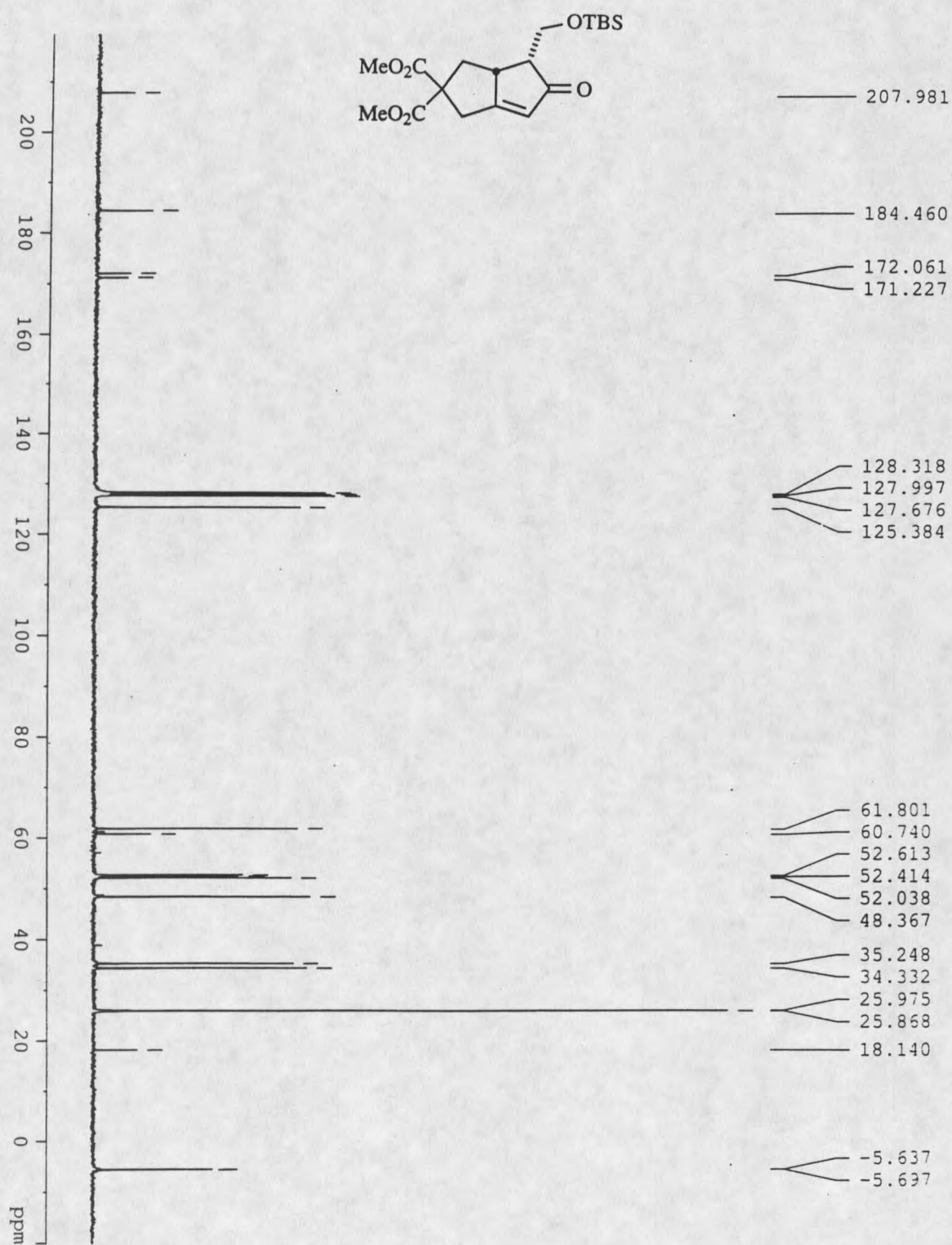
¹H NMR Spectrum of 176

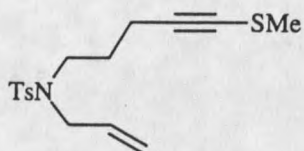
¹³C NMR Spectrum of 176

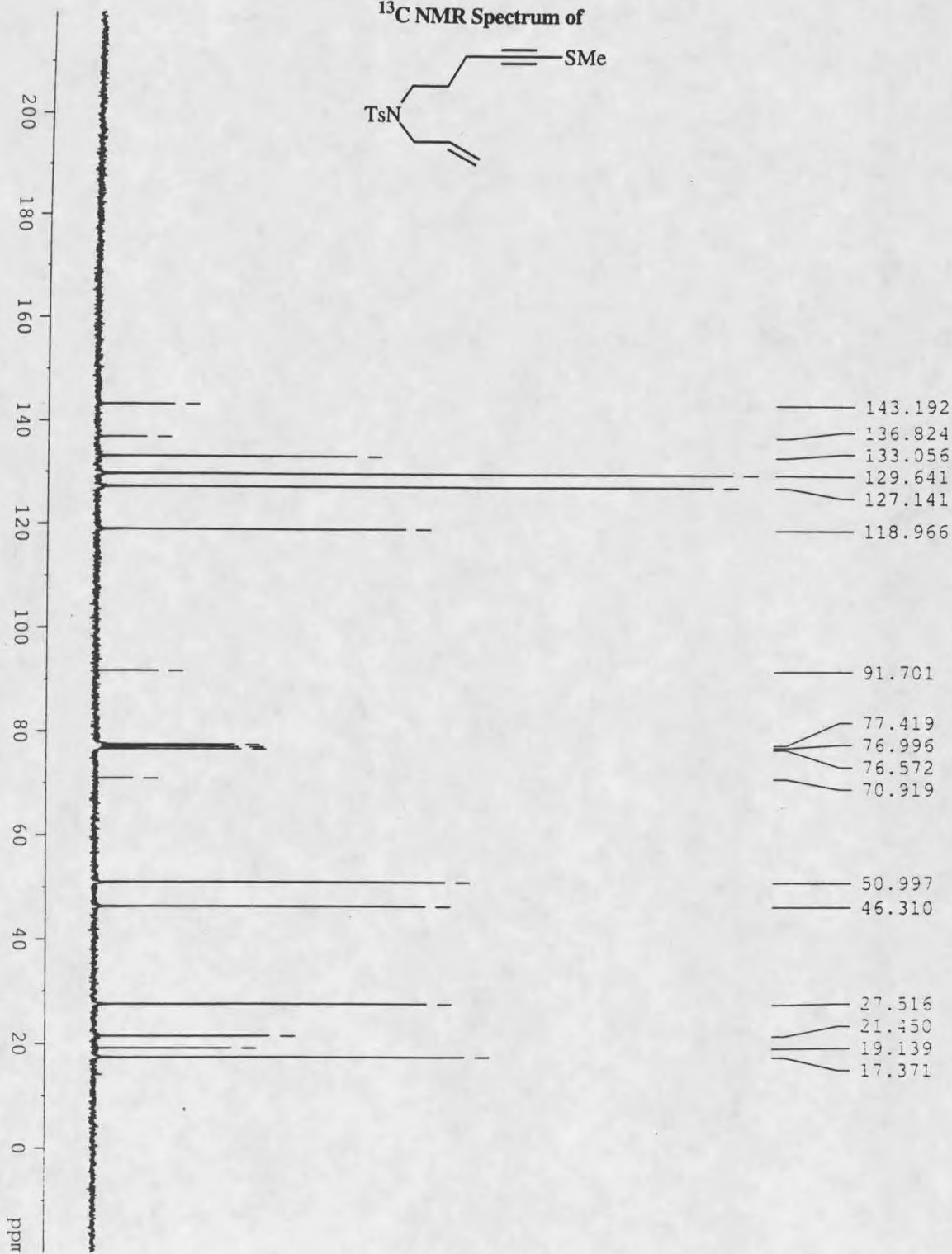
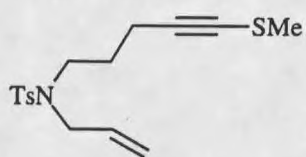
¹H NMR Spectrum of 177

