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Regioselective Carbocyclic Ring Formation
Mediated by Titanocene Chloride

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Pascal Rigollier

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John R. Stille
Major professor

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REGIOSELECTIVE CARBOCYCLIC RING FORMATION MEDIATED BY TITANOCENE CHLORIDE

By

Pascal Rigollier

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ABSTRACT

REGIOSELECTIVE CARBOCYCLIC RING FORMATION MEDIATED BY TITANOCENE CHLORIDE

By

Pascal Rigollier

A new method for selective carbocyclic ring formation is described. Soluble Ziegler-Natta type catalysts bearing an alkene tether were designed and shown to undergo intramolecular cyclization by olefin insertion into the carbon-titanium bond. Typically, the cyclization process is a syn addition of the carbon-metal bond on to alkene functionality, and proceeds very selectively in an exo manner.

A variety of alkene bromide substrates were synthesized and the corresponding Grignard reagents underwent transmetalation when treated with titanocene dichloride. Upon addition of a Lewis acid cocatalyst, the alkenyltitanocene chloride species were activated and intramolecular olefin insertion occurred. The 5-hexen-1-yl type ligands closed regioselectively to form cyclopentylmethyl units. Bicyclic systems, such as bicyclo[3.3.0]octane, *cis*-1-methyl bicyclo[3.3.0]octane and *cis*-1-methylbicyclo[4.3.0]nonane were obtained in good yield by intramolecular carbon-titanium addition on

a cyclopentene, methylenecyclopentane, or methylenecyclohexane preexisting ring.

Six-membered ring formation by cyclization of the 6-hepten-1-yl ligand was also studied. The reaction was regioselective, but somewhat sluggish compared to the counterpart five-membered ring formation. Activation of the double bond by a suitably positioned trimethylsilyl substituent was shown to cause rate enhancement for the olefin insertion reaction. Influence of the solvent and the Lewis acidic cocatalyst was also analyzed.

A mes Parents, Christine, et Violaine.

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LIST OF ABBREVIATIONS

Cp	cyclopentadienyl
DHP	dihydropyran
DMF	N,N-dimethylformamide
DMSO	dimethylsulfoxide
NBS	N-bromosuccinimide
PPTS	p-toluenesulfonic acid
PTSA	pyridinium p-toluenesulfonate
Red-Al	sodium bis(2-methoxyethoxy)aluminum hydride
TEA	triethylamine
THF	tetrahydrofuran
THP	tetrahydropyranyl
TMS	trimethylsilyl

INTRODUCTION

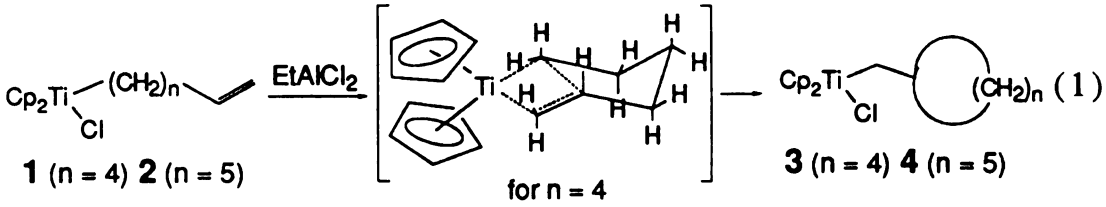
Carbon-carbon bond formation, along with functional groups manipulation is certainly one of the most fundamental processes in synthetic organic chemistry. In the last decades, organometallic compounds have played an increasing role in performing such a task. By careful design of "wonder" reagents, selective and very efficient organic reactions were invented.[1] Indeed, cyclopentyl- and cyclohexyl-units have been ideal targets for these transformations as they occur in many natural products of high architectural complexity.[2]

An efficient method for five- and six-membered carbocycle formation is presented. The principle behind this transformation is to use established reactivity of metal-carbon bonds for the insertion of alkene functionality.

Olefin insertion into a carbon-titanium bond is the fundamental step in Ziegler-Natta polymerization.[3] During the past 30 years, literature reports have emerged to establish the course of the event. Two major mechanisms, both supported by experimental evidence, were advanced. The Cossee mechanism[4] proposes direct alkene insertion by olefin coordination prior to chain elongation by β-alkyl migratory insertion. The Green and Rooney mechanism[5] involves a

metathesis step followed by olefin addition onto the metal-carbene. A process involving α-hydrogen "agostic" interaction has also been proposed.[6]

Soluble catalysts for Ziegler-Natta polymerization of ethylene were originally obtained by action of titanocene dichloride on alkylaluminum chloride co-catalysts.[7] Reaction of equimolar amounts of titanocene dichloride with diethylaluminum chloride in toluene, was proposed to generate an ethyltitanocene chloride/ethyl aluminum dichloride system, responsible for the polymerization process.[8] Coordination of the Lewis acidic aluminum center to the chloride ligand reduces the electron density on the transition metal, thus permitting olefin complexation and insertion. Direct preparation of $Cp_2Ti(Cl)Et$ was accomplished by action of ethylmagnesium bromide on titanocene dichloride.[9] Addition of $EtAlCl_2$ as a co-catalyst produced the Ziegler-Natta conditions for ethylene polymerization.[10] The experiment shown in Equation 1 was designed to probe for an isotope effect on the stereochemistry of the olefin insertion, by employing alkenyltitanocene chlorides **1** and **2** with a pendant olefin.[10a] They underwent single olefin insertion by intramolecular reaction upon treatment with ethylaluminum dichoride at -100 °C, to produce cyclopentyl- and cyclohexylmethyltitanocene chlorides (**3**) and (**4**) after quenching the co-catalyst with bipyridine.

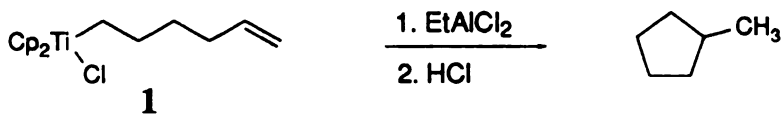


1 (n = 4) **2** (n = 5)

for n = 4

3 (n = 4) **4** (n = 5)

From the organic ligand viewpoint, this reaction offers a new approach to five- and six-membered ring formation. Protonolysis (HCl) of complex **3**, for example, would free the organic ligand of interest (Equation 2).



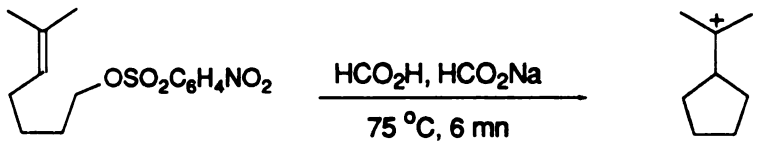
1

According to Baldwin's rules,[11] the 5-hexen-1-yl ligand undergoes a 5-exo-trig closure, whereas the 6-hepten-1-yl ligand cyclizes in a 6-exo-trig manner.

Intramolecular addition of a reactive carbon to an unactivated olefin via 5- or 6-exo-trig modes is a fundamental process for cyclopentane or cyclohexane ring formation. Traditionally, the reactive center has been in the form of a carbocation, a free radical or a carbanion species. Other methods involve metal promoted reactions. An overview is presented below. Examples were chosen to illustrate major concepts behind five- or six-membered carbocycle formation. They do not constitute an extensive and updated review on the subject.[12]

Carbocationic Cyclizations

Although carbocationic cyclizations do not usually proceed in an exo manner, they represent a powerful method for generating six-membered rings.[13] The regioselectivity is governed by the stability of the cation product. The endo cyclization process for the simple 5-hexen-1-yl cations is favored since a stable secondary carbocation is generated. However five-membered ring formation can be controlled by stabilizing the exo-carbocation product. Formolysis of sulfonate ester **5** under the conditions shown in Equation 3 gave cyclopentane products, all derived from **6**.[14] Evidently, the high stability of this tertiary cation precluded the formation of the less stable secondary carbocation endo-product.



5 **6** (3)

Other examples of 5-membered ring closure involve the use of a styryl internal trap, where a benzylic cation is produced upon exo-cyclization.[13] Even if such requirements cause structural restrictions on cyclopentane formation, the access to complex systems such as steroids by polyannulation reactions to cyclohexane units, makes the carbocationic cyclization a very valuable process.

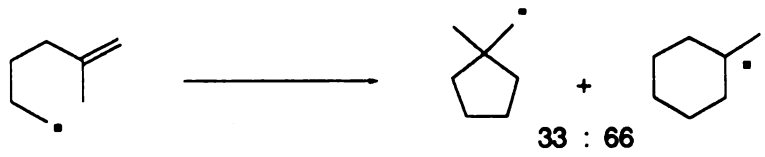
Free Radical Cyclizations

Free radical ring closure of 5-hexen-1-yl systems has been a subject of interest for physical organic chemists as early as the 1960's.[15] Reduction of 6-bromo-1-hexene with nBu_3SnH, initiated by AIBN, was elegantly used by Walling for cyclopentylmethyl radical formation by free radical addition on the tethered olefin.[16] Since then, the tin hydride method has become the most common way of generating and cyclizing 5-hexen-1-yl radicals. A better understanding of the reaction process was made possible by the stability and kinetic studies carried on the involved species.[17] More recently, a great amount of work has been invested in developing this reaction for synthetically useful purposes.[18] Access to structurally complex natural products was achieved by tandem cyclizations performed on carefully designed bromo or iodo polyalkenes.[19] However a fine control of the competitive reaction rates was crucial and limitations still remain.

Because both cyclized and uncyclized radicals are present in solution, quenching of these reactive species by hydrogen atom transfer can cause premature reaction termination, prior to cyclization.[20] Functionality is lost when hydrogen abstraction, by the carbon-centered radical **7** from Bu_3SnH, takes place during the transfer step shown below (Equation 4). To overcome the problem, functionalized traps have been designed.[21]

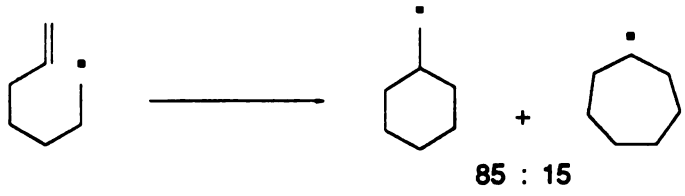
7 (4)

Five-exo cyclization is kinetically preferred over the 6-endo closure. However, highly stabilized cyanoester radicals, which undergo equilibration with the endo- and exo-products, favor the more stable 6-endo radical product.[22] The 5-methyl-5-hexen-1-yl system closes predominantly in a 6-endo-trig manner by producing the very stable tertiary cyclohexylmethyl radical (Equation 5).[23]



(5)

Formation of cyclohexylmethyl radical from 6-exo closure of 6-hepten-1-yl radical is an order of magnitude slower than the analogous reaction of the 5-hexen-1-yl radical.[18c] Tin hydride-mediated cyclization produced a 85:15 ratio of exo and endo products (Equation 6).[24]

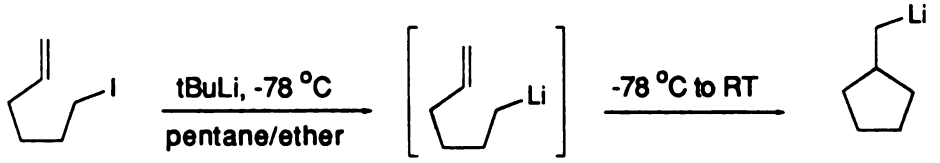


(6)

Free radicals have also been involved in carbocyclic ring forming reactions that are initiated or mediated by a transition metal species. Cobalt has received the most attention,[18b] but the use of vanadium,[25] chromium,[26] manganese[27], or titanium[28] has also been reported.

Anionic cyclizations

Anionic cyclizations at sp^3 centers remained, until very recently, unprecedented. Bailey pioneered the area in 1985 by reporting the preparation and cyclization of 5-hexen-1-yllithium.[29] Metal-halogen exchange took place when 6-iodo-1-hexene in a pentane/ether solution was treated with tBuLi at -78 °C. Ring closure followed as the temperature was raised to 23 °C (Equation 7).



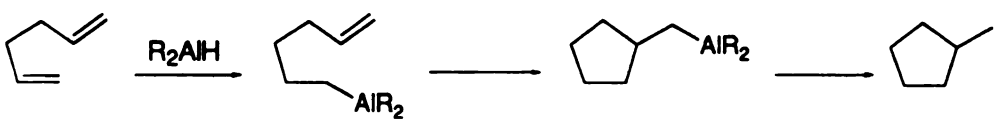
(7)

A reaction performed on the analogous 6-bromo-1-hexene gave a complex product mixture and was shown to proceed through radical intermediates.[30] Regiospecific ring closure of various iodoalkenes led to cyclopentylmethyl-containing products.[31] A *trans*-bicyclo[3.3.0]octane, hardly accessible by other methods,[32] was obtained in 87% yield by tandem cyclization of 4-ethenyl-6-hepten-1-yllithium.[33] Based on reported results, this method is the most efficient for five-membered ring formation. 6-Exo-trig closure of 6-hepten-1-yllithium in presence of 2 equivalents of TMEDA did not go to completion and produced a 68:32 ratio of methylcyclohexane and 1-heptene.[31a]

Metal Promoted Cyclizations

Reactive species in which the activated carbon center is not truly a free radical or a carbanion are included under this category. They include most organometallic compounds with a covalent metal-carbon bond. Halo alkenes and dienes are common starting materials. Only the cases where a 5-hexen-1-ylmetal intermediate, for 5-membered ring formation, is generated prior to cyclization are considered. The process by which the pendant olefin closes onto the activated carbon center is referred to as an insertion into the carbon-metal bond. Exo- or endo-ring closure determines the regioselectivity of the reaction.

Early work on the subject centered around aluminum complexes. Reactions involved the addition of a dialkylaluminum hydride to a diene, intramolecular insertion of the pendant olefin into the newly formed carbon-aluminum bond and hydrolysis (Equation 8). Thus, treatment of 1,5-hexadiene with 2.1 equivalents of diisobutylaluminum hydride at 70 °C for 16 hours produced n-hexane and methylcyclopentane in 2.4% and 97.6% respectively. However 1,6-heptadiene and longer chain dienes failed to cyclize.[34]

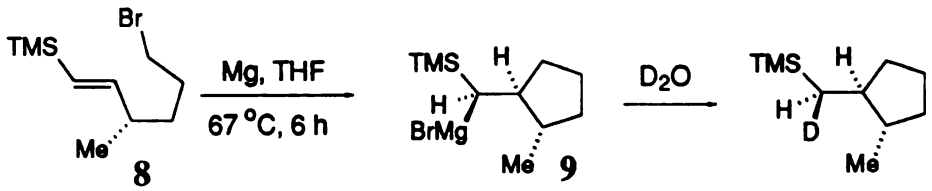


(8)

2-Methyl-1,5-hexadiene was submitted to similar reaction conditions by Stefani in a study of the regiochemical outcome of the aluminum cyclization reaction.[35] Addition of one equivalent of Et_2AlH

to 2-methyl-1,5-hexadiene for 24 hours at 23 °C generated after hydrolysis 1,3-dimethylcyclopentane and 1,1-dimethylcyclopentane in 32% and 65% yields respectively. The former requires alumination of the most substituted olefin followed by cyclization, whereas the later results from ring closure of 5-methyl-5-hexen-1-ylalane species.

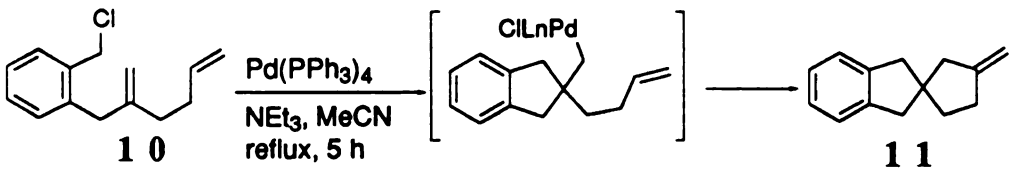
First reports mentioning five-membered ring formation mediated by magnesium appeared in 1966.[36] Upon hydrolysis, methylcyclopentane was obtained as a sideproduct (5%) while preparing the Grignard reagent of 6-bromo-1-hexene. Synthetic applications employed a trimethylsilyl activating group on the olefin.[37] Treatment of **8** with magnesium produced the Grignard reagent which cyclized in a very regio- and stereoselective manner to **9** (Equation 9). The methyl substituent controlled the relative stereochemistry at the two tertiary carbon centers and the syn addition of the carbon-magnesium bond onto the trans olefin established the configuration of the third stereocenter.



(9)

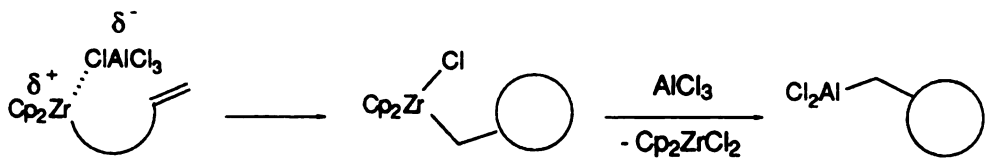
The most successful examples of late transition metal-mediated cyclization involve palladium. A variety of ways by which the initial carbon-palladium bond is formed exist. Usually, Heck reaction conditions are applied to an aryl, or vinyl iodide or bromide. A

limitation resides in the absence of β-hydrogens for the success of the reaction, as β-hydride elimination competes with the cyclization reaction. However, alkylpalladium species containing β-hydrogens can occur as intermediates which cyclize and undergo β-hydride elimination in the final step.[38] More recently, an intramolecular benzyl-palladation of alkene was reported.[39] Sequential carbopalladation conducted on **10** with a catalytic amount of palladium (0) generated the spiroalkene **11** in 57% yield (Equation 10).



10 **11** (10)

In a study of the preparation of organoaluminums by hydrozirconation-transmetalation, Schwartz reported the ring closure of 5-hexen-1-ylzirconocene chloride (**12**) to **14**, when treated with $AlCl_3$ (Equation 11).[40] Coordination of the Lewis acidic $AlCl_3$ to the chloride ligand of **12** and olefin insertion into the carbon-zirconium bond was proposed. Transmetalation between **13** and $AlCl_3$ freed zirconocene dichloride and **14**.



12 **13** **14** (11)

The zirconium/aluminum system, which resembled well known Ziegler-Natta catalysts, prompted our choice of the similar homogeneous titanocene catalyst to perform intramolecular olefin insertions. In chapters one and two, systems analogous to **1** were investigated. The regioselectivity of the intramolecular addition of a carbon-titanium bond to disubstituted olefins was studied. Once optimum reaction conditions were obtained for these simple substrates, the study was extended to bicyclic system formation. Single ring closure onto a preexisting cyclopentene, methylenecyclopentane or methylenecyclohexane tether generated fused [3.3.0] or [4.3.0] bicyclic skeletons.

By increasing the tether length by one or two carbons, cyclohexylmethyl- or cycloheptylmethyl-units are potential exo-cyclized products. In chapter three, such unit formation by the titanium based methodology with unactivated olefin terminators is presented. In an effort to improve our results, activation of the olefin with a trimethylsilyl substituent was investigated.

RESULTS AND DISCUSSION

Selective Formation of Five-Membered Carbocycles Mediated by Titanocene Chloride

1. Introduction

Our initial studies involved the simplest system, 5-hexen-1-yltitanocene chloride (**1**).[41] The preparation of **1** followed established procedures for the general two step formation of alkyltitanocene chlorides from alkylhalides.[9,10a] The 5-hexen-1-ylmagnesium bromide in THF was added to a suspension of Cp_2TiCl_2 in CH_2Cl_2 at -40 °C, and after 30 minutes the resulting homogeneous red solution was warmed to room temperature and stirred for 2 hours. Protonolysis of the mixture (HCl/MeOH, -78 °C) produced 1-hexene and methylcyclopentane in 98% yield from 5-hexen-1-ylmagnesium bromide in a 96:4 ratio. Quenching a sample of the Grignard reagent (HCl/H_2O, -78 °C to 23 °C) generated the same products, also in a 96:4 ratio;[42] thus, the transmetalation process did not result in further ligand cyclization.

Intramolecular cyclization of **1** to the cyclopentylmethyl titanocene chloride (**3**) was induced by the addition of

0.5 equivalent of $EtAlCl_2$ to a 0.1 *M* toluene solution of **1** at -78 °C.[43] After 30 minutes at -78 °C, the solution was quenched with HCl/MeOH, and a 1:99 mixture of 1-hexene to methylcyclopentane was produced in 88% yield from **1**.

In the present chapter, we investigate the effects of disubstituted olefin tethers on the insertion process. All three possible disubstituted alkenes, analogous to 6-bromo-1-hexene and bearing a methyl substituent, were synthesized. *cis*- and *trans*-1-Bromo-5-heptenes (**20**) and (**21**) were probes to establish the regioselectivity of carbon-titanium bond addition onto an internal olefin. As the geometry of the double bond was believed to influence the insertion process, pure geometric isomers **20** and **21** were tested individually. The third alkene substrate, 1-bromo-5-methyl-5-hexene (**26**) probed for the ease of insertion of terminal and disubstituted olefins into carbon-titanium bonds. Syn addition of the carbon-titanium bond in an anti-Markovnikov manner was expected to occur predominantly, by keeping away the bulky metal center from the newly formed cyclopentyl unit.

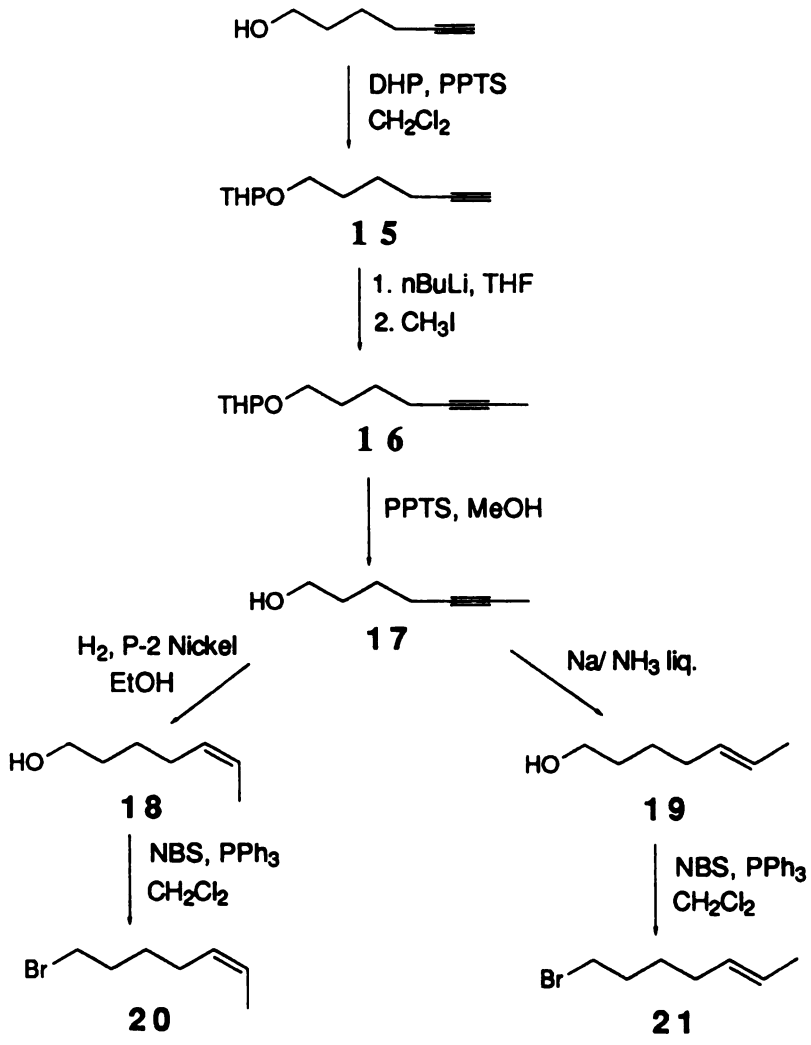
2. Synthesis of *cis*- and *trans*-1-Bromo-5-heptene and 1-Bromo-5-methyl-5-hexene

Alkene bromides **20**, **21**, and **26**, were chosen as substrates. They were prepared from commercially available starting materials, as outlined in Figure 1 and Figure 2. 5-Hexyn-1-ol was converted to its tetrahydropyranyl (THP) ether derivative **15** by reaction with

tetrahydropyran in CH_2Cl_2 containing a catalytic amount of pyridinium para-toluenesulfonate (PPTS).[44] Methylation conducted by sequential treatment of **15** with n-BuLi and then iodomethane, according to a reported procedure,[45] afforded the THP ether **16** in high yield. Deprotection catalyzed by PPTS[44] was run in anhydrous methanol and gave **17** in quantitative yield.

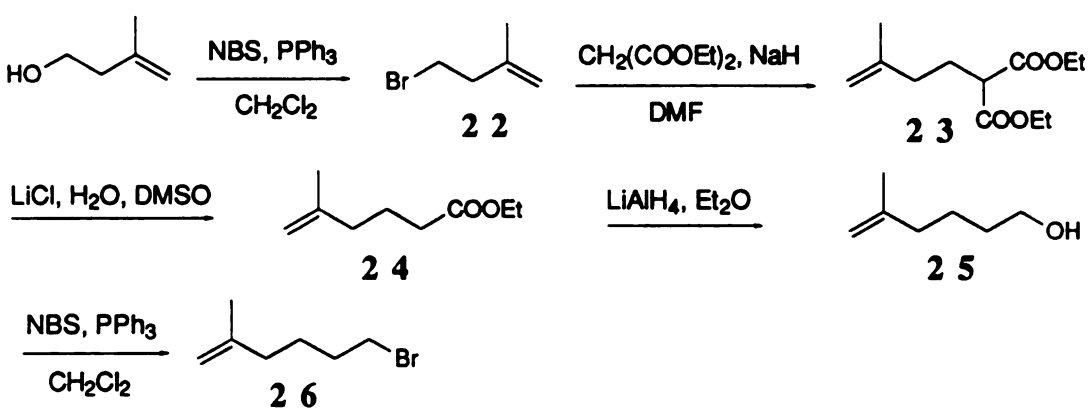
Alcohol **17** proved to be an ideal intermediate for diastereoselective reduction to alkenols **18** and **19**. Catalytic semi-hydrogenation utilized a procedure developed by Brown *et al.*[46] The "P-2 Nickel" catalyst, generated *in situ* and poisoned with ethylenediamine, selectively converted **17** to **18** under atmospheric pressure of H_2.

Reduction to the trans alkenol **19** caused more problem. Our initial attempt centered around the $LiAlH_4$-induced reduction in glyme solvents.[47] Reflux of **17** with $LiAlH_4$ in anhydrous diglyme for 12 hours generated **19** quantitatively but removal of the solvent proved to be difficult. Replacement of diglyme by the lower boiling monoglyme or the higher boiling tetraglyme did not promote reduction. Finally, when **16** was submitted to the same reaction conditions (diglyme under reflux) reduction occurred, but with the appearance of side products. Reduction with sodium in liquid ammonia, using reported procedures,[48] circumvented the problem and gave pure **19**. For the bromination of **18** and **19** to **20** and **21**, N-bromosuccinimide was added in small portions to a solution of the alcohol and triphenylphosphine in CH_2Cl_2 at 0 ^oC, using a modified procedure from those reported.[49]



Scheme 1. Synthetic Routes to *cis*- and *trans*-1-Bromo-5-heptene.

5-Methyl-5-hexen-1-ol (**25**) was prepared in 90% yield (based on GLC analysis) from 2-methyl-1,5-hexadiene by Sato *et al.*[50] Regioselective hydroalumination of the least substituted double bond of the diene with $LiAlH_4$, catalyzed by $TiCl_4$, followed by treatment with BF_3:OEt_2 gave the tri(5-methyl-5-hexenyl)borane, which was oxidized by alkaline hydrogen peroxide to the alcohol **25**. In our hands, 0.1 mole of 5-methyl-1,5-hexadiene produced **25** in 46% yield and in 95% purity. Thus, the two-carbon homologation of 3-methyl-3-buten-1-ol to **25** as shown in Scheme 2, was preferred.



Scheme 2. Synthetic Route to 1-Bromo-5-methyl-5-hexene.

Treatment of 3-methyl-3-buten-1-ol with NBS/PPh_3 in CH_2Cl_2 at 0 °C produced **22**, without double bond isomerization. Monoalkylation of diethylmalonate by **22**, carried in DMF, yielded **23**. The diester was deethoxycarboxylated by reaction with LiCl and water in DMSO heated to reflux. Reduction of the monoester **24** with

$LiAlH_4$ in Et_2O, produced alcohol **25** which was brominated to **26**, according to the general procedure.

3. Synthesis and Cyclization of *cis*- and *trans*-5-Hepten-1-yltitanocene Chlorides

Treatment of *cis*-1-bromo-5-heptene (**20**) with activated magnesium turnings in THF (1 *M*) at 65 °C for 5 hours produced *cis*-5-hepten-1-ylmagnesium bromide in quantitative yield. GLC analysis of a sample quenched with 10% aqueous HCl at 0 °C showed the presence of cyclized material in the extent of 4% (Table 1, entry 1).

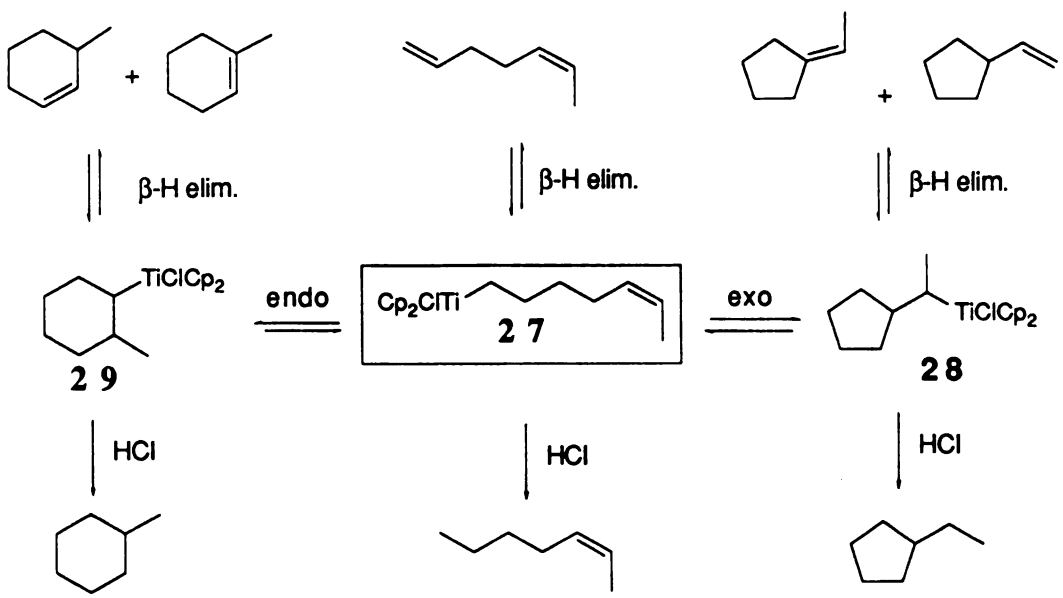
Table 1. Product Distribution from Quench of *cis*-2-Hepten-1-ylmetal Species and Isomers.

entry	quenched species				
1	Grignard R.	96	3	-	1
2	**27**	94	4	-	2
3	**27**	99	1	-	-
4	**28**	1	98	1	-

Transmetalation of the Grignard reagent to Cp_2TiCl_2 was achieved as described in the Experimental section. Prior to concentration, extraction and dilution in toluene (work up), GLC analysis of the crude solution provided the same composition of the

mixture (Table 1, entry 2). Thus, the transmetalation process did not modify the nature of the organic ligand, as expected. Concentration of the solution *in vacuo*, followed by addition of n-hexane, caused the precipitation of all magnesium salts. Filtration of the mixture, and subsequent washing of the salts with toluene, produced a solution of *cis*-5-hepten-1-yltitanocene chloride (**27**). Removal of solvents *in vacuo* produced a red brick paste, which was diluted to obtain a 0.1 *M* solution of **27** in toluene. This solution was somewhat different in composition, according to the species generated by HCl/MeOH quench (Table 1, entry 3). Obviously, the concentration *in vacuo* removed the volatile vinylcyclopentane. Production of ethylcyclopentane, to an extent of 4% from crude **27** (Table 1, entry 2), might have taken place during the quenching procedure (HCl/MeOH, -78 °C to 23 °C) since the solution of **27** was not free of the Lewis acidic magnesium dihalide salts. Species **27** was obtained in 78% yield from *cis*-5-hepten-1-ylmagnesium bromide by GLC analysis.

Addition of $EtAlCl_2$ to promote intramolecular olefin insertion could potentially result in a mixture of six products. Scheme 3 shows the paths to formation of each of these products from compound **27**.



Scheme 3. Potential Reaction Pathways of **27** with $EtAlCl_2$.

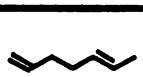
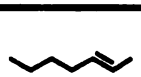
Intramolecular olefin insertion into the carbon-titanium bond through the exo mode would provide **28**, while endo cyclization would result in the less favorable species **29**. Decomposition of **27**, **28** or **29** by β-hydride elimination would produce *cis*-1,5-heptadiene, ethylidenecyclopentane, vinylcyclopentane, 1-methyl cyclohexene or 3-methylcyclohexene. Electrophilic quench of **27**, **28** and **29** (HCl for mixture analysis) would produce *cis*-2-heptene, ethylcyclopentane and methylcyclohexane respectively.

Treatment of **27** with 2.0 equivalents of $EtAlCl_2$ at -78 °C for 2 hours, followed by HCl/MeOH quench at -78 °C, produced a 1:98:1 ratio of *cis*-2-heptene, ethylcyclopentane and methylcyclohexane (Table 1, entry 4) in 79% yield from **27**, by GLC analysis. When **27** was submitted to the same conditions for 29 hours, the same product

ratio was observed. However, treatment with 2.0 equivalents of $EtAlCl_2$ at -78 °C for 2 hours, followed by removal of the cold bath for 0.5 hour and quenching at -78 °C, produced a 99:1 ratio of ethylcyclopentane and methylcyclohexane, with only a trace amount of *cis*-2-heptene. The absence of vinylcyclopentane and any products resulting from β-hydride elimination is noteworthy.

trans-5-Hepten-1-yltitanocene chloride (**30**) was obtained according to the method just described. *trans*-5-Hepten-1-ylmagnesium bromide produced from **21**, gave a 1:94:4:1 ratio of *trans*-1,5-heptadiene, *trans*-2-heptene, ethylcyclopentane and vinylcyclopentane when quenched with a 10% aqueous HCl solution at 0 °C (Table 2, entry 1). Here also, the ratio was somewhat different when the corresponding titanocene species **30** was quenched with HCl/MeOH at -78 °C. *trans*-2-Heptene, ethylcyclopentane and vinylcyclopentane amounted to a 98:1:1 distribution (Table 2, entry 2).

Table 2. Product Distribution from Quench of *trans*-2-Hepten-1-yl metal Species and Isomers.

entry	quenched species					
1	Grignard R.	1	94	4	-	1
2	**30**	-	98	1	-	1
3	**30**+$EtAlCl_2$	-	34	64	1	1
4	**30**+$EtAlCl_2$	-	-	98	2	-
5	**30**+$EtAlCl_2$	-	-	93	5	1

Cyclization of **30** proved to be more difficult than the corresponding cis isomer **27**. This is in accord with Schwartz's observation of olefin reactivity with hydrochlorozirconocene.[51] Treatment of a 0.1 *M* solution of **30** with 2.0 equivalents of $EtAlCl_2$ at -78 °C for 2 hours, followed by protonolysis, produced a 34:64:1:1 ratio of *trans*-2-heptene, ethylcyclopentane, methylcyclohexane and vinylcyclopentane (Table 2, entry 3). This ratio changed to a 4:94:2 distribution of *trans*-2-heptene, ethylcyclopentane and methyl cyclohexane when the solution was stirred for one additional hour after removal of the cold bath. Complete cyclization was achieved after 2.5 hours of reaction at 23 °C (Table 3, entry 4), ethylcyclopentane being produced in 59% yield from **30** (GLC analysis). The use of 10.0 equivalents of $EtAlCl_2$ for reaction at -78 °C for 2 hours on **30** drove the cyclization to completion (Table 2, entry 5), but endo cyclization occurred to a larger extent to form methylcyclohexane after protonolysis.

In order to avoid the long and tedious process of concentration *in vacuo* and filtration to obtain **30** as a pure complex in toluene, free of magnesium salts and Lewis basic solvents (THF and CH_2Cl_2), **30** was produced and cyclized according to the following procedure. A 1.0 *M* solution of *trans*-5-hepten-1-ylmagnesium bromide in the less Lewis basic Et_2O was transferred to 1.2 equivalent of Cp_2TiCl_2 in toluene at -40 °C. After 45 minutes at -40 °C and 5.5 hours at 23 °C, the reaction mixture was diluted to a 0.1 *M* solution by addition of toluene.

Subsequent protonolysis at -78 °C gave a 88:12 ratio of acyclic olefins and cyclic products (Table 3, entry 1). In the presence of the

less Lewis basic Et_2O, the magnesium dihalide salts produced during the transmetalation step appeared to have acted as a Lewis acid by promoting the cyclization reaction. The presence of the Lewis base Et_2O is thought to promote β-hydride elimination as the temperature was raised from -78 °C to 23 °C during protonolysis, thus explaining the formation of *trans*-1,5-heptadiene, vinylcyclopentane and ethylidenecyclopentane. If the 0.1 *M* solution of crude **30** was treated with 10.0 equivalents of $EtAlCl_2$ at -78 °C for 2.5 hours and quenched at -78 °C, GLC analysis showed a 85% cyclization rate with, here also, an appreciable amount of β-hydride elimination products (Table 3, entry 2).

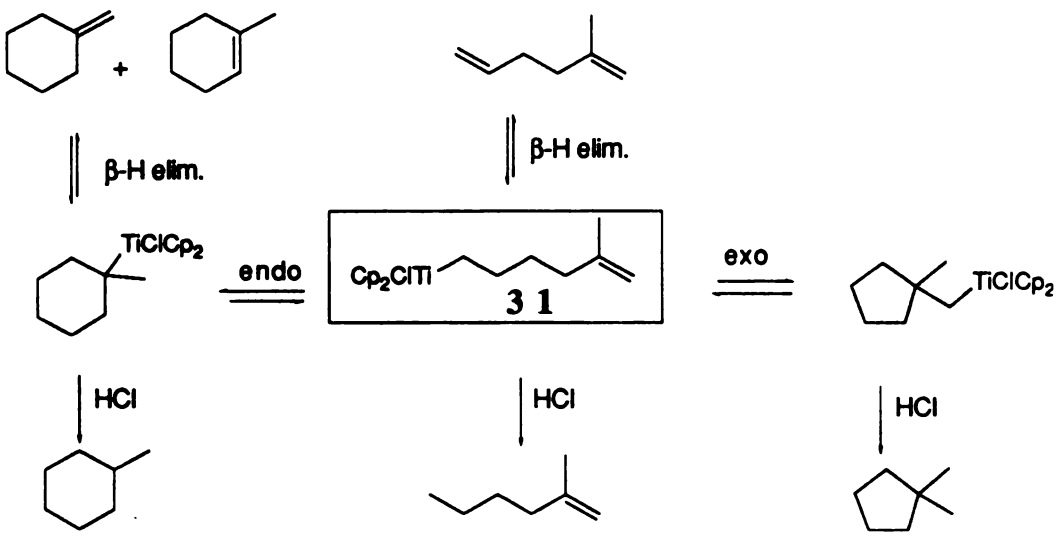
Table 3. Product Distribution from Quench of Crude **30** and Isomers.

entry						
1	2	86	8	3	1	-
2	3	13	13	9	33	2

In conclusion, this more convenient and direct procedure was not as efficient as the standard method. The presence of the Lewis acids and Lewis bases greatly promoted unwanted reactions and decomposition pathways of complex **30**. A pure and stable solution of **30** in toluene proved to be the best starting material to obtain clean and efficient intramolecular olefin insertion upon addition of $EtAlCl_2$.

4. Synthesis and Cyclization of 5-Methyl-5-hexen-1-yltitanocene Chloride

Cyclization of the 5-methyl-5-hexen-1-yl ligand is of great interest because it produces a quaternary carbon center by exo insertion of the terminal olefin into the carbon-titanium bond (Scheme 4). In the alternative endo cyclization mode, the metal center would be positioned on a tertiary carbon, a process which is not sterically and energetically favored.



Scheme 4. Potential Reaction Pathways of **31** with $EtAlCl_2$.

Species **31** was obtained from alkene bromide **26** in 59% yield (GLC analysis), as a 0.1 *M* solution in toluene It underwent facile and regioselective cyclization when treated with 2.0 equivalents of $EtAlCl_2$ at -78 °C for 4 hours. Protonolysis (HCl/MeOH,-78 °C) gave a 99:1 ratio of 1,1-dimethylcyclopentane (93% yield from **31** by GLC

analysis) and methylcyclohexane with only a trace amount (< 0.5%) of 2-methyl-1-hexene generated from **31**. If the cold bath was removed for 1 hour, after 4 hours of reaction at -78 °C, protonolysis of the solution under the same conditions, yielded the same products, in identical amount.

5. Compared Selectivities with the Free Radical nBu_3SnH-Initiated Ring Closure

Because our method for forming five-membered carbocycles utilizes bromoalkenes as starting material, it was interesting to compare it, in terms of selectivity, with the well established nBu_3SnH-induced free radical cyclization. Treatment of 0.05 *M* solutions of *cis*-1-bromo-5-heptene (**20**) or *trans*-1-bromo-5-heptene (**21**) in benzene at 70 °C, with 1.2 equivalents of nBu_3SnH and a catalytic amount of AIBN radical initiator gave the following results. Selective free radical cyclization of **20** and **21** produced ethylcyclopentane and methylcyclohexane in a 99:1 and 98:2[52] ratio respectively. In both cases, the alkene bromide was completely reduced by nBu_3SnH. However, the reaction mixture contained 9-12% of acyclic olefin, generated by nBu_3SnH quench of the uncyclized free radical by hydrogen abstraction. Closure of 1-bromo-5-methyl-5-hexene (**26**) mediated by nBu_3SnH has been reported.[23] Cyclization predominantly went *via* an endo mode of cyclization, 1,1-dimethylcyclopentane and methylcyclohexane were generated in a 40:60 ratio. Our method is of special interest since the

regioselectivity is reversed to yield the exo product almost exclusively.

6. Conclusion

From our studies on simple substrates such as **20**, **21**, and **26**, several features are noteworthy. The alkenyltitanocene chlorides **27**, **30**, and **31** were obtained from the readily accessible Grignard reagents, by transmetalation on Cp_2TiCl_2 in CH_2Cl_2. Once purified, by removal of all Lewis acids and Lewis bases involved in the synthesis, they showed a good stability in toluene solutions stored under inert atmosphere. Even if the $EtAlCl_2$-induced cyclization required longer reaction times and a larger amount of co-catalyst, compared to the parent 5-hexen-1-yltitanocene chloride system (**1**), total ring closure occurred at low temperature. This is of importance, especially for more elaborate substrates. Complete cyclization of the organic ligand has to take place before the carbon framework is released from the metal center, by external quench. Methods in which the reactive species is neutralized prior to cyclization in a competitive reaction (hydrogen abstraction on nBu_3SnH for the free radical process) can cause extensive waste of a valuable organic ligand.

Syn addition to the olefin occurred with an exceptional regioselectivity. The substitution pattern of the double bond had no dramatic influence. Alkenyltitanocene chlorides **27**, **30** and **31** gave exo to endo product ratios of 99:1, 98:2 and 99:1 respectively.

Finally, decomposition of the alkenyltitanocene chlorides by β-hydride elimination did not occur under optimum reaction conditions. Quite concentrated solutions could be employed with no problem of intermolecular olefin polymerization.

To extend the scope of this methodology, more elaborate substrates were tested in the Cp_2TiCl_2-mediated cyclization. A detailed study is presented in Chapter 2.

Selective Formation of Bicyclic Compounds Mediated by Titanocene Chloride

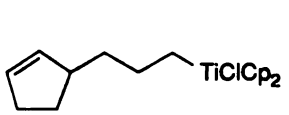
1. Introduction

Because the number of known condensed cyclopentanoid natural products continues to grow, and despite the fact that a collection of synthetic methods has been elaborated, new approaches are needed.[53] The application of our cyclization methodology in natural product synthesis will often require the construction of bicyclic structures. The *cis*-bicyclo[3.3.0]octane, *cis*-1-methyl bicyclo[3.3.0]octane, and *cis*-1-methylbicyclo[4.3.0]nonane systems are of special interest since they often constitute a part of the skeleton of cyclopentanoid compounds.

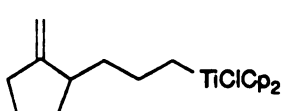
There are two ways in which the activated tether can be connected in an intramolecular exo fashion to produce a fused [3.3.0] bicyclic system. One way involves the cyclization of the activated

carbon onto a cyclopentene ring. With the tether attached at the allylic position, exo cyclization of **32** produces the *cis*-bicyclo[3.3.0]octane with the stereochemistry defined by the syn addition to the double bond and the cis constraint of the bicyclic system. Another route to these systems is achieved by the cyclization of **33**. Formation of a fused five-membered ring unit with a bridgehead methyl substituent is especially valuable. This framework is found in the carbon skeleton of triquinanes, a class of naturally occuring sesquiterpenes.

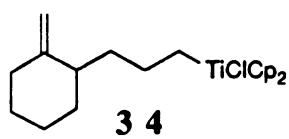
The fused bicyclo[4.3.0]nonane framework can potentially be prepared by ring closure of the analogous substituted cyclohexane system **34**. Cyclization of **34** in an exo manner generates the hydrindane carbon skeleton. Futhermore, the methyl substituted bridgehead carbon atom is identical to the C-13 quaternary center of the C-D ring system of steroids.



