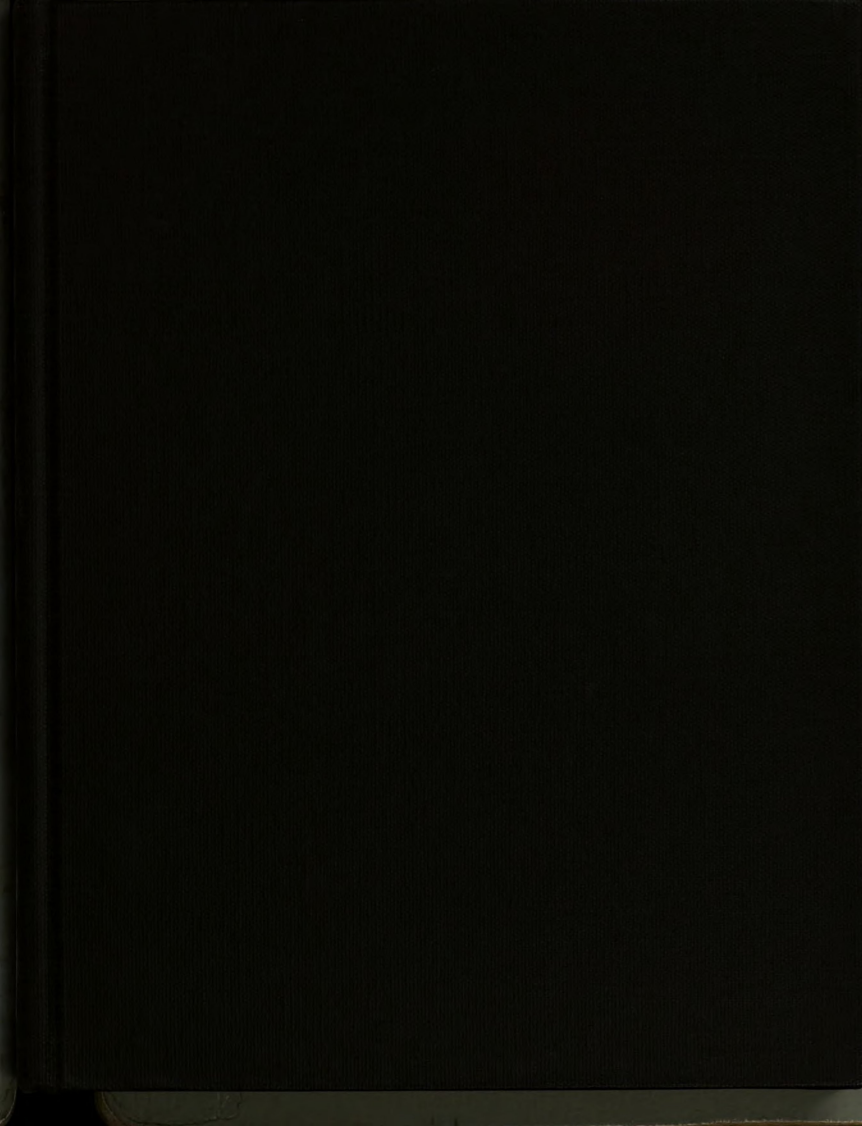






This is to certify that the

thesis entitled

STUDIES TOWARD
THE TOTAL SYNTHESIS
OF SEYSCHELLENE

presented by

KENNETH BRUCE WHITE

has been accepted towards fulfillment
of the requirements for

Ph.D. degree in Organic Chemistry

A handwritten signature in cursive script that reads "William Reusch".

Major professor

Date 10/25/77

STUDIES TOWARD THE TOTAL SYNTHESIS
OF SEYSCHELLENE

By
Kenneth Bruce White

A DISSERTATION

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

DOCTOR OF PHILOSOPHY

Department of Chemistry

1977

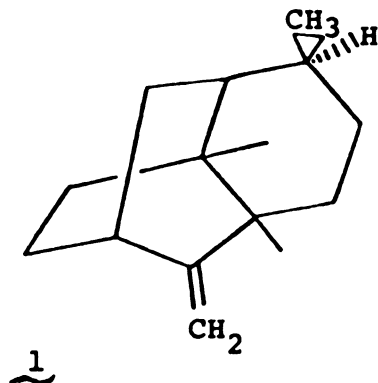
ABSTRACT

STUDIES TOWARD THE TOTAL SYNTHESIS
OF SEYSCHELLENE

By

Kenneth Bruce White

An approach to the synthesis of seyschellene (1) via bicyclo[2.2.2]octanone intermediates has been investigated.



The reactions of cross-conjugated dienolate anions derived from substituted cyclohexenones with methyl acrylate and vinyl ketones form bicyclo[2.2.2]octan-2-ones by a sequential Michael mechanism; however, the reaction of vinyl ketones must be conducted under amine-free conditions. Unexpectedly, the conjugate base from 2,3-dimethylcyclohex-2-enone gives only a single Michael adduct (2) with methyl vinyl ketone and if forced to react further undergoes an

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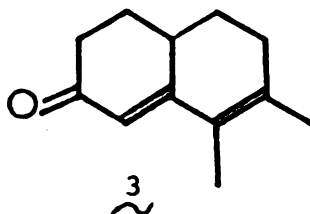
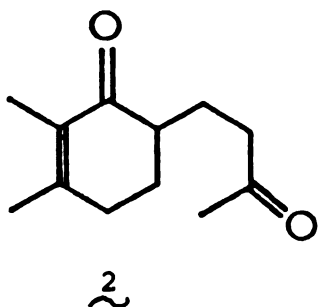
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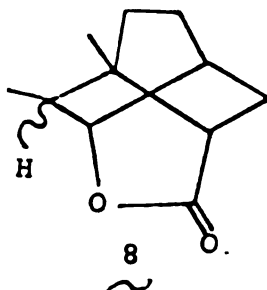
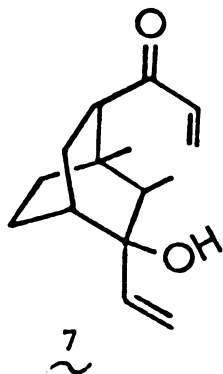
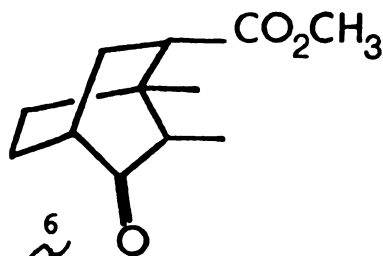
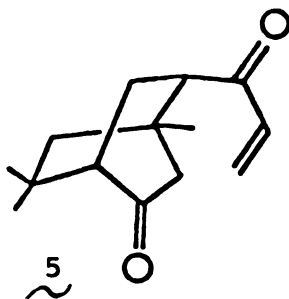
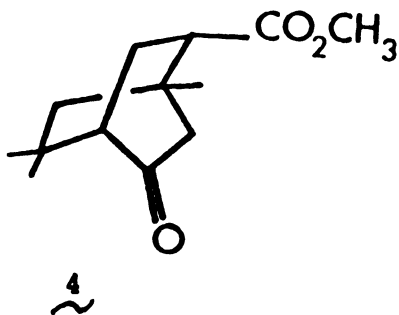
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intramolecular aldol condensation to give dienone 3.

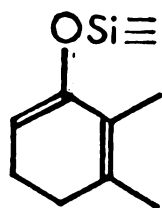


Keto-ester 4 was transformed into vinyl ketone 5 in four steps. The same route was applied to keto-ester 6 to give hydroxy-ketone 7. The corresponding hydroxy acid of 6 formed lactone 8, thus demonstrating that the C-5 carbo-methoxy group is syn to the carbonyl at C-2 in 6.

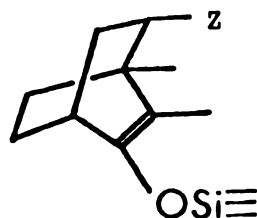


Kenneth Bruce White

Reaction of dienol silyl ether 9 with various dienophiles afforded Diels-Alder adducts 10.

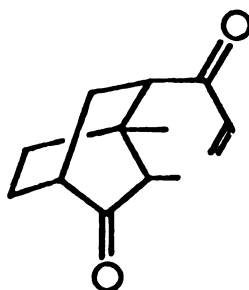


9



Z = CHO 10a
= COCH₃ 10b
= CN 10c

Aldehyde 10a was converted in two steps to vinyl ketone 11. Vinyl ketone 11 could be a possible precursor of seyschellene.



11

DEDICATION

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

To my sisters, who have been a source of joy and love.

ACKNOWLEDGMENTS

The author is deeply grateful to Professor William H. Reusch for his guidance, enthusiasm and encouragement during the course of this work.

Appreciation is also extended to my colleagues for stimulating and informative discussions and to my friends for their friendship, humor, and unending concern for my wellbeing.

Special thanks are extended to Beth Decker for her friendship and moral support.

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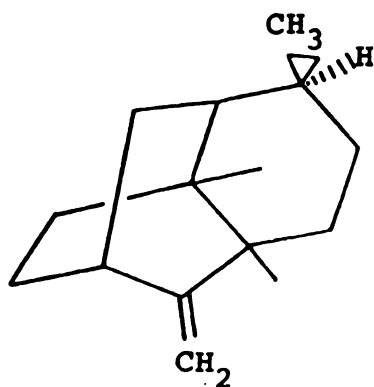
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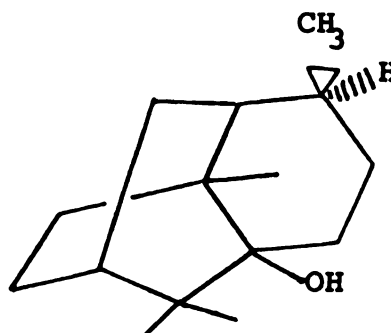
INTRODUCTION

Since the dawn of man, fragrant substances extracted from plants have played an important role in everyday life. One of the better known Eastern perfumes is Patchouli. According to Genders,¹ "Its odour is the most powerful of all scents derived from the botanical kingdom, and in its unadulterated form smells extremely unpleasantly of goats." The oil of Patchouli has an odor that is "sweet, powerful and persistent of old wood."² One sesquiterpene isolated from Patchouli oil obtained from the Seyschelles Islands is Seyschellene (1).³ Another sesquiterpene isolated from Patchouli oil is Patchouli alcohol (2).⁴



1

Seyschellene



2

Patchouli Alcohol

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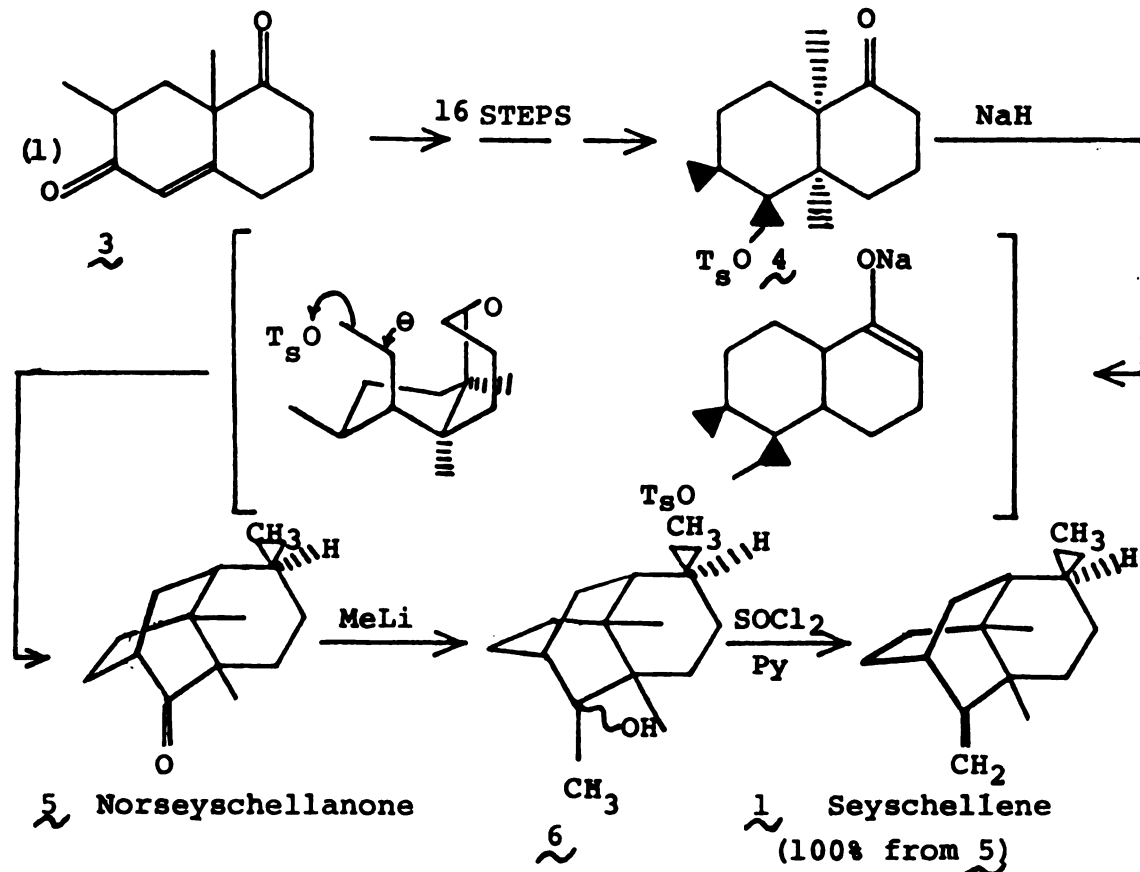
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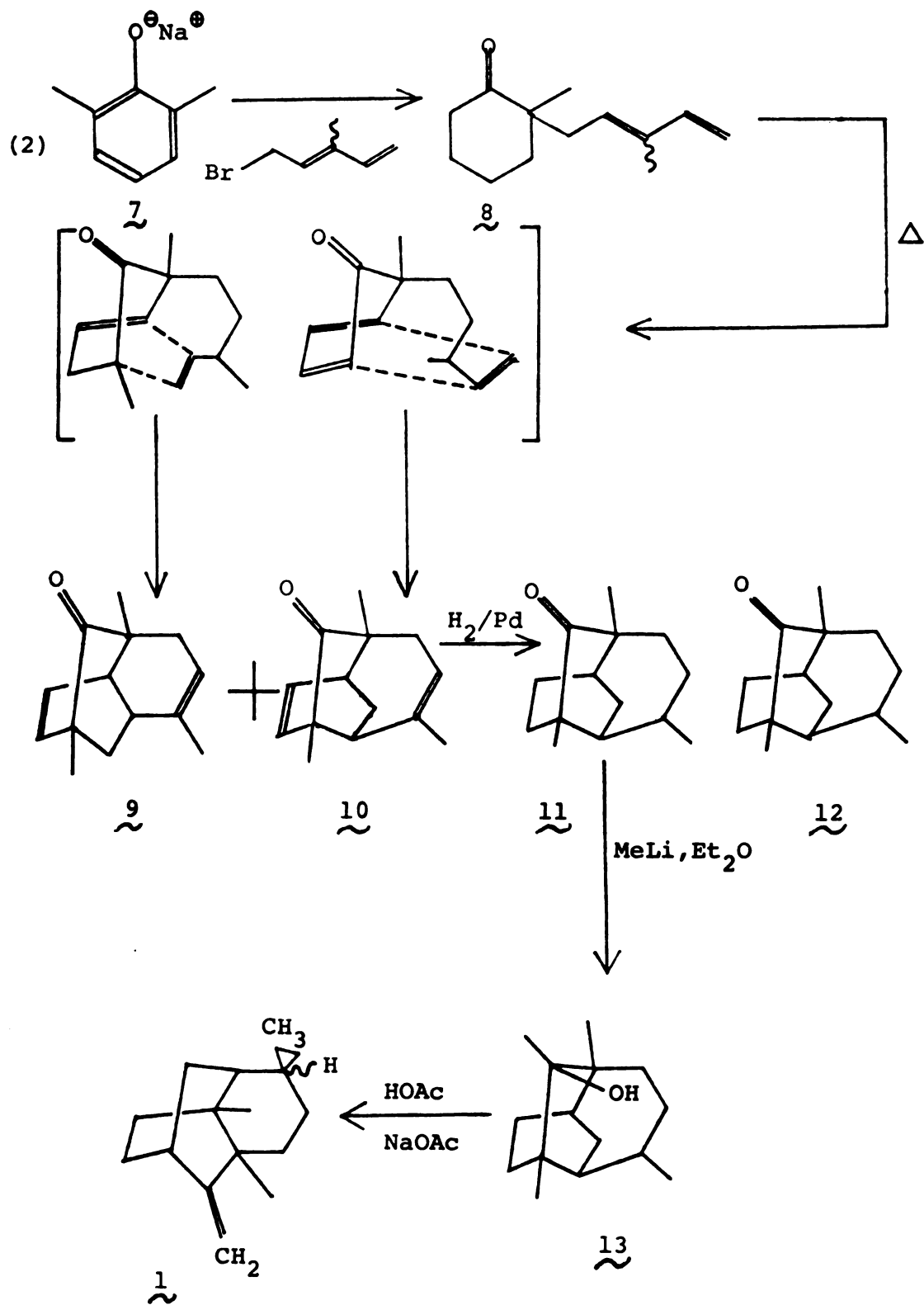
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Three different pathways have been employed in the construction of the tricyclic carbon skeleton of seyschellene (1). In the approach devised by Piers,⁵ Wieland-Miescher ketone (3) was transformed into the tosylate 4 in sixteen steps (eq. 1). Treatment of the tosylate 4 with sodium hydride afforded norseyschellanone 5, this being the key step in the formation of the tricyclic skeleton of seyschellene. Norseyschellanone (5) was treated first with methyl-lithium and next with a solution of pyridine and thionyl chloride to yield seyschellene 1. It is important to note that as a result of Pier's synthesis, a synthesis of norseyschellanone constitutes a synthesis of seyschellene.

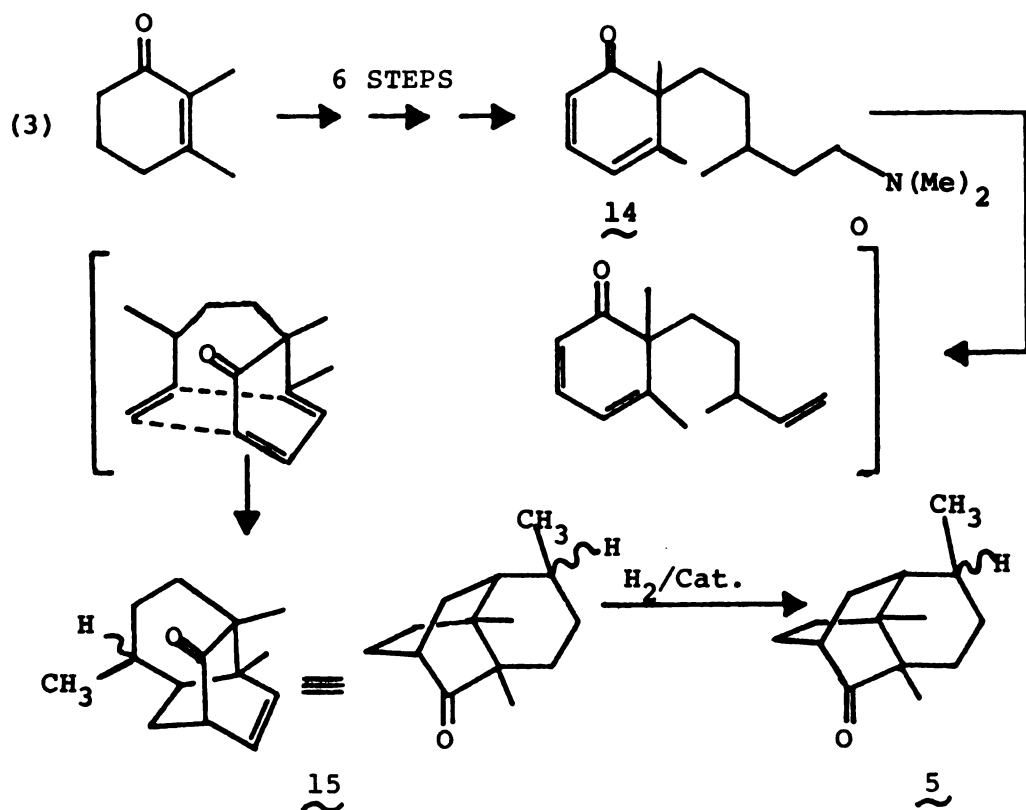


Another synthesis of seyschellene, devised by Frater,⁶ employs the Diels-Alder reaction (eq. 2). Alkylation of the phenolate 7 with cis and trans-5-bromo-3-methyl-1,3-pentadiene yielded ketone 8. This mixture of ketones was heated in benzene to form the tricyclic ketones 9 and 10. Hydrogenation of 9 and 10 afforded ketones 11 and 12. Ketone 11 was then treated with methyllithium to afford the alcohol 13. It should be noted that the tricyclic compounds 10, 11 and 13 do not have the carbon skeleton of seyschellene. In a very interesting rearrangement reaction, the alcohol 13 was heated with sodium acetate in acetic acid to yield seyschellene (1).

Frater suggests that this reaction proceeds via a Wagner Meerwein rearrangement.



A second total synthesis of seyschellene, using the Diels-Alder reaction to generate the tricyclic skeleton was reported by Yoskikose⁷ (eq. 3). In six steps, 2,3-dimethyl-2-cyclohexenone was converted into the N-oxide 14. Pyrolysis of the N-oxide 14 afforded a number (unreported) of products, one of which was the ketone 15. The yield of 15 was not reported; thus, it is unknown whether or not this was the major product. Hydrogenation of the ketone 15 gave norsey-schellanone (5).



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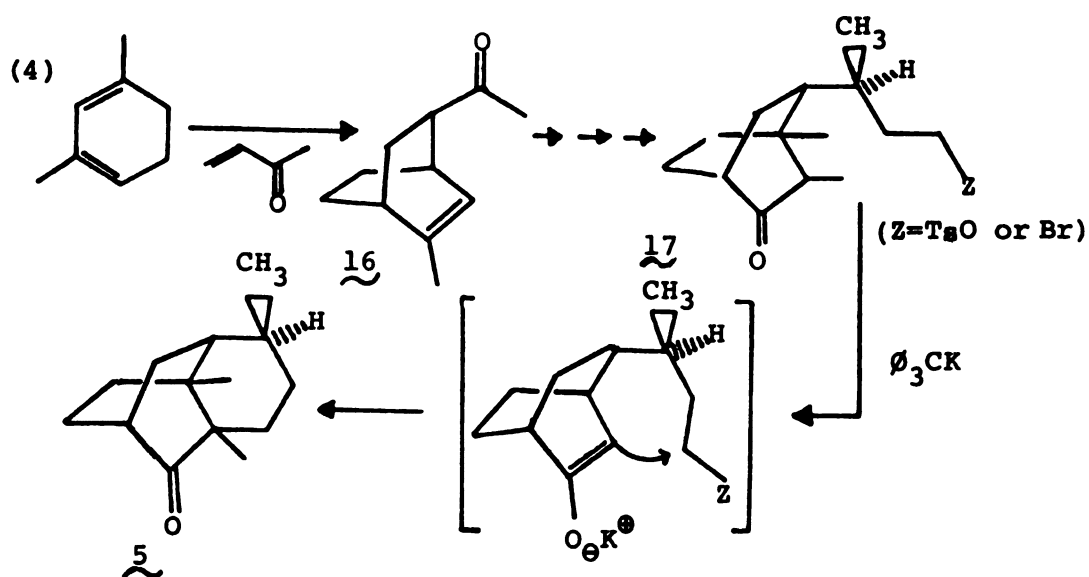
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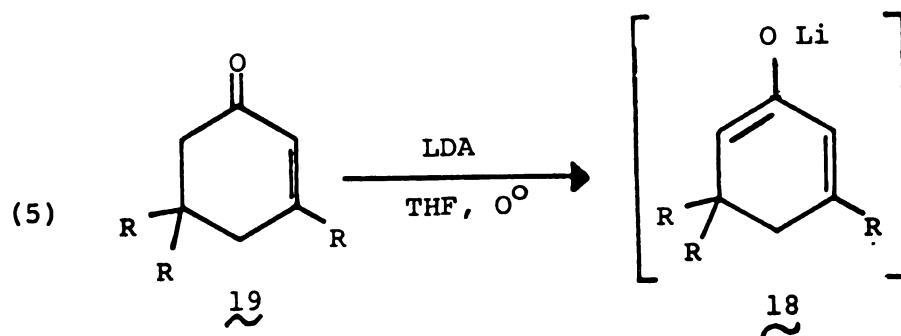
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The seyschellene synthesis effected by Mirrington⁸ (eq. 4), is based on the following strategy. First, a suitably functionalized bicyclo[2.2.2]octane was synthesized. Next, the six membered ring in the tricyclic carbon skeleton of seyschellene was annealed to form norseyschellone. The Diels-Alder reaction of 1,3-dimethyl-1,3-cyclohexadiene with methyl vinyl ketone affords the ketone 16,⁹ which was converted into the tosylate 17 in seven steps. Cyclization of the tosylate 17 was accomplished by treatment with trityl potassium to yield norseyschellanone (5). One major disadvantage of Mirrington's synthesis is the difficulty associated with the stereoselective construction of the non-rigid 4-carbon side chain in 17. Because of this difficulty, it was necessary at one stage in the synthetic sequence to separate a pair of epimeric compounds.⁵

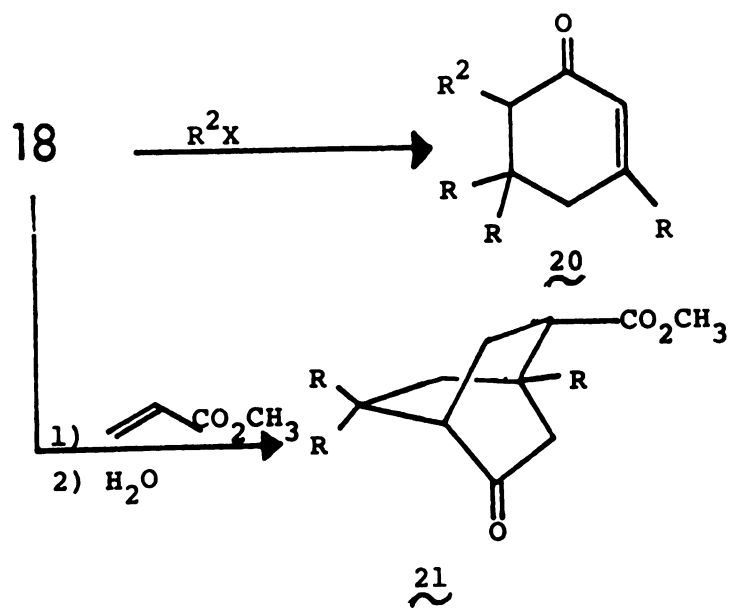


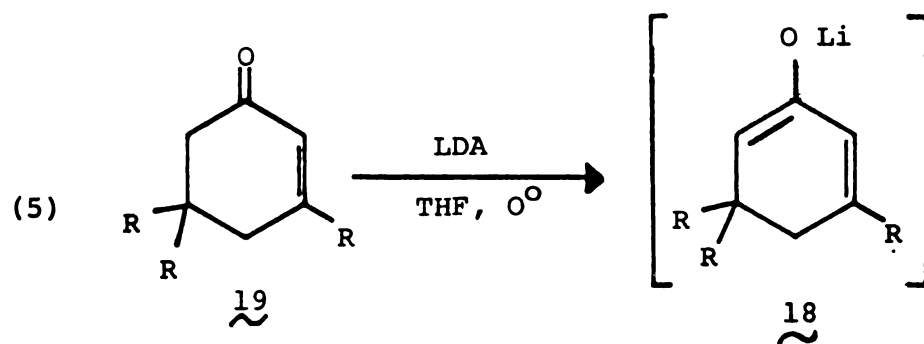
Every successful synthetic strategy has as its foundation at least one specific transformation of a versatile intermediate. In this study, the availability of the cross conjugated enolate anion 18 and its reactions prompted consideration of the total synthesis of seyschellene (eq. 5). Treatment of a cyclic α,β unsaturated ketone (19) with a lithium amide yields the cross conjugated enolate anion 18 (to be discussed later). This enolate can be alkylated to give α' alkyl α,β unsaturated ketones (20).¹⁰ A most unusual reaction is observed when a cross conjugated enolate anion is treated with methyl acrylate. A bicyclo[2.2.2]octanone (21) is formed in very high yield.¹¹

The formation of a suitable bicyclo[2.2.2]octanone would be a very useful intermediate in a synthetic pathway which follows a strategy similar to the approach used by Mirrington. This dissertation describes experiments which explore this type of synthetic pathway to the total synthesis of seyschellene.



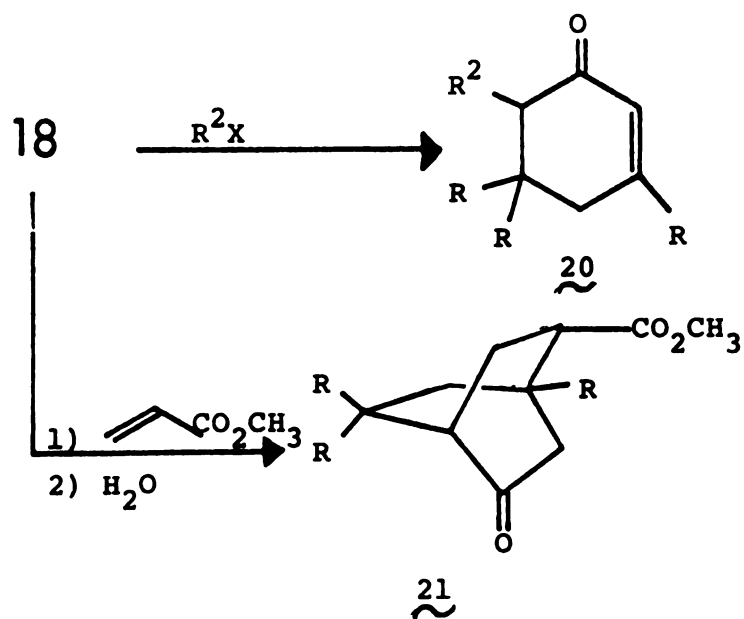
- a) $\text{R} = \text{H}$
 b) $\text{R} = \text{CH}_3$





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RESULTS AND DISCUSSION

The addition of methyl acrylate to the cross conjugated dienolate anion derived from isophorone gave keto ester 21 (eq. 5). There are two probable mechanisms by which this reaction might proceed. One consists of a sequence of two Michael reactions (eq. 6) and the other involves a Diels-Alder cycloaddition (eq. 7) in which the dienolate anion serves as the diene reactant. In view of the very high yields observed under exceptionally mild conditions with substrates of varying steric hindrance (to be discussed later), the sequential Michael mechanism was favored by Ross Lee in his initial investigation of this reaction.¹¹ In a study of the Michael reaction conducted by House et al.,¹² the reaction of an enolate anion with β -chloromethyl acrylate (eq. 8) gave unsaturated adduct via an addition-elimination mechanism. The same strategy was used here to study the mechanism of reaction eq. 5. Thus, addition of *cis*- β -chloro-methyl acrylate at -23° to the cross-conjugated dienolate anion derived from isophorone afforded the keto-ester 22 and starting material (eq. 9). A similar result was noted by Boeckman¹³ (eq. 10). These results clearly point to a double Michael reaction sequence, since

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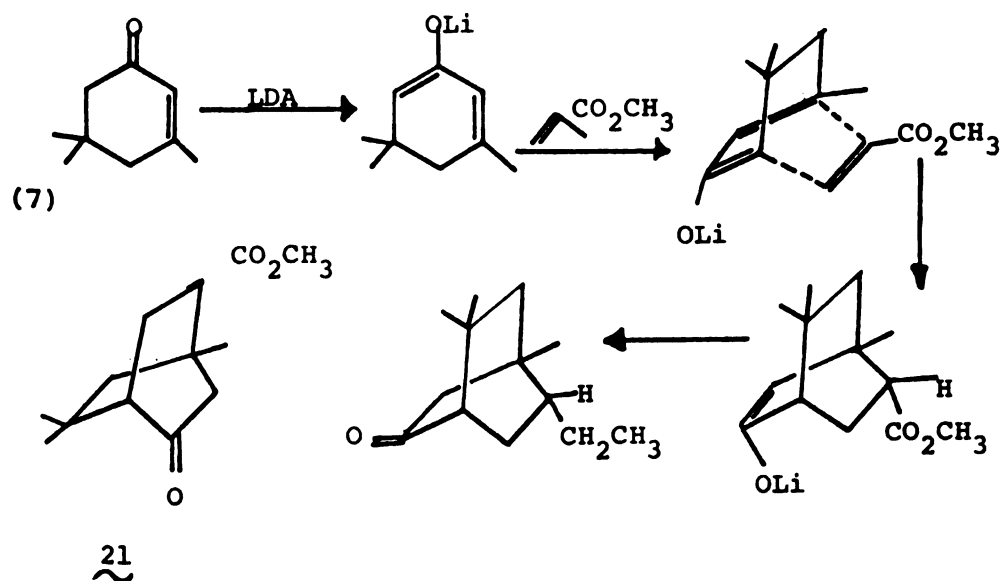
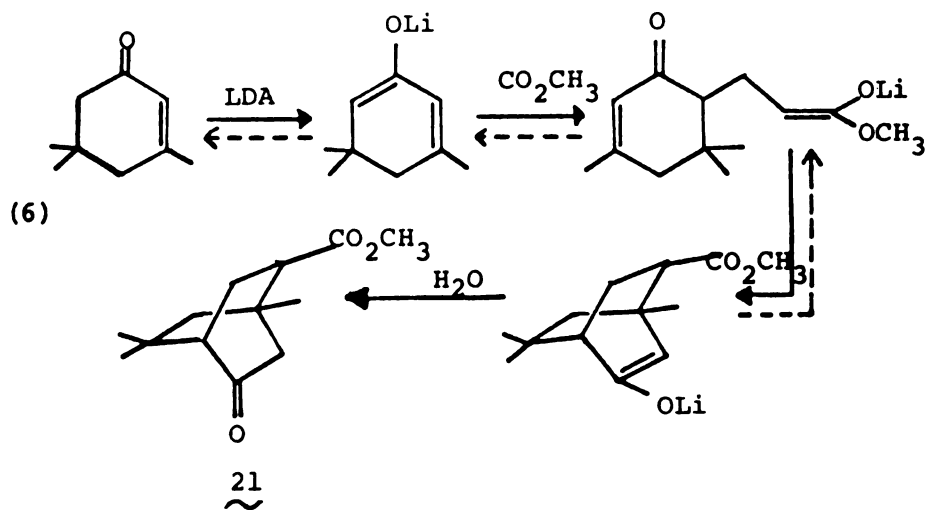
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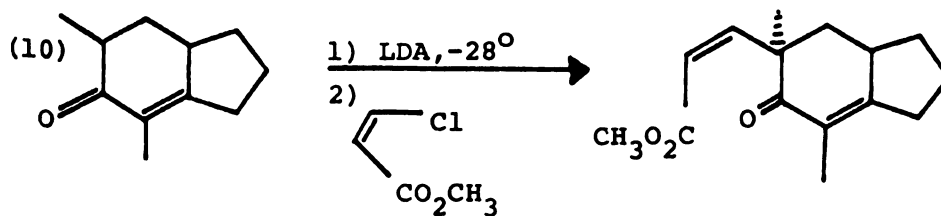
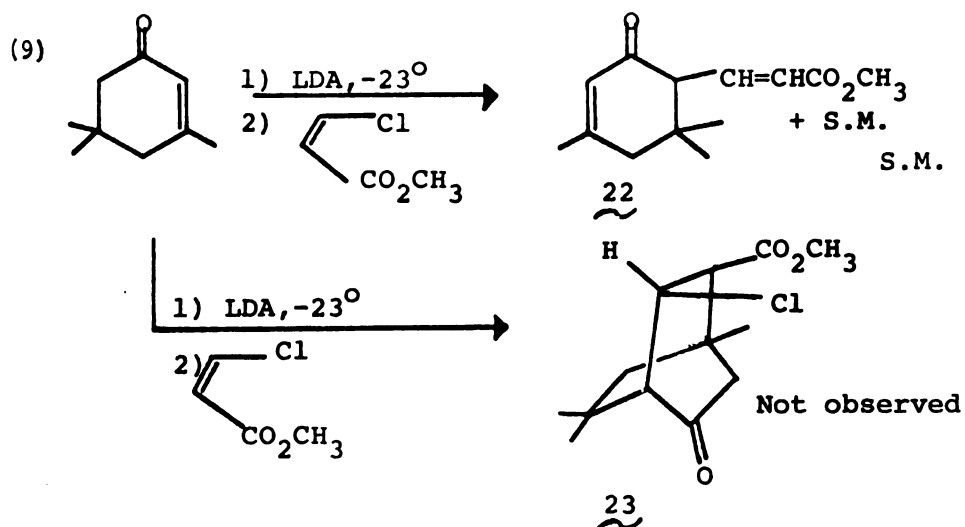
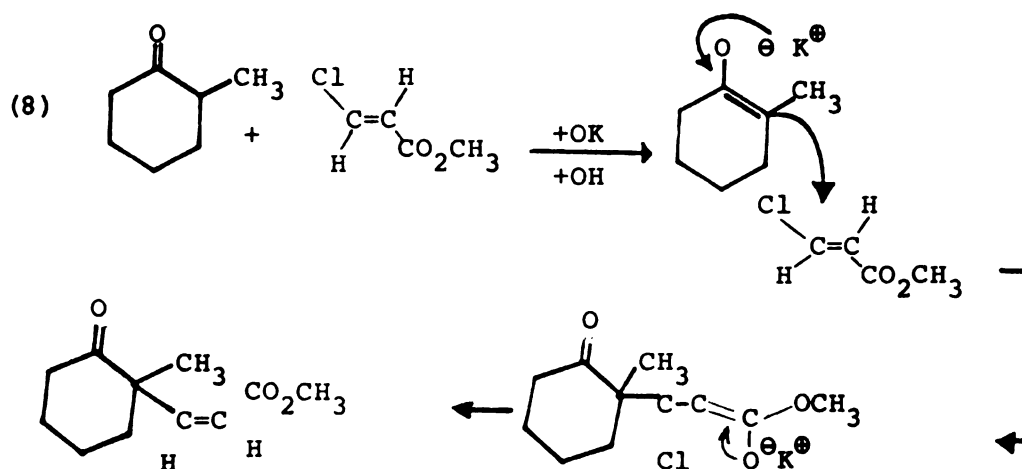
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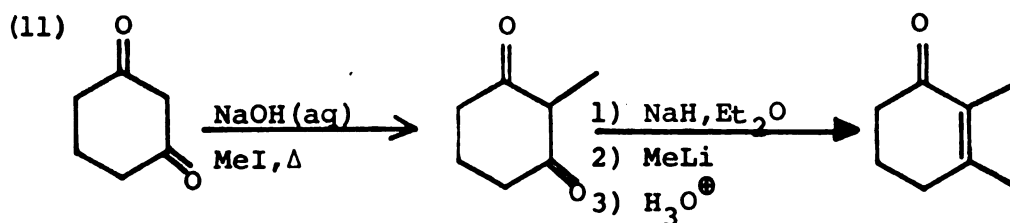
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the bicyclo[2.2.2]octanone product (23) expected from the Diels-Alder pathway should have been sufficiently stable to be isolated or otherwise observed.

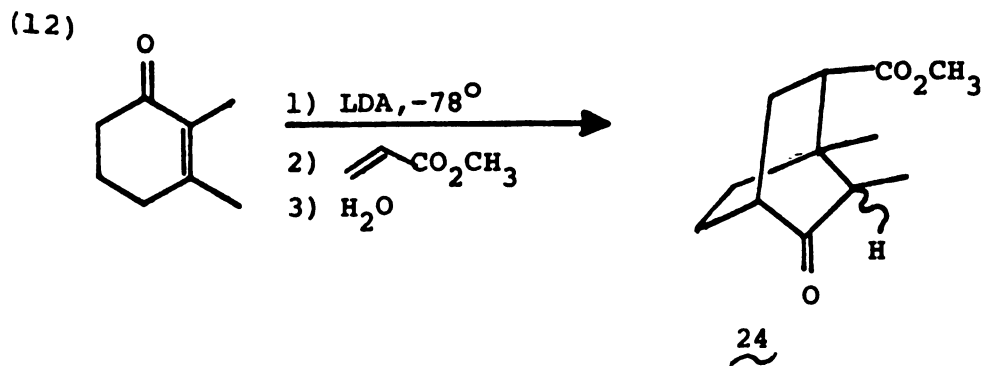




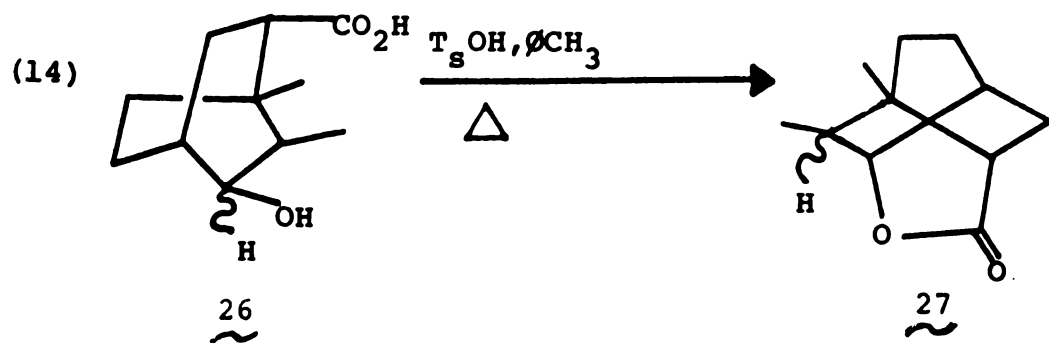
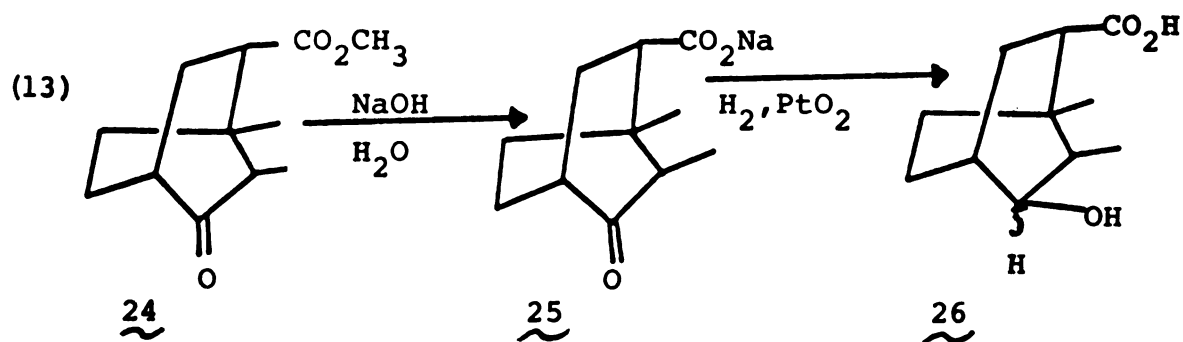
In order to use the sequential Michael synthesis to form the tricyclic carbon skeleton of seyschellene, it is necessary to begin with 2,3-dimethylcyclohexenone. This enone was prepared in two steps from cyclohexane-1,3-dione as shown in eq. 11.



Reaction of methyl acrylate with the cross-conjugated dienolate anion derived from 2,3-dimethylcyclohexenone afforded the keto-ester 24 in high yield (eq. 21).

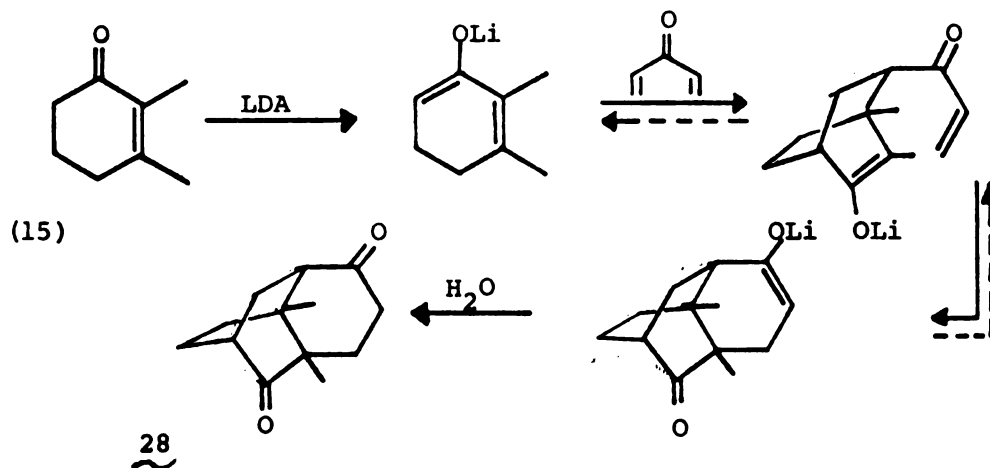


The configuration of the carbomethoxyfunction at C-5 in 24 was demonstrated by the following chemical approach. Keto-ester 24 was saponified to keto-carboxylate 25 (eq. 13) which was then reduced by catalytic hydrogenation to give hydroxy-acid 26. Lactonization of hydroxy acid 26 was accomplished in refluxing toluene containing para-toluene-sulfonic acid (eq. 14).



It should be noted, however, that, because of its easy accessibility, isophorone was used many times throughout this research project as a model compound for reactions to be applied to 2,3-dimethylcyclohexenone.

The success of double Michael reactions involving methyl acrylate suggested that a reaction between the cross-conjugated dienolate anion of 2,3-dimethylcyclohexenone and divinyl ketone might lead directly to a bis-nor-seyschellene derivative (28) as shown in eq. 15.

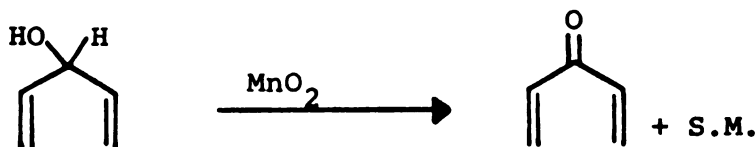


The synthesis of pure divinyl ketone turned out to be a difficult task. Oxidation of divinyl carbinol with manganese dioxide afforded divinyl ketone (~50%) and starting material (eq. 16). Attempts to purify divinyl ketone by spinning band column distillation failed to completely remove divinyl carbinol and a similar result was noted by Reed.¹⁴ It was, of course, unacceptable to use contaminated divinyl ketone as a Michael acceptor, since the alcoholic impurity would serve as a proton source which would destroy or isomerize the cross-conjugated dienolate anion.

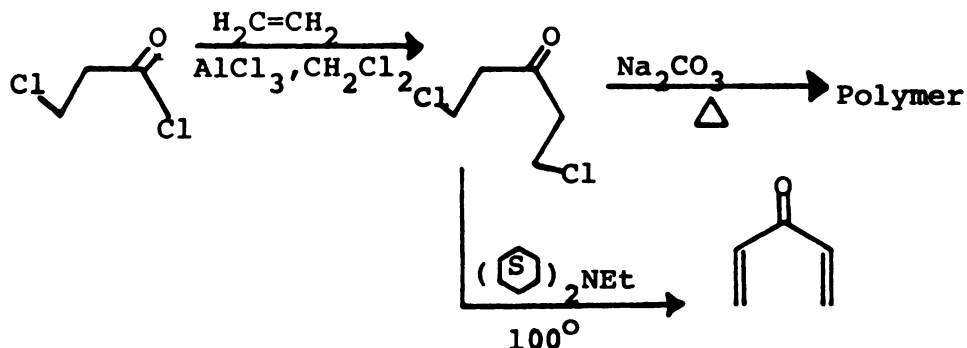
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Another approach to prepare divinyl ketone is the aluminum chloride catalyzed reaction of ethylene with β -chloro-acetyl chloride to yield 1,5-dichloro-3-pentanone (eq. 17), followed by bis-dehydrochlorination. Attempts to dehydrochlorinate 1,5-dichloro-3-pentanone using sodium carbonate by the procedure of Jones and Taylor failed.¹⁵ However, formation of divinyl ketone from 1,5-dichloro-3-pentanone was accomplished by using the method of dehydrochlorination developed by DeJongh and Wynberg.¹⁶ Thus, reaction of 1,5-dichloro-3-pentanone with ethyl dicyclohexyl amine at 100°C under vacuum yielded divinyl ketone which could be further purified by vacuum distillation (eq. 17).

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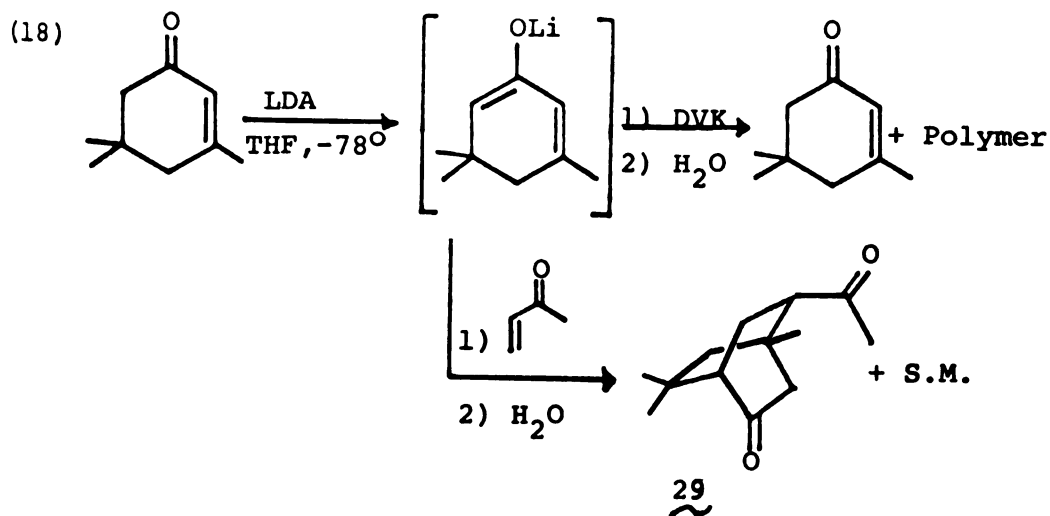


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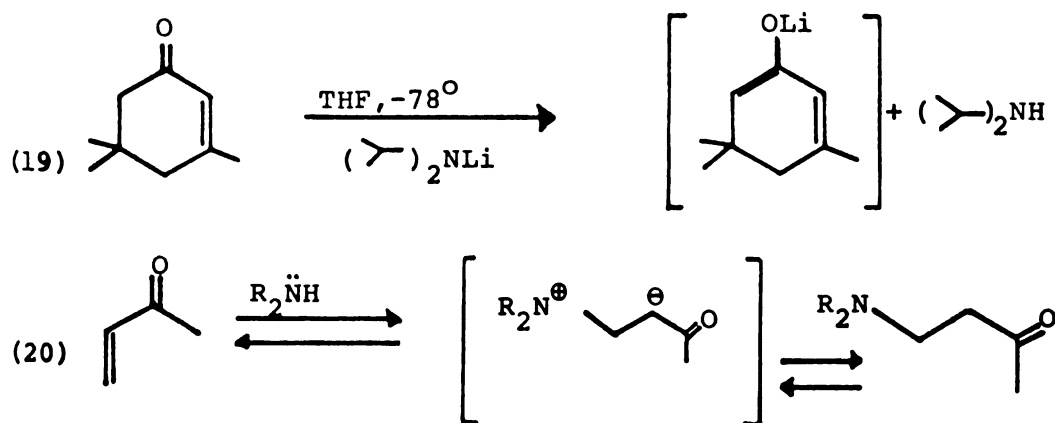
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Reaction of divinyl ketone with the cross-conjugated dienolate anion derived from isophorone led only to starting material and polymer (eq. 18). This disappointing result was matched by the reaction of methyl vinyl ketone with the same dienolate anion, which yielded mostly starting material and ~10% of the corresponding double Michael adduct (29, eq. 18). Thus, under reaction conditions that gave a successful double Michael reaction with methyl acrylate, methyl vinyl ketone was surprisingly unreactive.



The question that now had to be answered was: What factors are responsible for this difference in behavior between vinyl ketones and vinyl esters? Since the conjugated double bond of a vinyl ketone is more polar than the corresponding bond of a vinyl ester,¹⁷ vinyl ketones should in fact be more reactive in Michael reactions. In order to

reconcile these facts, it must be recognized that two nucleophiles are present in the reaction mixture: the dienolate anion and a 2° amine (eq. 19). If the amine reacts with the vinyl ketone by a 1,4 addition (eq. 20), the resulting adduct might initiate vinyl ketone polymerization, and in any event would hinder the desired reaction.

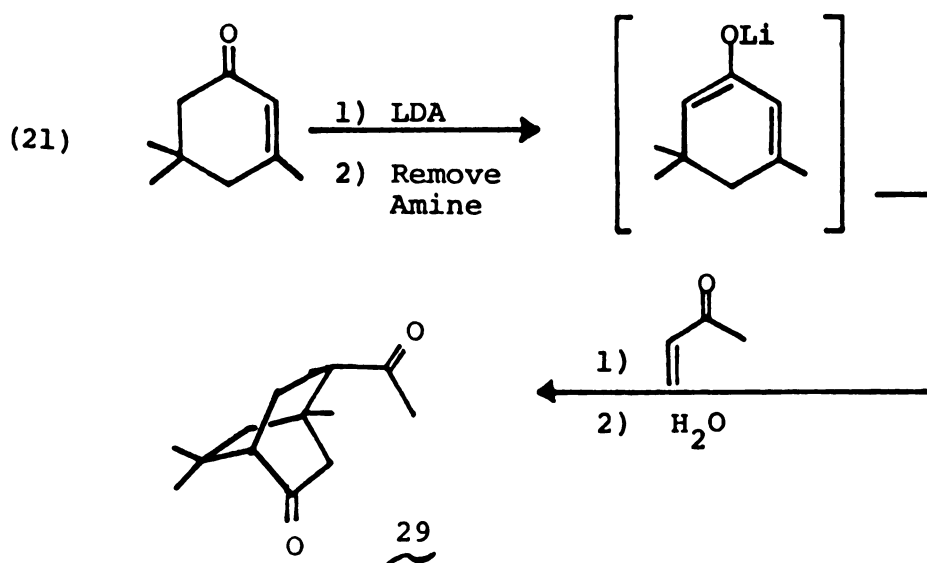


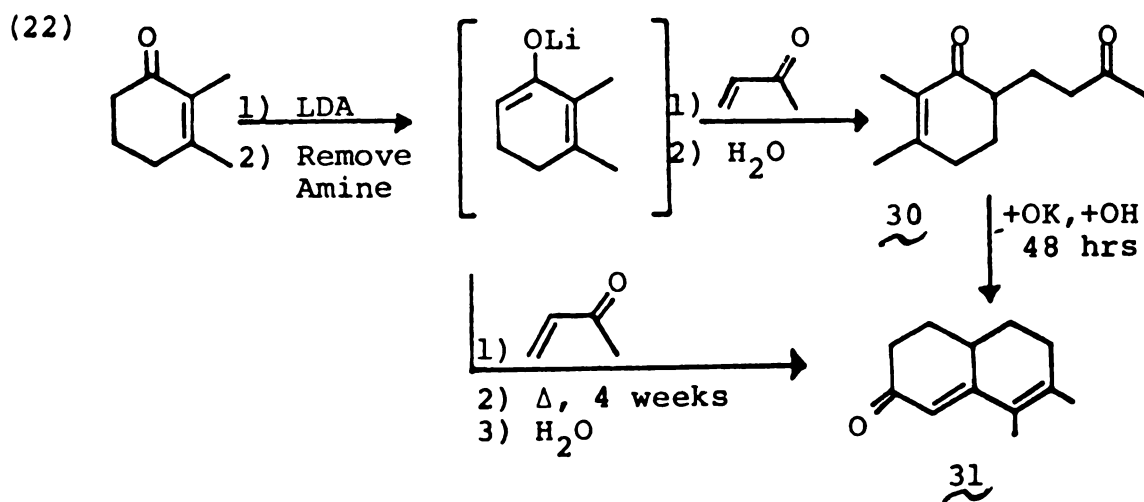
This argument suggests that removal of the amine after formation of the dienolate anion would facilitate subsequent double Michael reaction using vinyl ketones as Michael acceptors.

To test this premise, isophorone was treated with lithium diisopropyl amide (LDA). The resulting amine and solvent were removed by vacuum distillation from the reaction vessel. The remaining crystalline dienolate anion was

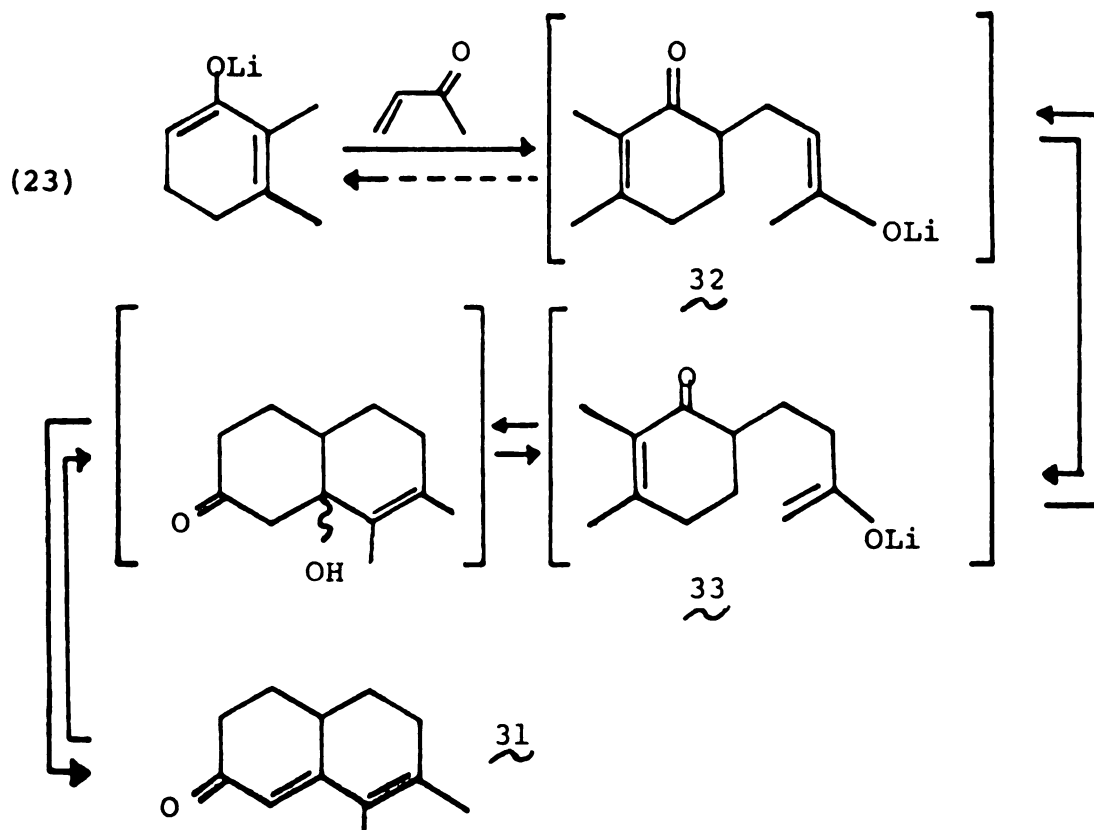
redissolved in THF under an argon atmosphere and then cooled to -78° . Addition of methyl vinyl ketone to this amine-free dienolate anion solution led to the desired bicyclo[2.2.2]octanedione 29 (eq. 21) in 75% yield.

Surprisingly, reaction of the amine-free conjugate base derived from 2,3-dimethyl-cyclohexenone with methyl vinyl ketone or ethyl vinyl ketone did not proceed to a bicyclo[2.2.2]octane product. Only the mono Michael product 30 was obtained under mild conditions, and more vigorous treatment (longer reaction time at a higher temperature) gave the decalone 31 (eq. 22). This same decalone was also obtained by stirring dione 30 in a THF solution of $+OK$ for 2 days at room temperature (eq. 22).

