



Substrate and reagent control of diastereoselectivity in transition metal mediated processes :
development of a catalytic photopromoted Pauson-Khand reaction
by Brian L Pagenkopf

A thesis submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy in
Chemistry
Montana State University
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Abstract:

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APPROVAL

of a thesis submitted by

Brian L. Pagenkopf

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.

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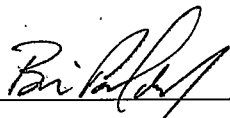
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For the Believers

Satisfaction lies in the effort not in the attainment. Full effort is full victory.

Mahatma Gandhi

Character is higher than intellect. A great soul will be strong to live, as well as to think.

Ralph Waldo Emerson

One science only will one genius fit: So vast is art, so narrow human wit.

Alexander Pope

There is no great genius without a tincture of madness.

Seneca

Don't be afraid to challenge the pros, even in their own backyard. Just as important, never neglect details, even to the point of being a pest.

Colin Powell

There is great ability in knowing how to conceal one's ability.

Francis, Duc de La Rochefoucauld

As for *work*, we haven't any of any consequence.

Henry David Thoreau

Not by years but by disposition is wisdom acquired.

Plautus

Four to six weeks in the lab can save you an hour in the library.

G. C. Quaderer, Dow Chemical

In matters of style, swim with the current; in matters of principle, stand like a rock.

Thomas Jefferson

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Abstract

Several of the factors that influence substrate based control of diastereoselection in $\text{Cp}_2\text{Zr(II)}$ mediated enyne cyclizations have been illuminated by examination of an extensive series of substituted enynes. An eminently practical, catalytic, photopromoted Pauson-Khand reaction that proceeds under mild reaction conditions (50 - 55 °C) under 1 atm of CO was developed. The photopromoted Pauson-Khand reaction is compatible with substrates bearing of a wide variety of functional groups and substitution patterns. In some instances, substrate modification resulted in improved yields and increased diastereoselection. Studies directed toward the synthesis of carbacyclin resulted in a short enantiocontrolled synthesis of the epi-carbacyclin core. The key steps of this synthesis were an Evans syn-aldol condensation and ring closure by the catalytic photopromoted Pauson-Khand reaction.

1. Introduction

In recent years, the development of new transition metal mediated processes has become one of the most active and exciting areas of research in synthetic chemistry. The power of metal mediated processes often lies in their ability to confer a high degree of molecular complexity to inexpensive and structurally simple starting materials with relatively little cost or effort. The direct formation of bicyclic metallocyclopentenenes from simple enynes by group IV metallocene reagents illustrates the synthetic potential of this class of reactions. Because the intermediate metallocyclopentenenes can be further functionalized by a variety of electrophiles, an array of cyclic products is available from the same acyclic precursor.

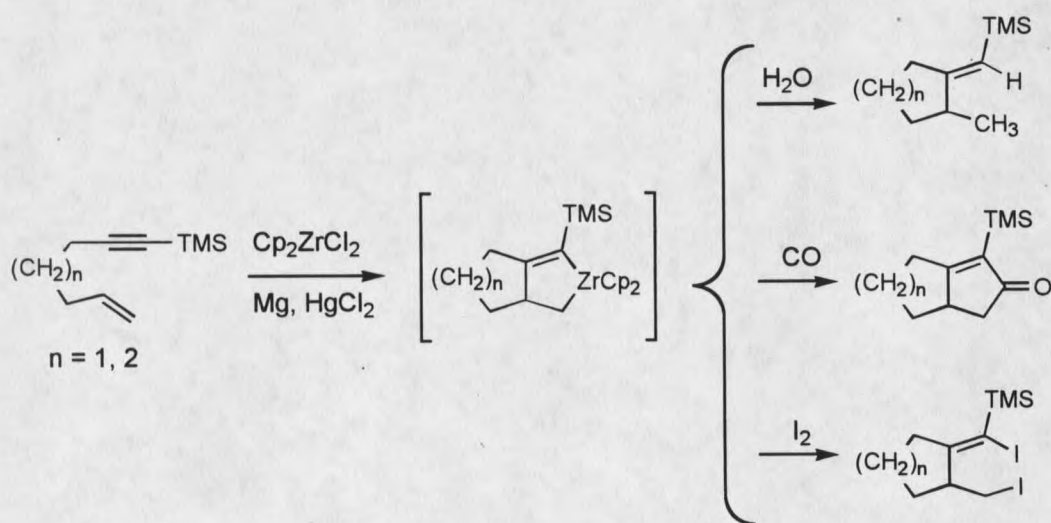
In order to further understand factors that contribute to substrate control of diastereoselectivity in $\text{Cp}_2\text{Zr(II)}$ mediated enyne cyclizations, a diverse series of substituted enynes has been synthesized and subsequently studied in cyclization reactions. The results of these experiments led to the evolution of several synthetic strategies directed toward the synthesis of carbacyclin. The key ring forming step of these synthetic endeavors focused on the use of a $\text{Cp}_2\text{Zr(II)}$ mediated enyne cyclization and tandem carbonylation sequence. The search for an improved

cyclization protocol to effect this transformation has led to the development of a novel, catalytic photopromoted Pauson-Khand reaction.

2. Background

2.1 Early Zirconium(II) Chemistry

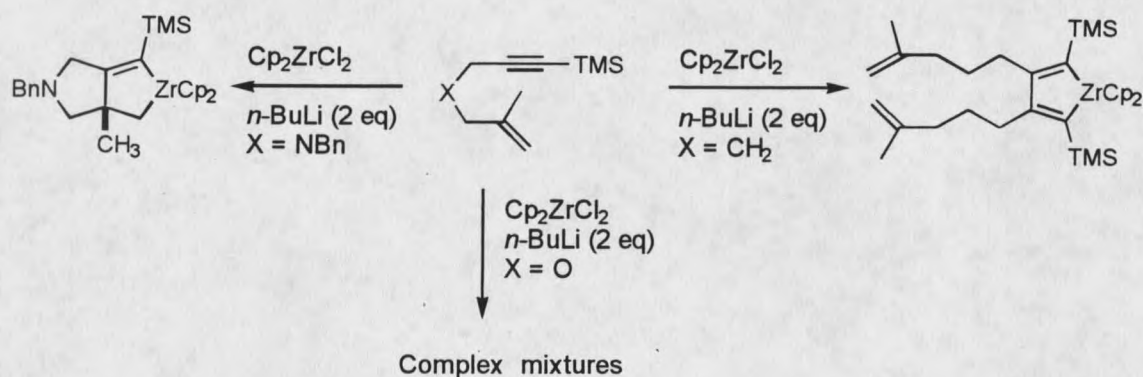
In 1985, Negishi reported that a zirconocene equivalent, i.e. "Cp₂Zr", generated by the treatment of Cp₂ZrCl₂ with Mg and HgCl₂ was effective for converting various non-terminal enynes to zirconocyclopentenenes (**Scheme 1**).¹ The chemistry of these metallocycles proved to be diverse and powerful, in that functionalized carbocycles could be obtained from simple acyclic precursors. The intermediate zirconocycles could be protonated to yield the methyldiene substituted cyclopentanes, treated with CO (1 atm), to provide the corresponding α -silyl



Scheme 1

cyclopentenones, or treated with I_2 , to give the 1-vinyl-4-alkyl diiodo derivatives, all in moderate yields. Negishi later reported that treatment of Cp_2ZrCl_2 with two equivalents of n -BuLi at low temperatures offered an easy and economical method for the *in situ* preparation of a zirconocene equivalent.² This disclosure resulted in the rapid acceptance of "zirconocene" as a useful synthetic reagent. The flourish of research since Negishi's initial disclosure has resulted in many contributions leading to the rich and interesting chemistry of zirconium(II) species.^{2b,3}

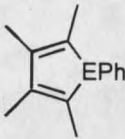
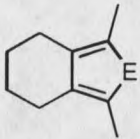
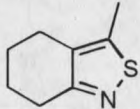
Some heteroatom linkages were found not only to be tolerant of the reaction conditions, but increased the reactivity of 1- or 2-substituted alkenynes (**Scheme 2**).⁴ Substituted alkenes with a carbogenic tether failed to react in the usual manner, but instead dimerized to give zirconocyclopentadienes in good yield. The heteroatom contraction offered by a benzylamine linkage resulted in the expected zirconocyclopentene product even with substituted alkenes. Oxygen tethers resulted in complex product mixtures,⁵ although with dienes (*vide infra*, section 2.3 (Chapter 2, subsection 3)) this reactivity has been attenuated to become a route to allylic- and propargyliczirconocene derivatives.⁶



Scheme 2

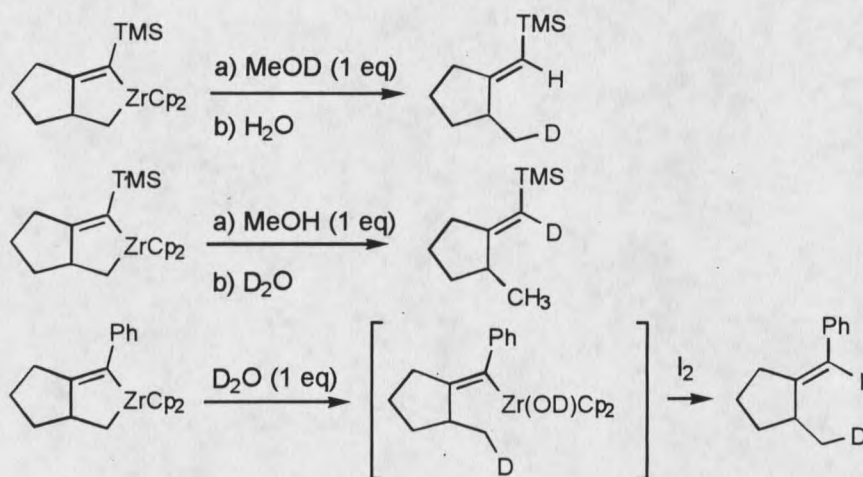
Fagan and Nugent later showed that zirconocyclopentadienes effectively transmetallated with main group electrophiles to afford main group heterocycles (Table 1).⁷ Substrates 1 and 2 were easily prepared from 2-butyne or 2,8-decadiyne. Entry 3 was prepared by the addition of 1-cyano-5-heptyne to a solution of $\text{Cp}_2\text{Zr}(n\text{-Bu})_2$ reduced *in situ* in the presence of bis(trimethylsilyl)acetylene. These preparations represented a superior route to these main group heterocycles.

Table 1. Main Group Heterocycles by Metallacycle Transfer from Zirconium.

Electrophile	Product	Element, (Yield)
1. PhECl ₂		E = P, (85%) As, (76%) Sb, (78%) Bi, (70%)
2. E ₂ Cl ₂		E = S, (55%) Se, (50%)
3. S ₂ Cl ₂		(65%) ^a

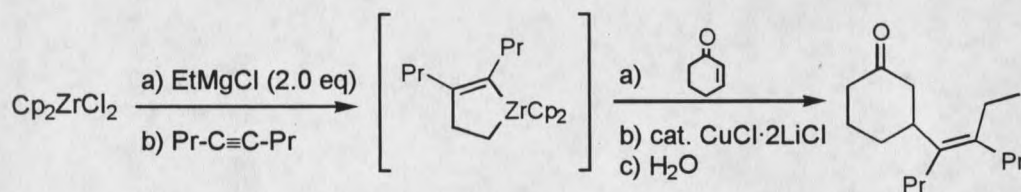
^a Based on recovered starting material.

Although both the sp^2 and sp^3 carbons bound to zirconium effectively transmetallate to main group electrophiles, they have sufficiently different nucleophilicity to allow selective mono functionalization. The sp^3 carbon reacts readily with one equivalent of electrophile, whereas initial reaction at the sp^2 carbon is virtually unknown. Deuteration of a zirconocyclopentene with deuterio-methanol (1 eq) followed by aqueous work-up afforded the cyclopentane in excellent yield with deuterium incorporation solely on the methyl group. Treatment of the zirconocycle with methanol (1 eq) followed by an acidic deuterium oxide quench provided the cyclopentane with deuterium incorporation solely at the vinylic position.⁸ Other electrophiles, such as iodine also followed the same reactivity pattern (Scheme 3).⁹



Scheme 3

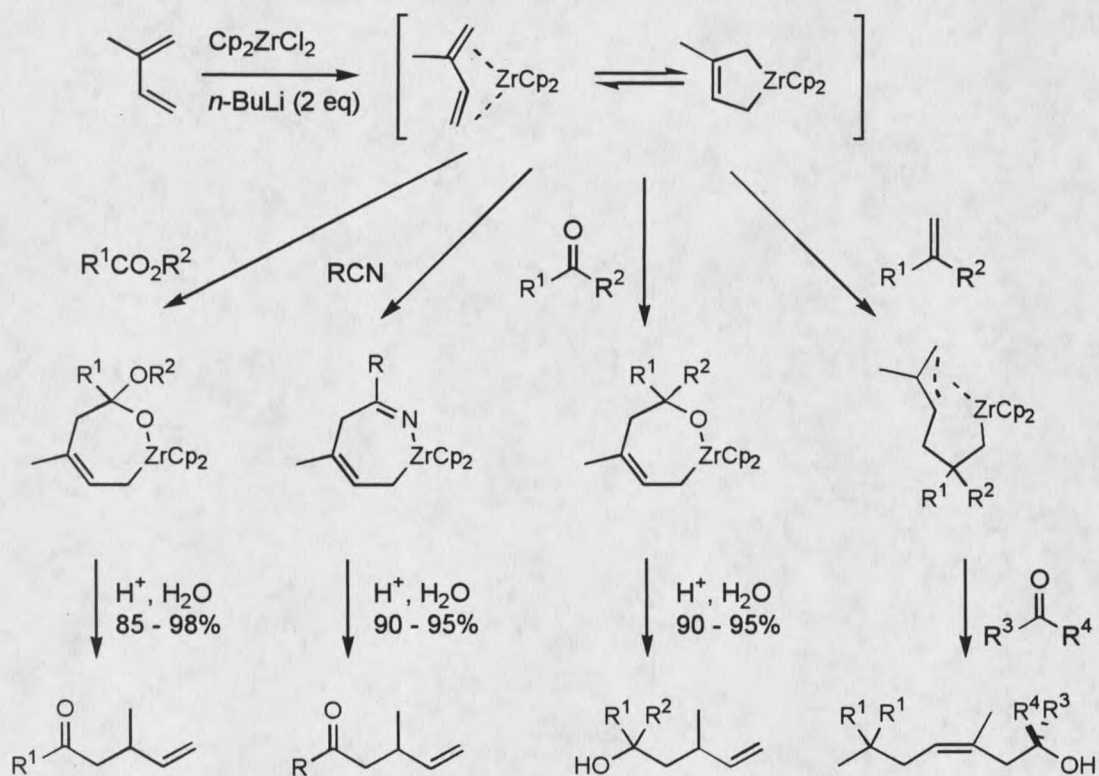
Lipshutz has shown that catalytic Cu(I) converted the zirconium bound sp^2 carbon of a zirconocyclopentene into a highly reactive cuprate intermediate that rapidly undergoes 1,4-addition to α,β -unsaturated enones (**Scheme 4**).¹⁰



Scheme 4

Zirconocyclopent-3-enes, derived from the reaction of Cp_2ZrCl_2 reduced *in situ* in the presence of *conjugated* dienes (e.g. isoprene), demonstrate diverse reactivity and high nucleophilicity (**Scheme 5**).^{4b} They may be viewed as allylzirconocene derivatives which react with polar or non-polar π -systems. It is

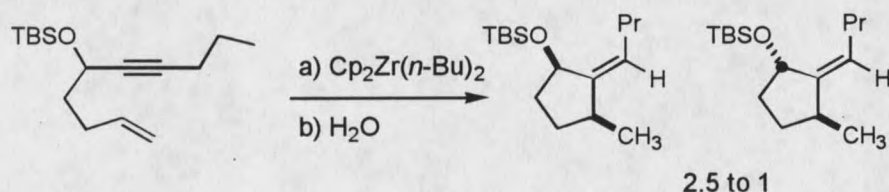
interesting to note that polar π -systems reacted adjacent to the methyl group while nonpolar π -systems reacted with the less hindered carbon.



Scheme 5

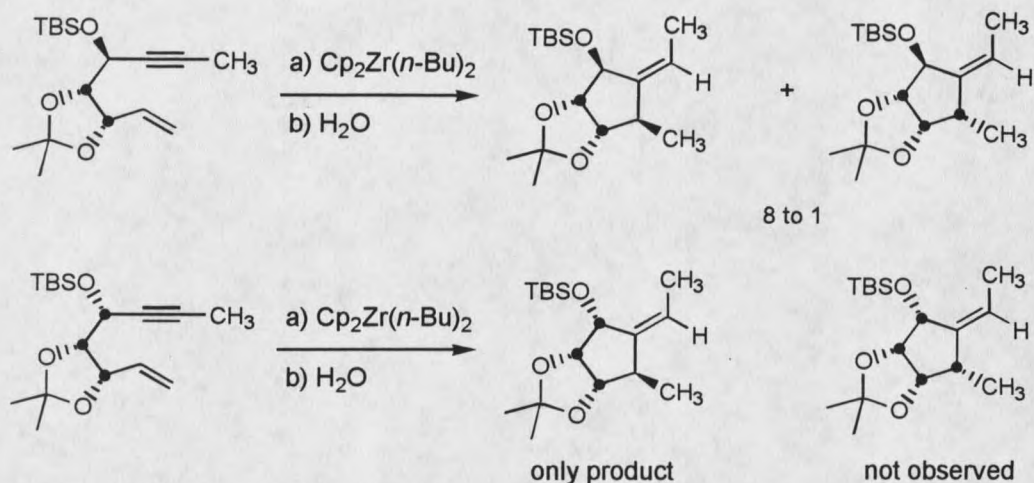
2.2 Diastereoselectivity in Zirconium(II) Enyne Cyclizations

The elucidation of processes that control the relative and absolute stereogenesis of chemical transformations is critical for mechanistic interpretations and planning synthetic strategies. In 1989, RajanBabu and Nugent described the first example of substrate control in stereoselective “zirconocene” mediated enyne cyclizations.¹¹ Cyclization of 6-siloxy-non-9-en-4-yne afforded *cis*- and *trans*-alkylidene-cyclopentanes in a 2.5 to 1 ratio in 94% overall yield (**Scheme 6**).



Scheme 6

Armed with the knowledge that “zirconocene” mediated enyne cyclizations occurred with moderate substrate derived stereocontrol, they prepared an enantiomerically pure 4 β ,5,6 α -trisubstituted enyne that cyclized to give diastereomeric alkylidines in an 8 to 1 ratio in 71% overall yield (**Scheme 7**). The epimeric trisubstituted enyne provided only one diastereomeric product.



Scheme 7

No rational analysis of the influences of ring substitution on stereoselection of zirconium(II) mediated enyne cyclizations was undertaken until Livinghouse and Lund, in a preliminary communication, examined a series of singly substituted enynes.¹² Excellent levels of diastereoselection were observed in that each example gave only a single diastereomeric product (**Table 2**). The intermediate zirconocyclopentenones formed from the zirconium(II) enyne cyclizations can equilibrate to the thermodynamically most stable product, although rationalization of the stereochemical outcome has also been based on kinetic arguments.¹³ Further exploration of stereoselection in zirconium(II) mediated cyclizations of monosubstituted enynes constitutes part of this thesis.¹⁴

Table 2. Diastereoselective Cyclizations with $\text{Cp}_2\text{Zr}(n\text{-Bu})_2$

Entry	Substrate	Product	Yield ^a
1	$\text{R}^1 = \text{TBS}, \text{R}^2 = \text{TMS}$		79%
2	$\text{R}^1 = \text{TBS}, \text{R}^2 = \text{SCH}_3$		53%
3	$\text{R}^1 = \text{Li}, \text{R}^2 = \text{SCH}_3$	$\text{R}^1 = \text{H}, \text{R}^2 = \text{SCH}_3$	70%
4	$\text{R} = \text{TBS}$		68%
5	$\text{R} = \text{Li}$	$\text{R} = \text{H}$	70%
6	$\text{R} = \text{TBS}$		78%
7	$\text{R} = \text{Li}$	$\text{R} = \text{H}$	81%

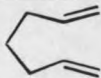
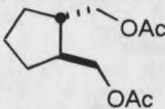
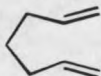
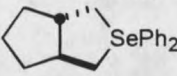
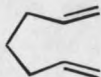
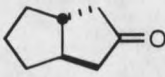
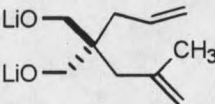
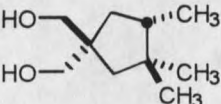
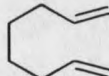
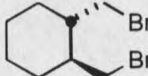
^a Isolated yield. No other diastereomers observed.

2.3 Zirconium(II) Diene Cyclizations

The zirconium(II) carbometallation reactions of non-conjugated dienes remained unexplored until 1989, when Nugent and Taber showed that dienes were efficient substrates for reductive bicyclization.¹⁵ The intermediate zirconium metallacyclopentanes can be trapped with a variety of electrophiles such as Br_2 , main group electrophiles (including BCl_3),¹⁶ and CO , usually in excellent yield.

(Table 3). Note in entry three the major diastereomer was the *trans*-bicyclo[3.3.0]octane.

Table 3. Cyclization of Dienes with $\text{Cp}_2\text{Zr}(n\text{-Bu})_2$ and varied Electrophilic Capture

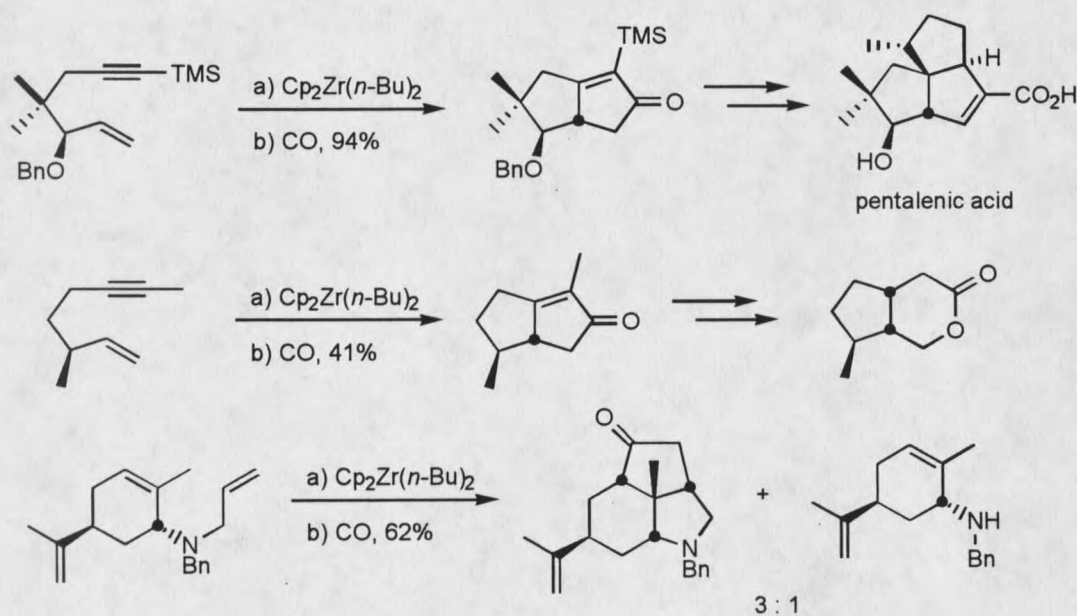
Entry	Diene	Electrophile	Product	Yield ^a
1		O_2		80% ^b
2		Ph_2SnCl_2		67%
3		CO		53% ^c
4		H^+		73%
5		Br_2		63%

^a Isolated yield of major diastereomer (shown). For entries 1 and 2 the presence of another diastereomer was not disclosed. ^b The crude product was treated with acetic anhydride / pyridine prior to chromatography. ^c 14 to 1 diastereomer ratio in 53% combined yield.

The use of Cp^*ZrCl_3 (Cp^* = pentamethylcyclopentadienyl anion) instead of Cp_2ZrCl_2 reversed the usual trend of *trans*-cyclopentanes (or *trans*-bicyclo[3.3.0]octanes) and gave *cis*-substituted cyclopentanes (or *cis*-bicyclo[3.3.0]octanes) as the major diastereomer. The high cost of Cp^* and the need for stoichiometric quantities of Cp^*ZrCl_3 has precluded the adaptation of this reagent in synthesis. However, the discovery that Cp_2ZrCl_2 could be used

$$\text{C}_6\text{H}_5\text{CH=CH}_2 + \text{C}_6\text{H}_5\text{CH=CH}_2 \xrightarrow[\text{C}_6\text{H}_5\text{CH=CH}_2]{\text{C}_6\text{H}_5\text{CH=CH}_2} \text{C}_6\text{H}_5\text{CH=CH}_2$$

transformed into a functionalized bicyclic enone which can be manipulated into more elaborate structures. Negishi's synthesis of pentalenic acid²⁰ and iridomyrmecin²¹ and Mori's formal synthesis of dendrobine^{22b} all demonstrate the utility of this powerful method (**Scheme 9**). In the last example, the substrate suffers from fragmentation of the nitrogen and propenyl moiety (c.f., **Scheme 2**).

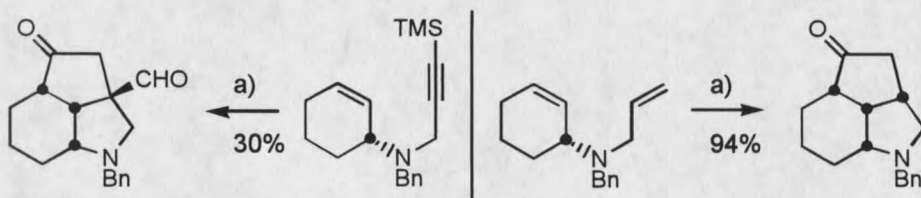


Scheme 9

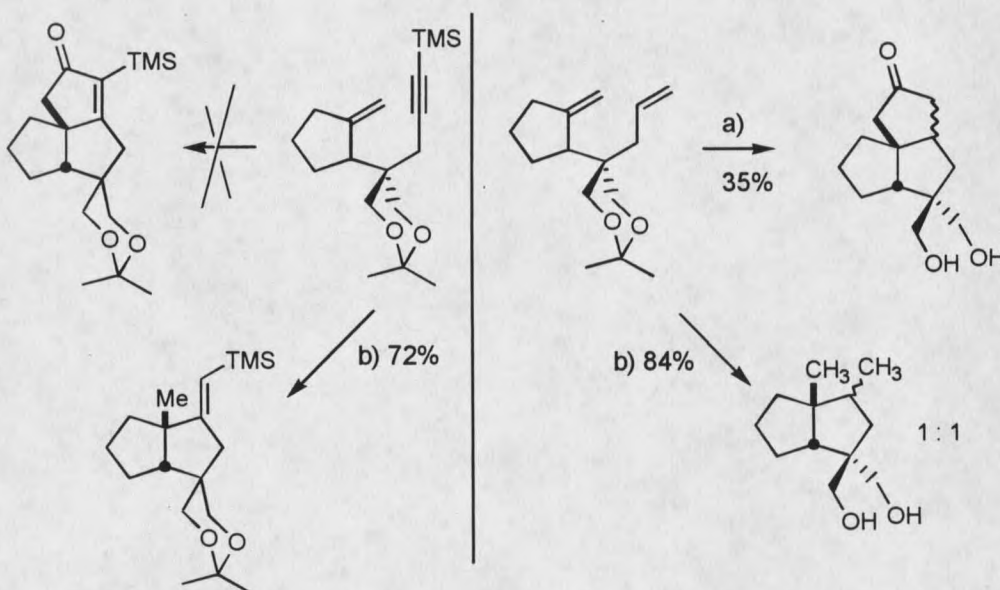
Yields of ketones obtained from zirconocycles are consistently better when derived from dienes compared to their enyne counterparts (**Scheme 10**). In the first example, the diene underwent cyclization and carbonylation in excellent yield, whereas the enyne was a poor substrate.²² The enyne in example one uniquely incorporated two equivalents of CO. In the second example, the corresponding enyne failed to incorporate any CO at all.²³ It is important to note that when the

intermediate zirconocyclopentene was quenched with water, the cyclized product was obtained in high yield. Zirconocyclopentanes have been converted into cyclopentanones by insertion of an isonitrile followed by hydrolysis of the resulting imide.²⁴

Example 1



Example 2



Reagents: (a) i. $\text{Cp}_2\text{Zr}(n\text{-Bu})_2$; ii. CO; iii. H_3O^+ ; (b) i. $\text{Cp}_2\text{Zr}(n\text{-Bu})_2$; ii. 10% HCl

Scheme 10

Several other highly successful methods exist for preparing bicyclic cyclopentenone derivatives. The elegant method of Buchwald used a catalytic amount of $\text{Cp}_2\text{Ti}(\text{PMe}_3)_2$ and a stoichiometric amount of isonitrile to convert enyne into bicyclopentenones (in 40-80% yield).²⁵ The key to the successful implementation of this methodology required the use trialkylsilylnitriles, which are in equilibrium with a small amount of trialkylsilylisonitrile; this essentially reduces the concentration of free isonitrile in solution to almost zero. The methodology worked with substrates that fail with titanocene or zirconocene, including enynes containing sensitive functional groups (e.g., esters, oxygen tethers). The method as initially described may not see widespread adoption because the extremely air and moisture sensitive nature of the catalyst necessitates that the reactions be performed in a dry box. However, the *in situ* generation of $\text{Cp}_2\text{Ti}(\text{PMe}_3)_2$ from air-stable Cp_2TiCl_2 and two equivalents of *n*-BuLi in the presence of PMe_3 appears to provide an easy route to an equally active catalyst.²⁶ The method is perhaps most limited in requiring only non-terminal alkynes. However, since this writing, a communication by Buchwald has appeared that employs the commercially available $\text{Cp}_2\text{Ti}(\text{CO})_2$ in catalytic quantities.²⁷ This methodology worked successfully with a variety of enynes containing sensitive functionality, 1,2-disubstituted alkenes and one example of a primary alkyne. However, the reaction required 2.3 atm of CO. Buchwald

suggested that the two catalyst systems do not go through the same titanacyclopentene intermediate, but offered no explanation.

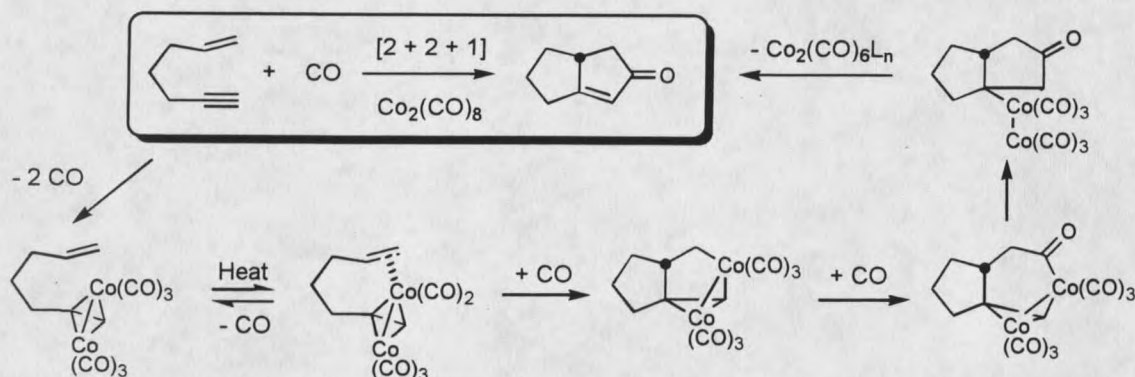
A second communication by Buchwald describing the synthesis of enones employing a nickel catalyst has appeared.²⁸ This catalyst system used a ligand derived from 1,2-diaminocyclohexane. The focus of this work is clearly to develop an asymmetric variation of this reaction.

2.5 The Pauson-Khand Reaction

Perhaps one of the most convergent methods for the synthesis of cyclopentenones is the Pauson-Khand reaction, which represents a formal [2+2+1] cycloaddition involving an alkyne, alkene and carbon monoxide (**Scheme 11**). This subject has been extensively reviewed.²⁹ The Pauson-Khand reaction successfully generates cyclopentenone derivatives by both inter- and intramolecular variations. In a typical procedure, the enyne is mixed with one equivalent of $\text{Co}_2(\text{CO})_8$ and then heated (either at reflux or in a sealed tube) for several hours to days. Common solvents are heptane, toluene and acetonitrile. The synthetic utility of the Pauson-Khand reaction was enhanced when it was disclosed that silica gel, tertiary amine *N*-oxides and DMSO markedly accelerate the reaction.³⁰ The Pauson-Khand reaction works with enynes containing sensitive functionality, including esters,

oxygen tethers and primary alkynes. (The first example of a zirconocene mediated cyclization-carbonylation reaction of a pseudo *terminal* alkyne was recently reported).³¹

The alkyne•Co₂(CO)₆ complexes formed in the initial stages of the reaction are typically air-stable compounds and are readily isolated and characterized. No later intermediates in the mechanistic pathway have yet been identified. The next step requires heat or amine oxides to promote CO disassociation followed by alkene complexation to the vacant coordination site on cobalt. Irreversible alkene insertion then occurs in the rate determining step, also setting the stereochemistry in chiral substrates. Next, migratory CO insertion followed by reductive elimination furnishes the enone as its Co₂(CO)₆ complex. Another reductive elimination affords the final product and regenerates the Co₂(CO)₆L_n metal catalyst. In principle, the thermal Pauson-Khand reaction should be catalytic. Indeed, low levels of catalytic turnover have been observed, but the high temperatures required for CO disassociation probably decompose the transient unbound Co₂(CO)₆L_n catalyst (*vide infra*, section 3.5).²⁹



Scheme 11

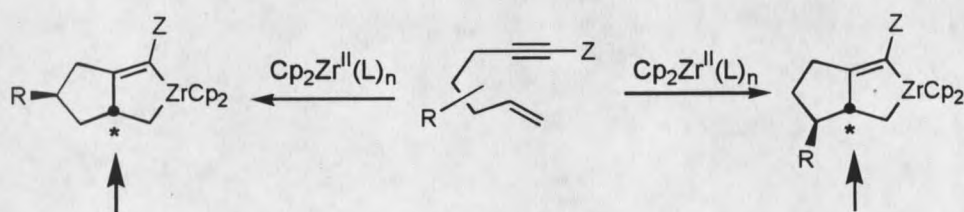
A major disincentive to the large scale use of the classical Pauson-Khand reaction rests in its requirement for stoichiometric quantities of $\text{Co}_2(\text{CO})_8$.³² However, Jeong and collaborators recently reported that selected 1,6-enynes could be converted to the corresponding cyclopentenones in the presence of CO (at 4-5 atm pressure), 3-5 mol % $\text{Co}_2(\text{CO})_8$ and 10-20 mol % $(\text{PhO})_3\text{P}$ at 120 °C.³³ Although highly significant as one of a very limited number of successful accounts involving truly catalytic quantities of $\text{Co}_2(\text{CO})_8$,³⁴ the relatively strenuous conditions of the Jeong procedure may discourage its widespread adoption in many laboratory settings or for use with sensitive substrates. The development of a photo-promoted catalytic Pauson-Khand reaction requiring only 1 atm of CO constitutes part of this thesis.

A variety of other reagents capable of effecting the Pauson-Khand reaction also exist. The tungsten based reagent $\text{W}(\text{CO})_5 \cdot \text{THF}$ has been shown to promote the Pauson-Khand reaction in a batch-catalytic manor, but in only poor to moderate

(ca. 25-65%) yields.³⁵ The Pauson-Khand reaction is also promoted by iron carbonyl complexes under strenuous conditions (2 eq $\text{Fe}(\text{CO})_5$, 135-140 °C, 4-5 atm CO, 21-64 h) and with poor to moderate yields.³⁶ Recently, Sato demonstrated that the $(\eta^2\text{-propenyl})\text{Ti}(\text{O-}i\text{-Pr})_2$ complex could mediate carbonylation of enynes.³⁷ Only two examples were given, both in poor yield. Finally, bicyclic enones are obtained from by treating a 1,6-diyne with catalytic $\text{Rh}(\text{acac})(\text{CO})_2$ in the presence of stoichiometric trialkylsilane under 15 atm of CO.³⁸

3. Results and Discussion

The elucidation of processes that control relative and absolute stereogenesis has become central to the practice of selective organic synthesis. In this context, transformations mediated by transition metals have gained increasing recognition as a powerful means for achieving reaction selectivity. This characteristic is derived, in part, from the ability of transition metals to serve as vehicles for both substrate³⁹ and reagent⁴⁰ based stereocontrol. The intramolecular Pauson-Khand reaction has been utilized quite frequently for the construction of fused 2-cyclopenten-1-ones (*vide supra*, section 2.5). Although numerous studies addressing the diastereoselective nature of this cobalt-centered annulation have appeared, comparatively little has been reported regarding the corresponding $\text{Cp}_2\text{Zr(II)}$ mediated cyclizations.⁴¹ The potential utility of Group IV metal templated cyclizations for the synthesis of bioactive [3,4] fused cyclopentenones warranted



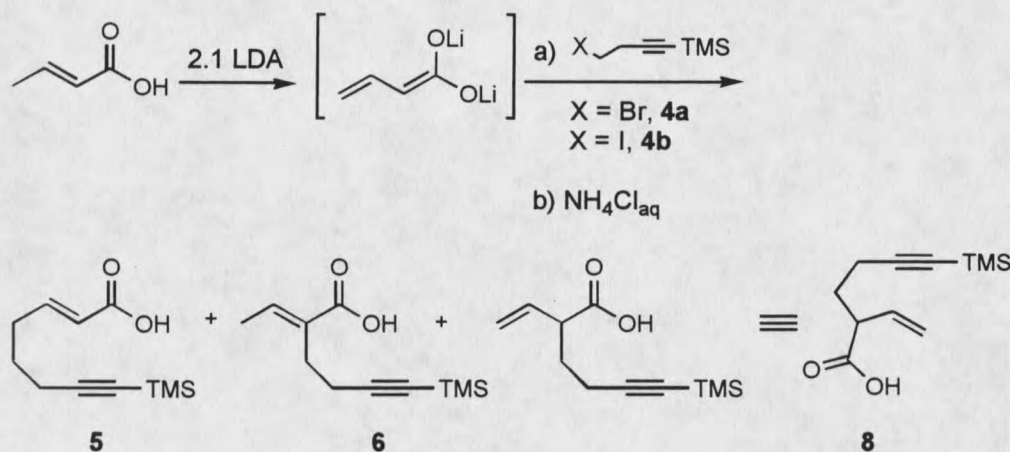
Scheme 12

continuation of the initial investigations of substrate directed stereocontrol in Zr-enyne cyclizations (**Scheme 12**).^{11,12}

3.1 Preparation of 5-Substituted-1,6-Heptenynes

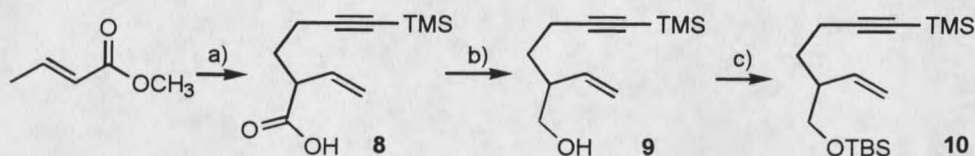
The first substrate targeted for study was 5-hydroxymethyl-1-trimethylsilyl-hept-7-en-1-yne **9** (**Scheme 13**). The analogous 5-hydroxy substrate showed excellent stereoselectivity in zirconocene mediated cyclizations (*vide supra*, section 2.2) and the stereochemistry of the product should be readily determined by NOE spectroscopy. Furthermore, the potential products derived from the 5-hydroxymethyl bearing substrate would closely resemble the prostaglandin skeleton. Early work by Katzenellenbogen prompted us to explore selective deconjugative α -alkylation of the dianion derived from crotonic acid.⁴² Unfortunately, this methodology is most successful with activated electrophiles (e.g. allylic and benzylic). The homopropargylic electrophiles **4** and **4b** are prone to elimination, further exacerbating the problem. Simple nonactivated electrophiles less prone to eliminate, such as butyl bromide, alkylated in moderate yield to provided the α -alkylated deconjugated acid. However, with competing elimination and γ -alkylation reactions, at best the desired product **8** was obtained inconsistently in exceedingly poor yield (< 10%) (**Scheme 14**). Of course, various solvents and

solvents and solvent mixtures (THF, Et₂O, 1,2-DME), bases (LDA, lithium diethylamine, KHMDS), and additives (HMPA, triethanolamineborate)⁴³ were tried and found to be ineffectual.



Scheme 13

Alkylation of methyl crotonate derived enolates proved somewhat more fortuitous. The best results afforded the desired *deconjugated* α-alkylation product ester **8** in 8% yield, which was reduced (LiAlH₄) to provide the desired substrate **9** (which was also protected as its TBS ether **10**) (**Scheme 14**). Although this procedure provided analytical quantities of the desired product, it offered no entry into a useable supply of material for serious study. The zirconocene cyclization studies concerning this compound are therefore incomplete.



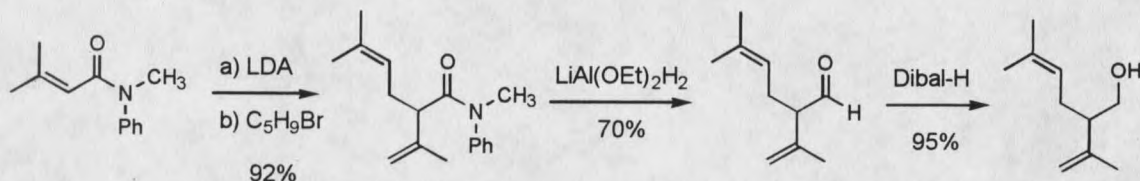
Reagents: (a) i. LDA; ii **4b**; (b) LAH; (c) TBDMSCI-imidazole

Scheme 14

Another avenue towards the desired enyne **10** was envisaged by alkylation of a crotonic acid derived Weinreb amide, because of the proven utility of *alkylation* of acetic acid Weinreb amides.⁴⁴ The crotonic acid Weinreb amide was deprotonated (LDA/THF, -78 °C) and treated with allylbromide as a model electrophile. However, no products derived from alkylation were observed, nor was any starting material recovered. This result was consistent with the observation that Weinreb amides bearing alpha substituents can undergo a unwelcomed retro-ene reaction after enolization.⁴⁵ Although possible, this mode of reactivity does not appear to happen with acetic acid Weinreb amides.

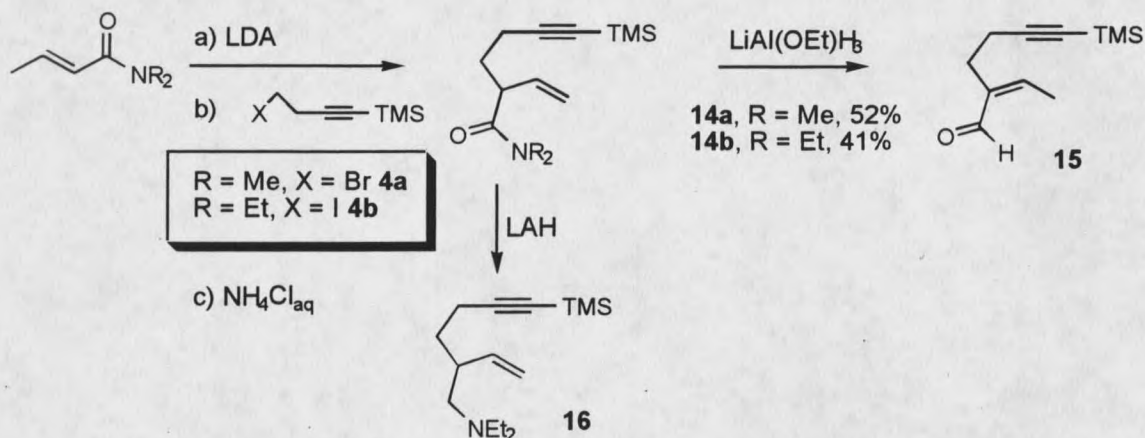
The deconjugative alkylation of crotonic acid tertiary amides was next examined. The alkylation of 3-alkyl (cyclic or acyclic) substituted crotonamides has been exploited by Sniekus for natural product synthesis (**Scheme 15**).⁴⁶ Although the successful conversion of amides to alcohols usually requires harsh reaction conditions,⁴⁷ Brown's $\text{LiAl}(\text{OEt})_2\text{H}_2$ reagent appeared to be an excellent candidate for a mild reduction of the deconjugated amides.^{46,48} Alkylation of *N*-methyl aniline crotonamide was initially investigated because these tertiary amides generally

reduce directly to the alcohol with LiAlH_4 . Unfortunately, alkylation of *N*-methyl aniline crotonamide with either bromo- or iodohomopropargylic electrophiles **4a** or **4b** was unsuccessful.



Scheme 15

Fortunately, the deconjugative alkylation of dialkyl tertiary crotonamides under identical conditions gratifyingly afforded the desired α -alkylated *deconjugated* amides **14a** and **14b** as the sole products, albeit in low (30-50%) yield (**Scheme 16**). For reproducible yields the choice of which electrophilic halide employed was found to be critical. The dimethyl and diethyl amide enolates required 1-iodo-4-trimethylsilyl-3-butyne **4a** and 1-bromo-4-trimethylsilyl-3-butyne **4b**, respectively, for appreciable product formation. It is interesting to note that two closely related amide enolates could have markedly different reactivities.

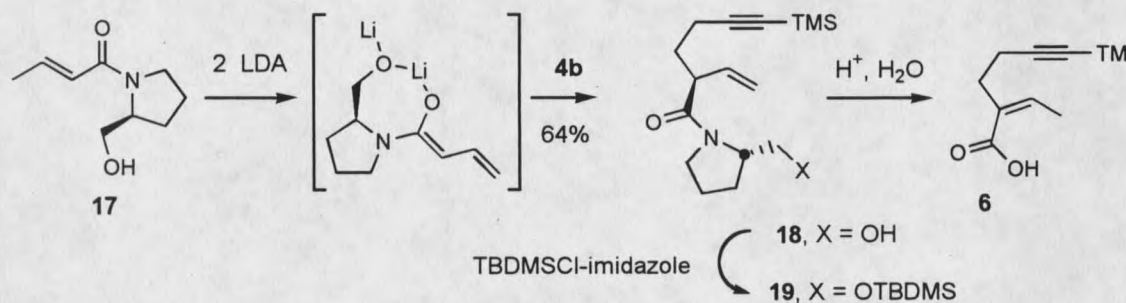


Scheme 16

With enynes **14a** and **14b** in hand, their reduction to the corresponding alcohols was examined. Surprisingly amides **14a,b** were found to be completely impervious to Brown's $\text{LiAl(OEt)}_2\text{H}_2$ reducing reagent. Eventually it was discovered that treating the tertiary amides at $-10\text{ }^\circ\text{C}$ with the monoethoxy complex LiAl(OEt)H_3 effectively reduced the amide to the reconjugated aldehyde **15** (Scheme 16). Apparently, the stabilizing influence of a 3-alkyl substituent (c.f., Scheme 15) is required to prevent reconjugation.⁴⁹ A variety of mild work-ups, such as inverse quenching into buffered solutions followed by *immediate* reduction to the alcohol, offered no improvement. However, this new reduction procedure represents a potentially valuable and mild method for the reduction of tertiary amides. Other reagents proven to be effective for converting tertiary amides to alcohols were investigated, including the ate complex derived from diisobutyl

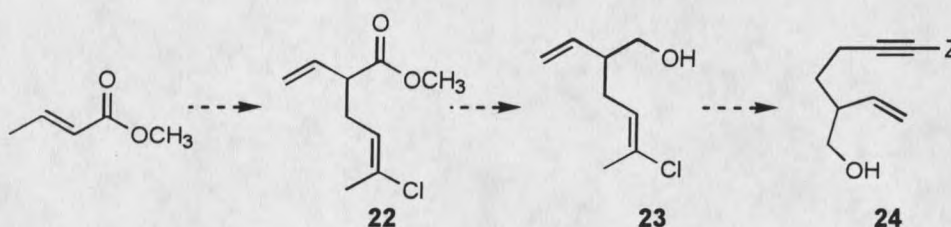
aluminum hydride⁵⁰ (Dibal-H) and *n*-butyllithium; lithium triethylborohydride⁵¹ (Super-Hydride[®]) and borane-lithium pyrrolidide.⁵²

Because β -hydroxy amides are readily hydrolyzable, Evans' prolinol based chiral auxiliary was examined for these alkylations.^{53,54} Although Evans had not demonstrated the utility of deconjugative alkylations, the Evans' chiral amide proved to be a remarkably effective alkylating agent (**Scheme 17**). The desired enyne **18** was procured in 64% isolated yield. The absolute stereochemical assignment of **18** is based on literature precedent.⁵³ Unfortunately, hydrolysis conditions for this β -hydroxy amide proved too harsh and resulted in reconnection.



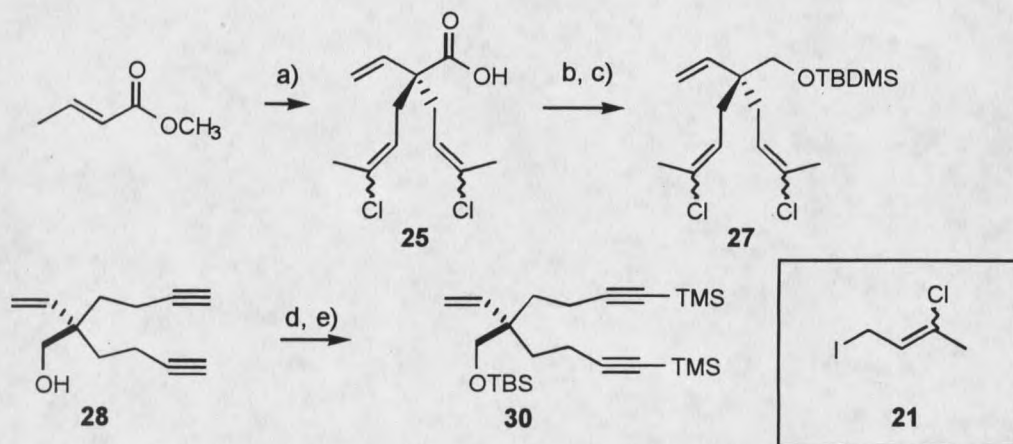
Scheme 17

The last attempt for an efficient synthesis of enyne **9** utilized a 4-bromobut-1-yne equivalent, as depicted in **Scheme 18**. It was anticipated that the activated electrophile 1-iodo-3-chloro-2-butene **21** should be a superior electrophile, without suffering from problematical elimination. The conversion to the terminal acetylene should proceed according to literature precedent.⁵⁵



Scheme 18

The commercially available 1-chloro-3-chloro-2-butene was converted quantitatively (NaI, acetone) into the light sensitive 1-iodo-3-chloro-2-butene **21** immediately before use. This allylic iodide was added to the enolate of methyl crotonate (LDA, -78°C) and provided the unexpected *dialkylation* product **25** in 88% unoptimized yield (Scheme 19). While experiments were undertaken to favor the monoalkylation product, triene **25** was converted to endiyne **30** as a test substrate. Triene **25** was reduced to the alcohol (LiAlH_4), silylated and treated with potassium 3-aminopropanamide to afford the endiyne **28**. Even though the silylether **27** was desilylated by the harsh conditions employed for the elimination, yields of endiyne **30** were found to improve dramatically when the silylated triene **27** was employed (83%, both steps). Endiyne **28** was subsequently converted to the bis-silylated enyne **30** [1. (a) *n*-BuLi; (b) TMSCl; (c) HCl_{aq} ; 2. TBDMSCl-imidazole (92% overall)]. This endiyne was subjected to zirconium(II) mediated cyclization conditions, afforded a plethora of unidentified products. Attempts to maximize formation of the monoalkylation product **22** were unsuccessful.



Reagents: (a) i. LDA; ii. **21**; (b) i. LAH; (c) i. TBDMSCl-imidazole; ii. $\text{KHN}(\text{CH}_2)_3\text{NH}_2$ (83%); (d) i. 2.1 eq $n\text{-BuLi}$; ii. 2.2 eq TMSCl iii. 10% HCl_{aq} , 6 hr (95%); (e) TBDMSCl-imidazole (97%).

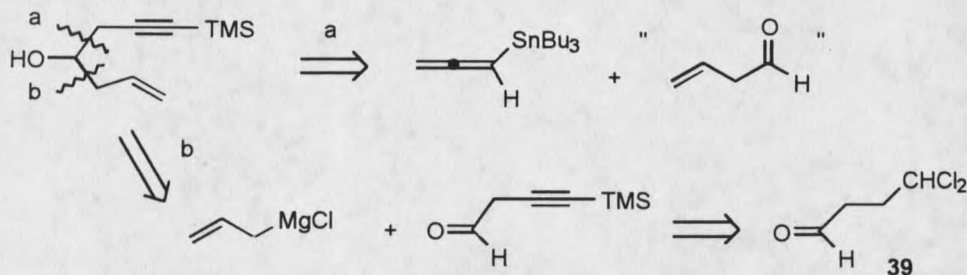
Scheme 19

Fortunately, the three novel amido enynes **14a,b** and **19** and the amine **16** were shown to be extraordinary substrates for zirconocene mediated enyne cyclization (*vide infra*, section 3.3).

3.2 Preparation of 4-Substituted-1,6-Heptenyne

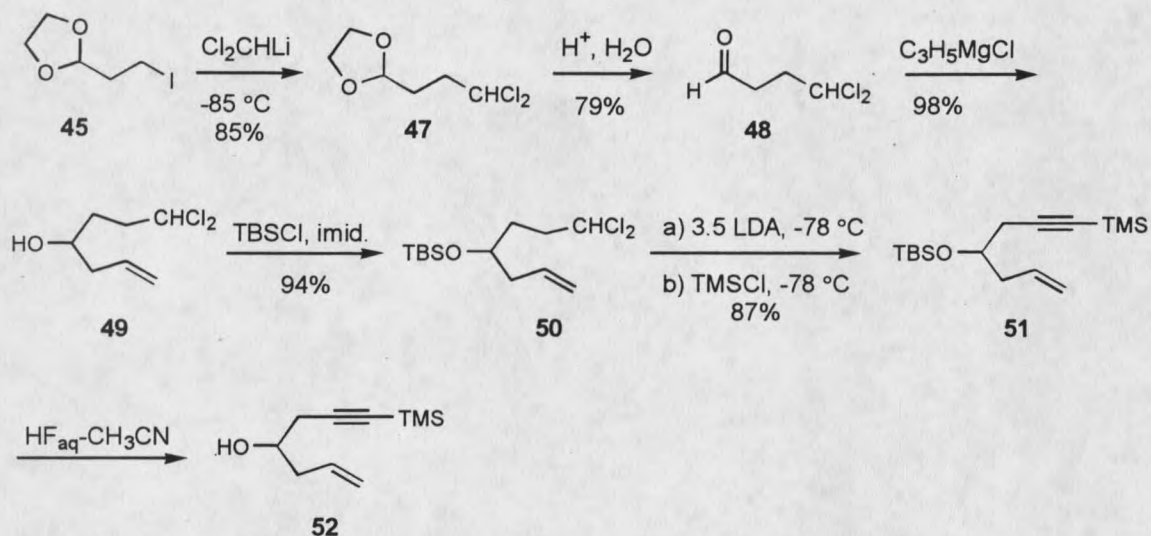
With a variety of 5-substituted-1,6-heptenyne in hand, the preparation of a series of 4-substituted-1-trimethylsilyl hept-6-en-1-yne afforded the next challenges. Retrosynthetic analysis of the desired enynes indicated that rupture of bond *a* would require the use of an allenic nucleophile and an unknown aldehyde. Cleavage of bond *b* would greatly simplify the nucleophilic component but would necessitate the use of an extremely unstable aldehyde. The solution was to use a

novel 4-trimethylsilyl but-3-yn-1-al equivalent (**Scheme 20**) based on the Normant acetylene synthesis,⁵⁶ and proceed via path *b*.



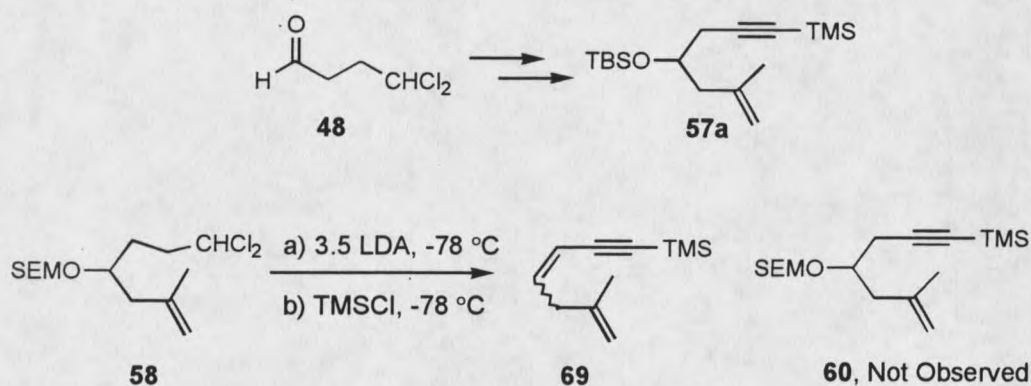
Scheme 20

The aldehyde surrogate, 4,4-dichlorobutanal **48**, was prepared in 67% overall yield by the addition of dichloromethyl lithium to bromo- or 2-(2'-iodoethyl)-1,3-dioxolane **45** at -85 °C, followed by hydrolysis of the dioxolane moiety (2:1 acetone:10% HCl_{aq}) (**Scheme 21**). Addition of allyl magnesium chloride to the aldehyde was uneventful and furnished the key intermediate **49** in 98% yield. *O*-silylation (TBSCl-imidazole) and conversion of the geminal dichloride **50** into terminal acetylene **51** required slow *portion-wise* addition of LDA (3.5 eq) at -78 °C followed by electrophilic capture with TMSCl⁵⁷ at -78 °C. This protocol provided the 1,6-enynes **51** and **52** after *O*-desilylation (HF_{aq}-CH₃CN).



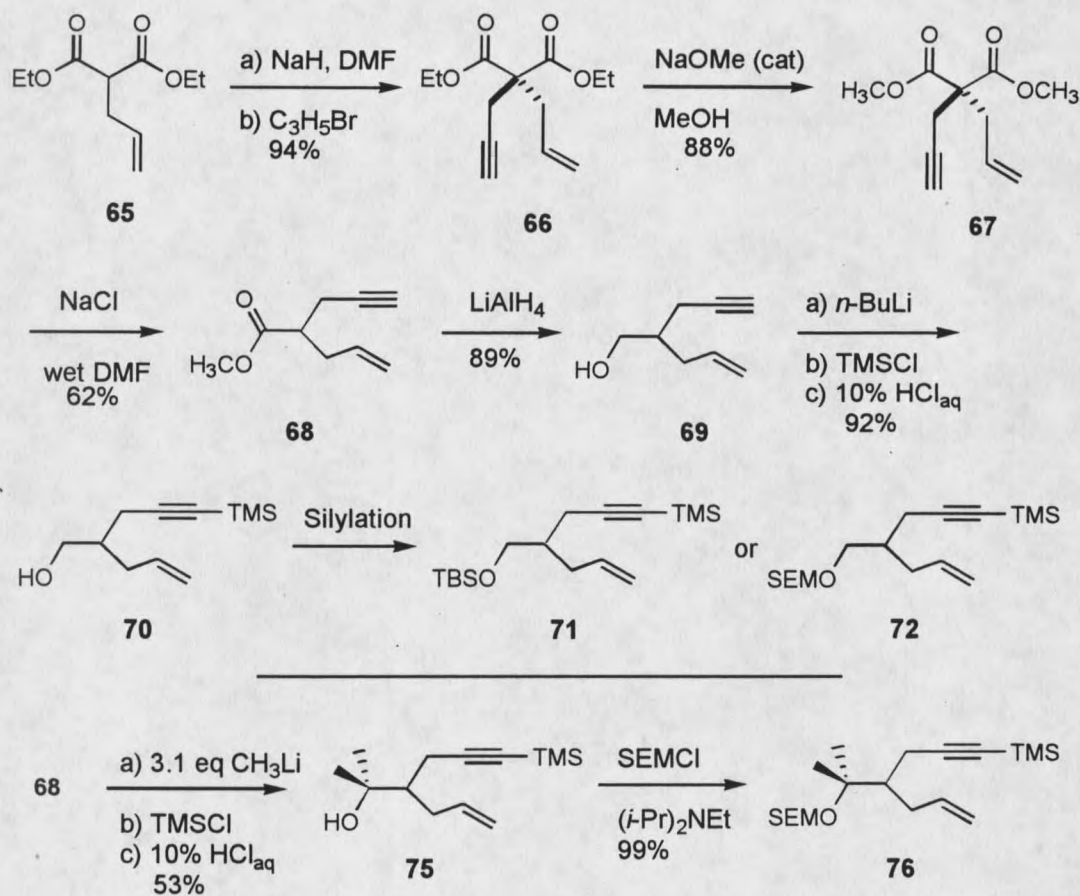
Scheme 21

A series of 4-substituted-6-methyl-1-trimethylsilyl hept-6-en-1-ynes was then prepared in a manner analogous to that used to prepare **51**, except aldehyde **48** was treated with methallyl magnesium bromide (**Scheme 22**). A SEM ether proved to be a much better leaving group than a TBS ether, and the only isolated material from the LDA mediated elimination was the bis-elimination product **69**. With an authentic sample of **69** in hand, it was found by G.C. analysis that **69** was present in the elimination reaction undertaken to form **57a**, although only as a minor component.



Scheme 22

The next targets were 4-hydroxymethyl-1-trimethylsilyl hept-6-en-1-yne and various derivatives. Alkylation of commercially available diethyl allyl malonate with propargyl bromide, *trans*-esterification to the methyl ester and decarboxylation (NaCl, wet DMF)⁵⁸ afforded key intermediate **68** (Scheme 23). The 4-(hydroxymethyl)-1-hepten-6-yne derivatives **71**, **72** and **76** were prepared by reduction [1. LiAlH₄; 2. (a) *n*-BuLi; (b) Me₃SiCl; (c) HCl_{aq}] and silylation [TBDMSCl-imidazole, DMF (48% overall for **71** or SEMCl/(*i*-Pr)₂NEt (37% overall for **72**)], or an exhaustive *methylation*/SEM ether formation protocol for **76** [1. (a) CH₃Li; (b) Me₃SiCl; (c) HCl_{aq}; 2. SEMCl/(*i*-Pr)₂NEt (34% overall)].



Scheme 23

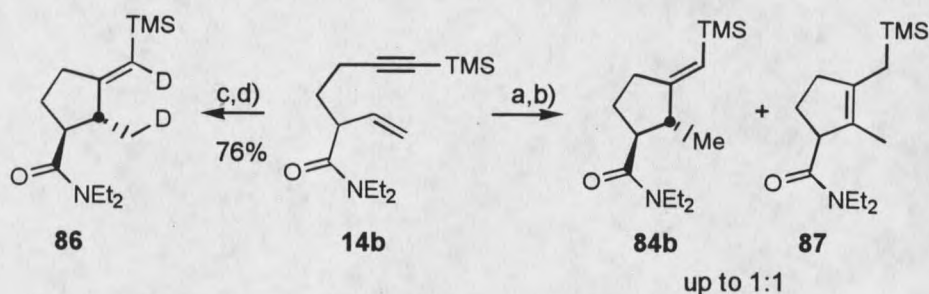
3.3 Cp₂(Zr) Mediated Enyne Cyclizations

With a variety of new substrates in hand, the focus of attention turned toward the further exploration of discoveries already communicated from these laboratories, specifically to the utilization of Cp₂Zr(II) complexes for the annulation of 2,3-disubstituted alkylidenecyclopentane derivatives. Zirconocene mediated

cyclization of enynes bearing carboxamido moieties at the 3-position (e.g., **14a,b** and **19**, counting from the alkene) initially proved problematic (c.f., **Scheme 24**), unlike their previously cyclized hydroxy substituted counterparts **80** and **81** (entries 1 and 2, **Table 4**). Although cyclization could be achieved to some extent using the standard set of reaction conditions, substrate to product conversion was typically below 70% even when 2.1 equiv of $\text{Cp}_2\text{Zr}(n\text{-Bu})_2$ was utilized. [The standard protocol involves treatment of 1 equiv Cp_2ZrCl_2 in THF with $n\text{-BuLi}$ (2 equiv) at $-78\text{ }^\circ\text{C}$ followed by the addition of the appropriate enyne substrate and subsequent stirring ($-78\text{ }^\circ\text{C}$, 0.5 h then $25\text{ }^\circ\text{C}$, 12 h) to generate the corresponding zirconocyclopentene].² In light of the possibility that **14a,b** and **19** might be anomalous with respect to their rate of cyclization, we theorized that competitive decomposition of the active Zr(II) species might be responsible for the observed inefficiency of conversion. It was previously shown that complexation with 4-dimethylaminopyridine (DMAP) conferred enhanced stability on low valent zirconocene complexes.⁵⁹ In accordance with the foregoing hypothesis, cyclization of carboxamides **14a,b** and **19** were performed in the presence of 1 equiv each of $\text{Cp}_2\text{Zr}(n\text{-Bu})_2$ and DMAP. Unfortunately, the yields did not improve. When 2 equiv each of $\text{Cp}_2\text{Zr}(n\text{-Bu})_2$ and DMAP were utilized, the *efficiency of cyclization was gratifyingly restored for the above substrates*, to provide the alkylidenecyclopentanes **84a,b** and **85** in 91%, 93% and 94% isolated yield

respectively. These results constituted the first examples of *carboxamido containing substrates* to successfully undergo zirconium(II) mediated bicyclization. It was possible, that the carboxamido functionality was involved in a previously unobserved Zr-ligation effect, and may have been responsible for observed turpitude of the intended cyclization. In addition, for each of the above cases a very high level of stereoselectivity was observed as a consequence of substrate controlled cyclization. Specifically, the alkylidenecyclopentanes **84a,b** and **85**, the indicated products were formed in greater than 30:1, 99:1 and 50:1 isomeric purity, respectively, as determined by capillary G.C. These results are summarized in **Table 4**. In no cases were any other diastereomers observed.

For carboxamido enynes **14,b** and **19** the use of *strictly alkoxide-free butyllithium* was essential for the successful implementation of this cyclization strategy. Apparently alkoxides catalyze the isomerization of the initial alkylidenecyclopentane to the indicated cyclopentene (**Scheme 24**). A deuterium quench showed no deuterium incorporation α to the carbonyl.



Reagents: (a) 2 eq $\text{Cp}_2\text{Zr}(n\text{-Bu})_2$, 2 eq DMAP with trace *alkoxides*; (b) H_2O ; (c) 2 eq $\text{Cp}_2\text{Zr}(n\text{-Bu})_2$, 2 eq DMAP; (d) D_2O

Scheme 24

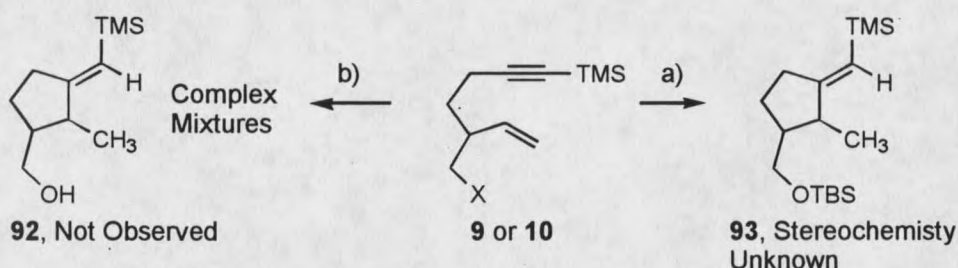
These stereochemical results are more easily understood when considered with the results previously reported from these laboratories for the cyclization of the allylic enynes **80** and **81** bearing a 5-silyloxy or hydroxy substituent (Table 4). Under the standard conditions (3 equiv of *n*-BuLi in the case of **80**), led to the formation of the *trans* alkylidenecyclopentanes **90** and **91** in a highly stereocontrolled fashion and in very good yield.¹² In the case of **80** two diastereomeric cyclization products were formed in a 14:1 ratio with the *trans* isomer predominating. For **81**, a single stereochemically homogeneous product **91** was formed as a consequence of $\text{Cp}_2\text{Zr(II)}$ mediated annulation. In the instances of **90** and **91**, evidence for relative stereochemistry derived both from NOE spectroscopy and single-crystal X-ray analysis. The splitting patterns and chemical shift data for the alkylidenecyclopentanes **90** and **91** were closely analogous with one another. Similarly, no observable NOE was detectable between H_a and H_b (although other strong NOE's from the C-2 methyl group to the vinylic methine

were observable). See Table 4 entry 1 for a definition of H_a and H_b . In the case of **91**, the *trans* relationship of the pendant methyl and hydroxy substituents as well as the *E* geometry of the alkylidene moiety were ultimately confirmed via single-crystal X-ray analysis of the corresponding 4-phenylbenzoate ester.¹² The assignment of relative stereochemistry for **84a,b** and **85** is tentative, as it rests strictly on the *absence* of NOE's between the vicinal hydrogens H_a and H_b and on analogy with the stereochemical outcome of the cyclizations that led to **90** and **91**.

In this connection, the cyclization of amine **31** might be seen as stereochemically informative (Table 4). Exposure of **31** to $\text{Cp}_2\text{Zr}(n\text{-Bu})_2$ under the standard set of experimental conditions (*no DMAP*) provided a predominant diastereomeric alkylidenecyclopentane **95** (stereoselectivity > 40:1) in 88% yield upon protonolysis. As in the previous cases, no detectable NOE was observed between H_a and H_b . However, a strong NOE was observable between H_b and the $\text{CH}_2\text{N}(\text{Et})_2$ methylene. In light of the corpus of data presented above, it is very likely that the stereochemical outcome of the cyclizations **84a,b** and **85** is analogous.

Unlike the 5-hydroxy substituted enyne **81** which cyclized in 81% yield, the diligently sought 5-hydroxymethyl enyne **9** failed to provide any recognizable cyclic products, although the enyne itself was *completely consumed during the course of the reaction* (Scheme 25). When converted to the corresponding TBS ether, enyne

7 cyclized in 50% yield under standard conditions as a sole diastereomer based strictly on capillary G.C. analysis. The highly acid-sensitive alkylidenecyclopentane **93** was inseparable from *unreacted* starting material by flash chromatography. Use of an excess of $\text{Cp}_2\text{Zr}(n\text{-Bu})_2$ (with or without the stabilizing influence of DMAP) conferred no better conversion but surprisingly resulted in an increase in side products. This reaction may have been further beleaguered by the necessity of performing the reaction on extremely small scales.

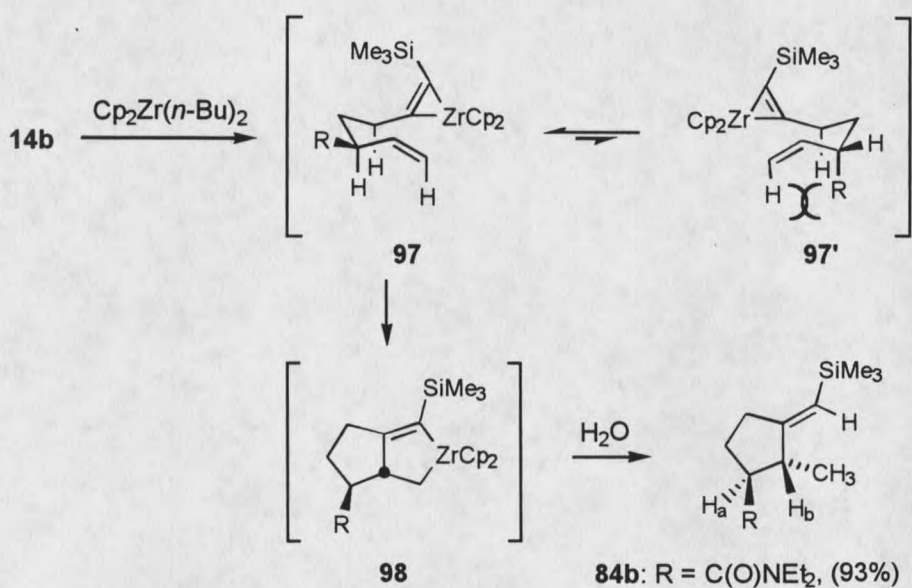


Reagents: (a) (**10**: X = OTBS) i. $\text{Cp}_2\text{Zr}(n\text{-Bu})_2$, -78°C to rt, 12 h; ii. H_2O , 50% conversion. (b) (**9**: X = OH) i. $n\text{-BuLi}$; ii. $\text{Cp}_2\text{Zr}(n\text{-Bu})_2$, -78°C to rt, 12 h; iii. H_2O

Scheme 25

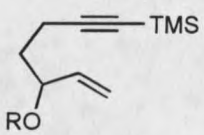
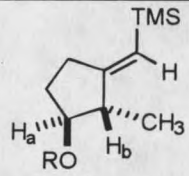
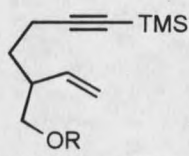
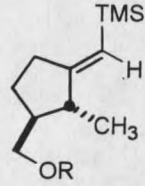
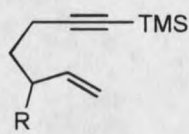
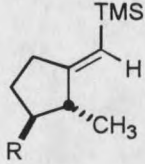
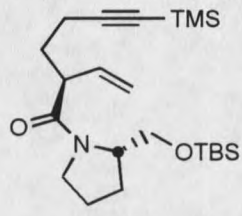
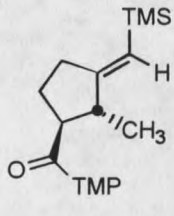
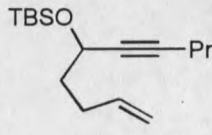
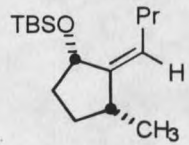
The excellent diastereoselectivity observed for the preceding five cyclizations of can be rationalized as arising from minimization of quasi 1,3-diaxial interactions and 1,3-allylic strain⁶⁰ by the adoption of conformers of the type **97** by the Cp_2Zr -alkyne complex prior to cyclization (**Scheme 26**). According to the following mechanistic interpretation, reductive elimination of butane from $\text{Cp}_2\text{Zr}(n\text{-Bu})_2$ followed by enyne complexation with loss of 1-butene² should generate the transient zirconacycloprenes **97** for which there are two extreme precyclization

conformers (e.g., **97** and **97'**). Conformers corresponding to **97'** are expected to be disfavored energetically as a consequence of 1,3-allylic strain between the proaxial substituent at C-5 and a methylene hydrogen bound to C-7 and by quasi 1,3-diaxial interactions. Accordingly, cyclization via conformers corresponding to **97**, in which allylic 1,3-strain is minimized, should occur preferentially to provide the exo substituted zirconocyclopentenenes **84b**. A complete summary of these cyclizations appears in **Table 4**.



Scheme 26

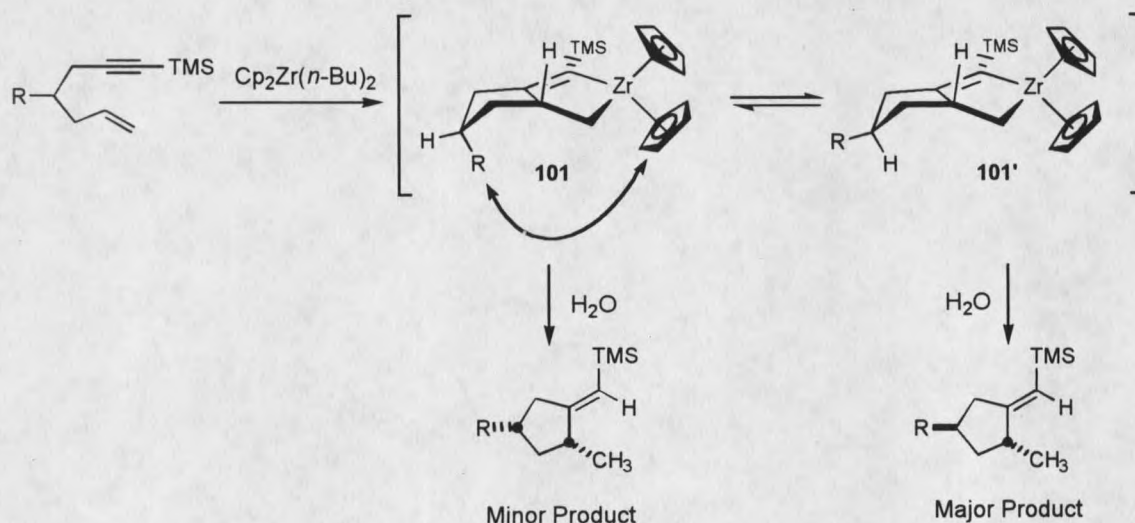
Table 4. Preparation of Alkylidene-cyclopentanes by Cyclization of Substituted Enynes with $\text{Cp}_2\text{Zr}(n\text{-Bu})_2$

Entry	Substrate	Product	Yield ^a
1 ^b 2 ^b	 80 , R = TBS 81 , R = H ^d	 90 91	78% 81%
4 5	 10 , R = TBS 9 , R = H ^d	 93 92	50% 0%
6 7 8	 14a , R = C(O)NMe ₂ 14b , R = C(O)NEt ₂ 31 , R = CH ₂ NEt ₂	 84a 84b 95	91% 93% 88%
9	 19	 85	94%
10 ^c			94%

^a Isolated yield. No other diastereomers observed. ^b Ref. 12. ^c Ref. 11. ^d The lithium alkoxide was pre-formed with $n\text{-BuLi}$ (1.0 eq) before addition of $\text{Cp}_2\text{Zr}(n\text{-Bu})_2$.

The Zr(II) mediated cyclization of several 1-hepten-6-yne substrates bearing a single C-4 substituent were subsequently examined. From the standpoint of substrate derived stereocontrol, substituents of this variety were not expected to be as influential as those proximate to the sites of ring formation. Accordingly, attempted cyclization of the alkoxide **70** failed and resulted in consumption of starting material as with alkoxide **6** (Table 5). Fortunately, cyclization of **71** under the usual conditions (*vide supra*, this section) proceeded without incident to furnish the predominately *trans* alkylidenecyclopentanes **99a** and **99b** (**99a** / **99b** = 2) in 89% yield. The size of the silyloxy protecting group had little effect on the diastereoselectivity, as **73** cyclized with nearly identical diastereoselection (**100a** / **100b** = 2.1). Cyclization of **76** under analogous conditions provided **105a** and **105b** (**105a** / **105b** = 11) in 99% isolated yield. In the case of **99a** and **99b**, the minor isomer **99b** gave a NOE between the C-2 and C-4 hydrogens as would be expected for a molecule possessing *cis* disposed substituents. In addition, the TBDMSOCH₂ ¹H resonance of the *minor* isomer **99b** appeared as multi-line pattern (2 dd, δ 3.40) which could possibly be a consequence of restricted rotation (as might be expected for the *cis* isomer) whereas the TBDMSOCH₂ signal of **99a** appeared as a sharp doublet centered at δ 3.46. For **100a** and **100b**, the *absence* of a NOE between the C-2 and C-4 methines of the major isomer **100a** is consistent

with a *trans* stereochemical relationship of these hydrogens. Although quite suggestive, the foregoing data must be viewed as inconclusive and accordingly, the precise stereochemical outcome for the cyclizations of **70-73** remains tentative. The diastereoselectivities observed for the cyclizations of **70-73** can be viewed as arising from nonbonded interactions that are related in origin but *smaller in magnitude* than those of the preceding series (i.e., **14a,b**, **19** and **31**). The precyclization conformer where the C4-substituent occupies a pseudoequatorial position would result in bicycle **101'** with the substituent on the exo face (**Scheme 27**). Accordingly, structure **101'** would be preferred because of a reduction in pseudodiaxial interaction between the C4-substituent and one of the cyclopentadienyl rings. Protonolysis would afford predominately the *trans* isomer.



Scheme 27

Cyclizations of enynes bearing oxygen substituents at the 4-position were next briefly examined. Exposure of **51** to $\text{Cp}_2\text{Zr}(n\text{-Bu})_2$ (1.1 equiv) in the usual manner gave the alkylidenecyclopentanes **103a** and **103b** (**103a** / **103b** = 1) in 80% yield after protonation. In concordance with both previous hydroxymethyl analogs, the alkoxide derived from *in situ* deprotonation of **50** [$\text{Cp}_2\text{Zr}(n\text{-Bu})_2 + n\text{-BuLi}$ (1 equiv)] also proved incompatible with Zr(II) mediated cyclization. Once again, the precycle was completely consumed under the normal reaction condition. This study showed that enynes bearing *remote* alkoxy substituents have been demonstrably inferior substrates resulting in low-yields of cyclized products compared to their ether counterparts. The observed stereochemical outcome of the C4-substituted enynes is directly related to the relative size of the substituent *ipso* to the C4 carbon. A complete summary of the 4-substituted enyne cyclizations appears in **Table 5**.

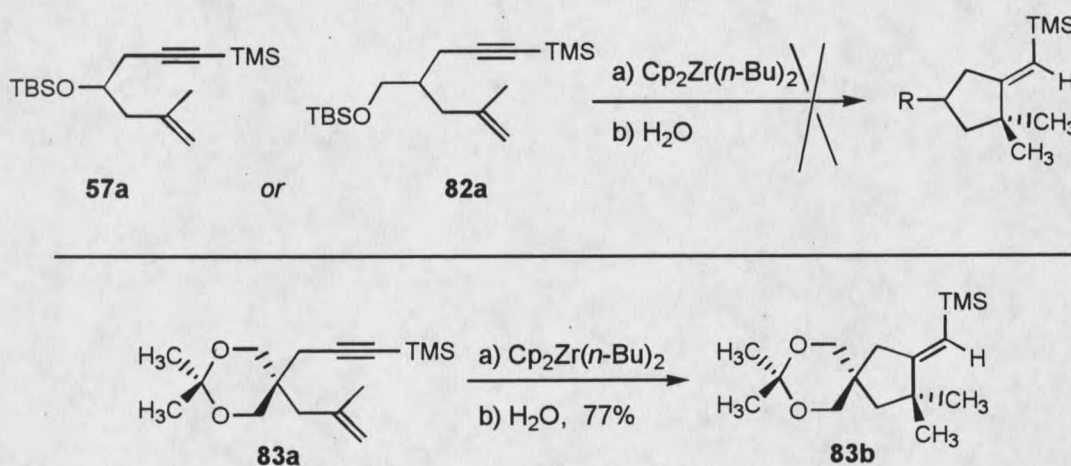
Table 5. Preparation of Alkylidenecyclopentanes by Cyclization of Substituted Enynes with $\text{Cp}_2\text{Zr}(n\text{-Bu})_2$

Entry	Substrate	Product (Major Diastereomer)	Ratio	Yield ^a
1	50 , R = OH ^b	102	-	0%
2	51 , R = OTBS	103	1:1	80%
3	70 , R = OH ^b	98 , R = OH	-	0%
4	71 , R = OTBS	99	2:1	80%
5	73 , R = OSEM	100	2.1:1	99%
6	75 , R = OH ^b	104 , R = OH	-	0%
7	76 , R = OSEM	105	11:1	99%

^a Isolated yield of combined diastereomers. ^b The lithium alkoxide was preformed with *n*-BuLi (1.0 eq) before addition of $\text{Cp}_2\text{Zr}(n\text{-Bu})_2$.

Enynes bearing substituted alkenes were next examined. Enynes **57a** and **82a** were treated with $\text{Cp}_2\text{Zr}(n\text{-Bu})_2$ (1.1 equiv) in the usual manner, however, the expected alkylidenecyclopentanes were not obtained. The use of non-coordinating solvents such as toluene did not improve the situation. Intermolecular dimerization

of two alkynes appeared to be the primary mode of reactivity. However, the enyne **83a** bearing geminal substitution at C-4 interestingly afforded the alkylidenecyclopentane **83b** (Scheme 28). This reactivity is consistent with the known reactivity of substituted alkenes (c.f., Scheme 2) and is a manifestation of the Thorpe-Ingold effect (*vide infra*, 3.4).

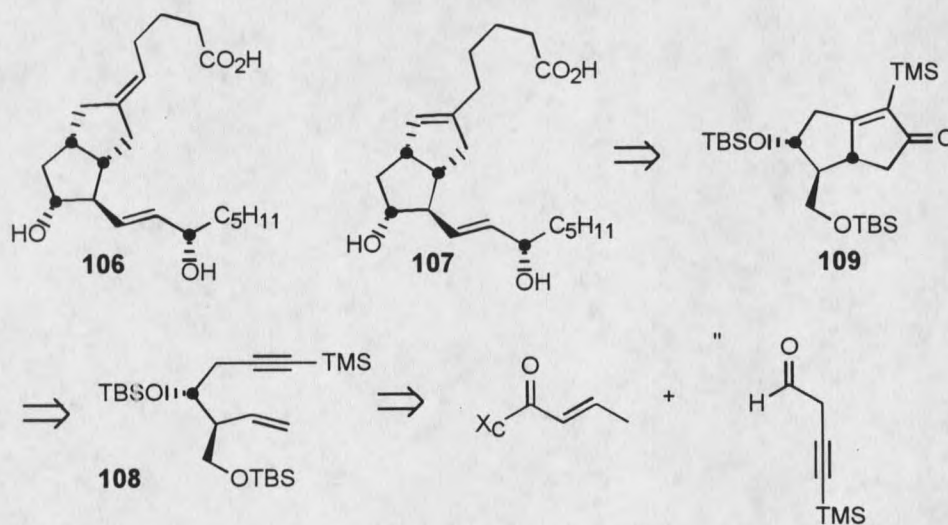


Scheme 28

In summary, several of the factors that appear to influence substrate based control of diastereoselection in $\text{Cp}_2\text{Zr}(\text{II})$ promoted enyne cyclizations have been illuminated. Although the stereochemical outcome for the preceding annulations has not yet been unequivocally established in all cases, it is evident that a high level of stereocontrol can often be achieved by way of this transition metal-based reaction.

3.4 Attempted Syntheses of Carbacyclin

With the successful zirconium mediated cyclization of a variety of substituted enynes, many of which showing excellent levels of substrate controlled diastereoselection, the synthesis of carbacyclin and isocarbacyclin was undertaken. There has been a great deal of interest recently in the synthesis of prostacyclin,⁶¹ carbacyclin **106**⁶² and of their analogs due to its promising pharmacology. A zirconium(II) mediated cyclization-carbonylation sequence could potentially construct the bicyclic core of carbacyclin in one step from a simple linear structure (Scheme 29).

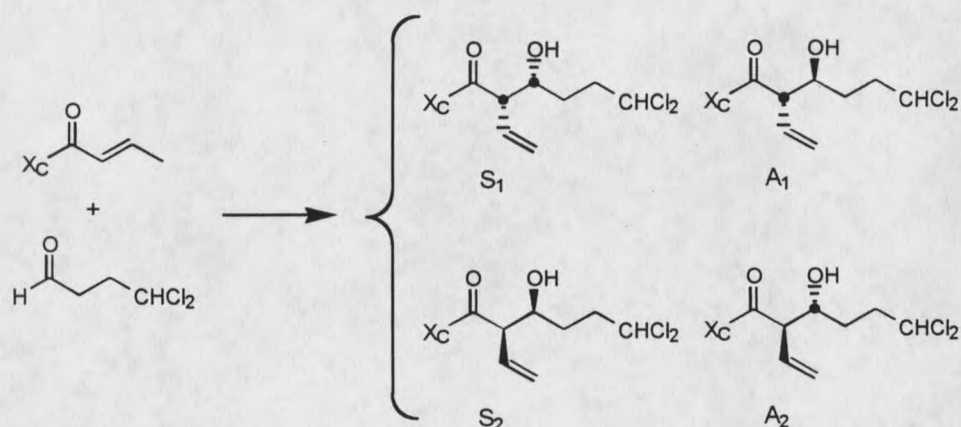


Scheme 29

The key cyclization step would require substrate derived stereocontrol of a *disubstituted enyne*. The competing or synergistic effect of the juxtaposed

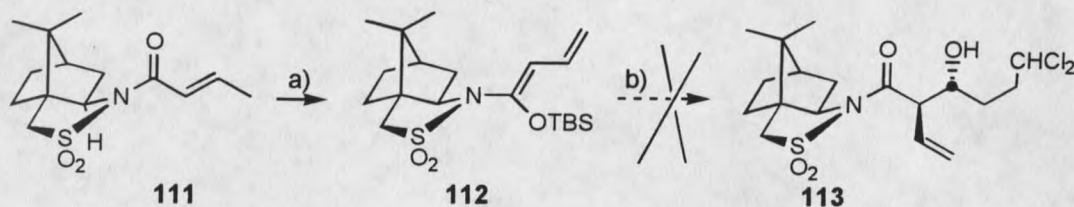
substituents on the stereochemical outcome of a zirconocene mediated cyclization was uncertain. In earlier zirconocene mediated cyclizations (*vide supra*) it was shown that 4-silyloxy substituted 1,6-enynes offered little stereocontrol whereas all the 5-substituted 1,6-enynes showed high levels of 1,2-stereoiduction. It was anticipated that the overwhelming influence of the more proximal substituent would determine the stereochemical outcome of the cyclization. As shown retrosynthetically (**Scheme 30**), the requisite precyclic enyne for the zirconocene cyclization-carbonylation protocol could be assembled quickly by a deconjugative anti-aldol employing a homochiral crotonate derived enolate and a 3-butyne-1-al surrogate.⁶³ The efficacy of 4,4-dichlorobutanal as a 3-butyne-1-al surrogate was amply demonstrated earlier. Finally, the absolute stereochemistry could be obtained by utilization of a suitable chiral auxiliary X_c .

In any given aldol reaction, four possible products could be obtained (**Scheme 30**): two diastereomers (syn vs. anti, S vs. A) and both enantiomers ($1_{R,R}$ vs. $2_{S,S}$). Therefore, both reaction diastereoselection ($S_1 + S_2$ vs. $A_1 + A_2$) and enantioselection (S_1 vs. S_2 or A_1 vs. A_2) must be considered. **Scheme 30** illustrates this specifically for the aldol reaction depicted retrosynthetically above. The carbacyclin core requires the anti (A) configuration with the absolute stereochemistry of (A_2).



Scheme 30

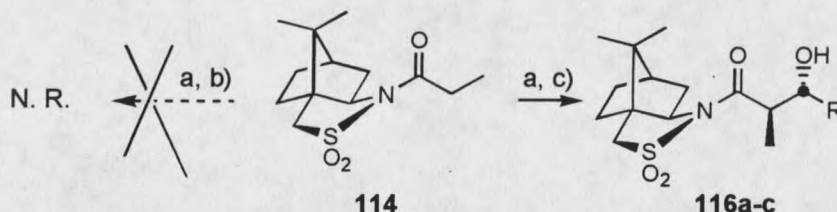
The first attempt to implement this aldol strategy employed the methodology of Oppolzer.⁶⁴ *N*-Acyl sultam **111** was converted to its silyl-*N,O*-ketene acetal **112** (TBDMSOTf, TEA, ~100%) which could be isolated as a white crystalline material or prepared and used in situ. Exposure of **112** to a solution of Lewis acid (TBDMSOTf, $ZnCl_2$ or $TiCl_4$) and 4,4-dichlorobutanal under the published conditions [(a) $-78^\circ C$, CH_2Cl_2 , 5 min; (b) NH_4Cl_{aq}] resulted in complete recovery of unreacted sultam **111** (Scheme 31). This result was clearly very surprising and unexpected because of the wide acceptance and use of chiral sultams in synthesis.



Reagents: (a) TBDMSOTf, TEA, ~100%; (b) 4,4-dichlorobutanal, Lewis Acid, -78 °C

Scheme 31

To verify the experimental integrity of the method, known propionoyl sultam **114** was prepared and treated with propanal (ref. 64b) according to the literature procedure but instead of the expected aldol product **116b**, the acyl sultam was *quantitatively recovered unchanged* (**Scheme 32**). The failure of this well documented and important industrial procedure was mildly perplexing. It was found that the aldol reaction of aldehydes **115a-c** with sultam **114** failed to react according the published procedure, and that allowing them to warm to rt resulted in poor diastereoselection. However, conditions were developed (-40 °C, 4-12 h) that proved gratifyingly efficient (85-95% G.C., typically ~70% isolated yields) for the construction of the advertised anti-aldols. Presumably, the erroneous protocol was a typographical oversight. With the demonstrated efficiency of this new procedure, efforts were made to condense the crotonoyl sultam **111** with aldehydes **115a-c**, but yields were disappointingly low (<30% isolated). Furthermore, crotonoyl sultam **111** failed to react altogether with 4,4-dichlorobutanal.

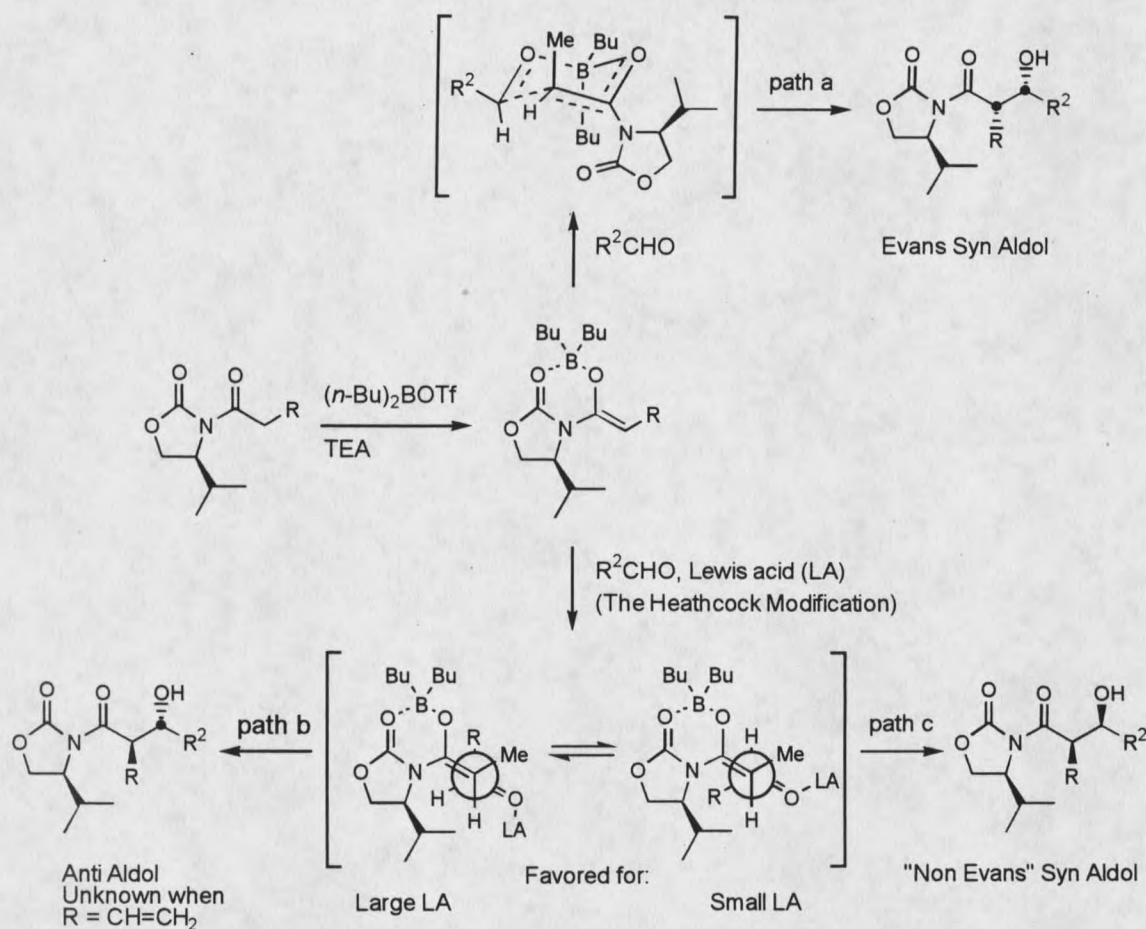


Key: For **115a-c** and **116a-c**: **a**: R = Me; **b**: R = Et; **c**: R = *i*-Pr.

Reagents: (a) TBDMSOTf, TEA, ~100%; (b) RCHO **115a-c**, Lewis acid, -78 °C; (c) RCHO **115a-c**, Lewis acid, -40 °C.

Scheme 32

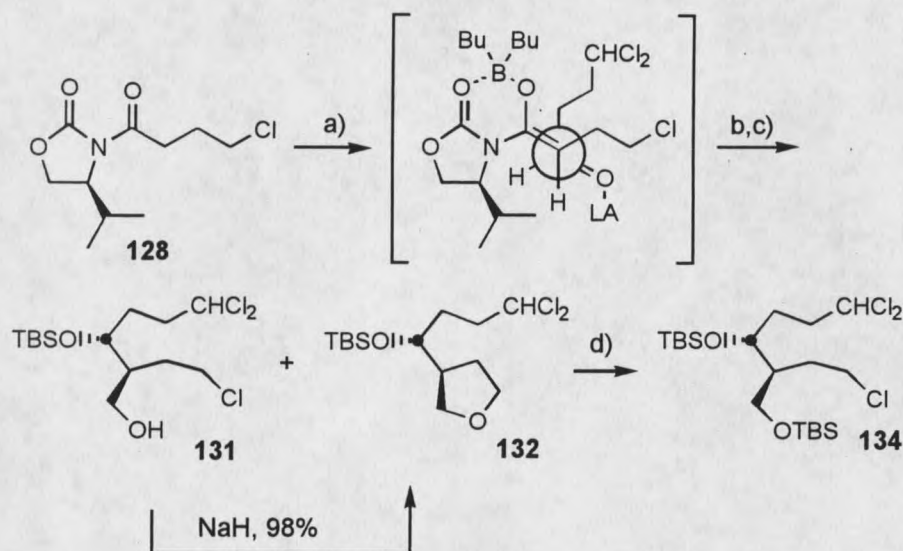
Another well established and proven chiral auxiliary for the preparation of enantiomerically pure syn-aldols was developed by Evans.⁶⁵ These amino acid or norephedrine derived oxazolidinone chiral auxiliaries have gained wide acceptance in academics and industry (S_1 **Scheme 30**, and path *a*, **Scheme 33**). This methodology was greatly extended by Heathcock to permit the fabrication of anti-aldols and “non-Evans” syn aldols *from the same starting oxazolidinones* (**Scheme 33**).⁶⁶ Heathcock showed that when the Evans' boronate enol ethers were treated with aldehydes precomplexed with Lewis acids, the stereochemistry was altered to provide anti-aldols (A_2 **Scheme 30**, and path *b*, **Scheme 33**) and “non-Evans” syn aldols (S_2 **Scheme 30**, and path *c*, **Scheme 33**) with excellent diastereoselectivity and yield (**Scheme 33**). The use of large Lewis acids, such as diethyl aluminum chloride, maximizes the formation of the anti-aldol product by favoring an open transition state (path *b*, **Scheme 33**).



Scheme 33

This methodology offered an attractively expedient route into the requisite carbacyclin precyclic chain (**Scheme 29**). Although the aldol reaction of chiral crotonic acid derived oxazolidinones for the preparation of *syn aldols* is well documented,^{65f} these imides suffer from undesirable side reactions and condensations in the presence of Lewis acids; therefore, the desired anti-aldol via *path b* when $R = CH::CH_2$ remains unobtainable by this course. Since the synthetic goal required the anti-aldol derived from a crotonoyl enolate, and the Oppolzer and

Evans methods were unsuitable, a new route was designed that offered the option of *delayed installation of the terminal olefin* by elimination of an innocuous leaving group later in the synthesis (**Scheme 34**).



Reagents: (a) i. $(n\text{-Bu})_2\text{BOTf}$, TEA; ii. RCO, Et_2AlCl , -110°C to -58°C ; (b) TBDMSOTf, 2,6-Lutidine; (c) NaBH_4 , LiCl, EtOH; (d) TBDMSOTf-imidazole. 42% overall

Scheme 34

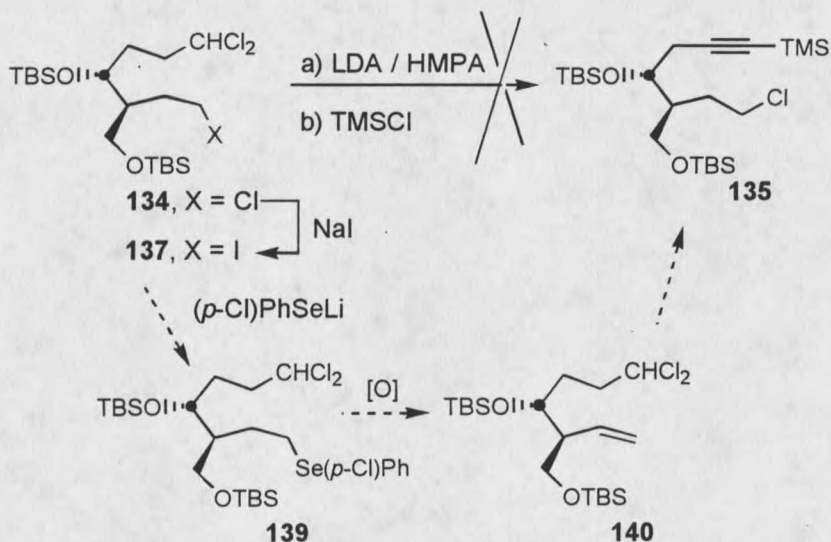
The synthesis began by treating the novel 4'-chlorobutenoyl imide **128** with dibutylborotriethylate and triethyl amine at 0°C . After one hour, the CH_2Cl_2 solution containing the boron enolate was cooled to -90°C and treated with a solution of 4,4-dichlorobutanal, precomplexed with Et_2AlCl at -110°C , and then warmed to -58°C and held at this temperature for 18 h. The extremely cold temperatures used for the aldehyde-Lewis acid complexation were absolutely necessary to prevent the formation of undesirable aldehyde self condensation products. The general

conditions employed were based on the experimental protocol best described by Hoffman.⁶⁷ Subsequent silylation of the secondary hydroxyl after oxidative work-up and reductive removal of the recyclable chiral auxiliary [1. (a) TBDMSOTf -2,6-lutidine; 2. NaBH₄, LiCl, EtOH; 3. TBDMSCl-imidazole) afforded the anti-aldol **131** in 42% overall yield for three steps. Alcohol **131** was converted to its Mosher's ester and found to be enantiomerically pure by G.C., ¹H and ¹³C NMR.

The interesting 2'-hydroxy-2-alkyl tetrahydrofuran **132** was likely formed by intramolecular attack of a transient alkoxide formed during the reduction step. Treating alcohol **131** with 1 equiv of NaH in THF for 10 min followed by aqueous work-up also afforded tetrahydrofuran **132** in near quantitative yield. This constitutes a new and powerful method for the general synthesis of homochiral 2'-hydroxy-2-alkyl tetrahydrofurans. Most importantly, because the relative and absolute stereochemistry is set by established aldol methodology, *all four possible tetrahydrofurans can be synthesized with equal ease*. There has been a great deal of recent interest in mono-substituted tetrahydrofurans, and this procedure appears to be superior to the other methods.⁶⁸

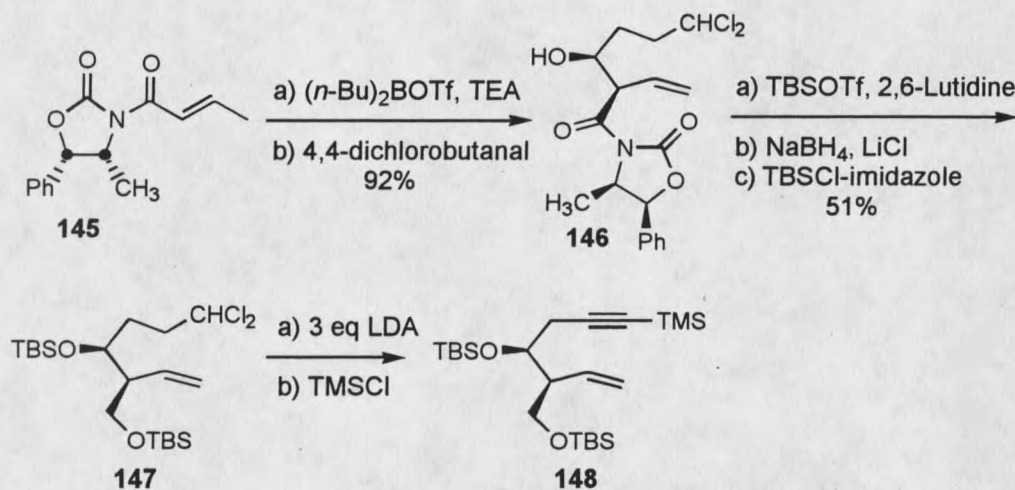
All that remained was the elimination of the *gem*-dihalide and the primary chloride into an alkyne and alkene, respectively, to furnish the desired precyclic enyne **108**. Chlorodecane was used as a model substrate to find suitable conditions for the elimination into 1-decene. It was found that chlorodecane could be

converted into 1-decene in >95% yield by treatment with LDA•THF and HMPA (1 equiv each) at 0° C for 3 days. It was anticipated that the cold and rapid conditions used for acetylene formation (*vide supra*) would convert **134** into acetylenic **135** while leaving the primary chloride unchanged. This halide could then be eliminated to the primary olefin in a second step. Unfortunately, the elimination / silylation conditions (LDA or KNH₂) proved incompatible with **134** and complex mixtures resulted. The primary chloride was then converted into the alkyl iodide **137** (NaI, acetone, cat K₂CO₃) which was then subjected to the usual elimination conditions, however, without improved results. The catalytic base used in the Finkelstein reaction was essential for any reasonable conversion without complete decomposition of both reactant and product. Even with this modification, clean conversion to **137** was never achieved. Another synthetic option could be to displace the primary chloride with a lithium aryl selenide, which could be converted into alkene **140** under mild oxidizing conditions. Towards this end, crude iodide **137** was treated with lithium *p*-chlorophenyl selenide in THF / DMF, but the only gradual decomposition of **137** was observed.



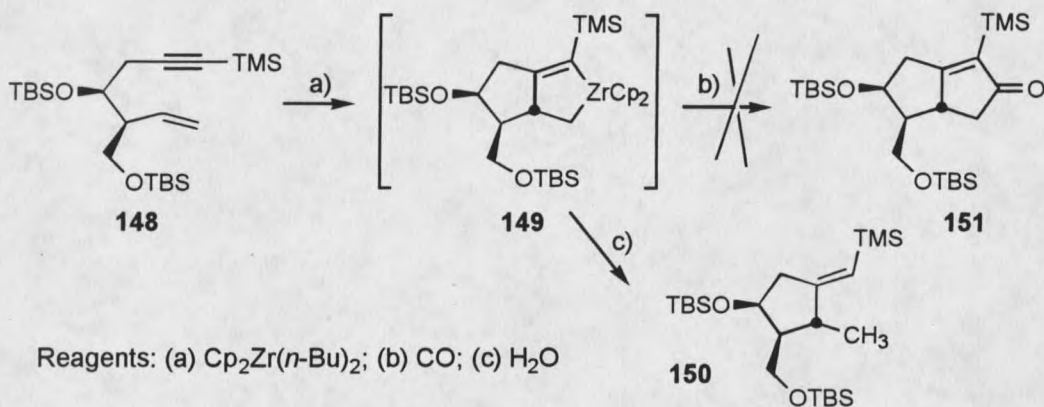
Scheme 35

Further studies concerning the elimination were delayed, because the synthesis of an epi-carbacyclin enyne was accomplished (**Scheme 36**). The boron enolate of *N*-butenoyl oxazolidinone **145** was treated with 4,4-dichlorobutanal ($-78^{\circ}\text{C} \rightarrow 0^{\circ}\text{C}$) to afford the syn-aldol **146** in 92% yield after oxidative work-up. Although TBS ether formation (TBDMSOTf, 2,6-lutidine) was uneventful, the reduction (NaBH_4 , LiCl, EtOH) occurred in only 55% unoptimized yield. Finally, TBS ether formation (TBDMSCl-imidazole, 99%) and elimination / alkyne transformation [(a) 3.3 equiv LDA / HMPA, (b) 1.1 equiv TMSCl] gratifyingly secured enyne **148**. Although enyne **148** possesses the incorrect stereochemistry at C-4, if bicyclopentenone formation were successful it was thought that the stereochemistry could be corrected later by Mitsunobu inversion.



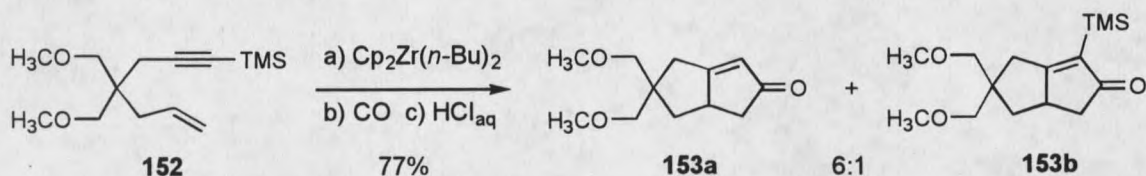
Scheme 36

Enyne **148** was then exposed to the key zirconium(II) mediated reductive bicyclization / carbonylation reaction (Scheme 37). After treatment with $\text{Cp}_2\text{Zr}(n\text{-Bu})_2$ ($-78\text{ }^\circ\text{C} \rightarrow \text{rt}$, 12 h) a quenched aliquot (H_2O) showed the absence of starting material and $>90\%$ conversion to a single material that was likely the alkylidene-cyclopentane **150**, formed by protonation of zirconocyclopentene **149**. However, upon treatment of zirconocyclopentene **149** with CO and then either I_2 or $5\% \text{HCl}_{\text{aq}}$, a multitude of products was obtained, none of which was identified as bicyclopentenone **151**.



Scheme 37

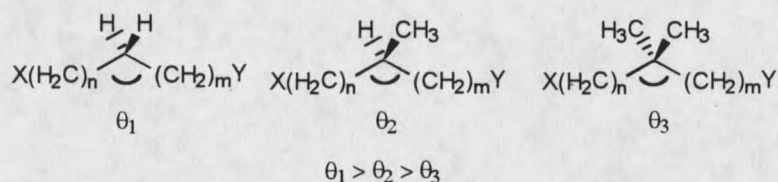
To test the efficacy of the zirconium(II) / carbonylation protocol, enyne **152** was exposed to the usual carbonylation conditions. Two bicyclopentenones were obtained in 77% combined isolated yield, with the predominant product being derived from desilylation of the relatively labile vinyltrimethylsilane (**Scheme 38**).



Scheme 38

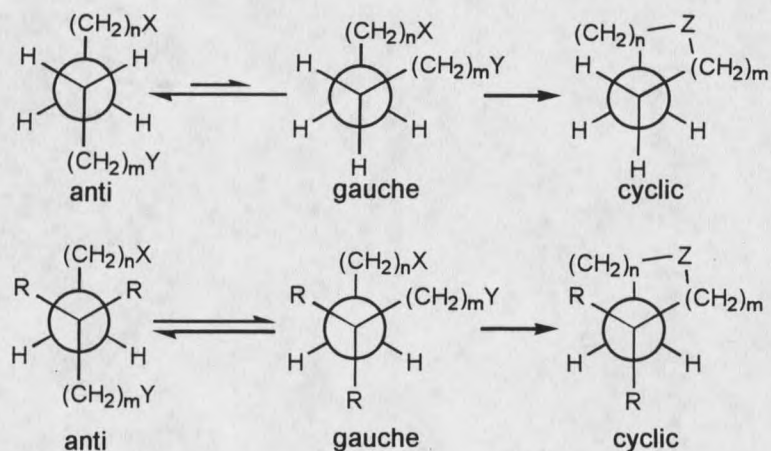
The failure of enyne **148** to successfully undergo the reductive bicyclization / carbonylation sequence was thoroughly disconcerting. One of the major limitations of the zirconium(II) cyclization / carbonylation protocol appears to be the necessity for *gem*-disubstitution along the tether connecting the reactive centers. The most suitable substrates for zirconium(II) mediated cyclization / carbonylation utilized such substitution (c.f., **Scheme 9**).

The increased reactivity of substrates bearing *gem*-substituents between the reactive centers has been known for some time as the Thorpe-Ingold Effect.⁶⁹ The Thorpe-Ingold Effect theorized that substitution about a central methylene causes an angular contraction of the internal angle θ (**Scheme 39**). This angular compression results in moving the two reactive substituents, *X* and *Y*, closer together so they can react more readily.



Scheme 39

It was later postulated that there are more syn rotamers (in the gauche conformation) with geminal substitution than in the unsubstituted case where the anti rotamer is clearly preferred (**Scheme 40**).⁷⁰ An excellent analysis of these two phenomenon was provided by Jung and Gervay.⁷¹ By studying an intramolecular Diels-Alder reaction that effectively separated angular compression and the rotamer effect, they were able to demonstrate that the enhanced reactivity is in fact due to the *reactive rotamer effect* and not simply angular compression. Regardless of semantics, the phenomena is still commonly referred to as the *Thorpe-Ingold effect*.



Scheme 40

In any case, the lack of geminal substitution about precyclic enyne **148** was undoubtedly the cause for the observed lack of efficient carbonylation. One possible solution may be to oxidize the C-4 hydroxy to a ketone and protect it as an acetal, thus providing *gem*-substitution. This option, however, clearly lacks any elegance. Although we sought to employ novel or relatively unexplored reagents to construct the bicyclic pentenone **109**, the use of an alternative cyclization / carbonylation reagent was now explored. Because the chemistry of $\text{Co}_2(\text{CO})_8$ for use in the stoichiometric Pauson-Khand reaction has been extensively developed and implemented in synthesis, it was applied to enyne **148**. Exposure of enyne **148** to stoichiometric $\text{Co}_2(\text{CO})_8$ in toluene for 1 h followed by heating to reflux under an atmosphere of CO for 12 h failed to provide pentenone **109**. This result was a strong impetus to explore / develop other carbonylating agents.

3.5 Catalytic Pauson-Khand Reactions

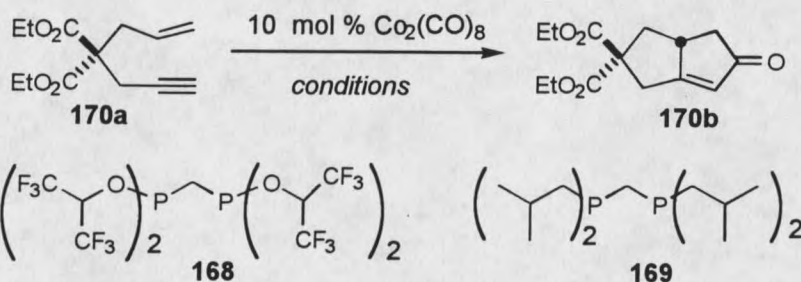
At about this time, Jeong and coworkers reported the first truly catalytic variation of the Pauson-Khand reaction.⁷² Although highly significant, the conditions employed are somewhat harsh (5 mol % $\text{Co}_2(\text{CO})_8$, 20 mol % $\text{P}(\text{OPh})_3$, 3 atm CO, 120 °C) and require the use of a high pressure bomb. Jeong proposed that the triphenyl phosphite served as a ligand to stabilize the unbound active catalyst. The use of *bridging* ligands in the Pauson-Khand reaction has not been reported, although the synthesis of methylene bridged phosphine and phosphite complexes of $\text{Co}_2(\text{CO})_8$ has.^{73,74} Ideally, the Pauson-Khand reaction should be catalytic and require only ambient temperatures and pressures. The favored enthalpy of a bidentate ligand could potentially effect the Pauson-Khand reaction by helping prevent scission of the Co-Co bond.⁷³ We hoped any potential stabilizing effect of a bridging ligand may allow the reaction to proceed at *ambient pressures* of CO. Even though mildly electron rich phosphines and phosphites cause disproportionation of $\text{Co}_2(\text{CO})_8$ to the ionic salt $[\text{Co}(\text{CO})_4]_2$,^{73a,b} this pathway could be initially circumvented by alkyne precomplexation prior to ligand addition.

Furthermore, the obvious goal for any ligand assisted catalytic Pauson-Khand reaction would be the generation of optically active products from achiral

substrates by the employment of a suitable homochiral ligand. Kerr⁷⁵ has demonstrated that when an achiral enyne- $\text{Co}_2(\text{CO})_6$ complex is treated with one equivalent of a homochiral carbohydrate derived diphenylphosphine, a nearly 1:1 diastereomeric mixture of phosphine bound complexes is obtained. Diastereomers are generated when the phosphine binds to a cobalt bound either to the terminal or internal carbon. Separation of these diastereomers by HPLC followed by Pauson-Khand cyclization generates *complementary* chiral enones each in >99 % ee.⁷⁶ This suggests that for an asymmetric, catalytic Pauson-Khand reaction, the use of a monodentate ligand must be precluded. The generation of a homochiral methylene bridged diphosphine could easily be imagined by analogy to DIOP, CHIRAPHOS, DuPHOS, or BINOL.

The bridging ligands **168** and **169** were chosen for initial study because of their similar sterics, but greatly differentiated electron properties. **Table 6** summarizes some results for the Pauson-Khand reaction with bridging ligands **168** and **169** under various conditions.

Table 6. Various Conditions in the Thermal Catalytic Pauson-Khand Reaction



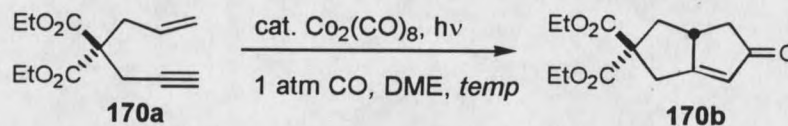
Entry	Solvent	Temp ^f	atm ^g	Time	Additives ^e	G.C. Yield ^a
1	DME	18 °C	3 atm	48 h	none	99% / 0%
2	DME	110 °C	3 atm	48 h	none	90% / 0%
3a	DME	rt	3 atm	72 h	12 mol % 168	80% / 10%
3b ^b	DME	130 °C	3 atm	6 h	"	- / 87%
4	DME	reflux	1 atm	12 h	"	80% / 0%
5	Diglyme	110 °C	1 atm	12 h	"	- / 45%
6	Diglyme	165 °C	3 atm	72 h	"	- / 34%
7a	DME	rt	3 atm	24 h	12 mol % 169	98% / 0%
7b ^b	DME	110 °C	3 atm	24 h	"	- / 94%
8	DME	110 °C	3 atm	24 h	24 mol % 169	70% / 18%
9	Diglyme	110 °C	1 atm	48 h	12 mol % 169	- / 21%
10	DME	reflux	1 atm	12 h	"	70% / 25%
11	DMA	110 °C	1 atm	48 h	"	100% / 0%
12	DMA	110 °C	1 atm	48 h	and CH ₃ CN (xs)	100% / 0%
13 ^c	DME	rt	3 atm	0.2 h	169 and sonication	- / 10%

^a Yields refer to (starting material / product). ^b Reactions 2b and 7b were simply placed into a preheated oil bath after the time indicated for part a. ^c No further catalytic activity was observed with extended times. ^d Isolated yield with 5 mol % Co₂(CO)₈. ^e For reactions employing ligands **168** or **169**, the Co₂(CO)₈ and enyne were premixed for 30 min followed by ligand complexation for 1 h prior to irradiation. ^f Boiling point of 1,2-DME: 85 °C; diglyme: 162 °C. ^g Reactions run at 3 atm were set to 3 atm initially. After heating internal pressure likely increased to 5-6 atm.

A few entries in **Table 6** are worthy of comment. Without the effect on any stabilizing ligands there is no observed catalytic activity (entries 1 and 2). Under identical conditions with *either* bidentate ligand the desired bicyclopentenone was obtained in excellent yield (entries 3b and 7b). This suggests that the catalyst is stabilized by either electron rich or poor bridging ligands. Jeong implied that only triphenyl phosphite was a suitable ligand. Employing two equivalents of bidentate ligand **169** was detrimental to the reaction (entry 8). However, attempts to perform the reaction at atmospheric pressure with either ligand met with only moderate success (entries 5 and 9). The data suggested that high pressures as well as high temperatures were essential. To maintain a sufficient concentration of dissolved CO in solution at high temperatures, high boiling solvents were required (compare entries 4 and 5).

None of these results were particularly encouraging until irradiation with a high intensity visible light was attempted. It has previously been disclosed that tertiary amine *N*-oxides and DMSO markedly accelerate stoichiometric Pauson-Khand reactions.⁸⁵ These reagents have been proposed to function via the oxidative removal of CO, thereby providing an empty coordination site for alkene complexation. For many years it has been known that various metal carbonyl complexes undergo photo-induced CO dissociation.⁷⁷ It is therefore most surprising that this simple expedient has not been reported in connection with

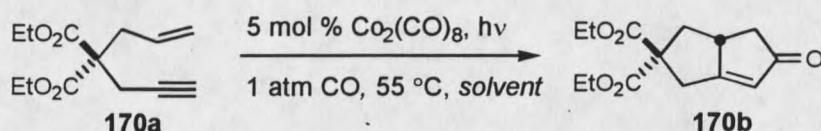
facilitating the Pauson-Khand reaction. The initial attempts at photo-promotion using 10 mol % $\text{Co}_2(\text{CO})_8$ under 1 atm CO were not satisfying in that only low levels (< 30%) of substrate conversion were realized. These results remained promising, because the method was sufficiently mild that there was no observed decomposition of either starting materials or products. Ultimately it was discovered that the *purity of $\text{Co}_2(\text{CO})_8$* ⁷⁸ as well as the choice of an appropriate light source⁷⁹ were both critically important for successful catalytic reactions (**Table 7**). In addition, reaction temperatures in the range of 50 °C seemed to be particularly advantageous. When enyne **170a** and 5 mol % Co_2CO_8 were stirred under an atmosphere of CO *in complete darkness*, a catalytic turnover of 6 was observed (entry 5). Higher temperatures lead to rapid decomposition of the active catalyst under otherwise identical conditions. The maximum catalyst observed turnover for the reaction was 60 (entry 2). Among the several light sources examined, the Q-Beam[®] MAX MILLION[™] 1,000,000 candlepower spotlight distributed by Brinkmann, Inc. proved extraordinary for photoinitiation.

Table 7. Photopromotion in the Pauson-Khand Reaction

Entry	Temp.	mol % cat.	hν source	Yield ^a
1	50 - 55 °C	5	Q-Beam [®] Irradiation	95%
2	50 - 55 °C	0.5	Q-Beam [®] Irradiation	30%
3	< 17 °C	5	Q-Beam [®] Irradiation	N.R.
4	52 °C	5	Vitalite [®] Irradiation	64%
5	52 °C	5	Darkness	28%

^a Isolated yields. All reactions ran for 12 h, except entry 1 which was complete in 4 hours.

After these initially exciting results, various solvents were then screened for the carbonylative cyclization of enyne **170a** to the corresponding cyclopentenone **170b** under 1 atm of CO (Table 8).

Table 8. Effect of Solvent on the Photopromoted Pauson-Khand Reaction

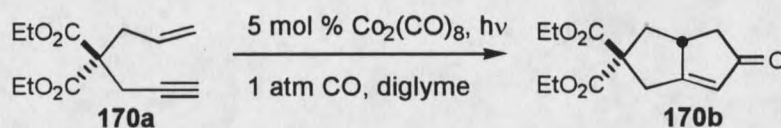
Entry	Solvent ^c	Time (h)	Yield (G.C. / Isolated) ^a
1	1,2-DME	4	98% / 95%
2	EtOAc	4	93% / 87%
3	Diglyme	12	81% / 69%
4	Toluene	4	76% / 62%
5	TFE	12	- / 59%
6	1,2-DCE	12	93% / 53% ^b
7	THF	4	60% / 53%
8	Hexane	4	17% / 5%
9	CH ₃ CN	4	N.R.
10	MeOH	4	N.R.

^a Products were isolated by preparative TLC. ^b There was a lot of apparent polymeric baseline material in this reaction. ^c Degassed.

Of the various solvents tested 1,2-DME was the most efficacious, although EtOAc, diglyme and toluene were also found to be reasonable. It may be possible to increase the yield in the industrially favored solvent toluene with additives. For effective photo-promotion it is critical that the solvent employed be rigorously degassed prior to use. Furthermore, 1,2-DME distilled from a deep blue solution of sodium benzophenone-ketyl immediately before use was sufficiently oxygen free that it required no further processing.

Because of Jeong's report,⁷² the potential stabilizing effect of triphenyl phosphite on the $\text{Co}_2(\text{CO})_8$ catalyst was examined under photo-promotion conditions. Interestingly, the phosphite was found to hinder product formation at both high and low temperatures (Table 9).

Table 9. Effect of Temp and $\text{P}(\text{OPh})_3$ on the Photopromoted Pauson-Khand Reaction



Entry	Temp.	Additives	Yield ^a
1	120 °C	20 mol % $\text{P}(\text{OPh})_3$	29%
2	120 °C	none	55%
3	50 - 55 °C	20 mol % $\text{P}(\text{OPh})_3$	61%
4	50 - 55 °C	none	69%

^a Products were isolated by preparative TLC.

At this point, the photopromoted Pauson-Khand reaction as designed appeared very promising. The initial goal of achieving enone formation under 1 atm CO had been realized, but the reaction required an air sensitive catalyst. As most alkyne- $\text{Co}_2(\text{CO})_6$ complexes are more stable than $\text{Co}_2(\text{CO})_8$, several of these complexes were prepared⁸⁰ and their efficacy as a $\text{Co}_2(\text{CO})_8$ equivalent retaining catalytic-Pauson Khand activity was examined. These complexes necessarily need to allow disassociation of free $\text{Co}_2(\text{CO})_6\text{L}_n$ and subsequent ligation to the enyne

substrate. That is, simply a formal trans-ligation from one alkyne to another was required. Electron poor alkynes, such bis-trifluoromethyl acetylene, are extremely stable compounds and no trans-ligation with them has been observed. Electron rich alkynes, such as *N,N*-diethylpropargyl amine readily undergo trans-ligation but are not air stable complexes. The propensity for several alkyne- $\text{Co}_2(\text{CO})_6$ complexes to undergo trans-ligation is (in increasing order): $(\text{CF}_3)_2 < (\text{COOCH}_3)_2 < (\text{C}_6\text{H}_5)_2 < (\text{CH}_3)(\text{C}_6\text{H}_5) < (\text{CH}_3)_2 < \text{H}(\text{C}_6\text{H}_5) \sim \text{H}(\text{CH}_3) < \text{H}_2 < (\text{CH}_2\text{NCH}_2\text{H}_5)_2$. It was not clear what effect irradiation might have on the ease of trans-ligation among various alkyne complexes.

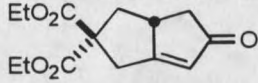
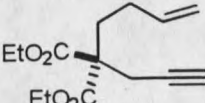
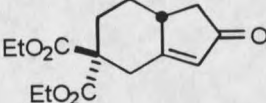
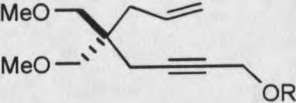
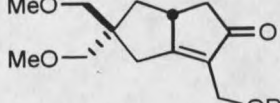
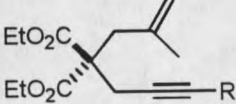
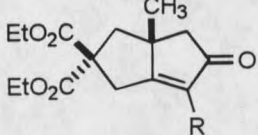
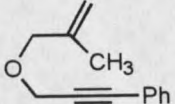
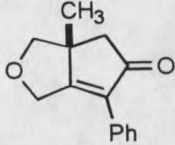
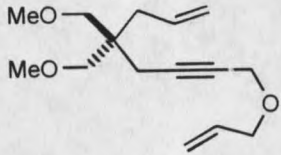
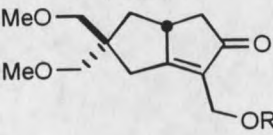
The alkyne- $\text{Co}_2(\text{CO})_6$ complexes derived from reaction of bis-trimethylsilylacetylene, diphenylacetylene, 2-butyne, acetylene or *N,N*-diethylpropargyl amine with $\text{Co}_2(\text{CO})_8$ were examined for catalytic photopromoted Pauson-Khand activity with enynes **170a** and **193a**. Only the complex derived from acetylene showed any catalytic activity. Specifically, a 0.1 M solution of tosamide **193a** in 1,2-DME containing 5 mol % of 2-butyne- $\text{Co}_2(\text{CO})_6$ was irradiated for 24 hours at 55 °C under 1 atm of CO, after which the reaction became heterogeneous. G.C. analysis of the crude reaction mixture showed 50% conversion to enone **193b**. No modifications were found to extend catalysis to terminal alkyne **170a**. Furthermore, only the bis-trimethylsilylacetylene and diphenylacetylene complexes proved to be appreciably air stable.

To test another means to circumvent the need for ultra-pure $\text{Co}_2(\text{CO})_8$, enynes **170a** and **193b** were treated with an excess (3 equiv) of low-grade, partially decomposed $\text{Co}_2(\text{CO})_8$ in 0.1 M DCM under an atmosphere of CO for 24 h. Isolation by chromatography on silica gel or alumina as previously described⁸⁰ afforded the desired alkyne- $\text{Co}_2(\text{CO})_6$ complexes. A catalytic amount (5 mol %) of these complexes demonstrated catalytic activity equal to the use of free $\text{Co}_2(\text{CO})_8$, if used immediately after purification.

3.6 Applications of the Photopromoted Pauson-Khand Reaction

To test the generality of this new reaction, a series of enynes were synthesized and subjected to the standard set of reaction conditions (5 mol % Co_2CO_8 , 0.1 M in 1,2-DME, $h\nu$, 50-55°C). Substrates **170a**, **180a**, **186a**, **189a** were prepared by the alkylation of various diethyl malonate derivatives (*vide supra*, section 3.2). The results from $\text{Co}_2(\text{CO})_8$ mediated catalytic photopromoted enyne-CO cyclizations involving a range of substituted malonate derivatives is shown in Table 10.

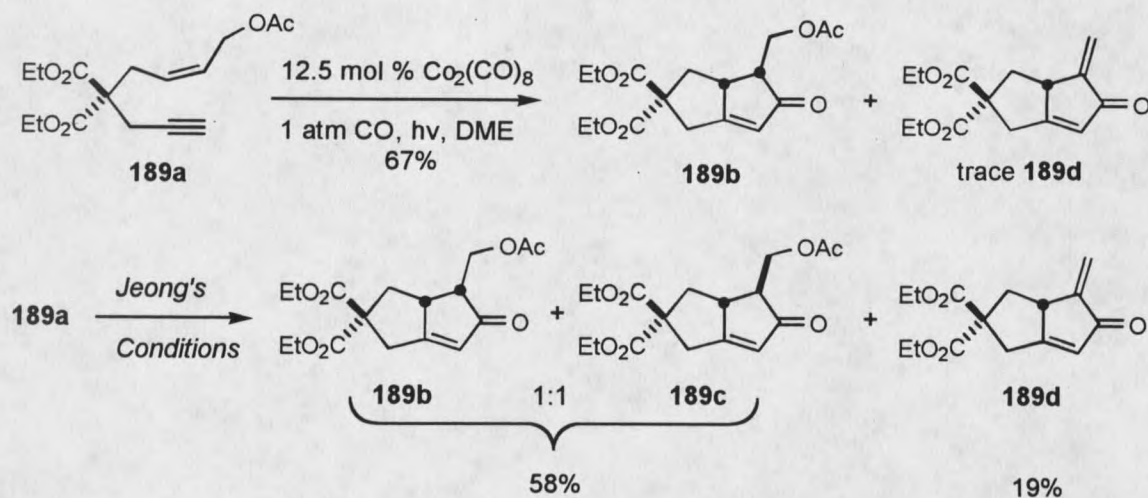
Table 10. Catalytic Pauson-Khand Photocyclizations of Malonate Derivatives Under 1 atm CO

Entry ^a	Substrate	Product	Yield ^b (%)
1	 170a	 170b	95 ^c
2	 171a	 171b	74
3	 173a , R = H 174a , R = TBS	 173b 174b	74 30
4	 176a , R = H 179a , R = Ph	 176b 179b	91 84
5	 182a	 182b	N.R.
6	 185a	 185b	67 ^d

^a Unless otherwise noted, all reactions were conducted using 5 mol % $\text{Co}_2(\text{CO})_8$ and substrate concentration of 0.1 M in 1,2-DME under irradiation for 12 h at 50–55 °C. ^b All yields given in this table correspond to isolated, chromatographically purified products. ^c Irradiation time = 4 h. ^d Reaction performed with 10 mol % $\text{Co}_2(\text{CO})_8$.

Several of the results presented in **Table 10** are worthy of comment. The successful conversion of **171a** to **171b** demonstrates the utility of this new photochemical procedure for the cyclization of 1,7-enynes. The efficient cyclization of **173a** shows the compatibility of the prescribed reaction conditions with a free hydroxyl moiety. The relatively labile primary propargylic silyl ether **174a** cyclized in considerably poorer yield. Entries 4 and 5 indicate the method tolerates both alkene and alkyne substitution. However, the corresponding disubstituted ether **182a** failed to cyclize under the usual conditions. Interestingly, carbonylative photocyclization of **185a** furnished **185b** to the complete exclusion of the isomeric 1*H*-cyclopenta[*c*]furan-5-one. The latter result and the failure of ether **182a** to undergo cyclization are presumably both manifestations of the Thorpe-Ingold effect (*vide supra*, section 3.4).

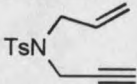
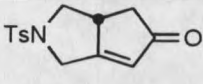
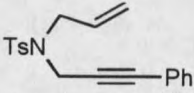
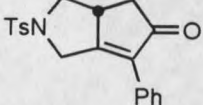
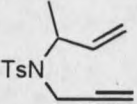
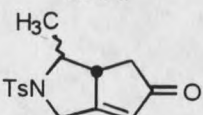
The *selective* cyclization of **189a** to **189b** is most significant. Cyclization of **189a** under Jeong's reaction conditions (120 °C) reportedly³³ gives rise to **189b** and **189c** (58%, 1:1 diastereomer ratio)^{33b} admixed with 19% of the elimination product **189d** (Scheme 41). However, under our photopromoted conditions, **189a** cyclized with complete stereochemical integrity in 67% isolated yield. Only a trace of the elimination product **189d** was observed.



Scheme 41

Several enynes with a *p*-toluenesulfonamide linker (prepared by the alkylation of various *p*-toluenesulfonamides [NaH , THF / DME or K_2CO_3 / acetone]) that underwent cyclization are presented in **Table 11**. These substrates further demonstrate the generality of the new photopromoted Pauson-Khand reaction.

Table 11. Catalytic Pauson-Khand Photocyclizations of Tosamide Derivatives Under 1 atm CO

Entry ^a	Substrate	Product	Yield ^b (%)
1	 192a	 192b	81
2	 193a	 193b	75
3	 195a	 195b,c	90

^aUnless otherwise noted, all reactions were conducted using 5 mol % $\text{Co}_2(\text{CO})_8$ and substrate concentration of 0.1 M in 1,2-DME under irradiation for 12 h at 50–55 °C. ^bAll yields given in this table correspond to isolated, chromatographically purified products, except where noted. ^cObtained as an inseparable 1.1 to 1 mixture of diastereomers.

3.7 Ligand Effects on Diastereoselectivity in the Photopromoted Pauson-Khand Reaction

The remarkable level of substrate controlled diastereoselection observed in the zirconium(II) mediated cyclizations appeared to be lacking in the photopromoted Pauson-Khand reaction (e.g., **195a** → **195b**). Two possible methods for improving diastereoselection may include reagent or substrate derived stereocontrol. The steric demands of the metal catalyst could be increased by

suitably coordinating ligands. For this tactic to be successful, the ligand would need to remain bound to the cobalt catalyst during the ring forming steps. Another option would be to modify the substrate, e.g., by utilizing alkyne protecting groups, for increased substrate derived stereocontrol.

It would clearly be a superior solution to develop one ligand-modified catalyst compatible with a variety of substrates than depending on substrate modification for enhanced diastereoselection. Towards this goal, a wide variety of ligands were screened, and the results tabulated in the following four tables (**Tables 12-15**). Substrates **170a** and **195a** served as models for testing the various ligands, some of which are presented graphically in **Figure 1**. The achiral enyne **170a** was used to screen some ligands for catalytic turnover, to minimize use of the more precious substrate **195a**. Ligands that passed this test were then examined with the **195a** to appraise the ligands influence on diastereoselection.

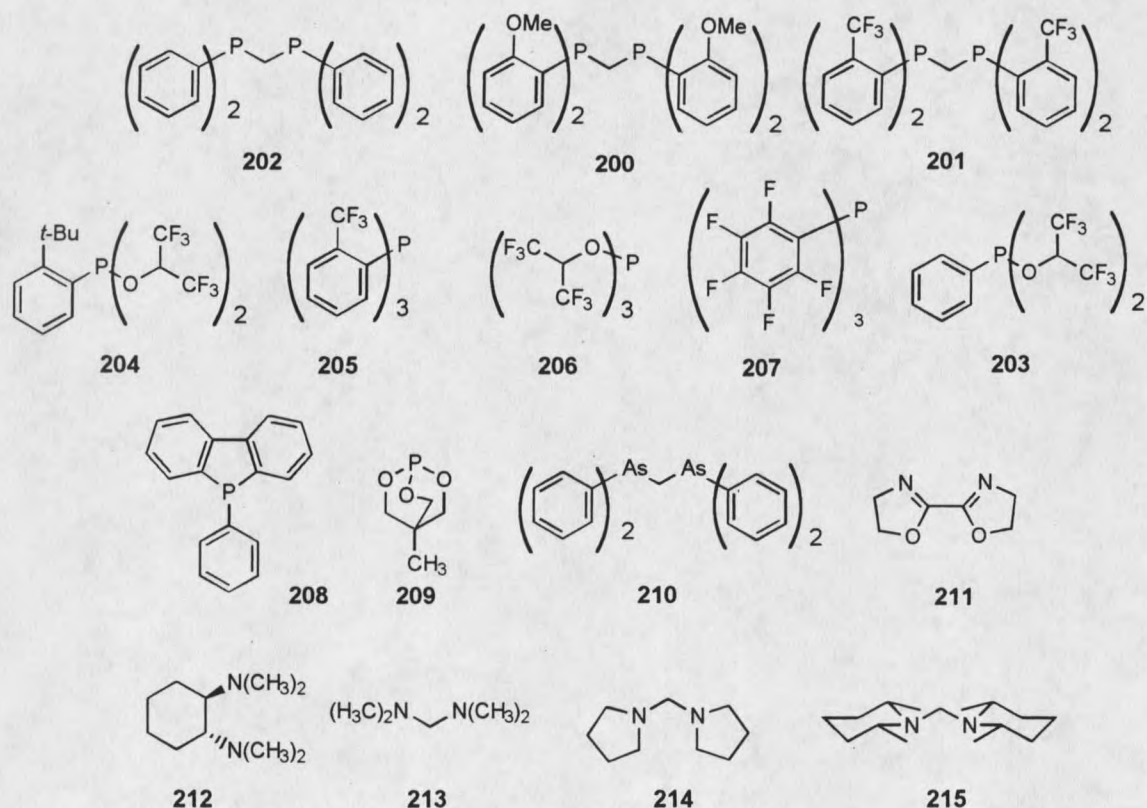
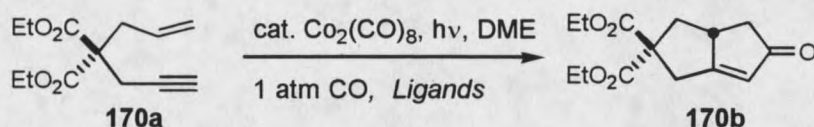
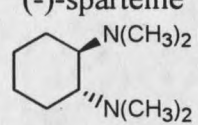


Figure 1

The reaction appears tolerant of a wide range of monodentate amines, except for the highly electron rich DMAP. Bidentate amines proved to be much more detrimental for the malonate substrate than for the tosamide (**Table 12**, entries 13-15 and **Table 14**, entries 7-11). The three electronically similar but sterically differentiated bidentate amines in **Table 14** demonstrate no obvious trends based on their increasing steric demands. Electron poor phosphines and phosphites were also suitable additives. Again two equivalents of electron rich monodentate phosphines or phosphites interfered more than one equivalent, but their methylene bridged bidentate analogues resulted in further attenuation of catalytic activity (**Table 13**).

Table 12. Effect of Nitrogen Based Ligands on Photopromoted Pauson-Khand Cyclizations

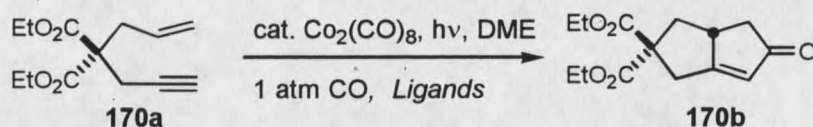


Entry	mol % cat	mol % ligand	ligand ^a	Yield ^c
1	5	-	none	95% ^g
2	5	-	none, 3 atm CO	87% / 10
3	10	11	pyridine	4% / 84%
4	10	22	"	3% / 91%
5	10	250	"	1% / 92%
6	10	11	2,6-lutidine	4% / 85%
7	10	22	"	4% / 92%
8	10	250	"	3% / 89%
9	10	11	DMAP	3% / 89%
10	10	21	"	3% / 90%
11	10	21	DABCO	3% / 90%
12	10	21	methylpyrrolidine	4% / 90%
13	4	11	(CH ₃) ₂ NCH ₂ N(CH ₃) ₂	28% / 61%
14	5	10.5	(-)-sparteine	- / >95% ^d
15	5	11		90% / 8%
16	5	11	"	89% / 9% ^e
17	5	-	(toluene)	- / 79% ^f
18	5	200	2,6-lutidine (toluene)	- / >95% ^f

^a Unless otherwise noted, the enyne and Co₂(CO)₈ were premixed for 30 min prior to addition of ligand and the resulting mixture was stirred for an additional ca. 30 min after ligand addition and before irradiation. ^b The Co₂(CO)₈ and ligand were premixed for 30 min prior to addition of ligand and the resulting mixture was stirred for an additional ca. 30 min after ligand addition and before irradiation. ^c Yields are G.C. yields and refer to (starting material / product). ^d Isolated in 65% yield; no optical rotation observed. ^e Solvent: 1,2-dichloroethane. ^f Solvent: toluene.

^g Isolated yield.

Table 13. Effect of Non-Nitrogen Based Ligands on Photopromoted Pauson-Khand Cyclizations

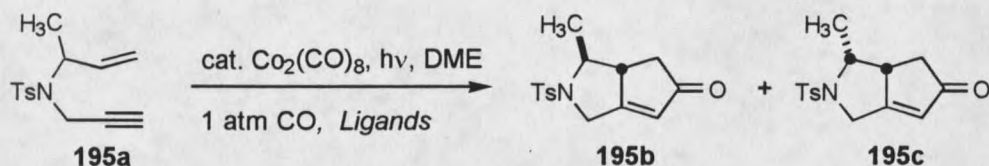


Entry	mol % cat	mol % ligand	ligand ^a	Yield ^c
1	5	-	none	95% ^d
2	5	5.5	$\text{Ph}_2\text{PCH}_2\text{PPh}_2$	84% / 6%
3	10	12	Ph_3P	70% / 16%
4	5	12	$\text{P}(\text{OPh})_3$	- / 56%
5	5	6	$(o\text{-MeOPh})_2\text{PCH}_2\text{P}(\text{''})$	93% / 5%
6	5	6	$(\text{F}_6\text{C}_2\text{CHO})_3\text{P}$	- / 86%
7	5	12	$(\text{F}_6\text{C}_2\text{CHO})_3\text{P}$	80% / 14%
8	10	12	$(\text{F}_6\text{C}_2\text{CHO})_2\text{PCH}_2\text{P}(\text{''})$	88% ^d
9	10	11	$(\text{C}_6\text{F}_5)_3\text{P}$	- / >95%
10	10	21	$(\text{C}_6\text{F}_5)_3\text{P}$	22% / 55%
11	5	11	phosphorole	52% / 35%
12	5	11	tripodolphosphite	60% / 35%
13	5	12	HMPA	95% / 0%
14	5	5.5	169^a	84% / 6%
15	5	5.5	169^e	95% / 0%
16	5	11	Ph_3As	- / 98%
17	5	11	MeAsPh_2	- / 80%
18	10	22	$(\text{C}_6\text{H}_{11})_3\text{As}^b$	61% / 20%
19	10	22	$(\text{C}_6\text{H}_{11})_3\text{As}^a$	25% / 66%
20	5	12	tetrahydrothiophene	63% / 33%
21	10	250	thiophene	- / >95%

^a Unless otherwise noted, the enyne and $\text{Co}_2(\text{CO})_8$ were premixed for 30 min prior to addition of ligand and the resulting mixture was stirred for an additional ca. 30 min after ligand addition and before irradiation. ^b The $\text{Co}_2(\text{CO})_8$ and ligand were premixed for 30 min prior to addition of ligand and the resulting mixture was stirred for an additional ca. 30 min after ligand addition and before irradiation. ^c Yields are G.C. yields and refer to (starting material / product). ^d Isolated yield. ^e The phosphine and $\text{Co}_2(\text{CO})_8$ were premixed for 33 h prior to addition of the enyne.

Although the additives appeared to have a similar effect on catalysis with chiral tosamide **195a**, in no case was a significant improvement in diastereoselection achieved. It is interesting that the electron rich tri-*t*-butyl phosphine did not initiate decomposition of the catalyst (**Table 15**, entry 10). This may be due to the large cone angle of this ligand.⁸¹ The very electron poor trifluorophosphine ligand had little effect on the diastereoselectivity, but is had a large influence on the rate of cyclization. Whereas most the entries in the following tables required at least 12 hours for completion, with PF₃, the cyclization was done cleanly in less than four hours.⁸² This apparent rate enhancement has not been examined with other substrates. The most efficacious ligands yet examined appears to be several amine based ligands (**Table 12**) and 2-methylthio-2-thiazoline (**Table 15**, entries 20-22). These ligands allowed for efficient substrate to product conversion with the best observed improvement in diastereoselectivity (1.4 to 1). However, when enyne **230a** was examined with the amine ligands not improvement in diastereoselectivity was observed. With enyne **230a** and the thiazoline ligand, catalytic activity was completely suppressed. This ligand survey should be considered as a preliminary study directed towards the logical design of homochiral ligands for asymmetric catalysis.

Table 14. Effect of Nitrogen Based Ligands on Diastereoselectivity in Photopromoted Pauson-Khand Cyclizations

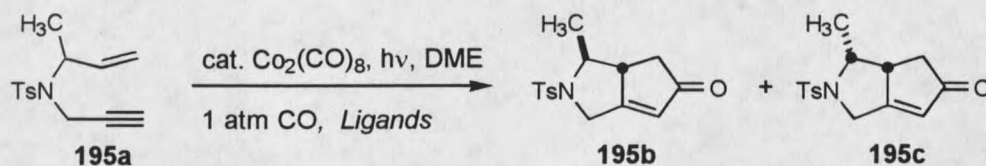


Entry	mol % cat	mol % ligand	ligand ^a	ratio exo to endo	Yield ^c
1	5	none	solvent: DME	1.1	90% ^e
2	5	none	solvent: TFE-DME, 2:1	1.3	2% / 86% ^d
3	5	none	solvent: TFE	1.4	- / 85%
4	10	100	2,6-lutidine	1.4	- / 100%
5	10	23	DMAP	1.5	57% / 33%
6	10	12	<i>N</i> -methylmorpholine	1.4	55% / 14%
7	10	12	(CH ₃) ₂ NCH ₂ N(CH ₃) ₂	1.4	4% / 87%
8	10	12		1.3	72% / 12%
9	10	12		1.1	5% / 72% ^a
10	10	12	"	0.8	6% / 76% ^b
11	10	12	2,2'-oxazoline	1.5	69% / 34%
12	10	12	"	1.4	5% / 72% ^d

^a Unless otherwise noted, the enyne and Co₂(CO)₈ were premixed for 30 min prior to addition of ligand and the resulting mixture was stirred for an additional ca. 30 min after alkyne addition and before irradiation. ^b The Co₂(CO)₈ and ligand were premixed for 30 min prior to addition of alkyne and the resulting mixture was stirred for an additional ca. 30 min after enyne addition and before irradiation.

^c Yields are G.C. yields and refer to (starting material / product). ^d Solvent: TFE-1,2-DME, 2:1. ^e Isolated yield.

Table 15. Effect of Non-Nitrogen Based Ligands on Diastereoselectivity in Photopromoted Pauson-Khand Cyclizations



Entry	mol % cat	mol % ligand	ligand ^a	ratio exo to endo	Yield ^c
1	5	none	solvent: DME	1.1	90% ^e
2	5	none	solvent: TFE-DME, 2:1	1.3	2% / 86% ^d
3	5	6	(F ₆ C ₂ CHO) ₂ PCH ₂ P(")	1.1	54% / 37%
4	10	12	(F ₆ C ₂ CHO) ₃ P	0.9	- / 83%
5	10	12	(F ₆ C ₂ CHO) ₂ PPh	1.0	- / 78%
6	10	12	(F ₆ C ₂ CHO) ₂ P(<i>o</i> - <i>t</i> -Bu)	1.2	24% / 44%
7	10	12	((<i>o</i> -CF ₃)Ph) ₂ PCH ₂ P(")	1.0	- / 65%
8	10	12	((<i>o</i> -CF ₃)Ph) ₃ P	1.3	39% / 54%
9	5	10.5	(C ₆ F ₅) ₃ P	1.2	55% ^e
10	10	21	(<i>t</i> -Bu) ₃ P	1.3	- / 79%
11	5	xs ^g	PF ₃		
12	10	11	DMA	1.1	80% / 10%
13	10	21	Ph ₃ As ^a	1.3	28% / 60%
14	10	21	Ph ₃ As ^b	1.3	35% / 55%
15	10	none	cat.: [Ph ₃ As•Co(CO) ₃] ₂	1.3	57% / 43% ^f
16	10	12	Ph ₂ AsCH ₂ AsPh ₂ ^a	1.2	28% / 60%
17	10	12	Ph ₂ AsCH ₂ AsPh ₂ ^b	1.2	35% / 55%
18	10	22	(C ₆ H ₁₁) ₂ As	1.4	7% / 93%
19	10	22	(C ₆ H ₁₁) ₂ As	1.4	6% / 94%
20	10	11	2-methylthio-2-thiazoline	1.4	- / 86%
21	10	21	"	1.4	- / 86%
22	10	200	"	1.4	- / 72%
23	10	2.1	thiophene	1.3	24% / 65%
24	5	200	thiophene	1.1	- / 85%

^{a,b} See Table 14. ^c Yields are G.C. yields and refer to (starting material / product). ^d Solvent: TFE-1,2-DME, 2:1. ^e Isolated yield. ^f Normalized ratio. ^g The atmosphere was supplied by a balloon filled with PF₃ and CO ca. 1 to 1.

Most of these ligands cause decomposition of free $\text{Co}_2(\text{CO})_8$ in solution, however, when bound as an alkyne complex little decomposition is observed. To attempt to quantify this phenomenon the alkyne complex $[\text{2-butyne}]\cdot\text{Co}_2(\text{CO})_6$ was prepared and exposed to several ligands and the resulting mixture was subsequently examined by NMR. The representative ligands examined were: triphenylphosphine, bis(diphenylphosphino)methane (DPM), triphenylarsine, tricyclohexylarsine, pyridine and DMAP. The complex was treated with two equivalents of each ligand, except for the bidentate DPM, of which only 1 equivalent was used. After mixing, each solution was examined by NMR after 30 min to 1 h. In no case was there any significant changes in the chemical shifts of either the ligand or the cobalt complex. However, there was considerable loss of *resolution* in the spectra of all the ligands in the presence of the cobalt - alkyne complex.

The samples were then Q-Beam irradiated for 30 min. The samples gradually warmed from room temperature to 50 °C over 25 min, and were irradiated at 50 °C for an additional 5 min. In the NMR spectra of the samples treated with either the PPh_3 or DPM ligand, changes were observed in the NMR spectra after irradiation. Specifically, a new, broad signal was observed at 2.2 ppm just upfield of the complexed alkyne CH_3 's at 2.8 ppm. Additionally, a new signal in the ^{13}C

NMR spectra was also observed slightly up field at 19.3 ppm from the cobalt complexed alkyne CH_3 at 20.3 ppm. No changes were observed in the ^{31}P NMR with Ph_3P . However, two new singlets at (-26.0 and -25.7 ppm) upfield from the DPM singlet (-21.8 ppm) was observed. Both the Ph_3As and $(\text{C}_6\text{H}_{11})_3\text{As}$ samples showed a similar change in the ^1H NMR. In the case of $(\text{C}_6\text{H}_{11})_3\text{As}$, a new signal at 21.0 ppm downfield from the cobalt complexed alkyne CH_3 at 20.1 ppm in the ^{13}C NMR spectra was clearly observable. The ^1H NMR spectra of the pyridine sample showed considerable deformation of the normal pyridine proton spectrum to two broad peaks, one centered at 9.3 ppm and the other at 7.4 ppm. Both the amine samples showed the growth of a very small signal at 1.7 ppm in the ^1H NMR spectra, but no changes in the ^{13}C NMR were observed.

After another 1.5 h of irradiation (1 h at 50-55 °C) both phosphine samples showed considerable decomposition and were not measurable by NMR spectroscopy, presumably due to the presence of paramagnetic material. However, neither arsine complex had decomposed and the apparently new signals mentioned above had grown considerably. Specifically, in the case of $(\text{C}_6\text{H}_{11})_3\text{As}$ the new signals mentioned above had grown to equal intensity of original signals (before irradiation).

Although these results suggest that the ligands modify the cobalt - alkyne complex, the nature of this modification is not clear. It is plausible that

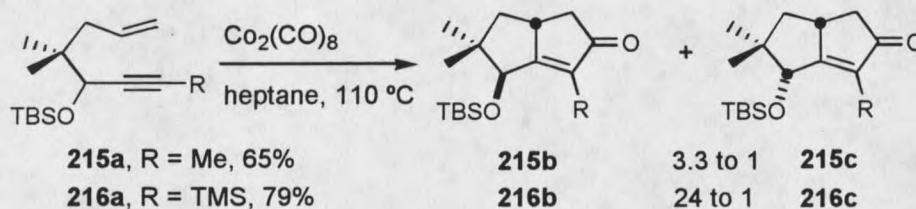
photopromoted CO disassociation generates a free coordination site on cobalt, which is subsequently filled by the ligand. Very little about the mode of action of external ligands on the photopromoted Pauson-Khand reaction can be inferred from these observations. That is, even if ligation were complete in these studies, in the photopromoted Pauson-Khand reaction other conditions must be considered: ligand binding may be incomplete, may not be present in the key ring forming steps, the ligated species may react slower than the uncoordinated catalyst, etc.

One of the few ligands that does not induce disproportionation of $\text{Co}_2(\text{CO})_8$ is Ph_3As . The known, stable $[\text{Ph}_3\text{As}\cdot\text{Co}(\text{CO})_3]_2$ complex was prepared and tested under standard photopromoted Pauson-Khand conditions.⁸³ With tosamide **195a** there was no observed improvement in diastereoselection and only poor catalytic turnover (**Table 15**, entry 14). This catalyst was also tested with enyne **215a**, but again poor catalytic turnover was observed with a decrease in diastereoselection.

3.8 Substrate Derived Stereocontrol in the Photopromoted Pauson-Khand Reaction

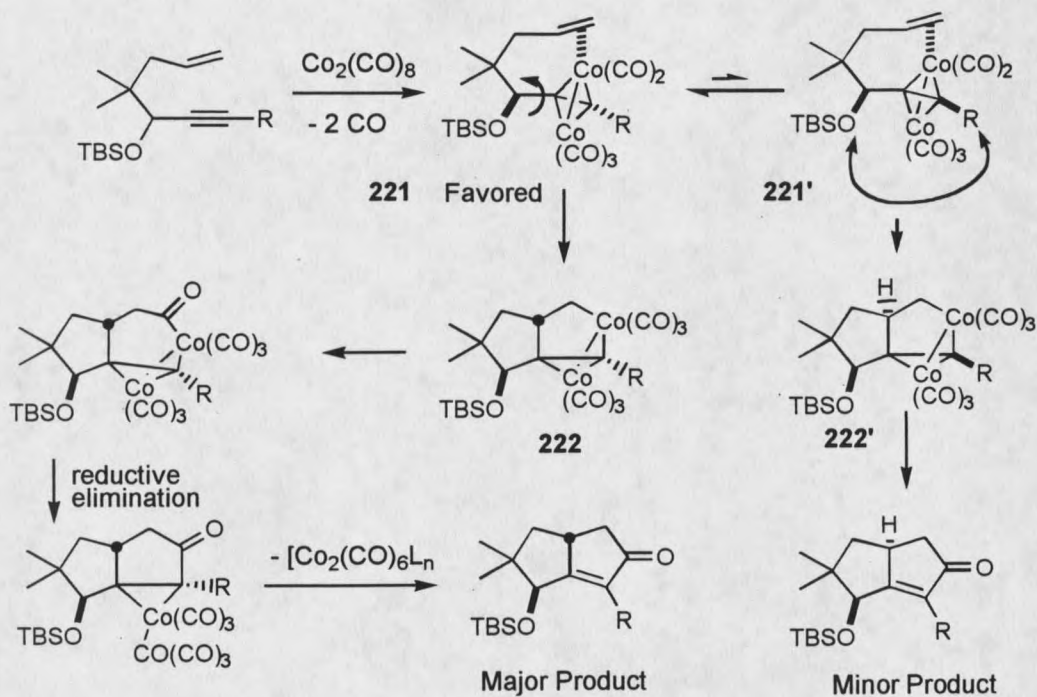
Since little improvement in diastereoselection was realized by reagent control, substrate modification was next examined. There have been many studies concerning substrate derived stereocontrol in the classical stoichiometric Pauson-

Khand reaction. For 5-substituted 1,6-enynes improved diastereomer ratios are obtained by increasing the steric demands of the alkyne terminus (**Scheme 42**).⁸⁴



Scheme 42

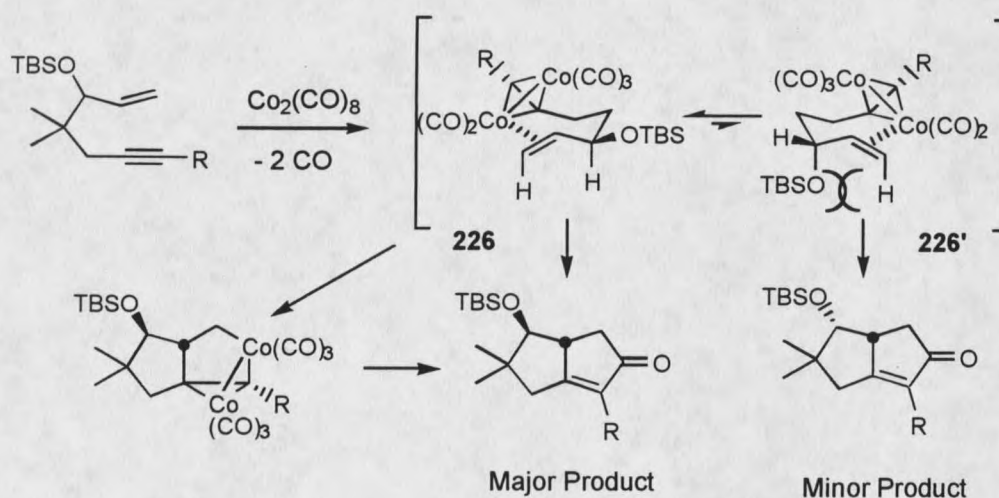
The accepted explanation for this phenomenon states that because of pseudodioxial interaction between the OTBS ether at the propargylic position in **221'** and the alkyne terminus *R* favors, alkene insertion is favored to occur by conformation **221** (**Scheme 43**). If alkene insertion occurs by conformation **221** to give intermediate cobalt complex **222**, then in the final product the OTBS ether will occupy the exo face.



Scheme 43

The same rationale is often used to explain a similar trend observed with 3-substituted 1,6-enynes, although the allylic substituent is much further away from the alkyne terminus. There was surprisingly scant experimental evidence to support this view, i.e., studies concerning systematic changes of the alkyne terminus *R* on a substrate with allylic substitution. Experiments presented later in this thesis offer evidence to support this hypothesis. However, studies in which the allylic group was modified suggest that increased steric requirements at the allylic position confer markedly improved diastereoselection. Instead of rationalizing this phenomenon simply by the reduction of pseudodiaxial interactions, a more plausible explanation rests in minimization of allylic 1,3 strain in the precyclization conformers (**Scheme**

44). If alkene insertion occurs via conformer **226** where the bulky allylic substituent occupies a pseudoequatorial position and $A^{(1,3)}$ strain is minimized, the substituent will occupy the exo face of the resultant bicycle. Furthermore, this mode of cyclization also minimizes any potential diaxial interaction.

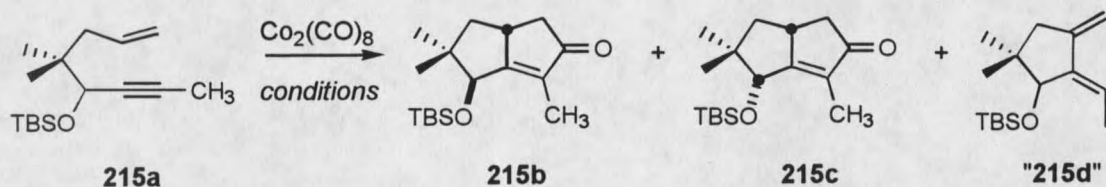


Scheme 44

To further explore substrate derived stereocontrol, enynes of the general type depicted in **Scheme 44** appeared to be excellent candidates for study. It was presumed that the alkyne terminus of substrate **230a** (**Scheme 45**) could easily be alkylated to prepare a variety of substrates with different protecting groups. When enynes **215a** or **230a** were exposed to the usual photopromoted Pauson-Khand conditions both failed to cyclize in greater than 50% yield, even with high catalytic loading. This was a disconcerting result since both substrates cyclized readily in the traditional Pauson-Khand reaction. Both substrates appeared to undergo cyclization

via a previously inoperative pathway to provide products consistent with **215d** (**Table 16**).⁸⁵ After considerable effort, it was a relief to discover that 2,2,2-trifluoroethanol (TFE) as a co-solvent alleviated the problem, and the desired enones were obtained in high yield.

The ratio of diastereomeric products obtained from cyclization of enyne **215a** was lower (2.5 to 1) than that reported in the literature (3.3 to 1). This discrepancy appears to be due to solvent effects (**Table 16**). When enyne **215a** was treated with stoichiometric $\text{Co}_2(\text{CO})_8$ at 55 °C, in a non-coordinating solvent such as hexane, the observed ratio increased to 3.6 to 1. However, when 2:1 TFE-1,2-DME was used as solvent, the ratio was identical to that obtained by the catalytic photopromoted Pauson-Khand (2.5 to 1). When the complex obtained from combining enyne **215a** with stoichiometric $\text{Co}_2(\text{CO})_8$ in TFE-1,2-DME as solvent, was treated with excess *N*-methylmorpholine-*N*-oxide at 0 °C, again the same ratio was obtained (2.5 to 1).

Table 16. Diastereoselectivity Dependence on Solvent

Entry	Equiv. $\text{Co}_2(\text{CO})_8$	Solvent ^a	Promoter	Ratio ^b b to c
1	0.05	DME	hν	2.1 to 1
2	0.05	TFE:DME	hν	2.5 to 1
3	1.0	Hexane	55 °C	3.6 to 1
4	1.0	TFE:DME	55 °C	2.5 to 1
5	1.0	TFE:DME	NMO, 0 °C	2.5 to 1

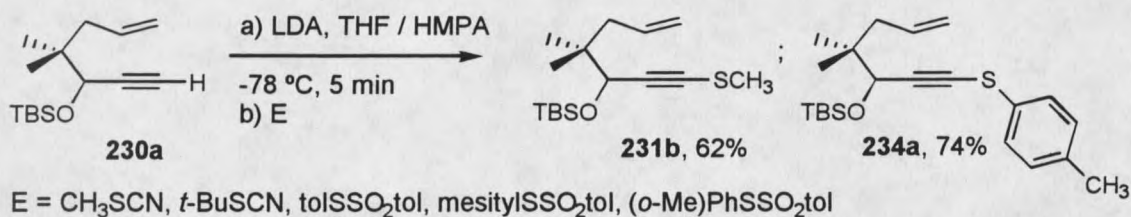
^a Ratio of TFE: DME = 2:1. ^b Determined by G.C. analysis of crude reaction mixtures.

These results suggested that the same diastereomeric ratios are obtained with either the conventional stoichiometric or photopromoted Pauson-Khand reaction. Although the NMO procedure (**Table 16**, entry 5) failed to improve the diastereomer ratio, this is not unprecedented;⁸⁶ it has been shown that for certain substrates *greatly improved diastereoselectivity* may be realized by conducting the oxidation at -78 °C.⁸⁷ For the photopromoted Pauson-Khand reaction cold conditions are not an option, as temperatures in the range of at least 55 °C appear necessary (*vide supra*, **Table 9**).

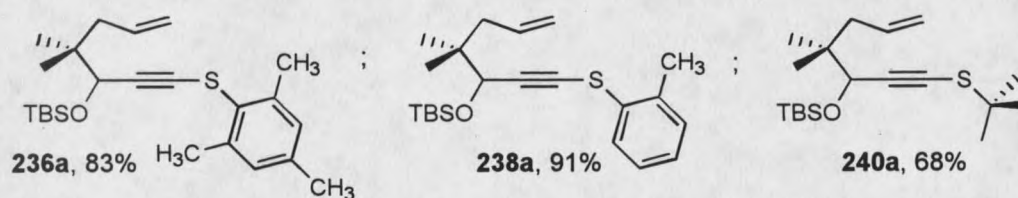
Although trimethylsilyl substituted alkynes are superb substrates in the stoichiometric Pauson-Khand reaction, the presence of the trimethylsilyl group inhibits cyclization in the photopromoted Pauson-Khand reaction (c.f., **Table 20**).

A search for a suitably bulky alternative protecting group began with aryl and alkyl sulfenyl ethers. Any potential group utilized for substrate derived diastereocontrol must obviously be readily removed after cyclization. Unlike the mildly acidic conditions required to desilylate a vinyl α -silyl enone, the strongly reducing conditions necessary to remove the sulfenyl ethers would likely reduce the bicyclic enones to ketones, a potentially serious disadvantage, and limit the variety of tolerant functionality. Regardless, a series of alkyne modified precyclization enynes was prepared by deprotonation of acetylene **230a** followed by electrophilic capture (Scheme 45) [(a) *n*-BuLi or LDA•THF, THF / HMPA, -78 °C, 5 min; (b) "E"].

The use of *n*-BuLi instead of LDA•THF improved yields and was essential in some cases to prevent allene formation. The ethoxy alkyne **244a** was prepared by the addition of lithium ethoxyacetylide to a solution 2,2-dimethyl-4-propenal followed by silylether formation [1. (a) $\text{LiC}\equiv\text{COEt}$, THF, -78 °C; (b) $\text{NH}_4\text{Cl}_{\text{aq}}$; 2. TBDMSCl-imidazole (71% overall)].



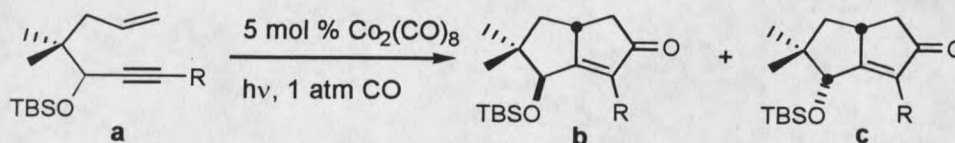
Prepared with $n\text{-BuLi}$:



Scheme 45

The cyclization study began with enyne **231a** which gratifyingly underwent photopromoted catalytic Pauson-Khand cyclization cleanly and in superb yield to provide cyclopentenones **231b,c** in 99% combined isolated yield as a 3.9 to 1 mixture of diastereomers. This substrate cyclized in better yield and with better selectivity than its parent primary acetylenic enyne, without the use of any TFE co-solvent.

Table 17. Effect of Alkyne Substitution on Propargyl Substituted Enynes



Entry	R	Solvent	Ratio b to c	Yield ^a
1, 230a	H	DME	-	< 50%
2, 230a	H	TFE: DME	1.6	80%
3, 231a	SCH ₃	DME	3.9	99%
4, 234a	STol	DME	2.4	95%
5, 236a	SMesityl	DME	2.1	55%
6, 238a	S(<i>o</i> -Me)Ph	DME	2.3	22%
7, 240a	S(<i>t</i> -Bu)	DME	2.2 (stoic) ^b	56%
8, 240a	S(<i>t</i> -Bu)	TFE: DME	1.9 (stoic) ^b	-
9, 244a	OEt	DME	0.72	84%

^a Isolated yield, except where noted. ^c Stoichiometric Co₂(CO)₈.

The toluoyl sulfenyl ether cyclized with moderate selectivity (2.5 to 1) in excellent yield (95%). Surprisingly, the increased steric bulk of the *ortho*-methyl and mesityl sulfenyl ethers resulted in a *decrease* of both selectivity and yield (Table 17, entries 5 and 6). These experiments do not clarify if electronics (phenyl vs. alkyl) or simple sterics interfere with the cyclization. The bulky sulfenyl *tert*-butyl group completely prevents any catalytic turnover despite its electronic similarity to the sulfenyl methyl group. Enones **240b,c** were prepared by Q-Beam[®] irradiation of a mixture containing *stoichiometric* Co₂(CO)₈ and enyne **240a** in 1,2-DME or TFE-1,2-DME solvent mixtures. Only poor diastereoselection was

observed. Of the sulfenyl ethers examined, the sulfenyl methyl is the most promising and potentially valuable for several reasons. It confers a synthetically useful improvement in diastereoselection, it should be easily removed, and it is easy to install. At this point, it appears that the sulfenyl based modifiers presented herein fail to improve diastereoselection as effectively as the trimethylsilyl group.

This is the first example of reversal of normal stereochemistry for a mono-substituted enyne without external ligands.⁸⁸ The assigned stereochemistry is based on the observed NOE's indicated below (**Figure 2**). Furthermore, the proton assignments are fully consistent with ^1H and ^{13}C heteronuclear correlation, ^{13}C 90 ° DEPT and ^{13}C 135 ° DEPT NMR experiments. All the other C4 or C6-substituted bicyclic enones prepared herein, the major product bears exo substitution. The endo and exo products are easily identifiable by simple one-dimensional ^1H NMR spectroscopy, as the endo proton is shielded by the enone, and is shifted upfield by as much as 1 ppm.

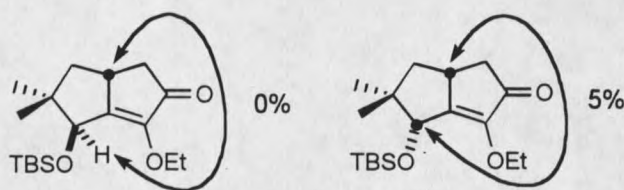
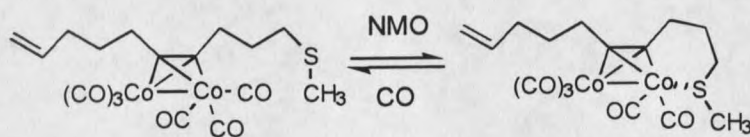


Figure 2

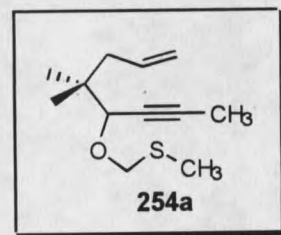
It was interesting to observe that presence of sulfur had a visible effect on the color of the reaction solution. With sulfur containing substrates the reaction's

color becomes nearly black within minutes, whereas with the other substrates, the solution remained a brilliant red. In nearly all cases the solution becomes heterogeneous with concurrent catalyst decomposition after the reaction was complete.