¹³C NMR Spectrum of 177

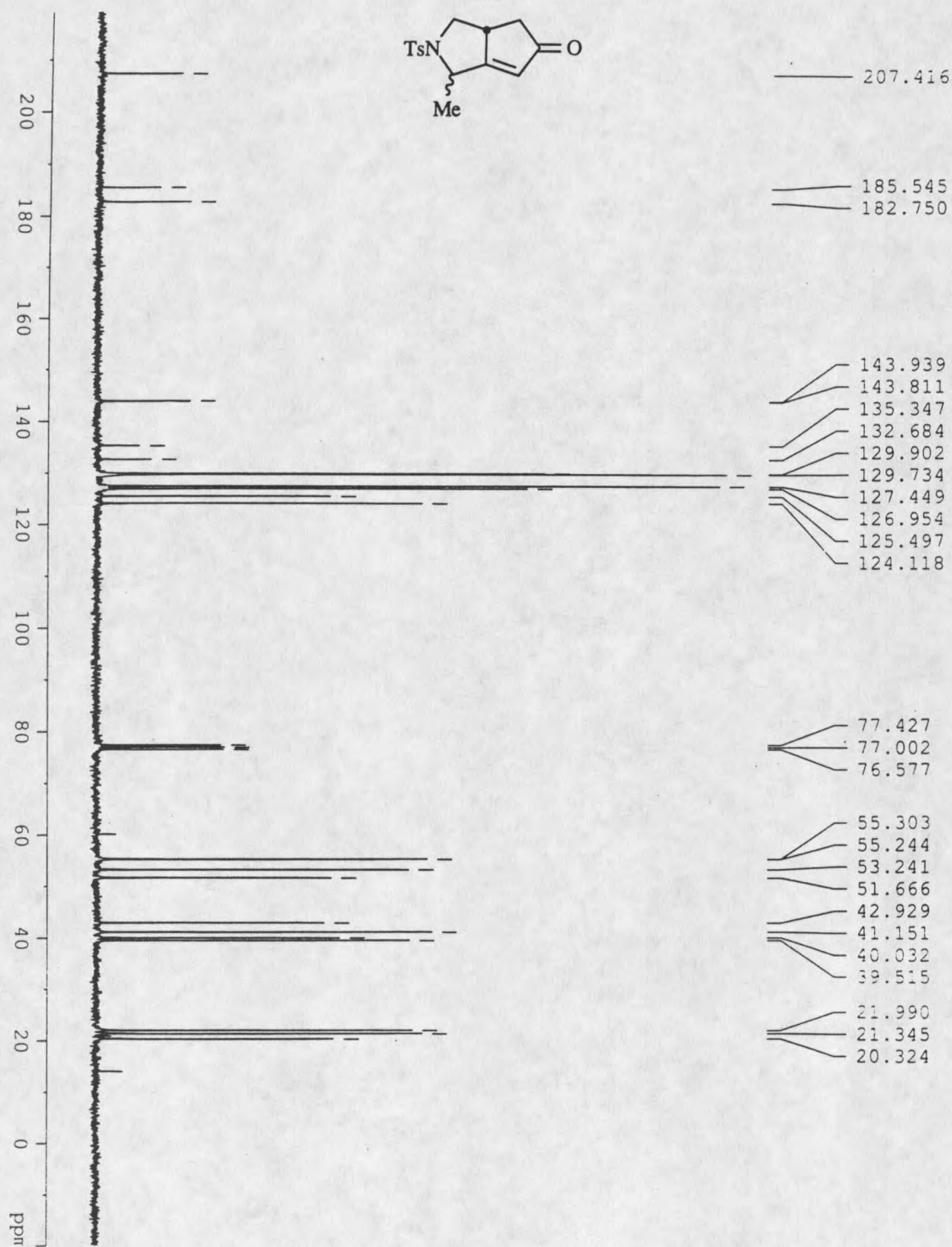
¹H NMR Spectrum of 178

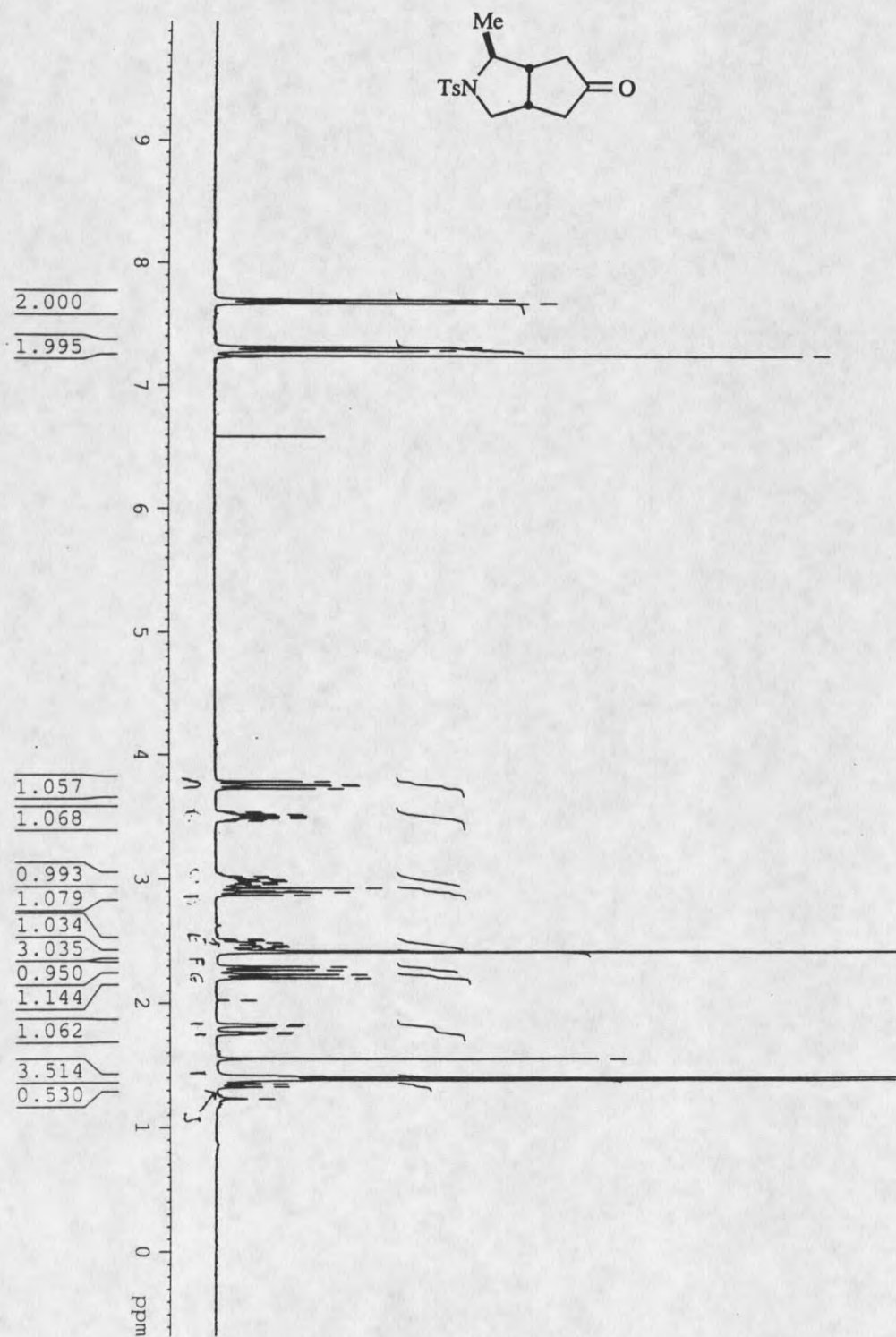
¹³C NMR Spectrum of 178

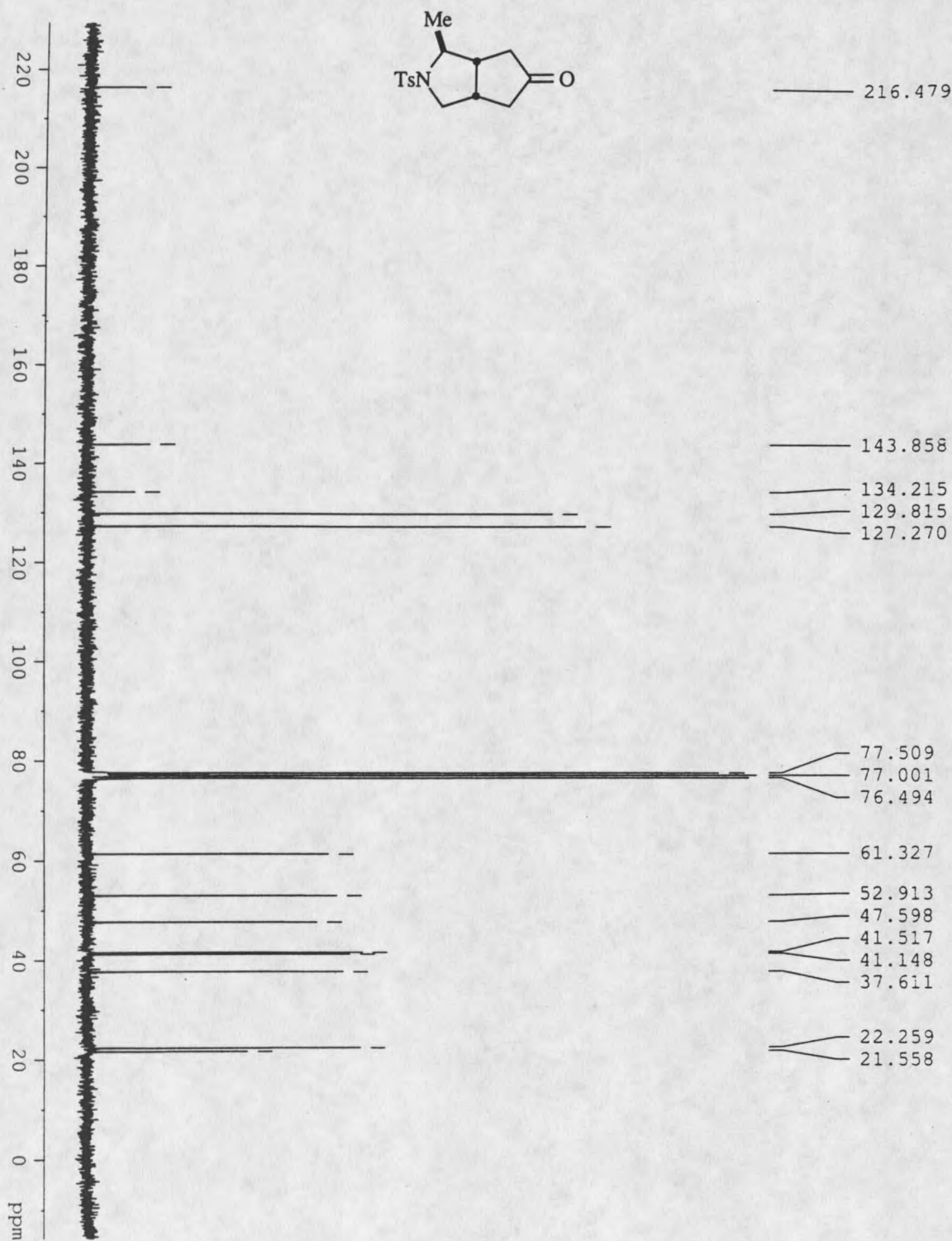
¹H NMR Spectrum of

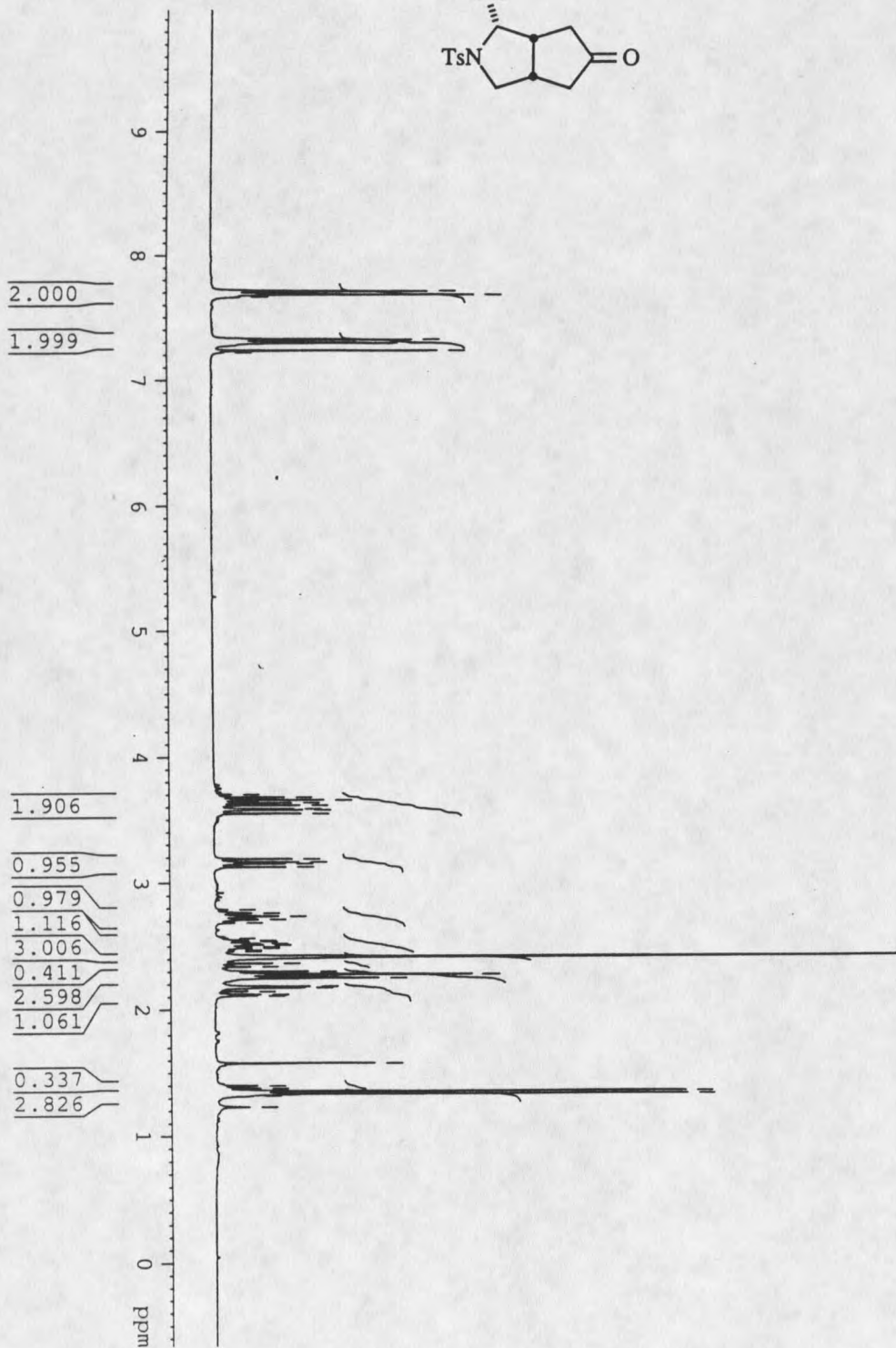