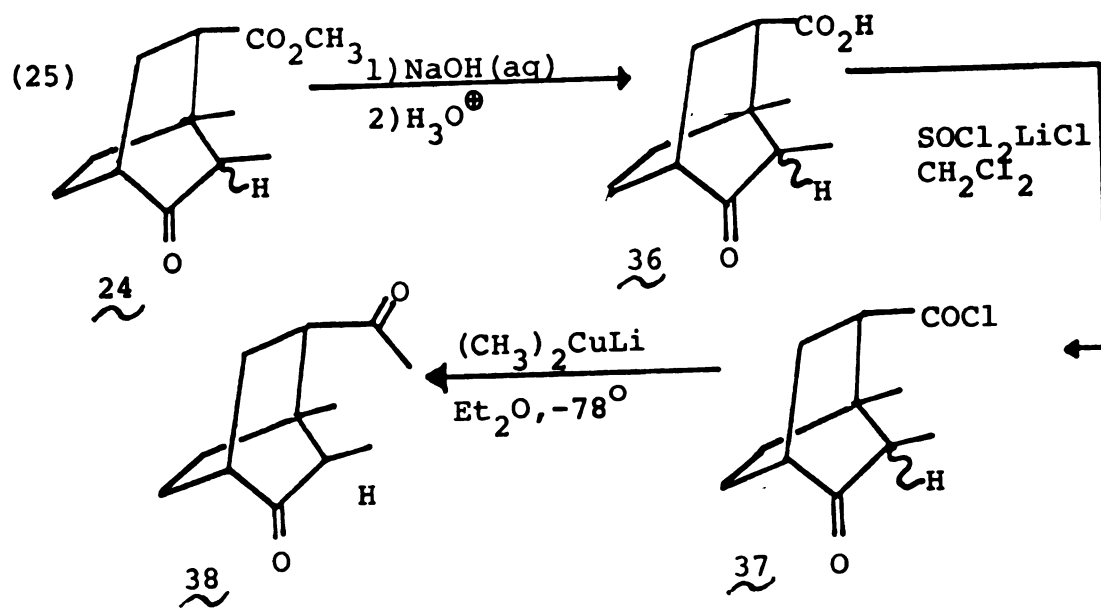
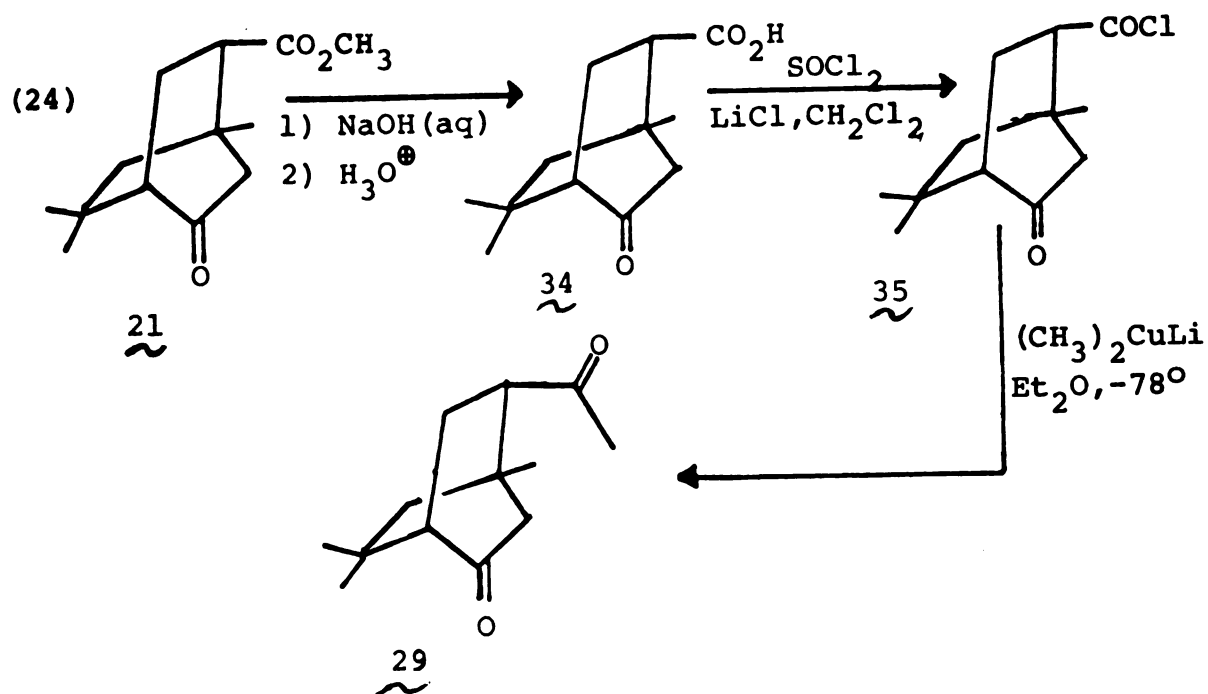




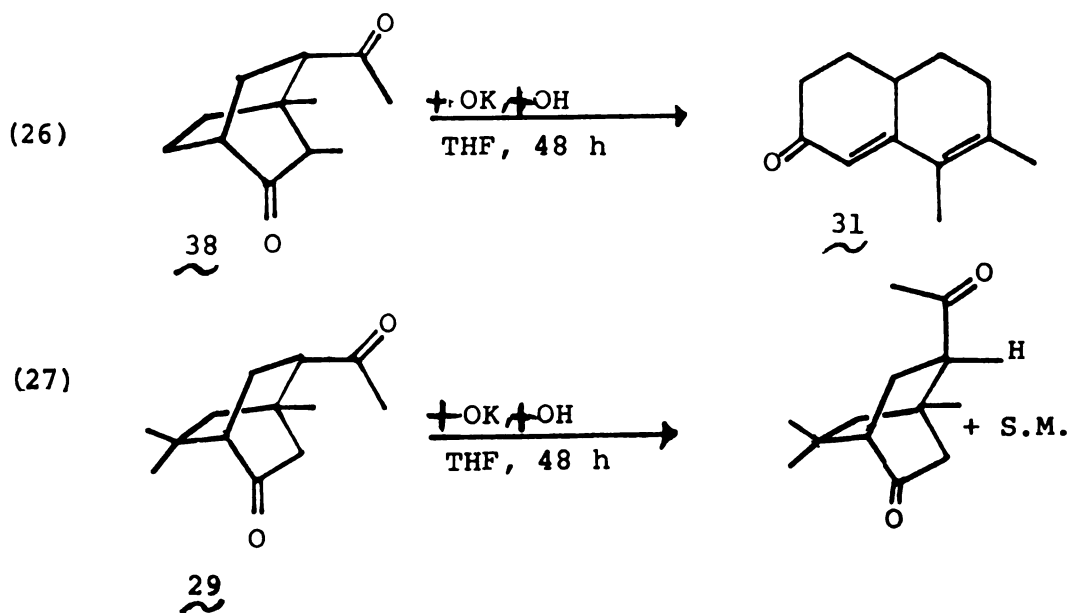
The formation of dienone 31 is not difficult to rationalize. Formation of the dione intermediate undoubtedly proceeds by an initial Michael reaction (eq. 23). Under more drastic reaction conditions interconversion of the enolate anions 32 and 33 (eq. 23) occurs and, the latter then suffers an adol condensation to form decalone 31 by a Robinson annelation.



In the course of studying these reactions, it was necessary to prepare authentic samples of the diones 29 and 38 by an alternative route. To this end, saponification of keto-ester 21 afforded keto acid 34 in 80% yield (eq. 24). Treatment of 34 with a methylene chloride solution of thionyl chloride and lithium chloride afforded keto-acid chloride 35 in 89% yield (eq. 24). Finally, reaction of 35 with dimethyl lithium cuprate gave dione 29 in 85% yield (eq. 24).¹⁸ Dione 38 was synthesized in the same way, starting with keto-ester 24 (eq. 25). As expected, the spectral properties (IR, NMR, MS) of dione 29 obtained by the double Michael reaction (eq. 21) and the aforementioned route were identical.

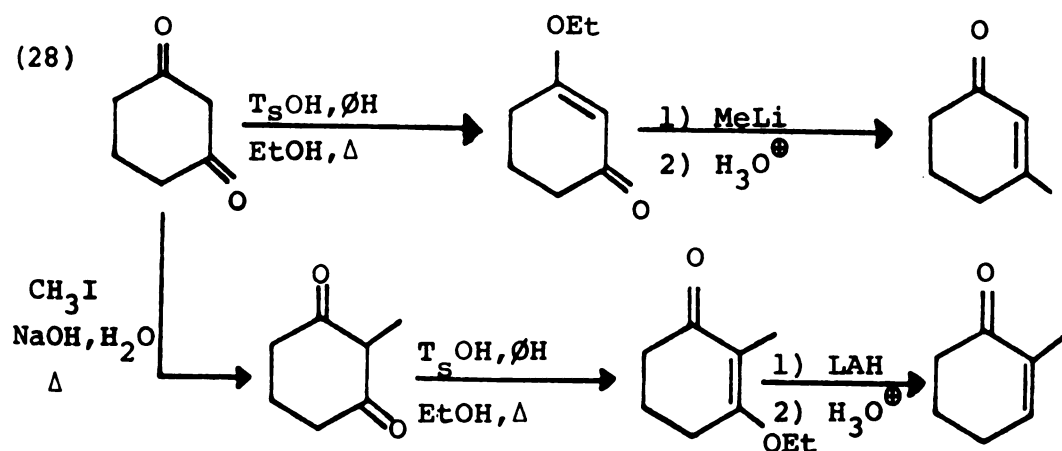


In an important experiment 38, on treatment with potassium t-butoxide at 25° for 2 days, was completely converted to the Robinson annelation product 31 (eq. 26). Similar treatment of 29 gave only slight epimerization to the exo isomer, over 90% of the diketone being recovered unchanged (eq. 27).



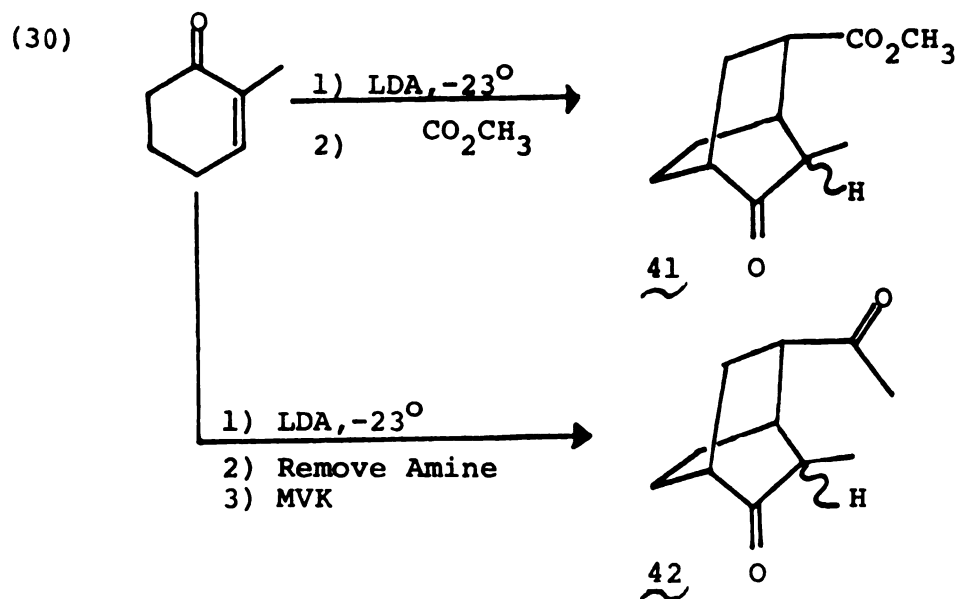
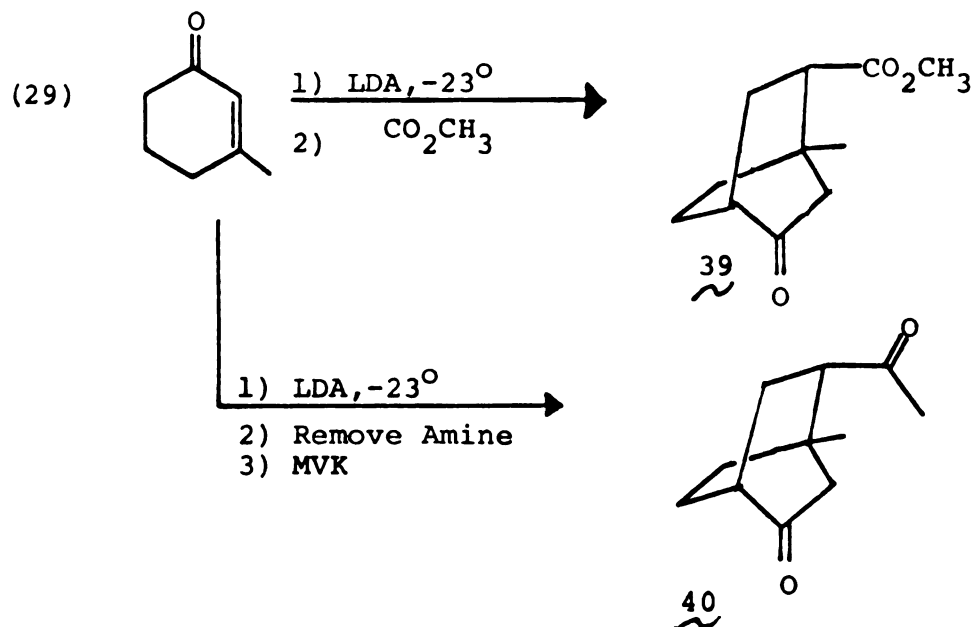
The effect of methyl groups on the course of the sequential Michael reactions of cyclohexenone dienolate anions with methyl vinyl ketone is indeed striking. It is also puzzling that this effect does not appear when the Michael acceptor is methyl acrylate. In order to explore this feature more fully a series of comparative cyclizations were conducted in which methyl groups were positioned at different sites on the cyclohexenone ring. For this purpose,

3-methylcyclohexenone was prepared in two steps from cyclohexan-1,3-dione (eq. 28) and 2-methylcyclohexenone was obtained in three steps from the same starting material (eq. 28).¹⁹

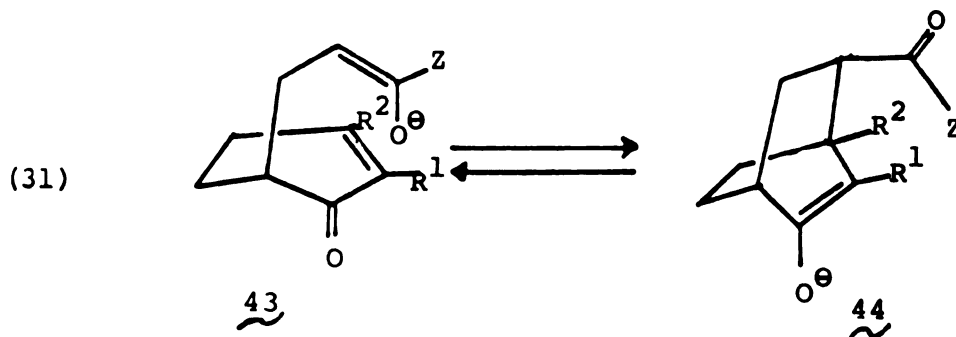


Reaction of the cross-conjugated dienolate anion derived from 3-methylcyclohexenone with methyl acrylate gave the keto-ester 39 (eq. 29). Likewise reaction of the cross-conjugated dienolate anion from 2-methylcyclohexenone with methyl acrylate afforded the epimeric keto-esters 41 (eq. 30). The reaction of the amine-free cross-conjugated dienolate anions of these methylcyclohexenones with methyl vinyl ketone also afforded the expected bicyclo[2.2.2]octane diones (eq. 29 and 30). Thus, the reaction of the conjugate

base derived from 2,3-dimethylcyclohexenone with methyl vinyl ketone is unique in not yielding the expected bicyclo[2.2.2]octane dione (eq. 22).

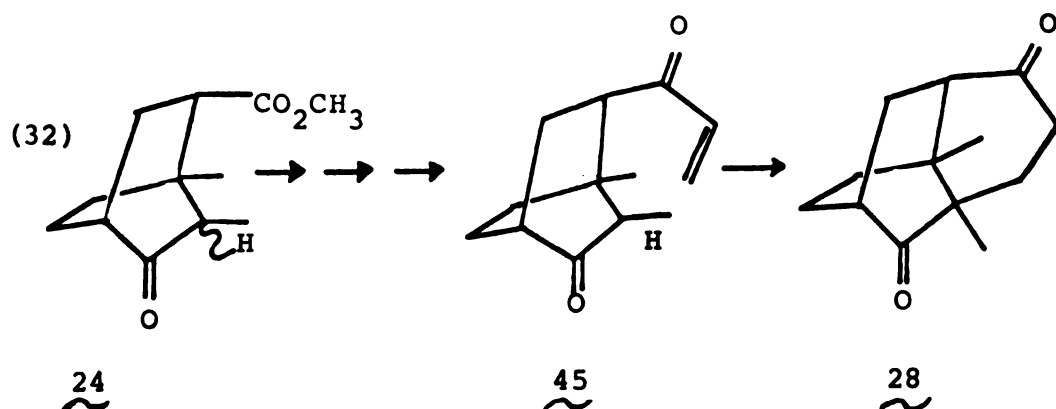


The variability of the enolate reactions described above can be rationalized in terms of steric and electronic factors influencing the second Michael addition (eq. 31).

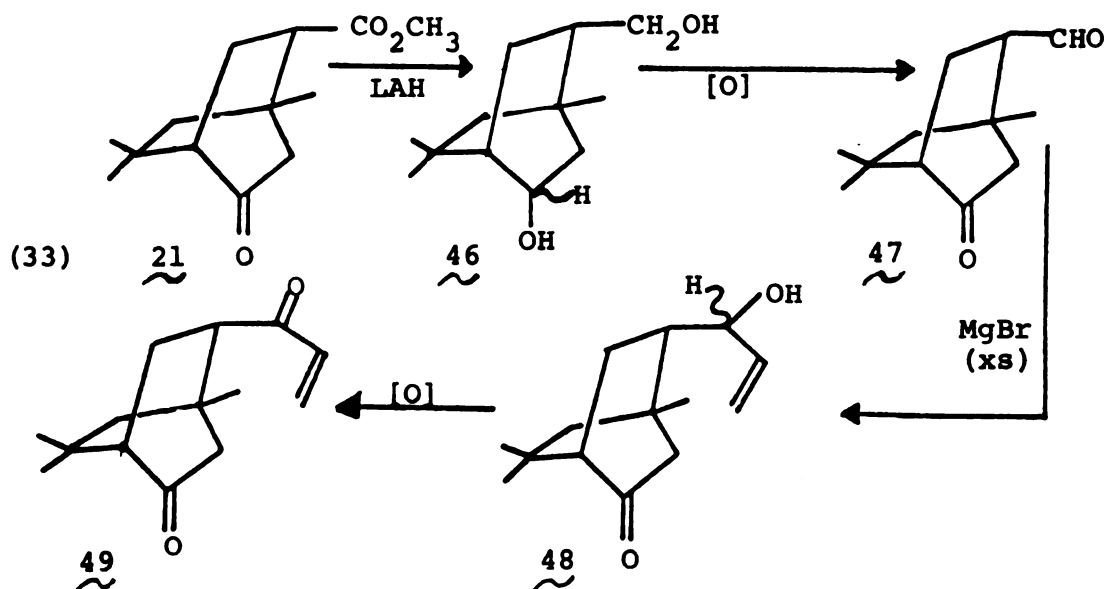


Since ester enolate bases are less stable and more reactive than ketone enolate anions (esters are over 10,000 times weaker as Bronsted acids than are ketones²⁰), there is a thermodynamic driving force favoring cyclization (43 $\rightarrow$ 44) of the intermediate formed from acrylate ester addition ($Z = \text{OCH}_3$ in equation 31). Vinyl ketone reactions, on the other hand, proceed through a series of ketone enolate anions among which this driving force is missing. In the absence of strong steric hindrance, the cyclization should still be favored because of the increase in bond energy that normally accompanys the conversion of π -bonds to σ -bonds. Indeed, this is observed for all cases in which at least one of the R substituents (R^1 or R^2) is a hydrogen atom. However, when both R^1 and R^2 are methyl, non-bonded repulsions destabilize the bicyclic product (44) relative to the monocyclic precursor and the latter (43) predominates.

As a consequence of the model experiments with vinyl ketones, the triple Michael reaction approach to seyschellene was abandoned. Nevertheless, approaches involving sequential Michael reactions still looked promising. This new strategy would require synthesis of the vinyl ketone 45 from the keto-ester 24, followed by intramolecular cyclization (eq. 32).

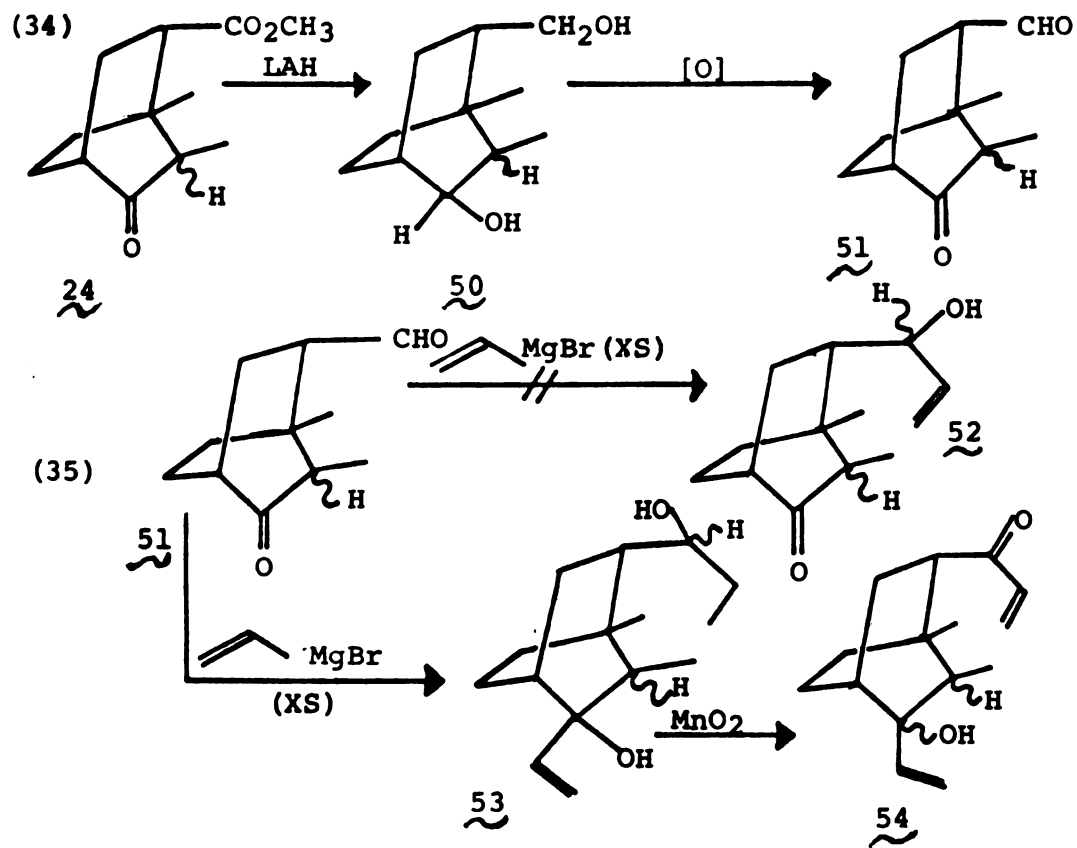


The easily accessible keto-ester 21 was used as a model compound for the proposed reactions of 24. To this end, reduction of 21 with lithium aluminum hydride afforded the diol 46 (eq. 33). This diol (46) was oxidized to keto-aldehyde 47 with pyridinium chlorochromate (eq. 33), and treatment of 47 with vinyl magnesium bromide afforded keto-alcohol 48. As expected, attack of the Grignard reagent occurred only at the less hindered carbonyl function of the aldehyde. Oxidation of 48 with manganese dioxide afforded the vinyl ketone 49.



With the promising results of model compound in hand, this synthesis was applied to keto-ester 24. Reduction of 24 with lithium aluminum hydride afforded the expected diol (50) in high yield (eq. 34) and oxidation with pyridinium chlorochromate gave the desired keto-aldehyde 51 (rq. 34). Unfortunately treatment of 51 with excess vinyl magnesium bromide proceeded with double addition, resulting in diol 53 rather than keto-alcohol 52 (eq. 35). The structure of 53 was based on mass spectral evidence. Attempts to obtain hydroxy ketone 52 using other reaction conditions (lower concentration of the Grignard reagent and lower temperature) also failed. Oxidation of 53 with manganese dioxide afforded vinyl ketone 54 (eq. 35). Thus it appears that the gem-dimethyl group in the model keto-aldehyde 47 blocked attack

of the Grignard reagent at the ketone. In keto-aldehyde 51, the gem-dimethyl group is no longer present and the Grignard reagent attacks both carbonyl functions with very little chemoselectivity.²²



At this point, it appeared doubtful whether any pathway to seyschellene could be achieved using Michael reactions of conjugated dienolate anions. Consequently, a new approach was devised. Earlier considerations of a Diels-Alder

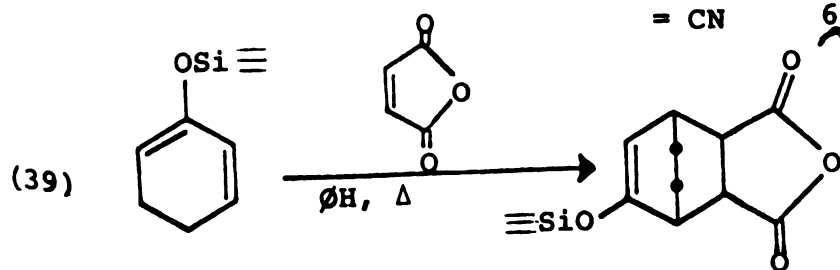
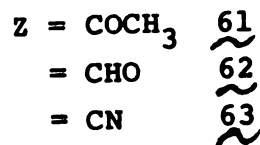
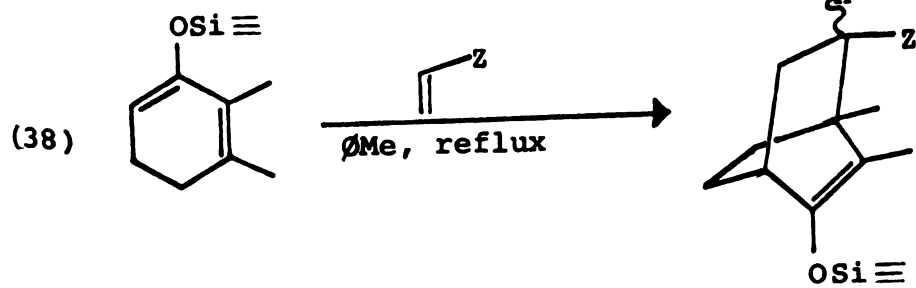
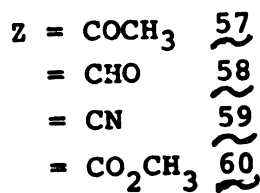
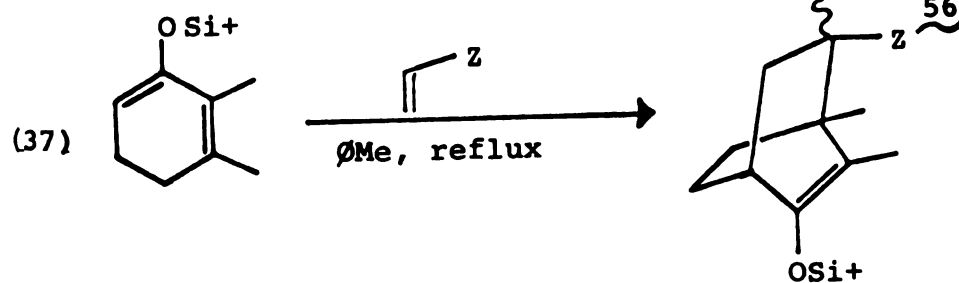
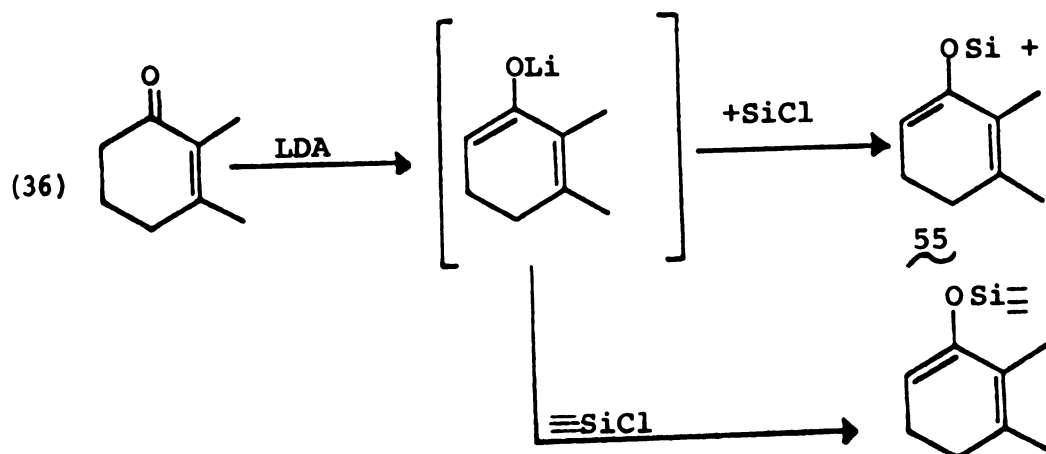


mechanism for the cross-conjugated dienolate anions suggested the possibility of using a Diels-Alder reaction to construct the bicyclic carbon skeleton of seyschellene.

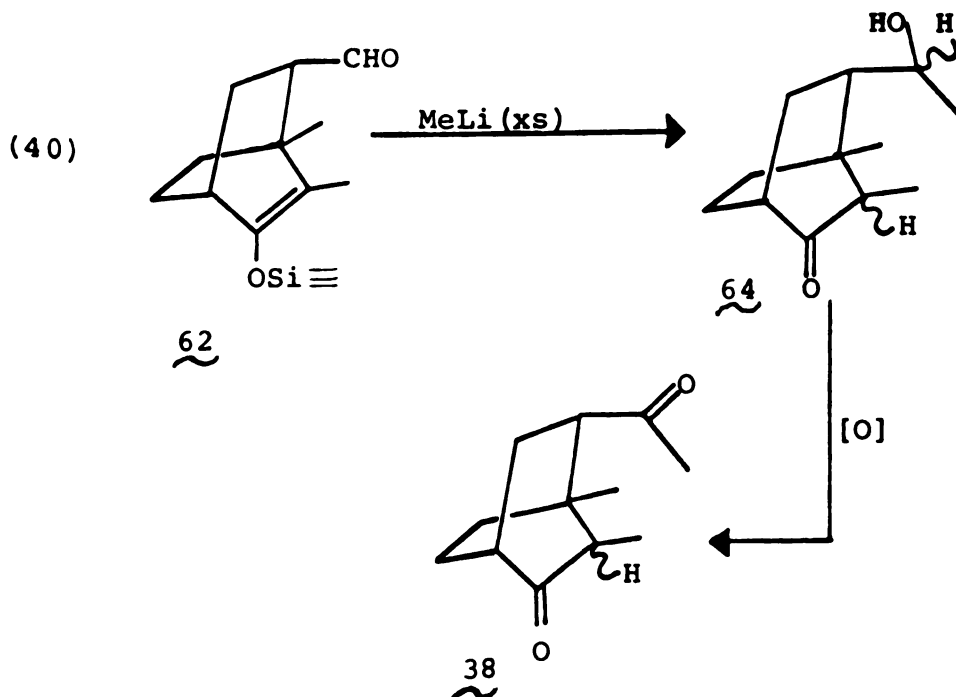
In order to use the Diels-Alder reaction in this way, it was necessary to begin with a cross-conjugated dienol ether derived from 2,3-dimethylcyclohexenone. This diene was readily prepared by silylation of the corresponding dienolate anion.²³ Thus, treatment of the cross-conjugated dienolate anion derived from 2,3-dimethylcyclohexenone with a THF:HMPA solution of t-butyl dimethyl silyl chlorosilane afforded t-butyl dimethyl dienol ether 55 (eq. 36). An equivalent reaction of the same dienolate anion with trimethyl chlorosilane afforded trimethyl silyloxy diene ether 56 (eq. 36). Diels-Alder cycloaddition of 55 with methyl vinyl ketone afforded the ketone 57 in 94% yield (eq. 37). Other dienophiles also reacted with this siloxy diene (eq. 37) to give corresponding Diels-Alder adducts.

As expected, trimethyl silyl dienol ether 56 also reacted with dienophiles to give Diels-Alder adducts (eq. 38). While this work was in progress, Rubottom and Krueger reported similar results for the Diels-Alder reactions between silyl dienol ethers derived from cyclohexenones with maleic anhydride or dimethyl acetylene-dicarboxylate (eq. 39).²⁴

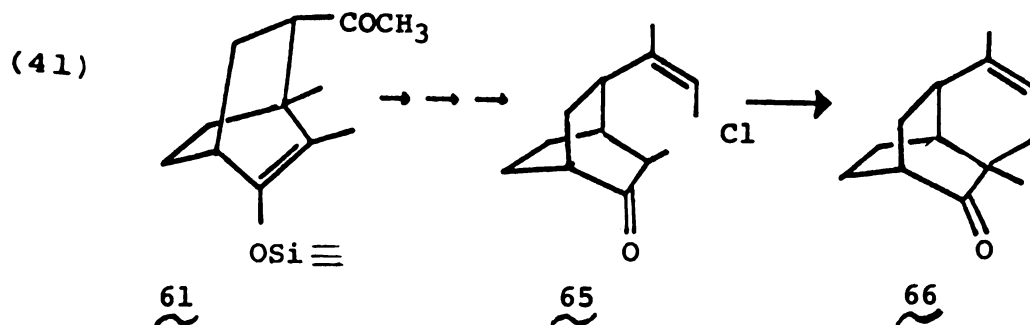
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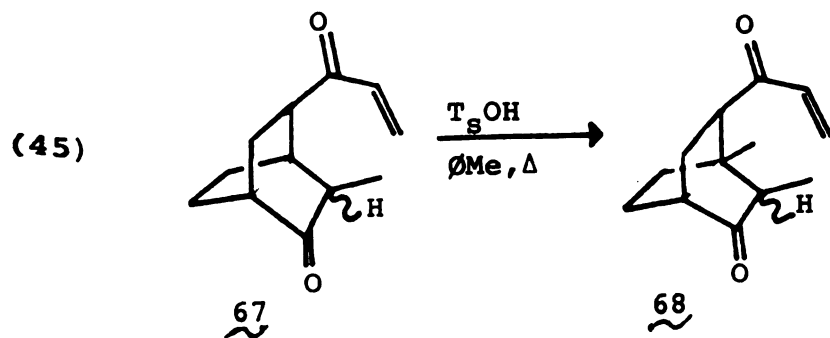
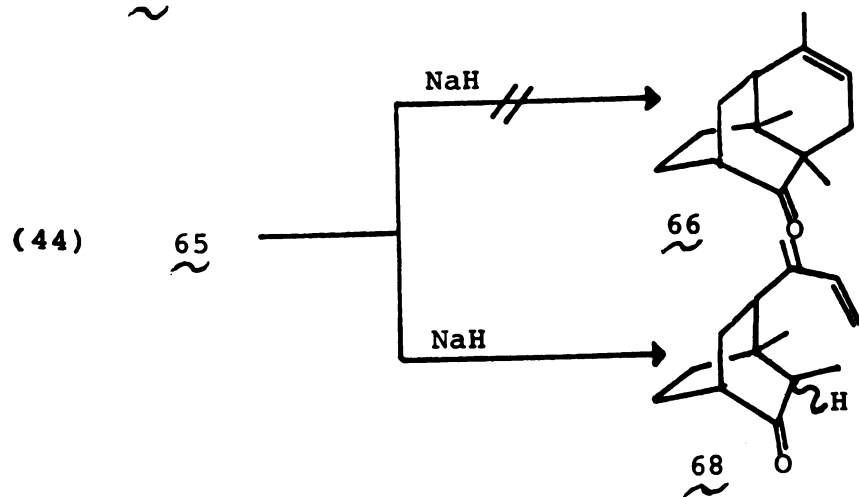
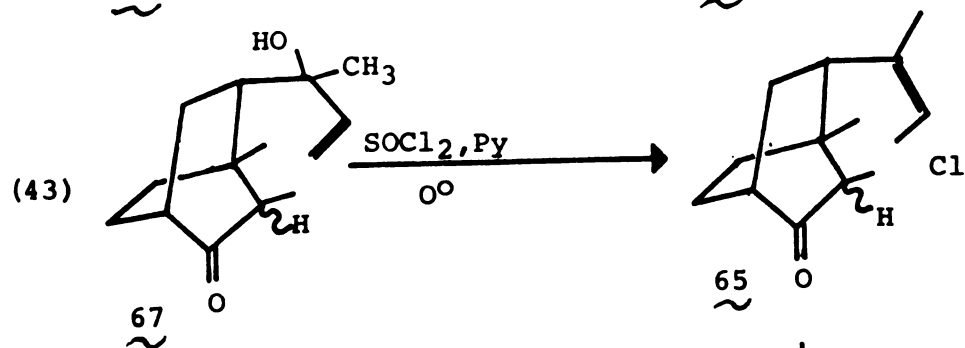
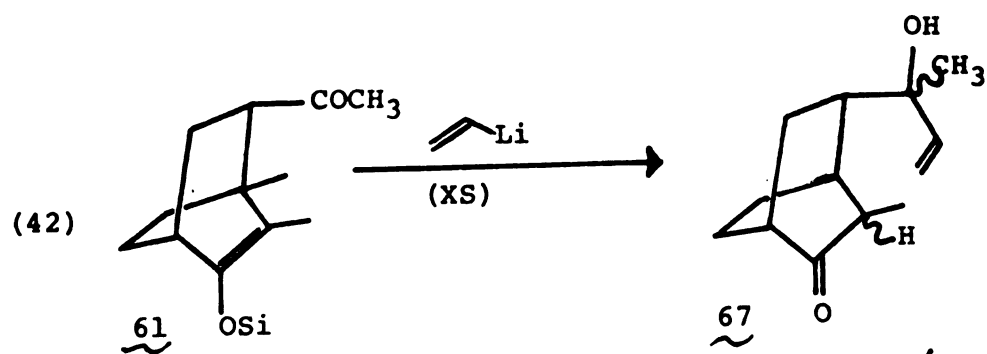


One question that had to be answered was: What is the configuration of the Diels-Alder adducts? Since there are four possible isomers, it is imperative to know which isomer (if any) was favored in the Diels-Alder reaction. To this end, treatment of aldehyde 62 with excess methyl lithium afforded keto-alcohol 64 (eq. 40) and oxidation of 64 with pyridinium chlorochromate gave dione 38. The spectral properties of dione 38 obtained in this fashion were identical to the spectral properties of dione 38 prepared by an alternate route (eq. 25). Thus, the Diels-Alder adducts appear to obey Alder's endo rule, and they have the configuration required for use in a seyschellene synthesis.



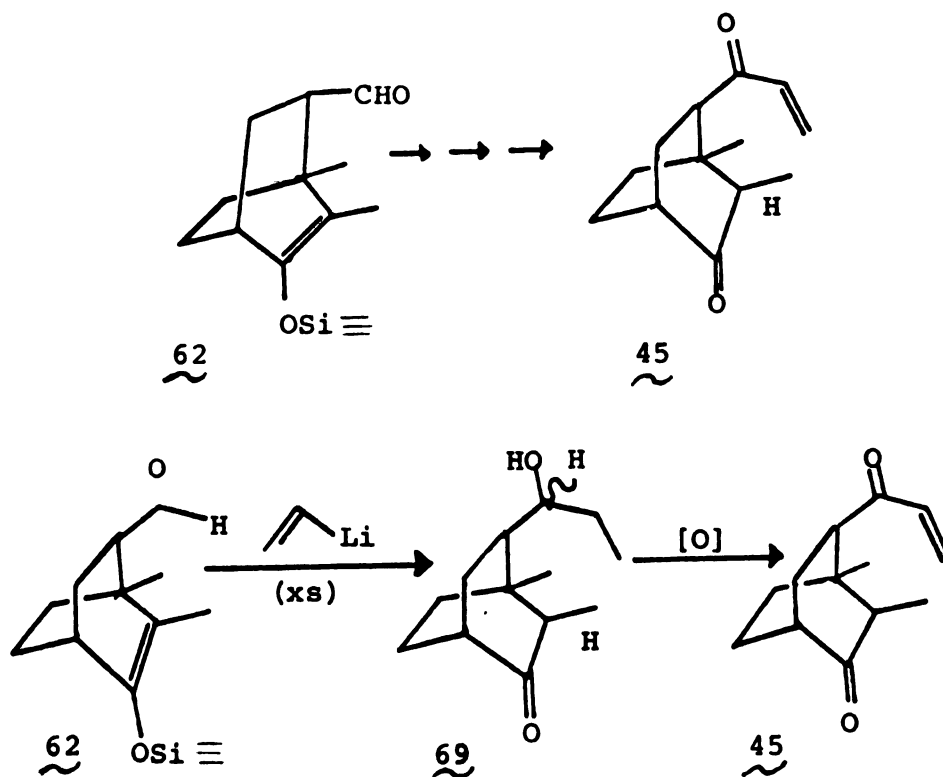
With the stereochemistry of the Diels-Alder adducts known, approaches involving the Diels-Alder adducts looked promising. One strategy would require synthesis of allyl chloride 65 from ketone 61, followed by intramolecular cyclization (eq. 41). To this end, treatment of ketone 61 with excess vinylolithium afforded allyl alcohol 67 (eq. 42). Treatment of 67 with thionyl chloride using the method of Morrow *et al.*,²⁵ gave the allyl chloride 65 (eq. 43). In an attempt to isolate 65 by preparative glpc, 65 underwent dehydrochlorination to form diene 68. Thus, treatment of crude allyl chloride 65 with sodium hydride gave the diene 68 and not the expected ketone 66 (eq. 44). Diene 68 was obtained by an alternate route. Treatment of allyl alcohol 67 with *para* toluenesulfonic acid in refluxing toluene gave 68 (eq. 45). Since the stereochemistry of the double bond of 65 was not determined, the possibility that the major isomer obtained was the *E* isomer existed. This might explain the failure of 65 to cyclize.





Another strategy which utilized a Diels-Alder adduct involved synthesis of dione 45 (eq. 46 and eq. 32) from aldehyde 62. Thus, treatment of aldehyde 62 with excess vinyl lithium afforded allyl alcohol 69 (eq. 47). Oxidation of 69 with manganese dioxide afforded vinyl ketone 45 (eq. 47).

The synthesis of vinyl ketone 45 accomplishes the primary goal of this dissertation since this compound is a possible precursor of norseyschellanone (5).



EXPERIMENTAL

General

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.

Melting points were taken on either the Hoover-Thomas apparatus (capillary tubes) or on a hot-stage microscope and are uncorrected.

Gas-liquid phase chromatographic analyses (glpc) were conducted with either a Varian 1200 flame ionization gas chromatograph or an Aerograph A-90P3 thermal conductivity instrument.

Micro-analyses were performed by Spang Microanalytical Labs, Ann Arbor, Michigan.

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2'-Carbomethoxy-6-vinyl-3,5,5-trimethyl-
cyclohex-2-en-1-one (22)

To a stirred solution of .340 mL (2.4 mmoles) of diisopropyl amine (DIA) in 80 mL of THF at -23° under an argon atmosphere was added 1.0 mL (2.2 mmoles) of 2.2 M n-butyllithium in hexane. After 20 min, a solution of .300 mL (2.0 mmoles) of isophorone in 5 mL of THF was then added dropwise to this mixture over a ten minute period. The reaction mixture was stirred for 1 hr, following which a solution of .264 g (2.2 mmoles) of cis-β-chloromethyl acrylate in 5 mL of THF was added dropwise over a five minute period. The reaction mixture was stirred for 2 hr at -23°. After warming to 25°, water and ether were added and the aqueous phase was extracted with ether. The combined ether extracts were washed three times with a 1 M HCl solution, once each with water and a saturated sodium sulfate solution and finally dried over MgSO₄. Removal of solvent gave .404 g (91%) of a reddish oil. Analysis by glpc showed a mixture of isophorone and keto-ester 22 (ratio 1:1). An analytical sample of 22 obtained by preparative glpc the following properties: Uv (95% EtOH) 242 nm ($\epsilon = 13,400$); ir (CDCl₃) 1725 cm⁻², 1670 cm⁻¹; pmr (CDCl₃) δ 6.3-6.1 (vinyl, 3H), 3.6 (s, 3H), 2.4-1.2 (m, 6H), 1.05 (s, 3H), 0.95 (s, 3H); mass spectrum (70 eV) m/e (rel intensity) 222(3)P, 190(27), 175(100).

Anal. Calcd. for $C_{13}H_{18}O_3$: C, 70.24; H, 8.16.

Found: C, 70.33; H, 8.25.

5-Carbomethoxy-3,4-dimethylbicyclo-
[2.2.2]octan-2-one (24)

To a stirred solution of 2.2 mmoles of lithium diisopropyl amide (LDA) in 80 mL of THF prepared in the usual manner, at -78° under an argon atmosphere was added a solution of .248 g (2.0 mmoles) of 2,3-dimethylcyclohexenone in 5 mL of THF over a 5 min period. The reaction mixture was stirred for 1 hr, following which a solution of .200 mL (2.2 mmoles) of methyl acrylate in 5 mL of THF was added dropwise over a 5 min period. The reaction mixture was stirred, first for 2 hr at -78° and then for 12 hr at 25° . Water and ether were added to the reaction mixture and the aqueous phase was extracted with ether. The combined ether extracts were washed three times with a 1 M HCl solution, once each with water and a saturated sodium sulfate solution and finally dried over $MgSO_4$. Removal of solvent gave .390 g (91%) of keto-ester 24 as a pale yellow oil, which was homogeneous by glpc (4% QF-1, 120°). An analytical sample obtained by preparative glpc (4% QF-1, 190°) exhibited the following properties: ir (CCl_4) 1730 cm^{-1} , 1190 cm^{-1} , 1160 cm^{-1} ; pmr (CCl_4) δ 3.6 (s, 3H), 2.9-1.3 (m, 9H), 1.1 (s, 3H) 0.9 (d, 3H); mass spectrum (70 eV) m/e (rel intensity) 210(5)P, 124(100).

Anal. Calcd. for $C_{12}H_{18}O_3$: C, 68.55; H, 8.63.

Found: C, 68.68; H, 8.66.

5-Carboxy-3,4-dimethylbicyclo-
[2.2.2]octan-2-ol (26)

The keto-ester 24 (.784 g, 4 mmoles) was added to a solution of 10% aqueous sodium hydroxide and stirred at rm temp for 5 hr (until homogeneous). Platinum oxide (170 mg) was then added and the solution was hydrogenated at 25° and atmospheric pressure for 2 days with theoretical uptake of hydrogen. After filtering off the catalyst through a celite mat, the solution was acidified with 6 M hydrochloric acid and extracted with ether. The combined ether extracts were washed once each with water and a saturated sodium sulfate solution and finally dried over $MgSO_4$. Removal of solvent gave .740 g (92%) of hydroxy acid 26 and starting material (8:2) as a white solid, mp 103-104°. An analytical sample obtained by preparative glpc (4% QF-1, 190°) exhibited the following properties: ir ($CDCl_3$) 3500 cm^{-1} , $3250-3000\text{ cm}^{-1}$, 1720 cm^{-1} ; pmr ($CDCl_3$) δ 8.2 (bs, 2H) 2.9-1.5 (m, 10H) 1.2-.9 (m, 6H); mass spectrum (70 eV) m/e (rel intensity) 198(2)P, 196(11)impurity, 124(100).

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2-Hydroxy-3,4-dimethylbicyclo[2.2.2]octan-5-
carboxylic acid δ -Lactone (27)

To a solution of 50 mL of toluene containing a small amount of para-toluenesulfonic acid was added .198 g (1 mmole) of hydroxy-acid 26 and the resulting mixture was refluxed 1 hr through a Dean-Stark water trap containing molecular sieves (4Å). Ether was added to the cooled solution and the organic mixture was washed with cold (3°) five percent sodium bicarbonate and saturated sodium sulfate solutions and finally dried over MgSO₄. Removal of solvent gave .092 g (51%) of lactone 27 as an oil. An analytical sample obtained by preparative glpc (4% QF-1, 190°) exhibited the following properties: ir (CDCl₃) 1755 cm⁻¹, 1270 cm⁻¹; mass spectrum (70 eV) m/e (rel intensity) 180(2)P, 152(10), 94(100).

5-Acetyl-4,7,7-trimethylbicyclo-
[2.2.2]octan-2-one (29)

To a stirred solution of 2.2 mmoles of LDA in 40 mL of THF, prepared by the usual manner, at -78° under an argon atmosphere was added a solution of .300 mL (2.0 mmoles) of isophorone in 5 mL of THF dropwise over a 5 min period, and the resulting solution was stirred at -78° for 1 hr. The reaction mixture was warmed to 25° and the solvent and amine were removed under vacuum being careful to avoid exposure

to the air. The resulting solid was dissolved in 80 mL of THF under an argon atmosphere and the solution was cooled to -78° . To this solution was added .178 mL (2.2 mmoles) of methyl vinyl ketone in 5 mL of THF over a 5 min period. The reaction mixture was stirred 2 hr at -78° and 12 hr at 25° . Water and ether were then added to the reaction mixture and the aqueous solution was extracted with ether. The combined ether extracts were washed three times with a 1 M HCl solution, once each with a water and a saturated sodium sulfate solution and finally dried over MgSO_4 . Removal of the solvent yielded .364 g of a yellow oil. Dione 29 (.310 g, 75%) was obtained as a white solid, mp $51-53^{\circ}$, by Kugelrohr distillation (110° , 5 microns). An analytical sample obtained by preparative glpc (4% QF-1, 190°) exhibited the following properties: ir (CCl_4) 1725 cm^{-1} ; pmr (CDCl_3) δ 2.8-2.25 (m, 2H), 2.15 (s, 3H), 1.95-1.30 (m, 6H) 1.15 (s, 3H), 1.0 (s, 3H), 0.9 (s, 3H); mass spectrum (70 eV) m/e (rel intensity) 208(15)P, 193(18), 138(28), 123(100).

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

Found: C, 74.91; H, 9.75.

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3'-Oxo-6-butyl-2,3-dimethylcyclohex-
2-enone (30)

To a stirred solution of 22 mmoles of LDA in 200 mL of THF, prepared by the usual manner, at -78° under an argon atmosphere was added a solution of 2.48 g (20 mmoles) of 2,3-dimethylcyclohexenone in 50 mL of THF dropwise over a 10 min period and the resulting solution was stirred at -78° for 1 hr. The reaction mixture was warmed to 25° , and the solvent and amine were removed under vacuum being careful to avoid exposure to the air. The resulting solid was dissolved in 400 ml of THF under an argon atmosphere and the solution was cooled to -78° . To this solution was added 1.80 mL (22 mmoles) of freshly distilled methyl vinyl ketone in 100 mL of THF over a 10 min period. The resulting mixture was stirred 3 hr at -78° and 12 hr at rm temperature. Water and ether were then added to the reaction mixture and the aqueous solution was extracted with ether. The combined ether extracts were washed three times with a 1 M HCl solution, once each with a water and a saturated sodium sulfate solution and finally dried over MgSO_4 . Removal of the solvent yielded 2.8 g of a yellow oil. Kugelrohr distillation (100° , 5 microns) of the oil afforded 2.41 g (60%) of dione 30 as a colorless oil which exhibited the following properties: Uv (95% EtOH) 245 nm ($\epsilon = 8,200$); ir (CCl_4) 1720 cm^{-1} , 1660 cm^{-1} ; pmr (CCl_4) δ 2.7-2.2 (m, 6H), 2.1 (s, 3H), 1.85

(bs,4H), 1.70 (d,4H) 0.9 (m,1H); mass spectrum (70 eV) m/e (rel intensity) 194(3)P, 137(41), 124(19), 96(100).

Anal. Calcd. for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34.

Found: C, 74.19; H, 9.20.

9,10-Dimethylbicyclo[4.4.0]deca-
2,9-diene-3-one (31)

To a stirred solution of .560 g (5 mmoles) of potassium t-butoxide and 5 mL of t-butyl alcohol in 80 mL of THF at 25° was added a solution of .388 g (2 mmoles) of dione 30 in 5 mL of THF. After stirring for 2 days at 25°, water and ether were added and the aqueous phase was extracted with ether. The combined ether extracts were washed twice with a 1 M HCl solution, once each with water and a saturated sodium sulfate solution and finally dried over $MgSO_4$. Removal of the solvent afforded .323 g (91%) of dienone 31 as an oil. An analytical sample obtained by preparative glpc (4% QF-1, 190°) exhibited the following properties: Uv (EtOH) λ_{max} 291 nm ($\epsilon = 19,600$; ir ($CHCl_3$) 1650 cm^{-1} , 1620 cm^{-1} ; pmr (CCl_4) δ 5.5 (bs,1H), 2.4-2.0 (m,7H) 1.8 (m,8H); mass spectrum (70 eV) m/e (rel intensity) 177(7)P+1, 176(56)P, 133(30), 105(100).

Anal. Calcd. for $C_{12}H_{16}O$: C, 81.77; H, 9.00

Found: C, 81.77; H, 9.00

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5-Carboxy-4,7,7-trimethylbicyclo-
[2.2.2]octan-2-one (34)

To 2.98 g (13.19 mmoles) of keto-ester 21 was added 100 mL of ten percent aqueous sodium hydroxide, and this solution was stirred for 5 hr at 25° (until homogeneous). After acidification with 6 M HCl solution, the solution was extracted three times with ether, and the combined extracts were washed with water and saturated sodium sulfate solution and finally dried over MgSO₄. Removal of the solvent gave 2.26 g (82%) of a solid. Recrystallization from hexane and ethyl acetate afforded keto acid 34 which exhibited the following properties: mp 148-150°, ir (CDCl₃) 3300-3000 cm⁻¹, 1720 cm⁻¹; pmr (CDCl₃) δ 9.6 (bs, 1H), 2.9-1.3 (m, 8H), 1.1 (s, 3H), 1.05 (s, 3H), 0.90 (s, 3H); mass spectrum (70 eV) m/e (rel intensity) 210(7)P, 138(35), 123(100).

5-Chloroformyl-4,7,7-trimethylbicyclo-
[2.2.2]octan-2-one (35)

To a stirred solution of 2.0 g (8.77 mmoles) of keto-acid 34 and 10 g of lithium chloride in 200 mL of CHCl₃ was added 20 mL of thionyl chloride. After stirring for 3 days at 25° under an argon atmosphere, the reaction was filtered, and removal of solvent from the filtrate afforded 1.78 g (89%) of acid chloride 35 as a solid. Recrystallization from CHCl₃ afforded 35 as a white solid which exhibited the

following properties: mp 63-65°; ir (CDCl₃) 1795 cm⁻¹, 1725 cm⁻¹; pmr (CDCl₃) δ 2.5-1.2 (m, 8H) 1.10 (s, 3H), 1.05 (s, 3H), 0.90 (s, 3H); mass spectrum (70 eV) m/e (rel intensity) 230(4)P+2, (228)P, 165(20), 138(28), 123(100).

Preparation of Dione 29 From Acid Chloride 35

To a stirred solution of 1.17 g (6 mmoles) of cuprous iodide in 80 mL of ether at -78° under an argon atmosphere was added 7.05 mL (12 mmoles) of a 1.7 M methyllithium in ether solution. The resulting reaction mixture was stirred for 20 min, following which a solution of .448 g (2 mmoles) of acid chloride 35 in 5 mL of ether was added. The reaction mixture was then stirred for 4 hr, followed by the addition of 1 ml of acetic acid.

After warming to 25°, water and ether were added and the aqueous phase was extracted three times with ether. The combined ether extracts were washed three times with a buffered ammonium hydroxide solution (pH 9), once each with water and a saturated sodium sulfate solution and finally dried over MgSO₄. Removal of solvent afforded 1.70 g (85%) of an oil which was homogeneous by glpc (4% QF-1, 160°). An analytical sample obtained by glpc (4% QF-1, 190°) exhibited the identical gas chromatographic and spectral properties as dione 29.

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5-Carboxy-3,4-dimethylbicyclo-
[2.2.2]octan-2-one (36)

To 1.71 g (8.14 mmol) of keto-ester 24 was added 100 mL of ten percent aqueous sodium hydroxide, and this solution was stirred for 6 hr at 25° (until homogeneous). After acidification with 6 M hydrochloric acid, the solution was extracted three times with ether, and the combined extracts were washed with water and saturated sodium sulfate and dried over MgSO₄. Removal of the solvent gave 1.30 g (82%) of a solid. Recrystallization from hexane and ethyl acetate afforded keto-acid 36 which exhibited the following properties: mp 112-115°, ir (CDCl₃) 3300-3000 cm⁻¹, 1720 cm⁻¹; pmr (CDCl₃) δ 8.0 (bs, 1H), 2.9-1.5 (m, 8H), 1.2-1.0 (m, 7H); mass spectrum (70 eV) m/e (rel intensity), 196 (9)P, 124 (100).

5-Chloroformyl-3,4-dimethylbicyclo-
[2.2.2]octan-2-one (37)

To a stirred solution of 1.58 g (8.5 mmol) of keto-acid 36 and 5 gm of lithium chloride was added 25 mL of thionyl chloride. After stirring for 4 days at 25° under an argon atmosphere, the reaction mixture was filtered, and removal of solvent from the filtrate afforded 1.69 g (89%) of acid chloride 37 as an oil which was homogeneous by glpc (4% QF-1, 160°). An analytical sample obtained by preparative glpc (4% QF-1, 190°) exhibited the following properties:

ir (CDCl₃) 1795 cm⁻¹, 1725 cm⁻¹; pmr (CDCl₃) δ 3.1-1.3 (m, 9H), 1.1 (s, 3H), 1.0 (d, 3H); mass spectrum (70 eV) m/e (rel intensity) 216(1)P+2, 214(2)P, 178(46), 124(37), 79(100).

5-Acetyl-3,4-dimethylbicyclo-
[2.2.2]octan-2-one (38)

To a stirred solution of 11.76 g (60 mmoles) of cuprous iodide in 400 mL ether at -78° under an argon atmosphere was added 70.5 mL (120 mmoles) of a 1.7 M methyllithium in ether solution. The resulting reaction mixture was stirred for 20 min, following which a solution of 4.28 g (20 mmoles) of acid chloride 37 in 50 mL of ether was added. The reaction mixture was then stirred for 4 hr, following which 2 mL of acetic acid was added. After warming to 25°, water and ether were added and the aqueous phase was extracted three times with ether. The combined ether extracts were washed three times with a buffered ammonium hydroxide solution (pH 9), once each with water and saturated sodium sulfate solution and finally dried over MgSO₄. Removal of the solvent afforded 2.00 g (52%) of dione 38 as an oil which was homogeneous by glpc (4% QF-1, 160°). An analytical sample obtained by preparative glpc (4% QF-1, 190°) exhibited the following properties: ir (CCl₄) 1720 cm⁻¹; pmr (CCl₄) δ 2.8-2.1 (m, 2H), 2.05 (s, 3H), 2.0-1.1 (m, 7H),

1.00 (s,1H), 0.90 (s,3H), 0.80 (d,3H); mass spectrum (70 eV) m/e (rel intensity) 194(20)F, 124(100).

Anal. Calcd. for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34.

Found: C, 74.17; H, 9.21.

Treatment of Dione 38 with Base

To a stirred solution of .560 g (5 mmoles) of potassium t-butoxide and 5 mL of t-butyl alcohol in 80 mL of THF at 25° was added a solution of .776 g (4 mmoles) of dione 38 in 5 mL of THF. After stirring at 25° for 2 days, water and ether were added and the aqueous phase was extracted with ether. The combined ether extracts were washed twice with a 1 M HCl solution, once each with water and a saturated sodium sulfate solution and finally dried over $MgSO_4$. Removal of the solvent afforded .437 g (62%) of an oil. An analytical sample collected by preparative glpc exhibited the identical spectral and gas chromatographic properties of dione 31.

Treatment of Dione 29 with Base

To a stirred solution of .560 g (5 mmoles) of potassium t-butoxide and 5 mL of t-butyl alcohol in 80 mL of THF at 25° was added a solution of .194 g (1 mmole) of dione 29 in 5 mL of THF. After stirring at 25° for 2 days, water and

ether were added and the aqueous phase was extracted with ether. The combined ether extracts were washed twice with a 1 M HCl solution, once each with water and a saturated sodium sulfate solution and finally dried over MgSO_4 . Removal of the solvent gave .139 g (77%) of an oil which showed two products, dione 29 and the epimer of dione 29 (ratio 9:1). An analytical sample of the major product obtained by preparative glpc (4% QF-1, 190°) exhibited the identical spectral and gas chromatographic properties as dione 29.

3-Methylcyclohex-2-enone

To a stirred solution of 4.90 g (35 mmol) of 3-ethoxy-2-cyclohexenone in 100 mL of ether under an argon atmosphere at 25° was added 25 mL (40 mmol) of 1.6 M methyl-lithium in ether. After 24 hr, the reaction mixture was poured into an ice and water mixture. The aqueous phase was extracted with ether and the combined ether extracts were washed three times with a 1 M HCl solution, once each with water and a saturated sodium sulfate solution and finally dried over MgSO_4 . Removal of the solvent afforded 2.69 g (70%) of crude 2-methylcyclohexenone. Distillation through a short-path still gave 2.11 g of colorless 3-methylcyclohexenone which exhibited the following properties: bp 98-100° (7 mm) (lit. bp 99.5-98 (8.0 mm)]²⁶;

ir (liquid film) 1675 cm^{-1} , 1640 cm^{-1} ; pmr (CDCl_3) δ 5.7 (m,1H), 2.4-2.0 (m,6H), 1.9 (s,1H); mass spectrum (70 eV) m/e (rel intensity) 110(37)P, 82(100).

3-Ethoxy-2-methylcyclohexenone

To a solution of 400 mL of toluene and 200 mL of absolute ethanol containing 3.0 gm of para-toluenesulfonic acid was added 37.8 g (0.3 moles) of 2-methylcyclohexane-1,3-dione, and the resulting mixture was refluxed for 18 hr through a Dean-Stark water trap. After cooling, the reaction mixture was washed with four 100 mL portions of ten percent aqueous sodium hydroxide which had been saturated with sodium chloride. The resulting organic solution was washed with successive 50 ml portions of water until the aqueous washings were neutral. Removal of the solvent afforded an oil which was purified by vacuum distillation to yield 14.4 g (31%) of a clear oil which exhibited the following properties: bp 80° , .300 mm; ir (CCl_4) 1665 cm^{-1} , 1630 cm^{-1} ; pmr (CCl_4) δ 4.0 (q,2H), 2.7-1.6 (m,6H), 1.45 (s,3H), 1.35 (t,3H); mass spectrum (70 eV) m/e (rel intensity) 155(6)P+1, 154(53)P, 110(42), 98(100).

2-Methylcyclohex-2-enone

To a stirred solution of .910 g (24 mmoles) of lithium aluminum hydride (LAH) in 300 mL of dry ether was added dropwise a solution of 14 g (92.5 mmoles) of 3-ethoxy-2-methylcyclohexenone in 100 mL of ether. The reaction mixture was refluxed for 24 hr, cooled and then carefully poured into a water and ice mixture which was acidified to a pH of two with 1 M HCl solution. The aqueous phase was extracted with ether, and the combined ether were washed three times with 1 M HCl solution and once each with water and a saturated sodium sulfate solution and finally dried over MgSO_4 . Removal of the solvent gave 8.5 g (82%) of an oil. Distillation through a short-path still afforded 7.4 gm of colorless 2-methylcyclohexenone which exhibited the following properties: bp. 57-60 (10 mm) [Lit. bp. 56 (9 mm)]²⁷; ir (liquid film) 1680 cm^{-1} ; pmr (CCl_4) δ 6.7 (bs, 1H), 2.5-1.8 (m, 6H), 1.65 (s, 3H); mass spectrum (70 eV) m/e (rel intensity) 110(37)P, 82(100).

5-Carbomethoxy-4-methylbicyclo-
[2.2.2]octan-2-one (39)

To a stirred solution of 5.5 mmoles of LDA in 80 mL of THF, prepared by the usual manner, at -23° under an argon atmosphere was added a solution of .550 g (5.0 mmoles) of

3-methylcyclohex-2-enone in 5 mL of THF dropwise to the reaction mixture over a 10 min period. The resulting mixture was stirred at -23° for 1 hr, following which a solution of .550 mL (6.0 mmoles) of methyl acrylate in 5 mL of THF was added dropwise over a 5 min period. After stirring for 2 hr at -23° , water and ether were added to the reaction mixture and the aqueous phase was extracted with ether. The combined ether extracts were washed three times with a 1 M HCl solution, once each with water and a saturated sodium sulfate solution and finally dried over MgSO_4 . Removal of the solvent gave .879 g (98%) of keto-ester 39 as a yellow oil which was homogeneous by glpc (4% QF-1, 130°). An analytical sample obtained by preparative glpc (4% QF-1, 190°) exhibited the following properties: ir (CDCl_3) 1725 cm^{-1} , 1175 cm^{-1} ; pmr (CDCl_3) δ 3.6 (s, 3H), 2.9-1.3 (m, 10H), 0.95 (s, 3H); mass spectrum (70 eV) m/e (rel intensity) 196(11)P, 110(100).

Anal. Calcd. for $\text{C}_{11}\text{H}_{16}\text{O}_3$: C, 67.32; H, 8.22.

Found: C, 67.44; H, 8.31.

