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dissertation entitled

Cyclobutanes in Organic Synthesis
Part I : Reglo and Stereoselective Rearrangements of Stereoisomeric 7-Oxirylbicyclo [4.2.0] Octan-7-ols
Part II: Solvolytic Studies of Ester Derivatives of Bicyclo [n.2.0] Alkanols (n = 3 or 4)

presented by

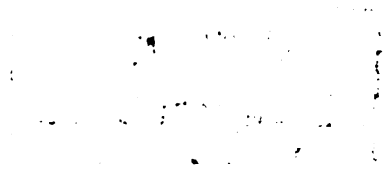
Chrong-Shiong Hwang

has been accepted towards fulfillment
of the requirements for

Ph.D. degree in Chemistry

William Reusch
Major professor

Date 8/26/88



CYCLOBUTANES IN ORGANIC SYNTHESIS
Part I : REGIO AND STEREOSELECTIVE REARRANGEMENTS OF STEREOISOMERIC 7-OXIRYLBICYCLO[4.2.0]OCTAN-7-0LS
Part II : SOLVOLYTIC STIDIES OF ESTER DERIVATIVE OF BICYCLO[n.2.0]ALKANOLS (n = 3 OR 4)

BY

Chrong-Shiong Hwang

A DISSERTATION

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1988

ABSTRACT

CYCLOBUTANES IN ORGANIC SYNTHESIS
Part I : REGIO AND STEREOSELECTIVE REARRANGEMENTS OF STEREOISOMERIC 7-OXIRYLBICYCLO[4.2.0]OCTAN-7-OLS
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Part I : The four racemic diastereomers of the title compound have been prepared by epoxidation of the related vinylcyclobutanols. Mild treatment of these isomers with boron trifluoride induced regio- and stereoselective rearrangement to ring-expanded hydroxymethyl bicyclo[4.2.0]nonanones. Curiously, one of the diastereomers did not react under these mild conditions. Other Lewis acids such as $Ti(i\text{-}PrO)_4$, $SnCl_4$ and $MgBr_2 \cdot Et_2O$ have also been examined. However, the results were not promising from a synthetic point of view. When the pair of diastereomers having an endo hydroxyl group (1 : 1 mixture) were treated with trifluoroacetic acid, rearrangement of the methine group occurred exclusively, followed by dehydration to cis-7-methylenebicyclo[4.3.0]nonan-8-one (**A**).The physical properties of this enone and its 8-methylene-7-

one regioisomer (**B**) were established by independent syntheses. Elimination of the hydroxymethyl products from the initial rearrangement gave **A** or **B**, thus identifying the regioselectivity of each rearrangement.

Several sequential reactions were then carried out to characterize the hydroxymethyl configurations. First, sodium borohydride reduction, followed by acetylation and hydroboration of **A** and **B** gave a pair of cis 1,3-diols, assuming normal convex facial-selectivity. Second, reduction of appropriate hydroxymethyl products with sodium triacetoxyborohydride gave a pair of trans 1,3-diols. Finally, the cis or trans configurations of these diols were confirmed by the relative rates of acetonide formation.

Part II : A two-carbon ring expansion involving solvolyses of 6-bicyclo[3.2.0]heptyl esters and 7-vinyl-7-bicyclo[4.2.0]octyl esters has been explored. Acetolysis of benzoates or 1,3-dinitrobenzoates in glacial acetic acid or aqueous acetic acid with an acetate buffer afforded 3-cycloheptenyl or 3-cyclooctenyl derivatives in good to excellent yields. The latter solvolysis required the addition of $LiClO_4$ for best results.

To My Grandmother And Parents

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PART I

REGIO AND STEREOSELECTIVE REARRANGEMENTS OF 7-OXIRYLBICYCO[4.2.0]OCTAN-7-OLS

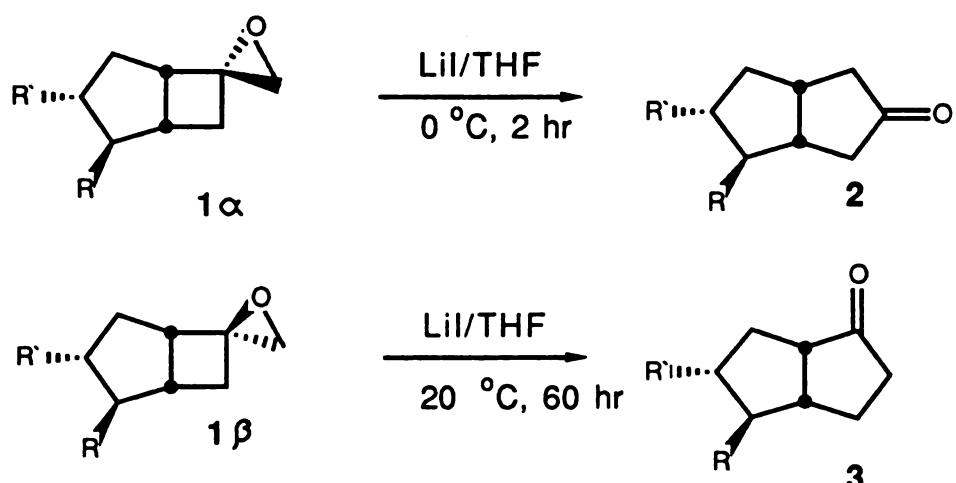
Introduction

The importance of carbocations as reactive intermediates in organic chemistry is well documented in both synthetic and mechanistic studies.[1] Prominent examples of reactions involving carbocation intermediates include biogenetic-like polyene cyclizations[2] and molecular rearrangements such as those involving steroid[3] or terpene[4] substrates.

The ring expansion of cyclobutane derivatives to cyclopentanes is an important transformation that normally proceeds via carbocation intermediates.[5] This has emerged as a powerful synthetic method which in some cases may proceed with good regio- and stereoselective control. The popularity of cyclobutane derivatives in syntheses may be attributed to several factors. First, cyclobutane derivatives are readily prepared by [$2\pi + 2\pi$] cycloaddition of olefins with ketenes,[6] [$2\pi + 2\pi$] photocyclization of olefins[7] together with several other facile methods[8] such as ring expansion of cyclopropane derivatives and ring closure by double alkylation of 1,3-dithiane with bromochloropropane. Second, the

high strain energy in cyclobutane rings (26.9 kcal/mole)[9] provides a thermodynamic driving force for ring cleavage or expansion. Finally, cyclopentane derivatives occur in a variety of natural products, including jasmones, pyrethrins,[10] prostaglandins[11] and triquinane sesquiterpenes.[12]

An instructive example of such ring expansion was reported by Hart and Comte.[13] Bicyclic ketones (**2** and **3**), which have been extensively used in the synthesis of prostacyclin analogues, were prepared by regiocontrolled ring expansions from epimeric epoxides **1α** and **1β** respectively. Rearrangement of epoxide **1α** proceeded rapidly in a regioselective manner (lithium iodide, THF, 20 °C, 4 hr) to yield ketone **2** (68%) and its isomer **3** (10%). In contrast to the cleavage of **1α**, epoxide **1β** underwent a slow, regioselective rearrangement to afford ketone **3** in 71% yield and less than 10% of ketone **2**.

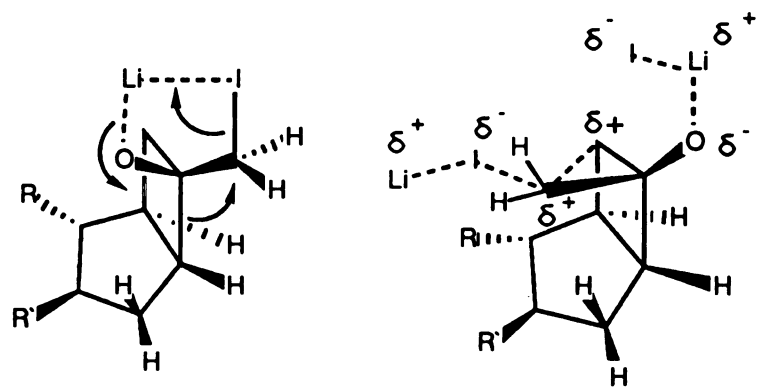


1α **2** **1β** **3**

R` = -OSiMe$_2$ ^{t}Bu

R = -CH=CHCHC$_5$H$_{11}$
OSiMe$_2$ ^{t}Bu

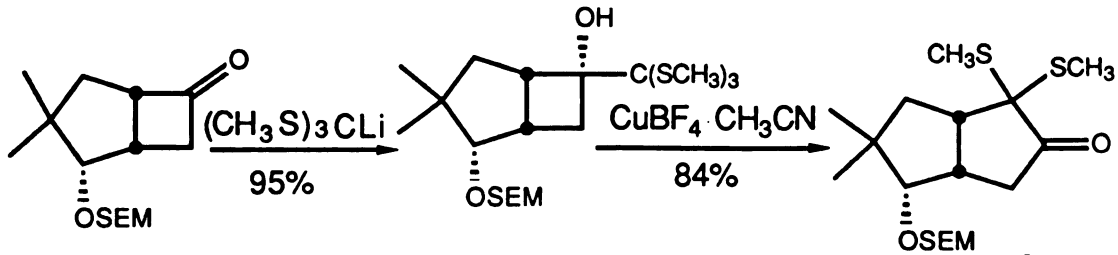
The regioselectivity of these epoxide-carbonyl rearrangements has been attributed to steric interactions and torsional strain inherent in the bicyclo[3.2.0]heptane system. For example, epoxide **1α**, being readily susceptible to nucleophilic attack, may form a five-membered anti-periplanar transition state **4**, which then undergoes a synchronous rearrangement to give ketone **2**. However, owing to steric congestion at the concave α-face, this path is not available to **1β**, which has been thought to give ketone **3** via transition state **5**.



4 **5**

Figure 1

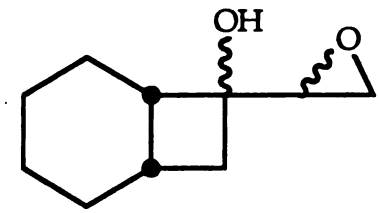
Another application of ring expansions of cyclobutane derivatives has been used recently to prepare a key bicyclic intermediate (**8**) for a total synthesis of the sesquiterpene (±)-coriolin by Knapp et al.[14] Treatment of ketone **6** with $(CH_3S)_3CLi$ led to a single product **7**, which was smoothly expanded to the keto thioketal **8** without formation of its regioisomer (80% overall) by treatment with $CuBF_4 \cdot CH_3CN$ in toluene solution.



6 7 8

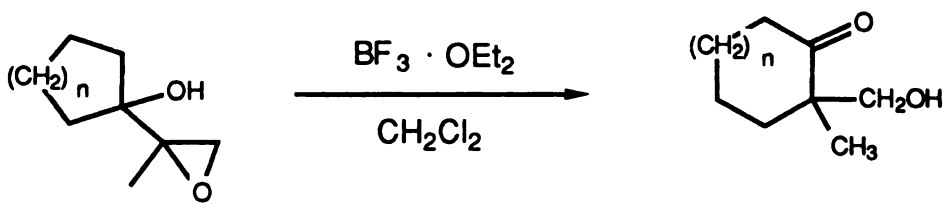
The high regioselectivity in this case (where either a methylene or methine carbon may migrate) has been attributed to the formation of a highly stabilized cationic intermediate, followed by a transition state in which there is substantial charge delocalization on the migrating carbon. On the other hand, examples of ring expansions with less[15] or even reversed[16] regioselectivity have been also reported. Since these reactions involve less stabilized cationic intermediates, the difference in electron-donating ability of the migrating atoms is not significant.

Recognizing that epoxides are excellent initiating groups for reactions proceeding via carbocation intermediates, such as polyene cyclizations[2] and molecular rearrangements,[3] we decided to examine the behavior of a group of stereoisomeric epoxycyclobutanols having the general structure **9**.



9

Surprisingly, a survey of the literature revealed only few examples of acid-catalyzed rearrangement of epoxy alcohols. Cheer and Johnson[17] found that monocyclic epoxyl alcohols **10** underwent acid-catalyzed rearrangements induced by $BF_3 \cdot OEt_2$ or acidic alumina to give hydroxymethyl ketone **11** in moderate yields (Scheme II).



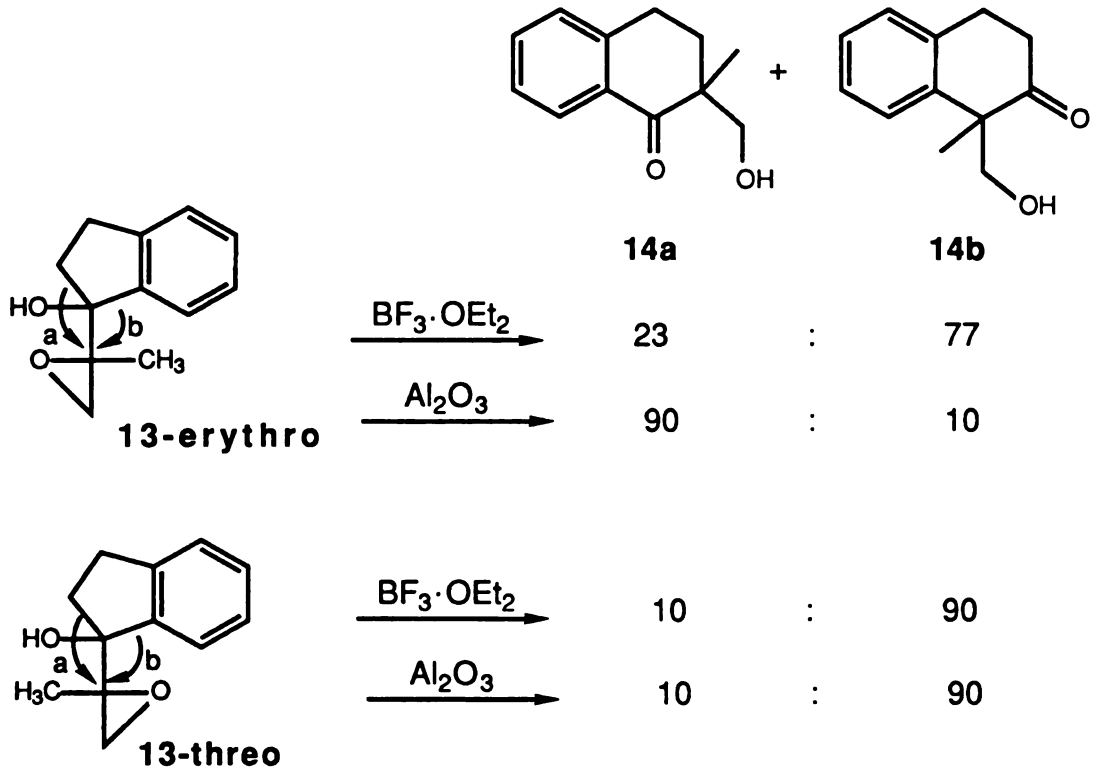
10 **11**

a : n = 0	63%
b : n = 1	49%
c : n = 2	15%

Scheme II

This study demonstrated that , as in the case of Tiffeneau-Demjanov rearrangement,[18] such rearrangements are a function of ring size, giving decreasing yield with increasing ring size. More significantly, the best yield was observed for the acid-catalyzed rearrangement of epoxycyclobutanol **10a**, affording hydroxymethyl cyclopentanone **11a** in 63% yield.

To investigate the stereochemical character of this rearrangement, Cheer and Johnson further examined the acid-catalyzed rearrangement of the diastereomeric epoxyl alcohols **13-erythro** and **13-threo**, derived from the epoxidation of 1-isopropenyl-1-indanol.[19]



Scheme III

The erythro- and threo- epoxy alcohols on treatment with $BF_3 \cdot OEt_2$ afforded hydroxymethyl ketones **14b** and **14a** in a ratio of 77 : 23 and 90 : 10 respectively (Scheme III). The ratio of **14a** to **14b** obtained in this study is probably best explained in terms of migratory aptitudes, in this case phenyl (path b) shifts preferentially over the primary alkyl group. On the other hand, the corresponding alumina-catalyzed rearrangement of **13-erythro** and **13-threo** gave **14a** and **14b** in a ratio of 90 : 10 (67%) and 10 : 90 (66%) respectively. Because of this high regioselectivity, the authors suggested that the alumina-catalyzed rearrangement

proceeded through a " surface-adsorbed " transition state, as shown in Figure 2.

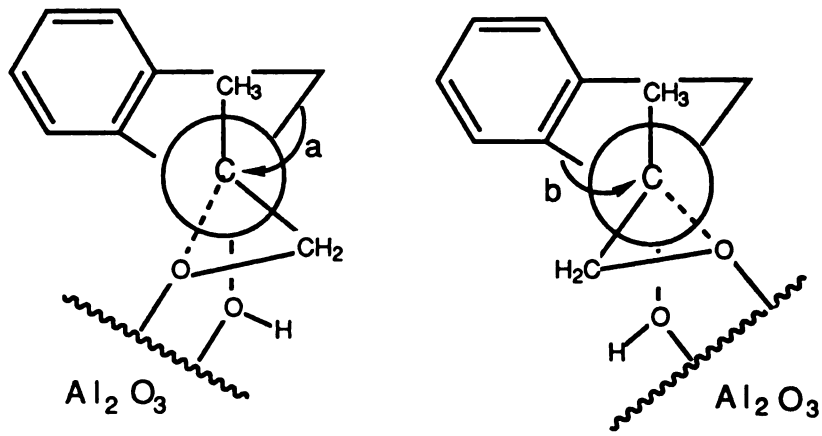
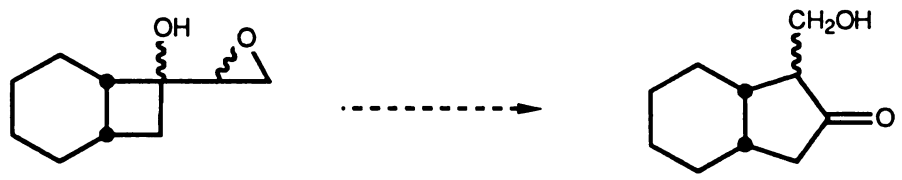


Figure 2

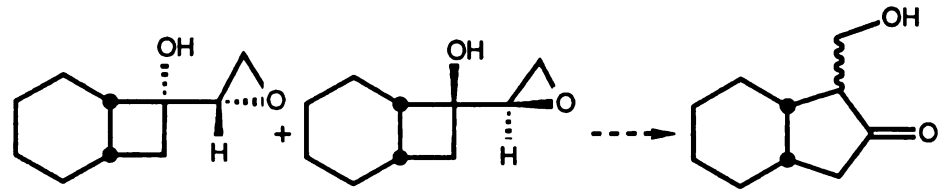
In this dissertation we present the results of our study of Lewis and Bronsted acid-catalyzed rearrangements of the four diastereomeric epoxycyclobutanols (**9a**, **9b**, **9c**, and **9d**). Our interest in this subject is related to Johnson and Cheer`s study. If previously determined migratory aptitudes are dominant, the methine residue should migrate preferentially and we would expect to obtain hydroxymethyl cyclopentanones **29a** or **29c** as major products. In contrast, a coordination-controlled pathway should favor regioselective and stereoselective rearrangements. Four possible regio- and stereoisomers, **29a**, **29b**, **29c** and **29d**, are formally possible from rearrangements of the isomers of **9** (Scheme IV).

A. Migratory Aptitude-Controlled Pathway

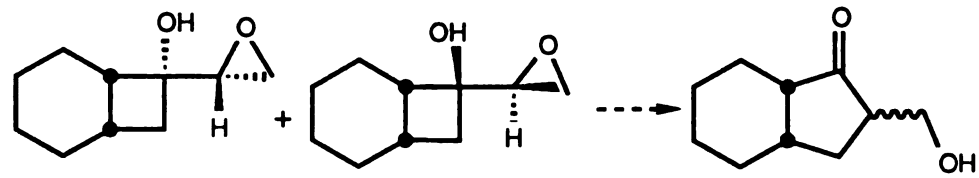


9a,b,c,d **29a,c**

B. Coordination-Controlled Pathway



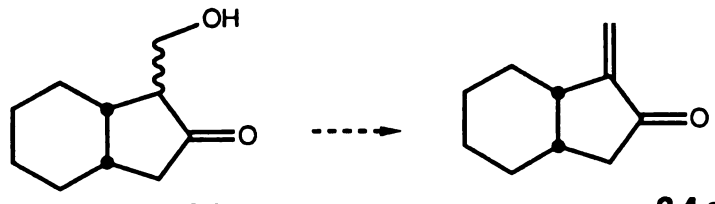
9a **9c** **29a,c**



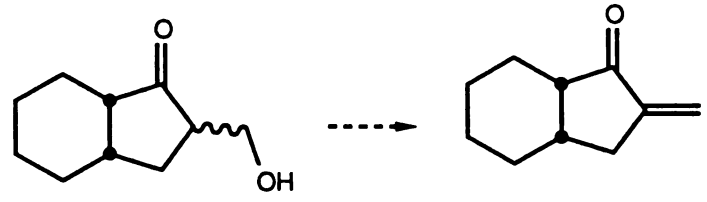
9b **9d** **29b,d**

Scheme IV

Hydroxymethyl ketones **29a** and **29c** can be distinguished from **29b** and **29d** by dehydration to methylene cyclopentanones **34a** or **34b** under suitable conditions.

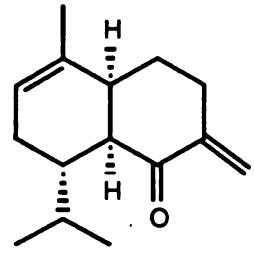


29a,c **34a**

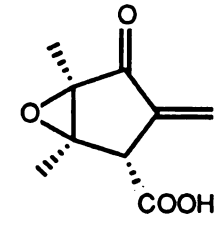


29b,d **34b**

α-Methylene ketones, such as **34a** and **34b**, are particularly attractive intermediates in synthetic organic chemistry. Quite a few natural products, such as the sesquiterpene chiloscyphone[20] and the antibiotic methylenomycin A,[21] possess this feature. Moreover, the potential synthetic utility of the highly reactive unsaturated carbonyl system (-C=C-C=O) has been demonstrated repeatedly in organic syntheses, including extended enolate alkylations,[22] reductive alkylations[23] and especially Michael addition reactions.[24]



Chiloscyphone



Methylenomycin A

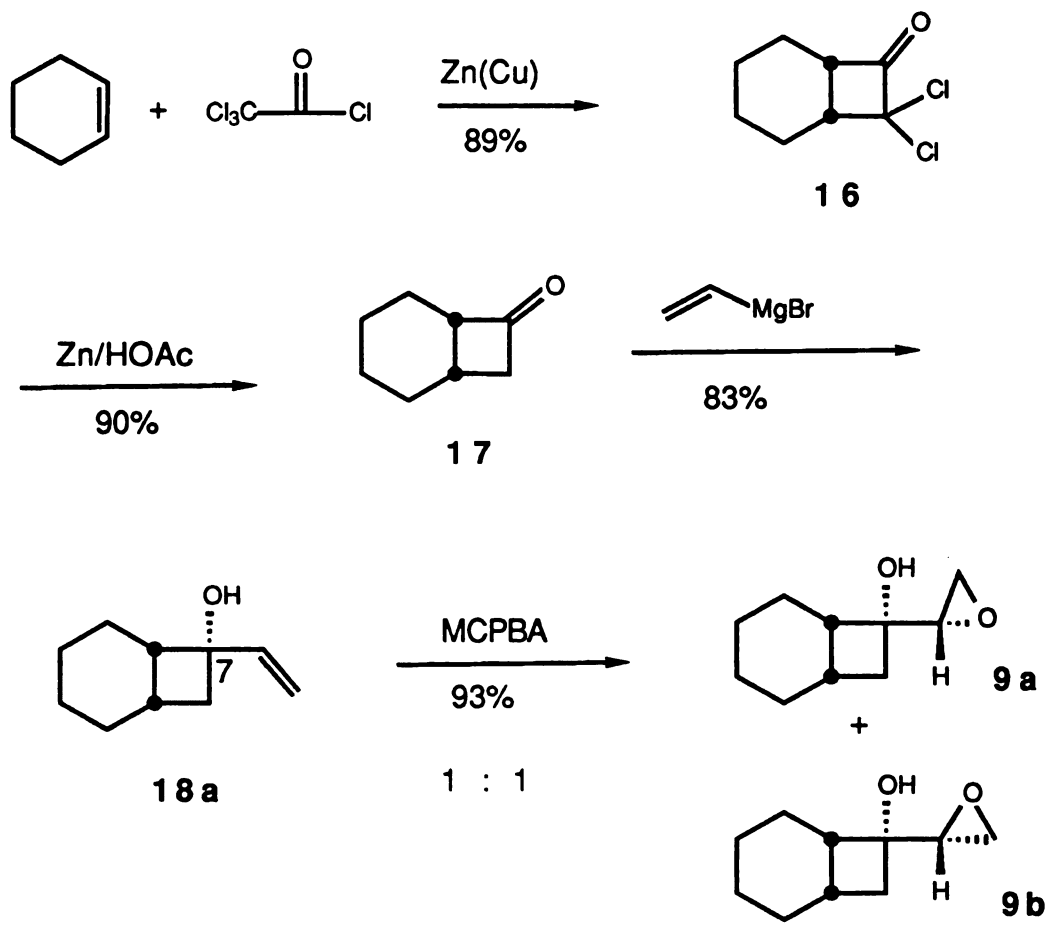
Results and Discussion

Preparation of Diastereomeric Epoxycyclobutanols

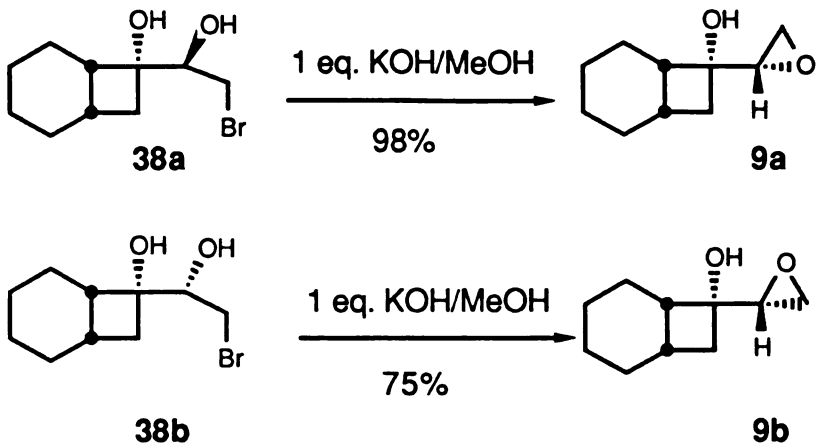
Cyclobutanone **17** is an obvious precursor to cyclobutanol **18a**. Several methods of preparing cyclobutanones have been described.[25] Among these the [2π + 2π] cycloaddition[26] of ketenes with alkenes is one of the most direct and simplest, and dichloroketene has been demonstrated to be particularly effective for this purpose.[27] Thus in situ cycloaddition of dichloroketene, prepared by the zinc dechlorination of trichloroacetyl chloride, with cyclohexene gave dichlorocyclobutanone **16** in 89% yield. Reductive removal of the chlorine atoms from **16** with zinc in acetic acid was easily accomplished to afford cyclobutanone **17** in excellent yield.

Subsequent addition of vinyl magnesium bromide to **17** yielded a single diastereomeric product (vinyl cyclobutanol **18a**). The stereochemistry at the C(7) center, as indicated in structure **18a**, was assigned on the basis of preferred reagent attack at the less hindered convex side of the substrate. Epoxidation of vinylcyclobutanol **18a** with MCPBA then provided epoxycyclobutanols **9a** and **9b** in 93% yield as a 1 : 1 mixture of diastereomers (determined by ^{1}H NMR). Unfortunately, these

isomers could not be separated by fractional distillation or flash chromatography (Scheme V).



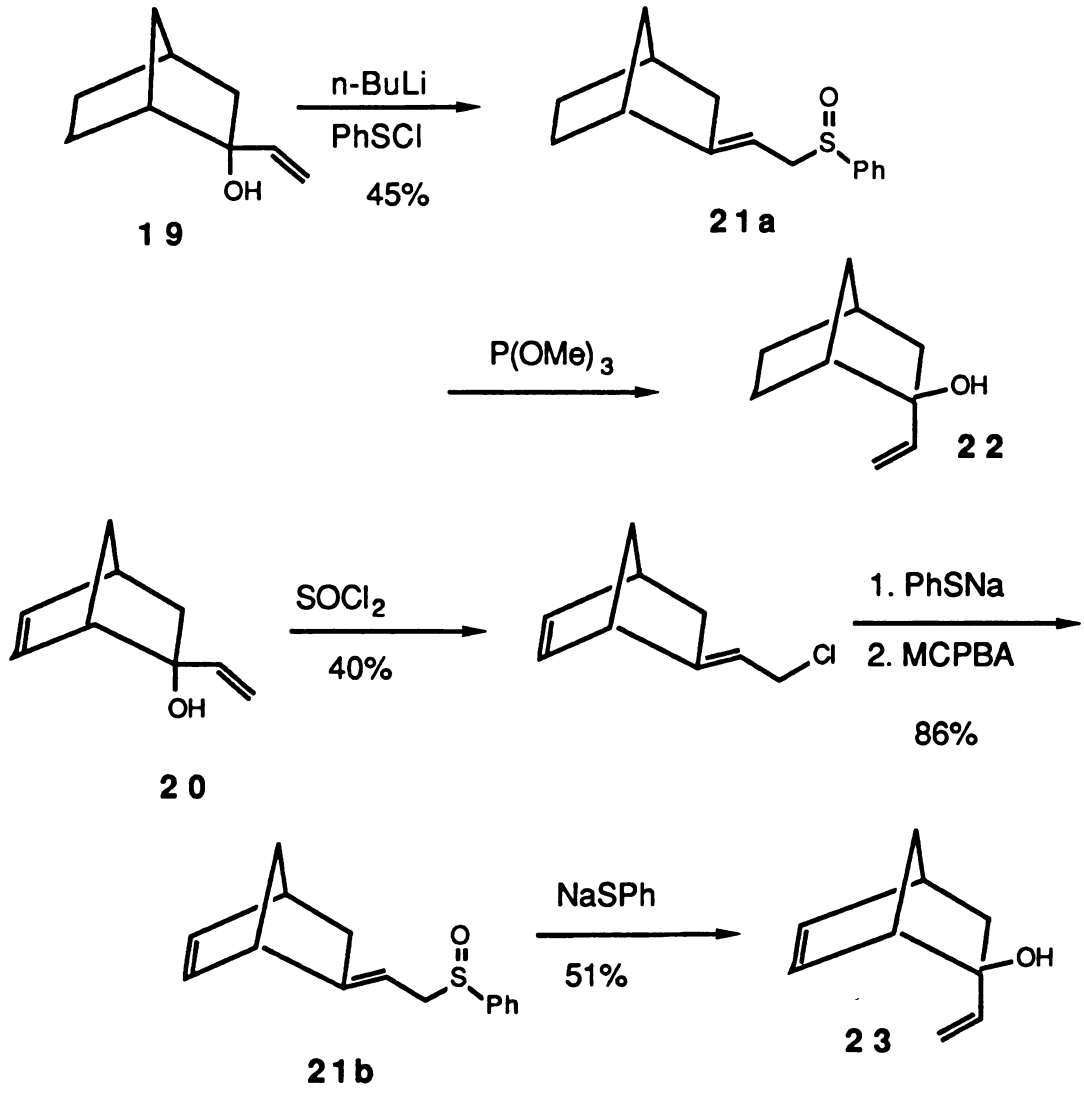
However, a pure sample of each isomer was eventually obtained from the derived bromohydrins, **38a** and **38b** respectively, by treatment with methanolic base.



With epoxycyclobutanols **9a** and **9b** in hand, we continued our effort to prepare the vinylcyclobutanol **18b**, a precursor of the other two diastereomeric epoxycyclobutanols (**9c** and **9d**).

Brown and Fallis[28] have reported a procedure for converting the endo vinyl alcohols **19** and **20** into the corresponding exo vinyl alcohols **22** and **23**, via allylic sulfoxides **21a** and **21b**. A [2,3] sigmatropic rearrangement of the sulfoxide moiety was assumed to occur preferentially across the less hindered exo faces of the double bond (Scheme VI).

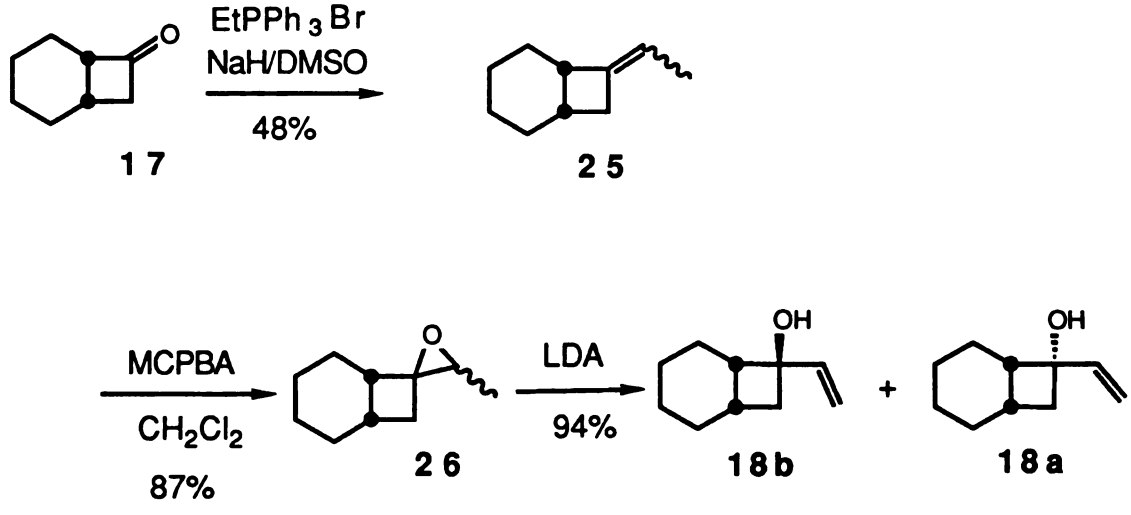
Since treatment of vinylcyclobutanol **18a** with either phenylsulfenyl chloride or thionyl chloride led to complicated mixtures, an alternative procedure was devised, as shown in Scheme VII. Of central importance to this approach was the ability to carry out a stereoselective epoxidation of ethylidenecyclobutane **25**, followed by a regioselective β-elimination of the resulting epoxides. We anticipated that a peracid reagent would prefer to attack olefin **25** from the less hindered convex side, thus leading to the desired β-epoxides.



Scheme VI

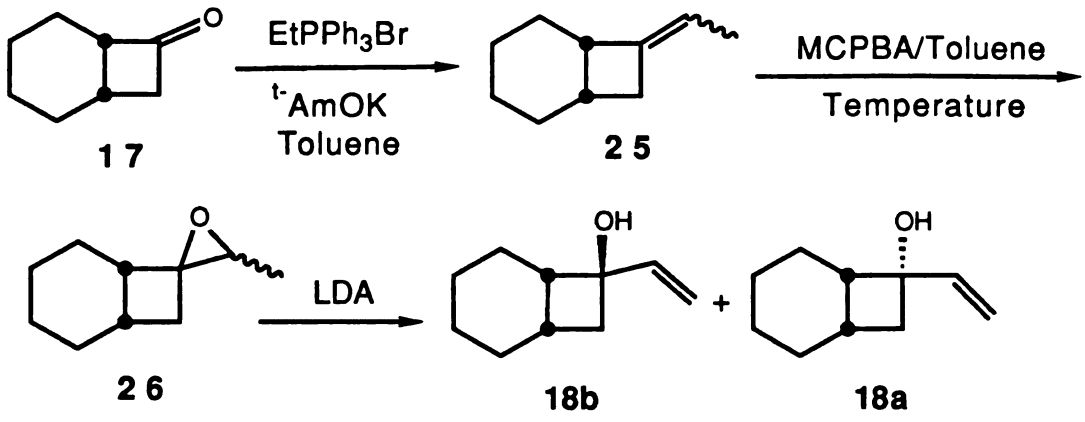
In the event, alkene **25** was prepared as a 1 : 1 E/Z mixture from cyclobutanone **17** by a Wittig reaction. Epoxidation of alkene **25** with MCPBA in methylene chloride solution yielded a diastereomeric mixture of epoxides **26**. Finally, base-catalyzed elimination of this epoxide mixture with lithium diisopropylamide

(LDA) yielded vinylcyclobutanols **18b** and **18a** in a 4 : 1 ratio (Scheme VII).



Scheme VII

Of the many reported procedures for effective Wittig reactions, we found that the conditions suggested by Schow and McMorris[32] (potassium tert-amylate in refluxing benzene or toulene) worked well in this case. In order to reduce the loss of the volatile olefin product (**25**) during workup, it was not purified and epoxidation was conducted on the crude product mixture. Thus, the effect of temperature changes on epoxidation stereoselectivity was studied in this solution. Table I summarized the results of this study, which provided the best experimental conditions for the desired exo-face epoxidation. The overall yield for conversion from **17** to **18b** was greater than 50%, which was nearly double that of the previous procedure (Table I).



17 25 26 18b 18a

Scheme VIII

Table I. Temperature Effect on Epoxidation of Olefin **25**

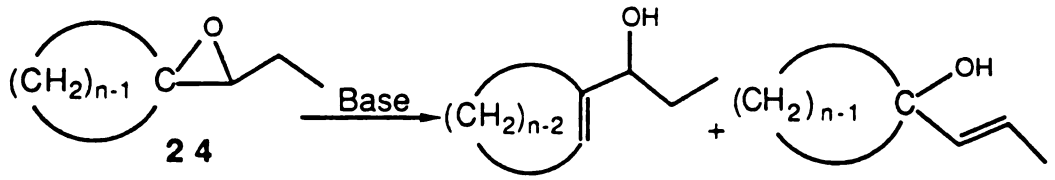
Temp. \ Yield(%) 18a+18b	Yield(%)* 18b	18b/18a
r. t.	70.6	54	3.3
0 °C	61.6	49.3	4.8
-78 °C	65.1	49.9	4.1

* : Overall yield from **17** to **18b**

The exclusive formation of tertiary alcohols (**18a** and **18b**) from epoxides **26** reported here should be contrasted with work of Thummel and Rickborn,[29] in which the base-induced rearrangement of propylidenecycloalkane oxides to allylic alcohols exhibited marked regioselectivity for endocyclic olefin products (Table II). An

exception was propylidenecyclohexane oxide, which gave 95% of the alternative product.

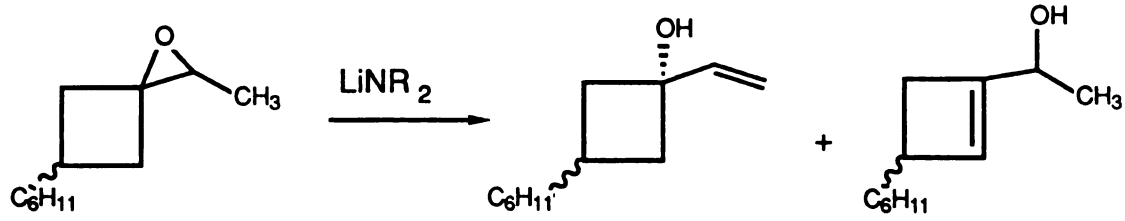
Table II. Base-Induced Rearrangement of Akylidenecycloalkane Oxides **24**



n =	4	77	15
	5	100	0
	6	5	95
	7	98	2
	8	100	0
	12	84	---

On the other hand, the same authors also reported[30] a highly selective base-induced rearrangement involving proton abstraction from the least substituted β-carbon atom of unsymmetrically substituted epoxides. Since there was no experimental data available for base-induced rearrangements of ethylidenecyclobutane oxide, we carried out our own study involving treatment of epoxides **27** with either lithium diisopropylamide (LDA) or lithium diethylamide in ether solution to afford allylic alcohols **28a** and **28b** in a ratio of 10 : 1 (90%) and 12 : 1 (83%), respectively. These results indicated a balance between the preference for endocyclic olefin formation and the preference for base attack at the less

substituted β-carbon in the case of epoxide derivatives of alkylidenecyclobutanes.



27 **28a** **28b**

It has been noted[31] that hydroxylic solvents such as t-BuOH may form hydrogen bonds with peracids, resulting in a decrease of the rate of epoxidation. With this in mind, we decided to explore the medium effect. We hoped that association of additional polyhydroxyl reagents or hydroxylic solvents with the peracid would increase the bulkiness of this reagent and the facial selectivity of the epoxidation of **25**. The results of this study are listed in Table III.

As shown in Table III , the addition of a polyhydroxyl co-reactant did not increase the facial selectivity. On the other hand, the facial selectivity increased to 6.5 : 1 when the epoxidation was carried out in methanol solution. Unfortunately, the lower yield of the reaction in MeOH offset this improvement.

Finally, epoxycyclobutanols **9c** and **9d** were obtained by epoxidation of **18b** with MCPBA in methylene chloride solution. Unlike their diastereomers (**9a** and **9b**), **9c** and **9d** were easily separated by flash chromatography.

Table III. Solvent Effect on Epoxidation of Olefin **25**

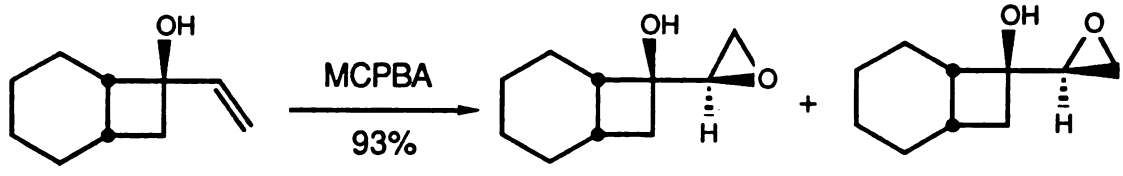
Solvent	Yield(%) **18a+18b** #	Yield(%) **18b** #	+ **18b/18a**	++ **18b/18a**
CH_2Cl_2	75.5	59.7	3.8	4.2
CH_2Cl_2 ROH*	76.2	59.3	3.5	4.1
ether	74.8	57.8	3.4	3.4
ether ROH*	77.2	58.8	3.2	3.1
MeOH	64	55.7	6.5	6.7

* : 1,1,1-Tris(hydroxymethyl) ethane

\# : Overall yield from **25** to **18a** + **18b**

\+ : The ratios were determined by the integrations of ^1H NMR

++ : The ratios were determined by the isolated yields

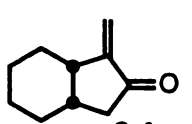
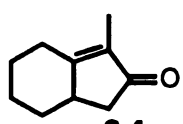
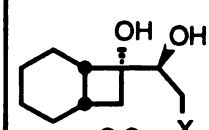
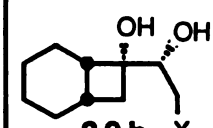


18b **9c** **9d**

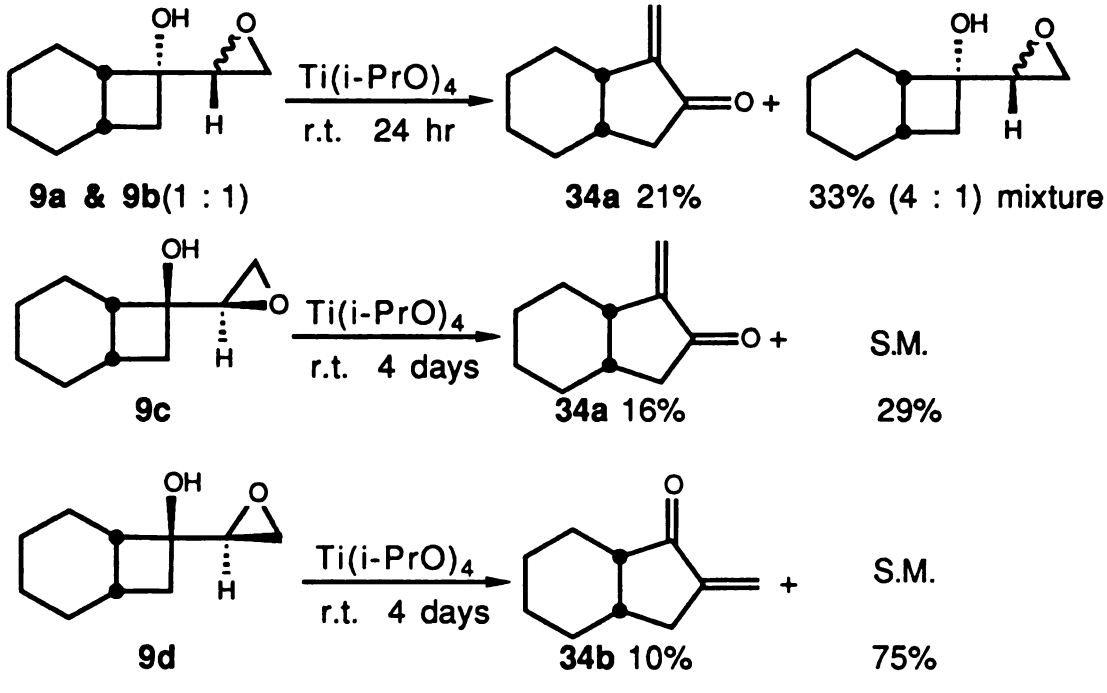
Reactions of Epoxycyclobutanols with Lewis Acids and Bronsted Acids

With the epoxycyclobutanols **9a, 9b, 9c** and **9d** in hand, we proceeded to study the Lewis acid-catalyzed rearrangement of these isomers. Since boron trifluoride rapidly converted a 1 : 1 mixture of **9a** and **9b** to a complex decomposition mixture at 0 °C in methylene chloride solution, milder acids such as $SnCl_4$, $Ti(i\text{-}PrO)_4$, $Ti(i\text{-}PrO)_3Cl$ and $MgBr_2$ were investigated. As noted in Table IV, ring expansion products (**34a** and **34c**) and halohydrins (**38a** and **38b**) were identified and obtained in amounts that varied markedly with the Lewis acids used and the conditions of the reaction.

Table IV. Reactions of Epoxycyclobutanols (**9a** + **9b**) with Lewis Acids

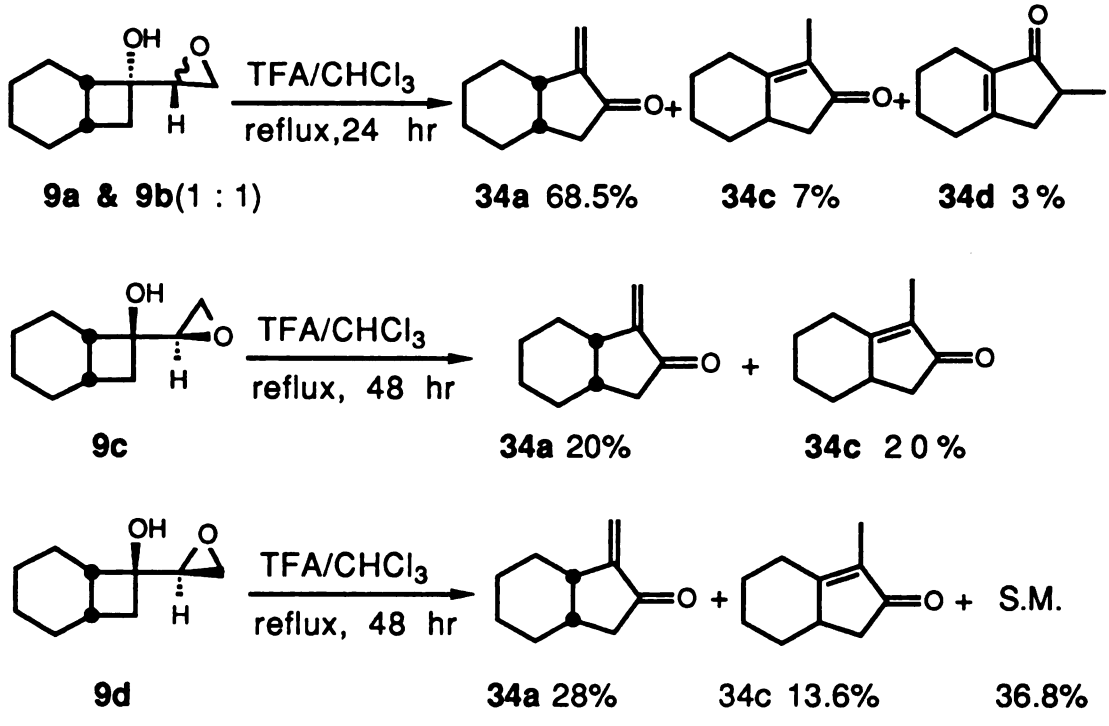
Products / Yields(%) / Lewis Acids	 **34a**	 **34c**	 **38a** X	 **38b** X
Cat. $SnCl_4$	33	< 3	X = Cl 6.4	X = Cl 5.4
Cat. $Ti(i\text{-}PrO)_3Cl$	10	< 3	X = Cl 3.7	X = Cl 3.6
1.1eq.$Ti(i\text{-}PrO)_3Cl$			X = Cl 50	X = Cl 50
$Ti(i\text{-}PrO)_4$	21	< 3		
1.1 eq. $MgBr_2$			X = Br 50	X = Br 50

Although these Lewis acid-catalyzed reactions of **9a** and **9b** proved to be unpromising from a synthetic point of view, several conclusions may be drawn from the data. First of all, reactions of epoxycyclobutanols **9a** and **9b** with one or more equivalents of Lewis acids which incorporate nucleophilic halogens gave halohydrins in near quantitative yields. Secondly, with catalytic amounts of such Lewis acids, low yields of enones **34a** and **34c** together with small amounts of halohydrins were obtained. Finally, an examination of the reaction of **9a** and **9b** with the weak Lewis acid, $Ti(i\text{-}PrO)_4$, revealed that diastereomer **9b** was substantially less reactive than **9a**. Similar results were observed for $Ti(i\text{-}PrO)_4$ catalyzed rearrangement of **9c** and **9d**, as shown in Scheme IX.



Scheme IX

Better conditions for the conversion of **9a** and **9b** into enones (**34a** and **34c**) were achieved by replacing the Lewis acid catalysts with the nonnucleophilic Bronsted acid, trifluoroacetic acid (TFA). Thus treatment of the 1 : 1 mixture of epoxycyclobutanols (**9a** and **9b**) with 1.1 equivalents of TFA in chloroform solution gave enones **34a** (68.5%), **34c** (7%) and **34d** (3%). Shorter reaction times gave lower yields of enones and recovery of starting material.

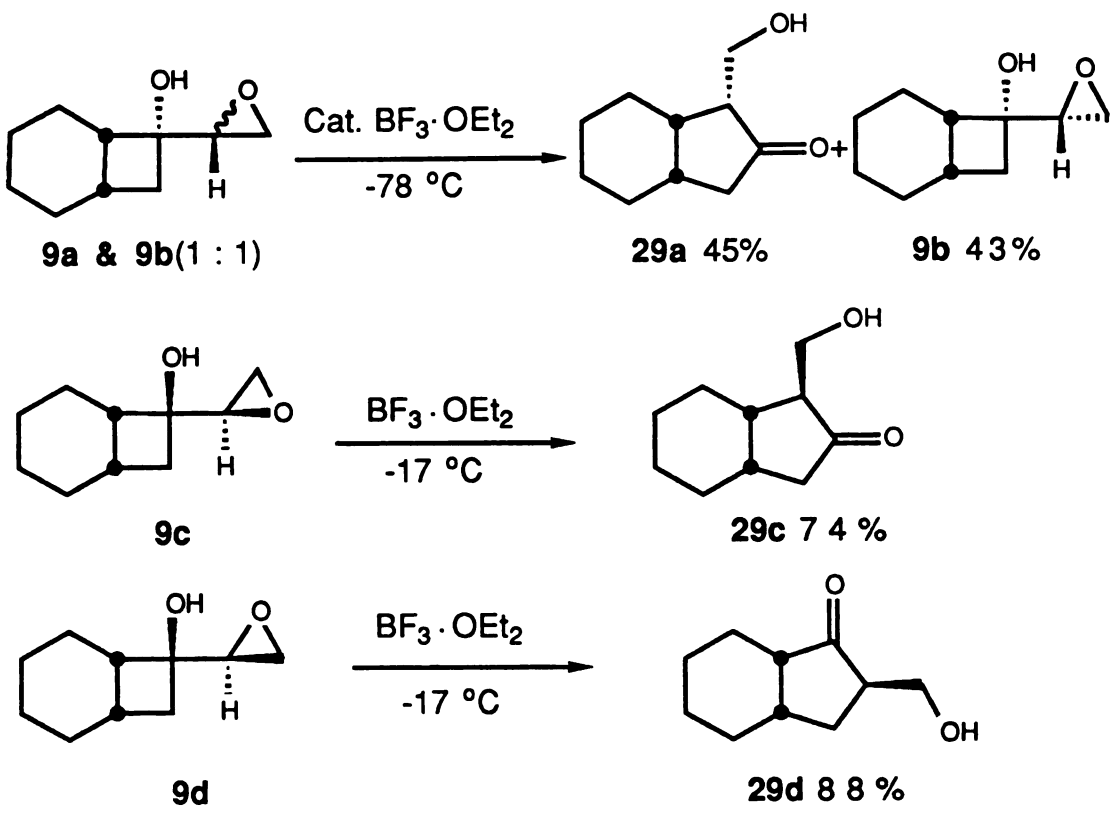


Scheme X

Not surprisingly, the migratory aptitudes displayed in these rearrangements favor the more substituted ring residue. In the case of α-epoxy alcohols **9a** and **9b**, the ratio of migratory aptitudes of the methine and methylene carbons is 11 : 1. On the other hand, methine carbon migration occurs almost exclusively in the reaction of β-epoxy alcohols **9c** or **9d** with TFA (Scheme X).

Since the ratio of recovered epoxycyclobutanols (**9a** : **9b**) remained unchanged, the reactivities of **9a** and **9b** with trifluoroacetic acid , unlike $Ti(i\text{-}PrO)_4$, are roughly the same. The more thermodynamically stable enones **34c** and **34d** may be derived from enones **34a** and **34b**, respectively, through keto-enol tautomerization and double bound isomerization under acidic conditions. Finally, the much slower rate of the reaction of **9c** and **9d** with TFA encouraged us to examine stronger Lewis acids, such as $BF_3{\cdot}OEt_2$, under milder conditions.

Remarkably, treatment of **9c** with 1.1 equivalents of $BF_3{\cdot}OEt_2$ in CH_2Cl_2 at -17 °C gave a single ketol **29c** in excellent yield. Under equivalent conditions, ketol **29d** was obtained in 74% yield from **9d**. We then examined the reaction of $BF_3{\cdot}OEt_2$ with **9a** and **9b** at lower temperatures. Surprisingly, treatment of **9a** and **9b** (1 : 1 mixture) with catalytic amounts of $BF_3{\cdot}OEt_2$ at -78 °C gave ketol **29a** (45%) together with recovered **9b** (43%). On more vigorous treatment (higher temperature or equimolar boron trifluoride), **9b** was transformed to an intractable mixture including polymeric products (Scheme XI).


OH
O
H
Cat. $BF_3 \cdot OEt_2$
-78 °C
OH
O+
OH
O
H
9a & 9b(1 : 1)
29a 45%
9b 43%
OH
O
H
$BF_3 \cdot OEt_2$
-17 °C
OH
O
9c
29c 74 %
OH
O
H
$BF_3 \cdot OEt_2$
-17 °C
O
OH
9d
29d 88 %

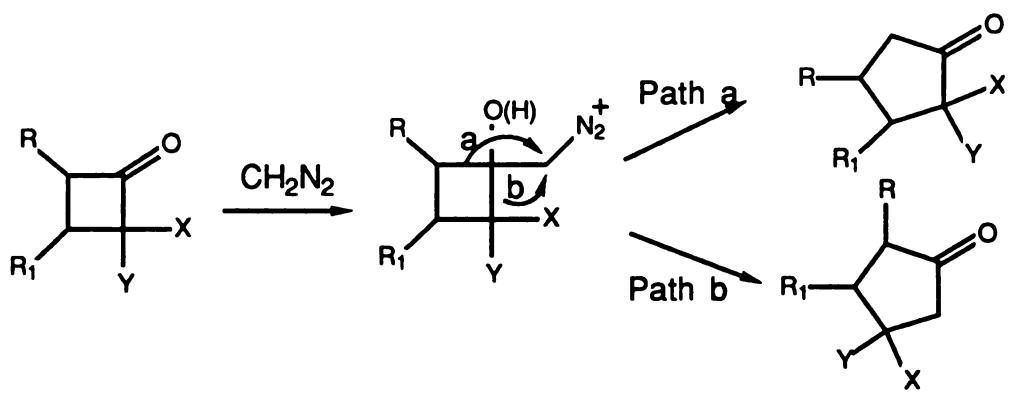
Scheme XI

Our interpretation and rationalization of the highly selective reactivity of stereoisomers **9a**, **b**, **c** and **d** with BF_3 etherate was complicated by the fact that none of the key compounds, including **9a** through **9d**, **34a**, **34b** and **29a** through **29d**, had been reported previously. Furthermore, although each of the diastereomers **9a** through **9d** exhibits characteristic properties, the corresponding ^1H and ^{13}C NMR spectra cannot be assigned unambiguously to a specific configuration. In addition, attempts to effect selective epoxidation of vinyl alcohols **18a** or **18b** with either m-chloroperbenzoic acid at low temperature (-78 °C) or titanium-mediated epoxidation with tert-butylperoxide[33] also gave a 1 : 1 ratio of diastereomeric epoxycyclobutanols. Consequently, a series of chemical correlations and interconversions were undertaken, which led ultimately to the structural assignments presented in Scheme XVIII.

Synthesis of regioisomeric Methylene cyclopentanones

Greene and Depres have examined the ring expansion reactions of certain alkyl-substituted cyclobutanones with diazomethane (Et_2O-MeOH, room temperature).[34] In the case of X = Y = H (Scheme XIII) the ring expansion proceeded quite smoothly to afford the corresponding cyclopentanones; however the regioselectivity of the migration was poor. The presence of α-chlorine substituent(s) (X, Y = H, Cl or X = Y = Cl) not only accelerated the rate of reaction, but also served to favor pathway a over pathway b, presumably due to stabilization of the positive charge which must be shared in the transition state. Although epoxide formation is generally observed in the reaction of larger ring ketones with CH_2N_2,[35] the reaction

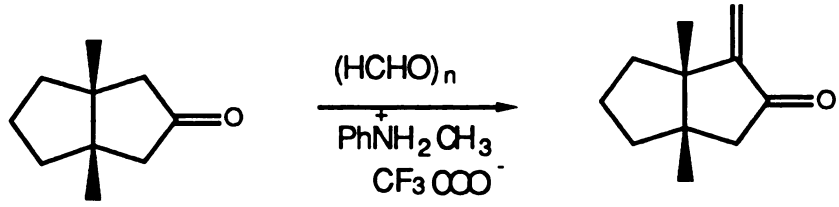
with cyclobutanones gave ring expansion products exclusively. The driving force in this case is probably the release of strain energy in the four-membered ring.



Scheme XIII

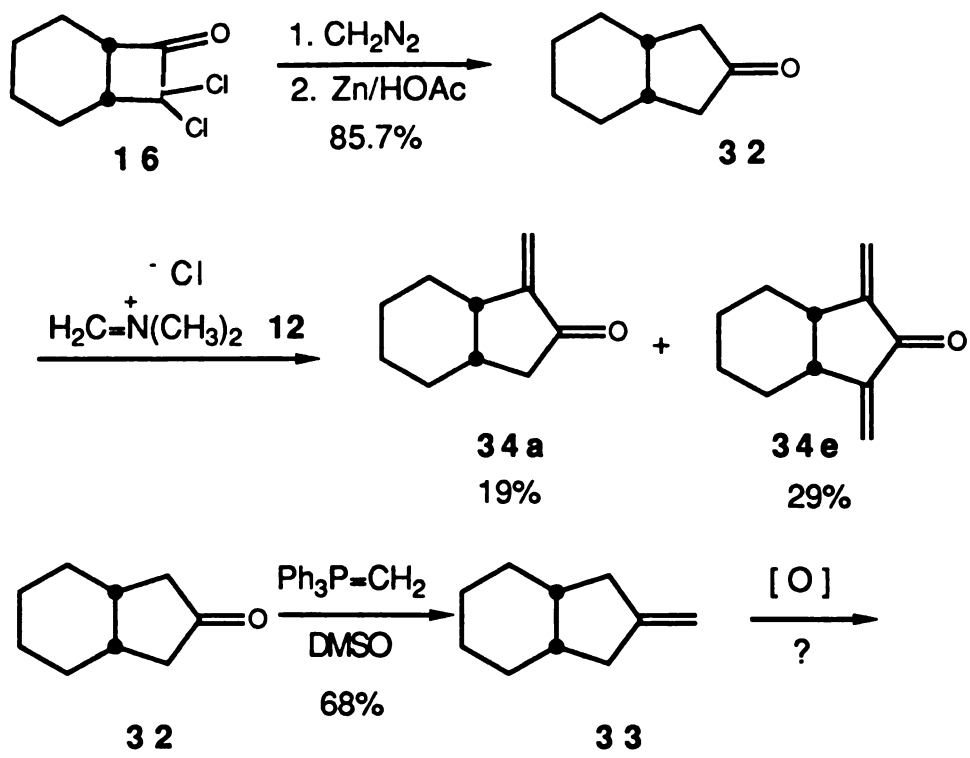
This reaction then served as the basis for our efforts to synthesize regioisomeric enones (**34a** and **34b**). Thus, ring expansion of dichlorocyclobutanone **16** with diazomethane, followed by zinc reduction, gave cyclopentanone **32** in excellent yield. Subsequent methylenation of **32** by Gras` procedure[36] [s-trioxane, N,N`-dimethylanilinium trifluoroacetate (TAMA) in dioxane or tetrahydrofuran solution] failed, returning starting material. Alternative procedures were then sought. A similar approach to methylene ketones has been reported by Paquette, et al.[37] Treatment of bicyclic ketone **30** with paraformaldehyde and TAMA in dioxane

solution provided the corresponding enone **31**. However, in our hands, this method also failed to give the desired enone **34a**.



30 **31**

Eventually **34a** was obtained in poor yield by a Mannich reaction of ketone **32** with ammonium salt **12**, prepared from the reaction of N, N, N`, N`-tetramethyl diaminomethane (aminal) and acetyl chloride in ether solution.[66] As noted , dimethylene ketone **34e** was the major product, even though less than one equivalent of **12** was used in the methylenation.

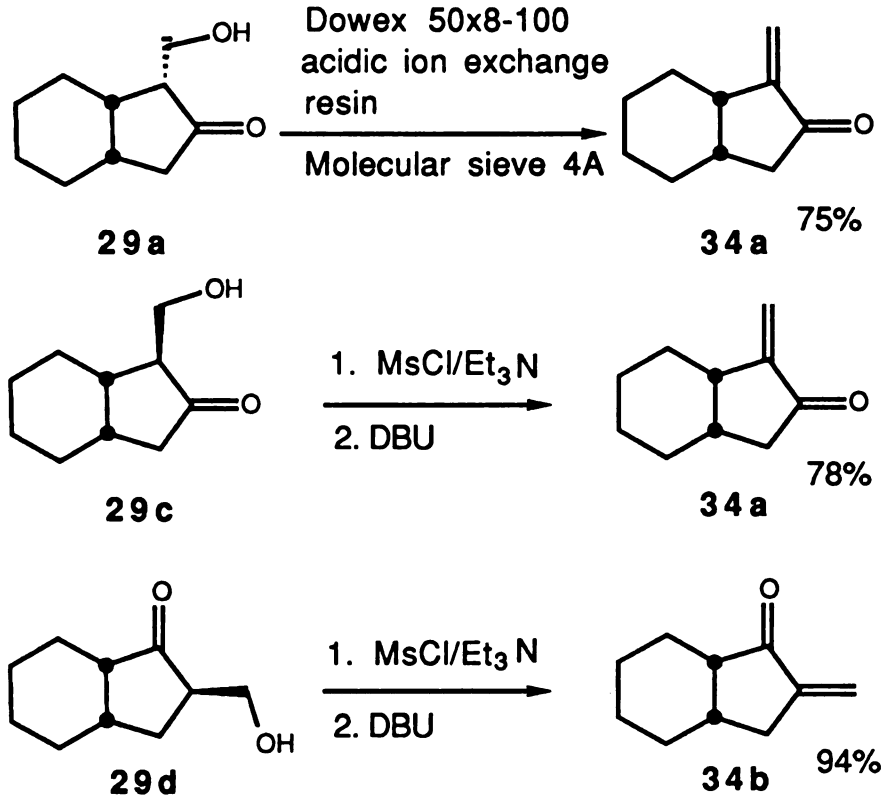


Scheme XII

Attempts to effect allylic oxidation of olefin **33**, obtained by Wittig reaction of ketone **32** with methylenephosphorane, through the action of either SeO_2[38] or CrO_3-Pyridine[39] resulted in complete recovery of starting material.

Treatment of ketol **29a** with Dowex 50x8-100 acidic ion exchange resin and molecular sieve 4A in refluxing chloroform yielded enone **34a**. Curiously, equivalent reactions of ketols **29c** or **29d** with the acidic ion exchange resin were sluggish under similar conditions. An alternative procedure, involving mesylation of ketol **29c** followed by elimination with 1,5-diazabicyclo[5.4.0]undeca-5-ene (DBU), gave enone **34a** in excellent yield (Scheme XIV). By the same procedure, enone **34b** was obtained from **29d** in 94% yield.

The characteristic properties of enone **34a** derived from dehydration of either ketol **29a** or **29c** were identical with the enone prepared by methylenation of cyclopetanone **32**. This result indicated that ketols **29a** and **29c** are epimeric isomers. The observed chemical shifts of the methylene protons of enone **34a** (δ 6.15, 5.15) and enone **34b** (δ 6.03, 5.30) enabled us to easily distinguish these two regioisomeric enones.



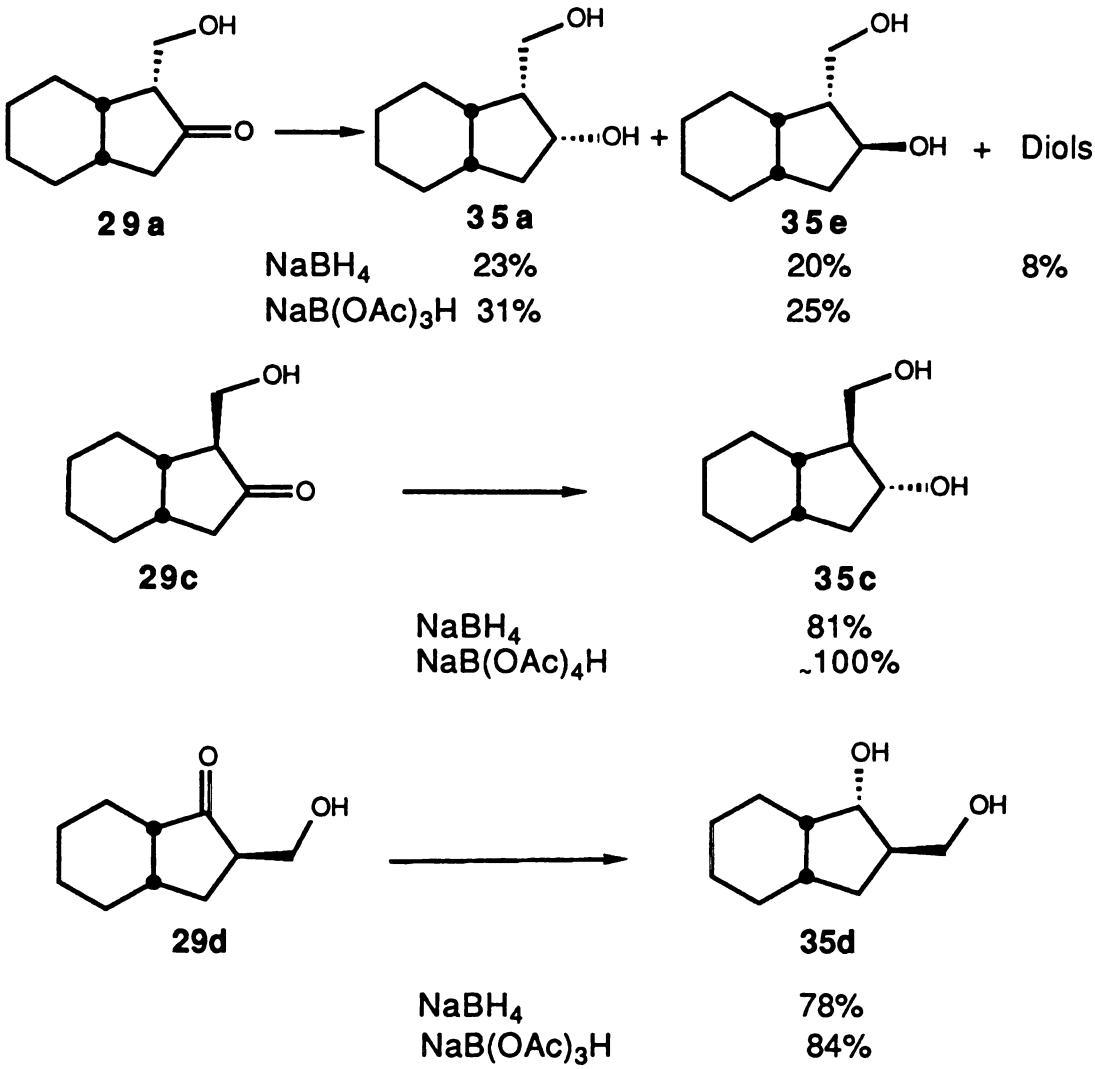
Scheme XIV

Identification of Stereoisomeric Hydroxymethyl Cyclopentanones

Having established the characteristics of enones **34a** and **34b**, we proceeded to define their stereoisomeric ketol precursors. Since the isomers **29a**, **29c** and **29d** could not be assigned configurations based on their spectroscopic characteristics alone, we planned to convert these ketols to 1,3-diols which would be defined as cis or trans from the expected stereoselectivity of the reaction. These assignments could then be checked by observing the rates of acetonide formation.

For this purpose we used sodium triacetyl borohydride, a highly selective reducing agent which reduces ketones only when a neighbouring hydroxyl group serves as a ligand for intramolecular delivery of hydride to the carbonyl function.[40] Of the three ketols obtained from the boron trifluoride-catalyzed rearrangements, both **29c** and **29d** have their hydroxymethyl group projecting from the convex face of the cis-bicyclononane ring system. In these cases we expected the normal convex facial-selectivity of the reduction would be enhanced by the neighbouring group effect. In the event, sodium triacetyl borohydride reduction of **29c** or **29d** gave high yields of diols **35c** or **35d**, respectively, which in each case were assigned trans configurations. On the other hand, isomer **29a** has a concave-face oriented hydroxymethyl group which, because of steric hindrance, is less easily bound to the reducing agent. Here reduction proceeded sluggishly at both faces of the carbonyl function and yielded both cis **35a** and trans **35e** diols.

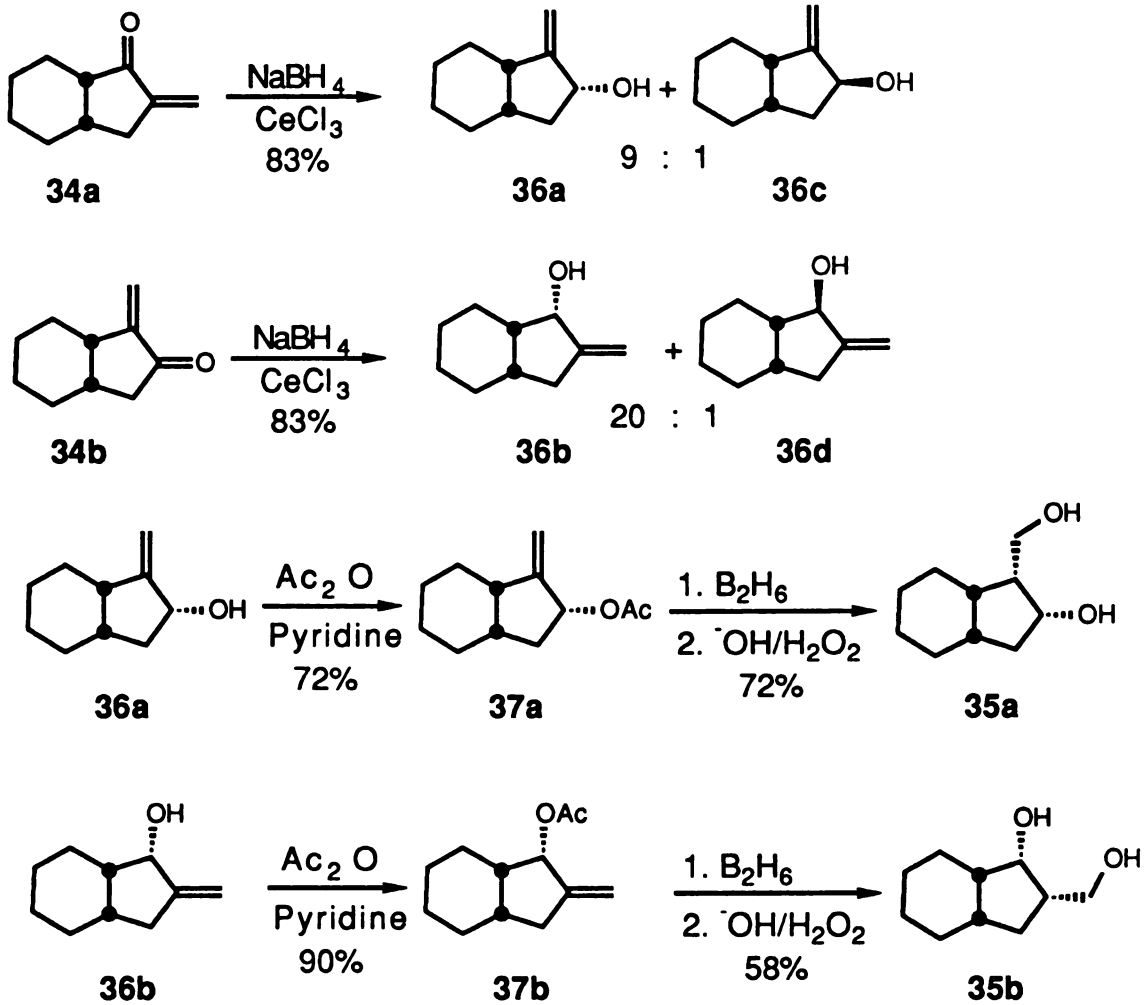
By comparison, sodium borohydride ($NaBH_4$) reduction of ketols **29c** or **29d** each gave a single product in lower yield. When ketol **29a** was treated with $NaBH_4$ in methanol solution, more than three



Scheme XV

compounds, including **35a** (31%), **35e** (25%) along with other unidentified diols (8%), were obtained. This was attributed to the epimerization of **29a** under the reaction condition (Scheme XV).

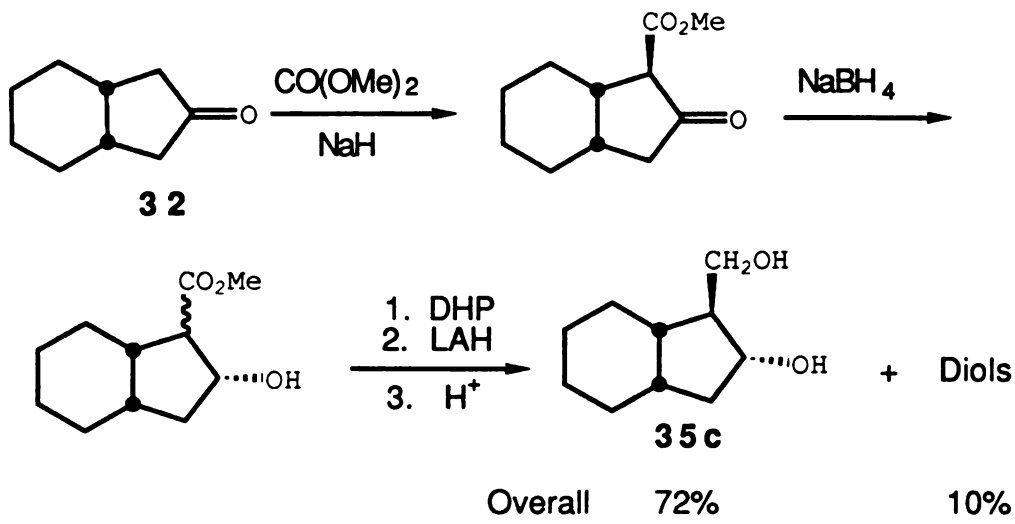
Alternative preparations of these diols from enones **34a** and **34b** were also explored. Reduction of enone **34a** with $NaBH_4$[41] gave a 9 : 1 ratio of epimeric allylic alcohols **36a** and **36c** which were separated by flash chromatography. Subsequent acetylation of the major alcohol **36a** followed by hydroboration/hydrogen peroxide oxidation gave diol **35a** in 42% overall yield from **34a**. Diol **35b** was also obtained in 50% yield from **34b** by this same procedure. This sequence of reactions, beginning with carbonyl reduction and ending with hydroboration oxidation, was assumed to proceed predominantly at the less hindered convex face, leading to the formation of cis-diols (Scheme XVI).



Scheme XVI

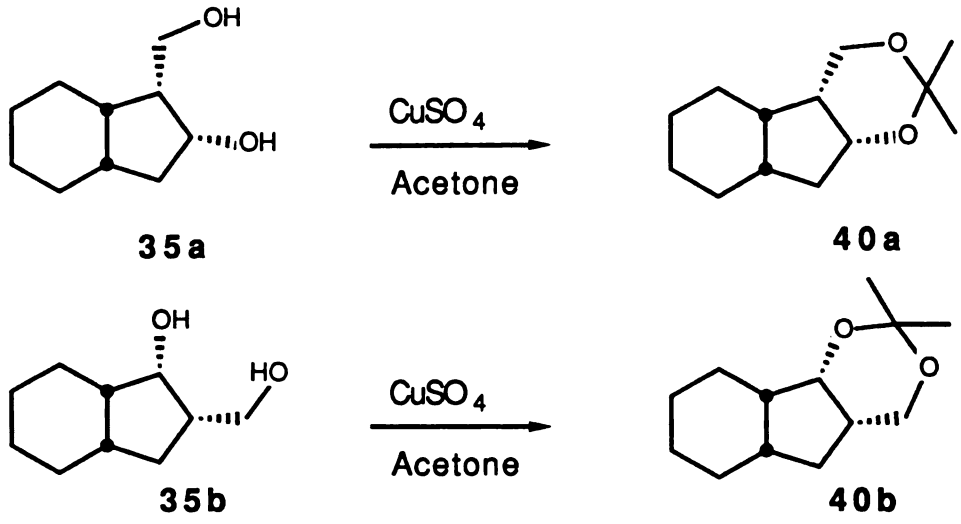
Diol **35c** was also prepared by an independent sequence of reactions. Thus, carboxymethylation of **32** followed by sodium borohydride reduction, dihydropyran protection, lithium aluminum hydride reduction and deprotection gave the trans-diol **35c** as a predominant product (72% yield overall). The trans configuration

assigned in this case can be rationalized on the basis of steric considerations.[42] Of course, this diol was found to be identical to the diol, derived from $NaB(OAc)_3H$ reduction of ketol **29c** (Scheme XVII).



Scheme XVII

As expected, the cis-diols **35a** and **35b** readily formed acetonide derivatives **40a** and **40b** respectively, on treatment with anhydrous copper sulfate in acetone solution[43] (> 50% yield in 2 hr at 25 °C). The trans isomers **35c** and **35d** reacted sluggishly, giving less than 5% acetonides under equivalent conditions.

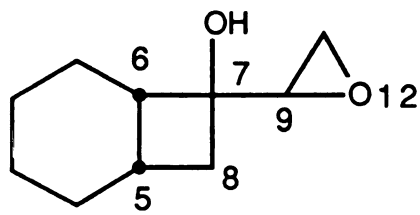


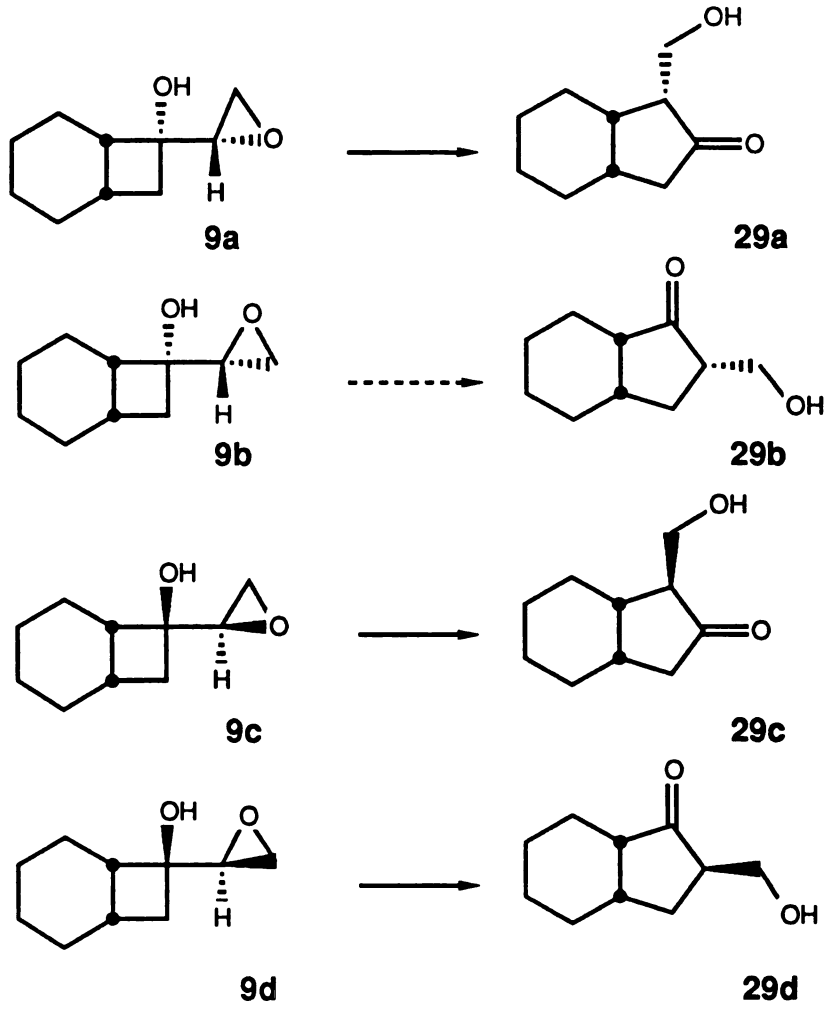
At this stage, we had established reasonable structures and configurations for regioisomeric enones **34a** and **34b** as well as stereoisomeric ketols **35a**, **35c** and **35d**. To rationalize the selective behavior of isomers **9a** through **9d** in the boron trifluoride-catalyzed rearrangements, we made the plausible assumption that the preferred transition state will have an anti-periplanar orientation of the oxirane CH-O bond and the migrating residue of the four-membered ring. Dihedral angles, calculated by MM2,[44] between the anti-periplanar ring residue and the CH-O bond of the most stable conformation in each epoxycyclobutanol are shown in Table V. Using this information together with Dreiding models and the assumption thst transition state energy difference will reflect ground state conformational energy difference, we propose the configurational relationships depicted in Scheme XVIII.

Table V. Dihedral Angle in the Most Stable Conformer of **9a** through **9d**

Compound	Potential Energy (Kcal/mole)	Dihedral Angle (Degree)*
9a	44.0	$176.2^{6,7,9,12}$
9b	44.4	$177.4^{8,7,9,12}$
9c	44.7	$172.1^{6,7,9,12}$
9d	44.3	$175.0^{8,7,9,12}$

* : atom number





Scheme XVIII

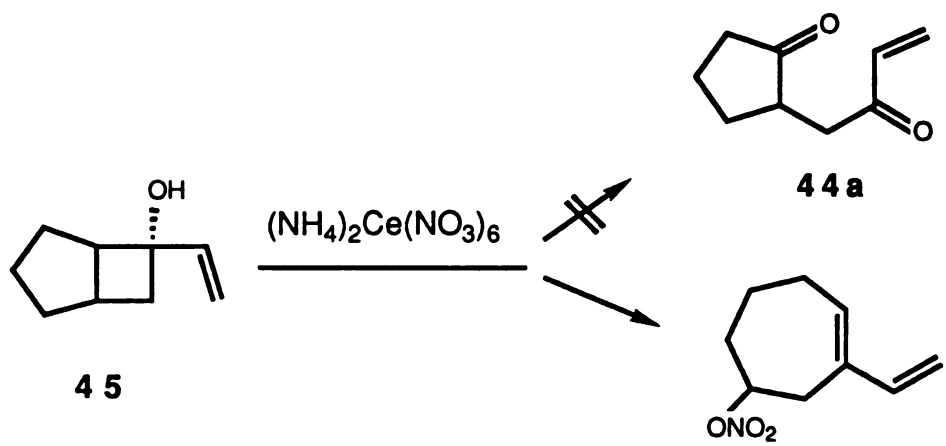
CYCLOBUTANES IN ORGANIC SYNTHESIS

PART II

SOLCOLYTIC STUDIES OF ESTER DERIVATIVES OF BICYCLO[n.2.0]ALKANOLS (n = 3 OR 4)

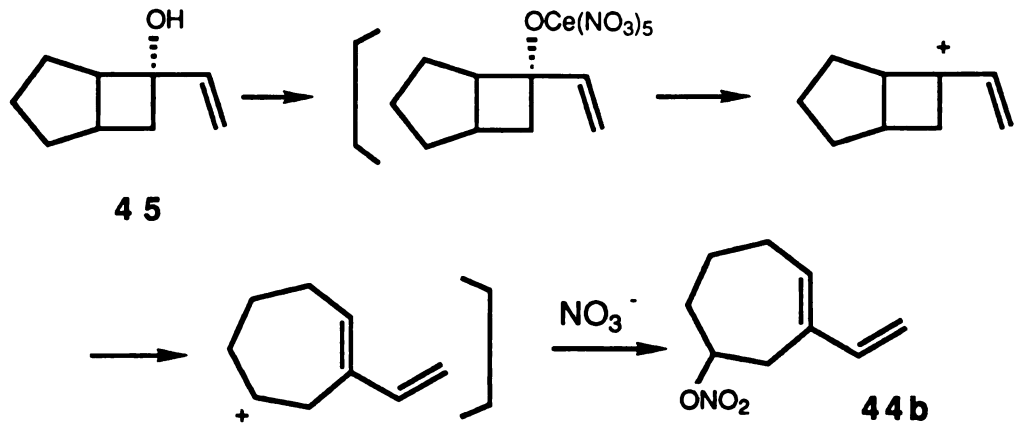
Introduction

This study began with an attempt to oxidize vinylcyclobutanol **45** by treatment with ceric ammonium nitrate in acetonitrile at reflux. Unexpectedly, we obtained the rearranged vinylcycloheptenyl nitrate **44b** (23%) together with a complicated mixture (35%), and were not able to detect any **44a**.



45 **44a** **44b** 23%

The ring-opened compound **44b** appeared to be a solvolytic product of **45** (NO_3- as nucleophile, $OCe(NO_3)_5$ as leaving group). Consequently, it seemed to us that better controlled conditions (pure substrates, specific media) should lead to better yields of useful cycloheptenyl derivatives.

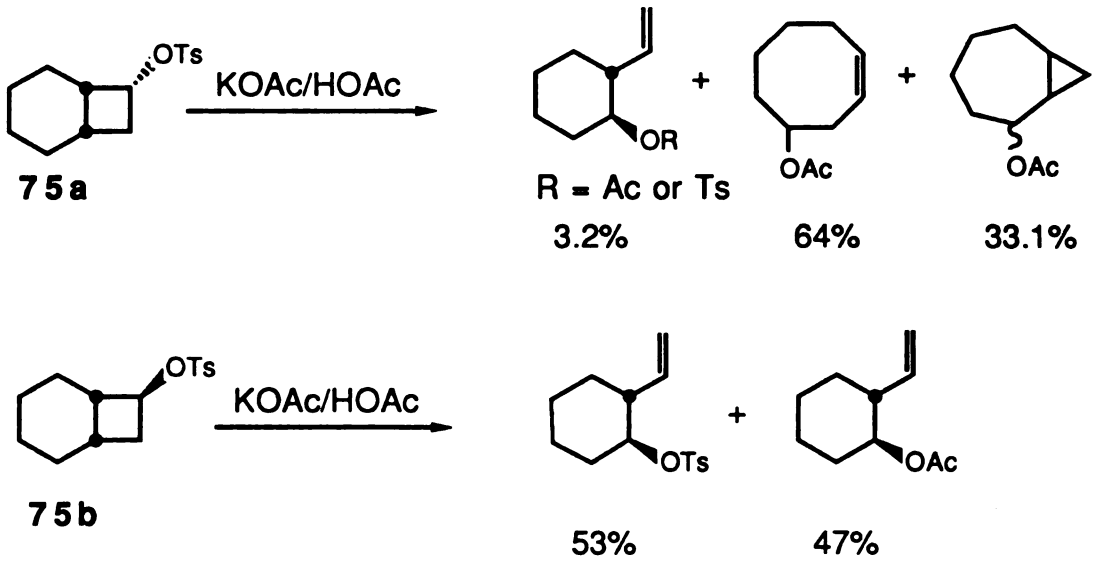


45

44b

Previous solvolytic studies of constrained cyclobutane derivatives demonstrated that the configuration of the four-membered ring and ionizing substituent were major factors in determining reactivity as well as product distribution.[45] A system in which epimeric esters showed different reactivity and gave different products was reported by Wiberg.[46] In the case of exo-bicyclo[4.2.0]ctyl-7 tosylate (**75b**) the formation of a vinylcyclohexyl ion occurs with a conformational change of the initially flattened cyclohexane ring into a normal chair form, and is an energetically favorable process. In the event, solvolysis of **75b** yielded only trans-2-vinylcyclohexyl tosylate and acetate. On the other hand, a similar reaction of **75a** proceeds with conversion of the cyclohexane ring to a higher energy boat conformation, and the vinylcyclohexyl products should not be favored. Alternatively, a disrotatory opening of the internal cyclobutane bond in **75a** would relieve strain without increasing nonbonded steric interactions. In this fashion, the solvolysis of **75a** gave 3-cyclooctenyl acetate and bicyclo[5.1.0]octyl-2 acetate along with only a small amount of

vinylcyclohexyl products. The rate enhancement of the latter reaction was attributed to release of strain and anchimetric assistance in the ionization process (Scheme XX).



75a

R = Ac or Ts

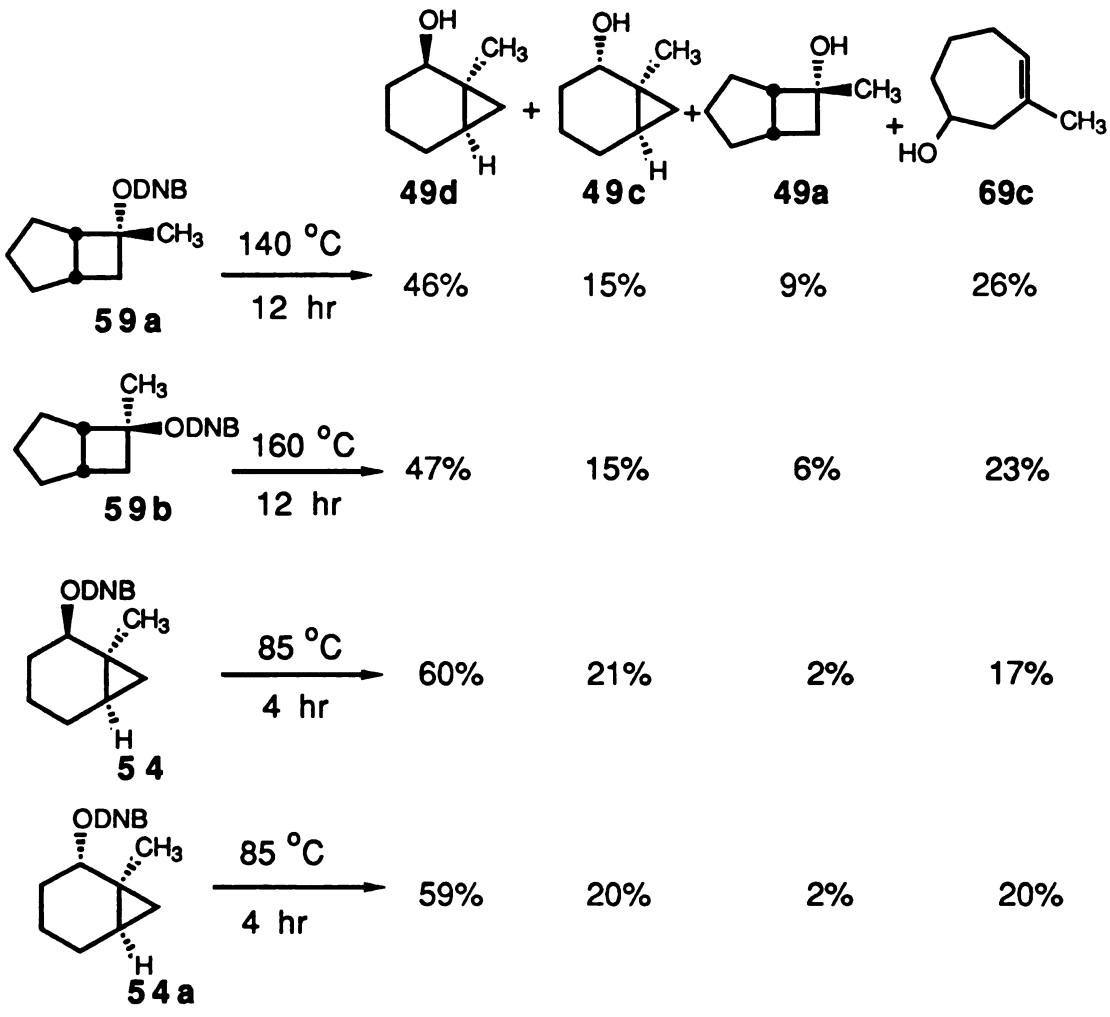
3.2% 64% 33.1%

75b

53% 47%

Scheme XX

The effect of configuration on the rates and products of solvolysis of bicyclo[3.2.0]heptyl-6 and bicyclo[4.1.0]heptyl-2 dinitrobenzoates in 80% aqueous acetone has been also studied.[47] The endo isomer (**59a**) has the configuration suitable for a concerted rearrangement while **59b** does not. This is reflected by the fact that **59a** solvolyzes faster than **59b**. However, a similar product distribution is observed for the solvolyses of **54**, **54a**, **59a** and **59b** (Scheme XXI). On the basis of these observations, the authors assumed that the 1-methyl bicyclo[4.1.0]heptyl-2 cation intermediate is formed in each of these cases and is a common intermediate leading to all the products.