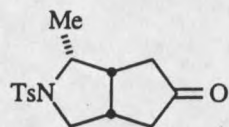
¹³C NMR Spectrum of

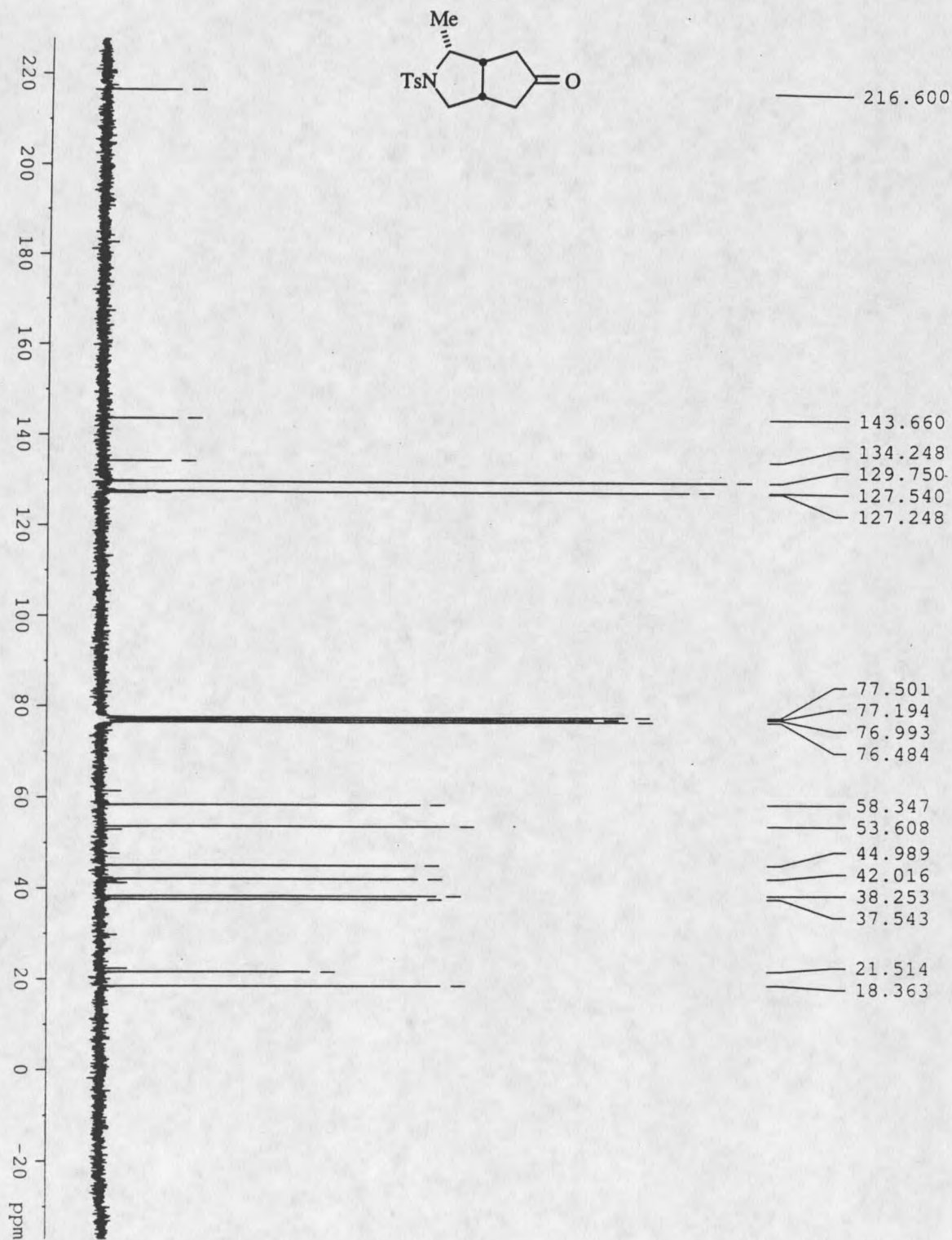
¹H NMR Spectrum of 188

¹³C NMR Spectrum of 188

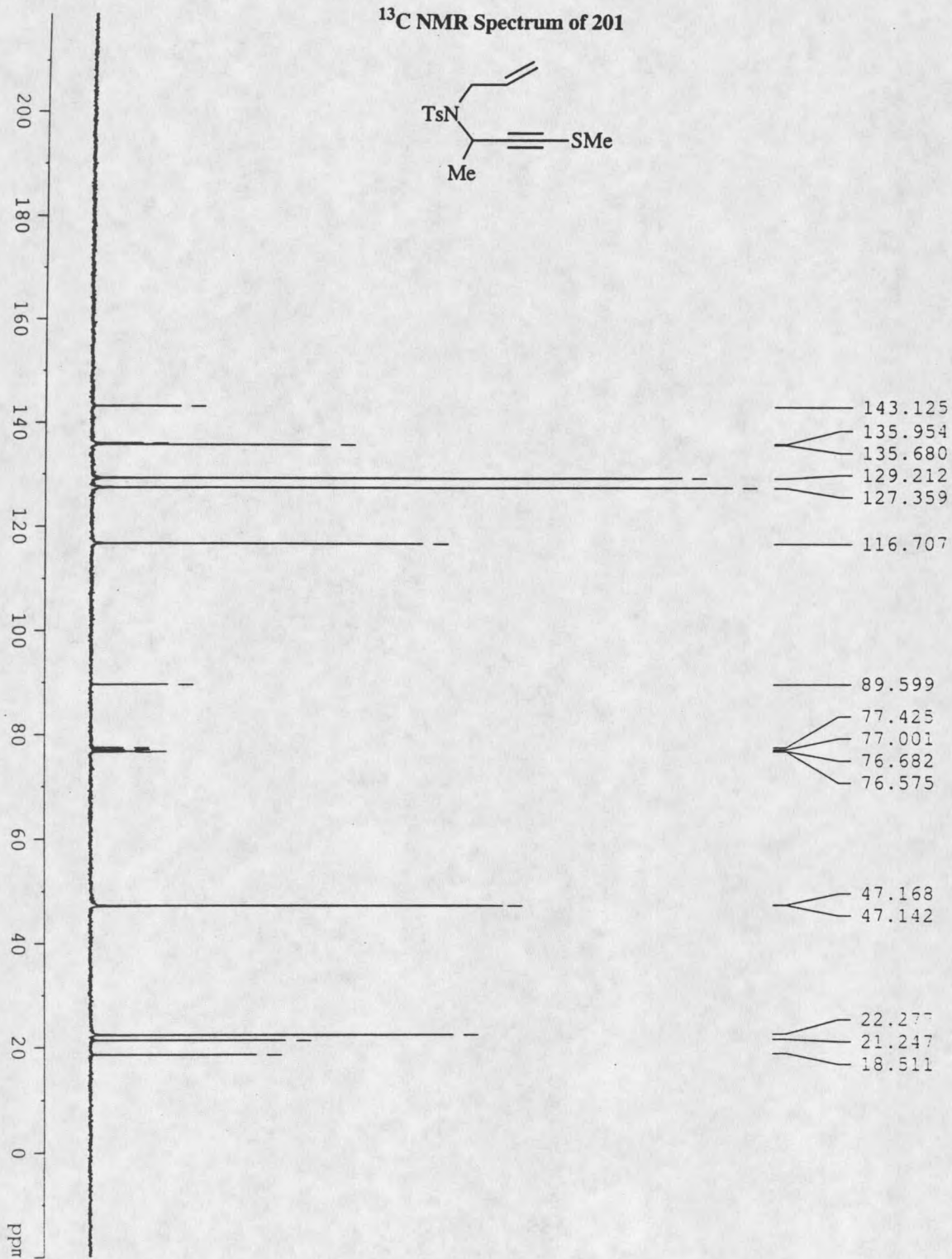
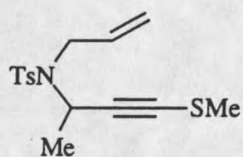
¹H NMR Spectrum of 188b