32



33

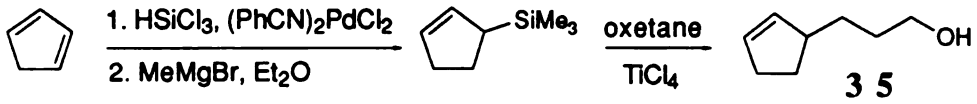


34

Our study started with the synthesis and cyclization of 3-(2-cyclopentenyl)propen-1-yltitanocene chloride (**32**).

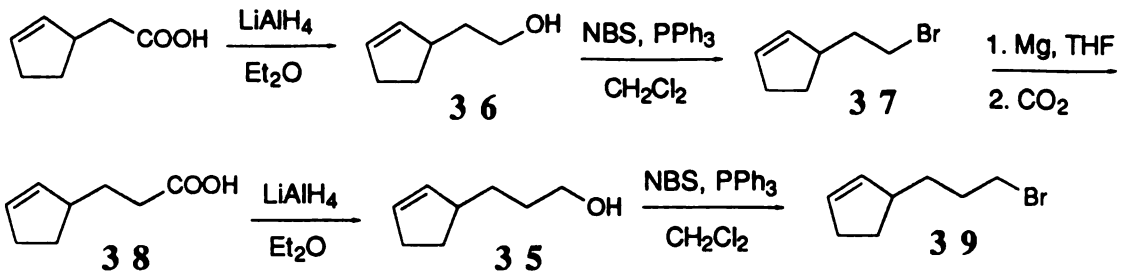
2. Synthesis and Cyclization of 3-(3-Bromopropyl)cyclopentene

The alcohol precursor **35** was reported by Weber *et al.* [54] (Equation 12)



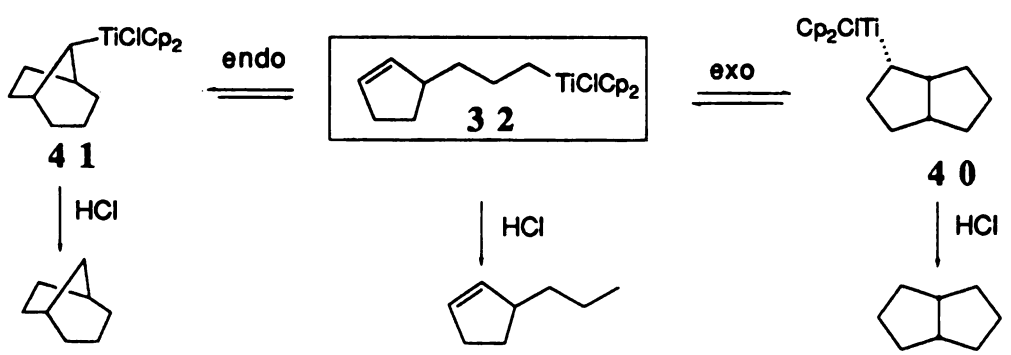
35 (12)

Hydrosilylation of cyclopentadiene with trichlorosilane, catalyzed by $(PhCN)_2PdCl_2$, at 105 °C for 65 hours gave 2-cyclo pentenyltrichlorosilane in 84% yield.[55] Methylation with methylmagnesium bromide in Et_2O afforded 2-cyclopentenyl trimethylsilane in 77% yield, which was converted to **35** as follows. Nucleophilic attack of 2-cyclopentenyltrimethylsilane on $TiCl_4$-activated oxetane resulted in the formation of **35**, along with appreciable amounts of 3-chloro-1-propanol (generated by competitive chloride ion attack of the activated oxetane). However, good yields of pure **35** could not be obtained by fractional distillation or flash column chromatography. A more classical route is presented in Scheme 5.



Scheme 5. Synthetic Route to **39**.

One-carbon homologation of 2-cyclopentene-1-acetic acid to carboxylic acid **38** was achieved by sequential $LiAlH_4$ reduction to alcohol **36** and bromination of **36** according to the standard NBS/PPh_3 method to the alkene bromide **37**. Treatment of a THF solution of the Grignard reagent of **37** with CO_2 (dry-ice) at -78 °C afforded the carboxylic acid **38**. $LiAlH_4$ reduction of **38** in Et_2O, followed by bromination, yielded **39** as a pure compound.



Scheme 6. Most Probable Reaction Pathway of **32** with $EtAlCl_2$.

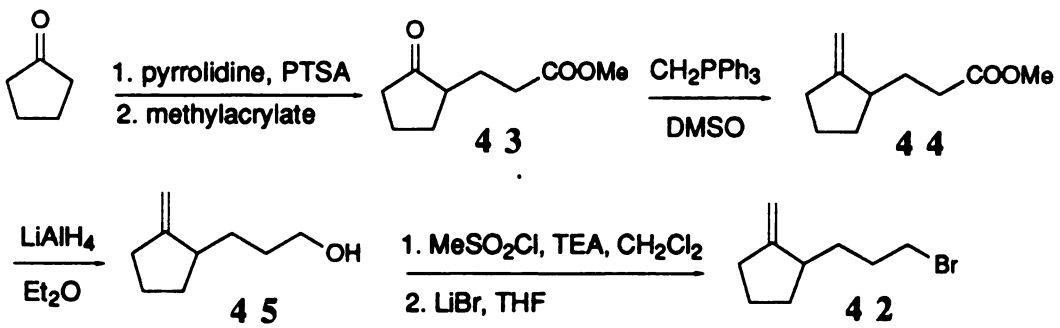
Intramolecular carbon-titanium bond syn addition onto the olefin can potentially result in the formation of **40** and **41** from **32** (Scheme 6). Potential β-hydride elimination products are not shown and quenched reaction mixtures were not analyzed for these compounds. Based on our previous results, the alkenyltitanocene chloride species do not decompose by β-hydride elimination under optimum reaction conditions. The non commercially available standard bicyclo[3.2.1]octane, resulting from protonolysis of **41**, was obtained from bicyclo[3.2.1]-2-octene, by H_2-hydrogenation on Pd/C at one atmosphere.[56] Hydrolysis of the Grignard reagent of **39** produced a sample of 3-propylcyclopentene.

Upon treatment of a 0.1 *M* toluene solution of **32** with 2.0 equivalents of $EtAlCl_2$ and subsequent protonolysis, a 97:3 mixture of *cis*-bicyclo[3.3.0]octane (83% yield from **32** by GLC analysis) and uncyclized product was observed. The closure regioselectivity was excellent since no endo type product occurred, no bicyclo[3.2.1]octane was detected in the reaction mixture. However, the cyclization reaction could not be driven to completion; treatment of **32** with 4.0 equivalents of $EtAlCl_2$ for 5 hours at -78 °C gave no better conversion.

3. Synthesis and Cyclization of 2-(3-Bromopropyl)-1-methylene cyclopentane

2-(3-Bromopropyl)-1-methylenecyclopentane (**42**) was prepared according to the synthetic sequence shown in Scheme 7.

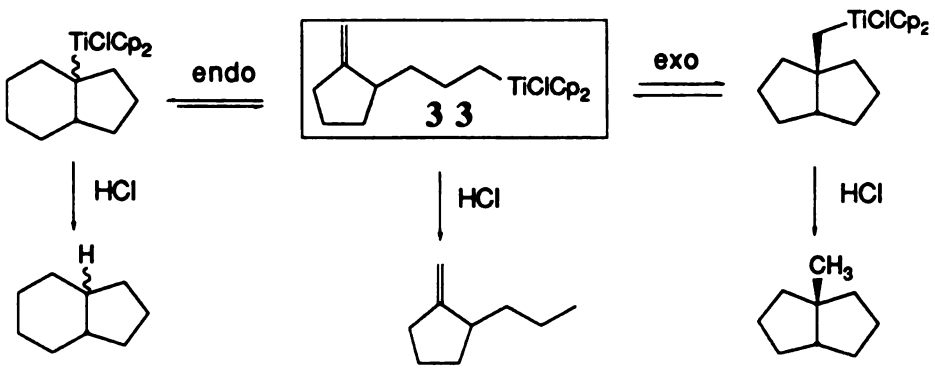
Condensation of pyrrolidinocyclopentane (obtained from cyclopentanone according to the method of Stork[57]) on methylacrylate gave methyl 3-(2-oxocyclopentenyl)propionate (**43**). Selective olefination of this keto-ester with methylene triphenylphosphane, generated by action of NaH on methyltriphenylphosphonium iodide in DMSO,[58] yielded the ester **44**, which was reduced to the alcohol **45** with $LiAlH_4$. Bromination of **45** with NBS/PPh_3 in CH_2Cl_2 at 0 °C, resulted in complete isomerization of the double bond. However, bromination of the mesyl derivative of **45** with LiBr in THF according to general methods[59] provided **42** as a pure compound.



Scheme 7. Synthetic Route to **42**.

The chlorotitanocene **33** was generated in 75% yield (GLC analysis) from **42** as a 0.1 *M* solution in toluene. Most probable reaction pathways of **33**, upon treatment with $EtAlCl_2$, are shown in Scheme 8. Addition of 2.0 equivalents of $EtAlCl_2$ at -78 °C for 1 hour produced a 1:99 ratio of 1-methylene-2-propylcyclopentane and *cis*-

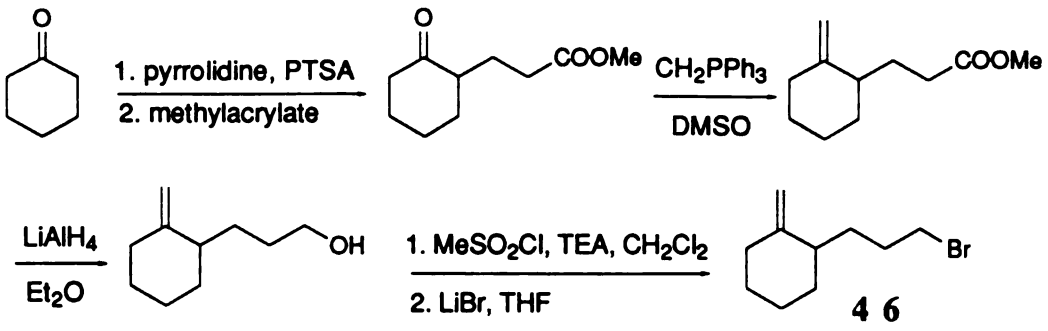
1-methylbicyclo[3.3.0]octane (84% yield from **33** by GLC analysis). As the major product was not commercially available, easy comparison of retention time, by GLC analysis, with an authentic sample could not be performed. An analytical sample was isolated as described in the Experimental section and gave satisfactory ^{1}H and ^{13}C NMR and MS spectra. *cis*- and *trans*-Bicyclo[4.3.0]nonane, resulting from endo closure by syn addition of the carbon-titanium bond on the α and β face respectively, were not formed during the reaction.



Scheme 8. Most Probable Reaction Pathways of **33** with $EtAlCl_2$.

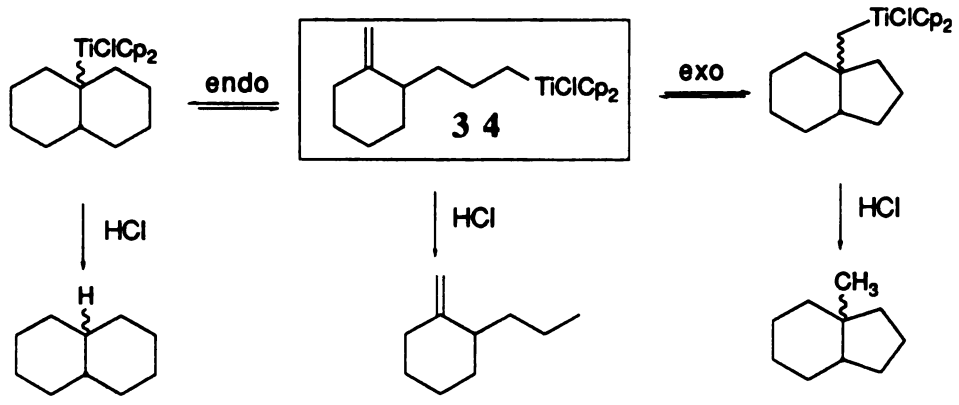
4. Synthesis and Cyclization of 2-(3-Bromopropyl)-1-methylene cyclohexane

2-(3-Bromopropyl)-1-methylenecyclohexane (**46**) was obtained by a method analogous to the synthesis of **42** (Scheme 9).[60]



Scheme 9. Synthetic Route to **46**.

A 0.1 *M* solution of the chlorotitanocene derivative **34** was produced under the usual experimental conditions in 81% yield from **46** (GLC analysis). Reaction with 1.0 equivalent of $EtAlCl_2$ for 3 hours at -78 °C generated *cis*-1-methylbicyclo[4.3.0]nonane as a single product, and in 74% yield (GLC analysis), after protonolysis (Scheme 10). It corresponded to a syn addition of the carbon-titanium bond onto the olefin in an exo fashion.

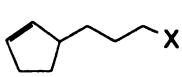
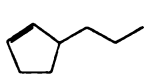
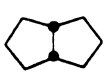
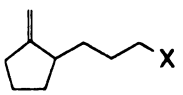
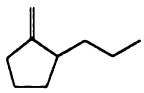
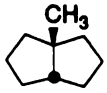
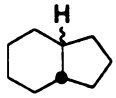
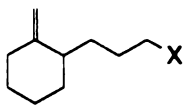
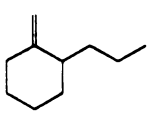
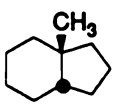
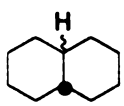


Scheme 10. Most Probable Reaction Pathways of **34** with $EtAlCl_2$.

5. Comparison of the Selectivities with the Free Radical Ring Closure

Free radical ring closure mediated by nBu_3SnH was performed on bromoalkenes **39**, **42**, and **46** in benzene solutions, as described in the Experimental section. Results are given in Table 4.

Table 4. Compared Selectivities with Free Radical Cyclization.

			
X = $TiClCp_2$	3	97	0
X = Br	3	97	0
			
X = $TiClCp_2$	1	99	0
X = Br	11	15	50:24 (cis:trans)
			
X = $TiClCp_2$	0	100	0
X = Br	47	17	5:31 (cis:trans)[20]

In each case, the bromoalkene starting materials were completely consumed under the reaction conditions utilized. However, radical quench by hydrogen abstraction prior to cyclization appeared to be a major drawback of this method, as uncyclized species composed 3 to 47% of the product mixtures. Another

limitation was the lack of selectivity. Exo- to endo-product ratios of 17:83 and 1:2 for **42** and **46** respectively, reflected the poor regioselectivity of the radical addition on the olefin.

6. Conclusion

The Cp_2TiCl_2-induced ring closure of **39**, **42** and **46** is a valuable and efficient process. *cis*-Bicyclo[3.3.0]octane, *cis*-1-methylbicyclo[3.3.0]octane and *cis*-1-methylbicyclo[4.3.0]nonane were obtained regioselectively and in high yields. The fused bicyclo[3.3.0] system was generated in the cis form exclusively by both nBu_3SnH- and Cp_2TiCl_2-initiated methods. 3-Propylcyclopentene occurred in the reaction mixture to an extent of 3% in both cases. However, a major difference in product distribution was observed for the ring closure of **42** and **46**. The radical mediated cyclization of **42** favored the quite stable bicyclic products, *cis*-bicyclo[4.3.0]nonane (strain energy 8.9 kcal/mol[76]), whereas the Cp_2TiCl_2 based method leads to the exclusive formation of the more constrained *cis*-1-methylbicyclo[3.3.0]octane system (strain energy for *cis*-bicyclo[3.3.0]octane 12.0 kcal/mol[76]). The same tendency was observed in the cyclization of **46**. Radical cyclization formed the stable *trans*-decalin as the major cyclized product. The titanium method, instead, produced the relatively instable *cis*-1-methylbicyclo[4.3.0]nonane system by effective irreversible cyclization.

A similar outcome was observed for anionic cyclizations performed on analogous substrates.[31a] 2-(3-Iodopropyl)-1-methylenecyclopentane and 2-(3-iodopropyl)-1-methylene cyclohexane underwent regio- and stereoselective isomerization to *cis*-1-methylbicyclo[3.3.0]octane and *cis*-1-methylbicyclo[4.3.0] nonane respectively, upon treatment with tBuLi in pentane/Et_2O solutions. However, the poor rate of isomerization represented a major problem for this method. Uncyclized products amounted 84% and 35% of the reaction mixture for 2-(3-iodopropyl)-1-methylenecyclopentane and 2-(3-iodopropyl)-1-methylene cyclohexane.

Six-membered Ring and Attempted Seven-membered Ring Formation Mediated by Titanocene Chloride

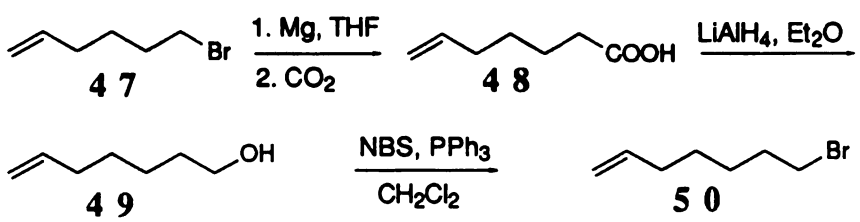
1. Introduction

According to Baldwin's rules,[11] favored processes for six-membered ring closure are 6-exo-tet, 6-exo-trig, 6-endo-trig and 6-endo-dig. Seven-membered ring formation via 7-exo-tet, 7-exo-trig, 7-endo-trig or 7-endo-dig closures are also favored. Although each mode of cyclization possesses literature precedents, existing methods have not, to date, been as versatile and numerous as those employed for five-membered ring closure. Intramolecular insertion of unactivated olefin into the carbon-titanium bond performed on

appropriate substrates is expected to generate 6- and 7-membered carbocycles in a regioselective fashion *via* 6-exo-trig and 7-exo-trig modes respectively. Thus, the methodology under investigation should complement and even improve the existing methods. The first tests were carried on the simplest system, 6-hepten-1-yltitanocene chloride (**2**).

2. Synthesis and Cyclization of 6-Hepten-1-yltitanocene Chloride Catalyzed by Various Lewis Acids

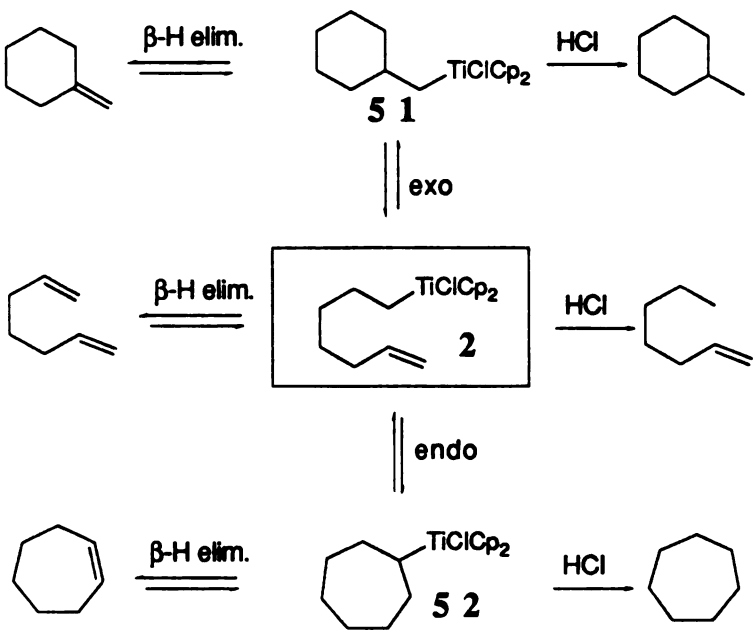
The organic precursor **50** to 6-hepten-1-yltitanocene chloride (**2**) was obtained by one-carbon homologation of 6-bromo-1-hexene (**47**) as depicted in Scheme 11. A solution of 5-hexen-1-ylmagnesium bromide in THF was treated with CO_2 (dry-ice) at -78 °C and acidified to generate carboxylic acid **48**. Reduction with $LiAlH_4$ provided **49**, which was brominated to **50** with NBS/ PPh_3 in CH_2Cl_2.



47 **48** **49** **50**

Scheme 11. Synthetic Route to 1-Bromo-7-octene (**50**)

Grignard reagent formation of **50** in THF, followed by transmetalation on Cp_2TiCl_2 according to the general procedure yielded **2** in 74% yield (GLC analysis) from **50**. Upon treatment with $EtAlCl_2$ or other Lewis acids, 6-hepten-1-yltitanocene chloride (**2**) could potentially generate the six products shown in Scheme 12, by protonolysis or decomposition by β-hydride elimination of the titanocene species. Reaction mixtures were analyzed for all compounds, except cycloheptene. Since endo cyclization of **2** to **52** is disfavored, only trace amounts of cycloheptene should appear, if any.



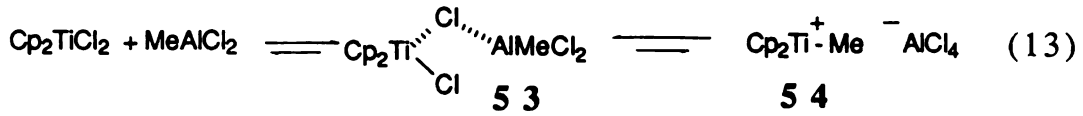
Scheme 12. Potential Reaction Pathways of **2** with $EtAlCl_2$.

Protonolysis of the 0.1 *M* toluene solution of **2** gave a 98:2 ratio of 1-heptene and methylcyclohexane. $EtAlCl_2$-induced cyclization by

addition of 2.0 equivalents of $EtAlCl_2$ at -78 °C for 1 hour afforded a 1:96:3 distribution of 1-heptene, methylcyclohexane, and methylenecyclohexane, after protonolysis at -78 °C. In this particular case, yields were somewhat dependent upon the concentration of **2**. Cyclization occurred in 45-55% yields (GLC analysis) at 0.1 *M* concentration of **2**, but in 83% yield if a 0.01 *M* solution of **2** was employed.

In an effort to overcome decomposition by β-hydride elimination, another Lewis acid was tested. Methylalumoxanes have been used extensively with Zr or Ti transition metals as catalysts for butene or propene polymerization, and the study of the stereochemical outcome of such reactions.[61] Thus, treatment of **2** with 3.0 equivalents of methylalumoxane, prepared according to published procedures,[62] at -78 °C resulted in an almost complete conversion to **51**. A 6:86:6 ratio of 1-heptene, methylcyclohexane and methylenecyclohexane resulted after protonolysis. The three products accounted for 80% of the starting material **2**. If the cold bath was removed and the solution allowed to warm up to ambient temperature, this ratio changed to 1:75:24. Although the three products were obtained in identical yield, decomposition of **51** by β-hydride elimination became a major problem, methylenecyclohexane accounted for 24% of the product mixture.

In the study of the carbotitanation of trimethyl(phenylethynyl) silane by titanocenedichloride in the presence of $MeAlCl_2$, Eisch *et al* [63] discussed the solvent influence on the following equilibria (Equation 13).



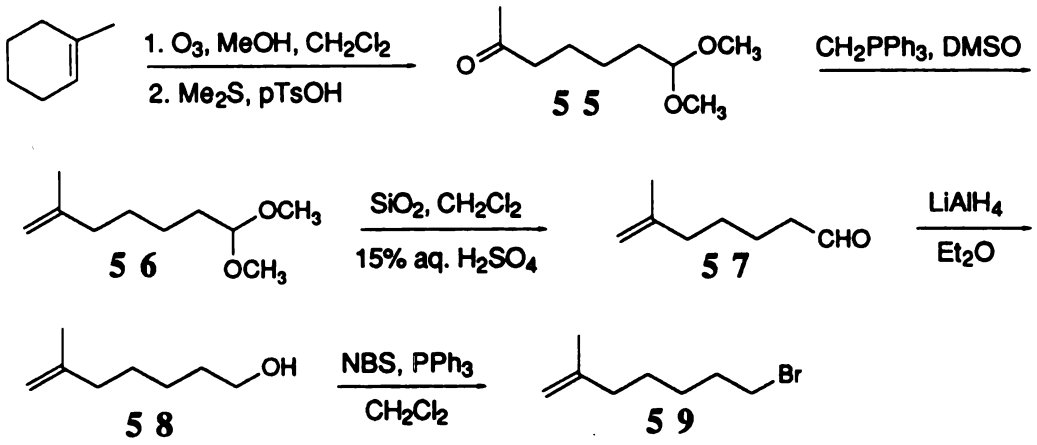
(13)

While Lewis basic solvents prevent the formation of **53** by coordination with $MeAlCl_2$, aromatic solvents, such as toluene, have a tendency to form complexes with **53**, thus pulling the first equilibrium to the left. Coordination of these π-bases to the cationic site of **54** also retards the olefin or acetylene insertion. However, polar and weakly donor solvents, such as haloalkanes, were shown to accelerate ethylene insertion process into **54**. Consequently, treatment of **2** in a 1,2-dichloroethane solution with 0.4 equivalent of $EtAlCl_2$ (1.0 *M* in n-pentane) at -32 °C resulted in complete cyclization of **2**. Protonolysis of the solution with 1 *M* HCl in Et_2O, 0.2 hour after the addition gave methylcyclohexane as the only product, in 64% yield from **2**. However, the reactive species were more prone to polymerization as the yields dropped at longer reaction times.

3. Synthesis and Cyclization of 6-Methyl-6-hepten-1-yltitanocene Chloride Catalyzed by Various Lewis Acids

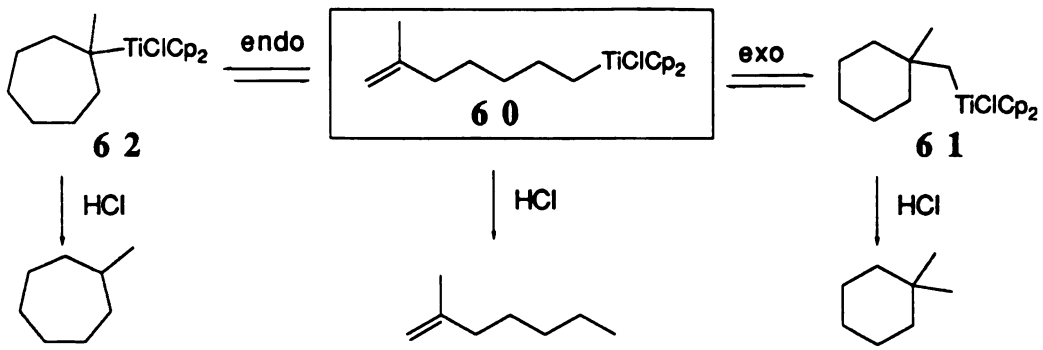
In view of the potential synthetic utility of our approach to cyclohexane ring formation, it was of interest to test a more elaborated substrate in the cyclization process. Alkene bromide **59** should preferentially undergo exo closure to form a gemdimethyl substituted cyclohexane ring. Such a skeleton is especially valuable in terpenoid chemistry, since it is often part of the carbon framework

of these naturally occurring compounds. Based on our results for five-membered ring formation, the external olefin should insert quite readily into the carbon-titanium bond. Finally, β-hydride elimination, which was of concern for the parent system **2**, does not take place on the exo cyclized species **61** (Scheme 14). Scheme 13 shows our approach to substrate **59** from 1-methylcyclohexene.



Scheme 13. Synthetic Route to **59**.

Ozonolysis of 1-methylcyclohexene and Me_2S-reduction of the hydroperoxide product yielded the ketoacetal **55**.[64] Wittig olefination of **55** according to the Corey modification[65] produced the acetal **56**, which was reduced to aldehyde **57** under mild acidic conditions.[66] $LiAlH_4$ reduction to **58** and bromination afforded **59** as a pure compound. Grignard reagent formation of **59** and transmetalation on Cp_2TiCl_2 produced **60** in 63% yield by GLC analysis. Exo-ring closure and endo-ring closure could generate **61** and **62** respectively (Scheme 14).



Scheme 14. Potential Reaction Pathways of **60** with Lewis Acids.

In this case, the olefin insertion did not occur as readily as for the parent system **50**. The steric hindrance caused by the methyl substituent probably made the required conformation for olefin insertion less favored. A variety of reaction conditions to form **61** were tested, our best results are given in Table 5.

Table 5. Cyclization of **60**: Experimental Conditions and Results

catalyst	solvent[a]	temp.	reaction time	non cyclized	exo-product[b]	yield[c]
$EtAlCl_2$, 2 eq	toluene	-78 °C	13 h	95	5	87%
$EtAlCl_2$, 2 eq	toluene	-20 °C	12 h	88	12	73%
$EtAlCl_2$, 1 eq	$Cl(CH_2)_2Cl$	-30 °C	15 mn	15	85	23%
Me_2AlCl, 0.3 eq	$Cl(CH_2)_2Cl$	-30 °C	15 mn	18	82	72%
$(CH_3AlO)_n$, 1 eq	$Cl(CH_2)_2Cl$	-30 °C	1.3 h	100	-	low

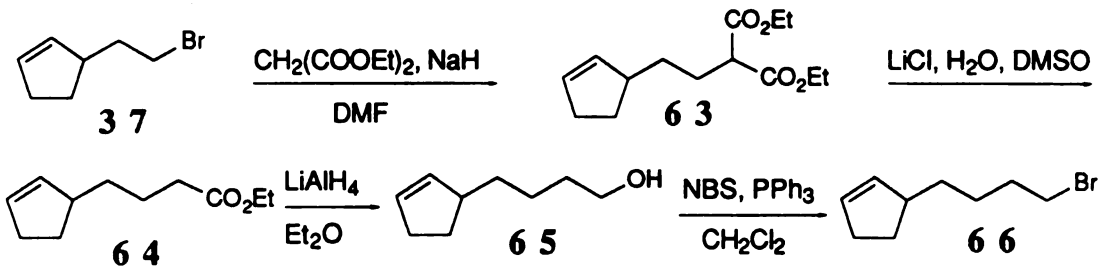
[a]All reactions were performed with 0.1 *M* solutions of **60**. [b]No endo-product was observed under these conditions. [c]Yields refer to both products (non cyclized and exo-product) and were obtained by GLC analysis of the hydrolyzed reaction mixtures.

In toluene, **60** underwent only partial cyclization upon treatment with 2.0 equivalents of $EtAlCl_2$. This process was somewhat promoted at higher temperature, since reaction at -20 °C for 12 hours resulted in a 12% conversion of **60** to 1,1-dimethylcyclohexane, after protonolysis. In 1,2-dichloroethane solvent and at -30 °C, the reactive species was more subject to decomposition, probably by intermolecular polymerization of **60**. Treatment of **60** with 1.0 equivalent of $EtAlCl_2$ for 15 minutes and subsequent quenching gave a 15:85 ratio of 2-methyl-1-heptene and 1,1-dimethylcyclohexane. However, this strong Lewis acid induced decomposition of **60**, 2-methyl-1-heptene and 1,1-dimethylcyclohexane accounted only for 23% of the initial material. The less Lewis acidic Me_2AlCl induced cyclization to the same extent, but in higher yield. Finally, methylalumoxane had no influence on the ring closure and destroyed most of the starting material. In all cases, a temperature rise of the 1,2-dichloroethane solution resulted in almost a complete disappearence of 2-methyl-1-heptene or 1,1-dimethylcyclohexane, by decomposition of the reactive species **60**.

4. Synthesis and Cyclization of 4-(2-Cyclopentenyl)but-1-yl titanocene Chloride Catalyzed by $EtAlCl_2$

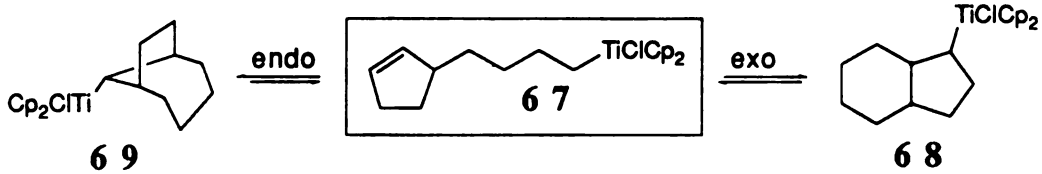
The two-carbon homologation of **37** as shown in Scheme 15, provided a synthesis of **66**. Monoalkylation of diethylmalonate by **37** in DMF provided the diethyl ester **63**, which was deethoxycarboxylated to ethyl ester **64**. $LiAlH_4$ reduction of **64** to

the alcohol **65**, followed by bromination with NBS/PPh_3 afforded 3-(4-bromobutyl)cyclopentane (**66**) in 53% overall yield.



Scheme 15. Synthetic Route to **66**.

The corresponding 4-(2-cyclopentenyl)but-1-yltitanocene chloride (**67**) can potentially generate *cis*-bicyclo[4.3.0]nonane and *trans*-bicyclo[4.3.0]nonane via exo type ring closure and bicyclo[4.2.1]nonane via endo ring closure. However, syn addition of the carbon-titanium bond onto the olefin, in an exo manner, should produce *cis*-bicyclo[4.3.0]nonane after acidic quench. *trans*-Bicyclo[4.3.0]nonane and bicyclo[4.2.1]nonane result from exo ring closure on the α face, and endo ring closure respectively. These processes are disfavored based on our previous results.

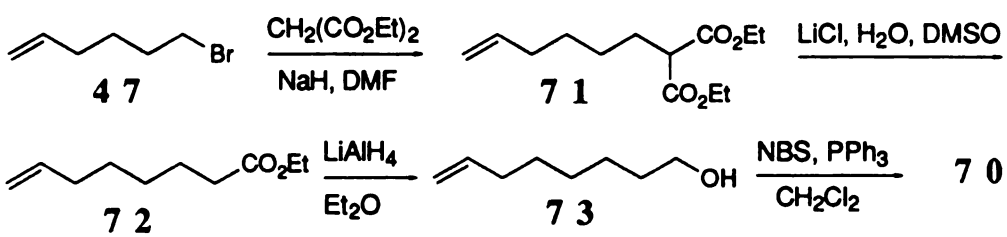


Scheme 16. Most Probable Cyclization Pathways of **67**.

Cyclization induced by addition of 2.0 equivalents of $EtAlCl_2$ at -78 °C to a 0.1 *M* solution of **67** in toluene did not occur after 18 hours. A 93:7 ratio of 3-butyl-1-cyclopentene and *cis*-bicyclo[4.3.0]nonane reflected the poor reaction mixture, if the solution was stirred an additional 0.5 hour at 0 °C. The two products were generated in 70% yield from **67** after HCl protonolysis. Longer reaction times did not give a better conversion; the structure of **67** was confirmed by ^{13}C NMR performed on a sample diluted in D6-benzene.[67]

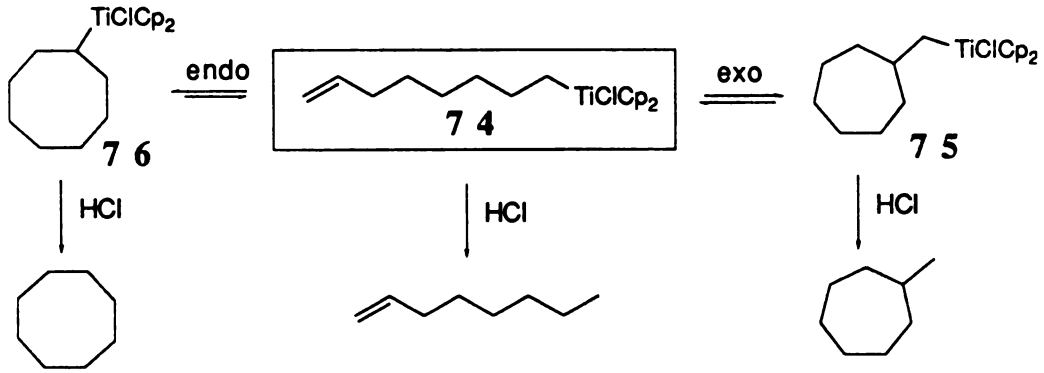
5. Synthesis and Attempted Cyclization of 7-Octen-1-yltitanocene Chloride

8-Bromo-1-octene (**70**) was prepared as follows. Alkylation of diethylmalonate with **47** in DMF afforded the diethyl ester **71**, which was deethoxycarboxylated to ethyl ester **72**, in presence of LiCl and water in DMSO. Reduction of **72** to 7-octen-1-ol (**73**) and bromination of **73** with NBS/ PPh_3 in CH_2Cl_2 gave **70** in 57% overall yield (Scheme 17).



Scheme 17. Synthetic Routes to **70**.

Treatment of 7-octen-1-yltitanocene chloride (**71**) with a Lewis acid can potentially generate **75** and **76**, which give methylcycloheptane and cyclooctane upon protonolysis (Scheme 18). The reaction mixture was also analyzed for methylenecycloheptane which resulted from the decomposition of **75** by β-hydride elimination.



Scheme 18. Exo and Endo Cyclization Products of **74**.

A variety of experimental conditions were tested (Table 6). Reaction of **74** with $EtAlCl_2$ or methylalumoxane in toluene or in 1,2-dichloroethane solutions did not result in ring closure. No methylcycloheptane product from exo-cyclized **74** was detected. Polymerization of **74** catalyzed by $EtAlCl_2$ accounted for low yields in 1-octene (0-5%). Methylalumoxane did not induce starting material decomposition when used at -78 °C in toluene, but it did not promote cyclization either. Since no trace of methylcycloheptane was observed under any reaction conditions, the 6-carbon chain

connecting the olefin to the titanium center is probably too long for an adequate conformation to be reached prior to olefin insertion.

Table 6. Reaction Conditions for Attempted Cyclization of **74**.

solvent	concentration	catalyst	temp.	reaction time	yield[a]
toluene	0.1 *M*	$EtAlCl_2$, 2 eq	-78 °C	0.2 h	low
toluene	0.01 *M*	$EtAlCl_2$, 2 eq	-78 °C	1 h	low
toluene	0.1 *M*	$(CH_3AlO)_n$, 0.6 eq	-78 °C	4 h	89%
toluene	0.1 *M*	$(CH_3AlO)_n$, 1.2 eq	-78 °C	11 h	75%
$Cl(CH_2)_2Cl$	0.1 *M*	$EtAlCl_2$, 1 eq	-30 °C	0.5 h	low

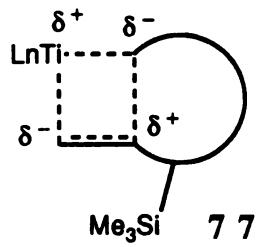
[a]Refers to yield of 1-octene from **74** obtained by GLC analysis.

6. Trimethylsilyl-Charge Accelerated Olefin Insertion for Six- and Seven-membered Ring Closure

Trialkylsilyl groups are known for exerting a strong stabilization of electron deficient carbon atoms at the β position to the silicon center (Si β-effect).[68] The initial insertion product of trimethyl(phenylethynyl)silane onto the Ziegler-Natta catalyst system, generated by reaction of equimolar amounts of Cp_2TiCl_2 and $MeAlCl_2$ in chloroform was isolated and characterized.[69] The carbometalation step was eased by the trimethylsilyl activating substituent, explained in terms of hyperconjugation effect. More recently, in a regiochemical study of the allyltrimethylsilane

insertion into a carbon-zirconium bond,[70] the outcome of the reaction of allyltrimethylsilane with $Cp_2Zr(pyridyl)^+$ resulted from the Me_3Si-stabilization of the polar 4-center transition state.

For six- and seven-membered ring formation, a Me_3Si substituent positioned on the olefin tether as depicted by **77** (Scheme 19) should cause a rate enhancement for the olefin insertion into the carbon-titanium bond, by interaction of the silicon atom with the β developing positive charge.



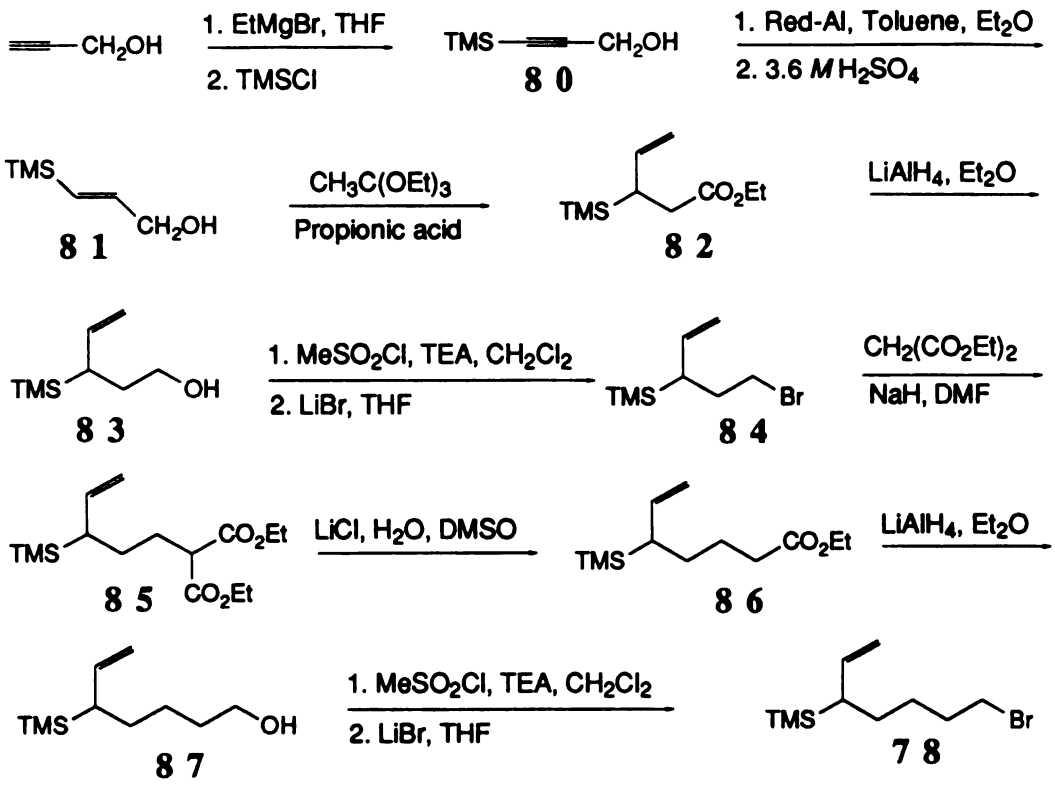
77

Scheme 19. TMS-Accelerated Olefin Insertion into C-Ti Bond.

By its remote position from the olefin, the Me_3Si substituent should not cause any unnecessary steric interactions with the crowded titanium center, contrarily to a vinyltrimethylsilane moiety for example. Thus $EtAlCl_2$-induced intramolecular olefin insertion was performed on the simplest systems, 7-bromo-3-(trimethylsilyl)-1-heptene (**78**) and 8-bromo-3-(trimethylsilyl)-1-octene (**79**).

7. Synthesis and Cyclization of 7-Bromo-3-(trimethylsilyl)-1-heptene

7-Bromo-3-(trimethylsilyl)-1-heptene (**78**) was obtained as follows. Trimethylsilylation of propargyl alcohol[71] in THF afforded **80**, which was reduced to **81** with Red-Al in toluene according to the method of Denmark.[72] Treatment of **81** with triethylorthoacetate under acidic conditions following a published procedure,[73] generated the Ortho Claisen type product **82**. Reduction with $LiAlH_4$ to **83** and bromination by action of LiBr on the corresponding mesylate completed the synthesis of intermediate **84**. The 2-carbon homologation of **84** by reaction on diethylmalonate provided **78** as shown in Scheme 20.

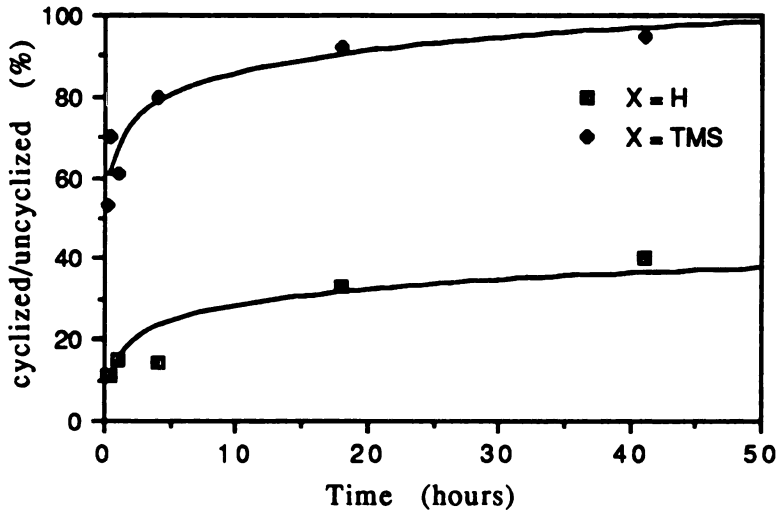


Scheme 20. Synthetic Route to **78**.

Action of **78** on Mg at 64 °C resulted solely in complete Grignard reagent formation.[74] Transmetalation on Cp_2TiCl_2 to generate 5-(trimethylsilyl)-6-hepten-1-yltitanocene chloride (**88**) and work up produced a solution of **88** in toluene (approximately 0.1 *M*). Treatment with $EtAlCl_2$ for 1 hour at -78 °C resulted in complete and clean cyclization of the organic ligand, as evidenced by HCl quench at -78 °C and GLC analysis of the crude mixture (Equation 14). In 1,2-dichloroethane, addition of 0.4 equivalent of $EtAlCl_2$ over a 15 minutes period at -30 °C was sufficient to induce complete ring closure.

