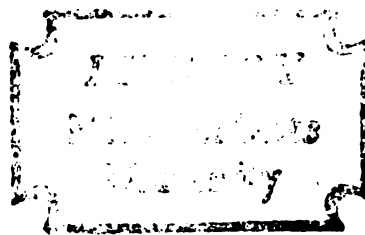


STUDIES TOWARD THE TOTAL SYNTHESIS OF
TETRACYCLIC TRITERPENES

Dissertation for the Degree of Ph. D.
MICHIGAN STATE UNIVERSITY
JERROLD LEROY MARTIN, JR.
1976



This is to certify that the
thesis entitled
Studies Toward the Total Synthesis
of Tetracyclic Triterpenes
presented by

Jerrold Leroy Martin, Jr.

has been accepted towards fulfillment
of the requirements for

Ph.D. degree in Organic Chemistry

William H. Reusch

Major professor

Date 8/23/76

ABSTRACT

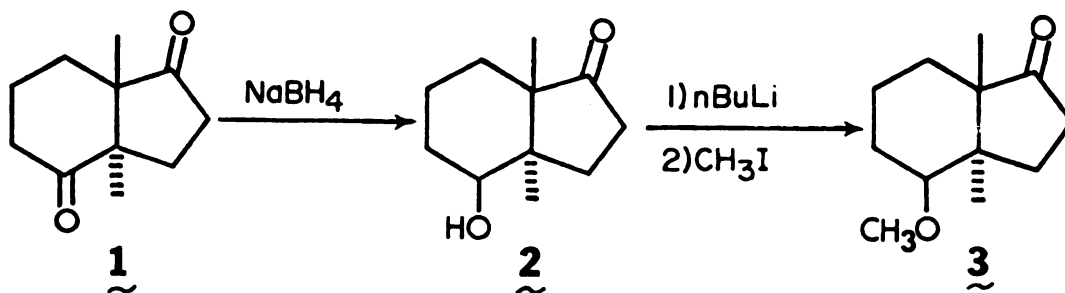
STUDIES TOWARD THE TOTAL SYNTHESIS OF TETRACYCLIC TRITERPENES

By

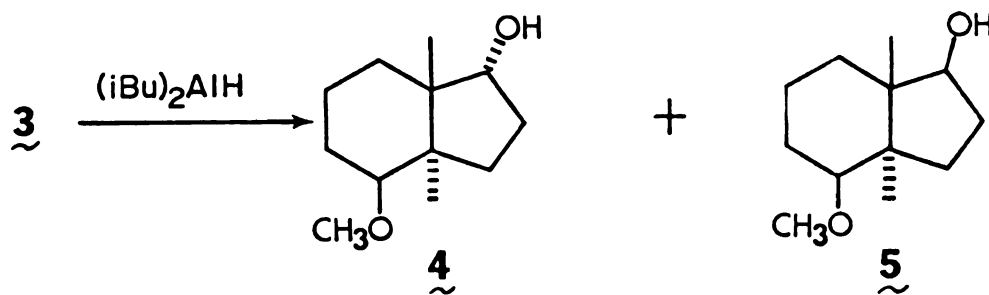
Jerrold Leroy Martin, Jr.

Perhydroindenedione 1 is a potentially useful starting material for the total synthesis of lanostane and euphane triterpenes.

The carbonyl function in the six-membered ring of 1 was reduced to an axial alcohol and formed adducts with Grignard reagents and ylides in the presence of the unprotected carbonyl group in the five-membered ring. By making use of this selective reactivity, derivative 3 was synthesized.

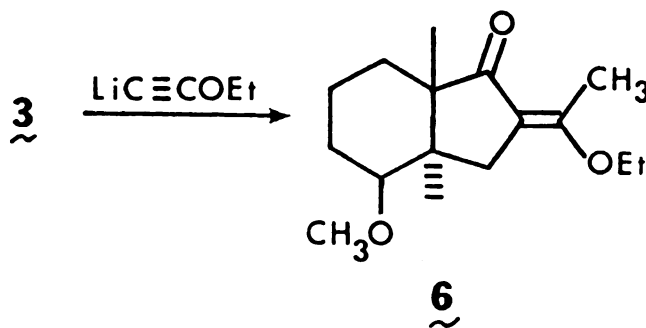


Treatment of 3 with diisobutyl aluminum hydride yielded alcohols 4 and 5.



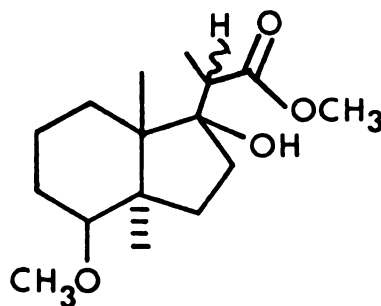
Epimer 4 showed an eight-fold preference for water loss (M-18) in its 15eV mass spectrum, relative to 5; however, mass spectral analysis of several deuterium labeled analogs of 4 and 5 failed to explain this phenomenon. The configurations of 4 and 5 were assigned by a comparison of the methyl shifts in their proton magnetic resonance spectra with known angular methyl shifts for the 5 α ,14 α -androstande series.

Approaches to building a terpene side chain onto 3 were explored. Although the carbonyl function in 3 resisted the addition of a wide variety of nucleophilic reagents, it did form an adduct with sodium acetylide. This adduct was completely resistant to all efforts to transform it into useful intermediates. Treatment of 3 with lithium ethoxyacetylene resulted in an unprecedented condensation product:



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Allyl magnesium bromide and crotyl magnesium bromide both formed adducts with 3. The adduct resulting from the crotyl Grignard reagent was transformed into a β -hydroxy ester side chain similar to that employed by other workers to elaborate a terpene side chain:



7

STUDIES TOWARD THE TOTAL SYNTHESIS
OF TETRACYCLIC TRITERPENES

By
Jerrold Leroy Martin, Jr.

A DISSERTATION

Submitted to
Michigan State University
in partial fulfillment of the requirements
for the degree of

DOCTOR OF PHILOSOPHY

Department of Chemistry

1976

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1976

This dissertation is dedicated to my
parents, who have provided a continuing
source of love and inspiration, and to
my future with Sally.

ACKNOWLEDGEMENTS

The author is indebted to Professor William H. Reusch for his instruction, for his vigorous intellectual example, and for his sincere counsel.

To friends in the lab and elsewhere, past and present, the author extends his gratitude.

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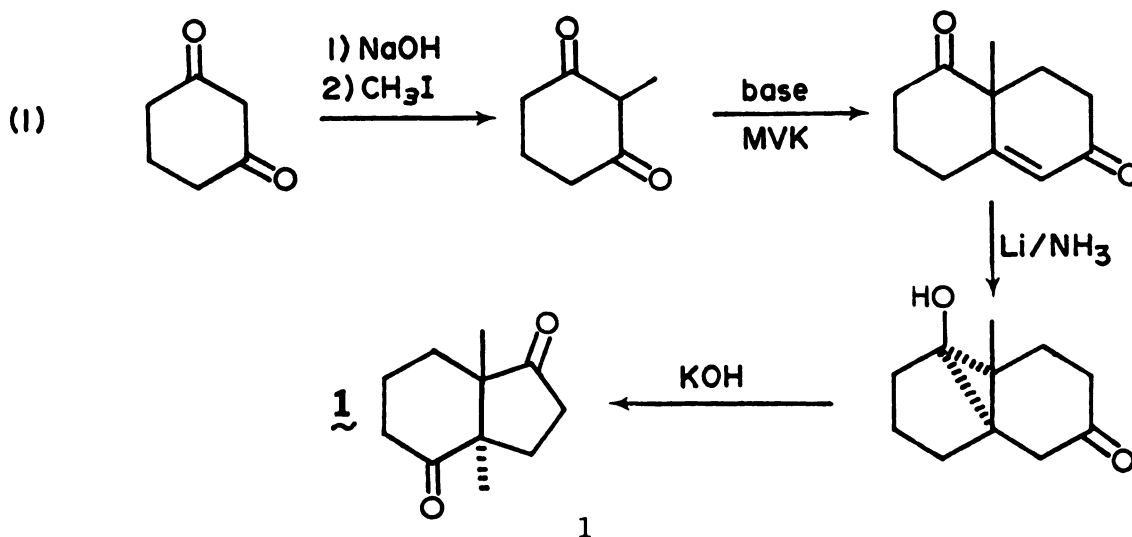
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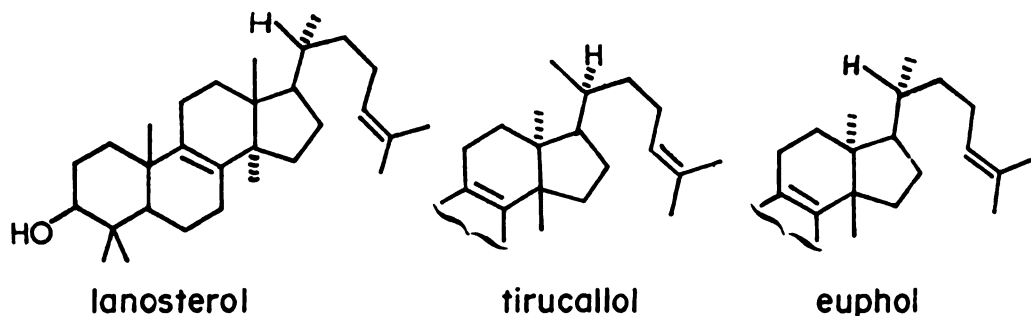
INTRODUCTION

The tetracyclic triterpenes and steroids constitute an area of vital interest to synthetic chemists. Their synthesis and modification pose a challenge which has not only tested and refined synthetic strategies, but also has led to the development of novel reagents or reaction conditions. The marked physiological properties¹ of some members of this group is an additional enticement in capturing the interest of the researcher.

Every successful synthetic strategy has as its foundation at least one specific transformation or versatile intermediate. In this study, the availability of *trans*-1,6-dimethylbicyclo[4.3.0]nonan-2,7-dione² (equation 1) prompted consideration of the total synthesis of the lanostane and euphane/tirucallane triterpenes.

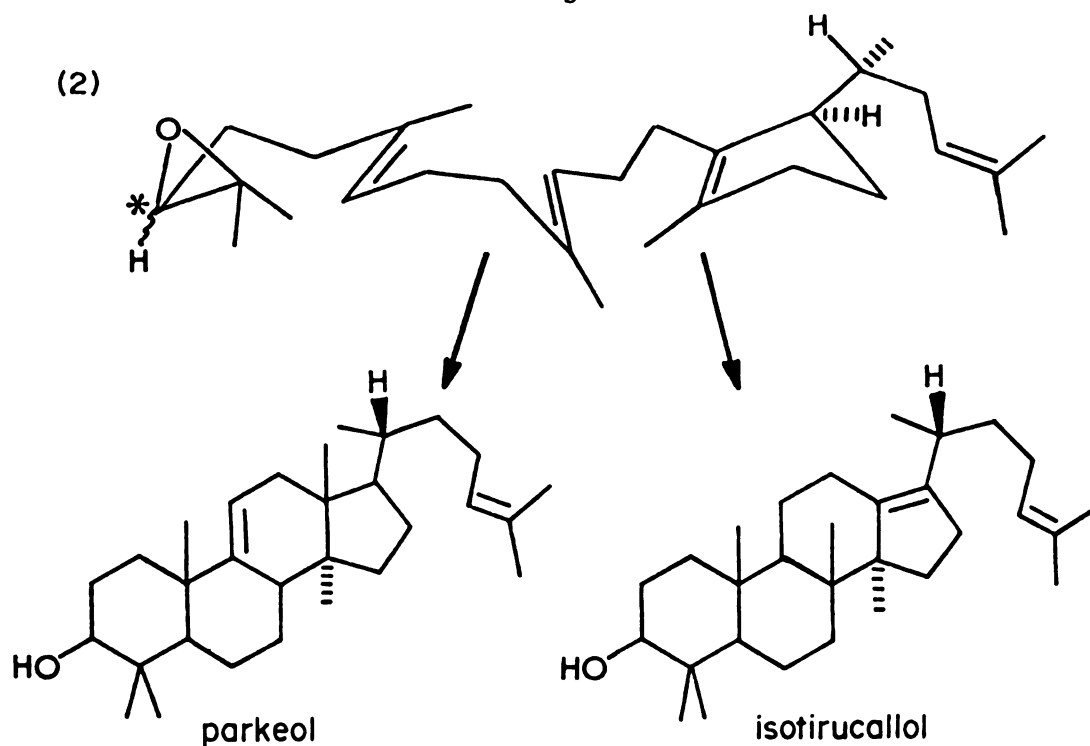


The tetracyclic triterpenes and steroids³ are formed in nature by enzymatic cyclizations of squalene,⁴ followed by rearrangement and loss of methyl groups. A chair-boat-chair-boat folding of squalene leads to the lanostane system, whereas a chair-chair-chair-boat arrangement leads to euphol and/or tirucallol derivatives.

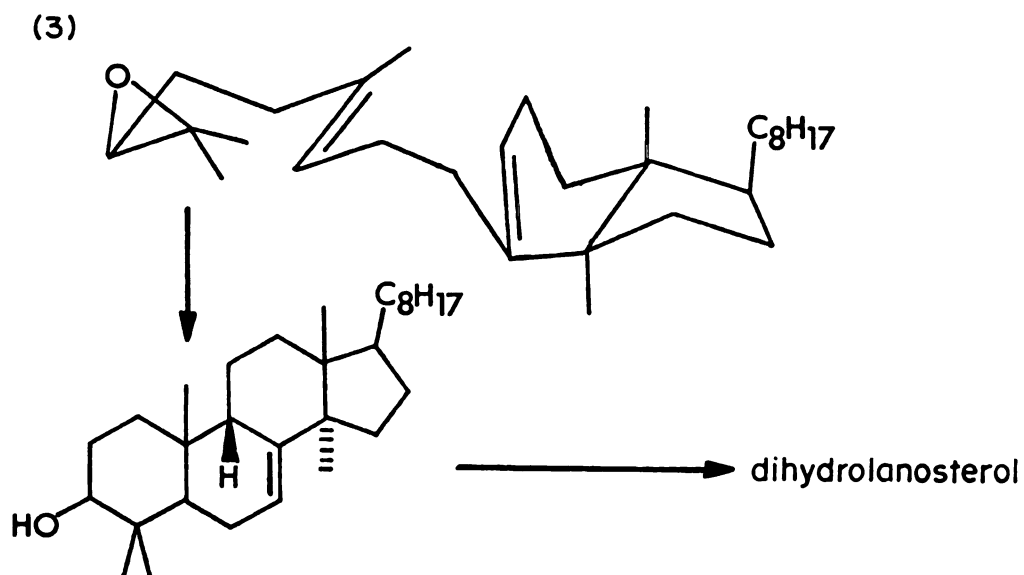


Treatment of squalene 2,3-oxide with an appropriate enzyme in the laboratory has in fact produced a mixture of lanosterol and cholesterol.⁵

Non-enzymatic, acid-catalyzed cyclization of appropriate polyene intermediates has also generated the lanostane skeleton. Thus, a polyene monoepoxide with a pre-formed D ring was cyclized to parkeol while the corresponding epimeric epoxide was cyclized to isotirucallol:⁶

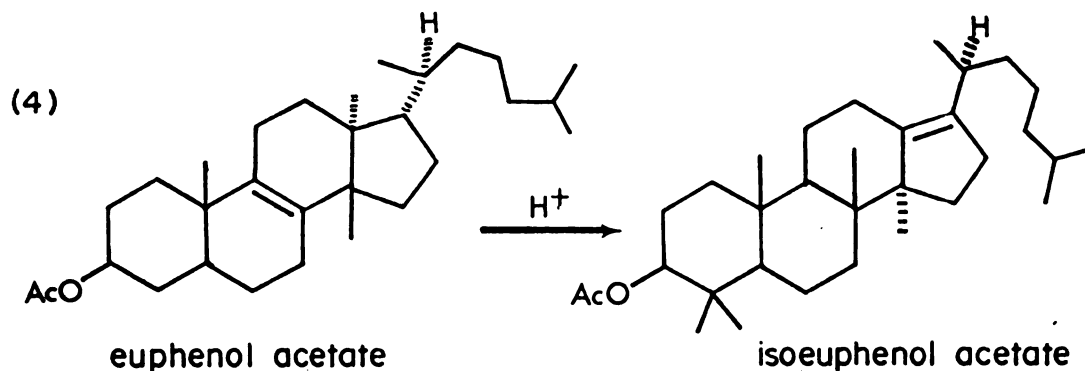


Cyclization of another polyene monoepoxide with a preformed CD moiety led to a dihydrolanosterol precursor:⁷

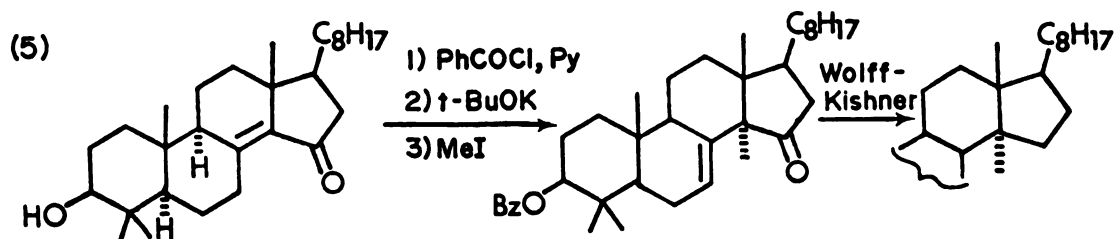


The euphane/tirucallane skeleton probably cannot be obtained by such polyene cyclizations, because of the ease

with which compounds of this family undergo acid-catalyzed rearrangement:⁸

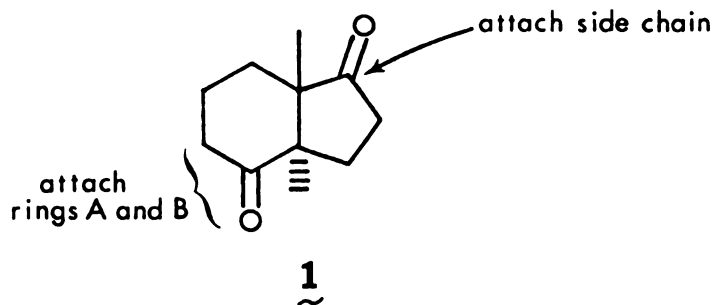


Another successful approach to the synthesis of 14 α -methyl steroids and triterpenes involves the methylation of 15-keto intermediates. This strategy was used in the first synthesis of lanosterol (from cholesterol)⁹ and was also used for the preparation of 14 α -methyltestosterone and 14 α -methylprogesterone analogs.¹⁰

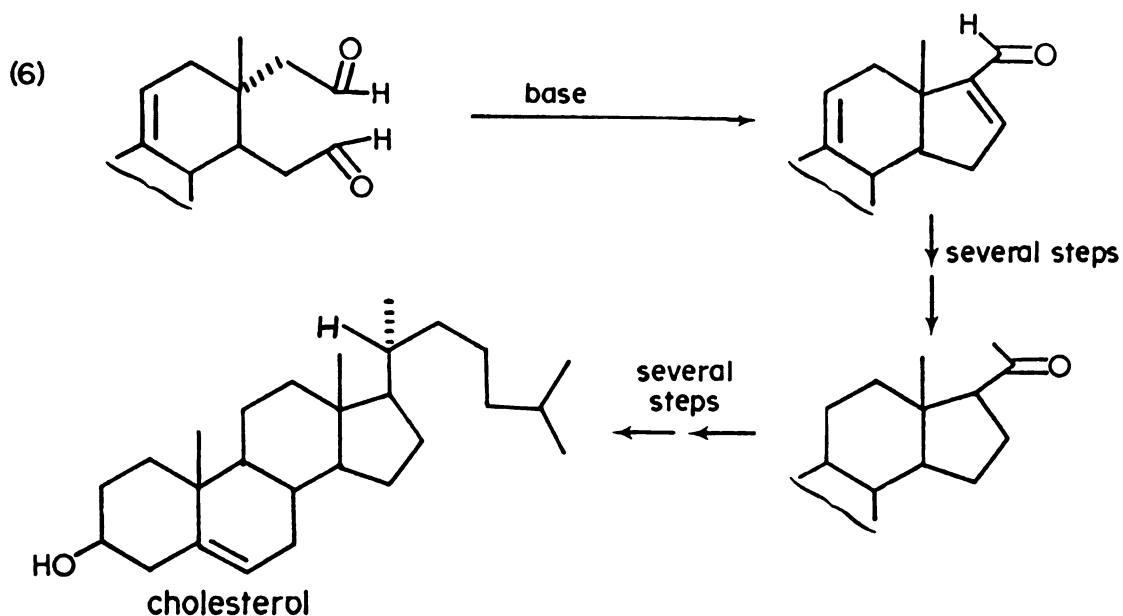


The use of 1 as the basis for a total synthesis of the lanostane and euphane triterpenes is particularly

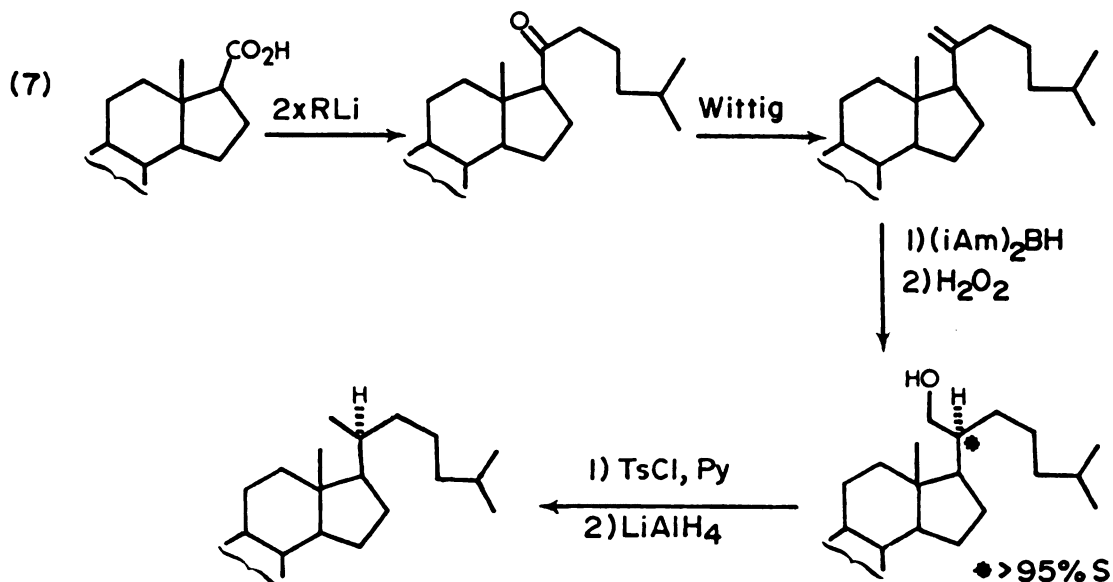
attractive since it would avoid a 14α -methylation step. Such a total synthesis would necessarily be conducted in two parts. First, the A and B rings must be joined to appropriate sites on the six-membered ring of 1. Second, a side chain must be attached to the carbonyl function of the five-membered ring:



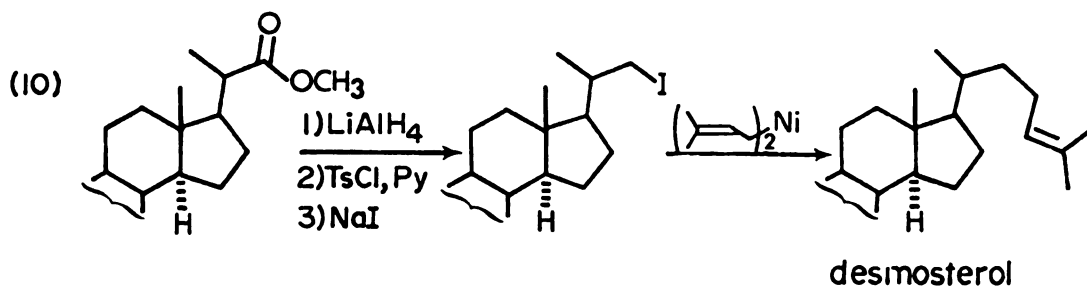
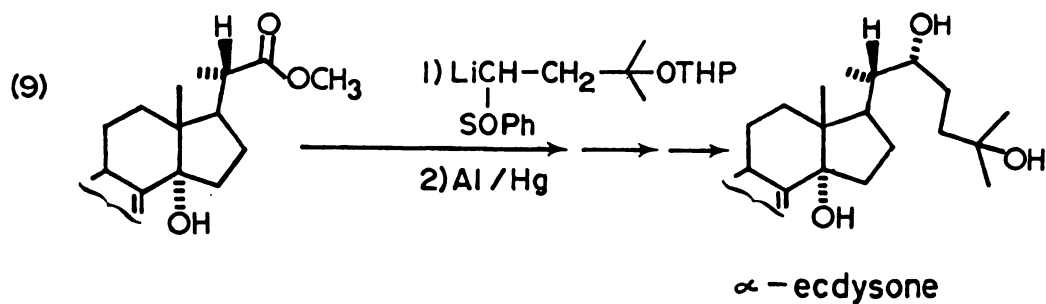
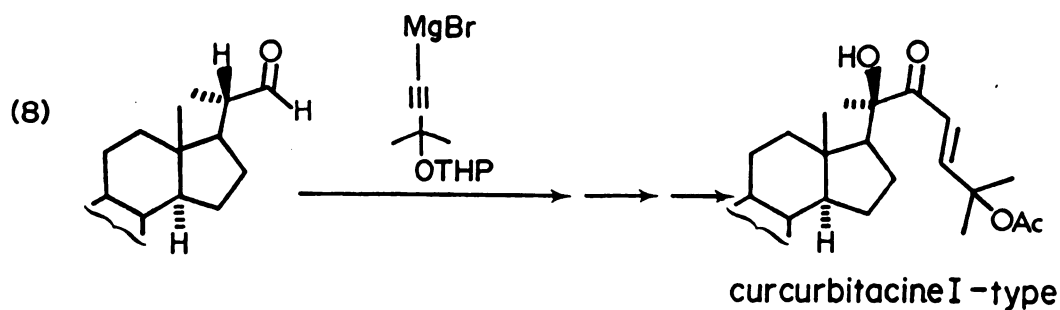
A literature search disclosed three general strategies which have been used for building the eight-carbon cholestane side chain. The first strategy, utilized in Woodward's cholesterol synthesis,¹¹ proceeds by a condensation to form the D ring, elaboration to a pregnane side chain, and addition of an isohexyl unit as the alkyl magnesium bromide (equation 6). The isohexyl unit has also been added as a Wittig reagent.¹²

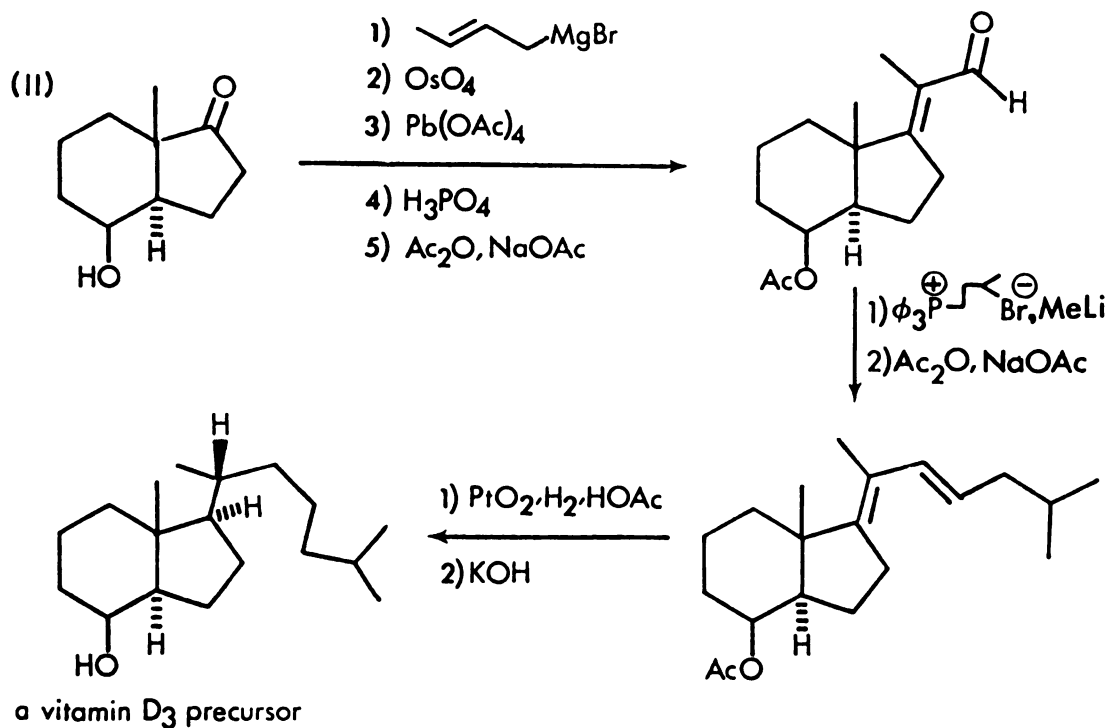


The second strategy results from a combination of two independent studies. It proceeds by addition of an isohexyl unit to a carboxylic acid,¹³ followed by a Wittig reaction,¹⁴ and a stereoselective hydroboration¹⁴ (equation 7):



The third route, used in the synthesis of the curcurbitacin I,¹⁵ ecdysone,¹⁶ desmosterol,¹⁷ and vitamin D₃¹⁸ side chains, proceeds through a C-22 carbonyl function and concludes with the addition of an isohexyl unit as illustrated below:





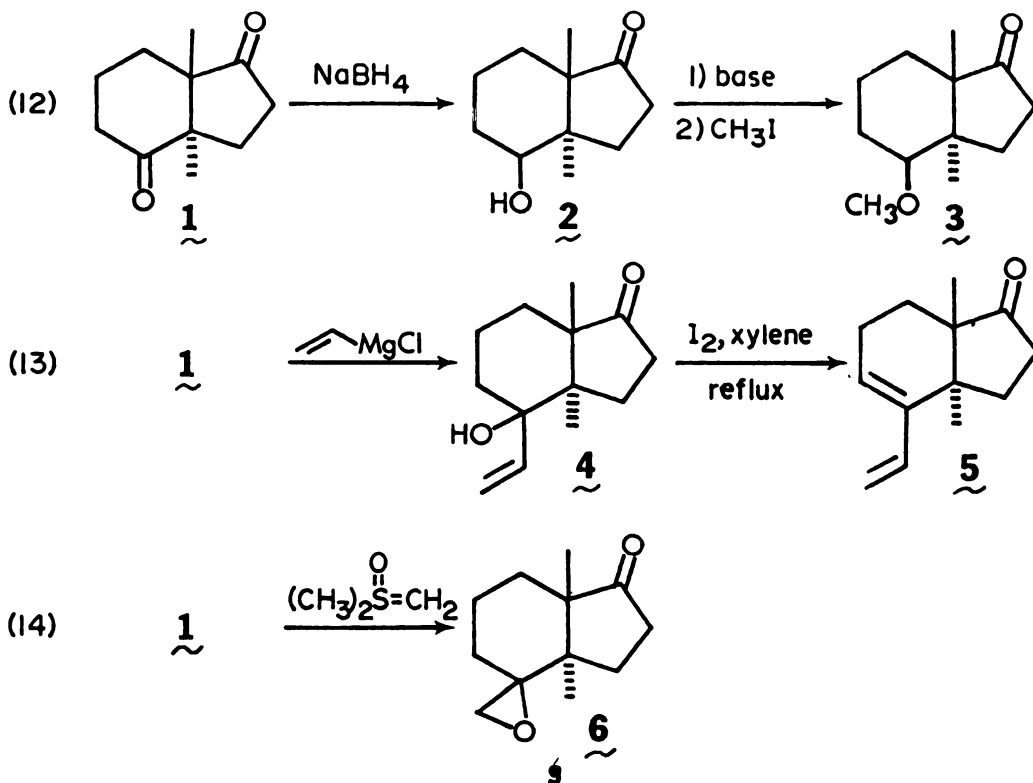
This dissertation describes experiments which explore the reactivity of the perhydroindenedione 1 and offer the possibility of attaching a side chain to the five-membered ring of 1 with the natural configuration.

RESULTS AND DISCUSSION

A. Survey of Carbonyl Reactivity in 1

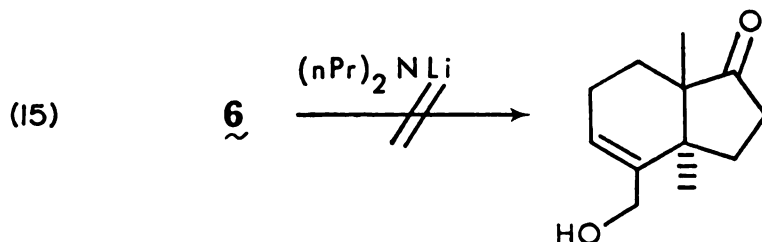
As well as being the potential basis of a total synthesis of several tetracyclic triterpenes, the perhydroindenedione, 1, offered a unique opportunity to study the comparative reactivity of five- and six-membered ring ketones with similar steric environments.

Some idea of the difference in reactivity between the five-membered ketone and the six-membered ketone can be gained by considering the selective transformations outlined in equations 12, 13, and 14:

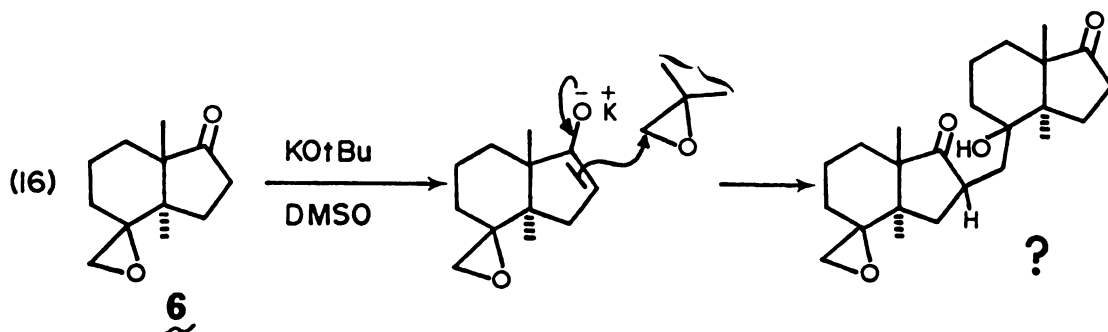


Thus, a very high degree of selectivity, favoring addition to the six-membered carbonyl group, was observed for sodium borohydride reduction, vinyl magnesium chloride addition and sulfoxonium ylide combination with 1. Subsequent transformations of these products have implications for future work to introduce fused rings A and B or a C-17 side chain. For example, protection of the hydroxyl group in 2 as an ester or ether derivative should permit chemical transformations of the relatively unreactive five-membered carbonyl function. To this end, compound 2 was methylated and yielded the expected methyl ether 3. Compound 3 was accompanied by small amounts of side products, presumably resulting from alkylation of the carbon atom alpha to the carbonyl function. The vinyl carbinol 4 proved to be difficult to dehydrate, but finally yielded to treatment with iodine in refluxing xylene¹⁹ to form the diene 5. The diene 5 did not form Diels-Alder adducts with maleic anhydride or tetracyanoethylene in refluxing xylene, or with benzoquinone in refluxing chlorobenzene.²⁰ Epoxide 6 was formed in excellent yield by reaction with dimethyloxosulfonium methylide²¹ in DMSO solution for more than one week at ambient temperature. Epoxide 6 was fairly resistant to boron trifluoride etherate at room temperature, yielding only small amounts of isomerized material which was not isolated. Treatment of 6 with lithium di-*n*-propyl amine

in refluxing ether²² failed to give the expected β -elimination product (equation 15):



However, treatment of **6** with potassium *tert*-butoxide in hot DMSO²³ gave a product, the mass spectrum of which suggested a condensation product of two units of **6** (equation 16):



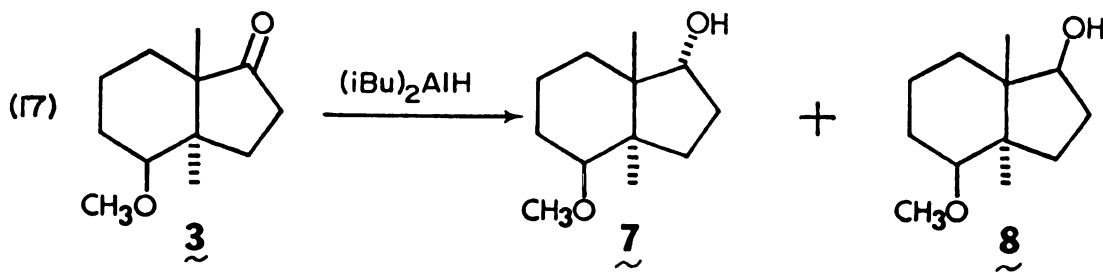
In retrospect, the greater reactivity of the six-membered ketone of **1** compared with the five-membered ketone is a good illustration of a general principle summarized over twenty years ago by Professor H. C. Brown:

"It follows that in the 5-membered ring the trigonal structure for one of the ring atoms is strongly favored over the tetrahedral arrangement, whereas the reverse is true in

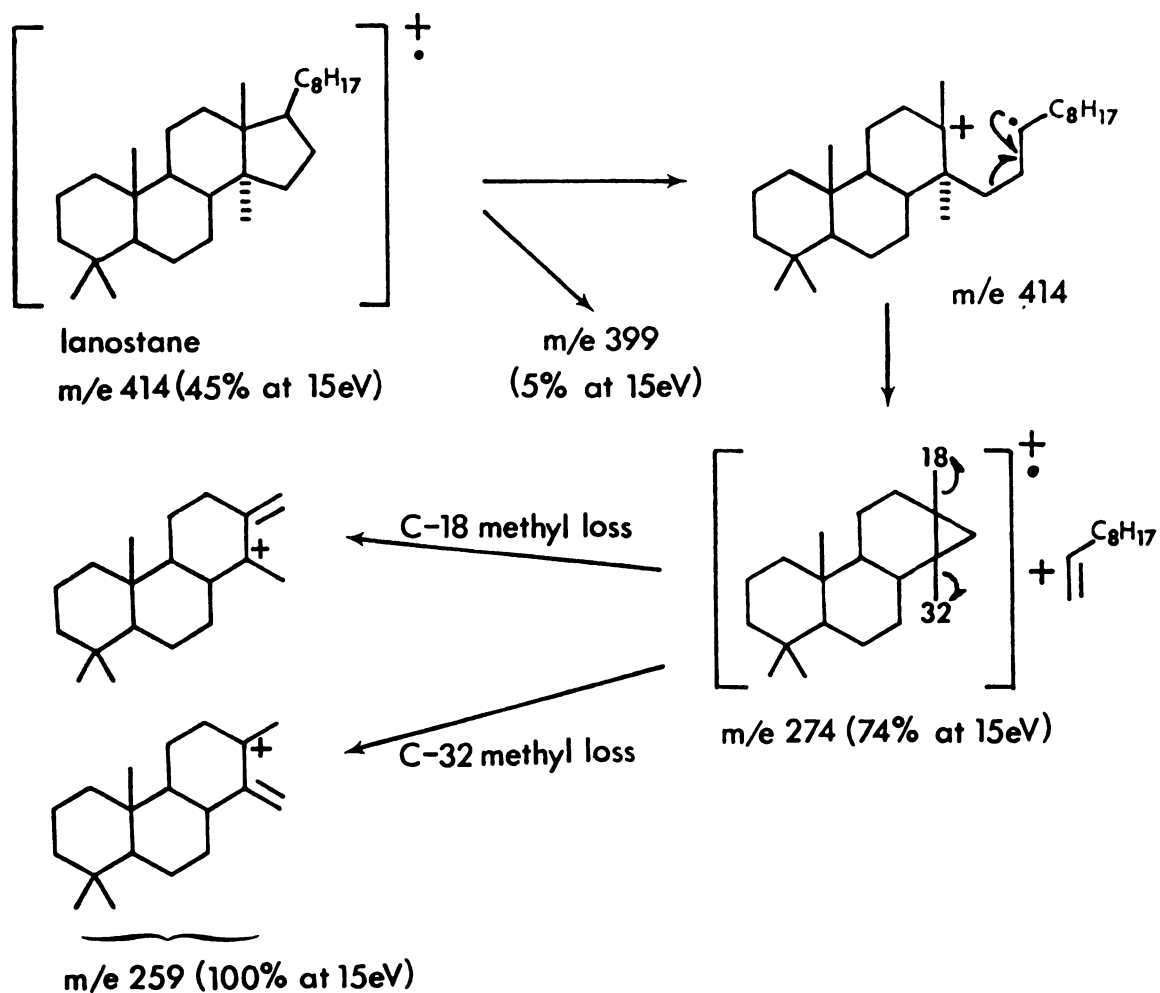
the 6-membered ring. Let us assume that this result will be generally true for all derivatives of 5- and 6-membered rings. In other words let us assume that an exo double bond in all 5-membered ring systems will be more stable toward changes involving loss of the exocyclic double bond than will the corresponding exo double bonds in 6-membered ring systems."²⁴

The methoxy ketone 3 was used as the starting material for all subsequent efforts directed toward a side chain synthesis. To this end, the widely studied 17-keto steroids²⁵ served as excellent models for many of the reactions that were investigated.

Although 3 can be reduced with excess lithium aluminum hydride, this reduction is best accomplished by treatment with diisobutyl aluminum hydride. A pair of epimeric alcohols were produced (equation 17), isolated, and analyzed spectroscopically.

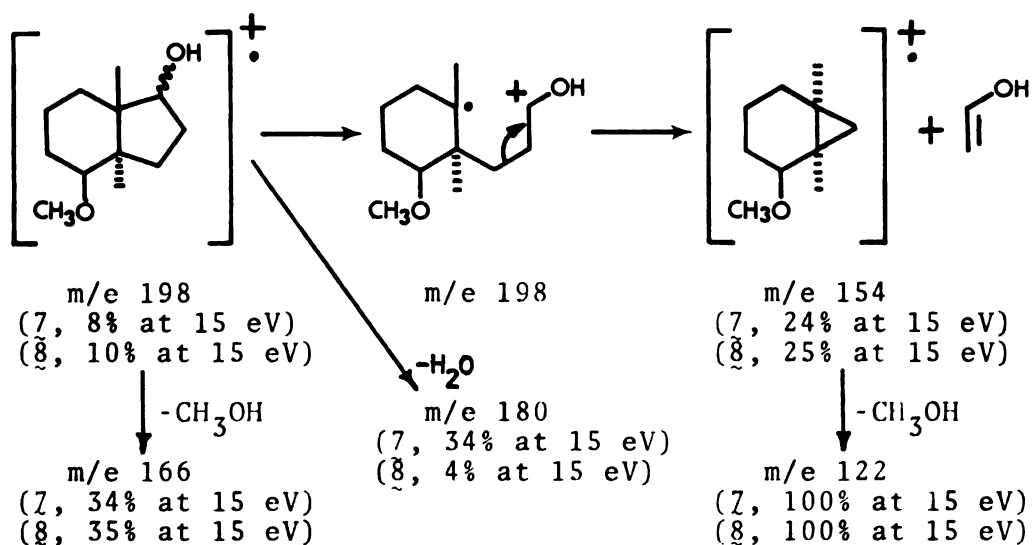


The mass spectra of 7 and 8 were studied because of the possible parallel fragmentation to the D ring cleavage in lanostane,²⁶ illustrated in part below:



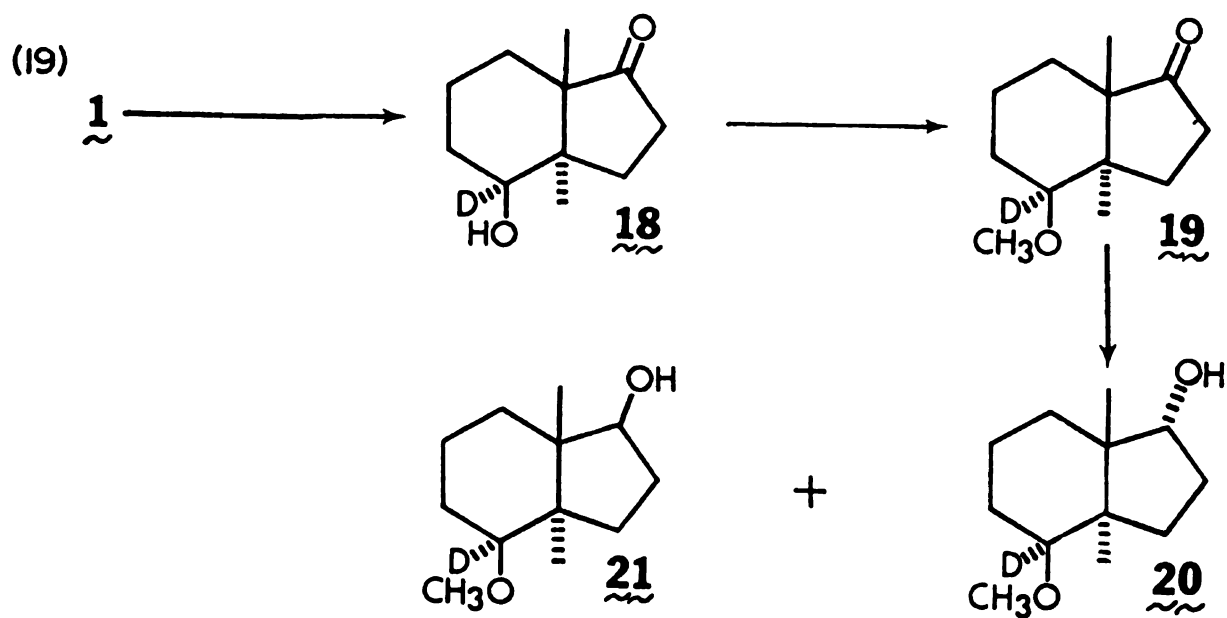
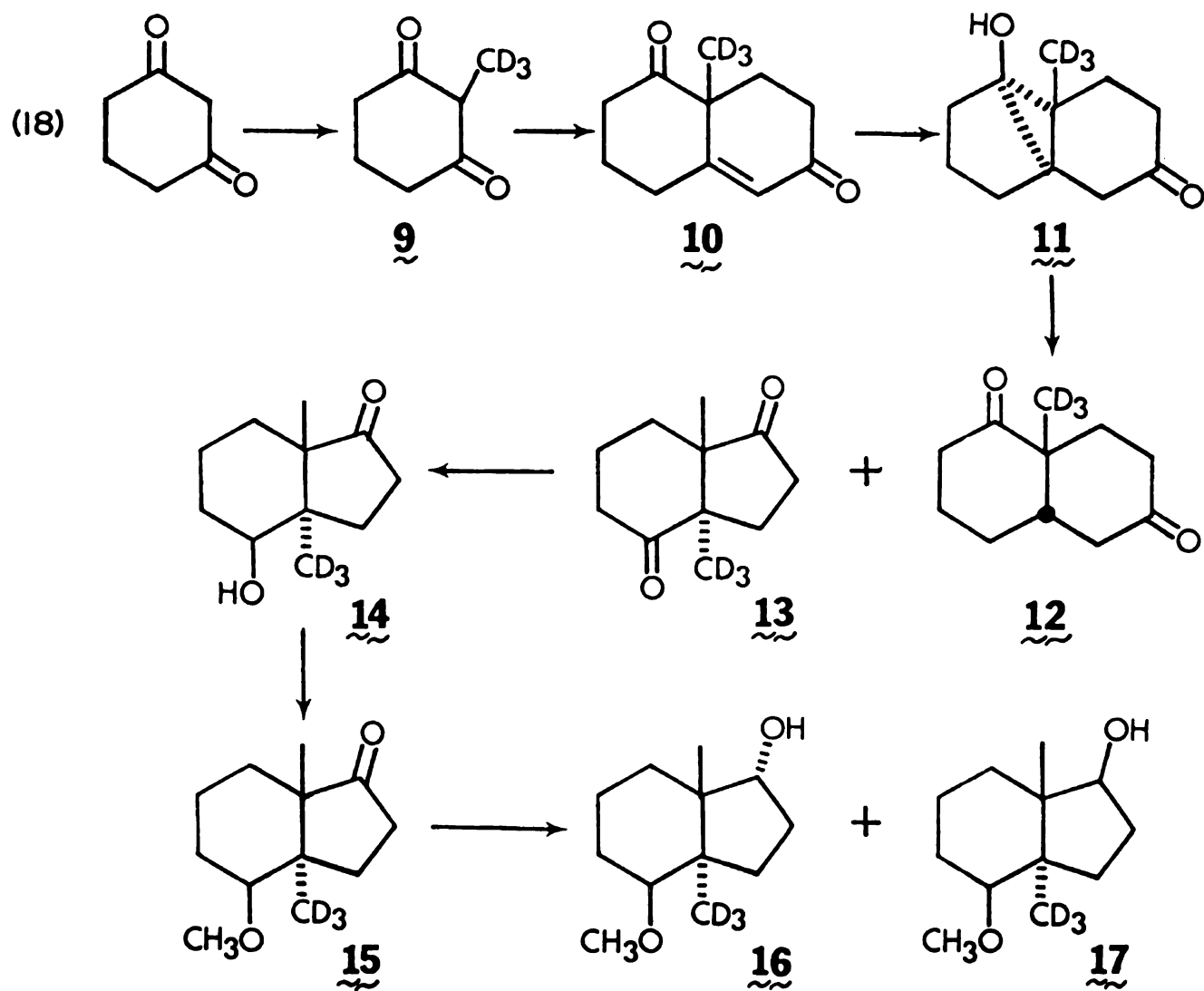
Scheme 1

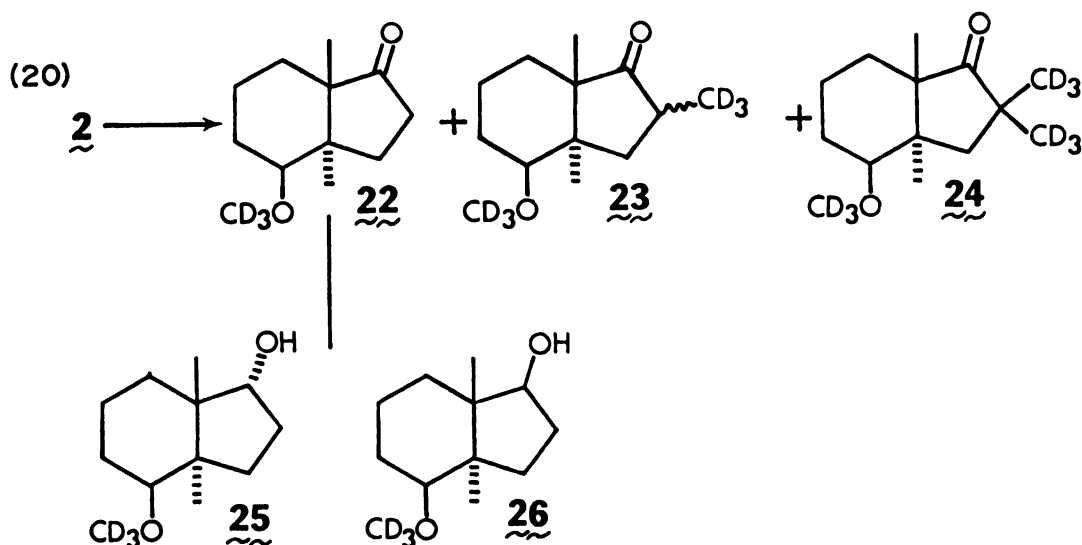
Indeed, the mass spectra of 7 and 8 were similar to that of lanostane with respect to the formation of an m/e 154 fragment by loss of C_2H_4O , and the lack of substantial methyl loss (M-15):



Scheme 2

An eight-fold preference for the loss of water (M-18) from 7 relative to 8 in the 15 eV mass spectra of these epimers must be related in some way to their different configurations. In an effort to determine the nature of this potentially useful stereochemical discrimination, three deuterium labeled analogs of 7 and 8 were prepared, as outlined in equations 18, 19, and 20.

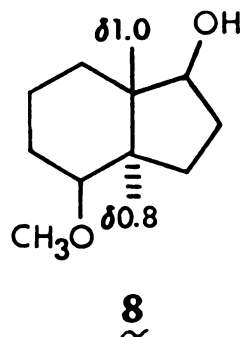
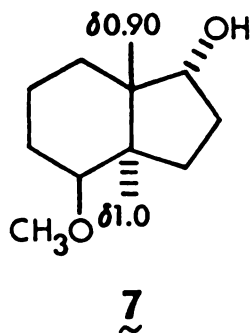




The formation of 22, 23, and 24 in nearly equal amounts is a dramatic example of the difference between methyl iodide and its d_3 analog, the latter being smaller and more able to "invade" the crowded environment of the five-membered ring.

Compounds 7, 16, 20, and 25 all have lower melting points and more abundant M-18 ions than their corresponding epimers (8, 17, 21, and 26). More importantly, no M-19 ion was observed in any of the deuterium labeled compounds. The mass spectra of 7 and 8 were therefore not helpful in assigning configurations to these isomers. Compound 7 moves faster than 8 on TLC and GLPC, as expected for that isomer having a pseudo-equatorial hydroxyl function. However, this difference is not sufficient to anchor an iron clad structure assignment.

Fortunately, the angular methyl resonance signals in 7 and 8 (with the aid of the selectively deuterated analogs 16 and 17) can be interpreted in a fashion that leads to a clear configuration and assignment.



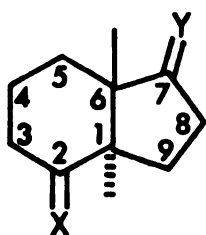
Bhacca and Williams²⁷ have tabulated the incremented effects of substituents on the chemical shift of C-18 and C-19 protons for the 5 α ,14 α -androstane series. After assigning the chemical shifts of the angular methyl groups bonded to C-1 and C-6 of the perhydroindenes 1, 2, 3, 7, and 8 (Table 1), the chemical shift difference for each compound was calculated from the appropriate steroid methyl increments and compared with the observed value (Table 2). Hydroxyl increments were used as an estimate for the methoxyl function in 3, 7, and 8. The good correlation of the observed and calculated chemical shift differences (Δ) for 7 and 8 seems to justify their assigned structures.

Table 1. Assignment of chemical shifts (ppm)

Compound	C-6 methyl	C-1 methyl	C-6 methyl (d_3 analog)
1 ~	0.85	1.15	0.95 (13)
2 ~	1.25	0.90	1.25 (14)
3 ~	1.15	0.85	1.10 (15)
7 ~	0.90	1.00	0.95 (16)
8 ~	1.00	0.80	1.05 (17)

Table 2. Calculated and observed Δ ($\delta_1 - \delta_6$) values (ppm)

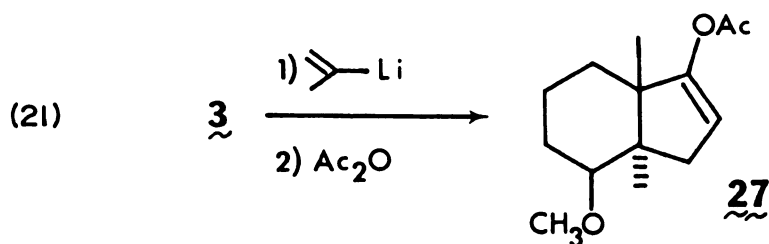
Compound	Δ obs	Δ calc	steroid increments used
1 ~	0.30	0.32	C-6: 17-oxo(C-18) + 4-oxo(C-19) C-1: 12-oxo(C-18) + 15-oxo(C-18)
2 ~	-0.35	-0.32	C-6: 17-oxo(C-18) + 4 β -OH(C-19) C-1: 15-oxo(C-18) + 12 α -OH(C-18)
3 ~	-0.30	-0.32	same as for 2
7 ~	0.10	0.05	C-6: 17 α -OH(C-18) + 4 β OH(C-19) C-1: 15 β -OH(C-18) + 12 α -OH(C-18)
8 ~	-0.20	-0.23	C-6: 17 β -OH(C-18) + 4 β OH(C-19) C-1: 15 α -OH(C-18) + 12 α -OH(C-18)



- 1, X = Y = 0
 2, X = β -OH, α -H; Y = 0
 3, X = β -OCH₃, α -H; Y = 0
 7, X = β -OCH₃, α -H; Y = β -H, α -OH
 8, X = β -OCH₃, α -H; Y = β -OH, α -H

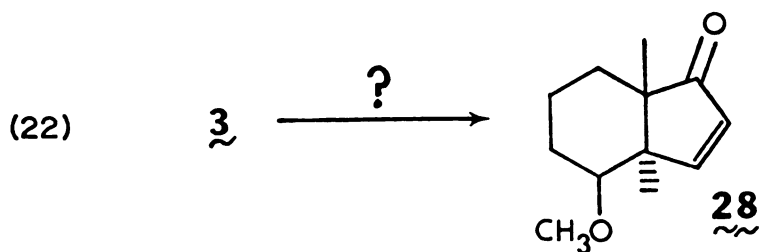
B. Approaches to Side Chain Synthesis

Treatment of 3 with isopropenyl lithium, vinyl lithium, vinyl magnesium chloride, and methyl lithium failed to yield a carbonyl adduct. However, when 3 was treated with isopropenyl lithium, followed by acetic anhydride, the enol acetate 27 was isolated (equation 21). This illustrated the propensity of 3 to form an enolate anion, rather than an adduct, in the presence of organometallic reagents.

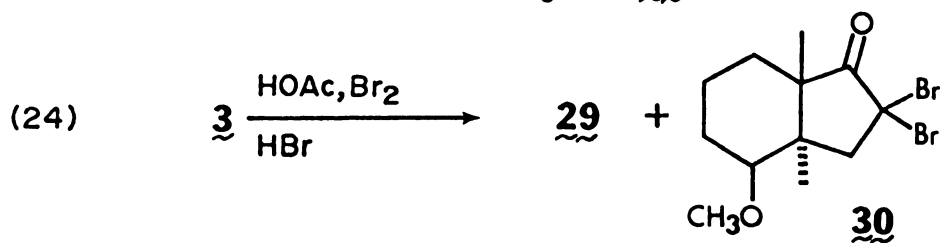
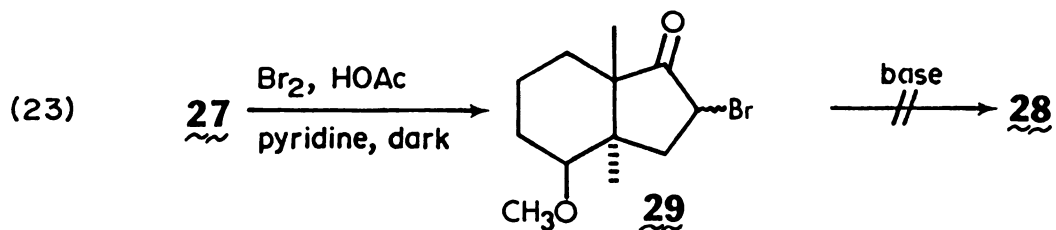


In order to avoid enolization of 3, under such reaction conditions, an attempt was made to synthesize the α,β -unsaturated compound 28, which is incapable of

enolization, but should still be subject to attack by carbon nucleophiles.

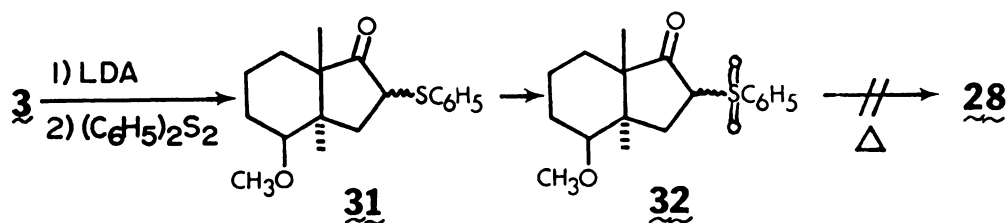


The bromide 29 was synthesized from both 3 and the enol acetate 27 ; 28 however, 29 proved to be resistant to dehydrobromination by pyridine-silver nitrate, potassium hydroxide, and potassium *tert*-butoxide.

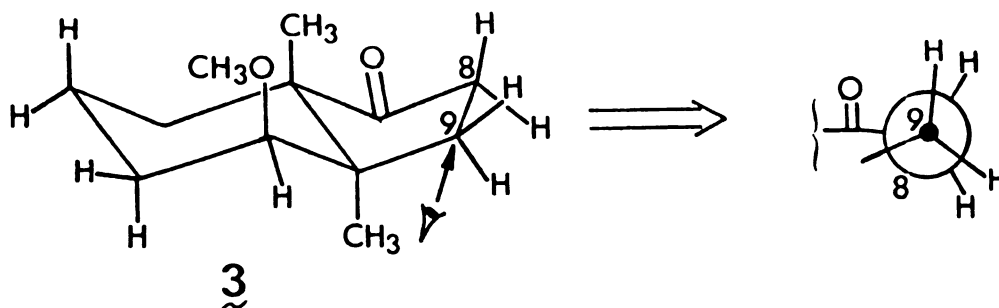


Likewise, the sulfone 32 failed to eliminate thermally, 29 in refluxing xylene, to give 28 .