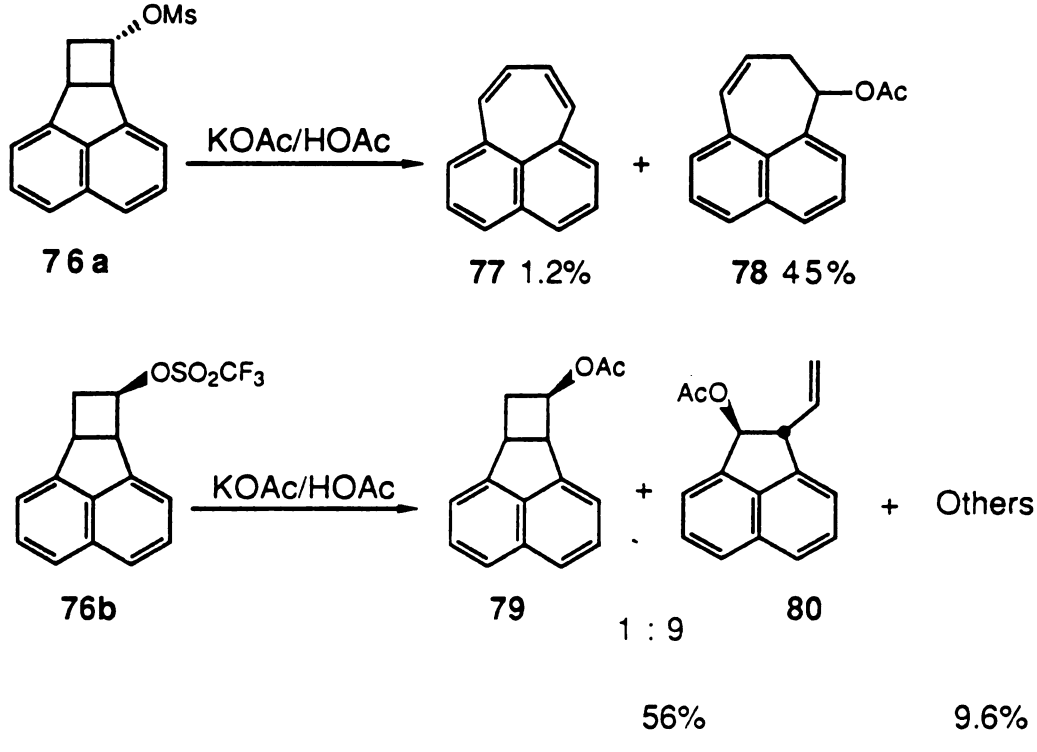


Reaction condition : 80% aqueous acetone

Scheme XXI

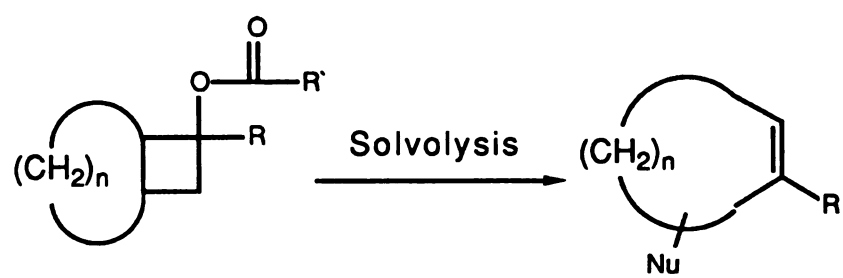
Wiberg`s studies have shown that in the cases of endo cyclobutyl derivatives, solvolysis proceeds with σ-bond participation, and the ring opening of the cyclobutane occurs so as to ensure maximum overlap between the orbital of bond being broken and the developing orbital. Thus the rate of endo isomer is faster than that of exo isomer.

In contrast, Meinwald et al.[48] has found that certain epimeric cyclobutanes under solvolytic conditions gave different products, but showed the same reactivity. For example, acetolysis of **76a** gave pleiadiene **77** (1.2%) and acetate **78** (45%), while in the case of **76b** a hydrocarbon fraction (9.5%) and three-component acetate fraction (56%) were obtained. On the other hand, the reactivity of epimeric esters (**76a** and **76b**) was found to be nearly the same. This is contrary to observation by Nelson[49], involving the solvolysis of bicyclo[3.2.0]heptyl-6 tosylates, wherein the endo isomer has a solvolytic rate at least 500 times larger than that of the exo isomer. The anomalously slow reaction rate of **76a** as well as the absence of cyclopropyl carbinyl products led Meinwald to question whether anchimetric assistance by σ-bond participation was involved in this solvolysis.



Scheme XXII

Continuing studies[50] have yielded additional insight into the relationship of reactivity and product distribution with the conformation of cyclobutane rings. In this respect, prompted by our earlier observation in the oxidation of vinylcyclobutanol **45**, we proceeded to study the solvolysis of ester derivatives of bicyclo-[n.2.0]alkanols (n = 3 or 4) as a general synthesis of substituted cycloheptenols or cyclooctenols (Scheme XXIII).



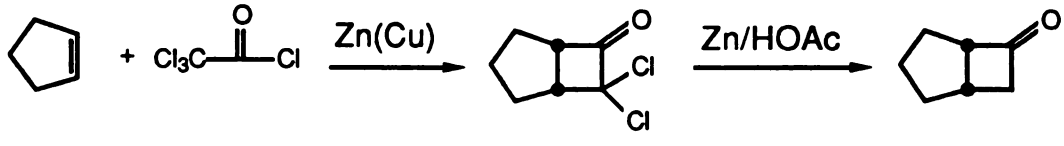
n = 3 or 4 n = 3 or 4

Scheme XXIII

Results and Discussion

Preparation of Ester Derivatives of Cyclobutanols

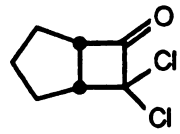
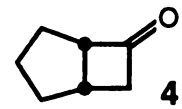
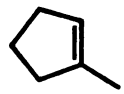
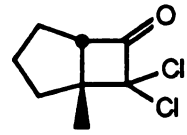
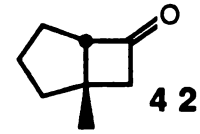
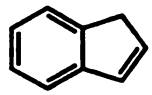
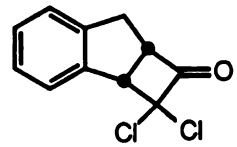
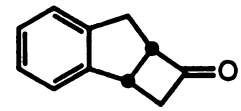
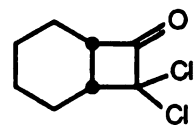
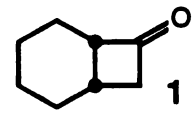
The in situ cycloaddition[26] of dichloroketene with an olefin to give a dichlorocyclobutanone, followed by reductive removal of the chlorine atoms with zinc and acetic acid is illustrated below for cyclopentene. Other related compounds used in this investigation are shown in Table VI.



41

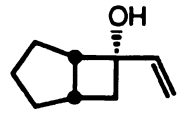
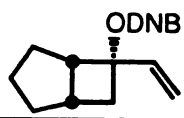
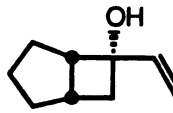
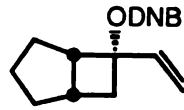
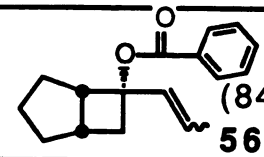
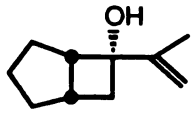
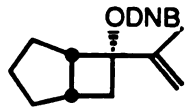
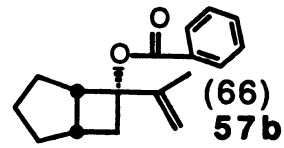
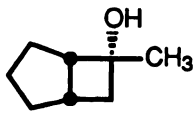
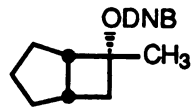
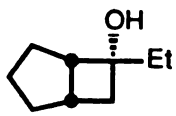
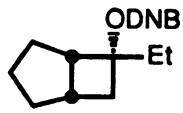
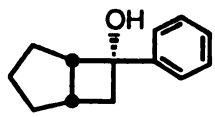
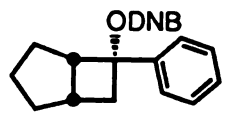
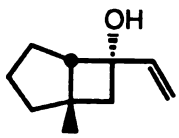
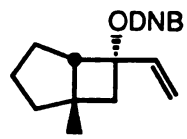
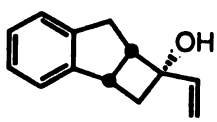
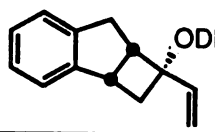
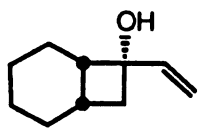
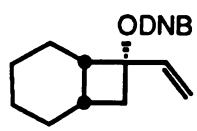
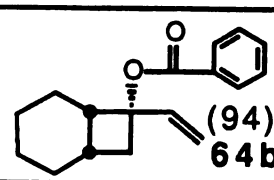
Subsequent addition of Grignard reagents to these cyclobutanones afforded cyclobutanols in good to excellent yields. Finally, benzoates (or dinitrobenzoates) was prepared by treatment of the cyclobutanols with 2 equivalents of benzoyl chloride (or 1, 3-dinitrobenzoyl chloride) in pyridine solution in the presence of catalytic amounts of 4-dimethylaminopyridine (DMAP). The yields of specific products are listed in Table VII.

Table VI. Cycloadducts of Dichloroketene and Olefins

Olefin	Cycloadduct	Reduction Product	Yield (%)
		 **41**	62
		 **42**	35
		 **43**	57
		 **17**	80

Attempts were made to convert vinylcyclobutanol **45** to the corresponding tosylate or methanesulfonate. However, these reactions did not proceed smoothly, probably due to steric hindrance of the endo tertiary alcohol and/or the extreme reactivity of 3°-allylic sulfonate ester.

Table VII. Adducts of Grignard Reagents with Cyclobutanones and their Ester Derivatives

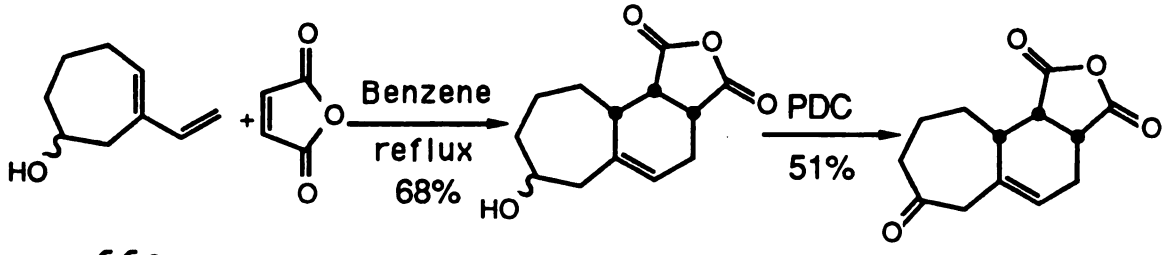
Product(yield %)	Dinotrobenzoate(yield %)	Benzoate(yield%)
 (75) **45**	 (77) **55**	
 (82) **46**	 (65) **56a**	 (84) **56b**
 (92) **47**	 (55) **57a**	 (66) **57b**
 (92) **49a**	 (83) **59a**	
 (82) **50**	 (79) **60**	
 (60) **51**	 (85) **61**	
 (85) **52**	 (83) **62**	
 (92) **53**	 (86) **63**	
 (83) **18a**	 (86) **64a**	 (94) **64b**

* : ODNB : 3,5-Dinitrobenzoate

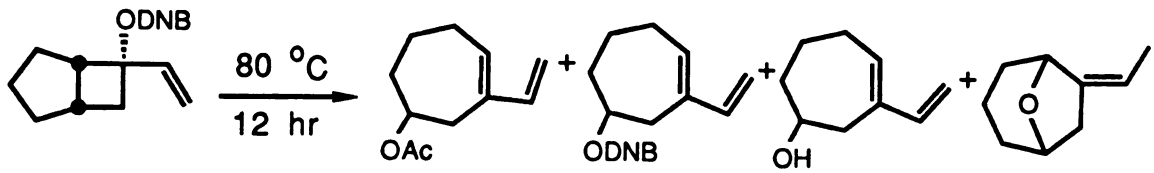
Acetolysis of 6-Alkenyl Bicyclo[3.2.0]heptyl-6 Ester Derivatives

Solvolytic reactions of **55** were carried out under various conditions, the best consisting of glacial or aqueous acetic acid solutions containing potassium acetate or triethylammonium acetate (TEAA) at 80 °C. The results of these experiments are summarized in Table VIII.

Much to our surprise, the only products formed under all reaction conditions were 3-vinyl cycloheptenol-3 (**66c**) and its ester derivatives (**66a** and **66b**). The structure of **66c** was assigned from spectroscopic data as well as chemical reactions. Thus, cycloaddition of **66c** with maleic anhydride provided a 1 : 1 ratio of diastereomeric Diels-Alder products (**82**), indicating the conjugated diene character of **66c**. Oxidation of **82** with pyridinium dichromate (PDC) in DMF solution gave a single isomer (**83**), which was assigned the endo configuration on the strength of Alder's rule.[51]



66c **82** **83**



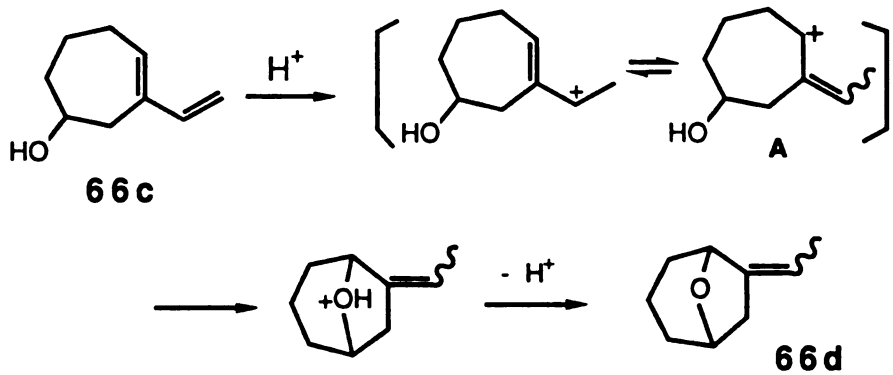
55 66a 66b 66c 66d

Table VIII. The Product Distribution from Solvolyses of Benzoate **55**

Reaction Condition	Yield(%) 66a	66b	66c	66d
4 eq. KOAc/H_2O	5		46	
4 eq. KOAc/HOAc	32	21		
10 eq. KOH HOAc : H_2O (6/1)	43			
2 eq. $^-$OAc* HOAc	66	8		
2 eq. $^-$OAc* HOAc : H_2O (3/1)	54		28	
2 eq. $^-$OAc* 4 eq. $LiClO_4$ HOAc : H_2O (3/1)	24.5	4.7	26.2	
4 eq. $LiClO_4$ H_2O			55	

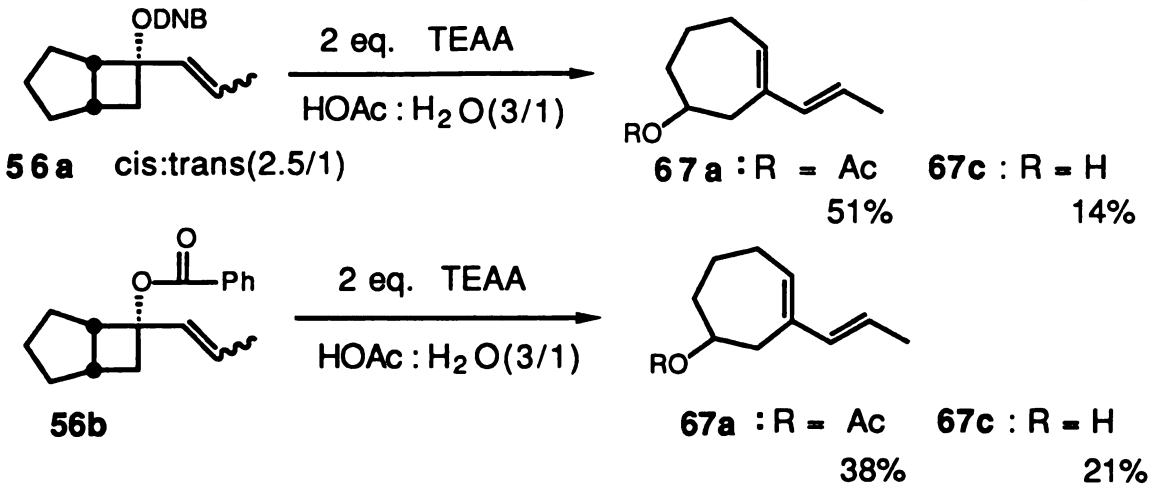
* : 0.1 M Et_3NHOAc in HOAc

Heterogeneous hydrolysis of **55** with 4 equivalents of $LiClO_4$ in H_2O yielded the interesting bicyclic ether **66d**, presumably by internal trapping of allylic cation intermediate **A** by the oxygen atom of the hydroxyl group, as shown in Scheme XXIV.



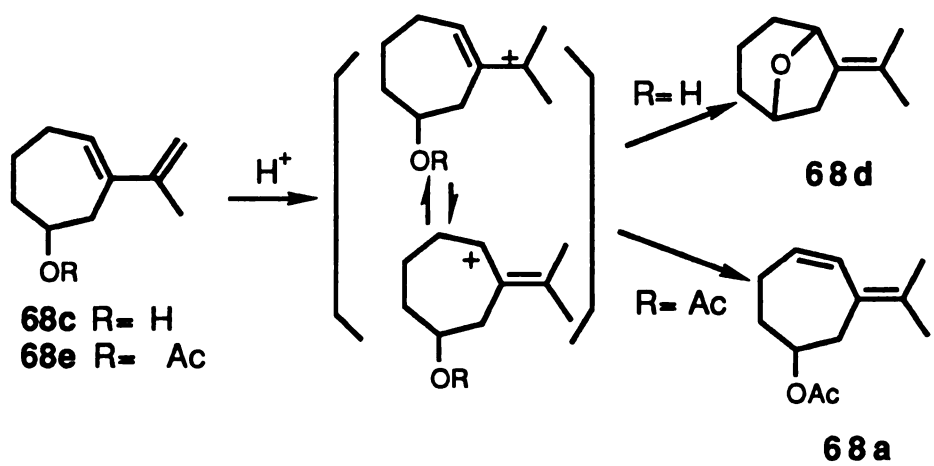
Scheme XXIV

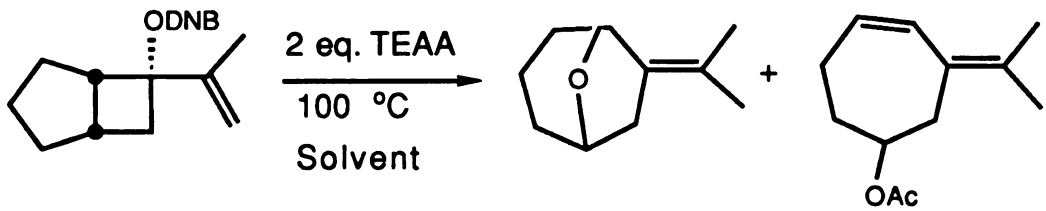
For the solvolysis of **56a** and **56b**, the same conditions which gave the best results for **55** were used. Thus, buffered acetolysis of **56a** (cis : trans = 2.5/1) with TEAA in aqueous acetic acid afforded acetate **67a** and alcohol **67c**. A similar result was obtained in the case of **56b** (Scheme XXV) That dienyl acetate **67a** was a single stereoisomer was confirmed by its ^{13}C NMR spectrum, and the trans configuration was indicated by the vicinal coupling constant (J = 15.1 Hz) of the olefinic protons in the ^{1}H NMR spectrum.



Scheme XXV

The product distribution from solvolysis of **57a** and **57b** was dependent on the reaction conditions, as shown in Table IX and Table X, respectively. Two points should be noted . First, **57a** solvolyzed faster than **57b** in agreement with the fact that dinitrobenzoate is a better leaving group than benzoate. Second, The formation of isomerized diene **68a** (or bicyclic ether **68d**) probably proceeds by way of the stable carbocation intermediate **B**, generating by protonation of **68c** (or **68e**). It should be noted that the ether product was only formed when aqueous solvent systems were used.

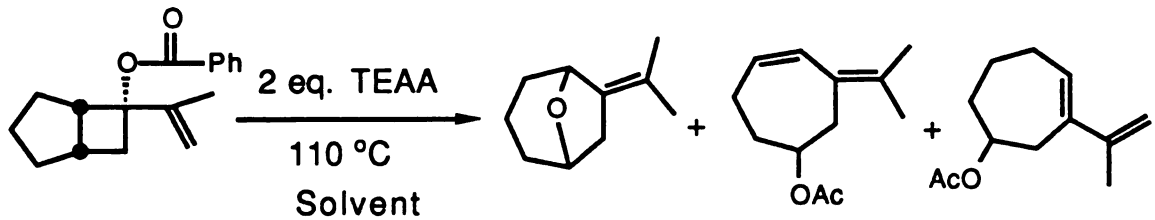




57a **68d** **68a**

Table IX. The product Distribution from Solvolyses of Benzoate **57a**

Reaction Condition(Solvent)	Yield(%) **68d**	**68a**
HOAc		85
HOAc : H_2O (14/1)	25	61
4 eq. $LiClO_4$ HOAc : H_2O (14/1)	35	53
4 eq. $LiClO_4$ HOAc : H_2O (3/1)	42	27
HOAc : H_2O (3/1)	53	27.3
HOAc : H_2O (1/1)	76	18
Reaction Cndition		
H_2O	>90	



57b **68d** **68a** **68e**

Table X. The Product Distribution from Solvolyses of Benzoate **57b**

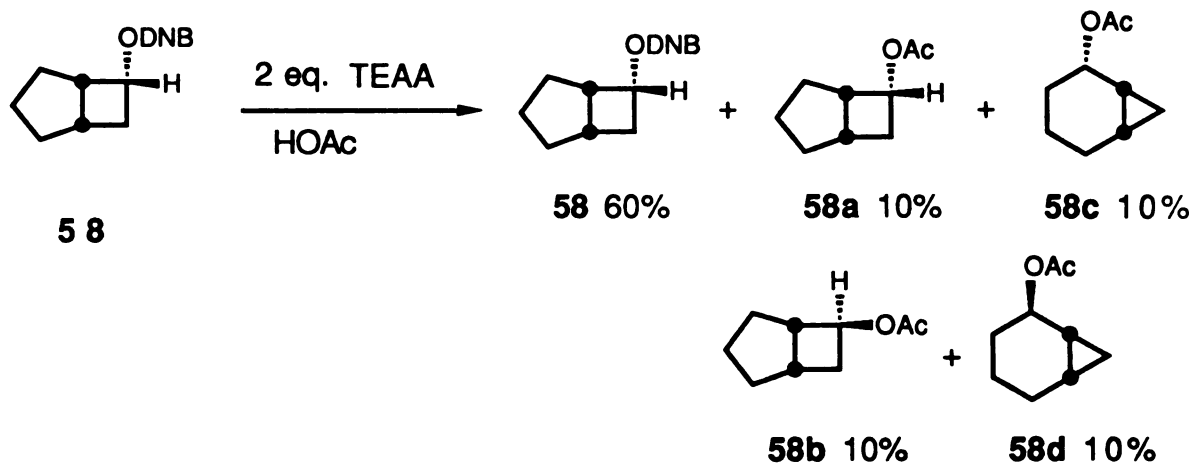
Reaction Condition(Solvent)	Yield(%) **68d**	**68a**	**68e**
HOAc		48.3	43.4
4 eq. $LiClO_4$ HOAc : H_2O (14/1)	39.1	27.5	
4 eq. $LiClO_4$ HOAc : H_2O (3/1)	61.9	28.2	
HOAc : H_2O (3/1)	52.8	35.2	
HOAc : H_2O (1/1)	63	20.1	
HOAc : H_2O (1/2)	77	12.4	
HOAc : H_2O (1/3)	75.7	7	
4 eq. $LiClO_4$ HOAc : H_2O (3/1)	80		
Reaction Condition			
H_2O	76.6		
4 eq. $LiClO_4$ H_2O	69		

Acetolysis of 6-Alkyl Bicyclo[3.2.0]heptyl-6 Ester Derivatives

Our finding that 6-alkenyl bicyclo[3.2.0]heptyl-6 esters (**55** through **57**) solvolyze with facile ring expansion to dienyl alcohols and their derivatives prompted us to explore the generality of this rearrangement by extending our study to the group of esters (**58** through **61**). The results are summarized in Scheme XXVI. Significantly, in all of these cases except **58**, ring expansion products were obtained without significant formation of unrearranged compounds, and yields ranged from 81 to 86%.

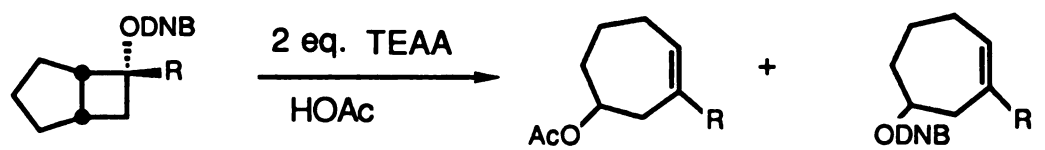
On consideration of the facts summarized in Scheme XXVI, several interesting points emerge. First of all, the high K_{CH_3}/K_H ratio is probably a reflection of the difficulty of forming the cyclobutyl cation in the absence of stabilization by substitution. Secondly, since both **59a** and **59b** led to the same products, although at different rates, both compounds probably react via the same ion(s) on the way to products. Thirdly, a factor of at least 5 was observed in the rate ratio of endo/exo **59**, indicating some anchimetric assistance by σ-bond participation. Finally, the formation of only **71a** and **71b** in the case of **61** was striking. Wiberg reported[47] that solvolysis of **61** in 80% aqueous acetone gave almost equal amounts of rearranged and unrearranged products. Consequently, Wiberg proposed that a phenyl group is able to stabilize the charge at the C_6 position sufficiently to suppress rearrangement. This view was supported by the Olah's observation[52] that ionization of 6-phenyl bicyclo[3.2.0]heptan-6-ol in FSO_3H/SO_2ClF at -149 ^oC gave the unrearranged parent ion by ^{13}C

NMR spectroscopy. Thus it is clear that solvolysis conditions have a marked effect on product distribution.



58 60% **58a** 10% **58c** 10%

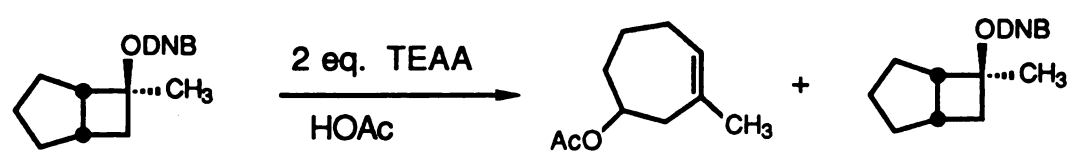
58b 10% **58d** 10%



59a: R = Me **69a** 72% **69b** 9%

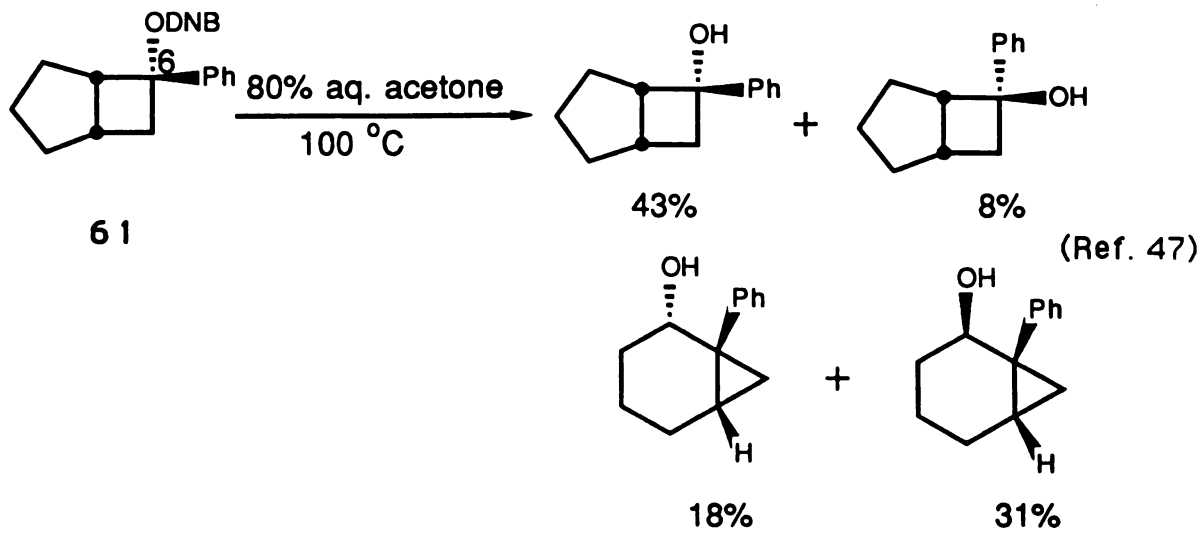
60 : R = Et **70a** 88%

61 : R = Ph **71a** 80% **71b** 6.7%

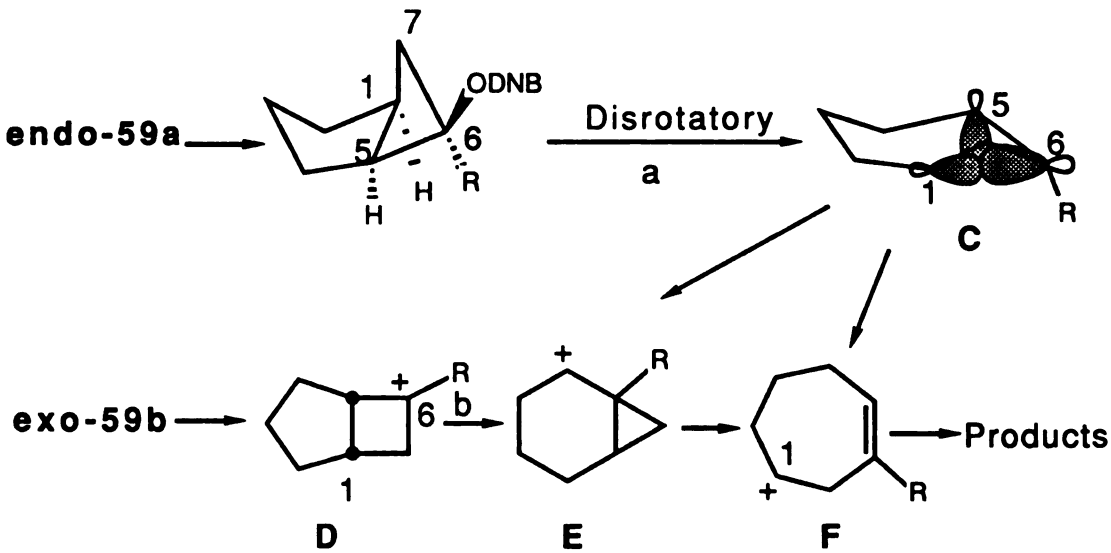


59b **69a** 14% **59b** 56%

Scheme XXVI



As described in the introduction, orbital symmetry considerations indicated[53] that the conversion of a cyclobutyl ion into a cyclopropyl carbinyl ion or a homoallylic ion should occur by disrotatory ring opening, and steric factors that hinder such a process are found to decelerate cyclobutyl solvolysis. Thus in the case of **59a**, to overlap the orbital of the bond being broken with the back side of the developing p orbital, movement occurs in such a way as to move the bridgehead hydrogens away from each other (pathway a). However, in **59b**, the same process would require that the bridgehead hydrogens move toward each other, and this is energetically unfavorable. Consequently, the solvolysis of **59b** probably proceeded through a classical ion which then undergoes a thermodynamically controlled process leading to homoallylic products (pathway b). Thus, both **59a** and **59b** solvolyzed to give the same products, but **59a** solvolyzed faster than **59b** (Scheme XXVII).



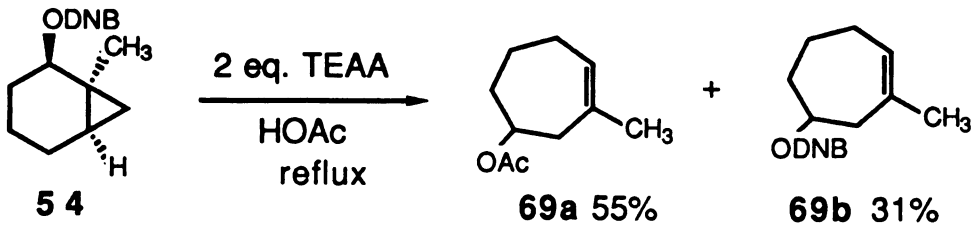
Scheme XXVII

To obtain a better understanding of the solvolysis mechanism, dinitrobenzoates (**54**, **62** and **63**) were synthesized by a slight modification of published procedures,[54] or by methods described in the previous section. For example, **54** was prepared from 2-chloro-2-methyl cyclohexanone by the following sequence : dehydrochlorination (LiCl in DMF), reduction (lithium aluminum hydride), cyclopropanation (CH_2I_2, Zn/Cu) and benzoylation (3,5-dinitrobenzoyl chloride in pyridine, catalytic amounts of DMAP) in 7.8% yield overall.

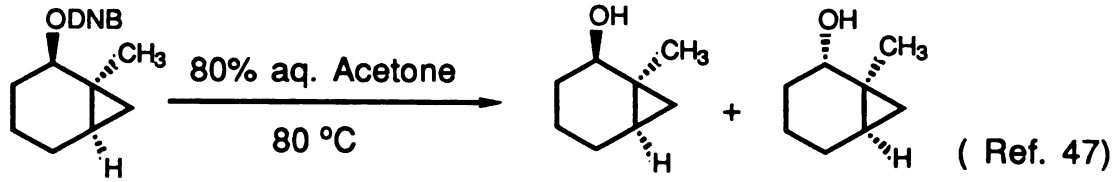
Acetolysis of **54** was carried out with 0.1M TEAA in glacial acetic acid at 90 °C, and the results are summarized in Scheme XXVIII. The data reported by Wiberg and Chen[47] for the same

substrate in aqueous acetone are given for comparison. The formation of ring opened acetate and dinitobenzoate in the less nucleophilic acetic acid medium is consistent with a longer lived carbotion intermediate.

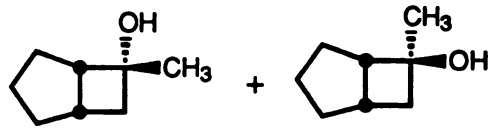
In studying the solvolyses of **55**, **62** and **63**, we found that **63** showed the lowest reactivity. A similar relationship has also been observed by Meinwald,[48] who found that acenaphthylene-fused cyclobutane **76a** has a rate at least 100 times smaller than that of any other endo esters of fused cyclobutanes. The nearly comparable reactivity of **55** and **62** was interesting, since the methyl group at the C_1 position should stabilize carbocation intermediate **F** in Scheme XXVII and facilitate ionization assisted by σ-bond participation.



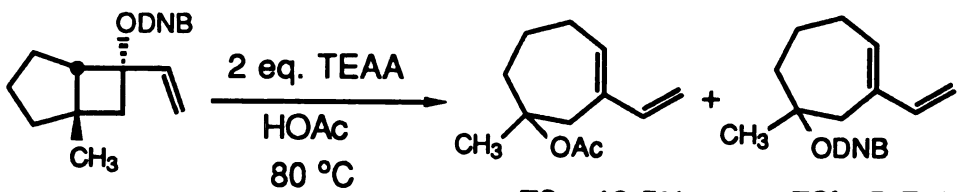
5 4 **69a** 55% **69b** 31%



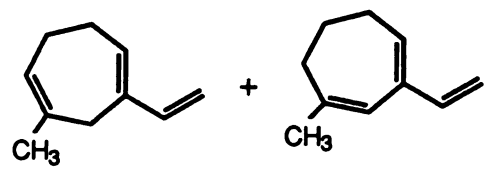
5 4 **49d** 60% **49c** 21% (Ref. 47)



49a 17% **49b** 2%



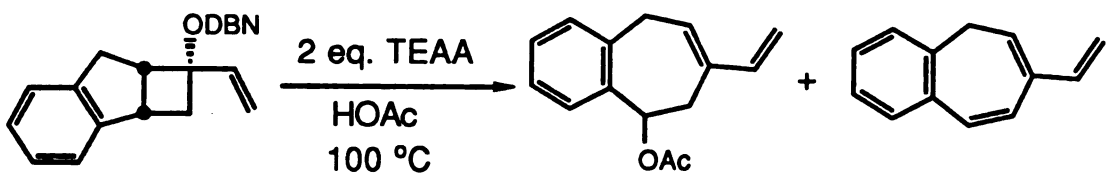
6 2 **72a** 43.5% **72b** 5.7%



72c **72d**

3.5 : 1

25%

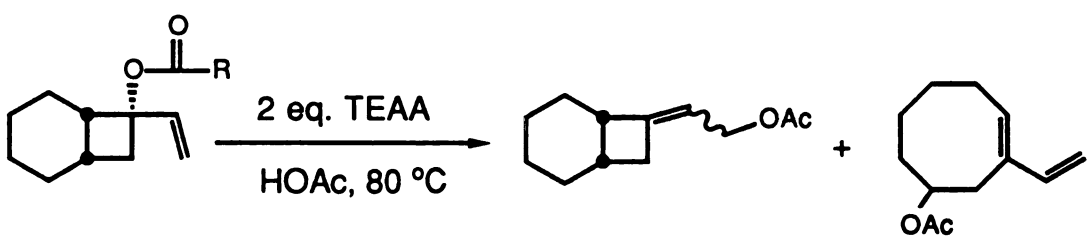


6 3 **73a** 25.3% **73b** 34.5%

Scheme XXVIII

Acetolysis of 7-Vinyl Bicyclo[4.2.0]octyl-7 Ester Derivatives.

Effecting the acetolysis of 7-vinyl endo bicyclo[4.2.0]octyl-7 dinitrobenzoate (**64a**) to a vinyl cyclooctenyl derivative proved to be challenging. Treatment of **64a** with 0.1M TEAA in glacial acetic acid as in the earlier studies afforded not only **74a** (10-15%) but also **74f** (60-75%). A variety of ester derivatives of vinylcyclobutanol **18a**, such as the trifluoroacetate, acetate, benzoate and p-nitrobenzoate were examined under different reaction conditions; however, in all cases the desired dienyl acetate (**74a**) was obtained in only poor yield (10-15%).



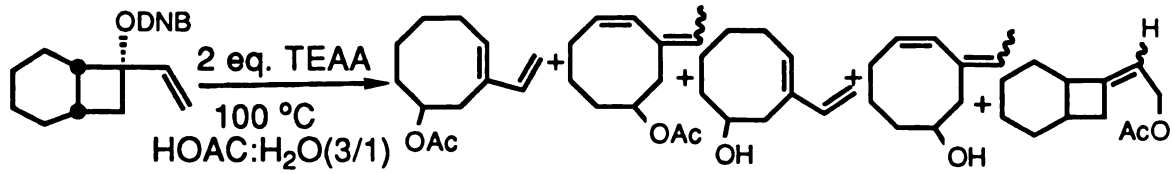
64 **74f** 60-75% **74a** 10-15%

R = CF_3, CH_3, Phenyl, p-Nitrophenyl, 3,5-Dinitrophenyl

We speculated that **74f** was derived by an S_N2' mechanism with nucleophilic attack at the 1°-carbon occurring in preference to conventional S_N2 displacement. In order to obtain a better yield of ring opened products, we decided to modify the reaction medium so as to enhance the formation of a carbocation intermediate in the solvolysis. The so-called " special salt effect " proposed by Winstein[55] for the acetolysis of organic halides or

benzenesulfonates is well-suited to this purpose. Added salts, such as lithium perchlorate or lithium bromide, not only increase the solvolysis rate of alkyl bromides[56] or benzenesulfonates[57] but also trap the solvent-separated ion pair intermediate to form $R^+||\ ClO_4^-$ which then goes on to products.

When ester **64a** was treated with TEAA in aqueous acetic acid in the presence of 2 equiv. of LiBr, an improved yield (25-35%) of cyclooctenyl derivatives was obtained. However, allylic acetate **74f** was still the predominant product (40-45%). Further analysis of the cyclooctenyl products by ^1H NMR indicated a complicated mixture, including not only acetates but also bromides. A similar result was also observed with lithium chloride. We then turned our attention to lithium perchlorate, an anion having little nucleophilic character, as the added salt for the solvolysis reactions. Promising results were obtained and are described in Table XI. With as little as 2 equivalents of $LiClO_4$ the derived vinylcyclooctenyl derivatives (**74a**, **74c**) were the major product. With larger amounts of salt, allylic acetate **74f** could not be detected, and **74a** together with **74c** were obtained in almost 70% yield (run 3). With 8 equivalents of added $LiClO_4$, the yield of the thermodynamically favored isomers (**74d** and **74e**) increased to roughly 20% at the expense of **74c.**

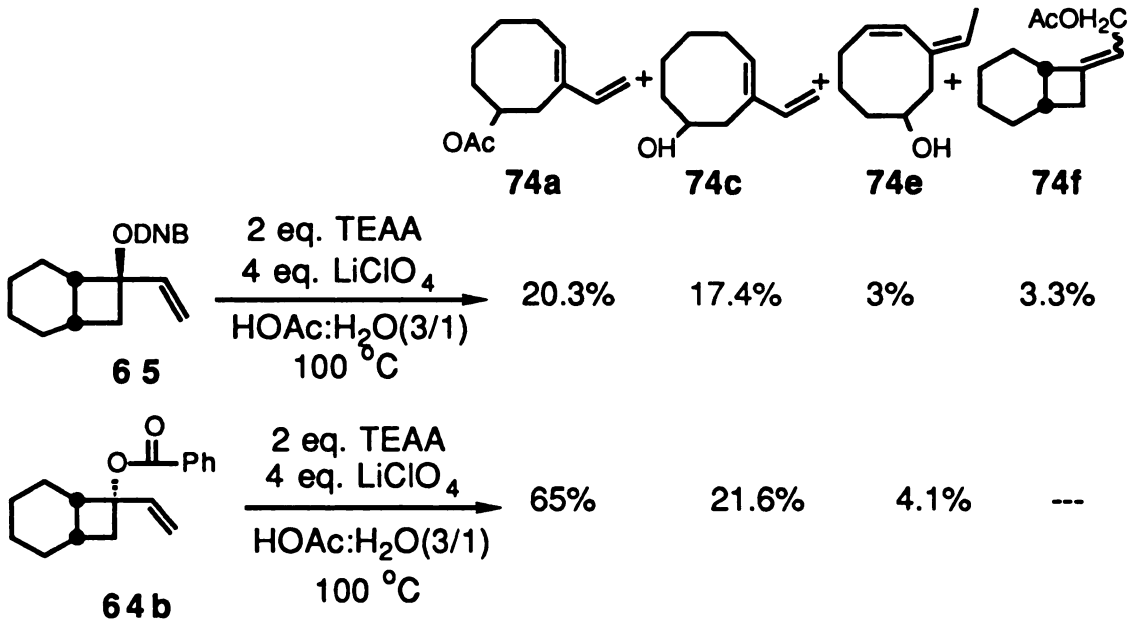


64a **74a** **74d** **74c** **74e** **74f**

Table XI. The Product Distribution from Solvolyses of Benzoate **65a**

Run	Reaction Condition	Yield(%)				
		74a	**74d**	**74c**	**74e**	**74f**
1	2 eq. $LiClO_4$	36.3	<2	14	3	14.5
2	4 eq. $LiClO_4$	40.8	<2	20.5		
3	6 eq. $LiClO_4$	42.8	<2	26.8		
4	8 eq. $LiClO_4$	45.9	16.4	8.2	4.8	

Not surprisingly, on treatment with TEAA and $LiClO_4$ in aqueous acetic acid, exo ester **65** reacted slower than endo ester **64a** to give **74a** (20.3%), **74c** (17.4%), and **74e** (3%) along with **74f** (3.2%). This was consistent with our previous observation in the acetolysis of bicyclo[3.2.0]heptyl-6 systems. Finally the most effective procedure for preparing the desired vinycyclooctenyl compoundswas the acetolysis of benzoate **64b**. This afforded vinyl cyclooctenyl derivatives in over 85% yield without any formation of **74f** (Scheme XXIX).



Scheme XXIX

In summary, we have identified conditions for the conversion of a variety of bicyclo[3.2.0]heptyl-6 derivatives to their corresponding cycloheptenol derivatives. The analogous 7-vinyl bicyclo[4.2.0]octyl-7 esters have also been converted to vinyl cyclooctenol derivatives in good to excellent yields. An advantage of this method is the facility with which alkyl or alkenyl cycloheptenols and their derivatives can be prepared from readily available bicyclo[3.2.0]heptanone-6 by three simple operations (Grignard reagent addition, benzoylation and acetolysis). In particular, The two ring functionalities (double bond and OR group) created in this process should allow further synthetic elaboration to proceed in any of several directions.

CYCLOBUTANES IN ORGANIC SYNTHESIS

PART I

REGIO AND STEREOSELECTIVE REARRANGEMENTS OF 7-OXIRYLBICYCO[4.2.0]OCTAN-7-OLS

Experimental Section

Unless otherwise indicated, all reactions were conducted under a dry argon or nitrogen atmosphere, using solvents distilled from appropriate drying agents. Reactions were monitored by thin layer chromatography (Silica Gel 60 F_{254}, E. Merck or Al Sil G/UV_{254}, Whatman) with visualization by ultraviolet fluorescence or chemical reagents (30% aqueous H_2SO_4 or ammonium molybdate in 10% aqueous H_2SO_4) followed by heating. Analytical samples were prepared by flash chromatography using Merck Silica Gel (230-400 mesh), as described by Still et al.[58]

Melting points were determined on either a Hoover-Thomas apparatus or a Reichert hot-stage microscopic, and are uncorrected. Infrared (IR) spectra were taken on a Perkin-Elmer 237 B or a Perkin-Elmer 599 spectrophotometers in dichloromethane solution unless indicated otherwise. ^1H NMR spectra and ^{13}C NMR spectra were taken in deuteriochloroform solution and recorded on a Bruker 250 MHz spectrometer operating at 69.8 MHz for carbon, and were calibrated in parts per million (δ) from tetramethylsilane (TMS) as an internal standard. UV absorption spectra (in 95% EtOH or CH_3CN) were measured with a Perkin-Elmer 200 spectrophotometer. Mass spectra (MS) were obtained with a Finnigan 400 GC/MS spectrometer and recorded as m/e vs relative intensity. High resolution mass measurements were made on a JEOL-HX 110 mass spectrometer. Elemental analyses were conducted by Spang Microanalytical Laboratory, Eagle Harbor, MI.

Cycloaddition of Cyclohexene with Dichloroketene

A solution of freshly distilled trichloroacetyl chloride (2.8 ml, 25 mmol) in dry ether (250 ml) was added over 4 hr to a stirred, refluxing mixture of cyclohexene (2.6 ml, 25 mmol) and activated zinc[27] (5 g) in Et_2O (250 ml). The reaction mixture was stirred at reflux overnight, then filtered through a pad of Celite. The filtrate was concentrated to c.a. 25% of its original volume, an equal amount of pentane was added, and this mixture was washed with cold water, cold saturated aqueous $NaHCO_3$, brine and dried over Na_2SO_4. Kugelrohr distillation of the product afforded dichlorocyclobutanone **16** (4.2 g, 87%).

Characteristic properties of **16**[59] : IR, 1800 cm^{-1}; ^1H NMR, 3.90 (1H, m), 2.93 (1H, m), 1.02-2.18 (8H, m).

Dechlorination of Dichlorocyclobutanone 16 with Zinc Dust

A stirred solution of ketone **16** (2.0 g, 10.4 mmol) in glacial acetic acid (25 ml) was cooled and stirred while zinc dust (2.5 g, 38 mmol) was added portionwise. The reaction mixture was warmed to 75 °C, stirred overnight and then filtered through Celite. The filtrate was mixed with ether, washed several times with cold water,followed by aqueous sodium bicarbonate, and dried. Kugelrohr distillation of the product (40-45 °C, 0.3 mmHg) afforded cyclobutanone **17** (1.15 g, 90%).

Characteristic properties of **17**[59] : IR, 1780 cm^{-1}; ^1H NMR, 3.27 (1H, m), 3.13 (1H, m), 2.50 (1H, m), 2.44 (1H, m), 2.15 (1H, m), 1.95 (1H, m), 1.10-1.80 (6H, m).

Preparation of Vinyl Alcohol 18a

To a stirred solution of Grignard reagent, prepared by treating vinyl bromide (7.7 ml, 10.8 mmol) in tetrahydrofuran (20 ml) solution with magnesium (3.18 g, 12.9 mmol), activated by 1,2-dibromoethane (0.3 ml), was added a solution of cyclobutanone **17** (5.34 g, 4.3 mmol) in THF (20 ml). The mixture was stirred overnight at room temperature, then quenched by addition of saturated aqueous ammonium chloride. Extraction with ether, followed by conventional workup and Kugelrohr distillation (48-50 °C, 0.25 mmHg), gave vinylcyclobutanol **18a** (4.433 g, 83%).

Characteristic properties of **18a**[60] : IR, 3450-3600 cm^{-1}; ^1H NMR, 6.15 (1H, dd, J = 10.7 & 17.4 Hz), 5.25 (1H, dd, J = 17.4 & 1.2 Hz), 5.00 (1H, dd, J = 10.7 & 1.2 Hz), 0.84-2.10 (13H, m); ^{13}C NMR, 143.5, 111.0, 73.1, 42.5, 37.1, 25.9, 23.5, 22.6, 21.7, 21.5.

Wittig Reaction of Ketone 17 in Toluene Solution

A mixture of ethyltriphenylphosphonium bromide (30 g, 81 mmol) with 0.5M ^{t}-AmOK in toluene (180 ml, 90 mmol) was refluxed for 30 min. A solution of cyclobutanone **17** (2.55 g, 21 mmol) in toluene (10 ml) was then added dropwise, and this mixture was refluxed for 2 hr, cooled and poured into ice water (100 ml).. The resulting mixture was extracted with toluene, and the extracts were washed with 10% aqueous HCl, saturated aqueous $NaHCO_3$, brine and dried over Na_2SO_4.

To one-third of the ethylidenecyclobutane solution thus obtained, cooled to 0 °C,was added m-chloroperbenzoic acid (MCPBA). The progress of this reaction was followed by TLC, and additional

MCPBA was occasionally added in order to complete the reaction. The reaction was quenched with 10% aqueous Na_2SO_3, brine and dried over Na_2SO_4. Removal of the solvent followed by flash chromatography of the residue (1 : 5, ether/hexane) gave a mixture of epoxides **26** which was used immediately in the next step.

To 1.55M n-butyl lithium in hexane (6.5 ml, 10.1 mmol) at 0 °C was added a solution of diisopropylamine (1.5 ml, 10.4 mmol) in ether (20 ml) . After 20 min., a solution of the epoxides **26** in ether (10 ml) was added. This mixture was then stirred at reflux for 2 hr, and the reaction was quenched with MeOH and diluted with ether and water. The organic layer was washed with cold 10% aqueous HCl, brine and dried over Na_2SO_4. Evaporation of the solvent followed by flash chromatography (3 : 1 pentane/ether) gave various ratios of vinylcyclobutanols **18a** and **18b**, depending on the reaction temperature. These results are listed in Table III.

Characteristic properties of **18b** : IR, 3300-3650 cm^{-1}; ^1H NMR, 6.09 (lH, dd, J = 10.7 & 17.0 Hz), 5.23 (1H, dd, J = 17.0 & 1.5 Hz), 5.12 (1H, J = 10.7 & 1.5 Hz), 2.62 (1H, m), 2.42 (1H, m), 2.18 (1H, m),1.92 (1H, m), 0.78-1.88 (9H, m); ^{13}C NMR, 141.5,113.7, 44.2, 36.4, 26.9, 25.8, 23.2, 22.4, 22.0; MS, 152 (2), 135 (49), 109 (13), 81 (31), 70 (100), 55 (80); High resolution MS, calculate for $C_{10}H_{16}O$, 152.1206, found, 152.1198.

Wittig Reaction of Ketone 17 in Dimethyl Sulfoxide Solution

A solution of dismyl sodium was prepared by heating a suspension of sodium hydride (0.612 g, 25.5 mmol) in DMSO (60 ml)

at 60 °C for 1 hr. After cooling to room temperature, a solution of ethyltriphenylphosphonium bromide (9.5 g, 25.5 mmol) in DMSO (30 ml) was added dropwise, the resulting red solution was stirred for 45 min., and a solution of cyclobutanone **17** (1.1926 g, 9.6 mmol) in DMSO (15 ml) was added. The resulting mixture was heated at 60 °C for 65 hr, cooled, poured into ice water (100 ml) and extracted with hexane. The hexane extracts were washed with cold 10% aqueous HCl, water, brine and dried over Na_2SO_4 . Evaporation of the solvent followed by chromatography on silica gel (hexane) gave a 1 : 1 E/Z mixture of ethylidenecyclobutanes **25** (0.628 g, 48%).
Characteristic properties of **25** : ^1H NMR, 5.12 (1H, m), 2.93 (1H, m), 2.52 (1H, m), 2.04-2.40 (2H, m), 0.80-1.96 (11H, m).

Preparation of Epoxy Cyclobutanols 9

Vinylcyclobutanols **18a** and **18b** were epoxidized by MCPBA. A solution of the substrate (1.00 g, 6.6 mmol) in methylene chloride (20 ml) was cooled (ice bath) and treated with MCPBA (ca. 10 mmol) by dropwise addition of a methylene chloride solution of the peracid. Following an overnight reaction period (25 °C), the reaction mixture was filtered and washed with 10% aqueous Na_2SO_3 and brine. The dried solution yielded an oily product which was purified by chromatography (1 : 3 pentane/ether) to give 1.028 g of a 1 : 1 mixture of
diastereomeric epoxycyclobutanols **9c** and **9d** (93%).
Characteristic properties of **9c** : IR, 3400-3650 cm^{-1}; ^1H NMR, 3.25 (1H, m), 2.74 (2H, m), 2.48 (2H, m), 1.10-2.30 (11H, m); ^{13}C NMR (acetone, d-6), 75.5, 52.5, 43.3, 42.2, 33.2, 27.0, 26.1, 23.2,

22.8, 22.2; MS, 168 (2), 149 (30), 139 (100), 86 (20); High resolution MS, calculated for $C_{10}H_{16}O_2$, 168.1151; found, 168.1160. Characteristic properties of **9d** : IR, 3450-3600 cm^{-1}; ^1H NMR, 3.28 (1H, dd, J = 4.1 & 2.8 Hz), 2.85 (1H, dd, J = 5.2 & 2.8 Hz), 2.75 (1H, dd, J = 5.2 & 4.1 Hz), 2.60 (1H, m), 2.36 (1H, m), 2.20 (1H, m), 1.20-2.20 (10H, m); ^{13}C NMR, 76.5, 54.3, 44.2, 43.3, 34.1, 27.1, 25.7, 22.4, 22.3, 21.9; MS, 168 (2), 167 (13), 149 (100), 123 (35), 108 (33), 97 (70), 73 (45); High resolution MS, calculated for $C_{10}H_{16}O_2$, 168.1151; found, 168.1158.

Isomers **9a** and **9b** were prepared from the corresponding bromohydrins (**38a** and **38b**) after chromatography separation, as described below.

Characteristic properties of **9a** : IR, 3500 cm^{-1}; ^1H NMR, 3.21 (1H, dd, J = 4.0 & 2.9 Hz), 2.83 (1H, dd, J = 5.0 & 2.8 Hz), 2.78 (1H, dd, J = 5.0 & 4.0 Hz), 1.01-2.45 (13H, m); ^{13}C NMR, 70.7, 56.7, 44.4, 39.5, 36.1, 26.1, 24.3, 22.6, 21.7, 21.1.

Characteristic properties of **9b** : IR, 3500 cm^{-1}; ^1H NMR, 3.27 (1H, dd, J = 2.5 & 5.0 Hz), 2.82 (1H, dd, J = 2.5 & 5.0 Hz), 2.77 (1H, dd, J = 5.0 & 5.0 Hz), 0.91-2.45 (13H, m); ^{13}C NMR, 71.5, 56.8, 44.1, 40.0, 35.1, 27.0, 24.8, 23.3, 22.4, 21.9.

Preparation of Bromohydrins 38

A solution of an epoxycyclobutanol isomer, **9abcd**, (0.3323 g, 2.0 mmol) in THF (10 ml) was stirred at room temperature while magnesium bromide etherate (0.68 g, 2.4 mmol) was added. Thirty minutes later the reaction mixture was quenched with water and carefully acidified by the addition of 1N hydrochloric acid. Ether

extraction in the usual manner gave crude bromohydrin which was purified by chromatography (1 : 3 pentane/ether). From a 1 : 1 mixture of **9a** and **9b** the respective bromohydrins (**38a** and **38b**) were obtained, each in 46% each isolated yield. The other isomers (**38c** and **38d**) were obtained from **9c** and **9d** respectively in > 95% yield.

Characteristic properties of **38a** : R_f = 0.30 (1 : 3 pentane/ether); mp, 110-112 °C; IR (KBr), 3500 cm^{-1}; ^1H NMR, 3.88 (1H, m) , 3.62 (1H, dd, J = 2.3 & 10.6 Hz), 3.49 (1H, dd, J = 10.6 & 9.6 Hz), 1.03-2.51 (14H, m); ^{13}C NMR (DMSO, d-6), 76.2, 75.8, 39.6, 37.6, 35.5, 27.3, 24.8, 23.2, 22.2, 20.8.

Characteristic properties of **38b** : R_f = 0.58 (1 : 3 pentane/ether); mp, 142-143 °C; IR (KBr), 3550 cm^{-1}; ^1H NMR, 3.91 (1H, dd, J = 10.1 & 2.3 Hz), 3.65 (1H, dd, J = 10.7 & 2.3 Hz), 3.51 (1H, dd, J = 10.1 & 10.7 Hz), 0.93-2.63 (14H, m); ^{13}C NMR, 76.8, 75.6, 38.2, 37.0, 35.9, 27.0, 24.8, 22.0, 21.4, 21.1.

Characteristic properties of **38c** : mp, 138-140 °C; IR (KBr), 3300-3650 cm^{-1}; ^1H NMR, 3.92 (1H, dd, J = 9.3 & 2.9 Hz), 3.50 (1H, dd, J = 10.8 & 9.3 Hz), 3.43 (1H, dd, J = 10.8 & 2.9 Hz), 1.01-2.90 (14H, m); ^{13}C NMR (acetone, d-6), 78.9, 76.2, 43.0, 36.9, 36.7, 27.3, 26.8, 23.5, 23.1, 22.1.

Characteristic properties of **38d** : mp, 97-98 °C; IR (KBr), 3250-3600 cm^{-1}; ^1H NMR, 3.97 (1H, dd, J = 7.6 & 4.8 Hz), 3.47 (2H, m), 1.02-2.90 (14H, m); ^{13}C NMR (acetone, d-6), 78.5, 75.0, 44.8, 36.3, 34.3, 26.8, 23.5, 23.1, 22.2.

Base-Induced Cyclization of Bromohydrins 38 to Epoxycyclobutanols 9

A stirred solution of bromohydrin **38a** (95 mg, 0.38 mmol) in methanol (5 ml) was treated with 1N sodium hydroxide in methanol (0.4 ml, 0.4 mmol). After 24 hr the reaction mixture was neutralized with dilute aqueous hydrochloric acid and diluted with ether. The organic layer was washed and dried; removal of the solvent gave 63 mg (98%) of epoxycyclobutanol **9a**.

In a similar reaction bromohydrin **38b** gave **9b** in 75% yield.

Boron Trifluoride-Catalyzed Rearrangement of 9

The following procedure is typical. To a stirred solution of **9a** and **9b** (0.331 g, 2 mmol) in CH_2Cl_2 (10 ml), cooled to -78 °C, was added ca. 0.2 mmol of $BF_3 \cdot OEt_2$ via syringe. This mixture was stirred for 90 min., quenched with water and mixed with more CH_2Cl_2. Conventional workup and evaporation of the solvent gave a residue which was purified by chromatography (1 : 3 pentane/ether) to provide ketol **29a** (0.15 g, 42.7%, R_f = 0.2), and recovered **9b** (0.16 g, 49.5%, R_f = 0.39).

Characteristic properties of **29a** : IR, 3300-3650, 1705 cm^{-1}; ^1H NMR, 3.90 (1H, dd, J = 11.2 & 7.4 Hz), 3.62 (1H, dd, J = 11.2 & 6.9 Hz), 2.59 (1H, m), 2.03-2.52 (5H, m), 1.31-1.83 (8H, m); ^{13}C NMR, 221.3, 58.9, 58.3, 38.6, 38.2, 33.3, 26.2, 24.5, 23.4, 19.8; MS, 168 (5), 108 (50), 95 (11), 67 (48), 55 (47), 41 (100); High resolution MS, calculated for $C_{10}H_{16}O_2$, 168.1151; found 168.1160.

Characteristic properties of **29c** : Yield, 88%; IR, 3350-3600, 1710 cm^{-1}; ^1H NMR, 3.84 (1H, dd, J = 10.8 & 5.2 Hz), 3.67 (1H, dd, J = 10.8

& 6.4 Hz), 0.85-2.59 (14H, m); ^{13}C NMR, 222.3, 62.9, 50.4, 47.6, 34.6, 29.5, 29.1, 24.4, 22.9, 22.7; MS, 168 (10), 150 (5), 12 (15), 95 (27), 81 (75), 67 (100), 55 (53), 41 (95).

Characteristic properties of **29d** : Yield, 73.8%; IR, 3450-3600, 1725 cm^{-1}; ^1H NMR, 3.79 (1H, dd, J = 4.3 & 11.7 Hz), 3.59 (1H, dd, J = 6.1 & 11.7 Hz), 2.10-2.51 (6H, m), 0.85-1.80 (8H, m); ^{13}C NMR, 222.3, 60.5, 50.4, 45.8, 36.7, 33.7, 28.5, 25.6, 24.3, 20.4; MS, 168 (5), 150 (5), 122 (6), 108 (58), 93 (21), 79 (38), 67 (58), 55 (50), 41 (100).

Trifluoroacetic Acid (TFA)-Catalyzed Rearrangement of 9

To a stirred solution of **9a** and **9b** (1.0987 g, 6.4 mmol) in $CHCl_3$ (50 ml) was added TFA (0.6 ml, 7.8 mmol). The mixture was refluxed with stirring for 24 hr, then quenched with water. Conventional workup followed by removal of the solvent gave an oil which was purified by chromatography, using 1 : 3 ether/pentane as eluent, to provide enones **34a** (622 mg, 68.5%, R_f = 0.5), **34c** (29 mg, 3%, R_f = 0.2) and **34d** (63.7 mg, 7%, R_f = 0.3).

Characteristic properties of **34a** : IR, 1720, 1640 cm^{-1}; UV (EtOH), λ_{max} 236 (ε_{max} 8000); ^1H NMR, 6.15 (1H, d, J = 3 0 Hz), 5.15 (1H, dd, J = 3.0 & 1.0 Hz), 0.84-2.37 (12H, m); ^{13}C NMR, 207.0, 146.8, 115.8, 44.1, 40.8, 33.3, 28.5, 25.8, 23.7, 20.4; MS, 150 (20), 108 (98), 93 (53), 79 (73), 41 (100), 39 (90); High resolution MS, calculated for $C_{10}H_{14}O$, 150.1045; found, 150.1039.

Characteristic properties of **34c**[61] : IR, 1675, 1625 cm^{-1}; UV (EtOH), λ_{max} 240 (ε_{max} 6500); ^1H NMR, 2.81 (1H, m), 2.49 (2H, m), 1.58 (3H, s), 0.78-2.18 (8H, m).

Characteristic properties of **34d**[62] : IR, 1685, 1645 cm^{-1}; UV (EtOH), λ_{max} 237 (ε_{max} 7800); ^1H NMR, 2.71 (1H, m), 1.13 (3H, d, J = 6.0 Hz), 1.10-2.42 (10H, m).

In a similar procedure, the reaction of **9c** with TFA in $CHCl_3$ gave enones, **34a** (20%) and **34c** (20%). Treatment of **9d** with TFA in $CHCl_3$ afforded **34a** (28%) and **34c** (13.6%), along with recovery of **9d** (36.8%).

Preparation of Enones 34 from Ketols 29

Method 1 : A mixture of ketol **29a** (75 mg, 0.45 mmol), Dowex 50x8-100 ion acidic exchange resin (50 mg) and molecular sieve 4A in $CHCl_3$ (20 ml) was refluxed overnight. Filtration, followed by evaporation of the solvent afforded enone **34a** (50.2 mg, 75%).

Method 2 : To a cold solution (ice bath) of ketol **29d** (159.5 mg, 0.95 mmol) and Et_3N (0.5 ml) in CH_2Cl_2 (20 ml) was added methanesulfonyl chloride (0.5 ml). This mixture was stirred for 2 hr at 0-5 °C before it was quenched by the addition of water (2 ml) and saturated aqueous ammonium chloride. The organic layer was washed with 10% aqueous citric acid, saturated aqueous $NaHCO_3$, brine and dried over Na_2SO_4. Evaporation of the solvent and chromatography of the crude product afforded mesylate (elution with 1 : 3 hexane/ether, R_f = 0.22).

Characteristic properties of mesylate of **29d** : IR, 1740, 1352, 1175 cm^{-1}; ^1H NMR, 4.42 (1H, dd, J = 4.8 & 9.7 Hz), 4.32 (1H, dd, J = 4.4 & 9.8 Hz), 2.95 (3H, s), 0.85-2.53 (13H, m); ^{13}C NMR, 217.0, 69.0, 50.1, 44.9, 36.6, 33.8, 29.2, 28.6, 24.0, 22.4.

To this mesylate in ether (20 ml) was added DBU (0.5 ml) at 0 °C. The mixture was stirred at the same temperature for 2 hr, and quenched with cold 10% aqueous HCl. Following workup, the crude product was chromatographed to give 134.5 mg of enone **34b** (94% yield overall).

Characteristic properties of **34b** : IR, 1710, 1636 cm^{-1}; UV (EtOH), λ_{max} 235 (ε_{max} 8500); ^1H NMR, 6.03 (1H, m), 5.30 (1H, m), 2.65 (1H, m), 2.95 (1H, m), 2.04-2.43 (2H, m), 0.80-1.75 (8H, m); ^{13}C NMR, 206.8, 144.0, 117.9, 49.6, 34.3, 33.4, 29.2, 24.0, 22.8, 22.5; High resolution MS, calculated for $C_{10}H_{14}O$, 150.1045; found, 150.1036.

Ketol **29c** was converted to a mesylate derivative and then eliminated by DBU treatment, as above. Chromatography of the crude product gave **34a** in 78% overall yield.

Characteristic properties of the mesylate derived from **29c** : IR, 1745, 1360, 1180 cm^{-1}; ^1H NMR, 4.43 (1H, dd, J = 10.0 & 4.0 Hz), 4.28 (1H, dd, J = 10.0 & 3.8 Hz), 2.92 (3H, s), 1.12-2.50 (13H, m); ^{13}C NMR, 216.8, 66.7, 47.4, 45.4, 36.5, 36.3, 33.1, 28.1, 25.0, 24.2, 19.8.

Preparation of Enone 34a from Dichlorocyclobutanone 16

To a solution of CH_2N_2 in ether, prepared by the reaction of KOH (5.6 g) with N-methyl-N-nitroso-p-toluenesulfonamide (10.7 g, 50 mmol) in 1 : 3 diethyleneglycol/ether (60 ml) solution,[65] was added a solution of ketone **16** (5.0416 g, 26 mmol) in Et_2O (10 ml), followed by MeOH (10 ml). Immediately, a brisk evolution of nitrogen ensued. After 30 min., excess diazomethane was destroyed with a few drops of AcOH. The solvent was evaporated to afford crude

dichlorocyclopentanone which was used immediately in the next step.

To a stirred solution of the foregoing crude product in glacial acetic acid (40 ml) was added zinc dust (10 g) in portion. The reaction mixture was raised to 70 °C, stirred for 3 hr and filtered through Celite. The filtrate was mixed with ether, washed several times with cold water followed by aqueous sodium bicarbonate and dried. Kugelrohr distillation of the crude product gave cyclopentanone **32** (2.95 g, overall 86%).

Characteristic properties of **32**[63] : IR, 1740 cm^{-1}; ^1H NMR, 1.88-2.36 (6H, m), 1.07-1.66 (8H, m).

An acetonitrile solution of ketone **32** (820.4 mg, 5.94 mmol) and N, N-dimethyl(methylene)ammonium chloride[66] (1.66 g, 19 mmol) was refluxed with stirring for 6 hr. After addition of K_2CO_3 , this mixture was stirred for 6 hr at room temperature. Removal of the solvent and the residue was diluted with ether and aqueous $NaHCO_3$ The organic layer was dried over Na_2SO_4. Evaporation of the solvent yielded an oily residue, which was purified by flash chromatography using 1 : 6 ether/hexane as eluent. This afforded enone **34a** (171.9 mg, 19%, R_f = 0.34), and dimethylene ketone **34e** (27.5 mg, 29%, R_f = 0.23).

Characteristic properties of **34e** : IR, 1700, 1640 cm^{-1}; ^1H NMR, 6.04 (2H, dd, J = 1.0 & 0.8 Hz), 5.27 (2H, dd, J = 1.0 & 0.5 Hz), 2.29 (2H, m), 1.24-1.73 (8H, m); ^{13}C NMR, 195.6, 149.0, 116.5, 39.4, 27.4, 22.0.

Preparation of Cis-Diols 35 from Enones 34

To enone **34b** (351 mg, 2.34 mmol) was added 0.4M $CeCl_3 \cdot 6H_2O$ in methanol solution (6 ml, 2.4 mmol), followed by addition of $NaBH_4$ (15 mg, 3 mmol)at 0 °C. The reaction mixture was allowed to react for 20 min., and then quenched with cold 5% aqueous HCl. After conventional workup, the residue was purified by chromatography (1 : 1 ether/pentane) to give allylic alcohol **36b** (308.4 mg, 88.4%) and its epimer **36d**.

Characteristic properties of **36b** : IR, 3560 cm^{-1}; ^1H NMR, 5.05 (1H, dd, J = 2.5 & 5.0 Hz), 4.94 (1H, dd, J = 2.5 & 5.0 Hz), 4.41 (1H, m), 0.70-2.40 (13H, m); ^{13}C NMR, 154.2, 107.0, 78.2, 42.7, 32.2, 31.0, 26.6, 24.3, 20.7.

A solution of **36b** (108 mg, 7.1 mmol) in pyridine (10 ml) was mixed with acetic anhydride (2 ml, 19 mmol), and this mixture was refluxed with stirring for 3 hr, cooled, and poured onto ice (20 ml). The aqueous solution was extracted twice with ether and the combined extracts were washed with 10% aqueous HCl, saturated aqueous $NaHCO_3$, and brine. The dried extract solution yielded an oily product which was chromatographed to give allylic acetate **37b** (137 mg, 98%).

Characteristic properties of **37b** : IR, 1725, 1235 cm^{-1}; ^1H NMR, 5.42 (1H, m), 5.02 (2H, m), 2.11 (3H, s), 0.90-2.50 (12H, m); ^{13}C NMR, 170.8, 148.8, 108.6, 79.1, 40.6, 33.1, 31.1, 26.5, 24.2, 21.5, 20.9, 20.7.

To a stirred solution of allylic acetate **37b** (63 mg, 0.32 mmol) in THF (5 ml) was added 1M B_2H_6 in THF (1 ml, 1 mmol) at 0 °C. The reaction mixture was stirred at 0 °C for 3 hr, then quenched

with 10% aqueous NaOH (10 ml) and 30% H_2O_2 (3 ml). Extraction with ether, followed by conventional workup and chromatography gave cis-diol **35b** (32.1 mg, 58%).

Characteristic properties of **35b** : IR, 3200-3600 cm^{-1}; ^1H NMR, 4.42 (1H, m), 3.76 (2H, m), 2.38 (4H, m), 1.98 (2H, m), 1.00-1.77 (9H, m); ^{13}C NMR, 77.6, 64.2, 43.6, 44.4, 35.7, 29.6, 27.9, 24.8, 22.0, 21.8; MS, 168 (3),152 (13), 108 (27), 95 (23), 81 (72), 67 (84), 55 (76), 41 (100).

In a similar procedure, reduction of **34a** with $NaBH_4$-$CeCl_3$ in MeOH gave allylic alcohols **36a** (74.7%) and **36c** (8.3%).

Characteristic properties of **36a** : IR, 3575 cm^{-1}; ^1H NMR, 5.18 (1H, dd, J = 2.2 & 2.2 Hz), 5.00 (1H, dd, J = 2.2 & 2.2 Hz), 4.52 (1H, m), 2.42 (1H, m), 1.00-2.12 (12H, m); ^{13}C NMR, 149.0, 97.4, 64.2, 42.8, 39.0, 36.2, 29.0, 28.4, 24.0, 23.8.

Characteristic properties of **36c** : IR, 3560 cm^{-1}; ^1H NMR, 5.22 (1H, dd, J = 2.1 & 1.8 Hz), 5.00 (1H, dd, J = 2.1 & 2.0 Hz), 4.56 (1H, m), 0.90-2.70 (13H, m); ^{13}C NMR, 125.7, 108.4, 74.2, 42.3, 39.4, 36.8, 28.2, 26.7, 23.8, 22.0.

Characteristic properties of acetate **37a**, derived from **36a** : IR, 1725, 1225 cm^{-1}; ^1H NMR, 5.52 (1H, m), 5.02 (1H, m), 5.14 (1H, m), 2.11 (3H, s), 1.18-2.50 (12H, m); ^{13}C NMR, 171.8, 153.7, 109.0, 75.8, 43.1, 36.8, 36.0, 29.2, 27.0, 24.0, 22.4, 21.1.

Characteristic properties of **35a**, derived from **37a** : mp, 68-69 °C; IR, 3500 cm^{-1}; ^1H NMR, 4.23 (1H, m), 3.82 (1H, dd, J = 10.1 & 6.2 Hz), 3.71 (1H, dd, J = 10.1 & 9.0 Hz), 2.40 (1H, broad), 0.82-2.22 (14H, m); ^{13}C NMR, 73.0, 59.7, 52.4, 41.3, 38.6, 38.3, 27.5, 26.4, 24.3, 21.5;

MS, 152 (9), 123 (8), 108 (56), 93 (29), 81 (44), 67 (54), 55 (57), 41 (100).

Reduction of Ketols 29 with $NaB(OAc)_3H$

The following is a typical procedure. Sodium borohydride (0.2 g, 5.1 mmol) was added portionwise to chilled glacial acetic acid (15 °C) and stirred until gas evolution ceased. Ketol **29d** (73 mg, 0.43 mmol) was added, and the mixture was stirred at room temperature for 4 hr. Following quenching with water and extractionby ether, the crude product was chromatographed to trans diol **35d** (77.5 mg, quantitative).

Characteristic properties of **35d** : mp, 78-80 °C; IR, 3550 cm^{-1}; ^1H NMR, 4.00 (1H, dd, J = 5.7 & 2.1 Hz), 3.80 (1H, dd, J = 5.7 & 4.4 Hz), 3.63 (1H, dd, J = 8.0 & 8.7 Hz), 1.10-2.31 (15H, m); ^{13}C NMR, 80.1, 67.1, 45.8, 43.9, 34.3, 27.7, 26.9, 24.6, 22.0, 21.0; MS, 152 (21), 121 (13), 108 (28), 93 (23), 81 (58), 67 (76), 55 (74), 41 (100).

Characteristic properties of **35c** : 84% yield; IR, 3580 cm^{-1}; ^1H NMR, 4.07 (1H, ddd, J = 8.3, 5.7 & 2.5 Hz), 3.75 (1H, dd, J = 10.4 & 4.9 Hz), 3.43 (1H, dd, J = 10.4 & 9.0 Hz), 3.06 (broad, OH), 1.10-2.12 (14H, m); ^{13}C NMR, 77.6, 65.5, 52.2, 39.7, 39.5, 36.8, 29.1, 26.9, 24.1, 22.5; MS, 152 (8), 108 (46), 93 (25), 79 (42), 67 (53), 55 (55), 41 (100).

Preparation of Acetonides 40

A solution of diol **35b** (79.6 mg, 0.47 mmol) in dry acetone (10 ml) was mixed with anhydrous copper sulfate (200 mg) and stirred at room temperature for 2 hr. Filtration and chromatography of the crude product from the filtrate resulted in some loss of the volatile

acetonide. In this case recovered **35b** amounted to 7 mg (9%) and the acetonide yield was 43 mg (44%).

Characteristic properties of **40b** : ^{1}H NMR, 4.07 (1H, dd, J = 5.2 & 5.2 Hz), 3.87 (1H, dd, J = 11.3 & 5.2 Hz), 3.48 (1H, dd, J = 11.3 & 5.8 Hz), 1.32 (3H, s),1.27 (3H, s), 0.90-2.02 (13H, m); ^{13}C NMR, 98.4, 75.5, 62.4, 43.0, 38.5, 37.1, 33.1, 30.6, 28.2, 24.0, 23.7, 21.1.

Characteristic properties of **40a** : 52% yield; ^{1}H NMR, 4.24 (1H, m), 3.84 (1H, dd, J = 7.0 & 11.7 Hz), 3.74 (1H, dd, J = 6.4 & 11.7 Hz), 1.32 (3H, s), 1.26 (3H, s), 0.96-2.02 (13H, m); ^{13}C NMR, 98.0, 71.2, 58.8, 43.3, 41.1, 37.0, 34.7, 26.9, 26.4, 25.7, 24.6, 21.4, 20.7.

CYCLOBUTANES IN ORGANIC SYNTHESIS

PART II

SOLCOLYTIC STUDIES OF ESTER DERIVATIVES OF BICYCLO[n.2.0]ALKANOLS (n = 3 OR 4)

General Procedure for the Preparation of Cyclobutanones

A solution of freshly distilled trichloroacetyl chloride (3 mmol) in dry ether (30 ml) was added over 20 min. to a stirred, refluxing mixture of olefin (3 mmol), dry ether (30 ml) and activated zinc[27] (0.6 g). The reaction mixture was stirred at reflux for an additional 16 hr after the addition was complete. The excess zinc was filtered and the filtrate was then concentrated to about 20 ml, and mixed with pentane (40 ml). Finally, the pentane solution was decanted from the precipitated zinc salts and evaporated to give a crude product which was used immediately in the next step.

To a cooled stirred solution of the previous product in glacial acetic acid (10 ml) was added zinc dust (0.5 g) portionwise. The reaction mixture was heated to 75 °C, stirred overnight and then filtered through Celite. The filtrates were mixed with ether, washed several times with cold water followed by aqueous sodium bicarbonate and dried over Na_2SO_4. After removal of the solvent, the residue was purified by Kugelrohr distillation or flash chromatography.

Characteristic properties of **41**[59] : Yield, 62%; IR, 1775 cm^{-1}; ^1H NMR, 3.55 (1H, m), 3.21 (1H, m), 2.89 (1H, m), 2.48 (1H, m), 1.42-2.08 (6H, m).

Characteristic properties of **42**[67] : Yield, 35%; IR, 1778 cm^{-1}; ^1H NMR, 2.98 (1H, m), 2.81 (1H, dd, J = 18.1 & 4.4 Hz), 2.65 (1H, dd, J = 18.1 & 2.9 Hz), 1.45-1.98 (6H, m), 1.41 (3H, s).

Characteristic properties of **43**[67] : Yield, 57%; IR, 1770 cm^{-1}; ^1H NMR, 7.17 (4H, m), 4.02 (2H, m), 3.58 (1H, m), 3.29 (1H, d, J = 17.4

Hz), 3.08 (1H, m), 2.87 (1H, d, J = 17.4 Hz); ^{13}C NMR, 211.9, 144.4, 142.8, 127.2, 125.2, 124.8, 62.6, 55.4, 36.4, 33.8.

General Procedure for the Addition of Grignard Reagents to Cyclobutanones

To a stirred solution of Grignard reagent, prepared by treating the appropriate alkenyl or alkyl bromide (7.5 mmol) in THF (10 ml) solution with magnesium (9 mmol), was added a solution of the cyclobutanone (3 mmol) in THF (10 ml). This mixture was stirred overnight at room temperature, and then quenched by addition of saturated aqueous ammonium chloride. Extraction with ether, followed by conventional workup and purification by flash chromatography yielded the corresponding cyclobutanol.

Characteristic properties of **45**[60] : Yield, 75%; IR, 3330-3650, 1640, 998, 920 cm^{-1}; ^{1}H NMR, 6.15 (1H, dd, J = 17.3 & 10.6 Hz), 5.20 (1H, dd, J = 1.2 & 17.3 Hz), 5.00 (1H, dd, J = 1.2 & 10.6 Hz), 2.71 (1H, m), 2.27-2.52 (2H, m), 1.76-2.02 (3H, m), 1.35-1.62 (5H, m); ^{13}C NMR, 146.7, 109.0, 71.0, 49.6, 39.4, 33.0, 30.9, 26.3, 26.0.

Characteristic properties of **46** : Yield, (**cis** + **trans**), 82%; **trans** : IR, 3350-3650, 1442, 1020 cm^{-1}; ^{1}H NMR, 5.75 (1H, m), 5.64 (1H, m), 2.53 (1H, m), 2.35 (1H, m), 2.26 (1H, m), 1.58 (3H, d, J = 5.4 Hz), 1.38-2.01 (8H, m); **cis** : ^{1}H NMR, 5.78 (1H, m), 5.52 (1H, m), 2.57 (1H, m), 2.42 (2H, m), 2.04 (1H, m), 1.73 (3H, dd, J = 7.3 & 1.7 Hz), 1.38-1.92 (7H, m).

Characteristic properties of **47** : Yield, 92%; IR, 3300-3650, 1642, 899 cm^{-1}; ^{1}H NMR, 5.01 (1H, m), 4.82 (1H, m), 2.70 (1H, m), 2.50 (1H, m), 2.41 (1H, m), 1.84 (3H, m), 1.72 (2H, m), 1.38-1.52 (6H, m);

^{13}C NMR, 149.8, 108.2, 73.5, 47.2, 37.9, 32.5, 31.0, 26.2, 25.8, 17.8; MS, 152 (2), 135 (17), 84 (70), 69 (100), 55 (31).

Characteristic properties of **49a**[47] : Yield, 92%; IR, 3350-3650 cm^{-1}; ^{1}H NMR, 2.48 (1H, m), 2.34 (1H, m), 2.08 (1H, m), 1.30-1.54 (4H, m), 1.64-1.92 (4H, m), 1.34 (3H, s).

Characteristic properties of **50** : Yield, 82%; IR, 3370-3650, 1440, 998 cm^{-1}; ^{1}H NMR, 2.48 (1H, m), 2.32 (1H, m), 2.15 (1H, m), 1.32-1.88 (10H, m), 0.92 (3H, t, J = 8 Hz).

Characteristic properties of **51**[47] : Yield, 62%; IR, 3350-3650, 1604, 1498, 1075 cm^{-1}; ^{1}H NMR, 7.20-7.68 (5H, m), 2.97 (1H, m), 2.53 (2H, m), 1.42-2.17 (8H, m).

Characteristic properties of **52** : Yield, 85%; IR, 3320-3610 cm^{-1}; ^{1}H NMR, 6.14 (1H, dd, J = 10.7 & 17.2 Hz), 5.20 (1H, dd, J = 17.2 & 0.9 Hz), 5.02 (1H, dd, J = 10.7 & 0.9 Hz), 2.64 (1H, broad), 2.25 (1H, dd, J = 1.7 & 8.4 Hz), 2.08 (1H, dd, J = 2.8 & 14.9 Hz), 1.29 (3H, s), 1.59-2.03 (7H, m); ^{13}C NMR, 145.8, 109.8, 69.3, 52.9, 44.9, 41.0, 37.8, 26.8, 25.6; MS, 152 (0.6), 135 (2), 109 (9), 83 (23), 70 (100), 67 (38), 55 (78).

Characteristic properties of **53** : Yield, 92%; IR, 3350-3650 cm^{-1}; ^{1}H NMR, 6.92-7.21 (4H, m), 6.01 (1H, dd, J = 17.2 & 10.7 Hz), 5.13 (1H, dd, J = 17.2 & 1.2 Hz), 4.93 (1H, dd, J = 10.7 & 1.2 Hz), 3.39 (1H, m), 3.27 (1H, dd, J = 17.8 & 2.7 Hz), 3.08 (1H, m), 2.99 (1H, dd, J = 17.8 & 9.6 Hz), 2.65 (1H, ddd, J = 12.6, 10.6 & 2.2 Hz), 1.93 (1H, broad), 1.83 (1H, ddd, J = 12.6, 5.0 & 0.9 Hz); ^{13}C NMR, 147.4, 144.2, 126.4, 124.7, 123.9, 110.6, 73.2, 47.6, 43.5, 37.9, 31.8; MS, 186 (0.51), 167 (1.5), 116 (100), 91 (10), 55 (24).

General Procedure for the Preparation of Dinitrobenzoates or Benzoates of Cyclobutanols

To a stirred solution of the selected cyclobutanol (2 mmol) and 4-dimethylaminopyridine (20 mg) in pyridine (15 ml) was added 3,5-dinitrobenzoyl chloride or benzoyl chloride (3 mmol). This mixture was stirred overnight, then poured into ice (50 ml) and extracted with ether. The combined ether layers were washed with cold 5% aqueous HCl and dried. Removal of the solvent and purification by flash chromatography gave the corresponding dinitrobenzoate or benzoate derivatives.

Characteristic properties of **55** : Yield, 77%; mp, 84-85 °C; IR, 1730, 1550, 1350, 900 cm^{-1}; ^{1}H NMR, 9.23 (1H, t, J = 2.0 Hz), 9.17 (2H, d, J = 2.0 Hz), 6.28 (1H, dd, J = 17.4 & 10.8 Hz), 5.35 (1H, d, J = 17.4 Hz), 5.26 (1H, d, J = 10.8 Hz), 3.17 (1H, m), 2.56-2.82 (2H, m), 1.52-2.12 (7H, m).; ^{13}C NMR, 160.7, 148.6, 139.7, 134.5, 129.2, 122.2, 113.8, 81.0, 49.0, 36.8, 32.4, 32.2, 27.2; MS, 332 (0.05), 315 (0.09), 247 (1.7), 195 (36), 120 (42), 92 (37), 68 (100); High resolution MS, calculated for $C_{16}H_{16}N_2O_6$; 332.1008, found, 332.1002.

Characteristic properties of **56a** : Yield, 58%; mp, 160-165 °C; IR, 1730, 1550, 1350, 1275, 900 cm^{-1}; ^{1}H NMR (**cis**), 9.27 (1H , m), 9.08 (2H, m), 6.08 (1H, dd, J = 12.4 & 1.7 Hz), 5.61 (1H, m), 3.05 (1H, m), 2.30 (2H, m), 1.69 (3H, dd, J = 1.7 & 7.1 Hz), 1.42-2.19 (7H, m). ^{1}H NMR (**trans**), 9.27 (1H, m), 9.13 (2H, m), 5.84 (1H, m), 5.55 (1H, m), 3.22 (1H, m), 2.30-2.81 (2H, m), 1.76 (3H, dd, J = 1.2 & 4.3 Hz), 1.42-2.19 (7H, m).

Characteristic properties of **56b** : Yield, 84%; IR, 1710, 1602, 1450, 1335, 1275, 1113, 992 cm^{-1}; ^1H NMR (**cis**), 7.39-8.45 (5H, m), 6.07 (1H, dd, J = 10.9 & 1.7 Hz), 5.53 (1H, dq, J = 10.9 & 7.2 Hz), 3.05 (1H, m), 2.51 (2H, m), 1.50-2.24 (7H, m), 1.64 (3H, dd, J = 1.7 & 7.2 Hz); ^1H NMR (**trans**), 7.39-8.45 (5H, m), 5.93 (1H, d, J = 15.5 Hz), 5.73 (1H, dq, J = 15.5 & 6.3 Hz), 3.05 (1H, m), 2.51 (2H, m), 1.72 (3H, dd, J = 1.4 & 6.3 Hz), 1.50-2.24 (7H , m).

Characteristic properties of **57a** : Yield, 55%; mp, 116-118 °C; IR, 1730, 1550, 1349, 1275, 900 cm^{-1}; ^1H NMR, 9.23 (1H, t, J = 2.2 Hz), 9.12 (2H, d, J = 2.2 Hz), 5.20 (1H, m), 5.05 (1H, m), 3.10 (1H, m), 2.86 (1H, m), 2.62 (1H, m), 1.50-2.20 (7H, m), 1.76 (3H, m); ^{13}C NMR, 160.5, 148.4, 144.6, 134.5, 129.1, 122.2, 110.4, 83.4. 48.3, 36.0, 32.6, 32.4, 27.4, 25.7, 17.9; MS, 346 (0.21), 317 (0.20), 278 (1.8), 195 (44), 119 (36), 67 (100); High resolution MS, calculate for $C_{17}H_{18}N_2O_6$, 346.1165; found, 346.1171.

Characteristic properties of **57b** : Yield, 66%; IR, 1725, 1275 1050 cm^{-1}; ^1H NMR, 8.06 (2H, m), 7.74 (1H, m), 7.54 (2H, m), 5.15 (1H, m), 4.97 (1H, m), 2.98 (1H, m), 2.85 (1H, m), 2.56 (1H, m), 2.13 (1H, m), 1.74 (3H, m), 1.50-1.98 (6H, m); ^{13}C NMR, 164.6, 142.2, 132.6, 130.8, 129.3, 128.2, 109.4, 80.7, 48.5, 36.0, 32.5, 25.5, 17.9; MS, 188 (9), 151 (1.5), 135 (4), 105 (100), 77 (34).

Characteristic properties of **58** : Yield, 84%; mp, 114-115 °C; ^1H NMR, 9.26 (1H, t, J = 2.1 Hz), 9.15 (2H, d, J = 2.1 Hz), 5.40 (1H, m), 3.22 (1H, m), 2.68 (1H, m), 1.35-1.98 (8H, m).

Characteristic properties of **59a**[47] : Yield, 83%; mp, 129-131 °C; IR, 1727, 1632, 1550, 1350, 1275, 926 cm^{-1}; ^1H NMR, 9.21 (1H, t, J

= 2.2 Hz), 9.11 (2H, d, J = 2.2 Hz), 2.91 (1H, m), 2.58 (1H, m), 2.44 (1H, m), 1.74 (3H, s), 1.54-2.05 (7H, m).

Characteristic properties of **59b**[47] : mp. 116-118 °C; IR, 2820-3058, 1725, 1550, 1350 cm^{-1}; ^1H NMR, 9.20 (1H, t, J = 2.1 Hz), 9.15 (2H, d, J = 2.1 Hz), 3.05 (1H, m), 2.89 (1H, m), 2.11 (1H, m), 2.02-2.45 (7H, m), 1.57 (3H, s).

Characteristic properties of **60** : Yield, 79%; mp, 103-105 °C; IR, 2860-3150, 1728, 1548, 1348 cm^{-1}; ^1H NMR, 9.14 (1H, t, J = 2.1 Hz), 9.04 (2H, d, J = 2.1 Hz), 2.88 (1H, m), 2.22-2.63 (2H, m), 2.08 (1H, m), 2.09 (2H, q, J = 7.4 Hz), 1.42-2.92 (6H, m), 0.85 (3H, t, J = 7.4 Hz); MS, 317 (0.44), 305 (2), 267 (6), 195 (80), 122 (18), 68 (100).

Characteristic properties of **61**[47] : Yield, 85%; mp, 114-116 °C; IR, 1725, 1630, 1450, 1348, 1275, 1170 cm^{-1}; ^1H NMR, 9.11-9.18 (3H, m), 7.12-7.60 (5H, m), 2.92 (1H, m), 2.43-2.69 (3H, m), 1.38-2.02 (6H, m).

Characteristic properties of **62** : Yield, 83%; mp, 112-114 °C; IR, 1723, 1545, 1345, 1270 cm^{-1}; ^1H NMR, 9.22 (1H, t, J = 2.1 Hz), 9.12 (2H, d, J = 2.1 Hz), 6.30 (1H, dd, J = 17.4 & 10.7 Hz), 5.38 (1H, d, J = 10.7 Hz), 5.30 (1H, d, J = 17.4 Hz), 2.65 (1H, m), 2.49 (1H, dd, J = 13.8 & 3.2 Hz), 2.22 (1H, d, J = 13.8 Hz), 1.29 (3H, s), 1.50-2.02 (6H, m). ^{13}C NMR, 160.7, 148.6, 139.9, 129.1, 122.1, 114.8, 79.8, 52.8, 42.3, 40.9, 39.8, 28.1, 26.5, 24.8; MS, 346 (0.03), 331 (0.29), 304 (1.1), 290 (0.53), 195 (12), 134 (13), 82 (100), 67 (25).

Characteristic properties of **63** : Yield, 86%; IR, 1723, 1542, 1342 cm^{-1}; ^1H NMR, 8.98 (1H, t, J = 2.1 Hz), 8.83 (2H, d, J = 2.1 Hz), 6.94-7.20 (4H, m), 6.24 (1H, dd, J = 10.8 & 17.4 Hz), 5.32 (1H, d, J = 17.4

Hz), 5.22 (1H, d, J = 10.8 Hz), 3.49 (2H, m), 3.33 (1H, m), 2.98-3.24 (2H, m), 2.33 (1H, dd, J = 4.8 & 13.1 Hz); ^{13}C NMR, 160.5, 148.4, 146.2, 144.2, 138.7, 134.1, 129.0, 126.7, 124.6, 123.8, 122.0, 114.7, 82.3, 48.4, 40.8, 39.1, 33.1; MS, 380 (0.12), 212 (1.5), 168 (27), 116 (100), 105 (7).

Characteristic properties of **64a** : Yield; 57%; mp, 103-104 °C; IR, 1725, 1550, 1350 cm^{-1}; ^{1}H NMR, 9.20 (1H, t, J = 2.1 Hz), 9.11 (2H, d, J = 2.1 Hz), 6.29 (1H, dd, J = 10.8 & 17.4 Hz), 5.42 (1H, d, J = 17.4 Hz), 5.30 (1H, d, J = 10.8 Hz), 2.72 (1H, m), 1.38-2.50 (2H, m), 2.27 (1H, m), 1.02-1.94 (8H, m); ^{13}C NMR, 160.9, 148.4, 137.6, 134.6, 129.2, 122.1, 113.3, 81.9, 42.6, 34.9, 25.1, 25.0, 22.4, 22.0, 21.4; MS, 317 (0.05), 290 (0.1), 212 (0.2), 195 (27), 134 (10), 82 (77), 67 (94), 55 (100).