Krafft found that bishomopropargylic sulfides can chelate to a vacant coordination site on cobalt, thus stabilizing the cobalt center and slowing cyclopentenone formation (**Scheme 46**). A homopropargylic sulfide substituent also chelated to cobalt, but did not retard cyclopentenone formation. If the sulfur were bound at a chiral position, the chelation effect may result in enhanced diastereoselectivities. To test this hypothesis, enyne **254a** bearing a MTM protecting group⁸⁹ was prepared and subjected to the usual catalytic photopromoted Pauson-Khand conditions, but no products were observed even with extensive reaction times.



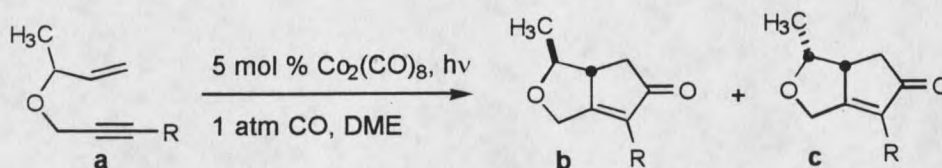
Scheme 46



Next, attention focused on exploring enynes with heterocyclic linkages. With the successful cyclization of several tosamide tethered substrates, ether linked enynes were considered. Initial accounts concerning ethereal substrates reported

only poor yields of cyclopentenones were obtained. However, the use of modifiers such as NMO, DMSO and silica gel allow for the preparation of cyclopenta[*c*]furan-5-ones in excellent yields.^{86,90} Attempts to cyclize methallyl propargyl ether **256a** by the usual catalytic photopromoted Pauson-Khand reaction met with minimal success, in that the desired cyclopentenone was obtained in only 22% yield (**Table 14**).⁹¹ No solvent or ligand modifications were found to defeat this shortcoming. Fortunately, when enyne **256a** was alkylated with methylsulfenyl cyanate, the resultant enyne **257a** readily underwent cyclization. The sulfenylmethyl moiety incorporated in the structure resulted in two beneficial consequences for this substrate: both the yield and diastereomeric ratio were increased to synthetically useful levels. Although the *tert*-butyl sulfenyl ether could be difficult to remove from the final product, it was examined strictly for theoretical considerations. In this case, the catalyst activity was not impinged upon, and the diastereoselectivity was markedly increased.

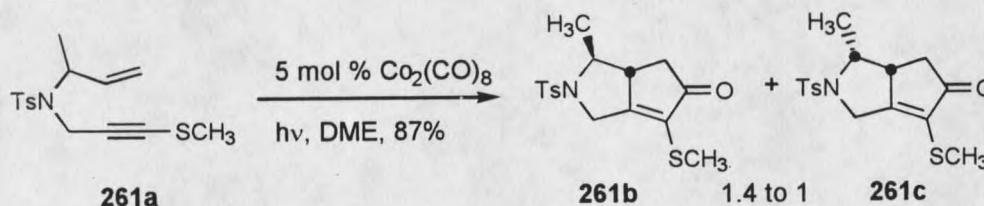
Table 18. Alkyne Substitution Effects with Allylic Ethers



Entry	Substituent, R =	Ratio b : c	Yield ^a
1, 256a	H	5 : 1	< 23%
2, 257a	SCH ₃	12 : 1	81%
3, 258a	S(<i>t</i> -Bu)	42 : 1	78%

^a Isolated yield.

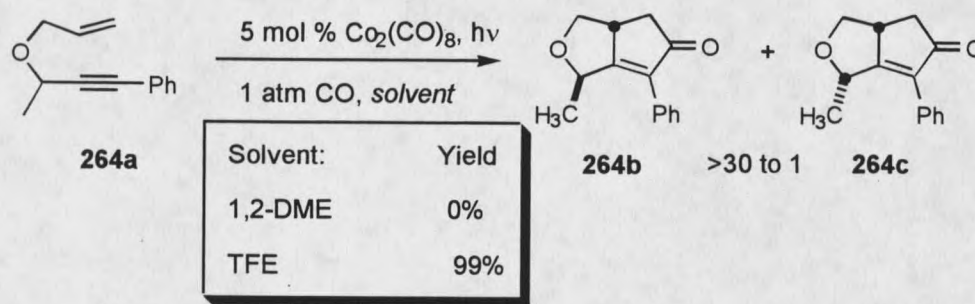
Because of the significant improvement in selectivity and yield achieved for enyne **256a** by simply introducing a sulfenyl methyl substituent, tosamide **195a** was converted to **261a** and subjected to the usual cyclization conditions (Scheme 47). Unfortunately, the diastereoselectivity only increased from 1.1 to 1 to 1.4 to 1. This somewhat surprising result offered no better improvement in selectivity than was achieved with the variety of ligands discussed above.



Scheme 47

Enyne **264a** (Scheme 48) bearing propargylic methyl substitution was prepared and subjected to the usual photopromoted Pauson-Khand conditions, but cyclization was arrested, even with TFE as co-solvent. However, when the reaction was performed in neat TFE, the desired cyclopentenone was obtained in an

astonishing 99% isolated yield as a 30 to 1 mixture of diastereomers. This striking example amply demonstrates the solvent dependency of the photopromoted Pauson-Khand reaction. Furthermore, the generation of enone **264b,c** by Buchwald's²⁶ method offers selectivity of only 5 to 1.

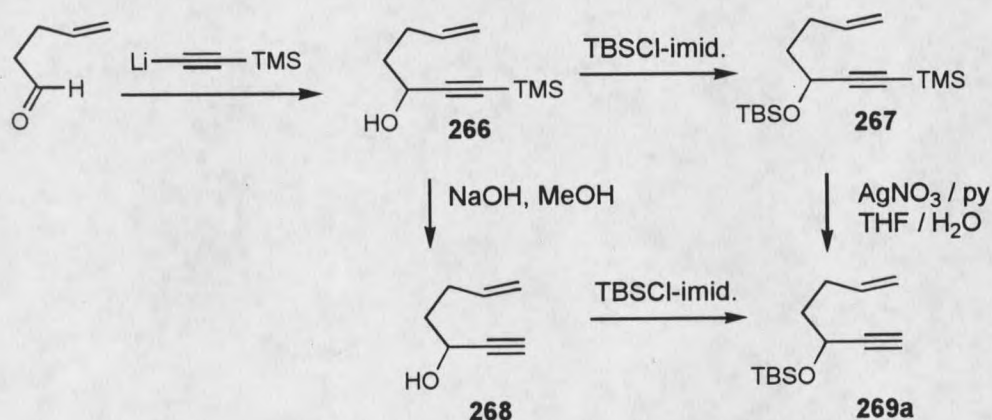


Scheme 48

All of the substrates subjected to photopromoted Pauson-Khand cyclizations to this point have benefited from either the Thorpe-Ingold effect or heteroatom contraction. Indeed, of the catalytic methods for cyclopentenone formation only Buchwald has successfully cyclized substrates linked by a simple unsubstituted or mono-substituted tether.²⁶ To further explore the scope of the new photopromoted Pauson-Khand reaction, two substrates designed specifically to address this issue were prepared and examined.

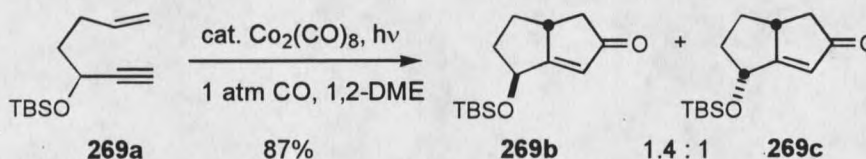
During the course of preparation of either enyne **269a** or **271a**, the classic method to effect acetylenic desilylation (cat. NaOH, MeOH) was found to result in poor yields due to product decomposition. Specifically, when allylic or propargylic

silyl ether moieties resided within the substrate, decomposition was the favored reaction path. Converting the silyl ethers to hydroxyl moieties resolved the decomposition problem, but necessitated extra steps, and an unstable and volatile alcohol was formed (**Scheme 49**). In a recent synthesis of calicheamicinone, Clive reported an undesired acetylenic desilylation while attempting an α -bromo dehalogenation (AgNO_3 , pyridine, THF, H_2O). After several trials, it was discovered that the amount of water in the reaction is critical for successful desilylation. With slightly less water than Clive described, the reaction becomes heterogeneous and desilylation fails to proceed beyond 10% conversion. Under optimized conditions, selective desilylation of **267** to **269a** was achieved in 88% isolated yield in less than one hour. Without any further misfortune, enynes **269a** and **271a** were both secured.



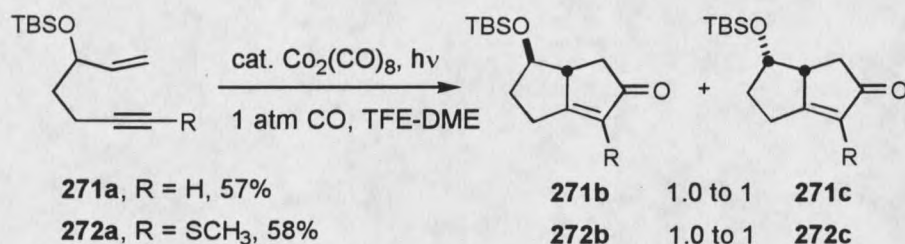
Scheme 49

Enyne **269a** cyclized without incident to afford bicyclopentenones **269b** and **269c** in excellent yield although only moderate diastereoselection was observed. This represents the first reported high-yielding synthesis of an "unactivated" bicyclopentenone derivative by transition metal catalysis. (Since the time of this writing, Buchwald has reported the successful conversion of similar aliphatic enynes in better yields, ref. 27, chapter 1, section 4).



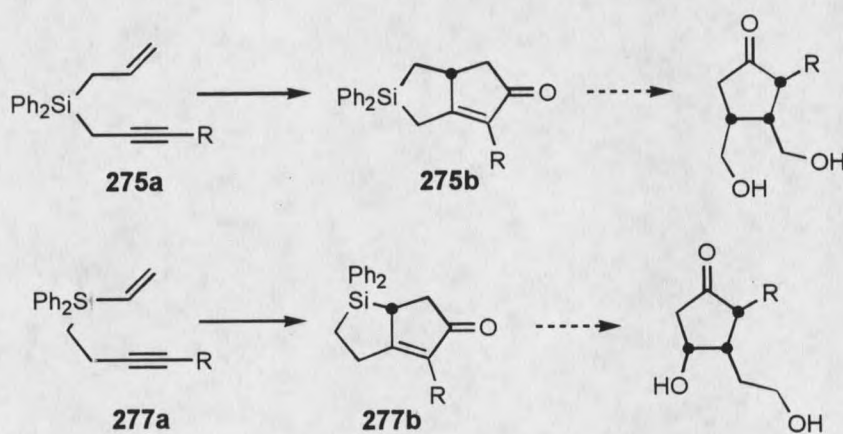
Scheme 50

Enone **271b,c**, however, proved to be a much more elusive goal, and enyne **271a** only underwent cyclization surreptitiously (Scheme 51). Not only was TFE required as a co-solvent, but enyne **271a** requires filtration through basic alumina *immediately prior to cyclization*. With proper substrate preparation and optimization of reaction conditions, enones **271b** and **271c** were consistently obtained in moderate yields as a 1.0 to 1 mixture of diastereomers. It was anticipated that sulfenyl methyl incorporation would improve both diastereoselectivity and yield of allylic ether enyne **272a**, but this was not realized. In contrast to prior examples, thiomethyl ether formation had unfortunately no effect on yield or diastereoselectivity. However, it did obviate the necessity for immediately prior purification.



Scheme 51

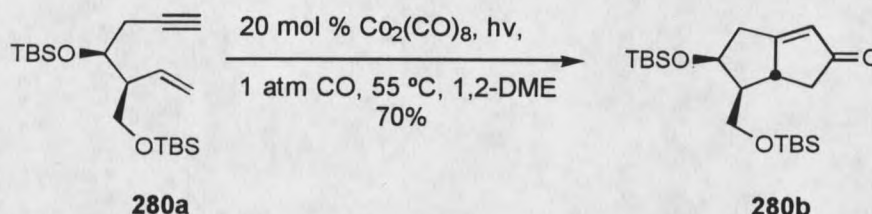
Silanes such as **275a** and **277a** would be interesting substrates because of the increase in molecular complexity readily achieved by sequential Pauson-Khand cyclization followed by silyl-to-hydroxyl conversion.⁹² With 5 mol % catalyst, enyne **277a** (R = H) appeared to have cyclized to only a limited extent (15% by G.C.), but more efficient conversion was not realized. Enynes similar to **275** were not examined.



Scheme 52

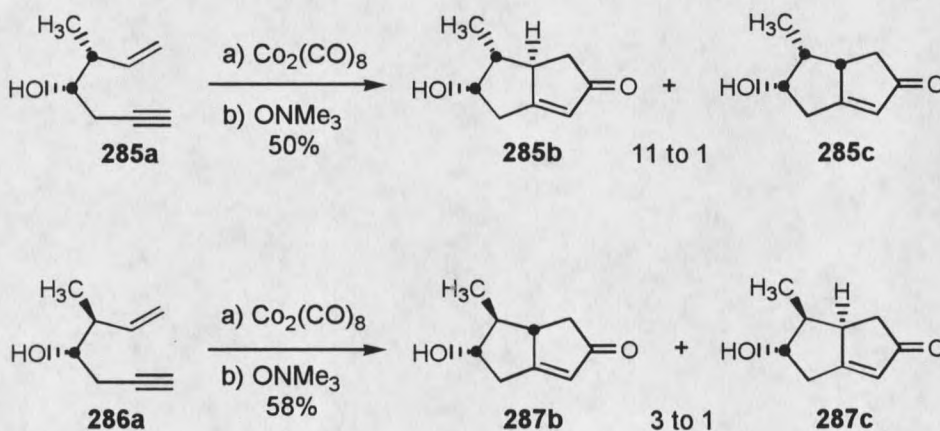
With such a diversity of enynes examined, attention then returned to the carbacyclin synthesis. Epi-carbacyclin precursor **148** was desilylated (NaOH, MeOH, 90%) and subjected to the usual photopromoted Pauson-Khand cyclization

conditions. Although catalytic turnover was poor, the desired enone **280b** was obtained in 70% unoptimized yield as a single isomer.



Scheme 53

The excellent diastereoselection observed in this cyclization is consistent with studies conducted by Schore.⁸⁸ He evaluated syn and anti 3,4-disubstituted enynes, and found that the syn-enyne **285a** afforded an 11 to 1 ratio of the expected exo-substituted enyne. In contrast, the anti enyne **286a** showed decreased diastereoselection and a 3 to 1 ratio of enones was obtained.



Scheme 54

A variety of enynes failed to participate in the photopromoted catalytic Pauson-Khand reaction (**Table 19**). These included all 1-trimethylsilyl-alkynes examined, most free alcohols and all intermolecular examples. Intermolecular studies were conducted with excess norbornene or 2,3-dihydrofuran either neat or in a variety of solvents (neat, toluene, 1,2-DME, TFE, 1,2-DME-TFE). Three different alkynes were examined under each set of reaction conditions: 1-octyne, 1-methylthio-1-octyne, and phenyl acetylene. The successful development of an intermolecular annulation strategy was not achieved.

Table 19. Unsuccessful Substrates for Photopromoted Pauson-Khand Cyclizations

Entry	Enyne	Anticipated Product	Yield ^a
1, 229			N.R.
2	$R^1 = H, R^2 = H$		N.R.
3, 216a	$R^1 = H, R^2 = TMS$		N.R.
4, 240a	$R^1 = TBS, R^2 = TMS$		N.R.
5, 254a	$R^1 = TBS, R^2 = S(t-Bu)$		N.R.
	$R^1 = MTM, R^2 = H$		N.R.
6, 152			N.R.
7, 196a			N.R.
8, 197a			N.R.
8, 182a			N.R.
9, 290a			N.R.
10, 291a	$R = H$		33%
11, 292a	$R = TMS$		42%
12, 297a			15%

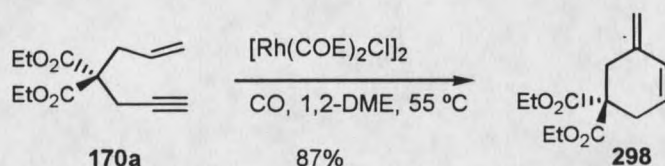
^a 5 mol % catalyst was usually employed. Yields are G.C. yields.

3.9 Rhodium Catalyzed Cycloisomerizations

The extremely intense visible light generated by the halogen bulb employed in these experiments was readily available without considerable financial investment until recent years. Photopromotion of the Pauson-Khand reaction may have been examined by other researches previously, but they undoubtedly met with minimal success. Since this light source is relatively new, other metal carbonyl catalysts (either prepared or purchased commercially) were examined for Pauson-Khand activity under irradiation with bench-mark enyne **170a**: $\text{Ru}_3(\text{CO})_{12}$, $[\text{CpMo}(\text{CO})_3]_2$, $\text{Ru}_3(\text{CO})_{12}$ with $(\text{F}_6\text{C}_2\text{CHO})_3\text{P}$ and phosphole, $\text{Fe}_2(\text{CO})_9$, $\text{Rh}(\text{acac})_2\text{-TMSOTf}$, $(\text{Indenyl})\text{Rh}(\text{COD})$, $[\text{Rh}(\text{COE})\text{Cl}]_2$ with $(\text{F}_6\text{C}_2\text{CHO})_3\text{P}$ and phosphole, $(\text{In})\text{Rh}(\text{COD})$ with $(\text{F}_6\text{C}_2\text{CHO})_3\text{P}$ and phosphole, $[\text{CpRu}(\text{CO})_2]_2$, $\text{Re}_2(\text{CO})_{10}$, $\text{CoBr}_2 / \text{Zn}$.⁹³ Only the first two metal carbonyls and $\text{Rh}(\text{acac})_2\text{-TMSOTf}$ showed cyclopentenone formation. With 5 mol % catalytic loading in 1,2-DME under the usual irradiation conditions, the ruthenium and molybdenum complexes each showed 2% conversion into bicyclic enone **170b** by G.C.M.S.. With 10 mol % catalytic loading the $\text{Rh}(\text{acac})_2\text{-TMSOTf}$ showed stoichiometric conversion to the desired cyclopentenone, but no catalytic activity.

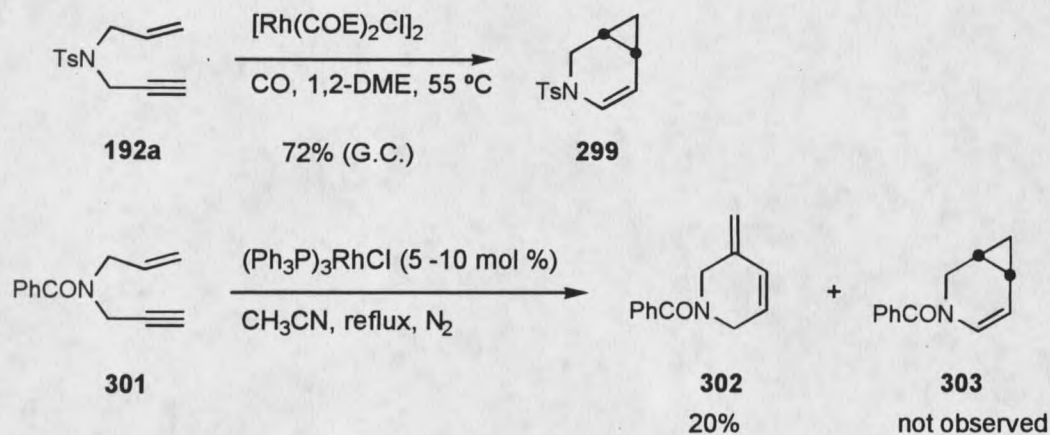
More significantly, of the rhodium catalysts examined, $[\text{Rh}(\text{COE})\text{Cl}]_2$ generated cycloisomerization products instead of the anticipated Pauson-Khand adduct. These reactions represent novel rhodium catalyzed cycloisomerization

reactions (**Schemes 54 and 55**).⁹⁴ Specifically, treatment of enyne **175a** with 1 or 2 equivalents $(C_2F_6CHO)_3P$ and $[Rh(COE)Cl]_2$ under an atmosphere of Ar or CO provided afforded alkylidene cyclohexene **298** in excellent (>80% G.C.) yields. Under optimized conditions (1 mol % $[Rh(COE)Cl]_2$, 2 mol % $(C_2F_6CHO)_3P$ under an atmosphere of CO at 55 °C, 24 h) provided diene **298** in 87% isolated yield. The use of a CO atmosphere generated a homogeneous and nearly colorless complex, whereas the use of Ar resulted in a much darker, heterogeneous solution with lower catalytic activity.



Scheme 55

Tosamide **192a** was next examined under the same reaction conditions, and the interesting cyclopropane moiety **299** was generated in 72% G.C. conversion. Using 5 mol % catalyst did not improve the conversion. Complexation of alkyne **192a** with $Co_2(CO)_8$ did not sufficiently change its R_f value to allow separation by silica gel chromatography. Final separation of the cyclopropane from unreacted starting material was achieved by subsequent Pauson-Khand cyclization.



Scheme 56

Cyclohexadiene **298** was previously synthesized by a similar isomerization reaction catalyzed by Wilkinson's catalyst (5 mol % Rh, acetonitrile, 80 °C, 73%).⁹⁵ Grigg also examined substrates with a heteroatom tether, and found that amide **301** produced cycloisomerization product **302** in poor yield without cyclopropane formation. Thus initially, this new catalyst appears to offer better yields and different reactivity with heteroatom tethered enynes.

4. Conclusions

Several of the factors that influence substrate based control of diastereoselection in $\text{Cp}_2\text{Zr(II)}$ mediated enyne cyclizations have been illuminated by examination of an extensive series of substituted enynes. It is evident that a high level of stereocontrol can often be achieved with the $\text{Cp}_2\text{Zr(II)}$ mediated enyne cyclization protocol. Based on the diastereoselectivity observed with model substrates in the $\text{Cp}_2\text{Zr(II)}$ cyclization study, several synthetic strategies directed toward the synthesis of carbacyclin have been examined. Failure of the $\text{Cp}_2\text{Zr(II)}$ methodology to effect the key cyclization of an epi-carbacyclin precycle led to the exploration of alternative reagents.

These efforts have resulted in the development of an eminently practical, catalytic, photopromoted Pauson-Khand reaction that proceeds under mild reaction conditions (50 - 55 °C) under 1 atm of CO. The photopromoted Pauson-Khand reaction has been shown to be compatible with substrates bearing of a wide variety of functional groups and substitution patterns. Many of the solvent and ligand dependencies of the reaction have been revealed. In some instances, substrate modification resulted in improved yields and increased diastereoselection.

Finally, synthetic studies directed toward the synthesis of carbacyclin have resulted in a short enantiocontrolled synthesis of the epi-carbacyclin core. The key

steps of this synthesis were a syn-aldol condensation and ring closure by the catalytic photopromoted Pauson-Khand reaction.

5. Experimental Section

5.1 General Experimental Details

The purification of common solvents and reagents is outlined in **Table 20**.

For a comprehensive listing of acronyms and abbreviations, see reference ⁹⁶.

Table 20. Purification of Common Materials

Material	Drying Agent	Method
THF, Et ₂ O, 1,2-DME	Na ⁰ Benzophenone-ketyl	Distillation
Acetonitrile	CaH ₂	"
2,6-Lutidine	"	"
2-Methoxyethyl Ether (Diglyme)	LiAlH ₄ -Triphenylmethane ^a	"
Methylcyclohexane	CaH ₂	"
Pyridine	LiAlH ₄ -Triphenylmethane ^a	"
Toluene	CaH ₂	"
<i>N,N</i> -Dimethyl Acetamide (DMA)	CaSO ₄	Vac. Distillation
<i>N,N</i> -Dimethyl Formamide (DMF)	"	"
Hexamethylphosphoramide (HMPA)	CaH ₂	"
2° and 3° amines	LiAlH ₄	Fract. Distillation
Triphenylphosphite [P(OPh) ₃]	-	Fract. Distillation
(<i>n</i> -Bu) ₃ SnCl	-	Fract. Distillation
4- <i>N,N</i> -Dimethylaminopyridine (DMAP)	-	Sublimation
Trifluoromethanesulfonic acid (Triflic acid, TfOH) ⁹⁷	-	Fract. Distillation

^a Material was distilled from a *red* solution of LiAlH₄-triphenylmethane.

Hydrocarbon solvents and benzene were purified by repeatedly stirring over fresh concentrated sulfuric acid until no discoloration occurred, washed with water and distillation from potassium. Zirconocene dichloride was purchased from Boulder Scientific and was purified by continuous extraction (45 g of zirconocene dichloride) through a pad of dry Celite (4 cm diameter by 10 cm) with CH_2Cl_2 (200 mL) and the resulting crystals were dried *in vacuo*. Dicobalt octacarbonyl was either purchased from Strem Chemicals, stored in a glove box and used as received, or was purified by recrystallization from hexane or by sublimation at 50 mTorr at 25 °C. Deuterated chloroform was purified by filtration through basic alumina (pipet) immediately before use.

The molarities for organolithium reagents were preferably determined by titration with *N*-pivaloyl-*o*-toluidine as previously described.⁹⁸ In addition, the molarities for organolithium and alkylmagnesium halide reagents were sometimes established by titration with 2-butanol and either 1,10-phenanthroline (at 0 °C) or 2,2'-bipyridyl (at 25 °C), respectively, as indicators. Unless otherwise noted, all reactions were carried out under an atmosphere of argon⁹⁹ in flamed, oven-dried Pyrex vessels.

^1H NMR and ^{13}C NMR were measured at 300 or 250 MHz and 75 or 62.9 MHz, respectively, with either a Bruker AC-300, DPX300 or DRX250 spectrometer, unless otherwise stated. ^1H NMR and ^{13}C NMR chemical shifts are

reported as δ values in ppm relative to the residual proton signals in CDCl_3 or C_6D_6 (^1H δ = 7.24 or 7.15) or the CDCl_3 or C_6D_6 triplet (^{13}C δ = 77.0 or 128.7). ^1H NMR coupling constants are reported in Hz and refer to apparent multiplicities and not true coupling constants. Multiplicity is indicated as follows: s (singlet); d (doublet); t (triplet); q (quartet); p (pentet); sx (sextet); br (broad); m (multiplet); app d (apparent doublet); app t (apparent triplet); dd (doublet of doublets); etc. NOE difference spectra for the $\text{Co}_2(\text{CO})_8$ derived cyclopentenones and later compounds were obtained on either a Bruker AC-300, DPX300 or DRX250 spectrometer with low decoupling irradiation power (typically 40L, or 70 dB) and long irradiation times (10 seconds). This extremely useful NOE protocol for *small molecules* was provided by Martha D. Bruch formerly of the University of Delaware NMR Spectrometry Center, and is gratefully acknowledged.

Infrared spectra were typically recorded on a Bruker IFS 25 IR, when available.

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 chromatographs were obtained for all products on a Varian Model 3700 gas chromatograph equipped with a flame ionization detector and either an Alltech Econocap SE-54 bonded phase column (15 m length, 0.54 mm id, and 1.2 μm film thickness) or a Heliflex (Alltech)

RSL150BP bonded phase column (30 m length, 0.32 mm id, and 0.25 μm film

thickness). Except where noted, diastereomer ratios were determined by G.C. analysis of crude reaction mixtures. Preparative gas chromatography was performed on a Varian 3300 Gas Chromatograph equipped with a 10% OV-17 on chromosorb column (2 m length, 2 mm id). Thin layer chromatography (TLC) was performed on Machery-Nagel Polygram[®] SIL G/UV₂₅₄ plates supplied by Alltech and Associates. Preparative thin layer chromatography was performed on 1 mm thick silica gel 60 glass plates manufactured by Whatman. Gradient flash¹⁰⁰ column chromatography was performed with Merck silica gel 60, unless otherwise described. Optical rotation measurements were measured without temperature control at approximately 25 °C with a Perkin-Elmer 241 MC Polarimeter.

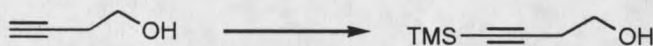
LDA•THF complex was prepared by dropwise addition of *n*-BuLi (5.1 mL, 9.8 M in heptane, 50 mmol) to a solution of *N,N*-diisopropylamine (7.0 mL, 50 mmol) in THF (4 mL, 50 mmol) and methylcyclohexane (34 mL) cooled to -78 °C. The solution was allowed to warm to 0 °C and this complex was titrated by the method of Vedejs¹⁰¹ prior to use. The solution was stable indefinitely at -20 °C and was only allowed to warm to 0 °C while in use.

The following materials were made according to literature methods: (4*S*,5*S*)-3-((*E*)-2-butenoyl)-4-methyl-5-phenyl-2-oxazolidinone,^{108c} (4*S*)-3-((*E*)-2-butenoyl)-4-(1-methylethyl)-2-oxazolidone (including spectral data),^{108c} D,L-10-camphorsulfonyl chloride,¹⁰² (+)-(1*S*)-10-camphorsulfonamide,¹⁰³

camphorsulfonamide,¹⁰³ (S)-camphor sultam,¹⁰³ Bu₂Mg,¹⁰⁴ di-*n*-butylboryl trifluoromethanesulfonate,¹⁰⁵ 2,2-dimethyl-4-pentenal,¹⁰⁶ lithium cyclopentadienide and lithium pentamethylcyclopentadienide,¹⁰⁷ (4*S*)-4-(1-methylethyl)-2-oxazolidinone,^{108a} (4*R*,5*S*)-4-methyl-5-phenyl-2-oxazolidinone,¹⁰⁸ methylenebis(dichlorophosphine),¹⁰⁹ tetrabutyl ammonium perruthenate (TBAP),¹¹⁰ *p*-toluoylsufenyltoluoylsulfonate,¹¹¹ 1-(tributylstannyl)-allene,¹¹² trifluorophosphine,¹¹³ [(trimethylsilyl)oxy]ethoxymethyl chloride (SEM-Cl),¹¹⁴ trimethylsilyl triflate (TMSOTf),¹¹⁵ *tert*-butyldimethylsilyl triflate (TBDMSOTf or TBSOTf),¹¹⁵ Cp₂M(PMe₃)₂, M = Ti or Zr,¹¹⁶ Cp*ZrCl₃,¹¹⁷ triethanolamine borate,¹¹⁸ Rieke magnesium (Mg*),¹¹⁹ zinc chloride TMEDA complex.¹²⁰

5.2 Enynes

4-Trimethylsilyl-3-butyne-1-ol.



A vigorously stirred solution of 3-butyne-1-ol (2.0 mL, 25 mmol) in THF (200 mL) was cooled to -78 °C and a solution of *n*-BuLi (5.30 mL, 9.90 M in heptane, 52.2 mmol) was added in one portion. The resulting viscous suspension was stirred for 1 h at -78 °C and then treated with chlorotrimethylsilane (6.98 mL, 55 mmol). The dry ice-acetone bath was removed and the reaction stirred for 12 h. The reaction

mixture was then poured into a separatory funnel containing H₂O (500 mL) and saturated aqueous NH₄Cl (100 mL). The mixture was extracted with hexane (3 x 100 mL) and the combined organic portions were washed with H₂O (25 mL), brine (50 mL) and concentrated *in vacuo*. The residue was transferred to a polyethylene beaker with the aid of EtOAc (30 mL) and treated with conc. HF (approx. 5 mL). After stirring 5 min the reaction was diluted with H₂O (500 mL), transferred to a separatory funnel and extracted with 1:3 EtOAc-hexane (4 x 75 mL). The combined organic phases were washed with H₂O (2 x 5 mL), saturated aqueous NaHCO₃ (2 x 15 mL), brine (20 mL), dried (Na₂SO₄), filtered and concentrated *in vacuo*. Bulb-to-bulb distillation (80 °C, 1 Torr) of the resultant oil afforded 3.31 g (92%) the title compound as a colorless oil: ¹H NMR (CDCl₃) δ 3.69 (t, *J* = 6.3 Hz, 2H, CH₂), 2.48 (t, *J* = 6.3 Hz, 2H, CH₂), 1.62 (s, 1H, OH), 0.14 (s, 9H, Si(CH₃)₃); ¹³C NMR (CDCl₃) δ 103.4, 85.5, 60.8, 24.1, -0.04.

4-Bromo-1-trimethylsilyl-1-butyne (**4a**).



A magnetically stirred solution of 4-trimethylsilyl-3-butyn-1-ol (3.32 g, 23 mmol) and PPh₃ (6.93 g, 26.45 mmol) in CH₂Cl₂ (120 mL) maintained at less than 10 °C was treated with finely powdered *N*-bromo-succinamide (4.50 g, 25.3 mmol) under an atmosphere of argon. After 5 min the reaction was warmed to rt, stirred for 30

min and quenched with methanol (0.5 mL). The flask containing the reaction mixture was concentrated on a rotary evaporator *in vacuo* at 35 °C until precipitates formed. Bulb-to-bulb distillation (80 °C, 0.5 Torr, 15 min) from the residue afforded 4.32 g (98%) of the title compound **4a** as a colorless oil: ^1H NMR (CDCl_3) δ 3.40 (t, $J = 7.4$ Hz, 2H, CH_2), 2.74 (t, $J = 7.4$ Hz, 2H, CH_2), 0.13 (s, 9H, $\text{Si}(\text{CH}_3)_3$); ^{13}C NMR δ (CDCl_3) 103.9, 87.2, 29.8, 25.0, 0.6; IR (thin film) 2959, 2177, 1419, 1270, 843, 860, 636 cm^{-1} .

4-Iodo-1-trimethylsilyl-1-butyne (**4b**).

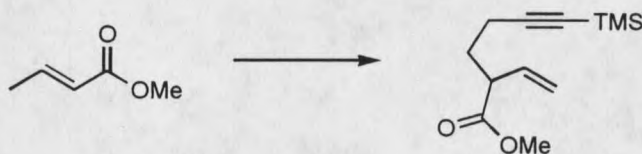


To a magnetically stirred solution of 4-trimethylsilyl-3-butyn-1-ol (6.45 g, 45.3 mmol), PPh_3 (15.5 g, 59.0 mmol), imidazole (5.25 g, 79.4 mmol) in 1:4 CH_3CN - Et_2O (250 mL) was added I_2 (11.5 g, 95.3 mmol) in Et_2O (60 mL) via canula at 25 °C. If necessary, additional Et_2O may be added to aid the transfer of I_2 . After 5 min the reaction was quenched with methanol (1 mL) and concentrated *in vacuo*. The solids were triturated with hexane (3 x 75 mL) and the combined organic layers washed with H_2O (20 mL), saturated aqueous $\text{Na}_2\text{S}_2\text{O}_6$ (2 x 20 mL), brine (20 mL), dried (MgSO_4), filtered and concentrated *in vacuo*. Bulb-to-bulb distillation (80 °C, 1 Torr) afforded 10.4 g (91%) of **4b** as a colorless oil: ^1H NMR (CDCl_3) δ 3.19 (t, J

= 7.6 Hz, 2H, CH₂), 2.76 (t, *J* = 7.6 Hz, 2H, CH₂), 0.13 (s, 9H, Si(CH₃)₃); ¹³C

NMR (CDCl₃) δ 105.8, 87.6, 25.8, 1.5, 0.6.

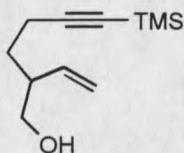
Methyl 2-ethenyl-6-(trimethylsilyl)-5-hexynoate (**8**).



According to the general procedure for the preparation of LDA for **14a**, a solution of methyl crotonate (0.5 g, 5 mmol) in THF (3 mL) was added to a magnetically stirred solution of LDA (5.1 mmol) in THF (15 mL) maintained at -78 °C. After 1 h a solution of 4-iodo-1-trimethylsilyl-1-butyne (1.51 g, 6.0 mmol) and HMPA (2.15 g, 12.0 mmol) in THF (8 mL) cooled to -78 °C was added dropwise over 3 min. After 3 h a solution of saturated aqueous NH₄Cl (5 mL) in THF (30 mL) was added in one portion. The reaction mixture was allowed to warm to rt and was diluted with H₂O (100 mL) and pentane (25 mL). The organic layer was separated and the aqueous layer was extracted with pentane (2 x 25 mL) and the combined organic layers were washed with H₂O (3 x 15 mL), saturated aqueous NaHCO₃ (10 mL), brine (10 mL), dried (Na₂SO₄), filtered and concentrated *in vacuo*. Chromatography of the residual oil on silica gel (hexane for elution) afforded 84 mg (8%) of the title compound as a colorless oil: ¹H NMR (CDCl₃) δ 5.78 (ddd, *J* = 18.5, 9.8, 8.7 Hz, 1H, CH=CH₂), 5.19-5.08 (m, 2H, CH=CH₂), 3.67 (s, 3H, OCH₃); 3.20-3.13 (m,

^1H , CH), 2.23-2.18 (m, 2H, $\text{CH}_2\text{C}\equiv\text{C}$), 2.03-1.90 (m, 1H, CHH), 1.76-1.68 (m, 1H, CHH), 0.12 (s, 9H, $\text{Si}(\text{CH}_3)_3$); IR (thin film) 3083, 2957, 2175, 1739, 1640, 1435, 1250, 1203, 1161, 923, 760, 699, 639 cm^{-1} .

1-(Trimethylsilyl)-5-(hydroxymethyl)-6-hepten-1-yne (**9**).

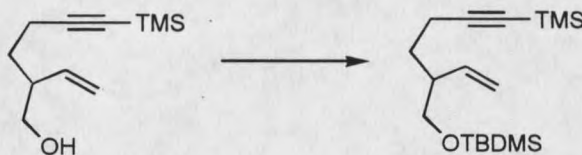


To a magnetically stirred suspension of LiAlH_4 (20.9 mg, 0.55 mmol) in Et_2O (1 mL) cooled to $0\text{ }^\circ\text{C}$ was added dropwise EtOH (32.2 μL , 0.55 mmol) over 1 min. The solution was warmed to rt for 2 h then cooled to $-15\text{ }^\circ\text{C}$ and dimethylcarboxamide **14a** (118 mg, 0.50 mmol) in Et_2O (0.5 mL) was added dropwise. The solution was warmed to $-10\text{ }^\circ\text{C}$ and stirred for 1 h. The reaction mixture was added dropwise to an aqueous solution of citric acid (5 mL, 0.5 M citric acid solution in half-saturated brine) maintained at or below $-5\text{ }^\circ\text{C}$. After the addition was complete the reaction mixture was transferred to a separatory funnel and the organic phase was separated and added to a pH 7.0 aqueous phosphate buffer solution (20 mL, 1.0 M) maintained at $0\text{ }^\circ\text{C}$. The aqueous phase was extracted with Et_2O (2 x 5 mL) and the combined organic layers were separated from the aqueous phosphate buffer and washed with a $0\text{ }^\circ\text{C}$ saturated aqueous solution of NaHCO_3 (2 x 5 mL) and dried (NaSO_4) for 5 min at $0\text{ }^\circ\text{C}$. The solution

was filtered and then added to a solution of LiAlH_4 (76 mg, 2.0 mmol) in Et_2O (2 mL) at rt over 3 min. After stirring for 15 min the remaining LiAlH_4 was cautiously quenched with aqueous 10% HCl (10 mL) and the organic layer separated. The aqueous layer was extracted with Et_2O (2 x 5 mL) and the combined organic layers were washed with brine (5 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo*. Chromatography of the residual oil on silica gel (2% EtOAc /hexane for elution) afforded 18 mg (18%, both steps, typical yields 0-22%) of the title compound as a colorless oil. Most of the recovered material (ca. 75% mass) was the alcohol from the reduction of the corresponding *conjugated* aldehyde (**15**).

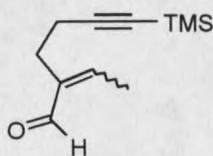
Alternatively, the title compound may be prepared by reduction of methyl 2-ethenyl-6-(trimethylsilyl)-5-hexynoate, **8**, with LiAlH_4 according to the general procedure utilized for **69**: ^1H NMR (CDCl_3) δ 5.57 (ddd, $J = 19.6, 10.8, 8.7$ Hz, 1H, CHCH_2), 5.18-5.07 (m, 2H, CHCH_2), 3.56 (app dd, $J = 10.7, 6.3$ Hz, 1H, CHHOH), 3.43 (app dd, $J = 10.7, 7.6$ Hz, 1H, CHHOH), 2.30 (s, 1H, OH), 2.30-2.10 (m, 3H, CH and CH_2), 1.68-1.57 (m, 2H, CH_3), 0.12 (s, 9H, $\text{Si}(\text{CH}_3)_3$); ^{13}C NMR (CDCl_3) δ 139.4, 118.6, 107.7, 85.6, 66.0, 46.7, 30.3, 18.3, 0.8.

1-(Trimethylsilyl)-5-[(1,1-dimethylethyl)dimethylsiloxymethyl]-6-hepten-1-yne (**10**).

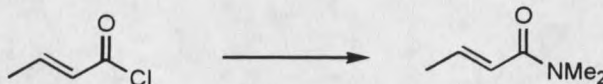


The title compound was prepared according to the general procedure for **71** to afford 8 mg (82%) of the title compound as a clear oil: ^1H NMR (CDCl_3) δ 5.57 (ddd, $J = 21.4, 10.7, 10.7$ Hz, $\text{CH}=\text{CH}_2$), 5.08-5.01 (m, 2H, $\text{CH}=\text{CH}_2$), 3.57-3.45 (m, 2H, CH_2O), 2.36-2.12 (m, 3H, CH and CH_2), 1.73-1.69 (m, 1H, CHH), 1.50-1.33 (m, 1H, CHH), 0.86 (s, 9H, $\text{C}(\text{CH}_3)_3$), 0.24 (s, 9H, $\text{Si}(\text{CH}_3)_3$), 0.00 (s, 6H, $\text{Si}(\text{CH}_3)_2$).

2-(Trimethylsilyl-3-butyne)-2-butenal (**15**).

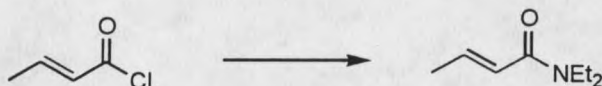


Attempts to separate the above aldehyde resulted in isolation of the conjugated crotonaldehyde: ^1H NMR (CDCl_3) δ 9.35 (s, 1H, CHO), 6.68 (q, $J = 7.0$ Hz, 1H, $\text{C}=\text{CHCH}_3$), 3.30 (t, $J = 7.2$ Hz, 2H, CH_2), 2.48 (t, $J = 7.2$ Hz, 2H, CH_2), 2.03 (d, $J = 7.0$ Hz, 3H, CHCH_3), 0.11 (s, 9H, $\text{Si}(\text{CH}_3)_3$).

N,N-Dimethyl-2-buteneoyl carboxamide.

An oven-dried, 1-L, three neck round-bottomed flask was equipped with a Teflon coated magnetic stir bar, reflux condenser, addition funnel, and a glass stopcock. A continuous argon inlet was attached to the top of the addition funnel and a CaSO₄ drying tube was attached to the top of the reflux condenser. The flask was cooled in a dry ice-acetone bath and charged with *N,N*-dimethylamine (24.8 g, 0.55 mol) and Et₂O (300 mL). A solution of 2-butenoyl chloride (26.1 mL, 0.20 mol) in Et₂O (100 mL) was added dropwise over 30 min to the vigorously stirred solution. The cold bath was subsequently removed and the reaction mixture was heated at reflux for 30 min. The mixture was cooled, and the resulting suspension was filtered through Celite (18 cm diameter by 10 cm) and the solids washed with Et₂O (4 x 25 mL). The filtrate was concentrated *in vacuo* and the residual oil was purified by fractional distillation (14 Torr) to afford 21.9 g (97%) of the title compound as a colorless oil: ¹H NMR (CDCl₃) δ 6.82 (dq, *J* = 14.9, 6.9 Hz, 1H, CHCH₃), 6.23 (dd, *J* = 15.0, 1.8 Hz, 1H, COCH), 3.02 (s, 3H, NCH₃), 2.95 (s, 3H, NCH₃), 1.83 (dd, *J* = 6.9, 1.6 Hz, 3H, CHCH₃); ¹³C (CDCl₃) δ 166.6, 140.6, 121.9, 37.1, 35.3, 17.9; IR (thin film) 3472, 3022, 2937, 1661, 1615, 1496, 1446, 1397, 1154, 924, 683, 628 cm⁻¹.

N,N-Diethyl-2-butenoyl carboxamide.



A solution of *N,N*-diethylamine (16.8 mL, 163 mmol) in Et₂O (60 mL) was added dropwise over 30 min to a magnetically stirred solution of 2-butenoyl chloride (6.83 g, 65.3 mmol) in Et₂O (100 mL) maintained at 0 °C. After the addition was complete the NaCl-ice bath was removed and the reaction was heated at reflux for 30 min. The resulting suspension was filtered through Celite (10 cm diameter by 10 cm) and the solids were subsequently washed with Et₂O (4 x 25 mL). The filtrate was concentrated *in vacuo* and the residual oil was purified by bulb-to-bulb distillation to afford 6.83 g (74%) of the title compound as a colorless oil: ¹H NMR (CDCl₃) δ 6.77 (dt, *J* = 6.9, 4.1 Hz, 1H, CHCH₃), 6.08 (app dd, *J* = 14.9, 1.6 Hz, 1H, COCH), 3.26 (app q, *J* = 7.3 Hz, 4H, NCH₂), 1.73 (dt, *J* = 6.9, 1.1 Hz, 3H, NCH₂CH₃), 1.02 (dt, *J* = 17.2, 7.1 Hz, 3H, CH₂CH₃); ¹³C NMR (CDCl₃) δ 165, 141, 122, 143, 141, 19, 15, 13; IR (thin film) 3533, 3223, 2972, 1665, 1615, 1455, 1288, 1148, 901, 683, 628 cm⁻¹.

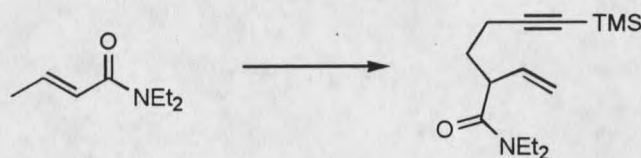
N,N-Dimethyl-1-(trimethylsilyl)-6-hepten-1-yne-5-carboxamide (**14a**).



A solution of *n*-BuLi (2.53 mL, 4.34 M in heptane, 11.0 mmol) was added dropwise to a magnetically stirred solution of DIPA (1.68 mL, 12.0 mmol) in THF (300 mL) maintained at -78 °C. After 10 min the mixture was warmed to 0 °C, then recooled to -78 °C. After stirring for an additional 15 min at -78 °C a solution of *N,N*-diethyl-2-butenecarboxamide (1.13 g, 10.0 mmol) in THF (10 mL) was added dropwise and the reaction mixture was stirred for 1 h at -78 °C. The resulting mixture was subsequently allowed to warm to 23 °C, held at this temperature for 1.5 h and then recooled to -78 °C. A solution of 4-iodo-1-trimethylsilyl-1-butyne (3.14 g, 12.0 mmol) in THF (10 mL) was then introduced and the reaction mixture allowed to warm to rt overnight. The resulting solution was diluted with half-saturated aqueous NH₄Cl (200 mL) and the organic phase separated. The aqueous phase was extracted with 1:1 Et₂O-CH₂Cl₂ (3 x 50 mL). The combined organic phases were washed with 10% aqueous H₂SO₄ (2 x 5 mL), H₂O (5 mL), saturated aqueous NaHCO₃ (5 mL), brine (10 mL), dried (MgSO₄), filtered and concentrated *in vacuo*. Chromatography of the residual oil on silica gel (20% EtOAc/hexane for elution) afforded 1.23 g (52%) of **14a** as a viscous yellow oil: ¹H NMR (CDCl₃) δ 5.75 (ddd, *J* = 17.0, 10.4, 8.5 Hz, 1H, CH=CH₂), 5.10 (m, 2H, CH=CH₂), 3.51 (app q, *J* = 7.8 Hz, 1H, COCH), 3.04 (s, 3H, NCH₃), 2.93 (s, 3H, NCH₃), 2.21 (t, *J* = 6.7 Hz, 2H, CH₂C≡C), 1.92 (app hx, *J* = 6.7 Hz, 1H, CHCH₂CH₂), 1.64 (app hx, *J* = 6.7 Hz, 1H, CHCH₂CH₂), 0.10 (s, 9H, Si(CH₃)₃); ¹³C NMR (CDCl₃) δ 173.5,

173.2, 117.7, 107.5, 86.1, 46.0, 37.3, 36.4, 31.5, 18.1, 0.8; IR (thin film) 3079, 2959, 2173, 1650, 1397, 1250, 1039, 842, 760, 698, 638 cm^{-1} .

N,N-Diethyl-2-ethenyl-6-(trimethylsilyl)-5-hexynamide (**14b**).



A solution of *n*-BuLi (2.53 mL, 4.34 M in heptane, 11.0 mmol) was added dropwise to a magnetically stirred solution of DIPA (1.68 mL, 12.0 mmol) in THF (300 mL) maintained at $-78\text{ }^{\circ}\text{C}$. After 10 min the mixture was warmed to $0\text{ }^{\circ}\text{C}$, then cooled to $-78\text{ }^{\circ}\text{C}$. After stirring for an additional 15 min at $-78\text{ }^{\circ}\text{C}$ a solution of *N,N*-diethyl-2-butenamide (1.41 g, 10.0 mmol) in THF (10 mL) was added dropwise over 5 min and the reaction mixture was then stirred for 1 h at $-78\text{ }^{\circ}\text{C}$. The resulting mixture was subsequently allowed to warm to $23\text{ }^{\circ}\text{C}$, held at this temperature for 1.5 h and then recooled to $-78\text{ }^{\circ}\text{C}$. A solution of 4-iodo-1-(trimethylsilyl)-1-butyne (3.02 g, 12.0 mmol) in THF (10 mL) was then introduced dropwise, the $-78\text{ }^{\circ}\text{C}$ bath was removed and the reaction mixture allowed to stir 9 h. The resulting solution was quenched with half-saturated aqueous NH_4Cl (200 mL) and the organic phase was separated. The aqueous phase was extracted with 1:1 $\text{Et}_2\text{O}-\text{CH}_2\text{Cl}_2$ (3 x 50 mL). The combined organic phases were washed with 10% aqueous H_2SO_4 (2 x 5 mL), H_2O (5 mL), saturated aqueous NaHCO_3 (5 mL), brine (10 mL), dried

(MgSO₄), filtered and concentrated *in vacuo*. Chromatography of the residual oil on silica gel (20% EtOAc/hexane for elution) afforded 1.08 g (41%) of **14b** as a light yellow oil: ¹H NMR (CDCl₃) δ 5.83 (ddd, *J* = 17.6, 10.4, 8.4, Hz, 1H, CH=CH₂), 5.10 (m, 2H, CH=CH₂), 3.34 (m, 5H, COCH and NCH₂), 2.2 (m, 2H, CH₂C≡C), 1.94 (app sx, *J* = 6.7 Hz, 1H, COHCH₂), 1.68 (app sx, *J* = 6.7 Hz, 1H, COHCH₂), 1.19 (t, *J* = 7.15 Hz, 3H, CH₃), 1.08 (t, *J* = 7.2 Hz, 3H, CH₃), 0.11 (s, 9H, Si(CH₃)₃); ¹³C NMR (CDCl₃) δ 172.7, 137.9, 117.3, 107.5, 86.0, 45.9, 42.4, 41.2, 32.0, 18.1, 15.5, 13.3, 0.8; IR (thin film) 2963, 2173, 1647, 1632, 1449, 1250, 1139, 1043, 918, 843, 638 cm⁻¹; *m/z* 265 (M⁺), 192, 165, 100, 73.

3-(Diethylaminomethyl)-7-(trimethylsilyl)-1-hepten-6-yne (**16**).

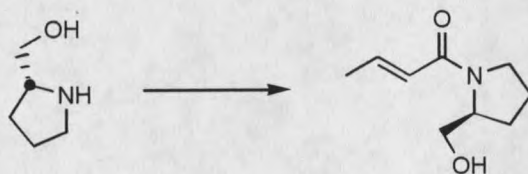


To a magnetically stirred solution of LiAlH₄ (8.5 mg, 2.2 mmol) in Et₂O (5 mL) at 22 °C was added a solution of **3c** (80 mg, 0.3 mmol) in Et₂O (0.3 mL) in one portion. The reaction mixture was heated at reflux for 36 h, then cooled to 0 °C.

To the cooled reaction mixture was added H₂O (2 mL) and aqueous NaOH (1 mL, 2.0 M). After 15 min of vigorous stirring at room temperature the organic layer was separated and the aqueous layer was extracted with Et₂O (3 x 5 mL). The combined organic layers were washed with brine (2 x 2 mL), dried (MgSO₄),

filtered and concentrated *in vacuo*. Chromatography of the residual oil on basic alumina (1% EtOAc/hexane for elution) afforded 56 mg (74%) of **3e** as a clear oil: ^1H NMR (CDCl_3) δ 5.51 (m, 1H, $\text{CH}=\text{CH}_2$), 5.02 (m, 2H, $\text{CH}=\text{CH}_2$), 2.48 (dt, $J = 6.9, 1.8$ Hz, 4H, $\text{N}(\text{CH}_2\text{CH}_3)$), 2.29 (m, 2H, NCH_2), 2.15 (m, 2H, $\text{CH}_2\text{C}\equiv\text{C}$), 1.75 (m, 1H, CH), 1.24 (m, 2H, $\text{CH}_2\text{CH}_2\text{C}\equiv\text{C}$), 0.96 (t, $J = 7.1$ Hz, 6H, CH_3), 0.11 (s, 9H, $\text{Si}(\text{CH}_3)_3$); ^{13}C NMR (CDCl_3) δ 141.1, 115.4, 107.6, 84.4, 57.9, 47.3, 41.5, 31.4, 17.6, 11.5, 0.1; IR (thin film) 3076, 2175, 1639, 1453, 1250, 1041, 914, 841, 760, 637 cm^{-1} ; m/z 149 ($\text{MH}^+ - \text{TMS}, -\text{Et}$), 121, 93, 73 (TMS).

(2*S*)-2-(hydroxymethyl)-1-(but-2'-enyl)pyrrolidine (**17**).



A mixture of (2*S*)-2-(hydroxymethyl)-pyrrolidine (3.401 g, 33.6 mmol) and 2-butenic acid anhydride (5.23 g, 35.3 mmol) was heated at 75 °C for 6 h then cooled to 20 °C and diluted with Et_2O (100 mL). The solution was washed with 2 M aqueous NaOH (1 x 50 mL, 3 x 10 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo*. Bulb-to-bulb distillation of the residue afforded 6.17 g (91%) of a colorless oil: ^1H NMR (CDCl_3) δ 6.92 (dq, $J = 14.9, 6.9$ Hz, 1H, CHCH_3), 6.10 (dd, $J = 15.0, 1.7$ Hz, 1H, CHCHCH_3), 5.0 (s, 1H, OH), 4.3 (m, 1H, NCHCH_2OH), 3.52-3.62 (m, 4H, CH_2OH and NCH_2), 1.81-1.96 (m, 6H), 1.6 (m,

^1H); ^{13}C NMR (CDCl_3) δ 167.9, 143.0, 123.5, 68.1, 61.9, 48.6, 28.9, 25.1, 18.7; IR (thin film) 3381, 2952, 2876, 1660, 1593, 1450, 1192, 1053, 965, 901, 827 cm^{-1} .

(2*S*,2'*S*)-1-[2'-Ethenyl-6'-(trimethylsilyl)-5'-hexynoyl]-2-(hydroxymethyl)pyrrolidine (18).

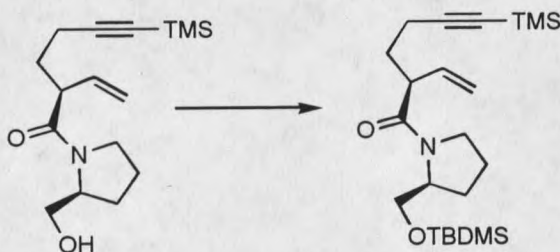


A solution of *n*-BuLi (4.39 mL, 4.78 M in heptane, 21.0 mmol) was added dropwise to a magnetically stirred solution of DIPA (3.08 mL, 22 mmol) in THF (60 mL) maintained at $-78\text{ }^{\circ}\text{C}$. The resulting mixture was warmed to $0\text{ }^{\circ}\text{C}$ and then recooled to $-78\text{ }^{\circ}\text{C}$. After stirring for an additional 15 min at $-78\text{ }^{\circ}\text{C}$, a solution of (2*S*)-2-(hydroxymethyl)-1-(2'-butenoyl)pyrrolidine (2.52 g, 10 mmol) in THF (20 mL) was added dropwise and the resulting mixture was stirred for 15 min at $-78\text{ }^{\circ}\text{C}$. The reaction mixture was allowed to warm to $22\text{ }^{\circ}\text{C}$, held at this temperature for 45 min and then recooled to $-78\text{ }^{\circ}\text{C}$. A solution of 4-iodo-1-(trimethylsilyl)-1-butyne (2.52 g, 10 mmol) in THF (10 mL) was then introduced and the resulting solution was stirred for a further 15 min at $-78\text{ }^{\circ}\text{C}$ whereupon stirring was continued for 6 h at $0\text{ }^{\circ}\text{C}$. After stirring for an additional 3 h at $25\text{ }^{\circ}\text{C}$ the reaction mixture was quenched with half-saturated aqueous NH_4Cl (10 mL) and

the mixture was concentrated *in vacuo* to approximately 20 mL. The resulting heterogeneous mixture was extracted with 1:1 CH_2Cl_2 - Et_2O (5 x 15 mL), washed with brine (5 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo*.

Chromatography of the residual oil on silica gel (50% EtOAc/hexane for elution) afforded 1.87 g (64%) of **18** as a colorless oil: ^1H NMR (CDCl_3) δ 5.50 (ddd, J = 16.0, 9.8, 8.5 Hz, 1H, $\text{CH}=\text{CH}_2$), 5.10 (m, 2H, $\text{CH}=\text{CH}_2$), 4.89 (m, 1H, OH), 4.18 (m, 1H, NCHCH_2OH), 3.65-3.48 (m, 4H, $\text{CH}_2\text{NCHCH}_2\text{OH}$), 3.37 (app q, J = 7.9 Hz, COCH), 2.21 (t, J = 6.6 Hz, 2H, $\text{CH}_2\text{C}\equiv\text{C}$), 1.91-1.84 (m, 4H), 1.64-1.55 (m, 2H), 0.09 (s, 9H, $\text{Si}(\text{CH}_3)_3$); ^{13}C NMR (CDCl_3) δ 174.7 (C), 136.7 (CH), 118.1 (CH_2), 107.1 (C), 86.2 (C), 67.8 (CH_2), 61.8 (CH), 48.3 (CH_2), 48.1 (CH), 30.9 (CH_2), 28.8 (CH_2), 25.0 (CH_2), 18.0 (CH_2), 0.7 (CH_3); IR (thin film) 3394, 3079, 2957, 2171, 1621, 1615, 1435, 1249, 1047, 842, 760, 668, 637 cm^{-1} .

(2*S*,2'*S*)-1-[2'-Ethenyl-6'-(trimethylsilyl)-5'-hexynoyl]-2-[[[(1,1-dimethylethyl)dimethylsilyloxy]methyl]pyrrolidine (**19**).

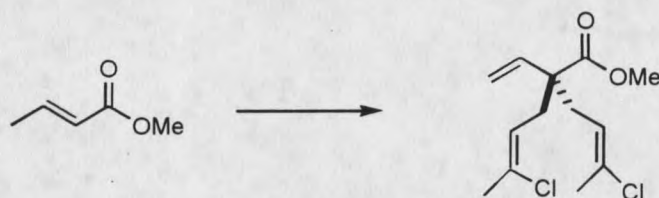


A solution of **16** (4.26 mmol, 1.25 g), imidazole (10.2 mmol, 0.696 g), and *t*-butyldimethylsilyl chloride (4.65 mmol, 0.706 g) in DMF (8 mL) was magnetically

stirred at 45 °C for 30 h. The cooled reaction mixture was poured into saturated aqueous NaHCO_3 (30 mL) and extracted with Et_2O (3 x 20 mL). The combined organic extracts were washed with 10% aqueous H_2SO_4 (5 mL), H_2O (5 mL), brine (10 mL), dried (MgSO_4), filtered and concentrated *in vacuo*. The resulting oil was initially purified by chromatography on silica gel (20% EtOAc /hexane for elution). Final purification by bulb-to-bulb distillation afforded 1.42 g (82%) of **19** as a viscous clear oil: $[\alpha]_D -21.0$ (*c* 8.2, C_6H_6), ^1H NMR (CDCl_3) δ 5.74 (ddd, $J = 18.5$, 10.4, 8.6 Hz, 1H, $\text{CH}=\text{CH}_2$), 5.09 (m, 2H, $\text{CH}=\text{CH}_2$), 4.13 (m, 1H, NCHCH_2O), 3.68 (d, $J = 4.5$ Hz, 2H, CH_2OSi), 3.52 (m, 2H, NCH_2), 3.32 (m, 1H, COCH), 2.21 (t, $J = 6.8$ Hz, 2H, $\text{CH}_2\text{C}\equiv\text{C}$), 2.10-1.07 (m, 6H, CH_2), 0.82 (s, 9H, $\text{C}(\text{CH}_3)_3$), 0.08 (s, 9H, $\text{Si}(\text{CH}_3)_3$), 0.00 (s, 3H, $\text{Si}(\text{CH}_3)_2$), 0.03 (s, 3H, $\text{Si}(\text{CH}_3)_2$); ^{13}C NMR (CDCl_3) δ 172.0, 137.4, 117.5, 107.6, 86.0, 59.1, 58.9, 48.2, 47.9, 31.1, 27.7, 26.5, 24.9, 22.6, 18.1, 0.8, -4.8; IR (thin film) 3082, 2241, 1643, 1490, 1467, 1379, 1260, 1117, 1057, 1002, 912, 733, 687, 645 cm^{-1} ; m/z 407 (M^+), 350, 262, 73; high resolution mass spectrum calcd for $\text{C}_{22}\text{H}_{41}\text{NO}_2\text{Si}_2$ (M^+) 407.2676; found 407.2667.

5.3 Endiynes Derivatives

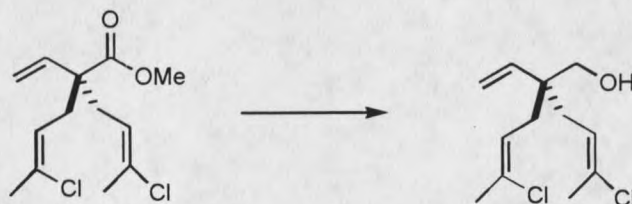
Methyl 2-ethenyl-2-(3-chlorobut-2-ene)-5-chloro-hex-6-eneoate (**24**).



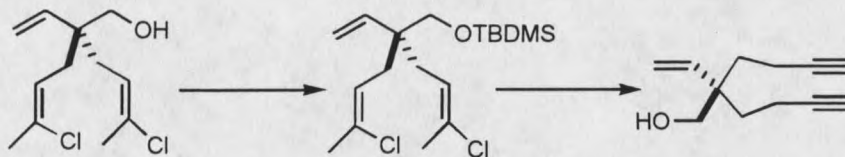
To a magnetically stirred solution of LDA (11.0 mmol) in 1:2 THF-DME (75 mL) (prepared according to the general procedure utilized for **14a**) cooled to $-78\text{ }^{\circ}\text{C}$ was added a solution of methyl crotonate (1.0 g, 10 mmol) in THF (2 mL) in one portion. After 1 h at $-78\text{ }^{\circ}\text{C}$ the reaction mixture was allowed to warm to $0\text{ }^{\circ}\text{C}$ and was maintained at that temperature for 1 h. The reaction mixture was cooled to $-78\text{ }^{\circ}\text{C}$ and a solution of *cis* and *trans*-2-chloro-4-iodo-2-butene (2.38 g, 11.0 mmol), HMPA (2.15 g, 12.0 mmol) in 1:2 THF-DME (10 mL) cooled to $-78\text{ }^{\circ}\text{C}$ was added via cannula. After 1 h the dry ice-acetone bath was removed and the reaction mixture was allowed to warm to rt. After 3 h a saturated aqueous solution of NH_4Cl (10 mL) was added and the solution was concentrated *in vacuo*. The residue was diluted with H_2O (10 mL) and hexane (10 mL). The organic layer was separated and the aqueous layer was extracted with hexane (2 x 10 mL) and the combined organic layers were washed with H_2O (10 mL), saturated aqueous NaHCO_3 (5 mL), brine (5 mL), dried (MgSO_4), filtered and concentrated *in vacuo*. Chromatography of the residual oil on silica gel (5% EtOAc/hexane for elution)

afforded 1.22 g (88% based on electrophile) of the title compound as a mixture of *cis/trans* isomers and as a colorless oil. ^1H NMR (CDCl_3) δ 5.96-5.86 (m, 1H, $\text{C}=\text{CHH}$), 5.35-5.29 (m, 2H, CH), 5.25-5.07 (m, 2H, $\text{C}=\text{CHH}$), 3.69-3.64 (m, 3H, OCH_3), 2.57-2.53 (m, 4H, CH_2), 2.04 (br s with fine structure, 6H, CH_3); ^{13}C NMR (CDCl_3) δ 175.3 (C), 140.0 (CH), 133.1 (C), 121.5 (CH), 116.2 (CH_2), 52.7 (CH_3), 35.6 (CH_2), 27.1 (CH_3); IR (thin film) 3083, 2553, 2520, 1735, 1665, 1438, 1342, 1207 (br), 1050, 820, 629 cm^{-1} .

5-Ethenyl-5-hydroxymethyl-2,8-dichloro-nona-2,7-diene (**26**).

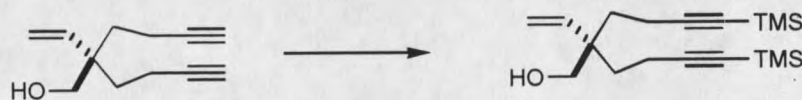


The title compound was prepared according to the general procedure utilized for **69** to afford **26** as a mixture of *cis/trans* isomers and as clear oil. ^1H NMR (CDCl_3) δ 5.74-5.64 (m, 1H, $\text{CH}=\text{CHH}$), 5.44-5.39 (m, 2H, $\text{CH} \times 2$), 5.21-5.15 (m, 1H, $\text{CH}=\text{CHH}$), 5.05-4.99 (m, 1H, $\text{CH}=\text{CHH}$), 3.41-3.39 (m, 2H, CH_2OH), 2.27-2.23 (m, 4H, CH_2), 2.08-2.02 (m, 6H, CH_3), 1.75-1.71 (m, 1H, OH); ^{13}C NMR (CDCl_3 , major isomer) δ 142.7, 132.6, 121.9, 115.7, 67.7, 46.1, 34.1, 27.0.

5-Ethylenyl-5-(hydroxymethyl)nona-1,8-diyne (**28**).

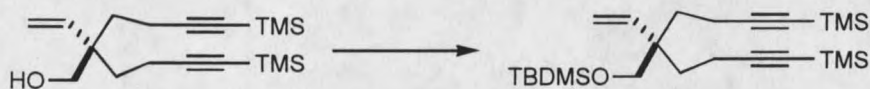
Alcohol **26** was silylated according to the general procedure utilized for **71** to afford 5-Ethenyl-5-[(1,1)-dimethylethyl]dimethylsiloxymethyl]-2,8-dichloro-non-2,7-diene (**27**) which was used without further purification. Silyl ether **27** was treated with potassium diaminopropane according to the general literature procedure to afford 0.56 g (83%, both steps) of alcohol **28** as a colorless oil after gradient silica gel chromatography (hexane to 10% EtOAc/hexane for elution): ^1H NMR (CDCl_3) δ 5.56 (dd, $J = 18.0, 11.2$ Hz, 1H, $\text{CH}=\text{CHH}$), 5.21 (app d with fine structure, $J = 11.2$ Hz, 1H, $\text{CH}=\text{CHH}$), 5.00 (app dd with fine structure, $J = 18.3, 0.9$ Hz, 1H, $\text{CH}=\text{CHH}$), 3.49 (s, 4H, CH_2OH), 2.13 (app dt, $J = 7.5, 2.6$ Hz, 4H, $\text{CH}_2\text{C}\equiv\text{C}$), 1.95 (t, $J = 2.6$ Hz, 2H, $\text{C}\equiv\text{CH}$), 1.65 (app t, $J = 7.5$ Hz, 4H, CH_2), (OH not observed); ^{13}C NMR (CDCl_3) δ 142.4 (CH), 116.5 (CH_2), 85.4 (C), 69.0 (CH), 66.0 (CH_2), 45.1 (C), 33.5 (CH_2), 13.8 (CH_2).

5-Ethyneyl-5-(hydroxymethyl)non-1,9-(trimethylsilyl)-1,8-diyne (29).



The title compound was prepared according to the general procedure utilized for **70** to afford 161 mg (95%) of **30** as a clear oil: ^1H NMR (CDCl_3) δ 5.52 (dd, $J = 17.6$, 11.0 Hz, 1H, $\text{CH}=\text{CHH}$), 5.17-5.13 (m, 1H, $\text{CH}=\text{CHH}$), 4.98-4.92 (m, 1H, $\text{CH}=\text{CHH}$), 3.46 (s, 2H, CH_2OH), 2.18-2.13 (m, 4H, $\text{CH}_2\text{C}\equiv\text{C}$), 1.65-1.58 (m, 4H, CH_2), 0.92-0.83 (m, 1H, OH), 0.09 (s, 18H, $\text{Si}(\text{CH}_3)_3$); ^{13}C NMR (CDCl_3) δ 142.7 (CH), 116.1 (CH_2), 108.3 (C), 85.2 (C), 66.0 (CH_2), 45.2 (C), 34.0 (CH_2), 15.2 (CH_2), 0.7 (CH_3); IR (thin film) 3412, 2083, 2175, 1636, 1454, 1418, 1250, 1042, 1002, 920, 840, 700, 690, 641 cm^{-1} .

5-Ethyenyl-5-[(1,1)-dimethylethyl]dimethylsiloxymethyl]non-1,9-(trimethylsilyl)-1,8-diyne (**30**).

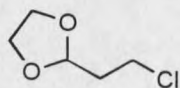


The title compound was prepared according to the general procedure utilized for **71** to afford 49 mg (97%) of **30** as a clear oil: ^1H NMR (CDCl_3) δ 5.58 (dd, $J = 18.0$, 11.1 Hz, 1H, $\text{CH}=\text{CHH}$), 5.06 (dd, $J = 11.1$, 0.8 Hz, 1H, $\text{CH}=\text{CHH}$), 4.90 (dd, $J = 18.0$, 0.8 Hz, 1H, $\text{CH}=\text{CHH}$), 3.37 (s, 2H, CH_2OSi), 2.13 (app dt, $J = 10.7$, 8.0 Hz, 4H, $\text{CH}_2\text{C}\equiv\text{C}$), 1.63 (app dt, $J = 8.5$, 7.6 Hz, 4H, CH_2), 0.86 (s, 9H, $\text{C}(\text{CH}_3)_3$), 0.11 (s, 18H, $\text{Si}(\text{CH}_3)_3$), 0.00 (s, 6H, $\text{Si}(\text{CH}_3)_2$); ^{13}C NMR (CDCl_3) δ 142.7 (CH), 115.1 (CH_2), 108.6 (C), 84.8 (C), 67.2 (CH_2), 44.9 (C), 34.4 (CH_2), 26.6 (CH_3), 18.9 (C),

15.4 (CH₂), 0.9 (CH₃), -4.9 (CH₃); IR (thin film) 3083, 2957, 5858, 2176, 1472, 1250, 1109, 1006, 760, 640 cm⁻¹; m/z 377 (M⁺ - 57), 303, 231, 147, 73.

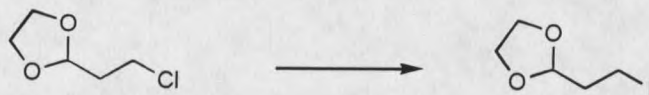
5.4 C4-Hydroxy-1,6-Heptenynes

2-(2'-Chloroethyl)-1,3-dioxolane (**44**).



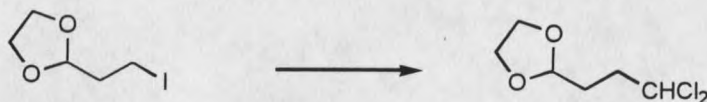
The title compound was prepared by a modified literature method.¹²¹ Accordingly, after the addition of acrolein the reaction was allowed to warm to 23 °C and was then transferred to a separatory funnel. After about one hour, the lower layer was removed and the remainder was extracted with an equal portion of CH₂Cl₂. The organic layers were combined and washed with H₂O (100 mL), transferred to a Erlenmeyer flask and treated with solid NaHCO₃ until the acid was neutralized. The reaction mixture was then filtered, washed with saturated aqueous NaHCO₃ (100 mL), brine (100 mL), dried (Na₂SO₄), filtered and concentrated *in vacuo*. Fractional distillation of the residual oil [Lit. 64 °C (14 mm)] afforded 114 g (58%) of the title compound **44** as a clear oil: ¹³C NMR (CDCl₃) δ 101.8 (CH), 64.8 (CH₂), 39.5 (CH₂), 36.8 (CH₂).

2-(2'-Iodoethyl)-1,3-dioxolane (**45**).



To a magnetically stirred solution of 2-(2'-chloroethyl)-1,3-dioxolane **44** (41 g, 0.3 mol) in acetone (350 mL) at 23 °C was added NaI (50 g, 0.33 mol) in one portion. After the ensuing exotherm subsided, the reaction mixture was heated at reflux for 12 hours in the dark. The reaction mixture was cooled to rt, concentrated *in vacuo*, and the residue was treated with H₂O (200 mL) and 20% EtOAc-hexane (200 mL) and the organic layer was separated. The aqueous layer was extracted twice with 200-mL portions of 20% EtOAc-hexane and the combined organic layers were washed with brine (100 mL), saturated aqueous sodium thiosulfate (40 mL), brine (100 mL), and dried (MgSO₄). The solution was filtered through a pad of neutral alumina (8 cm diameter by 10 cm) which was subsequently extracted with 20% EtOAc-hexane (3 x 20 mL). The filtrate was concentrated *in vacuo* to afford 65 g (95%) of the title compound **45** as a light sensitive, yellow oil which was suitable for use without further purification: ¹H NMR (CDCl₃) δ 4.88 (t, *J* = 4.4 Hz, 1H, CHO₂), 3.93-3.82 (m, 4H, CH₂O), 3.16 (t, *J* = 7.4 Hz, 2H, CH₂I), 2.20-2.11 (m, 2H, CH₂); ¹³C NMR (CDCl₃) δ 103.8 (CH), 84.9 (CH₂), 37.9 (CH₂), -2.0 (CH₂).

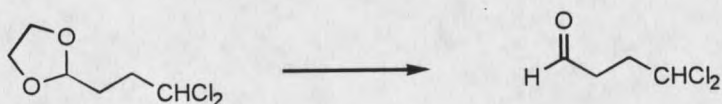
2-(3',3'-Dichloropropyl)-1,3-dioxolane (**47**).



To a magnetically stirred solution of *n*-BuLi (40 mL, 10 M in heptane, 0.40 mol) in Et₂O (150 mL) and THF (300 mL) cooled to -110 °C was added CH₂Cl₂ (38 mL, 0.6 mol) dropwise at such a rate that the internal reaction temperature was maintained below -90 °C. After 20 min at -90 °C, a solution of 2-(2'-iodoethyl)-1,3-dioxolane **45** (45.6 g, 0.2 mol) in THF (50 mL) was added dropwise while the temperature was maintained at -90 °C. The reaction mixture was then cooled to -110 °C and a solution of 1:1 THF-HMPA (200 ml) was added dropwise at such a rate that the internal reaction mixture's temperature was maintained below -90 °C. After the addition the solution was maintained at -90 °C for 30 min, and then warmed to -85 °C and maintained at this temperature for 20 min. A solution of 1:1 10% aqueous H₂SO₄-THF (280 mL) was then rapidly introduced and the reaction was allowed to warm to rt. The organic layer was separated and the aqueous layer was extracted with 20% EtOAc-hexane (2 x 200 mL) and the combined organic layers were concentrated *in vacuo*. The residue was diluted with hexane (400 mL) and washed with H₂O (2 x 50 mL), saturated aqueous NH₄Cl (2 x 200 mL), saturated aqueous NaSO₃ (50 mL), brine (100 mL), and dried (MgSO₄). The combined aqueous layers were treated with conc. HCl (150 mL) and heated at

reflux for 10 h before disposal. The dried organic solution was filtered through a pad of neutral alumina (8 cm diameter by 5 cm) which was subsequently extracted with 20% EtOAc-hexane (2 x 10 mL). The filtrate was concentrated *in vacuo* and purified by fractional distillation (118 °C, water aspirator) to afford 31.4 g (85%) of the title compound **47** as a clear oil: ^1H NMR (CDCl_3) δ 5.84 (t, $J = 6.0$ Hz, 1H, CHCl_2), 4.90 (t, $J = 2.9$ Hz, 1H, O_2CH), 3.97-3.82 (m, 4H, OCH_2), 2.31 (m, 2H, CH_2), 1.90 (m, 2H, CH_2); ^{13}C NMR (CDCl_3) δ 103.8, 74.0, 65.7, 38.4, 30.5; IR (thin film) 2958, 2885, 2762, 1476, 1411, 1236, 1141, 1028, 943, 906, 750, 651 cm^{-1} ; m/z 187, 185, 183 ($\text{M}^+ - \text{H}$), 148, 112, 73.

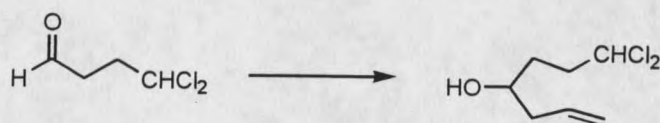
4,4-Dichlorobutanal (**48**).



A magnetically stirred solution of **47** (9.25 g, 50 mmol) in 1:1 10% aqueous HCl-acetone (200 mL) was heated at reflux for 24 h. The reaction mixture was subsequently concentrated *in vacuo* and then extracted with Et_2O (3 x 30 mL). The combined organic phases were washed with H_2O (15 mL), brine (15 mL), dried (MgSO_4), filtered and concentrated *in vacuo*. Fractional distillation of the resultant oil (93 °C, 14 mm Hg) afforded 5.57 g (79%) of the title compound **48** as a clear oil: ^1H NMR (CDCl_3) δ 9.64 (s, 1H, CHO), 5.78 (t, $J = 5.8$ Hz, 1H, CHCl_2), 2.66 (t, $J = 6.9$ Hz, 2H, COCH_2), 2.35 (m, 2H, CH_2CHCl_2); ^{13}C NMR (CDCl_3) δ 200.1,

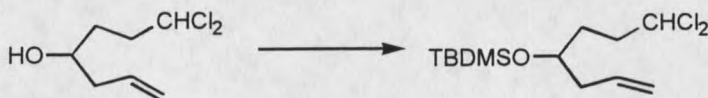
72.9, 40.1, 36.1; IR (thin film) 2939, 2848, 1726, 1446, 1352, 1255, 1133, 1071, 927, 746, 676 cm^{-1} ; m/z 144, 142, 140 (M^+), 105, 76, 75.

7,7-Dichloro-4-hydroxy-1-heptene (**49**).



To a magnetically stirred solution of 4,4-dichlorobutanal **48** (1.41 g, 10 mmol) in Et_2O (5 mL) maintained at -10°C was added a solution of allylmagnesium chloride (17 mL, 0.63 M in THF, 10.7 mmol) dropwise over 20 min. After stirring for 1 h at 0°C the reaction mixture was poured into ice cold H_2O (10 mL) and acidified with 10% aqueous H_2SO_4 . The resultant mixture was then extracted with Et_2O (3 x 10 mL) and the combined organic phases were washed with brine (3 x 5 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo*. Chromatography of the residual oil on silica gel (20% EtOAc /hexane for elution) afforded 1.78 g (98%) of the title compound **49** as a colorless oil: ^1H NMR (500 MHz, CDCl_3) δ 5.81 (m, 2H, CHCl_2 and $\text{CH}=\text{CH}_2$), 5.03 (m, 2H, $\text{CH}=\text{CH}_2$), 3.7 (m, 1H, CHOH), 2.45-2.35 (m, 1H, CH_2), 2.35-2.18 (m, 2H, CH_2), 2.18-2.10 (m, 1H, CH_2), 1.85 (s, 1H, OH), 1.75-1.65 (m, 1H, CH_2), 1.65-1.58 (m, 1H, CH_2); ^{13}C NMR (125 MHz, CDCl_3) δ 134.7, 119.6, 74.3, 70.3, 42.8, 40.7, 33.3; IR (thin film) 3380, 3078, 1640, 1448, 1234, 1071, 998, 924, 865, 784, 747 cm^{-1} .

7,7-Dichloro-4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1-heptene (**50**).



7,7-Dichloro-4-hydroxy-1-heptene (**49**) was silylated according to the general procedure utilized for **71** to afford 1.37 g (94%) of the title compound **50** as a clear oil which was suitable for use without further purification: ^1H NMR (CDCl_3) δ 5.74 (m, 2H, CHCH_2 and CHCl_2), 5.03 (m, 2H, CHCH_2), 3.75 (m, 1H, CHOH), 2.22 (m, 4H, CH_2), 1.68 (m, 2H, CH_2), 0.87 (s, 9H, $\text{C}(\text{CH}_3)_3$), 0.04 (s, 6H, $\text{Si}(\text{CH}_3)_2$); ^{13}C NMR (CDCl_3) δ 135.2, 117.9, 74.5, 71.6, 42.5, 40.2, 33.2, 26.6, 18.8, -3.6, -3.9; IR (thin film) 3078, 2852, 1642, 1472, 1255, 1091, 9160, 836, 775 cm^{-1} .

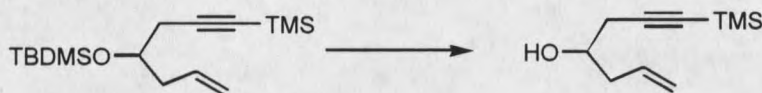
4-[[[(1,1-Dimethylethyl)dimethylsilyl]oxy]-1-(trimethylsilyl)-6-hepten-1-yne (**51**).



To a magnetically stirred solution of **50** (300 mg, 1.0 mmol) and HMPA (348 μL , 2.0 mmol) in THF (5 mL) maintained at -78°C was added a solution of $\text{LDA}\cdot\text{THF}$ (1.17 mL, 0.85 M in methylcyclohexane, 1.0 mmol). After approximately 10 min an additional solution of $\text{LDA}\cdot\text{THF}$ (1.17 mL, 0.85 M in methylcyclohexane, 1.0 mmol) was added followed by a further portion of $\text{LDA}\cdot\text{THF}$ (1.76 mL, 0.85 M

in methylcyclohexane, 1.5 mmol) 20 min later. The reaction mixture was stirred for 2 h and then warmed to 0 °C. After 45 min the reaction mixture was cooled to -78 °C and chlorotrimethylsilane (0.19 mL, 1.5 mmol) was introduced. After 2 h the reaction was quenched with 10% aqueous H₂SO₄ (5 mL). The mixture was allowed to warm to room temperature, extracted with hexane (3 x 10 mL) and the combined organic layers were washed with H₂O (5 mL), saturated aqueous NH₄Cl (5 mL), brine (3 x 5 mL), dried (MgSO₄), filtered and concentrated *in vacuo*. Chromatography of the residual oil on silica gel (1% EtOAc/hexane for elution) afforded 258 mg (87%) of **51** as a colorless oil: ¹H NMR (CDCl₃) δ 5.80 (dddd, *J* = 14.4, 10.6, 8.3, 8.3 Hz, 1H, CH=CH₂), 5.02 (m, 2H, CH=CH₂), 3.84 (m, 1H, CHO), 2.36 (m, 4H, CH₂), 0.87 (s, 9H, C(CH₃)₃), 0.12 (s, 9H, Si(CH₃)₃), 0.07 (s, 3H, Si(CH₃)₂), 0.05 (s, 3H, Si(CH₃)₂); ¹³C NMR (CDCl₃) δ 135.3, 118.1, 105.3, 86.9, 71.6, 42.1, 29.1, 27.2, 18.8, 0.7, -3.7, -3.8; IR (thin film) 3078, 2178, 1251, 1098, 916, 841, 808, 668, 642 cm⁻¹; *m/z* 295 (M⁺ - H), 255, 239, 223, 147, 73.

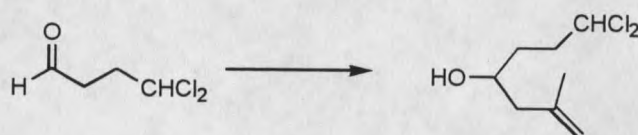
4-Hydroxy-1-(trimethylsilyl)-6-hepten-1-yne (**52**).



Enyne **52** was prepared by the O-desilylation of **51** according to a literature¹²² procedure: ¹H NMR (CDCl₃) δ 5.72 (m, 1H, CH=CH₂), 5.04 (m, 2H, CH=CH₂), 3.69 (m, 1H, CHOH), 2.33 (m, 2H, CH₂C≡C), 2.20 (m, 2H, CH₂), 1.90 (s, 1H,

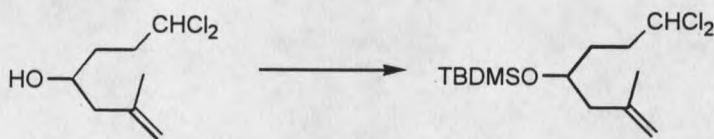
OH), 0.04 (s, 9H, Si(CH₃)₃); ¹³C NMR (CDCl₃) δ 134.1, 118.2, 103.0, 87.7, 69.1, 40.6, 28.1, 0.0; IR (thin film) 3417 (br), 3076, 2959, 2176, 1642, 1421, 1250, 1020, 917, 842, 760; m/z 182 (M⁺) 109, 73.

7,7-Dichloro-4-hydroxy-2 methyl-1-heptene (**53**).



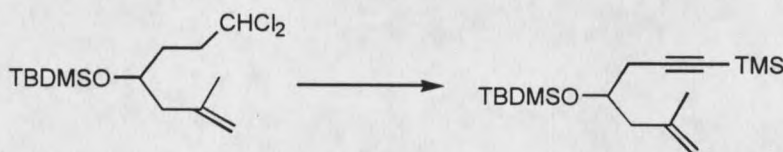
The title compound was prepared according to the general procedure utilized for **49** except that methallylmagnesium chloride was used instead of allylmagnesium chloride for afford 3.26 g (90%) of the title compound as a clear oil: ¹H NMR (CDCl₃) δ 5.82 (t, *J* = 5.8 Hz, 1H, CHCl₂), 4.87 (app t, *J* = 1.6 Hz, 1H, C=CHH), 4.78 (s, 1H, C=CHH), 3.77-3.69 (m, 1H, CHOH), 2.48-2.10 (m, 4H, overlapping CH₂'s), 1.83 (d, *J* = 2.8 Hz, 1H, OH), 1.78-1.58 (m, 2H, CH₂), 1.73 (s, 3H, CH₃); ¹³C NMR (CDCl₃) δ 142.8 (C), 114.6 (CH₂), 74.4 (CH), 68.4 (CH), 47.0 (CH₂), 40.8 (CH₂), 33.7 (CH₃), 23.0 (CH₃); IR (thin film) 3414, 3075, 2934, 1647, 1446, 1276, 1082, 895, 782, 747 cm⁻¹.

7,7-Dichloro-4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2 methyl-1-heptene (**54**).



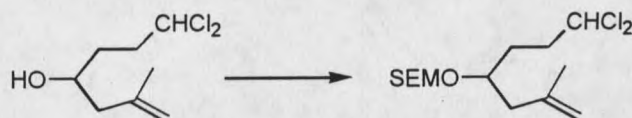
The title compound was prepared according to the general procedure utilized for **71**, and was purified by silica gel chromatography (10% EtOAc/hexane for elution) to afford 2.94 g (76%) of the title compound as a clear oil: ^1H NMR (CDCl_3) δ 5.76 (t, $J = 6.1$ Hz, 1H, CHCl_2), 4.77 (app t, $J = 1.7$ Hz, 1H, $\text{C}=\text{CHH}$), 4.70 (s, 1H, $\text{C}=\text{CHH}$), 3.92-3.83 (m, 1H, CHO), 2.45-2.05 (m, 4H, overlapping CH_2), 1.83-1.50 (m, 2H, CH_2), 1.71 (m, 3H, CH_3), 0.87 (s, 9H, $\text{C}(\text{CH}_3)_3$), 0.04 (s, 6H, $\text{Si}(\text{CH}_3)_3$); ^{13}C NMR (CDCl_3) δ 142.9 (C), 114.1 (CH_2), 74.7 (CH), 70.4 (CH), 46.6 (CH_2), 40.0 (CH_2), 33.1 (CH_2), 26.6 (CH_3), 23.6 (CH_3), 18.8 (C), -3.7 (CH_3), -3.9 (CH_3).

4-[[[(1,1-Dimethylethyl)dimethylsilyl]oxy]-1-trimethylsilyl-6-methyl-6-hepten-1-yne (57).



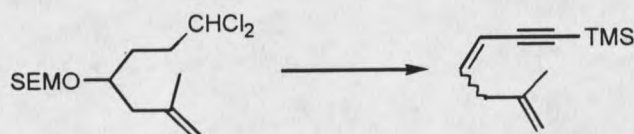
The title compound was prepared according to the general procedure utilized for **51**, and was purified by silica gel chromatography (hexane for elution) to afford 138 mg (43%, see **69**) of the title compound as a clear oil: ^1H NMR (CDCl_3) δ 4.78 (s, 1H, $\text{C}=\text{CHH}$), 4.70 (s, 1H, $\text{C}=\text{CHH}$), 3.98-3.89 (m, 1H, CHOSi), 2.40-2.10 (m, 4H, CH_2), 1.72 (s, 3H, CH_3), 0.87 (s, 9H, $\text{C}(\text{CH}_3)_3$), 0.13 (s, 9H, $\text{Si}(\text{CH}_3)_3$), 0.08 (s, 3H, $\text{Si}(\text{CH}_3)$), 0.05 (s, 3H, $\text{Si}(\text{CH}_3)$); IR (thin film) 3076, 2967, 2857, 2178, 1649, 1471, 1363, 1251, 1059, 1028, 839, 775, 643 cm^{-1} ; m/z 310 (M^+), 73.

7,7-Dichloro-4-[(2-trimethylsilylethoxy)methoxymethyl]-2 methyl-1-heptene (**58**).



The title compound was prepared according to the general procedure utilized for **76**: ^1H NMR (CDCl_3) δ 5.78 (t, $J = 6.1$ Hz, 1H, CHCl_2), 4.75 (d with fine structure, $J = 7.0$, 2H, $\text{C}=\text{CH}_2$), 4.65 (dd, $J = 12.5$ and 7.3 Hz, 2H, CH_2O), 3.82-3.63 (m, 1H, CHO), 3.64-3.54 (m, 2H, CH_2O), 2.40-2.26 (m, 3H), 2.12-2.08 (m, 1H), 1.85 (m, 1H), 1.72 (s, 3H, CH_3), 1.68-1.58 (m, 1H), 0.91 (s, 2H, CH_2Si), 0.00 (s, 9H, $\text{Si}(\text{CH}_3)_3$); ^{13}C NMR δ 142.7, 114.0, 94.3, 74.9, 74.3, 68.2, 43.8, 40.2, 31.1, 23.3, 18.8, -0.7.

6-Methyl-1-trimethylsilyl-3,6-heptadien-1-yne (**59**).



This product was occasionally generated in the elimination/silylation reaction for the preparation of compounds such as **57**, especially with SEM ethers. ^1H NMR (CDCl_3) δ 6.18 (dt, $J = 16.5$, 7.0 Hz, 1H, $\text{CH}=\text{CHC}\equiv\text{C}$), 5.54-5.48 (m, 1H, $\text{CH}=\text{CHC}\equiv\text{C}$), 4.76 (s, 1H, $\text{C}=\text{CHH}$), 4.70 (s, 1H, $\text{C}=\text{CHH}$), 2.76 (d, 2H, CH_2), 1.69 (s, 3H, CH_3), 0.16 (s, 9H, $\text{Si}(\text{CH}_3)_3$); ^{13}C NMR (CDCl_3) δ 143.7, 143.6, 112.5, 111.9, 104.6, 93.9, 42.1, 23.0, 0.6.

5.5 C4-Hydroxymethyl-1,6-Heptenyne

Diethyl 2-(2-propenyl)-2-(2-propynyl)propan-1,3-dioate (**66**).

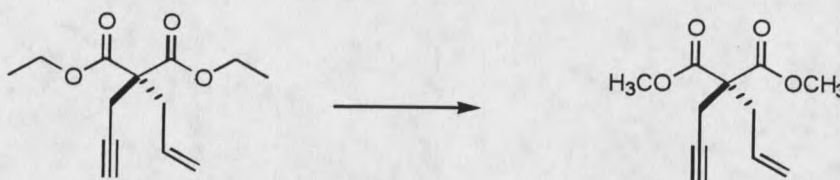


To a magnetically stirred solution of oil-free NaH (1.82 g, 55 mmol) in 2:5 THF-DMF (50 mL) maintained at 0 °C was added dropwise diethyl allyl malonate (10.0 g, 50.0 mmol). The reaction mixture was subsequently stirred for 1.5 h at 25 °C, recooled to 0 °C, and propargyl bromide (6.54 g, 55 mmol) was introduced and the reaction allowed to warm to rt. After 24 h the reaction was poured into ice-cold H₂O (100 mL). The organic layer was separated and the aqueous layer extracted with hexane (2 x 20 mL). The combined organic layers were washed with H₂O (2 x 15 mL), brine (20 mL), dried (MgSO₄), filtered and concentrated *in vacuo*.

Fractional distillation of the resulting oil afforded 11.1 g (94%) of **66** as a clear oil:

¹H NMR (CDCl₃) δ 5.61 (m, 1H, CH=CH₂), 5.15 (m, 2H, CH=CH₂), 4.18 (q, *J* = 7.2 Hz, 4H, OCH₂), 2.76 (m, 4H, CH₂), 1.98 (t, *J* = 2.7 Hz, 1H, C≡CH), 1.22 (t, *J* = 7.2 Hz, 6 H, CH₃); ¹³C NMR (CDCl₃) δ 170.3, 132.4, 120.3, 79.6, 71.9, 62.3, 37.1, 23.2, 14.7.

Dimethyl 2-(2-propenyl)-2-(2-propynyl)propan-1,3-dioate (**67**).

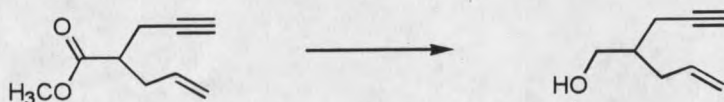


A magnetically stirred solution of diethyl ester **66** (2.38 g, 10.0 mmol) and NaOH (68 mg, 1.7 mmol) in methanol (15 mL) was heated at reflux. When G.C. analysis of a quenched (H₂O) aliquot indicated complete conversion of starting material after 14 h, the cooled reaction was subsequently concentrated *in vacuo* and the residue was dissolved in hexane (25 mL), washed with brine (10 mL), dried (MgSO₄), filtered and concentrated *in vacuo* to afford 1.85 g (88%) of **67** as a clear oil which was suitable for use without further purification: ¹H NMR (CDCl₃) δ 5.62 (m, 1H, CH=CH₂), 5.15 (m, 2H, CH=CH₂), 3.71 (s, 6H, OCH₃), 2.78 (m, 4H, CH₂), 1.98 (t, *J* = 2.6 Hz, 1 H, C≡CH); ¹³C NMR (CDCl₃) δ 170.0, 132.4, 120.4, 79.5, 72.1, 57.6, 53.3, 37.3, 23.4; IR (thin film) 3293, 3081, 2121, 1741, 1438, 1147, 926, 854, 654 cm⁻¹; *m/z* 210 (M⁺), 195, 151.

Better yields were achieved if the above reaction was performed with anhydrous sodium methoxide instead of sodium hydroxide.

Methyl-2-(2-propenyl)-5-pentynoate (**68**).

A magnetically stirred solution of dimethyl 2-(2-propenyl)-2-(2-propynyl)propan-1,3-dioate **67** (1.76 g, 8.82 mmol), NaCl (0.515 g, 8.82 mmol), H₂O (318 μ L, 17.6 mmol) in DMF (8 mL) was heated at reflux for 36 h. The cooled reaction mixture was subsequently poured into H₂O (100 mL), and extracted with hexane (4 x 25 mL). The combined organic fractions were washed with H₂O (10 mL), brine (20 mL), dried (MgSO₄), filtered and concentrated *in vacuo*. Chromatography of the residual oil on silica gel (10% EtOAc/hexane for elution) afforded 777 mg (62%) of the title compound **68** as a colorless oil: ¹H NMR (CDCl₃) δ 5.61 (m, 1H, CH=CH₂), 5.00 (m, 2H, CH=CH₂), 3.57 (s, 3H, CH₃), 2.5 (m, 1H, CHCO), 2.3 (m, 4H, CH₂), 1.90 (t, J = 2.5 Hz, 1H, C $\equiv$ CH); ¹³C NMR (CDCl₃) δ 174.4, 134.9, 118.0, 81.6, 70.5, 52.1, 44.4, 35.5, 20.8; IR (thin film) 3299, 3080, 2122, 1741, 1438, 921.4 cm⁻¹.

4-(Hydroxymethyl)-6-hepten-1-yne (**69**).

A solution of methyl 2-(2-propenyl)-5-pentynoate **68** (2.07 g, 13.5 mmol) in Et₂O (5 mL) was added dropwise to a magnetically stirred solution of LiAlH₄ (387 mg, 10.2 mmol) in Et₂O (100 mL) at a rate sufficient to maintain a gentle reflux. The reaction mixture was heated at reflux for 3 h, cooled to 0 °C and H₂O (20 mL) was added dropwise, followed by 10% aqueous H₂SO₄ (50 mL). The layers were separated and the aqueous phase was extracted with Et₂O (4 x 20 mL). The combined organic layers were washed with brine (15 mL), dried (Na₂SO₄), filtered and concentrated *in vacuo*. Chromatography of the residual oil on silica gel (10% EtOAc/hexane for elution) afforded 1.50 g (89%) of the title compound **69** as a colorless oil: ¹H NMR (CDCl₃) δ 5.72 (ddt, *J* = 17.4, 10.0, 2.5 Hz, 1H, CH=CH₂), 5.01 (m, 2H, CH=CH₂), 3.58 (m, 2H, HOCH₂), 2.33 (s, 1H, HO), 2.23 (m, 2H, CH₂CH=CH₂), 2.12 (t, *J* = 7.2 Hz, 2H, CH₂C≡C), 1.94 (t, *J* = 2.4 Hz, 1H, C≡CH), 1.7 (m, 1H, HOCH₂CH); ¹³C NMR (CDCl₃) δ 136.6, 117.4, 83.0, 70.4, 65.2, 40.1, 35.4, 20.4; IR (thin film) 3350 (br), 3303, 3078, 2117, 1641, 1438, 1033, 917 cm⁻¹; *m/z* 124 (M⁺), 83.

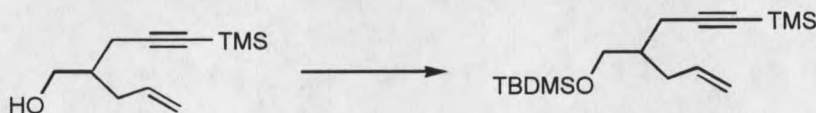
4-(Hydroxymethyl)-1-(trimethylsilyl)-6-hepten-1-yne (**70**).



A solution of *n*-BuLi (4.86 mL, 4.78 M in heptane, 23.3 mmol) was added to a magnetically stirred solution of 4-(hydroxymethyl)-6-hepten-1-yne (**69**) (1.37 g,

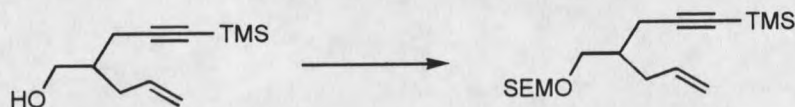
11.1 mmol) in THF (50 ml) maintained at -78°C . After 1 h, chlorotrimethylsilane (2.65 g, 24.4 mmol) was added in one portion and the reaction mixture was allowed to warm to room temperature. After 2 h, 10% aqueous HCl (30 mL) was added and the heterogeneous mixture was vigorously stirred for 6 h. The organic layer was separated and the aqueous phase was extracted with 1:4 EtOAc-hexane (3 x 20 mL). The combined organic layers were washed with brine (15 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo*. Chromatography of the residual oil on silica gel (20% EtOAc/hexane for elution) afforded 2.00 g (92%) of the title compound **70** as a colorless oil: ^1H NMR (CDCl_3) δ 5.70 (dddd, $J = 17.2, 10.0, 7.2, 7.2$ Hz, 1H, $\text{CH}=\text{CH}_2$), 4.99 (m, 2H, $\text{CH}=\text{CH}_2$), 3.54 (m, 2H, CH_2OH), 2.26 (m, 2H, $\text{CH}_2\text{C}\equiv\text{C}$), 2.12 (ddd, $J = 6.9, 6.9, 0.9$ Hz, 2H, $\text{CH}_2\text{CH}=\text{CH}_2$), 2.02 (s, 1H, OH), 1.78 (m, 1H, CH), 0.06 (s, 9H, $\text{Si}(\text{CH}_3)_3$); ^{13}C NMR (CDCl_3) δ 136.7, 117.42, 105.9, 87.1, 65.6, 40.4, 35.6, 22.1, 0.7; IR (thin film) 3354, 3078, 2174, 1938, 1641, 1250, 1034, 843, 760, 698 cm^{-1} ; m/z 196 (M^+), 165, 155, 123, 73.

4-[[[(1,1-Dimethylethyl)dimethylsilyl]oxymethyl]-1-(trimethylsilyl)-6-hepten-1-yne (71).



A solution of 4-(hydroxymethyl)-1-(trimethylsilyl)-6-hepten-1-yne **70** (282 mg, 1.44 mmol), imidazole (235 mg, 3.46 mmol), and *t*-butyldimethylsilyl chloride (238 mg, 1.58 mmol) in DMF (2.8 mL) was magnetically stirred at room temperature for 8 h. The reaction mixture was subsequently poured into saturated aqueous NaHCO₃ (50 mL) and the transfer was quantitated with hexane (5 mL). The organic phase was separated and the aqueous phase was extracted with hexane (3 x 10 mL). The organic layers were washed with H₂O (5 mL), brine (10 mL), dried (MgSO₄), filtered and concentrated *in vacuo* to afford 438 mg (98%) of **71** as a colorless oil which was suitable for use without further purification: ¹H NMR (CDCl₃) δ 5.78 (m, 1H, CH=CH₂), 5.00 (m, 2H, CH=CH₂), 3.55 (m, 2H, CH₂O), 2.25 (d, *J* = 6.2 Hz, 2H, CH₂C≡C), 2.12 (m, 2H, CH₂CH=CH₂), 1.73 (m, 1H, CH), 0.88 (s, 9H, C(CH₃)₃), 0.12 (s, 9H, Si(CH₃)₃), 0.03 (s, 6H, Si(CH₃)₂); ¹³C NMR (CDCl₃) δ 137.2, 117.1, 106.5, 87.0, 64.8, 40.6, 35.3, 26.6, 21.7, 21.4, 0.8, -4.7; IR (thin film) 3079, 2175, 1641, 1250, 1104, 841, 776 cm⁻¹; *m/z* 310 (M⁺), 253, 73.

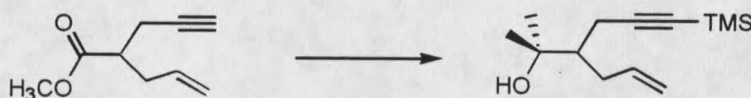
4-(2-(trimethylsilylethoxy)methoxymethyl)-1-trimethylsilyl-6-hepten-1-yne (**72**).



The title compound was prepared according to the general procedure for **76** to afford 70 mg (74%) of **72** as a clear oil: ¹H NMR (CDCl₃) δ 5.7 (m, 1H, CH=CH₂), 5.0 (m, 2H, CH=CH₂), 4.62 (s, 2H, OCH₂O), 3.6 (m, 2H, CH₂CH₂TMS), 3.47 (d, *J*

= 4.0 Hz, OCH₂CH), 2.15 (app dt, J = 7.2, 0.8 Hz, 2H, CH₂CC), 1.8 (m, 1H, CH), 0.9 (m, 2H, CH₂TMS), 0.11 (s, 9H, Si(CH₃)₃), -0.01 (s, 9H, Si(CH₃)₃); ¹³C NMR (CDCl₃) δ 136.7, 117.3, 105.8, 95.7, 86.6, 69.9, 65.6, 38.5, 35.6, 22.1, 18.8, 0.8, -0.7; IR (thin film) 3078, 2175, 1641, 1249, 1059, 937, 840, 760, 694 cm⁻¹.

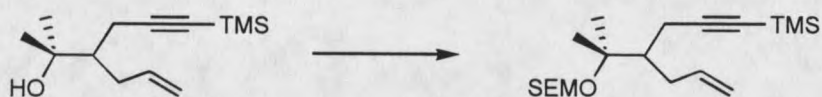
4-(1,1-Dimethyl-1-hydroxymethyl)-1-(trimethylsilyl)-6-hepten-1-yne (**75**).



To a magnetically stirred solution of methyllithium (11.6 mL, 1.38 M in Et₂O, 16.0 mmol) maintained at -35 °C was added **68** (761 mg, 5 mmol) dropwise over 45 min. After 1 h the reaction mixture was allowed to warm to 0 °C and then maintained at that temperature for 1 h. The solution was subsequently cooled to -78 °C, chlorotrimethylsilane (2.53 mL, 20 mmol) was added and the reaction mixture was allowed to warm to 22 °C. After 4 h, 10% aqueous HCl (20 mL) was added and the heterogeneous mixture was vigorously stirred for 12 h. The organic layer was separated, the aqueous layer was extracted with Et₂O (4 x 10 mL) and the combined organic extracts were washed with H₂O (2 mL), saturated aqueous NaHCO₃ (2 x 5 mL), brine (5 mL), dried (Na₂SO₄), filtered and concentrated *in vacuo*. Chromatography of the residual oil on silica gel (10% EtOAc/hexane for elution) afforded 597 mg (53%) of the title compound **75** as a clear oil: ¹H NMR

(CDCl₃) δ 5.72 (m, 1H, CH=CH₂), 5.00 (m, 2H, CH=CH₂), 2.40-2.03 (m, 4H, CH₂), 1.55 (m, 1H, CH), 1.19 (s, 3H, CH₃), 1.15 (s, 3H, CH₃), 0.06 (s, 9H, Si(CH₃)₃); ¹³C NMR (CDCl₃) δ 138.2, 116.9, 107.2, 87.8, 73.9, 47.9, 34.2, 28.9, 27.9, 20.1, 0.5; IR (thin film) 3420 (br), 3077, 2963, 2173, 1640, 1426, 1374, 1250, 994, 913, 813, 760, 698, 643 cm⁻¹.

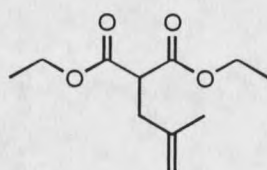
4-[1,1-Dimethyl-1-[(2-trimethylsilyl)ethoxymethyl]oxymethyl]-1-trimethylsilyl-6-hepten-1-yne (**76**).



A magnetically stirred solution of 4-(1,1-dimethyl-1-hydroxymethyl)-1-(trimethylsilyl)-6-hepten-1-yne **75** (103 mg, 0.459 mmol) in CH₂Cl₂ (1 mL) was treated with diisopropylethyl amine (289 μ L, 2.06 mmol) and SEMCl (80 mg, 0.48 mmol). After 1 h the reaction mixture was concentrated *in vacuo* and the residue was triturated with hexane (4 x 5 mL). The combined organic extracts were washed with H₂O (5 mL), brine (5 mL), dried (MgSO₄), filtered and concentrated *in vacuo*. Chromatography of the residual oil on silica gel (5% EtOAc/hexane for elution) afforded 162 mg (99%) of **76** as a clear oil: ¹H NMR (CDCl₃) δ 5.82 (m, 1H, CH=CH₂), 5.02 (m, 2H, CH=CH₂), 4.72 (s, 2H, OCH₂O), 3.60 (m, 2H, CH₂CH₂TMS), 2.41-2.08 (m, 4H, CH₂), 1.75 (m, 1H, CH), 1.21 (app d, *J* = 2.5 Hz, 6H, CH₃), 0.90 (m, 2H, CH₂TMS), 0.11 (s, 9H, Si(CH₃)₃), 0.00 (s, 9H, Si(CH₃)₃);

^{13}C NMR (CDCl_3) δ 138.6, 116.5, 107.7, 89.7, 86.5, 79.0, 65.6, 47.6, 34.3, 24.9, 24.7, 20.2, 18.9, 0.7, -0.7; IR (thin film) 3077, 2174, 1640, 1250, 1090, 1071, 916, 840, 760, 650 cm^{-1} ; m/z 354 (M^+), 281, 223, 131, 73.

Diethyl 2-(2-methyl-2-propenyl)propan-1,3-dioate (**77**).



This compound was prepared according to a general literature procedure: ^1H NMR (CDCl_3) δ 4.76 (s, 1H, $\text{C}=\text{CHH}$), 4.70 (s, 1H, $\text{C}=\text{CHH}$), 4.16 (q, $J = 7.1$ Hz, 4H, OCH_2), 3.54 (t, $J = 7.7$ Hz, 1H, CH), 2.58 (d, $J = 7.7$ Hz, 2H, CH_2), 1.72 (s, 3H, CH_3), 1.23 (t, $J = 7.1$ Hz, 6H, OCH_2CH_3).

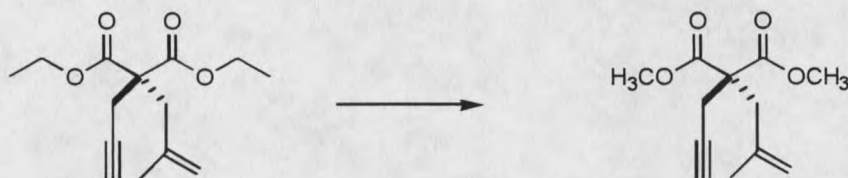
Diethyl 2-(2-methyl-2-propenyl)-2-(2-propynyl)propan-1,3-dioate (**78**).



Diethyl 2-(2-methyl-2-propenyl)propan-1,3-dioate **77** was alkylated according to the general procedure utilized for **66** (with propargyl bromide as the electrophile) to afford 2.47 g (98%) of the title compound as a clear oil after purification by short-path distillation (14 Torr): ^1H NMR (CDCl_3) δ 4.88 (app t, $J = 1.7$ Hz, 1H,

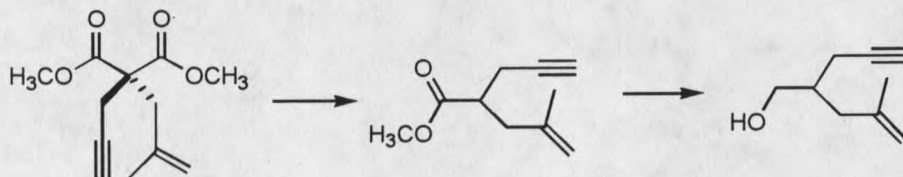
C=CHH), 4.83 (s, 1H, C=CHH), 4.25-4.10 (m, 4H, OCH₂), 2.81 (br s, 4H, overlapping CH₂), 2.00 (t, $J = 2.6$ Hz, 1H, C≡CH), 1.64 (s, 3H, CH₃), 1.23 (app t, $J = 14.3$ Hz, 6H, OCH₂CH₃); ¹³C NMR (CDCl₃) δ 170.8, 140.7, 116.8, 80.1, 72.2, 62.3, 57.1, 40.1, 23.9, 23.4, 14.7.

Dimethyl 2-(2-methyl-2-propenyl)-2-(2-propynyl)propan-1,3-dioate (**79a**).



Diethyl 2-(2-methyl-2-propenyl)-2-(2-propynyl)propan-1,3-dioate **78** was transesterified according to the general procedure utilized for **67** (except that 10 mol % NaOCH₃ was employed instead of NaOH) to afford the title compound as a clear oil which was used immediately in the next step: ¹H NMR (CDCl₃) δ 4.89 (app t, $J = 1.5$ Hz, 1H, C=CHH), 4.82 (s, 1H, C=CHH), 3.71 (s, 6H, OCH₃), 2.82 (s, 2H, CH₂), 2.81 (s, 2H, CH₂), 2.00 (t, $J = 2.7$ Hz, 1H, C≡CH), 1.62 (s, 3H, CH₃); ¹³C NMR (CDCl₃) δ 171.2, 140.6, 125.7, 117.0, 79.9, 72.3, 53.3, 40.3, 23.8, 23.5.

4-Hydroxymethyl-6-methyl-6-hepten-1-yne (**79b**).



Dimethyl 2-(2-methyl-2-propenyl)-2-(2-propynyl)propan-1,3-dioate **79a** was decarboxylated according to the general procedure utilized for **68** to afford methyl 2-(2'-methyl-2'-propenyl)-5-pentynoate as an oily material contaminated with up to 15 mol % of the diester. This crude material was reduced according to the general procedure utilized for **69**, and was easily purified by silica gel chromatography (10% EtOAc/hexane for elution) to afford 1.17 g (62%, both steps) of the title compound as a clear oil: ^1H NMR (CDCl_3) δ 4.68 (s, 1H, $\text{C}=\text{CHH}$), 4.63 (s, 1H, $\text{C}=\text{CHH}$), 3.59-3.46 (m, 2H, CH_2OH), 2.15 (dddd, $J = 30.0, 8.1, 5.5, 2.6$ Hz, 2H, $\text{CH}_2\text{C}\equiv\text{CH}$), 1.98 (d, $J = 7.3$ Hz, 2H, CH_2), 1.86 (t, $J = 2.6$ Hz, 1H, $\text{C}\equiv\text{CH}$), 1.85-1.77 (m, 2H, CH and OH), 1.61 (s, 3H, CH_3); ^{13}C NMR (CDCl_3) δ 144.0 (C), 113.1 (CH_2), 83.1 (C), 70.5 (C), 65.5 (CH_2), 39.8 (CH_2), 38.1 (CH), 22.8 (CH_3), 20.6 (CH_2).

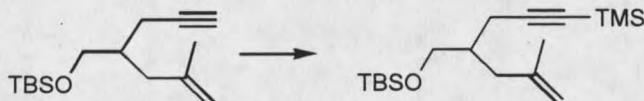
4-[(1,1-Dimethylethyl)dimethylsiloxymethyl]-6-methyl-6-hepten-1-yne (**81**).



The title compound was prepared according to the general procedure utilized for **71** to afford 1.93 g (95%) of **81** as a clear oil: ^1H NMR (CDCl_3) δ 4.76 (s, 1H, $\text{C}=\text{CHH}$), 4.70 (s, 1H, $\text{C}=\text{CHH}$), 3.60-3.50 (m, 2H, CH_2O), 2.22-2.20 (m, 2H, $\text{CH}_2\text{C}\equiv\text{CH}$), 2.05 (app d, $J = 6.4$ Hz, 2H, CH_2), 1.89 (t, $J = 2.5$ Hz, 1H, $\text{C}\equiv\text{CH}$),

1.88-1.80 (m, 1H, CH), 1.69 (s, 3H, CH₃), 0.87 (s, 9H, C(CH₃)₃), 0.03 (s, 6H, Si(CH₃)₂); ¹³C NMR (CDCl₃) δ 144.0, 112.9, 83.5, 70.0, 64.9, 39.4, 38.6, 26.6, 22.9, 20.4, 19.0, -4.7; IR (thin film) 3313, 3076, 3955, 2857, 2118, 1650, 1471, 1255, 1009, 1006, 837, 776, 622 cm⁻¹.

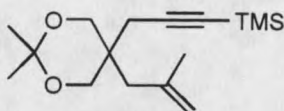
4-[(1,1-Dimethylethyl)dimethylsiloxymethyl]-6-methyl-1-(trimethylsilyl)-6-hepten-1-yne (**82a**).



To a magnetically stirred solution of **81** (374 mg, 1.47 mmol) in THF (8 mL) maintained at -78 °C was added a solution of *n*-BuLi (0.83 mL, 1.96 M in heptane, 1.63 mmol). After 1 h chlorotrimethylsilane (0.235 mL, 1.85 mmol) was added in one portion and the reaction mixture was allowed to warm to rt and then treated with saturated aqueous NH₄Cl (1 mL) and hexane (5 mL). The organic layer was separated and the aqueous layer was extracted with hexane (2 x 5 mL) and the combined organic layers were washed with brine (1 mL), saturated aqueous NaHCO₃ (2 x 2 mL), brine (2 mL), dried (MgSO₄), filtered and concentrated *in vacuo* to afford 474 mg (99%) of the title compound as a clear oil suitable for use without further purification: ¹H NMR (CDCl₃) δ 4.75 (s, 1H, C=CHH), 4.69 (s, 1H, C=CHH), 3.58-3.53 (m, 2H, CH₂O), 2.25-2.22 (m, 2H, CH₂C≡C), 1.85-1.80

(m, 1H, CH), 1.69 (s, 3H, CH₃), 0.87 (s, 9H, C(CH₃)₃), 0.09 (s, 9H, Si(CH₃)₃), 0.03 (s, 6H, Si(CH₃)₂); ¹³C NMR (CDCl₃) δ 144.3 (C), 112.8 (CH₂), 106.6 (C), 86.4 (C), 64.9 (CH₂), 39.4 (CH₂), 38.7 (CH), 26.6 (CH₃), 23.0 (CH₃), 21.8 (CH₂), 19.0 (C), 0.8 (CH₃), -4.7 (CH₃); IR (thin film) 3075, 2957, 2175, 1650, 1471, 1250, 1106, 841, 776, 645 cm⁻¹.

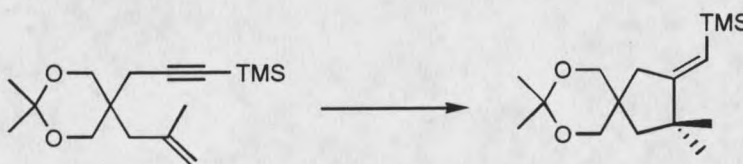
2,2-Dimethyl-[5-(2'-methyl-2'-propenyl)-5-(3'-trimethylsilyl-2'-propyne)-1,3-dioxane (83a).



The title compound was prepared according to the general procedure utilized for **82a** to afford 84 mg (99%) of **83a** as a clear oil suitable for use without further purification: ¹H NMR (CDCl₃) δ 4.88 (s, 1H, C=CHH), 4.75 (s, 1H, C=CHH), 3.64 (s, 4H, CH₂O), 2.40 (s, 2H, CH₂), 2.09 (s, 2H, CH₂), 1.76 (s, 3H, CH₃), 1.38 (s, 3H, CH₃), 1.37 (s, 3H, CH₃), 0.09 (s, 9H, Si(CH₃)₃); ¹³C NMR (CDCl₃) δ 141.6 (C), 116.0 (CH₂), 104.7 (C), 98.7 (C), 88.5 (C), 67.7 (CH₂), 40.6 (CH₂), 36.8 (C), 26.4 (CH₃), 25.8 (CH₃), 24.6 (CH₂), 22.7 (CH₃), 0.7 (CH₃); IR (thin film) 3075, 2960, 2862, 2174, 1642, 1452, 1370, 1250, 1220, 1112, 1071, 1039, 812, 760 cm⁻¹.

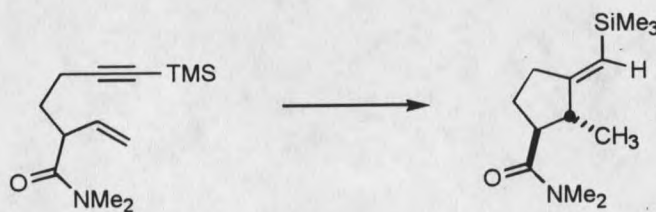
5.6 $Cp_2Zr(II)$ Mediated Cyclizations

2,2-([dimethyl]cyclopentylidene)methyl)trimethylsilane-4-spiro-5'-(2,2-dimethyl-1,3-dioxane) (**83b**).



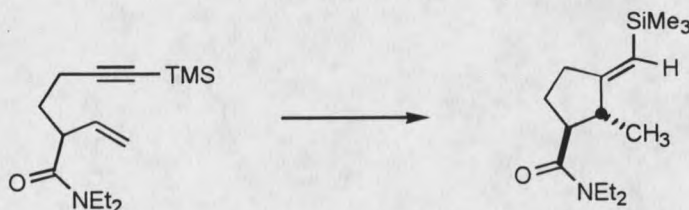
Enyne **83a** (42 mg, 0.15 mmol) was cyclized according to the general procedure utilized for **99** to afford 30 mg (71%) of **83b** in unoptimized yield. The product was found to be 100% homogeneous by analytical capillary G.C.: 1H NMR (C_6D_6) δ 5.46 (app t, $J = 1.9$ Hz, 1H, $C=CH$), 3.52 (s, 4H, CH_2O), 2.64 (d, $J = 1.9$ Hz, 2H, $CH_2=CH$), 1.47 (s, 3H, CH_3), 1.38 (s, 3H, CH_3), 1.28 (s, 2H, CH_2), 1.03 (s, 6H, $C(CH_3)_3$), 0.25 (s, 9H, $Si(CH_3)_3$); ^{13}C NMR (C_6D_6) δ 170.5, 118.0, 98.4, 70.1, 48.1, 43.5, 41.6, 40.4, 31.6, 27.1, 22.6, 0.7.

(1a,2b,3*E*)-*N,N*-Dimethyl-2-methyl-3-[(trimethylsilyl)methylene]cyclopentane-1-carboxamide (**84a**).



Enyne **14a** (59 mg, 0.25 mmol) was cyclized according to the procedure utilized for **14b** to afford 54 mg (91%) of the title compound as light yellow oil: ^1H NMR (C_6D_6) δ 5.43 (app d, $J = 4.3$ Hz, 1H, $\text{C}=\text{CH}$), 3.15 (m, 1H, CHCH_3), 2.68 (s, 3H, NCH_3), 2.63-2.47 (m, 2H, CH_2), 2.25 (m, 1H, COCH), 1.93-1.60 (m, 2H, CH_2), 1.09 (d, $J = 2.3$ Hz, 3H, CHCH_3), 0.18 (s, 9H, $\text{Si}(\text{CH}_3)_3$); ^{13}C NMR (C_6D_6) δ 174.3, 166.3, 117.5, 49.7, 46.6, 36.9, 36.0, 32.8, 29.1, 17.6, 0.6; IR (thin film) 3393, 1717, 1636, 1458, 1380, 1247, 1138, 840 cm^{-1} ; m/z 239 (M^+), 224, 167, 73.

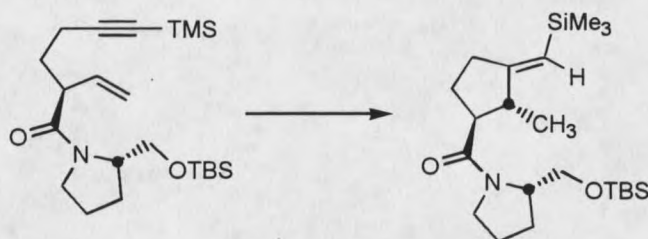
(1 α ,2 β ,3 E)-*N,N*-Diethyl-2-methyl-3-[(trimethylsilyl)methylene]cyclopentane-1-carboxamide (**84b**).



A solution of *n*-BuLi (0.36 mL, 5.9 M in heptane, 2.1 mmol) was added to a magnetically stirred solution of Cp_2ZrCl_2 (307 mg, 1.05 mmol) and DMAP (107 mg, 1.08 mmol) in THF (10 mL) maintained at -78°C . After 10 min the dry ice-acetone bath was removed and the vigorously stirred reaction mixture was allowed to warm to -10°C . As soon as the reaction mixture became homogeneous (usually at -20°C) the resulting yellow solution was recooled to -78°C . A solution of **14b** (132 mg, 0.5 mmol) in THF (0.15 mL) was then added dropwise and the

resulting mixture was held at $-78\text{ }^{\circ}\text{C}$ for 15 min. The dry ice-acetone bath was subsequently removed, the reaction flask was wrapped in foil and the vigorously stirred solution was allowed to gradually warm to $25\text{ }^{\circ}\text{C}$. After 10 h at $25\text{ }^{\circ}\text{C}$, H_2O (1 mL) was added, the reaction mixture was stirred for an additional 5 min and then 10% aqueous H_2SO_4 (1 mL) was added. After 1 h the supernatant solution was decanted and filtered through a pad of silica gel (1 cm diameter by 2 cm) which was subsequently extracted with Et_2O (3 x 10 mL). The filtrate was washed with H_2O (35 mL), and the organic layer was separated. The aqueous layer was extracted with Et_2O (3 x 15 mL) and the combined organic layers were washed with 10% aqueous H_2SO_4 (5 mL), H_2O (5 mL), saturated aqueous NaHCO_3 (5 mL), brine (5 mL), dried (MgSO_4), filtered and concentrated *in vacuo*. Chromatography of the residual oil on silica gel (15% EtOAc /hexane for elution) afforded 123 mg (93%) of **84b** as a colorless oil: ^1H NMR (CDCl_3) δ 5.19 (app d, $J = 2.1\text{ Hz}$, 1H, $\text{C}=\text{CH}$), 3.34 (app sx, $J = 7.1\text{ Hz}$, 4H, NCH_2), 2.79-2.67 (m, 1H, CHCH_3), 2.61-2.48 (m, 1H, CH_2), 2.36 (m, 1H, CHCO), 2.29 (m, 1H, CH_2), 1.90-1.65 (m, 2H, CH_2), 1.09 (dt, $J = 15.8, 7.0\text{ Hz}$, 6H, NCH_2CH_3), 0.9 (d, $J = 6.6\text{ Hz}$, 3H, CH_3), 0.04 (s, 9H, $\text{Si}(\text{CH}_3)_3$); ^{13}C NMR (CDCl_3) δ 174.5, 165.5, 117.3, 49.5, 46.4, 42.4, 41.2, 32.3, 29.5, 16.9, 15.7, 13.9, 0.4; IR (thin film) 3393, 2960, 1624, 1458, 1381, 1247, 1138, 840 cm^{-1} ; m/z 267 (M^+), 194, 167, 73; high resolution mass spectrum calcd for $\text{C}_{15}\text{H}_{29}\text{NOSi}$ (M^+) 267.2018, found 267.2010.

(1*E*,2 α *R*,3 β)-2-Methyl-3-[1-oxo-[-1-[2*S*-(1,1-dimethylethyl)dimethylsilyloxymethyl]pyrrolidino]]-methylcyclopentylidenemethyl]trimethylsilane (**85**).



The enyne **19** (205 mg, 0.25 mmol) was cyclized according to the procedure described above for **84b** to afford 193 mg (94%) of **85** as a light yellow oil. $[\alpha]_D^{25}$ -10 (*c* 1.0, C_6H_6); 1H NMR ($CDCl_3$) δ 5.18 (app t, $J = 2.3$ Hz, 1H, $C=CH$), 4.15 (m, 1H, $NCHCH_2$), 3.72-3.61 (m, 2H, CH_2O), 3.59-3.30 (m, 3H, NCH_2 and $COCH$), 2.62 (m, 1H, $CHCH_3$), 2.60-1.68 (m, 8H, CH_2), 0.99 (d, $J = 6.6$ Hz, 3H, $CHCH_3$), 0.82 (s, 9H, $C(CH_3)_3$), 0.03 (s, 9H, $Si(CH_3)_3$), 0.00 (s, 3H, $Si(CH_3)_2$), -0.02 (s, 3H, $Si(CH_3)_2$); ^{13}C NMR ($CDCl_3$) δ 173.4, 164.8, 116.7, 64.7, 63.1, 58.4, 51.1, 47.7, 46.0, 31.6, 27.6, 25.9, 21.8, 18.1, 16.4, -0.3, -5.4; IR (thin film) 3037, 2955, 2858, 1645, 1422, 1321, 1249, 1103, 841, 967 cm^{-1} ; m/z 409 (M^+), 352, 167, 73; high resolution mass spectrum calcd for $C_{22}H_{43}NO_2Si_2$ (M^+) 409.2832, found 409.2850.

Deuterated Diethyl cycle (**86**).



Enyne **14b** (66 mg, 0.25 mmol) was cyclized according to the procedure utilized for **84b**, except that after 12 h a solution of 80% AcOD in D₂O (2 mL) was added.

After 1 h H₂O (10 mL) and Et₂O (10 mL) were added and the organic layer separated. The aqueous phase was extracted with Et₂O (2 x 5 mL) and the combined organic layers were washed with 10% aqueous H₂SO₄ (2 mL), H₂O (2 mL), saturated aqueous NaHCO₃ (5 mL), brine (5 mL), dried (MgSO₄), filtered and concentrated *in vacuo*. Chromatography of the residual oil on silica gel (15% EtOAc/hexane for elution) afforded 51 mg (76%) of **86** as a colorless oil: ¹H NMR

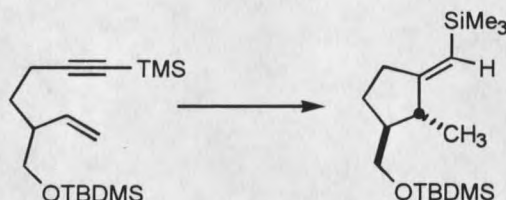
(C₆D₆) δ 3.22 (q, *J* = 7.1 Hz, NCH₂CH₃) 3.15 (shoulder, m, 1H, CHCH₃), 2.75 (q, *J* = 7.0 Hz, 2H, NCH₂CH₃), 2.55 (m, 1H, CHCO), 2.25 (m, 2H, CH₂CHCO), 1.95 (m, 1H, CH₂) 1.73 (m, 1H, CH₂) 1.07 (d, *J* = 5.6 Hz, CH₂D), 0.97 (t, *J* = 7.1 Hz, NCH₂CH₃), 0.70 (t, *J* = 7.2 Hz, 3H, NCH₂CH₃), 0.18 (s, 9H, Si(CH₃)₃). ¹³C NMR (C₆D₆) δ 173.8, 166.4, 117.4, 50.2, 47.1, 42.5, 41.6, 33.0, 30.1, 17.1 (t, *J* = 20.3 Hz), 15.8, 14.2, 0.6; *m/z* 269 (M⁺), 73.

N,N-Diethyl-2-methyl-3-[(trimethylsilyl)methyl]-1-cyclopentene-1-carboxamide
(87).



An analytical sample was purified by preparative gas chromatography. ^1H NMR (C_6D_6) δ 3.5 (m, 1H, CHCO), 3.25 (m, 2H, NCH_2), 2.85 (m, 2H, NCH_2), 2.55 (m, 1H, COCH), 2.25 (m, 1H, CHCH_2CH_2), 2.10 (m, 1H, CHCH_2), 1.90 (m, 1H, CHCH_2), 1.64 (s, 3H, CH_3), 1.58 (s, 1H, CH_2Si), 1.53 (s, 1H, CH_2Si), 0.97 (t, $J = 7.0$ Hz, 3H, NCH_2CH_3), 0.76 (t, $J = 7.0$ Hz, 3H, NCH_2CH_3), 0.08 (s, 9H, $\text{Si}(\text{CH}_3)_3$); ^{13}C NMR (C_6D_6) δ 174.5, 136.8, 101.6, 52.8, 42.5, 41.1, 39.1, 28.6, 20.3, 15.7, 14.1, 0.0; m/z 267 (M^+), 194, 167, 73.

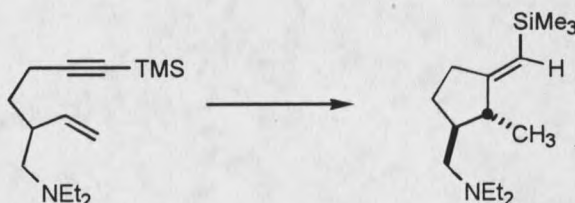
[[5-[(1,1-Dimethylethyl)dimethylsilyloxymethyl]-2-methylcyclopentylidene]-methyl]trimethylsilane) (93).



The enyne **10** was cyclized according to the general procedure utilized for **99** to afford an oil that possessed 93% of the theoretical mass. Analytical capillary G.C.

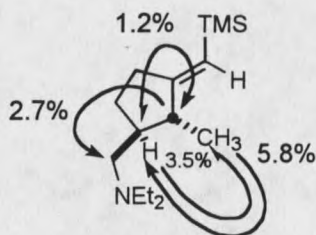
analysis of the crude reaction mixture indicated two peaks: one corresponding to 33% starting material (by coinjection) and another to 67% of a new material. ^1H NMR (CDCl_3) analysis of the crude reaction mixture showed an apparent quartet at 5.45 ppm, which is consistent with a vinyl proton of the title compound. No other characterization was successful.

(1 α ,2 β ,3 E)-1-(N,N -Diethylaminomethyl)-2-methyl-3-[(trimethylsilyl)methylene]cyclopentane (**95**).



Enyne **31** (38 mg, 0.15 mmol) was cyclized according to the general procedure utilized for **73** except after stirring for 10 h the reaction was treated with H_2O (2 mL) and heated at 35 °C for 2 h. The reaction mixture was allowed to cool and then treated with aqueous NaOH (1 mL, 2 M) and Et_2O (2 mL) and the organic layer was separated. The aqueous phase was extracted with Et_2O (4 x 2 mL) and the combined organic layers were washed with brine (2 x 2 mL), dried (MgSO_4), filtered and concentrated *in vacuo*. Chromatography of the residual oil on basic alumina (1% EtOAc /hexane for elution) afforded 31 mg (88%) of **95** as a pale yellow oil: ^1H NMR (CDCl_3) δ 5.48 (app q, $J = 2.4$ Hz, 1H, $\text{C}=\text{CH}$), 2.52-2.25 (m,

4H, NCH_2CH_3), 2.23-2.09 (m, 2H, NCH_2 and 1H, $\text{CH}_2\text{C}=\text{C}$), 1.95-1.86 (m, 1H, $\text{CH}_2\text{C}=\text{C}$), 1.86-1.78 (m, 1H, CHCH_3), 1.54-1.40 (m, 1H, CHCH_2N), 1.26-1.11 (m, 2H, CH_2), 0.95 (d, $J = 6.8$ Hz, 3H, CHCH_3), 0.90 (t, $J = 7.0$ Hz, 6H, NCH_2CH_3), 0.20 (s, 9H, $\text{Si}(\text{CH}_3)_3$); ^{13}C NMR (C_6D_6) δ 168.9, 117.6, 59.3, 48.6, 47.5, 46.5, 32.5, 31.3, 19.3, 13.1, 0.7; IR (thin film) 1621, 1459, 1382, 1247, 1203, 1068, 870, 839, 690 cm^{-1} ; m/z 253 (M^+), 180, 151, 86; high resolution mass spectrum calcd for $\text{C}_{15}\text{H}_{31}\text{NSi}$ (M^+) 253.2226, found 253.2230. The stereochemical assignment is consistent with the observed NOE's:



[[4-[(1,1-Dimethylethyl)dimethylsilyloxymethyl]-2-methylcyclopentylidene]methyl]trimethylsilanes (**99a** and **99b**).

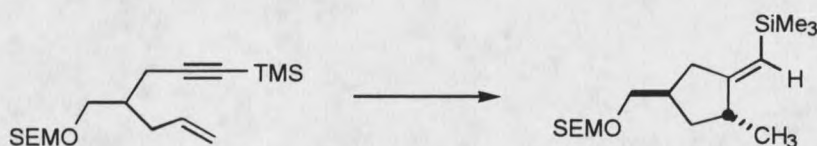


To a vigorously stirred mixture of **73** (77.6, 0.25 mmol) and Cp_2ZrCl_2 (80 mg, 0.27 mmol) in THF (3 mL) maintained at -78°C was added a solution of *n*-BuLi (116 μL , 4.78 M in heptane, 0.552 mmol). After 15 min the dry ice-acetone bath was removed, the reaction vessel was wrapped in foil, and the reaction mixture was

allowed to warm to 25 °C and stirred at this temperature for 10 h. The reaction mixture was quenched with H₂O (1 mL) followed by the addition of 10% aqueous H₂SO₄ (5 mL) 5 min later. After 1 h the resultant mixture was extracted with hexane (3 x 15 mL). The combined organic phases were washed with H₂O (5 mL), saturated aqueous NaHCO₃ (5 mL), brine (5 mL), dried (MgSO₄) and filtered through a pad of silica gel (1 cm diameter by 1.5 cm) which was subsequently extracted with hexane (3 x 2 mL). The filtrate was concentrated *in vacuo* to afford 69 mg (89%) of **99a** and **99b** as a colorless oil. GLC analysis indicated 99.6% conversion to a 2.1 to 1 mixture of diastereomers: *trans*-**99a**: ¹H NMR (C₆D₆) δ 5.42 (m, 1H, C=CH), 3.46 (d, *J* = 6.0 Hz, 2H, OCH₂), 2.62 (m, 1H, CH₂), 2.35 (m, 1H, CHCH₃), 2.22-2.10 (m, 2H, CH₂ and CH), 1.88 (m, 2H, CH₂), 1.09 (d, *J* = 6.8 Hz, CH₃), 0.97 (s, 9H, -C(CH₃)₃), 0.20 (s, 9H, Si(CH₃)₃), 0.05 (s, 6H, Si(CH₃)₂); *cis*-**15a** 5.40 (m, 1H, C=CH), 3.40 (2 dd, *J* = 6.4, 4.0 Hz, 2H, OCH₂), 2.62 (m, 1H, CH₂), 2.38 (m, 1H, CHCH₃), 2.22-2.10 (m, 2H, CH₂ and CH), 1.78 (m, 1H, CH₂), 1.30 (m, 1H, CH₂), 1.04 (d, *J* = 7.0 Hz, 3H, CH₃), 0.97 (s, 9H, -C(CH₃)₃), 0.19 (s, 9H, Si(CH₃)₃), 0.05 (s, 6H, Si(CH₃)₂); ¹³C NMR (C₆D₆) δ 168.0 and 162.4, 118.3 and 117.4, 67.7 and 67.4, 42.6 and 41.9, 41.2 and 40.8, 39.1 and 37.3, 37.4 and 36.6, 26.8, 21.1, 19.2, 0.6, -4.5; IR (thin film) 1632, 1471, 1249, 1099, 838, 774, 685 cm⁻¹; m/z 255 (M⁺ - *t*Bu), 180, 73; high resolution mass

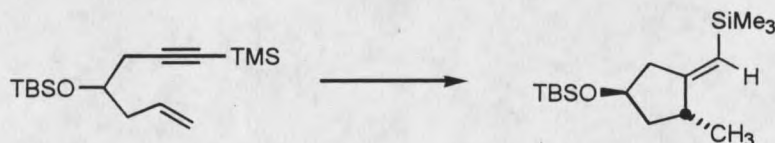
spectrum calcd for $C_{17}H_{36}OSi_2$ (M^+) 312.2305, found 312.2313 (*cis*) and 312.2321 (*trans*).

[[4-[1-(2-trimethylsilylethoxy)methoxymethyl]-2-methylcyclopentylidene]methyl]tri-methylsilane (**100a** and **100b**).



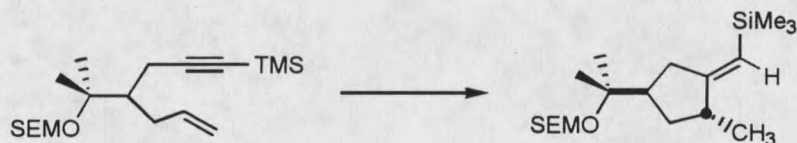
Enyne **73** (49 mg, 0.15 mmol) was cyclized according to the general procedure utilized for **99a,b** to afford 49 mg (99%) of **100a** and **100b** as a clear oil as a 2.1 to 1 (*trans*:*cis*) mixture of diastereomers: *trans*-**100a**: 1H NMR (C_6D_6) δ ; 5.42 (m, 1H, CCH), 4.61 (s, 2H, OCH_2O), 3.63 (m, 2H, CH_2CH_2TMS), 3.41 (m, 2H, $CHCH_2O$), 2.74-2.11 (m, 4H, CH_2), 1.90 (m, 1H, CH_2), 1.06 (d, $J = 6.7$ Hz, 3H, CH_3), 0.95 (m, 2H, CH_2TMS), 0.18 (s, 9H, $Si(CH_3)_3$), 0.00 (s, 9H, $Si(CH_3)_3$); ^{13}C NMR (δ) 167.2 (C), 117.5 (CH), 95.8 (CH_2), 72.6 (CH_2), 65.7 (CH_2), 42.5 (CH), 39.5 (CH_2), 37.8 (CH_2), 21.1 (CH), 19.1 (CH_3), 19.0 (CH_2), 0.6 (CH_3), -0.6 (CH_3); IR (thin film) 1623, 1376, 1248, 1109, 1058, 836, 691 cm^{-1} ; m/z 328 (M^+), 197, 73.

[[3-[(1,1-Dimethylethyl)dimethylsilyloxy]-5-methylcyclopentylidene]methyl]trimethylsilanes (**103a** and **103b**).



Enyne **51** (74 mg, 0.25 mmol) was cyclized according to the general procedure for **99a,b** to afford 60 mg (80%) of **103a** and **103b** as a colorless oil as a 1.1 to 1 mixture of diastereomers: ^1H NMR (C_6D_6) δ 5.47 (app q, $J = 2.3$ Hz, 1H, $\text{C}=\text{CH}$) and 5.43 (app q, $J = 2.4$ Hz, 1H, $\text{C}=\text{CH}$), 4.23-4.18 and 4.15-4.06 (m, 1H, OCH), 2.82 and 2.72 (m, 1H, CHCH_3), 2.55-2.25 (m, 4H, CH_2), 2.00-1.83 (m, 4H, CH_2), 1.13 (d, $J = 6.9$ Hz, 3H, CH_3) and 1.06 (d, $J = 6.9$ Hz, 3H, CH_3), 0.96 and 0.94 (s, 9H, CCH_3), 0.17 and 0.16 (s, 9H, $\text{Si}(\text{CH}_3)_3$), 0.05 (s, 12H, $\text{Si}(\text{CH}_3)_2$); ^{13}C NMR (C_6D_6) δ 166.1 and 165.3 (C), 118.8 and 118.6 (CH), 73.3 and 72.9 (CH), 44.9 and 44.7 (CH_2), 44.0 and 43.9 (CH_2), 40.3 and 39.4 (CH), 26.7 (CH_3), 20.3 and 19.8 (CH_3), 18.9 (C), 0.6 (CH_3), -3.8 (CH_3); IR (thin film) 643, 1462, 1248, 1055, 837, 774, 689 cm^{-1} ; m/z 297 ($\text{M}^+ - \text{H}$), 241, 167, 147, 133, 73; high resolution mass spectrum calcd for $\text{C}_{16}\text{H}_{34}\text{OSi}_2$ (M^+) 298.2148, found 298.2159 and 298.2159.

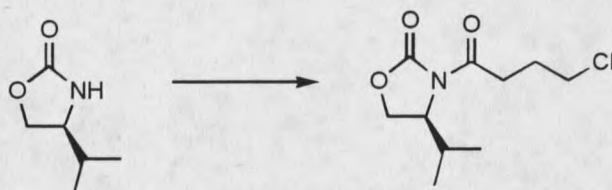
[[4-[1,1-Dimethyl-1-[(2-trimethylsilylethoxy)methoxymethyl]]-2-methylcyclopentylidene]methyl]trimethylsilanes (**105a** and **105b**).



Enyne **76** (71 mg, 0.20 mmol) was cyclized according to the general procedure for utilized **99a,b** to afford 73 mg (99%) of **105a** and **105b** as an 11 to 1 mixture of diastereomers: *trans*-**105a**: ^1H NMR (C_6D_6) δ 5.45 (app q, $J = 2.3$, 1H, $\text{C}=\text{CH}$), 4.72 (s, 2H, OCH_2O), 3.66 (m, 2H, $\text{CH}_2\text{CH}_2\text{TMS}$), 2.56 (m, 2H, CH_2), 2.35 (m, 1H, CHCH_3), 1.95-1.71 (m, 2H, CH_2), 1.14 (m, 9H, overlapping $\text{C}(\text{CH}_3)_2$ and CHCH_3), 0.94 (m, 2H, CH_2TMS), 0.21 (s, 9H, $\text{Si}(\text{CH}_3)_3$), 0.00 (s, 9H, $\text{Si}(\text{CH}_3)_3$); ^{13}C NMR (C_6D_6) δ 167.7, 116.8, 90.2, 76.8, 65.6, 50.2, 42.8, 36.9, 34.9, 25.8, 25.1, 19.1, 18.9, 0.7, -0.5; IR (thin film) 1632, 1459, 1379, 1248, 1056, 937, 768 cm^{-1} ; m/z 283 ($\text{M}^+ - \text{TMS}$), 225, 209, 131, 73; high resolution mass spectrum calcd for $\text{C}_{19}\text{H}_{40}\text{O}_2\text{Si}_2$ (M^+) 356.2567, found 356.2563.

5.7 Carbacyclin Synthesis

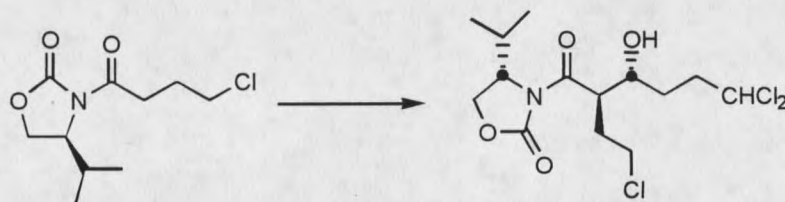
(4S)-3-(4'-chlorobutanoyl)-4-(methylethyl)-1,3-oxazolidin-2-one (**128**).



To a magnetically stirred solution of NaH (1.44 g, 60 mmol) in THF (300 mL) cooled to 0 °C was added (4S)-(-)-4-(methylethyl)-2-oxazolidinone (6.46 g, 50 mmol) in one portion. The reaction mixture was allowed to warm to rt and was stirred for 10 h. The thick suspension was then cooled to 0 °C and 4-chlorobutryl chloride (9.16 g, 65 mmol) was added and the solution was allowed to warm to rt. After 1.5 h saturated aqueous NH₄Cl (50 mL) was added dropwise with caution. Next, H₂O (50 mL) was added and volatile material was removed *in vacuo*. The resulting heterogeneous mixture was extracted with EtOAc (3 x 100 mL) and the combined organic phases were washed with 2.0 M aqueous NaOH (2 x 25 mL), saturated aqueous NaHCO₃ (25 mL), brine (25 mL), dried (Na₂SO₄), filtered and concentrated *in vacuo*. Initial purification by chromatography of the residual oil on silica gel (15% EtOAc/hexane for elution) followed by bulb-to-bulb distillation afforded 9.82 g (84%) of **128** as a white crystalline solid: mp 39-40 °C; [α]_D +77.5 (*c* 8.9); ¹H NMR (CDCl₃) δ 4.41-4.37 (m, 1H), 4.27-4.15 (m, 2H), 3.10-3.01 (m,

2H), 2.35-2.29 (m, 1H), 2.11-2.04 (m, 2H), 0.87 (d, $J = 7.2$ Hz), 0.83 (d, $J = 6.9$ Hz); ^{13}C NMR (CDCl_3) δ 172.1, 154.0, 63.5, 58.5, 44.0, 32.7, 28.5, 27.2, 17.9, 14.7, 10.5; IR (thin film) 1779, 1699, 1386, 1245 cm^{-1} .

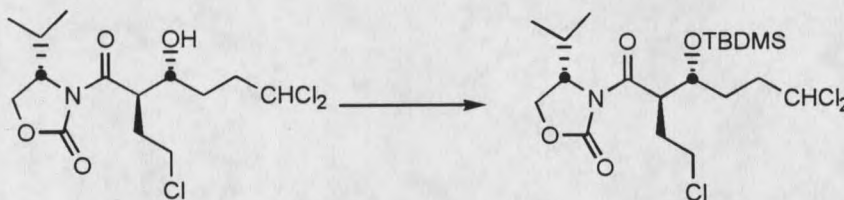
(4*S*,2'*R*,3'*R*)-3-(2'-(2-chloroethyl)-3'-hydroxy-6',6'-dichlorohexanoyl)-4-methylethyl-1,3-oxazolidin-2-one (**129**).



To a magnetically stirred solution of (4*S*)-3-(4'-chlorobutanoyl)-4-(methylethyl)-1,3-oxazolidin-2-one **128** (3.50 g, 15.0 mmol) in CH_2Cl_2 (60 mL) maintained at 0 °C was added TEA (2.40 mL, 17.2 mmol), followed by the dropwise addition of dibutylborotriylate (4.52 g, 16.5 mmol). The reaction mixture was stirred for 1 h at 0 °C and then cooled to -78 °C. Meanwhile, to a magnetically stirred solution of 4,4-dichlorobutanal (3.81 g, 27.0 mmol) in CH_2Cl_2 (54 mL) cooled to -110 °C was added a solution of diethylaluminum chloride (58 mL, 1.0 M in hexane, 58 mmol) cooled to -78 °C. The resulting aldehyde-Lewis acid solution was allowed to warm to -78 °C and was stirred for 5 min. To the cold aldehyde solution, the solution of the boron enolate was added dropwise via canula. The reaction mixture was gradually warmed to -58 °C over 20 min and maintained at this temperature for 18

h. The reaction mixture was then recooled to $-78\text{ }^{\circ}\text{C}$ and a solution of 30% aqueous H_2O_2 (5 mL) in MeOH (30 mL) was added dropwise, allowing 1 min between drops at first. After the addition was complete, a solution of 30% aqueous H_2O_2 (25 mL) in MeOH (75 mL) was added dropwise and the reaction mixture was allowed to warm to $0\text{ }^{\circ}\text{C}$ and was diluted with H_2O (100 mL). The phases were separated and the aqueous phase was extracted with three 100-mL portions of EtOAc. The combined organic phases were washed with saturated aqueous NaHCO_3 (2 x 10 mL), brine (50 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo*. Chromatography of the residual oil on silica gel (15% EtOAc/hexane for elution) afforded 5.50 g of a colorless oil containing a mixture of compounds.

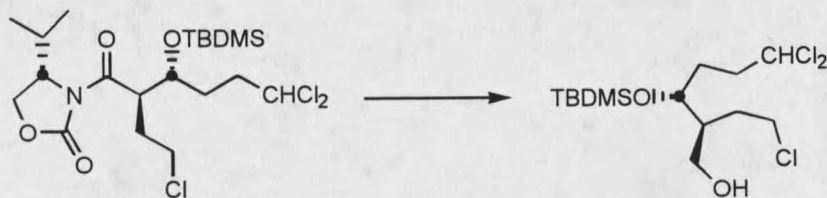
(4*S*,2'*R*,3'*R*)-3-(2'-(2-chloroethyl)-3'-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-6',6'-dichlorohexanoyl)-4-methylethyl-1,3-oxazolidin-2-one (**130**).



To a magnetically stirred solution of crude (4*S*,2'*R*,3'*R*)-3-(2'-(2-chloroethyl)-3'-hydroxy-6',6'-dichlorohexanoyl)-4-methylethyl-1,3-oxazolidin-2-one **129** (5.50 g, from the above reaction) and 2,6-lutidine (4.37 mL, 37.5 mmol) in CH_2Cl_2 (225 mL) maintained at $0\text{ }^{\circ}\text{C}$ was added dropwise *t*-butyldimethylsilyltriflate (5.17 mL,

22.5 mmol). After 10 min the reaction mixture was allowed to warm to 23 °C and stir for another 10 min. To the resulting solution was added saturated aqueous NH_4Cl (30 mL) and the resulting phases were separated. The aqueous phase was extracted with CH_2Cl_2 (3 x 30 mL) and the combined organic layers were washed with saturated aqueous NH_4Cl (2 x 20 mL), brine (20 mL), dried (MgSO_4) and filtered. Chromatography of the residual oil on silica gel (15% EtOAc/hexane for elution) afforded 8.07 g of an impure colorless oil. High resolution (CI/NH_3) mass spectrum calcd for $\text{C}_{20}\text{H}_{36}\text{Cl}_3\text{NO}_4\text{Si}$ ($\text{M}+\text{H}$)⁺ 488.1557, found 488.1541.

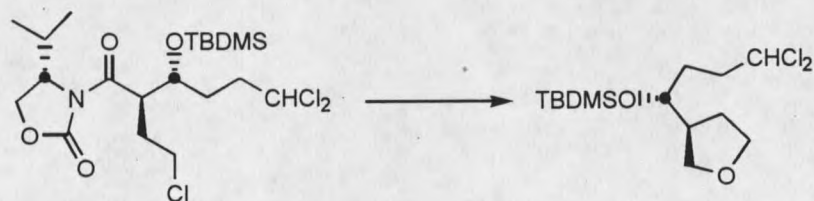
(2*R*,3*R*)-2-chloroethyl-3-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-6,6-dichlorohexanol (**131**).



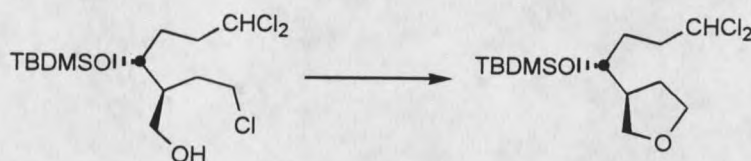
To a magnetically stirred solution of NaBH_4 (1.25 g, 33 mmol) and LiCl (1.40 g, 33 mmol) in EtOH (110 mL) cooled to 0 °C was added imide **130** (from the above reaction) in THF (30 mL). The reaction was allowed to warm to 23 °C and was stirred for 12 h. A solution of aqueous 10% HCl (100 mL) was added, cautiously at first. Volatiles were removed *in vacuo*. The resulting heterogeneous solution was extracted with EtOAc (4 x 200 mL) and the combined organic phases were washed

with saturated aqueous NaHCO_3 (50 mL), brine (50 mL), dried (Na_2SO_4) and filtered. Gradient chromatography of the residual oil on silica gel (5-10% EtOAc/hexane for elution) afforded 2.40 g (44%, three steps) of the title compound as a colorless oil. This compound was found to be >99% enantiomerically pure based on analysis of its Mosher's ester. $[\alpha]_D +6.2$ (c 14.9, CHCl_3); ^1H NMR (CDCl_3) δ 5.76 (t, $J = 5.6$ Hz, 1H, CHCl_2), 3.90-3.81 (m, 2H, CH_2O), 3.68-3.54 (m, 3H, CH and CH_2Cl), 2.54 (br s, 1H, OH), 2.22-2.14 (m, 2H), 2.03-1.98 (m, 1H), 1.89-1.78 (m 2H), 0.87 (s, 9H, $\text{C}(\text{CH}_3)_3$), 0.09 (s, 3H, SiCH_3), 0.08 (s, 3H, SiCH_3); ^{13}C NMR (CDCl_3) δ 74.3 (CH), 73.3 (CH), 61.5 (CH_2), 43.3 (CH_2), 40.8 (CH), 39.5 (CH_2), 31.2 (CH_2), 30.4 (CH_2), 25.8 (CH_3), 17.9 (C), -4.3 (CH_3), -4.6 (CH_3); IR (thin film) 3442, 2956, 2858, 1472, 1388, 1362, 1258, 1084, 837, 776, 660 cm^{-1} ; m/z (M^+); high resolution mass spectrum calcd for $\text{C}_{14}\text{H}_{29}\text{Cl}_3\text{O}_2\text{Si}$ (M^+) 362.1002, found 361.9998.

(2*S*,1*R*)-2-(1-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-4',4'-dichlorobutyl]-tetrahydrofuran (**132**).



From the above reaction, 0.303 g (5.6%) of the title compound was isolated after chromatography.



The title compound may be prepared by an alternative method. To a magnetically stirred solution NaH (3.6 mg, 0.15 mmol) in THF (1 mL) was added alcohol **131** (36.0 mg, 0.1 mmol) in THF (1.5 mL). After stirring at 23 °C for 18 hours, saturated aqueous NH₄Cl (10 mL) and EtOAc (5 mL) was added and the resulting phases were separated. The aqueous phase was extracted with EtOAc (2 x 5 mL) and the combined organic layers were washed with brine (5 mL), dried (MgSO₄) and filtered. Chromatography of the residual oil on silica gel (5% EtOAc/hexane for elution) afforded 32.0 mg (98%) of the title compound as a colorless oil: [α]_D -17 (c 3.4, CHCl₃); ¹H NMR (CDCl₃) δ 5.76 (t, *J* = 5.9 Hz, 1H, CHCl₂), 3.87-3.79 (m, 2H, CH₂O), 3.73-3.66 (m, 2H, CH₂O), 3.51 (app t, *J* = 8.1 Hz, 1H, CHO), 2.40-2.16 (m, 3H), 1.93-1.48 (m, 4H), 0.85 (s, 9H, C(CH₃)₃), 0.04 (s, 3H, SiCH₃), 0.03 (s, 3H, SiCH₃); ¹³C NMR (CDCl₃) δ 73.8 (CH), 73.1 (CH), 71.1 (CH₂), 68.2 (CH₂), 44.6 (CH), 38.2 (CH₂), 31.3 (CH₂), 28.7 (CH₂), 25.8 (CH₃), 18.0 (C), -4.1 (CH₃), -4.7 (CH₃); IR (thin film) 2930, 2857, 1472, 1387,

1472, 1387, 1361, 1256, 1082, 940, 837, 676 cm^{-1} ; High resolution mass spectrum calcd for $\text{C}_{14}\text{H}_{29}\text{O}_2\text{SiCl}_2$ ($\text{M}+\text{H}$) $^+$ 327.1313, found 237.1321.

(2*R*,3*R*)-1-chloro-3-[[[(1,1-dimethylethyl)dimethylsilyl]oxymethyl]-4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-7,7-dichloroheptane (**134**).

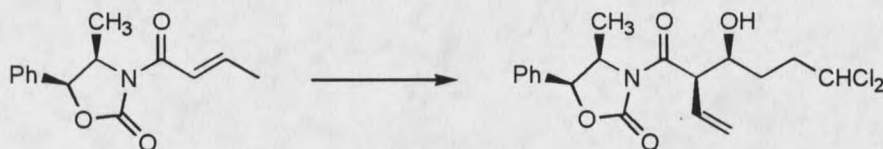


A solution of (2*R*,3*R*)-2-chloroethyl-3-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-6,6-dichlorohexanol **131** (1.56 g, 4.3 mmol), imidazole (0.73 g, 10.7 mmol), and *t*-butyldimethylsilyl chloride (0.71 g, 4.7 mmol) in DMF (8 mL) was magnetically stirred at room temperature for 8 h. The reaction mixture was subsequently poured into saturated aqueous NaHCO_3 (50 mL) and the transfer was quantitated with 6:1 hexane- Et_2O (10 mL). The organic phase was separated and the aqueous phase was extracted with 6:1 hexane- Et_2O (3 x 25 mL). The organic layers were washed with H_2O (5 mL), brine (10 mL), dried (MgSO_4), filtered and concentrated *in vacuo* to afford 1.93 g (94%) of the title compound as a colorless oil which was suitable for use without further purification: $[\alpha]_D^{+15.4}$ (c 13.3, CHCl_3); ^1H NMR (CDCl_3) δ 5.75 (t, 1H, CHCl_2), 3.91-3.94 (m, 1H, CHO), 3.66-3.48 (m, 4H, CH_2O and CH_2Cl), 2.39-2.25 (m, 1H), 2.22-2.18 (m, 1H), 1.98-1.86 (m, 2H), 1.76-1.57 (m, 3H), 0.87 (s, 18H, $\text{C}(\text{CH}_3)_3$), 0.08-0.02 (m, 12H, SiCH_3); ^{13}C NMR (CDCl_3) δ 73.8

(CH), 71.6 (CH), 62.8 (CH₂), 44.1 (CH), 43.8 (CH₂), 40.3 (CH₂), 30.0 (CH₂), 28.8 (CH₂), 25.9 (CH₃, not resolved), 18.2 (C), 18.0 (C), -4.3 (CH₃), -4.5 (CH₃), -5.4 (CH₃), -5.6 (CH₃); IR (thin film) 2955, 2858, 1982, 1472, 1388, 1361, 1258, 1090, 1005, 938, 836, 775, 667 cm⁻¹; High resolution mass spectrum calcd for C₂₀H₃₆Cl₃NO₄Si (M⁺) 476.1867, found 476.1863.

5.8 *epi*-Carbacyclin Synthesis

(2'*R*,3'*S*,4*R*,5*S*)-3-(2'-Ethenyl-3'-hydroxy-6',6'-dichlorohexanoyl-4-methyl-5-phenyl-1,3-oxazolidin-2-one (**146**).



To a magnetically stirred solution of imide **145** (1.47 g, 6.0 mmol) in CH₂Cl₂ (24 mL) cooled to -78 °C was added a solution of Bu₂BOTf (1.81 g, 6.6 mmol) in CH₂Cl₂ (6 mL), followed by TEA (0.79 g, 7.8 mmol) 5 min later. After stirring for 1 h at -78 °C, the reaction mixture was allowed to warm gradually to 0 °C, and the solution was maintained at this temperature for 45 min. The reaction mixture was recooled to -78 °C and a -78 °C solution of 4,4-dichlorobutanal **48** (1.27 g, 9.0 mmol) in CH₂Cl₂ (9 mL) was added via a micro 22 gauge cannula. After stirring for 1 h at -78 °C the reaction mixture was gradually warmed to 0 °C and maintained

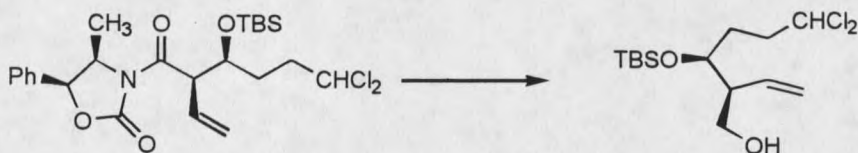
at this temperature for 1 h. A solution of MeOH (18 mL) and 1.0 M pH 7.0 phosphate buffer (6 mL) cooled to 0 °C was added in one portion, then a solution of 30% aqueous H₂O₂ (6 mL) and MeOH (6 mL) was added dropwise over 5 min. The resulting heterogeneous mixture was vigorously stirred for 2 h and then extracted with EtOAc-hexane 1:1 (3 x 50 mL). The combined organic phases were washed with saturated aqueous NaHCO₃ (25 mL), brine (25 mL), dried (Na₂SO₄), filtered and concentrated *in vacuo*. Chromatography of the residual oil on silica gel (5% EtOAc/hexane for elution) afforded 2.23 g (92%) of the title compound as a colorless oil: $[\alpha]_D^{20}$ (c 2.3, CHCl₃), ¹H NMR (CDCl₃) δ 7.42-7.23 (m, 5H, aromatic H's), 5.93 (ddd, *J* = 19.1, 9.9, 8.9 Hz, 1H, CH=CH₂), 5.82 (t, 1H, *J* = 6.0 Hz, CHCl₂), 5.65 (d, *J* = 7.3 Hz, 1H, PhCH), 5.40-5.34 (m, 2H, CH=CH₂), 4.83-4.74 (m, 1H, CHOH), 4.49 (dd, *J* = 8.9, 3.6 Hz, 1H, C₂-CH), 4.03-3.98 (m, 1H, CHCH₃), 3.12 (br s, 1H, OH), 2.51-2.20 (m, 2H, CH₂), 1.76-1.64 (m, 2H, CH₂), 0.83 (d, *J* = 6.7 Hz, 3H, CH₃); ¹³C NMR (CDCl₃) δ 173.6 (C), 152.4 (C), 133.0 (C), 130.6 (CH), 128.8 (CH), 128.7 (CH), 125.6 (CH), 121.6 (CH₂), 78.8 (CH), 73.5 (CH), 70.7 (CH), 54.6 (CH), 52.4 (CH), 40.0 (CH₂), 30.3 (CH₂), 14.1 (CH₃); IR (thin film) 3511, 3068, 2984, 2932, 1782, 1693, 1633, 1352, 1304, 933, 806, 767, 738, 700 cm⁻¹; high resolution mass spectrum calcd for C₁₈H₂₁Cl₂NO₄ (M⁺) 385.0847, found 385.0850.

(2'*R*,3'*S*,4*R*,5*S*)-3-(2'-Ethenyl-3'-[[1,1-dimethylethyl]dimethylsilyl]oxy]-6',6'-dichlorohexanoyl-4-methyl-5-phenyl-1,3-oxazolidin-2-one (**146**).



The title compound was prepared according to the general procedure utilized for **130** to afford 652 mg (90%) of **146** as a clear oil: $[\alpha]_D^{25}$ 15.9 (*c* 6.92, CHCl_3); ^1H NMR (CDCl_3) δ 7.46-7.23 (m, 5H, aromatic *H*'s), 5.99 (ddd, $J = 19.4, 10.2, 9.2$ Hz, 1H, $\text{CH}=\text{CH}_2$), 5.82 (t, 1H, $J = 5.6$ Hz, CHCl_2), 5.60 (d, $J = 7.1$ Hz, 1H, PhCH), 5.28-5.20 (m, 2H, $\text{CH}=\text{CH}_2$), 4.77-4.67 (m, 1H, CHOH), 4.49 (dd, $J = 9.2, 5.5$ Hz, 1H, $\text{C}_2\text{-CH}$), 4.17-3.32 (m, 1H, CHCH_3), 2.34-2.25 (m, 2H, CH_2), 1.91-1.80 (m, 2H, CH_2), 0.88-0.69 (m, 12H, CH_3 , and $\text{C}(\text{CH}_3)_3$), 0.06 (s, 3H, $\text{Si}(\text{CH}_3)_2$), 0.04 (s, 3H, $\text{Si}(\text{CH}_3)_2$); ^{13}C NMR (CDCl_3) δ 171.9 (C), 152.7 (C), 133.14 (C), 133.11 (CH), 128.9 (CH), 125.6 (CH), 119.7 (CH_2), 79.0 (CH), 73.7 (CH), 72.1 (CH), 55.2 (CH), 53.4 (CH), 38.7 (CH_2), 31.1 (CH_2), 25.8 (CH_3), 18.0 (C), 14.2 (CH_3), -1.2 (CH_3), -1.6 (CH_3); IR (thin film) 3080, 2931, 2858, 1782, 1699, 1699, 1637, 1456, 1349, 493 cm^{-1} ; high resolution mass spectrum calcd for $\text{C}_{24}\text{H}_{35}\text{Cl}_2\text{NO}_4\text{Si}$ (M^+) 499.1712, found 499.1719.

(3*S*,4*S*)-3-Hydroxymethyl-4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-7,7-dichloro-1-heptene.



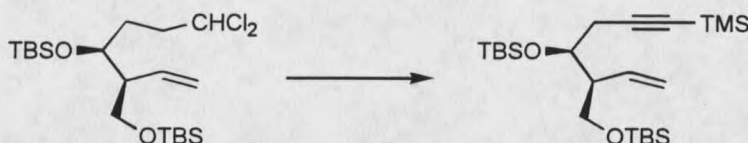
The title compound was prepared according to the general procedure utilized for **131** to afford 359 mg (55%) of the title compound as a clear oil: $[\alpha]_D$ not observed (c 0.83, CHCl_3); ^1H NMR (CDCl_3) δ 5.76-5.65 (m, 2H, $\text{CH}=\text{CH}_2$ and CHCl_2), 5.23-5.11 (m, 2H, $\text{CH}=\text{CH}_2$), 3.83 (dt, $J = 3.1, 6.2$ Hz, 1H, CHOSi), 3.72 (dd, $J = 10.6, 6.8$ Hz, 1H, CHHOH), 3.57 (dd, $J = 10.6, 7.5$ Hz, 1H, CHHOH), 2.42-2.34 (m, 2H, CH_2), 1.90 (br s, 1H, OH), 1.74-1.69 (m, 2H, CH_2), 0.88 (s, 9H, $\text{C}(\text{CH}_3)_3$), 0.08 (s, 3H, $\text{Si}(\text{CH}_3)$), 0.06 (s, 3H, $\text{Si}(\text{CH}_3)$); ^{13}C NMR (CDCl_3) δ 135.2 (CH), 118.9 (CH_2), 73.4 (CH), 72.4 (CH), 63.2 (CH_2), 51.5 (CH), 40.0 (CH_2), 30.4 (CH_2), 25.8 (CH_3), 18.0 (C), -4.3 (CH_3), -4.6 (CH_3); IR (thin film) 3403, 3076, 2956, 2857, 1640, 1463, 1254, 1103, 1034, 920, 837, 776, 663 cm^{-1} ; high resolution (CI/ NH_3) mass spectrum calcd for $\text{C}_{14}\text{H}_{29}\text{Cl}_2\text{O}_2\text{Si}$ (M^+) 327.1314, found 327.1298.

(3*S*,4*S*)-3-[[[(1,1-dimethylethyl)dimethylsilyl]oxymethyl]-4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-7',7'-dichloro-1-heptene (**147**).



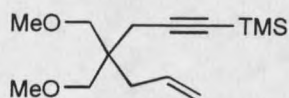
The title compound was prepared according to the general procedure utilized for **134** to afford 0.23 g (99%) of the title compound as a clear oil: $[\alpha]_D^{25}$ 1.48 (c 10.1, CHCl_3); ^1H NMR (CDCl_3) δ 5.32-5.28 (m, 2H, $\text{CH}=\text{CH}_2$ and CHCl_2), 5.16-5.05 (m, 2H, $\text{CH}=\text{CH}_2$), 3.90 (dt, $J = 2.5, 6.5$ Hz, 1H, CHOSi), 3.72 (dd, $J = 9.9, 7.9$ Hz, 1H, CHHOSi), 3.49 (dd, $J = 9.9, 6.1$ Hz, 1H, CHHOSi), 2.23-2.12 (m, 3H, CH_2 and CH), 1.74-1.66 (m, 2H, CH_2), 0.98 (s, 18H, $\text{C}(\text{CH}_3)_3 \times 2$), 0.06 (s, 6H, $\text{Si}(\text{CH}_3)_2$), 0.04 (s, 6H, $\text{Si}(\text{CH}_3)_2$); ^{13}C NMR (CDCl_3) δ 135.7 (CH), 117.9 (CH_2), 73.6 (CH), 70.1 (CH), 63.3 (CH_2), 51.8 (CH), 39.9 (CH_2), 31.5 (CH_2), 25.9 (CH_3 , not resolved), 18.1 (C , not resolved), -4.2 (CH_3), -4.6 (CH_3), -5.2 (CH_3), -5.3 (CH_3); IR (thin film) 3078, 2955, 2858, 1472, 1256, 1098, 1036, 919, 836, 775 cm^{-1} ; high resolution (CI/ NH_3) mass spectrum calcd for $\text{C}_{20}\text{H}_{43}\text{Cl}_2\text{O}_2\text{Si}_2$ ($\text{M}+\text{H}$) $^+$ 441.2178, found 441.2177.

(3*S*,4*S*)-3-[[[(1,1-dimethylethyl)dimethylsilyl]oxymethyl]-4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-8-trimethylsilyl-1-heptene-6-yne (**148**).