(25)

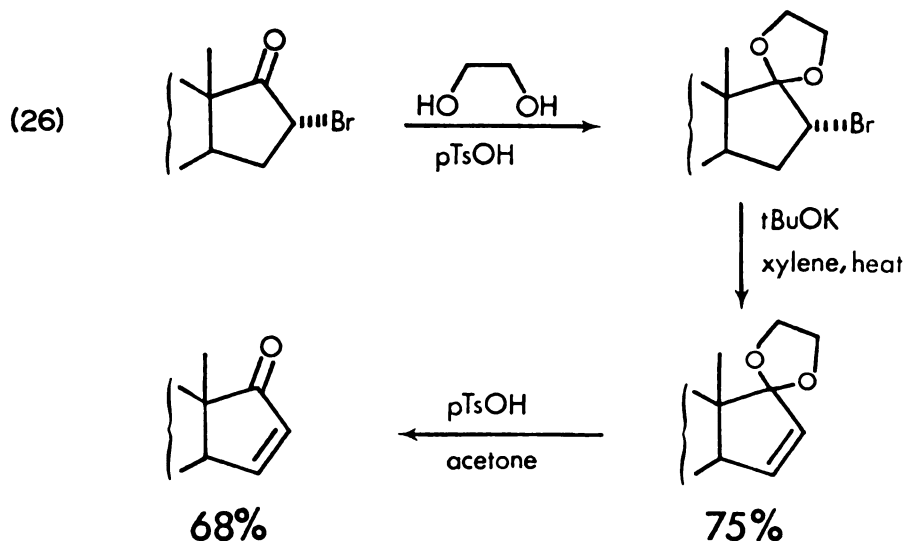


Examination of a Dreiding model of **3** indicates that its *trans*-configuration induces a puckering of the five-membered ring, analogous to the configuration of the 17-keto steroids:



It has been noted³⁰ in the case of the 16-bromo-17-keto steroids, that introduction of a double bond in the D ring would cause additional ring strain by flattening the ring, and this would in fact oppose dehydrohalogenation. Indeed, attempted dehydrohalogenation of such a steroid has led to extensive decomposition.³¹ Successful dehydrohalogenation of the 16-bromo-17-keto steroids can be effected, however, by protection of the 17-keto function

as an ethylene ketal during the dehydrohalogenation.³²



This approach is precluded in the present case because an ethylene ketal derivative of the keto function in 3 cannot be made.³³

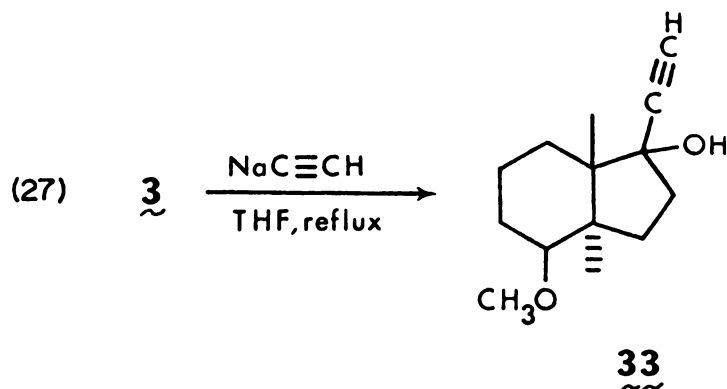
A variety of ylides and ester enolates also failed to form an adduct with the carbonyl function in 3 (Table 3). The addition of Wittig reagents,^{34,35} ylides,²¹ and Reformatsky reagents³⁹ to the 17-keto function of steroids has been successfully effected in the past.

The prospect for successful side-chain introduction improved temporarily with the discovery that freshly prepared sodium acetylide in THF solution gave an adduct with 3 (equation 27). In the context of previous failures, this success was not unexpected, since the acetylide nucleophile is smaller and less basic than the alkyl

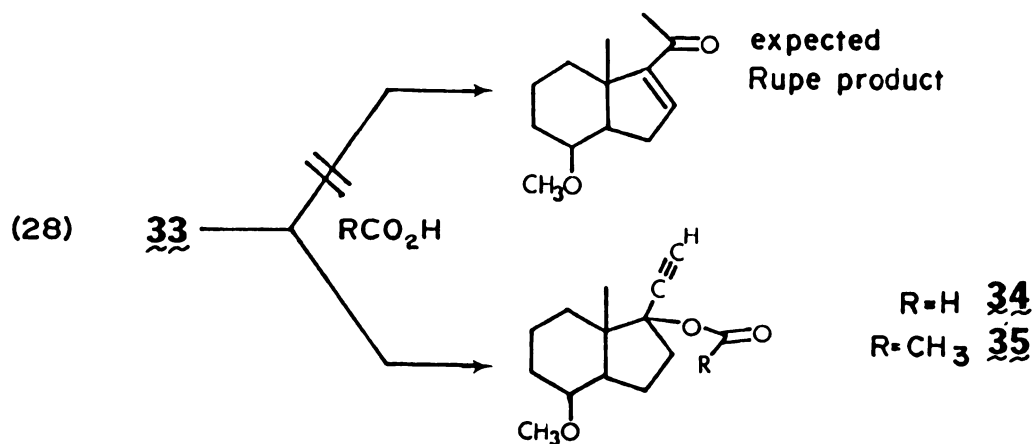
Table 3. Reagents which failed to form adducts to 3

REAGENT	REFERENCE
$(\text{C}_6\text{H}_5)_3\text{P}=\text{CH}-\text{CO}_2\text{Et}$	34
$(\text{EtO})_2\overset{\text{O}}{\underset{\text{ }}{\text{P}}}-\text{CH}=\text{CH}-\text{NHC}_6\text{H}_{11}, \text{NaH}$	35
$(\text{CH}_3)_2\overset{\text{O}}{\underset{\text{ }}{\text{S}}}=\text{CH}_2$	21
$\text{CH}_2=\text{C}\begin{matrix} \text{OLi} \\ \text{OtBu} \end{matrix}$	36
$(\text{CH}_3)_3\text{Si}-\text{CH}=\text{C}\begin{matrix} \text{OLi} \\ \text{OtBu} \end{matrix}$	37
$\text{CH}_2=\text{C}\begin{matrix} \text{OLi} \\ \text{OEt} \end{matrix}$	38
$\text{Br}-\text{CH}_2-\text{CO}_2\text{Et}, \text{Zn}$	39

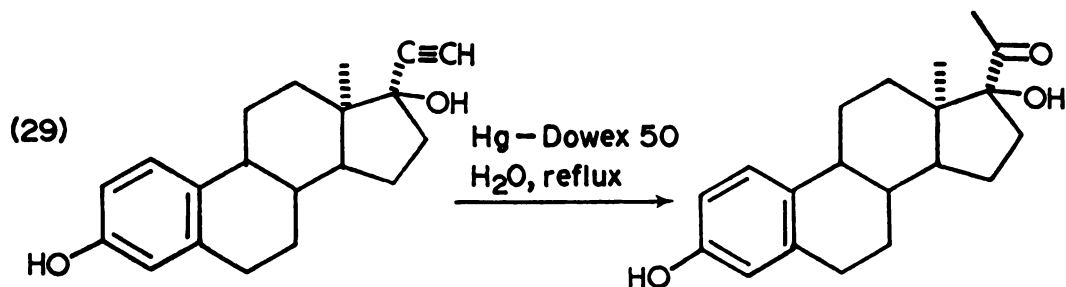
lithium reagents used earlier. Although the yield of adduct 33 was modest (41% isolated yield), it appeared as though elaboration of the ethynyl carbinol group to a terpene side chain would be a simple exercise in applying known procedures to an unexceptional substrate.



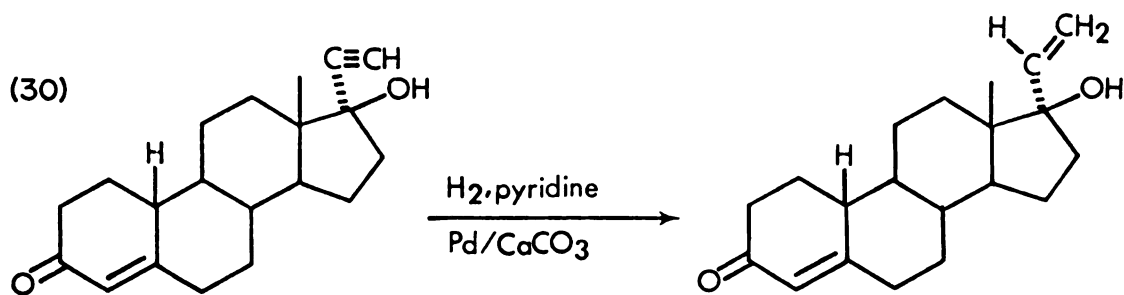
Unfortunately, adduct 33 proved to be completely resistant to all efforts to transform it into useful intermediates. The Rupe rearrangement,⁴⁰ for example, failed to proceed in either formic or acetic acid and yielded only the corresponding esters (equation 28).



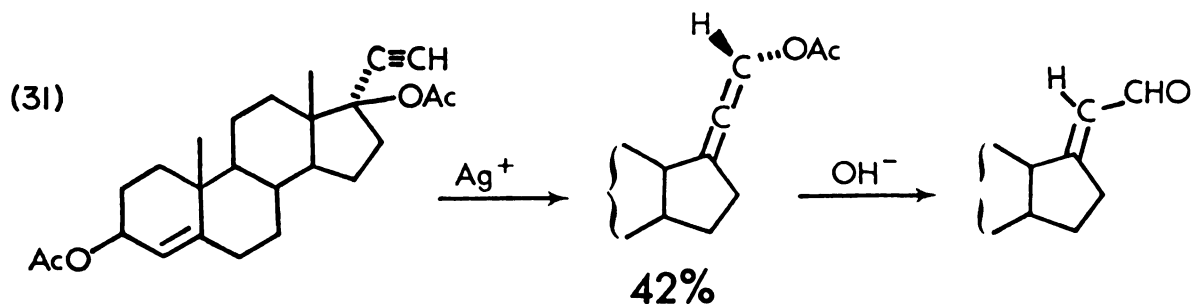
Attempts to effect hydrolysis of the triple bond by mercury catalyzed addition of water⁴¹ failed under a variety of conditions, some of which successfully transform 17-ethynylcarbinol derivatives of steroids⁴² (equation 29).



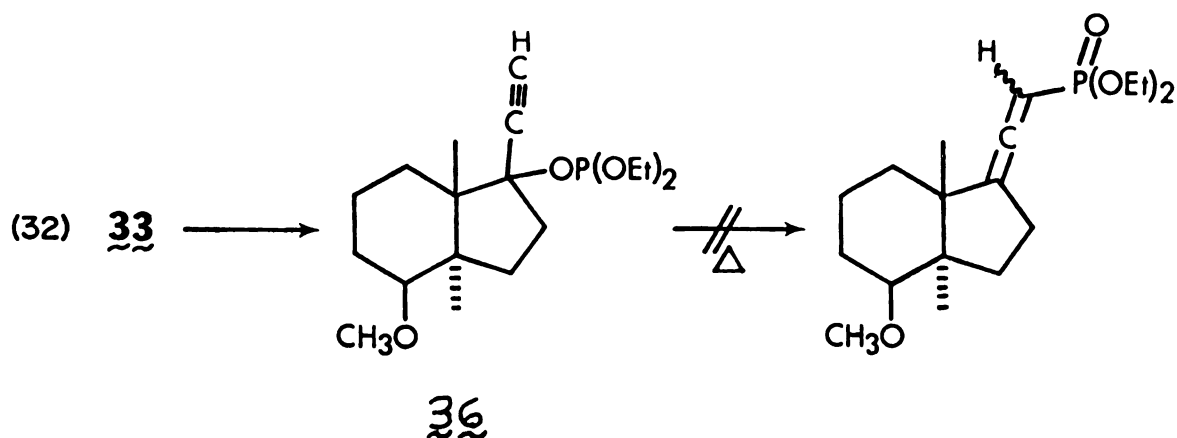
The ethynyl function of 33 also resisted reduction to a vinyl group by lithium aluminum hydride,⁴³ diisobutyl aluminum hydride,⁴⁴ and catalytic hydrogenation. Several hydrogenation conditions were explored, the least active of which has been used to reduce an ethynyl steroid⁴⁵ (equation 30).



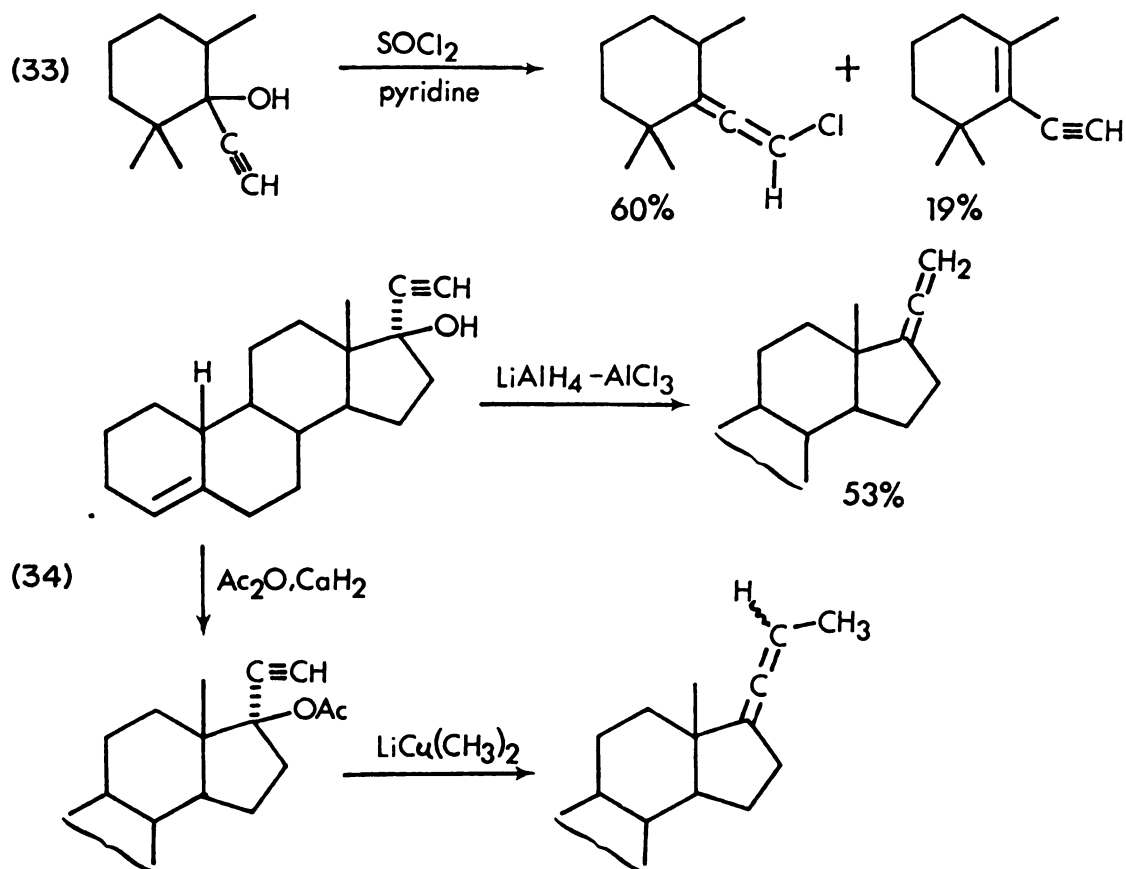
Experiments were then conducted with the objective of turning 33 or a derivative into an allene, but this effort proved to be equally frustrating. One series of experiments failed in the attempt to force a Claisen-Cope rearrangement of 34 and 35 by thermolysis, or by treatment of 35 with silver perchlorate in refluxing acetone,⁴⁶ a procedure successfully used with steroid analogs (equation 31).



Even the normally facile rearrangement of propargylic phosphites to phosphonate esters⁴⁷ failed to proceed (equation 32).

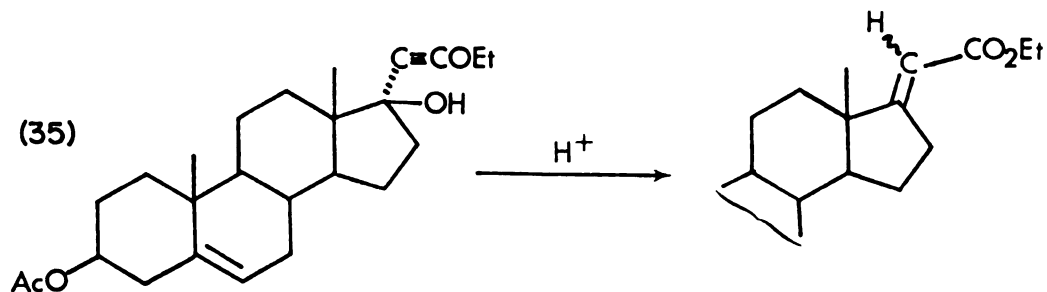


The ethynyl groups of 33 and 35 were also impervious to allene formation in the presence of thionyl chloride-pyridine,⁴⁸ lithium aluminum hydride--aluminum trichloride,⁴⁹ and dimethyl copper lithium,⁴⁹ the precedents for which are outlined below:

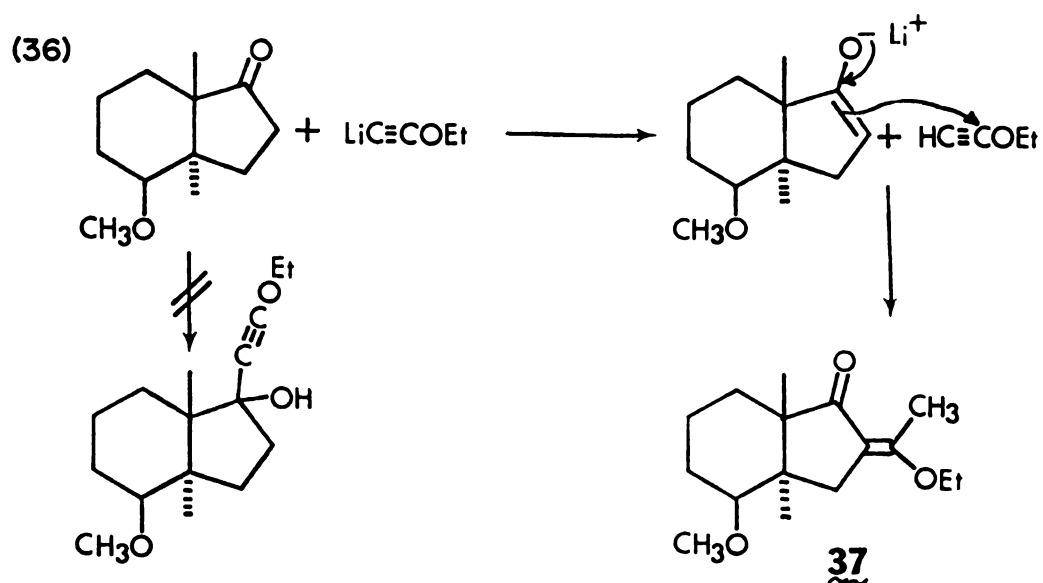


Some of the reaction conditions to which 3 was subjected, yielded unexpected results. Treatment of 3 with lithium ethoxyacetylene⁵⁰ gave a one-to-one adduct (37), as confirmed by its mass spectrum and elemental analysis. The infrared spectrum of 37 displayed a strong carbonyl band, and its C^{13} magnetic resonance spectrum displayed resonances which suggested a carbonyl (δ 113) and a double bond (δ 163 and 183). The above information implied that adduct 37 had undergone the known isomerization to an α,β -unsaturated ester

in the same fashion as the steroid isomerization⁵¹ shown in equation 35.

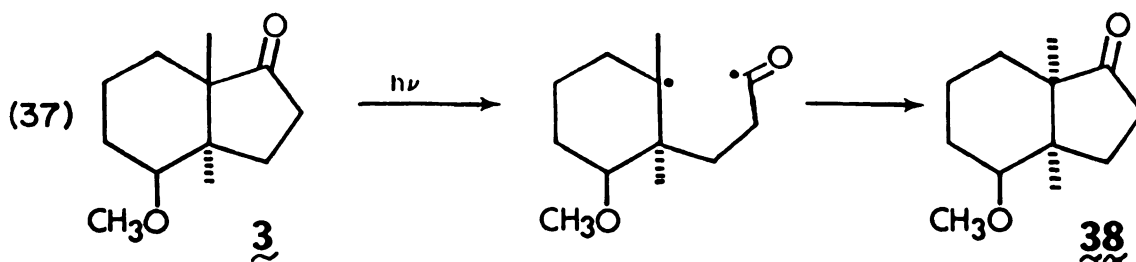


However, the lack of a resonance signal in the vinyl region of the proton magnetic resonance spectrum of 37 ruled out such a structure for this compound. Accordingly, an X-ray crystal structure determination⁵² of the yellow, crystalline solid was completed. The results of this analysis were surprising and are displayed in equation 36.



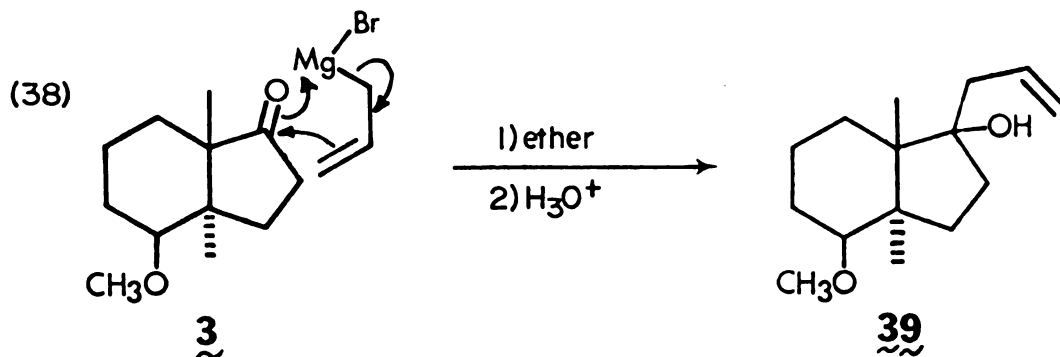
There is no precedent for an enolate condensing with ethoxyacetylene in this manner. However, amines, alcohols, and thiols do add in this fashion.⁵³

Since it has been shown⁵⁴ that certain acetylenes will add to ketones in a [2+2] manner upon photolysis, 3 was irradiated in the presence of ethoxyacetylene. The result of the experiment was to isomerize 3 into its *cis*-isomer 38:



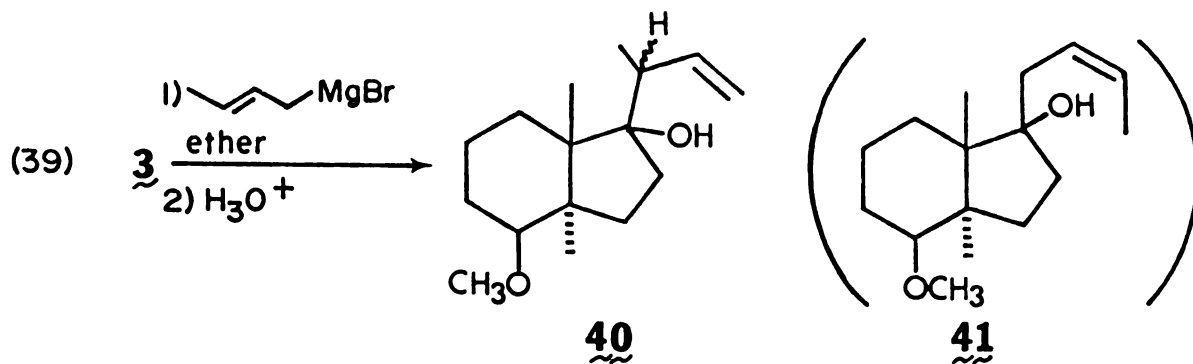
It may be noted that 38, or a modified version of it, is a potential starting material for the synthesis of 14 β -methyl steroids.

The ability of allyl and crotyl Grignard reagents⁵⁵ to form addition products with hindered ketones such as di-*tert*-butyl ketone in high yield⁵⁶ seemed worth exploring. Accordingly, 3 was reacted with allyl magnesium bromide in THF solution for two days, and recovered unchanged. However, a parallel experiment in ether solution proved successful, yielding 39 as the only product. One epimer of undetermined stereochemistry greatly predominated, as evidenced by the pmr spectrum of the product.

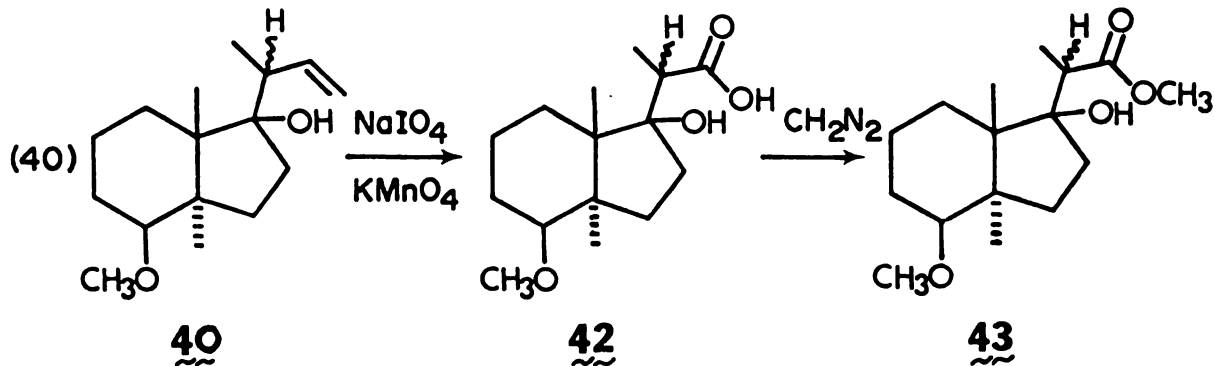


As shown in equation 38, the success of this addition reaction results from the ability of the magnesium, an electron deficient species, to coordinate with the ketone oxygen, thereby facilitating the known⁵⁵ cyclic mechanism by which allyl Grignards add to ketones. Apparently, THF complexes more strongly with the Grignard reagent than the ketone oxygen does, and the reaction is retarded in this solvent.⁵⁷

This reaction was extended to the case of crotyl magnesium bromide with excellent results. Reaction of 3 with this Grignard reagent produced the α -methyl alkyl adduct 40 after one hour's reaction time. Compound 3 had been totally consumed, and no trace of 41 was detected. However, longer reaction times (ca. one week) yield 41 as the only product, in accord with previous work.⁵⁵



Compound 40 was subjected to conditions which effected oxidative cleavage of the olefin bond.⁵⁸ The crude acid 42 was treated with excess diazomethane to form the β -hydroxy ester 43, which was obtained as a low melting solid after purification by high pressure liquid chromatography (HPLC), in 36% yield from 40.



Even though GLPC of 40 and 43 discloses a single peak in each case, analysis by HPLC shows that they are each a mixture of two compounds. These are presumably epimers at the position corresponding to C-20 on the steroid nucleus.

The synthesis of 43 accomplishes the primary goal of this dissertation, since this compound is closely related to other precursors to successful side chain syntheses.^{15,16,17,18}

EXPERIMENTAL

General

Except as indicated, all reactions were conducted under dry nitrogen or argon, using solvent purified by distillation from suitable drying agents. Magnetic stirring devices were used for most small scale reactions; larger reactions were agitated by paddle stirrers. Organic extracts were always dried over anhydrous sodium sulfate before being concentrated or distilled under reduced pressure. The progress of most reactions was followed by thin layer chromatography (TLC) and/or gas liquid phase chromatography (GLPC). Visualization of the thin layer chromatograms was effected by spray reagents such as 5% *p*-anisaldehyde in ethanol and 30% sulfuric acid with subsequent heating.

Analysis by GLPC was conducted with A-90-P3 or 1200 Varian-Aerograph instruments. Preparative layer chromatography was carried out on 2 mm silica gel F-254 adsorbent on 20 x 20 cm glass plates. Visualization of the preparative plates was effected by ultraviolet light and/or charring with a hot wire. Melting points were determined on either a Hoover-Thomas apparatus (capillary tube) or on a Reichert hot-stage microscope and are uncorrected.

Infrared spectra (ir) were recorded on a Perkin-Elmer 237B grating spectrophotometer. Proton magnetic resonance spectra (pmr) were taken in deuteriochloroform or CCl_4 solutions with a Varian T-60 spectrometer and are calibrated in parts per million (δ) downfield from tetramethylsilane as an internal standard. Ultraviolet spectra (UV) were recorded on a Unicam SP-800 spectrophotometer. Mass spectra (ms) were obtained with a Hitachi RMU 6 mass spectrometer. Carbon magnetic resonance spectra (cmr) were taken in deuteriochloroform solution with a Varian CFT-20 spectrometer and are calibrated in parts per million (δ) downfield from tetramethylsilane as an internal standard.

Microanalyses were performed by Spang Microanalytical Labs, Ann Arbor, Michigan.

Preparation of 2-Methylcyclohexan-1,3-Dione

A solution of 80.0 g (2.0M) of sodium hydroxide in 500 ml of water was added to 224 g (2.0M) of cyclohexan-1,3-dione. The solid quickly dissolved to form a red solution which was cooled to 0° ; then 312 g (2.2M/138 ml) of methyl iodide was added in one portion, and the mixture was refluxed for 12 hr. The reaction was cooled to 0° and the precipitated 2-methylcyclohexan-1,3-dione was filtered and rinsed with cold water to remove all traces of sodium iodide. The filtrate and washings were combined and placed in a reaction flask along with 40 ml of methyl iodide and refluxed 12 hr. The product was isolated in

the same manner described previously. The combined solid product was air dried for 24 hr, and then dried in a vacuum oven (40°/1 torr) for 12 hr. The product thus obtained (194 g, 77%) was suitable for use without further purification. It may be recrystallized (20 ml ethanol/5 g substrate) to give material with mp 209--211° (lit⁵⁹ mp 208--210°).

Preparation of 6-Methylbicyclo[4.4.0]dec-
1-ene-3,7-dione

A solution of 0.5 g (about 6 pellets) of potassium hydroxide in 500 ml of absolute methanol was added to 126 g (1.0M) of 2-methylcyclohexan-1,3-dione, followed by 77 g (1.1M) of methyl vinyl ketone (Aldrich). The mixture was refluxed for 3 hr, then cooled to room temperature, and the unreacted methyl vinyl ketone and methanol were removed under vacuum. The residual oil was dissolved in 500 ml of benzene in a one liter round bottom flask, equipped with a Dean-Stark trap and condenser, treated with 6 ml of pyrrolidine, and then refluxed for 90 min. At this point, 18 ml of water had collected in the Dean-Stark trap. Prior to cooling it to room temperature, 100 ml of benzene was then distilled from the reaction mixture. The dark solution was diluted with 300 ml of ether, washed with 4N hydrochloric acid until no more red colored material was removed, washed sequentially with water and brine, and dried. Removal of the solvents yielded 175 g of light brown oil which was diluted with

90 ml of ether and placed in the refrigerator. Crystallization yielded 113 g (63%) of slightly yellow, crystalline product which had mp 50--53° (ether) (lit⁶⁰ mp 47--50°).

Preparation of (1R*,5 α ,6 β)-5-Hydroxy-6-Methyl-Tricyclo[4.4.0.0^{1,5}]decan-9-One

It should be noted that all reaction apparatus was scrupulously clean and was flame dried under nitrogen. The reaction was conducted when the relative humidity in the laboratory was rather low (e.g., the last two weeks in January).

In a one liter, three neck, round bottom flask which contained a small lump of sodium metal, was condensed 500 ml of ammonia. The ammonia was then distilled through Tygon tubing into a two liter, three neck, round bottom flask containing 1.39 g (0.2M) of lithium ribbon. The reaction flask was equipped with a paddle stirrer, a dry ice condenser, a dry ice--isopropanol bath, and an addition funnel to which a nitrogen gas line was attached. A solution of 17.8 g (0.1M) of the enone dissolved in 250 ml of THF was placed in the addition funnel and added dropwise over a one hr period, during which an additional centimeter of lithium ribbon was added to the reaction. The blue color of the reaction was discharged by the dropwise addition of ethylene dibromide, following which 10 g of finely ground ammonium carbonate was added in one portion. The cooling bath was removed and the ammonia was evaporated into the hood under a stream of

nitrogen. The residue was taken up in 300 ml of water and this mixture was extracted four times with 200 ml of ether. The extracts were washed sequentially with water and brine, and then dried. After removal of the solvent, 17.2 g of light yellow oil was obtained, which was triturated with 10 ml of ether and placed in the refrigerator. Crystallization yielded 12.8 g (71%) of the white, crystalline cyclopropanol. An analytical sample had mp 98--100° (ether).

Preparation of 1

A solution of 1.57 g (0.028M) of potassium hydroxide in 30 ml of 50% v/v methanol--water was deoxygenated by bubbling nitrogen gas into it for 15 min. The solution was cooled to 0° and 4.5 g (0.025M) of the solid tricyclic cyclopropanol was added in one portion. The deep green solution was stirred at 0° for 24 hr, and the reaction was then neutralized with concentrated hydrochloric acid, whereupon it became yellow and a precipitate formed. The methanol was removed and the aqueous residue was dissolved in ether and water. This mixture was extracted with ether and the ether extracts were washed sequentially with water, 200 ml of 10% aqueous sodium bisulfite (in four portions), and brine. After drying and removal of the solvent, 3.27 g (72.5%) of solid 1 was obtained. An analytical sample displayed the following properties: mp 168--169° (ether); ir (CCl₄) 1705, 1735 cm⁻¹; pmr (CCl₄) δ 0.85 (s, 3H), 1.15 (s, 3H), 1.30--2.90 (m, 10H);

ms (70 eV) m/e (rel intensity) 180(85), 165(66), 154(10), 137(34), 125(252), 110(100), 95(72), 81(62), 67(63), 55(45), 41(81); cmr (rel intensity) δ 17.85(73), 20.59(97), 21.51(77), 24.34(100), 25.21(89), 32.74(98), 36.08(88), 54.45(25), 55.25(37), 176.25(18), 179.50(13).

Anal Calcd for $C_{11}H_{16}O_2$: C, 73.33; H, 8.88

Found: C, 73.05; H, 8.91

The sodium bisulfite extract was acidified with concentrated hydrochloric acid and extracted with chloroform. The chloroform extract was washed sequentially with water and brine. After drying and removal of the solvent, 0.69 g (15.3%) of *cis*-1-methylbicyclo[4.4.0]decan-2,8-dione was obtained (mp 65--67° [ether]).

Preparation of 2

To a solution of 27.0 g (0.15M) of 1 in 1350 ml of ethanol (cooled to 0°) was added dropwise a solution of 23.2 g (0.58M) of sodium hydroxide and 6.45 g (0.17M) of sodium borohydride (Ventron) in 100 ml of ethanol and 50 ml of water. This addition was effected over a 30 min period with vigorous stirring. After 3-1/2 hr at 0°, GLPC (130°, 4% SE-30) showed that 1 had been totally consumed. The ethanol was removed from the reaction mixture and the residue was dissolved in water and ether. The aqueous phase was extracted with ether and the combined ether extracts were washed sequentially with water and brine. After drying and removal of the solvent, 26.57 g (97.5%) of essentially pure 2 was obtained. An

analytical sample displayed the following properties:
 mp 170--180° (sealed tube); ir (CDCl₃) 3590, 3450, 1735
 cm⁻¹; pmr (CDCl₃) δ 0.9 (s,3H), 1.25 (s,3H), 1.3--2.7
 (m,11H), 3.8 (m,1H); ms (70 eV) m/e (rel intensity)
 182(41), 167(15), 154(5), 149(8), 138(10), 122(40),
 111(100), 109(85), 96(64), 81(58), 67(45), 55(62),
 41(80).

Anal Calcd for C₁₁H₁₈O₂: C, 72.49; H, 9.95

Found: C, 72.47; H, 9.97

Preparation of 3 via *n*-Butyl Lithium and Methyl Iodide

A solution of 9.1 g (0.05M) of 2 in 500 ml of THF was cooled to 0° and stirred vigorously while 27.0 ml of 1.85M *n*-butyl lithium in hexane (Ventron) was added. The resulting yellow suspension was stirred 15 min at 0°; then 7.8 g (0.055M) of methyl iodide was added. The reaction mixture was allowed to warm to room temperature, stirred for 12 hr, and then washed with brine and dried. After removal of the solvent, 10.08 g of brown oil was recovered. Analysis by GLPC (160°, 4% QF-1) showed that the oil was approximately 79% 3 and 21% 2. This oil was distilled at 70°/0.05 torr and yielded 6.62 g (67.5%) of 3 as a colorless oil. The residue weighed 3.1 g and consisted mainly of 2 which was recrystallized from ether and recycled in subsequent preparations. An analytical sample of 3 displayed the following properties: ir (neat) 1735 cm⁻¹; pmr (CCl₄) δ 0.85 (s,3H), 1.15 (s,3H), 1.20--2.70 (m,10H), 3.25 (m,1H), 3.3 (s,3H); ms (70 eV) m/e

(rel intensity) 196(5), 164(2), 148(5), 125(8), 120(9), 112(7), 109(8), 105(11), 97(8), 91(9), 85(9), 78(93), 71(13), 63(100), 61(15), 55(11), 45(14), 41(19); cmr (rel intensity) δ 16.89(86), 18.85(66), 22.84(59), 23.39(100), 25.98(87), 27.09(83), 32.98(74), 44.43(44), 51.17(35), 57.54(43), 83.69(72), 174.76(16).

Anal Calcd for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27

Found: C, 73.37; H, 10.17

Preparation of 3 via Dimethyl Sodium and Methyl Iodide

To 250 ml of dry DMSO was added 2.16 g (0.09M) of sodium hydride and the resulting suspension was heated at 70° for one hr to form a clear yellow solution. This dimethyl sodium solution was cooled to room temperature and 8.20 g (0.045M) of 2 was added in one portion. The solid quickly dissolved and the resulting solution was stirred one hr at room temperature, followed by the addition of 9.58 g (0.0675M) of methyl iodide in one portion. After this reaction mixture was stirred 19 hr at room temperature, it was poured into 250 ml of water, and the resulting aqueous mixture was extracted with benzene. The benzene extract was washed sequentially with water and brine, and then dried. After removal of the solvent, 8.54 g of yellow oil was recovered. This oil was distilled at 0.005 torr, and 6.50 g (73.7%) of 3 was collected between 51--53°.

Preparation of 4

To a solution of 1.80 g (0.001M) of 1 in 100 ml of THF at room temperature was added 10 ml of 2.5M vinyl magnesium chloride in TMF (Ventron) in one portion, and the resulting solution was stirred three days. The reaction was poured into saturated ammonium chloride and extracted with ether. The ether extracts were washed sequentially with water and brine, and then dried, to yield 2.81 g of light yellow amorphous solid after removal of the solvent. This solid was recrystallized from ethyl acetate--petroleum ether to yield 1.18 g (56.7%) of 4, which displayed the following properties: mp 111--112°; ir 3410, 1725, 1630, 990, 930 cm^{-1} ; pmr (CDCl_3) δ 0.85 (s, 3H), 1.3 (s, 3H), 1.35--3.7 (m, 11H), 5.1 (m, 2H), 5.9 (m, 1H); ms (70 eV) m/e (rel intensity) 208(8), 193(20), 190(11), 175(9), 133(25), 111(100), 96(36), 82(27), 67(25), 55(48), 41(43).

Anal Calcd for $\text{C}_{13}\text{H}_{20}\text{O}_2$: C, 74.96; H, 9.68

Found: C, 74.84; H, 9.77

Preparation of 5

A catalytic amount of iodine was added to a solution of 0.520 g (0.0025M) of 4 in 25 ml of xylene and the solution was refluxed for 12 hr. The reaction was cooled to room temperature and washed sequentially with 0.5M sodium thiosulfate and brine, and then dried. Analysis by GLPC (160°, 4% QF-1) and TLC (silica gel, 20% v/v ethyl

acetate--cyclohexane) showed that 4 had been totally consumed. The xylene solution was diluted with ether and filtered through silica gel. The solvents were removed to yield 0.436 g (91.8%) of 5 as a light yellow oily solid. An analytical sample of 5 displayed the following properties: UV (95% ethanol) 235 nm (ϵ $1.5[10^4]$); ir (neat) 3010, 1730, 1675, 990, 910 cm^{-1} ; pmr (CCl_4) δ 0.75 (s,3H), 0.85 (s,3H), 1.0--3.0 (m,8H), 5.0--7.0 (m,4H); ms (70 eV) m/e (rel intensity) 190(43), 175(16), 157(8), 147(10), 133(37), 119(100), 105(28), 91(14), 77(16), 65(9), 55(12), 41(12).

Anal Calcd for $\text{C}_{13}\text{H}_{18}\text{O}_2$: C, 82.06; H, 9.53

Found: C, 82.22; H, 9.70

Preparation of 6

To 300 ml of DMSO (dried over molecular sieves) was added 2.66 g (0.111M) of sodium hydride which had been rinsed with petroleum ether and weighed out as a dry solid. The mixture was heated with stirring at 70° for one hr, until a yellow solution had formed. The solution was cooled to 15° and 24.40 (0.111M) of solid trimethyl-oxosulfonium iodide was added in one portion. The mixture was stirred 30 min at room temperature until a solution had formed. Then a solution of 8.00 g (0.0455M) of 1 in 100 ml of DMSO was added in one portion and the resulting solution was stirred seven days at room temperature. The reaction was poured into 400 ml of ice water and the resulting mixture was extracted with five, 200 ml portions

of ether. The ether solution was washed sequentially with water and brine, and then dried. After removal of the solvent 7.33 g (83%) of 6 was recovered as a white solid. An analytical sample of 6 displayed the following properties: mp 159--161° (petroleum ether); ir 1735 cm^{-1} ; pmr (CCl_4) 1.0 (s, 3H), 1.1 (s, 3H), 1.15--2.2 (m, 10H), 2.3 (m, 2H); ms (70 eV) m/e (rel intensity) 194(28), 179(13), 166(17), 151(17), 136(44), 122(46), 107(100), 93(58), 79(45), 67(37), 55(42), 41(72).

Anal Calcd for $\text{C}_{12}\text{H}_{18}\text{O}_2$: C, 74.19; H, 9.34

Found: C, 74.16; H, 9.27

Preparation of 7 and 8

To a solution of 3.92 g (0.02M) of 3 in 100 ml of THF at 0° was added in one portion 43 ml of a 20% solution of diisobutyl aluminum hydride in hexane (Ventron). The reaction was placed in a refrigerator at 5° for two days, and was then poured into cold 4N hydrochloric acid and extracted with ether. The ether extracts were washed sequentially with 4N hydrochloric acid, water, and brine, and then dried. After removal of the solvent, 3.91 g (98.7%) of a clear oil was obtained which proved to be a mixture of the epimeric alcohols, 7 and 8. Analysis by GLPC (160°, 4% QF-1) showed that 3 had been completely consumed and that the two epimeric alcohols were present in the ratio of 1.4:1 (shorter retention alcohol:longer retention alcohol). Analytical samples of each of the alcohols were obtained by preparative

layer chromatography (20% v/v ethyl acetate--cyclohexane, double elution) of 0.1583 g of the epimeric mixture. The higher band on the plate yielded 0.0665 g of one epimer which corresponded to the shorter retention component on the GLPC. It was assigned configuration 7, and displayed the following properties: mp 84--85°; ir (CCl₄) 3610, 3480 cm⁻¹; pmr (CCl₄) δ 0.9 (s,3H), 1.0 (s,3H), 1.1--2.6 (m,11H), 3.05 (m,1H), 3.20 (s,3H), 3.6 (m,1H); ms (15 eV, ion source 100°) m/e (rel intensity) 198(8), 180(34), 166(34), 154(24), 148(63), 133(19), 122(100), 112(12), 93(16), 84(50), 71(20).

Anal Calcd for C₁₂M₂₂O₂: C, 72.68; M, 11.18

Found: C, 72.71; M, 11.16

The lower band on the plate yielded 0.0533 g of the other epimer which corresponded to the longer retention component on the GLPC. It was assigned configuration 8 and displayed the following properties: mp 106--108°; ir (CCl₄) 3615, 3500 cm⁻¹; pmr (CDCl₃) δ 0.8 (s,3H), 1.0(s,3H), 1.1--2.6 (m,11H), 3.0 (m,1H), 3.2 (s,3H), 3.8 (m,1H); ms (15 eV, source 100°) m/e (rel intensity) 198(10), 180(4), 166(35), 154(25), 148(39), 133(8), 122(100), 112(38), 93(8), 84(33), 71(16).

Anal Calcd for C₁₂M₂₂O₂: C, 72.68; M, 11.18

Found: C, 72.61; M, 11.18

Preparation of 9

A solution of 2.76 g (0.069M) of sodium hydroxide in 25 ml of water was added to 7.72 g (0.069M) of

cyclohexan-1,3-dione. The solid quickly dissolved to give an orange solution which was cooled to 0°, and heated with 10 g (0.069M) of CD₃I (Aldrich). The reaction was refluxed for two days, then cooled to room temperature, and placed in the refrigerator at 5° for 12 hr. The resulting solid was recovered by vacuum filtration, washed with water, and dried in a vacuum oven at 45°/one torr, to yield 6.00 g (67.5%) of 9, a light yellow solid which displayed the following properties: mp 184--188°; ms (70 eV) m/e (rel intensity) 130(5), 129(50), 101(62), 83(36), 73(35), 59(45), 55(100), 42(64), 32(77). The ir and pmr were not taken due to the low solubility of this compound in most common spectral solvents.

Preparation of 10

A mixture of 6.00 g (0.0465M) of 9, 30 ml of ethyl acetate, 10 ml of triethylamine, and 6.0 ml of methyl vinyl ketone was stirred 12 hr at room temperature. At this point, some of the starting material still had not dissolved, so an additional 2 ml of methyl vinyl ketone was added and the reaction was refluxed for 6 hr. The solution was cooled to room temperature and filtered. After removal of the solvent from the filtrate, 10.18 g of light brown gum was recovered which contained the desired Michael-adduct and some decomposed methyl vinyl ketone. A solution of the crude Michael-adduct, which was pure by GLPC (180°, 4% QF-1) in 200 ml of toluene, was

treated with 0.167 ml (0.142 g/0.002M) of pyrrolidine and 0.114 ml (0.120 g/0.002M) of glacial acetic acid and was refluxed for 12 hr. Analysis by GLPC indicated that the Michael-adduct had been consumed and that 10 was the only product. The reaction was diluted with 200 ml of ether and washed with 200 ml of 4N hydrochloric acid. The aqueous wash was treated with 15 ml of concentrated sulfuric acid and was extracted with ten, 100 ml portions of ether. The combined organic solutions were washed sequentially with water and brine, and then dried. After removal of the solvent, 6.95 g of brown oil was recovered. Continuous liquid-liquid extraction of the acid wash with chloroform gave 1.80 g of semi-solid material after removal of the solvent. This material was dissolved in ether and the resulting brown precipitate was removed by filtration. A further 0.32 g of crude product was obtained after removal of the solvent. The combined yield of crude product was 7.27 g. An ir of the crude product showed the presence of acidic material, so a solution of the crude product in ether was washed with saturated sodium bicarbonate. After removal of the solvent, 5.84 g (69.4%) of 10 was obtained which displayed the following properties: ir (neat) 2200, 1735, 1715, 1640 cm^{-1} ; pmr (CCl_4) δ 1.0--3.1 (m, 10H), 5.6 (s, 1H); ms (70 eV) m/e (rel intensity) 182(11), 181(58), 163(52), 139(80), 125(79), 121(100), 111(77), 93(75), 79(68), 69(80), 67(81), 41(75), 39(82).

Preparation of 11

Into a one liter, three neck, round bottom flask equipped with a dry ice--isopropanol cooling bath, paddle stirrer, dry ice--isopropanol condenser, pressure equalized addition funnel, and nitrogen line, containing 45 ml of THF and 0.452 g (0.065M) of lithium ribbon, was condensed 250 ml of dry ammonia (from sodium). A solution of 5.75 g (0.0318M) of 10 in 80 ml of THF was placed in the addition funnel and added to the reaction over 30 min. When the addition was complete, the blue color of the ammonia was discharged with a few drops of ethylene dibromide, then 6.7 g (0.07M) of ammonium carbonate was added in one portion. The ammonia was evaporated into the hood under a stream of nitrogen and the remaining material was taken up with 400 ml of water and then extracted with four, 100 ml portions of ether. The ether extracts were washed sequentially with water and brine, and then dried. After removal of the solvent, 5.18 g (89%) of 11 was recovered as a light brown solid which displayed the following properties: ir (CCl₄) 3375, 2200, 1700 cm⁻¹; pmr (CCl₄) δ 0.9--2.8 (m, 11H), 3.55 (m, 2H); ms (70 eV) (rel intensity) 184(16), 183(100), 165(28), 155(13), 140(26), 127(57), 113(70), 99(49), 84(53), 71(45), 55(33), 41(63).

Preparation of 13

To a deoxygenated solution of 1.72 g (0.0306M) of potassium hydroxide in 60 ml of 50% v/v methanol--water was added 5.10 g (0.0278M) of 11 and the resulting

solution was stirred six hr at room temperature. This solution was blue-green initially and gradually became brown. The reaction was neutralized with concentrated hydrochloric acid, and the resulting yellow, heterogeneous mixture was extracted with five, 100 ml portions of ether. The ethereal extract was analyzed by GLPC (160°, 4% QF-1) and the ratio of 13 to 12 was found to be 4:1. The ether extract was washed sequentially with three 25 ml portions of 10% sodium bisulfite, 4N hydrochloric acid, water, and brine, and then dried. After removal of the solvent, 2.65 g of yellow solid was recovered. This solid was recrystallized from ether--petroleum ether to give 1.29 g (25.3%) of 13 which displayed the following properties: mp 158--160°; ir (CCl₄) 2200, 1720, 1700 cm⁻¹; pmr (CDC1₃) δ 0.95 (s, 3H), 1.4--2.7 (m, 12H); ms (70 eV) m/e (rel intensity) 184(9), 183(64), 168(9), 165(56), 155(4), 141(21), 137(23), 128(50), 113(100), 99(63), 85(60), 69(30), 55(31), 41(49).

The combined aqueous washes were acidified with concentrated sulfuric acid and extracted continuously with chloroform in a liquid-liquid extractor. After isolation of the chloroform phase and removal of the solvent, 2.12 g of brown oil was recovered. Analysis by GLPC showed that the oil was a mixture of 12 and 13. The combined yield of 12 and 13 was 4.77 g (93.5%).

Preparation of 14

A solution of 1.25 g (0.0312M) of sodium hydroxide and 0.266 g (0.007M) of sodium borohydride in 3 ml of water was added to a solution of 1.00 g (0.00546M) of 13 in 50 ml of ethanol at 0°. The reaction was stirred 4-1/2 hr at 0°, then neutralized by the dropwise addition of concentrated hydrochloric acid. The ethanol was then removed and the residue was dissolved in ether and water. The mixture was extracted with ether and the extracts were washed sequentially with water and brine, and then dried. After removal of the solvent, 1.07 g of crude 14 was isolated as a solid, which was recrystallized from ether to yield 0.687 g (68.0%) of 14 as white crystals which displayed the following properties:

mp 176--177° (sealed tube); ir (CDCl₃) 3600, 3450, 2200, 1730 cm⁻¹; pmr (CDCl₃) δ 1.25 (s, 3H), 1.3--2.6 (m, 11H), 3.8 (m, 1H); ms (70 eV) m/e (rel intensity) 186(7), 185(55), 170(10), 167(10), 157(4), 152(4), 149(7), 143(6), 141(7), 139(8), 125(42), 114(78), 112(100), 99(80), 81(57), 69(53), 55(28), 43(33), 41(45).

Preparation of 15

To a solution of 0.617 g (0.003M) of 14 in 60 ml of THF at 0° was added dropwise 1.35 ml of 2.45M *n*-butyl lithium in hexane (Ventron), whereupon the lithium alkoxide of 14 formed a precipitate. The reaction mixture was stirred 15 min at 0°, then 0.206 ml (0.468 g/0.0033M) of iodomethane was added in one portion. The reaction was

warmed to room temperature and stirred for 12 hr, during which the alkoxide went into solution. This solution was poured into brine and the resulting mixture was extracted with ether. The ether extract was washed sequentially with 50% v/v water--brine and brine, and then dried. After removal of the solvent, 0.650 g of yellow oil was recovered, which was placed on 65 g of silica gel and eluted with 20% v/v ethyl acetate--cyclohexane, to yield 0.421 g (70.6%) of 15 as an oil, as well as 0.183 g of 14. Compound 15 displayed the following properties: ir (neat) 2215, 2200, 2050, 1735 cm^{-1} ; pmr (CCl_4) δ 1.1 (s,3H), 1.2--2.6 (m,10H), 3.15 (m,1H), 3.25 (s,3H); ms (70 eV) m/e (rel intensity) 200(8), 199(44), 184(4), 181(4), 171(5), 167(9), 157(2), 149(8), 143(11), 139(12), 128(40), 125(54), 115(59), 112(54), 97(51), 85(55), 71(100), 58(35), 41(43).

Preparation of 16 and 17

To a solution of 0.352 g (0.00177M) of 15 in 20 ml of THF at 0° was added in one portion 4.3 ml of a 20% solution of diisobutyl aluminum hydride in hexane (Ventron). The reaction was placed in a refrigerator at 5° for two days, and was then poured into cold 4N hydrochloric acid and extracted with ether. The ether extracts were washed sequentially with 4N hydrochloric acid, water, and brine, then dried. After removal of the solvent, 0.380 g of a clear oil was obtained which proved to be a mixture of the epimeric alcohols, 16 and 17.

Analysis by GLPC (160°, 4% QF-1) showed that 15 had been completely consumed and that the two epimeric alcohols were present in the ratio of 1.4:1 (shorter retention alcohol:longer retention alcohol).

Analytical samples of each of the alcohols were obtained by preparative layer chromatography (20% v/v ethyl acetate--cyclohexane, double elution) of the epimeric mixture. The higher band on the plate yielded 0.162 g of one epimer which corresponded to the shorter retention component on the GLPC. It was assigned configuration 16, and displayed the following properties: mp 76--78°; ir (CHCl₃) 3590, 3415, 2220, 2205, 2120, 2030 cm⁻¹; pmr (CDCl₃) δ 0.95 (s,3H), 1.1--2.6 (m,11H), 3.15 (m,1H), 3.25 (s,3H), 3.75 (m,1H); ms (15 eV, ion source 100°) m/e (rel intensity) 201(11), 186(1), 184(1), 183(12), 169(38), 157(35), 151(37), 125(100), 115(9), 112(9), 108(10), 84(49), 71(8).

The lower band on the plate yielded 0.124 g of the other epimer which corresponded to the longer retention component on the GLPC. It was assigned configuration 17, and displayed the following properties: mp 107--109°; ir (CHCl₃) 3580, 3410, 2215, 2205 cm⁻¹; pmr (CDCl₃) δ 1.05 (s,3H), 1.1--2.6 (m,11H), 3.05 (m,1H), 3.25 (s,3H), 3.9 (m,1H); ms (15 eV, ion source 100°) m/e (rel intensity) 201(12), 186(1), 184(1), 183(3), 170(6), 169(42), 157(32), 151(38), 125(100), 115(34), 112(8), 108(12), 84(14), 71(10).

Preparation of 18

To a solution of 0.42 g (0.01M) of sodium tetra-deuteridoborate (ICN) in 150 ml of absolute ethanol at 0°, was added in one portion 1.00 g (0.00556M) of 1. The reaction was stirred 3 hr at 0°, then the excess reducing agent was destroyed by the dropwise addition of concentrated hydrochloric acid. The ethanol was removed and the residue was dissolved in water and ether. The mixture was extracted with ether, and the extracts were washed with brine and dried. All of diketone 1 had been consumed by the reaction to form one product according to analysis by TLC (silica gel, ether) and GLPC (160°, 4% QF-1). The solvent was removed to yield 1.03 g (100%) of 18 as a white solid that displayed the following properties: mp 168--171°; ir (CHCl₃) 3600, 3450, 2400, 2090, 1735 cm⁻¹; pmr (CDCl₃) δ 0.82 (s, 3H), 1.15 (s, 3H), 1.20--2.6 (m, 11H); ms (70 eV) m/e (rel intensity) 184(7), 183(53), 168(18), 150(9), 141(6), 138(16), 123(45), 112(81), 110(100), 96(90), 82(52), 67(33), 55(46), 41(61).

Preparation of 19

To a solution of 0.732 g (0.004M) of 18 in 75 ml of THF at 0° was added dropwise 1.80 ml of 2.45M *n*-butyllithium in hexane (Ventron). The suspension which formed was stirred 15 min at 0°, then 0.275 ml (0.625 g/0.0044M) of iodomethane was added, and the reaction was stirred 1 hr at 0°, then warmed to room temperature, and stirred 12 hr. The reaction was diluted with 100 ml of ether,

and the solution was washed sequentially with 50% v/v water--brine and brine, and then dried. After removal of the solvent, 0.801 g of yellow oil was obtained which analysis by GLPC (160°, 4% QF-1) showed was a mixture of 19 and 18. This oil was placed on 80 g of silica gel and eluted with 20% v/v ethyl acetate--cyclohexane, to yield 0.550 g (69.9%) of 19, as well as 0.250 g of 18. The labeled methoxy ketone 19 displayed the following properties: ir (neat) 2175, 1740 cm^{-1} ; pmr (CCl_4) δ 0.82 (s,3H), 1.1 (s,3H), 1.2--2.6 (m,10H), 3.25 (s,3H); ms (70 eV) m/e (rel intensity) 198(7), 197(42), 182(5), 166(3), 165(8), 150(8), 141(10), 126(53), 123(41), 112(66), 110(55), 97(45), 86(57), 72(100), 59(30), 55(36), 41(51).

Preparation of 20 and 21

To a solution of 0.404 g (0.00205M) of 19 in 20 ml of THF at 0° was added in one portion 4.3 ml of a 20% solution of diisobutyl aluminum hydride in hexane (Ventron). The reaction was placed in a refrigerator at 5° for two days, after which it was poured into cold 4N hydrochloric acid and the resulting mixture was extracted with ether. The ether extracts were washed sequentially with 4N hydrochloric acid, water, and brine, and then dried. After removal of the solvent, 0.448 g of a clear oil was obtained which proved to be a mixture of the epimeric alcohols, 20 and 21. Analysis by GLPC (160°, 4% QF-1) showed that 19 had been completely consumed and

that the two epimeric alcohols were present in the ratio of 1.4:1 (shorter retention alcohol:longer retention alcohol). Pure samples of each of the alcohols were obtained by preparative layer chromatography (20% v/v ethyl acetate--cyclohexane, double elution) of the epimeric mixture. The higher band on the plate yielded 0.184 g of one epimer which corresponded to the shorter retention component on the GLPC. It was assigned configuration 20, and displayed the following properties: mp 70--72°; ir (CHCl₃) 3590, 3440, 2080 cm⁻¹; pmr (CDCl₃) δ 0.95 (s,3H), 1.05 (s,3H), 1.1--2.6 (m,11H), 3.2 (s,3H), 3.6 (m,1H); ms (15 eV, ion source 100°) m/e (rel intensity) 199(12), 181(17), 167(51), 155(39), 149(55), 134(11), 123(100), 112(15), 109(20), 108(15), 95(10), 85(70), 72(11).

The lower band on the plate yielded 0.153 g of the other epimer which corresponded to the longer retention component on the GLPC. It was assigned configuration 21, and displayed the following properties: mp 106--109°; ir (CHCl₃) 3590, 3440, 2075 cm⁻¹; pmr (CDCl₃) δ 0.82 (s,3H), 1.02 (s,3H), 1.1--2.6 (m,11H), 3.2 (s,3H), 3.8 (m,1H); ms (15 eV, ion source 90°) m/e (rel intensity) 199(7), 181(3), 167(36), 155(27), 149(35), 134(6), 123(100), 112(37), 109(17), 108(12), 95(6), 85(22), 72(9).

Preparation of 22

To a solution of 0.690 g (0.00379M) of 2 in 75 ml of THF at 0° was added 2.0 ml of 2.5M *n*-butyl lithium in

hexane (Ventron) in one portion, and the resulting suspension was stirred 15 min at 0°. The reaction was then treated with 0.322 ml (0.005M) of iodotrideuteriomethane (Aldrich) and stirred six hr at 0°. The reaction was then warmed to room temperature and stirred 12 hr. The reaction was diluted with 100 ml of ether and washed sequentially with 50% v/v water--brine and brine, and then dried. After removal of the solvent, 0.908 g of brown oil was recovered, which was filtered through silica gel in ether solution to give 0.732 g of light brown oil. This oil was chromatographed on an HPLC column (500 x 15 mm, silica gel, 5% v/v methanol--chloroform at 1 ml/min) to yield 0.524 g of deuterium labeled product as a clear oil and 0.145 g of 2. The deuterium labeled fraction was a mixture of three major components, present in roughly equal amounts. Pure samples of these components were isolated by preparative GLPC (200°, 10 ft 20% SE-30).

Collection of the component with the shortest retention yielded 0.142 g of 22 as an oil which displayed the following properties: ir (neat) 2210, 2175, 2100, 2045, 1735 cm^{-1} ; pmr (CCl_4) δ 0.82 (s,3H), 1.1 (s,3H), 1.2--2.6 (m,10H), 3.15 (m,1H); ms (70 eV) m/e (rel intensity) 200(4), 199(27), 184(3), 181(2), 171(3), 165(2), 164(6), 157(2), 156(3), 128(79), 121(34), 107(52), 93(56), 74(87), 67(50), 55(55), 41(100).

Collection of the component with the middle retention yielded 0.113 g of 23 as an epimeric mixture which displayed the following properties: ir (neat) 2205, 2175, 2105, 2045, 1735 cm^{-1} ; pmr (CCl_4) one epimer (63%) had δ 0.85 (s,3H), 1.05 (s,3H), the other epimer (37%) had δ 0.75 (s,3H), 1.15 (s,3H), the other peaks were δ 1.2--2.8 (m, 9H), 3.1 (m,1H); ms (70 eV) m/e (rel intensity) 217(3), 216(22), 201(2), 182(1), 181(4), 171(10), 153(6), 148(10), 143(13), 140(4), 138(19), 128(100), 114(34), 109(33), 107(28), 93(35), 81(43), 74(64), 67(33), 55(38), 41(75).

Collection of the component with the longest retention yielded 0.041 g of 24 as an oil which displayed the following properties: ir (neat) 2210, 2175, 2105, 2050, 1730 cm^{-1} ; pmr (CCl_4) δ 0.9 (s,3H), 1.15 (s,3H), 1.3--2.6 (m,8H), 3.15 (m,1H); ms (70 eV) m/e (rel intensity) 234(2), 233(14), 218(3), 215(1), 198(1), 171(9), 155(14), 146(25), 128(100), 119(30), 93(29), 81(35), 74(45), 67(28), 55(28), 41(63).