(14)

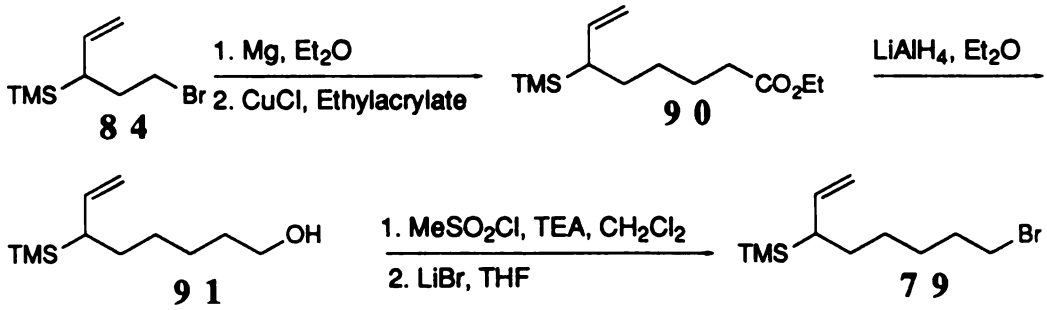
To measure the rate enhancement caused by the TMS substituent, an equimolar solution of **88** and 6-hepten-1-yltitanocene chloride (**2**) (0.14 *M* in toluene) was treated over a 15 minutes period with 0.4 equivalent of $EtAlCl_2$ at -78 °C. Immediate quench of an aliquot gave a 48:52 and a 84:16 ratio of uncyclized *versus* cyclized products for **88** and **2** respectively. After 41 hours, they changed to 5:95 and 60:40 (Scheme 21). Thus, introduction of a trimethylsilyl group on the tether resulted in an acceleration of the olefin insertion, probably by stabilizing the polar four-center transition state.



Scheme 21. Compared Rate of Cyclization of **88** (X=TMS) and **2** (X=H).

8. Synthesis and Attempted Cyclization of 8-Bromo-3-(trimethylsilyl)-1-octene

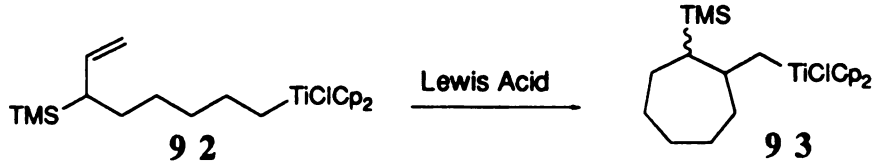
3-Carbon chain elongation of **84** was performed according to the synthetic sequence shown in Scheme 22.



Scheme 22. Synthetic Route to **79**.

Action of **84** on Mg, in Et_2O solution under reflux, generated the Grignard reagent, which was treated with ethylacrylate under CuCl catalysis[75] to give the 1,4-Michael addition product **90**. Ethyl ester **90** was converted to **79** by usual procedures.

6-(Trimethylsilyl)-7-octen-1-yltitanocene chloride (**92**) could generate, by exo insertion of the olefin, the substituted cycloheptylmethyltitanocene chloride **93** (Equation 15).



(15)

However, action of 2.0 equivalents of $EtAlCl_2$ at -78 °C on a 0.1 *M* solution of **92** in toluene had no effect after 12 hours. Raising the temperature to 23 °C resulted in oligomerization after 0.5 hour. Polymerized material also resulted when 1.0 equivalent of $EtAlCl_2$ was added to a 0.1 *M* solution of **92** in 1,2-dichloroethane at -30 °C.

9. Conclusion

We have shown that six-membered ring closure is a valuable process. The Cp_2TiCl_2 based methodology offered several advantages over the existing methods. Contrarily to the carbocationic cyclizations, the closure operated by exo insertion of the olefin. This process could be of special importance when endo ring closure did not fulfill the requirement of a synthetic sequence. Reactions were regioselective, the cycloheptane endo product did not occur under our reaction conditions. Activation of the double bond was not necessary. However, the reaction rates were enhanced when the 4-center transition state was stabilized by a suitably positioned trimethylsilyl group. Decomposition of the insertion product by β-hydride elimination was more of a concern, compared to the five-membered ring formation. It could nevertheless be minimized by careful operating conditions. Steric environment of the alkene had a major influence upon the success of the cyclization. Disubstituted olefins gave only partial ring closure, whereas trisubstituted tethered olefins were unreactive.

Seven-membered ring formation was not favored. Adequate conformations for the olefin insertion could not be reached. Electronic effects induced by a trimethylsilyl activating group did not overcome the steric effects. However 5- *versus* 7-membered ring formation can be beneficially employed for tandem type cyclization. 4-Vinyl-7-octen-1-yltitanocene chloride should preferentially undergo 5-exo type cyclization, followed by a 6-exo closure to the hydrindane system.

CONCLUSION

The present study on regioselective carbocyclic ring formation mediated by Cp_2TiCl_2 offers a new and quite general method for generating five- and six-membered rings.

The alkenyltitanocene chlorides were readily accessible. Transmetalation of the Grignard reagent of alkene bromide substrates on Cp_2TiCl_2 produced the organometallic species, which underwent cyclization upon treatment with a Lewis acidic co-catalyst.

The closure was typically a syn exo-addition of the carbon-titanium bond on the olefin tether. Acyclic substrates containing an internal or terminal carbon-carbon double bond, as well as cyclic substrates of the same nature, all showed great regioselectivity in the closure process. All reactions went near or to completion, depending on the concentration in organometallic species, the solvent and the co-catalyst utilized.

Following ring closure, the newly formed carbon-titanium bond is a potential handle for product functionalization,[79] and more work has to be accomplished in this area. Tandem type olefin insertion into carbon-titanium bond should have great potential for polycycle formation and natural product synthesis.

EXPERIMENTAL

General. Melting points were measured in glass capillary tubes on a Thomas Hoover melting point apparatus and are uncorrected. Infrared (IR) spectra were recorded on a Nicolet PC/IR Fourier transform spectrometer system equipped with a Nicolet IR/42 optical bench. ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra were recorded on a Varian VXR-300 S spectrometer. Chemical shifts are reported in parts per million (δ scale) from residual proton resonance ($CHCl_3$, δ 7.24 ppm) or from ^{13}C resonance ($CHCl_3$, δ 77.00 ppm). Multiplicities are recorded by the following abbreviations: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. Electron impact (70 eV) mass spectra (MS) were recorded on a Finnigan 400 with an Incos 4021 data system, or on a Hewlett Packard GC/MS system 5970 B equipped with a capillary DB-5 column. Gas chromatography (GLC) was conducted on a Perkin-Elmer 8500 using a 50-meter capillary column, SE-54 type (column A), or a Hewlett-Packard 5880 A using a 25-meter long capillary column (ID = 0.25 nm), liquid phase GB-1 (column B). Both chromatographs were equipped with flame ionization detectors and helium was used as a carrier gas, unless noted otherwise. Preparative gas chromatography was performed on a Varian Aerograph 90-P instrument with a gas conductivity type detector and a one-meter long column packed with SE-30 Chrom W.

Helium was used as a carrier gas. Thin layer chromatography was performed on glass precoated Merck Silica Gel 60 F_{254} plates (0.25 mm thick) and an aqueous potassium permanganate solution was used as a visualisation reagent. Flash chromatography was performed with Merk Silica Gel 60 (230-400 mesh, ASTM) according to the method of Still.[77] Elemental analyses were performed by Galbraith Laboratories, Knoxville, TN.

Unless overwise indicated, all reagents were obtained from commercial suppliers and used without purification. Ethylaluminum dichloride in toluene was purchased from Aldrich Chemical Co. and used as a known molarity, $EtAlCl_2$ refers to a 1.8 *M* solution of ethylaluminum dichloride in toluene unless overwise stated. Dimethylsulfoxide (DMSO) and dimethylformamide (DMF) were purchased from Aldrich Chemical Co. as 99+% pure chemicals. N-bromosuccinimide (NBS) was recrystallized from water (600 ml of water for 70 g of NBS) and dried under vacuum overnight. For Grignard reactions, Mg was activated by sequential treatment of magnesium turnings with a 10% aqueous HCl solution, water and Et_2O, and was dried while heated under high vacuum. For ozonolysis reactions, ozone was generated by a Welsbach ozonator. Quenched reaction mixtures were compared with authentic samples, whenever possible. Analytical samples of 1,5-hexadiene, 1-hexene, methylcyclopentane, methylenecyclopentane, cyclohexane, cyclohexene, 3-methyl-1-cyclohexene, 2-methyl-1,5-hexadiene, methylenecyclohexane, *cis*-decalin, *trans*-decalin, 1-heptene, 1,6-heptadiene, 1-octene, cyclooctane, and 1,1-dimethylcyclohexane were obtained from Aldrich Chemical Co. *trans*-1,5-Heptadiene, *cis*-

1,5-heptadiene, *trans*-2-heptene, *cis*-2-heptene, vinylcyclopentane, ethylcyclopentane, ethylidenecyclopentane, 1,1-dimethylcyclo pentane, 2-methyl-1-hexene, *trans*-bicyclo[4.3.0]nonane, *cis*-bicyclo[4.3.0]nonane, *cis*-bicyclo[3.3.0]octane, cycloheptane, and methylcycloheptane were obtained from Wiley Organics. Methylcyclohexane was purchased from Fisher, and 1-methyl-1-cyclohexene from Chemical Samples Co. Other standards were obtained from the corresponding Grignard reagents or synthesized from commercially available compounds. Tetrahydrofuran (THF), diethylether (Et_2O), toluene, benzene, n-pentane and n-hexane were distilled under nitrogen from sodium/benzophenone ketyl immediately prior to use. CH_2Cl_2, triethylamine and 1,2-dichloroethane were distilled from calcium hydride immediately before use. All reactions were performed under a positive pressure of N_2 in flame-dried glass apparatus. Alkenyltitanocene chloride syntheses and cyclization reactions were performed under an atmosphere of dry, oxygen-free argon that had been passed through a 6-cm x 60-cm glass column containing an activated copper catalyst, using standard Schlenk line techniques. Brine refers to a saturated aqueous solution of NaCl. For extractions, Et_2O was purchased from Columbus Chemical Industries Inc. and petroleum ether (35-60 ^oC boiling fraction) was purchased from E.M. Science Co.

Methyltriphenylphosphonium Iodide. A solution of 13.1 g (50 mmol) of triphenylphosphine and 16.2 g (115 mmol) of methyliodide in 50 ml of benzene was heated under reflux overnight. The voluminous precipitate was filtered, washed with 200 ml of benzene

and dried under high vacuum at 55 °C overnight. A quantitative yield of methyltriphenylphosphonium iodide (46.9 g) was obtained. Melting point 185-185.5 °C.

Pyridinium p-Toluenesulfonate (PPTS). A solution of 3.8 g (20 mmol) of p-toluenesulfonic acid in 8.1 ml (100 mmol) of pyridine was stirred at ambient temperature for 20 minutes. The excess of pyridine was removed by rotatory evaporation and the residue was recrystallized from acetone. The white crystals were dried under vacuum to afford 3.77 g (75% yield) of PPTS. Melting point 118-119 °C.

1-(Tetrahydropyranyloxy)-5-hexyne (15). Into a 500-ml, three-necked round-bottomed flask equipped with a condenser, was placed a solution of 9.81 g (0.1 mol) of 5-hexyn-1-ol, 12.62 g (0.15 mol) of dihydropyran and 2.51 g (0.01 mol) of PPTS in CH_2Cl_2 (300 ml). The solution was stirred at room temperature until completion. The solvent was removed and the residue was partitioned between Et_2O (100 ml) and brine (100 ml). The aqueous layer was extracted with Et_2O (3 x 30 ml), the organics were combined and dried on $MgSO_4$. Concentration and distillation under reduced pressure gave 17.6 g (97% yield) of a colorless oil. Boiling point 99-100 °C (7 mmHg).

1-(Tetrahydropyranyloxy)-5-heptyne (16). A 200-ml three-necked round-bottomed flask was fitted with a condenser and a thermometer. A solution of 10 g (54.9 mmol) of **15** in 90 ml of THF

was introduced *via* syringe. To this solution, cooled to -78 °C, 24.2 ml of a 2.5 *M* solution of nBuLi in hexanes (60.4 mmol) were added slowly and allowed to react for 1.5 hour. The cold bath was removed for 10 minutes to allow complete metalation. It was then replaced, and 4.1 ml (65.9 mmol) of methyliodide were added for reaction at -78 °C. The temperature was increased to 23 °C 0.5 hour after, and the reaction was complete after 2 hours. The mixture was partitioned between brine (200 ml) and Et_2O (200 ml). The aqueous layer was extracted with Et_2O (2 x 50 ml). The organics were combined, washed with water (100 ml) and dried on $MgSO_4$. Distillation under reduced pressure yielded 11 g of **16** (91% of theorical). Boiling point 92 °C (11 mmHg).

5-Heptyn-1-ol (17). A solution of 14.64 g (74.6 mmol) of **16** and 1.88 g (7.5 mmol) of PPTS in 500 ml of anhydrous methanol was stirred at 55 °C until complete consumption of the starting material (about 4 hours). The solution was concentrated, partitioned between Et_2O (100 ml) and brine (100 ml). The aqueous phase was extracted with Et_2O (2 x 80 ml). The organics were washed with water (50 ml) and dried ($MgSO_4$). Distillation afforded 4.15 g (92% of the theorical yield) of **17** as a colorless oil. Boiling point 83-85 °C (7 mmHg).

***cis*-5-Hepten-1-ol (18).** A 250-ml round-bottomed flask fitted with a hydrogen inlet and a rubber septum was flashed with hydrogen and charged with 0.56 g (2.25 mmol) of nickel acetate tetrahydrate in 80 ml of 95% ethanol. To this suspension was added 2.25 ml (2.25 mmol) of a 1 *M* solution of sodium borohydride in

ethanol. When gas evolution ceased, the black suspension obtained was treated with 0.31 ml (4.5 mmol) of ethylenediamine, followed by 2.02 g (18 mmol) of **17**. The rubber septum was replaced by a new one to avoid any leak, and the solution was stirred under a positive pressure of H_2. All of the starting material was reduced when 470 ml of H_2 approximately were consumed. The crude solution was filtered through a pad of silica gel, washed with 100 ml of a 50% saturated aqueous NaCl solution and 40 ml of water. The aqueous phase was extracted with Et_2O (2 x 50 ml) and the combined organic phases were dried on $MgSO_4$. After distillation, 3.87 g (86% yield) of **18** were obtained. Boiling point 83-86 °C (15 mmHg). Purity by GLC 96%, the remaining 4% were 1-heptanol.

***cis*-1-Bromo-5-heptene (20).** A one-liter round-bottomed flask was charged with 12.31 g (46.9 mmol) of triphenylphosphine, 4.46 g (39.1 mmol) of **18** and 300 ml of CH_2Cl_2. The flask was fitted with an addition funnel for solids containing 8.35 g (46.9 mmol) of NBS, and cooled to 0 °C. NBS was added in small portions and the solution was stirred until completion of the reaction. After concentration under reduced pressure, petroleum ether (200 ml) was added to precipitate the byproducts. The solution was filtered and the filtrate was cooled to -20 °C overnight to precipitate more solids. The solution was filtered again, dried on $MgSO_4$, passed through a small pad of basic alumina (Brockman Activity I, 80-200 mesh) and concentrated. Distillation under reduced pressure gave 3.66 g (53% yield) of **20**. Boiling point 85-90 °C (33 mmHg); IR (neat) ν max 3013, 2961, 2936, 2859, 1655, 1456, 1439, 1404, 1372, 1287, 1250, 1032, 739, 700,

644 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.41 (m, 2 H), 3.40 (t, J = 6.9 Hz, 2 H), 2.05 (q, J = 7.2 Hz, 2 H), 1.86 (quintet, J = 7.2 Hz, 2 H), 1.59 (dd, J = 6.4 Hz, J = 0.5 Hz, 3 H), 1.48 (quintet, J = 7.5 Hz, 2 H) ppm; ^{13}C NMR ($CDCl_3$) δ 129.78, 124.46, 33.71, 32.33, 28.00, 25.89, 12.72 ppm; MS (EI-70 eV) m/e (relative intensity) 178 (M+2, 11), 176 (M, 12), 137 (5), 135 (5), 109 (7), 97 (84), 95 (24), 83 (25), 81 (30), 69 (57), 68 (11), 67 (22), 57 (15), 56 (8), 55 (100). Anal. Calcd for $C_7H_{13}Br$: C, 47.48; H, 7.40. Found: C, 47.30; H, 7.51.

***trans*-5-Hepten-1-ol (19).** A one-liter round-bottomed flask fitted with a Claisen adapter, a dry-ice condenser and a drying tube was immersed into a dry-ice/isopropanol bath (-78 °C). NH_3 was introduced into the flask until 440 ml were liquified, followed by 5.52 g (240 mmol) of dry and clean sodium, cut in small pieces. Into the dark blue solution produced, 4.48 g (40 mmol) of **17** were injected by syringe. After 3 hours of reaction, the excess of sodium was destroyed by addition of NH_4Cl and the ammonia was allowed to evaporate slowly. The reaction mixture was partitioned between 75 ml of a saturated aqueous NH_4Cl solution and 150 ml of Et_2O. The aqueous phase was extracted with 100 ml of Et_2O. The organics were washed with brine (100 ml), water (80 ml) and dried on $MgSO_4$. Distillation gave 4.15 g of a colorless liquid (91% yield). Boiling point 84-85 °C (14 mmHg).

***trans*-1-Bromo-5-heptene (21).** Treatment of 5.72 g (50.1 mmol) of **19** with 15.76 g (60.1 mmol) of triphenylphosphine and 10.69 g (60.1 mmol) of NBS in 370 ml of CH_2Cl_2 was done according to the

general procedure. By distillation under reduced pressure, 7.79 g (88% yield) of **21** were collected. Boiling point 88-89 °C (34 mmHg); IR (neat) ν max 3025, 2963, 2936, 2857, 1453, 1439, 1377, 1283, 1250, 1200, 1074, 966, 733, 641 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.39 (m, 2 H), 3.38 (t, J = 6.9 Hz, 2 H), 1.99 (q, J = 6.8 Hz, 2 H), 1.85 (quintet, J = 7.2 Hz, 2 H), 1.62 (d, J = 4.6 Hz, 3 H), 1.47 (quintet, J = 7.3 Hz, 2 H) ppm; ^{13}C NMR ($CDCl_3$) δ 130.59, 125.46, 33.75, 32.24, 31.62, 28.03, 17.86 ppm; MS (EI-70 eV) m/e (relative intensity) 178 (M+2, 2), 176 (M, 2), 136 (2), 134 (2), 97 (12), 81 (11), 70 (4), 69 (26), 67 (11), 56 (7), 55 (100).

4-Bromo-2-methyl-1-butene (22). Reaction of 10 g (116.0 mmol) of 3-methyl-3-buten-1-ol with 36.51 g (139.2 mmol) of triphenylphosphine and 24.78 g (139.2 mmol) of NBS in CH_2Cl_2 (600 ml) according to the general procedure gave 12.96 g (75% yield) of **22** after work up and distillation under reduced pressure. Boiling point 83-86 °C (200 mmHg); ^1H NMR ($CDCl_3$) δ 4.84 (m, 1 H), 4.75 (m, 1 H), 3.45 (t, J = 7.4 Hz, 2 H), 2.56 (t, J = 7.4 Hz, 2 H), 1.73 (m, 3 H) ppm; ^{13}C NMR ($CDCl_3$) δ 142.37, 112.61, 40.88, 30.71, 21.90 ppm.

Diethyl (3-Methyl-3-buten-1-yl)propanedioate (23). To a suspension of 0.78 g (32.4 mmol) of NaH in 30 ml of DMF maintained at 0 °C, 4.93 ml (32.4 mmol) of diethylmalonate were added dropwise, and were allowed to react for 2 hours at room temperature. The solution was then cooled to 0 °C, treated with 4.40 g (29.5 mmol) of **22** and stirred at room temperature until complete consumption of the starting material. Water (75 ml) and Et_2O (50 ml)

were added. The aqueous phase was extracted with Et_2O (3 x 20 ml). The organic extracts were combined, washed with water (50 ml), dried on $MgSO_4$ and concentrated. Distillation under reduced pressure yielded 6.53 g (97% of theorical) of a colorless oil. Boiling point 90-95 °C (1 mmHg); IR (neat) v max 3077, 2982, 2940, 2876, 1736, 1651, 1449, 1370, 1323, 1298, 1221, 1152, 1098, 1030, 891, 862 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.72 (broad s, 1 H), 4.67 (broad s, 1 H), 4.16 (q, J = 7.2 Hz, 4 H), 3.30 (m, 1 H), 2.02 (m, 4 H), 1.69 (s, 3 H), 1.24 (t, J = 7.1 Hz, 6 H) ppm; ^{13}C NMR ($CDCl_3$) δ 169.41, 144.06, 111.14, 61.25, 51.33, 35.21, 26.62, 22.13, 14.04 ppm; MS (EI-70 eV) m/e (relative intensity) 228 (6), 183 (20), 182 (11), 173 (20), 161 (8), 160 (100), 155 (8), 154 (18), 139 (15), 137 (59), 136 (11), 133 (53), 132 (18), 127 (7), 115 (9), 114 (18), 111 (7), 109 (44), 108 (14), 105 (13), 119 (14), 99 (7), 88 (27), 87 (8), 86 (33), 82 (6), 81 (42), 80 (19), 79 (13), 73 (12), 69 (13), 68 (32), 67 (20), 58 (5), 55 (63), 53 (14), 45 (10), 43 (10).

Ethyl 5-Methyl-5-hexenoate (24). A 100-ml round-bottomed flask was charged with 44 ml of DMSO, 1.77 g (41.8 mmol) of LiCl, 0.4 ml (22.0 mmol) of water and 5.61 g (22.0 mmol) of **23**. The solution was heated to reflux and stirred until complete comsumption of the starting material. The mixture was poured into cold water (30 ml) and Et_2O (30 ml), extracted with Et_2O (2 x 30 ml). The organics were washed with a saturated aqueous $NaHCO_3$ solution (40 ml), water (40 ml) and dried on $MgSO_4$. After distillation, 2.52 g (74% yield) of **24** were obtained. Boiling point 79-80 °C (16 mmHg); ^1H NMR ($CDCl_3$) δ 4.69 (m, 1 H), 4.65 (m, 1 H), 4.09 (q, J = 7.1 Hz, 2 H), 2.25 (t, J = 7.5

Hz, 2 H), 2.01 (t, J = 7.4 Hz, 2 H), 1.73 (m, 2 H), 1.69 (s, 3 H), 1.22 (t, J = 7.1 Hz, 3 H) ppm; ^{13}C NMR ($CDCl_3$) δ 173.61, 144.76, 110.57, 60.15, 37.03, 33.71, 22.76, 22.13, 14.20 ppm.

5-Methyl-5-hexen-1-ol (25). To a suspension of 2.7 g (71.1 mmol) of $LiAlH_4$ in 200 ml of Et_2O maintained at 0 °C, 10.1 g (64.6 mmol) of **24** in 50 ml of Et_2O were added. After complete reaction, water (2.7 ml), a 15% aqueous NaOH solution (2.7 ml) and water (8.1 ml) were successively added at 0 °C. The white precipitate was removed by suction filtration and the solution was dried on $MgSO_4$ and concentrated. Distillation under reduced pressure afforded 6.57 g (89% yield) of **25**. Boiling point 92-93 °C (16 mmHg); ^1H NMR ($CDCl_3$) δ 4.66 (m, 1 H), 4.63 (m, 1 H), 3.57 (t, J = 6.3 Hz, 2 H), 2.06 (broad s removed by D_2O exchange, 1 H), 1.98 (t, J = 7.0 Hz, 2 H), 1.66 (s, 3 H), 1.38-1.58 (m, 4 H) ppm; ^{13}C NMR ($CDCl_3$) δ 145.65, 109.86, 62.64, 37.43, 32.25, 23.65, 22.22 ppm.

1-Bromo-5-methyl-5-hexene (26). Treatment of 6.49 g (56.8 mmol) of **25** with 17.89 g (68.2 mmol) of triphenylphosphine and 12.14 g (68.2 mmol) of NBS in CH_2Cl_2 (100 ml) was done according to the general procedure. After distillation under reduced pressure, 8.21 g (82% yield) of **26** were collected. Boiling point 67-69 °C (31 mmHg); IR (neat) ν max 3075, 2967, 2938, 2865, 1653, 1456, 1439, 1375, 1250, 889, 733, 644 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.68 (m, 2 H), 3.40 (t, J = 6.7 Hz, 2 H), 2.02 (t, J = 7.5 Hz, 2 H), 1.84 (quintet, J = 7.1 Hz, 2 H), 1.70 (s, 3 H), 1.56 (quintet, J = 7.5 Hz, 2 H) ppm; ^{13}C NMR ($CDCl_3$) δ 145.11, 110.32, 36.80, 33.69, 32.26, 25.98, 22.19 ppm; MS (EI-70 eV)

m/e (relative intensity) 178 (M+2, 2), 176 (M, 2), 137 (1), 123 (1), 109 (1), 98 (3), 97 (39), 96 (36), 95 (10), 83 (7), 81 (100), 79 (34), 77 (11).

2-Cyclopentene-1-ethanol (36). Treatment of 15.0 g (118.9 mmol) of 2-cyclopentene-1-acetic acid with 4.96 g (130.8 mmol) of $LiAlH_4$ in 220 ml of Et_2O according to the general procedure gave 10.36 g (78% yield) of **36** after distillation. Boiling point 85-87 °C (14 mmHg); IR (neat) ν max 3335, 3052, 2932, 2853, 1653, 1615, 1458, 1431, 1360, 1200, 1059, 1010, 910, 876, 719 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.71 (dq, J = 5.7 Hz, J = 2.0 Hz, 1 H), 5.65 (dq, J = 5.6 Hz, J = 2.0 Hz, 1 H), 3.65 (two t, J = 6.8 Hz, 2 H), 2.63-2.80 (broad m, 1 H), 2.15-2.40 (m, 2 H), 2.03 (ddt, J = 4.9 Hz, J = 12.7 Hz, J = 8.2 Hz, 1 H), 1.8 (broad s exchanded with D_2O, 1 H), 1.30-1.75 (three m, 3 H) ppm; ^{13}C NMR ($CDCl_3$) δ 134.85, 130.82, 61.68, 41.94, 38.69, 31.72, 29.56 ppm; MS (EI-70 eV) m/e (relative intensity) 112 (1), 94 (30), 93 (7), 91 (4), 80 (8), 79 (100), 78 (4), 77 (15), 68 (6), 67 (82), 66 (27), 65 (14), 55 (4), 53 (12), 51 (7), 50 (4).

3-(2-Bromoethyl)cyclopentene (37). Treatment of 5.38 g (48.0 mmol) of **36** with 15.11 g (57.6 mmol) of triphenylphosphine and 10.25 g (57.6 mmol) of NBS in CH_2Cl_2 (100 ml) according to the general procedure, gave 6.97 g (83% yield) of **37** after distillation under reduced pressure. Boiling point 69-70 °C (15 mmHg); IR (neat) ν max 3052, 2934, 2851, 1439, 1362, 1256, 1211, 912, 721, 563 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.75 (dq, J = 5.9 Hz, J = 2.2 Hz, 1 H), 5.64 (dq, J = 5.7 Hz, J = 2.0 Hz, 1 H), 3.41 (two t, J = 7.3 Hz, 2 H), 2.7-2.9 (broad

m, 1 H), 2.2-2.4 (broad m, 2 H), 1.7-2.2 (three m, 3 H), 1.3-1.5 (m, 1 H) ppm; ^{13}C NMR ($CDCl_3$) δ 133.42, 131.28, 44.25, 39.06, 32.09, 31.87, 29.26 ppm; MS (EI-70 eV) m/e (relative intensity) 176 (M+2, 5), 174 (M, 5), 95 (4), 93 (2), 91 (2), 81 (2), 79 (8), 77 (5), 68 (5), 67 (100), 66 (5), 65 (9), 63 (2), 55 (2), 53 (4), 51 (3).

3-(2-Cyclopenten-1-yl)propanoic acid (38). A 100-ml round-bottomed flask equipped with a condenser was charged with 2.74 g (112.8 mmol) of Mg and 40 ml of THF. The flask was heated to 45 °C and 4.95 g (28.2 mmol) of **37** were added in small portions over a 2.5-hour period. The solution was stirred for 5 hours at 60 °C, cooled to ambient temperature and added by cannula to a large excess of CO_2 (dry ice) in 50 ml of THF at -78 °C. The cold bath was removed, and CO_2 bubbled through the solution while reacting with the Grignard reagent. After complete evaporation of CO_2, the solution was diluted with Et_2O (100 ml), treated with a 10% aqueous HCl solution (20 ml), extracted with Et_2O (2 x 40 ml), washed with brine (40 ml) and dried on Na_2SO_4. Concentration and distillation under reduced pressure gave 3.21 g (81% yield) of **38**. Boiling point 95-98 °C (3 mmHg); IR (neat) ν max 3052, 2940, 2855, 2674, 1709, 1453, 1414, 1287, 1260, 1211, 1073, 939, 721 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.68 (dq, J = 5.9 Hz, J = 2.2 Hz, 1H), 5.63 (dq, J = 5.9 Hz, J = 2.0 Hz, 1 H), 2.68 (m, 1 H), 2.15-2.50 (m with one t at 2.36 ppm, J = 7.7 Hz, 4 H), 2.04 (ddt, J = 5.0 Hz, J = 12.8 Hz, J = 8.4 Hz, 1 H), 1.54-1.82 (m, 2 H), 1.20-1.50 (m, 2 H) ppm; ^{13}C NMR ($CDCl_3$) δ 180.45, 133.89, 131.20, 44.77, 32.35, 31.95, 30.58, 29.33 ppm; MS (EI-70 eV) m/e (relative intensity) 140 (4), 122 (18), 95 (3), 94 (7), 93 (3), 91 (4), 81 (25), 80 (88), 79 (40),

78 (3), 77 (13), 68 (7), 67 (100), 66 (12), 65 (17), 63 (3), 60 (3), 55 (6), 54 (3), 53 (9), 52 (4), 51 (7), 50 (4), 45 (14). Anal. Calcd for $C_8H_{12}O_2$: C, 68.54; H, 8.63. Found: C, 68.76; H, 8.88.

2-Cyclopentene-1-propanol (35). Treatment of 3.21 g (22.9 mmol) of **38** with 0.87 g (22.9 mmol) of $LiAlH_4$ in 40 ml of Et_2O according to the general procedure gave 2.45 g (85% yield) of **35** after distillation. Boiling point 82-85 °C (10 mmHg); IR (neat) ν max 3341, 3052, 2936, 2851, 1453, 1362, 1055, 1013, 914, 718 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.69 (dq, J = 5.7 Hz, J = 2.0 Hz, 1 H), 5.64 (dq, J = 5.7 Hz, J = 1.9 Hz, 1 H), 3.62 (t, J = 6.6 Hz, 2 H), 2.55-2.70 (m, 1 H), 2.15-2.40 (m, 2 H), 2.02 (ddt, J = 5.0 Hz, J = 12.8 Hz, J = 8.3 Hz, 1 H), 1.50-1.63 (m, 2 H), 1.20-1.50 (m, 4 H) ppm; ^{13}C NMR ($CDCl_3$) δ 134.87, 130.42, 63.16, 45.28, 32.04, 31.95, 31.08, 29.75 ppm; MS (EI-70 eV) m/e (relative intensity) 126 (3), 108 (7), 93 (15), 91 (6), 82 (6), 81 (5), 80 (59), 79 (26), 77 (9), 68 (6), 67 (100), 66 (17), 65 (14), 55 (4), 53 (7), 51 (5).

3-(3-Bromopropyl)cyclopentene (39). Treatment of 2.45 g (19.4 mmol) of **35** with 6.11 g (23.3 mmol) of triphenylphosphine and 4.15 g (23.3 mmol) of NBS in CH_2Cl_2 (80 ml) according to the general procedure gave 2.80 g (76% yield) of **39** after distillation. Boiling point 81-82 °C (11 mmHg); IR (neat) ν max 3052, 3005, 2938, 2949, 1653, 1612, 1458, 1439, 1359, 1277, 1246, 1203, 1036, 910, 775, 720, 642, 561 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.71 (dq, J = 5.6 Hz, J = 2.2 Hz, 1 H), 5.63 (dq, J = 5.7 Hz, J = 2.0 Hz, 1 H), 3.39 (t, J = 6.8 Hz, 2 H), 2.55-2.70 (m, 1 H), 2.15-2.40 (m, 2 H), 2.03 (ddt, J = 12.8 Hz, J = 5.0 Hz, J =

8.4 Hz, 1 H), 1.87 (quintet, J = 7.3 Hz, 2 H), 1.30-1.60 (two m, 3 H) ppm; ^{13}C NMR ($CDCl_3$) δ 134.47, 130.77, 44.83, 34.53, 34.06, 31.97, 31.25, 29.68 ppm; MS (EI-70 eV) m/e (relative intensity) 190 (4), 188 (4), 109 (3), 95 (3), 93 (1), 91 (2), 82 (10), 81 (5), 80 (3), 79 (7), 77 (4), 68 (6), 67 (100), 66 (9), 65 (7), 53 (4), 52 (2), 51 (3). Anal. Calcd for $C_8H_{13}Br$: C, 50.81; H, 6.93. Found: C, 50.95; H, 7.05.

Methyl 3-(2-Oxocyclopentyl)propionate (43). A solution of 42.06 g (500 mmol) of cyclopentanone, 60.45 g (820 mmol) of pyrrolidine and 0.95 g (5 mmol) of p-toluenesulfonic acid in 150 ml of benzene was heated to reflux until complete removal of the water by azeotropic distillation. Most of the solvent was evaporated and the yellow residue was distilled under reduced pressure to give 52.64 g (77% yield) of pyrrolidinocyclopentanone. Boiling point 85-89 °C (12 mmHg). A solution of 47.8 g (555 mmol) of methylacrylate and 43.20 g (315 mmol) of pyrrolidinocyclopentanone in dioxane (120 ml) was stirred for 2 hours and heated to reflux for 10 minutes. Water (24 ml) was then added and allowed to react for 15 hours under reflux. Concentration to an oil, dilution in Et_2O (800 ml), washing with a 5% aqueous HCl solution (2 x 200 ml) and water (300 ml) gave a colorless liquid which was dried on Na_2SO_4. Concentration and distillation under reduced pressure yielded 32.23 g (60% of theorical) of **43**. Boiling point 100-101 °C (2.5 mmHg); ^1H NMR ($CDCl_3$) δ 3.62 (s, 3 H), 2.38 (t, J = 7.4 Hz, 2 H), 1.40-2.35 (several m, 9 H) ppm; ^{13}C NMR ($CDCl_3$) δ 220.22, 173.59, 51.50, 48.17, 37.90, 31.87, 29.47, 24.86, 20.55 ppm.

Methyl 3-(2-Methylenecyclopentyl)propionate (44). To 40 ml of DMSO, 1.44 g (66 mmol) of NaH were added and stirred at 80 °C until complete evolution of H_2. A solution of 24.25 g (60 mmol) of methyltriphenylphosphonium iodide in warm DMSO (80 ml) was injected at 0 °C and allowed to react at ambient temperature for 15 minutes. To the reactive methylenetriphenylphosphane produced, 8.51 g (50 mmol) of **43** were added for overnigth reaction at room temperature. The crude solution was poured onto 40 ml of cold water and extracted with petroleum ether (5 x 100 ml). The organic extracts were combined and washed with water (20 ml), a 75% methanol solution in water (20 ml) and water (20 ml), dried on Na_2SO_4 and concentrated. Fractional distillation gave 4.12 g (49% yield) of **44**. Boiling point 85-87 °C (8 mmHg); ^1H NMR ($CDCl_3$) δ 4.87 (broad s, 1 H), 4.77 (broad s, 1 H), 3.64 (s, 3 H), 2.20-2.40 (broad m, 5 H), 1.20-2.0 (broad m, 6 H) ppm; ^{13}C NMR ($CDCl_3$) δ 174.27, 155.68, 104.87, 51.45, 43.31, 32.97, 32.34, 29.29, 24.06 ppm; MS (EI-70 eV) m/e (relative intensity) 168 (2), 137 (14), 136 (13), 108 (48), 95 (66), 94 (60), 93 (52), 79 (100), 55 (56).

3-(2-Methylenecyclopentyl)propanol (45). A solution of 11.59 g (68.9 mmol) of **44** in 50 ml of Et_2O was added slowly to a suspension of 2.87 g (75.8 mmol) of $LiAlH_4$ in 200 ml of Et_2O at 0 °C. After completion of the reaction, the solution was treated successively with water (2.87 ml), a 15% NaOH aqueous solution (2.87 ml) and water (8.6 ml) at 0 °C. The voluminous white precipitate formed was filtered, and the filtrate was dried on $MgSO_4$ and concentrated to an oil. Pure **45** was obtained by distillation, 9.25

g (96% yield) were collected. Boiling point 99-100 °C (7 mmHg); ^1H NMR ($CDCl_3$) δ 4.84 (m, 1 H), 4.75 (m, 1 H), 3.63 (t, J = 6.6 Hz, 2 H), 2.15-2.40 (m, 3 H), 1.80-2.00 (m, 1 H), 1.40-1.75 (m and one s at 1.62 ppm removed by D_2O exchange, 6 H), 1.10-1.35 (m, 2 H) ppm; ^{13}C NMR ($CDCl_3$) δ 156.68, 104.21, 63.18, 43.69, 33.13, 32.66, 30.99. 30.41, 24.14 ppm.

2-(3-Bromopropyl)-1-methylenecyclopentane (42). To a solution of 1.83 g (13.1 mmol) of **45** and 2.7 ml (19.6 mmol) of triethylamine in 65 ml of CH_2Cl_2 cooled to -10 °C, 1.12 ml (14.4 mmol) of freshly distilled methanesulfonyl chloride was added slowly. After 15 minutes of reaction at -10 °C, the solution was diluted with 50 ml of CH_2Cl_2 , washed with a 10% HCl aqueous solution (40 ml), a $NaHCO_3$ saturated aqueous solution (25 ml) and brine (40 ml). Mesyl 3-(2-methylenecyclopentyl)propanol in CH_2Cl_2 was dried ($MgSO_4$), concentrated, added *via* syringe to 2.68 g (26.1 mmol) of lithium bromide dissolved in 40 ml of THF at 0 °C, and allowed to react at room temperature until completion. The crude mixture was diluted in Et_2O (100 ml) and washed with a $NaHCO_3$ saturated aqueous solution (2 x 200 ml) and brine (20 ml). The organic phase was dried on $MgSO_4$, concentrated and purified by flash column chromatography on silica gel using petroleum ether as eluant. 20-ml fractions were collected and those containing the product were combined and concentrated. The residue was distilled under reduced pressure using a Kugehlrohr apparatus and gave 1.90 g (72% yield) of **42** as a colorless liquid. Boiling point 60-65 °C (5 mmHg); IR (neat) ν max 3071, 2955, 2868, 1653, 1450, 1433, 1285,

1246, 1202, 880, 646 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.86 (m, 1 H), 4.77 (m, 1 H), 3.40 (two t, J = 6.8 Hz, 2 H), 2.30 (m, 3 H), 1.80-2.00 (m, 3 H), 1.60-1.80 (m, 2 H), 1.18-1.60 (m, 3 H) ppm; ^{13}C NMR ($CDCl_3$) δ 156.20, 104.51, 43.20, 34.02, 33.06, 32.91, 32.62, 31.12, 24.15 ppm; MS (EI-70 eV) m/e (relative intensity) 204 (M+2, 3), 202 (M, 3), 123 (3), 109 (3), 107 (3), 96 (16), 95 (35), 94 (3), 93 (6), 91 (5), 82 (31), 81 (100), 80 (9), 79 (31), 78 (3), 77 (11), 68 (6), 67 (35), 65 (7), 55 (11), 54 (6), 53 (18), 52 (5), 51 (7). Anal. Calcd for $C_9H_{15}Br$: C, 53.22; H, 7.44. Found: C, 52.94; H, 7.24.

2-(3-Bromopropyl)-1-methylenecyclohexane (46). Boiling point 70-72 °C (1 mmHg); IR (neat) ν max 3081, 3069, 2932, 2855, 1645, 1444, 1292, 1254, 891, 652, 558 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.64 (broad s, 1 H), 4.55 (broad s, 1 H), 3.40 (t, J = 6.7 Hz, 2 H), 2.13-2.47 (m, 1 H), 1.93-2.10 (m, 2 H), 1.2-1.9 (several m, 10 H) ppm; ^{13}C NMR ($CDCl_3$) δ 152.21, 106.00, 42.52, 34.46, 34.23, 33.87, 30.89, 30.64, 28.72, 24.00 ppm; MS (EI-70 eV) m/e (relative intensity) 218 (M+2, 1), 216 (M, 1), 137 (5), 110 (6), 109 (15), 96 (72), 95 (100), 93 (13), 91 (11), 82 (11), 81 (54), 79 (25), 77 (16), 68 (13), 67 (65), 65 (11), 55 (26), 53 (18). Anal. Calcd for $C_{10}H_{17}Br$: C, 55.31; H, 7.89. Found: C, 55.20; H, 7.88.

6-Bromo-1-hexene (47). Treatment of 7.01 g (70.0 mmol) of 5-hexen-1-ol with 20.20 g (77.0 mmol) of triphenylphosphine and 13.70 g (77.0 mmol) of NBS in CH_2Cl_2 (100 ml) according to the general procedure gave 9.08 g (80% yield) of **47** after distillation. Boiling point 64-65 °C (35 mmHg); IR (neat) ν max 3079, 2938, 2859,

1642, 1455, 1439, 1284, 1252, 991, 914, 739 cm^{-1}; ^{13}C NMR ($CDCl_3$) δ 137.02, 115.52, 50.83, 40.13, 31.87, 26.39 ppm.

6-Heptenoic acid (48). 5-Hexen-1-ylmagnesium bromide was obtained by reacting 8.15 g (50.0 mmol) of **47** with 4.86 g (200.0 mmol) of Mg in 60 ml of THF. Treatment with CO_2 (dry-ice) at -78 °C according to the general procedure gave 5.21 g (82% yield) of **47** after distillation. Boiling point 95-97 °C (8 mmHg); IR (neat) ν max 3081, 2978, 2940, 2658, 1705, 1642, 1466, 1418, 1292, 1242, 1204, 995, 912 cm^{-1}; ^{13}C NMR ($CDCl_3$) δ 183.45, 137.65, 115.18, 38.71, 32.50, 31.20, 16.70 ppm; MS (EI-70 eV) m/e (relative intensity) 128 (3), 87 (5), 82 (5), 75 (3), 74 (100), 73 (13), 67 (9), 56 (12), 55 (26), 53 (5), 45 (13).

6-Hepten-1-ol (49). Treatment of 5.00 g (39.0 mmol) of **48** with 1.48 g (39.0 mmol) of $LiAlH_4$ in 100 ml of Et_2O according to the general procedure gave 3.81 g (86% yield) of **49** after distillation. Boiling point 80-81 °C (8 mmHg); IR (neat) ν max 3337, 3079, 2959, 2924, 2876, 1822, 1642, 1458, 1379, 1040, 993, 909, 764, 637 cm^{-1}; ^{13}C NMR ($CDCl_3$) δ 138.86, 114.32, 68.06, 35.16, 32.27, 31.12, 16.39 ppm; MS (EI-70 eV) m/e (relative intensity) 114 (<1), 96 (12), 82 (7), 81 (96), 79 (10), 71 (33), 68 (13), 67 (28), 58 (18), 57 (35), 56 (16), 55 (100), 54 (73), 53 (17).

7-Bromo-1-heptene (50). Treatment of 2.10 g (18.4 mmol) of **49** with 5.80 g (22.1 mmol) of triphenylphosphine and 3.93 g (22.1 mmol) of NBS in CH_2Cl_2 (80 ml) according to the general procedure

afforded 1.33 g (41% yield) of **50** after distillation. Boiling point 68-70 °C (17 mmHg); IR (neat) ν max 3077, 3000, 2961, 2936, 2859, 1642, 1460, 1439, 1269, 1242, 1200, 993, 912, 729, 644, 563 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.80 (ddt, J = 17.0 Hz, J = 10.3 Hz, J = 6.7 Hz, 1 H), 5.00 (ddt, J = 17.1 Hz, J = 1.7 Hz, J = 1.8 Hz, 1 H), 4.94 (ddt, J = 10.3 Hz, J = 2.0 Hz, J = 1.1 Hz, 1 H), 3.40 (t, J = 6.8 Hz, 2 H), 2.06 (broad q, J = 6.7 Hz, 2 H), 1.86 (quintet, J = 7.1 Hz, 2 H), 1.3-1.5 (broad m, 4 H) ppm; ^{13}C NMR ($CDCl_3$) δ 138.56, 114.58, 33.79, 33.50, 32.65, 28.01, 27.62 ppm; MS (EI-70 eV) m/e (relative intensity) 178 (M+2, <1), 176 (M, <1), 148 (3), 137 (6), 135 (6), 134 (5), 107 (3), 97 (31), 95 (3), 81 (9), 79 (2), 69 (28), 68 (8), 67 (14), 56 (7), 55 (100), 54 (13), 53 (13), 51 (4).

1,1-Dimethoxyheptan-6-one (55). A solution of 14.43 g (150 mmol) of 1-methyl-1-cyclohexene in 75 ml of methanol and 40 ml of CH_2Cl_2 was treated with ozone at -78 °C until a blue color persisted. The solution was degassed with N_2 and poured into 0.37 g of p-toluenesulfonic acid dissolved in 45 ml of dimethylsulfur at -78 °C. The mixture was stirred at ambient temperature for 3 hours, diluted with 400 ml of CH_2Cl_2, washed successively with a 3 *N* HCl aqueous solution (120 ml), water (3 x 150 ml) and dried on Na_2SO_4. Concentration and bulb-to-bulb distillation under reduced pressure gave 19.23 g (74% yield) of **55**. Boiling point 75-85 °C.(0.1 mmHg); IR (neat) ν max 2946, 2832, 1717, 1364, 1161, 1129, 1074, 1053 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.30 (t, J = 5.7 Hz, 1 H), 3.26 (s, 6 H), 2.39 (t, J = 7.4 Hz, 2 H), 2.09 (s, 3 H), 1.5-1.6 (m, 4 H), 1.2-1.4 (m, 2 H) ppm; ^{13}C NMR ($CDCl_3$) δ 209.25, 104.36, 52.54, 43.35, 32.05, 29.59, 23.84, 23.27

ppm; MS (EI-70 eV) m/e (relative intensity) 173 (M-1, <1), 143 (2), 111(2), 85 (3), 84 (9), 83 (15), 75 (100), 71 (8), 67 (5), 61 (12), 58 (5), 55 (6), 47 (14), 45 (8), 43 (46).