5-Acetyl-4-methylbicyclo[2.2.2]-
octan-2-one (40)

To a stirred solution of 2.2 mmoles of LDA in 40 mL of THF, prepared by the usual manner, at -78° under argon was added a solution of .220 gm (2.0 mmoles) of 3-methylcyclohex-2-enone in 5 mL of THF over a 10 min period and the

resulting solution was stirred at -78° for 1 hr. The reaction mixture was warmed to 25° and the solvent and amine were removed under vacuum being careful to avoid exposure to air. The resulting solid was dissolved in 80 mL of THF under an argon atmosphere and was cooled to -78° . To this reaction mixture was added .180 mL (2.2 mmol) of methyl vinyl ketone in 10 mL of THF over a 10 min period. The resulting mixture was stirred 3 hr at -78° and 12 hr at 25° . Water and ether were then added to the reaction mixture and the aqueous solution was extracted with ether. The combined ether extracts were washed three times with a 1 M HCl solution, once each with a water and a saturated sodium sulfate solution and finally dried over MgSO_4 . Removal of the solvent gave .262 g (73%) of dione 40 as a pale yellow oil which was homogeneous by glpc (4% QF-1, 160°). An analytical sample obtained by preparative glpc (4% QF-1, 190°) exhibited the following characteristics: ir (CCl_4) 1735 cm^{-1} ; pmr (CCl_4) δ 2.8-2.2 (m, 3H), 2.1 (s, 3H), 2.0-1.2 (m, 7H), 0.95 (s, 3H); mass spectrum (70 eV) m/e (rel intensity) 180(49)P, 110(100).

Anal. Calcd. for $\text{C}_{11}\text{H}_{16}\text{O}_2$: C, 73.30; H, 8.95.

Found: C, 73.33; H, 8.93.

5-Carbomethoxy-3-methylbicyclo-
[2.2.2]octan-2-one (41)

To a stirred solution of 2.2 mmoles of LDA in 80 mL of THF, prepared by the usual manner, at -78° under an argon atmosphere was added a solution of .220 g (2.0 mmoles) of 2-methylcyclo-hex-2-enone in 5 mL of THF dropwise to the reaction mixture over a 10 min period. The resulting mixture was stirred at -23° for 1 hr, following which a solution of .210 mL (2.4 mmoles) of methyl acrylate in 5 mL of THF was added dropwise over a 5 min period. The reaction mixture was stirred for 2 hr at -23° . Water and ether were added to the reaction mixture and the aqueous phase was extracted with ether. The combined ether extracts were washed three times with a 1 M HCl solution, once each with water and a saturated sodium sulfate solution and finally dried over MgSO_4 . Removal of the solvent gave .315 g (81%) of keto-ester 41 as a pale yellow oil which was a mixture of C-3 epimers by glpc (4% QF-1, 160°). An analytical sample obtained by preparative glpc (4% QF-1, 190°) exhibited the following properties: ir (CDCl_3) 1730 cm^{-1} , 1250 cm^{-1} , 1150 cm^{-1} ; pmr (CDCl_3) δ 3.65 (s, 3H), 2.8-0.90 (m, 13H); mass spectrum (70 eV) m/e (rel intensity) 196(20)P, 110(100).

Anal. Calcd. for $\text{C}_{11}\text{H}_{16}\text{O}_3$: C, 67.32; H, 8.22.

Found: C, 67.34; H, 8.18.

5-Acetyl-3-methylbicyclo[2.2.2]-
octan-2-one (42)

To a stirred solution of 2.2 mmoles of LDA in 40 mL of THF, prepared by the usual manner, at -78° under an argon atmosphere was added a solution of .220 g (2.0 mmoles) of 2-methylcyclohexenone in 5 mL of THF dropwise to the reaction mixture over a 10 min period. After stirring for 1 hr at -78° , the reaction was warmed to 25° and the solvent and amine were removed under vacuum being careful to avoid exposure to air. The resulting solid was dissolved in 80 mL of THF under an argon atmosphere and the solution was cooled to -78° . To this solution was added .180 mL (2.2 mmoles) of methyl vinyl ketone in 10 mL of THF over a 10 min period. The resulting mixture was stirred 2 hr at -78° and 12 hr at 25° . Water and ether were then added to the reaction mixture and the aqueous solution was extracted with ether. The combined ether extracts were washed three times with a 1 M HCl solution, once each with a water and a saturated sodium sulfate solution and finally dried over MgSO_4 . Removal of the solvent gave .308 g (81%) of dione 42 as a pale yellow oil. Glpc analysis (4% QF-1, 160°) showed a mixture of epimers and starting material (9:1). An analytical sample obtained by preparative glpc (4% QF-1, 190°) exhibited the following properties: ir (CCl_4) 1730 cm^{-1} ; pmr (CCl_4) δ 2.8-2.2 (m, 3H), 2.15 (s, 3H), 2.0-1.0

(m,10H); mass spectrum (70 eV) m/e (rel intensity)
181(6)P+1, 180(44)P, 110(100).

Anal. Calcd. for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95.

Found: C, 73.12; H, 8.97.

5-Hydroxymethyl-4,7,7-trimethylbicyclo-
[2.2.2]octan-2-ol (46)

To a stirred solution of .228 g (6 mmoles) of LAH in 300 mL of ether at 25° was added dropwise a solution of 1.12 g (5 mmoles) of keto-ester 21 in 15 mL of ether. The reaction mixture was refluxed for 24 hr, cooled and then carefully poured into a water and ice mixture which was acidified to a pH of two with 1 M HCl solution, the aqueous phase was extracted with ether and the combined ether extracts were washed twice with water, once with a saturated sodium sulfate solution and finally dried over $MgSO_4$. Removal of the solvent afforded .894 g (89%) of a white solid, mp 135°. Recrystallization from acetone gave diol 46 which exhibited the following properties: mp 137°; ir (nujoil) 3240 cm^{-1} , 1170 cm^{-1} , 1025 cm^{-1} ; pmr (D_6 -acetone) δ 3.45 (d,2H), 3.14 (m,1H), 2.78 (s,2H, disappears with D_2O), 1.4-1.0 (m,7H), 0.9 (s,3H), 0.8(s,3H); mass spectrum (70 eV) m/e (rel intensity) 198(3)P, 180(35), 180(30), 93(100).

Anal. Calcd. for $C_{12}H_{22}O_2$: C, 72.68; H, 11.13.

Found: C, 72.80; H, 11.13.

5-Formyl-4,7,7-trimethylbicyclo-
[2.2.2]octan-2-one (47)

To a mechanically stirred solution of .537 g (2.5 mmoles) of pyridinium chlorochromate in 100 mL of CH_2Cl_2 at 25° was added a solution of .198 g (1 mmole) of diol 46 in 20 mL of CH_2Cl_2 . After 3 hr, 50 mL of ether was added and the superatant was decanted from the black gum. The insoluble residue was washed three times throughly with 50 mL portions of ether whereupon it became a black granular solid. The combined organic solution was passed through a short pad of florisel and was washed with 30 mL portions of a solution of 5 mL of acetyl acetone in 300 mL of a 20% sodium hydroxide solution and twice with water, once with saturated sodium sulfate solution and finally dried over MgSO_4 . Removal of the solvent gave .165 g (84%) of keto-aldehyde 47 as an oil which was homogeneous by glpc (4% QF-1, 160°). An analytical sample collected by glpc (4% QF-1, 190°) exhibited the following properties: ir (CCl_4) 2855 cm^{-1} , 2700 cm^{-1} , 1730 cm^{-1} ; pmr (CCl_4) δ 9.5 (s, 1H), 2.5(bs, 2H), 1.9-1.5 (m, 5H), 1.1 (s, 4H), 0.9 (s, 4H); mass spectrum (70 eV) m/e (rel intensity) 194(4)P, 180(10) impurity, 179(17), 138(38), 123(100).

5-(1'-hydroxyallyl)-4,7,7-trimethylbicyclo-
[2.2.2]octan-2-one (48)

To a stirred solution of .194 g (1.0 mmole) of keto-aldehyde 47 in 100 mL of THF at 25° was added dropwise 1.25 mL (3 mmoles) of 2.4 M vinyl magnesium bromide in THF. After 3 hr, the reaction mixture was poured into an ice and water mixture. The aqueous phase was extracted with ether and the combined ether extracts were washed twice with water, once with a saturated sodium sulfate solution and finally dried over MgSO₄. Removal of the solvent gave .200 g (90%) of hydroxyketone 48 as a yellow oil, which was homogeneous by glpc (4% QF-1, 190°). An analytical sample obtained by preparative glpc (4% QF-1, 190°) exhibited the following properties: ir (CHCl₃) 3600 cm⁻¹, 3460 cm⁻¹, 1720 cm⁻¹; pmr (CDCl₃) δ 6.1-5.5 (vinyl, 3H), 4.5 (bs, 1H), 2.0-1.5 (m, 6H), 1.3 (m, 3H), 1.1 (s, 6H), 0.9 (s, 3H); mass spectrum (70 eV) m/e (rel intensity) 222(2)P, 204(4), 138(30), 123(100).

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

Found: C, 75.75; H, 9.89.

8-Acryloyl-4,7,7-trimethylbicyclo-
[2.2.2]octan-2-one (49)

To a mechanically stirred solution of 30 g of manganese dioxide in 400 mL of CH₂Cl₂ at 25° was added 3.0 g (13.6 mmoles) of hydroxyketone 48 in 30 mL of CH₂Cl₂. After 24 hr,

100 mL of ether was added and the supernatant was decanted from the brown residue. The insoluble residue was then washed three times with ether and the combined organic solution was passed through a short pad of celite and finally dried over MgSO_4 . Removal of the solvent yielded 2.31 g (78%) of dione 49 as a yellow oil which was homogeneous by glpc (4% QF-1, 190°). An analytical sample obtained by preparative glpc (4% QF-1, 190°) exhibited the following properties: ir (CCl_4) 1725 cm^{-1} , 1675 cm^{-1} ; pmr (CCl_4) δ 6.3-5.5 (vinyl, 3H), 2.8-1.2 (m, 10H), 1.1 (s, 3H), 0.95 (s, 3H); mass spectrum (70 eV) m/e (rel intensity) 221(5)P+1, 220(34)P, 138(59), 55(100).

Anal. Calcd. for $\text{C}_{14}\text{H}_{20}\text{O}_2$: C, 76.33; H, 9.15.

Found: C, 76.22; H, 9.09.

5-Hydroxymethyl-3,4-dimethylbicyclo-
[2.2.2]octan-2-ol (50)

To a stirred solution of .36 g (9.5 mmoles) of LAH in 300 mL of ether at 25° was added dropwise a solution of 1.79 g (8.5 mmoles) of keto-ester 24 in 50 mL of ether. The reaction mixture was refluxed for 24 hr under an argon atmosphere, cooled and then carefully poured into a water and ice mixture which was acidified to a pH of two with 1 M HCl solution. The aqueous phase was extracted with ether and the combined ether extracts were washed twice with

water, once with a saturated sodium sulfate solution and finally dried over MgSO_4 . Removal of the solvent gave 1.35 g (86%) of diol 50 as a white solid, mp 183-186°. An analytical sample obtained by preparative glpc (4% QF-1, 190°) exhibited the following properties: ir (CHCl_3) 3600 cm^{-1} , 3400 cm^{-1} ; pmr (D_6 -acetone) δ 3.6 (m, 3H), 2.8 (s, 2H), 1.9-1.2 (m, 7H), 1.05-0.9 (m, 6H); mass spectrum (70 eV) m/e (rel intensity): 184(1)P, 108(100).

Anal. Calcd. for $\text{C}_{11}\text{H}_{20}\text{O}_2$: C, 70.92; H, 11.90.

Found: C, 71.61; H, 11.01.

5-Formyl-3,4-dimethylbicyclo-
[2.2.2]octan-2-one (51)

To a mechanically stirred solution of 14.8 g (69 mmoles) of pyridinium chlorochromate in 300 mL of CH_2Cl_2 at 25° was added a solution of 3.18 g (17.3 mmoles) of diol 50 in 30 mL of CH_2Cl_2 . After 5 hr, 50 mL of ether was added and the supernatant was decanted from the black gum. The insoluble residue was washed three times thoroughly with 100 ml portions of ether whereupon it became a black granular solid. The combined organic solution was passed through a short pad of florisil and was washed with a solution of 5 mL of acetyl acetone in 300 mL of a 20% sodium hydroxide solution and twice with water, once with saturated sodium sulfate and finally dried over MgSO_4 . Removal of the

solvent gave 2.08 g (67%) of a yellow oil. Further purification by Keigelrohr distillation (85°, 5 microns) afforded 51 as a clear liquid, ir (CCl₄) 2930 cm⁻¹, 1720 cm⁻¹, 1690 cm⁻¹; pmr (CDCl₃) δ 9.85 (d, 1H), 2.8-1.6 (m, 9H), 1.4-0.9 (m, 6H); mass spectrum (70 eV) m/e (rel intensity) 180(35)P, 124(100).

Anal. Calcd. for C₁₁H₁₆O₂: C, 73.30; H, 8.95.

Found: C, 73.29; H, 8.97.

5-(1'-Hydroxyallyl)-3,4-dimethyl-2-vinyl-
bicyclo[2.2.2]octan-2-ol (53)

To a stirred solution of 2.08 g (11.55 mmoles) of keto-aldehyde 51 in 100 mL of THF at 25° was added 9.2 mL (22 mmoles) of 2.4 M vinyl magnesium bromide in THF. After 5 hr, the reaction was poured into an ice-water mixture. The aqueous phase was extracted with ether and the combined ether extracts were washed twice with water and once with a saturated sodium sulfate solution and finally dried over MgSO₄. Removal of solvent gave 2.41 g (88%) of diol 53 as an oil which was homogeneous by glpc (4% QF-1, 160°). An analytical sample obtained by preparative glpc (4% QF-1, 190°) exhibited the following property: mass spectrum (70 eV) m/e (rel intensity) 236(1)P, 218(1), 124(23), 85(100).

5-Acryloyl-3,4-dimethyl-2-vinylbicyclo-
[2.2.2]octan-2-ol (54)

To a stirred solution of 25 g of manganese dioxide in 400 mL of CH_2Cl_2 at 25° was added 2.36 g (10 mmoles) of diol 53 in 30 mL of CH_2Cl_2 . After 24 hr, 100 mL of ether was added and the supernatant was decanted from the brown residue. The insoluble residue was then washed three times with ether and the combined organic solution was passed through a short pad of celite and finally dried over MgSO_4 . Removal of the solvent yielded 2.12 g (91%) of an oil which contained hydroxy ketone 54 and ~5% starting material as shown by glpc (4% QF-1, 160°). An analytical sample obtained by preparative glpc (4% QF-1, 190°) exhibited the following properties: ir (CCl_4) 3220 cm^{-1} , 1725 cm^{-1} ; pmr (CCl_4) δ 6.4-4.4 (m, 6H), 4.1 (m, 1H), 2.8-1.9 (m, 9H) 1.0-0.8 (m, 6H); mass spectrum (70 eV) m/e (rel intensity) 234(1)P, 219(4), 206(10), 124(22), 41(100).

3-t-Butyldimethylsilyloxy-1,2-dimethyl-
cyclohexa-1,3-diene (55)

To a stirred solution of 55.5 mmoles of LDA, prepared in the usual manner, in 300 mL of THF at -78° under an argon atmosphere was added a solution of 6.2 g (50 mmoles) of 2,3-dimethylcyclohexenone in 100 mL of THF dropwise over a 10 min period. The reaction mixture was stirred for 1 hr and then 5 mL of HMPA was added. After the reaction mixture

warmed to 0°, a solution of 10.5 g (70 mmol) of t-butyldimethylchlorosilane in 100 mL of THF was added over a 10 min period. The reaction mixture was stirred for 18 hr at 25°, water and ether were then added and the aqueous phase was extracted with ether. The combined ether extracts were washed three times with water and once with a saturated sodium sulfate solution and finally dried over MgSO₄. Removal of the solvent gave a clear oil. Purification by vacuum distillation (123°, 6mm) yielded 10.0 g (88%) of dienol ether 55 as a clear oil with the following properties: ir (neat) 1645 cm⁻¹, 1620 cm⁻¹; pmr (CCl₄) δ 4.6 (bs, 1H), 2.1-1.6 (m, 10H), 0.95 (s, 9H), 0.20 (s, 6H); mass spectrum (70 eV) m/e (rel intensity) 238(5)P, 236(5), 75(100).

Anal. Calcd. for C₁₄H₂₆OSi: C, 70.52; H, 10.99

Found: C, 70.47; H, 10.84.

1,2-Dimethyl-3-trimethylsilyloxy-
cyclohexa-1,3-diene (56)

To a stirred solution of 55.5 mmol of LDA, prepared in the usual manner, in 300 mL of THF at -78° under an argon atmosphere, was added a solution of 6.2 g (50 mmol) of 2,3-dimethylcyclohexenone in 100 mL of THF dropwise over a 10 min period. The reaction mixture was stirred for 1 hr and then 5 mL of HMPA was added. After the reaction mixture warmed to 0°, a solution of 12.6 mL (100 mmol) of trimethylchlorosilane in 100 mL of THF was added over a 10 min

period. The reaction mixture was stirred for 18 hr at 25°, water and ether were then added and the aqueous phase was extracted with ether. The combined ether extracts were washed three times with water and once with a saturated sodium sulfate solution and finally dried over MgSO_4 . Removal of the solvent gave a clear oil. Purification by vacuum distillation (104°, 7 mm) yielded 8.58 g (87%) of ether 56 as a clear oil with the following properties: ir (neat) 1640 cm^{-1} , 1620 cm^{-1} ; pmr (CCl_4) δ 4.75 (bs, 1H), 2.05 (m, 4H), 1.7 (m, 6H), 0.20 (s, 9H); mass spectrum (70 eV) m/e (rel intensity) 198(5)P, 196(59), 73(100).

Anal. Calcd. for $\text{C}_{11}\text{H}_{20}\text{OSi}$: C, 67.28; H, 10.26.

Found: C, 67.17; H, 10.07.

5-Acetyl-2-t-butyltrimethylsilyloxy-3,4-dimethyl-
bicyclo[2.2.2]oct-2-ene (57)

To a stirred solution of 2.38 g (10 mmoles) of dienol ether 55 in 200 mL of toluene containing ~10 mg of hydroquinone was added 1.62 mL (20 mmoles) of methyl vinyl ketone. This reaction mixture was refluxed for 24 hr under an argon atmosphere. Removal of the solvent afforded 2.84 g (92%) of ketone 57 as an oil which was homogeneous by glpc (4% QF-1, 100°). An analytical sample obtained by preparative glpc (4% QF-1, 190°) exhibited the following properties: ir (CCl_4) 1700 cm^{-1} , 1650 cm^{-1} ; pmr (CCl_4) δ 2.5-2.0 (m, 3H),

1.95 (s, 3H), 1.8-1.2 (m, 8H), 1.1 (s, 3H), 0.9 (s, 9H), 0.2 (bs, 6H); mass spectrum (70 eV) m/e (rel intensity) 308(8)P, 238(15), 75(100).

Anal. Calcd. for $C_{18}H_{32}O_2Si$: C, 70.07, H, 10.45.

Found: C, 70.07; H, 10.38.

From a pmr experiment using EuFOD, 57 was found to be epimeric at C-5 (ratio; syn:anti, 80:20).

2-t-Butyldimethylsilyloxy-3,4-dimethyl-5-formyl-
bicyclo[2.2.2]oct-2-ene (58)

To a stirred solution of 2.38 g (10 mmoles) of dienol ether 55 in 200 ml of toluene containing ~10 mg of hydro-Quinone was added 1.34 mL (20 mmoles) of acrolein. This reaction was refluxed for 23 hr under an argon atmosphere. Removal of solvent afforded 2.90 g (98%) of aldehyde 58 as an oil which was homogeneous by glpc (4% QF-1, 100°). An analytical sample obtained by preparative glpc (4% QF-1, 190°) exhibited the following properties: ir (neat) 1730 cm^{-1} , 1680 cm^{-1} ; pmr ($CDCl_3$) δ 9.1 (d, 1H), 2.4-1.3 (m, 11H), 1.2 (m, 3H), .9 (bs, 9H), 0.2 (m, 6H); mass spectrum (70 eV) m/e (rel intensity) 294(6), 238(31), 75(100).

From a pmr experiment using EuFOD, 58 was found to be epimeric at C-5 (ratio; syn:anti, 80:20).

2-t-Butyldimethylsilyloxy-5-cyano-3,4-dimethyl-
bicyclo[2.2.2]oct-2-ene (59)

To a stirred solution of 2.38 g (10 mmoles) of dienol ether 55 in 200 mL of toluene containing ~10 mg of hydroquinone was added 1.30 mL (20 mmoles) of acrylonitrile. This reaction mixture was refluxed for 24 hr under an argon atmosphere. Removal of the solvent afforded 2.36 g (81%) of nitrile 59 as an oil which was homogeneous by glpc (4% QF-1, 100°). An analytical sample obtained by preparative glpc (4% QF-1, 190°) exhibited the following properties: ν (neat) 2225 cm^{-1} , 1670 cm^{-1} ; pmr (CCl_4) δ 2.5-1.5 (m, 10H), 1.3 (m, 6H), 0.9 (d, 9H), 0.1 (d, 6H); mass spectrum (70 eV) m/e (rel intensity) 291(30)P, 238(44), 182(100), 75(85).

Anal. Calcd. for $\text{C}_{17}\text{H}_{29}\text{OSiN}$: C, 70.04; H, 10.02

Found: C, 70.03; H, 10.03.

From a pmr experiment 59 was found to be epimeric at C-5 (ratio; syn:anti, 50:50).

2-t-Butyldimethylsilyloxy-5-carbomethoxy-3,4-
dimethylbicyclo[2.2.2]oct-2-ene (60)

To a stirred solution of 2.38 g (10 mmoles) of dienol ether 55 in 200 mL of toluene containing ~10 mg of hydroquinone was added 1.80 mL (20 mmoles) of methyl acrylate. This reaction mixture was refluxed for 24 hr under an argon atmosphere. Removal of the solvent afforded 3.20 g (95%)

of 60 as an oil which was homogeneous by glpc (4% QF-1, 100°). An analytical sample obtained by preparative glpc (4% QF-1, 190°) exhibited the following properties: ir (CCl₄) 1735 cm⁻¹, 1660 cm⁻¹; pmr (CCl₄) δ 3.5 (d, 3H), 2.3-1.0 (m, 14H), 0.9 (s, 9H), 0.1 (d, 3H); mass spectrum (70 eV) m/e (rel intensity) 325(8)P+1, 324(28)P, 238(59), 182(100).

From a pmr experiment using EuFOD, 60 was found to be epimeric at C-5 (ratio; syn:anti, 70:30).

5-Acetyl-3,4-dimethyl-2-trimethylsilyloxybicyclo-
[2.2.2]oct-2-ene (61)

To a stirred solution of .880 g (5 mmoles) of dienol ether 56 in 200 mL of toluene containing ~10 mg of hydroquinone was added 1.22 mL (15 mmoles) of methyl vinyl ketone. This reaction mixture was refluxed for 24 hr under an argon atmosphere. Removal of the solvent afforded 1.31 g (97%) of ketone 61 as an oil which was homogeneous by glpc (4% QF-1, 100°). An analytical sample obtained by preparative glpc (4% QF-1, 190°) exhibited the following properties: ir (neat) 1725 cm⁻¹, 1680 cm⁻¹; pmr (CDCl₃) δ 2.5-1.3 (m, 14H), 1.1 (s, 3H), 0.2 (d, 9H); mass spectrum (70 eV) m/e (rel intensity) 266(12)P, 196(100).

Anal. Calcd. for C₁₅H₂₆O₂Si: C, 67.61; H, 9.83.

Found: C, 67.61; H, 9.78.

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3,4-Dimethyl-5-formyl-2-trimethylsilyloxy-
bicyclo[2.2.2]oct-2-ene (62)

To a stirred solution of 1.98 g (10 mmoles) of dienol ether 56 in 200 mL of toluene containing ~10 mg of hydroquinone was added 1.35 mL (20 mmoles) of acrolein. This reaction mixture was refluxed for 24 hr under an argon atmosphere. Removal of the solvent afforded 2.30 g (92%) of aldehyde 62 as an oil which was homogeneous by glpc (4% QF-1, 100°). An analytical sample obtained by preparative glpc (4% QF-1, 190°) exhibited the following properties: ir (neat) 1680 cm⁻¹, 1635 cm⁻¹; pmr (CDCl₃) 9.15 (d, 1H), 2.5-0.9 (m, 14H), 0.1 (s, 9H); mass spectrum (70 eV) m/e (rel intensity) 2526(6)P, 196(100).

Anal. Calcd. for C₁₄H₂₄O₂Si: C, 66.61; H, 9.58.

Found: C, 66.41; H, 9.61.

5-Cyano-3,4-dimethyl-2-trimethylsilyloxy-
bicyclo[2.2.2]oct-2-ene (63)

To a stirred solution of .588 g (3 mmoles) of dienol ether 56 in 200 mL of toluene containing ~10 mg of hydroquinone was added .795 mL (12 mmoles) of acrylonitrile. This reaction mixture was refluxed for 24 hr under an argon atmosphere. Removal of the solvent afforded .689 g (92%) of nitrile 63 as an oil which was homogeneous by glpc (4% QF-1, 100°). An analytical sample obtained by

preparative glpc (4% QF-1, 190°) exhibited the following properties: ir (CHCl_3) 2230 cm^{-1} , 1670 cm^{-1} ; pmr (CDCl_3) δ 2.5-1.0 (m, 14H), 0.2 (d, 9H); mass spectrum (70 eV) m/e (rel intensity) 249(13)P, 196(100).

Anal. Calcd. for $\text{C}_{11}\text{H}_{23}\text{O Si N}$: C, 67.41; H, 9.29.

Found: C, 67.53; H, 9.32.

3,4-Dimethyl-5-(1'-hydroxyethyl)bicyclo-
[2.2.2]octan-2-one (64)

To a stirred solution of 2.66 g (10 mmoles) of aldehyde 62 in 100 mL of ether was added 18.6 mL (30 mmoles) of 1.6 M methyllithium in ether at 25° under an argon atmosphere. After 4 days, the reaction mixture was poured into an ice-water mixture. The aqueous phase was extracted with ether and the combined ether extracts were washed twice with water and once with a saturated sodium sulfate solution and finally dried over MgSO_4 . Removal of the solvent gave 1.59 g (81%) of hydroxy ketone 64 as an oil, which was homogeneous by glpc (4% QF-1, 160°). An analytical sample obtained by preparative glpc (4% QF-1, 190°) exhibited the following properties: ir (CHCl_3) 3600 cm^{-1} , 3430 cm^{-1} , 1720 cm^{-1} ; pmr (CDCl_3) ratio methyl to nonmethyl protons (1:1); mass spectrum (70 eV) m/e (rel intensity) 196(8)P, 178(55), 124(100).

Oxidation of Alcohol 64

To a stirred solution of 1.07 g (5 mmoles) of pyridinium chlorochromate in 100 mL CH_2Cl_2 at 25° was added a solution of .364 g (2 mmoles) of hydroxy ketone 64 in 30 mL CH_2Cl_2 . After 3 hr, 100 mL of ether was added and the supernatant was decanted from the black gum. The insoluble residue was washed three times thoroughly with 50 mL portions of ether whereupon it became a black granular solid. The combined organic solution was passed through a short pad of florisel and was washed three times with 40 mL portions of a solution of 5 mL of acetyl acetone in 300 mL of a 20% sodium hydroxide solution and once each with water and a saturated sodium sulfate solution and finally dried over MgSO_4 . Removal of the solvent gave .300 g (83%) of an oil which was homogeneous by glpc. An analytical sample obtained by preparative glpc (4% QF-1, 190°) exhibited identical spectral properties as dione 38.

5-(3'-Hydroxy-3'-but-1'-enyl)-3,4-dimethylbicyclo-
[2.2.2]octan-2-one (67)

To a stirred solution of 2.66 g (10 mmoles) of ketone 61 in 100 mL of THF at 25° under an argon atmosphere was added 9.8 mL (22 mmoles) of 2.25 M vinyl lithium in THF. After 4 days, the reaction mixture was poured into an ice-water mixture. The aqueous phase was extracted with ether

and the combined ether extracts were washed twice with water and once with a saturated sodium sulfate solution and finally dried over MgSO_4 . Removal of the solvent gave 1.86 g (83%) of hydroxy ketone 67 as an oil, which was homogeneous by glpc (4% QF-1, 160°). An analytical sample obtained by preparative glpc (4% QF-1, 190°) exhibited the following properties: ir (CHCl_3) 3590 cm^{-1} , 3450 cm^{-1} , 1720 cm^{-1} ; pmr (CDCl_3) δ 6.2-5.5 (m, 4H), 2.4-1.4 (m, 10H), 1.3 (s, 3H), 1.1-0.9 (m, 6H); mass spectrum (70 eV) m/e (rel intensity) 218 (25) impurity, 204 (6) m- H_2O , 123 (100).

Anal. Calcd. for $\text{C}_{14}\text{H}_{22}\text{O}_2$: C, 75.63; H, 9.97.

Found: C, 76.45; H, 9.99.

5-(2'-Buta-1',3'-diene)-3,4-dimethylbicyclo-
[2.2.2]octan-2-one (68)

To a solution of 200 mL of toluene containing 50 mg of para-toluene-sulfonic acid was added .654 g (3 mmoles) of hydroxy ketone 67, and the resulting mixture was refluxed for 24 hr through a Dean-Stark water trap. Ether was added to the cooled solution and the organic mixture was washed with saturated sodium carbonate and saturated sodium sulfate solutions and finally, dried over MgSO_4 . Removal of the solvent under reduced pressure gave .404 g (65%) of diene 68 as an oil which was homogeneous by glpc (4% QF-1, 160°). An analytical sample obtained by preparative glpc (4% QF-1, 190°) exhibited the following properties: ir (CCl_4):

3090 cm^{-1} , 1730 cm^{-1} ; pmr (CCl_4) δ 6.6-4.8 (m, 5H), 3.0-1.6 (m, 10H), 1.2-0.9 (m, 7H); mass spectrum (70 eV) m/e (rel intensity) 204(31)P, 124(42), 55(100).

Anal. Calcd. for $\text{C}_{14}\text{H}_{20}\text{O}$: C, 82.30; H, 9.87.

Found: C, 82.16; H, 9.87.

Preparation of Diene 68 via Allyl Chloride 65

To a stirred solution of .654 g (3 mmoles) of 67 and .241 mL (3 mmoles) of pyridine in 40 ml of ether at 0° was added .238 mL (3.3 mmoles) of thionyl chloride. The reaction mixture was stirred for 10 min at 0° and then concentrated to dryness under reduced pressure. The resulting oil was dissolved in toluene and concentrated to dryness three times. The residue was dissolved in water and ether, and the ether layer was washed with cold (3°) sodium bicarbonate and water and finally dried over MgSO_4 . Removal of the solvent gave .4218 g (58%) of a dark oil which was homogeneous by glpc (4% QF-1, 160°). A sample obtained by preparative glpc (4% QF-1, 190°) had the identical pmr as diene 68. The crude pmr was different from the pmr of diene 68.

To a stirred solution of .500 g (2.08 mmoles) of the crude product in 50 ml of glyme under an argon atmosphere at 25° was added .170 gm (3 mmoles) of sodium hydride. After stirring for 24 hrs at room temperature, water and

ether were added and the aqueous solution was extracted with ether. The combined ether extracts were washed once each with water and a saturated sodium sulfate solution and finally dried over MgSO_4 . Removal of solvent gave .302 g (70%) of an oil which exhibited the identical gas chromatographic and pmr properties as diene 68.

3,4-Dimethyl-5-(1'-hydroxyallyl)bicyclo-
[2.2.2]octan-2-one (69)

To a stirred solution of 1.4 g (5.55 mmoles) of aldehyde 62 in 100 mL of THF at 25° was added 6.7 mL (15 mmoles) of 2.25 M vinyl lithium in THF under an argon atmosphere at 25°. After 4 days, the reaction mixture was poured into an ice-water mixture. The aqueous phase was extracted with ether and the combined ether extracts were washed twice with water and once with a saturated sodium sulfate solution and finally dried over MgSO_4 . Removal of the solvent gave .920 g (84%) of hydroxy ketone 45 as an oil, which was homogeneous by glpc (4% QF-1, 160°). An analytical sample obtained by preparative glpc (4% QF-1, 190°) exhibited the following properties: ir (CCl_4) 3600 cm^{-1} , 3400 cm^{-1} ; pmr (CDCl_3) δ 6.2-4.8 (m, 3H), 3.0-1.3 (m, 10H), 1.0-0.9 (m, 6H); mass spectrum (70 eV) m/e (rel intensity) 208(6)P, 190(23), 124(31), 123(100).

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

Found: C, 74.92; H, 9.68.

5-Acryloyl-3,4-dimethylbicyclo-
[2.2.2]octan-2-one (45)

To a stirred solution of 5 g of manganese dioxide in 200 mL of CH_2Cl_2 at 25° was added .500 g (2.4 mmoles) of keto-alcohol 69 in 10 mL CH_2Cl_2 . After 24 hr, 100 ml of ether was added and the supernatant was decanted from the brown residue. The insoluble residue was then washed three times with ether and the combined organic solution was passed through a short pad of celite and finally dried over MgSO_4 . Removal of the solvent afforded .400 g (81%) of dione 45 as a yellow oil which contained 10% impurities by glpc (4% QF-1, 160°). An analytical sample obtained by preparative glpc (4% QF-1, 190°) exhibited the following properties: ir (CCl_4) 1725 cm^{-1} , 1615 cm^{-1} , pmr: (CDCl_3) ratio vinyl: nonvinyl protons, 3:17; mass spectrum (70 eV) m/e (rel intensity) 206(9)P, 156(10), 56(100).

REFERENCES

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REFERENCES

1. Roy Genders, "A History of Scent", Hamish Hamilton Ltd., London, England 1972, p. 112.
2. M. Billot and F. V. Wells, "Perfumery Technology; Art: Science:Industry", Halsted Press, New York, 1975, p. 87.
3. G. Wolff and G. Davisson, Tetrahedron, 25, 4903 (1969).
4. G. Buchi, W. D. MacLeod Jr. and J. Podella, J. Amer. Chem. Soc., 86, 4438 (1964).
5. E. Piers, W. DeWaals, and R. Britton, J. Amer. Chem. Soc., 93, 5113 (1971).
6. G. Frater, Helv. Chim. Acta, 57, 172 (1974).
7. N. Fukamiya, M. Kato and A. Yoskikoshi, J. C. S. Chem. Comm., 1120 (1971).
8. K. Schmalzl and R. Minington, J. Org. Chem., 37, 2877 (1972).
9. K. Schmalzl and R. Minington, J. Org. Chem., 34, 2358 (1969).
10. R. Lee, C. McAndrews, K. Patel, and W. Reusch, Tetrahedron Lett., 965 (1973).
11. R. Lee, Ph.D. Thesis, Michigan State University, 1973; Ross Lee, Tetrahedron Lett., 3333 (1973).
12. H. O. House, W. L. Roelofs and B. M. Trost, J. Org. Chem., 31, 646 (1966).
13. B. Boeckman, Private Communication.
14. S. Reed, J. Org. Chem., 27, 4116 (1962).
15. N. Jones and H. T. Taylor, J. Chem. Soc., 1345 (1961).

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16. H. A. P. DeJongh and H. Wynberg, Rec. Trav. Chim. 82, 202 (1963).
17. E. D. Bergmann, D. Ginsburg, and R. Pappo, Organic Reactions, 10, 205 (1959).
18. G. H. Posner, C. E. Whitten, and P. E. McFarland, J. Am. Chem. Soc., 94, 5107 (1972).
19. W. F. Gannon and H. O. House, Org. Synth., Coll. Vol. V, 539 (1973).
20. H. O. House, "Modern Synthetic Reactions", Second Edition, New York, 1972, p. 494.
21. E. J. Corey and J. W. Suggs, Tetrahedron Lett., 31, 2647 (1975).
22. B. M. Trost, H. C. Arndt, P. E. Strege, and T. R. Verhoeven, Tetrahedron Lett., 39, 3477 (1976).
23. K. M. Patel, Ph.D. Thesis, Michigan State University, (1974).
24. G. M. Rubottom and D. S. Krueger, Tetrahedron Lett., 7, 611 (1977).
25. D. F. Morrow, T. P. Culbertson, and R. M. Hofer, J. Org. Chem., 32, 361 (1967).
26. Beil, 7(2), 56.
27. H. Born, R. Pappo, and J. Szmuszkowicz, J. Chem. Soc., 1779 (1953).

APPENDIX

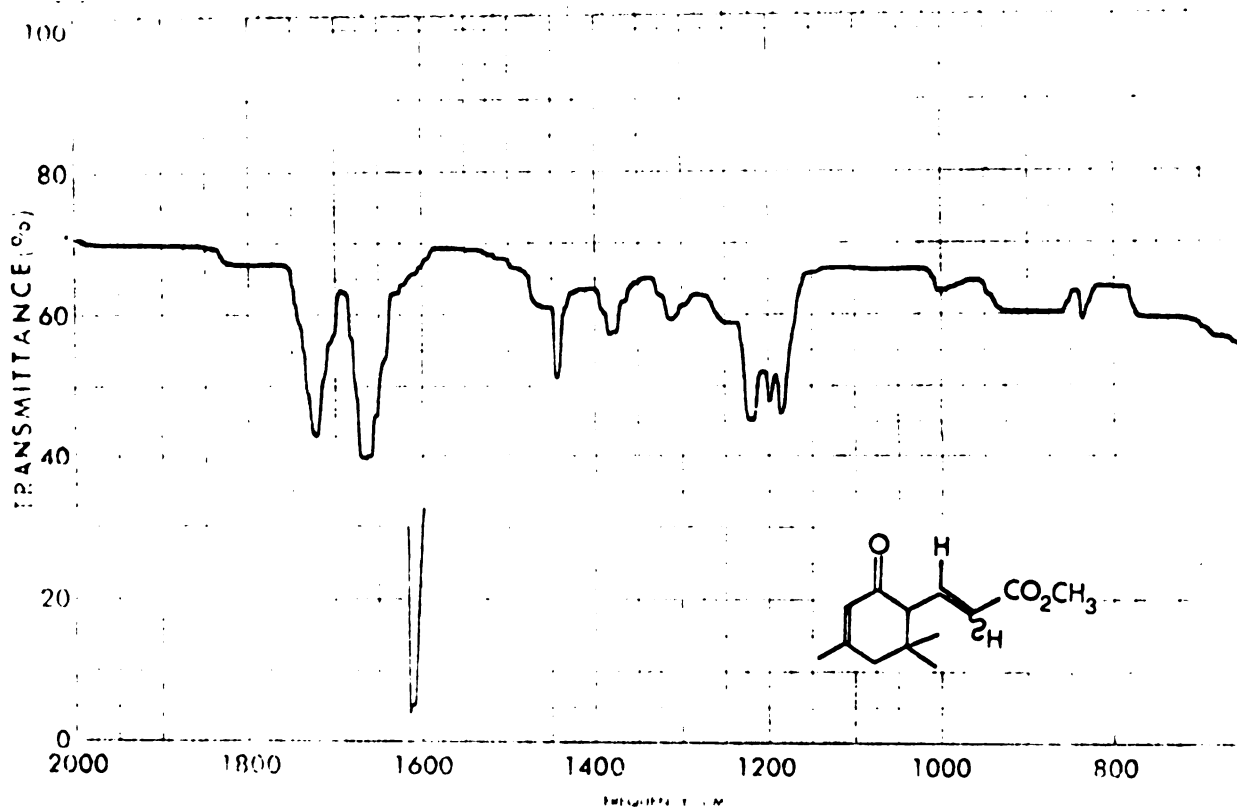
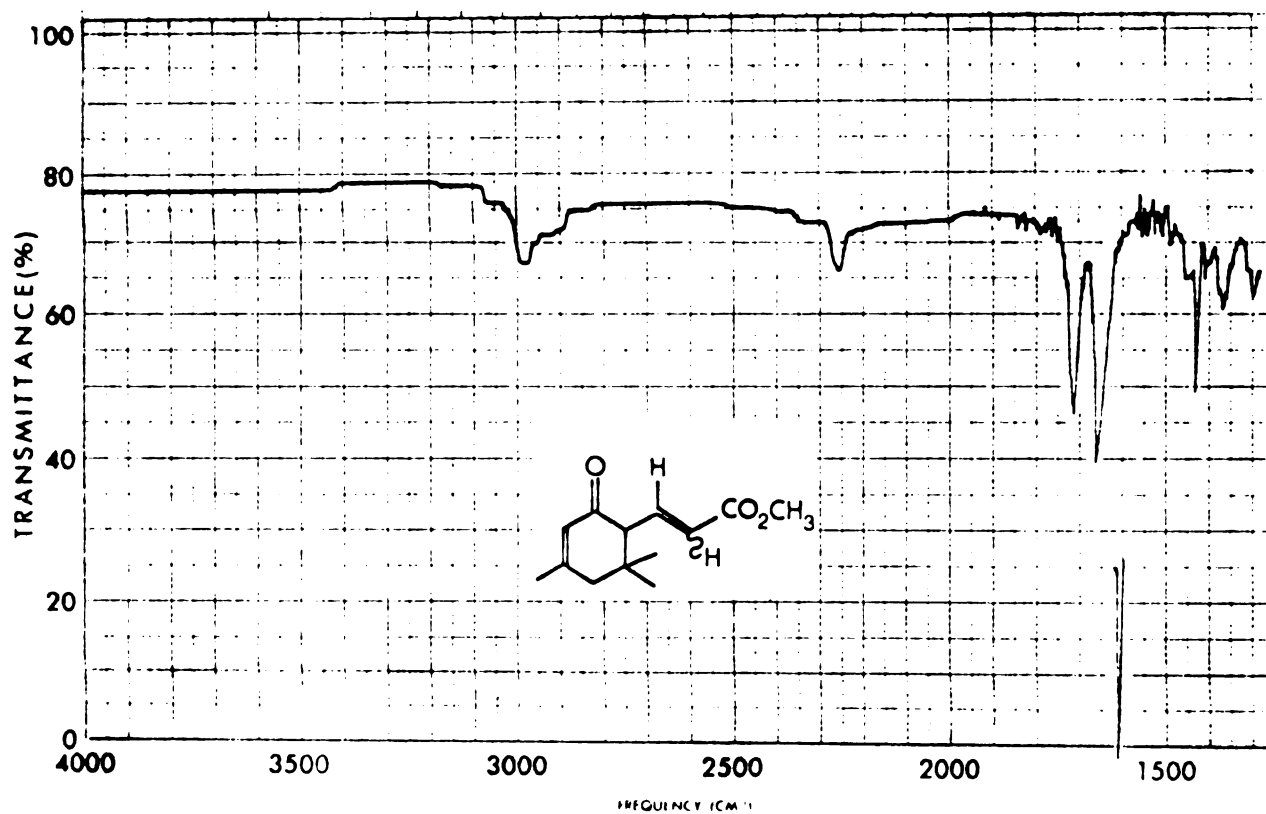


Figure 1. Infrared spectrum of 22.



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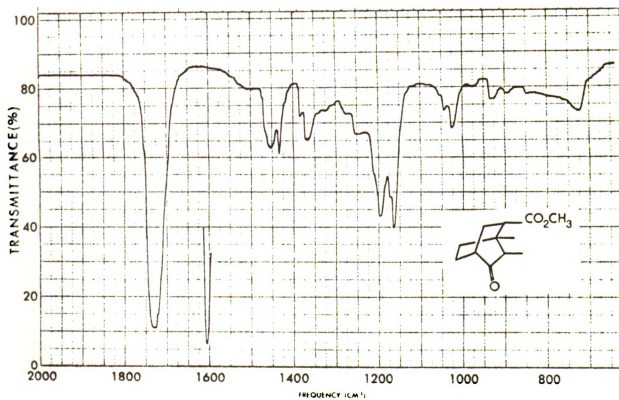
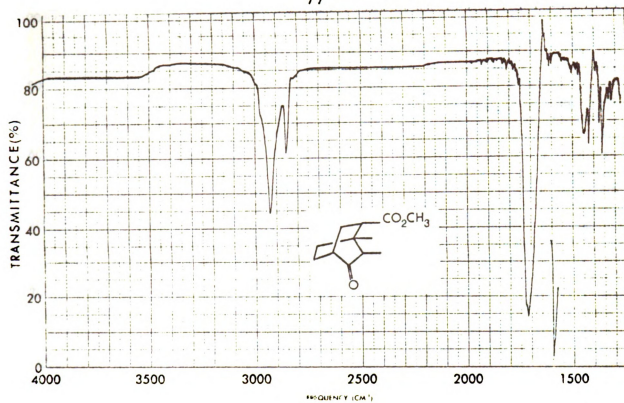
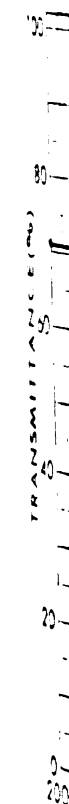
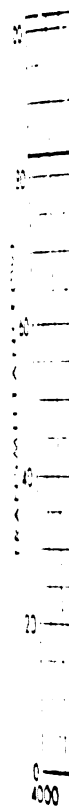


Figure 2. Infrared spectrum of 24.



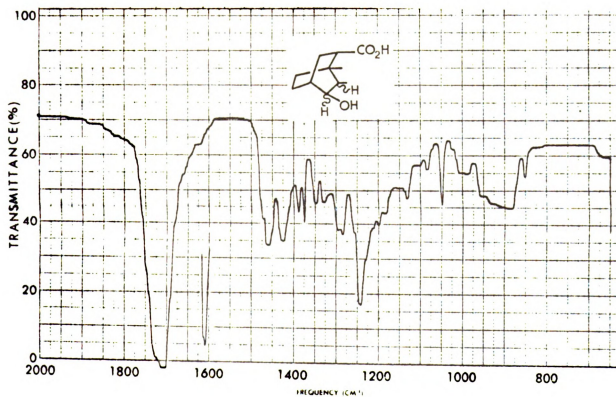
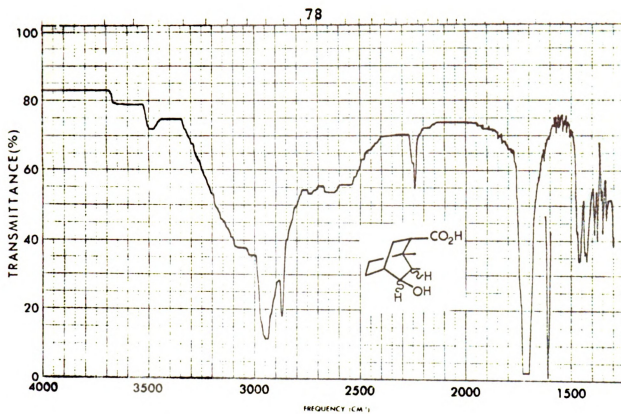


Figure 3. Infrared spectrum of 26.

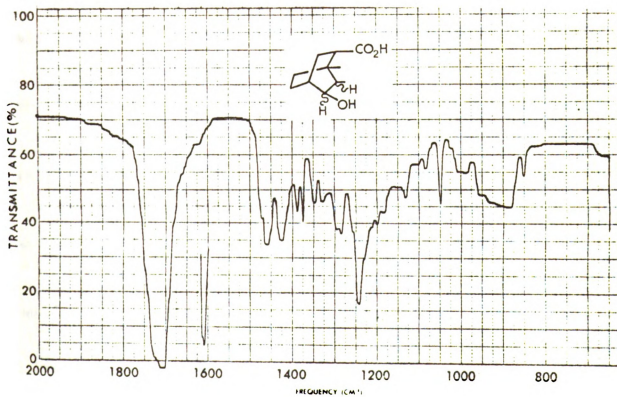
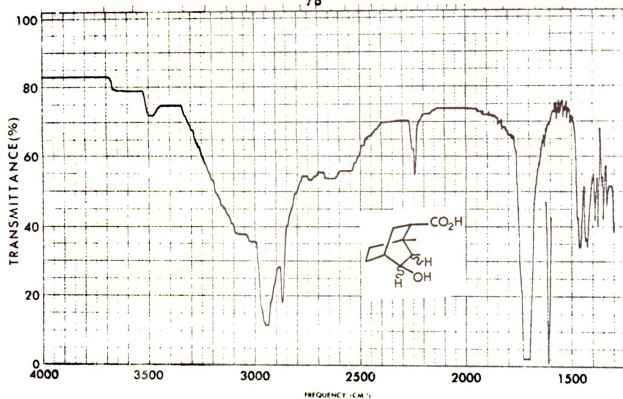


Figure 3. Infrared spectrum of 26.

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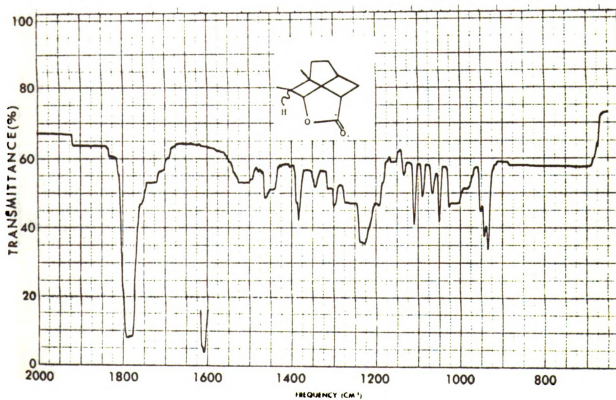
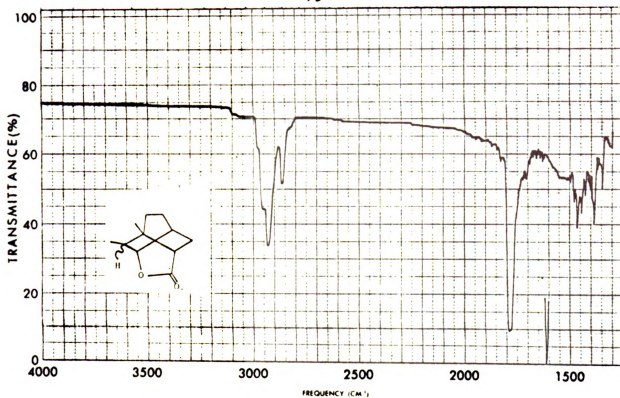


Figure 4. Infrared spectrum of 27.

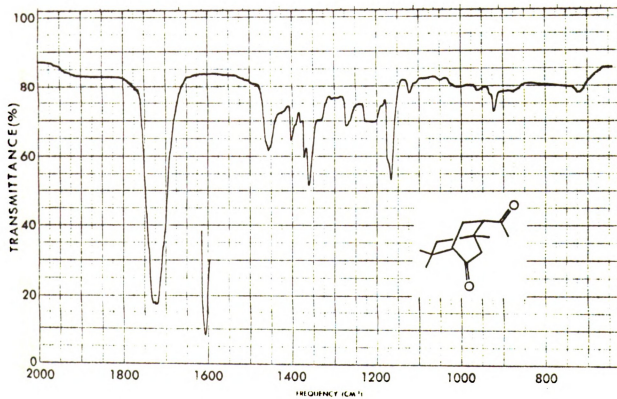
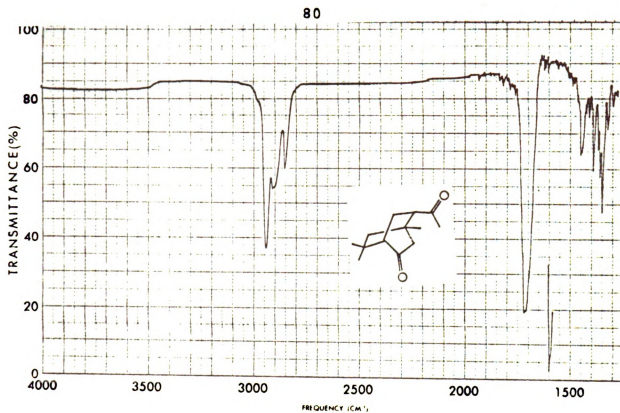


Figure 5. Infrared spectrum of 29.

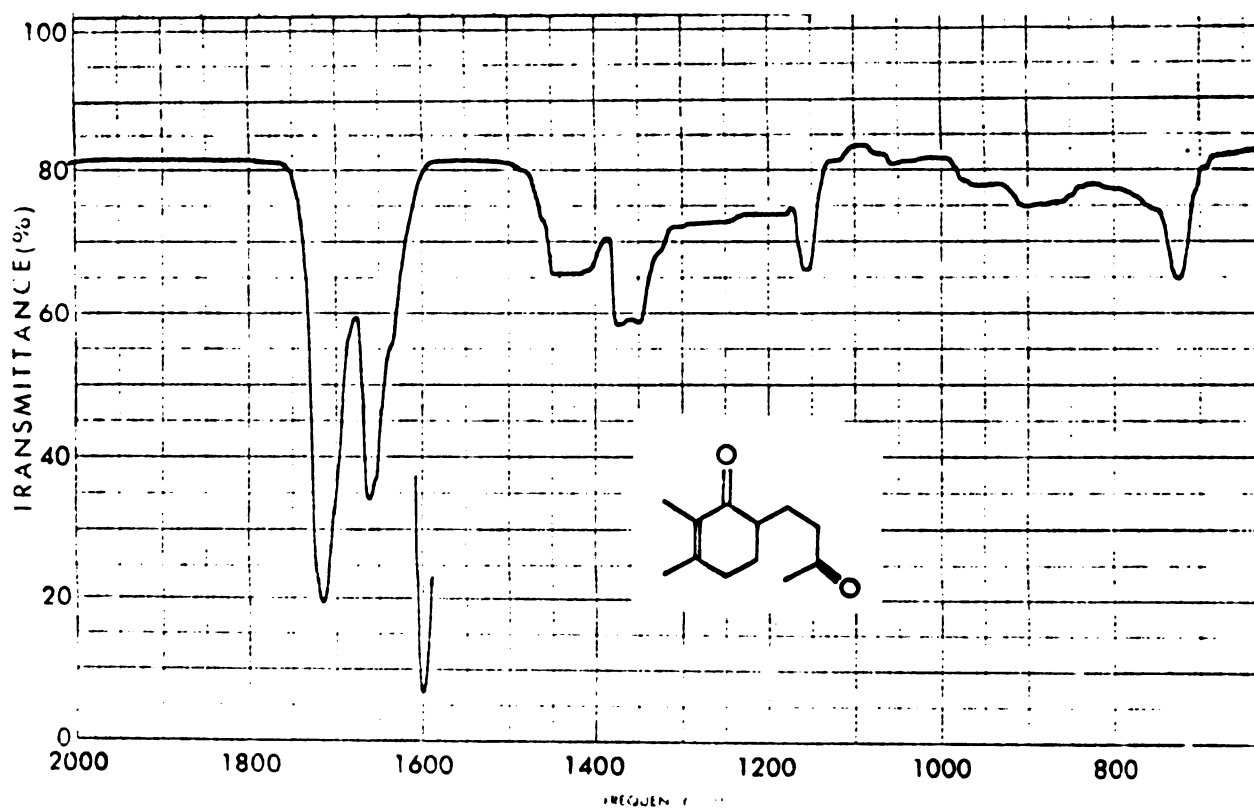
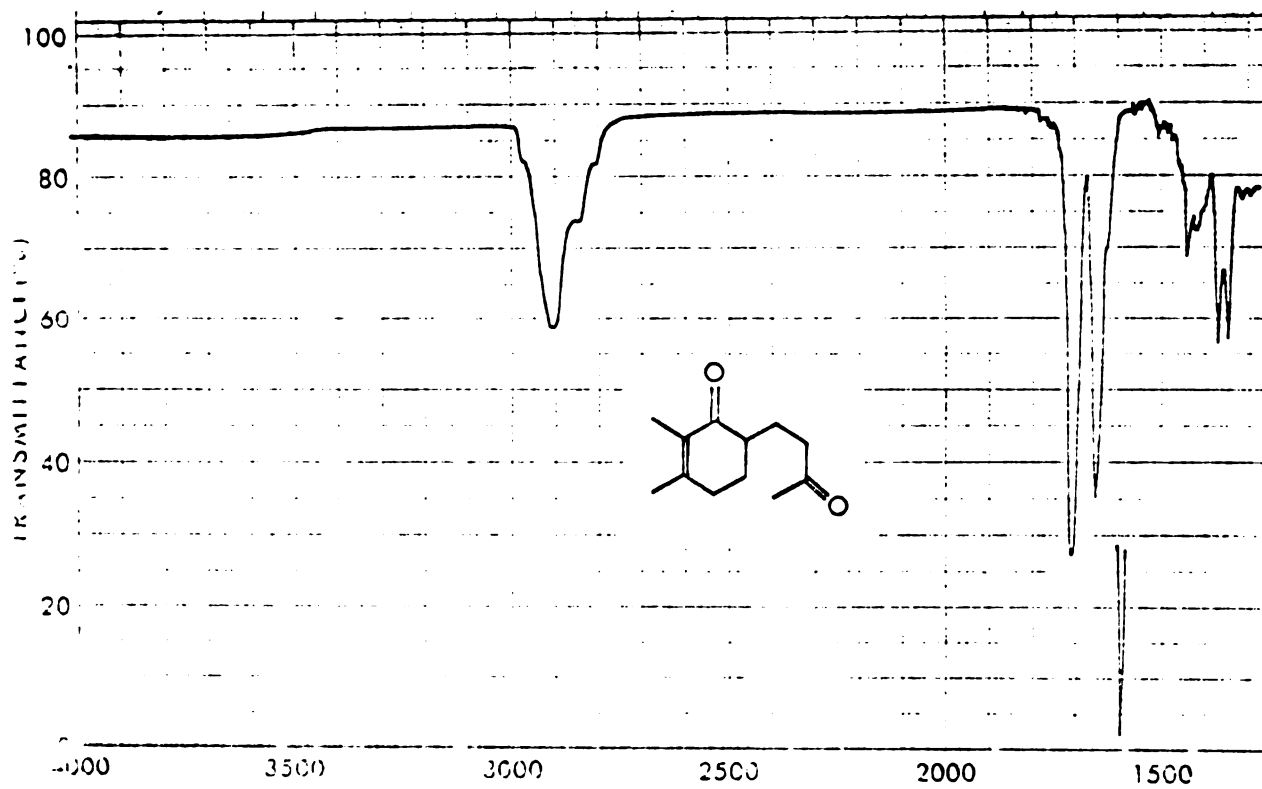


Figure 6. Infrared spectrum of 30.

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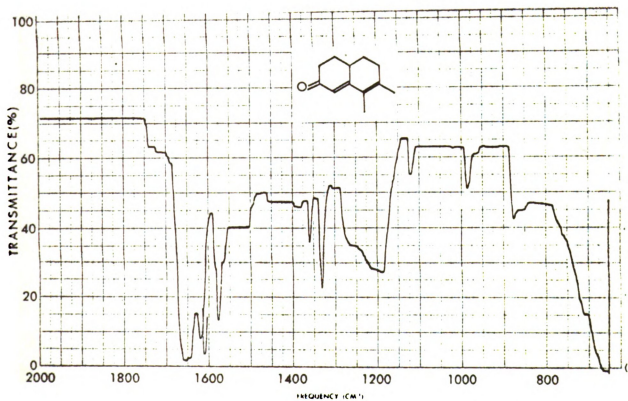
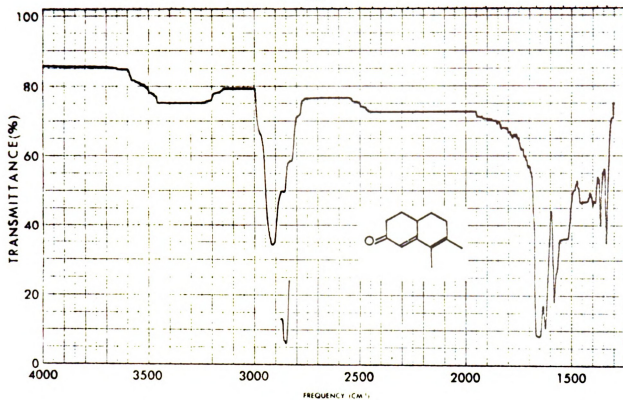


Figure 7. Infrared spectrum of 31.

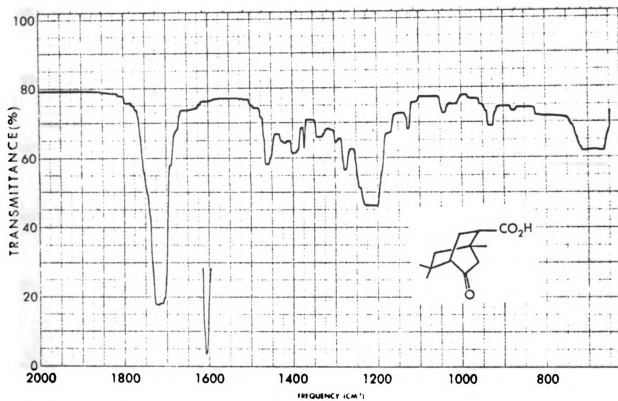
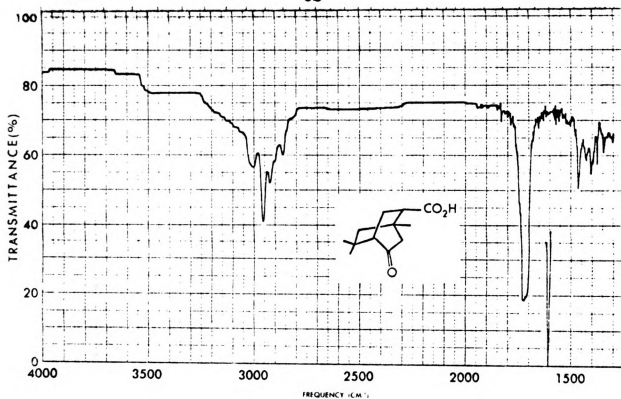


Figure 8. Infrared spectrum of **34**.

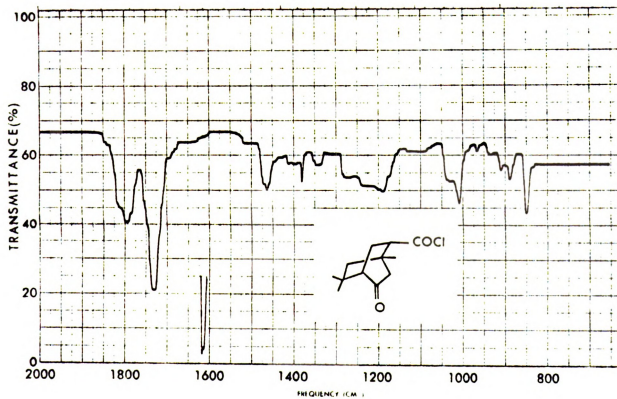
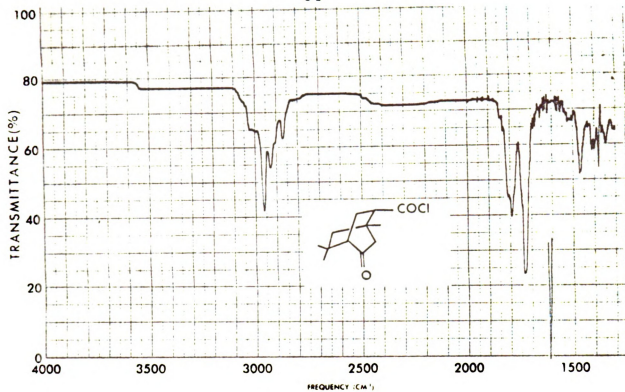


Figure 9. Infrared spectrum of 35.