Preparation of 25 and 26

To a solution of 0.137 g (0.000690M) of 22 in 20 ml of THF at 0° was added in one portion 2.26 ml of a 20% solution of diisobutyl aluminum hydride in hexane (Ventron). The reaction was placed in a refrigerator at 5° for two days, then poured into cold 4N hydrochloric acid and extracted with ether. The ether extracts were washed sequentially with 4N hydrochloric acid, water,

and brine, and then dried. After removal of the solvent, 0.141 g of a clear oil was obtained. Analysis by GLPC (160°, 4% QF-1) showed that the oil was a mixture of 22, 25, and 26 and that the two epimeric alcohols were present in the ratio of 1:2.5 (shorter retention alcohol: longer retention alcohol). Pure samples of each of the alcohols were obtained by preparative layer chromatography (20% v/v ethyl acetate--cyclohexane, double elution) of the mixture. The higher band on the plate yielded 0.057 g of one epimer which corresponded to the shorter retention component on the GLPC. It was assigned configuration 25, and displayed the following properties: mp 83--85°; ir (CHCl₃) 3590, 2210, 2175, 2100, 2045 cm⁻¹; pmr (CDCl₃) δ 0.95 (s, 3H), 1.05 (s, 3H), 1.1--2.6 (m, 11H), 3.1 (m, 1H), 3.65 (m, 1H); ms (15 eV, ion source 110°) m/e (rel intensity) 202(2), 201(10), 184(3), 183(19), 166(36), 157(25), 148(46), 133(8), 122(100), 112(10), 108(14), 95(4), 94(4), 87(51), 74(11).

The lower band on the plate yielded 0.042 g of the other epimer which corresponded to the longer retention component on the GLPC. It was assigned configuration 26, and displayed the following properties: mp 109--111°; ir (CHCl₃) 3590, 2210, 2170, 2045 cm⁻¹; pmr (CDCl₃) δ 0.8 (s, 3H), 1.02 (s, 3H), 1.1--2.6 (m, 11H), 3.02 (m, 1H), 3.82 (m, 1H); ms (15 eV, ion source 110°) m/e (rel intensity) 202(2), 201(11), 183(5), 166(38), 157(25), 148(36), 133(6), 122(100), 112(37), 108(13), 95(4), 94(5), 87(13), 74(9).

Treatment of 3 with Isopropenyl Lithium

To a solution of 3.33 ml of a 0.15M stock solution of isopropenyl lithium (from isopropenyl bromide) in ether and 5 ml of tetramethylethylenediamine in 12.5 ml of THF at -78° , was added dropwise a solution of 0.098 g (0.0005M) of 3 in 12.5 ml of THF. On completion of the addition, the reaction was stirred a further hour at -78° , then warmed to room temperature and stirred 24 hr. The reaction was then cooled to -78° , a second 3.33 ml of 0.15M isopropenyl lithium added, stirring continued one hr at -78° , and then warmed to room temperature and stirred 24 hr. The reaction was quenched by the addition of saturated aqueous ammonium chloride and extracted with ether. The extracts were washed sequentially with water and brine, and then dried. After removal of the solvent, 1.15 g of brown oil was recovered. The crude product was placed on 100 g of silica gel and eluted with 30% v/v ether--pentane, to yield 0.83 g of material which displayed spectral properties identical to those of the starting material.

Treatment of 3 with Vinyl Lithium

To a solution of 0.196 g (0.001M) of 3 in 20 ml of THF at -78° was added 0.6 ml of 2.5M vinyl lithium in THF (Ventron) in one portion. The reaction was stirred at -78° for one hr, then at 0° for one hr, and at room temperature for 12 hr. The reaction was poured into water and extracted with ether. The extracts were washed

sequentially with water and brine, and then dried. After removal of the solvents, 0.190 g of yellow oil was recovered which had spectral properties and GLPC retention (160°, 4% QF-1) identical with those of 3.

Treatment of 3 with Vinyl Magnesium Chloride

To a solution of 0.204 g (0.00104M) of 3 in 20 ml of THF and 0.42 ml (0.003M) of HMPA, was added 1.3 ml of 2.3M vinyl magnesium chloride in THF (Ventron) in one portion, and the resulting solution was refluxed for two days. The reaction was poured into 4N hydrochloric acid and extracted with ether. The ether extracts were washed sequentially with water and brine, and then dried. After removal of the solvent, 0.174 g of brown oil was obtained which displayed spectral properties and GLPC retention (160°, 4% QF-1) identical with those of 3.

Treatment of 3 with Methyl Lithium

To a solution of 0.196 g (0.001M) of 3 in 10 ml of THF and 0.3 ml of tetramethylethylenediamine, was added 1.21 ml of 1.65M methyl lithium in ether (Ventron) in one portion, and the resulting solution was stirred at room temperature for five days. The reaction was poured into cold 4N hydrochloric acid and then extracted with ether. The ether extract was washed sequentially with 4N hydrochloric acid, water, and brine, and then dried. After removal of the solvent, 0.225 g of brown oil was recovered

which displayed spectral properties and GLPC retention (160°, 4% QF-1) identical with those of 3.

Preparation of 27

To a solution of 3.33 ml of a 0.15M stock solution of isopropenyl lithium (from 2-bromopropene) in ether, 2.5 ml of tetramethylethylenediamine, and 6.5 ml of THF was added dropwise a solution of 0.049 g (0.00025M) of 3 in 6.5 ml of THF at room temperature. The resulting solution was refluxed for 24 hr. The reaction was cooled to room temperature, and then quenched by the addition of 1.08 g (0.0106M) of acetic anhydride in one portion. The cloudy, brown reaction became translucent at this point. The reaction mixture was poured into water and extracted with ether. The ether extracts were washed sequentially with water and brine, and then dried. The solvent was removed to yield 0.89 g of brown oil, which was placed on 80 g of silica gel and eluted with 30% v/v ether--pentane and later 50% v/v ether--pentane, to yield 0.140 g of hydrocarbon grease, 0.210 g (35.3%) of 27, and 0.326 g of 3. The enol-acetate 27 displayed the following properties: ir (neat) 1760, 1640, 895, 805 cm^{-1} ; pmr (CCl_4) δ 1.1 (s,3H), 1.15 (s,3H), 1.2--2.8 (m,8H), 2.05 (s,3H), 3.15 (m,1H), 3.2 (s,3H), 5.2 (m,1H); ms (70 eV) m/e (rel intensity) 238(1), 196(22), 181(10), 178(9), 164(33), 149(100), 135(23), 131(14), 121(30), 119(19), 117(30), 107(25), 93(24), 91(24), 79(25), 73(25), 71(52), 67(23), 55(39), 45(34), 43(86), 41(62).

Anal Calcd for $C_{14}H_{22}O_3$: C, 70.56; H, 9.30

Found: C, 70.64; H, 9.18

Preparation of 29 from 27

To a solution of 0.129 g (0.000543M) of 27 in 60 ml of 10% v/v pyridine--acetic acid was added a solution of 1.04 g (0.0065M) of bromine in 3 ml of acetic acid. The reaction was stirred in the dark at room temperature for 24 hr, after which 25 ml of 10% Na_2SO_3 was added. The mixture was extracted with ether. Analysis by TLC (silica gel, 30% v/v ether--pentane) of the ether solution showed that 27 had been consumed in the reaction. After drying and removal of most of the solvent, 1.27 g of oil was recovered which contained acetic acid. This oil was placed on 100 g of silica gel and eluted with 30% v/v ether--pentane. The products obtained from the chromatography were assumed to comprise both epimeric bromo ketones, since their TLC retentions were different from 27 and 3. Early fractions yielded 0.0205 g of a mixture of both epimers. The later fractions yielded 0.0648 g (43.5%) of one epimer of 27 as yellow crystals which displayed the following properties: mp 69--79° (decomposition); ir (CCl_4) 1755 cm^{-1} ; pmr (CCl_4) δ 0.89 (s,3H), 1.42 (s,3H), 1.3--2.9 (m,8H), 3.25 (m,1H), 3.35 (s,3H), 4.15 (t,1H); ms (70 eV) m/e (rel intensity) 276(9), 274(9), 196(8), 194(2), 168(5), 163(11), 140(65), 125(100), 109(44), 93(38), 84(95), 71(94), 55(45), 41(71).

Preparation of 29 and 30 from 3

To a solution of 0.613 g (0.00313M) of 3 in 55 ml of acetic acid was added a solution of 0.550 g (0.0034M) of bromine in 5 ml of acetic acid, followed by one drop of fuming hydrobromic acid. The reaction was stirred at 55° for eight hr. After cooling to room temperature, 50 ml of 10% sodium sulfite was added to the reaction mixture which was then poured into 200 ml of water. This aqueous mixture was extracted with ether and the ether extracts were washed sequentially with water and brine, and then dried. After removal of the solvent, 0.982 g of oil was recovered. Analysis by GLPC (150°, 4% SE-30) of the oil showed the presence of 3, 29, and a third component subsequently identified as 30. The oil was placed on 100 g of neutral alumina (act 1) and eluted with 5% v/v ether--benzene. Early fractions yielded 0.196 g of 30 as a solid which displayed the following properties: mp 100--105°; ir (nujol) 1765 cm^{-1} ; pmr (CCl_4) δ 1.20 (s,3H), 1.55 (s,3H), 1.5--2.8 (m,8H), 3.1 (m,1H) 3.35 (s,3H); ms (70 eV) m/e (rel intensity) 356(0.3), 354(0.4), 352(0.3), 296(0.2), 294(0.4), 292(0.2), 276(1.5), 274(1.6), 215(1.5), 213(1.5), 163(3.0), 140(95), 125(100), 109(24), 108(26), 93(26), 91(23), 84(22), 71(79), 55(26), 41(55).

Later fractions yielded 0.229 g (26.8% yield from 3) of 29, identical in all its spectral properties to the bromide isolated in the previous preparation.

Treatment of 29 with Pyridine--Silver Nitrate

To a solution of 0.0475 g (0.000173M) of 29 in 1.5 ml of pyridine was added 0.0295 g (0.000173M) of solid silver nitrate and the mixture was refluxed for 48 hr. The reaction was cooled to room temperature, diluted with benzene, and then filtered through alumina. The benzene solution was then washed sequentially with 4N hydrochloric acid and brine, and then dried. After removal of the solvent, 0.0452 g of oil was recovered whose spectral properties and GLPC retention were identical to those of 29.

Treatment of 29 with Ethanolic Potassium Hydroxide

A solution of 0.065 g of 29 and 0.7 g of potassium hydroxide in 5 ml of absolute ethanol was refluxed for 24 hr. Analysis of the reaction by GLPC and TLC (neut alumina, act 1, 5% v/v ether--benzene) showed that 29 had remained unchanged.

Treatment of 29 with Potassium *Tert*-Butoxide

A solution of 0.100 g (0.000365M) of 29, and 0.045 g (0.0004M) of potassium *tert*-butoxide in 1.5 ml of DMSO was heated at 100° for 24 hr. The reaction was cooled to room temperature and dissolved in water and ether. The ether phase was isolated and dried. After removal of the solvent, 0.0633 g of oil was recovered which later crystallized. The product was identical to 29 by its spectral and chromatographic properties.

Preparation of 32

To a solution of 0.506 g (0.005M) of diisopropylamine in 90 ml of THF was added 2.32 ml of 2.15M *n*-butyllithium in hexane (Ventron) in one portion, and the mixture was stirred 10 min at room temperature. After this solution was cooled to -78°, a solution of 0.410 g (0.0021M) of 3 in 5 ml of THF was added in one portion and the resulting solution was stirred 10 min at -78°. A solution of 1.09 g (0.005M) of diphenyldisulfide and 0.87 ml (0.895 g/0.005M) of HMPA in 5 ml of THF was then added in one portion and the reaction was stirred two hr at -78°, followed by 12 hr at room temperature. The reaction mixture was washed sequentially with acidified brine and neutral brine, and then dried. After removal of the solvent, 1.78 g of brown oil was recovered. An ethyl acetate solution of this material was filtered through silica gel and the solvent was removed from the filtrate to yield 1.28 g of crude 31 as a yellow oil. This oil was dissolved in 10 ml of acetic acid, treated with 5% aqueous potassium permanganate until the purple color persisted, and stirred a further 15 min at room temperature. The color was discharged by the addition of 0.5M sodium bisulfite. The mixture was extracted with chloroform and the extracts were washed sequentially with water and brine, and then dried. After removal of the solvent, 1.08 g of yellow oil was recovered. The oil was dissolved in a minimum of hot 50% v/v ethyl acetate--petroleum ether

and placed in the refrigerator. A precipitate was recovered and found to be 0.341 g of diphenyldisulfide. After removal of the solvent from the mother liquor, 0.617 g of brown oil was recovered. Preparative layer chromatography (20% v/v ethyl acetate--hexane) of this oil yielded 0.090 g (13.3% from 3) of 32 as an oil which displayed the following properties: ir (CDCl₃) 3025, 1745, 1575 cm⁻¹; pmr (CDCl₃) (approx a 1:2.67 mixture of epimers from comparison of the peaks in the methyl region) δ 0.85 (s,3H), 1.35 (s,3H), 1.4--2.0 (m,8H), 3.2 (m,1H), 3.3 (s,3H), 3.85 (m,1H), 7.5 (m,5H); ms (70 eV) m/e (rel intensity) 304(1), 292(2), 276(2), 252(9), 194(14), 179(10), 163(10), 151(10), 140(27), 135(28), 125(71), 111(80), 108(65), 95(45), 83(67), 77(100), 71(99), 55(76), 43(50).

Attempted Thermolysis of 32

A solution of 0.0585 g of 32 in 10 ml of xylene was refluxed for 18 days. The reaction was cooled to room temperature and the solvent was removed to yield 0.113 g of residue. Preparative layer chromatography (20% v/v ethyl acetate--cyclohexane) of the crude product yielded 0.0494 g of unchanged 32.

Attempted Conversion of 3 to a Homologous Unsaturated Ester Using a Wittig Reagent

To a solution of 0.098 g (0.0005M) of 3 in 10 ml of DMSO was added 0.348 g (0.001M) of the solid Wittig

reagent isolated from sodium hydroxide treatment of an aqueous solution of the salt prepared from triphenyl phosphine and ethyl bromoacetate. The mixture was heated at 110° for 12 hr, then cooled to room temperature, poured into water, and extracted with ether. The extracts were washed sequentially with water and brine, and then dried. The orange solution was filtered through silica gel and the solvent was removed to yield 0.120 g of brown oil, the major component of which was unreacted 3.

Attempted Conversion of 3 to a Homologous Unsaturated Aldehyde Using a Wittig Reagent

To a stirred suspension of 0.0254 g (0.0011M) of sodium hydride in 10 ml of THF at 0° was added a solution of 0.288 g (0.0011M) of diethyl 2-(cyclohexylamino)vinylphosphonate in 10 ml of THF in one portion. The resulting solution was stirred 15 min at 0°, then a solution of 0.196 g (0.001M) of 3 in 10 ml of THF was added in one portion. The reaction was stirred at 0° and monitored at intervals by GLPC (160°, 4% QF-1) over a 24 hr period. The ketone 3 remained unchanged. The expected imine would have yielded a homologous aldehyde derivative of 3 upon acid hydrolysis.

Attempted Conversion of 3 to a Spiro Epoxide

To 10 ml of DMSO was added 0.024 g (0.001M) of sodium hydride and the mixture was heated at 70° for one hr. The resulting yellow solution was cooled to 0°. To this was

added a solution of 0.220 g (0.001M) of trimethyloxosulfonium iodide in 10 ml of THF in one portion, and the solution was stirred 15 min at 0°. Then a solution of 0.196 g (0.001M) of 3 in 10 ml of THF was added in one portion and the reaction was stirred two hr at 0°. The reaction was warmed to room temperature, stirred two days, then poured into brine, and extracted with ether. The extracts were washed sequentially with water and brine and then dried. After removal of the solvent, 0.154 g of clear oil was recovered whose spectral properties and GLPC retention were identical to 3.

Treatment of 3 with the Lithium Enolate
Anion of *Tert*-Butyl Acetate

To a solution of 0.002M of lithium diisopropyl amine in 2 ml of THF at -78° was added 0.232 g (0.002M/0.168 ml) of *tert*-butyl acetate in one portion. The solution was stirred 15 min at -78°, then a solution of 0.196 g (0.001M) of 3 in 2 ml of THF was added dropwise. The solution was stirred at -78° for four hr, then 4 ml of 0.03N hydrochloric acid was added, and the reaction was warmed to room temperature. The mixture was extracted with ether and the extracts were washed sequentially with water and brine, and then dried. After removal of the solvent, 0.181 g of unreacted 3 was recovered.

In another trial of this experiment, the reaction was quenched with acetic anhydride at -78°, then warmed to room temperature. The isolated product was 3.

Treatment of $\tilde{3}$ with the Lithium Enolate Anion
of *Tert*-Butyl Trimethylsilylacetate

To a solution of 0.0005M of lithium isopropyl cyclohexyl amine in 10 ml of THF at -78° was added 0.094 g (0.0005M) of *tert*-butyl trimethylsilylacetate in one portion. The solution was stirred five min at -78° , then a solution of 0.098 g (0.0005M) of $\tilde{3}$ in one ml of THF was added dropwise. The reaction was stirred 10 min at -78° , warmed to room temperature, poured into 4N hydrochloric acid, and then extracted with ether. The ether extract was washed sequentially with 4N hydrochloric acid and brine, and then dried. After removal of the solvent, 0.134 g of yellow oil was recovered whose spectral properties, GLPC behavior (130° , 4% SE-30), and TLC retention (silica gel, 20% v/v ethyl acetate--hexane) were identical to those of $\tilde{3}$.

Treatment of $\tilde{3}$ with the Lithium
Enolate of Ethyl Acetate

To a solution of 0.002M of lithium diisopropyl amine in 10 ml of THF at -78° was added 0.22 g (0.0025M) of ethyl acetate in one portion. The solution was stirred 15 min at -78° , then a solution of 0.196 g (0.001M) of $\tilde{3}$ in one ml of THF was added dropwise. The reaction was stirred four hr at -78° , then quenched by the addition of 0.15 ml of glacial acetic acid. The reaction was warmed to room temperature, poured into water, and extracted with ether. The ether extracts were washed with brine and dried. After removal of the solvent, 0.208 g of

light yellow oil was recovered whose spectral properties, GLPC behavior, and TLC retention were identical to those of 3.

Treatment of 3 with a Reformatsky Reagent

To a solution of 0.196 g (0.001M) of 3 in 15 ml of benzene and one ml of dimethoxyethane was added 0.196 g (0.003M) of zinc dust and 0.501 g (0.003M) of ethyl bromoacetate. The mixture was brought to reflux. After 30 min most of the zinc was consumed. Refluxing was continued for a total of 24 hr, then the reaction was cooled to room temperature and a further 0.003M of zinc dust and 0.003M of ethyl bromoacetate were added. The reflux was resumed for another 24 hr, then the reaction was cooled to room temperature and poured into 2N sulfuric acid. The mixture was extracted with ether and the extracts were washed sequentially with water and brine, and then dried. After removal of the solvent, 0.370 g of orange oil was recovered. Preparative layer chromatography (20% v/v ethylacetate--cyclohexane, double elution) of the oil yielded 0.160 g of oil whose spectral properties, GLPC behavior, and TLC retention were identical to those of 3.

Preparation of 33

Acetylene gas, scrubbed by concentrated sulfuric acid, was bubbled over a six hr period into a stirred slurry of 1.15 g (0.05M) of sodium sand in 200 ml of THF

which was maintained at 50°. The acid in the scrubber was changed when it began to darken and turn yellow. A solution of 1.78 g (0.00908M) of 3 in 10 ml of THF was added in one portion to the sodium acetylide--THF slurry and the mixture was refluxed for 2 days under argon. The reaction was cooled to room temperature and poured slowly into ice water. The aqueous mixture was extracted with ether and the extracts were washed sequentially with water and brine, and then dried. After removal of the solvent, 1.87 g of yellow oil was recovered which later solidified. Recrystallization from ethyl acetate yielded 0.831 g (41.1%) of 33. An analytical sample of 33 displayed the following properties: mp 104--107°; ir (CCl₄) 3590, 3350 cm⁻¹; pmr (CCl₄) δ 0.8 (s,3H), 0.95 (s,3H), 1.2--2.4 (m,12H), 3.05 (m,1H), 3.3 (s,3H); ms (70 eV) m/e (rel intensity) 222(1), 207(1), 198(2), 188(3), 166(10), 154(14), 148(29), 133(28), 122(100), 112(30), 107(65), 93(30), 81(29), 71(90), 55(39), 41(58).

Anal Calcd for C₁₄H₂₂O₂: C, 75.63; H, 9.97

Found: C, 75.58; H, 10.00

Recovery of 34 from the Treatment
of 33 with Formic Acid

A solution of 0.350 g (0.00158M) of 33 in 1.65 ml of 88% formic acid was heated at 85--90° for 12 hr. The reaction was cooled to room temperature and made alkaline by the addition of 5% aqueous sodium hydroxide. The aqueous mixture was extracted with ether and the extracts

were washed sequentially with water and brine, and then dried. After removal of the solvents, 0.400 g of light brown oil was recovered. This oil was placed on 40 g of silica gel and eluted with 50% v/v ether--pentane, to yield 0.256 g (64.8%) of 34 as a crystalline white solid, as well as 0.057 g of 33. An analytical sample of 34 displayed the following properties: mp 37--39°; ir (CCl₄) 1725 cm⁻¹; pmr (CCl₄) δ 0.95 (s,3H), 1.1 (s,3H), 1.2--2.6 (m,11H), 3.15 (m,1H), 3.35 (s,3H), 8.05 (s,1H); ms (70 eV) m/e (rel intensity) 250(1), 226(1), 211(1), 194(3), 180(18), 165(19), 148(34), 133(59), 122(100), 107(96), 93(59), 84(95), 79(54), 71(42), 59(30), 53(35).

Regeneration of 33 from 34

To a solution of 0.060 g (0.000240M) of 34 in 3 ml of methanol was added 0.1 ml of 30% w/w potassium hydroxide--methanol. The reaction was stirred at room temperature for 20 min. The methanol was then removed and the residue was dissolved in ether and water. The ether phase was isolated and dried. After removal of the solvent, 0.0552 g (96.3%) of 33 was recovered, as evidenced by spectra, TLC retention (silica gel, 50% v/v ether--pentane), and GLPC behavior (150°, 4% SE-30) of the product.

Recovery of 35 from Treatment of 33
with Sulfuric Acid--Acetic Acid

To a solution of 0.0550 g (0.000248M) of 33 in one ml of glacial acetic acid was added one drop of concentrated sulfuric acid and the resulting solution was heated at 50° for 30 min. The reaction was cooled to 0°, neutralized with 30% aqueous sodium hydroxide, and extracted with ether. The ether extract was dried and analyzed by GLPC (150°, 4% SE-30) and TLC (silica gel, 50% v/v ether--pentane). A single product had formed from 33. After removal of the solvent, 0.038 g (58%) of crude 35 was obtained, whose spectral properties and GLPC retention were identical to the acetate derivative of 33 which was subsequently prepared from a pyridine--acetic anhydride medium.

Preparation of 35 from 33 in
Pyridine--Acetic Anhydride

A solution of 1.00 g (0.0045M) of 33 in 30 ml of pyridine and 1.38 ml of acetic anhydride was refluxed for 12 hr, then cooled to room temperature. The pyridine was removed and the residue was dissolved in ether. The ether solution was washed sequentially with 4N hydrochloric acid, water, and brine, and then dried. After removal of the solvent, 1.11 g of brown oil was obtained. Analysis by GLPC (160°, 4% QF-1) indicated that this was nearly pure 35. The oil was distilled at 0.15 torr and the desired acetate was collected at 67°, to yield 1.02 g (85.7%) of 35, which displayed the following properties:

ir (neat) 1735 cm^{-1} ; pmr (CCl_4) δ 0.92 (s,3H), 1.05 (s,3H), 1.95 (s,3H), 1.2--2.6 (m,11H), 3.1 (m,1H), 3.30 (s,3H).

A satisfactory mass spectrum could not be obtained.

Treatment of 33 with Mercuric
Oxide and Aqueous Acid

A mixture of 0.109 g (0.0005M) of red mercuric oxide and 10 ml of 5% aqueous sulfuric acid was heated at 60° until a solution had formed. Then 0.111 g (0.0005M) of solid 33 was added and the resulting mixture was heated at 60° for 24 hr. The reaction was cooled to room temperature, extracted with ether, the extracts were dried, and the solvent was removed to yield 0.055 g of unreacted 33.

Treatment of 33 with Mercuric
Sulfate and Acetic Acid

To a solution of 0.055 g (0.00025M) of 33 in one ml of glacial acetic acid was added 0.075 g (0.00025M) of mercuric sulfate and the resulting mixture was heated at 60° for 12 hr. The reaction was cooled to room temperature, diluted with water, and extracted with ether. The ether extract was washed sequentially with water and brine, and then dried. After removal of the solvent, 0.0585 g (87.9%) of the acetate 35 was isolated. Analysis of the crude product by TLC (silica gel, 50% v/v ether--pentane) and GLPC (150° , 4% SE-30) disclosed that it was essentially pure.

Treatment of 35 with Mercuric Acetate

A solution of 0.257 g of 35 and 0.5 g of mercuric acetate in 20 ml of ethyl acetate was stirred 24 hr at room temperature. Then hydrogen sulfide gas (generated from Al_2S_3 and water) was bubbled into the reaction for 10 min. The black precipitate which formed was removed by filtration through celite. After removal of the solvent from the filtrate, 0.257 g of unreacted 35 was recovered.

Treatment of 35 with Mercuric
Oxide and Aqueous Acid

A mixture of 0.109 g (0.0005M) of red mercuric oxide and 10 ml of 5% aqueous sulfuric acid was heated at 55--60° until a solution had formed. To this was added in one portion a solution of 0.132 g (0.0005M) of 35 in 5 ml of THF. The homogeneous reaction mixture was heated at 55--60° for 24 hr, then cooled to room temperature, diluted with water, and extracted with ether. The ether extracts were washed with brine and dried. After removal of the solvent, 0.110 g of crude 33 was obtained.

Attempted Reduction of the Ethynyl Group
of 33 using Lithium Aluminum Hydride

To a solution of 0.111 g (0.0005M) of 33 in 10 ml of diglyme was added 0.0378 g (0.001M) of solid lithium aluminum hydride in one portion. The heterogeneous mixture was refluxed for 18 hr. The reaction was cooled to room temperature, poured into ice water, neutralized with

4N hydrochloric acid, and extracted with chloroform. The chloroform extracts were washed sequentially with water and brine, and then dried. The solution was filtered through silica gel and the solvent was removed from the filtrate to yield 0.117 g of unreacted 33 as a white amorphous solid.

Attempted Reduction of the Ethynyl Group
of 33 using Diisobutyl Aluminum Hydride

To a solution of 0.222 g (0.001M) of 33 in 5 ml of benzene at 0° was added 7 ml of a 20% solution of diisobutyl aluminum hydride in hexane (Ventron) and the resulting solution was stirred five min at 0°. The reaction was heated at 60° for 3-1/2 days. After cooling to room temperature, five ml of 50% v/v methanol--benzene was added to the reaction followed by 10 ml of 50% v/v methanol--water. The resulting precipitate was filtered off, then most of the methanol was removed from the filtrate. The residue was diluted with water and extracted with ether. The ether extract was washed sequentially with water and brine, and then dried. After removal of the solvent, 0.198 g of unreacted, solid 33 was recovered.

Summary of the Attempted Catalytic
Hydrogenation of the Ethynyl Group
of 33 under Several Conditions

Ethynyl carbinol 33 was subjected to each of the following hydrogenation media under one atmosphere of

hydrogen and at room temperature: pyridine, 2% palladium on calcium carbonate, 24 hr; dioxane, 2% palladium on calcium carbonate, 1 hr; methanol, palladium on carbon, 6 hr; acetic acid, palladium on carbon, 24 hr; methanol, platinum oxide, 24 hr. In each case, 33 was recovered unchanged.

Attempted Claisen-Cope Rearrangement of 34

Formate 34 (0.119 g) was heated at 250° for 19-1/2 hr in an evacuated, sealed tube and recovered unchanged.

Attempted Claisen-Cope Rearrangement of 35 by Flow Pyrolysis

A solution of 0.359 g of 35 in 50 ml of cyclohexane was introduced dropwise (one drop/s) into the top of a Vigreux column packed with Pyrex beads which was maintained at 300°. The system was flushed by a stream of nitrogen (40 bubbles/min through a U-tube charged with mineral oil) during the course of the pyrolysis. The effluent was collected in two cold traps connected in series which were maintained at -78°. After removal of the solvent, 0.157 g of unchanged 35 was recovered.

Attempted Ag(I) Catalyzed Claisen-Cope Rearrangement of 35

To a solution of 0.395 g of 35 in 20 ml of acetone was added one drop of silver perchlorate monohydrate and the resulting solution was refluxed for five days. The reaction was cooled to room temperature, diluted with

five ml of saturated ammonium chloride, and stirred for 15 min. The mixture was diluted with ether and filtered through silica gel. After removal of the solvent, 0.340 g of brown oil was recovered, which was a mixture of 35 and 33.

Conversion of 33 to a Phosphite Ester
(36) and Attempted Thermal Claisen-
Cope Rearrangement of the Derivative

To a solution of 0.204 g (0.00092M) of 33 in 20 ml of triethylamine at room temperature was added 0.15 ml of diethyl chlorophosphite (Aldrich) in one portion and the reaction was stirred for 24 hr. The reaction was diluted with water and washed sequentially with water and brine, and then dried. After removal of the solvent, 0.269 g of yellow oil was recovered. Preparative layer chromatography (50% v/v ethyl acetate--cyclohexane) of the oil yielded 0.140 g of 33 and 0.078 g of 36. The phosphite ester 36 displayed the following properties: ir (neat) 1265, 1070, 1025, 970 cm^{-1} ; pmr (CCl_4) δ 0.9 (s,3H), 1.05 (s,3H), 1.3 (t,6H), 1.4--2.6 (m,11H), 3.0 (m,1H), 3.2 (s,3H), 3.9 (m,4H).

A sample of 36 was heated at 100° for 24 hr in an evacuated, sealed tube and later recovered unchanged.

Attempted Conversion of 33 to a Chloro-Allene
with Thionyl Chloride--Pyridine

To a solution of 0.111 g of 33 in 10 ml of pyridine was added 2.5 ml of thionyl chloride in one portion. The

dark brown solution was stirred at room temperature for 24 hr and the product isolated in the usual way. Analysis by TLC (silica gel, 40% v/v ether--pentane) and spectra of the product showed that it was unreacted 33.

Attempted Conversion of 33 to an Allene
using Lithium Aluminum
Hydride--Aluminum Trichloride

A solution of 0.222 g (0.001M) of 33 in seven ml of THF was added in one portion to a stirred slurry of 0.0756 g (0.002M) of lithium aluminum hydride and 0.200 g (0.0015M) of aluminum trichloride in eight ml of THF at room temperature. The mixture was then refluxed for 24 hr. The reaction was cooled to room temperature, poured into ice water, and the aqueous mixture was extracted with ether. The ether extracts were washed sequentially with water and brine, and then dried. After removal of the solvent, 0.220 g of 33 was recovered.

Attempted Conversion of 35 to a
Methyl-Substituted Allene

To a stirred suspension of 1.90 g (0.01M) of cuprous iodide in 25 ml of ether at 0° was added 10.9 ml of 2.3M methyl lithium in ether solution (Ventron) in one portion. The mixture was stirred 2.5 hr at 0° at which point a clear solution was obtained. The solution was cooled to -78° and a solution of 0.528 g (0.002M) of 35 in 10 ml of ether was added dropwise. The reaction was stirred 15 min at -78°, then warmed to room temperature and

stirred six hr. The reaction was diluted with ether and washed with pH 8 ammonium hydroxide (saturated ammonium chloride whose pH was adjusted with concentrated ammonium hydroxide) until most of the blue Cu(II) was removed. After drying and removal of the solvent, 0.563 g of light green oil was recovered. This oil was placed on 50 g of silica gel and eluted with 20% v/v ethyl acetate--petroleum ether to yield 0.214 g of 35 and 0.287 g of 33.

Preparation of 37

To a solution of 0.280 g (0.004M) of ethoxyacetylene (Farchan) in 10 ml of ether was added 1.93 ml of 2.08M *n*-butyl lithium in hexane (Ventron) and the resulting cloudy solution was stirred 10 min at room temperature. A solution of 0.434 g (0.00221M) of 3 in 10 ml of ether was then added in one portion, followed by 0.70 ml (0.72 g/0.004M) of HMPA. The reaction was stirred 12 hr, and then poured into cold 4N hydrochloric acid, and extracted with ether. The ether extracts were washed sequentially with 4N hydrochloric acid, water, and brine, and then dried. After removal of the ether, the residue was dissolved in methanol, norit was added, and the mixture was heated on a steam bath for five min. After filtration of the hot mixture, the methanol was removed to yield 0.579 g (98.3%) of light yellow, crystalline 37. An analytical sample of 37 displayed the following properties: mp 132--134° (petroleum ether--ethyl acetate);

ir (CCl₄) 1700, 1630, 1265 cm⁻¹; pmr (CCl₄) δ 0.9 (s,3H), 1.05 (s,3H), 1.25 (t,3H), 1.4--2.9 (m,11H), 3.15 (m,1H), 3.25 (s,3H), 3.9 (q,2H); UV (95% ethanol) 272 nm (ε 992); ms (70 eV) m/e (rel intensity) 267(13), 266(53), 251(4), 237(4), 234(60), 219(26), 205(50), 196(65), 177(35), 163(45), 157(45), 129(55), 109(58), 97(100), 71(60), 55(86), 43(95), 41(87); cmr (CDCl₃) δ (rel intensity) 13.57(77), 15.32(82), 17.08(91), 20.08(75), 23.67(100), 24.08(68), 25.73(97), 33.10(92), 42.03(53), 52.44(33), 57.70(58), 62.26(68), 83.58(87), 113.03(21), 163.46(15), 182.69(13).

Anal Calcd for C₁₆H₂₆O₃: C, 72.14; H, 9.84

Found: C, 72.13; H, 9.84

Preparation of 38

A solution of 0.098 g of 3 and 0.1 ml of ethoxyacetylene in five ml of benzene was irradiated for 3-1/2 hr with a Hanovia lamp using a Corex filter. After removal of the solvent, 0.112 g of yellow oil was recovered. The pmr spectrum of the crude product indicated that no adduct had formed and that 3 had isomerized to its *cis*-isomer as evidenced by the methyl shifts.

Accordingly, a solution of 0.105 g of 3 in five ml of benzene was irradiated as before. After removal of the solvent, 0.102 g of clear oil was recovered. The GLPC retention (160°, 4% QF-1) of the product was nearly coincident with that of the starting material but the pmr

spectrum of the product indicated that 3 had completely isomerized to 38. The *cis*-fused perhydroindene, 38, displayed the following properties: ir (neat) 1735 cm^{-1} ; pmr (CCl_4) δ 0.85 (s,3H), 0.92 (s,3H), 1.0--2.4 (m,10H), 3.2 (m,1H), 3.25 (s,3H); ms (70 eV) m/e (rel intensity) 197(5), 196(26), 181(8), 164(19), 149(19), 136(21), 122(35), 109(100), 97(65), 81(39), 71(45), 58(43), 41(68).

Anal Calcd for $\text{C}_{12}\text{H}_{20}\text{O}_2$: C, 73.43; H, 10.27

Found: C, 73.24; H, 10.34

Treatment of 3 with Allyl Magnesium Bromide in THF

A solution of 0.242 g (0.002M) of allyl bromide in 20 ml of THF was stirred with 0.048 g (0.002M) of magnesium turnings for three hr at room temperature, at which point all the magnesium had dissolved to form a clear solution. Then a solution of 0.196 g (0.001M) of 3 in one ml of THF was added to the Grignard solution. The reaction was stirred two days at room temperature, then poured into water, extracted with ether, and the extracts were washed sequentially with water and brine, and then dried. After removal of the solvent, 0.199 g of clear oil was recovered, the pmr spectrum of which indicated it to be unreacted 3.

Preparation of 39

A solution of 0.484 g (0.004M) of allyl bromide in 15 ml of ether was stirred with 0.096 g (0.004M) of magnesium turnings for three hr at room temperature, at

which point all the magnesium had dissolved to form a clear solution. Then a solution of 0.196 g (0.001M) of 3 in five ml of ether was added to the Grignard solution. The reaction was stirred for 12 hr at room temperature, then refluxed for two hr. The reaction was cooled to room temperature, poured into saturated aqueous ammonium chloride, and extracted with ether. The ether extracts were washed sequentially with water and brine, and then dried. After removal of the solvent, 0.212 g (89.1%) of 39 was obtained as a colorless oil. Analysis by GLPC (160°, 4% QF-1) of the product indicated that 3 had been completely consumed. An analytical sample of 39 displayed the following properties: ir (neat) 3520, 3025, 1630, 985, 905 cm^{-1} ; pmr (CCl_4) δ 1.0 (s,3H), 1.1 (s,3H), 1.2--2.4 (m,13H), 3.0 (m,1H), 3.15 (s,3H), 5.0 (m,2H), 5.7 (m,1H); ms (70 eV) m/e (rel intensity) 238(0.1), 220(0.6), 206(0.8), 197(0.6), 188(0.5), 179(2), 165(3), 147(8), 122(9), 107(6), 93(4), 91(4), 81(5), 71(9), 58(30), 43(100).

Anal Calcd for $\text{C}_{15}\text{H}_{26}\text{O}_2$: C, 75.58; H, 10.99

Found: C, 75.51; H, 11.05

Preparation of 40

A mixture of 7.2 g (0.3M) of magnesium turnings, a small crystal of iodine, and 30 ml of ether was stirred until the iodine color had lightened appreciably (about 15 min). Then a solution of 13.5 g (0.1M) of crotyl bromide (Aldrich) in 70 ml of ether was added dropwise

to the magnesium turnings over five hr at room temperature. After the addition was complete, the metallic gray solution was stirred a further 30 min. Then a solution of 10 g (0.051M) of 3 in 100 ml of ether was added to the Grignard solution over one hr. The reaction was stirred for another hour after the addition was complete, then poured into cold, saturated ammonium chloride. The aqueous mixture was extracted with ether and the extracts were washed sequentially with water and brine, and then dried. Analysis by GLPC (160°, 4% QF-1) of the ether solution indicated that 3 had been totally consumed. After removal of the solvent, 12.40 g (96.5%) of 40 was recovered as a clear oil. An analytical sample of 40 displayed the following properties: ir (neat) 3520, 3025, 1630, 990, 905 cm^{-1} ; pmr (CCl_4) δ 0.95 (d,3H), 1.1 (bs,6H), 1.15--2.6 (m,12H), 3.0 (m,1H), 3.15 (s,3H), 4.9 (m,2H), 5.8 (m,1H); ms (70 eV) m/e (rel intensity) 252(0.3), 240(0.2), 237(0.2), 234(2), 224(6), 220(3), 210(2), 202(2), 197(7), 179(19), 165(30), 147(100), 125(32), 122(37), 105(35), 91(25), 81(31), 71(52), 55(51), 41(56).

Anal Calcd for $\text{C}_{16}\text{H}_{28}\text{O}_2$: C, 76.14; H, 11.18

Found: C, 76.00; H, 11.15

Preparation of 43

A solution of 57.7 g (0.27M) of sodium metaperiodate and 0.30 g of potassium permanganate in 1000 ml of water

was added to a solution of 11.3 g (0.045M) of 40 in 250 ml of *tert*-butanol and 100 ml of 5% aqueous potassium carbonate, over 30 min at room temperature. The reaction was maintained at pH 8 during the addition by adding two further 100 ml portions of 5% aqueous potassium carbonate, at equally spaced intervals, to the reaction. The reaction was stirred four hr at room temperature after the addition was complete, then acidified with concentrated sulfuric acid. The reaction was extracted with four, 200 ml portions of chloroform, and the extracts were washed sequentially with water and brine, and then dried. After removal of the solvent, 12.27 g of the crude acid, 42, was recovered. Analysis of 42 by TLC (silica gel, 20% v/v ethyl acetate--cyclohexane) indicated the absence of 40. The neat ir spectrum of 42 displayed: 3600--2300 (broad), 1700 (strong) cm^{-1} .

The crude acid, 42, was dissolved in 100 ml of ether and treated with an ether solution of diazomethane (approx 0.05M in 500 ml) at 0°. The excess diazomethane and most of the ether were boiled off on a steam bath. The remainder of the ether was removed under reduced pressure to yield 11.72 g of clear viscous oil. Analysis of the oil by TLC indicated an absence of 42. Analysis by GLPC (160°, 4% QF-1) indicated one major peak at long retention and some volatile impurities. This material was purified by HPLC (15 x 500 mm silica gel, 20% v/v ethyl acetate--hexane, one ml/min) in 20 portions to

yield 4.64 g (36.2%) of 43 as a colorless oily solid which displayed the following properties: ir (neat) 3480, 1710 cm^{-1} ; pmr (CCl_4) δ 0.9--2.0 (m, 21H), 3.05 (m, 1H), 3.2 (s, 3H), 3.6 (s, 3H); ms (70 eV) m/e (rel intensity) 284(0), 266(1), 252(0.6), 234(1.3), 219(0.8), 208(13), 196(46), 164(11), 147(17), 125(62), 121(69), 112(61), 97(54), 85(60), 71(100), 57(75), 41(84).

APPENDIX

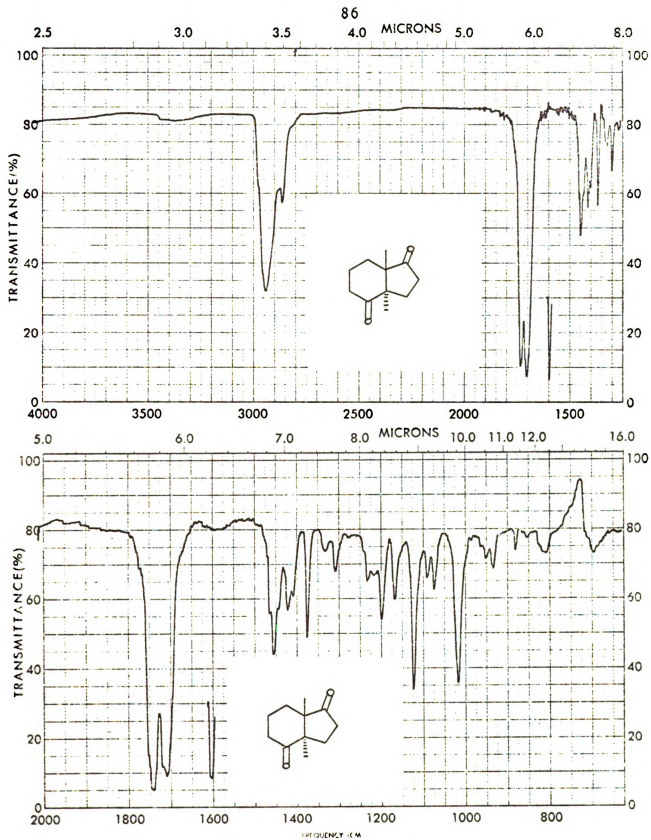


Figure 1. Infrared spectrum of 1.

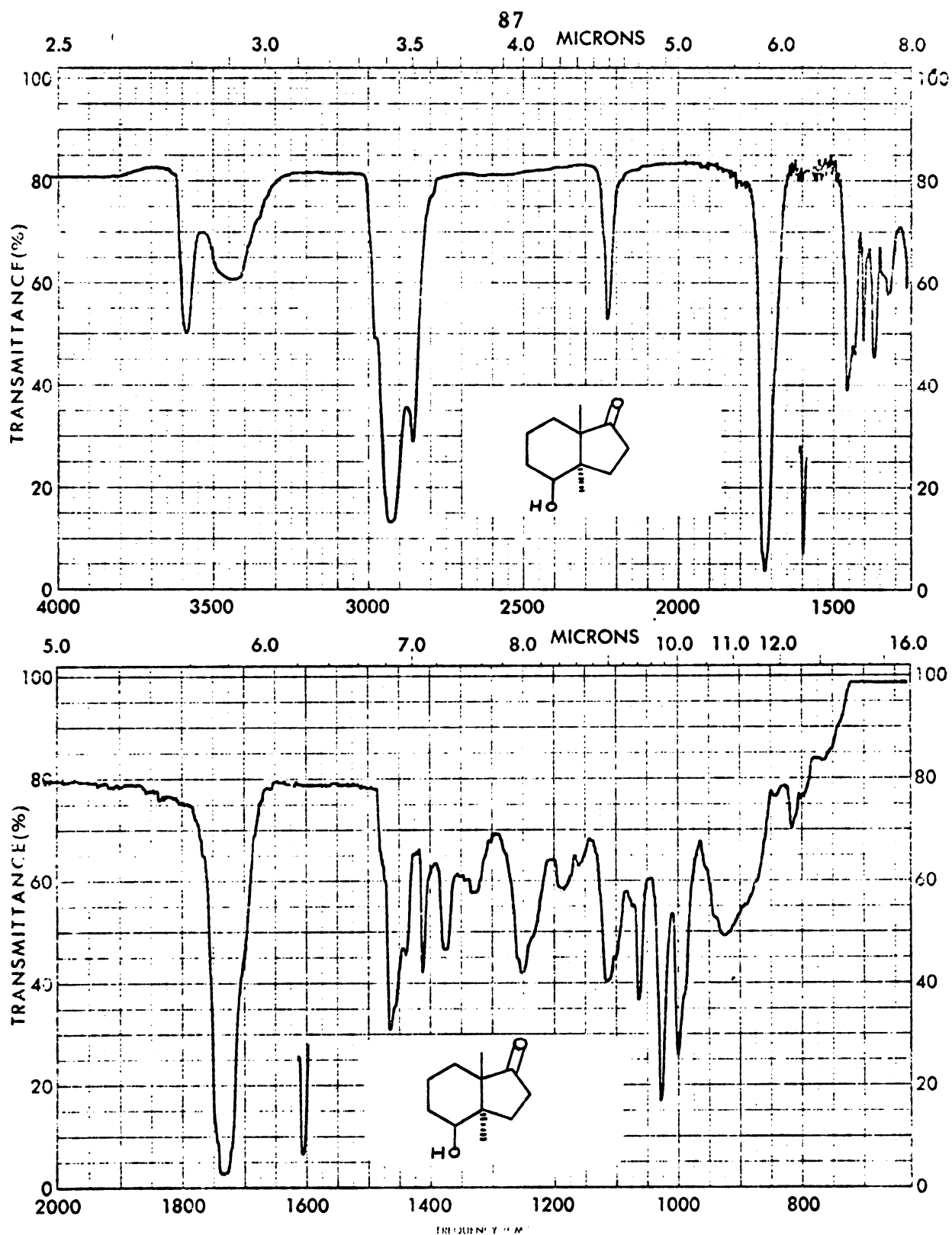


Figure 2. Infrared spectrum of 2 (CDCl_3).

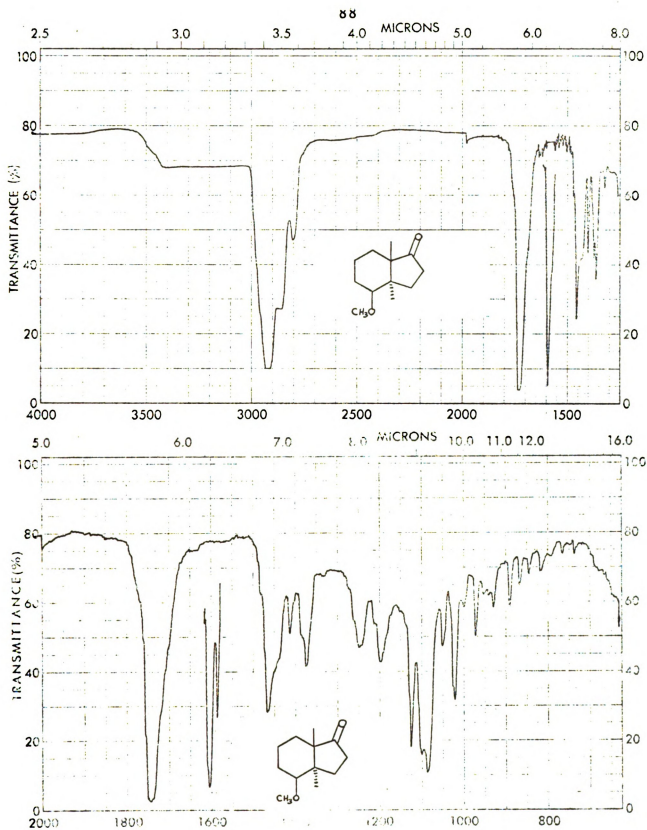


Figure 3. Infrared spectrum of 3.

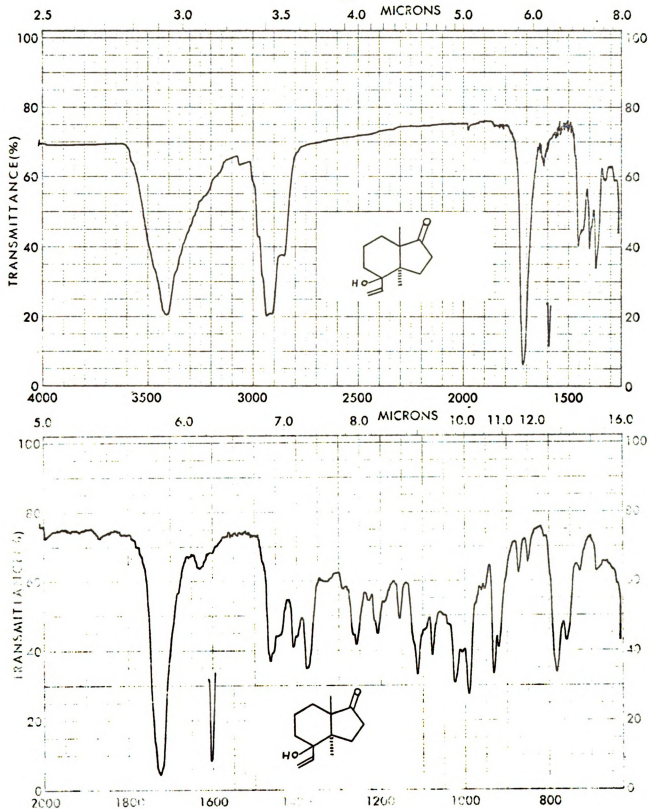


Figure 4. Infrared spectrum of 4.

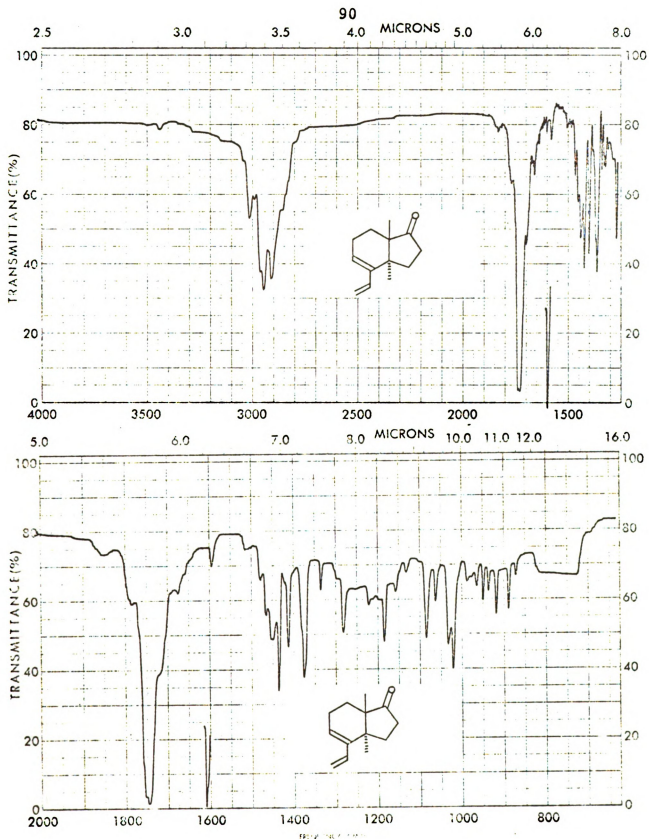


Figure 5. Infrared spectrum of 5.

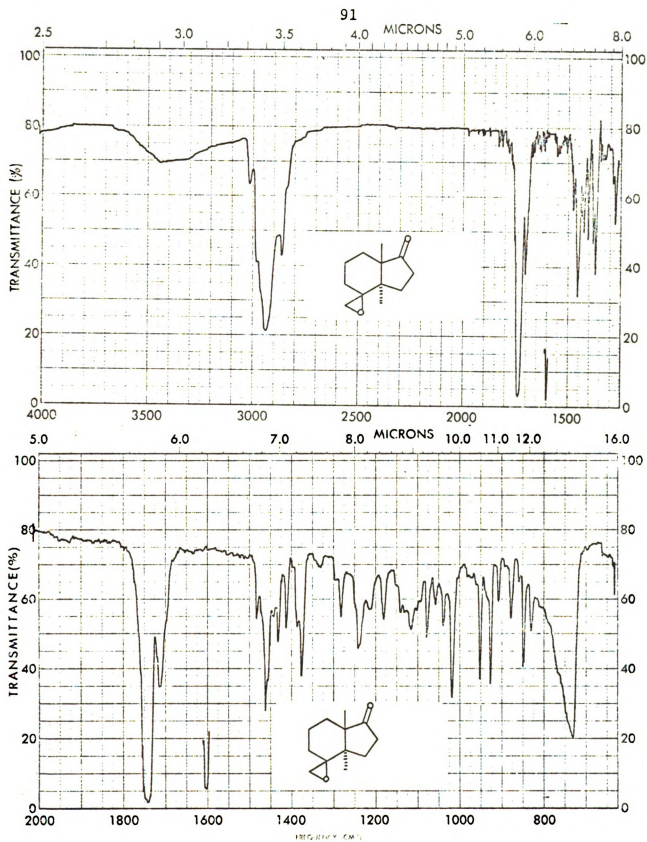


Figure 6. Infrared spectrum of 6.

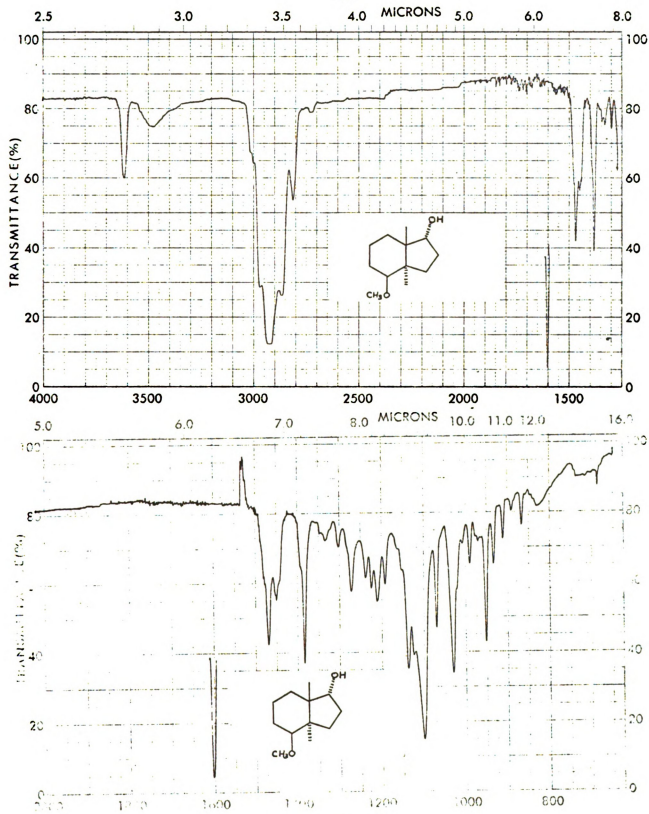


Figure 7. Infrared spectrum of 7.

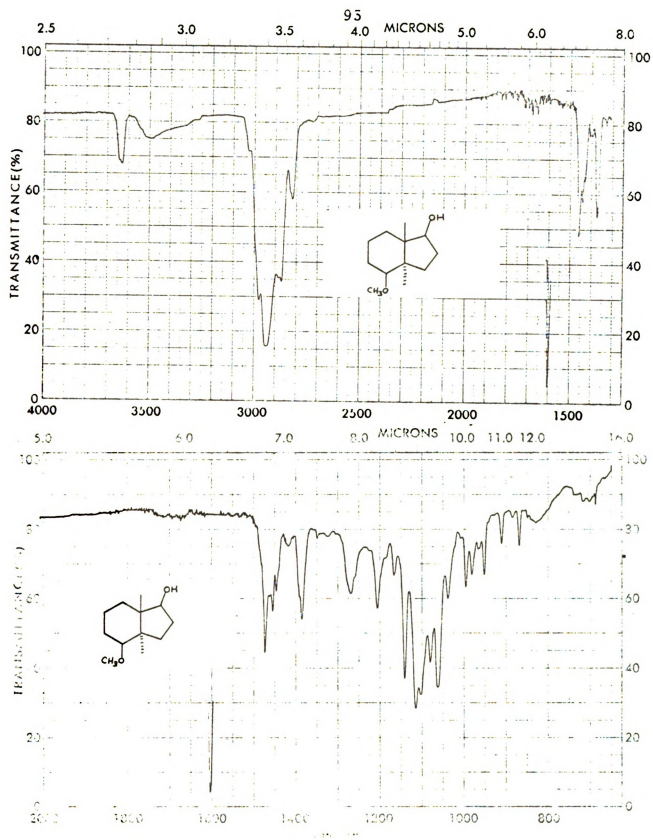


Figure 8. Infrared spectrum of 8.

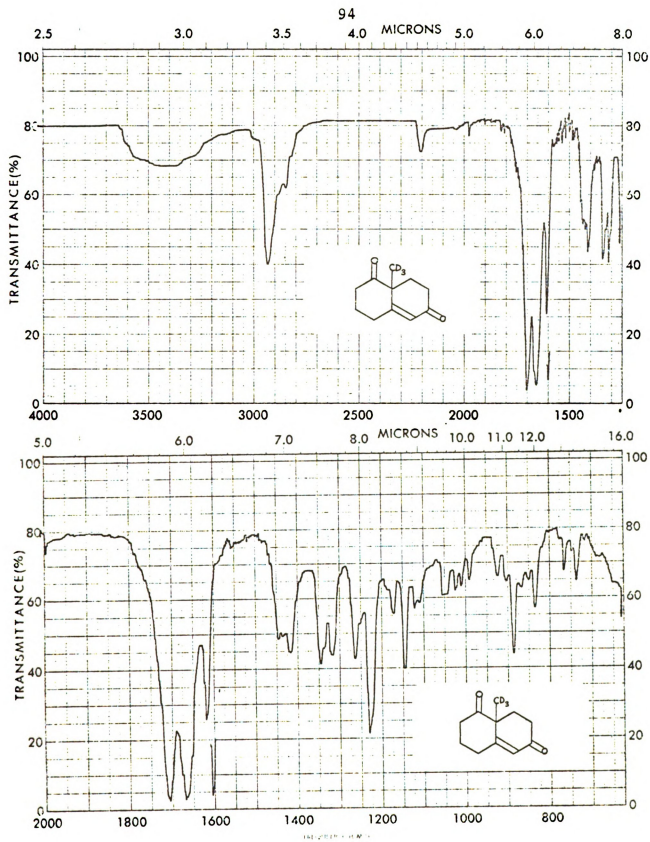


Figure 9. Infrared spectrum of 10.

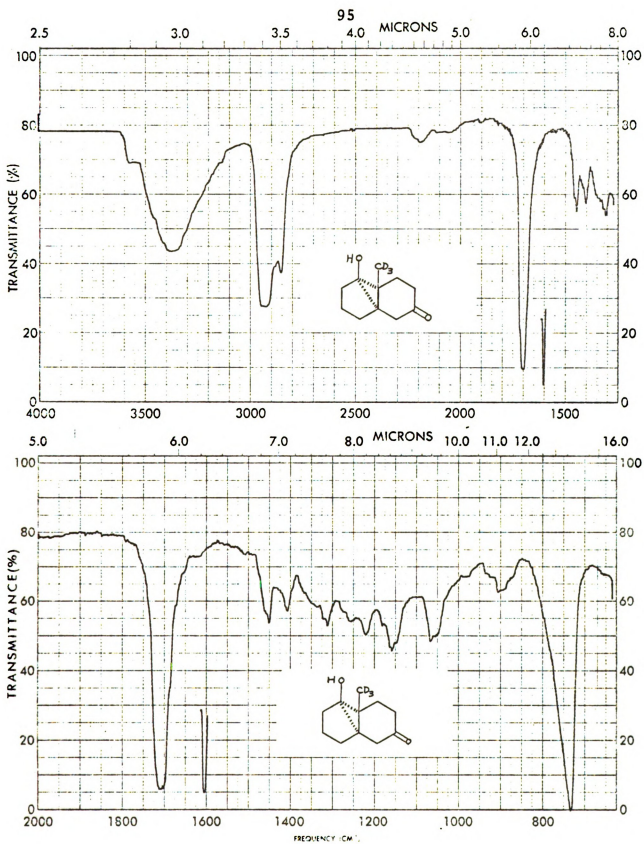


Figure 10. Infrared spectrum of 11.