7,7-Dimethoxy-2-methyl-1-heptene (56). A suspension of 3.12 g (130 mmol) of NaH in 90 ml of DMSO was stirred at 0 °C for one hour. A solution of 52.55 g (130 mmol) of methyltriphenylphosphonium iodide dissolved in warm DMSO (180 ml) was added to the yellow sodium methylsulfinyl carbanion solution cooled to 0 °C, and was allowed to react at room temperature for 15 minutes. Addition of 17.42 g (100 mmol) of **55** *via* syringe and overnight reaction at 22 °C gave the crude olefinated product. The reaction mixture was poured into iced water (250 ml) and methanol (50 ml) and extracted with n-pentane (3 x 200 ml). The organics were washed with 80 ml of a 3:1 mixture of methanol and water, 50 ml of water and dried on Na_2SO_4. Concentration to an oil followed by bulb-to-bulb distillation afforded 14.30 g (83% yield) of **56**. Boiling point 60-70 °C (0.1 mmHg); IR (neat) ν max 3075, 2942, 2863, 2830, 1651, 1456, 1387, 1375, 1192, 1161, 1129, 1078, 1053, 961, 887 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.65 (m, 1 H), 4.62 (m, 1H), 4.32 (t, J = 5.7 Hz, 1 H), 3.27 (s, 6 H), 1.96 (t, J = 7.5 Hz, 2 H), 1.67 (s, 3 H), 1.57 (q, J = 7.1 Hz, 2 H), 1.2-1.5 (m, 5 H) ppm; ^{13}C NMR ($CDCl_3$) δ 146.06, 109.89, 104.56, 52.43, 37.49, 32.14, 27.19, 24.01, 22.07 ppm; MS (EI-70 eV) m/e (relative intensity) 172 (<1), 140 (1), 109 (22), 108 (15), 93 (9), 84 (9), 81 (5), 75 (100), 71 (13), 69 (4), 67 (17), 58 (7), 55 (11), 53 (5), 47 (15), 45 (8), 43 (7). Anal. Calcd for $C_{10}H_2O_2$: C, 69.72; H, 11.70. Found: C, 69.73; H, 11.44.

6-Methyl-6-heptenal (57). To a suspension of SiO_2 (80 g) in CH_2Cl_2 (180 ml), were added 8 ml of a 15% H_2SO_4 aqueous solution. After adsorption on the silica gel (5 minutes), 8.0 g (46.4 mmol) of **56** were injected for overnight reaction at ambient temperature. The mixture was quenched with 1.0 g of $NaHCO_3$ and the solids were removed by suction filtration. The filtrate was washed with water (100 ml) and dried on Na_2SO_4. After evaporation of the solvent, 7.56 g of a yellow oil were obtained. It was utilized for the next step without further purification. IR (neat) ν max 3075, 2936, 2863, 1727, 1653, 1456, 1375, 1127, 1080, 887 cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.73 (t, J = 1.8 Hz, 1 H), 4.67 (broad s, 1 H), 4.63 (broad s, 1 H), 2.41 (td, J = 7.1 Hz, J = 1.9 Hz, 2 H), 1.99 (t, J = 7.4 Hz, 2 Hz), 1.67 (s, 3 H), 1.3-1.6 (two m, 4 H) ppm; ^{13}C NMR ($CDCl_3$) δ 202.62, 145.23, 110.12, 43.69, 37.37, 26.93, 22.20, 21.59 ppm.

6-Methyl-6-hepten-1-ol (58). A solution of 7.6 g of crude **57** in Et_2O (100 ml) was stirred at 0 °C with 1.76 g (46.4 mmol) of $LiAlH_4$. After usual workup and concentration, 4.61 g (78% yield) of **58** were obtained by distillation. Boiling point 95-97 °C (15 mmHg); IR (neat) ν max 3345, 3075, 2936, 2861, 1651, 1456, 1375, 1128, 1053, 885 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.67 (m, 1 H), 4.64 (m, 1 H), 3.62 (t, J = 6.7 Hz, 2 H), 2.00 (t, J = 7.4 Hz, 2 H), 1.68 (s, 3 H), 1.56 (quintet, J = 7.0 Hz, 5 H) ppm; ^{13}C NMR ($CDCl_3$) δ 145.93, 109.75, 62.95, 37.71, 32.63, 27.34, 25.36, 22.32 ppm.

7-Bromo-2-methyl-1-heptene (59). By following the general procedure, 3.49 g (27.0 mmol) of **58** were treated with 8.50 g (32.4 mmol) of triphenylphosphine and 5.77 g (32.4 mmol) of NBS in CH_2Cl_2 (100 ml). After distillation, 3.03 g (59% yield) of **59** were obtained. Boiling point 75-77 °C (15 mmHg); IR (neat) ν max 3075, 2936, 2859, 1649, 1454, 1441, 1375, 1262, 887, 646 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.68 (m, 1 H), 4.65 (m, 1 H), 3.39 (t, J = 6.8 Hz, 2 H), 2.00 (t, J = 6.7 Hz, 2 H), 1.85 (q, J = 7.0 Hz, 2 H), 1.69 (s, 3 H), 1.35-1.50 (m, 4 H) ppm; ^{13}C NMR ($CDCl_3$) δ 145.65, 109.93, 37.52, 33.82, 32.70, 27.78, 26.68, 22.31 ppm; MS (EI-70 eV) m/e (relative intensity) 192 (M+2, <1), 190 (M, <1), 137 (1), 135 (1), 111 (14), 109 (1), 107 (1), 95 (2), 79 (1), 70 (2), 69 (32), 68 (3), 67 (8), 65 (1), 57 (11), 56 (100), 55 (38), 54 (4), 53 (8), 52 (1), 51 (2). Anal. Calcd for $C_8H_{15}Br$: C, 50.28; H, 7.91. Found: C, 50.84; H, 8.30.

Diethyl 2-[2-(2-Cyclopenten-1-yl)ethyl]propanedioate (63). A solution of 6.7 ml (44 mmol) of diethylmalonate in DMF (60 ml) was treated with 1.06 g (44.0 mmol) of NaH. Alkylation by 7.00 g (40 mmol) of **37** produced 8.81 g (82% yield) of **63** after distillation. Boiling point 100-103 °C (0.2 mmHg); IR (neat) ν max 3050, 2982, 2940, 2909, 2853, 1753, 1736, 1453, 1370, 1337, 1298, 1279, 1246, 1221, 1177, 1156, 1098, 1030, 914, 860, 721 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.69 (dq, J = 5.7 Hz, J = 2.2 Hz, 1 H), 5.62 (dq, J = 5.7 Hz, J = 2.0 Hz, 1 H), 4.16 (q, J = 7.0 Hz, 4 H), 3.27 (t, J = 7.5 Hz, 1 H), 2.55-2.70 (m, 1 H), 2.15-2.40 (m, 2 H), 1.95-2.10 (m, 1 H), 1.85-1.95 (m, 2 H), 1.30-1.50 (m, 3 H), 1.24 (t, J = 7.1 Hz, 6 H) ppm; ^{13}C NMR ($CDCl_3$) δ 169.48, 134.38, 130.71, 61.23, 52.23, 45.19, 33.56, 31.93, 29.51, 27.08, 14.06

ppm; MS (EI-70 eV) m/e (relative intensity) 208 (M-46, 2), 191 (4), 180 (4), 173 (27), 163 (6), 162 (5), 161 (9), 160 (12), 135 (3), 134 (9), 133 (11), 127 (2), 117 (14), 115 (3), 114 (3), 107 (4), 106 (7), 105 (5), 101 (8), 94 (7), 93 (22), 92 (12), 91 (9), 88 (3), 86 (6), 81 (9), 80 (100), 79 (27), 77 (11), 73 (8), 69 (4), 67 (46), 66 (7), 65 (9), 55 (16), 53 (6), 51 (3).

Ethyl 4-(2-Cyclopenten-1-yl)butanoate (64). A solution of 3.88 g (15.3 mmol) of **63**, 1.23 g (29.0 mmol) of LiCl and 0.28 ml (15.3 mmol) of water in 40 ml of DMF was heated to reflux until completion of the reaction. Distillation under reduced pressure afforded 2.18 g (78% yield) of **64**. Boiling point 90-93 °C (6 mmHg); IR (neat) ν max 3052, 2980, 2942, 2851, 1738, 1460, 1373, 1238, 1177, 1134, 1034, 719 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.69 (dq, J = 5.7 Hz, J = 2 Hz, 1 H), 5.64 (dq, J = 5.6 Hz, J = 2.0 Hz, 1 H), 4.10 (q, J = 7.1 Hz, 2 H), 2.15-2.40 (m with t at 2.27 ppm , J = 7.3 Hz, 4 H), 2.55-2.70 (m, 1 H), 2.01 (ddt, J = 5.0 Hz, J = 12.8 Hz, J = 8.3 Hz, 1 H), 1.63 (quintet, J = 7.6 Hz, 2 H), 1.18-1.50 (m with t at 1.23 ppm, J = 7.1 Hz, 6 H) ppm; ^{13}C NMR ($CDCl_3$) δ 173.74, 134.77, 130.41, 60.14, 45.26, 35.52, 34.56, 31.94, 29.69, 23.34, 14.23 ppm; MS (EI-70 eV) m/e (relative intensity) 182 (2), 137 (5), 136 (32), 135 (6), 121 (2), 119 (13), 108 (7), 107 (3), 101 (6), 95 (9), 94 (35), 93 (32), 92 (7), 91 (12), 88 (17), 87 (4), 81 (6), 80 (19), 79 (27), 77 (13), 73 (5), 70 (7), 68 (6), 67 (100), 66 (12), 65 (14), 61 (7), 60 (10), 55 (9), 53 (10), 52 (4), 51 (5). Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.95. Found: C, 71.82; H, 9.94.

4-(2-Cyclopenten-1-yl)butanol (65). A Solution of 4.43 g (24.3 mmol) of **64** in Et_2O (40 ml), was stirred with 0.93 g (24.3 mmol) of $LiAlH_4$. Distillation gave 3.25 g (96% yield) of **65**. Boiling point 82-85 °C (5 mmHg); IR (neat) ν max 3329, 3052, 2934, 2851, 1458, 1360, 1057, 1036, 912, 718 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.69 (dq, J = 5.7 Hz, J = 1.9 Hz, 1 H), 5.65 (dq, J = 5.7 Hz, J = 1.9 Hz, 1 H), 3.63 (t, J = 6.6 Hz, 2 H), 2.55-2.70 (broad m, 1 H), 2.15-2.40 (m, 2 H), 2.01 (ddt, J = 4.8 Hz, J = 12.8 Hz, J = 8.4 Hz, 1 H), 1.55 (quintet, J = 6.9 Hz, 2 H), 1.20-1.45 (m, 6 H) ppm; ^{13}C NMR ($CDCl_3$) δ 135.11, 130.23, 45.54, 35.89, 33.03, 31.96, 29.79, 24.10 ppm; MS (EI-70 eV) m/e (relative intensity) 140 (1), 122 (8), 107 (3), 95 (2), 94 (11), 93 (25), 91 (4), 81 (9), 80 (32), 79 (26), 78 (2), 77 (8), 68 (7), 67 (100), 66 (16), 65 (11), 55 (7), 53 (7), 51 (4).

3-(4-Bromobutyl)cyclopentene (66). A solution of 3.25 g (23.2 mmol) of **65** in CH_2Cl_2 (100 ml) was treated with 7.29 g (27.8 mmol) of triphenylphosphine and 4.95 g (27.8 mmol) of NBS according to the general procedure. After distillation, 4.09 g (87% yield) of **66** were obtained. Boiling point 90-95 °C (10 mmHg); IR (neat) ν max 3052, 3005, 2940, 2849, 1651, 1613, 1458, 1439, 1360, 1267, 1237, 1111, 1049, 986, 719, 846, 719, 646, 563 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.70 (dq, J = 5.7 Hz, J = 2.0 Hz, 1 H), 5.65 (dq, J = 5,7 Hz, J = 1.9 Hz, 1 H), 3.40 (t, J = 6.8 Hz, 2 H), 2.62 (broad m, 1 H), 2.18-2.40 (m, 2 H), 2.02 (ddt, J = 4.9 Hz, J = 12.7 Hz, J = 8.4 Hz, 1 H), 1.85 (broad quintet, J = 7.0 Hz, 2 H), 1.20-1.50 (m, 5 H) ppm; ^{13}C NMR ($CDCl_3$) δ 134.88, 130.40, 45.37, 35.16, 33.89, 33.02, 31.96, 29.76, 26.50 ppm; MS (EI-70 eV) m/e (relative intensity) 204 (M+2, 1), 202 (M, 1), 137 (2), 135

(2), 123 (9), 95 (4), 82 (3), 81 (14), 80 (2), 79 (6), 77 (4), 68 (6), 67 (100), 66 (10), 65 (6), 55 (4), 54 (2), 53 (4), 51 (2). Anal. Calcd for $C_9H_{15}Br$: C, 53.22; H, 7.44. Found: C, 53.04; H, 7.27.

Diethyl 2-(5-Hexen-1-yl)propanedioate (71). Treatment of 7.22 g (44.3 mmol) of **47** with 7.40 g (48.7 mmol) of diethylmalonate and 1.17 g (48.7 mmol) of NaH in 45 ml of DMF under the usual conditions gave 8.66 g (81% yield) of **71**. Boiling point 74-78 °C (0.2 mmHg); IR (neat) ν max 3079, 2982, 2938, 2878, 1752, 1642, 1466, 1449, 1269, 1304, 1230, 1152, 1034, 997, 912, 864 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.75 (ddt, J = 10.3 Hz, J = 17.0 Hz, J = 6.7 Hz, 1 H), 4.96 (ddt, J = 17.0 Hz, J = 2.2 Hz, J = 1.7 Hz, 1 H), 4.91 (ddt, J = 10.1 Hz, J = 2.2 Hz, J = 1.1 Hz, 1 H), 4.16 (q, J = 5.3 Hz, 4 H), 3.28 (t, J = 7.4 Hz, 1 H), 2.02 (q, J = 7.0 Hz, 2 H), 1.87 (q, J = 7.6 Hz, 2 H), 1.17-1.50 (m and one t at 1.24 ppm, J = 7.1 Hz, 10 H) ppm; ^{13}C NMR ($CDCl_3$) δ 169.49, 138.52, 114.53, 61.22, 52.01, 33.36, 28.55, 28.43, 26.73, 14.05 ppm; MS (EI-70 eV) m/e (relative intensity) 201 (M-41, 3), 198 (3), 197 (22), 196 (7), 187 (53), 169 (9), 161 (36), 160 (100), 151 (77), 155 (33), 141 (35), 139 (9), 135 (15), 133 (56), 132 (16), 127 (31), 123 (33), 122 (66), 115 (53), 114 (22), 113 (11), 105 (19), 104 (16), 99 (26), 95 (52), 94 (27), 93 (13), 88 (29), 87 (63), 86 (41), 85 (10), 83 (21), 82 (67), 81 (51), 80 (13), 79 (24), 77 (9), 71 (8), 70 (7), 69 (91), 68 (14), 67 (67), 65 (5), 58 (6), 55 (90), 54 (44), 53 (30), 51 (6), 45 (27). Anal. Calcd for $C_{13}H_{22}O_4$: C, 64.44; H, 9.15. Found: C, 64.63; H, 9.26.

Ethyl 7-Octenoate (72). Reaction of 8.66 g (35.7 mmol) of **71** with 2.87 g (67.8 mmol) of LiCl and 0.64 ml (35.7 mmol) of water in 90 ml of DMSO under the usual conditions gave 5.30 g (87% yield) of **72**. Boiling point 85-88 °C (12 mmHg); IR (neat) ν max 3079, 2978, 2932, 2876, 2853, 1738, 1642, 1460, 1371, 1290, 1117, 1096, 1034, 995, 912 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.77 (ddt, J = 17.0 Hz, J = 10.3 Hz, J = 6.7 Hz, 1 H), 4.97 (ddt, J = 17.0 Hz, J = 2.2 Hz, J = 1.7 Hz, 1 H), 4.91 (ddt, J = 10.0 Hz, J = 2.0 Hz, J = 1.1 Hz, 1 H), 4.10 (q, J = 7.2 Hz, 2 H), 2.26 (t, J = 7.5 Hz, 2 H), 2.02 (q, J = 7.0 Hz, 2 H), 1.60 (quintet, J = 7.4 Hz, 2 H), 1.26-1.44 (m with one t at 1.23 ppm , J = 7.1 Hz, 7 H) ppm; ^{13}C NMR ($CDCl_3$) δ 173.77, 138.80, 114.36, 60.14, 34.31, 33.52, 28.57, 28.50, 24.81, 14.23 ppm; MS (EI-70 eV) m/e (relative intensity) 170 (1), 155 (4), 128 (7), 125 (16), 115 (6), 101 (5), 97 (14), 96 (17), 95 (7), 89 (6), 88 (56), 87 (17), 83 (27), 82 (80), 81 (22), 79 (6), 73 (12), 71 (5), 70 (25), 69 (23), 68 (6), 67 (27), 61 (24), 60 (30), 59 (14), 57 (6), 56 (21), 55 (100), 54 (15).

7-Octen-1-ol (73). Treatment of 5.30 g (31.1 mmol) of **72** with a suspension of 1.30 g (34.3 mmol) of $LiAlH_4$ in Et_2O (60 ml) produced 3.64 g (91% yield) of **73**. Boiling point 88-91 °C (15 mmHg); IR (neat) ν max 3333, 3079, 2959, 2928, 2874, 1642, 1458, 1379, 1059, 995, 963, 909, 633 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.78 (ddt, J = 17.0 Hz, J = 10.3 Hz, J = 6.7 Hz, 1 H), 4.97 (ddt, J = 17.3 Hz, J = 2.0 Hz, J = 1.7 Hz, 1 H), 4.91 (ddt, J = 10.3 Hz, J = 2.0 Hz, J = 1.2 Hz, 1 H), 3.61 (t, J = 6.6 Hz, 2 H), 2.02 (q, J = 7.3 Hz, 2 H), 1.55 (quintet, J = 7.0 Hz, 2 H), 1.20-1.45 (m and one s at 1.35 ppm exchanged by D_2O, 7 H) ppm; ^{13}C NMR ($CDCl_3$) δ 139 02, 114.22, 62.99, 33.67, 32.71, 28.86, 28.83, 25.57

ppm; MS (EI-70 eV) m/e (relative intensity) 110 (M-18, 5), 96 (4), 95 (43), 86 (8), 83 (6), 82 (27), 81 (71), 79 (7), 71 (44), 70 (5), 69 (46), 68 (61), 67 (72), 57 (18), 56 (64), 55 (100), 54 (38), 53 (22), 51 (7), 45 (13), 43 (45).

8-Bromo-1-octene (70). Treatment of 3.64 g (28.4 mmol) of **73** were treated with 8.94 g (34.1 mmol) of triphenylphosphine and 6.06 g (34.1 mmol) of NBS in CH_2Cl_2 (40 ml) according to the general procedure produced 4.81 g (89% yield) of **70** after distillation. Boiling point 80-84 °C (15 mmHg); IR (neat) ν max 3077, 2998, 2930, 2857, 1642, 1462, 1439, 1292, 1258, 1221, 993, 910, 727, 646, 561 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.78 (ddt, J = 17.1 Hz, J = 10.3 Hz, J = 6.7 Hz, 1 H), 4.98 (ddt, J = 17.1 Hz, J = 2.2 Hz, J = 1.7 Hz, 1 H), 4.51 (ddt, J = 10.2 Hz, J = 2.2 Hz, J = 1.1 Hz, 1 H), 3.39 (t, J = 6.8 Hz, 2 H), 2.03 (q, J = 7.0 Hz, 2 H), 1.84 (quintet, J = 7.0 Hz, 2 H), 1.2-1.5 (m, 6 H) ppm; ^{13}C NMR ($CDCl_3$) δ 138.86, 114.37, 33.90, 33.61, 32.76, 28.67, 28.20, 28.00 ppm; MS (EI-70 eV) m/e (relative intensity) 192 (M+2, 1), 190 (M, 1), 150 (56), 148 (64), 69 (68), 55 (55), 41 (100).

3-Trimethylsilyl-2-propyn-1-ol (80). A three-liter, three-necked, round-bottomed flask equipped with a thermometer, was fitted with a Claisen adapter, on which was mounted a 250-ml pressure equalizing addition funnel and a reflux condenser. The flask was charged with 48.7 g (2.0 mol) of magnesium turnings and 1 liter of THF. To the stirred suspension were added dropwise 149.5 ml (2.0 mol) of bromoethane over a 4-hour period, maintaining the temperature below 50 °C. The solution was heated with a steam bath

at 50 °C for one hour and then cooled to 5 °C on ice. 41.6 ml (0.72 mol) of propargyl alcohol in 42 ml of THF was added over 4 hours at 5-10 °C and was allowed to react at ambient temperature for 20 hours. The resulting solution was cooled to 5 °C and treated with 254 ml (2.0 mol) of chlorotrimethylsilane at 5-10 °C. The suspension was then heated to reflux for 2.5 hours with a steam bath, cooled to 22 °C and quenched with 800 ml of 1.4 *M* aqueous H_2SO_4, maintaining the temperature below 45 °C. The resulting solution was stirred for an additional hour and was diluted in 600 ml of Et_2O. The aqueous phase was extracted with Et_2O (2 x 400 ml), the organic extracts were washed with water (2 x 1 liter) and brine (800 ml), and dried on $MgSO_4$. After concentration, the residue was distilled under reduced pressure to give 79.95 g (86% yield) of **80**. Boiling point 73-78 °C (20 mmHg); IR (neat) ν max 3366, 2961, 2901, 2178, 1636, 1410, 1250, 1038, 985, 837, 760, 700, 648 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.23 (s, 2 H), 1.95 (broad s, 1 H), 0.15 (s, 9 H) ppm; ^{13}C NMR ($CDCl_3$) δ 103.86, 90.61, 51.55, -0.25 ppm; MS (EI-70 eV) m/e (relative intensity) 115 (M-15, 83), 99 (4), 97 (7), 87 (20), 85 (18), 83 (4), 76 (7), 75 (100), 74 (7), 73 (71), 67 (4), 61 (52), 60 (5), 59 (45), 58 (11), 57 (6), 55 (10), 53 (9), 47 (13), 45 (36).

(E)-3-Trimethylsilyl-2-propen-1-ol (81). A solution of 25.7 g (0.2 mol) of **80** in 120 ml of Et_2O was added dropwise over a two-hour period to 82 ml (0.28 mol) of a 3.4 *M* solution of Red-Al in toluene, diluted in Et_2O (120 ml), at ice-bath temperature. After 2 hours of reaction at 22 °C, the reaction mixture was treated with 600 ml of a 3.5 *M* aqueous solution of H_2SO_4 at O °C. The aqueous phase

was extracted with Et_2O (200 + 150 ml), the organics were washed with water (2 x 150 ml), brine (150 ml), dried on $MgSO_4$ and concentrated. Distillation of the residue under reduced pressure afforded 22 g (85% yield) of **81** as a colorless liquid. Boiling point 74-77 °C (18 mmHg); IR (neat) ν max 3326, 2957, 2899, 2859, 1622, 1420, 1248, 1073, 991, 864, 841, 768, 692, 613 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.14 (dt, J = 18.7 Hz, J = 4.4 Hz, 1 H), 5.88 (dt, J = 18.7 Hz, J = 1.7 Hz, 1 H), 4.13 (dd, J = 1.7 Hz, J = 4.4 Hz, 2 H), 1.92 (s, 1 H), -0.04 (s, 9 H) ppm; ^{13}C NMR ($CDCl_3$) δ 144.78, 129.47, 65.41, -1.40 ppm; MS (EI-70 eV) m/e (relative intensity) 115 (M-15, 83), 99 (4), 97 (7), 87 (20), 85 (18), 83 (4), 76 (7), 75 (100), 74 (7), 73 (71), 67 (4), 61 (52), 60 (5), 59 (45), 58 (11), 57 (6), 55 (10), 53 (9), 47 (13), 45 (36).

Ethyl 3-(Trimethylsilyl)-4-pentanoate (82). A 100-ml round-bottomed flask equipped with a short-path distillation head was charged with 2.61 g (20 mmol) of **81**, 25.7 ml (140 mmol) of triethylorthoacetate and a few drops of propionic acid. The flask was slowly heated to 140 °C over a 4-hour period during which 2.5 ml of liquid were collected (boiling point 70 °C). Most of the solvent was evaporated and the residue was distilled under reduced pressure. A low boiling fraction was collected at 40 °C (10 mmHg) and 3.35 g (84% yield) of **82** distilled at 67-70 °C (6 mmHg). IR (neat) ν max 3080, 2975, 1740, 1628, 1370, 1250, 1179, 1094, 1038, 999, 899, 839, 752, 693, 637 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.70 (ddd, J = 17.0 Hz, J = 10.6 Hz, J = 8.4 Hz, 1 H), 4.87 (ddd, J = 10.5 Hz, J = 1.5 Hz, J = 1.0 Hz, 1 H), 4.82 (dt, J = 17.0 Hz, J = 1.4 Hz, 1 H), 4.08 (q, J = 7.1 Hz, 2 H), 2.36 (d, J = 6.7 Hz, 1 H), 2.35 (d, J = 8.9 Hz, 1 H), 2.05 (tddd, J = 7.7 Hz, J =

8.5 Hz, J = 1.1 Hz, J = 1.1 Hz, 1 H), 1.21 (t, J = 7.1 Hz, 3 H), -0.03 (s, 9H) ppm; ^{13}C NMR ($CDCl_3$) δ 173.47, 138.23, 112.14, 60.24, 33.72, 30.74, 14.26, -3.48 ppm; MS (EI-70 eV) m/e (relative intensity) 200 (1), 185 (2), 157 (3), 155 (4), 119 (8), 117 (4), 103 (6), 97 (4), 82 (13), 81 (2), 75 (31), 74 (9), 73 (100), 61 (2), 59 (5), 58 (3), 57 (2), 55 (5), 54 (29), 53 (4), 47 (3), 45 (20).

3-(Trimethylsilyl)-4-penten-1-ol (83). Treatment of 26.33 g (131.4 mmol) of **82** with 5.00 g (131.4 mmol) of $LiAlH_4$ in 260 ml of Et_2O gave 18.05 g (87% yield) of **83**. Boiling point 78-80 °C (8 mmHg); IR (neat) ν max 3333, 3079, 2901, 1626, 1412, 1248, 1040, 995, 897, 856, 839, 750, 690, 637 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.62 (ddd, J = 16.7 Hz, J = 10.6 Hz, J = 9.2 Hz, 1 H), 4.86 (dd, J = 10.6 Hz, J = 2.0 Hz, 1 H), 4.84 (ddd, J = 16.7 Hz, J = 2.0 Hz, J = 0.6 Hz, 1 H), 3.50-3.70 (two m, 2 H), 1.54-1.74 (m with broad s exchanged by D_2O at 1.57 ppm, 4 H), -0.04 (s, 9 H) ppm; ^{13}C NMR ($CDCl_3$) δ 139.69, 112.39, 62.81, 31.48, 31.26, -3.46 ppm; MS (EI-70 eV) m/e (relative intensity) 143 (M-15, 1), 103 (3), 97 (3), 75 (48), 74 (9), 73 (100), 69 (5), 68 (65), 67 (77), 61 (5), 59 (7), 58 (3), 55 (5), 54 (3), 53 (15), 47 (5), 45 (30), 43 (17).

5-Bromo-3-(trimethylsilyl)-1-pentene (84). Treatment of 13.09 g (82.7 mmol) of **83** with 7.1 ml (91.0 mmol) of freshly distilled methanesulfonyl chloride in 400 ml of CH_2Cl_2 according to the general method produced the mesylate derivative of **80** after work up. This mesylate was added to a solution of 17.02 g (165.4 mmol) of LiBr in 250 ml of THF. Distillation under reduced pressure

gave 15.69 g (86% yield) of **84**. Boiling point 75-77 °C (11 mmHg); IR (neat) ν max 3079, 2959, 2899, 1628, 1429, 1305, 1250, 1215, 1074, 999, 901, 839, 752, 692, 638 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.53 (ddd, J = 17.0 Hz, J = 10.3 Hz, J = 9.5 Hz, 1 H), 4.93 (ddd, J = 10.3 Hz, J = 1.7 Hz, J = 0.6 Hz, 1 H), 4.87 (ddd, J = 17.0 Hz, J = 1.8 Hz, J = 1.0 Hz, 1 H), 3.50 (m, 1 H), 3.28 (dt, J = 9.5 Hz, J = 8.1 Hz, 1 H), 1.83-2.00 (m, 2 H), 1.68 (td, J = 9.8 Hz, J = 4.7 Hz, 1 H), -0.03 (s, 9 H) ppm; ^{13}C NMR ($CDCl_3$) δ 137.92, 113.44, 33.89, 33.87, 31.94, -3.44 ppm; MS (EI-70 eV) m/e (relative intensity) 222 (M+2, <1), 139 (18), 137 (18), 109 (3), 75 (3), 74 (8), 73 (100), 69 (5), 68 (90), 67 (54), 54 (6), 58 (3), 55 (4), 54 (3), 53 (12), 45 (26). Anal. Calcd for $C_8H_{17}BrSi$: C, 43.44; H, 7.75. Found: C, 43.35; H, 7.86.

Diethyl 2-(3-Trimethylsilyl-4-pentenyl)propionate (85). Treatment of 3.78 g (17.1 mmol) of **84** with 2.86 g (18.8 mmol) of diethylmalonate and 0.45 g (18.8 mmol) of NaH in 40 ml of DMF under the usual conditions, gave 4.13 g (81% yield) of **85**. Boiling point 111-118 °C (0.1 mmHg); IR (neat) ν max 3077, 2959, 2909, 1752, 1734, 1626, 1448, 1370, 1333, 1250, 1107, 1038, 895, 858, 839, 639 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.56 (ddd, J = 17.0 Hz, J = 10.3 Hz, J = 8.9 Hz, 1 H), 4.88 (dd, J = 10.3 Hz, J = 2.0 Hz, 1 H), 4.81 (ddd, J = 17.0 Hz, J = 2.0 Hz, J = 0.8 Hz, 1 H), 4.15 (m, 4 H), 3.28 (dd, J = 8.4 Hz, J = 7.0 Hz, 1 H), 2.02 (m, 1 H), 1.74 (m, 1 H), 1.43 (broad m, 3 H), 1.24 (t, J = 7.1 Hz, 3 H), 1.23 (t, J = 7.2 Hz, 3 H), -0.06 (s, 9 H) ppm; ^{13}C NMR ($CDCl_3$) δ 169.56, 169.45, 139.21, 112.54, 61.22, 61.19, 51.82, 34.55, 28.52, 26.02, 14.09, 14.07, -3.94 ppm; MS (EI-70 eV) m/e (relative intensity) 300 (<1), 285 (1), 246 (3), 245 (13), 233 (5), 217 (5), 209

(4), 181 (6), 173 (10), 171 (7), 167 (5), 140 (18), 137 (6), 136 (7), 129 (5), 127 (19), 119 (6), 117 (4), 115 (5), 109 (9), 108 (12), 81 (8), 80 (8), 79 (6), 75 (16), 74 (9), 73 (100), 67 (12), 59 (7), 55 (20), 54 (11). Anal. Calcd for $C_{15}H_{28}O_4Si$: C, 59.96; H, 9.39. Found: C, 59.94; H, 9.53.

Ethyl 5-(Trimethylsilyl)-6-heptenoate (86). Reaction of 4.02 g (13.4 mmol) of **85** with 1.08 g (25.5 mmol) of LiCl and 0.24 ml (13.4 mmol) of water in 40 ml of DMSO under the usual conditions gave 2.52 g (83% yield) of **86**. Boiling point 100-105 °C (8 mmHg); IR (neat) ν max 3077, 2957, 1734, 1626, 1373, 1248, 1177, 1099, 1034, 999, 895, 837, 750, 691, 638 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.56 (ddd, J = 17.0 Hz, J = 10.3 Hz, J = 9.2 Hz, 1 H), 4.86 (dd, J = 10.6 Hz, J = 2.0 Hz, 1 H), 4. 80 (ddd, J = 17.0 Hz, J = 2.0 Hz, J = 0.8 Hz, 1 H), 4.10 (q, J = 7.1 Hz, 2 H), 2.24 (m, 2 H), 1.30-1.80 (broad m, 5 H), 1.22 (t, J = 7.1 Hz, 3 H), -0.06 (s, 9 H) ppm; ^{13}C NMR ($CDCl_3$) δ 173.76, 139.70, 112.19, 60.13, 34.59, 34.59, 34.11, 27.82, 24.71, 14.25, -3.37 ppm; MS (EI-70 eV) m/e (relative intensity) 228 (<1), 183 (3), 174 (5), 173 (35), 129 (9), 117 (10), 103 (6), 101 (4), 93 (5), 82 (8), 81 (6), 79 (3), 75 (20), 74 (9), 73 (100), 68 (6), 67 (11), 59 (7), 58 (3), 55 (27), 54 (8). Anal. Calcd for $C_{12}H_{24}O_2Si$: C, 63.10; H, 10.59. Found: C, 62.07; H, 10.38.

5-(Trimethylsilyl)-6-hepten-1-ol (87). Treatment of 2.41 g (10.6 mmol) of **86** with 0.44 g (11.6 mmol) of $LiAlH_4$ in suspension in Et_2O (20 ml) produced 1.87 g (95% yield) of **87**. Boiling point 105-107 °C (8 mmHg); IR (neat) ν max 3333, 3077, 2934, 2859, 1626, 1412, 1248, 1055, 997, 895, 837, 748, 691, 638 cm^{-1}; ^1H NMR ($CDCl_3$)

δ 5.57 (ddd, J = 17.0 Hz, J = 10.3 Hz, J = 9.2 Hz, 1 H), 4.85 (dd, J = 10.3 Hz, J = 2.0 Hz, 1 H), 4.79 (ddd, J = 17.0 Hz, J = 2.1 Hz, J = 0.8 Hz, 1 H), 3.60 (t, J = 6.4 Hz, 2 H), 1.15-1.70 (m, 8 H), -0.06 (s, 9 H) ppm; ^{13}C NMR ($CDCl_3$) δ 140.14, 111.91, 62.93, 34.89, 32.57, 28.18, 25.43, -3.34 ppm; MS (EI-70 eV) m/e (relative intensity) 186 (<1), 171 (1), 143 (1), 129 (3), 96 (2), 95 (2), 91 (2), 81 (14), 77 (2), 76 (3), 75 (35), 74 (9), 73 (100), 68 (13), 67 (39), 66 (4), 59 (7), 55 (9), 54 (32), 53 (4). Anal. Calcd for $C_{10}H_{22}OSi$: C, 64.45; H, 11.90. Found: C, 64.18; H, 12.03.

7-Bromo-3-(trimethysilyl)-1-heptene (78). A solution of 1.75 g (9.4 mmol) of **87** in CH_2Cl_2 (75 ml) was treated with 1.06 ml (13.7 mmol) of freshly distilled methanesulfonyl chloride according to the general procedure. The mesylate obtained was added to a solution of 2.55 g (24.8 mmol) of LiBr in 50 ml of THF and 2.15 g (92% yield) of a colorless oil were collected by distillation. Boiling point 94-95 °C (7 mmHg); IR (neat) ν max 3077, 2959, 2857, 1626, 1458, 1439, 1412, 1248, 997, 897, 837, 750, 691, 638, 563 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.57 (ddd, J = 17.0 Hz, J = 10.3 Hz, J = 8.9 Hz, 1 H), 4.86 (dd, J = 10.3 Hz, J = 2.0 Hz, 1 H), 4.80 (ddd, J = 17.0 Hz, J = 2.0 Hz, J = 0.6 Hz, 1 H), 3.37 (t, J = 7.0 Hz, 2 H), 1.65-1.95 (m, 2 H), 1.40-1.65 (m, 5 H), -0.05 (s, 9 H) ppm; ^{13}C NMR ($CDCl_3$) δ 139.86, 112.12, 34.73, 33.79, 32.70, 27.92, 27.59, -3.33 ppm; MS (EI-70 eV) m/e (relative intensity) 250 (<1), 248 (<1), 193 (1), 191 (1), 139 (10), 137 (10), 109 (2), 107 (1), 96 (2), 95 (5), 93 (2), 83 (2), 81 (16), 79 (3), 75 (5), 74 (13), 73 (100), 71 (2), 69 (2), 68 (12), 67 (58), 66 (8), 59 (9), 58 (5), 55 (12), 54 (32). Anal. Calcd for $C_{10}H_{21}BrSi$: C, 48.18; H, 8.49. Found: C, 48.06; H, 8.57.

Ethyl 6-(Trimethylsilyl)-7-octenoate (90). A solution of 4.43 g (20.0 mmol) of **84** in 10 ml of Et_2O was added in small portions over a two-hour period to 1.94 g (80.0 mmol) of Mg in 20 ml of Et_2O at 34 °C. The funnel was rinsed with 5 ml of Et_2O. After 4 hours of reaction under reflux, the solution was transferred into a Schlenck tube, cooled to -40 °C and treated with 1.09 ml (10.0 mmol) of ethylacrylate over a three-hour period. During the addition, catalytic amounts of CuCl were added (5 times). Stirring for 1 hour at -40 °C and 15 min at 23 °C completed the reaction. 10% aqueous HCl solution (40 ml) cooled to 0 °C was added and the two-phase solution was extracted with Et_2O (2 x 60 ml), washed with saturated aqueous $NaHCO_3$ (40 ml), water (40 ml) and dried on Na_2SO_4. The solution was concentrated and the oil was passed through a column of silica gel (eluent n-pentane, followed by Et_2O). The fractions containing **90** (Et_2O) were combined and concentrated. Distillation under reduced pressure gave 1.89 g (78% yield) of **90**. Boiling point 110-113 °C (7mmHg); IR (neat) ν max 3077, 2959, 2859, 1734, 1626, 1373, 1250, 1177, 1034, 997, 895, 839, 750, 691, 638 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.56 (ddd, J = 17.0 Hz, J = 10.3 Hz, J = 9.2 Hz, 1 H), 4.84 (dd, J = 10.3 Hz, J = 2.0 Hz, 1 H), 4.76 (ddd, J = 17.0 Hz, J = 2.1 Hz, J = 1.0 Hz, 1 H), 4.09 (q, J = 7.2 Hz, 2 H), 2.25 (t, J = 7.6 Hz, 2 H), 1.4-1.7 (m, 6 H), 1.22 (t, J = 7.1 Hz, 4 H), -0.06 (s, 9 H) ppm; ^{13}C NMR ($CDCl_3$) δ 173.85, 140.10, 111.90, 60.14, 34.72, 34.32, 28.83, 28.04, 24.82, 14.24, -3.32 ppm; MS (EI-70 eV) m/e (relative intensity) 242 (8), 197 (14), 173 (53), 160 (7), 129 (9), 117 (20), 103 (6), 95 (8), 81 (7), 80 (16), 75

(16), 73 (100), 55 (15). Anal. Calcd for $C_{13}H_{26}O_2Si$: C, 64.41; H, 10.81. Found: C, 64.42; H, 10.87.

6-(Trimethylsilyl)-7-octen-1-ol (91). Treatment of 2.13 g (8.8 mmol) of **90** with 0.37 g (9.7 mmol) of $LiAlH_4$ in suspension in Et_2O (20 ml) produced 1.66 g (95% yield) of **87**. Boiling point 108-110 °C (6 mmHg); IR (neat) ν max 3337, 3077, 2932, 2857, 1626, 1458, 1412, 1248, 1057, 997, 895, 858, 837, 691, 638 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.57 (ddd, J = 17.0 Hz, J = 10.3 Hz, J = 9.2 Hz, 1 H), 4.84 (dd, J = 10.4 Hz, J = 2.1 Hz, 1 H), 4.78 (ddd, J = 17.0 Hz, J = 2.0 Hz, J = 1.0 Hz, 1 H), 3.61 (t, J = 6.6 Hz, 2 H), 1.1-1.6 (m, 9 H), 1.64 (broad s exchanged by D_2O, 1 H), -0.06 (s, 9 H) ppm; ^{13}C NMR ($CDCl_3$) δ 140.30, 111.71, 62.76, 34.82, 32.58, 29.06, 28.31, 25.50, -3.34 ppm; MS (EI-70 eV) m/e (relative intensity) 200 (17), 185 (9), 157 (17), 129 (17), 110 (6), 109 (7), 95 (23), 91 (14), 82 (33), 81 (54), 75 (77), 74 (31), 73 (100), 69 (17), 68 (49), 67 (49), 59 (22), 55 (21), 54 (77). Anal. Calcd for $C_{11}H_{24}OSi$: C, 65.93; H, 12.07. Found: C, 65.83; H, 11.66.

8-Bromo-3-(trimethylsilyl)-1-octene (79). A solution of 1.55 g (7.7 mmol) of **91** in CH_2Cl_2 (40 ml) was treated with 0.67 ml (8.6 mmol) of freshly distilled methanesulfonyl chloride according to the general procedure. The mesylate obtained was added to a solution of 1.59 g (15.4 mmol) of LiBr in 25 ml of THF, and 1.66 g (82% yield) of a colorless oil were collected. Boiling point 105-108 °C (6 mmHg); IR (neat) ν max 3077, 2930, 2855, 1626, 1460, 1248, 997, 895, 837, 750, 691, 638, 563 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.57 (ddd, J = 17.0 Hz, J = 10.2 Hz, J = 9.4 Hz, 1 H), 4.84 (dd, J = 10.4 Hz, J = 2.1 Hz, 1 H), 4.78

(ddd, J = 17.0 Hz, J = 2.0 Hz, J = 0.8 Hz, 1 H), 3.38 (t, J = 6.8 Hz, 2 H), 1.83 (quintet, J = 6.7 Hz, 2 H), 1.1-1.5 (m, 7 H), -0.05 (s, 9 H) ppm; ^{13}C NMR ($CDCl_3$) δ 140.17, 111.89, 34.84, 34.00, 32.79, 28.48, 28.22, 28.01, -3.31 ppm; MS (EI-70 eV) m/e (relative intensity) 264 (M+2, 8), 262 (M, 8), 139 (31), 137 (31), 110 (5), 109 (5), 95 (18), 82 (40), 81 (54), 75 (12), 74 (26), 73 (100), 69 (9), 68 (25), 67 (28), 59 (16), 55 (15), 54 (59). Anal. Calcd for $C_{11}H_{23}BrSi$: C, 50.18; H, 8.80. Found: C, 50.66; H, 9.20.

Bicyclo[3.2.1]octane. A solution of 1.39 g (12.8 mmol) of bicyclo[3.2.1]octene in 7 ml of anhydrous methanol was treated with 0.14 g of 10% Pd on C, with stirring, under a positive pressure of H_2. After completion of the reaction monitored by GLC, the mixture was filtered through Celite and purified by preparative GC (oven temperature 100 °C). A white solid was obtained. ^{13}C NMR ($CDCl_3$) δ 39.66, 35.16, 32.81, 28.86, 19.15 [lit[78] ^{13}C NMR ($CDCl_3$) δ 39.7, 35.2, 32.8, 28.9, 19.1 ppm].

Methylenecycloheptane. A suspension of 0.13 g (5.5 mmol) of NaH in 10 ml of DMSO was stirred at 0 °C for 45 minutes. A solution of 2.22 g (5.5 mmol) of methyltriphenylphosphonium iodide in warm DMSO (5 ml) was added to the yellow sodium methylsulfinyl carbanion solution, cooled to 0 °C, and was allowed to react at room temperature for 15 minutes. Addition of 0.59 ml (5.0 mmol) of cycloheptanone *via* syringe and reaction at 22 °C for 1.5 hour gave the crude olefinated product. After usual workup the solution was concentrated by distillation under atmospheric pressure and an

analytical sample of methylenecycloheptane was obtained by preparative G. C. (oven temperature 120 °C). IR (neat) ν max 3071, 2980, 2934, 2853, 1638, 1447, 882 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.66 (quintet, J = 1.0 Hz, 2 H), 2.26 (m, 4 H), 1.45-1.60 (broad m, 8 H) ppm; ^{13}C NMR ($CDCl_3$) δ 152.26, 110.27, 36.17, 29.48, 28.40 ppm; MS (EI-70 eV) m/e (relative intensity) 110 (20), 96 (4), 95 (55), 91 (3), 83 (4), 82 (72), 81 (37), 79 (15), 77 (8), 69 (13), 68 (41), 67 (100), 66 (6), 65 (10), 63 (3), 56 (26), 55 (31), 54 (53), 53 (26), 52 (6), 51 (11), 50 (5).

General Procedure for the Preparation of the Alkenyltitanocene Chloride Solutions. Synthesis of *cis*-5-Hepten-1-yltitanocene Chloride (27). Addition of 0.356 g (2.0 mmol) of *cis*-1-bromo-5-heptene (**20**) in small portions, to 0.199 g (8.0 mmol) of activated magnesium in 2 ml of THF, maintained at 65 °C was accomplished over a 1 hour period. After 5 hours of reaction, the solution mixture was cooled to 23 °C and slowly transferred to a stirred suspension of 0.598 g (2.4 mmol) of Cp_2TiCl_2 in 8 ml of CH_2Cl_2 at -45 °C. The red brick solution was stirred at -45 °C for 0.5 hour, after what the cold bath was removed for reaction at ambient temperature during 3.5 hours. The solution was concentrated in vacuo to a volume of 1-2 ml, diluted in n-hexane (5 ml) and toluene (8 ml) prior to filtration under argon. The solids were washed with toluene (3 x 5 ml) and the combined fractions were concentrated in vacuo until complete evaporation of THF, CH_2Cl_2, n-hexane and toluene. The red brick paste obtained, was then diluted in toluene to a 0.1 *M* solution of **27**. Compound **27** was produced in 61% from **20**

by comparison of the GLC peak area of the quenched material with that of an internal standard (n-octane; response factor 1.14). It was stored under argon at -20 °C, although it was quite stable at ambient temperature under an inert atmosphere.