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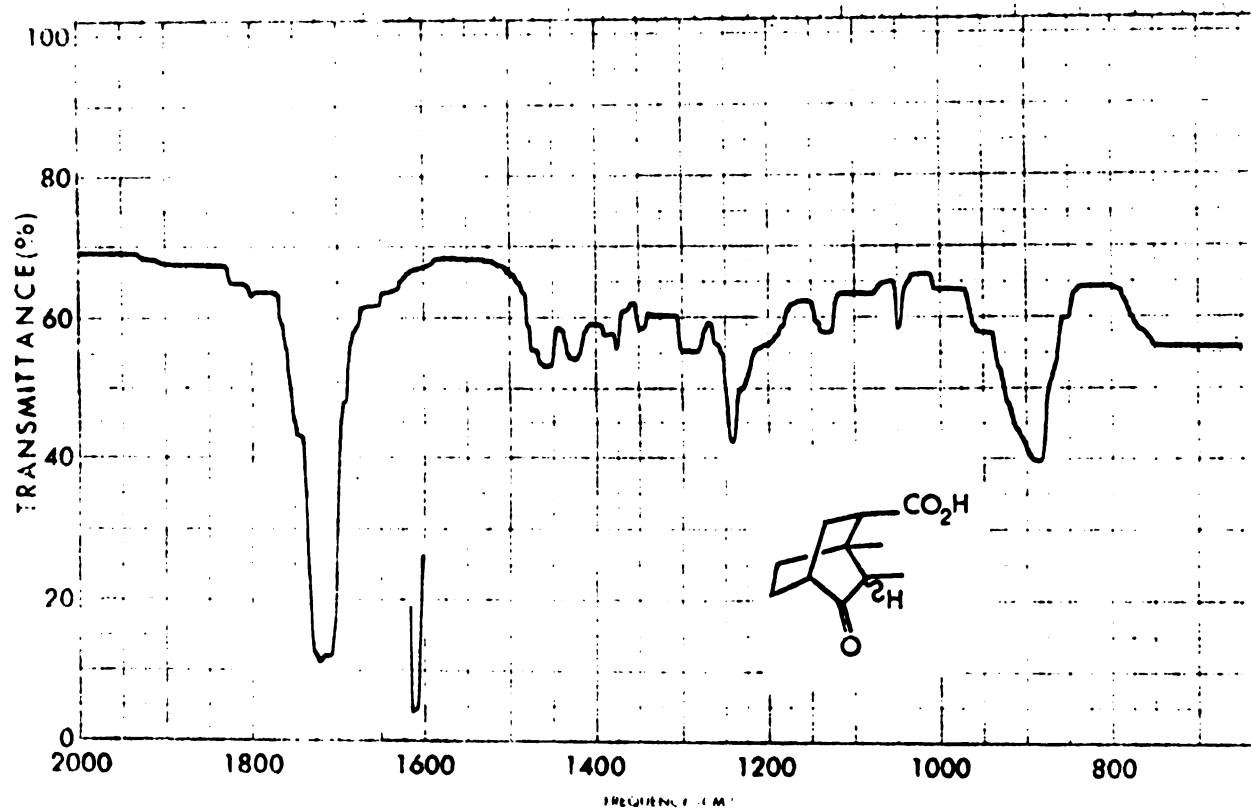
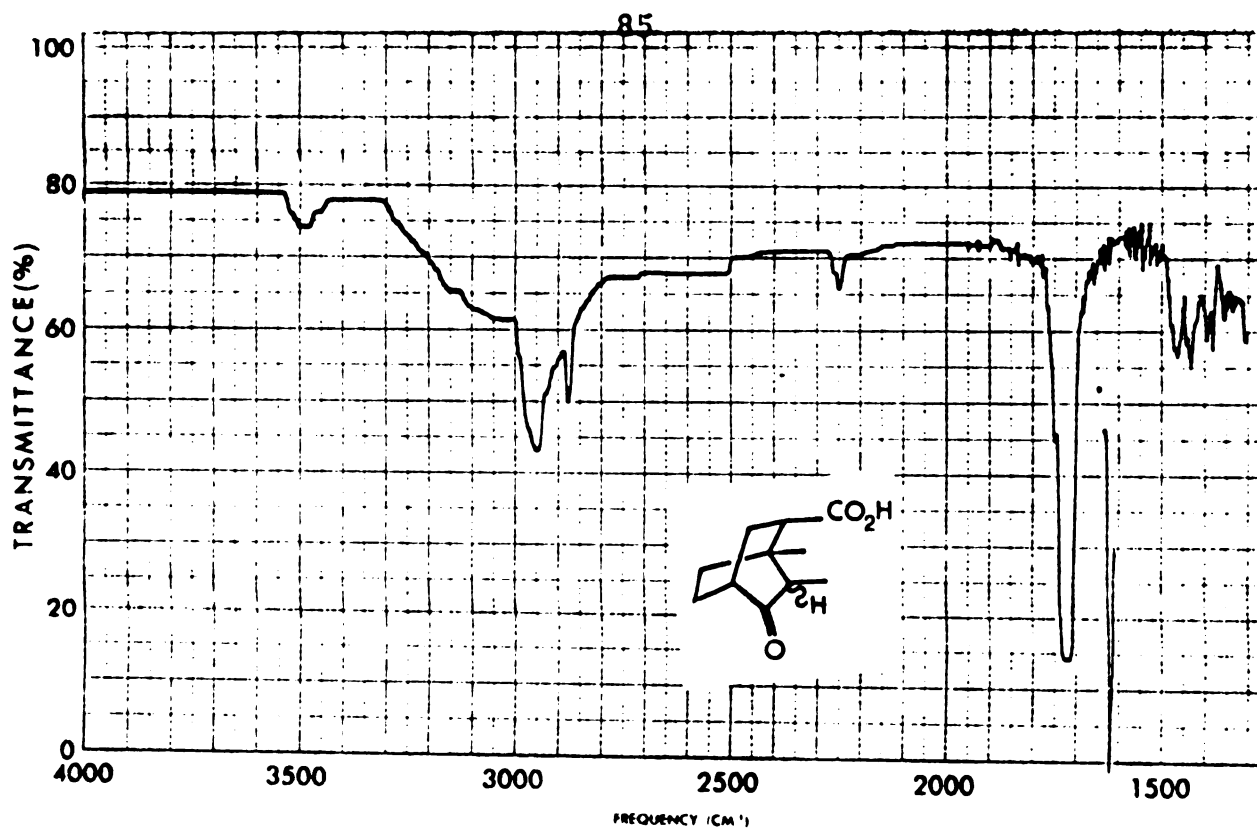


Figure 10. Infrared spectrum of 36.

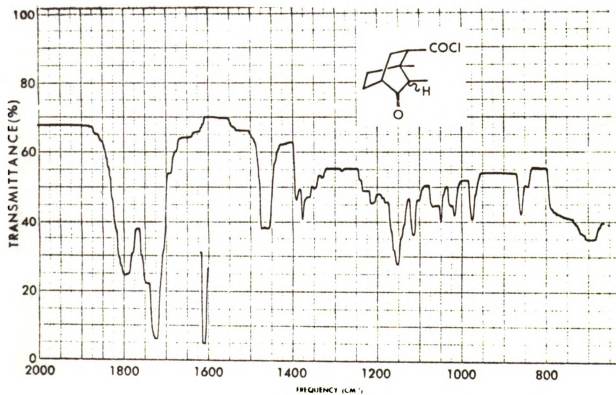
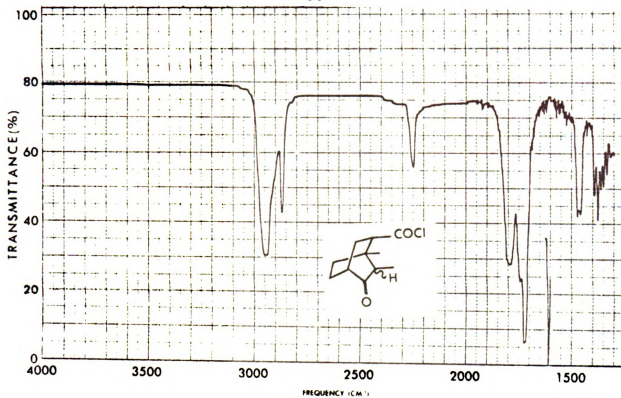


Figure 11. Infrared spectrum of 37.

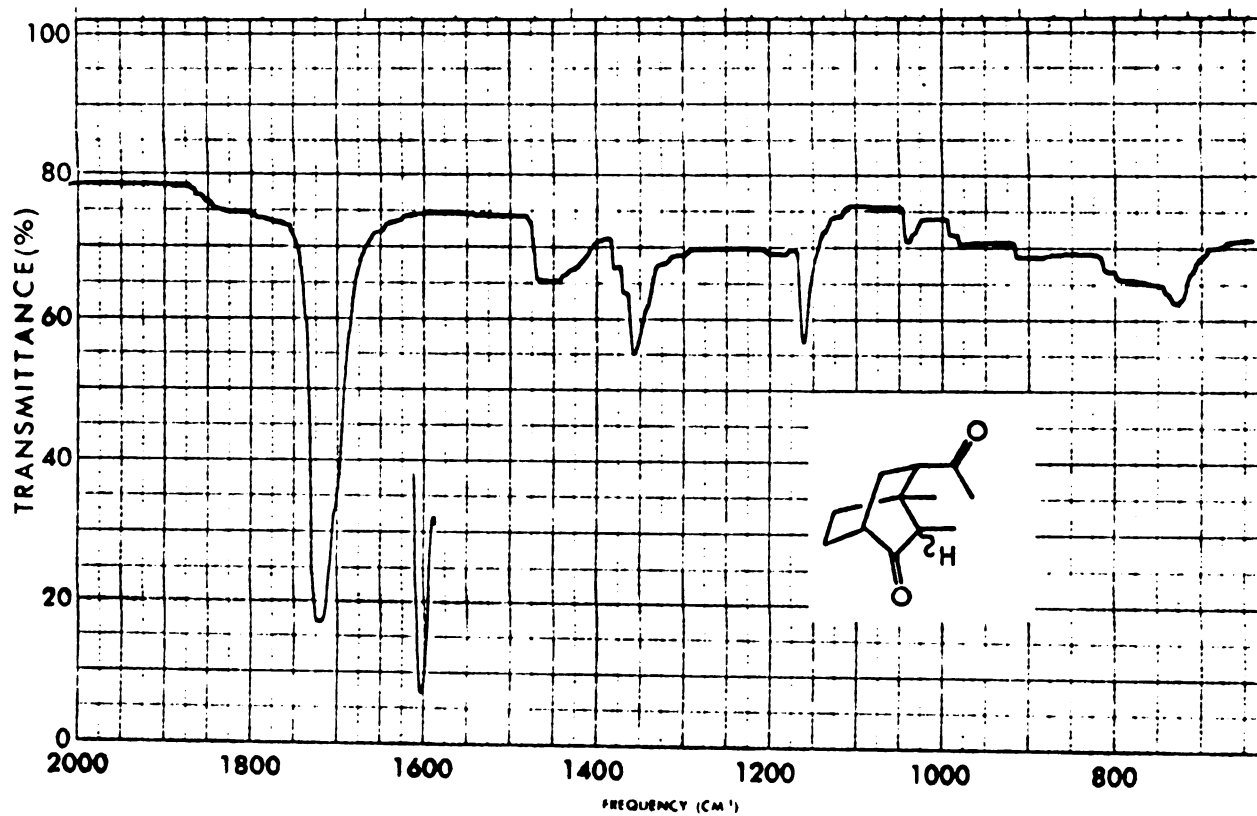
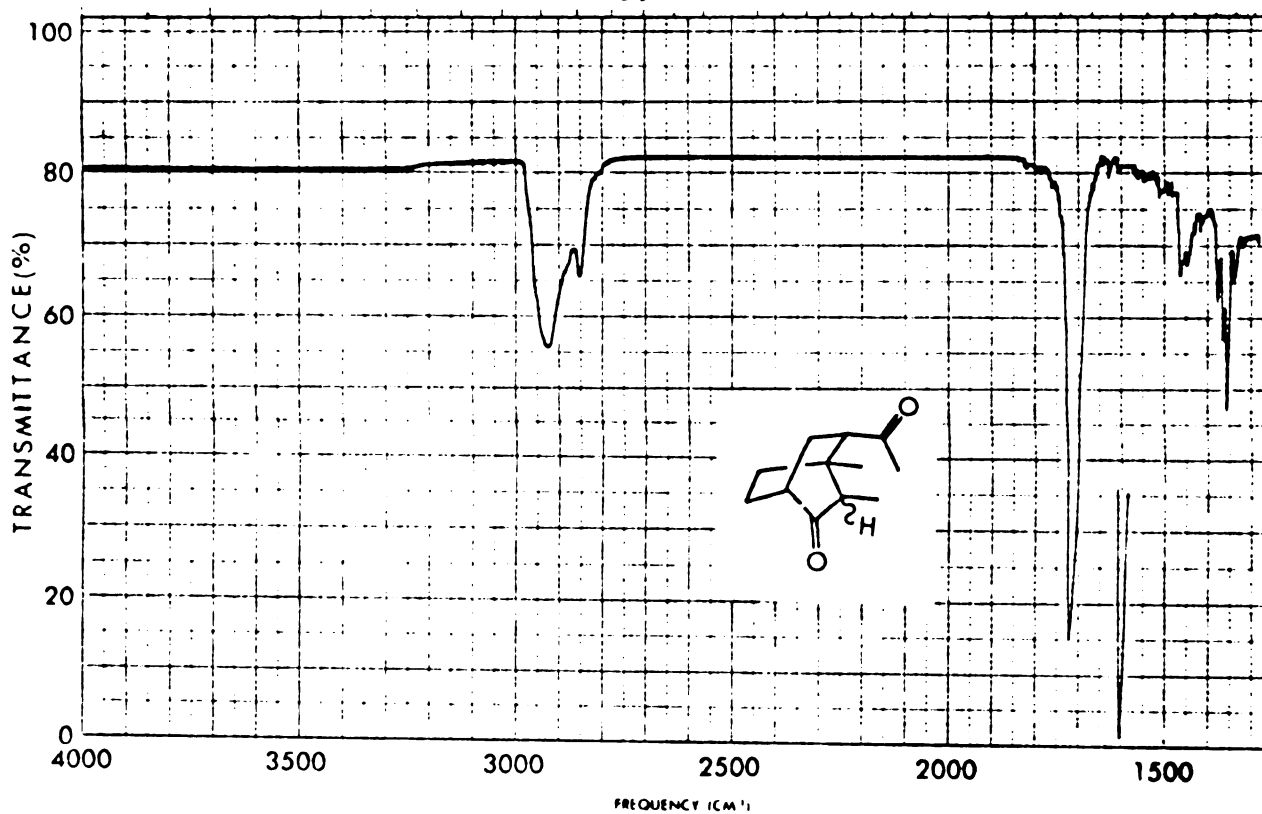


Figure 12. Infrared spectrum of 38.

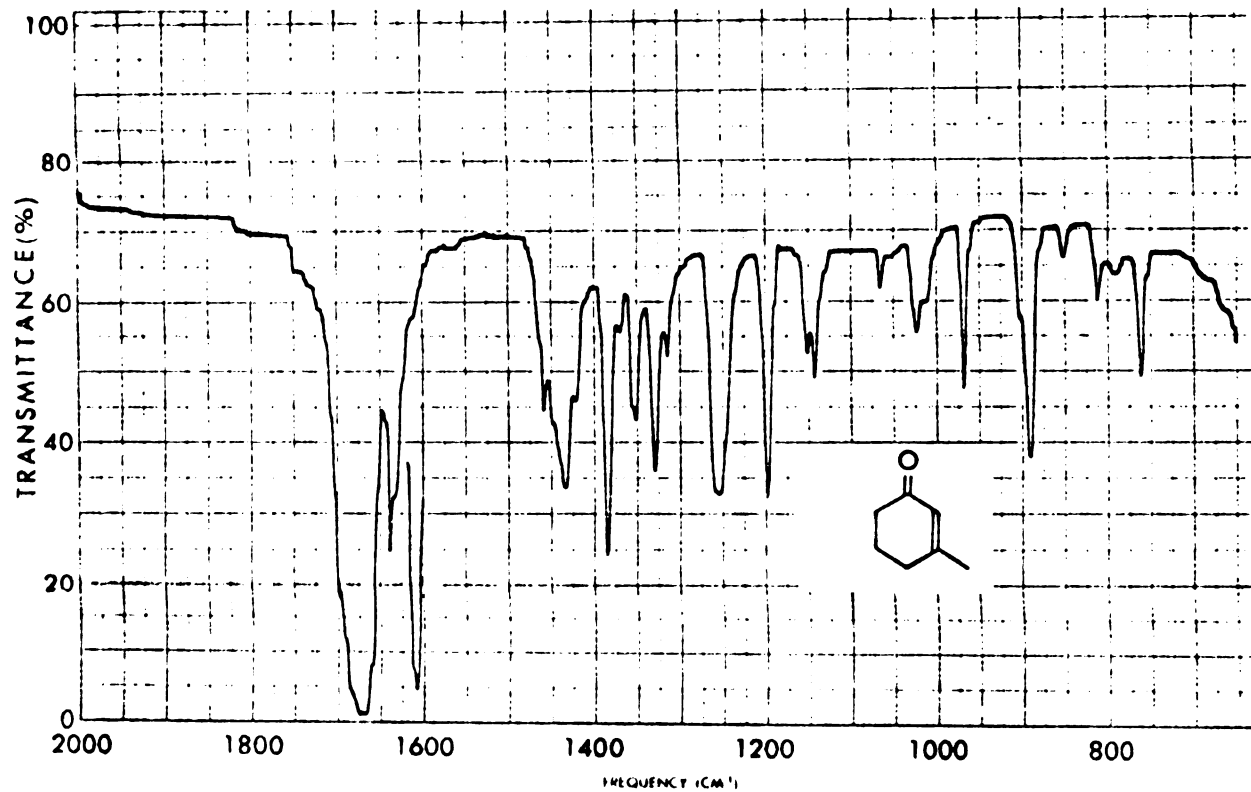
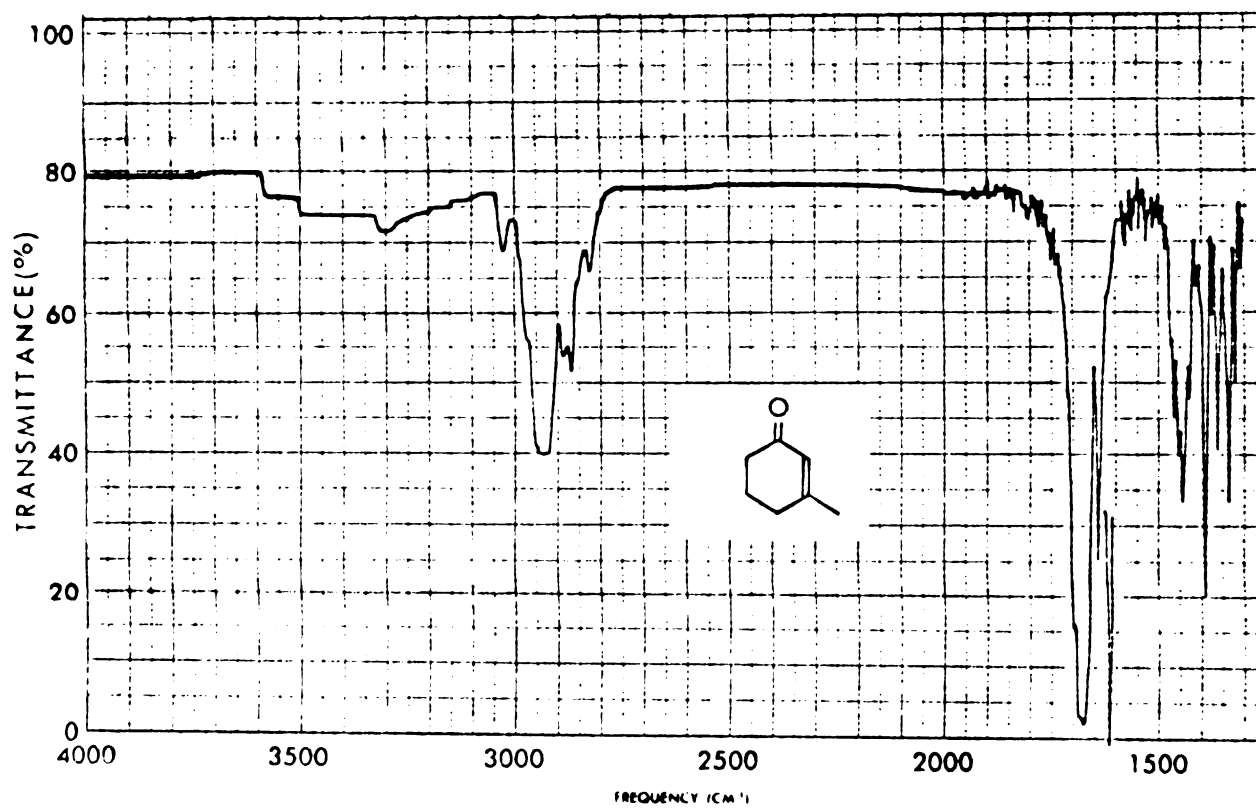


Figure 13. Infrared spectrum of 3-methylcyclohex-2-enone.

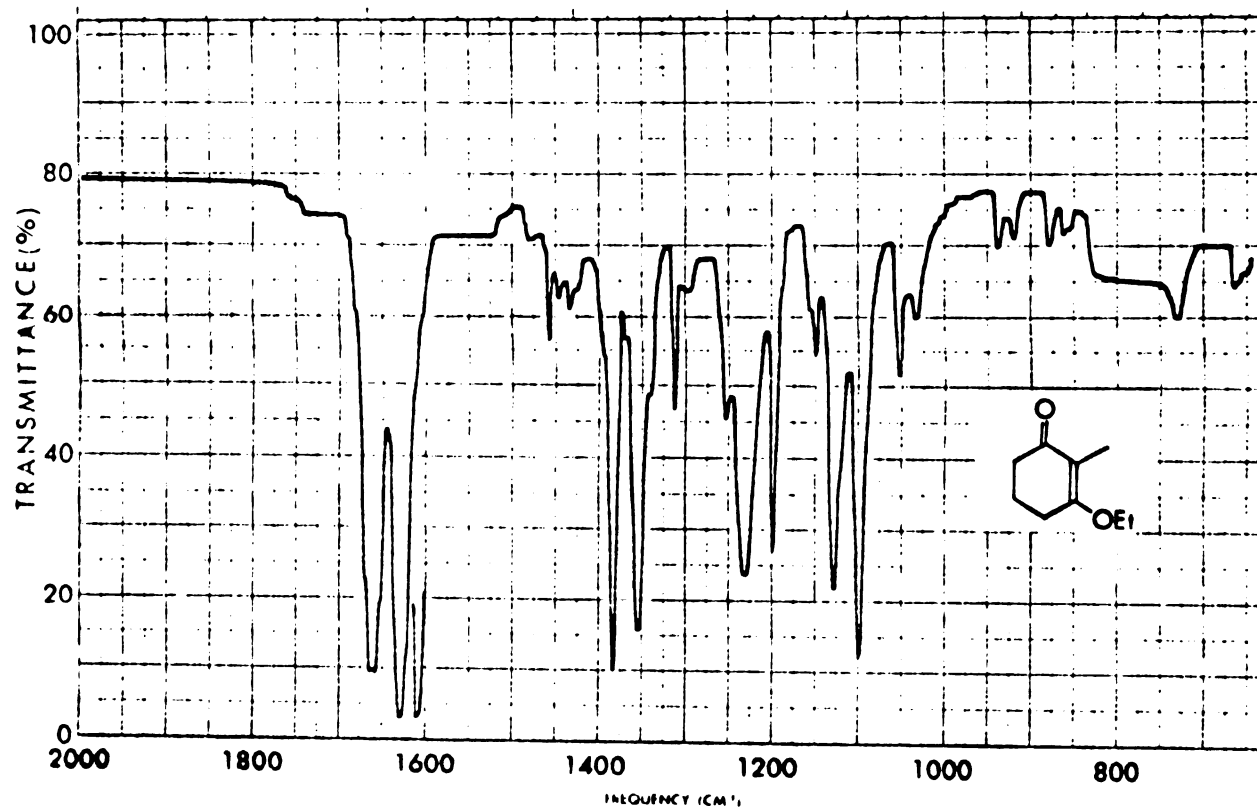
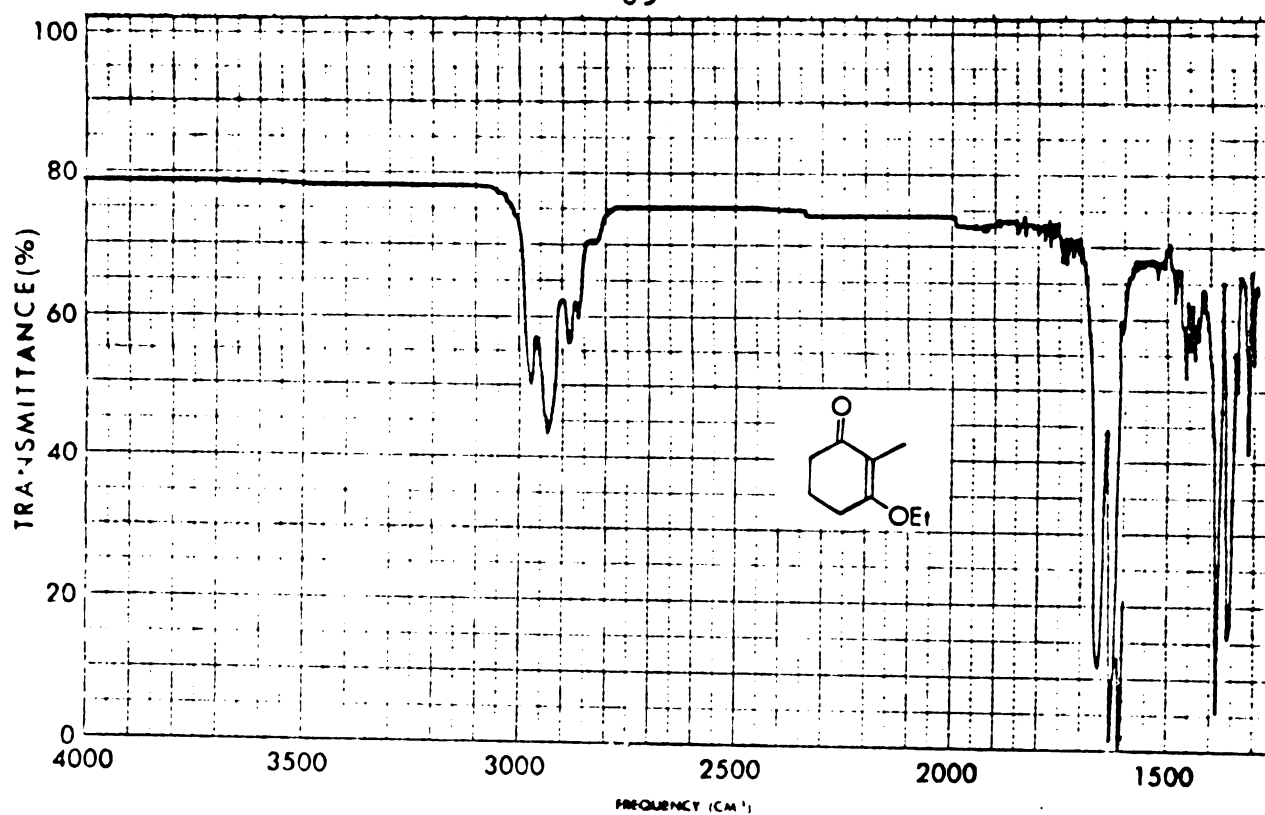


Figure 14. Infrared spectrum of 3-ethoxy-2-methylcyclohexenone.

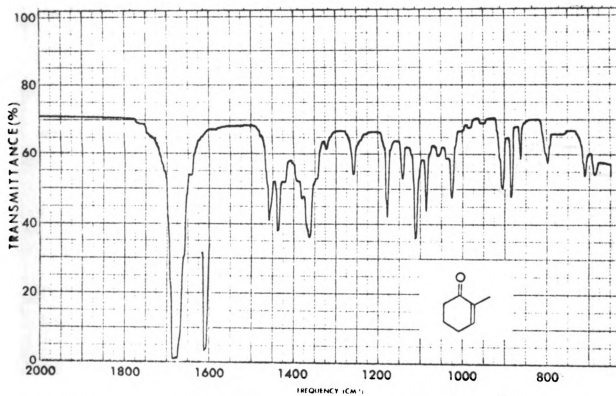
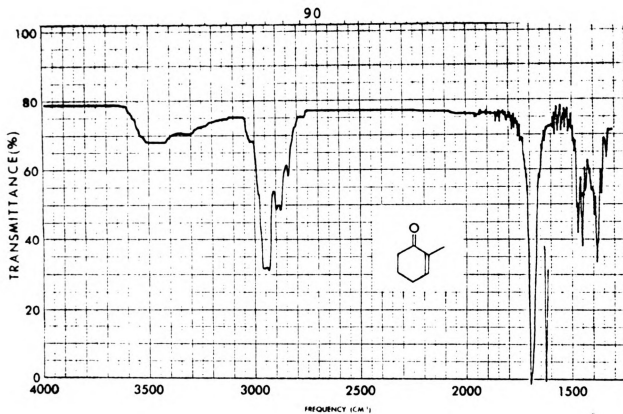


Figure 15. Infrared spectrum of 2-methylcyclohex-2-enone.

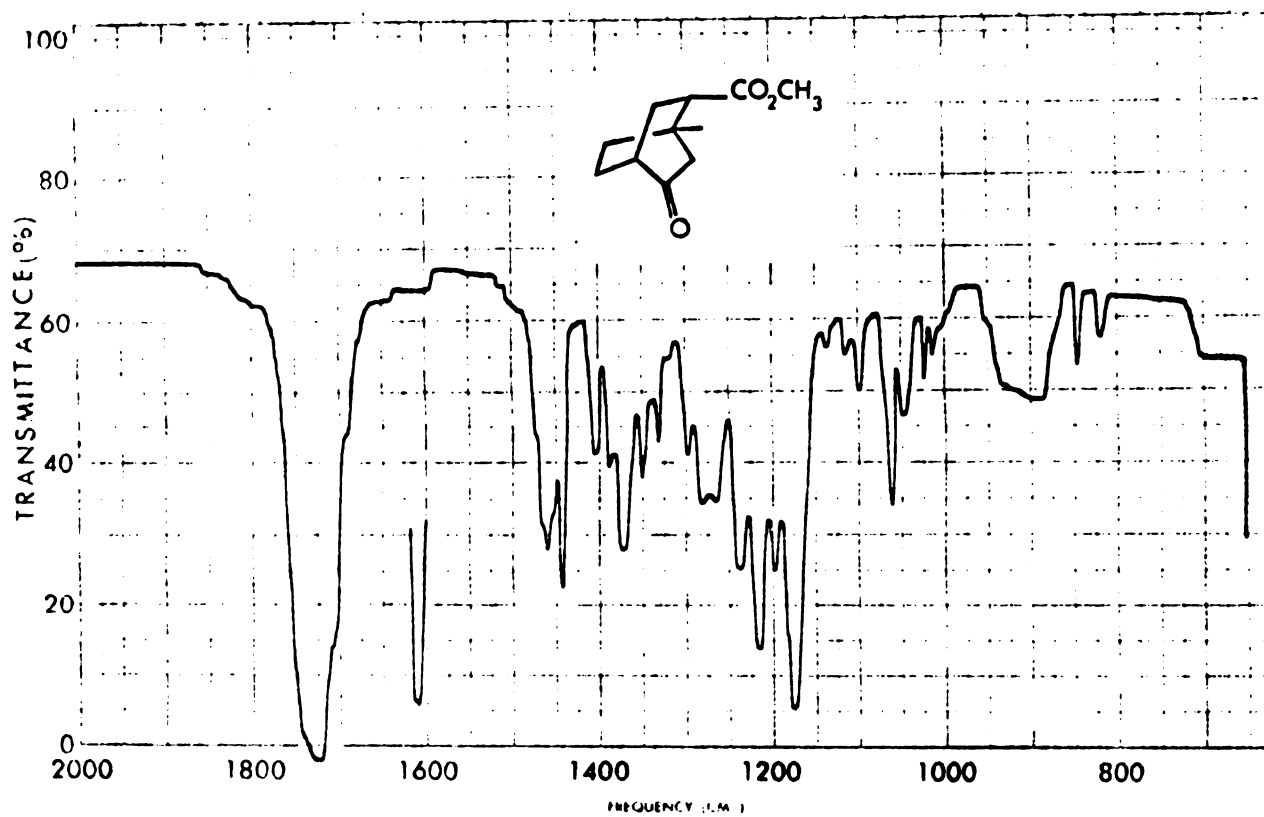
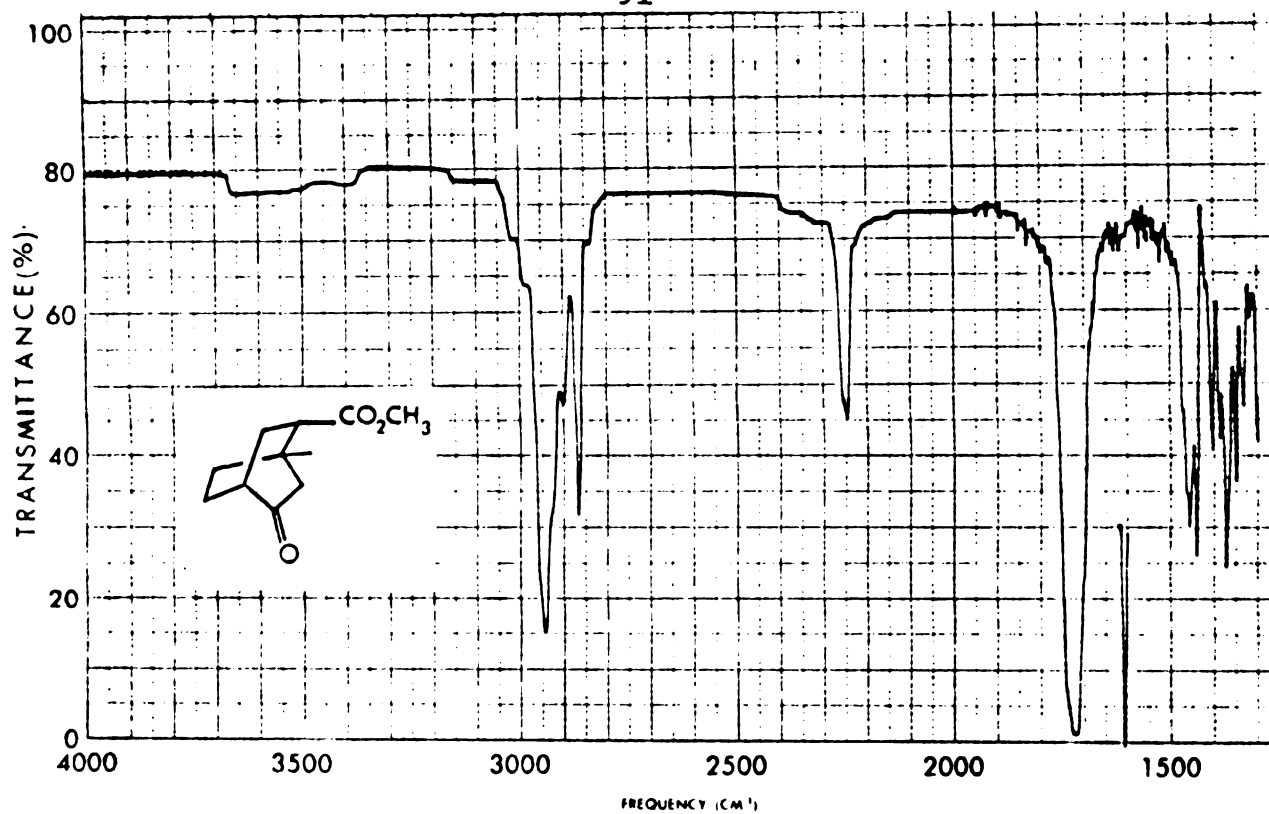


Figure 16. Infrared spectrum of 39.

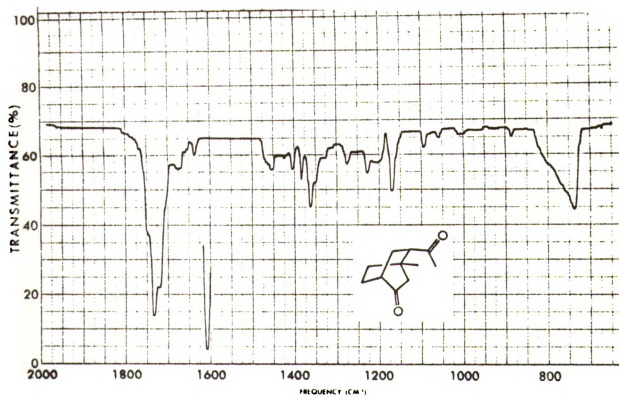
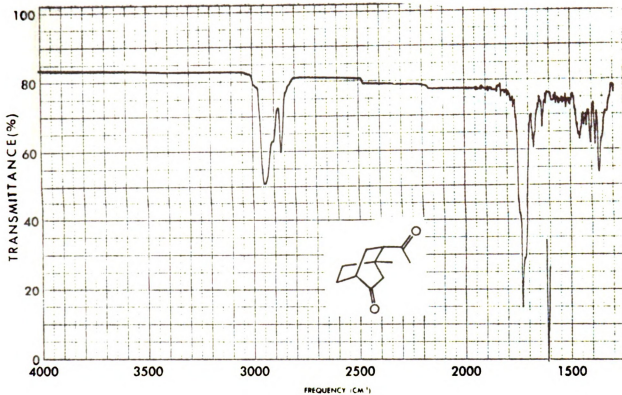


Figure 17. Infrared spectrum of 40.

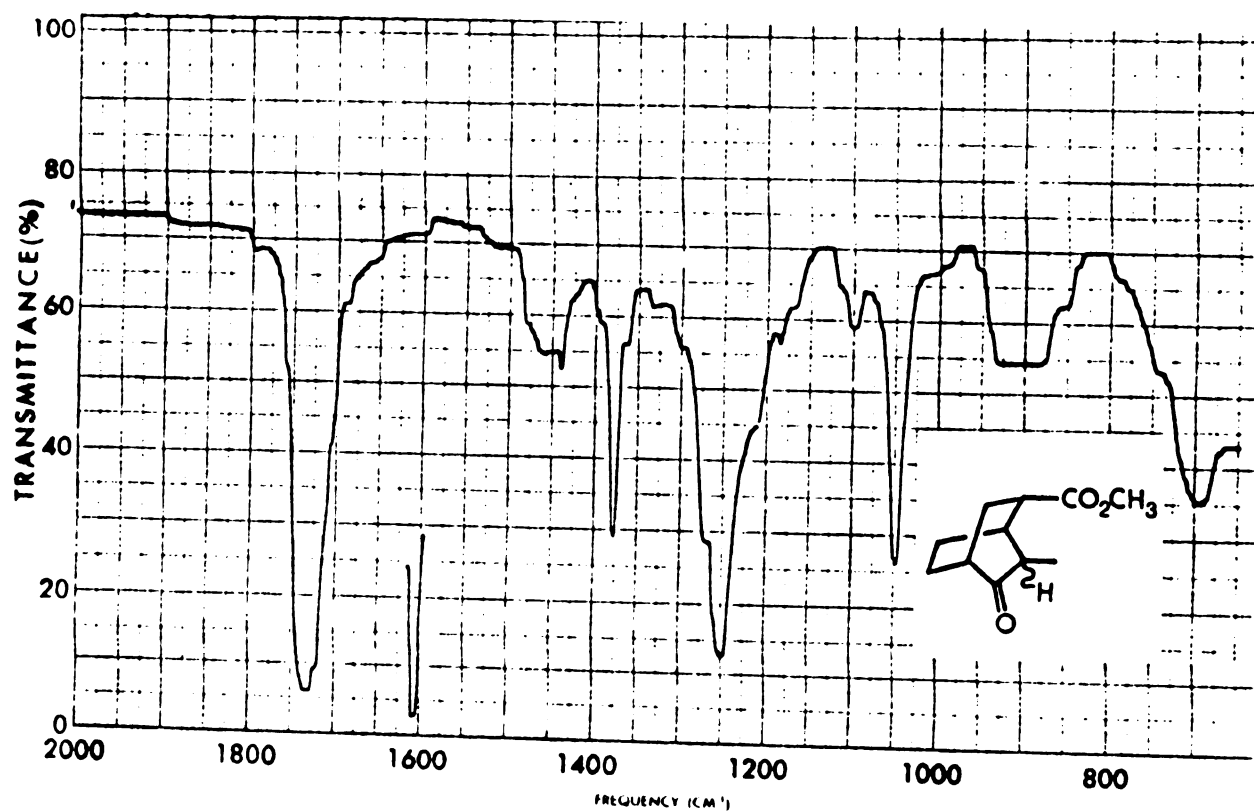
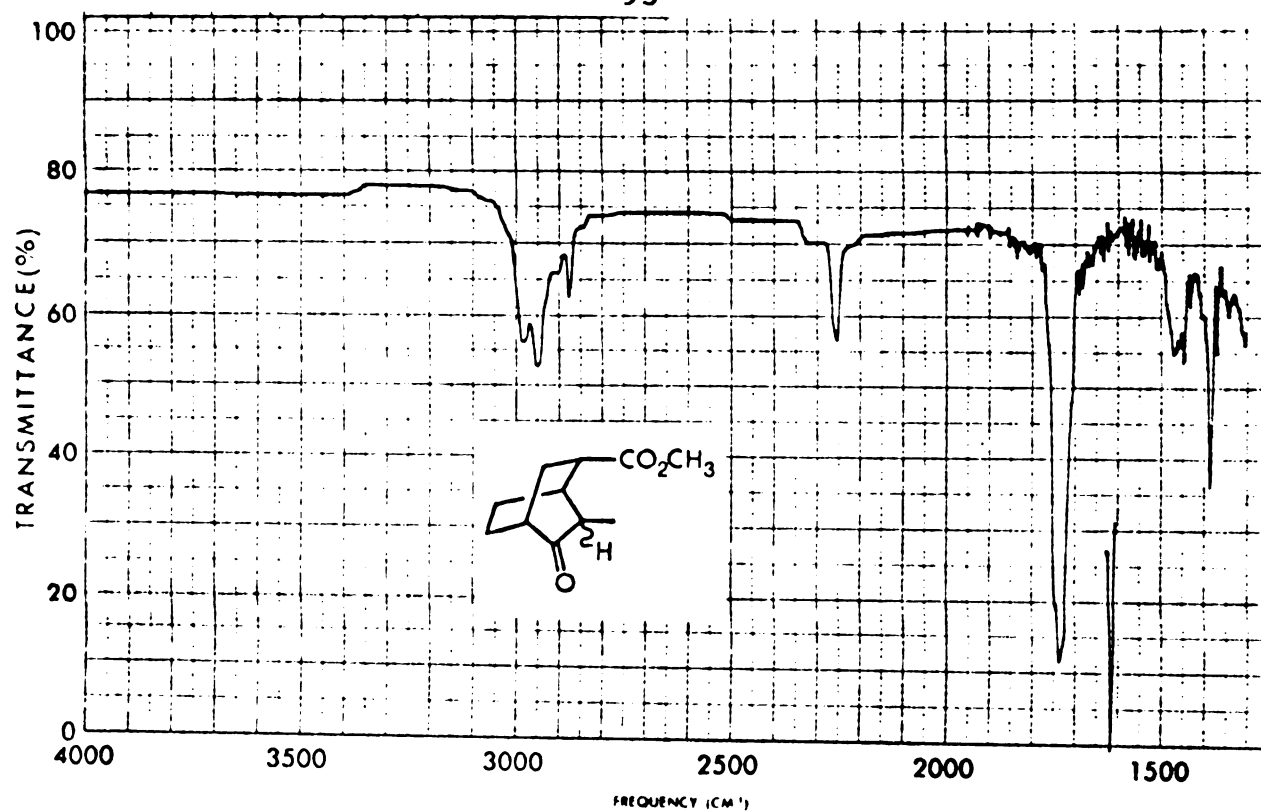


Figure 18. Infrared spectrum of 41.

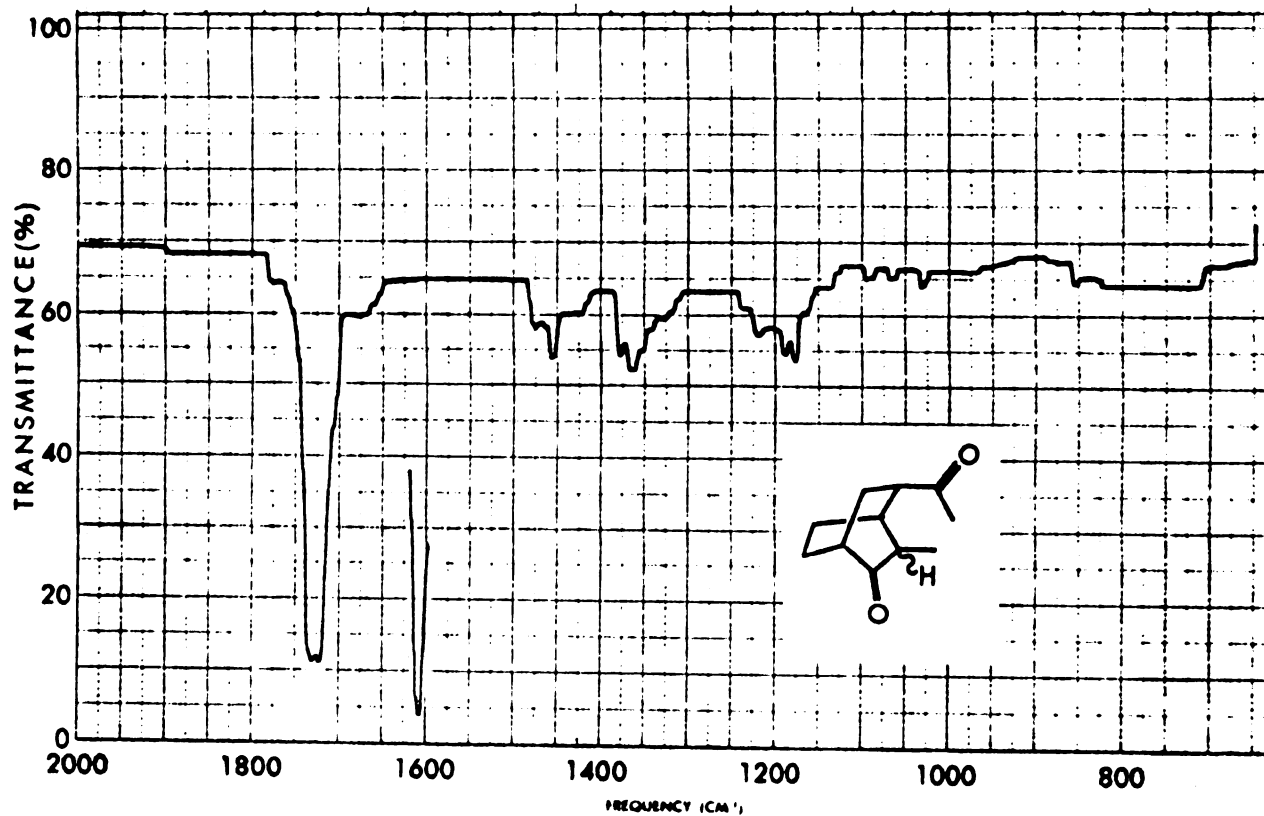
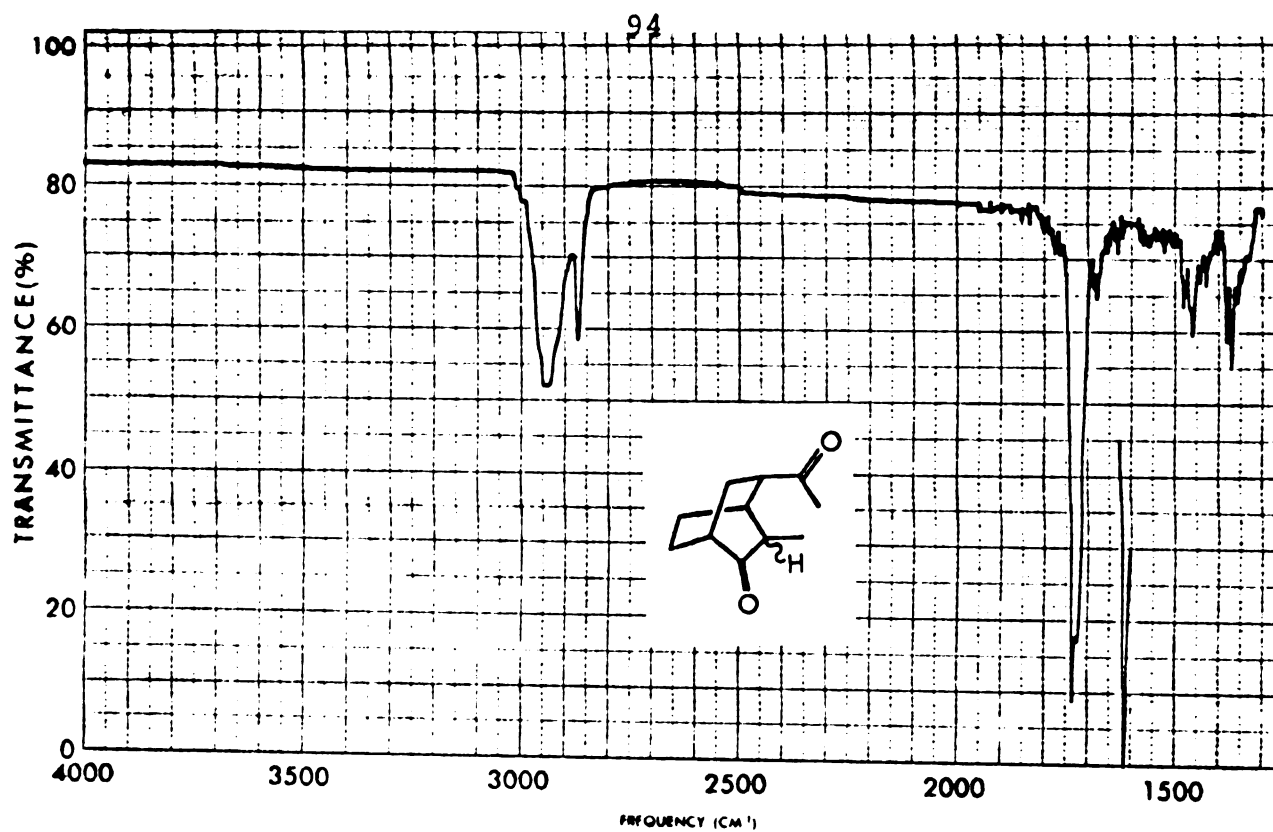


Figure 19. Infrared spectrum of 42.

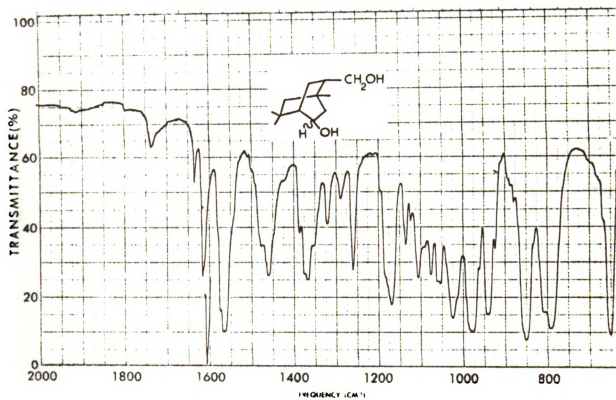
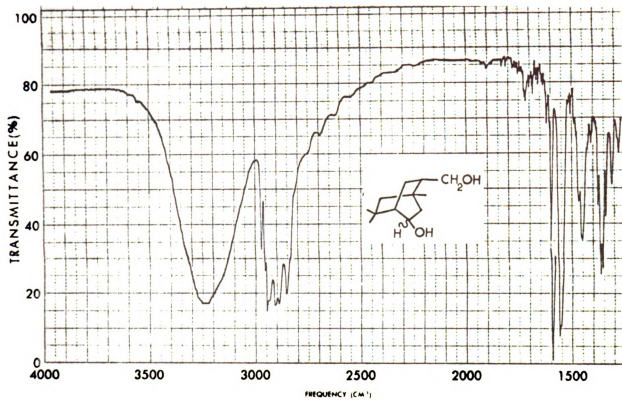


Figure 20. Infrared spectrum of 46.

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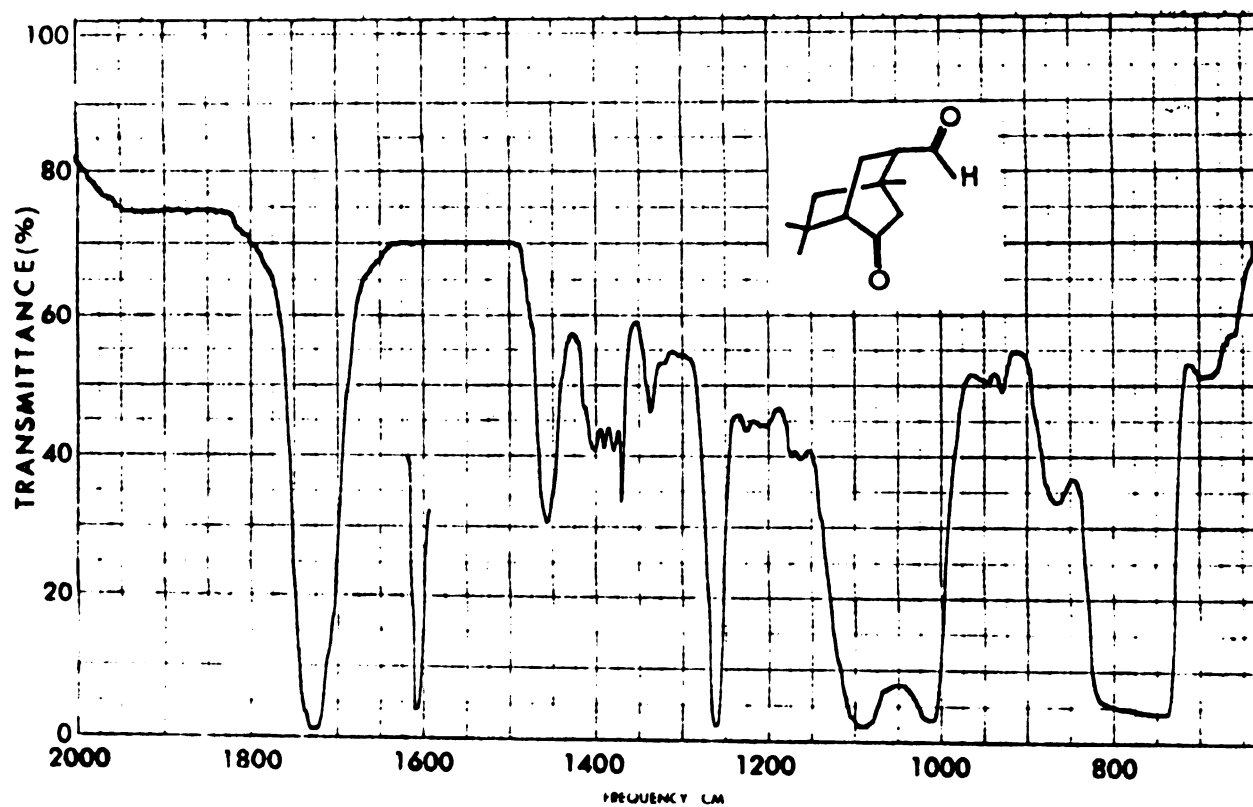
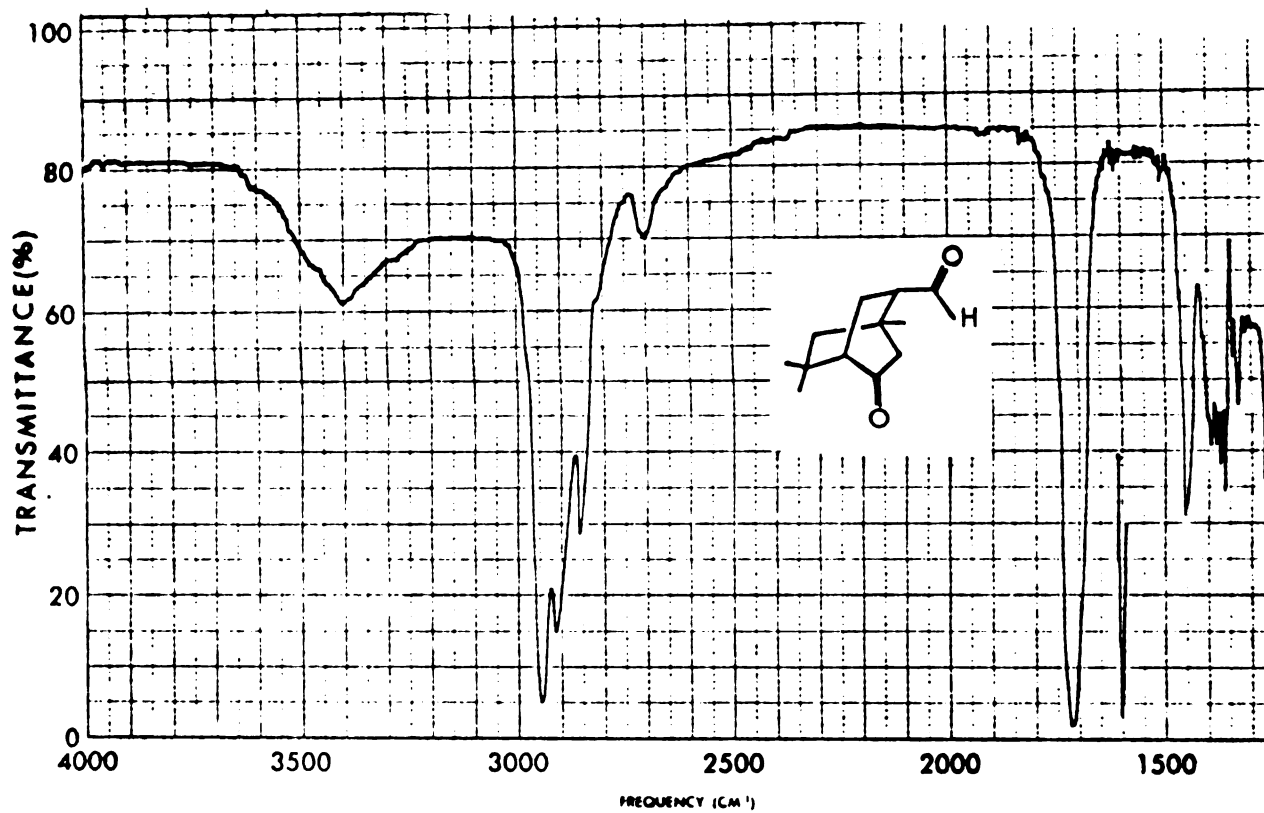


Figure 21. Infrared spectrum of 47.

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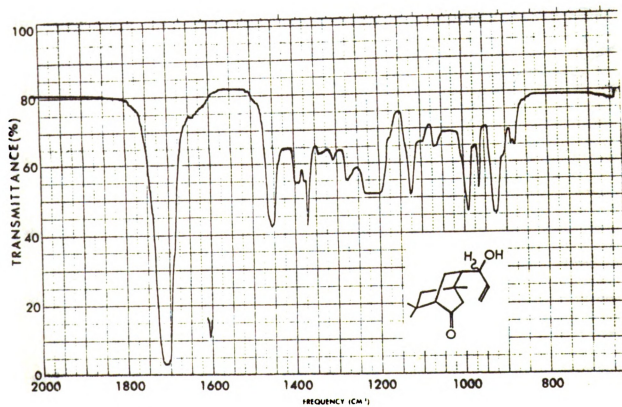
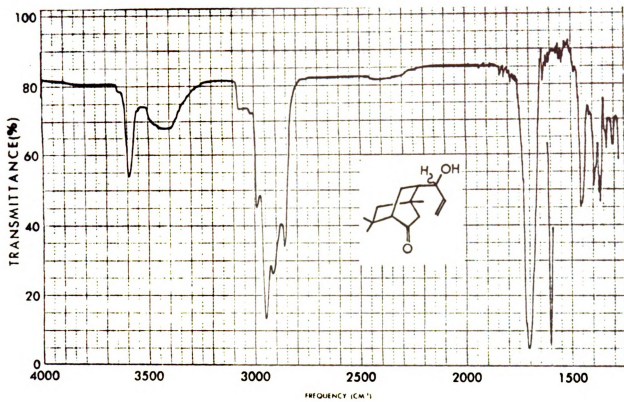


Figure 22. Infrared spectrum of 48.