¹³C NMR Spectrum of 188b

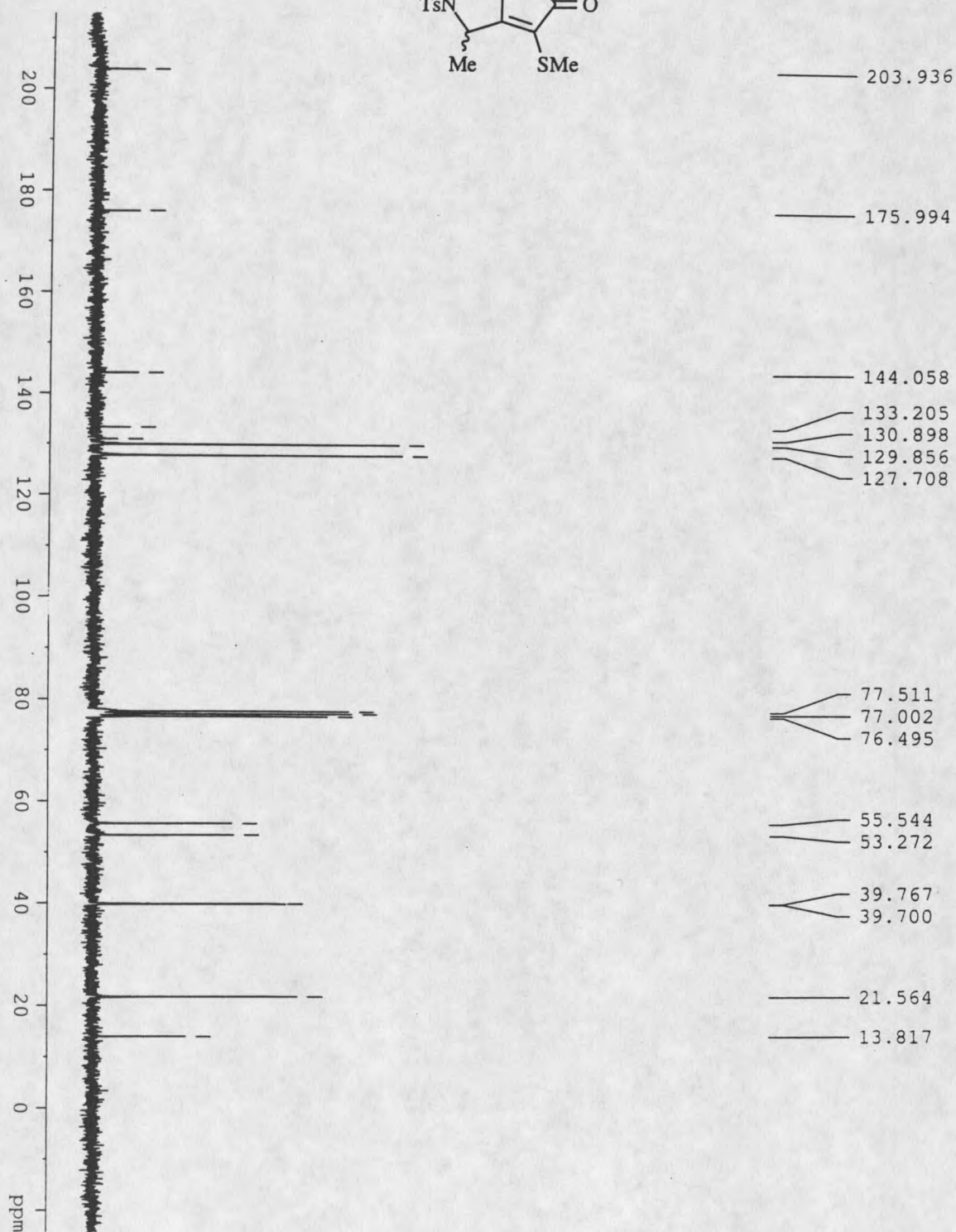
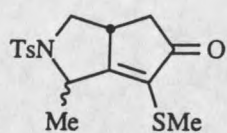
¹H NMR Spectrum of 188c