General Procedure for the Cyclization of the Alkenyltitanocene Chlorides. Cyclization of *cis*-5-Hepten-1-yltitanocene Chloride (27). In a Sclenck tube cooled to -78 °C, 2 ml (0.2 mmol) of the 0.1 *M* solution of **27** in toluene were treated by slow addition of 0.22 ml (0.4 mmol) of a 1.8 *M* solution of $EtAlCl_2$ in toluene. The initially red brick solution turned to dark green in presence of $EtAlCl_2$. Two hours of reaction at -78 °C and subsequent protonolysis, by slow addition of a HCl solution in methanol at -78 °C, afforded an orange reaction mixture, which was analyzed by GLC without purification. Column A was used under the following condition: oven temperature 100 °C. For identification of the product mixture, a solution of authentic standards in toluene was injected and gave the following retention times (minutes): *cis*-1,5-heptadiene (17.8); *cis*-2-heptene (19.1); vinylcyclopentane (20.8); methylcyclohexane (21.2); ethylcyclopentane (22.1); 3-methylcyclohexene (22.7); toluene (25.0); 1-methylcyclohexene (26.4); ethylidenecyclopentane (27.2); n-octane (internal standard, 30.0). Thus, analysis of the crude solution revealed the following mixture: *cis*-2-heptene (1%); ethylcyclopentane (98%); methylcyclohexane (1%) in 79% yield from **27** (internal standard n-octane).

Synthesis and Cyclization of *trans*-5-Hepten-1-yltitanocene Chloride (30). A 0.1 *M* solution of **30** in toluene was produced according to the general procedure. Treatment of 2 ml (0.2 mmol) of this solution with 0.22 ml (0.4 mmol) of $EtAlCl_2$ in toluene at -78 °C for 2 hours and at 23 °C for 2.5 hours, followed by protonolysis (HCl/MeOH) produced ethylcyclopentane (98%) and methylcyclohexane (2%). This distribution was obtained by GLC analysis under the experimental conditions described above and by comparison of retention times (minutes) with those of authentic samples: *trans*-1,5-heptadiene (17.0); *trans*-2-heptene (18.1); vinylcyclopentane (20.8); methylcyclohexane (21.2); ethylcyclopentane (22.1); 3-methylcyclohexene (22.7); toluene (25.0); 1-methylcyclohexene (26.4); ethylidenecyclopentane (27.2); n-octane (internal standard, 30.0).

Synthesis and Cyclization of 5-Methyl-5-hexenyltitanocene Chloride (31). A 0.1 *M* solution of **31** in toluene was produced according to the general procedure. Treatment of 2 ml (0.2 mmol) of this solution with 0.22 ml (0.4 mmol) of $EtAlCl_2$ in toluene at -78 °C for 4 hours resulted in complete ring closure to 1,1-dimethylcyclopentane and methylcyclohexane in a 99:1 ratio and in 93% yield from **31** determined by GLC analysis (internal standard n-octane; response factor 1.14). Mixture analyses were run on column A under the following conditions: oven temperature 70 °C; carrier gas H_2. Retention times (minutes) were compared with those of authentic samples: 2-methyl-1,5-hexadiene (15.3); 1,1-dimethylcyclopentane (15.7); 2-methyl-1-hexene (16.6); methylcyclohexane (21.9);

methylenecyclohexane (24.5); toluene (27.4); 1-methylcyclohexene (29.5); n-octane (internal standard, 36.5).

Synthesis and Cyclization of 3-(2-Cyclopentenyl)prop-1-yltitanocene Chloride (32). Four ml (0.4 mmol) of a 0.1 *M* solution of **32** in toluene, produced according to the general procedure were treated at -78 °C with 0.43 ml (0.4 mmol) of $EtAlCl_2$ in toluene. A 97:3 ratio of *cis*-bicyclo[3.3.0]octane and 3-propylcyclopentene was obtained after 1 hour of reaction at -78 °C and protonolysis. *cis*-Bicyclo[3.3.0]octane was generated in 83% yield (determined by GLC analysis) from **32** (internal standard n-octane; response factor 1.00). Mixtures were analyzed by GLC on column A at oven temperature 130 °C. Authentic samples had the following retention times (minutes): toluene (12.3); n-octane (13.6); 3-propylcyclopentene (15.3); *cis*-bicyclo[3.3.0]octane (19.8); bicyclo[3.2.1]octane (20.6).

Synthesis and Cyclization of 3-(2-Methylenecyclopentyl) prop-1-yltitanocene Chloride (33). Over a 80-minutes period, 0.401 g (1.97 mmol) of **42** was added in small portions to 0.193 g (7.95 mmol) of Mg in 3 ml of THF maintained at 60 °C. After 4 hours of reaction, the reaction was cooled to 23 °C and transferred to a suspension of 0.599 g (2.4 mmol) of Cp_2TiCl_2 in 8 ml of CH_2Cl_2 at -50 °C, and allowed to react at 23 °C for 3.5 hours. Usual work up gave a red brick paste which was diluted in 8 ml of toluene. 1.1 ml (1.98 mmol) of $EtAlCl_2$ was added in small portions over a 70-minute period to this solution at -78 °C. After one hour at -78 °C, 5% HCl in

MeOH (3 ml) was added slowly at -78 °C and the temperature was raised to 23 °C. The crude mixture was extracted with n-pentane (5 ml) and filtered through a small pad of alumina. Analyzis by GLC on column B (oven temperature 50 °C) revealed the presence of *cis*-1-methylbicyclo[3.3.0]octane as the only product. Under the same conditions, authentic standards gave the following retention times (minutes): *cis*-1-methylbicyclo[3.3.0]octane (see below for isolation, 4.7); n-nonane (internal standard; response factor 1.00, 5.2); 1-methylene-2-propylcyclopentane (5.6). An analytical sample of *cis*-1-methylbicyclo[3.3.0]octane was obtained by preparative GC at oven temperature 110 °C. A volatile and colorless liquid was collected. ^{1}H NMR ($CDCl_3$) δ 1.05 (s, 3 H), 1.1-1.9 (four m, 13 H) ppm [lit[31a] ^{1}H NMR ($CDCl_3$) δ 1.05 (s, 3 H), 1.27-1.81 (m, 13 H) ppm]; ^{13}C NMR ($CDCl_3$) δ 25.91, 29.13, 34.48, 41.81, 49.71, 50.81 ppm [lit[31a] ^{13}C NMR ($CDCl_3$) δ 25.94, 29.10, 34.50, 41.86, 49.74, 50.90 ppm]; MS (EI-70eV) m/e (relative intensity) 124 (4), 109 (4), 95 (27), 81 (100), 67 (35), 55 (20), 53 (11), 41 (30).

Synthesis and Cyclization of 3-(2-Methylenecyclohexyl) prop-1-yltitanocene Chloride (34). To 0.148 g (6.1 mmol) of Mg in 2 ml of THF maintained at 60 °C, was added 0.324 g (1.49 mmol) of **46** over a one hour period. After 6 hours at 60 °C, transmetalation with 0.448 g (1.18 mmol) of Cp_2TiCl_2 for 5.5 hours according to the general procedure afforded a solution of **34** in toluene (15 ml). Cyclization was induced by addition of 1.0 ml (1.8 mmol) of $EtAlCl_2$ at -78 °C and was complete within 3 hours. After HCl/MeOH quench. The crude mixture was analyzed by GLC with column B at oven

temperature of 60 °C. Authentic samples in toluene, eluted from the column with the following retention times (minutes): n-decane (internal standard; response factor 1.00, 7.3); 1-methylene-2-propylcyclohexane (7.4); *cis*-1-methylbicyclo[4.3.0]nonane (see below for isolation, 8.3); *trans*-1-methylbicyclo[4.3.0]nonane (9.2); *trans*-decalin (9.7); *cis*-decalin (12.8). An analytical sample of *cis*-1-methylbicyclo[4.3.0]nonane was purified by preparative GLC at oven temperature 130 °C. A colorless liquid was obtained. ^{1}H NMR ($CDCl_3$) δ 0.93 (s, 3 H), 1.1-1.9 (m, 15 H) ppm [lit[31a] ^{1}H NMR ($CDCl_3$) δ 0.93 (s, 3 H), 0.85-1.69 (m, 15 H) ppm]; ^{13}C NMR ($CDCl_3$) δ 20.65, 22.43, 22.79, 26.73, 26.80, 28.97, 33.79, 38.19, 40.50, 44.98 ppm [lit[31a] ^{13}C NMR ($CDCl_3$) δ 20.69, 22.46, 22.82, 26.80, 29.03, 33.85, 38.24, 40.53, 45.04 ppm].

Synthesis and Cyclization of 6-Hepten-1-yltitanocene Chloride (2). The Grignard reagent of **50** was obtained by reaction of 0.361 g (2.03 mmol) of **50** with 0.198 g (8.10 mmol) of Mg in 3 ml of THF. Transmetalation on 0.61 g (2.44 mmol) of Cp_2TiCl_2 in 3 ml of CH_2Cl_2 and work up produced **2** in 74% yield from **50** by GLC analysis (internal standard n-heptane; response factor 1.00). To 10 ml (0.2 mmol) of a 0.01 *M* solution of **2** in toluene was added 0.22 ml (0.4 mmol) of $EtAlCl_2$ for reaction at -78 °C during 1 hour, followed by HCl/MeOH quench. GLC analyses were conducted at oven temperature 100 °C on column A. Retention times (minutes) of the various standards ordered as follow: 1,6-heptadiene (12.4); 1-heptene (13.1); n-heptane (13.8); methylcyclohexane (16.3); methylenecyclohexane (17.6); toluene (19.2); cycloheptane (23.7). A

96:1:3 distribution of methylcyclohexane, 1-heptene and methylenecyclohexane resulted.

Synthesis and Cyclization of 6-Methyl-6-hepten-1-yltitanocene Chloride (60). 6-Methyl-6-hepten-1-ylmagnesium bromide was obtained by reaction of 0.380 g (2.0 mmol) of **59** on 0.199 g (8.2 mmol) of Mg in THF (2 ml) and was added to 0.598 g (2.4 mmol) of Cp_2TiCl_2 in CH_2Cl_2 (8 ml). After work up a 63% yield (by GLC analysis and comparison with an internal standard n-nonane; response factor 1.12) of **60** resulted. Product mixture analyses were performed at oven temperature 100 °C with column A. Authentic samples eluted from the column with the retention times (minutes): toluene (17.7); 2-methyl-1-heptene (19.5); 1,1-dimethylcyclohexane (20.8); methylcycloheptane (30.4); n-nonane (36.5). All cyclizations were carried on 1-2 ml sample of **60** (0.1 *M* in toluene). Then necessary, toluene was completely evaporated and replaced by 1,2-dichloroethane. Thus addition of 14 µl (0.025 mmol, 1.8 *M* solution in n-hexane) of Me_2AlCl to 2.5 ml (0.1 mmol) of **60** in 1,2-dichloroethane at -30 °C produced a dark green solution which was quenched by slow addition of a 1 *M* HCl solution in Et_2O, after 15 minutes of reaction. GLC analysis gave a 18:82 ratio of 2-methyl-1-heptene and 1,1-dimethylcyclohexane, which accounted for 72% of the starting material. Ring closures induced by other Lewis acids in other solvents were conducted in a similar way (see Table 5 in Results and Discussion section).

Synthesis and Cyclization of 4-(2-Cyclopentenyl)but-1-yltitanocene Chloride (53). A 0.1 *M* solution of **67** in toluene (82% yield from **66** by GLC analysis; internal standard n-nonane; response factor 1.00) was generated by action of 0.411 g (2.02 mmol) of **66** on 0.204 g (8.40 mmol) of Mg in 2 ml of THF, transmetalation on 0.605 g (2.43 mmol) of Cp_2TiCl_2 in 8 ml of CH_2Cl_2 and work up according to the general procedure. GLC analyses were conducted on column B under the following condition: oven temperature 50 °C. n-Nonane, 3-butyl-1-cyclopentene, *trans*-bicyclo[4.3.0]nonane and *cis*-bicyclo[4.3.0]nonane eluted from the column at 5.6, 6.1, 7.6 and 9.4 minutes respectively. Cyclizations were run according to the general procedure.

Synthesis of 7-Octen-1-yltitanocene Chloride (74). Reaction of 0.383 g (2.0 mmol) of **70** on 0.202 g (8.3 mmol) of Mg in THF (2 ml) at 60 °C for 6 hours and transmetalation on 0.598 g (2.4 mmol) of Cp_2TiCl_2 afforded **74** in 80% yield (by GLC analysis, internal standard n-octane; response factor 1.00). Cyclizations were carried on a 0.1 *M* solution of **74** in toluene. For reaction mixture analyses, authentic samples gave the following retention times (minutes): 1-octene (12.3); n-octane (12.9); methylcycloheptane (17.7); methylenecycloheptane (18.1); cyclooctane (23.2) for elution through column A at oven temperature 130 °C.

Synthesis and Cyclization of 5-(Trimethylsilyl)-6-hepten-1-yltitanocene Chloride (88). The Grignard reagent of **78** was prepared by addition of 0.25 g (1.0 mmol) of **78** on 0.10 g (4.0

mmol) of Mg in THF (2 ml) at 44 °C, followed by reaction at 64 °C for 10 hours. Transmetalation on 0.29 g (1.2 mmol) of Cp_2TiCl_2 in CH_2Cl_2 (5 ml) for 4 hours afforded **88** in toluene (10 ml) after usual work up. Analysis of the solution by GLC after HCl/Et_2O quench, revealed one single peak at 8.7 mn (column A, oven temperature 200 °C). This retention time was identical to the product obtained by quench of the Grignard reagent. To a Schlenck tube cooled to -78 °C and containing 2 ml (0.2 mmol) of **88** in toluene, was added 0.22 ml (0.4 mmol) of $EtAlCl_2$, for reaction at -78 °C for 1 hour. The solution was quenched with HCl/Et_2O at -78 °C. GLC analysis showed one single peak at 11.5 mn under the same operating conditions.

General Procedure for the nBu_3SnH Free Radical Cyclization of Disubstituted Bromo Alkenes. Cyclization of *cis*-1-Bromo-5-heptene (20). A solution of 0.177 g (1.0 mmol) of **20**, 0.33 ml (1.2 mmol) of nBu_3SnH and 0.01 g of AIBN in benzene (20 ml) was introduced into a 100-ml glass tube. Under external cooling with liquid nitrogen, the tube was degassed by applying high vacuum, and closed. The solution was stirred at 70 °C for 14 hours, cooled to ambient temperature and analyzed by GLC. Experimental conditions identical to those utilized for the titanium based methodology, gave a 12:87:1 distribution of *cis*-2-heptene, ethylcyclopentane and methylcyclohexane.

Free Radical Cyclization of *trans*-1-Bromo-5-heptene (21). A solution of 0.177 g (1.0 mmol) of 21, 0.33 ml (1.2 mmol) of nBu_3SnH and 0.01 g of AIBN in 20 ml of benzene was submitted to the

mentioned above reaction conditions for 14 hours. GLC analysis of the crude mixture gave a 9:89:2 distribution of *trans*-2-heptene, ethylcyclopentane and methylcyclohexane.

Free Radical Cyclization of 3-(3-Bromopropyl)cyclopantene (39). A solution of 0.04 g (0.2 mmol) of **39**, 0.07 ml (0.24 mmol) of nBu_3SnH and 0.01 g of AIBN in benzene (20 ml) was submitted to the usual reaction conditions for 6 hours. GLC analysis of the crude mixture gave a 3:97 ratio of 3-propylcyclopentene and *cis*-bicyclo[3.3.0]octane.

Free Radical Cyclization of 1-(3-Bromopropyl)-2-methylene cyclopentane (42). A solution of 0.03 g (0.15 mmol) of **42**, 0.05 ml (0.18 mmol) of nBu_3SnH and 0.01 g of AIBN in 15 ml of benzene was submitted to the usual reaction conditions for 5 hours. GLC analysis of the crude mixture gave the following product distribution: 1-methylene-3-propylcyclopentane (11%), *cis*-1-methylbicyclo[3.3.0] octane (15%), *cis*-bicyclo[4.3.0]nonane (50%) and *trans*-bicyclo[4.3.0]nonane (24%).

Free Radical Cyclization of 1-(3-Bromopropyl)-2-methylene cyclohexane (46). A solution of 0.043 g (0.20 mmol) of **46**, 0.07 ml (0.18 mmol) of nBu_3SnH and 0.01 g of AIBN in 20 ml of benzene was heated to 70 °C for 12 hours according to the general procedure. GLC analysis conducted on column B at 60 °C gave the following results. 1-methylene-2-propylcyclohexane (47%), *cis*-1-methylbicyclo[4.3.0] nonane (17%), *trans*-decalin (31%), and *cis*-decalin (5%) eluted from

the column at 7.5, 8.5, 9.9 and 13.1 minutes respectively [lit[20] 1-methylene-2-propylcyclohexane (56%); *cis*-1-methylbicyclo[4.3.0] nonane (15%), *trans*-decalin (25%), and *cis*-decalin (4%)].

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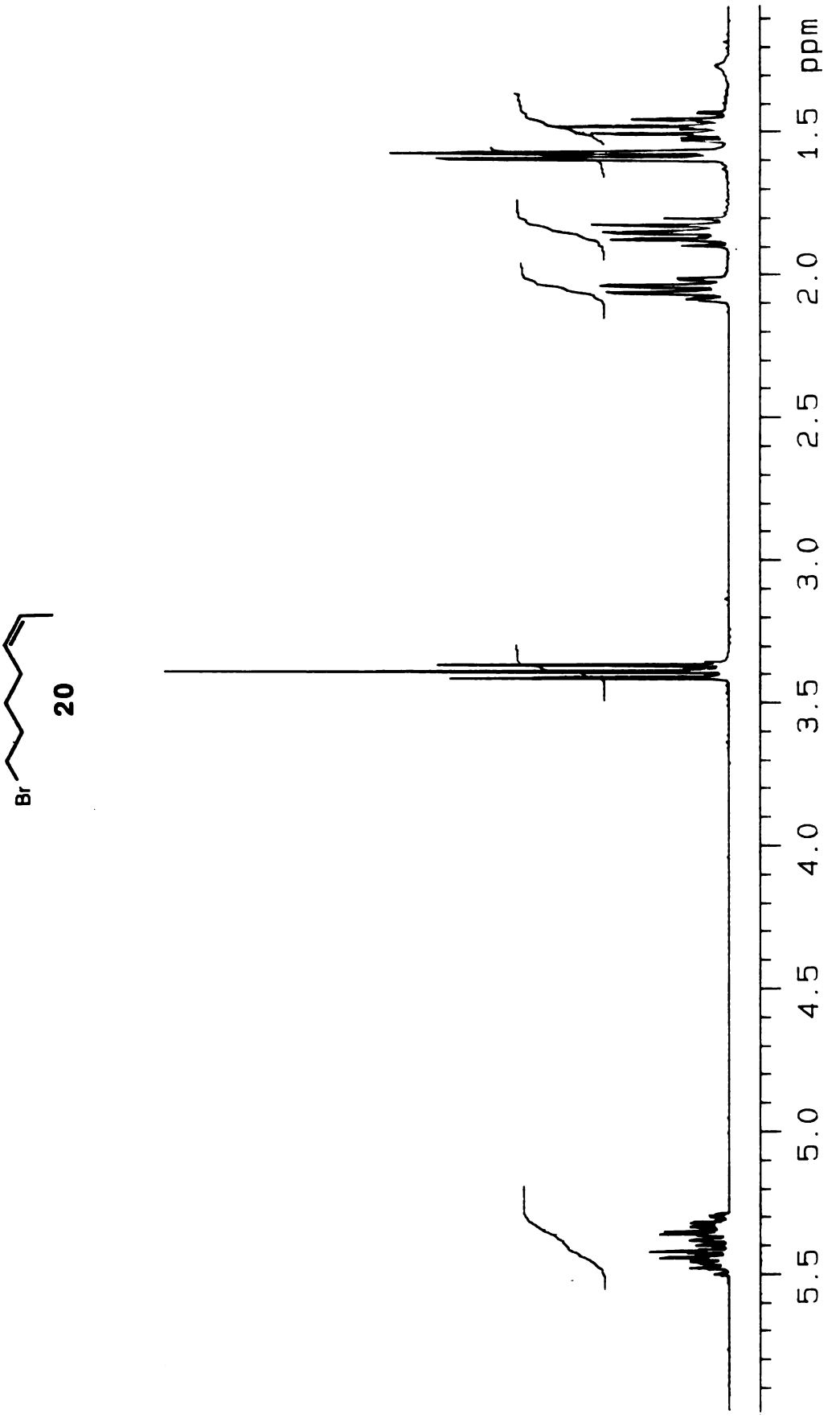
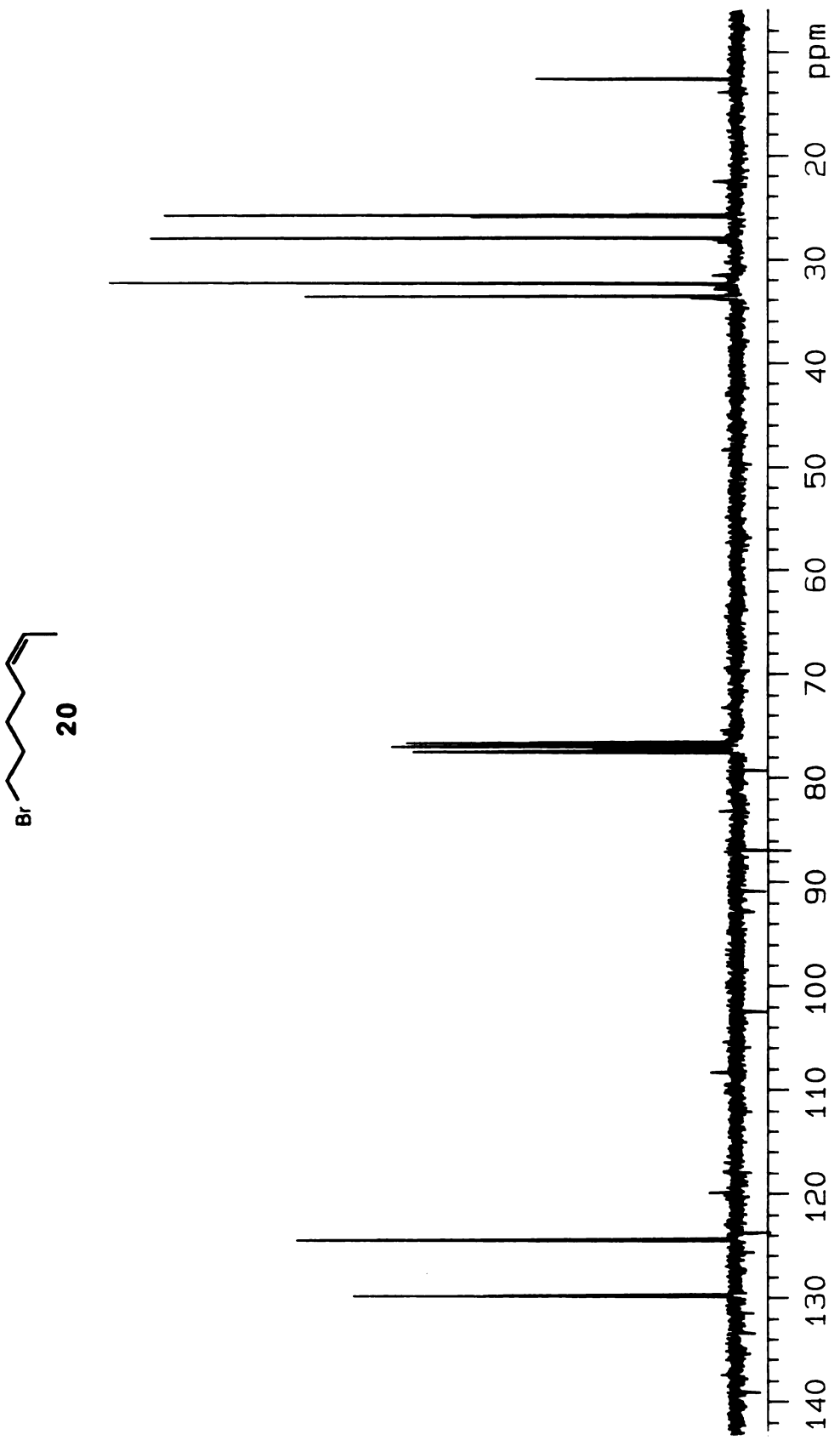
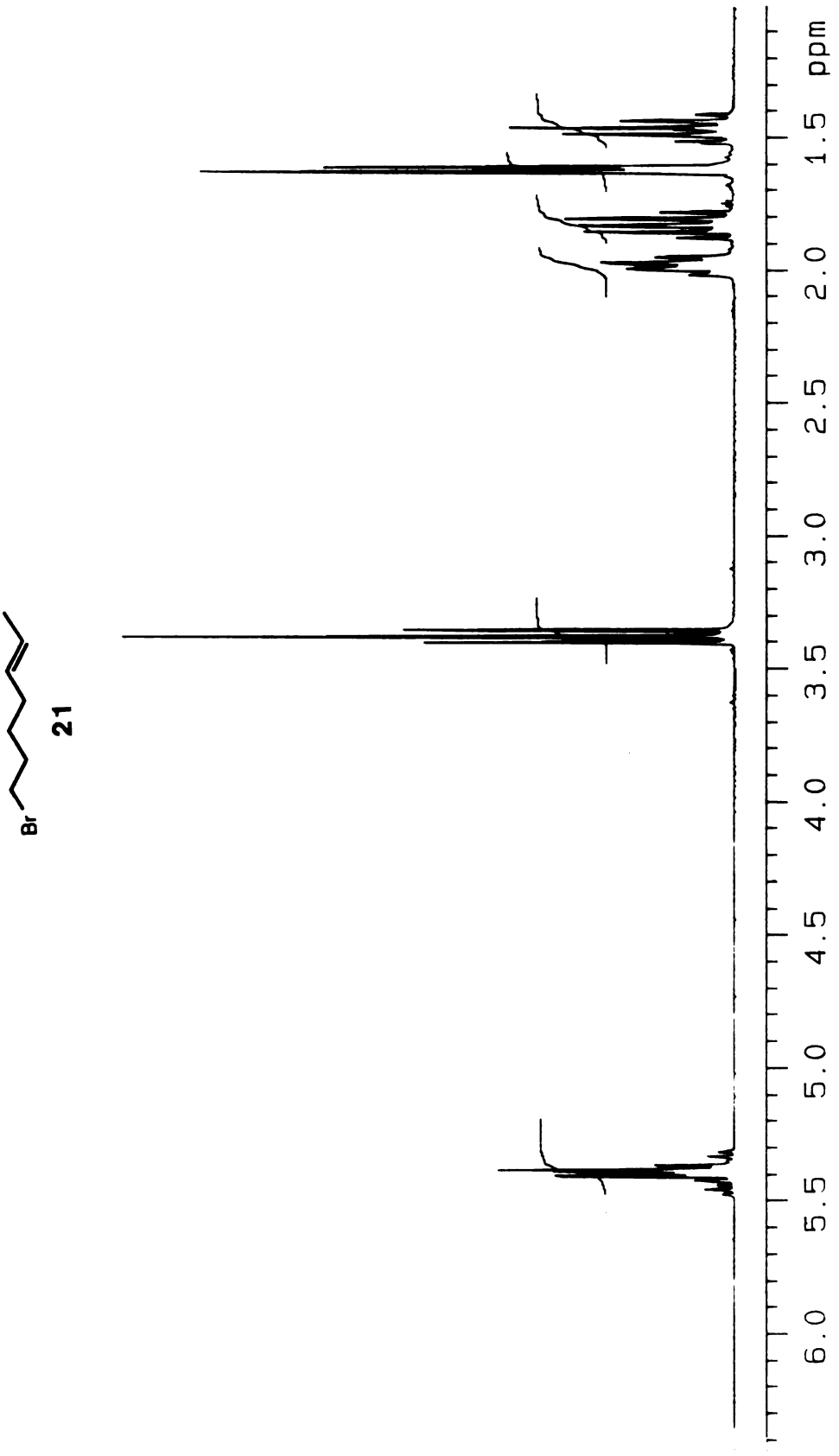
APPENDIX



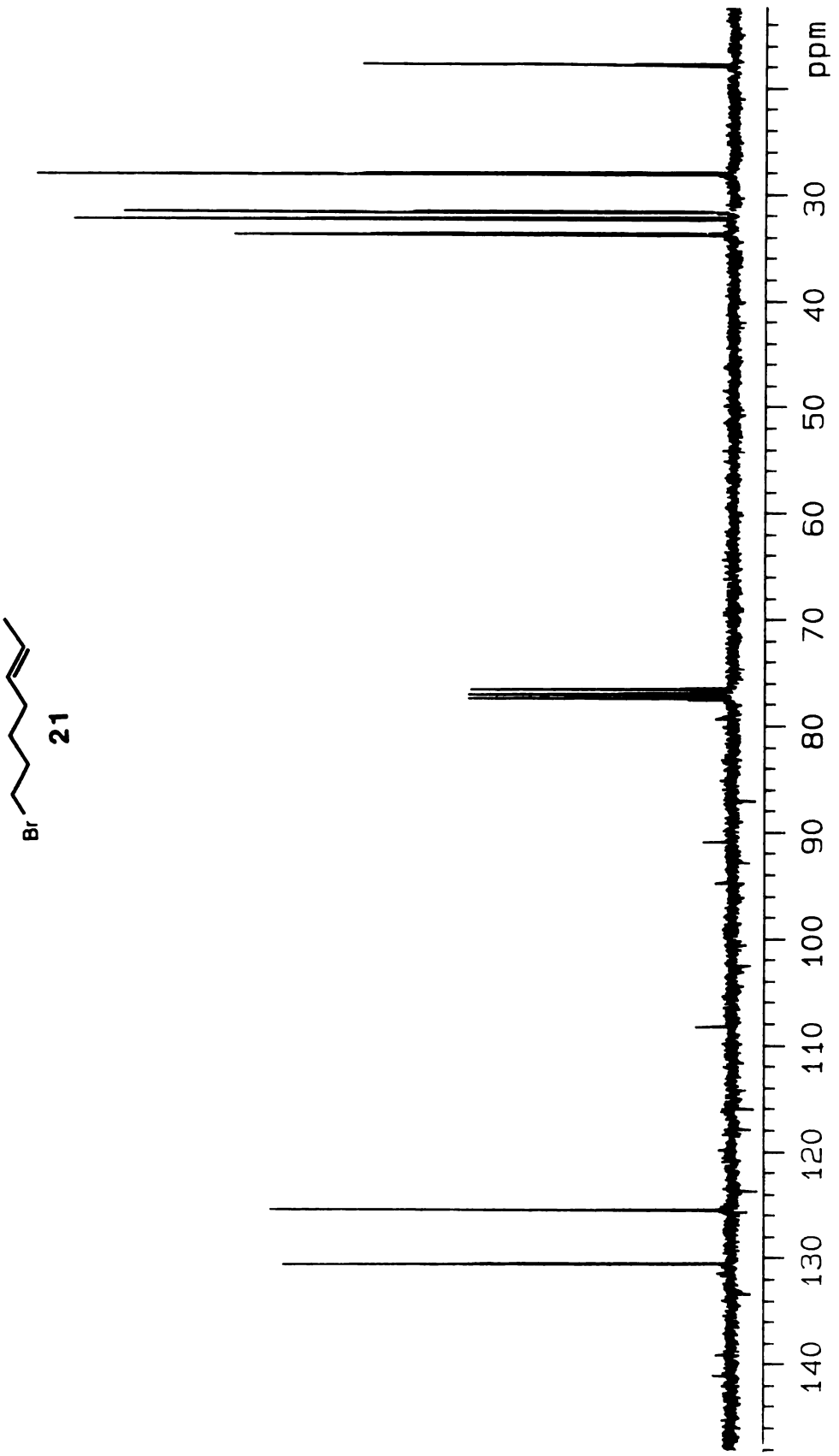
Scheme 23. ^{1}H NMR Spectrum of **20**.



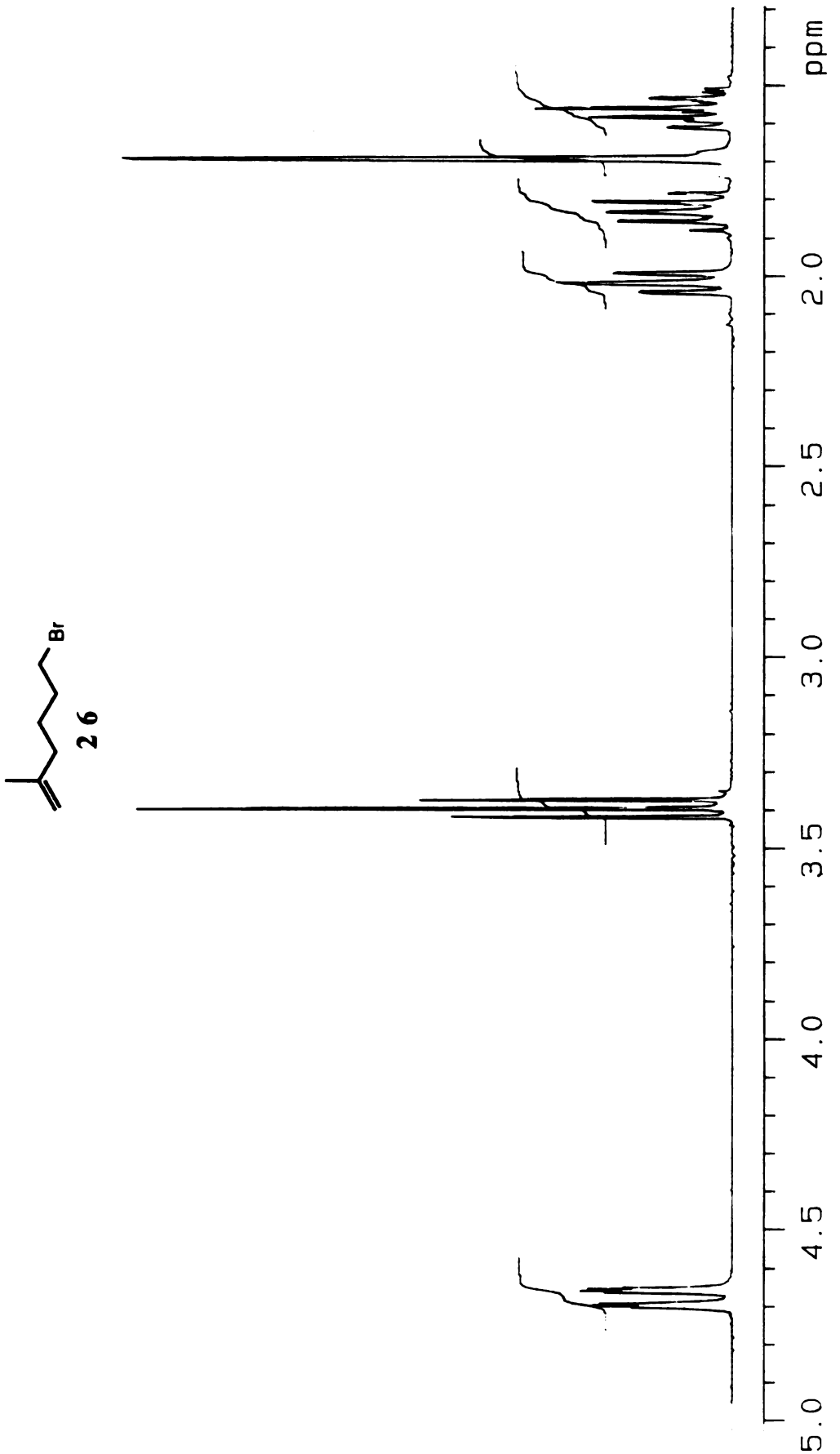
Scheme 24. ^{13}C NMR Spectrum of **20**.



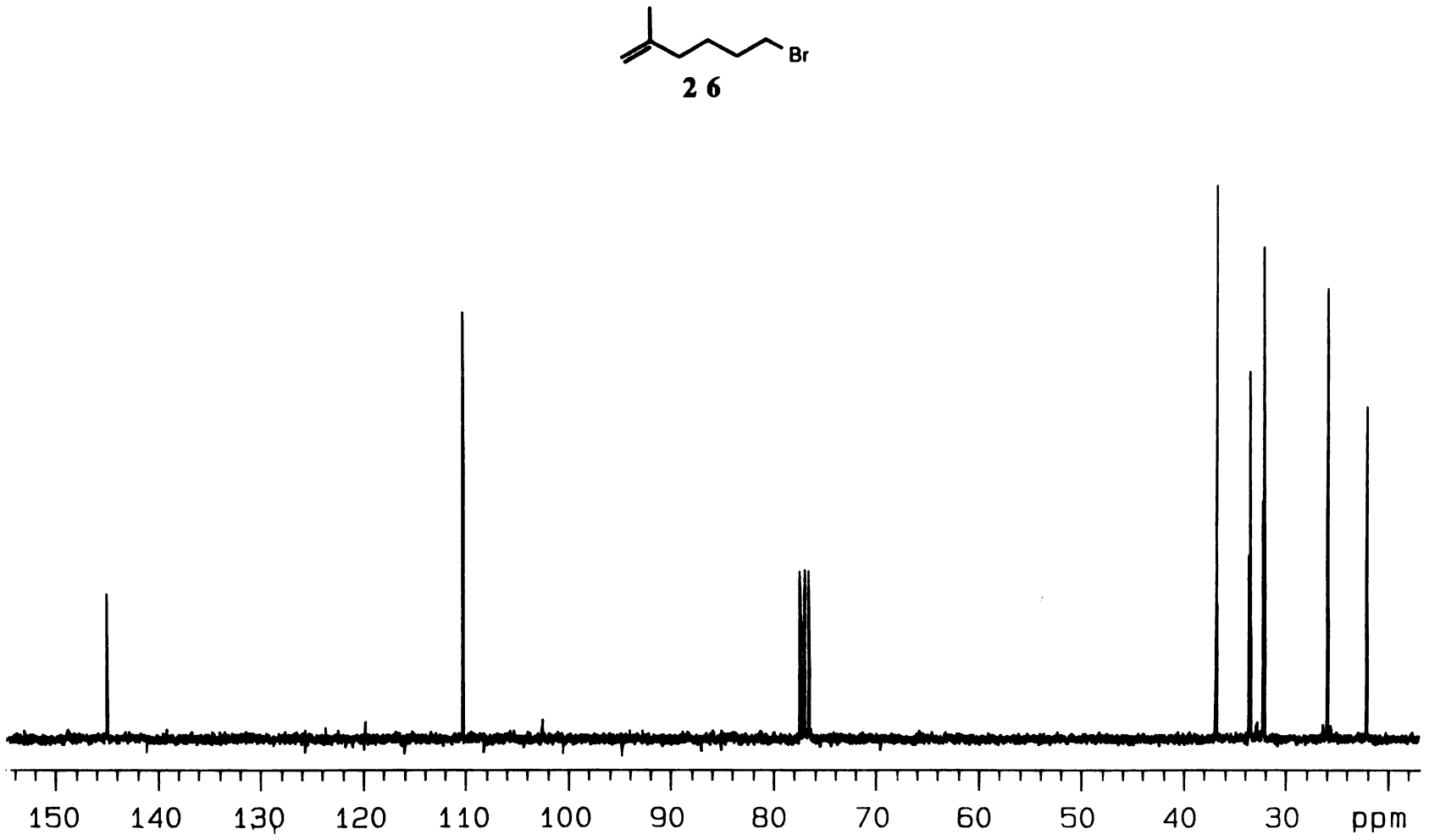
Scheme 25. ^{1}H NMR Spectrum of **21**.



Scheme 26. ^{13}C NMR Spectrum of **21**.

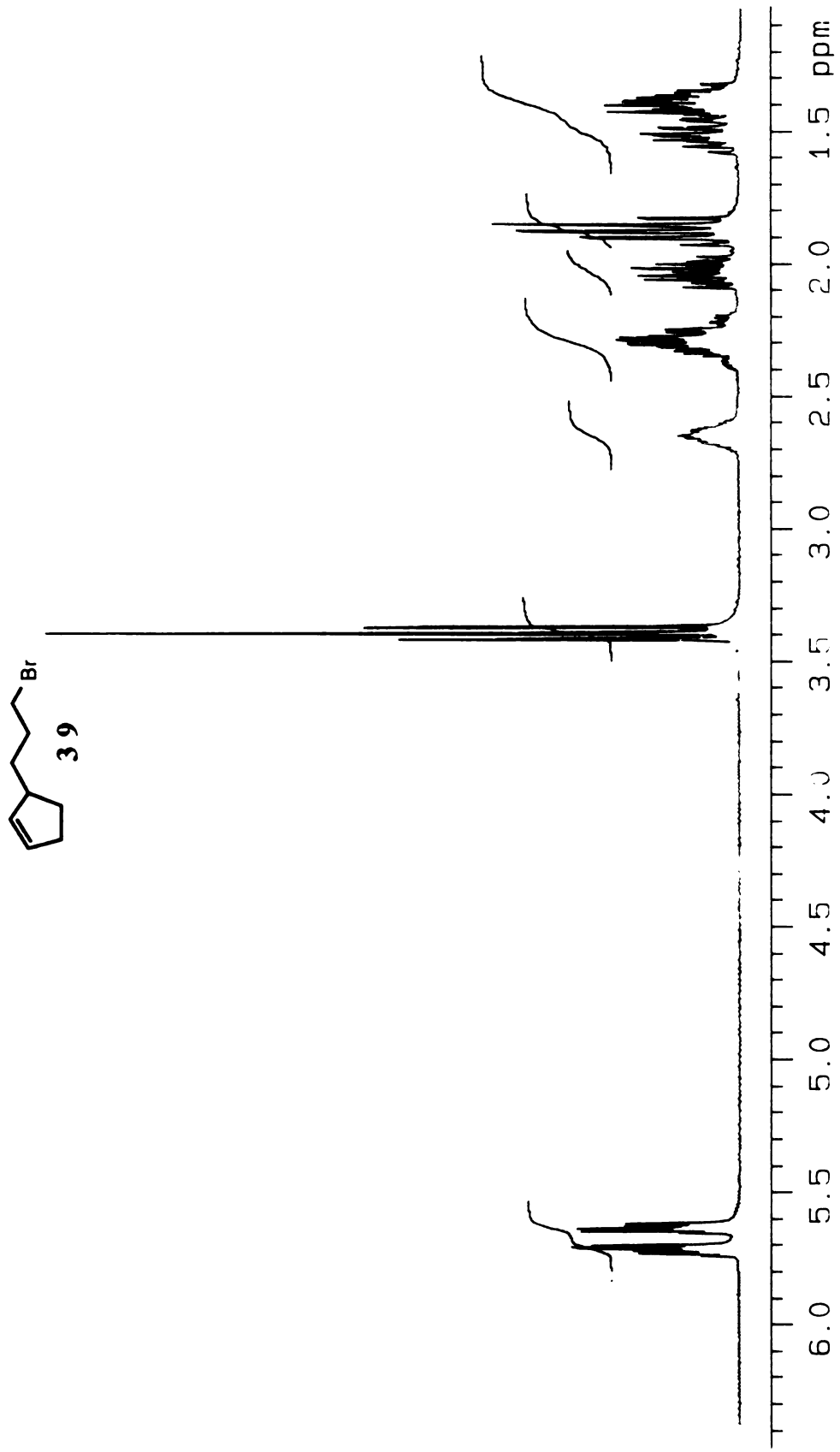


Scheme 27. ^{1}H NMR Spectrum of **26**.