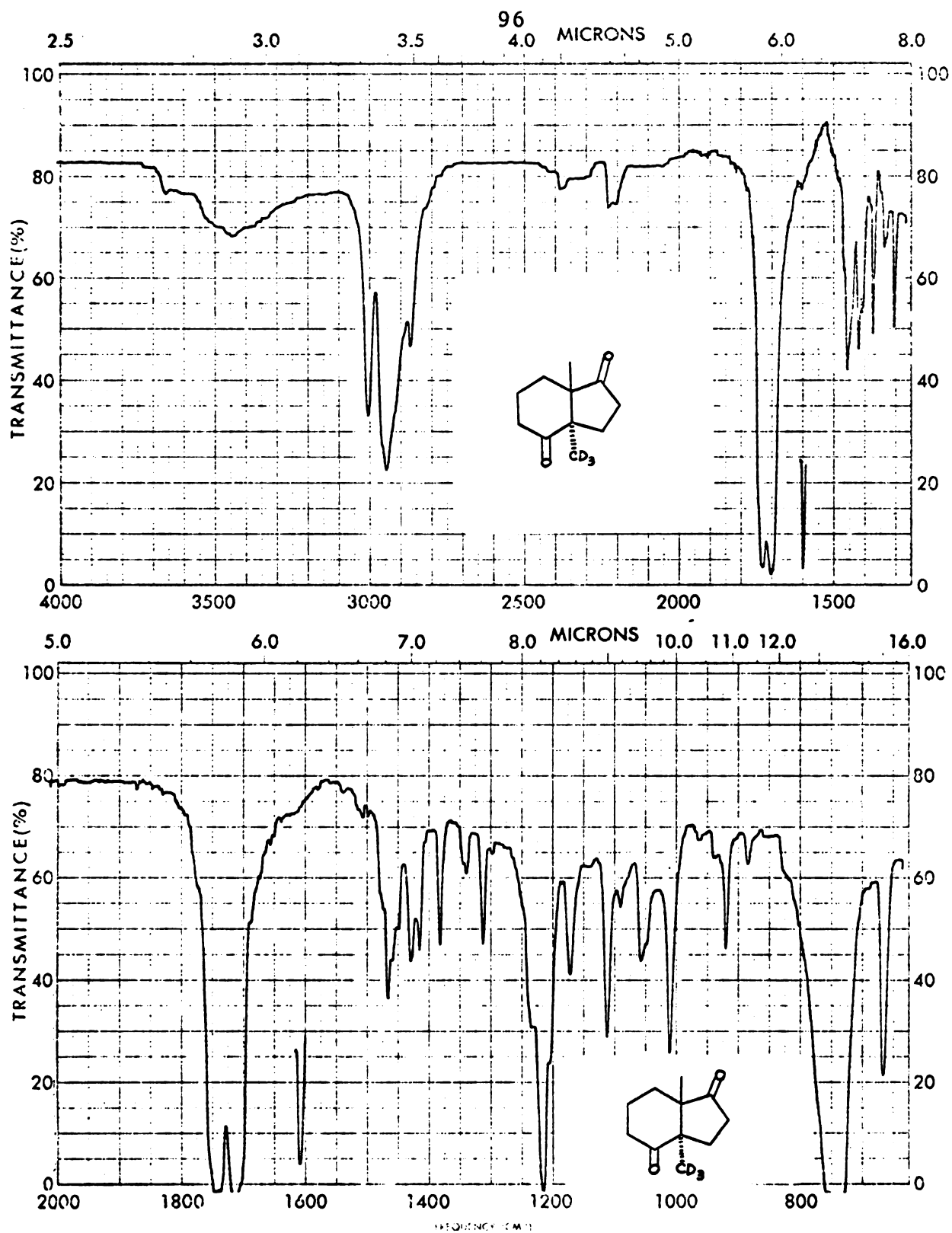


Figure 11. Infrared spectrum of 13.

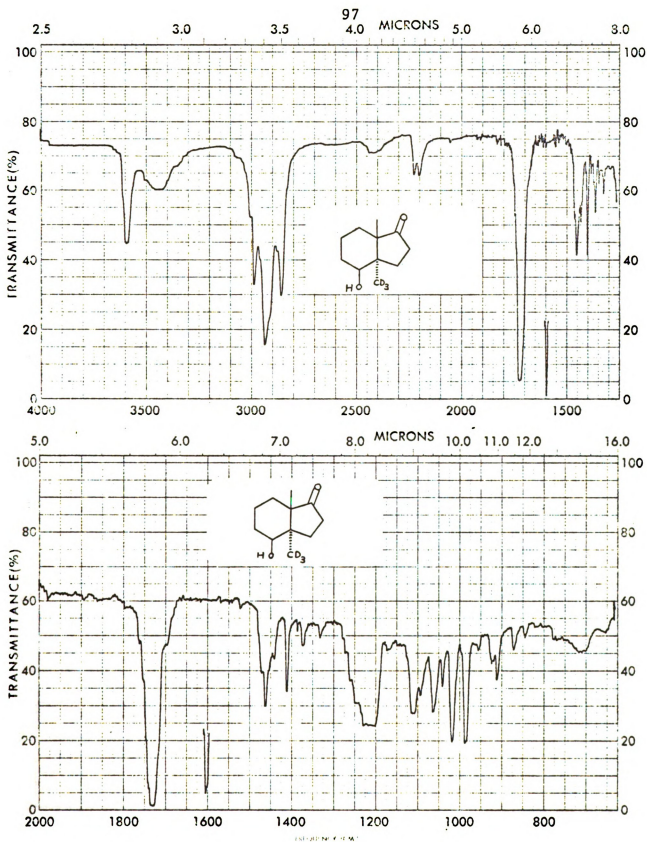


Figure 12. Infrared spectrum of 14.

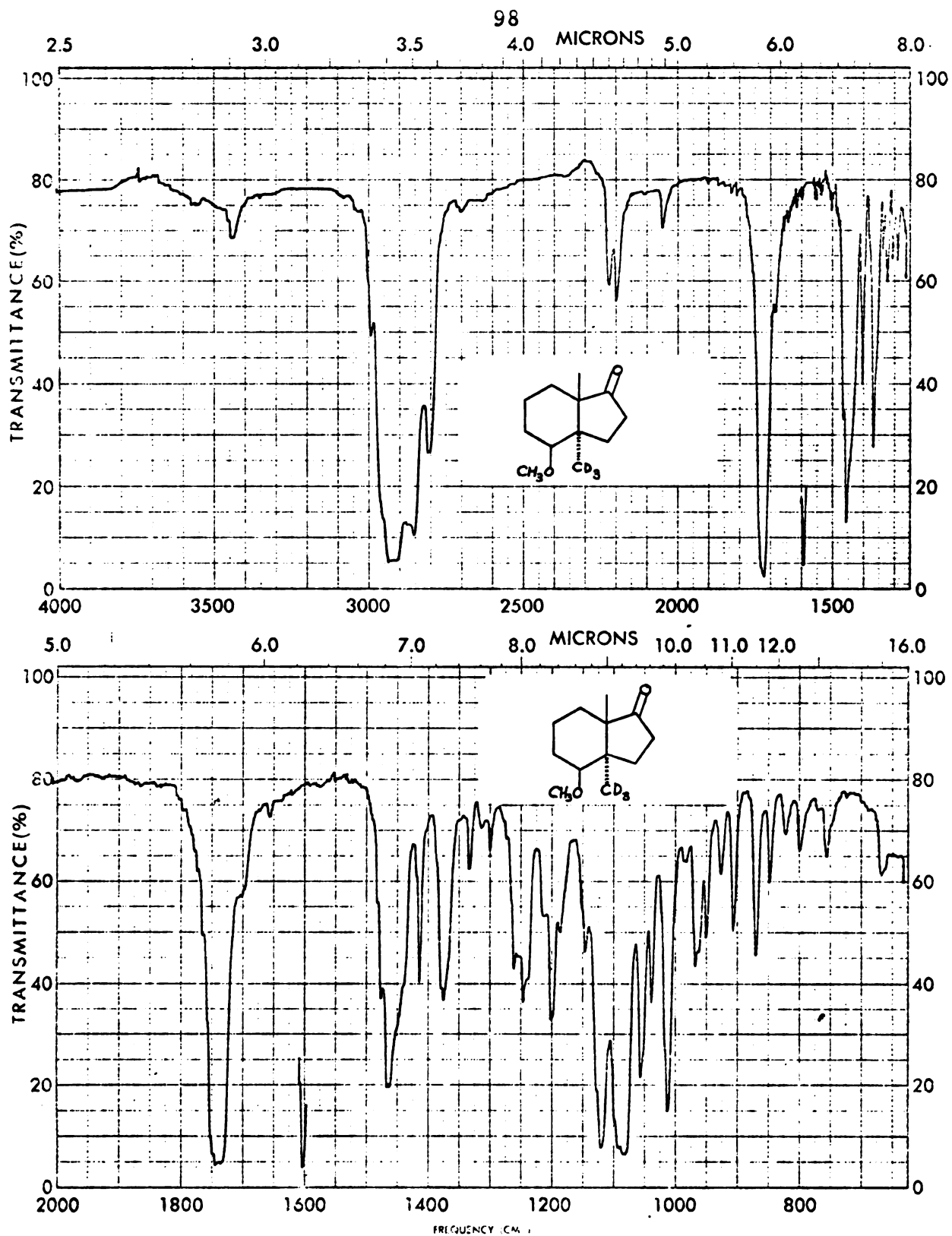


Figure 13. Infrared spectrum of 15.

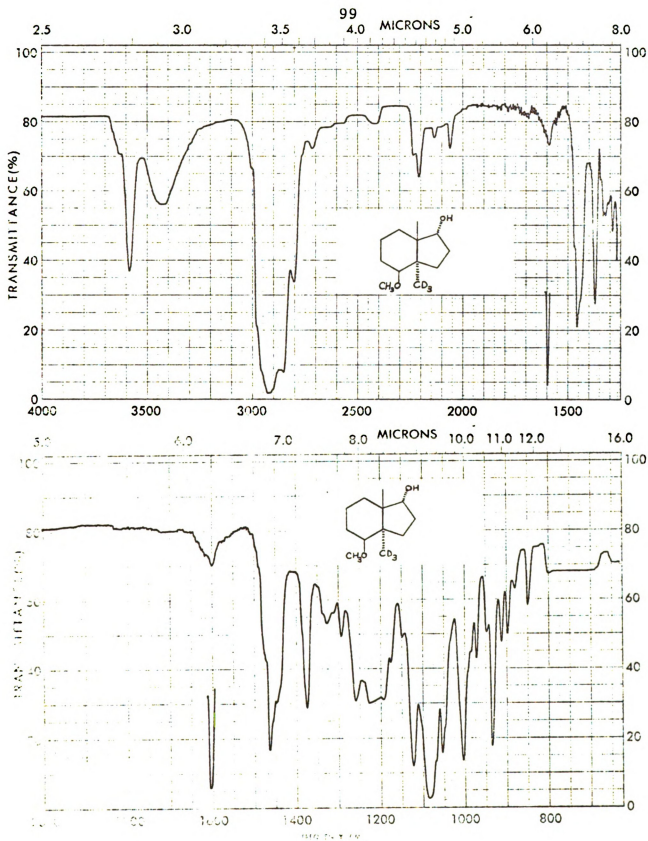


Figure 14. Infrared spectrum of 16.

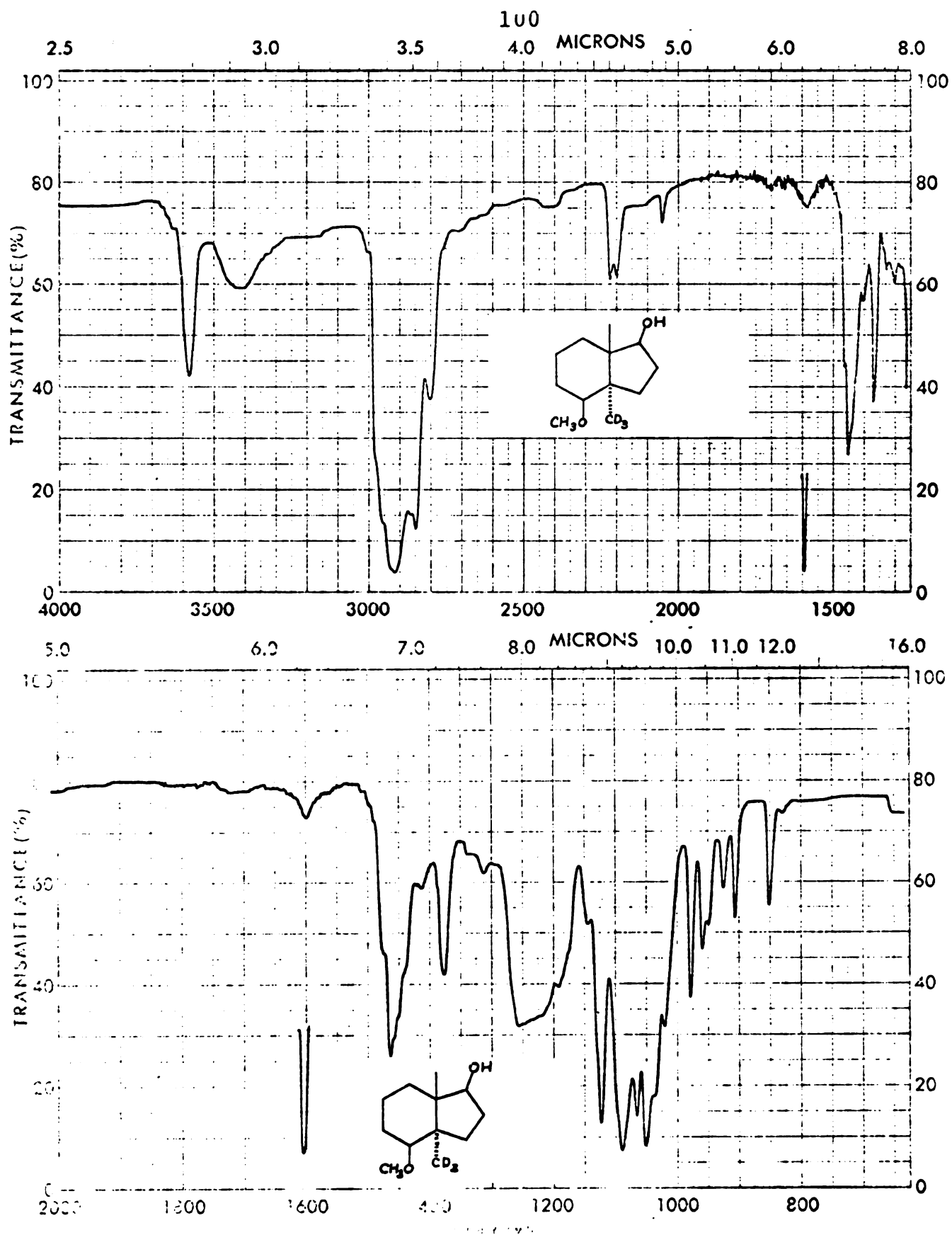


Figure 15. Infrared spectrum of 17.

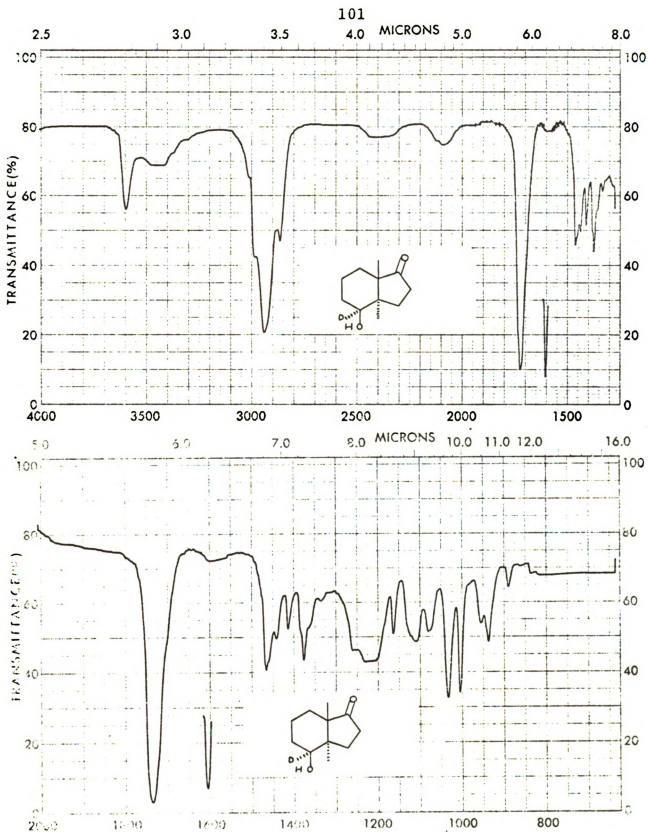


Figure 16. Infrared spectrum of 18.

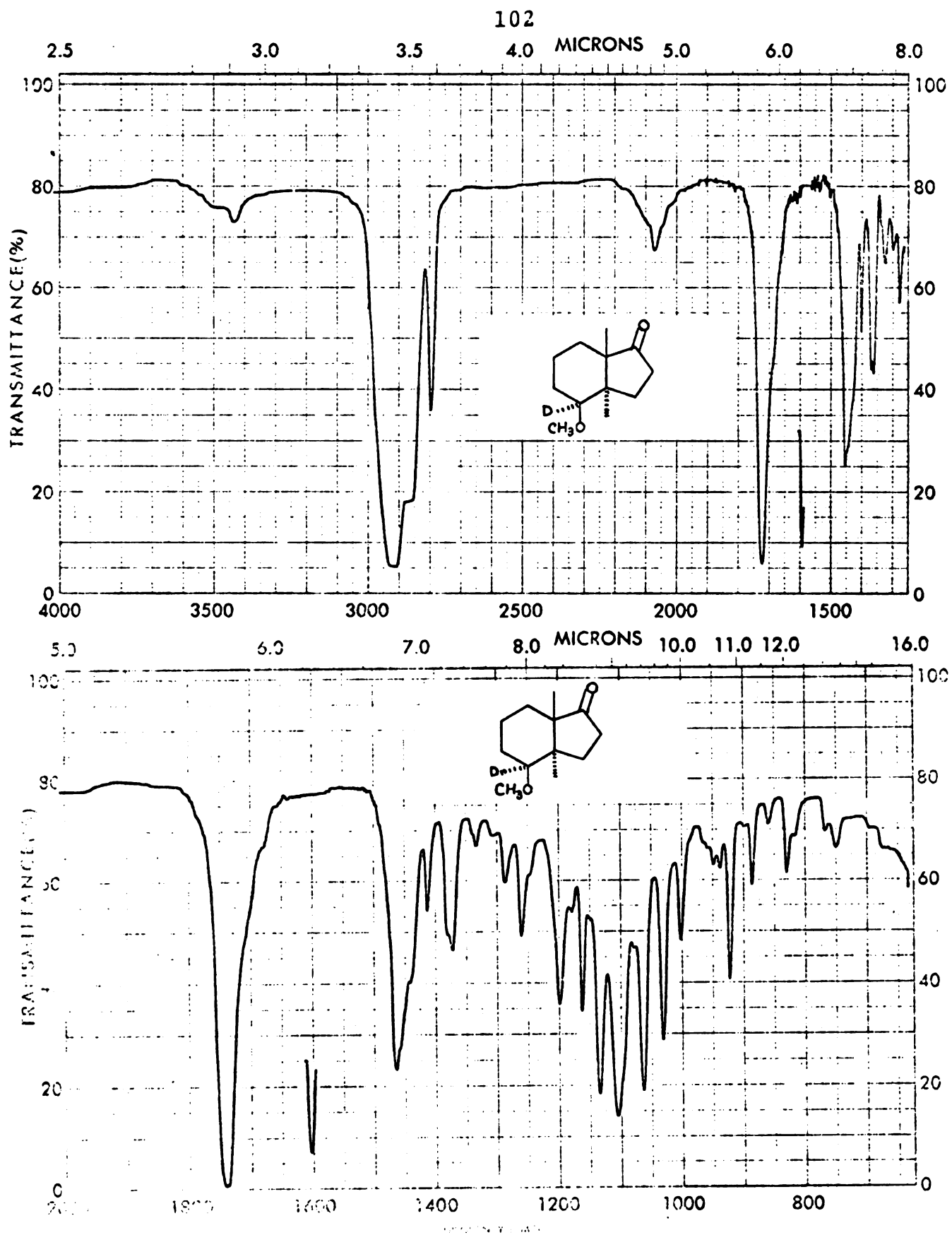


Figure 17. Infrared spectrum of 19.

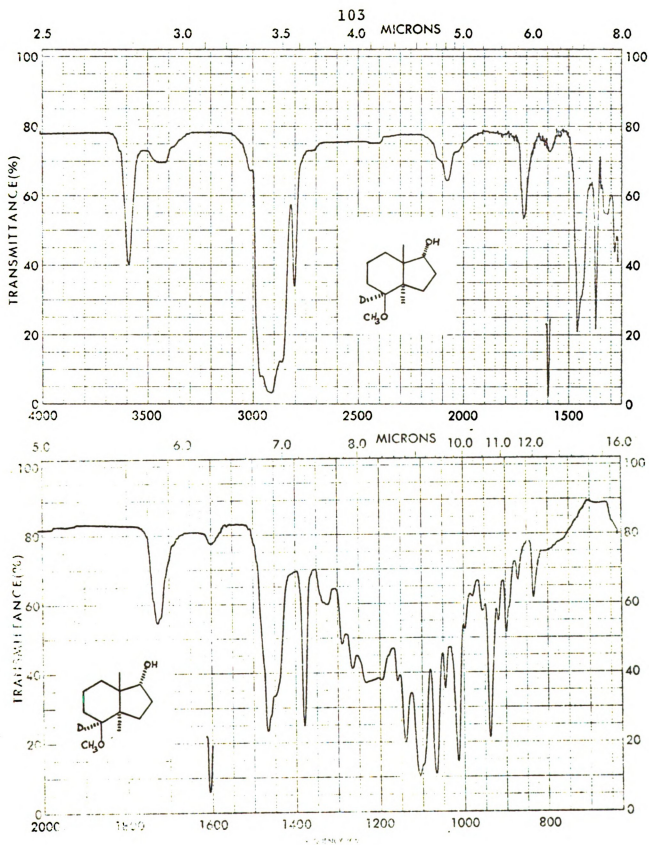


Figure 18. Infrared spectrum of 20.

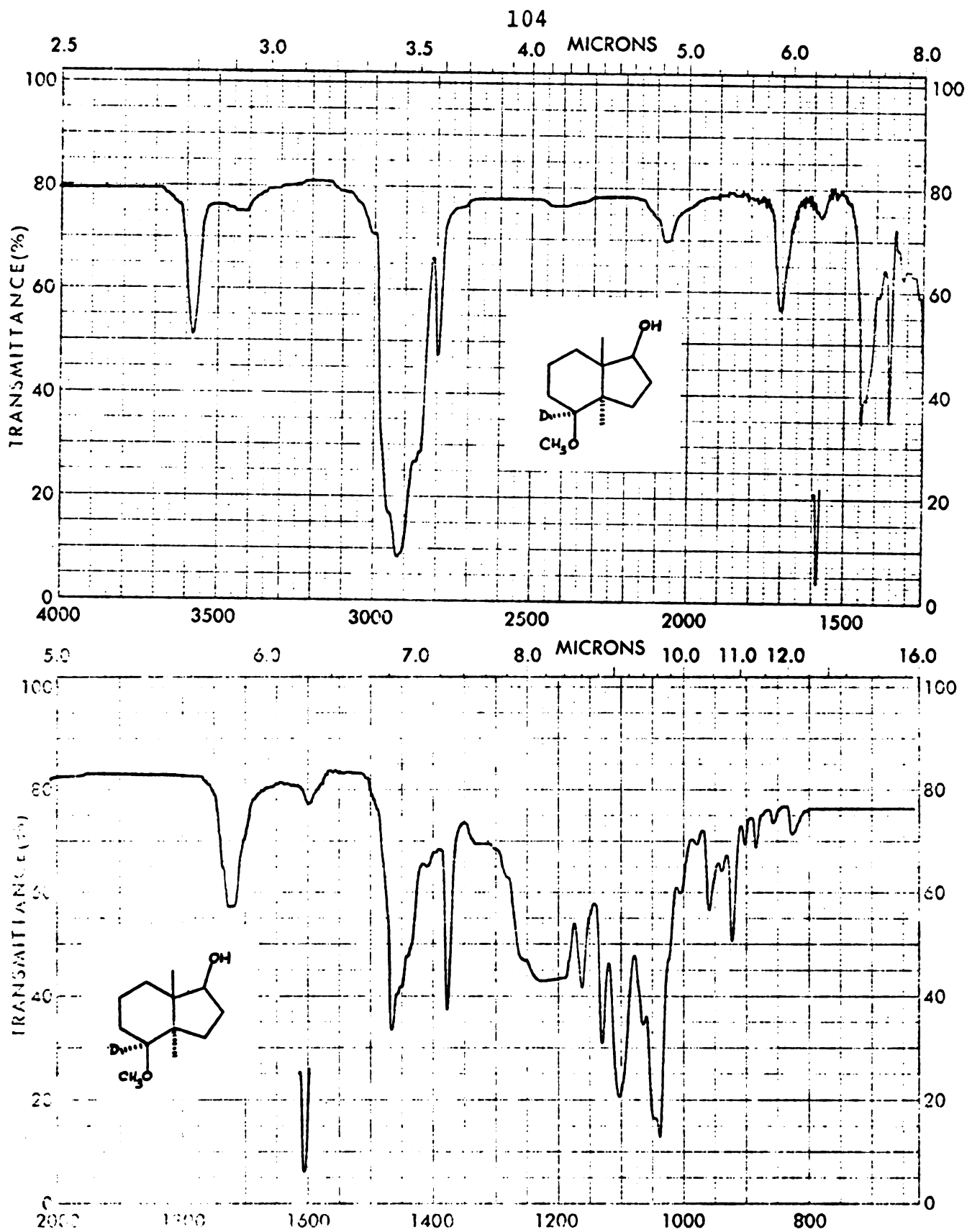


Figure 19. Infrared spectrum of 21.

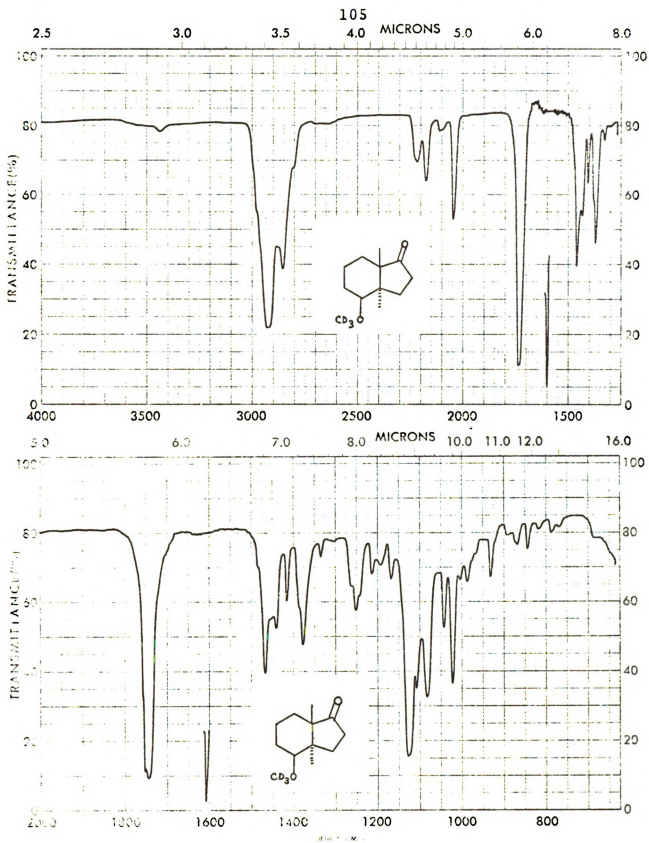


Figure 20. Infrared spectrum of 22.

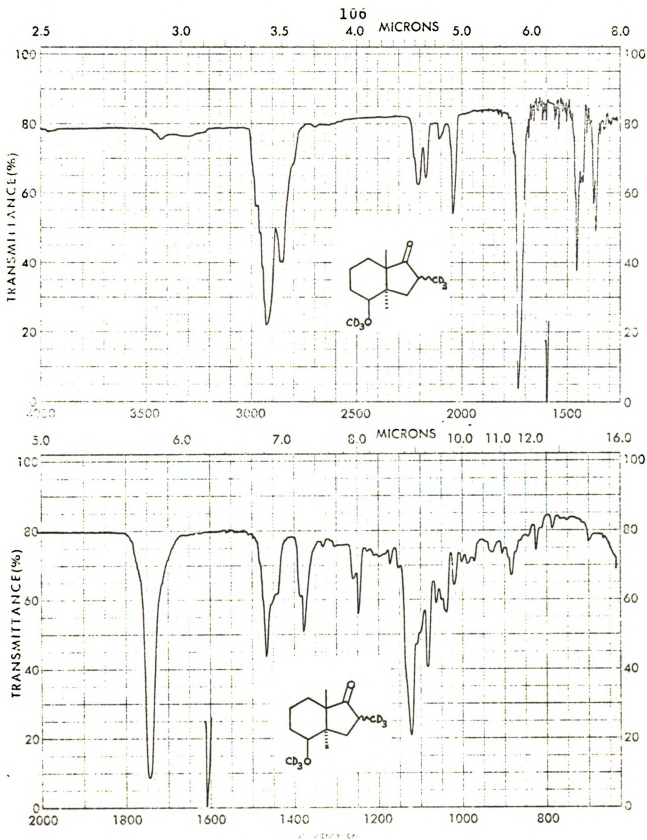


Figure 21. Infrared spectrum of 23.

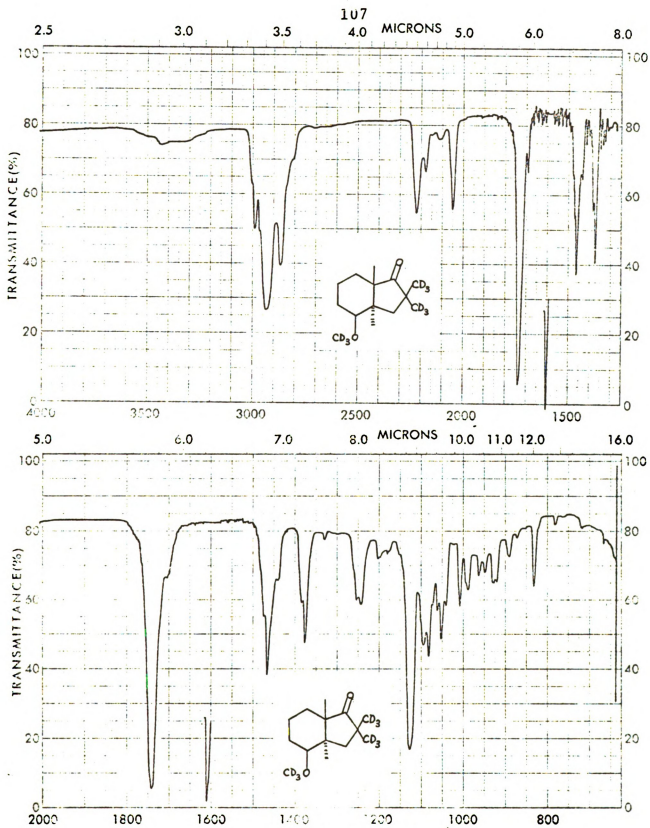


Figure 22. Infrared spectrum of 24.

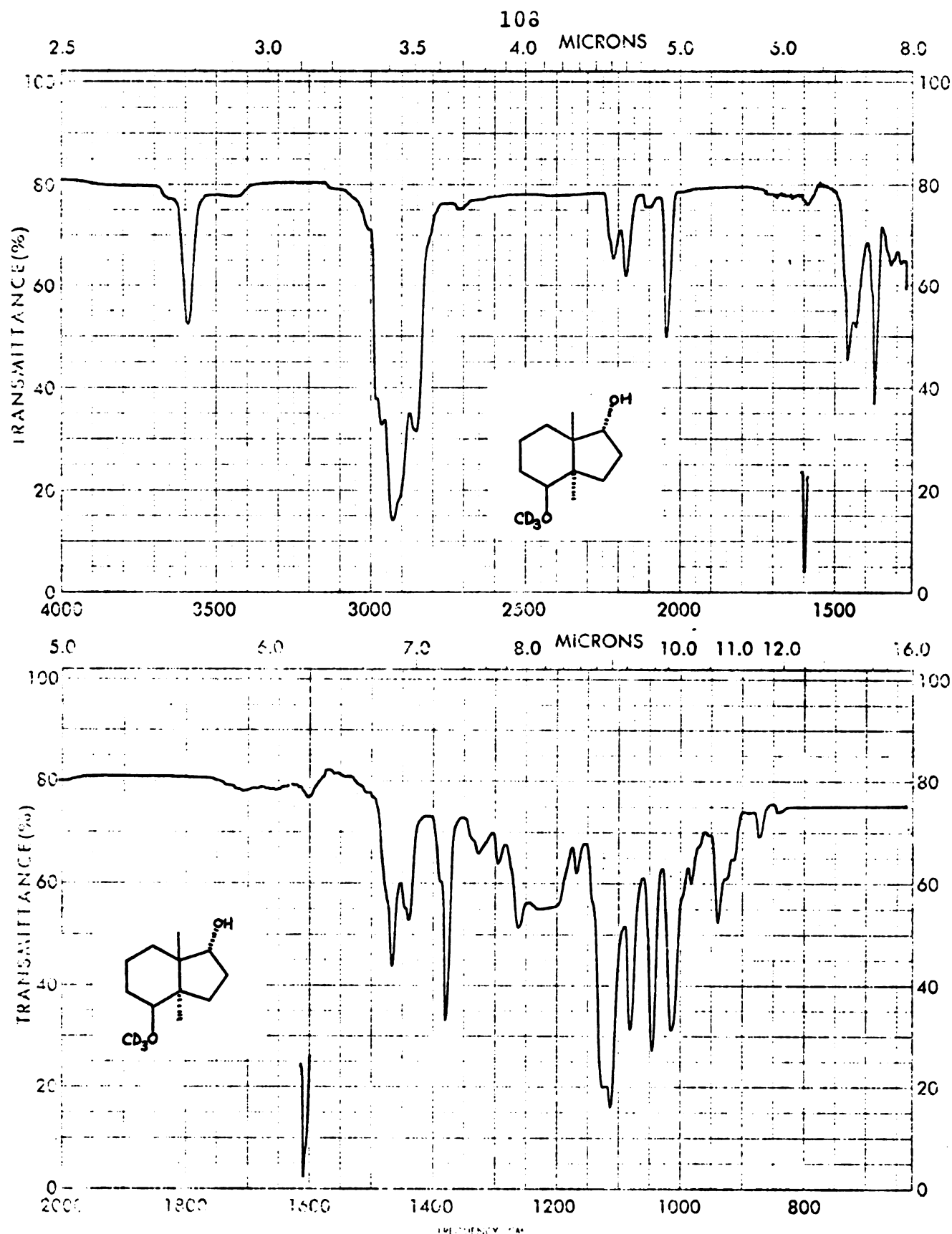


Figure 23. Infrared spectrum of 25.

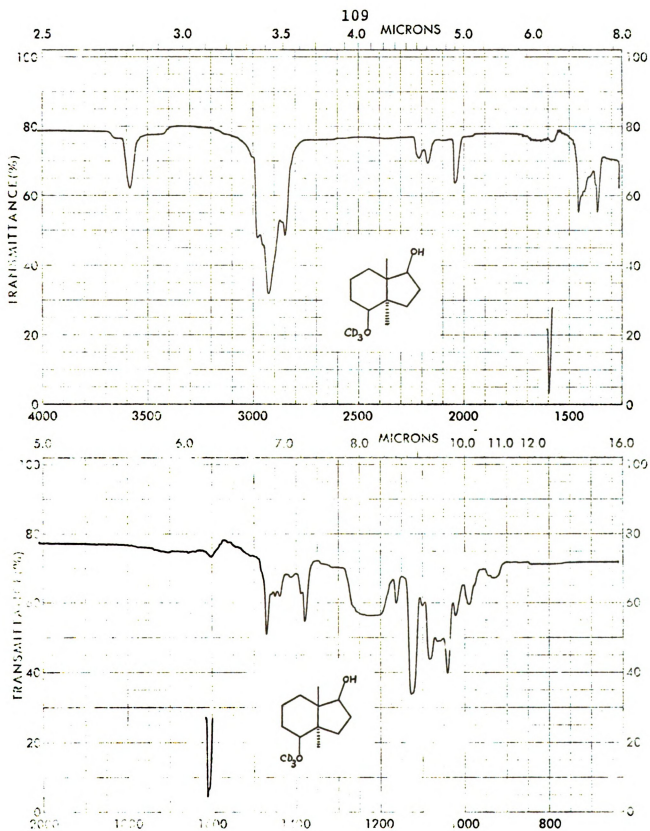


Figure 24. Infrared spectrum of 26.

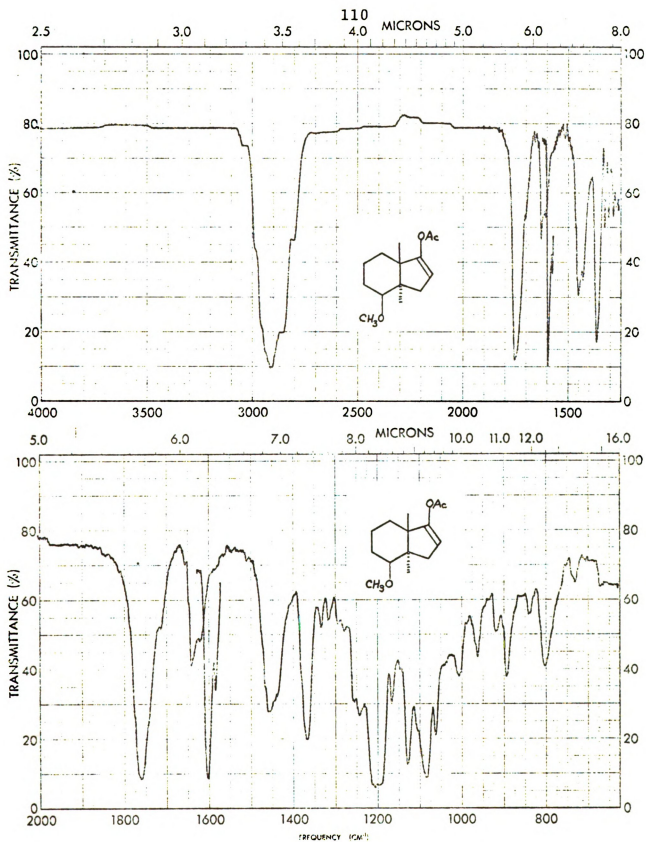


Figure 25. Infrared spectrum of 27.

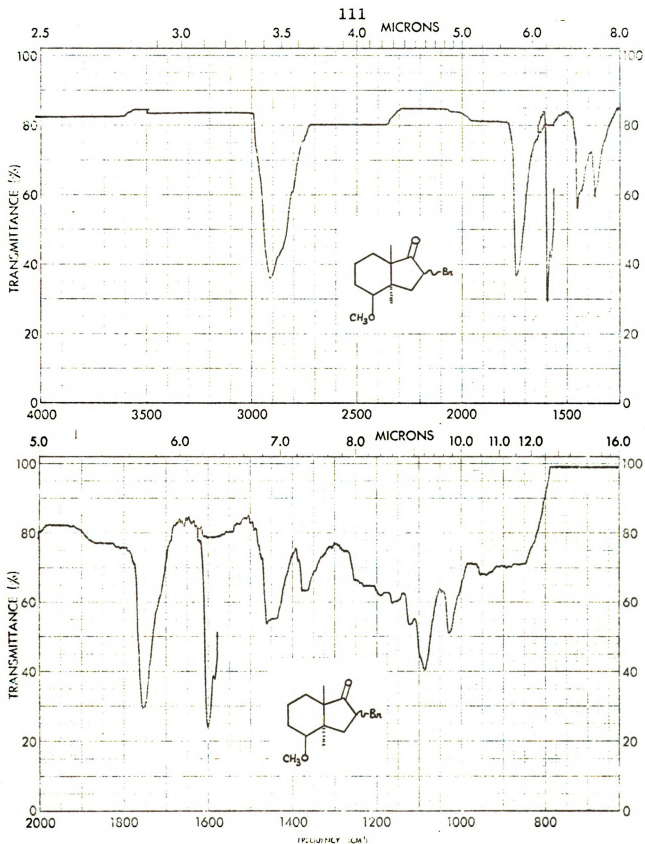


Figure 26. Infrared spectrum of 29.

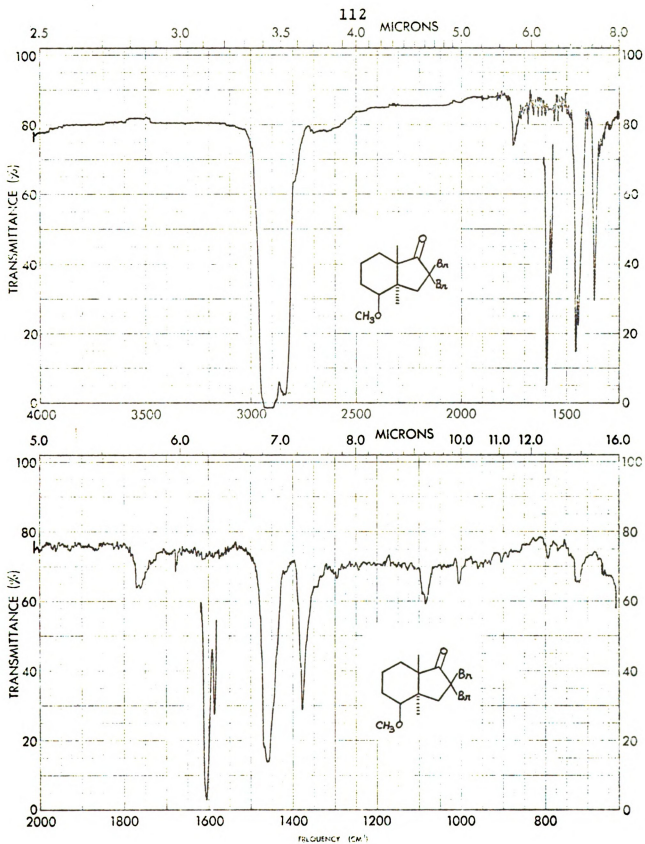


Figure 27. Infrared spectrum of 30.

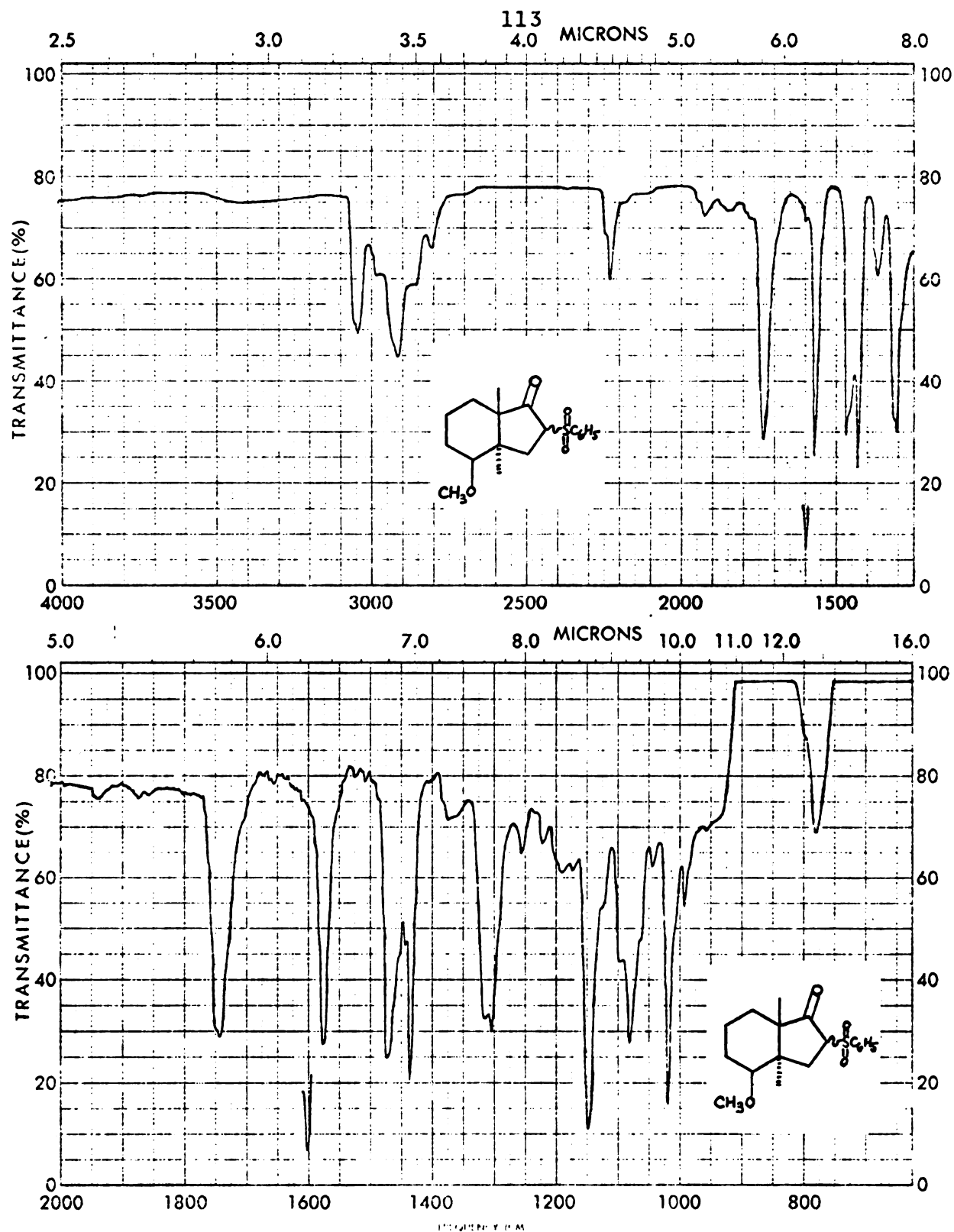


Figure 28. Infrared spectrum of 32 (CDCl₃).

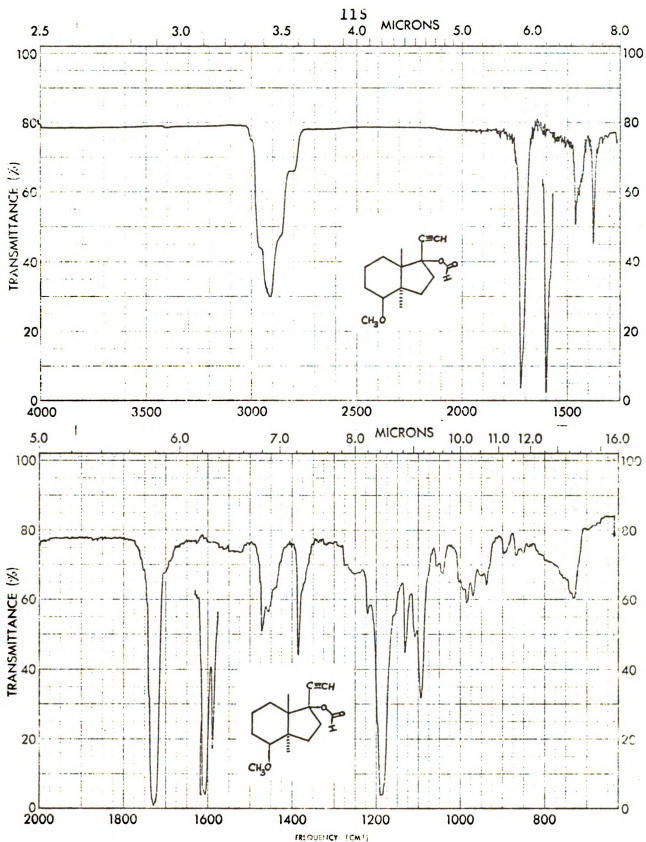


Figure 30. Infrared spectrum of 34.

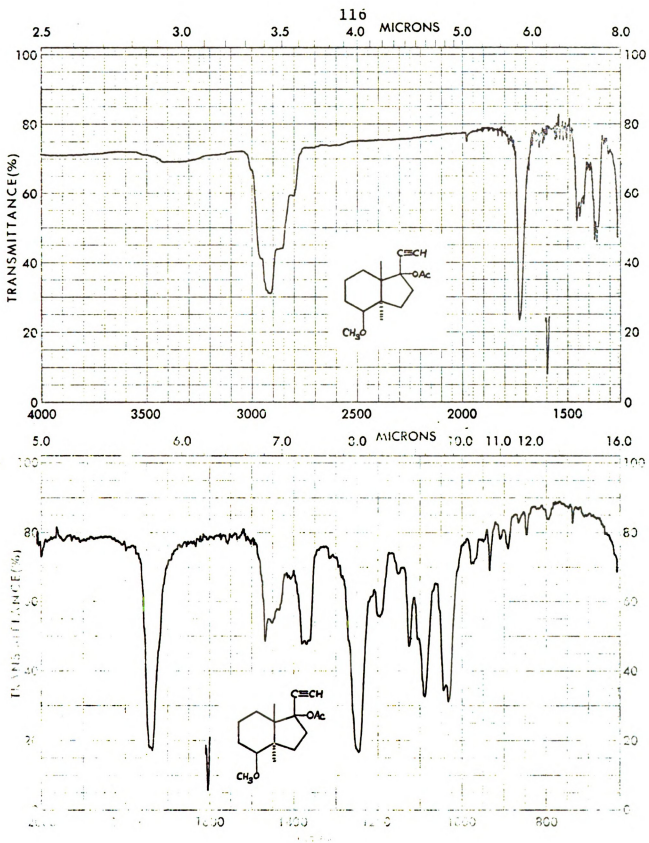


Figure 31. Infrared spectrum of 35.

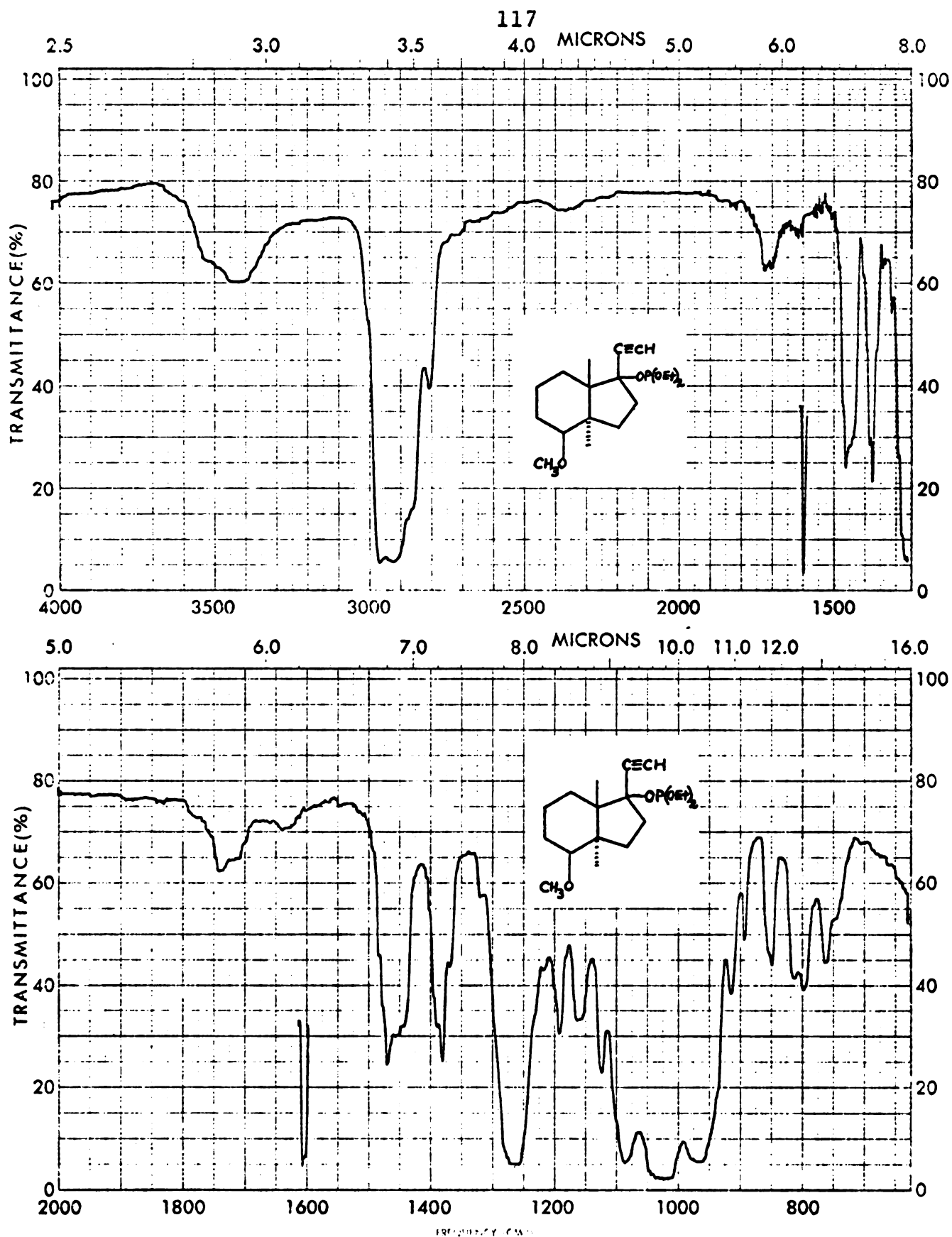


Figure 32. Infrared spectrum of 36.

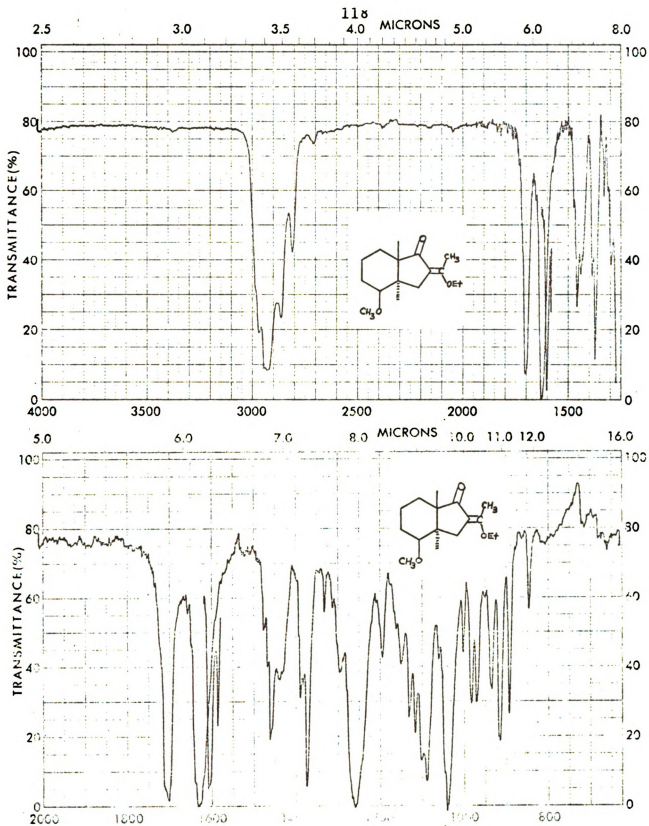


Figure 33. Infrared spectrum of 37.

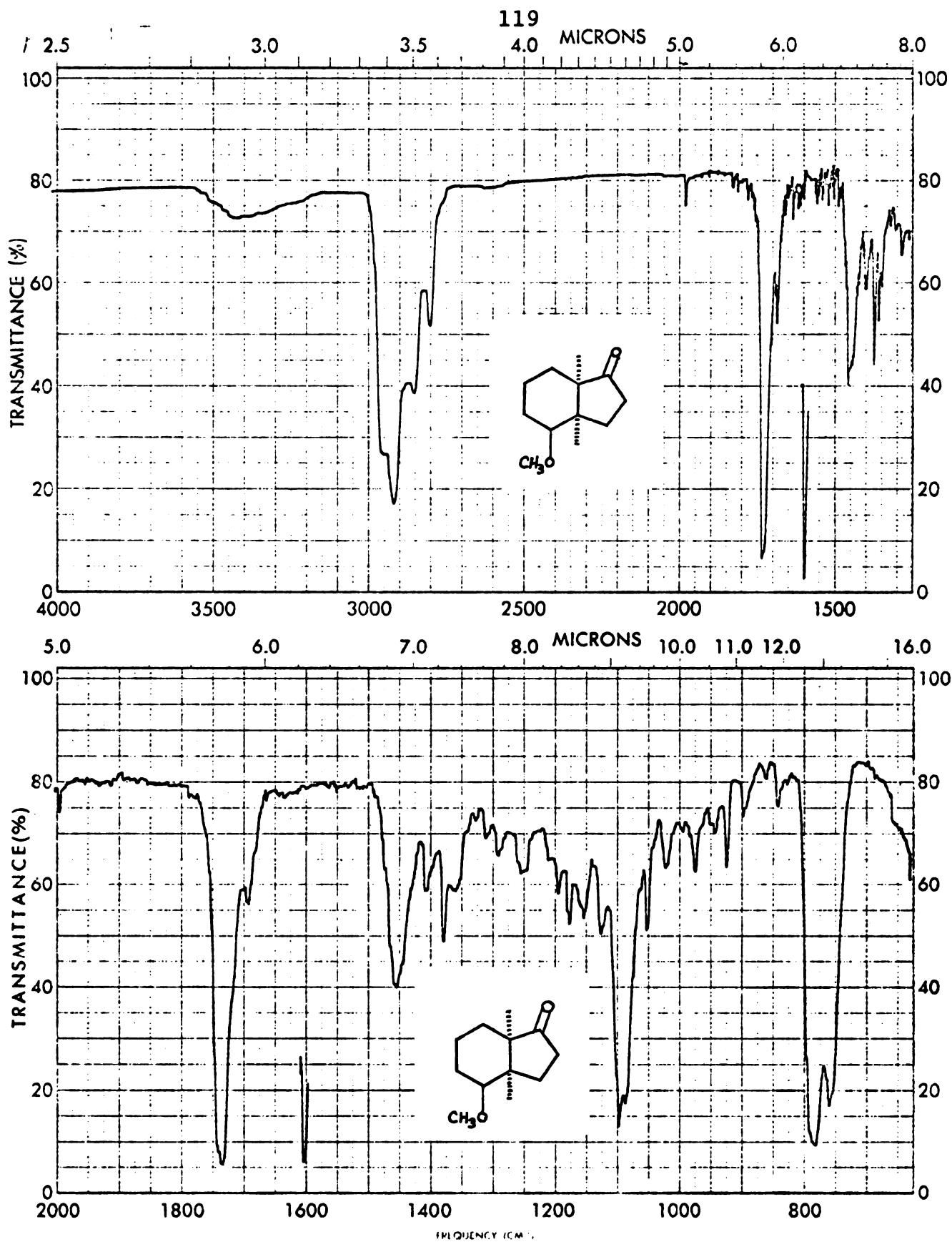


Figure 34. Infrared spectrum of 38.

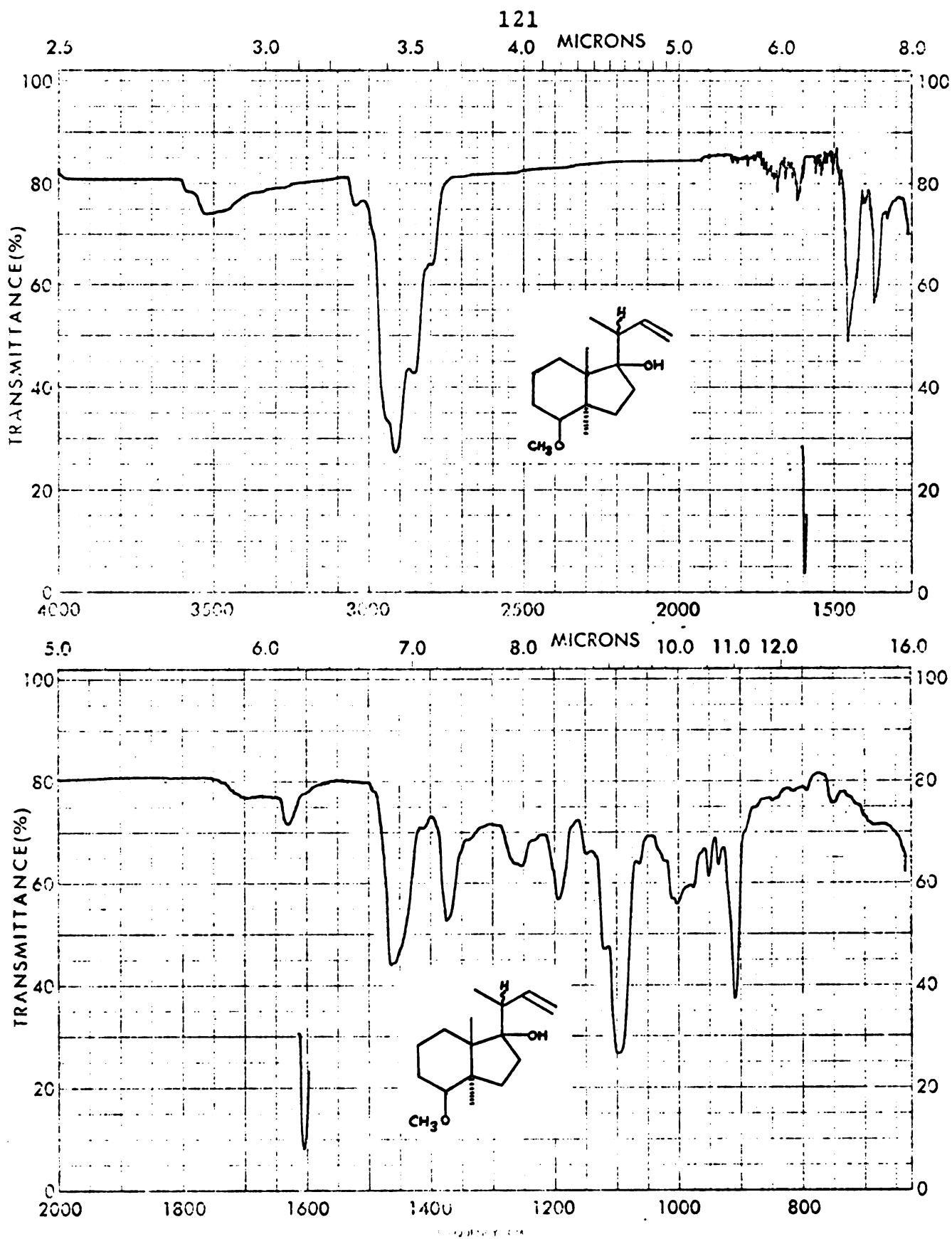


Figure 36. Infrared spectrum of 40.