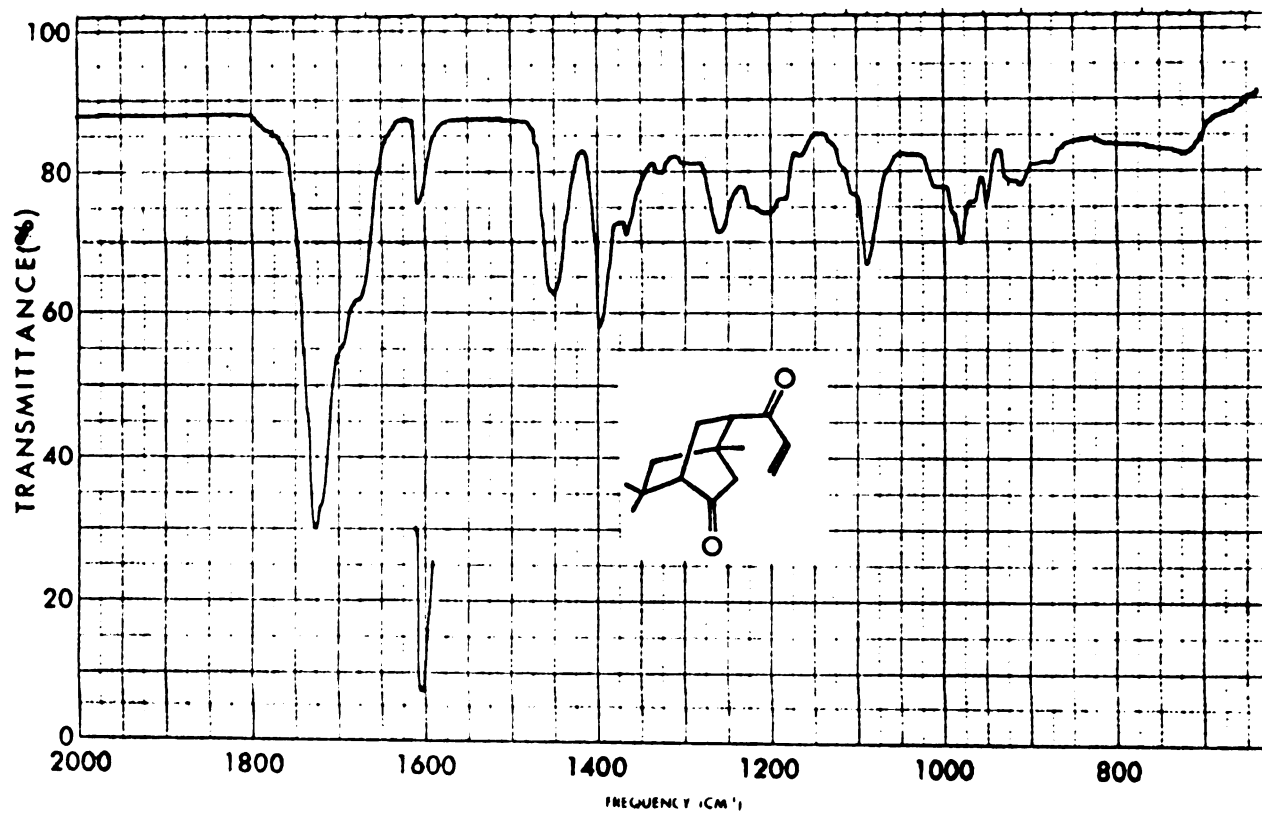
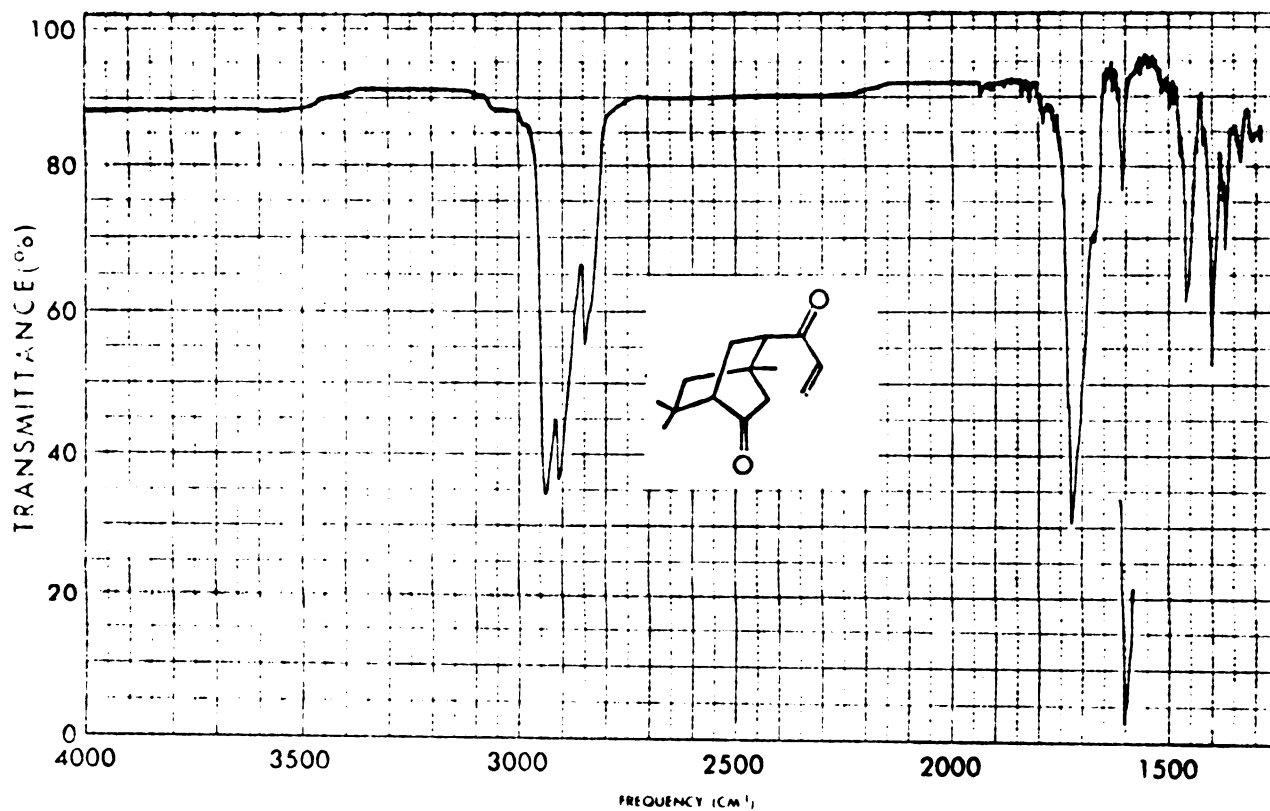


Figure 23. Infrared spectrum of 49.

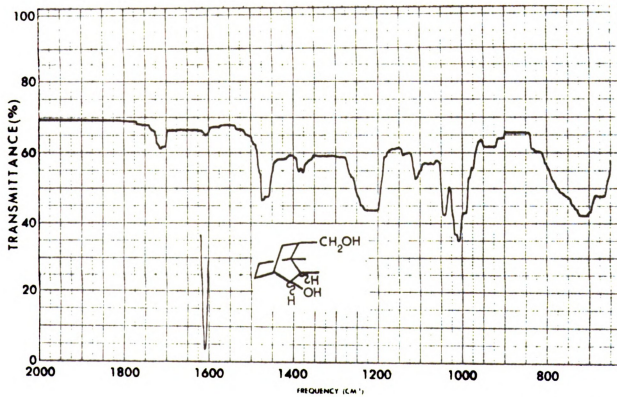
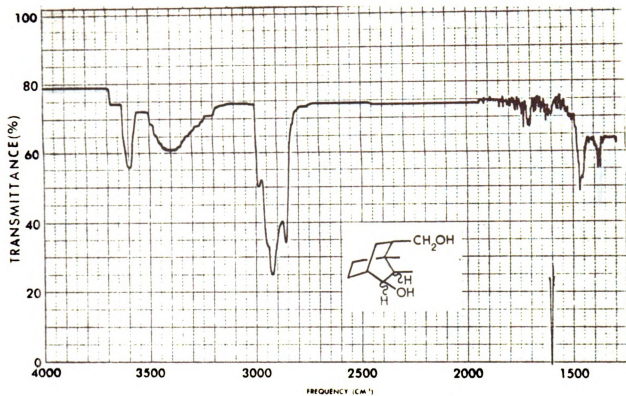


Figure 24. Infrared spectrum of 50.

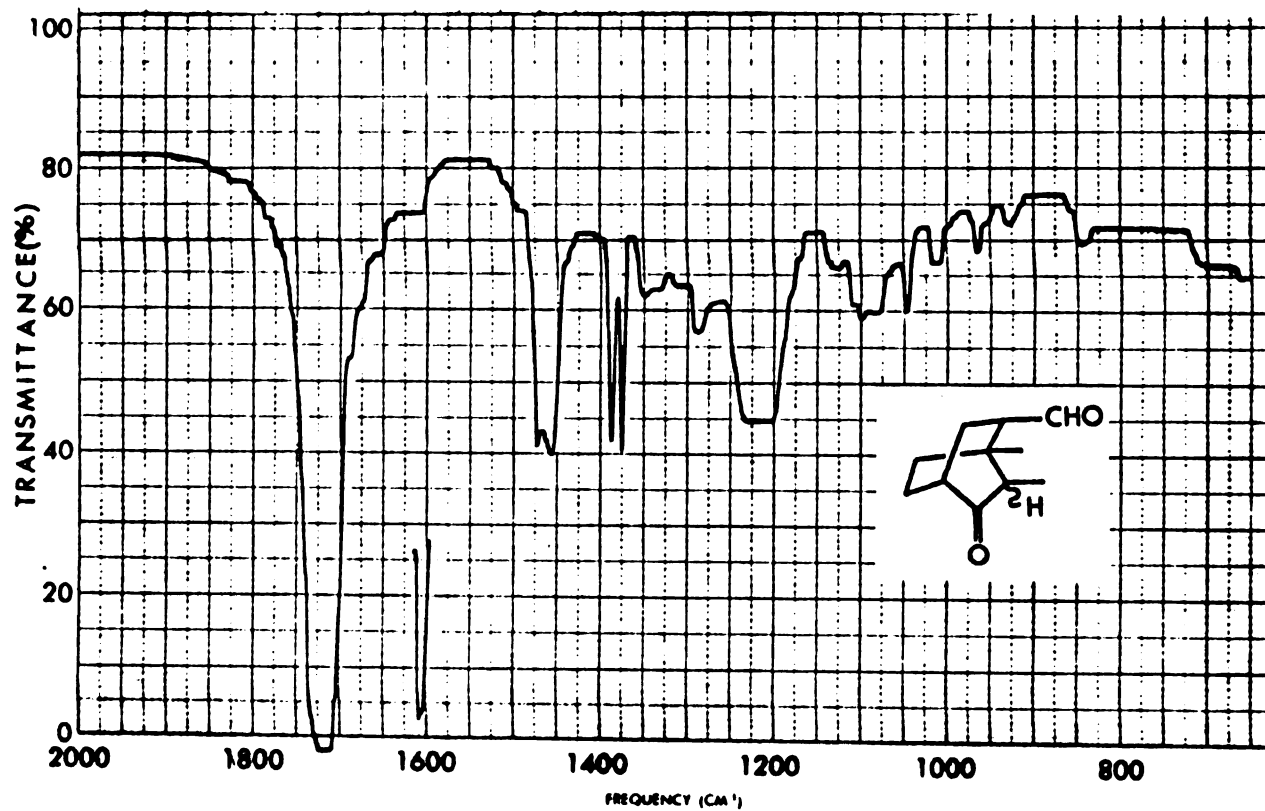
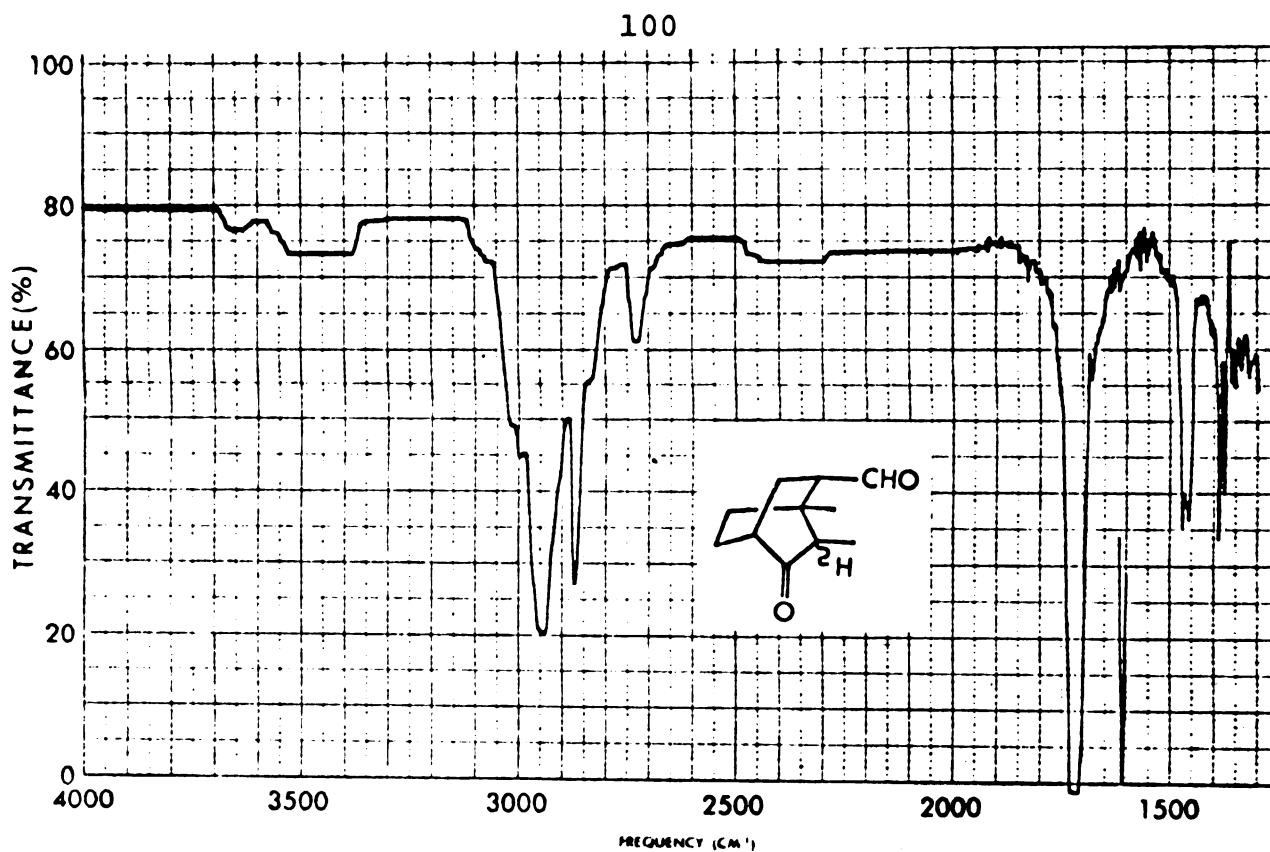


Figure 25. Infrared spectrum of 51.

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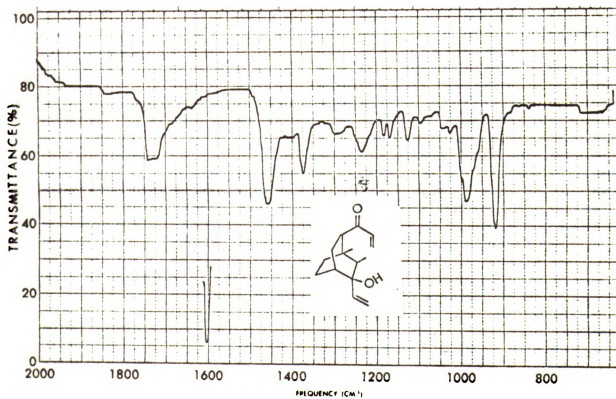
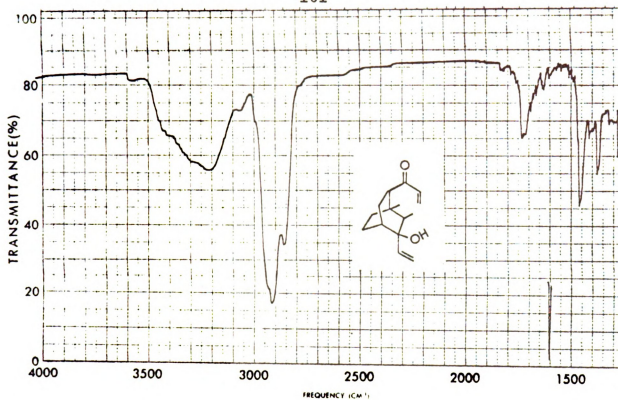


Figure 26. Infrared spectrum of 54.

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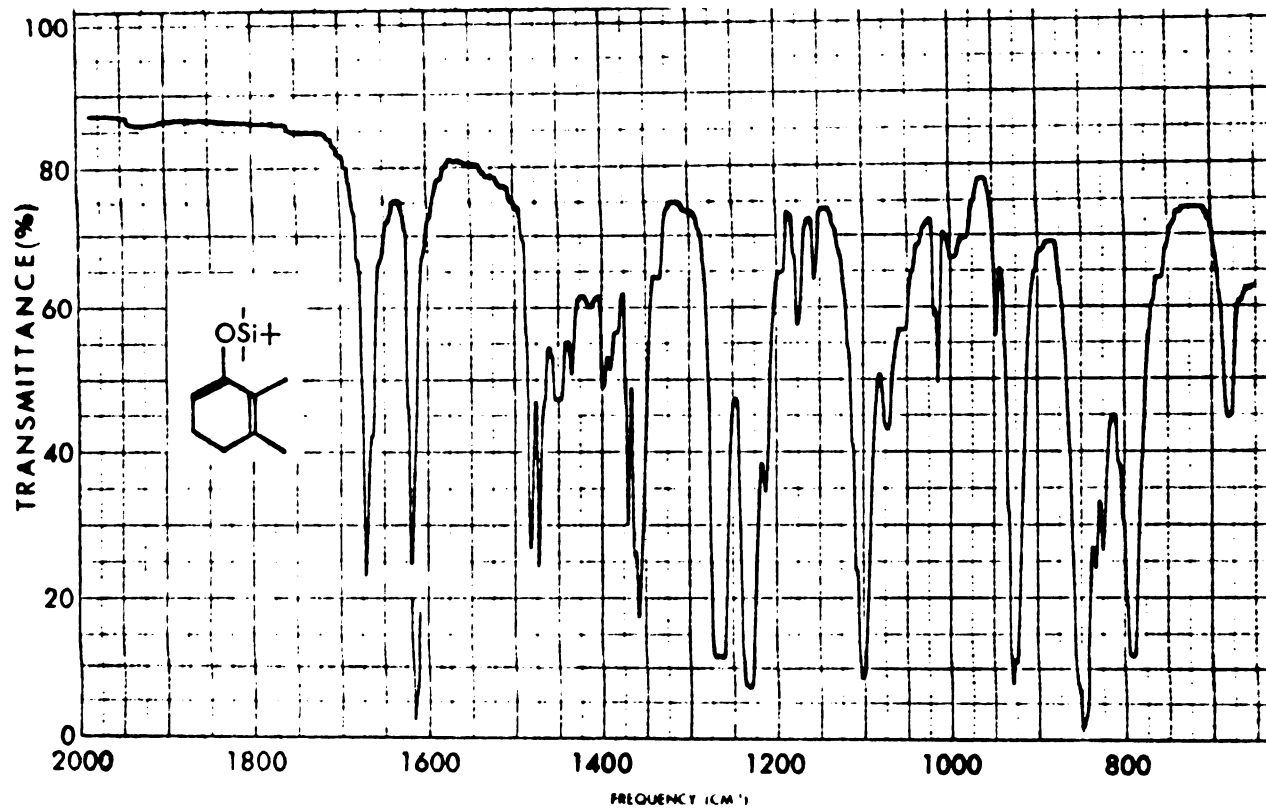
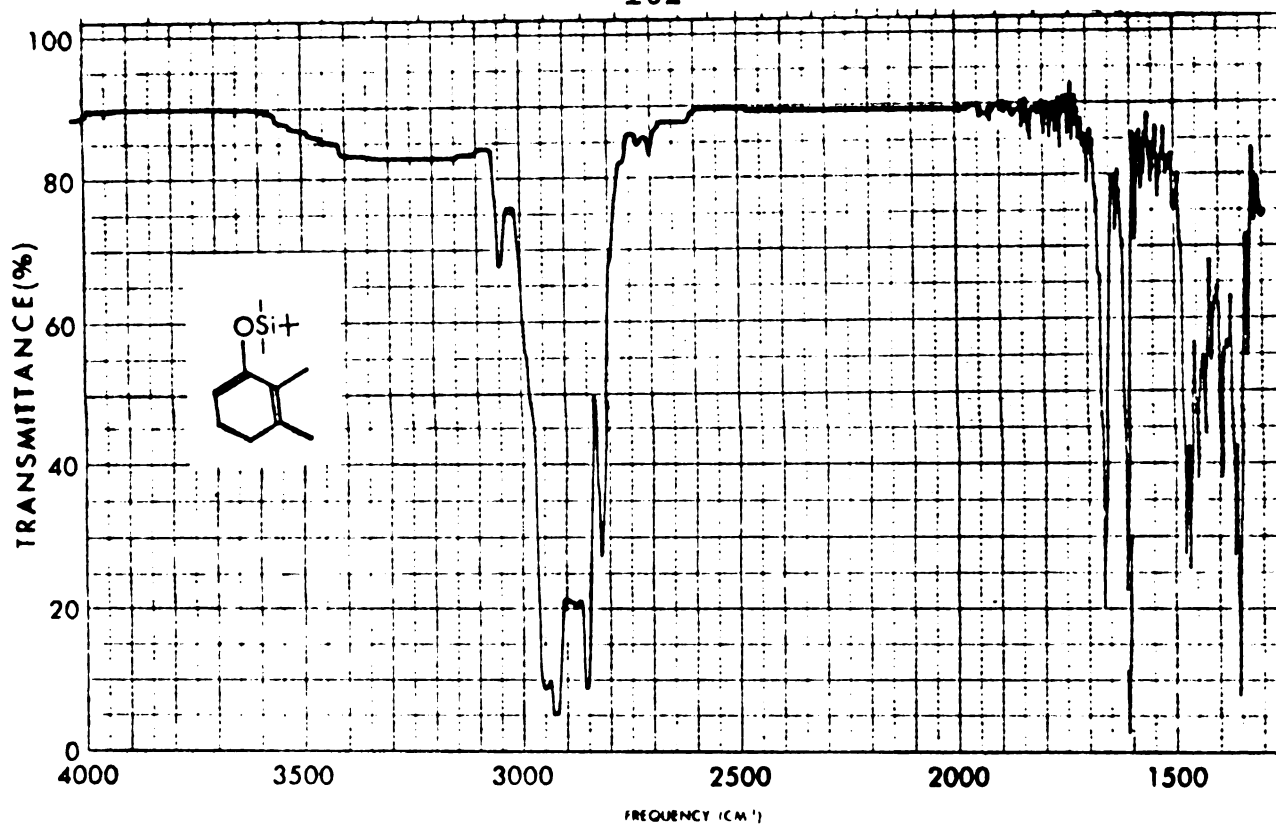


Figure 27. Infrared spectrum of 55.

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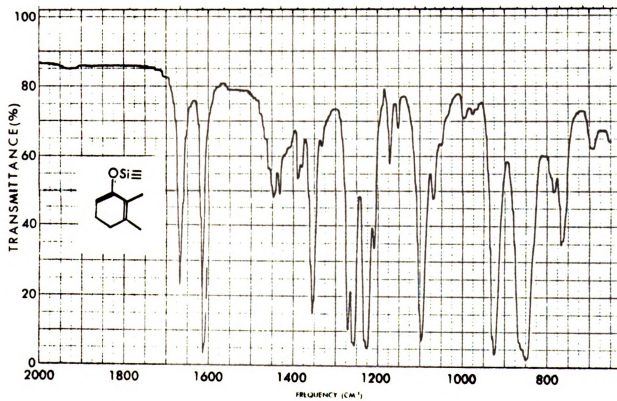
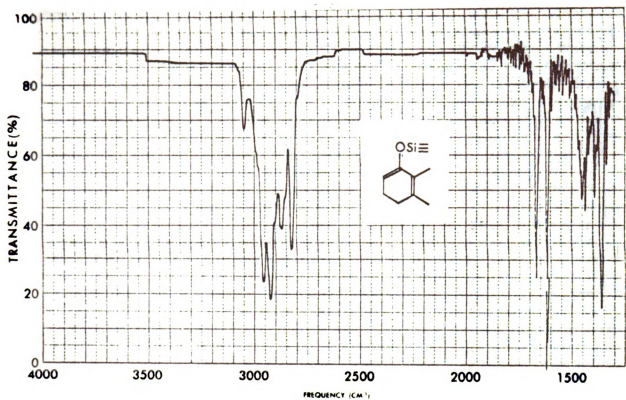
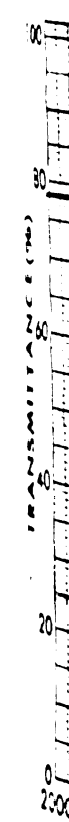
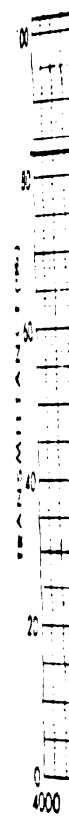


Figure 28. Infrared spectrum of 56.



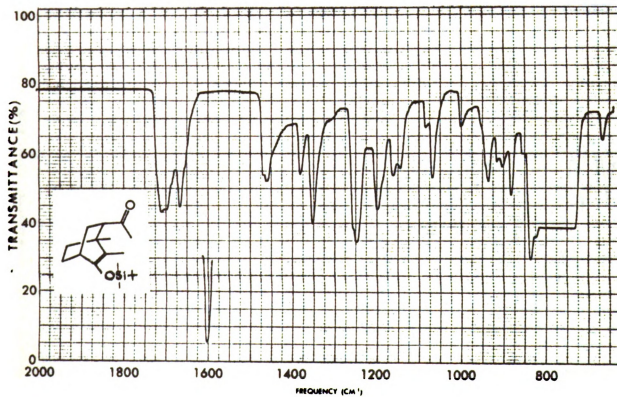
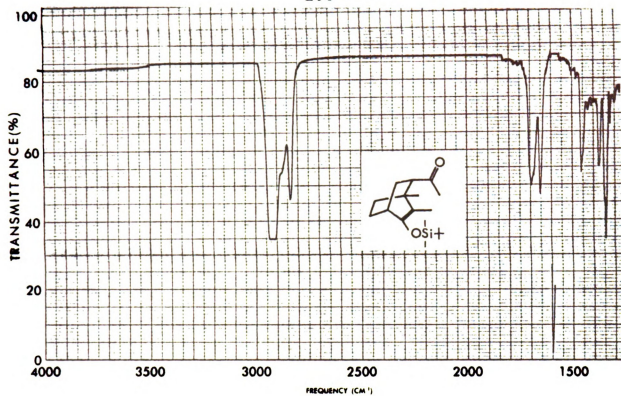


Figure 29. Infrared spectrum of 57.

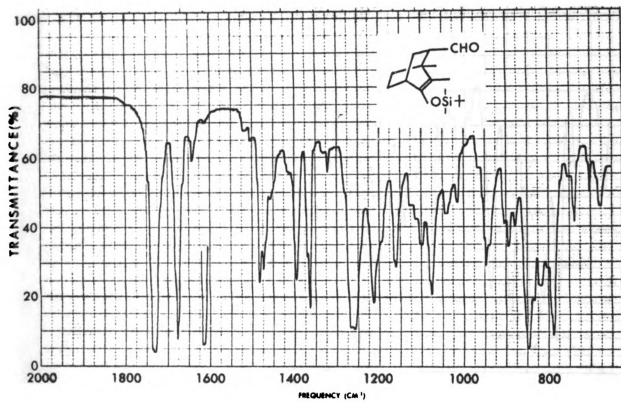
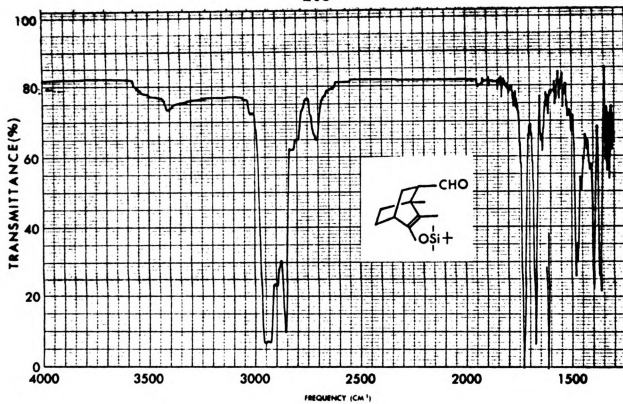


Figure 30. Infrared spectrum of 58.

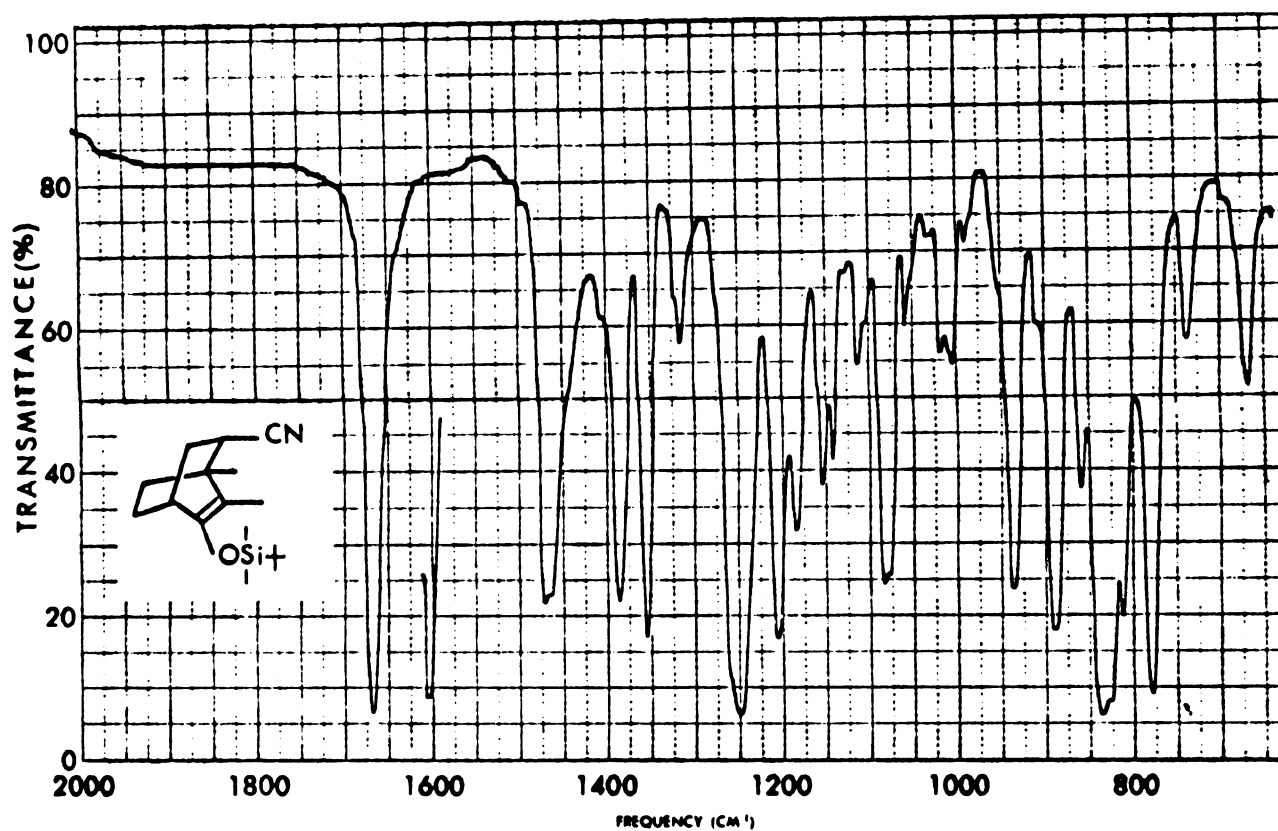
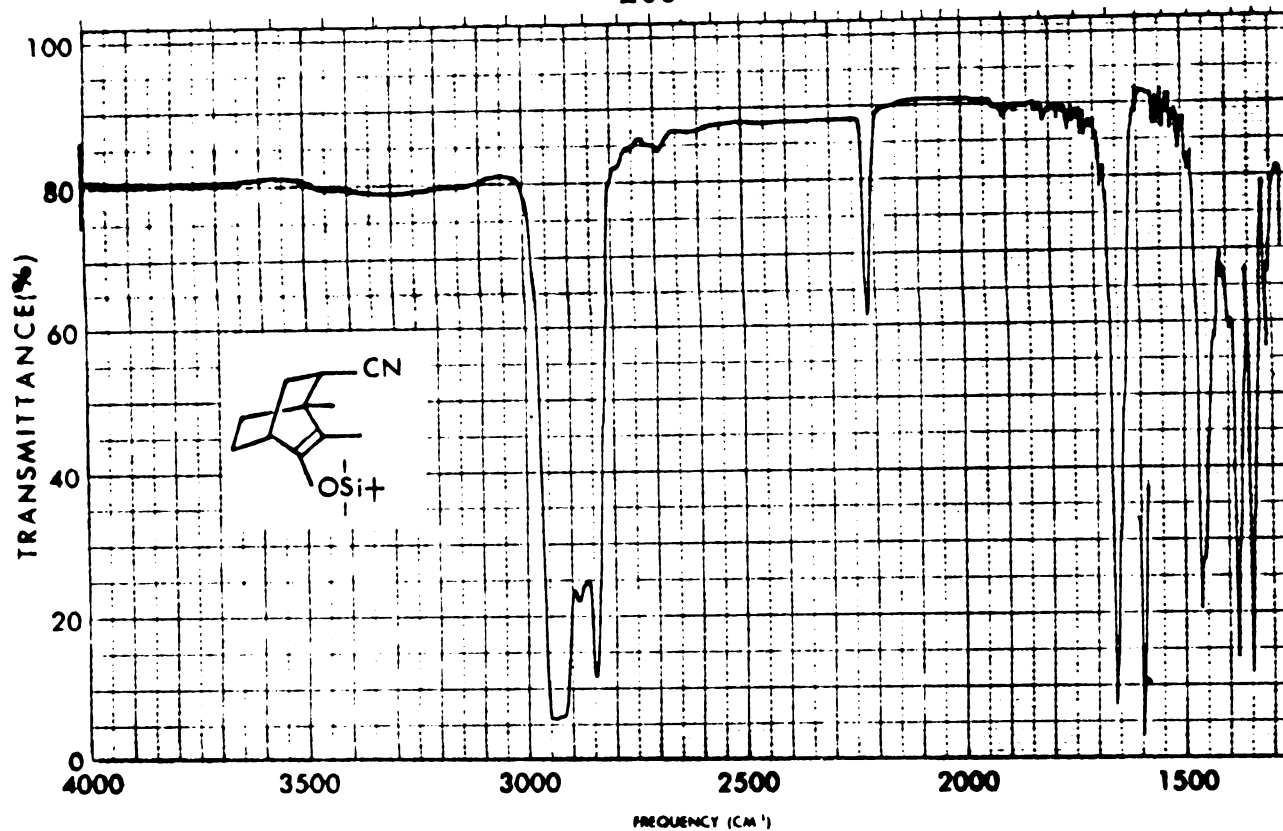


Figure 31. Infrared spectrum of 59.

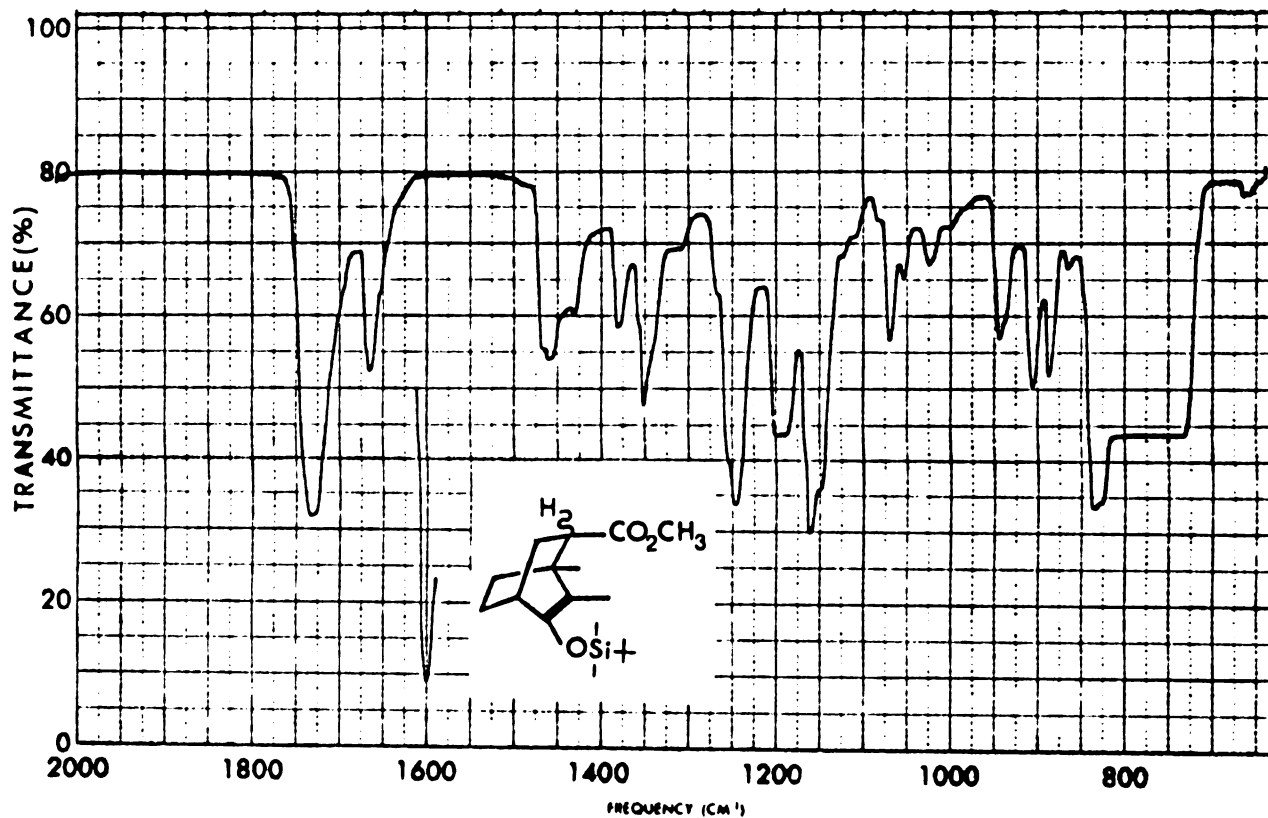
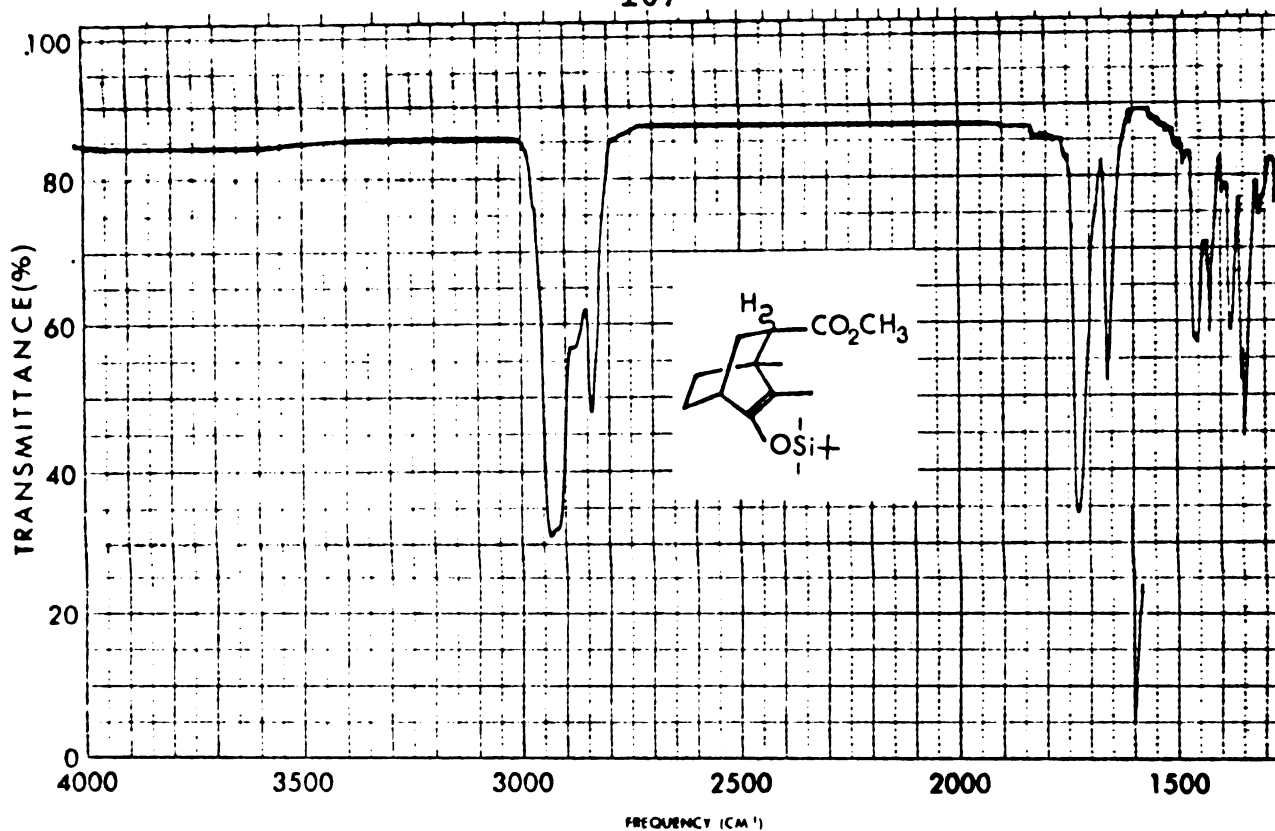


Figure 32. Infrared spectrum of 60.

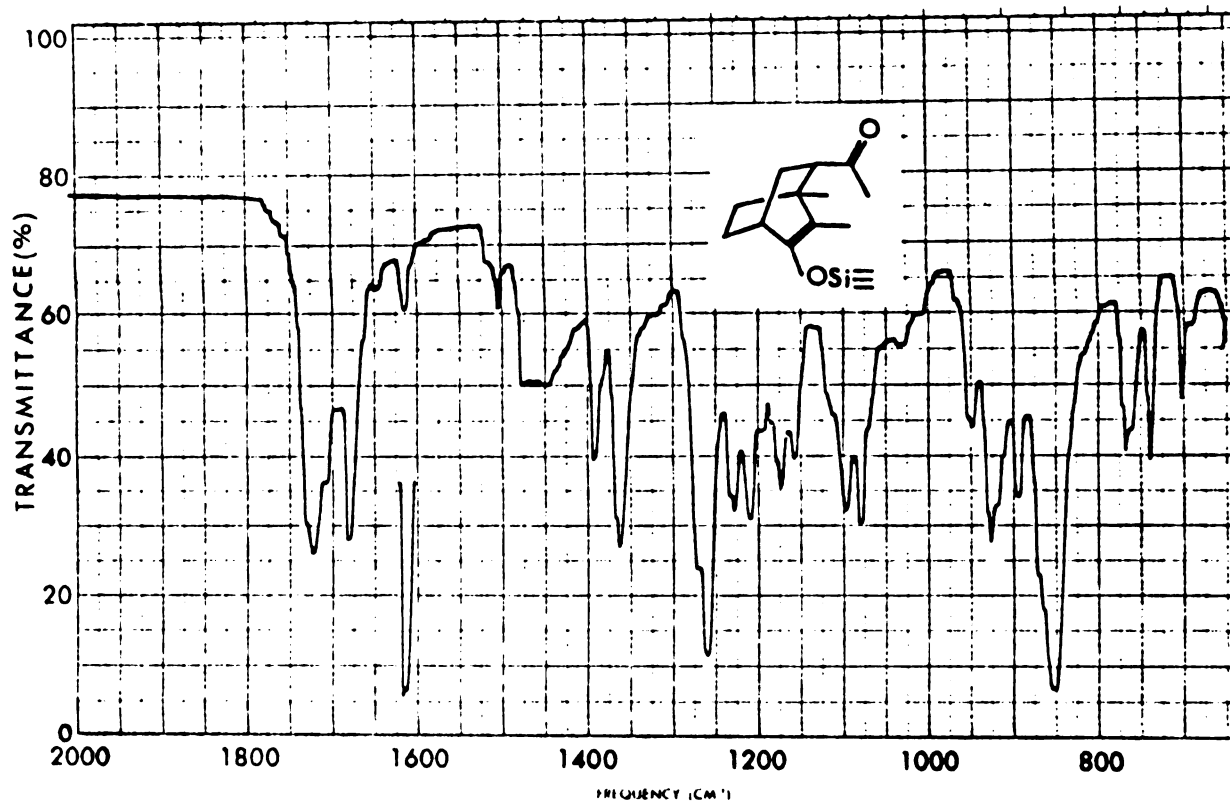
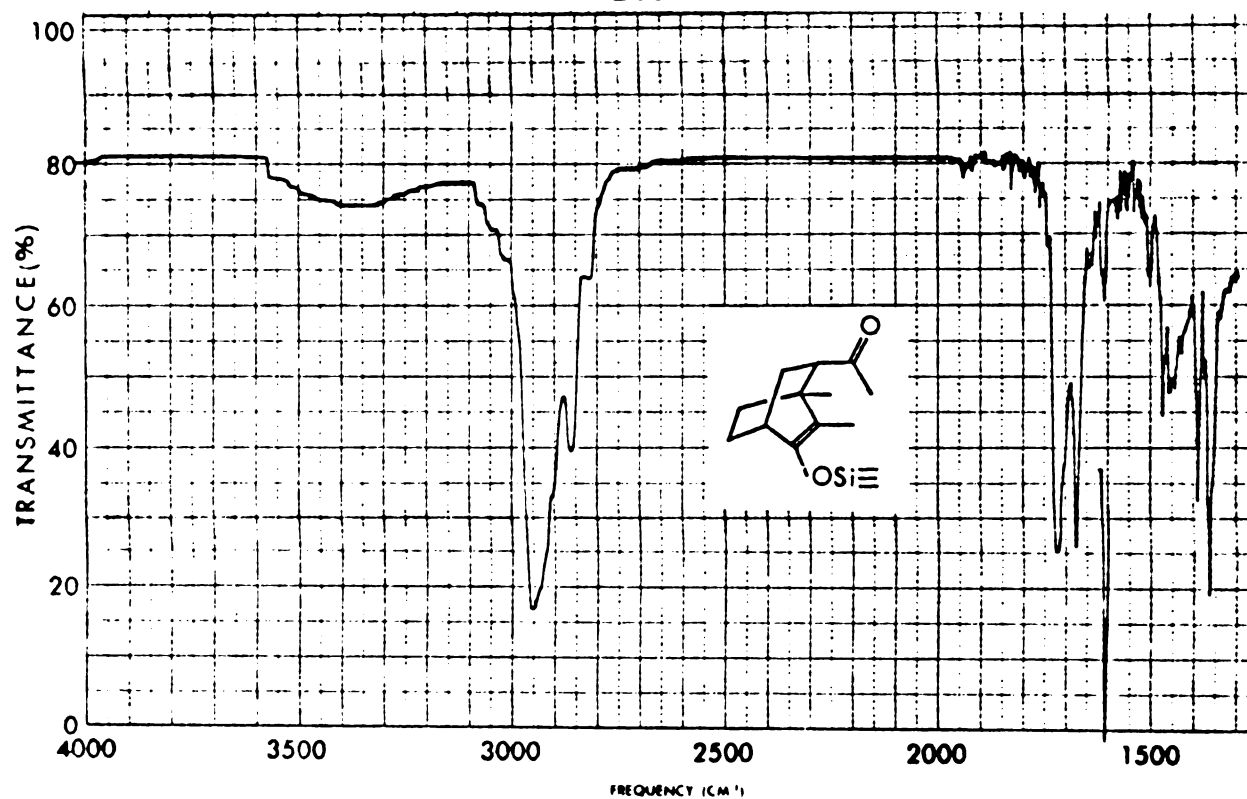


Figure 33. Infrared spectrum of 61.

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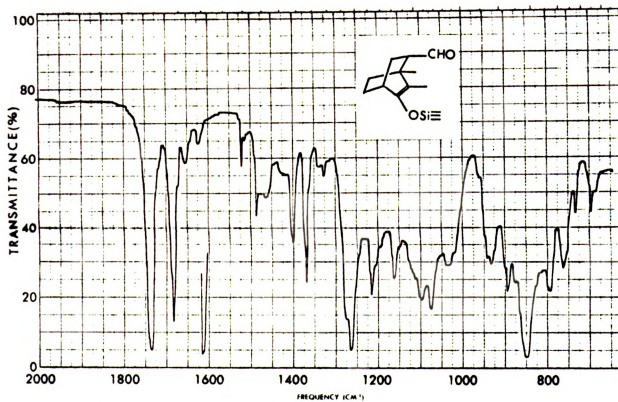
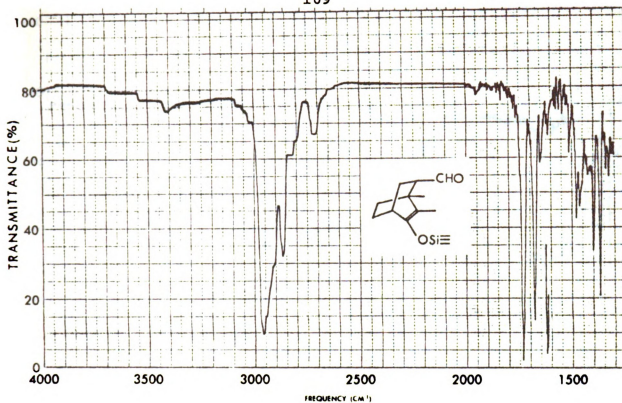


Figure 34. Infrared spectrum of 62.

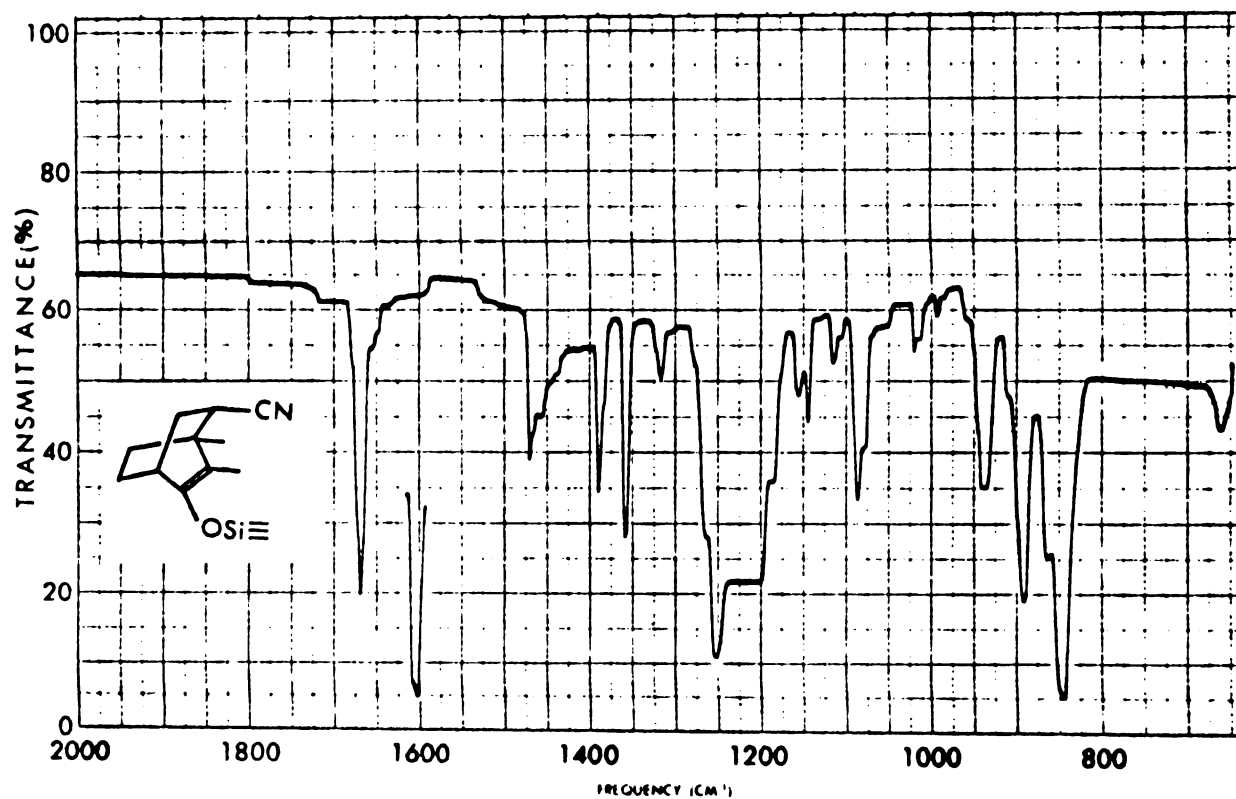
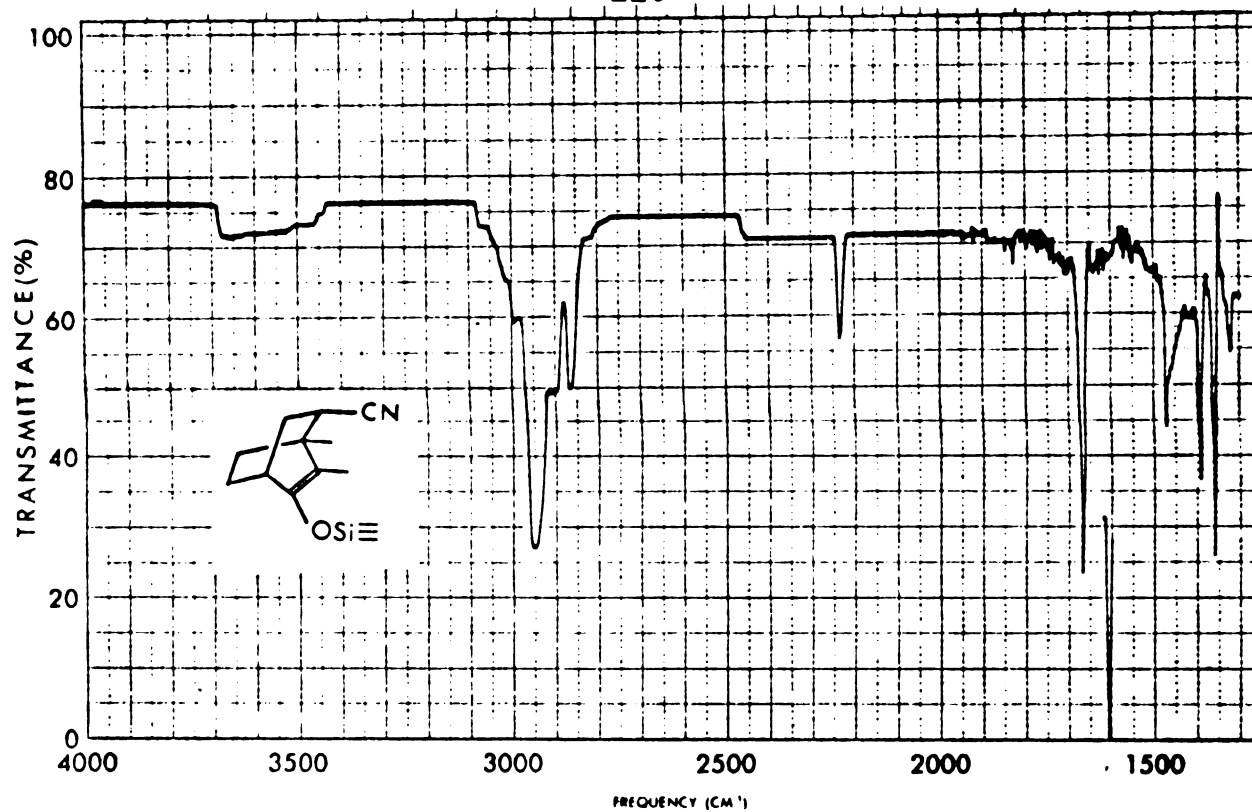


Figure 35. Infrared spectrum of 63.

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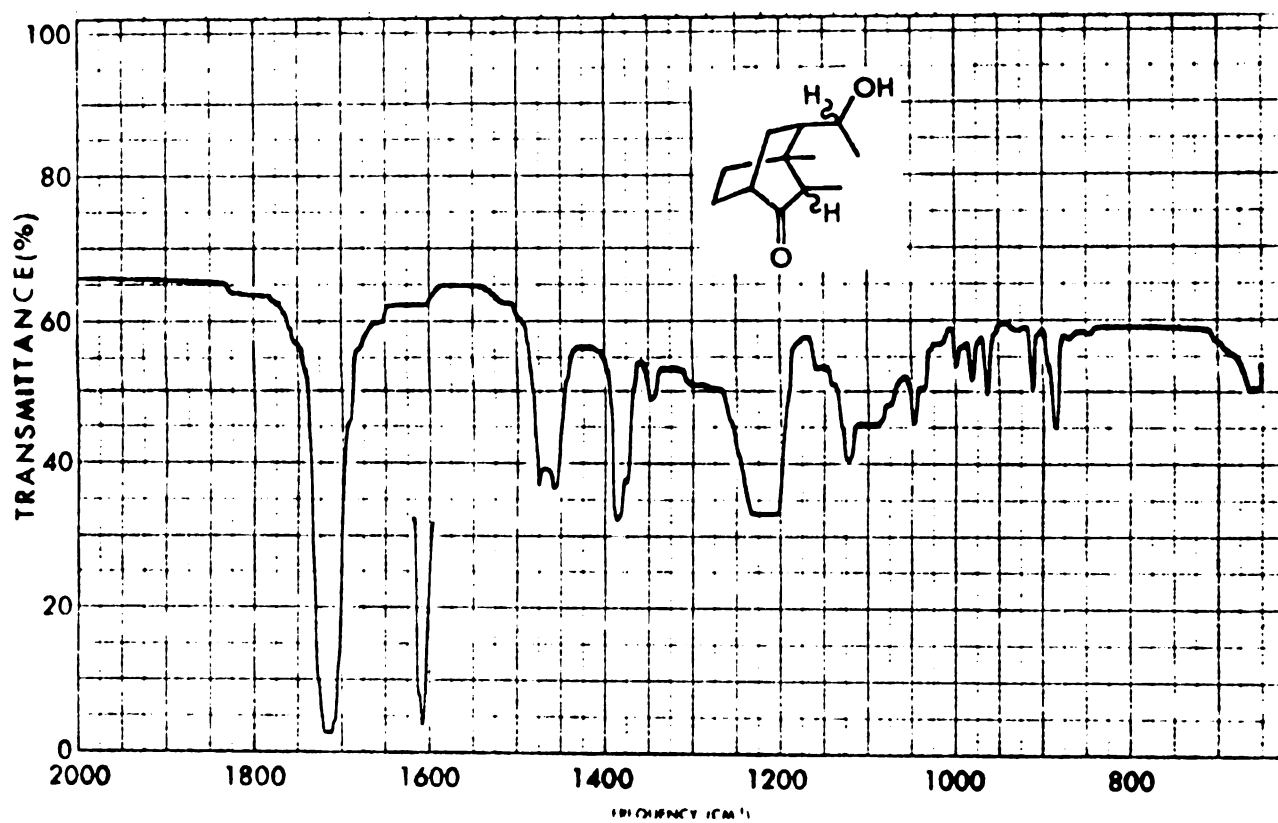
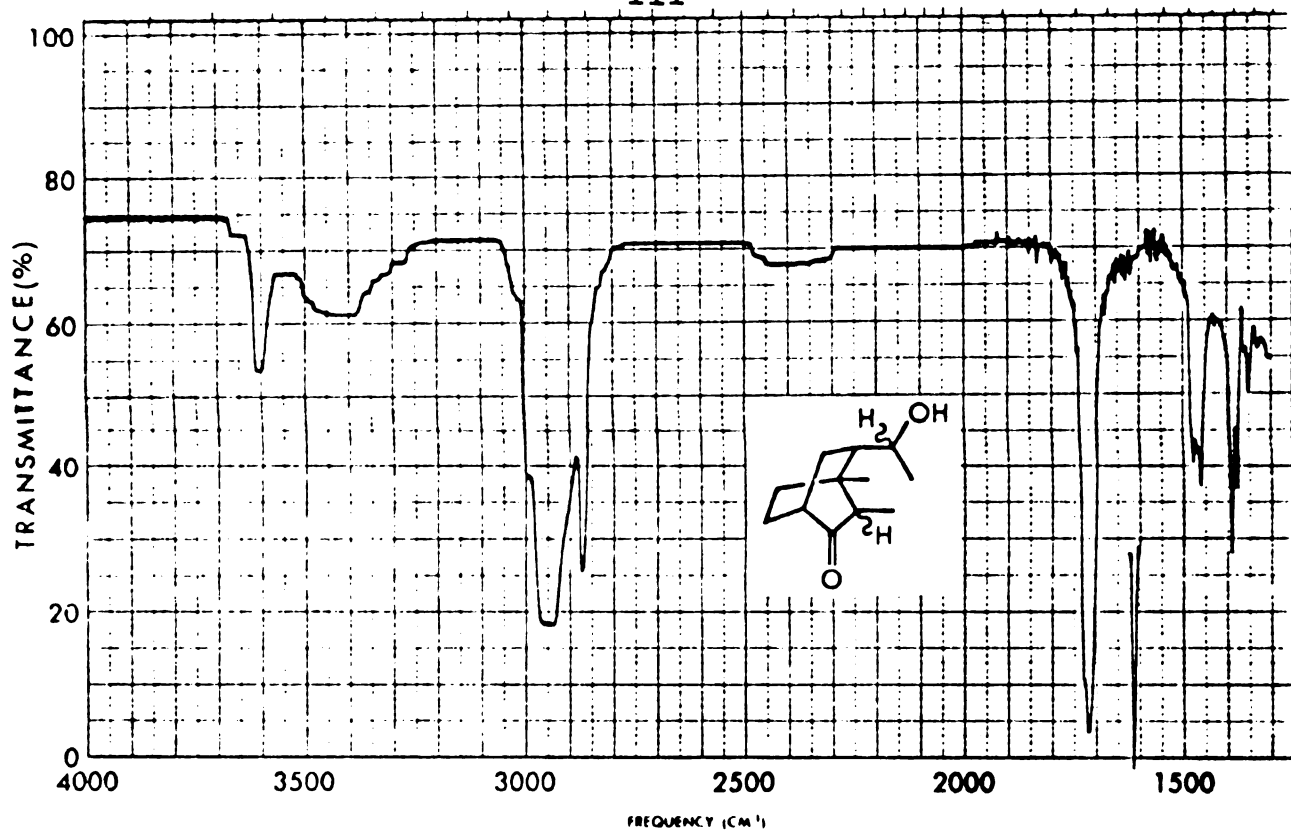


Figure 36. Infrared spectrum of 64.