Characteristic properties of **64b** : Yield, 93%; IR, 1715, 1275, 1110 cm^{-1}; ^{1}H NMR, 7.96 (2H, m), 7.46 (1H, m), 7.37 (2H, m), 6.25 (1H, dd, J = 17.3 & 10.7 Hz), 5.29 (1H, dd, J = 0.9 & 17.3 Hz), 5.16 (1H, dd, J = 0.9 & 10.7 Hz), 2.64 (1H, m), 2.41 (2H, m), 2.25 (1H, m), 1.02-1.94 (8H, m); ^{13}C NMR, 165.1, 139.0, 132.7, 130.9, 129.5, 128.2, 113.7, 79.6, 42.7, 35.2, 25.4, 25.2, 22.5, 22.0, 21.5; MS, 256 (0.08), 151 (0.81), 135 (2.4), 105 (100), 77 (51); High resolution MS, calculated for $C_{17}H_{20}O_2$, 256.1463; found, 256.1477.

Characteristic properties of **65a** : Yield, 84%, mp, 121-123 °C; IR, 1725, 1550, 1335 cm^{-1}; ^{1}H NMR, 9.12 (1H, t, J = 2.1 Hz), 9.05 (2H, d, J = 2.1 Hz), 6.18 (1H, dd, J = 17.4 & 10.7 Hz), 5.30 (1H, broad), 5.23 (1H, dd, J = 10.7 & 1.0 Hz), 2.79 (1H, m), 1.45 (2H, m), 1.12-1.84 (9H, m); ^{13}C NMR, 161.2, 148.6, 136.0, 134.9, 129.3, 122.0, 117.8, 88.1, 42.3, 35.0, 27.0, 26.5, 22.8, 22.2, 22.0; MS, 346 (0.08), 303 (0.31),

290 (0.33), 212 (0.13), 195 (19), 134 (20), 82 (100), 67 (93), 55 (39).

Acetolysis of Dinitrobenzoates or Benzoates in Glacial Acetic Acid Containing Triethylammonium Acetate

The following is a typical procedure. A solution of benzoate **55** (166 mg, 0.5 mmol) in 0.1 M triethylammonium acetate in glacial acetic acid (10 ml) was stirred at 80 °C for 12 hr. The reaction mixture was cooled, quenched with water and extracted with ether. The organic extracts were washed with saturated aqueous sodium bicarbonate, and dried. Evaporation of the solvent followed by flash chromatography gave dienyl acetate **66a** (59.4 mg, 66%) and dienyl dinitrobenzoate **66b** (13.3 mg, 8%).

Characteristic properties of **66a** : IR, 2800-3150, 1730, 1500, 1350, 1175, 925 cm^{-1}; UV (EtOH), λ_{max} 232 (ε_{max} 15600); ^1H NMR, 6.29 (1H, dd, J = 10.8 & 17.4 Hz), 5.95 (1H, dd, J = 6.7 & 7.1 Hz), 5.11 (1H, d, J = 17.4 Hz), 4.92 (1H, d, J = 10.8 Hz), 4.66 (1H, m), 2.54 (2H, m), 2.00 (3H, s), 1.29-2.28 (6H, m); ^{13}C NMR, 170.3, 139.4, 136.4, 133.6, 111.3, 73.7, 31.4, 29.2, 27.2, 21.2; MS, 180 (0.5), 120 (21), 105 (33), 92 (31), 79 (33), 43 (100).

Characteristic properties of **66b** : mp, 96-99 °C; IR, 2840-3150, 1730, 1550, 1349, 1265, 1172 cm^{-1}; UV (CH_3CN), λ_{max} 232 (ε_{max} 15000); ^1H NMR, 9.28 (1H, t, J = 2.0 Hz), 9.23 (2H, d, J = 2.0 Hz), 6.35 (1H, dd, J = 17.4 & 10.8 Hz), 6.07 (1H, dd, J = 7.0 & 6.9 Hz), 5.13 (1H, d, J = 17.4 Hz), 5.07 (1H, m), 4.95 (1H, d, J = 10.8 Hz), 2.28 (2H, m), 1.48-2.33 (6H, m); ^{13}C NMR, 160.8, 147.7, 138.9, 135.2, 134.6,

133.6, 128.4, 121.2, 110.0, 73.0, 35.9, 30.6, 26.4, 22.3; MS, 212 (5), 195 (42), 149 (36), 120 (79), 105 (100), 92 (75), 79 (54).

Acetolysis of Dinitrobenzoates or Benzoates with Triethylammonium Acetate - Lithium Perchlorate in Aqueous Acetic Acid

To a solution of $LiClO_4$ (213 mg, 2 mmol) in water (3.3 ml) was added a solution of 0.1M triethylammonium acetate in glacial acetic acid (10 ml), followed by benzoate **55** (166 mg, 0.5 mmol). This mixture was stirred at 80 °C for 12 hr, then cooled and quenched with water. After conventional workup and chromatography of the product, acetate **66a** (22.1 mg, 24.5%), benzoate **66b** (7.8 mg, 4.7%) and alcohol **66c** (18.1 mg, 26.2%) were obtained.

The studies of product distribution in acetolysis of benzoate **55** under different reaction conditions are listed in Table VIII.

The studies of product distribution in acetolysis of benzoate **57a** under different reaction conditions are listed in Table IX.

The studies of product distribution in acetolysis of benzoate **57b** under different reaction conditions are listed in Table X.

Characteristic properties of **66c** : IR, 3250-3650, 2810-3100, 1638, 1608, 1038, 998 cm^{-1}; UV (EtOH), λ_{max} 234 (ε_{max} 14000); ^1H NMR, 6.32 (1H, dd, J = 17.4 & 10.7 Hz), 5.97 (1H, dd, J = 7.0 & 6.8 Hz), 5.16 (1H, d, J = 17.4 Hz), 4.88 (1H, d, J = 10.7 Hz), 3.65 (1H, m), 2.48-2.57 (2H, m), 2.09-2.20 (2H, m), 1.29-2.30 (5H, m); ^{13}C NMR, 140.2, 136.9, 135.6, 110.6, 68.4, 41.0, 35.0, 27.8, 23.4; MS, 138 (4), 120 (29), 105 (54), 91 (45), 79 (100), 67 (49); High resolution MS, calculated for $C_9H_{14}O$, 138.1045; found, 138.1049.

Characteristic properties of **66d** : IR, 2800-3080, 1549, 1110, 1018, 867 cm^{-1}; ^1H NMR, 5.30 (1H, m), 4.46 (2H, m), 2.66 (1H, m), 2.33 (1H, m), 1.66 (3H, d, J = 6.1 Hz), 1.30-1.98 (6H, m); ^{13}C NMR, 140.6, 112.7, 78.6, 75.1, 33.2, 32.5, 30.6, 16.0, 14.7; MS, 138 (40), 121 (52), 109 (100), 95 (76), 81 (61), 67 (52).

Characteristic properties of **68a** : IR, 2810-3050, 1725, 1430, 1372, 1238, 1027 cm^{-1}; UV (EtOH), λ_{max} 238 (ϵ_{max} 22800); ^1H NMR, 6.28 (1H, d, J = 11.2 Hz), 5.58 (1H, m), 4.99 (1H, m), 1.96 (3H, s), 1.69 (3H, s), 1.67 (3H, s), 1.55-2.78 (6H, m); ^{13}C NMR, 170.6, 131.6, 129.1, 125.9, 73.3, 35.5, 32.0, 24.3, 21.4, 20.6; MS, 194 (3), 152 (5), 134 (31), 119 (69), 91 (87), 78 (22), 56 (26), 43 (100).

Characteristic properties of **68d** : IR, 2820-3100, 1550, 1172, 1010, 880, 869 cm^{-1}; ^1H NMR, 4.68 (1H, m), 4.42 (1H, m), 1.64 (3H, m), 1.58 (3H, s), 1.20-2.72 (8H, m); ^{13}C NMR, 134.7, 120.0, 76.4, 75.4, 34.8, 30.7, 30.2, 21.1, 20.4, 16.4; MS, 152 (43), 135 (52), 109 (100), 95 (40), 81 (62), 67 (43), 55 (24); High resolution MS, calculated for $C_{10}H_{16}O$, 152.1211; found, 152.1206.

Acetolysis of dinitrobenzoate **56a** and **56b** was carried out with two equivalents of 0.1M triethylammonium acetate in aqueous acetic acid (HOAc : H_2O = 3/1) at 110 °C for 12 hr. Conventional workup and chromatography of the product from **56a** gave acetate **67a** (51%) and alcohol **67c** (14%).

Conventional workup and chromatography of the product from **56b** gave acetate **67a** (38%) and alcohol **67c** (21%).

Characteristic properties of **67a** : IR, 2820-3085, 1725, 1370, 1235, 1025, 970 cm^{-1}; UV (EtOH), λ_{max} 233 (ϵ_{max} 13000); ^1H NMR, 6.01 (1H, d, J = 15.1 Hz), 5.84 (1H, dd, J = 6.7 & 6.9 Hz), 5.64 (1H, m),

4.65 (1H, m), 2.57 (2H, m), 2.01 (3H, s), 1.76 (3H, d, J = 6.5 Hz), 1.31-2.20 (6H, m); ^{13}C NMR, 170.2, 136.4, 134.4, 131.9, 122.2, 71.3, 37.2, 32.9, 27.4, 23.9, 21.2, 18.0; MS, 194 (2), 152 (3), 134 (100), 119 (99), 106 (45), 91 (48), 43 (79); High resolution MS, calculated for $C_{12}H_{18}O_2$, 194.1307; found, 194.1310.

Characteristic properties of **67c** : IR, 3300-3600, 2875-3035, 1450, 1035, 975 cm^{-1}; UV (EtOH), λ_{max} 237 (ϵ_{max} 15200); ^1H NMR, 6.05 (1H, dd, J = 0.6 & 15.6 Hz), 5.86 (1H, dd, J = 6.9 & 6.9 Hz), 5.70 (1H, m), 3.68 (1H, m), 2.57 (2H, m), 2.00-2.25 (4H, m), 1.76 (3H, dd, J = 0.5 & 6.3 Hz), 1.30-1.88 (3H, m); ^{13}C NMR, 136.4, 134.9, 132.3, 122.1, 68.4, 41.0, 36.0, 27.7, 23.6, 18.0; MS, 152 (35), 134 (39), 119 (100), 106 (52), 91 (88), 79 (59), 65 (20); High resolution MS, calculated for $C_{10}H_{16}O$, 152.1202; found, 152.1207.

Acetolysis of dinitrobenzoate **59a** was carried out with two equivalents of 0.1M triethylammonium acetate in acetic acid at 110 °C for 24 hr. Conventional workup and chromatography of the product gave acetate **69a** (72%) and benzoate **69b** (9.0%).

Characteristic properties of **69a** : IR, 2800-3100, 1722, 1550, 1370, 1235, 1026 cm^{-1}; ^1H NMR, 5.66 (1H, m), 4.71 (1H, ddd, J = 10.0, 3.6 & 2.3 Hz), 2.52 (2H, dd, J = 10.8 & 9.8 Hz), 2.04 (3H, s), 1.78 (3H, s), 1.50-2.18 (6H, m); ^{13}C NMR, 170.3, 134.1, 127.6, 71.2, 39.3, 37.4, 27.3, 26.1, 24.1, 21.3; MS, 125 (1), 109 (100), 93 (58), 67 (8), 43 (53).

Characteristic properties of **69b** : IR, 1725, 1550, 1350, 1235 cm^{-1}; ^1H NMR, 9.23 (1H, t, J = 2.1 Hz), 9.13 (2H, d, J = 2.1 Hz), 5.78 (1H, m), 5.10 (1H, m), 2.74 (1H, m), 1.40-2.42 (7H, m), 1.82 (3H, s); ^{13}C

NMR, 161.7, 148.6, 134.6, 133.4, 129.4, 128.4, 122.2, 74.4, 39.1, 27.3, 27.2, 26.2, 24.0; MS, 195 (3), 108 (100), 93 (52), 80 (10).

Acetolysis of dinitrobenzoate **59b** was carried out with two equivalents of 0.1M triethylammonium acetate in acetic acid at 110 °C for 24 hr. Conventional workup and chromatography of the product gave acetate **69a** (14%) and starting material (56%).

Acetolysis of dinitrobenzoate **60** was carried out with two equivalents of 0.1M triethylammonium acetate in acetic acid at 110 °C for 24 hr. Conventional workup and chromatography of the product gave acetate **70a** (88%).

Characteristic properties of **70a** : IR, 2810-3100, 1725, 1550, 1235 cm^{-1}; ^1H NMR, 5.62 (1H, m), 4.64 (1H, m), 2.51 (2H, m), 2.00 (3H, s), 1.52-2.22 (8H, m), 0.96 (3H, t, J = 7.3 Hz); ^{13}C NMR, 170.3, 139.8, 126.2, 71.7, 38.1, 37.7, 32.8, 27.3, 24.3, 12.5; MS, 122 (39), 107 (27), 93 (75), 79 (26), 55 (11), 43 (100); Elemental analysis, calculated for $C_{11}H_{18}O_2$: C, 72.48; H, 9.96

found : C, 72.33; H, 9.91

Acetolysis of dinitrobenzoate **61** was carried out with two equivalents of 0.1M triethylammonium acetate in acetic acid at 110 °C for 24 hr. Conventional workup and chromatography of the product gave acetate **71a** (80%) and dinitrobenzoate **71b** (6.7%).

Characteristic properties of **71a** : IR, 2820-3100, 1725, 1369, 1228, 1024 cm^{-1}; UV (EtOH), λ_{max} 247 (ε_{max} 17800), 205 (ε_{max} 12900); ^1H NMR, 7.12-7.40 (5H, m), 6.19 (1H, dd, J = 7.6 & 7.2 Hz), 4.84 (1H, ddd, J = 9.7, 3.4 & 2.6 Hz), 2.86 (2H, m), 2.03 (3H, s), 1.40-2.38 (6H, m); ^{13}C NMR, 170.3, 143.9, 138.5, 131.7, 128.1, 126.5,

125.7, 71.4, 38.2, 37.7, 27.8, 23.8, 21.3; MS, 230 (1), 170 (43), 155 (34), 142 (66), 129 (40), 91 (36), 77 (16).

Characteristic properties of **71b** : mp. 93-95 °C; IR, 2860-3100, 1728, 1540, 1350, 1275, 1072 cm^{-1}; UV (EtOH), λ_{max} 238 (ϵ_{max} 28000), 206 (ϵ_{max} 32000); ^1H NMR, 8.99 (1H, t, J = 2.1 Hz), 8.96 (2H, d, J = 2.1 Hz), 6.9-7.27 (5H, m), 6.15 (1H, dd, J = 7.0 & 6.8 Hz), 5.08 (1H, m), 3.00 (1H, dd, J = 14.3 & 10.0 Hz), 2.83 (1H, d, J = 14.3 Hz), 1.42-2.36 (6H, m); ^{13}C NMR, 161.7, 148.4, 143.4, 137.7, 134.1, 132.1, 129.2, 128.1, 126.6, 125.5, 122.0, 74.3, 37.7, 27.7, 23.5; MS, 382 (4), 195 (17), 170 (100), 155 (61), 142 (93), 129 (44), 115 (29), 91 (56), 75 (37);

Elemental analysis, calculated for $C_{20}H_{18}N_2O_6$: C, 62.81; H 4.75.

found : C, 62.98; H, 4.70

Acetolysis of dinitrobenzoate **62** was carried out with two equivalents of 0.1M triethylammonium acetate in acetic acid at 110 °C for 24 hr. Conventional workup and chromatography of the product gave trienes **72c** and **72d** (25%, 3.5 : 1 ratio), acetate **72a** (43.5%) and dinitrobenzoate **72b** (4.5%).

Characteristic properties of **72a** : IR, 1728, 1250 cm^{-1}; UV (EtOH), λ_{max} 234 (ϵ_{max} 17000); ^1H NMR, 6.24 (1H, dd, J = 10.8 & 17.4 Hz), 5.85 (1H, dd, J = 6.8 & 6.8 Hz), 5.14 (1H, d, J = 17.4 Hz), 4.88 (1H, d, J = 10.8 Hz), 2.87 (1H, d, J = 14.2 Hz), 2.68 (1H, d, J = 14.2 Hz), 1.93 (3H, s), 1.44 (3H, s), 1.45-2.03 (6H, m); ^{13}C NMR, 170.4, 140.4, 137.3, 134.2, 111.0, 82.0, 42.6, 35.8, 23.7, 22.5, 22.3.

Characteristic properties of **72b** : ^1H NMR, 9.07 (1H, t, J = 2.1 Hz), 9.02 (2H, d, J = 2.1 Hz), 6.37 (1H, dd, J = 10.8 & 17.4 Hz), 5.96 (1H, dd, J = 6.8 & 6.8 Hz), 5.24 (1H, d, J = 17.4 Hz), 5.03 (1H, d, J = 10.8

Hz), 3.03 (1H, d, J = 14.2 Hz), 2.82 (1H, d, J = 14.2 Hz), 1.66 (3H, s), 1.45-2.10 (6H, m).

Characteristic properties of **72c** : ^{1}H NMR, 6.25 (1H, dd, J = 10.8 & 17.4 Hz), 5.76 (1H, dd, J = 6.8 & 6.9 Hz), 5.44 (1H, m), 5.04 (1H, d, J = 17.4 Hz), 4.85 (1H, d, J = 10.8 Hz), 2.92 (2H, broad), 2.06-2.31 (4H, m), 1.70 (3H, d, J = 0.7 Hz); ^{13}C NMR, 140.9, 133.3, 133.0, 124.6, 110.1, 109.5, 30.1, 29.7, 26.7, 25.9.

Characteristic properties of **72d** : ^{1}H NMR, 6.26 (1H, dd, J = 10.8 & 17.4 Hz), 5.76 (1H, m), 5.10 (1H, d, J = 17.4 Hz), 4.92 (1H, d, J = 10.8 Hz), 4.65 (1H, broad), 1.42-2.42 (6H, m), 1.39 (3H, s).

Acetolysis of dinitrobenzoate **63** was carried out with two equivalents of 0.1M triethylammonium acetate in acetic acid at 110 °C for 24 hr. Conventional workup and chromatography of the product gave acetate **73a** (34.5%) and dinitrobenzoate **73b** (25.3%).

Characteristic properties of **73a** : IR, 1725, 1250 cm^{-1}; UV (EtOH), λ_{max} 233 (ε_{max} 9100); ^{1}H NMR, 6.98-7.32 (4H, m), 6.28 (1H, dd, J = 3.9 & 10.0 Hz), 6.20 (1H, dd, J = 10.8 & 17.5 Hz), 5.86 (1H, t. J = 7.0 Hz), 4.94 (1H, d, J = 17.5 Hz), 4.82 (1H, d, J = 10.8 Hz), 3.66 (1H, d, J = 17.0 Hz), 3.36 (1H, dd, J = 17.0 & 7.0 Hz), 2.70 (1H, d, J = 14.5 Hz), 2.53 (1H, d, J = 14.5 Hz), 2.11 (3H, s); MS, 168 (26), 153 (5), 129 (10), 116 (100).

Characteristic properties of **73b** : UV (EtOH), λ_{max} 236 (ε_{max} 17400), 276 (ε_{max} 4100); ^{1}H NMR, 7.03-7.32 (5H, m), 6.68 (1H, d, J = 11.8 Hz), 6.29 (1H, dd, J = 10.8 & 17.5 Hz), 5.74 (1H, dd, J = 7.0 & 7.1 Hz), 5.16 (1H, d, J = 17.5 Hz), 4.96 (1H, d, J = 10.8 Hz), 3.02 (2H, d, J = 7.1 Hz); ^{13}C NMR, 137.4, 135.5, 130.0, 128.6, 128.5, 127.4, 126.7,

126.2, 125.7, 113.0, 34.2; MS, 168 (87), 167 (100), 152 (32), 141 (32), 115 (51), 98 (16), 63 (26).

The studies of product distribution in acetolysis of benzoate **64a** were carried out with 0.1M triethylammonium acetate and lithium perchlorate in aqueous acetic acid. The results under different reaction conditions are listed in Table XI.

Characteristic properties of **74a** : IR, 1725, 1640, 1608, 1242, 903 cm^{-1}; UV (EtOH), λ_{max} 232 (ε_{max} 13200); ^1H NMR, 6.33 (1H, dd, J = 17.5 & 10.9 Hz), 5.78 (1H, dd, J = 8.3 & 8.2 Hz), 5.30 (1H, d, J = 17.5 Hz), 4.98 (1H, d, J = 10.9 Hz), 4.95 (1H, m), 2.61 (2H, m), 2.04 (3H, s), 2.01-2.22 (2H, m), 1.32-1.78 (6H, m); ^{13}C NMR, 170.5, 139.5, 136.5, 133.8, 111.4, 73.9, 31.3, 29.1, 27.0, 21.7, 21.4; MS, 194 (3), 134 (37), 119 (39), 105 (41), 91 (35), 43 (100).

Characteristic properties of **74c** : IR, 3320-3630, 1638, 1607, 1075, 902 cm^{-1}; UV (EtOH), λ_{max} 236 (ε_{max} 14000); ^1H NMR, 6.36 (1H, dd, J = 17.4 & 10.8 Hz), 5.76 (1H, dd, J = 8.3 & 8.3 Hz), 5.25 (1H, d, J = 17.4 Hz), 4.96 (1H, d, J = 10.7 Hz), 3.8 (1H, m), 2.58 (2H, m), 2.26 (2H, m), 1.15-1.86 (7H, m); ^{13}C NMR, 140.2, 136.8, 133.6, 110.7, 71.2, 34.9, 32.3, 28.8, 26.8, 21.2; MS, 152 (37), 134 (40), 123 (60), 119 (100), 105 (49), 93 (95), 91 (89), 79 (78), 55 (37).

Characteristic properties of **74d** : ^1H NMR, 6.14 (1H, d, J = 12.0 Hz), 5.67 (1H, q, J = 5.7 Hz), 5.37 (1H, ddd, J = 12.0, 8.5 & 3.4 Hz), 5.04 (1H, m), 2.81 (2H, dd, J = 6.8 & 16.4 Hz), 2.42 (2H, m), 2.06 (3H, s), 1.82 (3H, d, J = 5.7 Hz), 1.44-1.90 (4H, m).

Acetolysis of benzoate **64b** was carried out with 2 equivalents of 0.1M triethylammonium acetate in aqueous acetic acid at 110 °C for 24 hr. Conventional workup and chromatography of the product

gave dienyl acetate **74a** (65%), dienyl alcohols **74c** (21.6%) and **74e** (4%).

Acetolysis of benzoate **65a** was carried out with 2 equivalents of 0.1M triethylammonium acetate in aqueous acetic acid at 110 °C for 24 hr. Conventional workup and chromatography of the product gave dienyl acetate **74a** (20.3%), dienyl alcohols **74c** (17.4%) and **74e** (3%), and allylic acetate **74f** (3.2 %).

Diels-Alder Reaction of Diene 66c and Maleic Anhydride

A solution of dienyl alcohol **66c** (92.6 mg, 0.67 mmol) and maleic anhydride (131.5 mg, 1.34 mmol) in benzene (25 ml) was refluxed with stirring for 16 hr. The solvent was removed, and the residue was purified by flash chromatography to yield cycloadduct products **82a** and **82b** (107.2 mg, 68%, 1 : 1 mixture).

Characteristic properties of **82a** : mp, 119-122 °C; IR (CH_3Cl), 3200-3600, 1846, 1779, 1264, 1228, 966 cm^{-1}; ^1H NMR, 5.83 (1H, m), 3.72 (1H, broad), 3.58 (1H, ddd, J = 1.6, 9.3, & 7.0 Hz), 3.50 (1H, dd, J = 5.1 & 9.3 Hz), 3.40 (1H, m), 2.57 (1H, ddd, J = 15.5, 7.0 & 1.7 Hz), 2.48 (1H, m), 1.88-2.42 (7H, m), 1.12-1.64 (2H, m); ^{13}C NMR, 175.9, 173.7, 143.8, 123.8, 73.6, 47.7, 46.8, 42.6, 42.1, 40.8, 29.6, 26.2, 25.6; MS, 236(4.6), 218 (4), 190 (39), 145 (100), 118 (52), 93 (58), 71 (58).

Characteristic properties of **82b** : mp, 103-107 °C; IR (CH_3Cl), 3290-3610, 1846, 1778 cm^{-1}; ^1H NMR, 5.73 (1H, m), 4.02 (!H, m), 3.58 (1H, ddd, 1.8, 9.0 & 7.0 Hz), 3.51 (1H, m), 3.19 (1H, broad), 2.35 (1H, ddd, J = 7.0, 1.7 & 14.9 Hz), 1.42-2.48 (10H, m); ^{13}C NMR, 176.2, 173.8, 143.5, 124.9, 68.2, 76.6, 42.8, 42.6, 41.8, 38.1, 30.3,

25.5, 23.9; MS, 236 (1.3), 218 (5.5), 190 (56), 145 (100), 118 (30), 93 (29).

Oxidation of 82 to 83

A mixture of epimeric alcohols **82a** and **82b** (45 mg, 0.19 mmol) was added to a stirred solution of pyridinium dichromate (PDC, 144 mg, 0.4 mmol) in dimethylformamide (DMF, 10 ml). After stirring overnight at room temperature, the solution was diluted with water and extracted with ether. The extract was washed with brine and dried over magnesium sulfate. Evaporation of the solvent yielded ketone **83** (22.8 mg, 51%) as a yellowish solid. An analytical sample was prepared by recrystallization (ethyl acetate) to give **83** as a colorless solid : mp, 136-137 °C; IR (CH_3Cl), 1849, 1781,1707, 1224, 1212 cm^{-1}; ^1H NMR, 5.70 (1H, m), 3.48 (2H, m), 3.18 (1H, d, J = 15.0 Hz), 2.83 (1H, d, J = 15.0 Hz), 2.13-2.52 (4H, m), 1.68-2.10 (5H, m), 1.39 (1H, m); ^{13}C NMR, 206.8, 175.8, 173.6, 138.5, 125.1, 50.9, 47.0, 43.6, 41.1, 40.3, 28.5, 24.6, 20.1; MS, 234 (50), 206 (32), 188 (34), 118 (51), 105 (61), 91 (100), 68 (72); High resolution MS, calculated for $C_{13}H_{14}O_4$, 234.0892, found, 234.0898.

APPENDIX

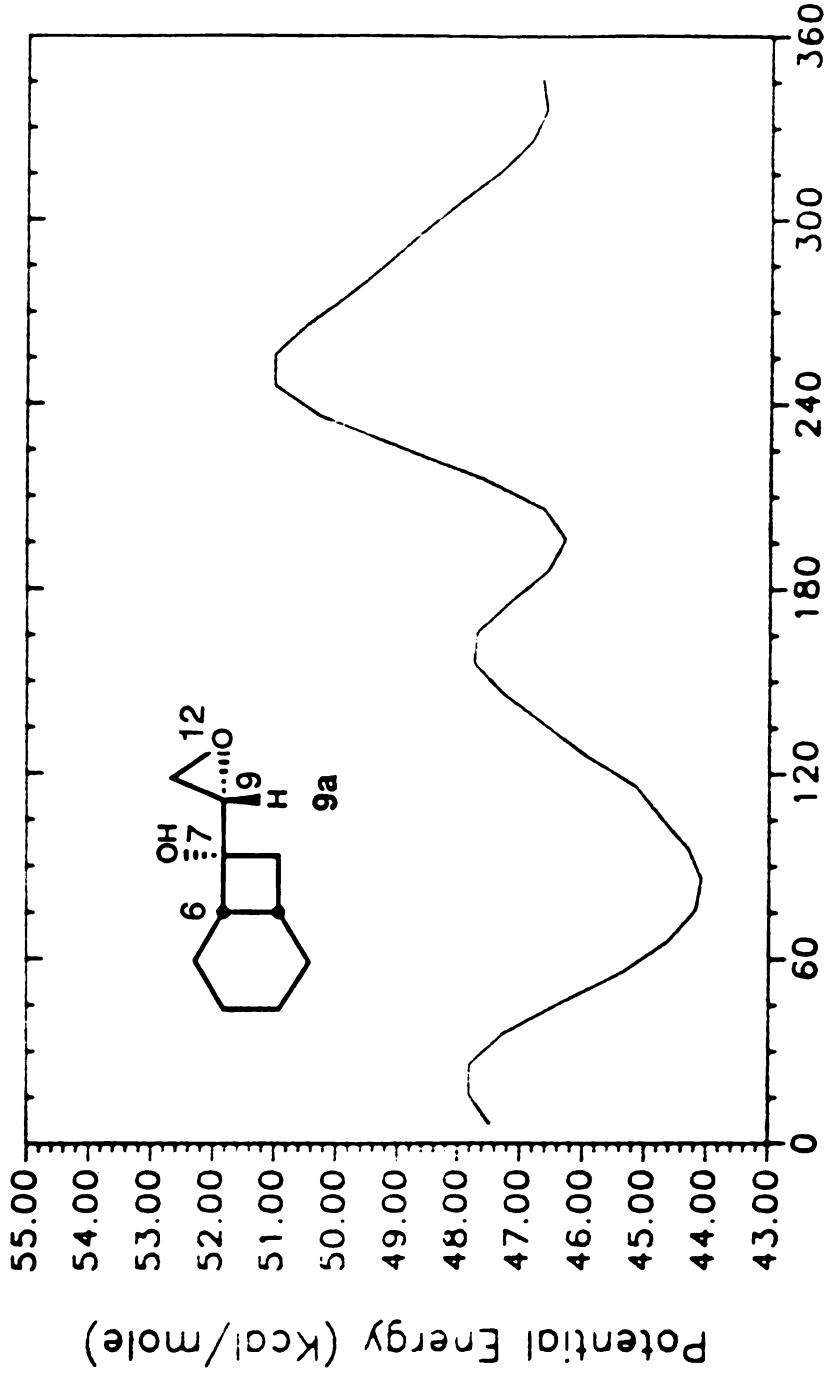


Figure 3. Diagram of Potential Energy vs. Dihedral Angle in **9a**

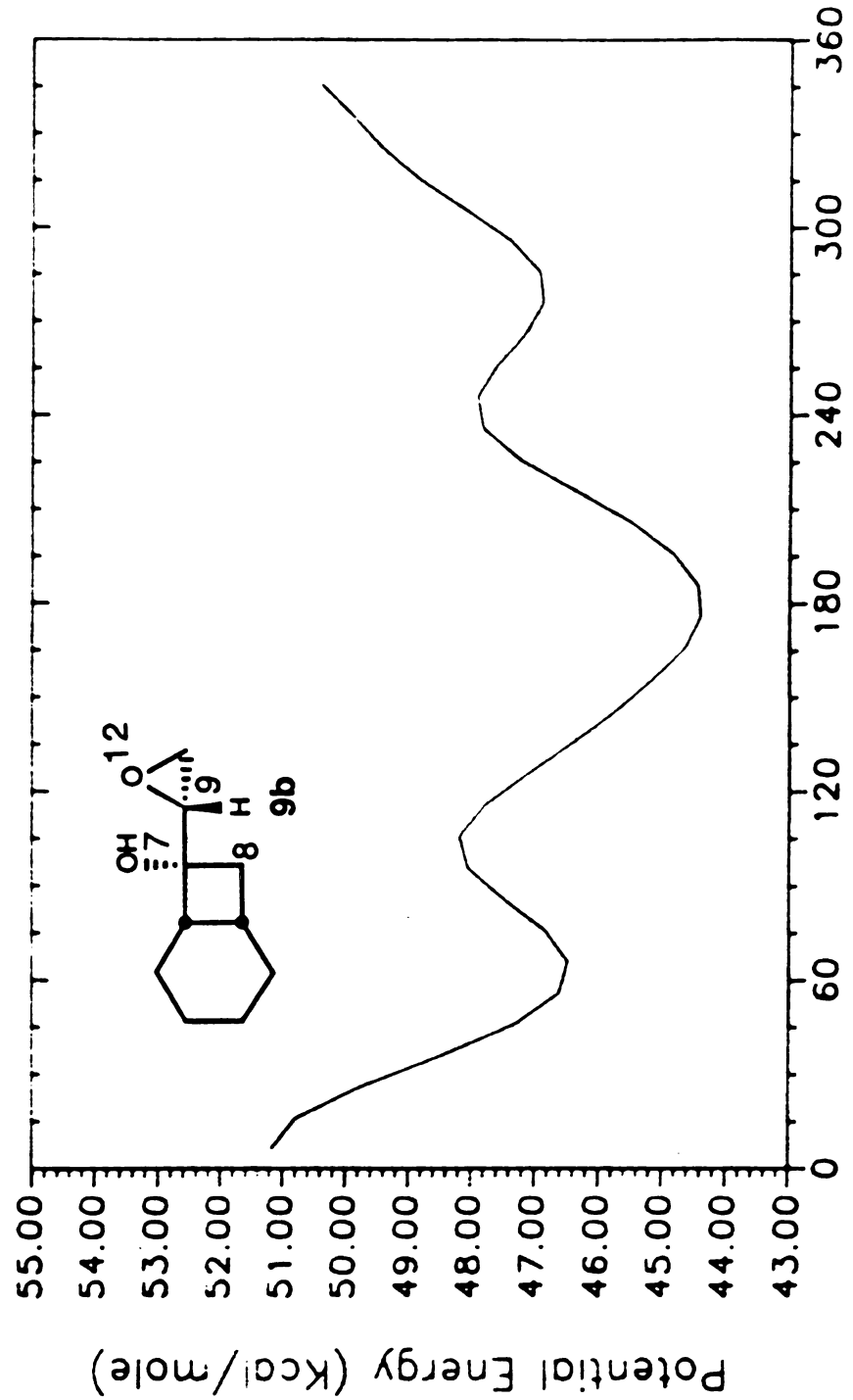


Figure 4. Diagram of Potential Energy vs. Dihedral Angle in **9b**

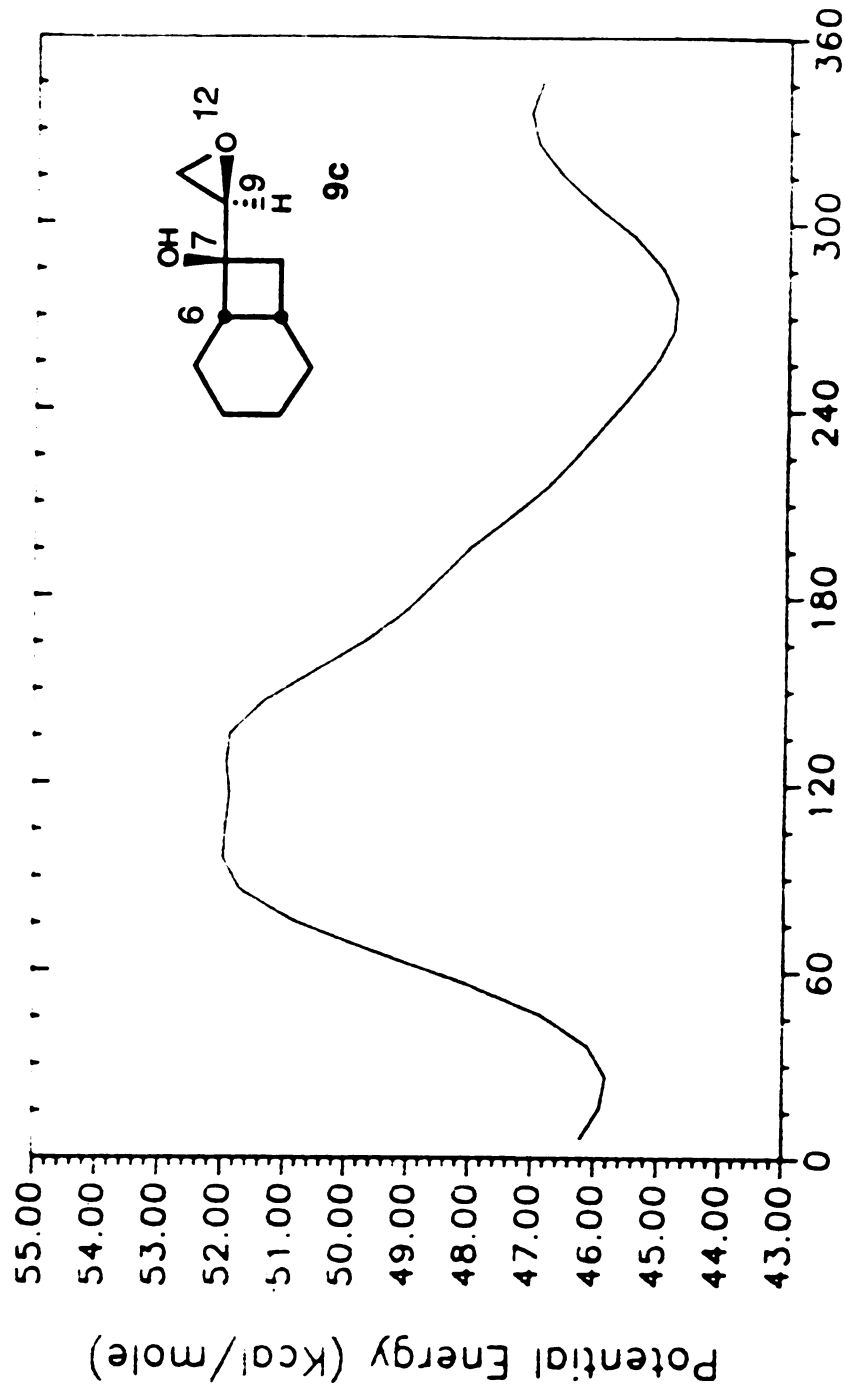


Figure 5. Diagram of Potential Energy vs. Dihedral Angle in **9c**

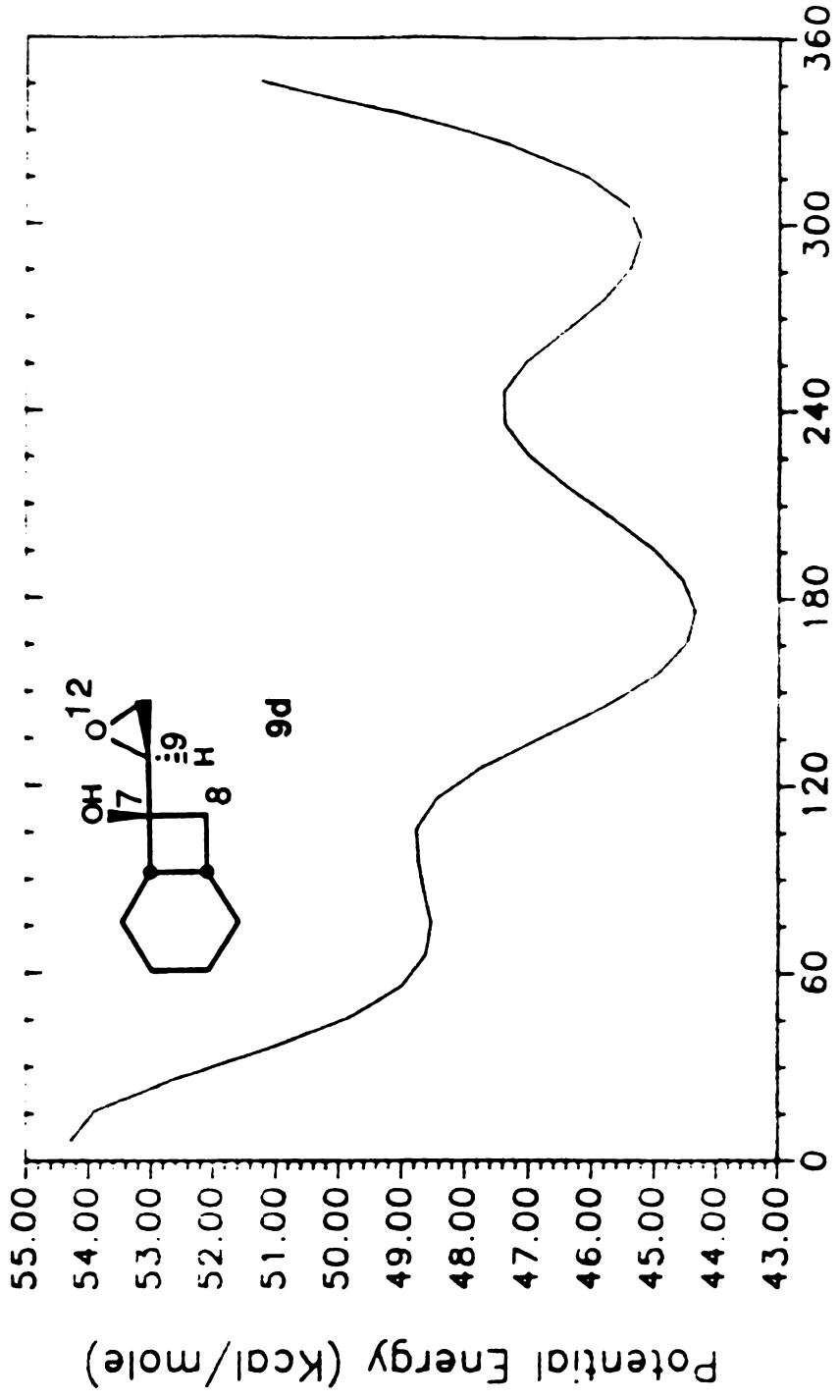


Figure 6. Diagram of Potential Energy vs. Dihedral Angle in **9d**

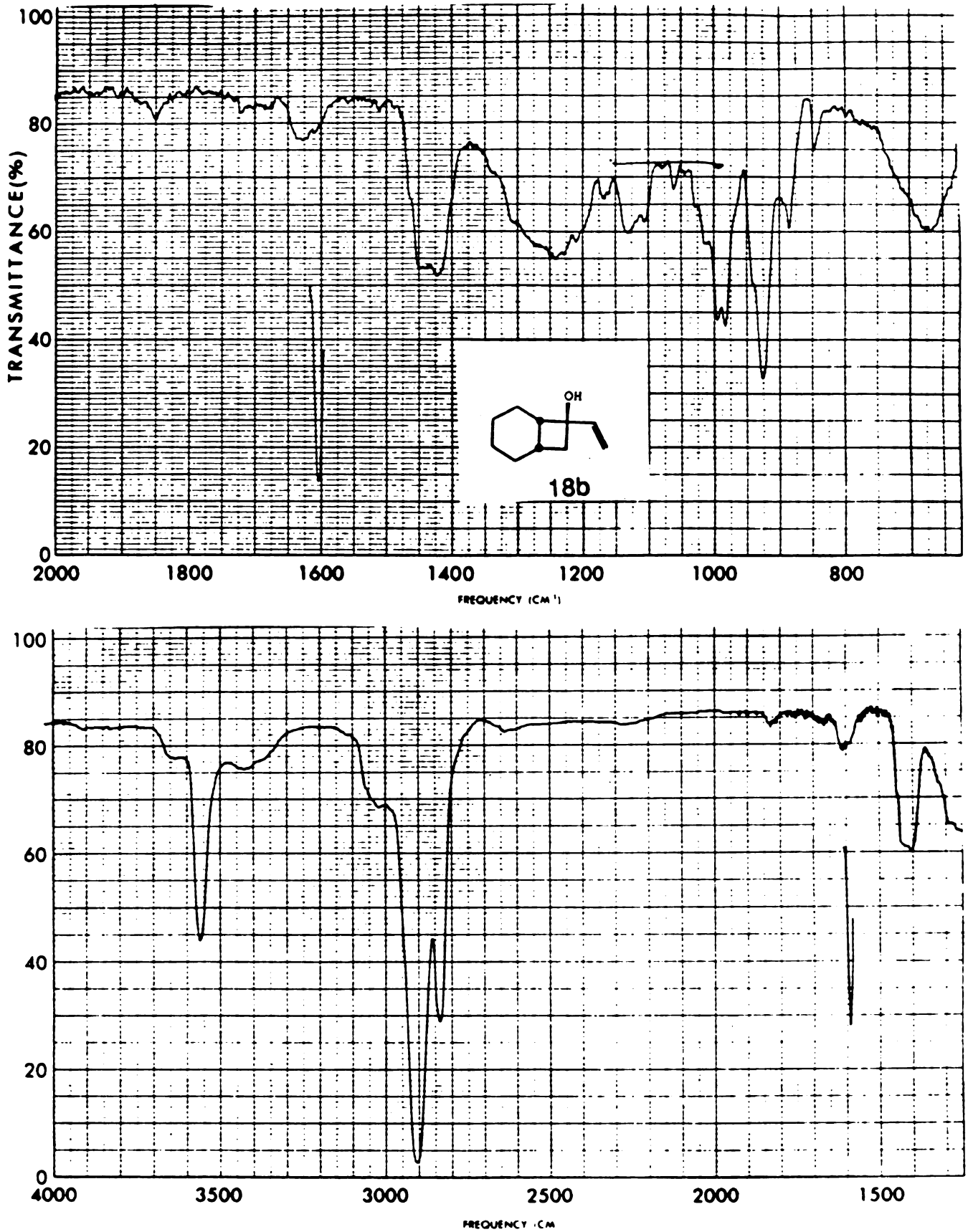


Figure 7. Infrared Spectrum of **18b**

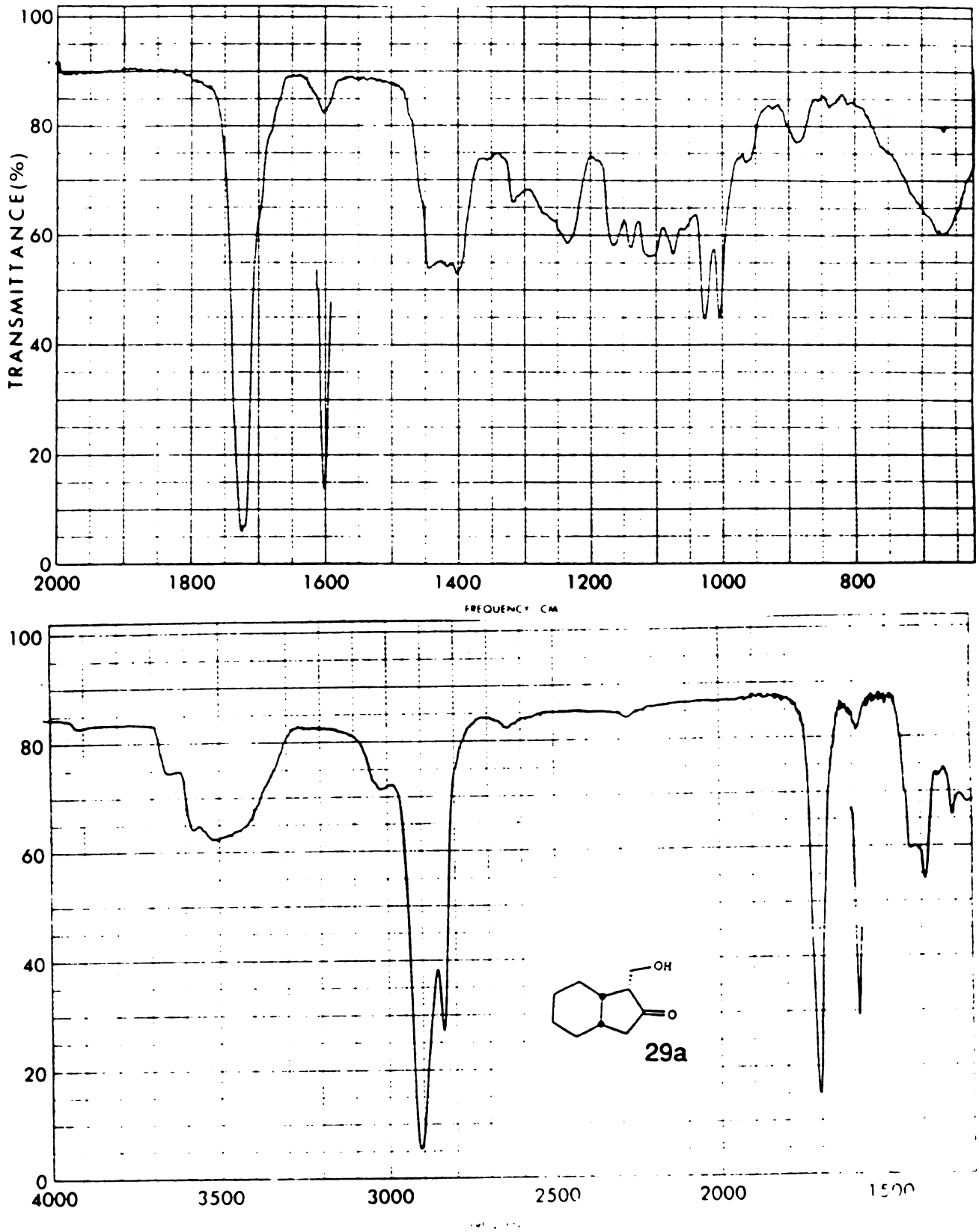


Figure 8. Infrared Spectrum of **29a**

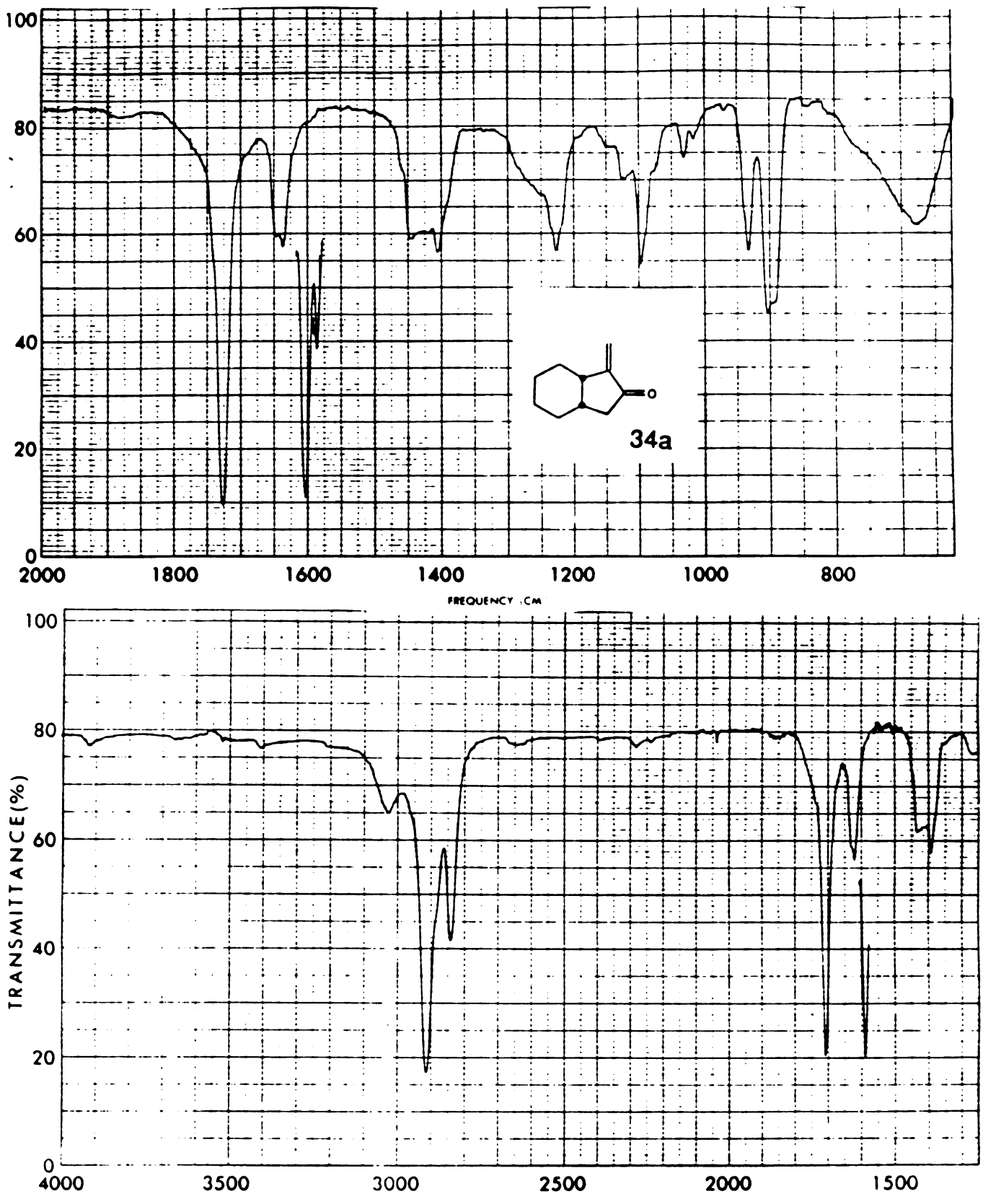


Figure 9. Infrared Spectrum of **34a**

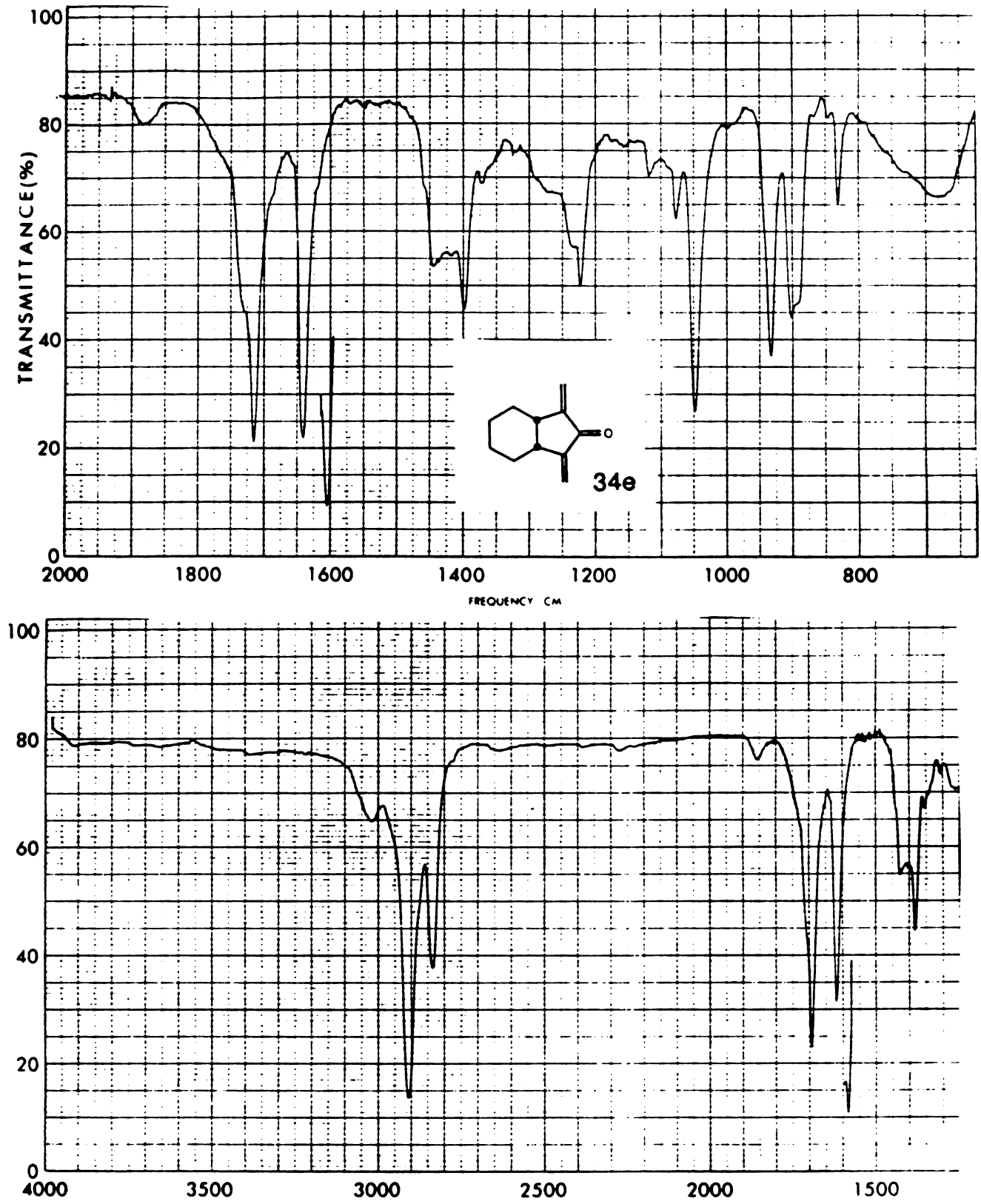


Figure 10. Infrared Spectrum of **34e**

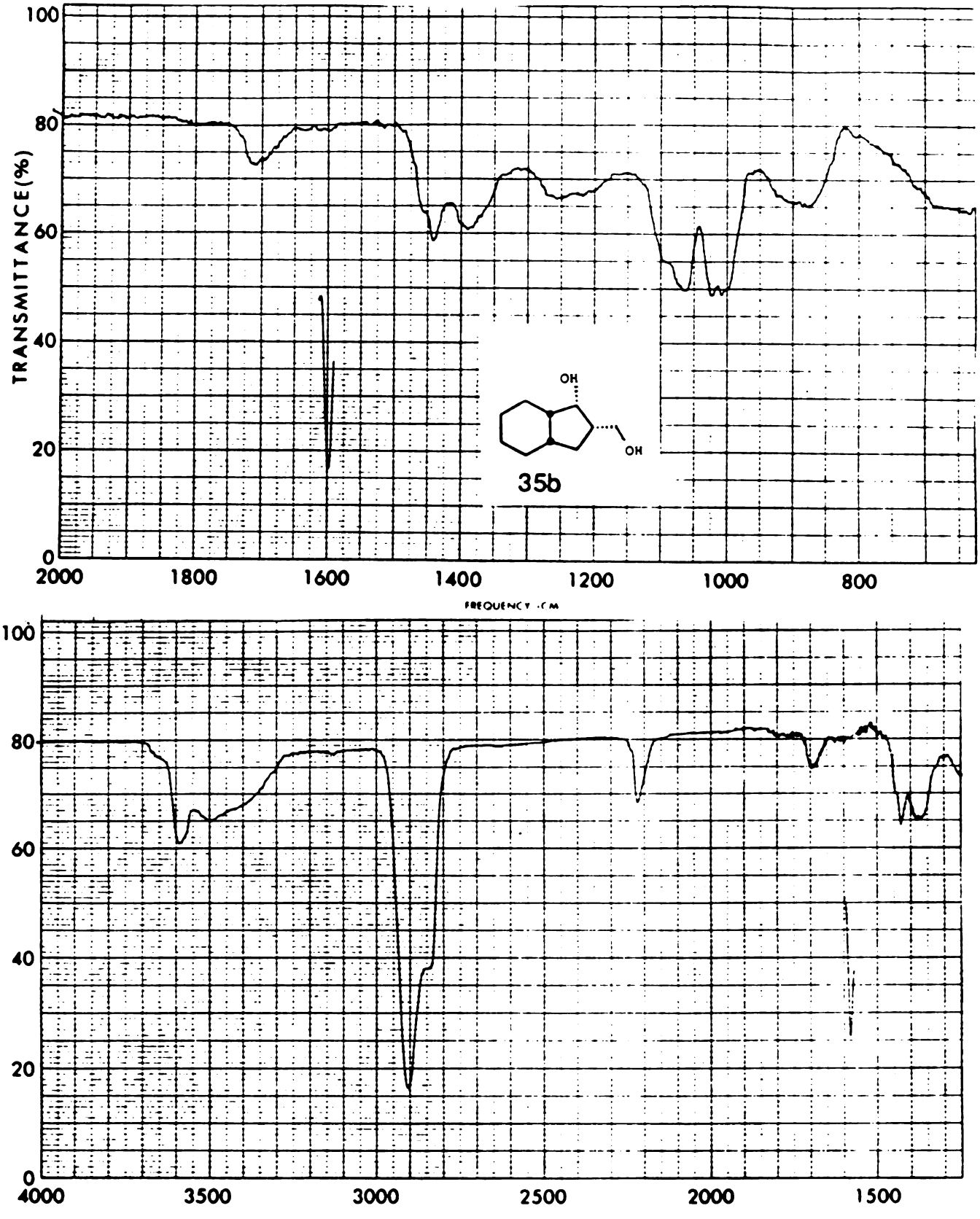


Figure 11. Infrared Spectrum of **35b**

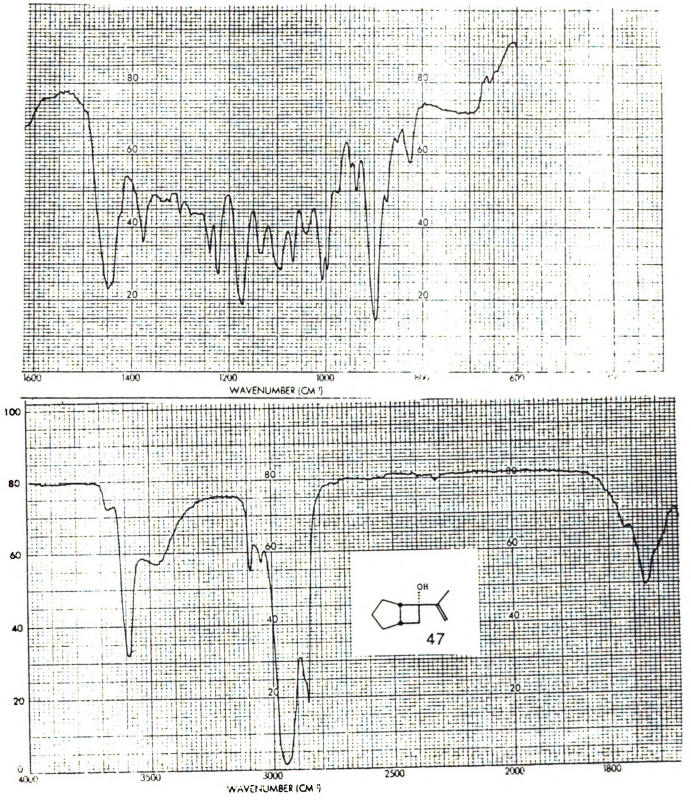


Figure 12. Infrared Spectrum of **47**

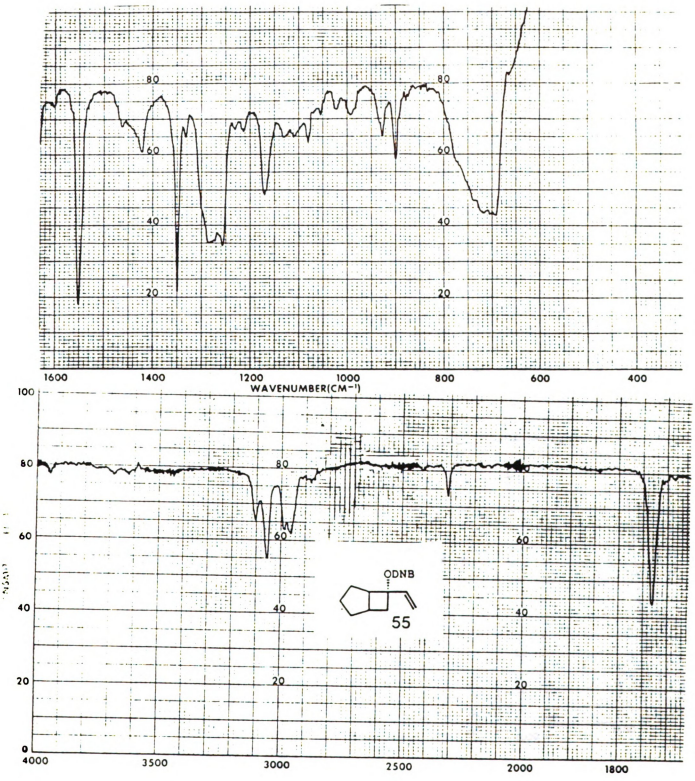


Figure 13. Infrared Spectrum of **55**

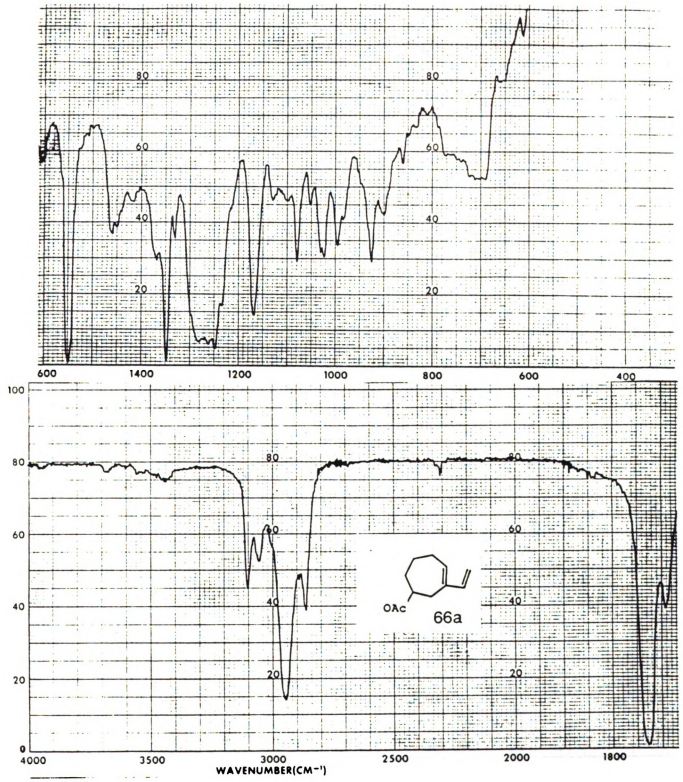


Figure 14. Infrared Spectrum of **66a**

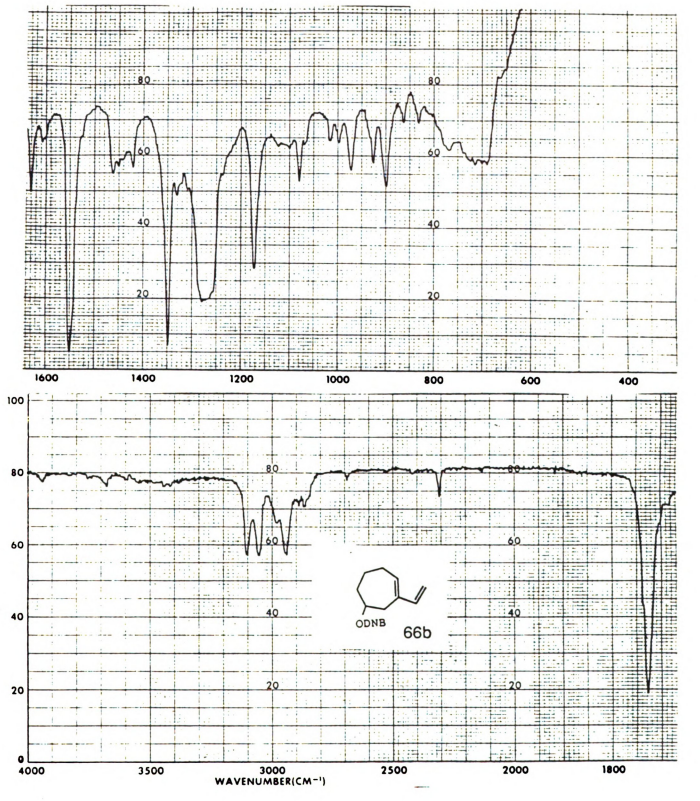


Figure 15. Infrared Spectrum of **66b**

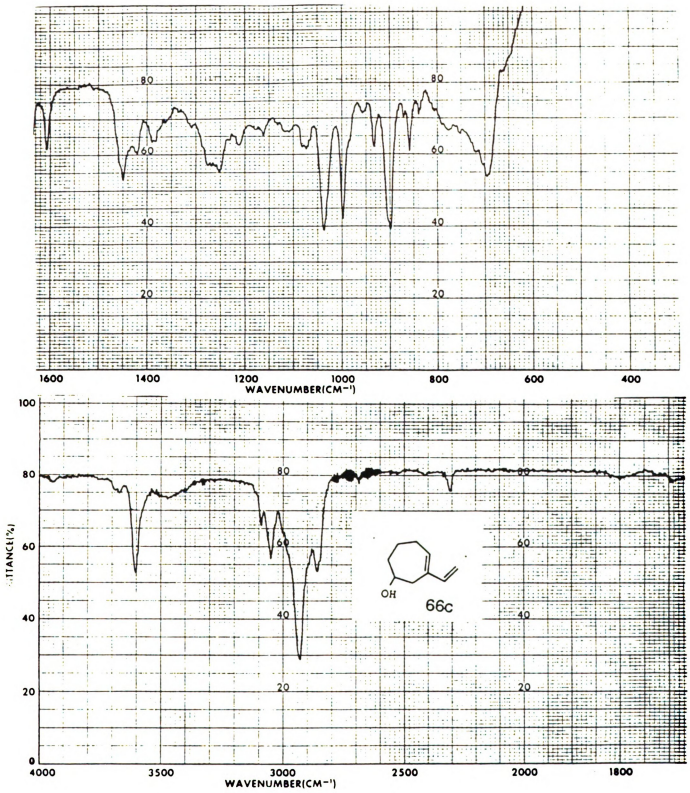


Figure 16. Infrared Spectrum of **66c**

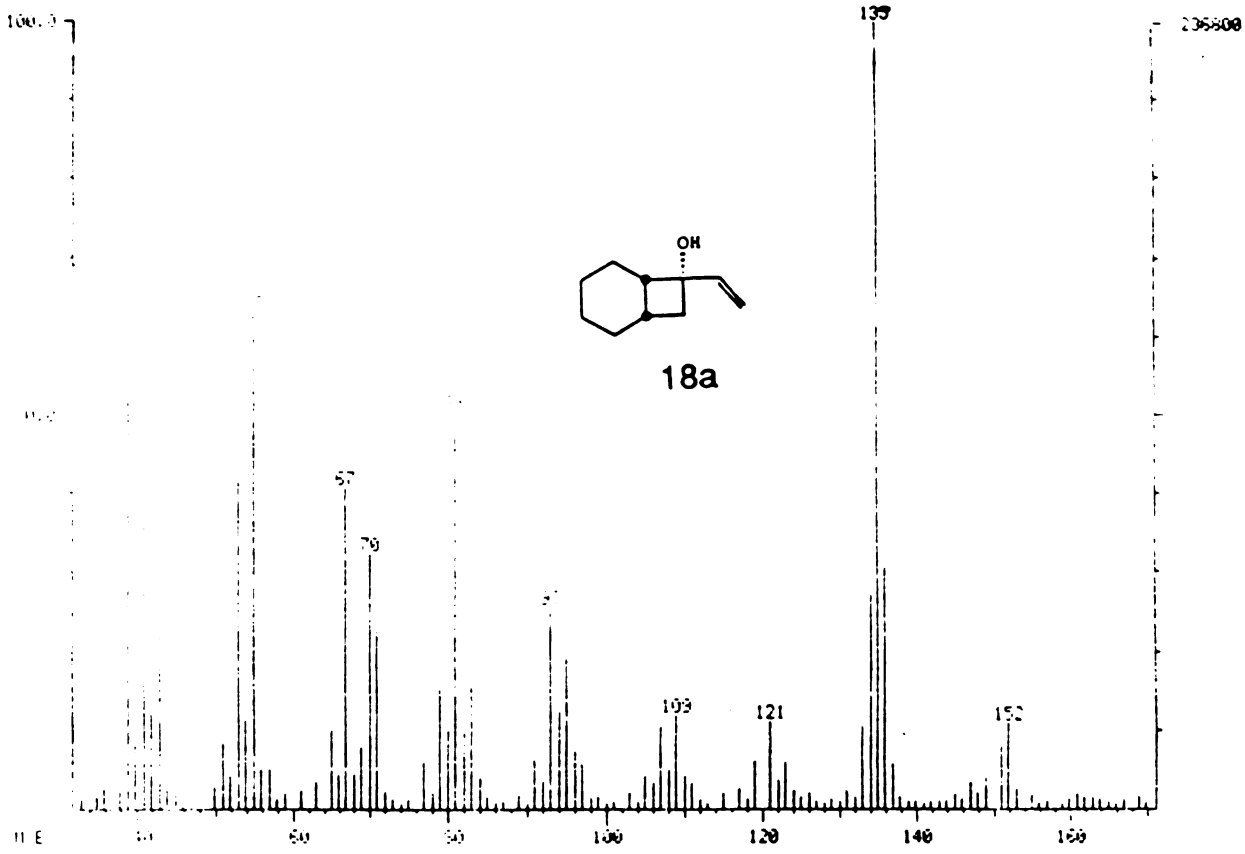


Figure 17. Mass Spectrum of **18a**

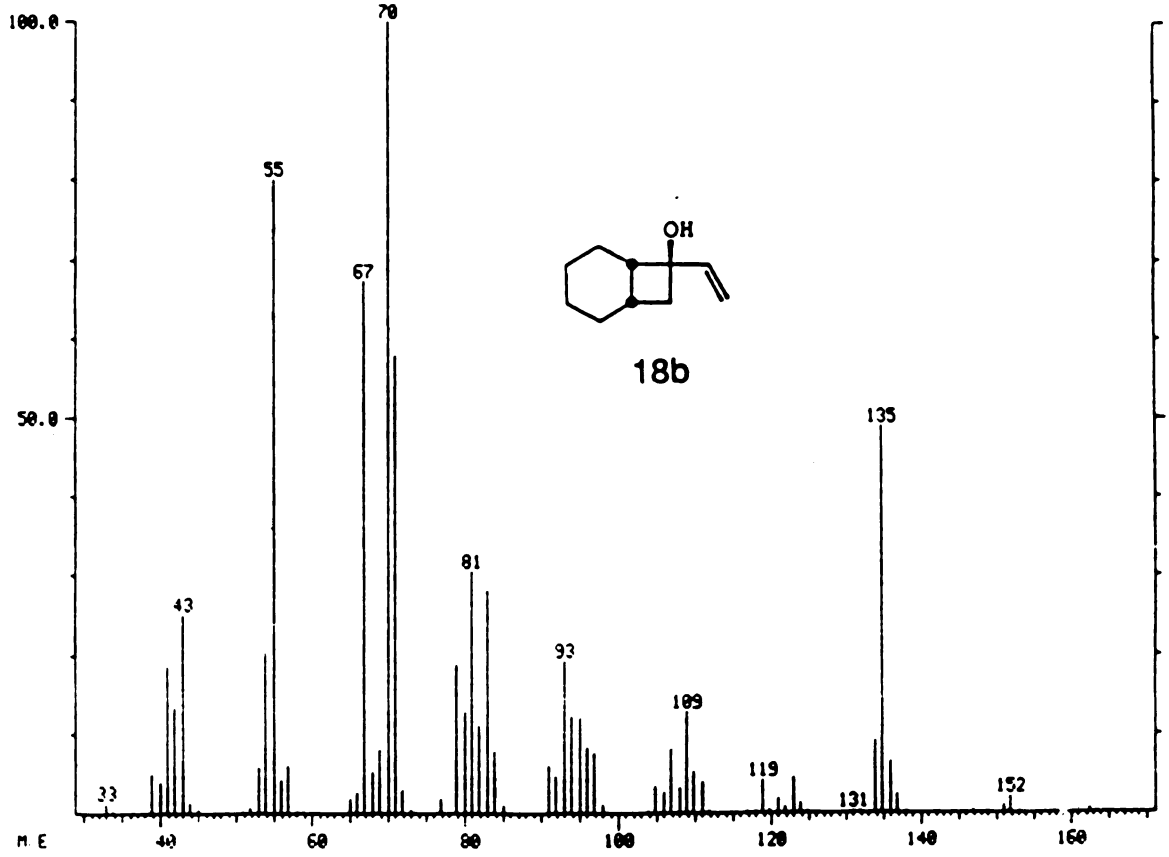


Figure 18. Mass Spectrum of **18b**

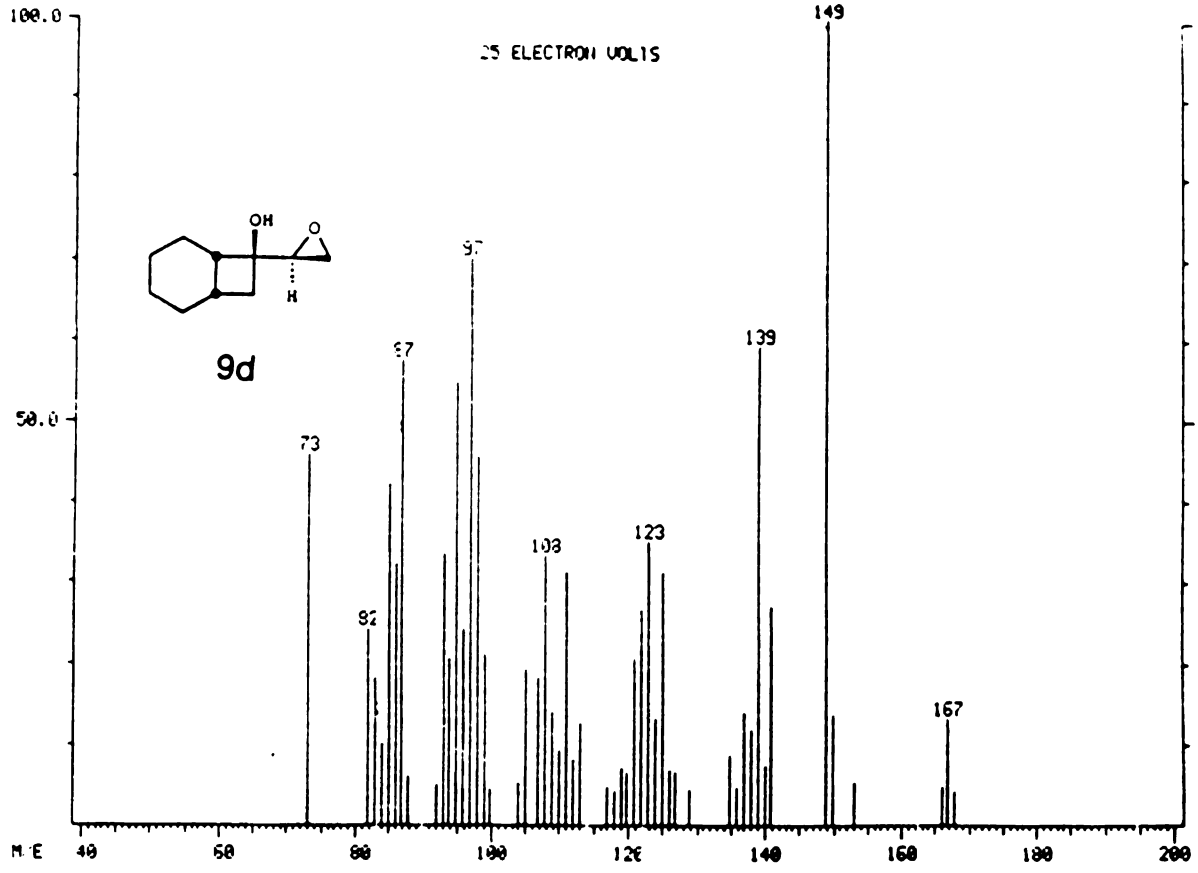


Figure 20. Mass Spectrum of **9d**

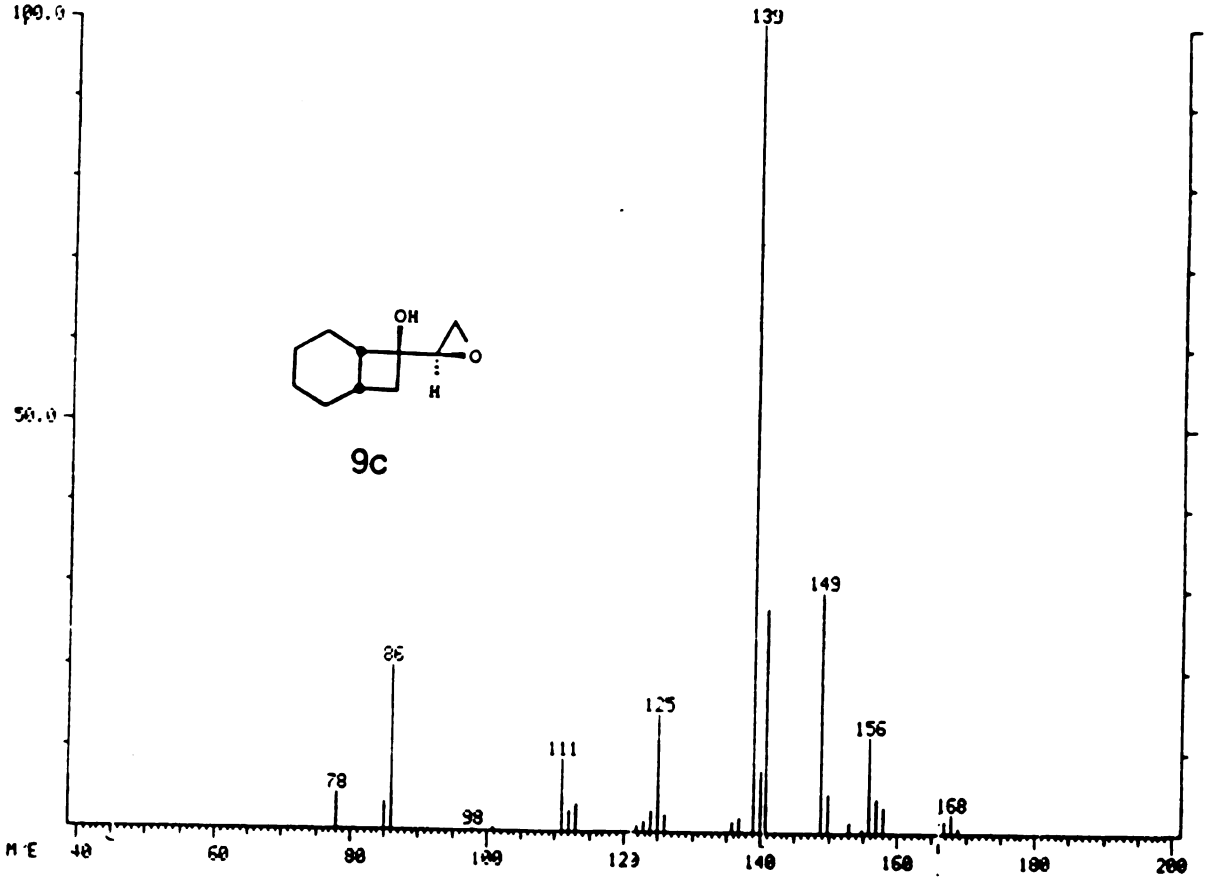
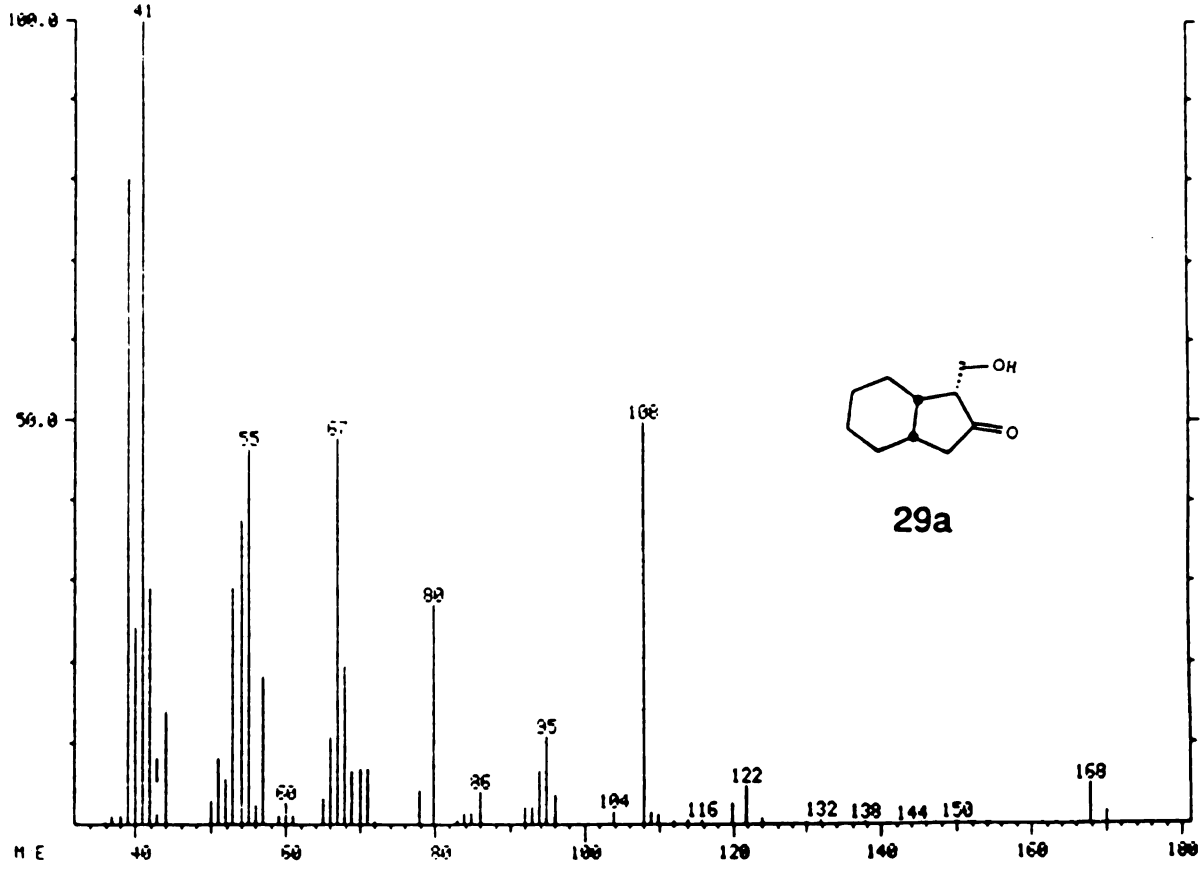
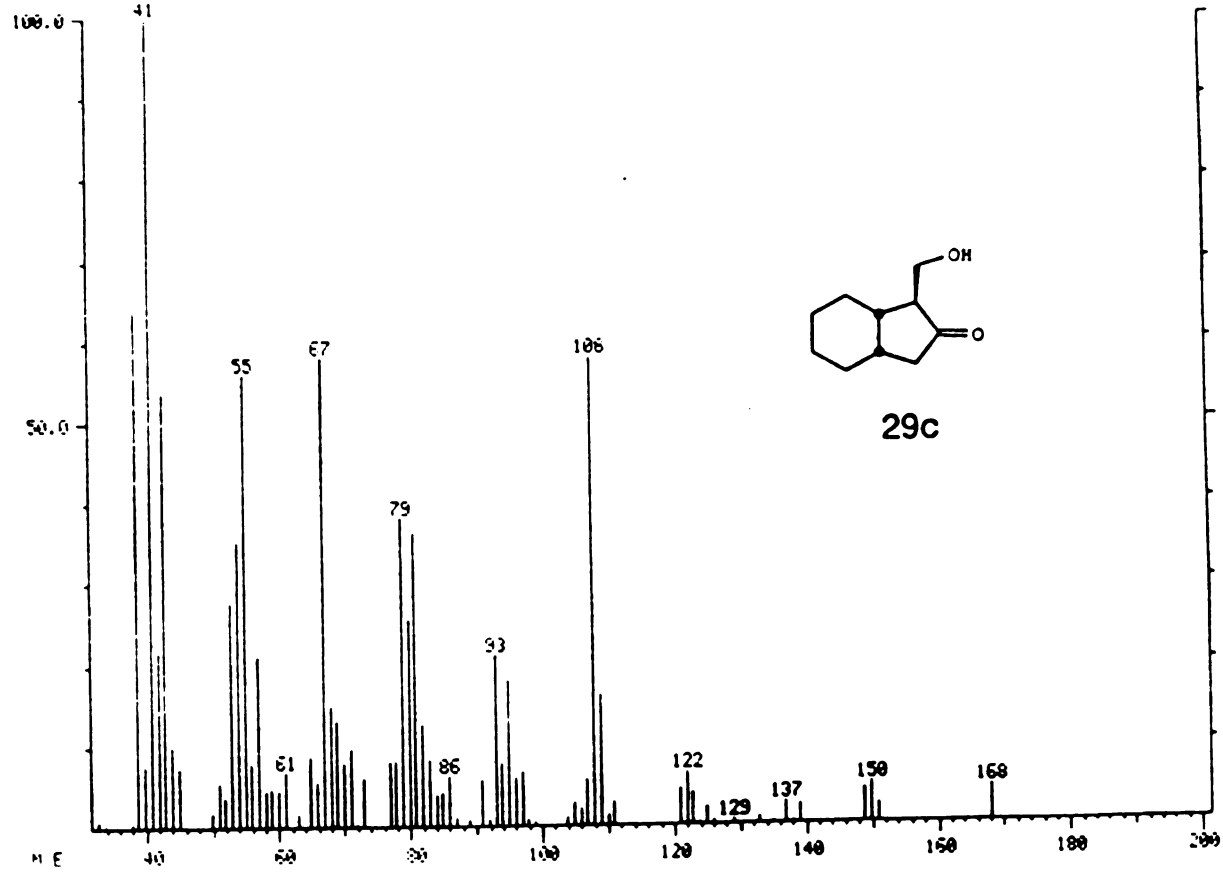