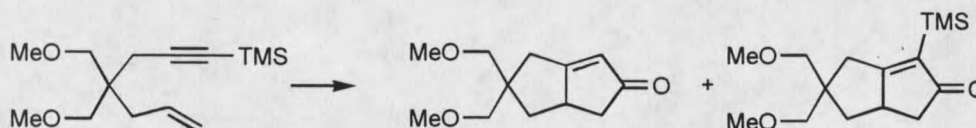


The title compound was prepared according to the general procedure utilized for **51** to afford the title compound **148** as a clear oil in excellent yield: $[\alpha]_D$ 6.9 (*c* 2.03, CHCl_3); ^1H NMR (CDCl_3) δ 5.73-5.61 (m, 1H, $\text{CH}=\text{CH}_2$), 5.17-5.10 (m, 2H, $\text{CH}=\text{CH}_2$), 4.08 (dt, $J = 1.9, 6.2$ Hz, 1H, CHOSi), 3.62 (dd, $J = 10.0, 9.1$ Hz, 1H, CHHOSi), 3.48 (dd, $J = 10.0, 6.2$ Hz, 1H, CHHOSi), 2.54-2.45 (m, 1H, CH), 2.33-2.31 (m, 2H, CH_2), 0.88 (s, 9H, $\text{C}(\text{CH}_3)_3$), 0.86 (s, 9H, $\text{C}(\text{CH}_3)_3$), 0.12 (s, 9H, $\text{Si}((\text{CH}_3)_3)$), 0.06 (s, 6H, $\text{Si}(\text{CH}_3)$), 0.03 (s, 3H, $\text{Si}(\text{CH}_3)$), 0.02 (s, 3H, $\text{Si}(\text{CH}_3)$); ^{13}C NMR (CDCl_3) δ 134.7 (CH), 118.4 (CH_2), 104.4 (C), 86.3 (C), 69.5 (CH), 63.3 (CH_2), 51.8 (CH), 27.0 (CH_2), 25.94 (CH_3), 25.87 (CH_3), 18.2 (C), 18.1 (C), 0.1 (CH_3), -4.3 (CH_3), -4.9 (CH_3), -5.1 (CH_3), -5.3 (CH_3); IR (thin film) 3076, 2956, 2858, 2177, 1472, 12514, 1105, 1037, 920, 838, 776, 667, 642 cm^{-1} ; high resolution (CI/ NH_3) mass spectrum calcd for $\text{C}_{23}\text{H}_{49}\text{O}_2\text{Si}_3$ ($\text{M}+\text{H}$) $^+$ 441.3040, found 441.3045.

Bis(4,4-methoxymethyl)hept-6-en-1-yne (**152**).



Bis[2,2-methoxymethyl]-3,3a,4,5,6-pentahydro-(1*H*)-pentalene-5-one (**153a**) and 6-Trimethylsilyl-bis[2,2-methoxymethyl]-3,3a,4,5-tetrahydro-(1*H*)-pentalene-5-one (**153b**).



To a solution of enyne **152** (254 mg, 1.0 mmol) and Cp_2ZrCl_2 (321 mg, 1.1 mmol) in THF (8 mL) cooled to -78°C was added dropwise a solution of *n*-BuLi (0.84 mL, 2.5 M in heptane, 2.1 mmol). After stirring for 10 min at -78°C the solution was allowed to warm slowly to rt and stir for an additional 18 h. The flask was subsequently immersed in -5°C cold bath and the Ar atmosphere was exchanged for CO with the internal reaction temperature being maintained at 0°C . After stirring for 1 h at 0°C , the reaction mixture was allowed to warm to rt and was stirred for an additional 18 h. A degassed solution of aqueous 10% HCl was then added and after stirring for 10 min EtOAc (10 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 x 10 mL) and the combined organic layers were washed with saturated aqueous NaHCO_3 (10 mL),

brine (10 mL) dried (Na_2SO_4), filtered and concentrated *in vacuo*. The residual material was purified by chromatography on silica gel to afford 140 mg (66%) of desilylated pentenone **153a** and 30 mg (11%) of **153b**. **153a**: ^1H NMR (C_6D_6) δ 5.75 (s, 1H, $\text{C}=\text{CH}$), 3.11 (s, 3H, OCH_3), 3.08 (d, $J = 3.1$ Hz, 2H, OCH_2), 3.05 (s, 3H, OCH_3), 2.95 (app q, $J = 8.8$ Hz, 2H, OCH_2), 2.64-2.57 (m, 1H), 2.35 (dd, $J = 17.6, 6.6$ Hz, 1H), 2.23 (dd, $J = 25.5$ and 17.6 Hz, 1H), 1.85-1.77 (m, 2H), 0.76 (app t, $J = 12.2$ Hz, 1H); ^{13}C NMR (C_6D_6) δ 208.3, 186.7, 125.1, 125.0, 77.4, 77.0, 58.9, 58.8, 49.6, 44.2, 42.7, 37.3, 34.0; IR (thin film) 3171, 2740, 1705, 1634, 1456, 1107 cm^{-1} . **153b**: ^1H NMR (C_6D_6) δ 3.17-2.90 (m, 10H, CH_2OCH_3), 2.34 (dd, $J = 16.8, 7.1$ Hz, 1H), 2.01 (dd, $J = 8.3, 3.7$ Hz, 1H), 1.77 (dd, $J = 16.9, 4.6$ Hz, 1H), 1.68 (dd, $J = 12.2, 7.7$ Hz, 1H), 1.22 (dd, $J = 11.9, 10.0$ Hz, 1H), 0.90-0.81 (m, 2H), 0.38 (s, 9H, $\text{Si}(\text{CH}_3)_3$).

5.9 Photopromoted Pauson-Khand Reactions

Photopromoted Pauson-Khand Reactions should not be performed in standard round-bottomed flasks unless some precautions are taken to prevent the warm solvent vapors from contacting the rubber septum. The best solution to this problem was to utilize schlenk flasks equipped with a 15 cm air or water cooled condenser between the rubber septum and the top of the flask. The schlenk flasks also allow for efficient flushing of the reaction vessel with CO.

General procedures for the preparation of bicyclopentenones by the photopromoted Pauson-Khand Reaction:

Procedure A: A solution of enyne (0.5 mmol) and dicobalt octacarbonyl (8.5 mg, 0.025 mmol, 5 mol %) in degassed 1,2-DME (5 mL) was magnetically stirred at rt under an atmosphere of CO. After 30 min, the reaction was irradiated. During the course of the irradiation, the position of the lamp was adjusted such that the internal reaction temperature was maintained between 50-55 °C. After 12 h the irradiation was discontinued and the cooled reaction mixture was diluted with EtOAc (15 mL), washed with brine (2 × 2 mL), dried (Na₂SO₄), filtered and concentrated *in vacuo*. The residual material was purified by flash chromatography on silica gel (30% EtOAc/hexane to 50% EtOAc/hexane gradient for elution) to afford the enone.

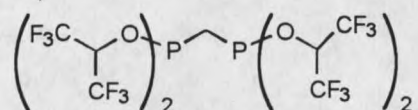
Procedure B: The experiment was performed as described for procedure A, except that after the irradiation the reaction solution was concentrated *in vacuo* and then purified by flash chromatography on silica gel (30% EtOAc/hexane to 50% EtOAc/hexane gradient for elution) to afford the enone without any additional work-up.

Procedure C: A solution of enyne (0.5 mmol) and dicobalt octacarbonyl (8.5 mg, 0.025 mmol, 5 mol %) in degassed 1,2-DME (1.7 mL) was magnetically stirred at rt under an atmosphere of CO for 30 minutes. The solution was then treated with TFE (3.3 mL), and after 5 min, the reaction was irradiated. During the course of the irradiation, the position of the lamp was adjusted such that the internal reaction temperature was maintained between 50-55 °C. After 12 h the irradiation was discontinued and the cooled reaction mixture reaction solution was concentrated *in vacuo* and then purified by flash chromatography on silica gel (30% EtOAc/hexane to 50% EtOAc/hexane gradient for elution) to afford the enone.

For preparative scale, longer irradiation times are required. Accordingly, a solution of enyne **170a** (4.76 g, 20.0 mmol) and dicobalt octacarbonyl (274 mg, 0.8 mmol, 4 mol %) in degassed 1,2-DME (200 mL) was magnetically stirred at rt under an atmosphere of CO for 30 min. The reaction was then irradiated for 16 h at 50-55 °C. The reaction mixture was concentrated *in vacuo* and the resulting oil was purified by flash chromatography on silica gel (10% EtOAc/hexane to 50%

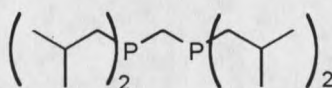
EtOAc/hexane gradient for elution) to afford 4.41 g (83%) of enone **170b** as a yellow oil.

Methane bis[bis(1,1,1,3,3,3-hexafluoroisopropyl)phosphite] (**168**).



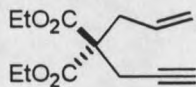
^1H NMR (CDCl_3) δ 4.62-4.50 (m, 4H, CH), 2.50 (t, $J = 7.1$ Hz, 2H, CH_2); ^{13}C NMR (CDCl_3) δ 120.5 (dt, $J = 21.3, 282.1$ Hz), 75.1 (m), 46.1 (t, $J = 34.7$ Hz).

Methane bis[bis((1-methyl)ethyl)phosphine] (**169**).



^1H NMR (C_6D_6) δ 1.70 (app p, $J = 7.1$ Hz, 4H, CH), 1.35 (br s, 2H, CH_2), 1.12-1.05 (m, 24H, CH_3); ^{13}C NMR (C_6D_6) δ 25.4 (t, $J = 5.1$ Hz, CH), 20.8 (t, $J = 8.7$ Hz, CH_3), 20.1 (t, $J = 6.8$, CH_3), 15.4 (t, $J = 60.4$ Hz, CH_2); IR (thin film) 2947, 2866, 1460, 1382, 1363, 880, 776.

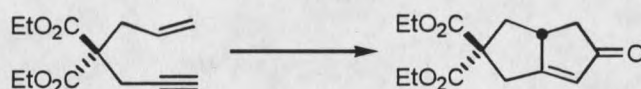
Diethyl 2-(2-propenyl)-2-(2-propynyl)propan-1,3-dioate (**170a**).



^1H NMR (CDCl_3) δ 5.67-5.52 (m, 1H, $\text{CH}=\text{CH}_2$), 5.18-5.08 (m, 2H, $\text{CH}=\text{CH}_2$), 4.17 (q, $J = 7.2$ Hz, 4H, 2 CH_2O), 2.78-2.75 (m, 4H, 2 CH_2), 1.87 (t, $J = 2.6$ Hz,

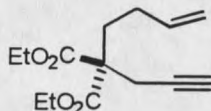
1H, C $\equiv$ CH), 1.21 (t, J = 7.2 Hz, 6H, 2 CH₃); ¹³C NMR (CDCl₃) δ 169.6 (C), 131.7 (C), 119.7 (CH₂), 78.9 (C), 71.3 (CH), 61.6 (CH₂), 56.6 (C), 36.3 (CH₂), 22.6 (CH₂), 14.0 (CH₃); IR (thin film) 3287, 3078, 2982, 2937, 2126, 1734, 1441, 1323, 1248, 1013, 653 cm⁻¹.

3,3a,4,5-Tetrahydro-5-oxo-2,2(1*H*)-pentalenedicarboxylic acid diethyl ester (**170b**).



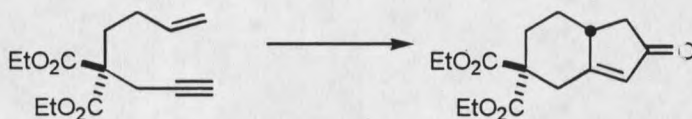
Enyne **170a** was cyclized according to general procedure A except that only 4 h of irradiation were required to give 127 mg (95%) of the title compound **170b** as a slightly yellow oil after chromatographic purification. ¹H NMR (CDCl₃) δ 5.89 (s, with fine structure, 1H, C=CH), 4.24-4.13 (m, 4H, 2 CH₂O), 3.35-3.18 (m, 2H), 3.14-3.00 (m, 1H), 2.76 (dd, J = 12.7, 7.6 Hz), 2.59 (dd, J = 17.9, 6.4 Hz, 1H), 2.09 (dd, J = 17.8, 3.2 Hz, 1H), 1.70 (app t, J = 12.7 Hz, 1H), 1.21 (app q, J = 7.3 Hz, 6H); ¹³C NMR (CDCl₃) δ 209.1 (C), 185.2 (C), 171.3 (C), 170.6 (C), 125.4 (CH), 61.9 (CH₂), 61.8 (CH₂), 60.8 (C), 44.9 (CH), 42.0 (CH₂), 38.8 (CH₂), 35.0 (CH₂), 13.8 (CH₃); IR (thin film) 3086, 2982, 2938, 1733, 1636, 1465, 1445, 1278, 1254, 1179, 1063, 900, 860 cm⁻¹.

Diethyl 2-(3-butenyl)-2-(2-propynyl)propane-1,3-dioate (**171a**).



The title compound was prepared by the alkylation of diethyl propargyl malonate according to the general procedure utilized for **66**. ^1H NMR (CDCl_3) δ 5.56-5.63 (m, 1H, $\text{CH}=\text{CH}_2$), 4.58-4.86 (m, 2H, $\text{CH}=\text{CH}_2$), 4.07 (q, $J = 7.1$ Hz, 4H, CH_2O), 2.22-2.19 (m, 2H, $\text{CH}_2\text{C}\equiv\text{C}$), 2.06-1.99 (m, 2H, CH_2), 1.93-1.82 (m, 3H, CH_2 and $\text{C}\equiv\text{CH}$), 1.13 (t, $J = 7.1$ Hz, 6H, 2 CH_3); ^{13}C NMR (CDCl_3) δ 169.7 (C), 137.1 (CH), 114.9 (CH_2), 78.6 (CH), 71.1 (C), 61.2 (CH_2), 56.3 (C), 30.9 (CH_2), 28.0 (CH_2), 22.6 (CH_2), 13.8 (CH_3); IR (thin film) 3286, 3079, 2981, 2939, 2123, 1734, 1642, 1448, 1367, 1271, 1240, 915, 859, 643 cm^{-1} ; high resolution (CI/ NH_3) mass spectrum calcd for $\text{C}_{14}\text{H}_{21}\text{O}_4$ ($\text{M}+\text{H}$) $^+$ 253.1440, found 253.1451.

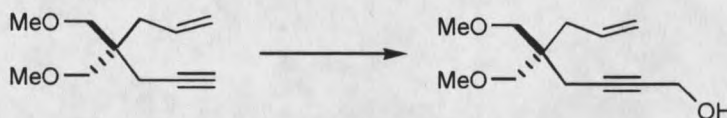
1,2,4,6,7,7a-hexahydro-2-oxo-5*H*-indene-5,5-dicarboxylic acid diethyl ester (**171b**).



Enyne **179a** was cyclized according to general procedure A to afford 126 mg (74%) of the title compound **179b** as a clear oil. ^1H NMR (CDCl_3) δ 5.87 (s, 1H, $\text{C}=\text{CH}$), 4.16-4.06 (m, 4H, CH_2O), 3.39 (dd, $J = 4.2, 0.6$ Hz), 2.65-2.39 (m, 4H), 2.12-2.04 (m, 1H), 1.96-1.80 (m, 2H), 1.28-1.23 (m, 1H), 1.16 (dt, $J = 1.9, 7.2$ Hz, 6H, CH_3);

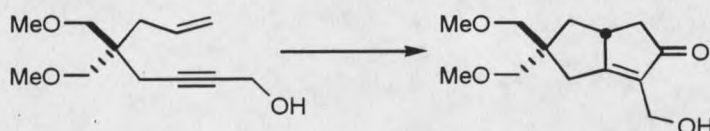
^{13}C NMR (CDCl_3) δ 207.8 (C), 178.7 (C), 170.7 (C), 169.3 (C), 129.4 (CH), 61.8 (CH₂), 61.4 (CH₂), 56.3 (C), 41.7 (CH₂), 40.5 (CH), 35.2 (CH₂), 30.49 (CH₂), 30.46 (CH₂), 13.8 (CH₃); IR (thin film) 3072, 2981, 2935, 2871, 1731, 1710, 1628, 1447, 1367, 1276, 1196, 1142, 1069, 1025, 860 cm^{-1} ; high resolution mass spectrum calcd for $\text{C}_{15}\text{H}_{20}\text{O}_5$ (M^+) 280.1311, found 280.1312.

Bis(5,5-methoxymethyl)oct-7-en-2-yn-1-ol (**173a**).



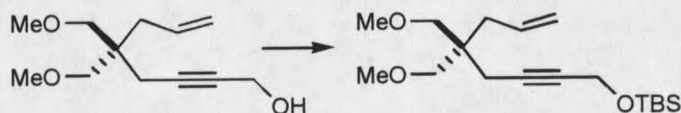
The title compound was prepared by the general hydroxymethylation protocol described for **181**. ^1H NMR (CDCl_3) δ 5.77-5.63 (m, 1H $\text{CH}=\text{CH}_2$), 5.04-4.97 (m, 2H, $\text{CH}=\text{CH}_2$), 4.16 (br s, 2H, $\text{C}\equiv\text{CCH}_2\text{OH}$), 3.24 (s, 6H, 2 CH_3), 3.19-3.12 (m, 4H, CH_2O), 2.76 (br s, 1H, OH), 2.14 (t, $J = 3.1$ Hz, 1H, $\text{C}\equiv\text{CH}$), 2.06 (d, $J = 7.5$ Hz, 2H, CH_2CH); ^{13}C NMR (CDCl_3) δ 133.7 (CH), 117.8 (CH₂), 82.5 (C), 80.4 (C), 74.3 (CH₂), 59.1 (CH₃), 50.9 (CH₂), 41.7 (C), 36.2 (CH₂), 22.3 (CH₂); IR (thin film) 3145, 3075, 2890, 2752, 2067, 1639, 1747, 1438, 1108, 1011, 918 cm^{-1} ; high resolution (CI/ NH_3) mass spectrum calcd for $\text{C}_{12}\text{H}_{21}\text{O}_3$ ($\text{M}+\text{H}$)⁺ 213.1491, found 213.1483.

6-[(hydroxy)methyl]-bis[2,2-(methoxymethyl)]-3,3a,4,5-tetrahydro-(1*H*)-pentalene-5-one (**173b**).



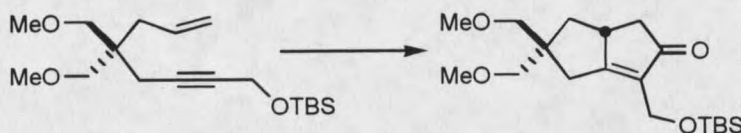
Enyne **185a** was cyclized according to general procedure B except that more polar solvents for flash chromatography on silica gel were utilized (50% EtOAc/hexane to EtOAc gradient for elution) to afford 96 mg (80%) of the title compound **185b** as a clear oil. ^1H NMR (CDCl_3) δ 4.24 (br s, 1H, $\text{C}=\text{CH}$), 3.32-3.28 (m, 5H, CH_3O and OCH_2), 3.25 (s, 3H, CH_3O), 3.17 (dd, $J = 16.8, 8.9$ Hz, 2H), 3.08-2.97 (m, 1H), 2.86 (br s, 1H, OH), 2.59-2.45 (m, 3H), 2.08-1.97 (m, 2H), 1.02 (app t, $J = 12.3$ Hz, 1H); ^{13}C NMR (CDCl_3) δ 210.3 (C), 184.1 (C), 134.4 (C), 77.4 (CH_2), 77.0 (CH_2), 59.2 (CH_3), 59.1 (CH_3), 56.1 (CH_2), 50.0 (C), 42.8 (CH_2), 42.1 (CH_2), 37.2 (CH_2), 32.8 (CH_2); IR (thin film) 3431, 2958, 2876, 2741, 1701, 1663, 1199, 1107, 989, 940, 874 cm^{-1} ; high resolution (CI/ NH_3) mass spectrum calcd for $\text{C}_{13}\text{H}_{21}\text{O}_4$ ($\text{M}+\text{H}$) $^+$ 241.1449, found 241.1440.

Bis(5,5-methoxymethyl)-1-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-7-octen-2-yne (**174a**).



The title compound was prepared by the general procedure utilized for **71**. ^1H NMR (CDCl_3) δ 5.83-5.69 (m, 1H, $\text{CH}=\text{CH}_2$), 5.08-5.02 (m, 2H), 4.29 (t, $J = 2.1$ Hz, 2H, $\text{CH}_2\text{C}\equiv\text{C}$), 3.29 (s, 6H, 2 CH_3O), 3.24-3.18 (m, 4H), 2.19 (t, $J = 2.1$ Hz, 1H, $\text{C}\equiv\text{CH}$), 2.12 (d, $J = 7.5$ Hz, 2H, CH_2CH), 0.88 (s, 9H, $\text{C}(\text{CH}_3)_3$), 0.10 (s, 6H, $\text{Si}(\text{CH}_3)_2$); ^{13}C NMR (CDCl_3) δ 134.0 (CH), 117.8 (CH_2), 81.9 (C), 80.7 (C), 74.5 (CH_2), 59.2 (CH_3), 52.0 (CH_2), 41.9 (C), 36.4 (CH_2), 25.8 (CH_3), 22.4 (CH_2), 18.3 (C), -5.1 (CH_2); IR (thin film) 3079, 2953, 2810, 1639, 1473, 1370, 1255, 1199, 1109, 1079, 1000, 917, 808, 777, 667 cm^{-1} .

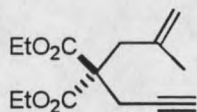
6-[[1,1-dimethylethyl[(dimethylsilyl)oxy]]methyl]-bis[2,2-(methoxymethyl)]-3,3a,4,5-tetrahydro-(1*H*)-pentalene-5-one (**174b**).



Enyne **173b** was cyclized according to the general procedure in 32% G.C. yield. Alternatively, this compound was prepared by silylation of penenone **173b** by the general procedure utilized for **71**. ^1H NMR (CDCl_3) δ 4.42-4.32 (m, 2H), 3.35-3.34 (m, 5H, CH_3O and CH_2O), 3.27 (s, 3H), 3.18 (dd, $J = 17.5, 8.8$ Hz, 2H), 3.05-2.93 (m, 1H), 2.76 (d, $J = 18.3$ Hz, 1H), 2.55 (dd, $J = 18.0, 6.4$ Hz, 1H), 2.43 (d, $J = 18.4$ Hz, 1H), 2.10-1.94 (m, 2H), 0.99 (app dd, $J = 12.3, 12.3$ Hz, 1H), 0.87 (s, 9H, $\text{C}(\text{CH}_3)_3$), 0.04 (s, 3H, $\text{Si}(\text{CH}_3)_3$), 0.03 (s, 3H, $\text{Si}(\text{CH}_3)_3$); ^{13}C NMR (CDCl_3) δ

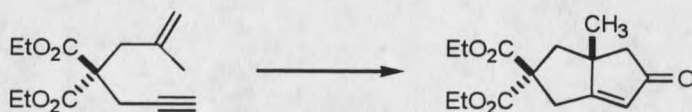
208.7 (C), 183.9 (C), 135.0 (C), 77.5 (CH₂), 77.0 (CH₂), 59.3 (CH₃), 59.1 (CH₃), 57.3 (CH₂), 50.0 (C), 42.9 (CH), 42.2 (CH₂), 37.4 (CH₂), 33.5 (CH₂), 25.9 (CH₃), 18.3 (C), -5.5 (CH₃); IR (thin film) 2955, 2928, 2826, 1706, 1671, 1472, 1461, 1256, 1190, 1109, 837, 778, 668 cm⁻¹; high resolution mass spectrum calcd for C₁₉H₃₄O₄Si (M⁺) 354.2226, found 354.2219.

Diethyl 2-(2-methyl-2-propenyl)-2-(2-propynyl)propan-1,3-dioate (**176a**).



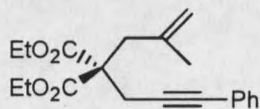
The title compound was prepared by the alkylation of diethyl methallyl malonate according to the general procedure utilized for **66**. ¹H NMR (CDCl₃) δ 4.83 (t, *J* = 1.5 Hz, 1H, C=CHH), 4.79 (s, 1H, C=CHH), 4.23-4.07 (m, 4H, OCH₂), 2.77-2.74 (m, 4H, CH₂), 1.96 (t, 1H, C≡CH), 1.60 (s, 3H, CH₃), 1.19 (app t, *J* = 7.1 Hz, 6H); ¹³C NMR (CDCl₃) δ 169.9 (C), 139.9 (C), 115.0 (CH₂), 79.2 (C), 71.4 (CH), 61.5 (CH₂), 56.3 (C), 39.3 (CH₂), 23.1 (CH₃), 22.6 (CH₂), 13.8 (CH₃); IR (thin film) 3286, 3079, 2983, 2939, 2123, 1734, 1645, 1446, 1206, 1076, 1020, 903 cm⁻¹.

3,3a,4,5-Tetrahydro-3a-methyl-5-oxo-2,2(1*H*)-pentalenedicarboxylic acid diethyl ester (**176b**).



Enyne **180a** was cyclized according to general procedure A to afford 127 mg (91%) of the title compound **180b** as a yellow oil. ^1H NMR (CDCl_3) δ 5.75 (d, $J = 1.6$ Hz, 1H, $\text{C}=\text{CH}$), 4.19 (q, $J = 7.2$, 2H, OCH_2), 4.11 (dq, $J = 1.1$, 7.0 Hz, OCH_2), 3.44 (dd, $J = 17.7$, 2.2 Hz, 1H), 3.12 (d, $J = 17.7$ Hz, 1H), 2.51 (d, $J = 13.7$ Hz, 1H), 2.31 (s, 2H), 2.17 (d, $J = 13.7$ Hz), 1.23-1.14 (m, 6H, CH_2CH_3), 1.09 (s, 3H, CH_3); ^{13}C NMR (CDCl_3) δ 208.8 (C), 188.2 (C), 171.4 (C), 171.1 (C), 124.2 (CH), 124.1 (CH), 62.0 (CH_2 , two peaks), 60.0 (C), 51.7 (CH_2), 49.7 (C), 44.4 (CH_2), 34.2 (CH_2), 26.5 (CH_3), 13.9 (CH_3), 13.8 (CH_3); IR (thin film) 3076, 2981, 2874, 1734, 1715, 1637, 1232, 1179, 1061, 859 cm^{-1} .

Diethyl 2-(2-methyl-2-propenyl)-2-(3-phenyl-2-propynyl)propan-1,3-dioate (**179a**).



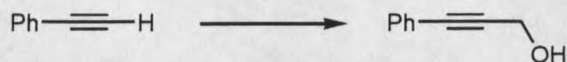
The title compound was prepared by the alkylation of diethyl methallyl malonate according to the general procedure utilized for **66**. ^1H NMR (CDCl_3) δ 7.35-7.23 (m, 5H), 4.91 (t, $J = 1.5$ Hz, 1H), 4.88 (t, $J = 0.6$ Hz, 1H), 4.25-4.05 (m, 4H), 3.03

(s, 2H), 2.80 (s, 2H), 1.68 (s, 3H), 1.24 (t, $J = 14.4$ Hz, 3H); ^{13}C NMR (CDCl_3) δ 170.1 (C), 140.0 (C), 131.5 (CH), 128.1 (CH), 127.8 (CH), 123.2 (C), 116.1 (CH₂), 84.7 (C), 83.6 (C), 61.5 (CH₂), 56.6 (C), 39.5 (CH₂), 23.4 (CH₂), 23.2 (CH₃), 13.9 (CH₃); IR (thin film) cm^{-1} .

3,3a,4,5-Tetrahydro-3a-methyl-5-oxo-1-phenyl-2,2(1*H*)-pentalenedicarboxylic acid diethyl ester (**179b**).



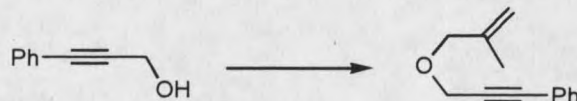
Enyne **179a** (79 mg, 0.25 mmol) was cyclized according to general procedure B to afford 78 mg (91%) of the title compound **179b** as a clear oil. ^1H NMR (CDCl_3) δ 7.51-7.30 (m, 5H), 4.26 (q, $J = 7.1$ Hz, 3H), 4.07-4.02 (m, 3H), 3.77 (d, $J = 18.3$ Hz, 1H), 3.24 (d, $J = 18.3$ Hz, 1H), 2.60 (d, $J = 13.6$ Hz, 1H), 2.55 (s, 2H), 2.55 (d, 13.6 Hz, 2H), 2.26 (d, $J = 13.6$ Hz, 1H) 1.28 (t, $J = 7.1$ Hz, 3H), 1.20 (s, 3H), 1.14 (t, $J = 7.1$ Hz, 3H); ^{13}C NMR (CDCl_3) δ 206.9 (C), 182.0 (C), 171.8 (C), 171.2 (C), 134.1 (C), 130.8 (C), 128.7 (CH), 128.4 (CH), 128.2 (CH), 62.2 (CH₂), 62.1 (CH₂), 60.7 (C), 52.4 (CH₂), 47.8 (C), 44.2 (CH₂), 34.6 (CH₂), 26.9 (CH₃), 14.0 (CH₃), 13.8 (CH₃); IR (thin film) cm^{-1} ; high resolution mass spectrum calcd for $\text{C}_{21}\text{H}_{24}\text{O}_5$ (M^+) 356.1624, found 356.1629.

3-Phenyl-2-butyne-1-ol (**181**).

To a solution of phenylacetylene (11.0 mL, 100 mmol) in Et₂O (100 mL) cooled to ca. -78 °C was added a solution of *n*-BuLi (46 mL, 2.5 M in heptane, 115 mmol) in one portion. After 5 min the dry ice-acetone bath was removed and the reaction was allowed to warm to 0 °C and was maintained at this temperature for 15 min.

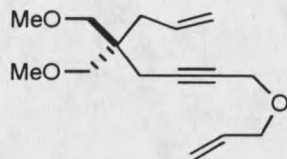
Paraformaldehyde (2.16 g, 120 mmol) was subsequently added portion-wise over 15 min by temporary removal of the reaction flask's septum. Thereafter, the ice bath was removed and the resultant mixture was allowed to warm to rt and was diluted with THF (30 mL) to facilitate stirring. After 3 h the reaction was poured into a separatory funnel containing saturated aqueous NH₄Cl (150 mL) and the organic layer was separated. The aqueous layer was extracted with a 50-mL portion of ether the combined organic layers were washed with brine, dried (Na₂SO₄), filtered and concentrated *in vacuo*. The resulting material was purified by bulb-to-bulb distillation (0.2 mm Hg, 0 °C trap) to afford 12.6 g (95%) of the title compound as a clear oil. ¹H NMR (CDCl₃) δ 7.46-7.16 (m, 5H, Aromatic *H*), 4.47 (s, 2H), 2.7 (br s, 1H, OH); ¹³C NMR (CDCl₃) δ 131.6, 128.3, 128.2, 122.6, 87.3, 85.4, 51.3; IR (thin film) 3327, 3081, 3060, 2922, 2864, 2235, 1598, 1489, 1442, 1258, 1032, 953, 756, 691 cm⁻¹.

1-(2-methyl-2-propenyloxy)-3-phenyl-2-propyne (**182**).



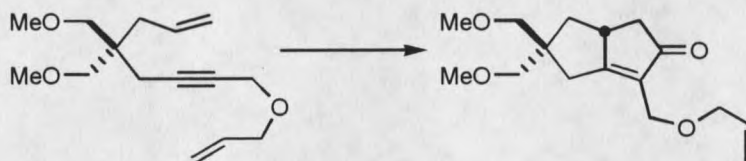
A solution of 3-phenyl-2-butyn-1-ol (2.64 g, 20.0 mmol, **181**) in THF (2.5 mL) was added portion-wise over 10 min to a suspension of NaH (0.576 g, 24.0 mmol) cooled in an ice bath. The reaction mixture was subsequently allowed to warm to rt, and a solution of methallyl chloride (3 mL, ca. 30 mmol) and cat. NaI (10 mol %, 0.26 g) in THF (10 mL) was added via cannula. The ice bath was removed after 15 min and the reaction was allowed to warm to rt. The resulting solution was diluted with water (400 mL) and hexane (50 mL). The organic layer was removed and the aqueous layer was extracted with hexane (3 x 50 mL) and the combined organic layers were washed with water (25 mL), brine (25 mL), dried (MgSO₄), filtered and concentrated *in vacuo*. The resulting material was purified by bulb-to-bulb distillation (0.25 mm Hg, 0 °C trap, 100 °C tank) to afford 3.43 g (92%) of the title compound as a clear oil in excellent yield. ¹H NMR (CDCl₃) δ 7.46-7.43 (m, 2H, Aromatic *H*), 7.30-7.28 (m, 3H, Aromatic *H*), 5.03 (s, with fine structure, 1H, C=CHH), 4.94 (s, with fine structure, 1H, C=CHH), 4.34 (s, 2H), 4.03 (s, 2H), 1.77 (s, 3H); ¹³C NMR (CDCl₃) δ 141.6 (C), 131.7 (CH), 128.3 (CH), 128.2 (CH), 123.8 (C), 112.9 (CH₂), 86.1 (C), 85.2 (C), 73.7 (CH₂), 57.7 (CH₂), 19.5 (CH₃); IR (thin film) 3079, 2849, 2283, 1490, 1442, 1085, 901, 757, 691 cm⁻¹.

Bis(5,5-methoxymethyl)-1-(2-propenoxy)-oct-7-en-2-yne (**185a**).



^1H NMR (CDCl_3) δ 5.95-5.68 (m, 2H, $\text{CH}=\text{CH}_2$), 5.23-5.01 (m, 4H, $\text{CH}=\text{CH}_2$), 4.11 (t, $J = 1.9$ Hz, 2H, $\text{C}\equiv\text{CCH}_2\text{O}$), 4.01 (d, $J = 5.7$ Hz, 2H, OCH_2CH), 3.27 (s, with fine structure, 6H), 3.22-3.16 (m, 4H), 2.19 (t, $J = 1.8$ Hz, 2H, $\text{CH}_2\text{C}\equiv\text{C}$), 2.11 (d, $J = 7.6$ Hz, 2H); ^{13}C NMR (CDCl_3) δ 134.2 (CH), 133.8 (CH), 117.8 (CH_2), 117.4 (CH_2), 83.6 (C), 77.8 (C), 74.4 (CH_2), 70.1 (CH_2), 59.1 (CH_3), 57.6 (CH_2), 41.8 (C), 36.3 (CH_2), 22.3 (CH_2); IR (thin film) 3076, 2979, 2923, 2810, 2753, 1635, 1448, 1108, 919 cm^{-1} ; high resolution mass spectrum calcd for $\text{C}_{15}\text{H}_{24}\text{O}_3$ (M^+) 252.1725, found 252.1719.

6-[(2-propenoxy)methyl]-bis[2,2-(methoxymethyl)]-3,3a,4,5-tetrahydro-(1*H*)-pentalene-5-one (**185b**).



Enyne **186a** was cyclized according to general procedure A, except that 12.5 mol % dicobalt octacarbonyl was used, to give 113 mg (67%) of the title compound **186b** as a clear oil. ^1H NMR (CDCl_3) δ 5.93-5.80 (m, 1H, $\text{CH}=\text{CH}_2$), 5.28-5.11 (m, 2H,

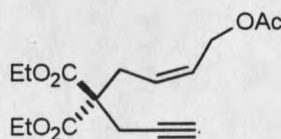
CH=CH₂), 4.16-4.04 (m, 2H), 3.94 (dt, $J = 5.6, 1.1$ Hz, CH₂), 3.34 (d, $J = 1.4$ Hz, 2H), 3.33 (s, 3H, CH₃O), 3.27 (s, 3H, CH₃O), 3.19 (app dd, $J = 13.8, 8.9$ Hz, 2H), 3.06-3.00 (m, 1H), 2.59-2.45 (m, 3H), 2.10-1.97 (m, 2H), 1.16 (app t, $J = 12.2$ Hz, 1H); ¹³C NMR (CDCl₃) δ 208.7 (C), 185.8 (C), 134.7 (CH), 132.8 (C), 116.9 (CH₂), 77.4 (CH₂), 77.0 (CH₂), 71.7 (CH₂), 62.6 (CH₂), 59.2 (CH₃), 59.1 (CH₃), 49.9 (C), 42.8 (CH), 42.1 (CH₂), 37.3 (CH₂), 33.3 (CH₂); IR (thin film) 3085, 2923, 2824, 2737, 1705, 1668, 1450, 1199, 1106 cm⁻¹; high resolution mass spectrum calcd for C₁₆H₂₄O₄ (M⁺) 280.1675, found 280.1673.

4-Acetoxy-2-buten-1-ol (**188**).



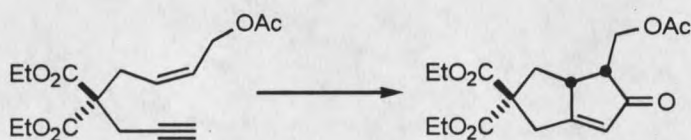
¹H NMR (CDCl₃) δ 5.81-5.73 (m, 1H), 5.59-5.51 (m, 1H), 4.59 (d, $J = 6.9$ Hz, 2H), 4.17 (d, $J = 6.4$ Hz), 2.68 (br s, 1H, OH), 1.99 (s, 3H, CH₃); ¹³C NMR (CDCl₃) δ 133.3, 125.2, 60.0, 58.1, 20.8; IR (thin film) 3419, 3030, 2939, 1738, 1374, 1237, 1030, 842 cm⁻¹.

cis-Diethyl 2-(4-acetoxy-2-butenyl)-2-(2-propynyl)propan-1,3-dioate (**189a**).

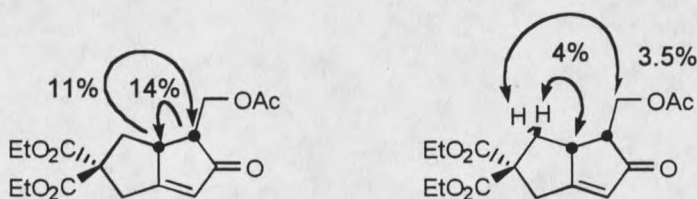


To solution of 4-acetoxy-2-buten-1-ol (1.12 g, 8.68 mmol) in ether (25 mL) cooled to 0 °C was added methanesulfonyl chloride (1.04 g, 9.12 mmol) followed by the careful dropwise addition of triethylamine (1.02 g, 9.98 mmol) over 3 min. The resulting solution was allowed to warm to rt and was stirred for 1 h and then filtered. The clear solution was added to the anion of diethyl allyl malonate and processed as previously described for **66** to afford the title compound in excellent yield. ^1H NMR (CDCl_3) δ 5.73-5.63 (m, 1H $\text{CH}=\text{CH}$), 5.47-5.37 (m, 1H, $\text{CH}=\text{CH}$), 4.62 (dd, $J = 6.9, 1.6$ Hz, 2H), 4.16 (app dq, $J = 2.5, 7.1$ Hz, 4H, CH_2O), 2.84 (d, with fine structure, $J = 8.1$ Hz, CH_2CH), 2.74 (d, $J = 2.8$ Hz, 2H, $\text{CH}_2\text{C}\equiv\text{C}$), 2.01 (s, 3H, COCH_3), 1.99 (t, $J = 2.5$ Hz, 1H $\text{C}\equiv\text{CH}$), 1.21 (t, $J = 7.1$ Hz, 6H, 2 CH_3); ^{13}C NMR (CDCl_3) δ 170.7 (C), 169.5 (C), 128.3 (CH), 127.4 (CH), 78.7 (CH), 71.6 (C), 61.7 (CH_2), 60.2 (CH_2), 56.5 (C), 30.1 (CH_2), 22.7 (CH_2), 20.8 (CH_3), 14.0 (CH_3); IR (thin film) 3282, 2983, 2993, 1732, 1446, 1372, 1289, 1209, 1096, 1027, 956, 857 cm^{-1} .

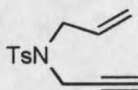
trans-4-[(acetoxy)methyl]-3,3a,4,5-tetrahydro-5-oxo-2,2(1H)-pentalenedicarboxylic acid diethyl ester (**189b**).



Enyne **189a** was cyclized according to general procedure A, except that 10 mol % of dicobalt octacarbonyl was used, to furnish 113 mg (67%) of the title compound **189b** as a clear oil. ^1H NMR (CDCl_3) δ 5.90 (s, with fine structure, 1H, $\text{C}=\text{CH}$), 4.24-4.13 (m, 5H, CH_2O), 4.02 (app dd, $J = 11.3, 8.9$ Hz, 1H CHHO), 3.38-3.18 (m, 3H), 2.87 (app ddd, $J = 8.7, 6.9, 4.6$ Hz, 1H, CHCH_2O), 2.58 (dd, $J = 12.7, 7.6$ Hz, 1H), 1.98 (s, 3H, COCH_3), 1.88 (app t, $J = 12.9$ Hz, 1H), 1.23 (app q, $J = 7.4$ Hz, 6H); ^{13}C NMR (CDCl_3) δ 207.4 (C), 185.2 (C), 171.3 (C), 170.6 (C), 170.4 (C), 124.5 (CH, two peaks), 62.3 (CH_2), 62.2 (CH_2), 62.0 (CH_2), 61.4 (CH_2), 60.5 (C), 48.4 (CH), 47.7 (CH), 35.2 (CH_2), 34.0 (CH_2), 20.7 (CH_3), 13.9 (CH_3); IR (thin film) 2982, 1733, 1638, 1446, 1326, 1252, 1186, 860 cm^{-1} . The indicated stereochemistry is consistent with the following observed NOE's:



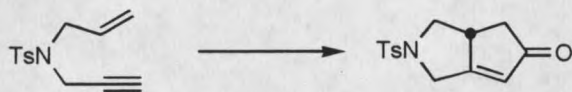
N-(2-propenyl)-*N*-(2-propynyl)-4-methylphenylsulfonamide (**192a**).



mp 60.8-61.5 $^{\circ}\text{C}$ (EtOAc /hexane); ^1H NMR (CDCl_3) δ 7.62 (d, $J = 8.3$ Hz, 2H, Aromatic H), 7.17 (d, $J = 8.1$ Hz, 2H, Aromatic H), 5.60-5.53 (m, 1H $\text{CH}=\text{CH}_2$), 5.20-5.10 (m, 2H, $\text{CH}=\text{CH}_2$), 3.97 (d, $J = 2.4$ Hz, 2H, $\text{CH}_2\text{C}\equiv\text{C}$), 3.70 (d, $J = 6.5$

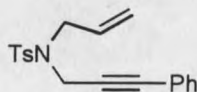
Hz, 2H, $\text{CH}_2\text{CH}=\text{CH}_2$), 2.30 (s, 3H, CH_3), 1.89 (t, $J = 2.4$ Hz, 1H, $\text{C}\equiv\text{CH}$); ^{13}C NMR (CDCl_3) δ 143.5 (C), 136.3 (C), 132.0 (CH), 129.5 (CH), 127.7 (CH), 119.8 (CH₂), 73.6 (CH₂), 49.0 (CH₂), 35.8 (CH₂), 21.5 (CH₃); IR (thin film) 3257, 3049, 2987, 2885, 2117, 1646, 1601, 1425, 1330, 1165, 989, 809 cm^{-1} .

2,3,3a,4-tetrahydro-2-[(4-methylphenyl)sulfonyl]-cyclopenta[*c*]pyrrol-5(1*H*)-one (**192b**).



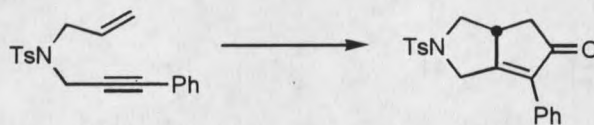
Enyne **192a** was cyclized according to general procedure A to afford 112 mg (81%) of the title compound **192b** as a yellow solid, which was recrystallized to a slightly tan solid. mp 145.2-148.0 °C (EtOAc/hexane); ^1H NMR (CDCl_3) δ 7.60 (d, $J = 8.3$ Hz, 2H, Aromatic *H*), 7.23 (d, $J = 8.2$ Hz, 2H, Aromatic *H*), 5.87 (s, 1H $\text{C}=\text{CH}$), 4.21 (d, $J = 16.5$ Hz, 1H), 3.94-3.88 (m, 2H), 3.10-2.96 (m, 1H), 2.53-2.43 (m, 2H), 2.32 (s, 3H, CH_3), 1.98-1.90 (m, 1H); ^{13}C NMR (CDCl_3) δ 207.2 (C), 178.6 (C), 144.0 (C), 133.7 (C), 129.9 (CH), 127.4 (CH), 126.1 (CH), 52.4 (CH₂), 47.5 (CH₂), 43.9 (CH), 39.7 (CH₂), 21.4 (CH₃); IR (KBr) 3067, 1711, 1648, 1343, 1162, 1090, 827, 673 cm^{-1} .

N-(1-Methyl-2-propenyl)-*N*-(3-phenyl-2-propynyl)-4-methylphenylsulfonamide
(**193a**).



mp 73.5-75.2 °C (EtOAc/hexane); ^1H NMR (CDCl_3) δ 7.67 (d, J = 8.3 Hz, 2H, Aromatic H), 7.17-7.09 (m, 5H, Aromatic H), 6.95 (dd, J = 7.7, 1.4 Hz, 2H, Aromatic H), 5.76-5.63 (m, 1H, $\text{CH}=\text{CH}_2$), 5.25-5.14 (m, 2H, $\text{CH}=\text{CH}_2$), 4.20 (s, 2H, $\text{CH}_2\text{C}\equiv\text{C}$), 3.78 (d, J = 6.5 Hz, 2H, $\text{CH}_2\text{CH}=\text{CH}_2$), 2.22 (s, 3H, CH_3); ^{13}C NMR (CDCl_3) δ 143.4 (C), 136.2 (C), 132.1 (CH), 131.5 (CH), 129.5 (CH), 128.4 (CH), 128.1 (CH), 127.8 (CH), 122.3 (C), 119.7 (CH_2), 85.7 (C), 81.8 (C), 49.3 (CH_2), 36.8 (CH_2), 21.4 (CH_3); IR (KBr) 3086, 3056, 3015, 2963, 2908, 2855, 1696, 1596, 1441, 1350, 1162, 1119, 943, 901, 816 cm^{-1} ; high resolution mass spectrum calcd for $\text{C}_{19}\text{H}_{19}\text{NO}_2\text{S}$ (M^+) 325.1136, found 325.1129.

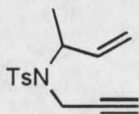
2,3,3a,4-tetrahydro-2-[(4-methylphenyl)sulfonyl]-6-phenyl-cyclopenta[*c*]pyrrol-5(1*H*)-one (**193b**).



Enyne **193a** was cyclized according to general procedure A to afford 149 mg (75%) of the title compound **193b** as a yellow solid, which was recrystallized to a white

solid. mp 165.2-166.5 °C (EtOAc/hexane); ^1H NMR (CDCl_3) δ 7.67 (d, $J = 8.1$ Hz, 2H, Aromatic H), 7.40-7.24 (m, 7H, Aromatic H), 4.58 (d, $J = 16.8$ Hz, 1H), 4.06-3.98 (m, 2H), 3.20-3.07 (m, 1H), 2.72 (dd, $J = 17.8, 6.4$ Hz), 2.57 (dd, $J = 10.6, 9.8$ Hz), 2.34 (s, 3H, CH_3), 2.19 (dd, $J = 17.9, 3.7$ Hz, 1H); ^{13}C NMR (CDCl_3) δ 205.2 (C), 171.7 (C), 143.8 (C), 135.9 (C), 133.9 (C), 129.8 (CH), 128.8 (CH), 128.5 (CH), 128.1 (CH), 127.2 (CH), 51.9 (CH_2), 48.2 (CH_2), 41.7 (CH), 40.6 (CH_2), 21.3 (CH_3); IR (KBr) 3056, 2923, 1709, 1661, 1245, 1158, 1093, 904, 816 cm^{-1} ; high resolution mass spectrum calcd for $\text{C}_{20}\text{H}_{19}\text{NO}_3\text{S}$ (M^+) 353.1086, found 353.1088.

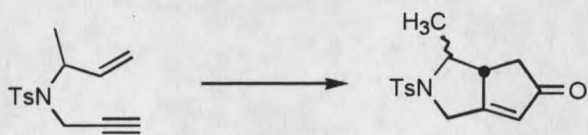
N-(1-Methyl-2-propenyl)-*N*-(2-propynyl)-4-methylphenylsulfonamide (**195a**).



A suspension of methallyl tosamide (4.63 g, 20.5 mmol), K_2CO_3 (3.69 g, 1.3 eq, 26.7 mmol) and propargyl bromide (3.18 g, 1.3 eq, 26.7 mmol) in acetone (42 mL) was heated at reflux. After 24 h the reaction was determined to be complete by TLC and was subsequently concentrated *in vacuo*. The residue was dissolved in H_2O (25 mL) and EtOAc (40 mL) and the organic layer was separated. The aqueous layer was further extracted with another 40-mL portion of EtOAc and the combined organic phases were washed with brine (12 mL), dried (MgSO_4), filtered

and concentrated *in vacuo*. The residue was recrystallized from 0.5 mL of ether and 25 mL of 20% EtOAc/Hex to afford 3.75 g (69%) of the title material as nearly white crystals from the first recrystallization: mp 64.2-65.3 °C (EtOAc/hexane); ^1H NMR (CDCl_3) δ 7.78 (d, $J = 7.9$ Hz, 2H, Aromatic H), 7.26 (d, $J = 8.0$ Hz, 2H, Aromatic H), 5.80-5.68 (m, 1H, $\text{CH}=\text{CH}_2$), 5.16-5.10 (m, 2H, $\text{CH}=\text{CH}_2$), 4.56-4.48 (m, 1H, CH), 4.13 (dd, $J = 18.8$ and 2.4 Hz, 1H, $\text{CHHC}\equiv\text{C}$), 3.85 (dd, $J = 18.8$, 2.4 Hz, 1H, $\text{CHHC}\equiv\text{C}$), 2.40 (s, 3H, CH_3), 2.13 (t, $J = 2.4$ Hz, 1H, $\text{C}\equiv\text{CH}$), 1.25 (d, $J = 6.8$ Hz, 3H, CHCH_3); ^{13}C NMR (CDCl_3) δ 143.2 (C), 137.9 (C), 137.4 (CH), 129.4 (CH), 127.5 (CH), 117.0 (CH_2), 80.2 (CH), 72.2 (C), 54.8 (CH), 32.3 (CH_2), 21.4 (CH_3), 17.1 (CH_3); IR (KBr) 3254, 2989, 2113, 1597, 1334, 1149, 1094, 1014, 893 cm^{-1} ; high resolution mass spectrum calcd for $\text{C}_{14}\text{H}_{17}\text{NO}_2\text{S}$ (M^+) 263.0980, found 263.0987.

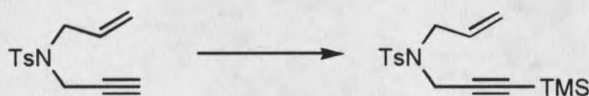
2,3,3a,4-tetrahydro-2-[(4-methylphenyl)sulfonyl]-3-methyl-cyclopenta[*c*]pyrrol-5(1*H*)-ones (**195b,c**).



Enyne **195a** was cyclized according to general procedure A to afford 130 mg (90%) of the title compound **195b** as an oily paste, which was found to be a 1.1 to 1 diastereomeric mixture. ^1H NMR (CDCl_3) δ 7.71 (d, $J = 8.2$ Hz, 2H, Aromatic H),

7.62 (d, $J = 8.2$ Hz, 2H, Aromatic H), 7.30-7.27 (m, 4H, Aromatic H), 6.02 (s, 1H, $C=CH$), 5.79 (s, 1H, $C=CH$), 4.36 (d, $J = 16.7$ Hz, 1H), 4.23-4.09 (m, 4H), 2.97-2.27 (m, 3H), 2.50 (dd, $J = 17.8, 6.3$ Hz, 1H), 2.37 (s with shoulder, 6.5 H), 2.30 (d, $J = 6.6$ Hz, 0.5H), 2.05 (dd, $J = 14.8, 3.5$ Hz, 1H), 1.93 (dd, $J = 17.9, 3.2$ Hz, 1H), 1.55 (d, $J = 5.9$ Hz, 3H), 0.98 (d, $J = 6.7$ Hz, 3H); ^{13}C NMR (CDCl_3) δ 208.0 (C), 206.8 (C), 178.6 (C), 176.2 (C), 144.0 (C), 143.8 (C), 135.8 (C), 133.6 (C), 129.9 (CH), 129.8 (CH), 127.4 (CH), 127.0 (CH), 126.2 (CH, two peaks), 125.2 (CH, two peaks), 61.9 (CH), 56.3 (CH), 52.0 (CH), 49.8 (CH_2 , two peaks), 47.3 (CH), 46.3 (CH_2), 39.3 (CH_2), 37.2 (CH_2), 21.4 (CH_3), 20.5 (CH_3), 15.9 (CH_3); IR (KBr) 2971, 2928, 2973, 1715, 1652, 1598, 1448, 1344, 1164, 1092, 818, 700 cm^{-1} ; high resolution mass spectrum calcd for $\text{C}_{15}\text{H}_{17}\text{NO}_3\text{S}$ (M^+) 291.0921, found 291.0929 and 291.0926.

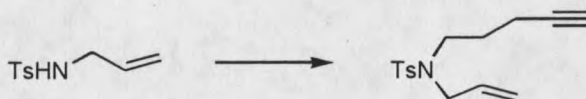
N-(2-propenyl)-*N*-(3-trimethylsilyl-2-propynyl)-4-methylphenylsulfonamide (**196a**).



The title compound was prepared by the general method utilized for **51**. mp 60.0-61.1 $^{\circ}\text{C}$ (EtOAc/hexane); ^1H NMR (CDCl_3) δ 7.69 (d, $J = 8.4$ Hz, 2H, Aromatic H), 7.26 (d, $J = 8.4$ Hz, 2H, Aromatic H), 5.77-5.65 (m, 1H, $\text{CH}=\text{CH}_2$), 5.28-5.19 (m, 2H, $\text{CH}=\text{CH}_2$), 4.07 (s, 2H, $\text{CH}_2\text{C}\equiv\text{C}$), 3.78 (d, $J = 6.5$ Hz, 2H, CH_2CH), 2.39

(s, 3H, CH₃), 0.04 (s, 9H, Si(CH₃)₃); ¹³C NMR (CDCl₃) δ 143.3 (C), 136.3 (C), 132.0 (CH), 129.5 (CH), 127.8 (CH), 119.7 (CH₂), 98.0 (C), 91.0 (C), 48.9 (CH₂), 36.8 (CH₂), 21.5 (CH₃), -0.4 (CH₃); IR (KBr) 3083, 3042, 2966, 2175, 1445, 1442, 1347, 1323, 1254, 1162, 843, 812 cm⁻¹.

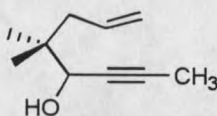
N-(4-pentenyl)-*N*-(2-propenyl)-4-methylphenylsulfonamide (**197a**).



¹H NMR (CDCl₃) δ 7.66 (dt, *J* = 8.2, 1.9 Hz, 2H), 7.27 (d, *J* = 8.2 Hz, 2H), 5.67-5.54 (m, 1H), 5.19-5.09 (m, 2H), 3.76 (d, *J* = 6.4 Hz, 2H), 3.17 (d, *J* = 7.3 Hz, 2H), 2.39 (s, 3H), 2.17 (dt, *J* = 2.6, 7.1 Hz, 2H), 1.92 (t, *J* = 2.6, 1H), 1.74 (app p, *J* = 7.3 Hz, 2H); ¹³C NMR (CDCl₃) δ 143.7 (C), 137.2 (C), 133.5 (CH), 130.1 (CH), 127.6 (CH), 119.4 (CH₂), 83.6 (C), 69.4 (CH), 51.5 (CH₂), 46.8 (CH₂), 27.7 (CH₂), 21.9 (CH₃), 16.2 (CH₂); IR (thin film) 3288, 3084, 3070, 2118, 1643, 1340, 1160, 1092 cm⁻¹; high resolution mass spectrum calcd for C₁₅H₁₉NO₂S (M⁺) 277.1136, found 277.1142.

5.10 Diastereoselective Photopromoted-PKR Cyclizations

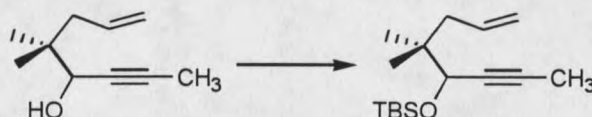
5,5-Dimethyl-1-octen-6-yne-4-ol (**214**).



To a solution of propyne (3.12 g, 77.9 mmol) in THF (75 mL) cooled to -78°C was added a solution of *n*-BuLi (30.5 mL, 2.30 M in heptane, 70.0 mmol, 0.9 eq) over 10 min. The resulting reaction mixture was stirred for an additional 1 h, and was then treated with a solution of 2,2-dimethyl-4-penten-1-al (7.00 g, 62.3 mmol, 0.8 eq) in THF (15 mL) in one portion. The dry-ice acetone bath was removed and the exothermic reaction was allowed to warm to rt. After being stirred for an additional 1 h, the reaction mixture was treated with saturated aqueous NH_4Cl (25 mL). The organic phase was separated and the aqueous phase was extracted with Et_2O (3 x 25 mL) and the combined organic fractions were washed with brine (25 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo*. The residue was subjected to gradient flash chromatography on silica gel (hexane to 5% EtOAc/hexane for elution) to afford 7.96 g (84%) of the title compound as a colorless oil: ^1H NMR (CDCl_3) δ 5.86-5.73 (m, 1H), 5.05-4.99 (m, 2H), 3.99-3.98 (m, 1H), 2.13-2.01 (m, 2H), 1.95 (br s, 1H), 1.80 (d, $J = 2.3$ Hz, 3H), 0.90 (d, $J = 3.4$ Hz, 6H); ^{13}C NMR (CDCl_3) δ 135.1 (CH), 117.3 (CH_2), 81.9 (C), 78.7 (C), 70.4 (CH), 42.7 (CH_2),

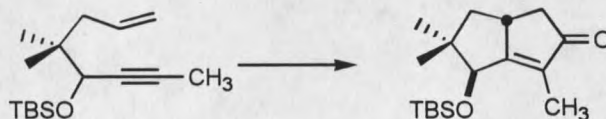
38.6 (C), 22.6 (CH₃), 22.4 (CH₃), 3.4 (CH₃); IR (thin film) 3418, 3075, 2228, 1639, 1024 cm⁻¹.

5,5-Dimethyl-4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1-octen-6-yne (**215a**).



The title compound was prepared from 0.552 g (3.63 mmol) of **215a** according to the general experimental procedure utilized for **71**, except that the reaction required 48 h, to afford 0.88 g (91%) of **215a** as a colorless oil: ¹H NMR (CDCl₃) δ 5.87-5.73 (m, 1H), 5.02-4.98 (m, 2H), 3.96 (app q, *J* = 2.1 Hz, 1H), 2.16-2.04 (m, 2H), 1.81 (d, *J* = 2.1 Hz, 3H), 0.89-0.85 (m, 15H), 0.12 (s, 3H), 0.07 (s, 3H); ¹³C NMR (CDCl₃) δ 135.6, 116.9, 81.2, 79.4, 70.8, 42.6, 39.2, 25.9, 22.7, 22.6, 18.2, 3.42, -4.3, -5.2; IR (thin film) 3079, 1640, 1076 cm⁻¹.

Trans-4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-4,5,6,6a-tetrahydro-3,5,5-trimethyl-2(1*H*)-pentalenone (**215b**).



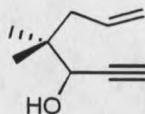
Enyne **215a** (66 mg, 0.25 mmol) was cyclized according to general procedure C to afford 54 mg (74%) of a 2.5 to 1 diastereomeric mixture of bicyclopentenones **215b** and **215c** as determined by G.C. analysis of the crude reaction mixture. **215b**:

^1H NMR (CDCl_3) δ 4.06 (s, 1H), 3.26-3.18 (m, 1H), 2.68 (dd, $J = 18.1, 6.2$ Hz, 1H), 2.02-1.93 (m, 2H), 1.72 (m, 3H), 1.09 (s, 3H), 1.01 (dd, $J = 12.7, 7.0$ Hz, 1H), 0.85 (s, 9H), 0.78 (s, 3H), 0.08 (s, 3H), 0.01 (s, 3H); ^{13}C NMR (CDCl_3) δ 211.5 (C), 180.6 (C), 132.0 (C), 76.2 (CH), 45.1 (C), 44.0 (CH_2), 43.1 (CH_2), 39.3 (CH), 29.0 (CH_3), 25.7 (CH_3), 24.0 (CH_3), 18.1 (C), 8.8 (CH_3), -4.6 (CH_3), -4.9 (CH_3); IR (thin film) 1713, 1676, 1472, 1257, 1090, 766 cm^{-1} .

Cis-4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-4,5,6,6a-tetrahydro-3,5,5-trimethyl-2(1*H*)-pentalenone (**215c**).



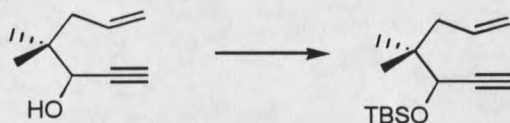
^1H NMR (CDCl_3) δ 4.55 (s, 1H), 2.84-2.24 (m, 1H), 2.62 (dd, $J = 17.9, 6.7$ Hz, 1H), 1.98-1.88 (m, 2H), 1.80 (t, $J = 1.83$ Hz, 3H), 1.23 (dd, $J = 13.2, 8.4$ Hz, 1H), 0.94 (s, 9H), 0.81 (s, 3H), 0.11 (s, 6H); ^{13}C NMR (CDCl_3) δ 210.7 (C), 179.8 (C), 132.2 (C), 80.5 (CH), 44.0 (CH_2), 43.8 (C), 43.7 (CH_2), 35.2 (CH), 28.9 (CH_3), 25.9 (CH_3), 24.6 (CH_3), 18.0 (C), 7.8 (CH_3), -4.4 (CH_3); IR (thin film) 1711, 1671, 1472, 1252, 1133 cm^{-1} .

4,4-Dimethyl-7-hepten-1-yne-3-ol (**229**).

To a solution of bis-trimethylsilyl acetylene (2.81 g, 16.5 mmol, 1.1 eq) in THF (60 mL) cooled in a NaCl-ice bath was added LiBr (1.56 g, 18.0 mmol, 1.2 eq) in three portions. When the internal reaction temperature returned to $< 5^{\circ}\text{C}$, a 0°C solution of methyllithium (15.8 mL, 1.0 M in 90% cumene-THF, 15.8 mmol, 1.05 eq) was added in one portion, and the resulting solution was allowed to warm to rt. After being stirred for 24 h, the reaction flask was cooled in a NaCl-ice bath and a solution of 2,2-dimethyl-4-penten-1-al (1.68 g, 15.0 mmol) in THF (5 mL) was added at such a rate that the internal reaction temperature remained below 20°C . After stirring 4 h at rt, the reaction mixture was treated with saturated aqueous NH_4Cl (50 mL) and concentrated *in vacuo*. The resulting heterogeneous mixture was diluted with Et_2O (50 mL) and the organic phase was separated. The aqueous phase was extracted with Et_2O (2 x 50 mL) and the combined organic fractions were washed with H_2O (15 mL), brine (25 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo*. The residual oil was diluted with MeOH (20 mL) and subsequently treated with NaOH (1 pellet, ca. 60 mg). After stirring for 24 the solution was concentrated *in vacuo* and the residue was subjected to gradient flash chromatography on silica gel (hexane to 5% EtOAc/hexane for elution) to afford

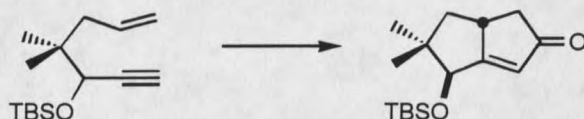
1.08 g (52%) of the title compound as a colorless oil: ^1H NMR (CDCl_3) δ 5.90-5.76 (m, 1H), 5.09-5.04 (m, 1H), 4.05 (d, $J = 2.0$ Hz, 1H), 2.43 (d, $J = 2.0$ Hz, 1H), 2.27-2.03 (m, 2H), 0.95 (s, 3H), 0.94 (s, 3H); ^{13}C NMR (CDCl_3) δ 134.7 (CH), 117.7 (CH_2), 83.4 (CH), 74.1 (C), 70.0 (CH), 42.6 (CH_2), 38.4 (C), 22.5 (CH_3), 22.3 (CH_3); IR (thin film) 3418 (br), 3307, 3076, 2115, 1639, 1040 cm^{-1} .

4,4-Dimethyl-5-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1-hepten-6-yne (**230a**).



The title compound was prepared from 0.69 g (5.0 mmol) of **229** according to the general experimental procedure utilized for **71** except that the reaction required 48 h to afford 0.98 g (78%) of **230a** as a colorless oil: ^1H NMR (CDCl_3 , 250 MHz) δ 5.88-5.63 (m, 1H), 5.06-4.98 (m, 2H), 4.00 (d, 2.25), 2.09 (app d with fine structure, $J = 7.5$ Hz, 2H), 0.92 (s, 3H), 0.91 (s, 3H), 0.89 (s, 9H), 0.14 (s, 3H), 0.08 (s, 3H); ^{13}C NMR (CDCl_3) δ 135.8 (CH), 118.0 (CH_2), 84.8 (C), 74.2 (CH), 71.1 (CH), 43.2 (CH_2), 39.7 (C), 26.5 (CH_3), 23.3 (CH_3), 23.2 (CH_3), 18.9 (C), -3.7 (CH_3), -4.6 (CH_3); IR (thin film) 3311, 3077, 1640, 1472, 1252, 1091, 838 cm^{-1} .

Trans-5,5-dimethyl-4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-4,5,6,6a-tetrahydro-2(1*H*)-pentalenone (**230b**).



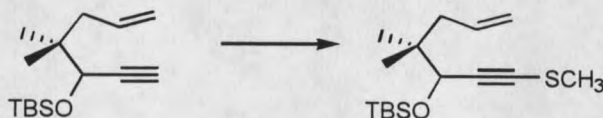
Enyne **230a** (63 mg, 0.25 mmol) was cyclized according to general procedure C except that 10 mol % $\text{Co}_2(\text{CO})_8$ was employed to afford 56 mg (80%) of a 1.6 to 1 diastereomeric mixture of bicyclopentenones **230b** and **230c** as determined by G.C. analysis of the crude reaction mixture. **230b**: ^1H NMR (CDCl_3 , 250 MHz) δ 5.9 (d, $J = 2.5$ Hz, 1H), 4.08 (s, 1H), 3.49-3.26 (m, 1H), 2.66 (dd, $J = 18.0, 6.8$ Hz, 1H), 2.05-1.94 (m, 2H), 1.08 (s, 3H), 1.07 (dd, $J = 12.8, 8.0$ Hz, 1H), 0.88 (s, 3H), 0.87 (s, 9H), 0.07 (s, 9H), 0.01 (s, 3H); ^{13}C NMR (CDCl_3) δ 211.0 (C), 188.8 (C), 125.0 (CH), 77.0 (CH), 44.7 (C), 44.3 (CH_2), 43.0 (CH_2), 41.6 (CH), 28.8 (CH_3), 25.4 (CH_3), 23.4 (CH_3), 17.9 (C), -4.7 (CH_3), -5.2 (CH_3); IR (thin film) 3076, 1717, 1645, 1471, 1250, 1082, 838 cm^{-1} .

Cis-5,5-dimethyl-4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-4,5,6,6a-tetrahydro-2(1*H*)-pentalenone (**230c**).



^1H NMR (CDCl_3 , 250 MHz) δ 5.94 (app t, $J = 2.0$ Hz, 1H), 4.45 (d, $J = 1.6$ Hz, 1H), 3.02-2.89 (m, 1H), 2.63 (dd, $J = 17.8, 6.7$ Hz, 1H), 2.06-1.92 (m, 2H), 1.28 (dd, $J = 13.2, 8.4$ Hz, 1H), 1.15 (s, 3H), 0.90 (s, 9H), 0.82 (s, 3H), 0.07 (s, 3H), 0.06 (s, 3H); ^{13}C NMR (CDCl_3) δ 210.1 (C), 192.2 (C), 124.0 (CH), 79.4 (CH), 44.7 (CH), 44.0 (CH_2), 43.9 (C), 37.2 (CH), 29.2 (CH_3), 25.8 (CH_3), 24.6 (CH_3), 18.2, -4.7 (CH_3), -4.9 (CH_3).

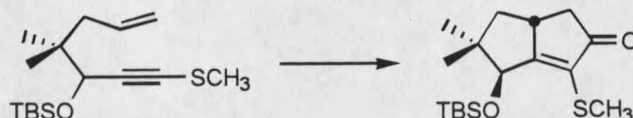
4,4-Dimethyl-5-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-7-thiomethyl-1-hepten-6-yne (**231a**).



To a solution of alkyne **230a** (315 mg, 1.2 mmol) in THF (3 mL) was added a -20 °C solution of LDA•THF (2.04 mL, 0.67 M solution in methyl cyclohexane, 1.1 eq). After stirring for 30 min, CH_3SCN (97 mL, 1.15 eq) was added neat and the resulting solution was allowed to warm to rt and stir overnight. The solution was subsequently treated with half-saturated aqueous NaHCO_3 (10 mL) and the resulting mixture was extracted with three 10-mL portions of ether. The combined organic phases were washed with H_2O (5 mL), brine (5 mL), dried (MgSO_4), filtered and concentrated *in vacuo*. The residue was subjected to flash chromatography on silica gel (hexane for elution) to afford 234 mg (63%) of the

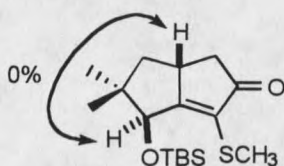
title compound as an air-sensitive yellow oil: ^1H NMR (CDCl_3) δ 5.86-5.73 (m, 1H), 5.03-4.98 (m, 2H), 4.08 (s, 1H), 2.35 (s, 3H), 2.14-2.00 (m, 2H), 0.88 (s with fine structure, 15H), 0.12 (s, 3H), 0.07 (s, 3H); ^{13}C NMR (CDCl_3) δ 135.2 (CH), 117.1 (CH_2), 93.4 (C), 71.4 (CH), 42.7 (CH_2), 39.4 (C), 25.8 (CH_3), 22.8 (CH_3), 22.7 (CH_3), 19.0 (CH_3), 18.2 (C), -4.2 (CH_3), -5.1 (CH_3); IR (thin film) 3075, 2186, 1639, 1091, 837 cm^{-1} ; high resolution mass spectrum calcd for $\text{C}_{17}\text{H}_{30}\text{O}_2\text{SiS}$ (M^+) 326.1736, found 326.1733.

Trans-5,5-dimethyl-4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3-methylthio-4,5,6,6a-tetrahydro-2(1*H*)-pentalenone (**231b**).



Enyne **231a** (75 mg, 0.25 mmol) was cyclized according to general procedure B except that 10 mol % $\text{Co}_2(\text{CO})_8$ was employed to afford 80 mg (98%) of a 3.9 to 1 diastereomeric mixture of bicyclopentenones **231b** and **231c** as determined by G.C. analysis of the crude reaction mixture. **231b**: R_f = 0.45 (10% EtOAc/Hex); ^1H NMR (CDCl_3) δ 4.19 (s, 1H), 3.11-3.21 (m, 1H), 2.72 (dd, J = 17.9, 6.8 Hz, 1H), 2.33 (s, 3H), 2.08-2.01 (m, 2H), 1.10 (s, 3H), 1.06 (dd, J = 13.0, 6.6 Hz, 1H), 0.85 (s, 9H), 0.81 (s, 3H), 0.11 (s, 3H), 0.02 (s, 3H); ^{13}C NMR (CDCl_3) δ 207.2 (C), 183.8 (C), 130.6 (C), 76.9 (CH), 45.0 (C), 44.7 (CH_2), 42.9 (CH_2), 39.8 (CH), 28.9 (CH_3),

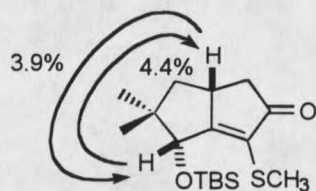
25.7 (CH₃), 23.8 (CH₃), 18.1 (C), 14.4 (CH₃), -4.5 (CH₃), -4.9 (CH₃); IR (thin film) cm⁻¹; high resolution mass spectrum calcd for C₁₇H₃₀O₂SiS (M⁺) 326.1736, found 326.1736. The assigned stereochemistry is consistent with the following observed NOE data:



Cis-5,5-dimethyl-4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3-methylthio-4,5,6,6a-tetrahydro-2(1*H*)-pentalenone (**231c**).



R_f = 0.23 (10% EtOAc/Hex); ¹H NMR (CDCl₃) δ 4.58 (s, 1H), 2.92-2.83 (m, 1H), 2.70 (dd, *J* = 17.1, 7.0 Hz), 2.32 (s, 3H), 2.08 (dd, *J* = 17.7, 3.5 Hz), 1.94 (dd, *J* = 13.1, 10.0 Hz, 1H), 1.28 (dd, *J* = 13.1, 8.2 Hz), 1.14 (s, 3H), 0.95 (s, 9H), 0.85 (s, 3H), 0.19 (s, 3H), 0.10 (s, 3H); ¹³C NMR (CDCl₃) δ 206.6 (C), 183.8 (C), 130.5 (C), 80.3 (CH), 44.1 (CH₂), 43.6 (CH₂), 36.3 (CH), 29.6 (C), 28.7 (CH₃), 26.1 (CH₃), 24.6 (CH₃), 18.2 (C), 15.0 (CH₃), -4.1 (CH₃), -4.3 (CH₃); IR (thin film) 1711, 1620, 1249, 1132, 838 cm⁻¹; high resolution mass spectrum calcd for C₁₇H₃₀O₂SSi (M⁺) 326.1736, found 326.1730. The assigned stereochemistry is consistent with the following observed NOE's:

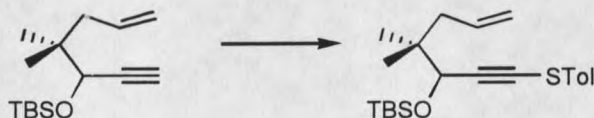


Allene elimination product (**232**).



$R_f = 0.51$ (Hex); ^1H NMR (CDCl_3 , 250 MHz) δ 6.09 (d, $J = 16.2$ Hz, 1H), 5.79-5.63 (m, 1H), 5.50 (d, $J = 16.2$ Hz, 1H), 5.03-4.94 (m, 2H), 2.03 (dt, $J = 7.4$, 1.1 Hz, 2H), 1.40 (s, 9H), 0.98 (s, 6H); ^{13}C NMR (CDCl_3) δ 153.2 (CH), 135.5 (CH), 118.0 (CH_2), 107.3 (CH), 95.9, 48.6 (C), 47.6 (CH_2), 37.6 (C), 31.0 (CH_2), 27.1 (CH_3); IR (thin film) cm^{-1} .

4,4-Dimethyl-5-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-7-[(4-methylphenyl)thio]-1-hepten-6-yne (**234a**).



The title compound was prepared from 252 mg (1.0 mmol) of enyne **230a** as described for the preparation of **231a** (except that the during work-up the combined organic phases were washed with 2.0 M aqueous NaOH (5 mL)) which afforded 268 mg (75%) of **234a** as a slightly yellow oil; ^1H NMR (CDCl_3) δ 7.32 (d, $J = 8.2$

Hz, 2H), 7.13 (d, $J = 8.2$ Hz, 2H), 5.42-5.38 (m, 1H), 5.11-5.05 (m, 2H), 4.24 (s, 1H), 2.32 (s, 3H), 2.22-2.10 (m, 2H), 0.97 (d, $J = 3.4$ Hz, 6H), 0.92 (s, 9H), 0.16 (s, 3H), 0.11 (s, 3H); ^{13}C NMR (CDCl_3) δ 136.4 (C), 135.1 (CH), 129.9 (CH), 129.4 (C), 126.6 (CH), 117.3 (CH_2), 98.9 (C), 71.6 (CH), 42.8 (CH_2), 39.6 (C), 25.8 (CH_3), 22.9(CH_3), 22.8(CH_3), 20.9(CH_3), 18.2 (C), -4.2(CH_3), -5.1(CH_3); IR (thin film) 3075, 2182, 1640, 1492, 1250, 1090, 837 cm^{-1} ; high resolution mass spectrum calcd for $\text{C}_{22}\text{H}_{34}\text{OSSi}$ (M^+) 374.2100, found 374.2109.

Trans-5,5-dimethyl-4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3-[(4-methylphenyl)thio]-4,5,6,6a-tetrahydro-2(1*H*)-pentalenone (**234b**).



Enyne **234a** (90 mg, 0.25 mmol) was cyclized according to general procedure B except that 10 mol % $\text{Co}_2(\text{CO})_8$ was employed to afford 92 mg (95%) of a 2.4 to 1 diastereomeric mixture of bicyclopentenones **23b** and **234c** as determined by G.C. analysis of the crude reaction mixture. **234b**: $R_f = 0.37$ (10% EtOAc/Hex); ^1H NMR (CDCl_3) δ 7.18 (d, $J = 6.3$ Hz, 2H), 7.03 (d, $J = 8.2$ Hz, 2H), 4.28 (s, 1H), 3.40-3.30 (m, 1H), 2.81 (dd, $J = 17.9, 6.9$ Hz, 1H), 2.27 (s, 3H), 2.13-2.04 (m, 2H), 1.14 (overlapping, s with fine structure, 4H), 0.88 (s, 9H), 0.82 (s, 3H), 0.13 (s, 3H), 0.04 (s, 3H); ^{13}C NMR (CDCl_3) δ 205.9 (C), 187.1 (C), 136.9 (C), 132.0 (C), 130.4

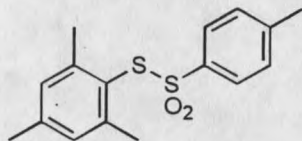
(CH), 129.5 (CH), 129.4 (C), 76.8 (CH), 45.0 (C), 44.7 (CH₂), 43.0 (CH₂), 40.2 (CH), 29.0 (CH₃), 25.8 (CH₃), 24.0 (CH₃), 21.0 (CH₃), 18.1 (C), -4.4 (CH₃), -4.9 (CH₃); IR (thin film) 1721, 1627, 1492, 1251, 1086, 837 cm⁻¹; high resolution mass spectrum calcd for C₂₃H₃₄OSSi (M⁺) 402.2049, found 402.2059.

Cis-5,5-dimethyl-4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3-[(4-methylphenyl)thio]-4,5,6,6a-tetrahydro-2(1*H*)-pentalenone (**234c**).



R_f = 0.13 (10% EtOAc/Hex); ¹H NMR (CDCl₃) δ 7.20 (d, *J* = 6.2 Hz, 2H), 7.00 (d, *J* = 8.2 Hz, 2H), 4.69 (s, 1H), 3.02-2.93 (m, 1H), 2.71 (dd, *J* = 17.7, 7.1 Hz, 1H), 2.26 (s, 3H), 2.07-1.98 (m, 2H), 1.35 (dd, *J* = 13.2, 8.0 Hz, 1H), 1.20 (s, 3H), 0.92 (s with fine structure, 12H), 0.17 (s, 3H), 0.11 (s, 3H); ¹³C NMR (CDCl₃) δ 205.0 (C), 186.9 (C), 136.0 (C), 130.8 (C), 130.1 (CH), 129.4 (CH), 128.8 (C), 80.5 (CH), 44.2 (C), 44.1 (CH₂), 43.6 (CH₂), 36.6 (CH), 28.9 (CH₃), 26.1 (CH₃), 24.8 (CH₃), 21.0 (CH₃), 18.2 (C), -4.1 (CH₃), -4.3 (CH₃); IR (thin film) 1717, 1622, 1250, 1250, 1162 cm⁻¹; high resolution mass spectrum calcd for C₂₃H₃₄OSSi (M⁺) 402.2049, found 402.2046.

(4-methylphenyl)-2,4,6-trimethylphenyl)sulfenyl sulfonate (**235**).



A three neck, 250-mL round bottomed flask was equipped with a magnetic stirring bar, thermometer, rubber septum and Dewar-type cold finger. The top of the cold finger was sealed with a rubber septum and was connected to an oil bubbler. The flask was charged with mesitylthiol (5.67 g, 37.3 mmol) and CCl_4 (40 mL). The cold finger was cooled to $-78\text{ }^\circ\text{C}$ and chlorine gas (previously condensed and tared in a test tube) was slowly introduced via cannula directly above the CCl_4 solution. The chlorine gas was introduced at such a rate that HCl evolution was not too vigorous, nor did the internal reaction temperature exceed $35\text{ }^\circ\text{C}$ (about 20 min). The cold finger was then adjusted to $0\text{ }^\circ\text{C}$, and argon was bubbled through the solution for 20 min. After this time, the flask was immersed in an ice bath and after the internal reaction temperature was below $5\text{ }^\circ\text{C}$, sodium *p*-toluenethiosulfonate trihydrate (8.58 g, 37.0 mmol) was added in one portion. The ice bath was removed and the reaction was allowed to warm to rt. After stirring at rt for 4 h, H_2O (40 mL) and CH_2Cl_2 (20 mL) were added and the organic layer was separated. The aqueous phase was extracted with CH_2Cl_2 (2 x 20 mL). The combined organic fractions were washed with saturated aqueous K_2CO_3 (20 mL), brine (30 mL), dried (MgSO_4), filtered and concentrated *in vacuo* from a $35\text{ }^\circ\text{C}$ water bath. When nearly

all the CCl_4 was removed, the warm flask was disconnect from the rotary evaporator and hexane (100 mL) was rapidly introduced with swirling. The resulting white crystals (8.12 g, 71%) were suitable for use without further purification: ^1H NMR (CDCl_3) δ 7.47 (dt, $J = 2.0, 8.0$, 2H), 7.21 (d, $J = 8.0$ Hz, 2H), 6.90 (s, 2H), 2.41 (s, 3H), 2.27 (s, 3H), 2.12 (s, 6H); ^{13}C NMR (CDCl_3) δ 145.3 (C), 144.7 (C), 142.0 (C), 141.7 (C), 129.7 (C), 127.4 (CH), 123.6 (C), 21.7 (CH_3), 21.6 (CH_3), 21.3 (CH_3); IR (KBr) 3027, 1731, 1654, 1140, 661 cm^{-1} .

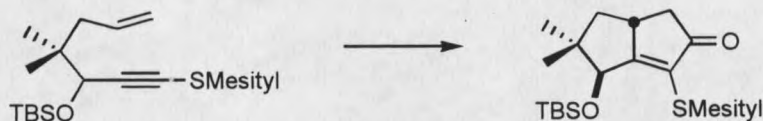
4,4-Dimethyl-5-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]- 7-[[[(2,4,6-trimethylphenyl)thio]-1-hepten-6-yne (**236a**).



To a solution of enyne **230a** (165 mg, 0.65 mmol) and HMPA (140 mg, 0.78 mmol, 1.2 eq) in THF (2 mL) cooled to -78°C was added a solution of *n*-BuLi (0.33 mL, 2.20 M in heptane, 0.73 mmol, 1.1 eq) dropwise over 1 min. After 5 min, a solution of mesityl sulfonate **235** (240 mg, 0.78 mmol, 1.2 eq) in THF (2 mL) cooled to -78°C was added via cannula and the resulting solution was allowed to warm to rt was stirred overnight. After 10 h, the solution was treated with half-saturated aqueous NH_4Cl (6 mL) and the aqueous phase was separated. The aqueous phase was extracted with Et_2O (3 x 15 mL) and the combined organic

fractions were washed with H₂O (3 x 5 mL), brine (20 mL), dried (MgSO₄), filtered and concentrated *in vacuo*. The residue was purified by silica gel chromatography (hexane for elution) and afforded 218 mg (83%) of the title compound as a colorless oil: $R_f = 0.67$ (5% EtOAc/Hex); ¹H NMR (CDCl₃) δ 6.92 (s, 2H), 5.83-5.69 (m, 1H), 5.02-4.93 (m, 2H), 4.03 (m, 1H), 2.93 (s, 6H), 2.26 (s, 3H), 2.11-1.96 (m, 2H), 0.86 (s with fine structure, 15H), 0.03 (s, 3H), 0.01 (s, 3H); ¹³C NMR (CDCl₃) δ 141.9 (C), 139.1 (C), 135.3 (CH), 129.2 (CH), 126.5 (C), 117.1 (CH₂), 91.2 (C), 74.8 (C), 71.4 (CH), 42.7 (CH₂), 39.6 (C), 25.8 (CH₃), 22.8 (CH₃), 22.7 (CH₃), 21.8 (CH₃), 21.0 (CH₃), 18.2 (C), -4.4 (CH₃), -5.2 (CH₃); IR (thin film) 3077, 2182, 1470, 1249, 1090, 836 cm⁻¹; high resolution mass spectrum calcd for C₂₄H₃₈OSSi (M⁺) 402.2413, found 402.2412.

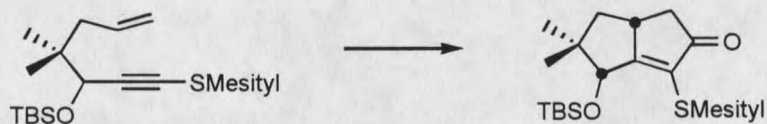
Trans-5,5-dimethyl-4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-4,5,6,6a-tetrahydro-3-[(2,4,6-trimethylphenyl)thio]-2(1*H*)-pentalenone (**236b**).



Enyne **235a** (90 mg, 0.26 mmol) was cyclized according to general procedure B except that 10 mol % Co₂(CO)₈ was employed to afford 92 mg (94%) of a 2.4 to 1 diastereomeric mixture of bicyclopentenones **236b** and **236c** as determined by G.C. analysis of the crude reaction mixture. **236b**: ¹H NMR (CDCl₃) δ 6.82 (s, 2H), 4.33

(s, 1H), 3.28-3.18 (m, 1H), 2.61 (dd, $J = 17.6, 6.7$ Hz, 1H), 2.48 (s, 6H), 2.23 (s, 3H), 2.04-1.91 (m, 2H), 1.21 (s, 3H), 1.00 (dd, $J = 12.8, 8.4$, 1H), 0.96 (s, 3H), 0.89 (s, 9H), 0.17 (s, 3H), 0.13 (s, 3H); ^{13}C NMR (CDCl_3) δ 205.3 (C), 179.6 (C), 142.7 (C), 138.4 (C), 130.5 (C), 128.8 (CH), 125.4 (C), 76.8 (CH), 45.4 (C), 43.9 (CH_2), 43.7 (CH_2), 40.3, 29.3 (CH_3), 25.8 (CH_3), 24.0 (CH_3), 22.4 (CH_3), 21.0 (CH_3), 18.2 (C), -4.3 (CH_3), -4.7 (CH_3); IR (thin film) 1716, 1601, 1463, 1251, 1127, 1084, 837 cm^{-1} ; high resolution mass spectrum calcd for $\text{C}_{25}\text{H}_{38}\text{O}_2\text{SiS}$ (M^+) 430.2362, found 430.2354.

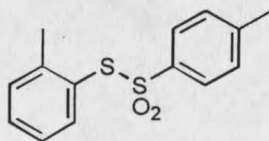
Cis-5,5-dimethyl-4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-4,5,6,6a-tetrahydro-3-[(2,4,6-trimethylphenyl)thio]-2(1*H*)-pentalenone (**236c**).



^1H NMR (CDCl_3) δ 6.85 (s, 2H), 4.66 (s, 1H), 2.88-2.78 (m, 1H), 2.52 (dd, $J = 17.5, 6.8$ Hz, 1H), 2.45 (s, 6H), 2.22 (s, 3H), 1.69-1.90 (m, 2H), 1.28 (dd, $J = 13.0, 8.8$ Hz, 1H), 1.19 (s, 3H), 0.98 (s, 9H), 0.96 (s, 3H), 0.26 (s, 9H), 0.14 (s, 3H); ^{13}C NMR (CDCl_3) δ 204.2 (C), 178.8 (C), 142.6 (C), 137.8 (C), 129.9 (C), 128.6 (CH), 126.2 (C), 80.5 (CH), 44.4 (CH_2), 44.2 (C), 43.7 (CH_2), 36.1 (CH), 29.2 (CH_3), 26.2 (CH_3), 25.1 (CH_3), 24.4 (CH_3), 21.0 (CH_3), 18.2 (C), -3.9 (CH_3), -4.0 (CH_3);

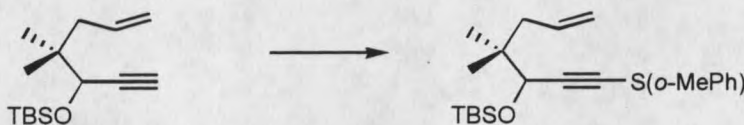
IR (thin film) 1716, 1601, 1463, 1251, 1127, 1084, 837 cm^{-1} ; high resolution mass spectrum calcd for $\text{C}_{25}\text{H}_{38}\text{O}_2\text{SiS}$ (M^+) 430.2362, found 430.2361.

(4-methylphenyl)-2,4,6-trimethylphenyl)sulfenyl sulfonate (**237**).



The title compound was prepared by the general procedure utilized for **235** to afford 18.0 g (76%) of **237** as white crystals: ^1H NMR (CDCl_3) δ 7.40 (d, $J = 8.1$ Hz, 2H), 7.19 (d, $J = 8.1$ Hz, overlapping with 7.38-7.09 (m), 6H), 2.40 (s, 3H), 2.13 (s, 3H); ^{13}C NMR (CDCl_3) δ 145.1 (C), 144.6 (C), 141.1 (C), 138.7 (CH), 132.2 (CH), 131.4 (CH), 129.8 (CH), 127.9 (CH), 127.7 (C), 127.3 (CH), 22.1 (CH_3), 21.0 (CH_3); IR (KBr) 3064, 1731, 1620, 1322, 1142, 1079, 792, 679 cm^{-1} .

4,4-Dimethyl-5-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-7-[(2-methylphenyl)thio]-1-hepten-6-yne (**238a**).



The title compound was prepared from 218 mg (0.83 mmol) of enyne **230a** as described for the preparation of **236a** which afforded 412 mg (91%) of **238a** as a slightly yellow oil: ^1H NMR (CDCl_3) δ 7.65 (d, $J = 7.8$ Hz), 7.24-7.19 (m, 1H),

7.12 (d, $J = 4.2$ Hz), 6.90-5.76 (m, 1H), 5.07-5.02 (m, 2H), 4.25 (s, 1H), 2.31 (s, 3H), 2.23-2.08 (m, 2H), 0.98 (s, 3H), 0.97 (s, 3H), 0.93 (s, 9H), 0.14 (s, 3H), 0.12 (s, 3H); ^{13}C NMR (CDCl_3) δ 135.5 (CH), 135.4 (C), 132.5 (C), 130.6 (CH), 127.2 (CH), 127.0 (CH), 126.8 (CH), 117.8 (CH_2), 99.7 (C), 72.0 (CH), 71.8 (C), 43.2 (CH_2), 40.0 (C), 26.2 (CH_3), 23.3 (CH_3), 23.2 (CH_3), 19.8 (CH_3), 18.6, -3.8 (CH_3), -4.8 (CH_3); IR (thin film) 3072, 2182, 1639, 1590, 1470, 1250, 836 cm^{-1} ; high resolution mass spectrum calcd for $\text{C}_{22}\text{H}_{34}\text{OSSi}$ (M^+) 374.2100, found 374.2108.

Trans-5,5-dimethyl-4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3-[(2-methylphenyl)thio]-4,5,6,6a-tetrahydro-2(1*H*)-pentalenone (**238b**).



Enyne **238a** (133 mg, 0.35 mmol) was cyclized according to general procedure B to afford 31 mg (22%) of a 2.4 to 1 diastereomeric mixture of bicyclopentenones **238b** and **238c** as determined by G.C. analysis of the crude reaction mixture. **238b**: R_f = 0.56 (20% EtOAc/Hex); ^1H NMR (CDCl_3) δ 7.14-6.92 (m, 4H), 4.28 (s, 1H), 3.44-3.35 (m, 1H), 2.86 (dd, $J = 17.9, 6.9$ Hz, 1H), 2.43 (s, 3H), 2.19-2.07 (m, 2H), 1.14 (s and m overlapping, 3H and 1H), 0.88 (s, 3H), 0.86 (s, 9H), 0.11 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (CDCl_3) δ 206.5 (C), 189.3 (C), 137.6 (C), 133.2 (C), 103.7 (CH_2), 129.0 (CH_2), 128.7, 126.8 (CH_2), 126.7 (CH_2), 77.2 (CH_2), 45.4 (C), 44.9 (CH_2),

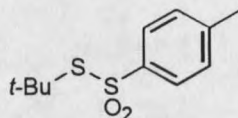
43.5 (CH₂), 40.9 (CH), 29.5 (CH₃), 26.5 (CH₃), 24.4 (CH₃), 20.9 (CH₃), 18.5 (C), -4.02 (CH₃), -4.44 (CH₃); high resolution mass spectrum calcd for C₂₃H₃₄O₂SSi (M⁺) 402.2049, found 402.2051.

Cis-5,5-dimethyl-4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3-[(2-methylphenyl)thio]-4,5,6,6a-tetrahydro-2(1*H*)-pentalenone (**238c**).



R_f = 0.38 (20% EtOAc/Hex); ¹H NMR (CDCl₃) δ 7.12-6.93 (m, 4H), 4.70 (s, 1H), 3.07-2.97 (m, 1H), 2.75 (dd, *J* = 17.8, 7.0 Hz, 1H), 2.41 (s, 3H), 2.13-2.00 (m, 2H), 1.38 (dd, *J* = 13.3, 8.2 Hz, 1H), 1.20 (s, 3H), 0.96 (s, 3H), 0.90 (s, 9H), 0.13 (s, 3H), 0.10 (s, 3H); ¹³C NMR (CDCl₃) δ 205.4, 188.6, 137.4, 134.2, 130.4, 128.2, 126.4, 126.1, 80.7, 44.7, 44.3, 40.0, 37.3, 29.3, 26.4, 25.2, 20.9, 18.6, -3.8, -3.9; IR (thin film) 3061, 1722, 1625, 1470, 1251, 1086, 838 cm⁻¹; high resolution mass spectrum calcd for C₂₃H₃₄O₂SSi (M⁺) 402.2049, found 402.2049.

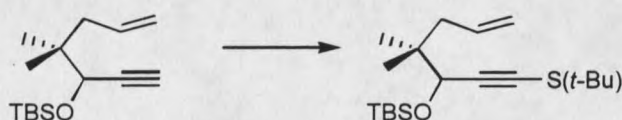
(4-Methylphenyl)-[1,1-(dimethylethyl)sulfonyl] sulfonate (**239**).



R_f = 0.29 (10% EtOAc/Hex); ¹H NMR (CDCl₃) δ 7.8 (d, *J* = 8.3 Hz, 2H), 7.29 (d, *J* = 8.3 Hz, 2H), 2.42 (s, 3H), 1.42 (s, 9H); ¹³C NMR (CDCl₃) δ 144.4 (C), 144.1 (C),

129.8 (C), 127.1 (CH), 55.2 (C), 30.9 (CH₃), 21.7 (CH₃); IR (KBr) 3090, 3068, 1593, 1460, 1117, 814 cm⁻¹.

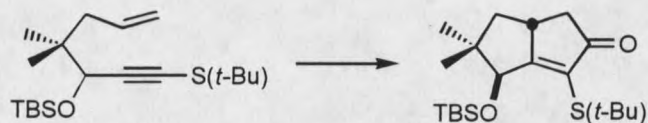
4,4-Dimethyl-5-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]- 7-[(1,1-dimethylethyl)thio]-1-hepten-6-yne (**240a**).



The title compound was prepared from 284 mg (1.12 mmol) of enyne **230a** as described for the preparation of **231a**, except utilizing *t*-butylthiocyanate as electrophile, which afforded 290 mg (98%) of **240a** as a slightly yellow oil:

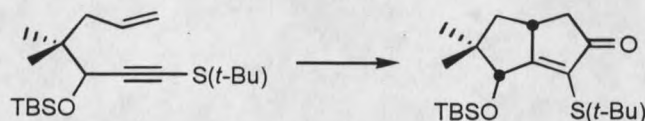
¹H NMR (CDCl₃) δ 5.88-5.72 (m, 1H), 5.05-4.56 (m, 2H), 4.15 (s, 1H), 2.19-2.04 (m, 2H), 1.39 (s, 9H), 0.93 (s, 3H), 0.91 (s, 3H), 0.88 (s, 9H), 0.13 (s, 3H), 0.07 (s, 3H); ¹³C NMR (CDCl₃) δ 135.3 (CH), 117.2 (CH), 97.5 (C), 74.6 (C), 71.6 (CH), 47.5 (C), 42.9 (CH₂), 39.7 (C), 30.7 (CH₃), 30.5 (CH₃), 25.9 (CH₃), 22.9 (CH₃), 18.3 (C), -4.1 (CH₃), -5.1 (CH₃); IR (thin film) 3076, 2176, 1639, 1471, 1250, 1091, 1051, 837 cm⁻¹; high resolution (CI/NH₃) mass spectrum calcd for C₁₉H₃₇OSSi (M+1)⁺ 341.2334, found 341.2324.

Trans-5,5-dimethyl-4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3-[(1,1-dimethylethyl)thio]-4,5,6,6a-tetrahydro-2(1*H*)-pentalenone (**240b**).



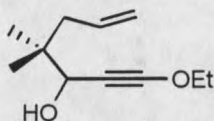
A solution of enyne **240a** (85 mg, 0.25 mmol) and $\text{Co}_2(\text{CO})_8$ (91 mg, 0.27 mmol, 1.1 eq) in 2:1 TFE-DME was irradiated for 12 h under an atmosphere of CO and the resulting material was purified by chromatography on silica gel (10-30% EtOAc/hexane for elution) to afford 52 mg (56%) of a 1.9 to 1 diastereomeric mixture of bicyclopentenones **240b** and **240c** as determined by G.C. analysis of the crude reaction mixture. **240b**: waxy solid; $R_f = 0.43$ (10% EtOAc/Hex); ^1H NMR (CDCl_3) δ 4.24 (s, 1H), 3.33-3.21 (m, 1H), 2.79 (dd, $J = 17.5, 6.9$ Hz, 1H), 2.12-2.01 (m, 2H), 1.34 (s, 9H), 1.11 (s, 3H), 1.10 (dd, $J = 13.0, 7.1$ Hz, 1H), 0.88 (s, 3H), 0.84 (s, 9H), 0.13 (s, 3H), 0.01 (s, 3H); ^{13}C NMR (CDCl_3) δ 208.7 (C), 191.0 (C), 129.6 (C), 76.9 (CH), 42.2 (C), 45.1 (C), 44.7 (CH_2), 43.4 (CH_2), 40.5 (CH), 32.5 (CH_3), 29.4 (CH_3), 25.9 (CH_3), 24.3 (CH_3), 18.3 (C), -4.2 (CH_3), -4.7 (CH_3); high resolution mass spectrum calcd for $\text{C}_{20}\text{H}_{36}\text{O}_2\text{SSi}$ (M^+) 368.2205, found 368.2211.

Cis-5,5-dimethyl-4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3-[(1,1-dimethylethyl)thio]-4,5,6,6a-tetrahydro-2(1*H*)-pentalenone (**240c**).



$R_f = 0.23$ (10% EtOAc/Hex); mp = 89.9-97.4 °C; ^1H NMR (CDCl_3) δ 4.62 (s, 1H), 2.94-2.84 (m, 1H), 2.72 (dd, $J = 17.2, 7.0$ Hz, 1H), 2.05 (dd, $J = 17.3, 4.0$ Hz, 1H), 1.97 (dd, $J = 13.2, 10.2$ Hz, 1H), 1.32 (s and m overlapping, 10H), 1.16 (s, 3H), 0.95 (s, 9H), 0.90 (s, 3H), 0.20 (s, 3H), 0.09 (s, 3H); ^{13}C NMR (CDCl_3) δ 208.1, 189.8, 129.3, 80.6, 46.9, 43.9, 43.2, 37.0, 32.2, 29.7, 28.9, 26.3, 25.0, 18.3, -3.6, -3.3; IR (melt) 1716, 1609, 1742, 1250, 1084, 838 cm^{-1} ; high resolution mass spectrum calcd for $\text{C}_{20}\text{H}_{36}\text{O}_2\text{SSi}$ (M^+) 368.2205, found 368.2198.

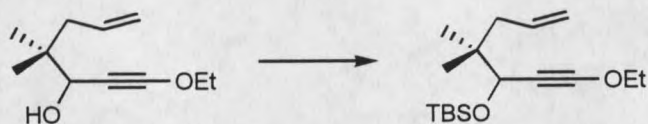
4,4-Dimethyl-1-ethoxy-7-hepten-1-yne-3-ol (**243**).



To a solution of ethoxy acetylene (0.84 g of a 50% solution in hexane, 6.0 mmol, 1.2 eq) in THF (10 mL) cooled to -78 °C was added a solution of *n*-BuLi (2.37 mL, 2.32 M in heptane, 5.5 mmol, 1.1 eq) dropwise over 5 min and the reaction mixture was stirred for an additional 5 min. Next, 2,2-dimethyl-4-penten-1-al (0.56 g, 5.0 mmol, 1.0 eq) was added neat. The dry-ice acetone bath was removed and the

reaction mixture was allowed to warm to rt while being vigorously stirred. After stirring for 10 min at 26 °C, the reaction mixture was treated with a saturated aqueous solution of NaHCO_3 (5 mL) and diluted with Et_2O (15 mL). The organic layer was separated and the aqueous layer was extracted with Et_2O (2 x 15 mL) and the combined organic fractions were washed with H_2O (5 mL), brine (10 mL) and concentrated *in vacuo*. The residue was purified by gradient flash chromatography on silica gel (2-10% EtOAc /Hex for elution with ca. 0.1 % TEA added) to afford 0.847 g (93%) of the title compound as a colorless oil: ^1H NMR (CDCl_3) δ 5.89-5.75 (m, 1H), 5.07-4.99 (m, 2H), 4.07 (q, $J = 7.1$ Hz, 2H), 4.06 (s, 1H), 2.15-2.04 (m, 2H), 1.70 (br s, 1H), 1.35 (t, $J = 7.1$ Hz, 3H), 0.91 (s, 3H), 0.90 (s, 3H); ^{13}C NMR (CDCl_3) δ 135.7 (CH), 117.7 (CH_2), 95.0 (C), 74.9 (CH_2), 70.6 (CH), 43.3 (CH_2), 39.3 (C), 38.2 (C), 23.1 (CH_3), 23.0 (CH_3), 14.8 (CH_3); IR (thin film) 3440 (br), 3075, 2263, 1640, 1234, 1007, 912 cm^{-1} .

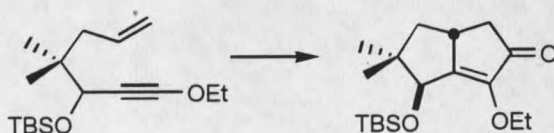
4,4-Dimethyl-5-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-7-ethoxy-1-hepten-6-yne (244a).



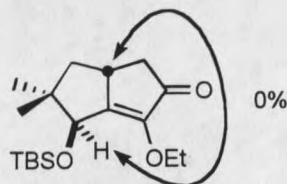
A solution of TBSCl (178 mg, 1.18 mmol, 1.05 eq) and imidazole (191 mg, 2.80 mmol, 2.5 eq) in DMF (1 mL) was stirred for 10 min at rt and subsequently treated

with a solution of alcohol **243** (205 mg, 1.12 mmol) in DMF (0.25 mL). The resulting solution was stirred for 96 h and then diluted with 6:1 hexane-ether (20 mL) and saturated aqueous K_2CO_3 (20 mL). The organic layer was separated and the aqueous layer was washed with 6:1 hexane-ether (2 x 15 mL). The aqueous layers were combined and washed with a 25-mL portion of water, brine (25 mL), dried ($MgSO_4$), filtered and concentrated *in vacuo*. The residual material was purified by flash chromatography on silica gel (hexane for elution) to afford 248 mg (76%) of the title compound as a colorless oil. 1H NMR ($CDCl_3$) δ 5.87-5.73 (m, 1H), 5.02-4.97 (m, 2H), 4.05 (q, $J = 7.1$ Hz, 2H), 4.06 (s, 1H), 2.14-2.01 (m, 2H), 1.35 (t, $J = 7.1$ Hz, 3H), 0.89 (s, 9H), 0.88 (s, 3H), 0.87 (s, 3H), 0.12 (s, 3H), 0.06 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 136.1 (CH), 117.2 (CH_2), 94.4 (C), 74.5 (CH_2), 70.9 (CH), 43.1 (CH_2), 39.8 (C), 38.8 (C), 26.2 (CH_3), 23.2 (CH_3), 23.1 (CH_3), 18.6 (C), 14.8 (CH_3), -3.7 (CH_3), -4.8 (CH_3); IR (thin film) 3076, 2264, 1640, 1250, 1067, 1005, 837 cm^{-1} ; high resolution (CI/ NH_3) mass spectrum calcd for $C_{17}H_{33}O_2Si$ (M^+) 297.2250, found 297.2244.

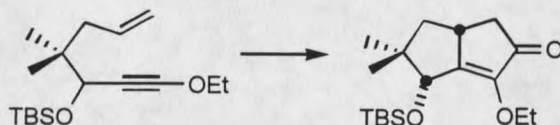
Trans-5,5-dimethyl-4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3-[(ethyl)oxy]-4,5,6,6a-tetrahydro-2(1*H*)-pentalenone (**244b**).



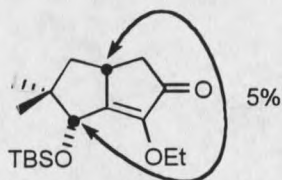
Enyne **244a** (74 mg, 0.25 mmol) was cyclized according to general procedure B, except that flash chromatography was performed with 2% EtOAc/hexane for elution, to afford 68 mg (84%) of a 0.72 to 1 diastereomeric mixture of bicyclopentenones **244b** and **244c** as determined by G.C. analysis of the crude reaction mixture. **244b**: R_f = 0.22 (5% EtOAc/Hex); ^1H NMR (CDCl_3) δ 4.28 (s, 1H), 4.24-4.13 (m, 2H), 3.17-3.10 (m, 1H), 2.65 (dd, J = 18.2, 6.4 Hz, 1H), 2.02-1.91 (m, 2H), 1.29 (t, J = 7.0 Hz, 3H), 1.08 (s, 3H), 1.03 (dd, J = 12.8, 7.6 Hz, 1H), 0.87 (s, 3H), 0.86 (s, 3H), 0.08 (s, 3H), 0.02 (s, 3H); ^{13}C NMR (CDCl_3) δ 205.6 (C), 158.5 (C), 148.0 (C), 76.6 (CH), 66.2 (CH_2), 46.5 (C), 44.2 (CH_2), 43.2 (CH_2), 36.6 (CH), 29.8 (CH_3), 26.2 (CH_3), 24.3 (CH_3), 18.6 (C), 15.9 (CH_3), -4.1 (CH_3), -4.5 (CH_3); IR (thin film) 1712, 1663, 1472, 1257, 1127, 838 cm^{-1} ; high resolution (CI/ NH_3) mass spectrum calcd for $\text{C}_{18}\text{H}_{34}\text{O}_3\text{Si}$ ($\text{M}+1$) $^+$ 325.2199, found 324.2192. The indicated stereochemistry is consistent with the following NOE data:



Cis-5,5-dimethyl-4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3-[(ethyl)oxy]-4,5,6,6a-tetrahydro-2(1*H*)-pentalenone (**244c**).



^1H NMR (CDCl_3) δ 4.42 (s, 1H), 4.24-4.13 (m, 2H), 2.76-2.68 (m, 1H), 2.56 (dd, J = 17.7, 6.4 Hz, 1H), 1.97 (dd, J = 17.7, 2.8 Hz, 1H), 1.84 (dd, J = 12.9, 9.2 Hz, 1H), 1.24 (t, J = 7.0 Hz, overlapping with CHH, 4H), 1.10 (s, 3H), 0.91 (s, 9H), 0.90 (s, 3H), 0.12 (s, 3H), 0.09 (s, 3H); ^{13}C NMR (CDCl_3) δ 205.6 (C), 163.9 (C), 149.0 (C), 79.7 (CH), 66.3 (CH_2), 45.0 (C), 44.7 (CH_2), 42.8 (CH_2), 33.4 (CH), 29.0 (CH_3), 26.3 (CH_3), 25.4 (CH_3), 18.7 (C), 16.0 (CH_3), -4.4 (CH_3); IR (thin film) cm^{-1} ; high resolution (CI/ NH_3) mass spectrum calcd for $\text{C}_{18}\text{H}_{34}\text{O}_3\text{Si}$ (M^+) 324.2199, found 324.2195. The indicated stereochemistry is consistent with the following NOE data:

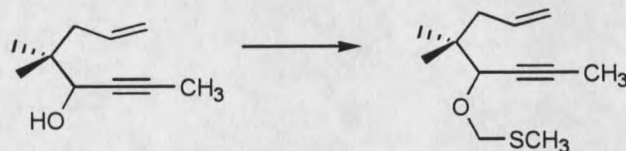


7-Chloro-4,4-dimethyl-5-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1-hepten-6-yne
(**244a**).



^1H NMR (CDCl_3) δ 5.85-5.71 (m, 1H), 5.05-4.98 (m, 2H), 4.00 (s, 1H), 2.15-2.00 (m, 2H), 0.91 (s, 6H), 0.90 (s, 9H), 0.13 (s, 3H), 0.07 (s, 3H); ^{13}C NMR (CDCl_3) δ 135.0 (CH), 117.4 (CH_2), 70.9 (CH), 69.6 (C), 63.3 (C), 42.6 (CH_2), 39.4 (CH_3), 25.8 (CH_3), 22.6 (CH_3), 22.5 (CH_3), 18.2 (C), -4.4 (CH_3), -5.3 (CH_3); IR (thin film) 3077, 2234, 1640, 1472, 1250, 1101, 1062, 837 cm^{-1} .

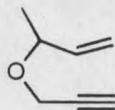
4,4-Dimethyl-5-[[[(methylthio)methyl]oxy]-1-hepten-6-yne (**254a**).



To a solution of alcohol **214** (152 mg, 1.0 mmol) in DMSO (3 mL) cooled to 10 $^{\circ}\text{C}$ was added a mixture of acetic anhydride (2.15 mL) and acetic acid (384 μL) over 1 min. After 3 d the resulting solution was poured into a sat. aqueous solution of NaHCO_3 (50 mL) cooled to 0 $^{\circ}\text{C}$, and the resulting mixture was vigorously stirred for 3 h while warming to rt. The resulting mixture was extracted with three 50-mL

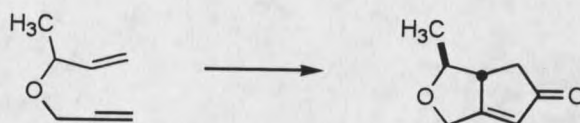
portions of CH_2Cl_2 and the combined organic phases were washed with H_2O (2 x 50 mL), sat. aqueous NaHCO_3 (50 mL), dried (MgSO_4), filtered and concentrated *in vacuo* to afford 35 mg (16%) of the title compound after chromatography on silica gel (1% EtOAc/Hex for elution). ^1H NMR (CDCl_3) δ 5.87-5.77 (m, 1H), 5.04-5.02 (m, 2H), 4.76 (app d, $J = 2.7$ Hz, 2H), 4.13 (app q, $J = 2.0$ Hz, 1H), 2.10 (m, 5H), 1.84 (d, $J = 2.0$, 3H), 0.93 (s, 3H); ^{13}C NMR (CDCl_3) δ 135.0 (CH), 117.2 (CH_2), 82.9 (C), 75.9 (C), 73.9 (CH), 72.9 (CH_2), 43.0 (CH_2), 38.0 (C), 23.2 (CH_3), 22.9 (CH_3), 14.2 (CH_3), 3.5 (CH_3); IR (thin film) 3075, 2228, 1639, 1471, 1300, 1050 cm^{-1} ; high resolution mass spectrum calcd for $\text{C}_{12}\text{H}_{20}\text{OS}$ (M^+) 212.1235, found 212.1242.

3-Methyl-3-(2-propynloxy)-1-propene (**256a**).



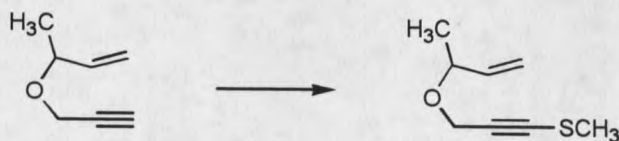
^1H NMR (CDCl_3) δ 5.72-5.60 (m, 1H), 5.24-5.15 (m, 2H), 4.18-3.98 (m, 3H), 2.36 (t, $J = 2.4$ Hz, 1H), 1.25 (d, $J = 6.1$ Hz, 3H); ^{13}C NMR (CDCl_3) δ 139.2 (CH), 116.9 (CH_2), 80.3 (CH), 75.9 (CH), 73.7 (C), 55.1 (CH_2), 21.1 (CH_3); IR (thin film) 3301, 3081, 2115, 1647, 1084 cm^{-1} .

Trans-3a,4-dihydro-3-methyl-1*H*-cyclopenta[*c*]furan-5(3*H*)-one (**256b**).



Enyne **256a** (110 mg, 1.0 mmol) was cyclized according to general procedure B, except that flash chromatography was performed with 10% EtOAc/Hex for elution to afford 31 mg (22%) of a 5.0 to 1 diastereomeric mixture of bicyclopentenones **256b** and **256c** as determined by G.C. analysis of the crude reaction mixture. **256b**: R_f = 0.20 (50% EtOAc/Hex); ^1H NMR (CDCl_3) δ 6.00 (app q, J = 2.0 Hz, 1H), 4.72 (d, J = 16.2 Hz, 1H), 4.56 (d, J = 16.2 Hz, 1H), 3.56-3.45 (m, 1H), 2.46-2.26 (m, 1H), 2.57 (ddd, J = 17.6, 6.4, 0.6 Hz, 1H), 2.07 (ddd, J = 17.6, 3.6, 0.6 Hz, 1H), 1.39 (d, J = 6 Hz, 3H); ^{13}C NMR (CDCl_3) δ 209.0 (C), 185.3 (C), 124.5 (CH), 79.6 (CH), 66.2 (CH_2), 52.3 (CH), 38.6 (CH_2), 19.3 (CH_3); IR (thin film) 3083, 1716, 1651, 1645, 999, 846 cm^{-1} .

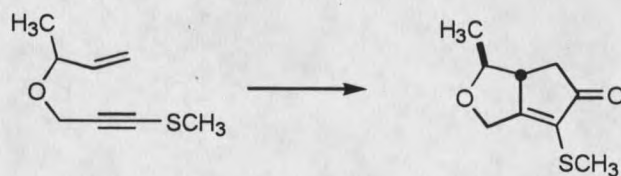
3-methyl-3-(3-methylthio-2-propynloxy)-1-propene (**257a**).



The title compound was prepared from 220 mg (2.0 mmol) of enyne **257a** as described for the preparation of **236a** to afford 96 mg (31%) of **257a** as a slightly yellow oil: R_f = 0.41 (5% EtOAc/Hex); ^1H NMR (CDCl_3) δ 5.65 (ddd, J = 17.7,

10.2, 7.7 Hz, 1H), 5.23-5.12 (m, 2H), 4.22 (d, 1H), 4.08 (d, $J = 16.2$ Hz, 1H), 4.04-4.16 (m, 1H), 2.35 (s, 3H), 1.23 (d, $J = 6.3$ Hz, 3H); ^{13}C NMR (CDCl_3) δ 139.2 (CH), 117.0 (CH_2), 89.5 (C), 77.7 (C), 75.6 (CH), 56.1 (CH_2), 21.1 (CH_3), 19.0 (CH_3); IR (thin film) 3078, 2180, 1642, 1081 cm^{-1} ; high resolution mass spectrum calcd for $\text{C}_8\text{H}_{13}\text{OS}$ (M^+) 157.0687, found 157.0691.

Trans-3a,4-dihydro-3-methyl-6-methylthio-1*H*-cyclopenta[*c*]furan-5(3*H*)-one (257b).



Enyne **257a** (65 mg, 0.42 mmol) was cyclized according to general procedure B to afford 63 mg (81%) of a 11.9 to 1 diastereomeric mixture of bicyclopentenones **257b** and **257c** as determined by G.C. analysis of the crude reaction mixture. **257b**: $R_f = 0.45$ (50% EtOAc/Hex); white crystals, mp: 67-78 $^{\circ}\text{C}$; ^1H NMR (CDCl_3) δ 4.71 (dd, $J = 16.3, 1.5$ Hz, 1H), 4.55 (dt, $J = 16.3, 1.43$ Hz, 1H), 3.49-3.40 (m, 1H), 2.76-2.68 (m, 1H), 2.64 (dd, $J = 6.4, 17.1$ Hz, 1H), 2.36 (s, 3H), 2.11 (dd, $J = 17.4, 2.9$ Hz, 1H), 1.36 (d, $J = 6.0$ Hz, 3H); ^{13}C NMR (CDCl_3) δ 205.1 (C), 176.1 (C), 132.9 (C), 79.9 (CH), 66.6 (CH_2), 51.3 (CH), 38.8 (CH_2), 19.4 (CH_3), 14.6 (CH_3); IR (thin film) 1709, 1629, 1442, 1067 cm^{-1} ; high resolution mass spectrum calcd for $\text{C}_9\text{H}_{12}\text{O}_2\text{S}$ (M^+) 184.0558, found 184.0556.

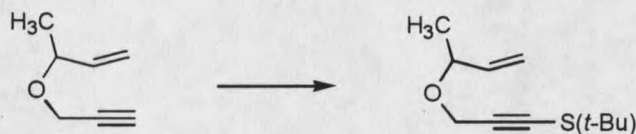
Cis-3a,4-dihydro-3-methyl-6-methylthio-1*H*-cyclopenta[*c*]furan-5(3*H*)-one (**257c**).



$R_f = 0.32$ (50% EtOAc/Hex); waxy tan colored semi-solid; ^1H NMR (CDCl_3)

δ 4.59 (s with fine structure, 2H), 4.54-4.43 (m, 1H), 3.42-3.34 (m, 1H), 2.63 (dd, $J = 18.0, 6.6$ Hz), 2.40 (s, 3H), 2.17 (dd, $J = 16.7, 3.5$ Hz, 1H), 0.94 (d, $J = 6.6$ Hz, 3H); high resolution mass spectrum calcd for $\text{C}_9\text{H}_{12}\text{O}_2\text{S}$ (M^+) 184.0558, found 184.0553.

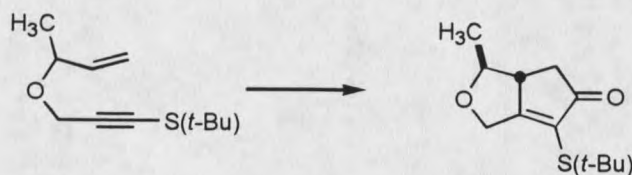
3-methyl-3-(3-[(1,1-dimethylethyl)thio]-2-propynoxy)-1-propene (**258a**).



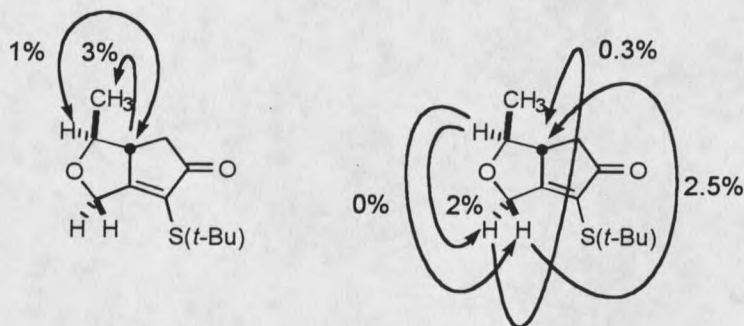
The title compound was prepared from 146 mg (1.3 mmol) of enyne **256a** as described for the preparation of **236a** to afford 186 mg (71%) of **258a** as a slightly yellow oil: $R_f = 0.31$ (5% EtOAc/Hex); ^1H NMR (CDCl_3) δ 5.65 (ddd, $J = 17.5, 10.2, 7.6$ Hz, 1H), 5.21-5.10 (m, 2H), 4.28 (d, 16.4 Hz, 1H), 4.15 (d, $J = 16.4$ Hz, 1H), 4.10-3.99 (m, 1H), 1.36 (s, 9H), 1.23 (s, 3H), 1.20 (s, 3H); ^{13}C NMR (CDCl_3) δ 139.4 (CH), 117.0 (CH_2), 93.9 (C), 75.7 (C), 75.4 (CH), 56.3 (CH_2), 47.7 (C),

30.3 (CH₃), 21.2 (CH₃); IR (thin film) 3079, 2175, 1643, 1366, 1083 cm⁻¹; high resolution mass spectrum calcd for C₁₁H₁₈OS (M⁺) 198.1078, found 198.1071.

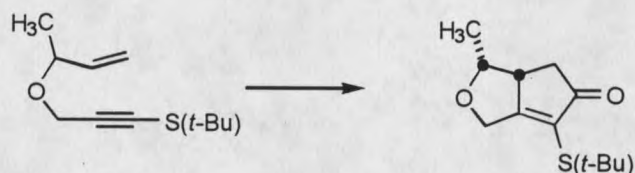
Trans-3a,4-dihydro-6-[(1,1-dimethylethyl)thio]-3-methyl-1*H*-cyclopenta[*c*]furan-5(3*H*)-one (**258b**).



Enyne **258a** (40 mg, 0.20 mmol) was cyclized according to general procedure B except that gradient flash chromatography was performed with 5-10% EtOAc/Hex for elution to afford 35 mg (78%) of a 41.6 to 1 diastereomeric mixture of bicyclopentenones **258b** and **258c** as determined by G.C. analysis of the crude reaction mixture. **258b**: colorless needles, mp 70-71 °C; ¹H NMR (CDCl₃) δ 4.76 (dd, *J* = 17.0, 1.0 Hz, 1H), 4.61 (dt, *J* = 17.0, 1.2 Hz, 1H), 3.56-3.47 (m, 1H), 2.89-2.82 (m, 1H), 2.73 (dd, *J* = 17.6, 6.6 Hz, 1H), 2.15 (dd, *J* = 17.1, 3.6 Hz, 1H), 1.40 (d, *J* = 6.0 Hz, 3H), 1.27 (s, 9H); ¹³C NMR (CDCl₃) δ 205.4 (C), 191.2 (C), 129.4 (C), 79.9 (CH), 67.0 (CH₂), 50.7 (CH), 48.4 (C), 38.4 (CH₂), 31.7 (CH₃), 19.2 (CH₃); IR (thin film) 1713, 1633, 1365 cm⁻¹; high resolution mass spectrum calcd for C₁₂H₁₈O₂S (M⁺) 226.1028, found 225.1021. The structural assignment is consistent with the following NOE data:

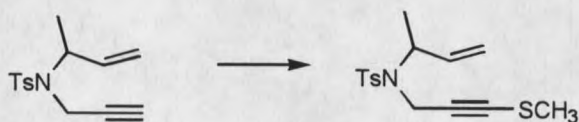


Cis-3a,4-dihydro-6-[(1,1-dimethylethyl)thio]-3-methyl-1*H*-cyclopenta[*c*]furan-5(3*H*)-one (**258c**).



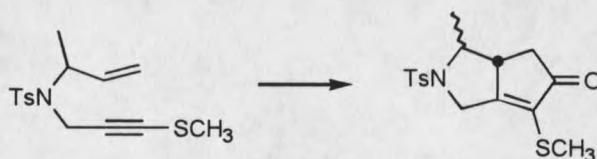
^1H NMR (CDCl_3) δ 4.67 (s with fine structure, 2H), 4.64 (m, 1H), 3.54-3.95 (m, 1H), 2.71 (dd, $J = 17.9, 6.7$ Hz, 1H), 2.22 (dd, $J = 17.9, 4.0$ Hz, 1H) 1.2 (s, 9H), 0.95 (d, $J = 6.6$ Hz, 3H); high resolution mass spectrum calcd for $\text{C}_{12}\text{H}_{18}\text{O}_2\text{S}$ (M^+) 226.1028, found 225.1034.

N-(1-Methyl-2-propenyl)-*N*-(3-methylthio-2-propynyl)-4-methylphenylsulfonamide (**261a**).



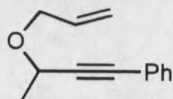
The title compound was prepared by alkylation of enyne **195a** (132 mg, 0.5 mmol) according to the general procedure utilized for **231a** to afford 66 mg (43%) of **261a** as a yellow oil: ^1H NMR (CDCl_3) δ 7.76 (d, $J = 8.2$ Hz, 2H), 7.27 (d, $J = 8.2$ Hz, 2H), 5.78-5.68 (m, 1H), 5.13-5.08 (m 2H), 4.57-4.49 (m, 1H), 4.20 (d, $J = 18.7$ Hz, 1H), 3.95 (d, $J = 18.7$ Hz, 1H), 2.39 (s, 3H), 2.21 (s, 3H), 1.20 (d, $J = 6.9$ Hz, 3H); ^{13}C NMR (CDCl_3) δ 143.1 (C), 138.1 (C), 137.6 (CH), 129.3 (CH), 127.3 (CH), 116.8 (CH_2), 89.1 (C), 75.9 (C), 54.8 (CH), 33.7 (CH_2), 21.4 (CH_3), 18.6 (CH_3), 17.1 (CH_3); IR (thin film) 3087, 3067, 2187, 1639, 1597, 1336, 1157 cm^{-1} ; high resolution mass spectrum calcd for $\text{C}_{15}\text{H}_{19}\text{NO}_2\text{S}_2$ (M^+) 309.0857, found 309.0864.

2,3,3a,4-tetrahydro-2-[(4-methylphenyl)sulfonyl]-3-methyl-6-methylthio-cyclopenta[c]pyrrol-5(1H)-ones (**261b,c**).



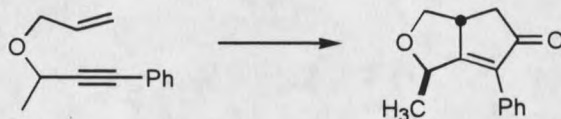
Enyne **261a** (33 mg, 0.11 mmol) was cyclized according to general procedure B, to afford 31 mg (87%) of a 1.4 to 1 diastereomeric mixture of bicyclopentenones **261b** and **261c** as determined by G.C. analysis of the crude reaction mixture. Due to the poor diastereoselection observed, the inseparable tosamides were not further characterized.

3-(1-Methyl-3-phenyl-2-propynloxy)-1-propene (**264a**).



^1H NMR (CDCl_3) δ 7.50-7.49 (m, 2H), 7.44-7.28 (m, 3H), 6.02-5.90 (m, 1H), 5.39-5.19 (m, 2H), 4.43 (q, $J = 6.7$ Hz, 1H), 4.33 (app dd, $J = 11.2, 5.1$ Hz), 4.05 (app dd, $J = 12.5, 6.3$ Hz, 1H), 1.53 (d, $J = 6.7$ Hz, 3H); ^{13}C NMR (CDCl_3) δ 134.6 (CH), 131.7 (CH), 128.2 (CH), 124.9 (C), 122.8 (C), 117.2 (CH_2), 89.0 (C), 85.0 (C), 69.6 (CH_2), 65.0 (CH), 22.2 (CH_3); IR (thin film) cm^{-1} .

Trans-3a,4-dihydro-1-methyl-6-phenyl-1*H*-cyclopenta[*c*]furan-5(3*H*)-one (**264b**).

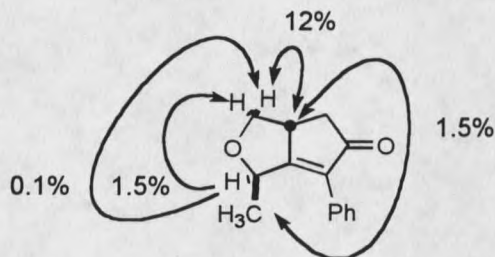


Enyne **264a** (93 mg, 0.5 mmol) was cyclized according to general procedure C except that the alkyne and $\text{Co}_2(\text{CO})_8$ were precomplexed 1 h before irradiation to afford 106 mg (99%) of a 50 to 1 diastereomeric mixture of bicyclopentenones

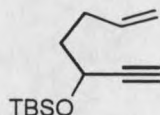
264b and **264c** as determined by G.C. analysis of the crude reaction mixture. **264b**:

^1H NMR (CDCl_3) δ 7.50-7.30 (m, 5H), 4.84 (q, $J = 6.5$ Hz, 1H), 4.34 (t, $J = 7.6$ Hz, 1H), 3.42-3.33 (m, 1H), 3.24 (dd, $J = 11.0, 7.6$ Hz, 1H), 2.78 (dd, 18.0, 6.3 Hz), 2.26 (dd, $J = 18.0, 3.5$ Hz, 1H), 1.54 (d, $J = 6.4$ Hz, 3H); ^{13}C NMR (CDCl_3) δ 207.0 (C), 179.9 (C), 134.7 (C), 130.8 (C), 128.4 (CH), 128.3 (CH), 72.3 (CH),

71.2 (CH₂), 41.7 (CH), 39.6 (CH₂), 21.2 (CH₃); IR (thin film) 3057, 1744, 1710, 1496, 1445, 1133, 1045 cm⁻¹. The structural assignment is consistent with the following NOE data:

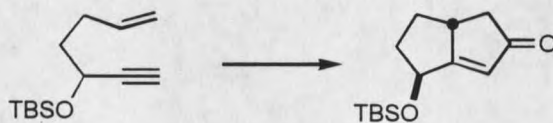


5-[[[(1,1-Dimethylethyl)dimethylsilyl]oxy]-1-hepten-6-yne (**269a**).



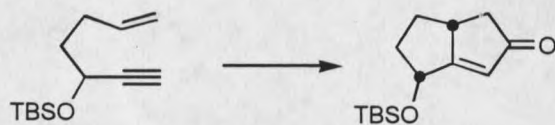
¹H NMR (CDCl₃) δ 5.78 (dddd, *J* = 16.9, 10.0, 6.5 Hz, 1H), 5.04 (m, 2H), 4.32 (dt, *J* = 6.4, 2.0 Hz, 1H), 2.35-2.12 (m, 3H), 1.77-1.68 (m, 2H), 0.86 (s, 9H), 0.14 (s, 3H), 0.08 (s, 3H); ¹³C NMR (CDCl₃) δ 137.9 (CH), 114.9 (CH₂), 85.5 (C), 72.2 (CH), 62.2 (CH), 37.8 (CH₂), 29.3 (CH₂), 25.8 (CH₂), 18.2 (C), -4.5 (CH₃), -5.0 (CH₃); IR (thin film) 3311, 3080, 1641, 1472, 1252, 1094, 837 cm⁻¹.

Trans-4-[[[(1,1-Dimethylethyl)dimethylsilyl]oxy]-4,5,6,6a-tetrahydro-2(1*H*)-pentalenone (**269b**).



Enyne **269a** (90 mg, 0.40 mmol) was cyclized according to general procedure B, except that gradient flash chromatography was performed with hexane to 10% EtOAc/Hex for elution to afford 88 mg (87%) of a 1.4 to 1 diastereomeric mixture of bicyclopentenones **269b** and **269c** as determined by G.C. analysis of the crude reaction mixture. **269b**: $R_f = 0.42$ (30% EtOAc/Hex); ^1H NMR (CDCl_3) δ 5.90 (d, $J = 2.2$ Hz, 1H); 4.72 (app t, $J = 5.6$ Hz, 1H); 3.24-3.12 (m, 1H), 2.65 (dd, $J = 18.1$, 6.3 Hz, 1H), 2.14-2.13 (m, 2H), 2.04 (dd, $J = 18.1$, 2.9 Hz, 1H), 1.94-2.81 (m, 1H), 1.11-1.08 (m, 1H), 0.86 (m, 1H), 0.09 (s, 9H), 0.05 (s, 3H); ^{13}C NMR (CDCl_3) δ 211.2 (C), 188.3 (C), 125.0 (CH), 68.5 (CH), 42.9 (CH), 42.8 (CH_2), 37.0 (CH_2), 28.5 (CH_2), 25.8 (CH_3), 18.1 (C), -4.5 (CH_3), -4.7 (CH_3); IR (thin film) 3015, 1716, 1640, 1472, 1463, 1253 cm^{-1} ; high resolution mass spectrum calcd for $\text{C}_{14}\text{H}_{24}\text{O}_2\text{Si}$ (M^+) 252.1546, found 252.1551.

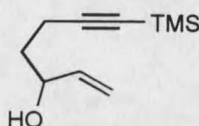
Cis-4-[[[(1,1-Dimethylethyl)dimethylsilyl]oxy]-4,5,6,6a-tetrahydro-2(1*H*)-pentalenone (**269c**).



$R_f = 0.35$ (30% EtOAc/Hex); ^1H NMR (CDCl_3) δ 5.99 (t, $J = 1.8$ Hz, 1H), 4.94 (app dd, $J = 9.4$, 4.4 Hz, 2.96-2.85 (m, 1H), 2.62 (dd, $J = 18.0$, 6.4 Hz, 1H), 2.40-2.28 (m, 1H), 2.15-2.04 (m, 2H), 1.88-1.76 (m, 1H), 1.53-1.40 (m, 1H), 0.89 (s,

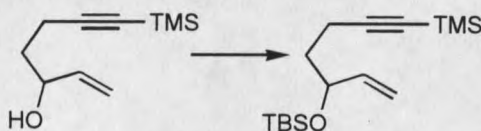
9H), 0.09 (s, 3H), 0.08 (s, 3H); ^{13}C NMR (CDCl_3) δ 210.0 (C), 192.0 (C), 124.4 (CH), 70.5 (CH), 43.5 (CH_2), 41.7 (CH), 35.5 (CH_2), 29.0 (CH_2), 25.8 (CH_3), 18.2 (C), -4.8 (CH_3), -4.9 (CH_3); IR (thin film) 1712, 1644, 1252, 1112, 838 cm^{-1} ; high resolution mass spectrum calcd for $\text{C}_{14}\text{H}_{24}\text{O}_2\text{Si}$ (M^+) 252.1546, found 252.1553.

7-(Trimethylsilyl)-1-hepten-6-yn-3-ol (**81**).



^1H NMR (CDCl_3) δ 5.85 (m, 1H, $\text{C}=\text{CH}$), 5.18 (m, 2H, $\text{C}=\text{CH}_2$), 4.25 (app q, $J = 6.2$ Hz, 1H, OCH), 2.75 (br s, 1H, OH), 2.32 (m, 2H, CH_2), 1.72 (app dd, 2H, CH_2), 0.12 (s, 9H, CH_3); ^{13}C NMR (CDCl_3) δ 140.3, 114.7, 85.0, 71.7, 35.4, 15.9, 0.0; IR (CCl_4) 3542, 3084 cm^{-1} ; high resolution mass spectrum calcd for $\text{C}_{10}\text{H}_{18}\text{OSi}$ (M^+) 182.1122, found 182.1116.

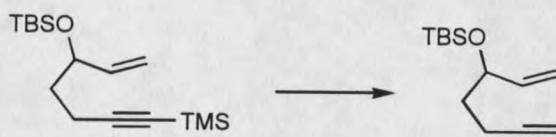
3-[(1,1-Dimethylethyl)dimethylsilyloxy]-7-(trimethylsilyl)-1-hepten-6-yne (**80**).



^1H NMR (CDCl_3) δ 5.76 (m, 1H, $\text{C}=\text{CH}$), 5.08 (m, 2H, $\text{C}=\text{CH}_2$), 4.22 (app q, $J = 6.2$ Hz, 1H, OCH), 2.25 (m, 2H, CH_2), 1.65 (m, 2H, CH_2), 0.88 (s, 9H, CH_3), 0.12 (s, 9H, CH_3), 0.05 (s, 3H, CH_3), 0.02 (s, 3H, CH_3); ^{13}C NMR (CDCl_3) δ 141.2,

114.2, 107.2, 84.7, 72.2, 36.8, 25.9, 18.2, 15.9, 0.2, -4.3, -4.8; IR (CCl₄) 3084, 2173 cm⁻¹; high resolution mass spectrum calcd for C₁₆H₃₂OSi₂ (M⁺) 296.1983, found 296.1982.

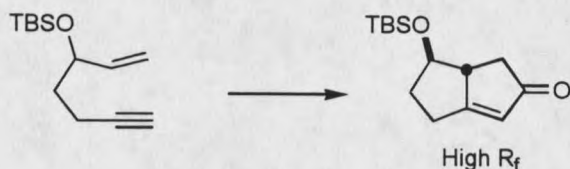
3-[(1,1-Dimethylethyl)dimethylsilyloxy]-1-hepten-6-yne (**271**).



To a solution of silyl acetylene **81** (0.593 g, 2.0 mmol) in THF (21 mL) was added pyridine (0.85 mL, 5.25 eq, 10.5 mmol), H₂O (4.5 mL), and AgNO₃ (1.07 g, 3.15 eq, 6.3 mmol). The flask was immediately flushed with Ar, sealed with a polyethylene stopper and wrapped in foil. After 1 hr G.C. analysis indicated with reaction was complete. Brine (40 mL) was then added and the heterogeneous slurry was vigorously stirred for 20 min. The mixture was then filtered through a pad of Celite and the phases were separated, and the aqueous phase was extracted with CH₂Cl₂ (3 x 20 mL). The combined organic phases were dried (MgSO₄), filtered, concentrated *in vacuo*, and *immediately* subjected to chromatography on basic alumina (hexane for elution) to afford 0.380 g (85%) of the title compound as a colorless oil: ¹H NMR (CDCl₃) δ 5.87-5.63 (m, 1H), 5.19-5.01 (m, 2H), 4.25-4.17 (m, 1H), 2.25-2.18 (m, 2H), 1.92 (t, *J* = 2.7 Hz, 1H), 0.88 (s, 3H), 0.05 (s, 3H), 0.02 (s, 3H); ¹³C NMR (CDCl₃) δ 141.1 (CH), 114.4 (CH₂), 84.5 (C), 72.3 (CH),

68.4 (CH), 36.7 (CH₂), 26.0 (CH₃), 18.3 (C), 14.4 (CH₂), -4.3 (CH₃), -4.8 (CH₃); IR (thin film) 3314, 3081, 2120, 1645, 1252, 1090, 838 cm⁻¹; high resolution mass spectrum calcd for C₁₃H₂₅OSi (M+1) 225.1661, found 225.1668.

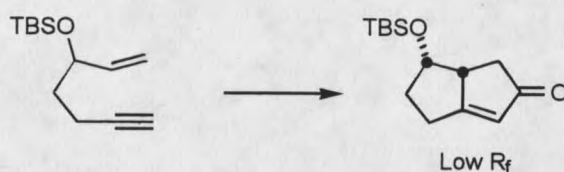
Trans-6-[[[(1,1-Dimethylethyl)dimethylsilyl]oxy]-4,5,6,6a-tetrahydro-2(1*H*)-pentalenone (**271b**).



Enyne **271a** (112 mg, 0.50 mmol) was cyclized according to general procedure C, except that 12.5 mol % Co₂(CO)₈ was employed and *immediately prior to cyclization* enyne **271a** was subjected to chromatography on basic alumina (hexane for elution). These modifications afforded 72 mg (57% optimized yield) of a 1.0 to 1 diastereomeric mixture of bicyclopentenones **271b** and **271c**. The diastereomeric ratio was determined by NMR integration of the C3-vinyl protons after minimal chromatography on silica gel. **271b**: R_f = 0.37 (20% EtOAc/Hex); ¹H NMR (CDCl₃) δ 5.85 (d, *J* = 1.2 Hz, 1H), 3.73 (app dd, *J* = 16.5, 9.0 Hz, 1H), 2.99-2.91 (br m, 1H), 2.84-2.72 (m, 1H), 2.64-2.44 (m, 2H), 2.27-2.10 (m, 3H), 0.86 (s, 9H), 0.04 (s, 6H); ¹³C NMR (CDCl₃) δ 210.3 (C), 187.0 (C), 126.5 (CH), 77.3 (CH), 53.8 (CH), 40.8 (CH₂), 35.0 (CH₂), 25.8 (C), 25.2 (CH₃), 18.0 (C), -4.6 (CH₃), -4.7 (CH₃); IR (thin film) 3074, 1715, 1639, 1623, 1255, 1082, 1048 cm⁻¹; high

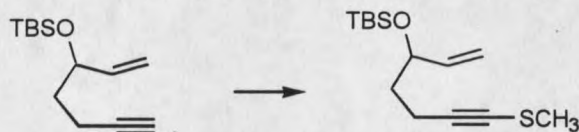
resolution (CI/NH₃) mass spectrum calcd for C₁₄H₂₅O₂Si (M+H)⁺ 253.1524, found 253.1625.

Cis-6-[[[(1,1-Dimethylethyl)dimethylsilyl]oxy]-4,5,6,6 α -tetrahydro-2(1*H*)-pentalenone (**271c**).



R_f = 0.28 (20% EtOAc/Hex); ¹H NMR (CDCl₃) δ 5.89 (d, J = 1.8 Hz, 1H), 4.20 (t, J = 3.75 Hz, 1H), 2.96-2.88 (m, 1H), 2.66-2.55 (m, 2H), 2.33-2.11 (d, J = 4.8 Hz, 2H), 2.23-2.11 (m, 1H), 2.04-1.93 (m, 1H), 0.80 (s, 9H), 0.01 (app d, J = 4.2 Hz, 6H); ¹³C NMR (CDCl₃) δ 211.9 (C), 189.4 (C), 125.6 (CH), 70.7 (CH), 52.9 (CH), 36.8 (CH₂), 36.2 (CH₂), 25.7 (CH₃), 24.3 (CH₂), 18.1 (C), -4.6 (CH₃), -5.0 (CH₃); high resolution (CI/NH₃) mass spectrum calcd for C₁₄H₂₅O₂Si (M+H)⁺ 253.1524, found 253.1628.

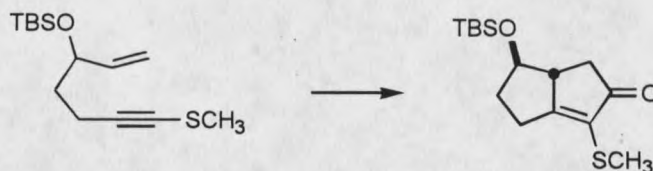
3-[[[(1,1-Dimethylethyl)dimethylsilyl]oxy]-7-methylthio-1-hepten-6-yne (**272a**).



The title compound was prepared by alkylation of enyne **271a** (224 mg, 1.0 mmol) according to the general procedure utilized for **236a** to afford 238 mg (88%) of **272a** as a yellow oil: ¹H NMR (CDCl₃) δ 5.76 (ddd, J = 17.1, 10.4, 6.0), 5.15 (app

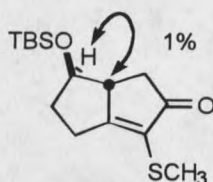
dt, $J = 17.1, 1.5$ Hz, 1H), 5.02 (app dt, $J = 10.5, 1.5$ Hz, 1H), 4.18 (app q, $J = 18.3$ Hz, 1H), 2.32 (s, 3H), 2.32-2.25 (m, 2H), 1.66-1.60 (m, 2H), 0.97 (s, 9H), 0.05 (s, 3H), 0.01 (s, 3H); ^{13}C NMR (CDCl_3) δ 141.4 (CH), 114.6 (CH_2), 93.3 (C), 72.7 (CH), 70.5 (C), 37.2 (CH_2), 26.3 (CH_3), 19.6 (CH_3), 18.6 (C), 16.4 (CH_2), -3.9 (CH_3), -4.5 (CH_3); IR (thin film) 3076, 2190, 1643, 1252, 1090, 837 cm^{-1} ; high resolution mass spectrum calcd for $\text{C}_{14}\text{H}_{26}\text{OSSi}$ (M^+) 270.1474, found 270.1483.

Trans-4-[[[(1,1-Dimethylethyl)dimethylsilyl]oxy]-3-methylthio 4,5,6,6 α -tetrahydro-2(1*H*)-pentalenone (**272b**).

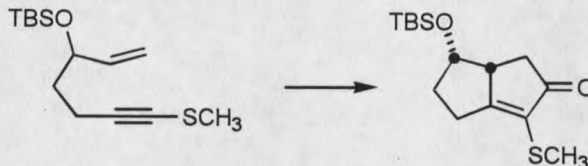


Enyne **272a** (67 mg, 0.25 mmol) was cyclized according to general procedure C, except that gradient flash chromatography was performed with 2-10% EtOAc/Hex for elution, to afford 44 mg (59%) of a 1.1 to 1 diastereomeric mixture of bicyclopentenones **272b** and **272c** as determined by G.C. analysis of the crude reaction mixture. **272b**: $R_f = 0.27$ (10% EtOAc/Hex); ^1H NMR (250 MHz, CDCl_3) δ 3.70 (app q with fine structure, 1H), 2.95-2.85 (m, 1H), 2.81-2.50 (m, 3H), 2.35 (s, 3H), 2.27-2.11 (m, 2H), 2.06-1.89 (m, 1H), 0.86 (s, 9H), 0.03 (s, 6H); ^{13}C NMR (CDCl_3) δ 205.9 (C), 180.1 (C), 132.5 (C), 77.3 (CH), 52.3 (CH), 40.5 (CH_2), 34.9

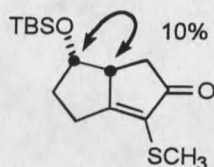
(CH₂), 25.7 (CH₃), 25.4 (CH₂), 18.0 (C), 14.3 (CH₃), -4.6 (CH₃), -4.7 (CH₃); IR (thin film) 1707, 1622, 1471, 1254, 836 cm⁻¹; high resolution mass spectrum calcd for C₁₅H₂₆O₂SiS (M⁺) 298.2423, found 298.1423. The indicated stereochemistry is consistent with the following NOE data:



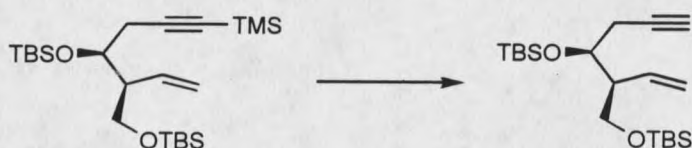
Cis-4-[[[(1,1-Dimethylethyl)dimethylsilyl]oxy]-3-methylthio-4,5,6,6a-tetrahydro-2(1*H*)-pentalenone (**272c**).



R_f = 0.15 (10% EtOAc/Hex); ¹H NMR (CDCl₃) δ 4.23 (app t, J = 3.6 Hz, 1H), 2.91-2.86 (m, 1H), 2.73-2.50 (m, 2H), 2.41-2.36 (m, 2H), 2.31 (s, 3H), 2.22-2.08 (m, 1H), 2.04-1.97 (m, 1H), 0.79 (s, 9H), 0.02 (s, 3H), 0.01 (s, 3H); ¹³C NMR (CDCl₃) δ 207.4 (C), 184.1 (C), 131.4 (C), 70.6 (CH), 51.3 (CH), 36.3 (CH₂), 35.9 (CH₂), 25.6 (CH₃), 24.5 (CH₂), 18.1 (C), 14.8 (CH₂), -4.6 (CH₂), -5.0 (CH₂); IR (thin film) cm⁻¹; high resolution mass spectrum calcd for C₁₅H₂₆O₂SiS (M⁺) 298.2423, found 298.1426. The indicated stereochemistry is consistent with the following NOE data:



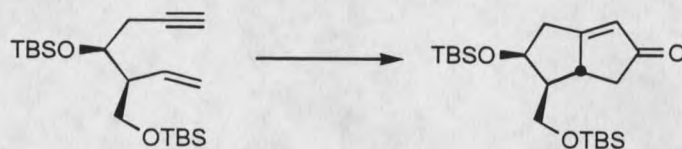
(3*S*,4*S*)-3-[[[(1,1-dimethylethyl)dimethylsilyl]oxymethyl]-4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-hept-1-ene-6-yne (**280a**).



To a solution of **148** (163 mg, 0.37 mmol) in MeOH (4 mL) was added NaOH (1.4 mg, 10 mol %). The reaction vessel was subsequently flushed with Ar, sealed with a polyethylene stopper and the solution was stirred for 24 h. The resulting solution was concentrated *in vacuo* and the residue was purified by chromatography on silica gel (5-10% EtOAc/Hex gradient for elution) to afford 123 mg (90%) of the title compound as a colorless oil. ^1H NMR (CDCl_3) δ 5.75-5.63 (m, 1H), 5.19-5.13 (m, 2H), 4.09 (ddd, $J = 8.0, 5.9, 2.0$ Hz, 1H), 3.63 (dd, $J = 10.0, 8.7$ Hz, 1H), 3.50 (dd, $J = 10.0, 6.1$ Hz, 1H), 2.56-2.48 (m, 1H), 2.32-2.27 (m, 2H), 1.94 (t, $J = 2.7$ Hz, 1H), 0.87 (s, 9H), 0.86 (s, 9H), 0.06 (s, 6H), 0.03 (s, 3H), 0.02 (s, 3H); ^{13}C NMR (CDCl_3) δ 134.6 (CH), 118.6 (CH_2), 81.5 (CH), 70.0 (C), 69.4 (CH), 63.4 (CH_2), 50.0 (CH), 25.9 (CH_3), 25.8 (CH_3), 25.5 (CH_2), 18.0 (C), -4.3 (CH_3), -4.9 (CH_3), -5.2 (CH_3), -5.3 (CH_3); IR (thin film) 3315, 3078, 2129, 1640, 1472, 1256,

1101, 836, cm^{-1} ; high resolution (CI/ NH_3) mass spectrum calcd for $\text{C}_{20}\text{H}_{41}\text{O}_2\text{Si}_2$ ($\text{M}+\text{H}^+$) 369.2645, found 369.2641.

(5*S*,6*S*,6*aR*)-5-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-4-[[[(1,1-dimethylethyl)dimethylsilyl]oxymethyl]-4,5,6,6*a*-tetrahydro-2(1*H*)-pentalenone (280b).



A solution of **280a** (57 mg, 0.15 mmol) and $\text{Co}_2(\text{CO})_8$ (5.2 mg, 10 mol %) in 1,2-DME was stirred under a CO atmosphere for 30 min, whereupon the resulting red solution was Q-Beam irradiated for 24 h. G.C. analysis of several aliquots indicated that the reaction stopped at 50% conversion so an additional portion of $\text{Co}_2(\text{CO})_8$ was added (5.2 mg in 0.5 mL 1,2-DME, 10 mol %, 20 mol % total). After a further 12 h of irradiation the reaction was complete. The resulting solution was concentrated *in vacuo* and the residue was purified by chromatography on silica gel (EtOAc/Hex gradient for elution) to afford 43 mg (70%) of the title compound as a colorless oil and as a single diastereomer: R_f = 0.58 (30% EtOAc/Hex); ^1H NMR (CDCl_3) δ 5.86 (app q, J = 1.7 Hz, 1H), 4.48 (app t, J = 4.9 Hz, 1H), 3.86 (dd, J = 10.0, 6.4 Hz, 1H), 3.70 (dd, J = 10.0, 7.6 Hz, 1H), 3.11-3.03 (m, 1H), 2.90 (dd, J = 20.0, 5.5 Hz), 2.64-2.51 (m, 2H), 2.15 (dd, J = 18.1, 3.3 Hz, 1H), 1.62-1.51 (m,

1H), 0.86 (s, 18H), 0.05 (s, 6H), 0.01 (s, 6H); ^{13}C NMR (CDCl_3) δ 210.4 (C), 188.0 (C), 125.5 (CH), 73.9 (CH), 62.7 (CH_2), 53.6 (CH), 47.3 (CH), 42.2 (CH_2), 39.0 (CH_2), 25.9 (CH_3), 25.7 (CH_3), 18.2 (C), 18.0 (C), -4.6 (CH_3), -5.1 (CH_3), -5.3 (CH_3); IR (thin film) 1713, 1636, 1472, 1256, 1067, 853 cm^{-1} ; high resolution mass spectrum calcd for $\text{C}_{21}\text{H}_{41}\text{Si}_2$ (M^+) 397.2554, found 397.2582.

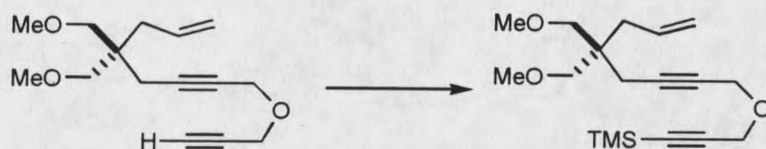
(4*S*)-3-(4'-chlorobutanoyl)-4-(methylethyl)-1,3-oxazolidin-2-one.



A solution of oxazoline **128** (3.25 g, 13.9 mmol) and NaI (2.71 g, 15.0 mmol) in acetone (20 mL) was gently heated to reflux for 36 h in the dark, after which time H_2O (20 mL) was added and the mixture was concentrated *in vacuo*. The residue was dissolved in CH_2Cl_2 (50 mL) and was subsequently washed with half-saturated $\text{Na}_2\text{S}_2\text{O}_3$ (10 mL), saturated aqueous NaHCO_3 (10 mL) and brine (10 mL). The solution was dried (MgSO_4), filtered and concentrated *in vacuo*. The solid residue was recrystallized from toluene/hexane to afford 4.20 g (93%) of the title compound as yellow needles. mp 63–65 °C (toluene/hexane) ^1H NMR (CDCl_3) δ 4.38 (app p, $J = 3.9$ Hz, 1H), 4.25 (t, $J = 8.6$ Hz, 1H), 4.19 (dd, $J = 9.1, 3.2$ Hz, 1H), 3.23 (t, $J = 6.9$ Hz, 2H), 3.12–2.94 (m, 2H), 2.37–2.27 (m, 1H), 2.14 (app p, $J = 6.9$ Hz, 2H), 0.87 (d, $J = 7.1$ Hz, 3H), 0.83 (d, $J = 6.9$ Hz, 3H); ^{13}C NMR (CDCl_3) δ 171.6 (C),

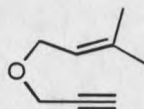
154.0 (C), 63.4 (CH₂), 58.4 (CH), 36.2 (CH₂), 28.3 (CH), 27.8 (CH₂), 17.9 (CH₃), 14.6 (CH₃), 5.3 (CH₂); IR (thin film) 1786, 1698, 1488, 1388, 1209 cm⁻¹.

Bis-(5,5-methoxymethyl)-1-[3-(trimethylsilyl)-2-propynoxy]-oct-7-en-2-yne (**292**).



The title compound was prepared by the general procedure utilized for **51**. ¹H NMR (CDCl₃) δ 5.49-5.35 (m, 1H, CH=CH₂), 4.76-4.69 (m, 2, CH=CH₂), 3.88 (s, with fine structure, 4H, CH₂OCH₂), 2.95 (s, 6H, 2 CH₃O), 2.90-2.84 (m, 4H, 2 CH₂O), 1.87 (t, *J* = 2.0 Hz, CH₂C≡C), 1.79 (d, *J* = 7.5 Hz, 2H, CH₂CH), -0.18 (s, 9H, Si(CH₃)); ¹³C NMR (CDCl₃) δ 133.8 (CH), 117.9 (CH₂), 100.9 (C), 91.6 (C), 84.3 (C), 77.0 (C), 74.4 (CH₂), 59.2 (CH₃), 56.9 (CH₂), 56.8 (CH₂), 41.8 (C), 36.4 (CH₂), 22.4 (CH₂), -0.2 (CH₃); IR (thin film) 3076, 2958, 2810, 2751, 2174, 1639, 1446, 1345, 1251, 1109, 1051, 1044, 917, 844, 760 cm⁻¹.

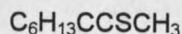
1,1-Dimethyl-3-(2-propynloxy)-1-propene (**293**).



¹H NMR (CDCl₃) δ 5.33-5.28 (m, 1H), 4.08 (d, *J* = 2.4 Hz, 2H), 4.02 (d, *J* = 7.1 Hz, 2H), 2.39 (t, *J* = 2.4 Hz, 1H), 1.72 (s, 3H), 1.67 (s, 3H); ¹³C NMR (CDCl₃)

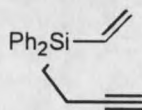
δ 138.1 (C), 120.3 (CH), 80.1 (CH), 74.0 (C), 66.0 (CH₂), 56.8 (CH₂), 25.7 (CH₃), 18.0 (CH₃); IR (thin film) 3298, 2115, 1674, 1442, 1075 cm⁻¹.

1-(Methylthio)-1-octyne (**296**).



¹H NMR (CDCl₃) δ 2.32 (s, 3H), 2.25 (t, J = 7.0 Hz, 2H), 1.47 (p, J = 7.3 Hz, 2H), 1.26-1.21, m, 6H), 0.86 (t, J = 6.7 Hz, 3H); ¹³C NMR (CDCl₃) δ 93.3 (C), 69.7 (C), 31.3 (CH₂), 28.7 (CH₂), 22.5 (CH₂), 20.0 (CH₂), 19.3 (CH₃), 14.0 (CH₃); IR (thin film) 1466, 1312, 976 cm⁻¹.

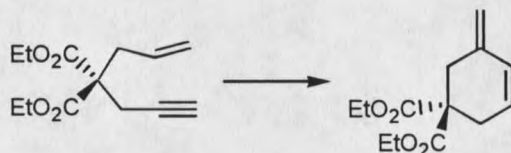
3-Butenyl-2-diphenyl-1-ethenylsilane (**297a**).



A solution of 4-trimethylsilyl-3-butenylmagnesium bromide (4.8 mmol) in THF (5 mL) was added vinyl-diphenylchlorosilane (4.4 mmol, 1.07 g) neat and the resulting solution was heated to reflux for 7 h. The resulting solution was treated with H₂O (15 mL) and 50% Et₂O-hexane (15 mL) and the organic layer was separated. The aqueous layer was extracted with 50% Et₂O-hexane (2 x 10 mL) and the combined organic layers were dried (MgSO₄), filtered, concentrated *in vacuo* and filtered through a silica gel plug (1 cm d x 3 cm, 20% EtOAc/hexane for elution) to afford 1.51 g of a colorless oil. A portion of this oil (483 mg, 1.44 mmol) was dissolved

in MeOH (5 mL) and a pellet of NaOH (97 mg, 1.7 mmol) was added and the resulting solution was vigorously stirred for 4 h after which time the resulting solution was treated with H₂O (50 mg, 2.7 mmol) and concentrated *in vacuo*. The residual material was purified by flash chromatography on silica gel (5% EtOAc/hexane for elution) to afford 0.215 g (57%, two steps) of the title compound as a thick, slightly yellow oil. ¹H NMR (CDCl₃) δ 7.57-7.26 (m, 10H), 6.49 (dd, *J* = 20.2, 14.7 Hz, 1H), 6.25 (dd, *J* = 14.7, 3.7 Hz, 1H), 5.80 (dd, *J* = 20.2, 3.7 Hz, 1H), 2.28 (dt with fine structure, *J* = 2.6, 8.6 Hz, 2H), 1.95 (t, *J* = 2.6 Hz, 1H), 1.50 (t with fine structure, *J* = 8.4 Hz, 2H); ¹³C NMR (CDCl₃) δ 136.3 (CH₂), 135.2 (CH), 133.9 (CH), 133.7 (C), 129.6 (CH), 127.9 (CH), 86.4 (C), 67.8 (CH), 13.2 (CH₂), 12.9 (CH₂); IR (thin film) 3301, 3068, 3049, 2115, 1589, 1428, 1112, 900 cm⁻¹.

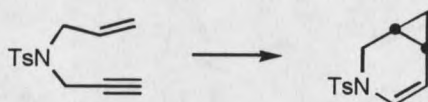
Rhodium derived cyclohexadiene (**298**).



¹H NMR (CDCl₃) δ 6.43 (dd, *J* = 17.5, 10.6 Hz, 1H), 5.53 (s, 1H), 5.07 (d, *J* = 6.0 Hz, 1H), 5.03 (s, 1H), 4.16 (q, *J* = 7.1 Hz, 4H), 3.06 (app d, *J* = 8.4 Hz, 2H), 1.21 (t, *J* = 7.1 Hz, 6H); ¹³C NMR (CDCl₃) δ 171.9 (C), 140.0 (C), 132.4 (CH), 126.8

(CH), 114.8 (CH₂), 61.4 (CH₂), 58.8 (C), 40.7 (CH₂), 39.1 (CH₂), 13.9 (CH₃); IR (thin film) 3090, 3049, 1733, 1644, 1596, 1250 cm⁻¹.

Rhodium derived cyclopropane (**299**).



¹H NMR (CDCl₃) δ 7.62 (d, *J* = 8.1 Hz, 2H), 7.28 (d, *J* = 8.1 Hz, 2H), 6.30 (d, *J* = 8.1 Hz, 1H), 5.37 (dd, *J* = 8.1, 5.5 Hz, 1H), 3.85 (d, *J* = 11.5 Hz, 1H), 3.02 (dd, *J* = 11.5 Hz, 1H), 2.40 (s, 3H), 1.55-1.47 (m, 1H), 1.14-1.05 (m, 1H), 0.77 (app dt, *J* = 8.3, 4.6 Hz, 1H), 0.32 (app q, *J* = 4.8 Hz, 1H); ¹³C NMR (CDCl₃) δ 143.6 (C), 135.1 (C), 129.7 (CH), 127.0 (CH), 121.2 (CH), 111.9 (CH), 40.9 (CH₂), 21.5 (CH₃), 18.3 (CH), 13.4 (CH₂), 7.1 (CH); IR (thin film) 3103, 3076, 3006, 1936, 1645, 1343, 1175, 1105 cm⁻¹; high resolution mass spectrum calcd for C₁₃H₁₅NO₂S (M⁺) 239.0823, found 239.0816.