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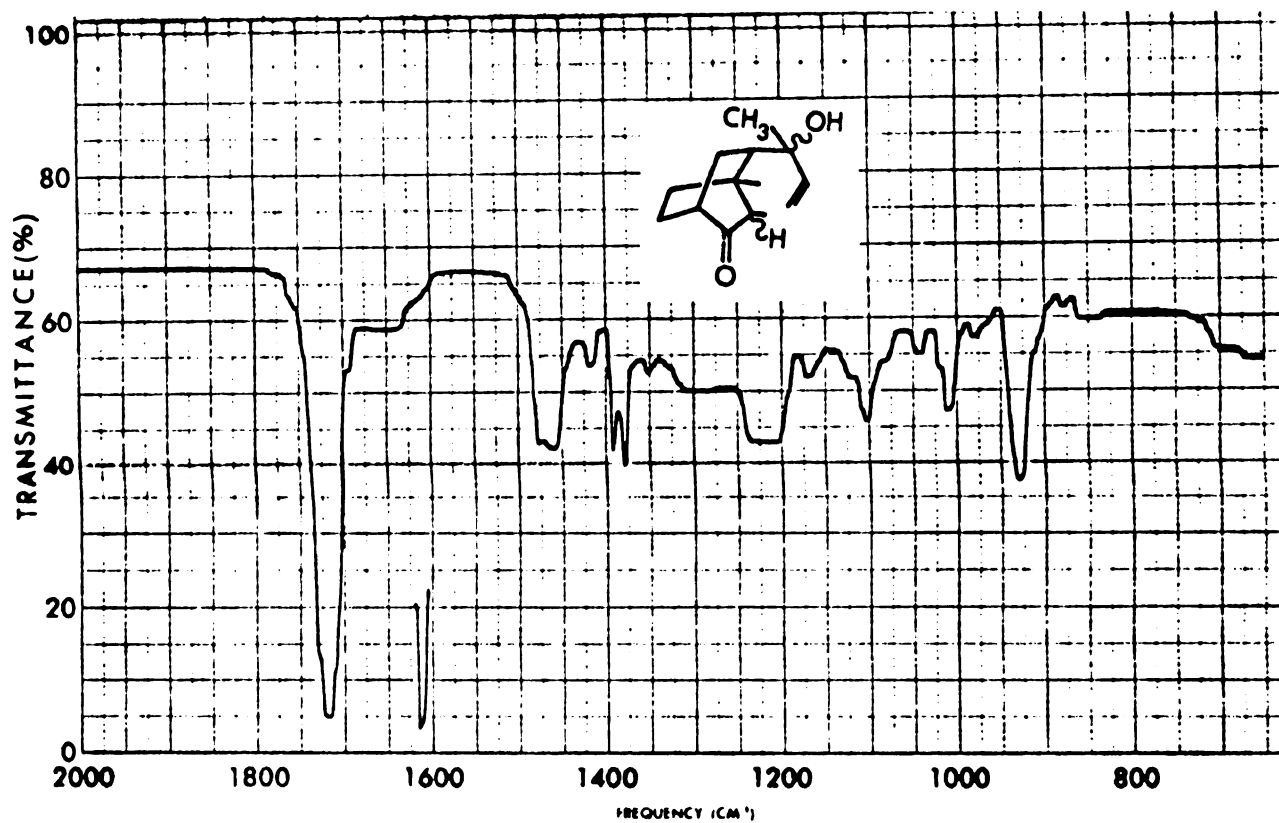
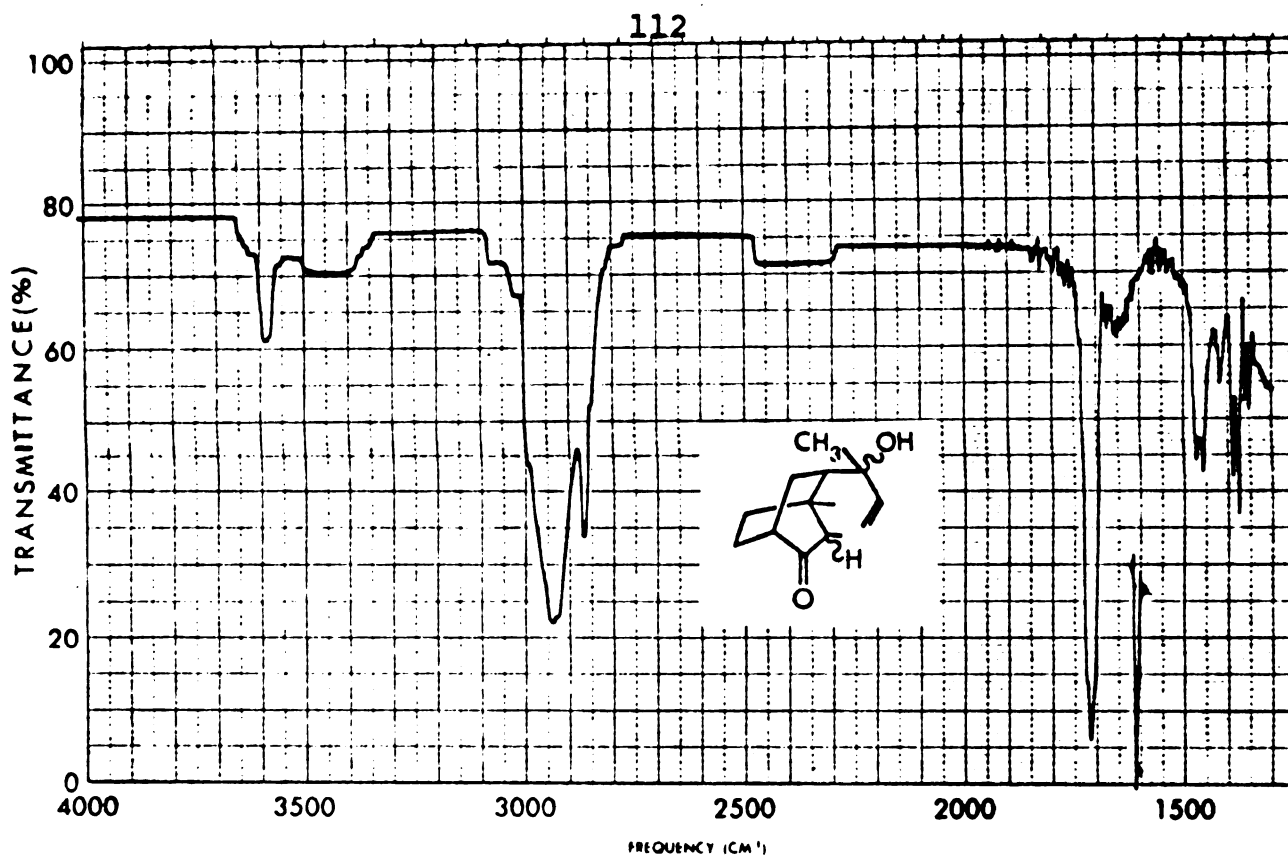


Figure 37. Infrared spectrum of 67.

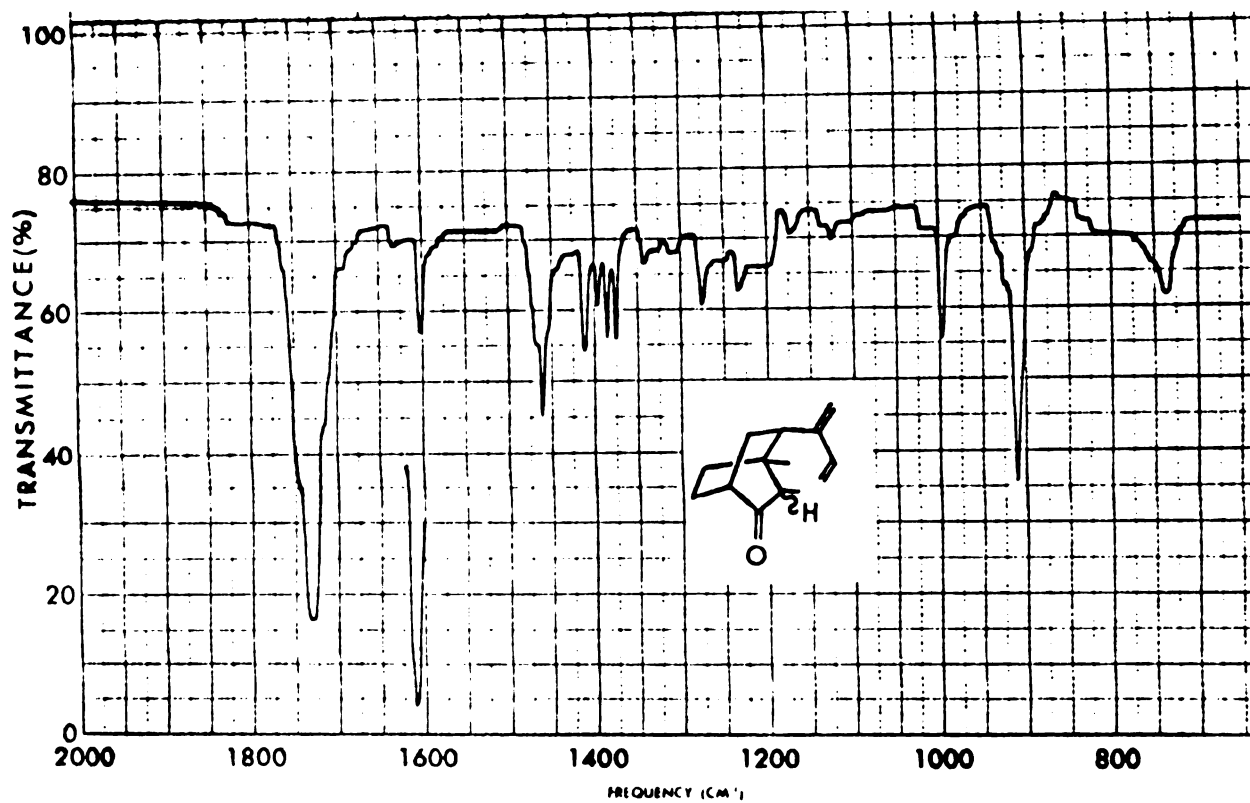
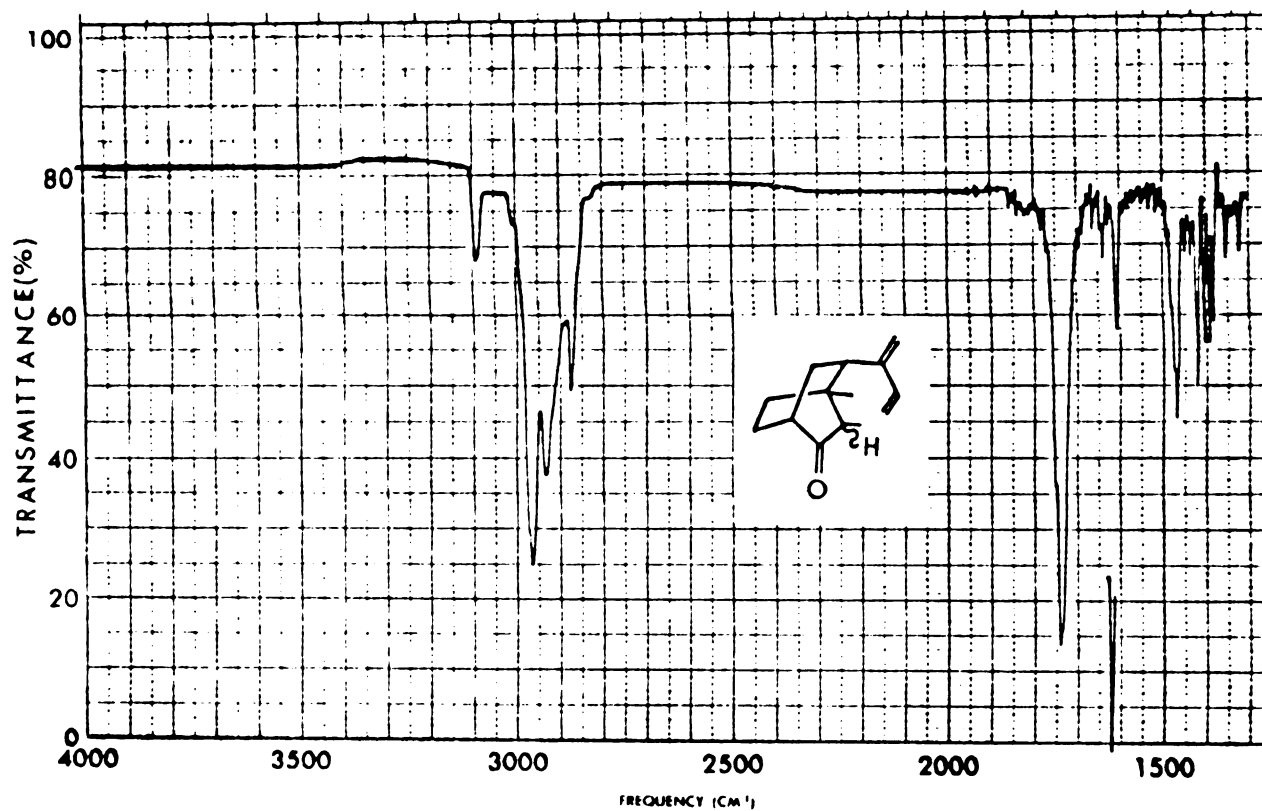


Figure 38. Infrared spectrum of 68.

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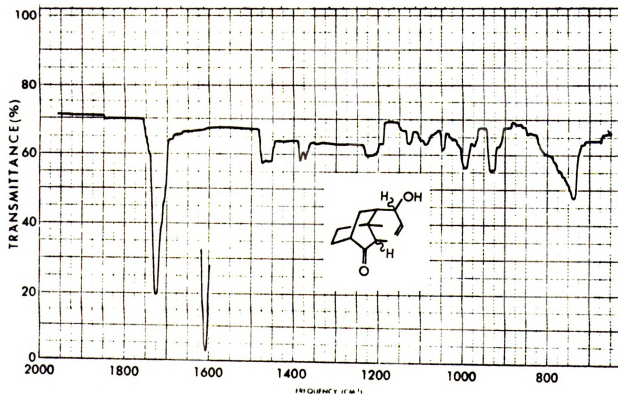
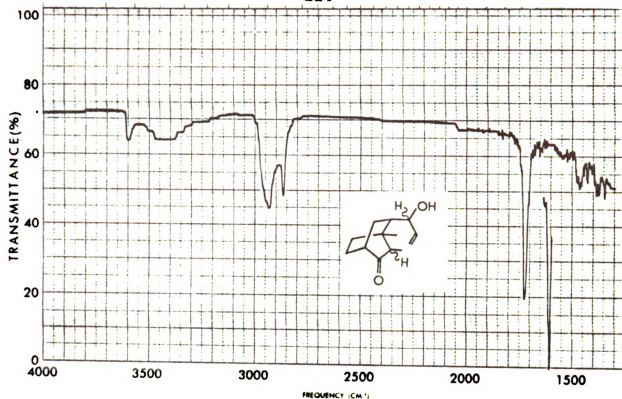


Figure 39. Infrared spectrum of 69.

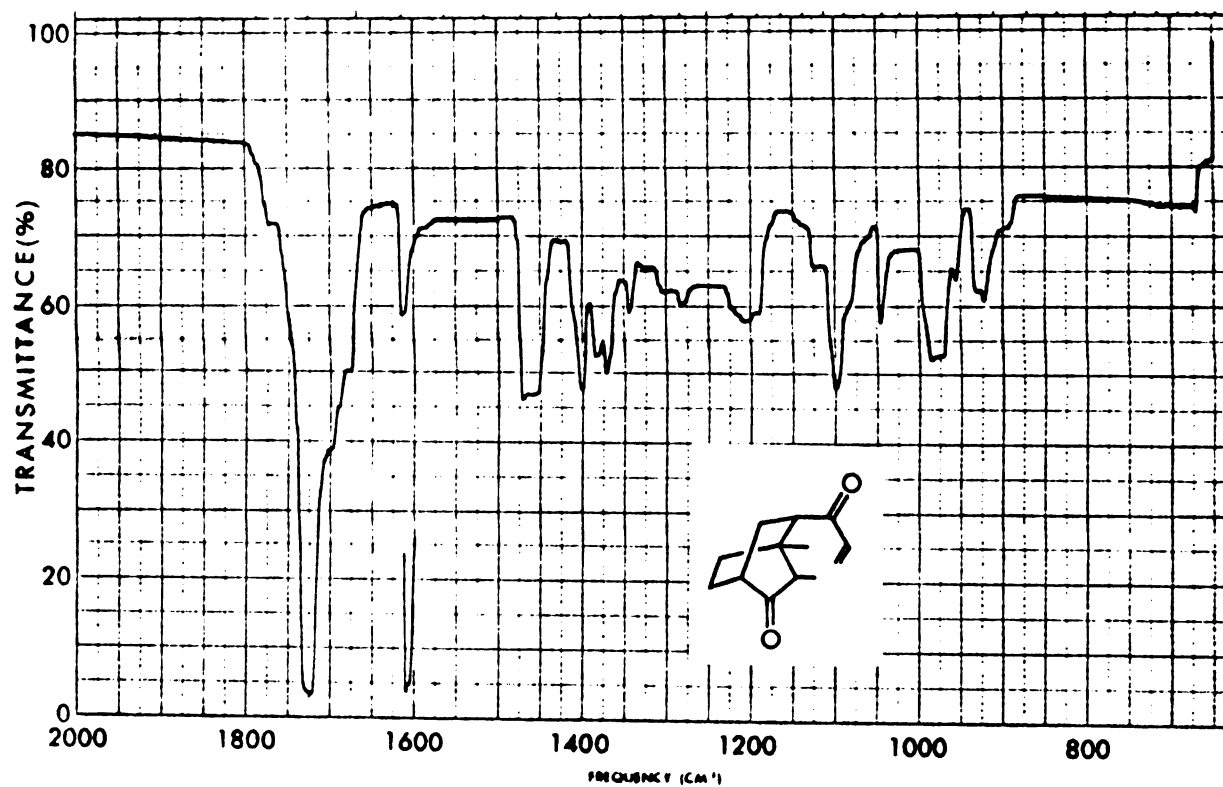
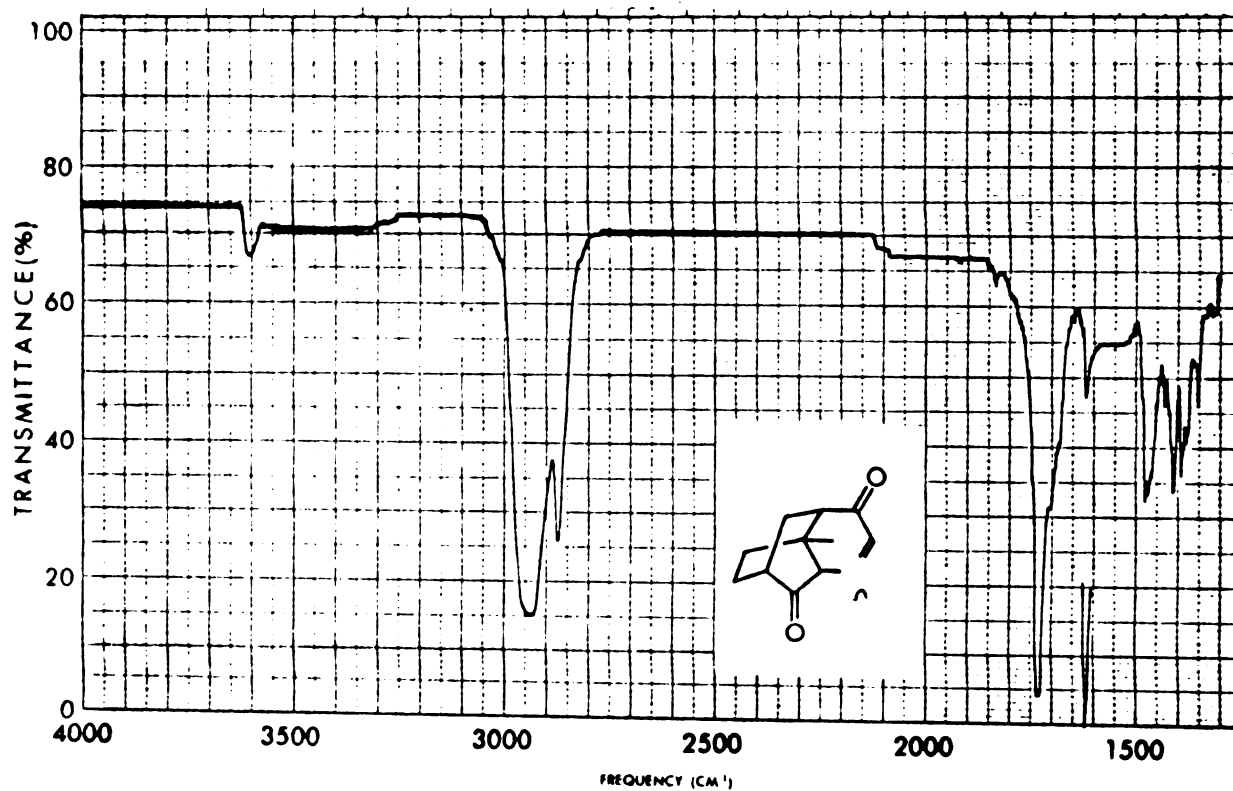
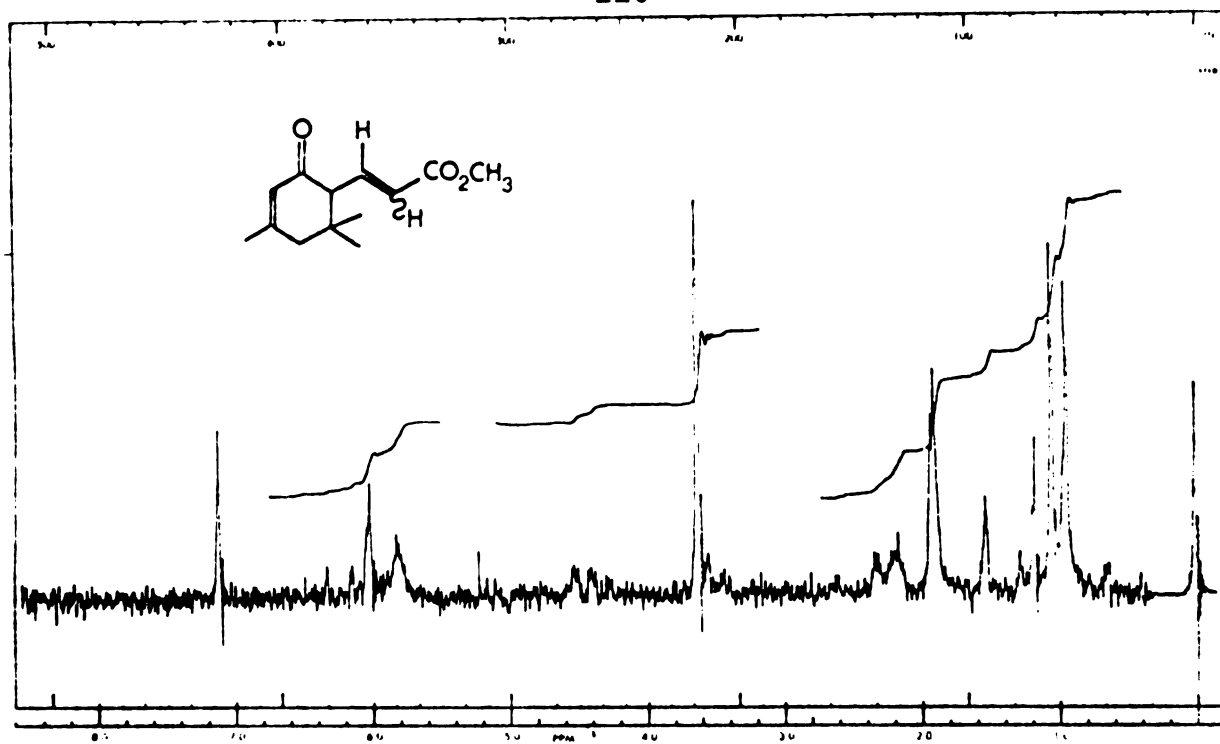
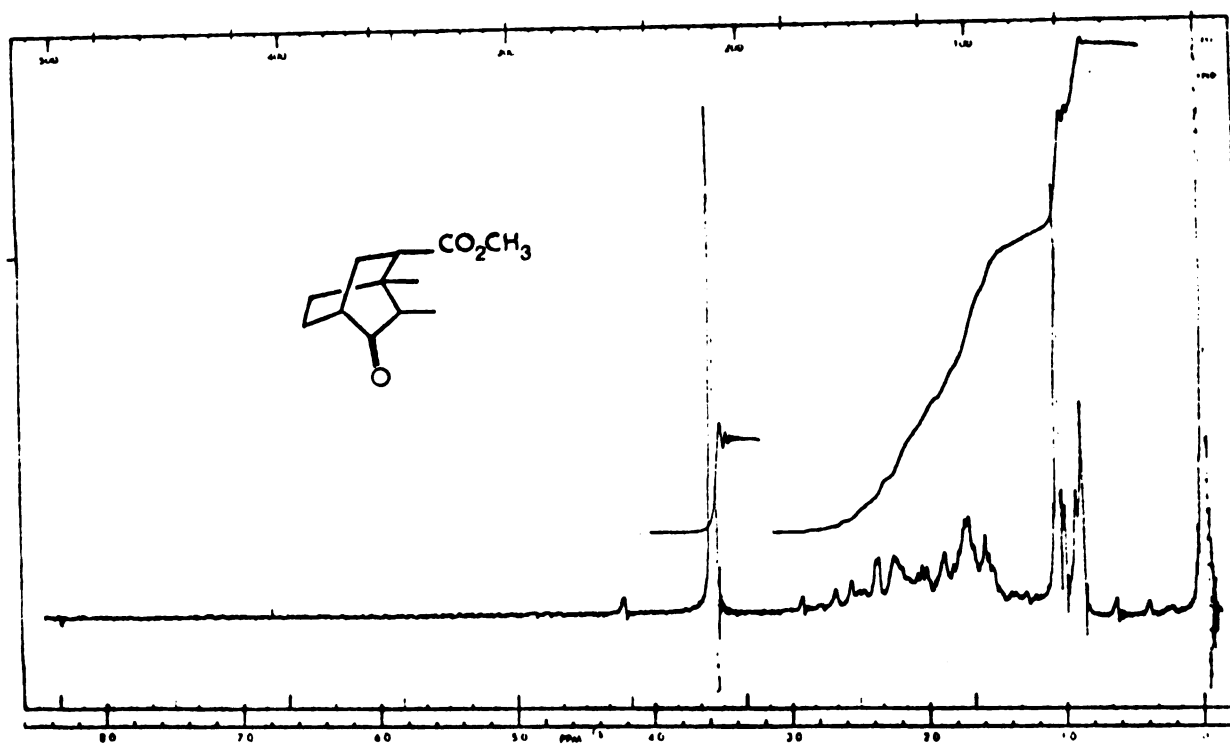


Figure 40. Infrared spectrum of 45.

Figure 41. Pmr spectrum of 22.Figure 42. Pmr spectrum of 24.

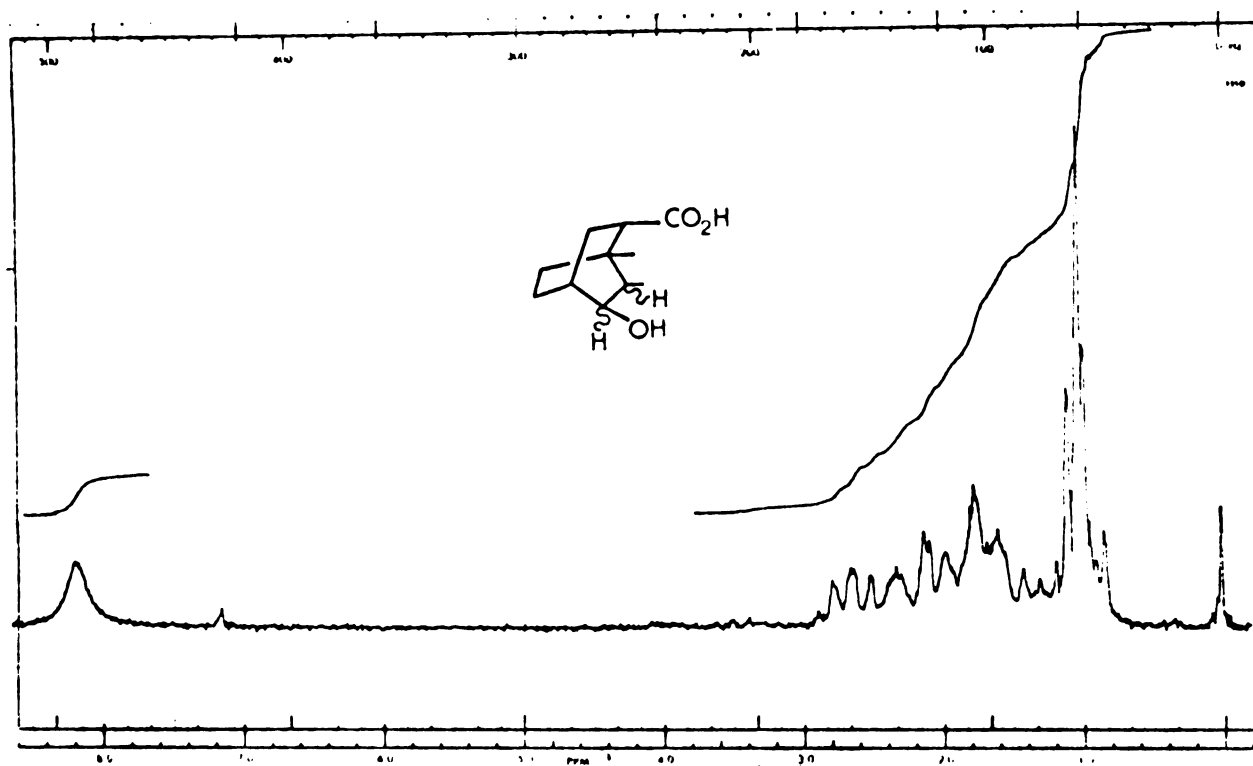


Figure 43. Pmr spectrum of 26.

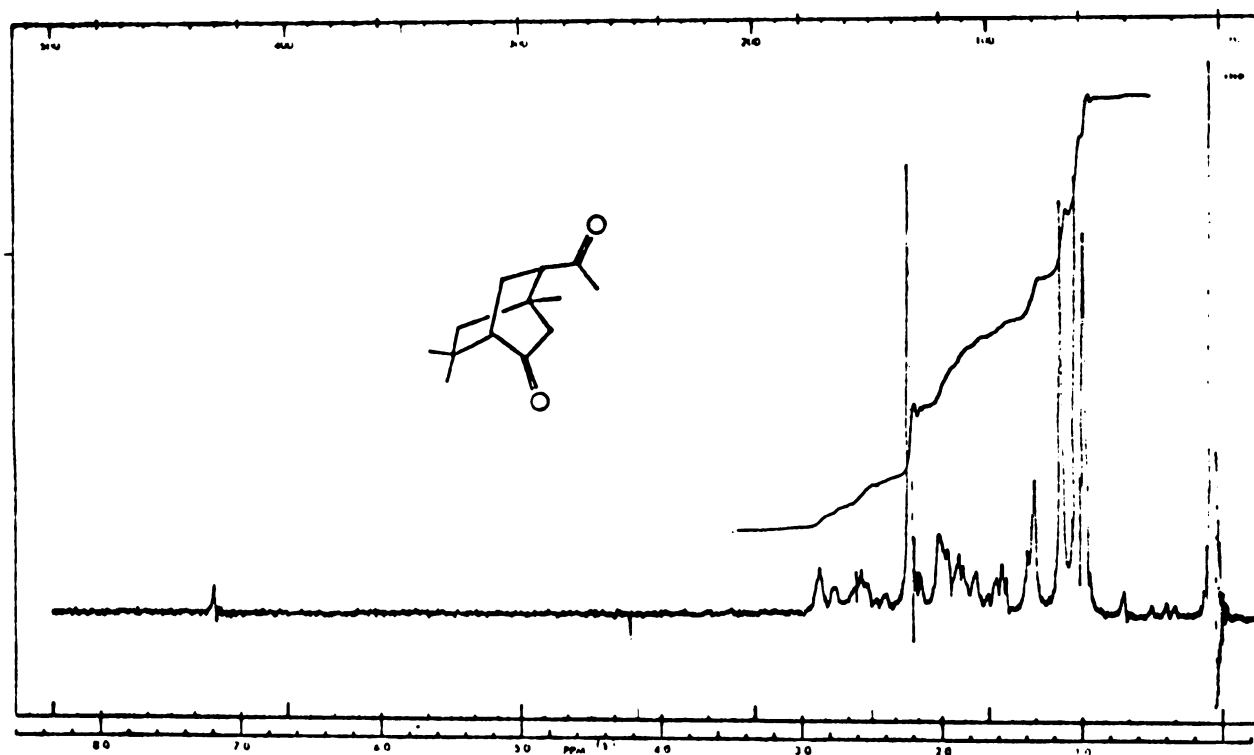


Figure 44. Pmr spectrum of 29.

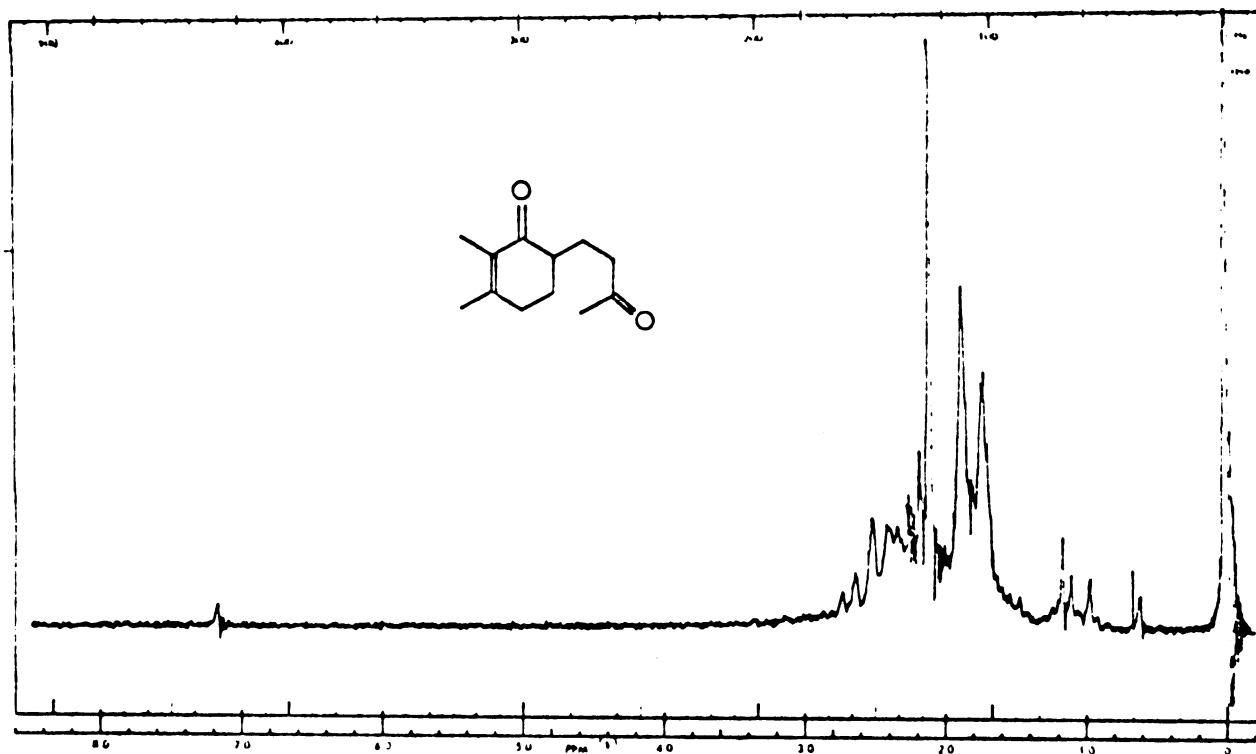


Figure 45. Pmr spectrum of 30.

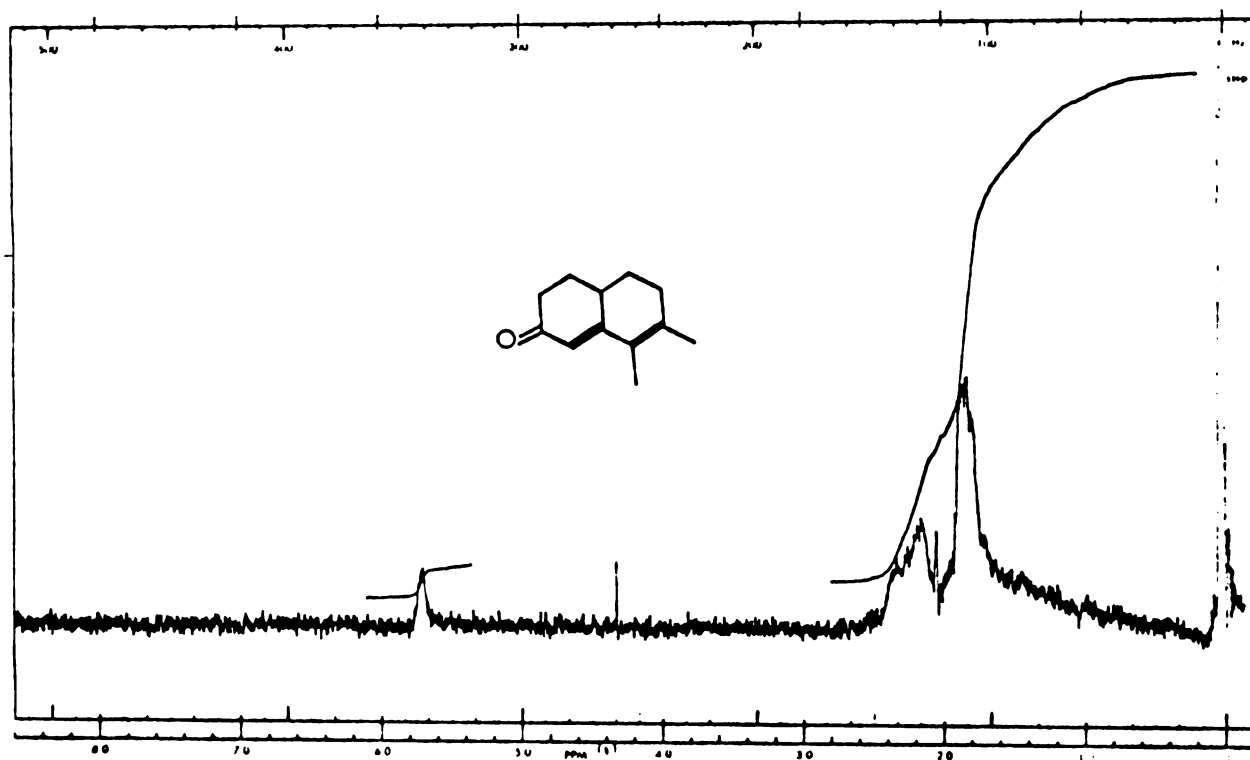


Figure 46. Pmr spectrum of 31.

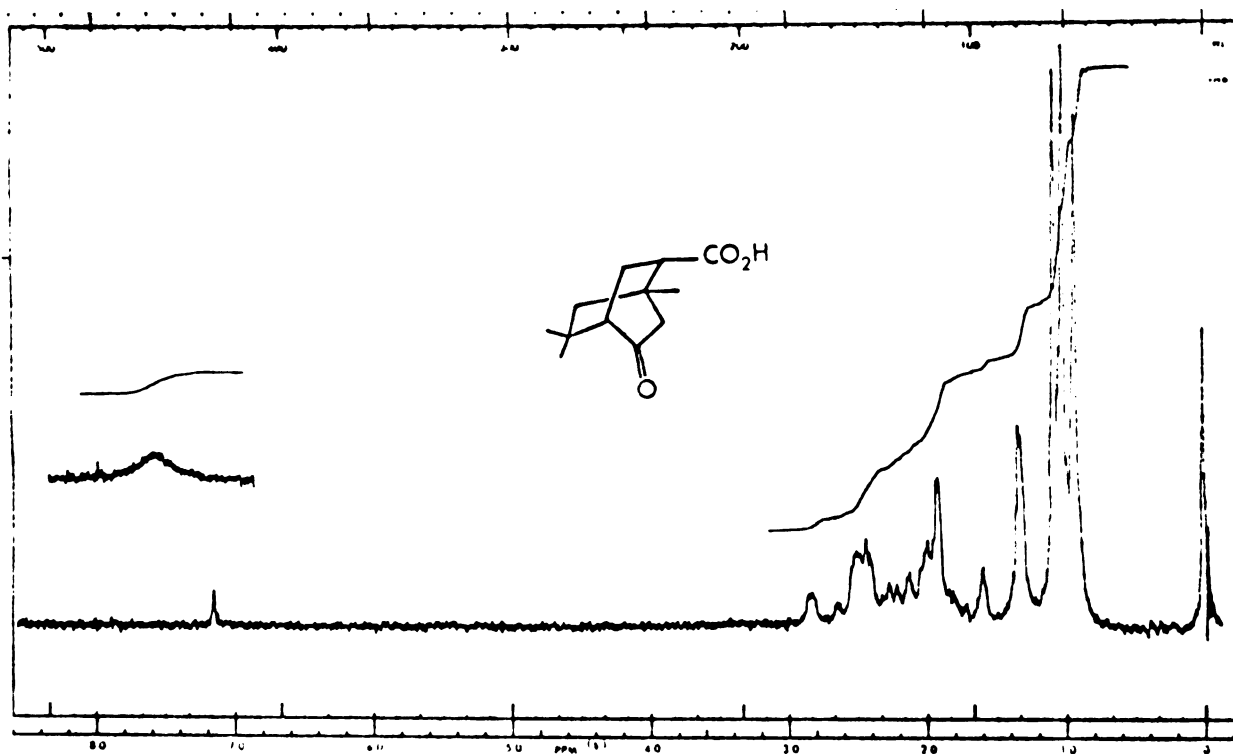


Figure 47. Pmr spectrum of 34.

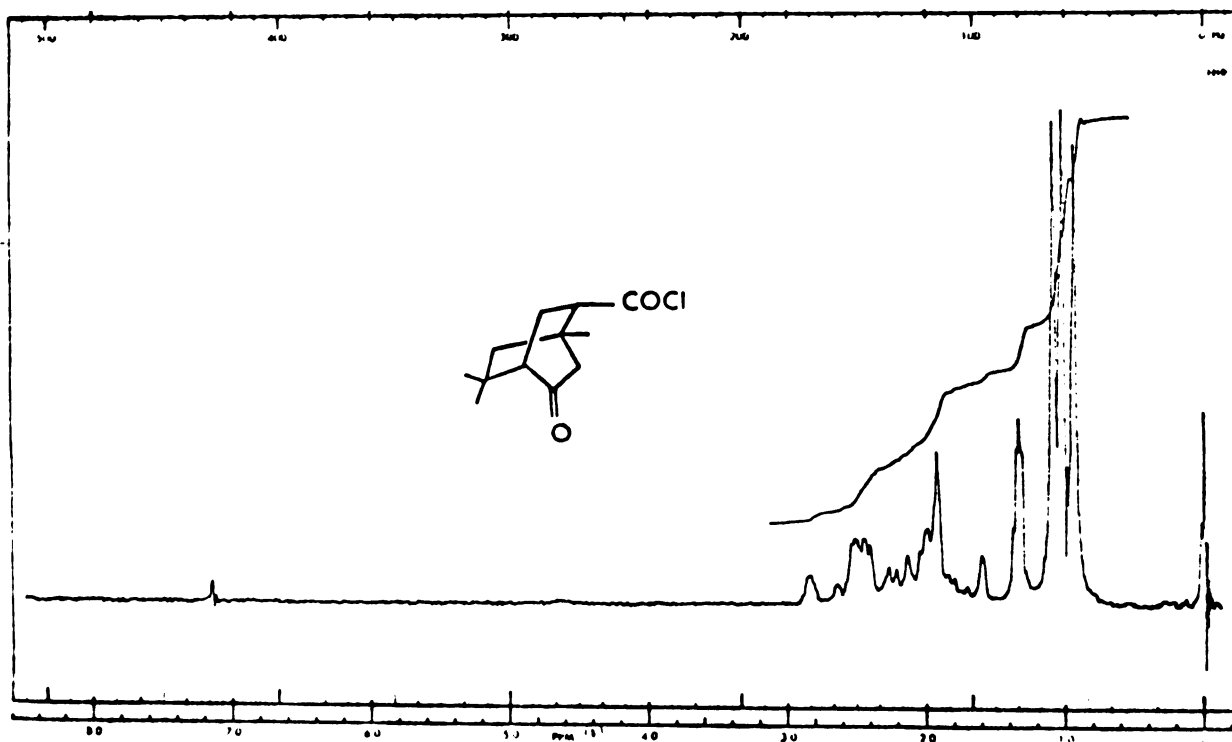


Figure 48. Pmr spectrum of 35.

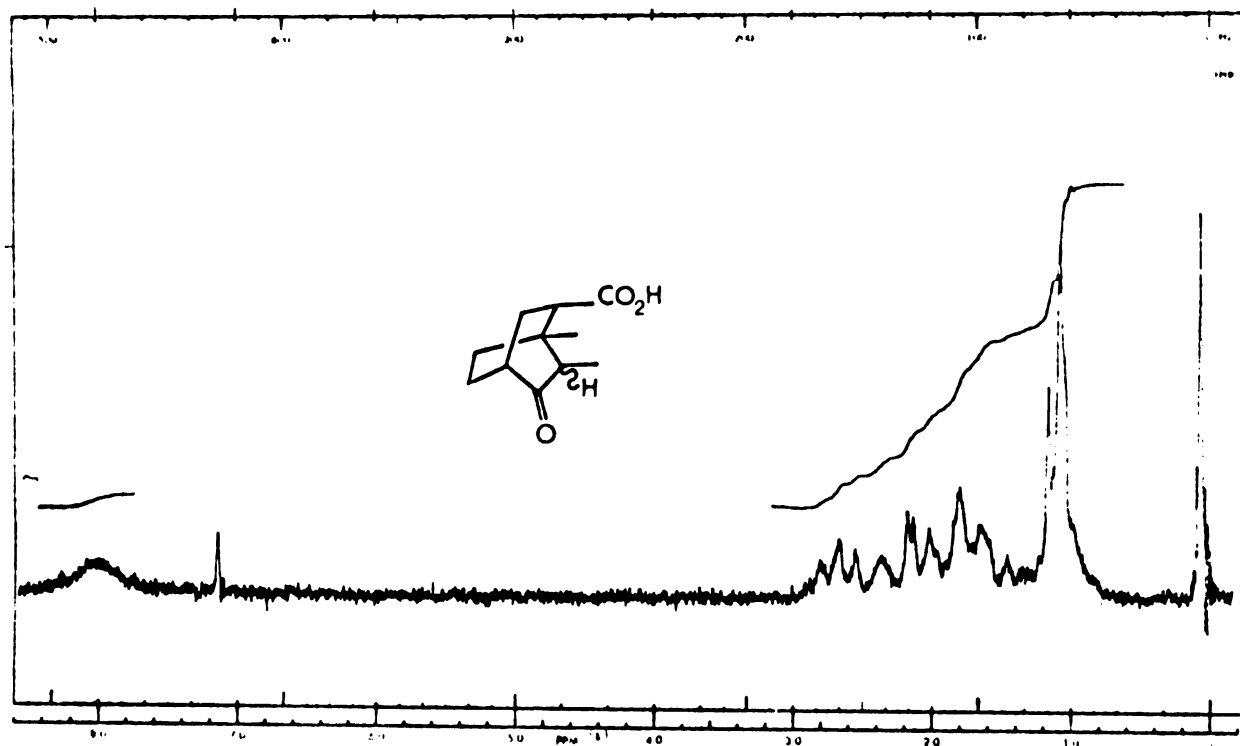


Figure 49. Pmr spectrum of 36.

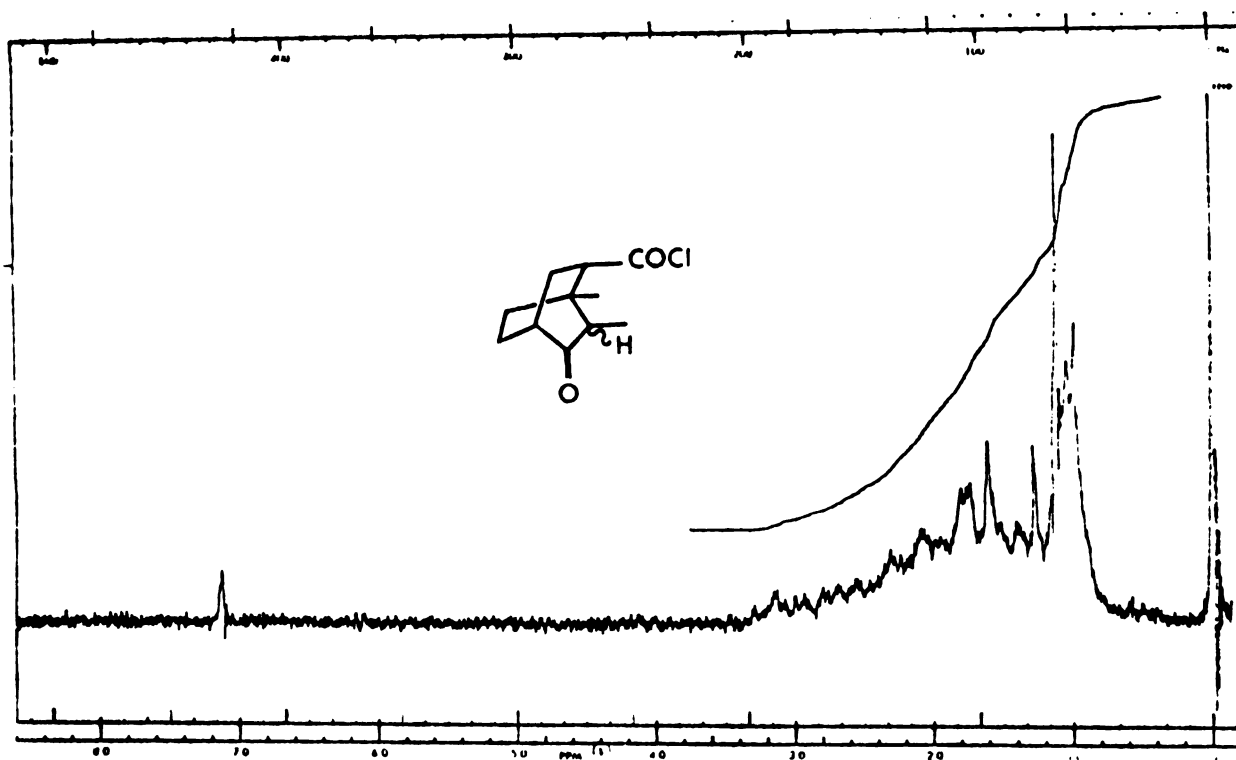


Figure 50. Pmr spectrum of 37.

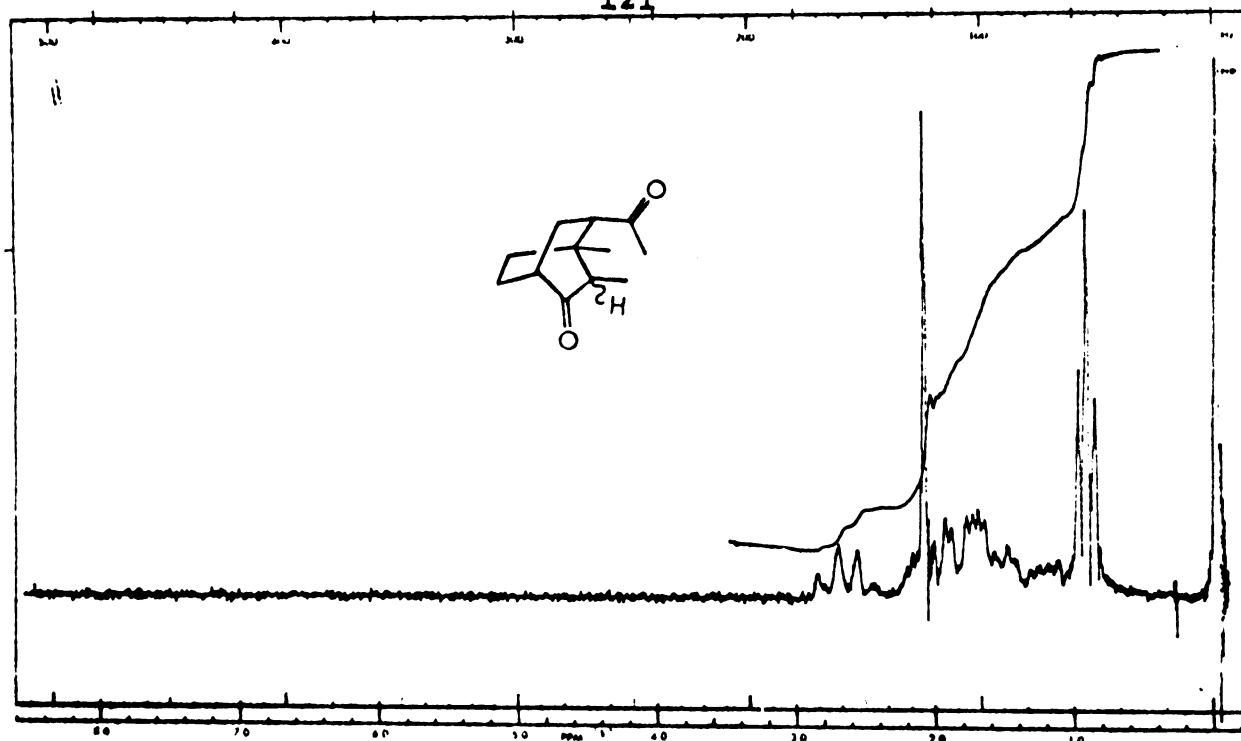


Figure 51. Pmr spectrum of 38.

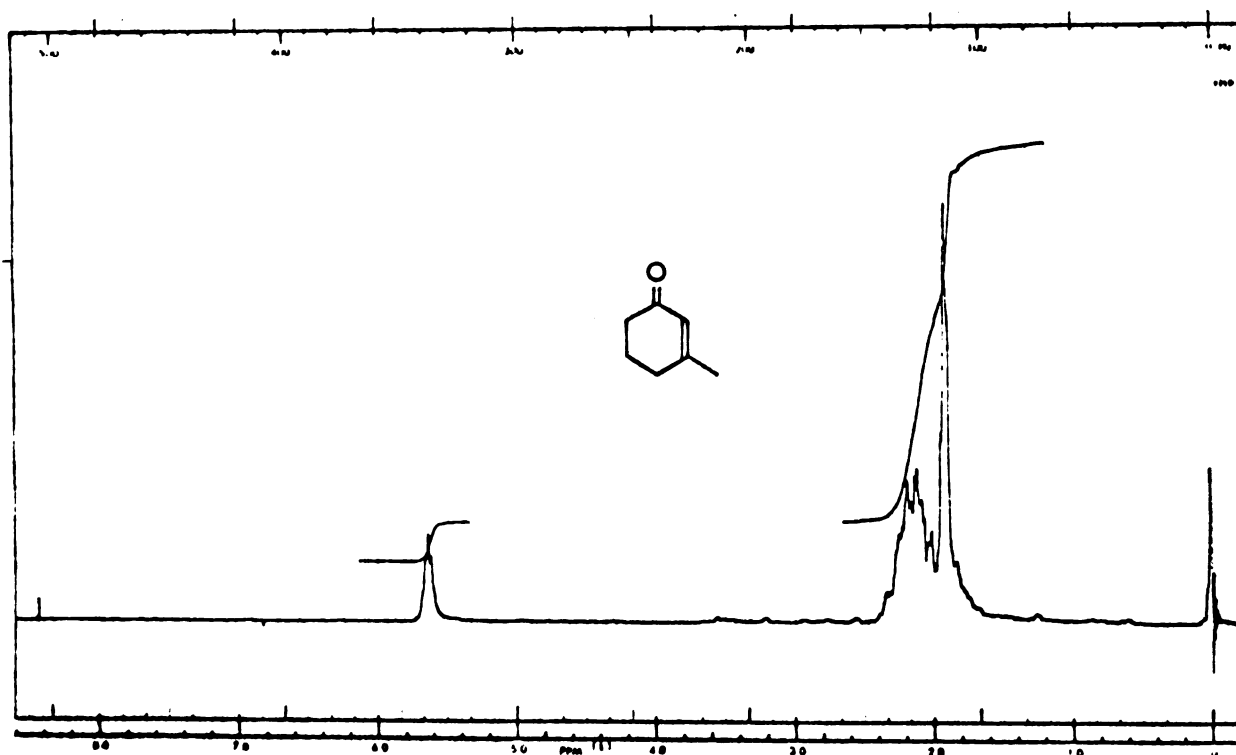


Figure 52. Pmr spectrum of 3-methylcyclohex-2-enone.

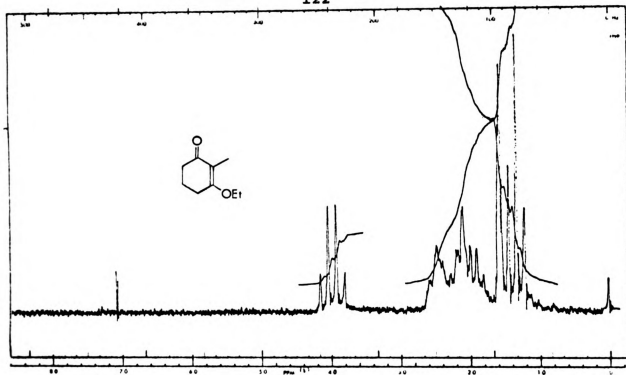


Figure 53. Pmr spectrum of 3-ethoxy-2-methylcyclohexenone.

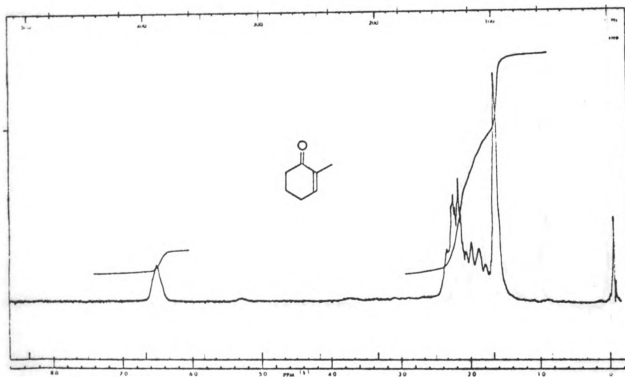


Figure 54. Pmr spectrum of 2-methylcyclohex-2-en-1-one.

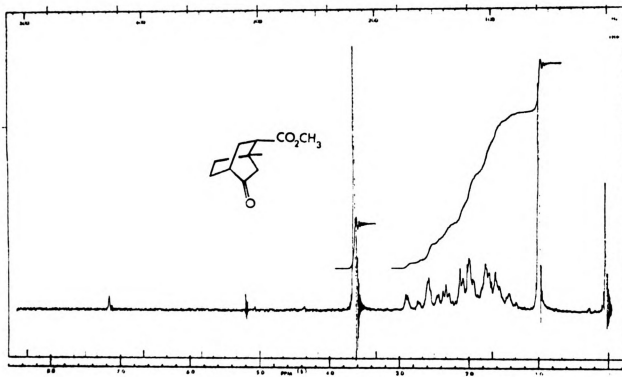


Figure 55. Pmr spectrum of 39.

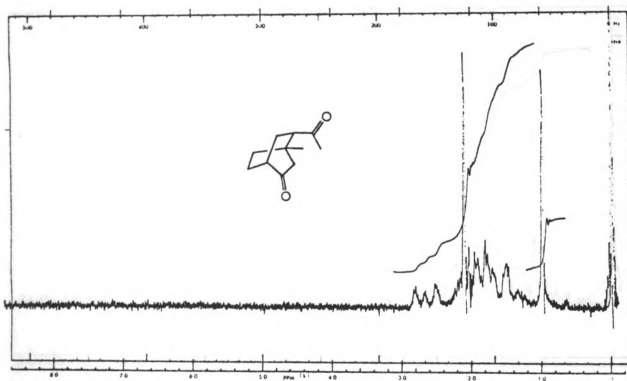


Figure 56. Pmr spectrum of 40.

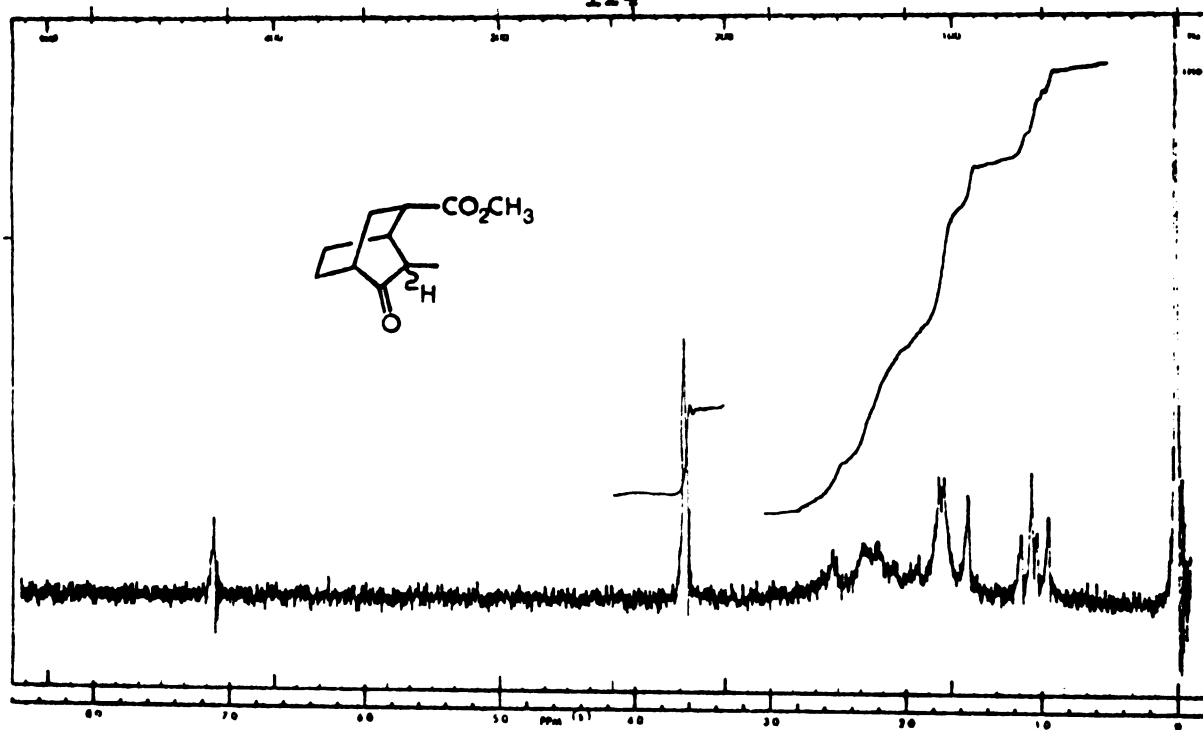


Figure 57. Pmr spectrum of 41.