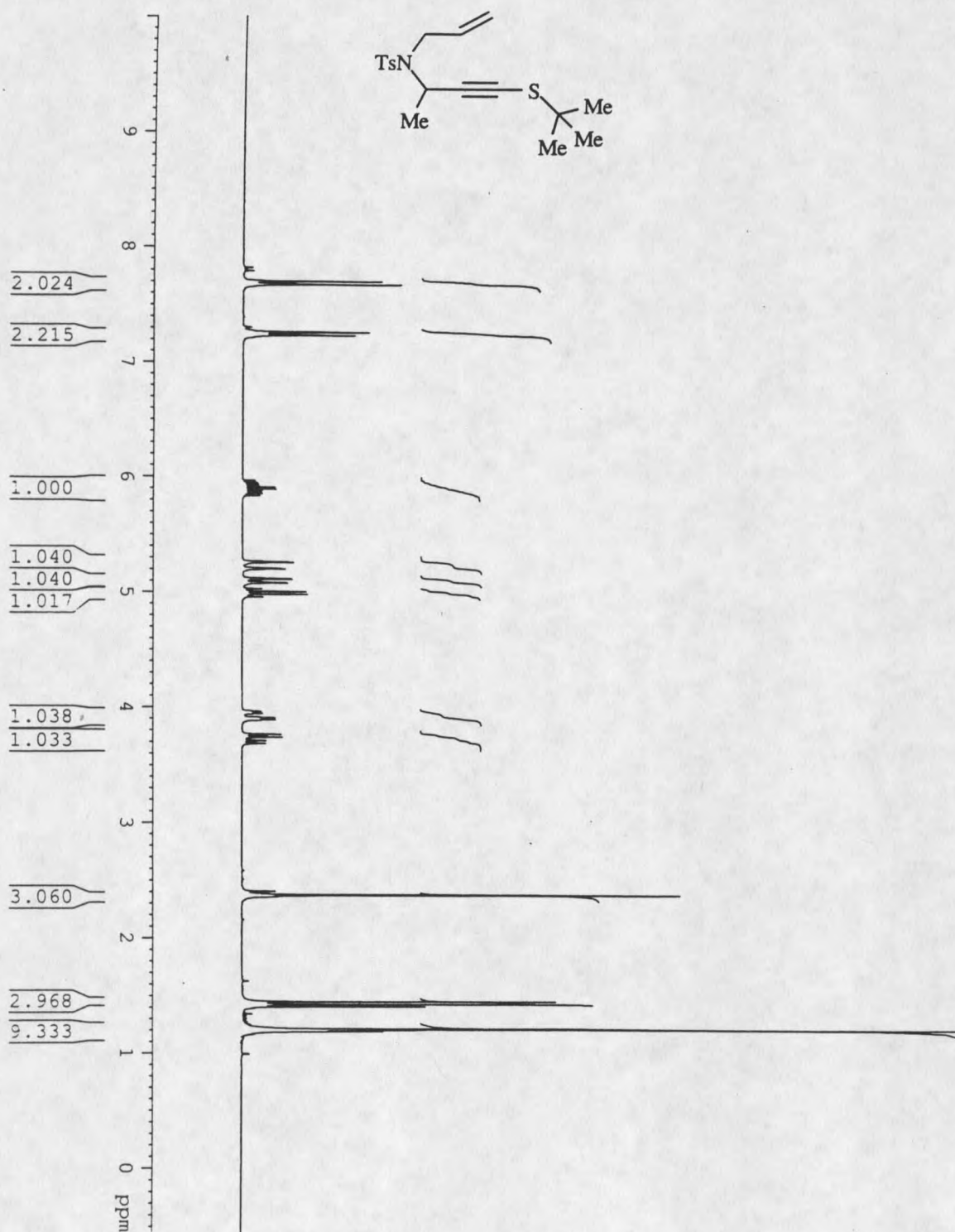
¹³C NMR Spectrum of 188c

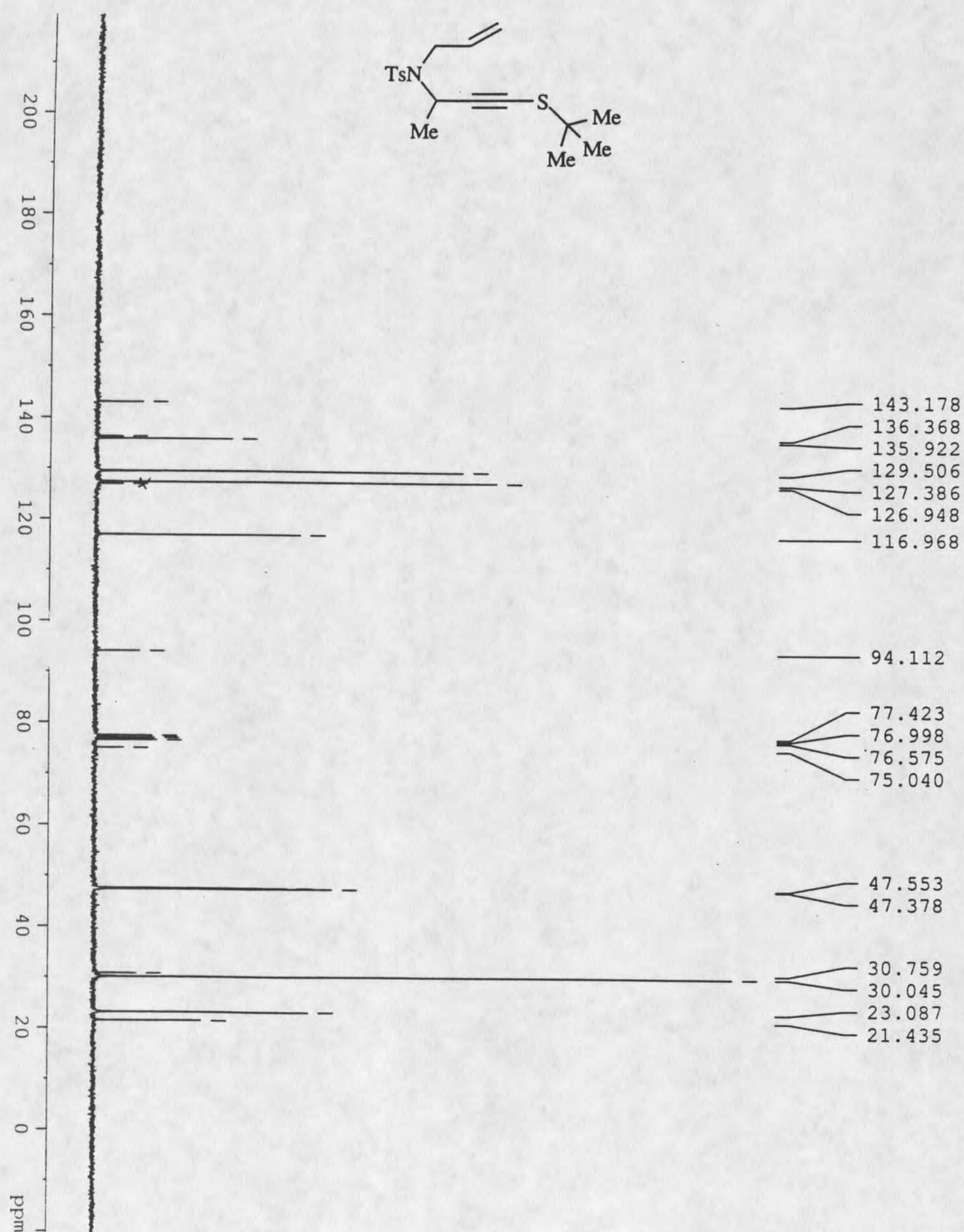
¹H NMR Spectrum of 201

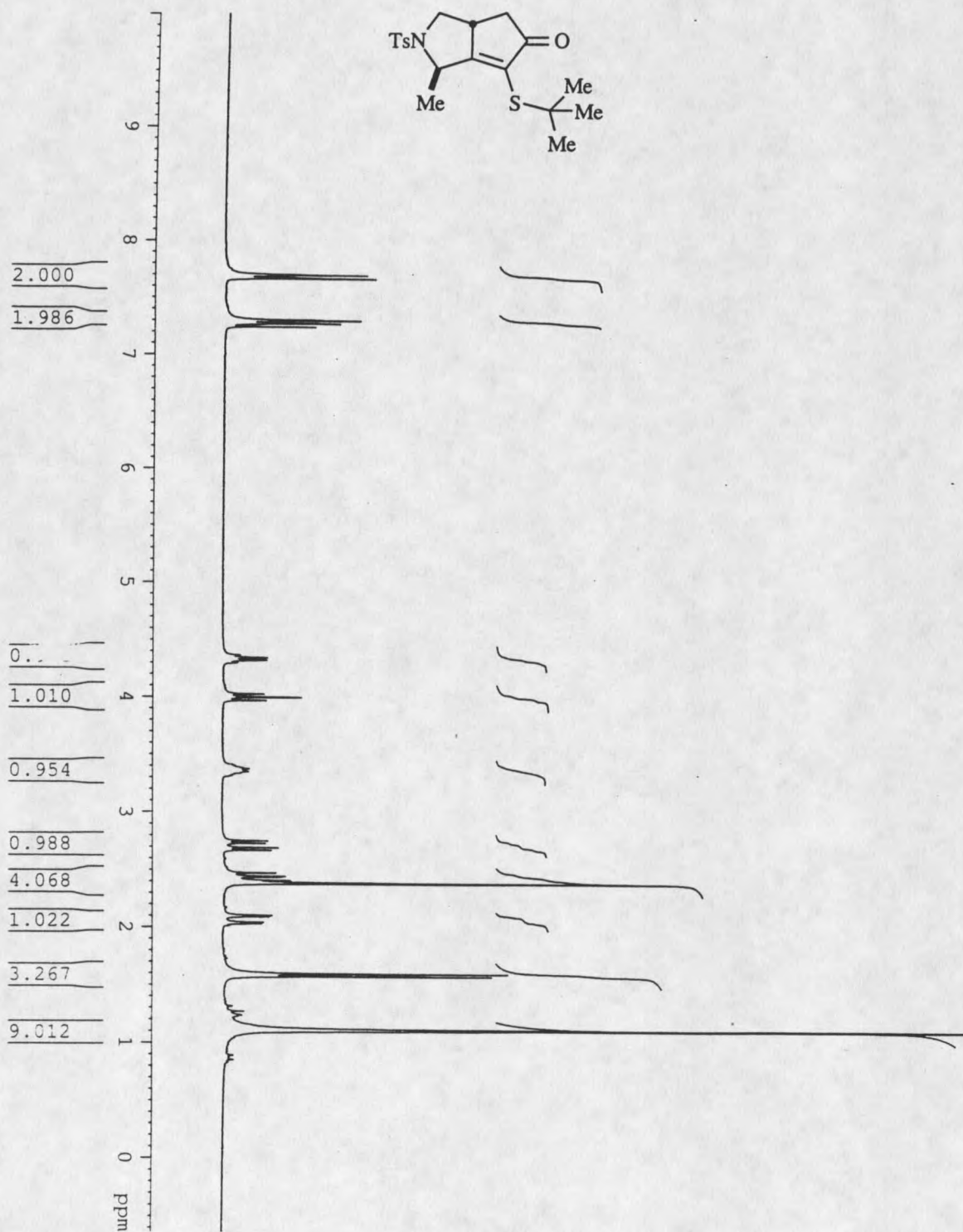
¹³C NMR Spectrum of 201

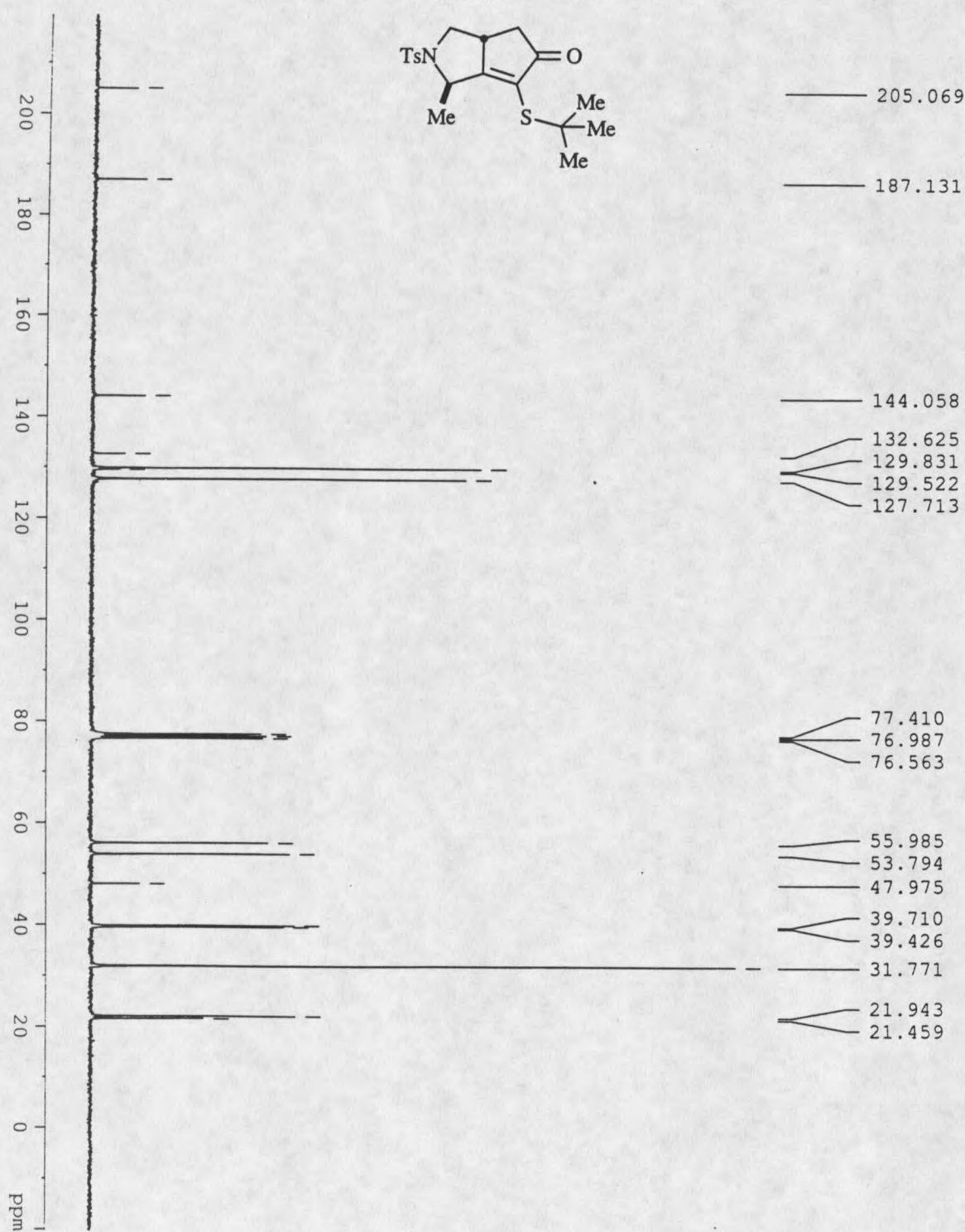
¹H NMR Spectrum of 206