Figure 19. Mass Spectrum of **9c**



29a

Figure 21. Mass Spectrum of **29a**



29c

Figure 22. Mass Spectrum of **29c**

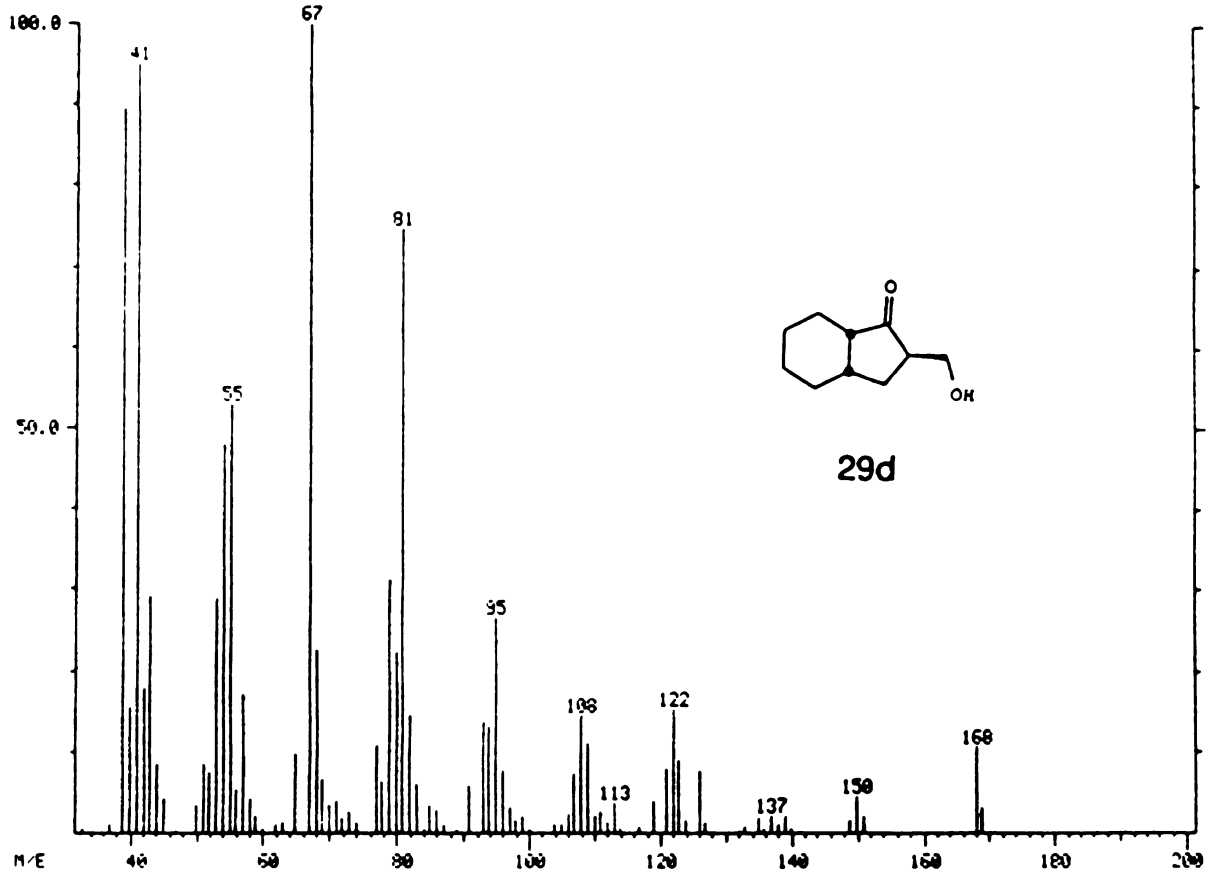


Figure 23. Mass Spectrum of **29d**

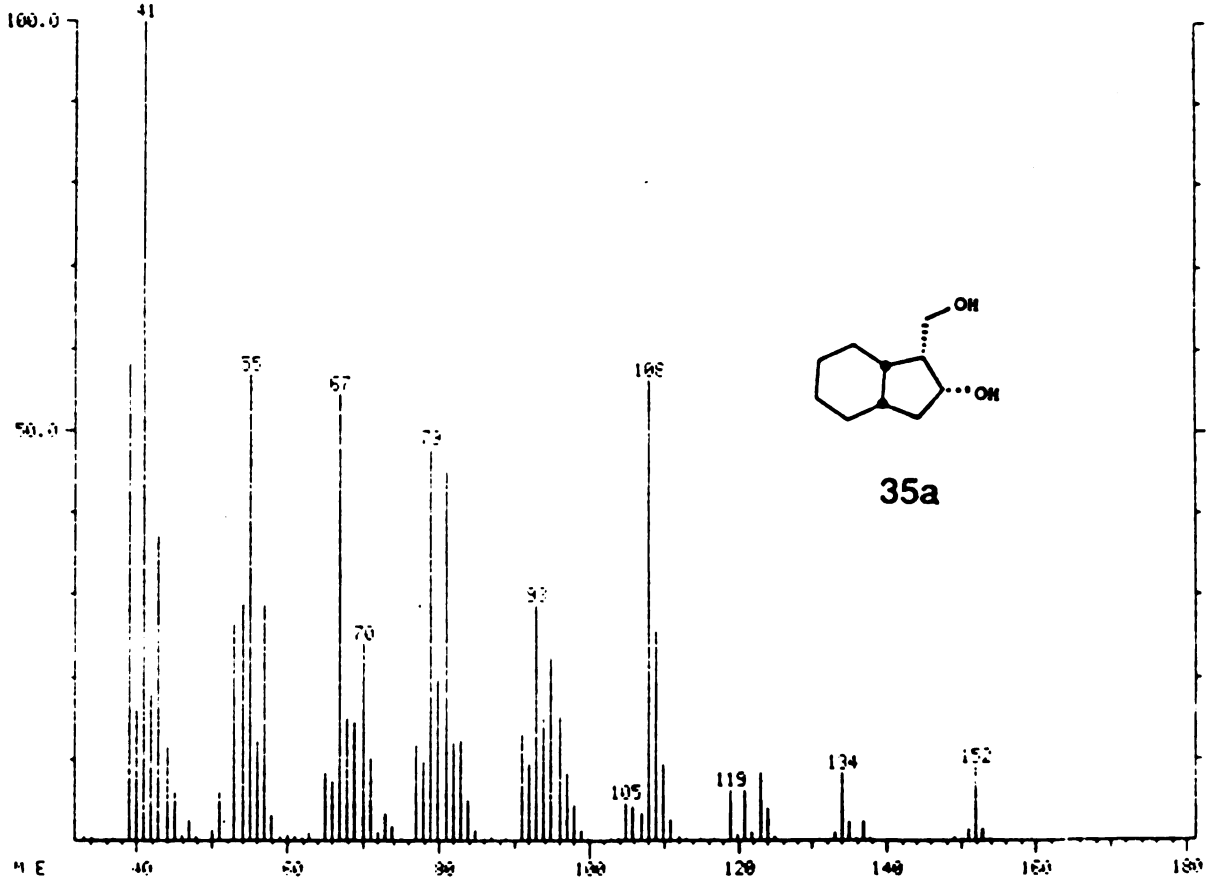


Figure 24. Mass Spectrum of **35a**

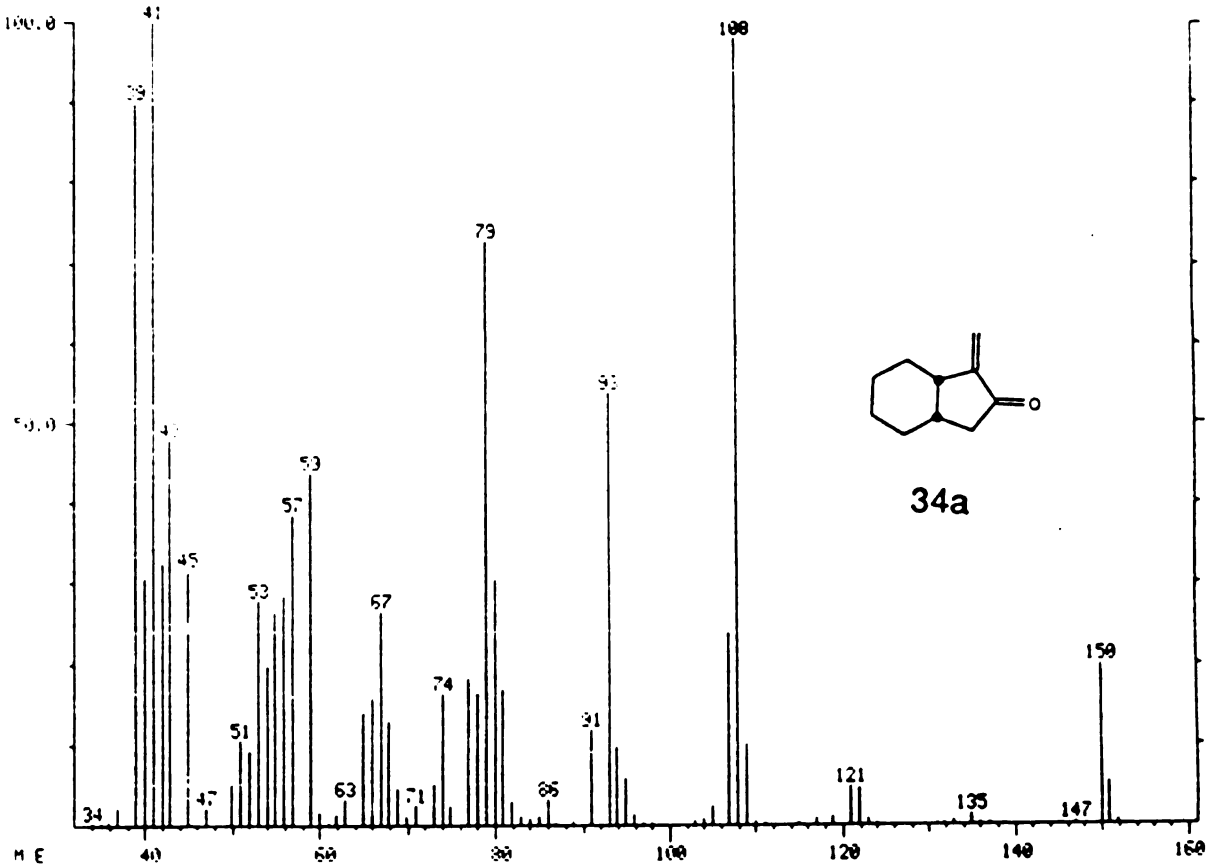


Figure 25. Mass Spectrum of **34a**

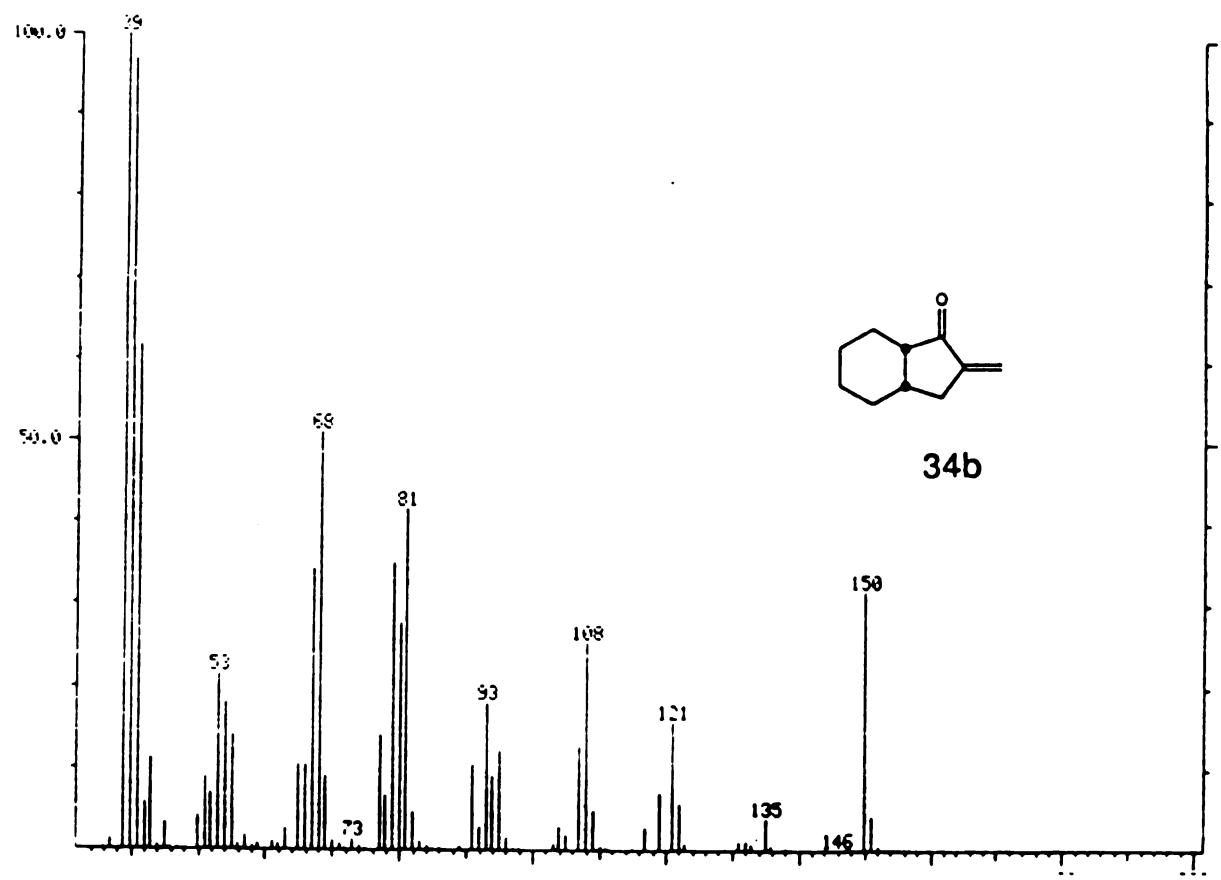


Figure 26. Mass Spectrum of **34b**

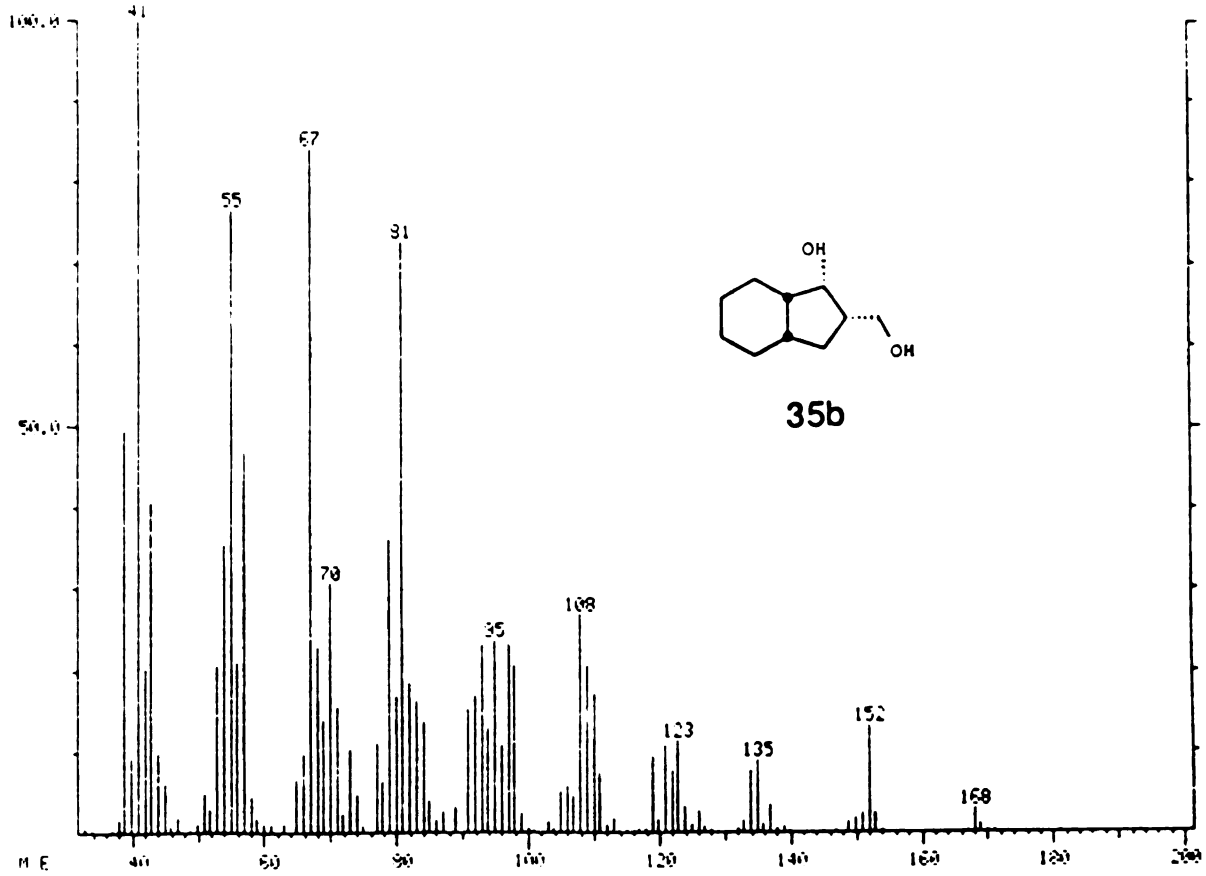


Figure 27. Mass Spectrum of **35b**

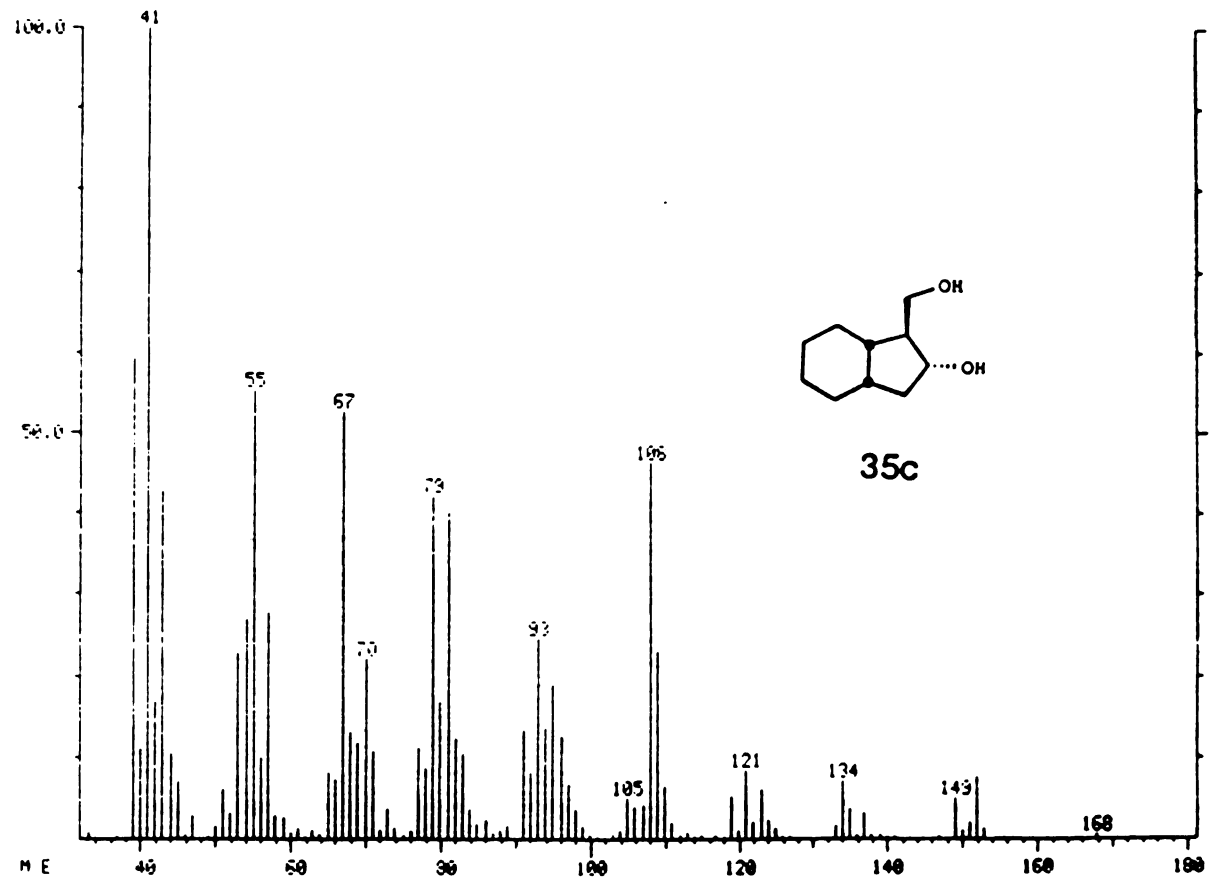


Figure 28. Mass Spectrum of **35c**

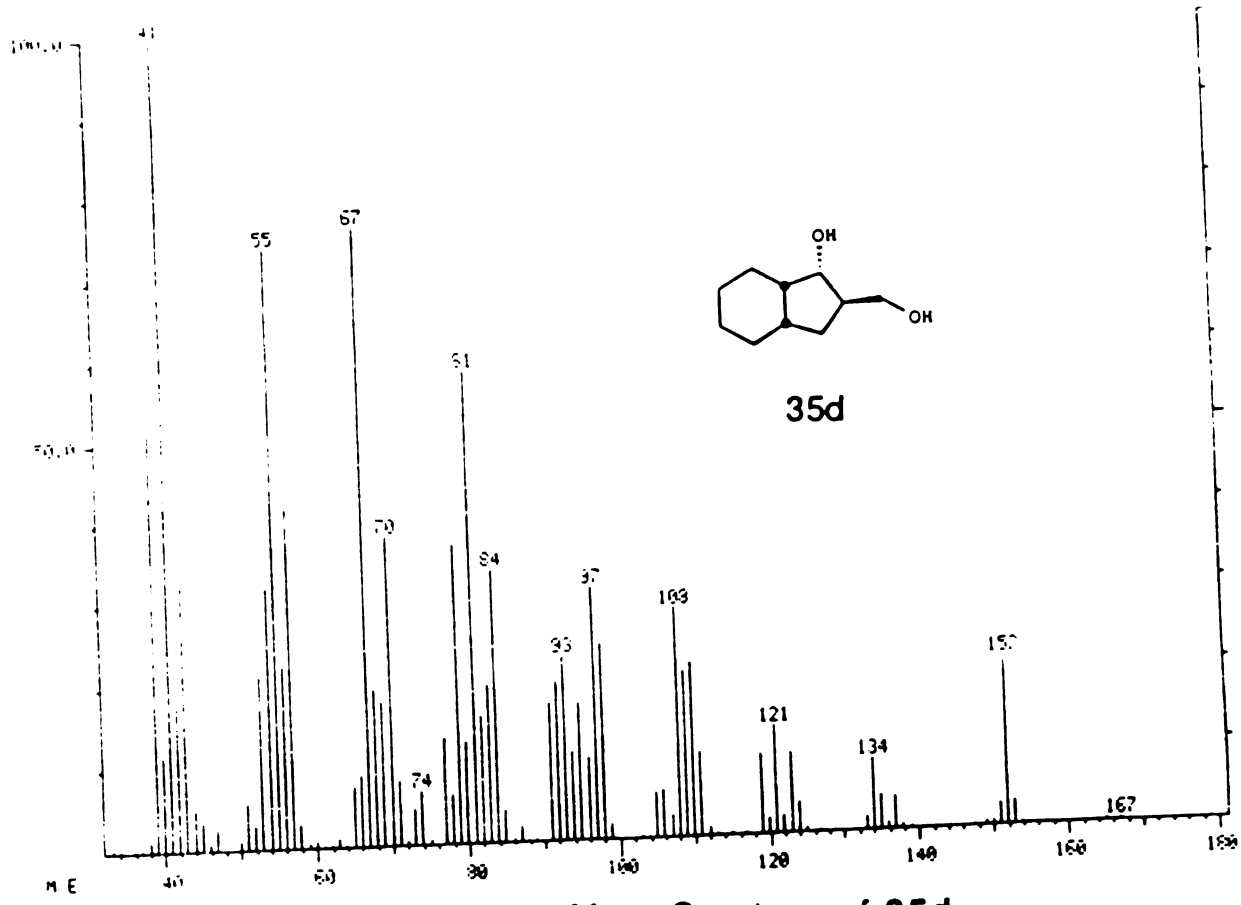


Figure 29. Mass Spectrum of **35d**

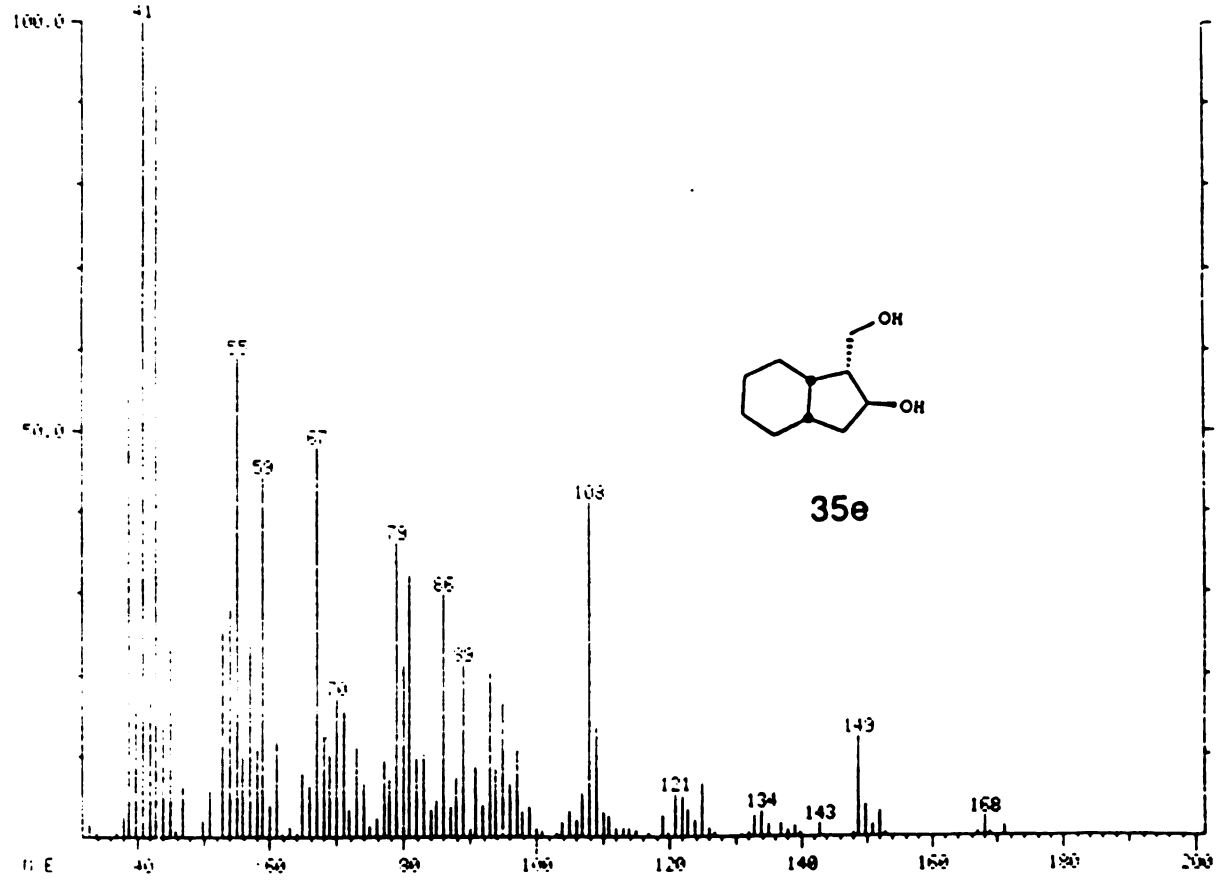


Figure 30. Mass Spectrum of **35e**

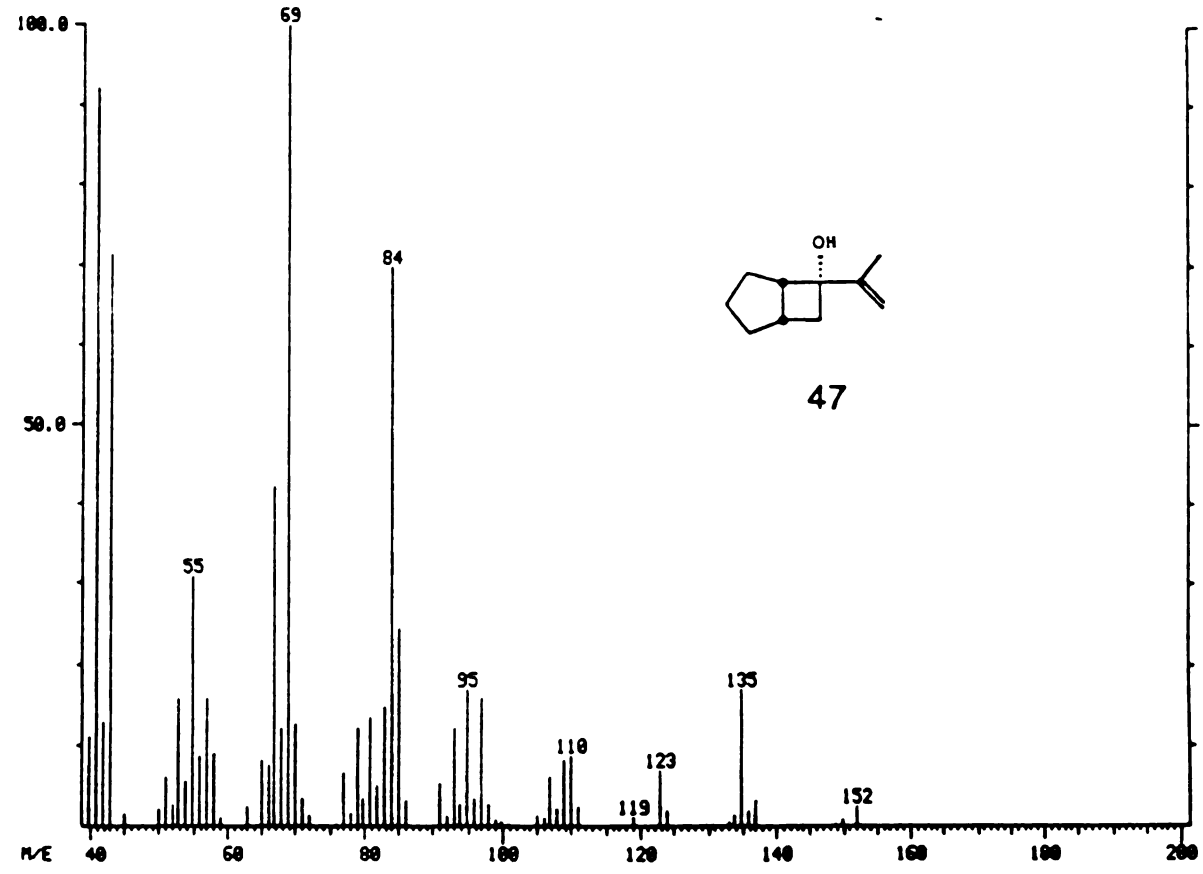


Figure 31. Mass Spectrum of **47**

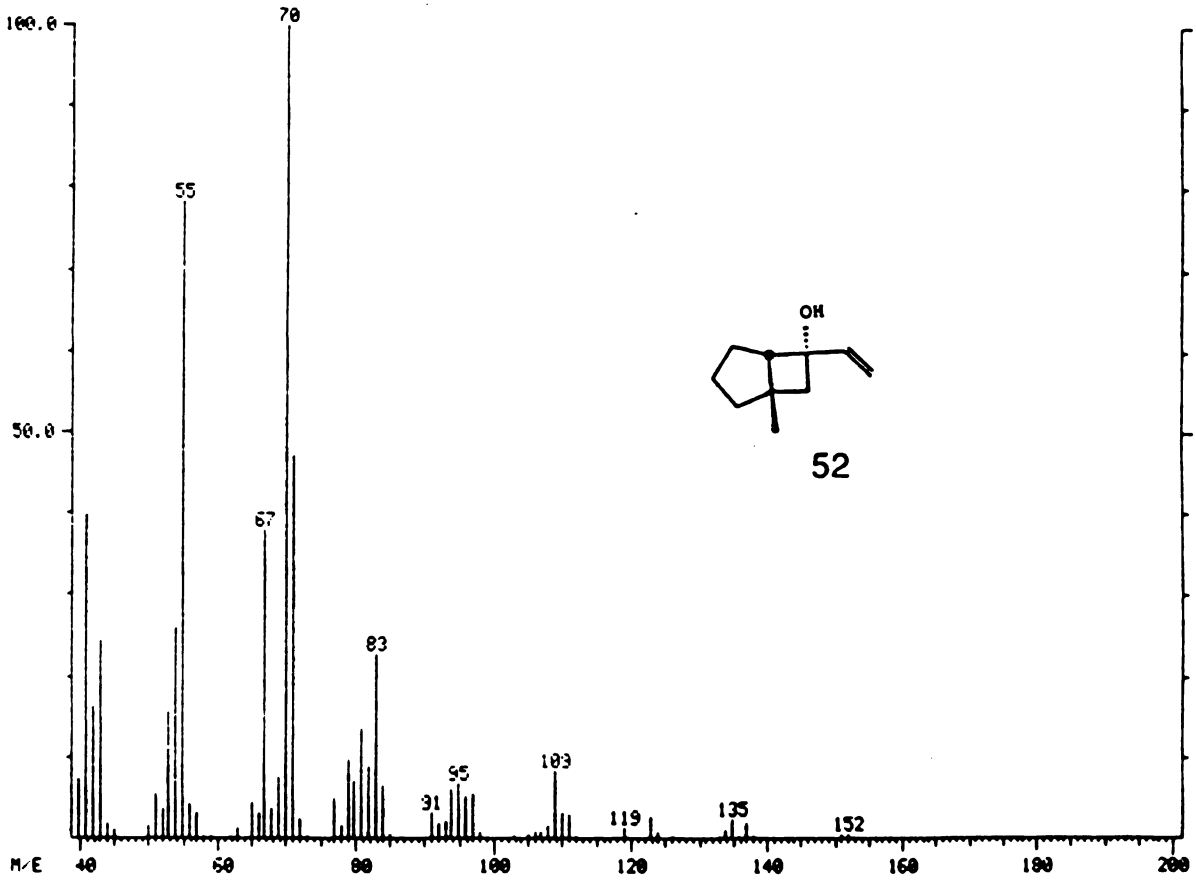


Figure 32. Mass Spectrum of **52**

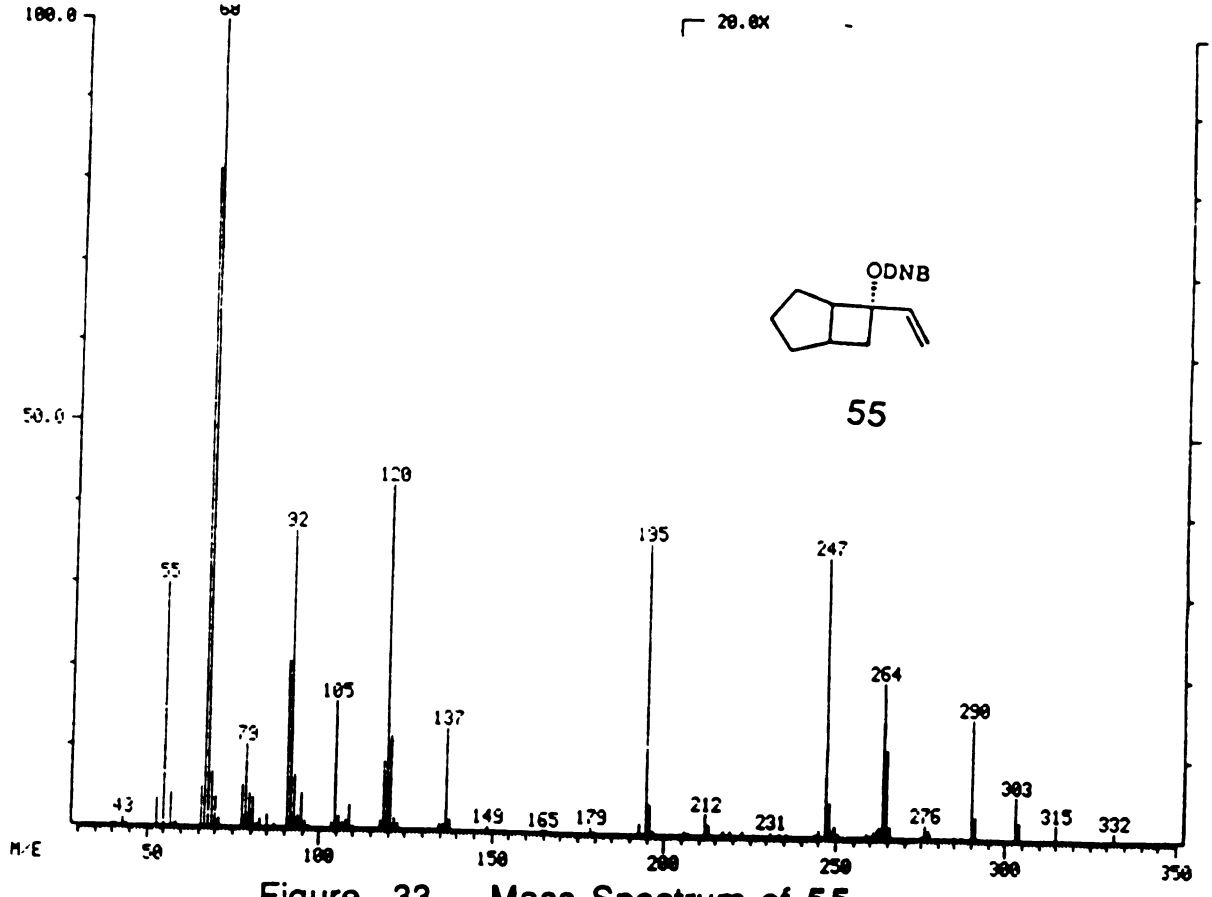


Figure 33. Mass Spectrum of **55**

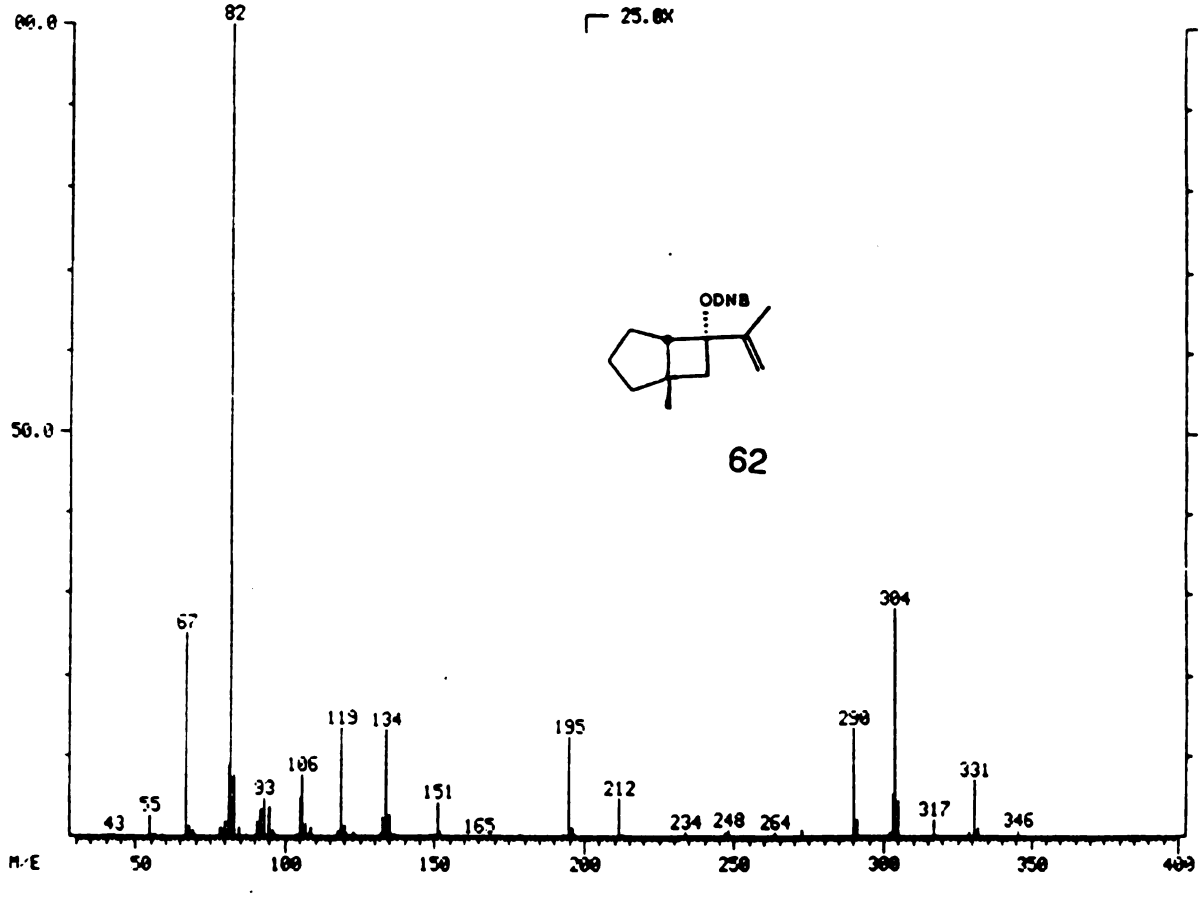
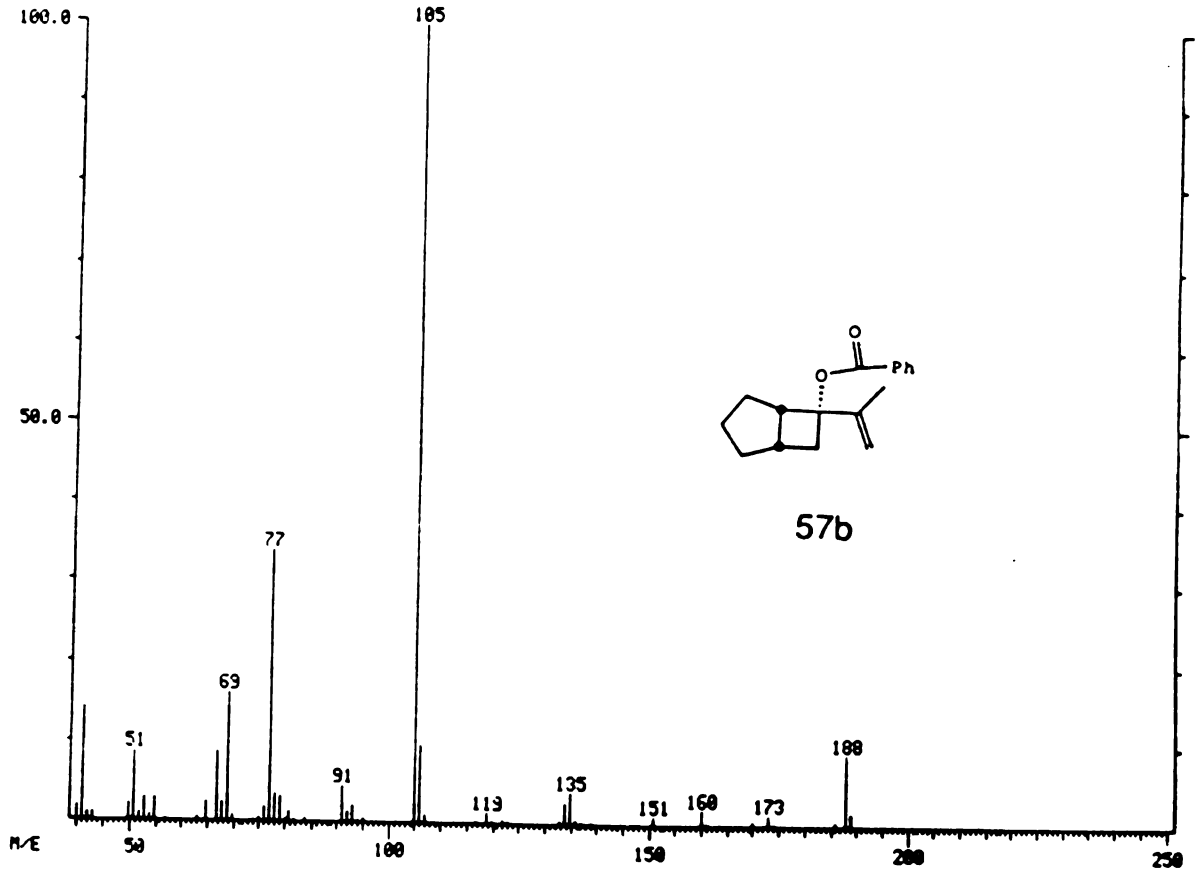
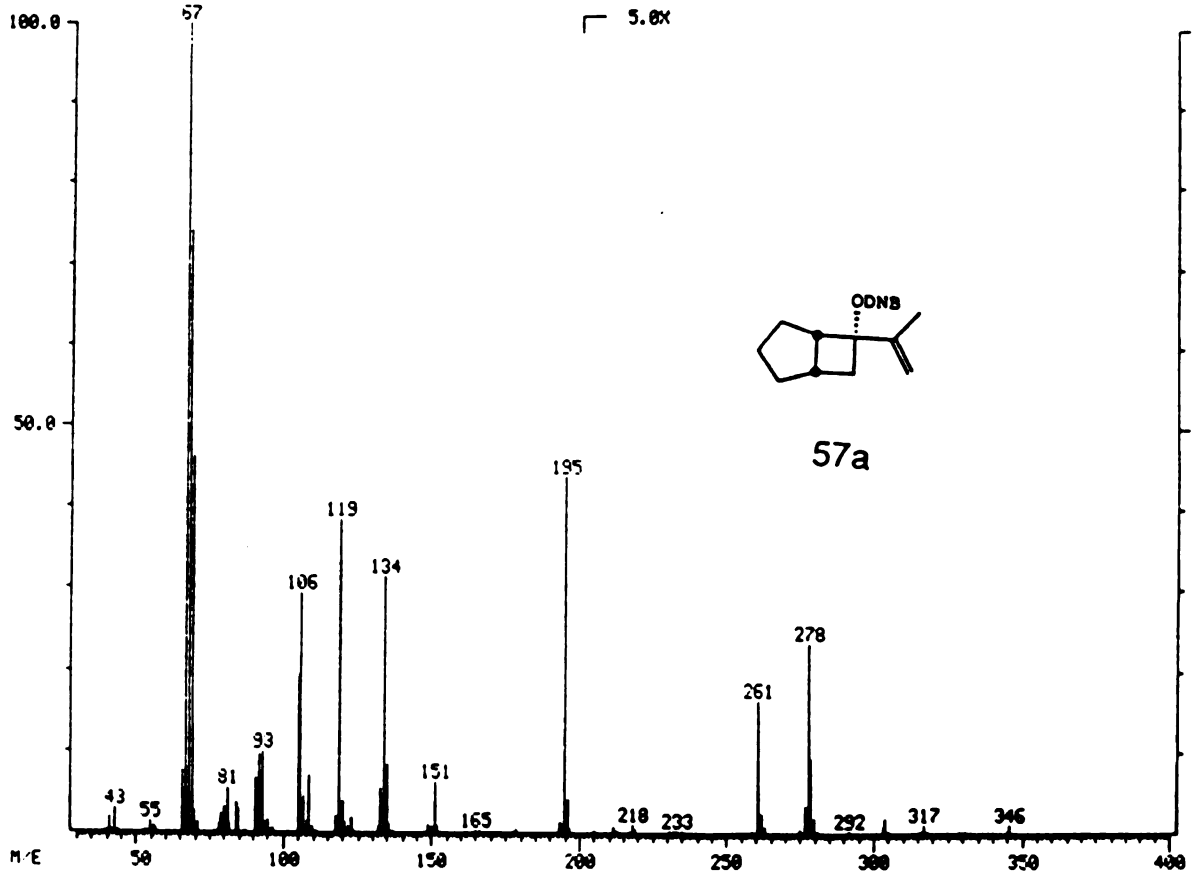


Figure 34. Mass Spectrum of **62**



57b

Figure 36. Mass Spectrum of **57b**



57a

Figure 35. Mass Spectrum of **57a**

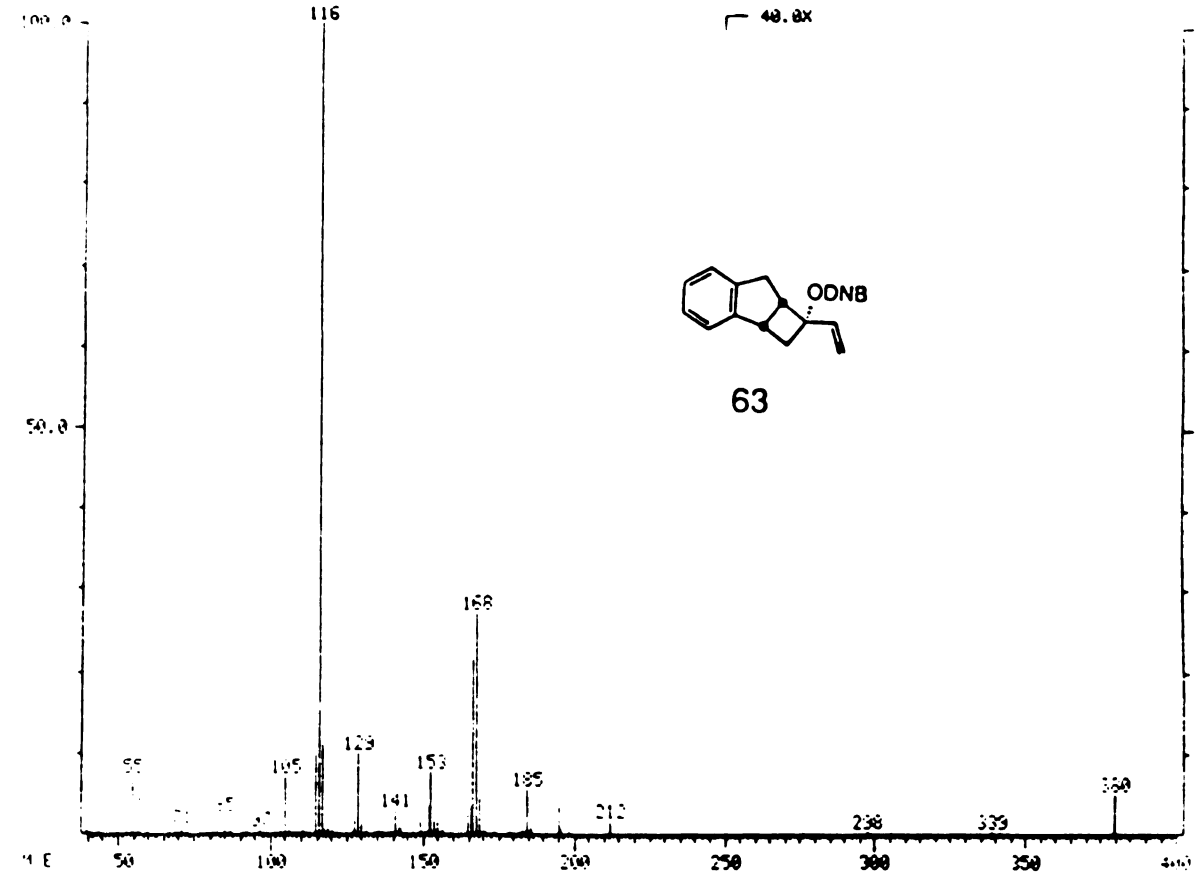


Figure 37. Mass Spectrum of **63**

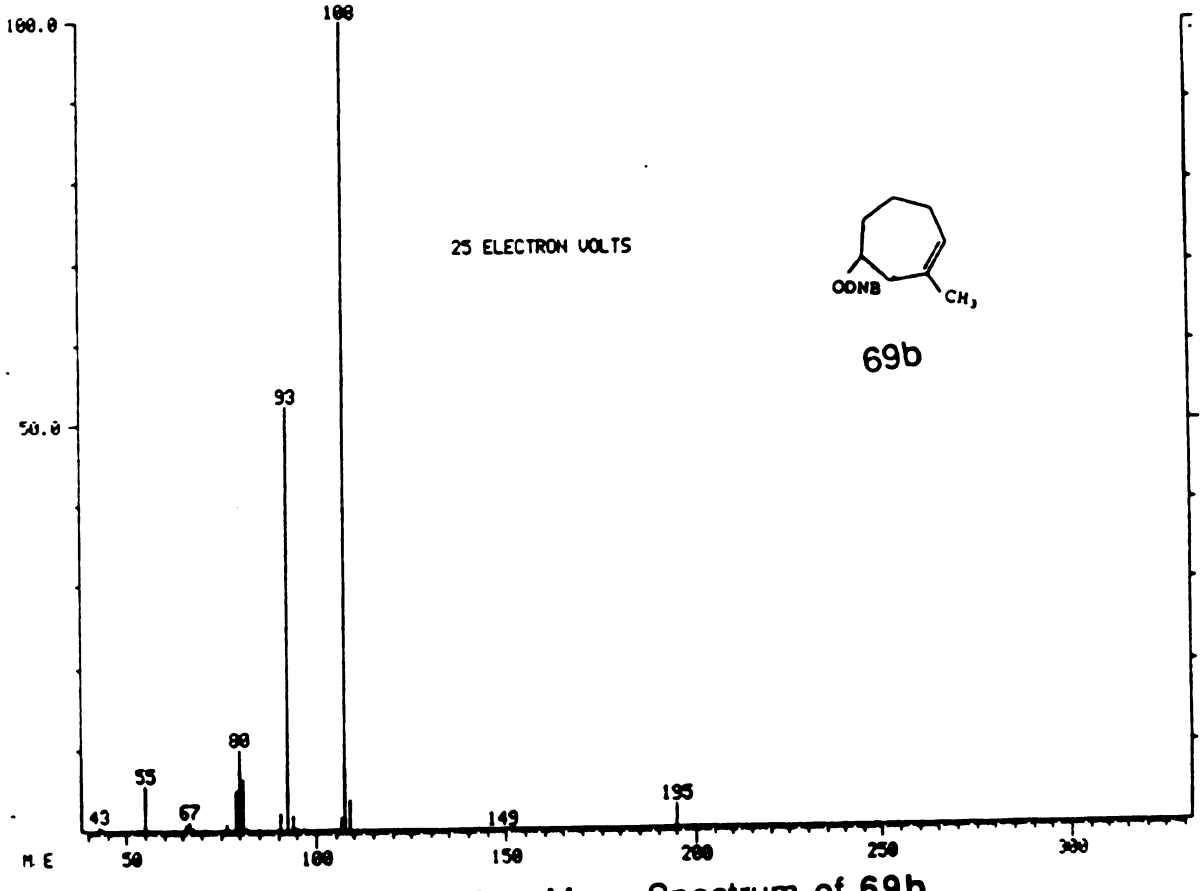


Figure 38. Mass Spectrum of **69b**

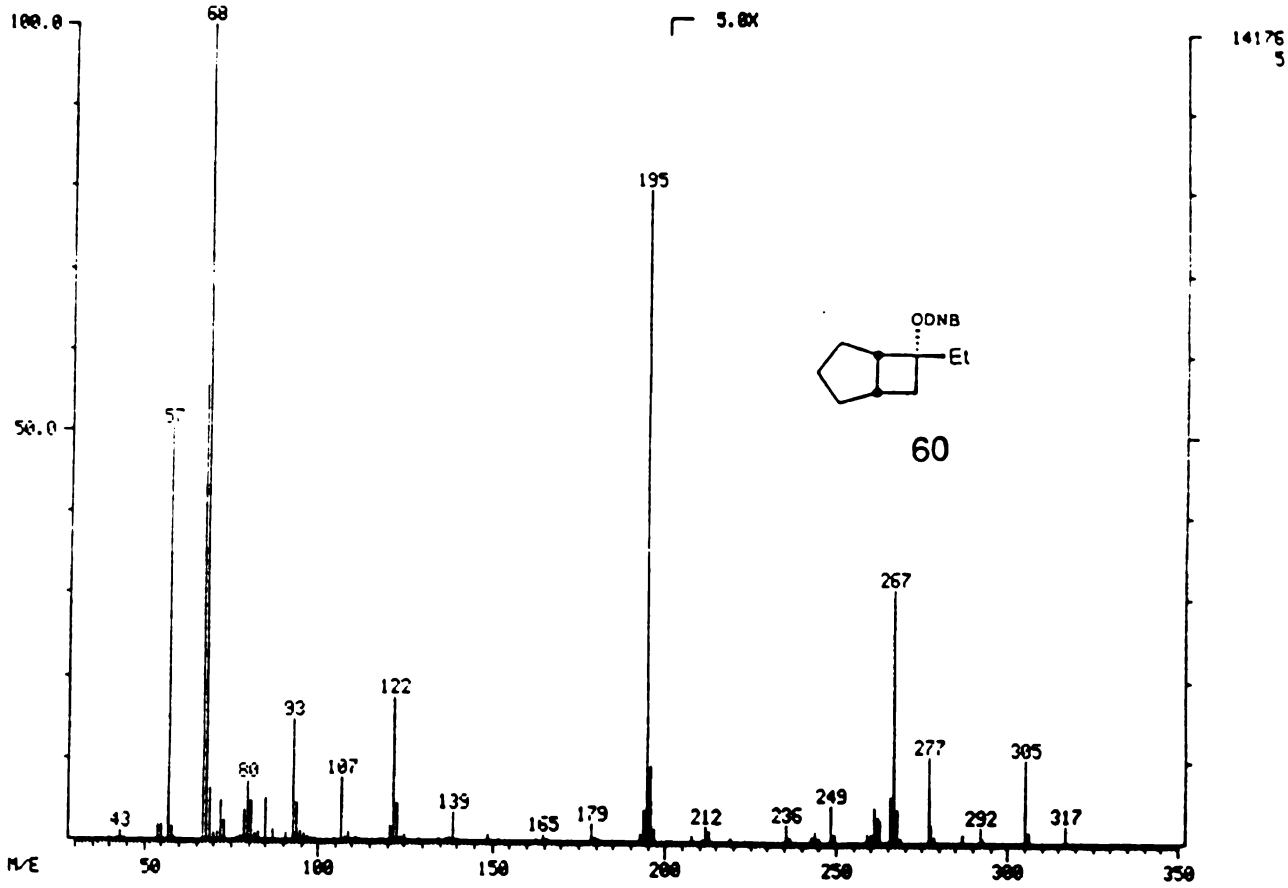


Figure 39. Mass Spectrum of **60**

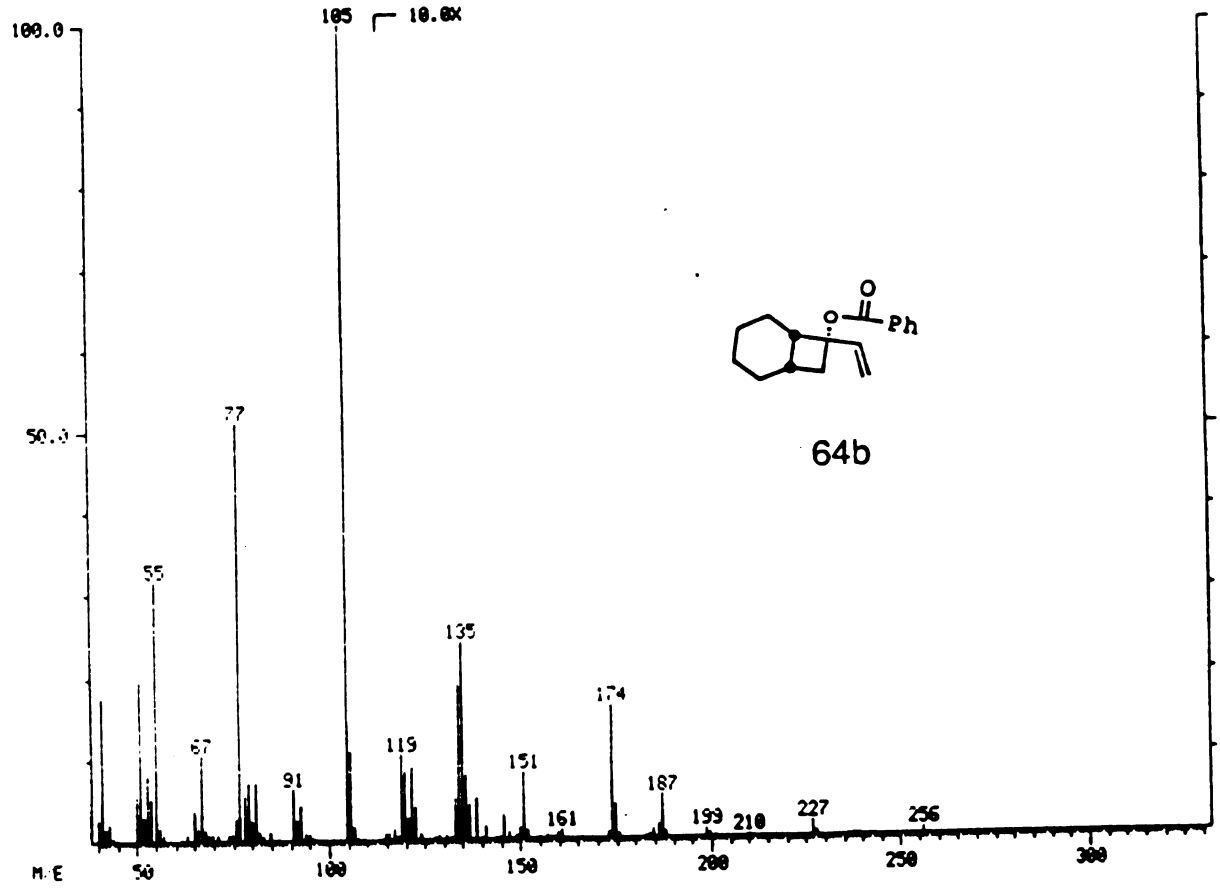


Figure 40. Mass Spectrum of **64b**

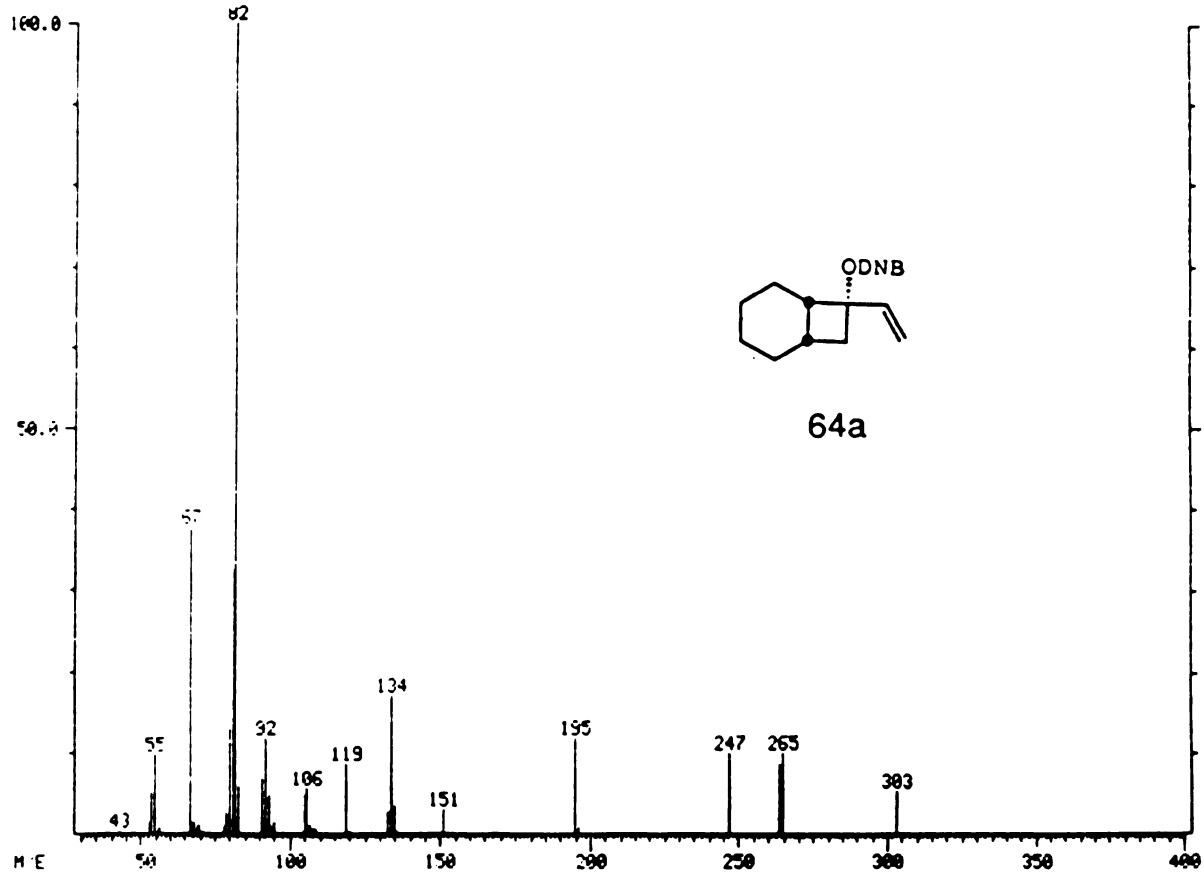


Figure 41. Mass Spectrum of **64a**

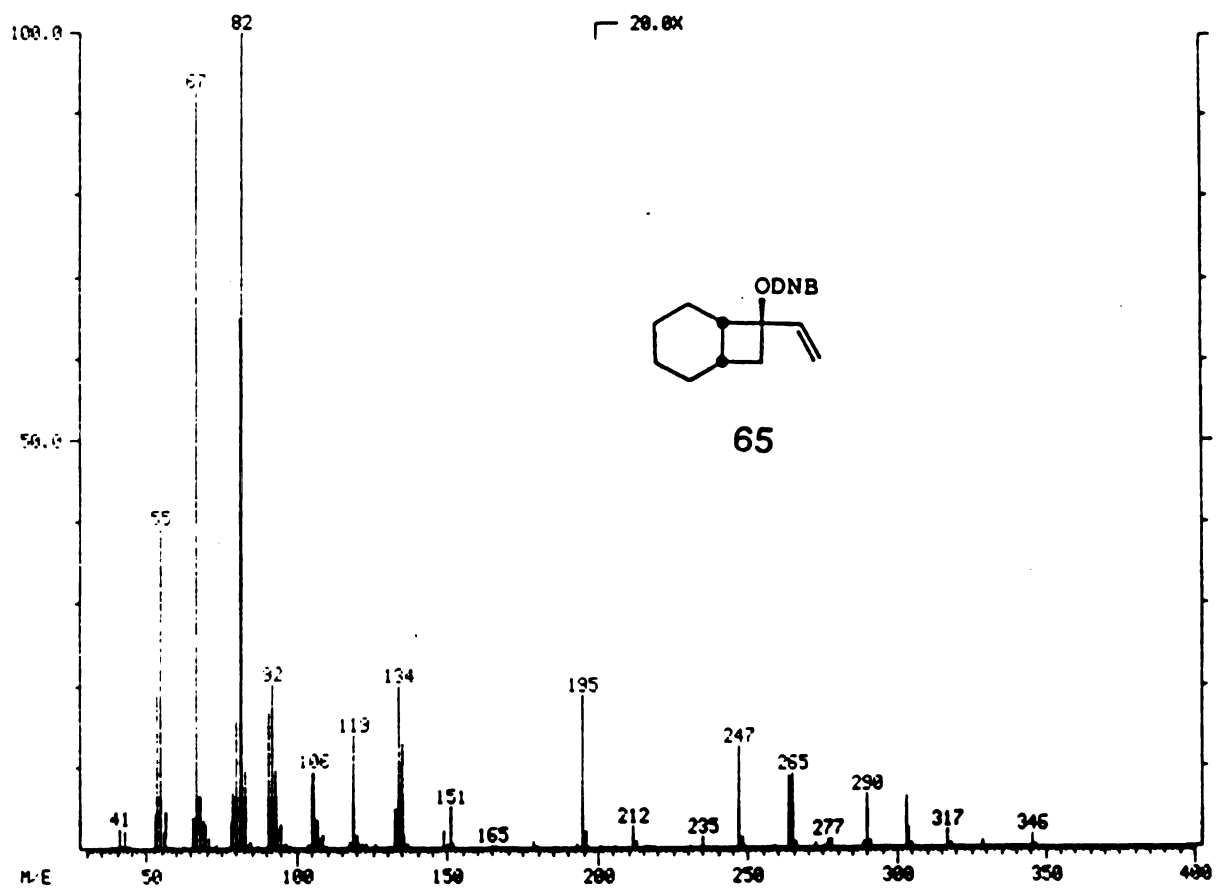


Figure 42. Mass Spectrum of **65**

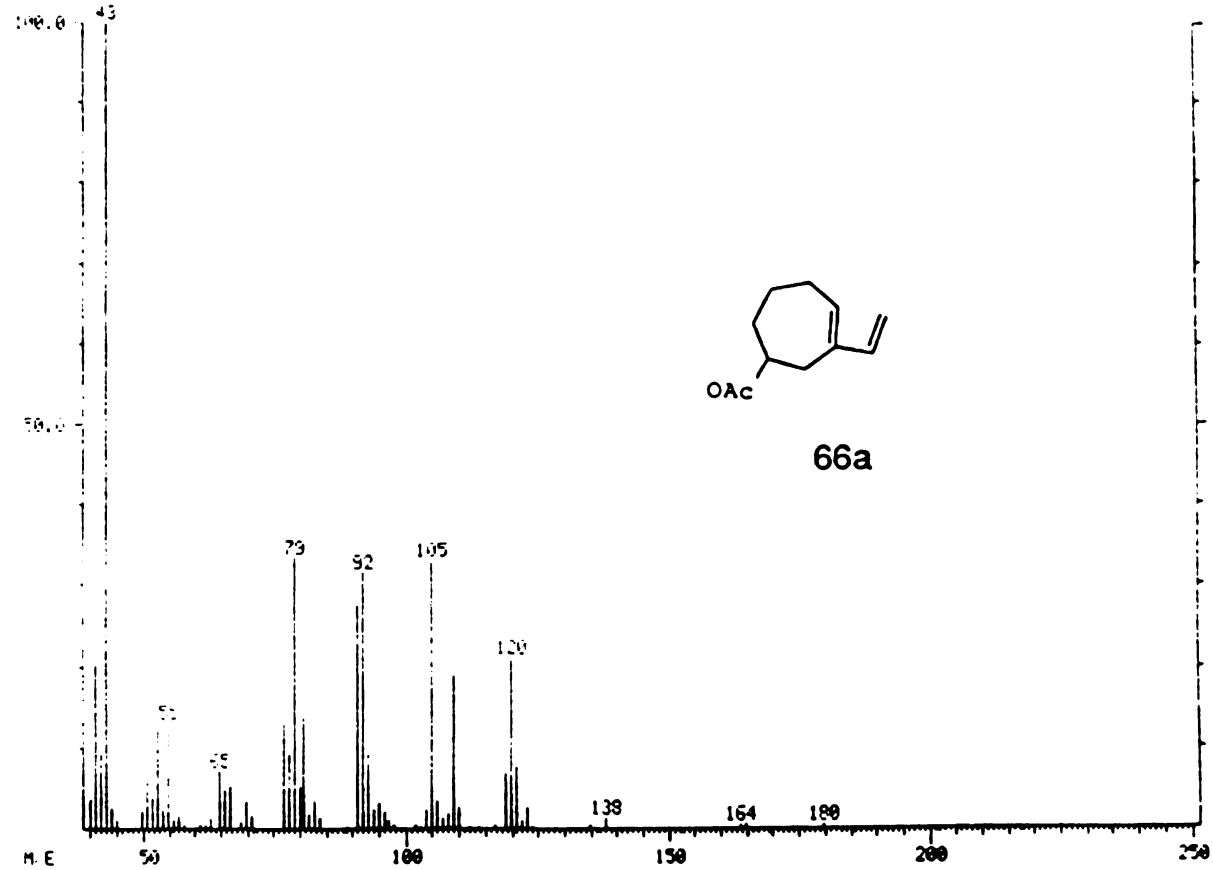


Figure 43. Mass Spectrum of **66a**

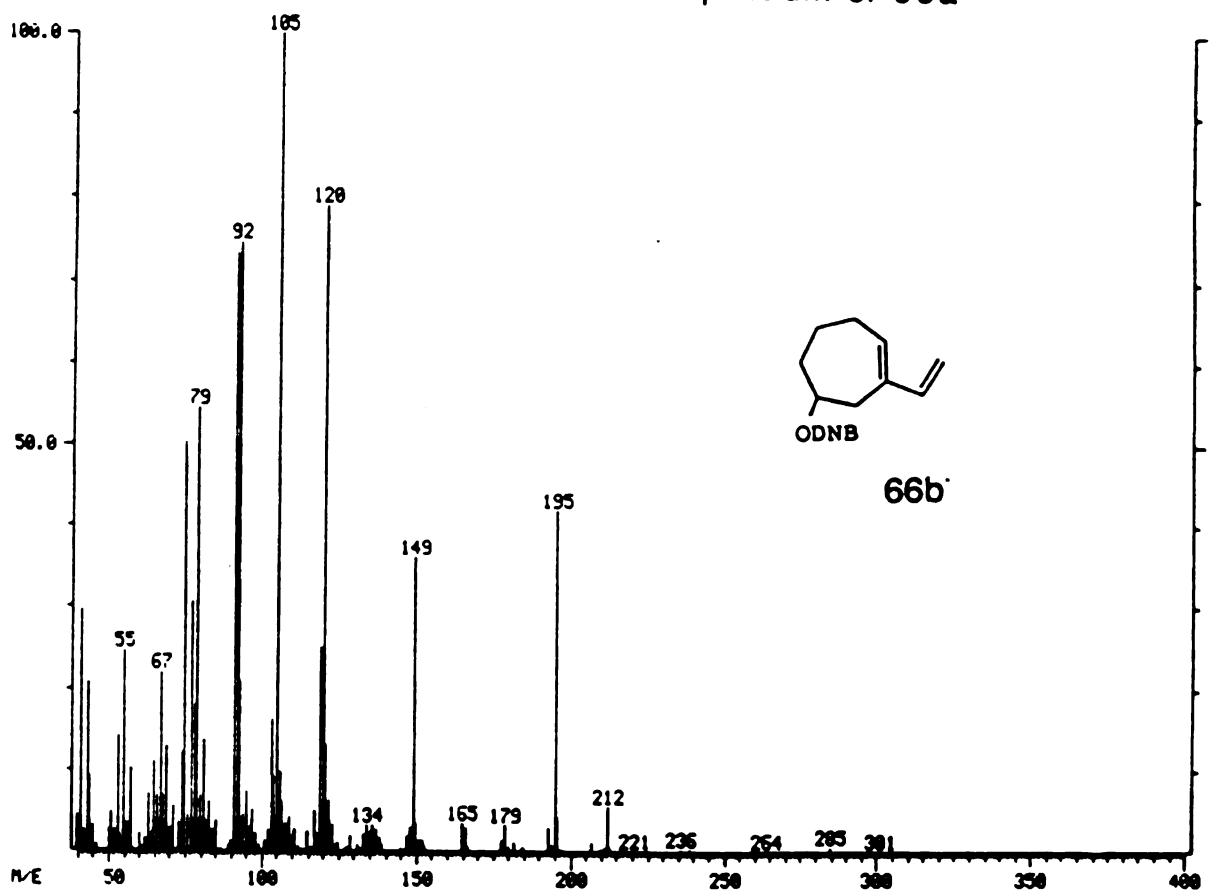


Figure 44. Mass Spectrum of **66b**

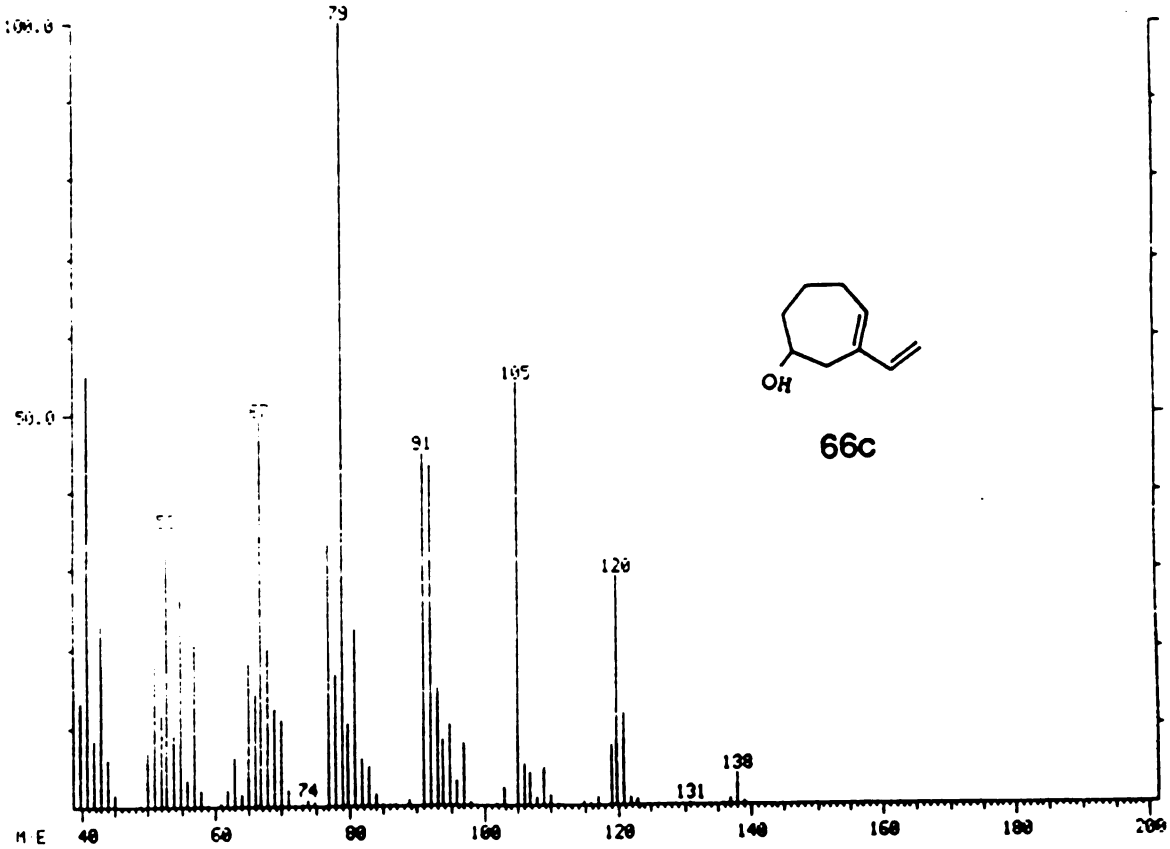


Figure 45. Mass Spectrum of **66c**

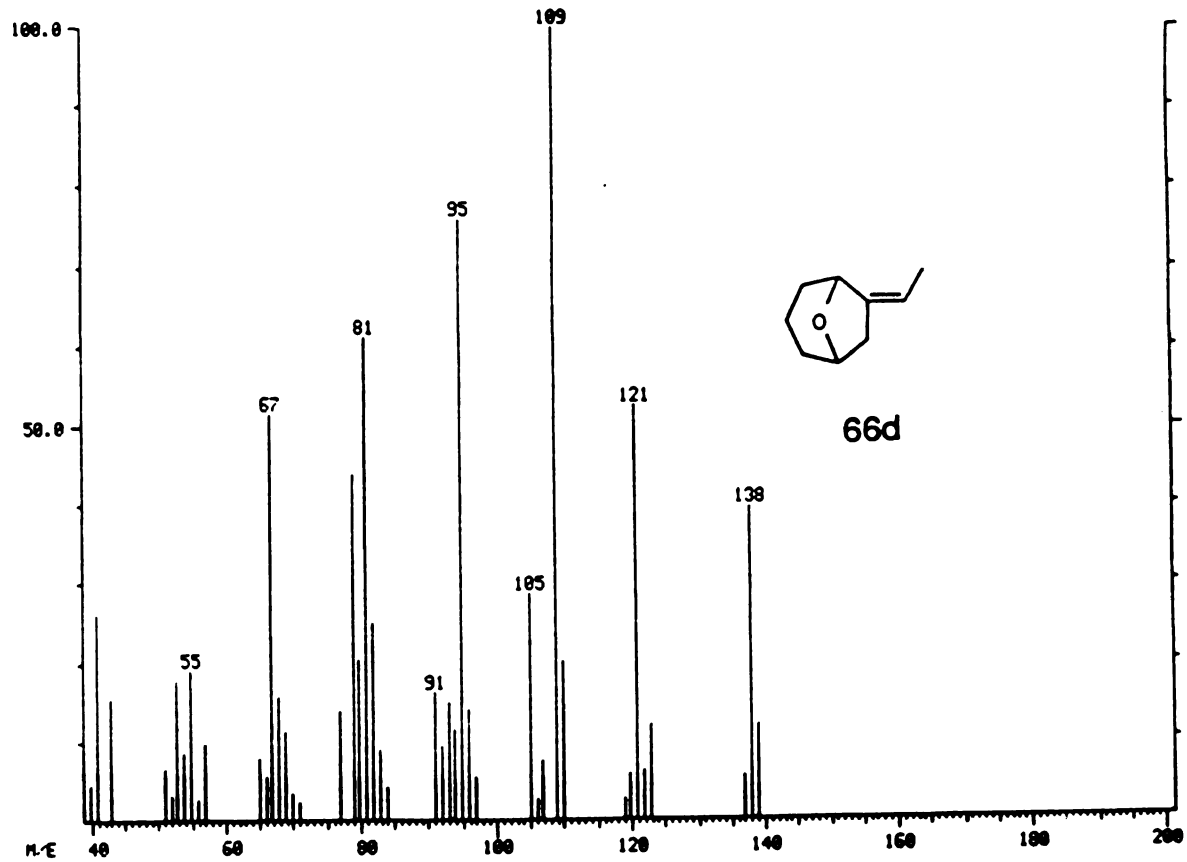
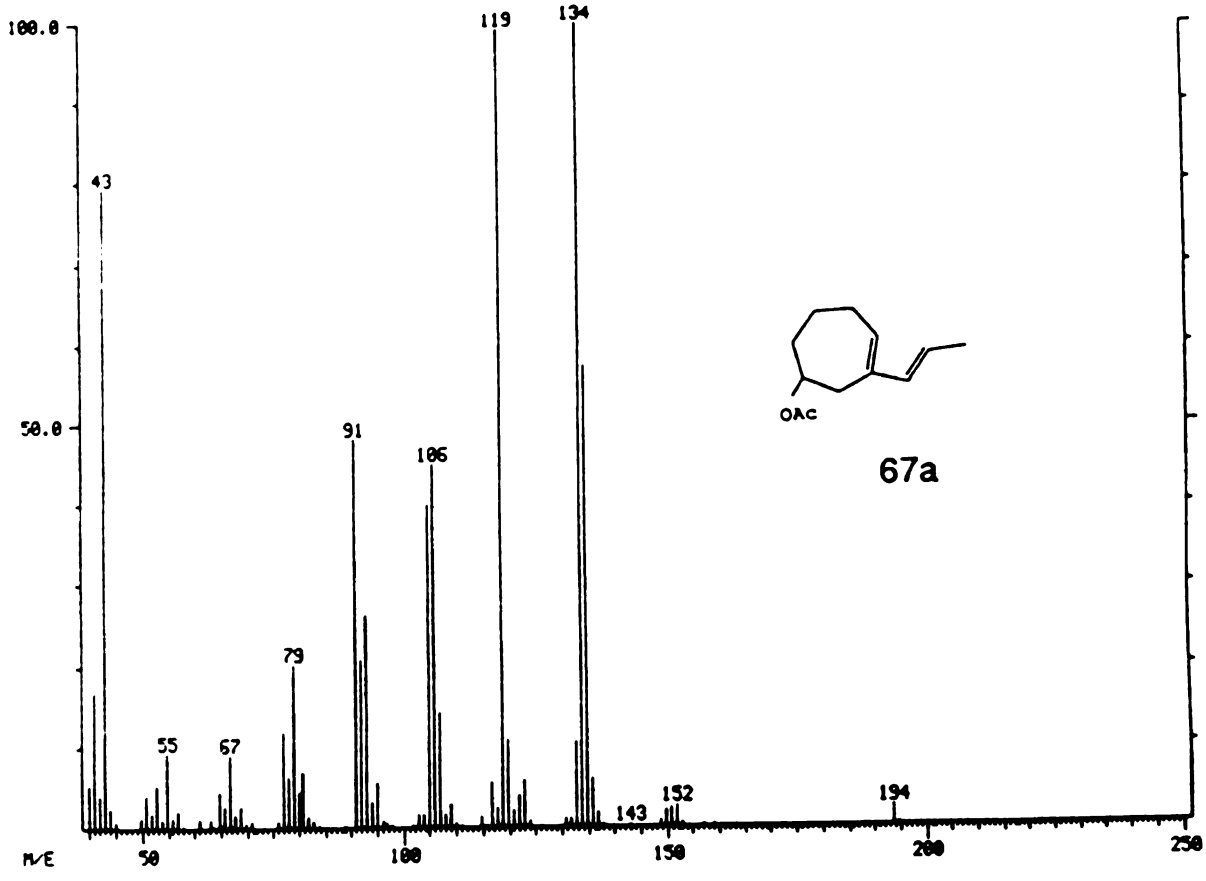
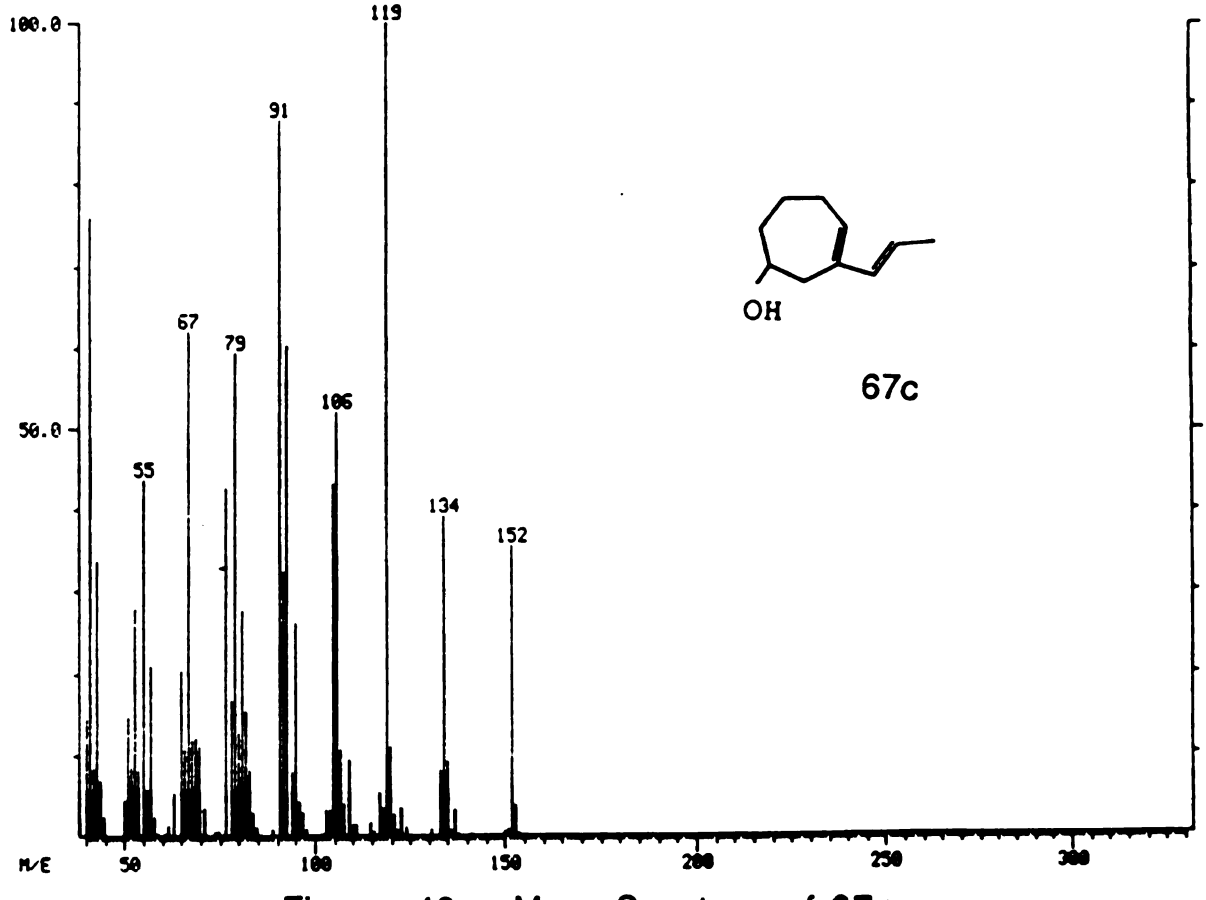