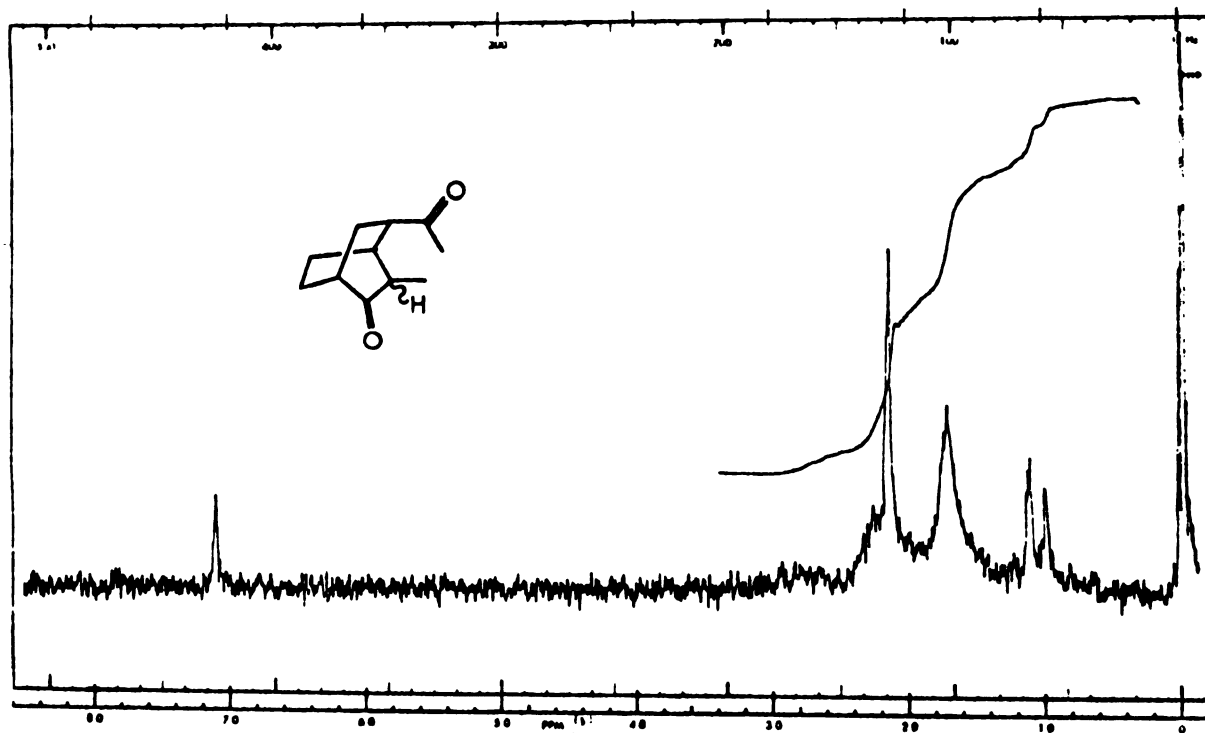


Figure 58. Pmr spectrum of 42.

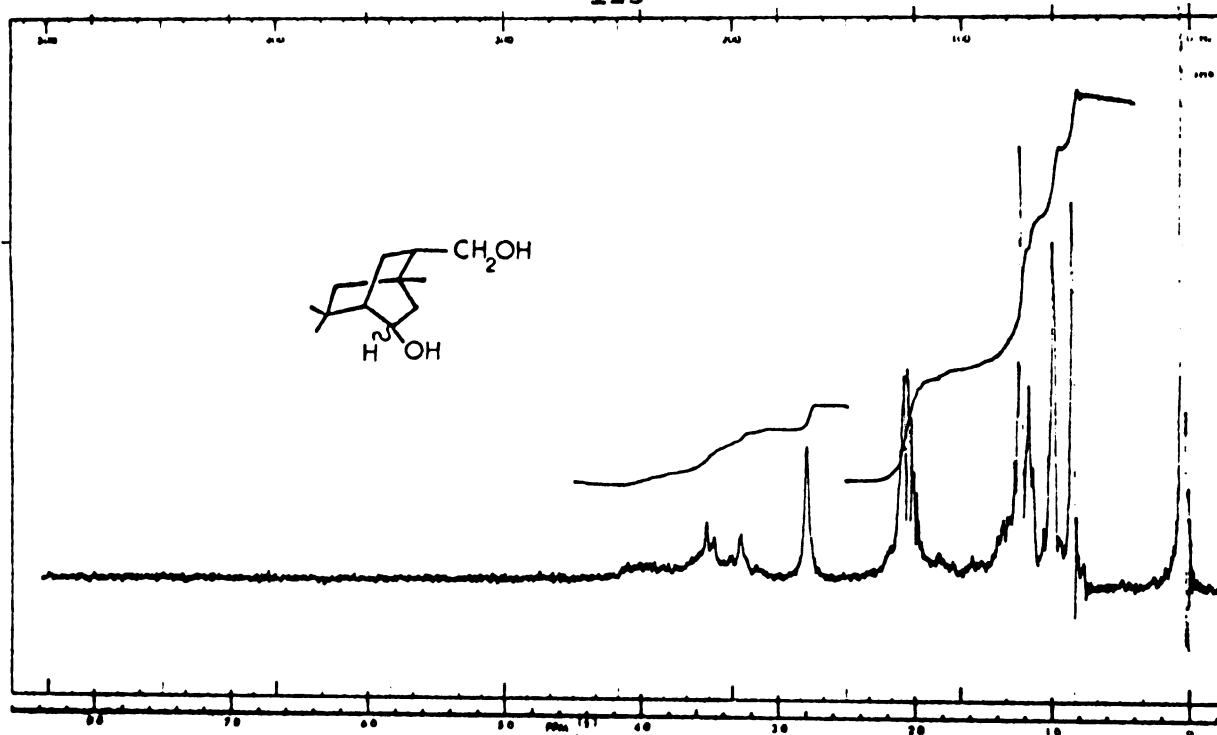


Figure 57. Pmr spectrum of 46.

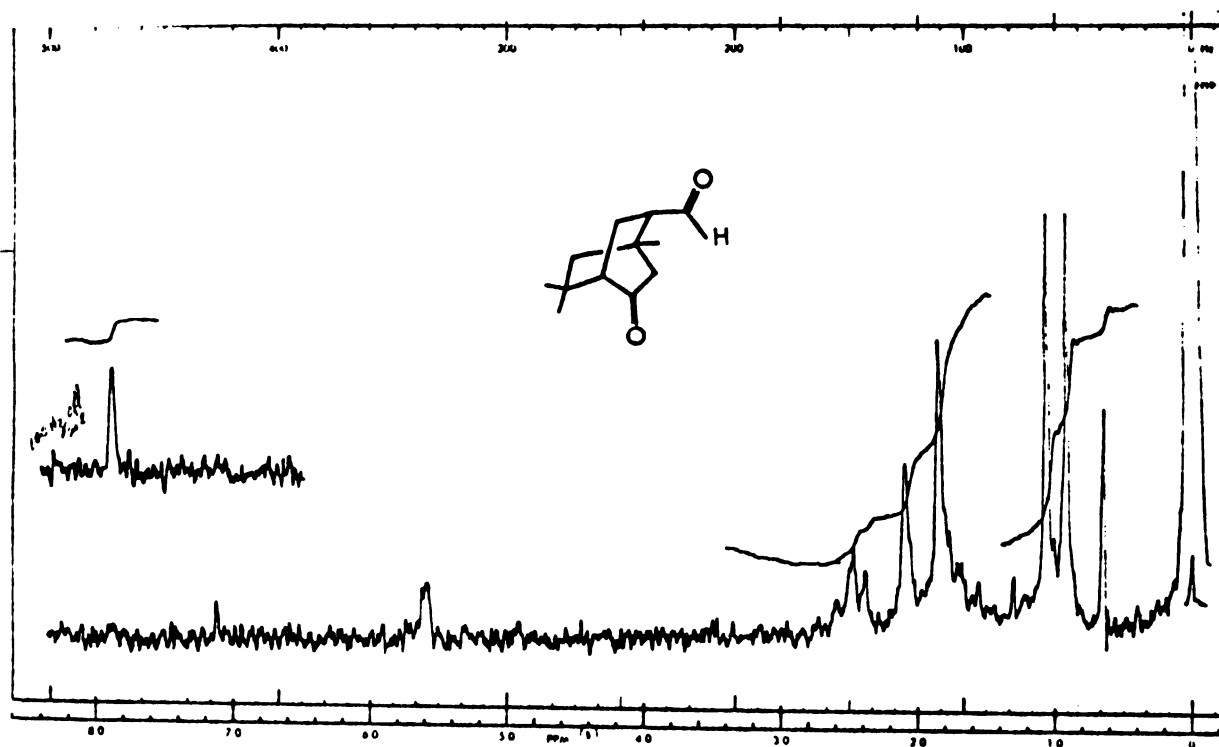


Figure 60. Pmr spectrum of 47.

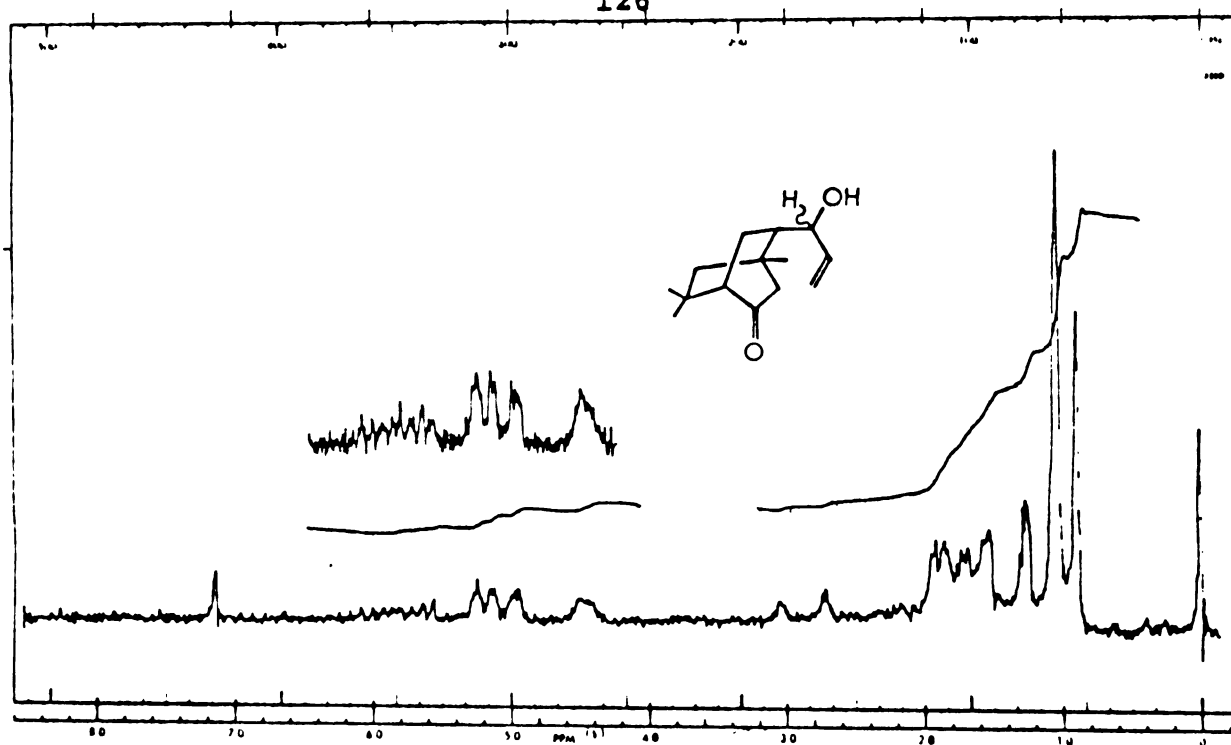


Figure 61. Pmr spectrum of 48.

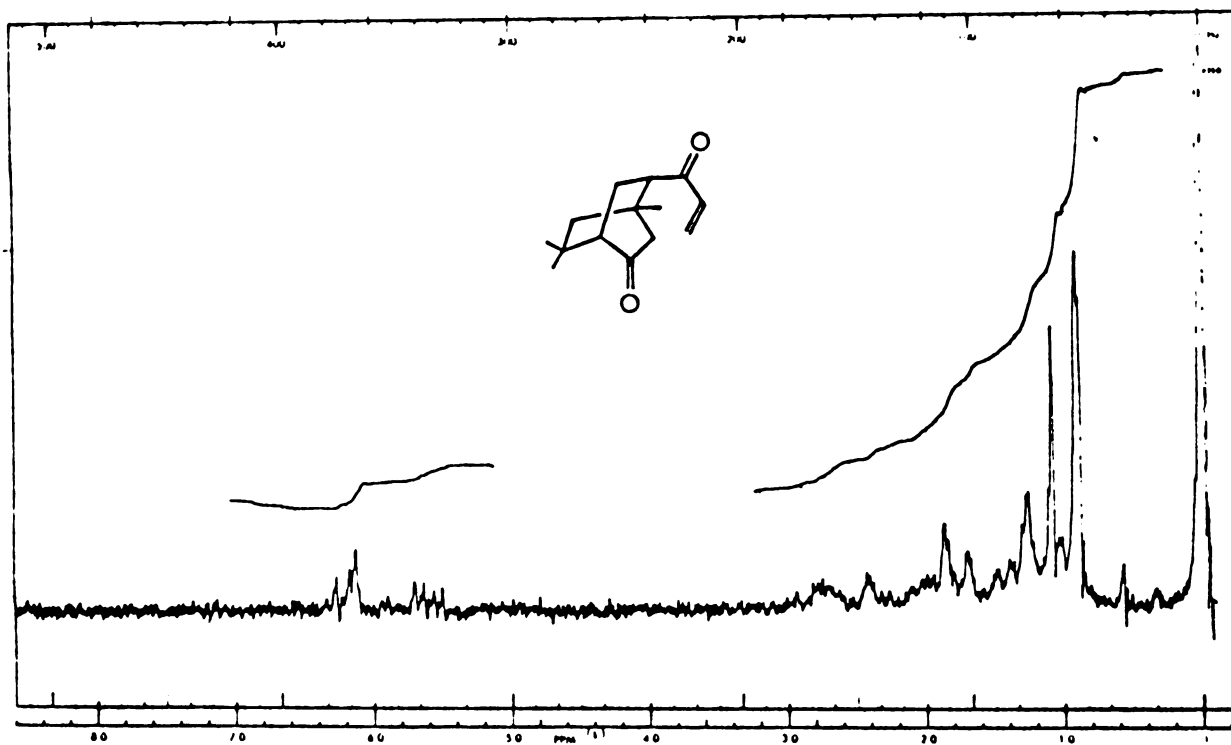


Figure 62. Pmr spectrum of 49.

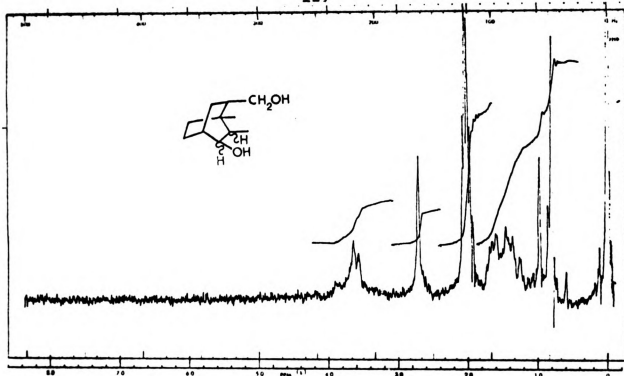


Figure 63. PMR spectrum of 50.

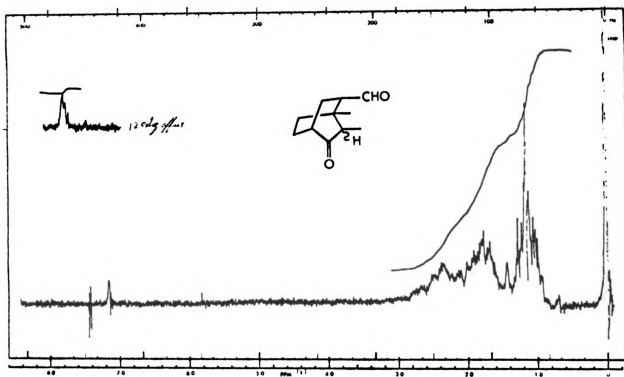


Figure 64. PMR spectrum of 51.

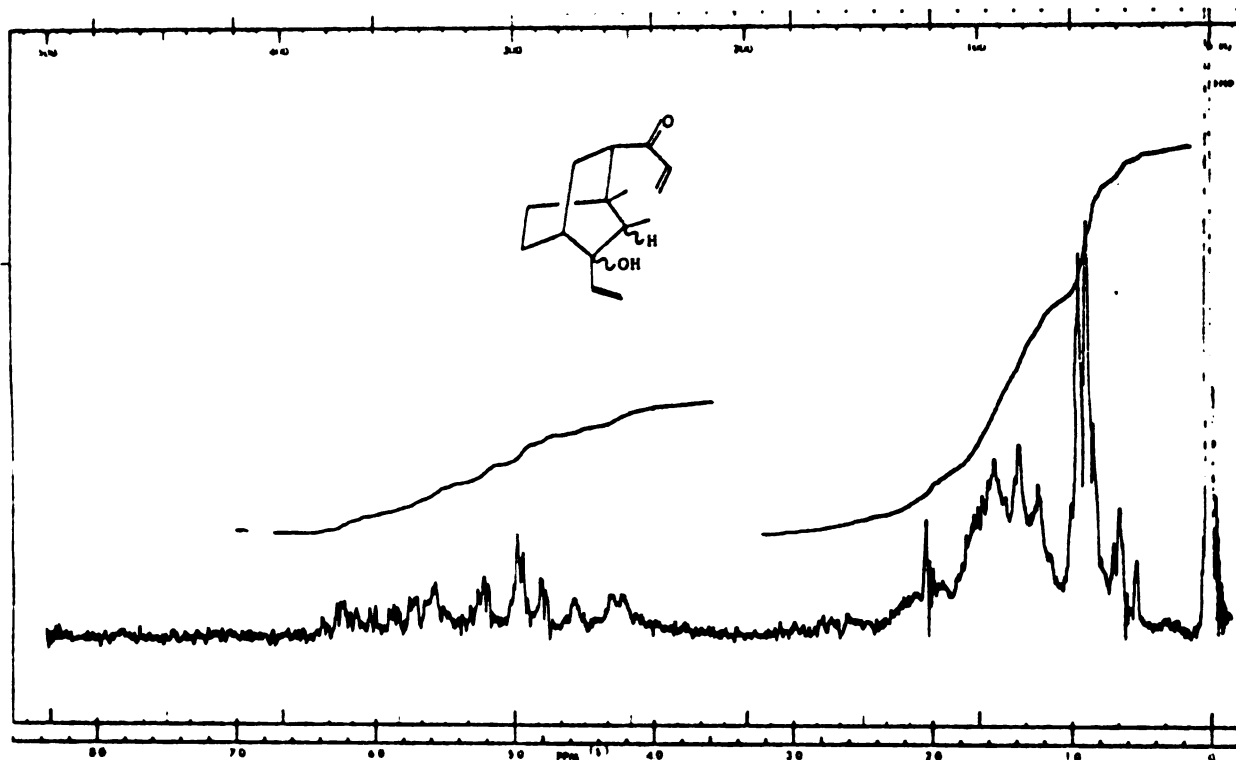


Figure 65. Pmr spectrum of 54.

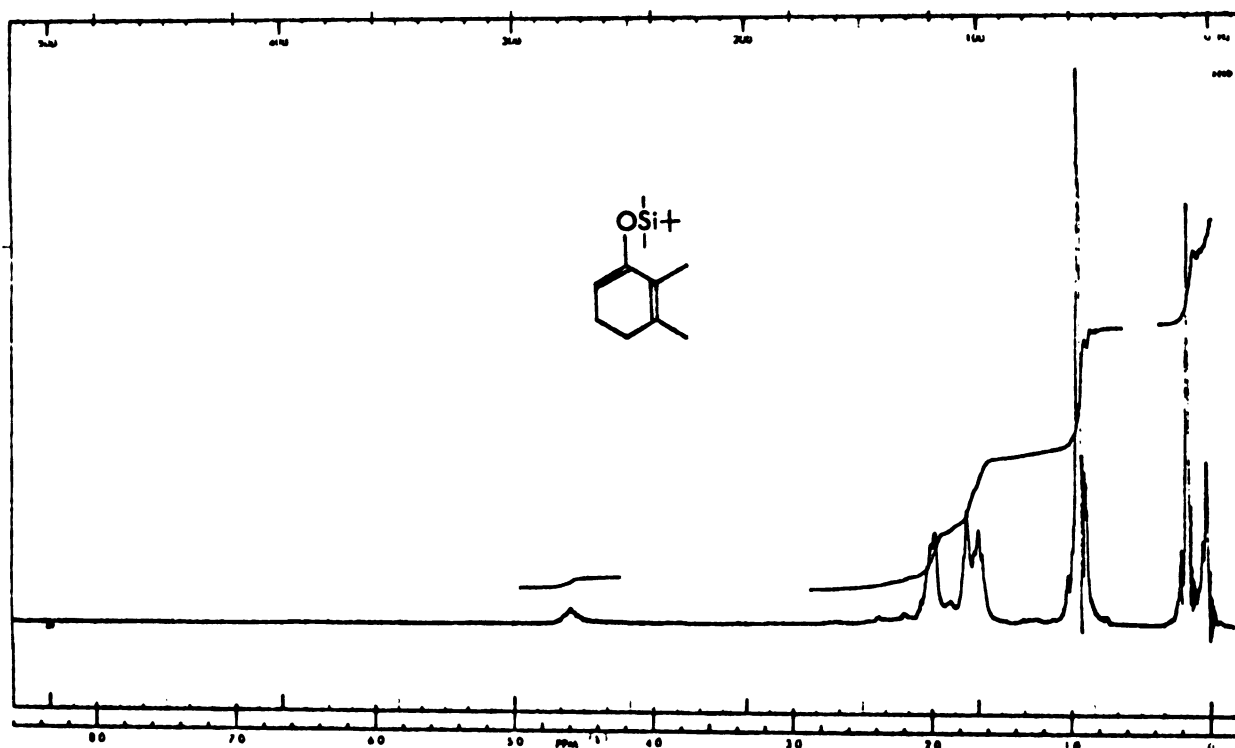


Figure 66. Pmr spectrum of 55.

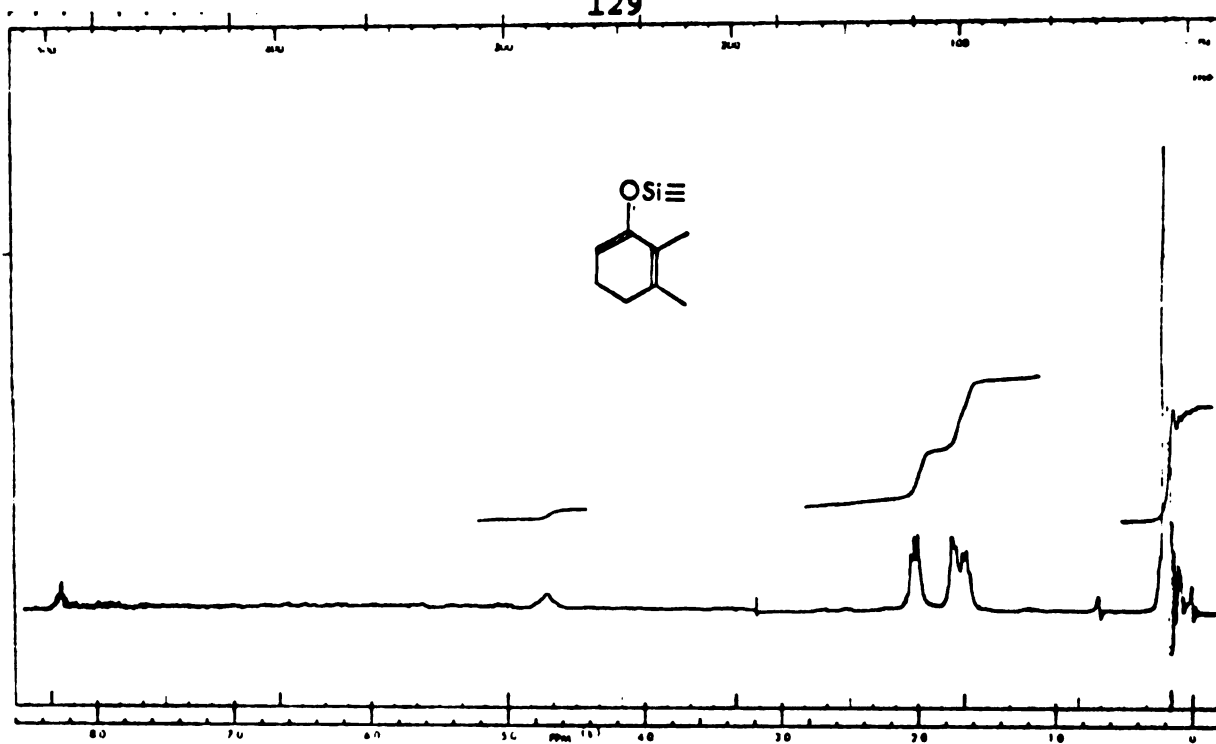


Figure 67. Pmr spectrum of 56.

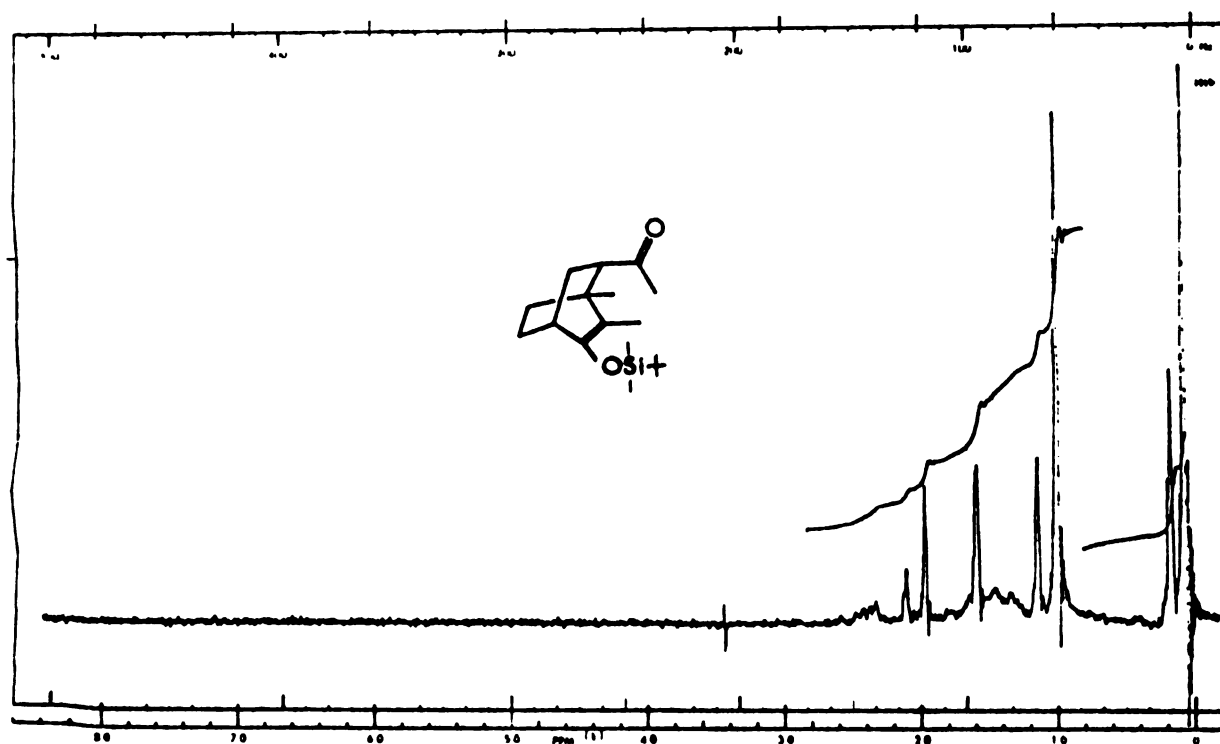


Figure 68. Pmr spectrum of 57.

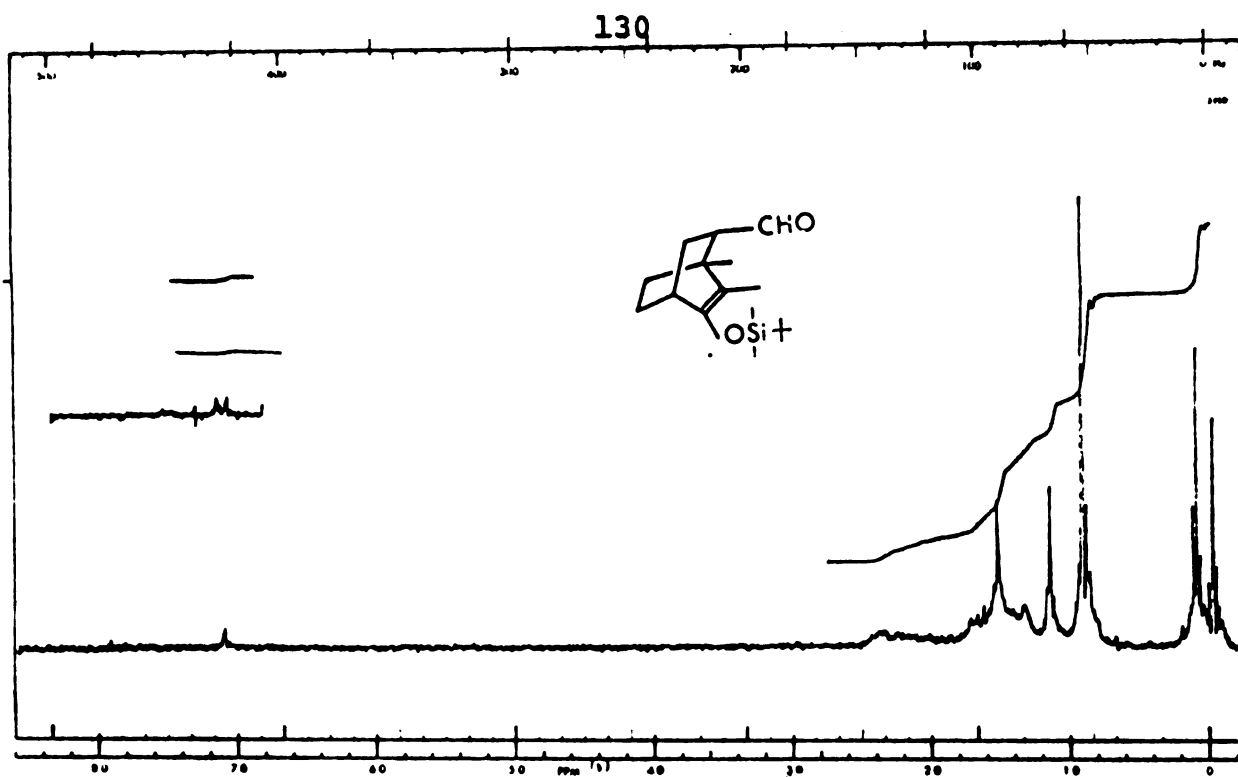


Figure 69. Pmr spectrum of 58.

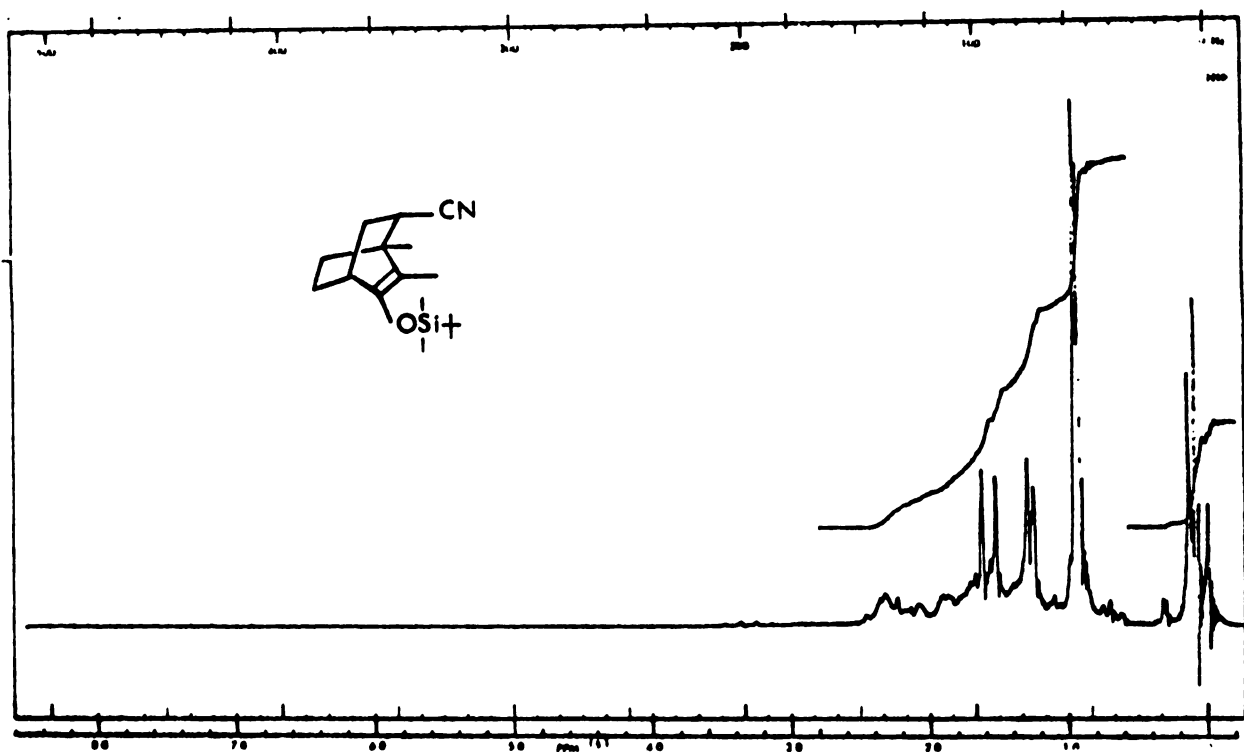
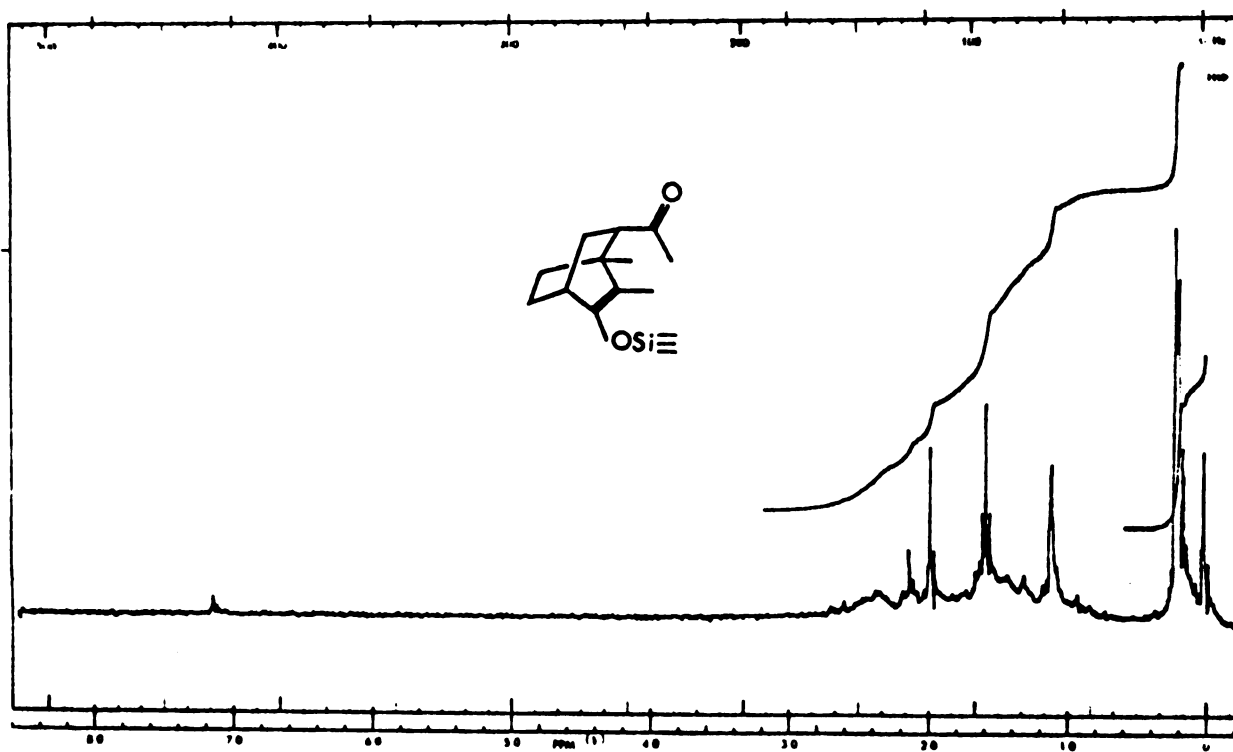
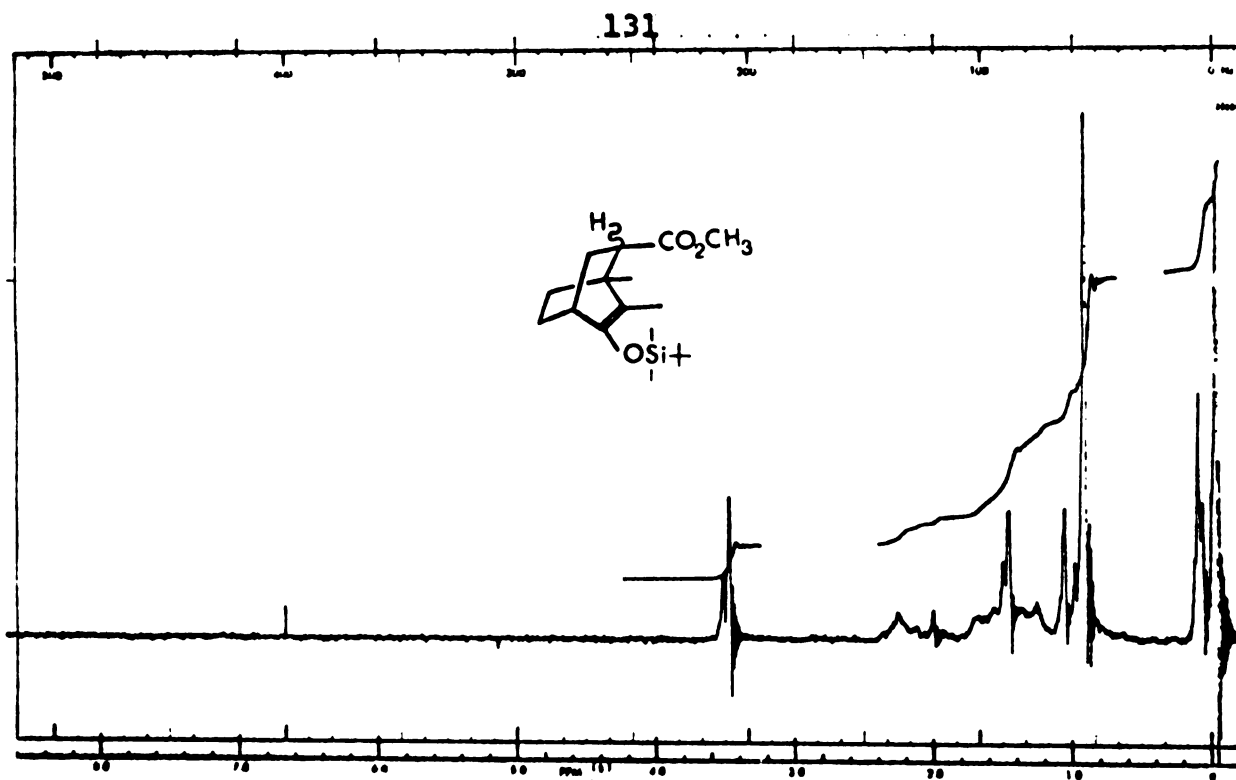


Figure 70. Pmr spectrum of 59.



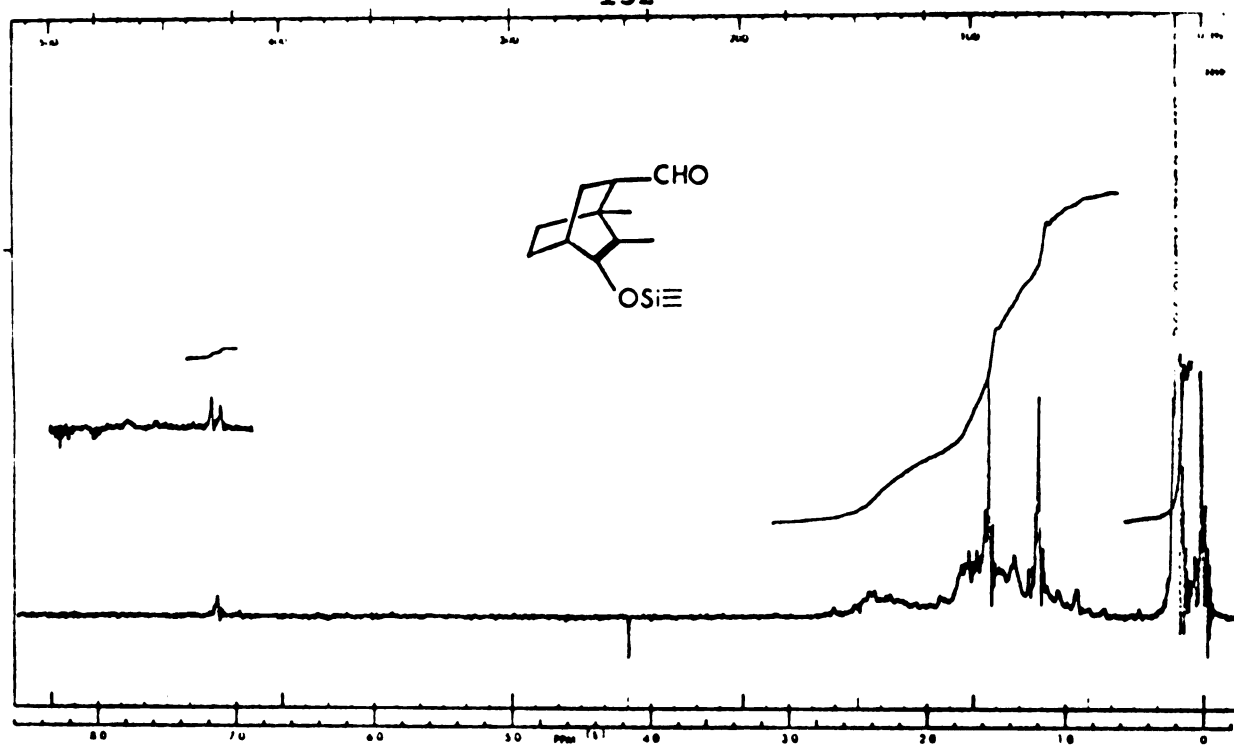


Figure 73. Pmr spectrum of 62.

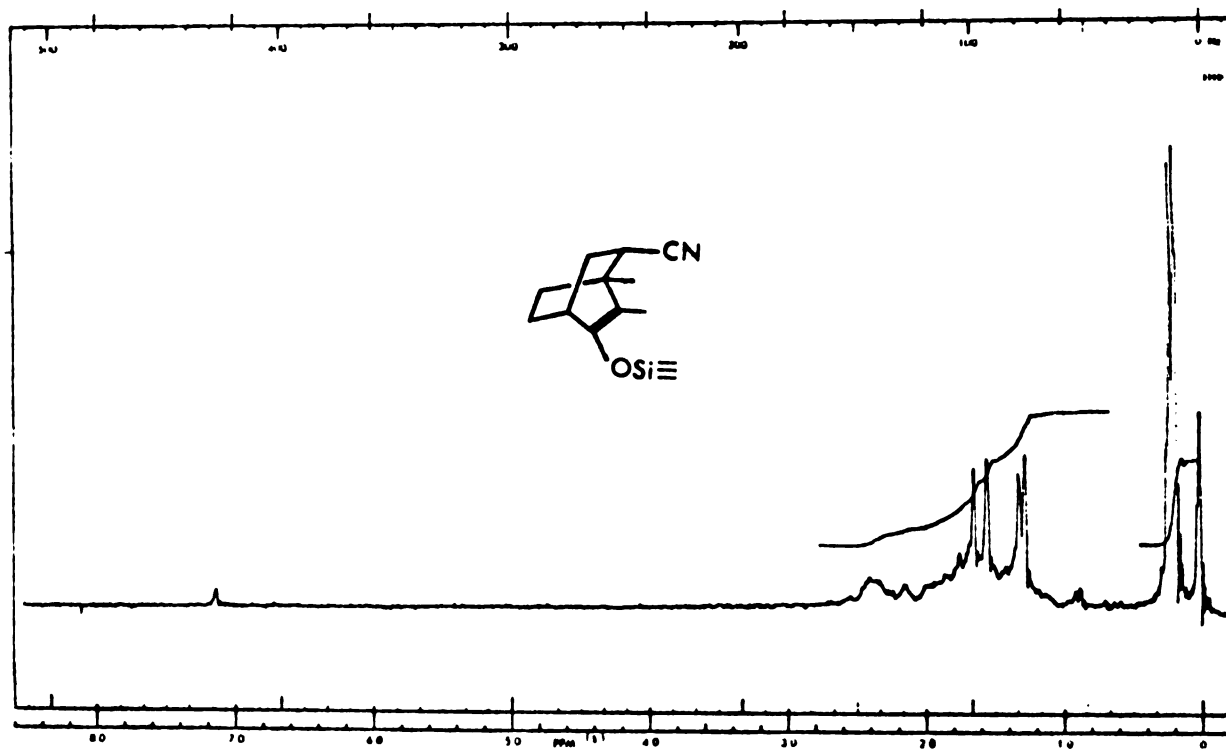


Figure 74. Pmr spectrum of 63.

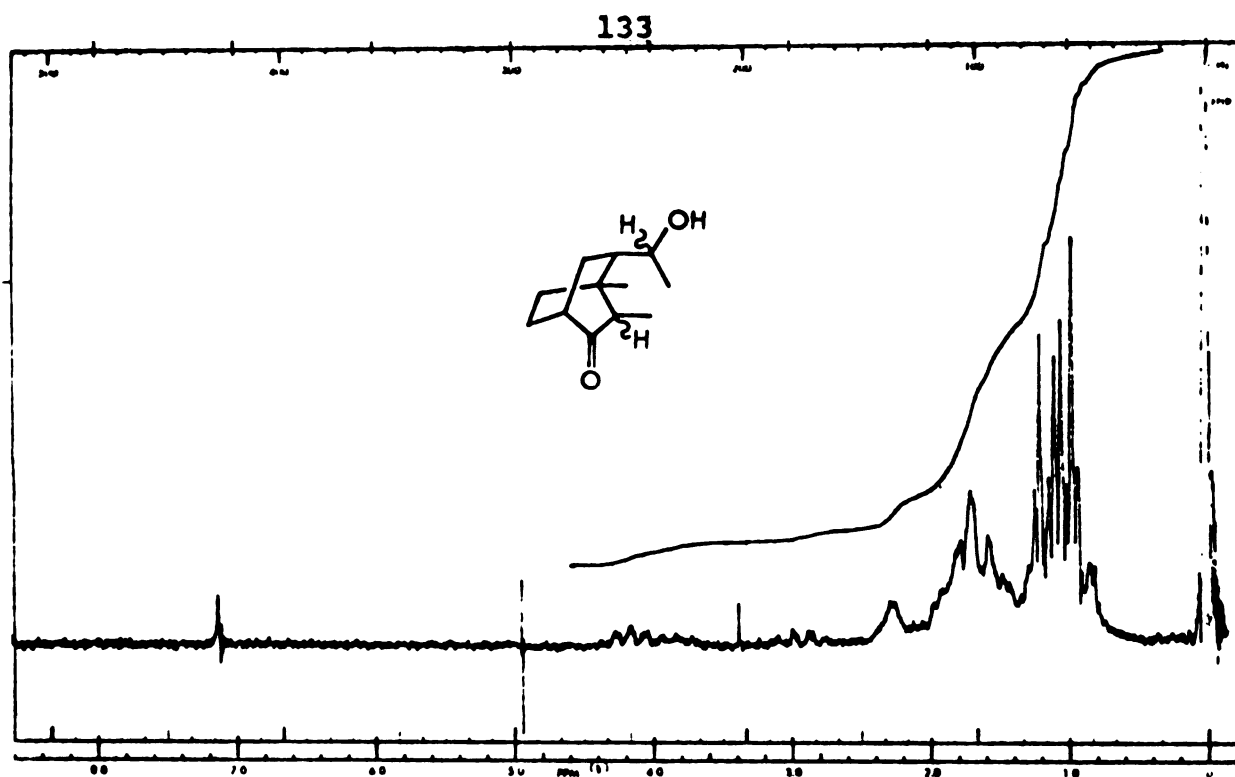


Figure 75. Pmr spectrum of 64.

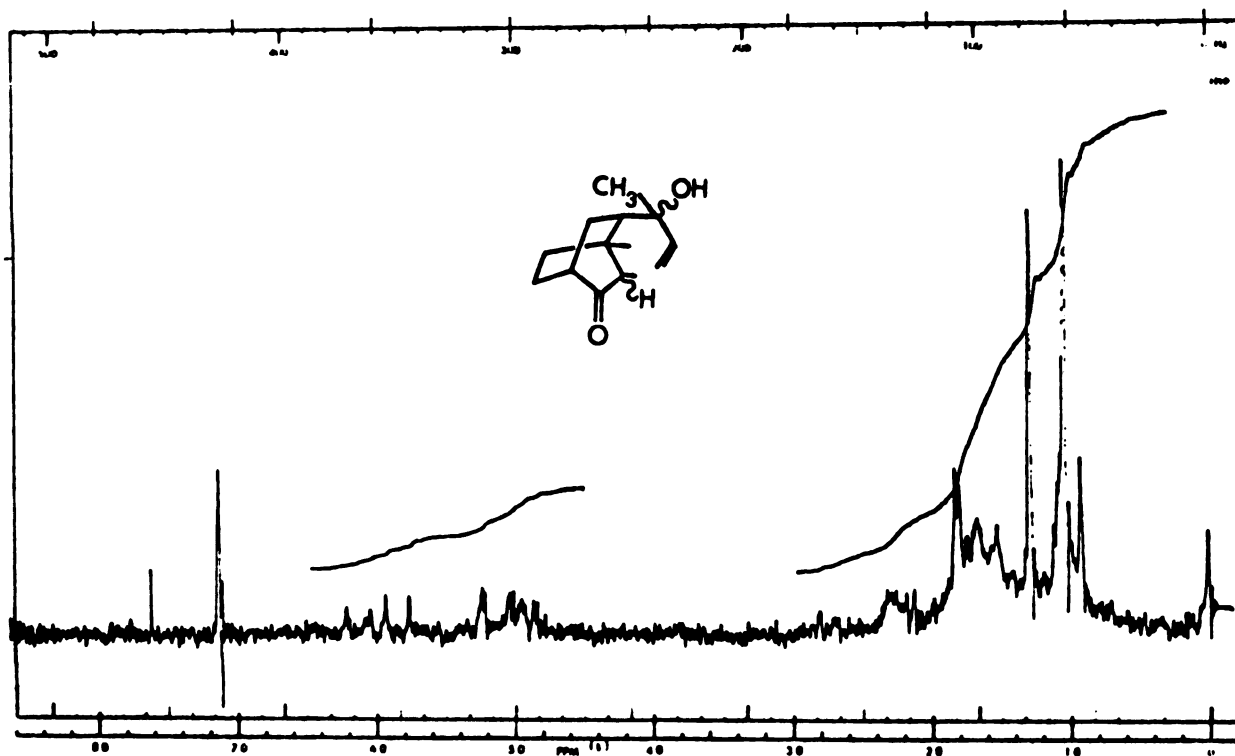


Figure 76. Pmr spectrum of 67.

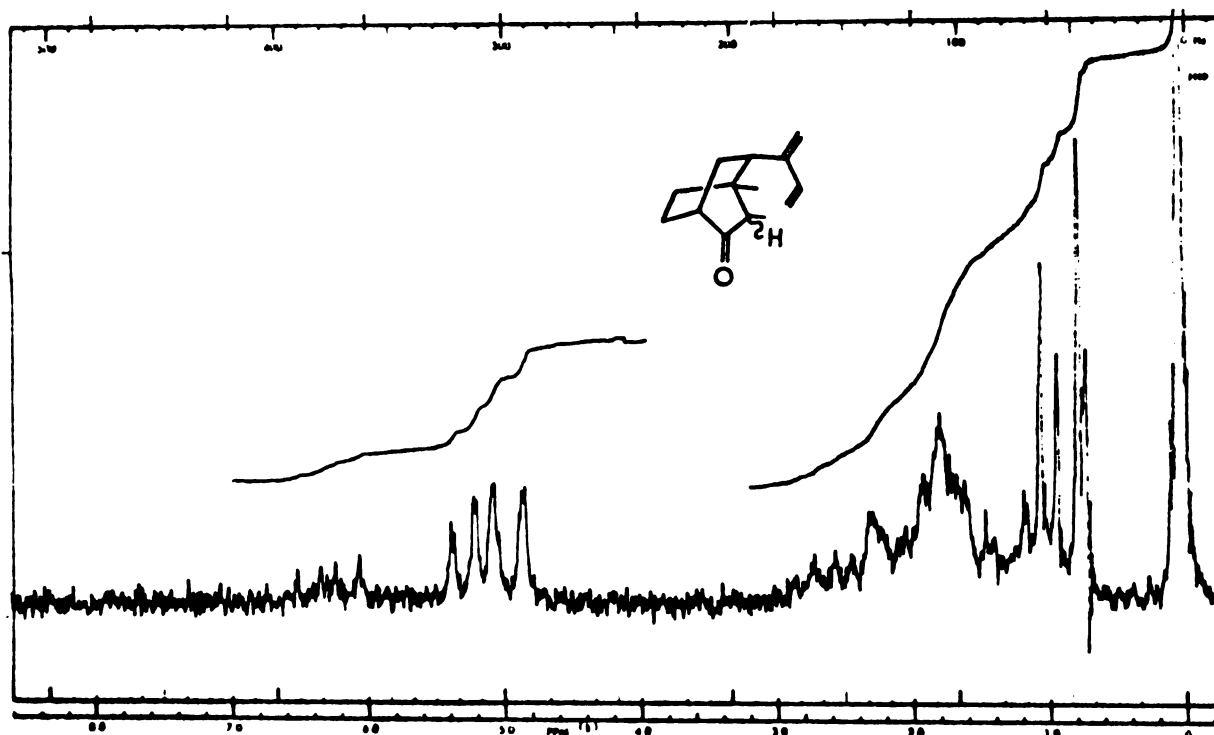


Figure 77. Pmr spectrum of 68.

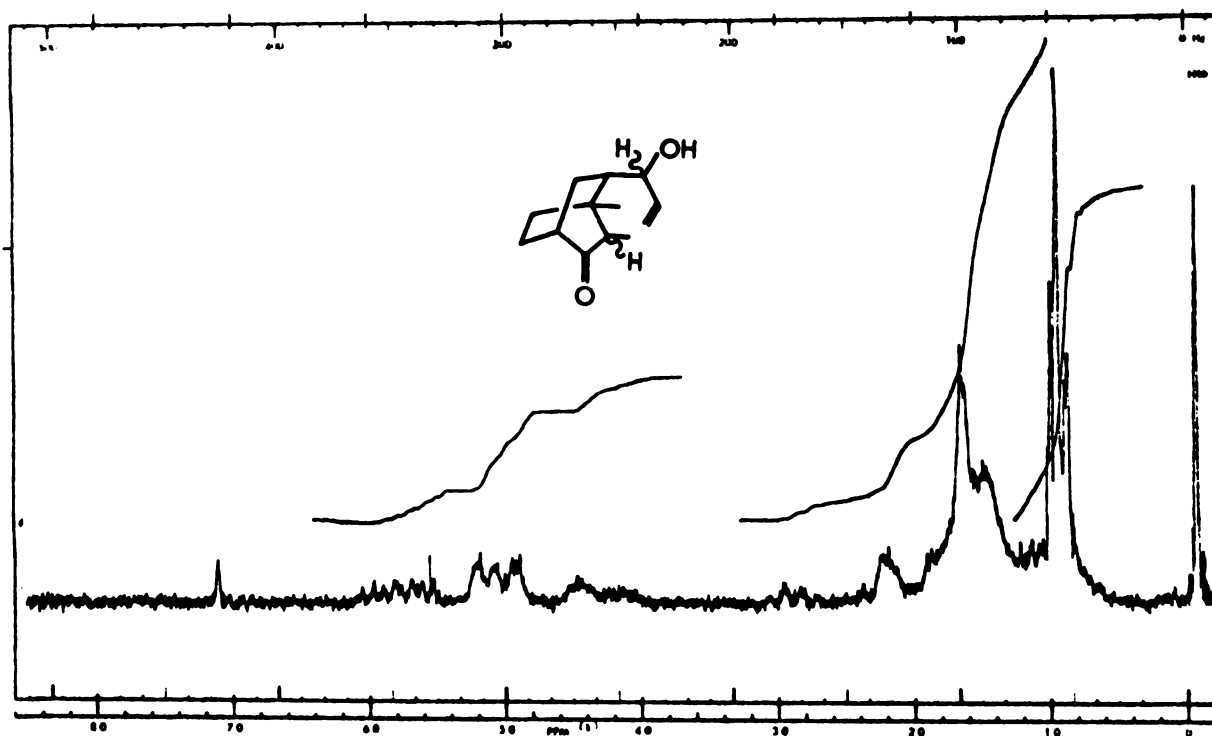


Figure 78. Pmr spectrum of 69.

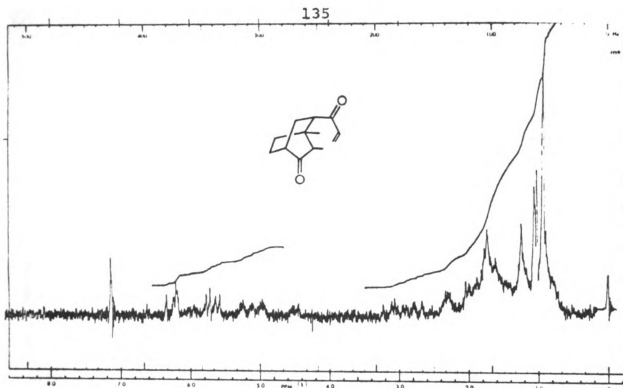


Figure 79. Pmr spectrum of 45.

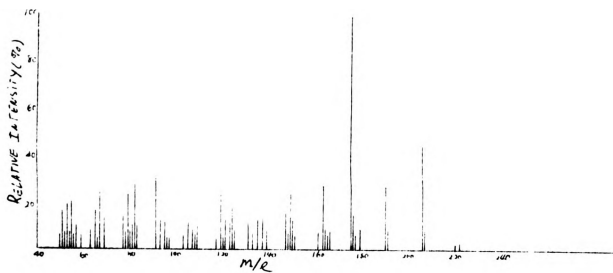
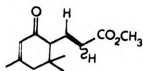
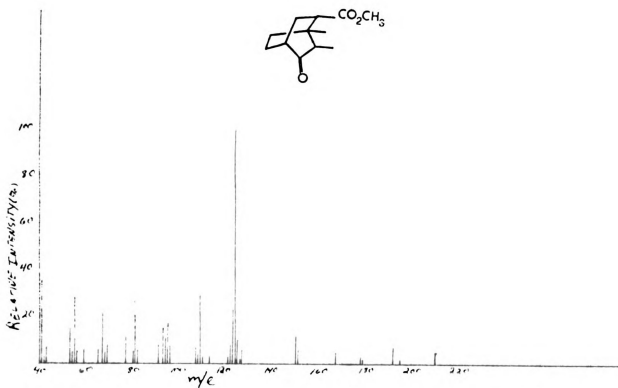
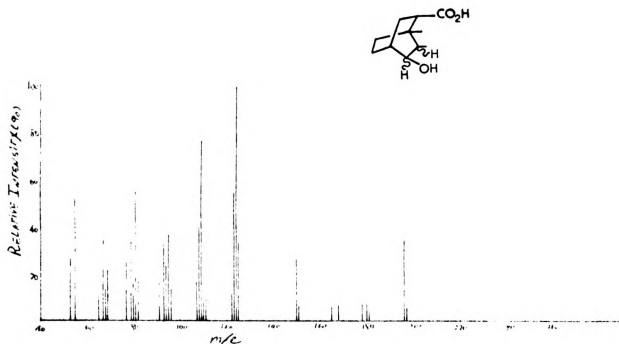
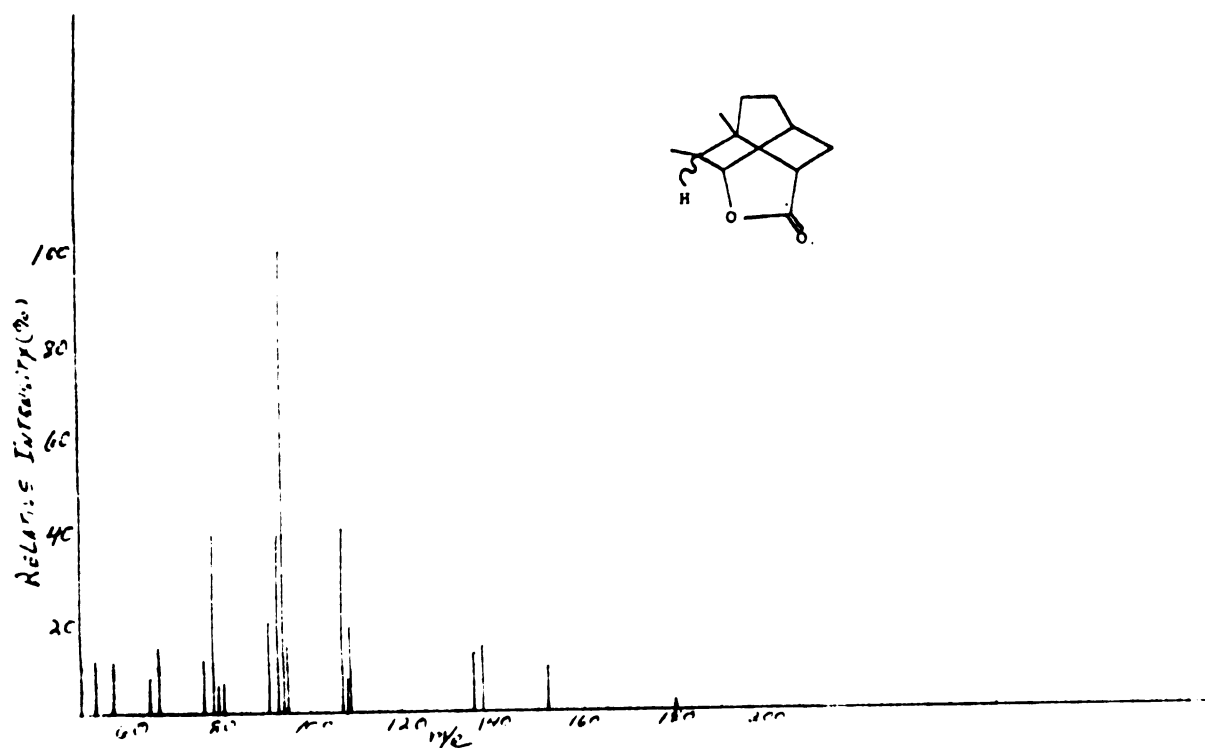
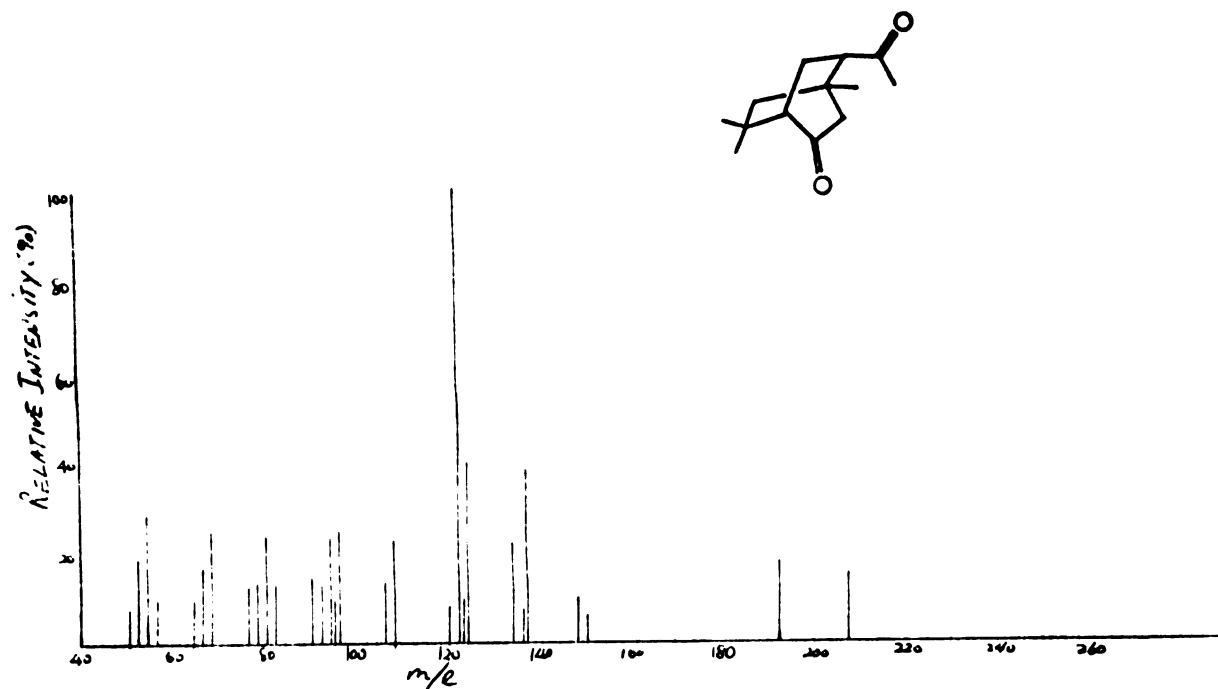


Figure 80. Mass spectrum of 22.