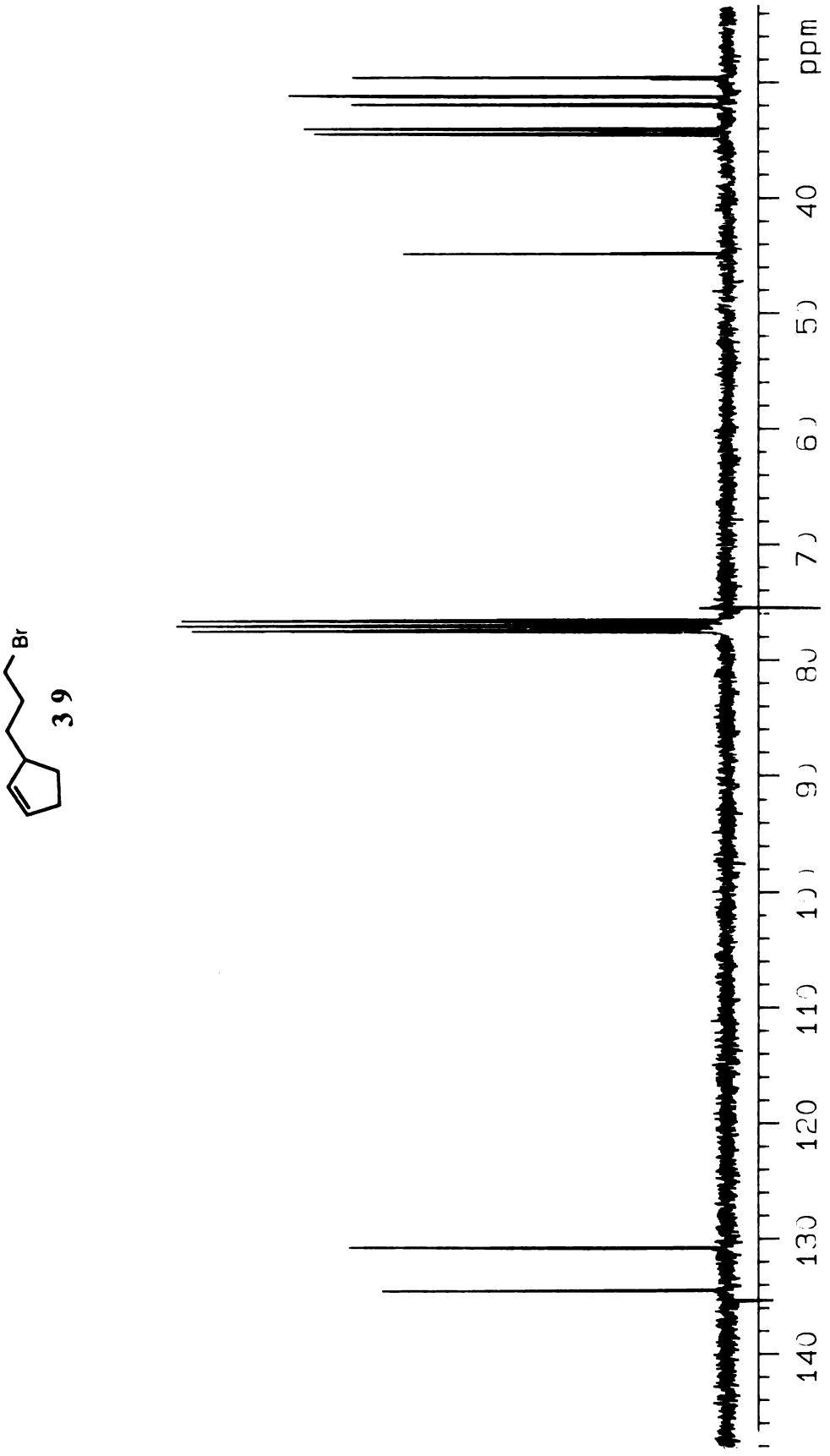


26

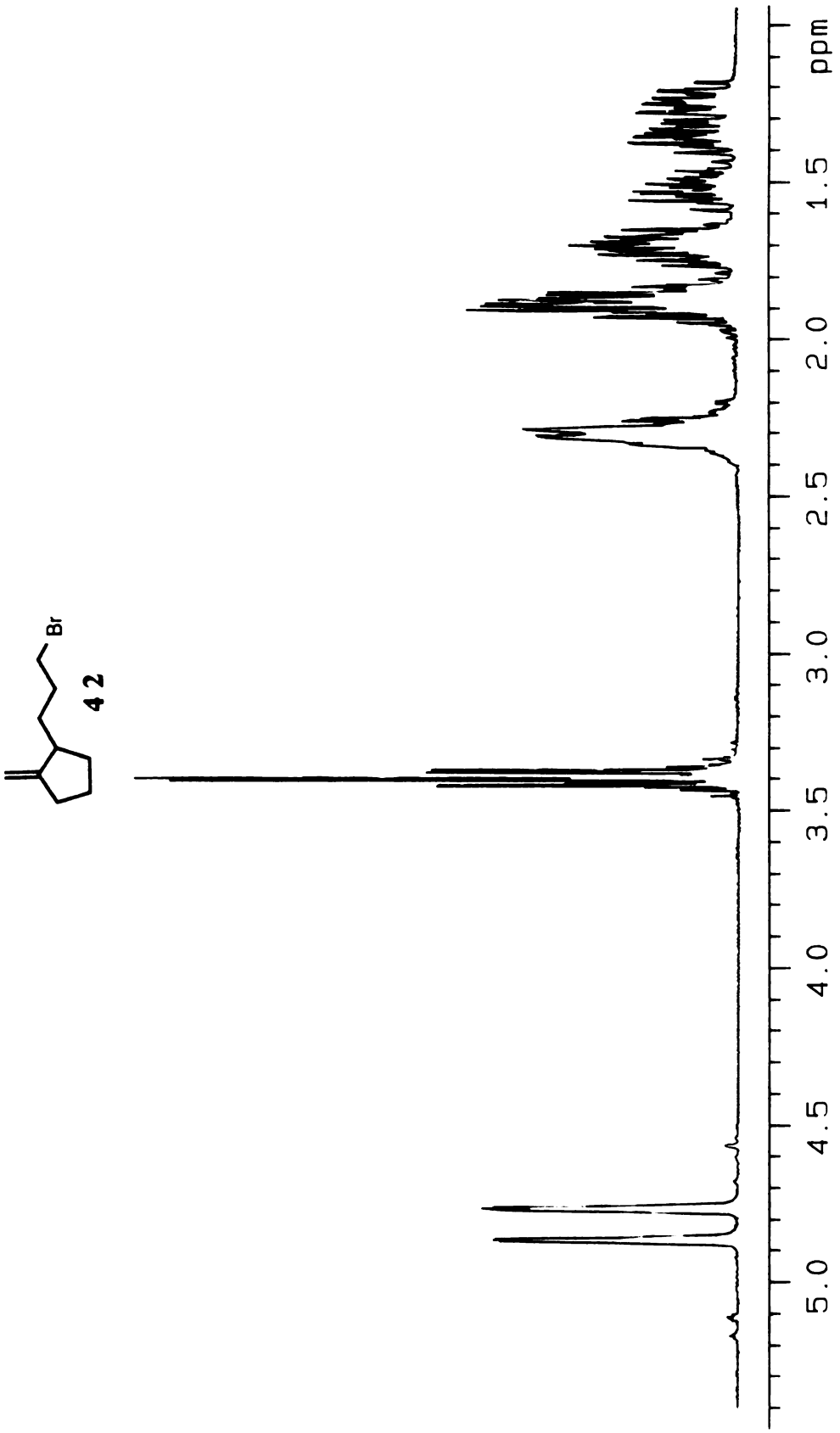
Scheme 28. ^{13}C NMR Spectrum of **26**.



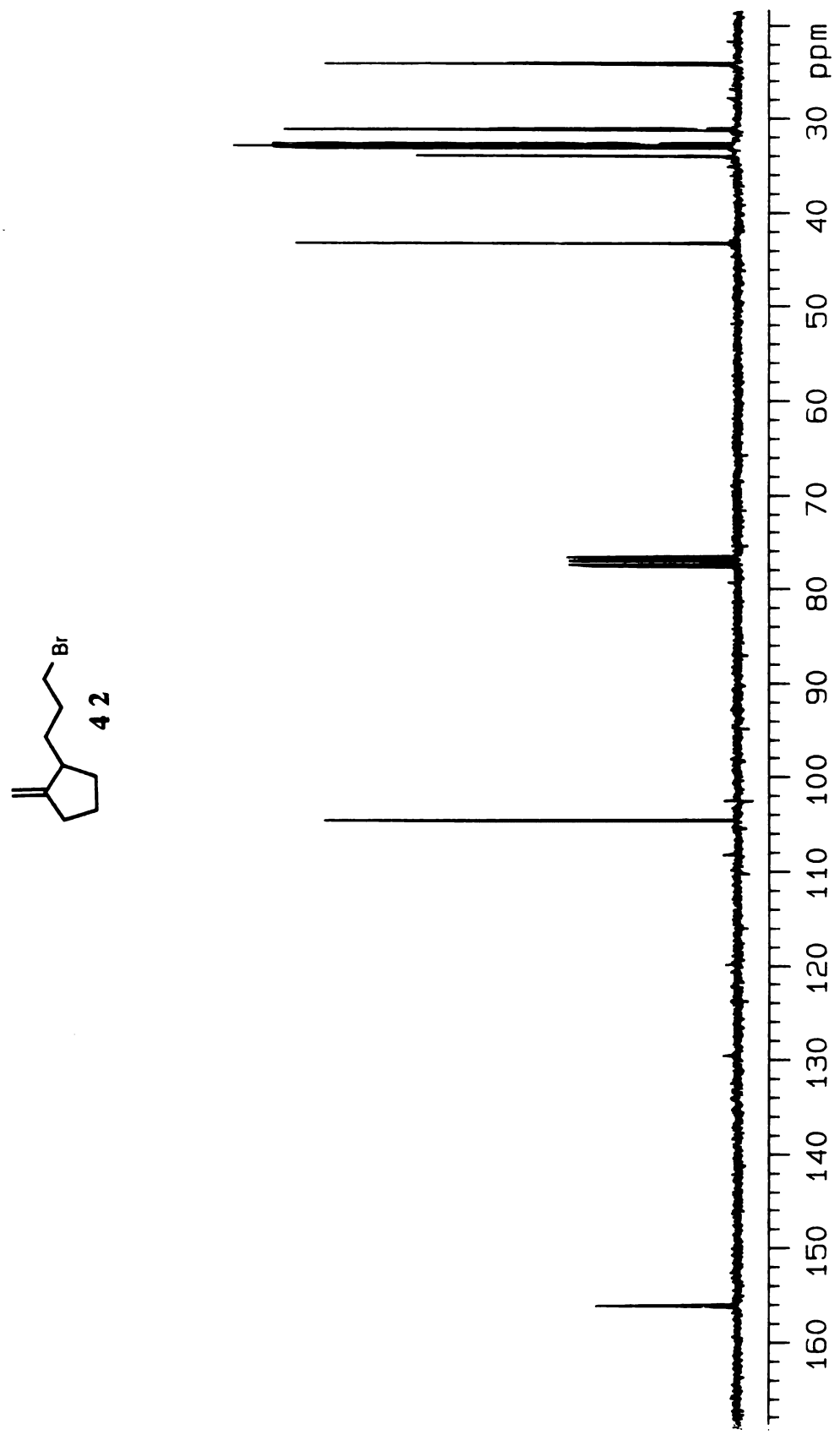
Scheme 29. ^{1}H NMR Spectrum of **39**.



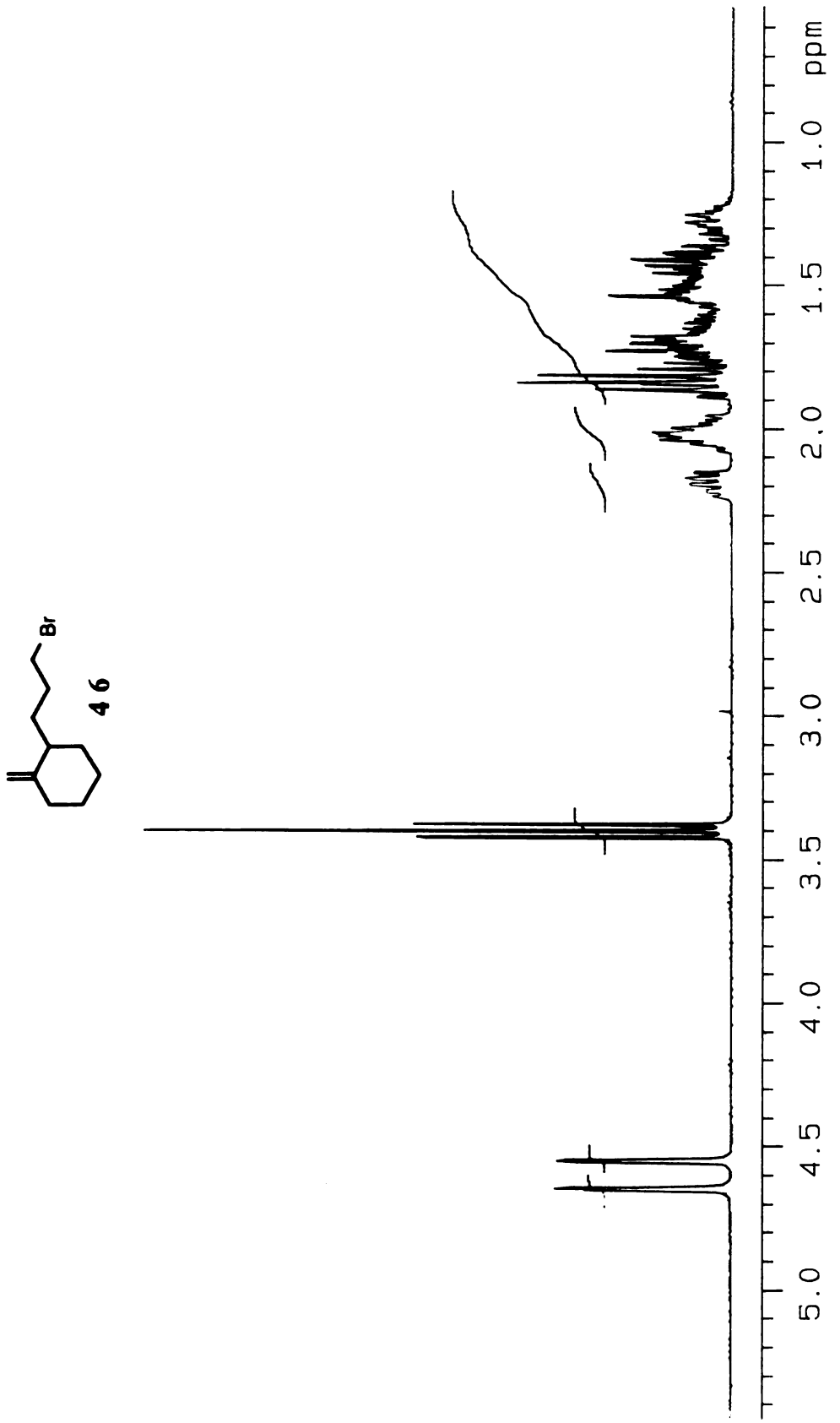
Scheme 30. ^{13}C NMR Spectrum of **39**.



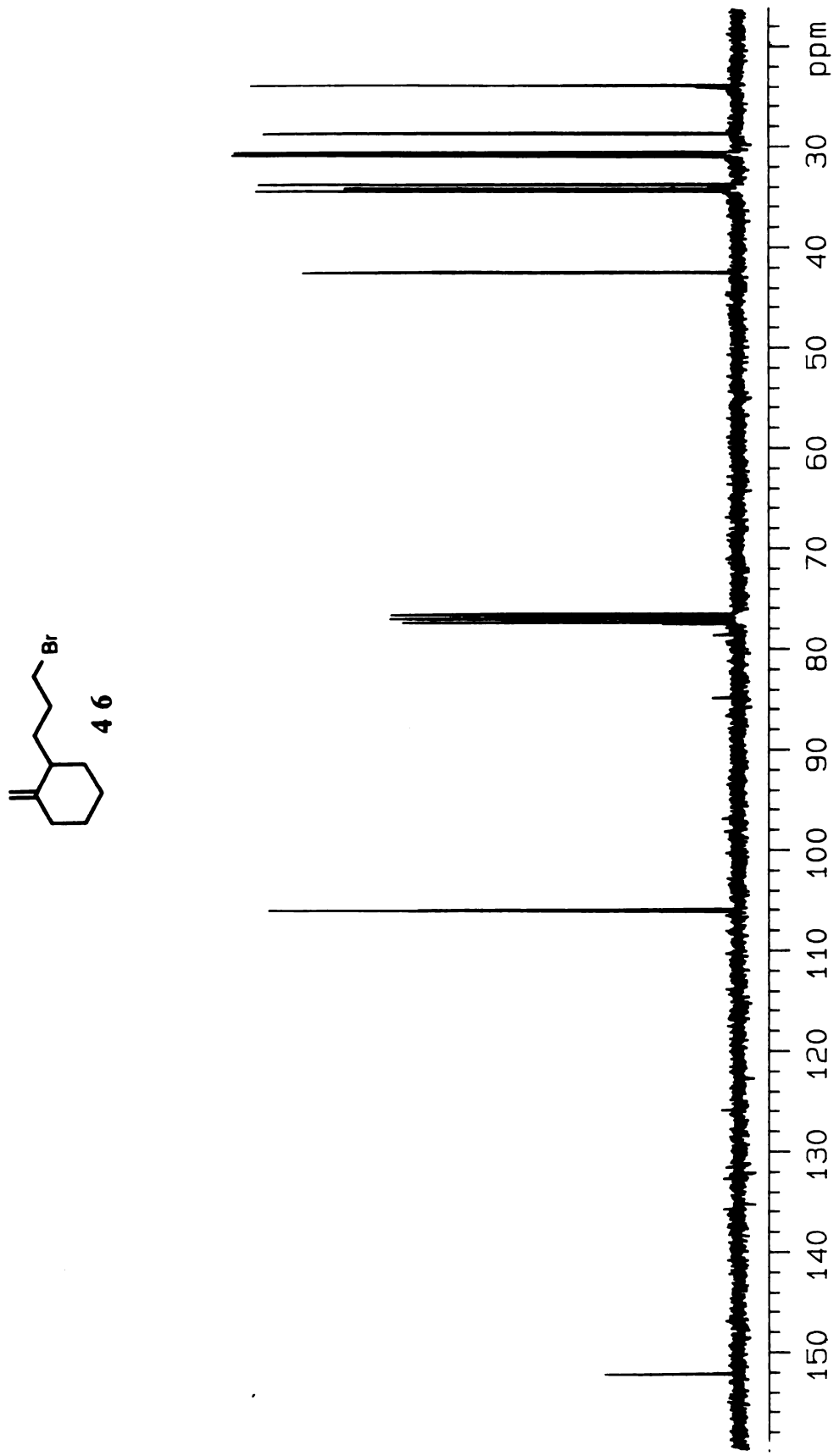
Scheme 31. ^{1}H NMR Spectrum of **42**.



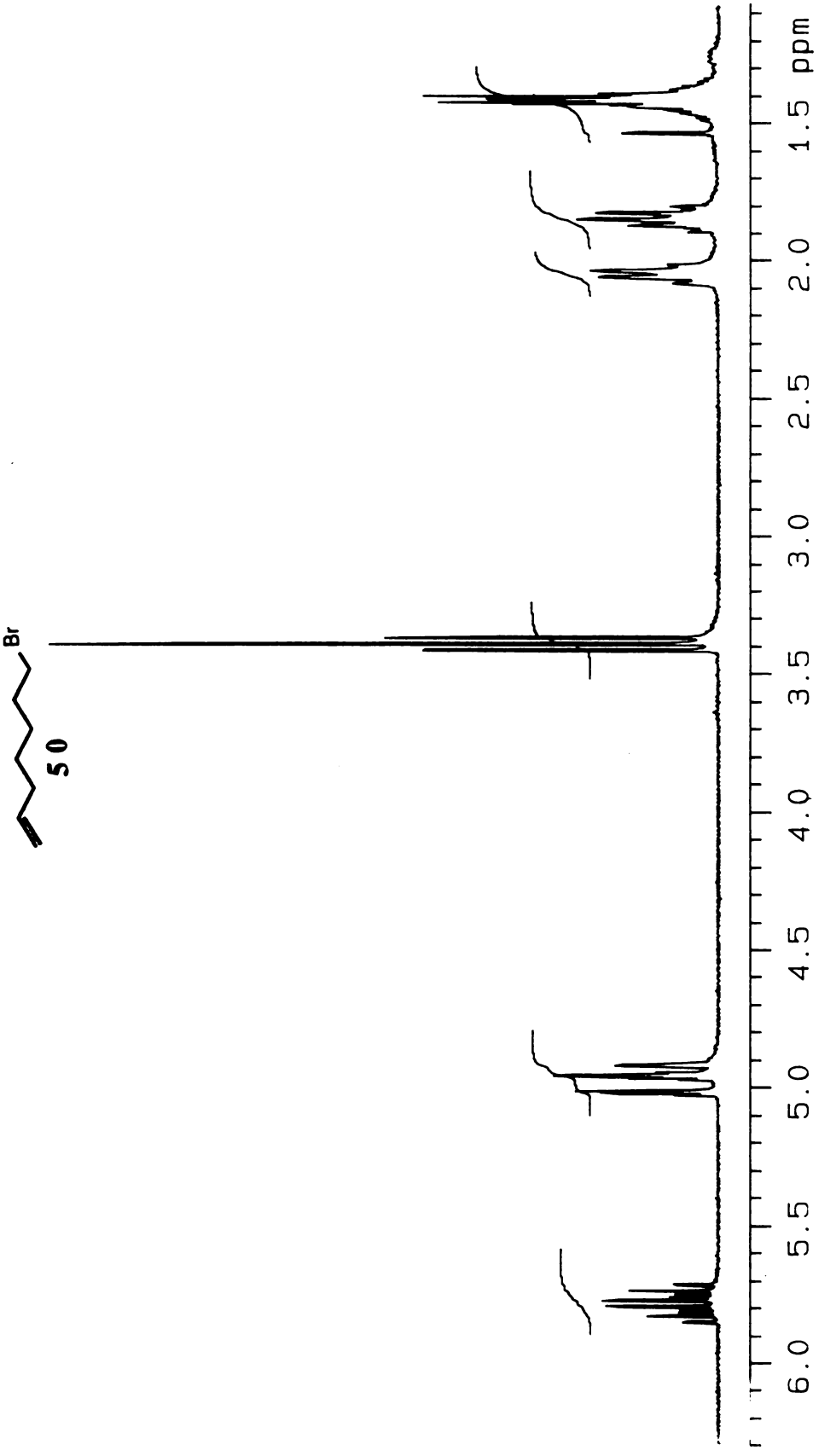
Scheme 32. ^{13}C **NMR Spectrum of 42.**



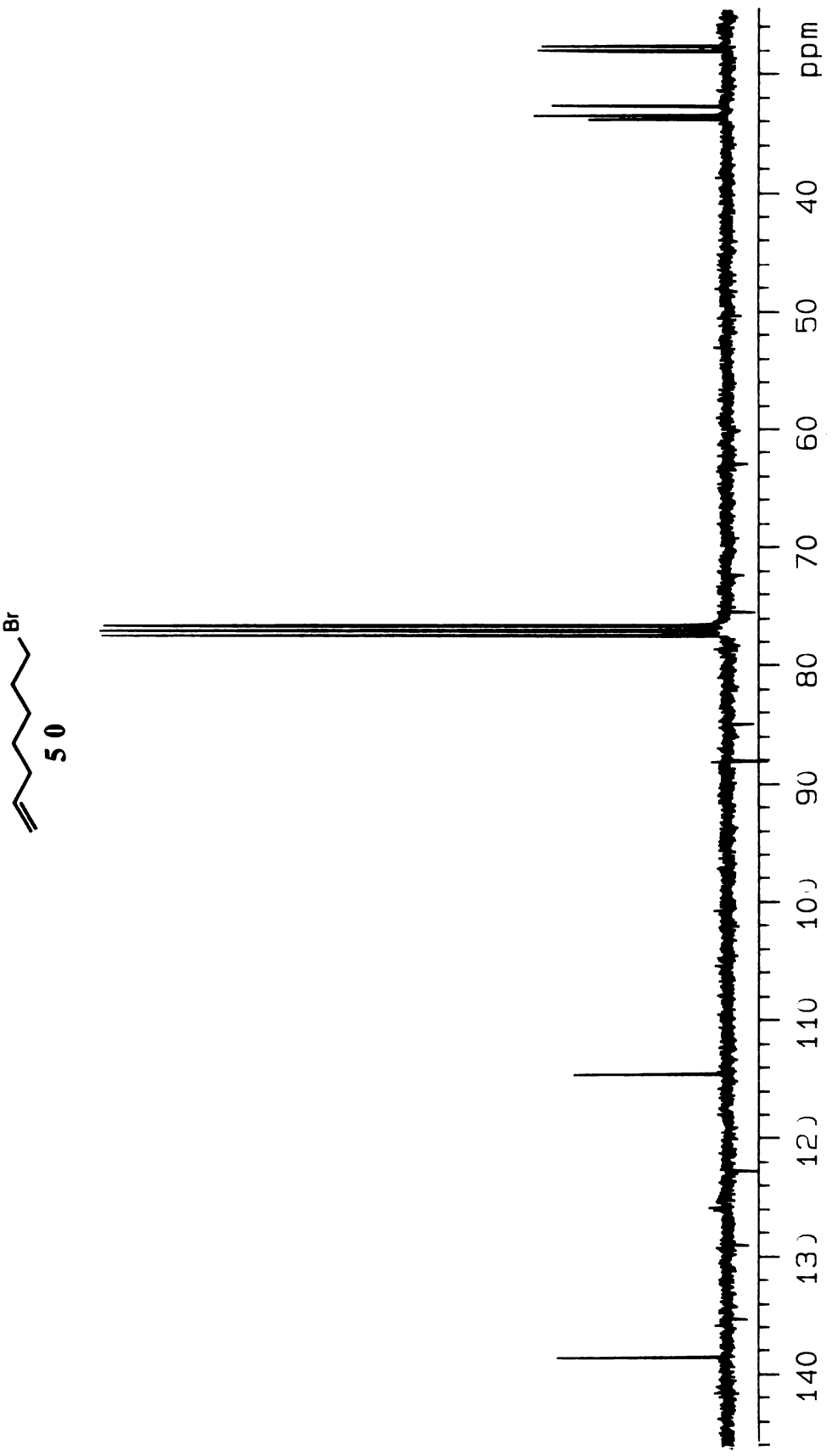
Scheme 33. ^{1}H NMR Spectrum of 46.



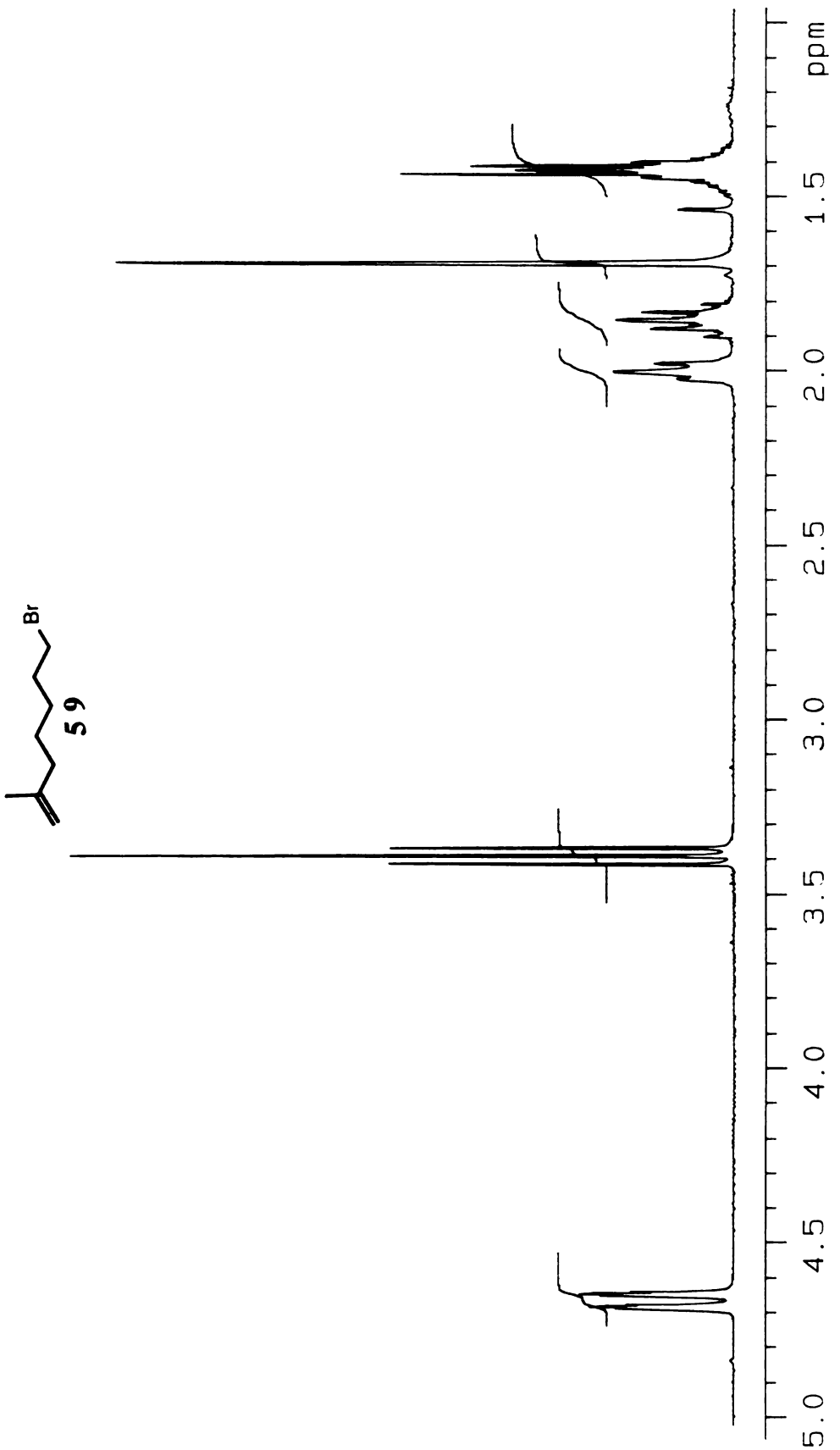
Scheme 34. ^{13}C **NMR Spectrum of 46.**



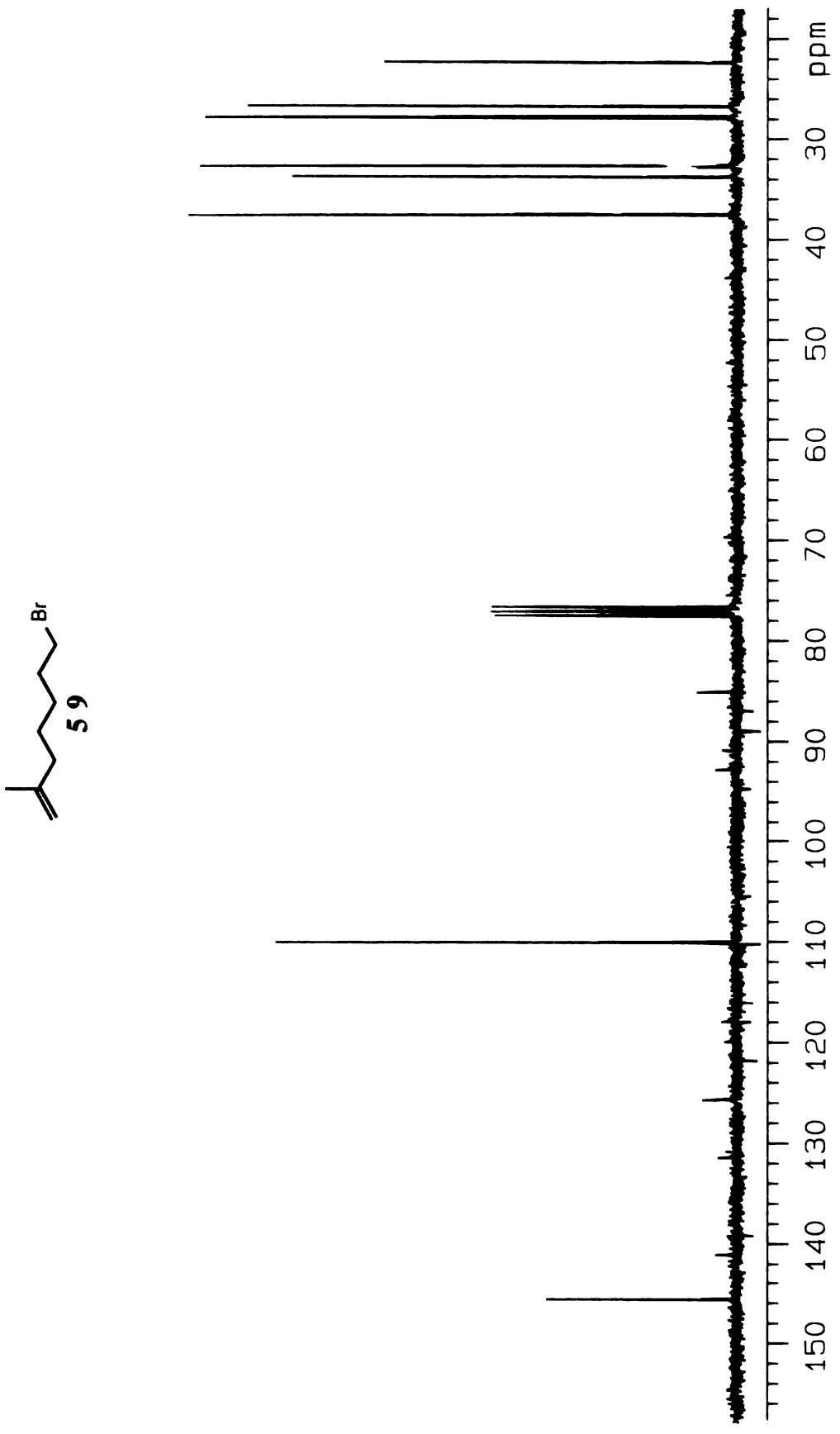
Scheme 35. ^{1}H NMR Spectrum of 50.



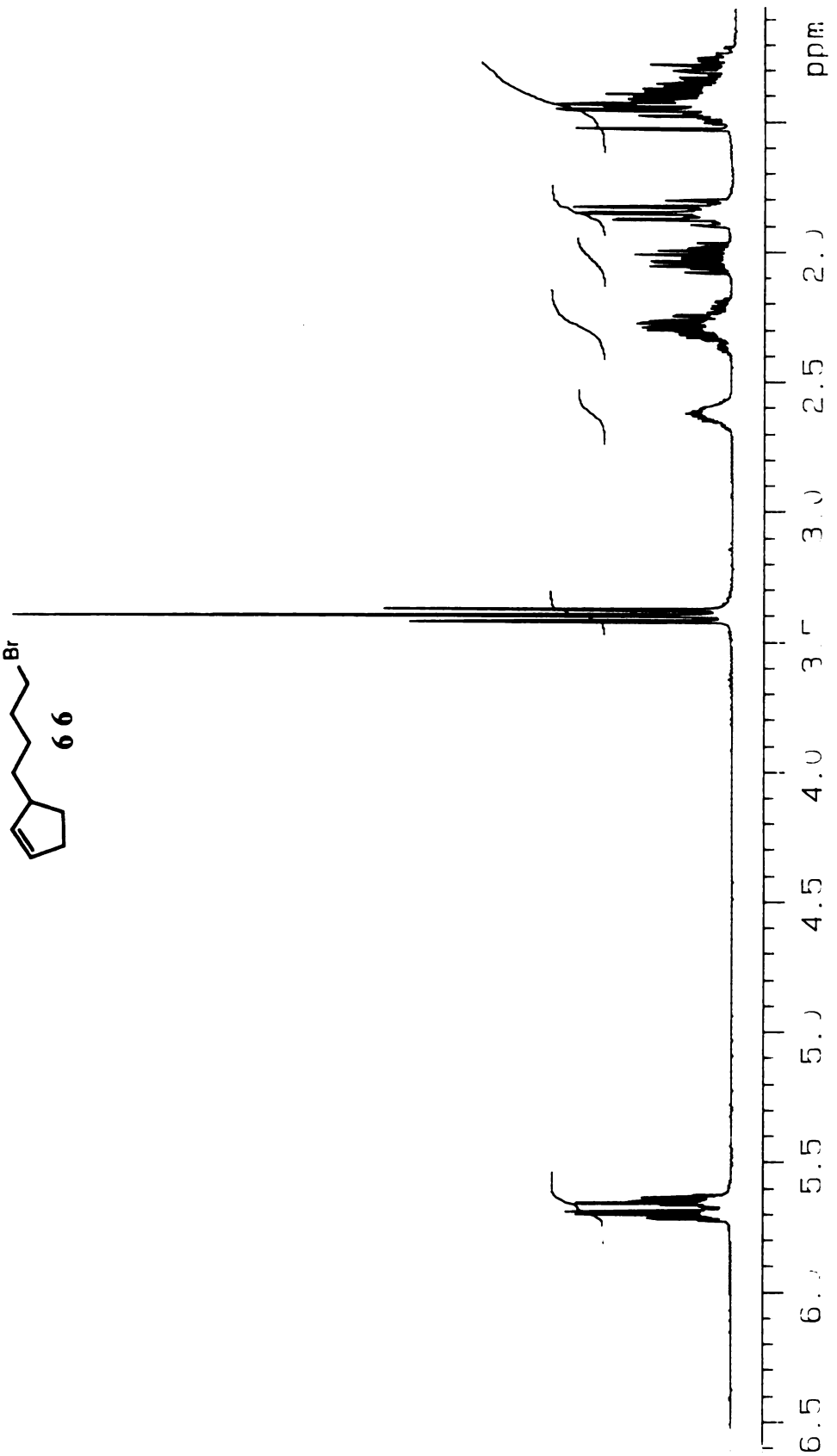
Scheme 36. ^{13}C NMR Spectrum of **50**.



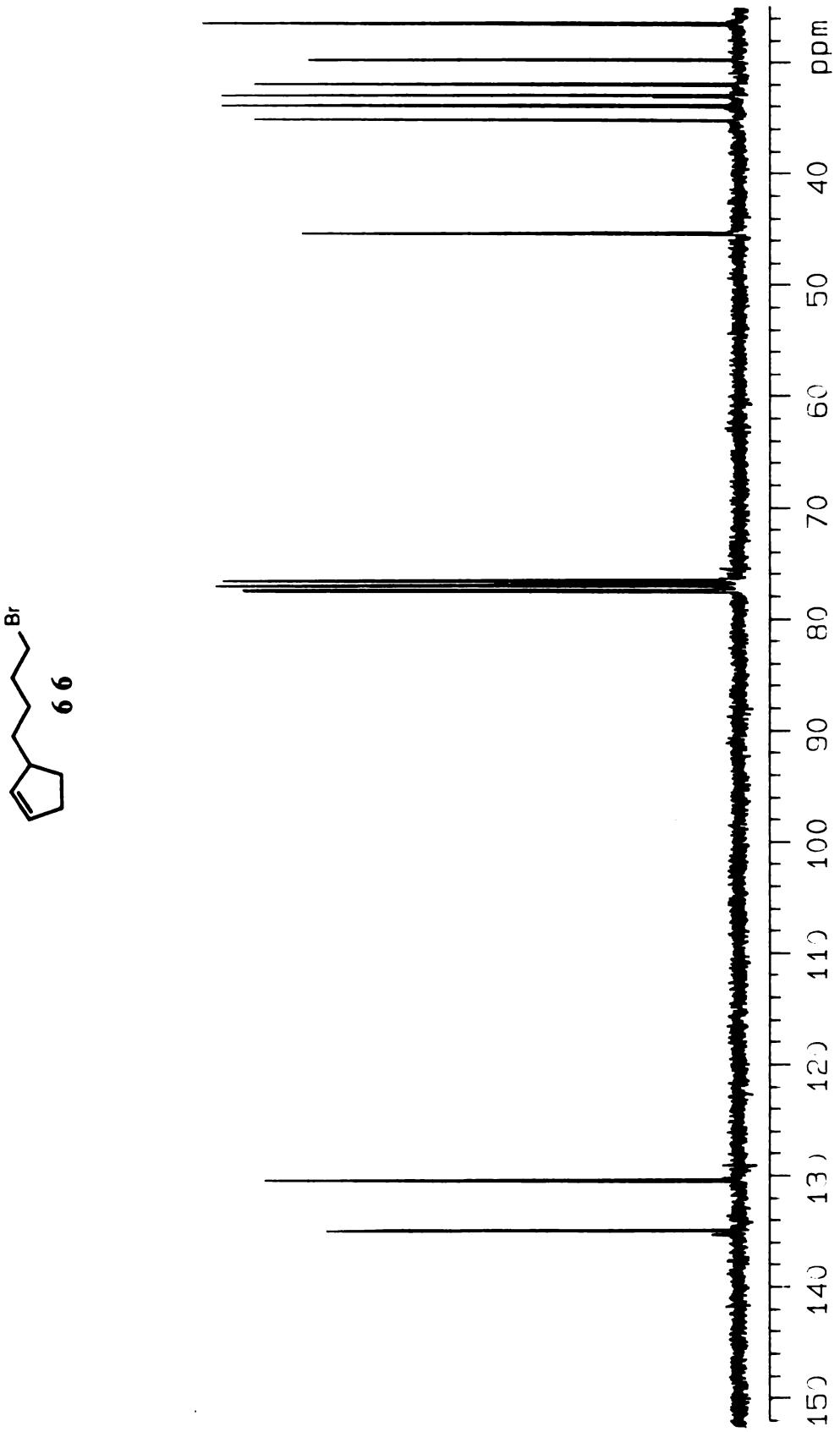
Scheme 37. ^{1}H **NMR Spectrum of 59.**



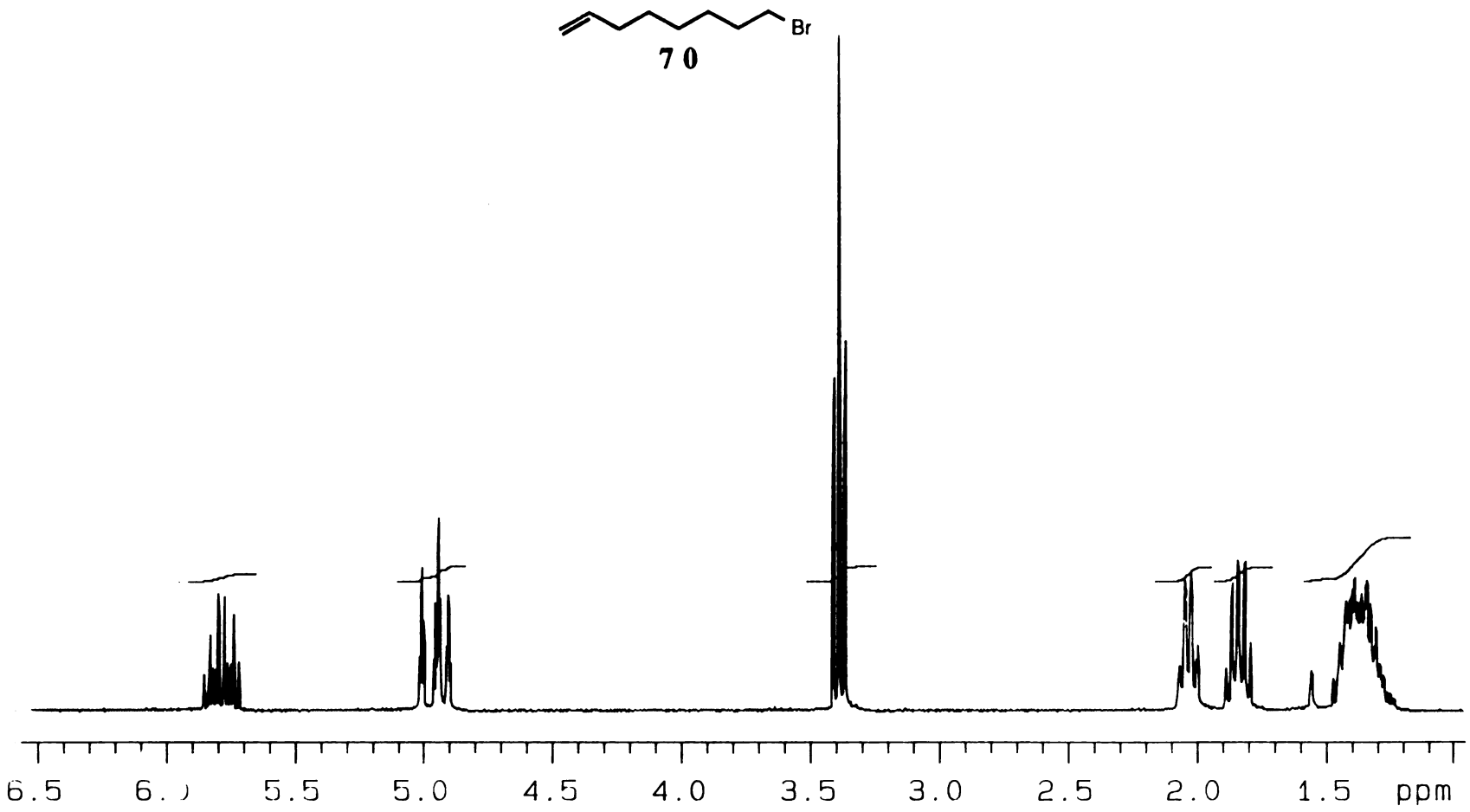
Scheme 38. ^{13}C NMR Spectrum of **59**.