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- ¹ (a) Negishi, E.; Holmes, S. J.; Tour, M. J.; Miller, J. A. *J. Am. Chem. Soc.* **1985**, 107, 2568. (b) For the first example with an anionic terminal acetylene, see: Takahashi, T.; et al. *J. Chem. Soc., Chem. Commun.* **1995**, 1503.
- ² (a) Negishi, E.; Cederbaum, F. E.; Takahashi, T. *Tetrahedron Lett.* **1986**, 27, 2829. (b) For a detailed mechanistic analysis of zirconocene formation and early

- review, see: Negishi, E.; Holmes, S. J.; Tour, J. M.; Miller, J. A.; Cederbaum, F. E.; Swanson, D. R.; Takahashi, T. *J. Am. Chem. Soc.* **1989**, *111*, 3336.
- ³ For a recent review, see: Negishi, E.; Takahashi, T. *Acc. Chem. Res.* **1994**, *27*, 124.
- ⁴ (a) Negishi, E.; Swanson, D. R.; Cederbaum, F. E.; Takahashi, T. *Tetrahedron Lett.* **1987**, *28*, 917. (b) For a review see: Negishi, E.; Takahashi, T. *Synthesis* **1988**, 1.
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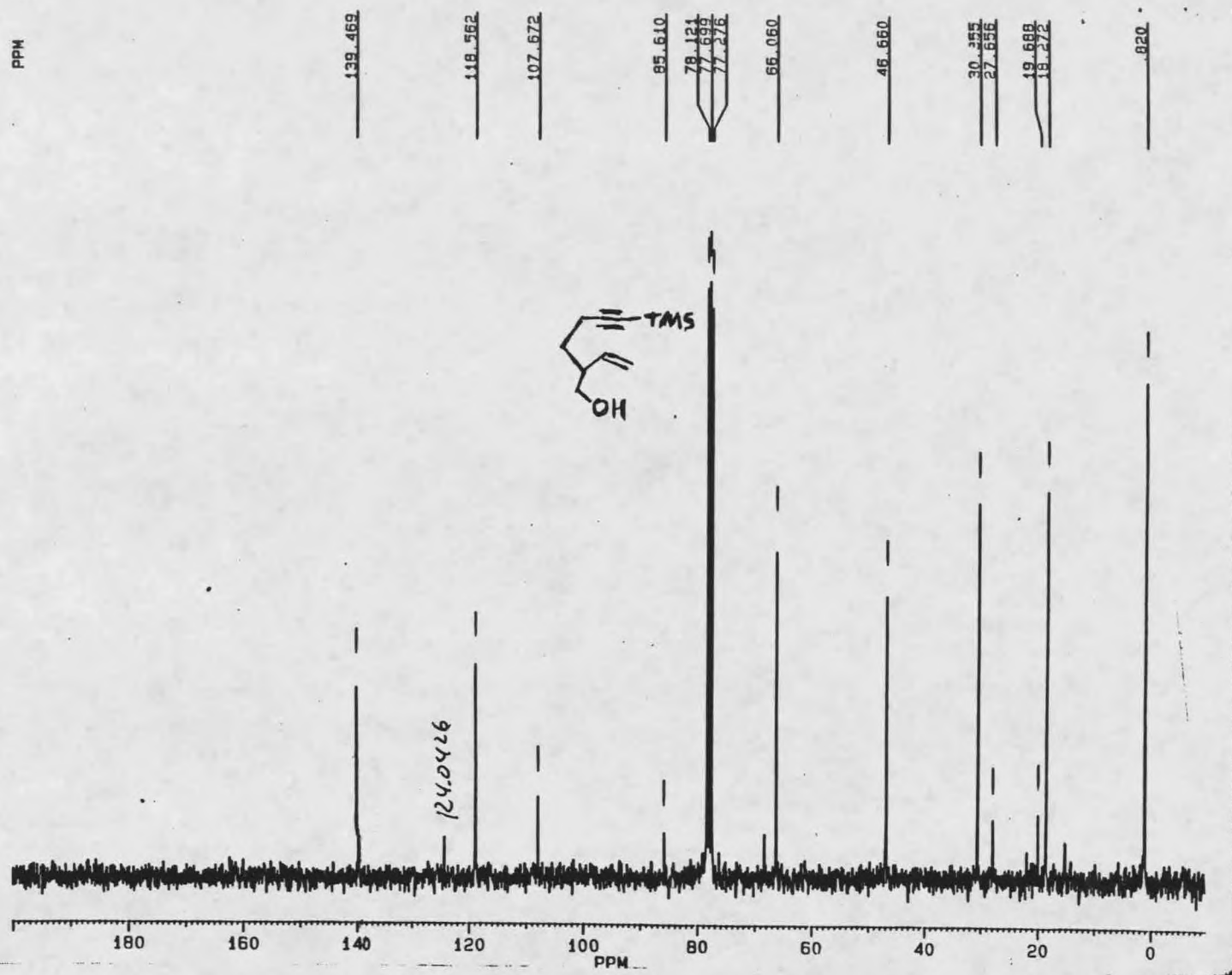
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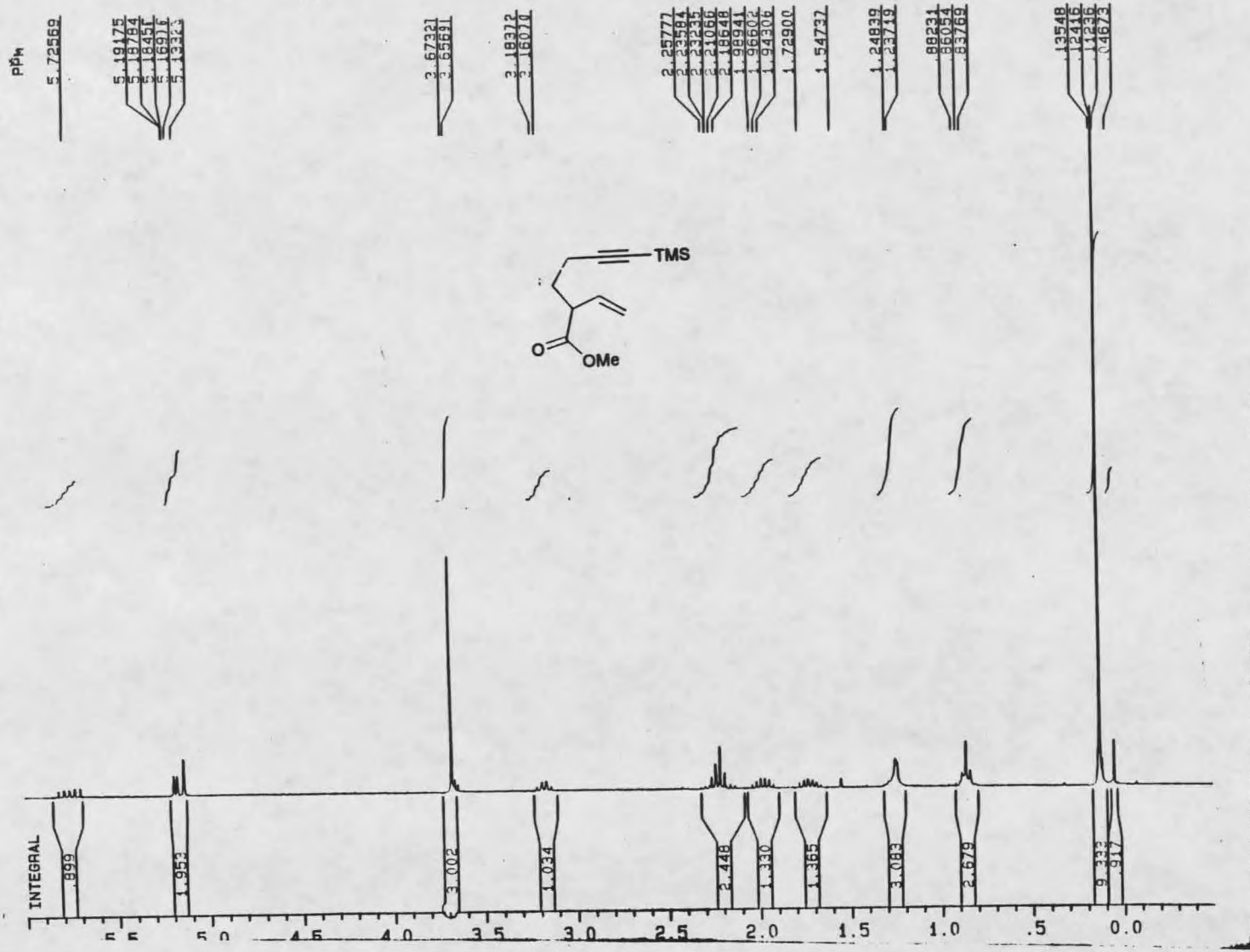
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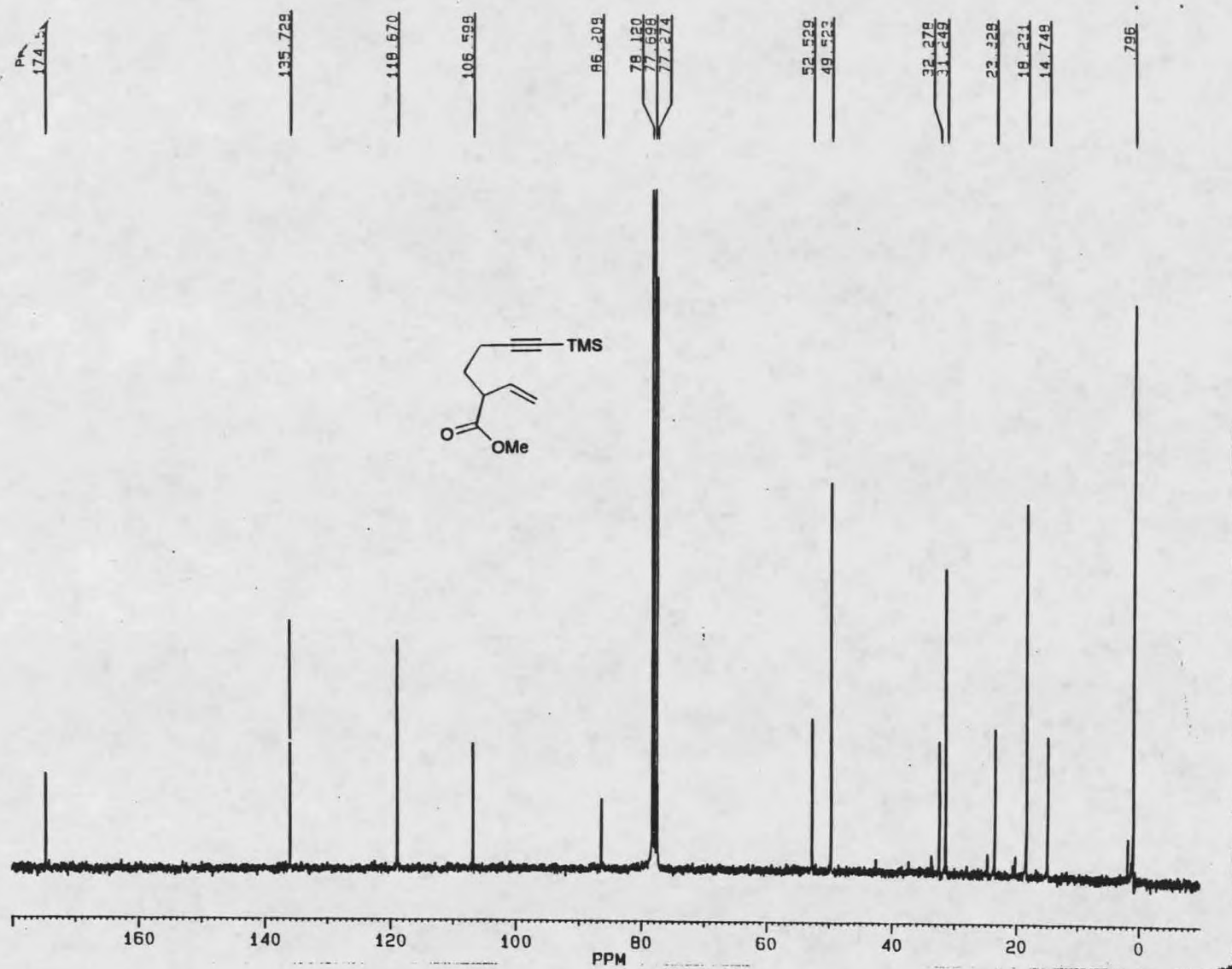
- ¹¹⁴ (a) For the preparation of SEM ethers, see: Lipshutz, B. H.; Pegram, J. J. *Tetrahedron Lett.* **1980**, *21*, 3343. (b) For an improved procedure for the removal of SEM ethers, see: Lipshutz, B. H.; Miller, T. A. *Tetrahedron Lett.* **1989**, *30*, 7149.
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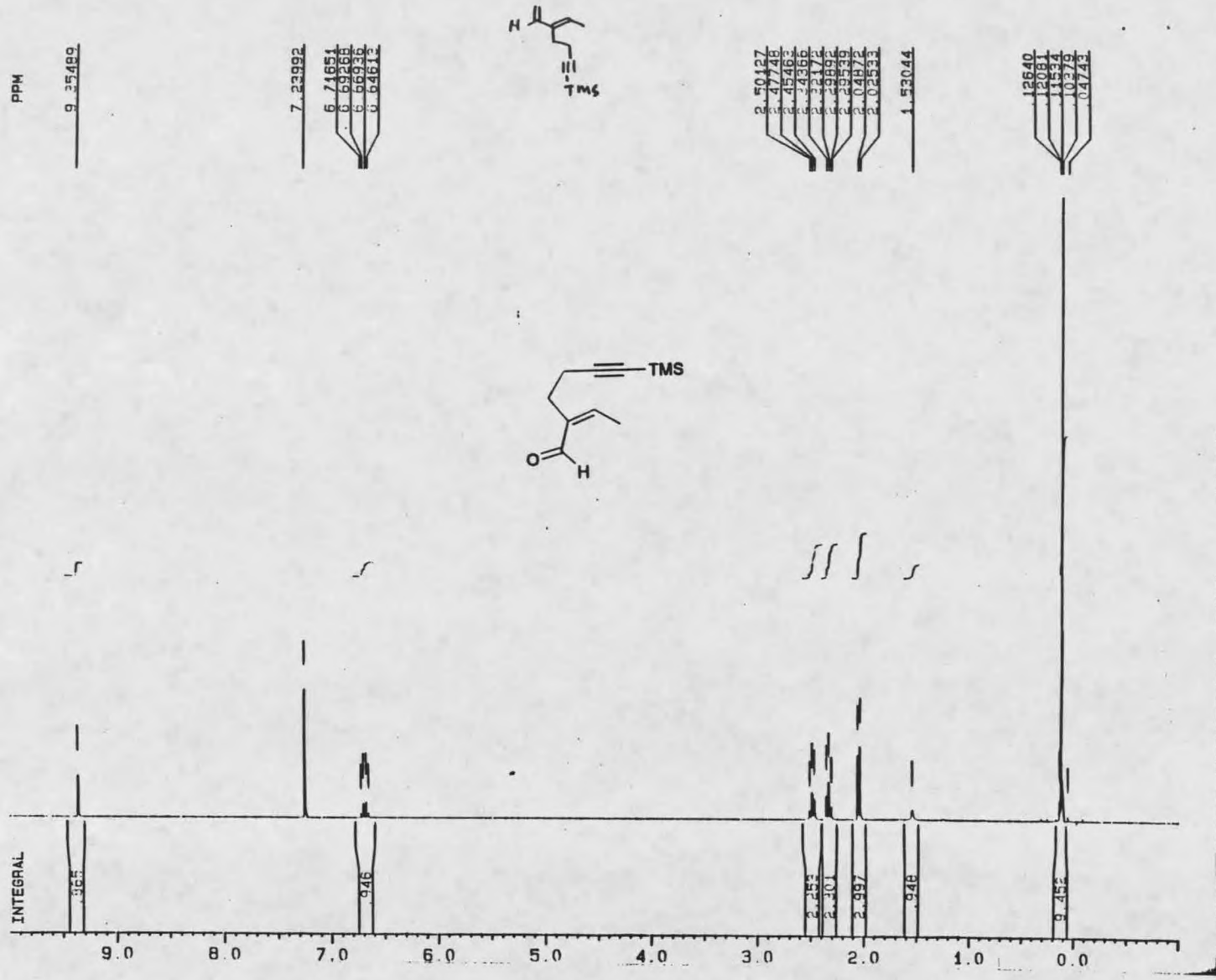
Appendix

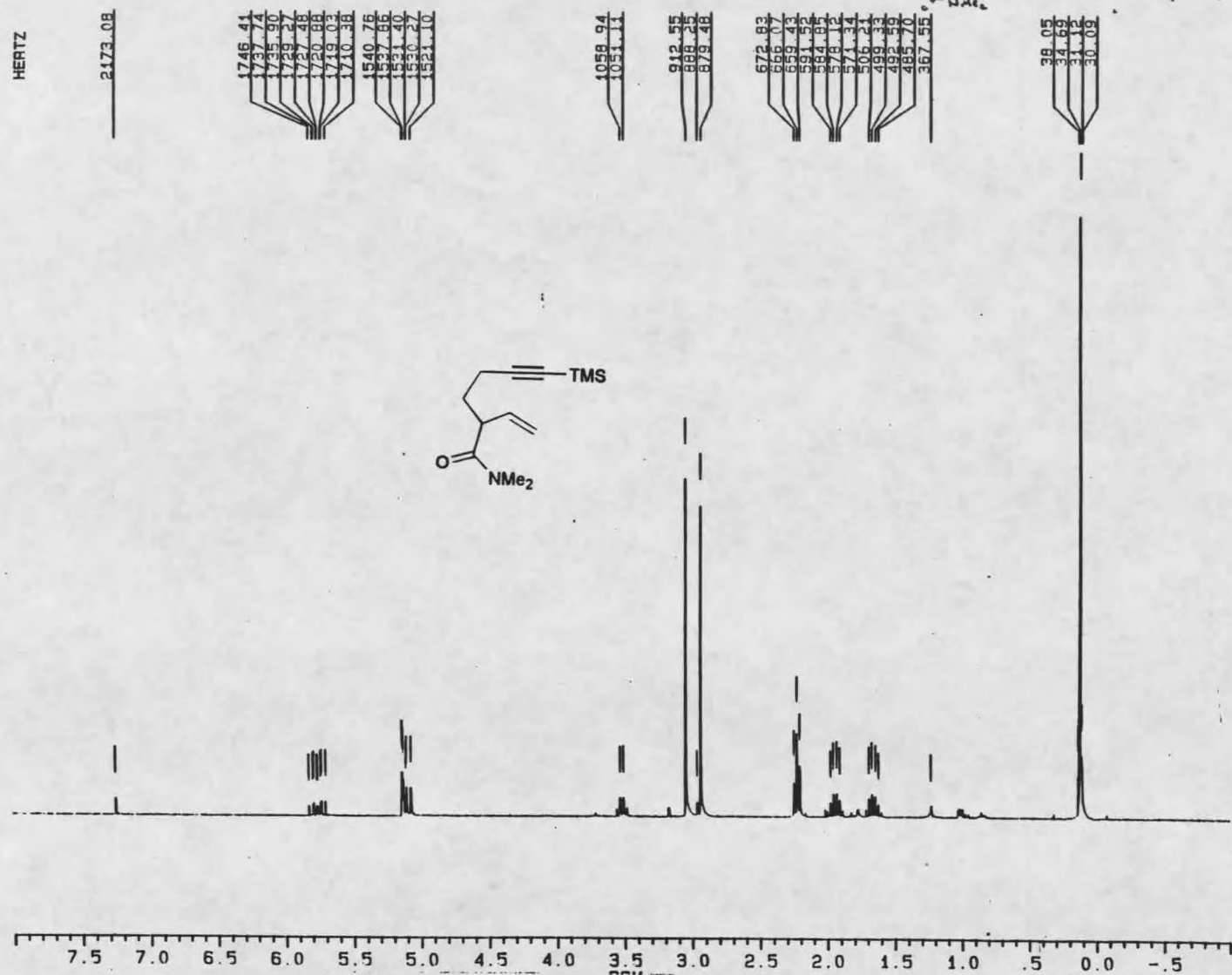


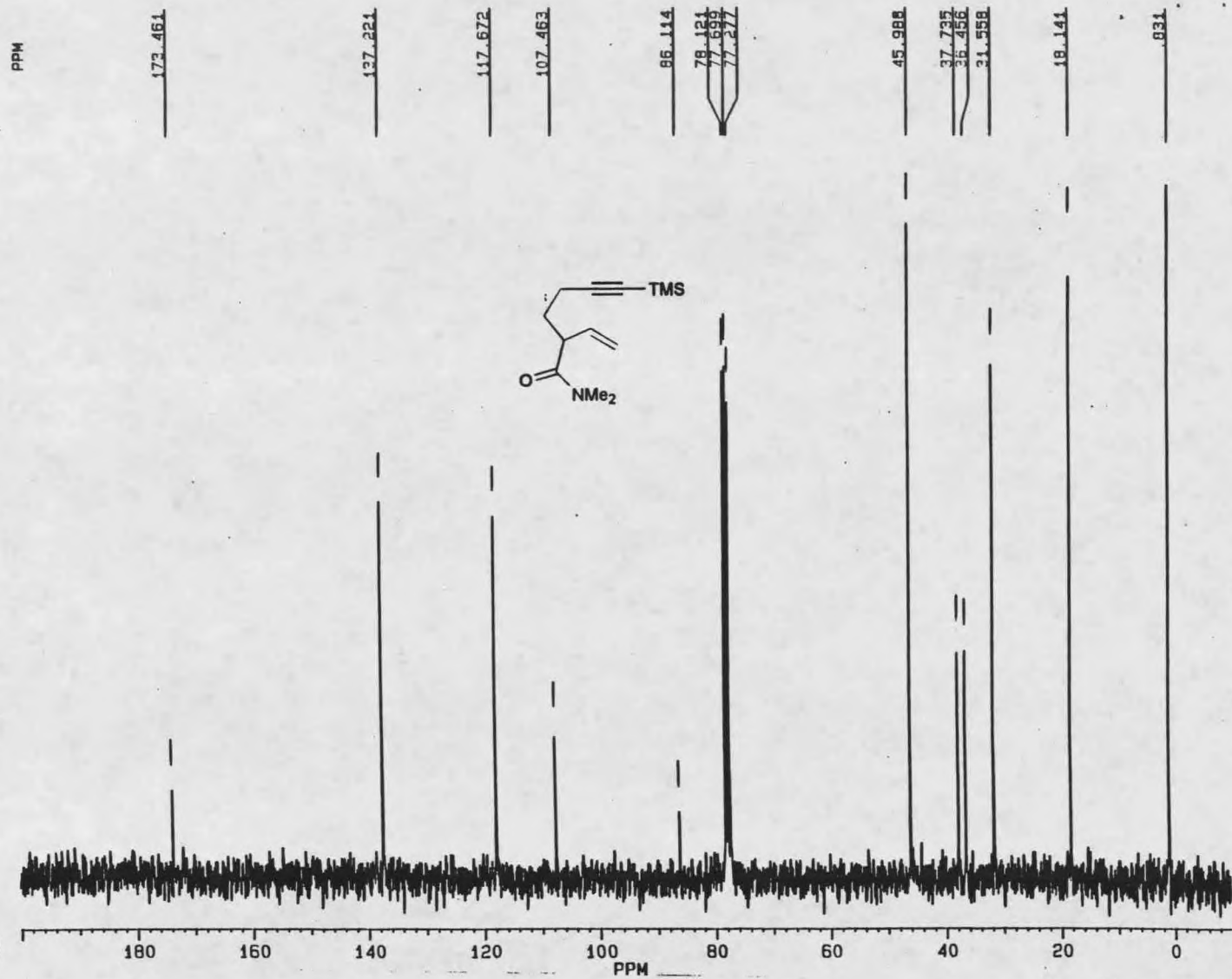






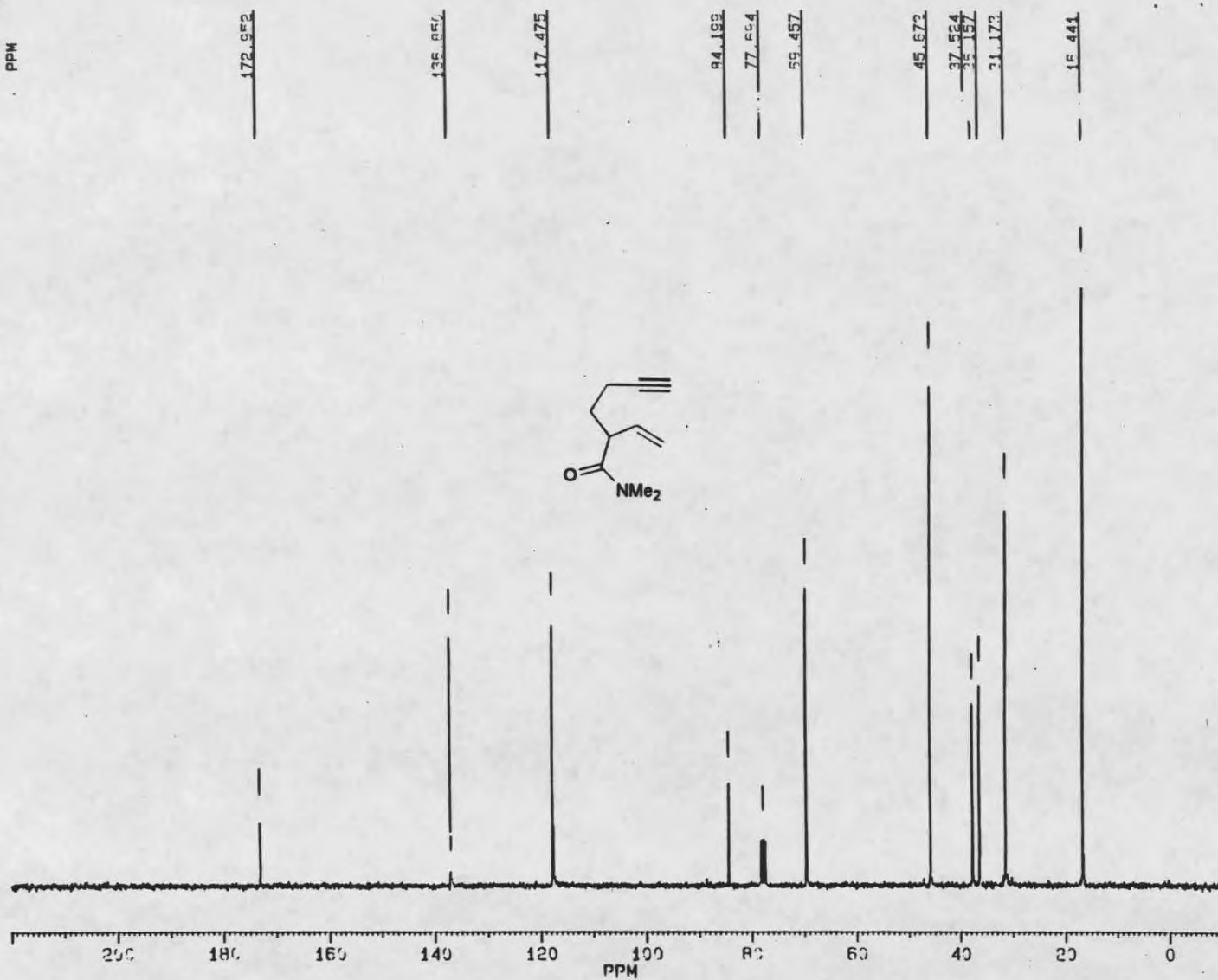


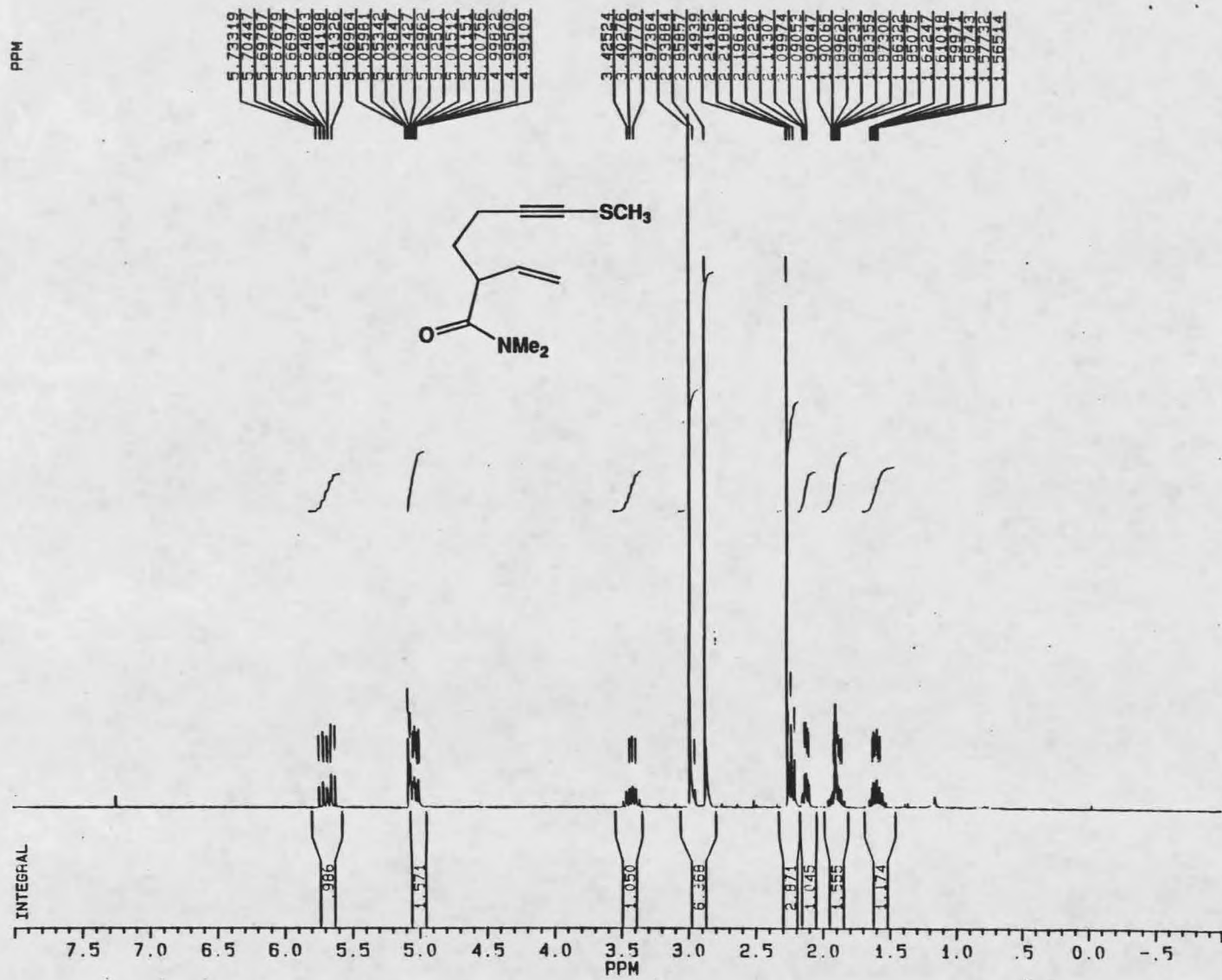


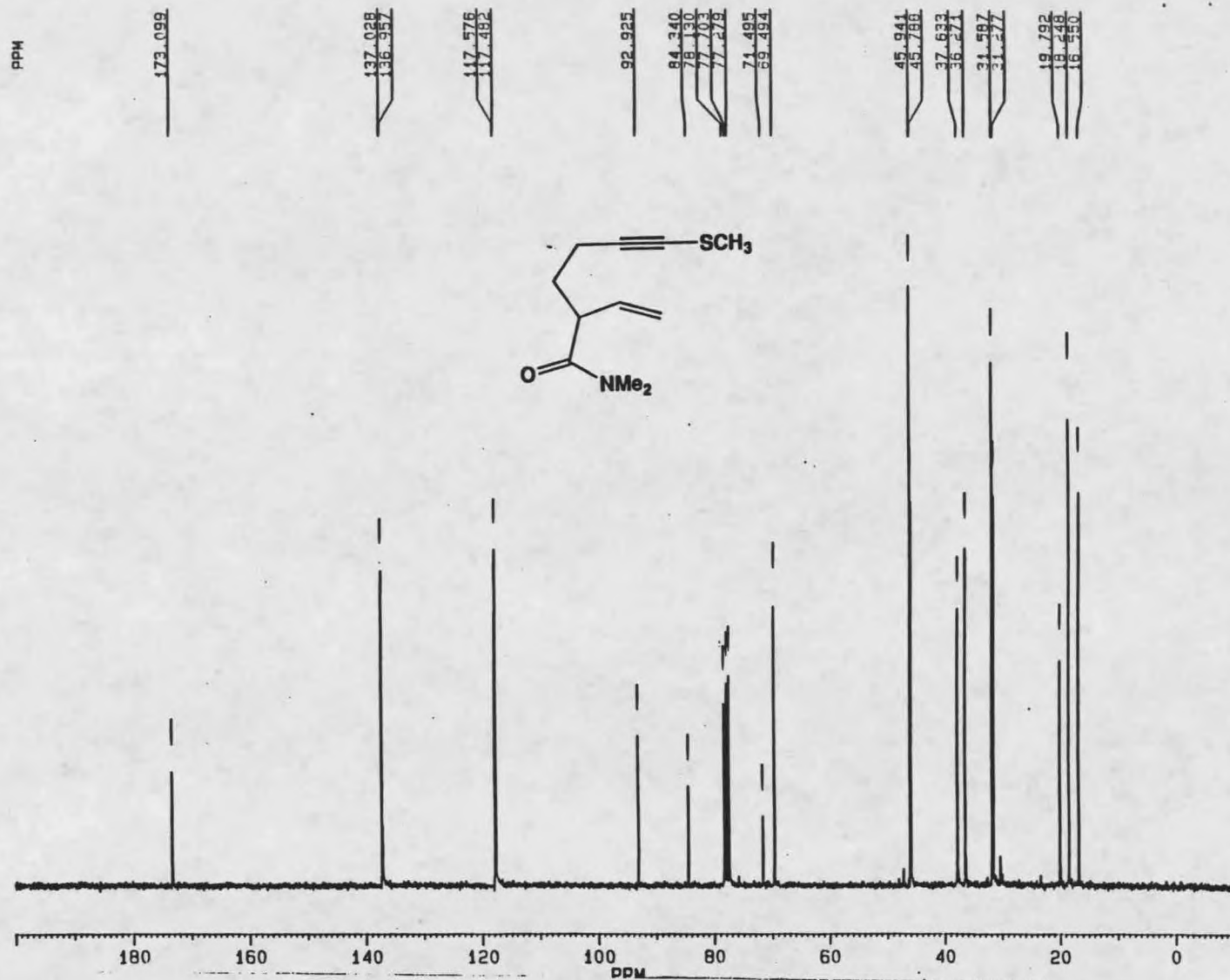




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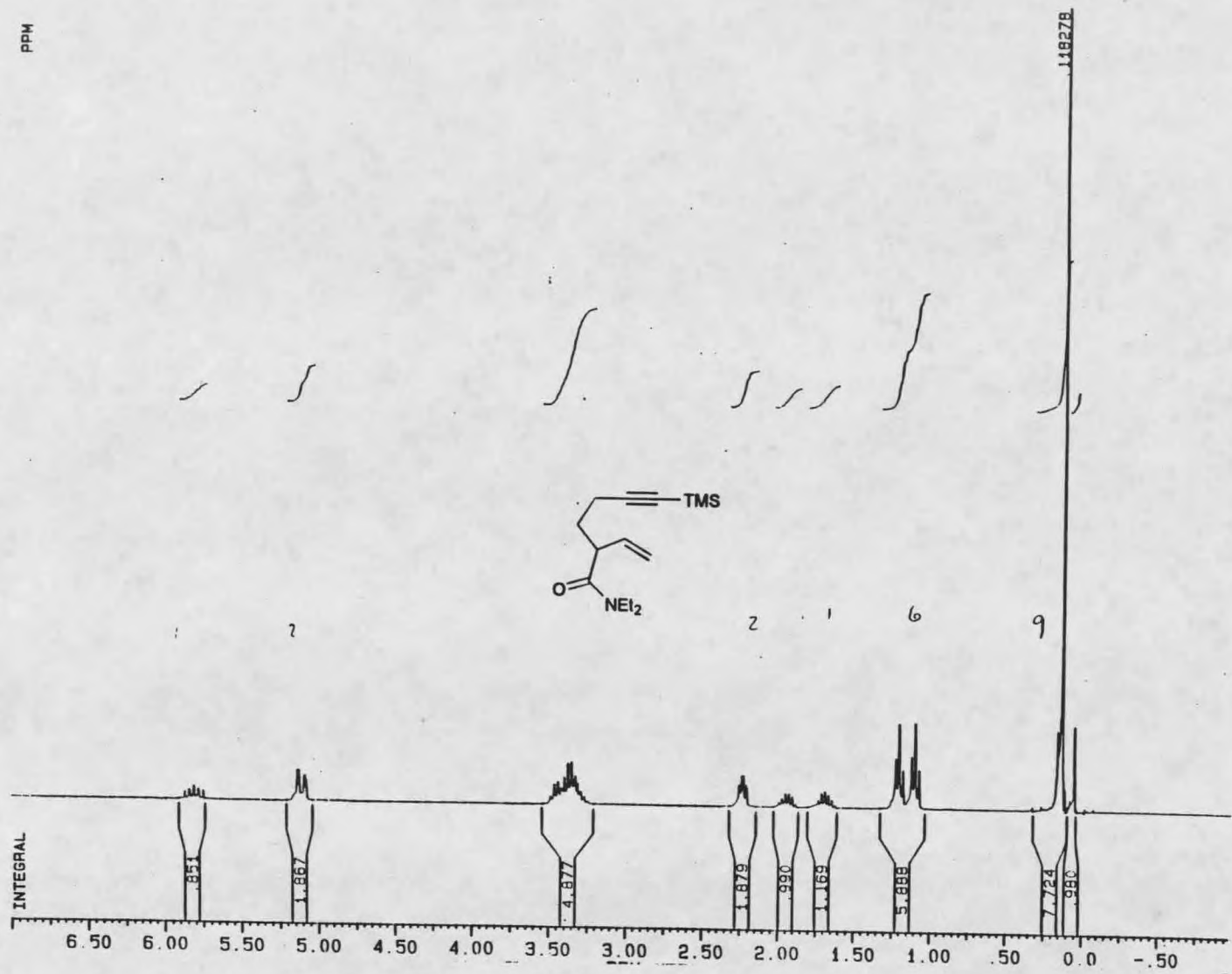






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107.582

86.029

79.116

77.892

77.269

45.984

42.490

41.231

32.021

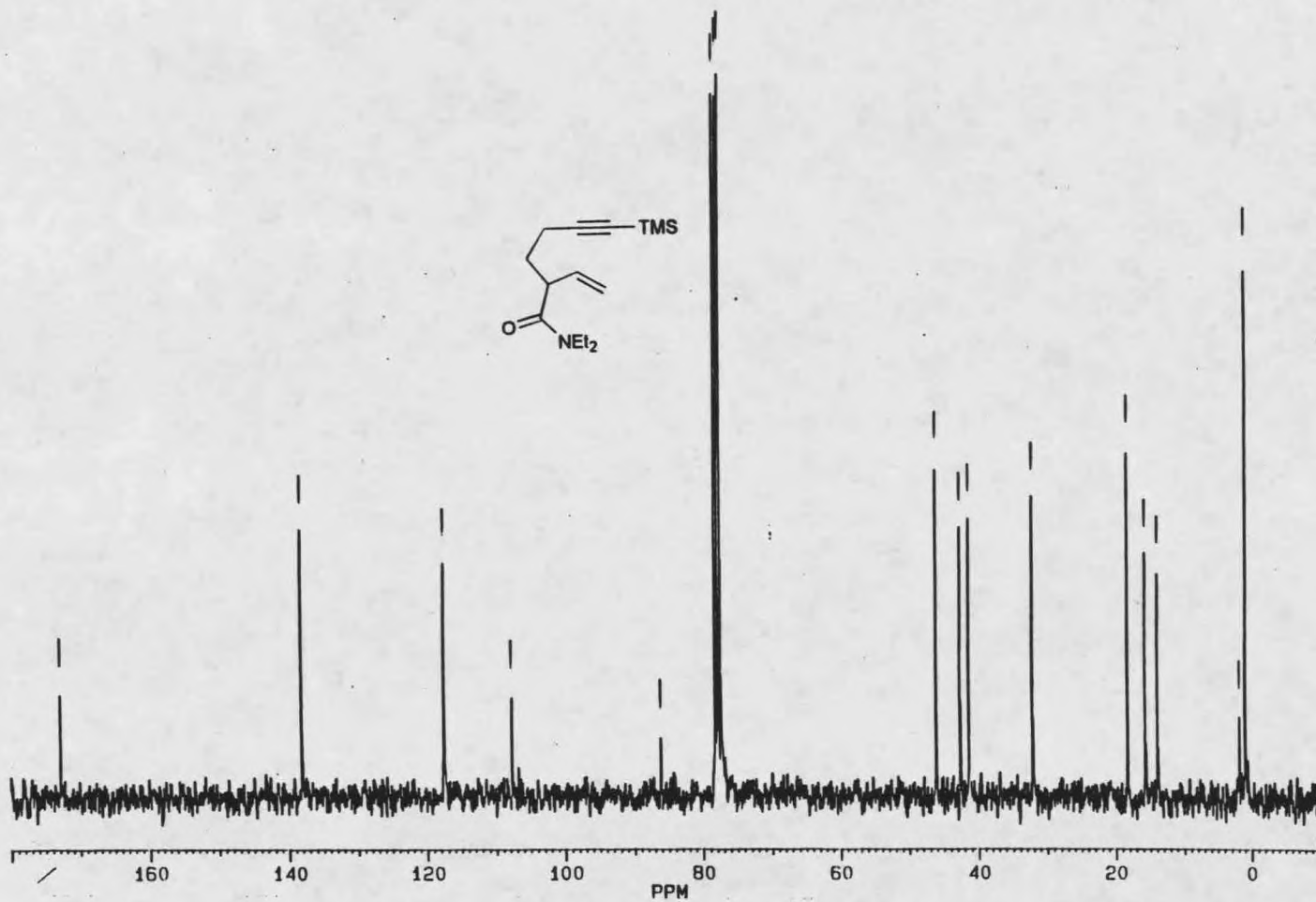
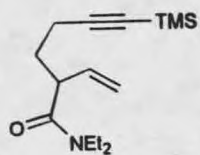
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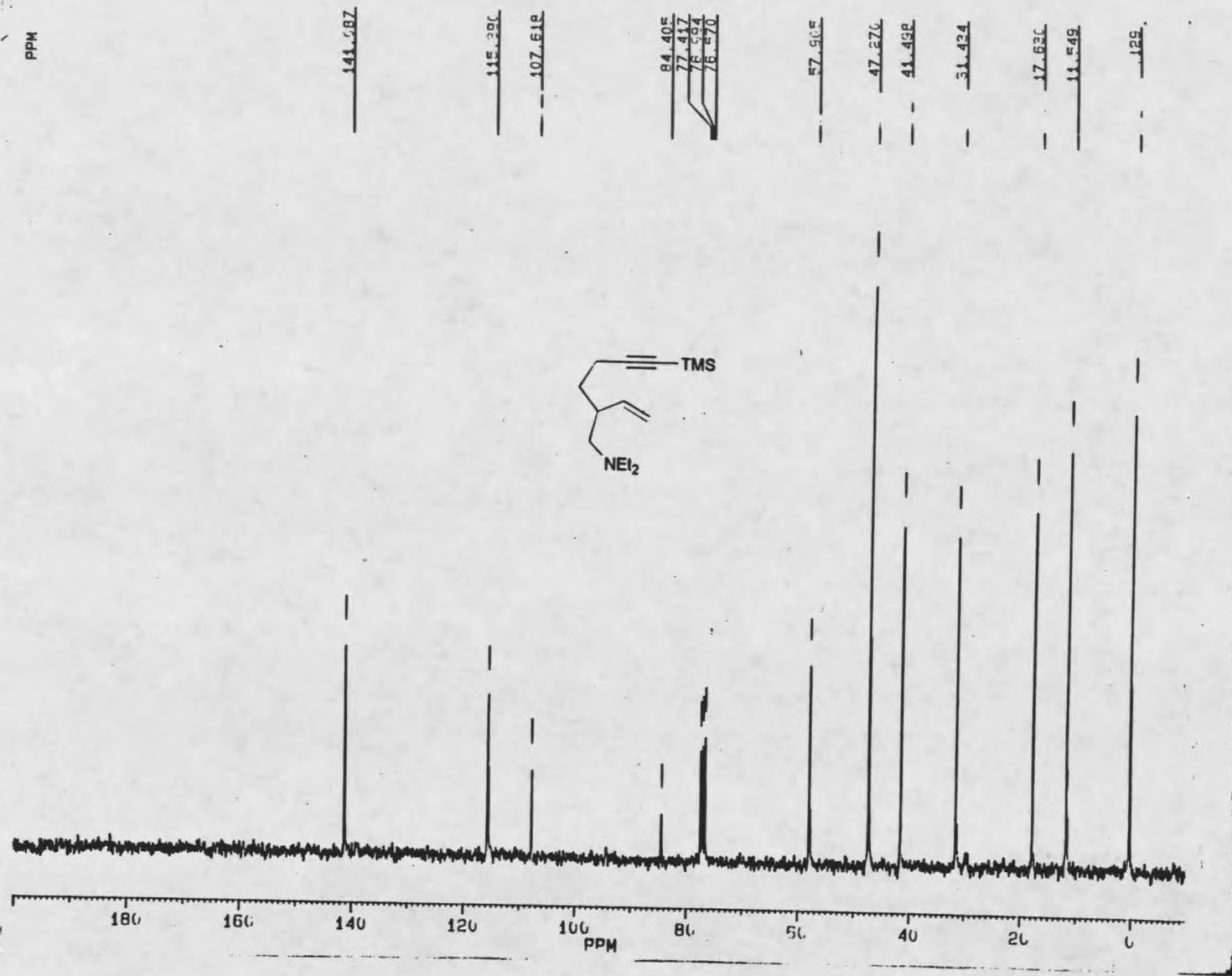
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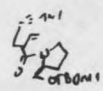
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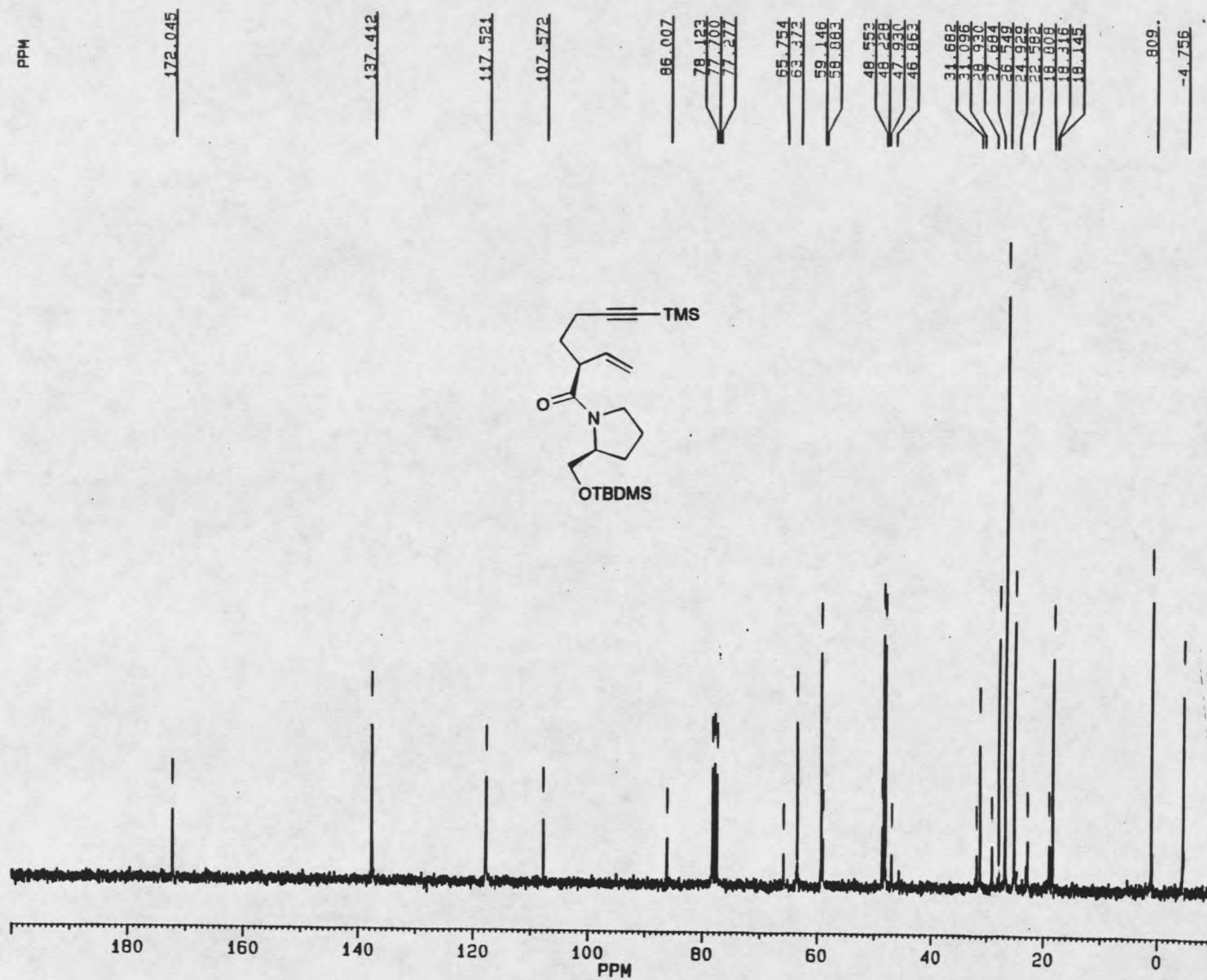
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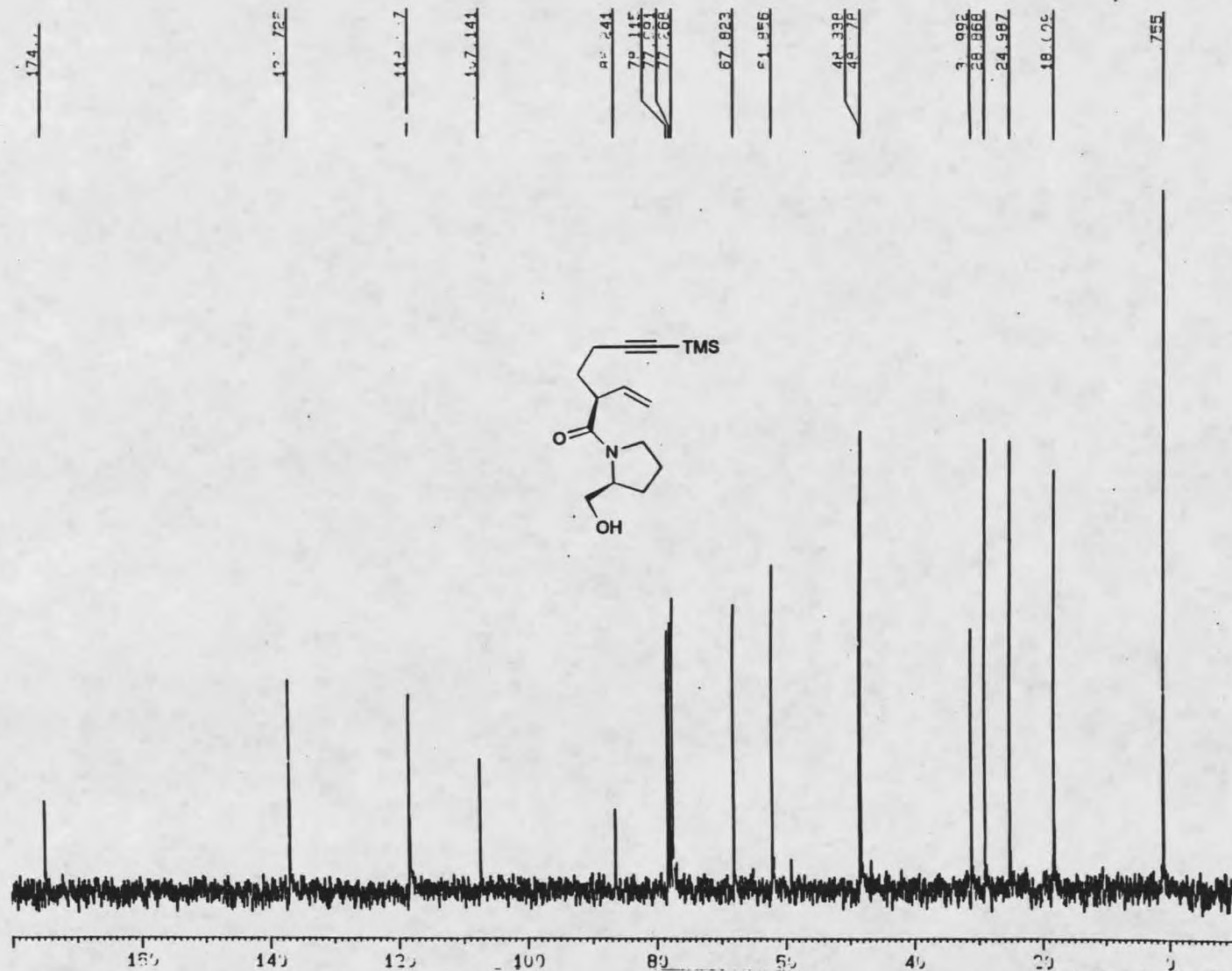


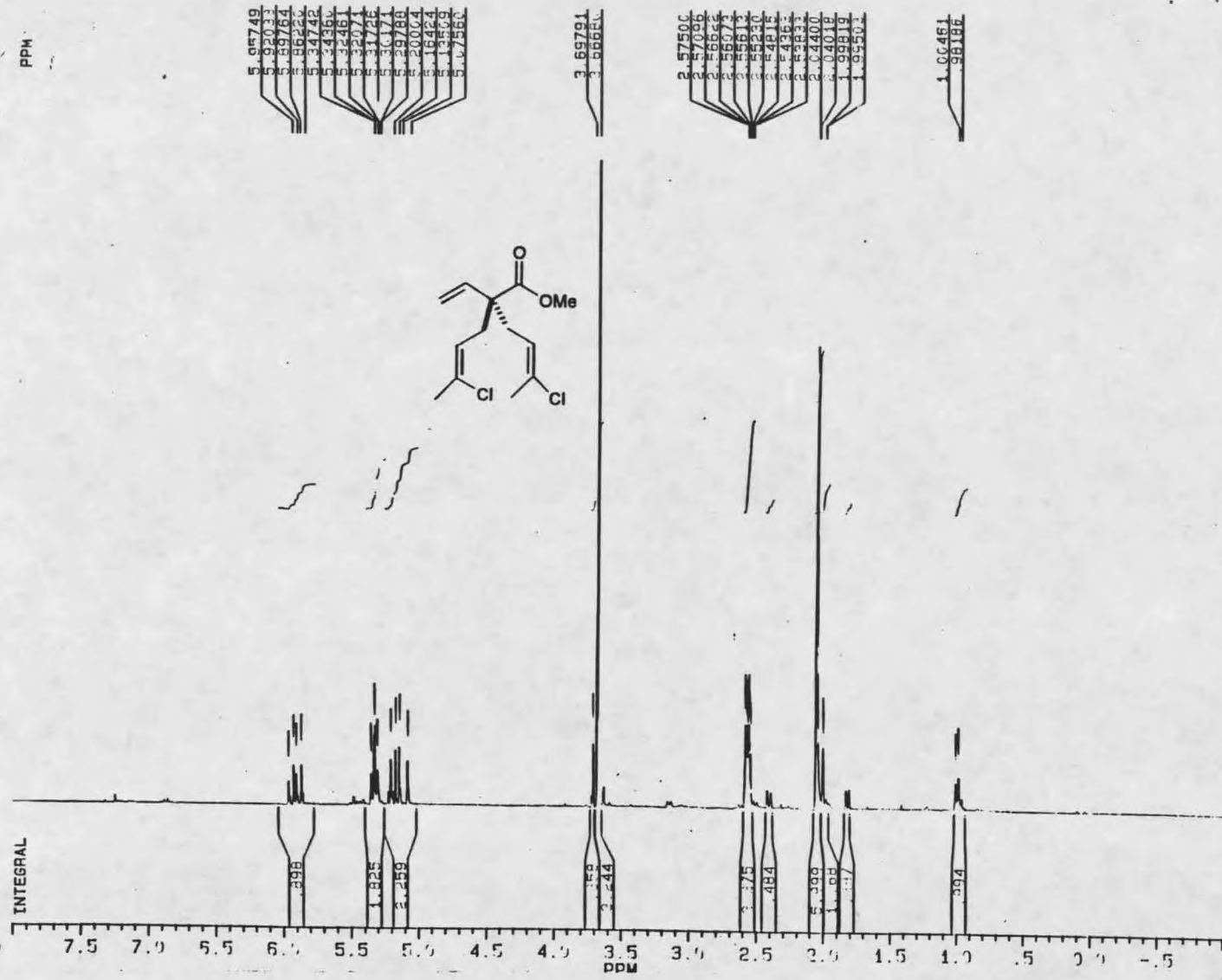












Mad

175.102

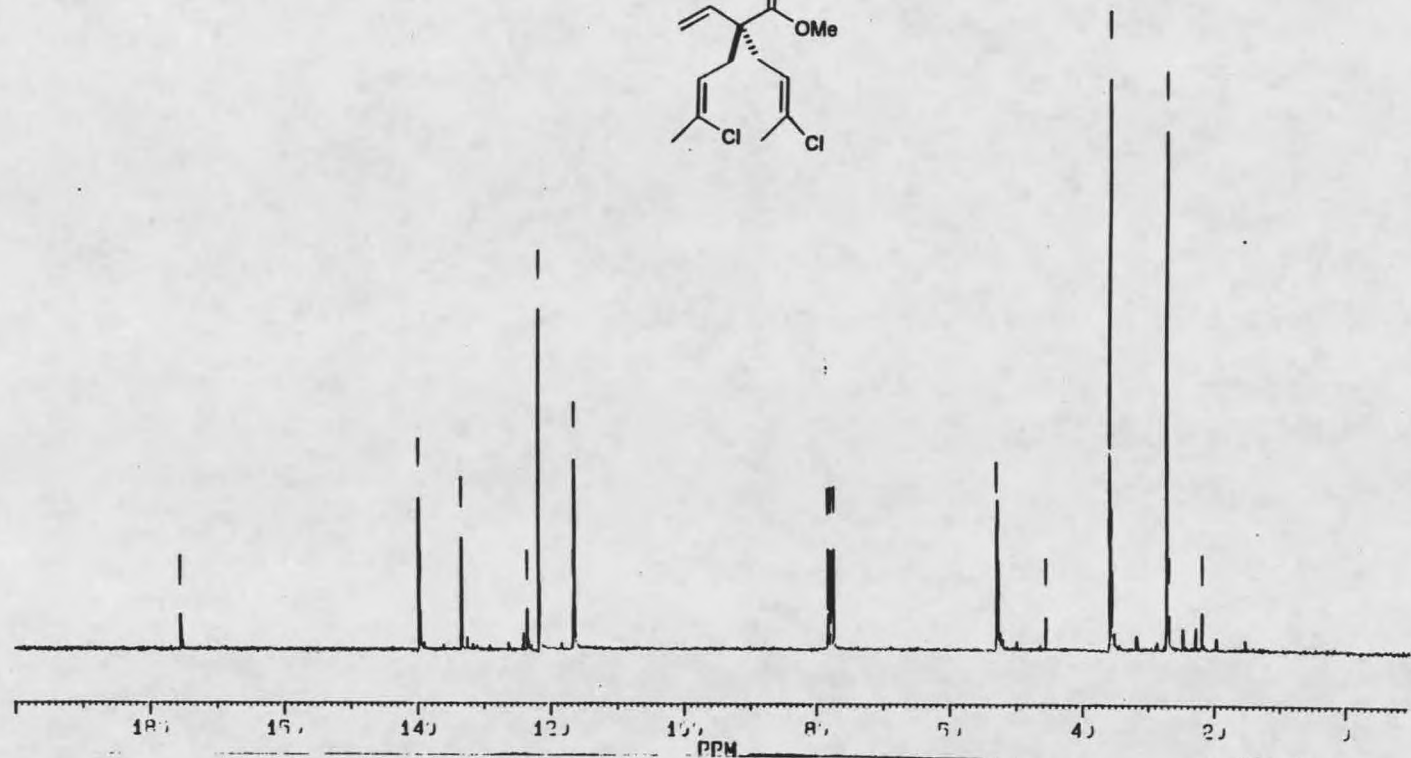
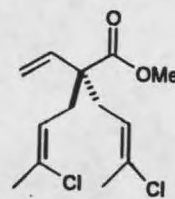
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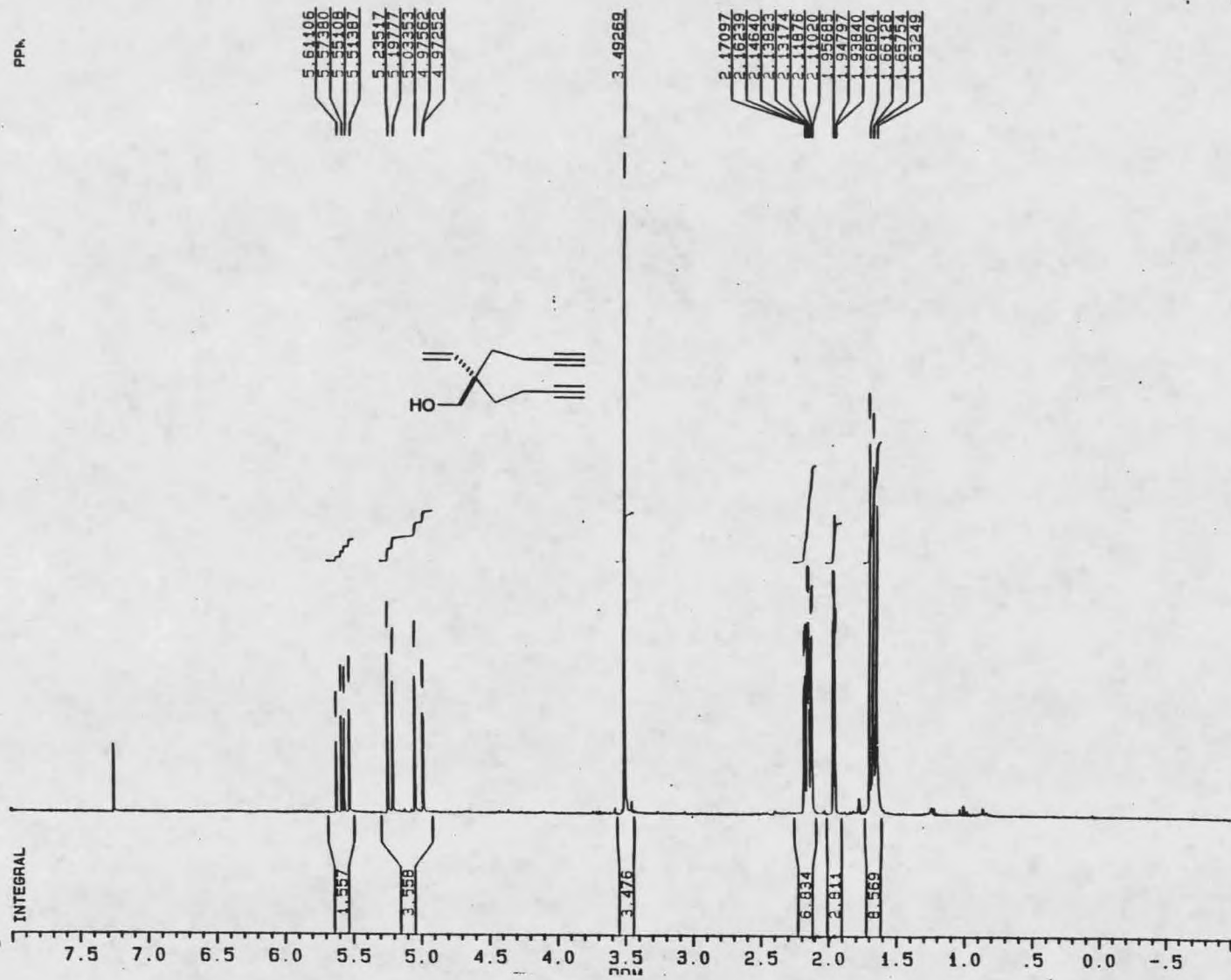
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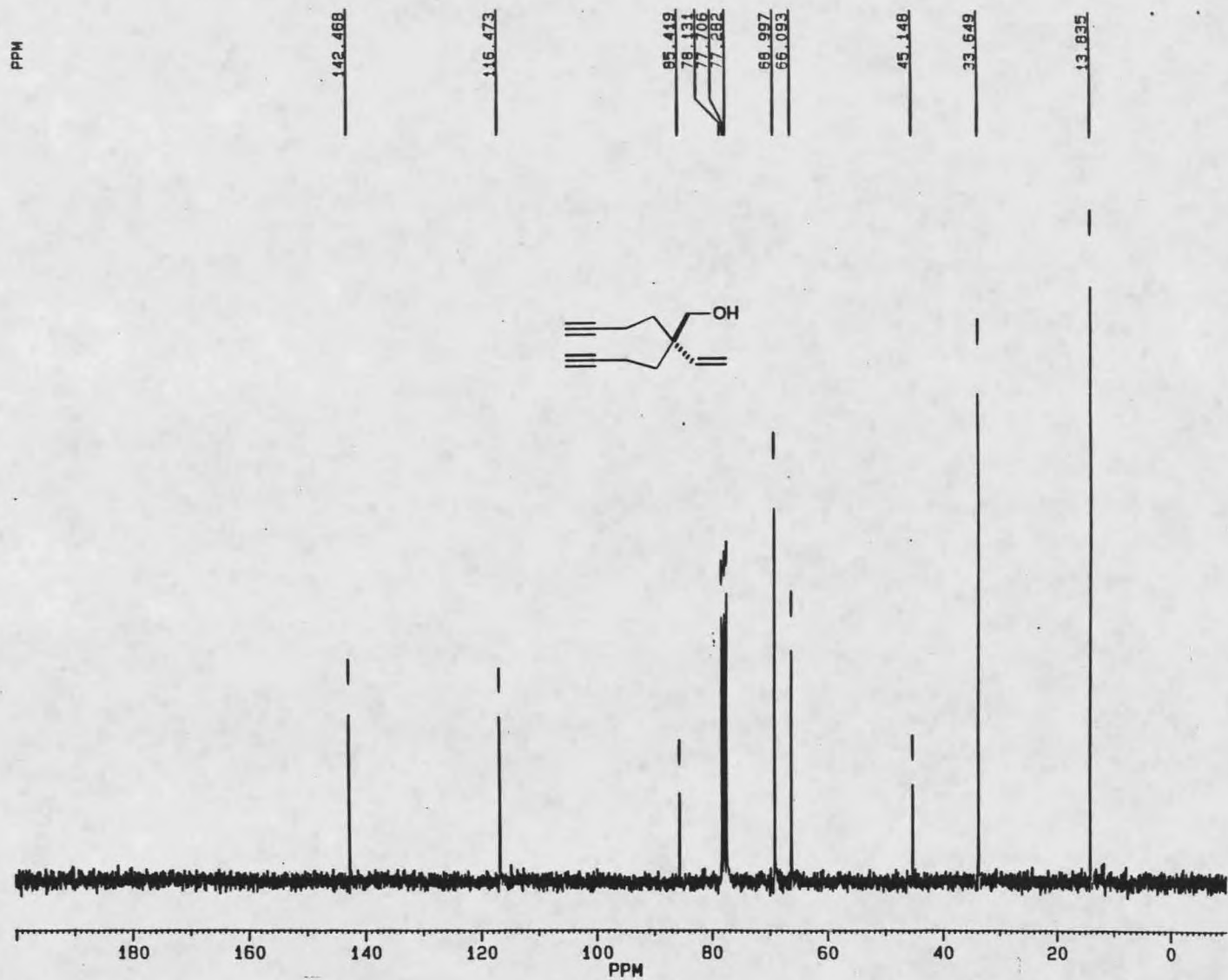
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76.116
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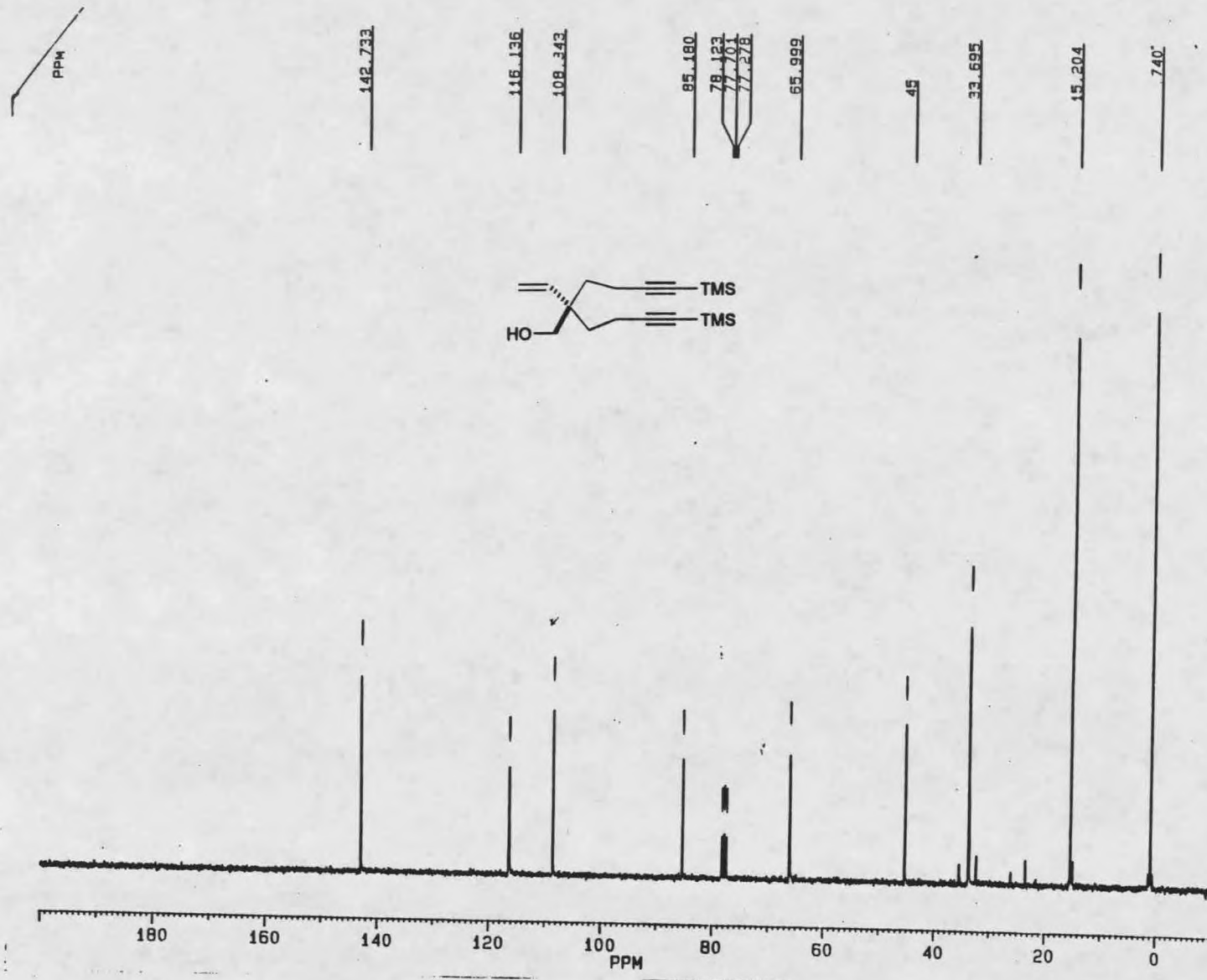
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53.710
45.375

31.112
31.110
31.108
31.106
27.112
27.110
27.108
27.106









INTEGRAL

7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 .5 0 0 - .5

PPM

≡

7.49

≡

5.076

—

3.3727

≡

2.16150

≡

1.65775

—

0.6505

≡

0.772

≡

0.118

≡

0.001

≡

0.070

≡

0.041



4.0

5.61732
5.59004
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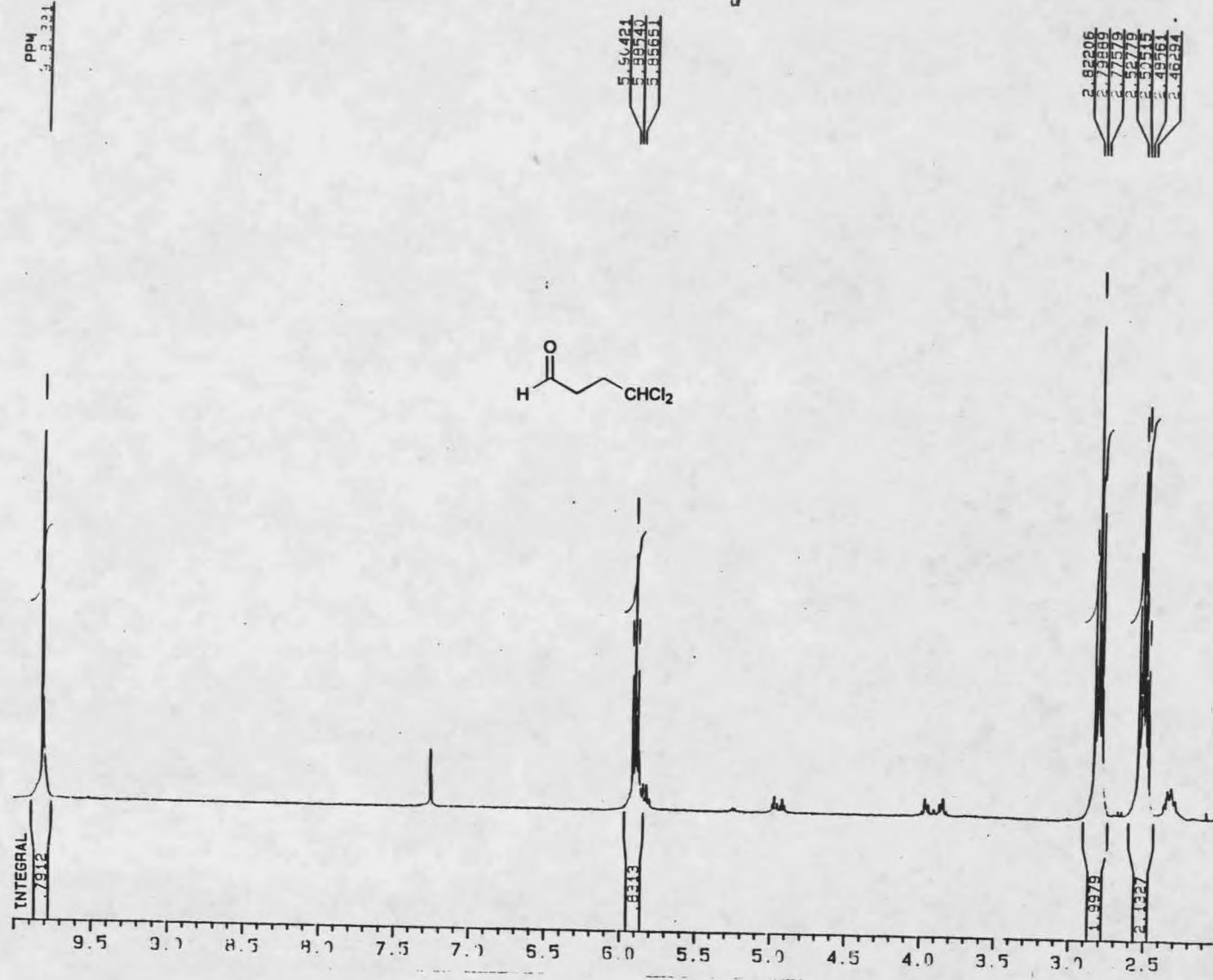
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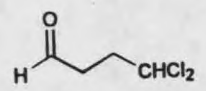
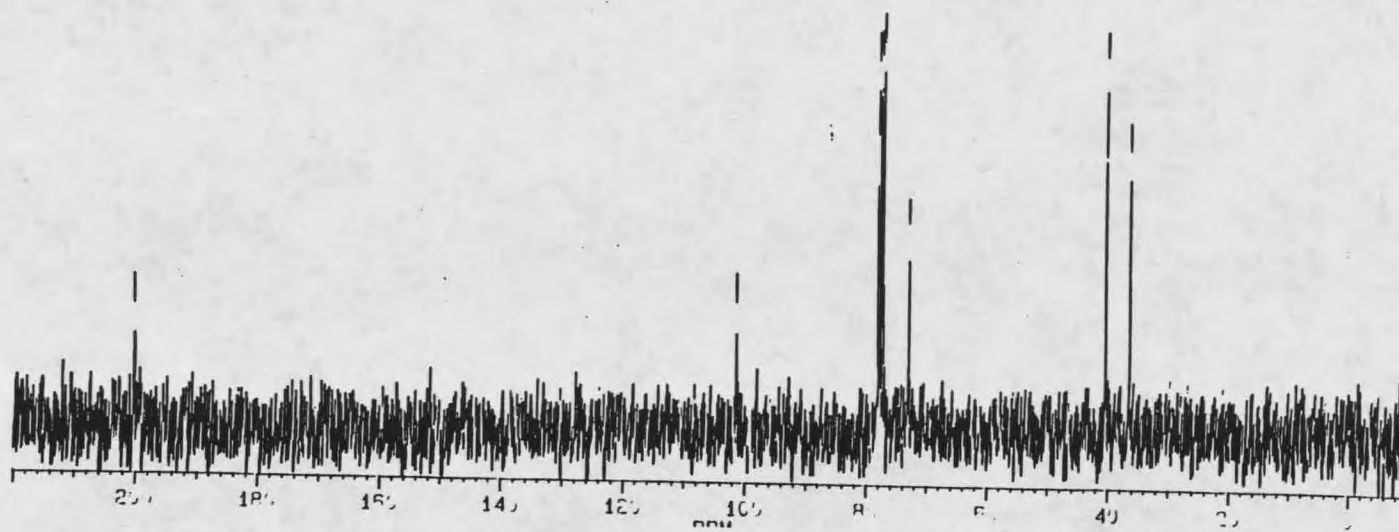
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ppm

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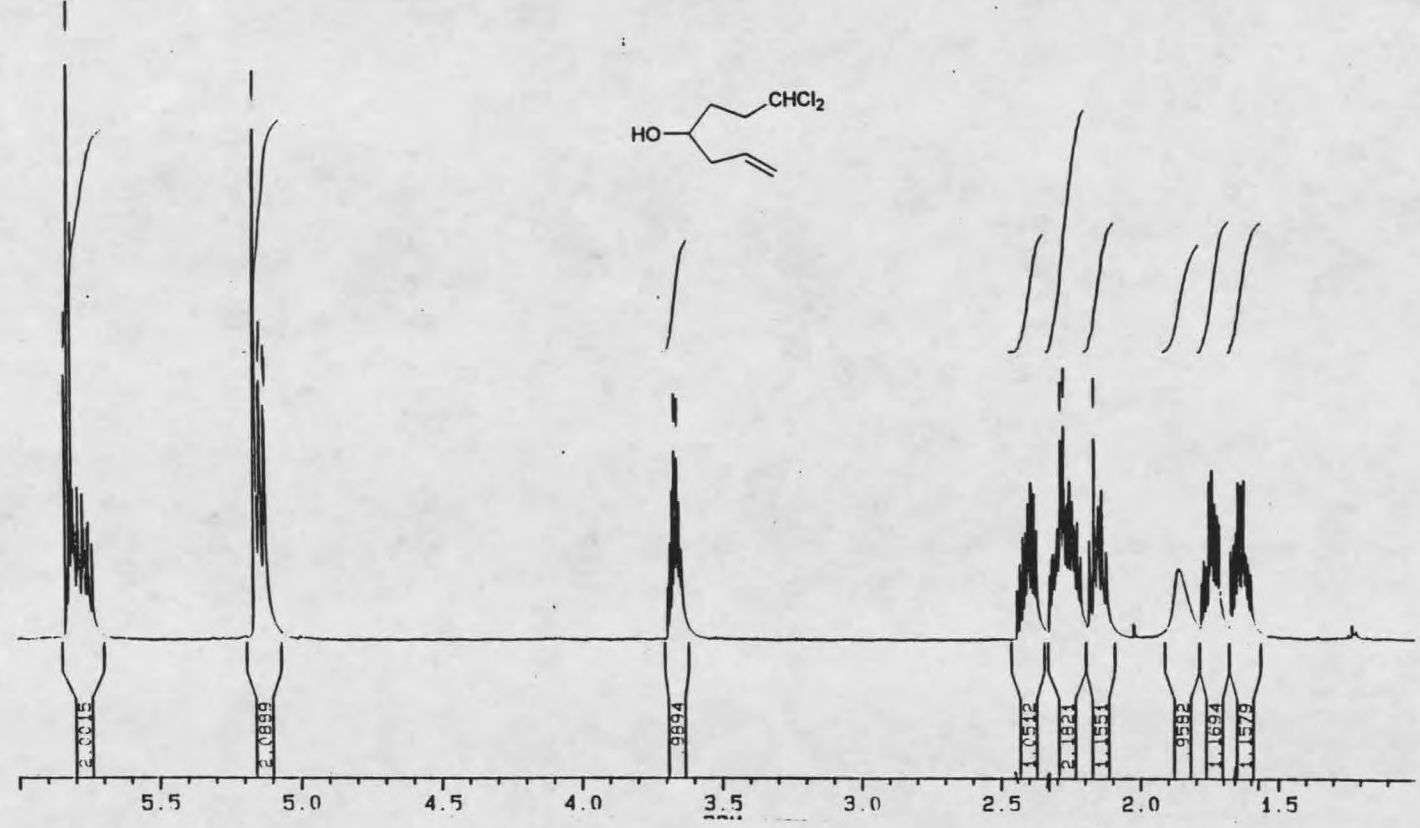
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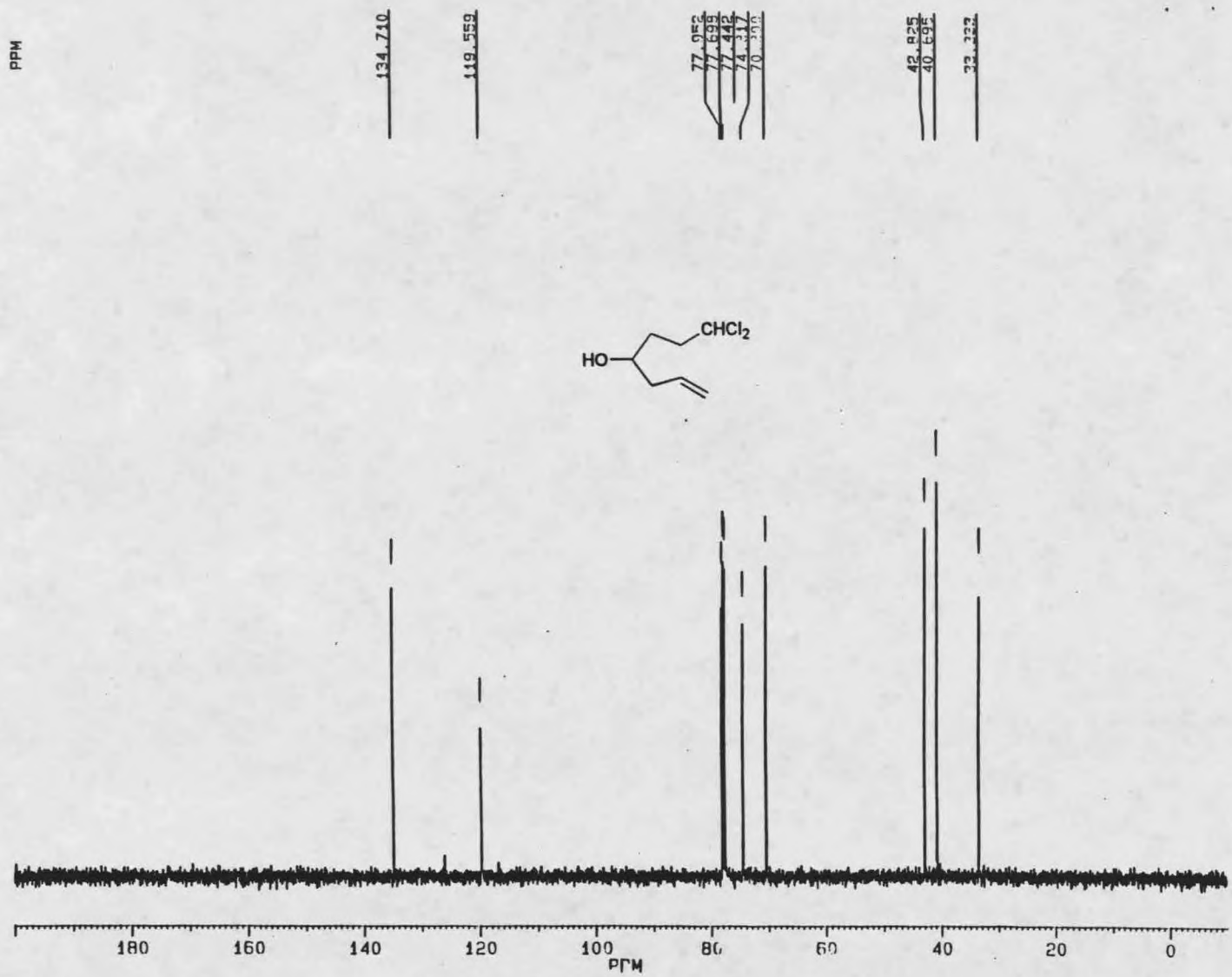
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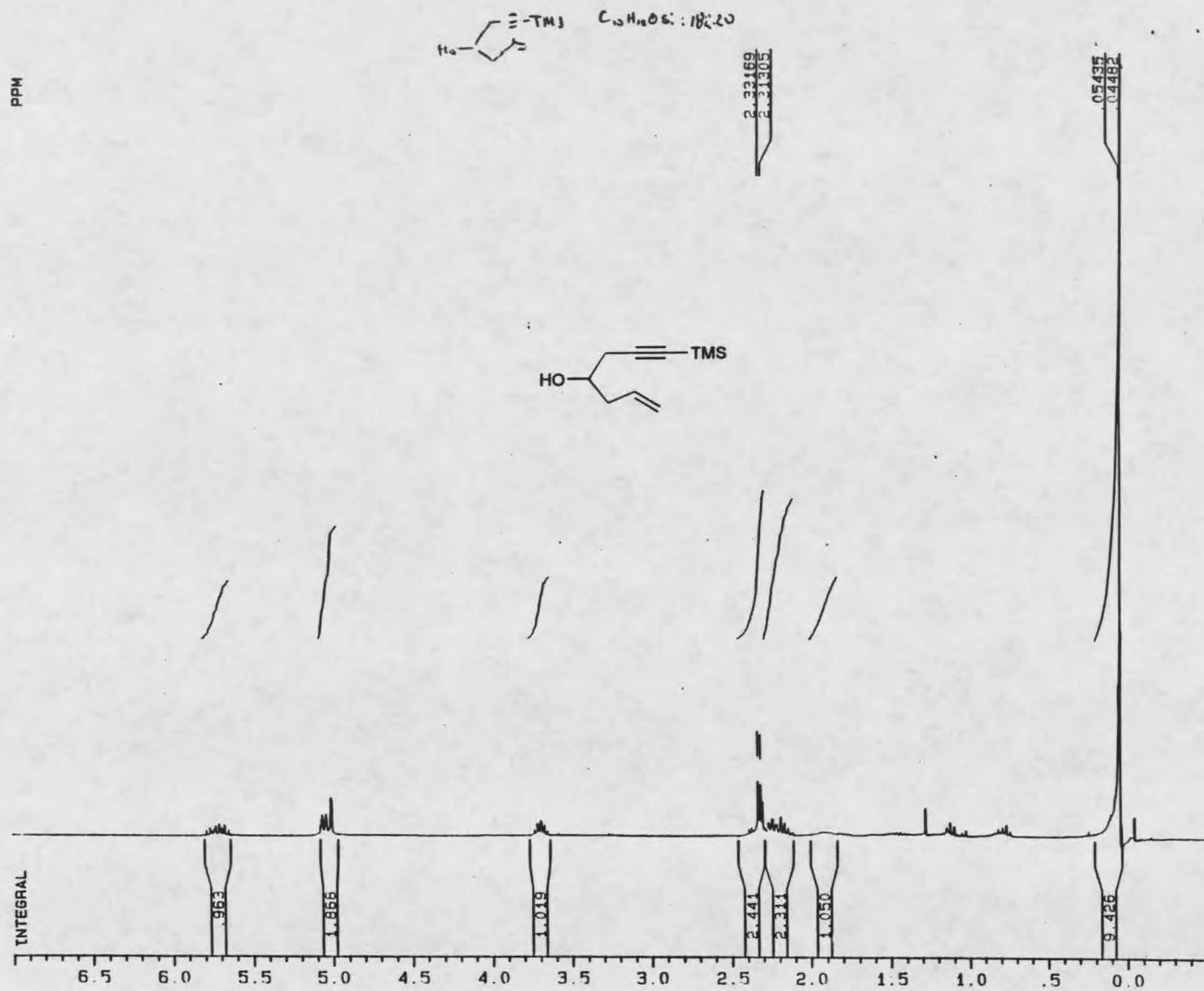
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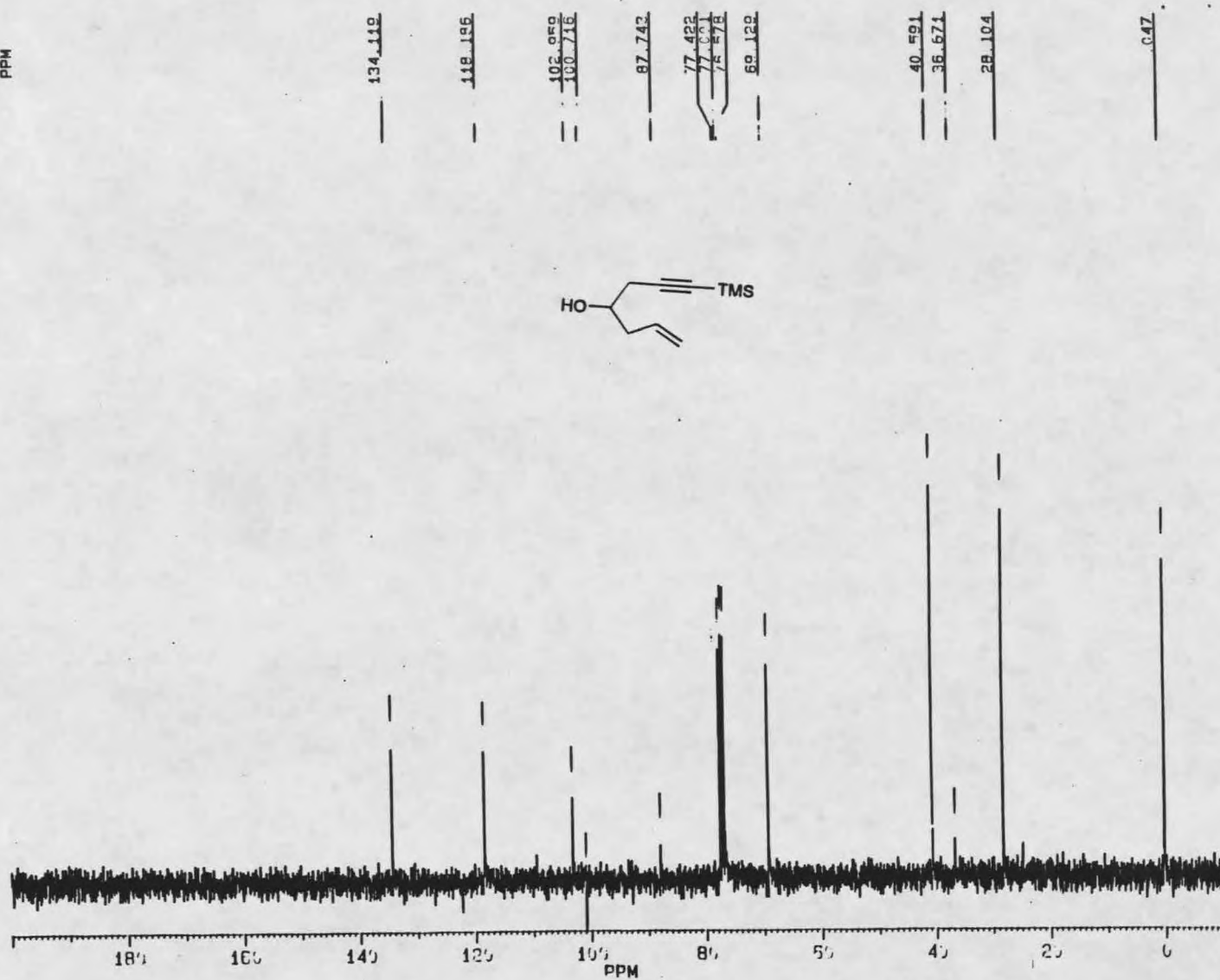
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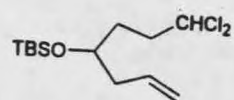


PPM



PPM

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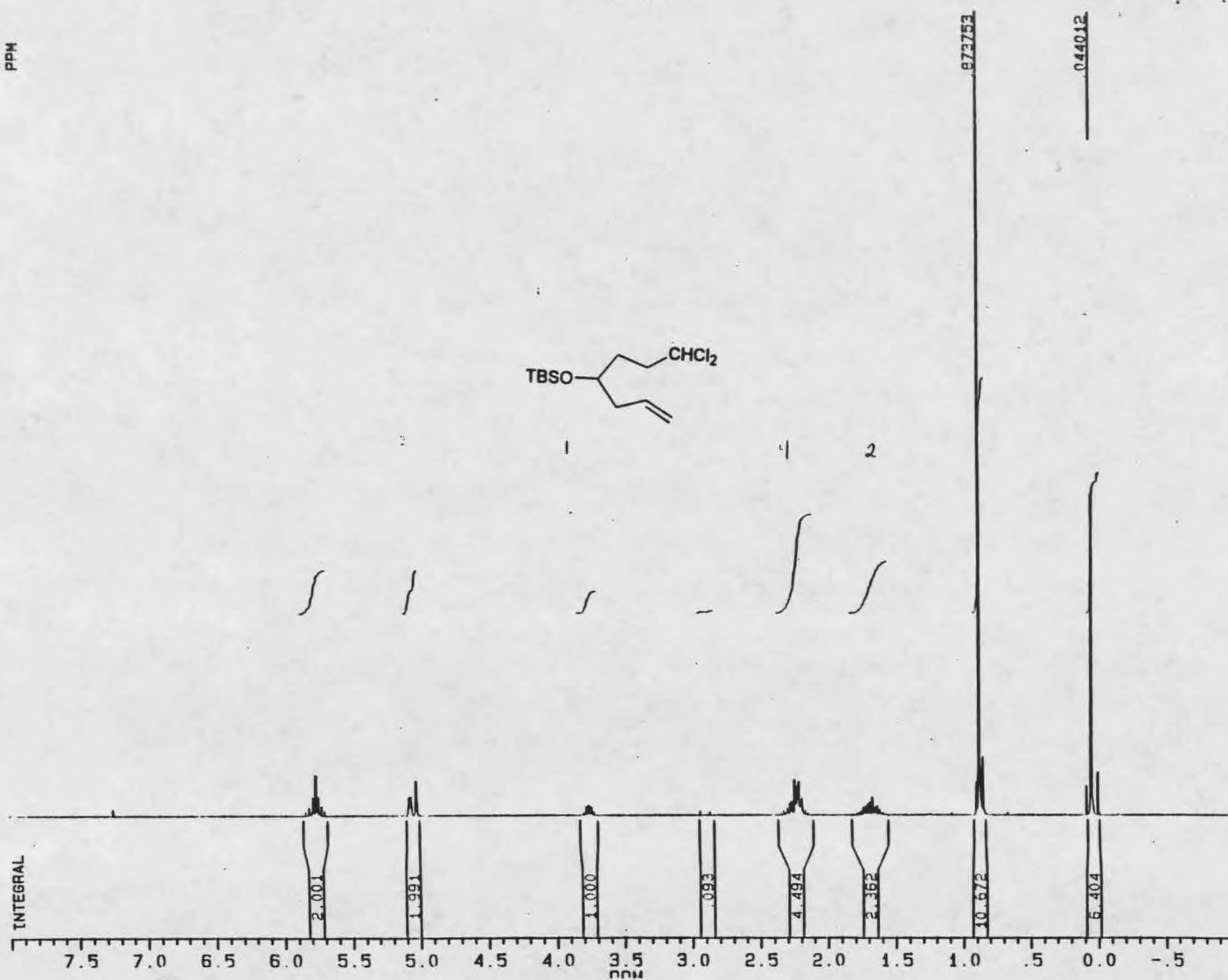


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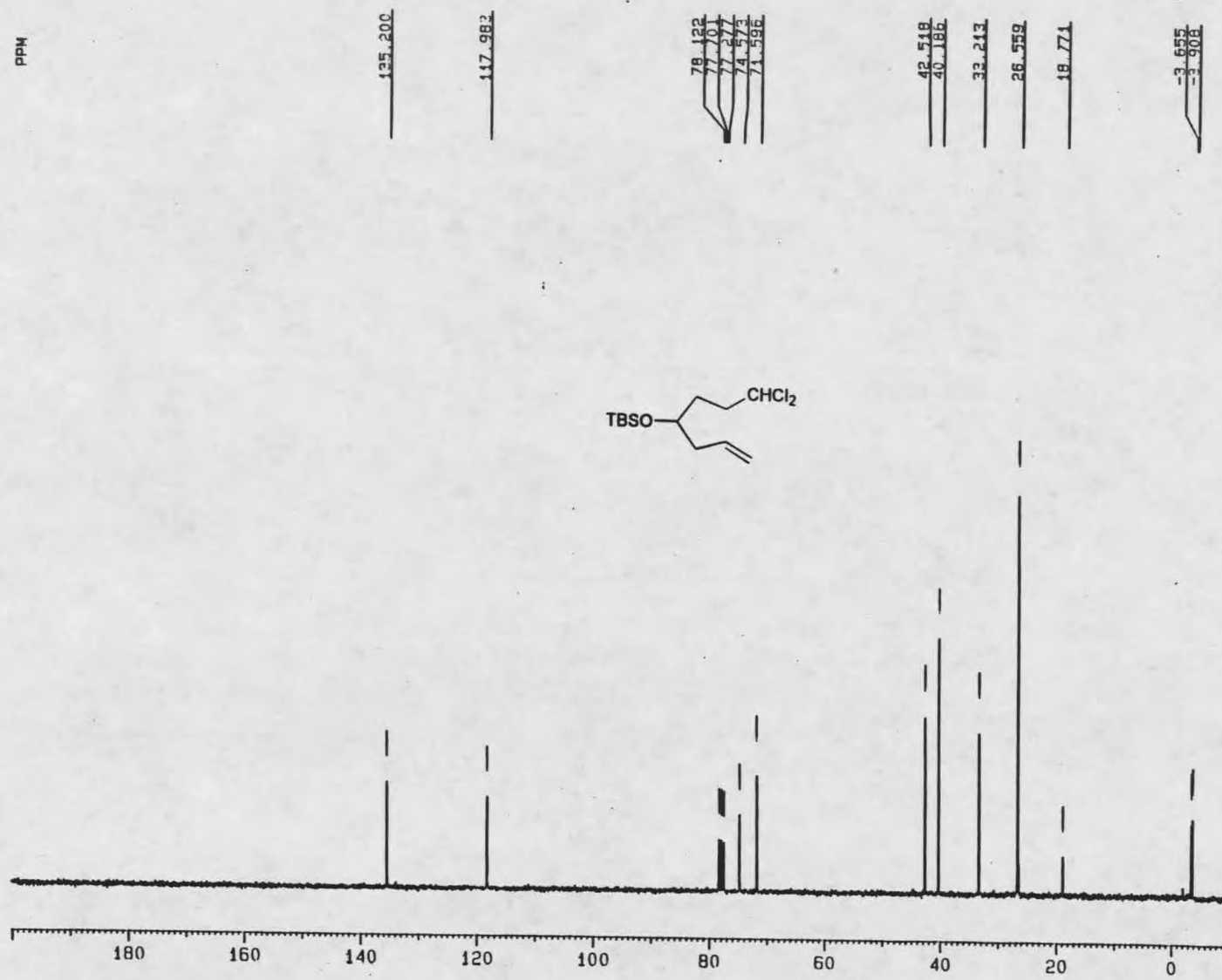
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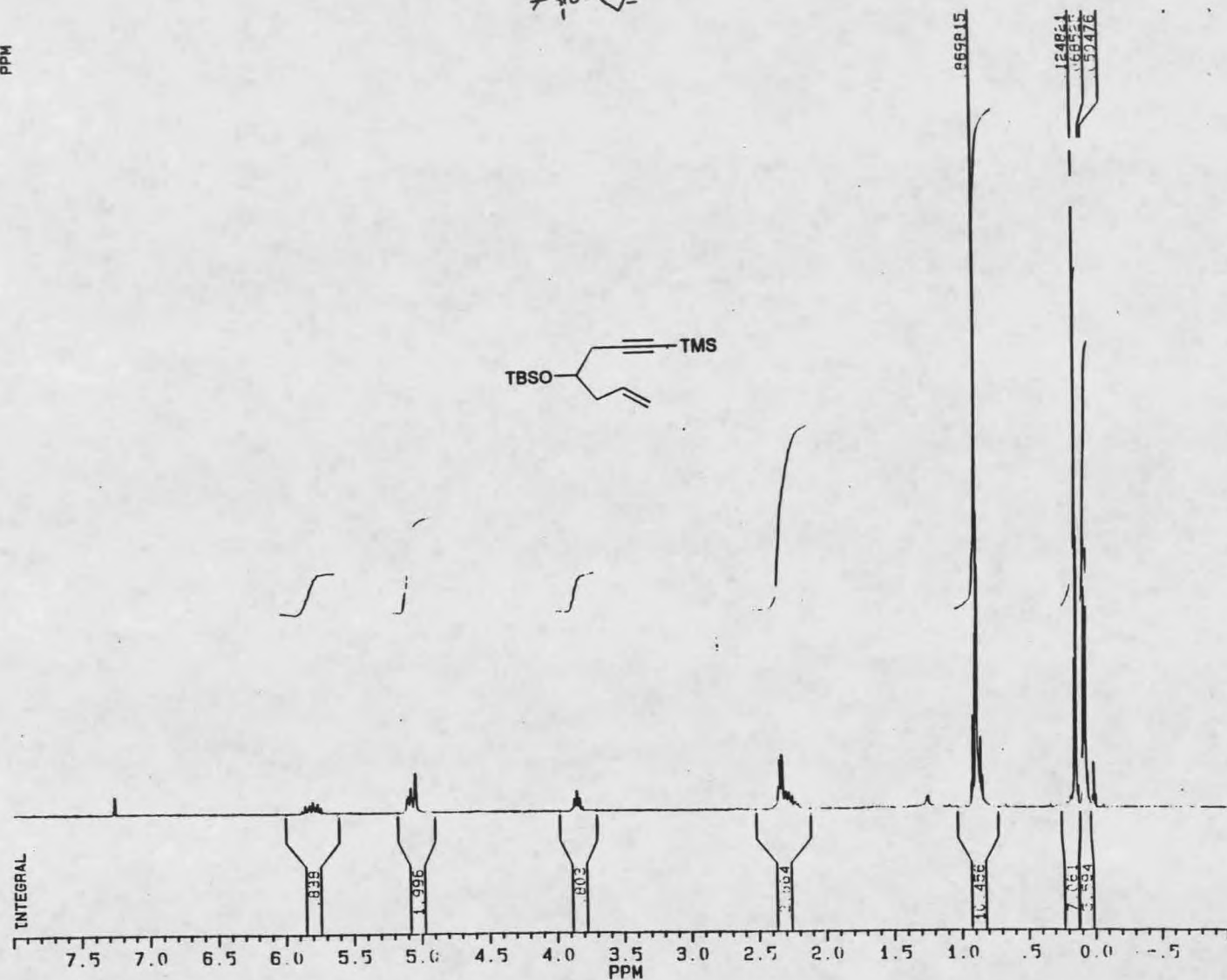
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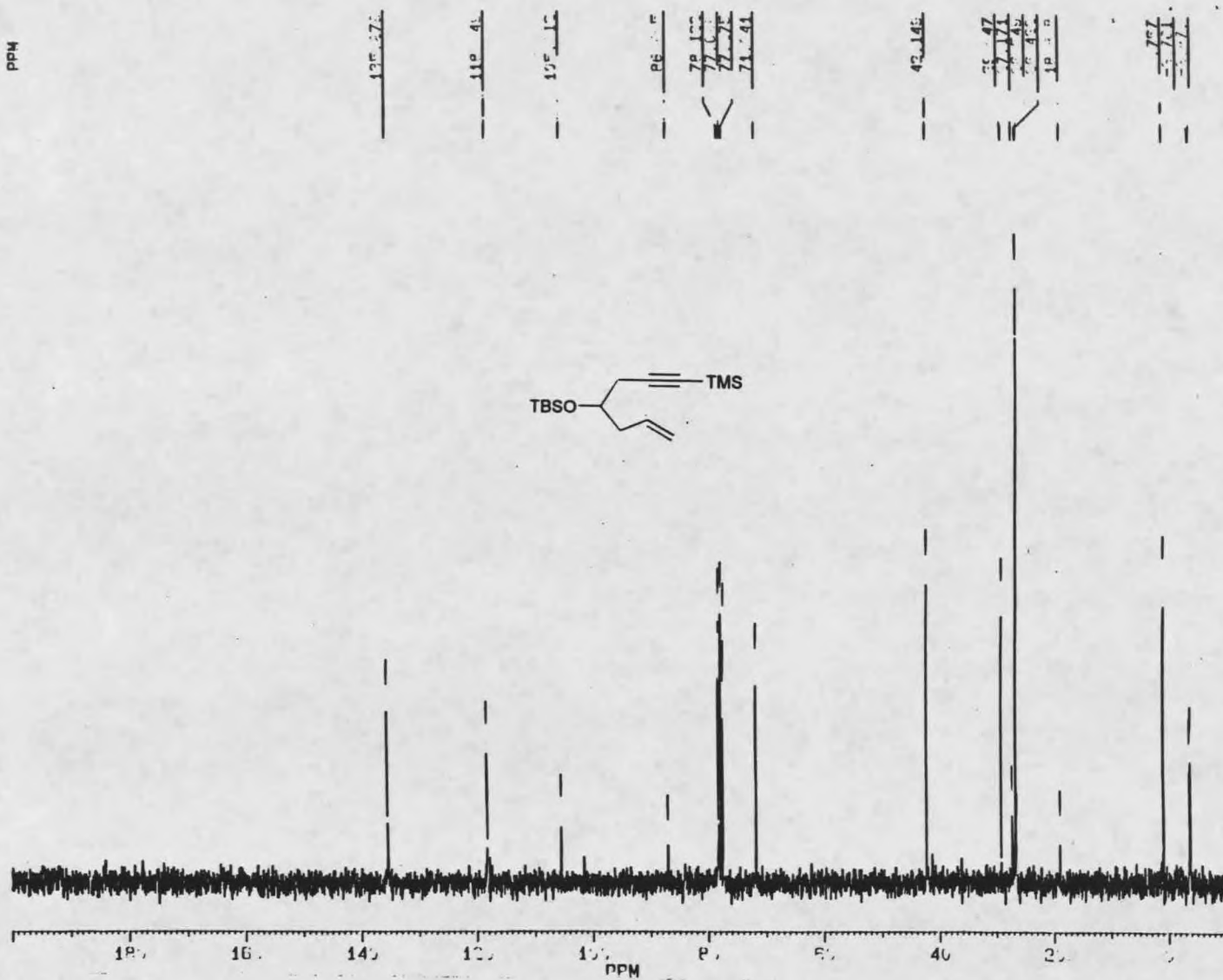
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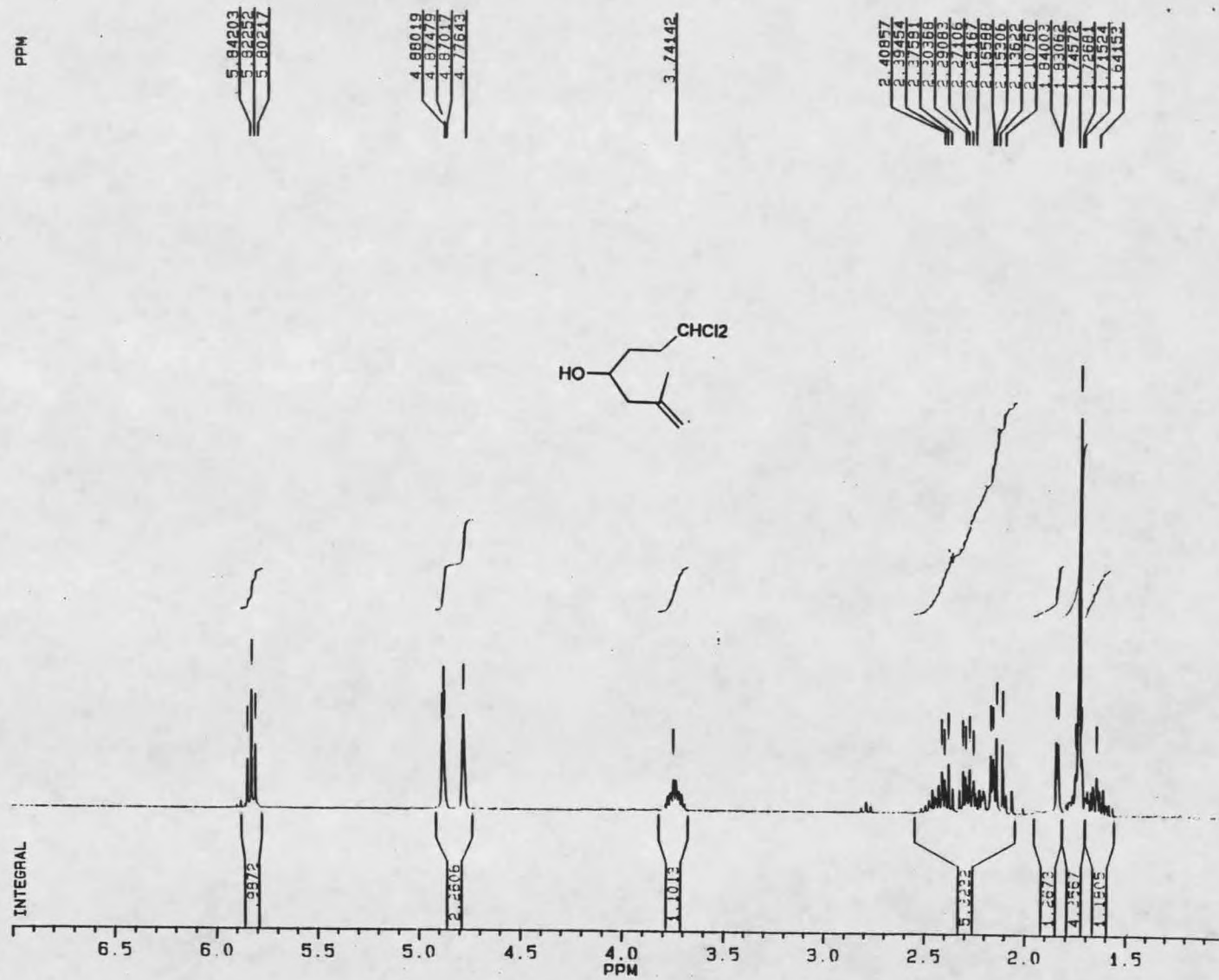


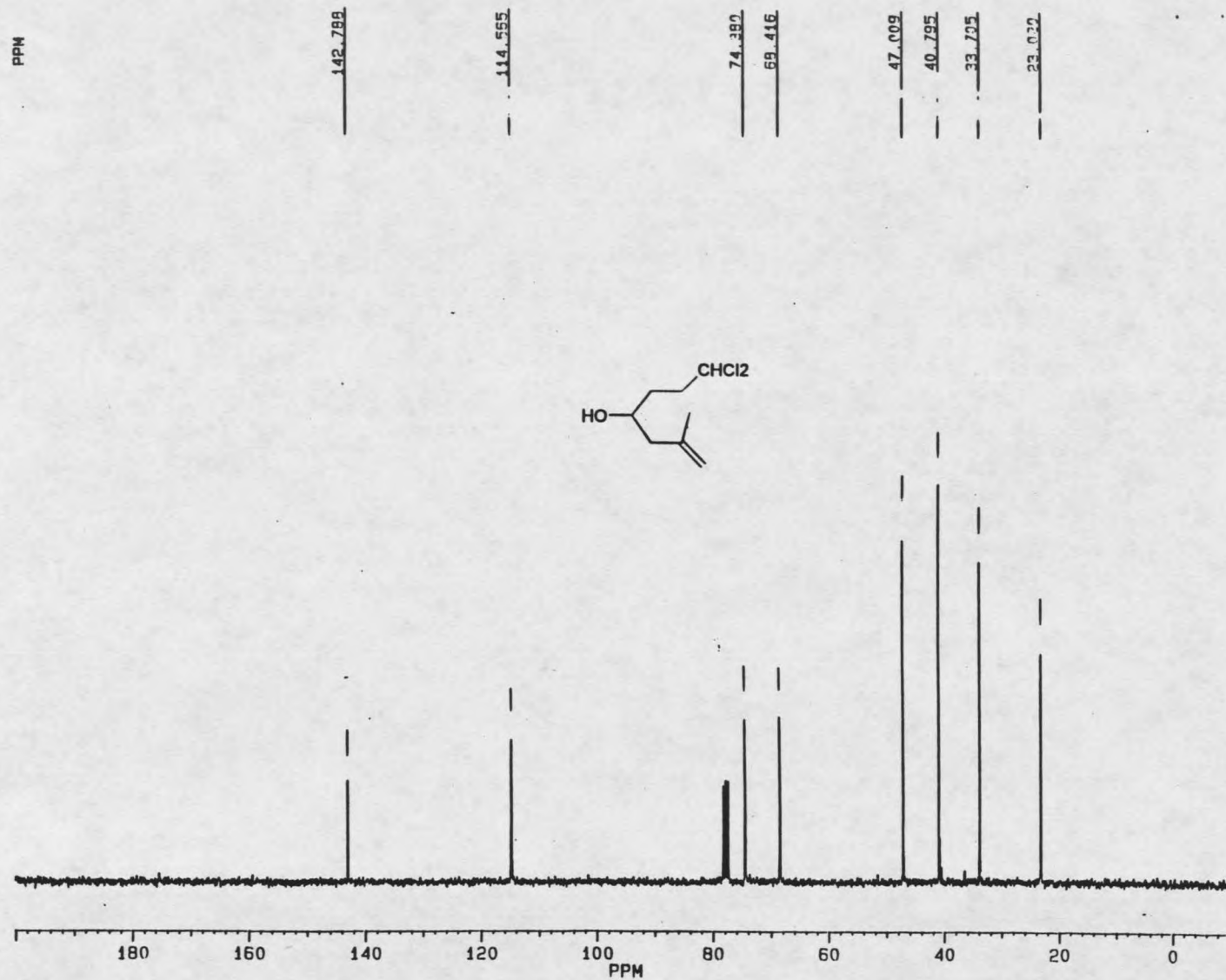
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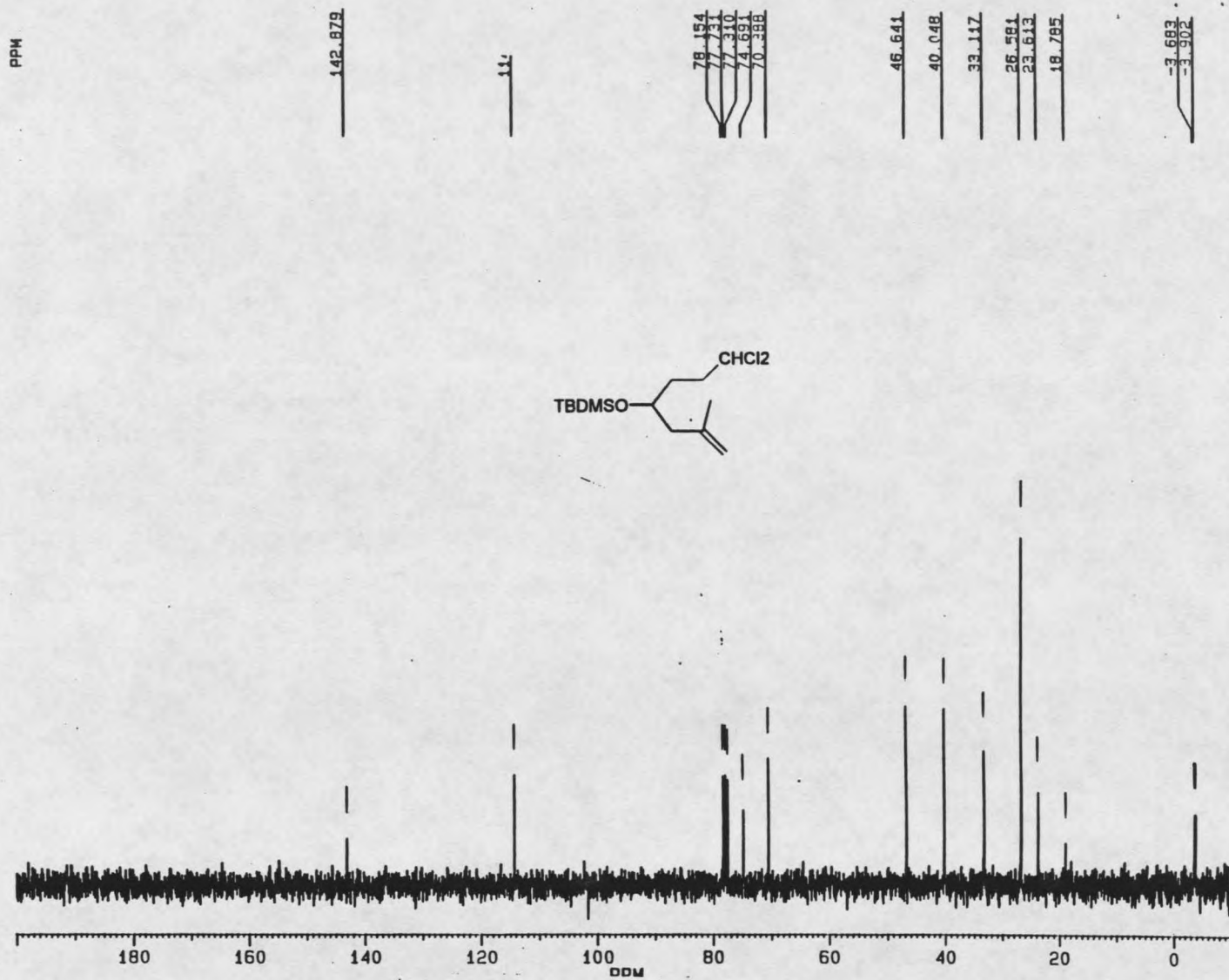


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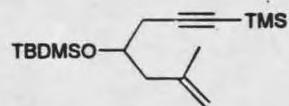


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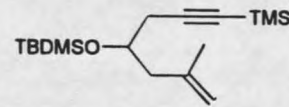
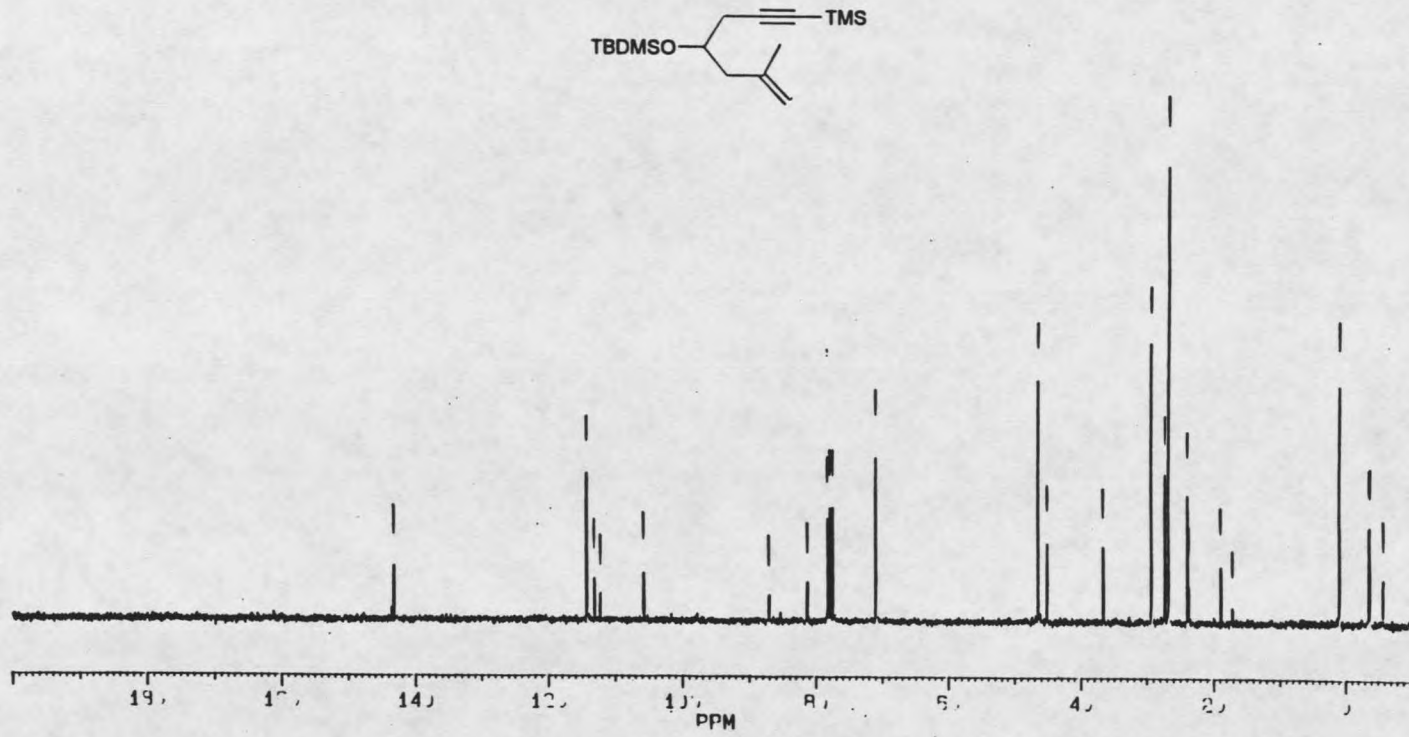
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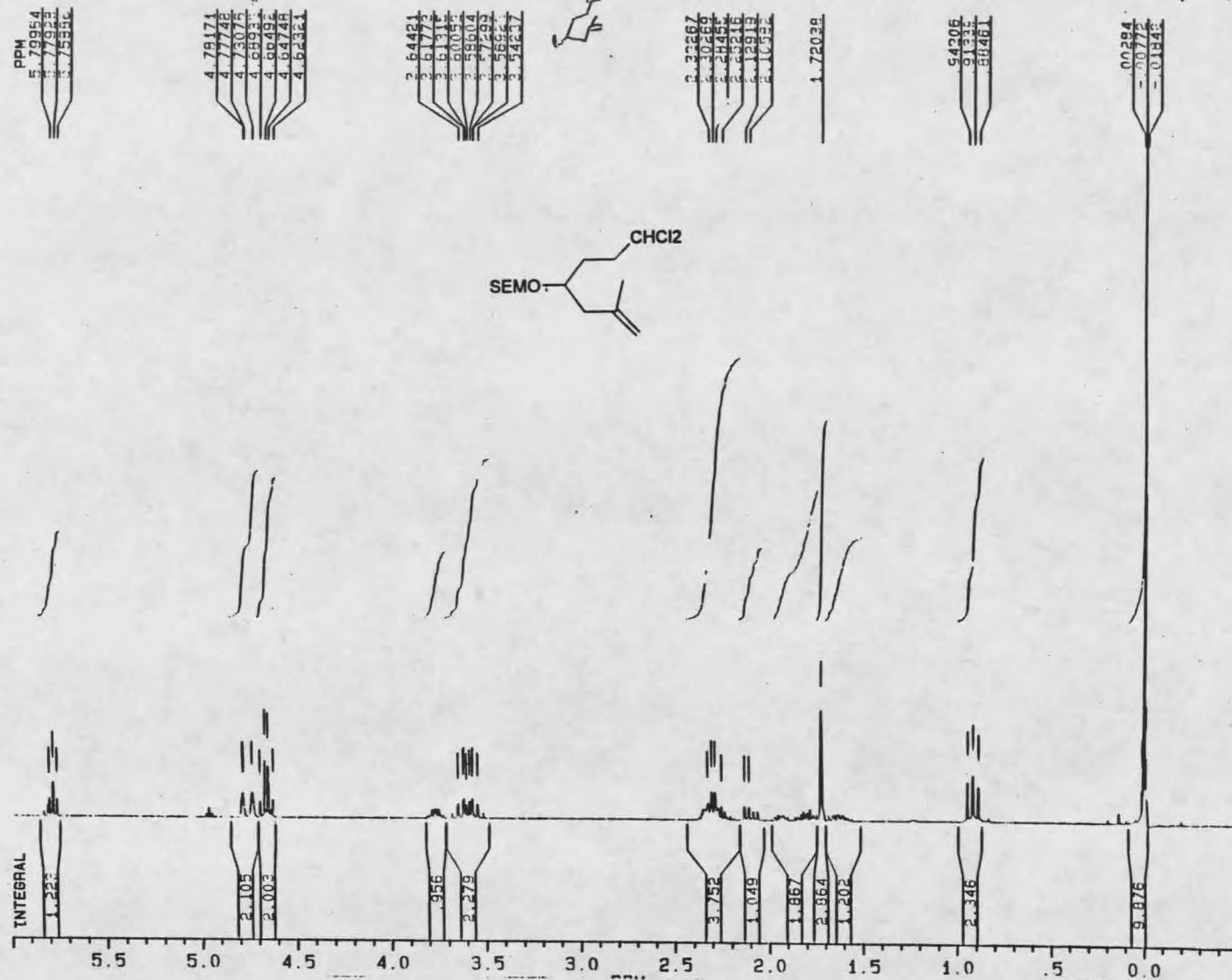
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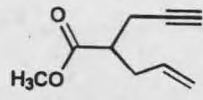
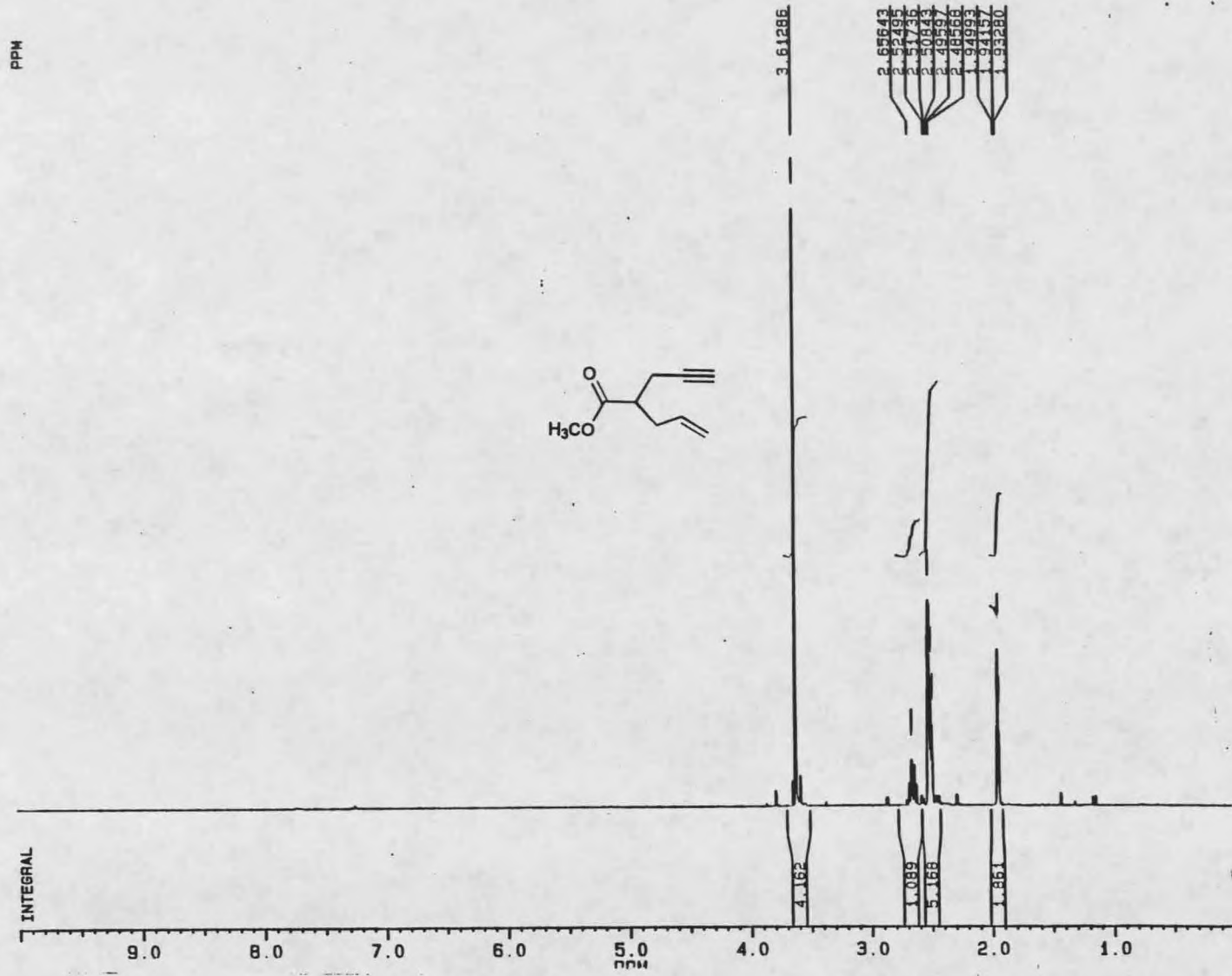
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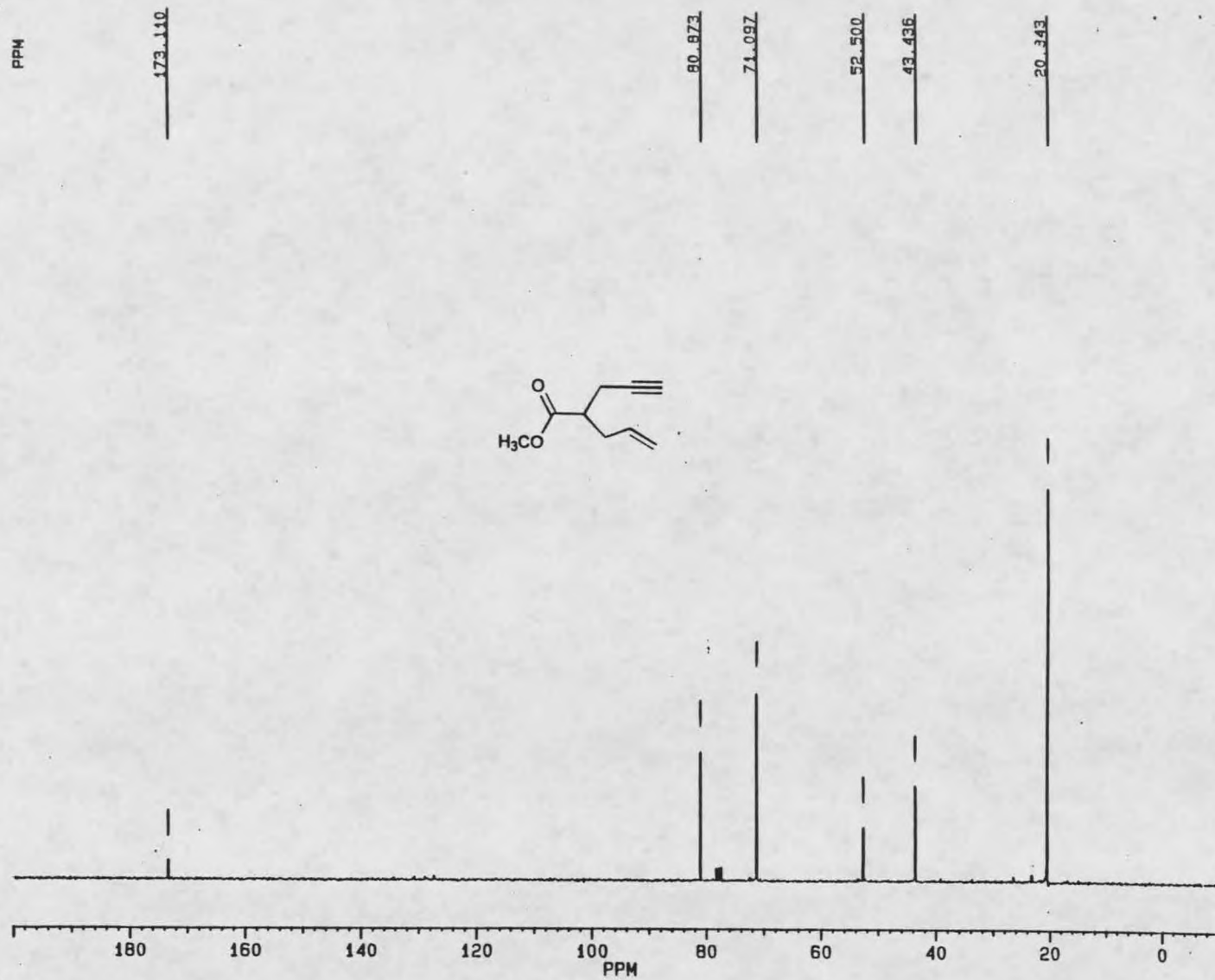
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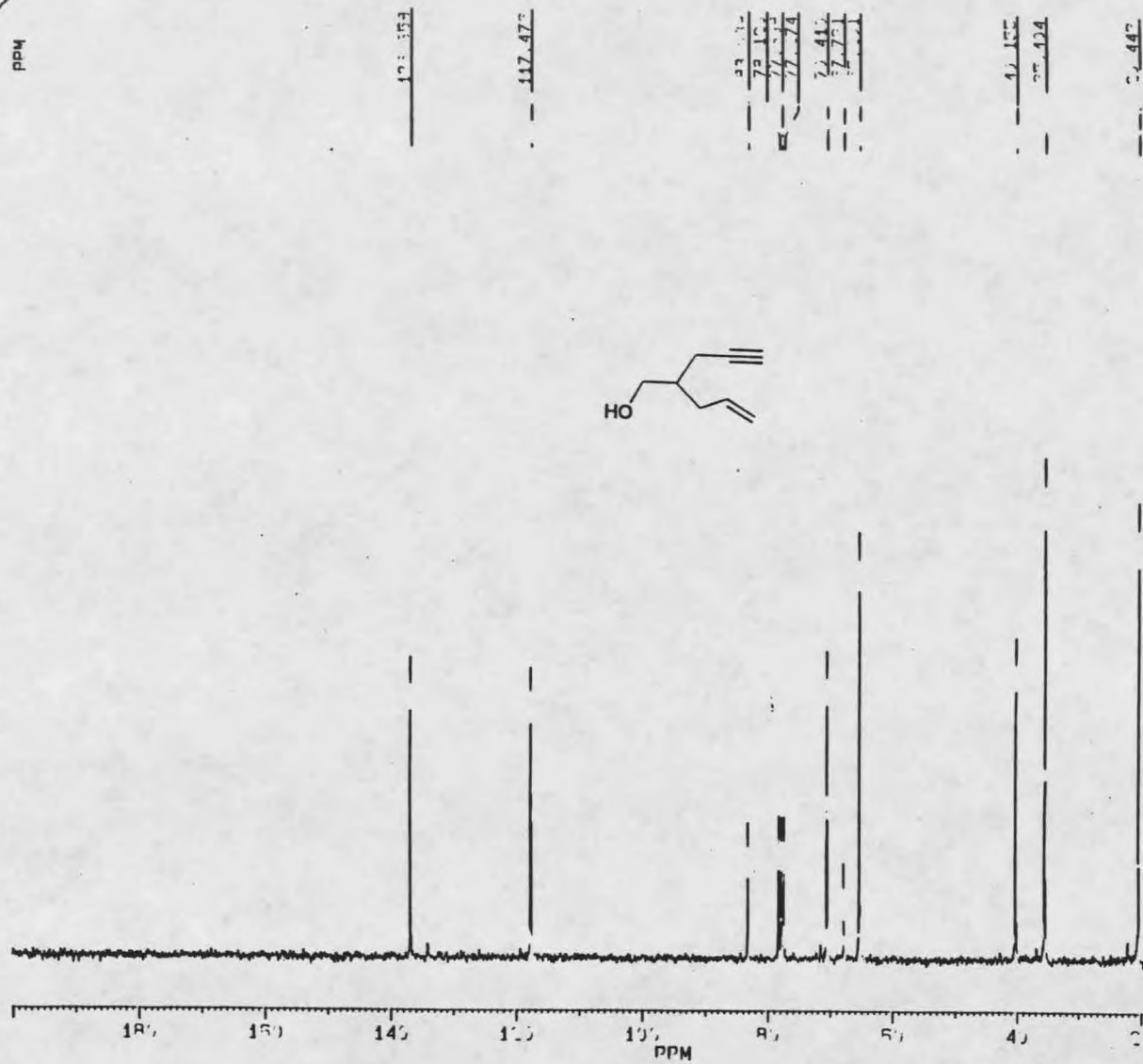


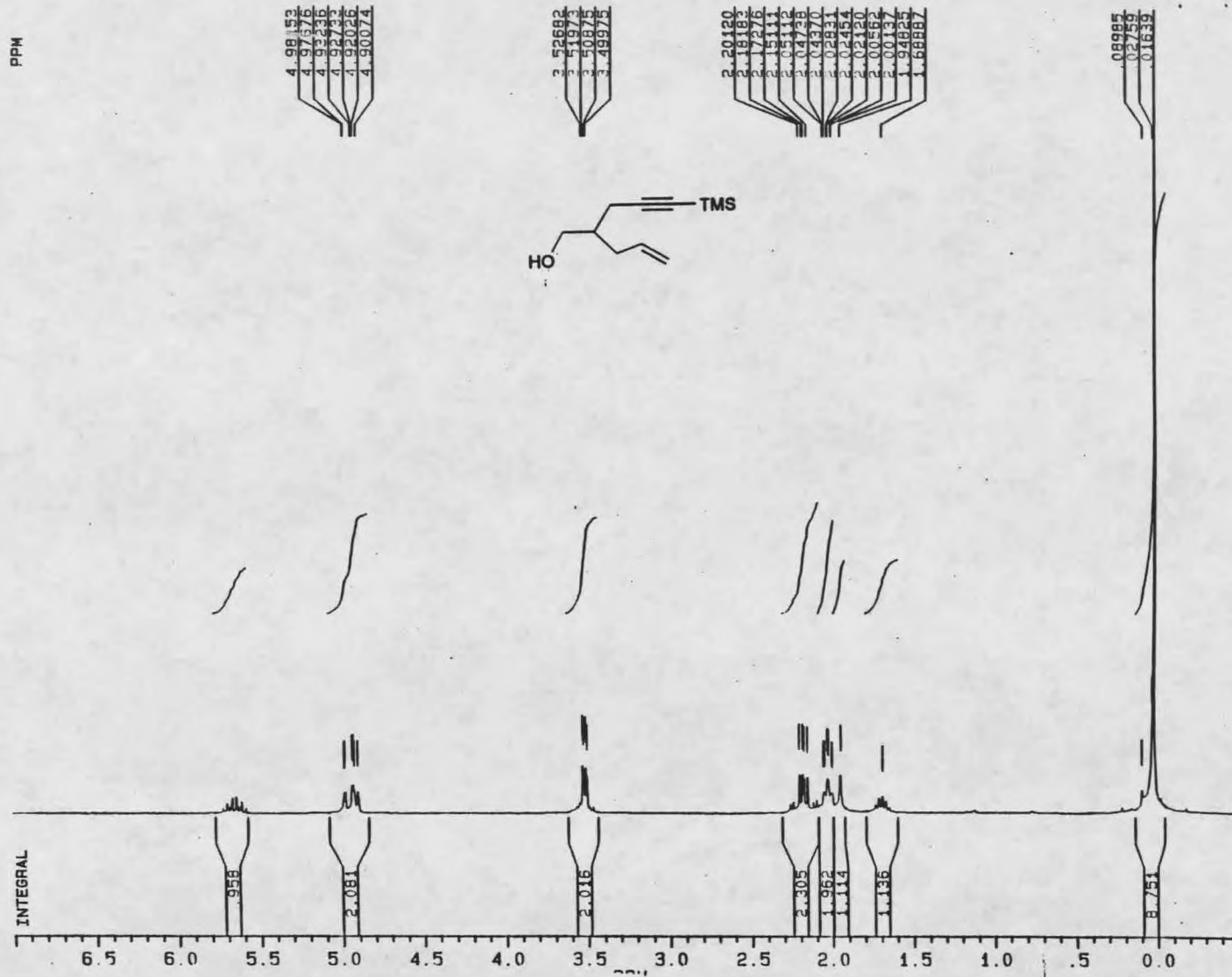




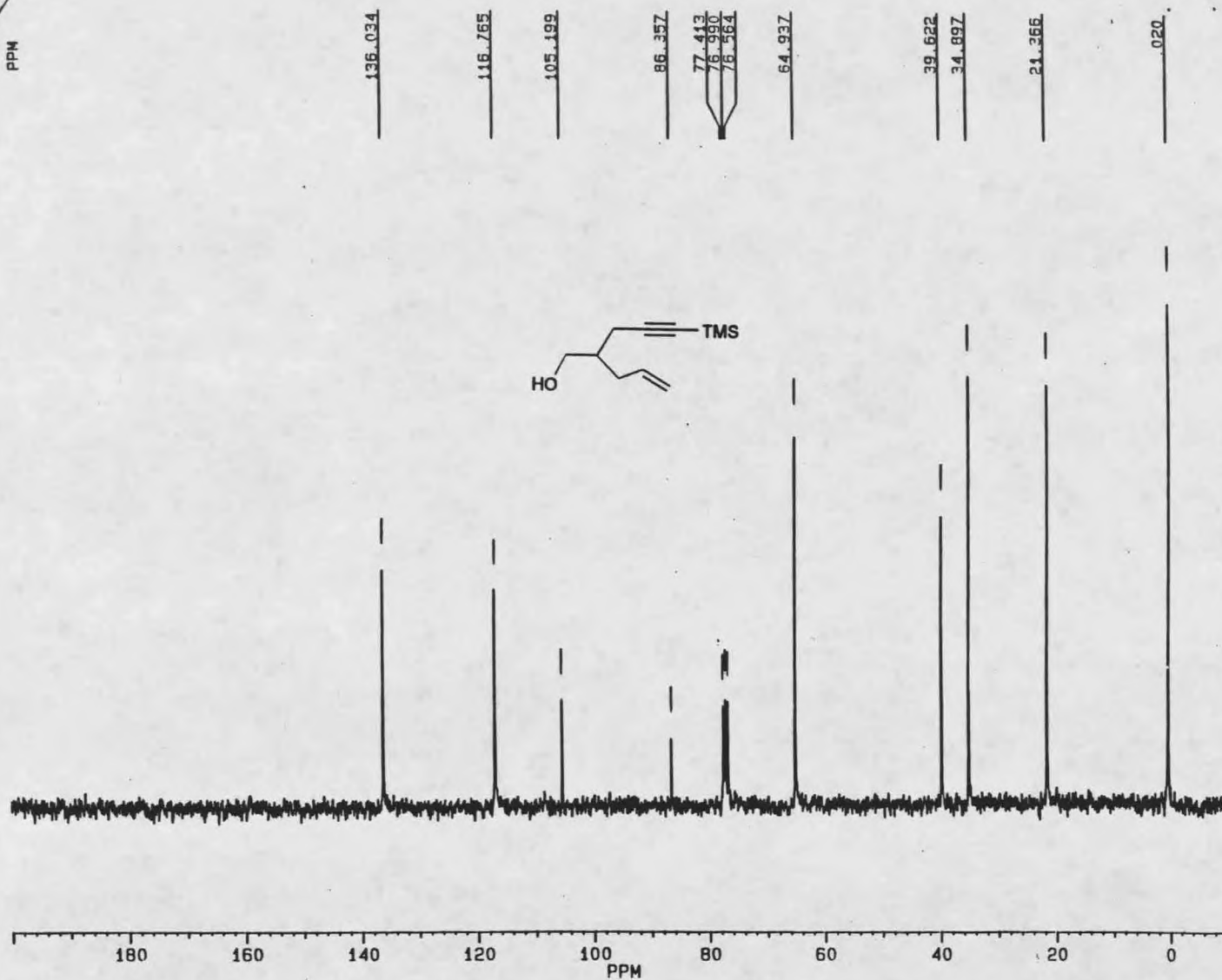


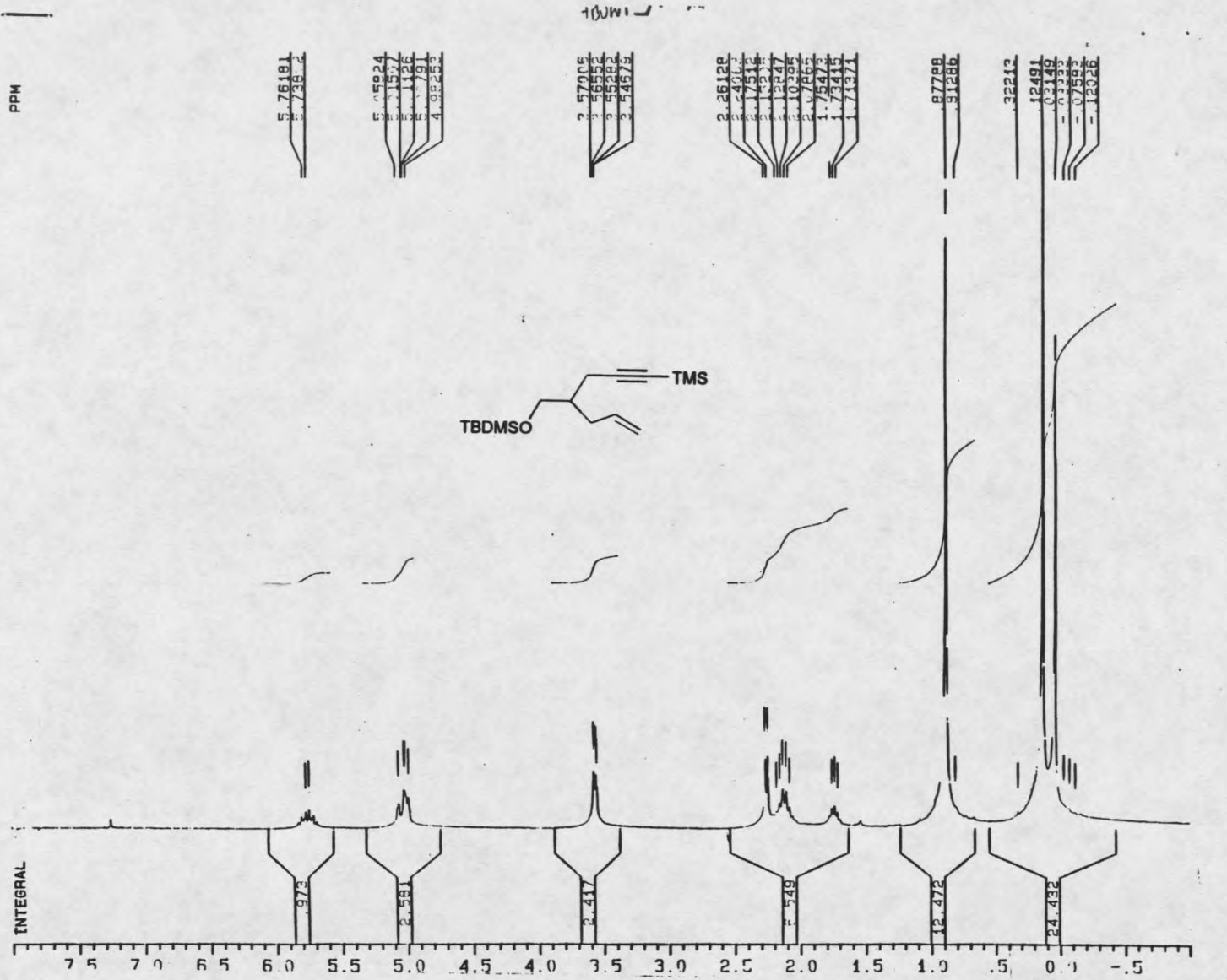
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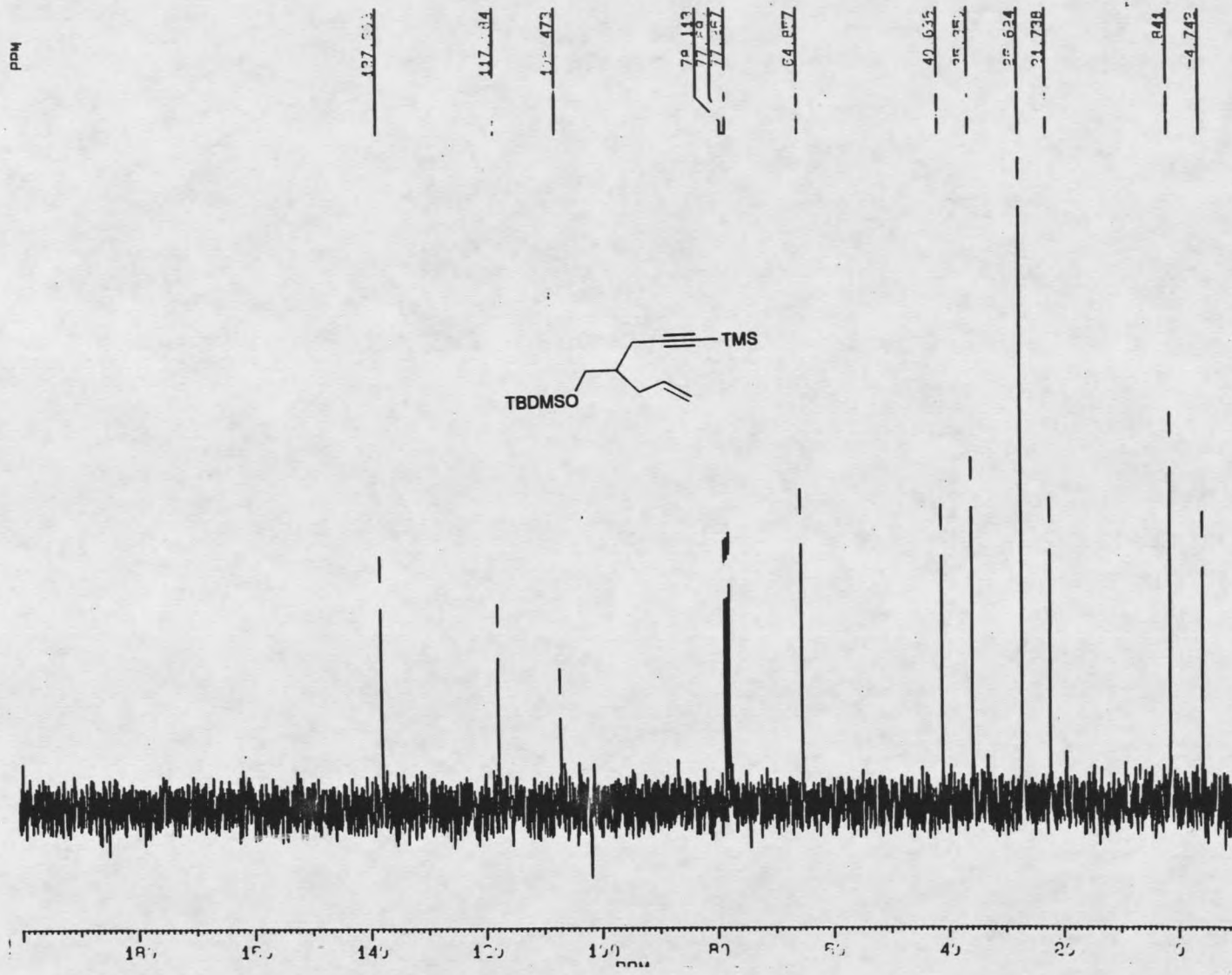


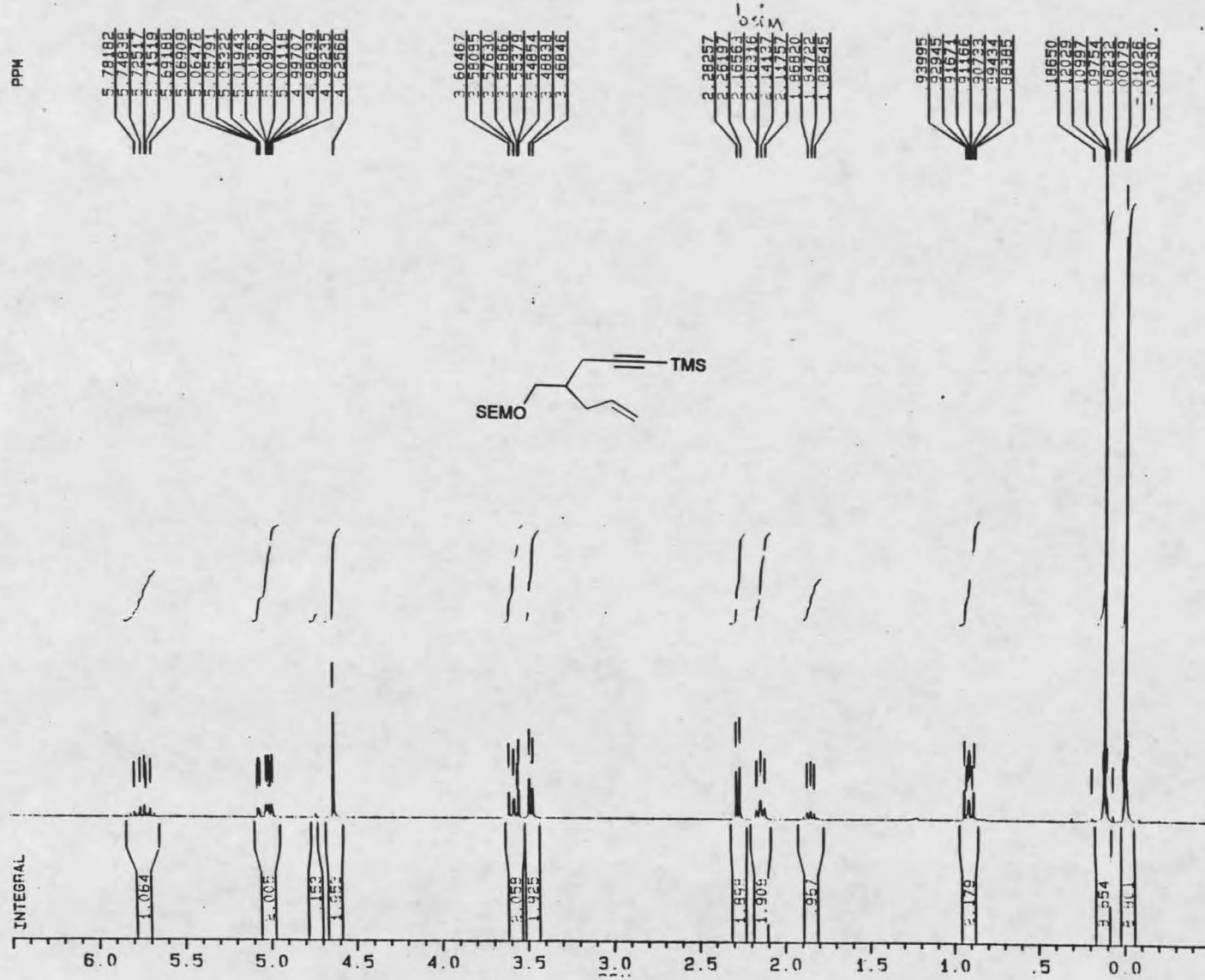


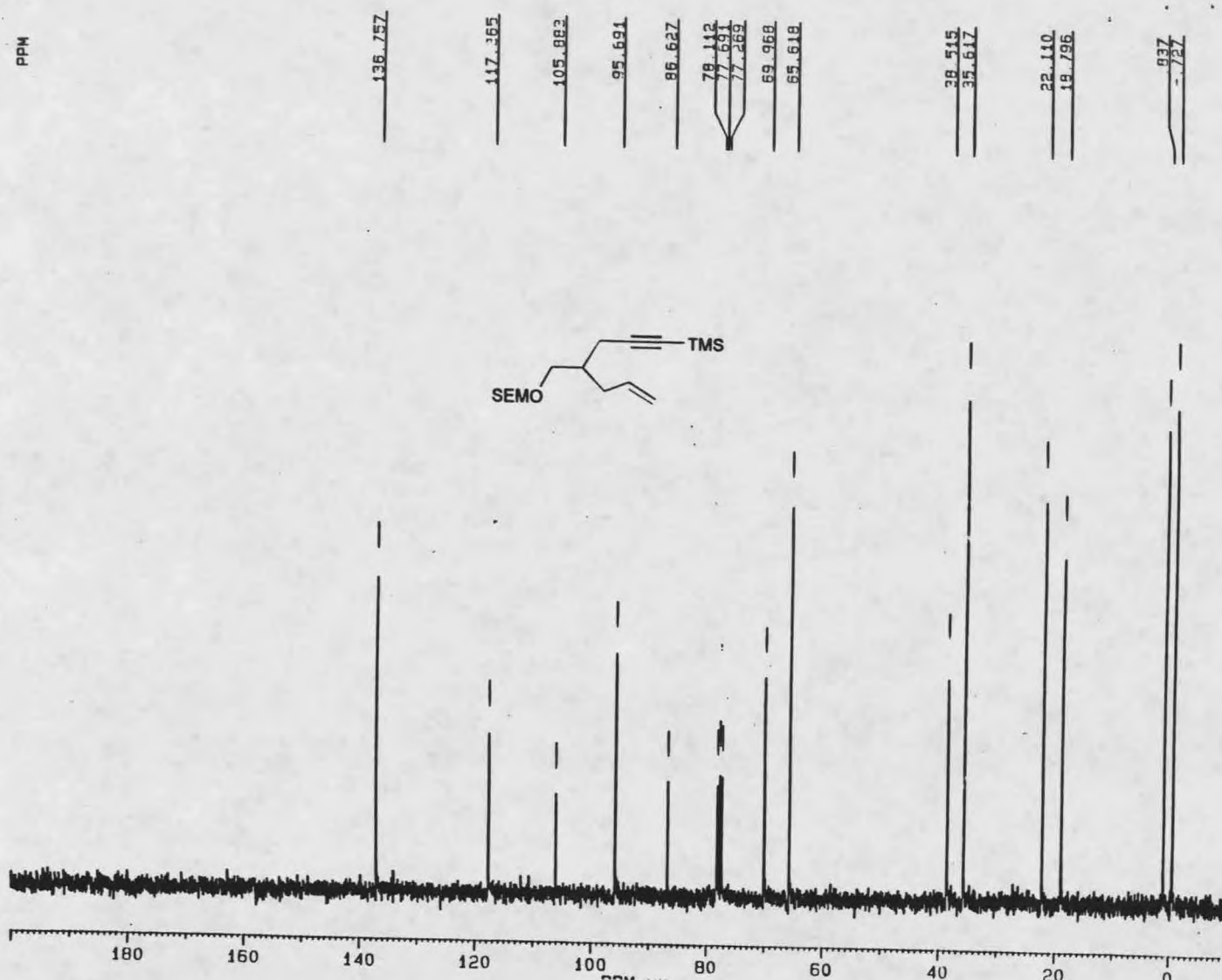
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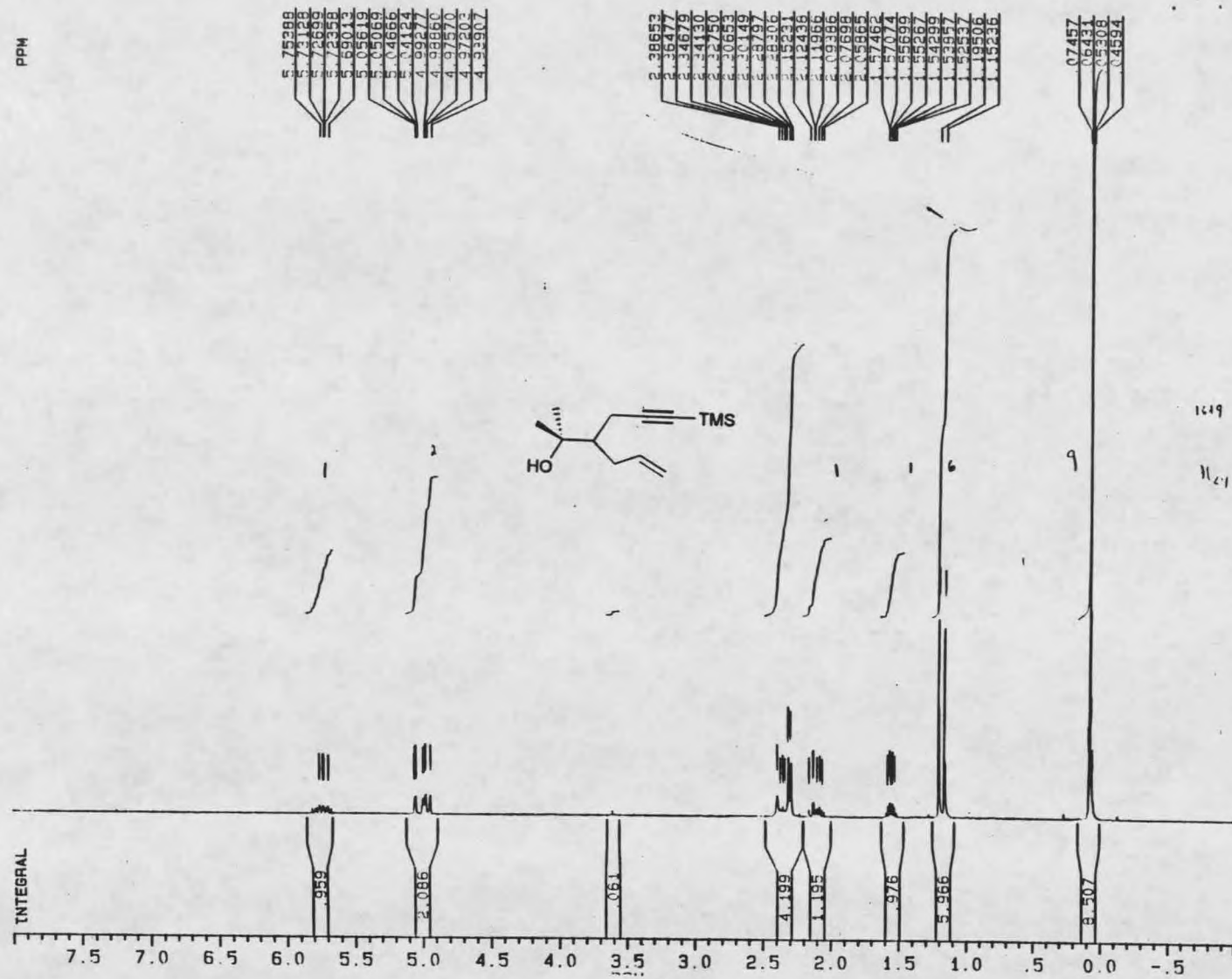




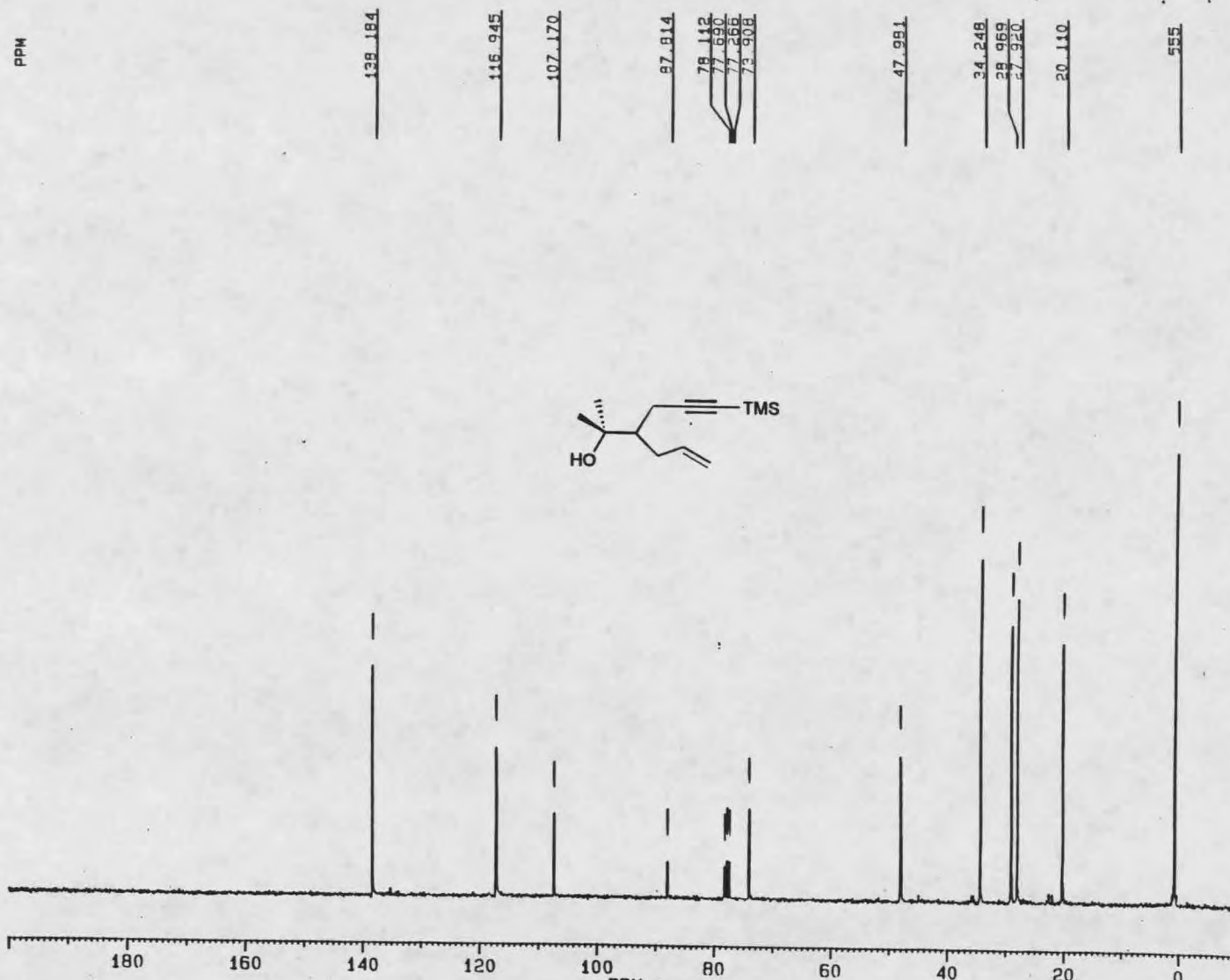


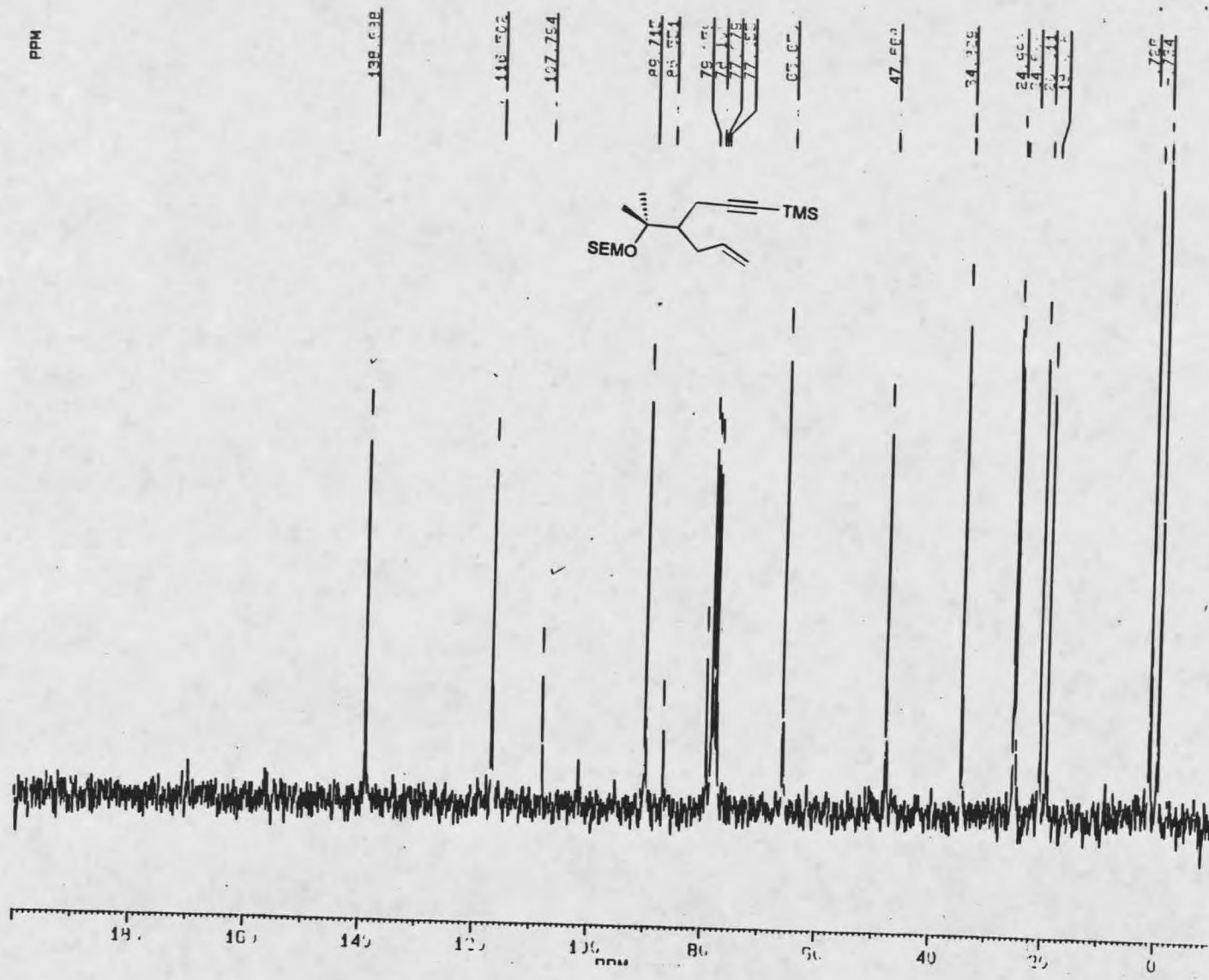


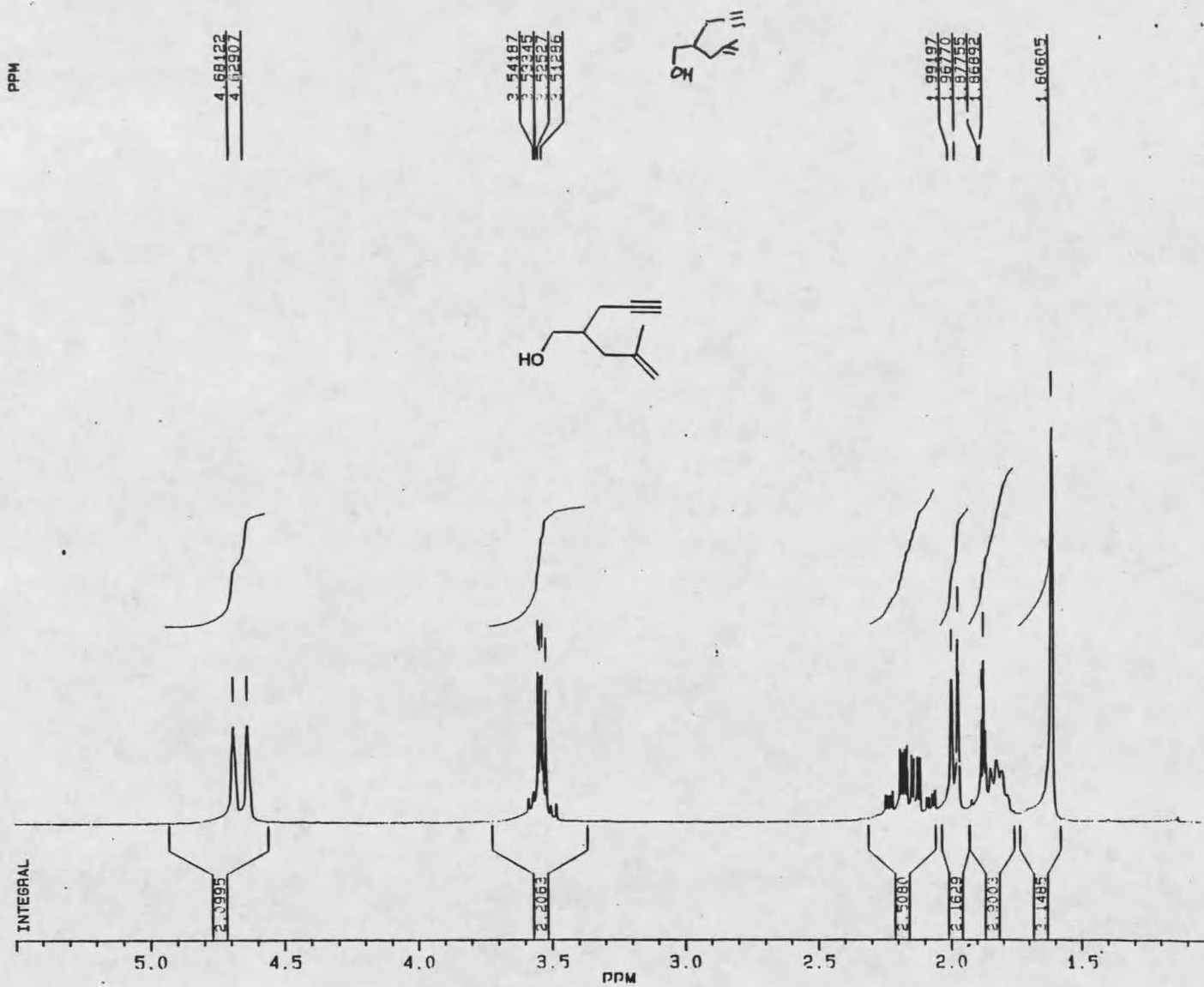


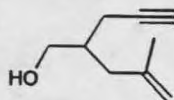
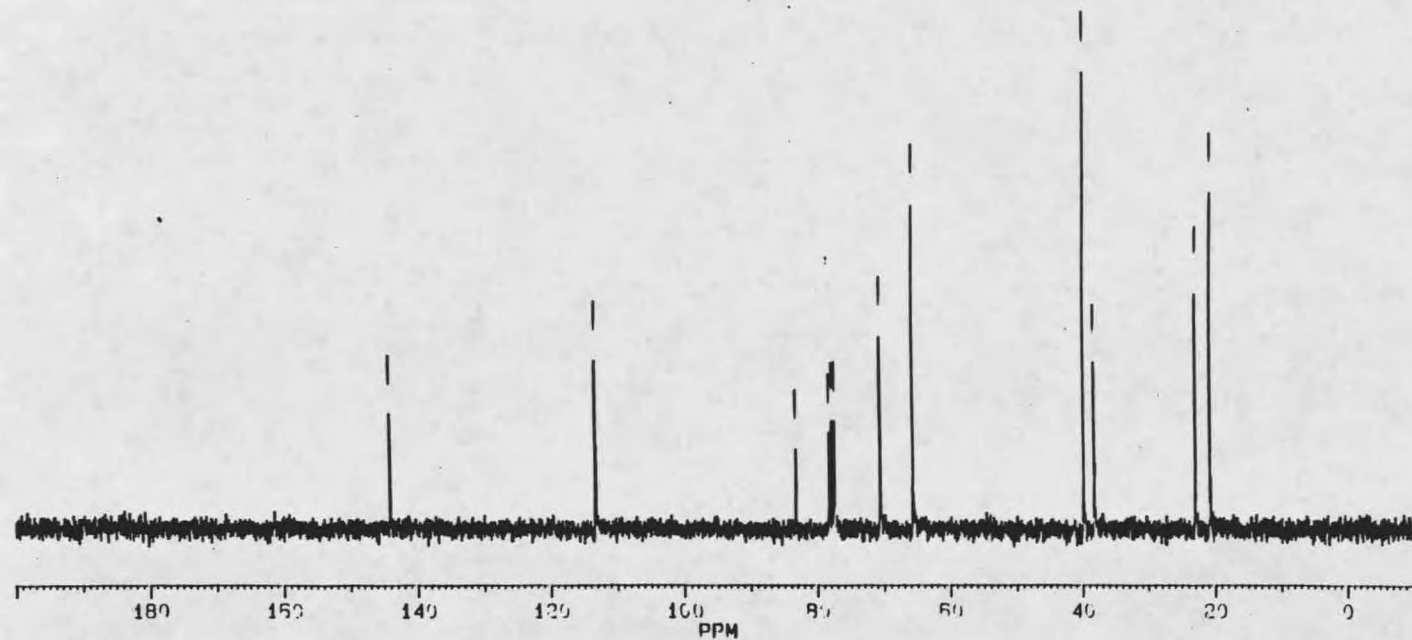


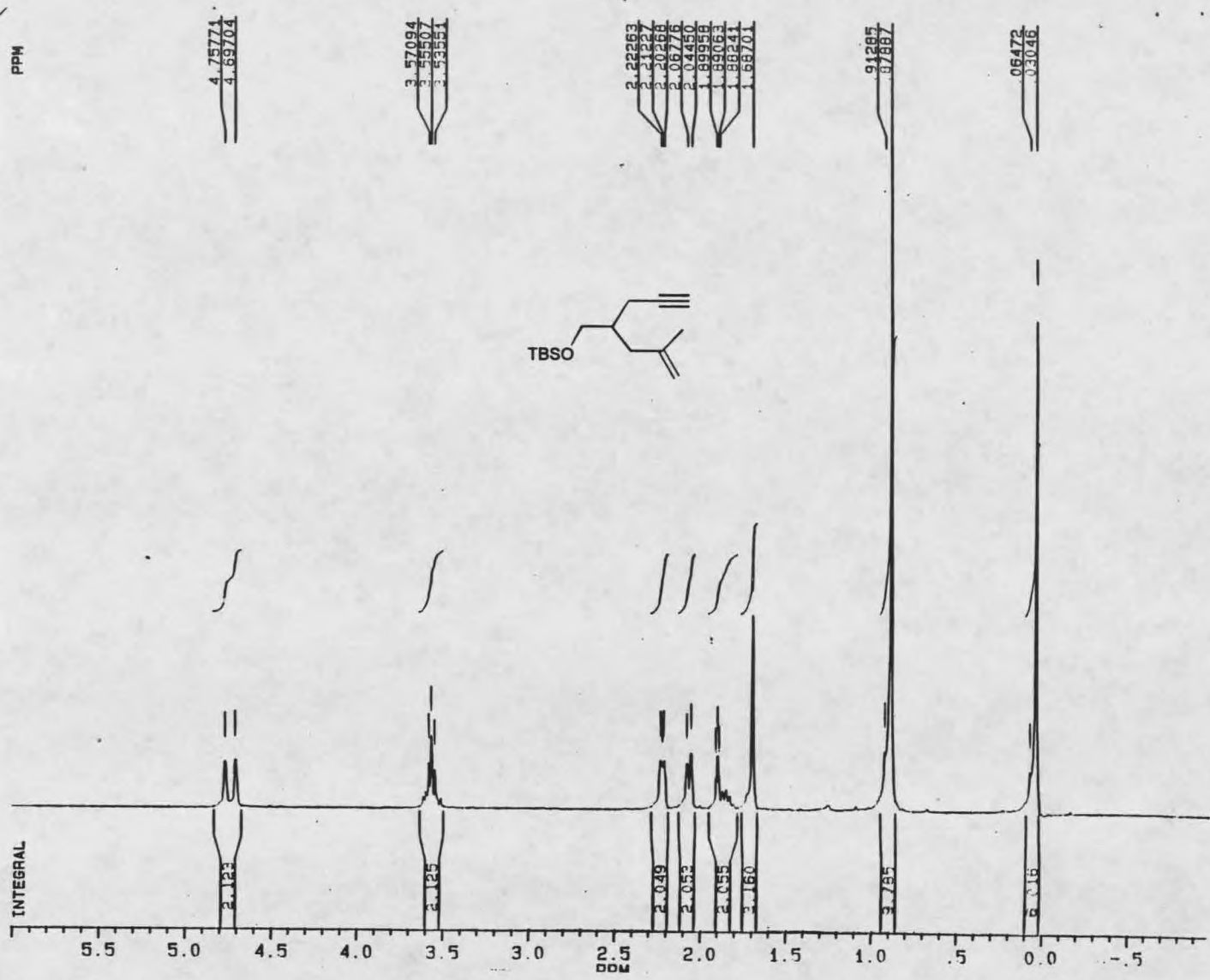
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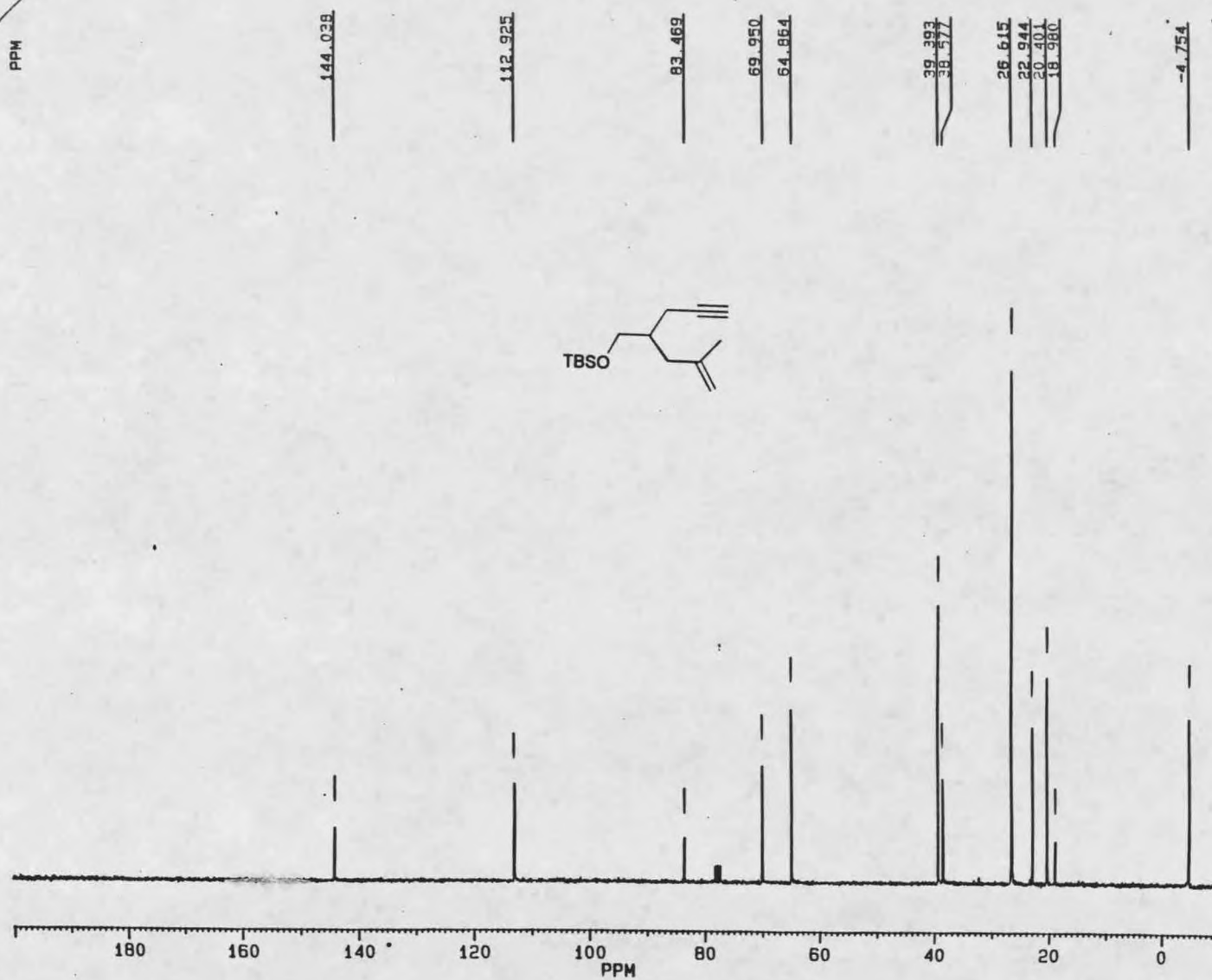