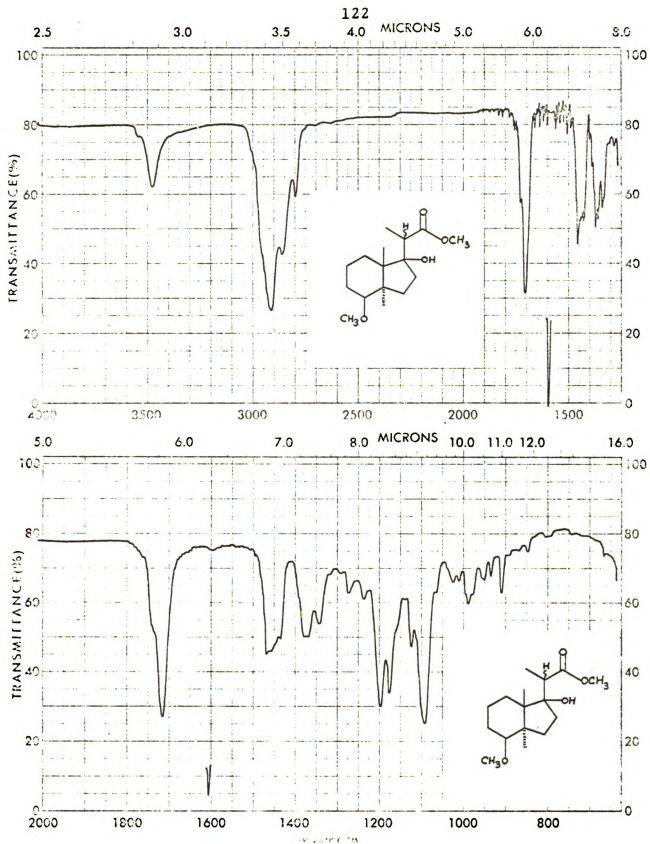


Figure 37. Infrared spectrum of 43.

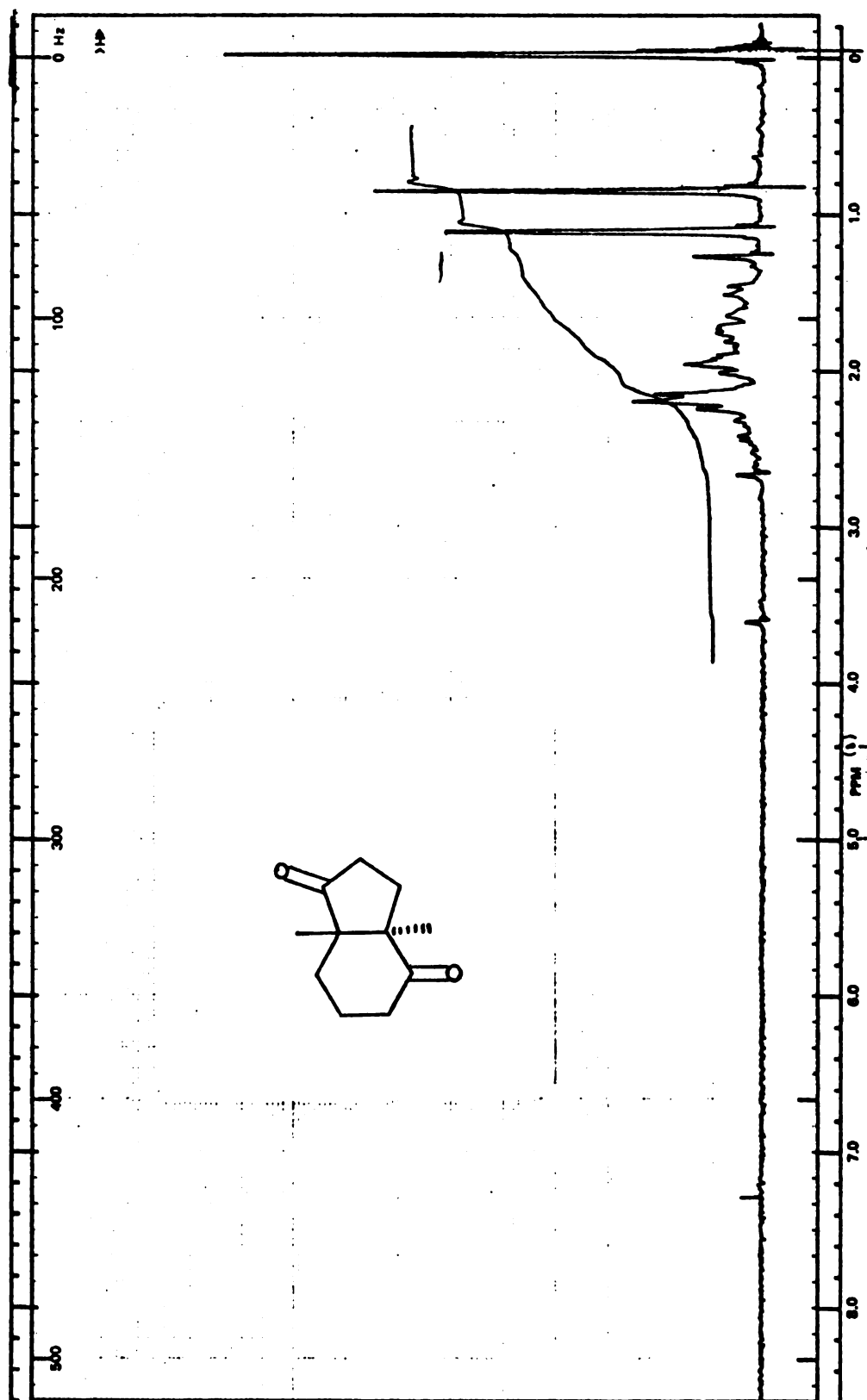


Figure 38. Pmr spectrum of 1.

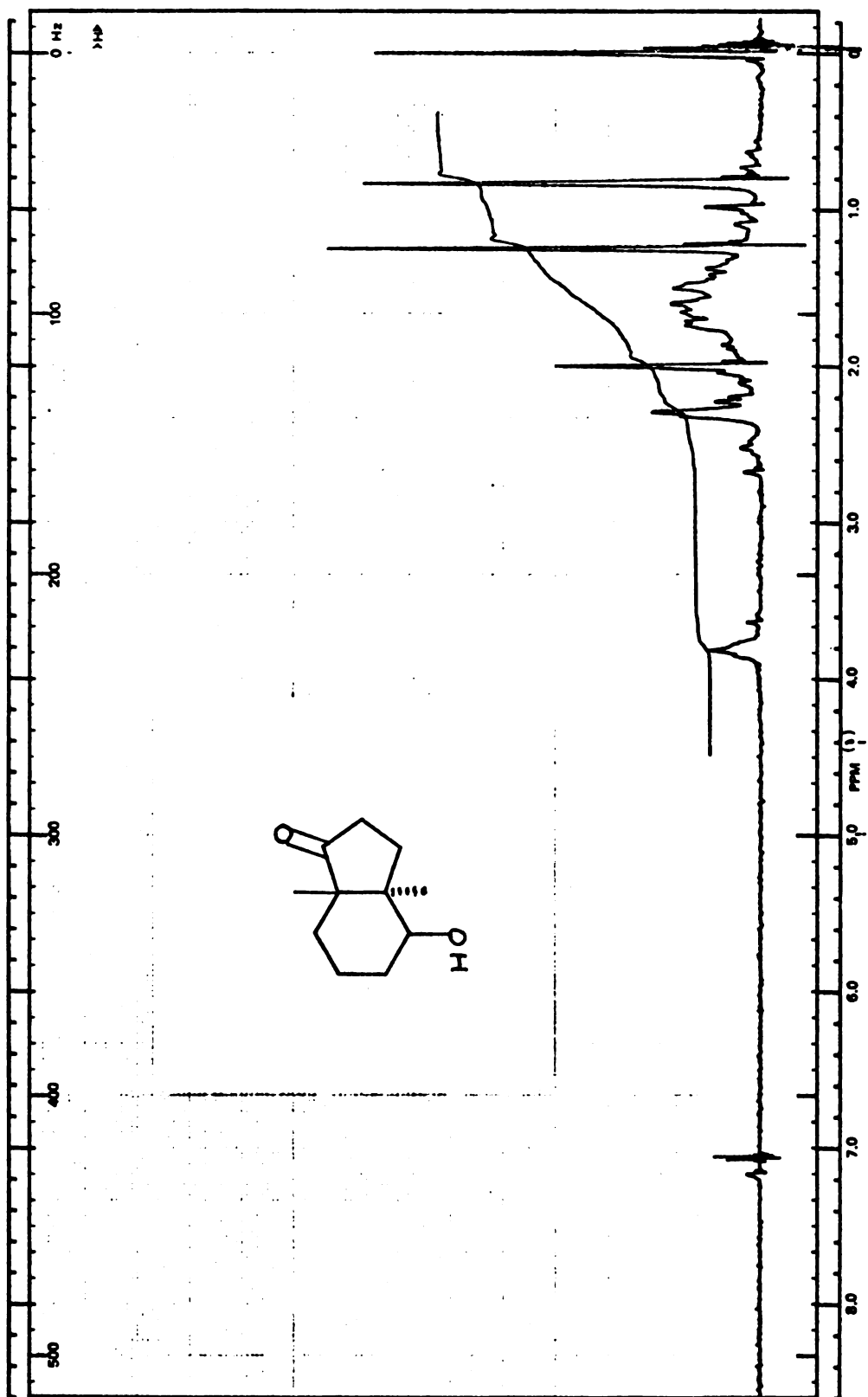


Figure 39. Pmr spectrum of 2.

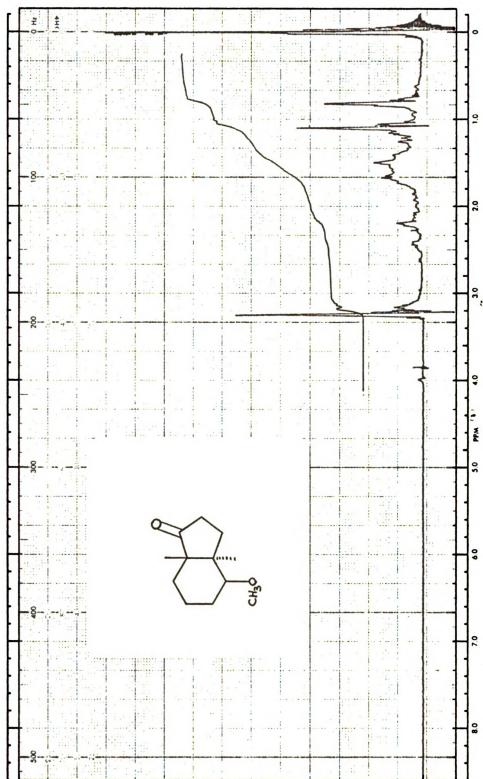


Figure 40. Pmr spectrum of 3.

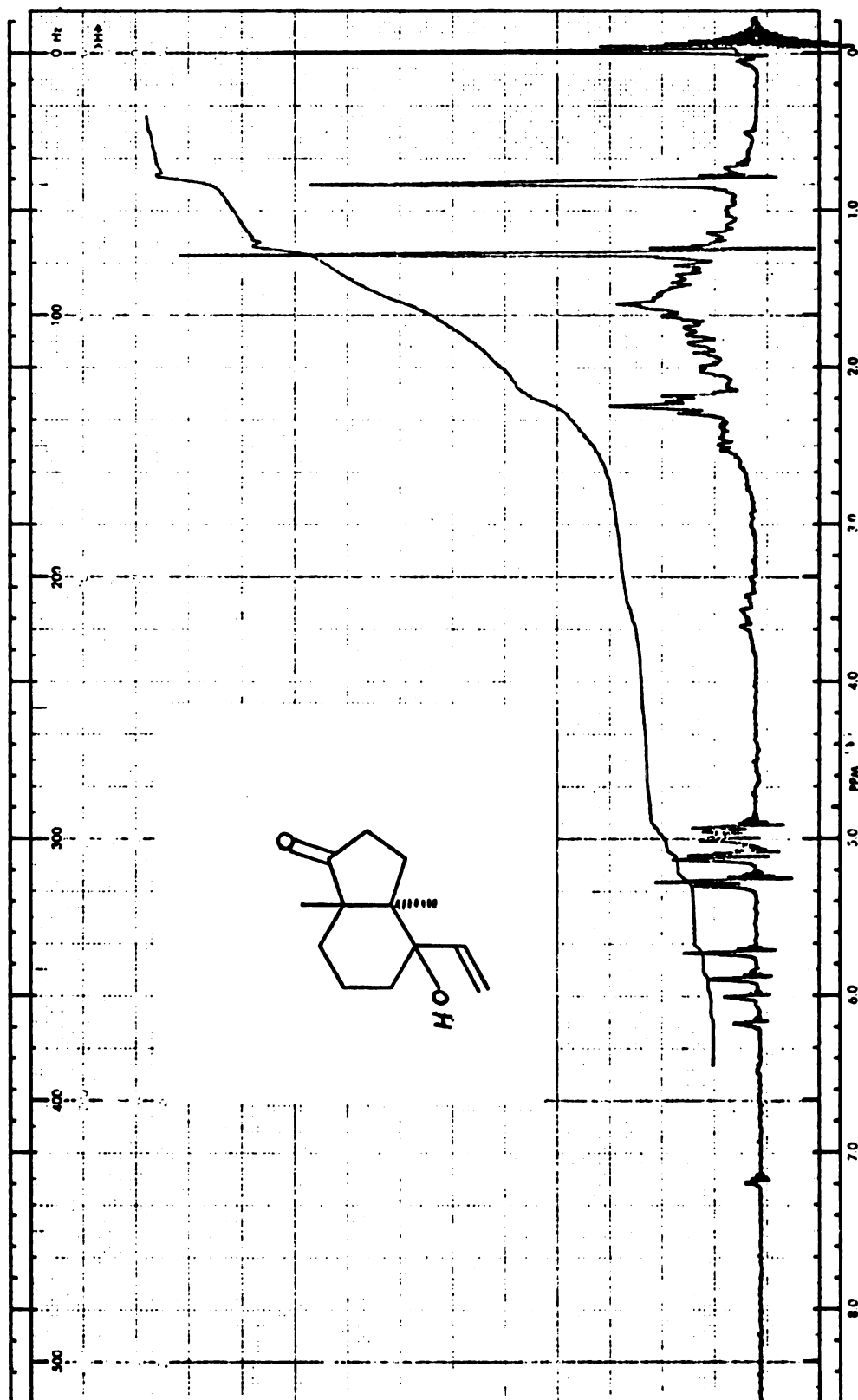


Figure 41. Pmr spectrum of 4.

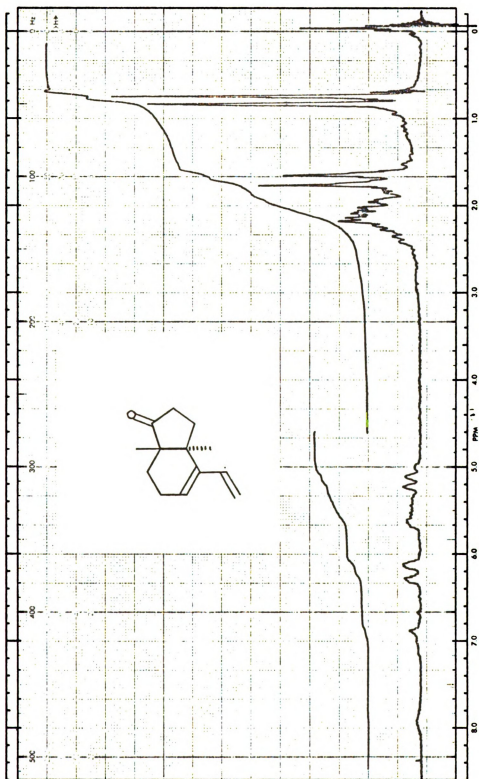


Figure 42. Pmr spectrum of 5.

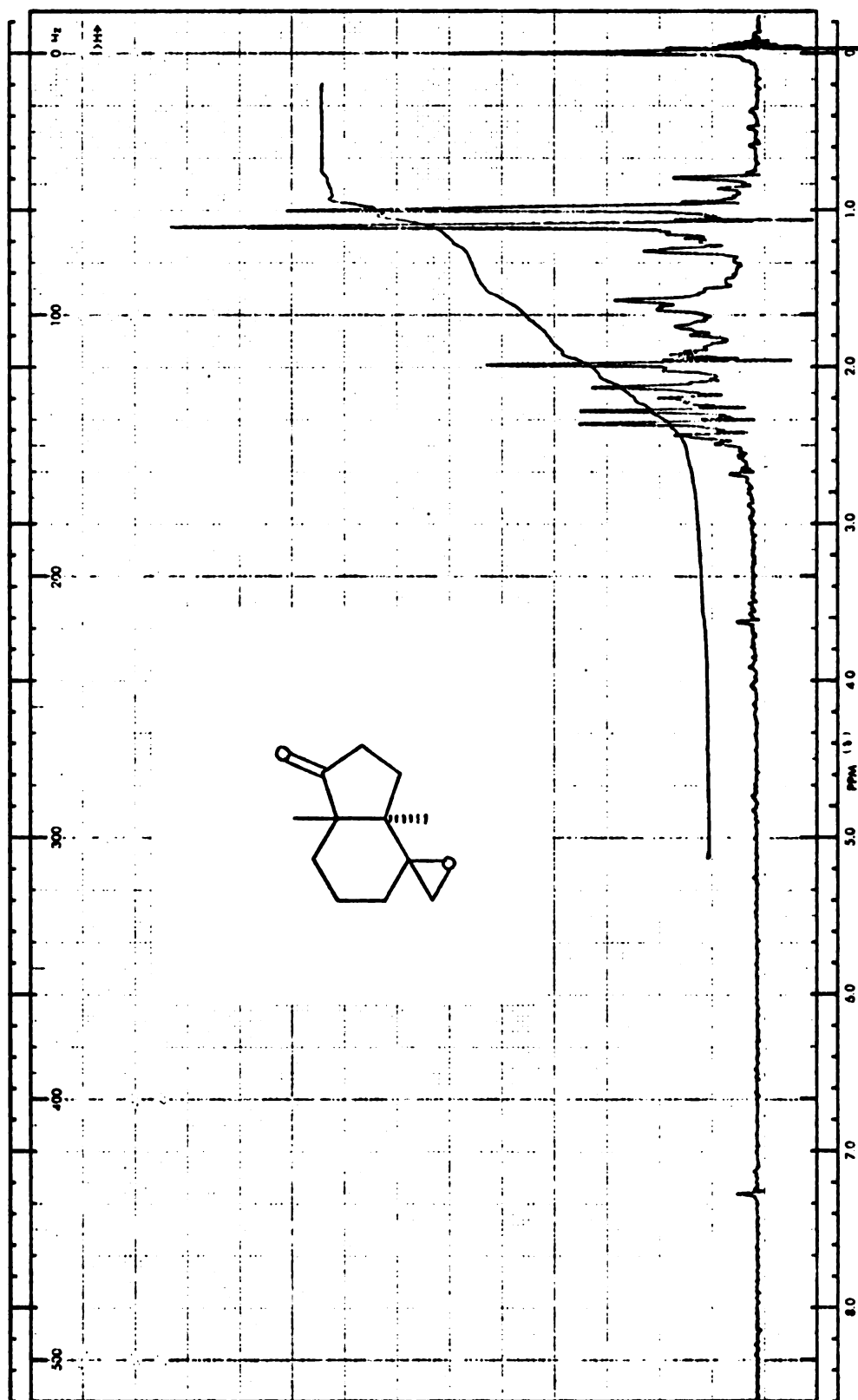


Figure 43. Pmr spectrum of 6.

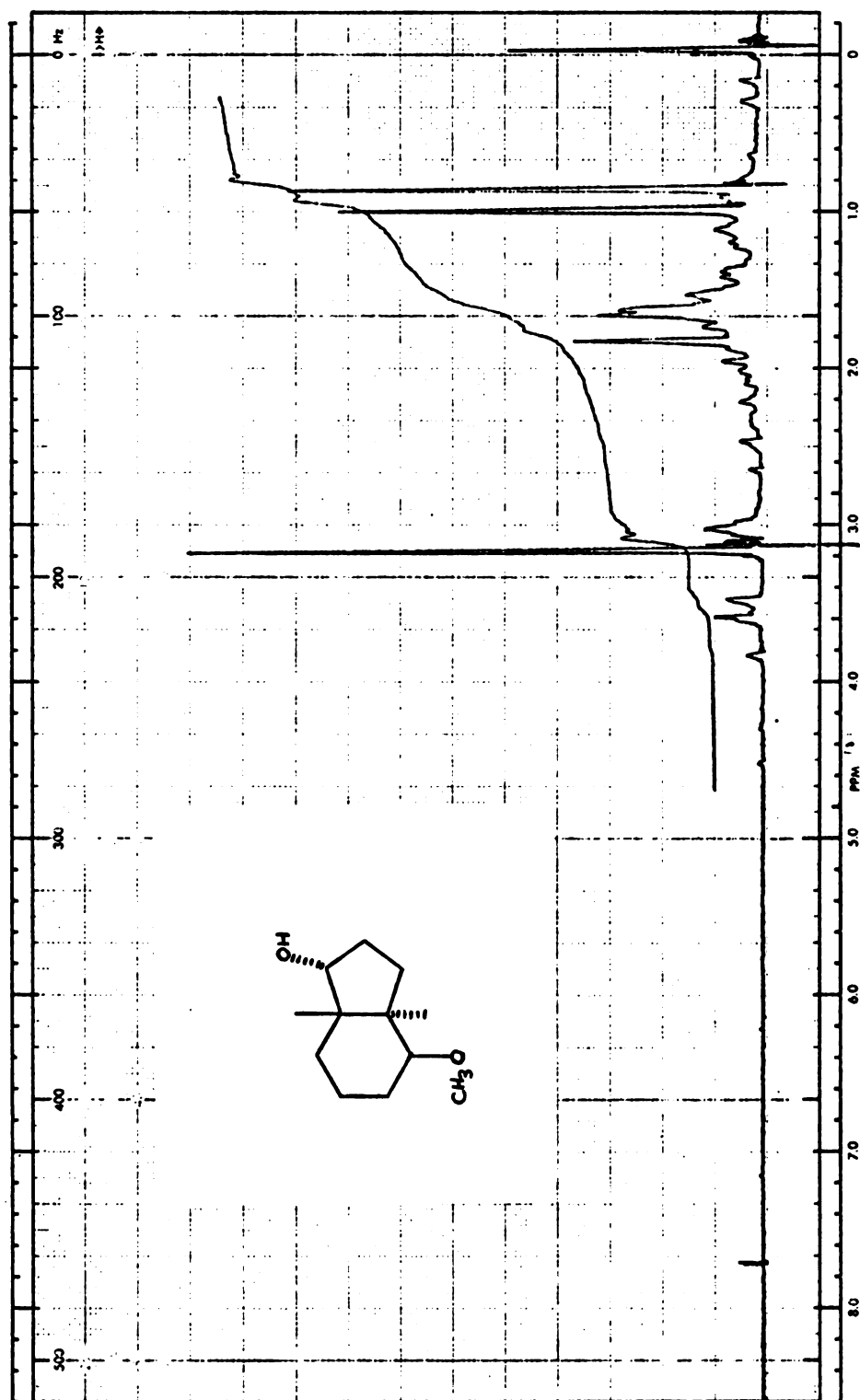


Figure 44. Pmr spectrum of 7.

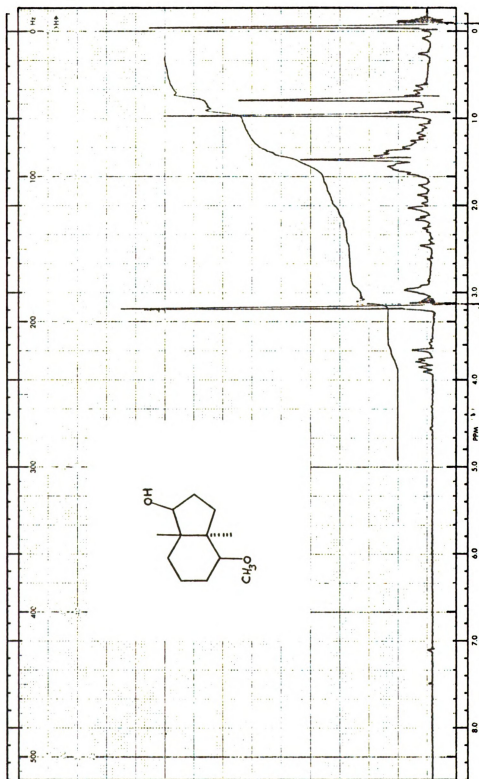


Figure 45. Pmr spectrum of 8.

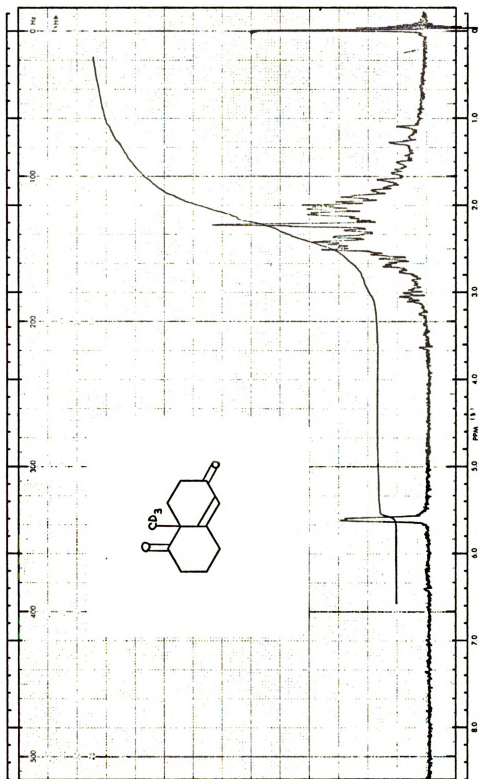


Figure 46. Pmr spectrum of 10.

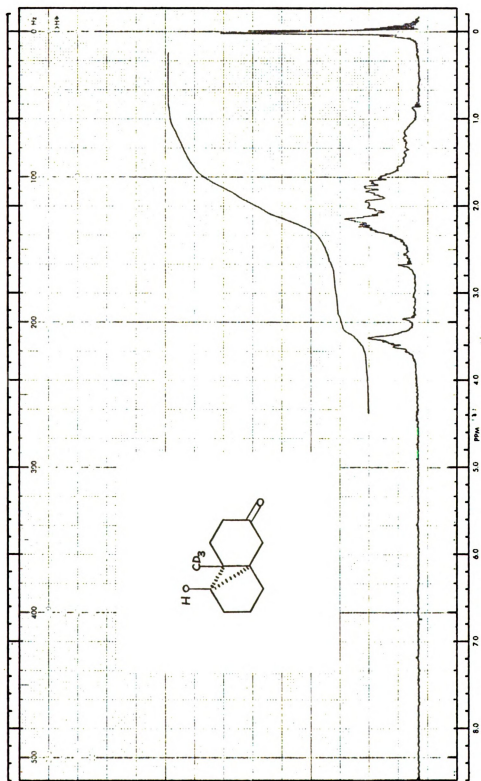


Figure 47. Pmr spectrum of 11.

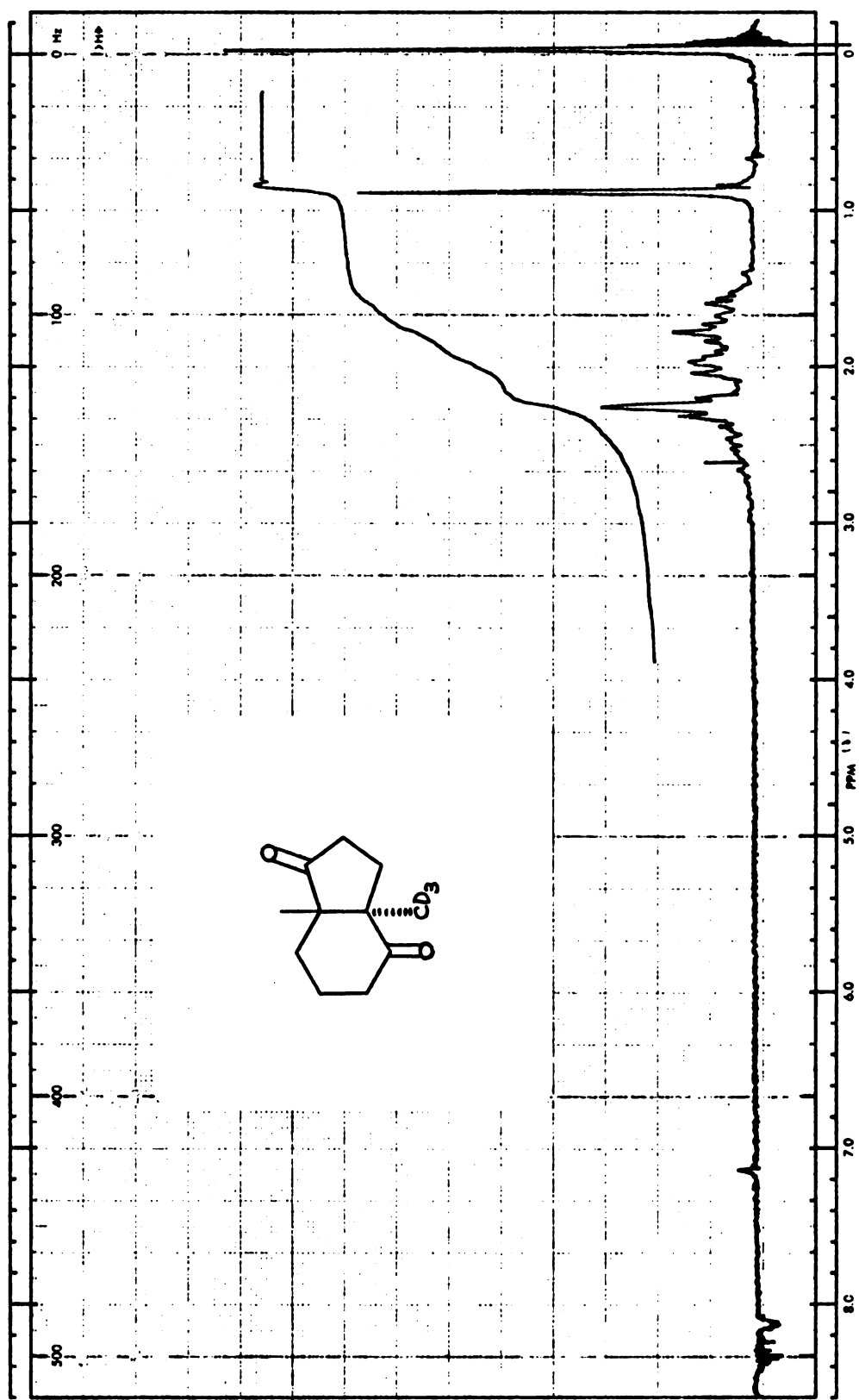


Figure 48. Pmr spectrum of 13.

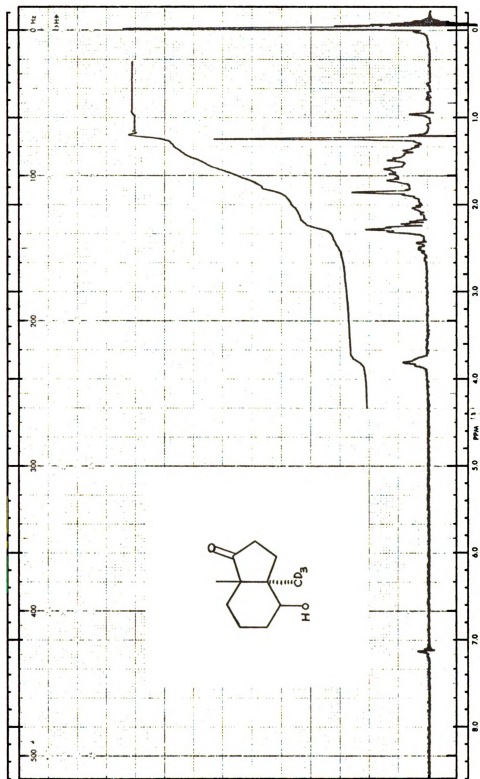


Figure 49. Pmr spectrum of 14.

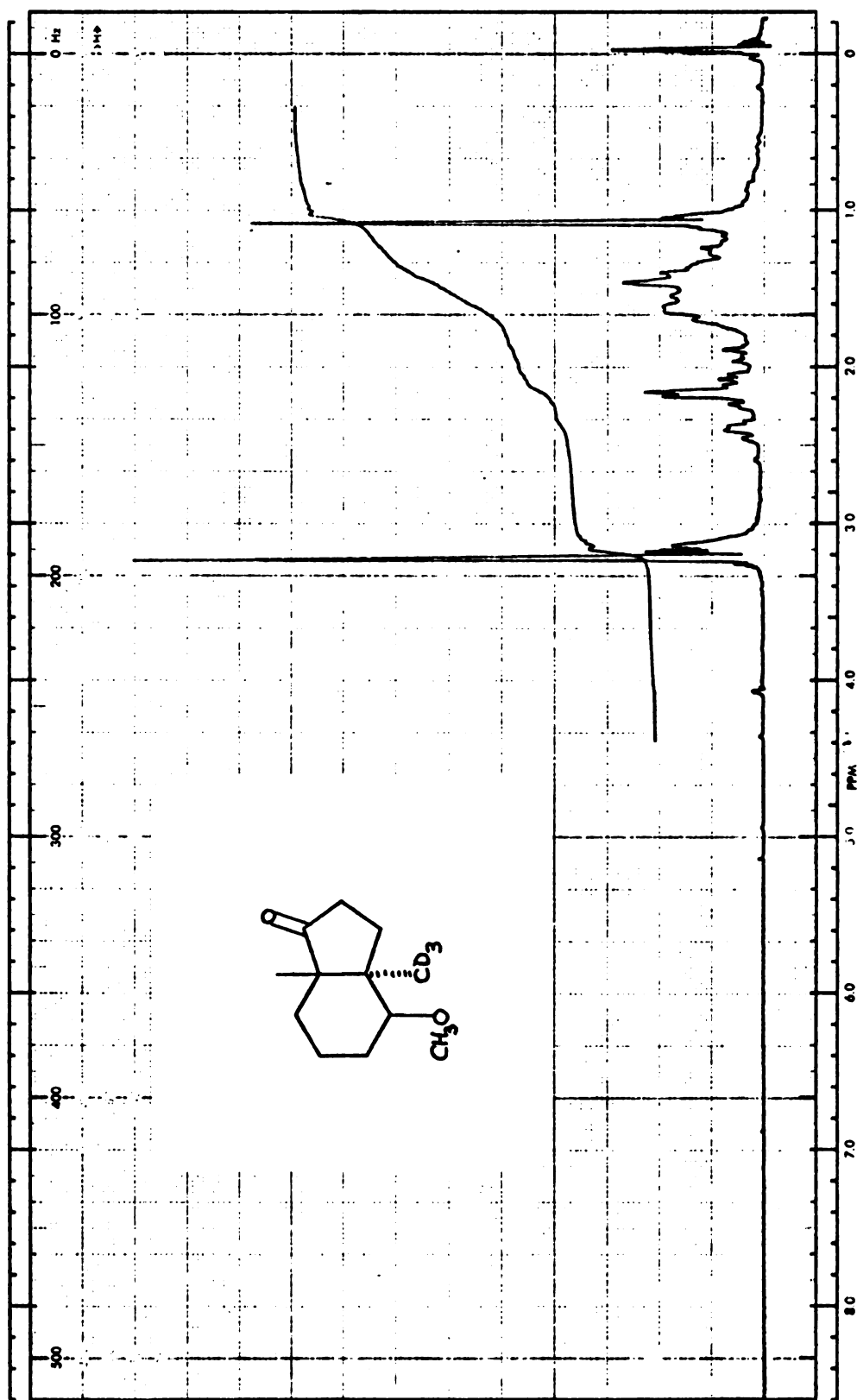


Figure 50. Pmr spectrum of 15.

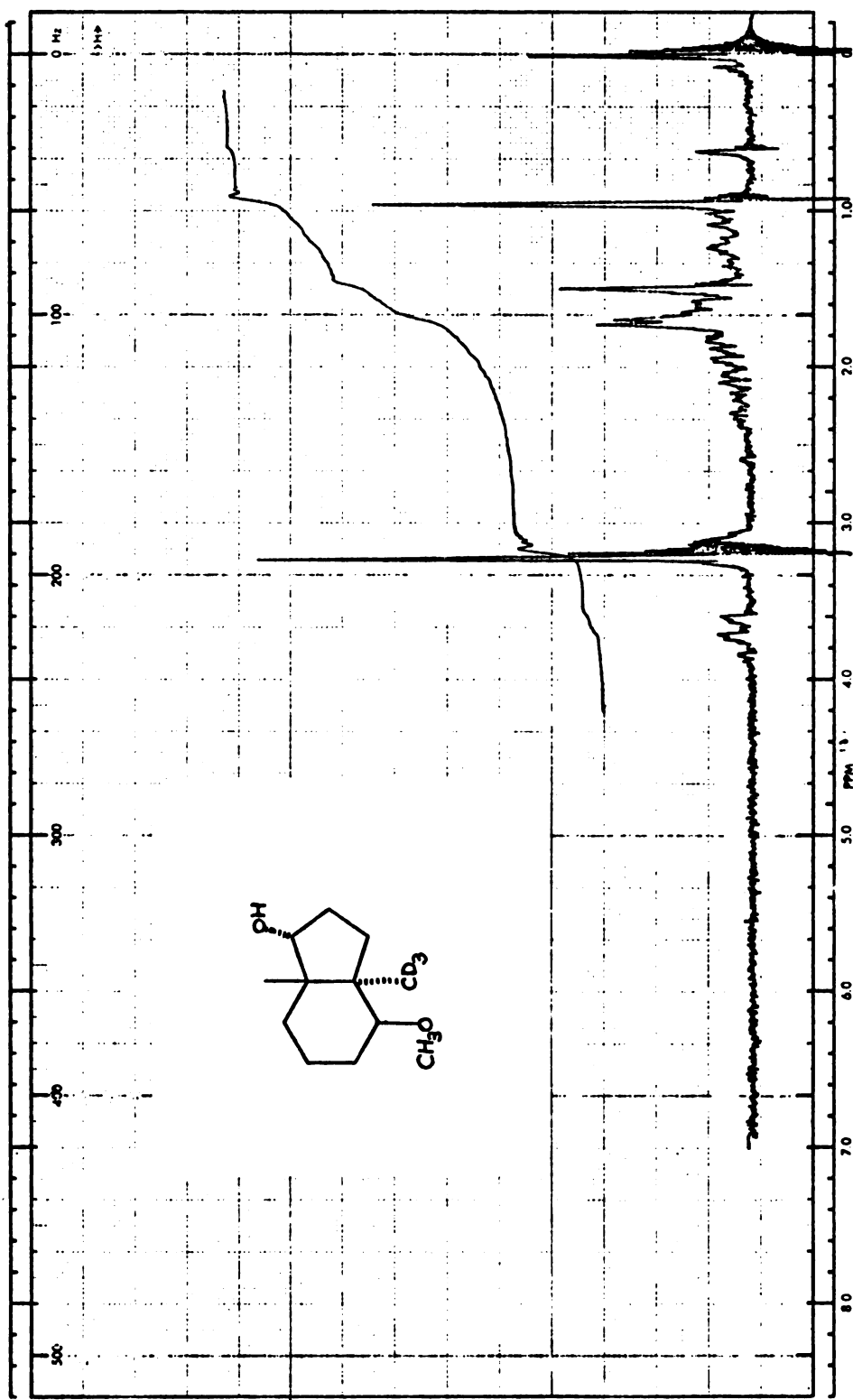


Figure 51. Pmr spectrum of 16.

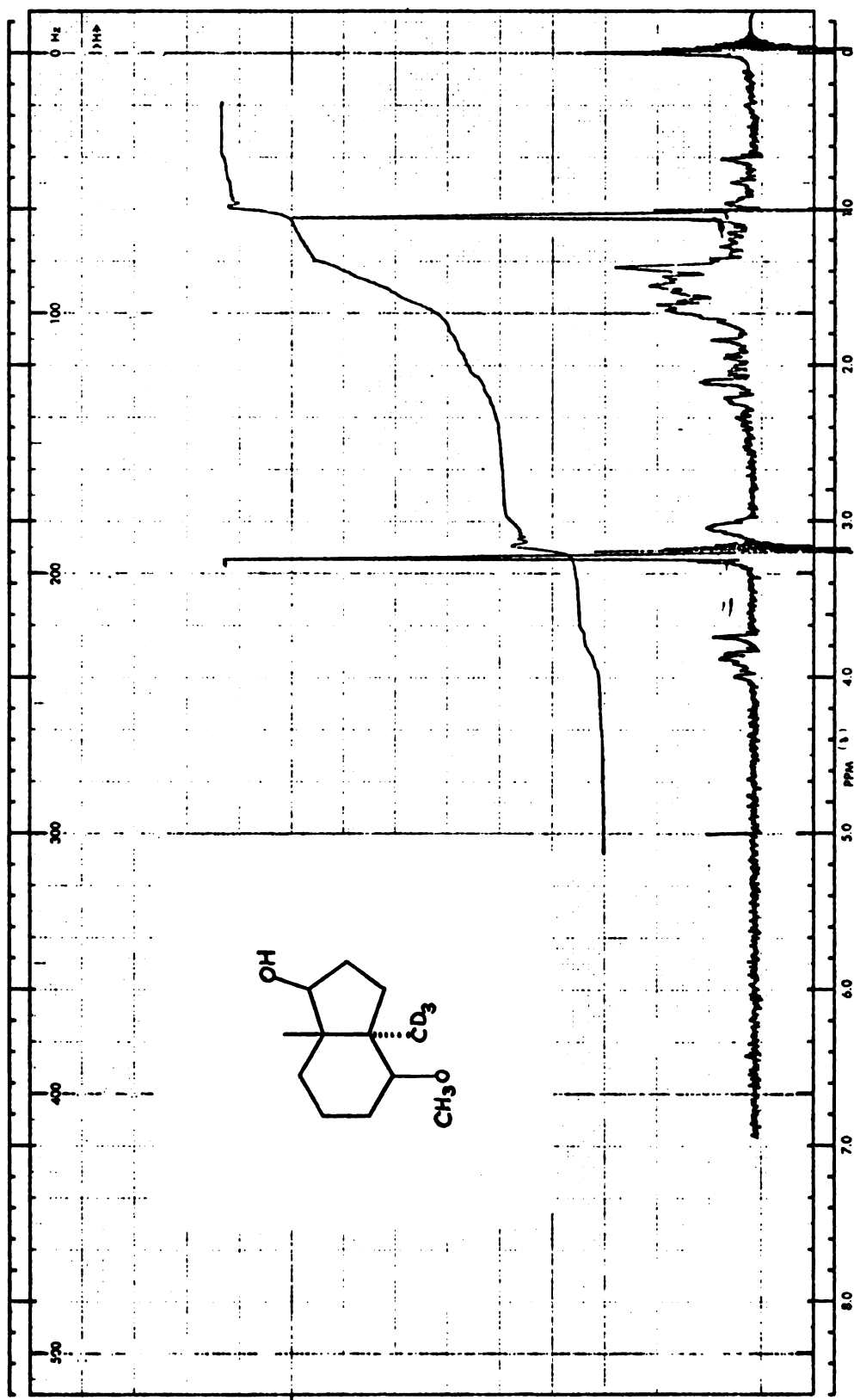


Figure 52. Pmr spectrum of 17.

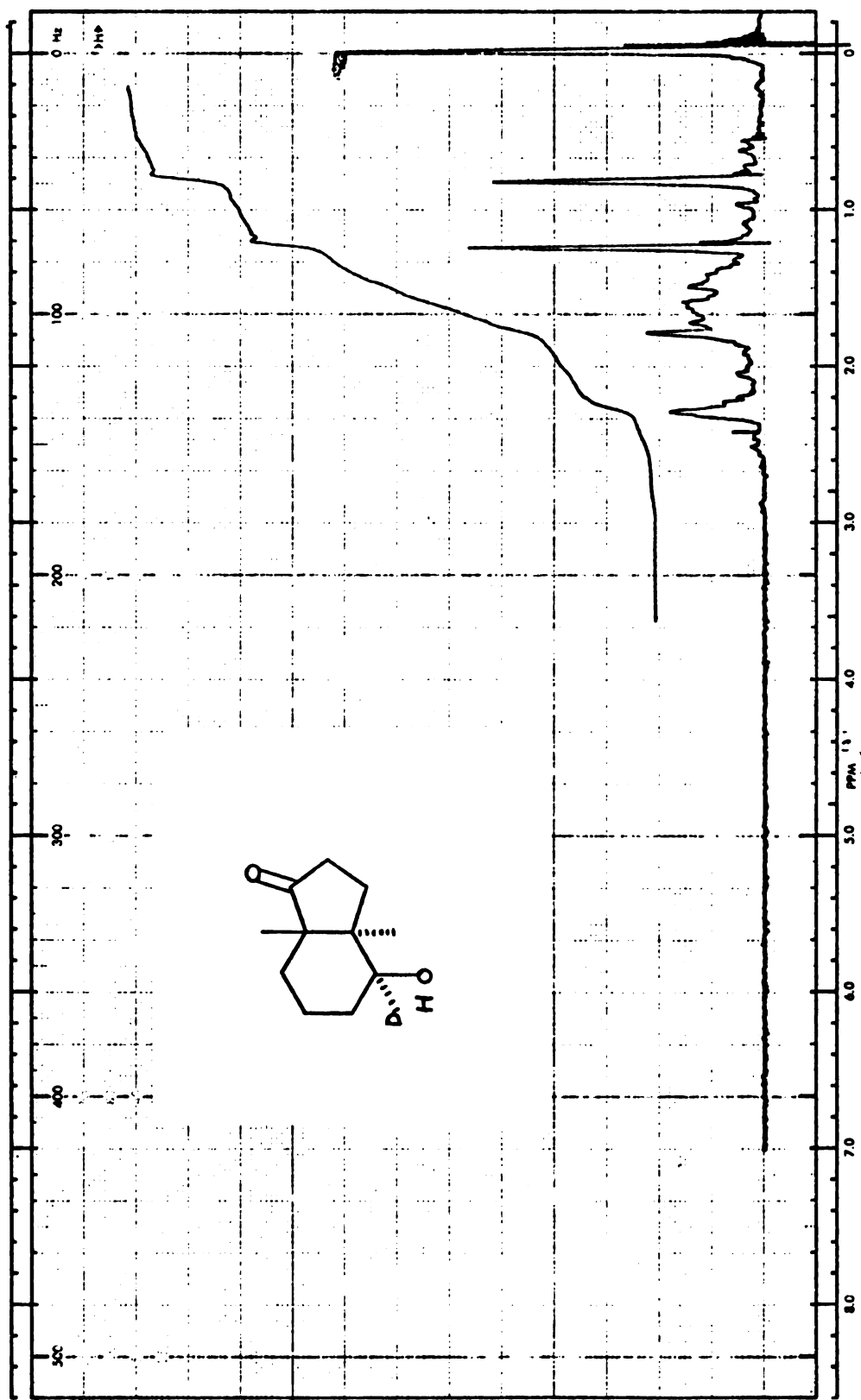


Figure 53. Pmr spectrum of 18.

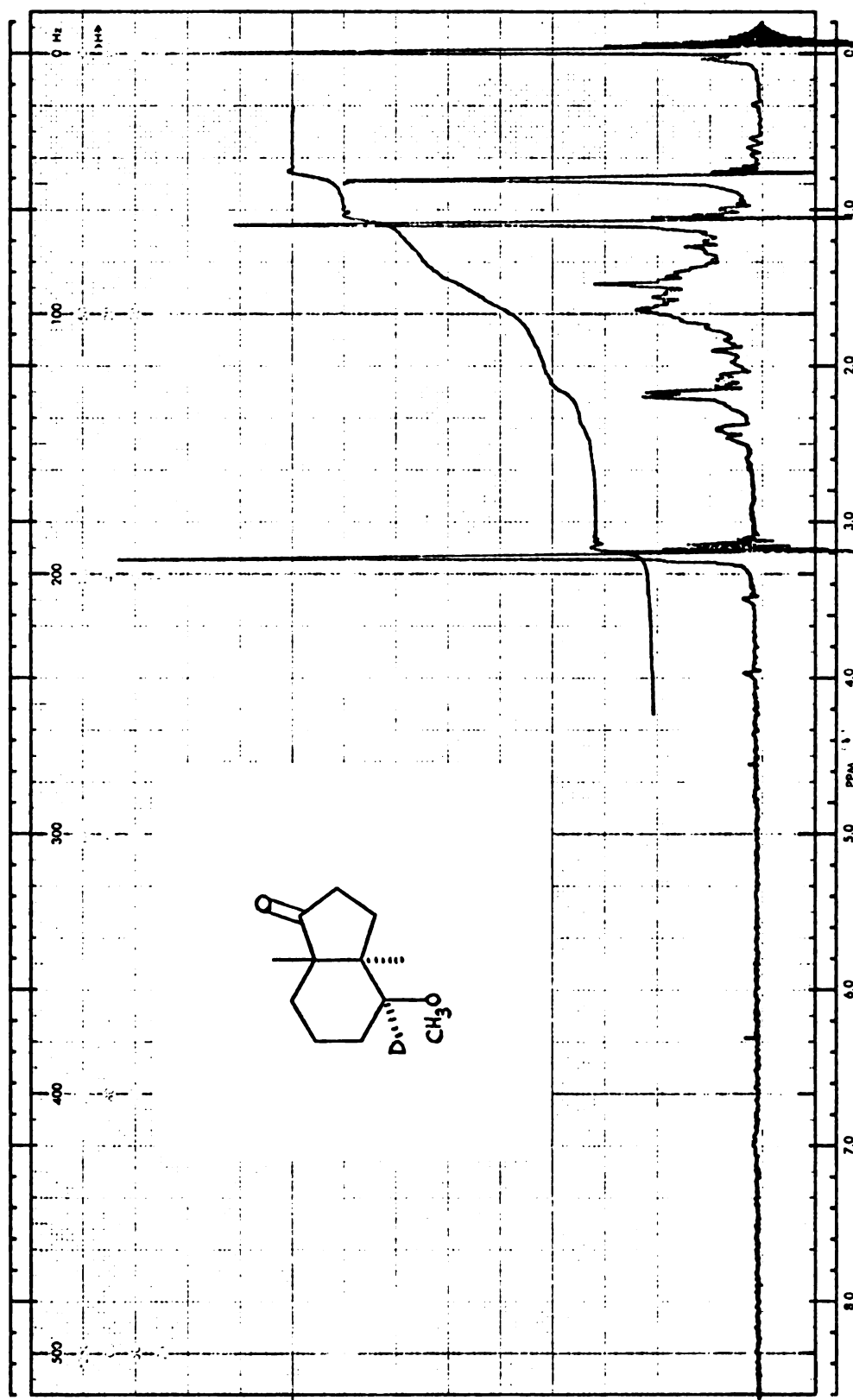


Figure 54. Pmr spectrum of 19.

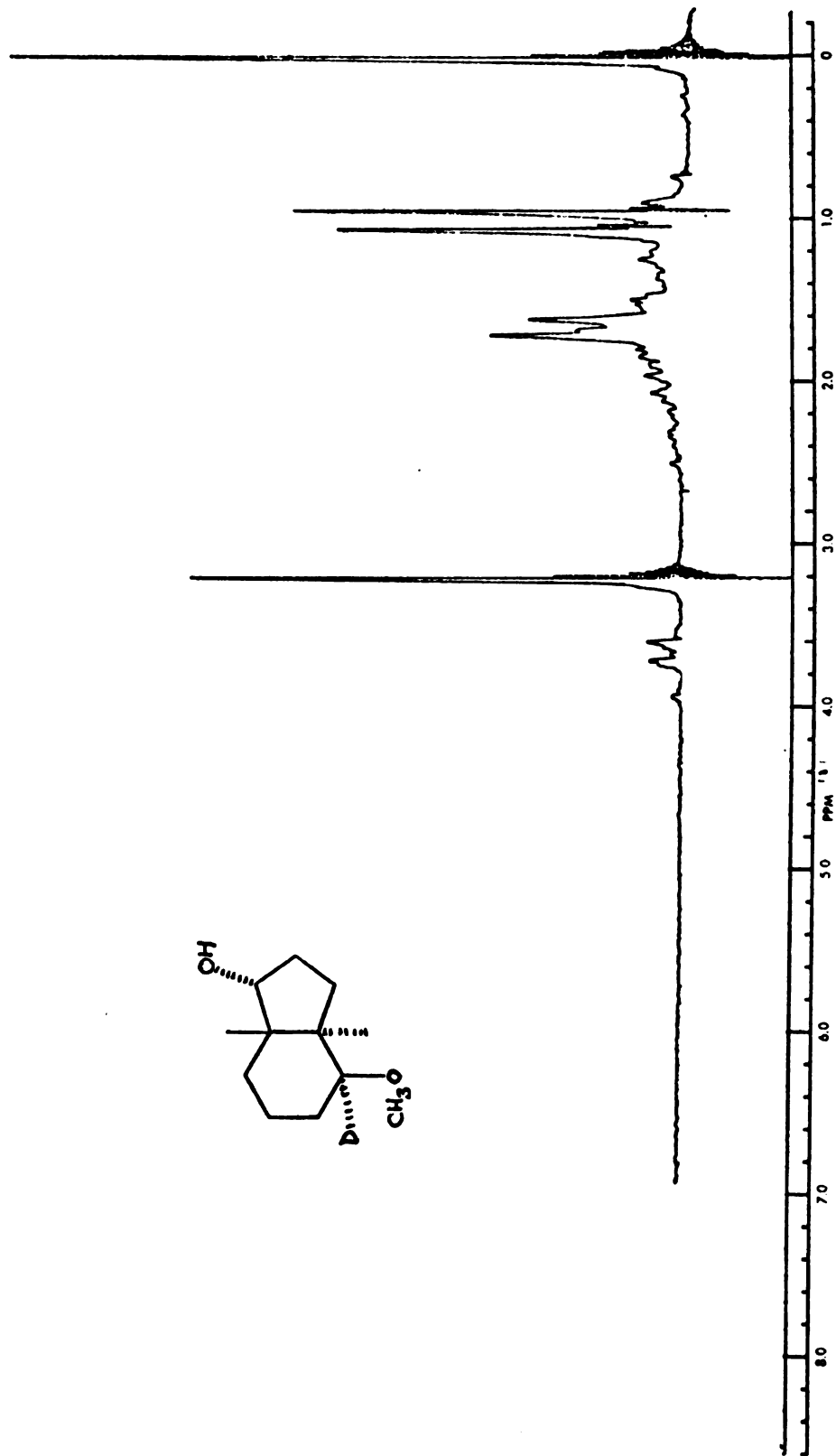


Figure 55. PMR spectrum of 20.

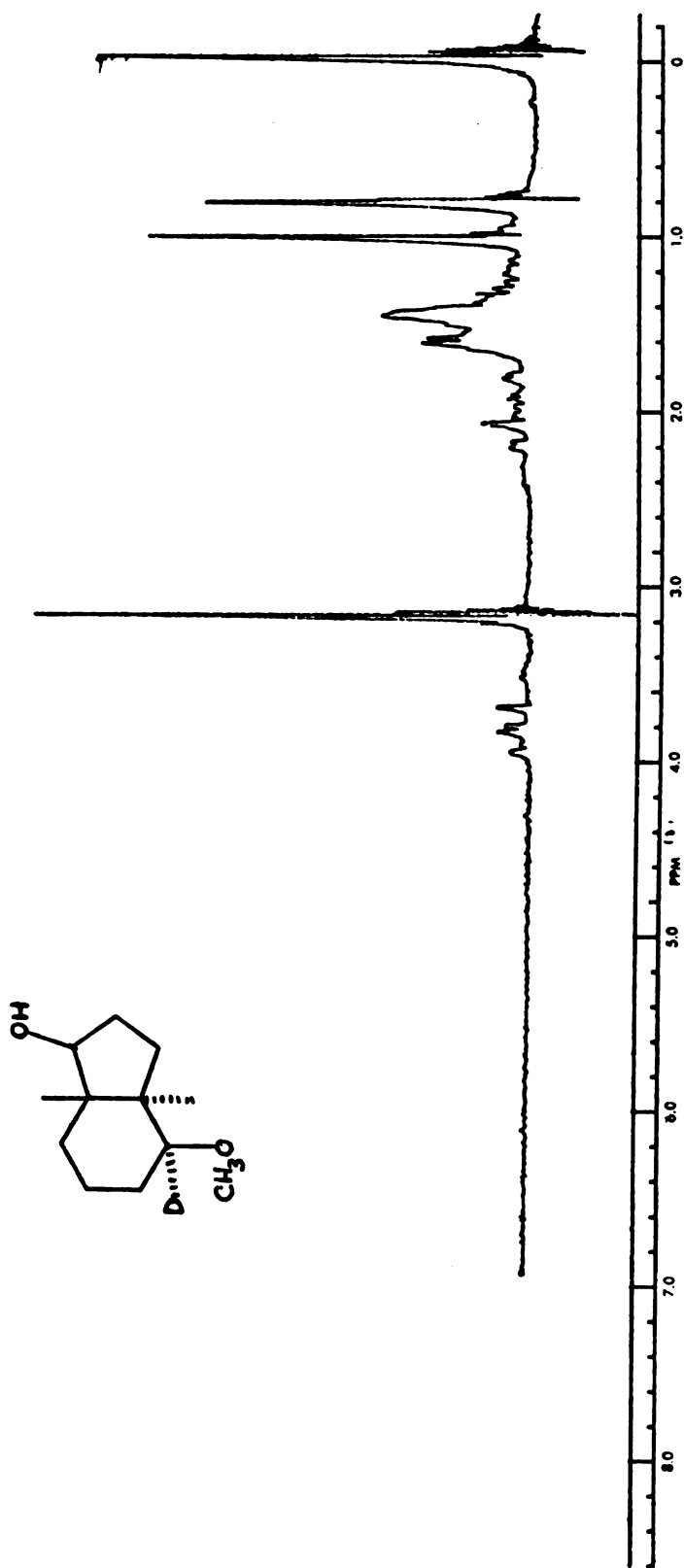


Figure 56. PMR spectrum of 21.

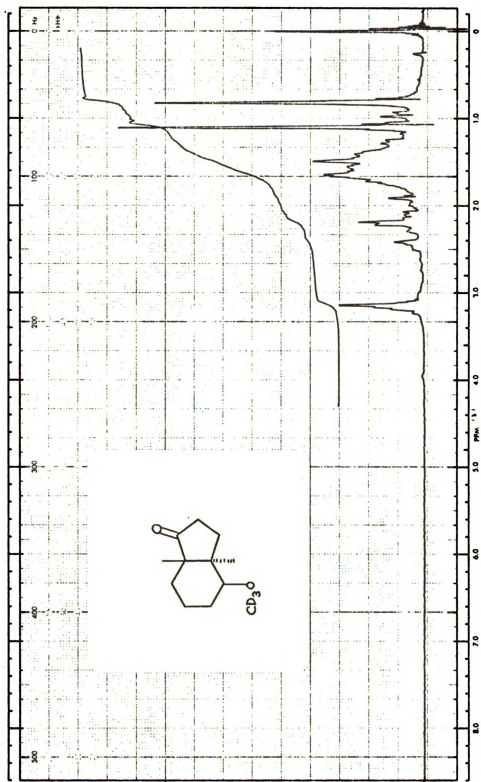


Figure 57. Pmr spectrum of 22.

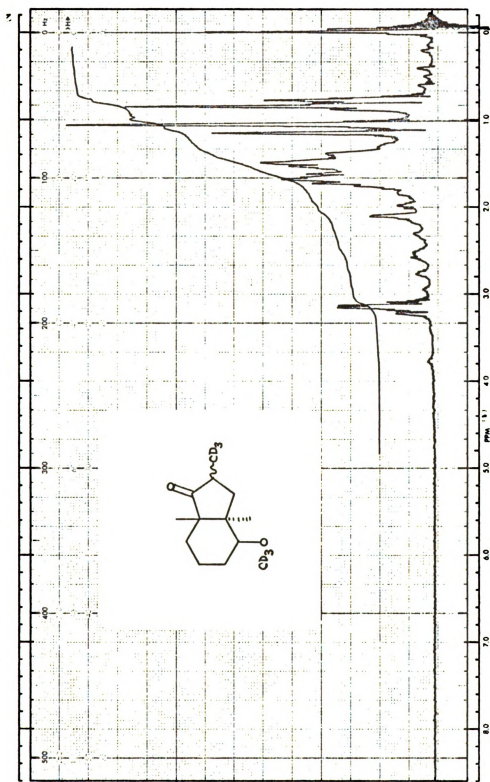


Figure 58. Pmr spectrum of 23.

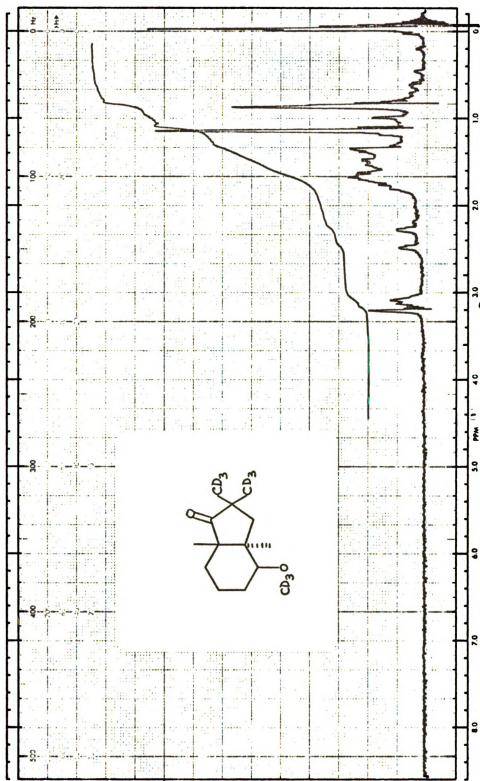


Figure 59. Pmr spectrum of 24.