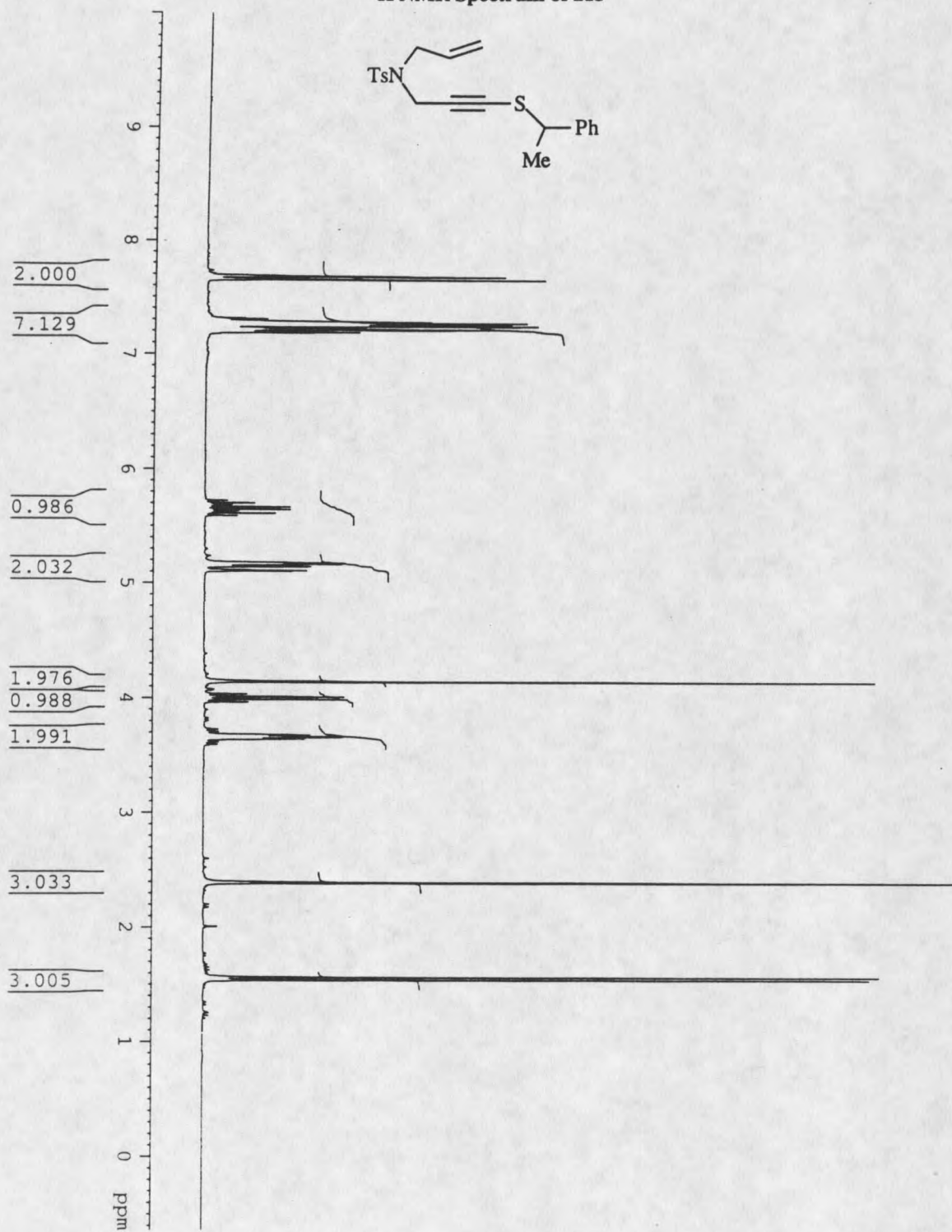
¹³C NMR Spectrum of 206

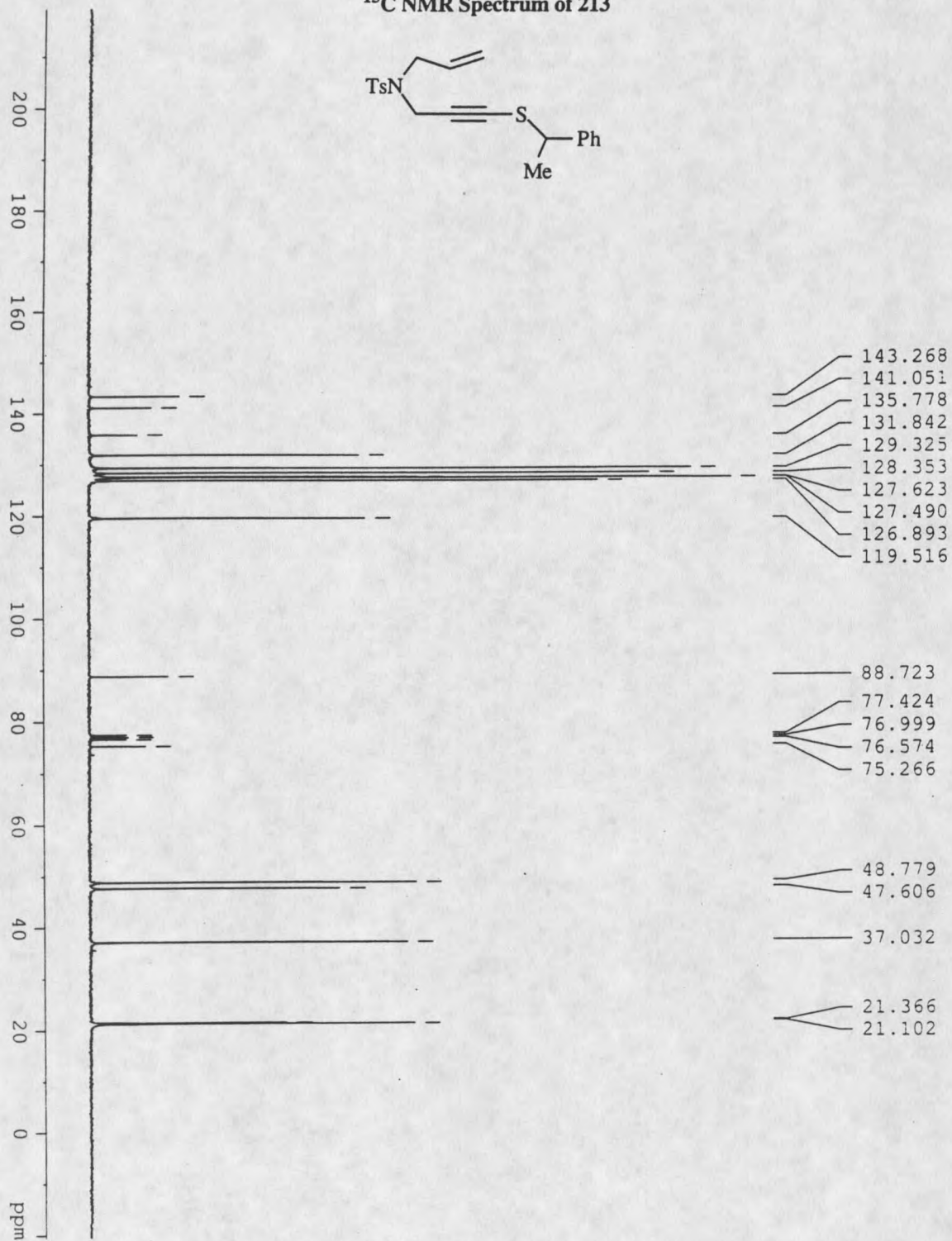
¹H NMR Spectrum of 212

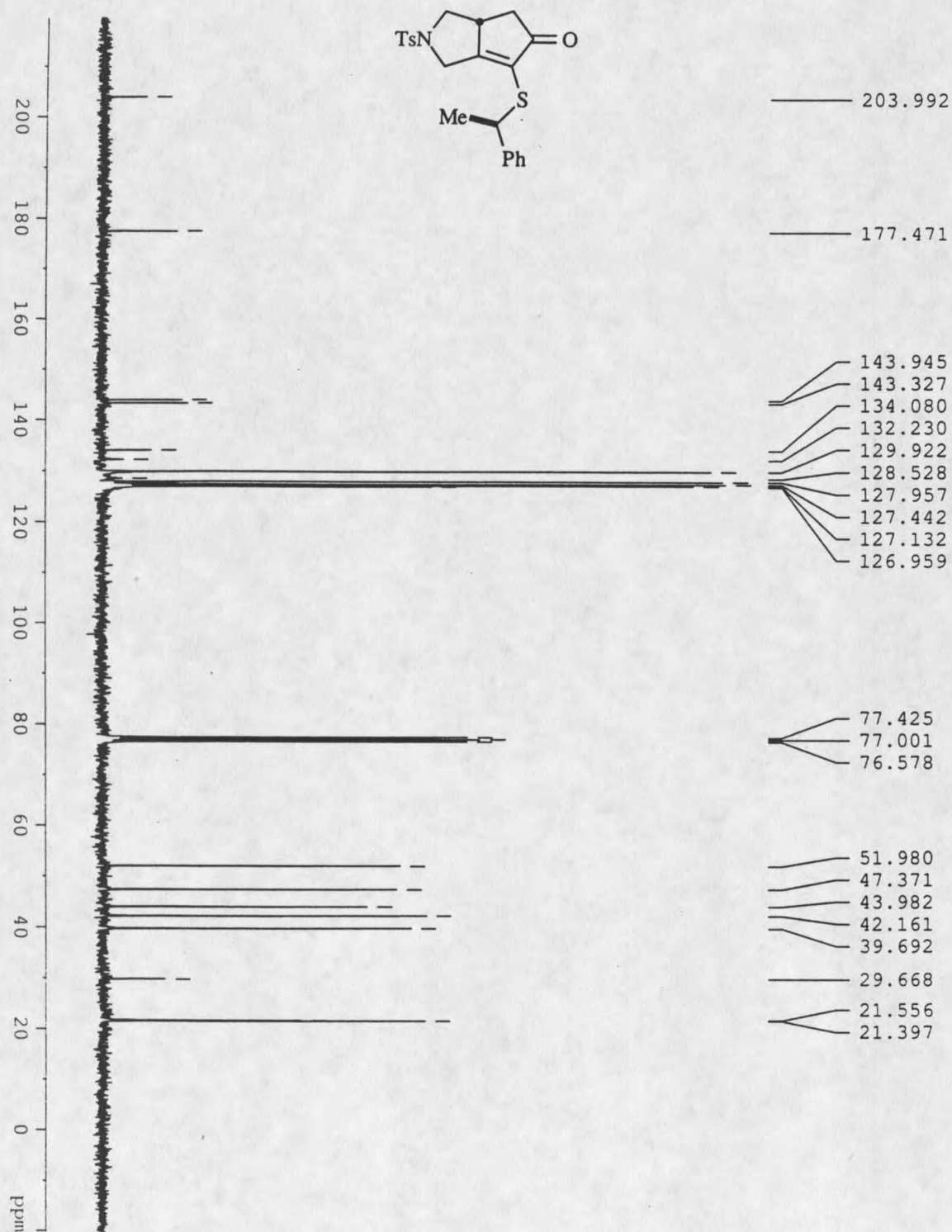
¹³C NMR Spectrum of 212

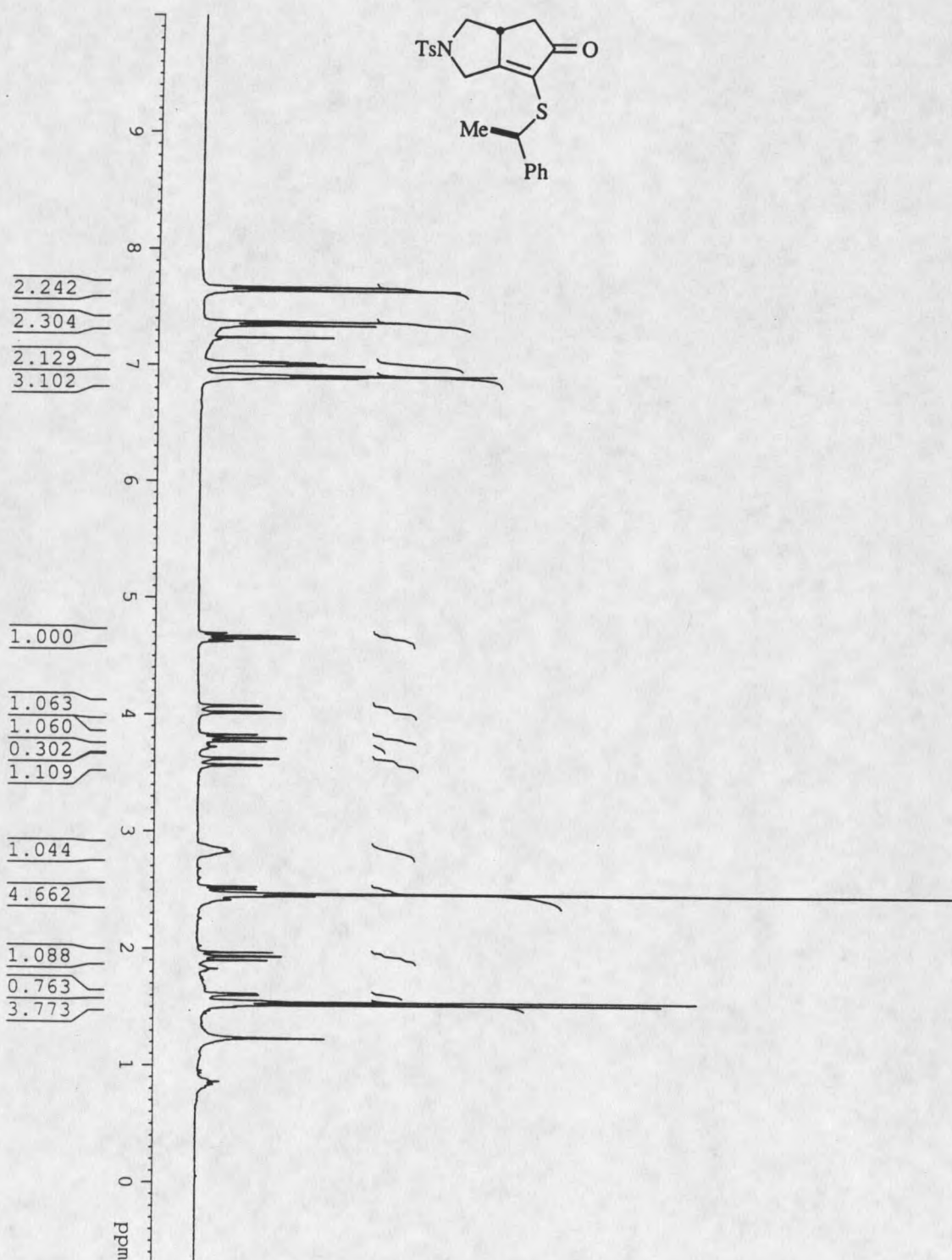