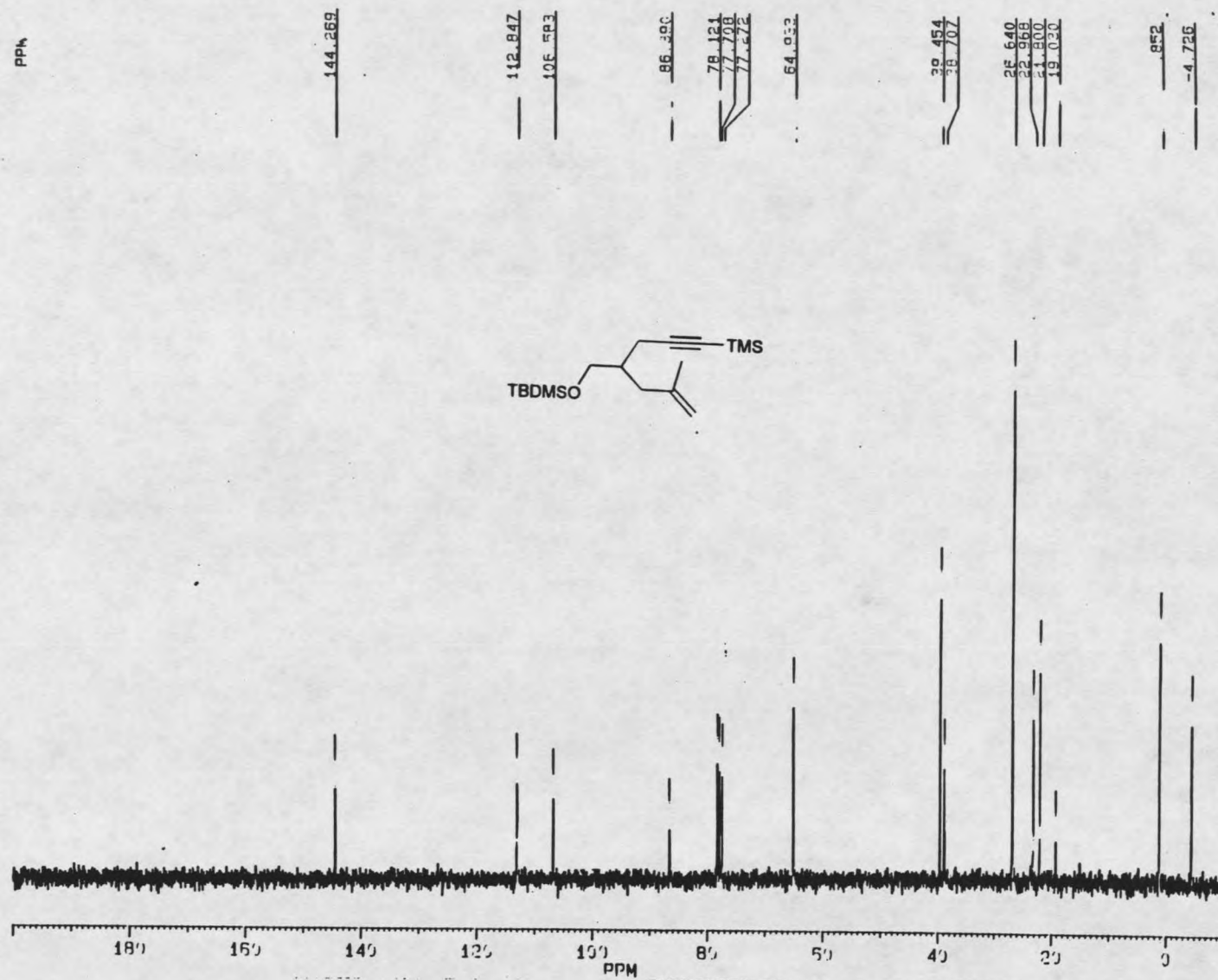


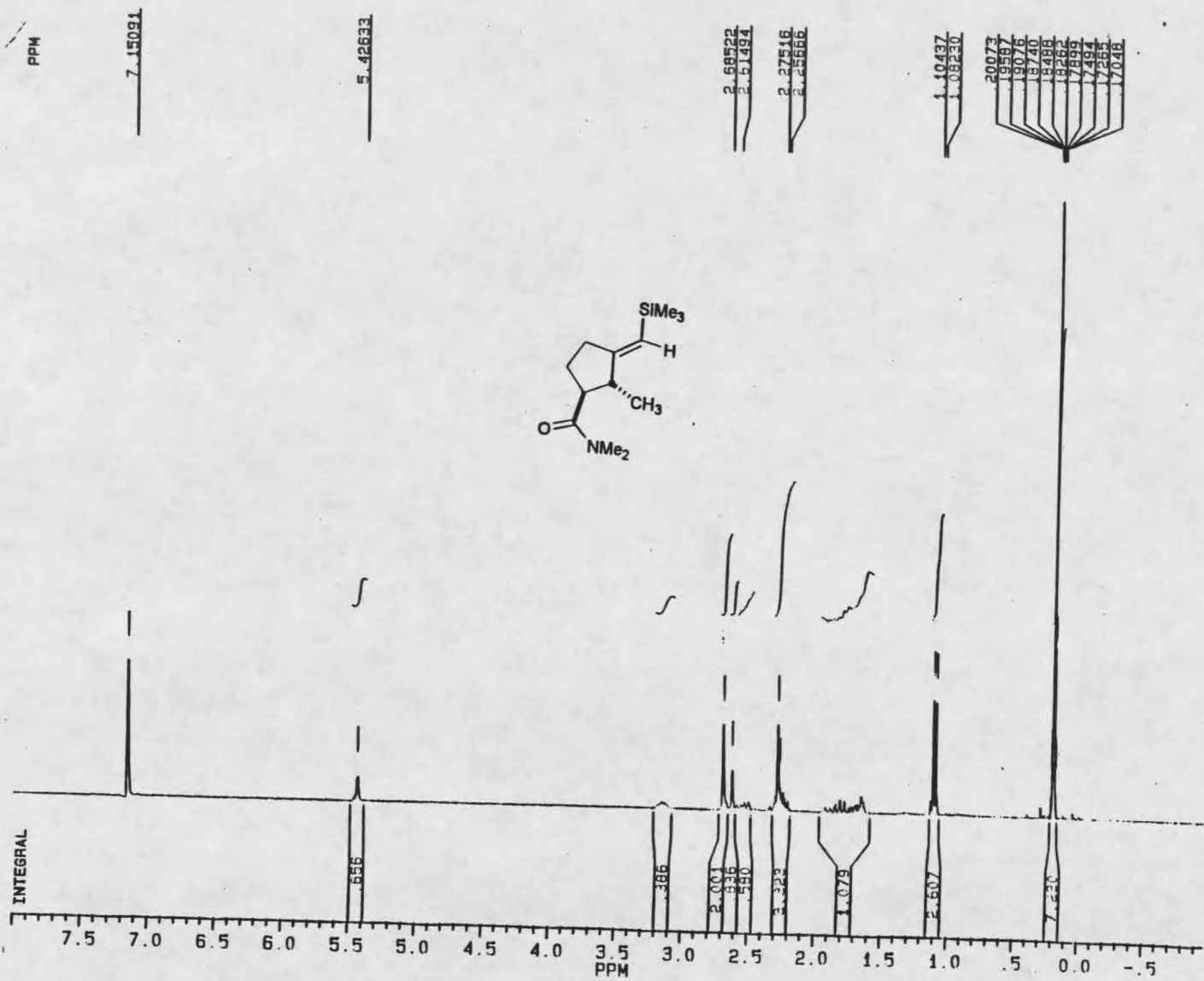


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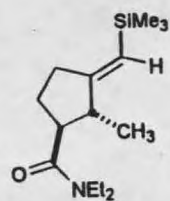
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9.070

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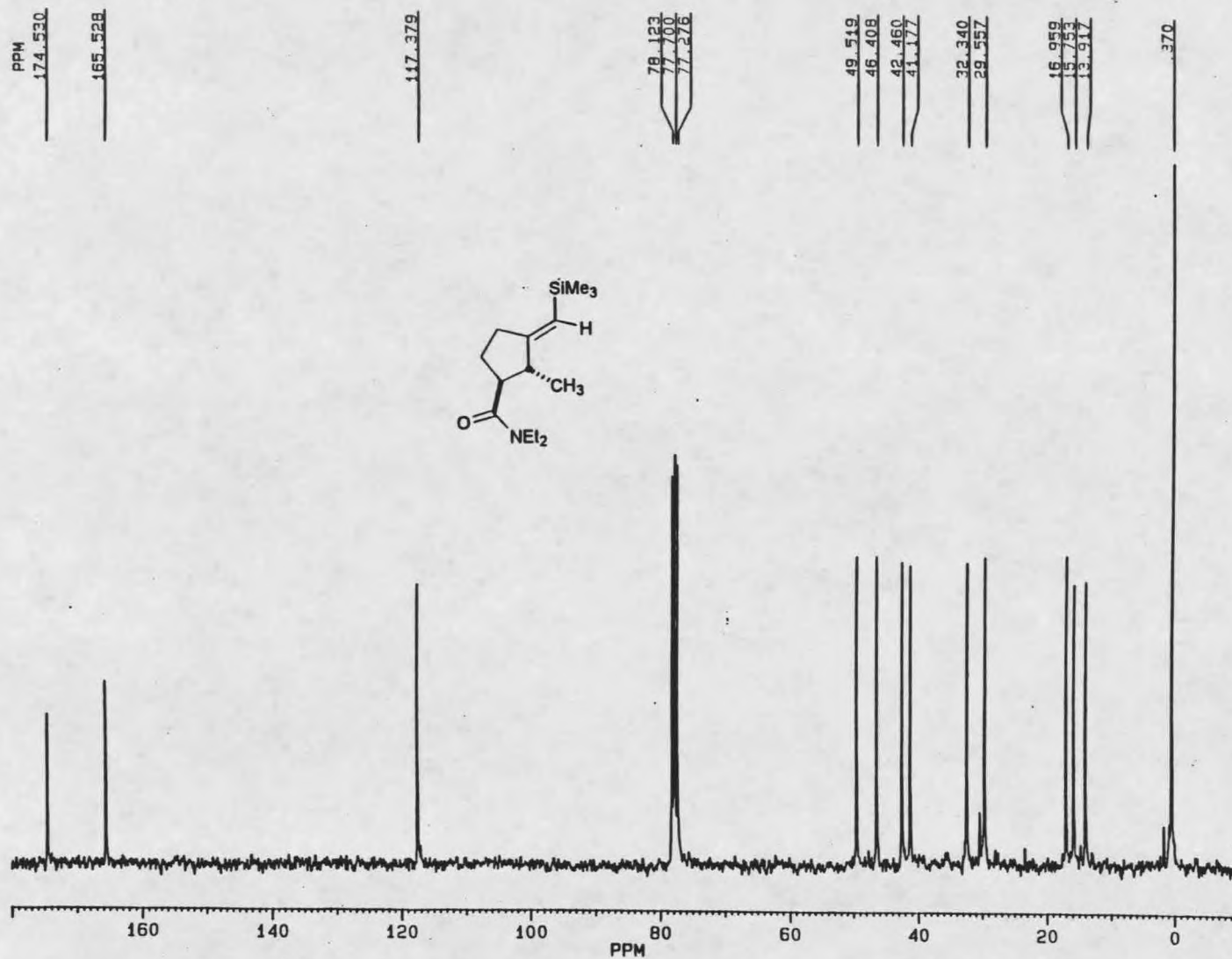
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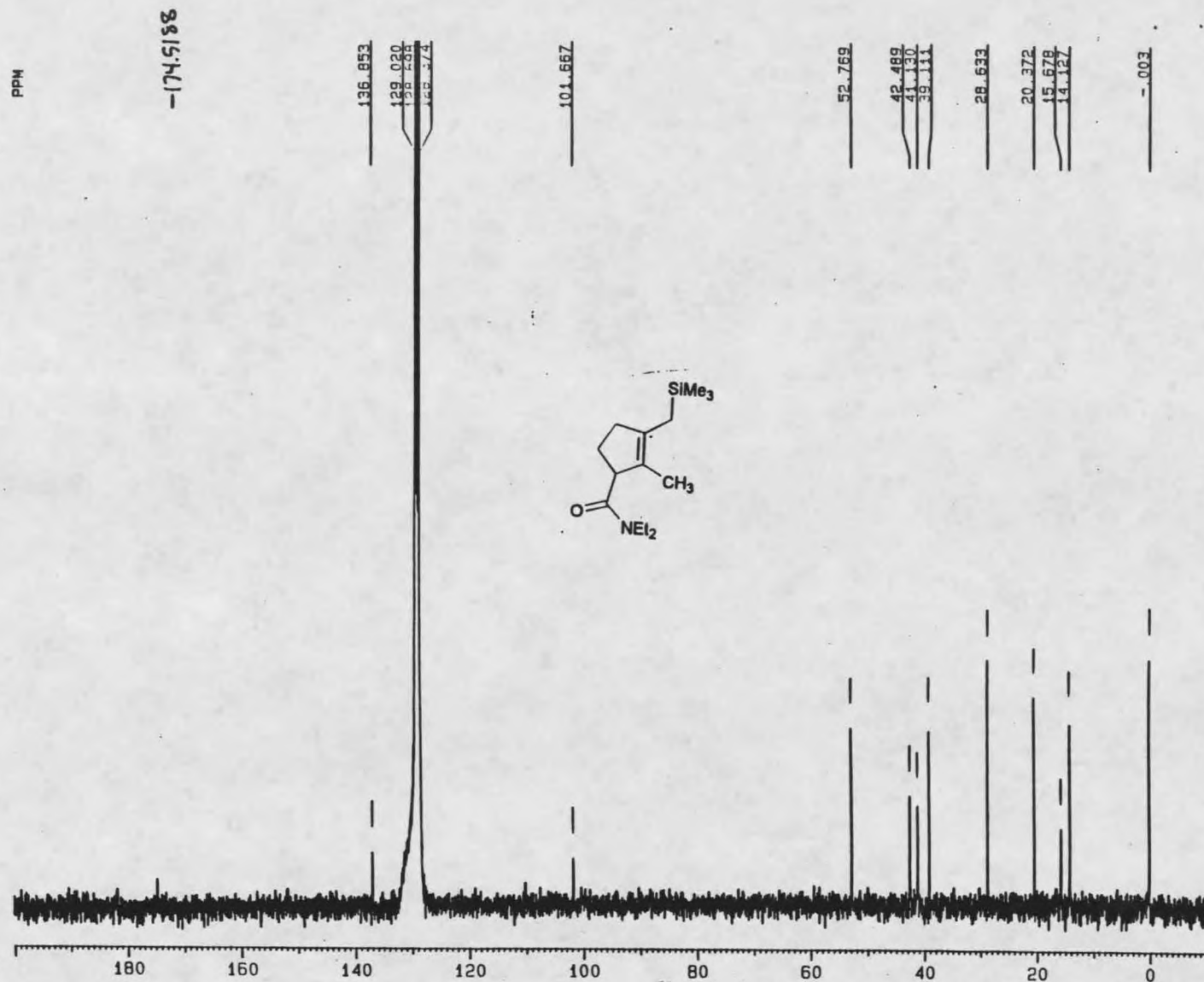
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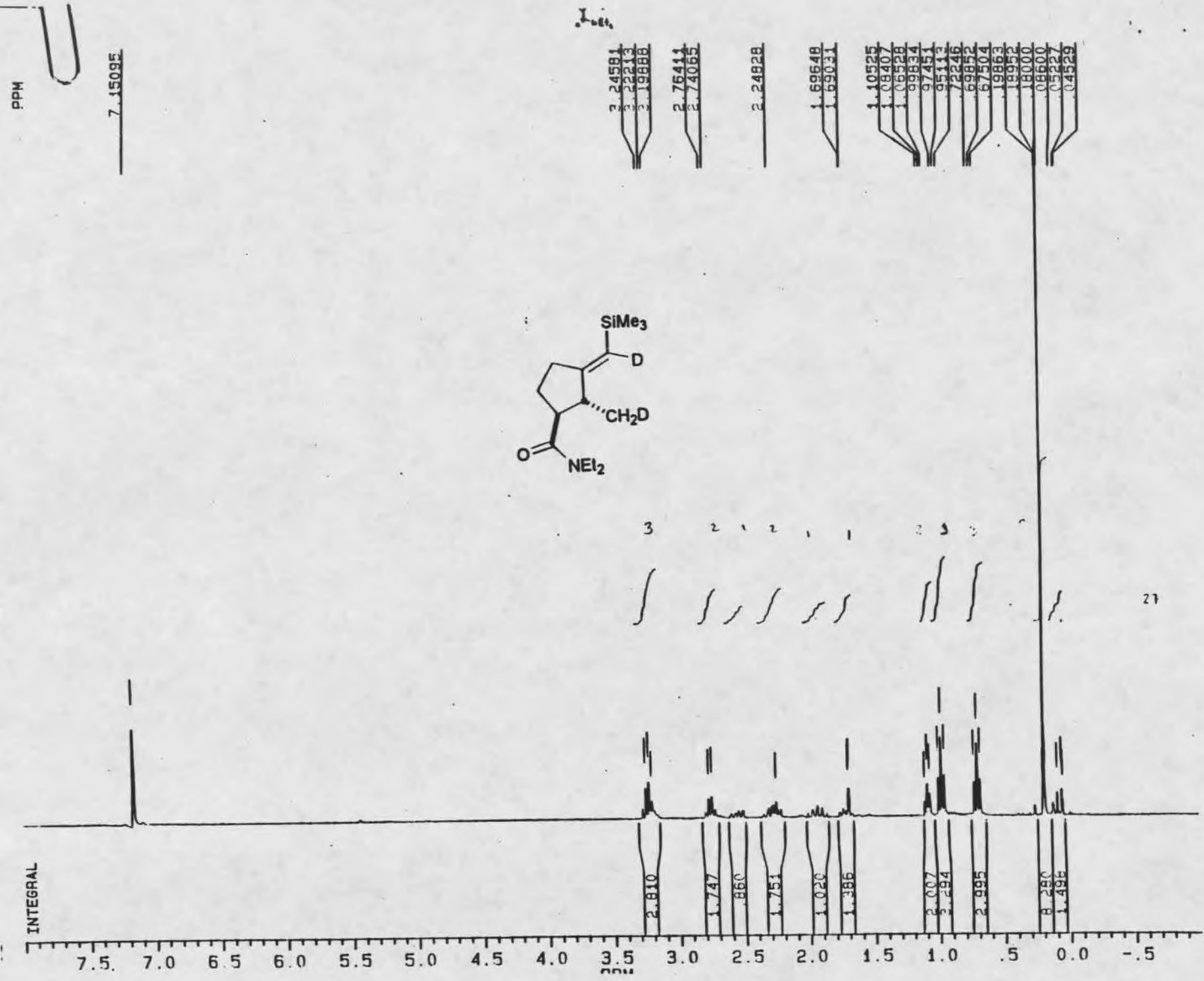
- .5

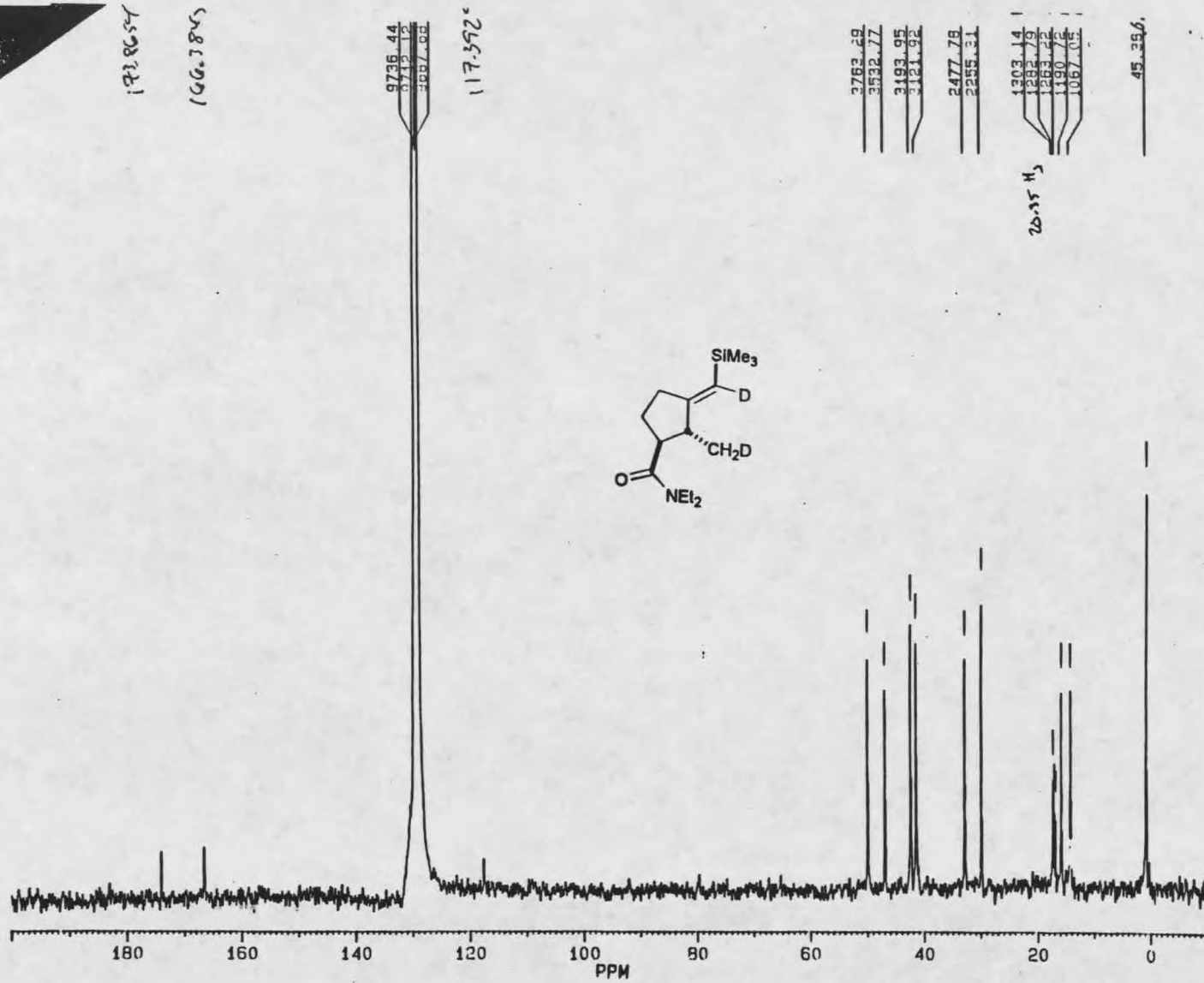
BPL-II-203-1











340

BP-11-202-1

ppm
174.672
174.081

165.542
165.434

117.435

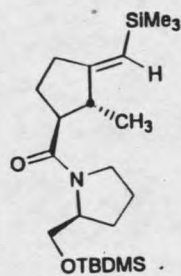
78.131
77.703
77.280

63.795
59.148

51.848
49.352
47.312
46.687

32.322
29.956
29.090
28.300
27.759
26.568
25.037
23.537
19.000
18.049
17.181

385
094
567.4



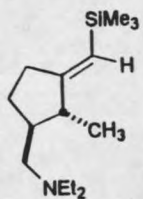
Chemical structure of the compound is shown above the spectrum:

CN(CC1C=CC(C1)C)C

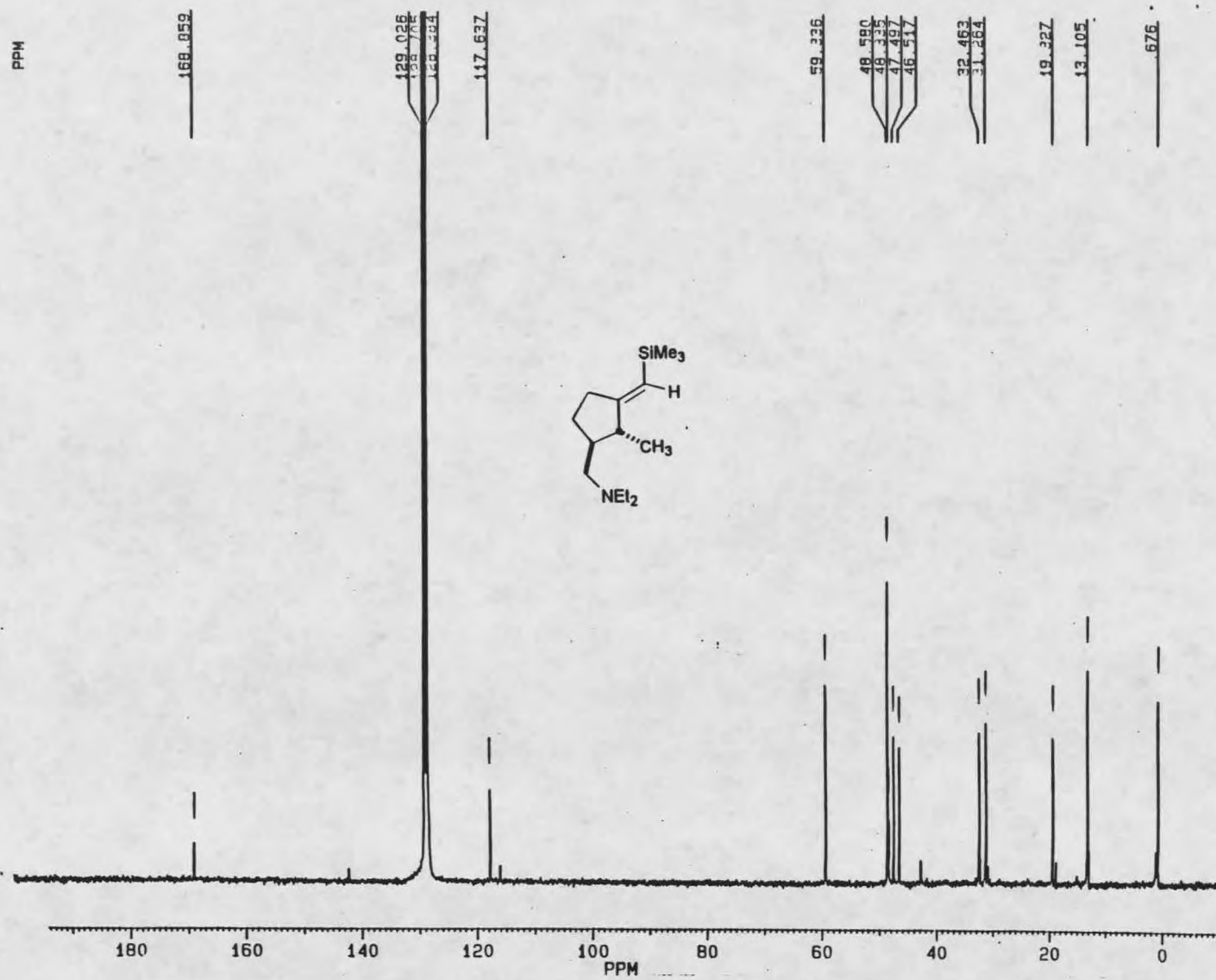
The spectrum displays several peaks corresponding to the structure:

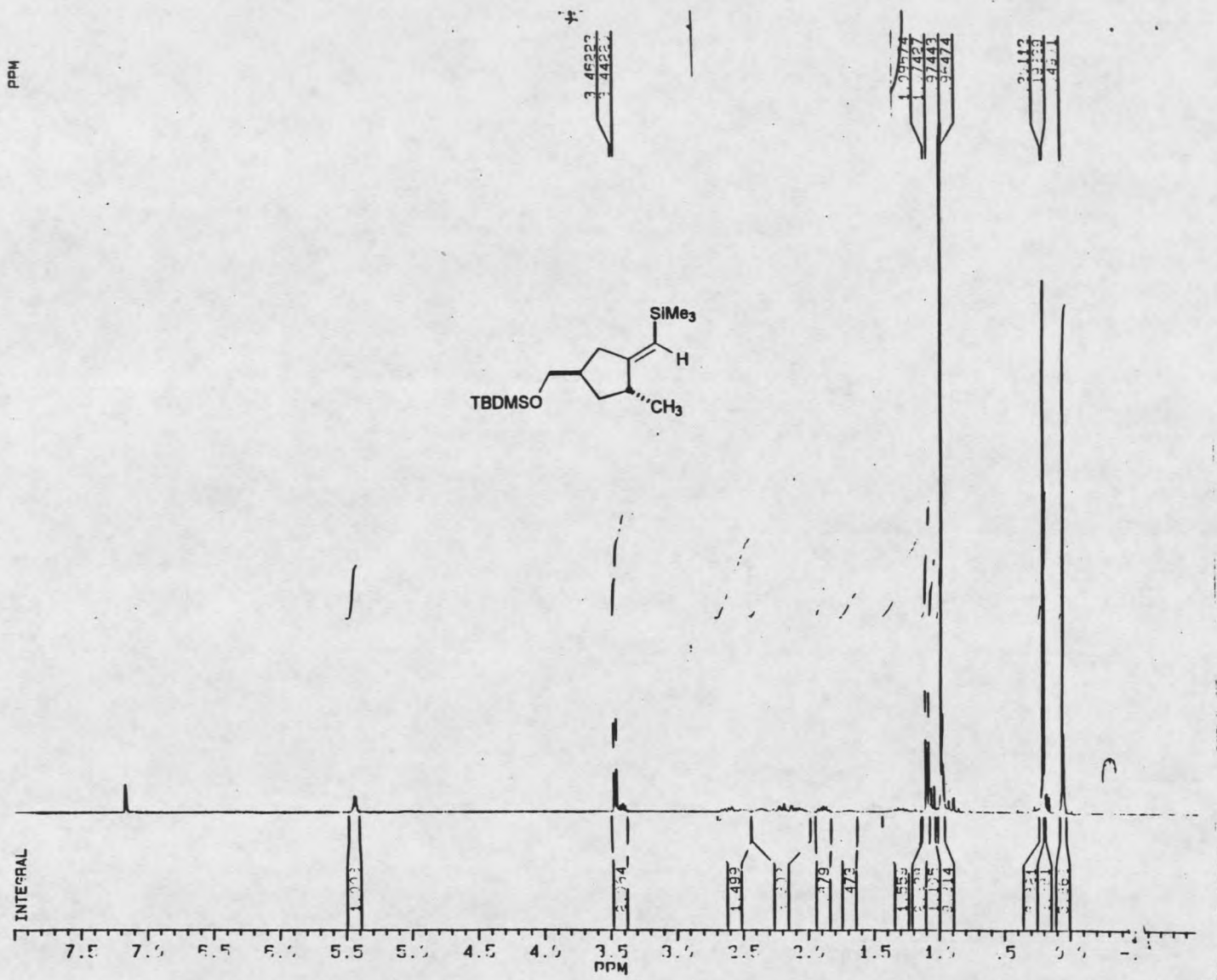
- Peak at ~5.5 ppm: NH_2 group.
- Peak at ~2.5 ppm: CH_2 group adjacent to the NH_2 group.
- Peak at ~1.2 ppm: CH_3 group.
- Peak at ~0.9 ppm: CH_2 group adjacent to the CH_3 group.

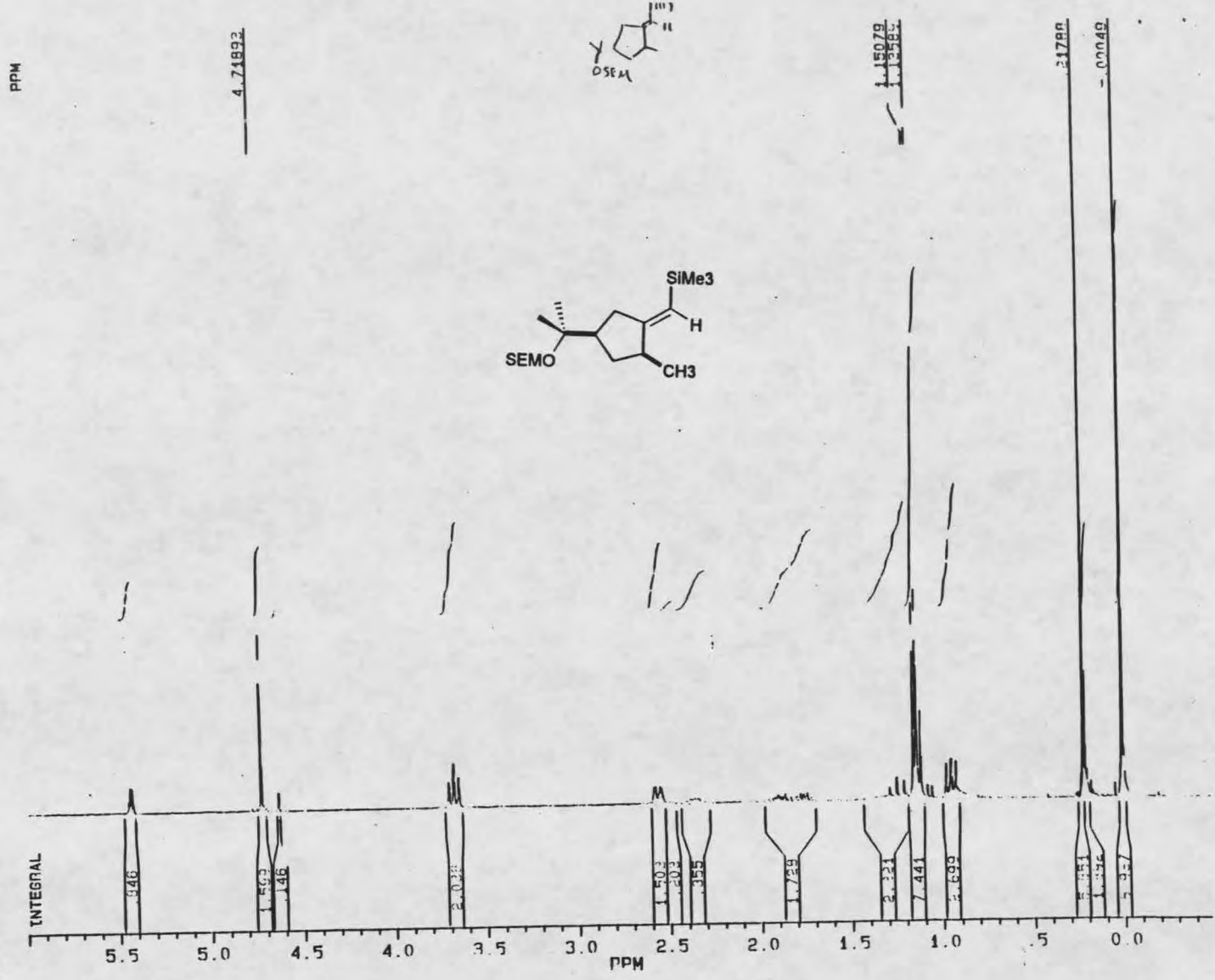
The x-axis is labeled PPM (ranging from 0.0 to 5.5) and the y-axis is labeled PPM (ranging from 0.0 to 5.5).

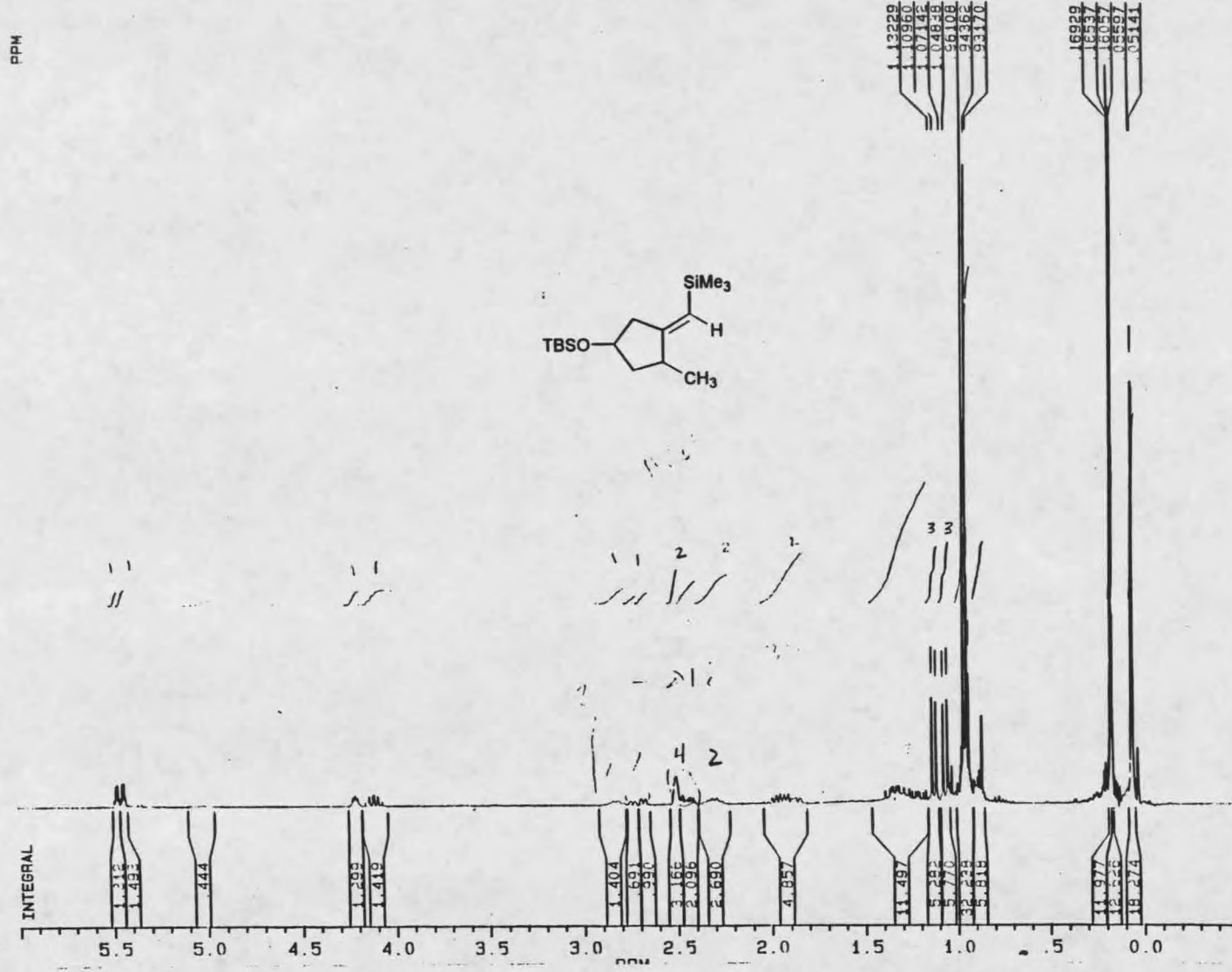


343



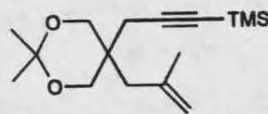
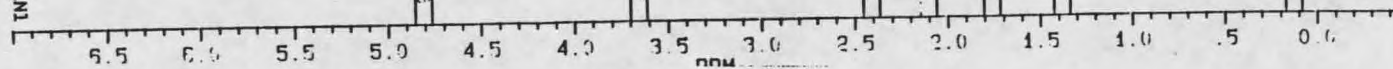


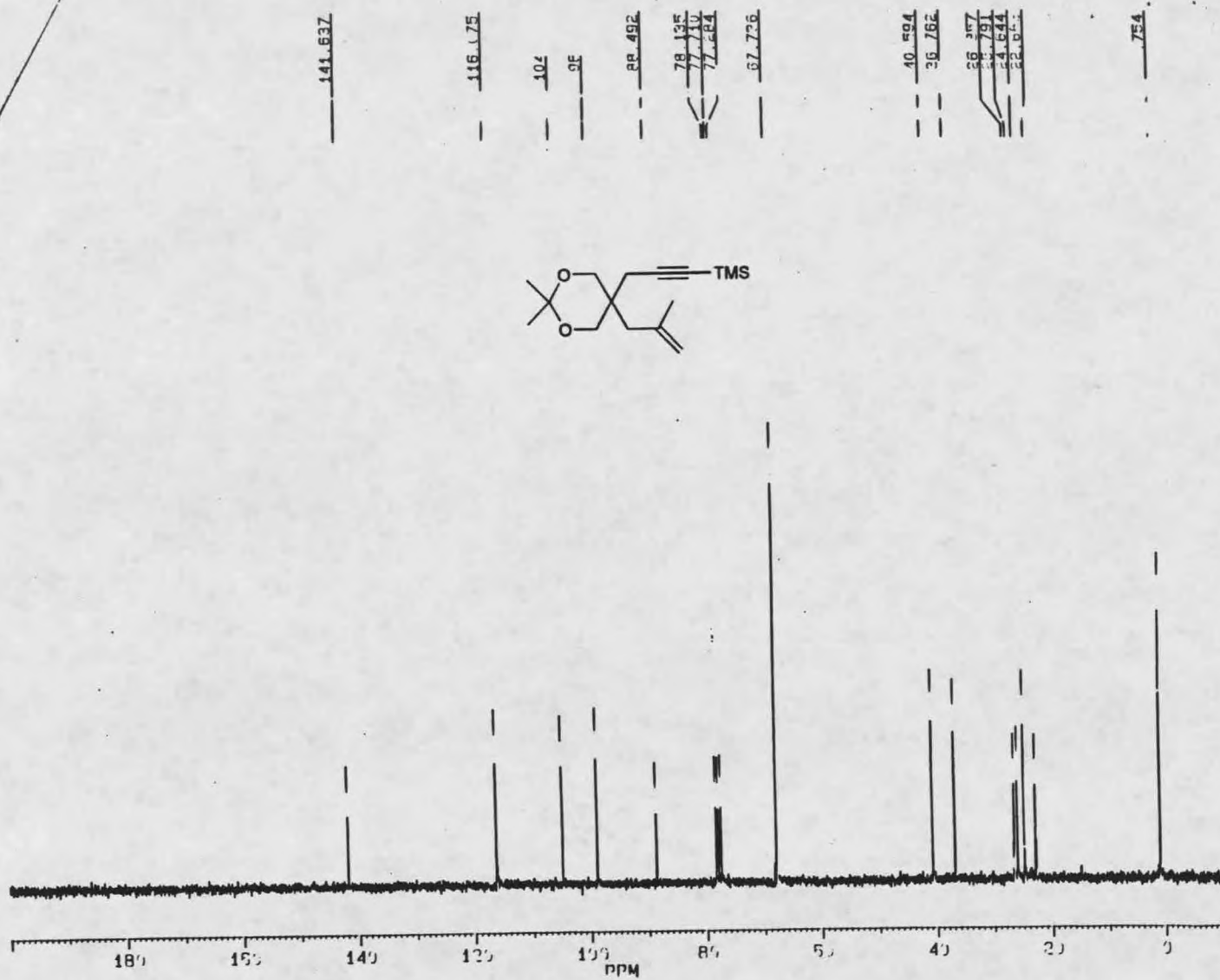


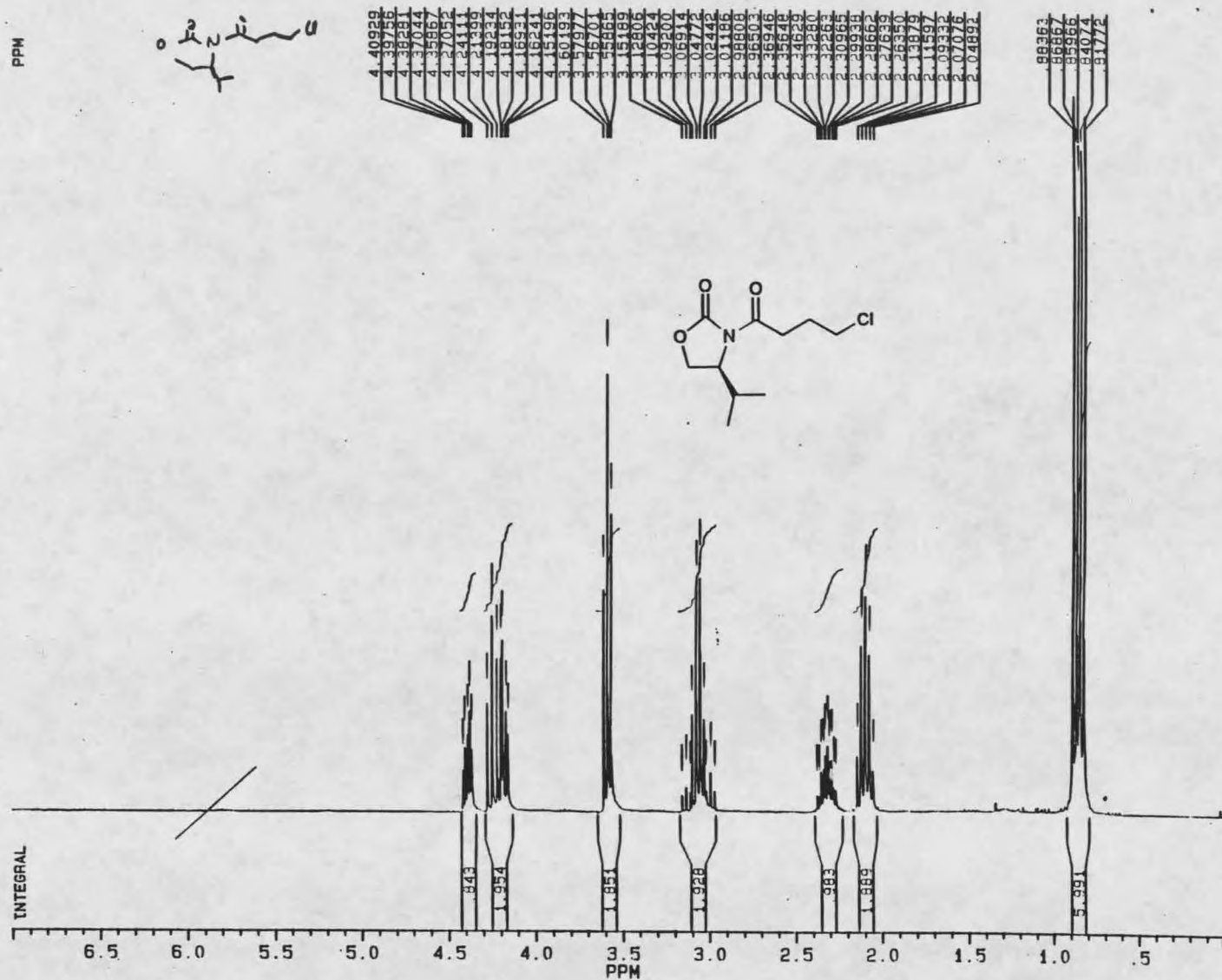


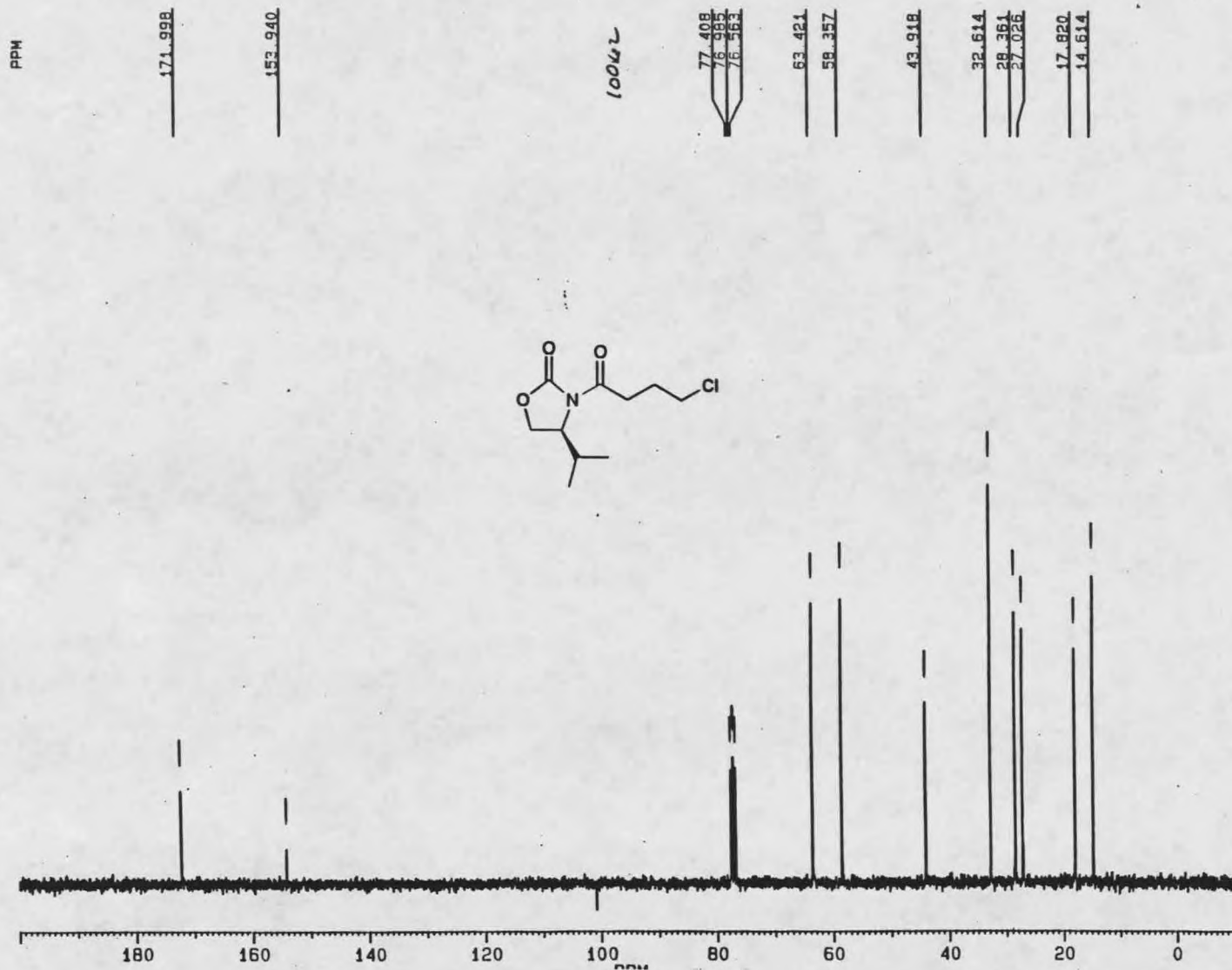
PPM

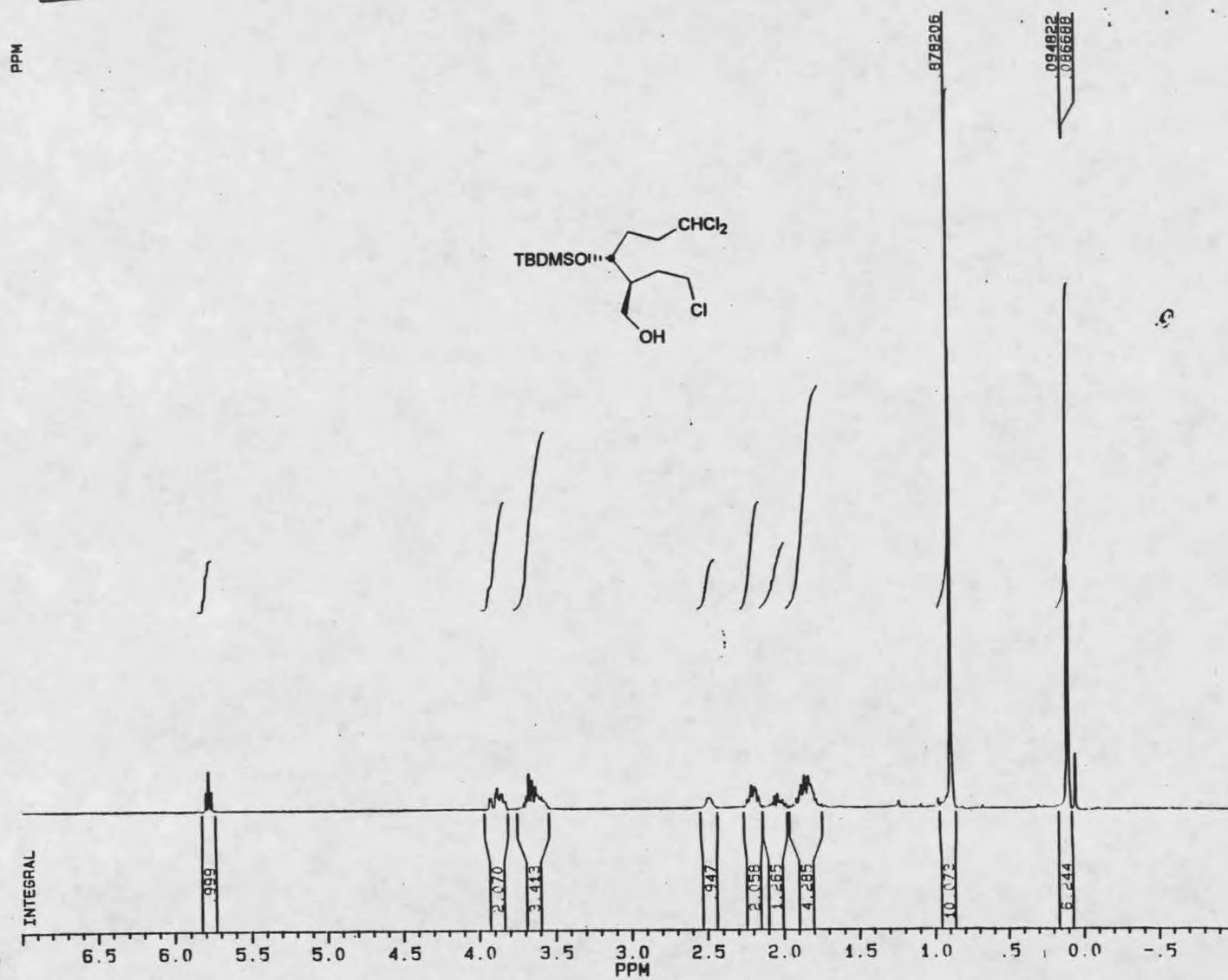
INTEGRAL

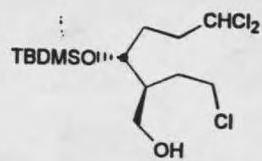
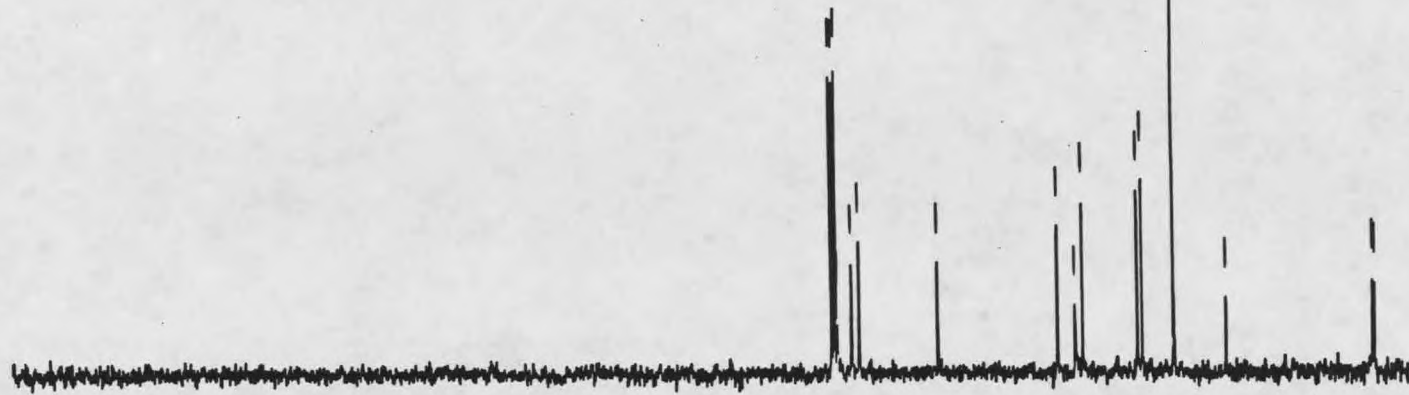












77.4167
76.9934
76.5700
74.3803
73.2552

61,4805

$$\begin{array}{r} 43.3408 \\ \hline 40.7276 \\ \hline 29.4976 \end{array}$$

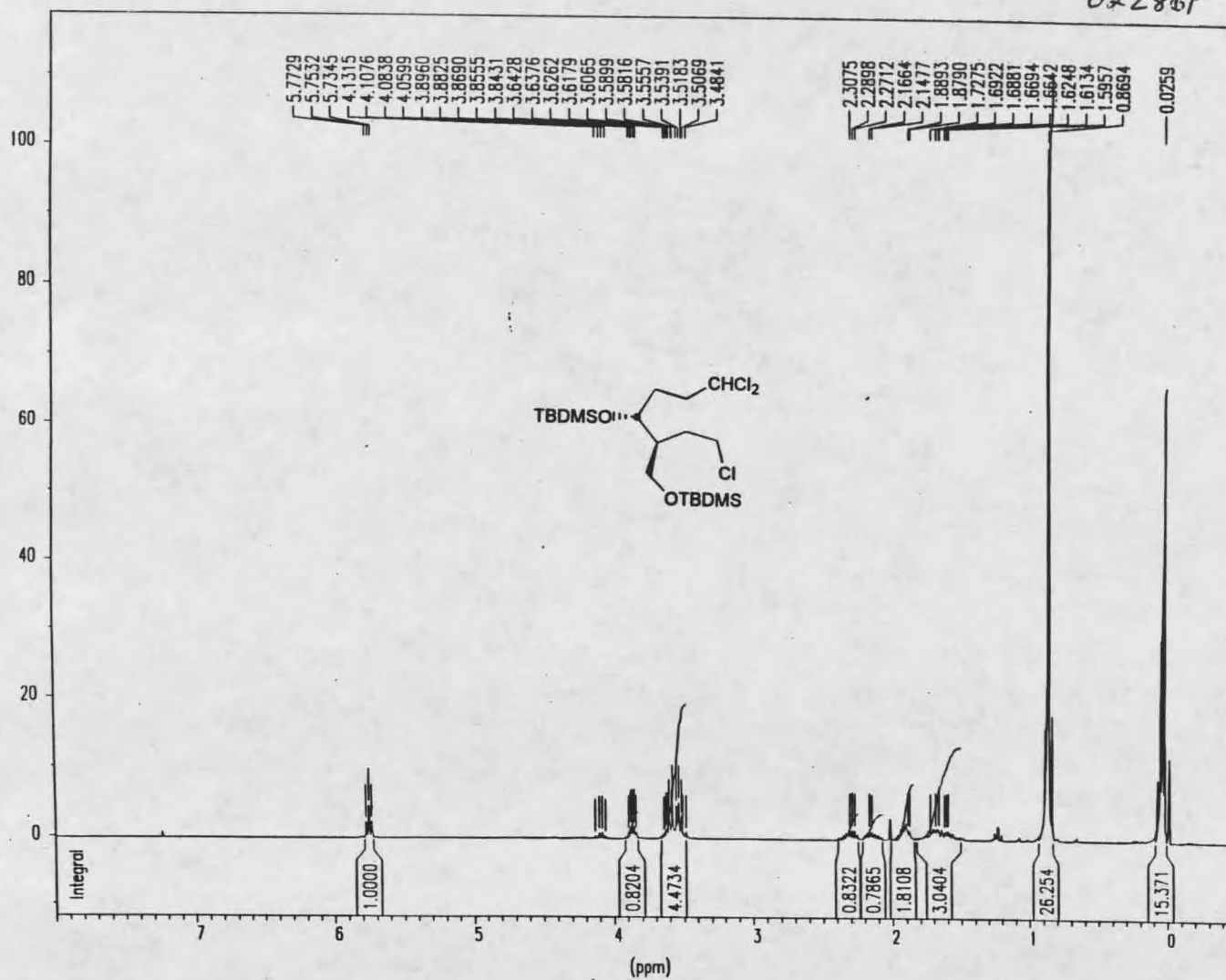
31.2557
30.5044

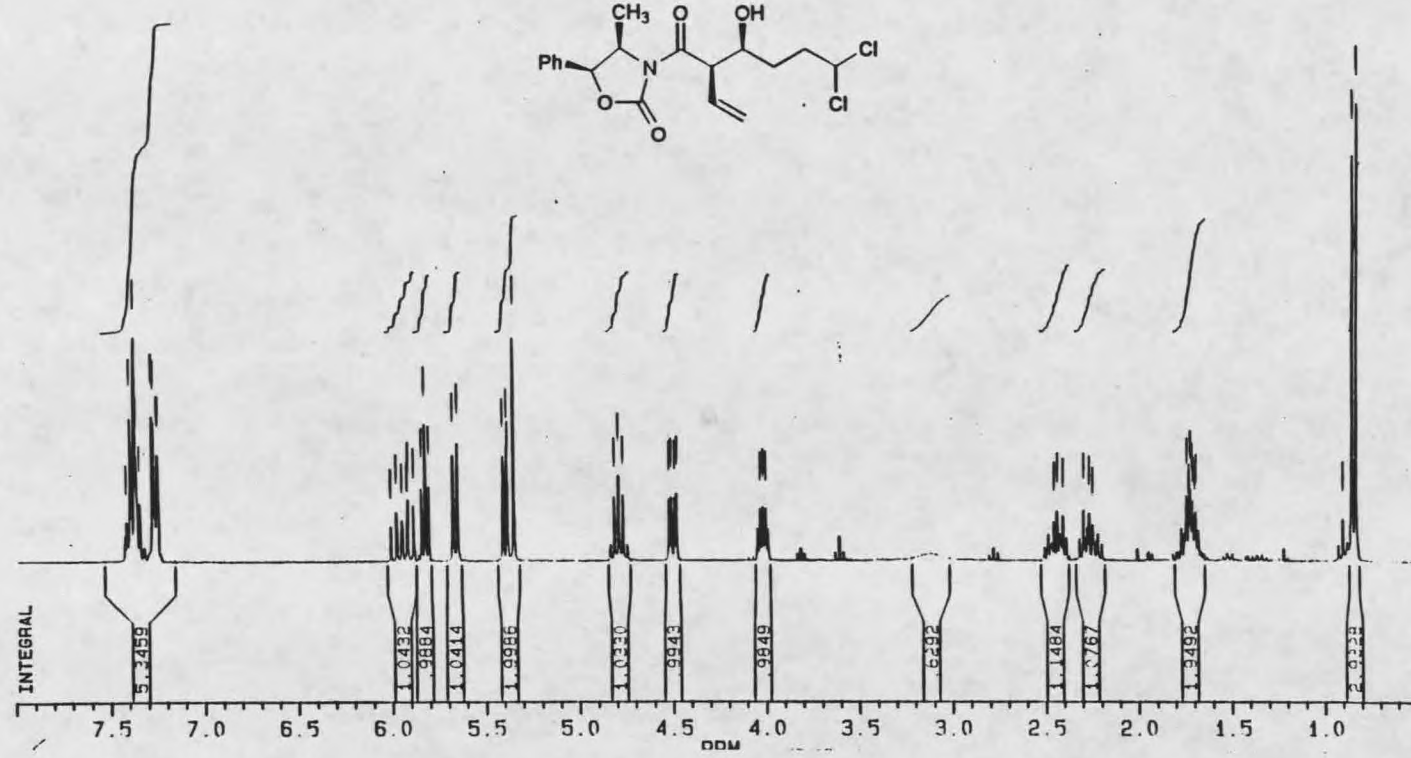
25.8130

17.9161

$$\begin{array}{r} -4,3181 \\ -4,5262 \\ \hline \end{array}$$

357





ppm

7.40608

7.38570

7.37541

7.36056

7.35238

7.34033

7.32799

7.31571

7.30134

7.24149

7.23857

5.99938

5.96971

5.94181

5.91351

5.90811

5.87862

5.83656

5.81643

5.79636

5.66810

5.64366

4.39900

4.37886

4.37198

4.34280

4.80746

4.78429

4.76067

4.54563

4.50365

4.48616

4.47398

4.02598

4.01172

3.99699

2.44977

2.43155

2.40048

2.29075

2.26006

2.24029

1.73512

1.72383

1.71659

1.70623

1.70214

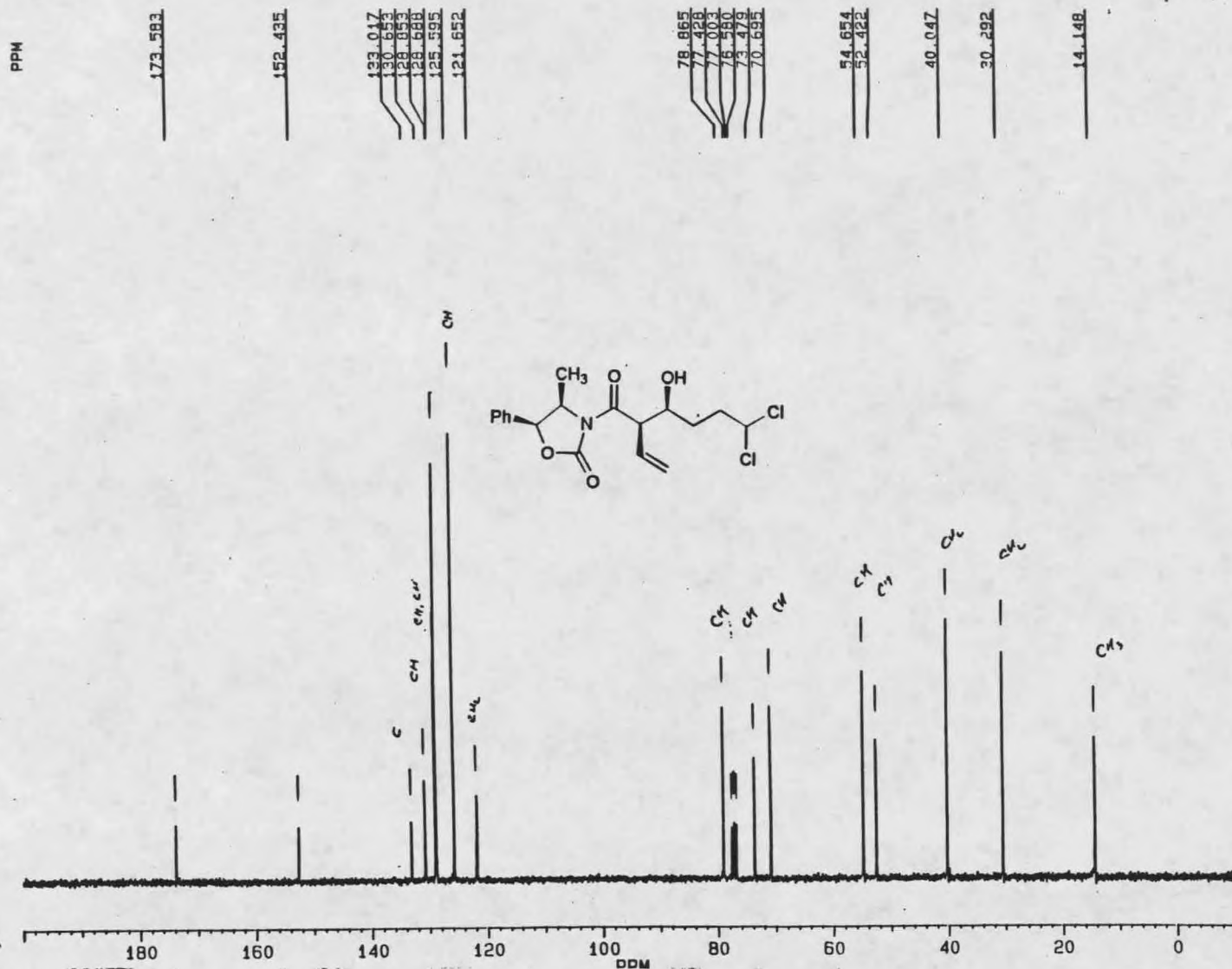
1.69291

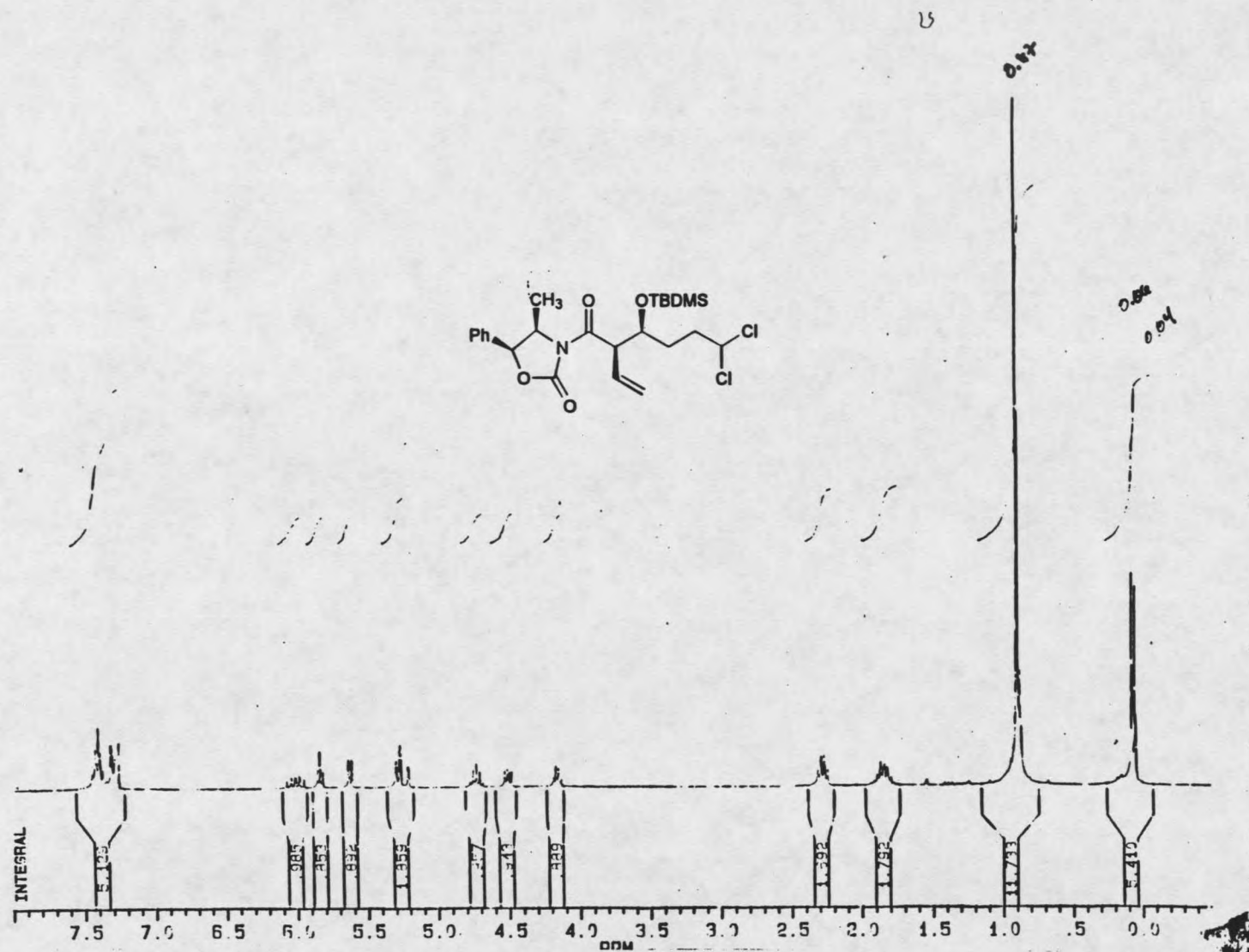
1.68662

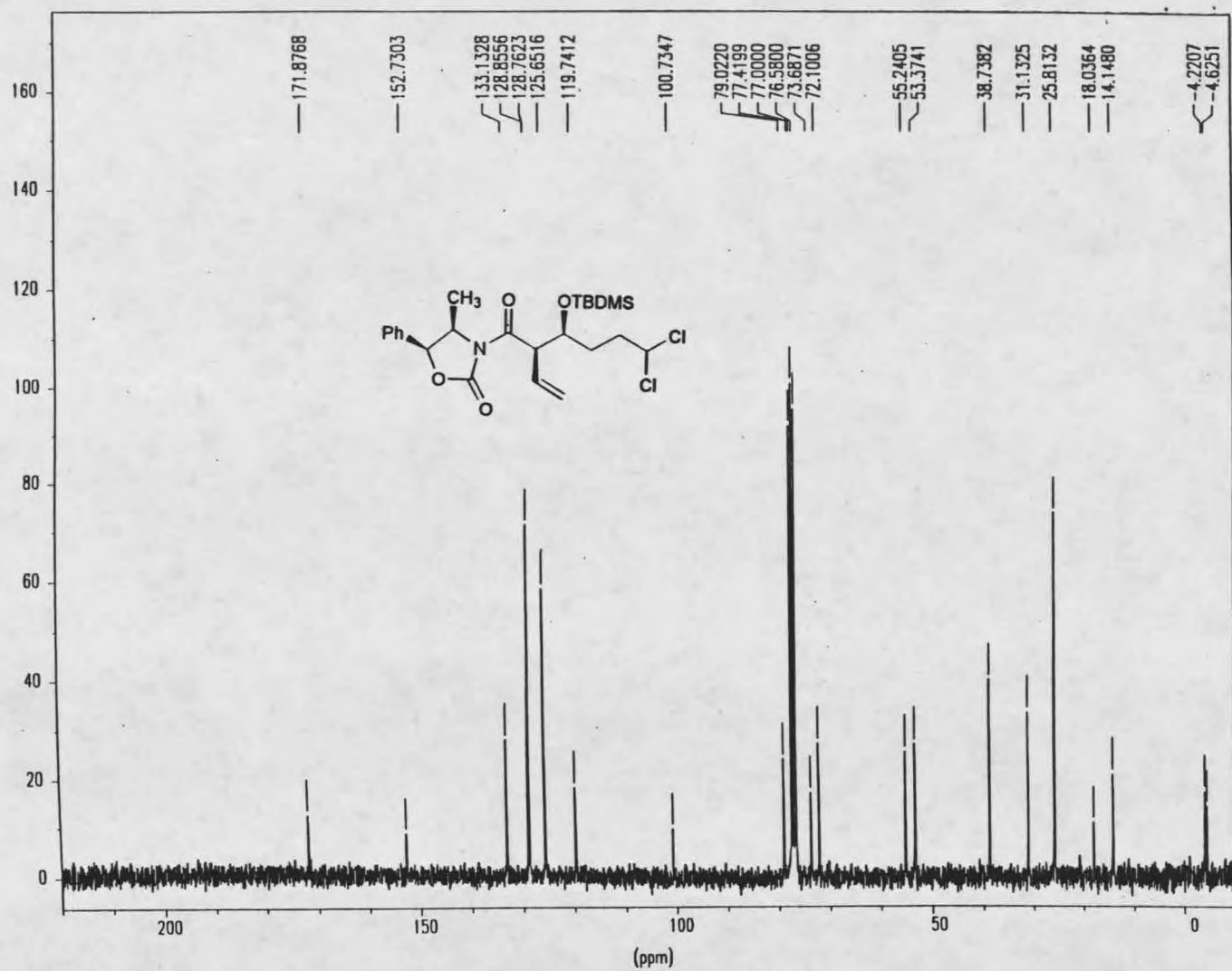
0.9455

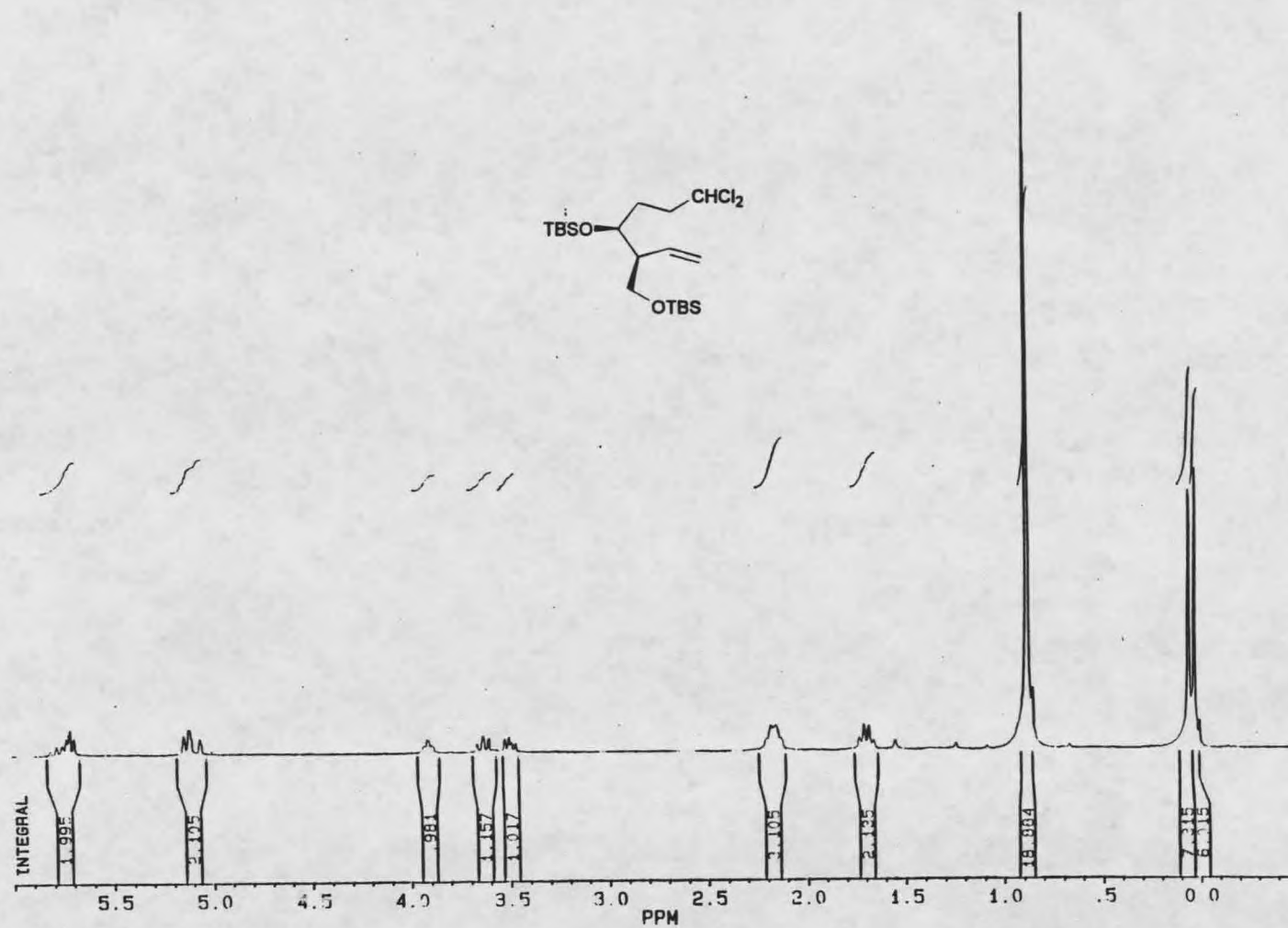
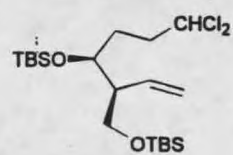
0.94617

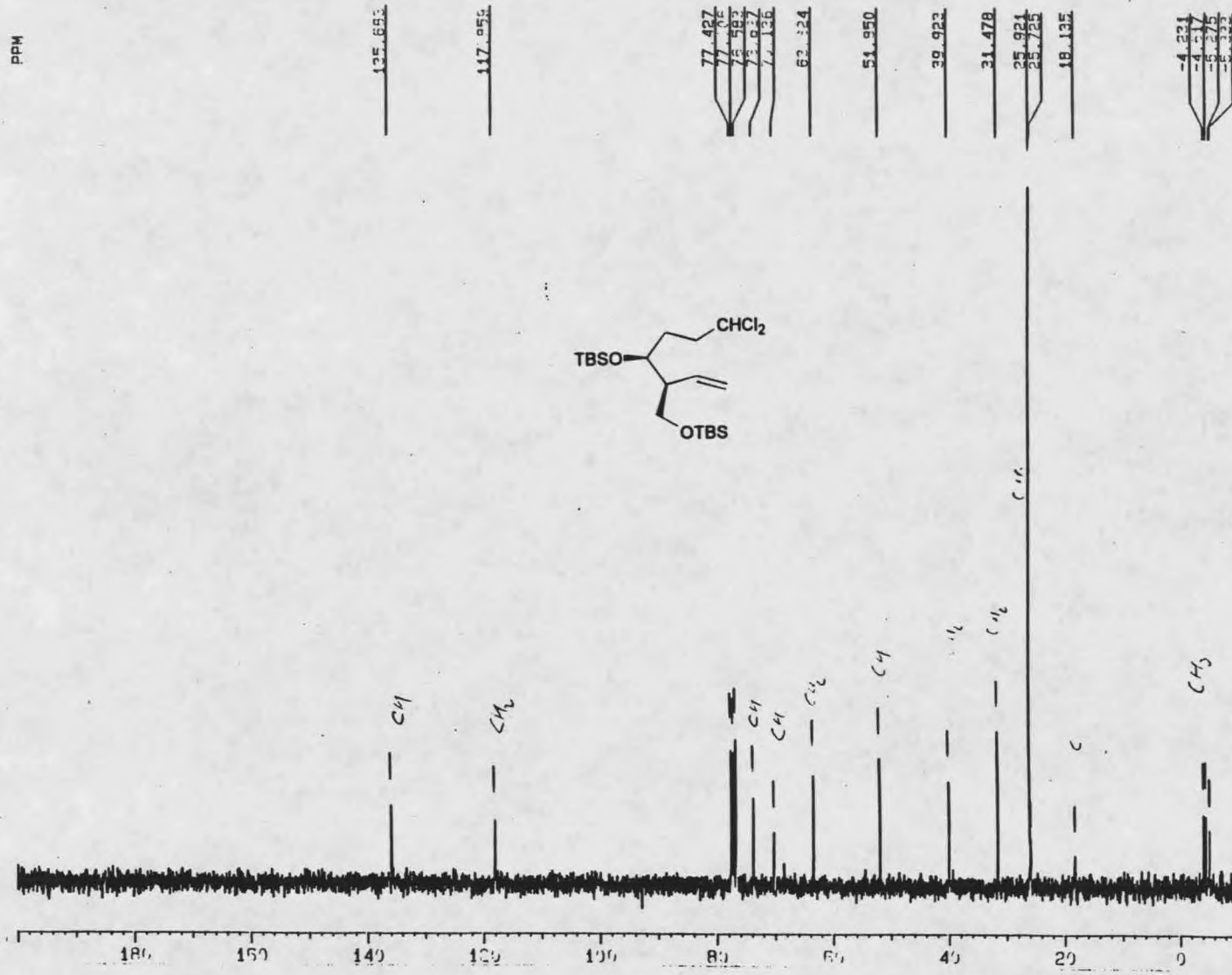
0.93857



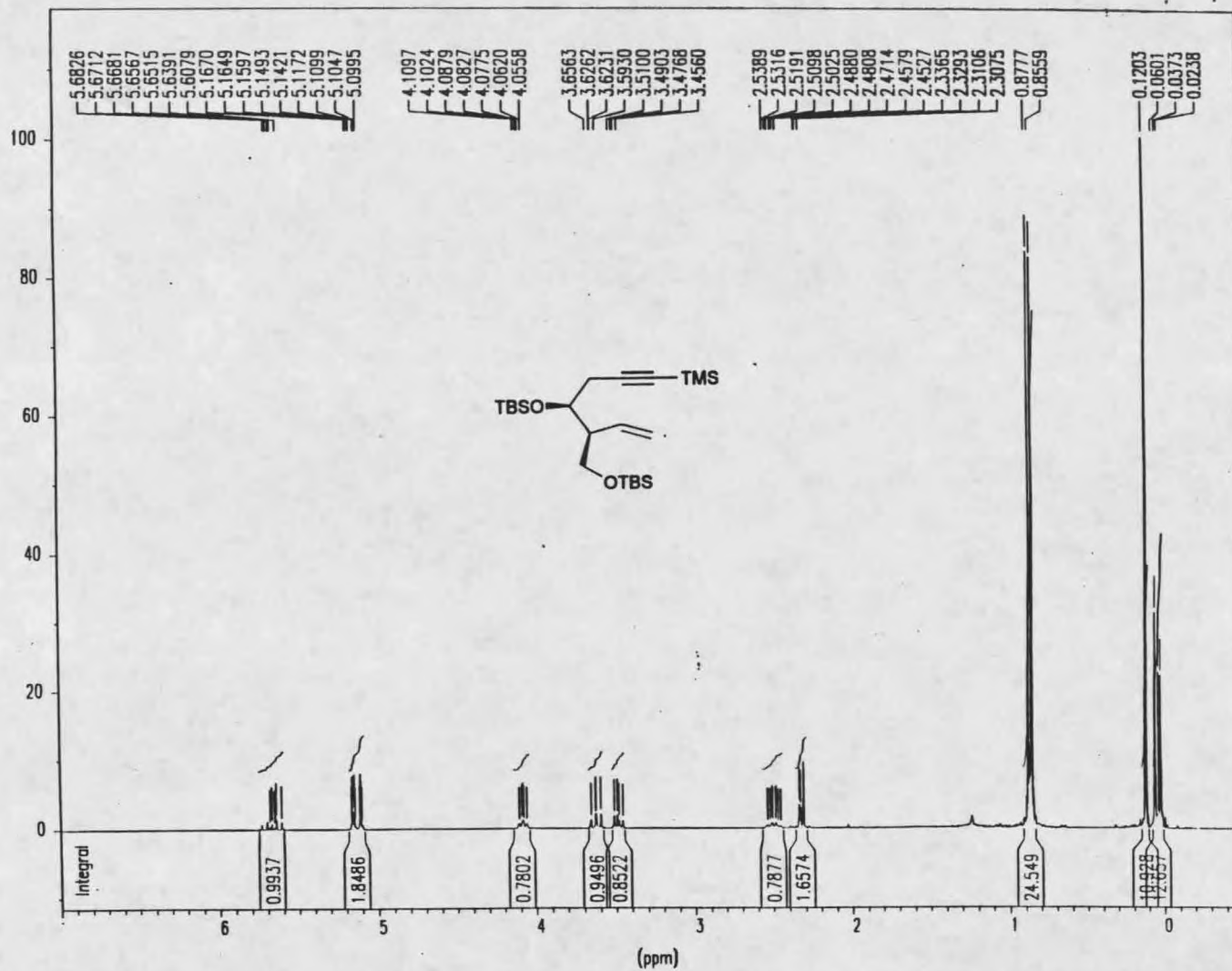


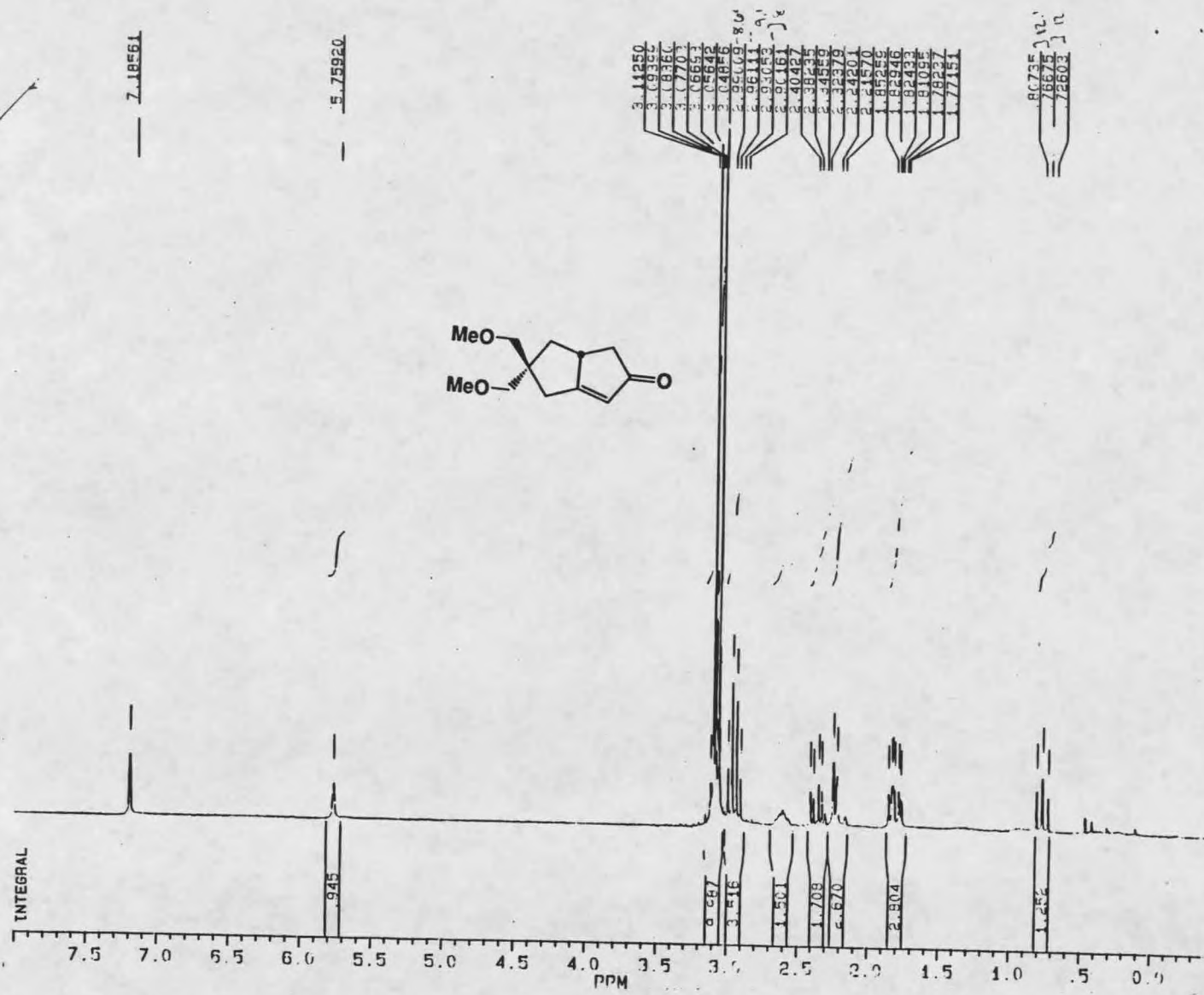


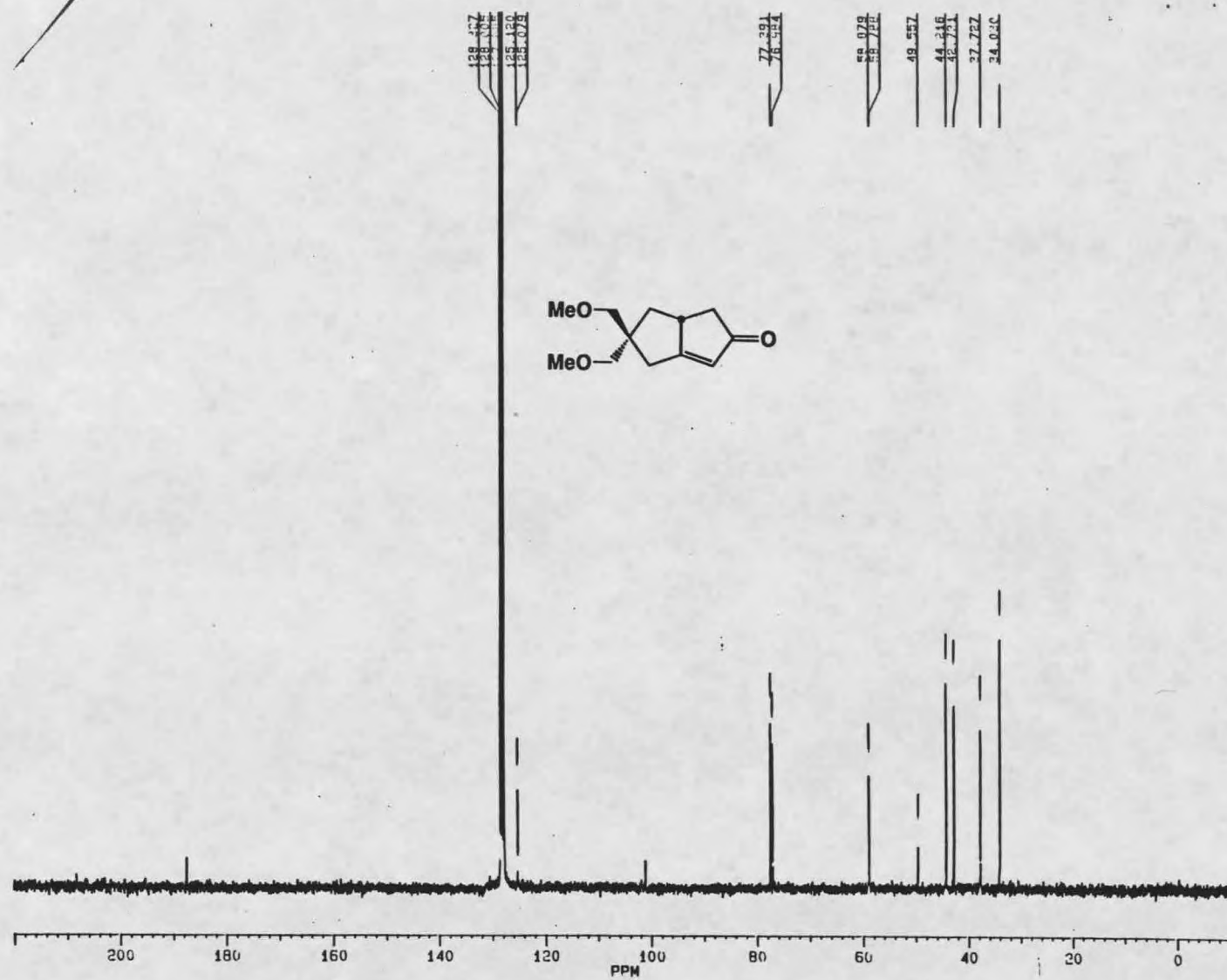


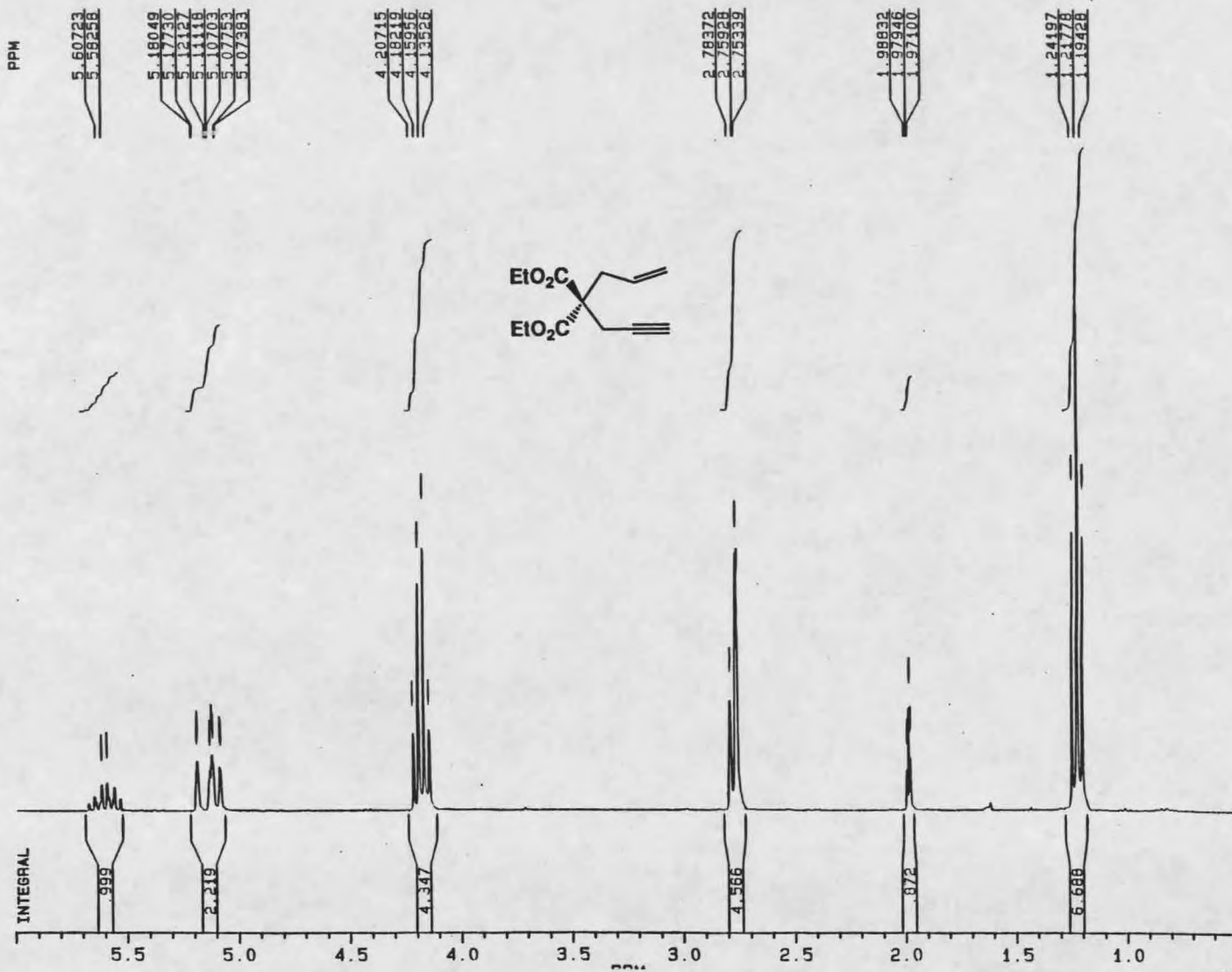


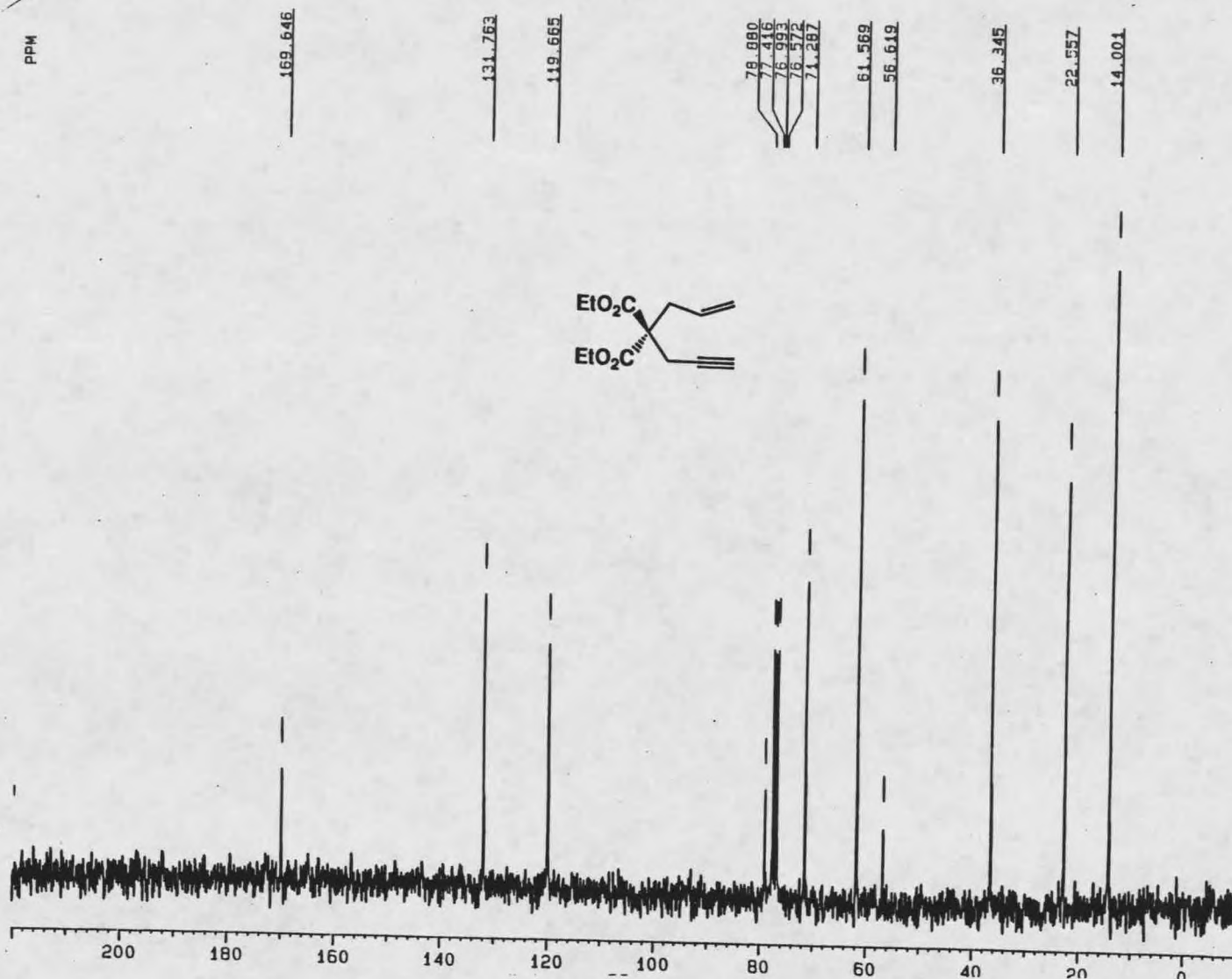
366

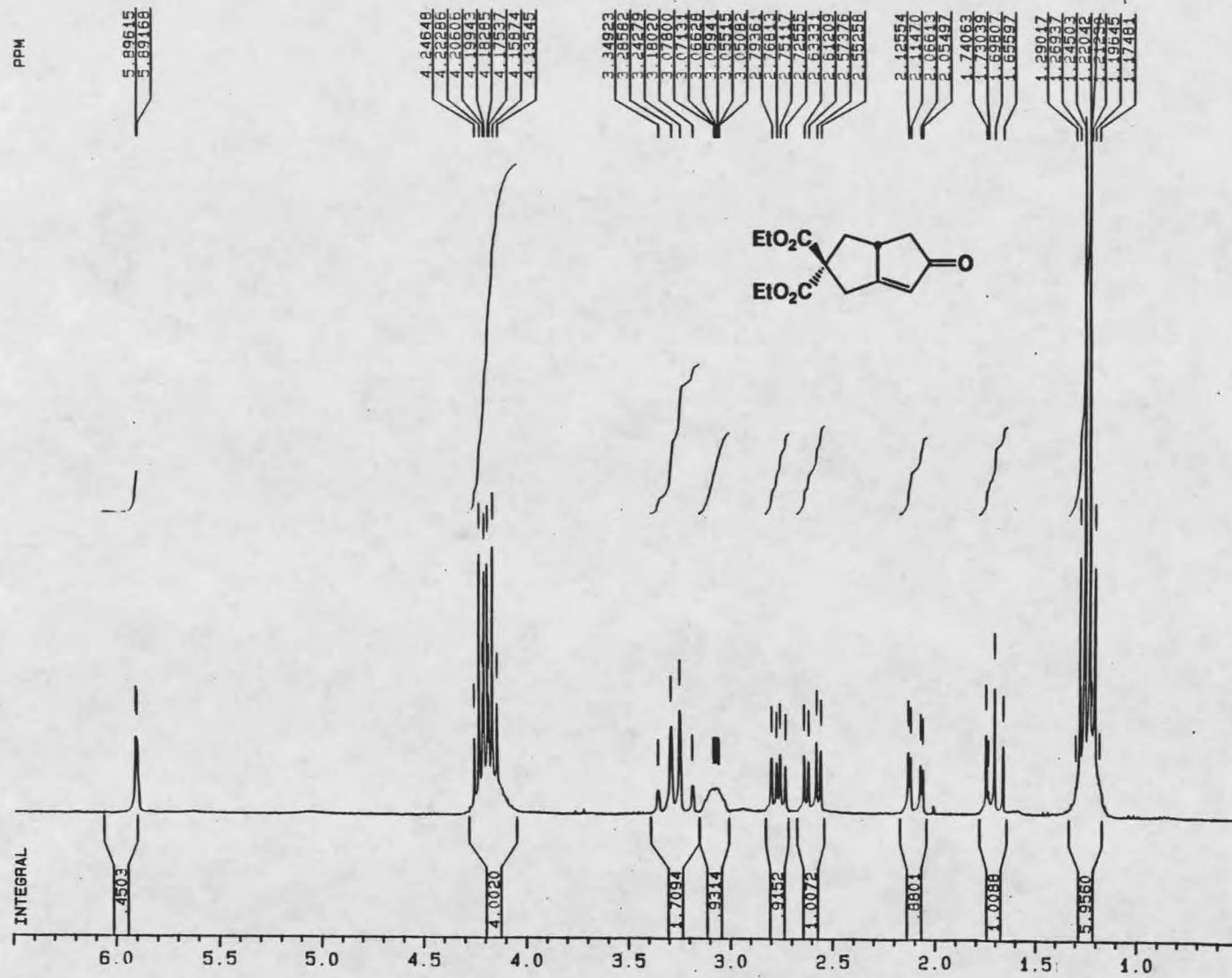


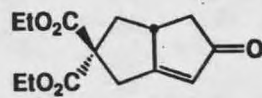
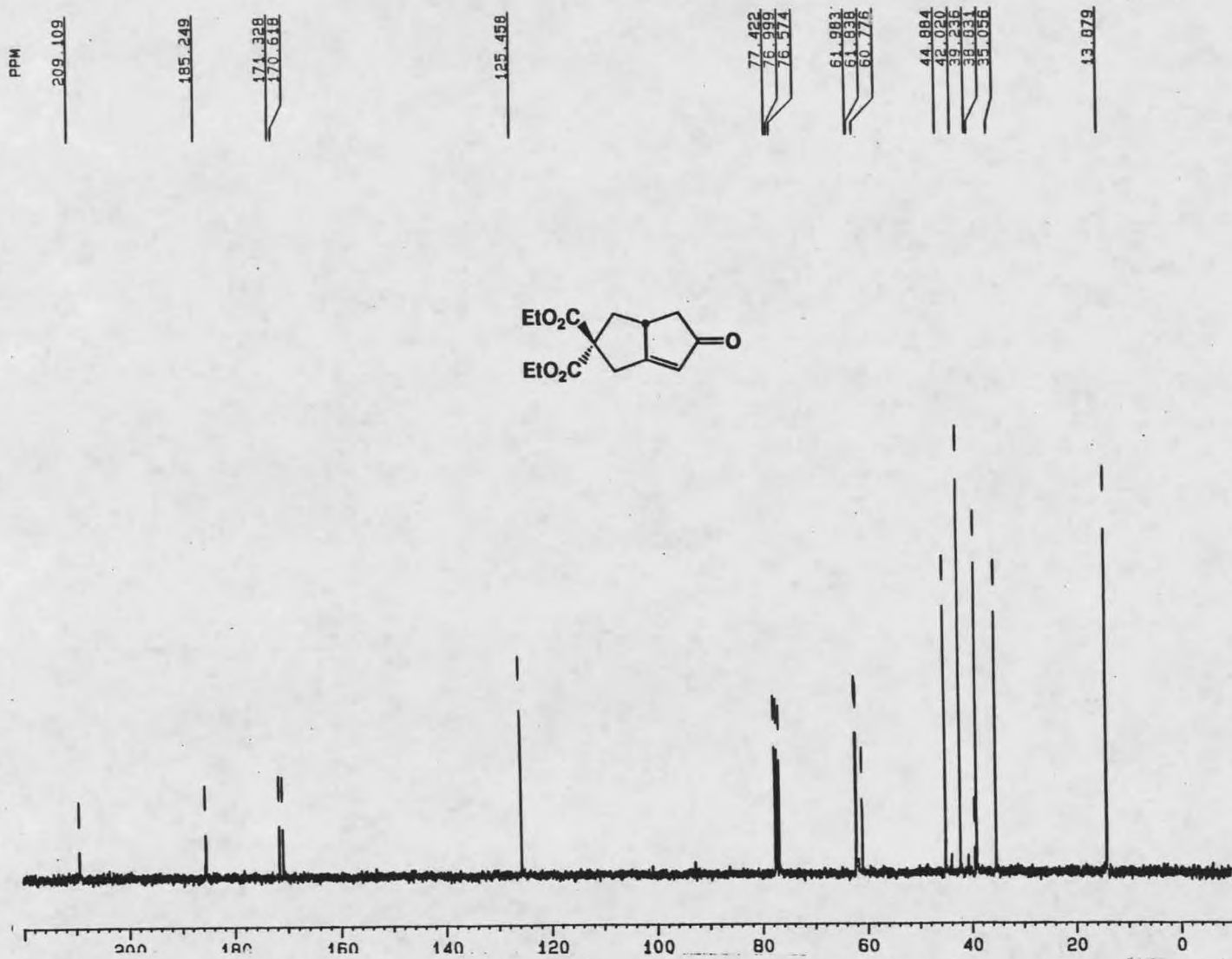


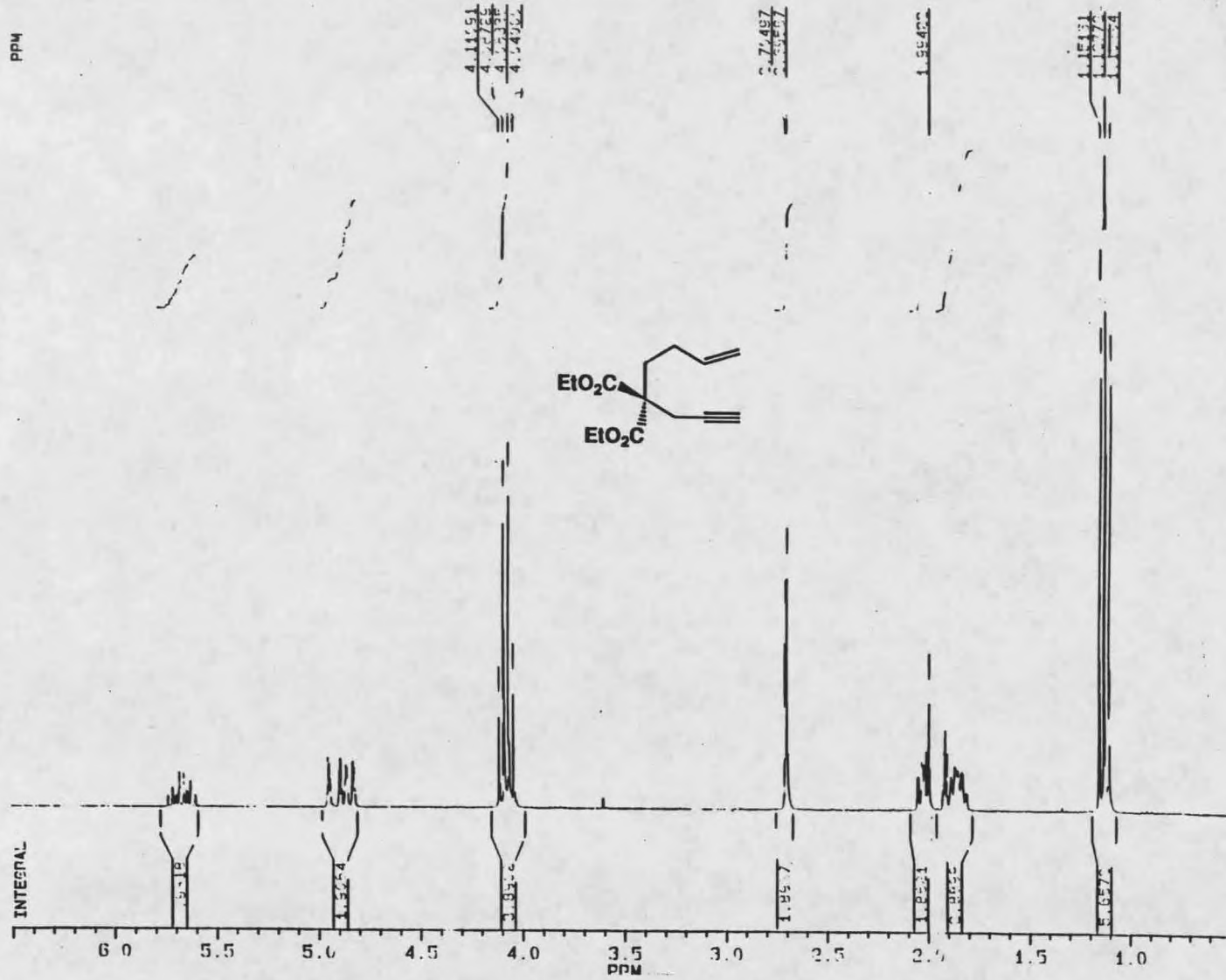


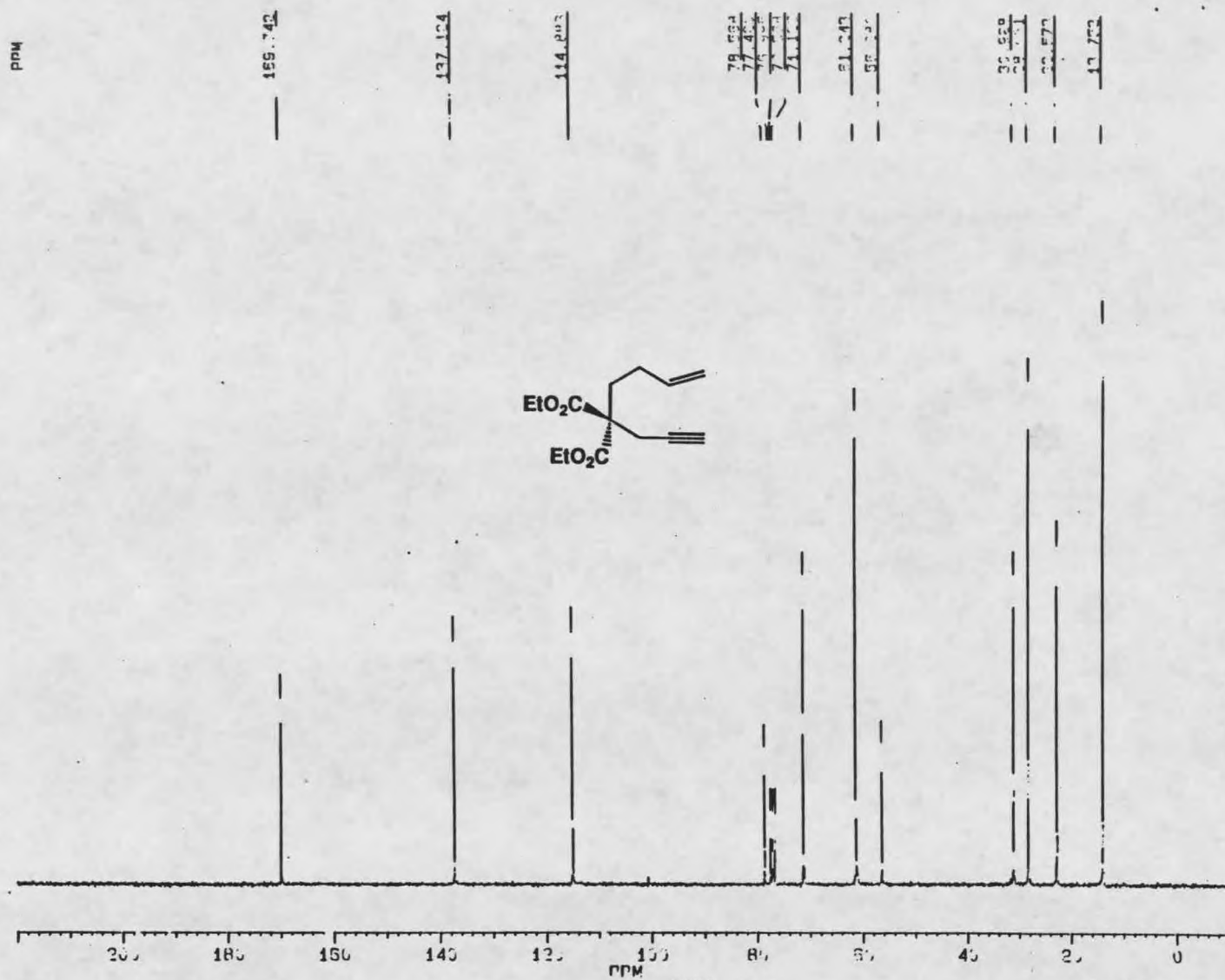


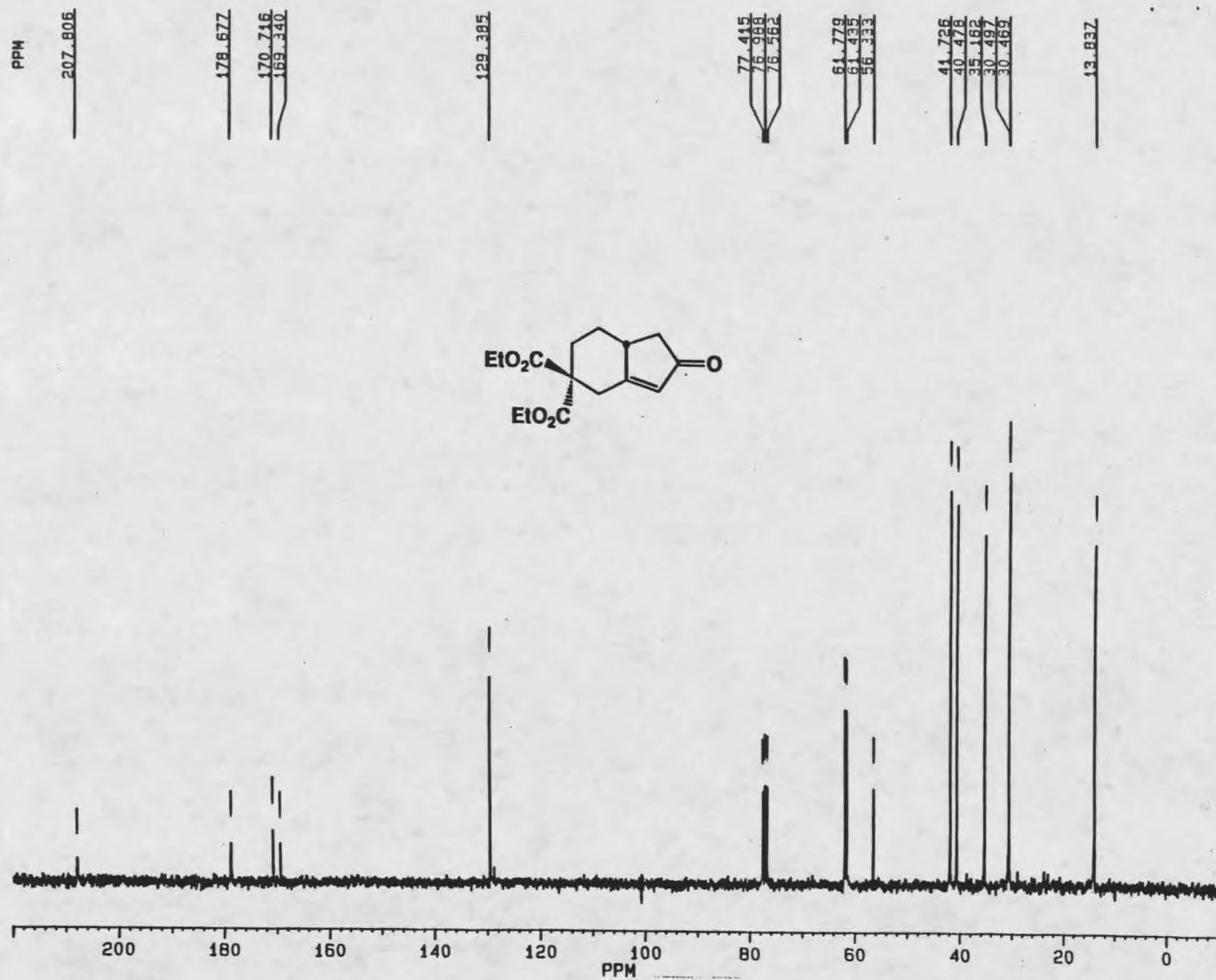






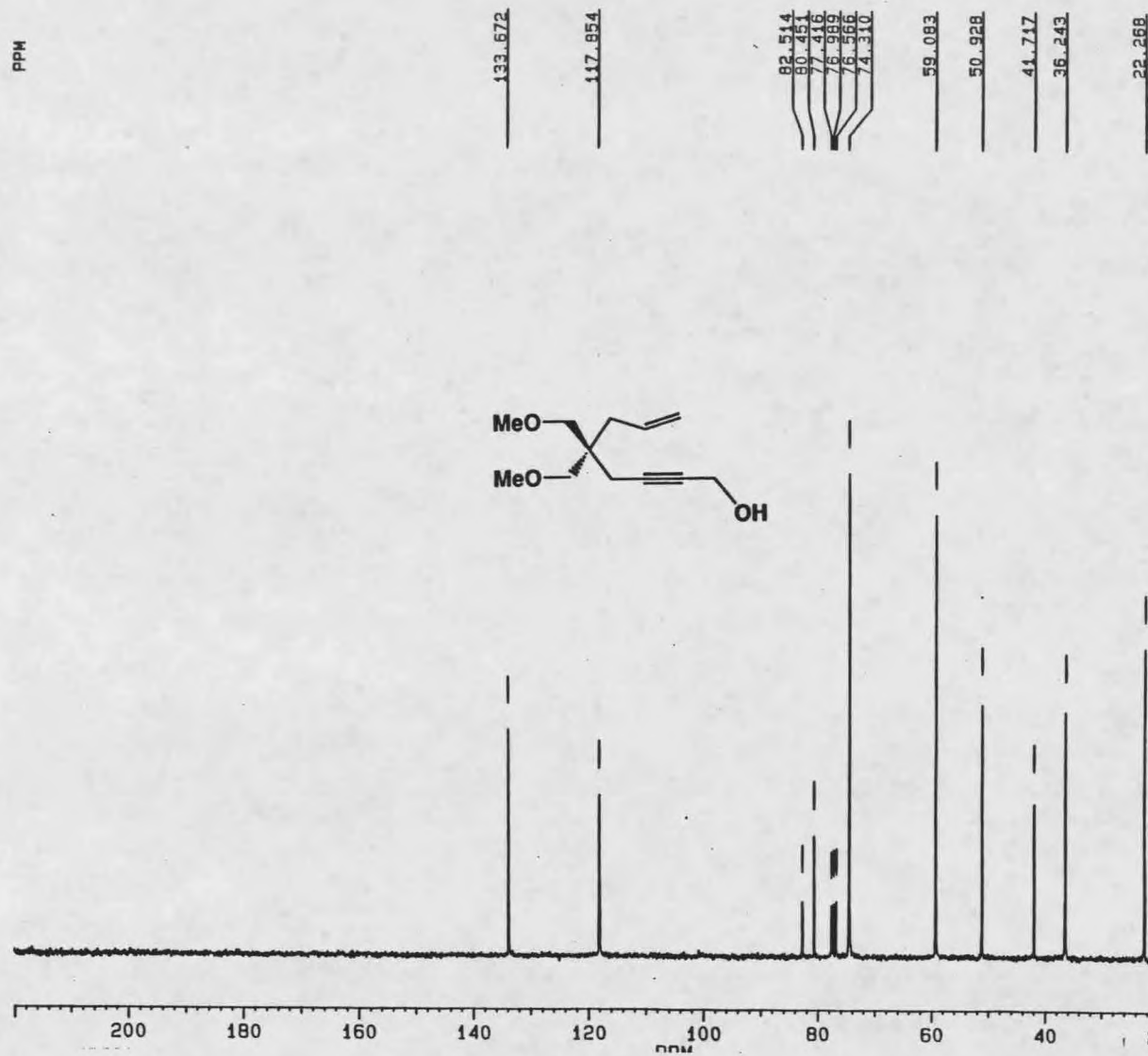


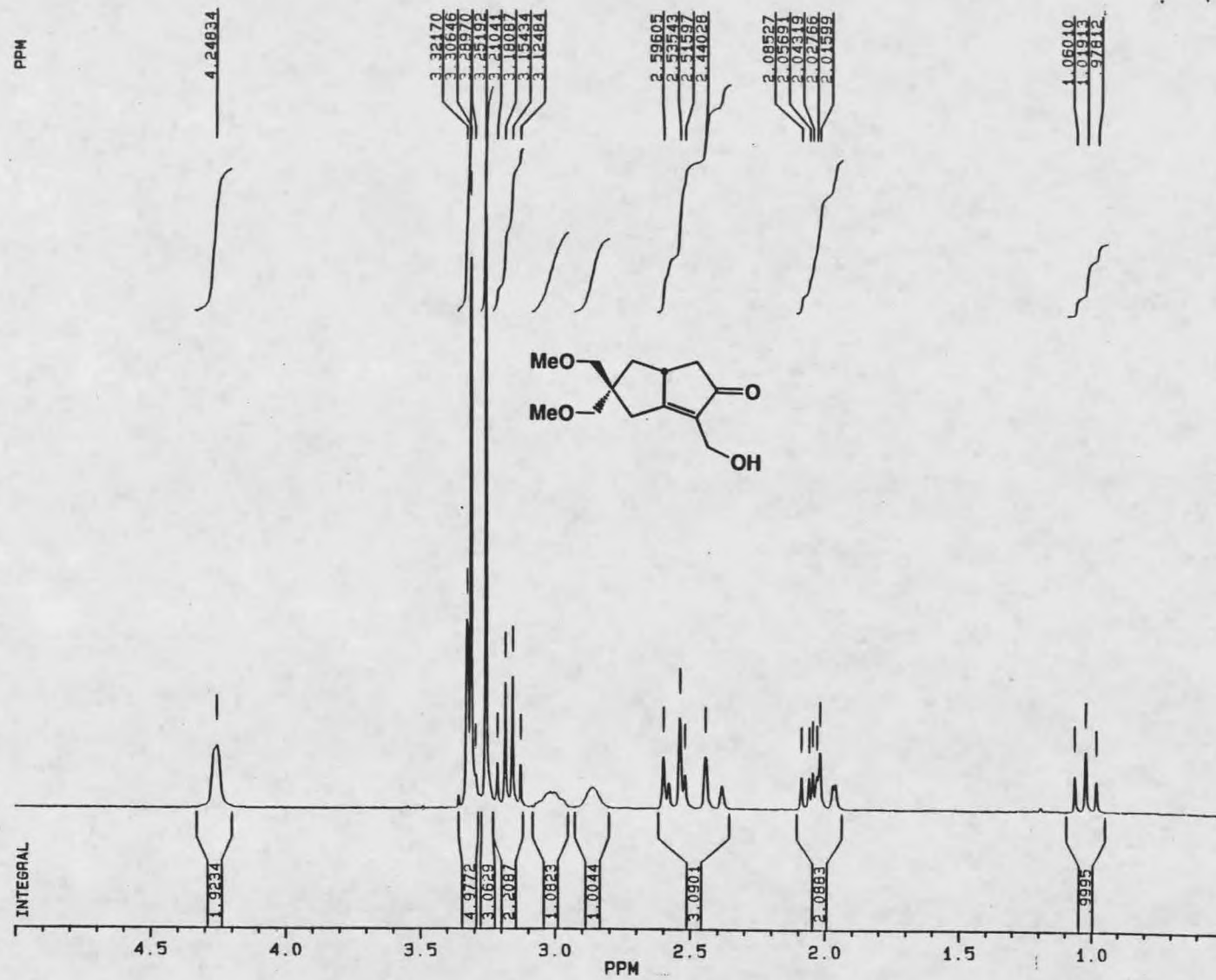


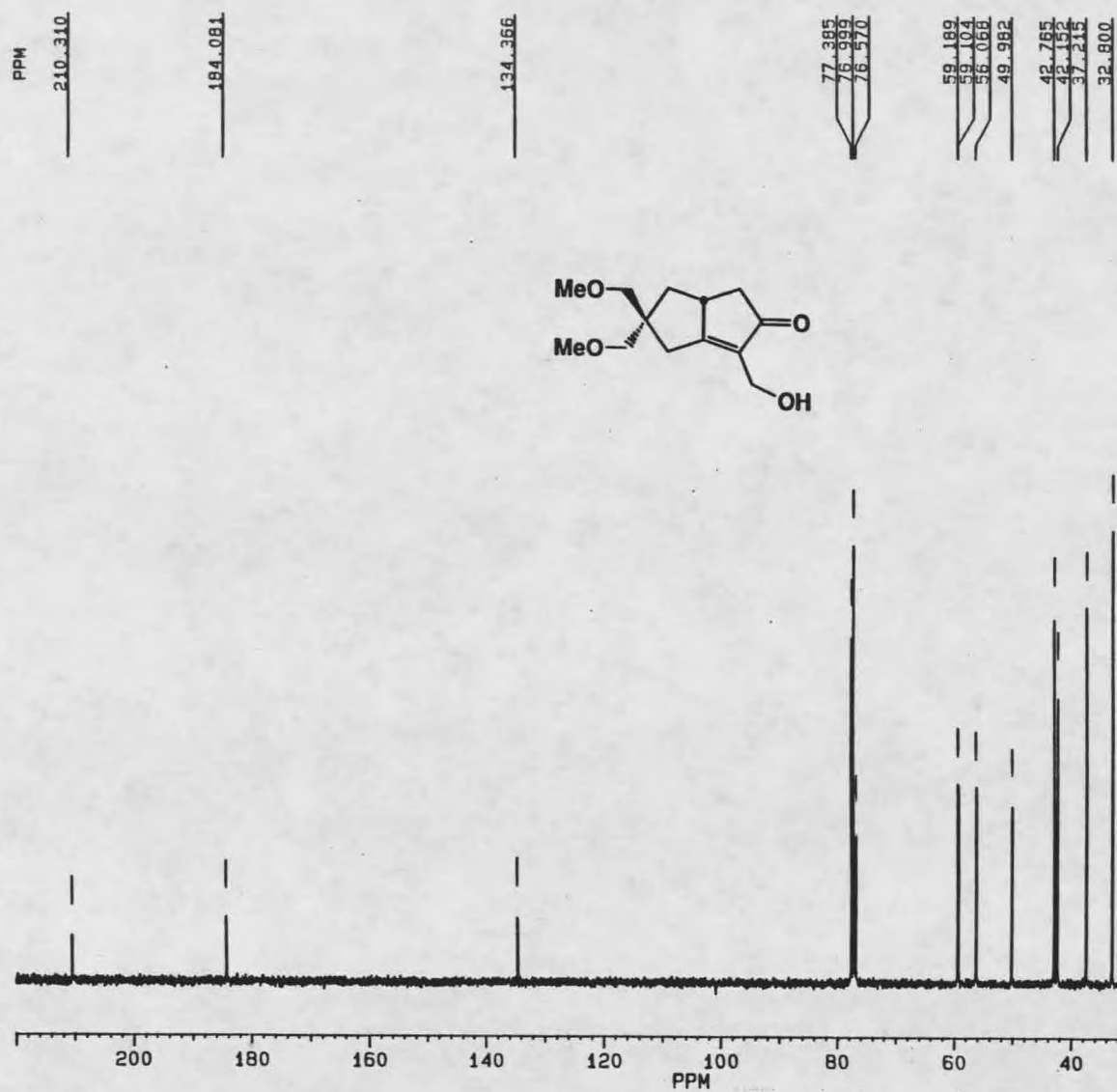


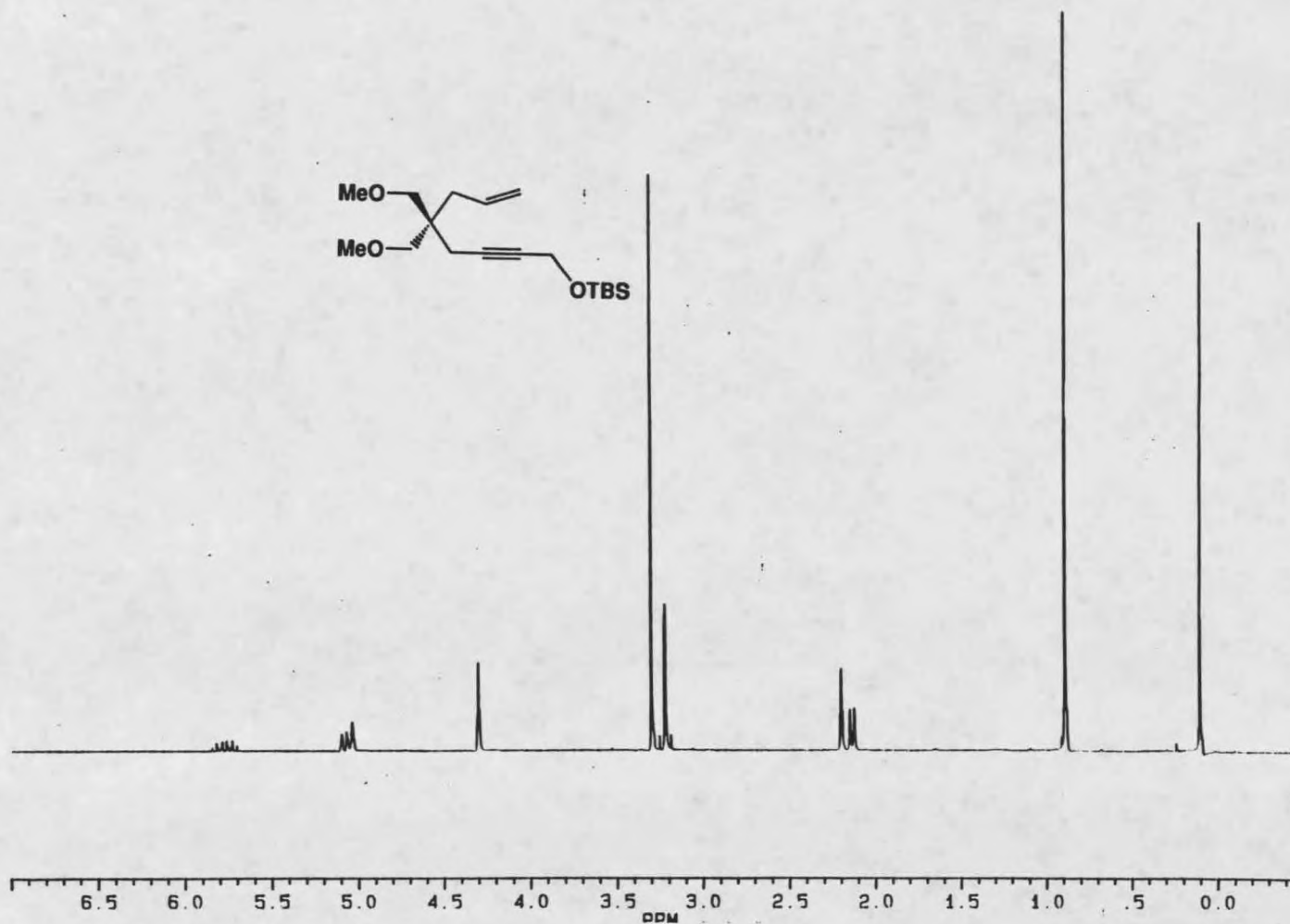
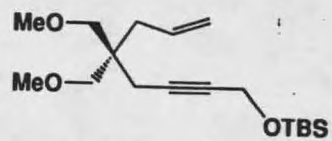


PPM

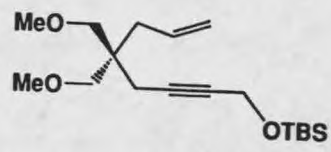
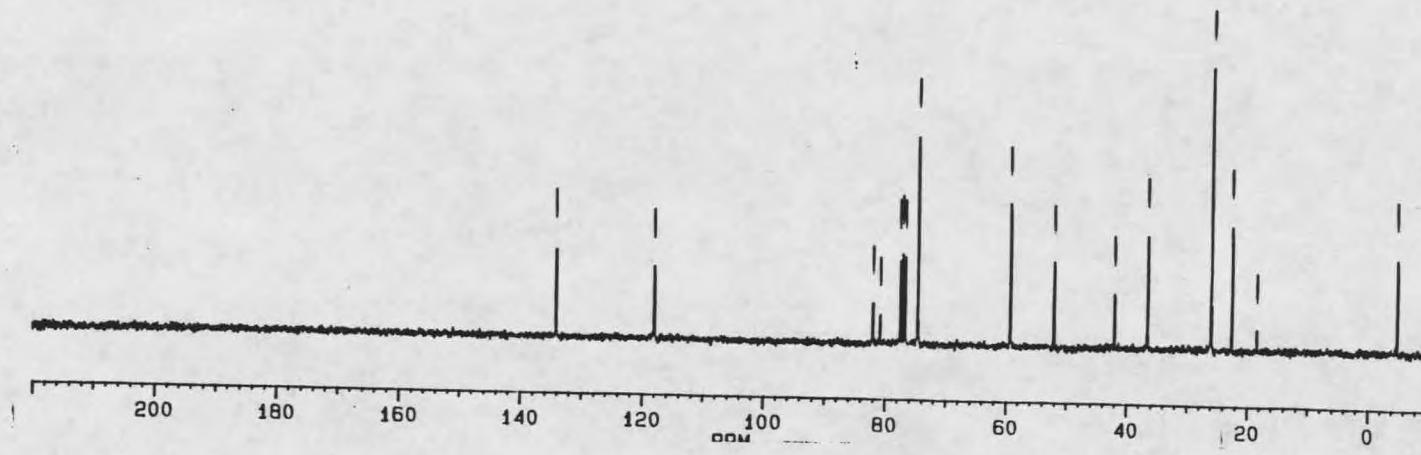








384



133.994

117.826

81.915
80.712
77.412
76.989
76.566
74.508

59.208

51.973

41.927

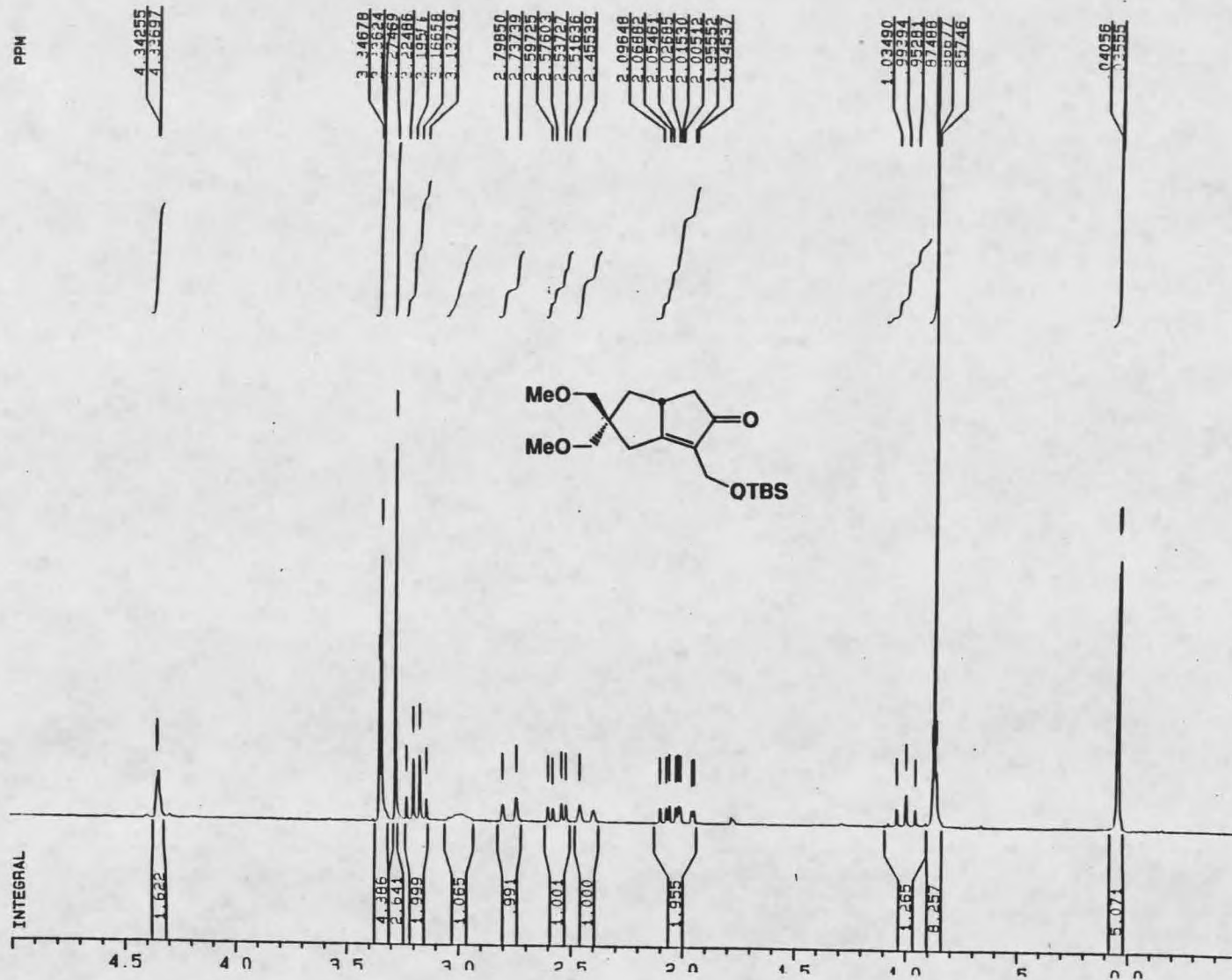
36.426

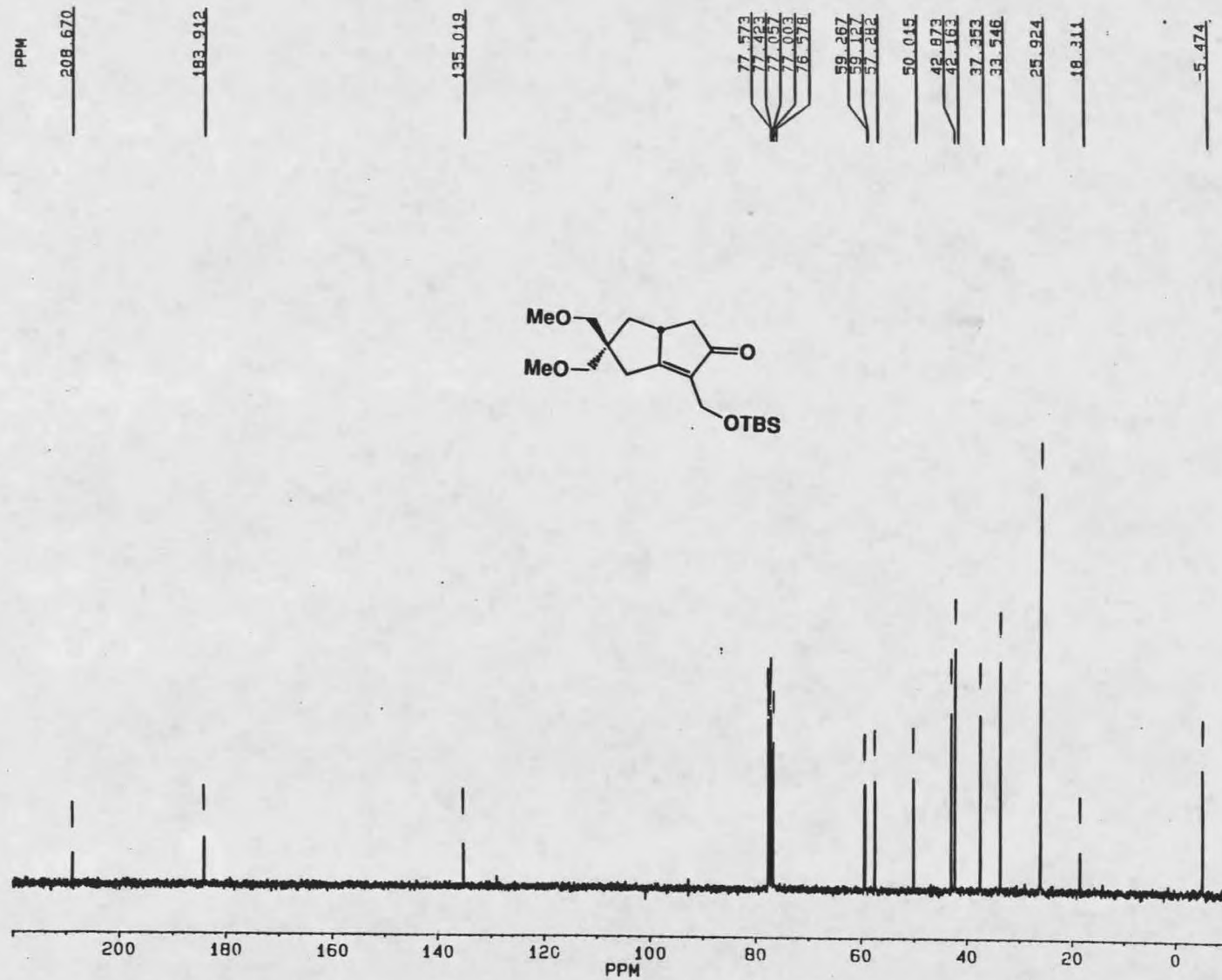
25.830

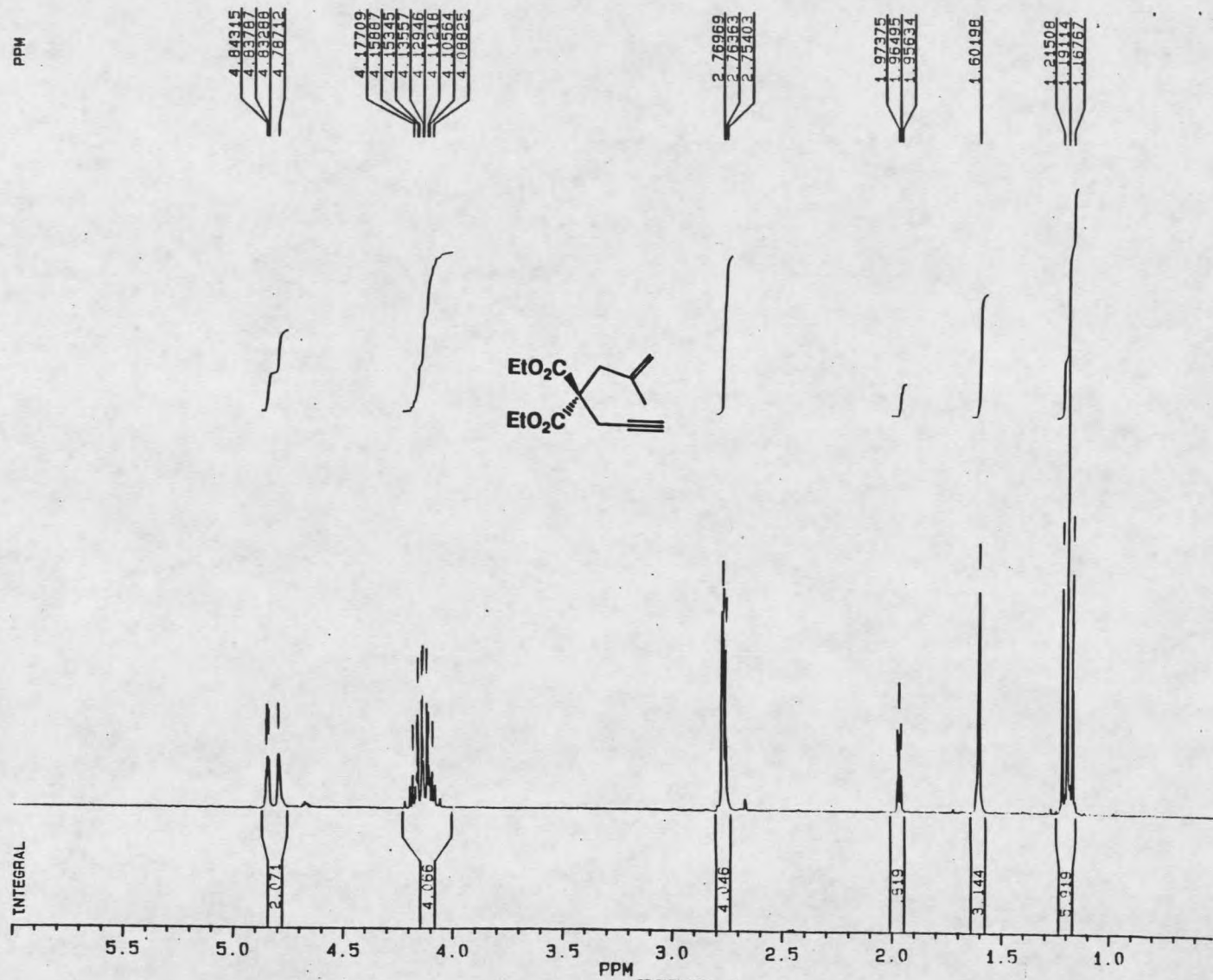
22.443

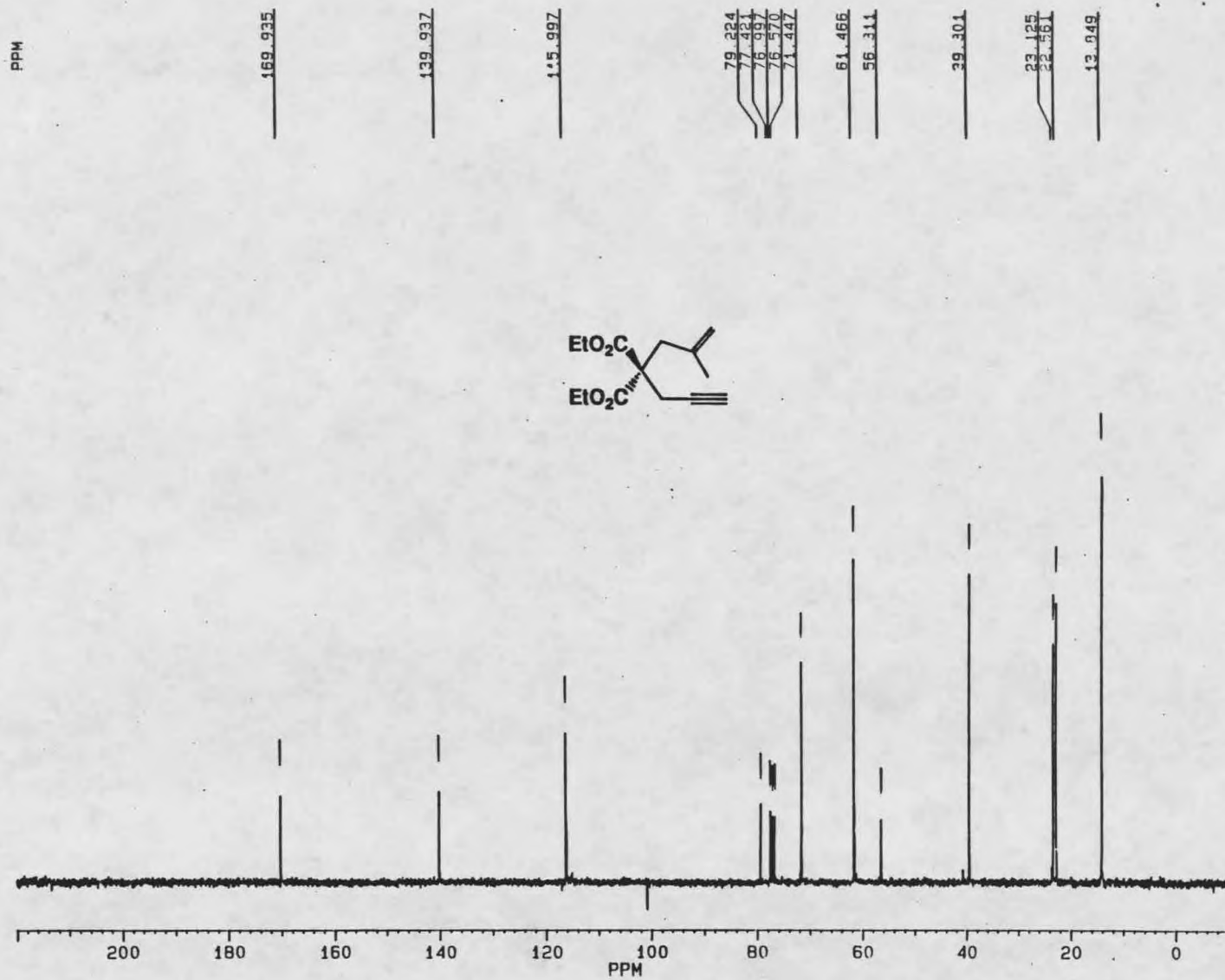
19.287

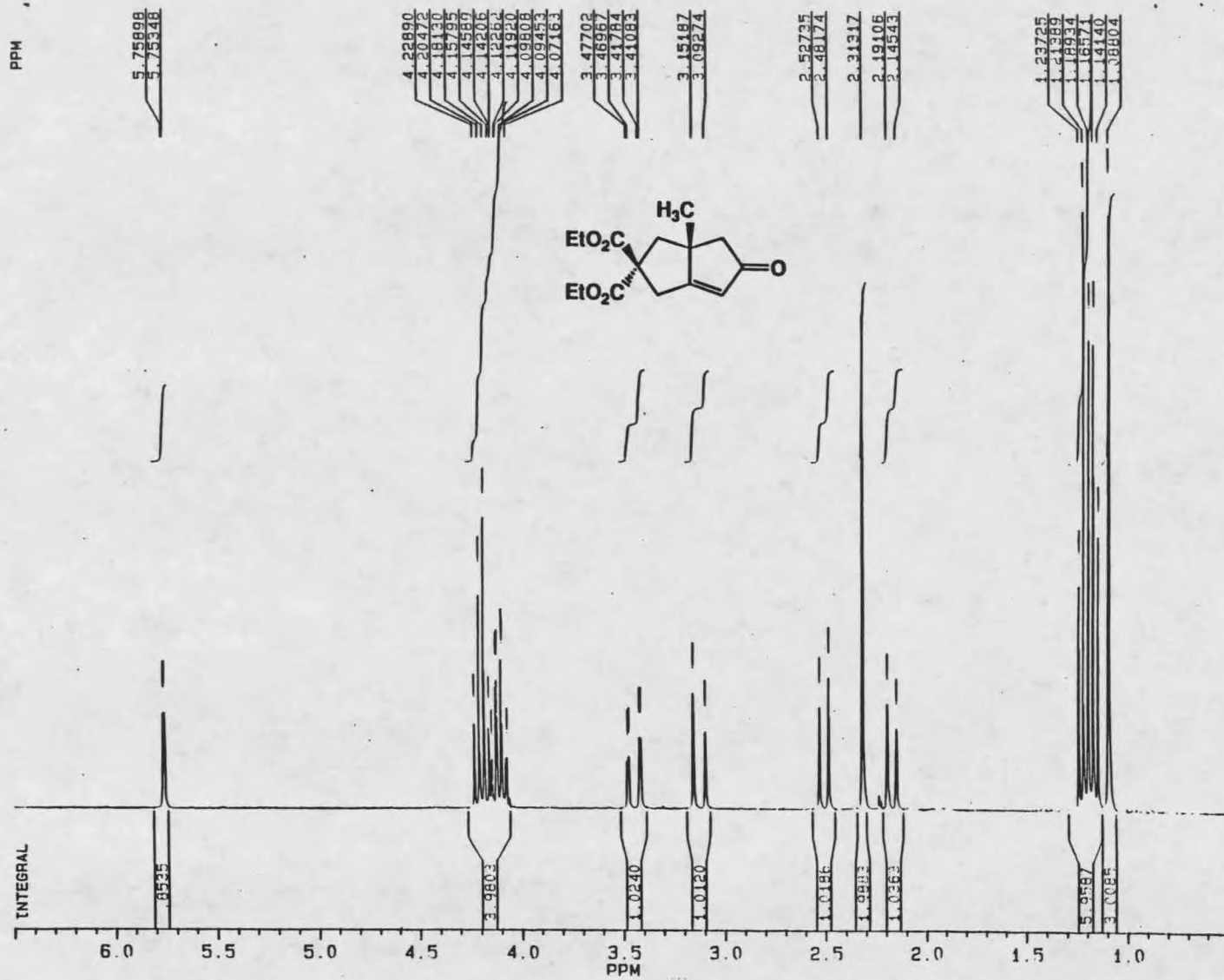
-5.109



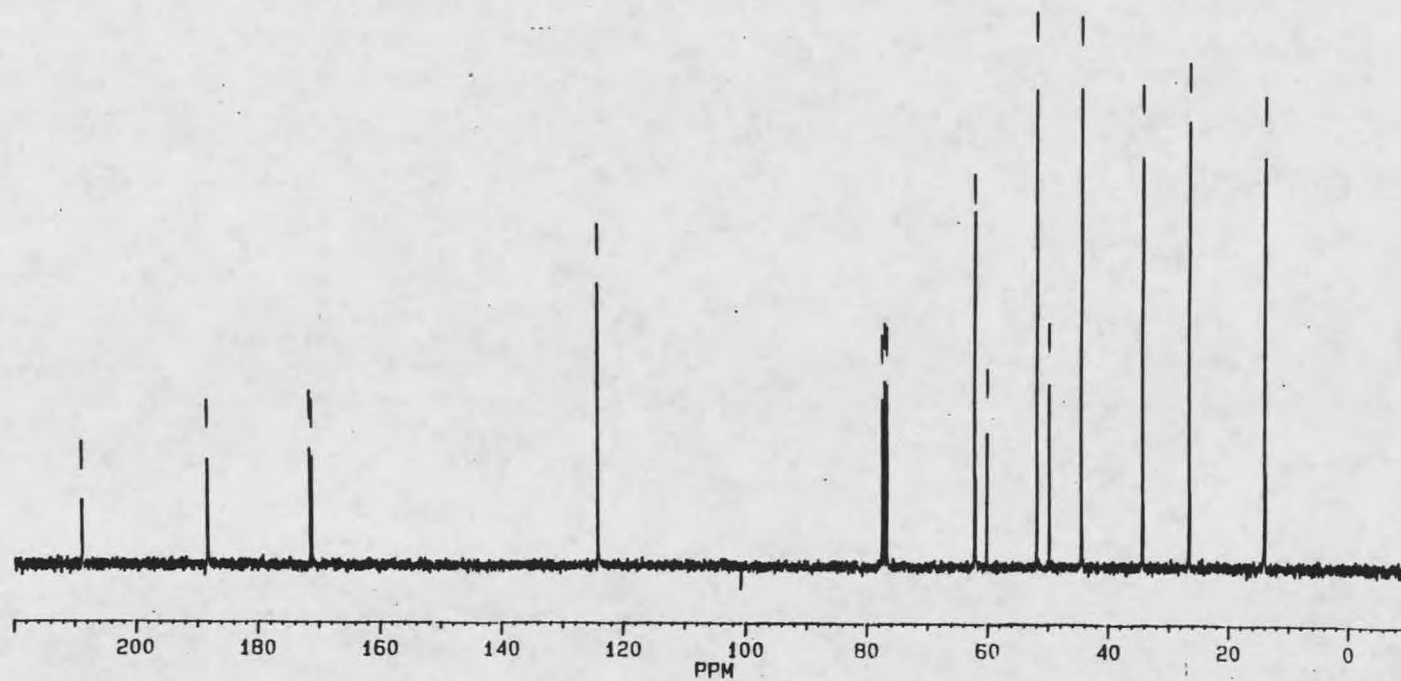
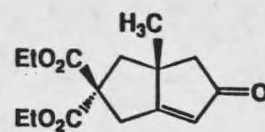


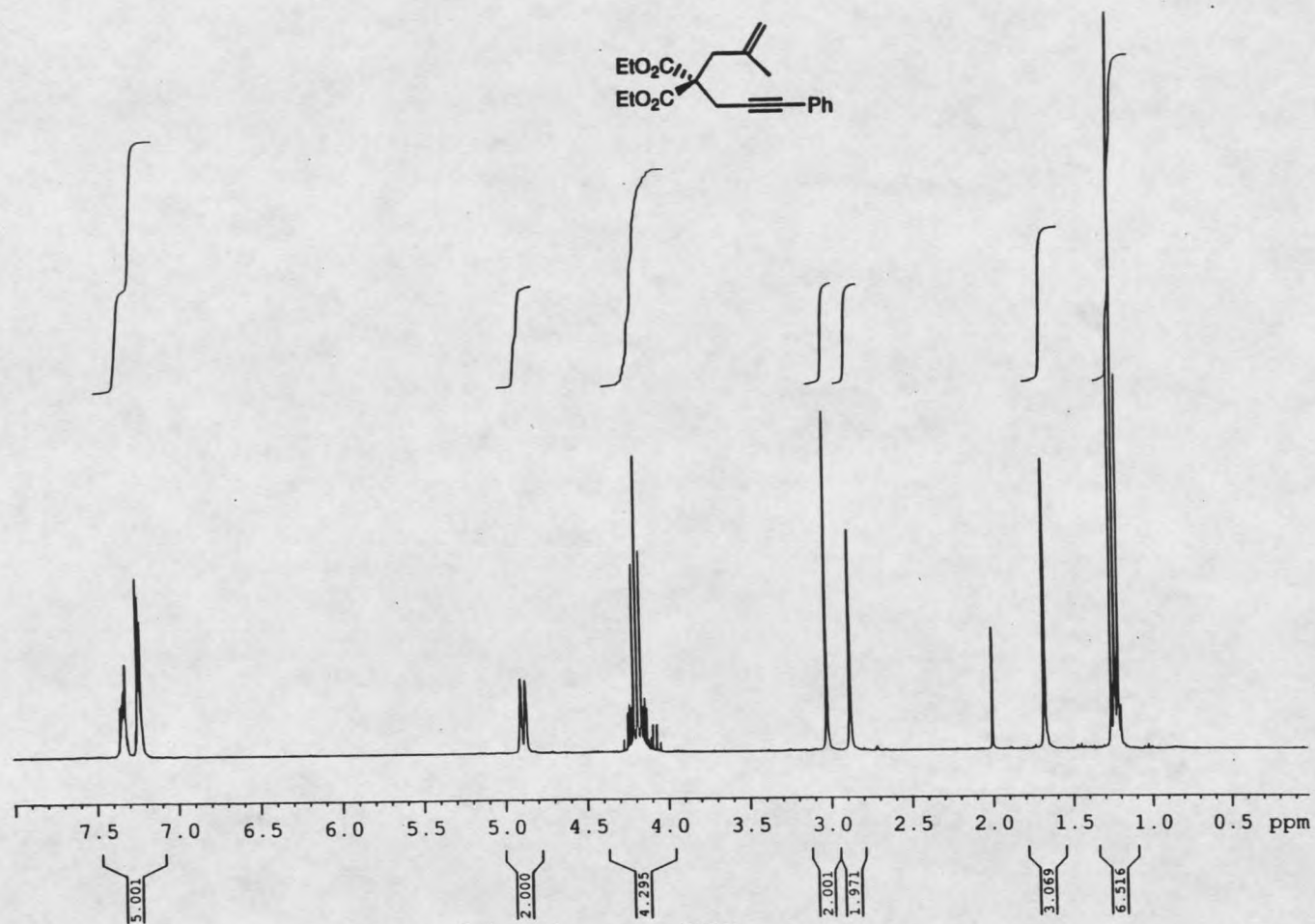


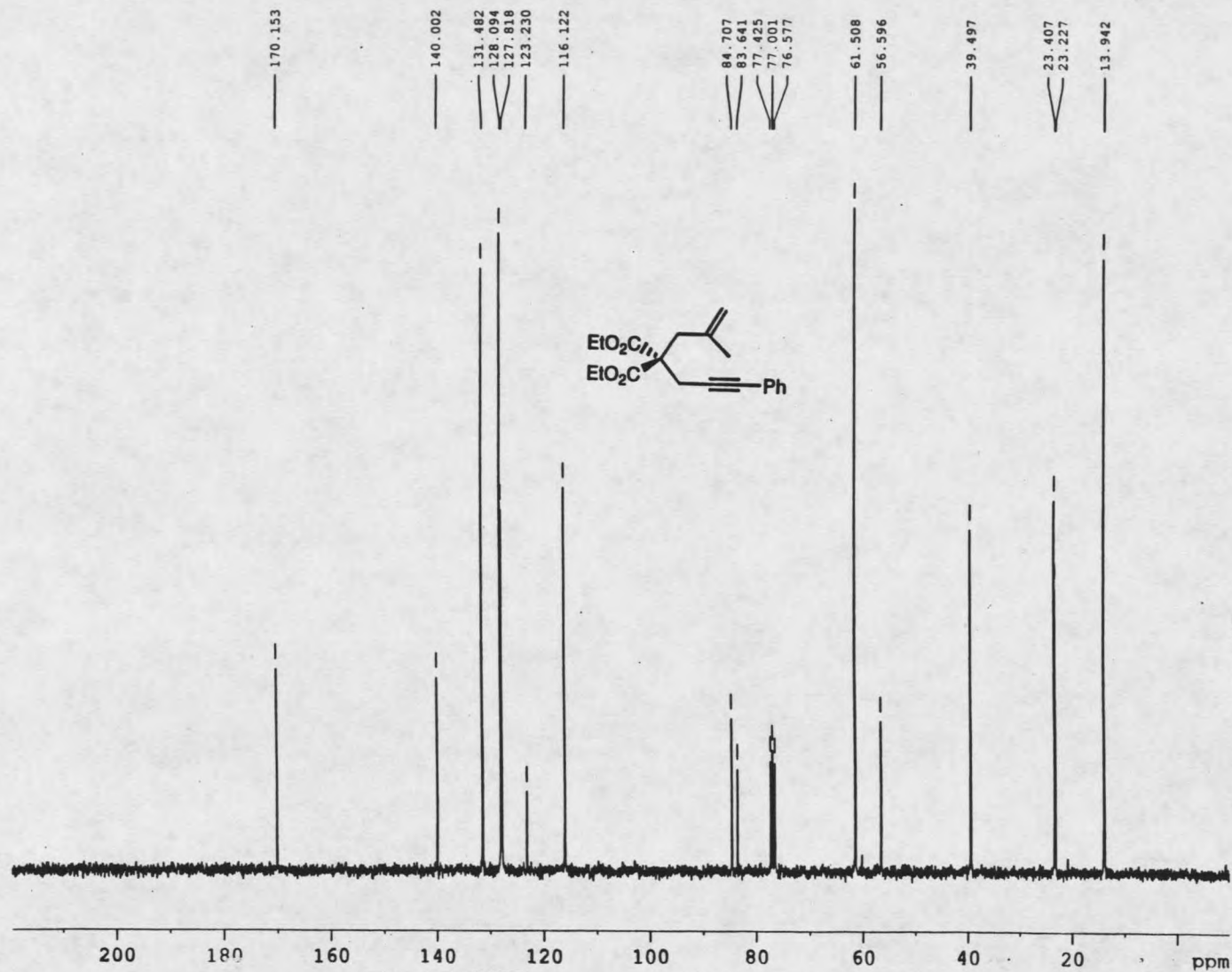


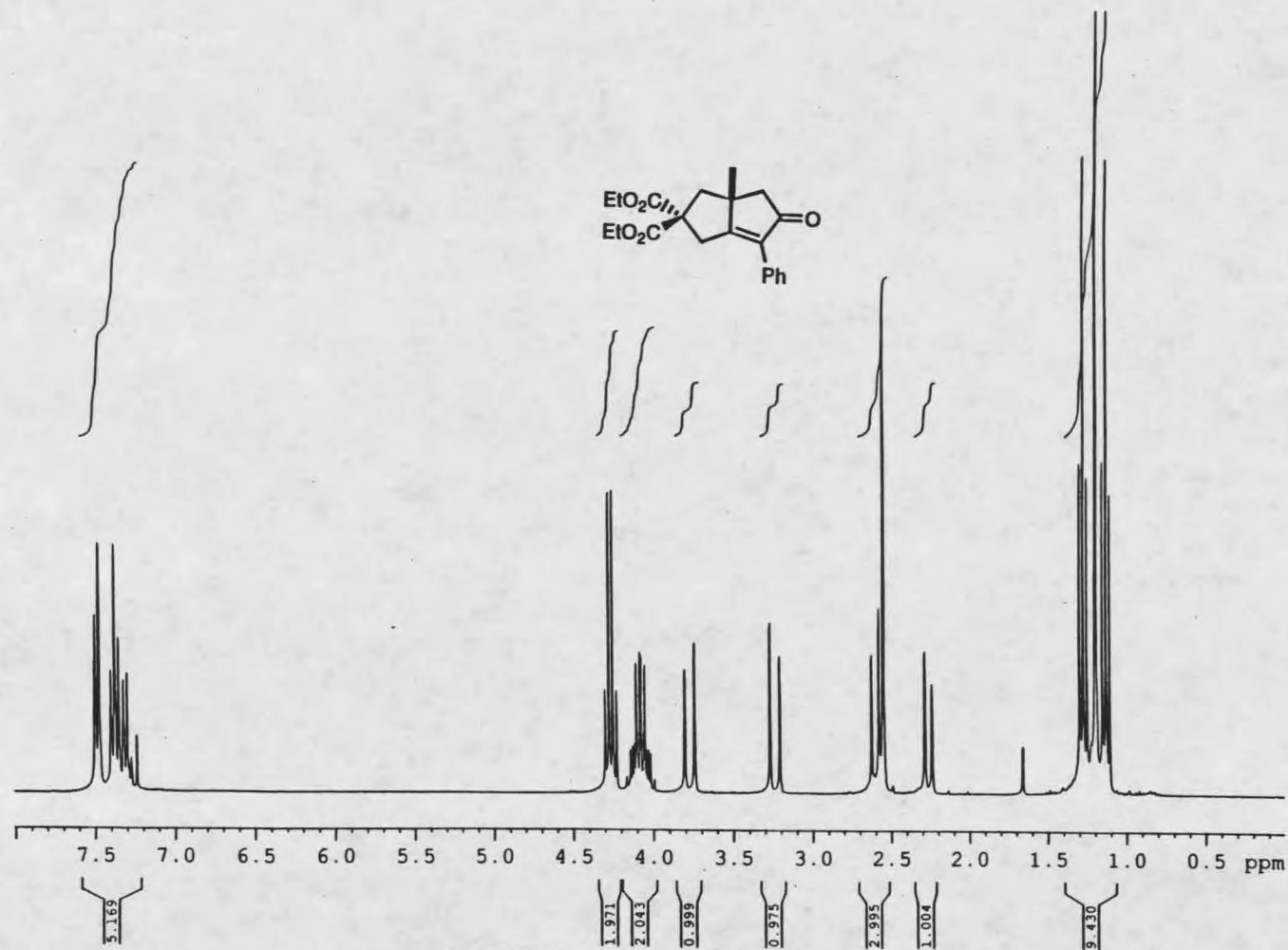


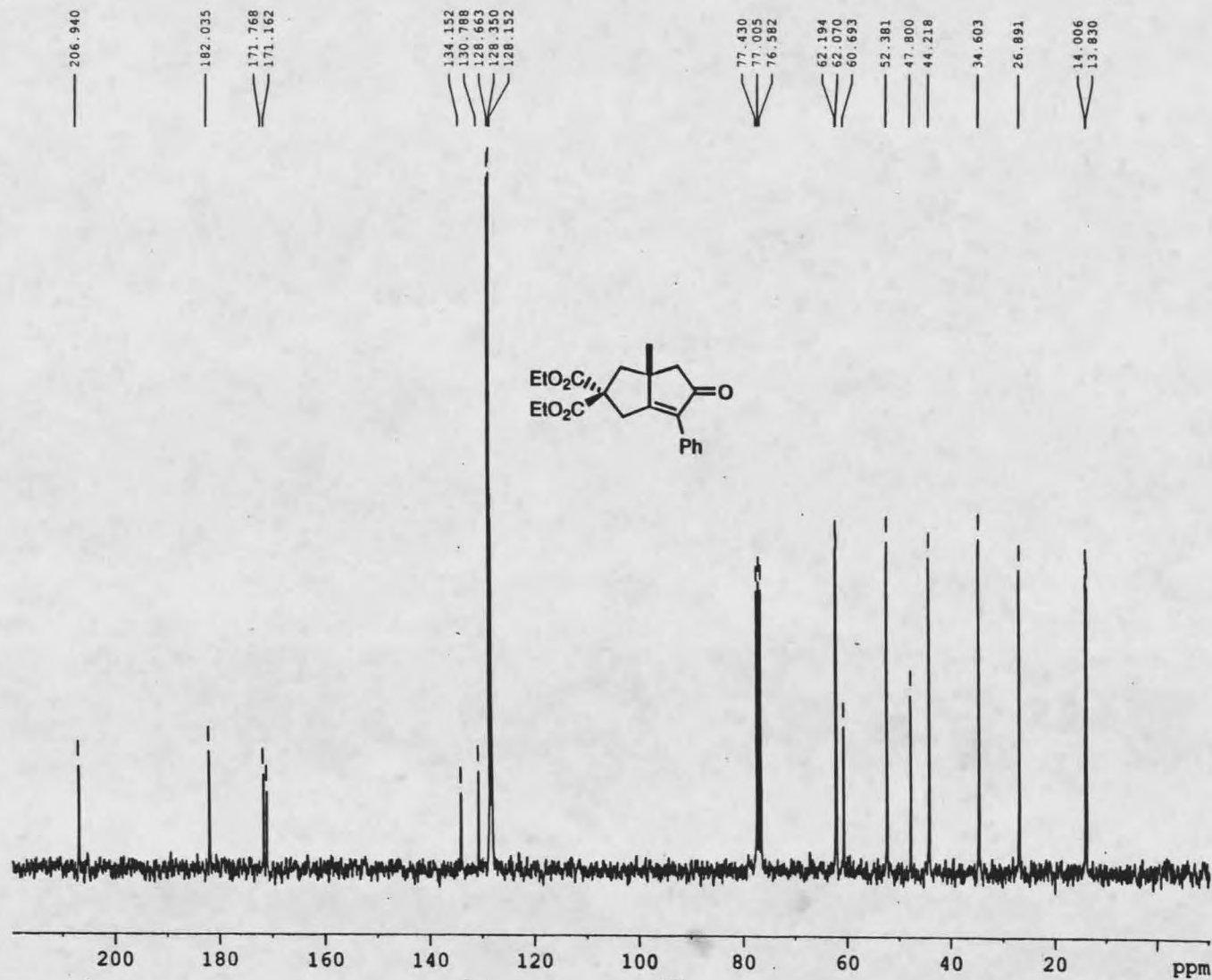
PPM
 208.783
 188.237
 171.454
 171.111
 124.155
 124.127
 77.426
 77.002
 76.579
 62.024
 61.980
 59.495
 51.749
 49.732
 44.366
 34.205
 26.467
 13.975
 13.040