Figure 46. Mass Spectrum of **66d**



67a

Figure 47. Mass Spectrum of **67a**



67c

Figure 48. Mass Spectrum of **67c**

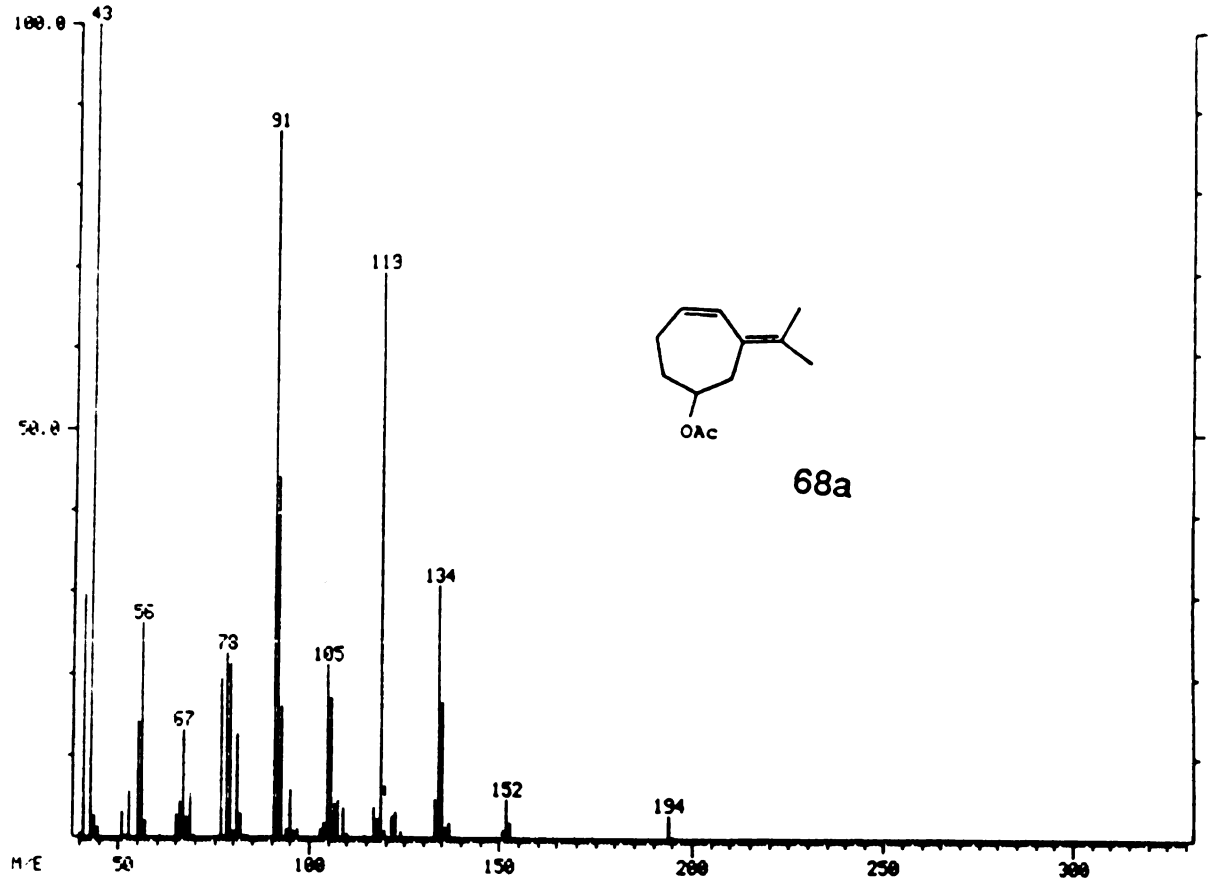


Figure 49. Mass Spectrum of **68a**

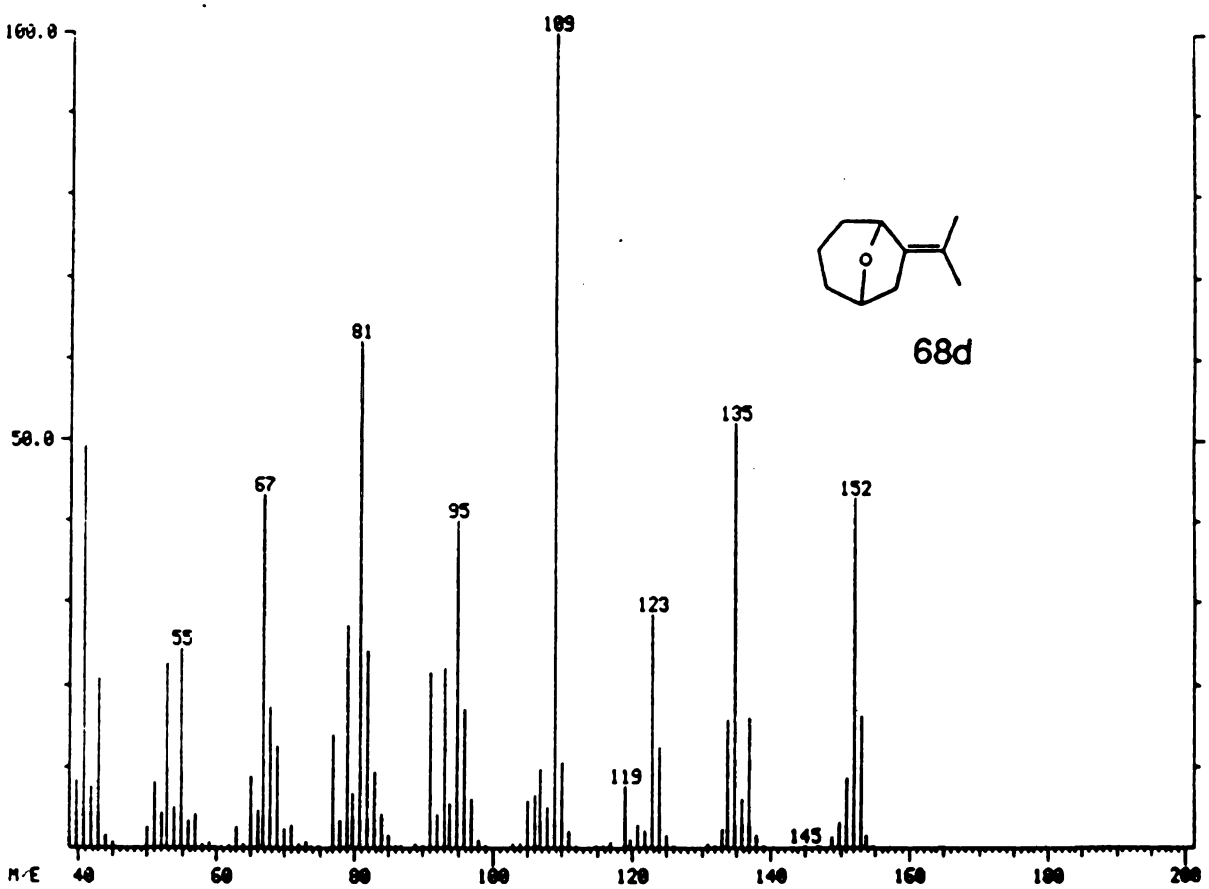


Figure 50. Mass Spectrum of **68d**

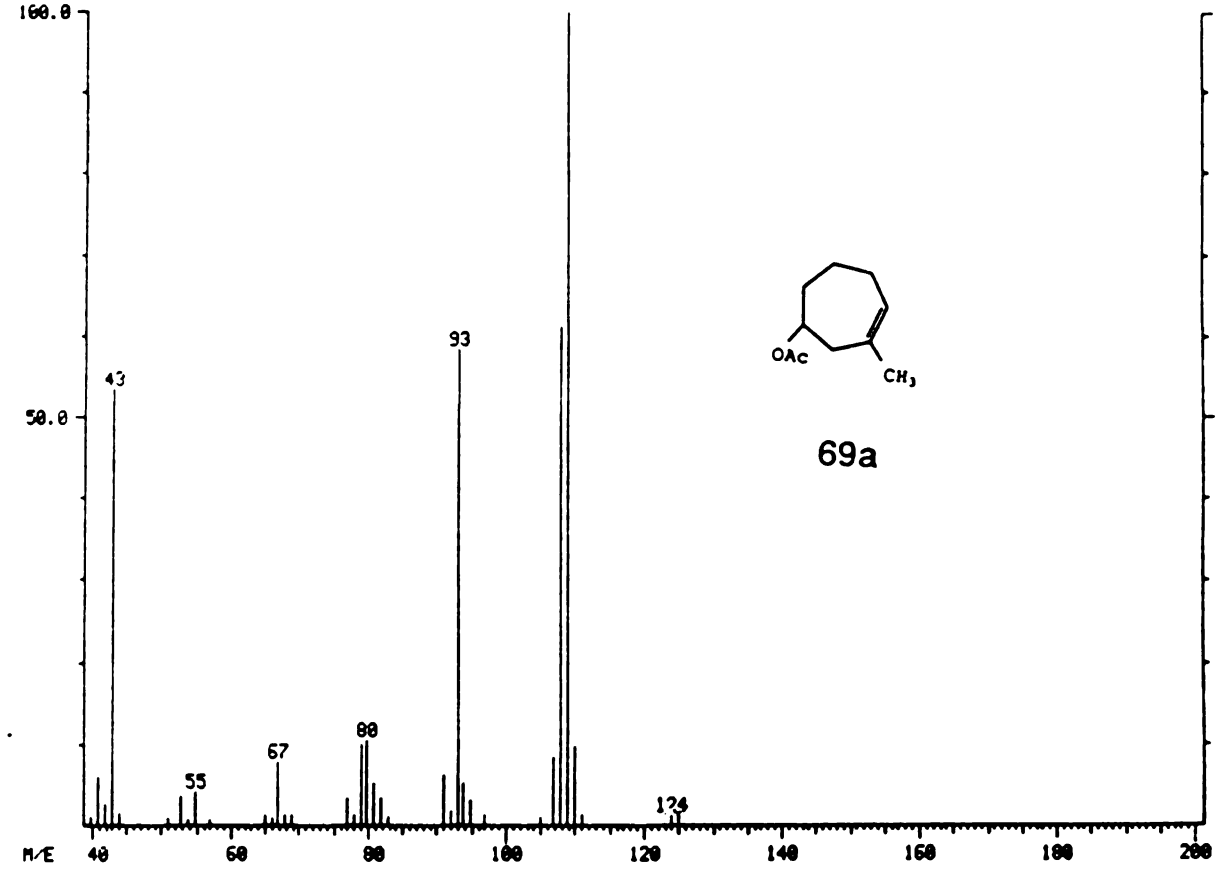


Figure 51. Mass Spectrum of **69a**

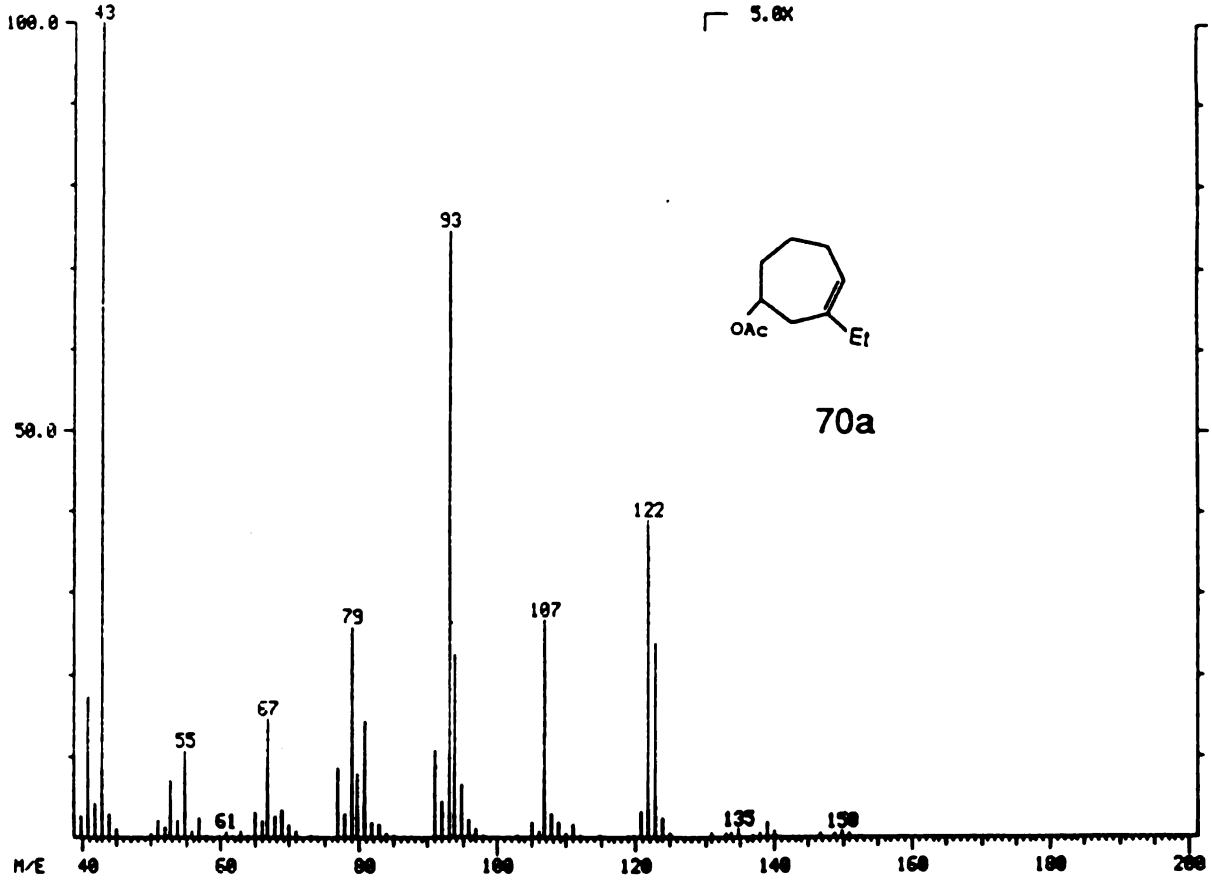


Figure 52. Mass Spectrum of **70a**

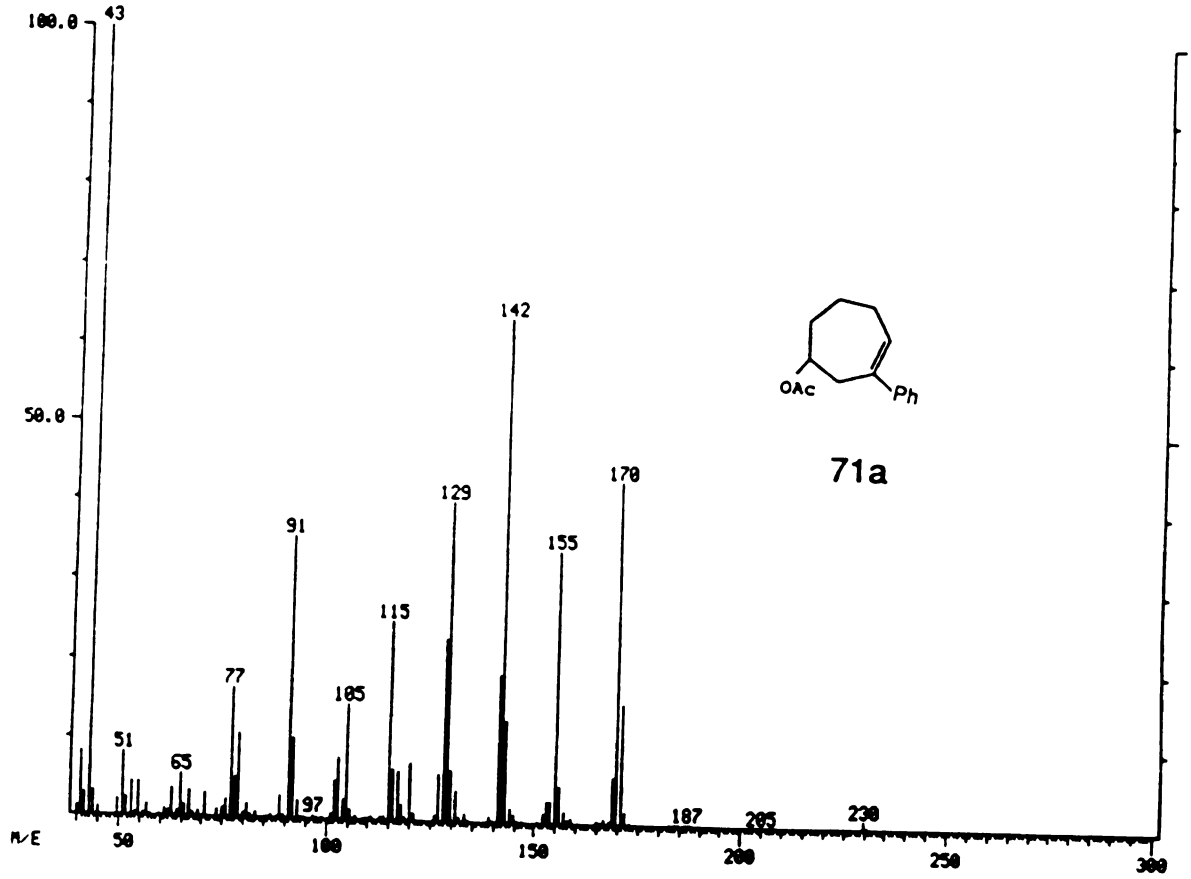


Figure 53. Mass Spectrum of **71a**

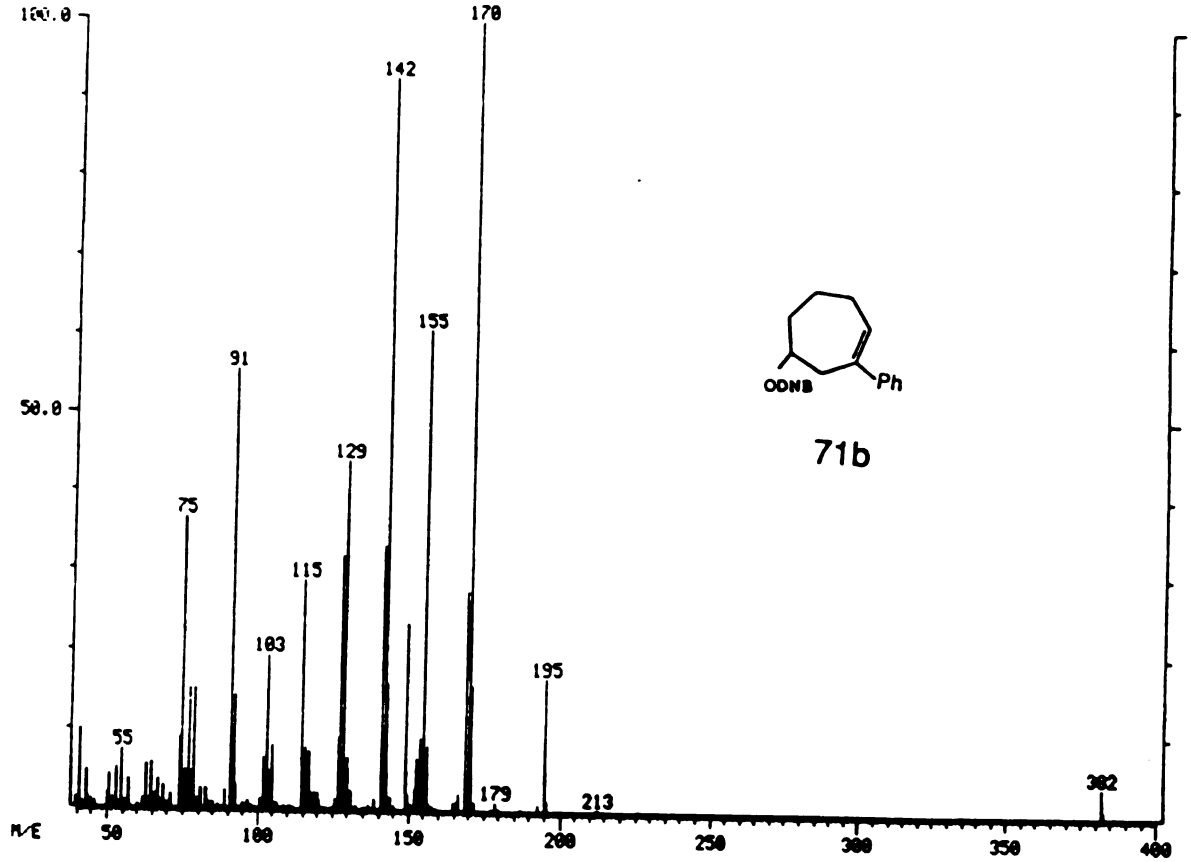


Figure 54. Mass Spectrum of **71b**

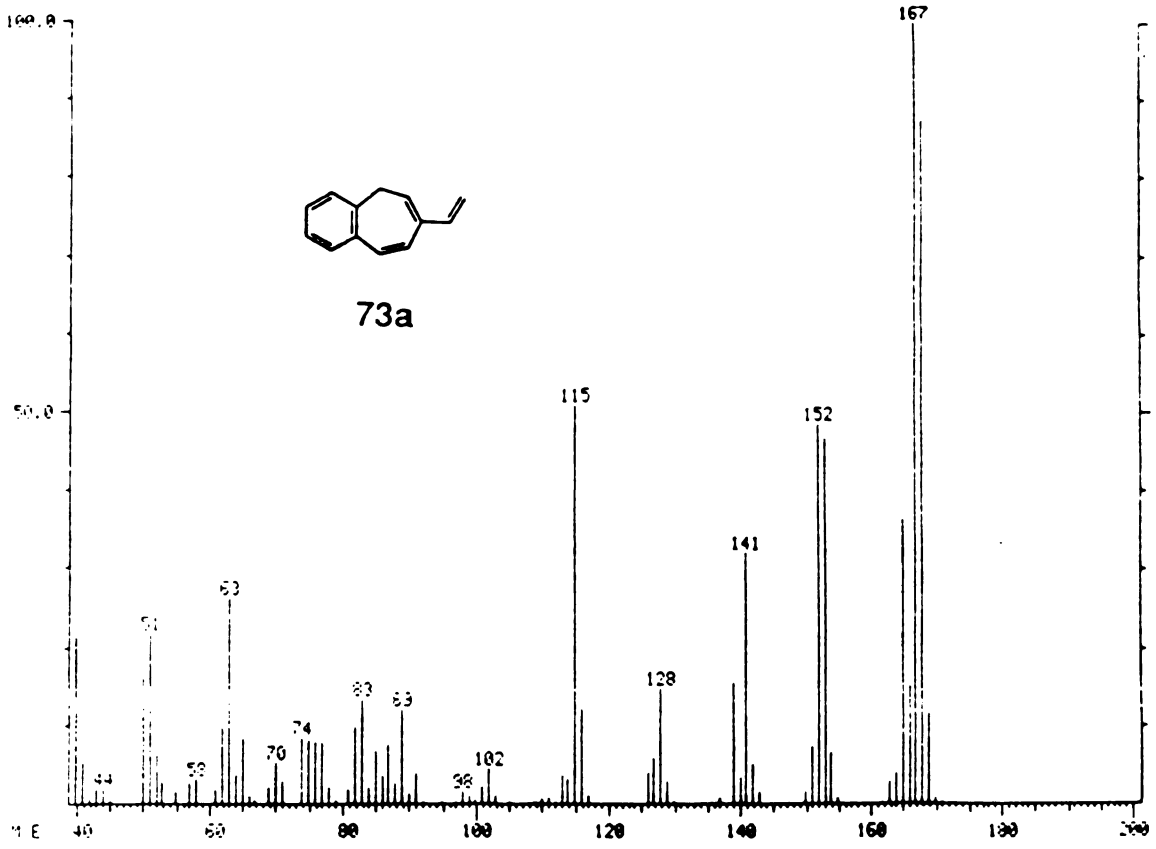


Figure 55. Mass Spectrum of **73a**

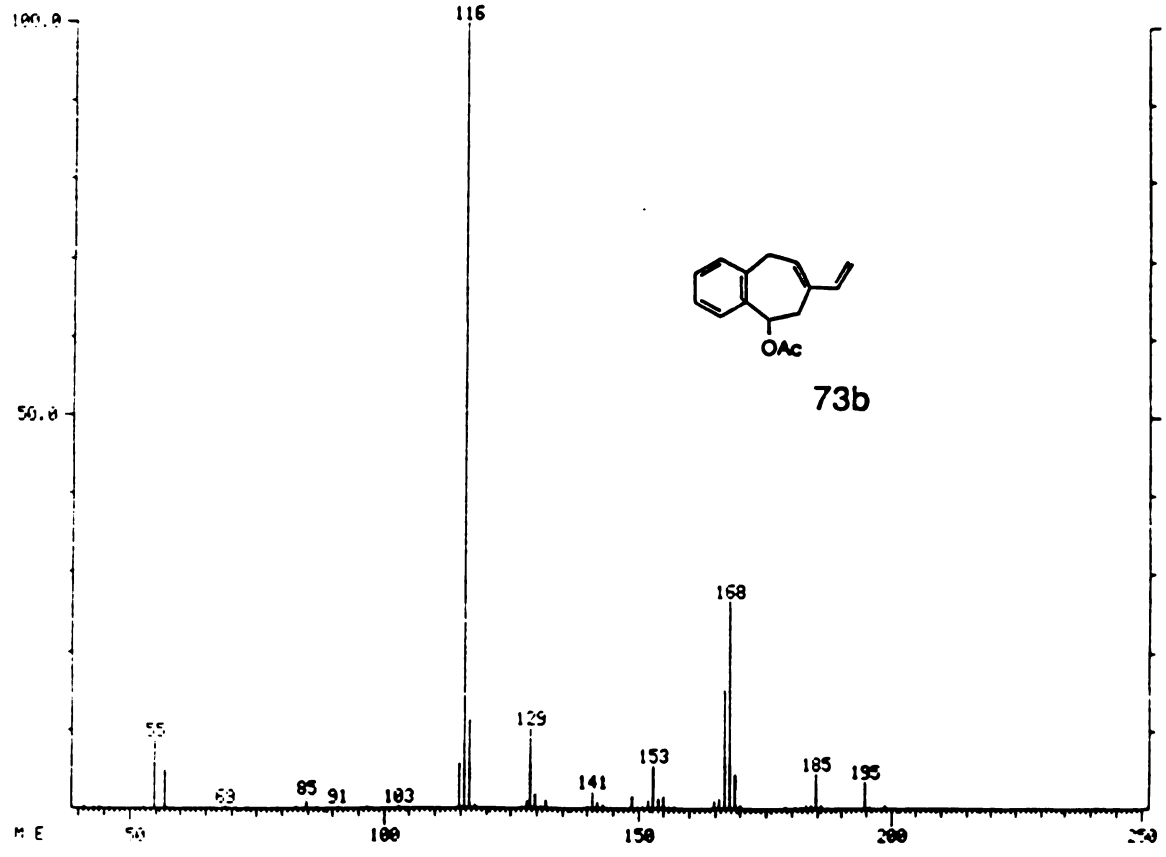


Figure 56. Mass Spectrum of **73b**

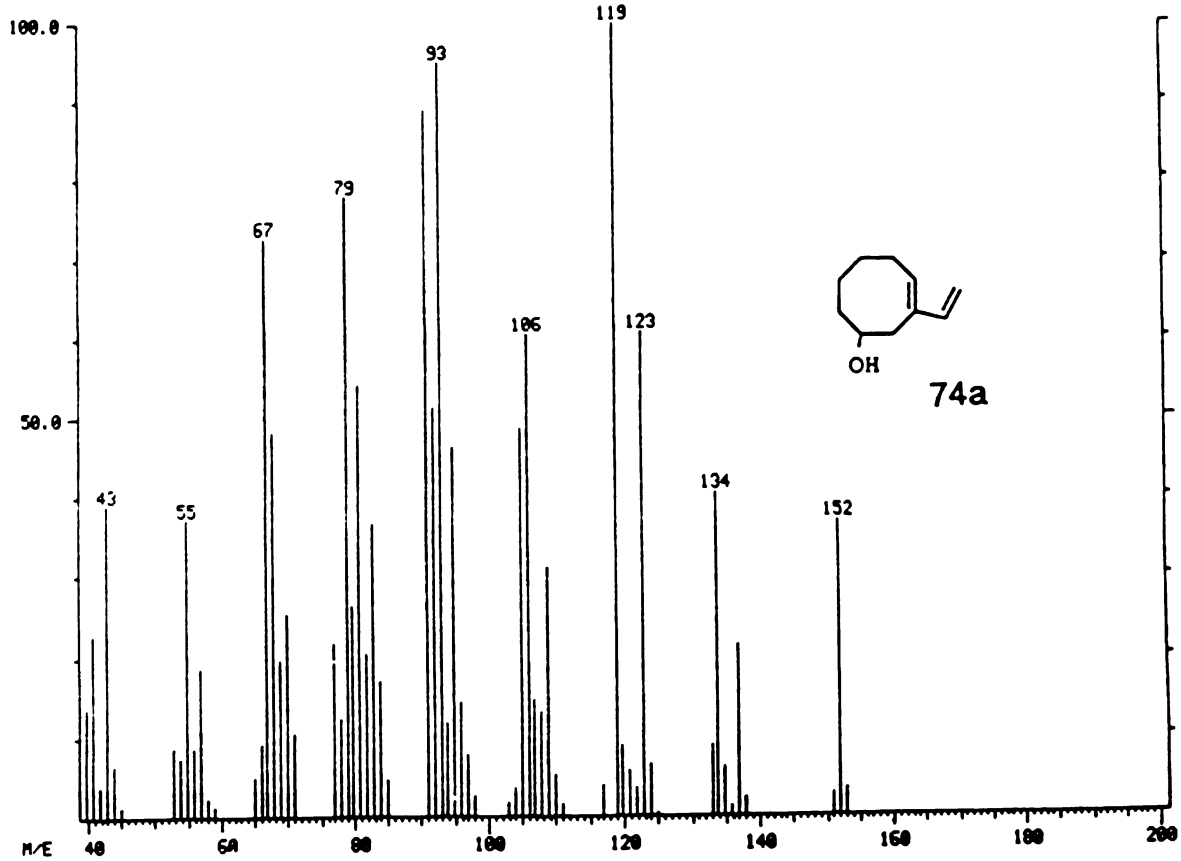


Figure 57. Mass Spectrum of **74a**

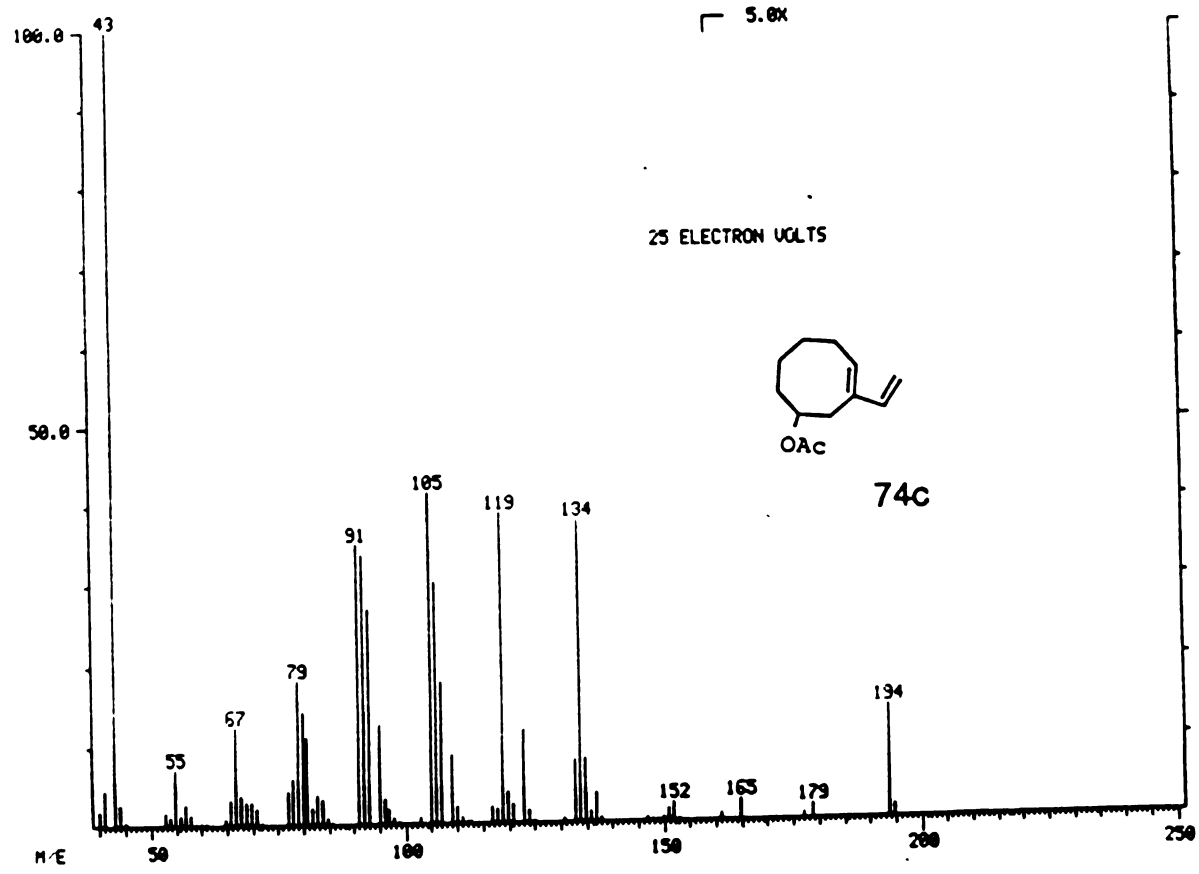


Figure 58. Mass Spectrum of **74c**

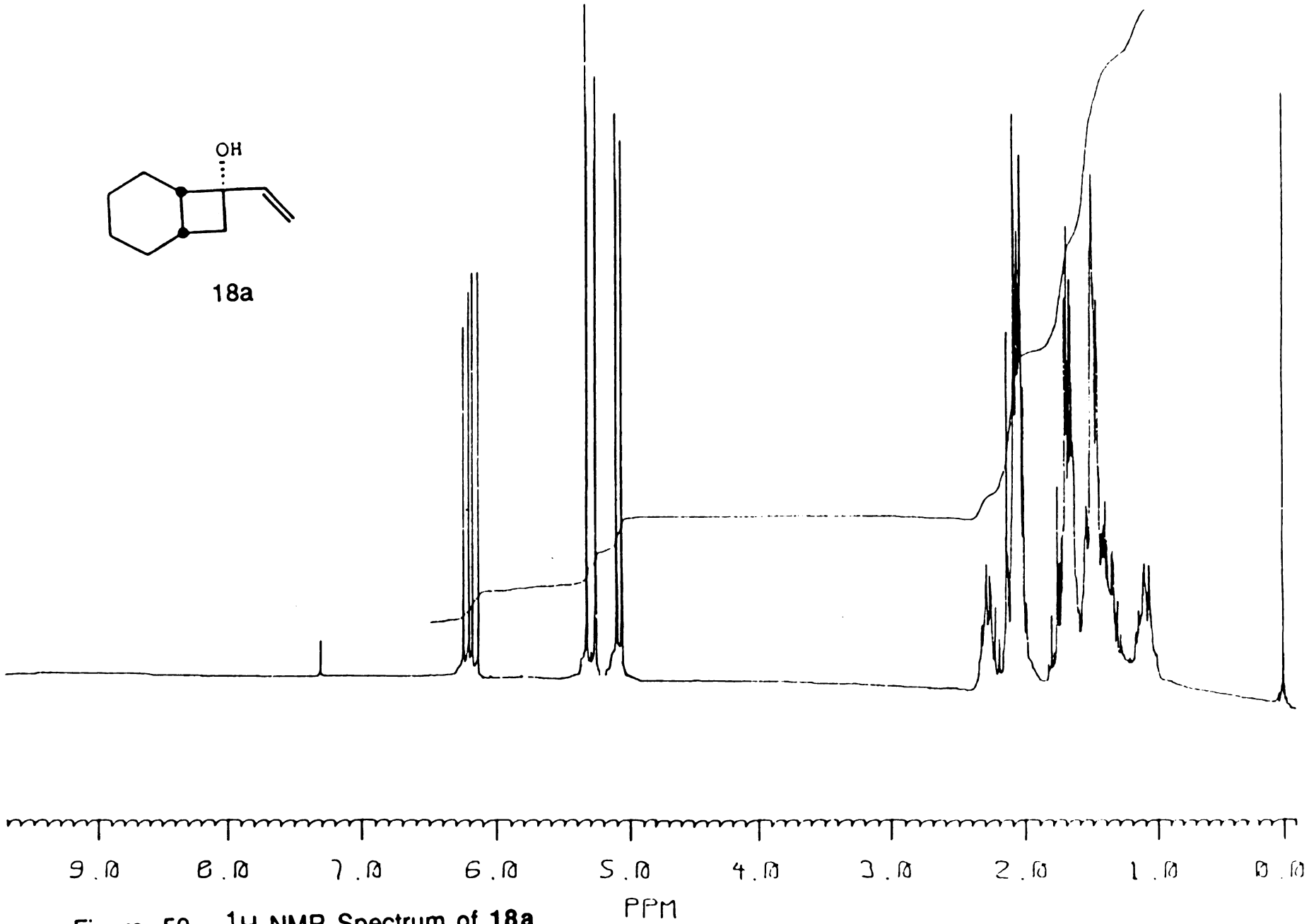


Figure 59. ^{1}H NMR Spectrum of **18a**

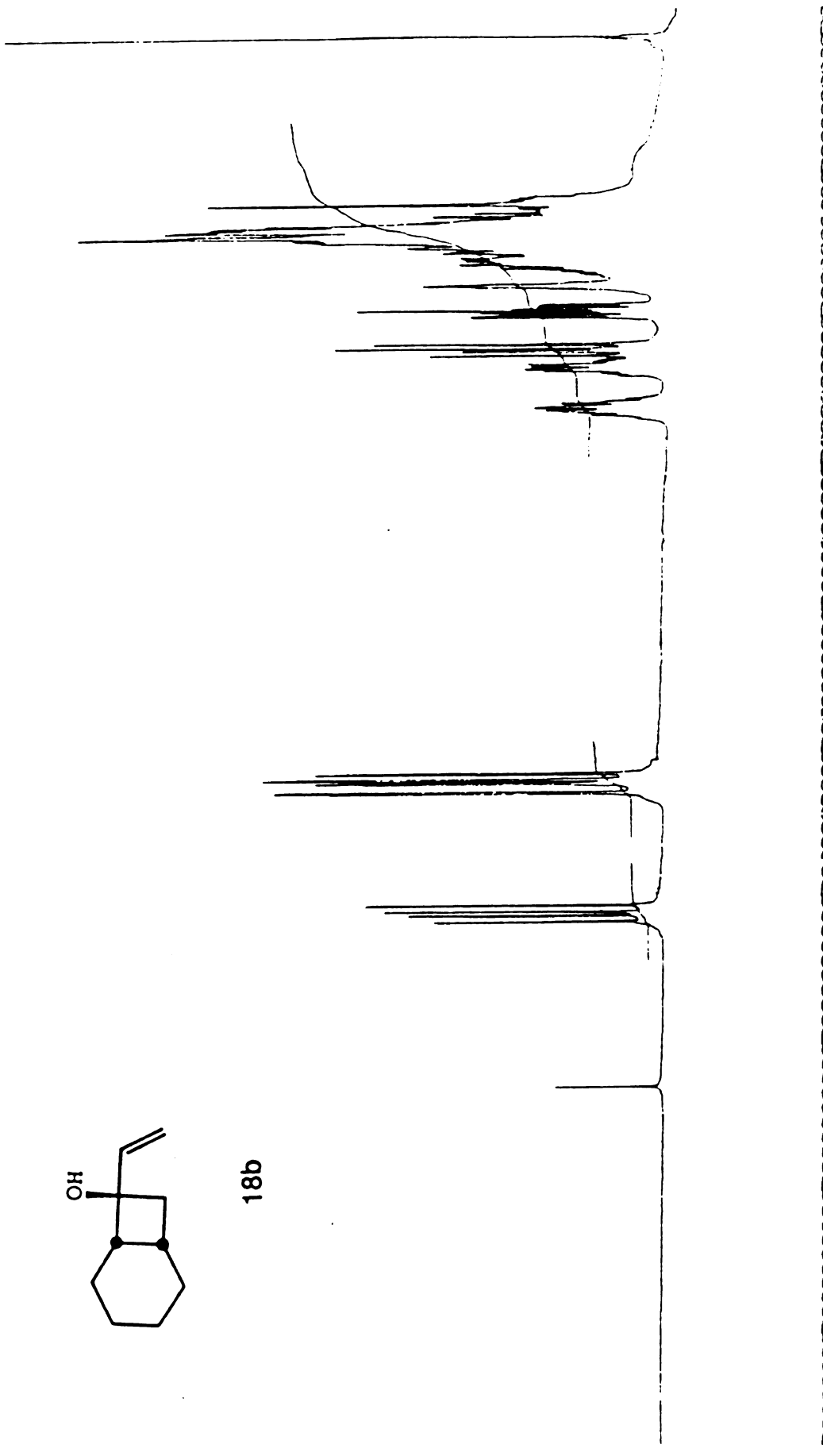
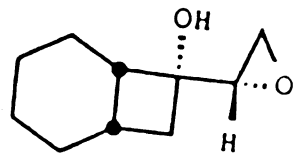


Figure 60. ^{1}H **NMR Spectrum of 18b**



9a

Figure 61. ^{1}H NMR Spectrum of **9a**

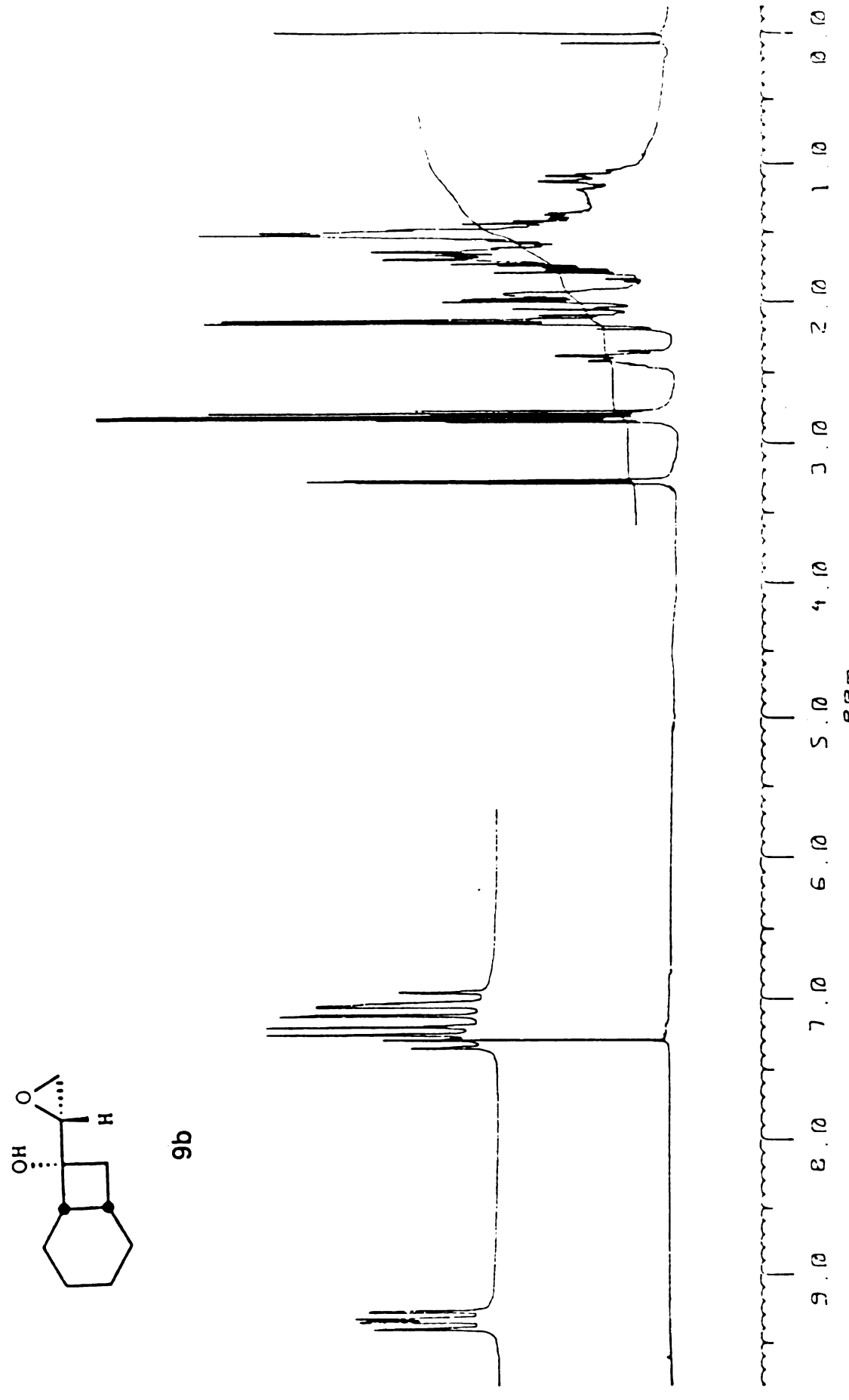


Figure 62. ^{1}H NMR Spectrum of **9b**

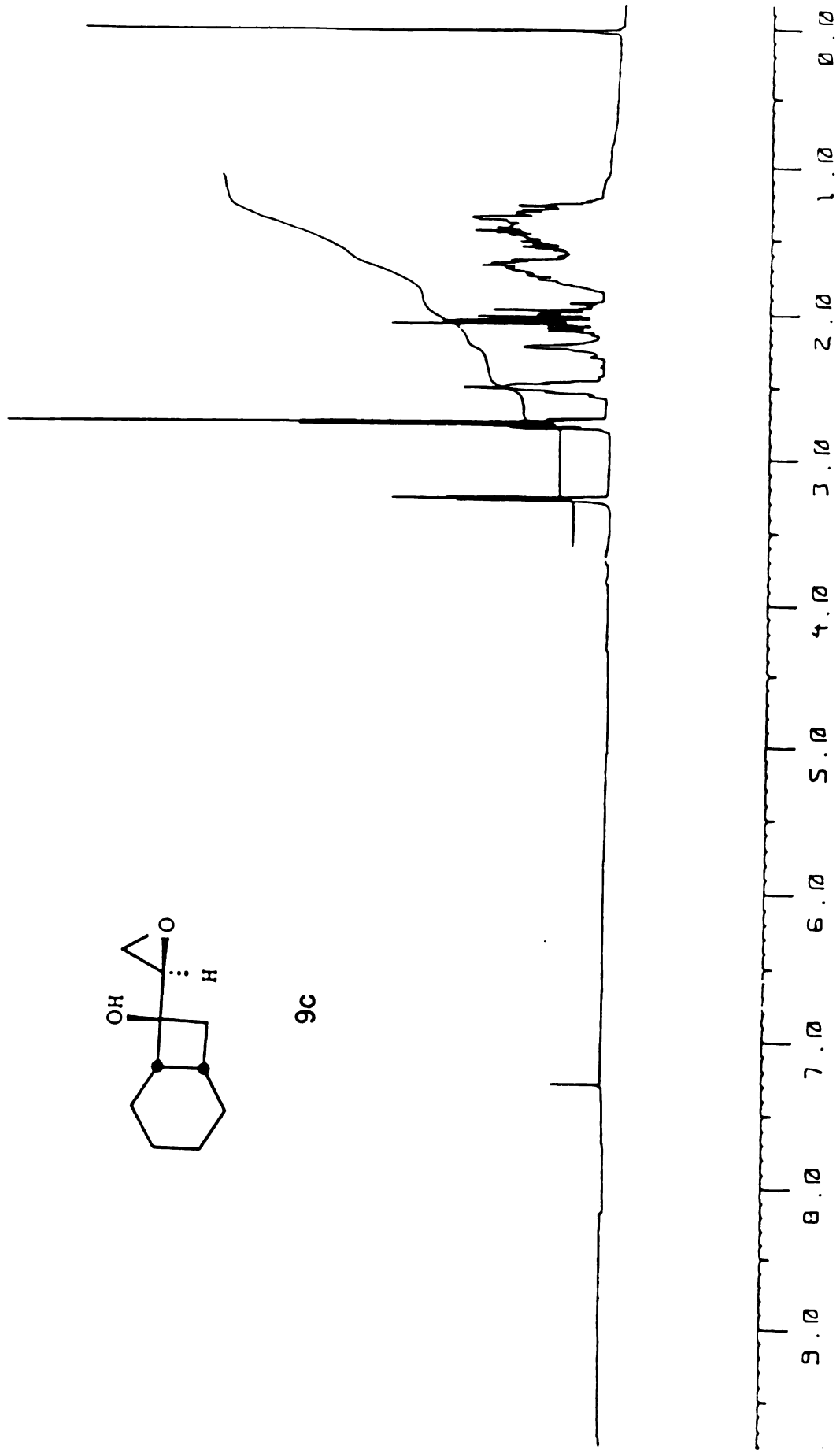


Figure 63. ^{1}H NMR Spectrum of **9c**

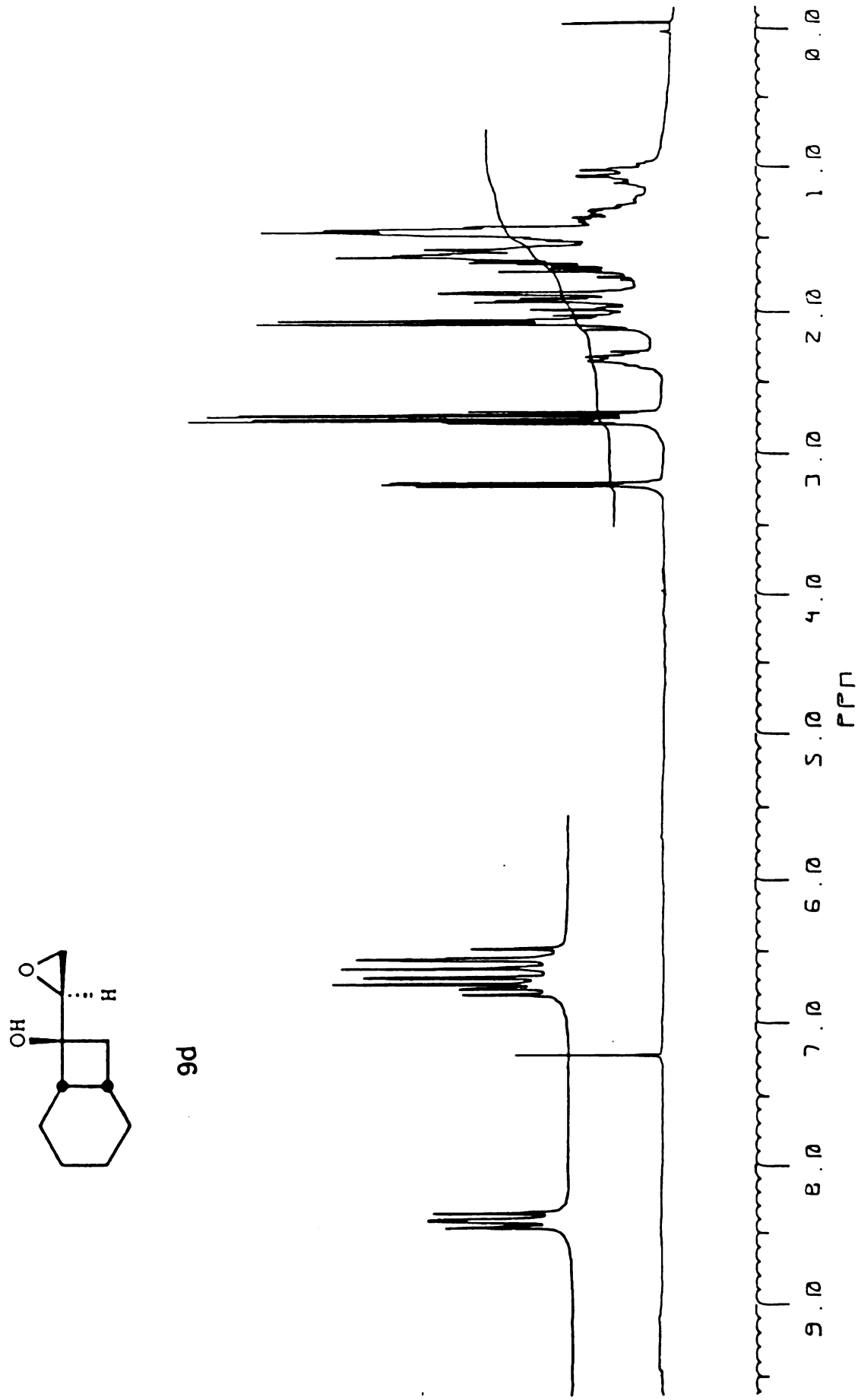


Figure 64. ^{1}H NMR Spectrum of **9d**

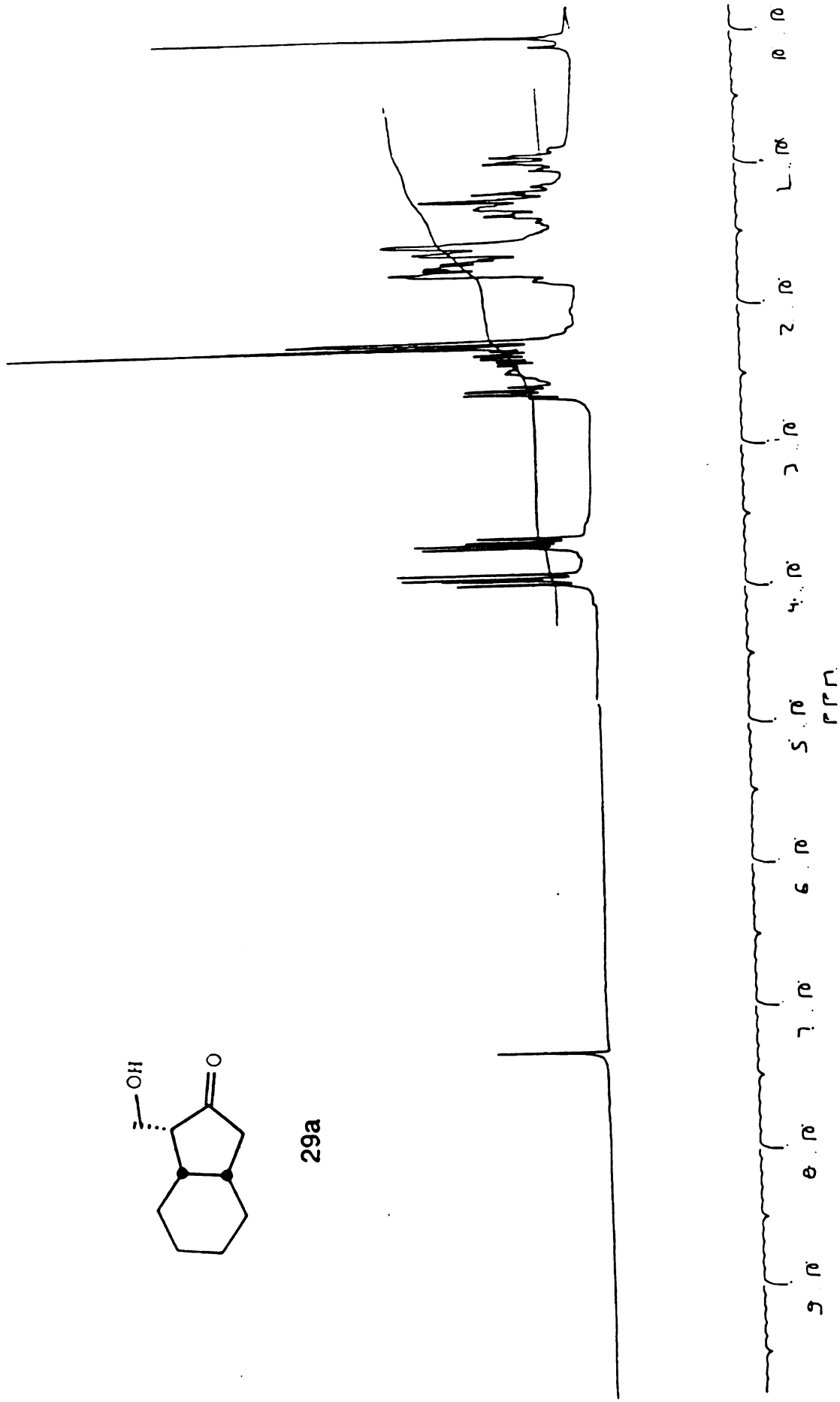


Figure 65. ^{1}H NMR Spectrum of **29a**

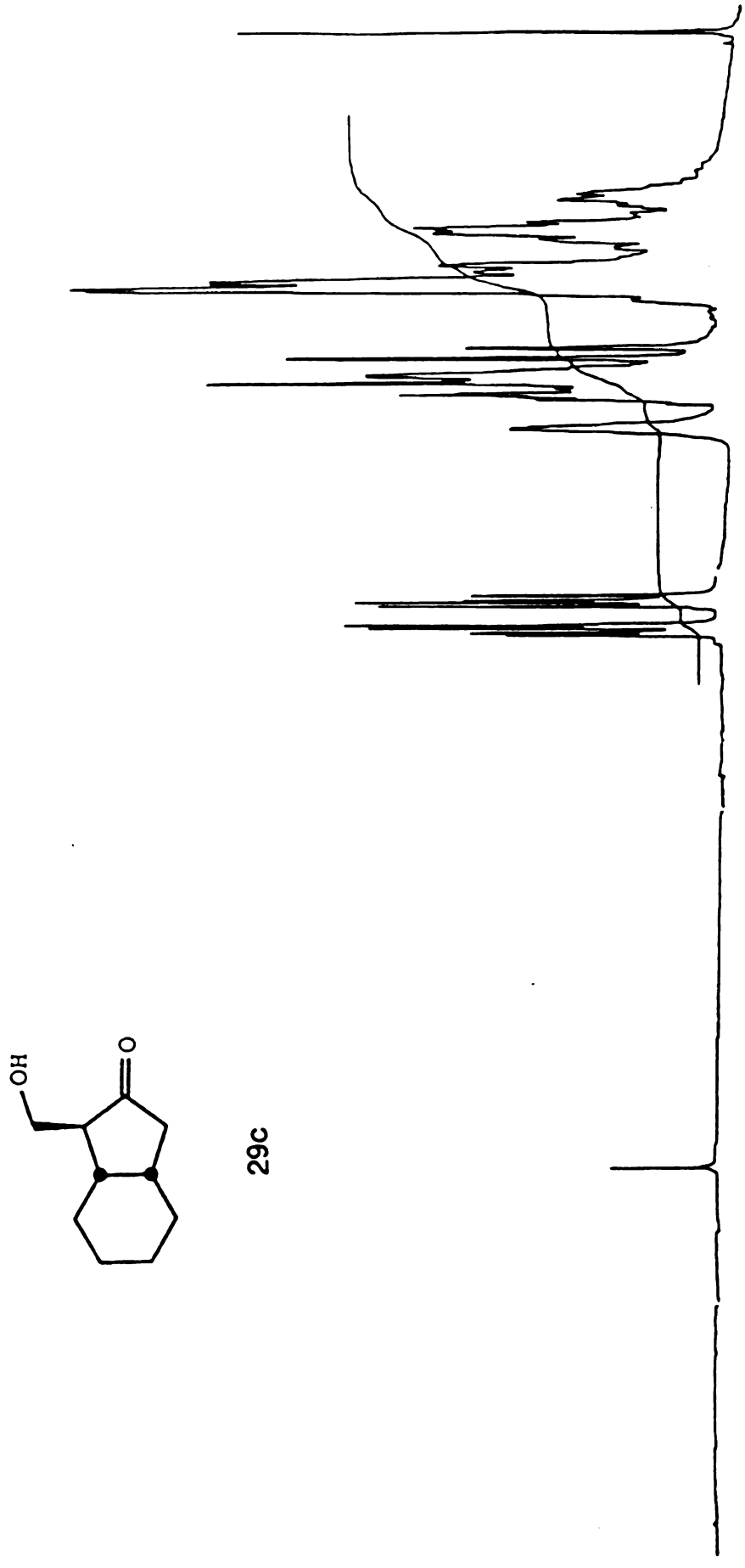


Figure 66. ^{1}H NMR Spectrum of **29c**

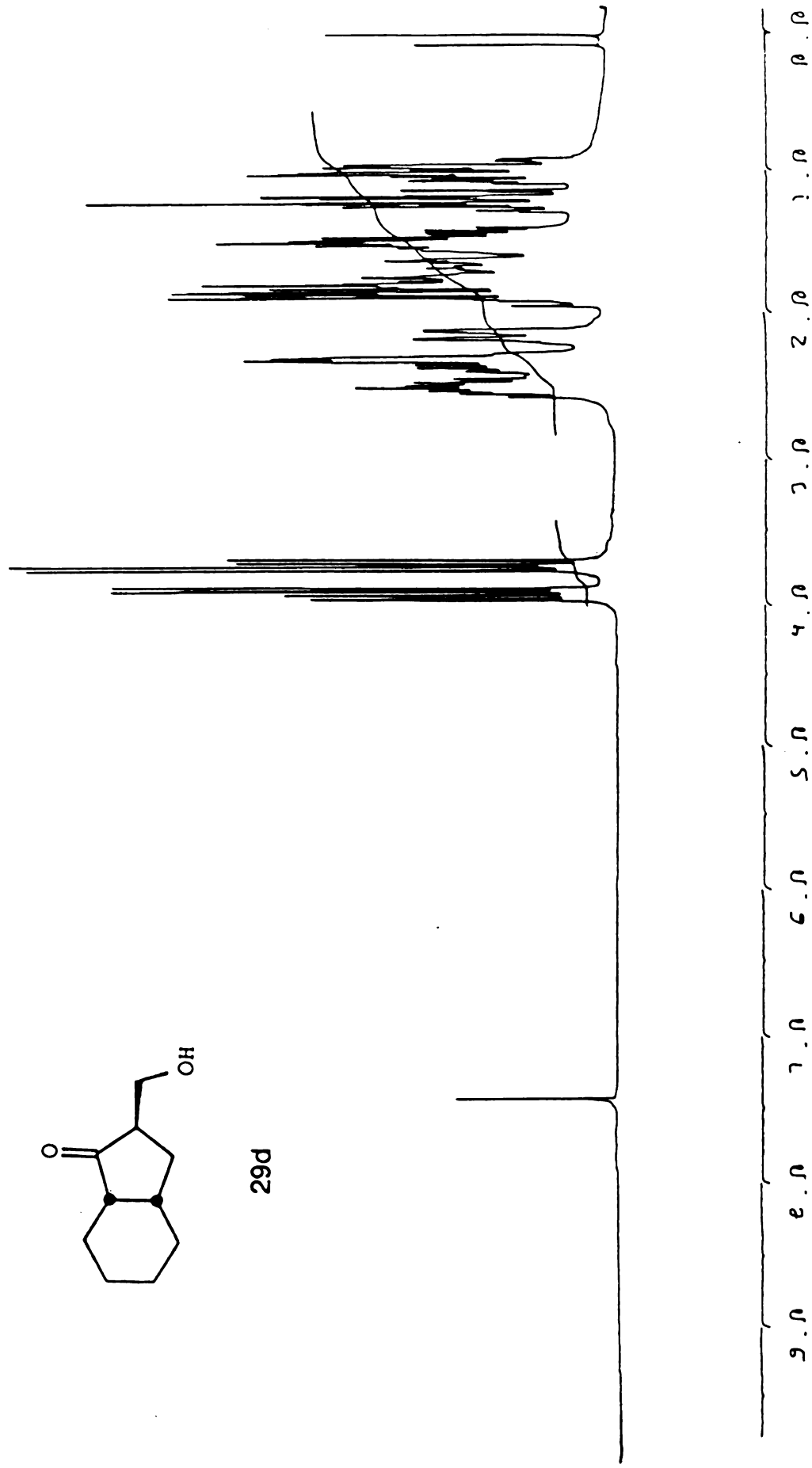


Figure 67. ^{1}H NMR Spectrum of **29d**

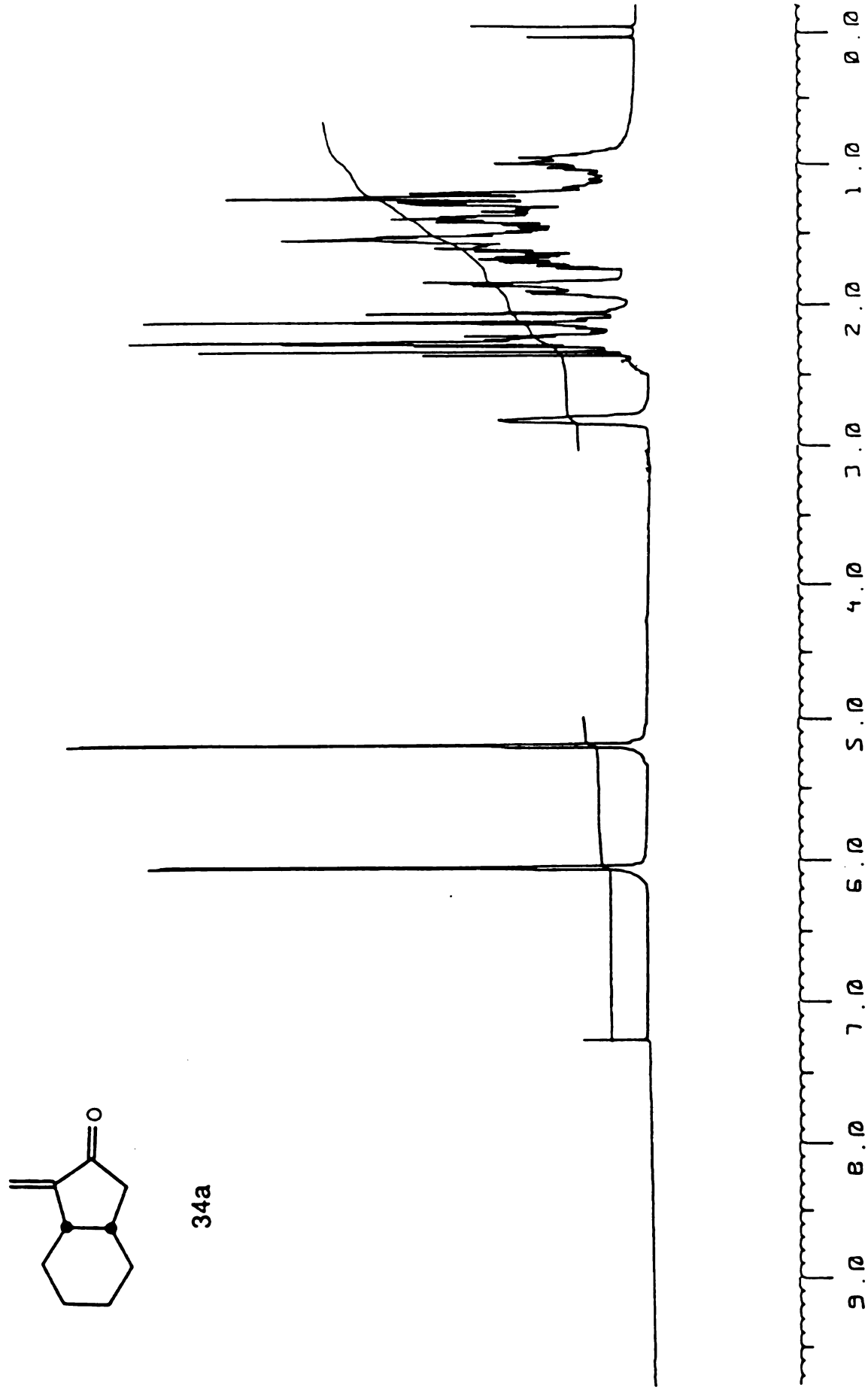


Figure 68. ^{1}H NMR Spectrum of **34a**

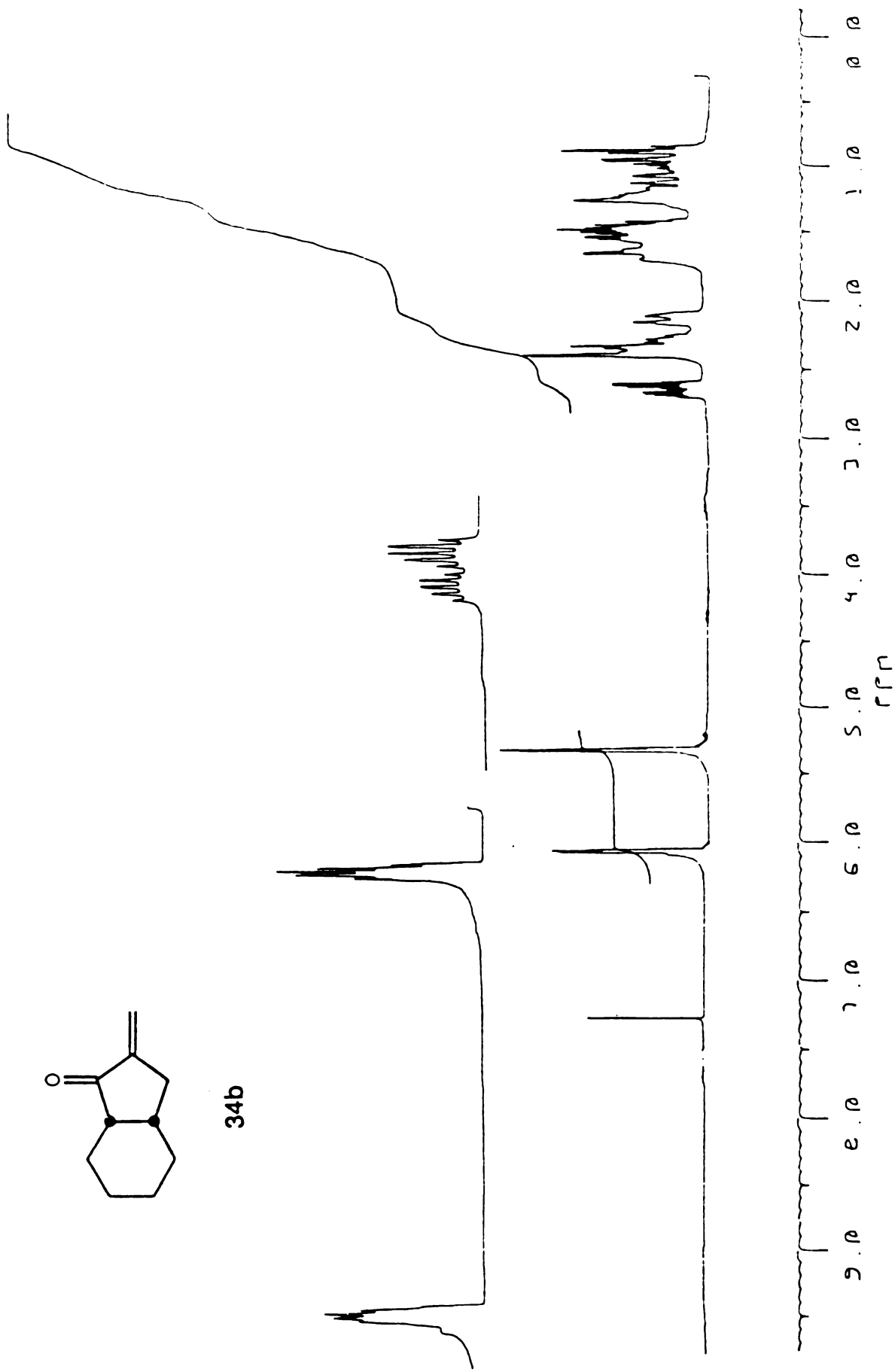


Figure 69. ^{1}H NMR Spectrum of **34b**

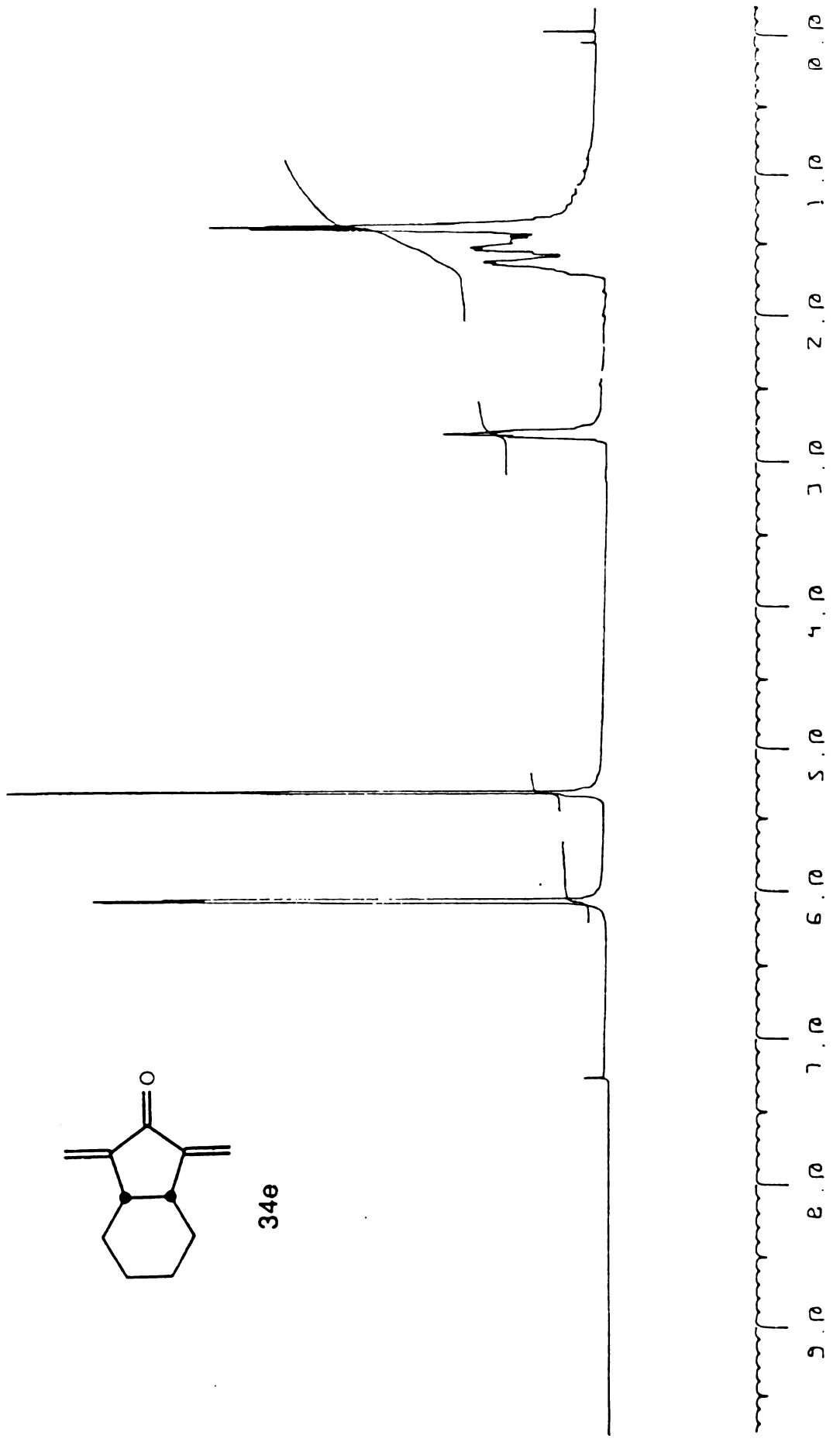


Figure 70. ^{1}H NMR Spectrum of **34e**

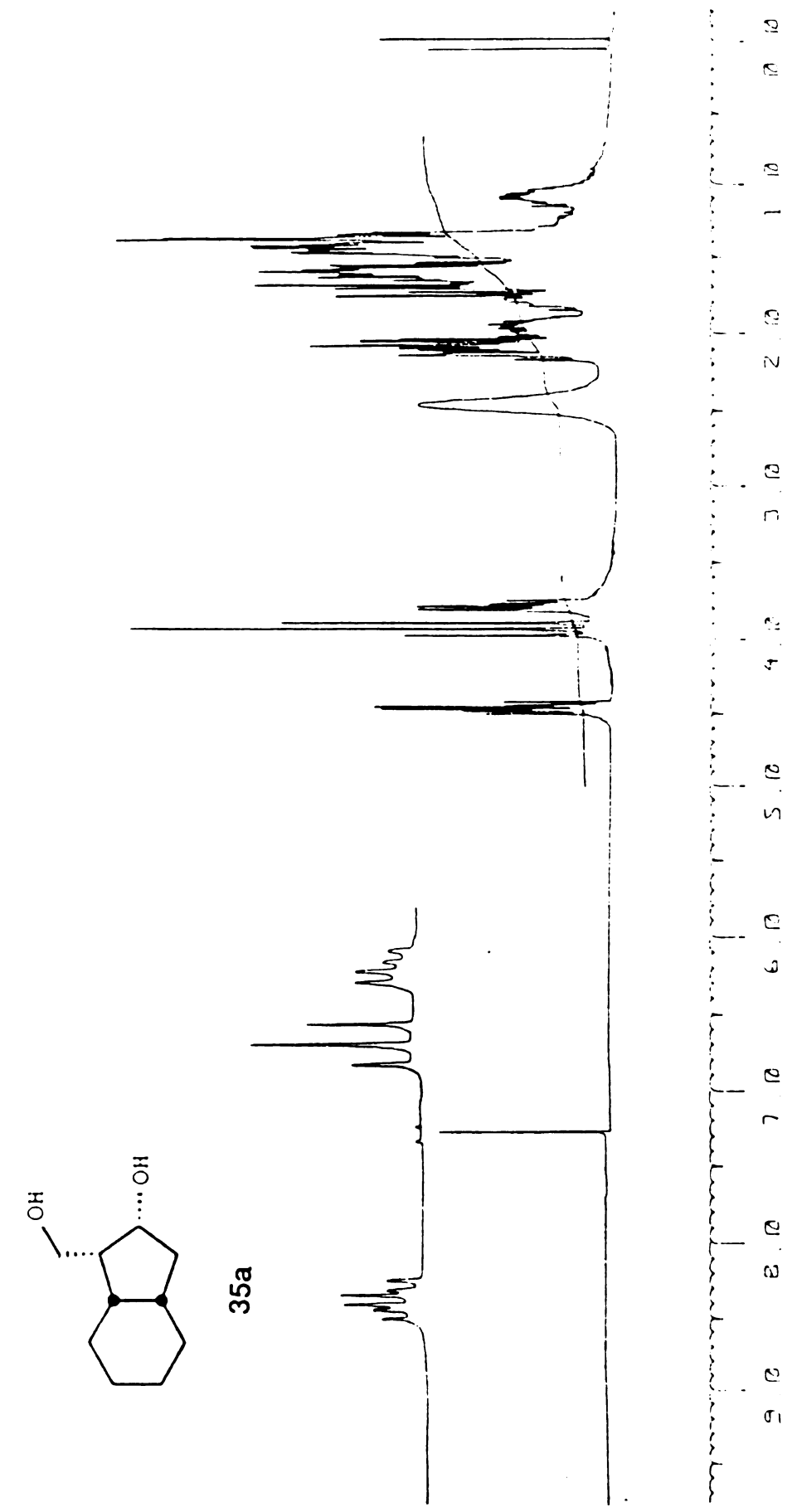


Figure 71. ^{1}H NMR Spectrum of **35a**

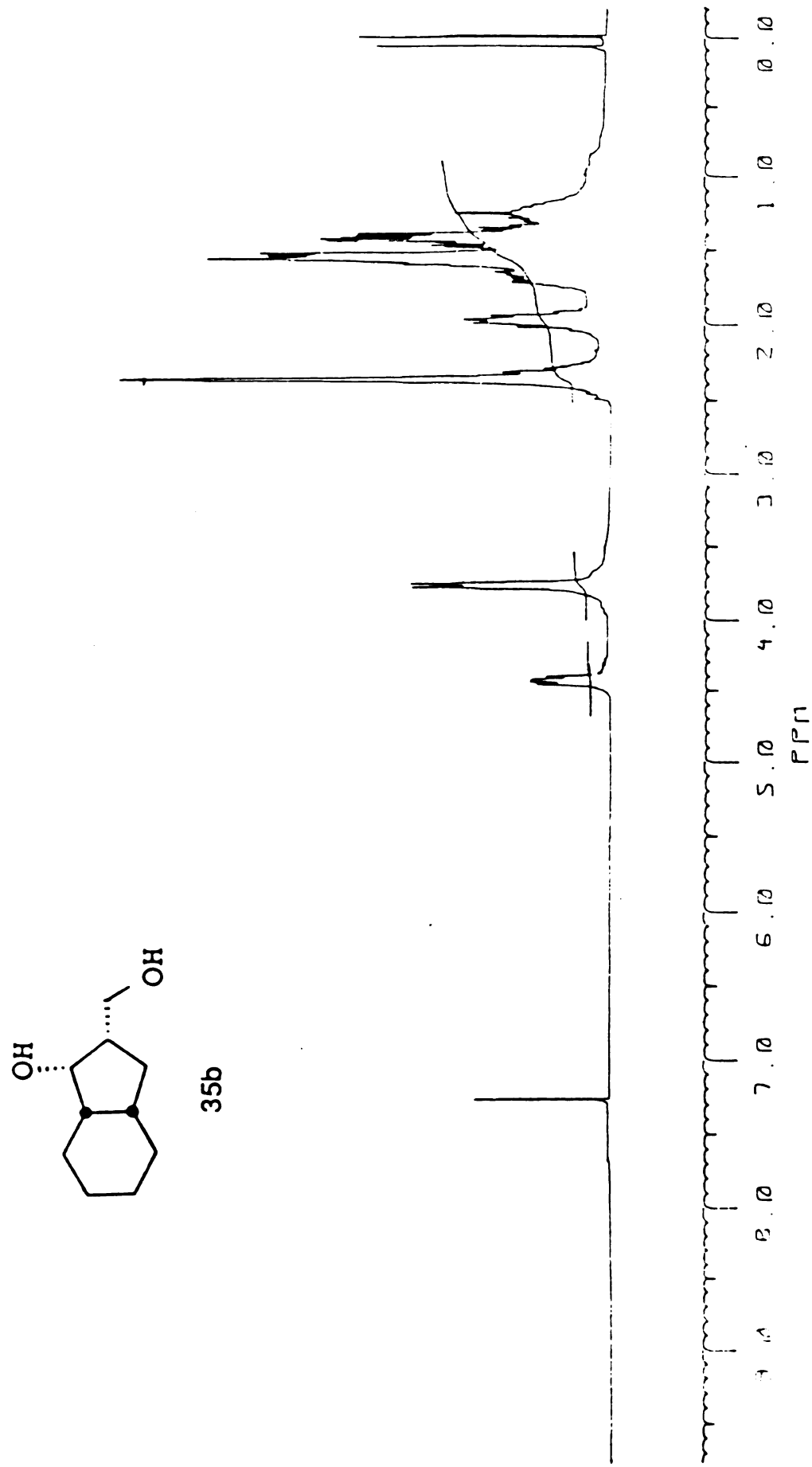


Figure 72. ^{1}H NMR Spectrum of **35b**

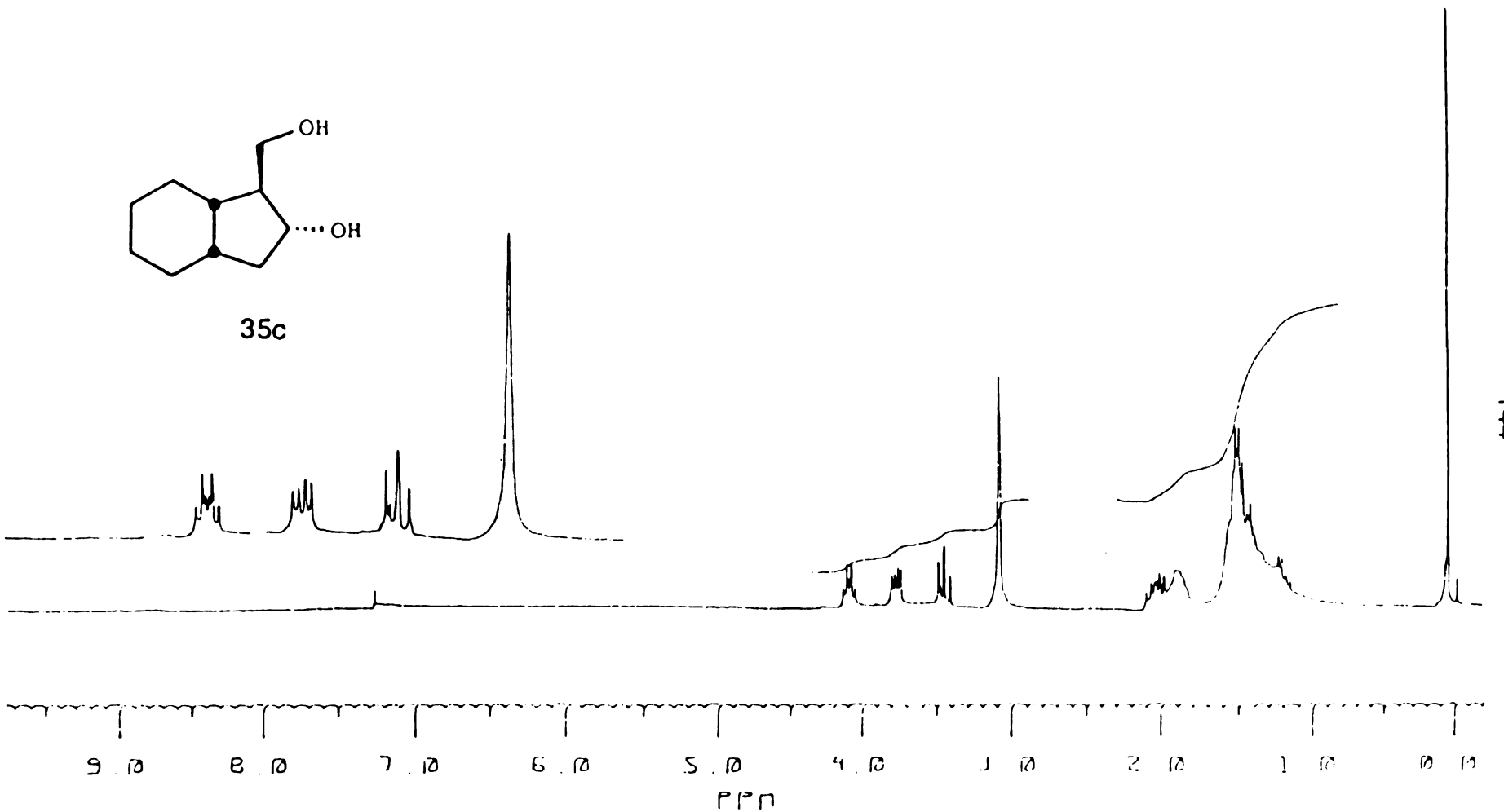


Figure 73. ^{1}H NMR Spectrum of **35c**

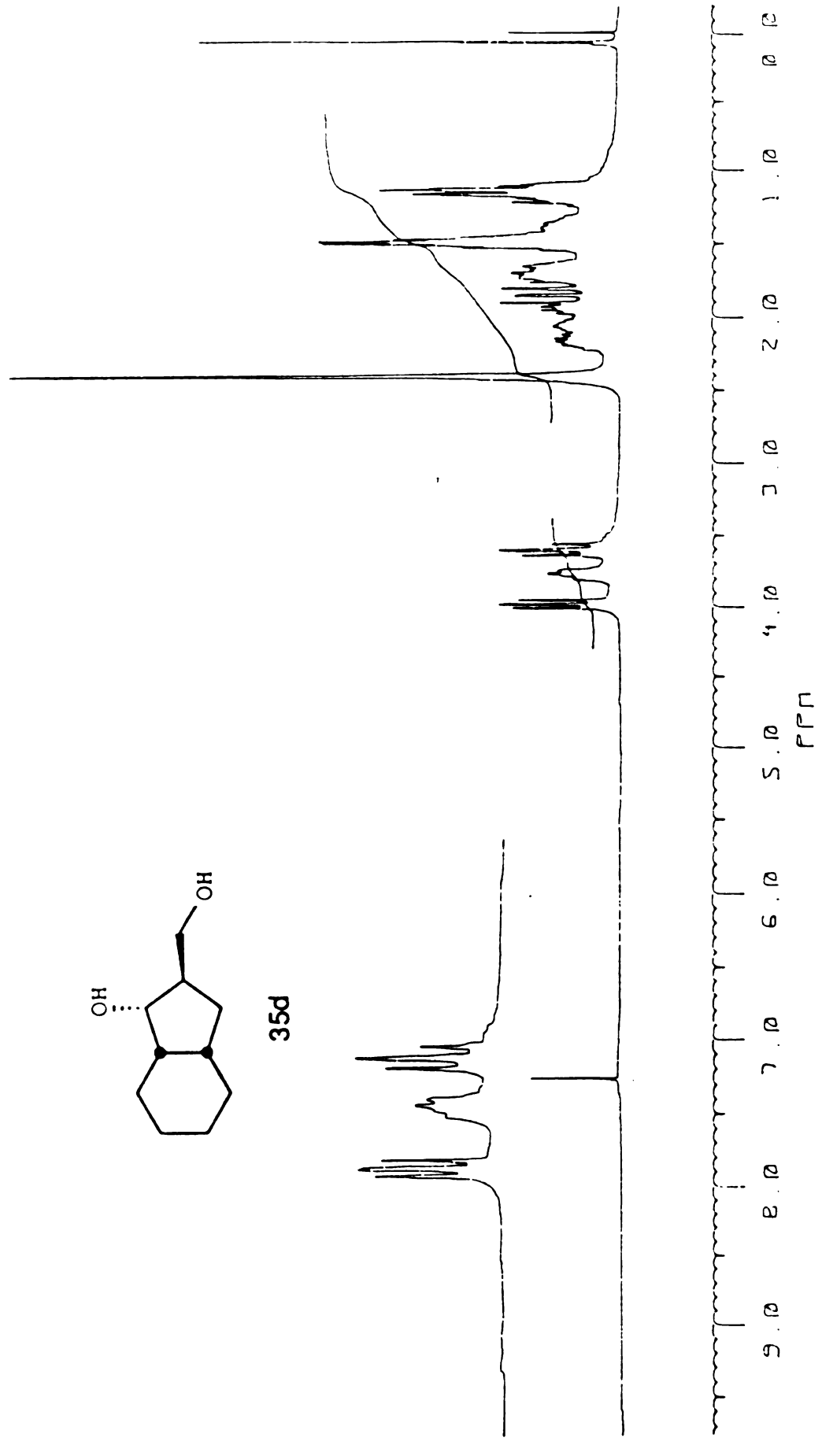


Figure 74. ^{1}H NMR Spectrum of **35d**

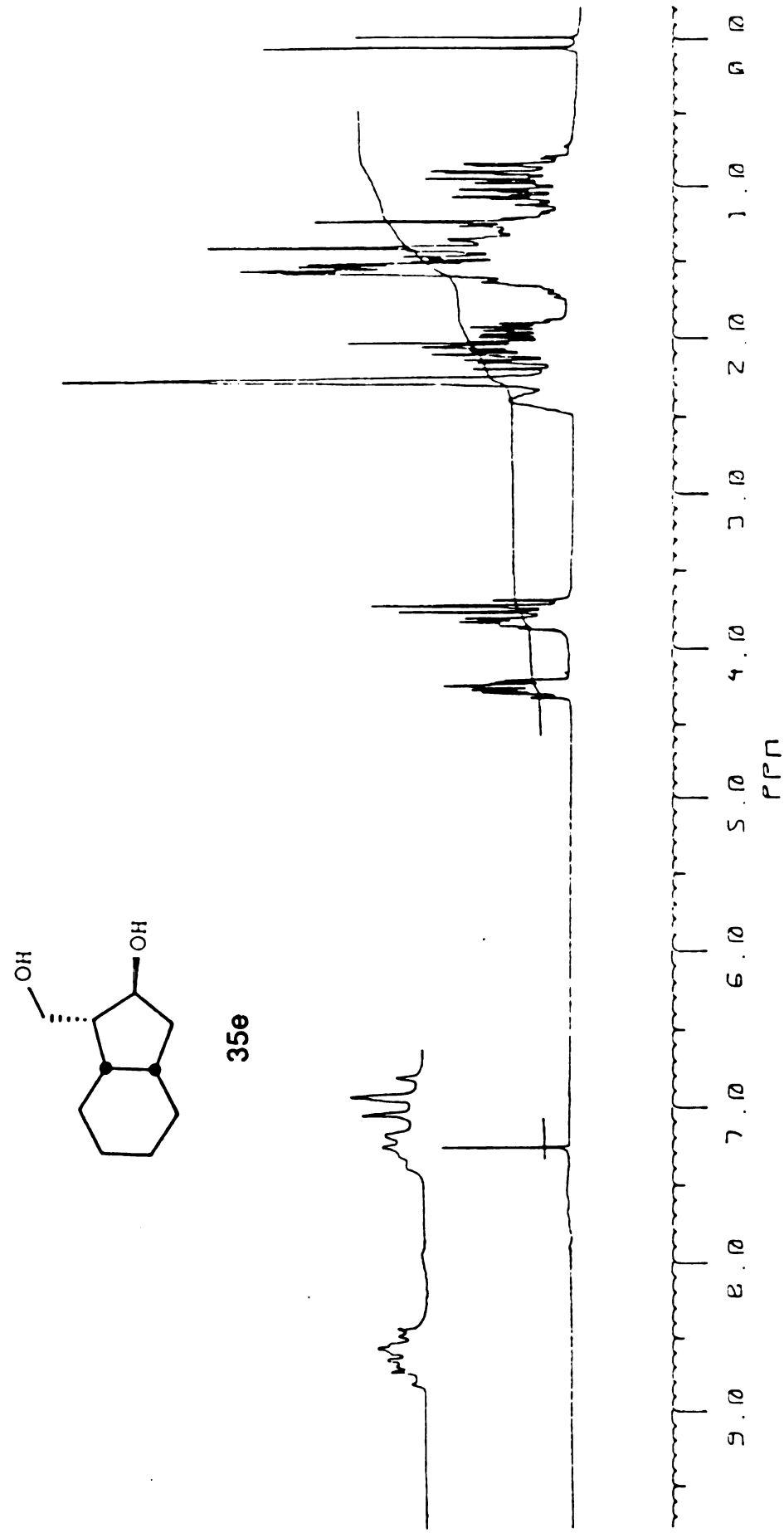


Figure 75. ^{1}H NMR Spectrum of **35e**

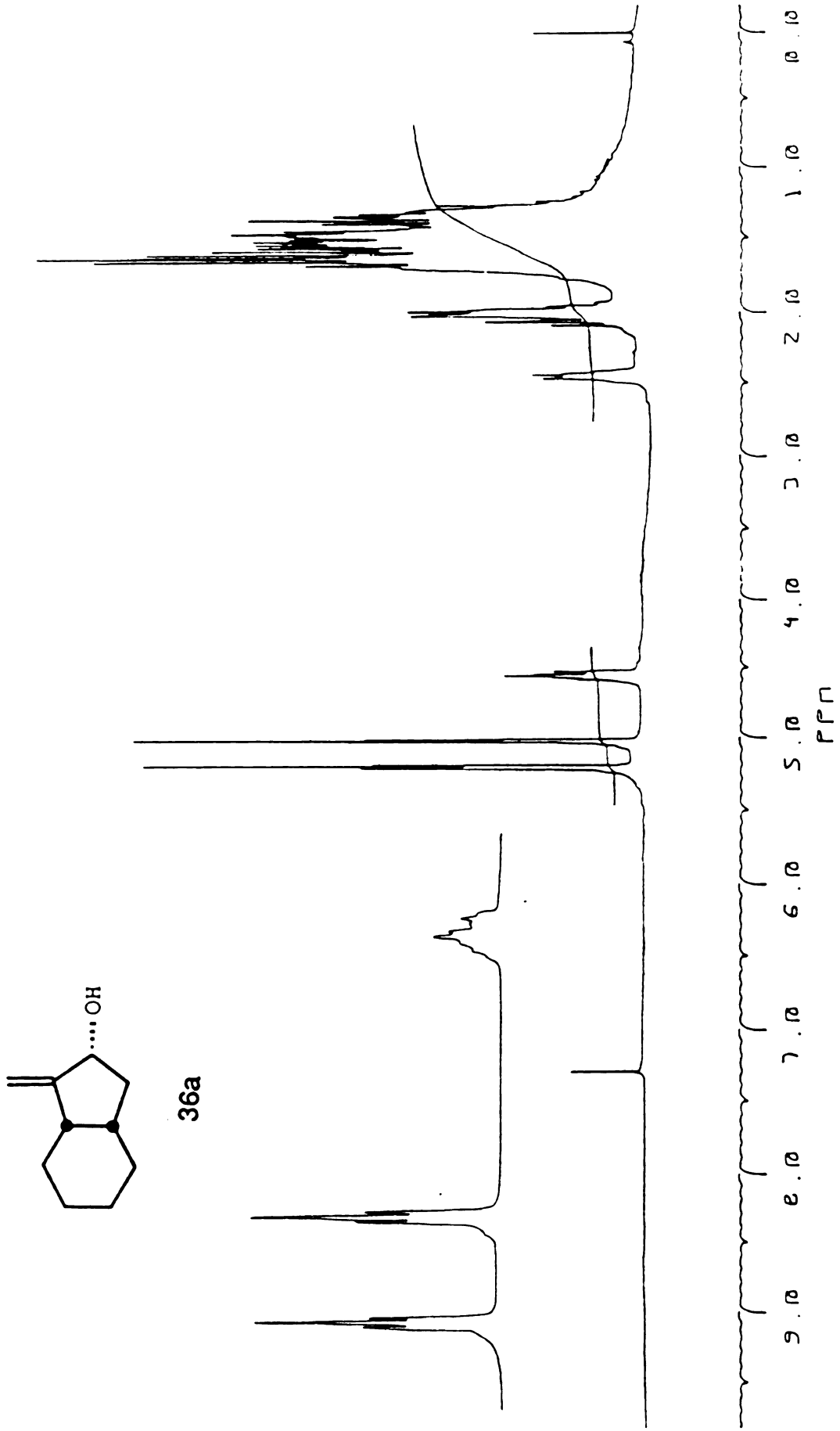
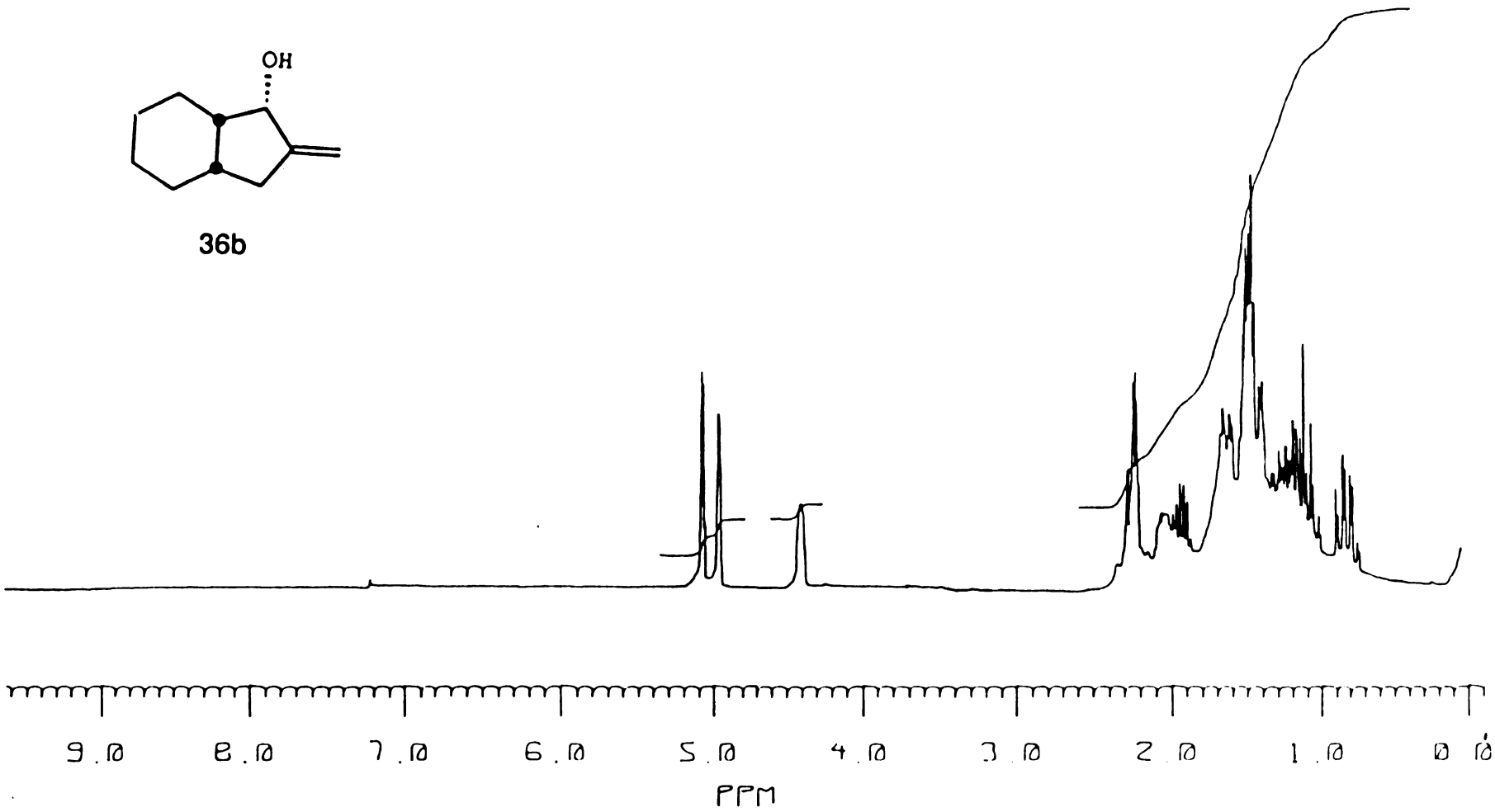