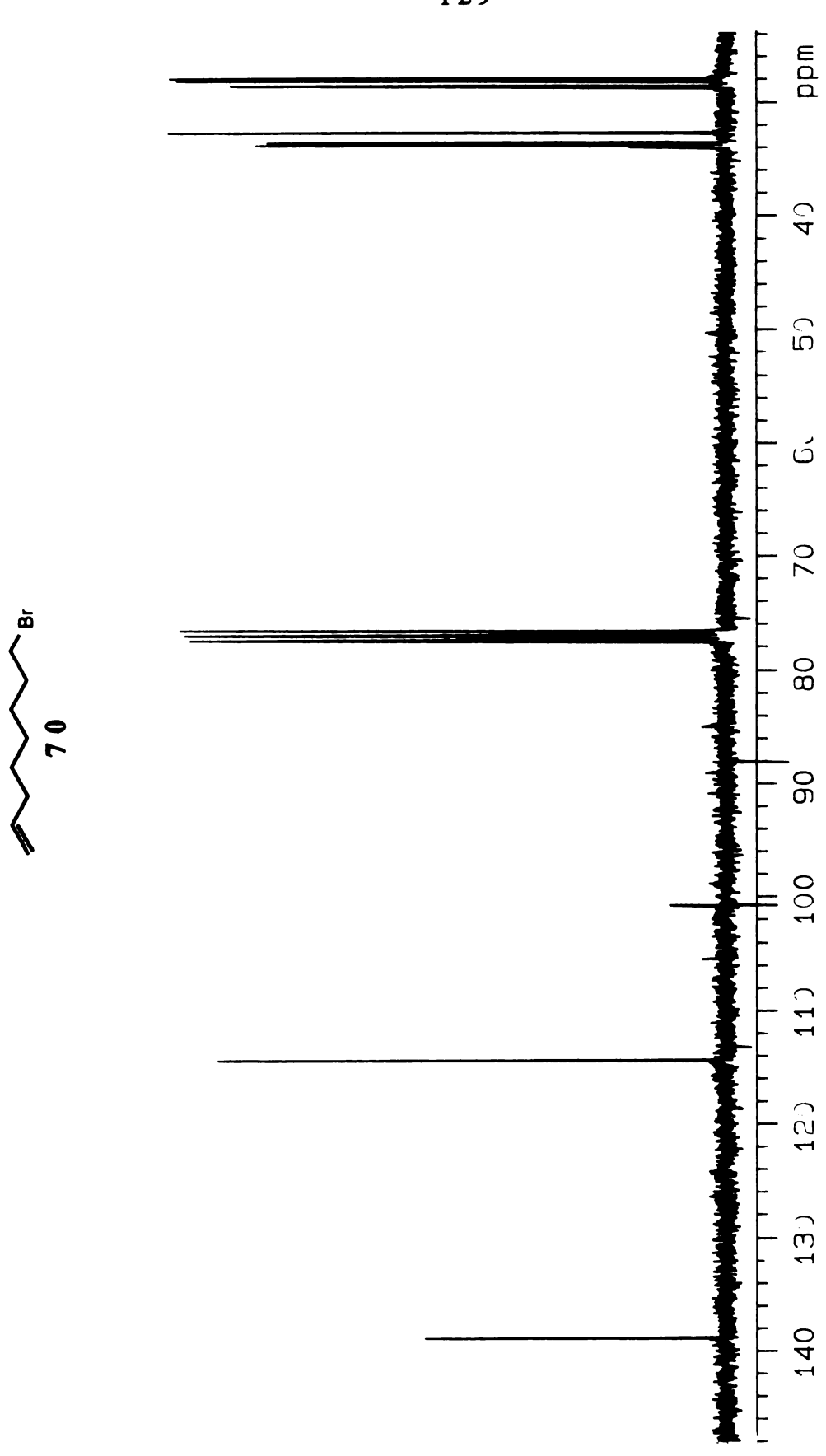
Scheme 39. ^{1}H NMR Spectrum of **66**.



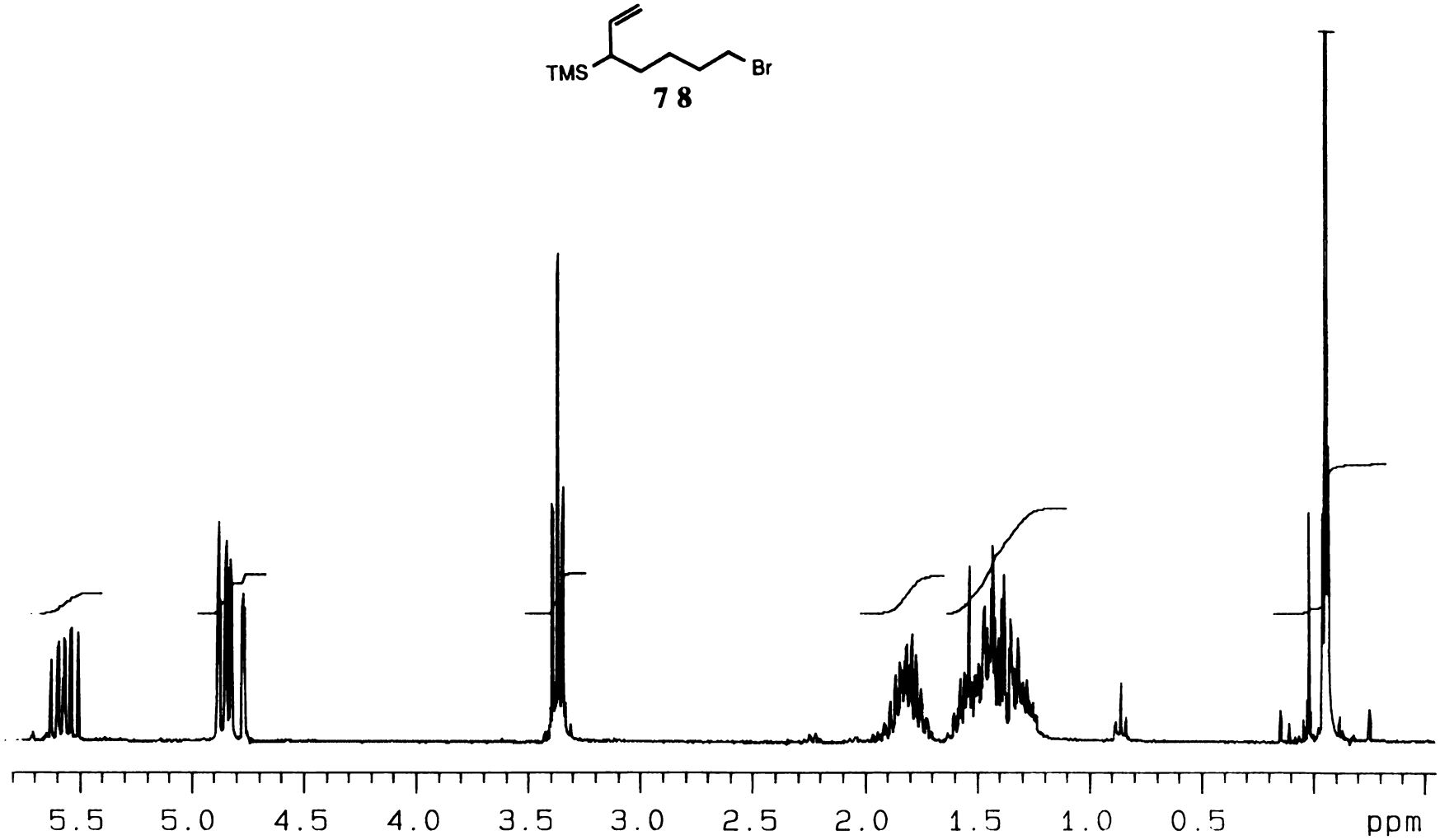
Scheme 40. ^{13}C NMR Spectrum of **66**.



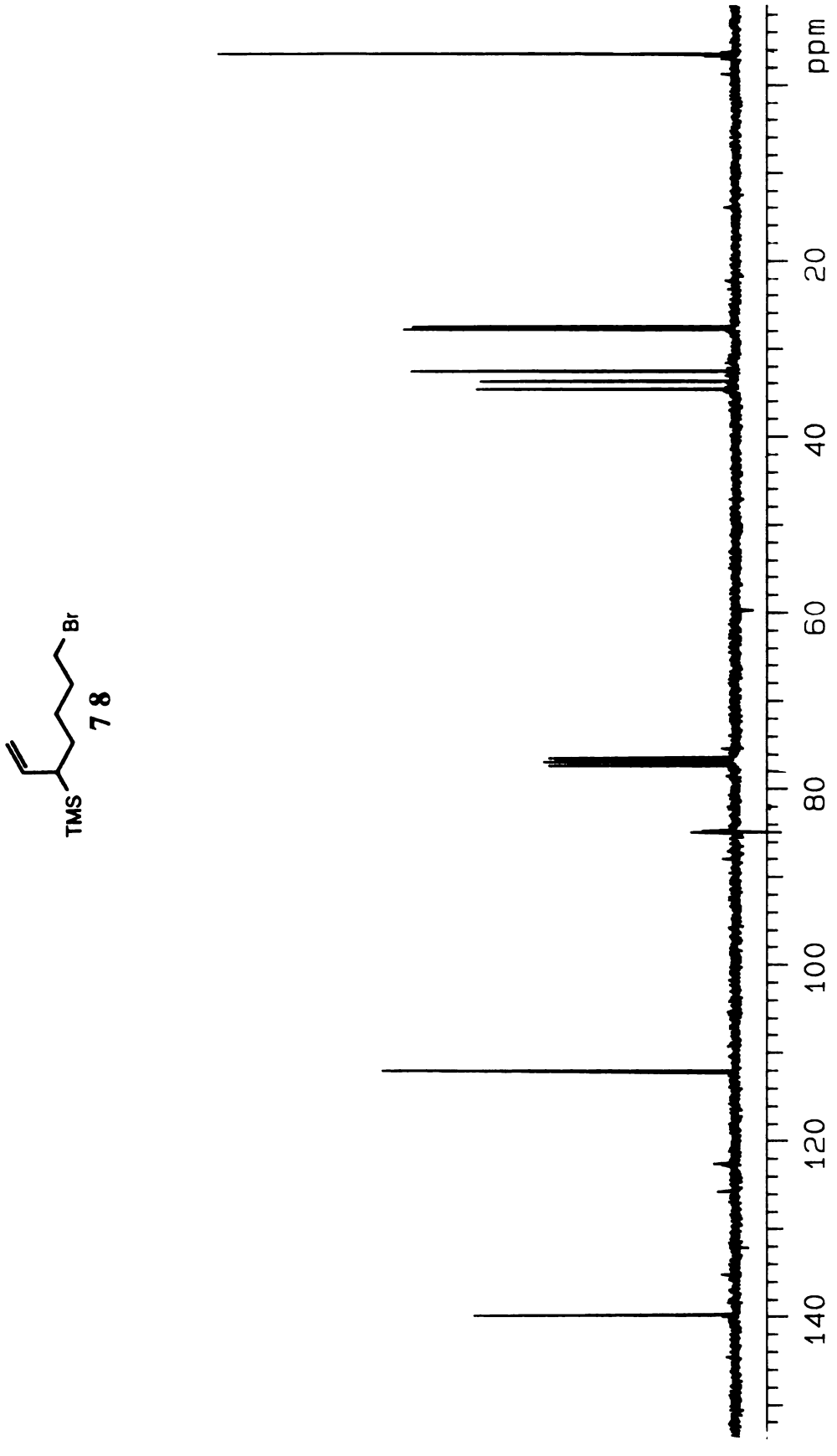
Scheme 41. ^{1}H NMR Spectrum of **70**.



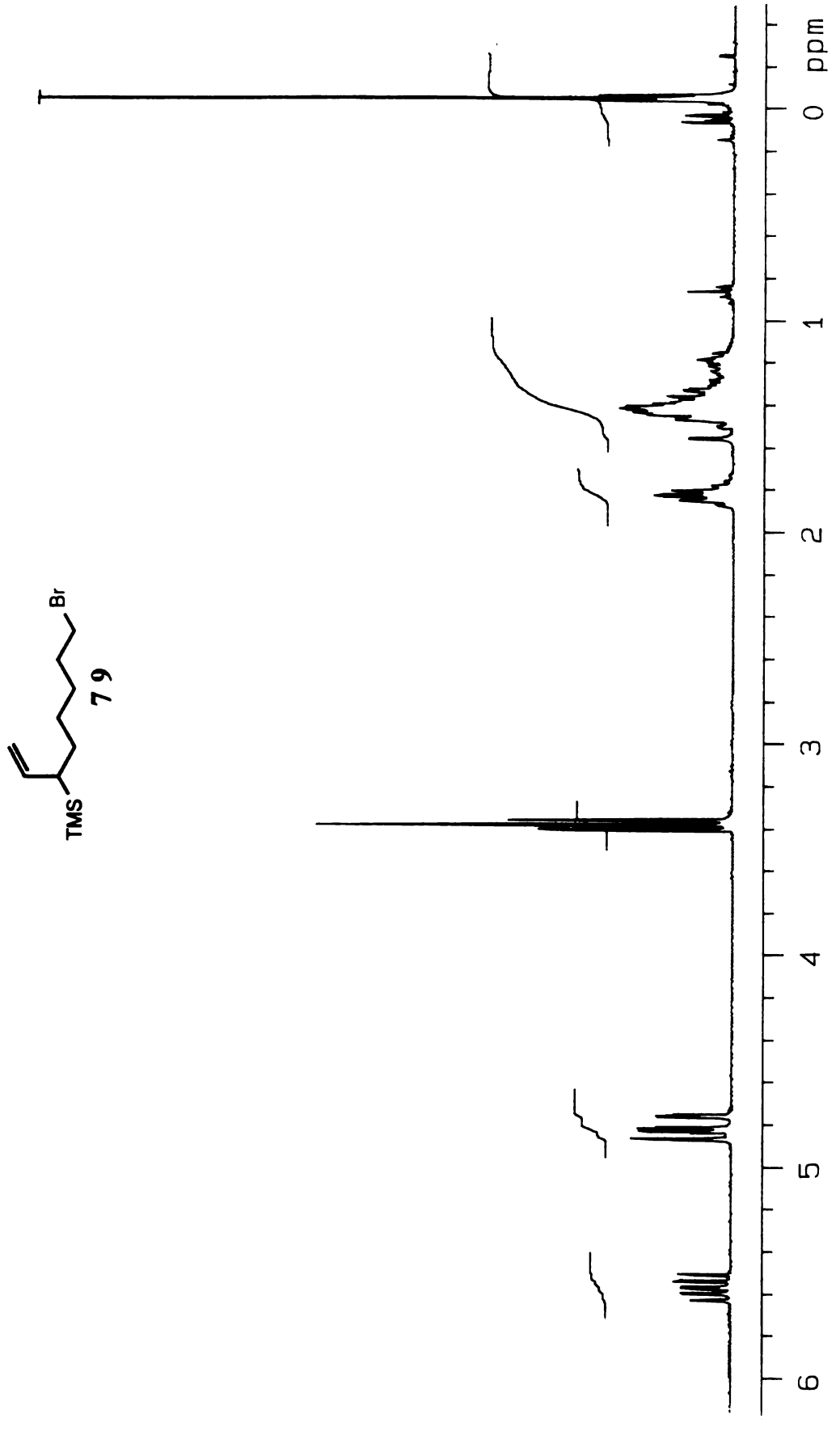
Scheme 42. ^{13}C NMR Spectrum of **70**.



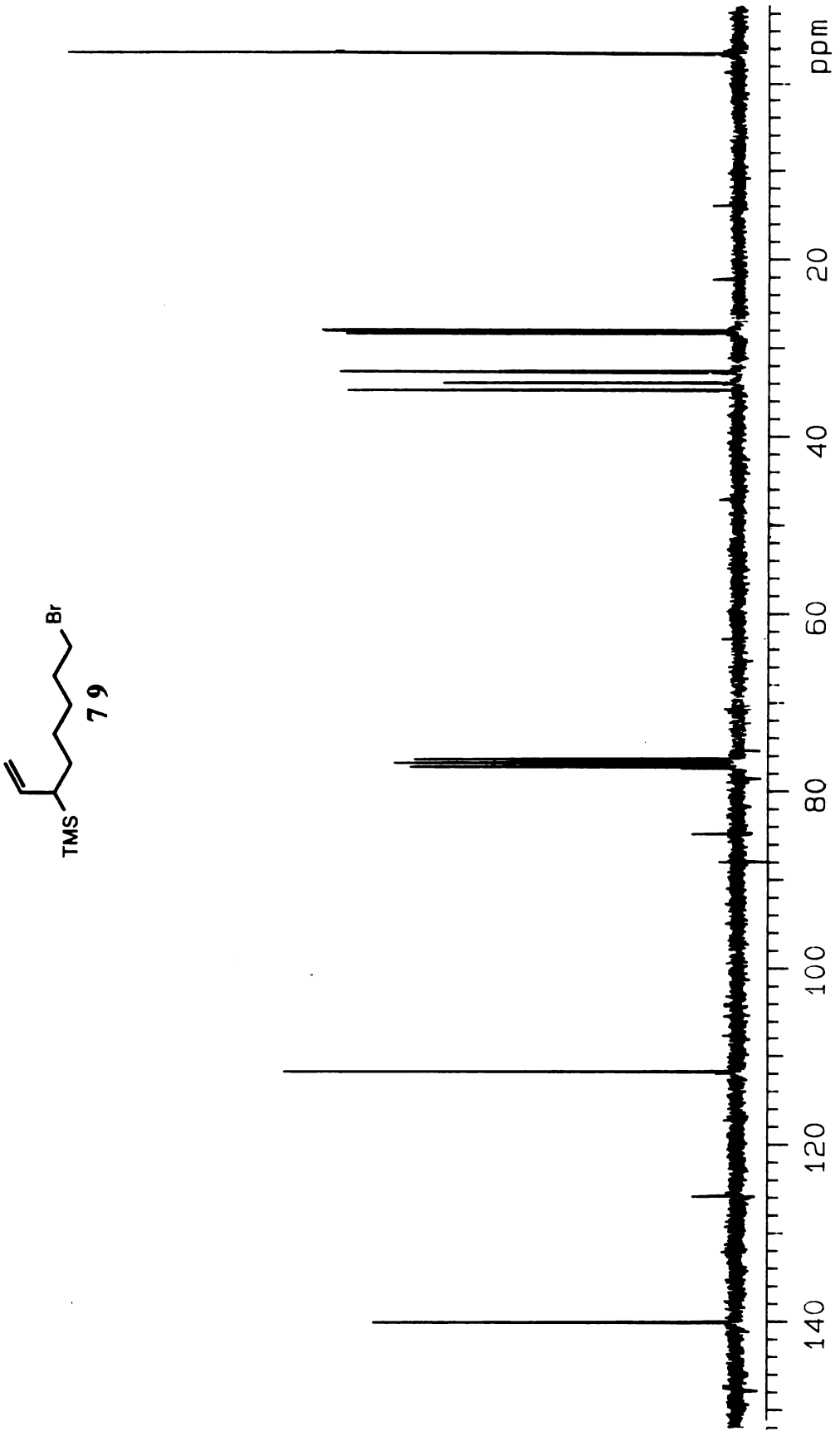
Scheme 43. ^{1}H NMR Spectrum of **78**.



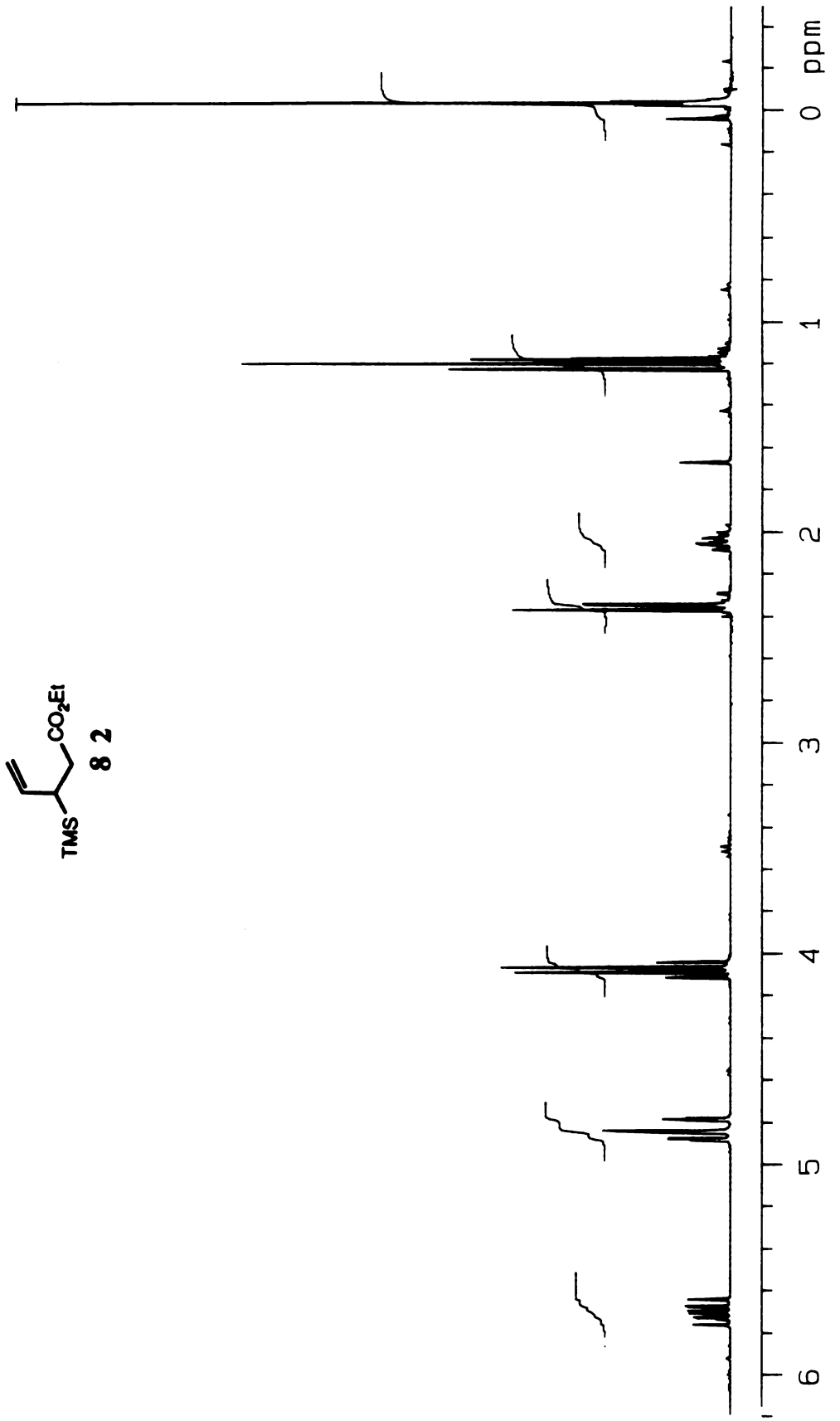
Scheme 44. ^{13}C NMR Spectrum of **78**.



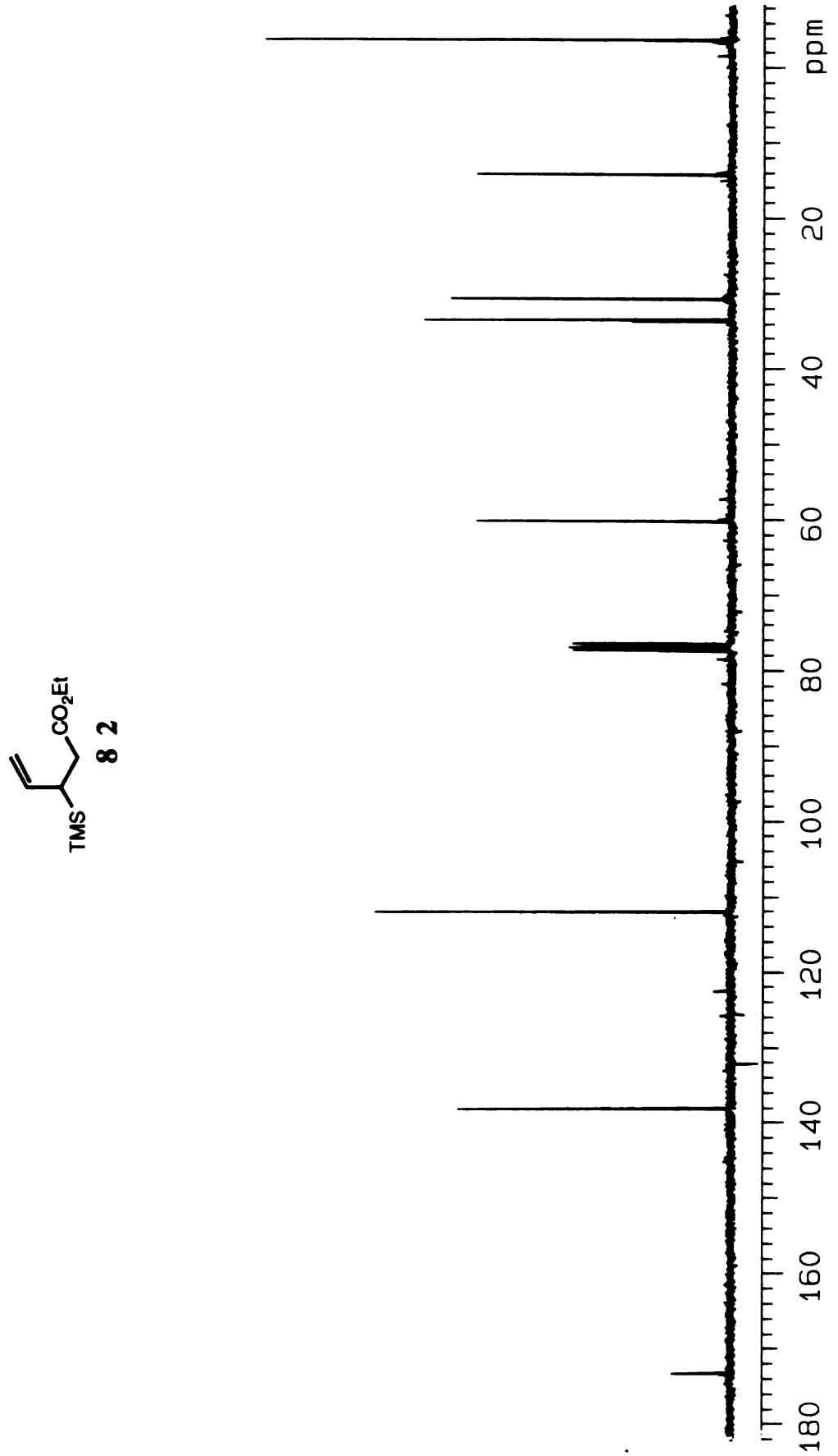
Scheme 45. ^{1}H NMR Spectrum of **79**.



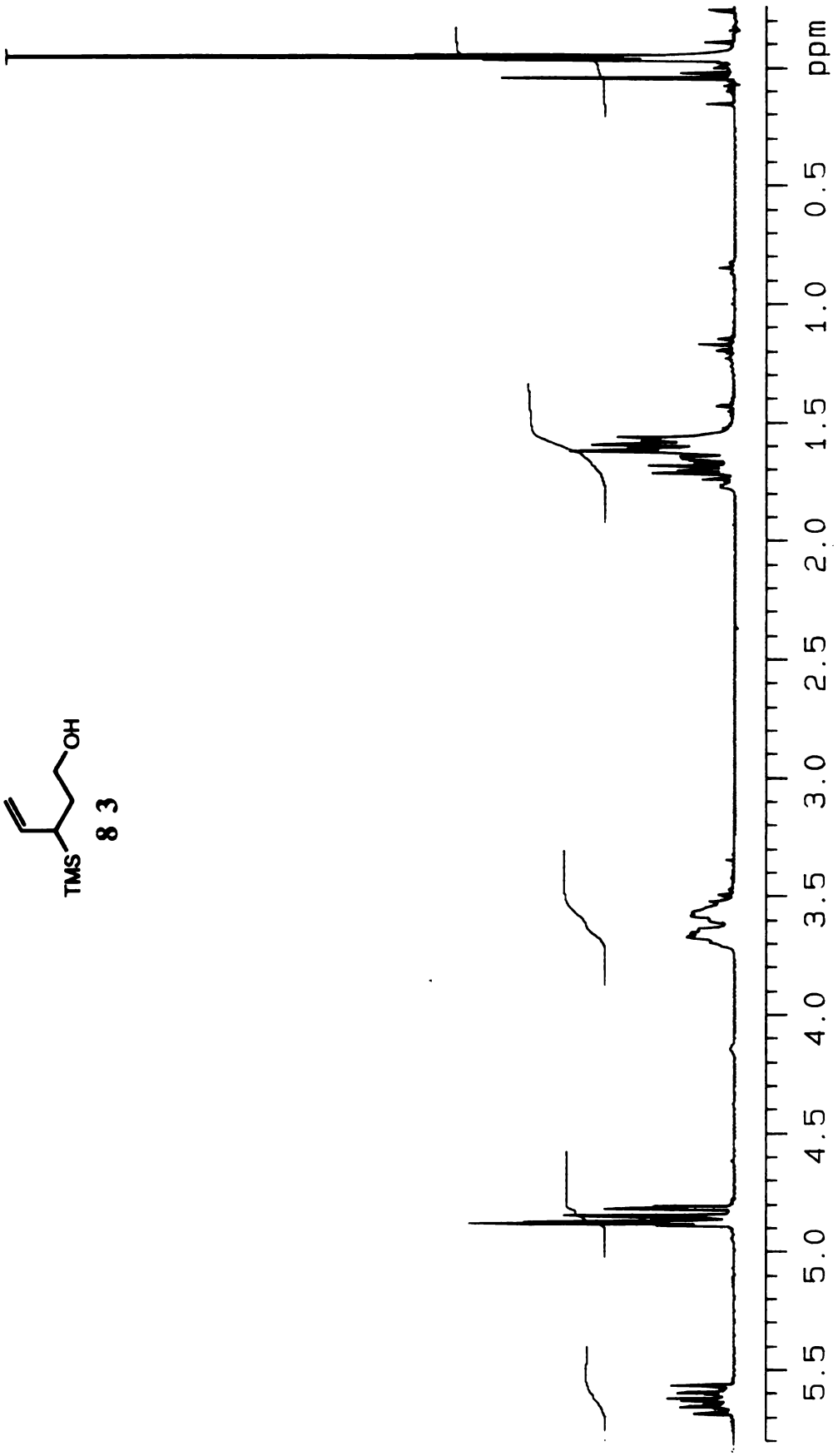
Scheme 46. ^{13}C NMR Spectrum of **79**.



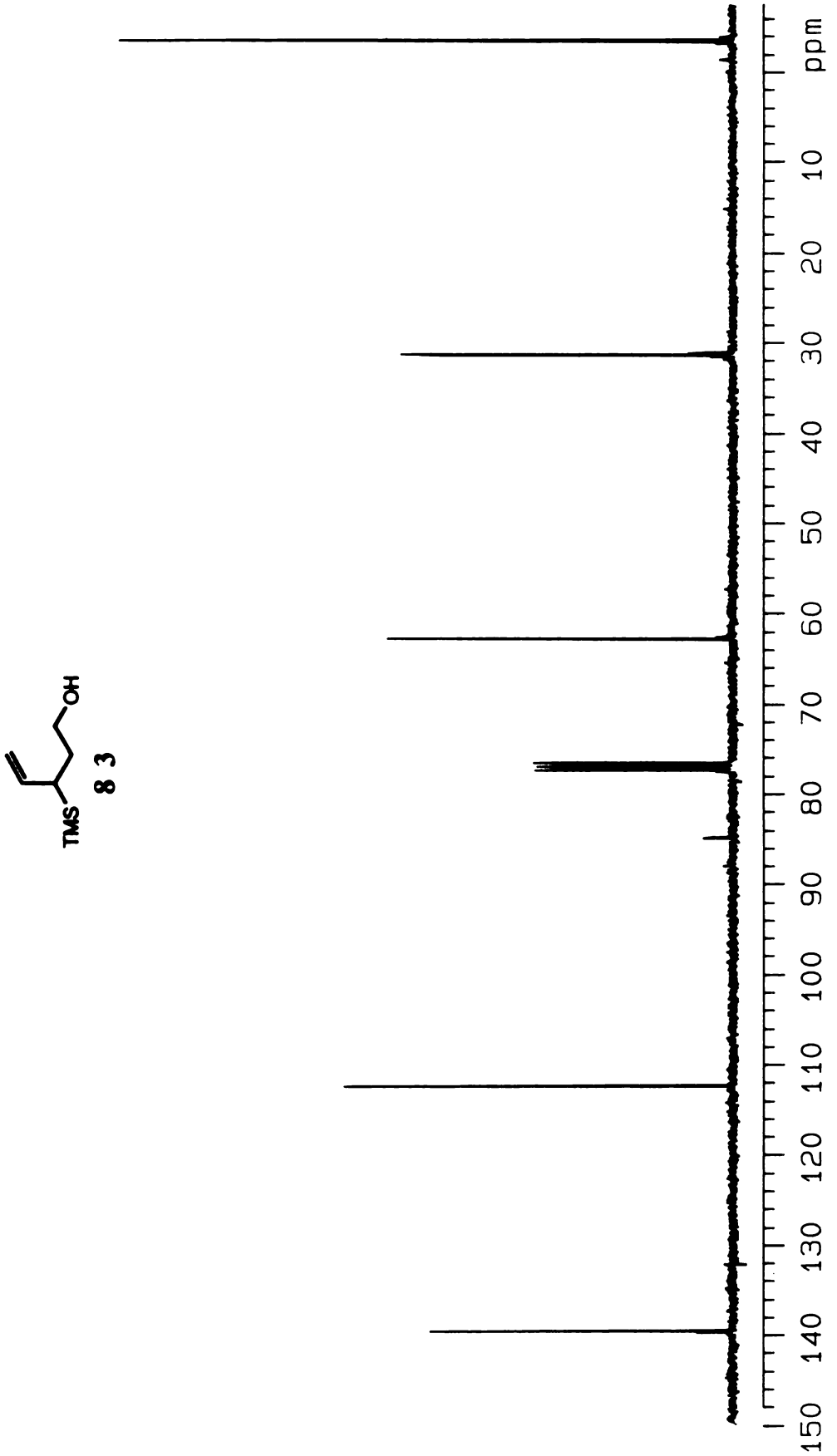
Scheme 47. ^{1}H NMR Spectrum of **82**.



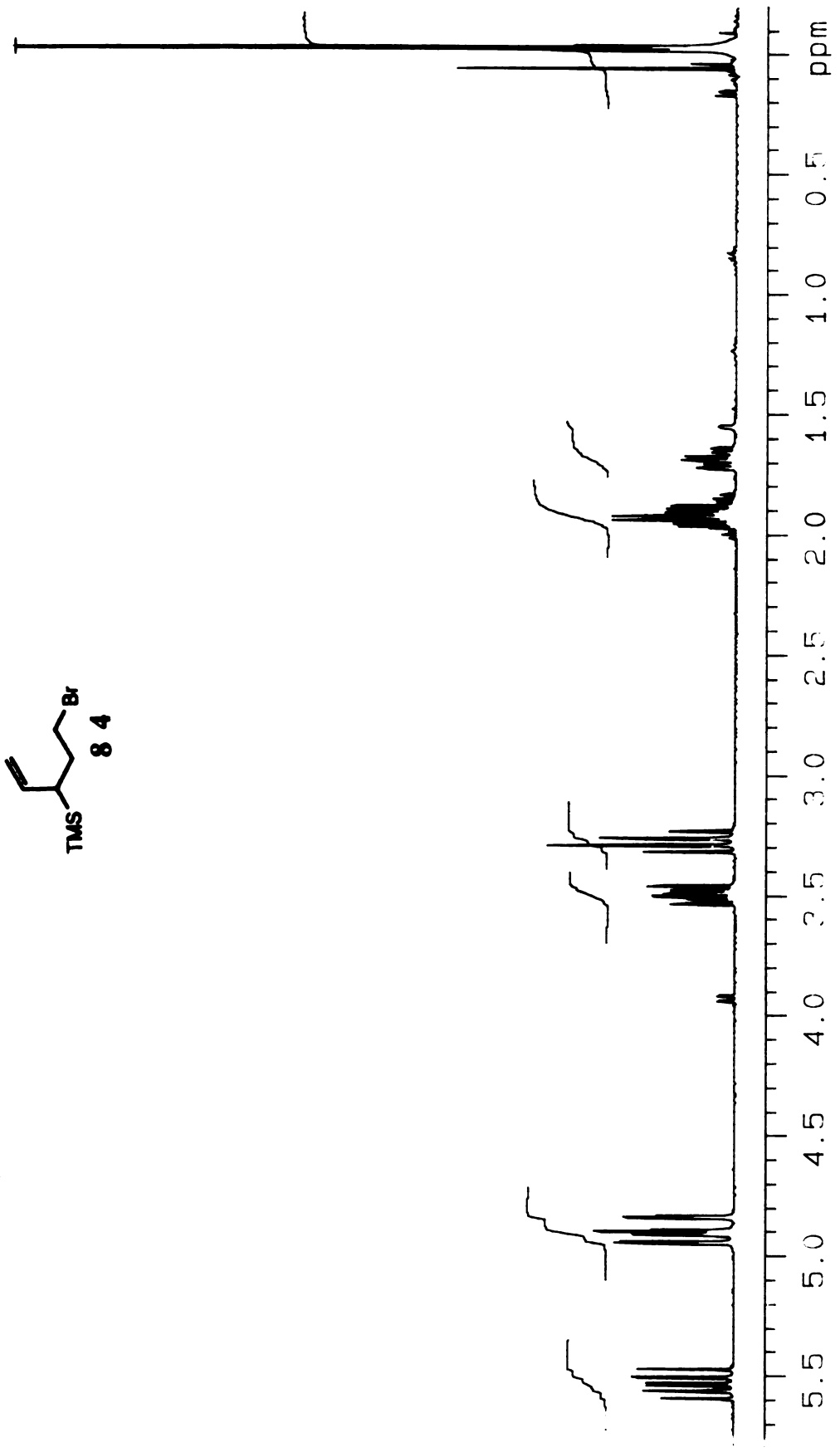
Scheme 48. ^{13}C NMR Spectrum of **82**.



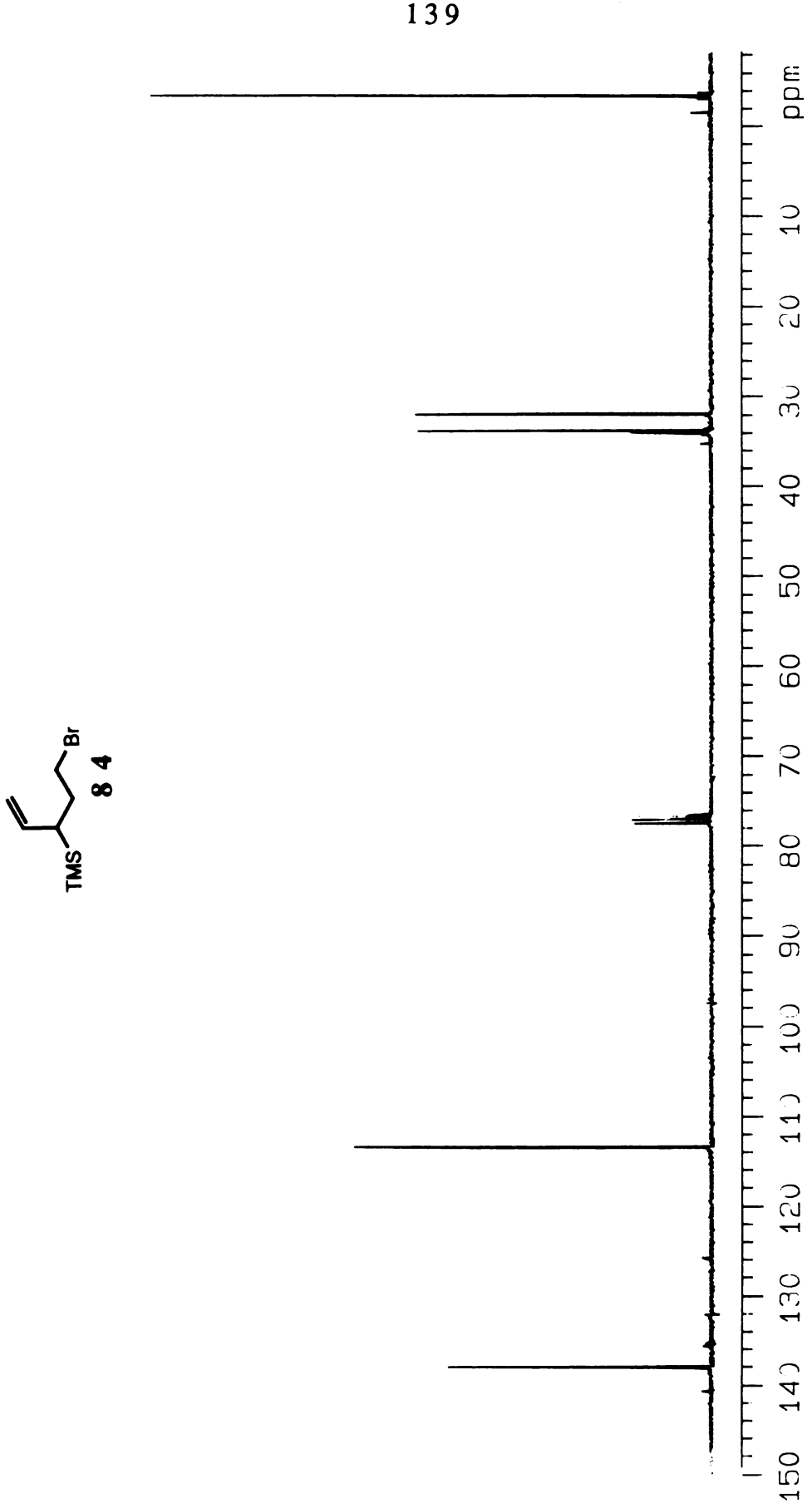
Scheme 49. ^{1}H NMR Spectrum of **83**.



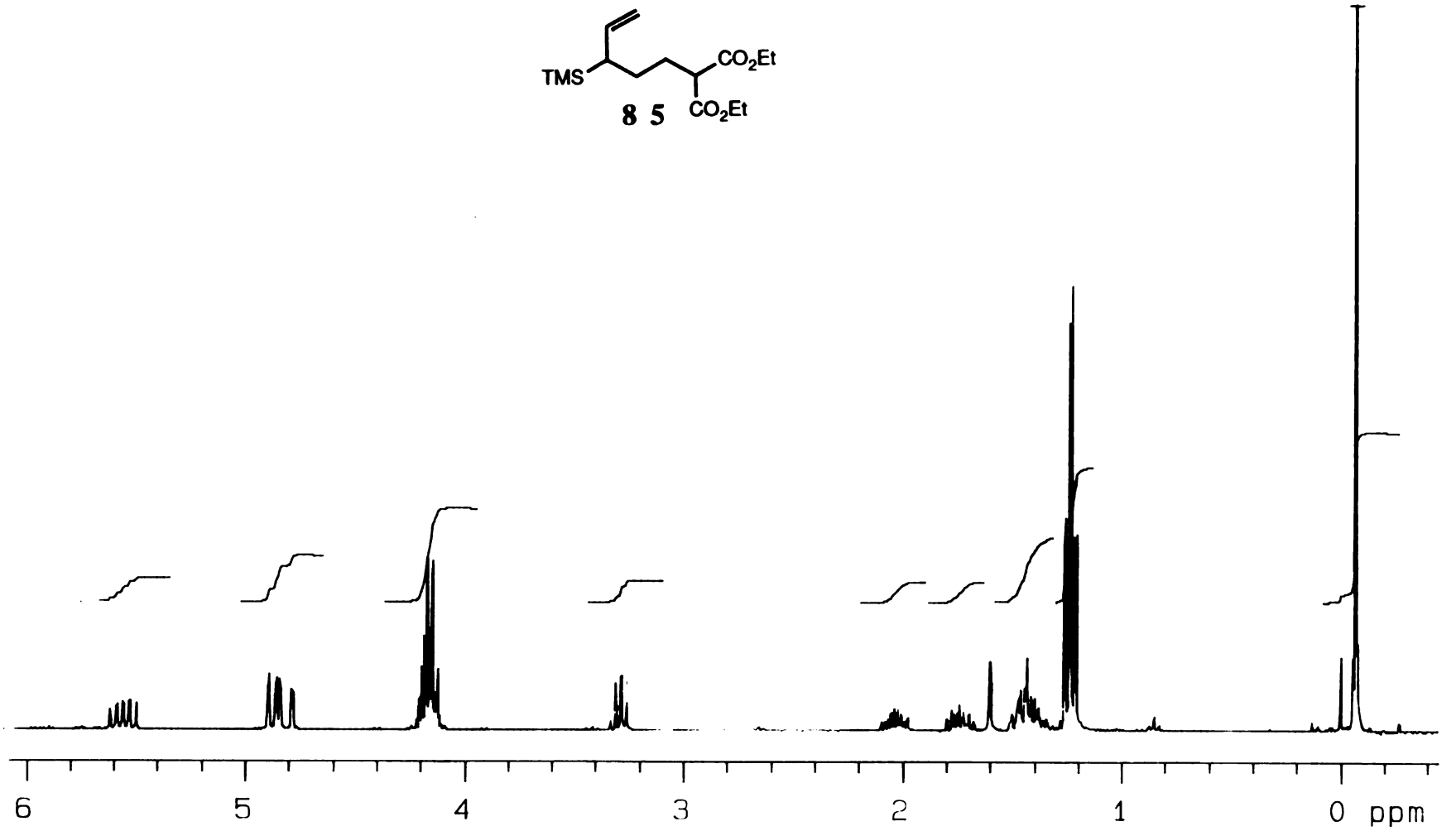
Scheme 50. ^{13}C NMR Spectrum of **83**.