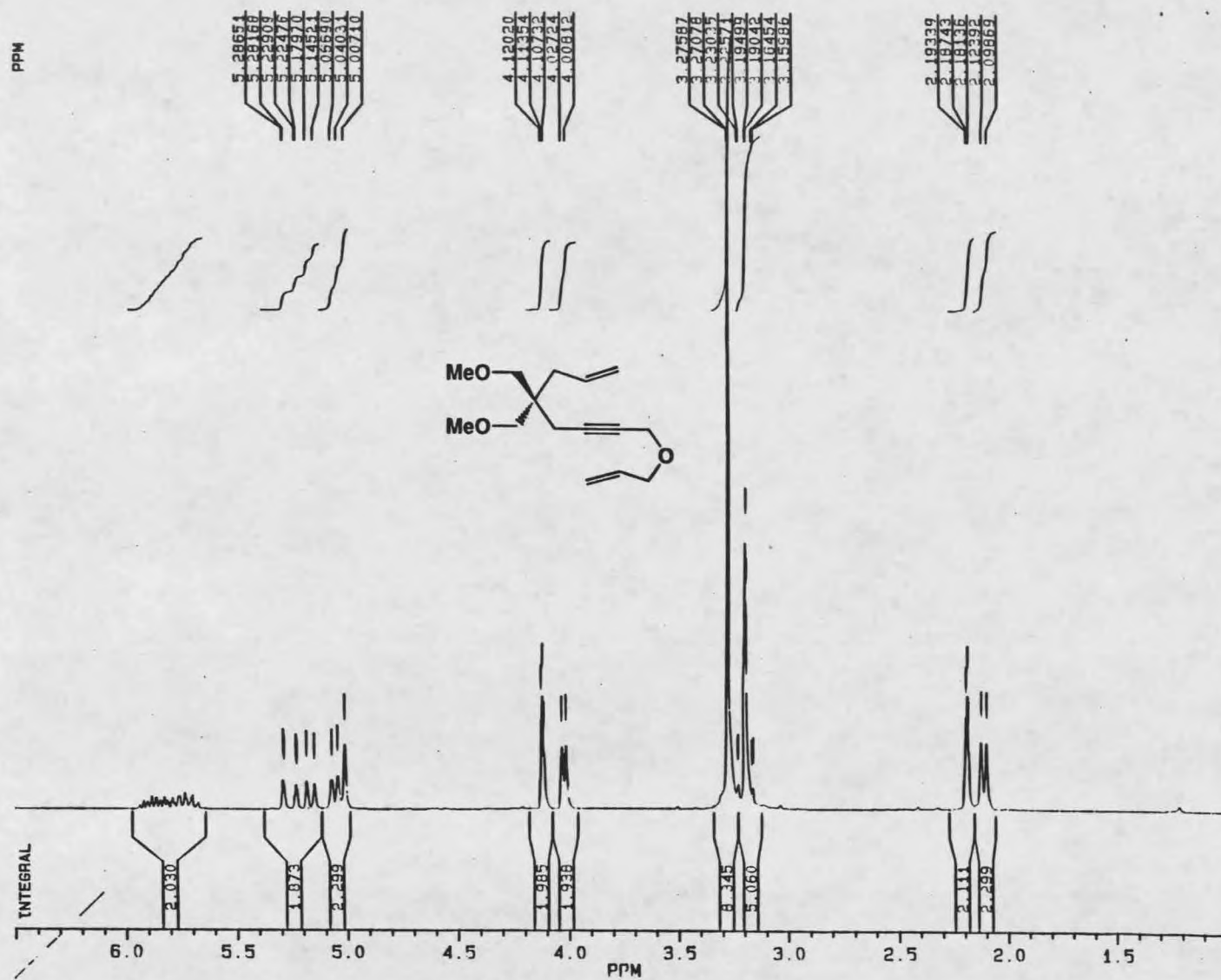


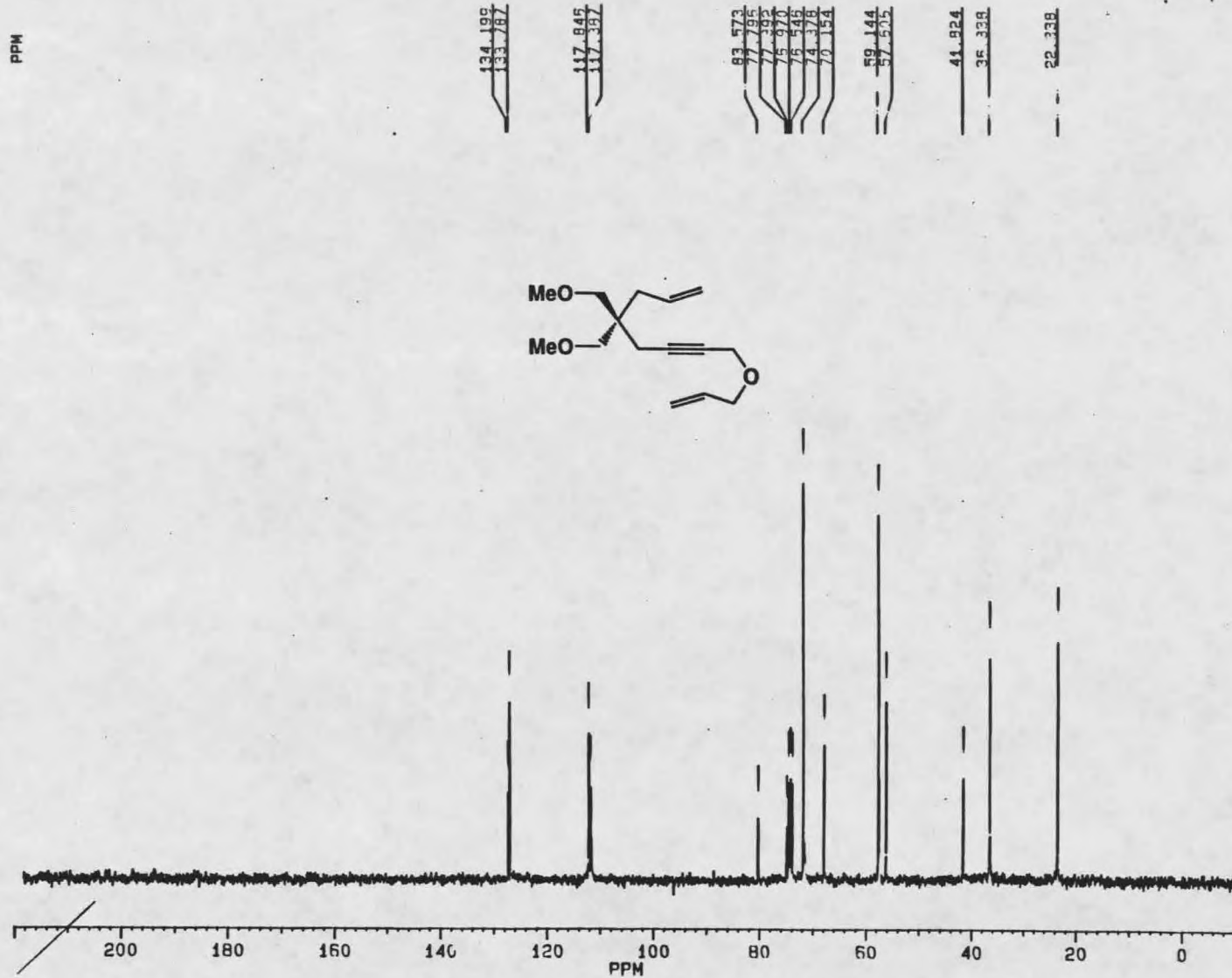


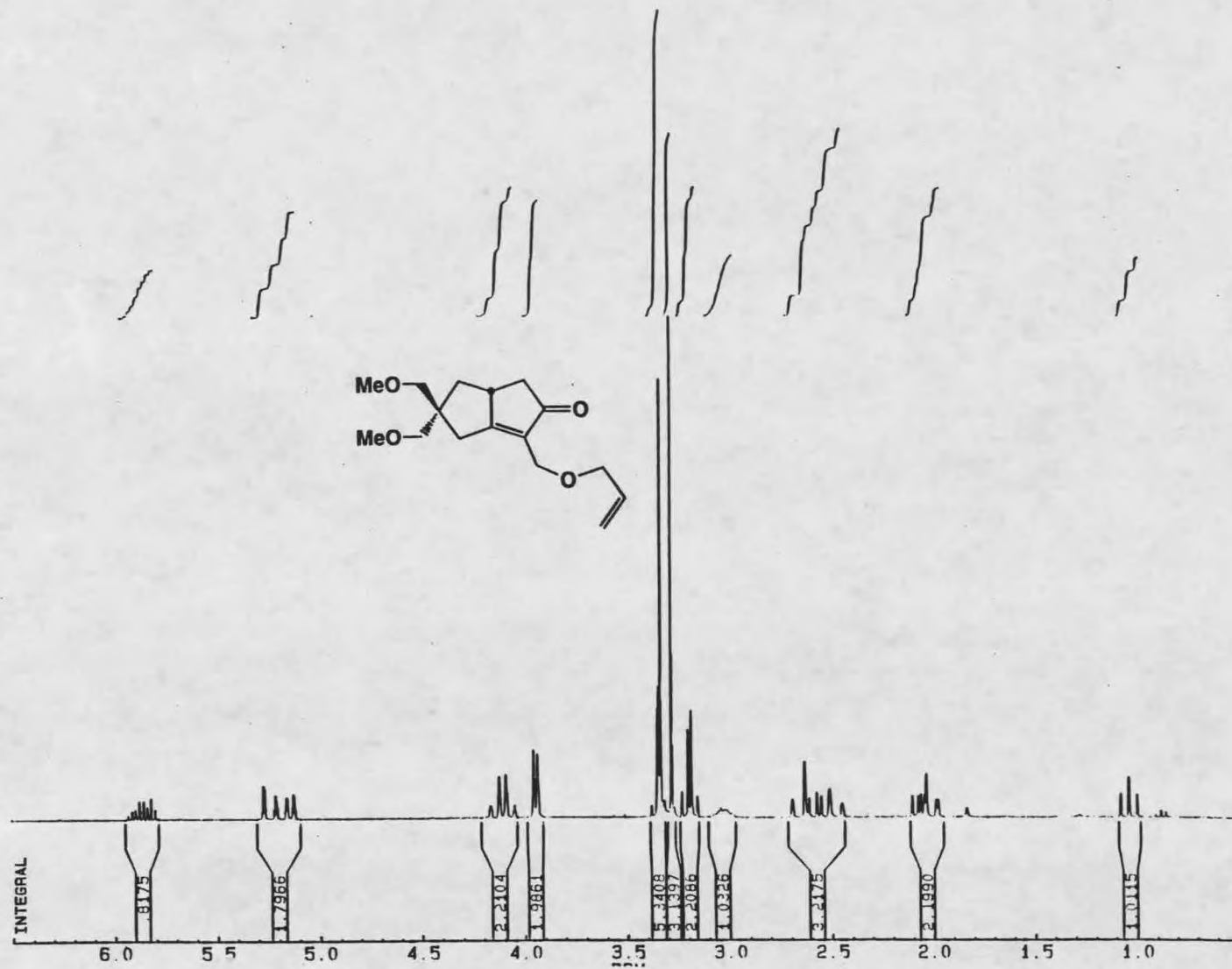


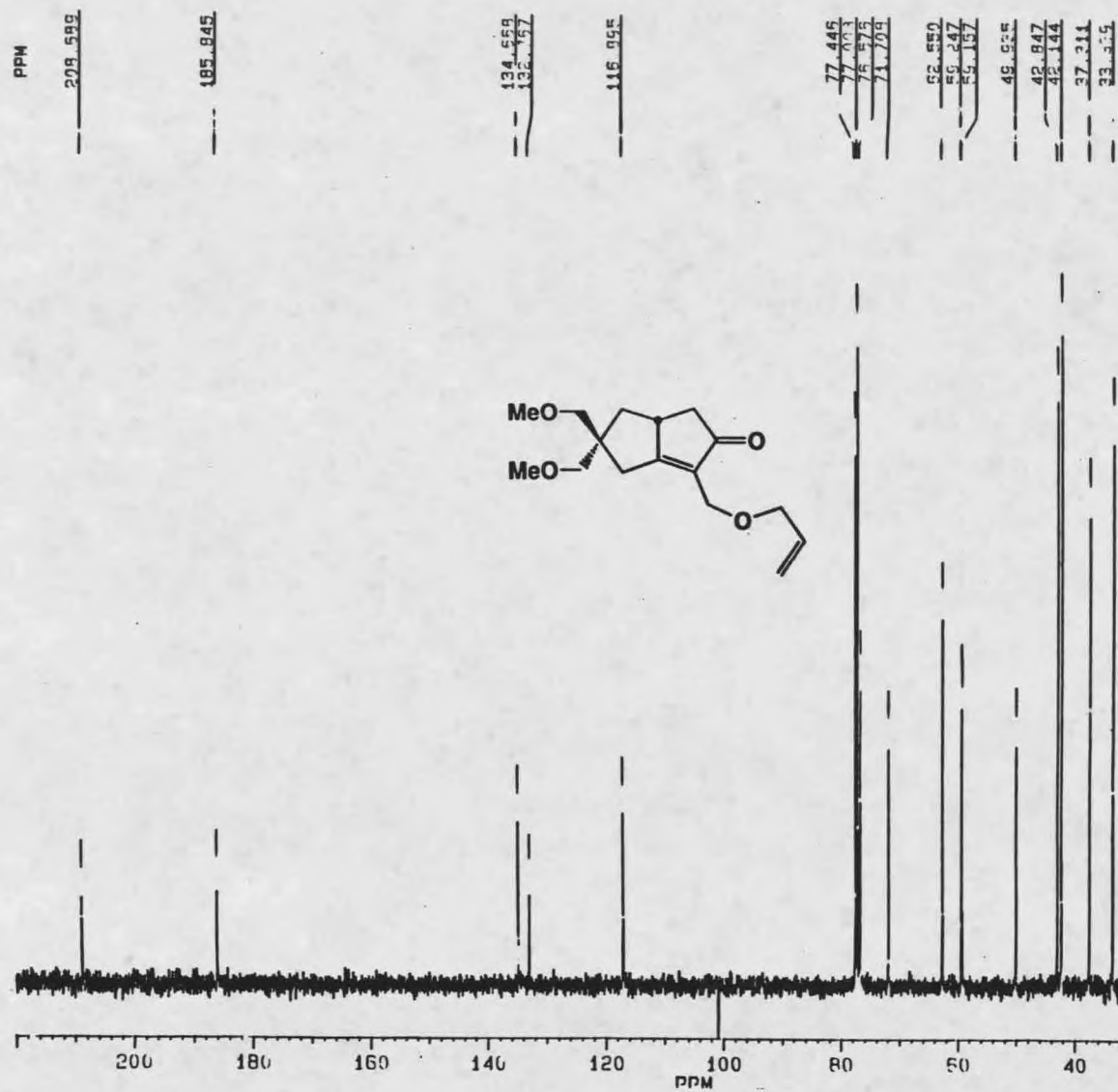


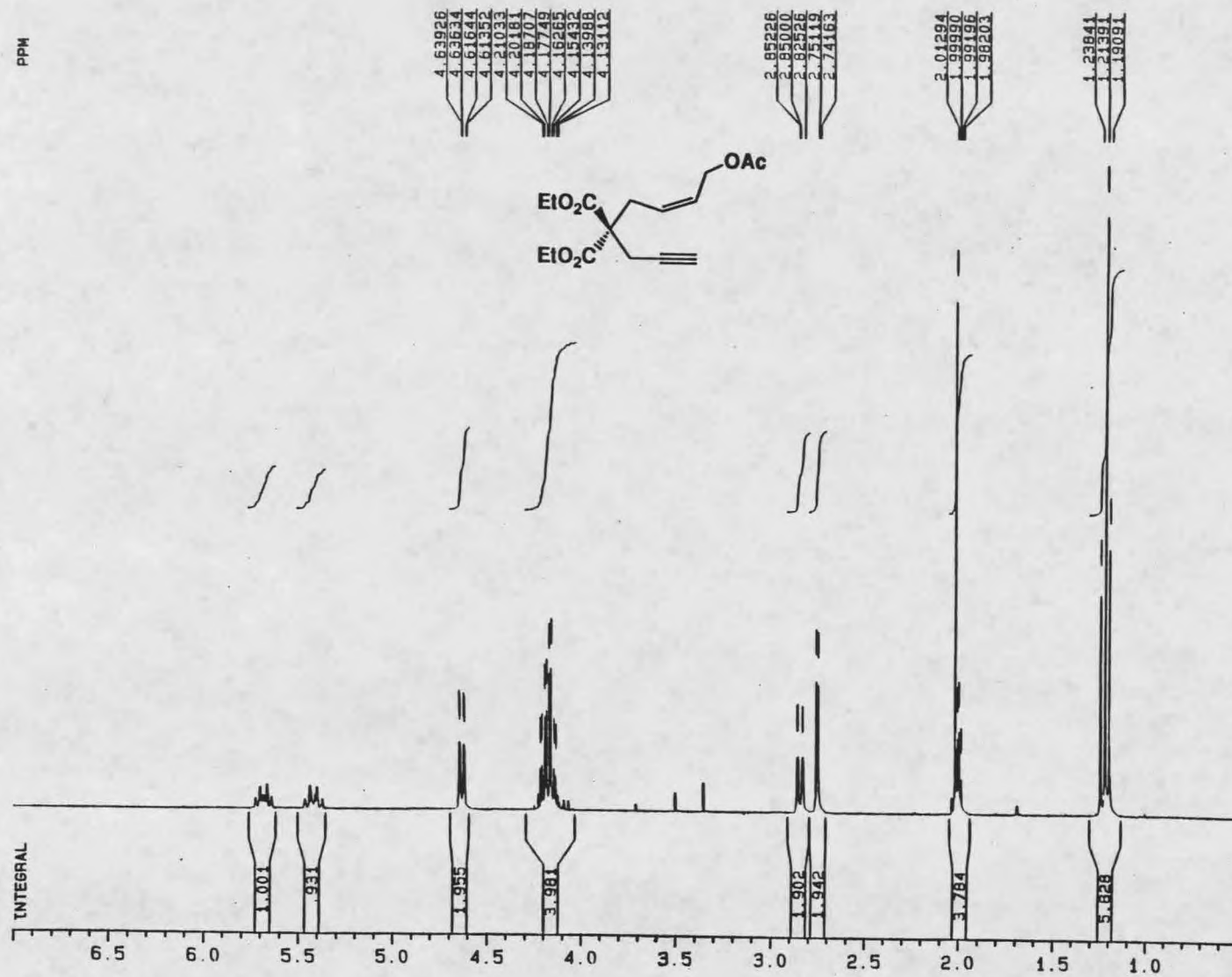


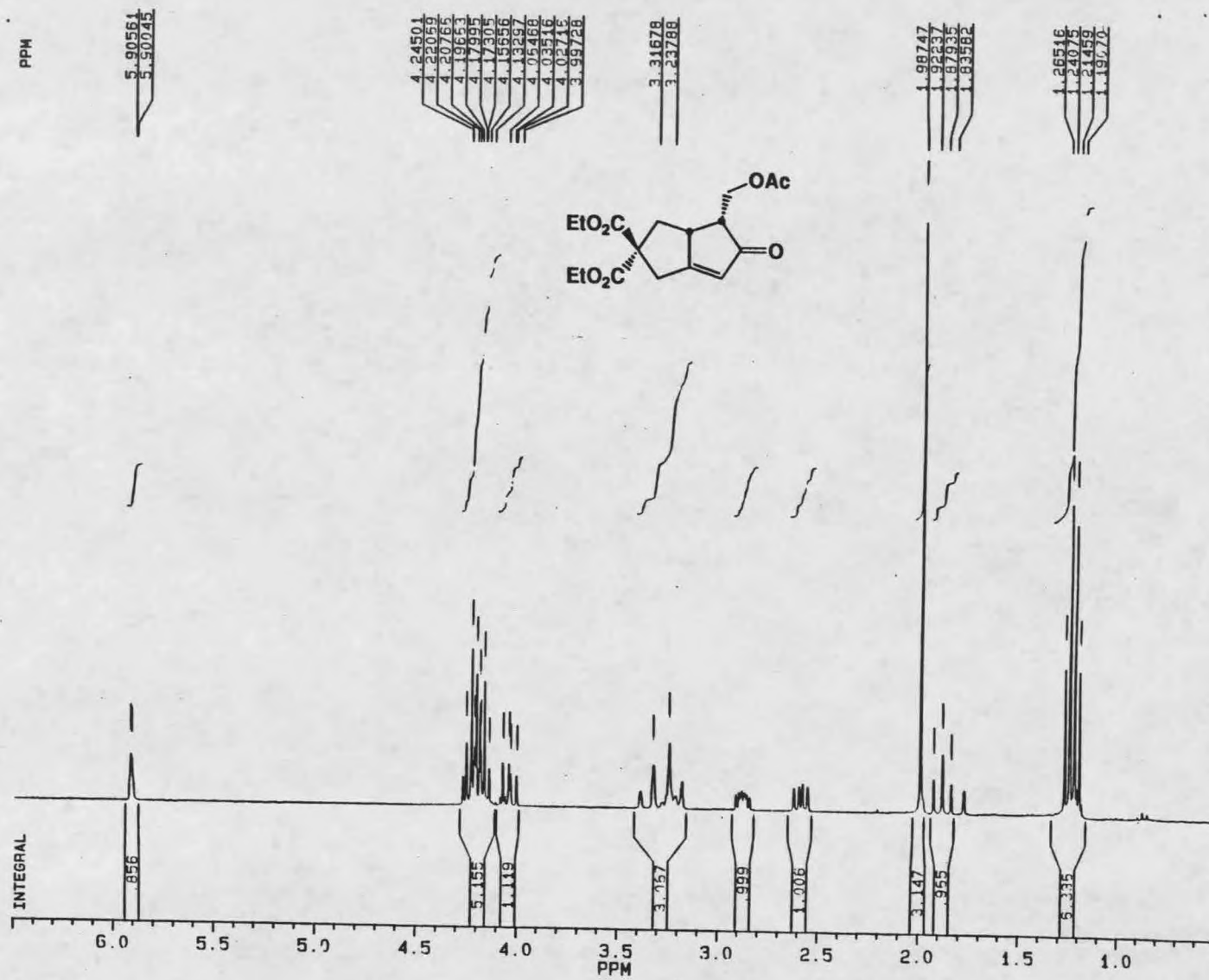


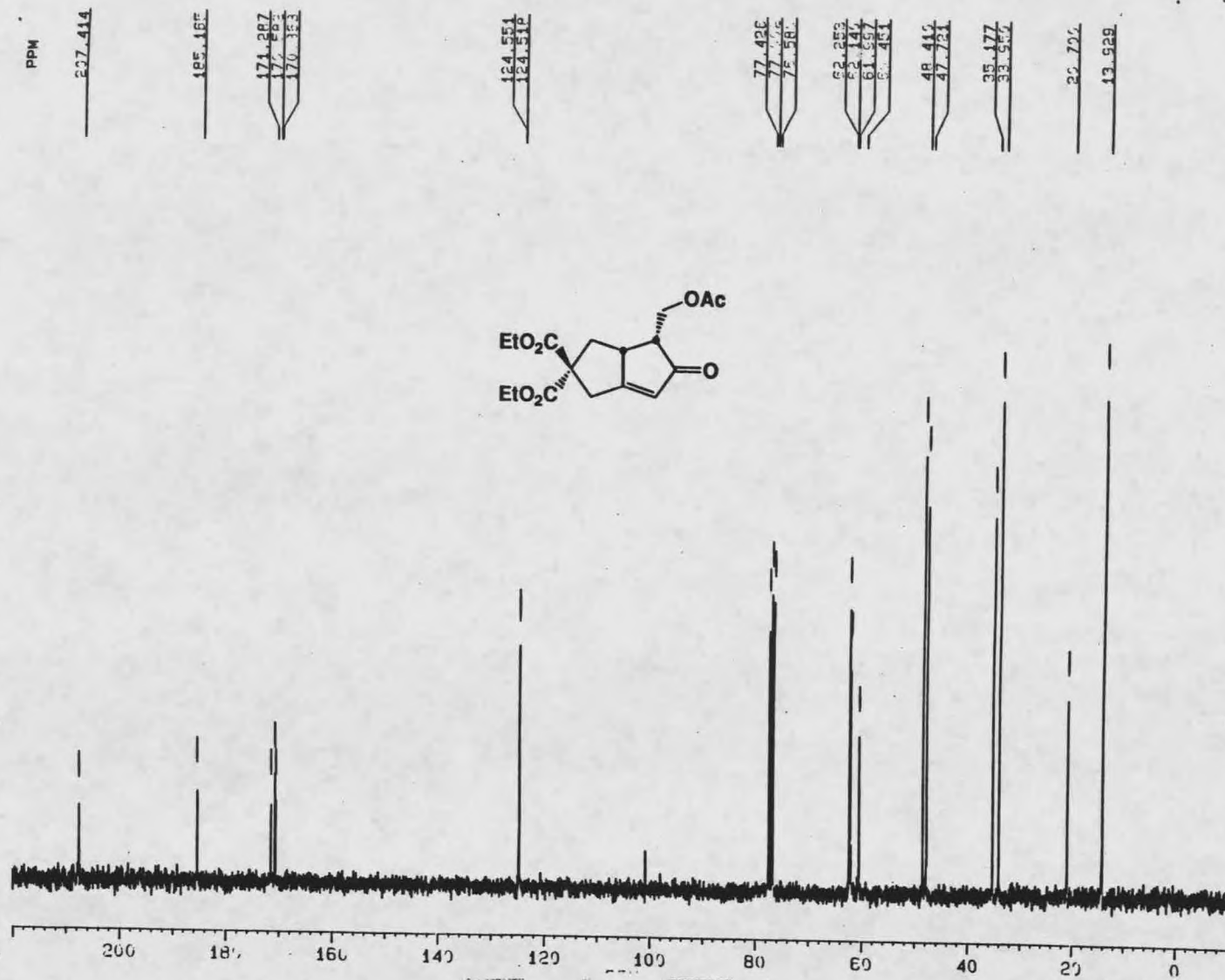


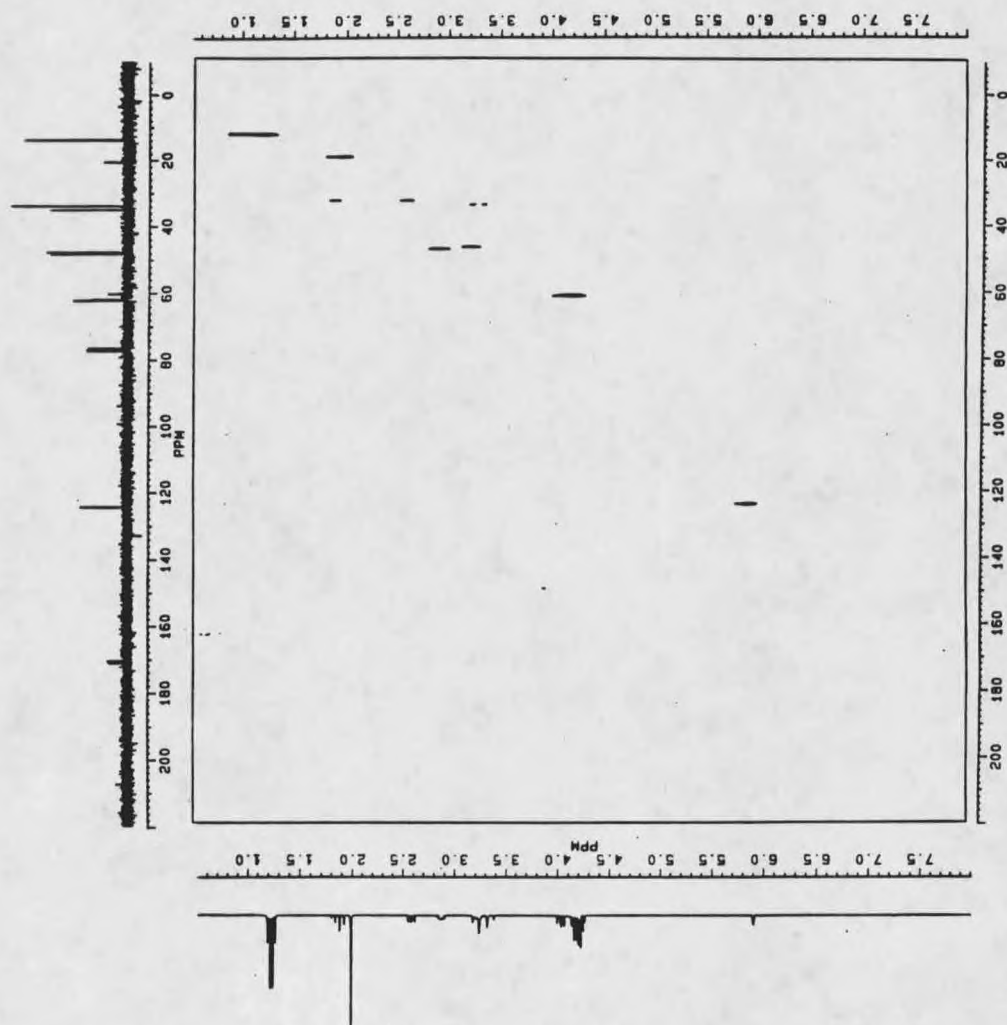
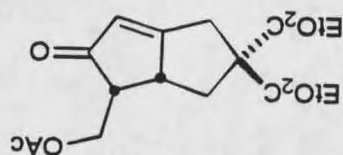


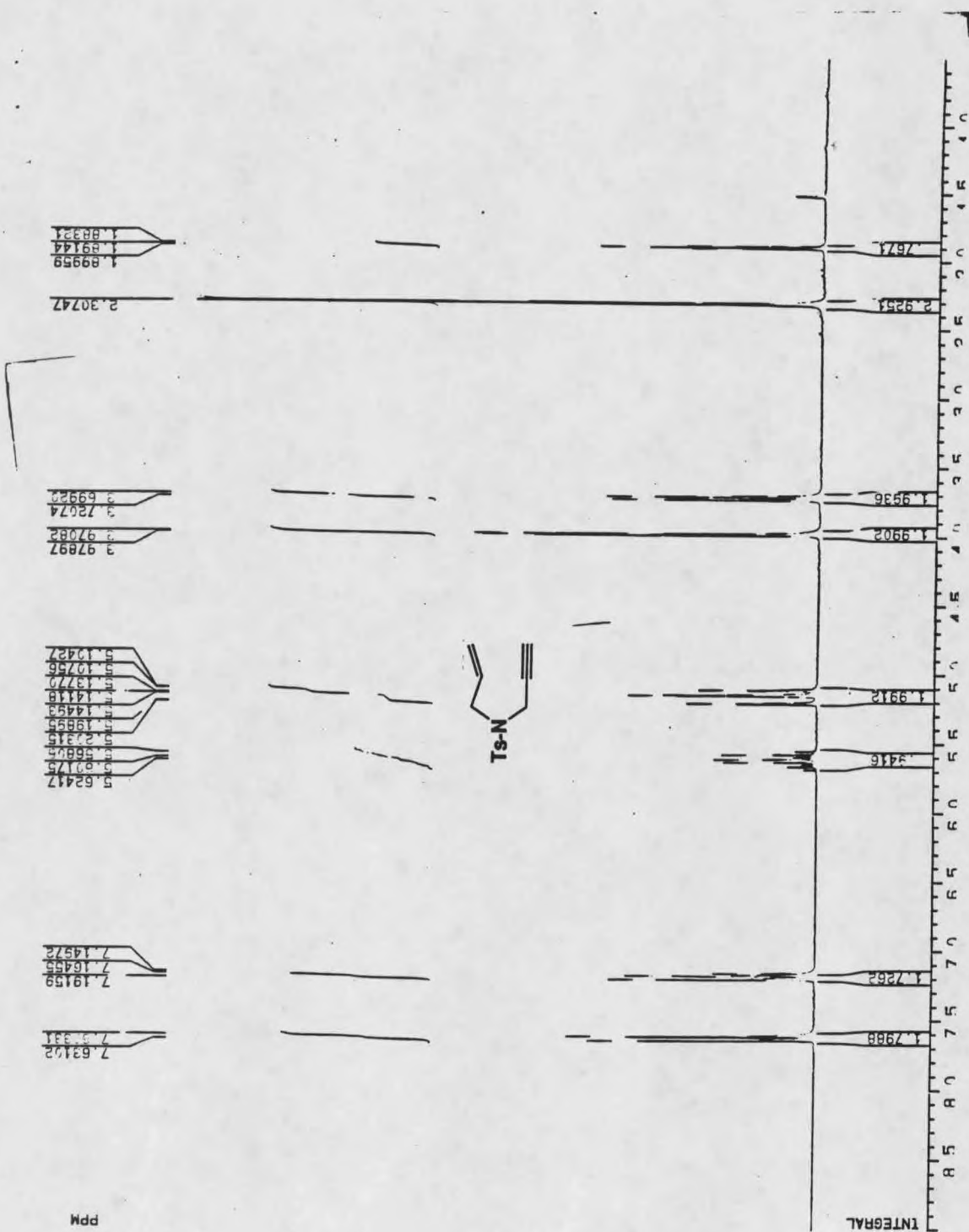


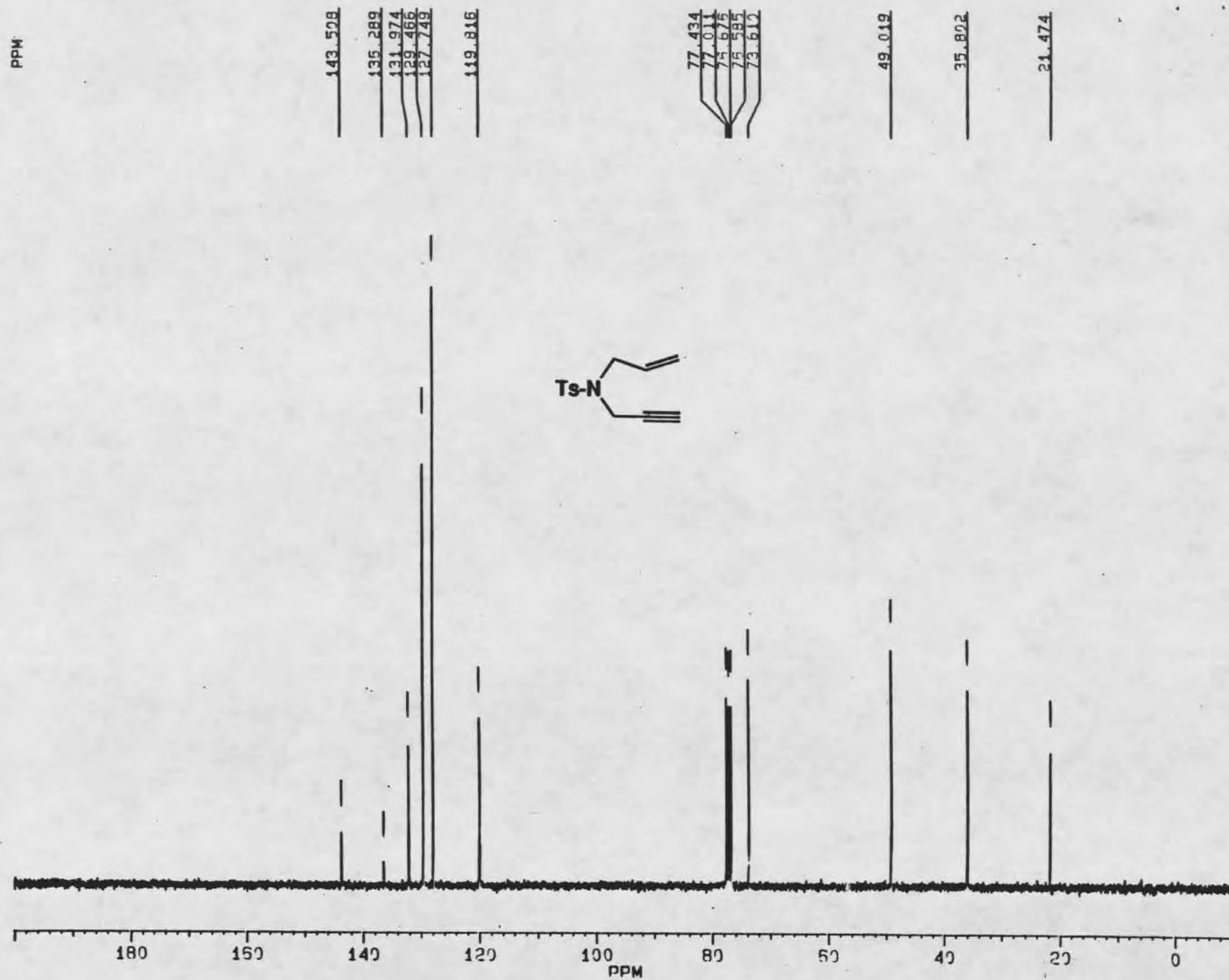


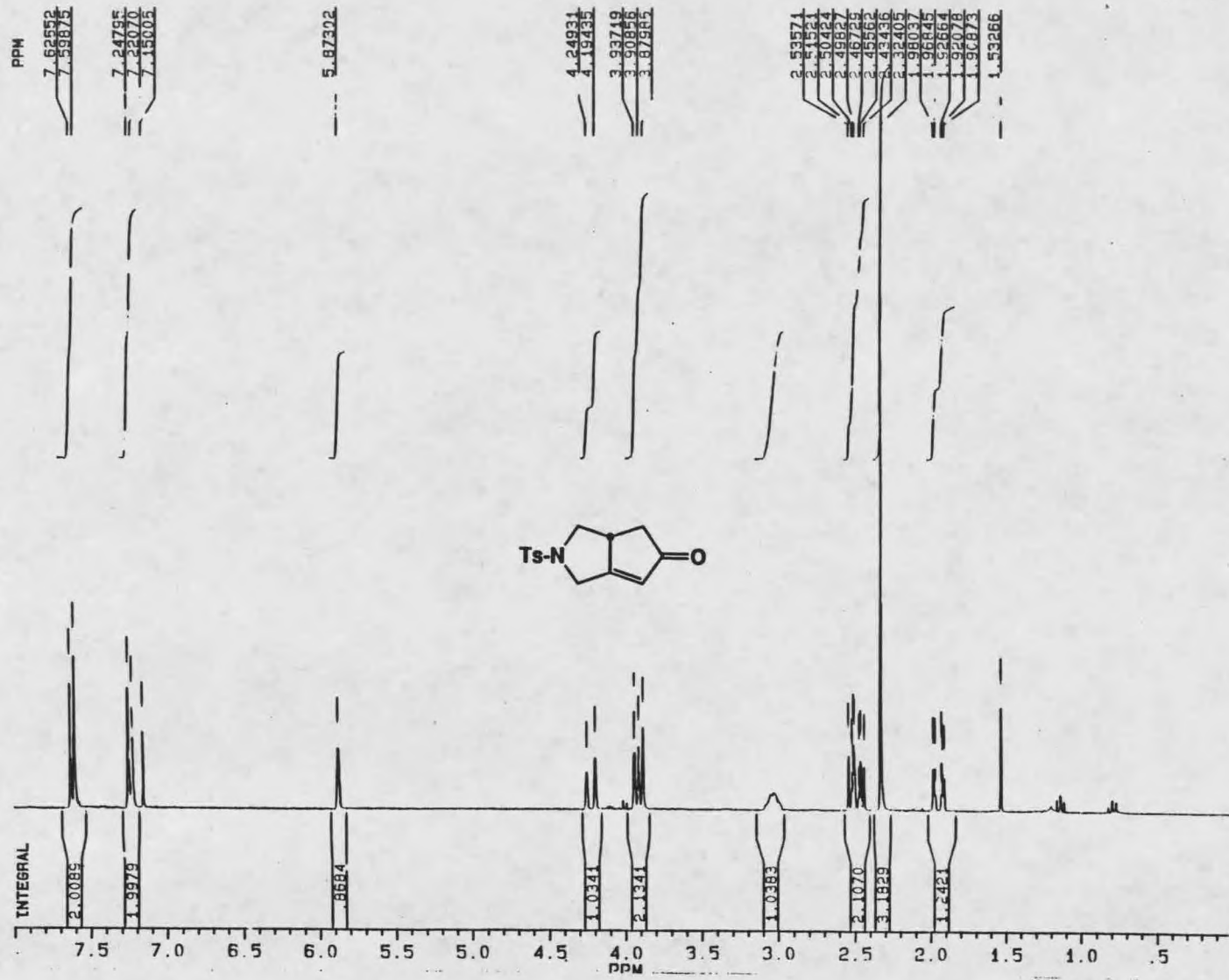


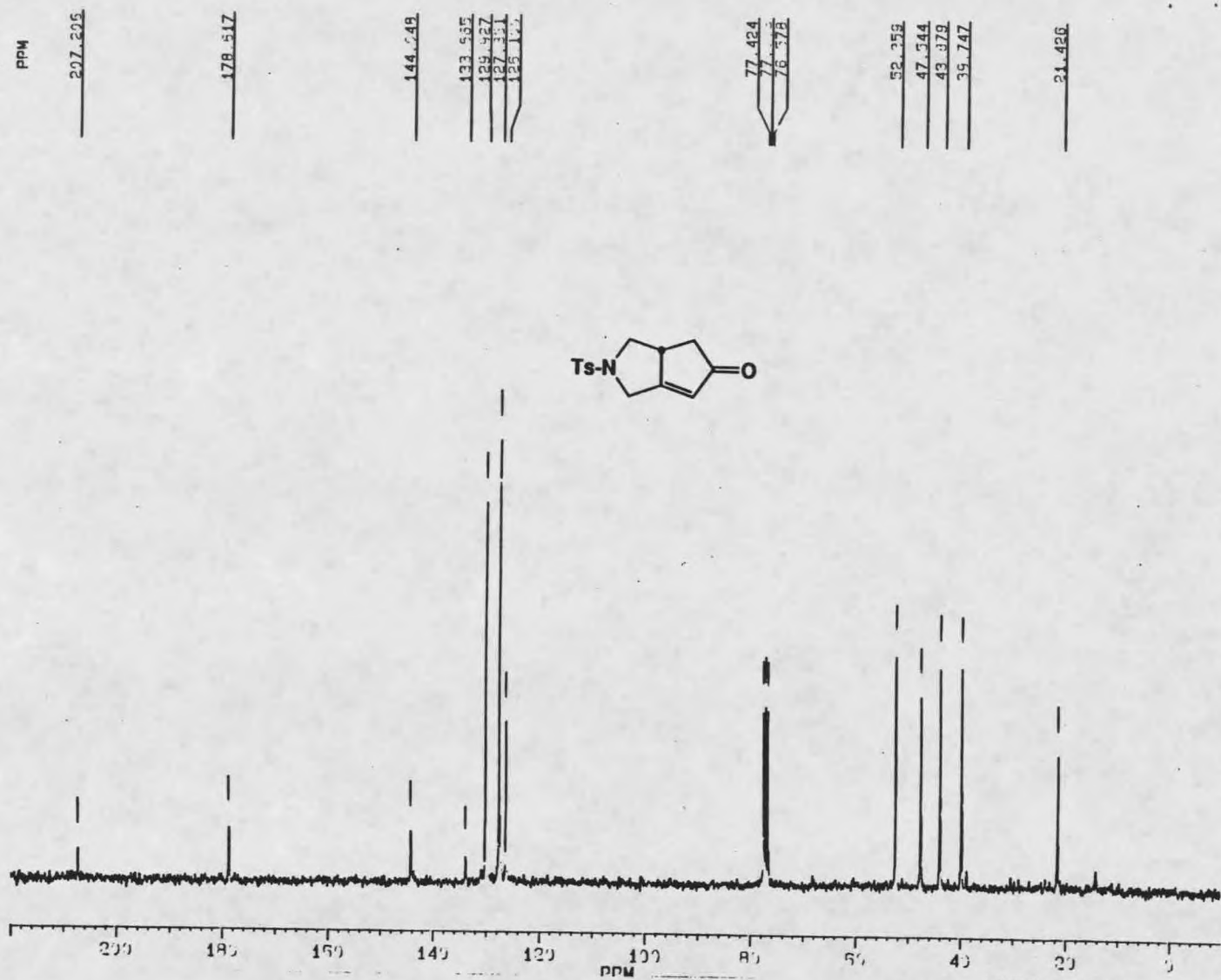


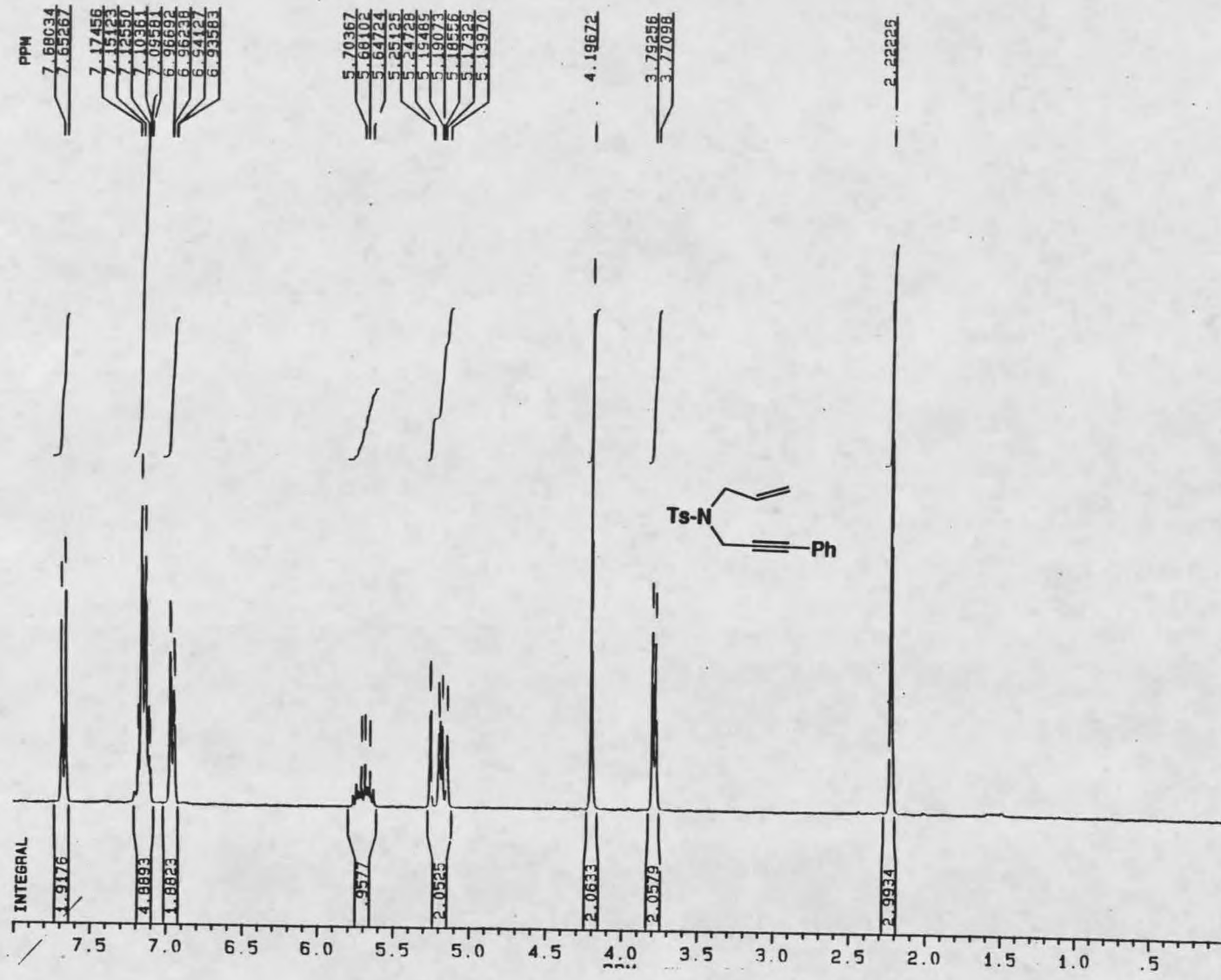


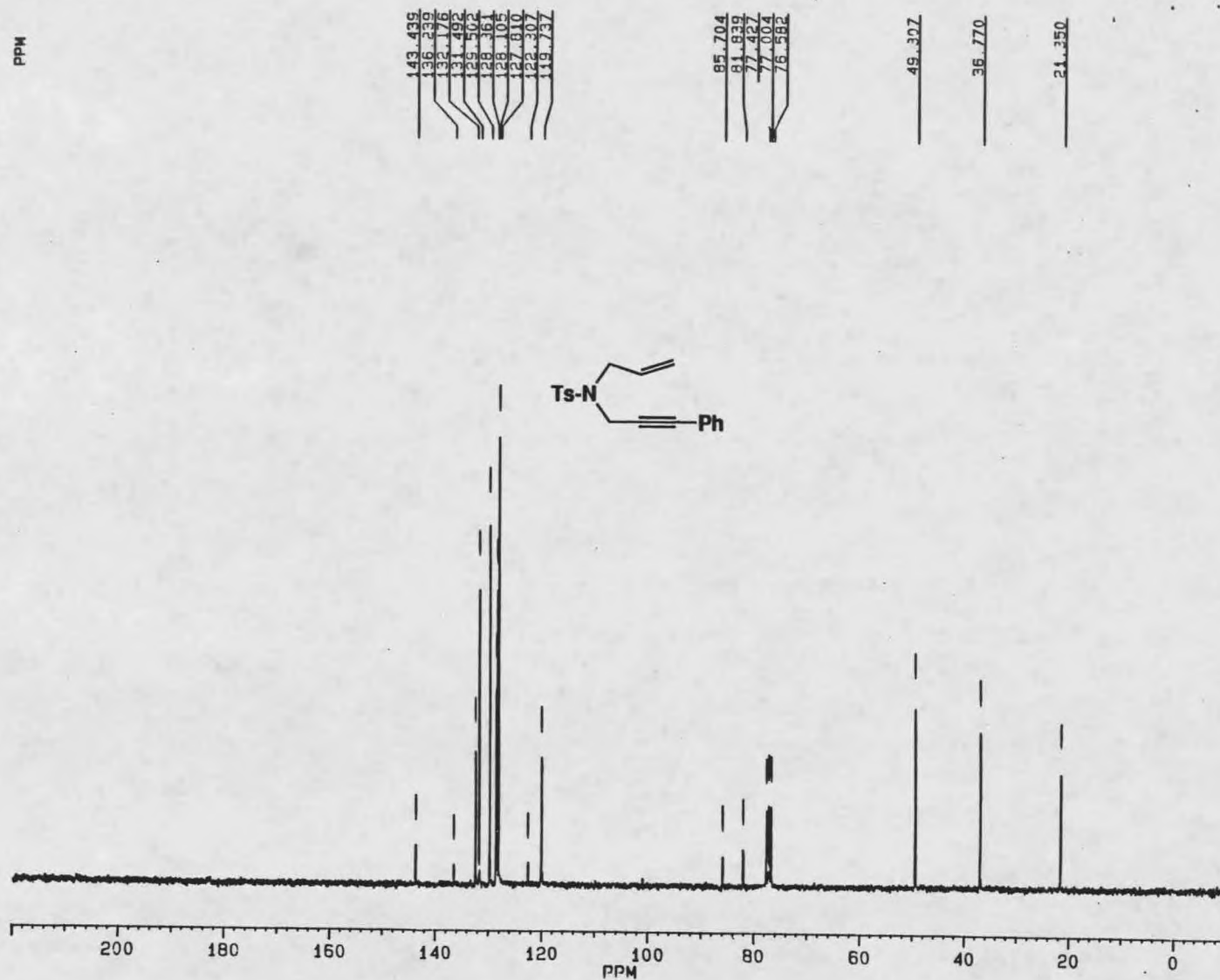


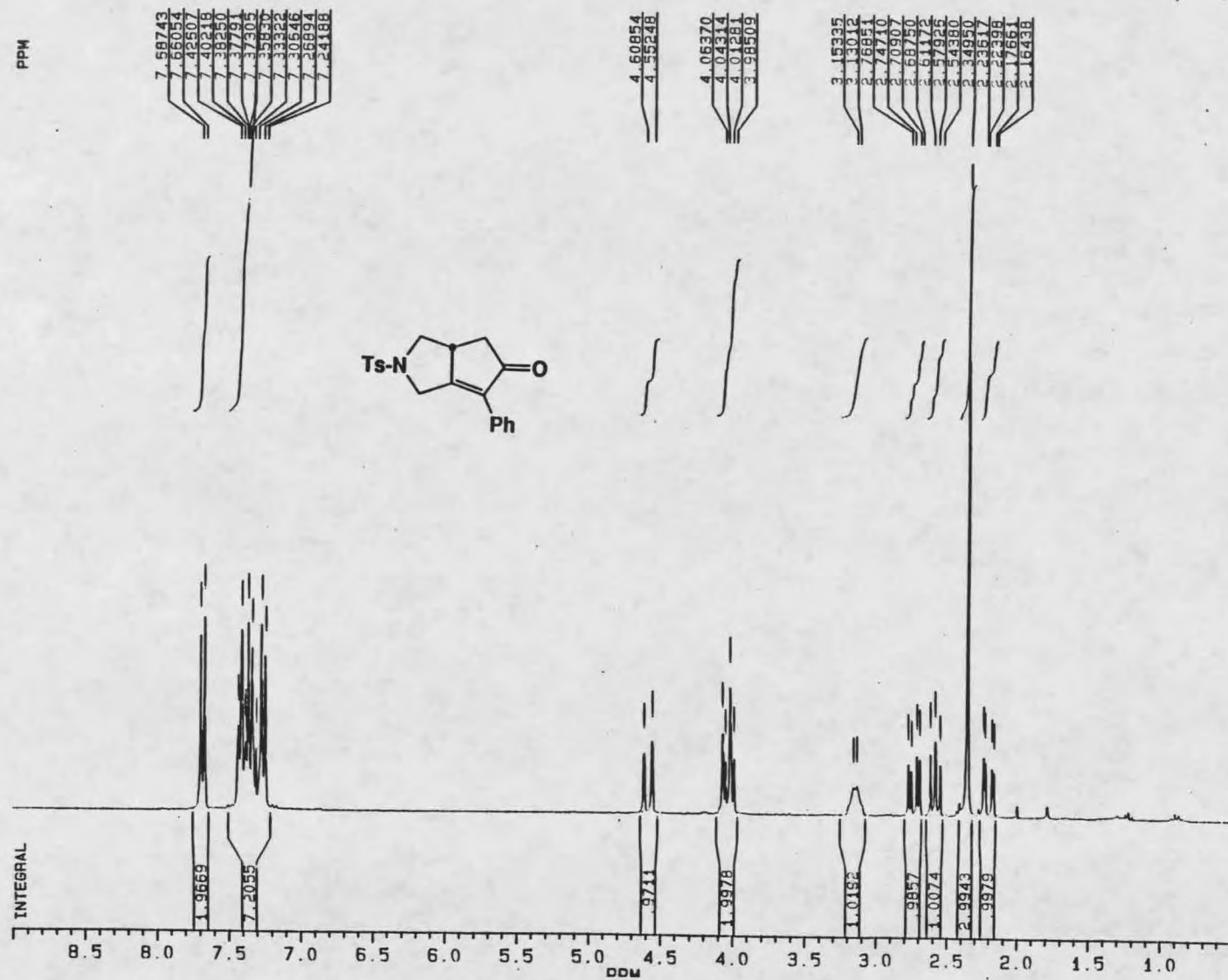


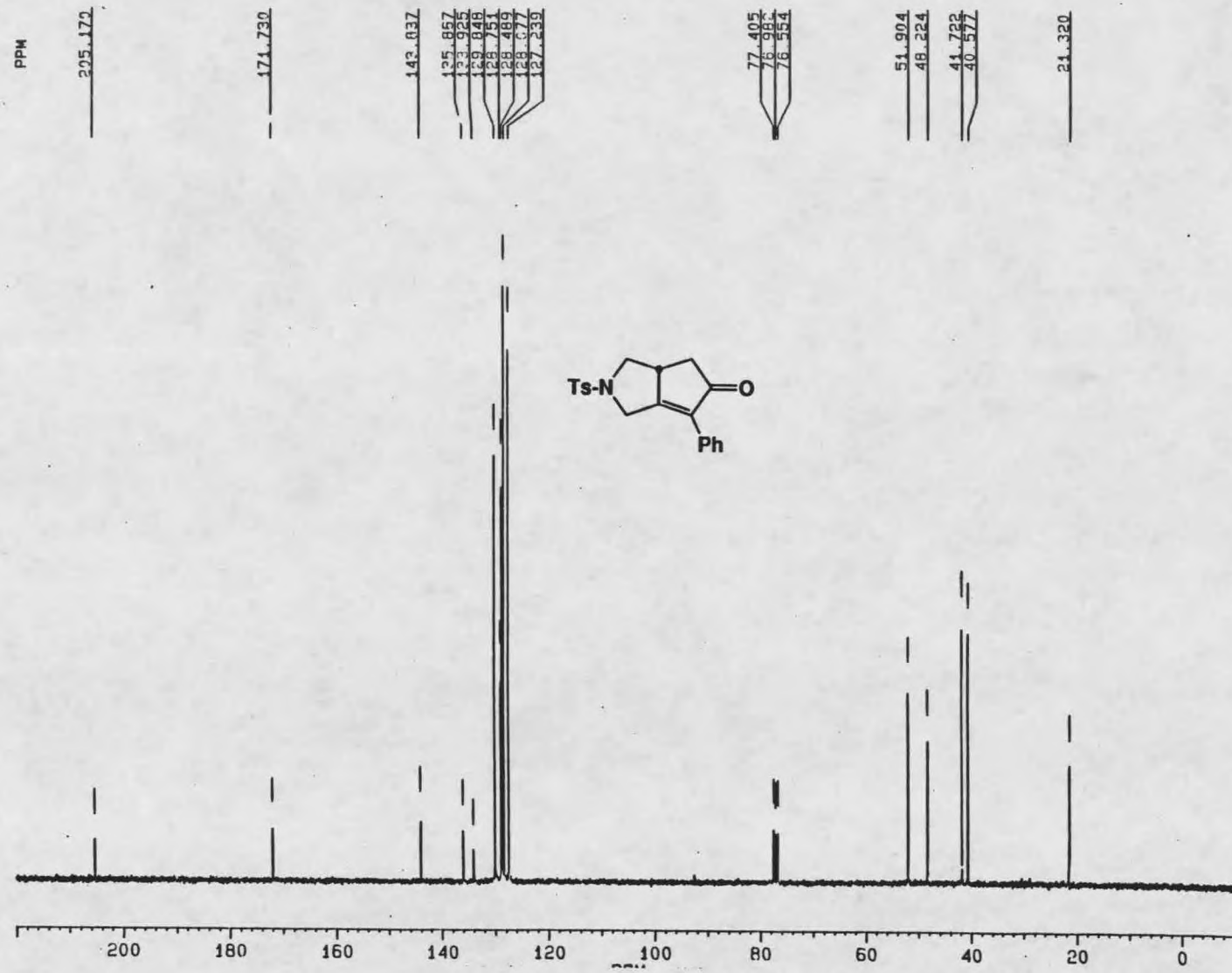


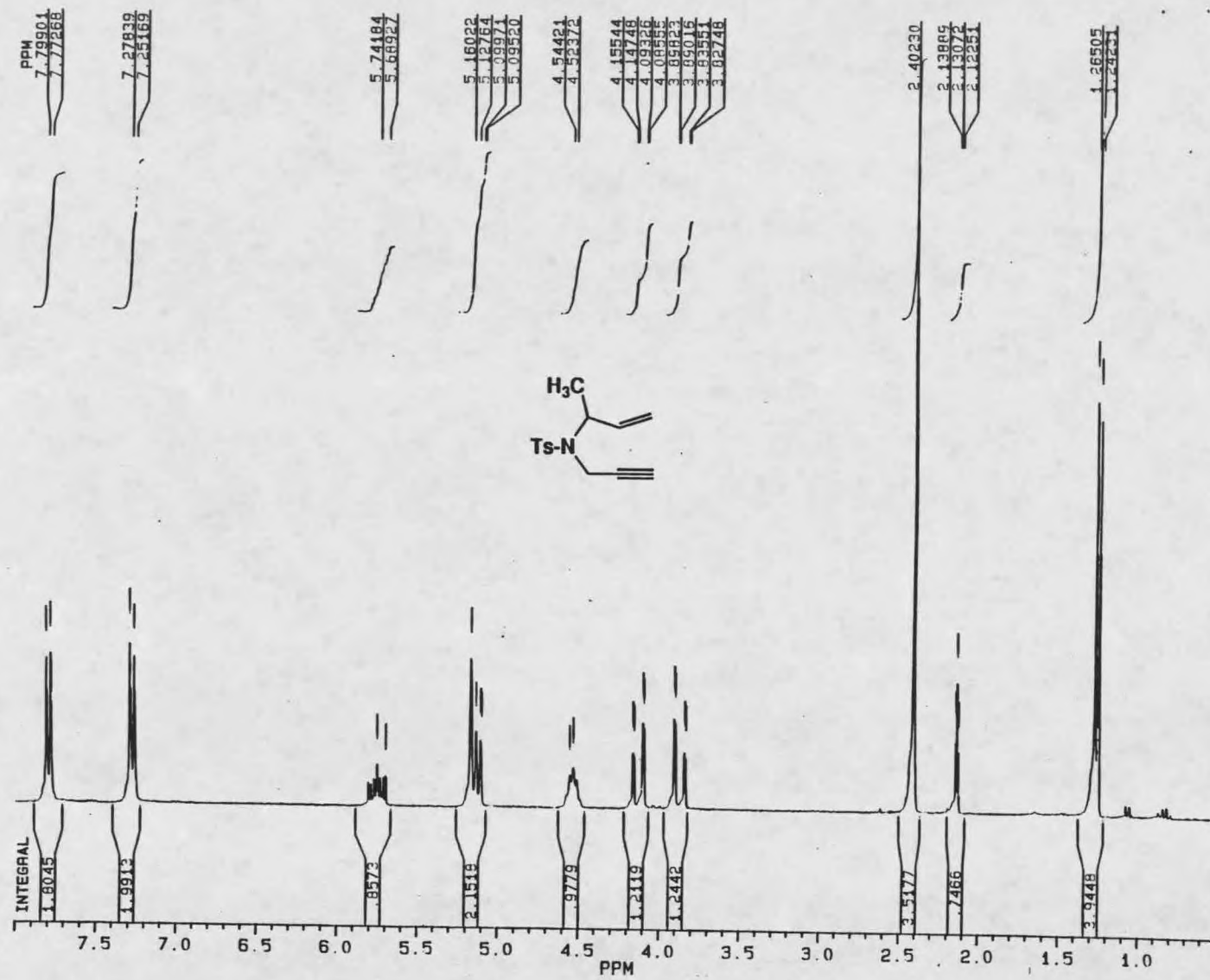


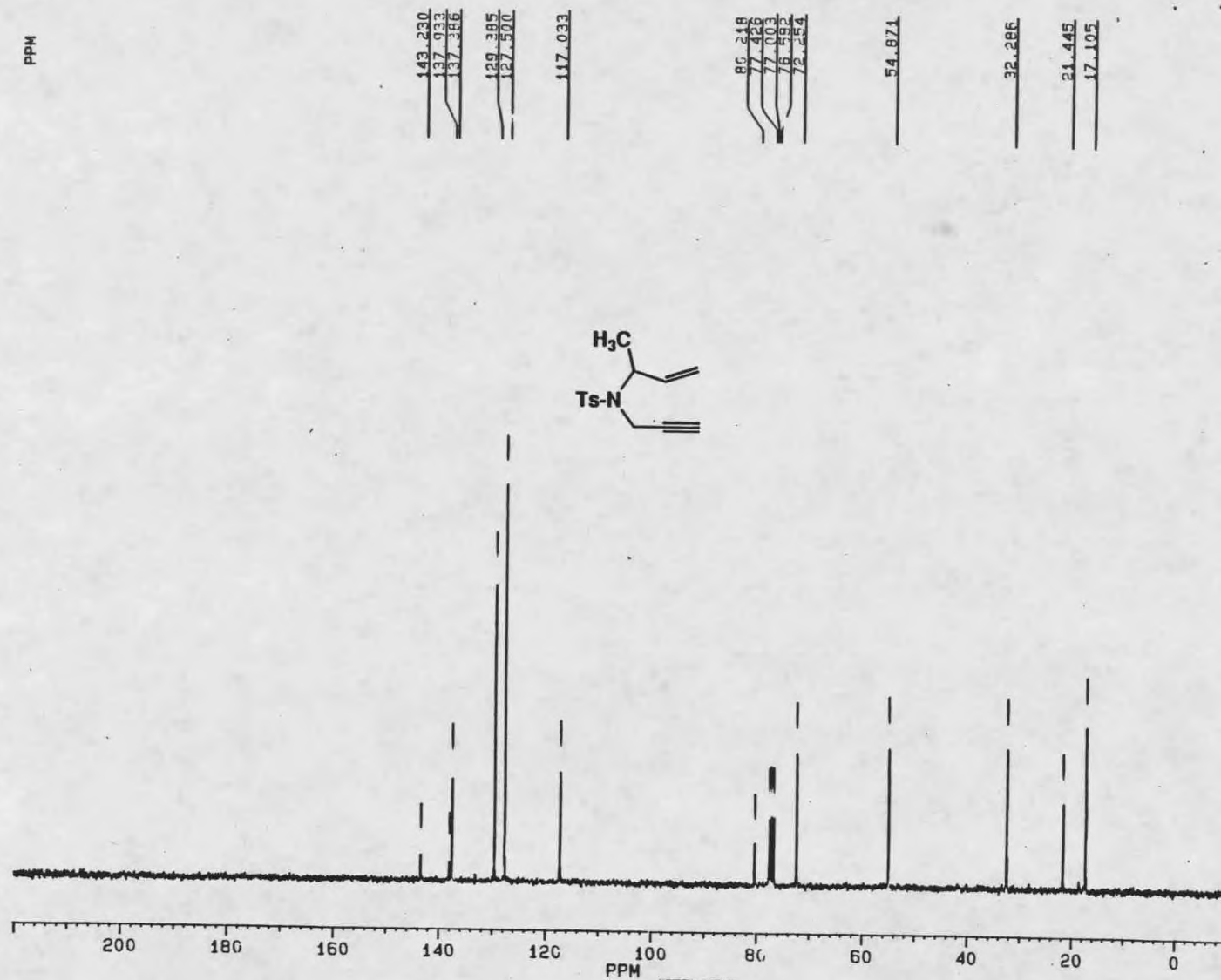


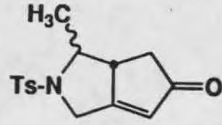
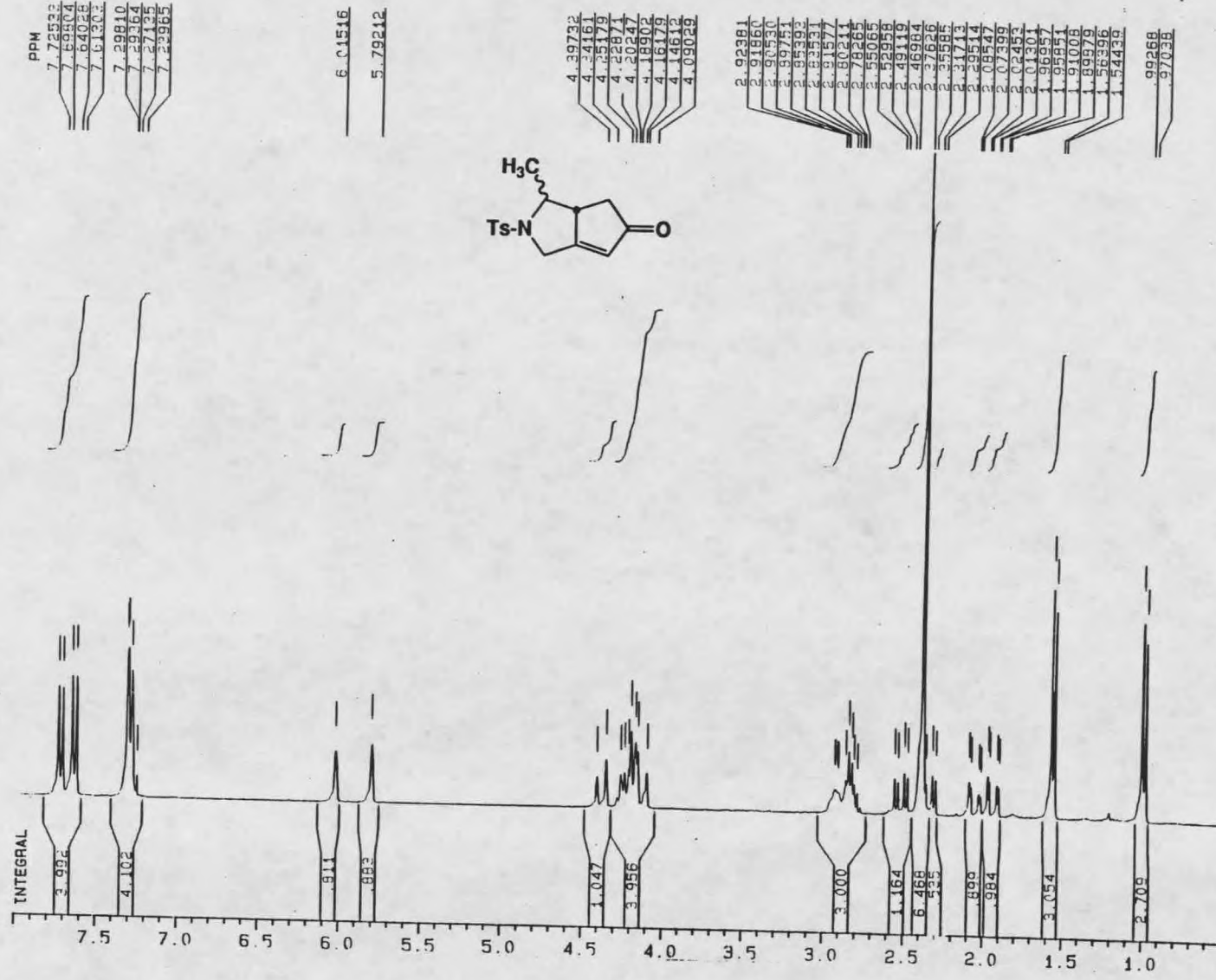


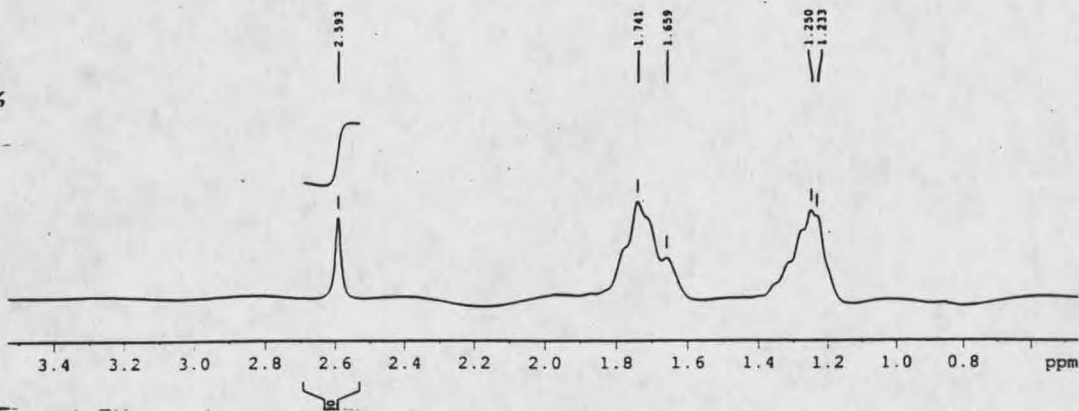
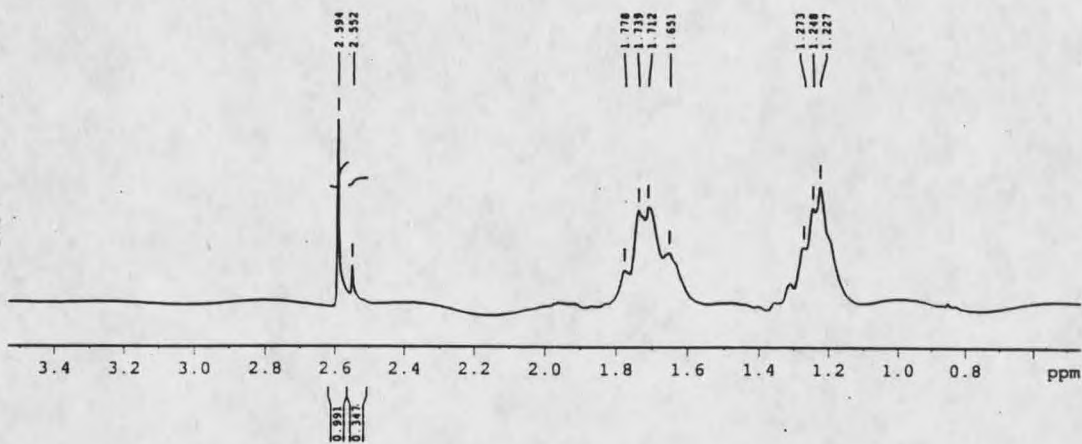
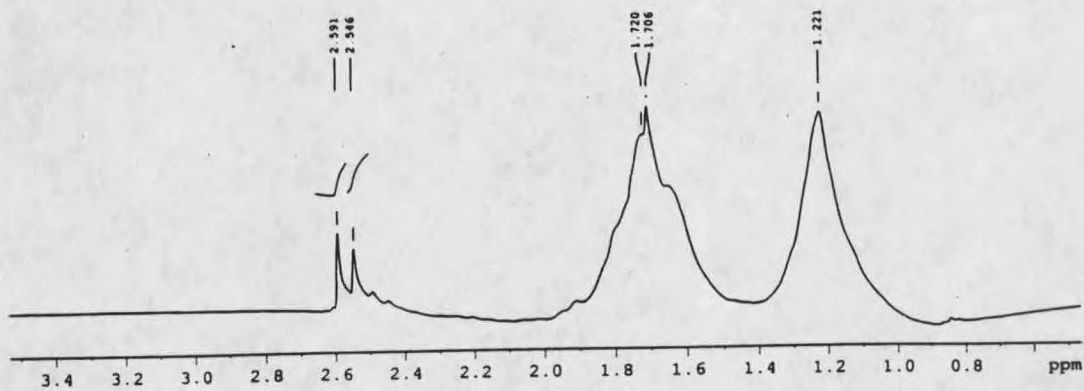


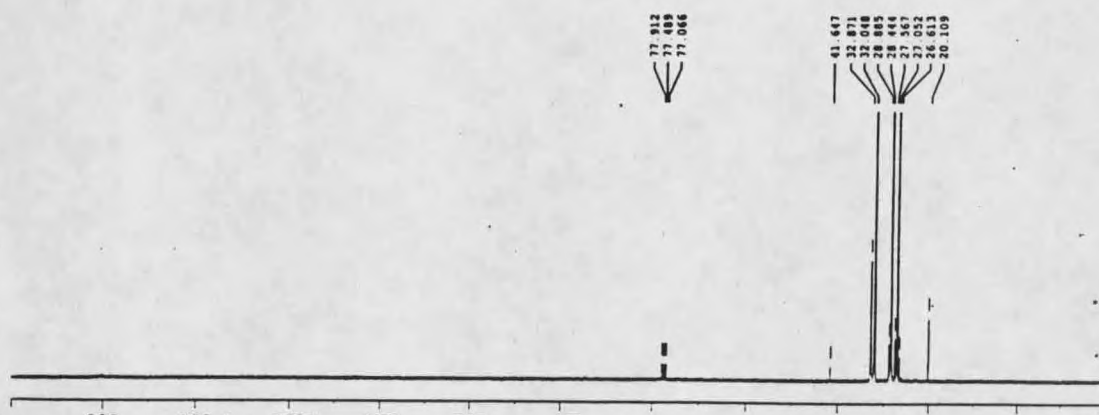
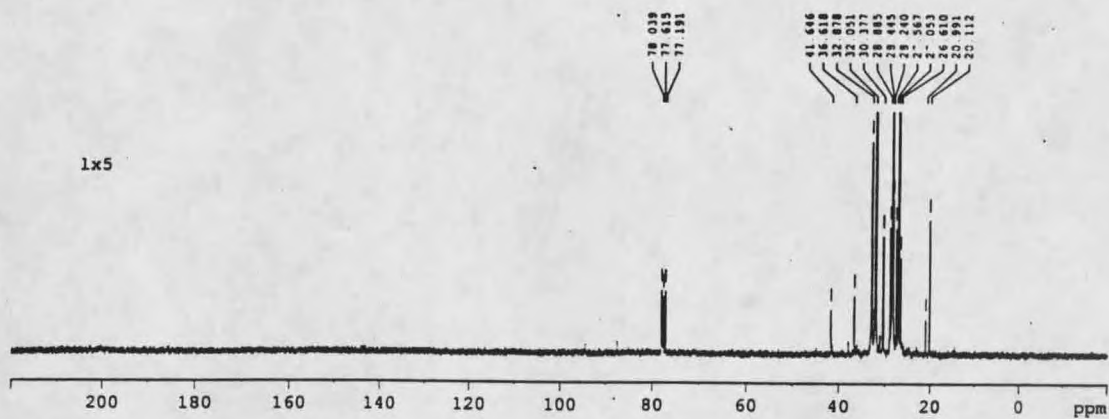
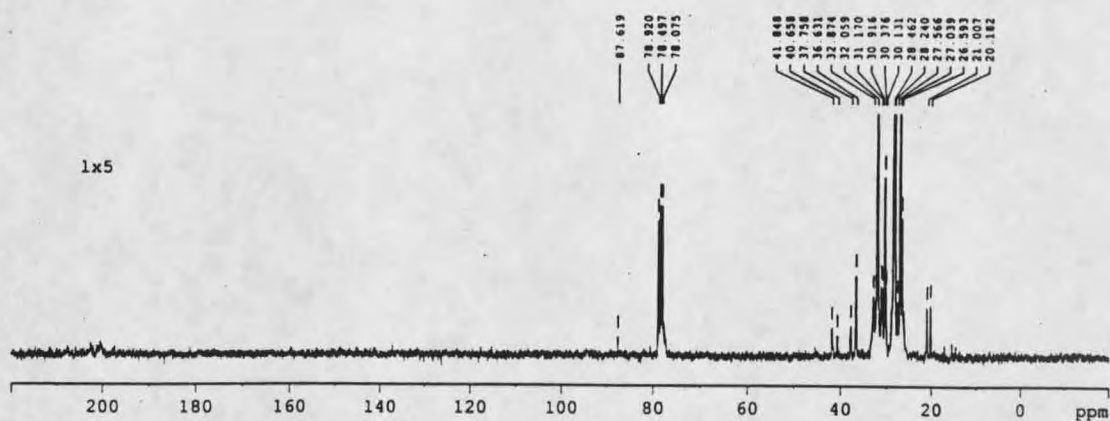


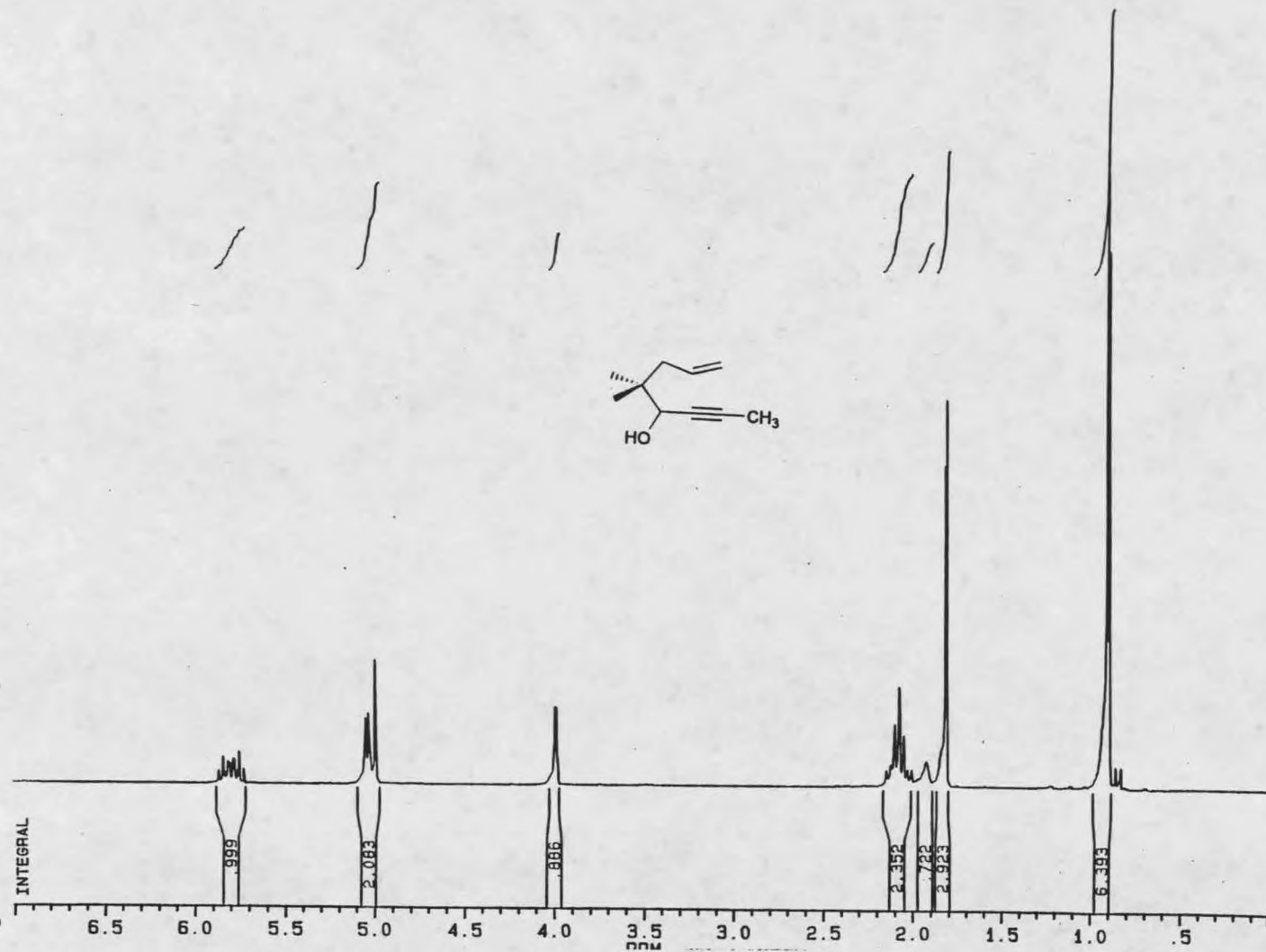




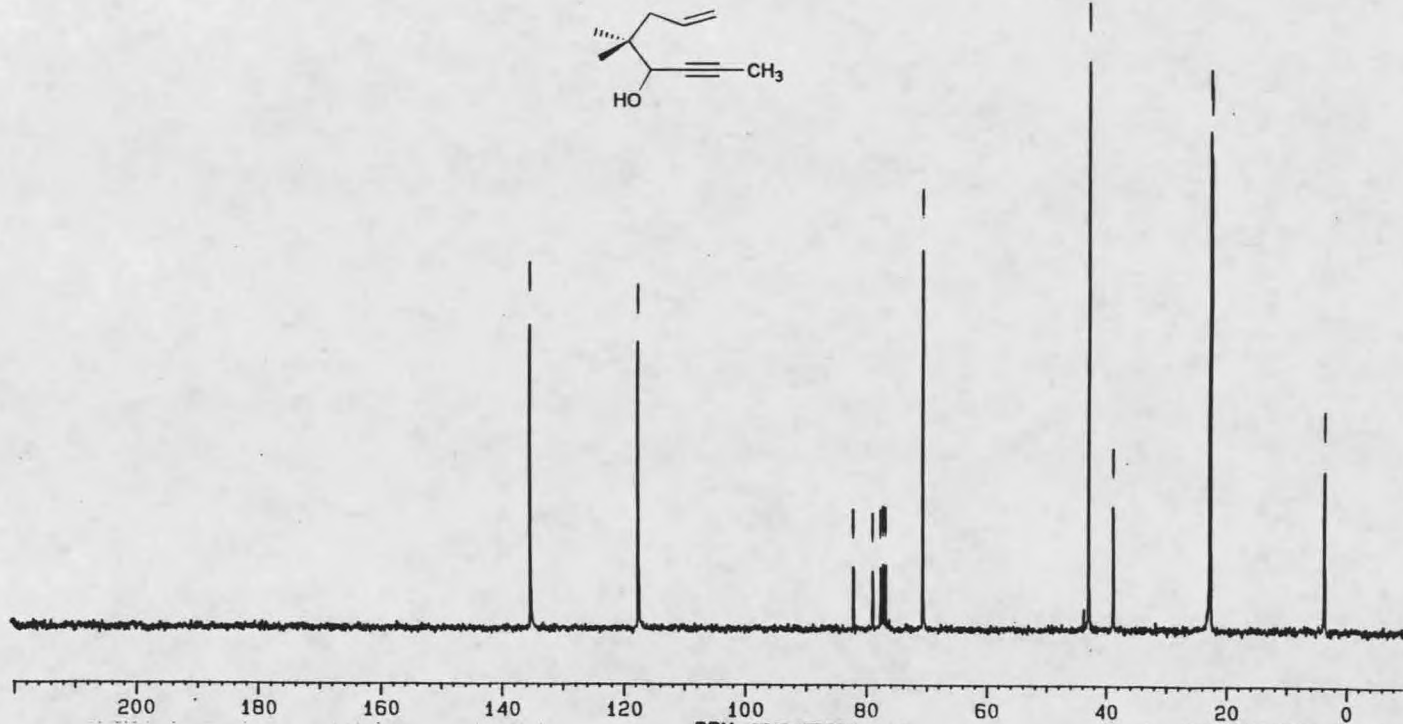


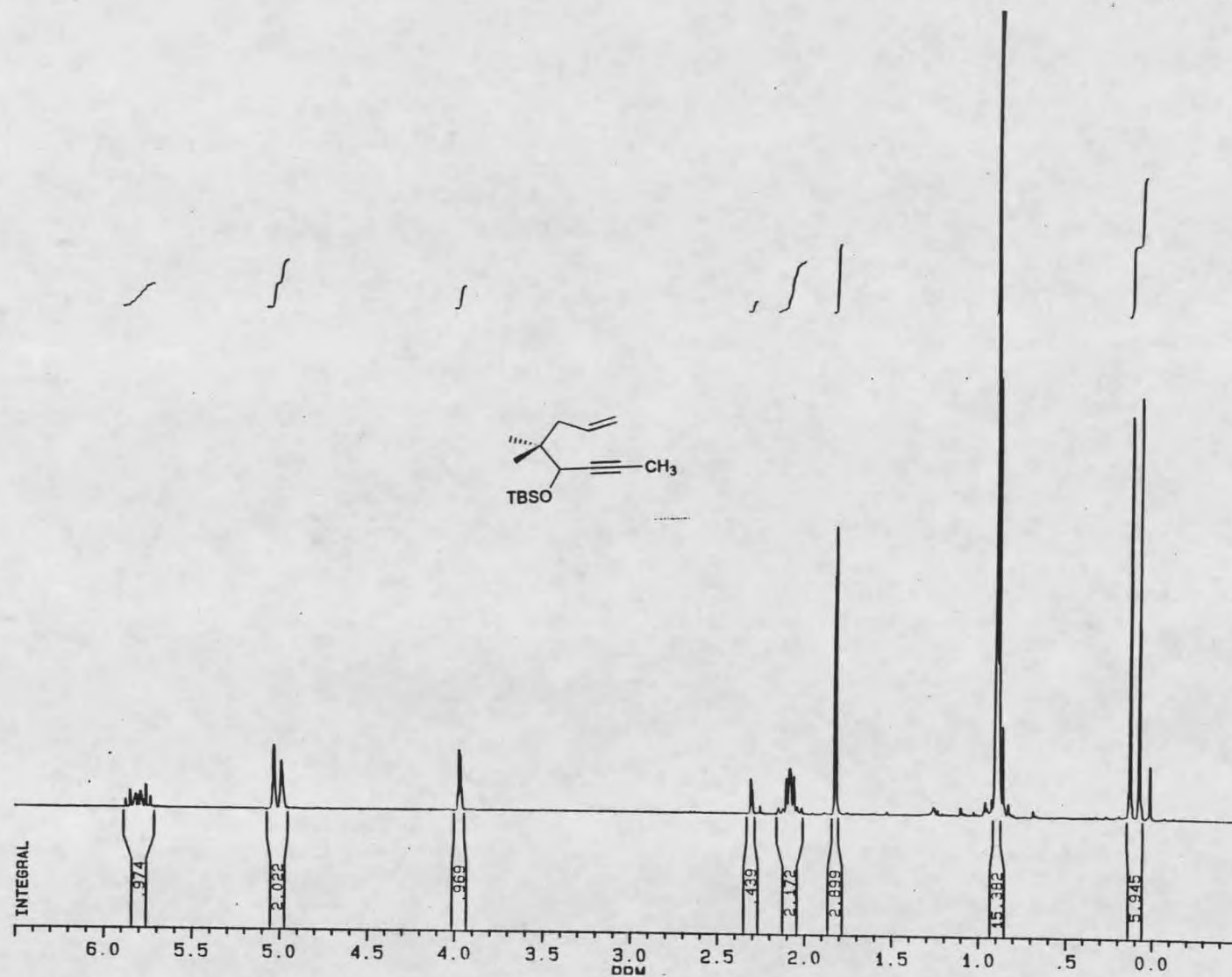


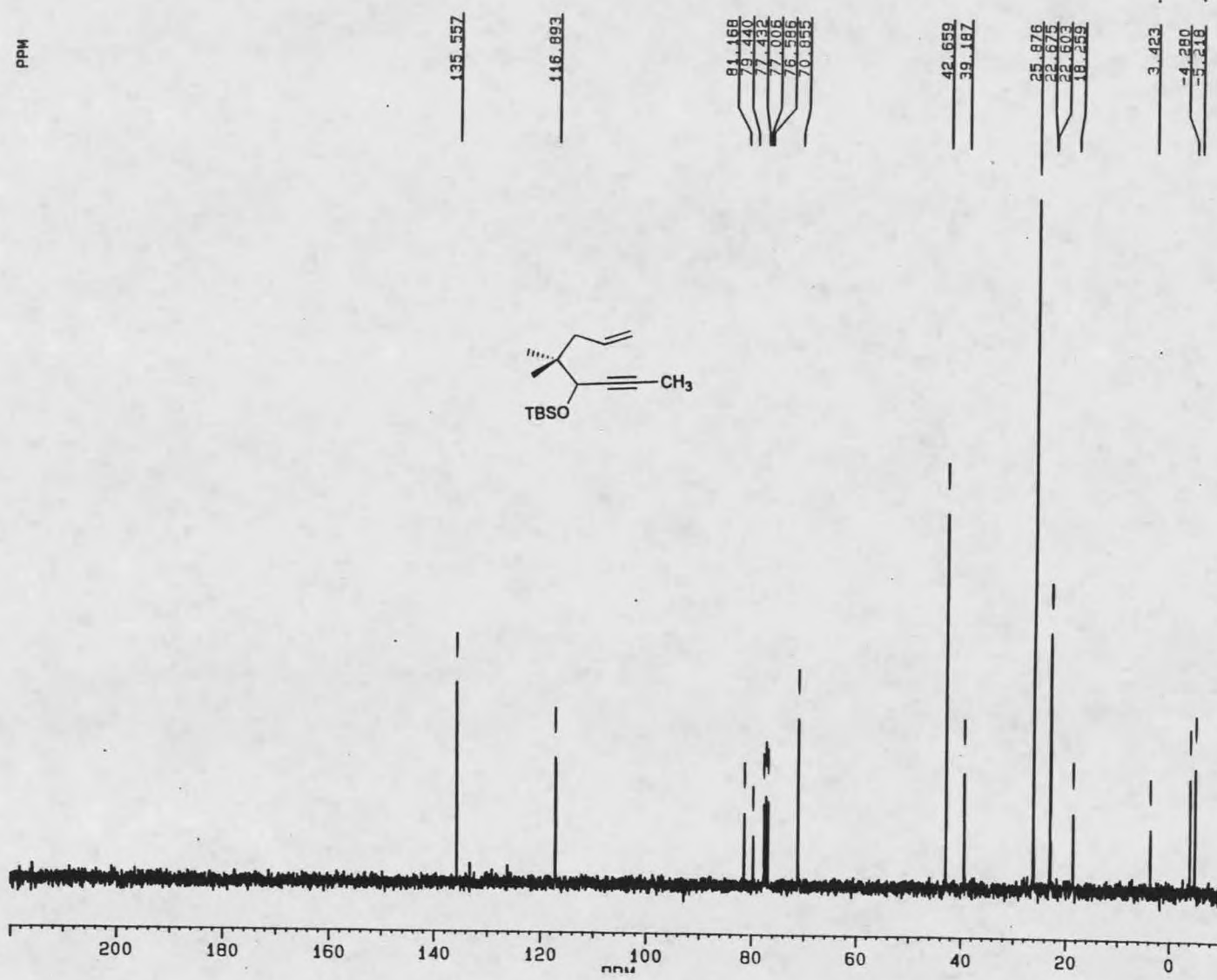


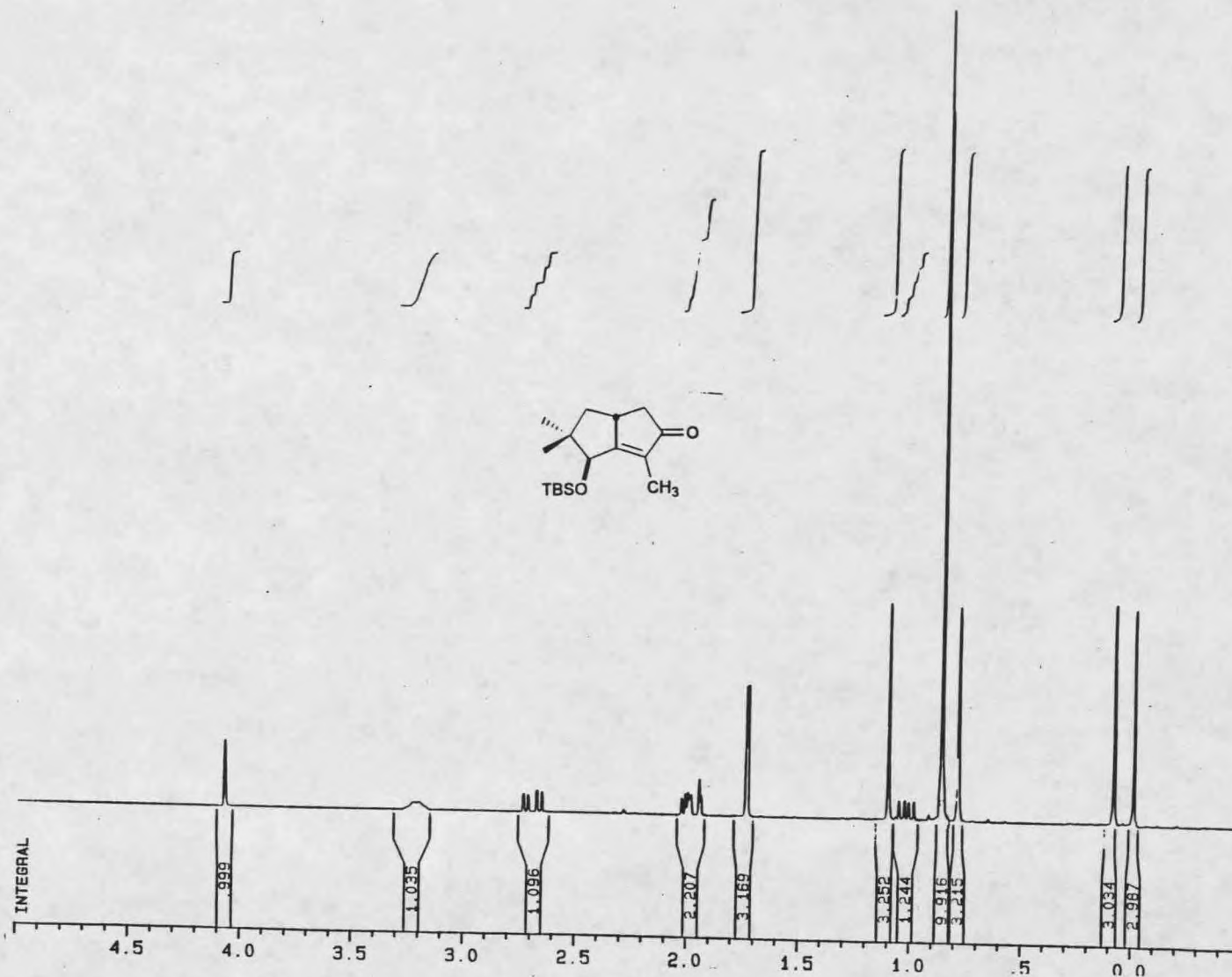
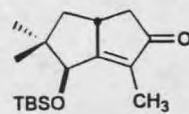


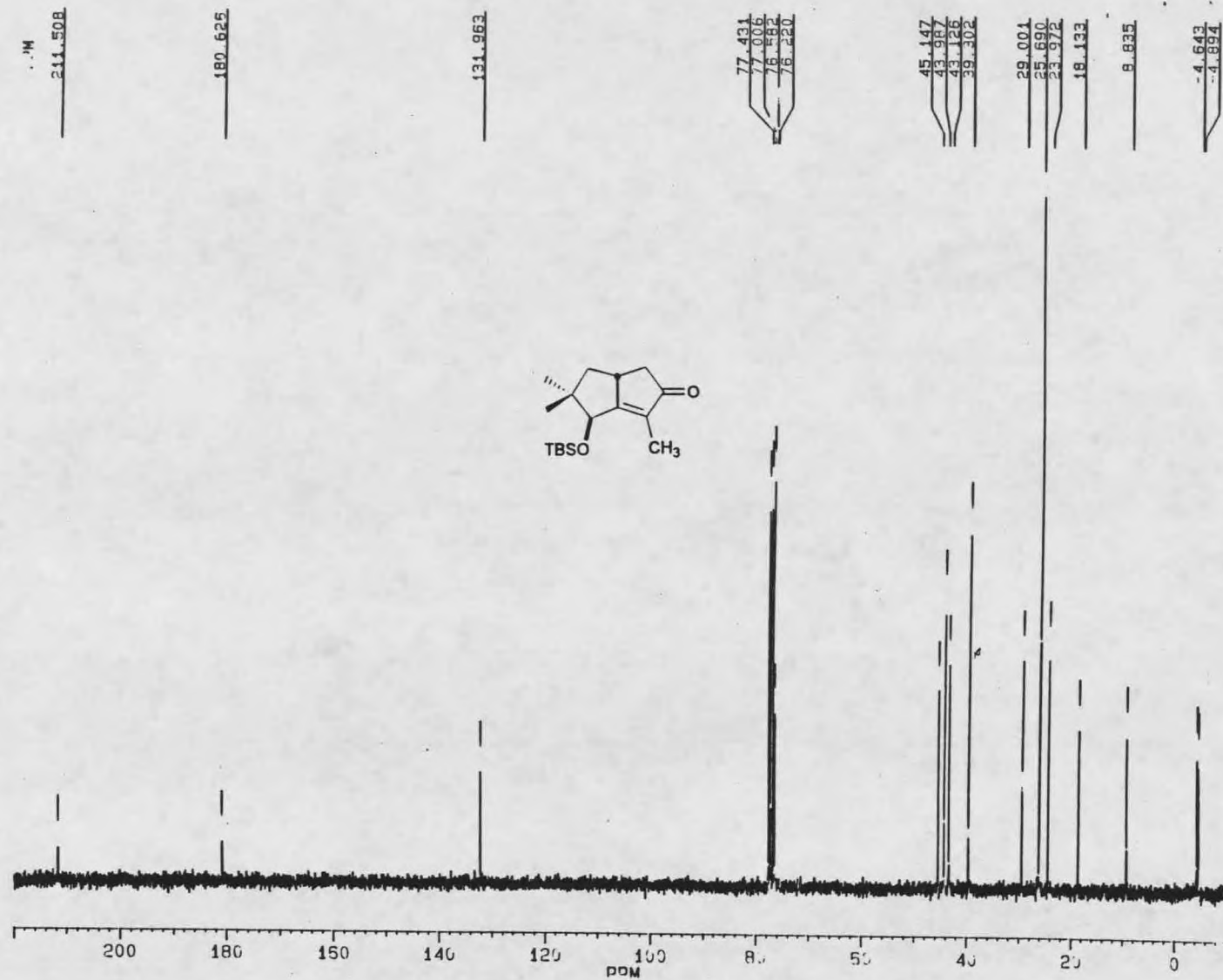
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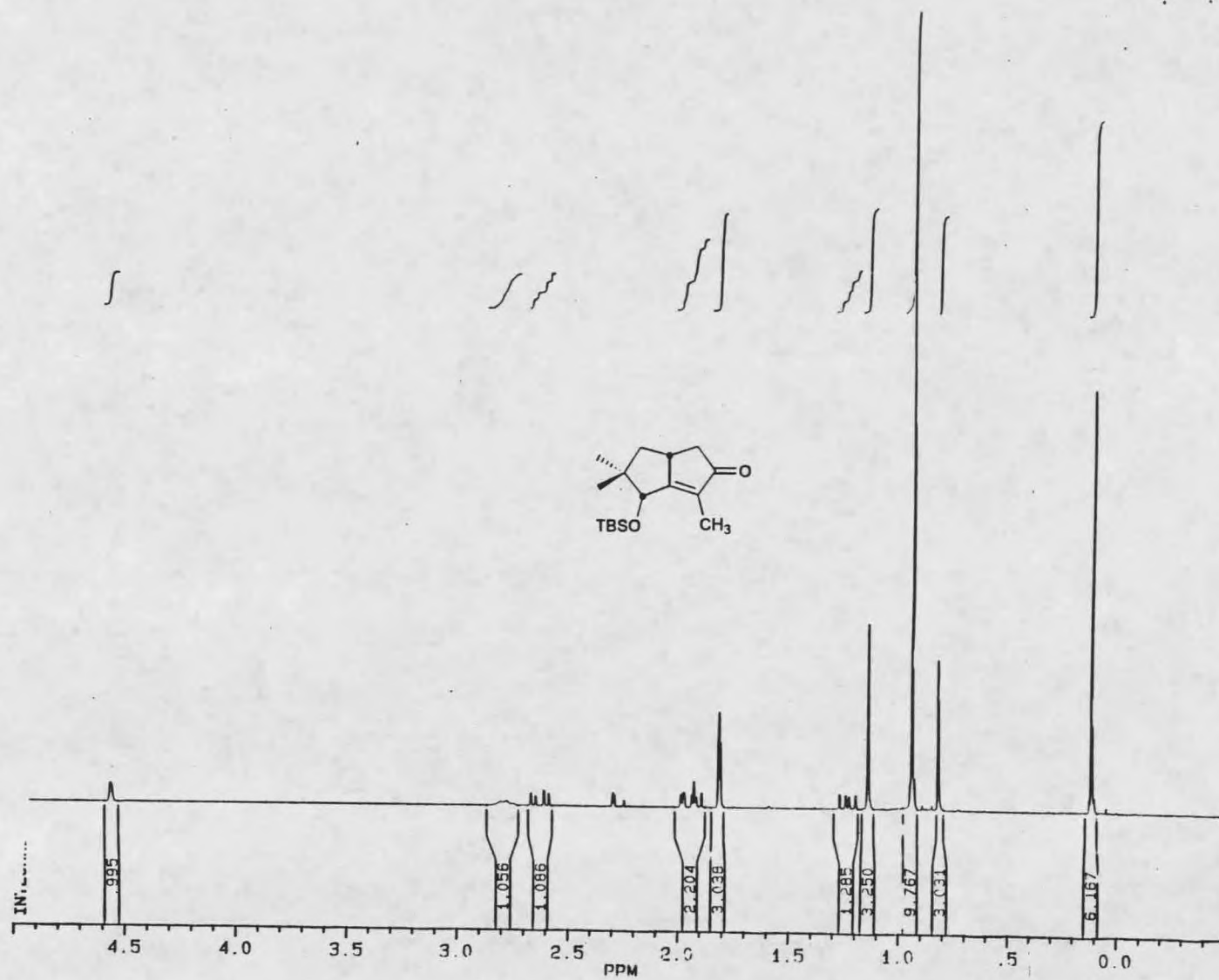


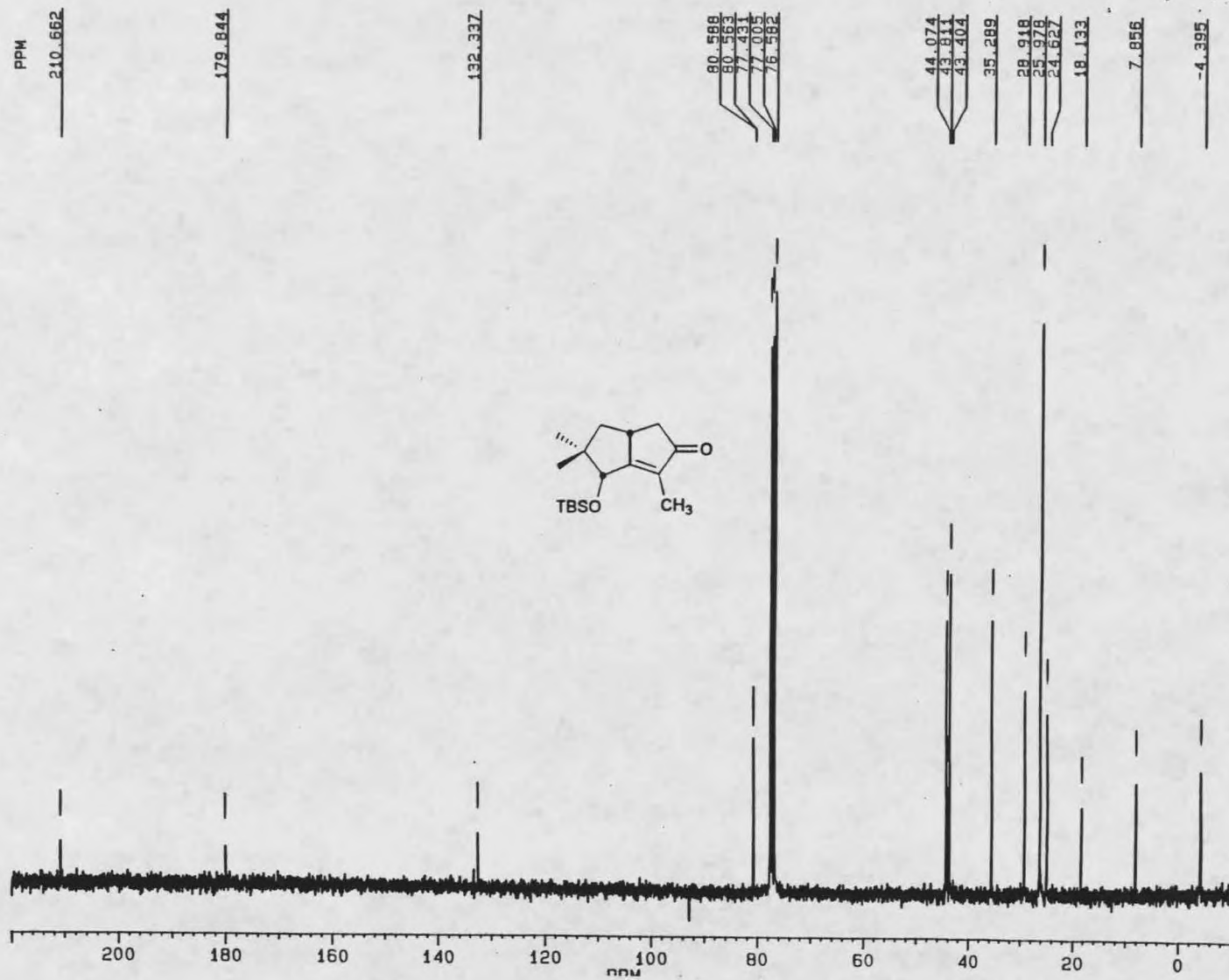


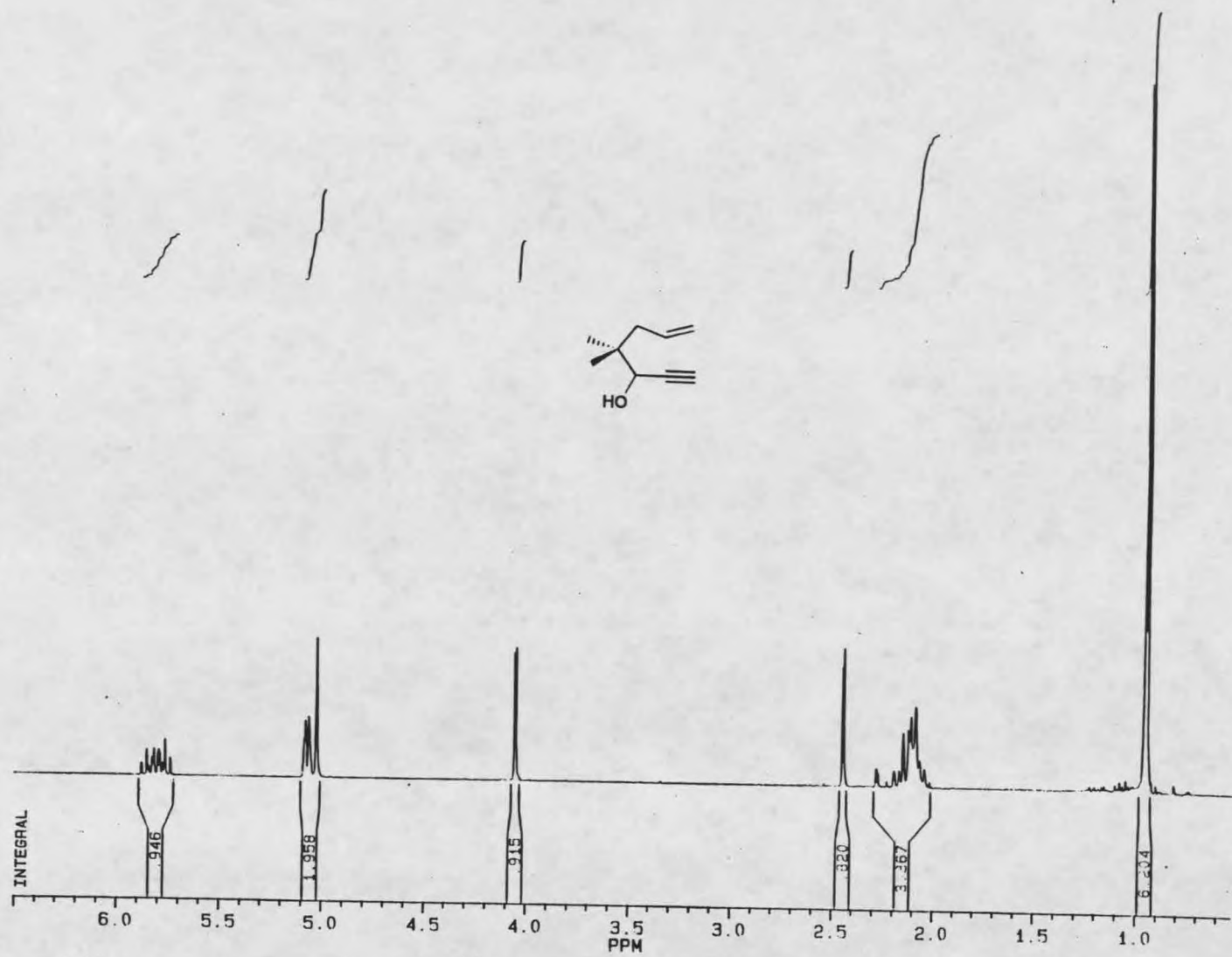


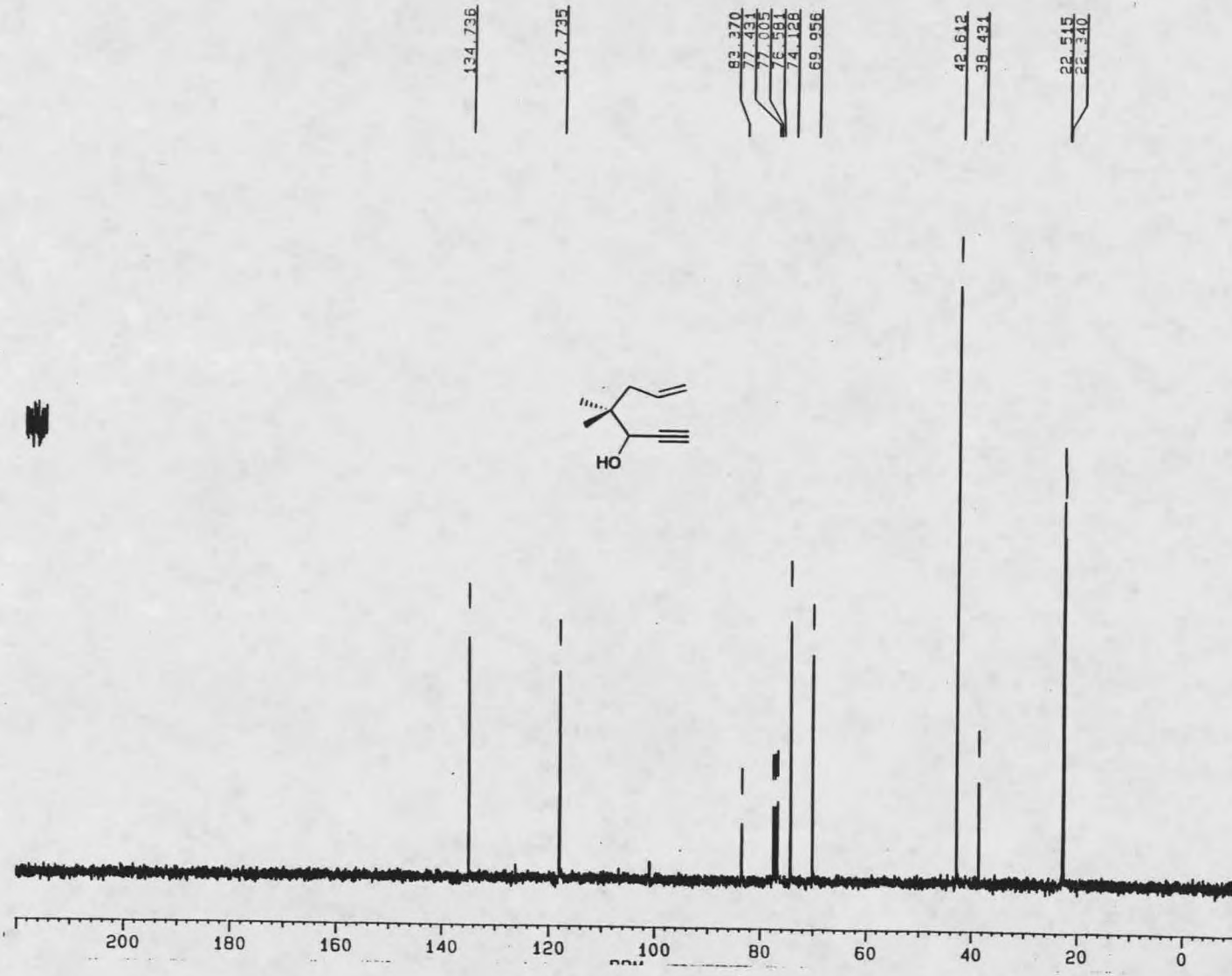
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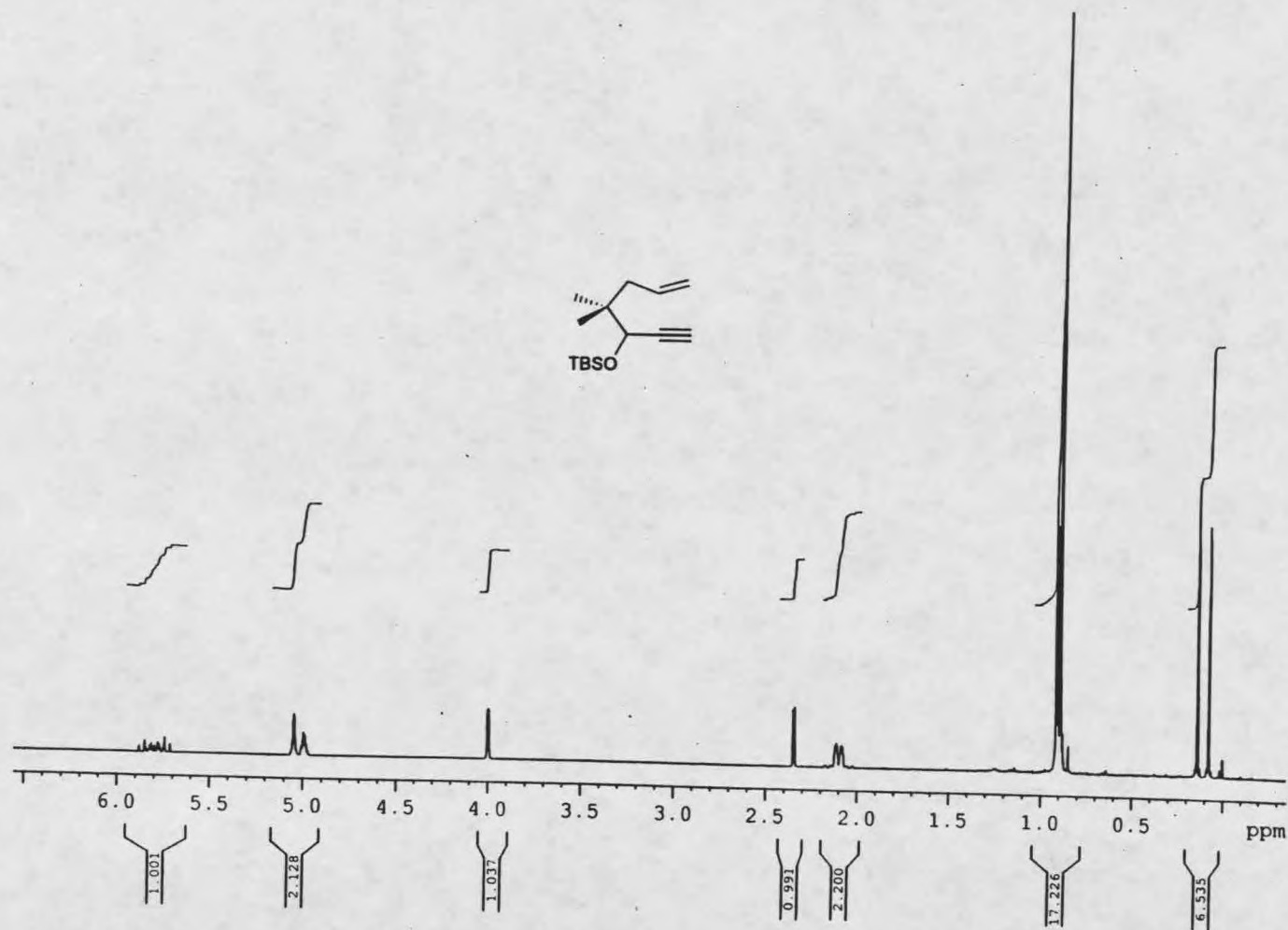
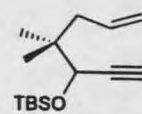


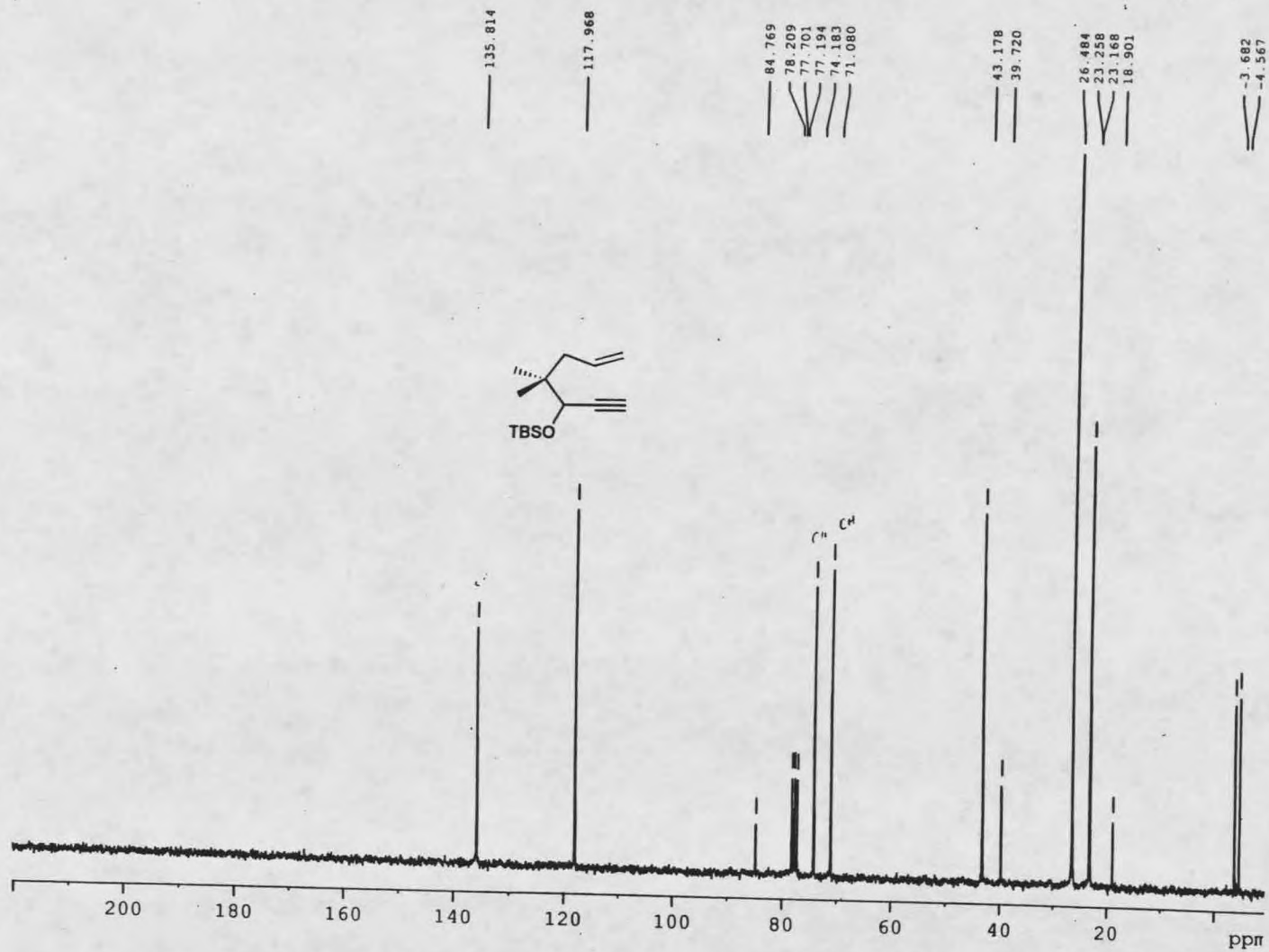




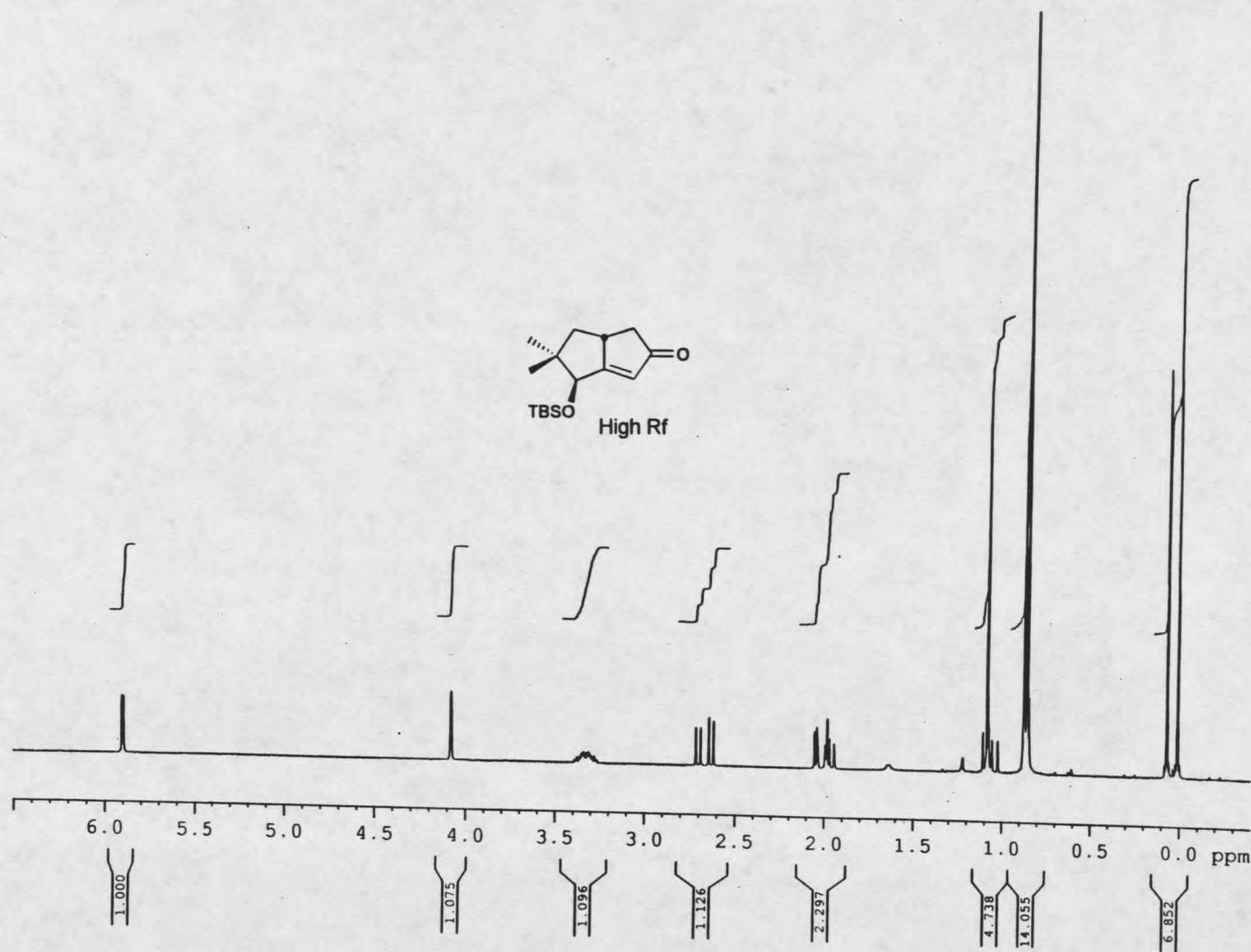


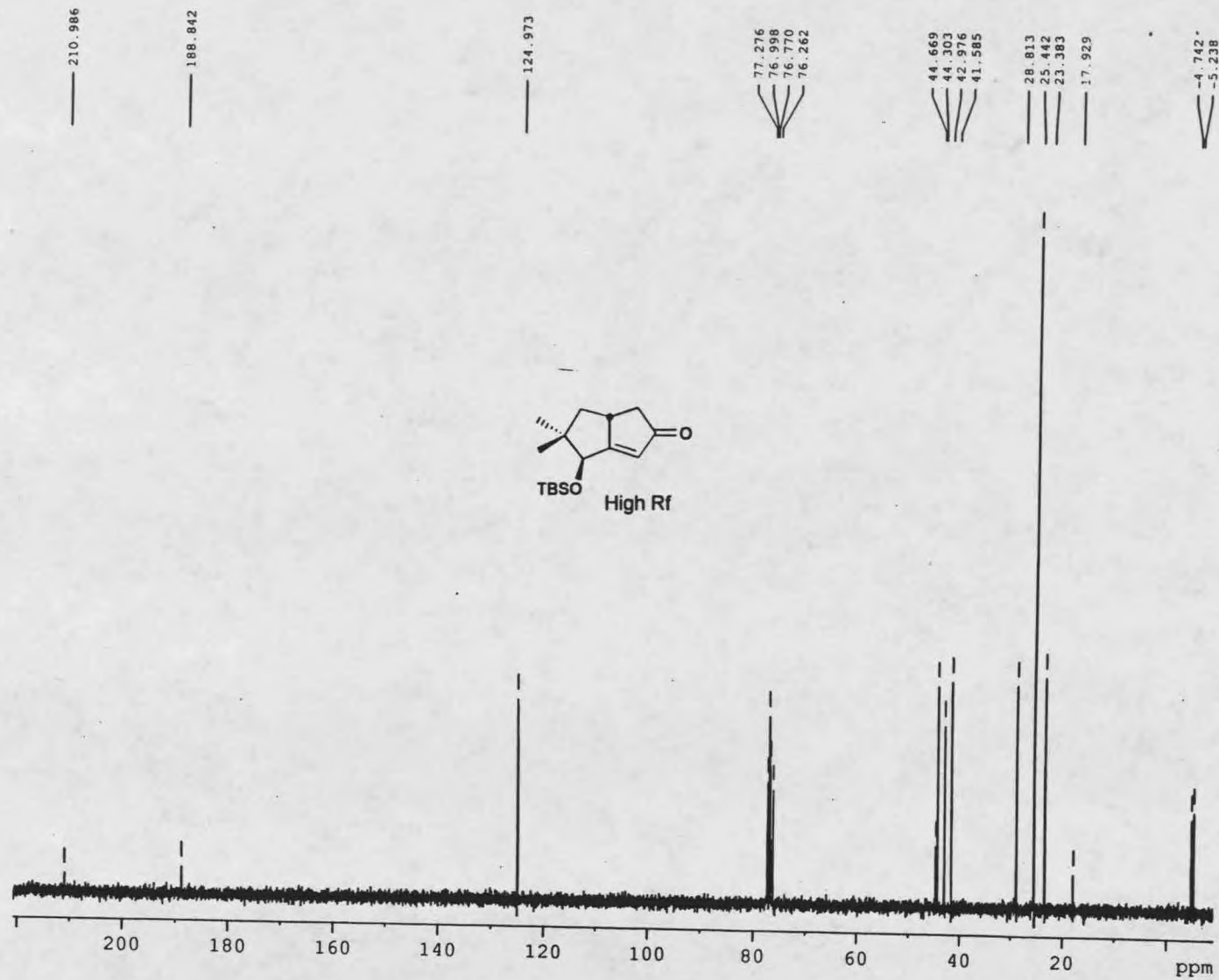




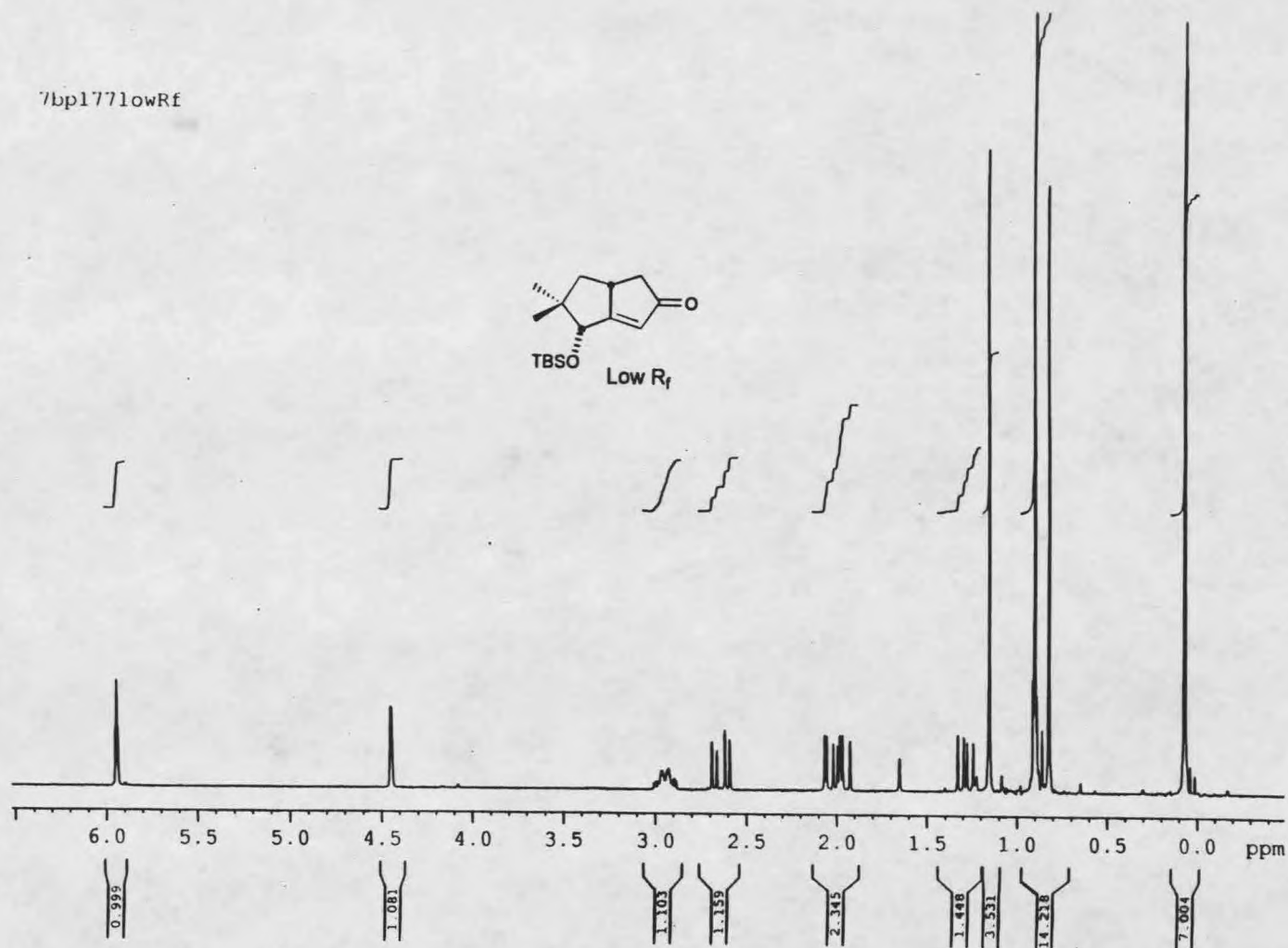
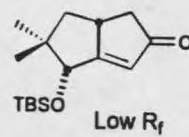


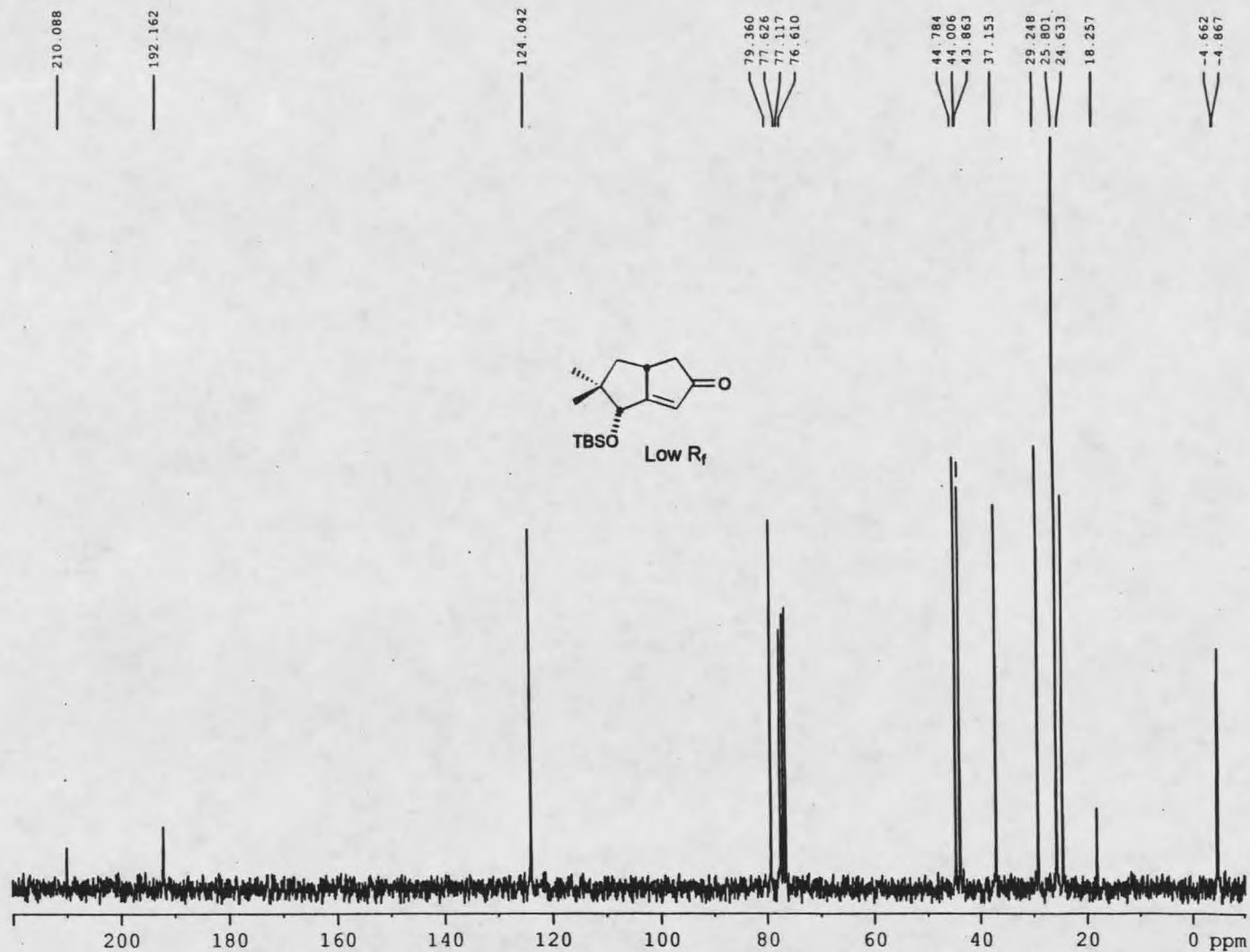
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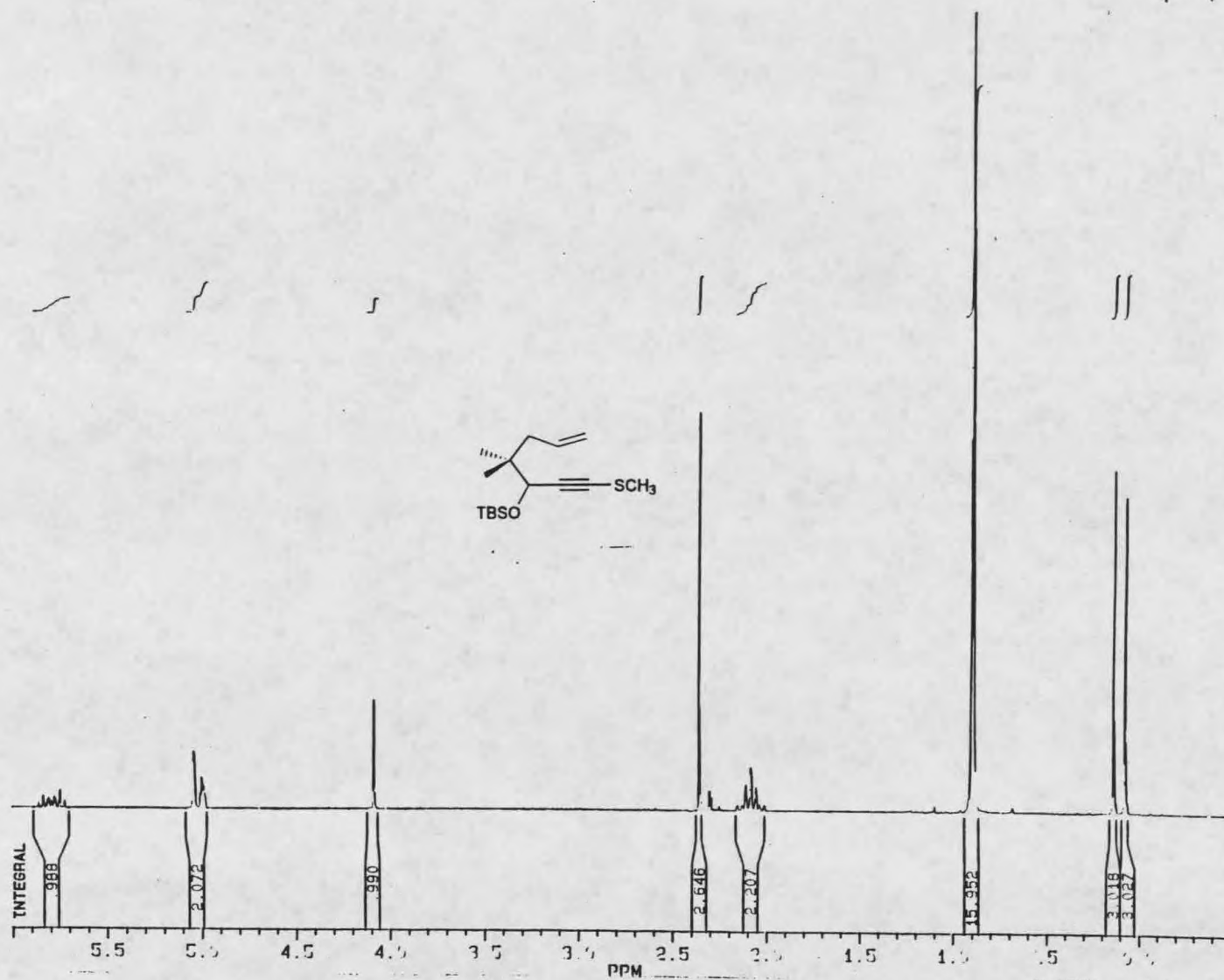


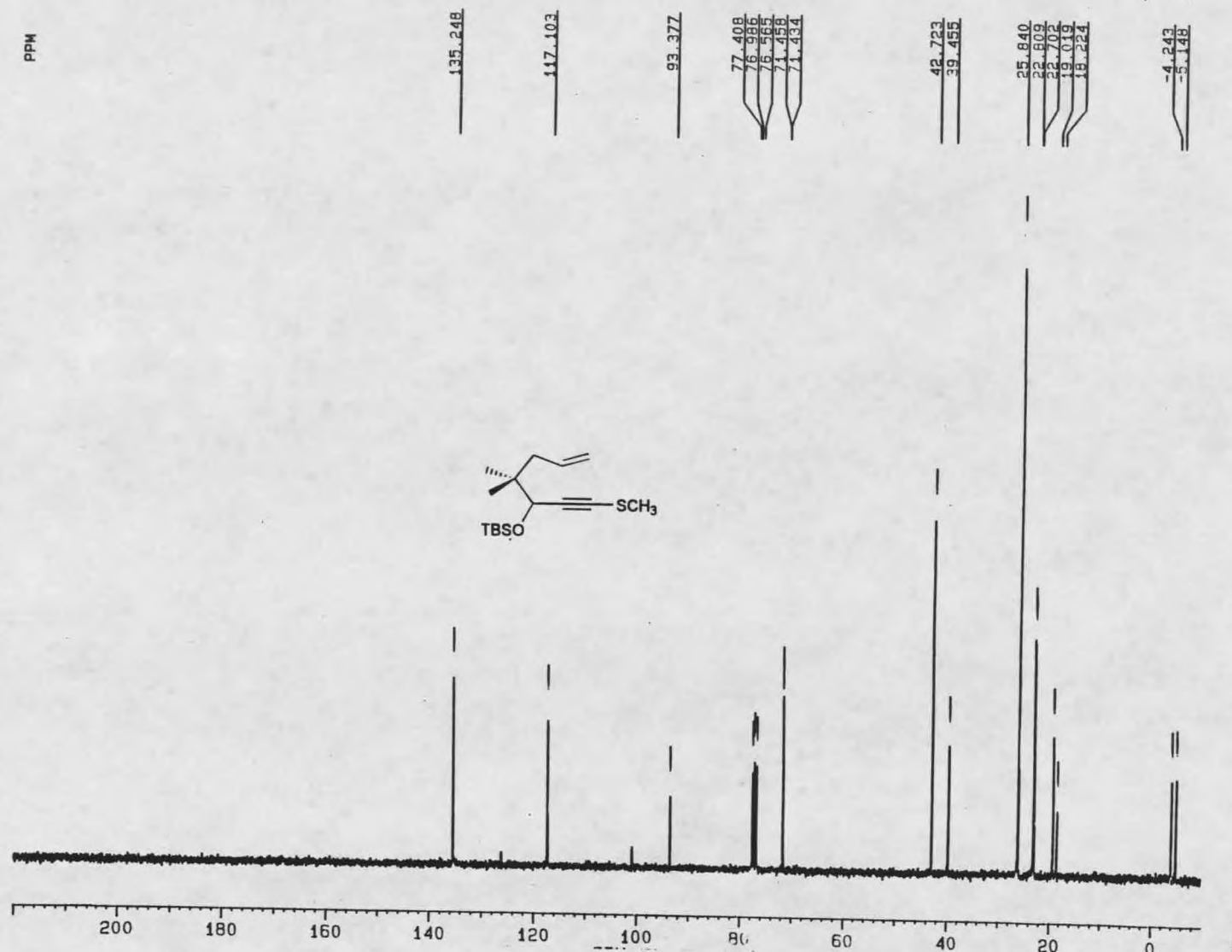


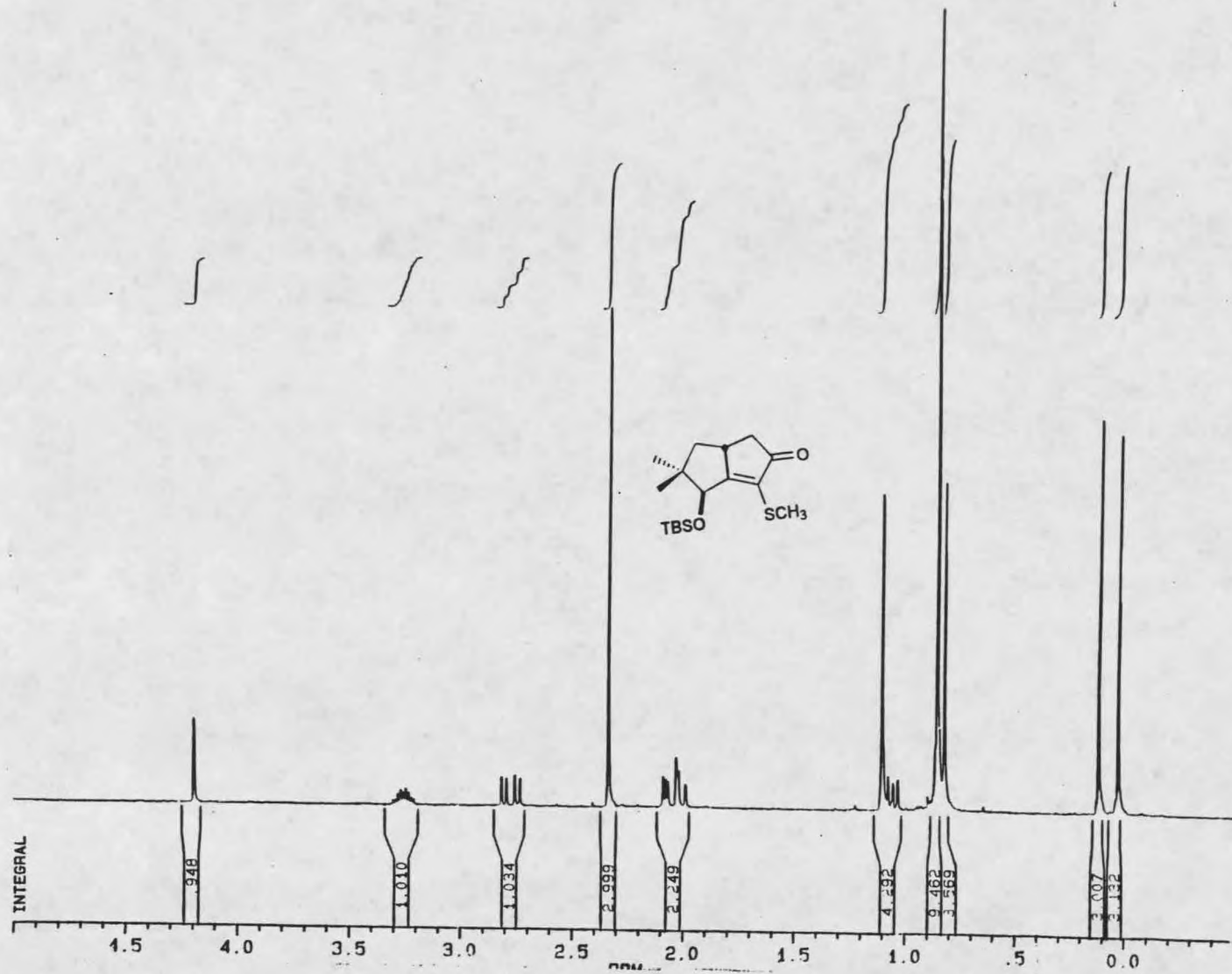
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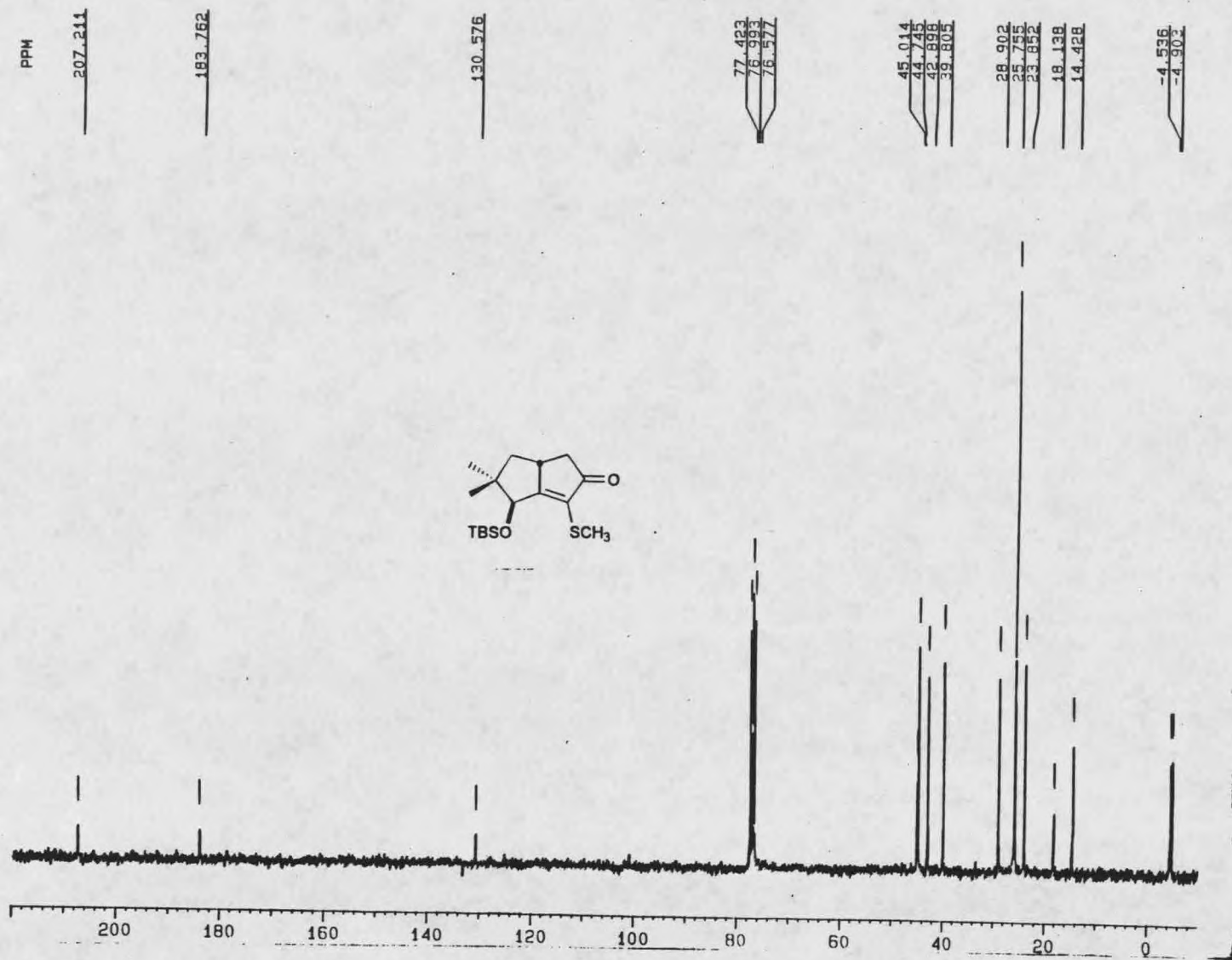