Figure 76. ^{1}H NMR Spectrum of **36a**



36b

Figure 77. ^{1}H NMR Spectrum of **36b**

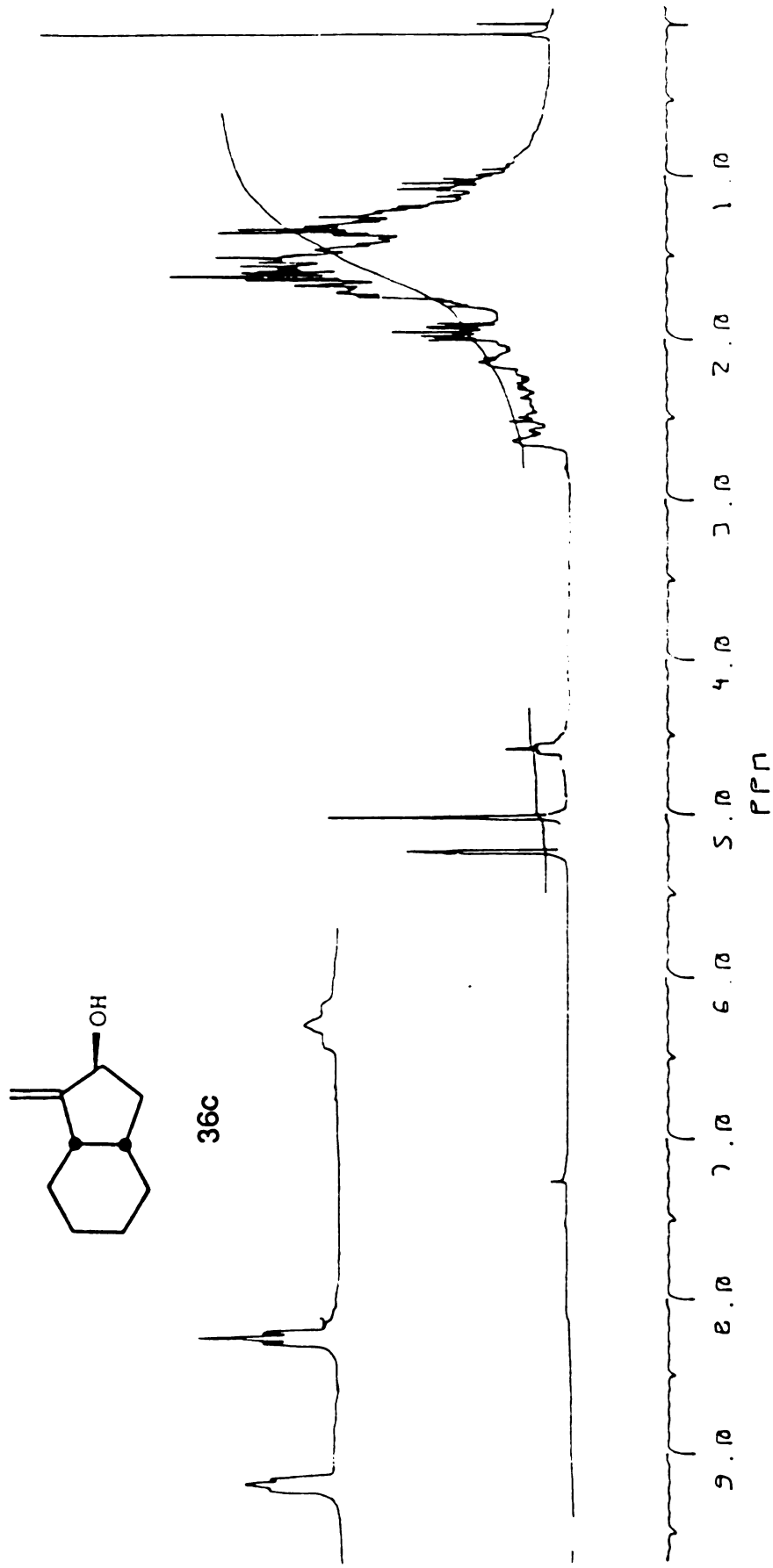


Figure 78. ^{1}H NMR Spectrum of **36c**

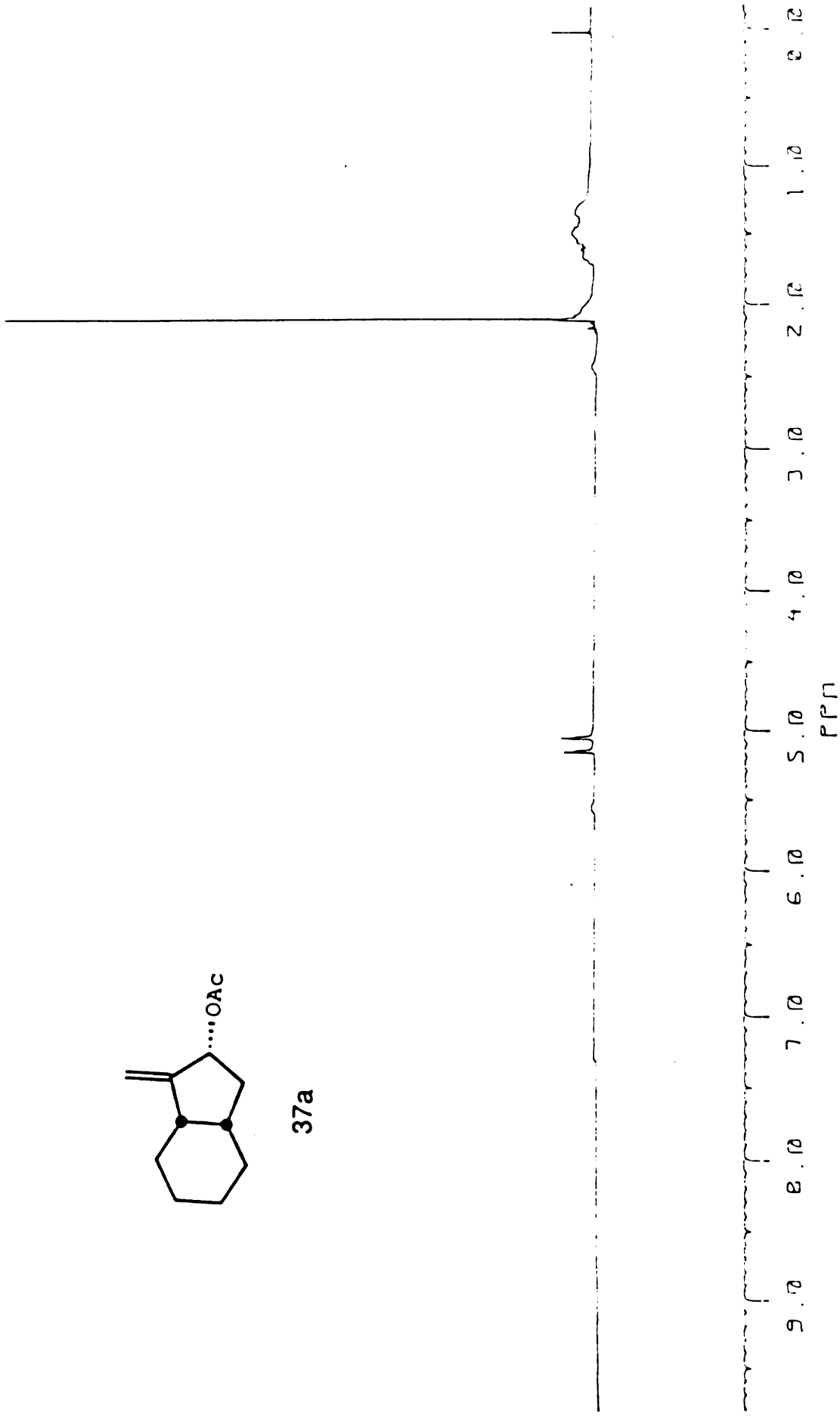


Figure 79. ^{1}H NMR Spectrum of 37a

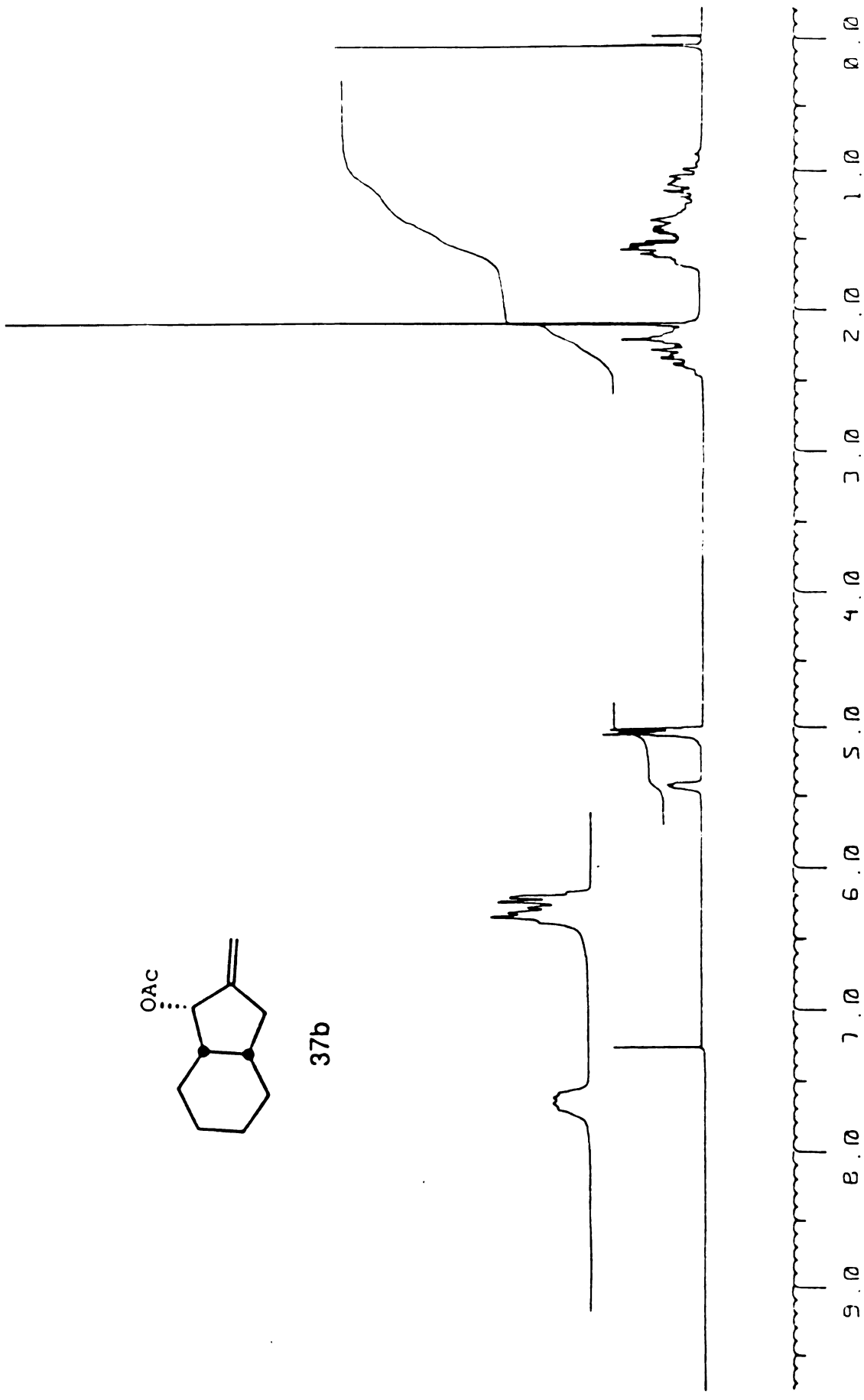


Figure 80. ^{1}H NMR Spectrum of **37b**

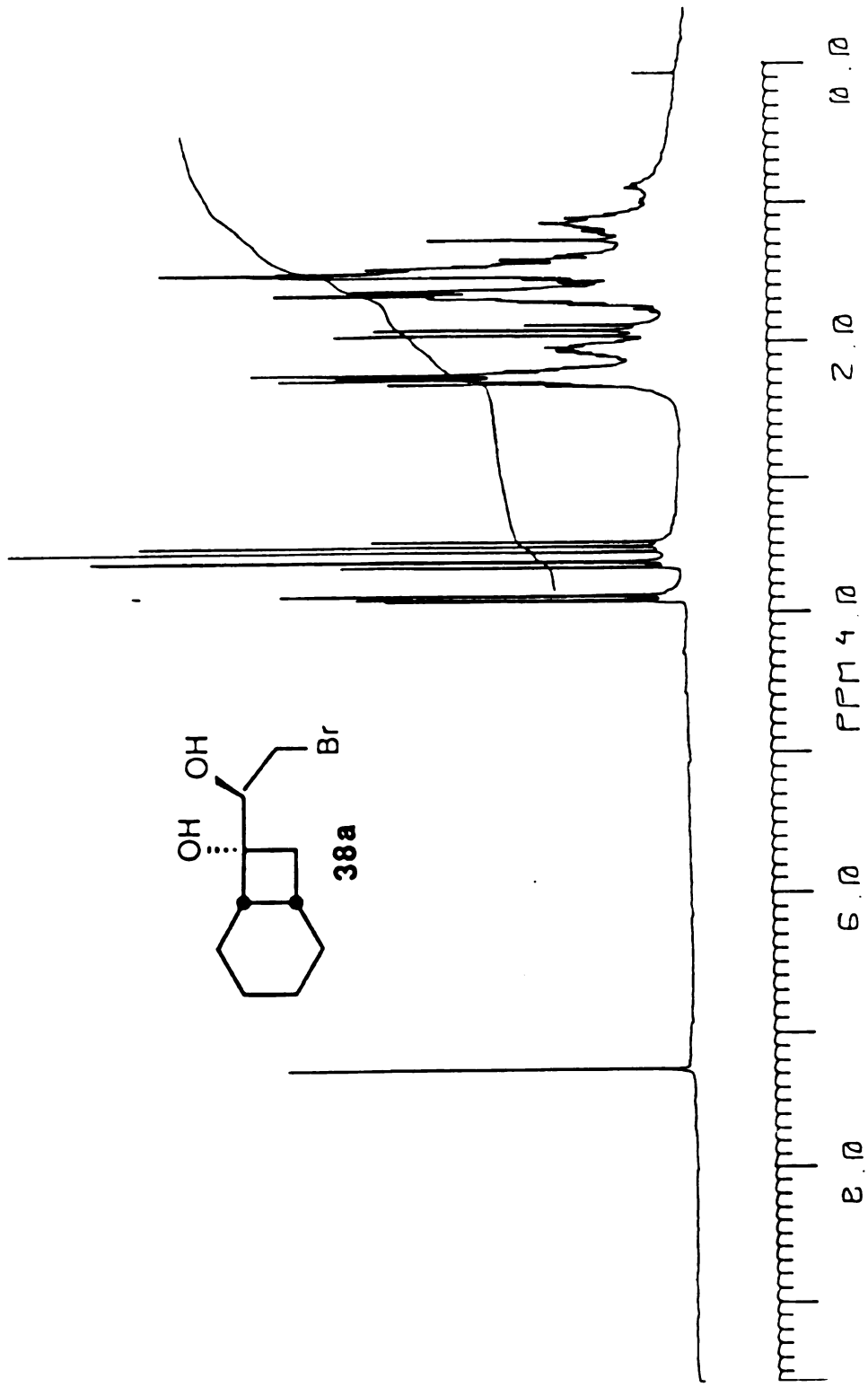


Figure 81. ^{1}H NMR Spectrum of **38a**

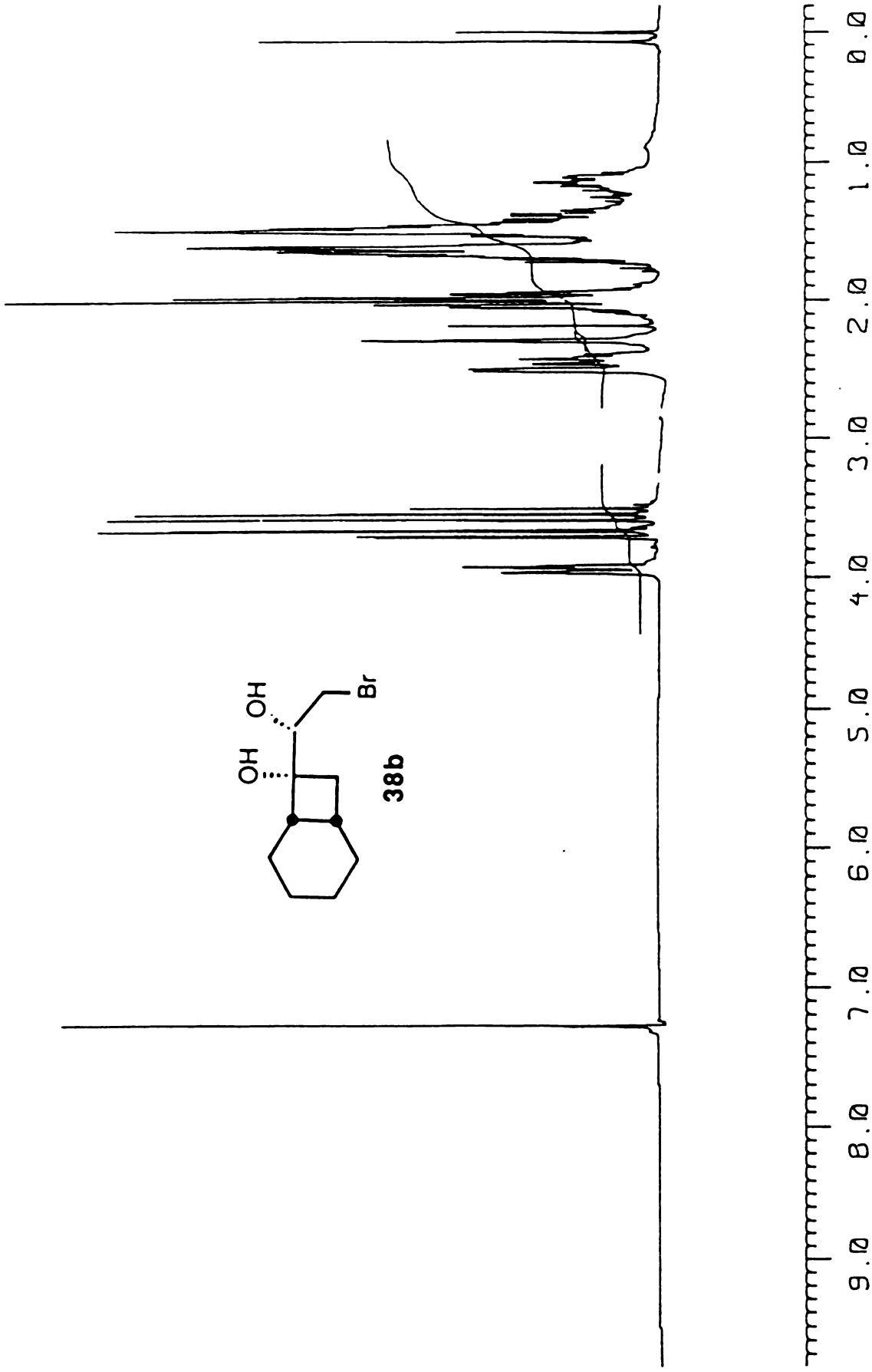


Figure 82. ^{1}H NMR Spectrum of **38b**

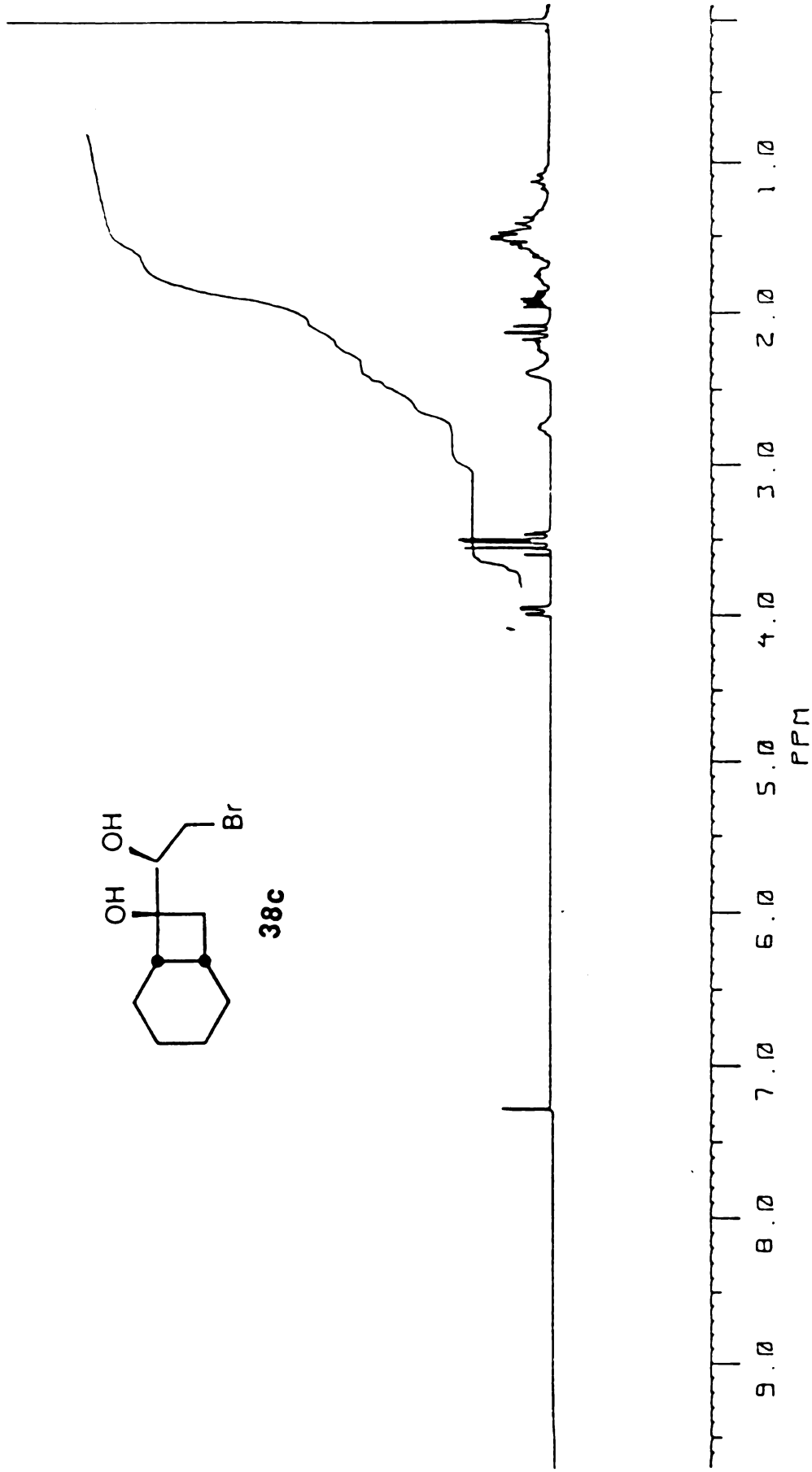


Figure 83. ^{1}H NMR Spectrum of **38c**

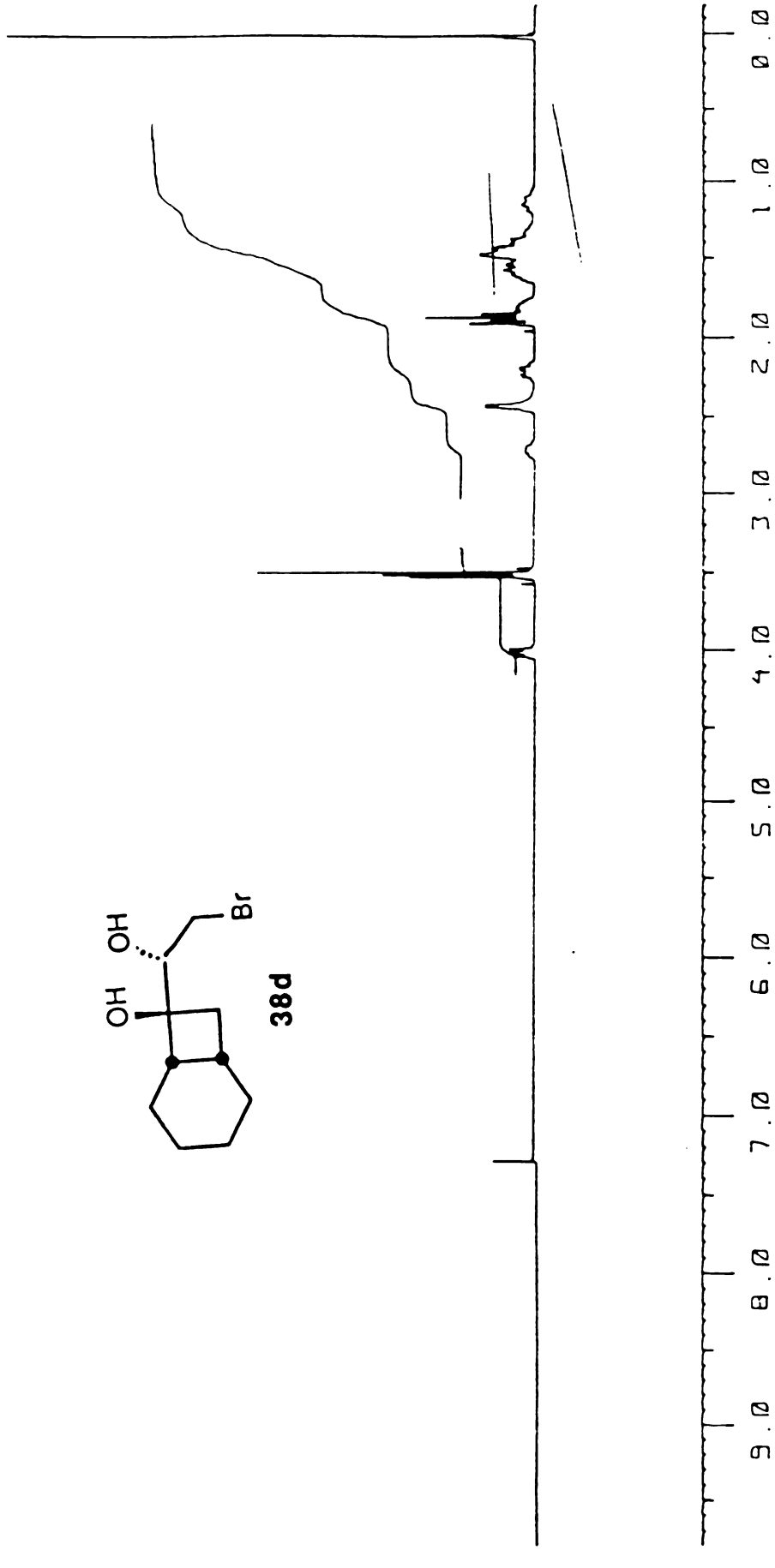


Figure 84. ^{1}H NMR Spectrum of **38d**

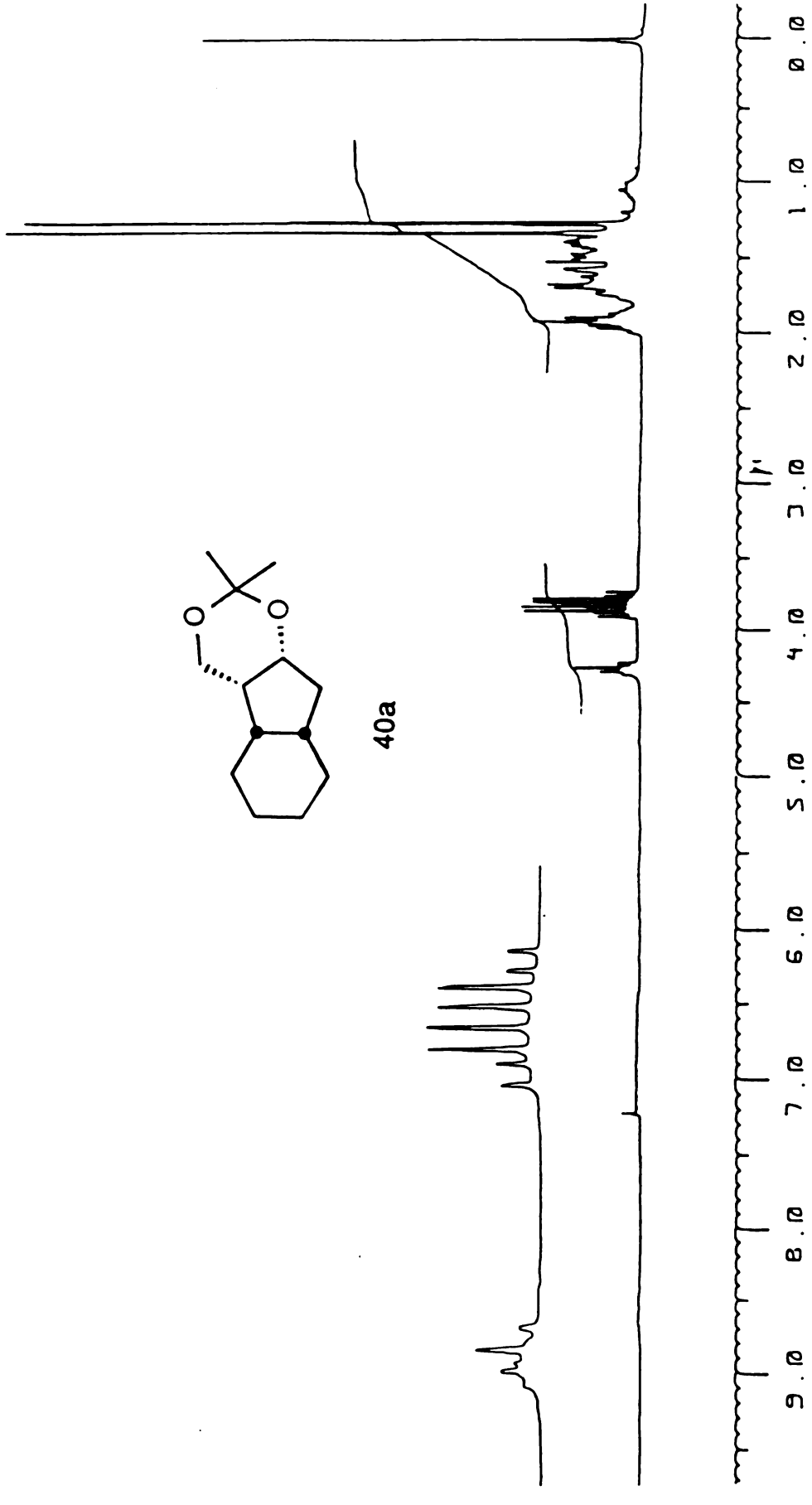


Figure 85. ^{1}H NMR Spectrum of **40a**

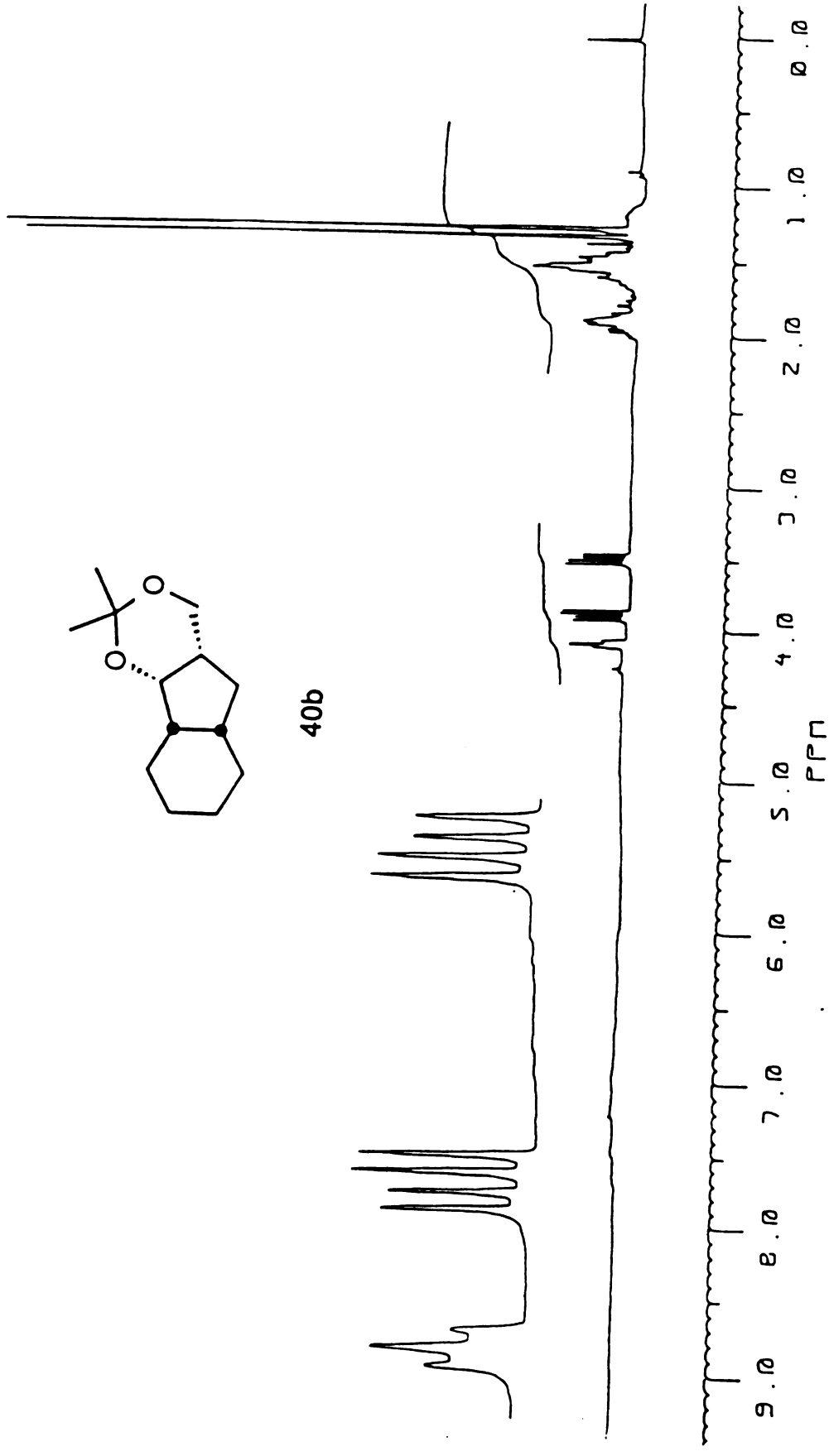


Figure 86. ^{1}H NMR Spectrum of **40b**

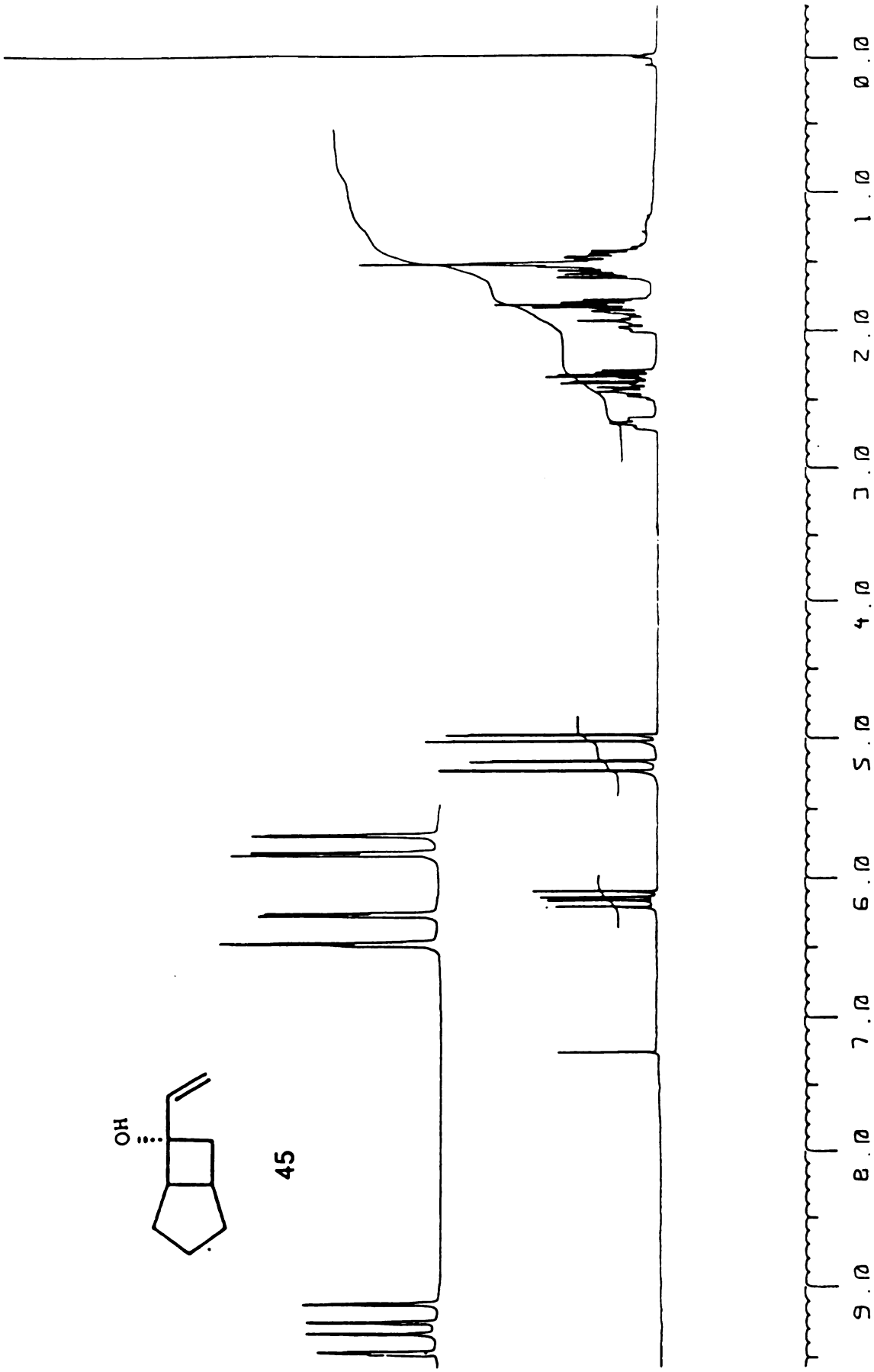


Figure 87. ^{1}H NMR Spectrum of **45**

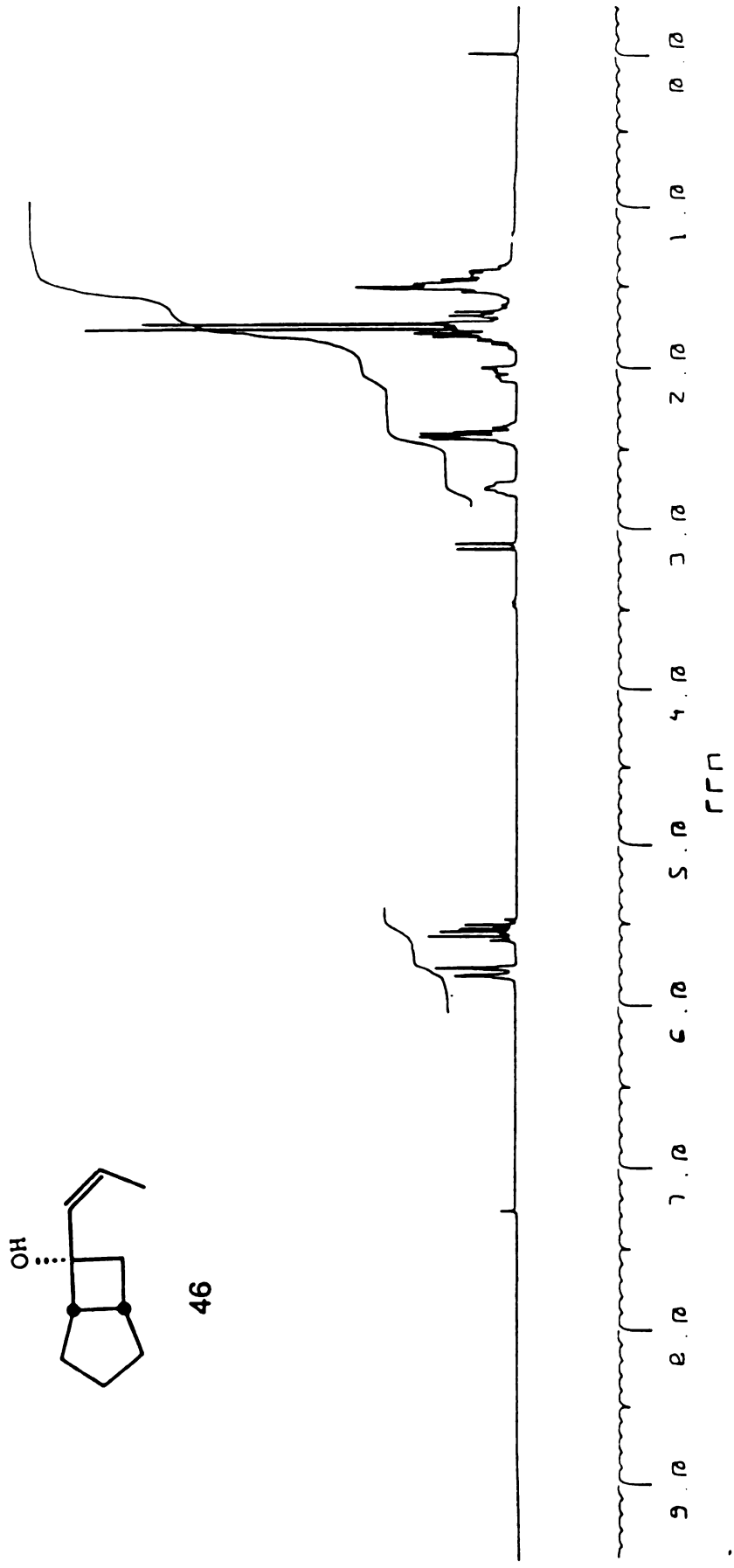


Figure 88. ^{1}H NMR Spectrum of **46** (**cis**)

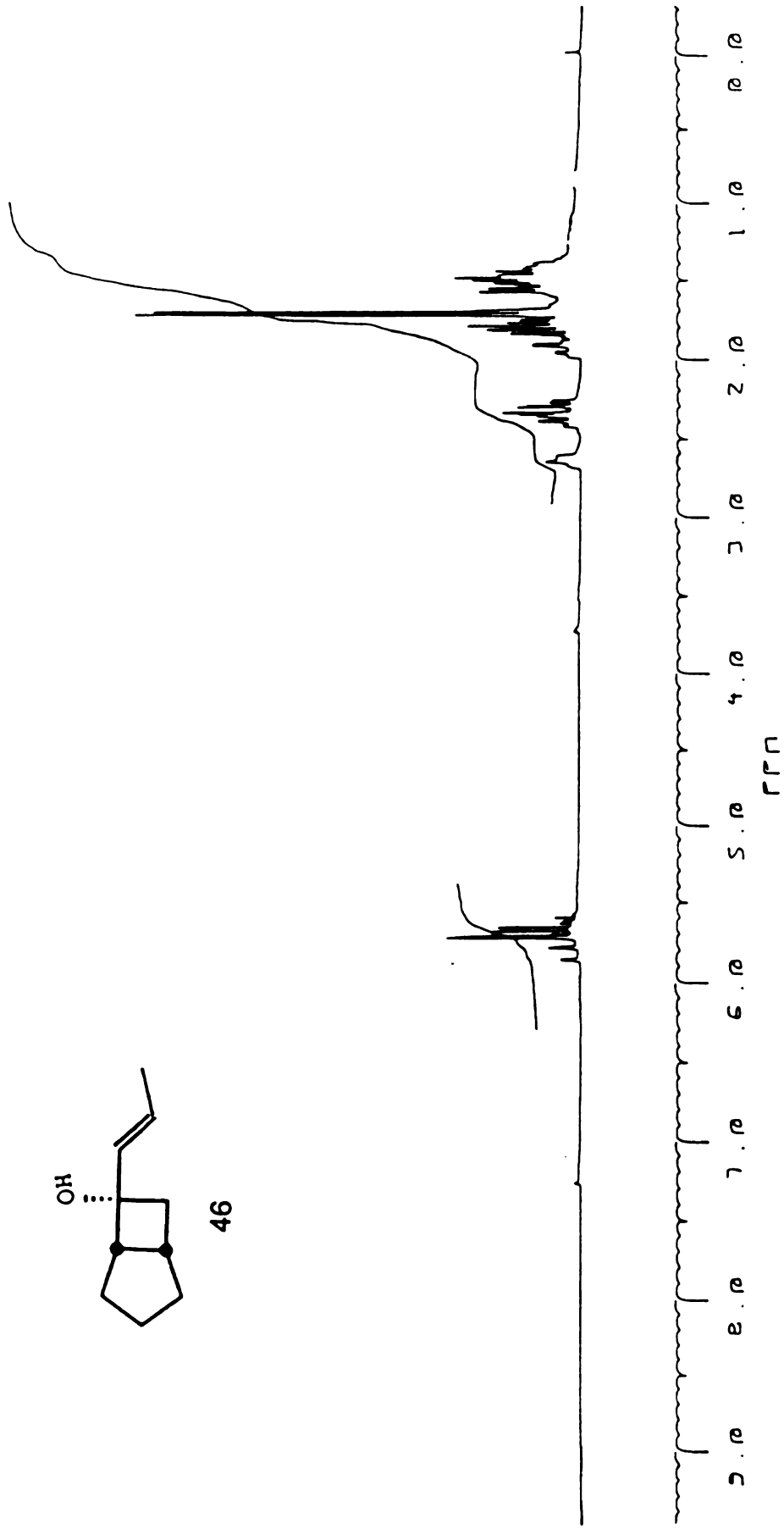


Figure 89. ^{1}H NMR Spectrum of **46** (tran)