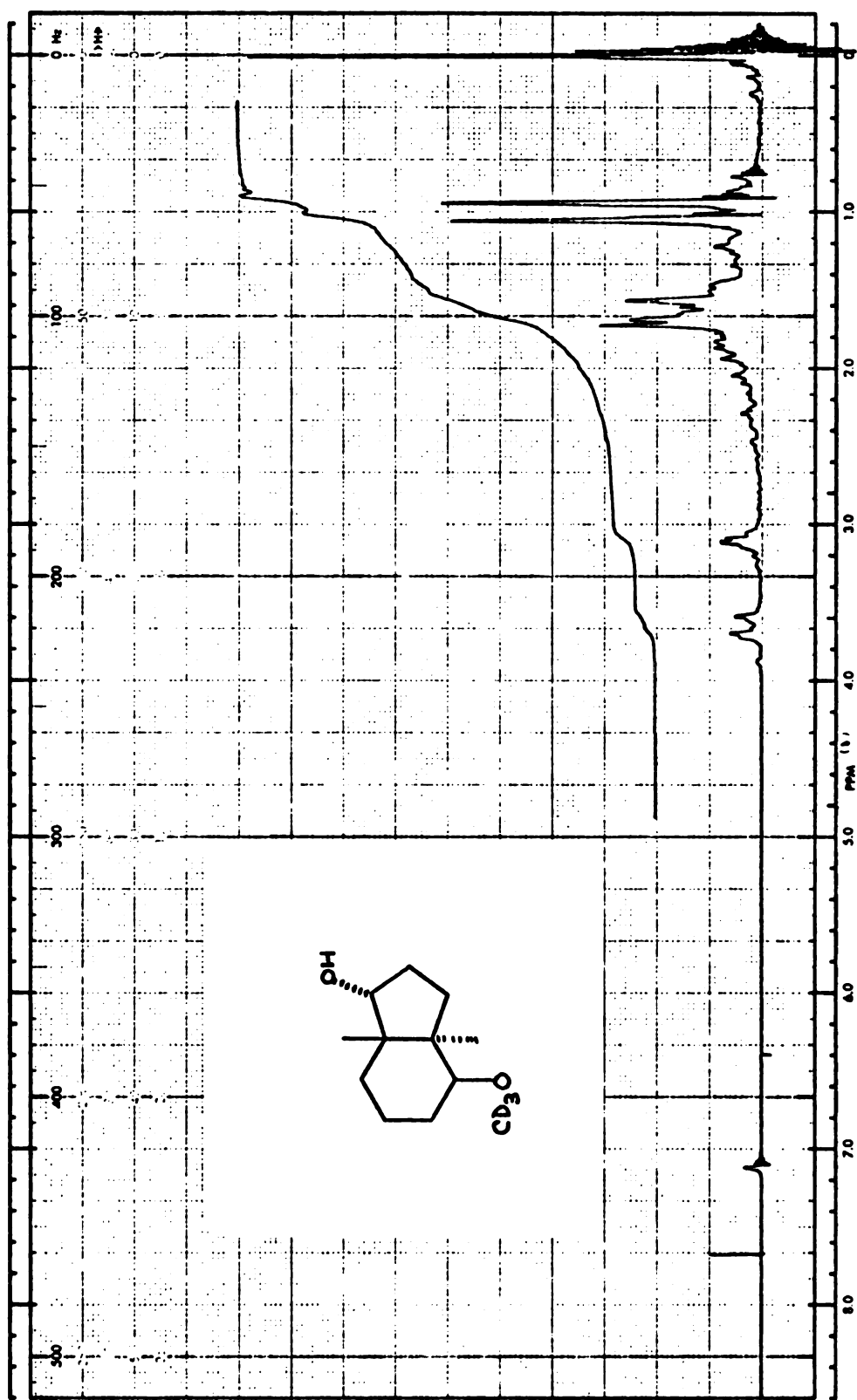


Figure 60. Pmr spectrum of 25.

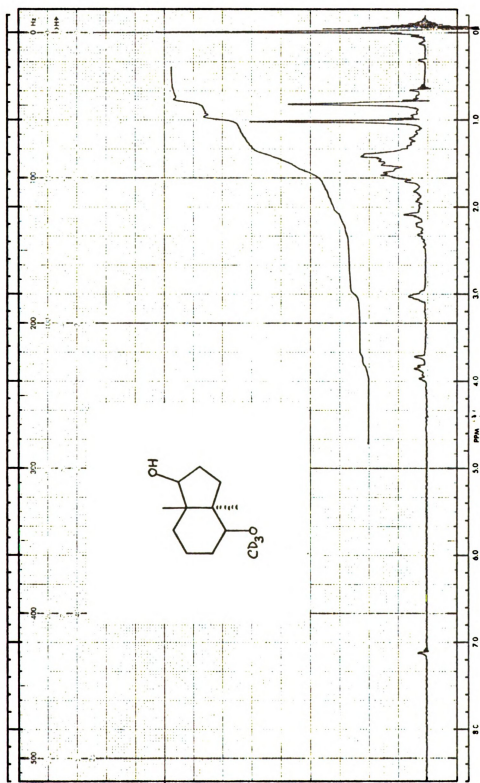


Figure 61. Pmr spectrum of 26.

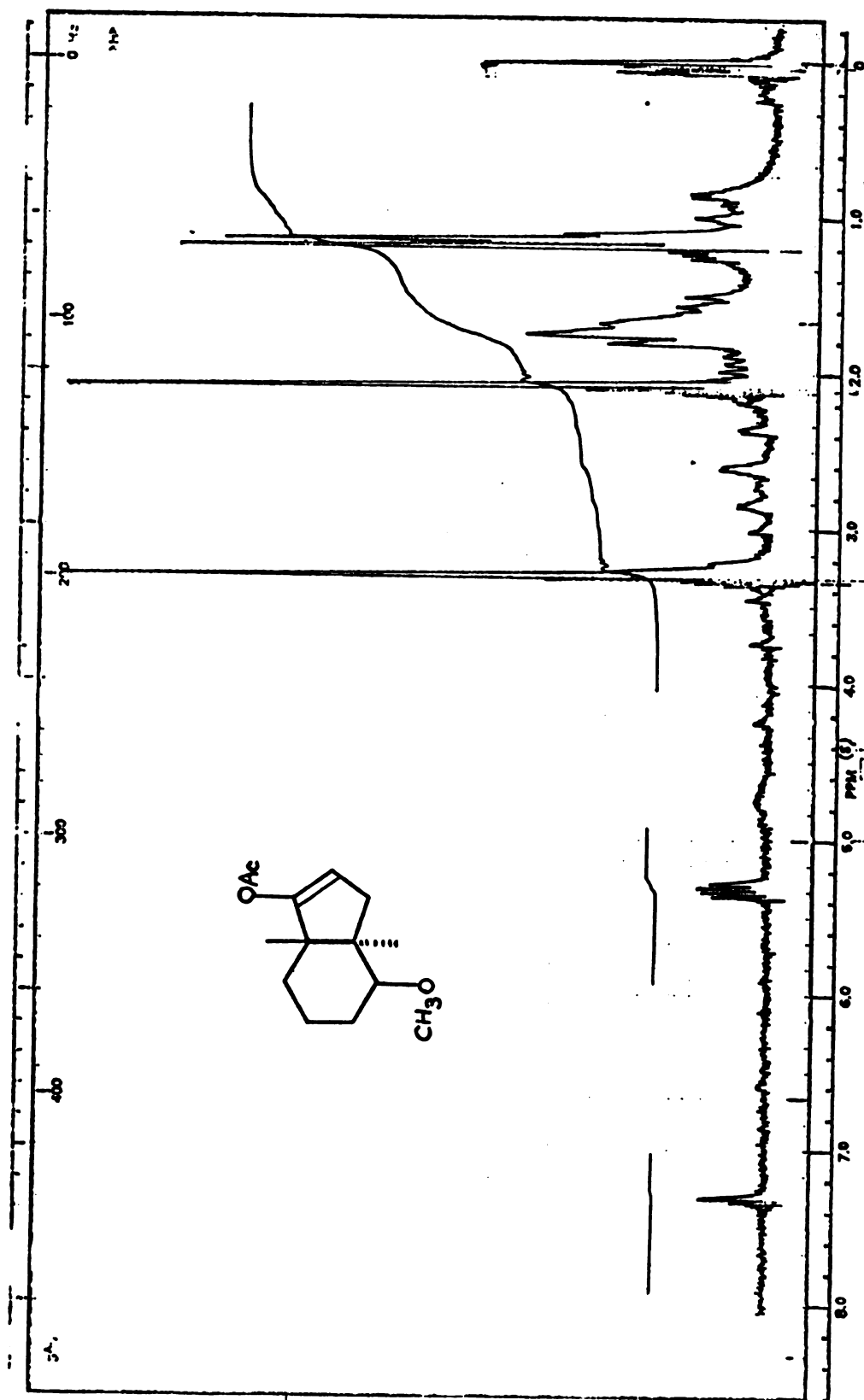


Figure 62. Pmr spectrum of 27.

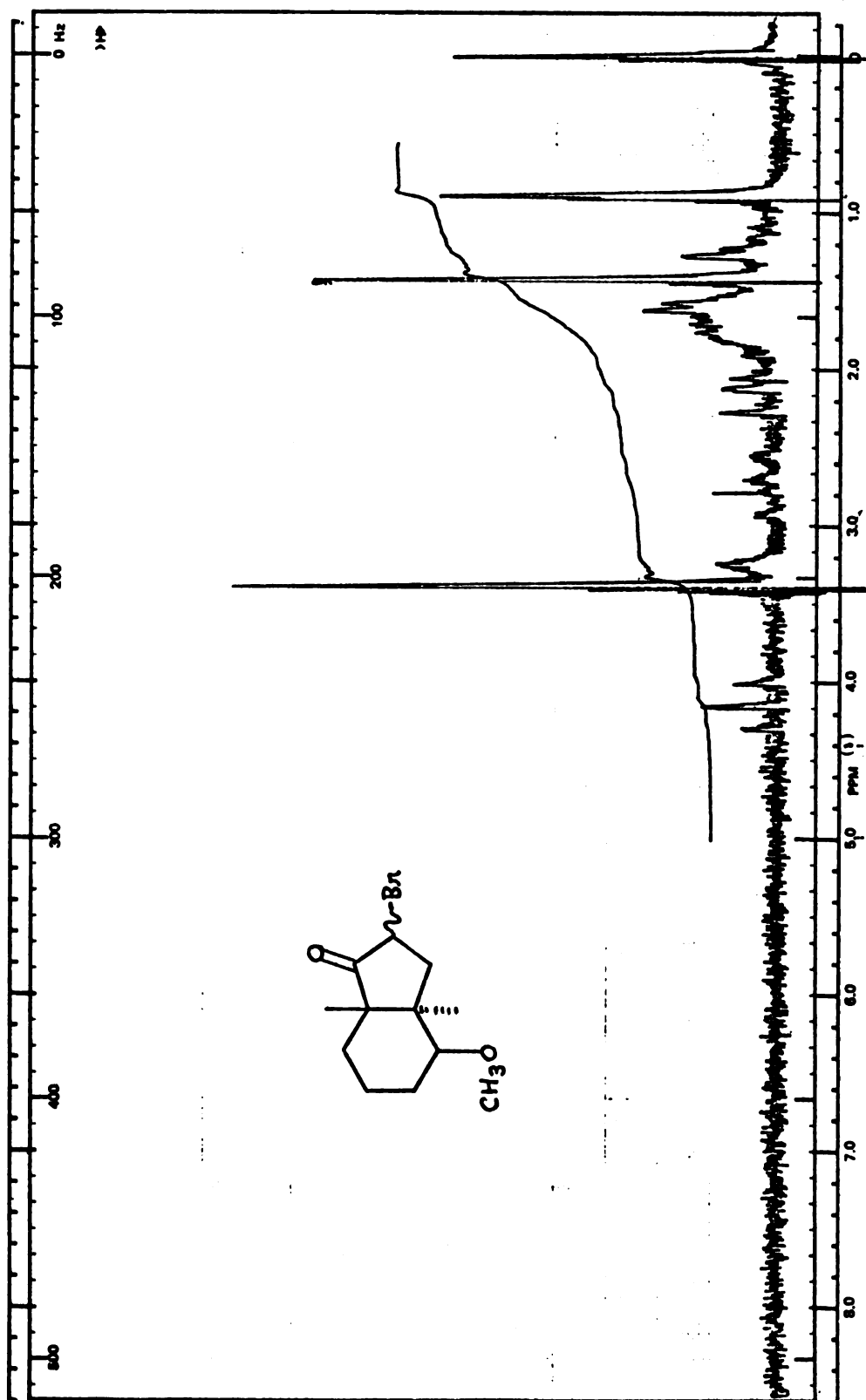


Figure 63. Pmr spectrum of 29.

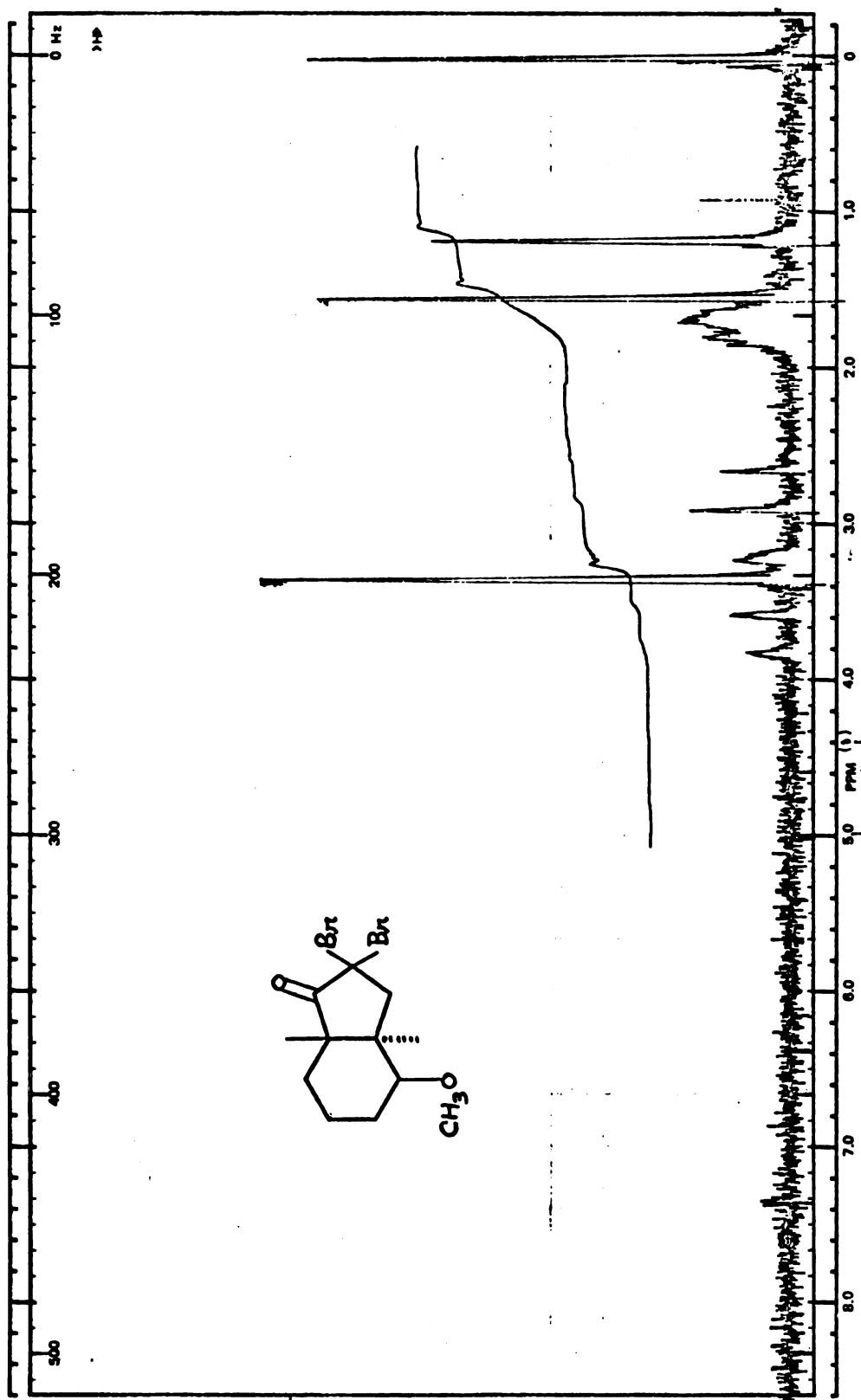


Figure 64. Pmr spectrum of 30.

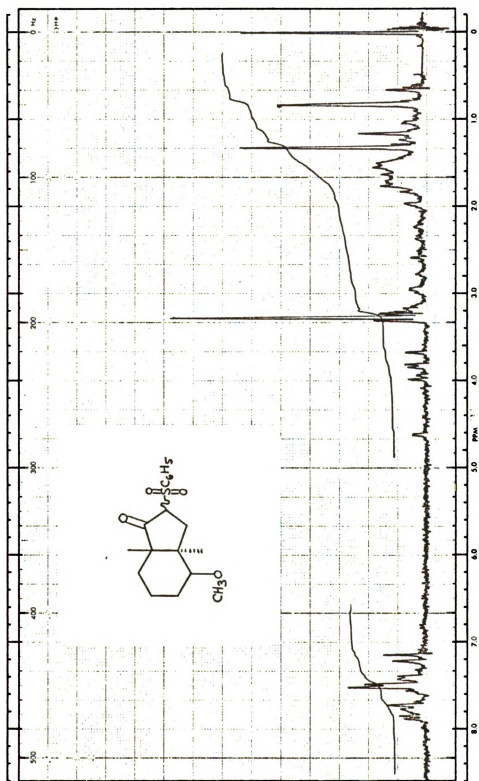


Figure 65. Pmr spectrum of 32.

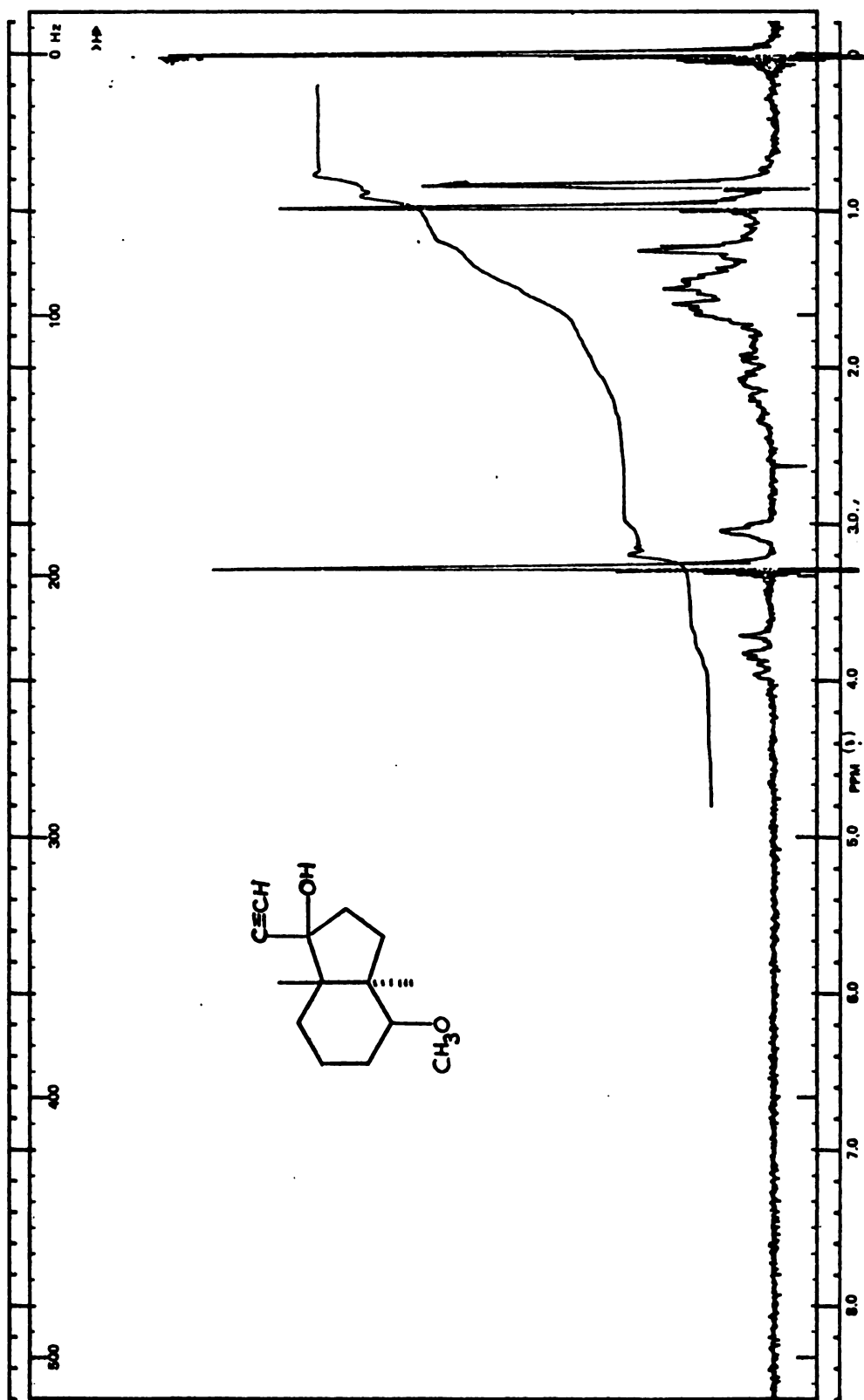


Figure 66. Pmr spectrum of 33.

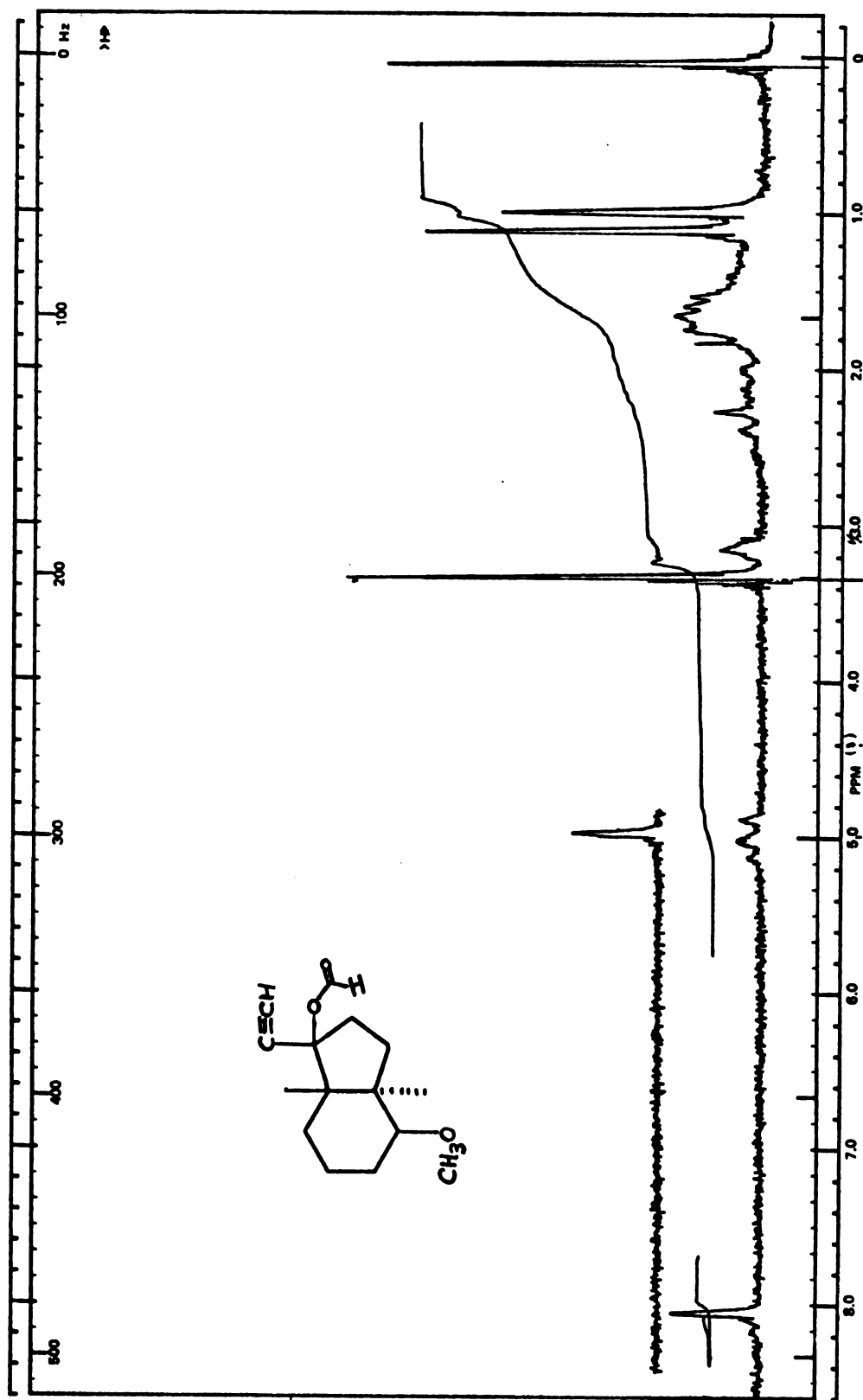


Figure 67. Pmr spectrum of 34.

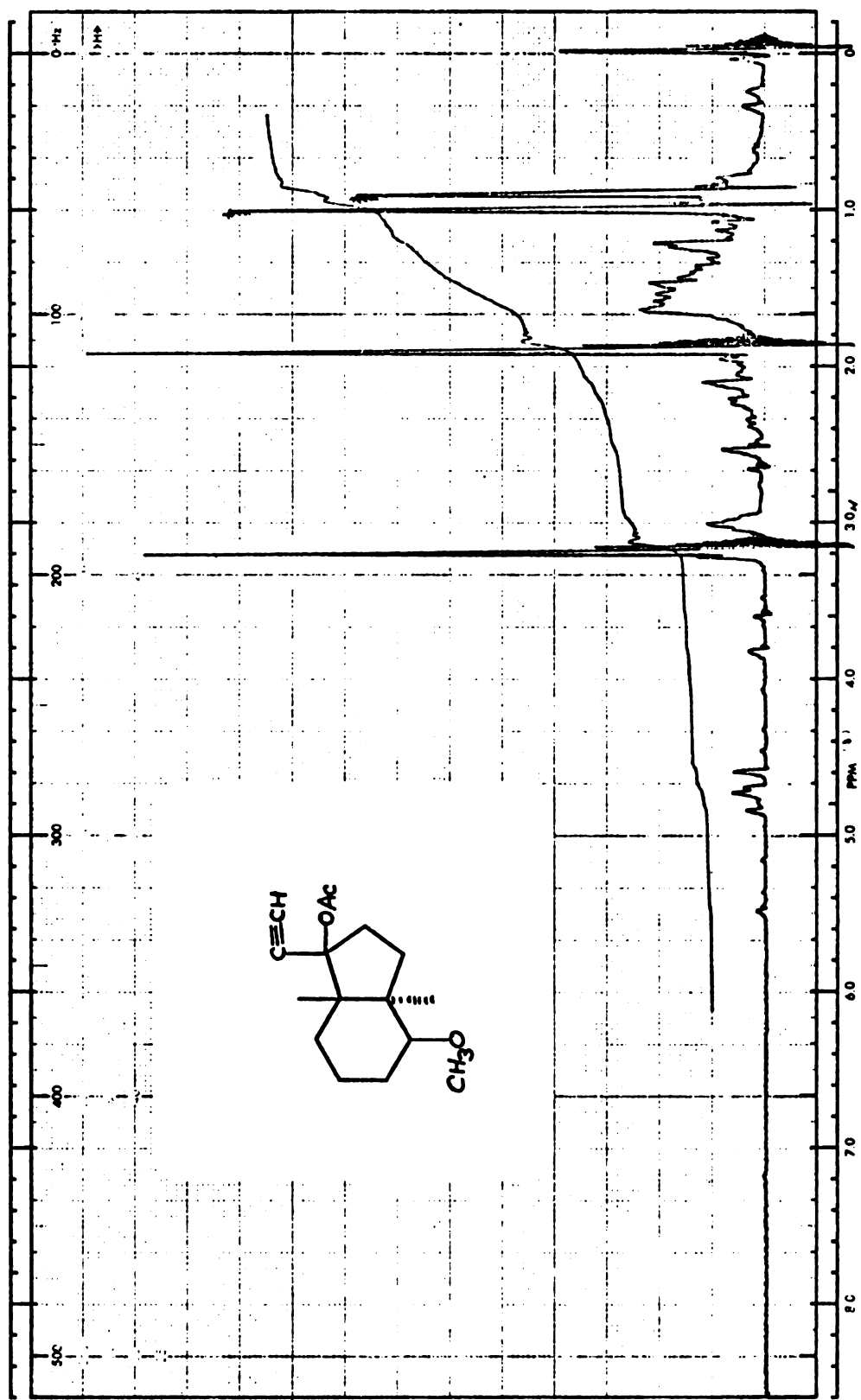


Figure 68. Pmr spectrum of 35.

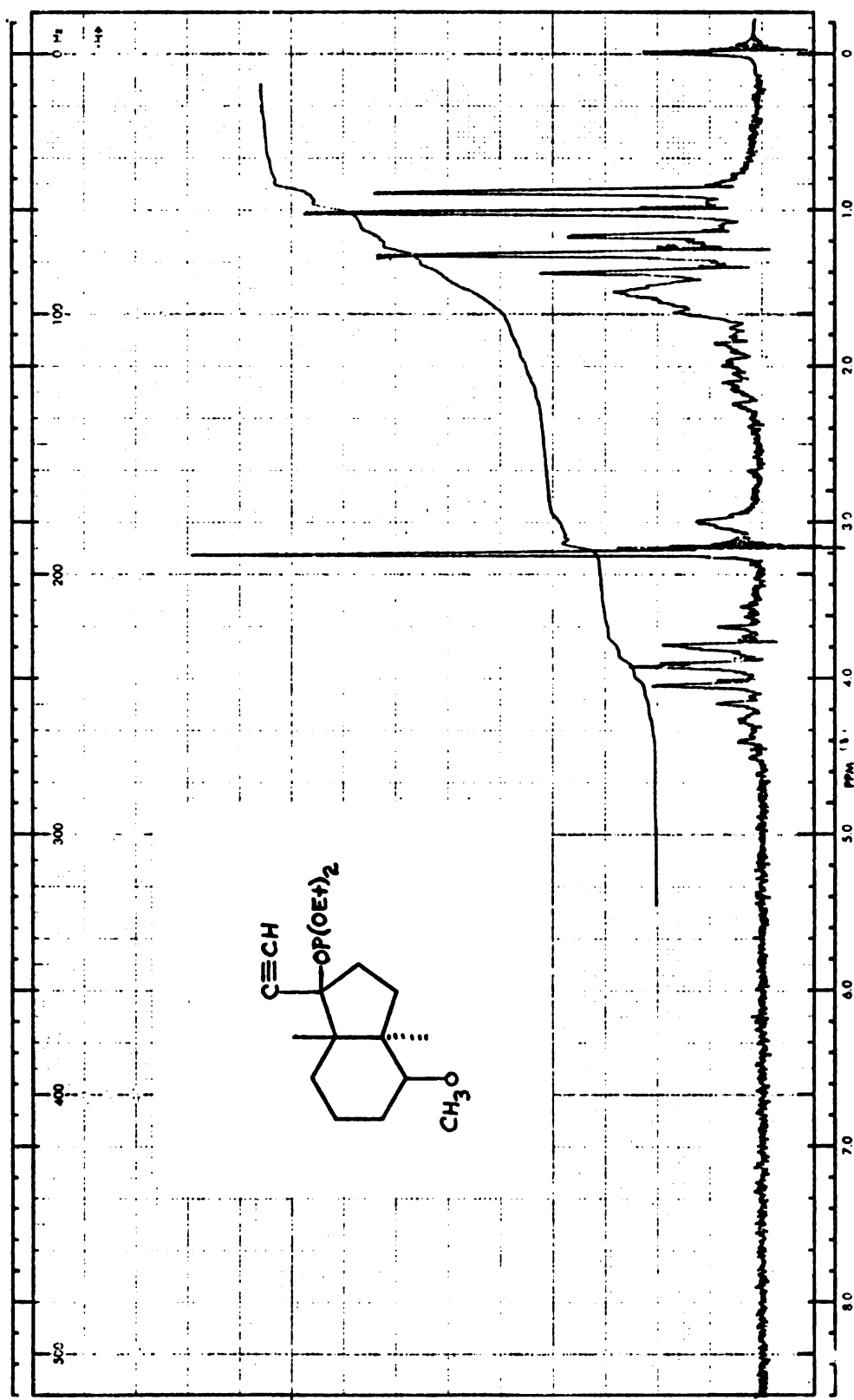


Figure 69. Pmr spectrum of 36.

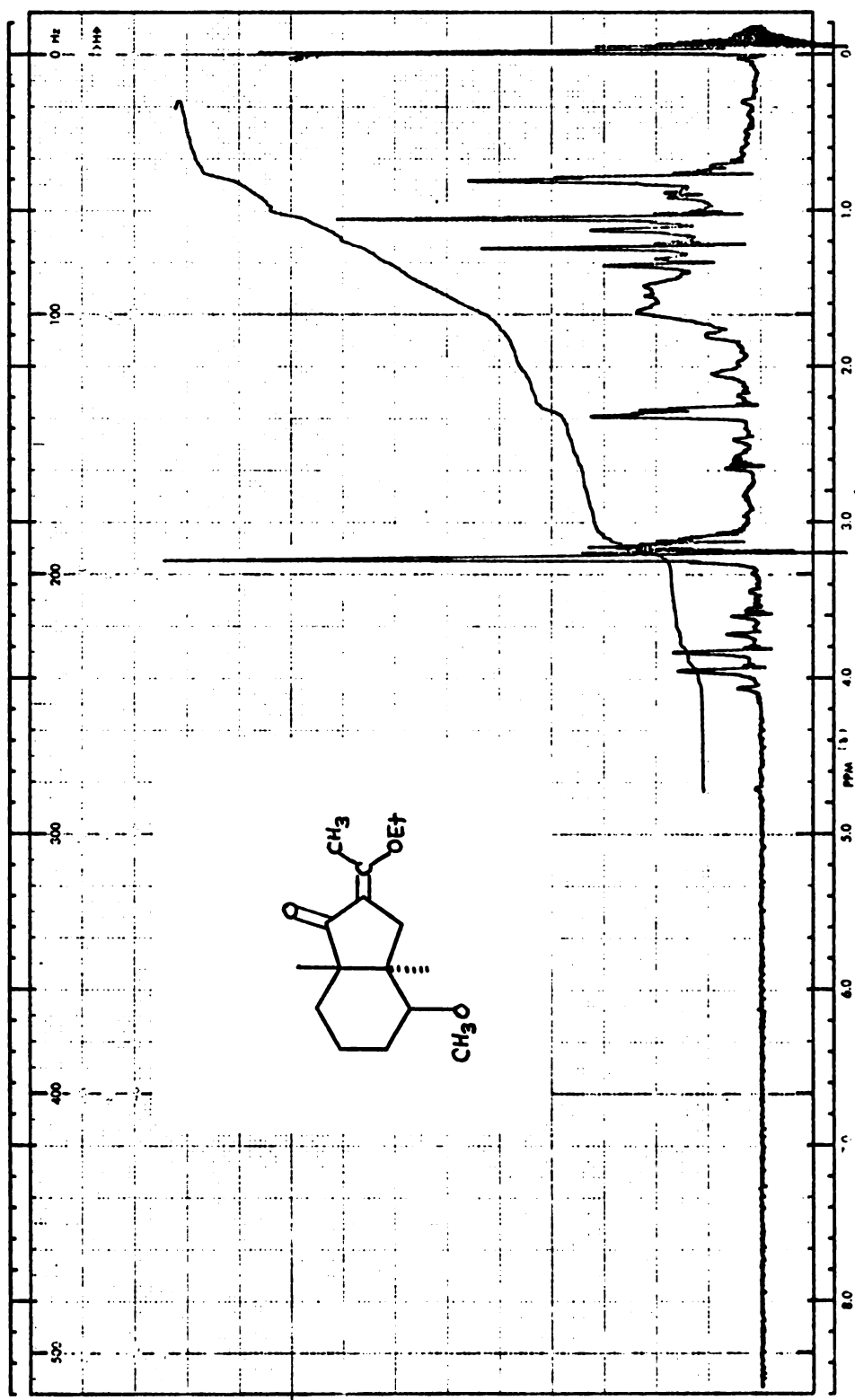


Figure 70. Pmr spectrum of 37.

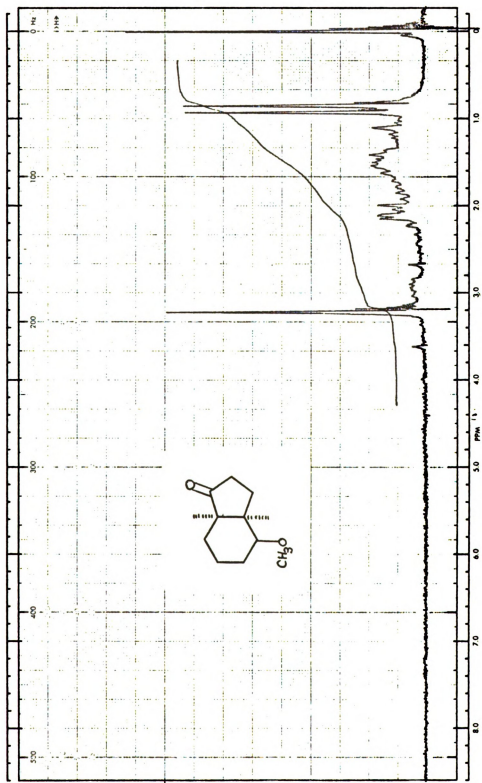


Figure 71. Pmr spectrum of 38.

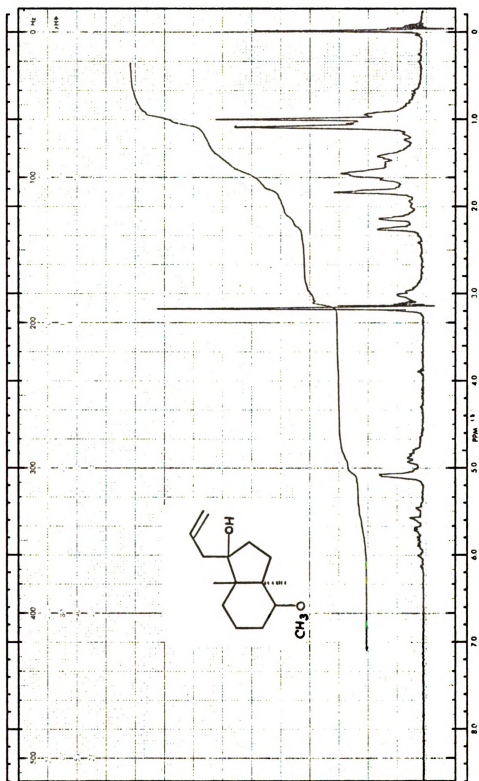


Figure 72. Pmr spectrum of 39.

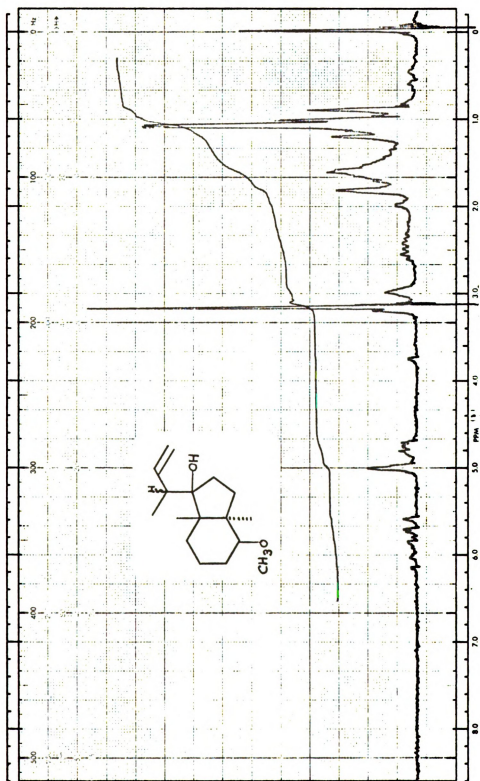


Figure 73. Pmr spectrum of 40.

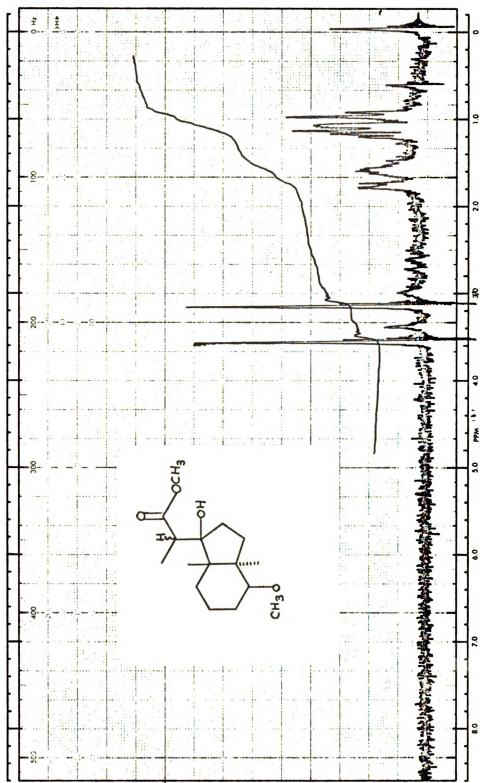


Figure 74. Pmr spectrum of 43.

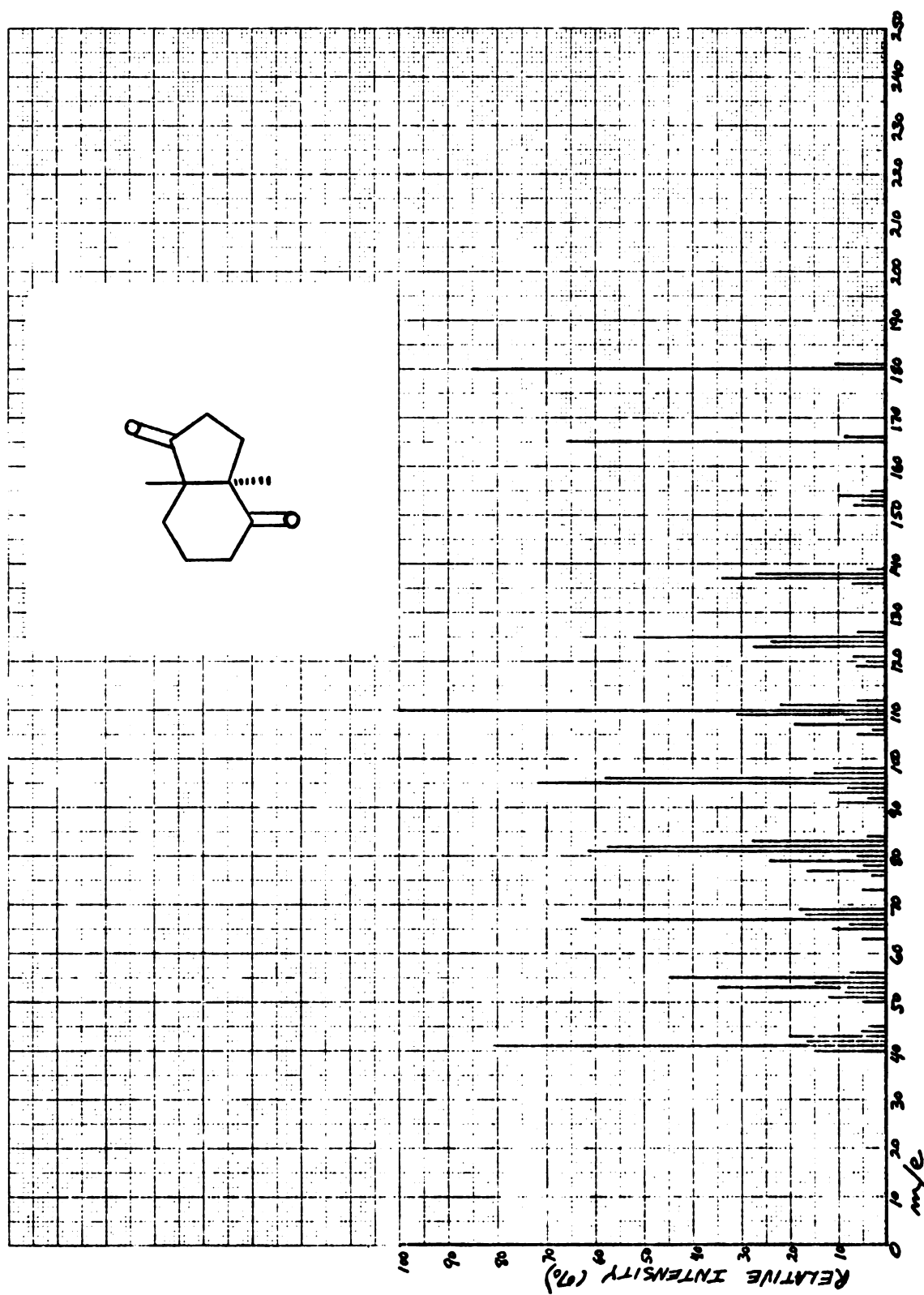


Figure 75. Mass spectrum of \tilde{I} (70 eV)

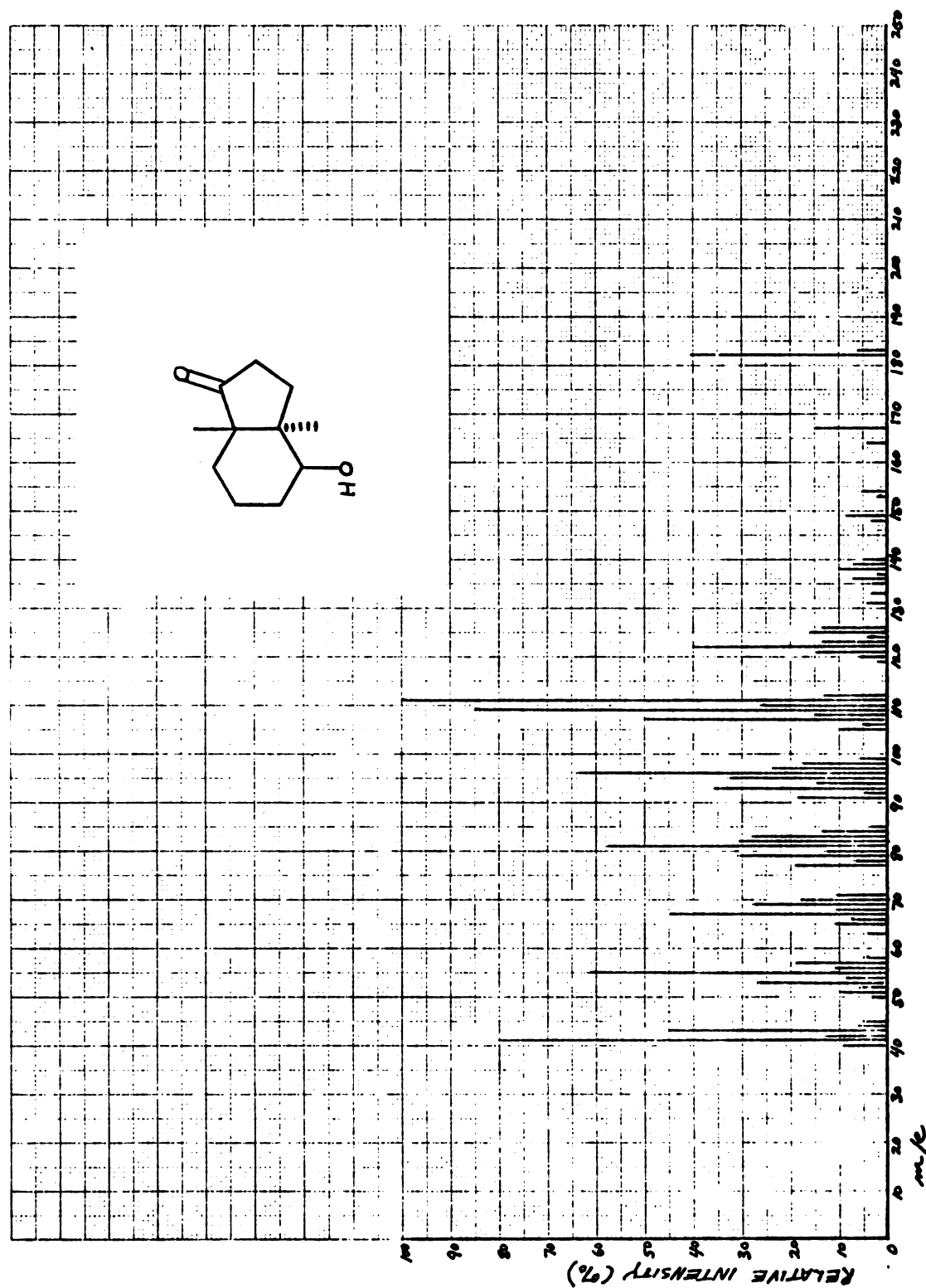


Figure 76. Mass spectrum of 2 (70 eV).

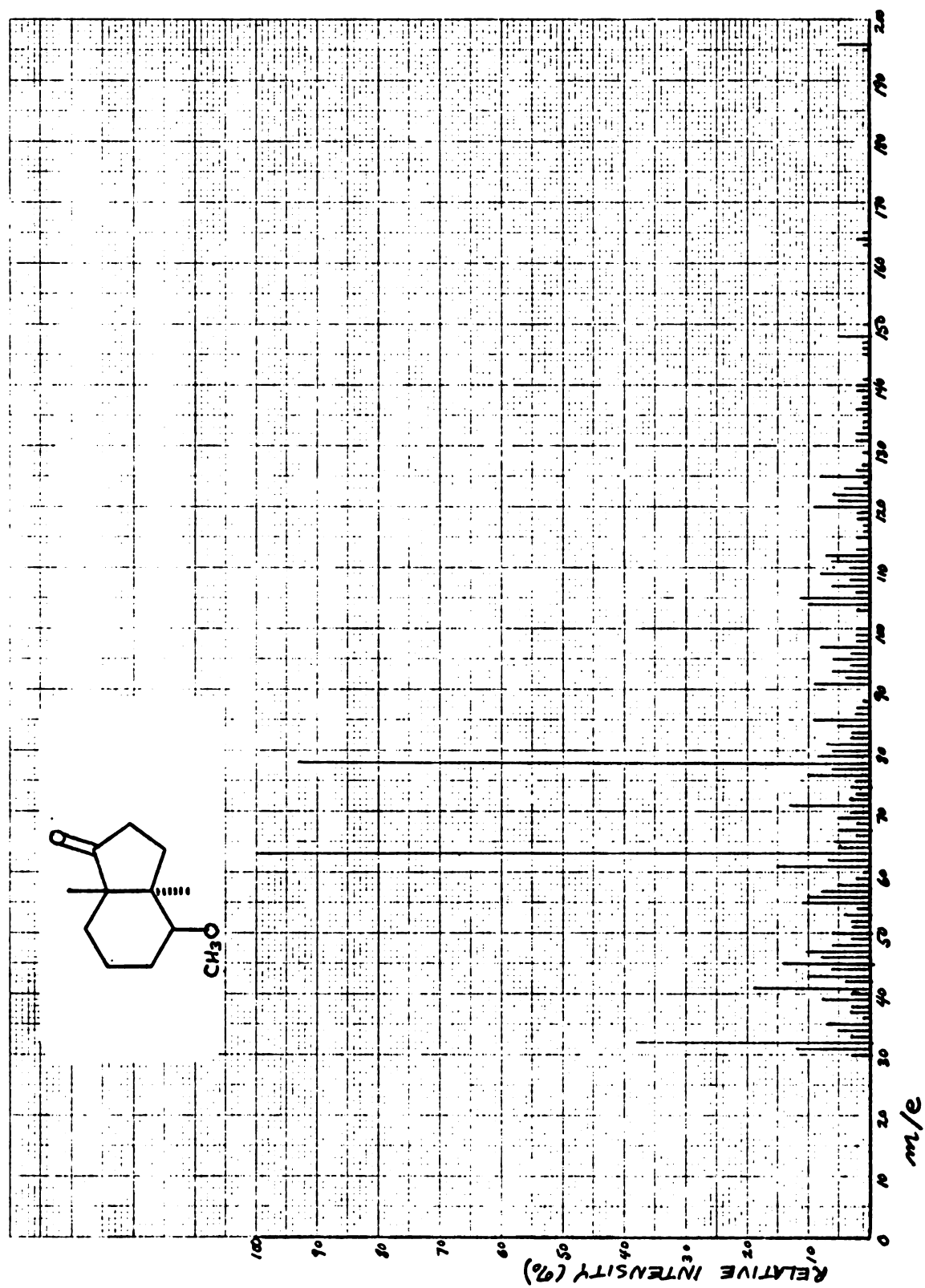


Figure 77. Mass spectrum of **3** (70 eV).

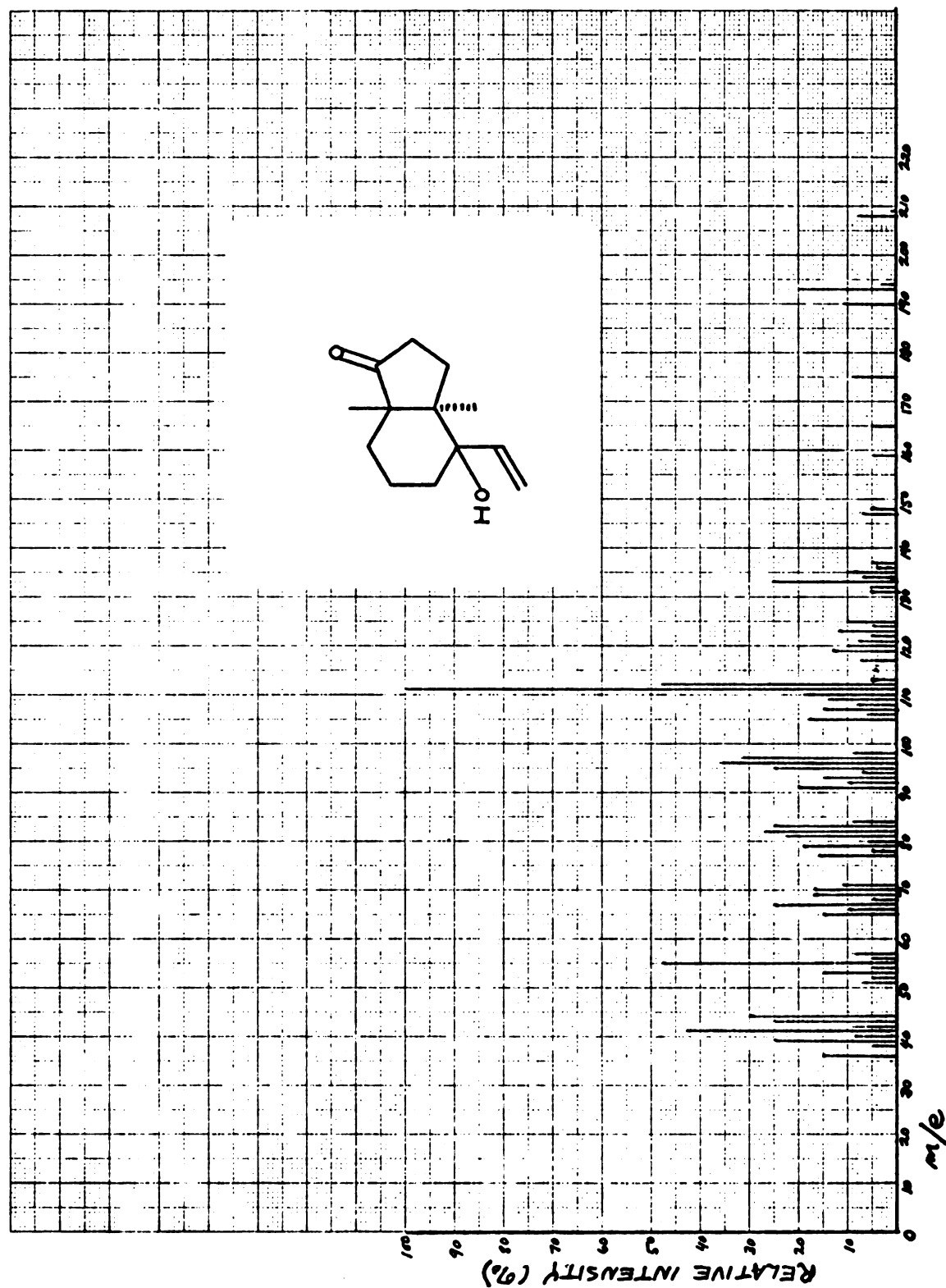


Figure 78. Mass spectrum of 4 (70 eV).

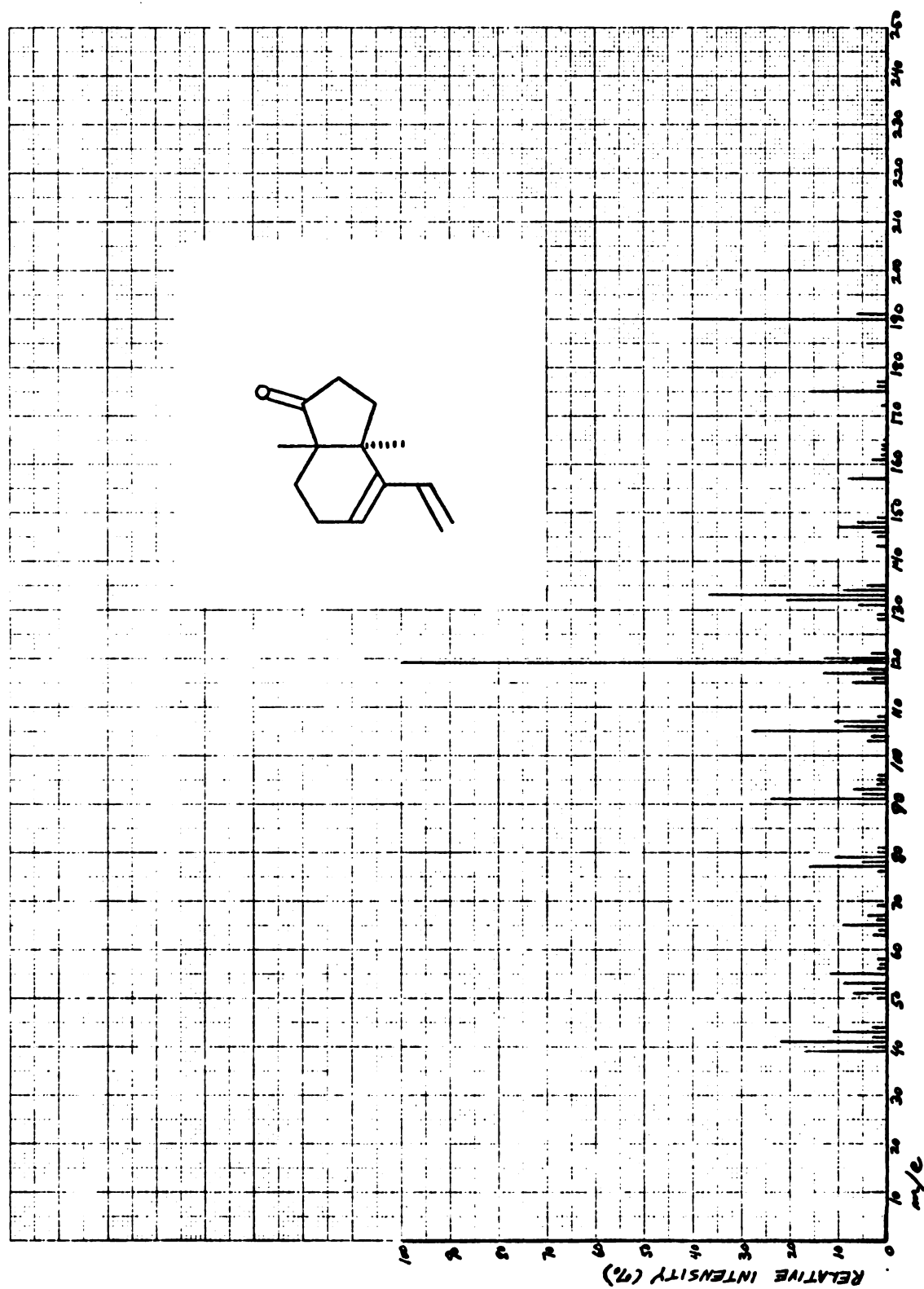


Figure 79. Mass spectrum of 5 (70 eV).