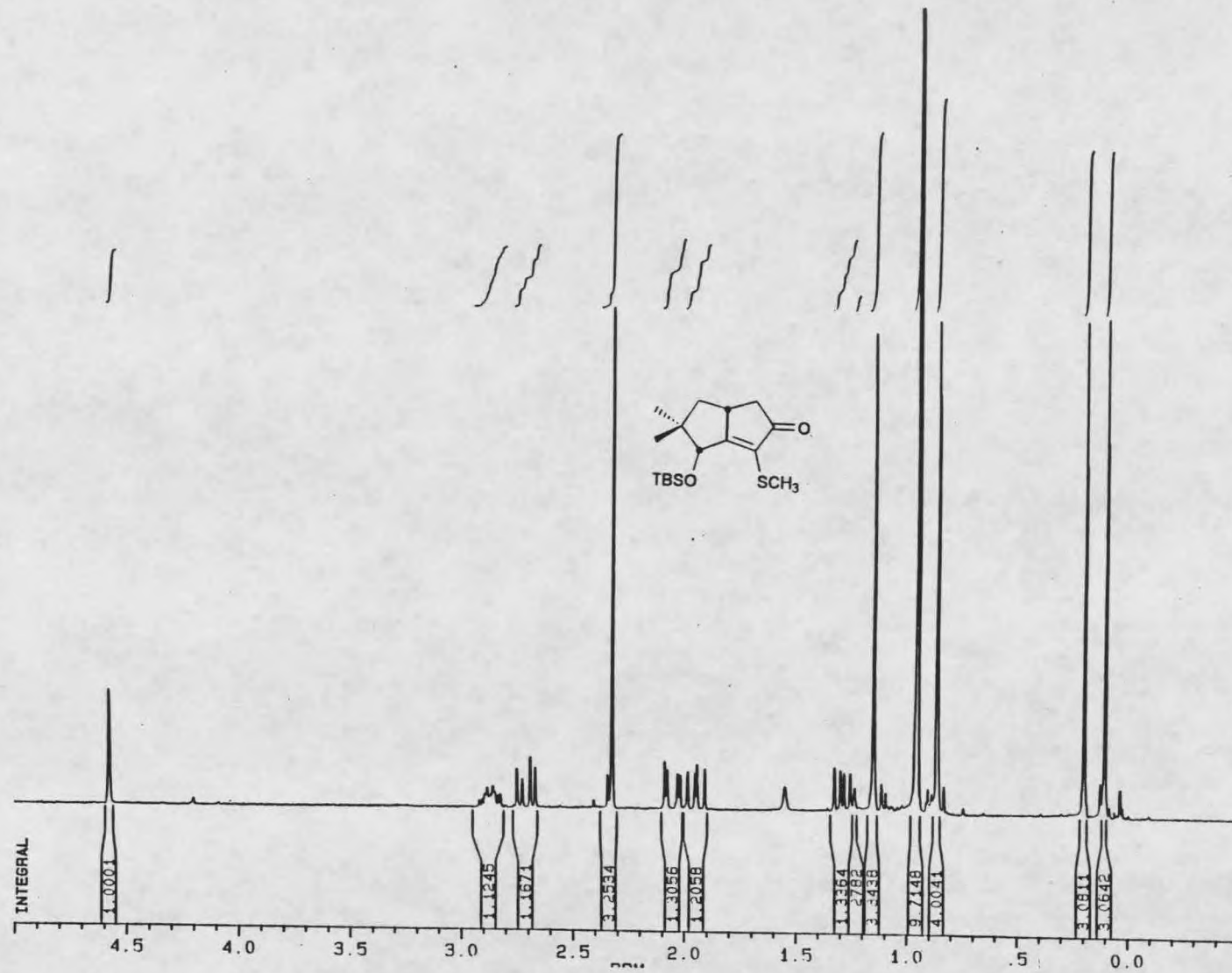


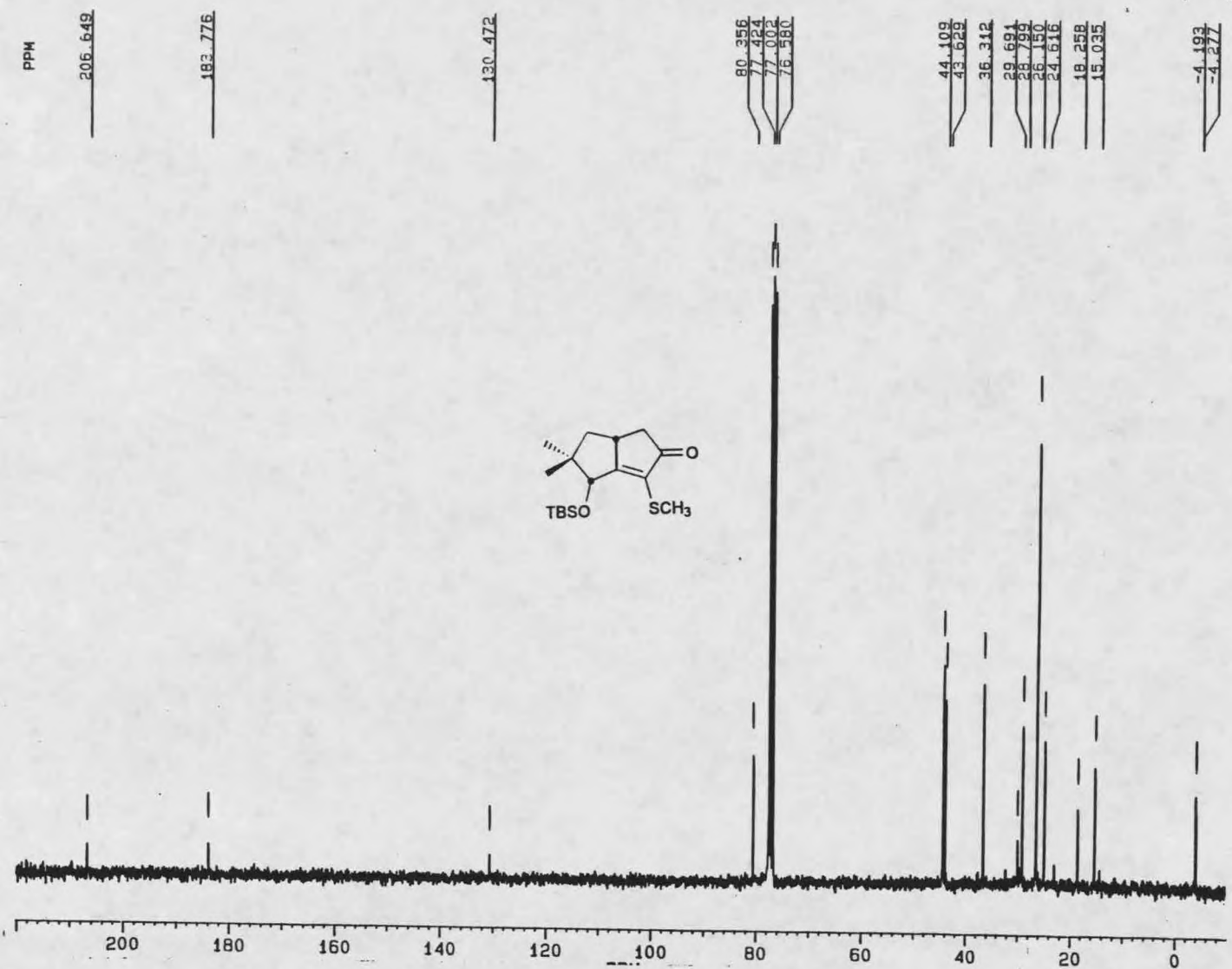


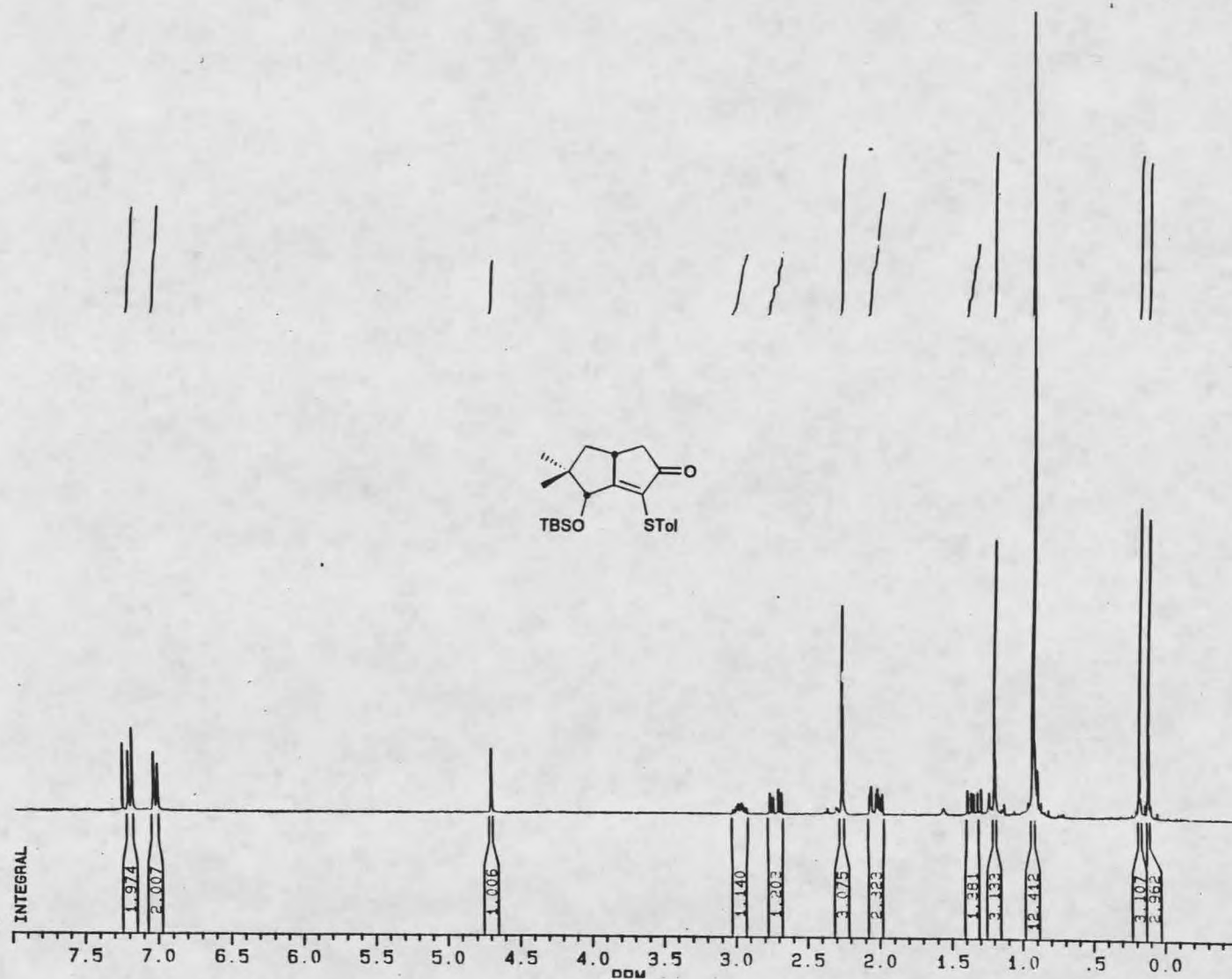




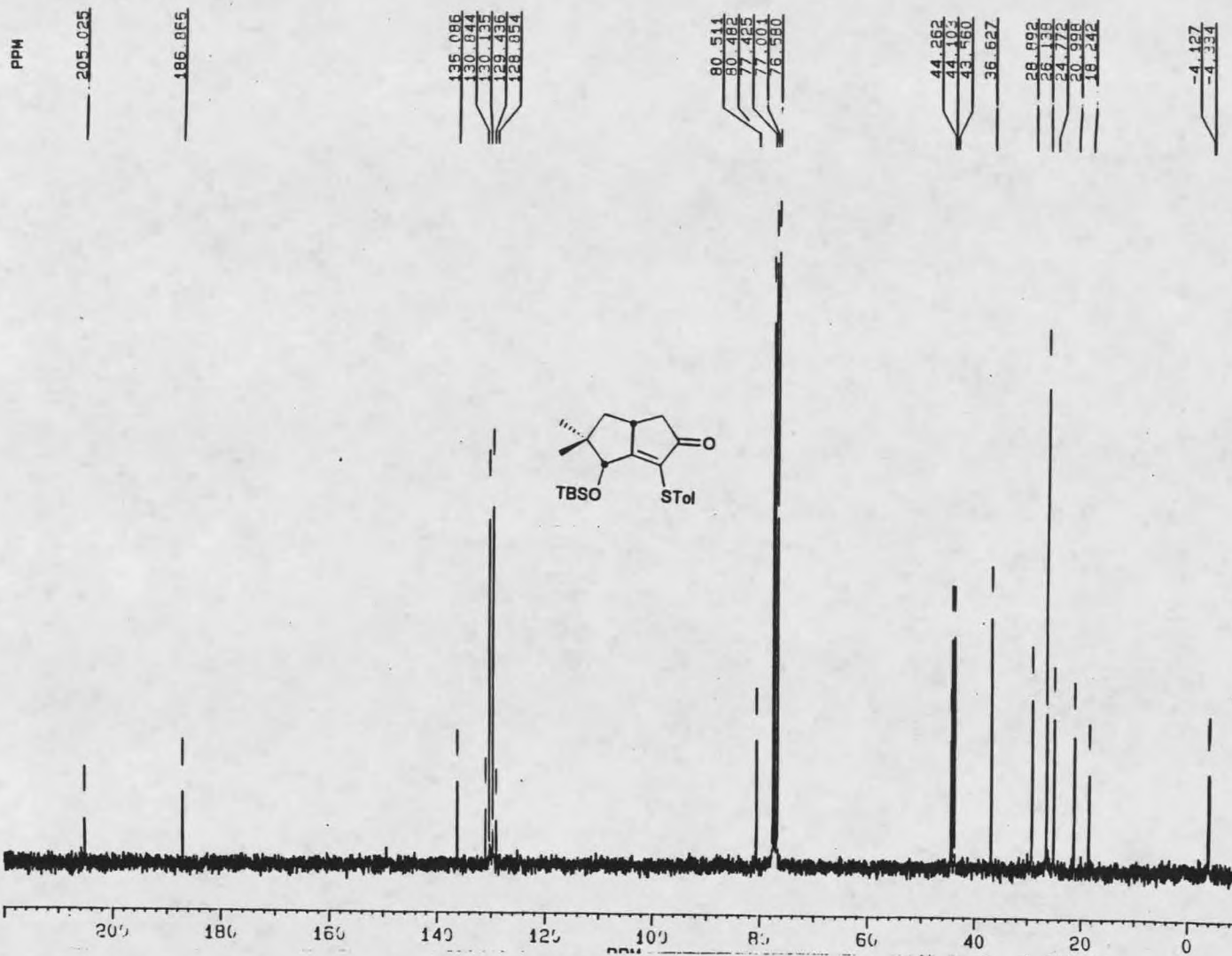


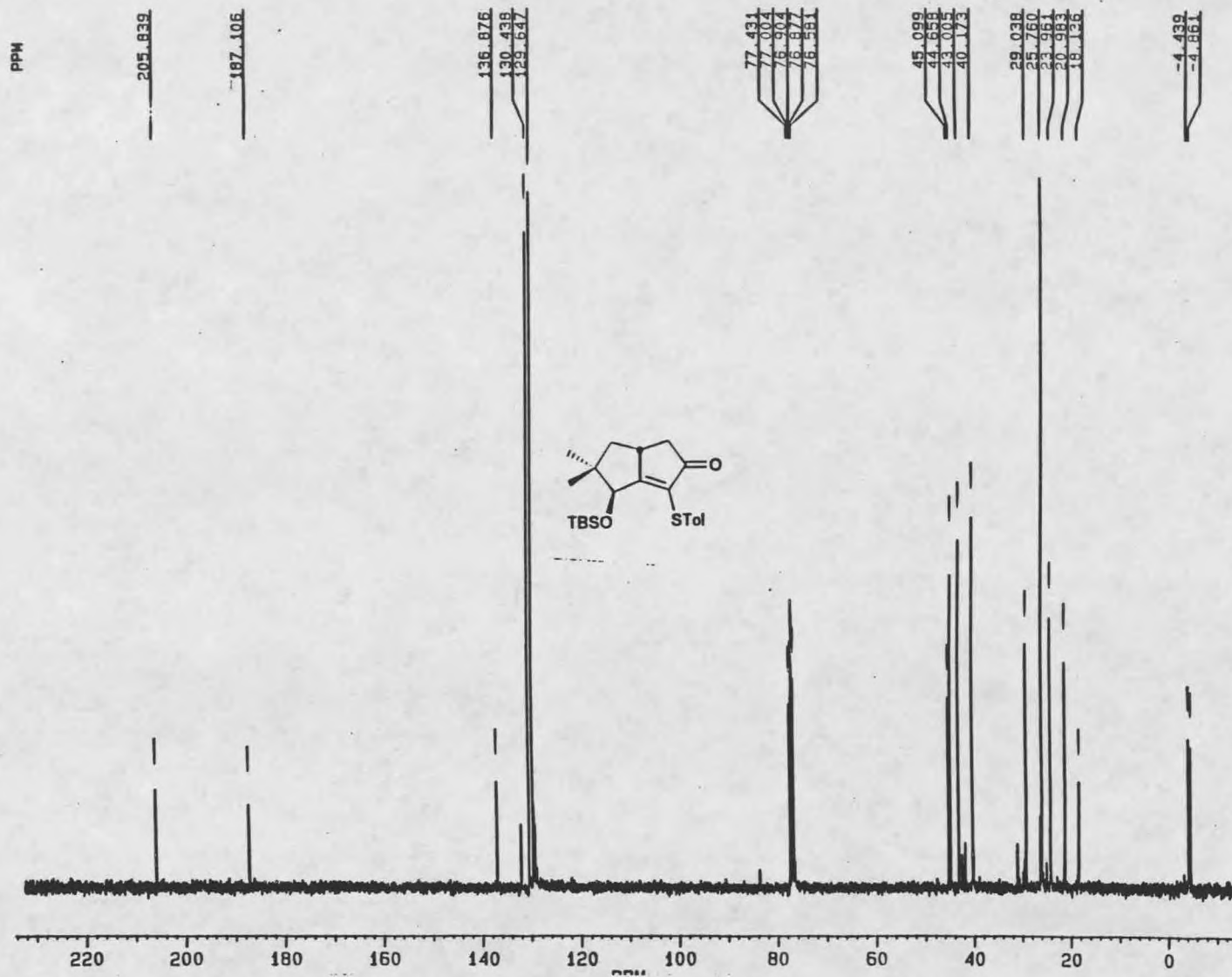




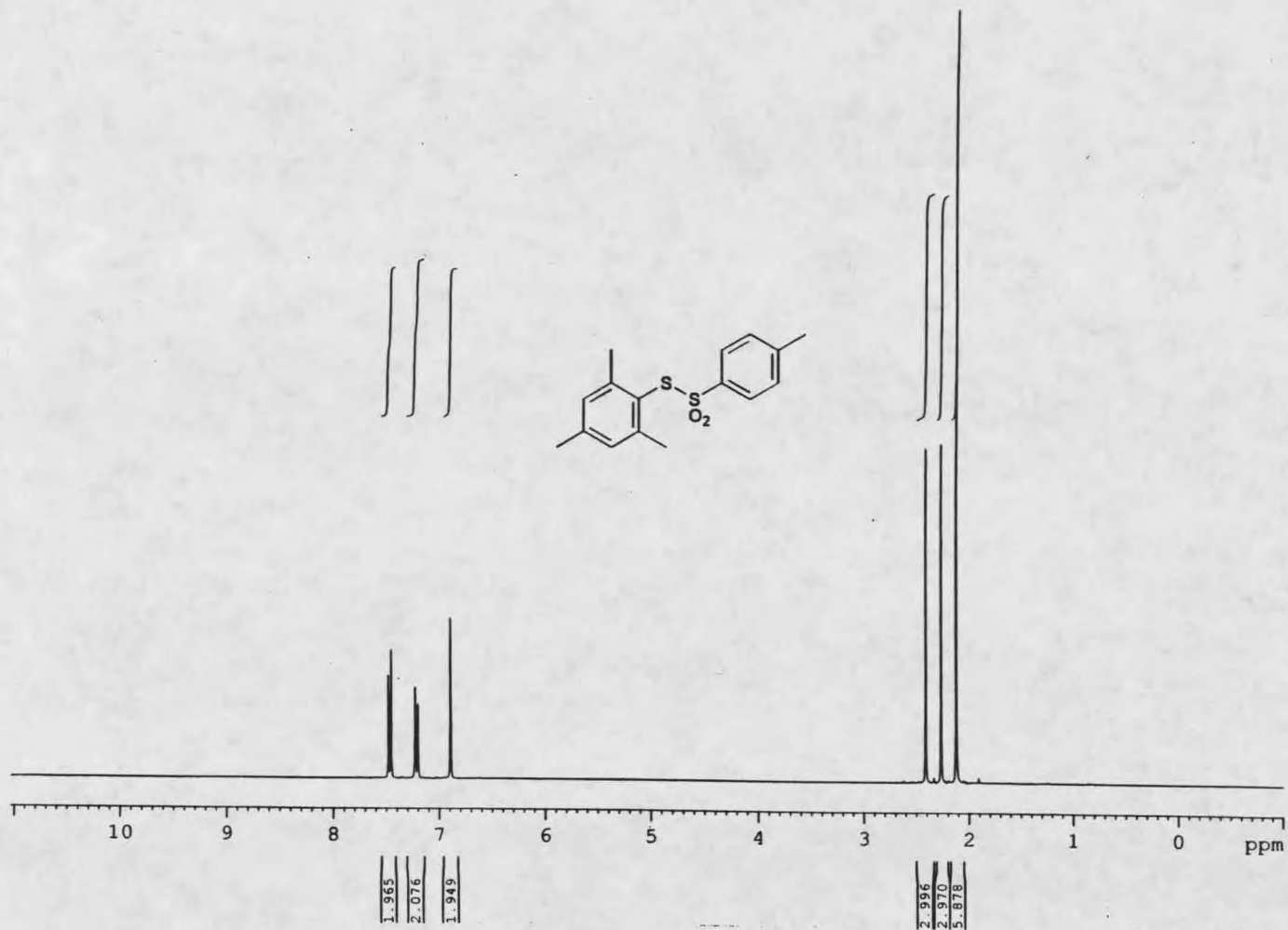


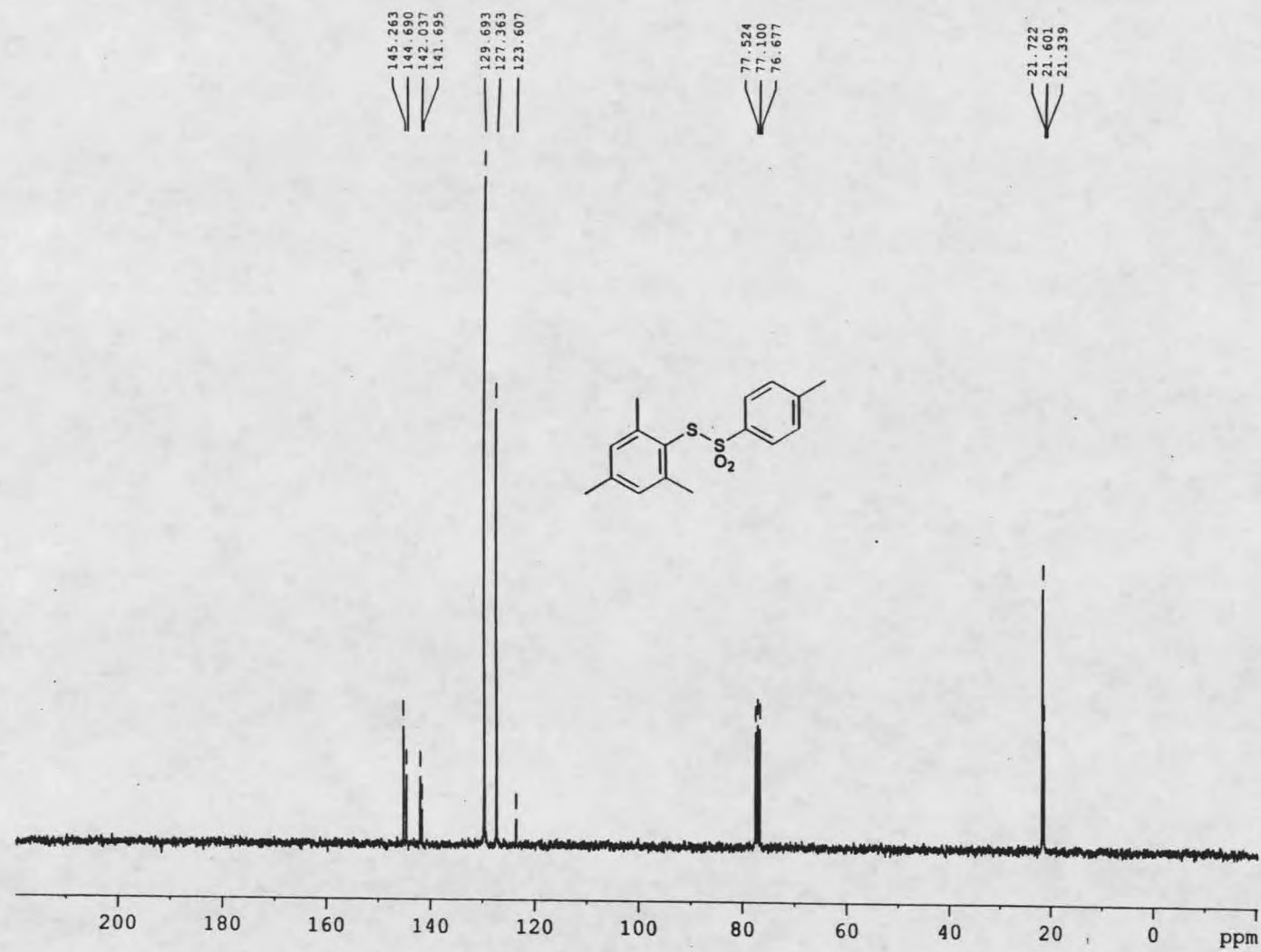
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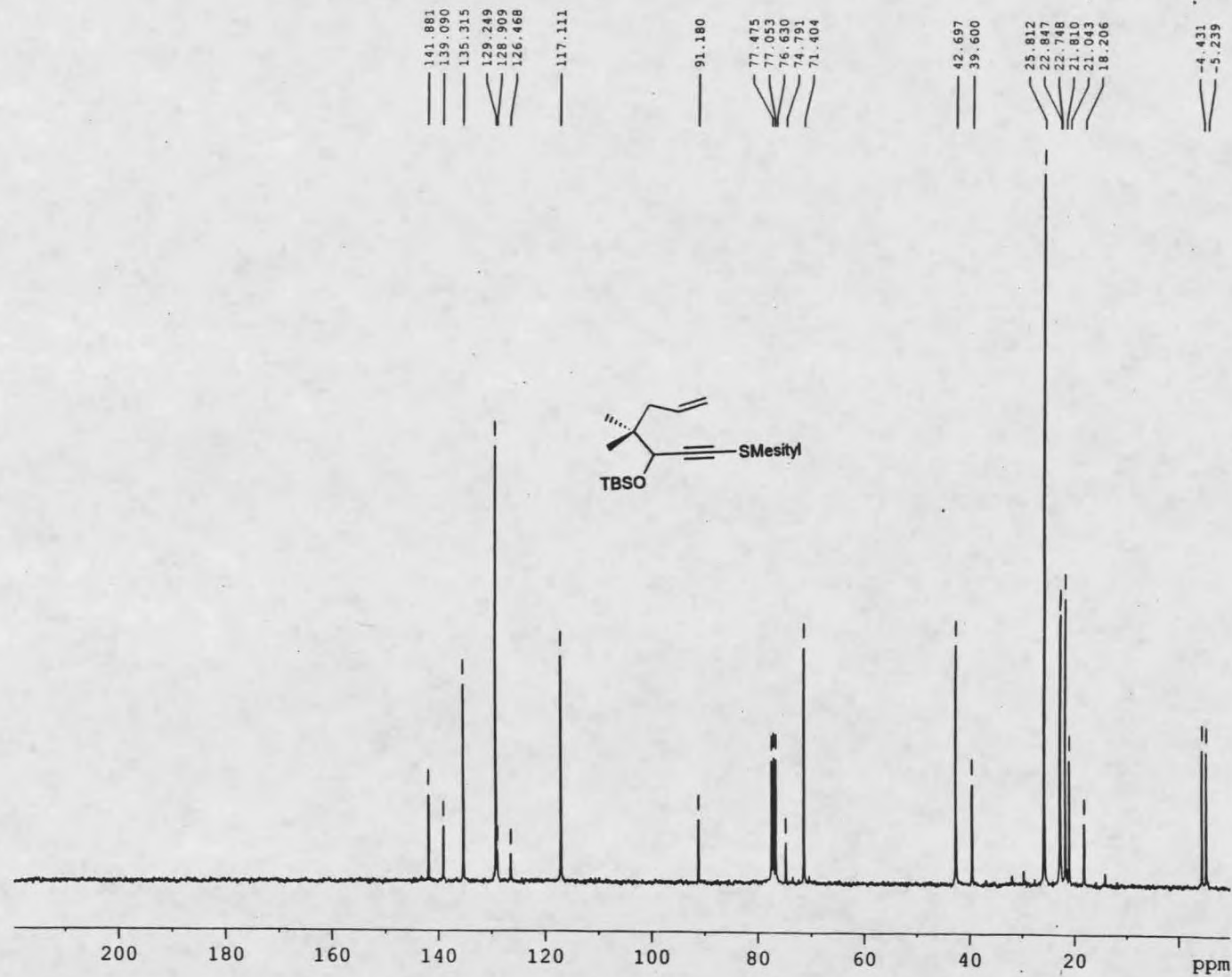


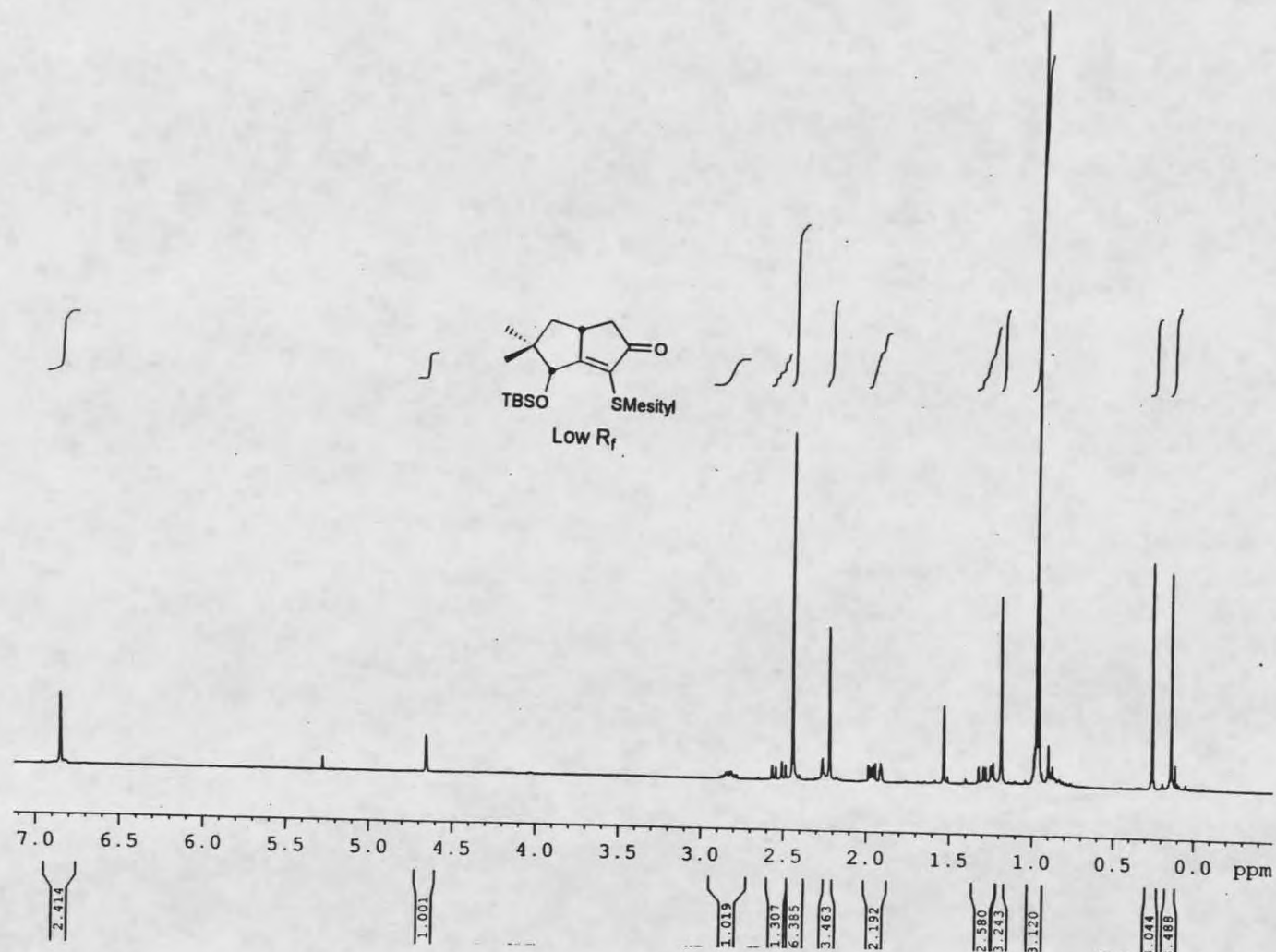
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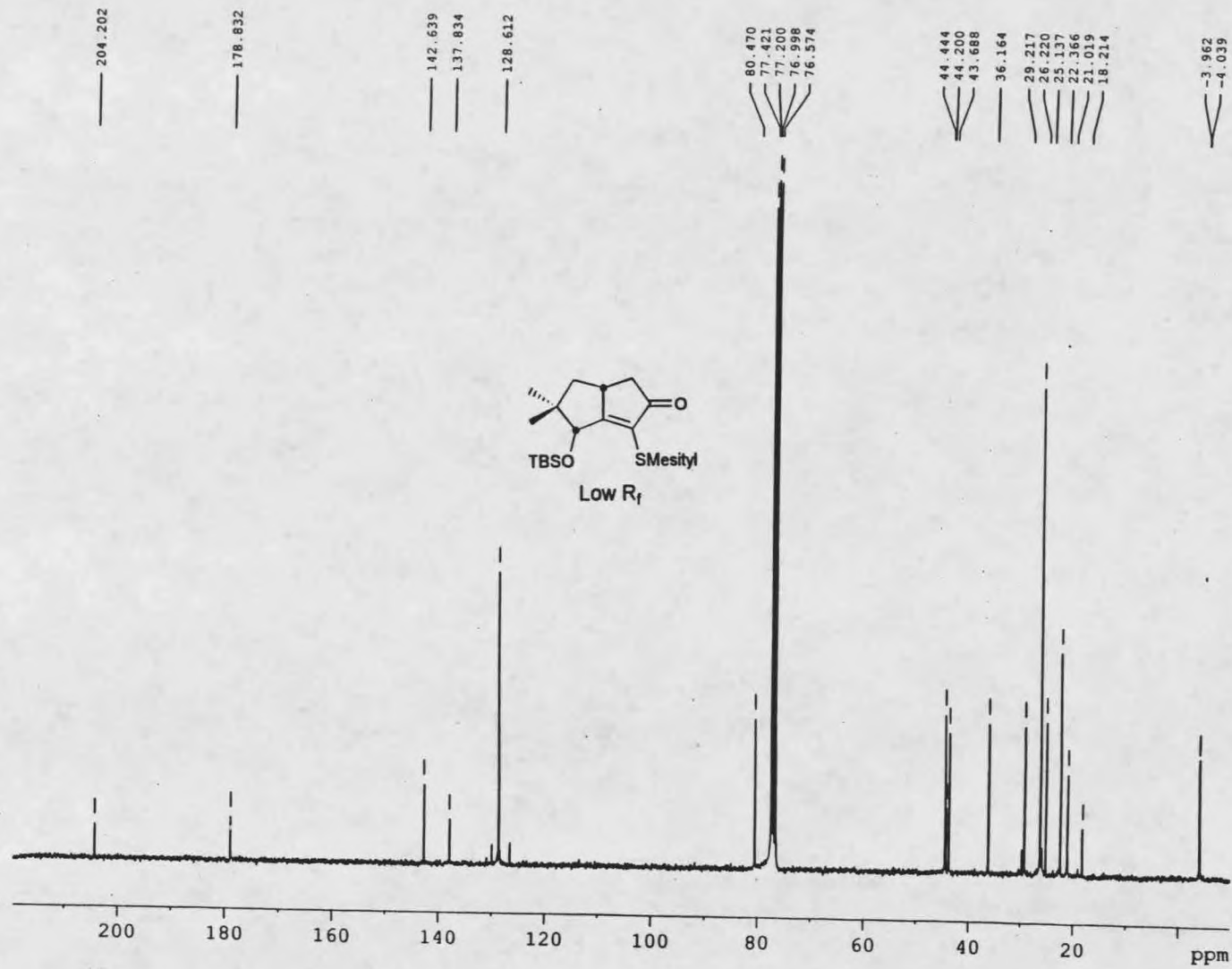


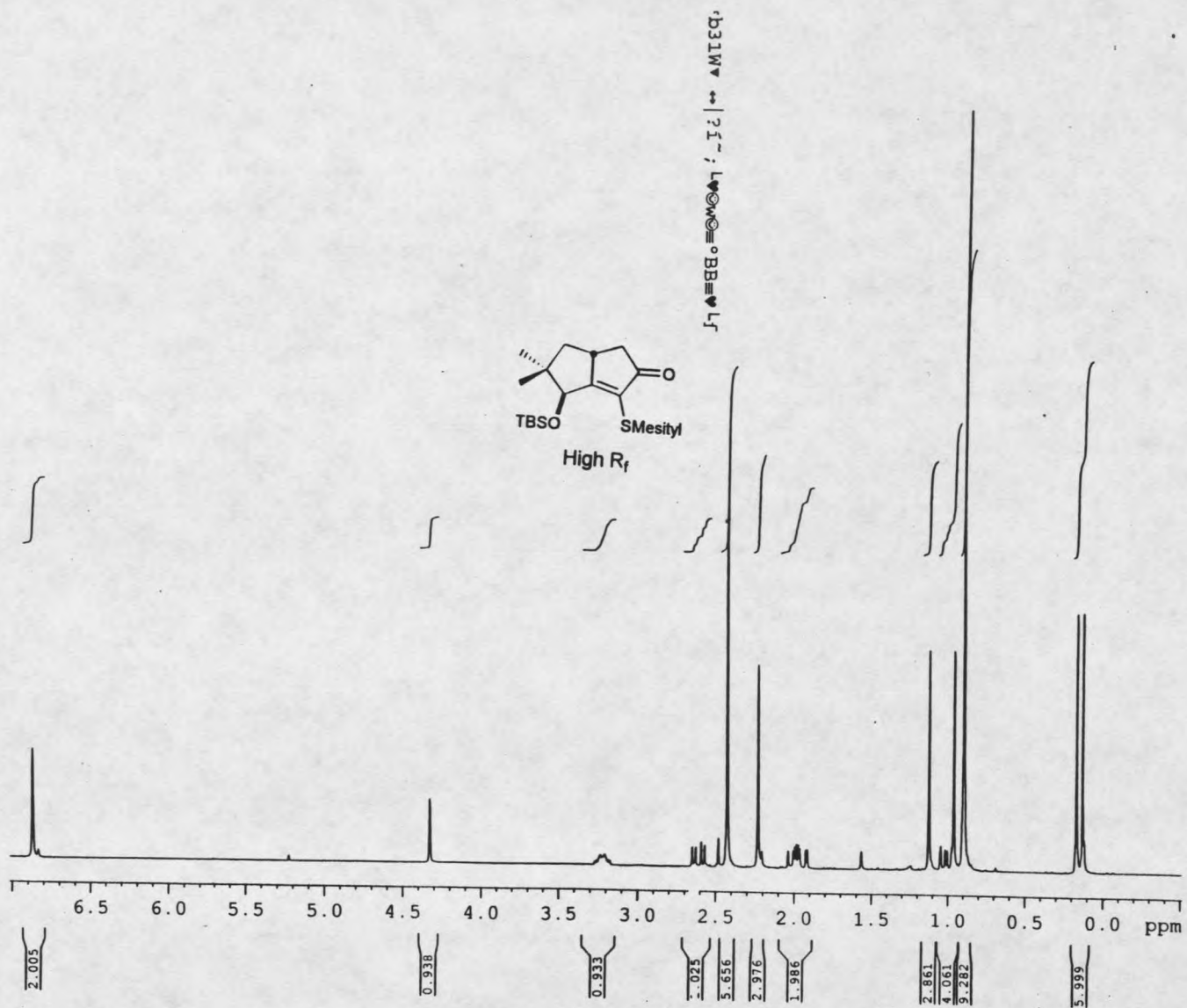




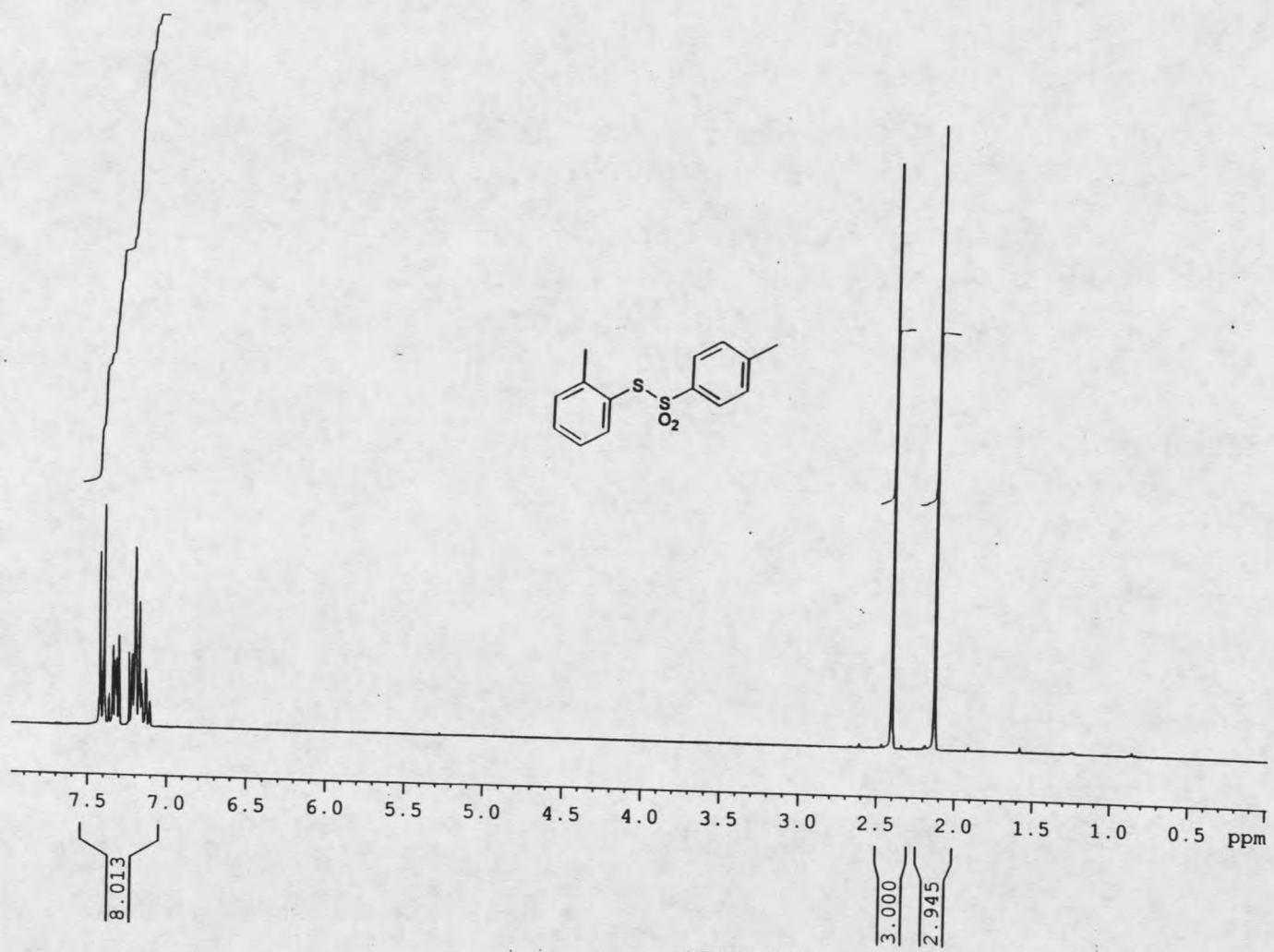


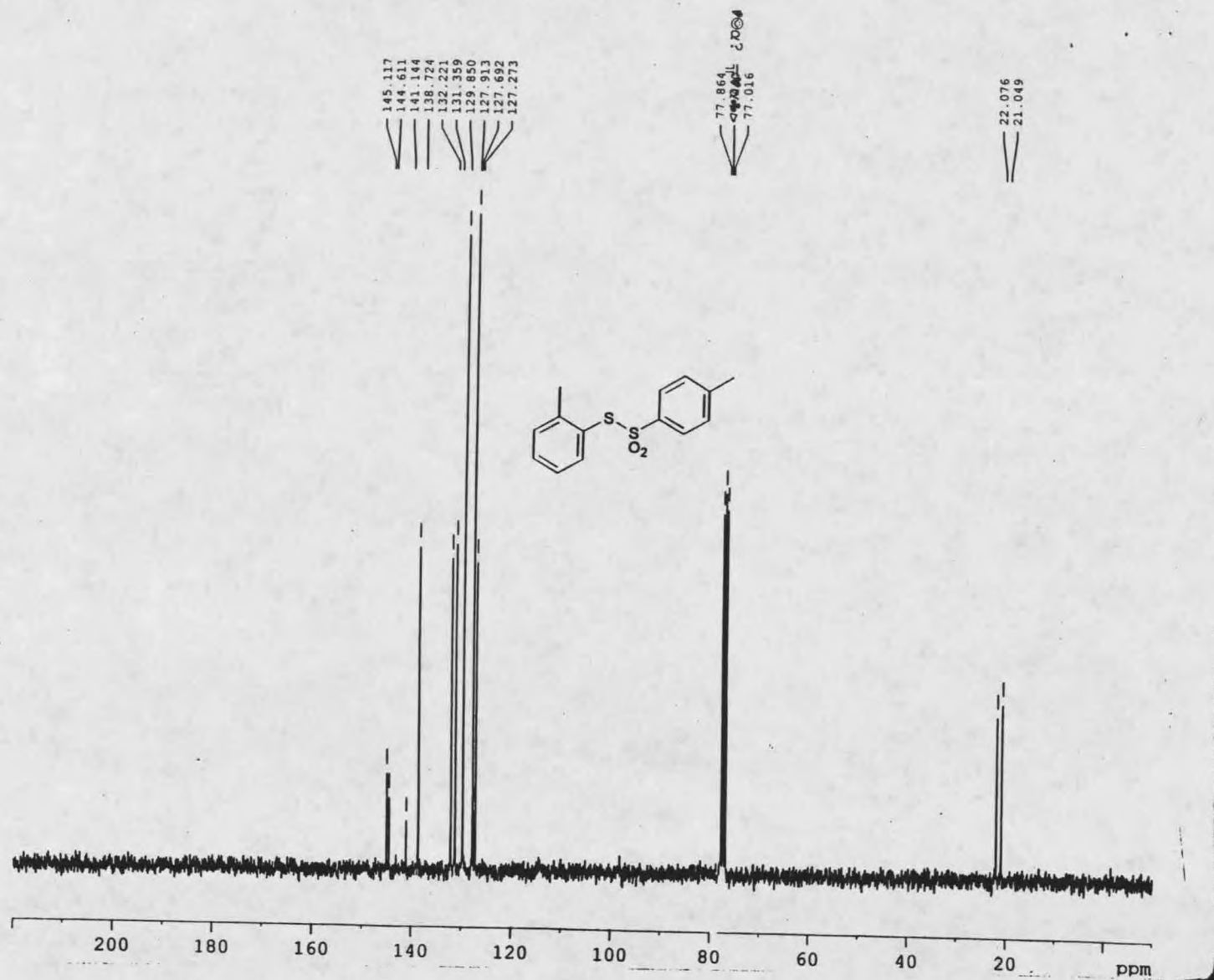


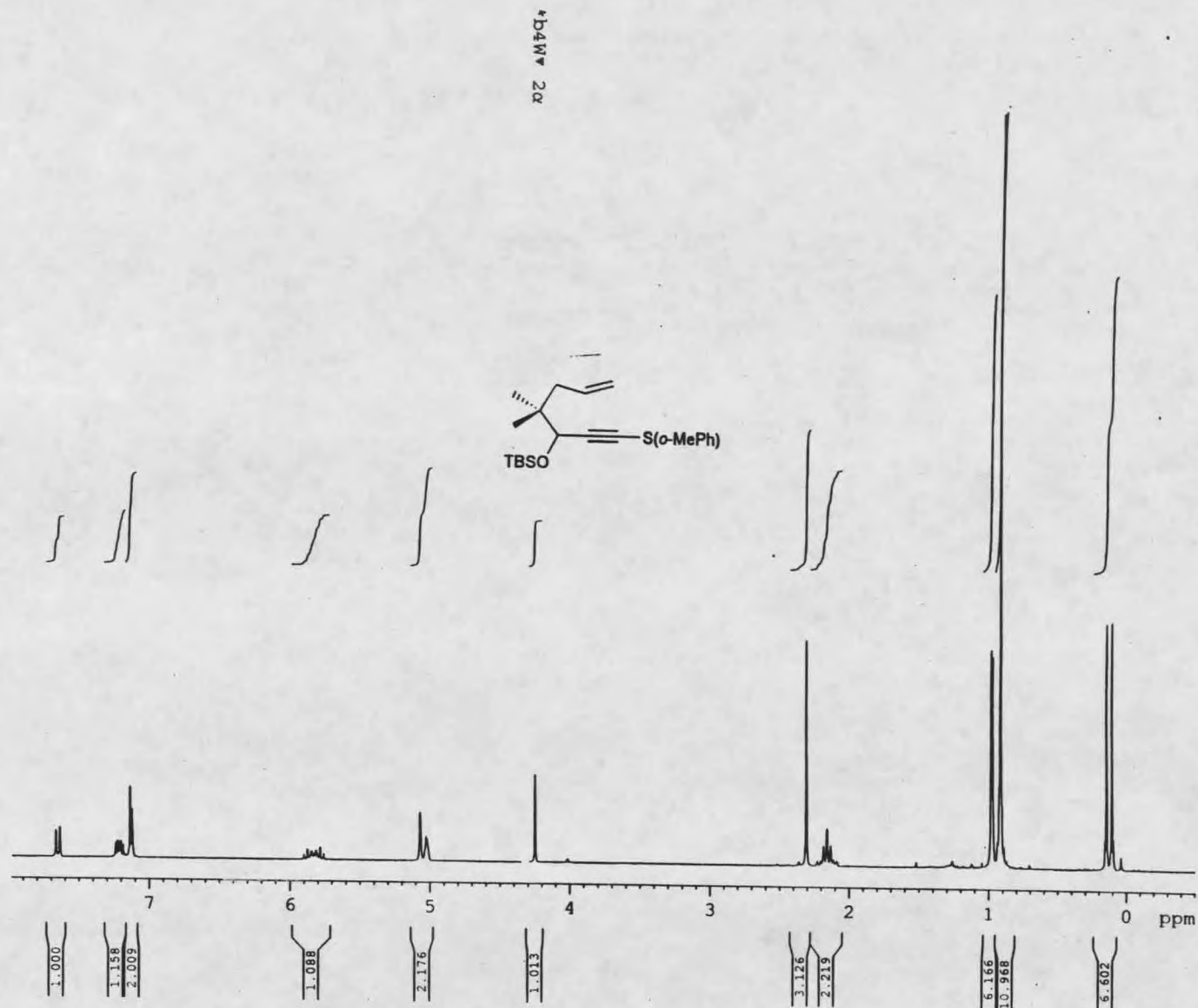


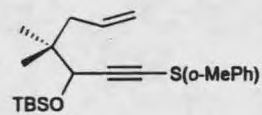


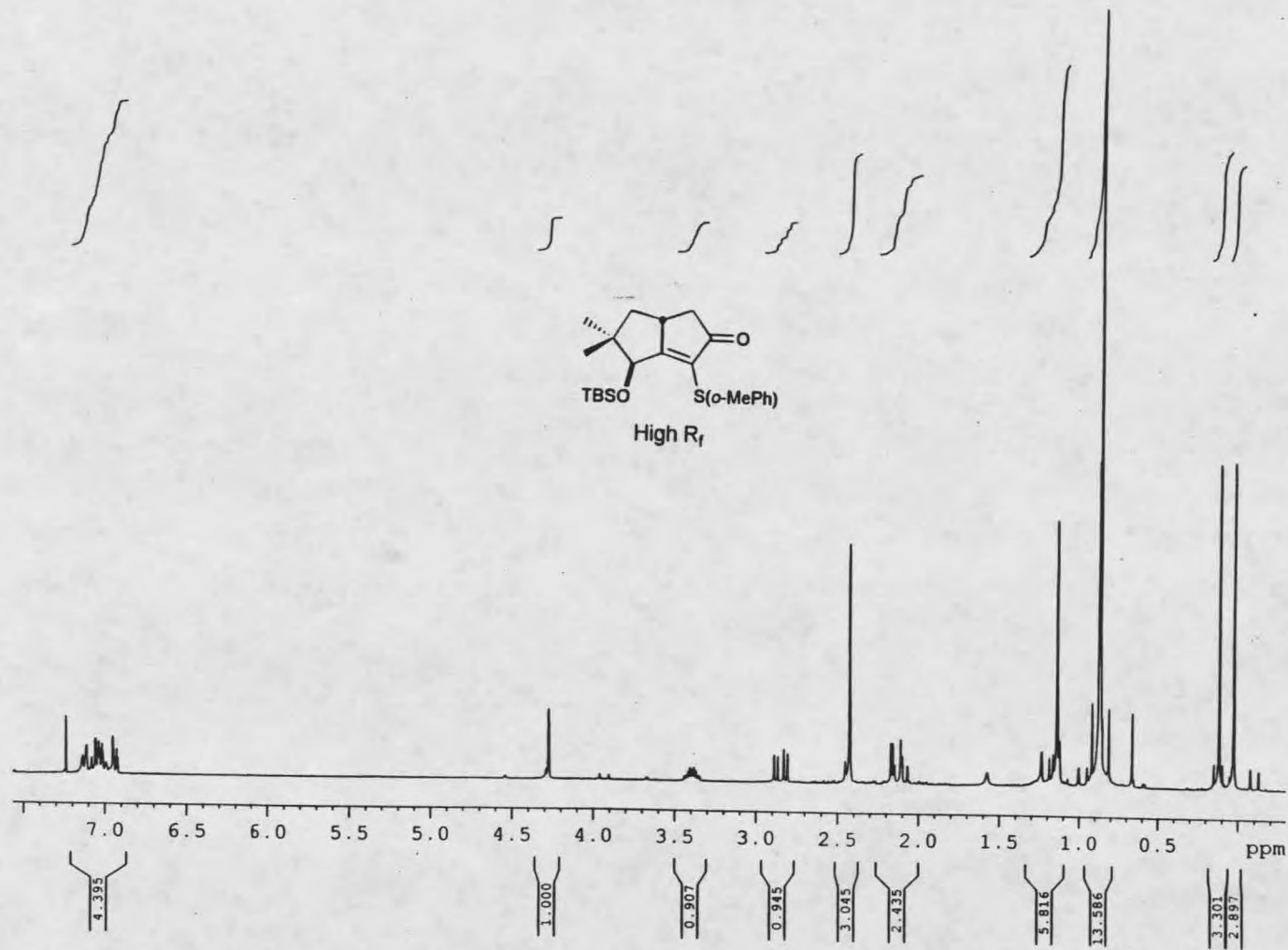
1H NMR Spectrum 1



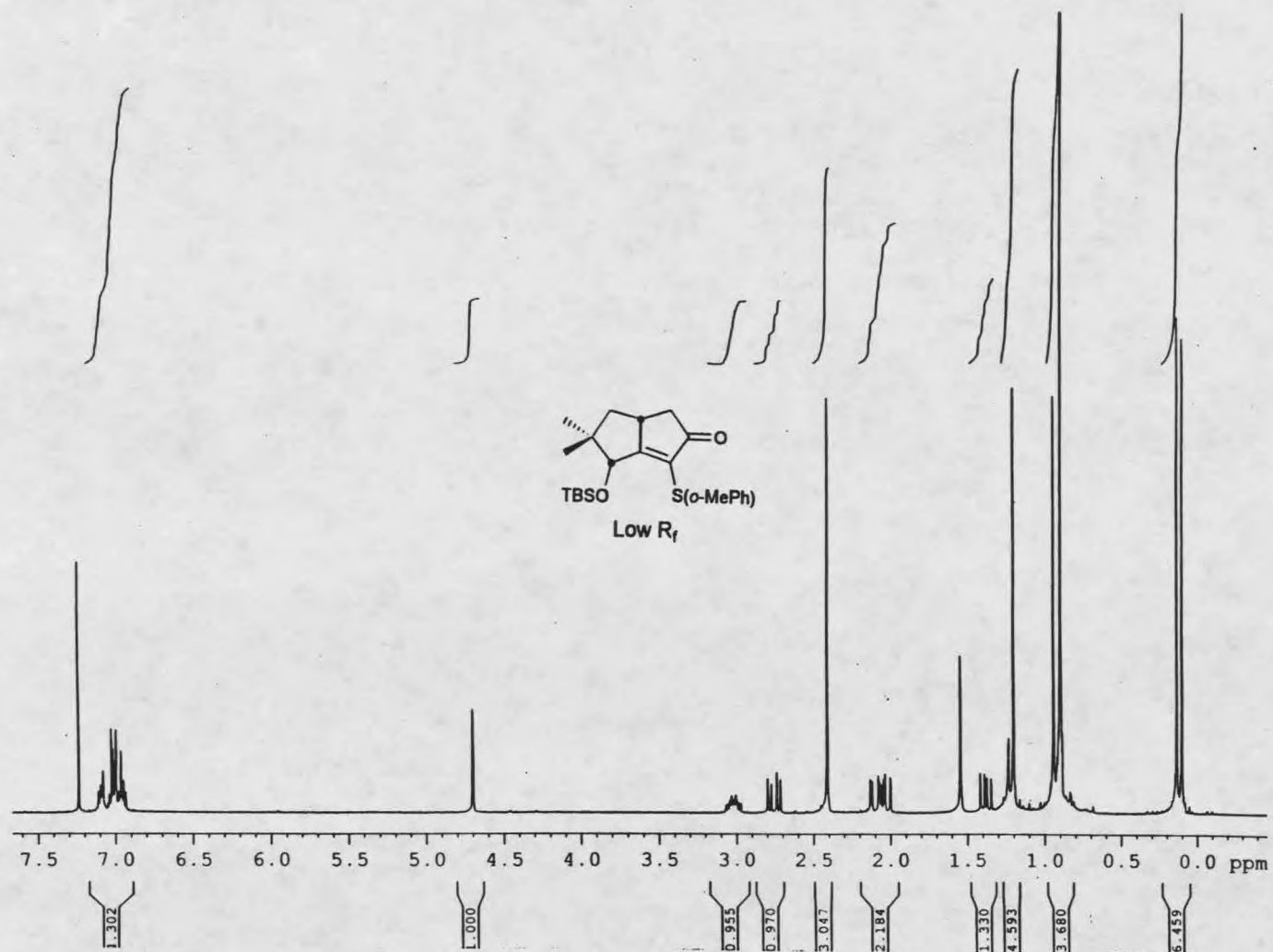


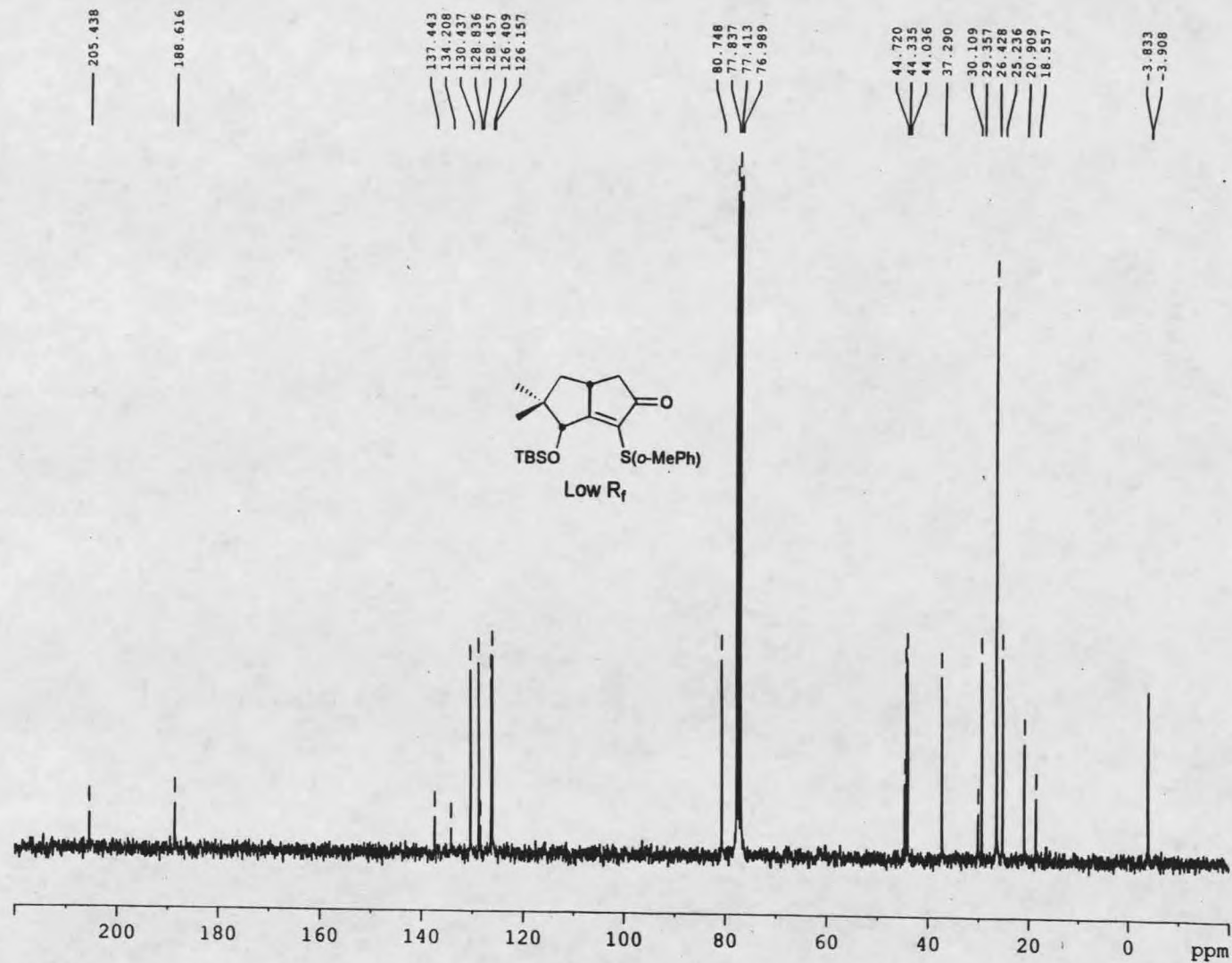
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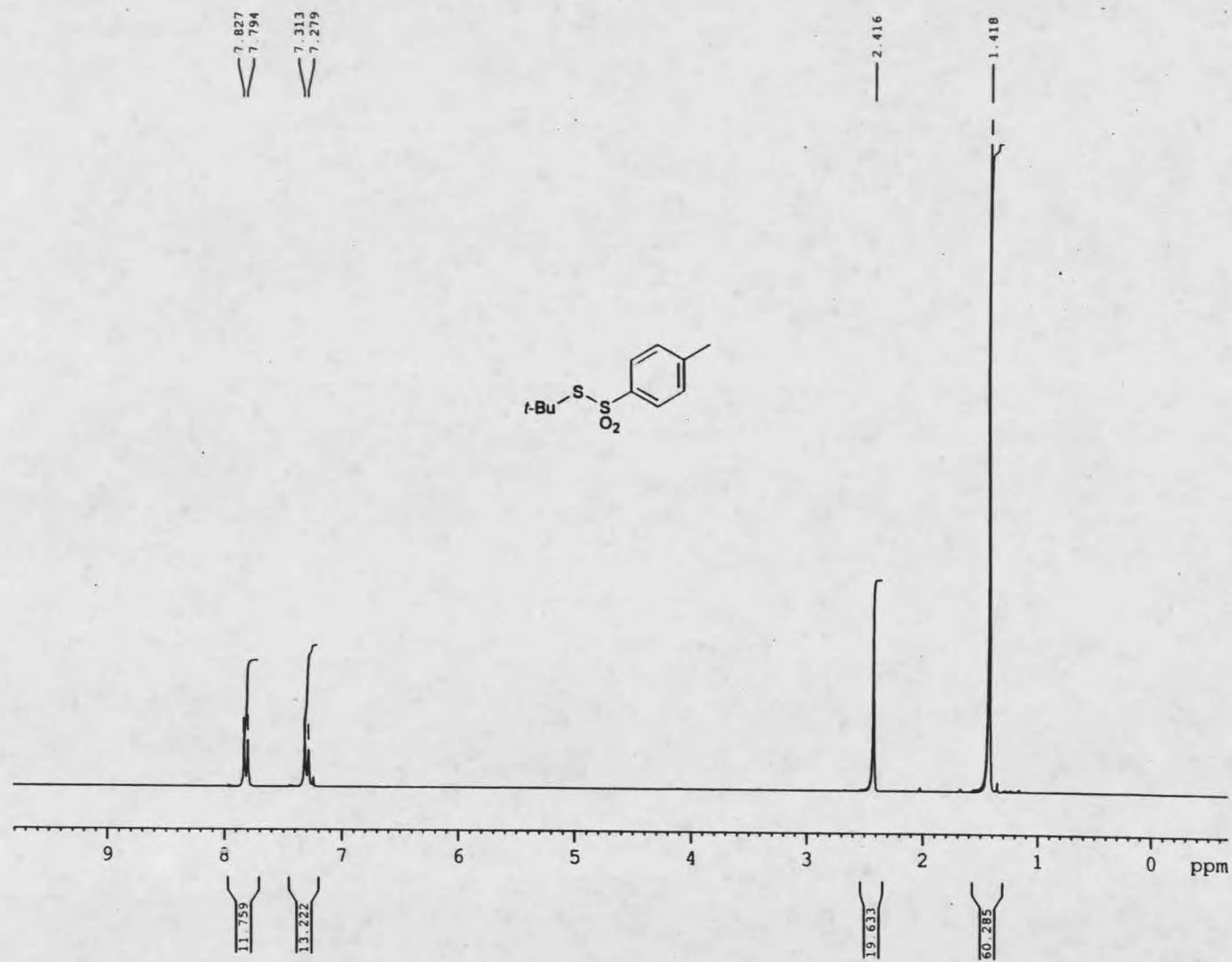


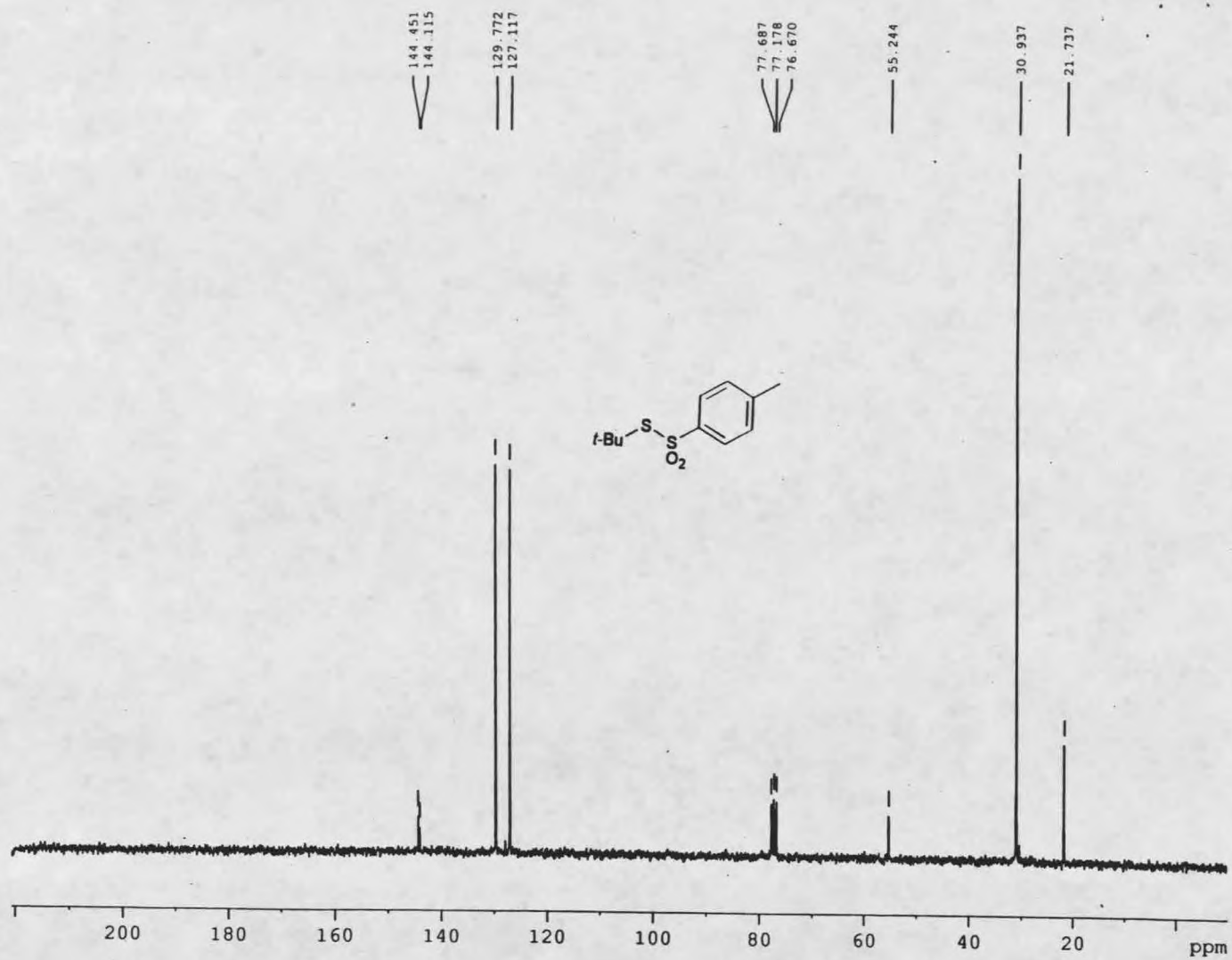




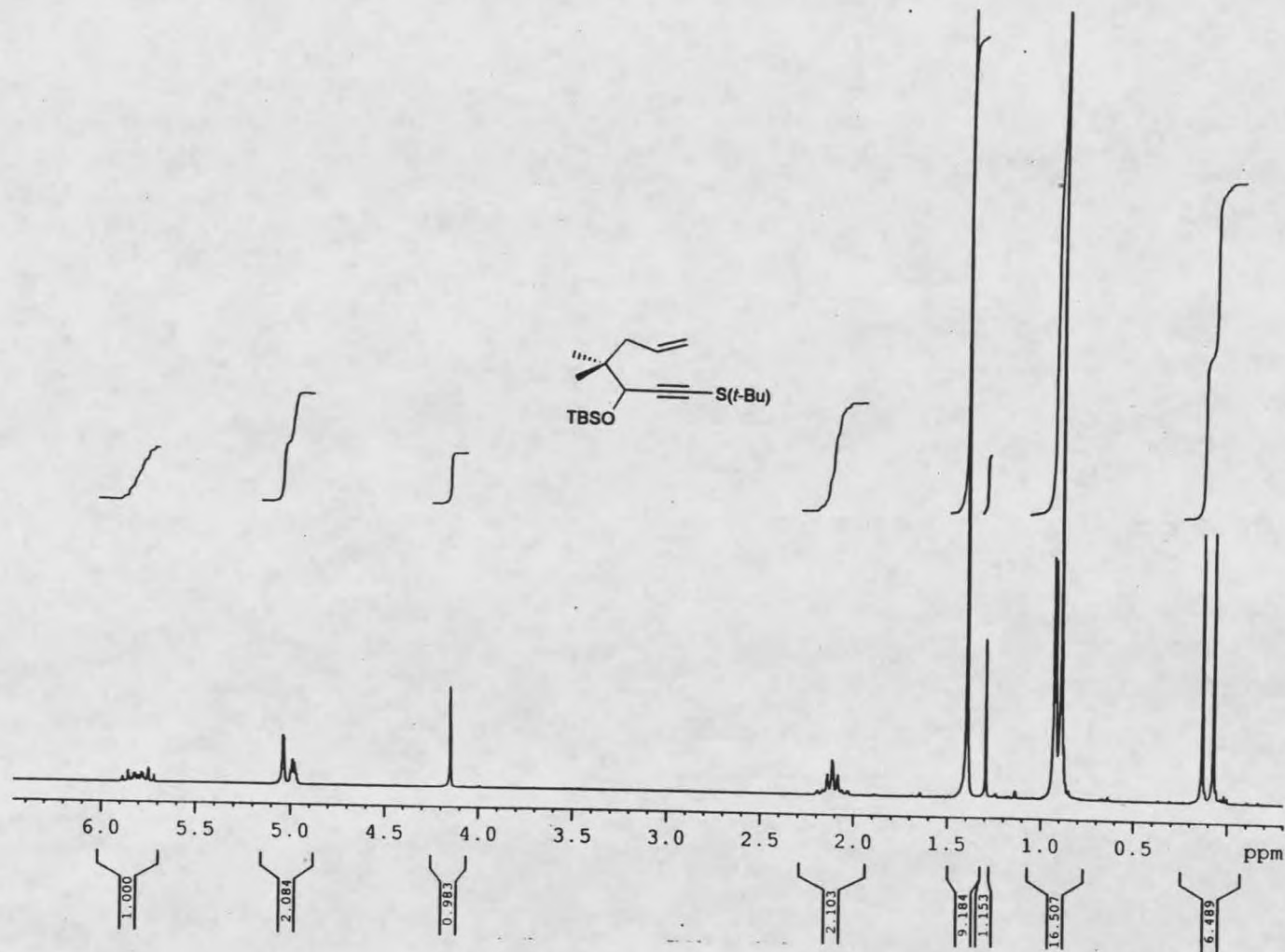




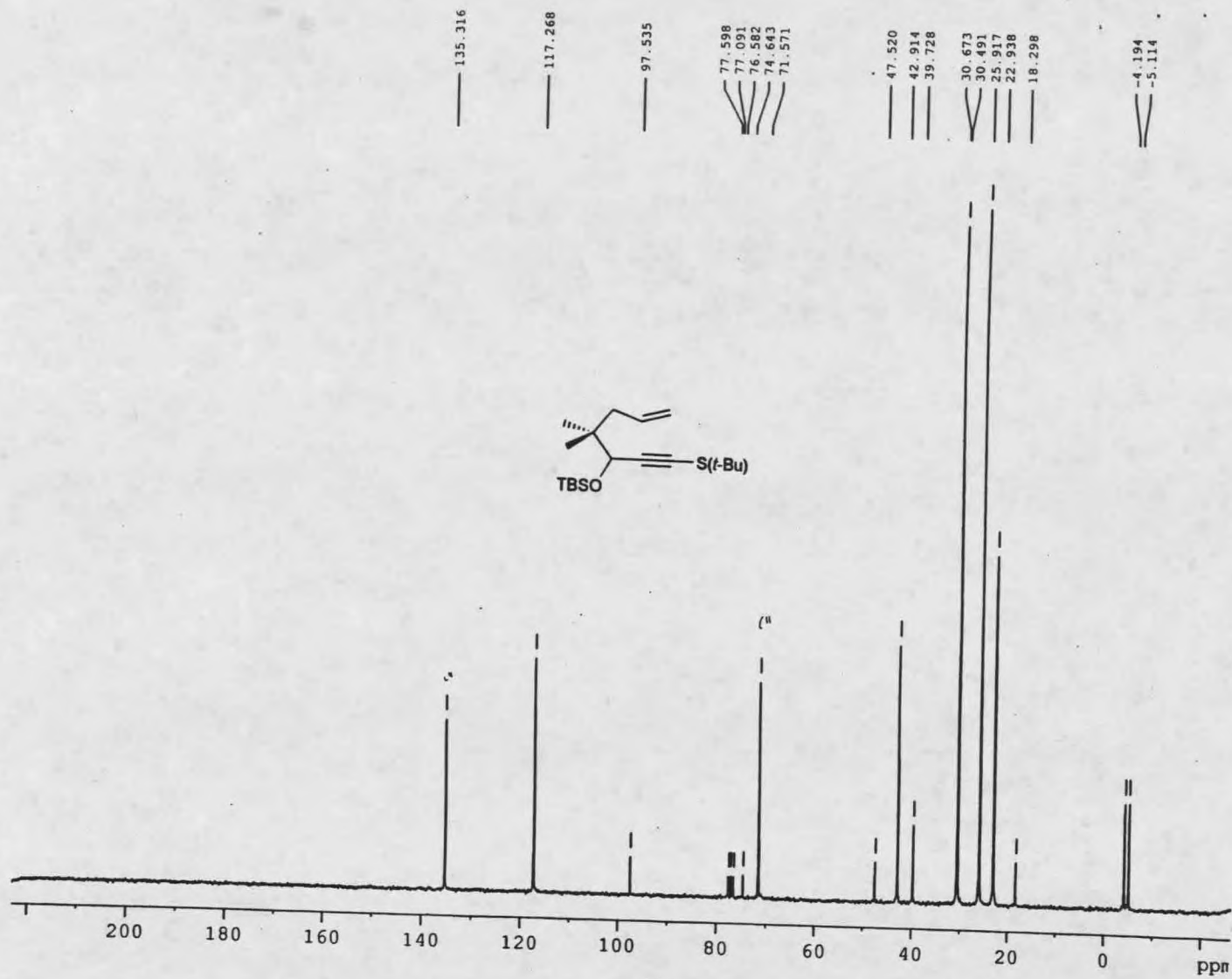




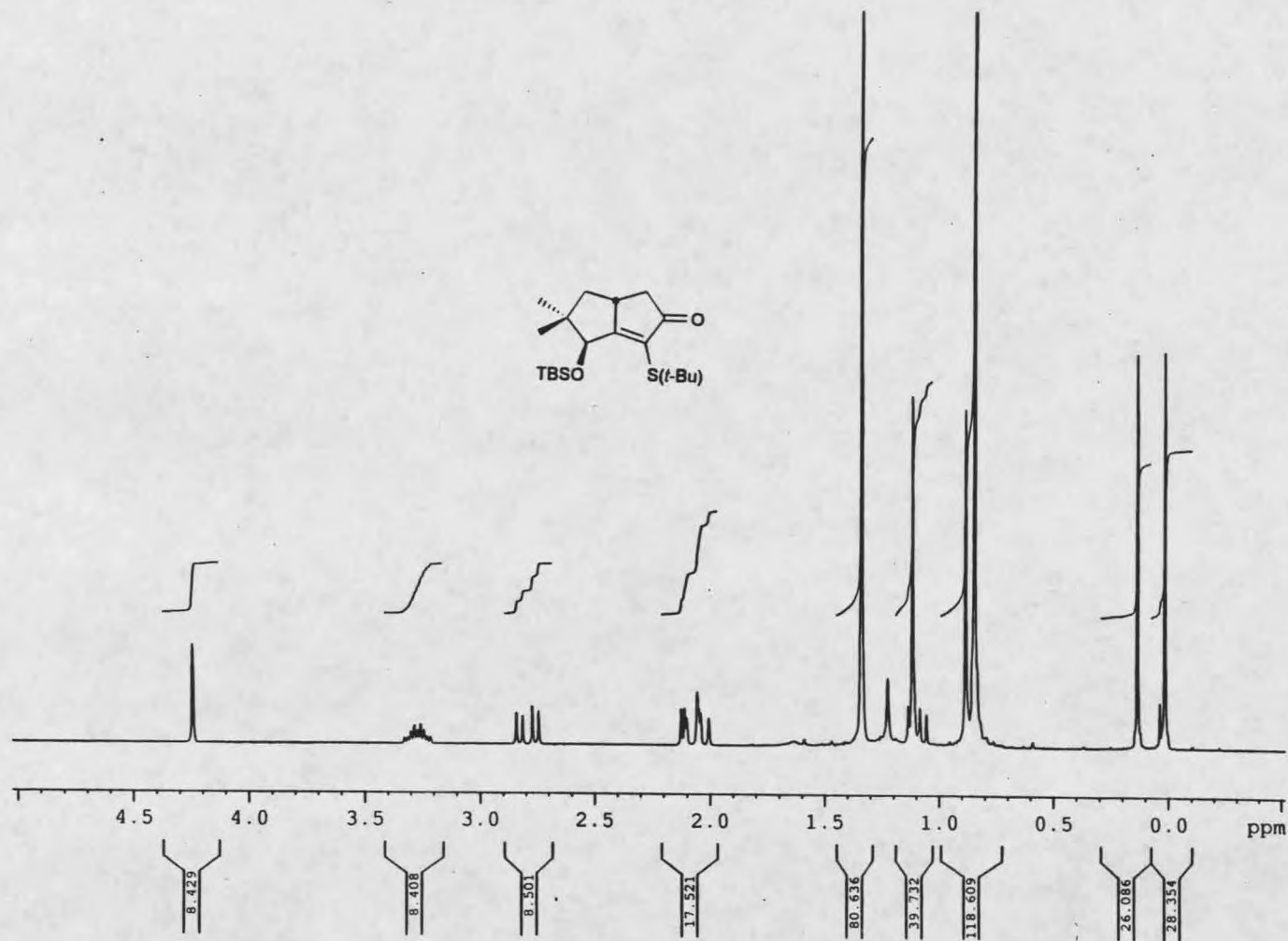
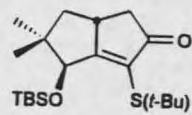
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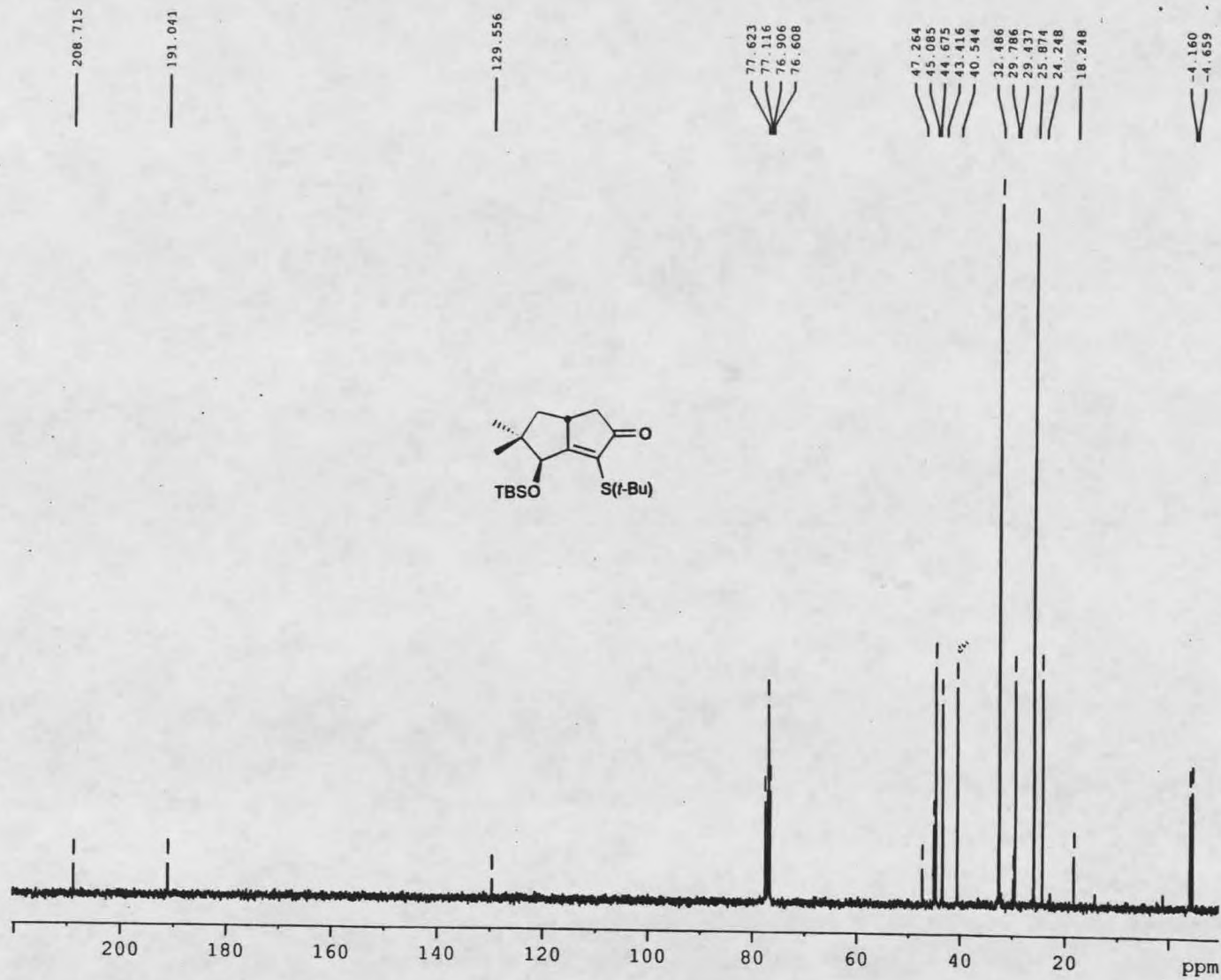
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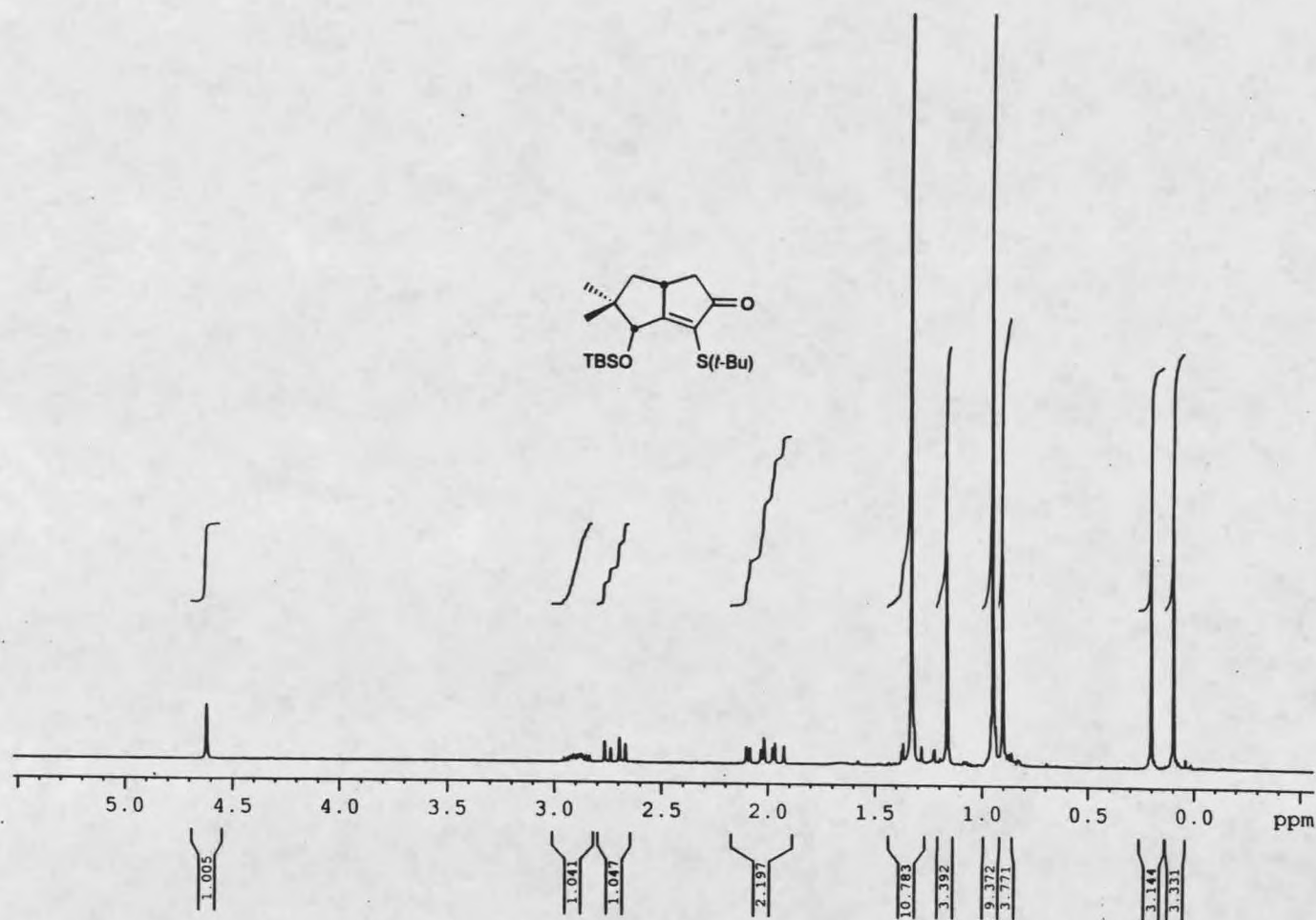


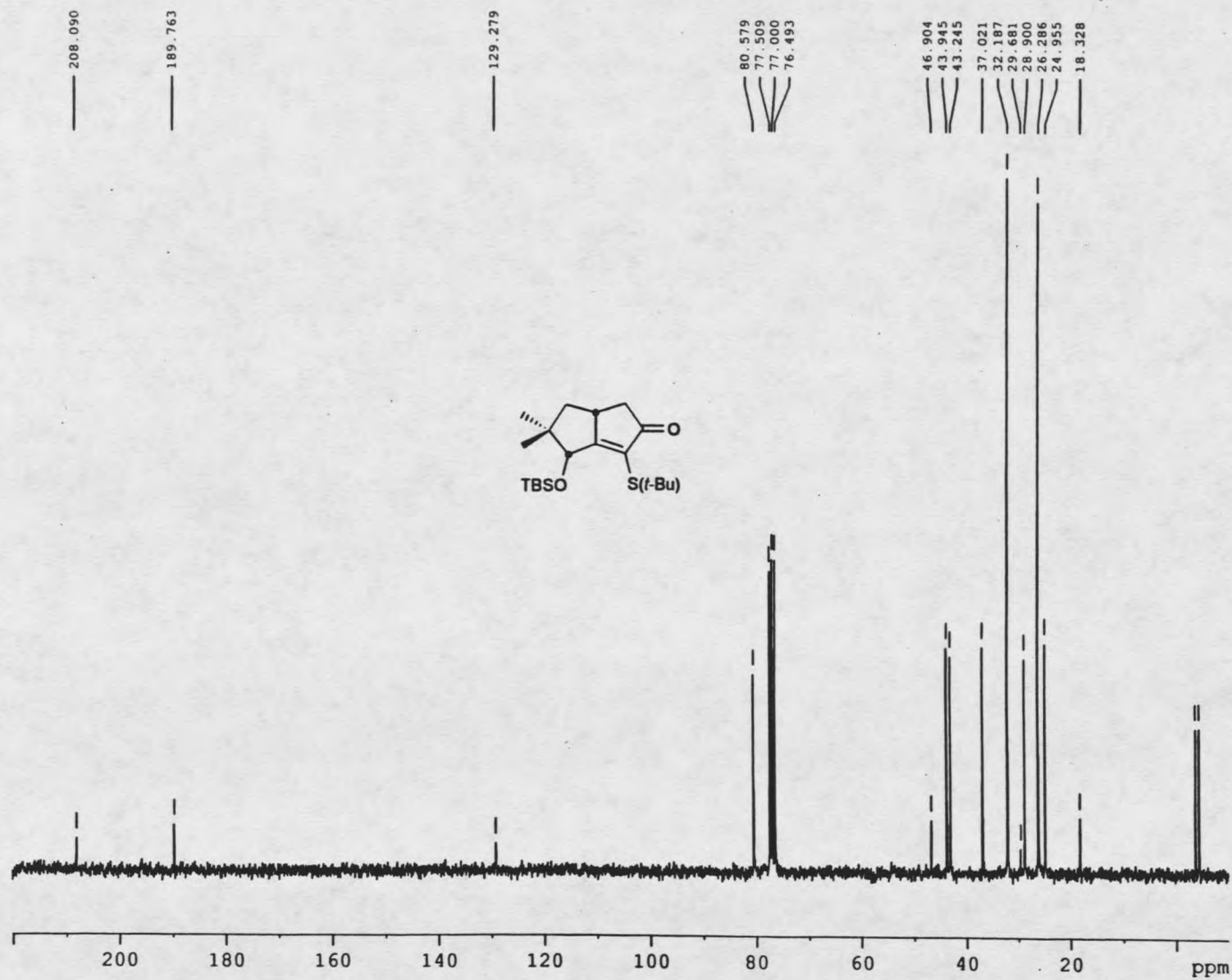
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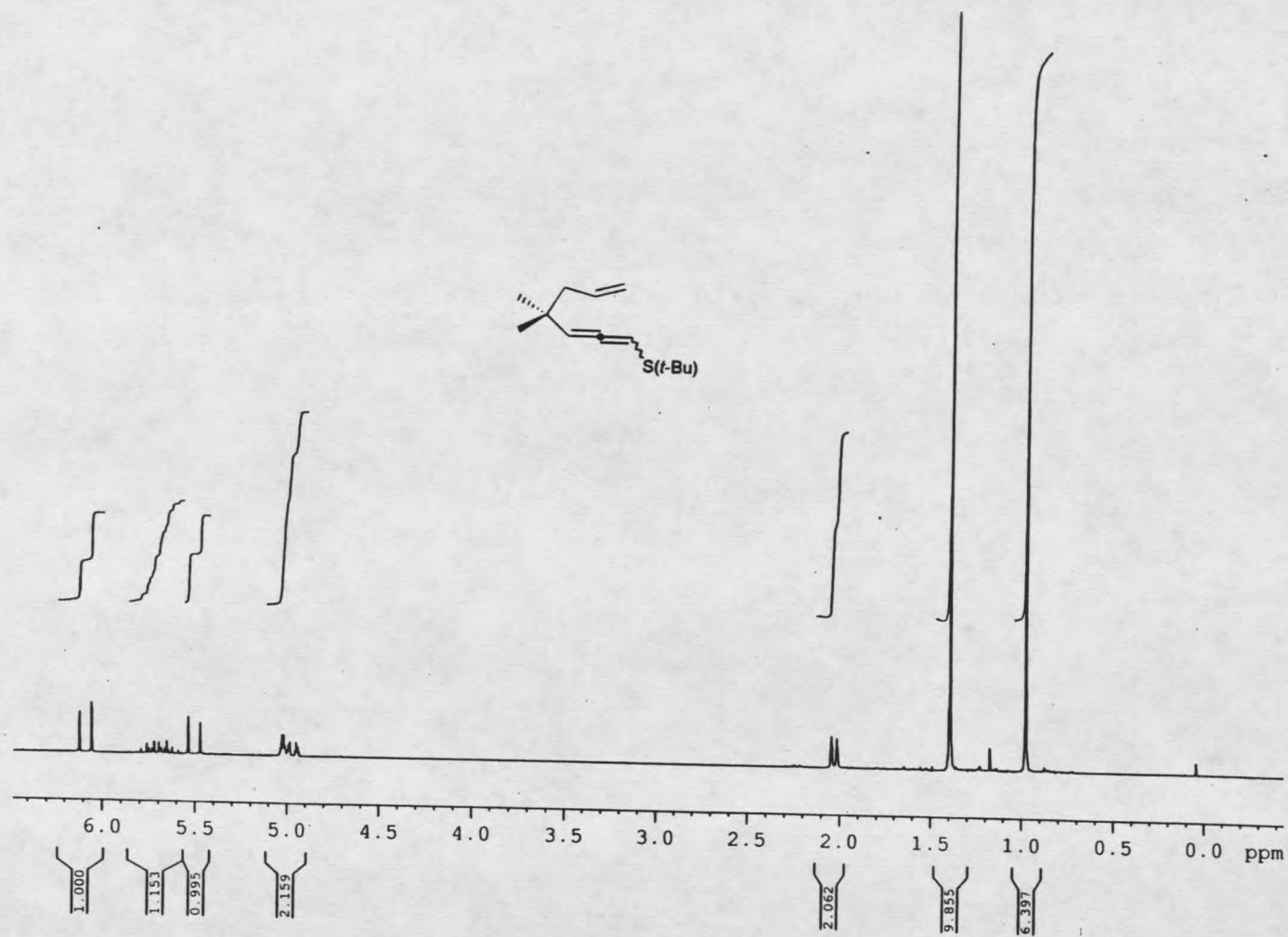


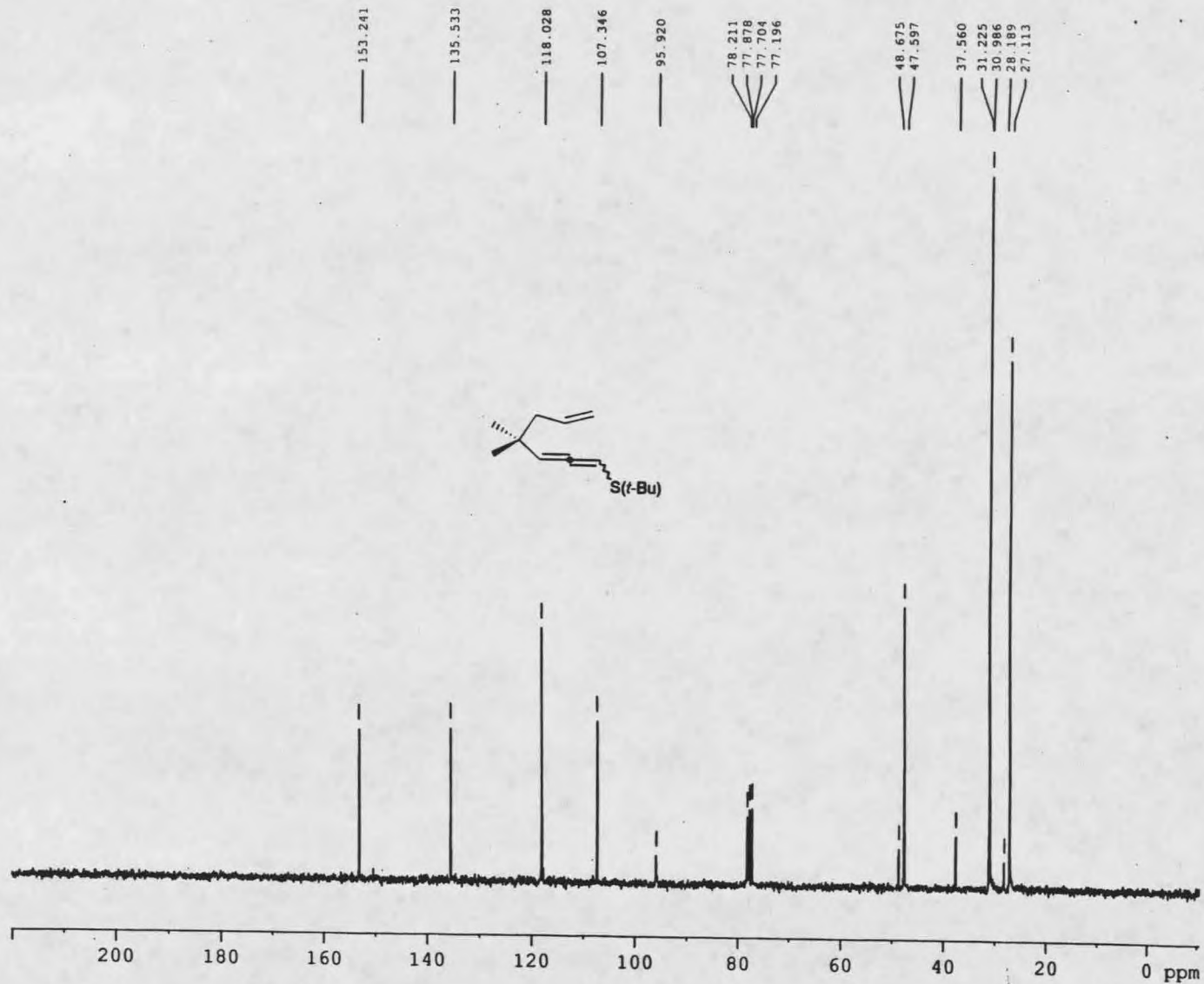
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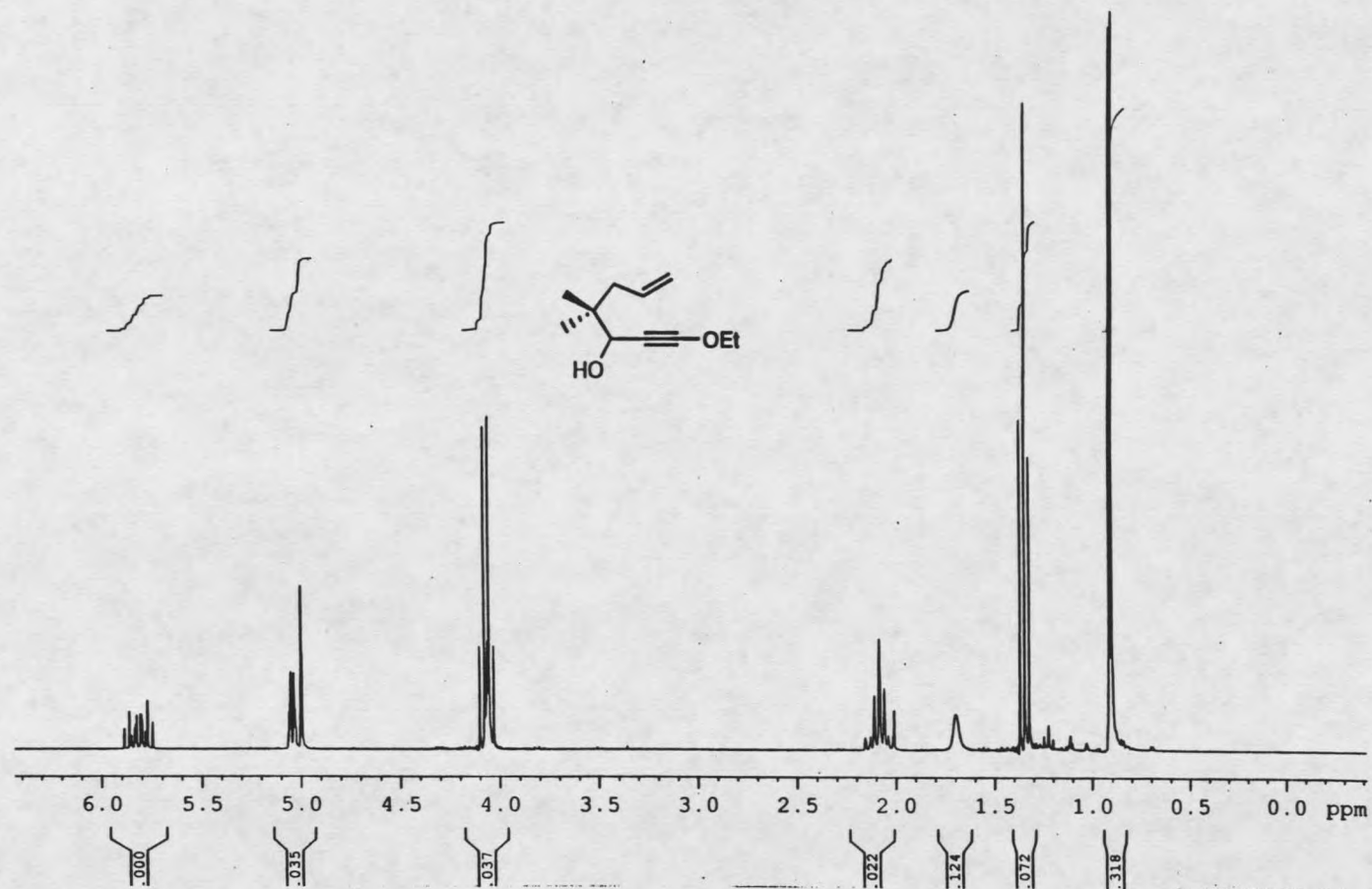


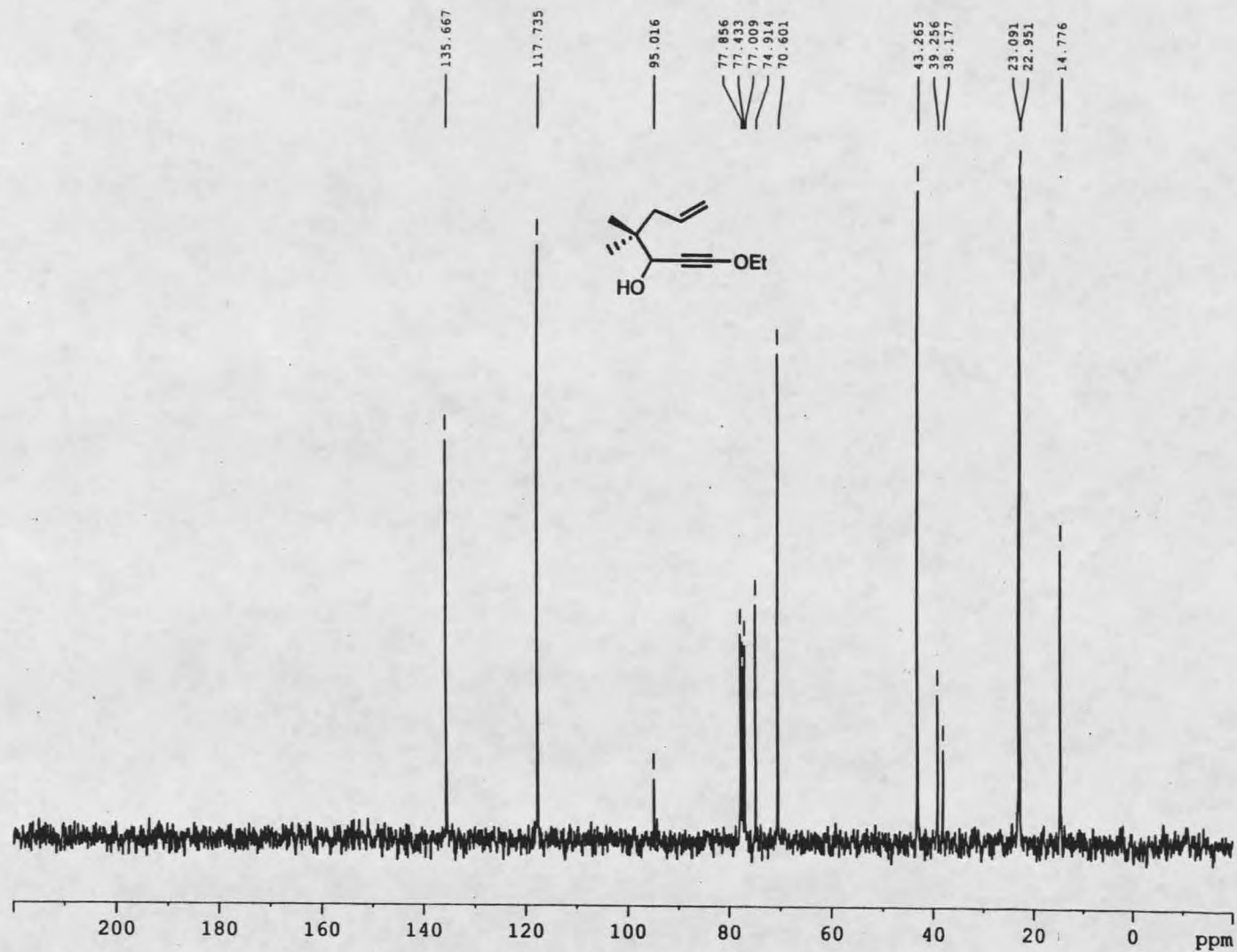


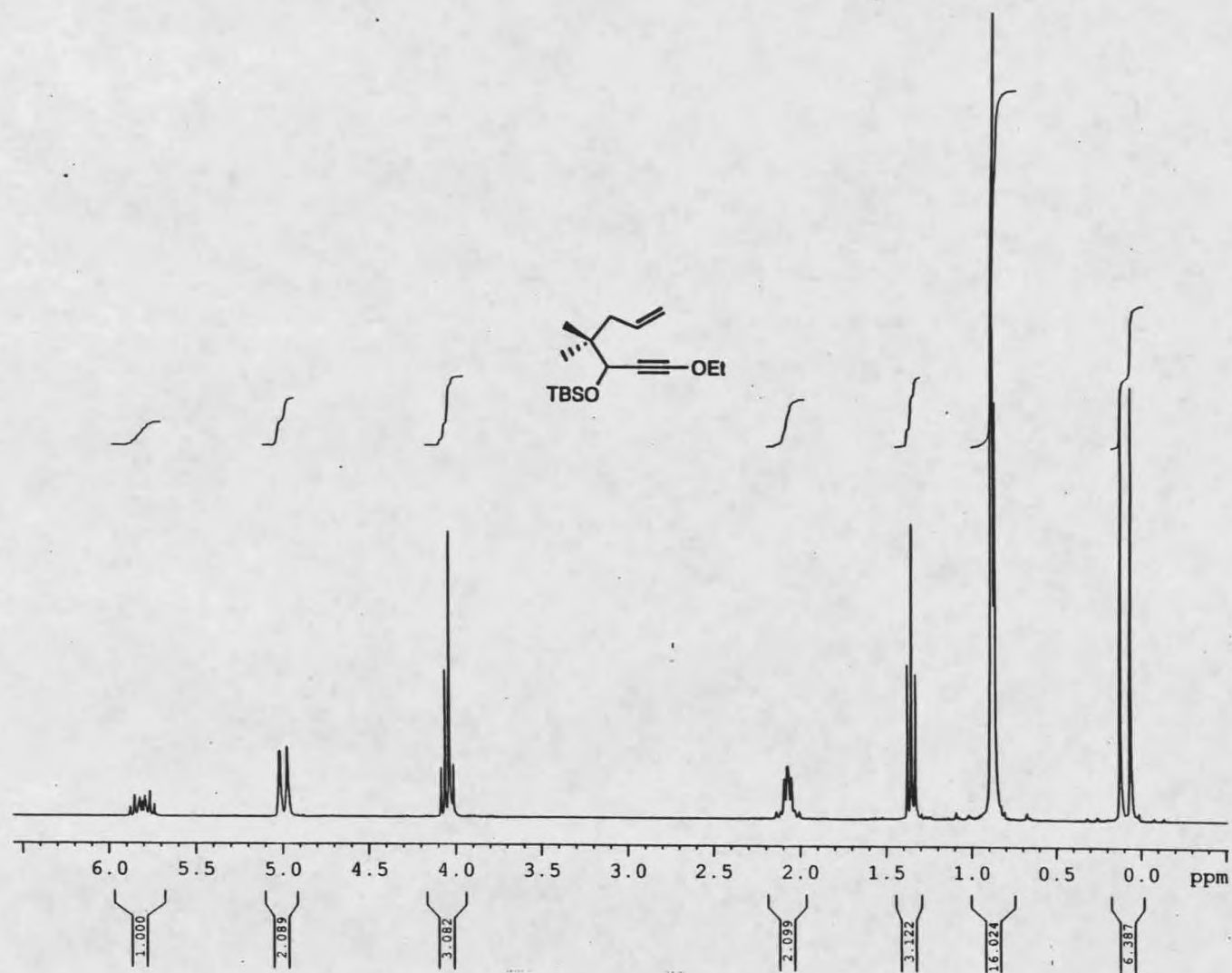


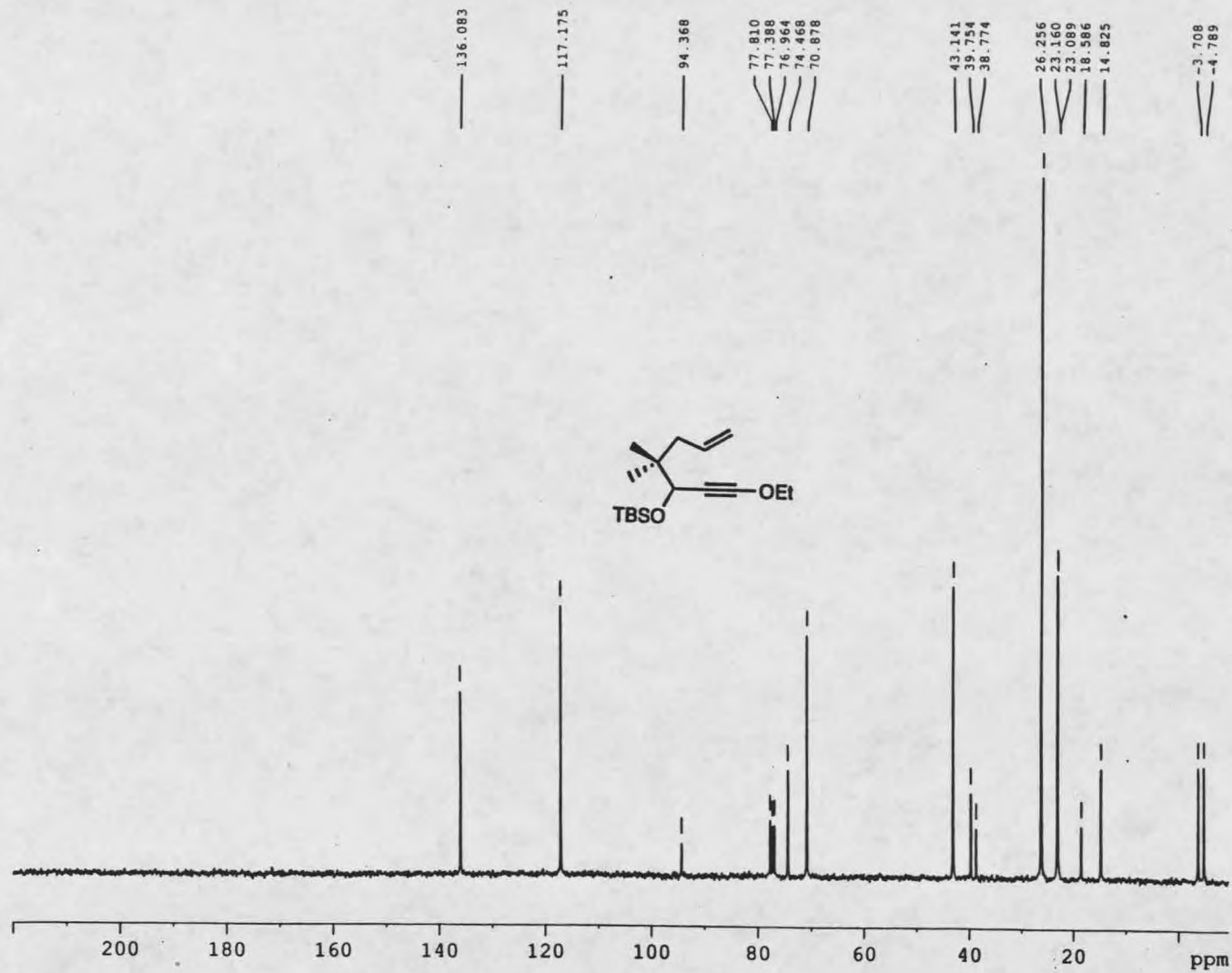




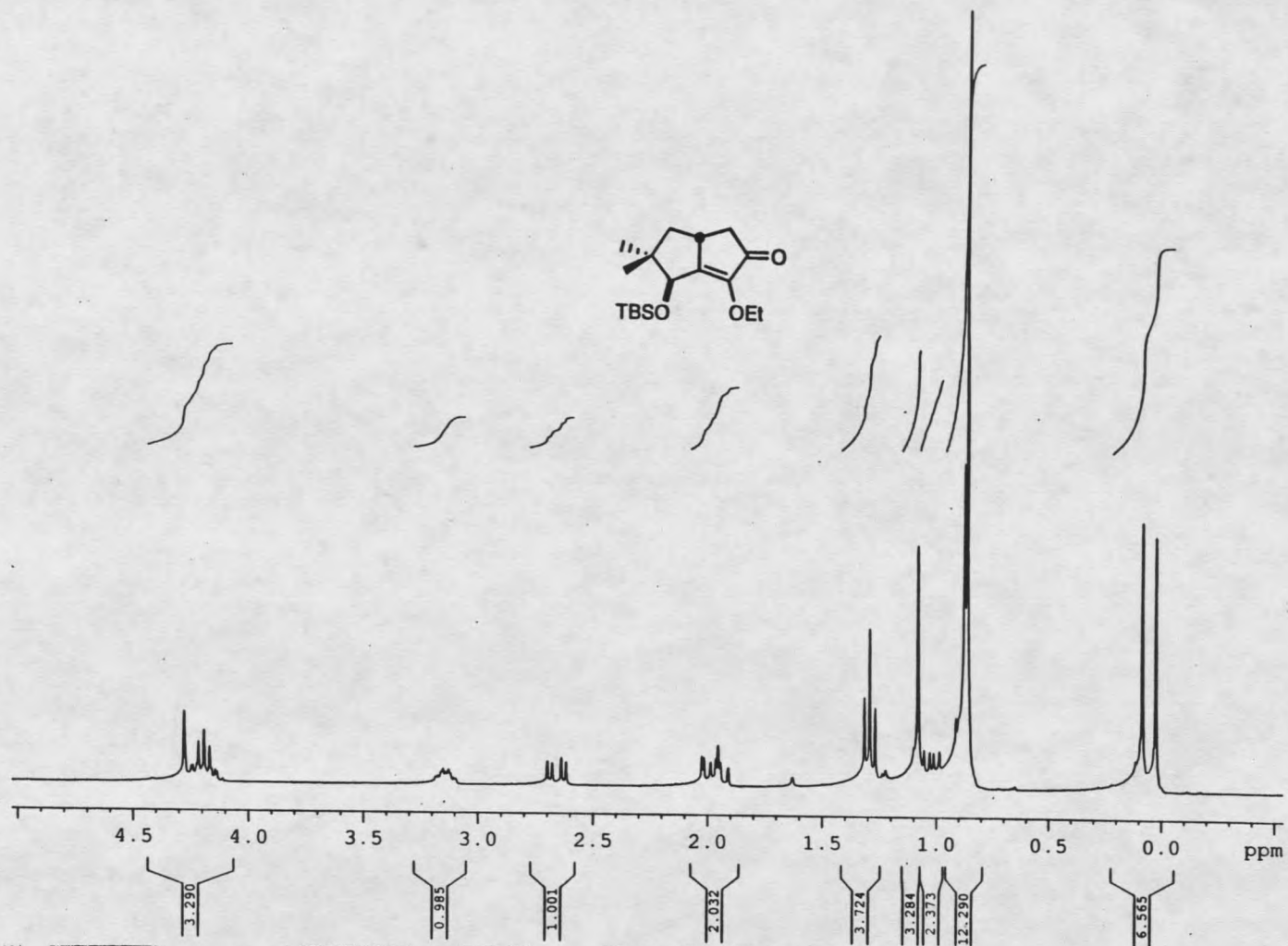
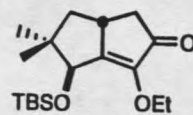




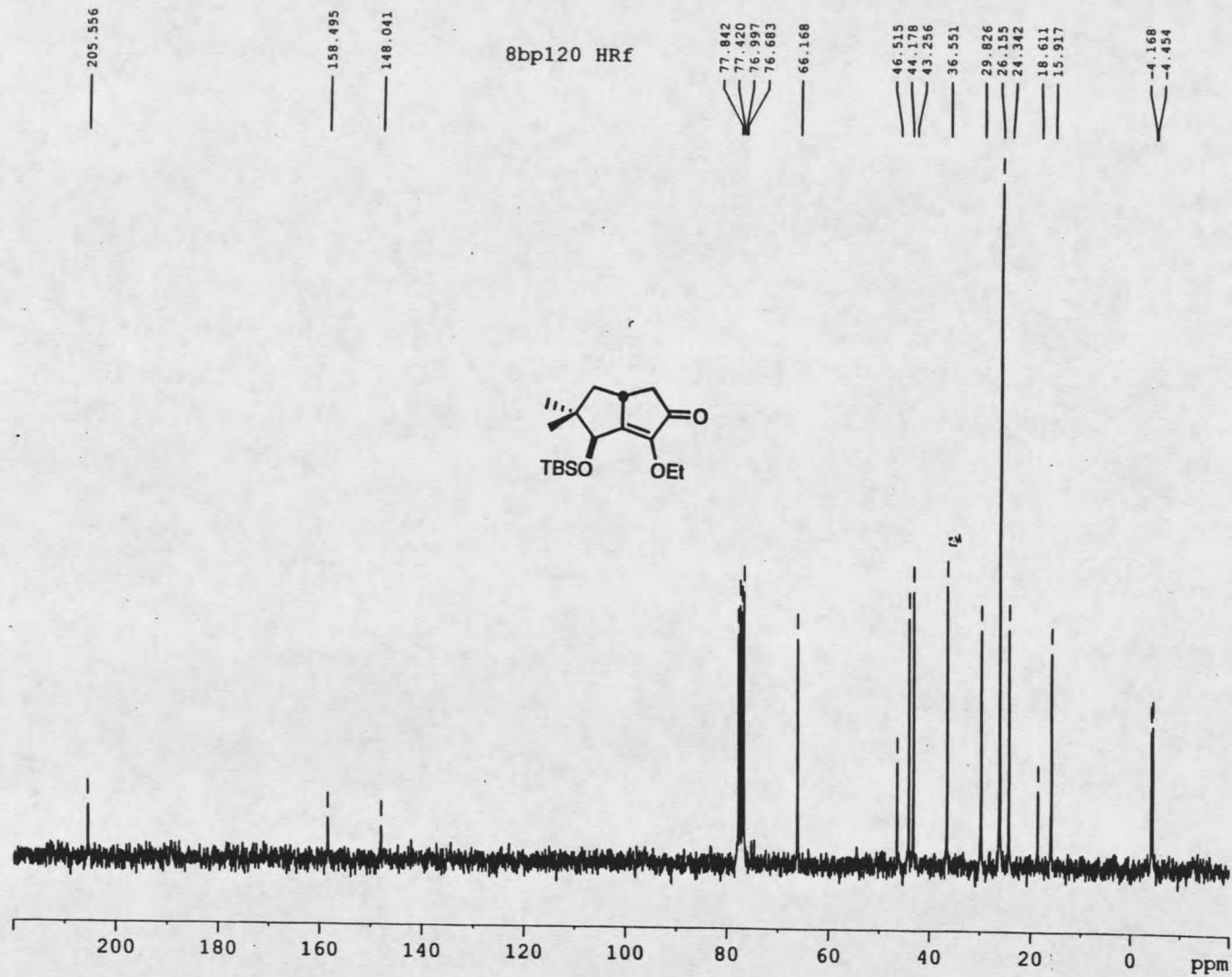




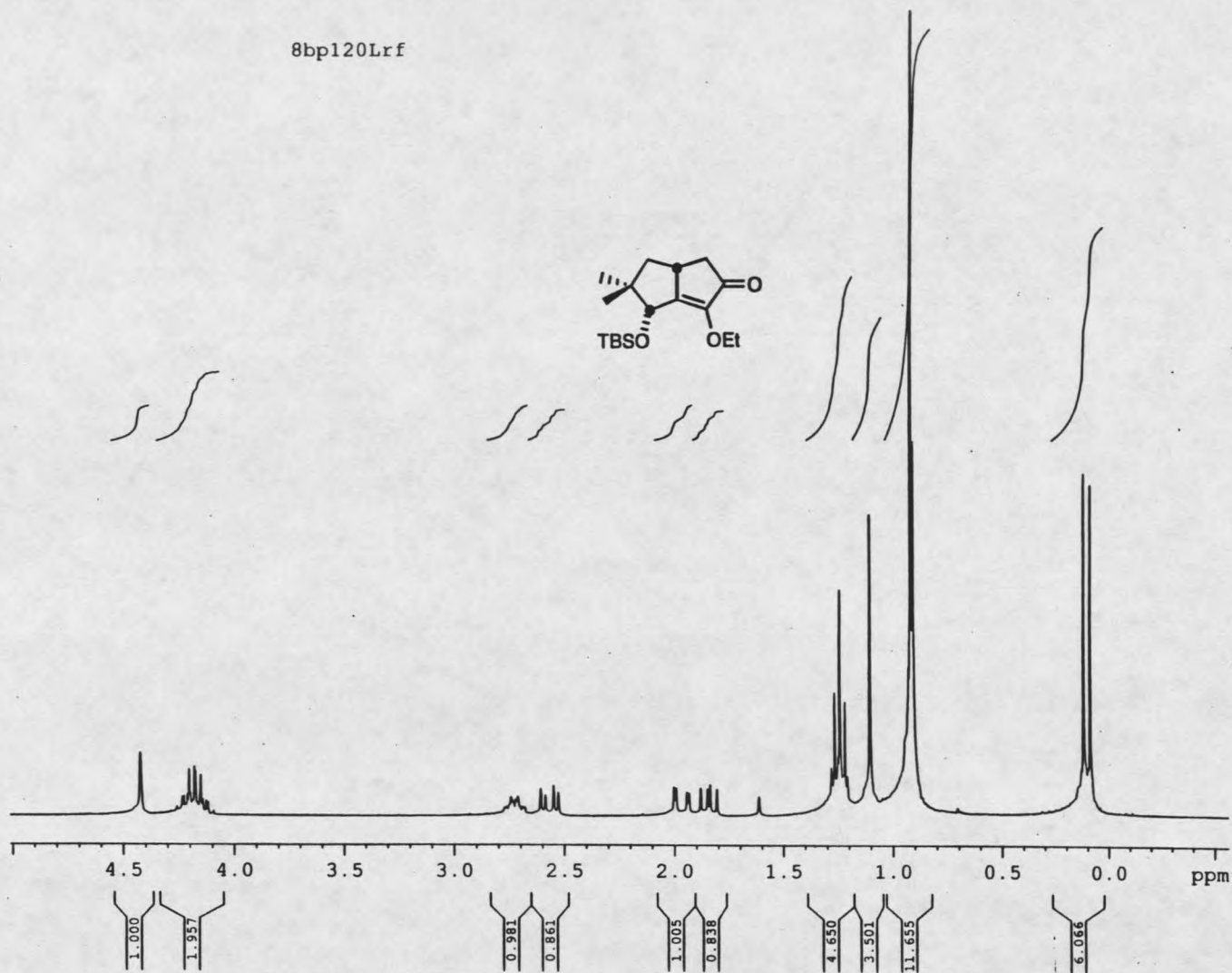
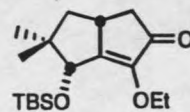
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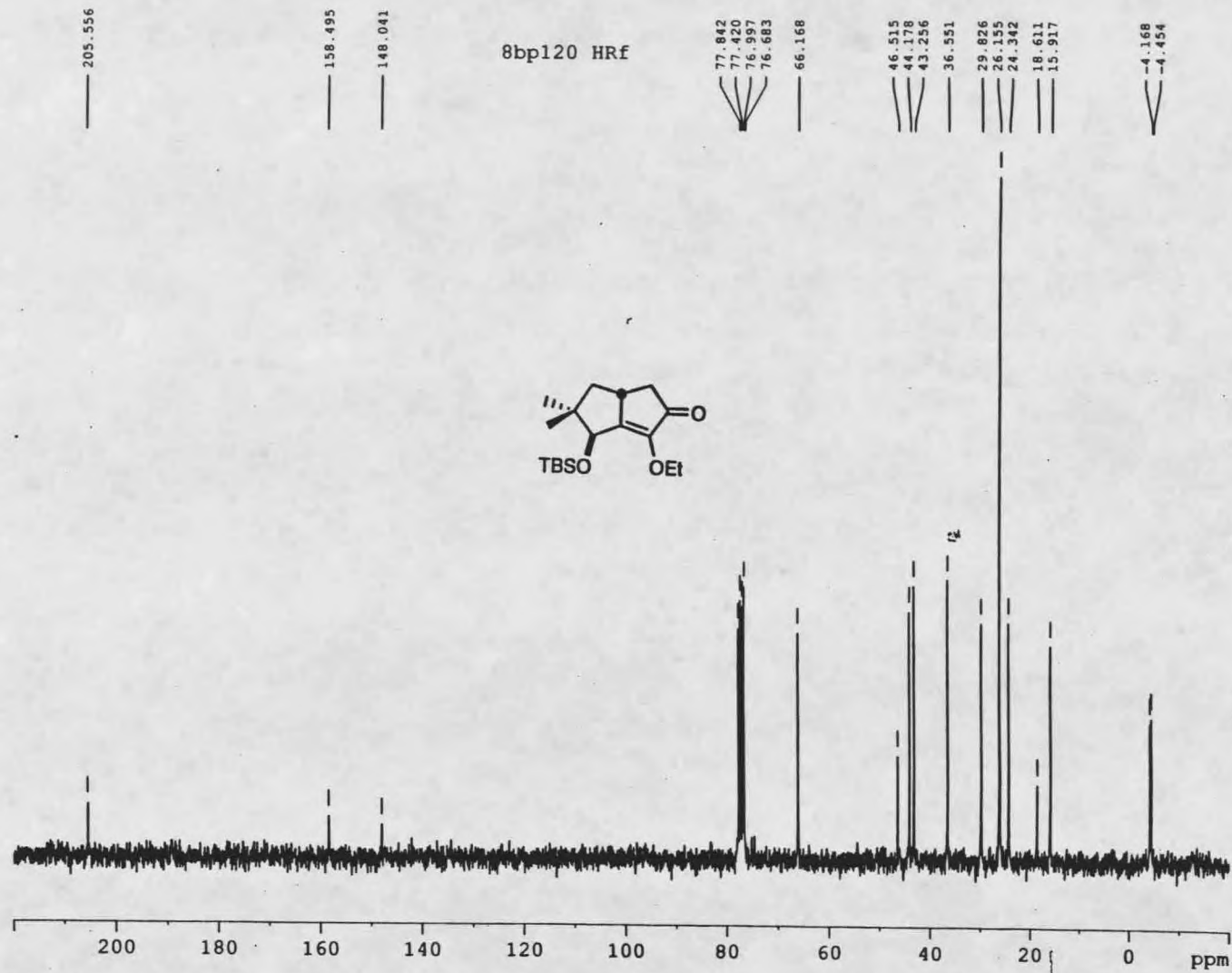


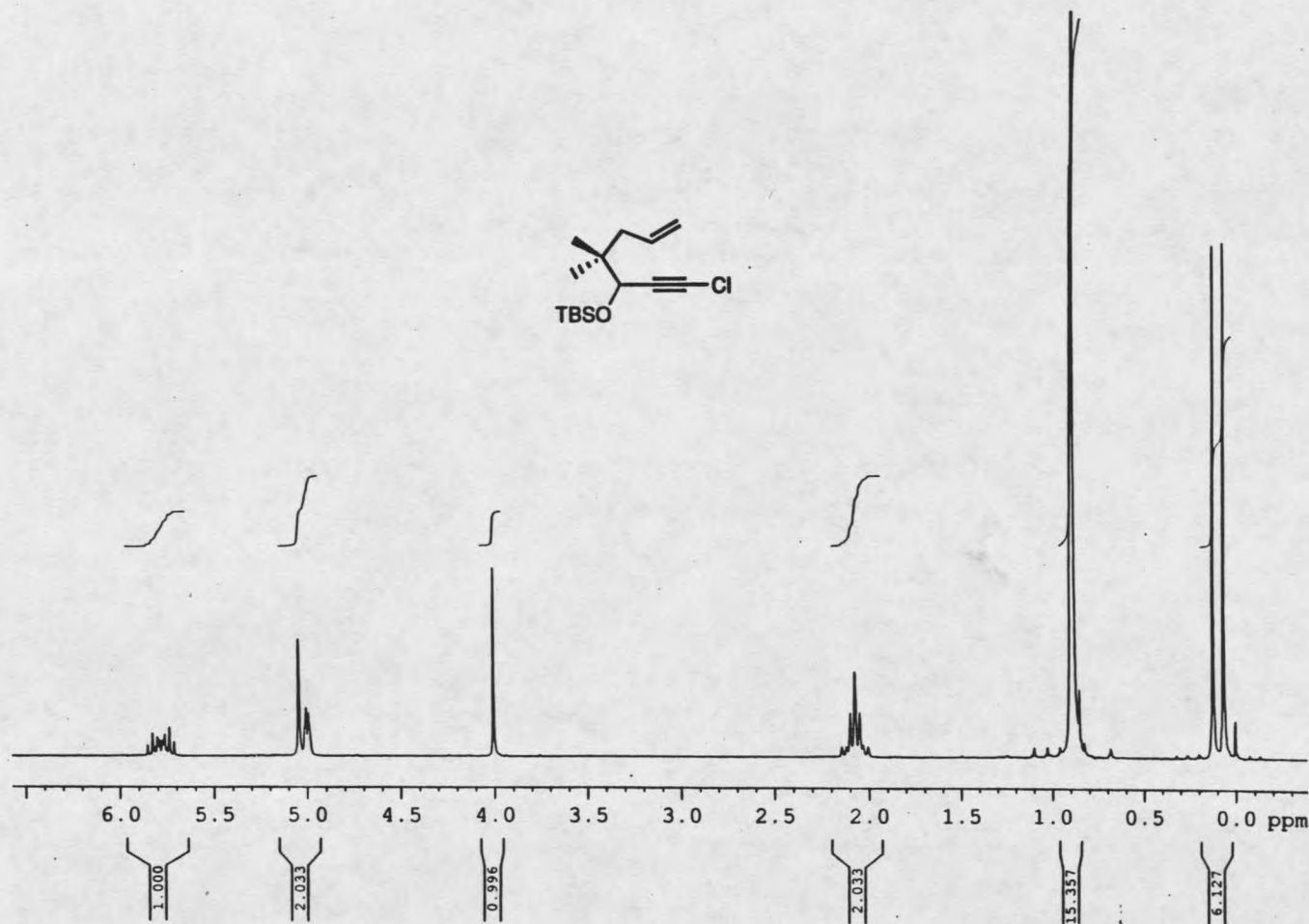
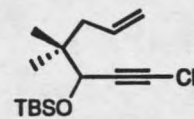
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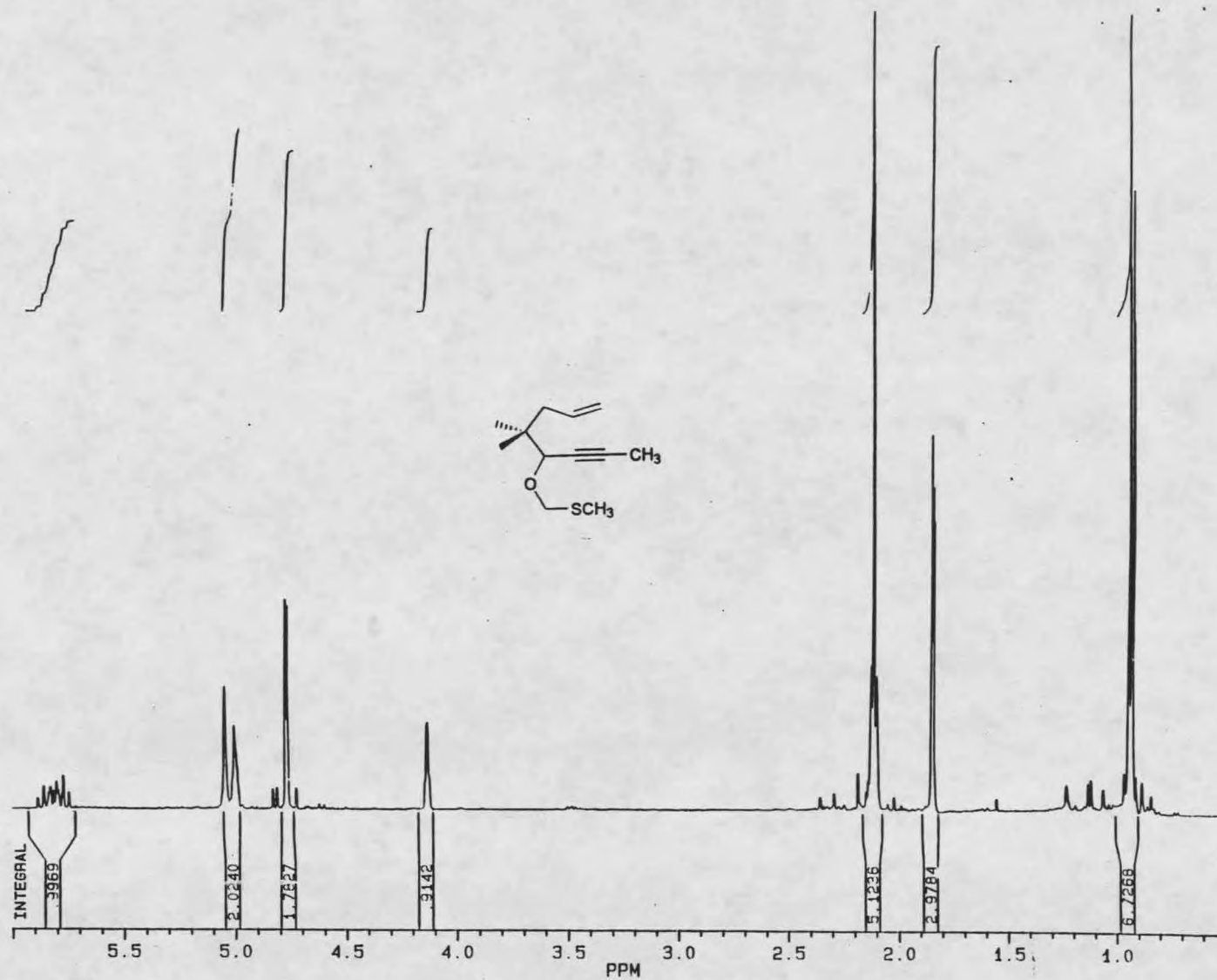


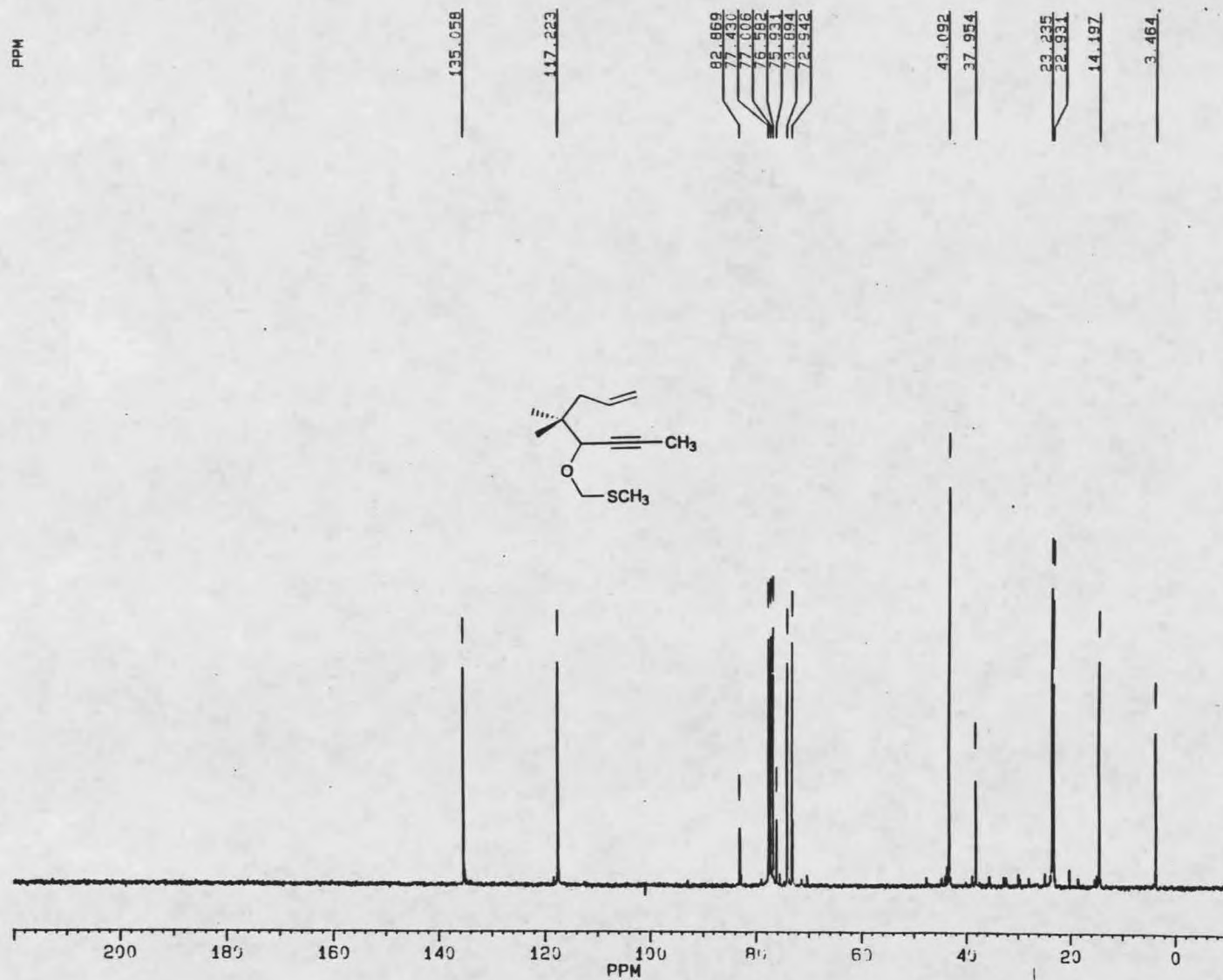
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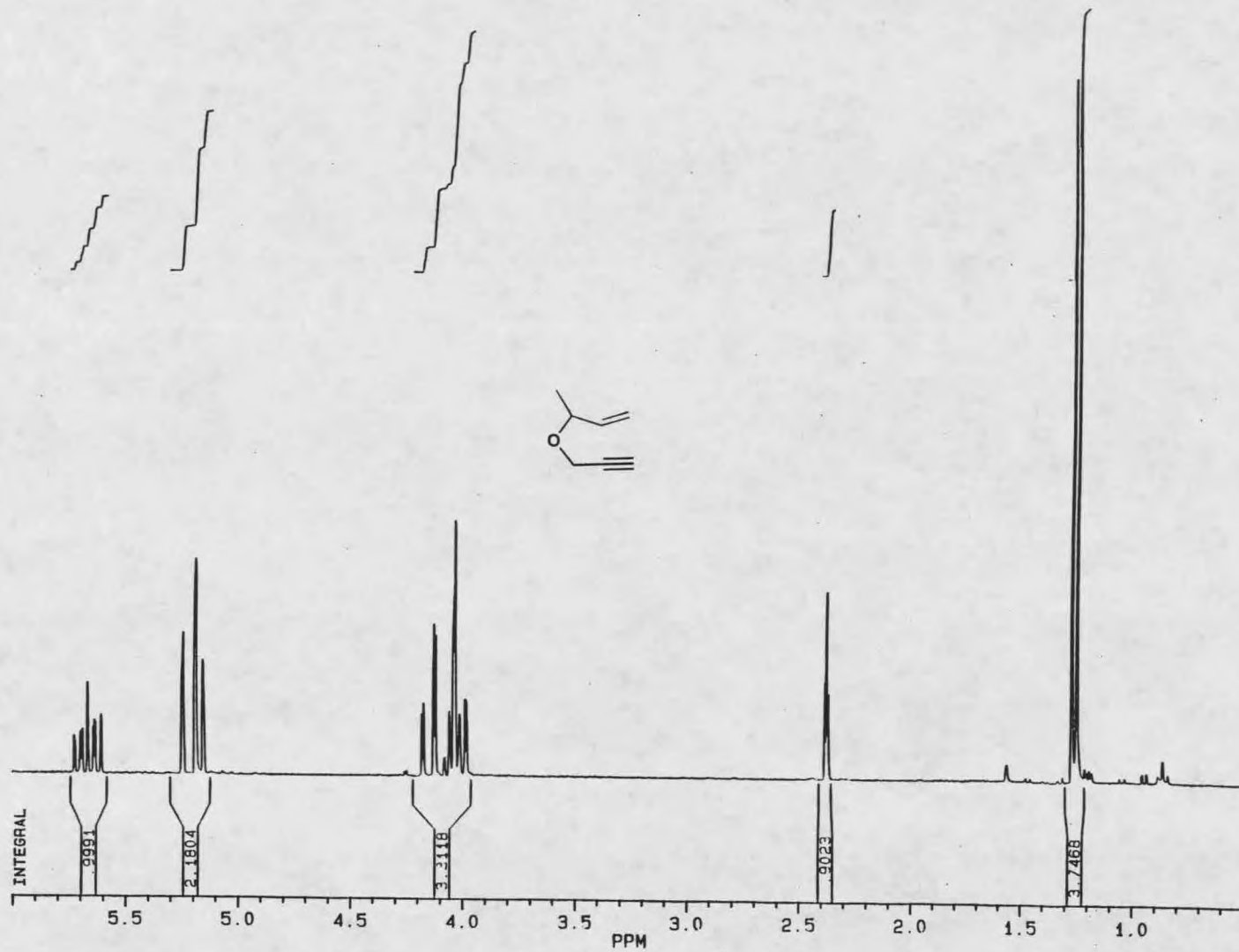


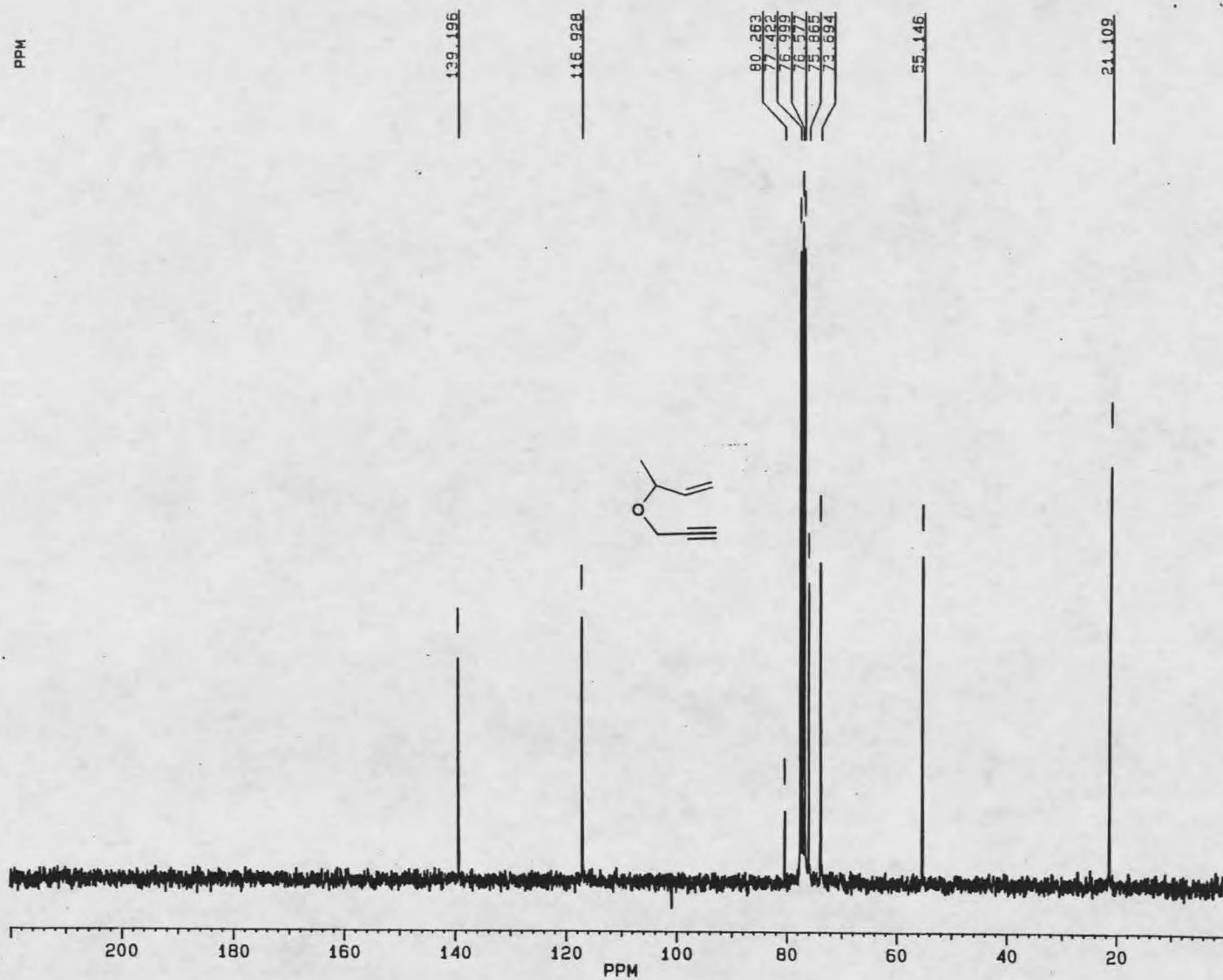


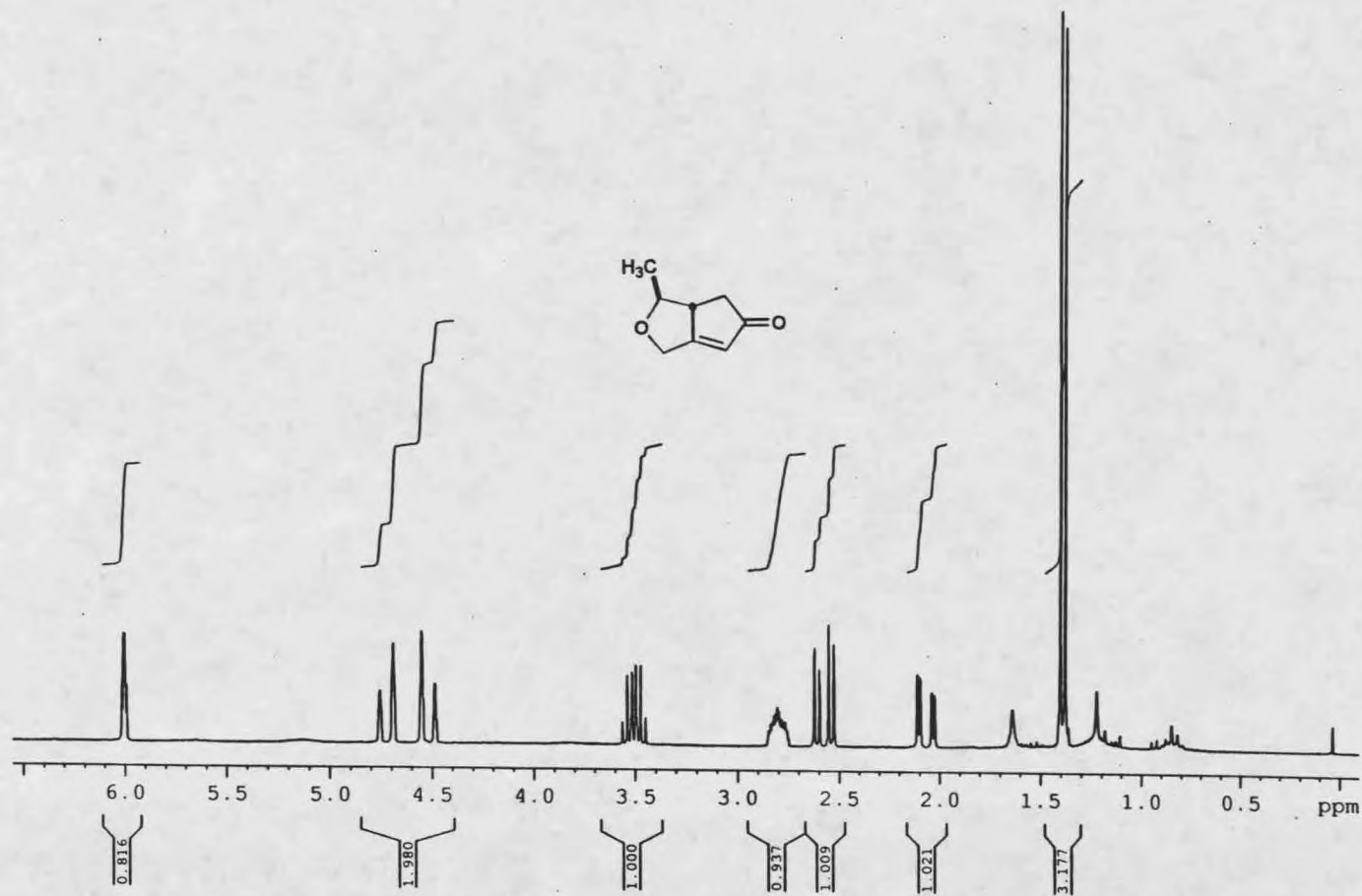


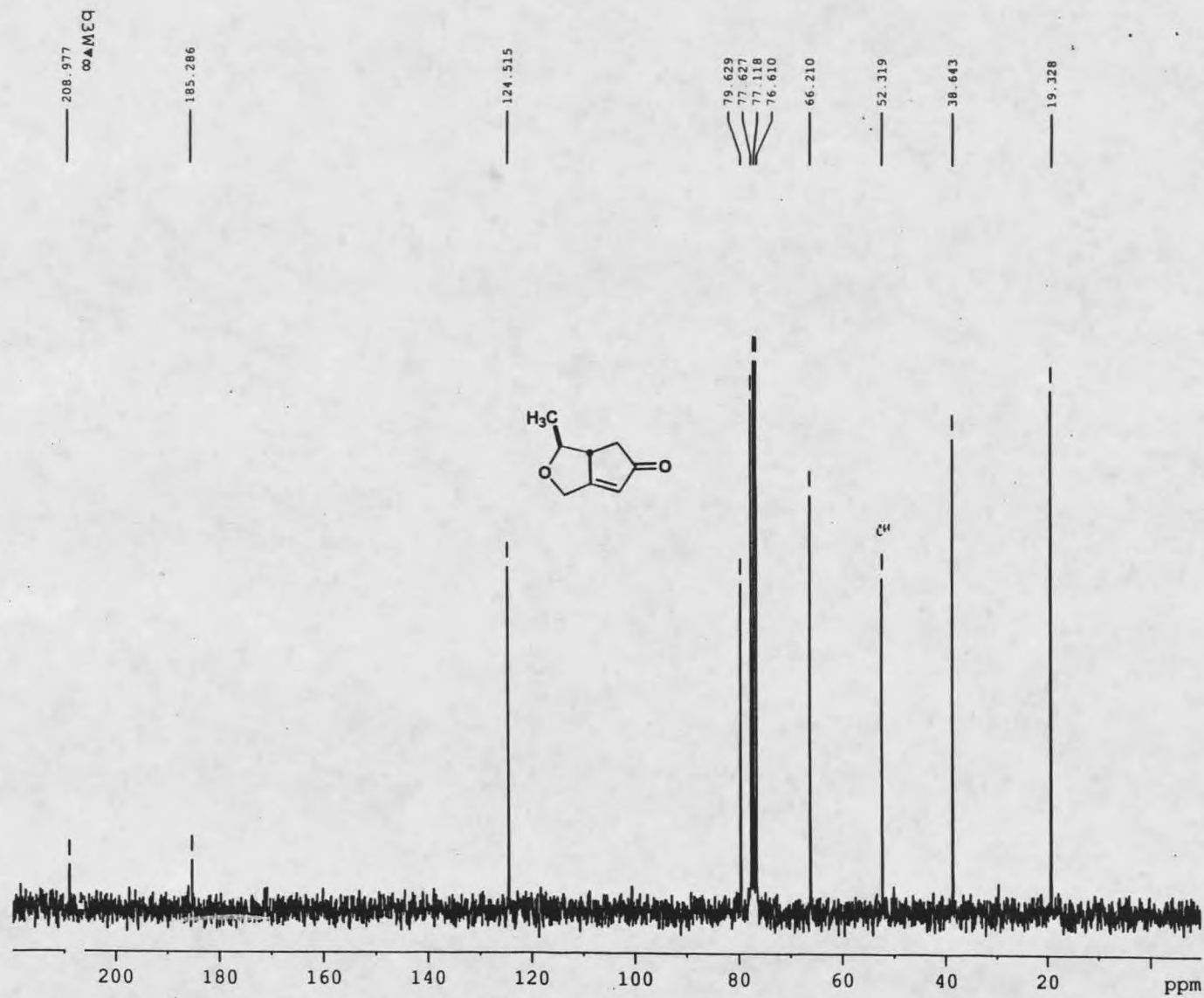


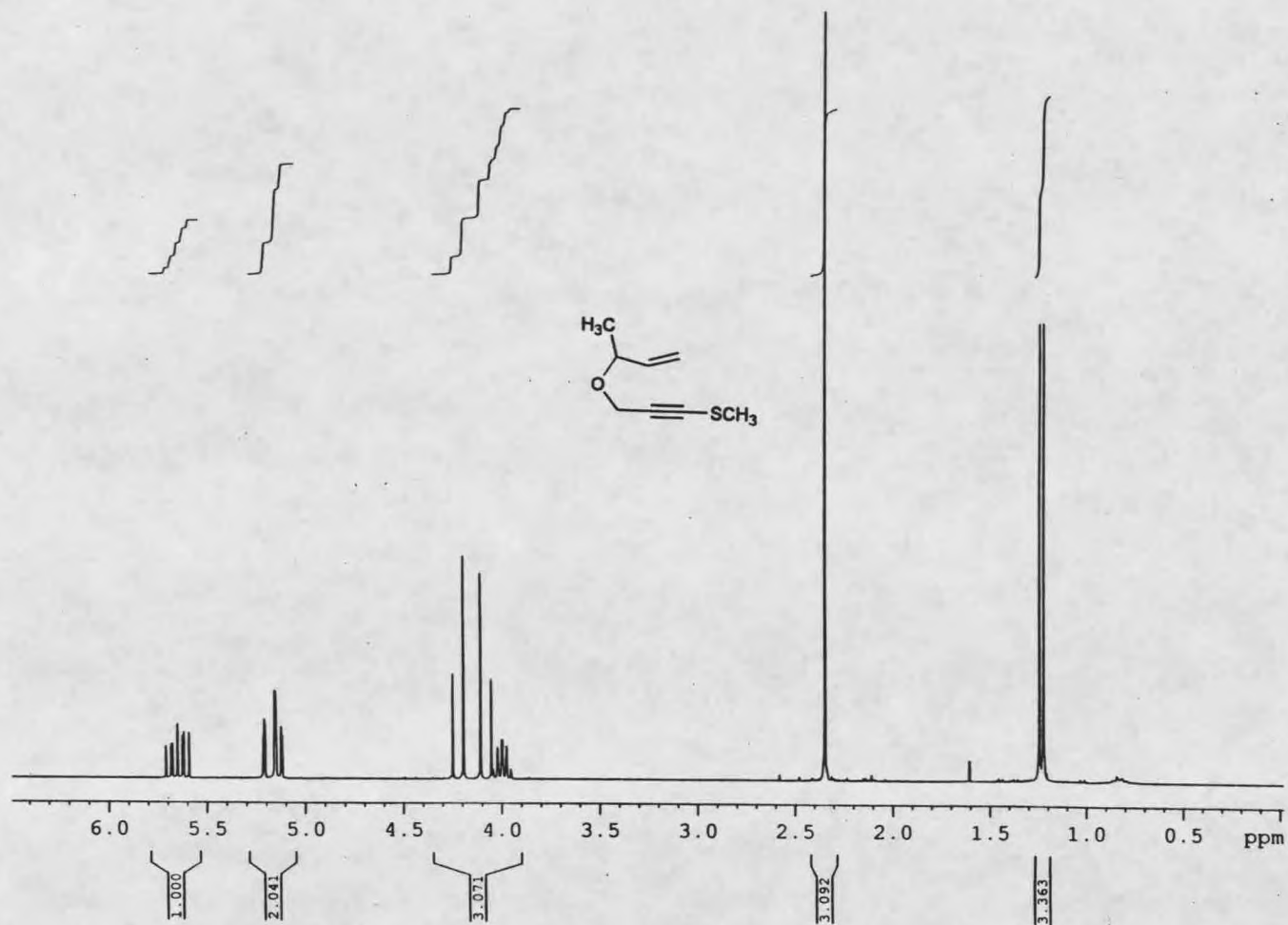


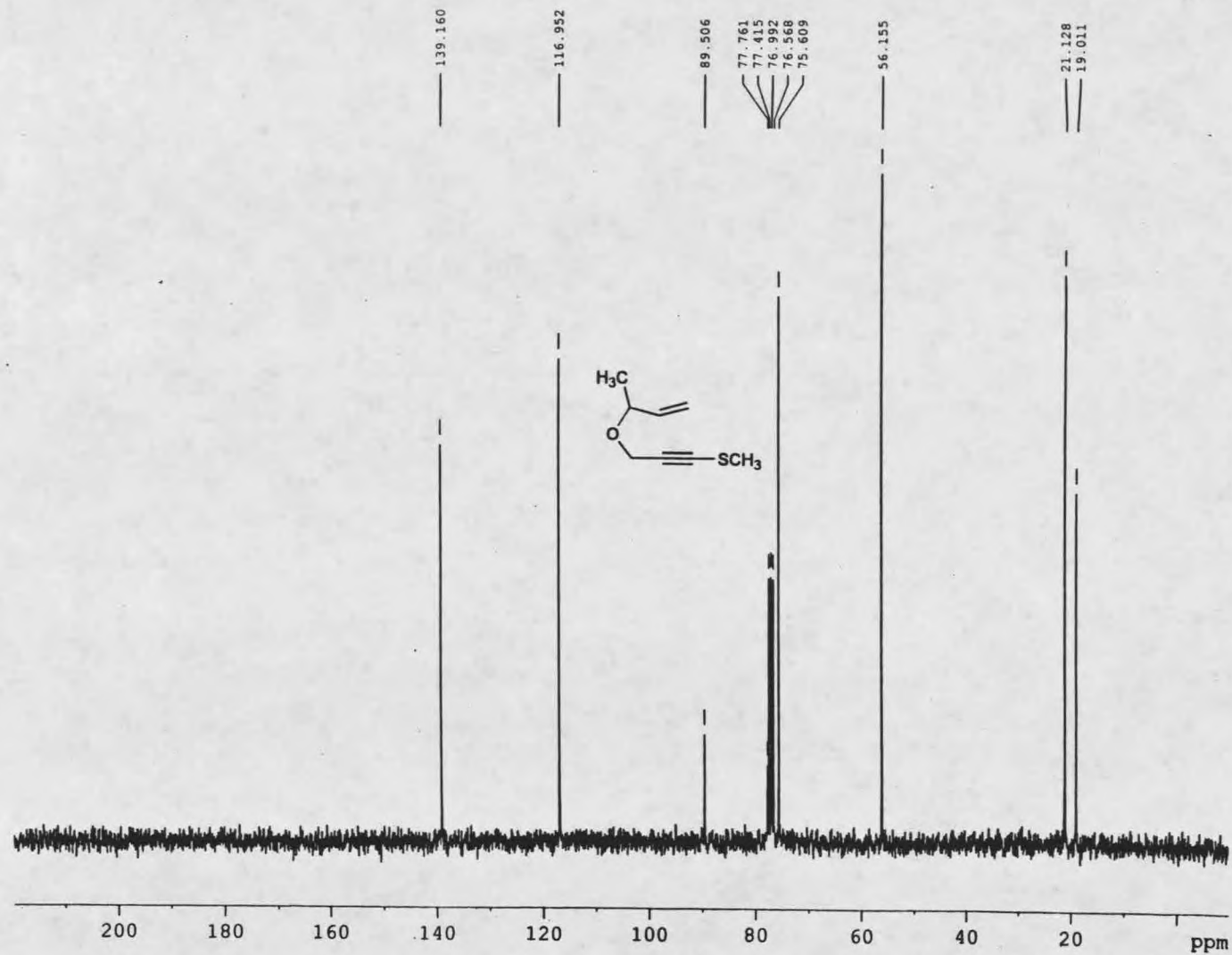


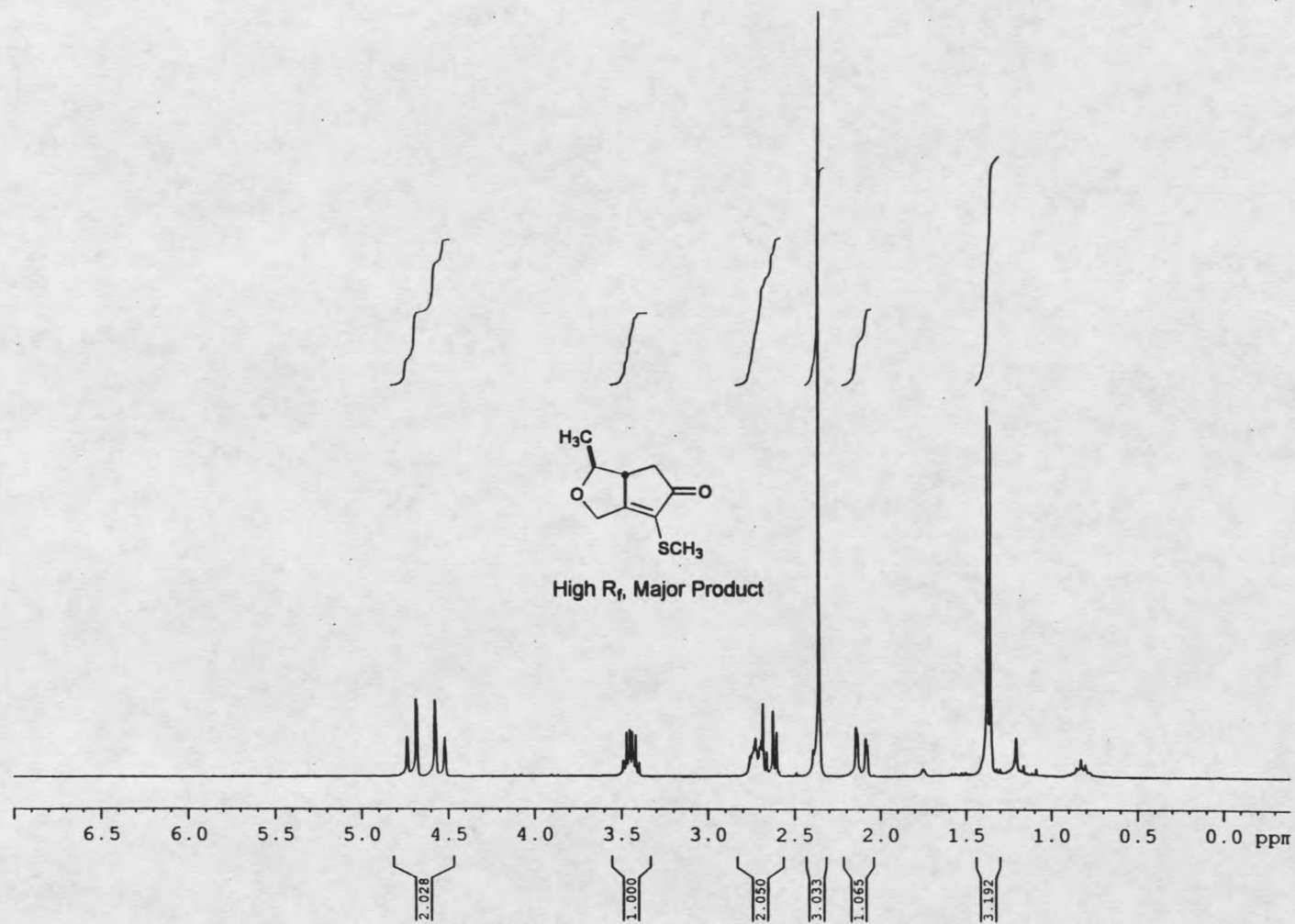


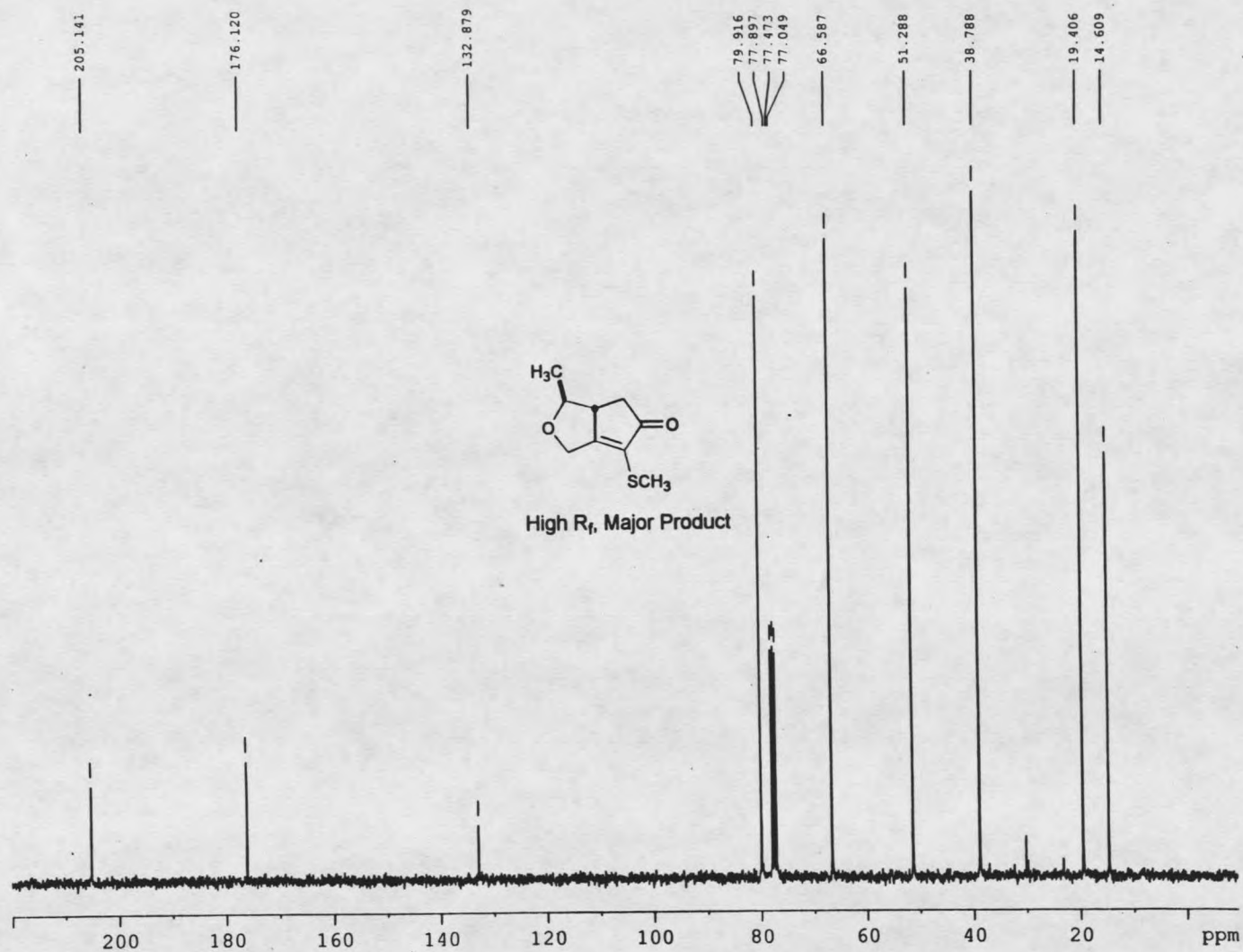


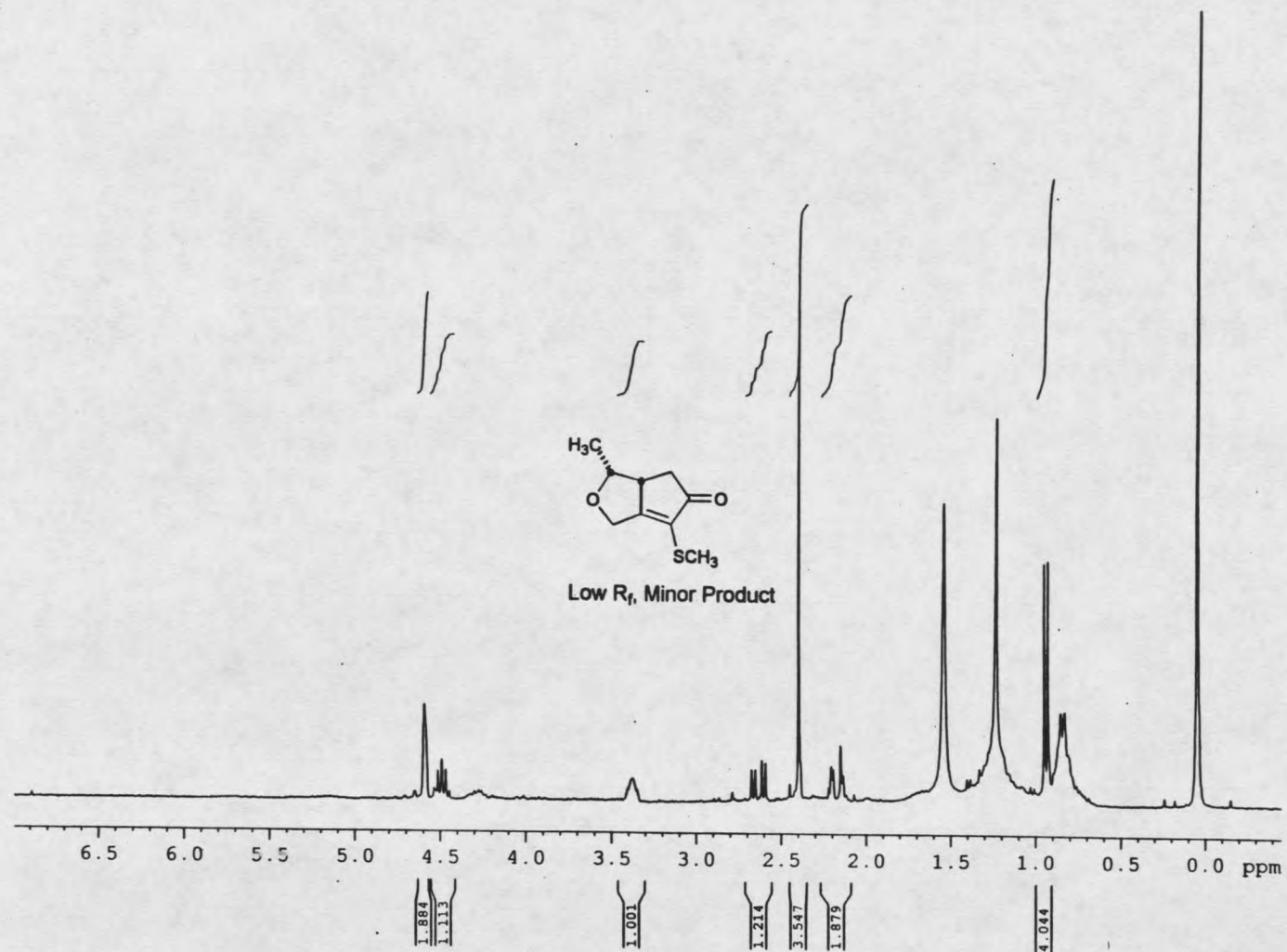


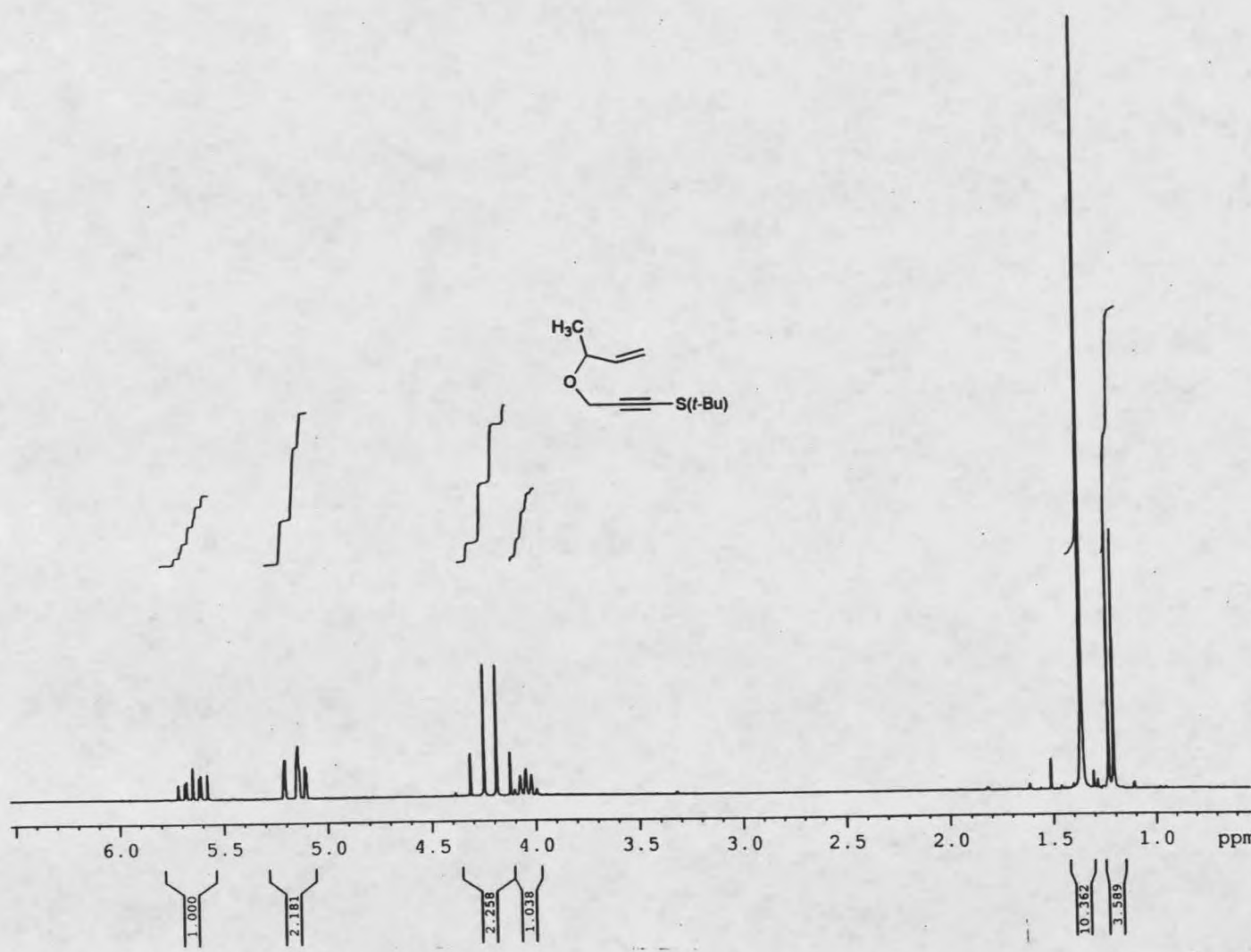
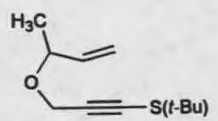