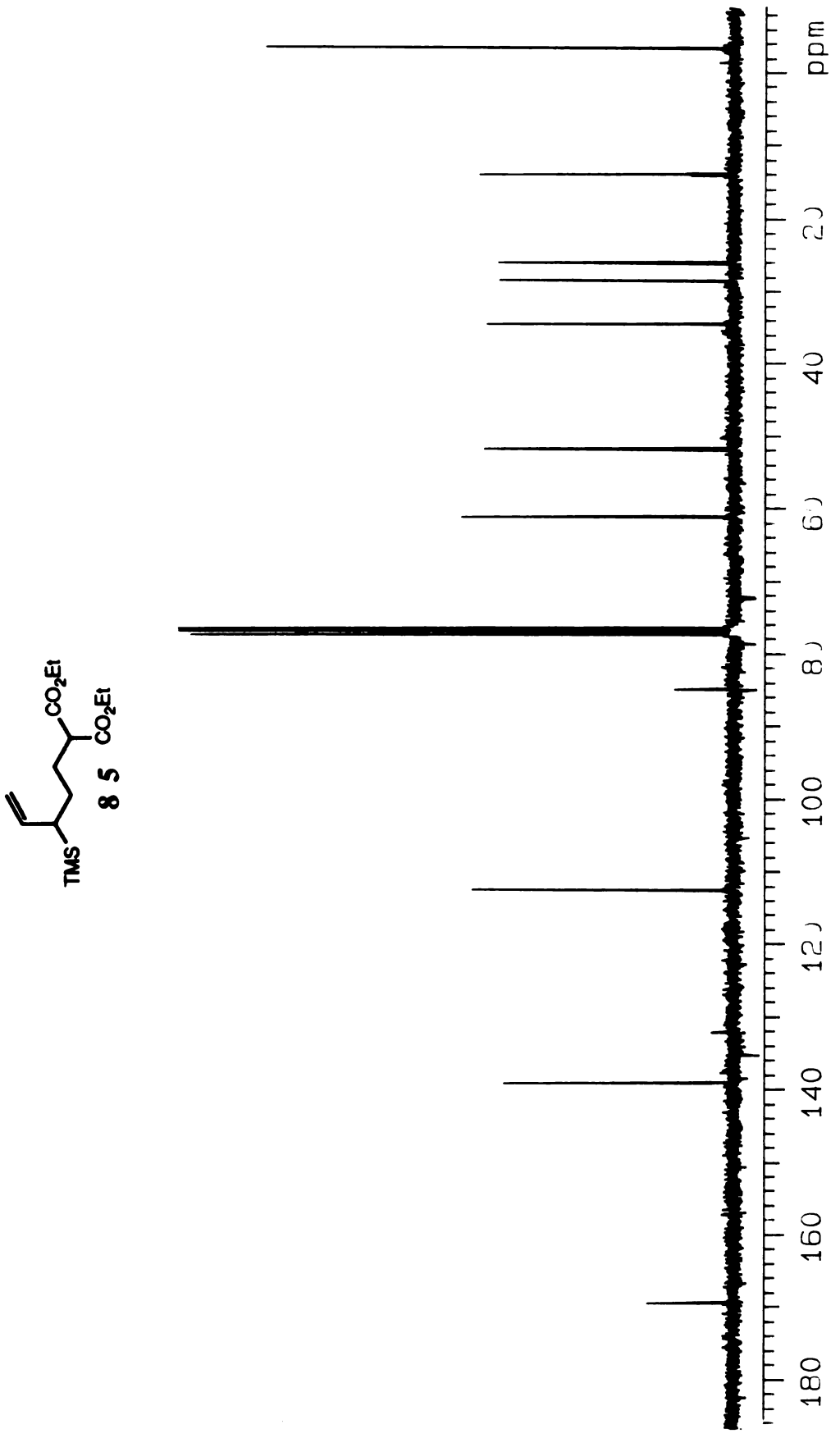
Scheme 51. ^{1}H NMR Spectrum of **84**.



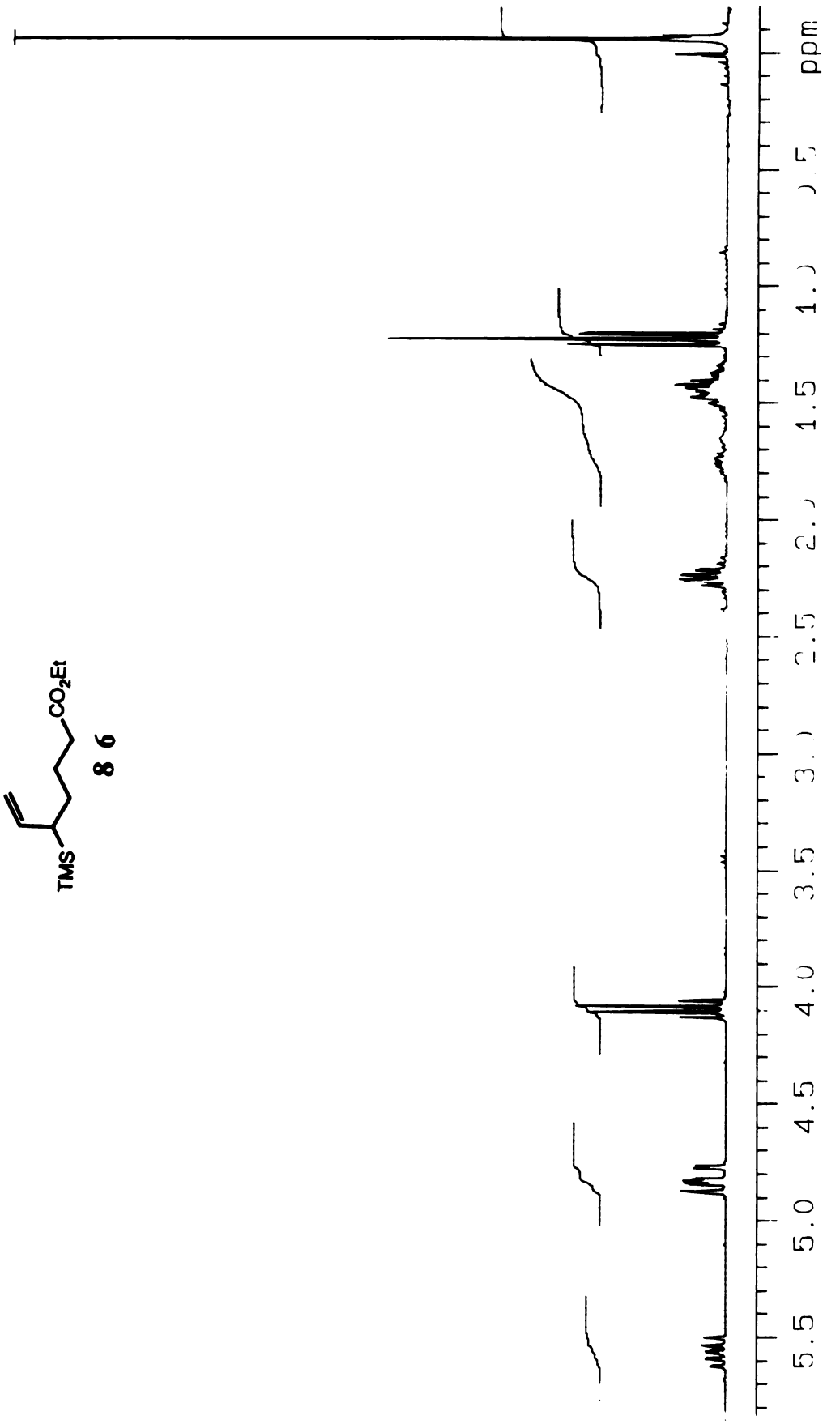
Scheme 52. ^{13}C NMR Spectrum of **84**.



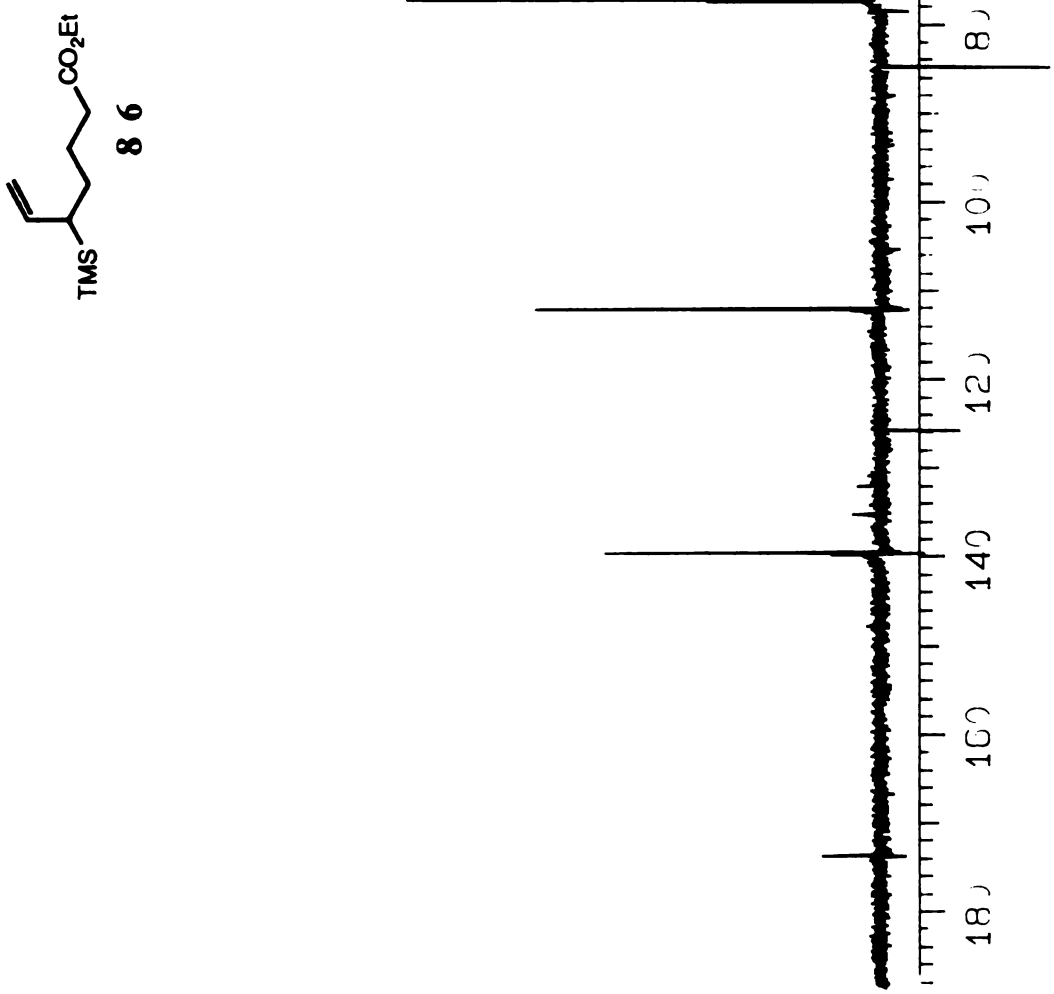
Scheme 53. ^{1}H NMR Spectrum of **85**.



Scheme 54. ^{13}C NMR Spectrum of **85**.



Scheme 55. ^{1}H NMR Spectrum of **86**.



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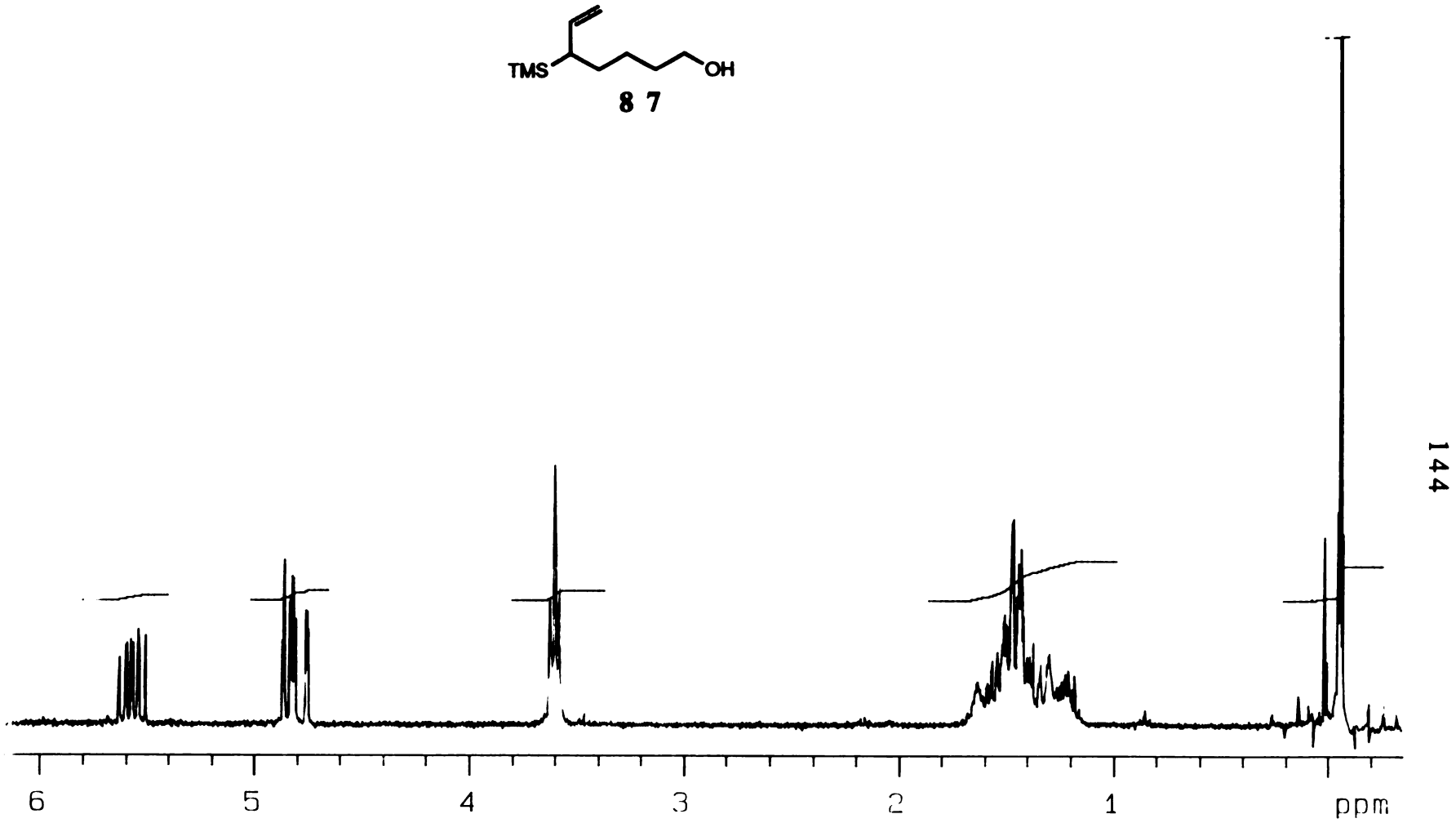
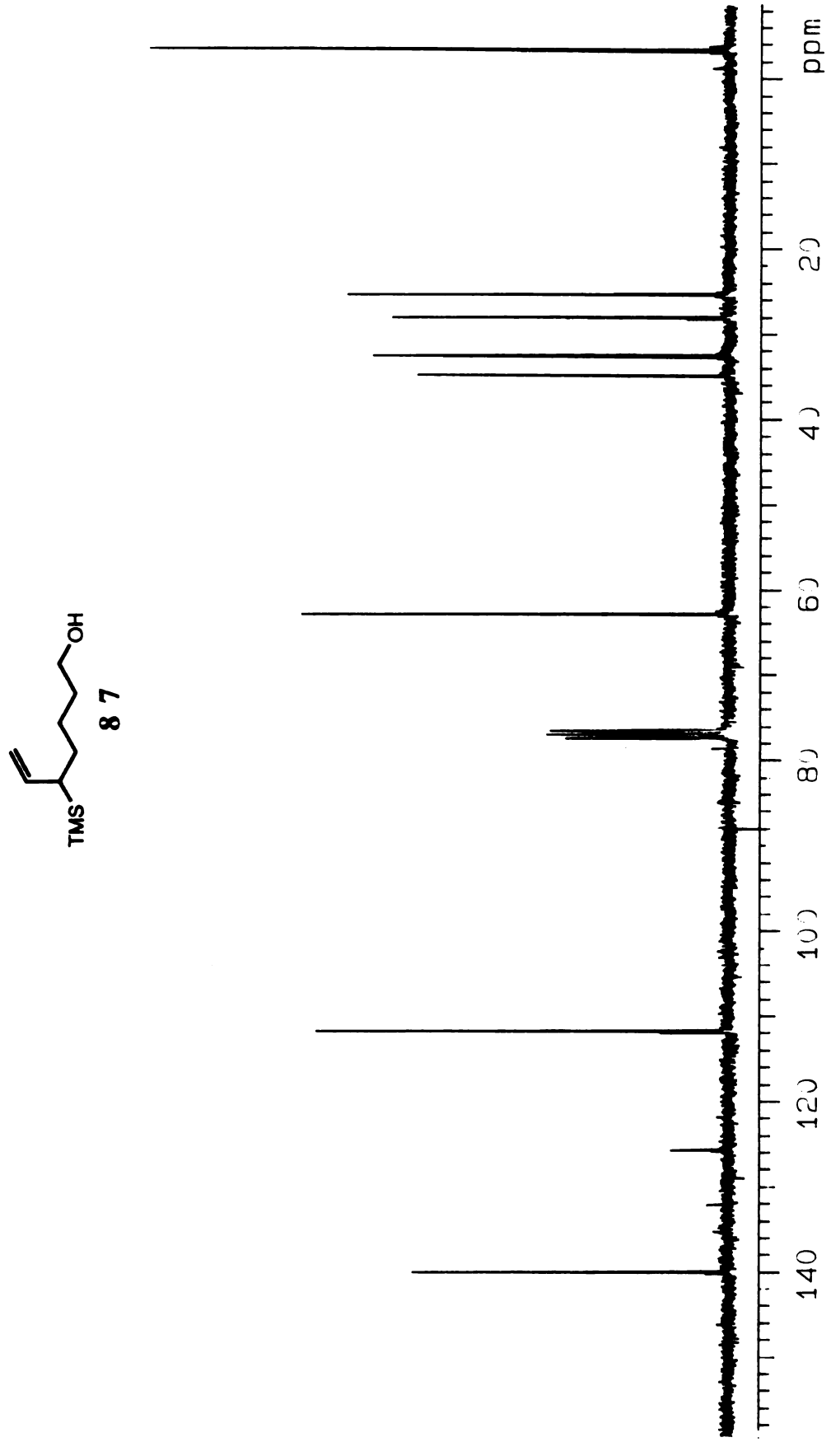
Scheme 56. ^{13}C NMR Spectrum of **86**.

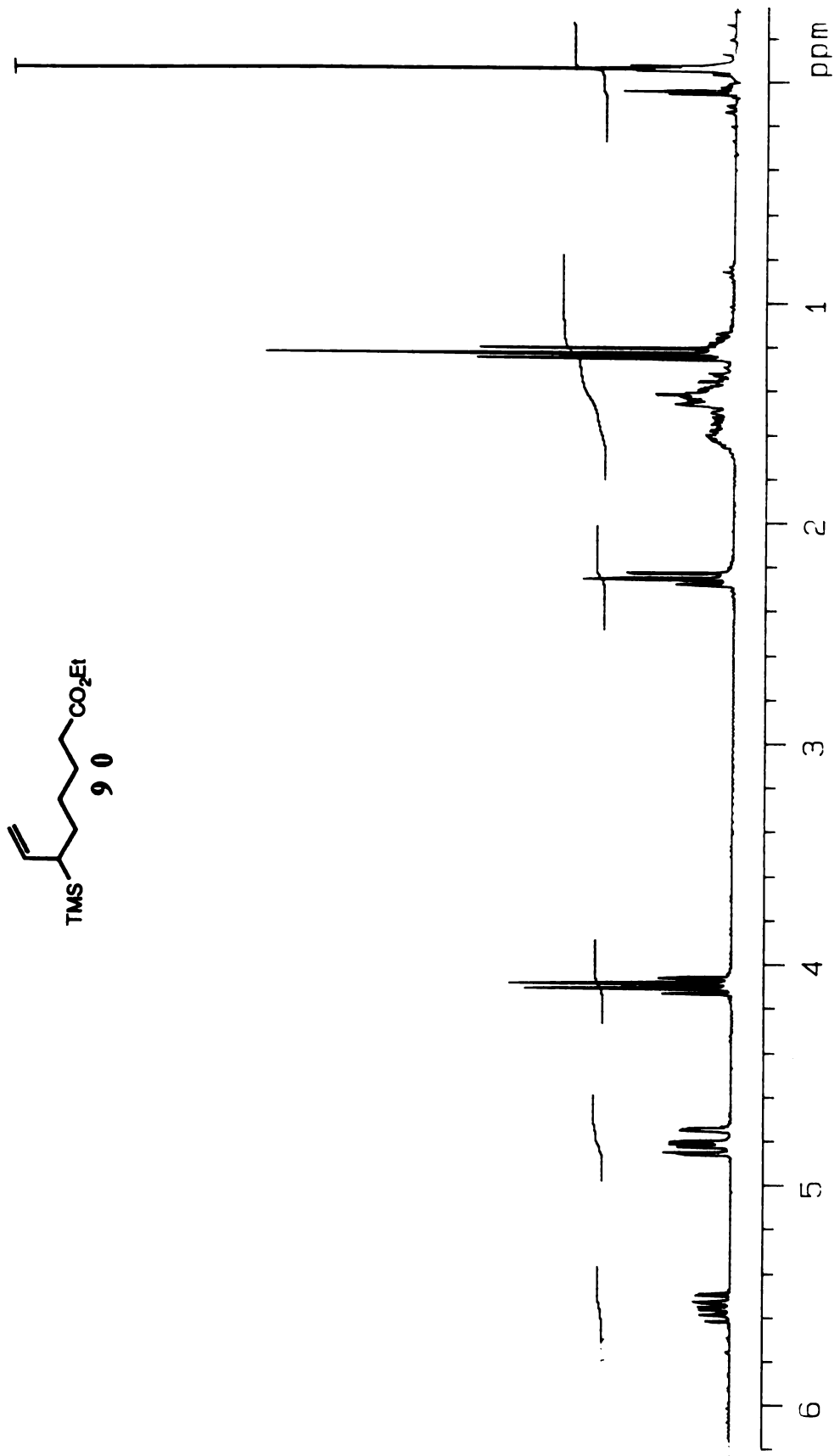


8 7

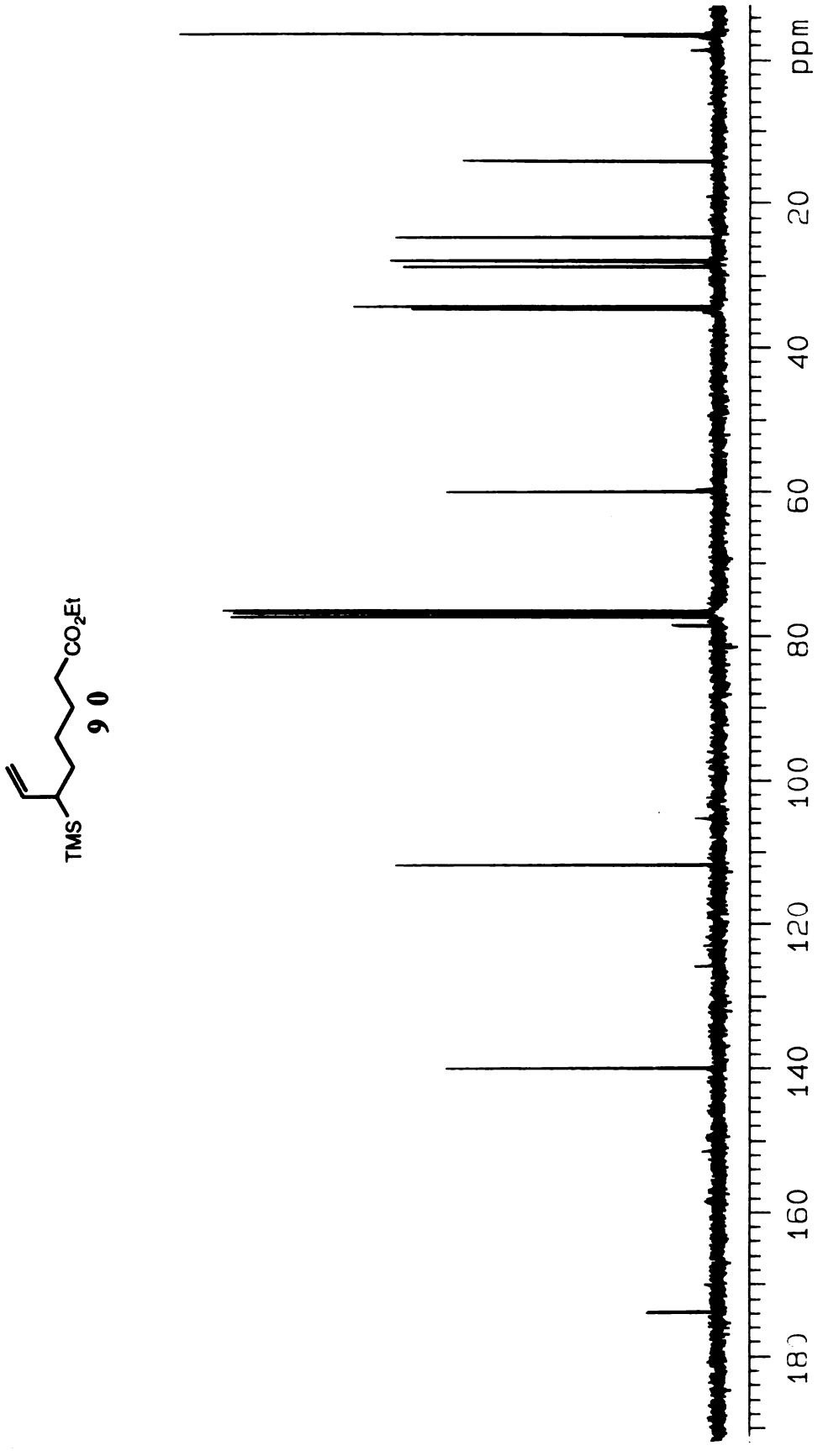
Scheme 57. ^{1}H NMR Spectrum of **87**.



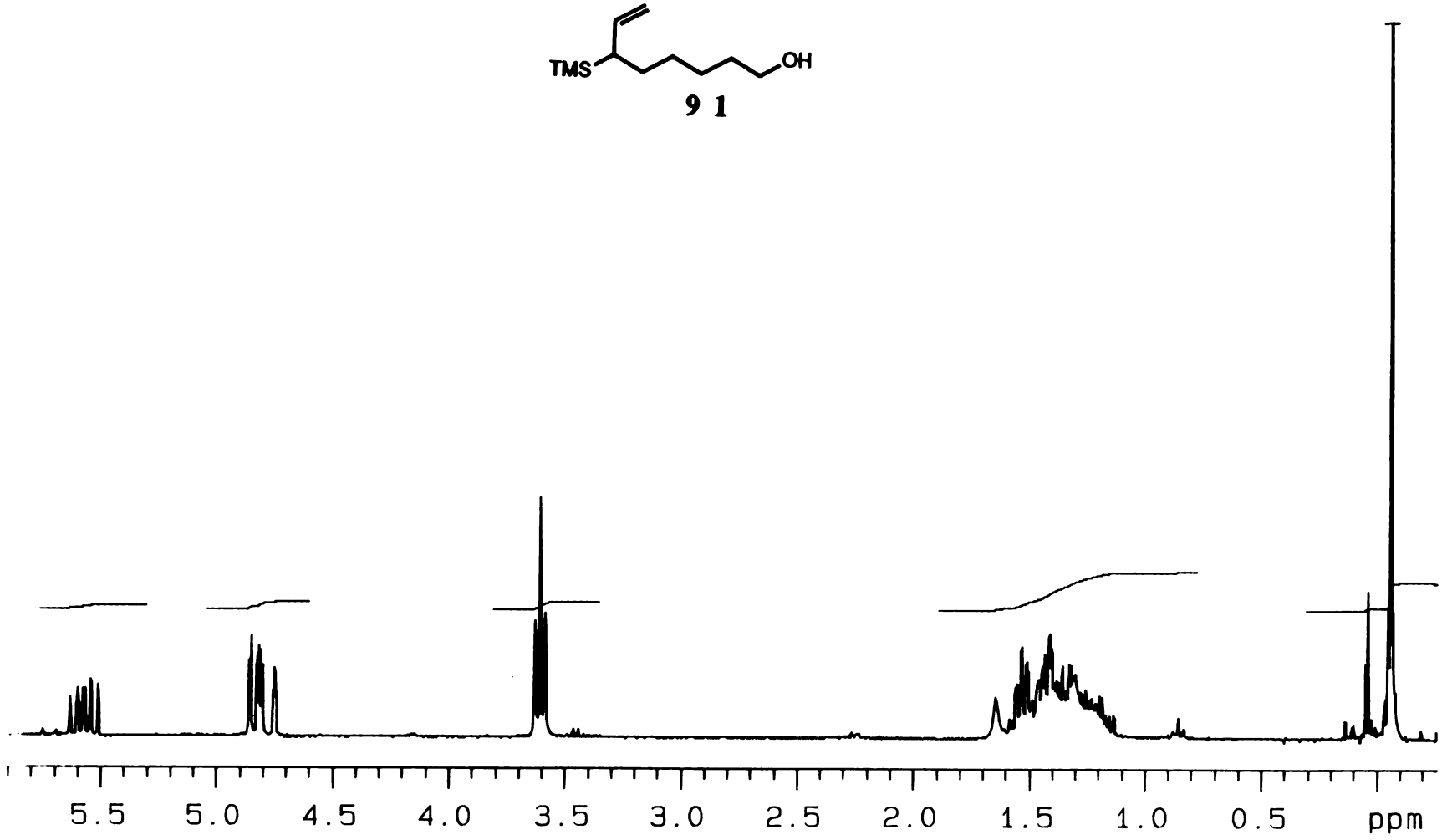
Scheme 58. ^{13}C NMR Spectrum of **87**.



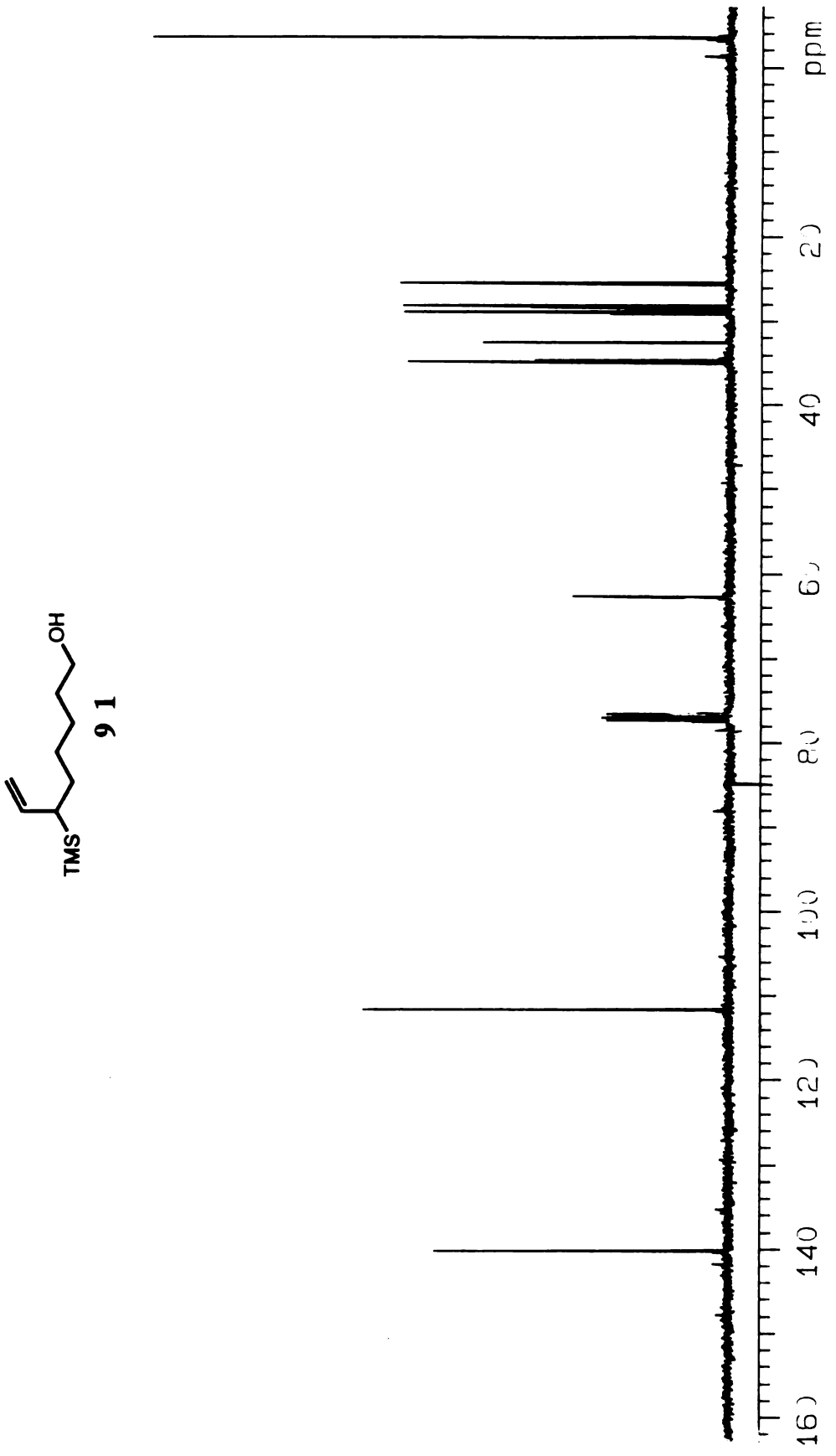
Scheme 59. ^{1}H NMR Spectrum of **90**.



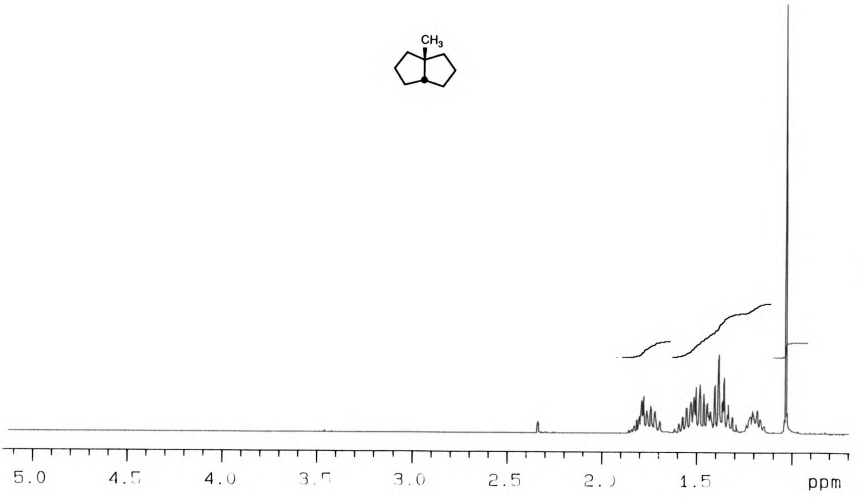
Scheme 60. ^{13}C NMR Spectrum of 90.



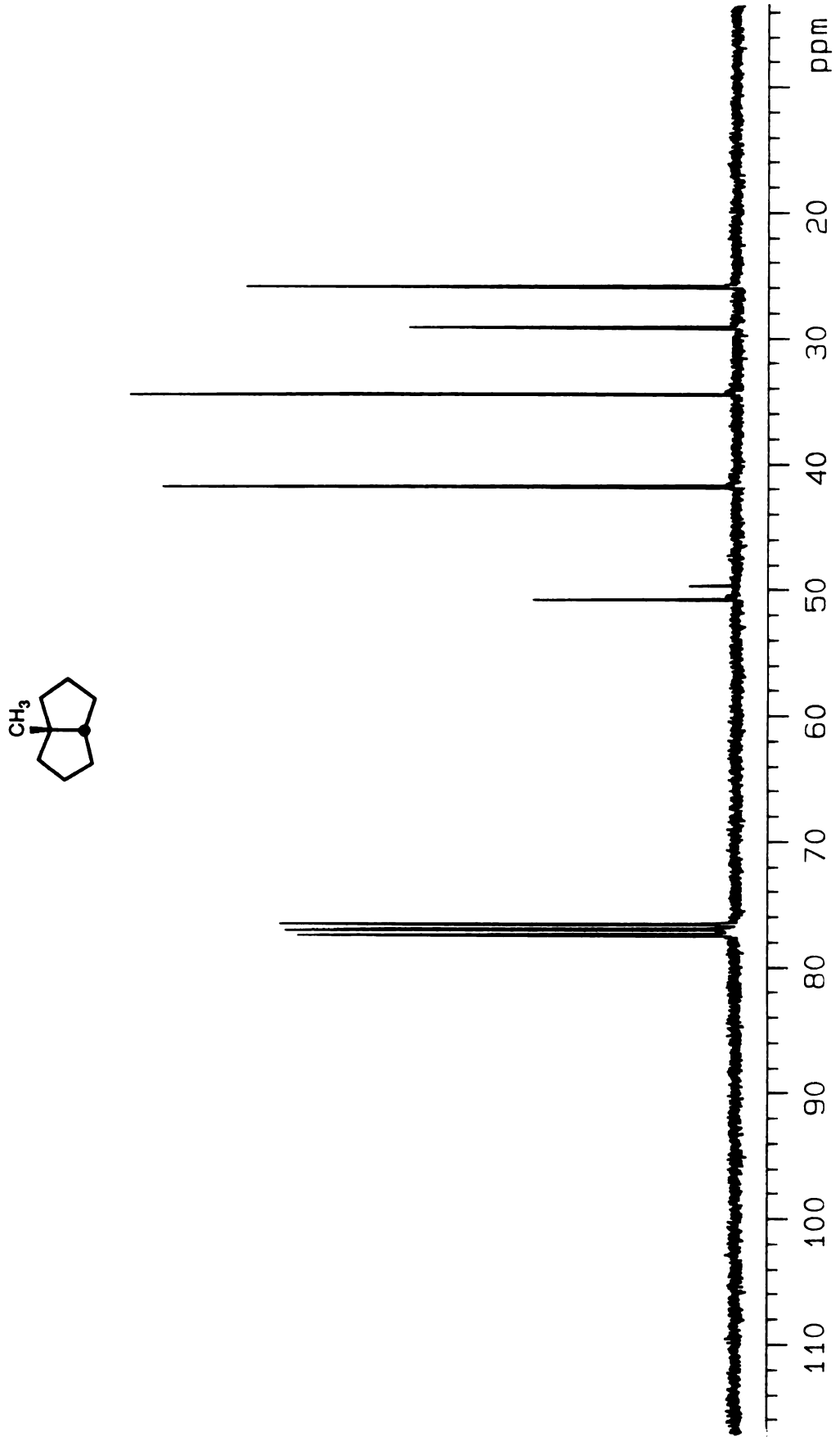
Scheme 61. ^{1}H NMR Spectrum of **91**.



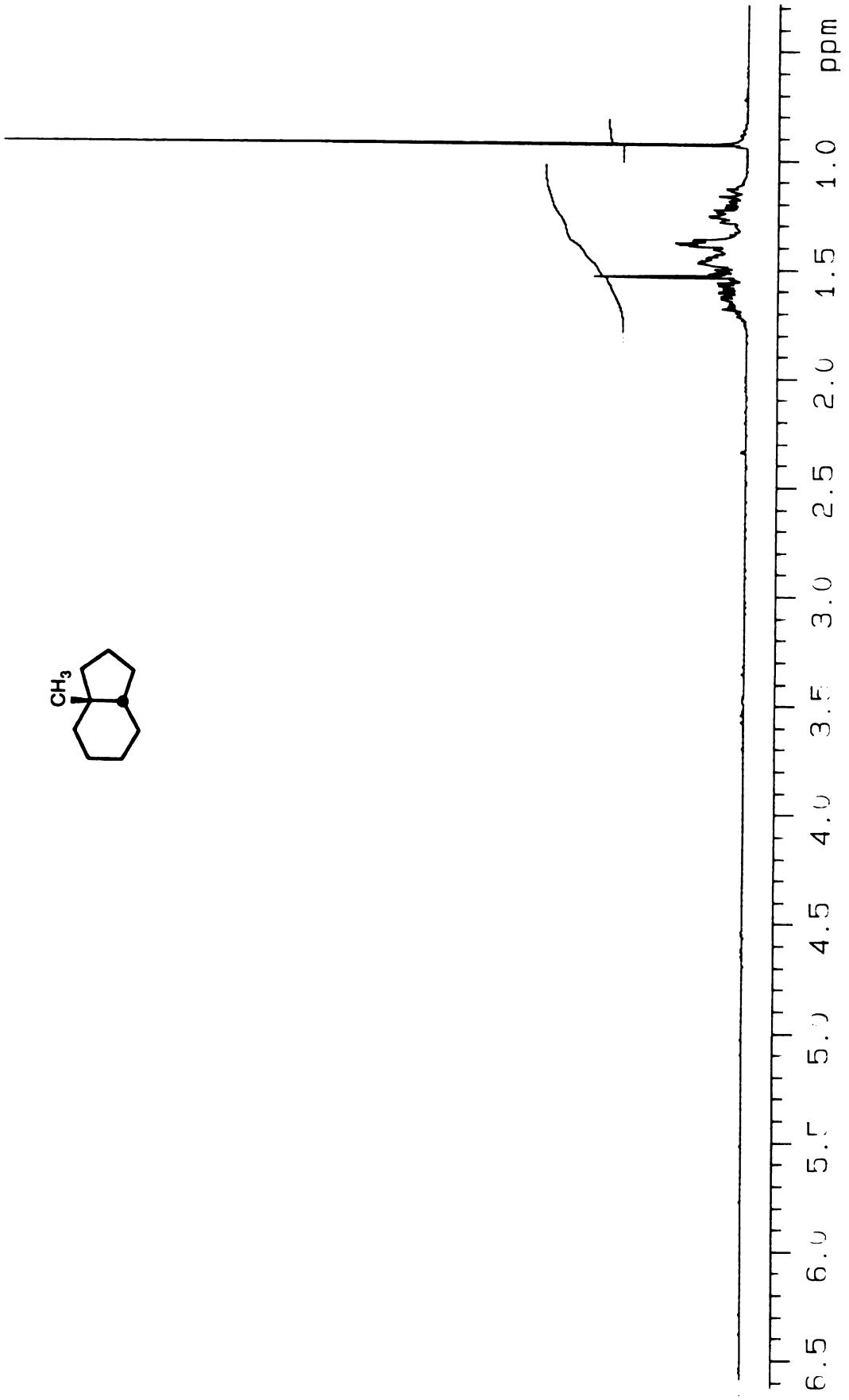
Scheme 62. ^{13}C NMR Spectrum of **91**.



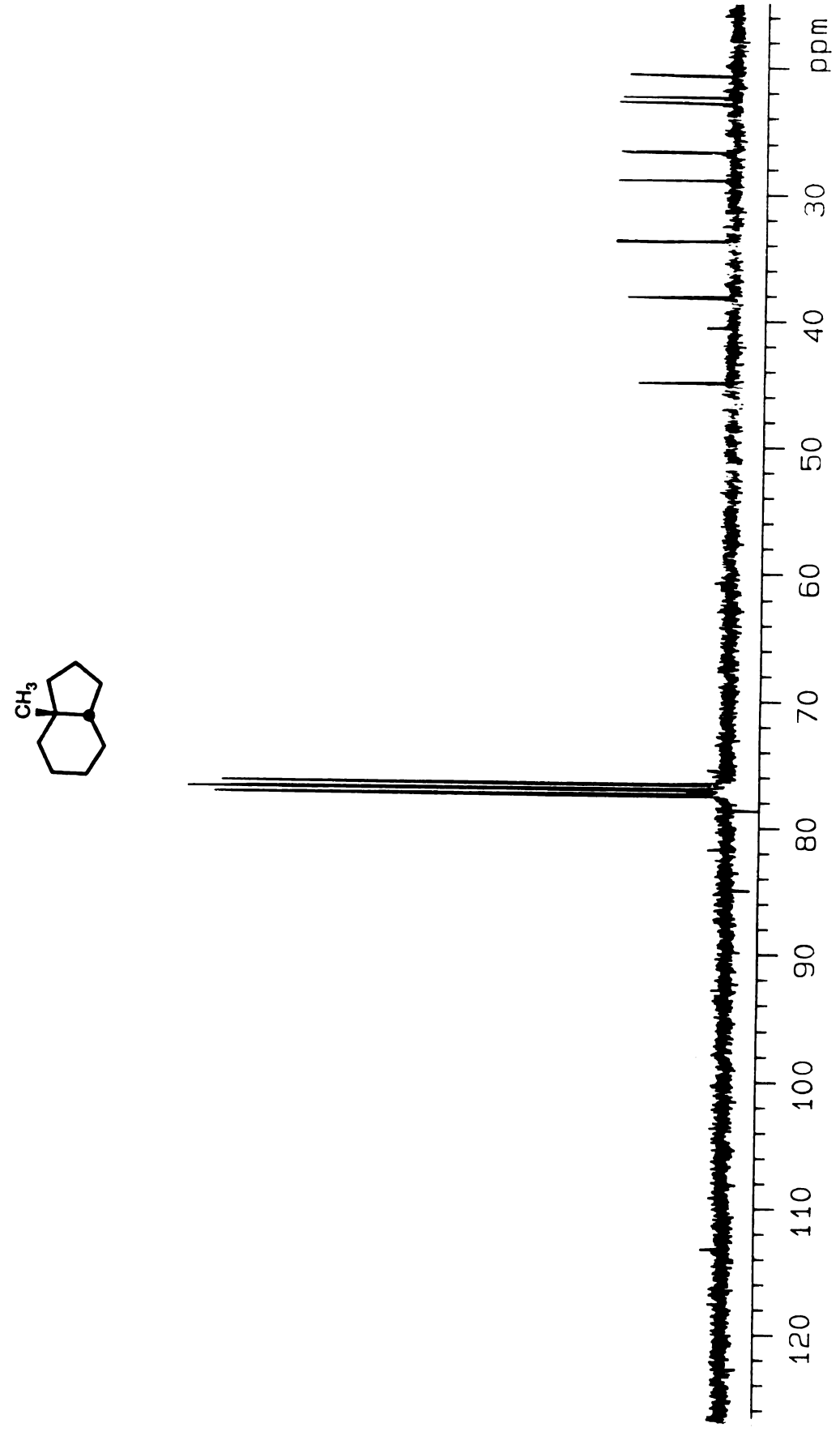
Scheme 63. ^{1}H NMR Spectrum of *cis*-1-methylbicyclo[3.30]octane.



Scheme 64. ^{13}C NMR Spectrum of *cis*-1-methylbicyclo[3.30]octane.



Scheme 65. ^{1}H NMR Spectrum of *cis*-1-methylbicyclo[4.30]nonane.



Scheme 66. ^{13}C NMR Spectrum of *cis*-1-methylbicyclo[4.30]nonane.