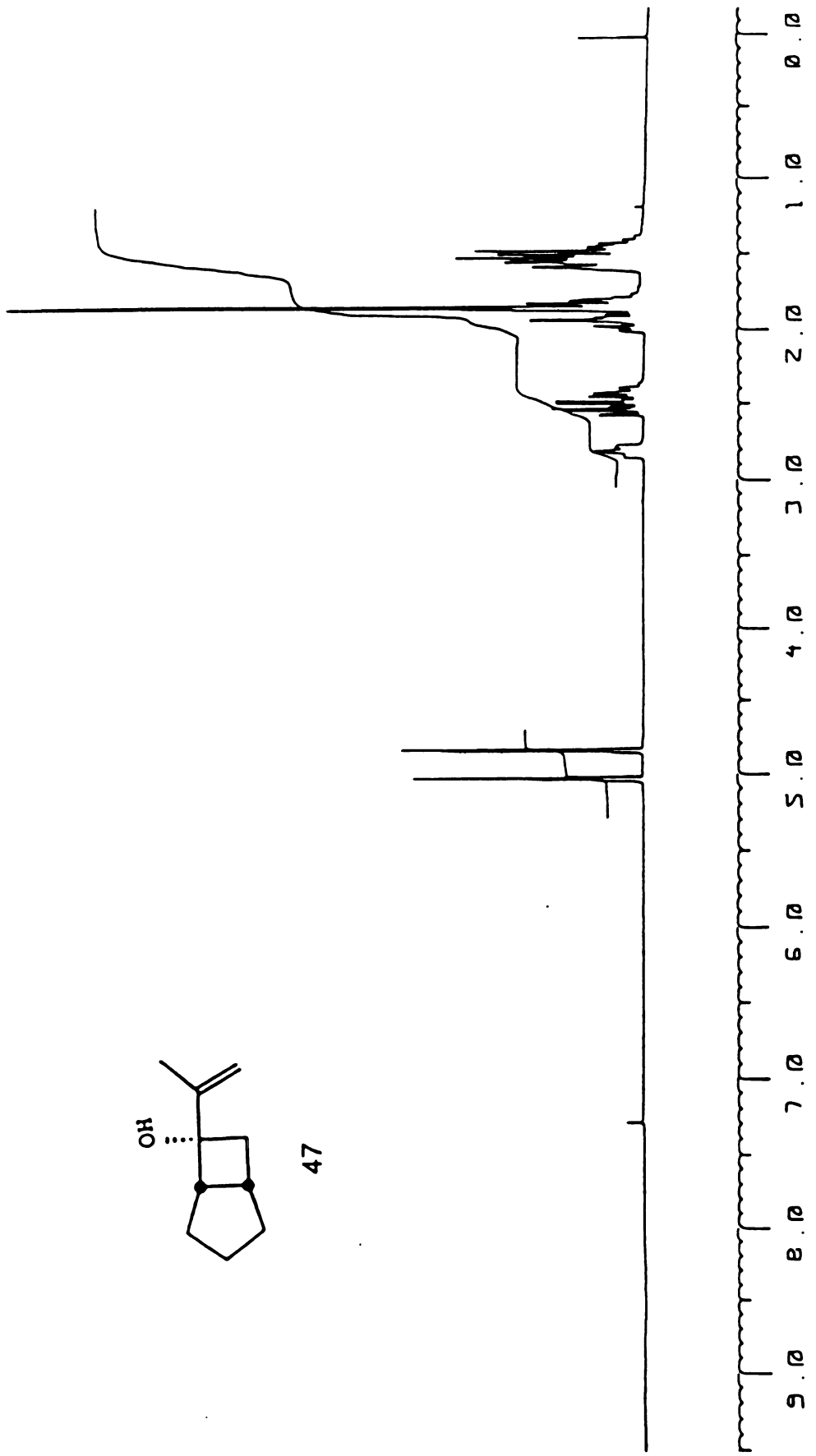


Figure 90. ^{1}H NMR Spectrum of **47**

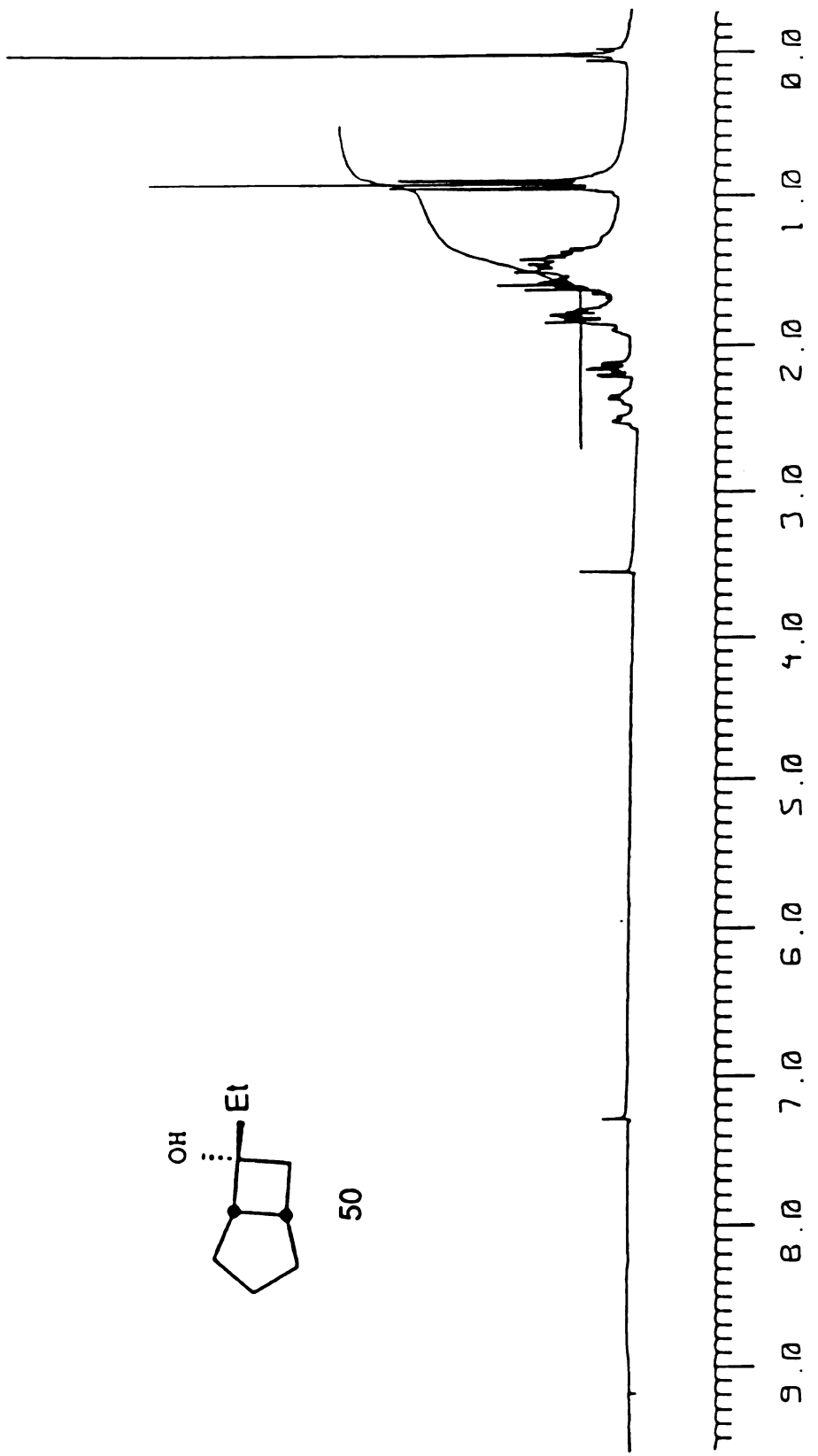


Figure 91. ^{1}H NMR Spectrum of **50**

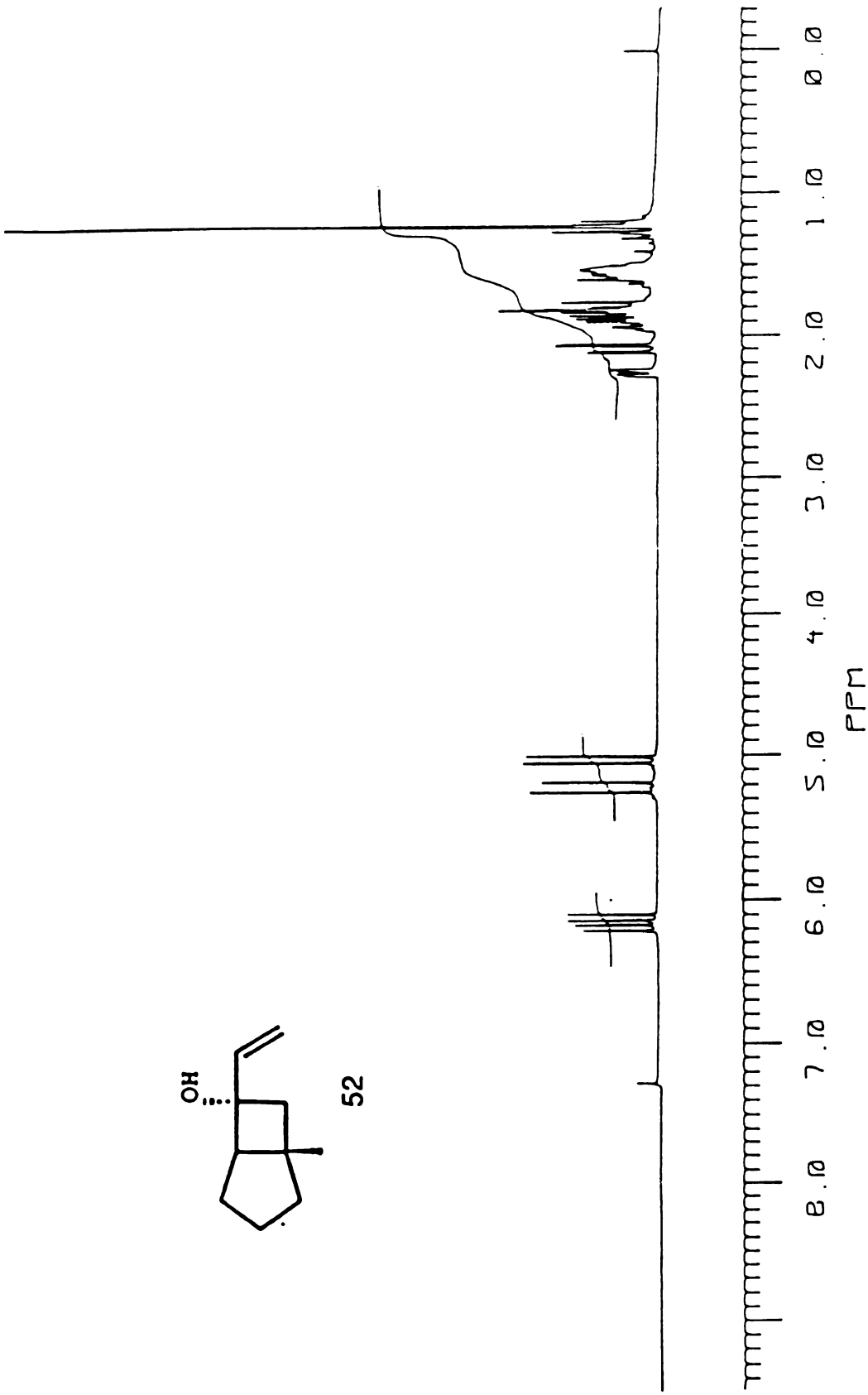


Figure 92. ^{1}H NMR Spectrum of **52**

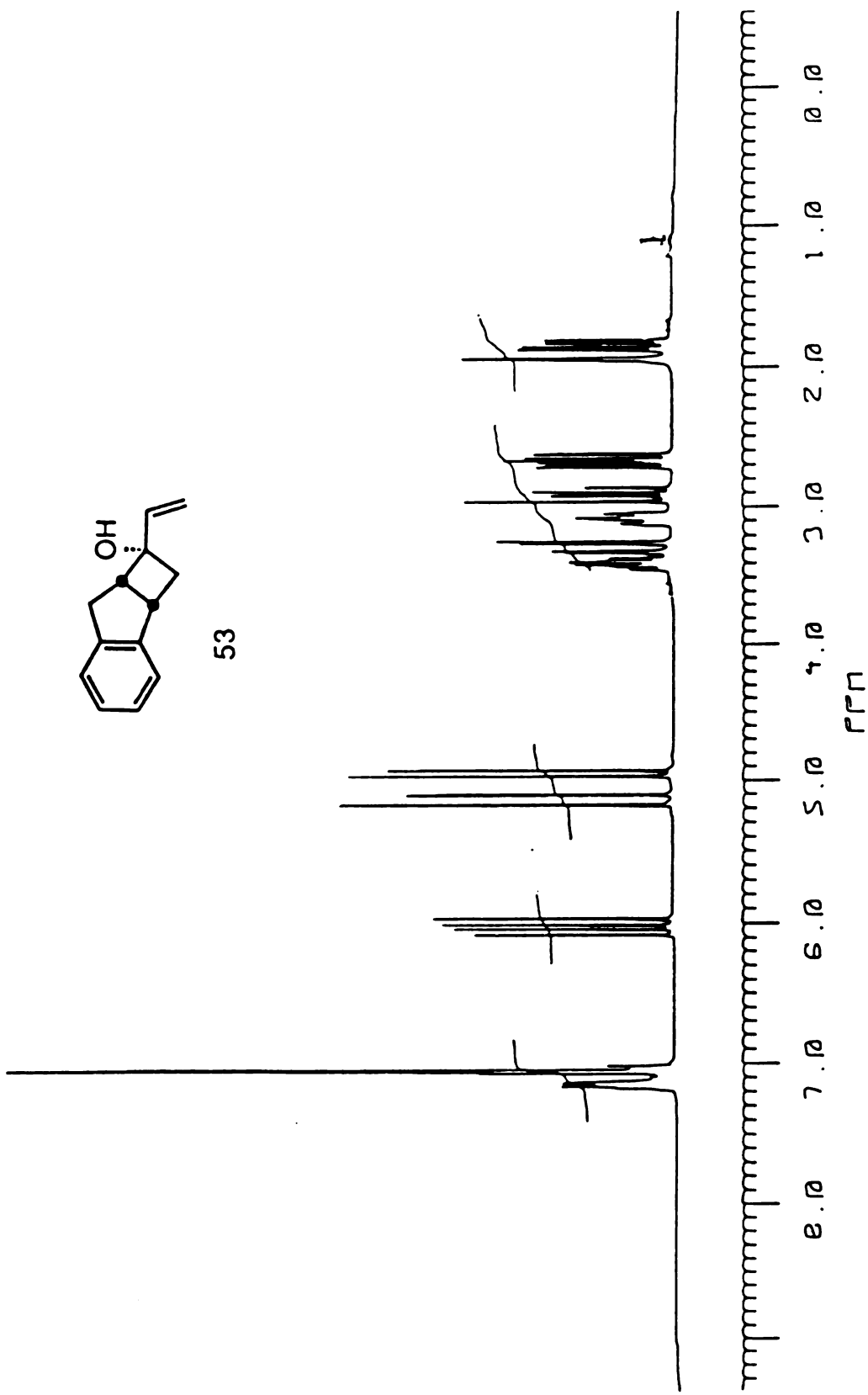


Figure 93. ^{1}H NMR Spectrum of **53**

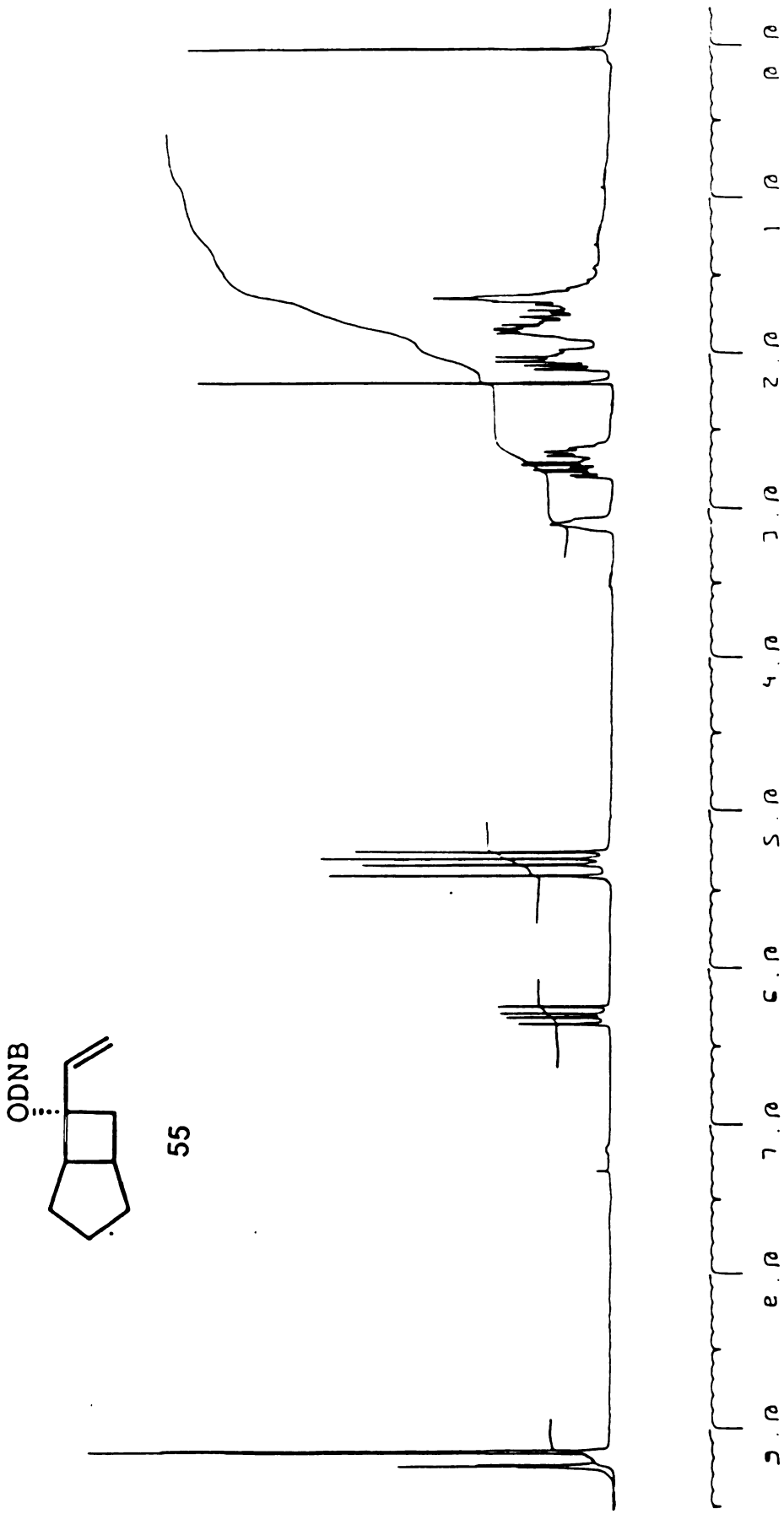


Figure 94. ^{1}H NMR Spectrum of **55**

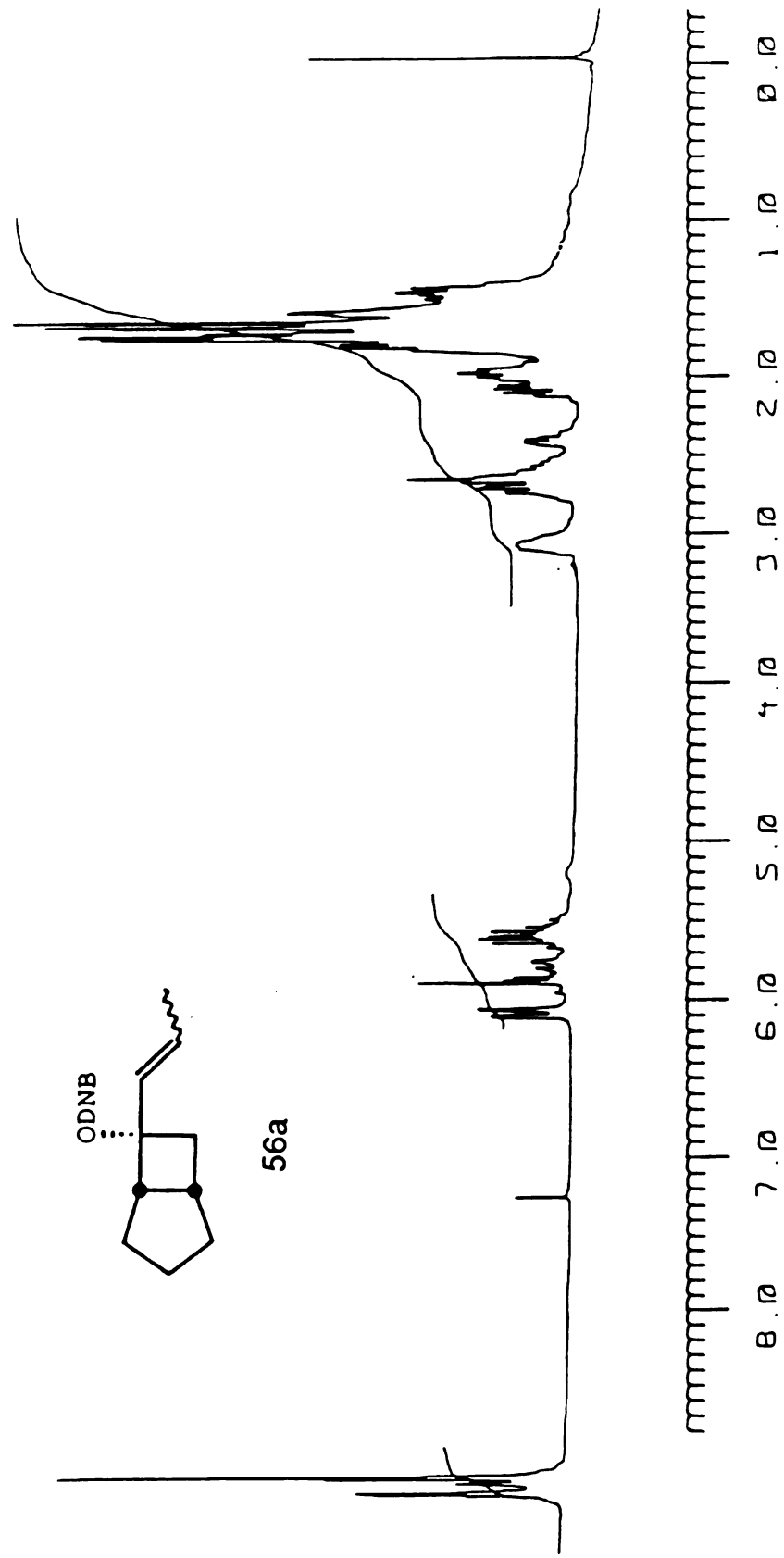


Figure 95. ^{1}H NMR Spectrum of **56a**

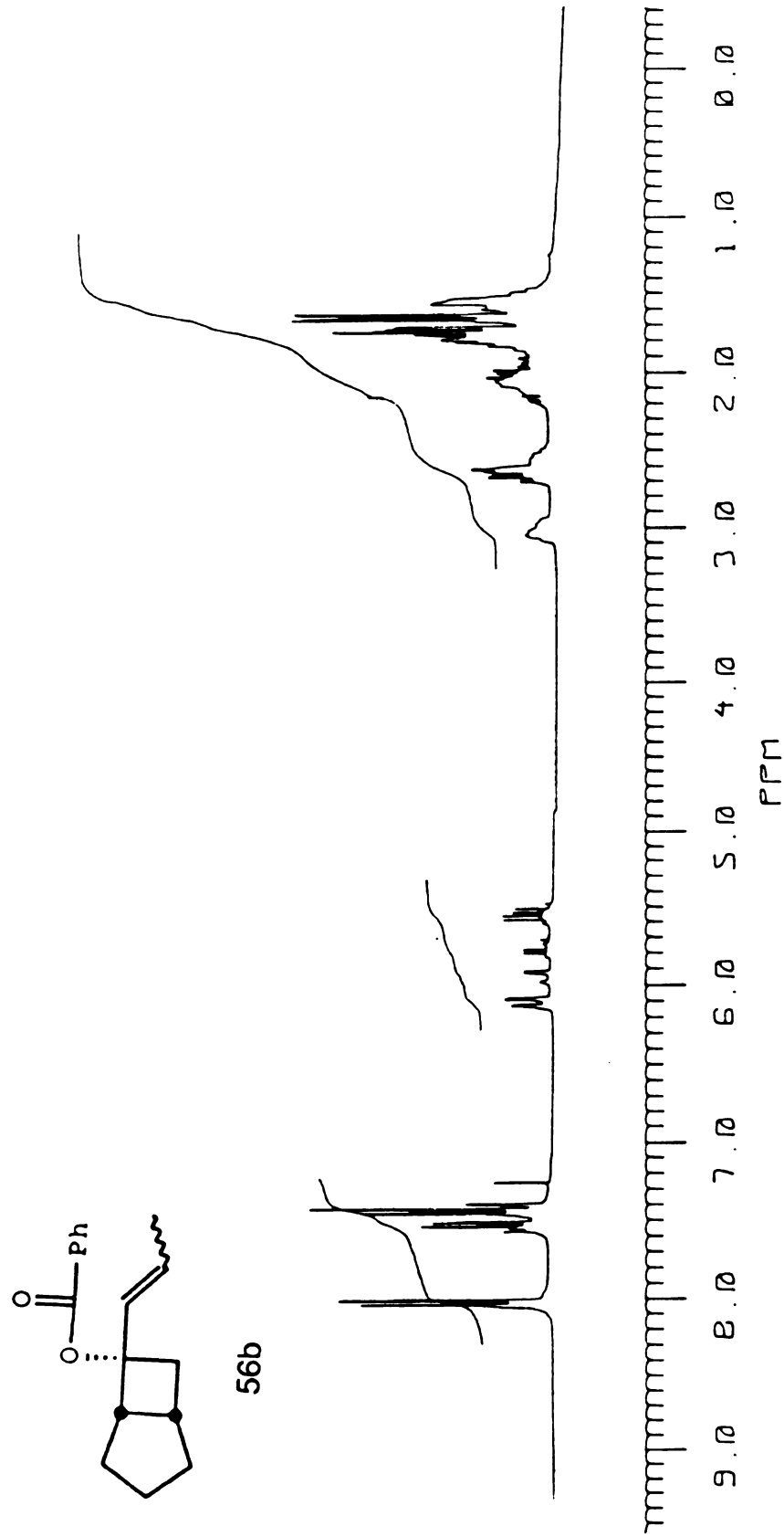


Figure 96. ^{1}H NMR Spectrum of **56b**

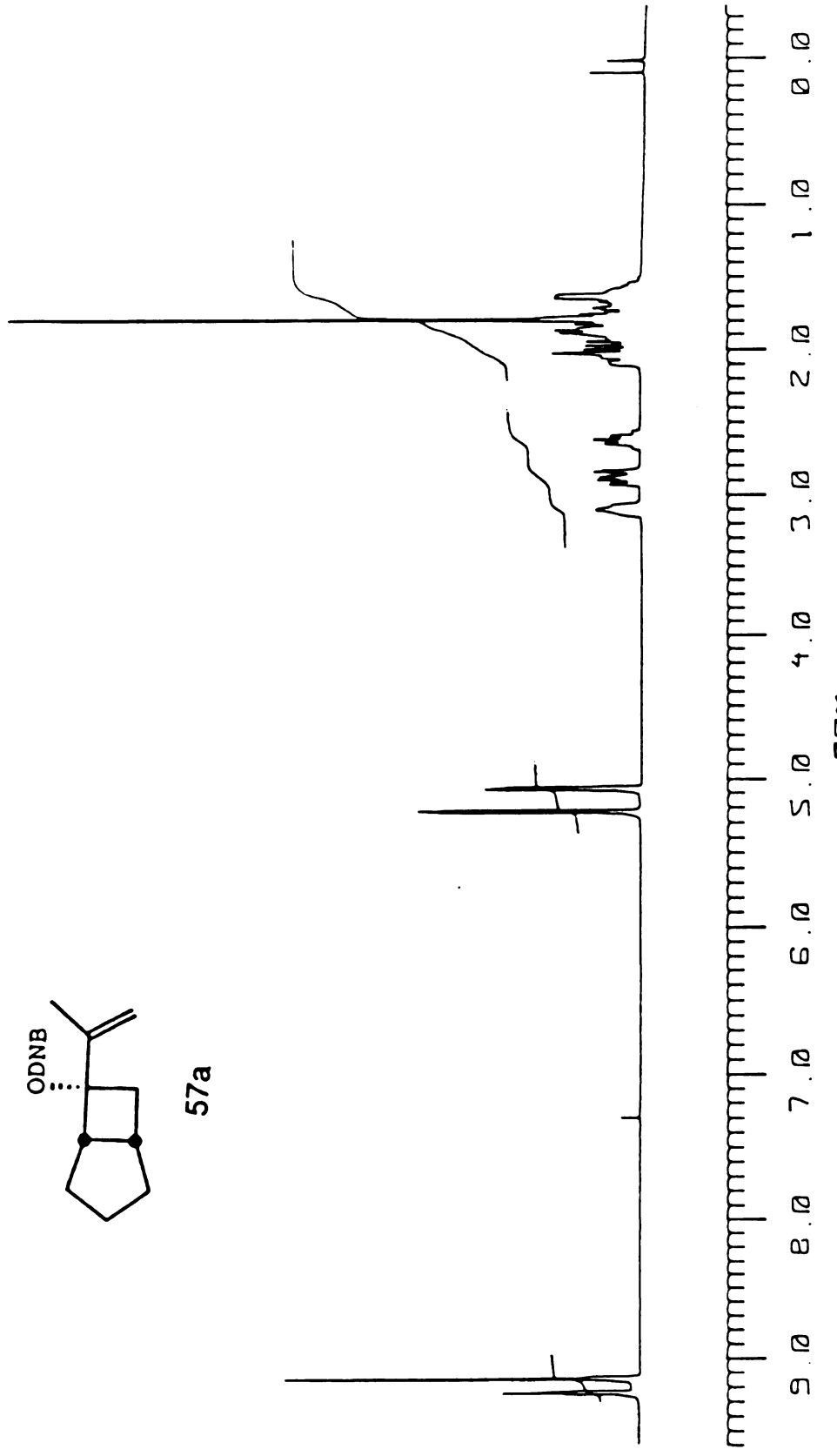


Figure 97. ^{1}H NMR Spectrum of **57a**

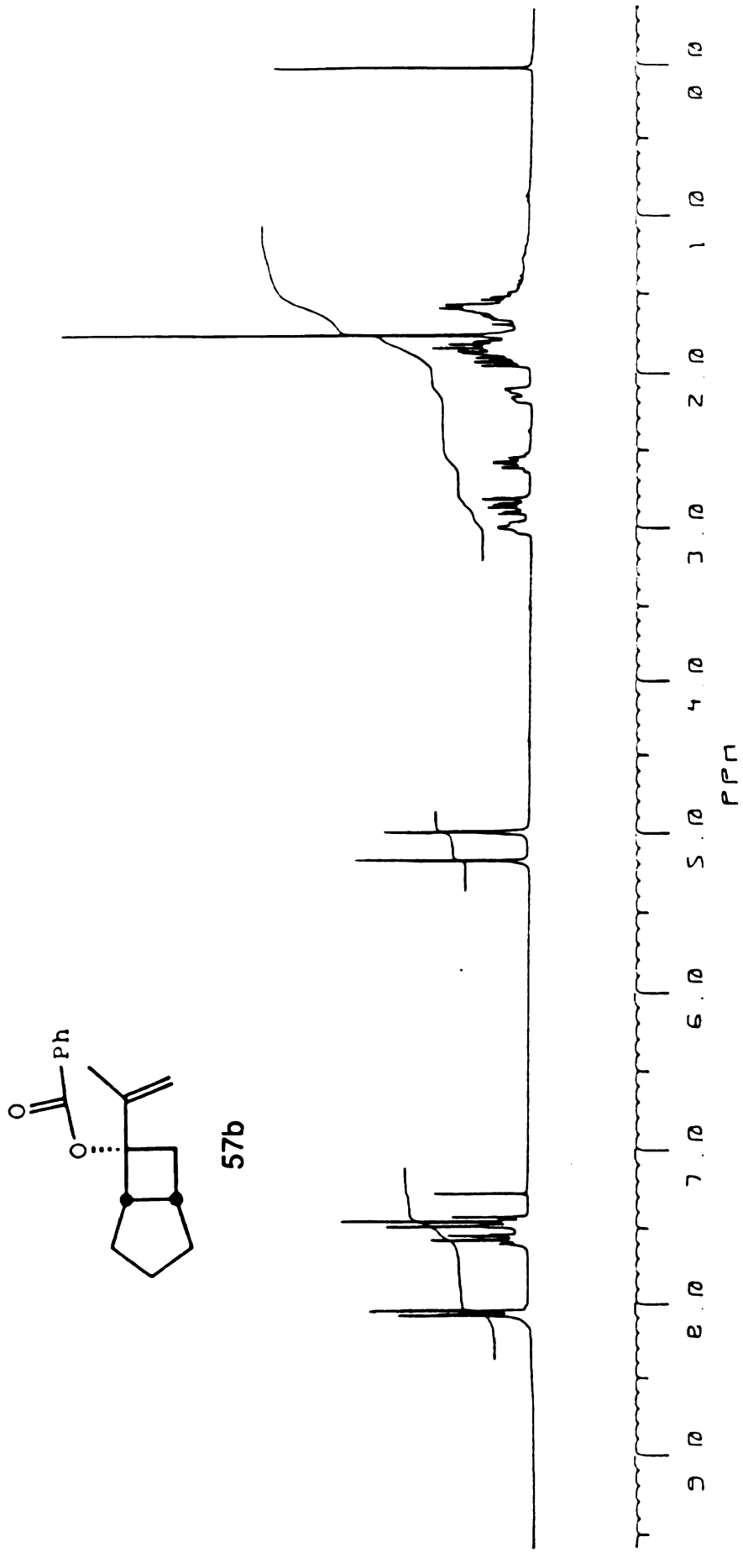


Figure 98. ^{1}H NMR Spectrum of **57b**

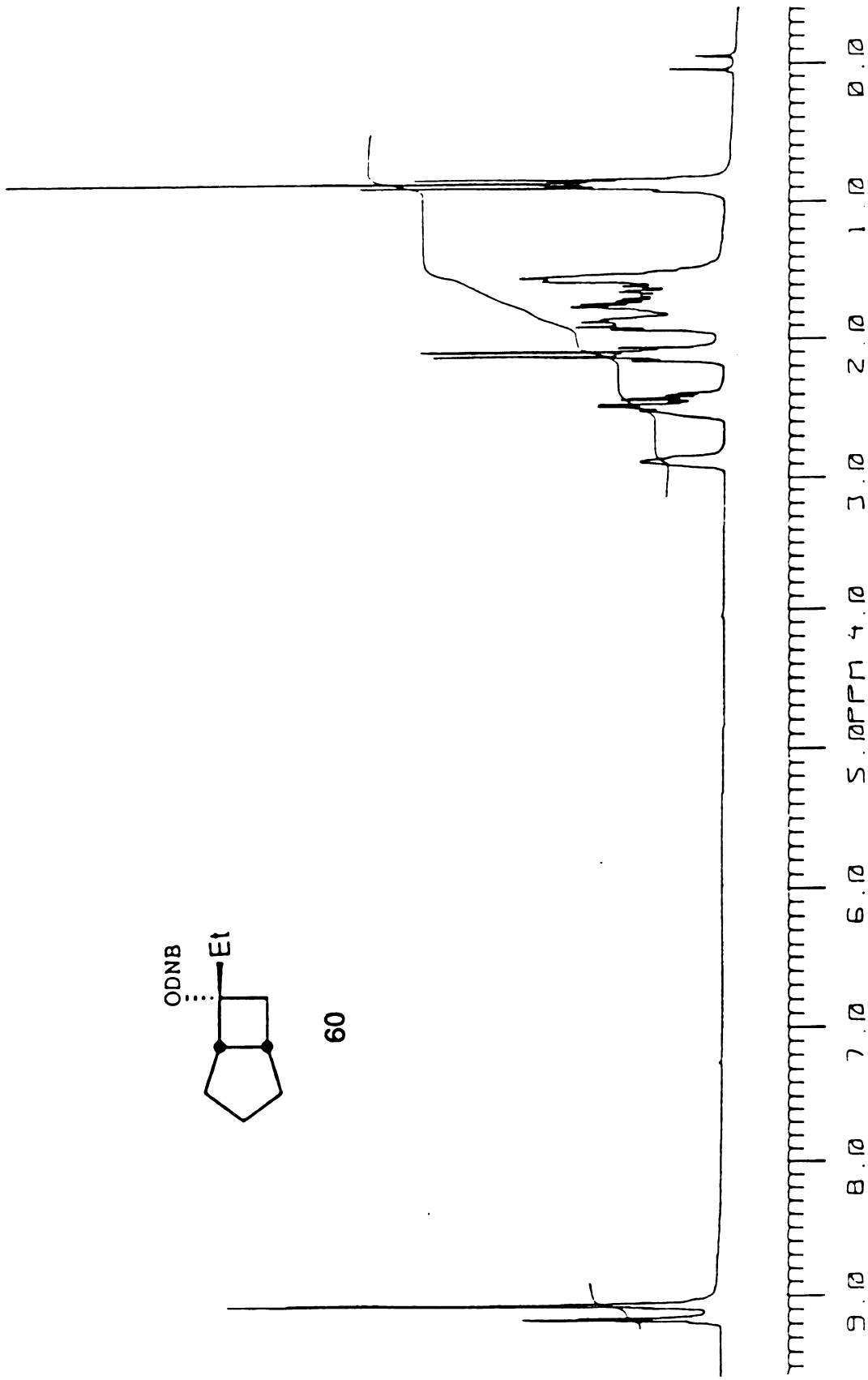


Figure 99. ^{1}H NMR Spectrum of **60**

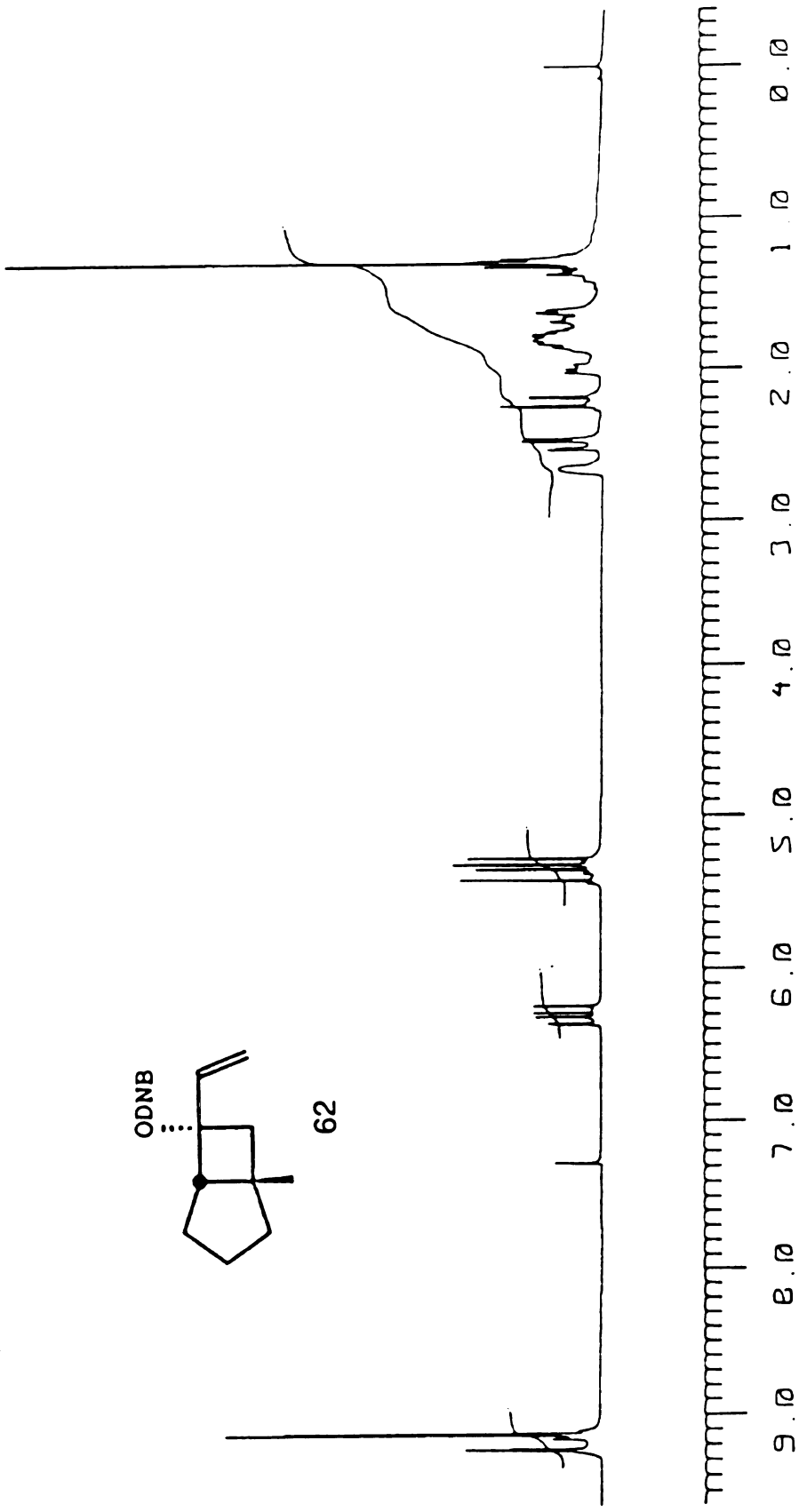


Figure 100. ^{1}H NMR Spectrum of **62**

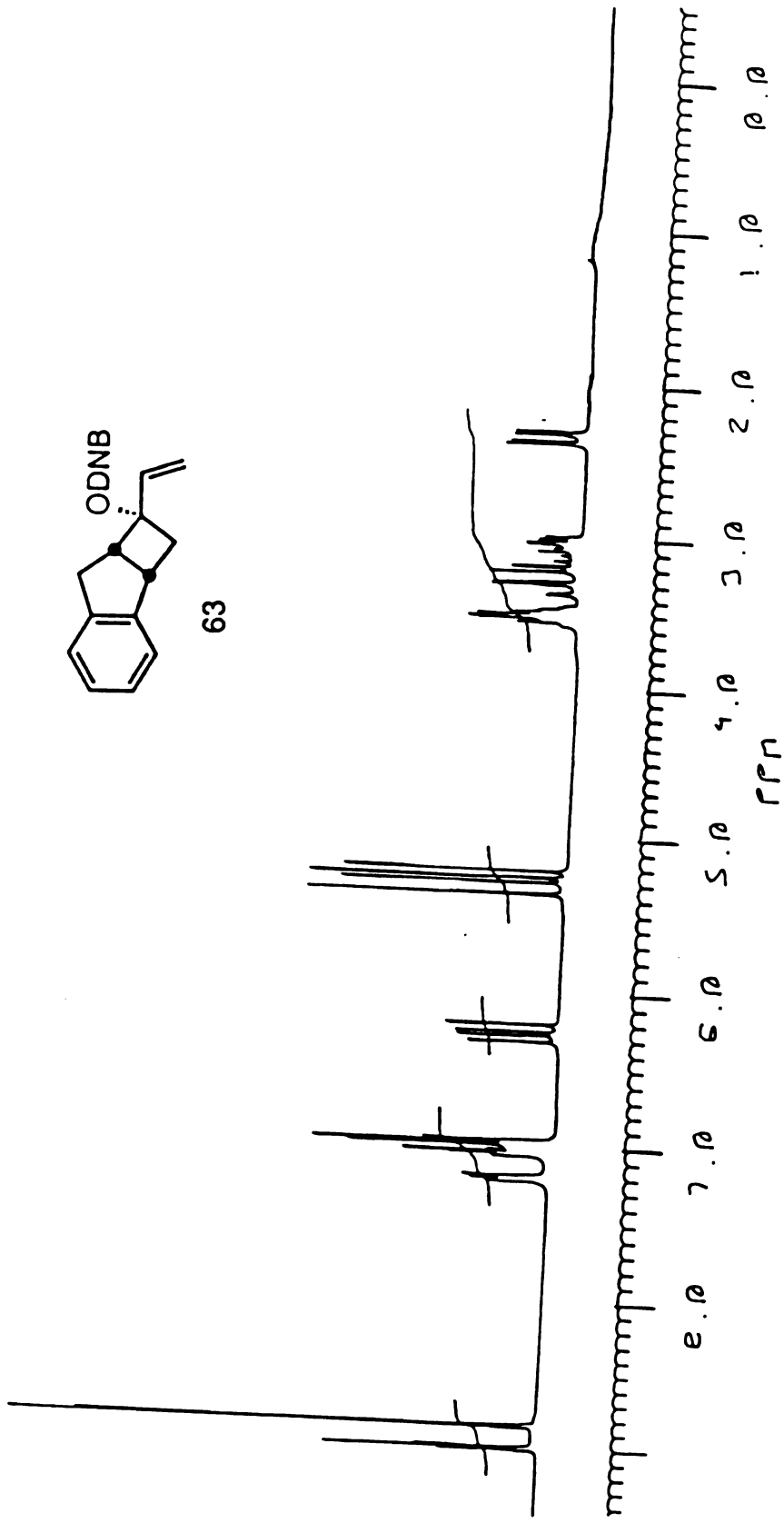


Figure 101. ^{1}H NMR Spectrum of **63**

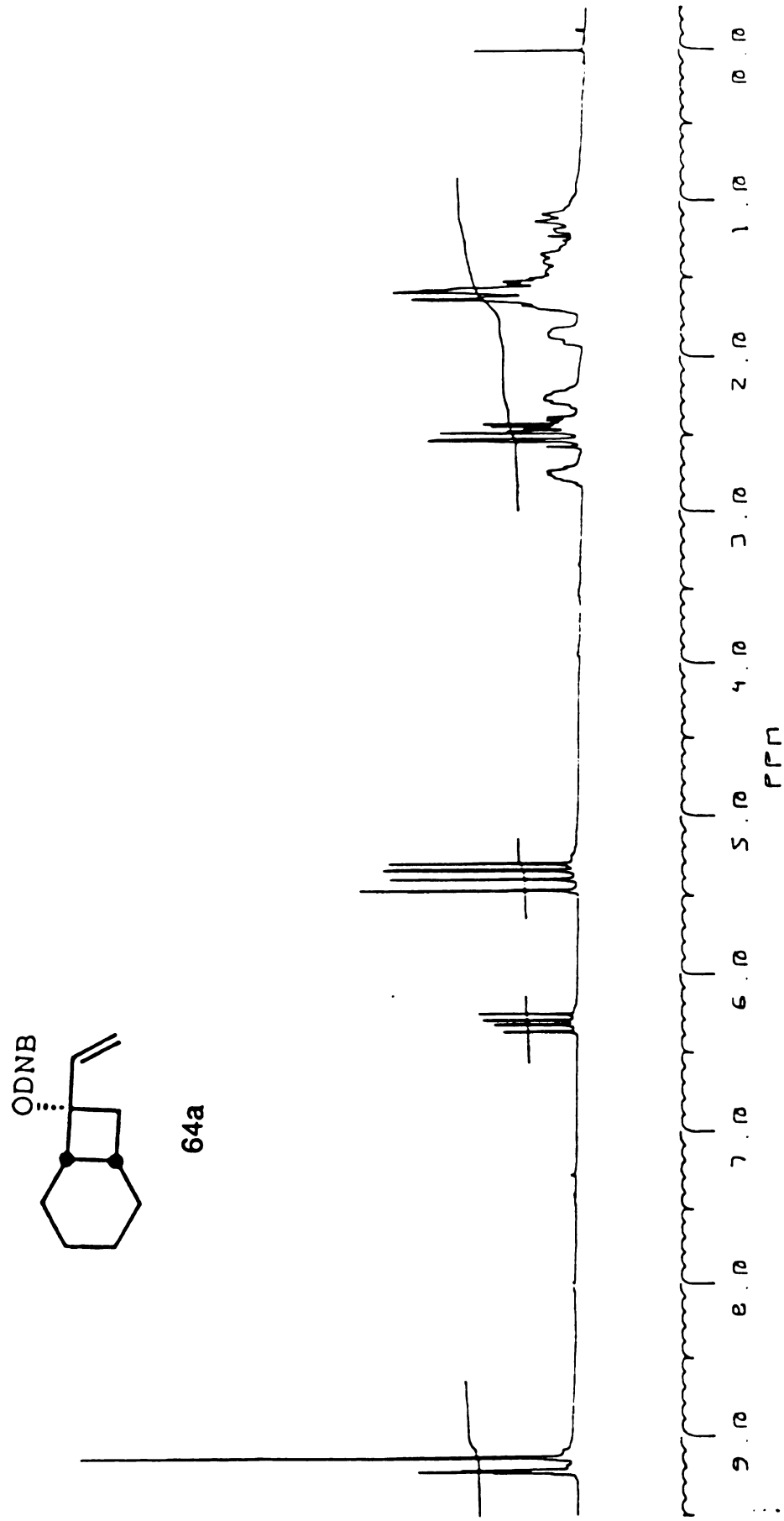


Figure 102. ^{1}H NMR Spectrum of **64a**

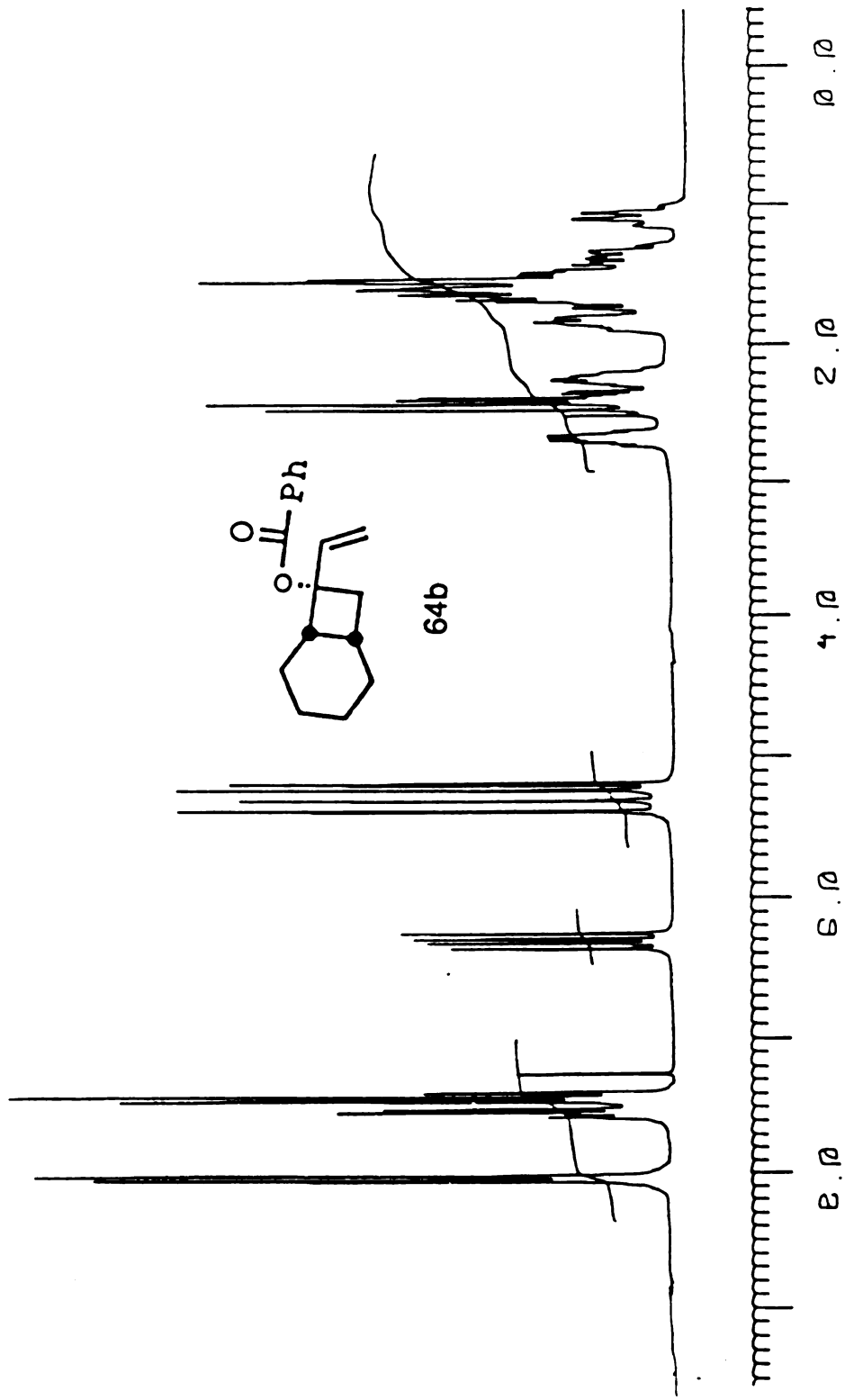


Figure 103. ^{1}H NMR Spectrum of **64b**

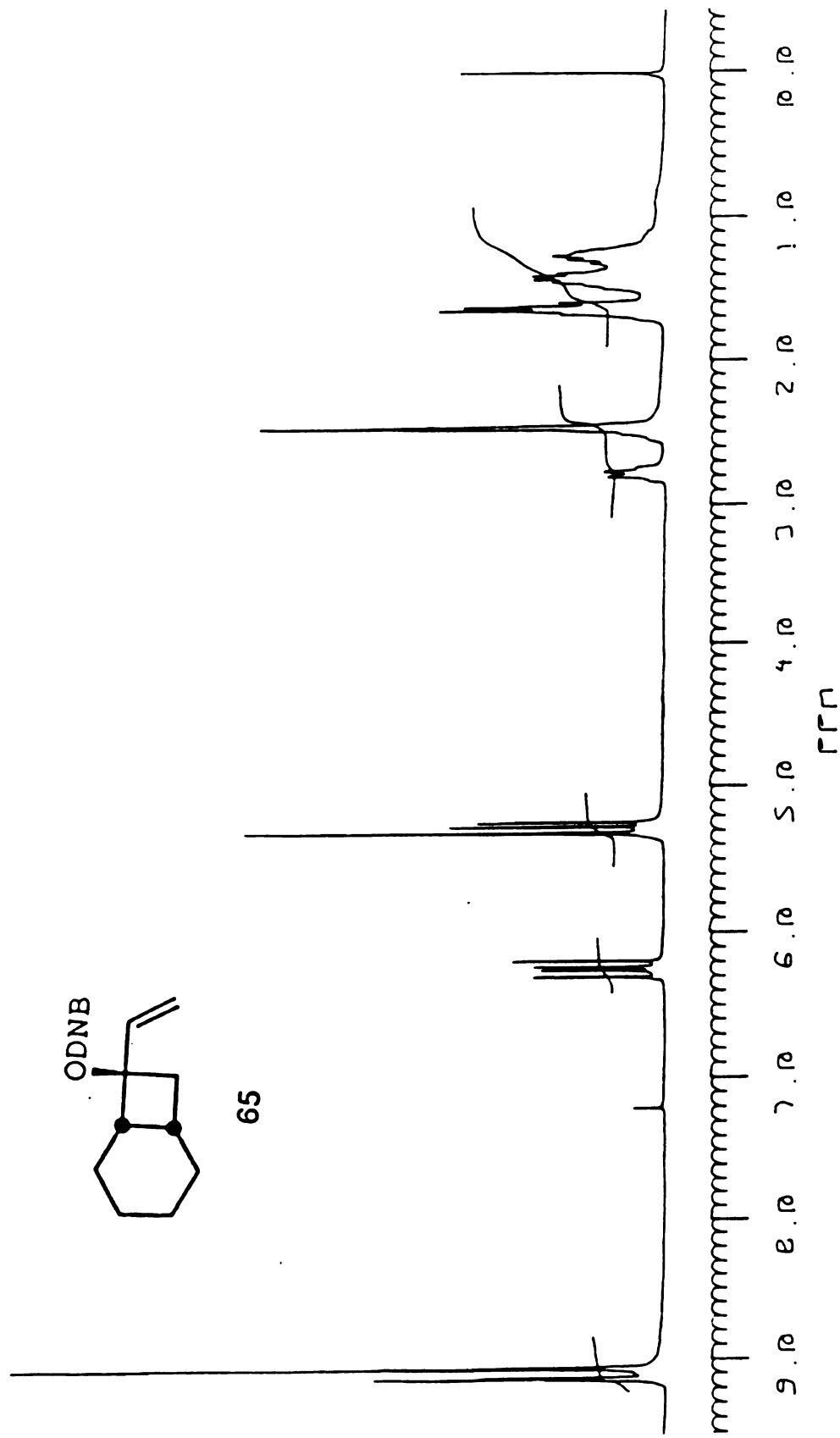


Figure 104. ^{1}H NMR Spectrum of **65**

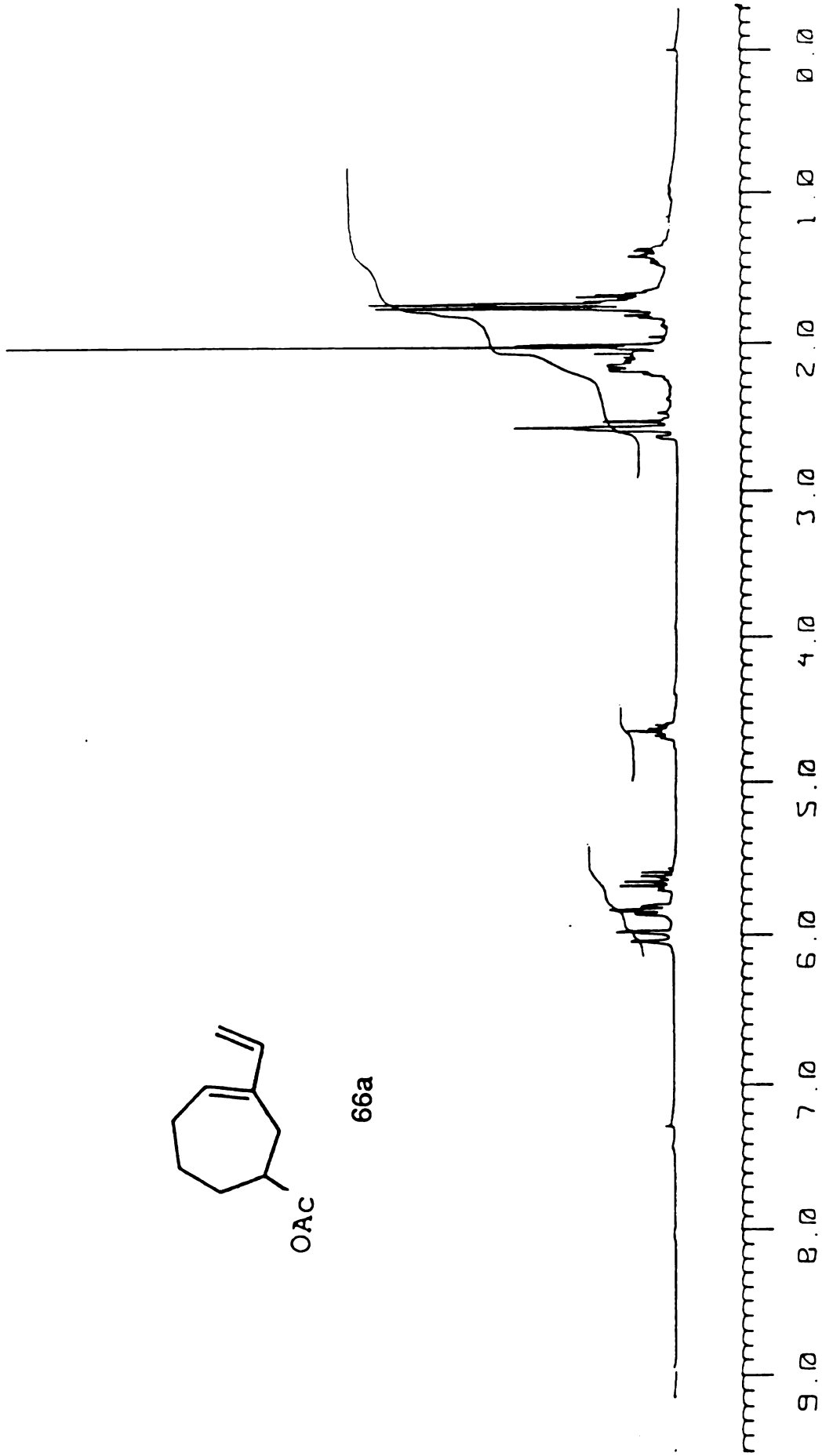


Figure 105. ^{1}H NMR Spectrum of **66a**

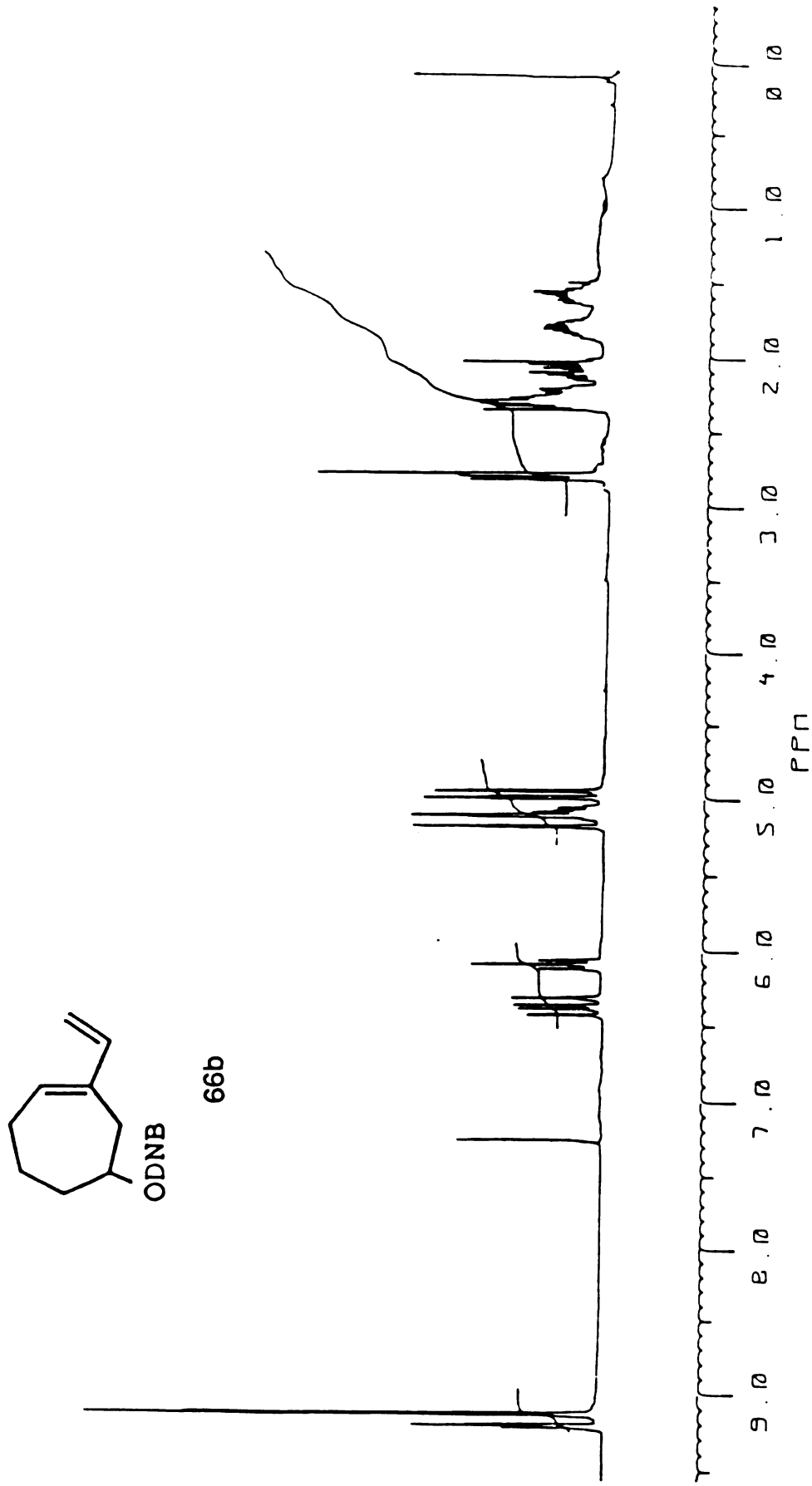


Figure 106. ^{1}H NMR Spectrum of **66b**

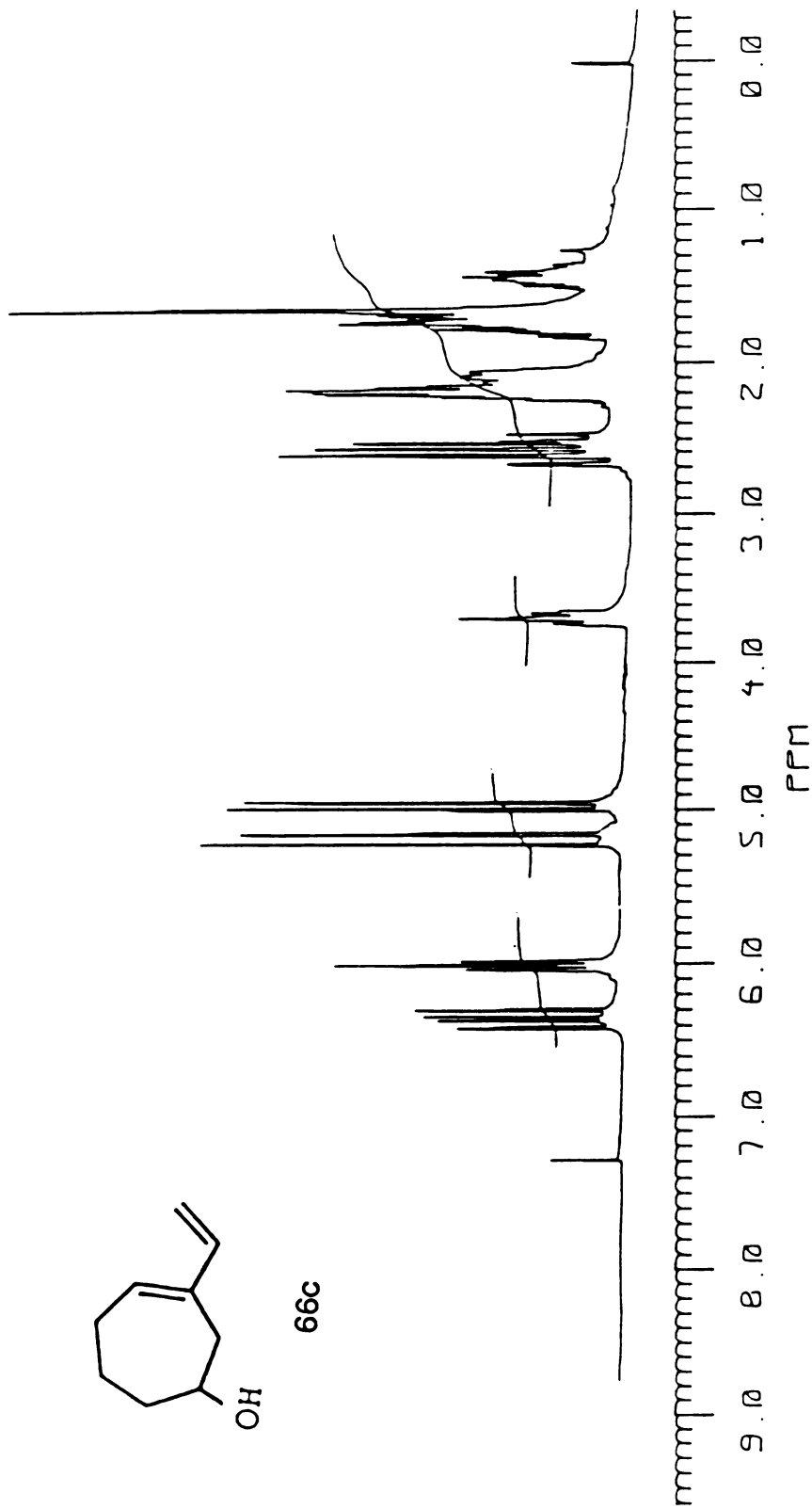


Figure 107. ^{1}H NMR Spectrum of **66c**

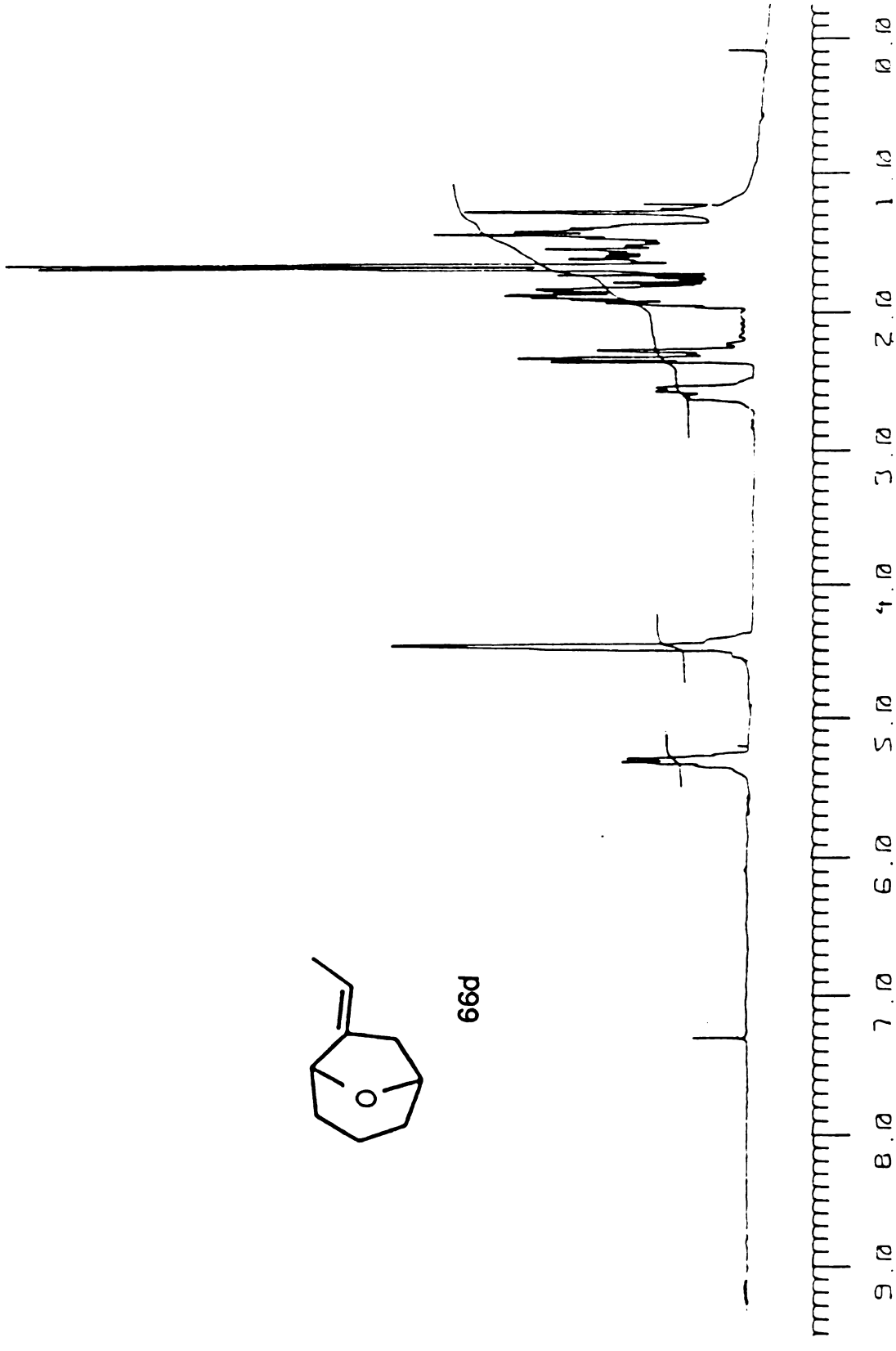


Figure 108. ^{1}H NMR Spectrum of **66d**

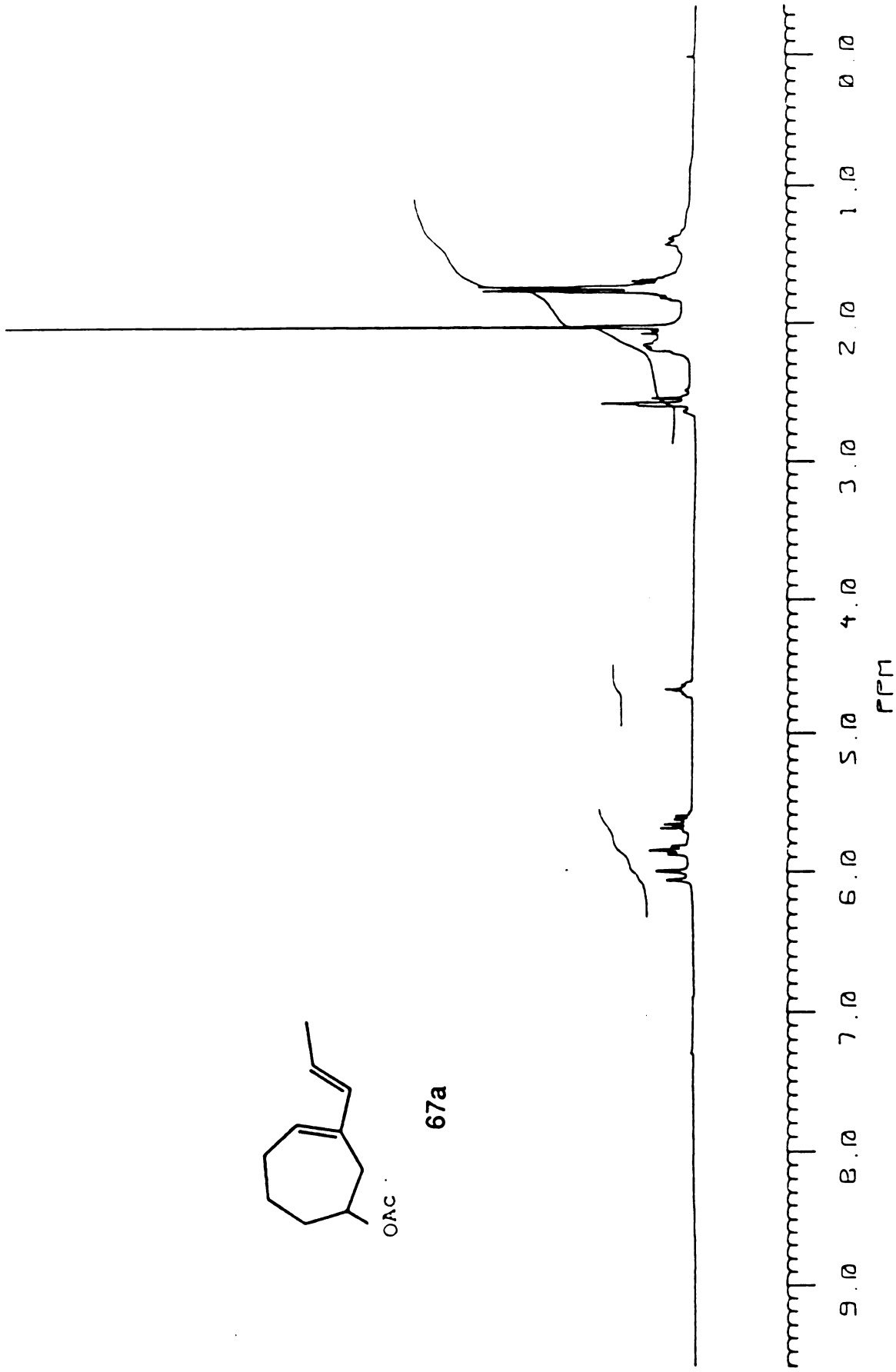


Figure 109. ^{1}H NMR Spectrum of **67a**

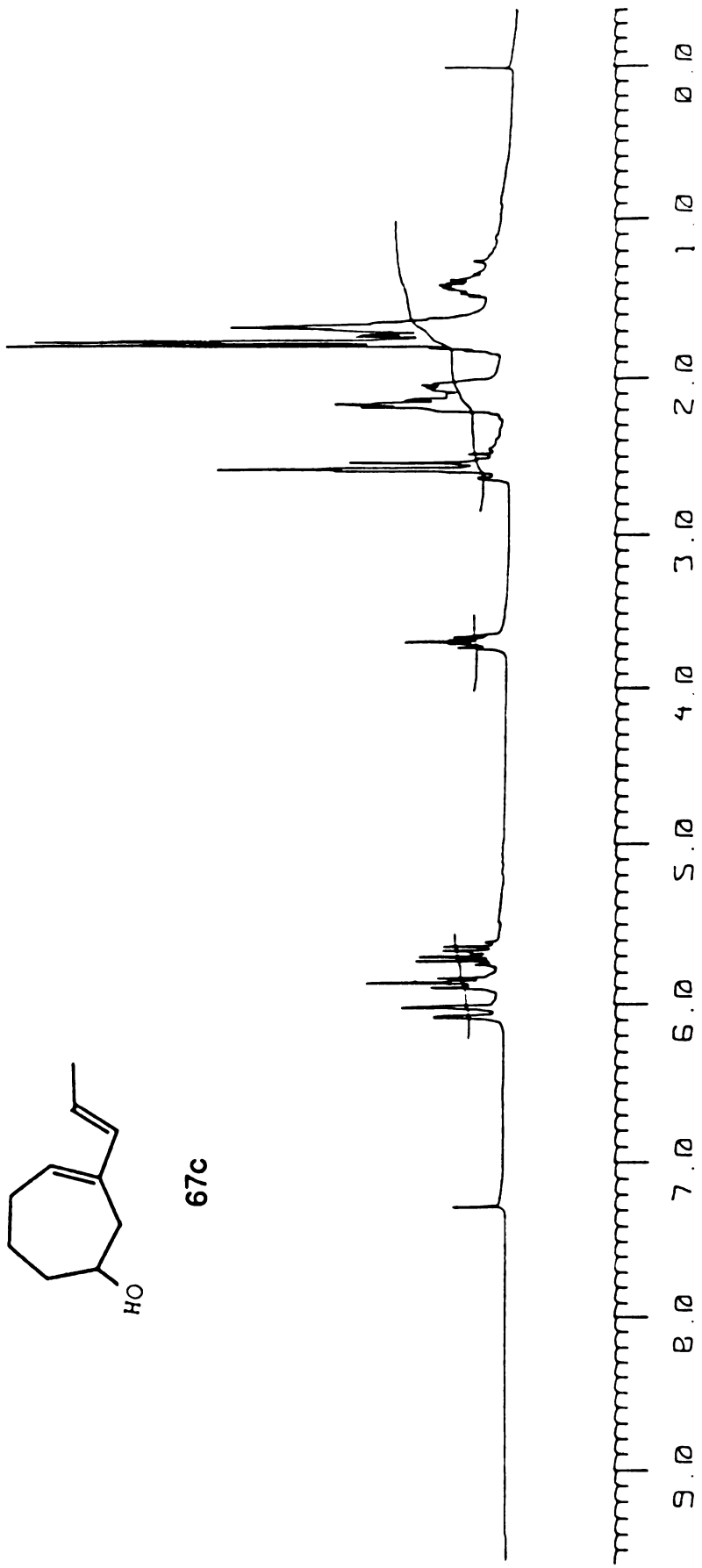


Figure 110. ^{1}H NMR Spectrum of **67c**

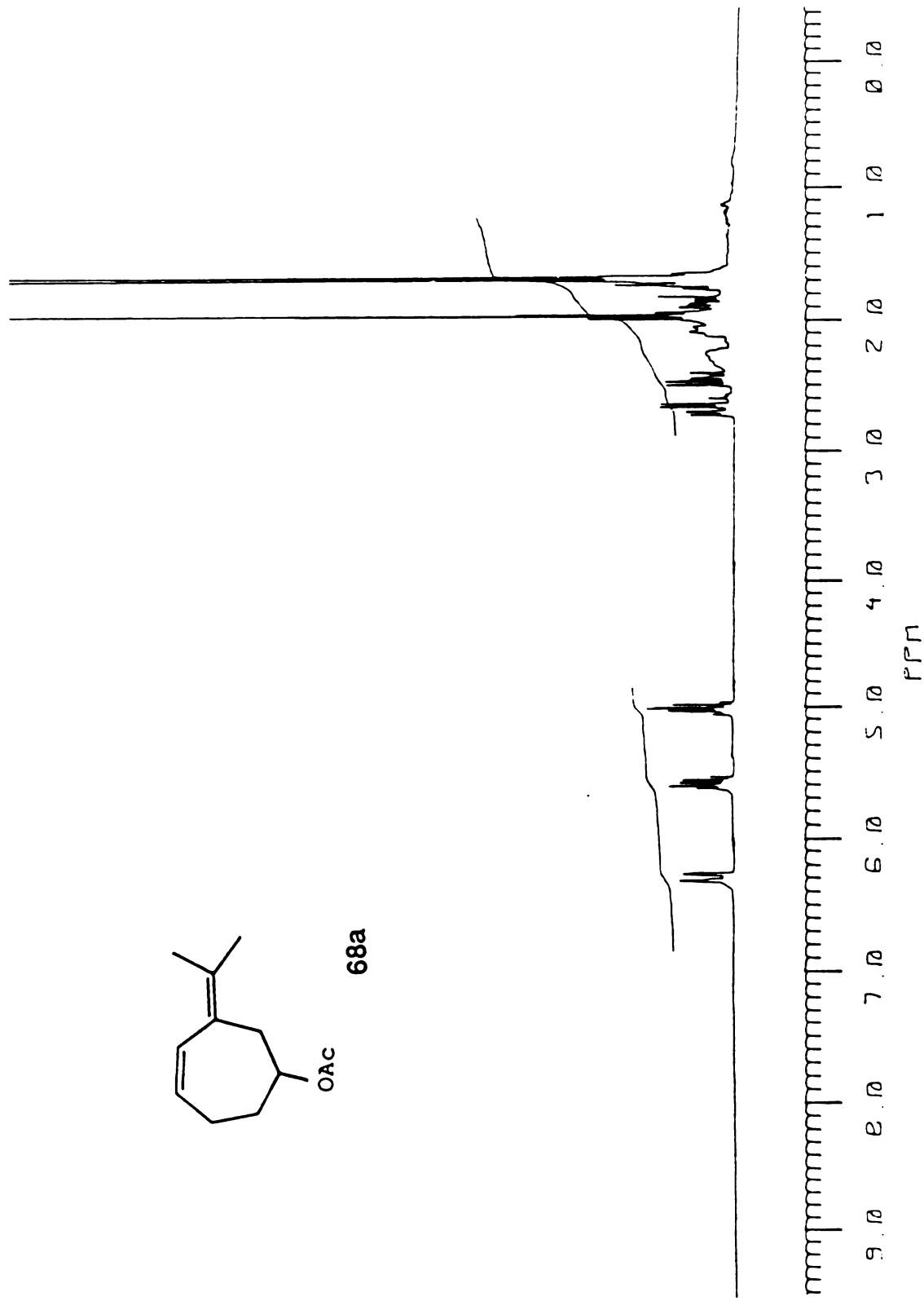


Figure 111. ^{1}H NMR Spectrum of **68a**

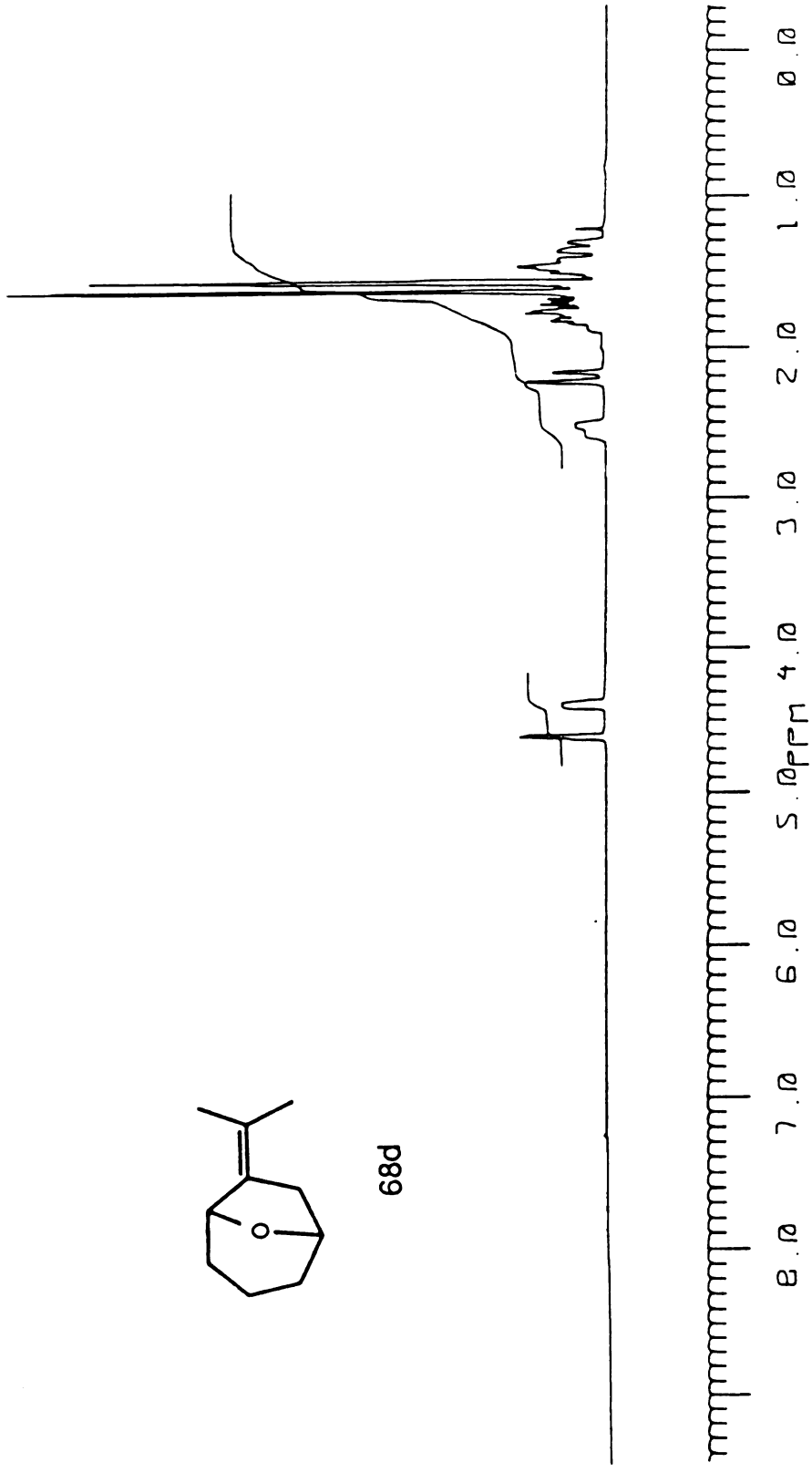


Figure 112. ^{1}H NMR Spectrum of **68d**

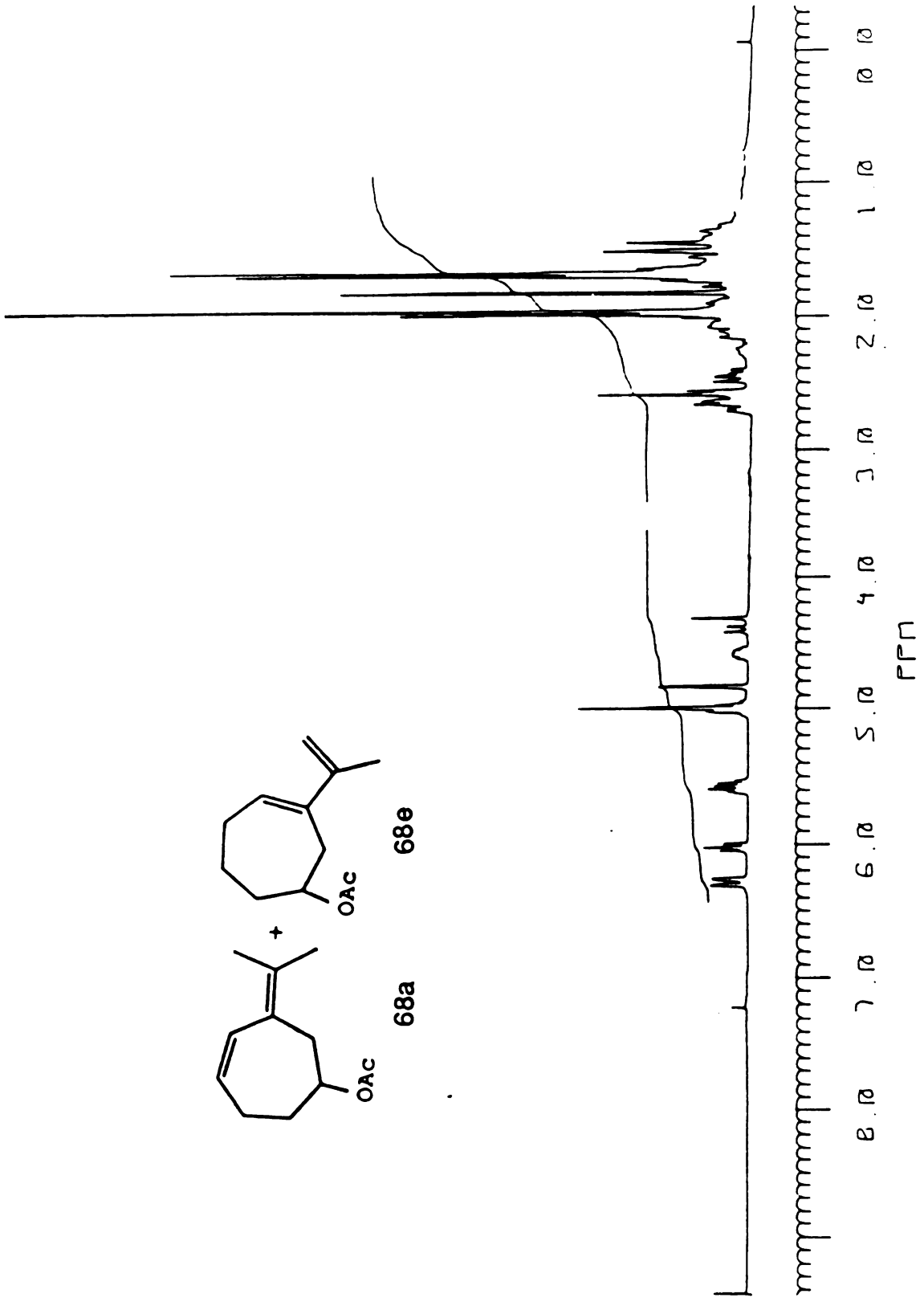


Figure 113. ^{1}H NMR Spectrum of **68a + 68e**

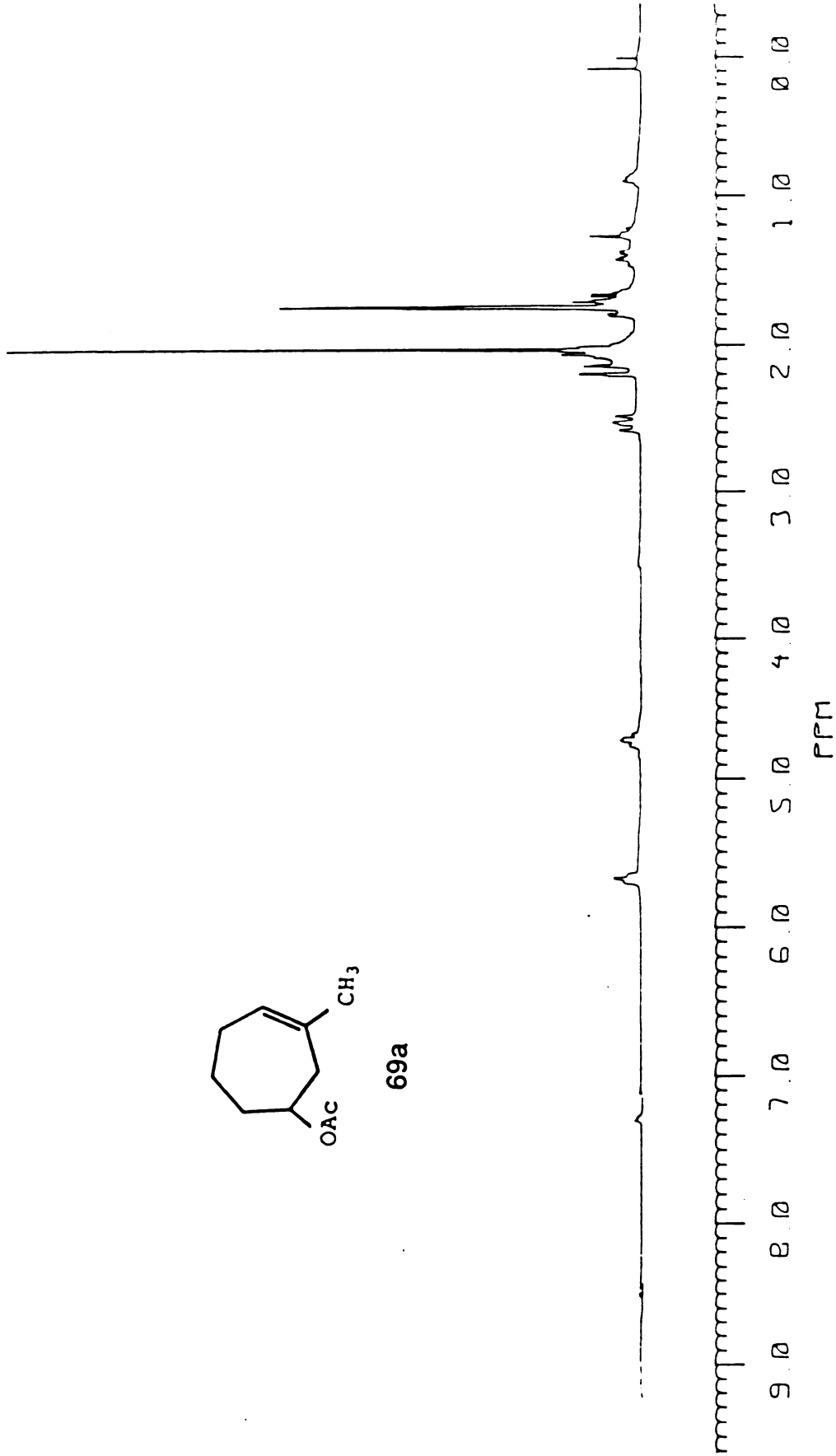


Figure 114. ^{1}H NMR Spectrum of **69a**

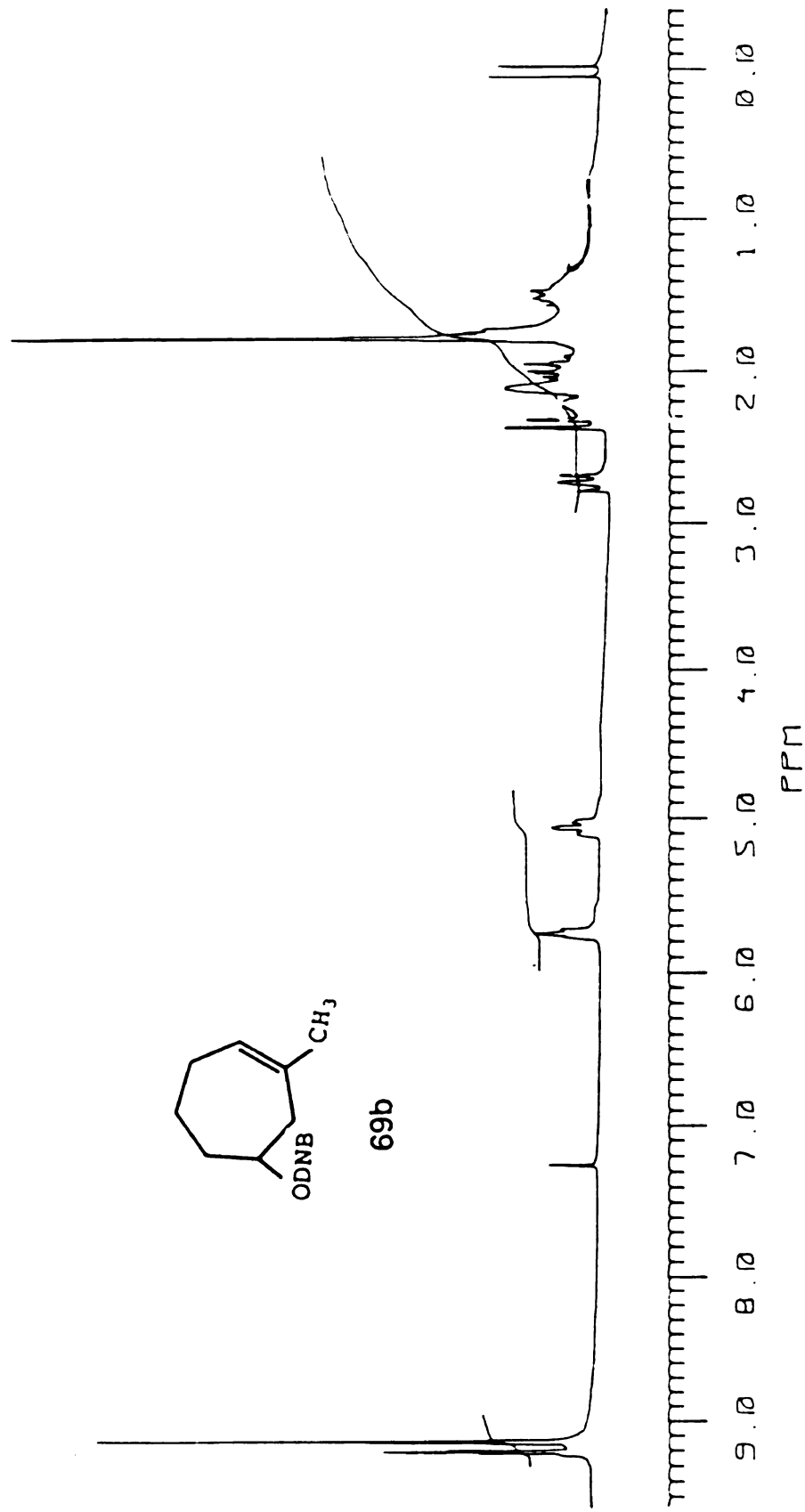


Figure 115. ^{1}H NMR Spectrum of **69b**

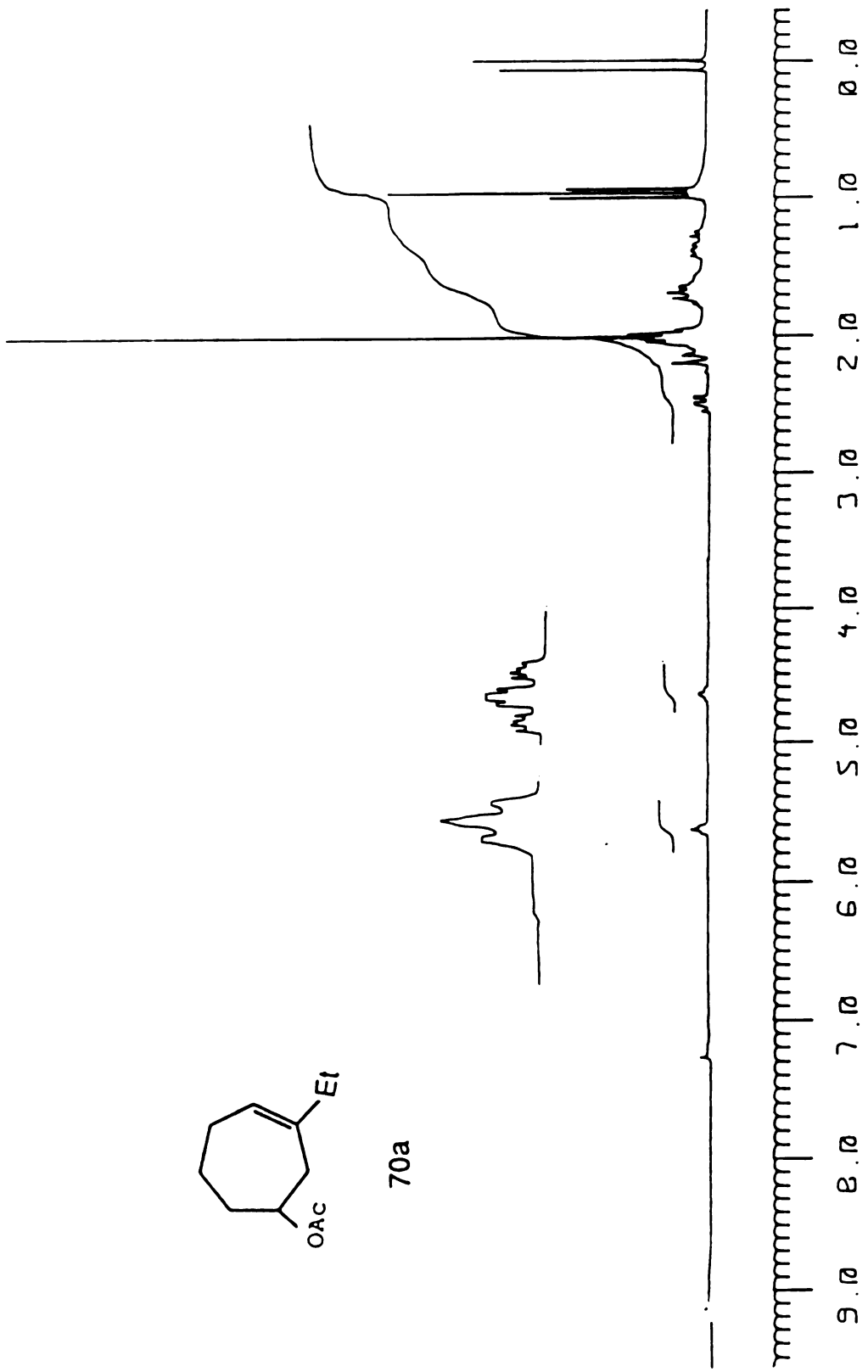


Figure 116. ^{1}H NMR Spectrum of **70a**

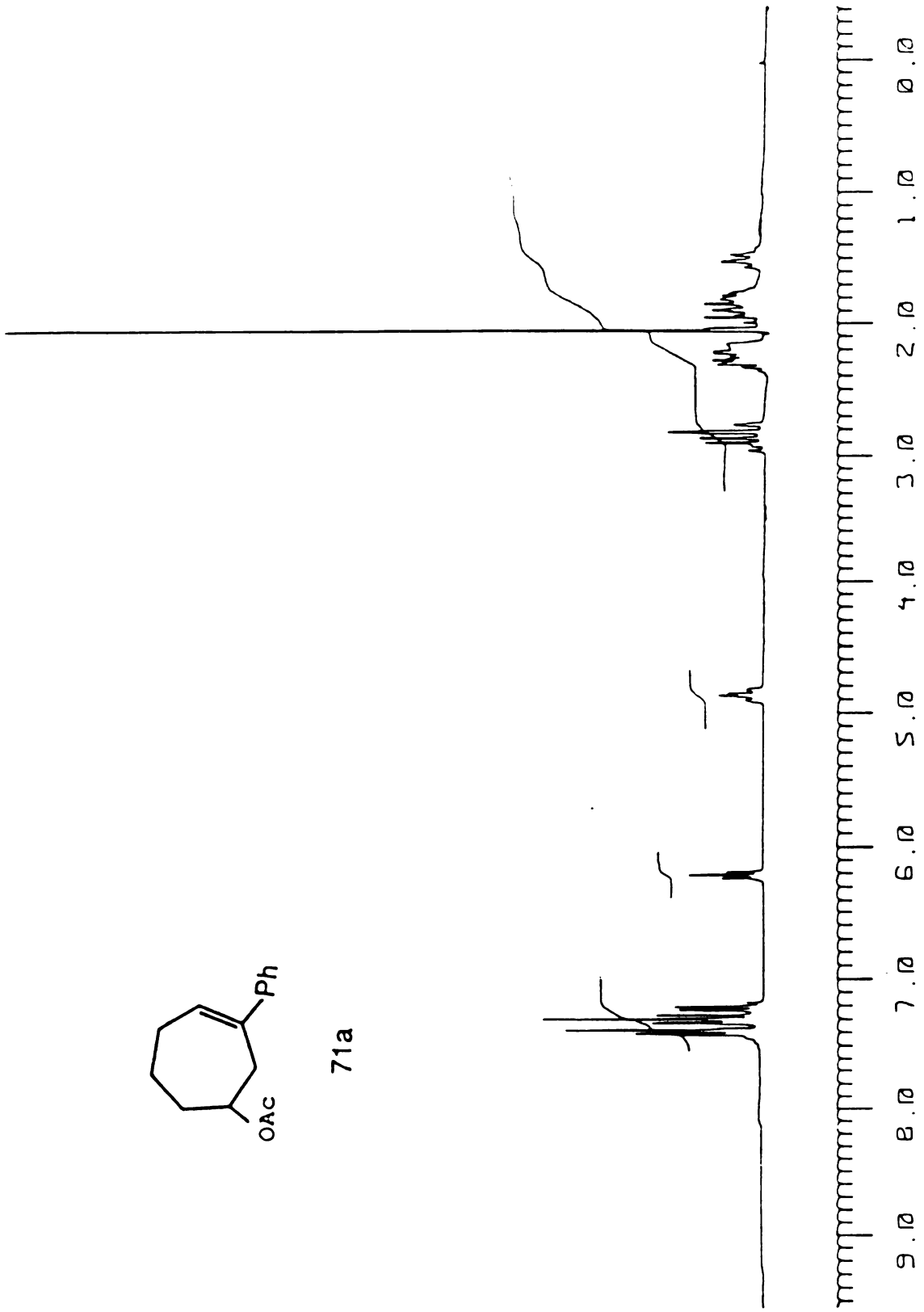


Figure 117. ^{1}H **NMR Spectrum of 71a**

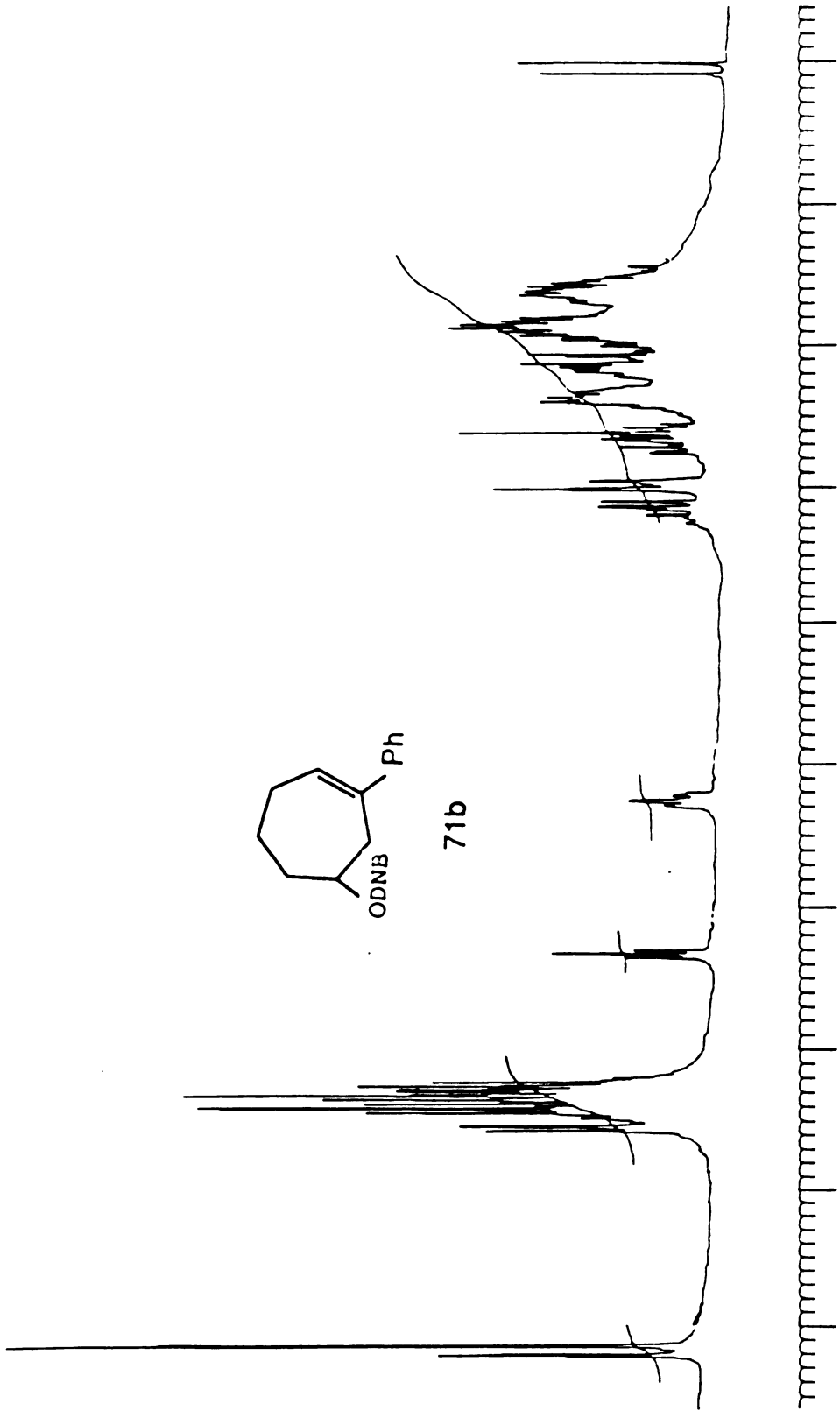


Figure 118. ^{1}H NMR Spectrum of **71b**

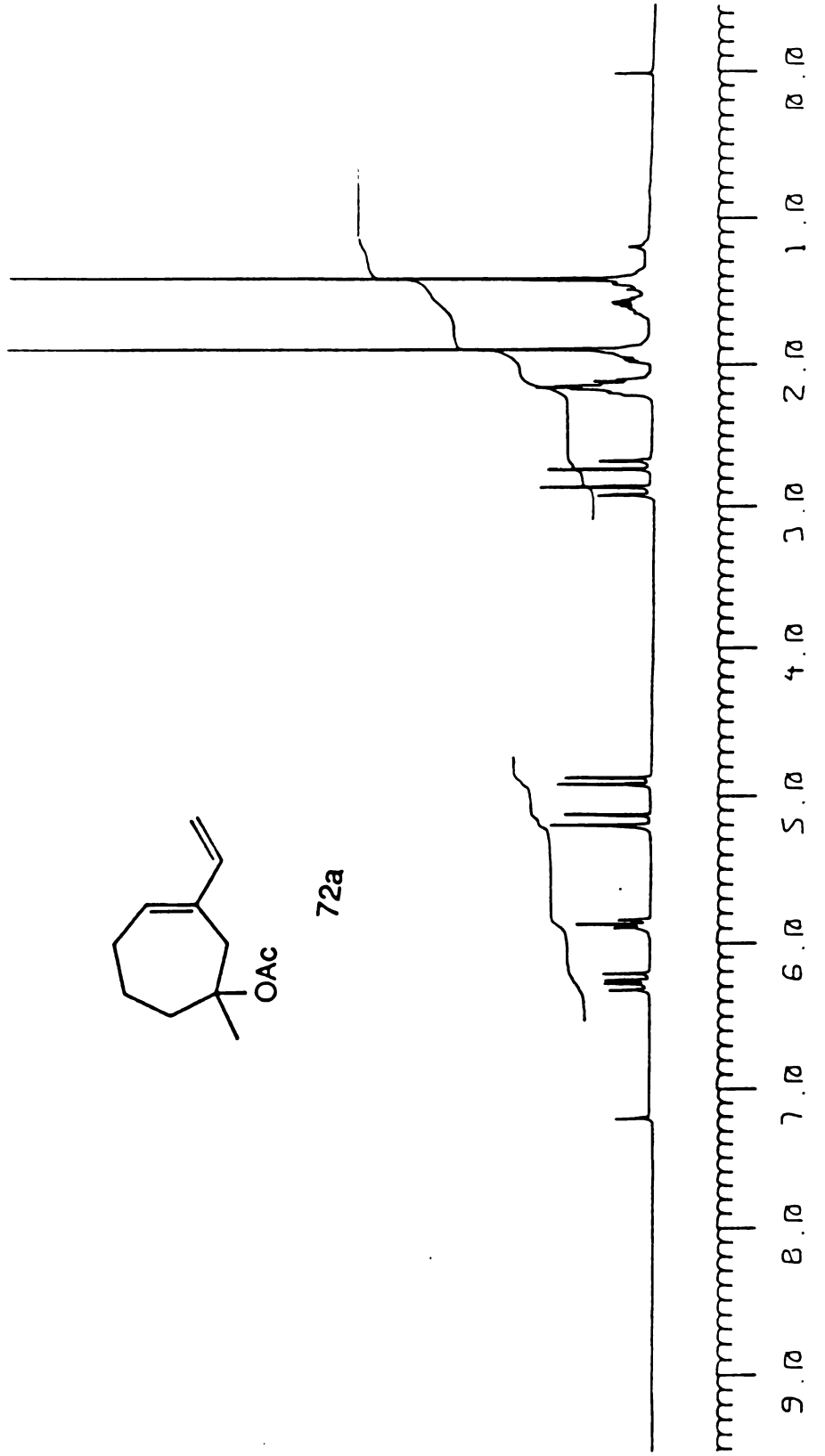


Figure 119. ^{1}H NMR Spectrum of **72a**

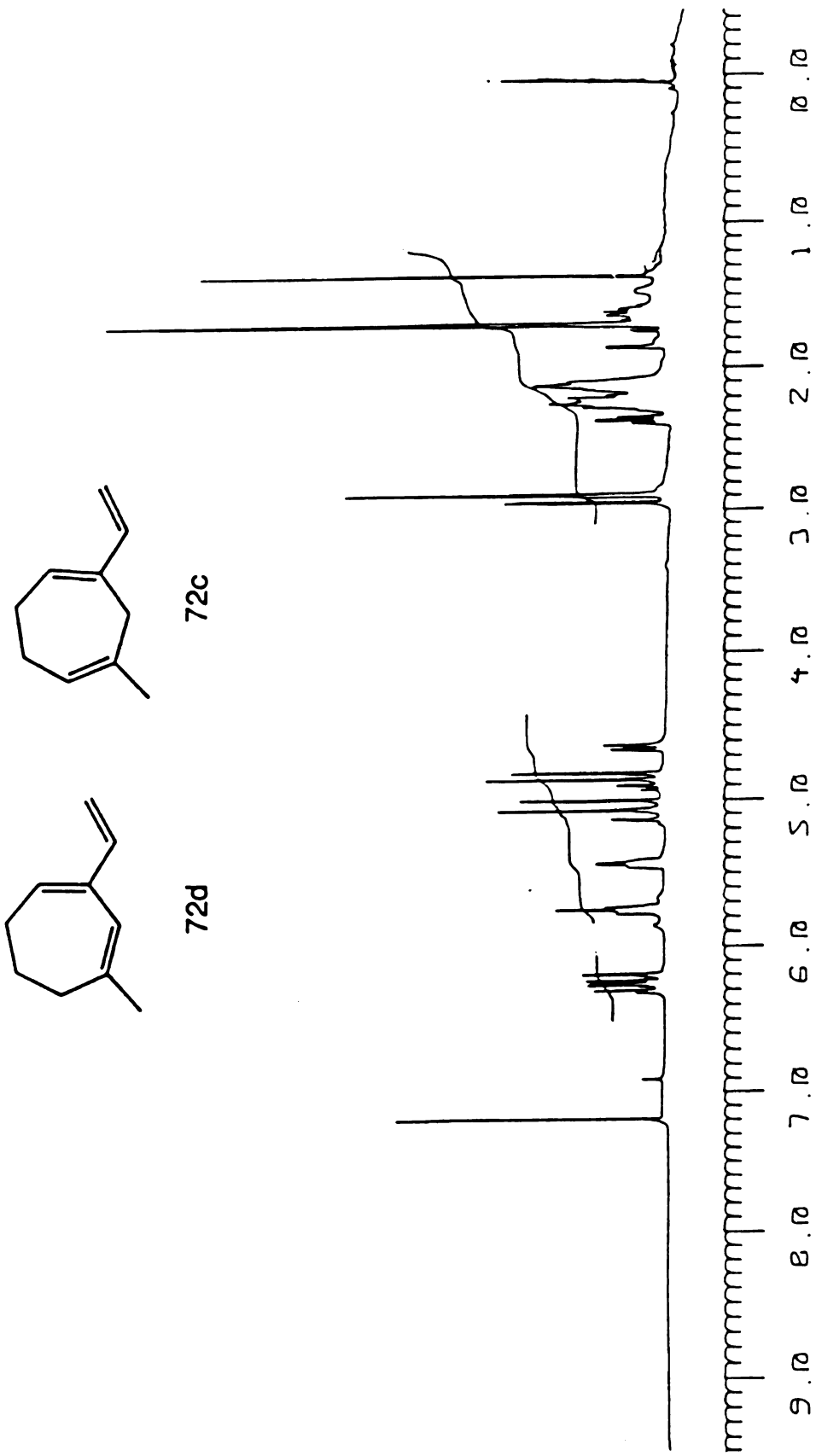


Figure 120. ^{1}H NMR Spectrum of **72c** + **73d**

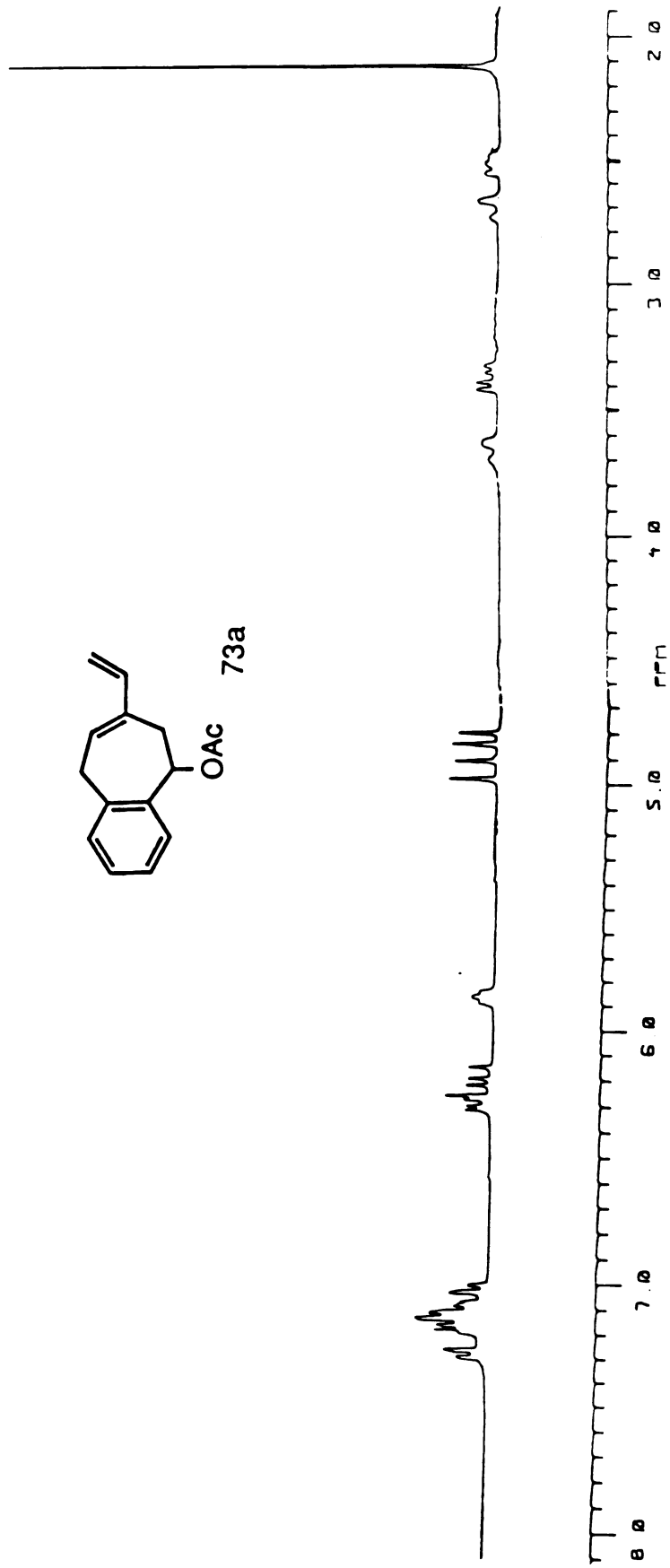
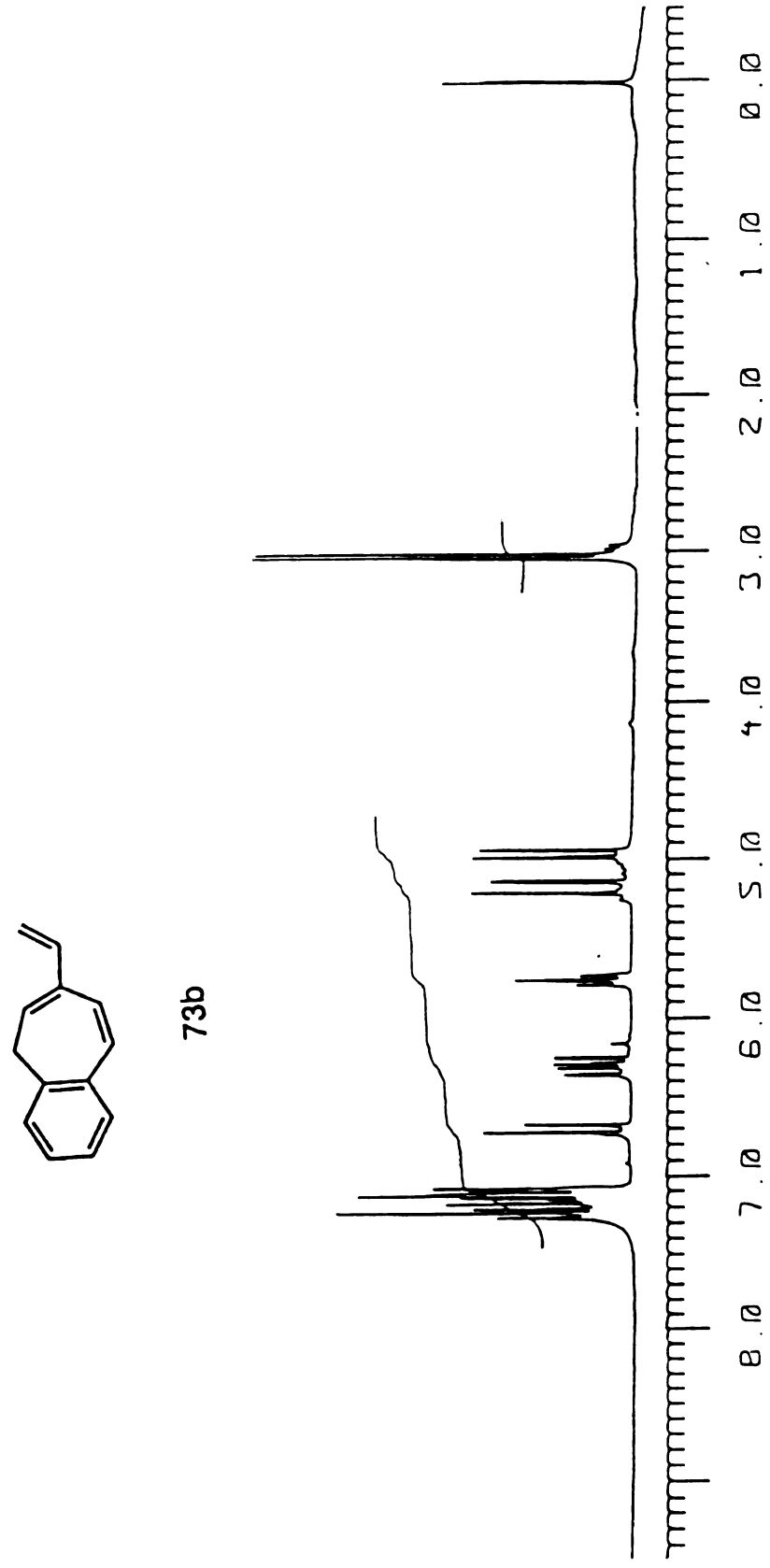


Figure 121. ^{1}H NMR Spectrum of **73a**



73b

Figure 122. ^{1}H NMR Spectrum of **73b**

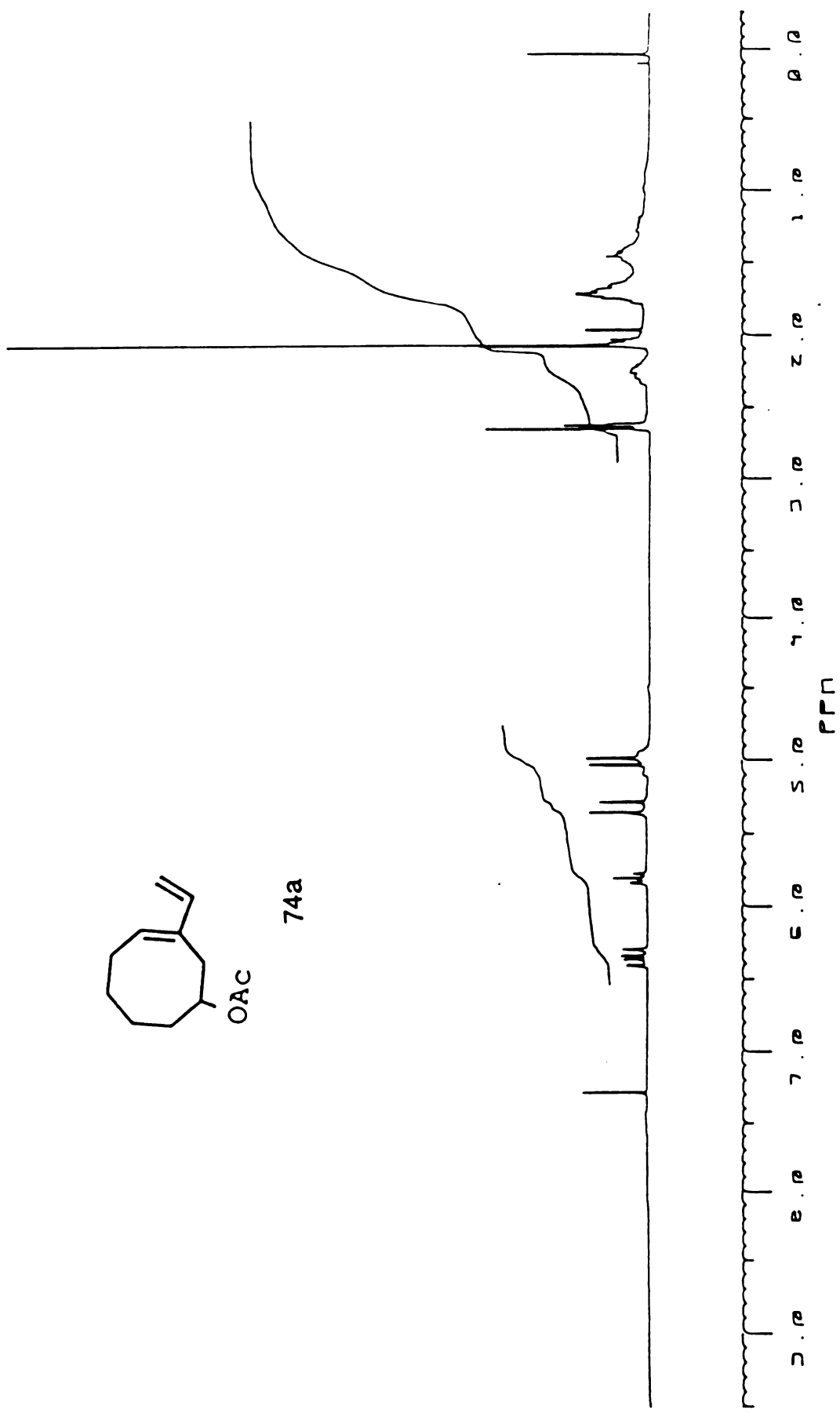


Figure 123. ^{1}H NMR Spectrum of **74a**

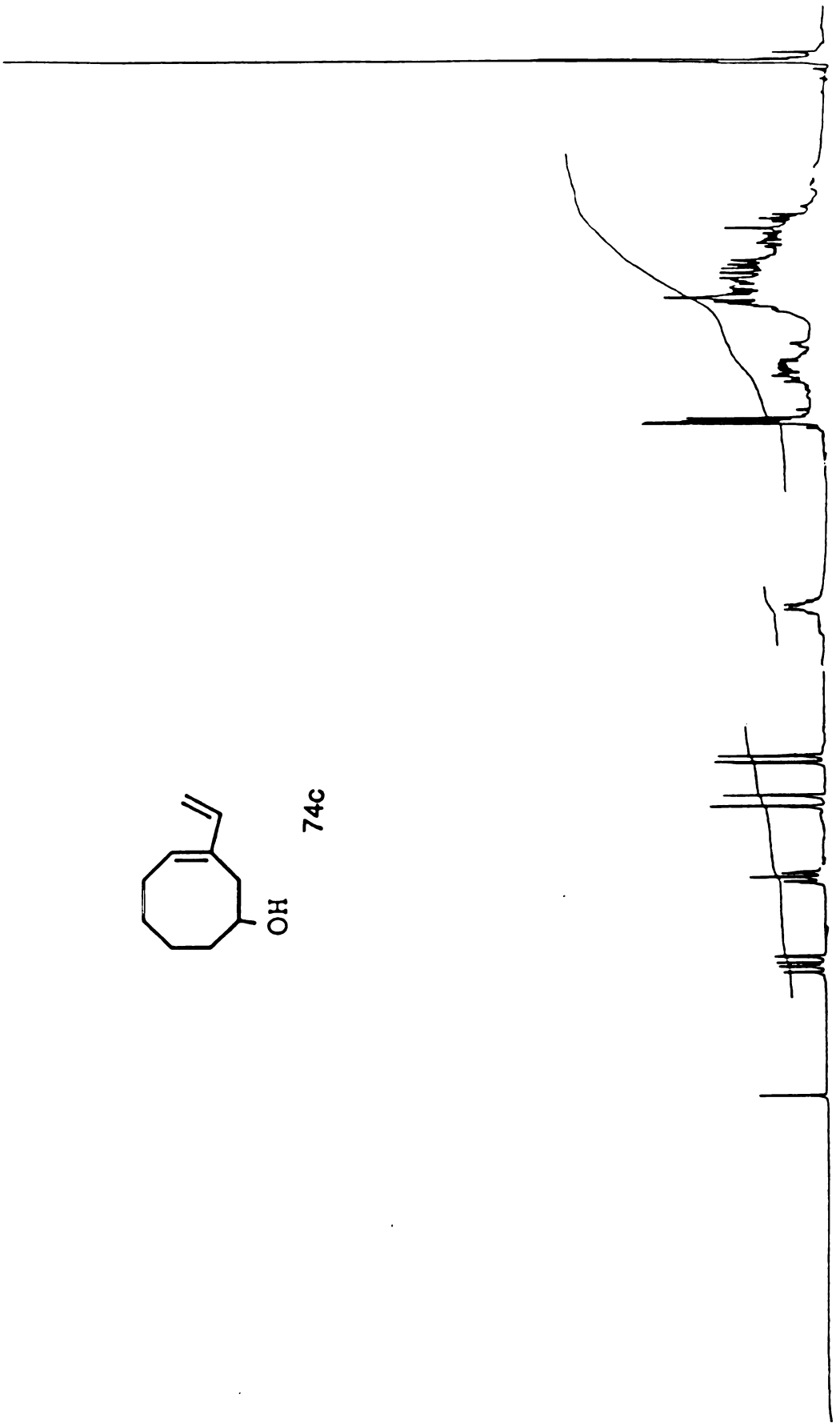


Figure 124. ^{1}H NMR Spectrum of **74c**

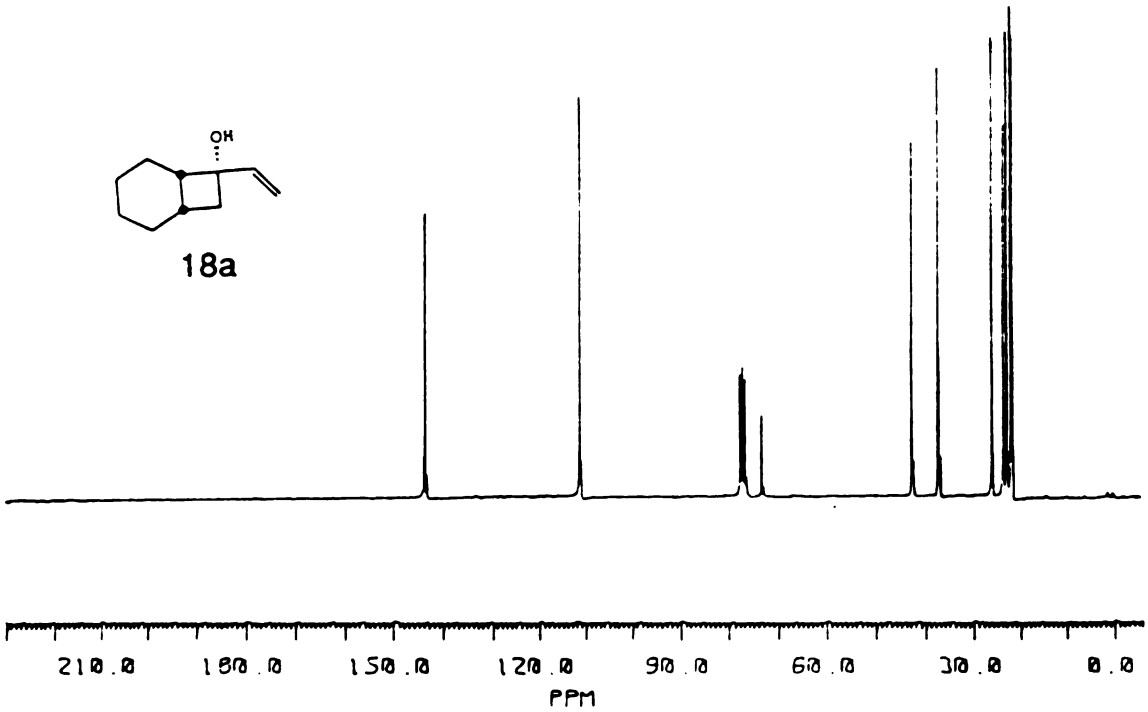


Figure 125. ^{13}C NMR Spectrum of **18a**

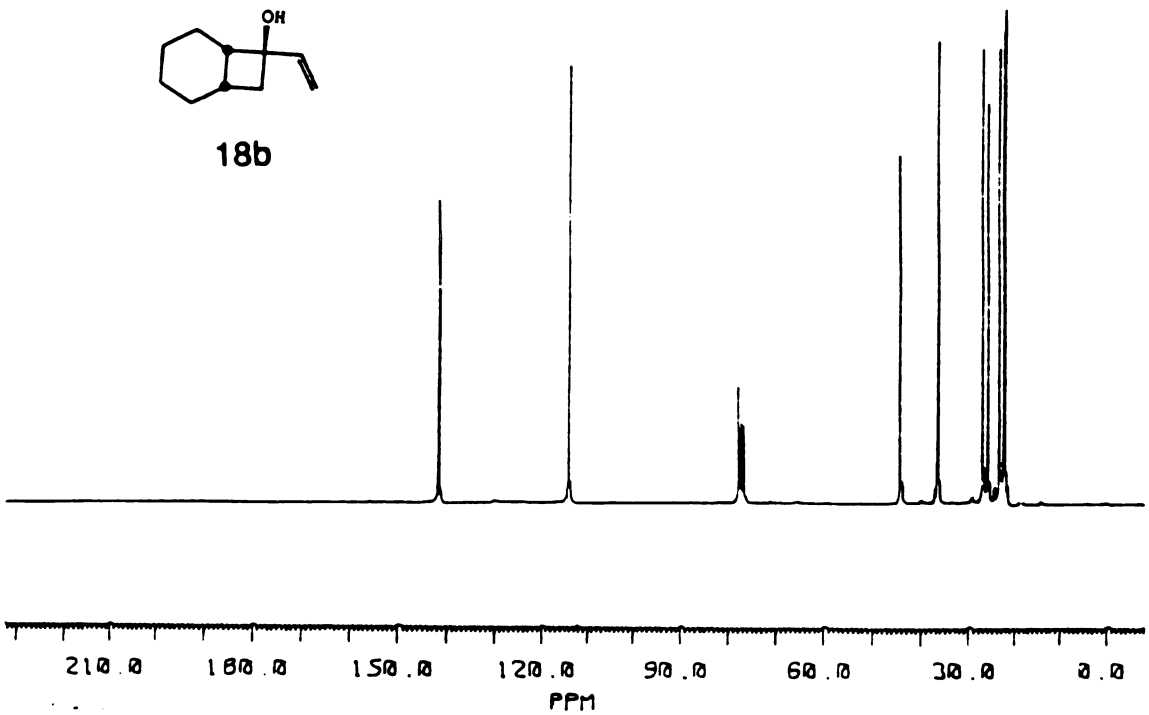


Figure 126. ^{13}C NMR Spectrum of **18b**

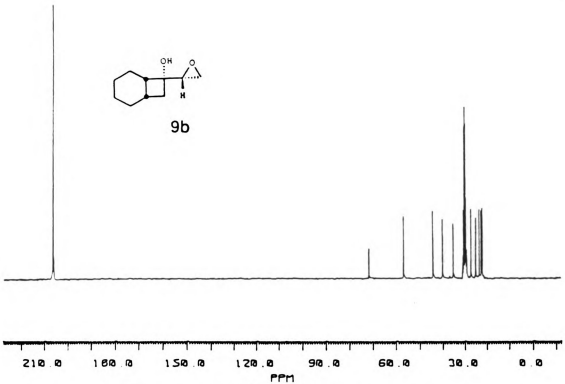


Figure 128. ^{13}C NMR Spectrum of **9b**

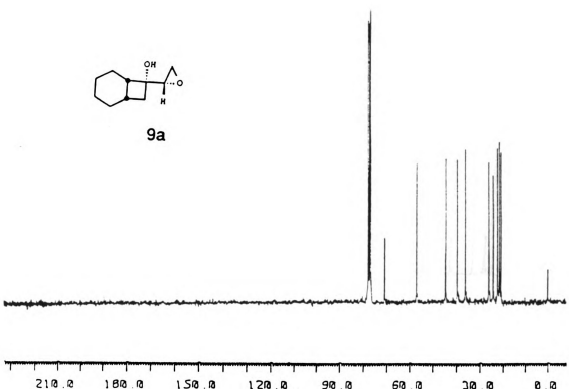
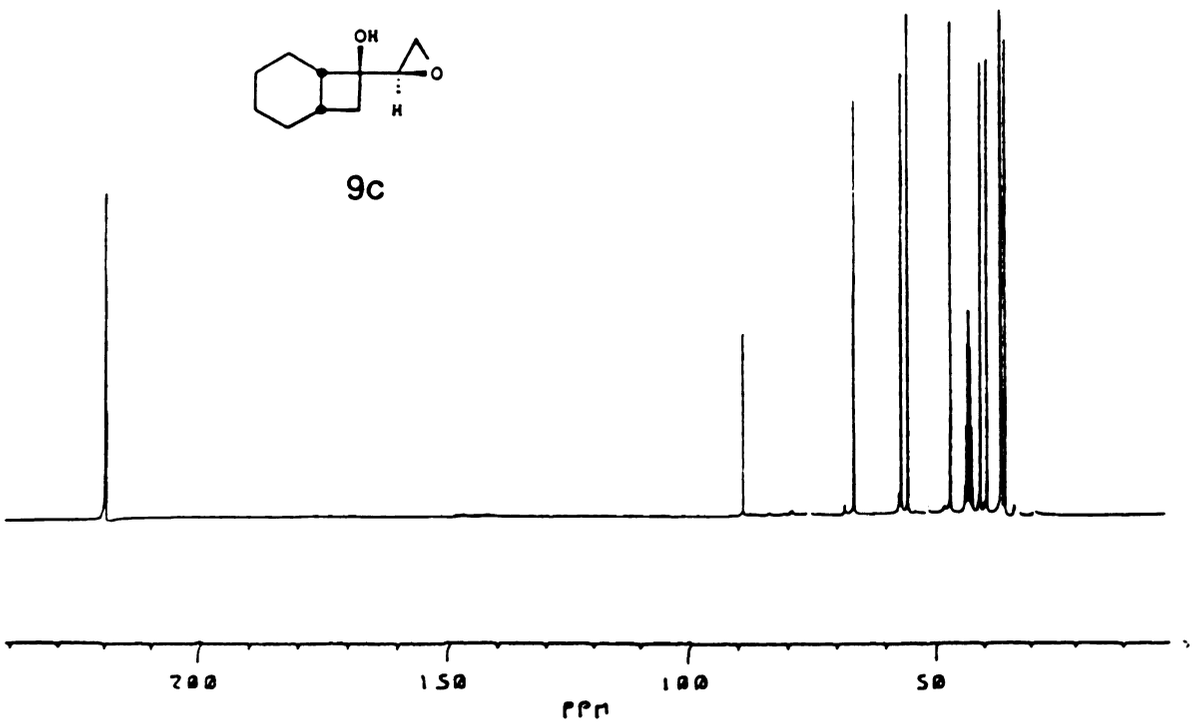
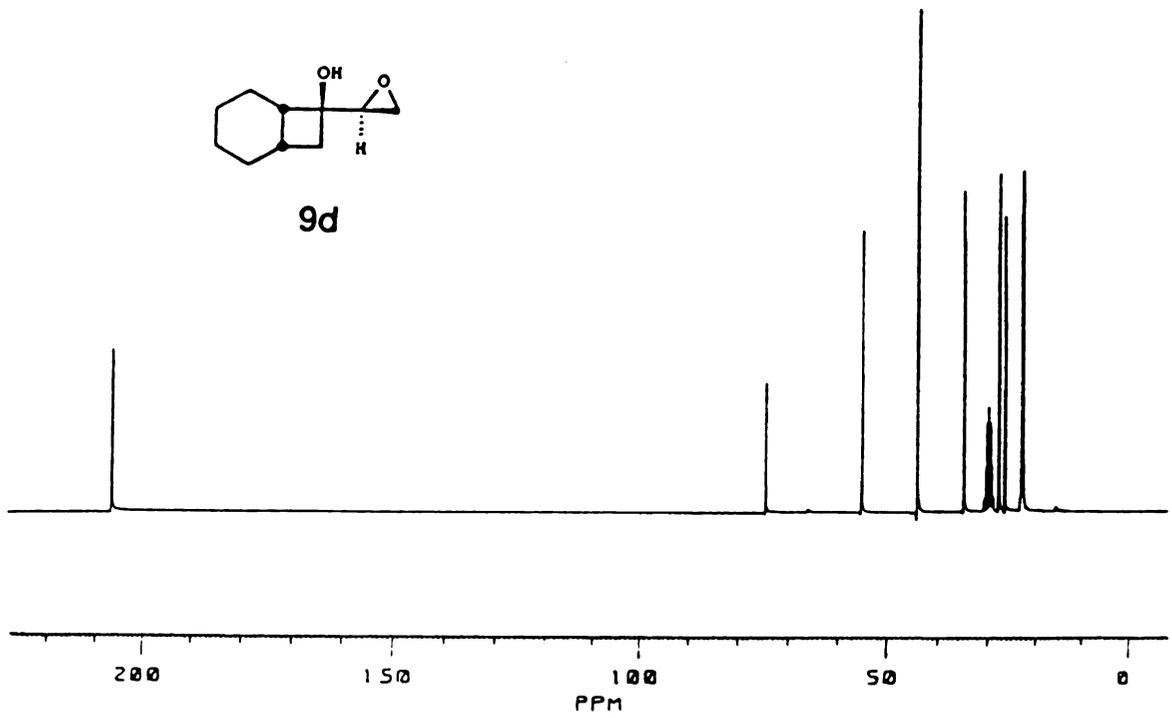