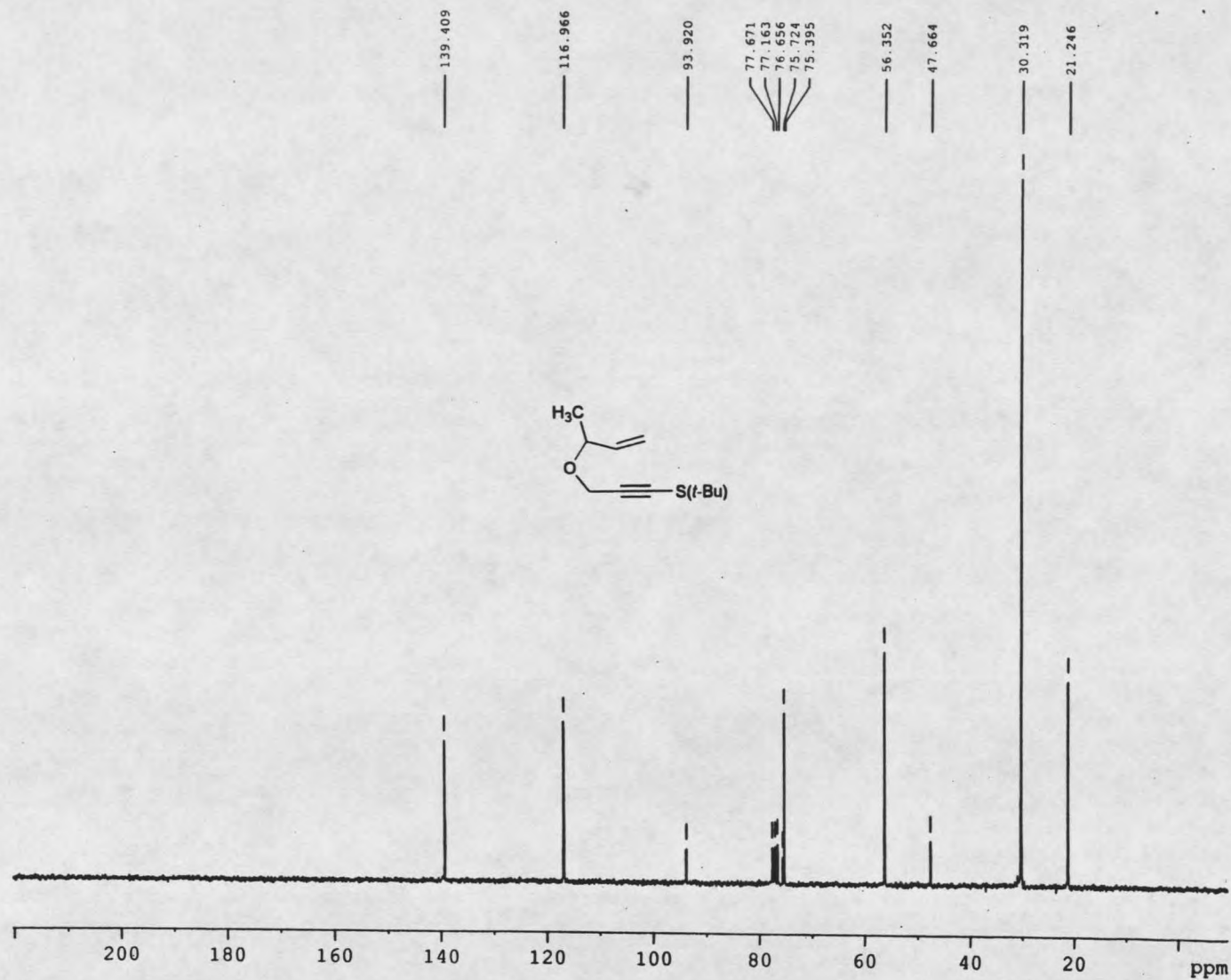


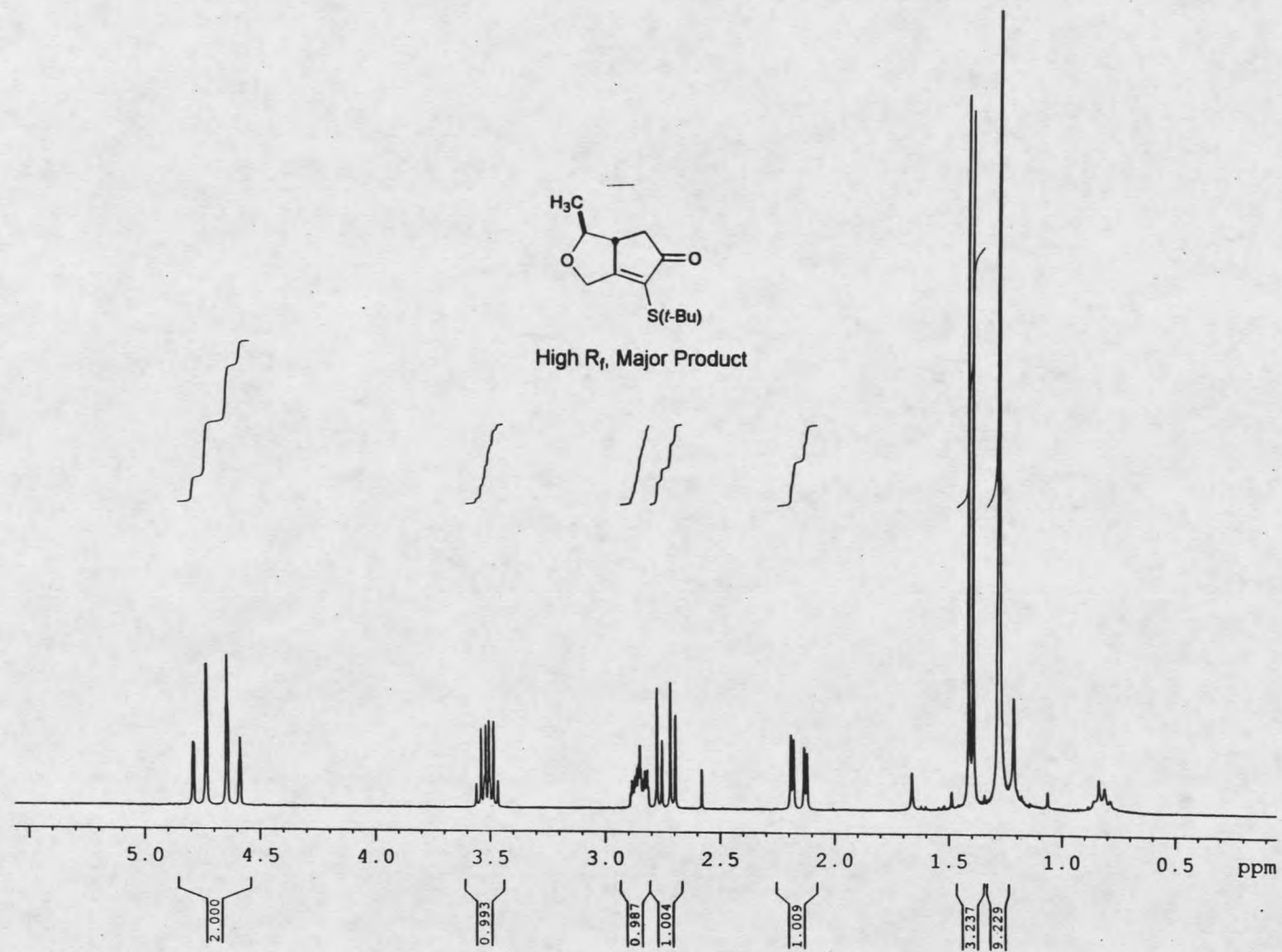


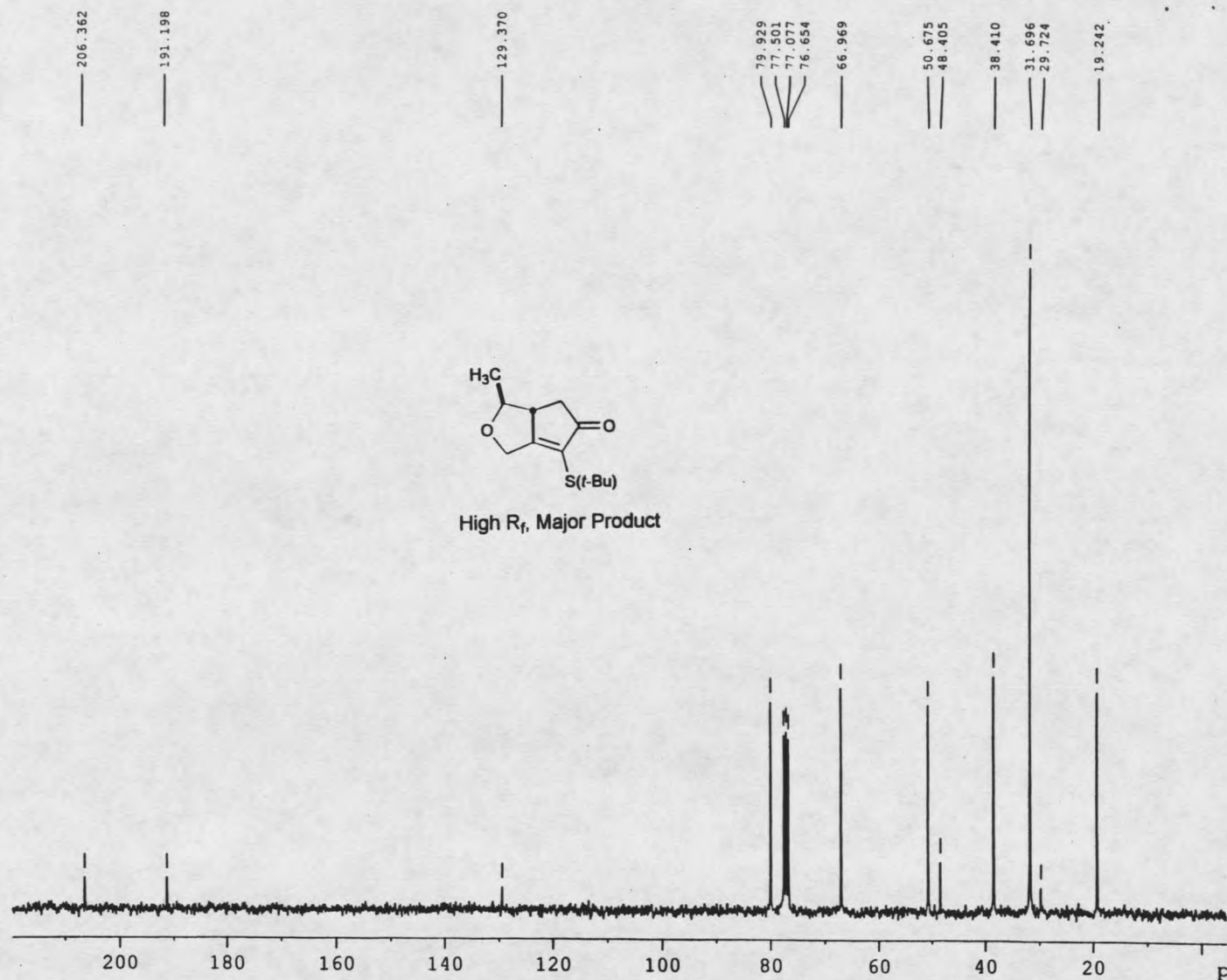


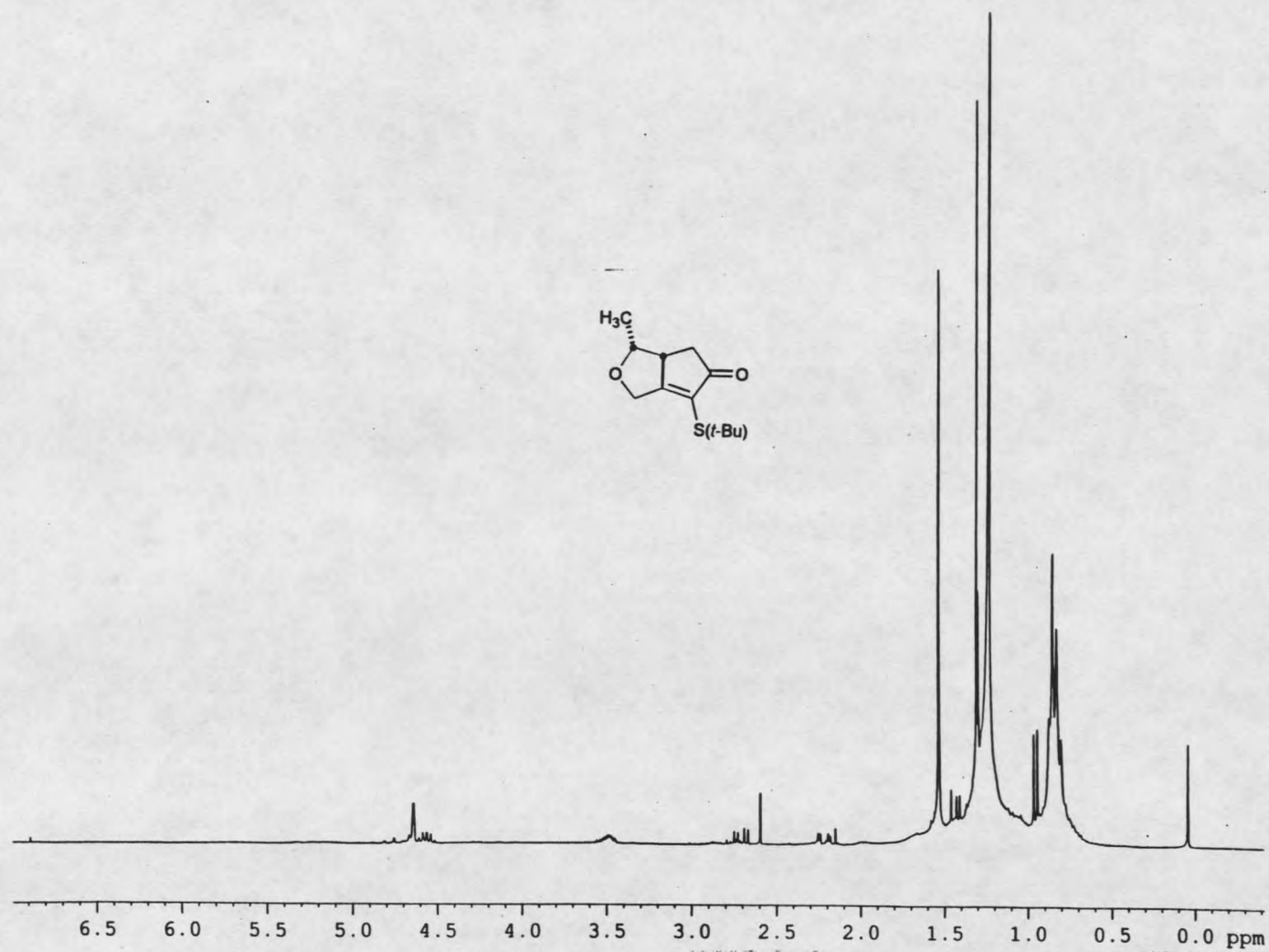


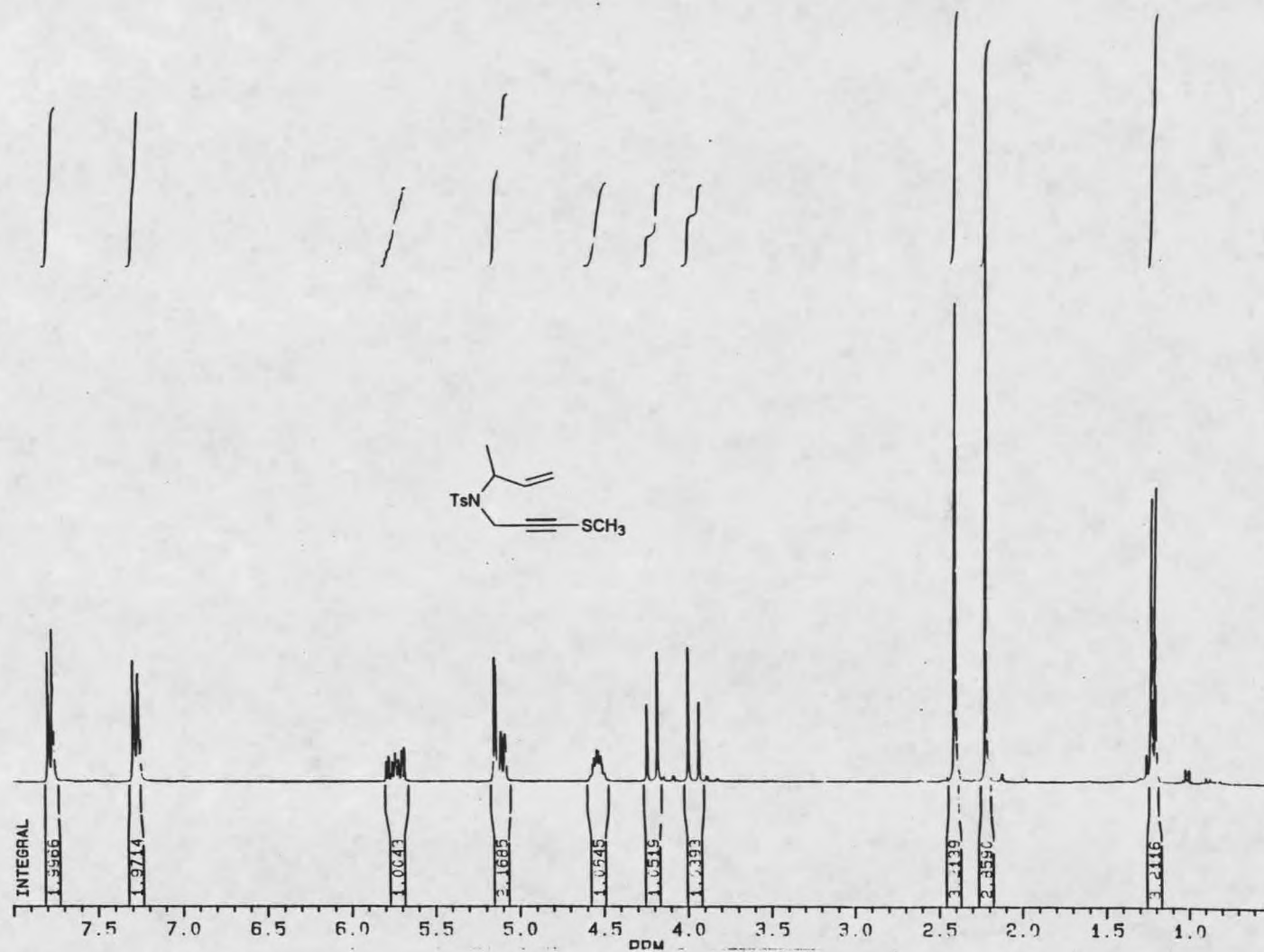


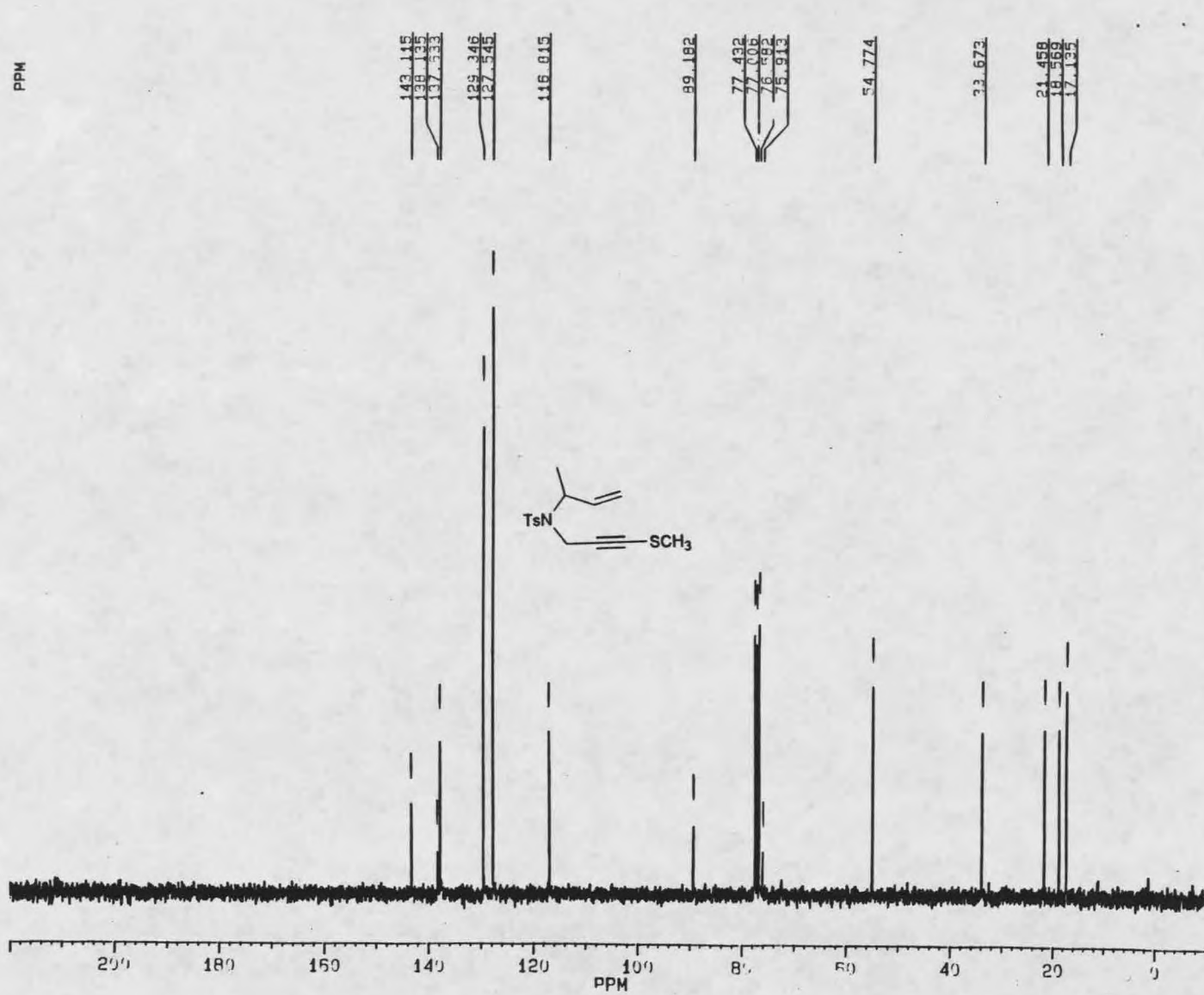


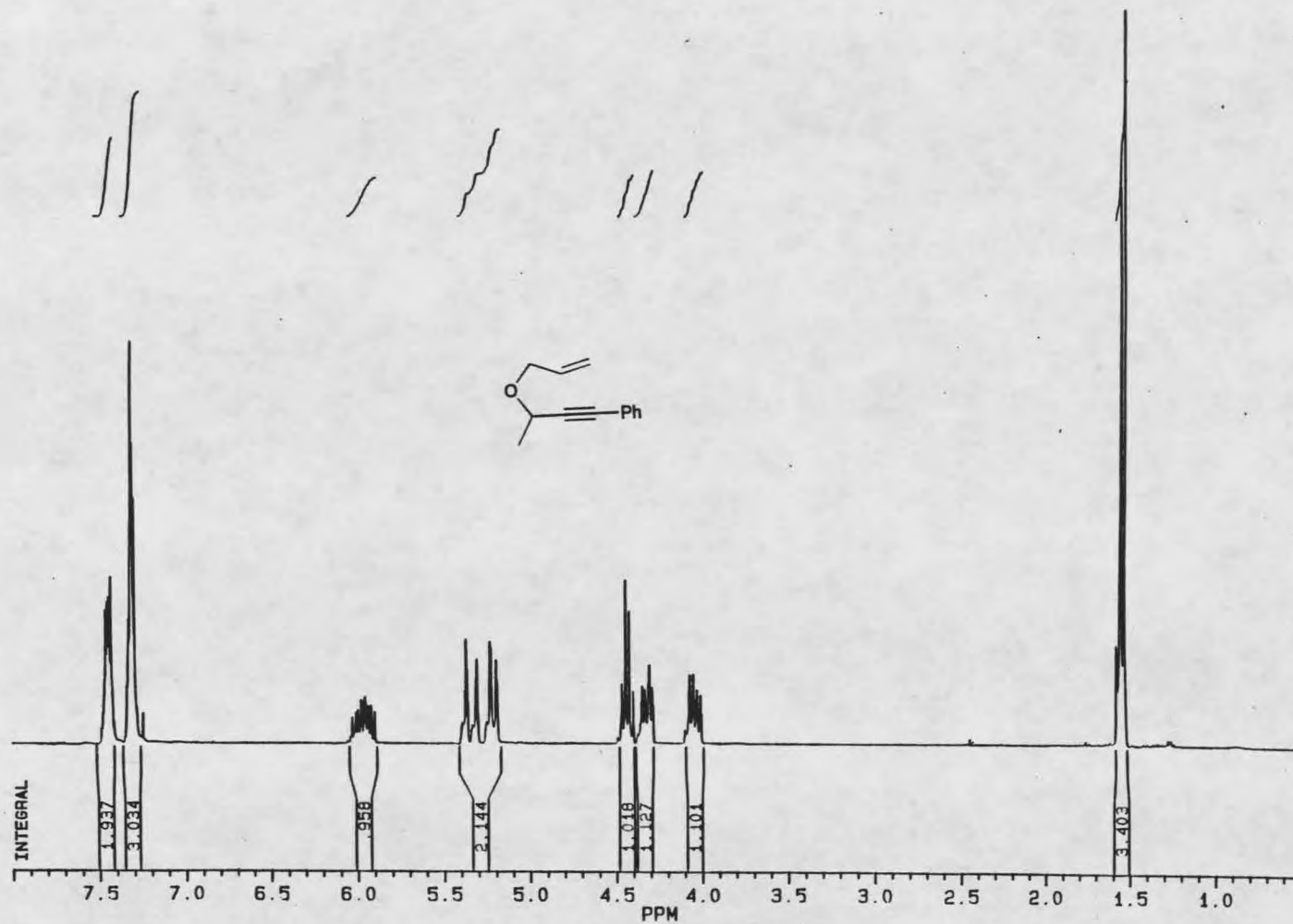


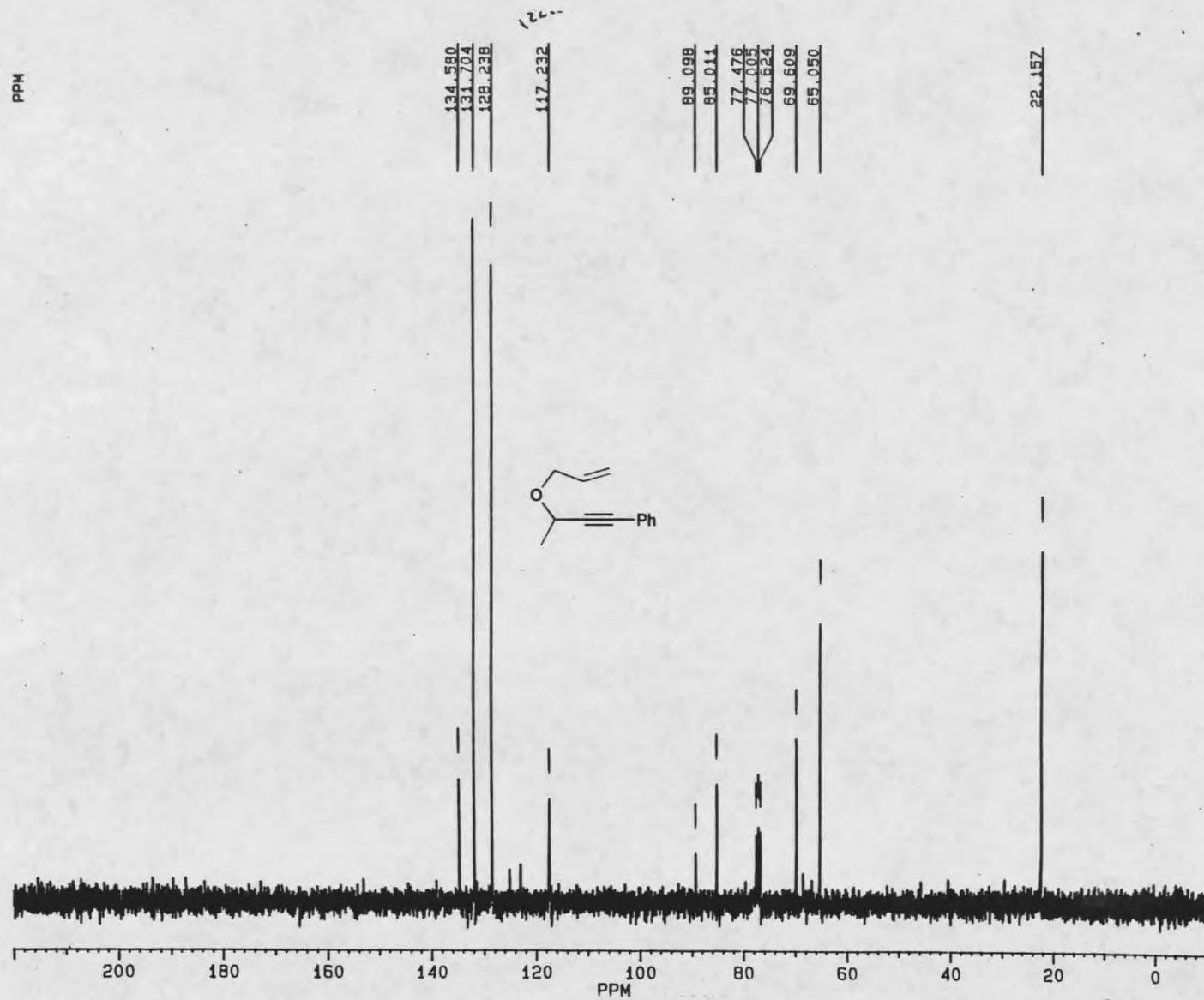


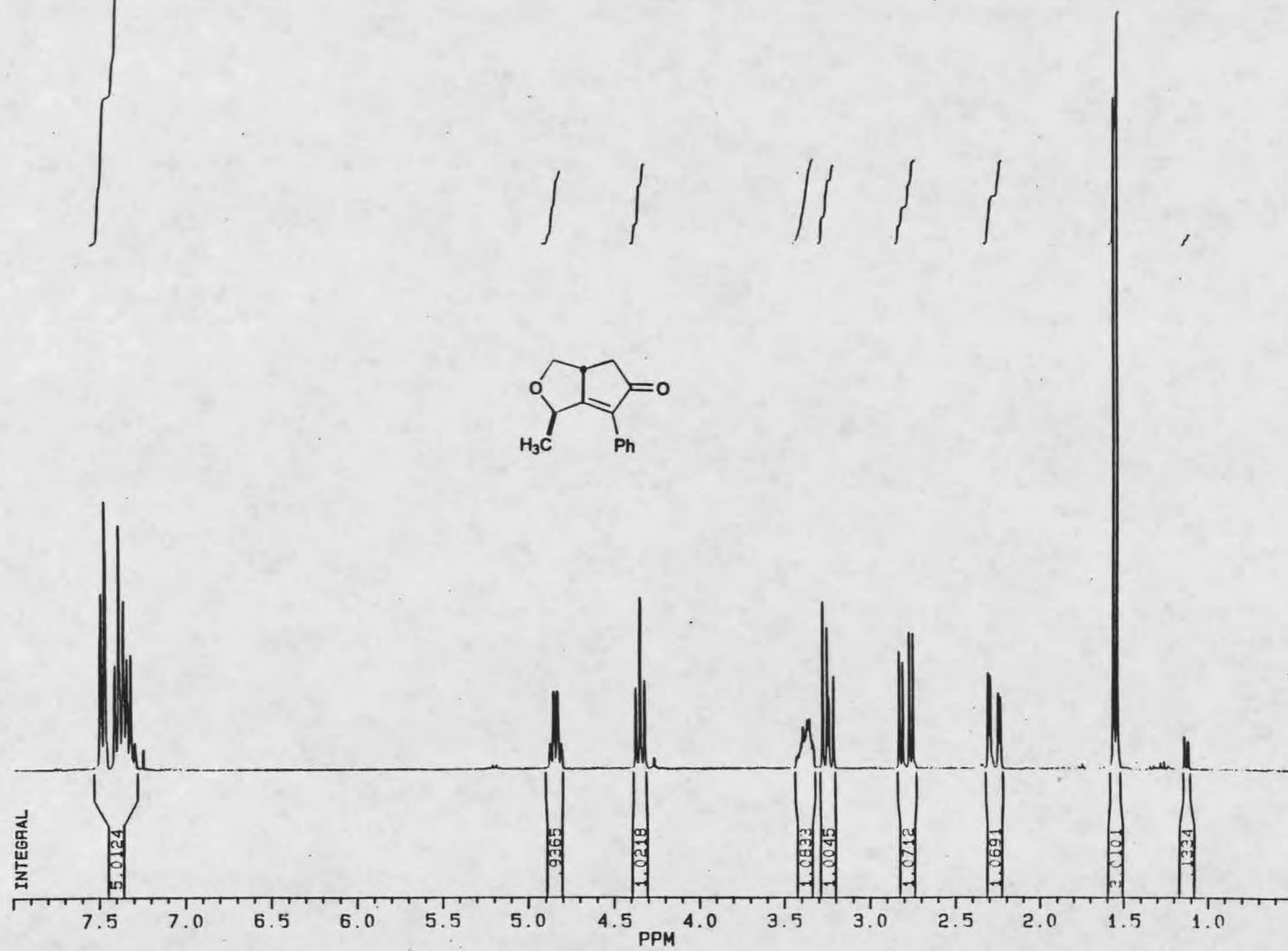


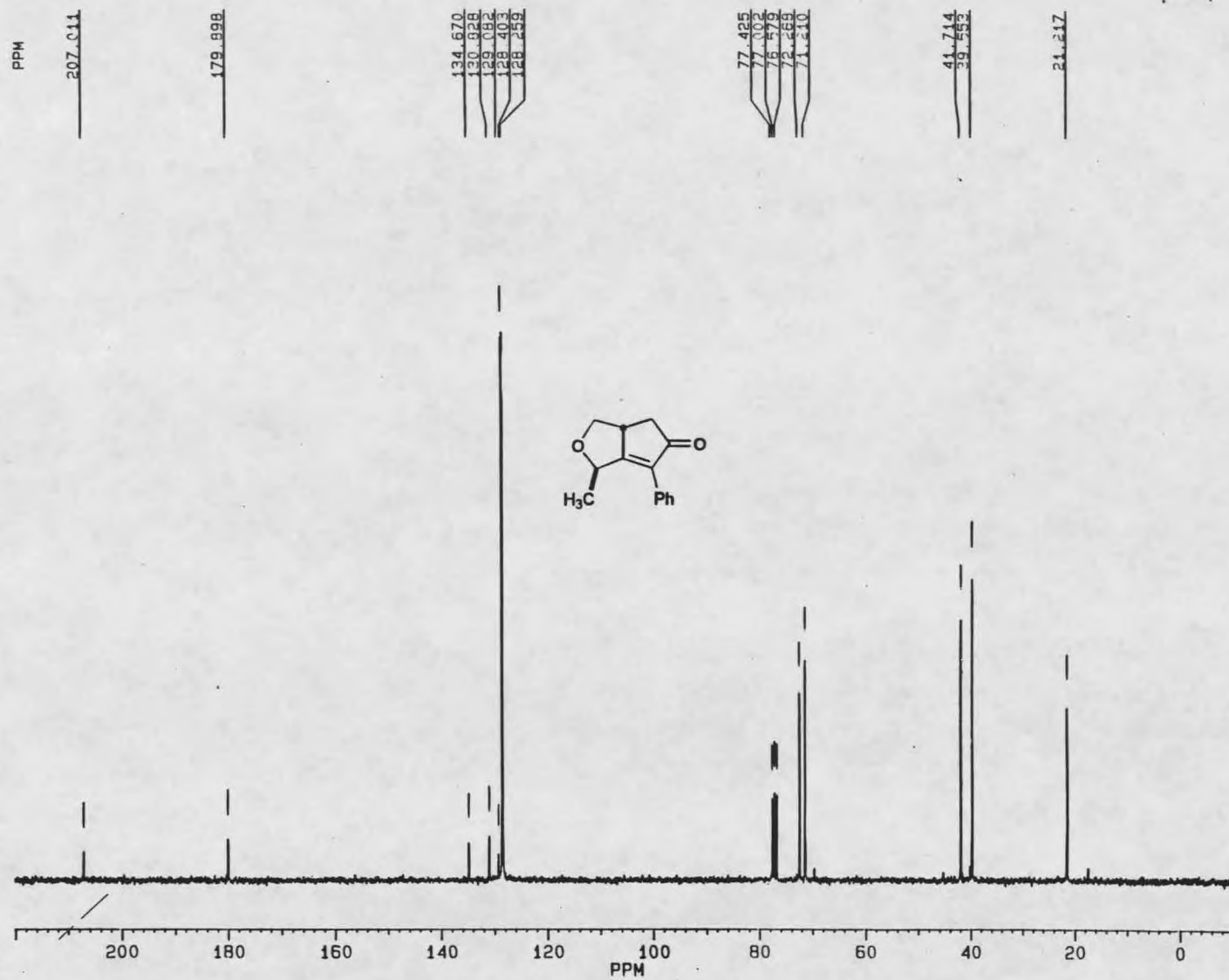


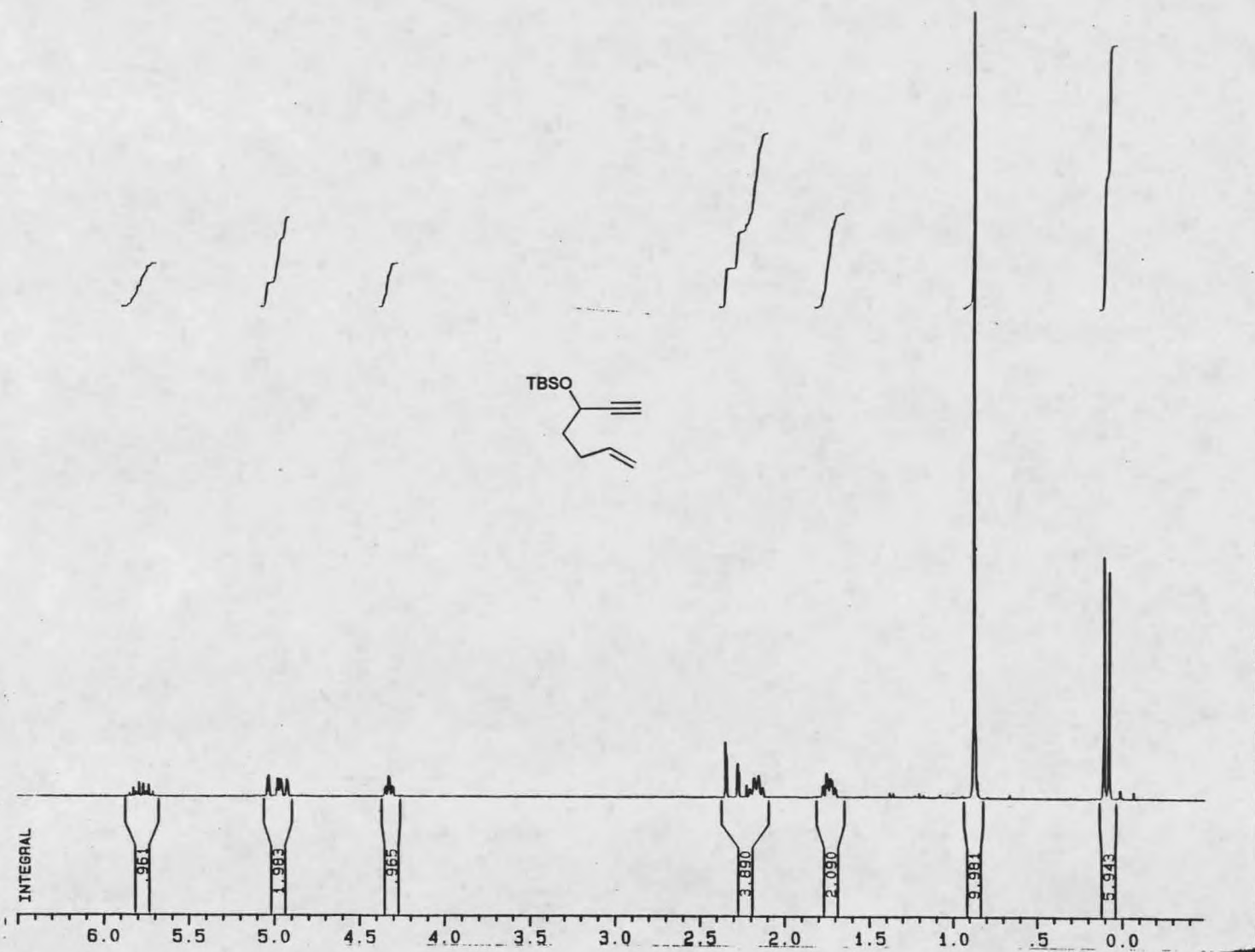


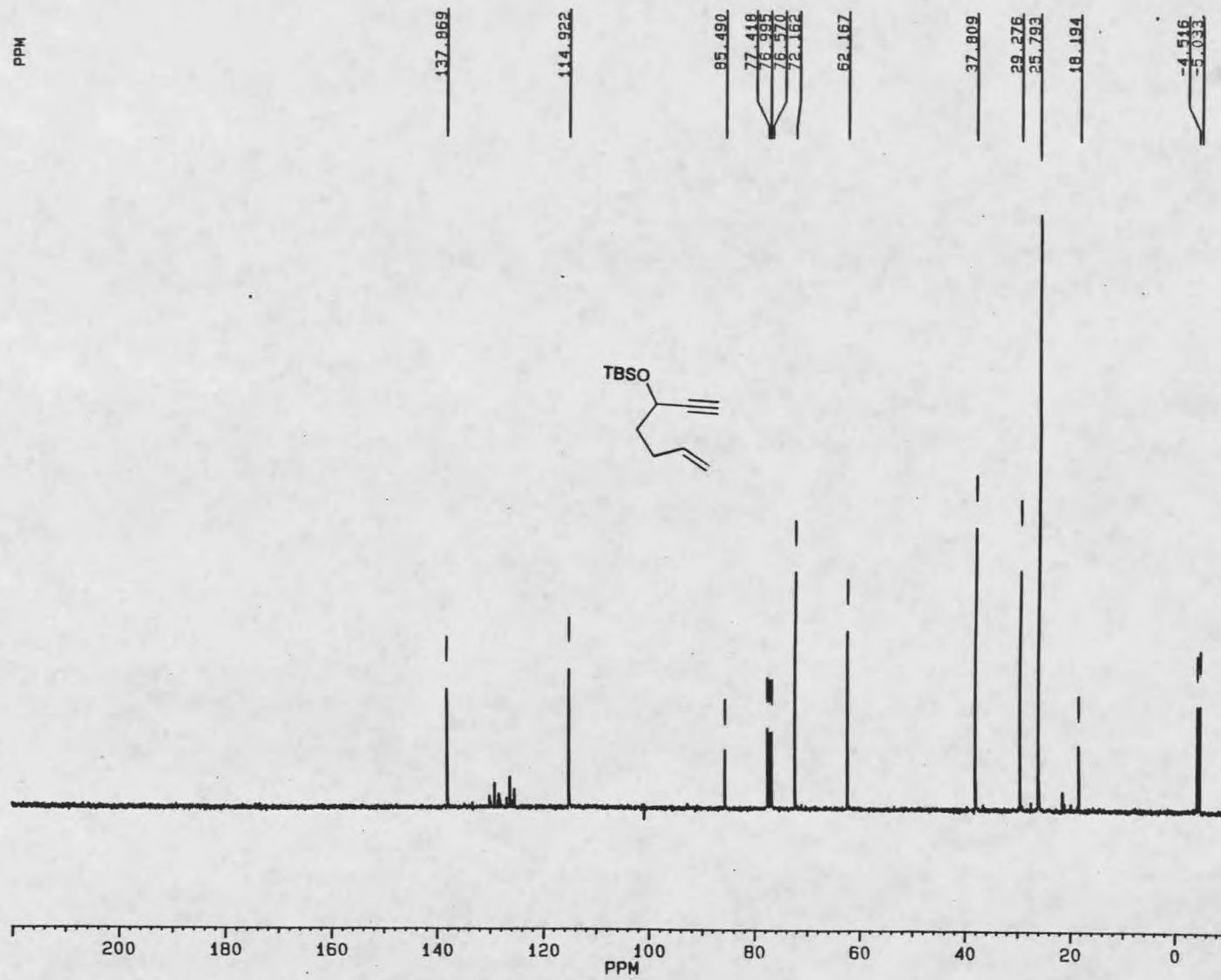


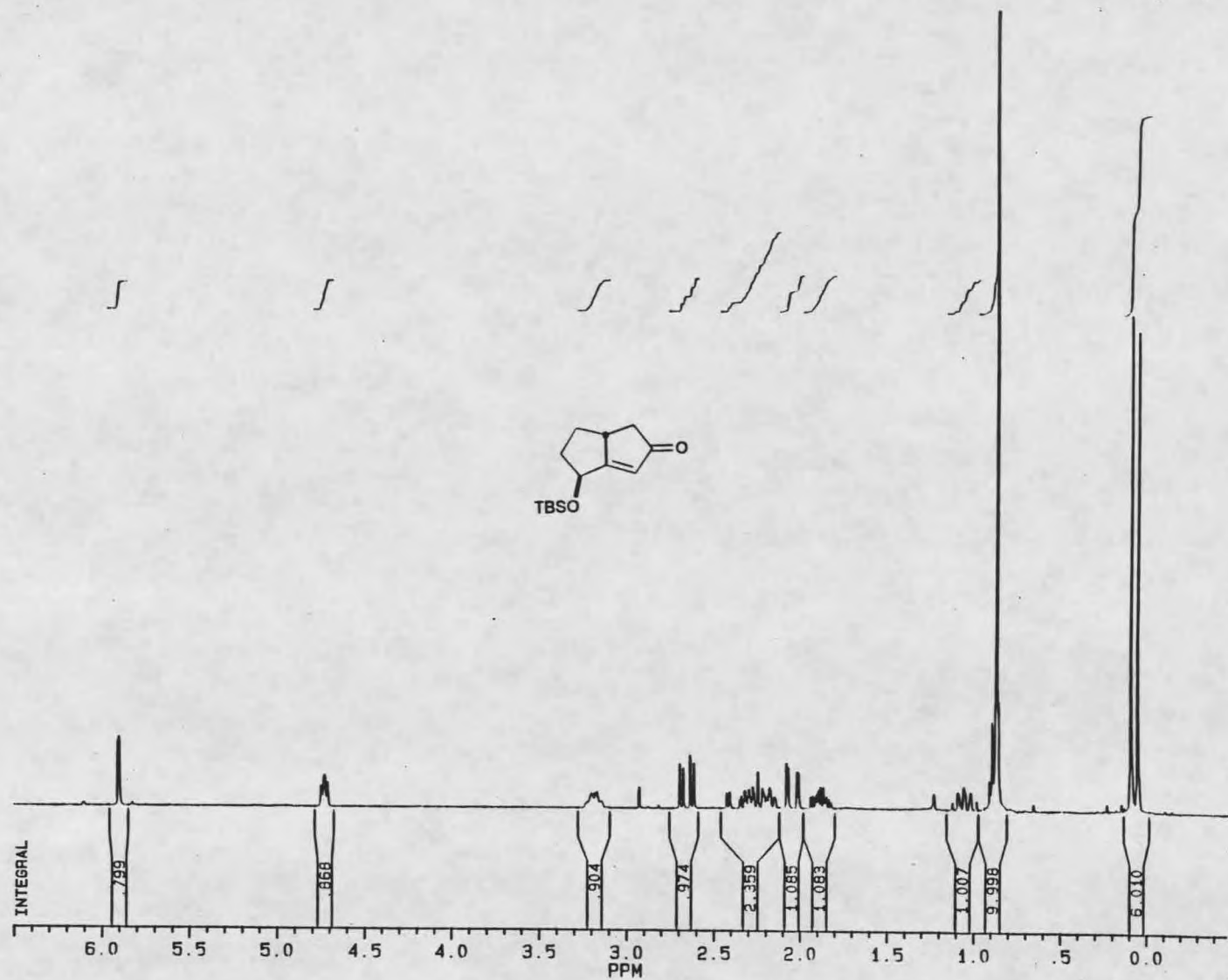




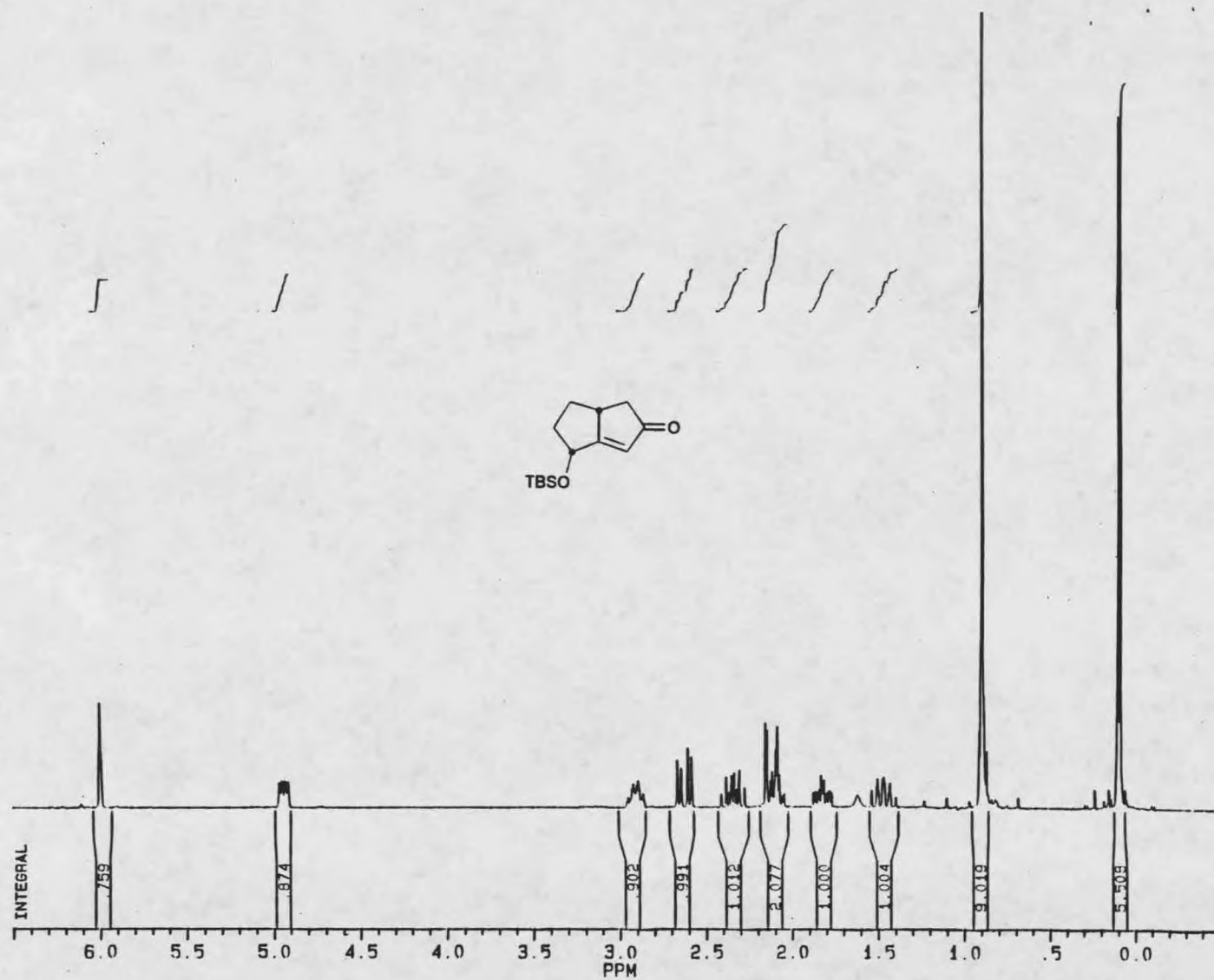


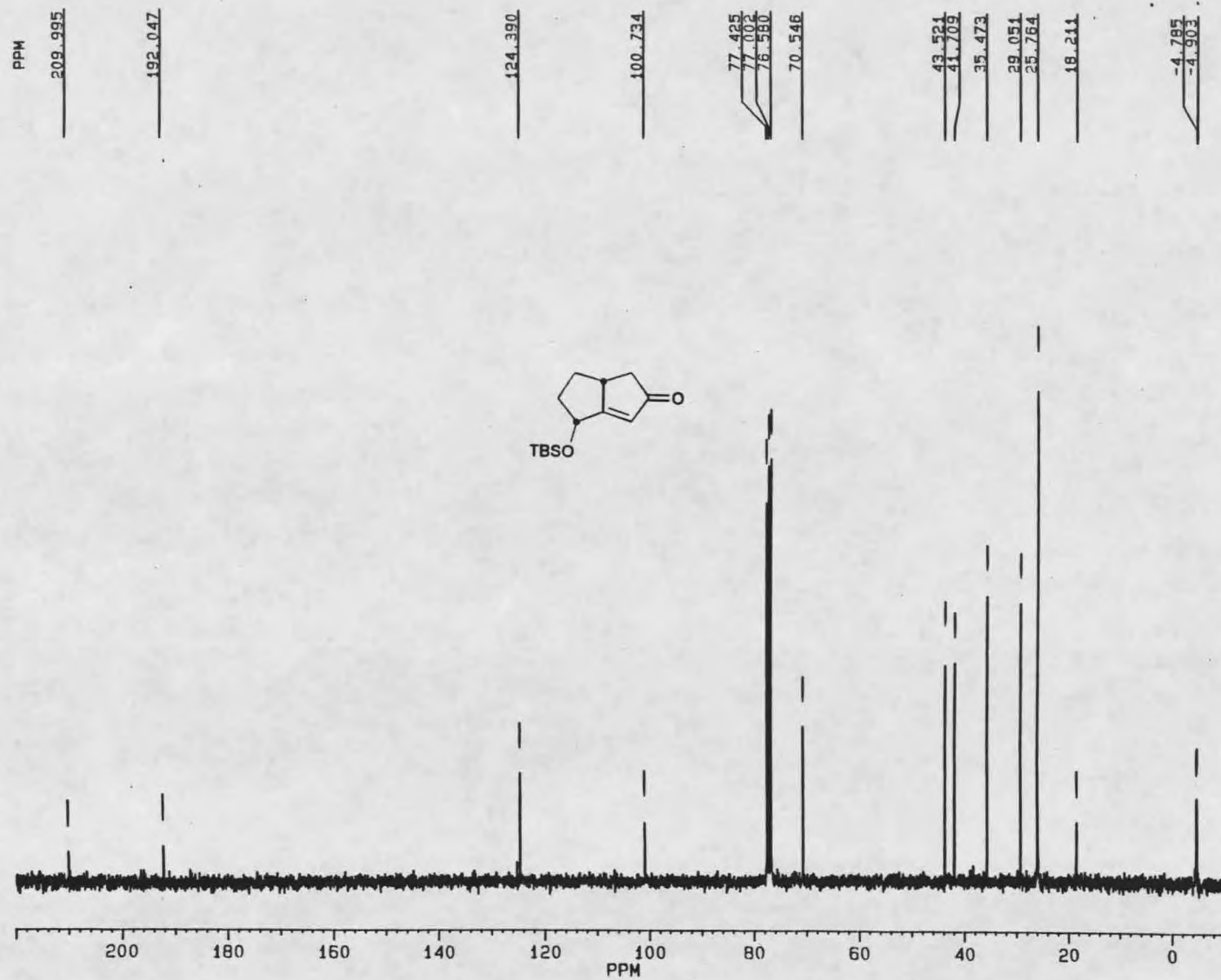




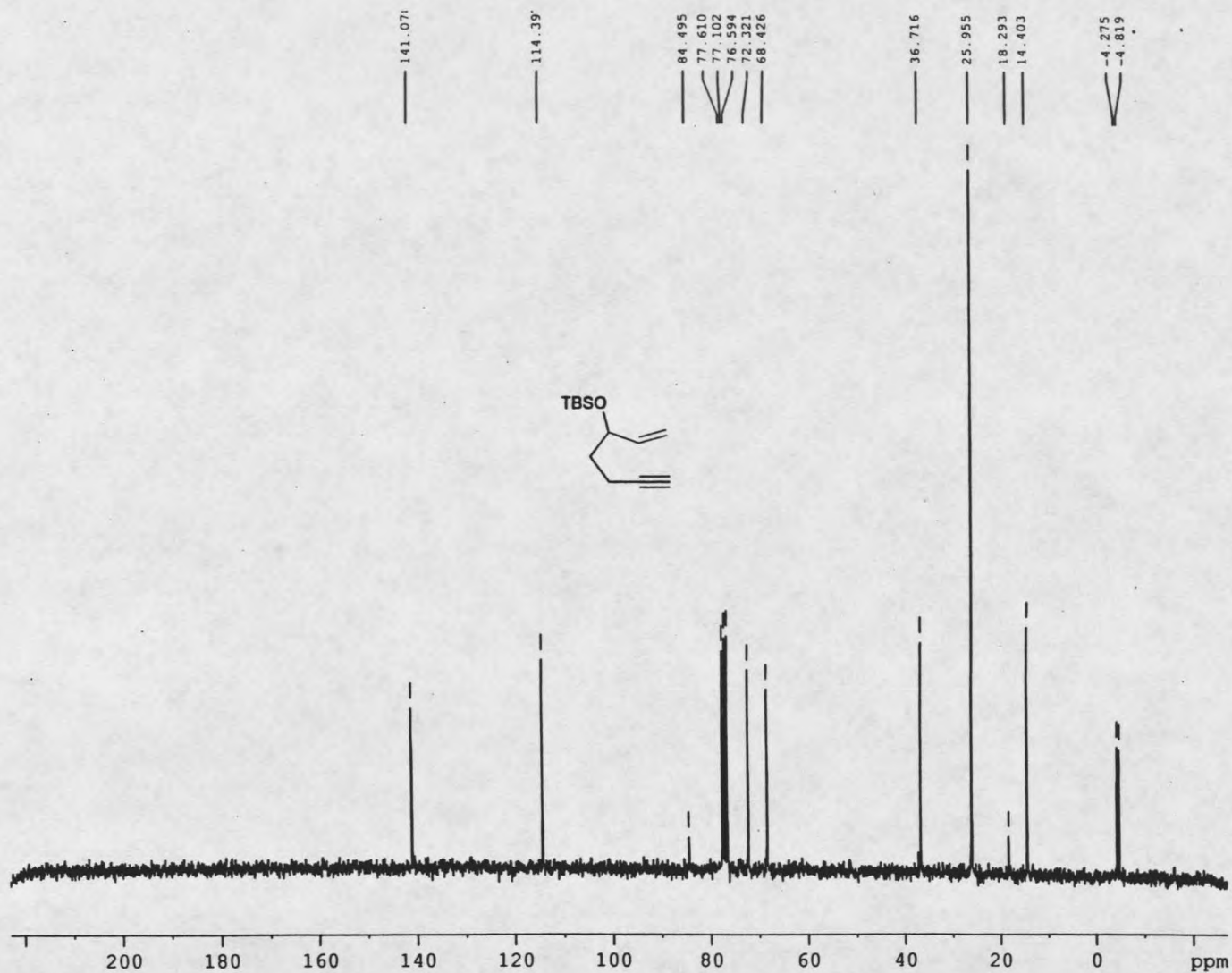




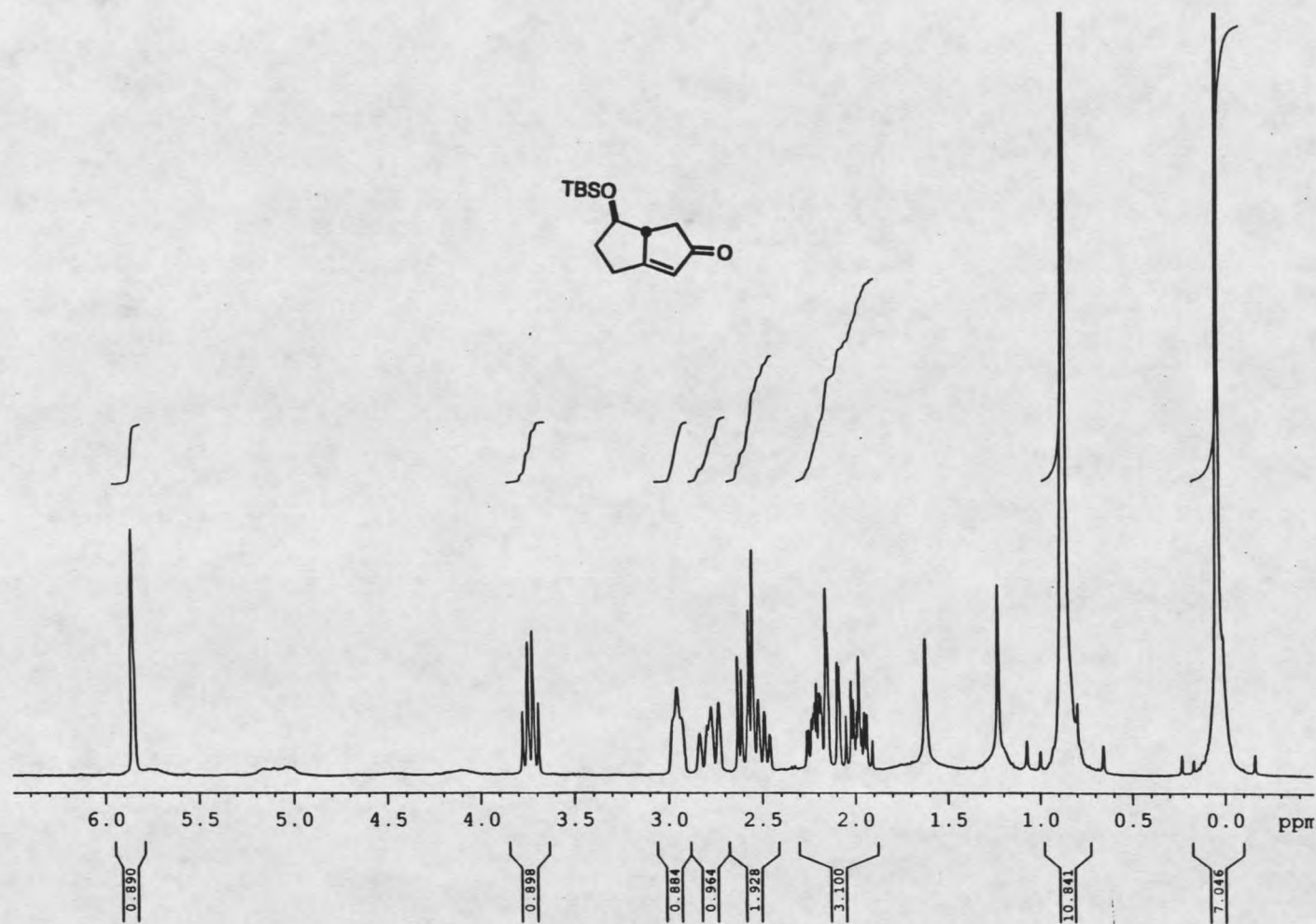


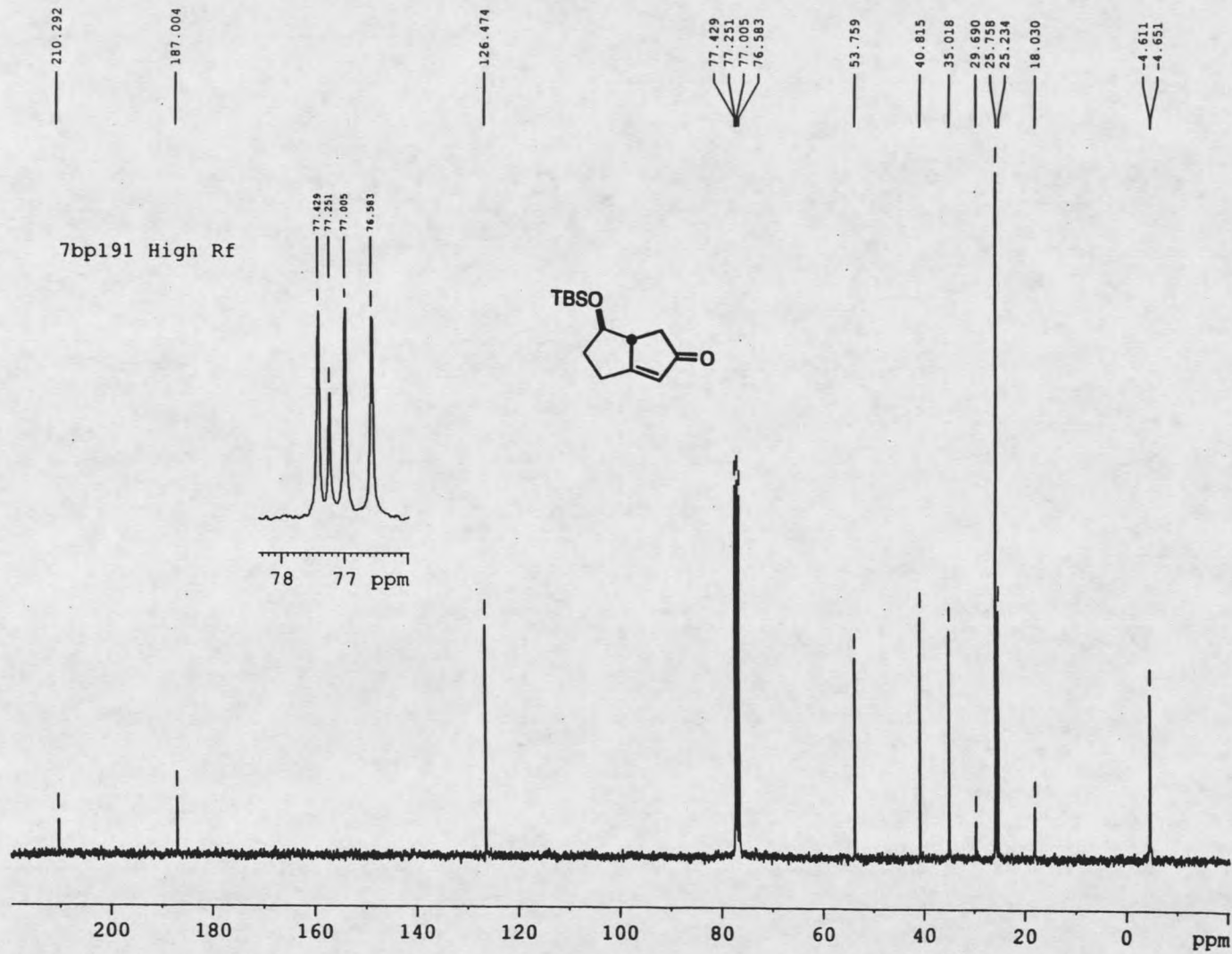


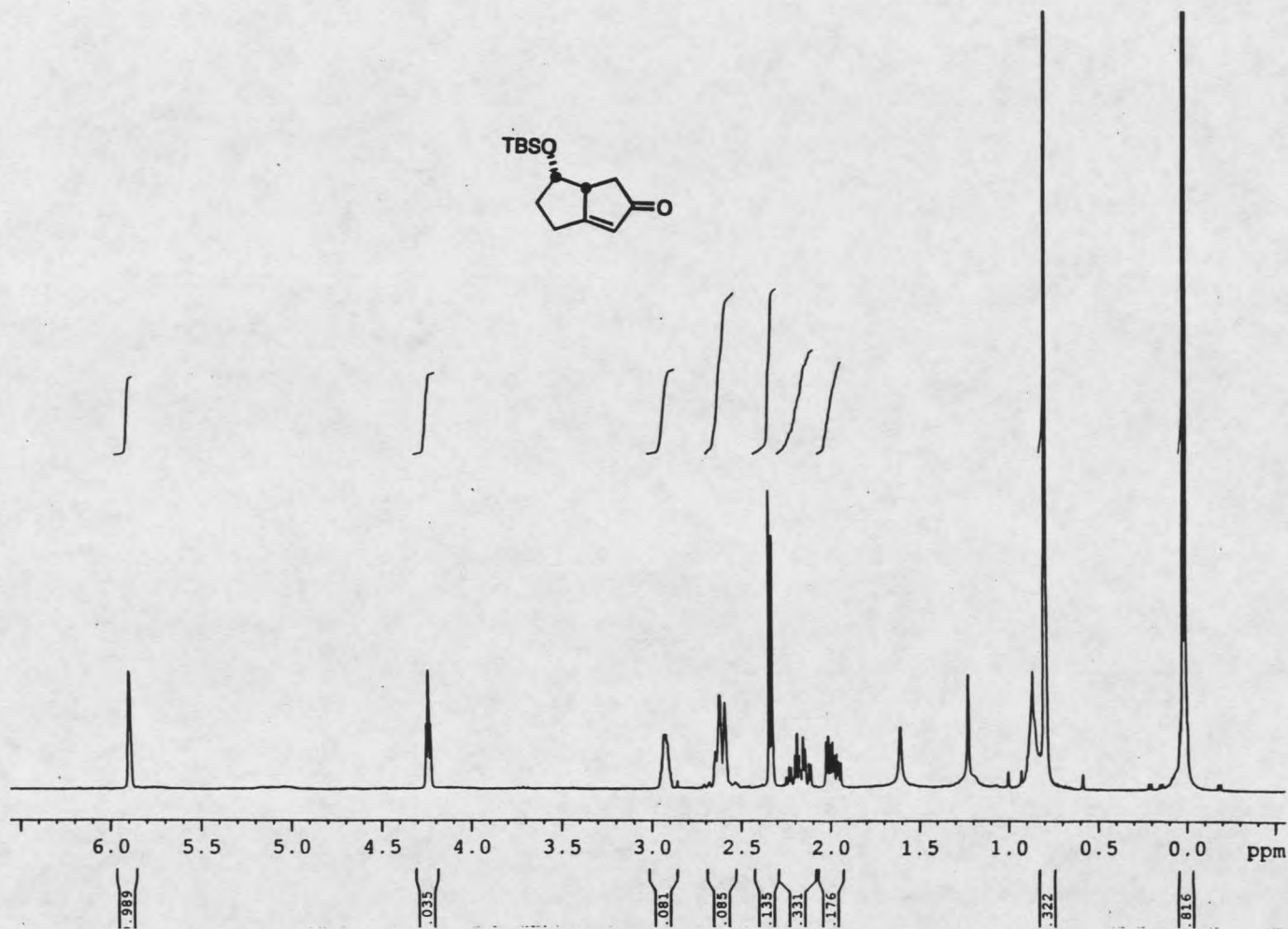




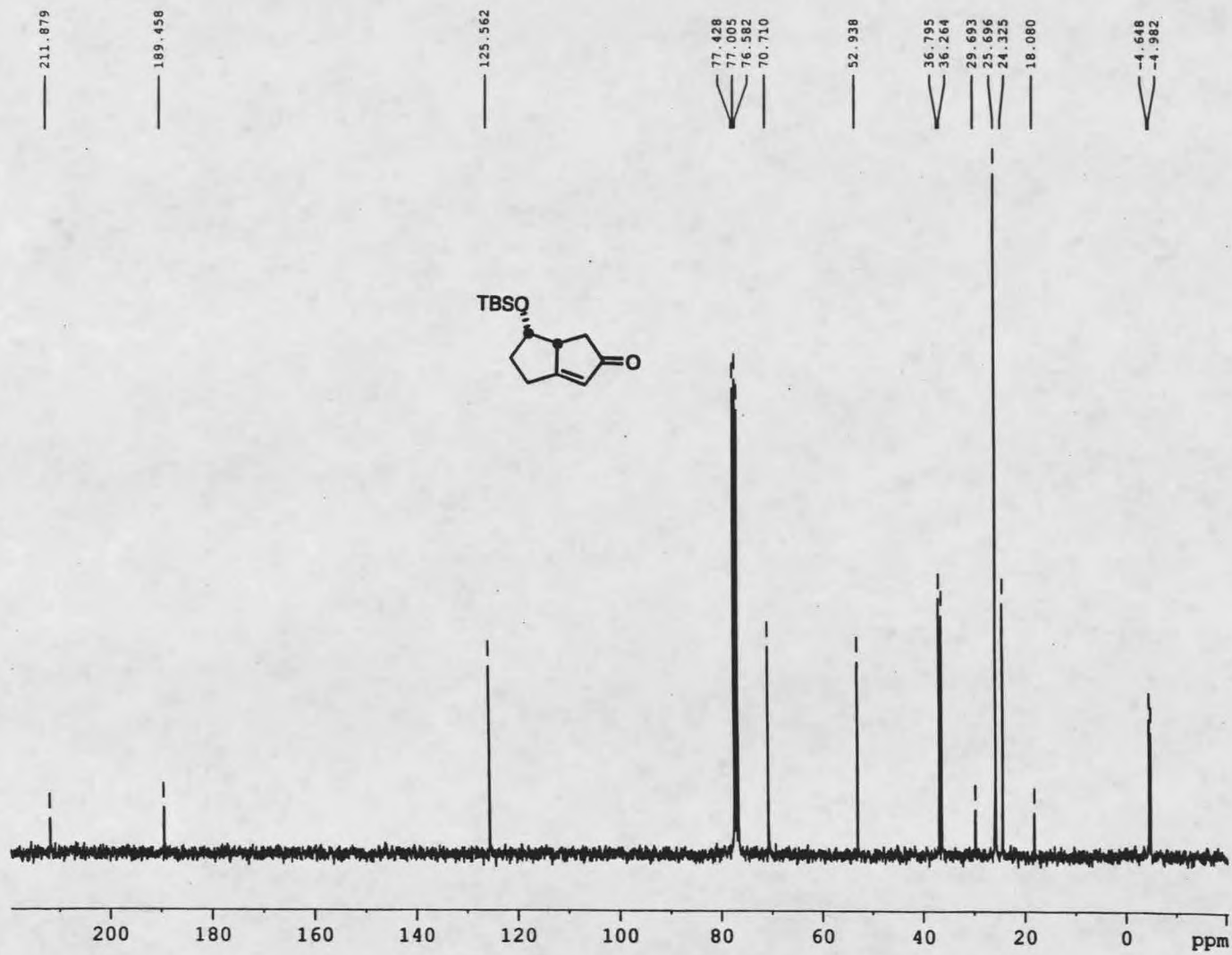
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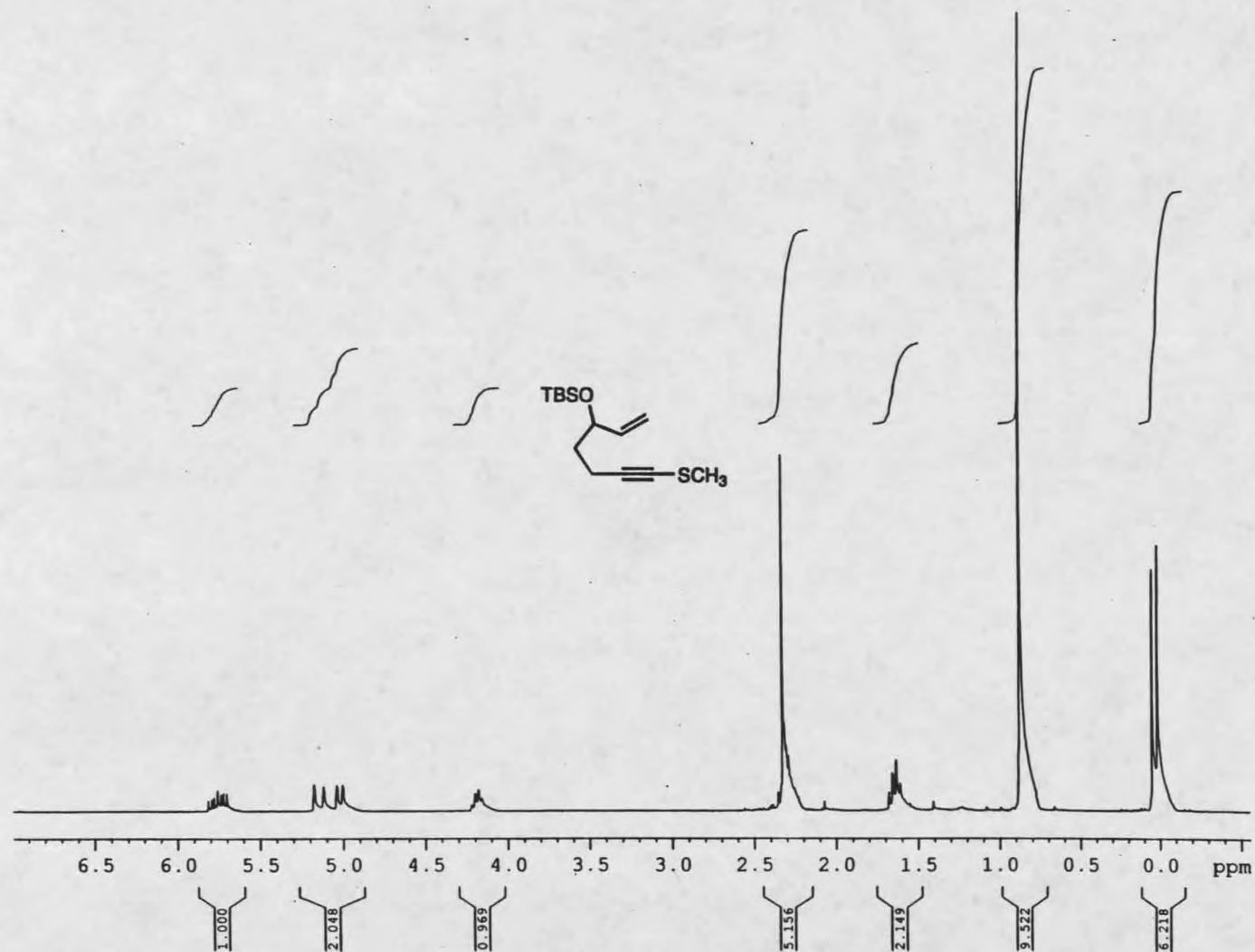


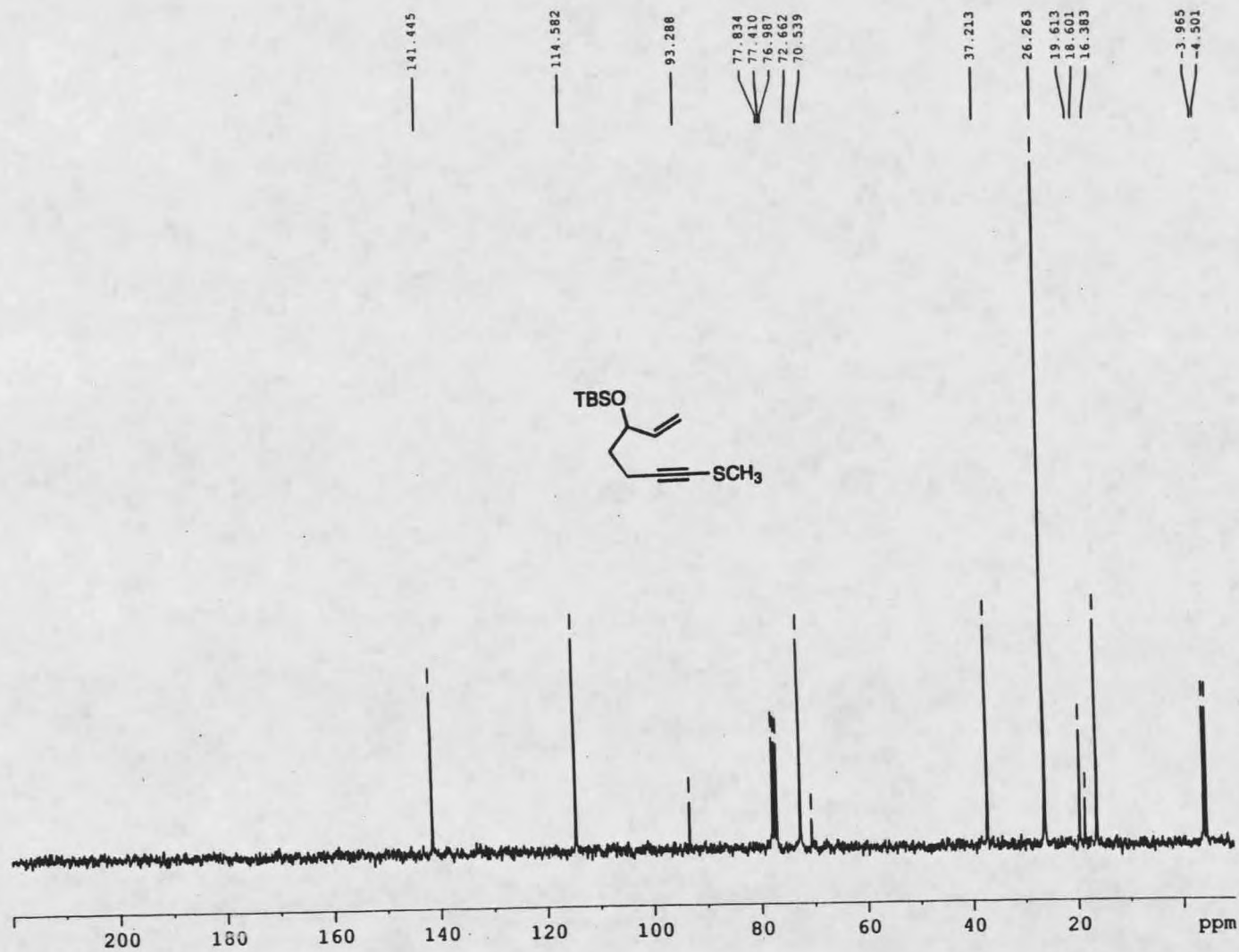


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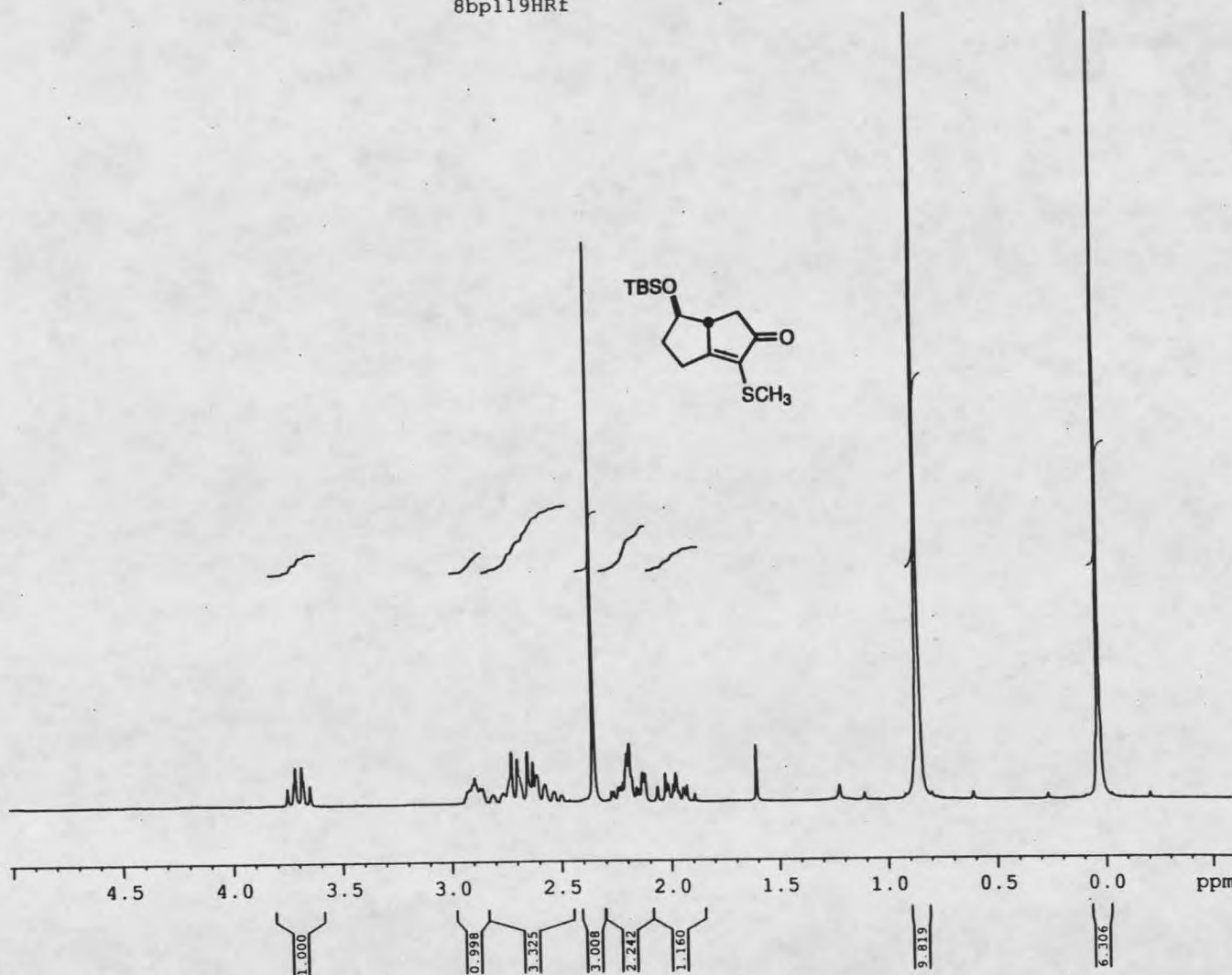
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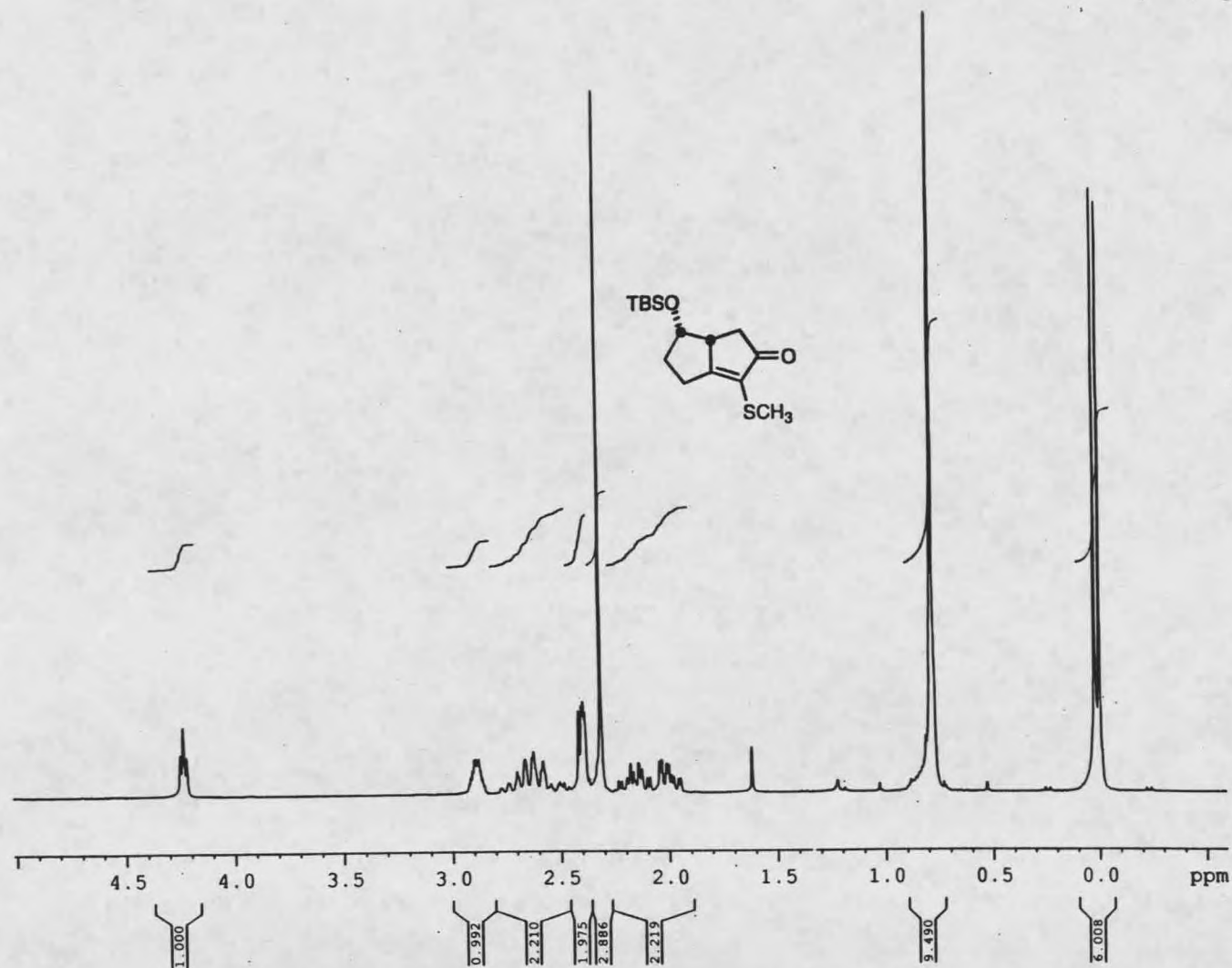


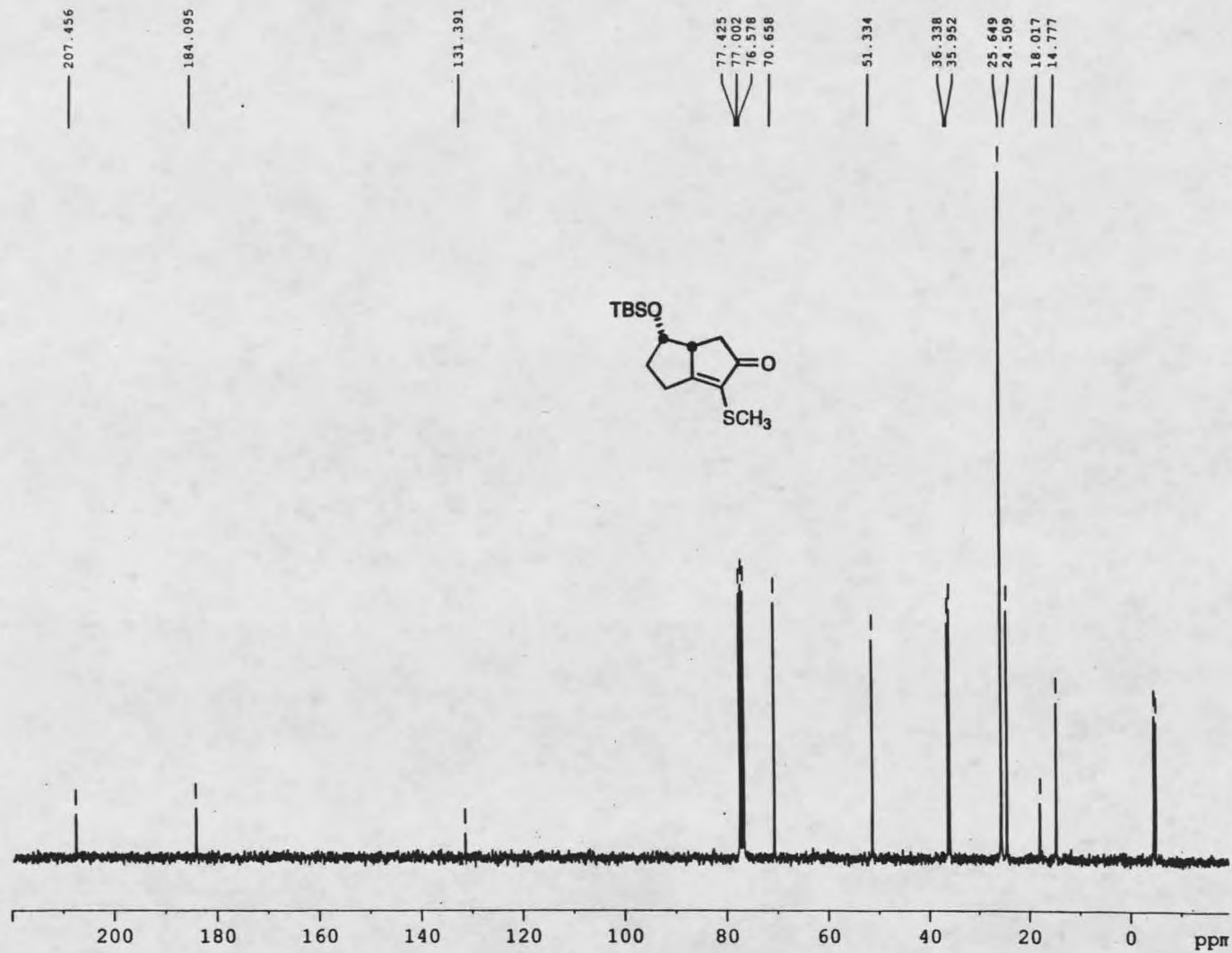


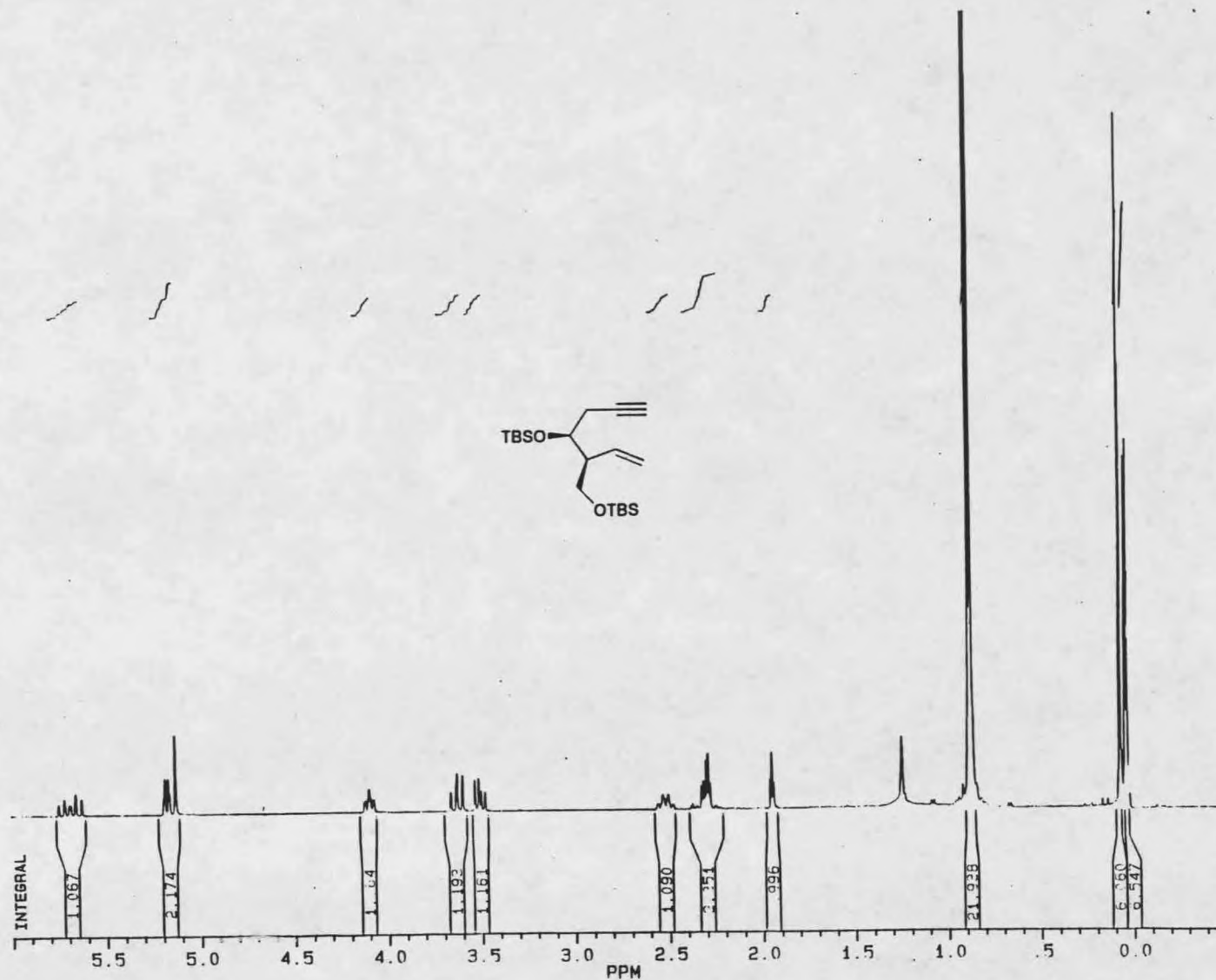
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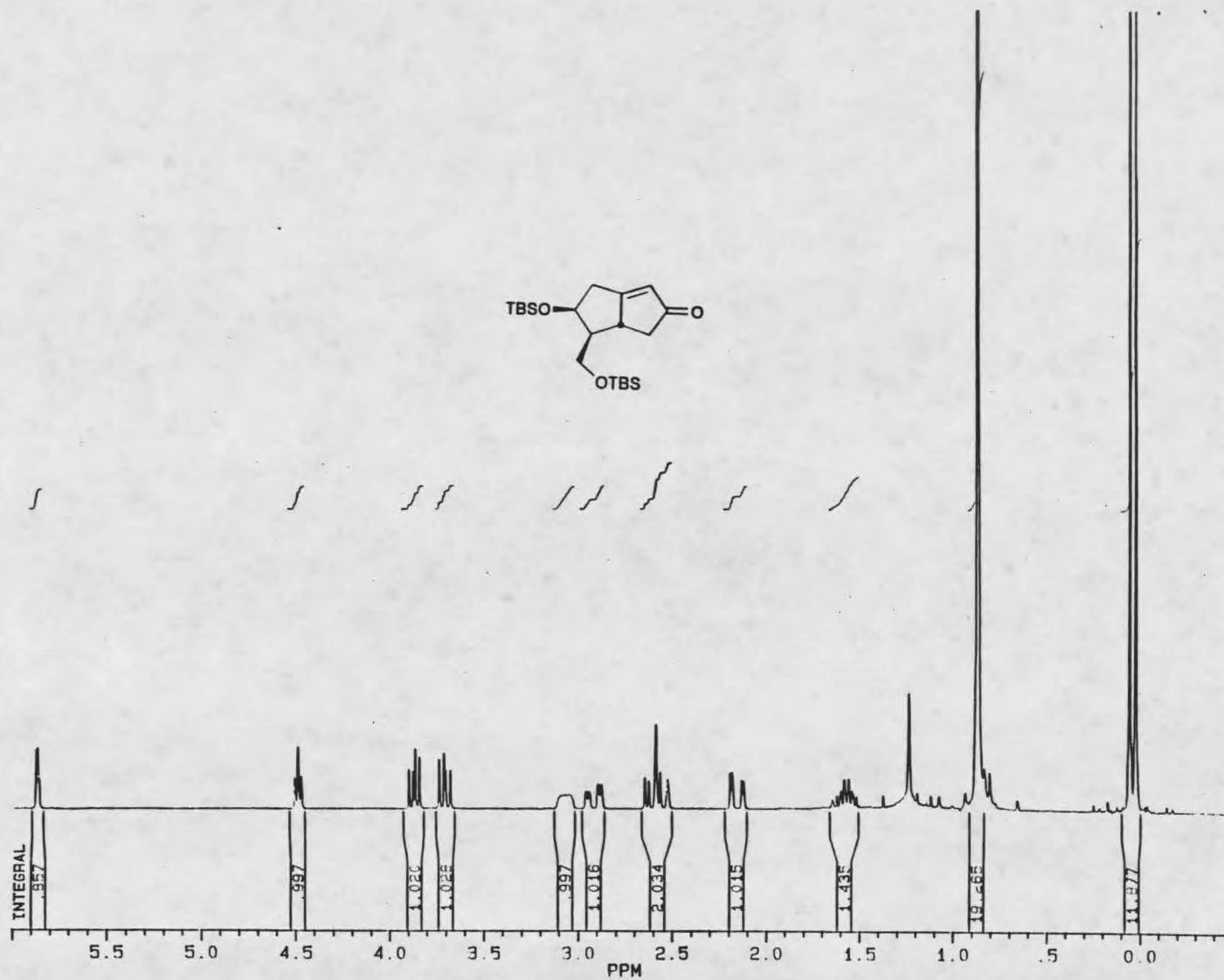


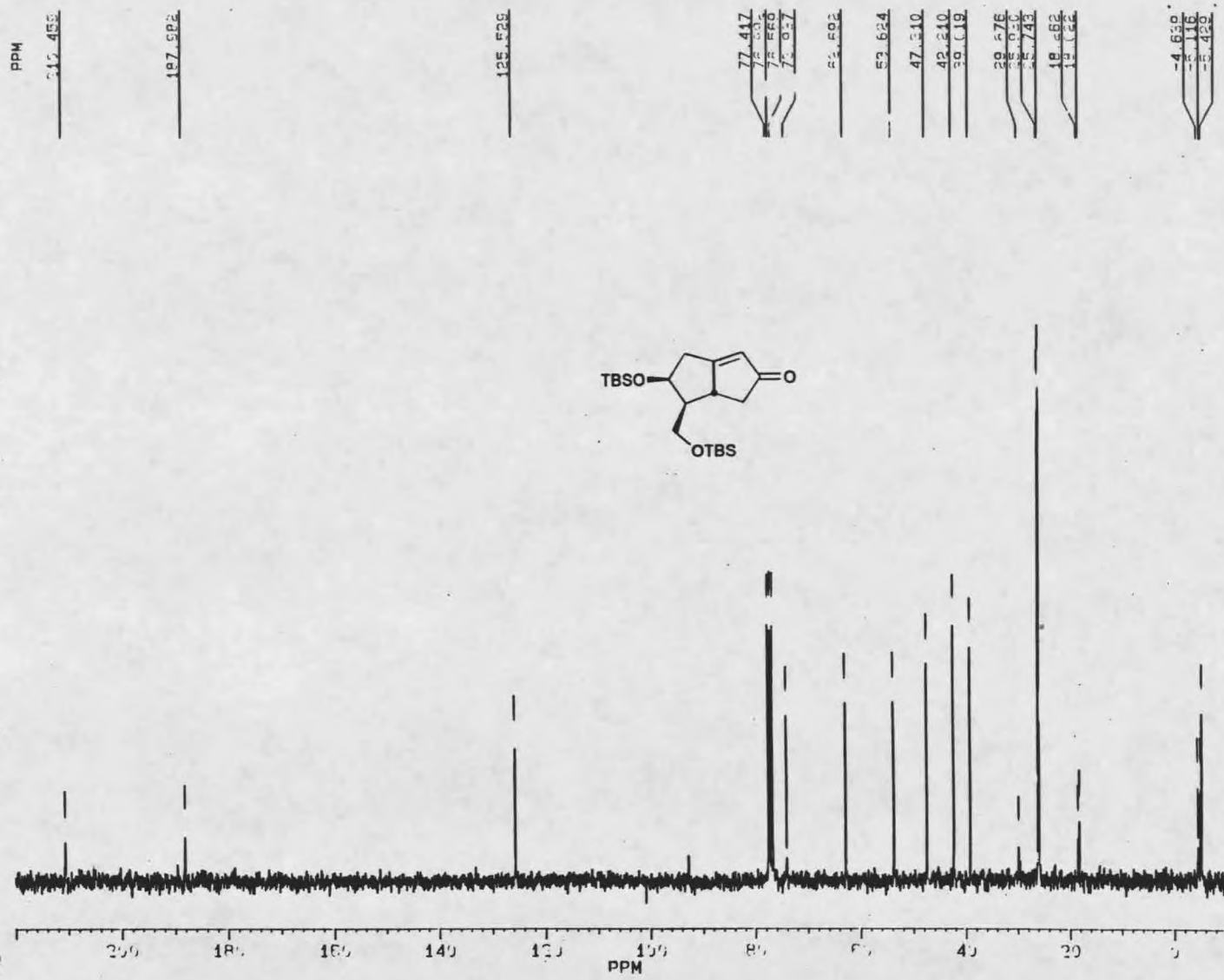
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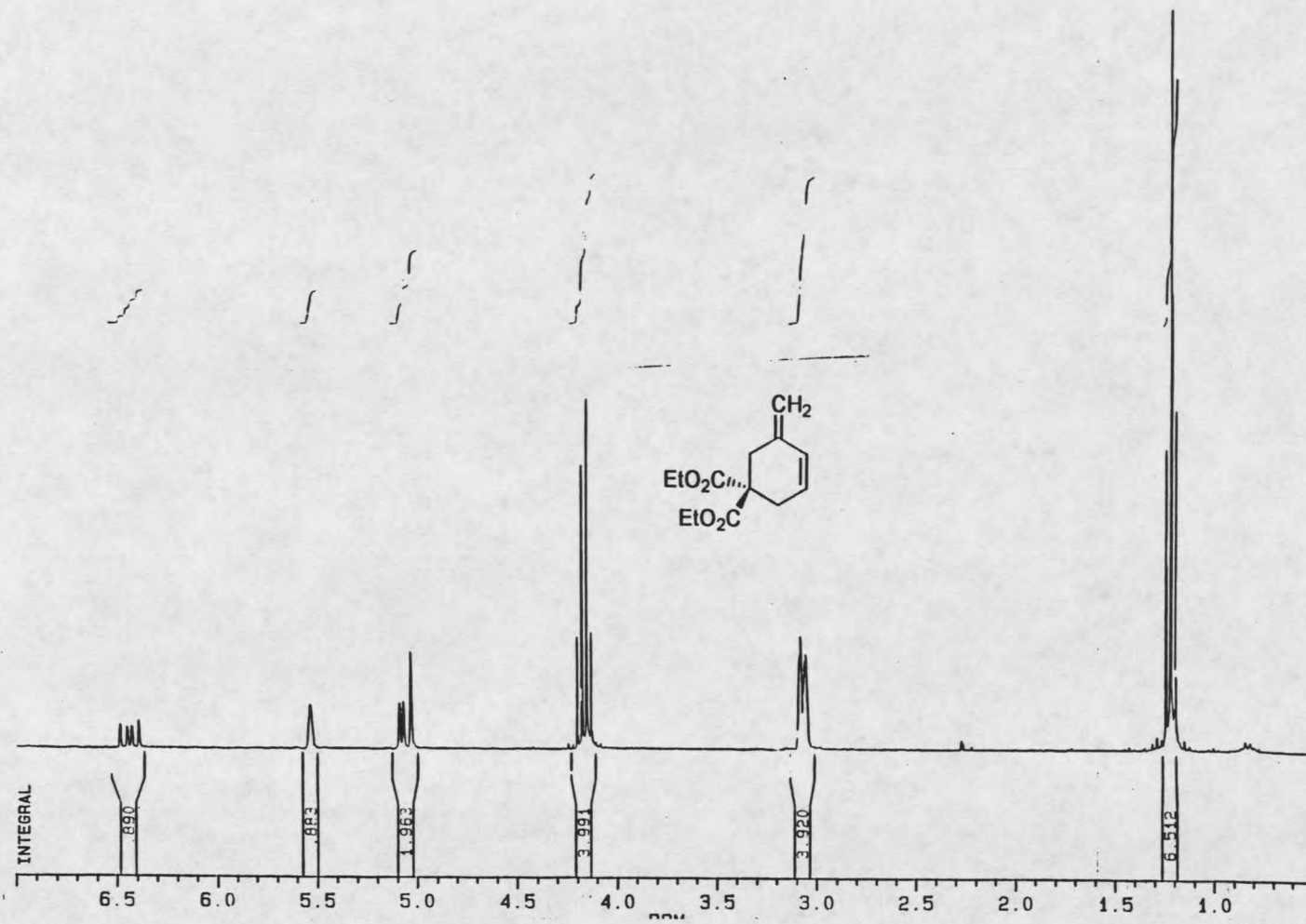


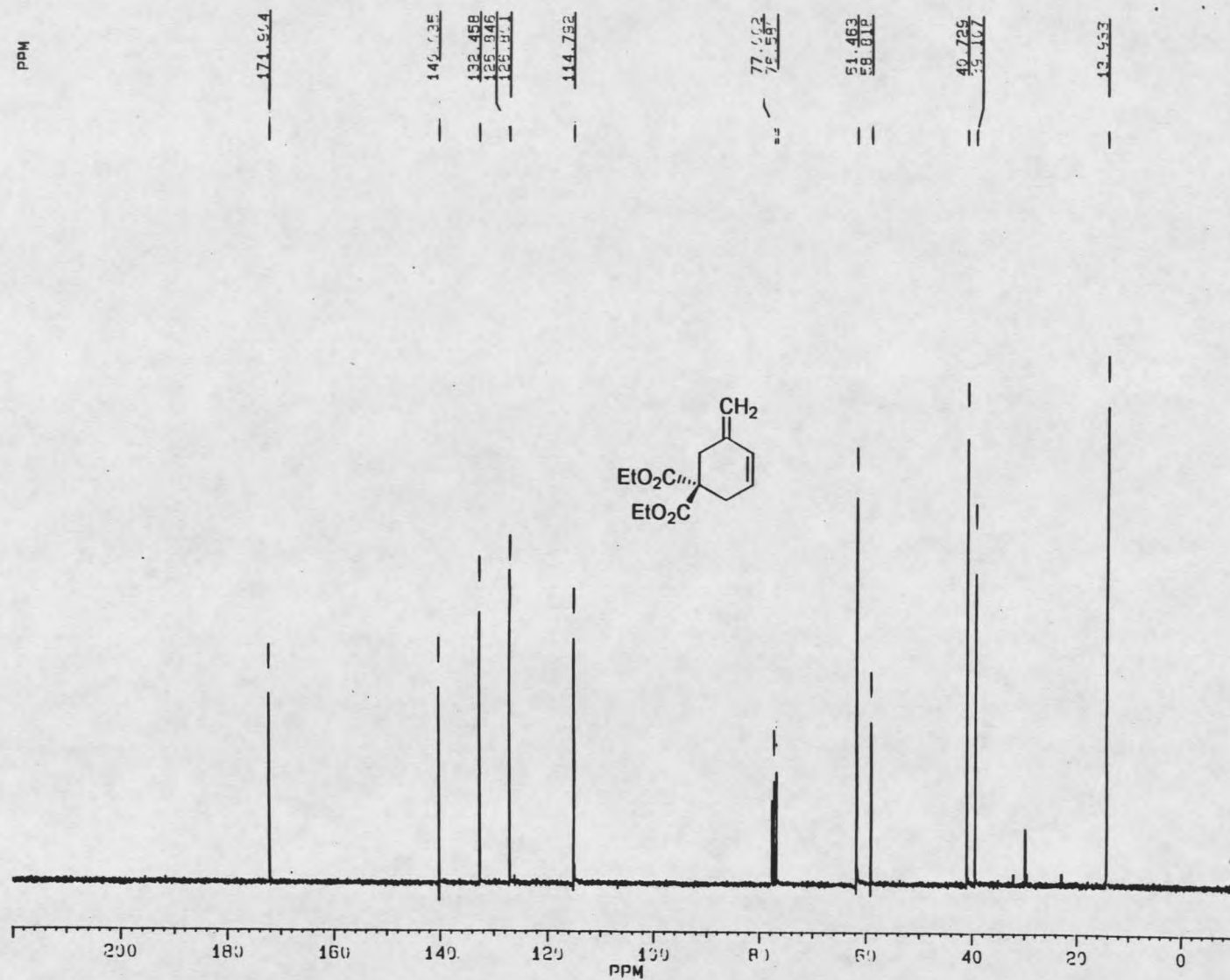


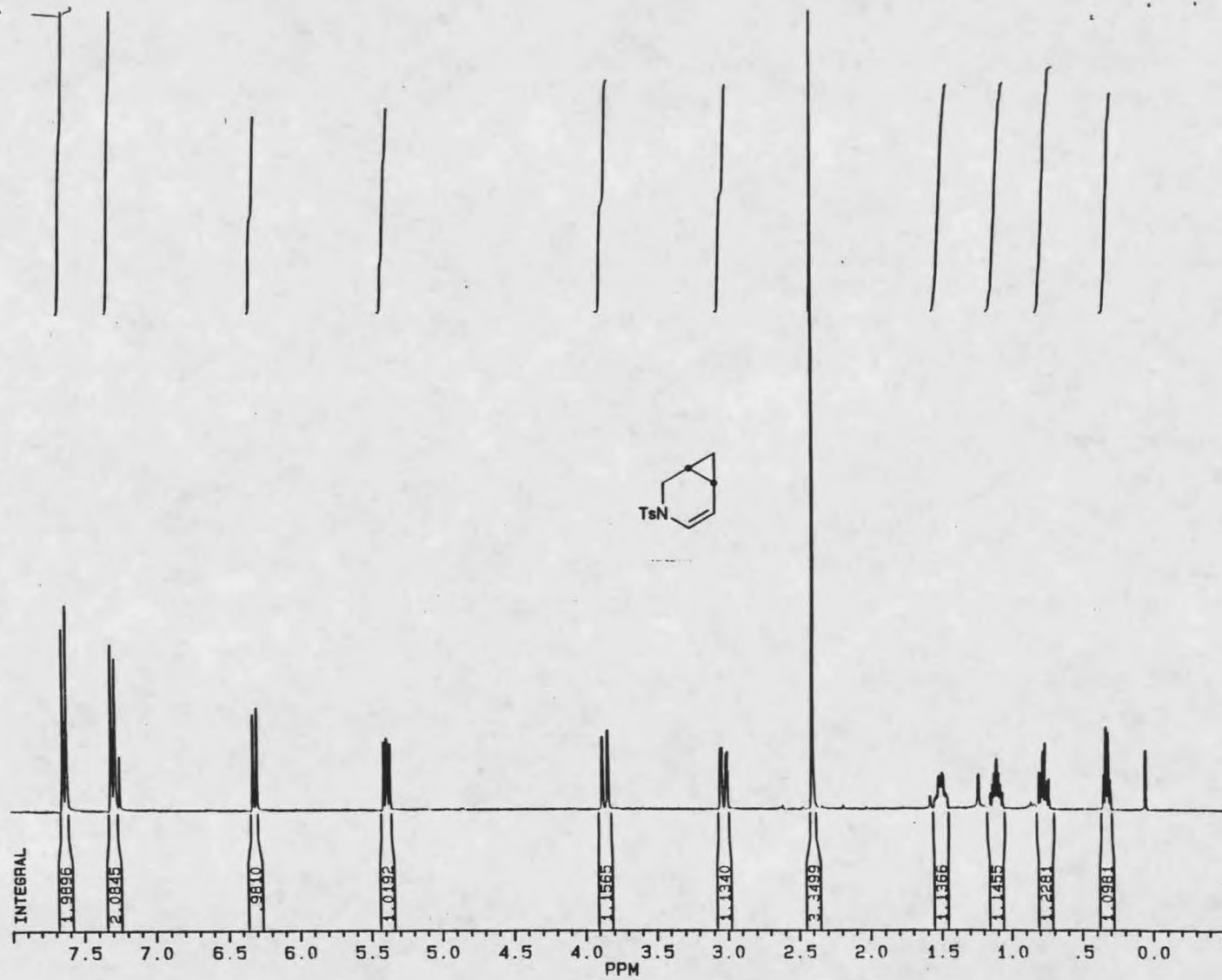


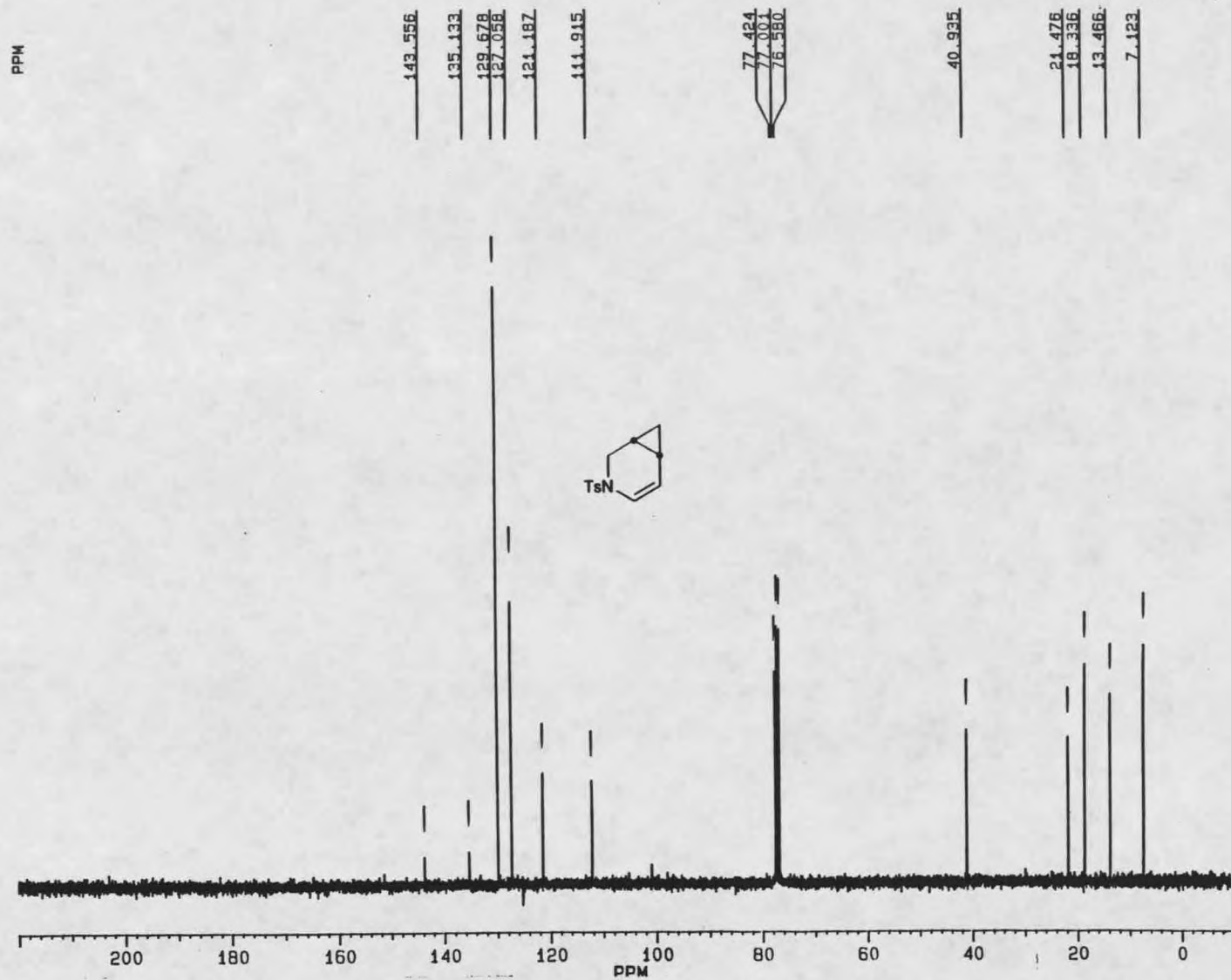


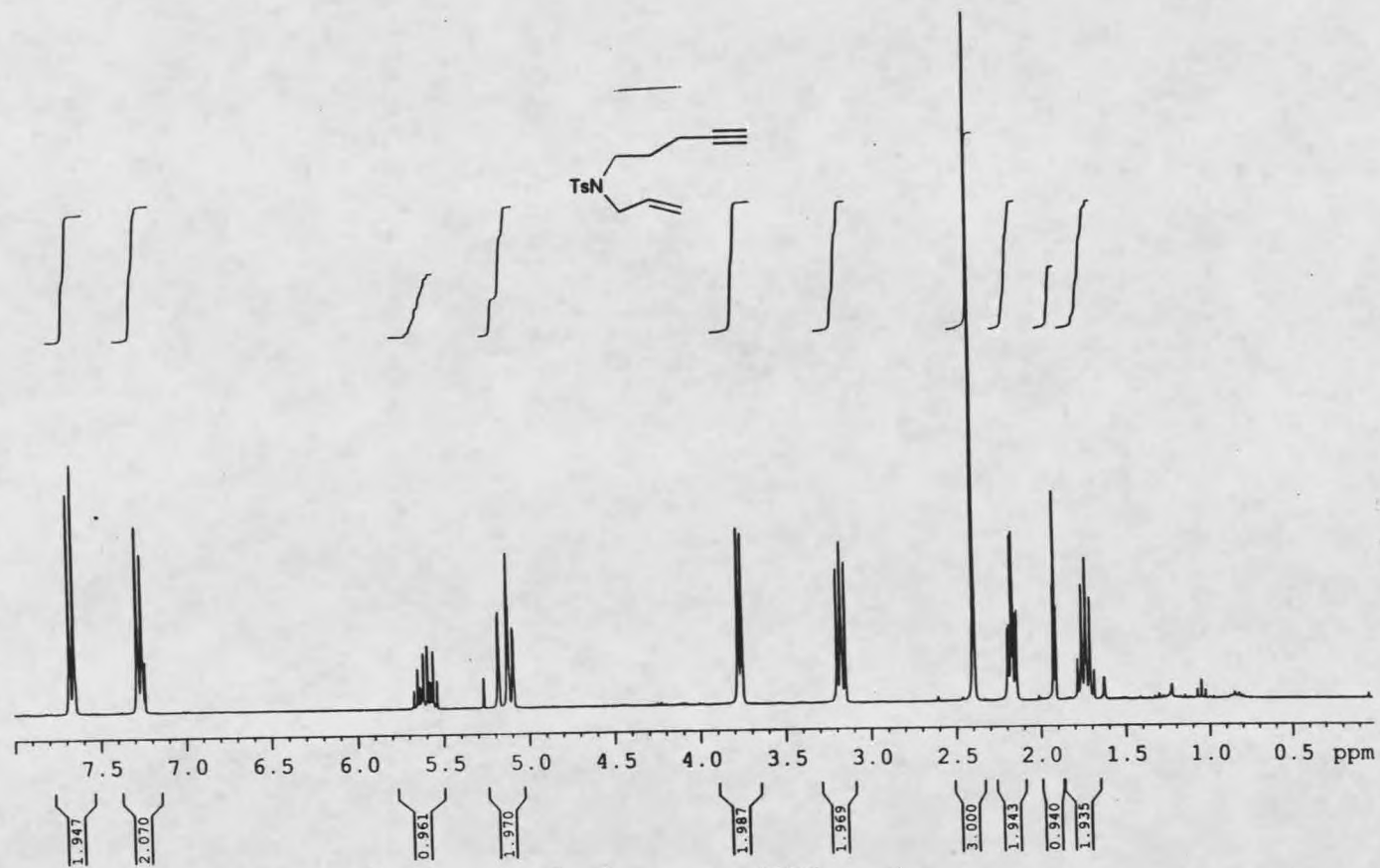


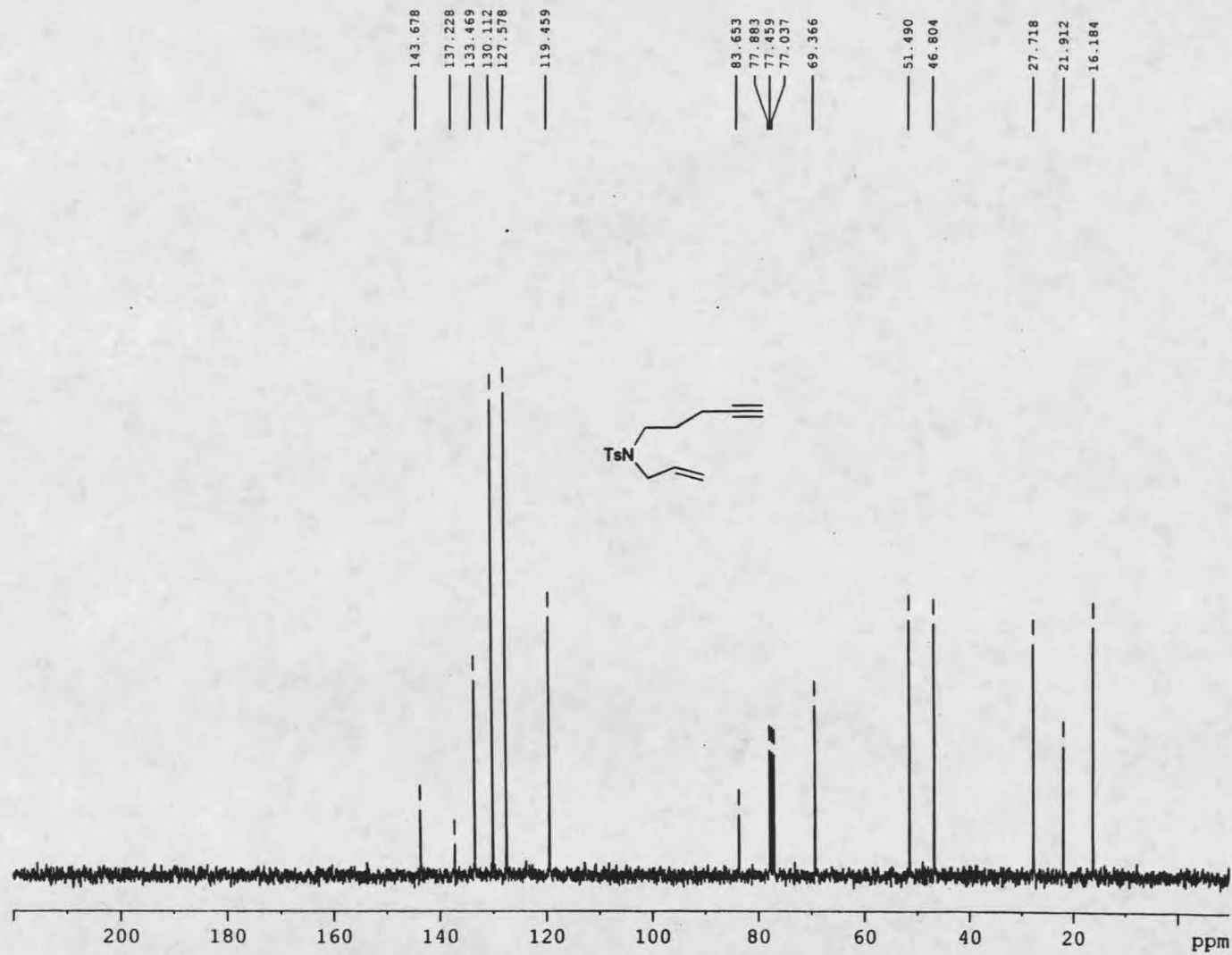


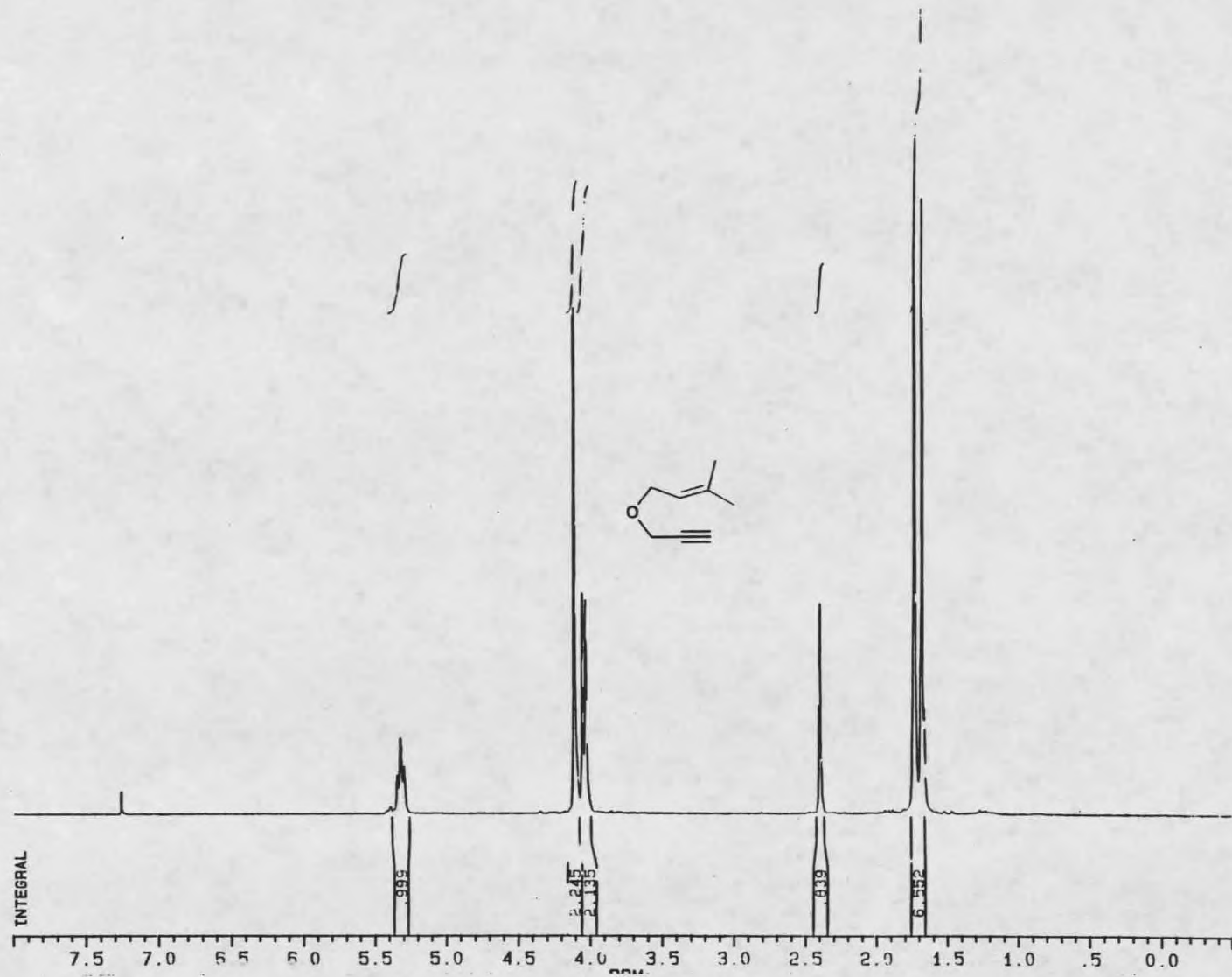


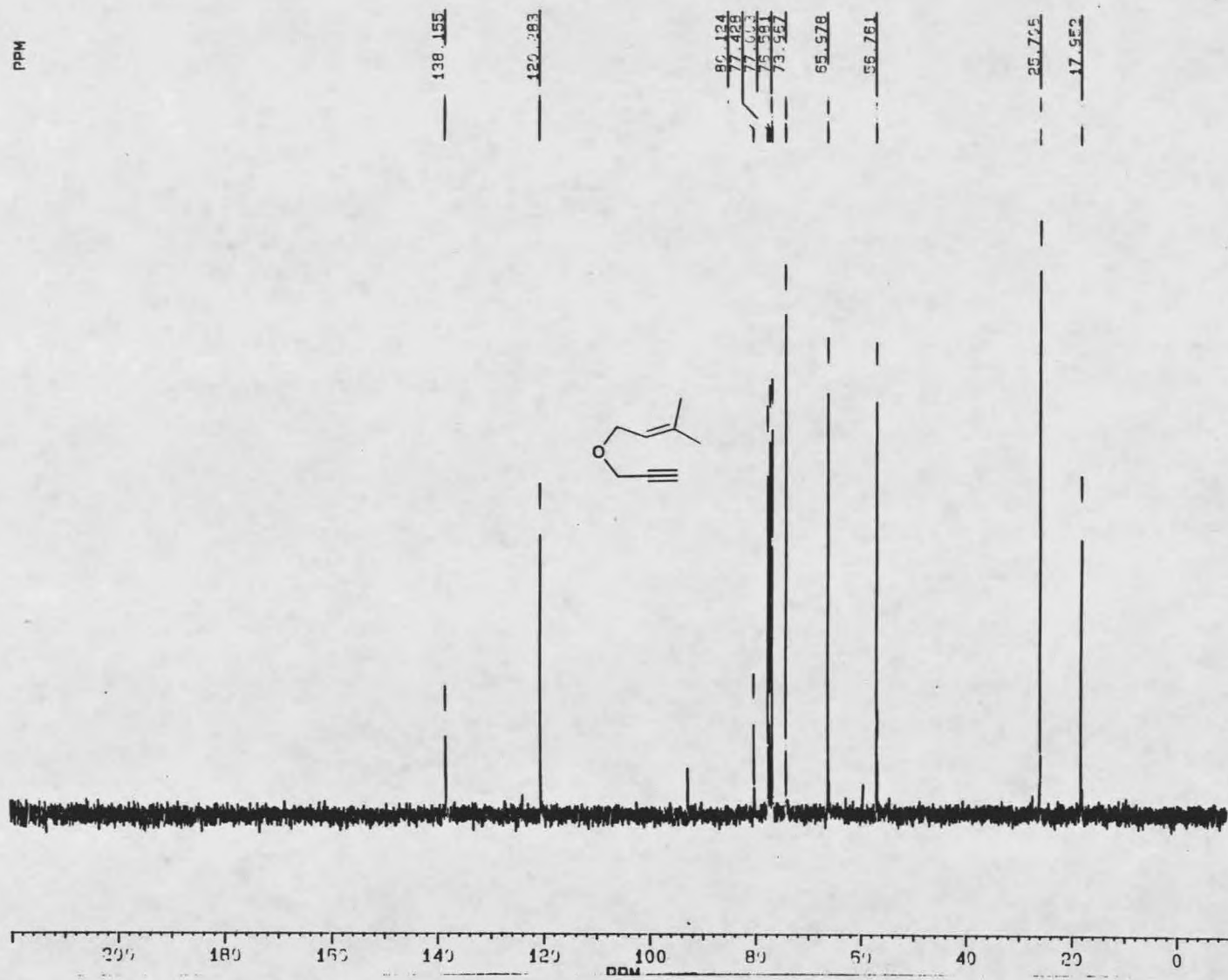


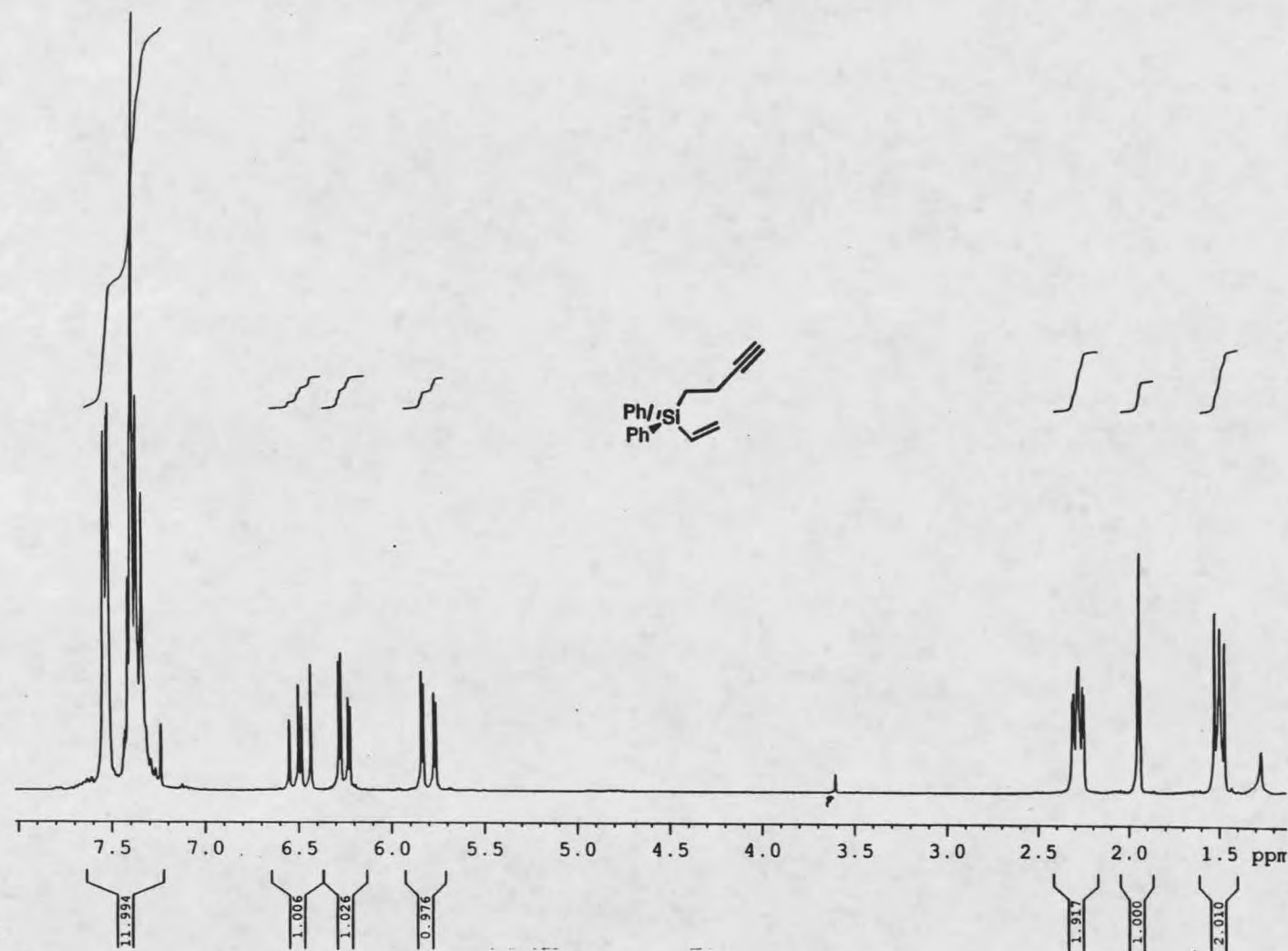


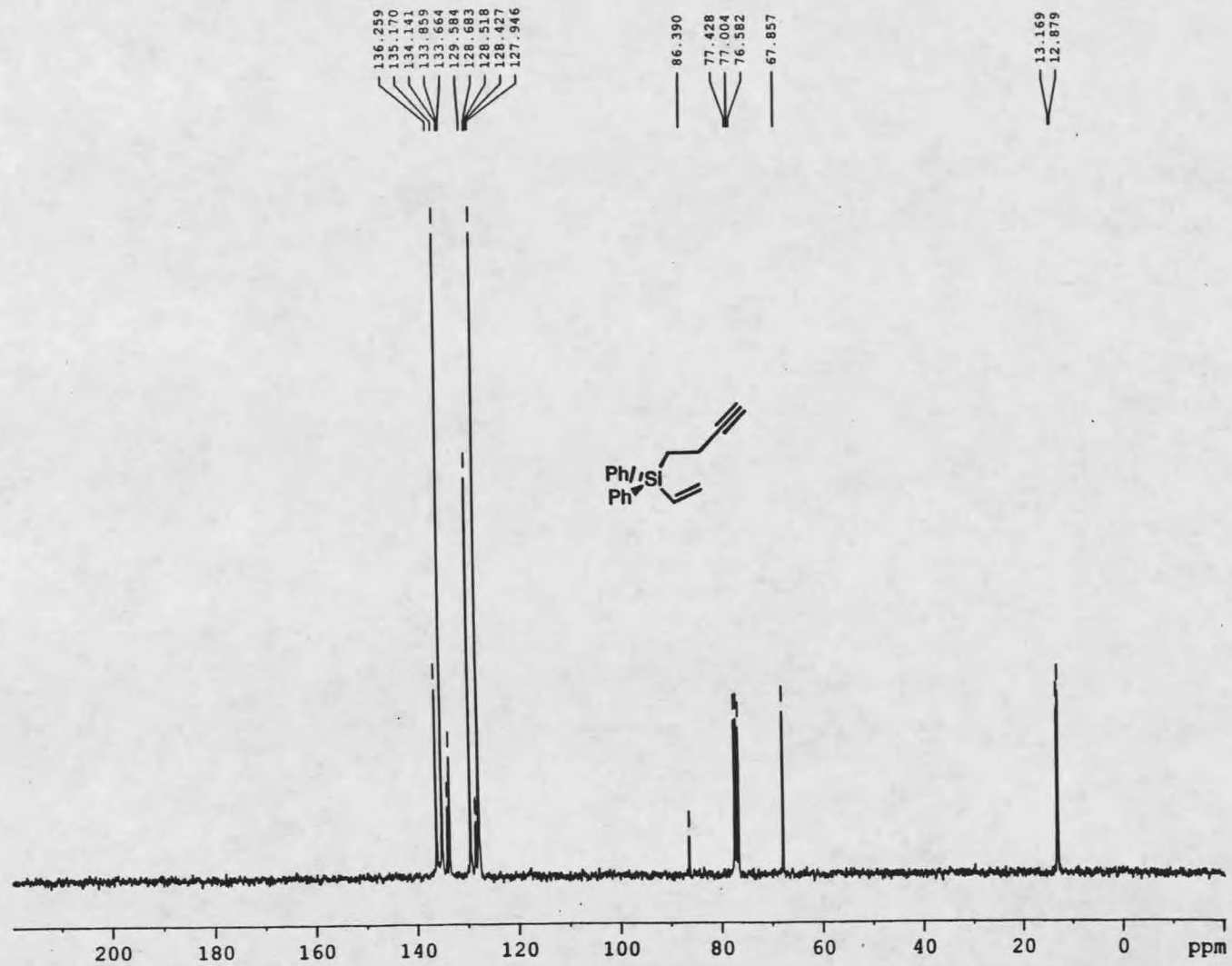


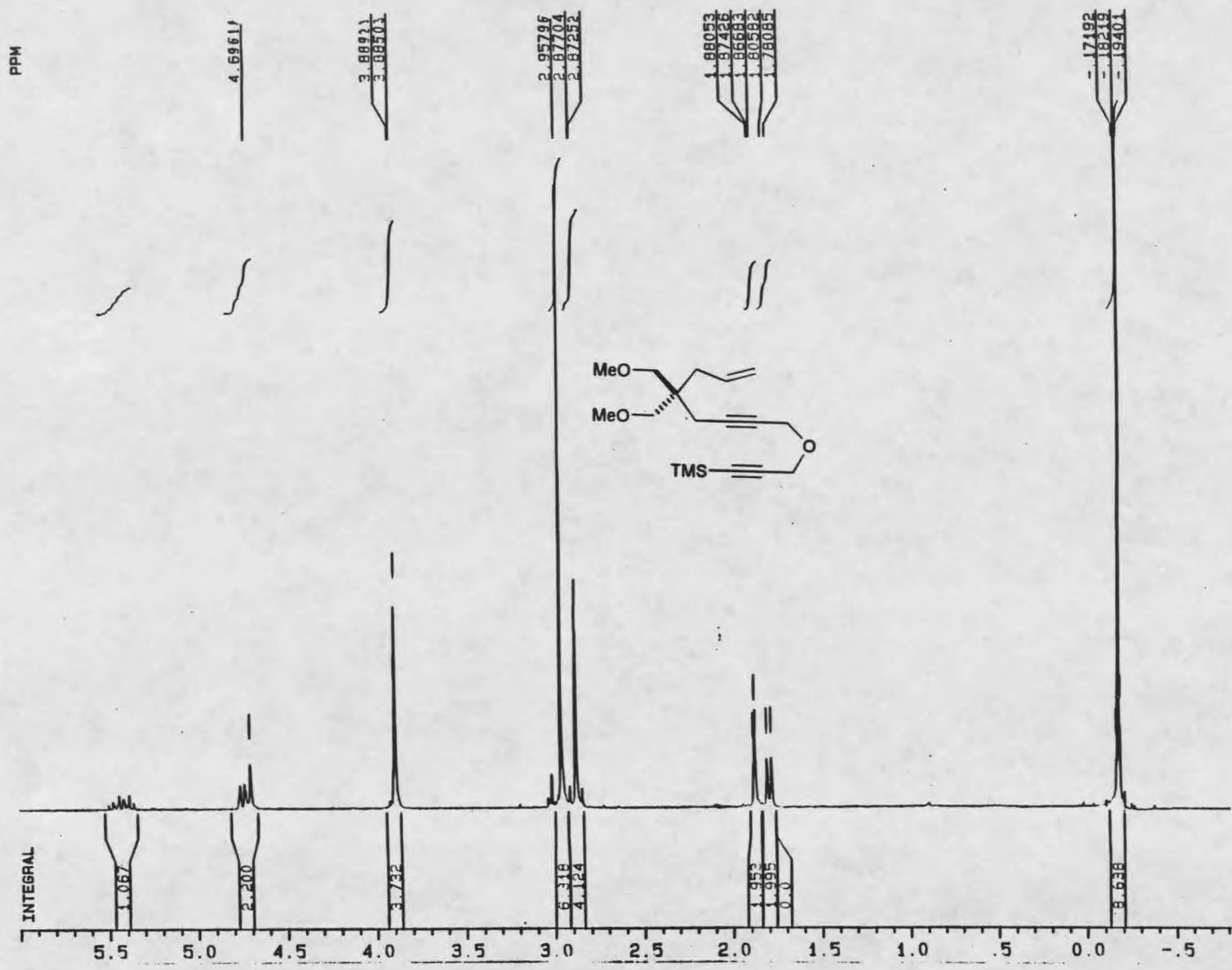


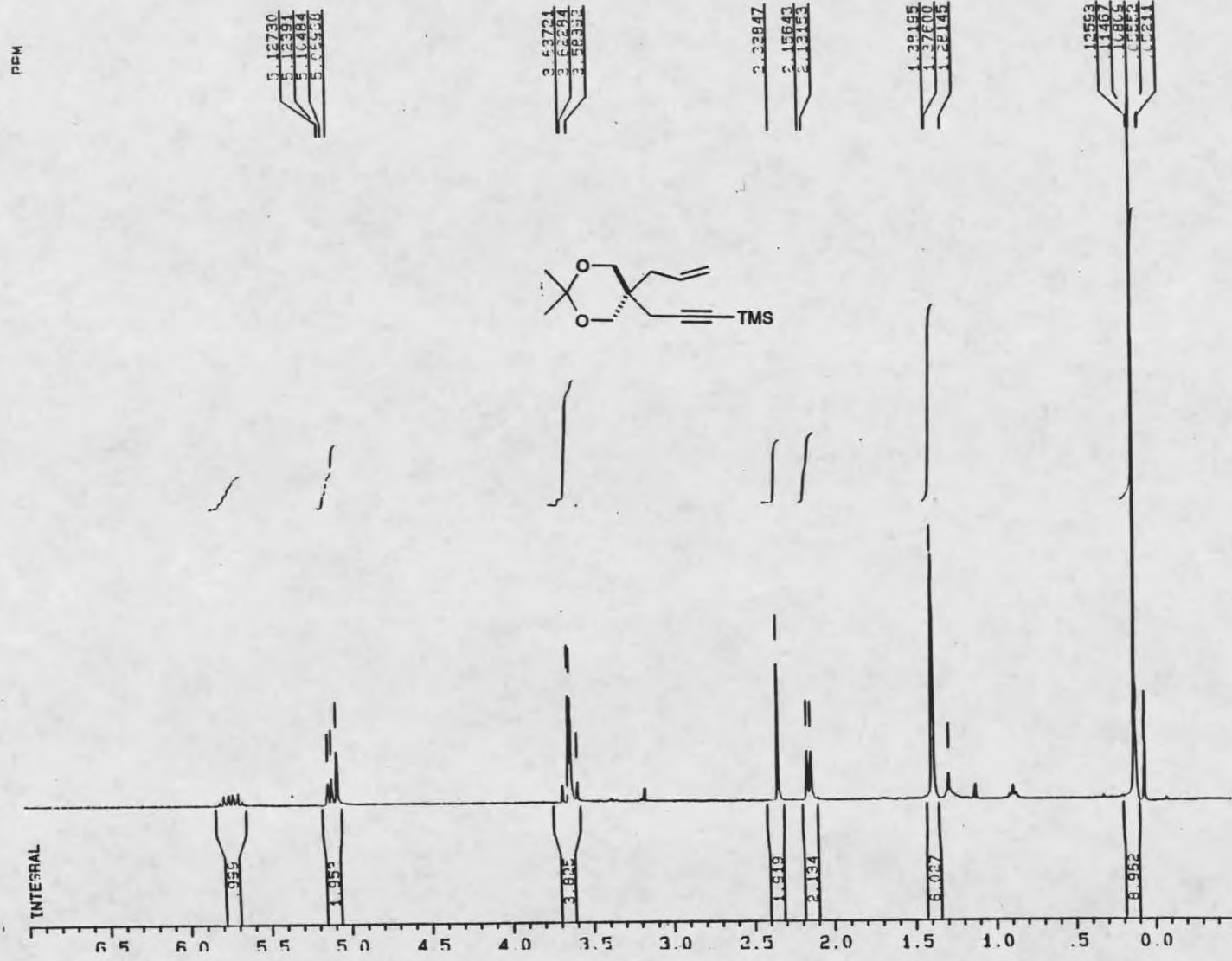


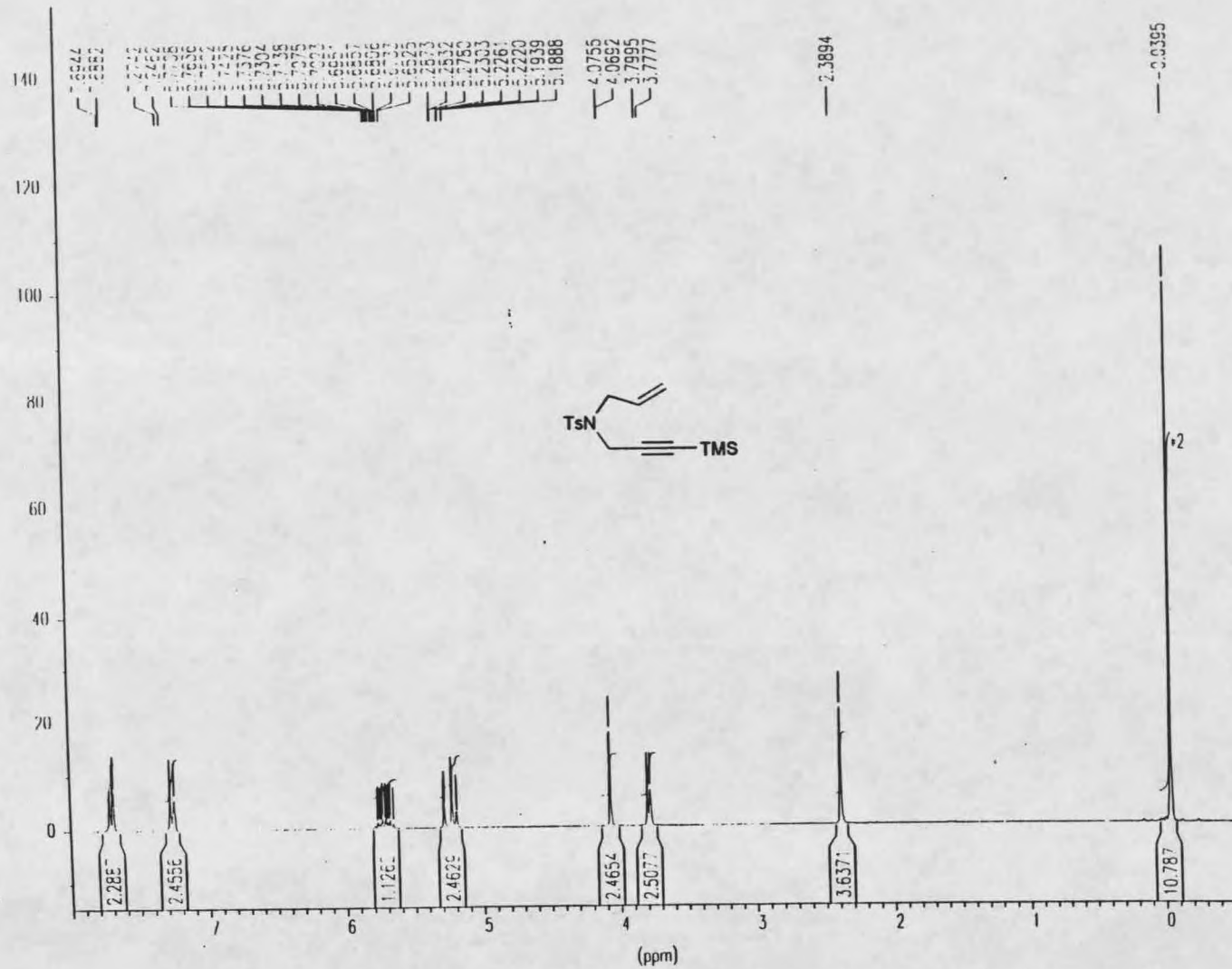


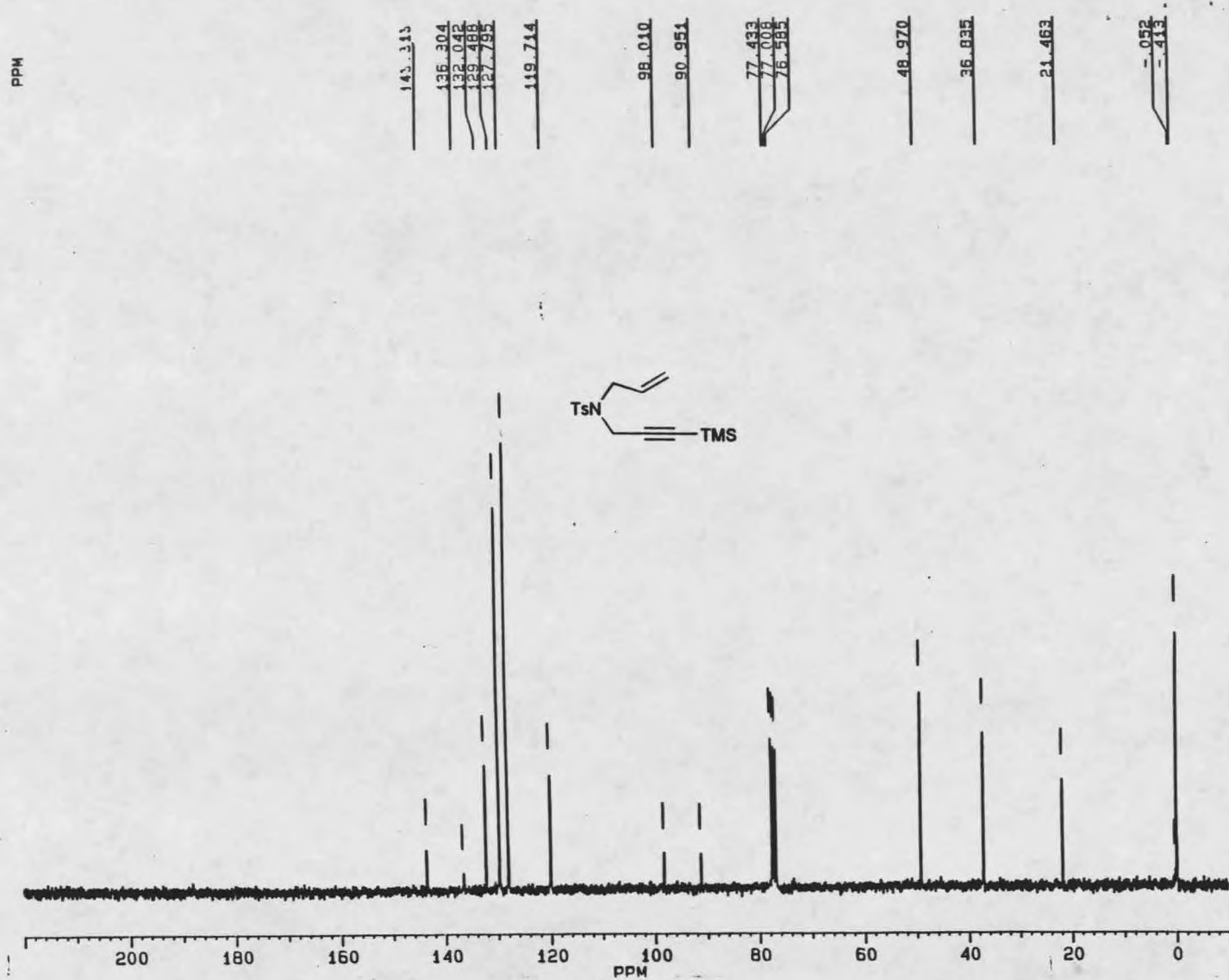


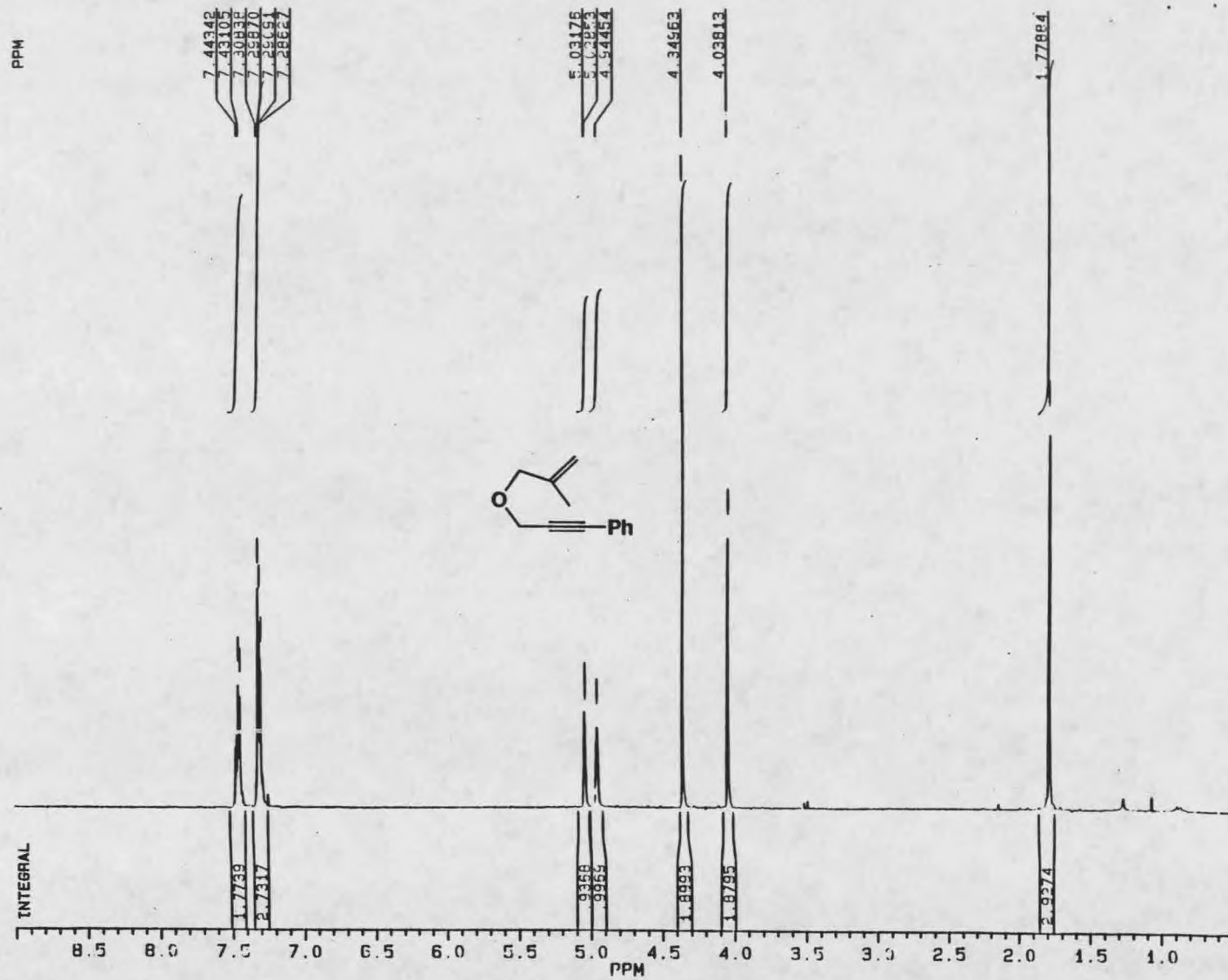


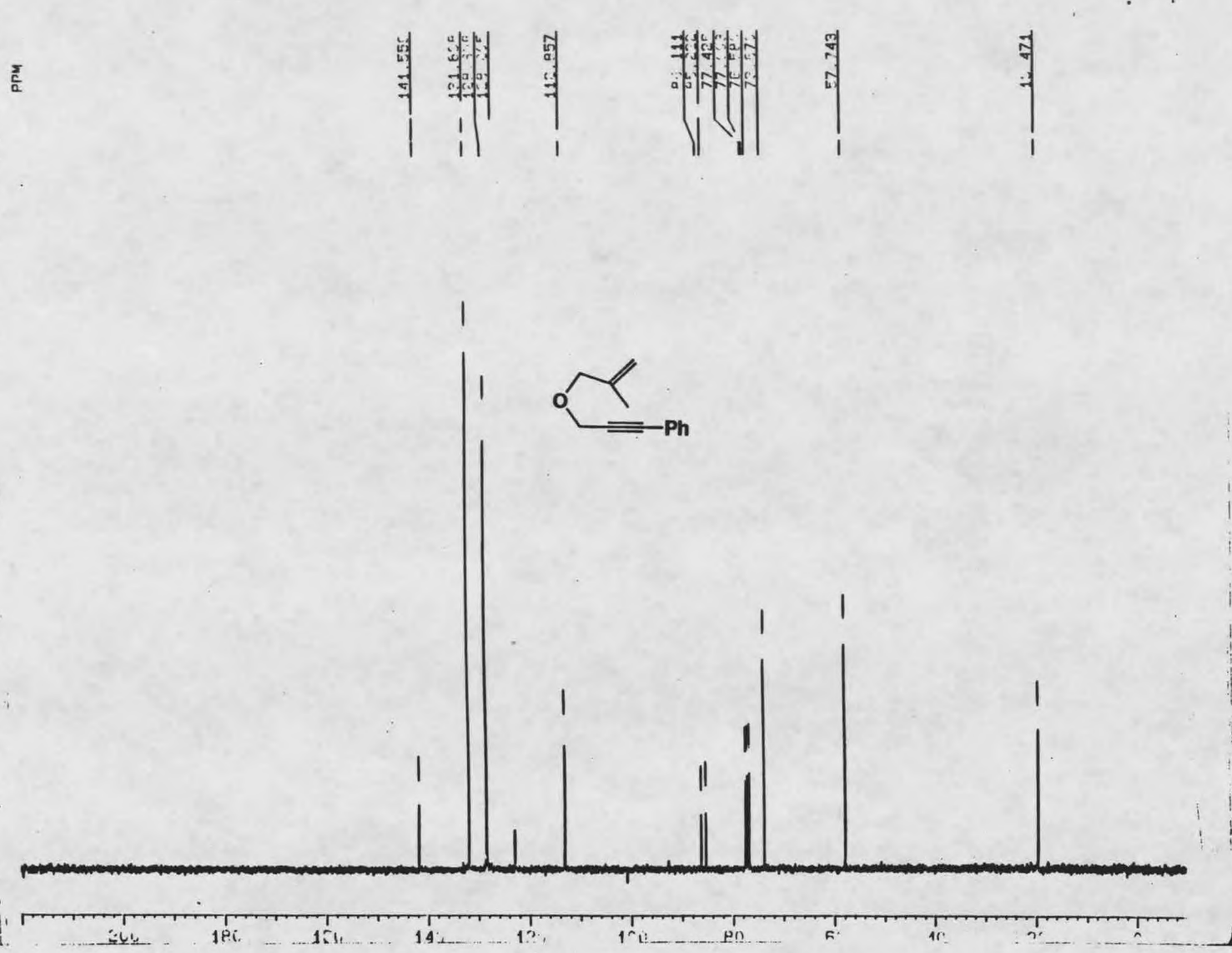


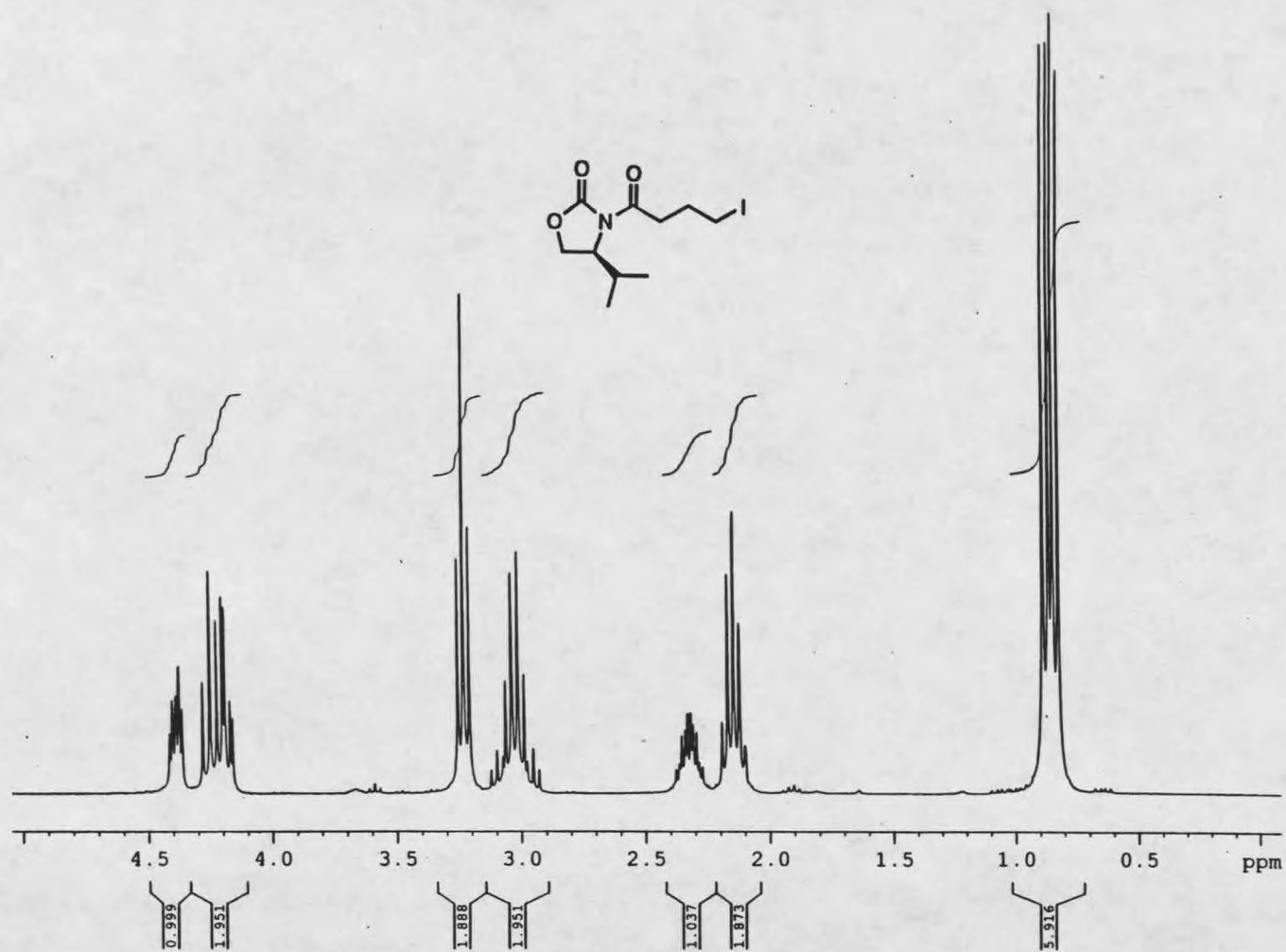


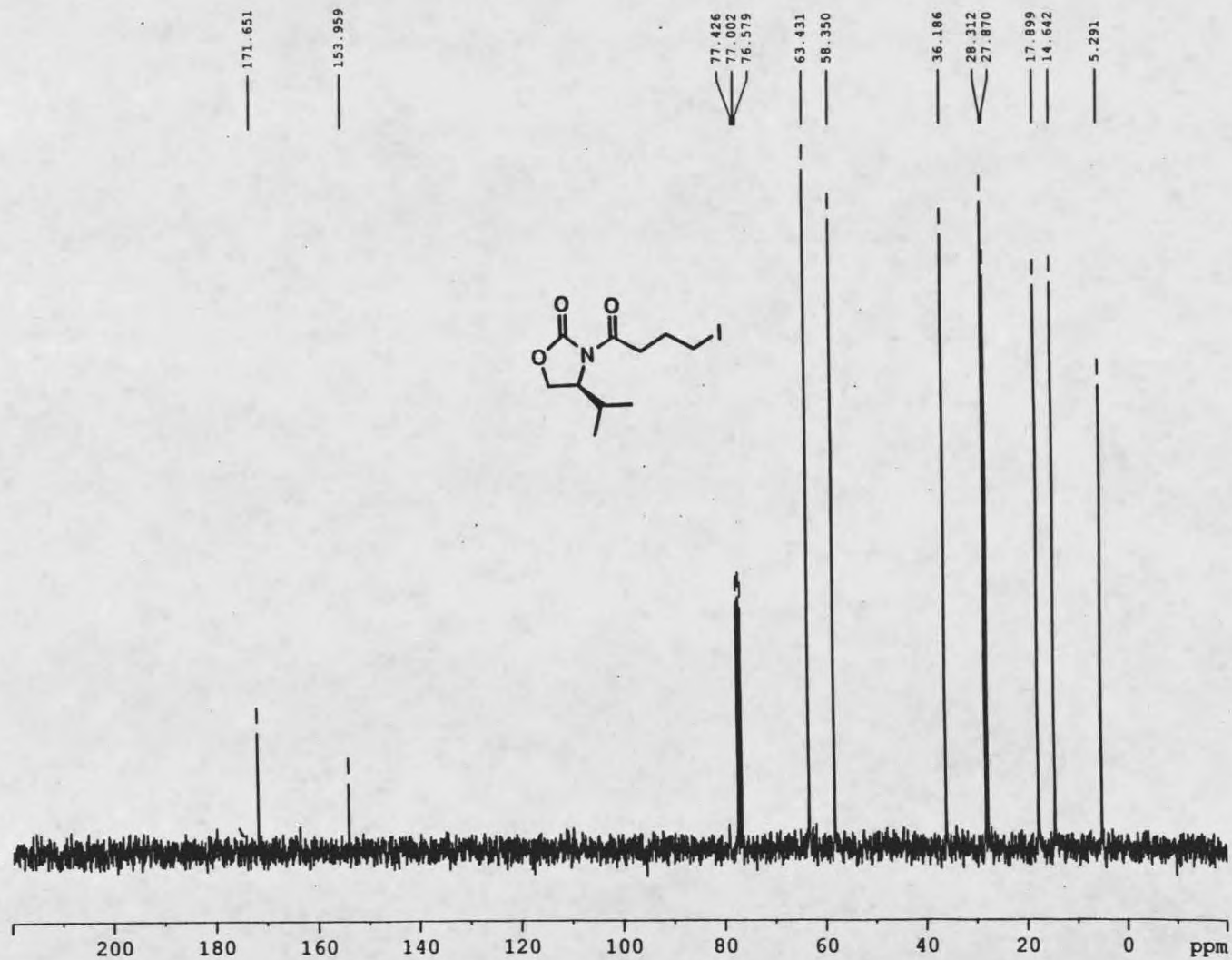


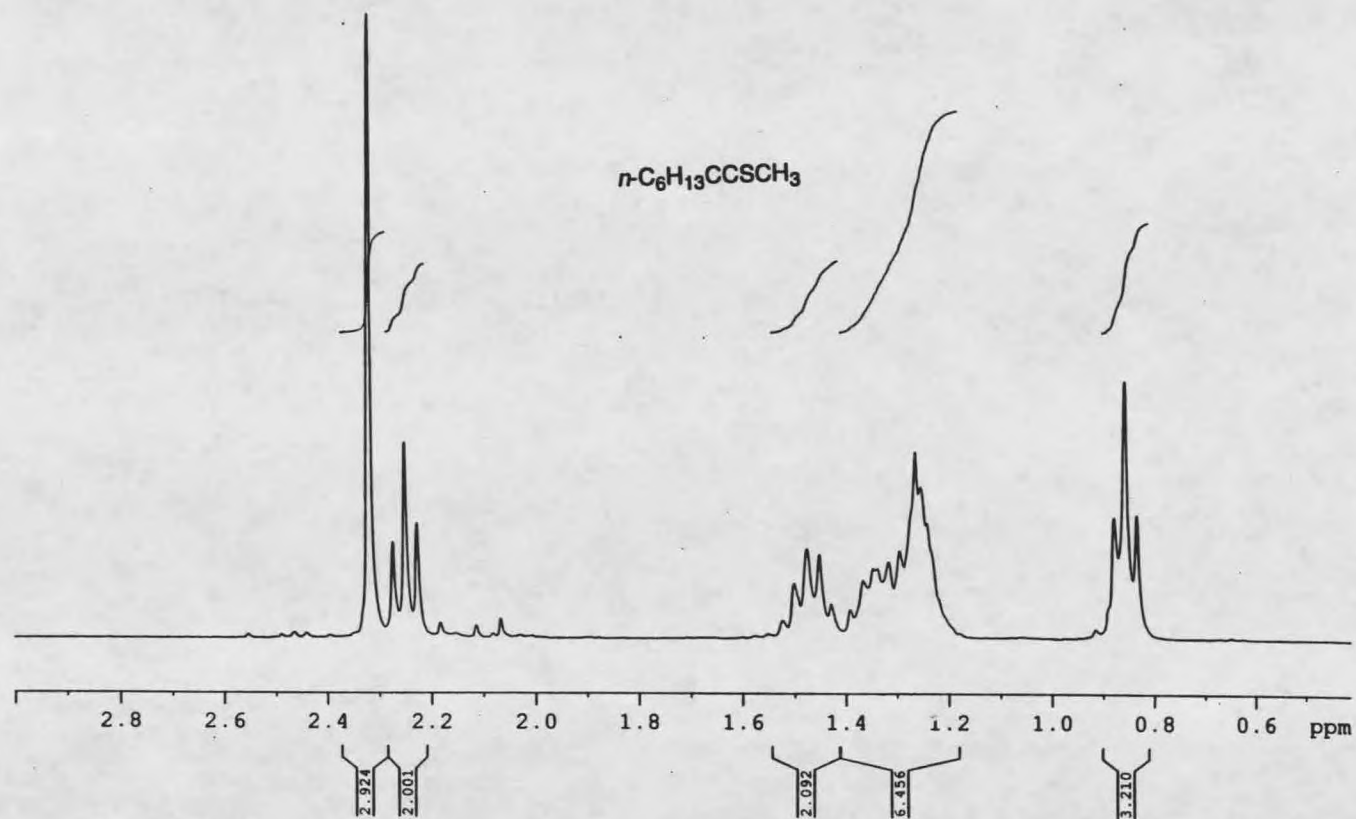


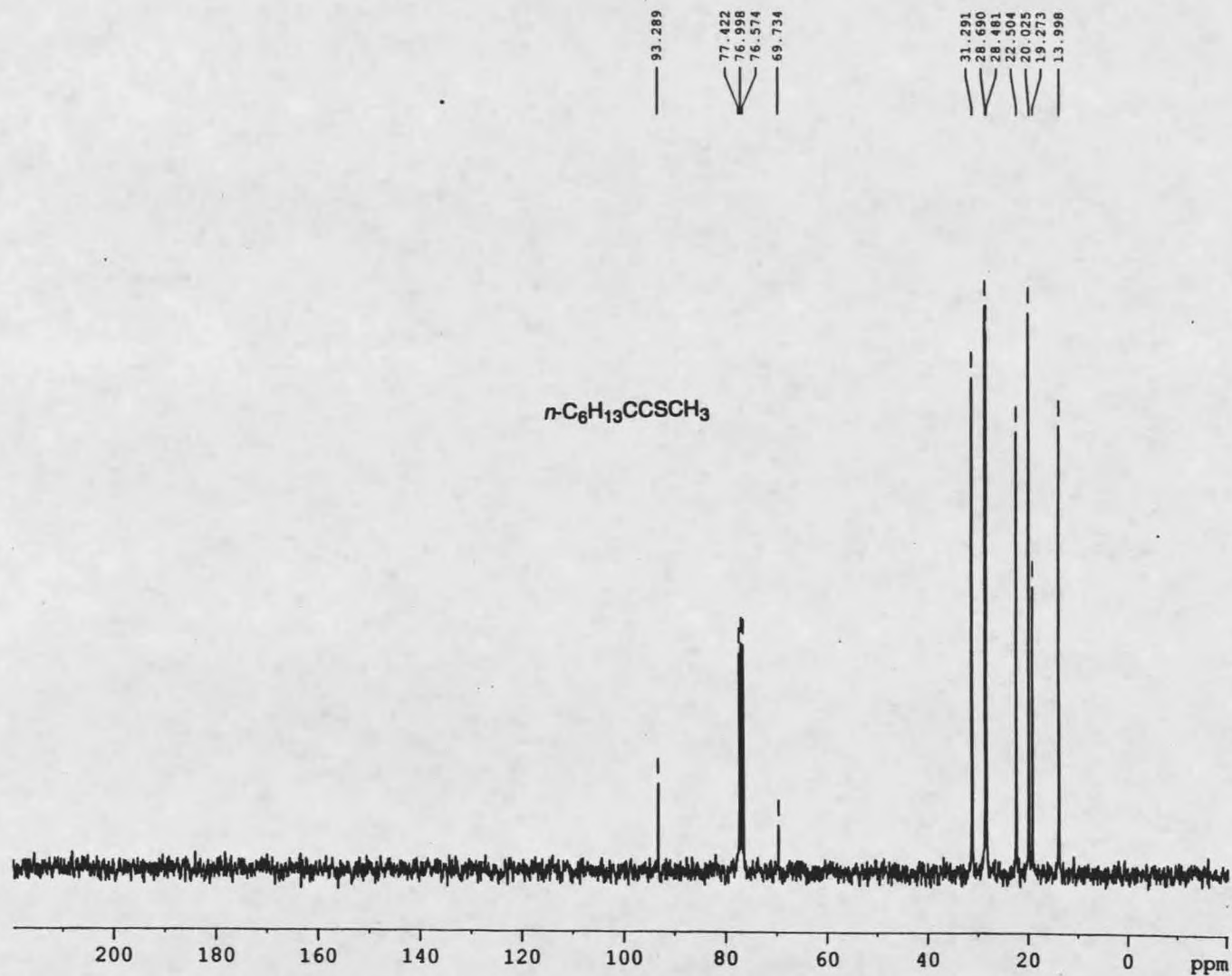












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