¹H NMR Spectrum of 206

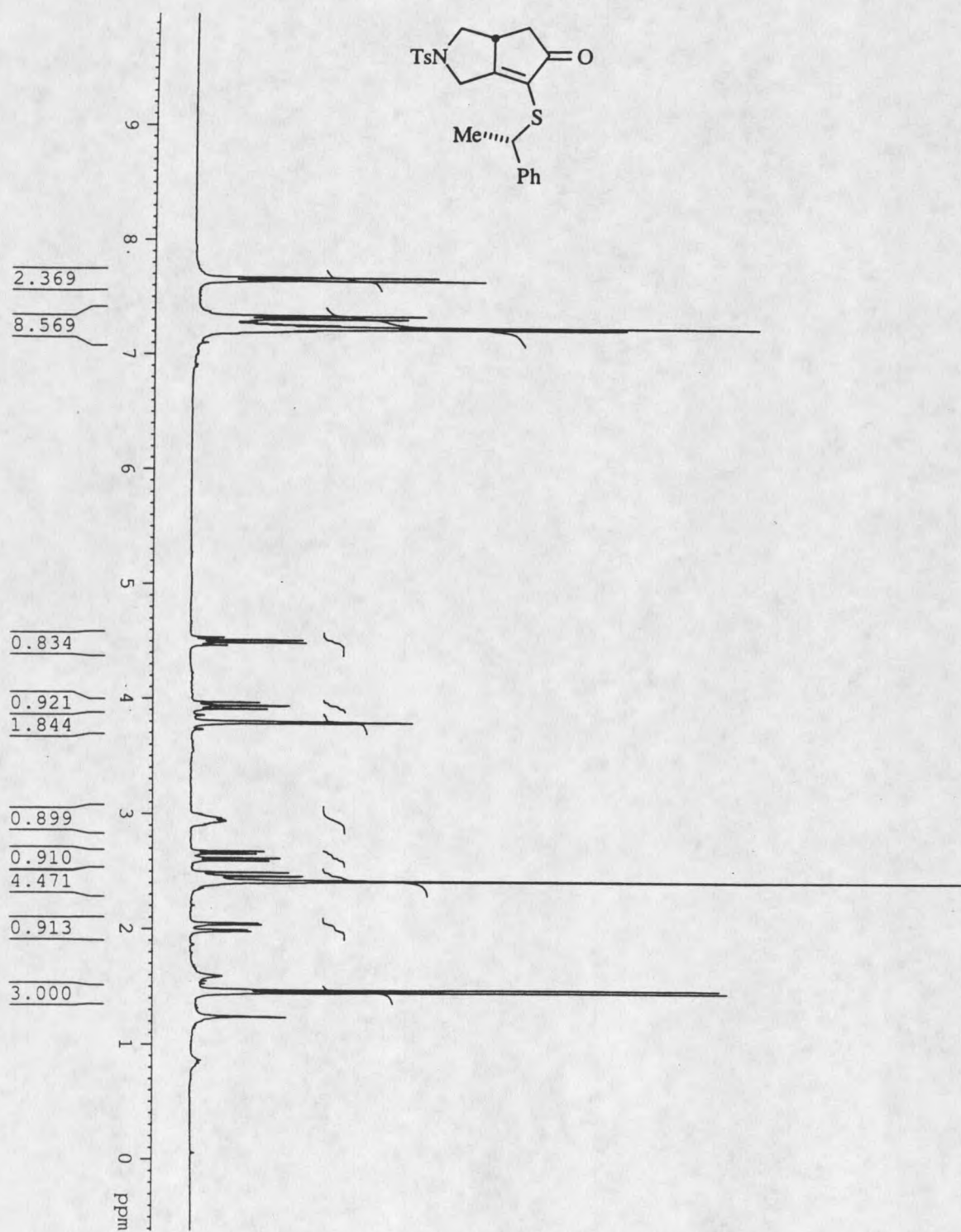
¹³C NMR Spectrum of 206

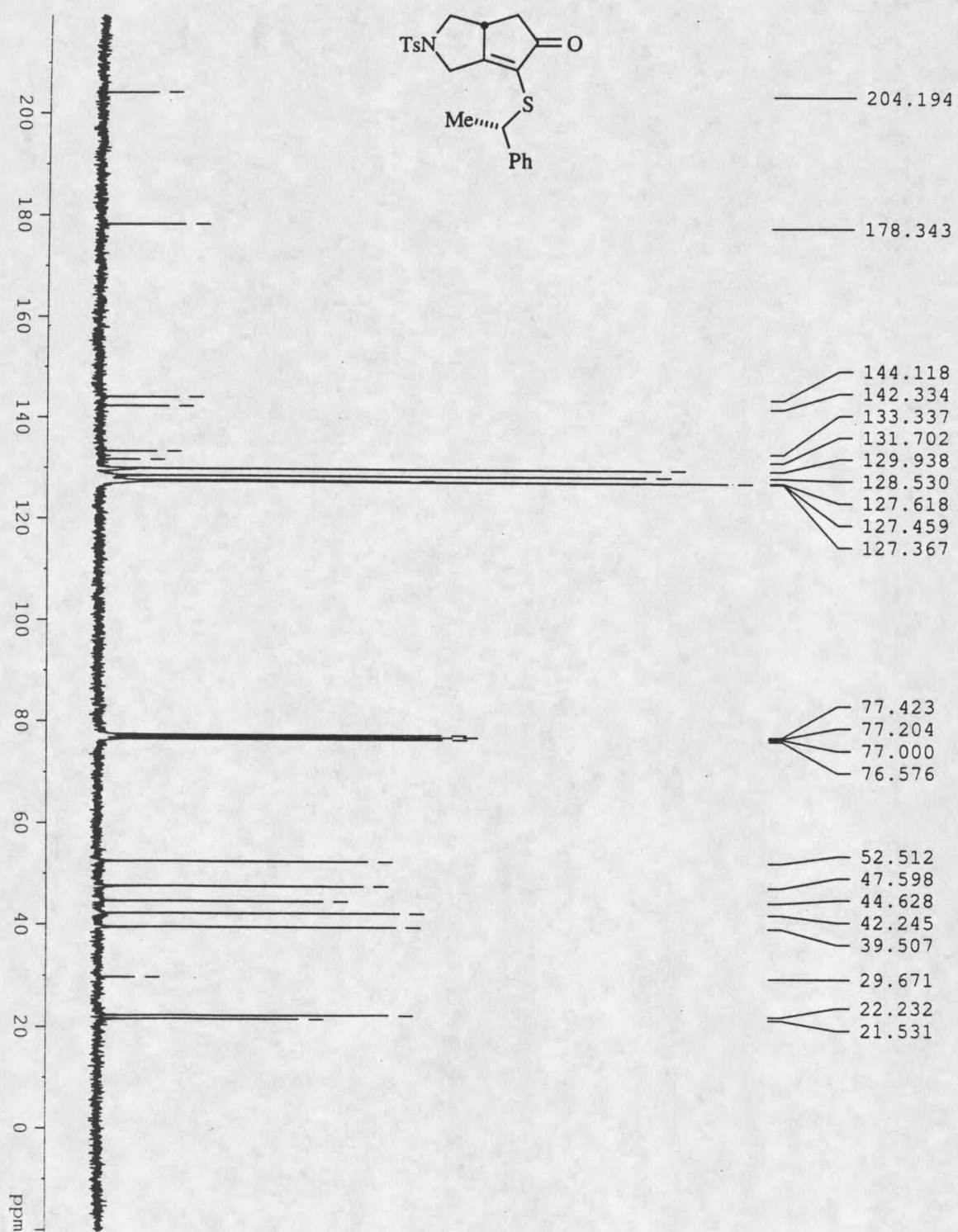
¹H NMR Spectrum of 213

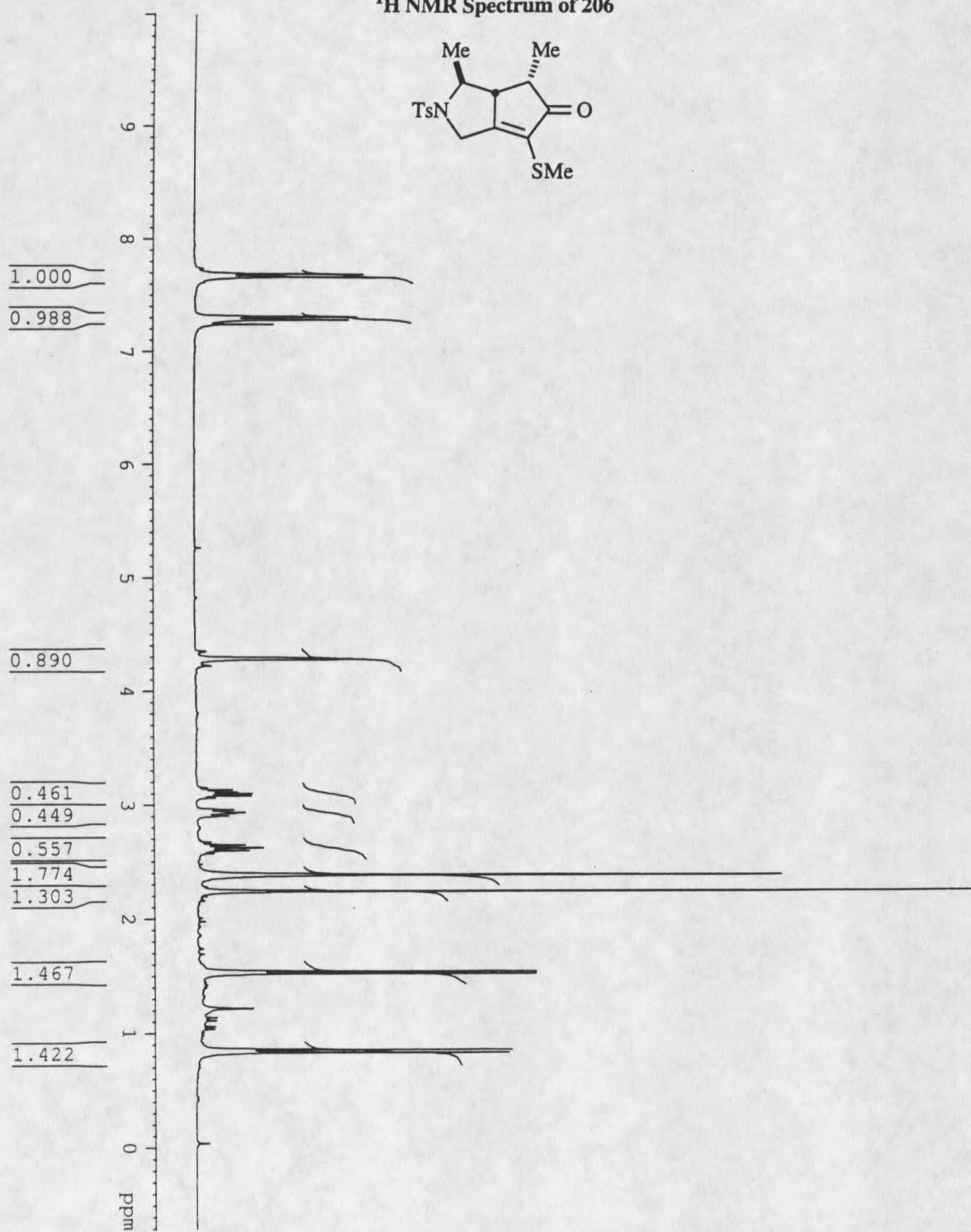
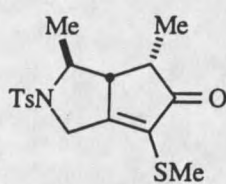
¹³C NMR Spectrum of 213