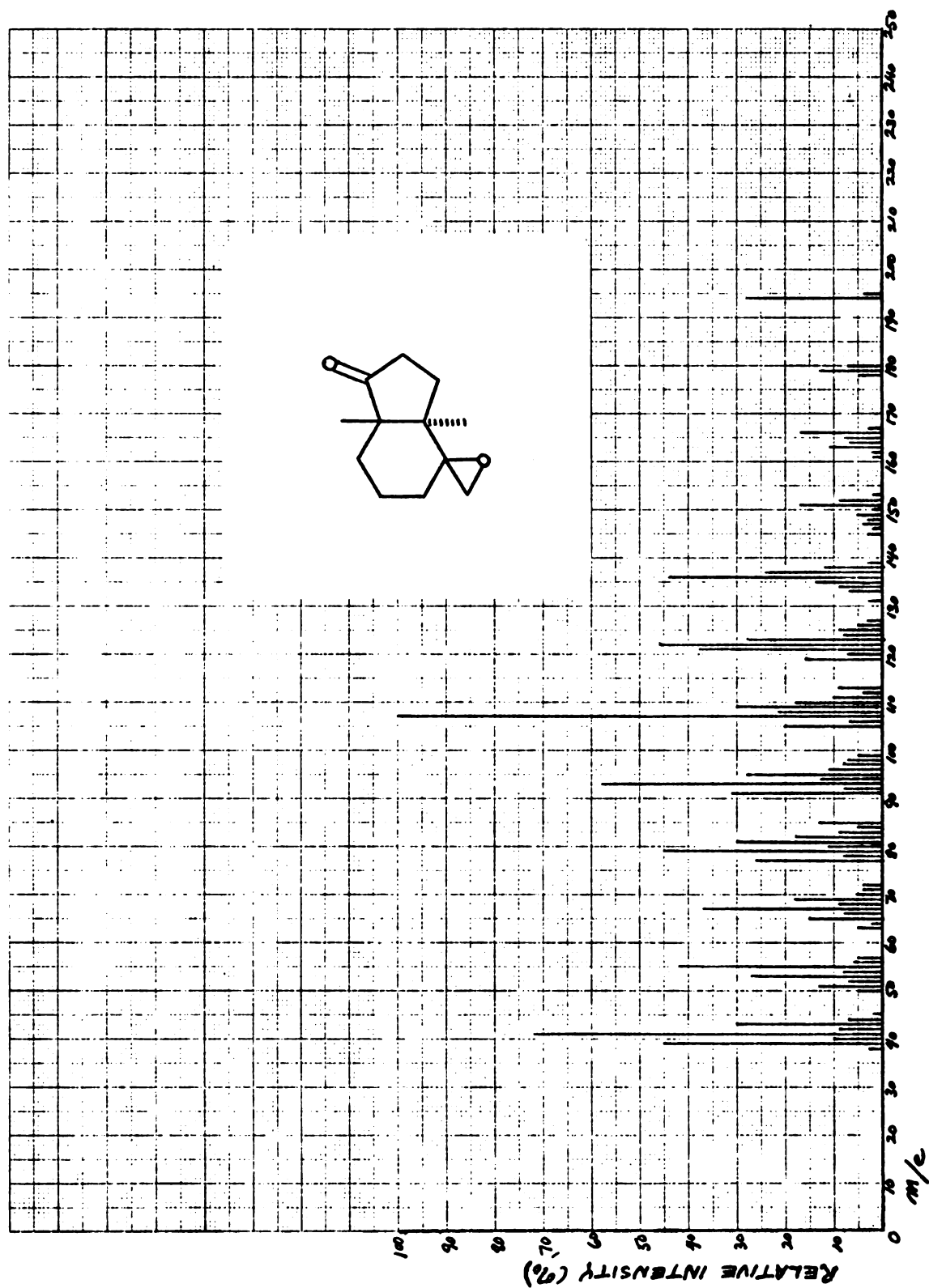


Figure 80. Mass spectrum of 6 (70 eV).

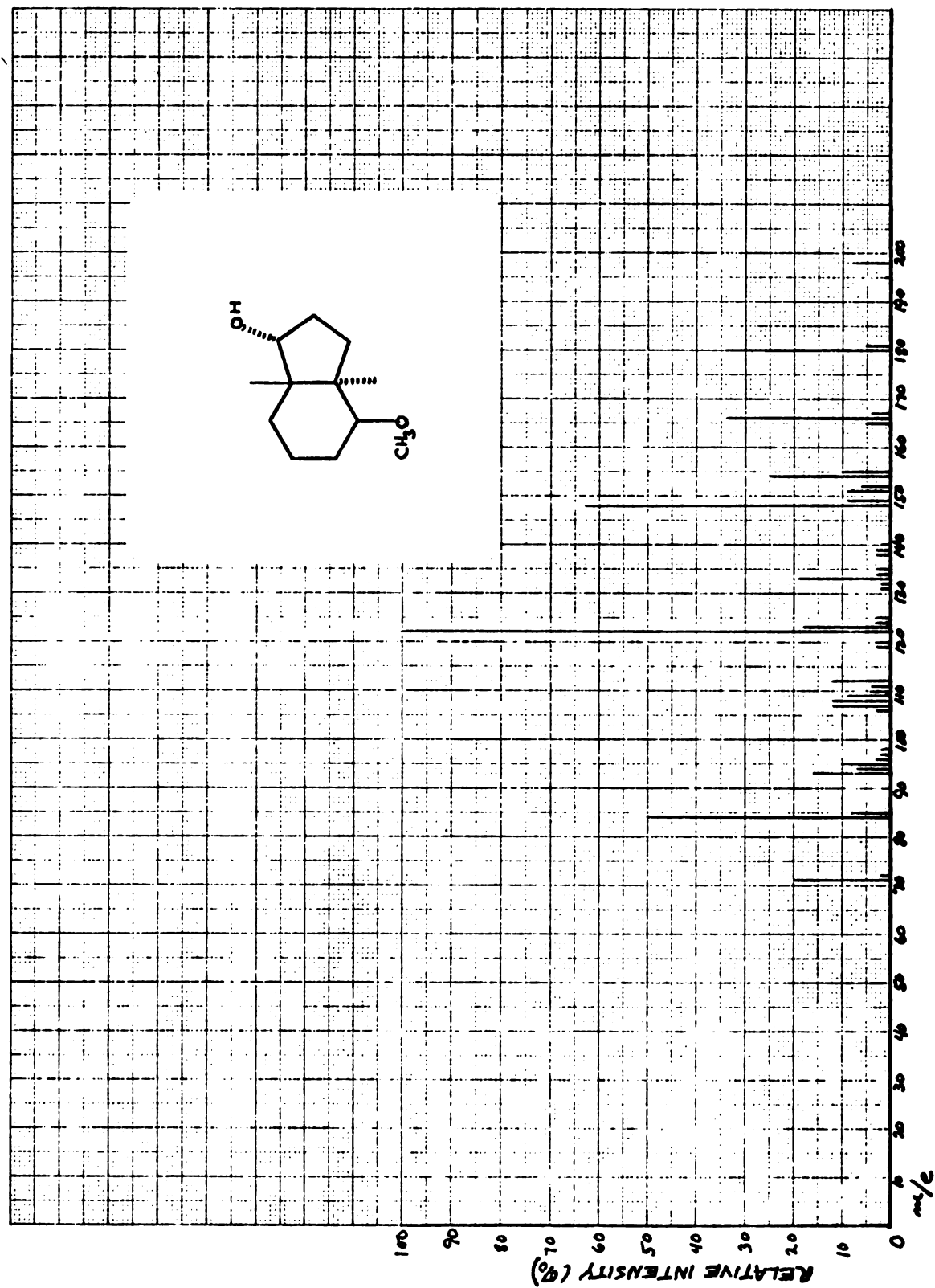


Figure 81. Mass spectrum of 7 (15 eV, ion source 100°).

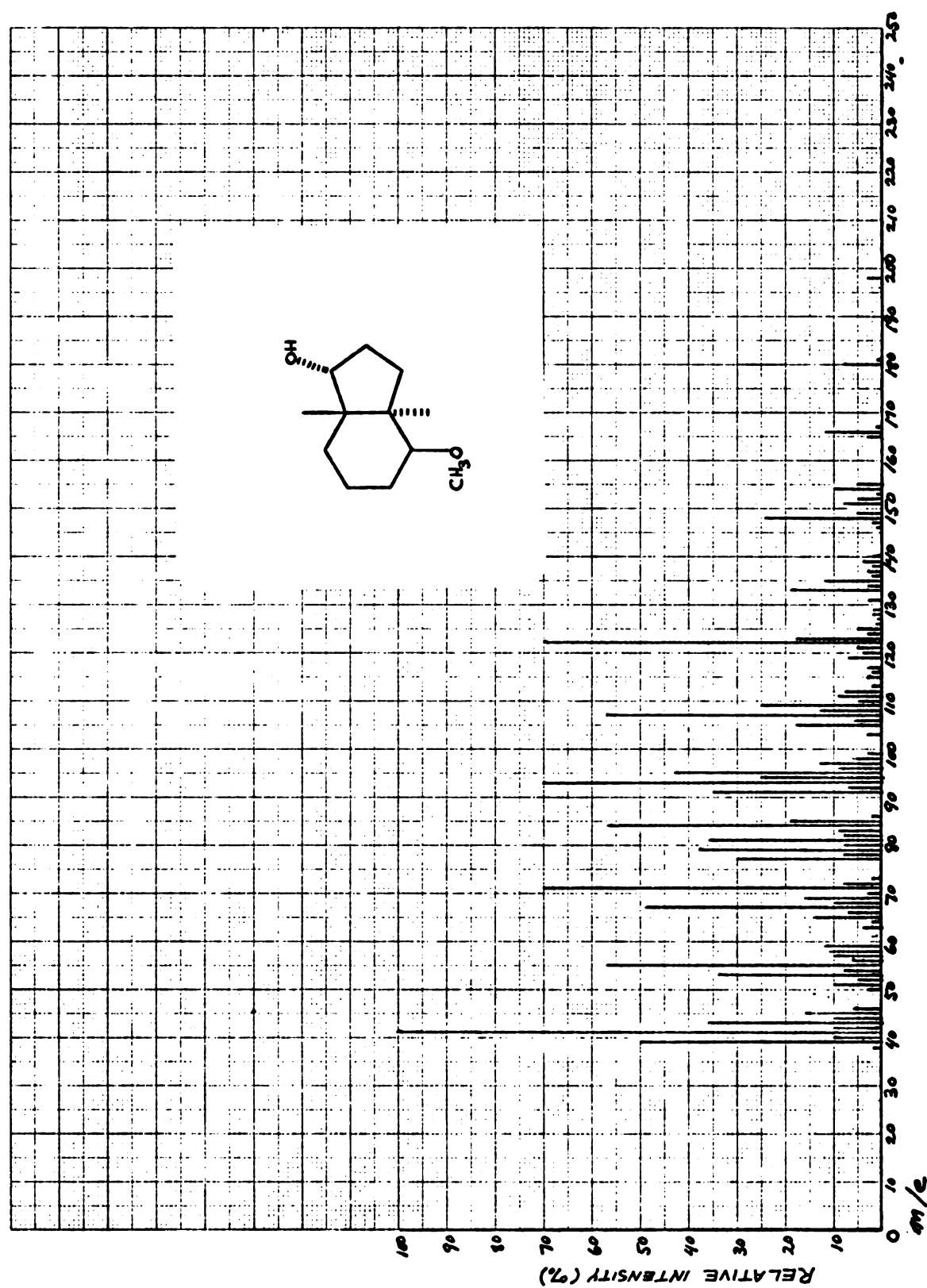


Figure 82. Mass spectrum of **7** (70 eV, ion source 115°).

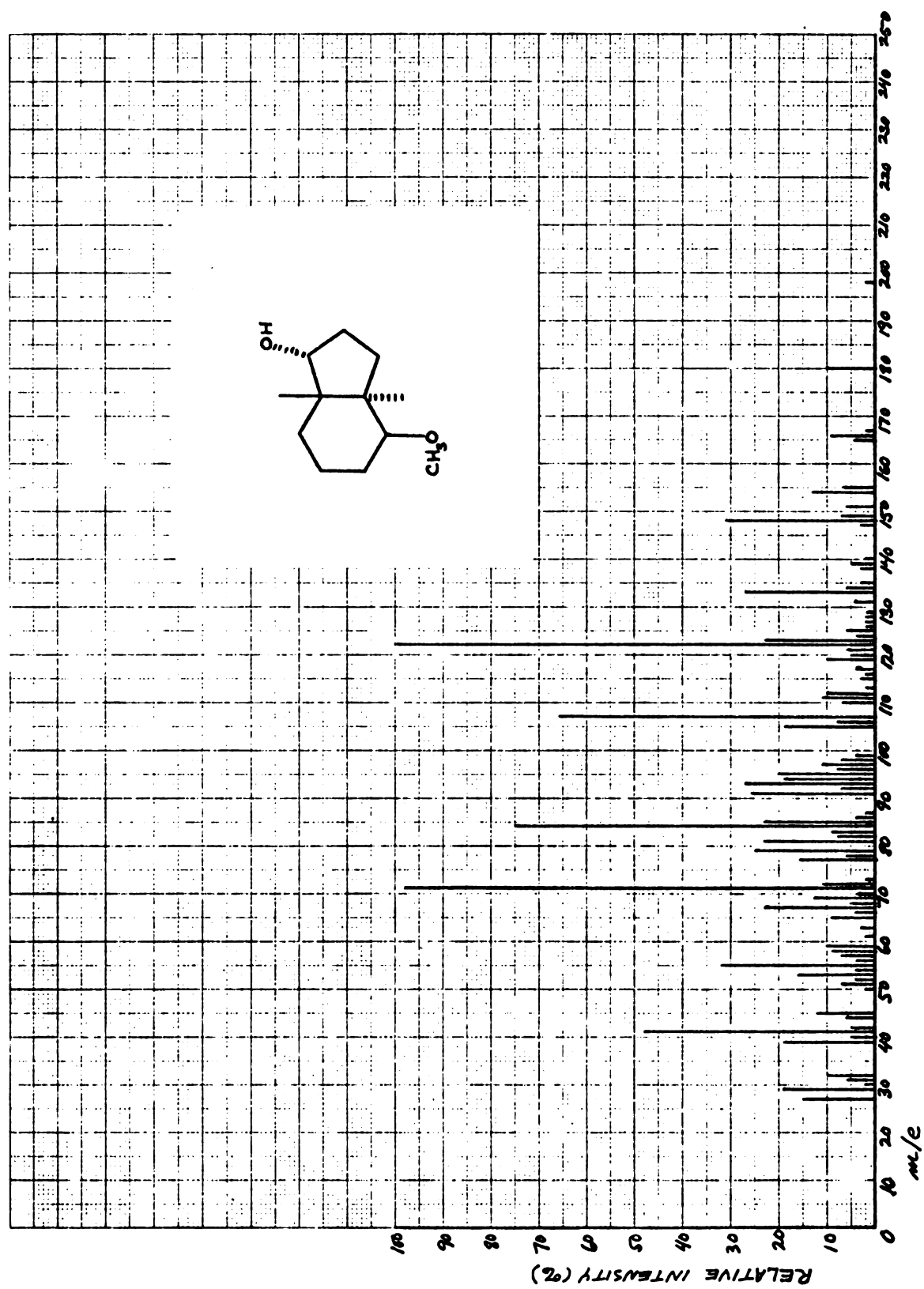


Figure 83. Mass spectrum of 7 (70 eV, ion source 250°).

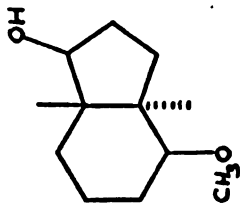


Figure 84. Mass spectrum of 8 (15 eV, ion source 100°).

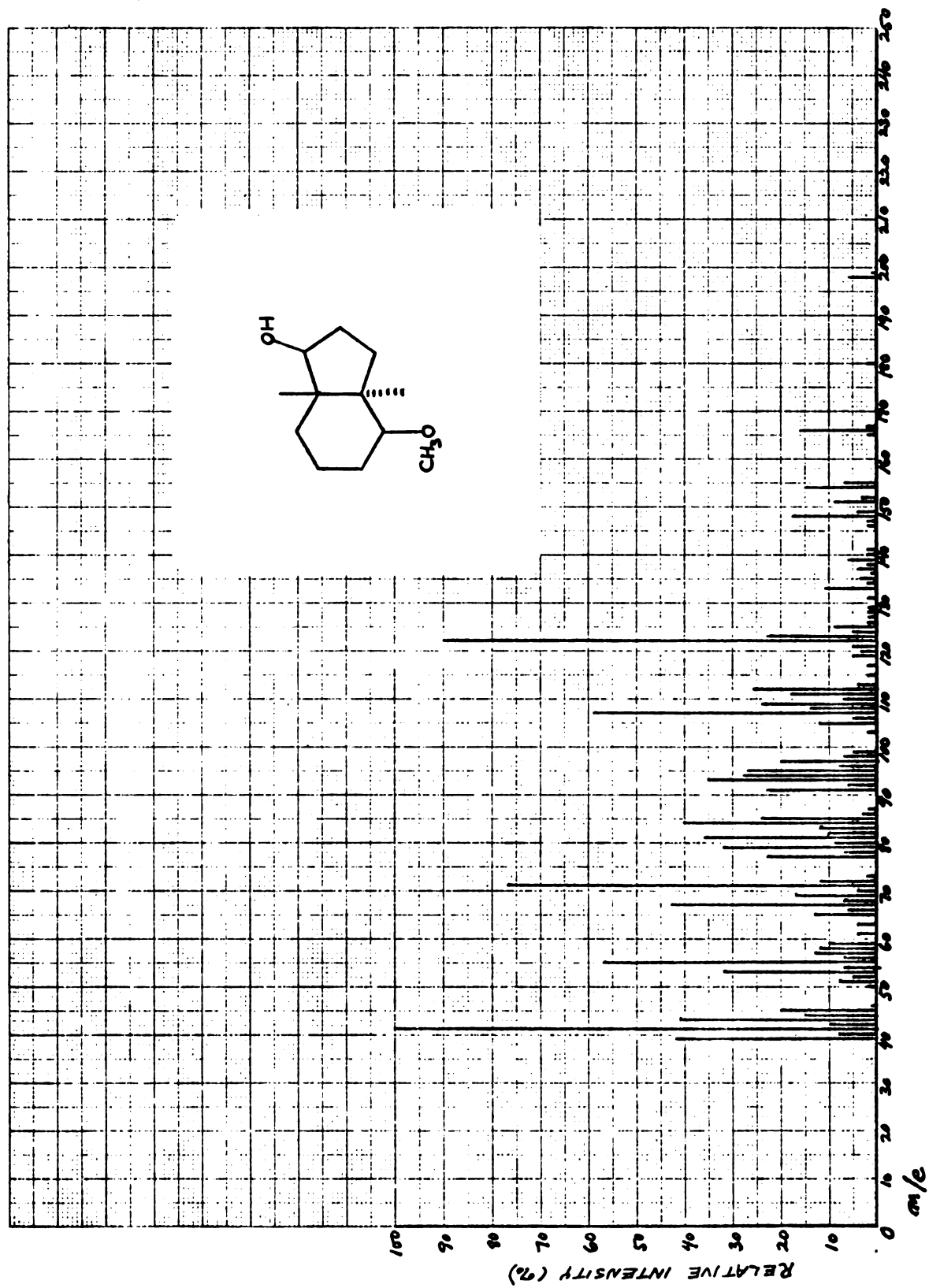


Figure 85. Mass spectrum of 8 (70 eV, ion source 115°).

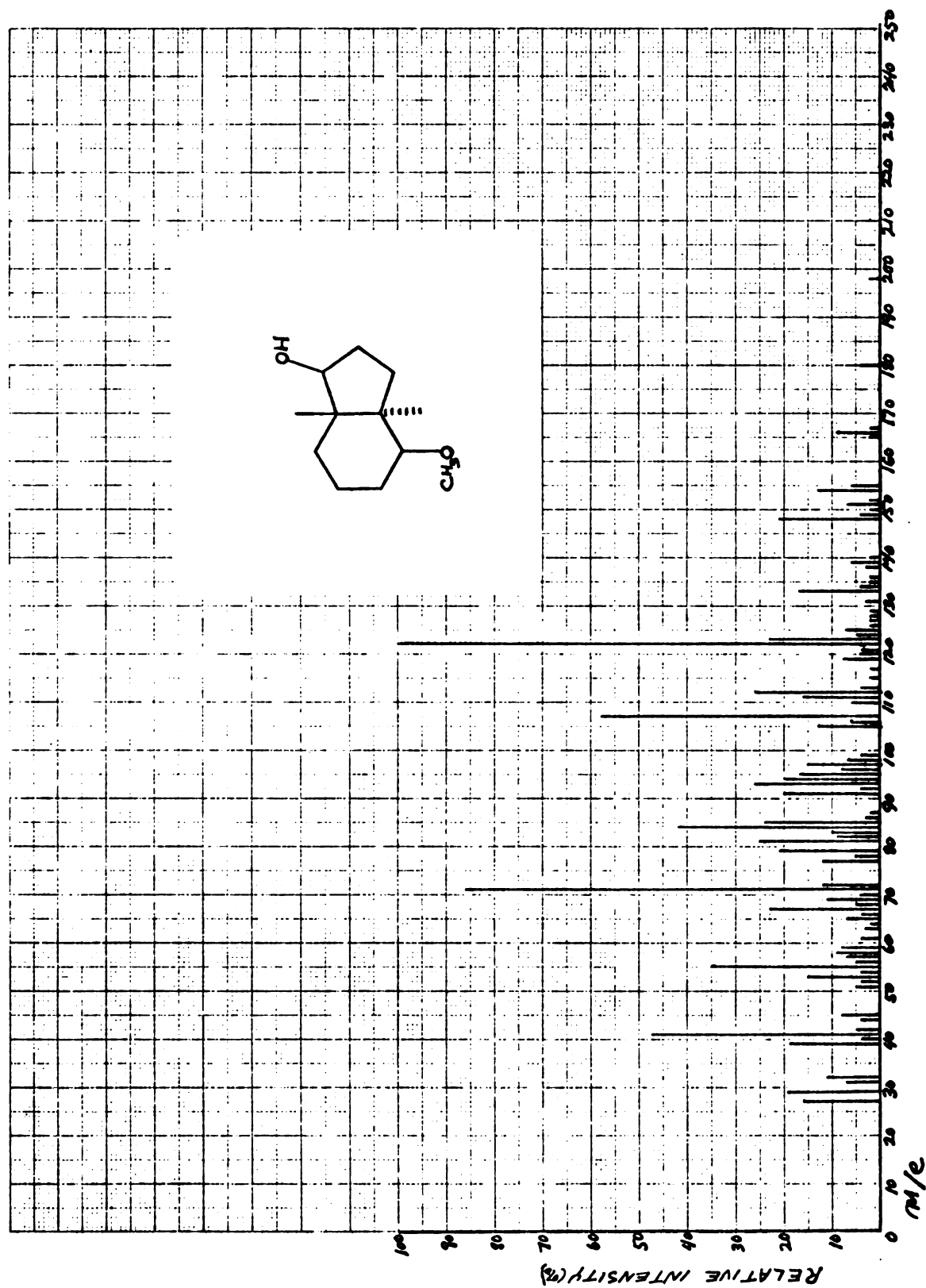


Figure 86. Mass spectrum of 8 (70 eV, ion source 250°).

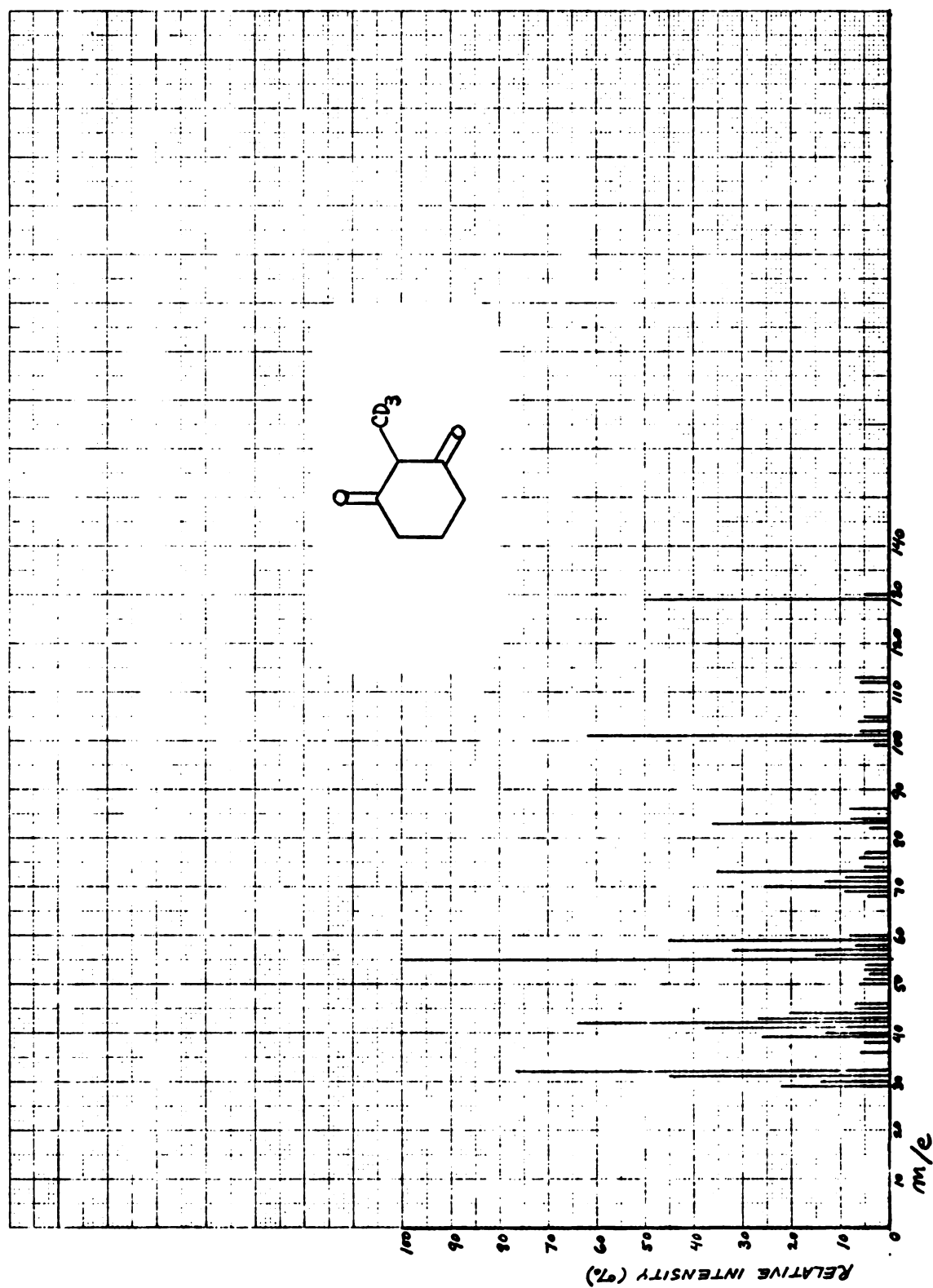


Figure 87. Mass spectrum of 9 (70 eV).

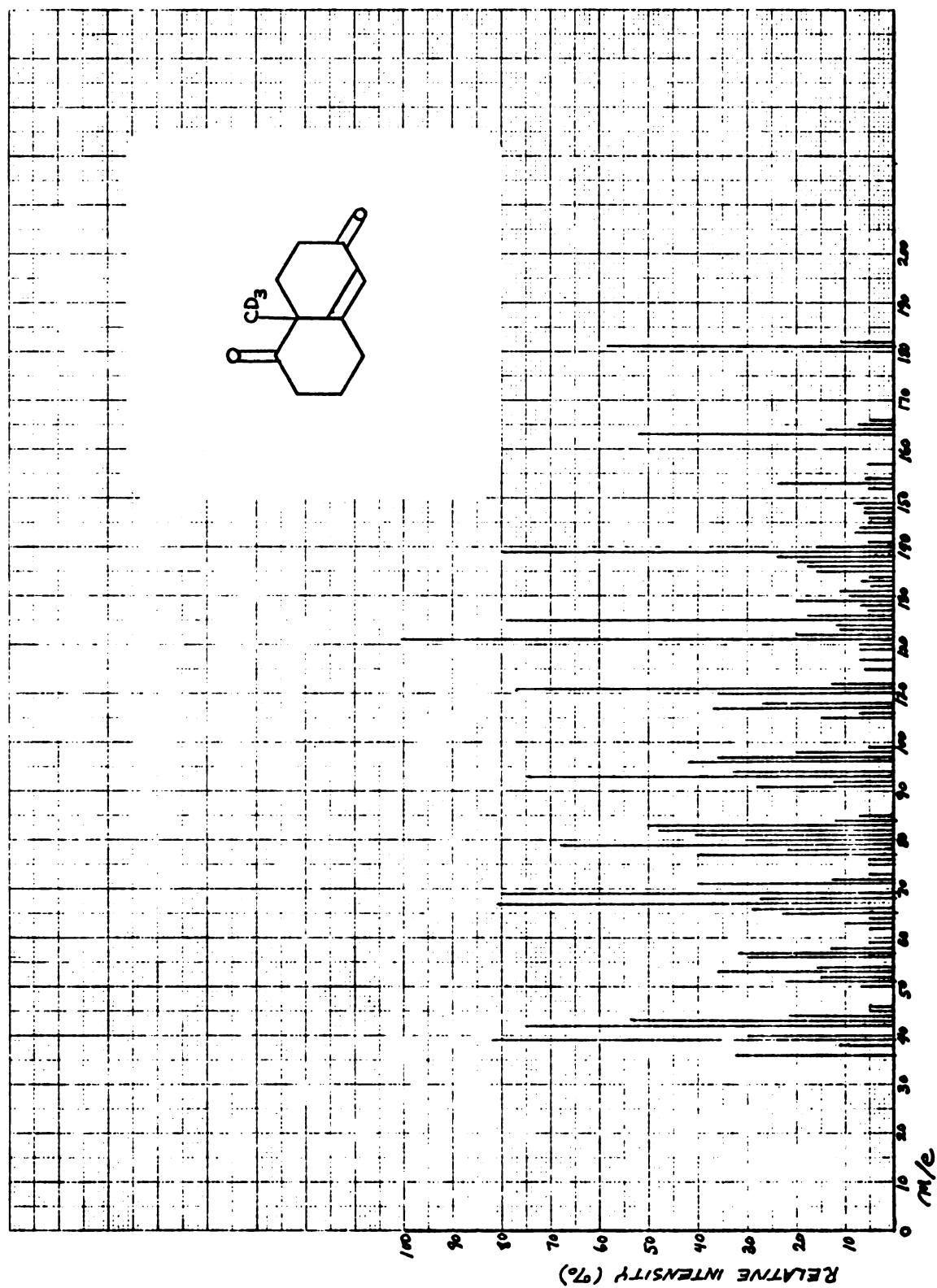


Figure 88. Mass spectrum of 10 (70 eV).

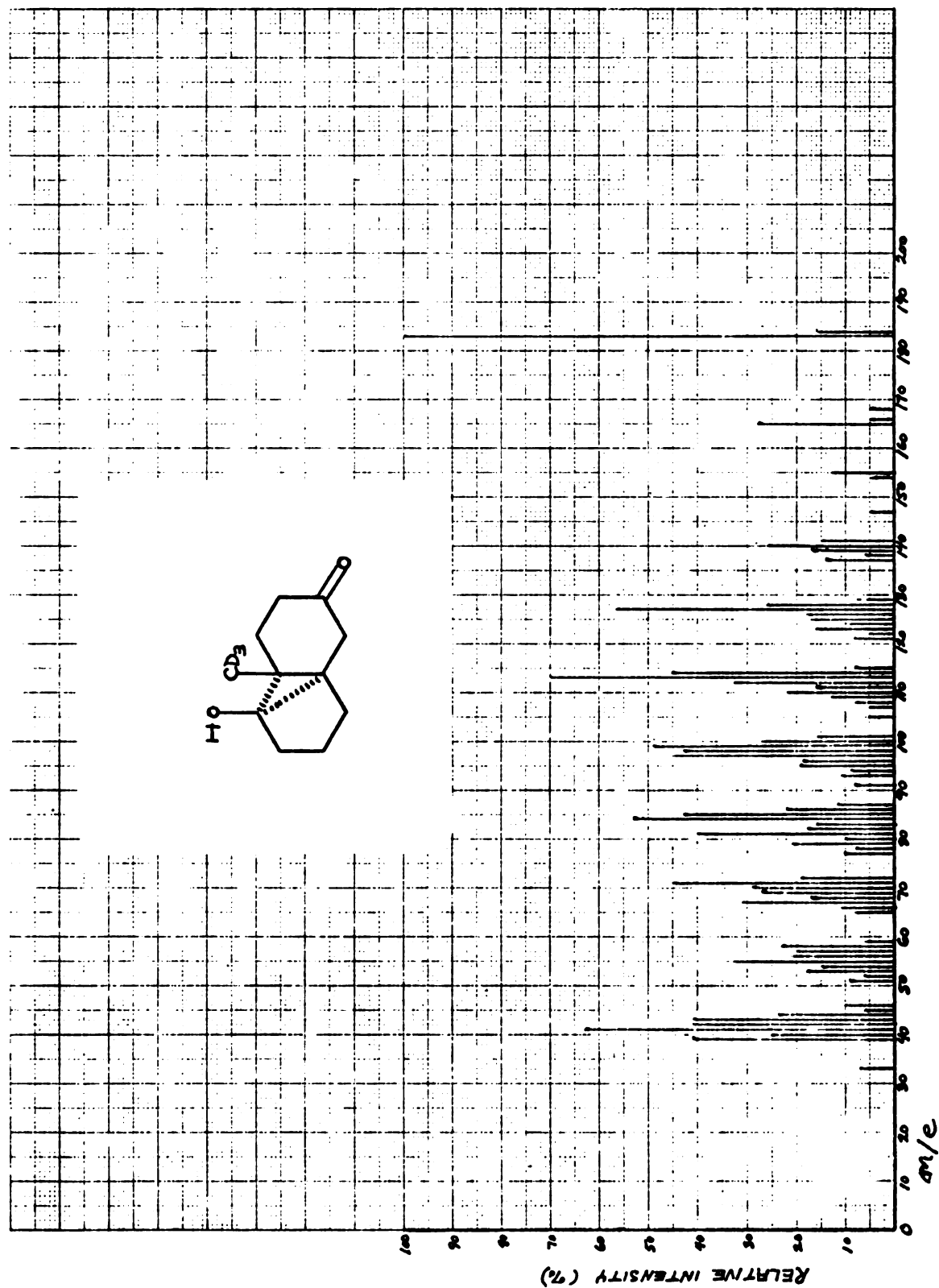


Figure 89. Mass spectrum of 11 (70 eV).

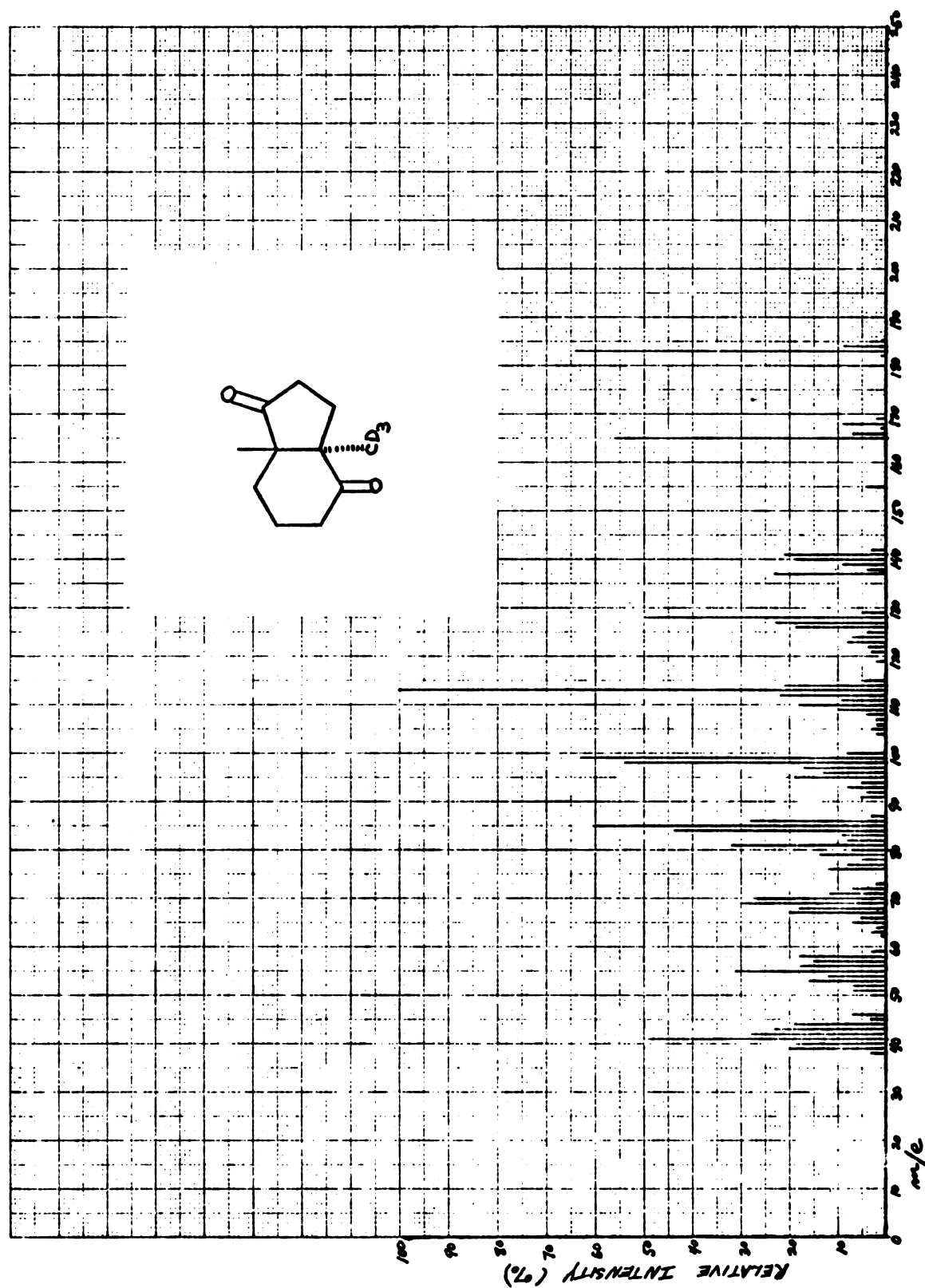


Figure 90. Mass spectrum of 13 (70 eV).

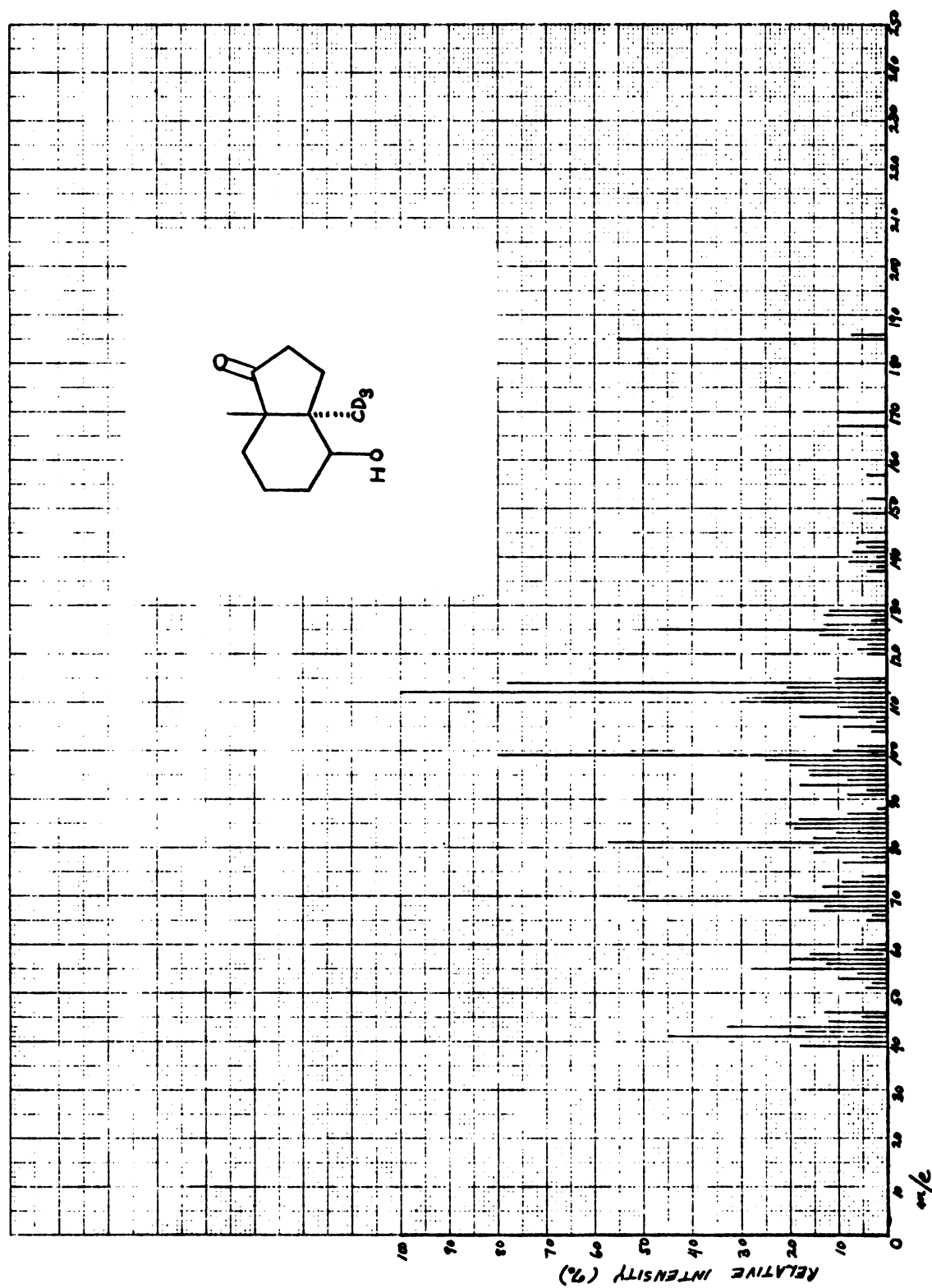


Figure 91. Mass spectrum of 14 (70 eV).

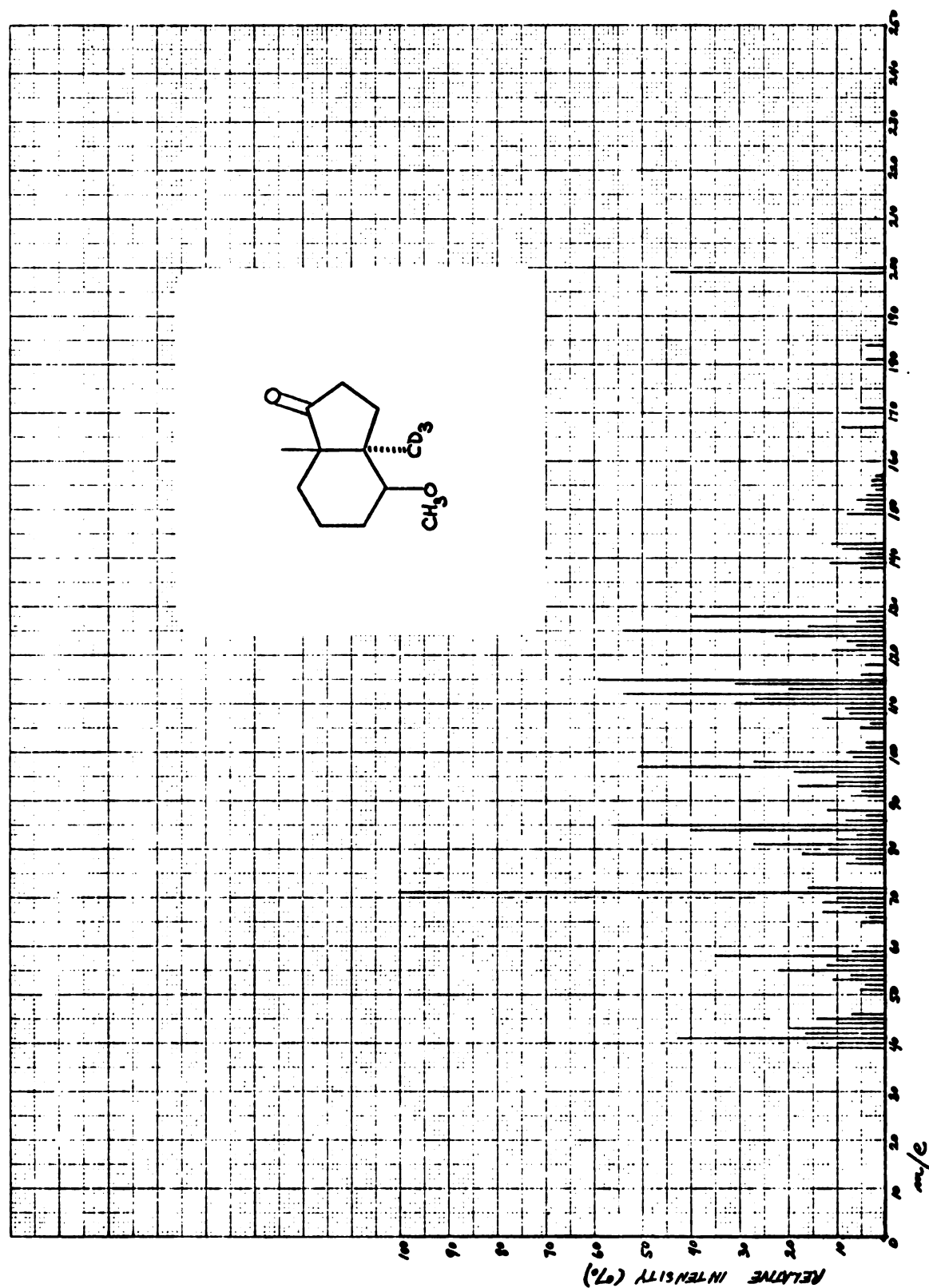


Figure 92. Mass spectrum of 15 (70 eV).

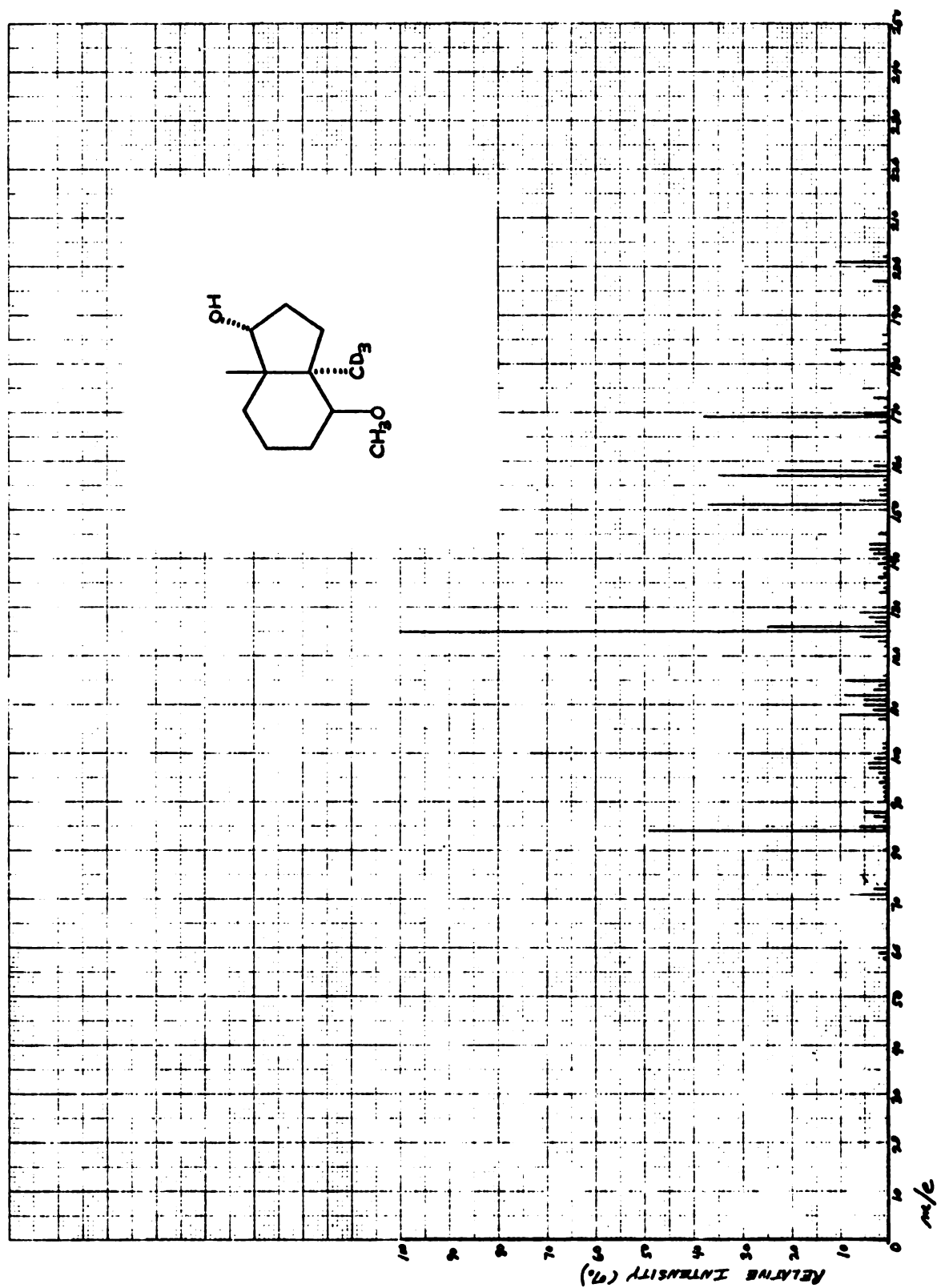


Figure 93. Mass spectrum of 16 (15 eV, ion source 100°).

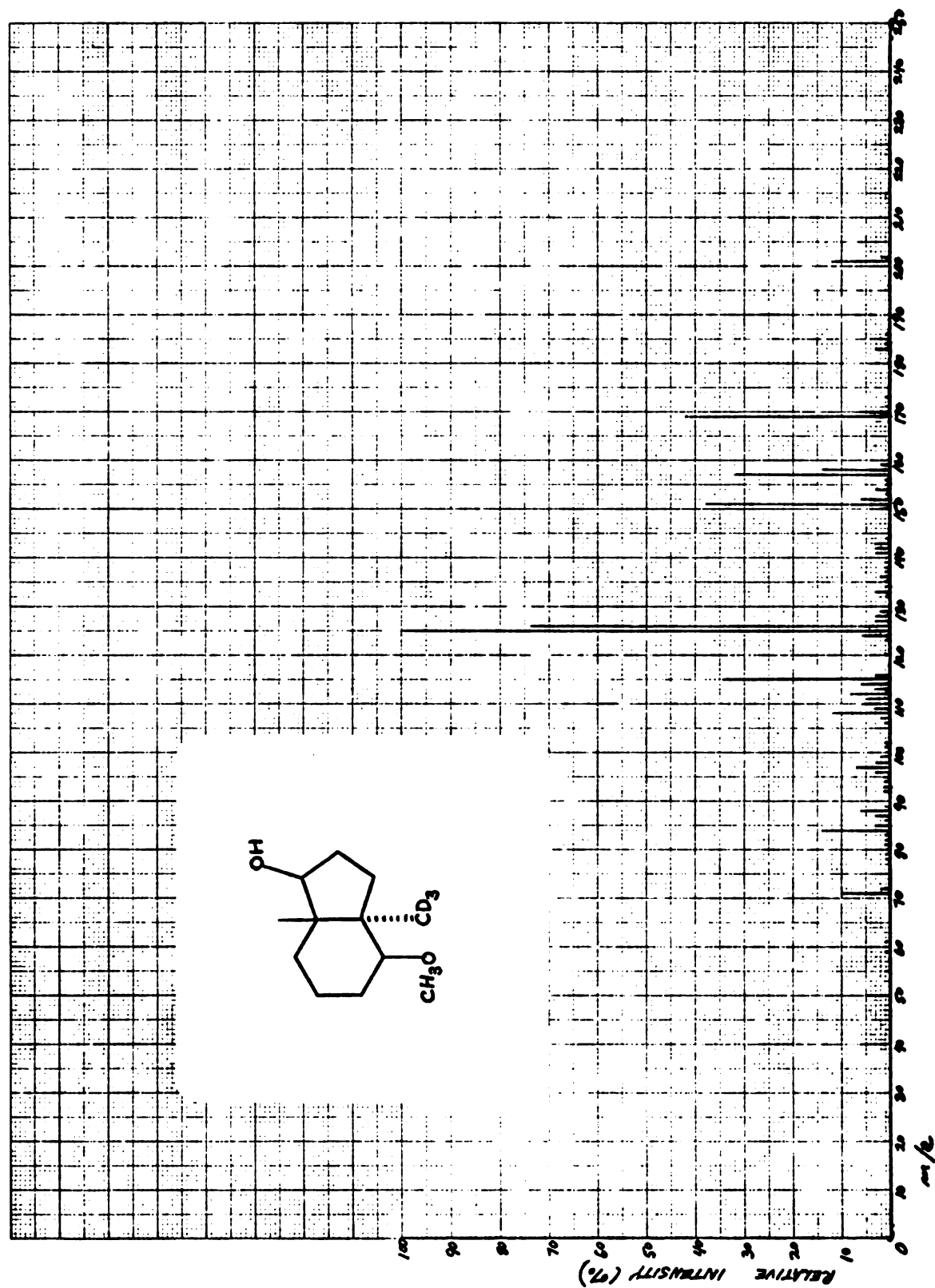


Figure 94. Mass spectrum of 17 (15 eV, ion source 100°).

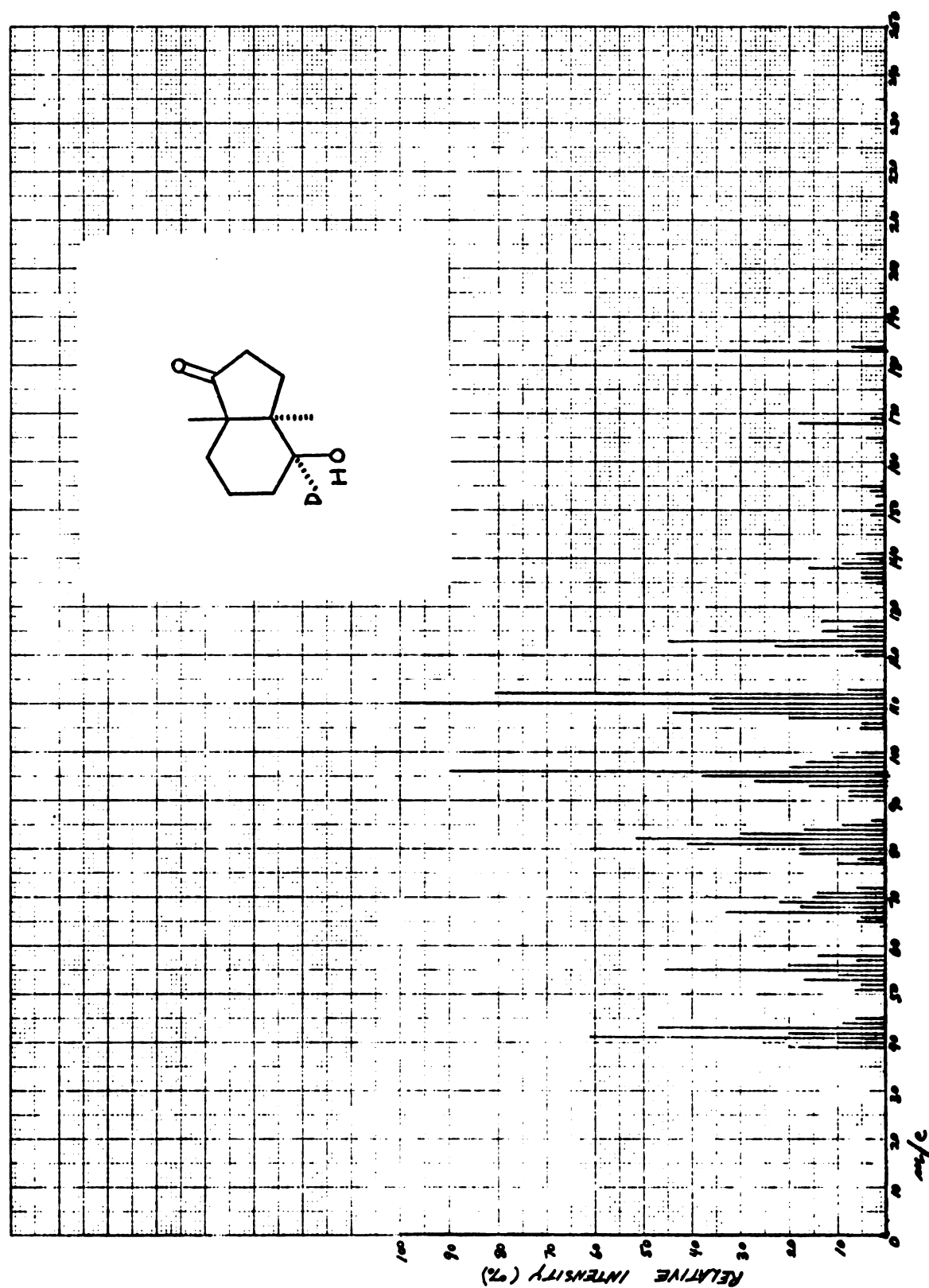


Figure 95. Mass spectrum of 18 (70 eV).

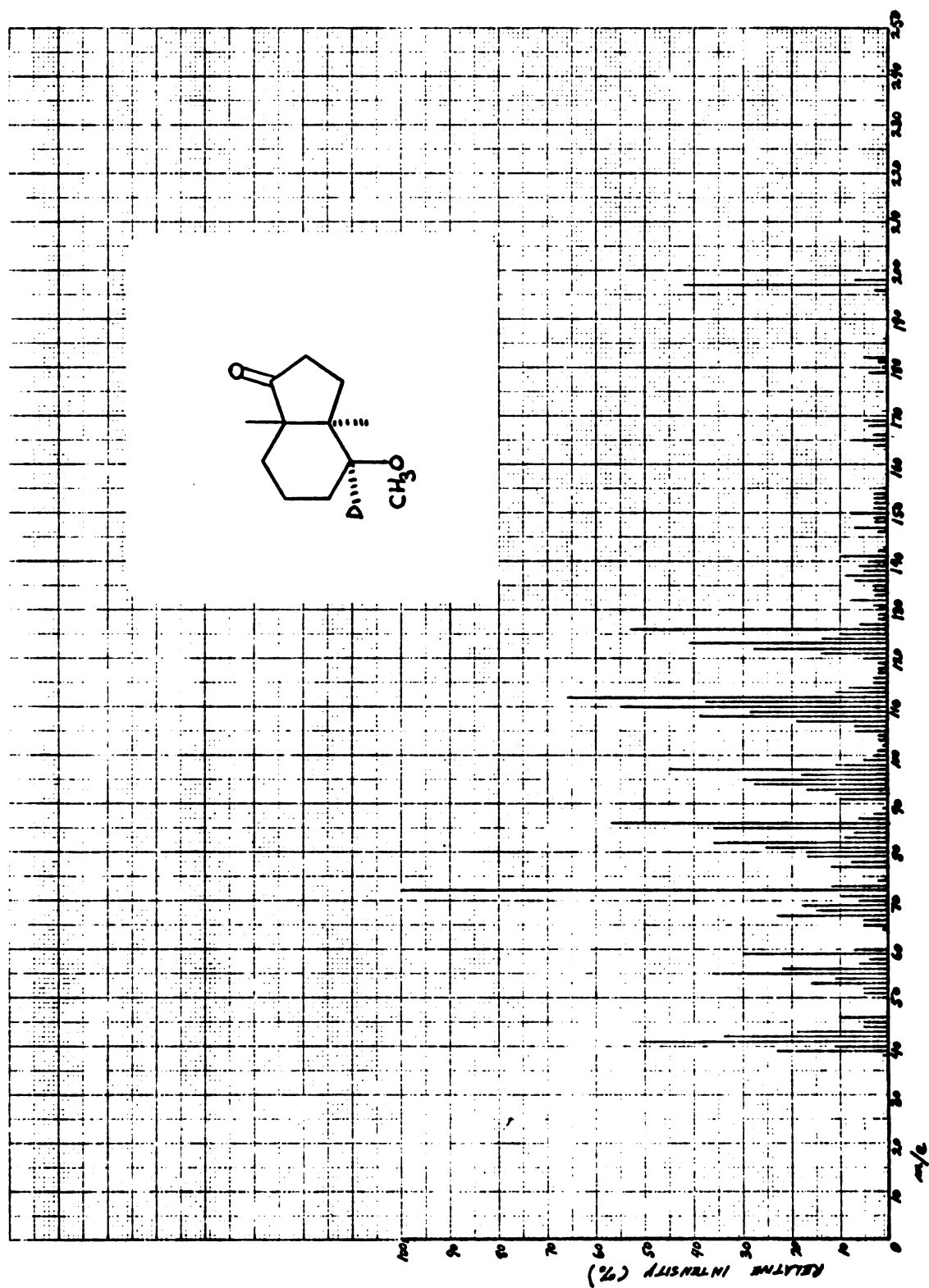


Figure 96. Mass spectrum of 19 (70 eV).