Figure 127. ^{13}C NMR Spectrum of **9a**



9c

Figure 129. ^{13}C NMR Spectrum of **9c**



9d

Figure 130. ^{13}C NMR Spectrum of **9d**

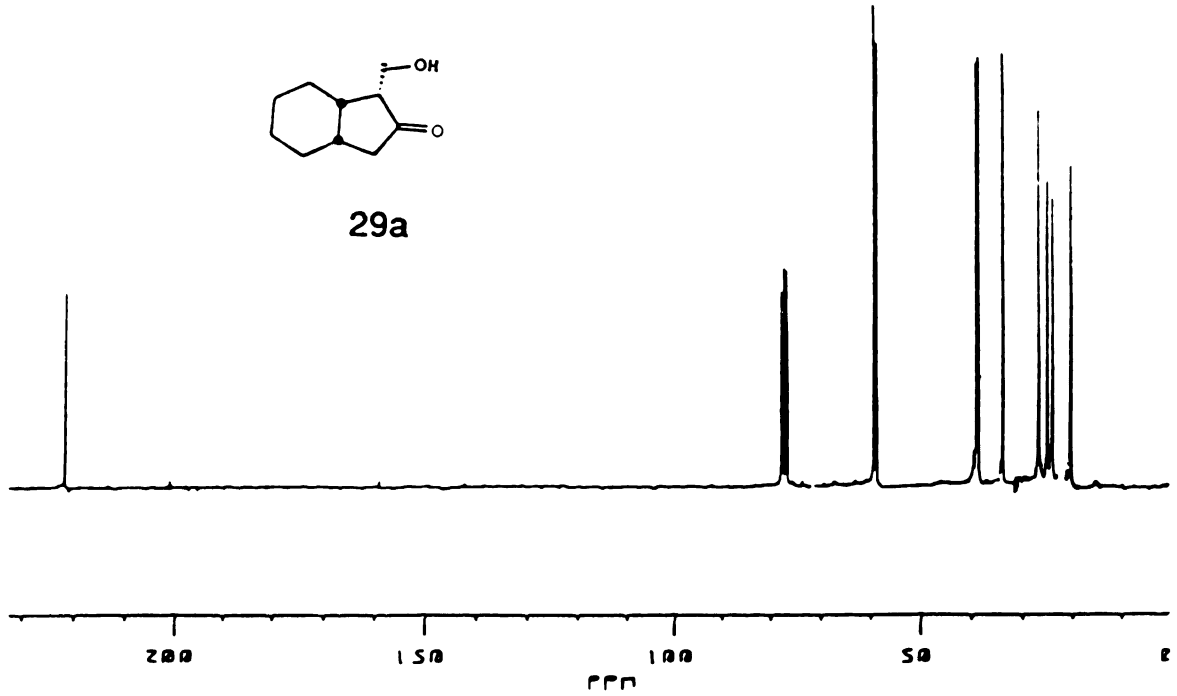


Figure 131. ^{13}C NMR Spectrum of **29a**

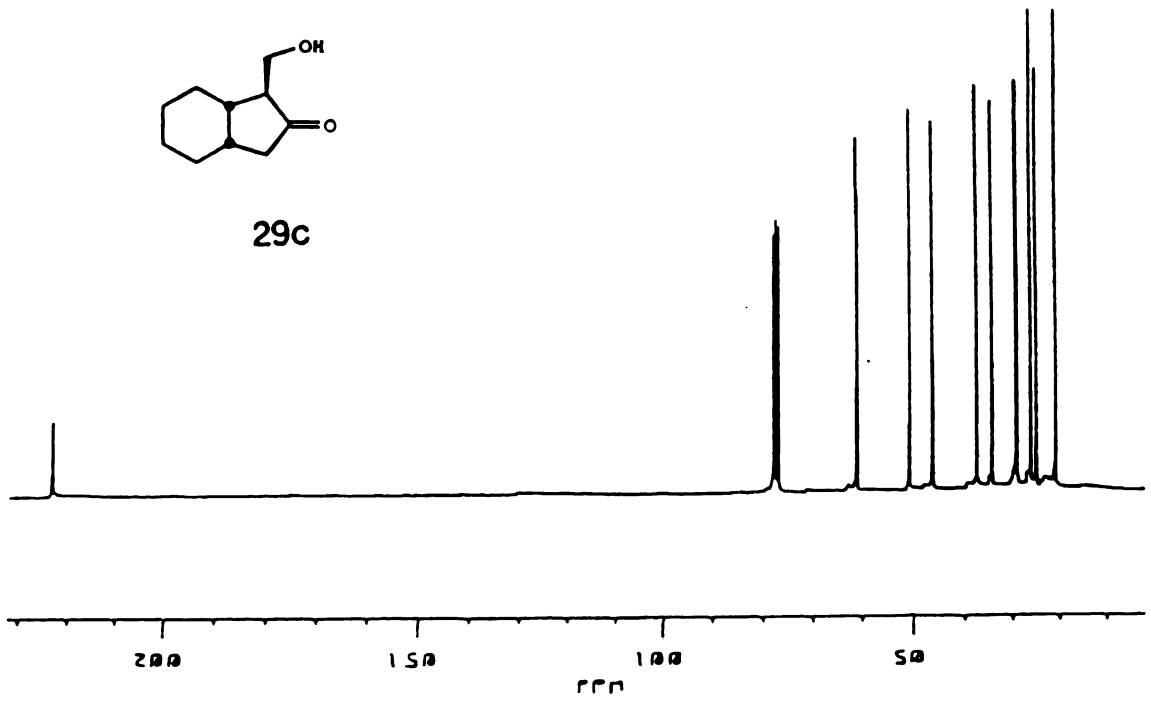
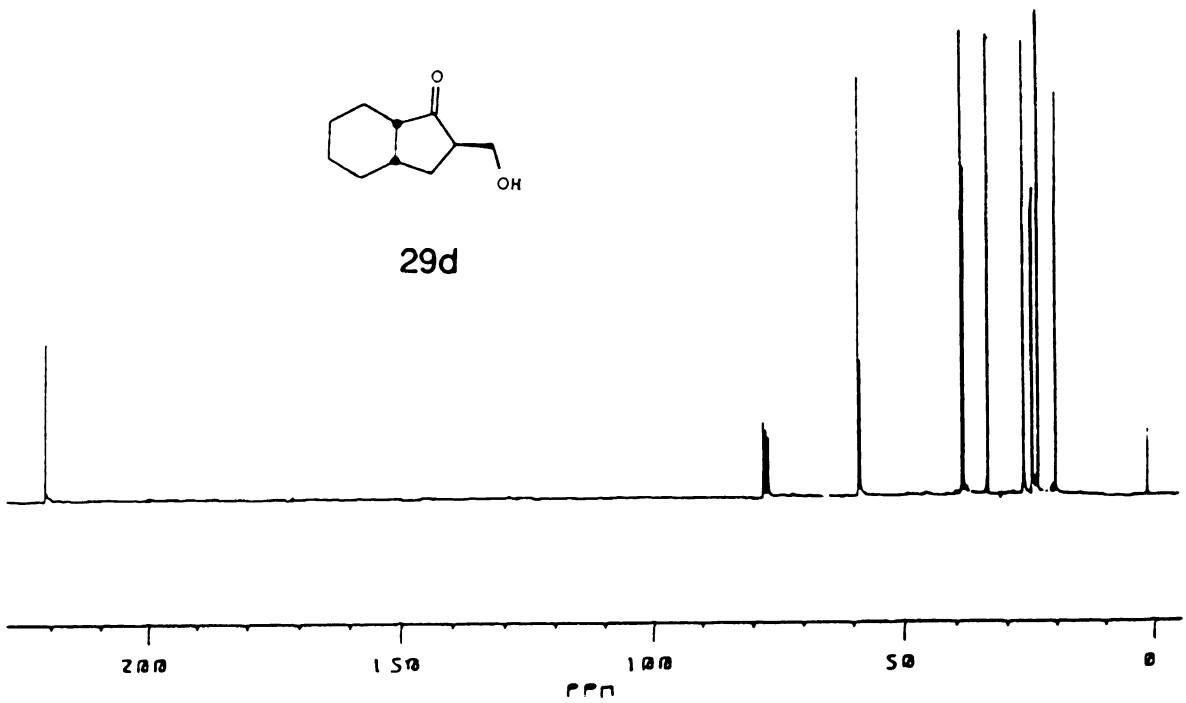
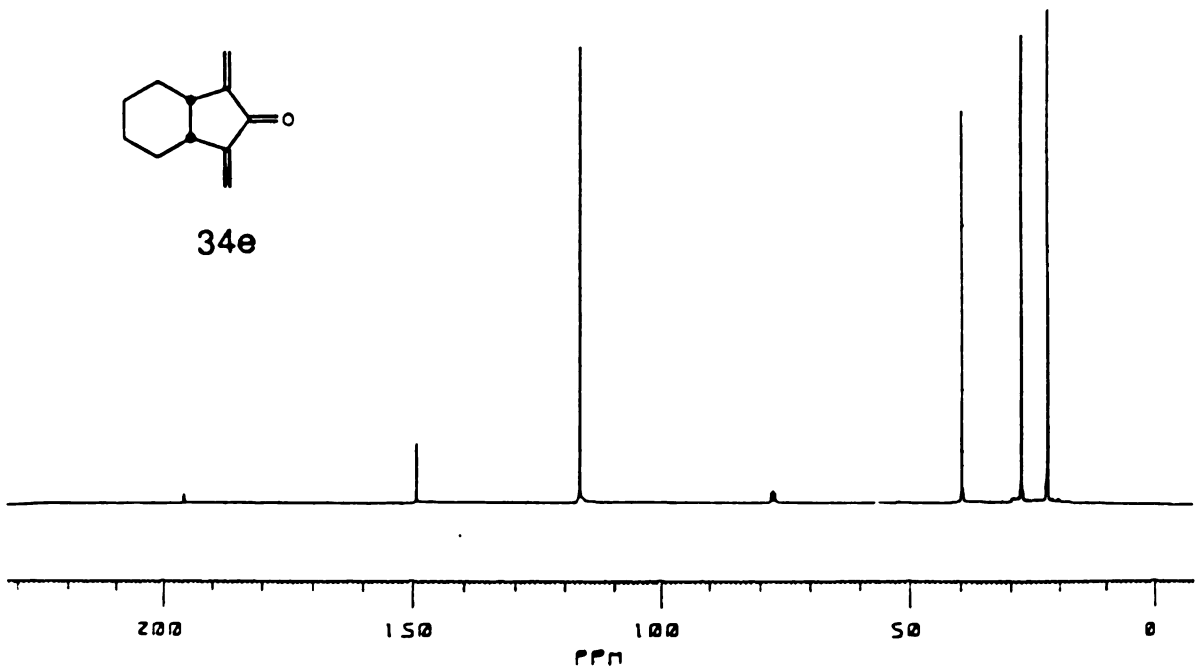


Figure 132. ^{13}C NMR Spectrum of **29c**



29d

Figure 133. ^{13}C NMR Spectrum of **29d**



34e

Figure 134. ^{13}C NMR Spectrum of **34e**

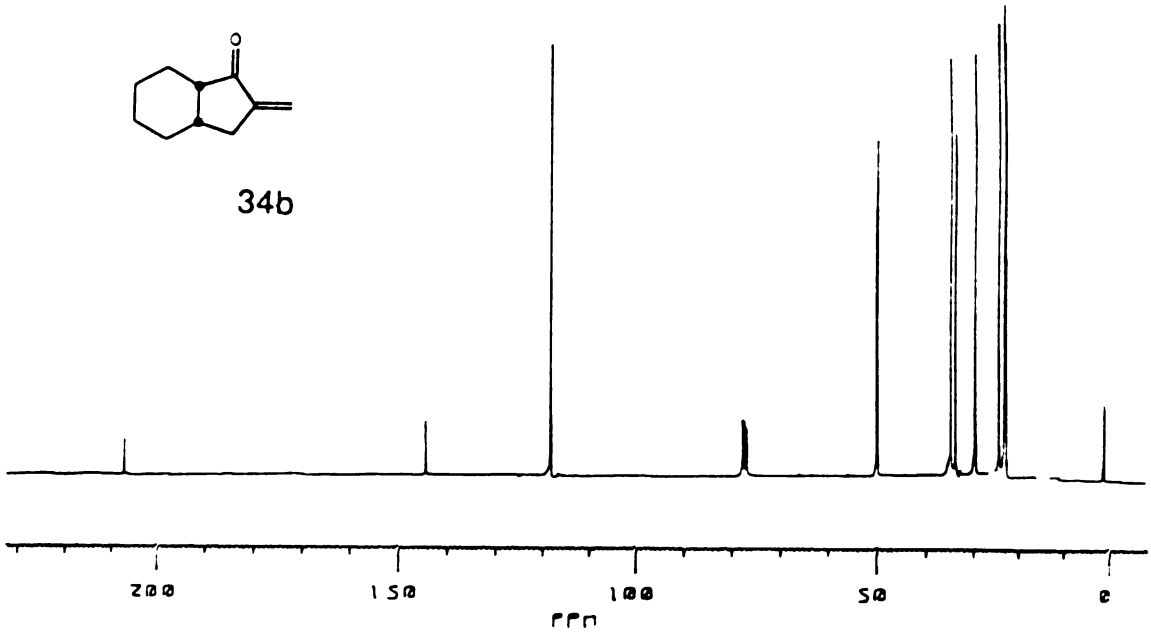


Figure 136. ^{13}C NMR Spectrum of **34b**

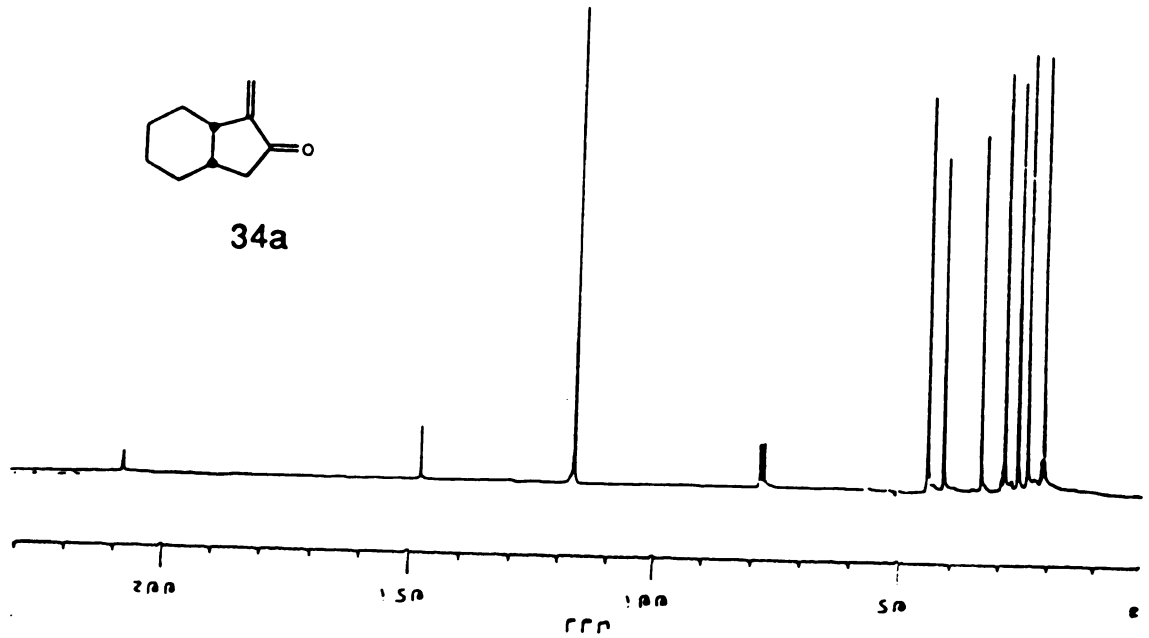


Figure 135. ^{13}C NMR Spectrum of **34a**

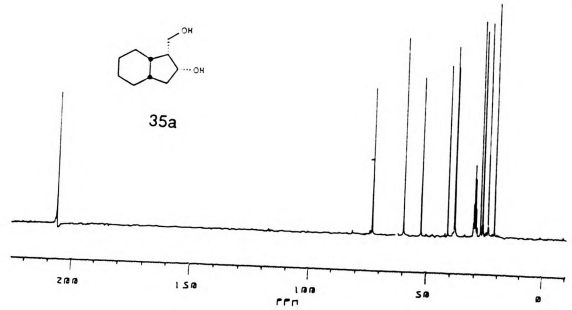


Figure 137. ^{13}C NMR Spectrum of **35a**

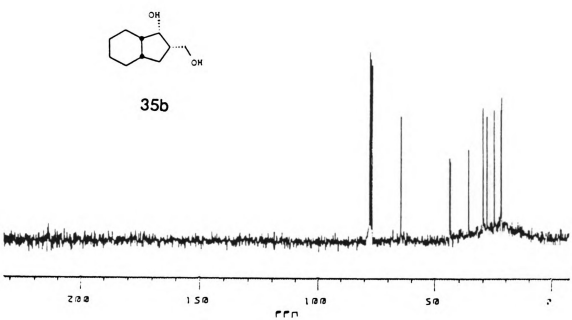


Figure 138. ^{13}C NMR Spectrum of **35b**

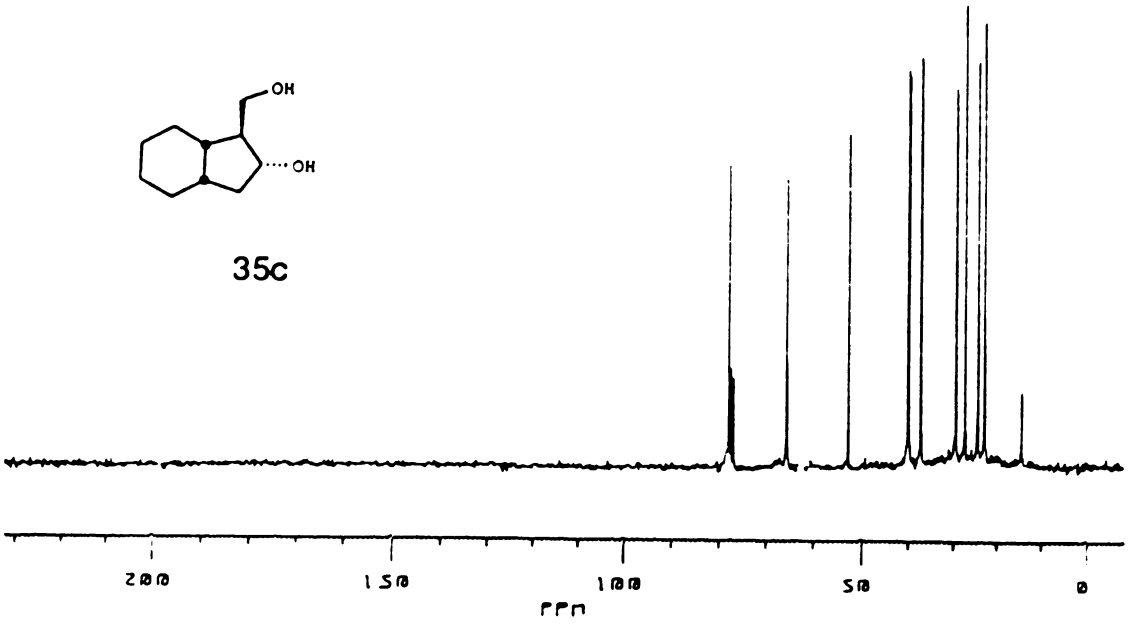


Figure 139. ^{13}C NMR Spectrum of **35c**

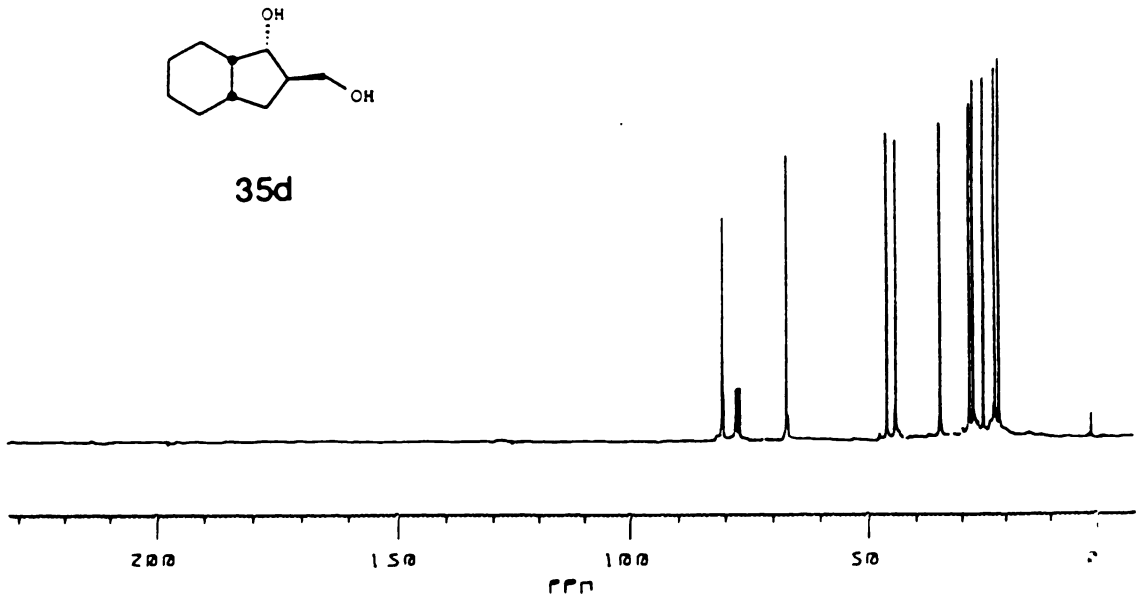
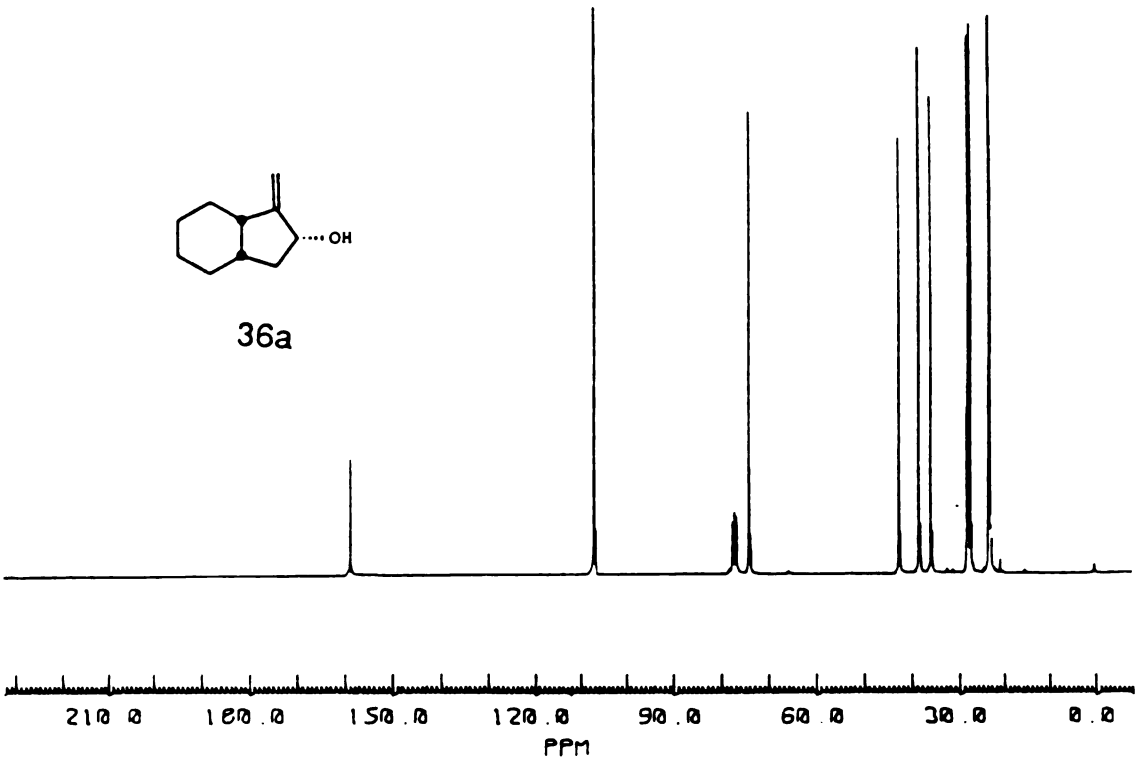
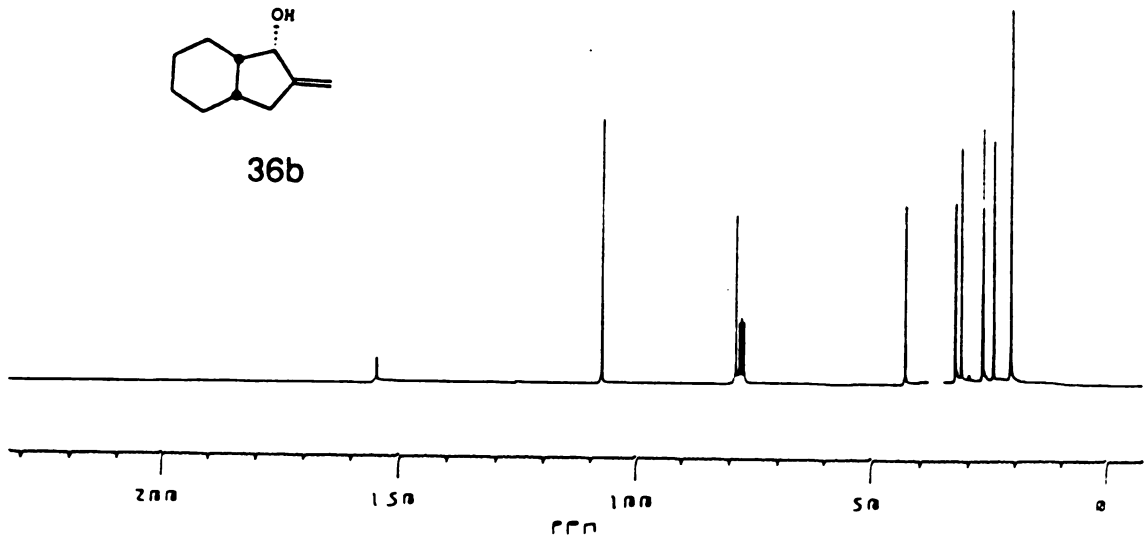


Figure 140. ^{13}C NMR Spectrum of **35d**



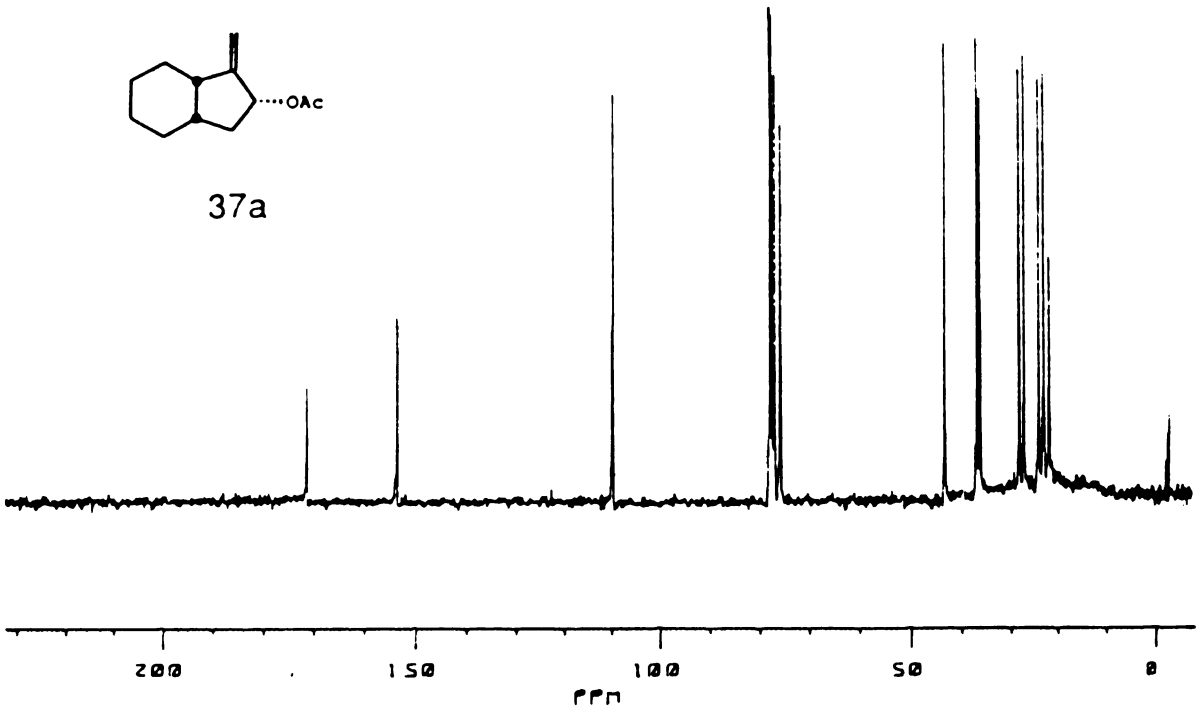
36a

Figure 141. ^{13}C NMR Spectrum of **36a**



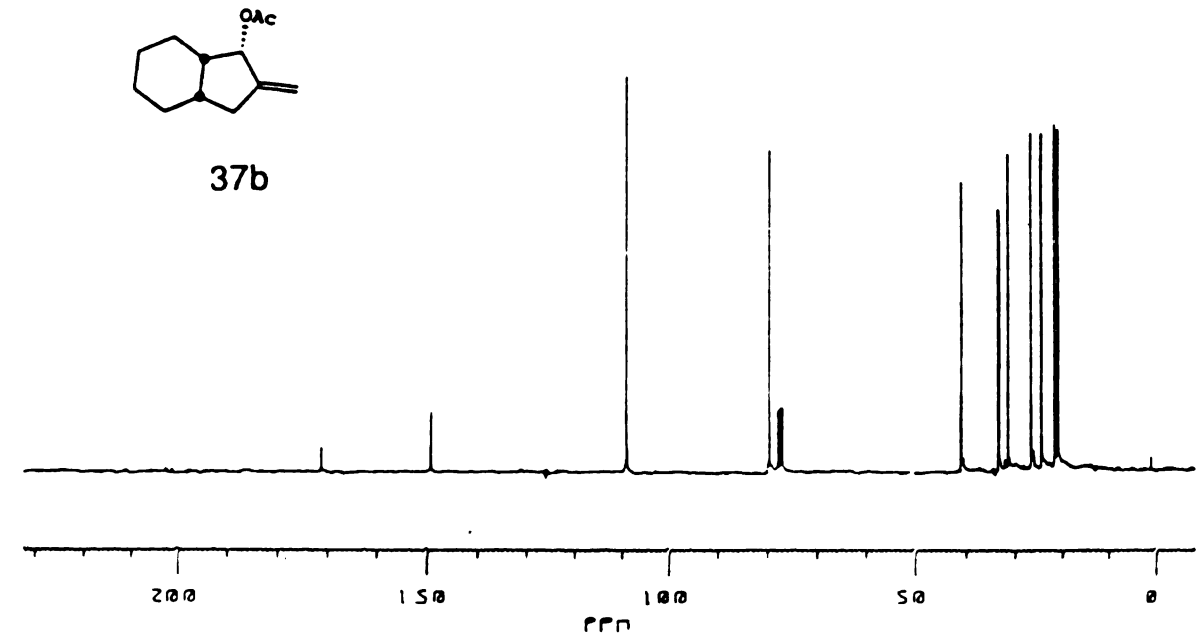
36b

Figure 142. ^{13}C NMR Spectrum of **36b**



37a

Figure 143. ^{13}C NMR Spectrum of **37a**



37b

Figure 144. ^{13}C NMR Spectrum of **37b**

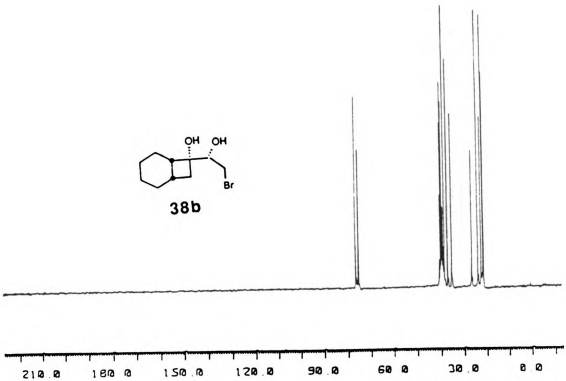


Figure 146. ^{13}C NMR Spectrum of **38b**

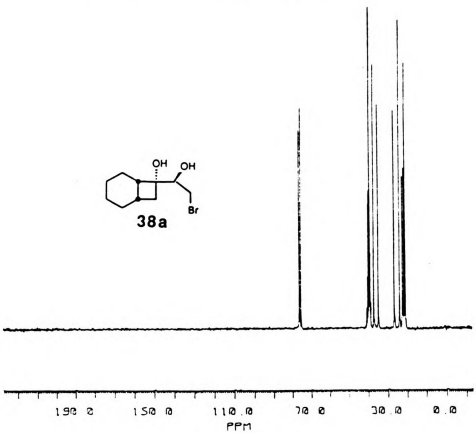


Figure 145. ^{13}C NMR Spectrum of **38a**

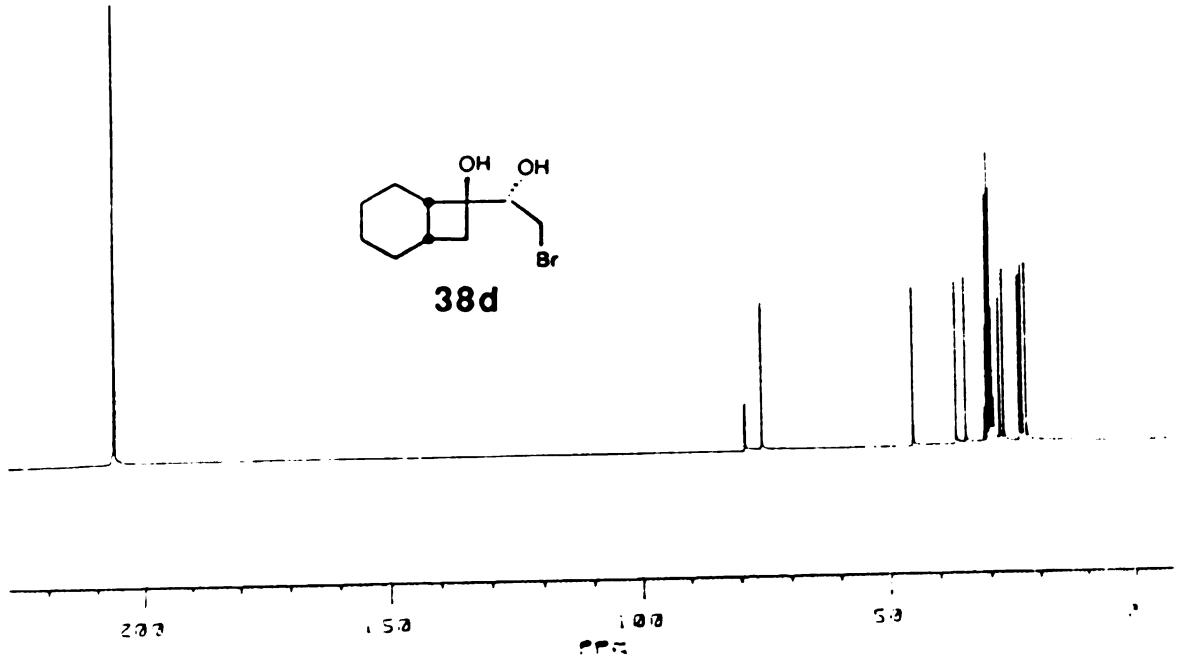


Figure 148. ^{13}C NMR Spectrum of **38d**

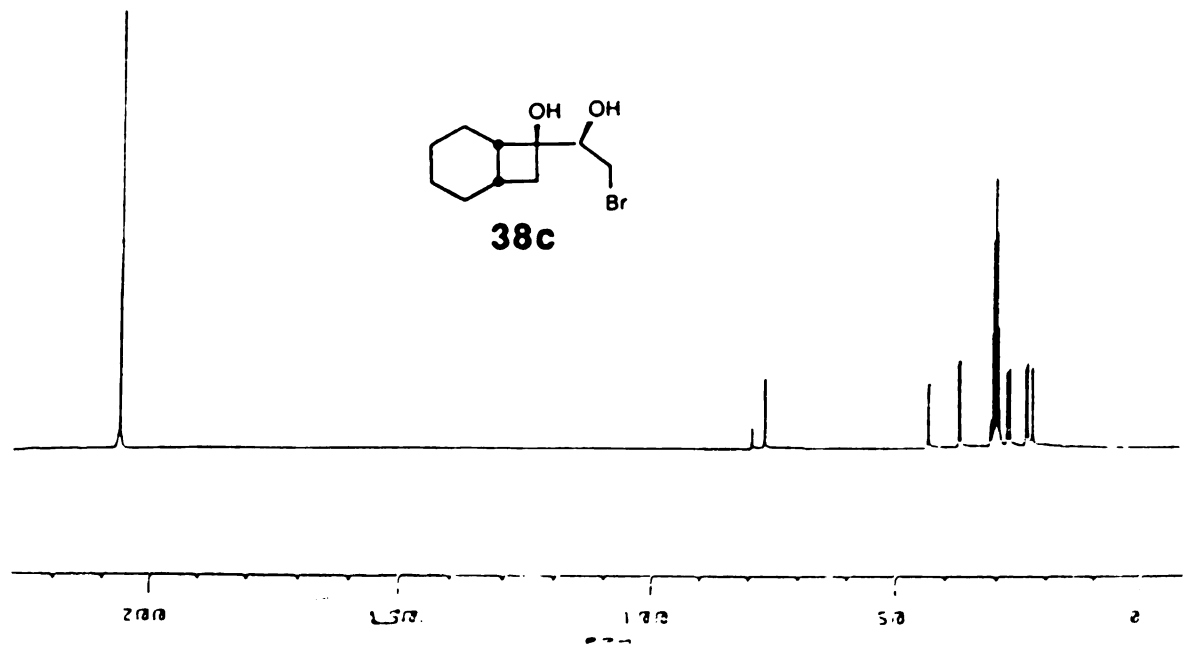


Figure 147. ^{13}C NMR Spectrum of **38c**

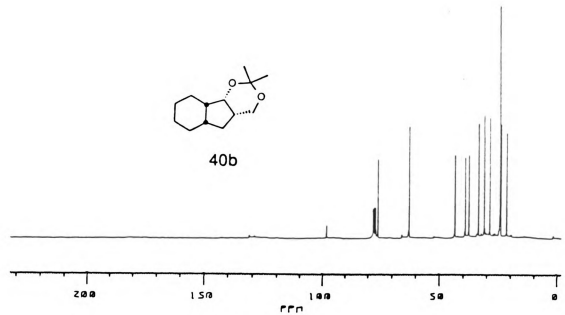


Figure 149. ^{13}C NMR Spectrum of **40b**

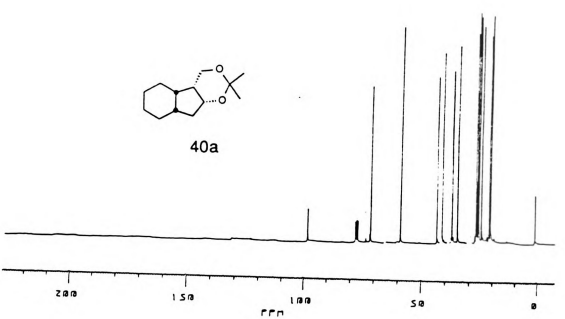


Figure 150. ^{13}C NMR Spectrum of **40a**

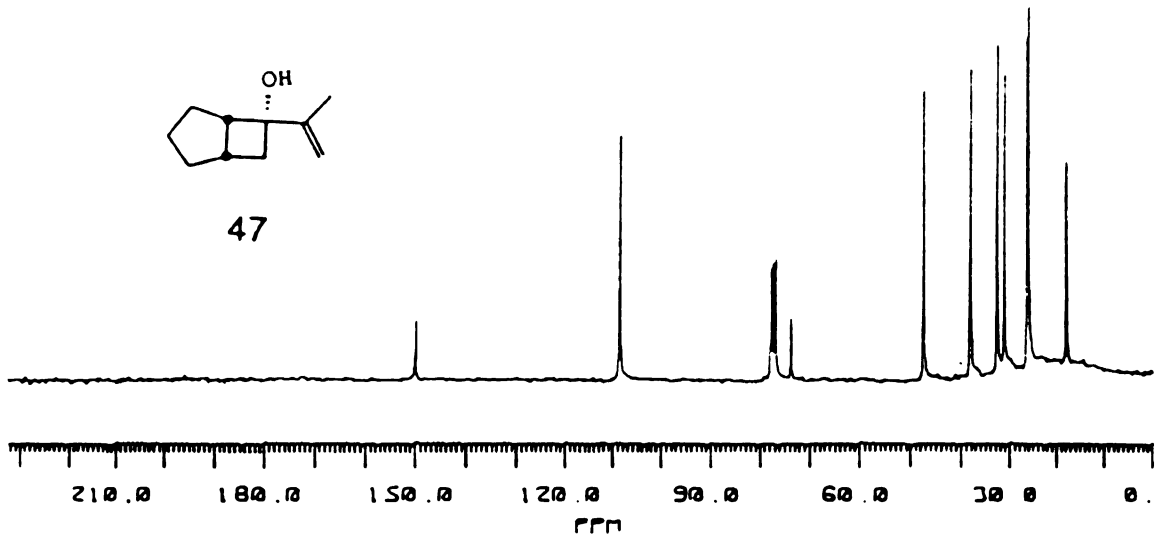


Figure 151. ^{13}C NMR Spectrum of **47**

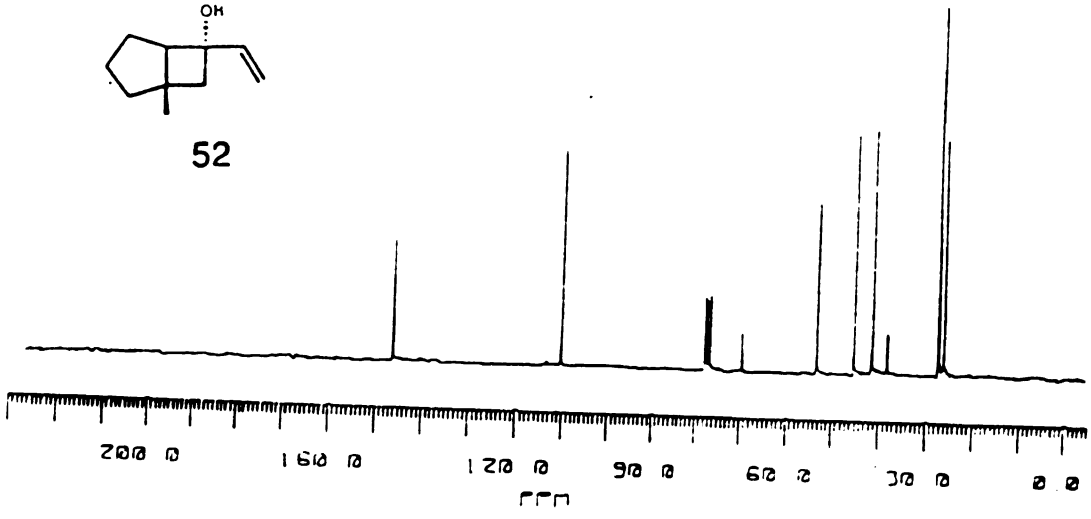


Figure 152. ^{13}C NMR Spectrum of **52**

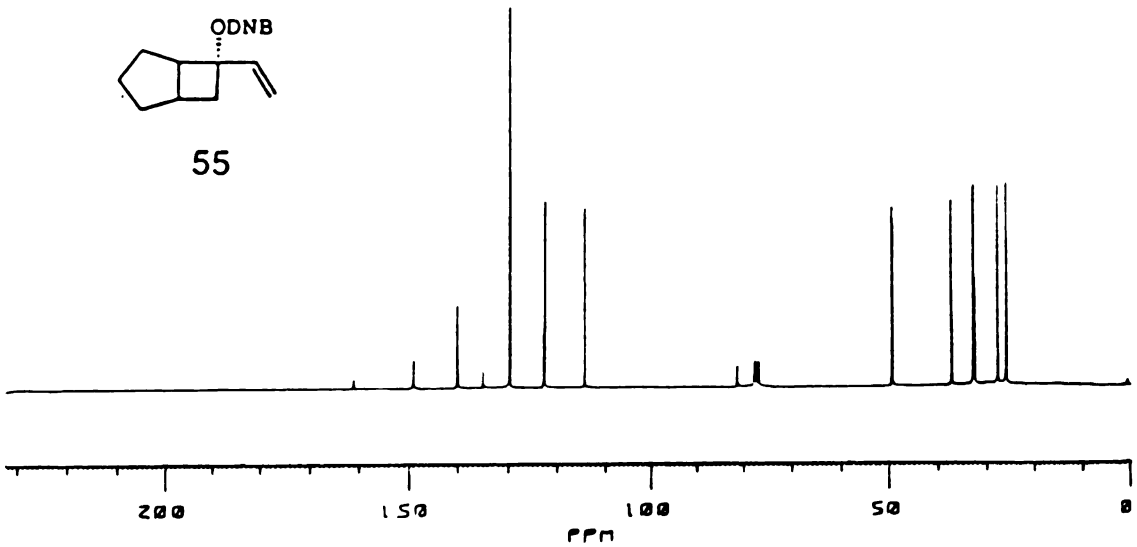


Figure 153. ^{13}C NMR Spectrum of **55**

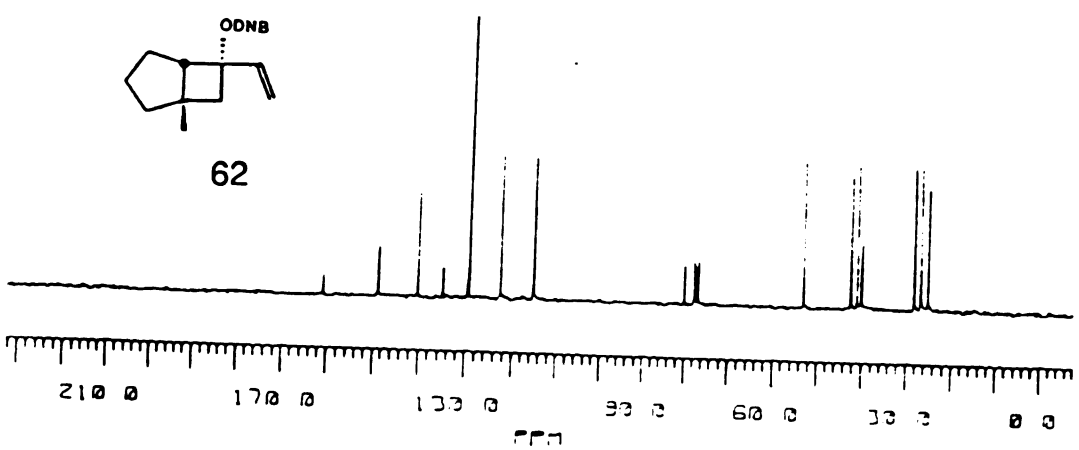


Figure 154. ^{13}C NMR Spectrum of **62**

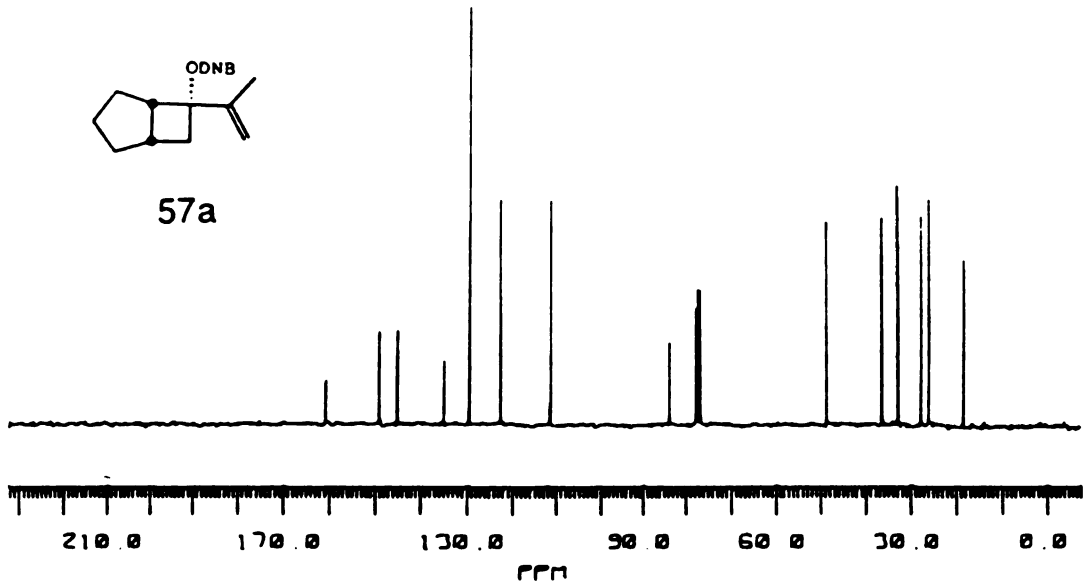


Figure 155. ^{13}C NMR Spectrum of **57a**

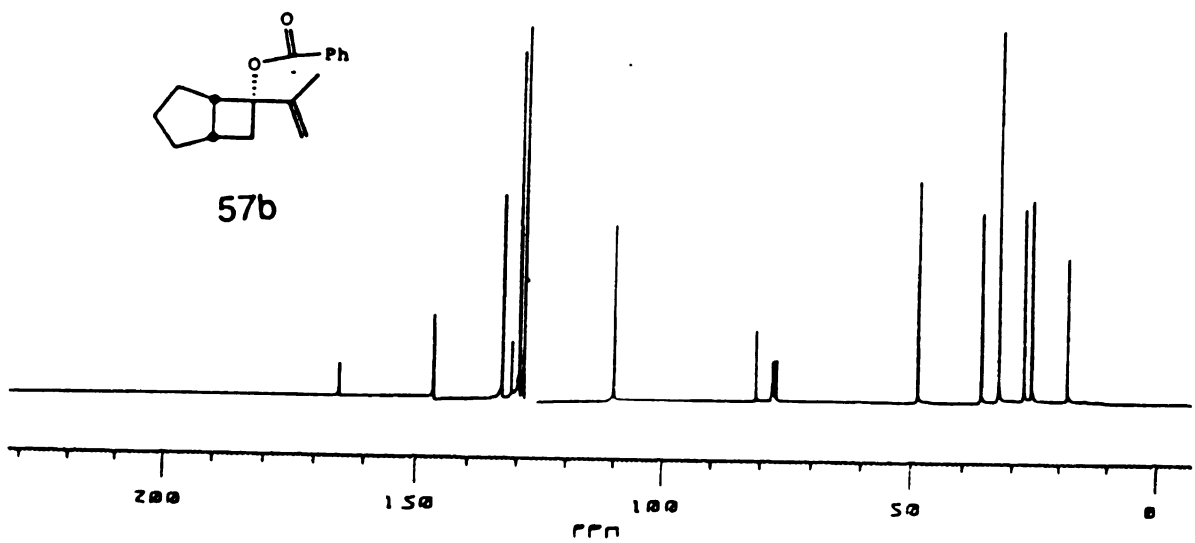


Figure 156. ^{13}C NMR Spectrum of **57b**

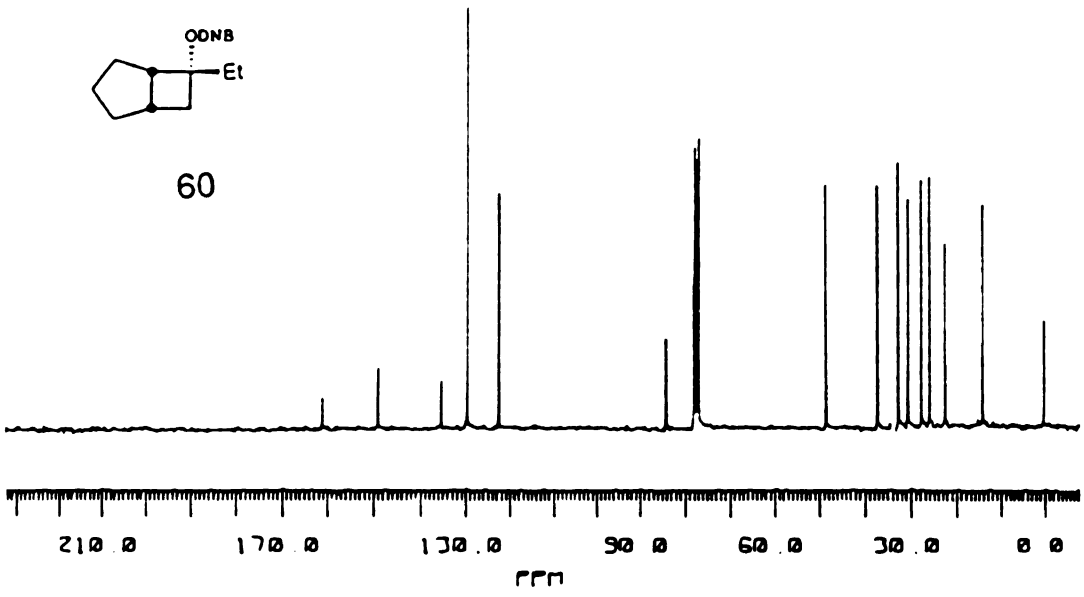


Figure 157. ^{13}C NMR Spectrum of **60**

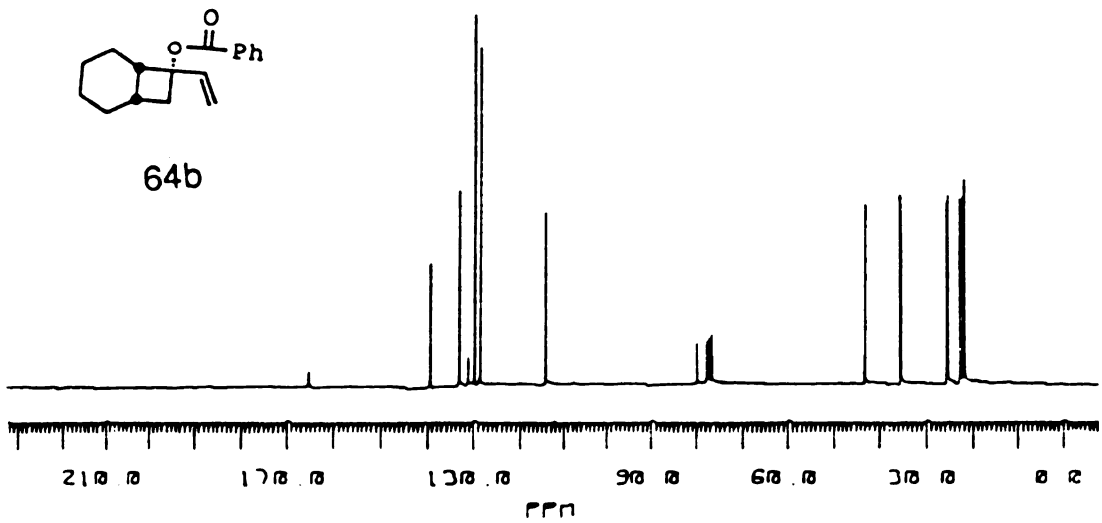


Figure 158. ^{13}C NMR Spectrum of **64b**

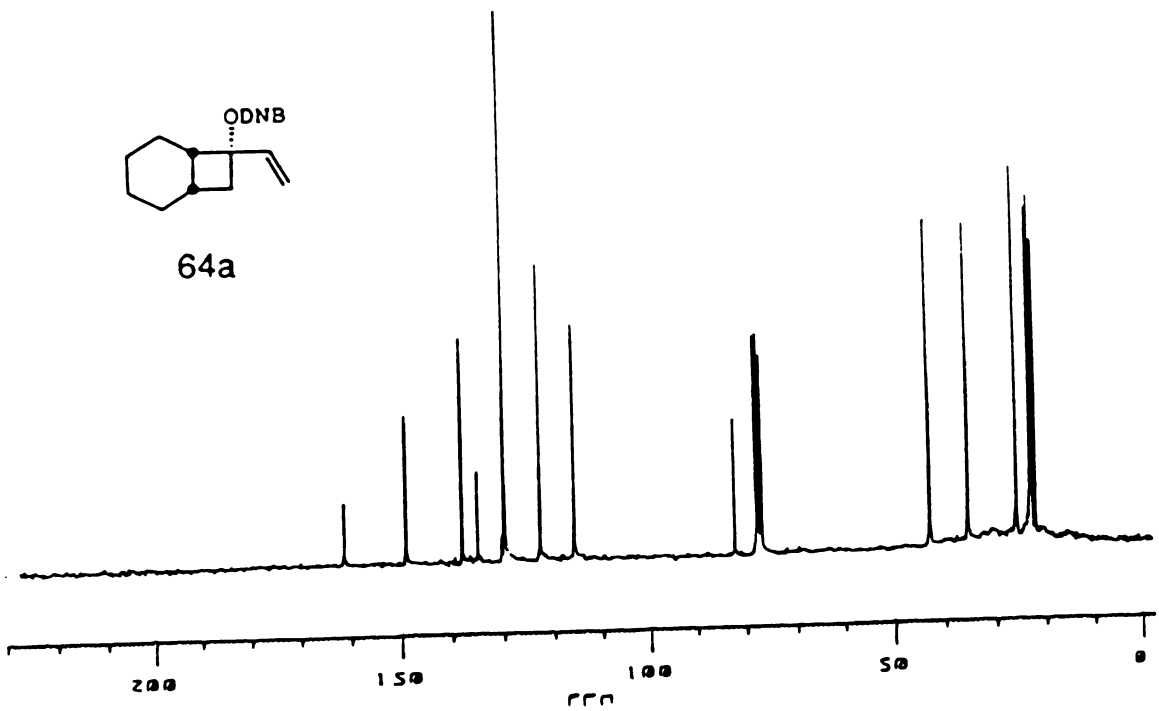


Figure 159. ^{13}C NMR Spectrum of **64a**

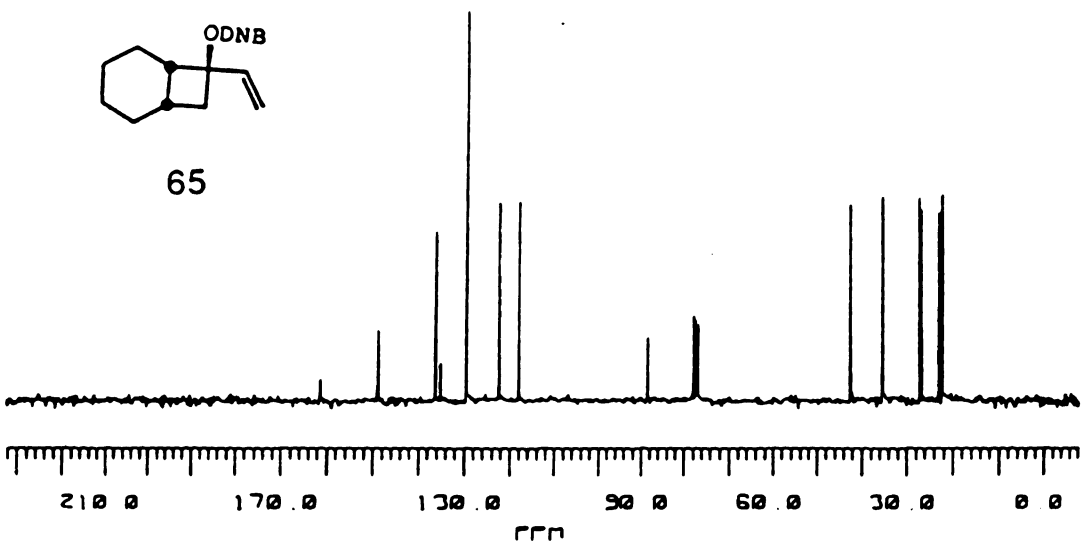


Figure 160. ^{13}C NMR Spectrum of **65**

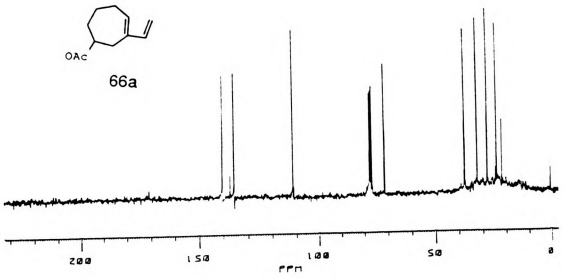


Figure 161. ^{13}C NMR Spectrum of **66a**

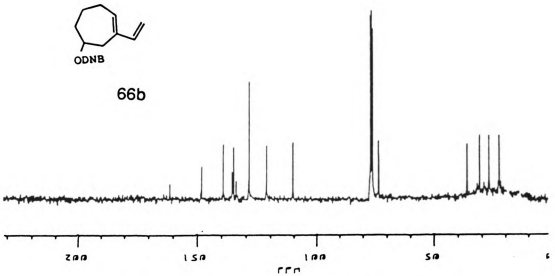


Figure 162. ^{13}C NMR Spectrum of **66b**

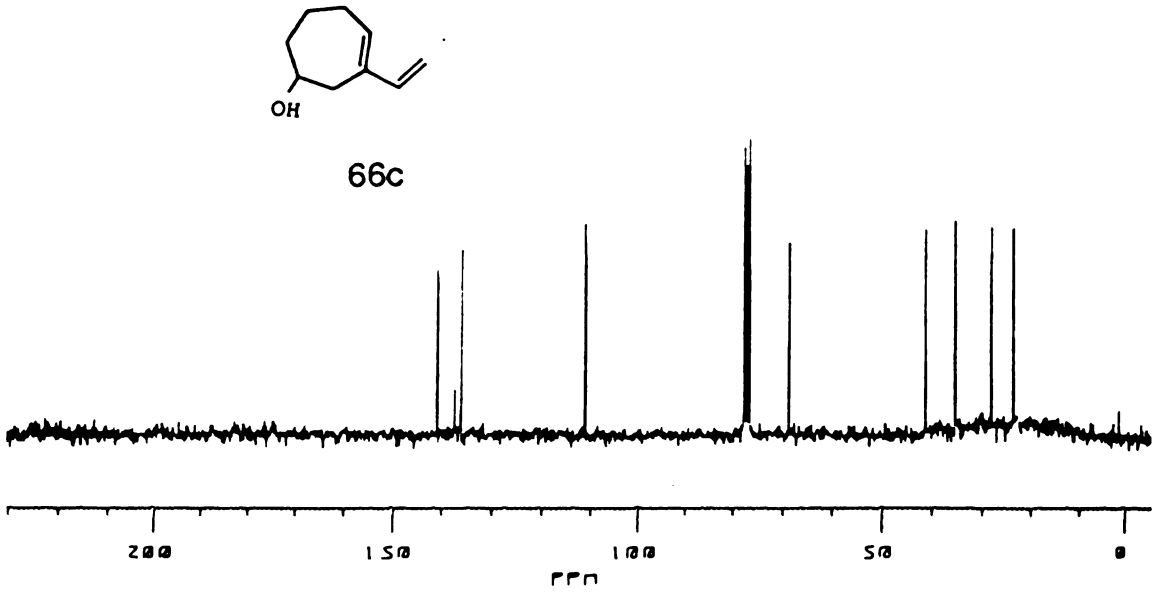


Figure 163. ^{13}C NMR Spectrum of **66c**

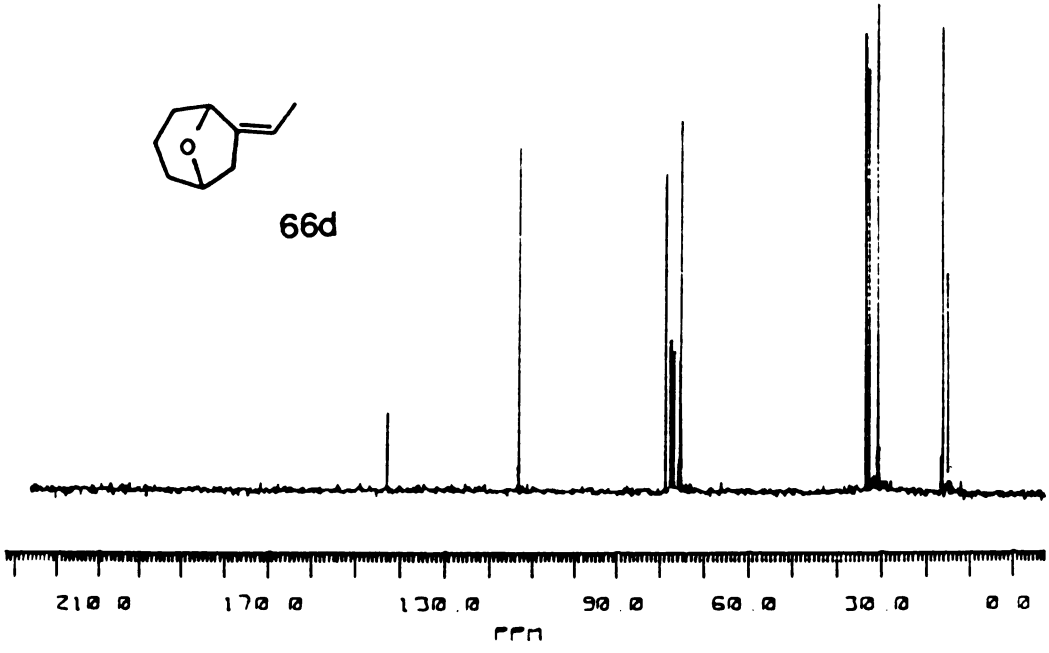


Figure 164. ^{13}C NMR Spectrum of **66d**

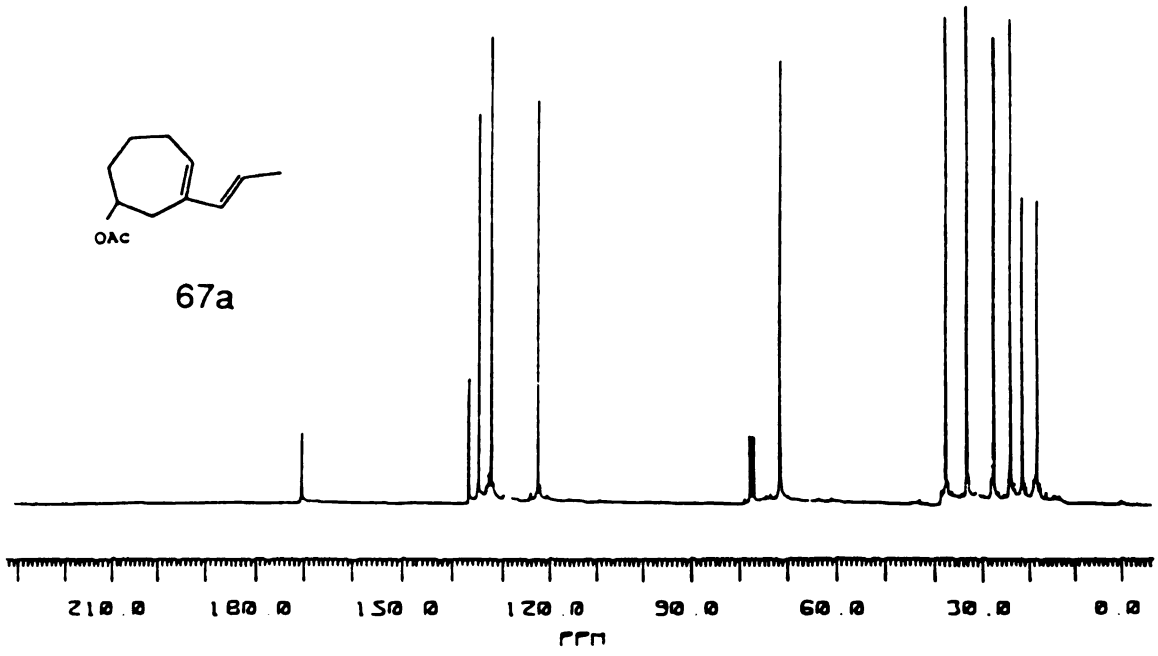


Figure 165. ^{13}C NMR Spectrum of **67a**

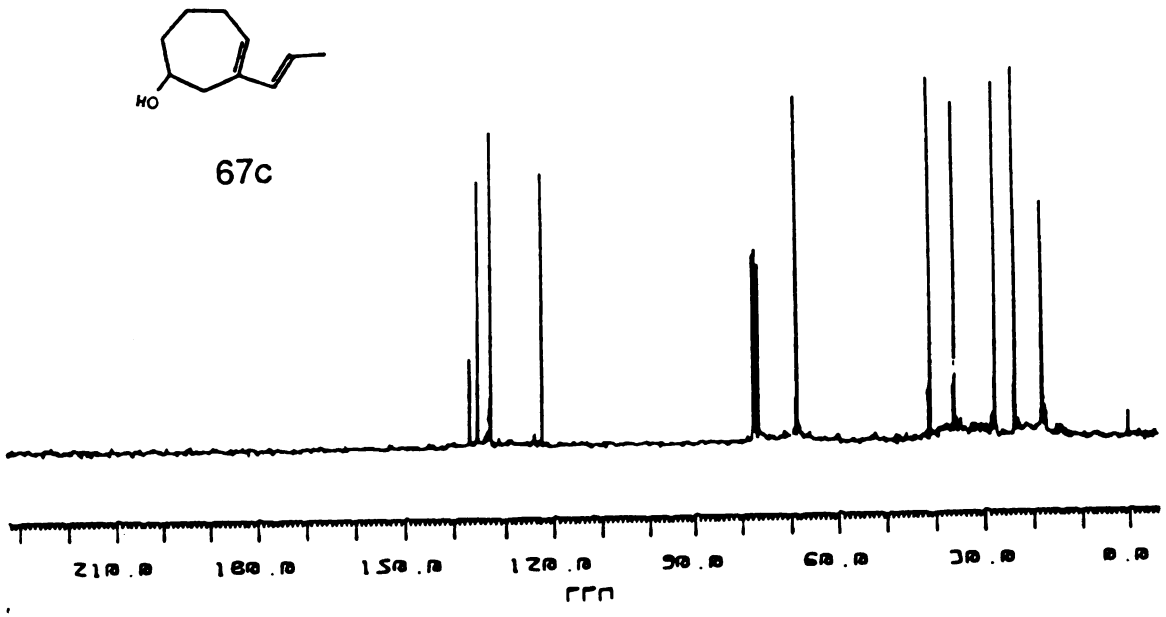


Figure 166. ^{13}C NMR Spectrum of **67c**

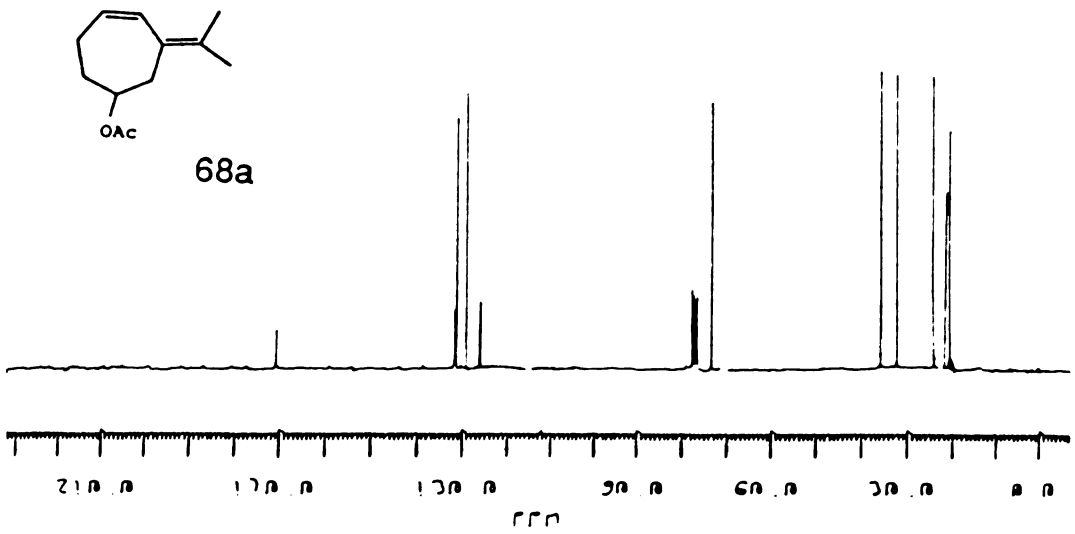


Figure 167. ^{13}C NMR Spectrum of **68a**

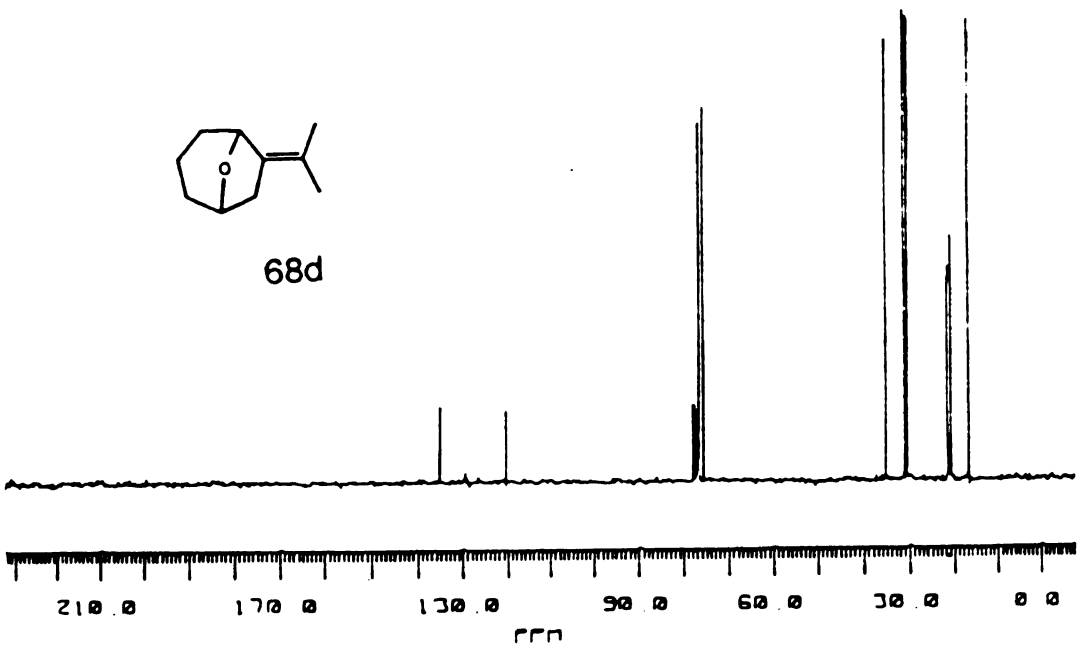


Figure 168. ^{13}C NMR Spectrum of **68d**

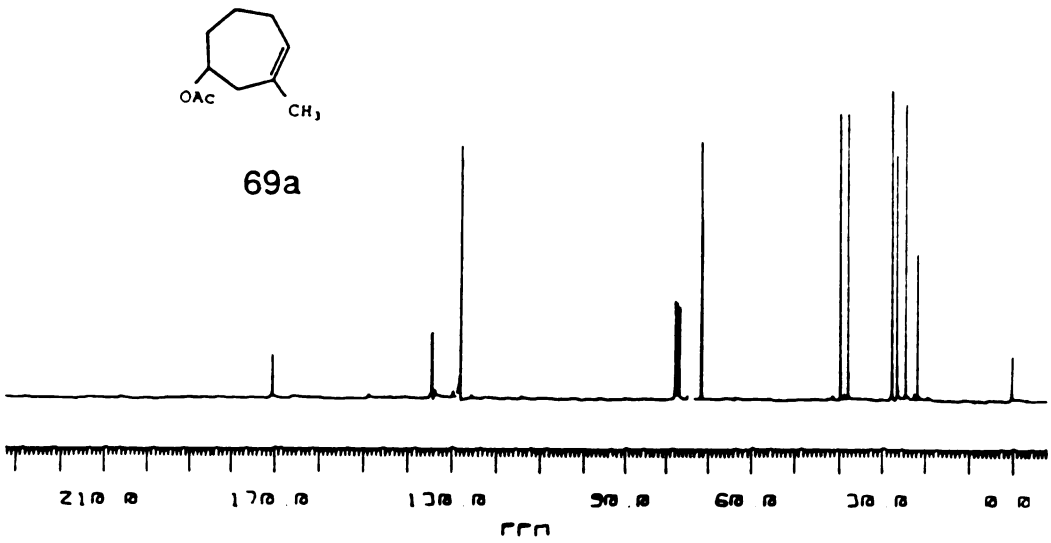


Figure 169. ^{13}C NMR Spectrum of **69a**

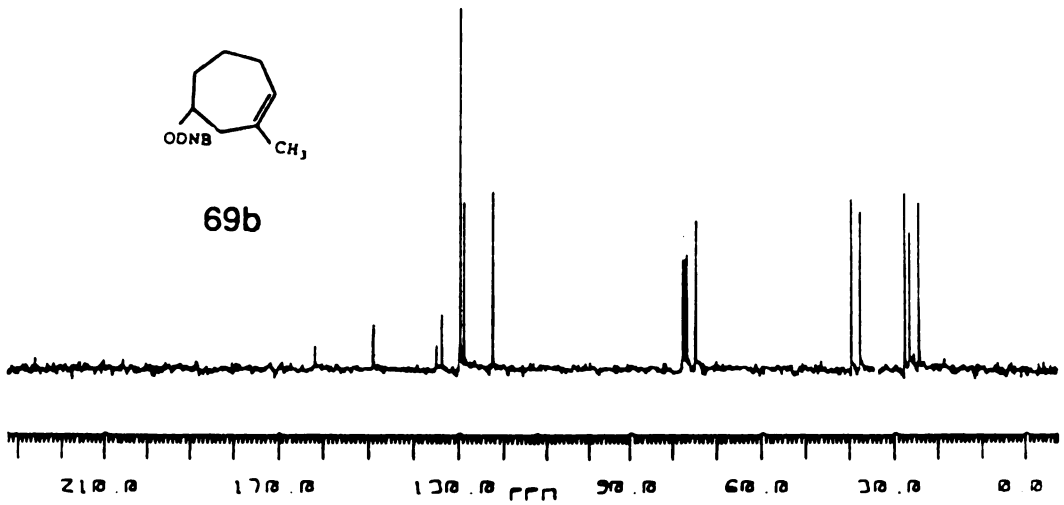


Figure 170. ^{13}C NMR Spectrum of **69b**

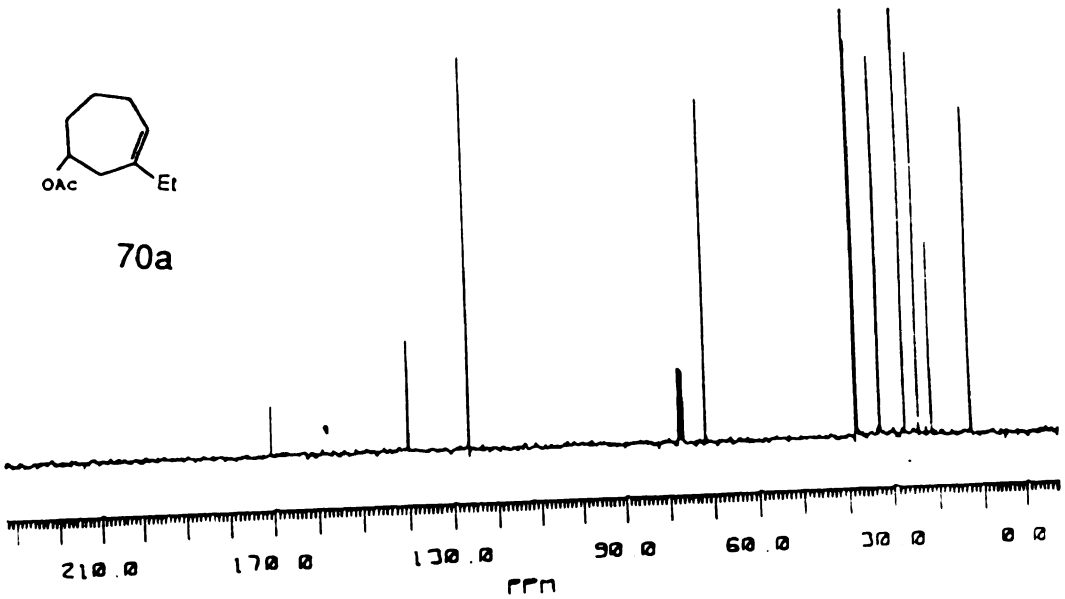


Figure 171. ^{13}C NMR Spectrum of **70a**

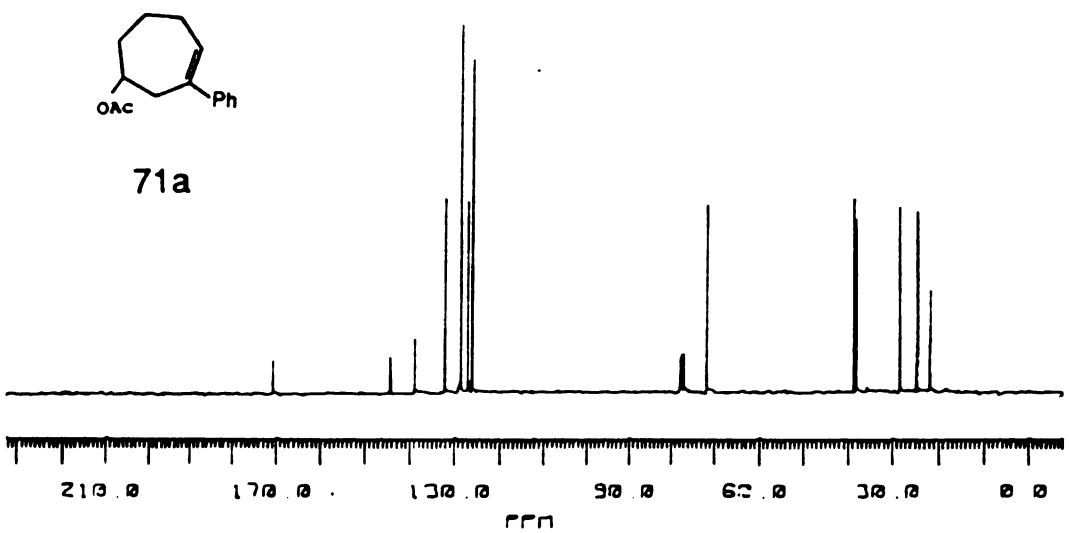


Figure 172. ^{13}C NMR Spectrum of **71a**

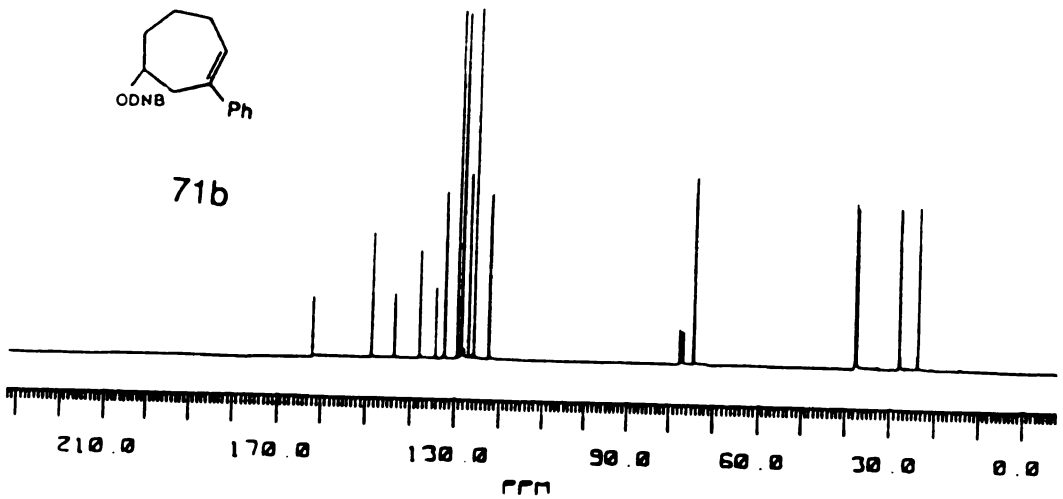


Figure 173. ^{13}C NMR Spectrum of **71b**

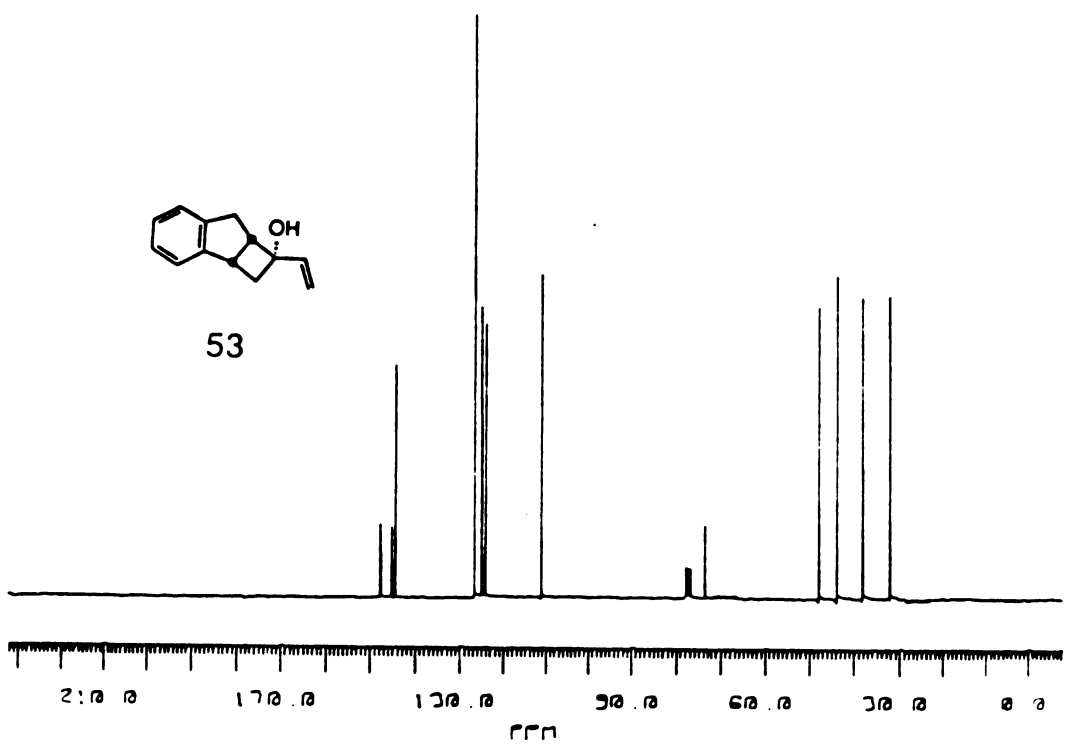
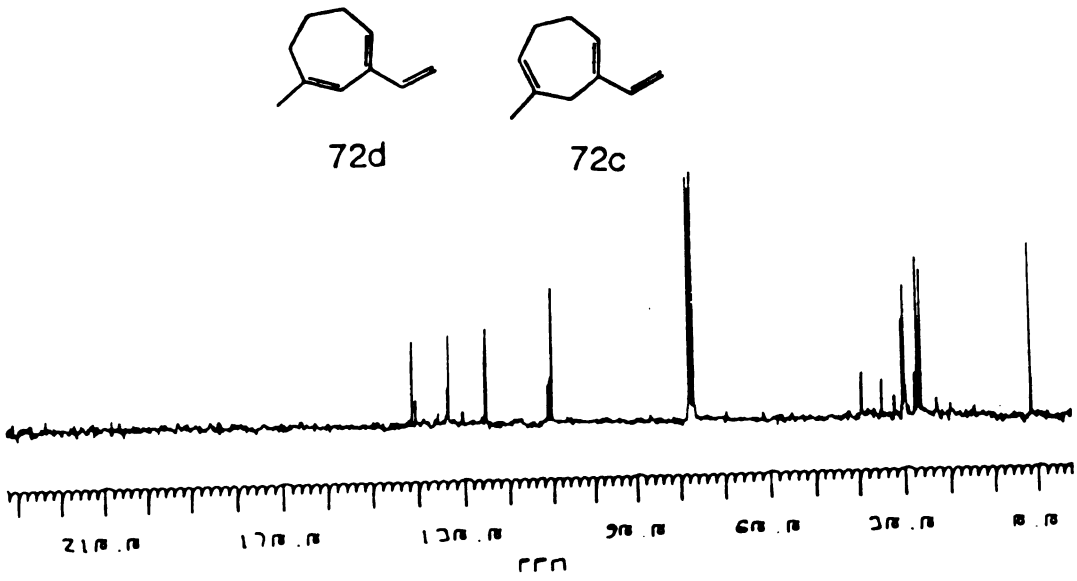
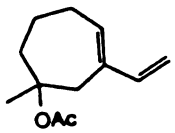


Figure 174. ^{13}C NMR Spectrum of **53**



72d 72c

Figure 175. ^{13}C NMR Spectrum of **72c + 73d**



72a

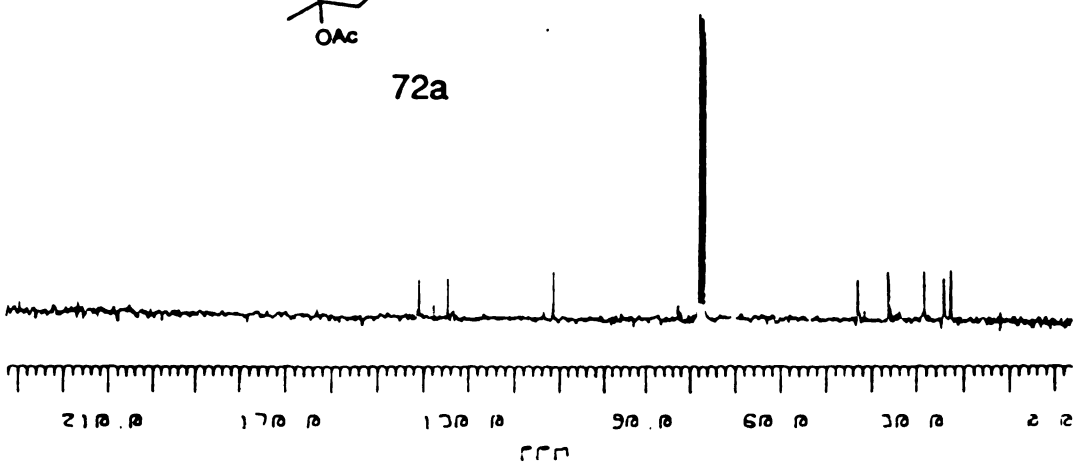


Figure 176. ^{13}C NMR Spectrum of **72a**

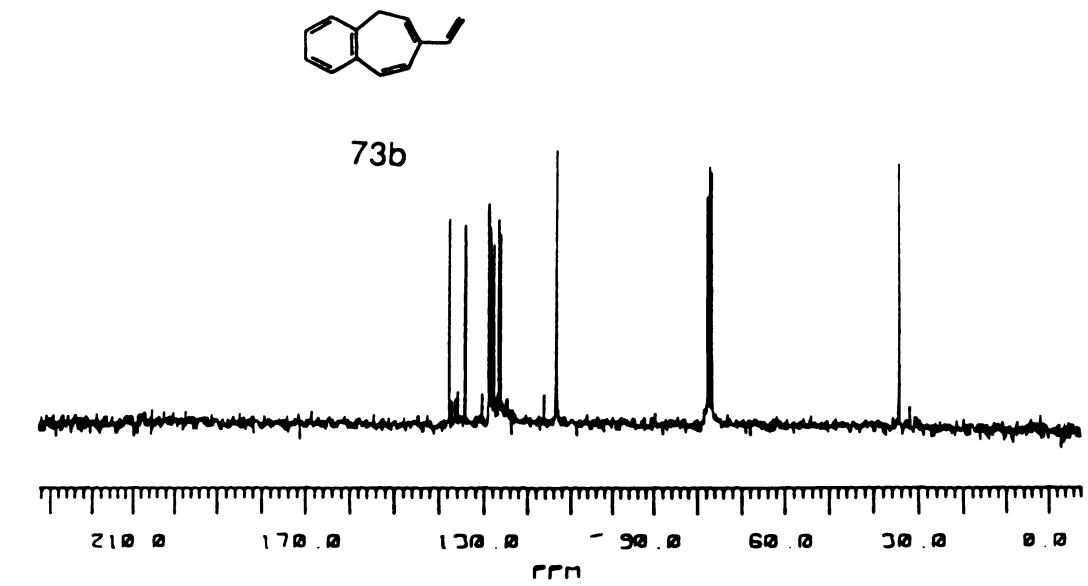


Figure 177. ^{13}C NMR Spectrum of **73b**

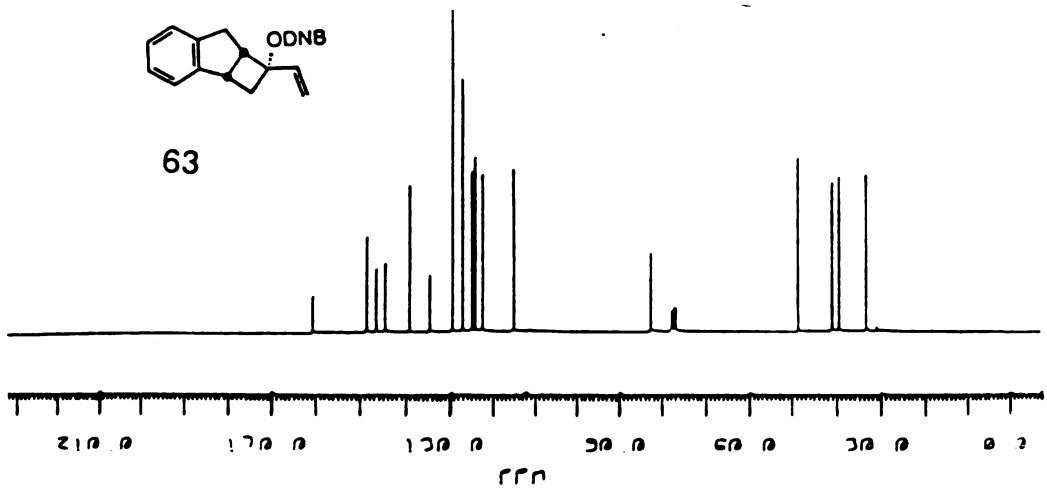


Figure 178. ^{13}C NMR Spectrum of **63**

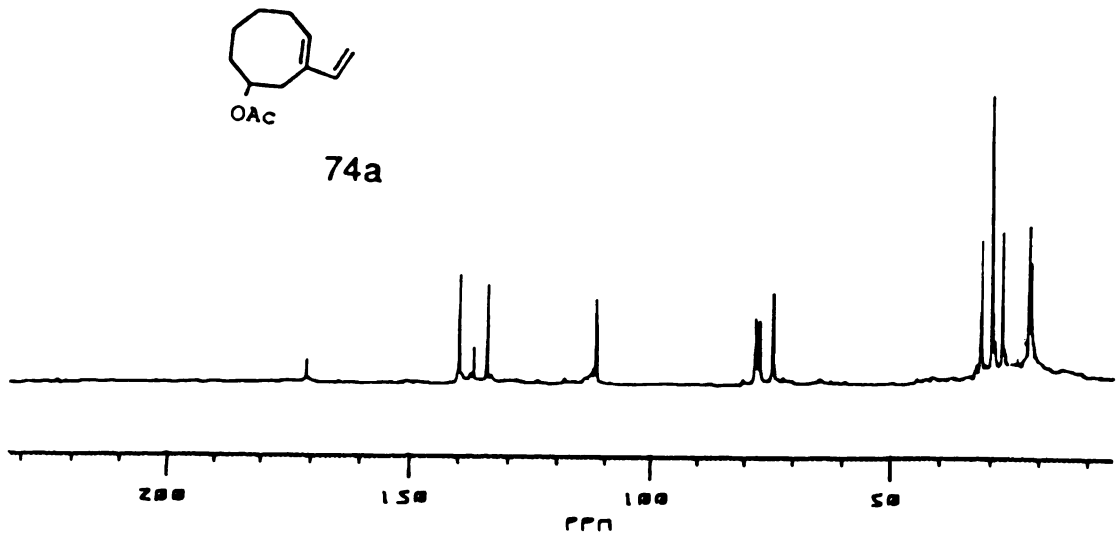


Figure 179. ^{13}C NMR Spectrum of **74a**

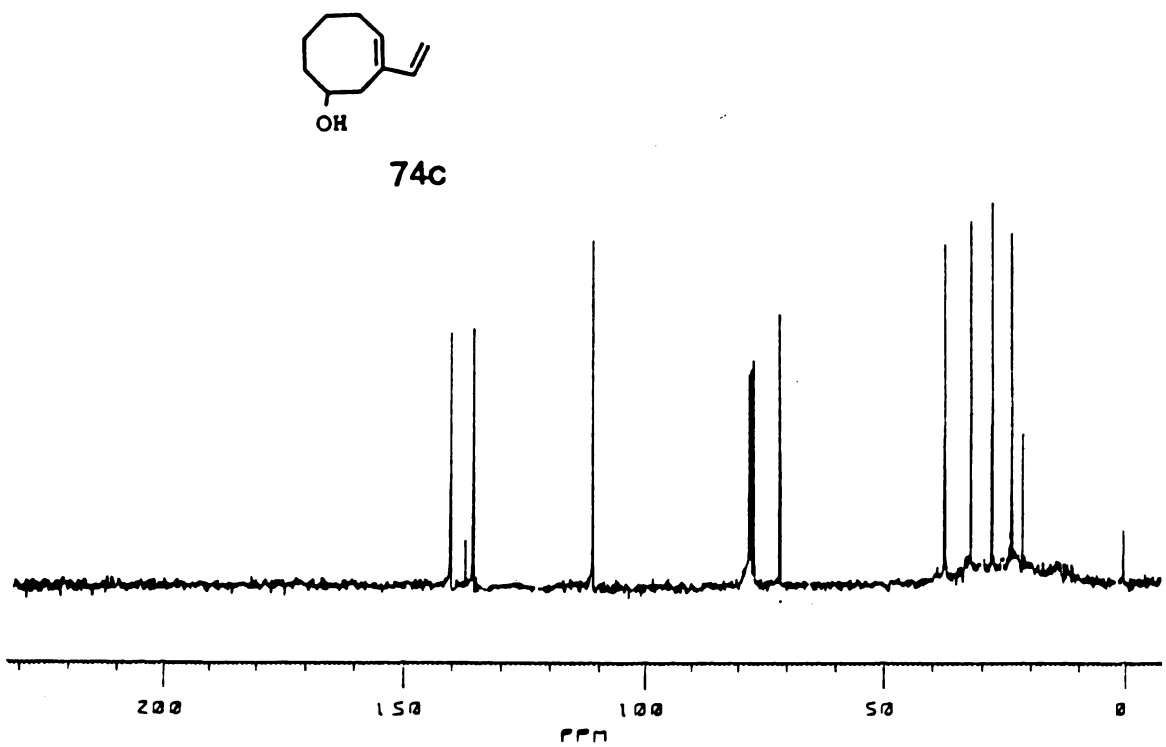


Figure 180. ^{13}C NMR Spectrum of **74c**

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