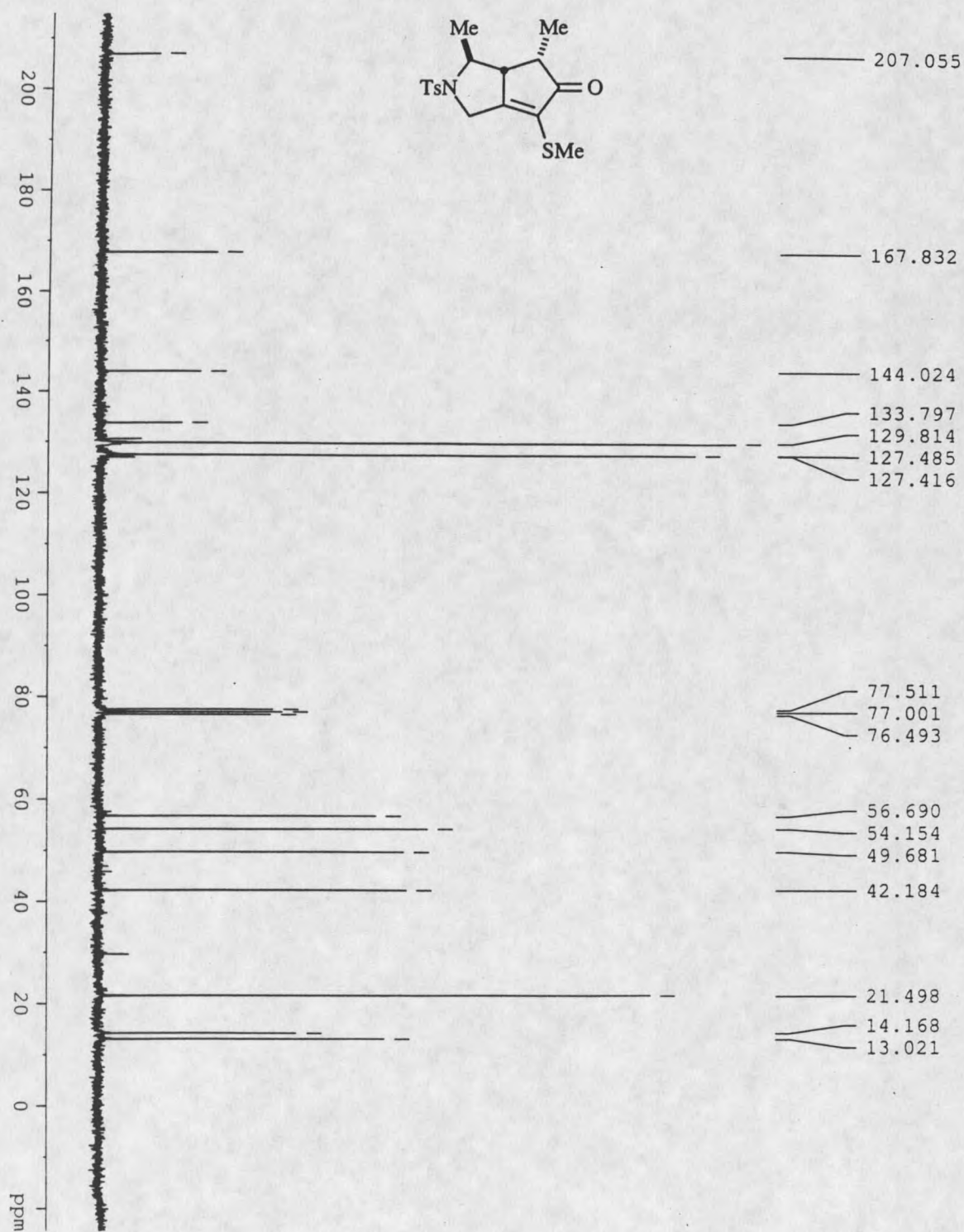
¹H NMR Spectrum of 214a

¹³C NMR Spectrum of 214a

¹H NMR Spectrum of 214b

¹³C NMR Spectrum of 214b

¹H NMR Spectrum of 206

¹³C NMR Spectrum of 206

MONTANA STATE UNIVERSITY - BOZEMAN



3 1762 10332019 6