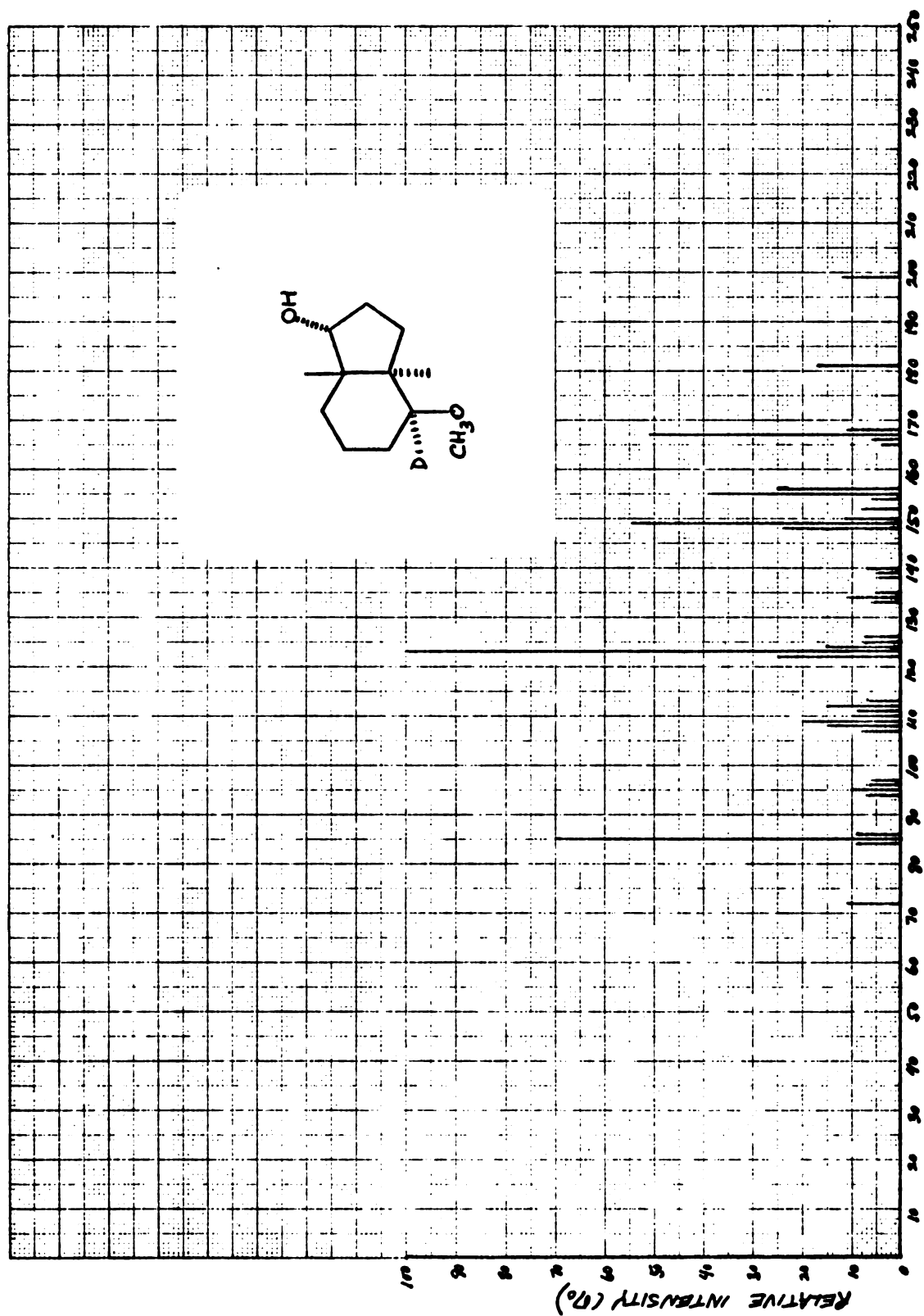


Figure 97. Mass spectrum of 20 (15 eV, ion source 100°).

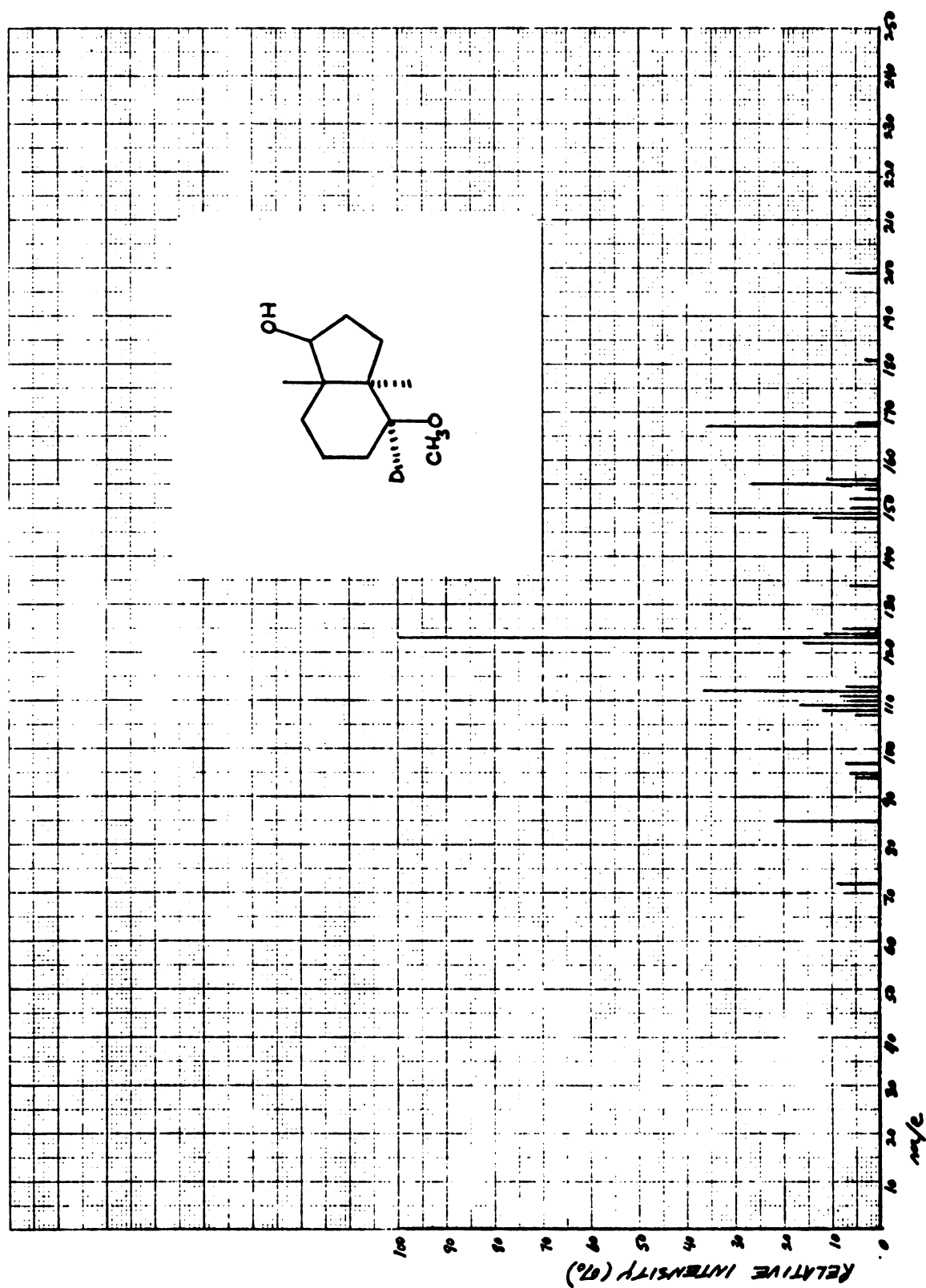


Figure 98. Mass spectrum of 21 (15 eV, ion source 90°).

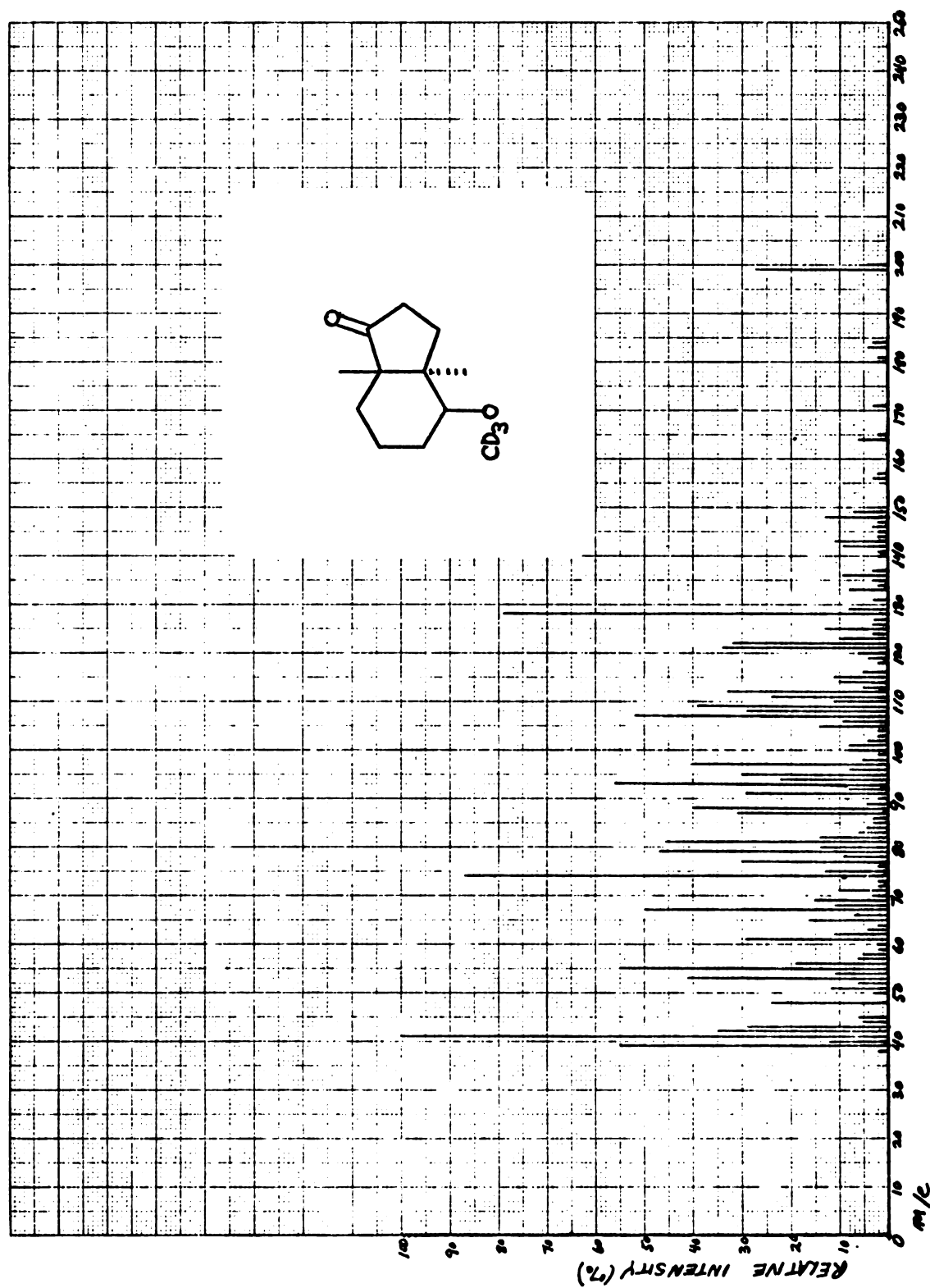


Figure 99. Mass spectrum of 22 (70 eV).

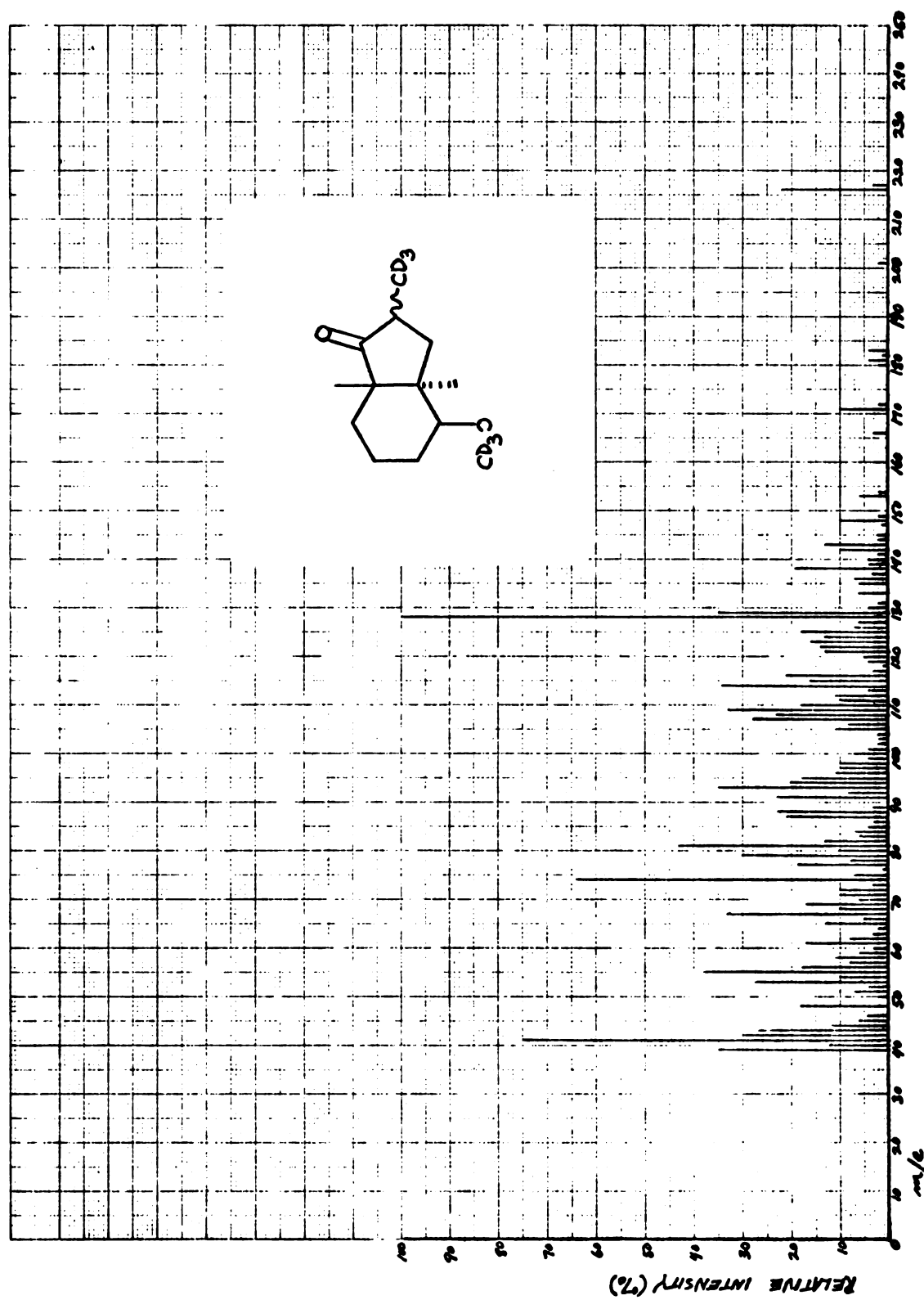


Figure 100. Mass spectrum of 23 (70 eV).

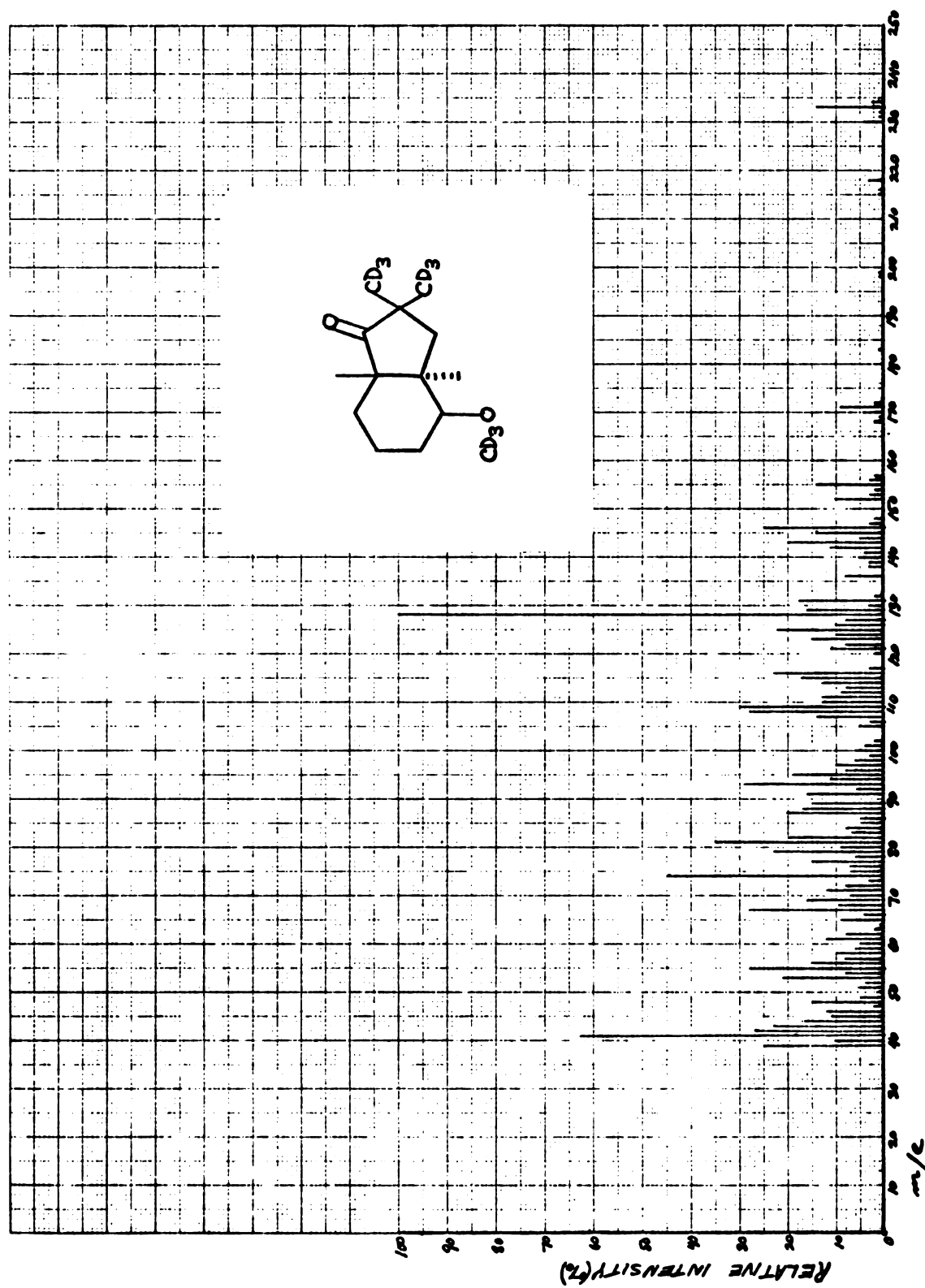


Figure 101. Mass spectrum of 24 (70 eV).

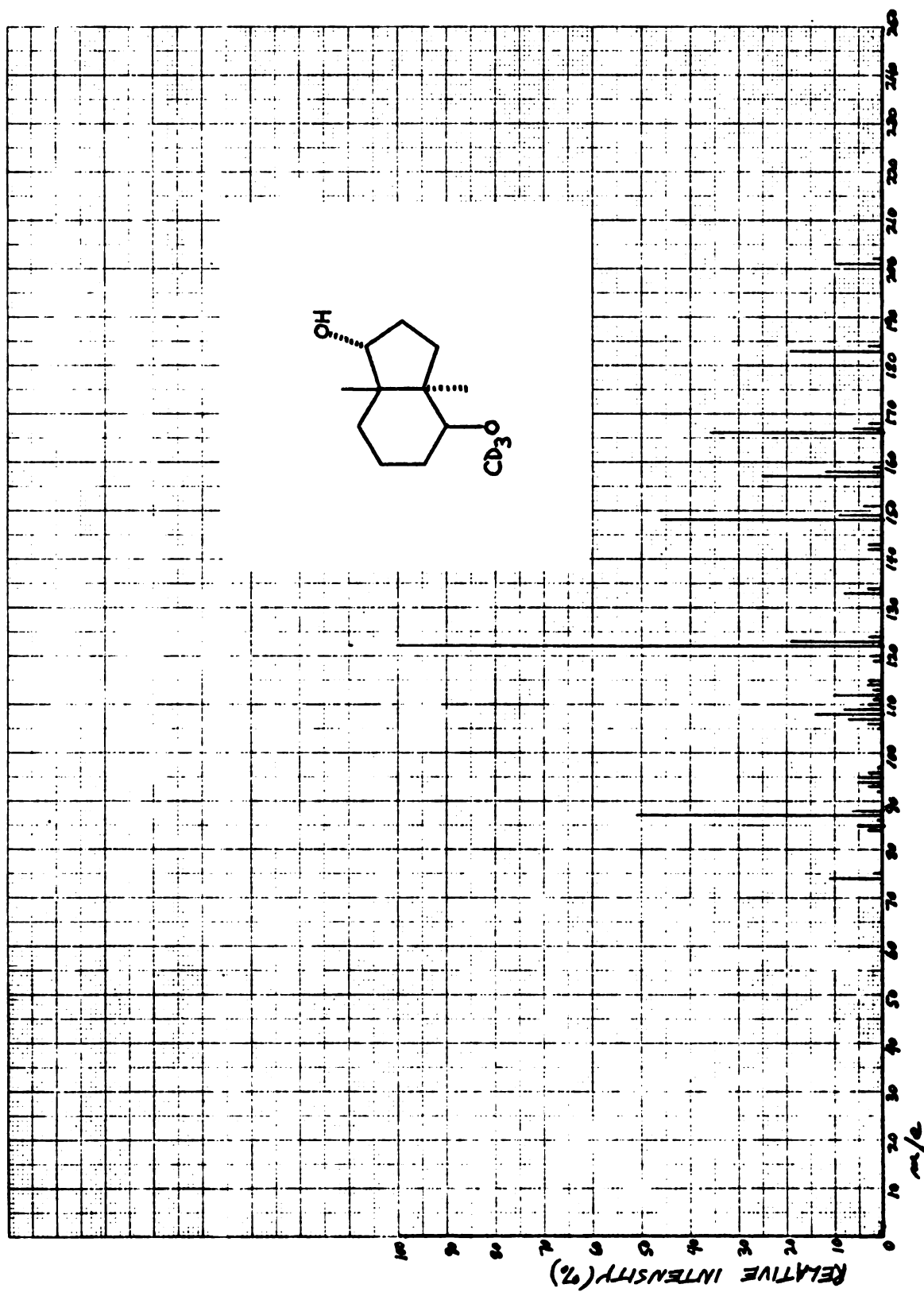


Figure 102. Mass spectrum of 25 (15 eV, ion source 110°).

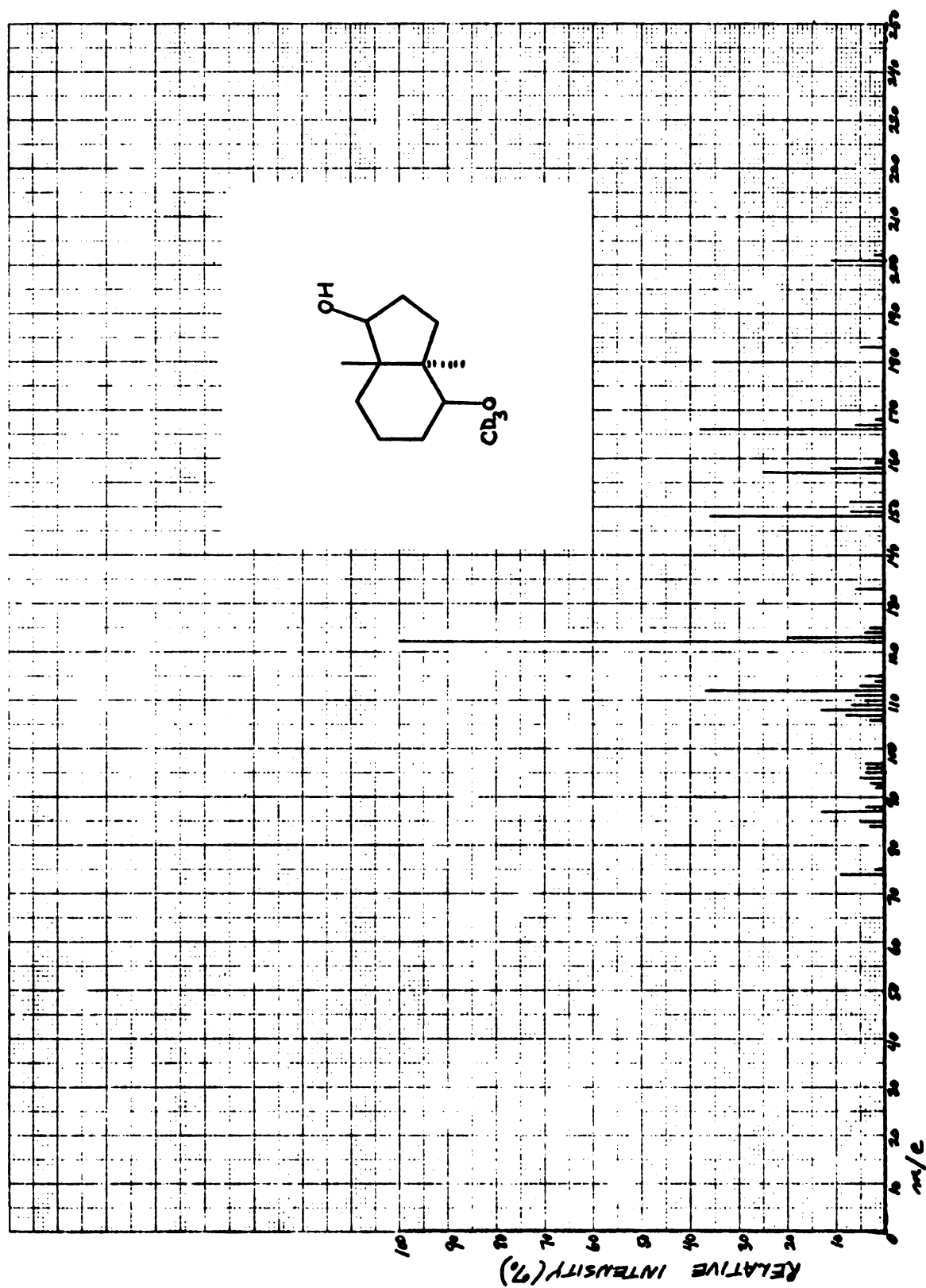


Figure 103. Mass spectrum of 26 (15 eV, ion source 110°).

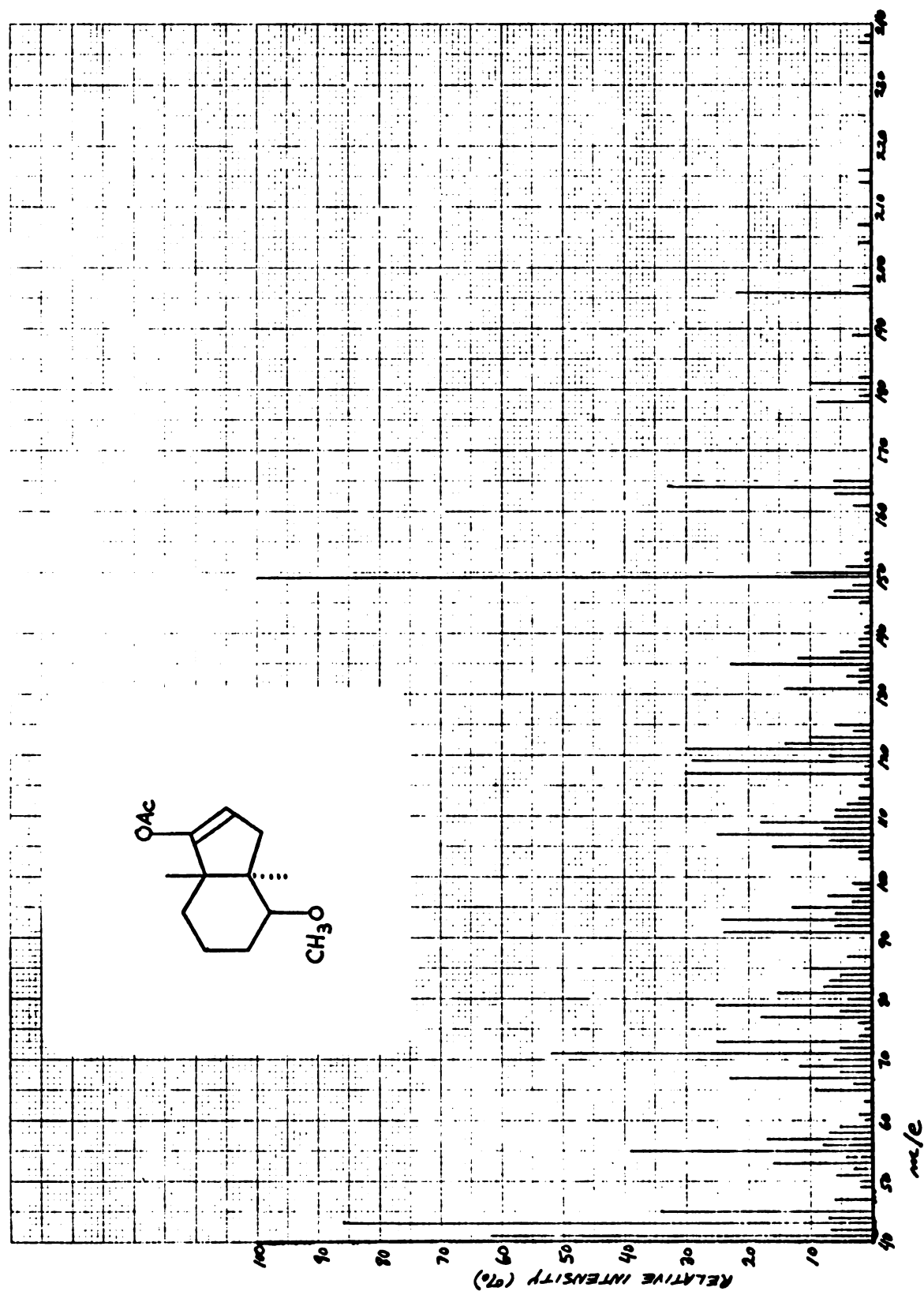
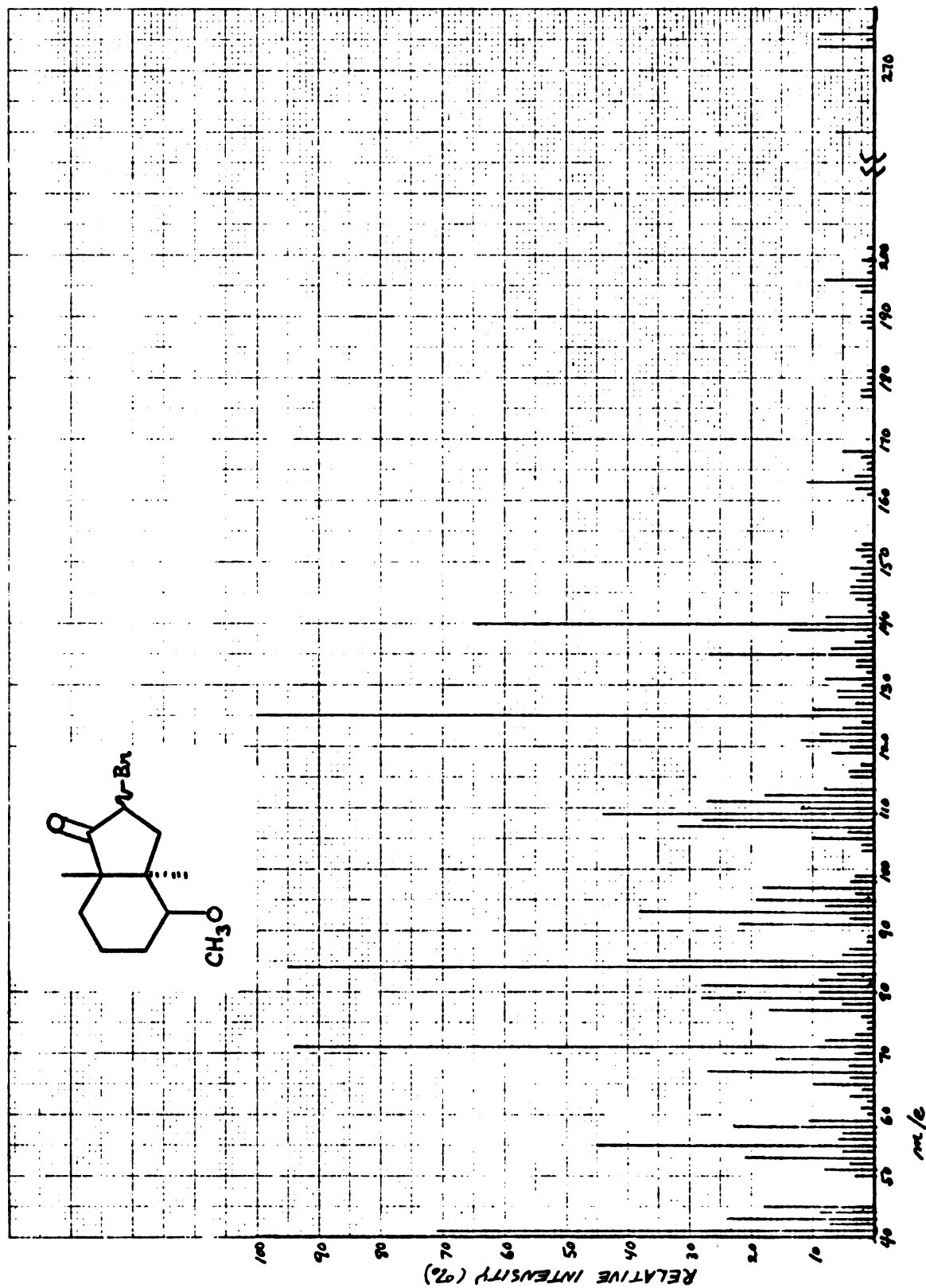


Figure 104. Mass spectrum of 27 (70 eV).



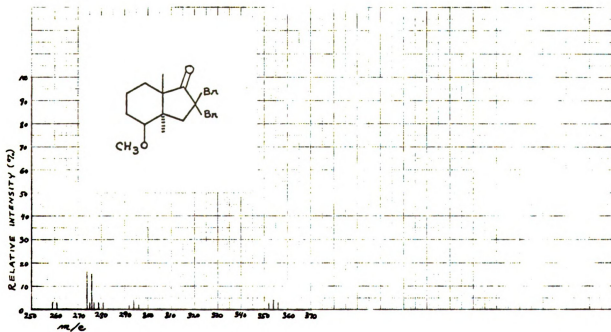
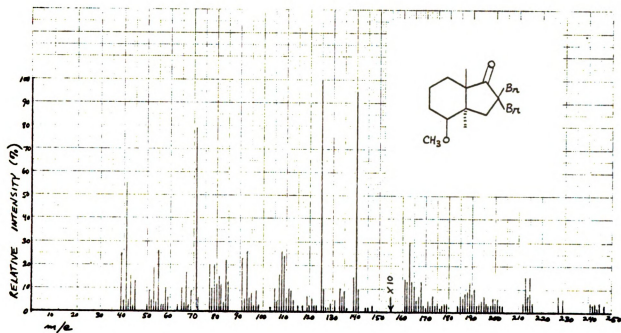


Figure 106. Mass spectrum of 30 (70 eV).

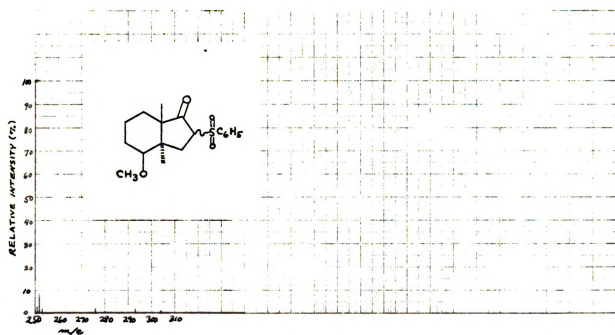
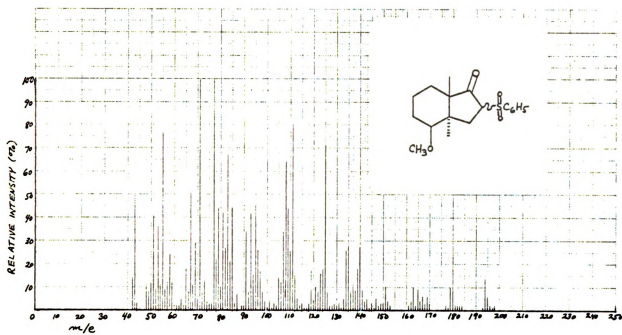


Figure 107. Mass spectrum of 32 (70 eV).

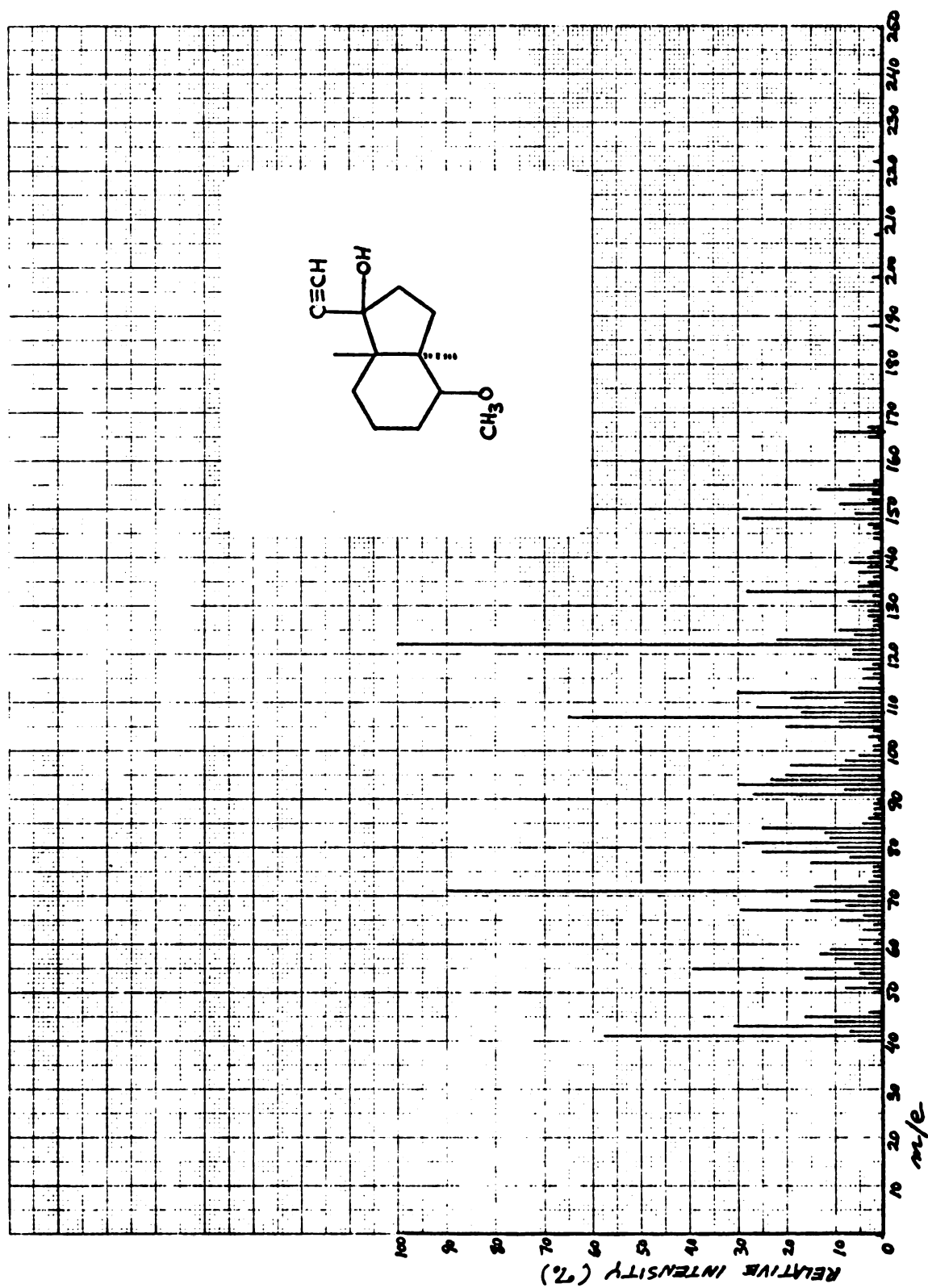


Figure 108. Mass spectrum of 33 (70 eV).

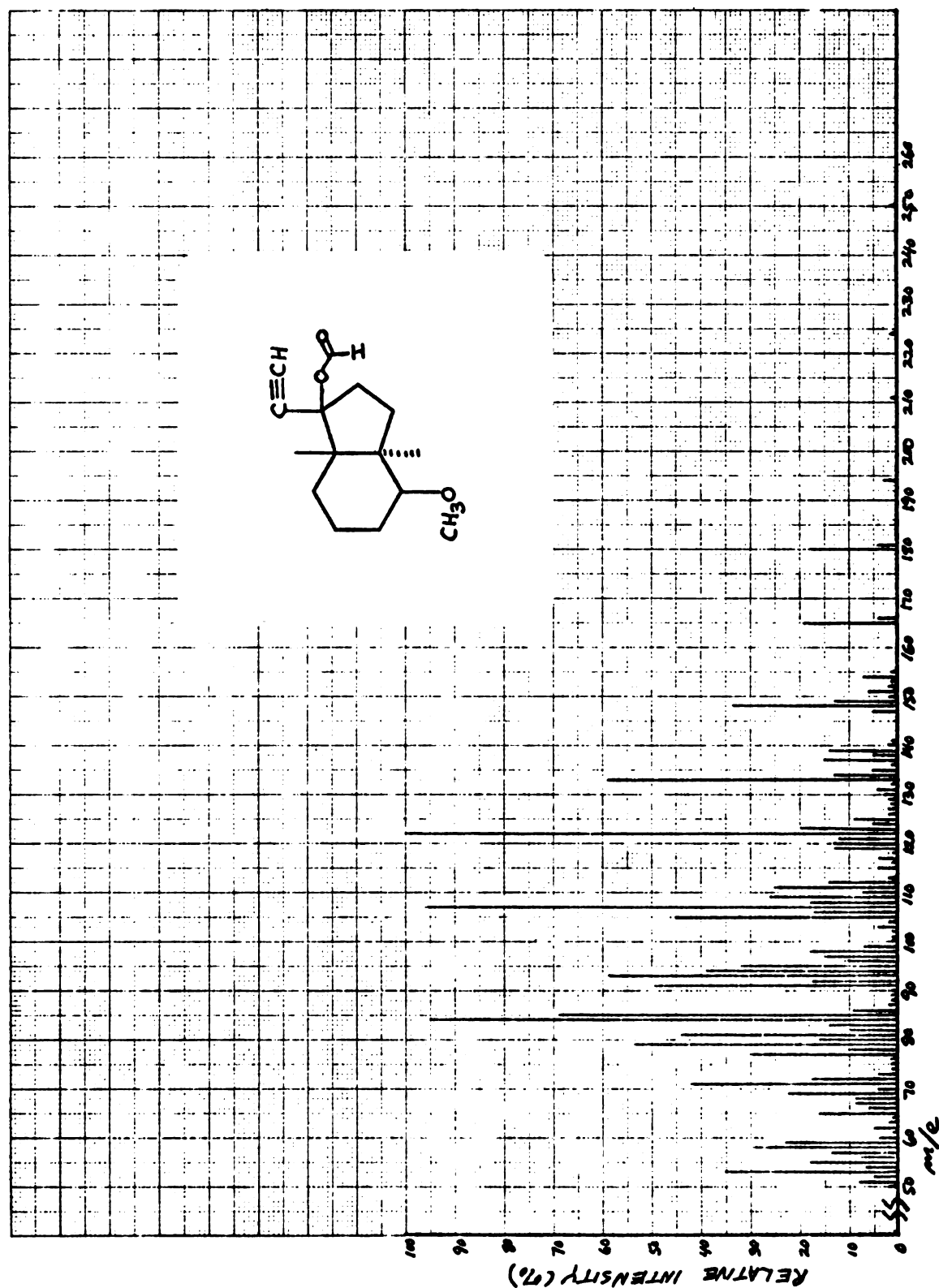


Figure 109. Mass spectrum of 34 (70 eV).

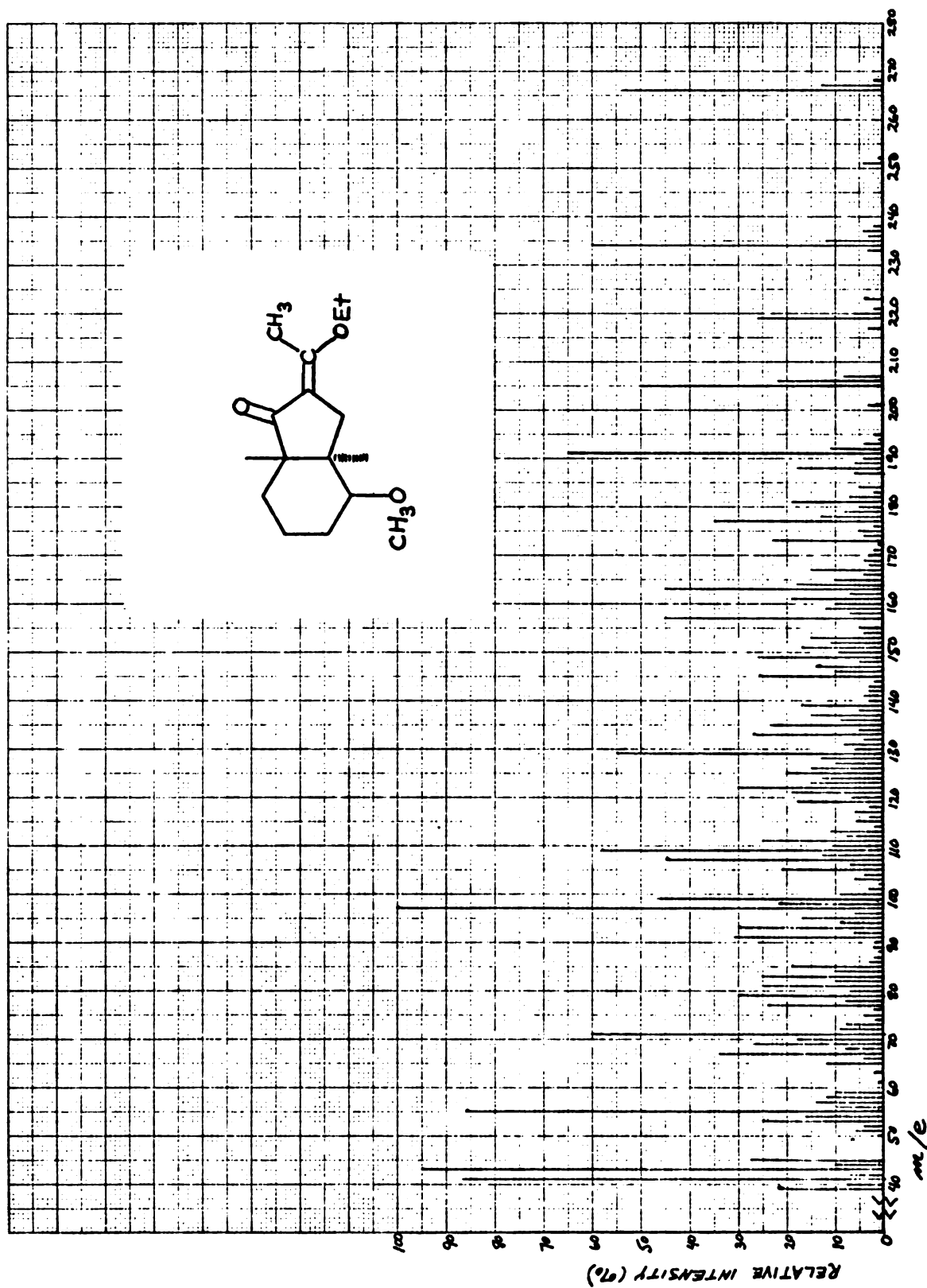


Figure 110. Mass spectrum of 37 (70 eV).

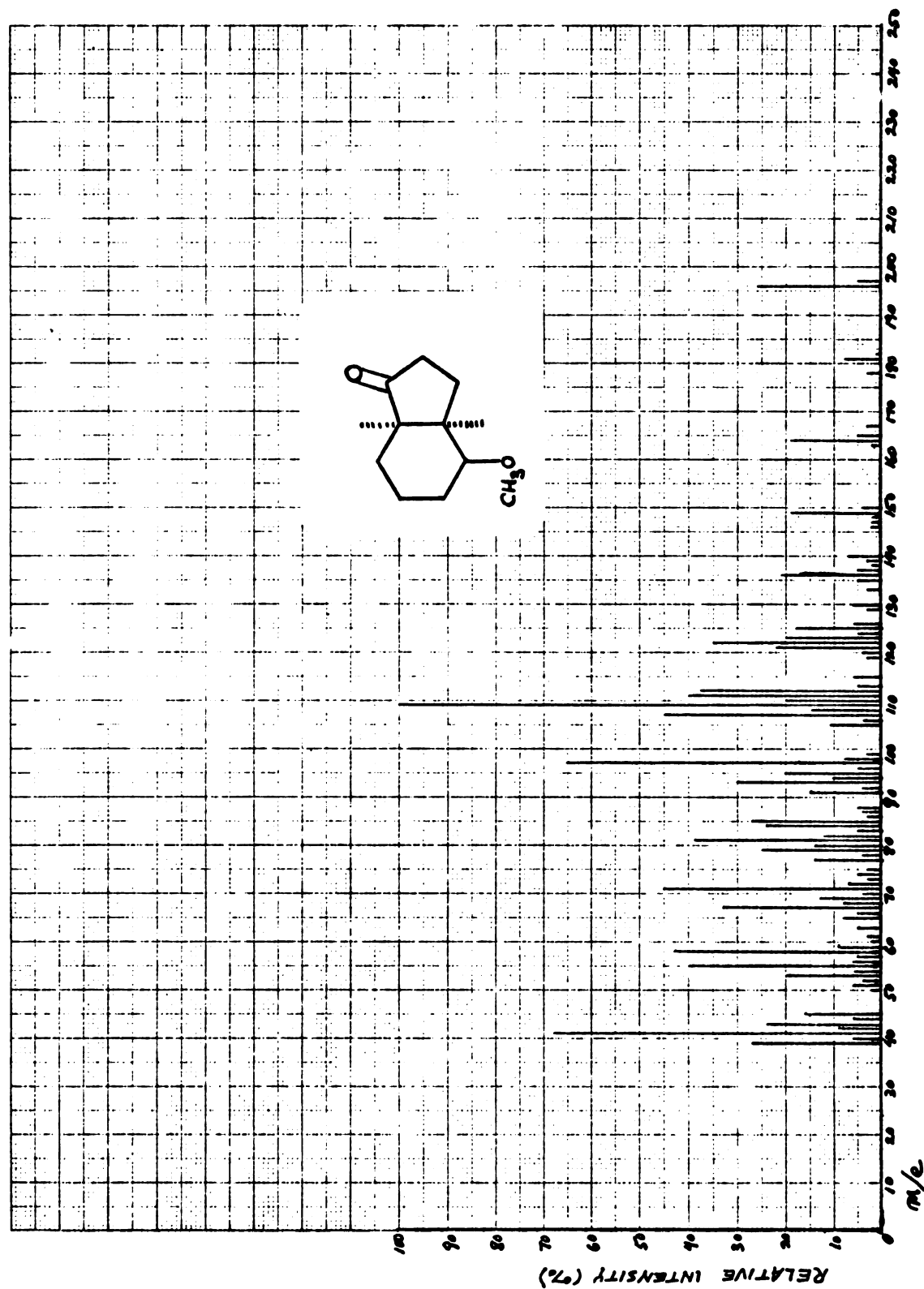


Figure 111. Mass spectrum of 38 (70 eV).

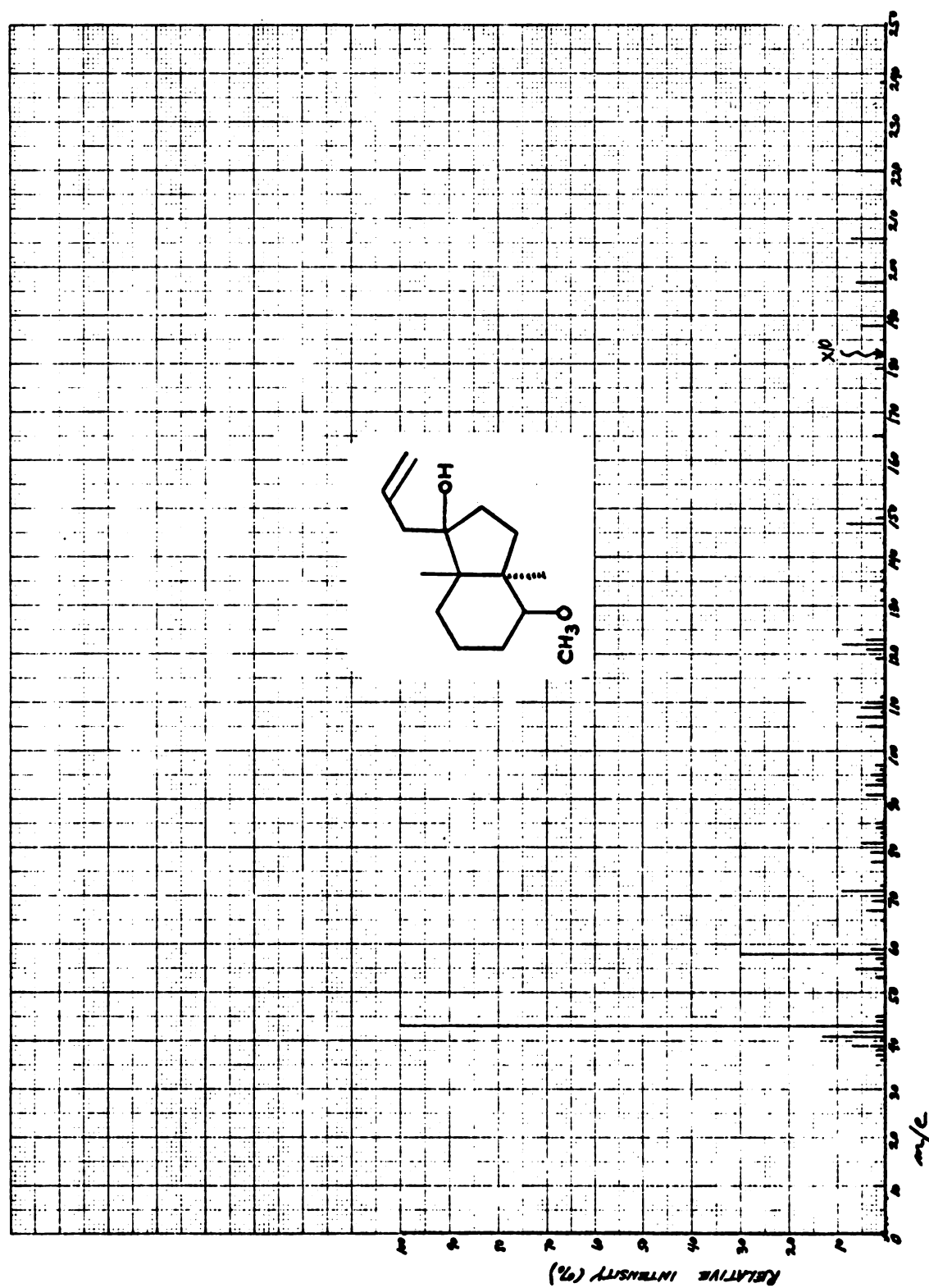


Figure 112. Mass spectrum of 39 (70 eV).

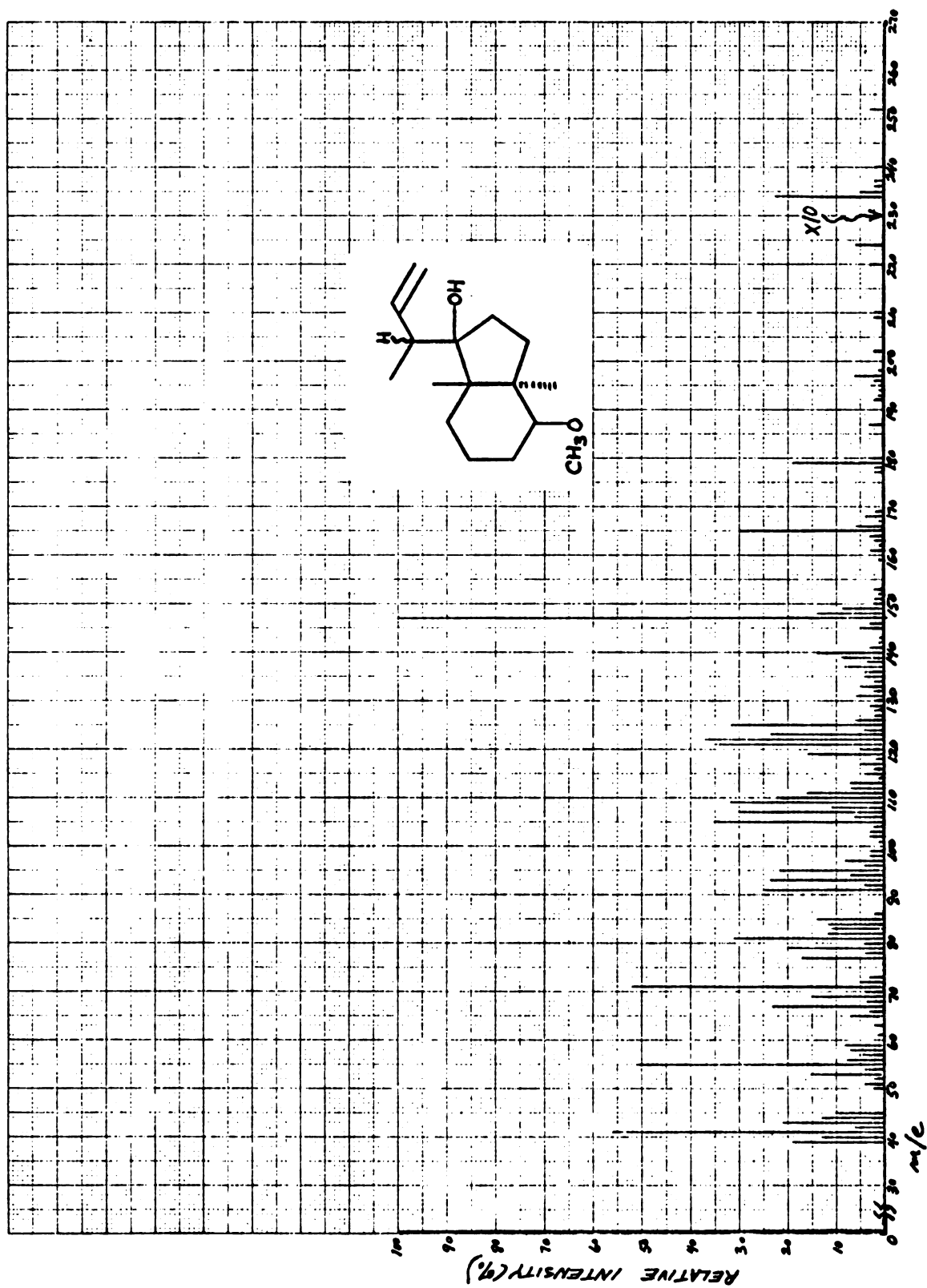


Figure 113. Mass spectrum of 40 (70 eV).

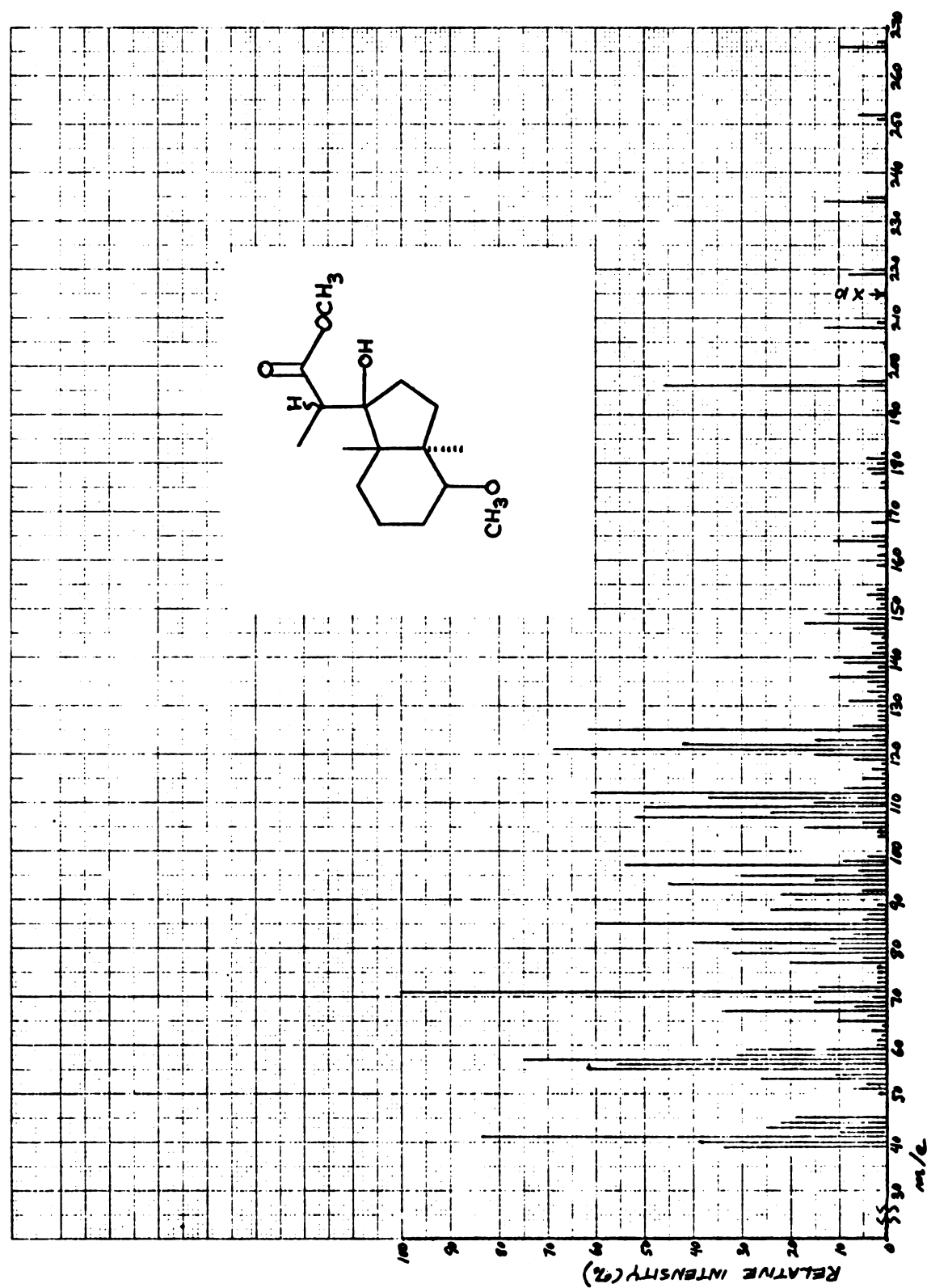


Figure 114. Mass spectrum of 43 (70 eV).

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