Figure 81. Mass spectrum of 24.Figure 82. Mass spectrum of 26.

Figure 83. Mass spectrum of 27.Figure 84. Mass spectrum of 29.

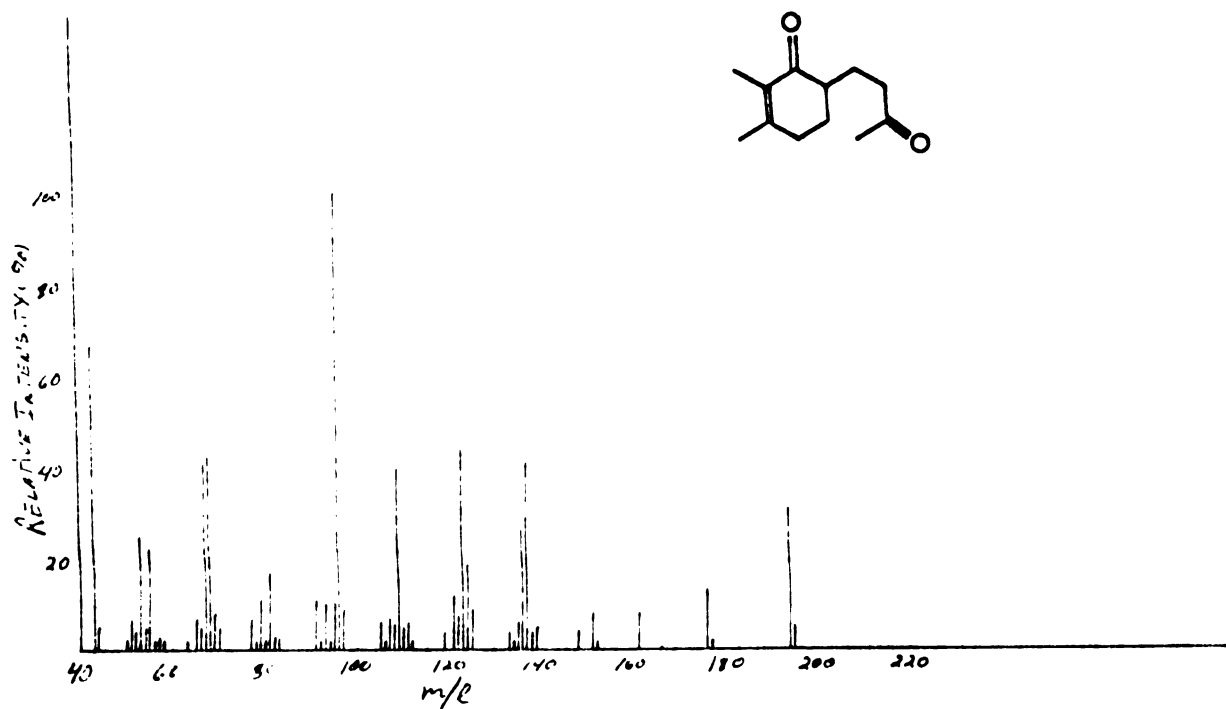


Figure 85. Mass spectrum of 30.

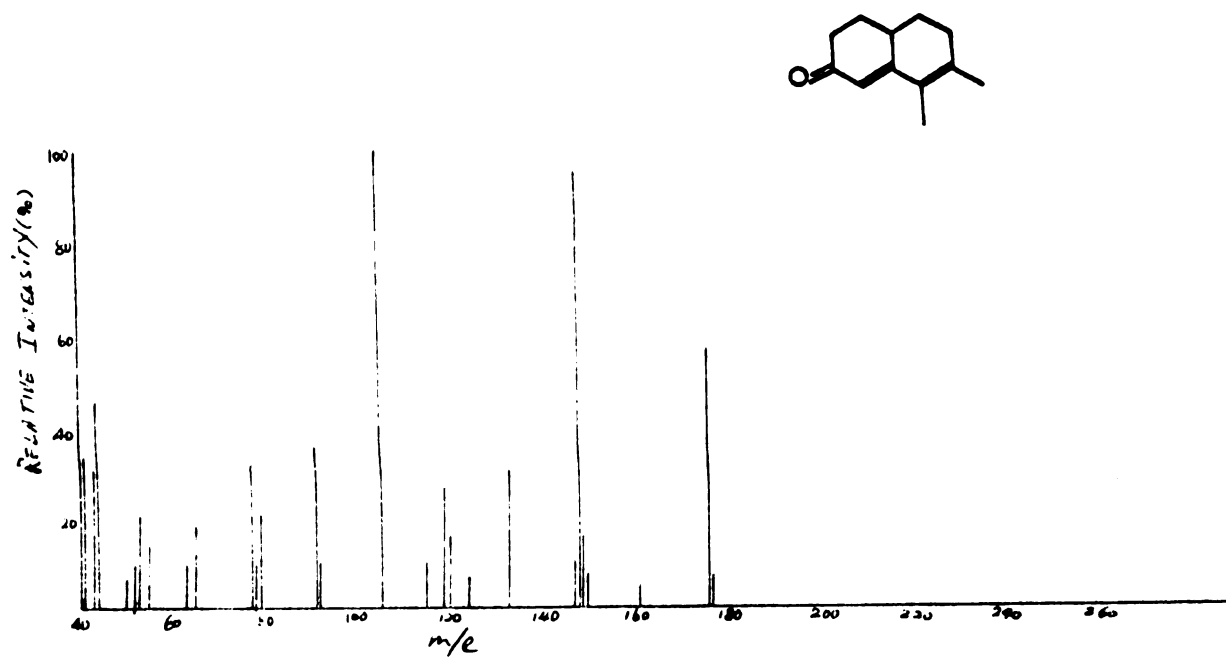
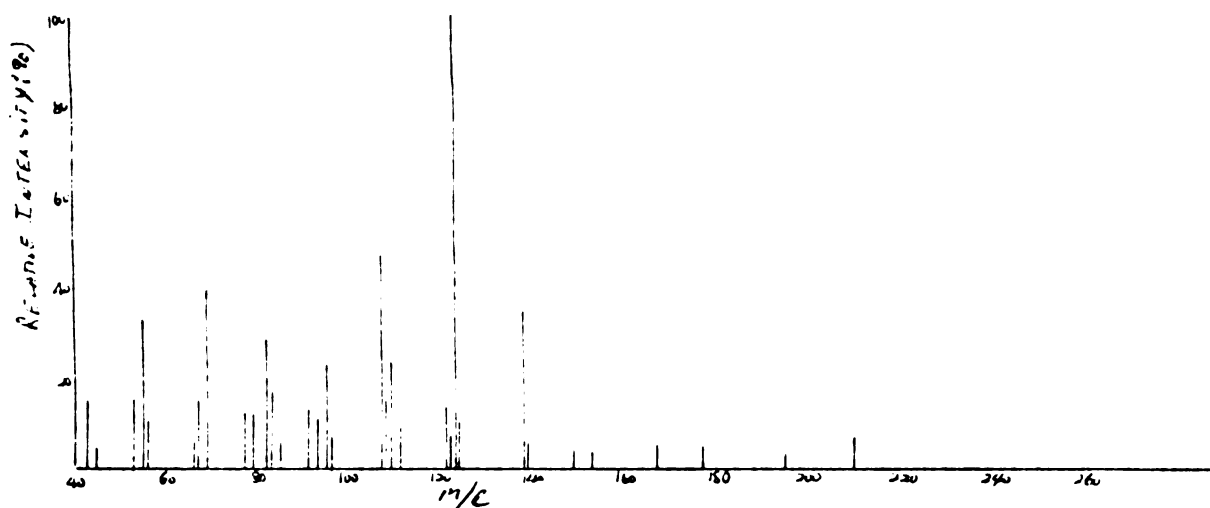
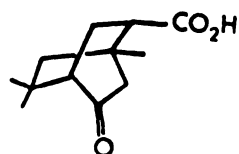


Figure 86. Mass spectrum of 31.



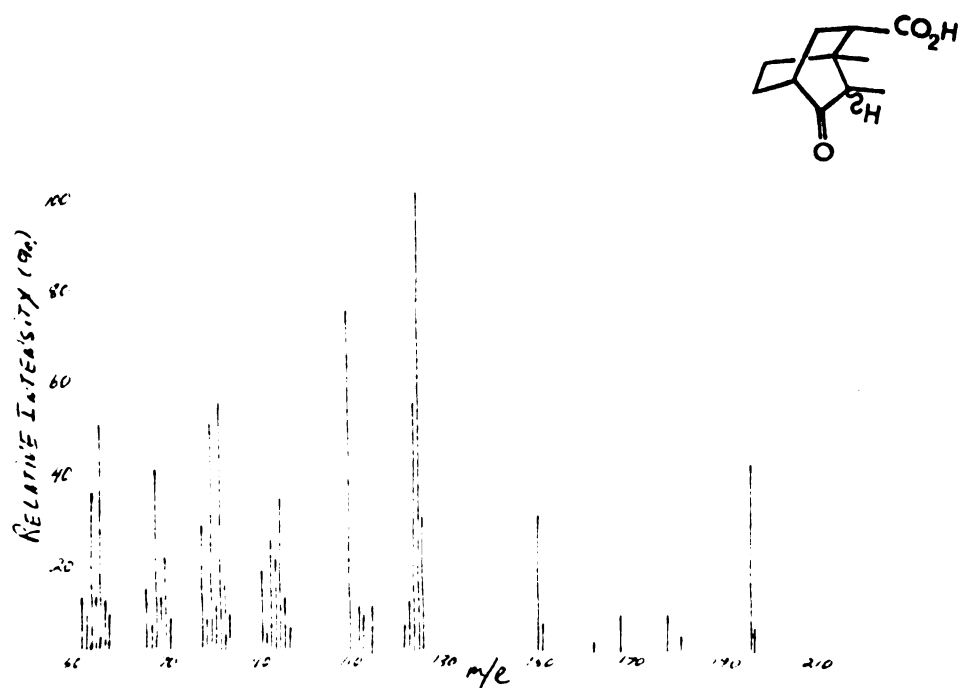


Figure 89. Mass spectrum of 36.

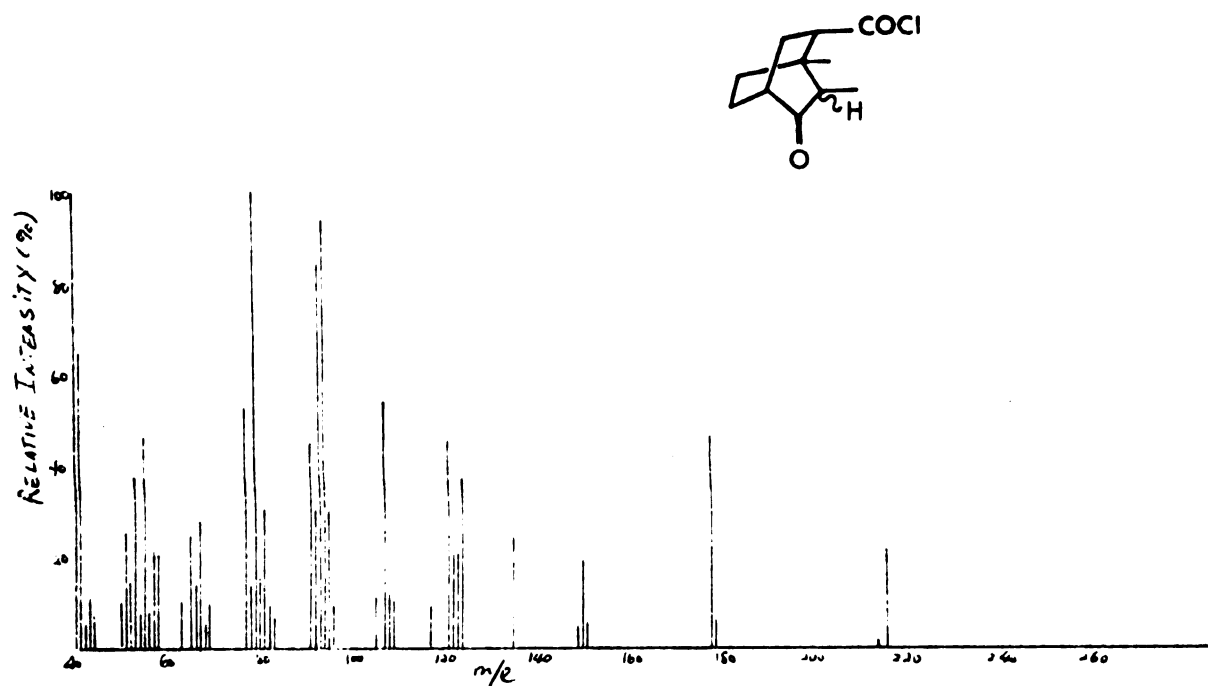


Figure 90. Mass spectrum of 37.

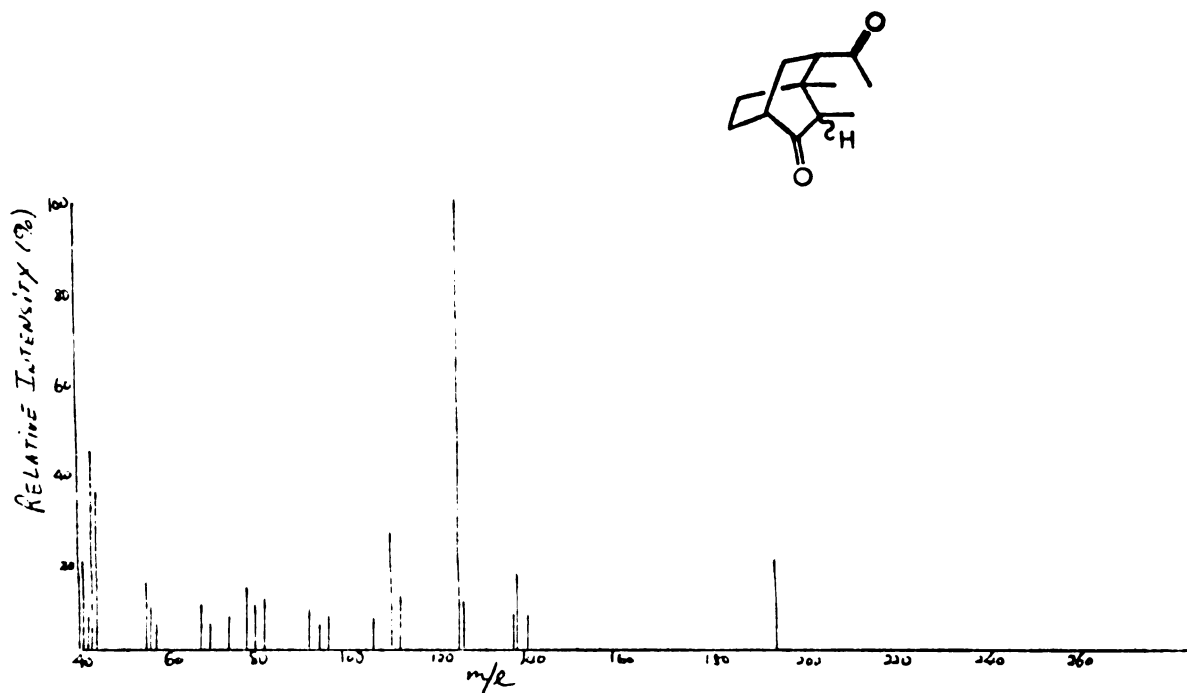


Figure 91. Mass spectrum of 38.

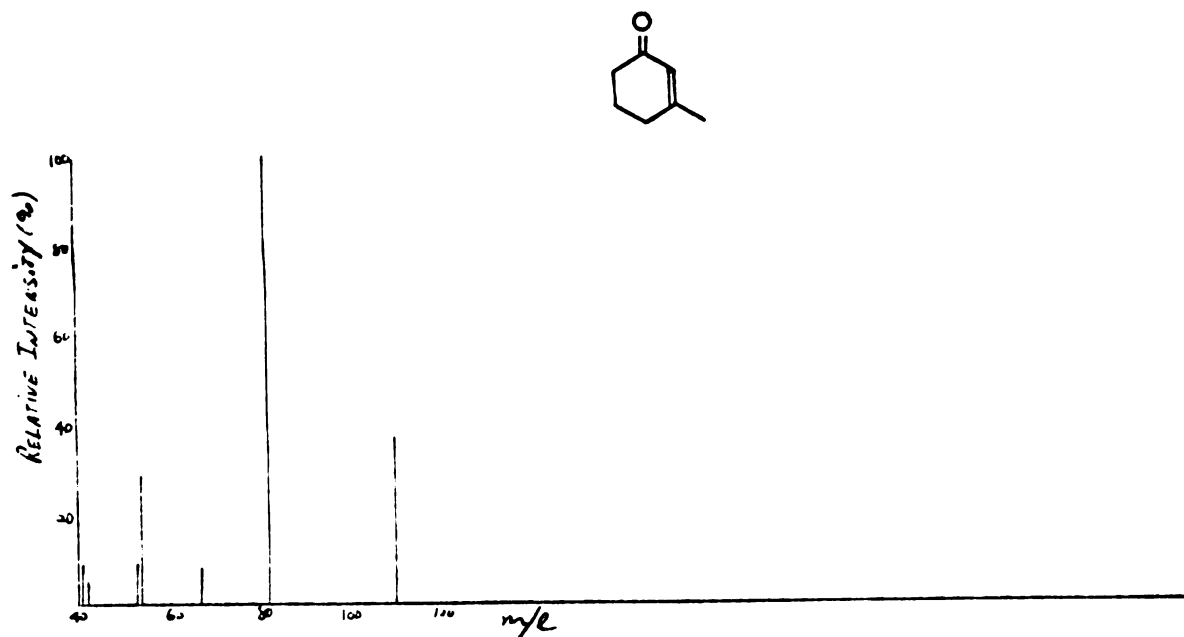


Figure 92. Mass spectrum of 3-methylcyclohex-2-enone.

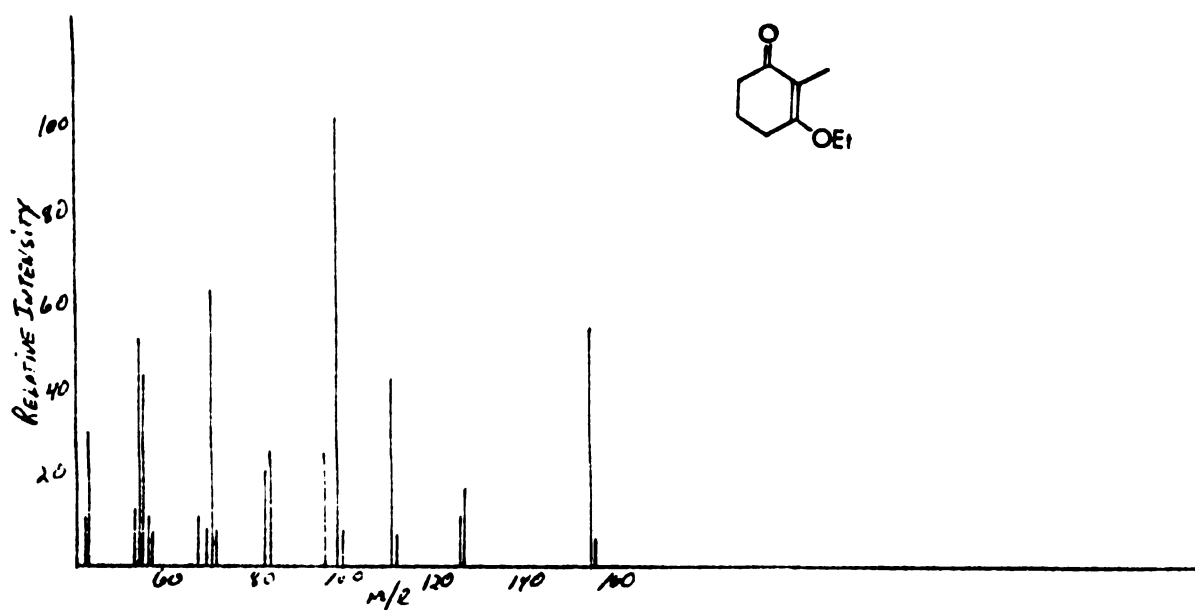


Figure 93. Mass spectrum of 3-ethoxy-2-methylcyclohexenone.

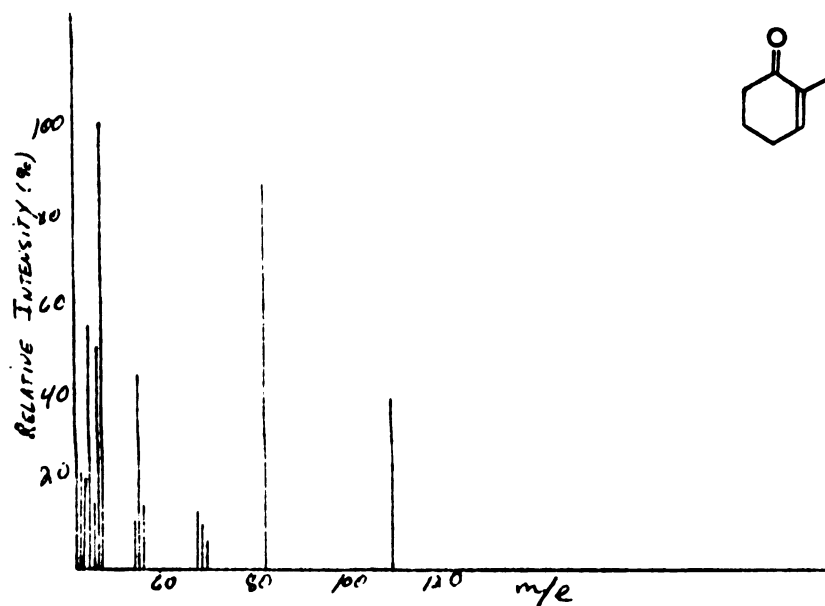


Figure 94. Mass spectrum of 2-methylcyclohex-2-enone.

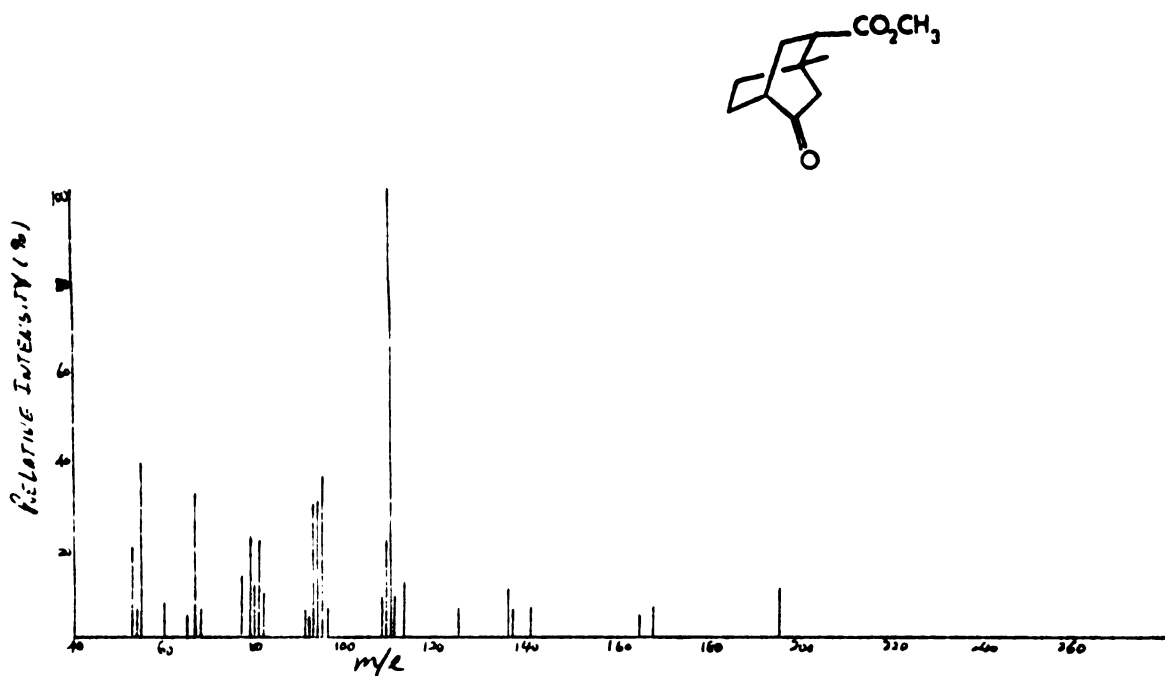


Figure 95. Mass spectrum of 39.

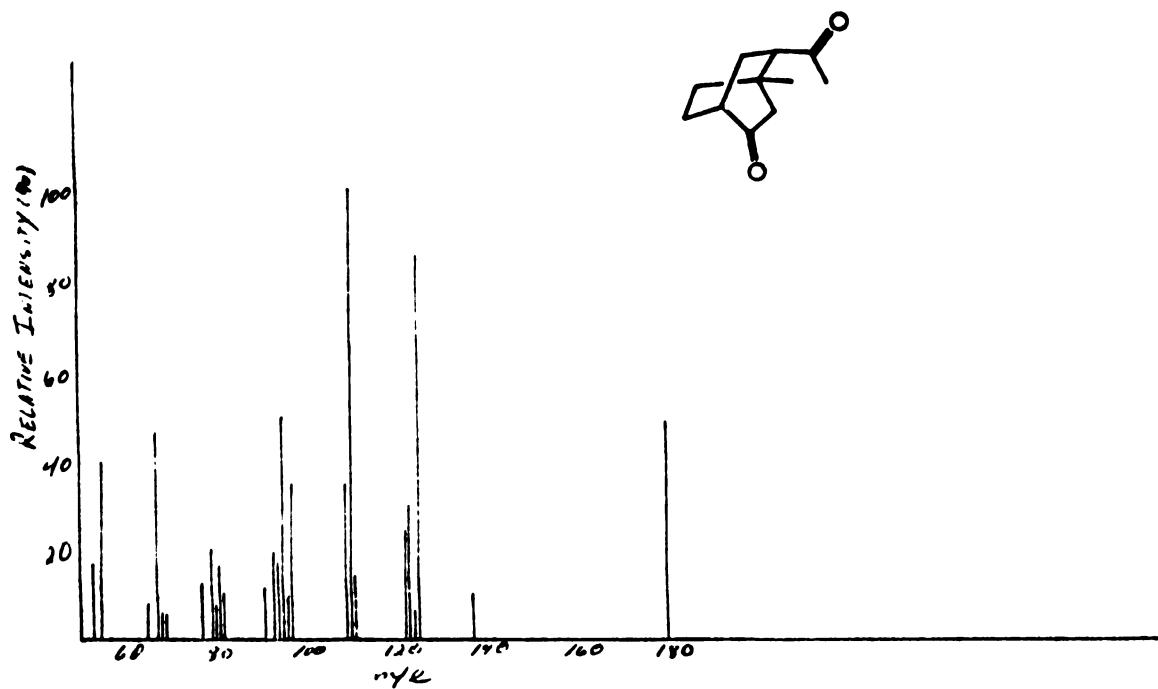


Figure 96. Mass spectrum of 40.

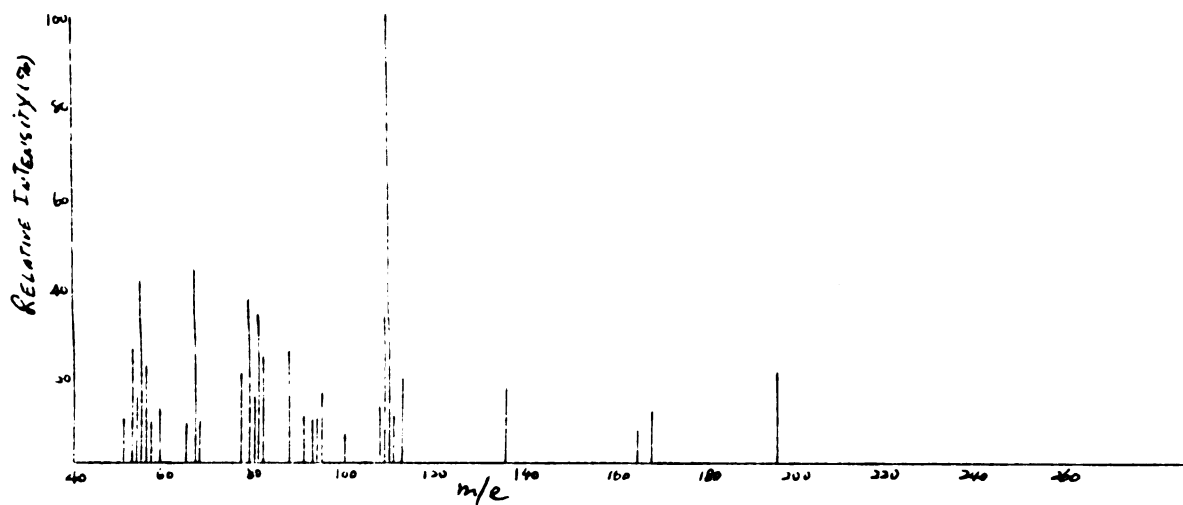
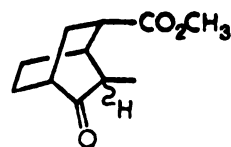


Figure 97. Mass spectrum of 41.

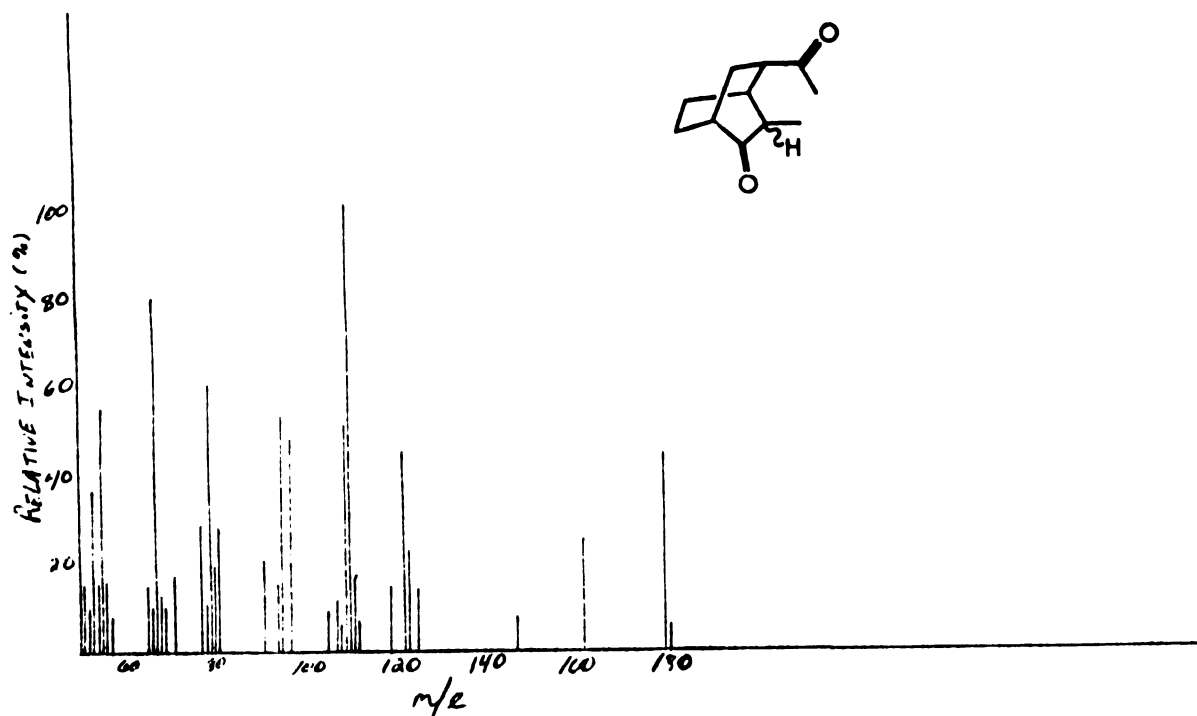
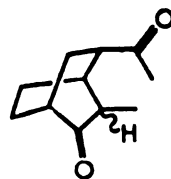


Figure 98. Mass spectrum of 42.

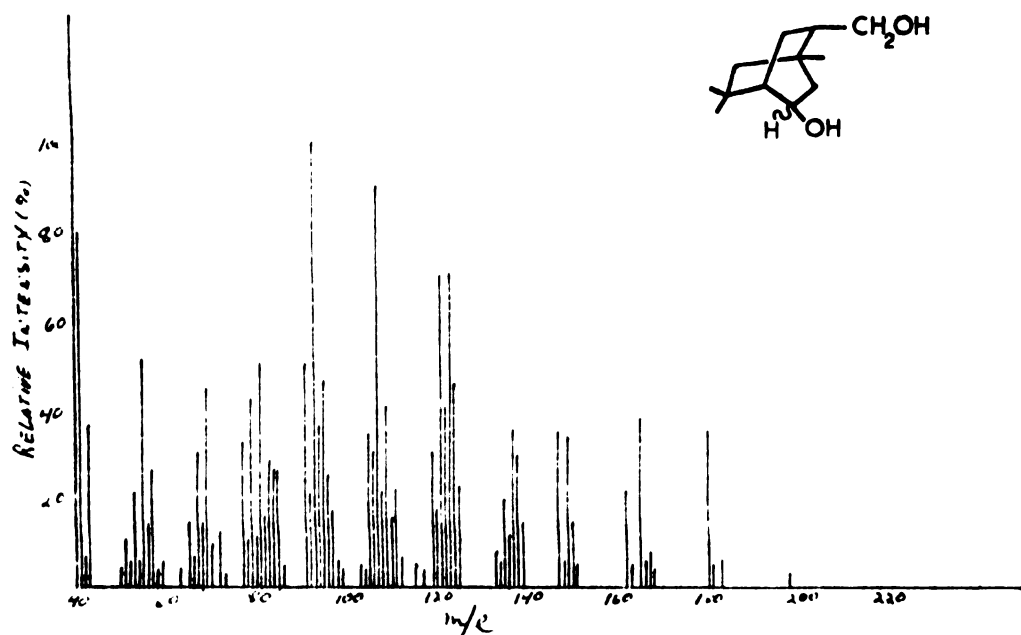


Figure 99. Mass spectrum of 46.

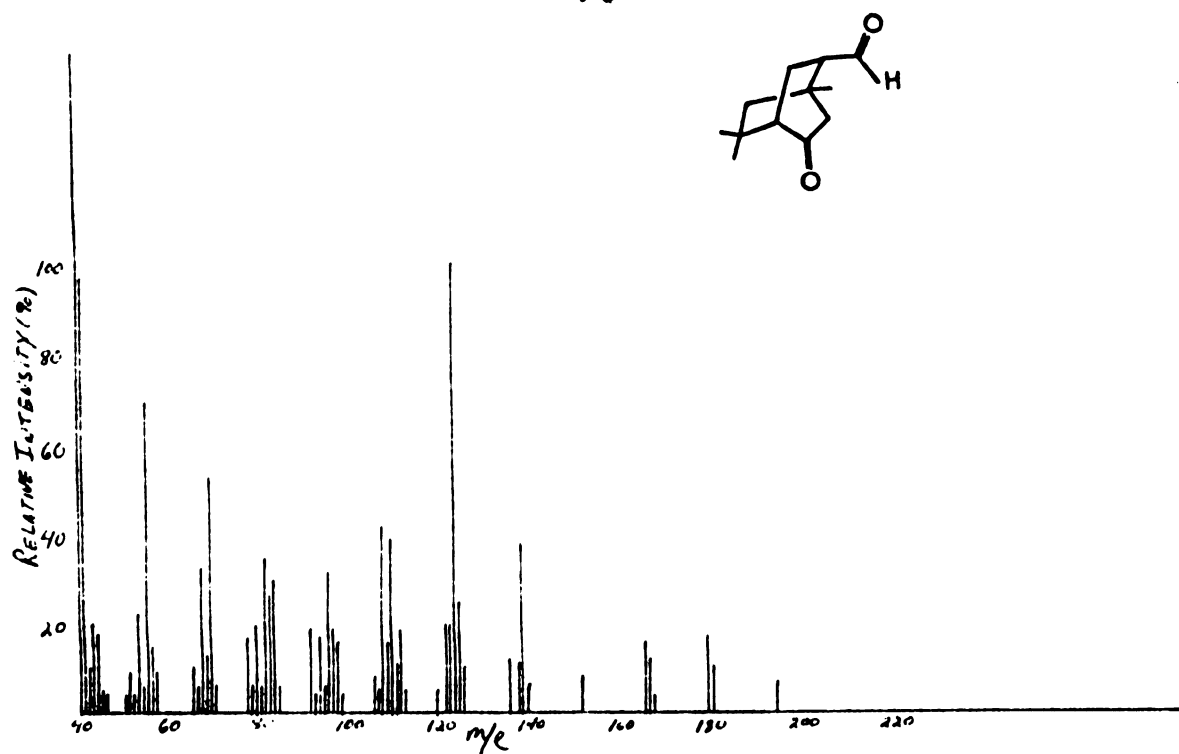


Figure 100. Mass spectrum of 47.

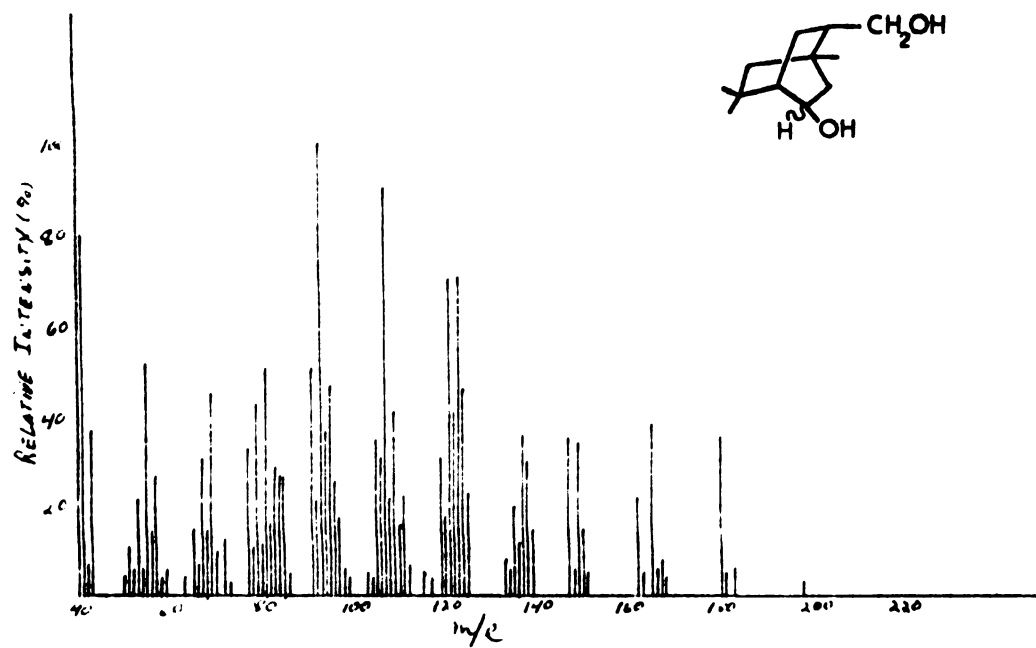


Figure 99. Mass spectrum of 46.

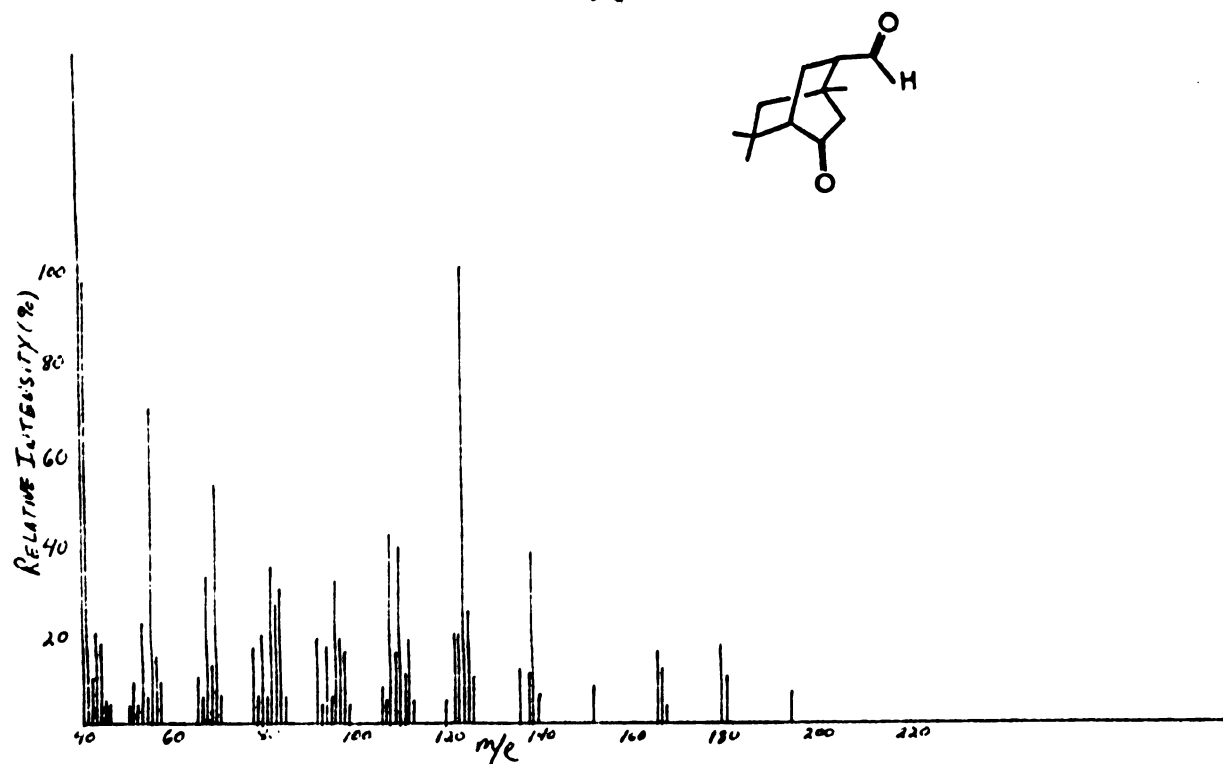


Figure 100. Mass spectrum of 47.

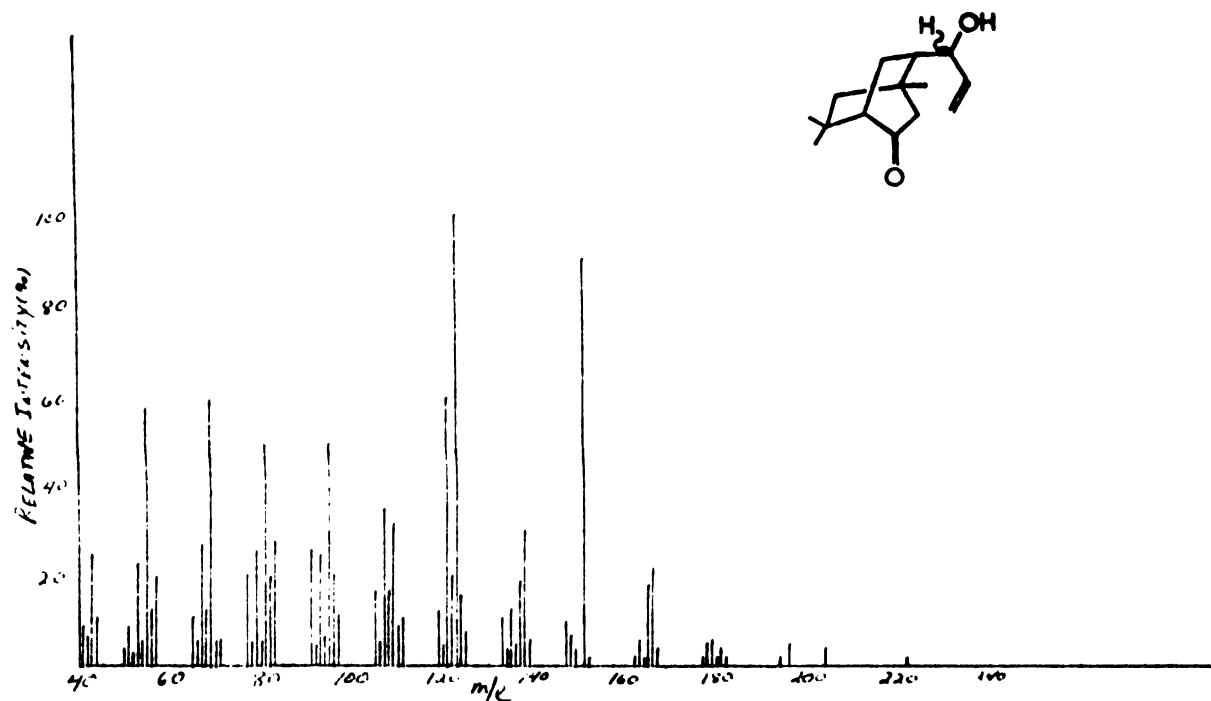


Figure 101. Mass spectrum of 48.

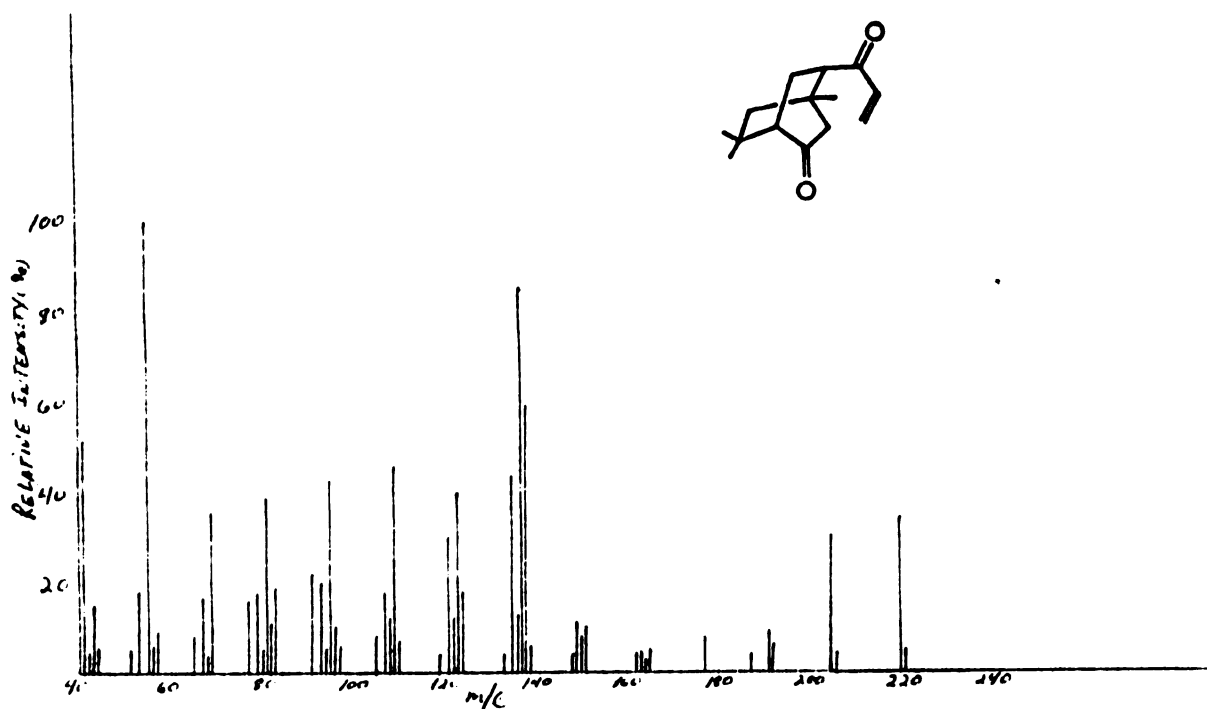
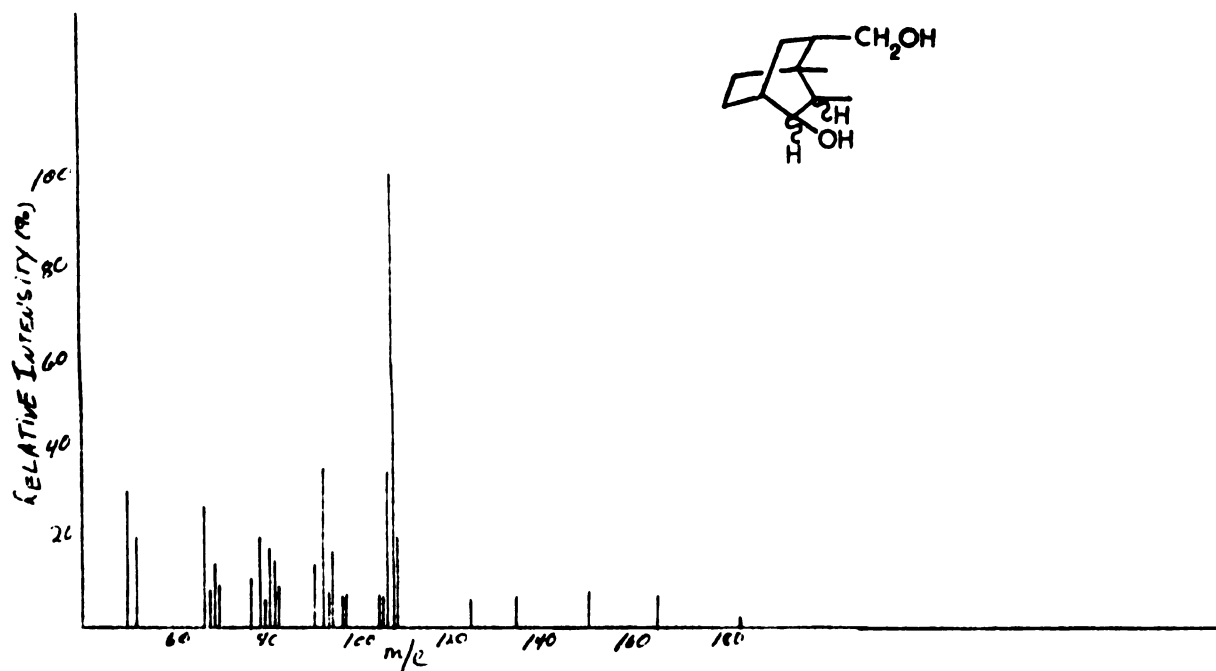
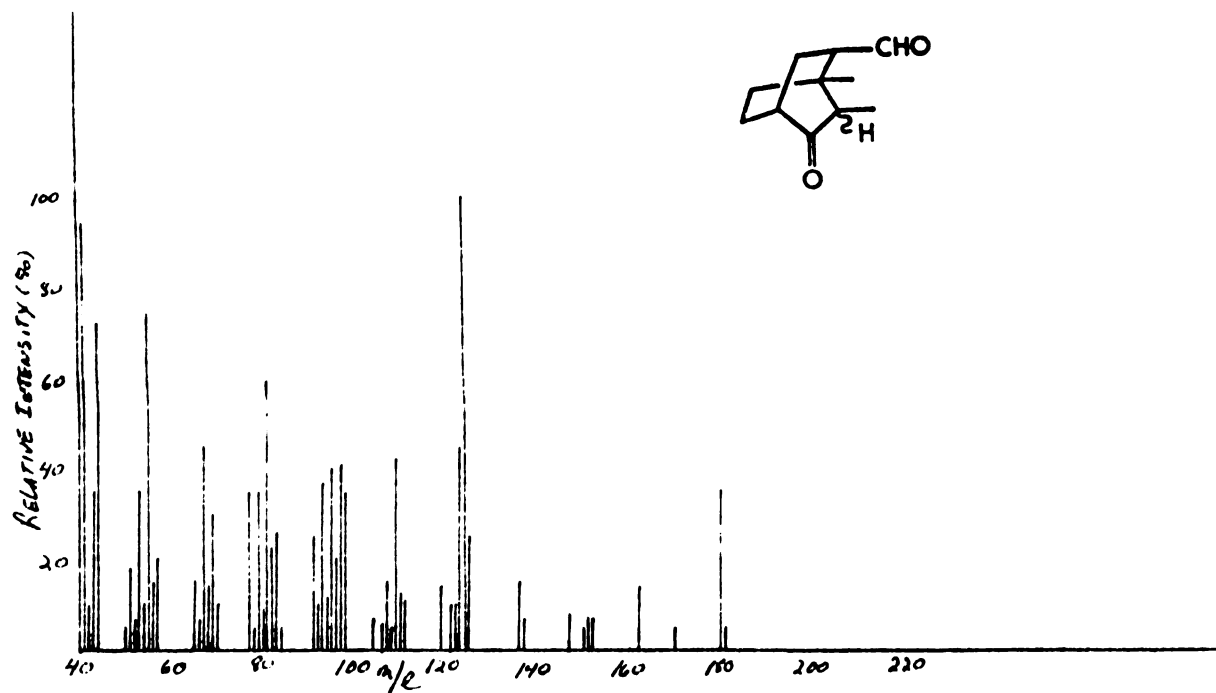


Figure 102. Mass spectrum of 49.

Figure 103. Mass spectrum of 50.Figure 104. Mass spectrum of 51.

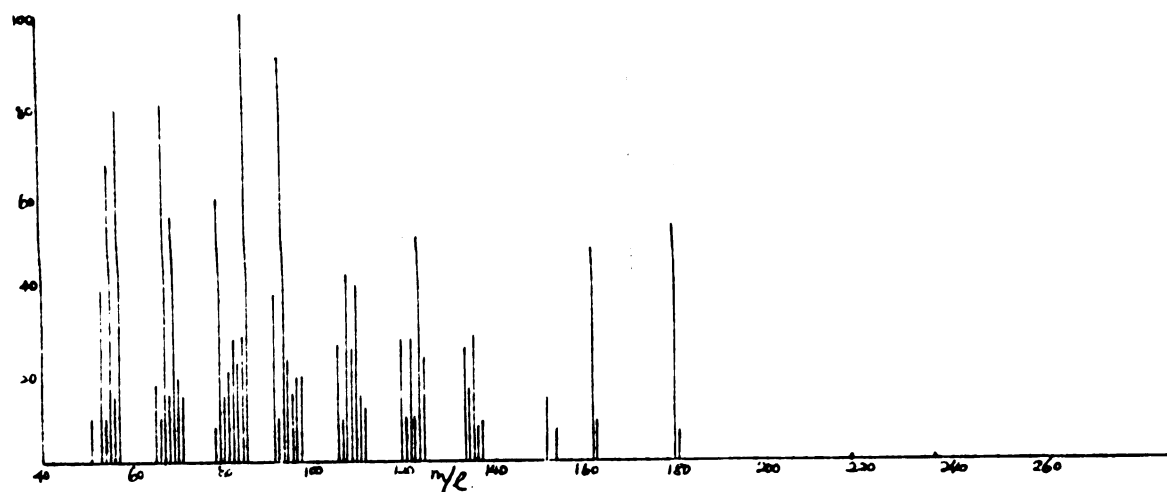
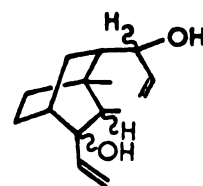


Figure 105. Mass spectrum of 53.

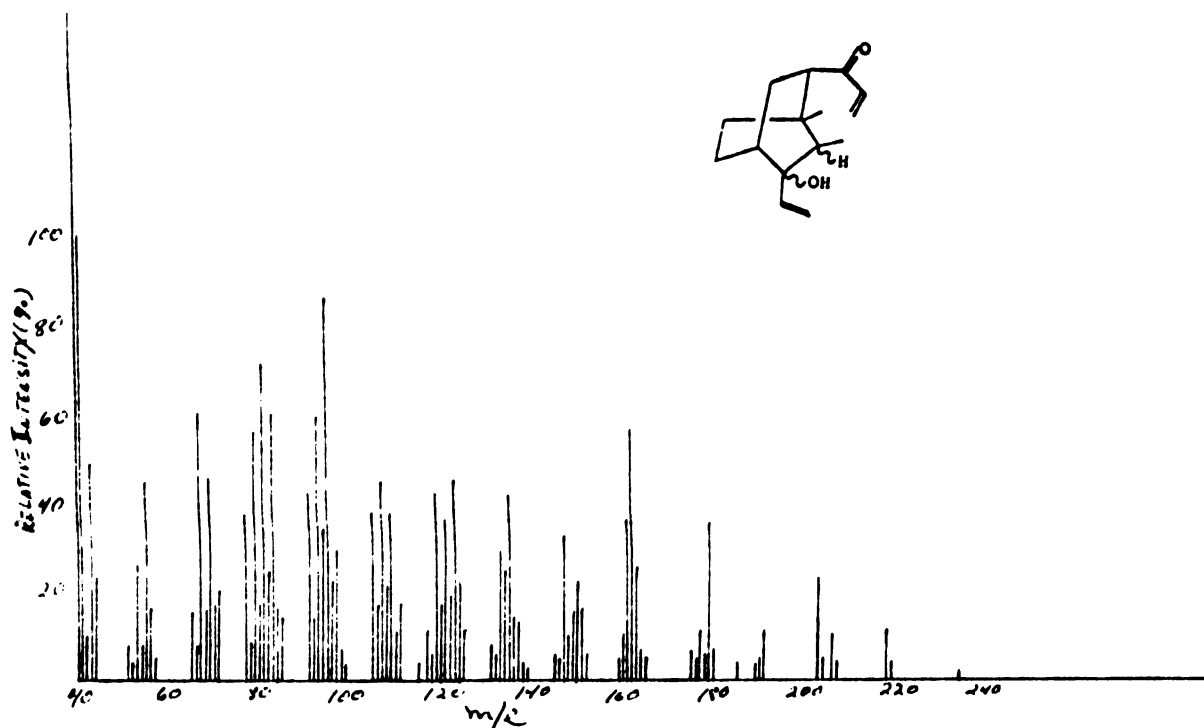
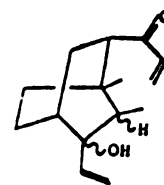


Figure 106. Mass spectrum of 54.

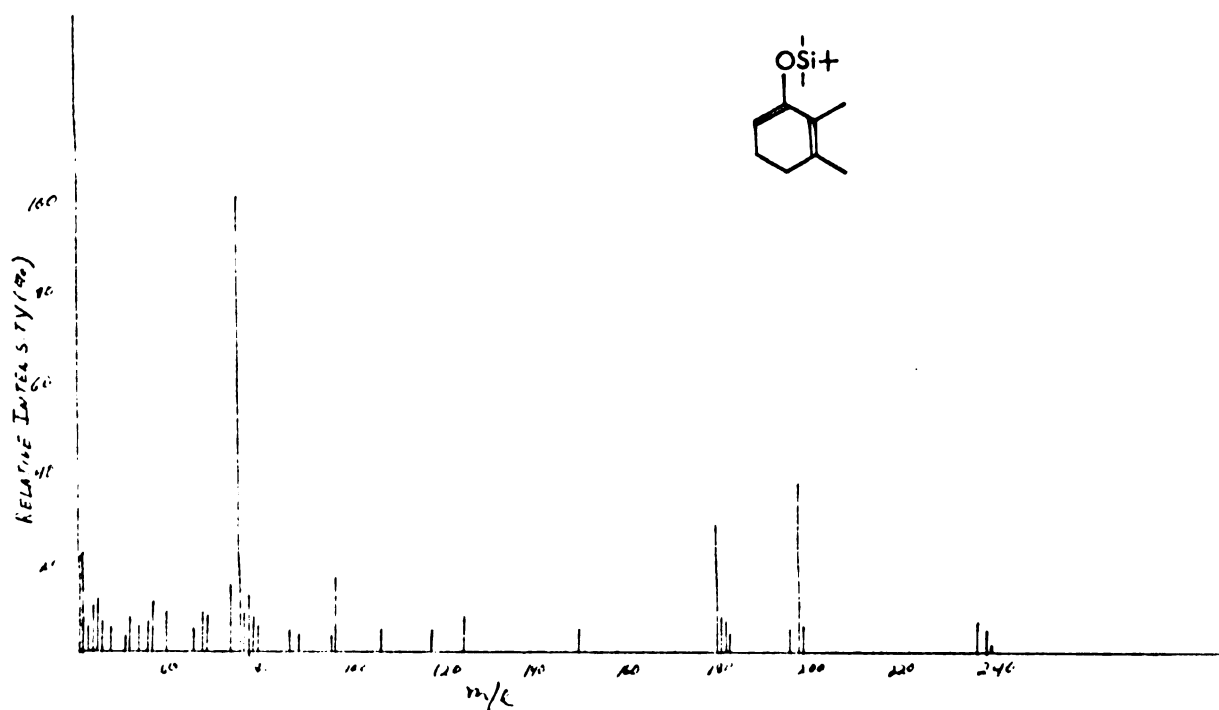


Figure 107. Mass spectrum of 55.

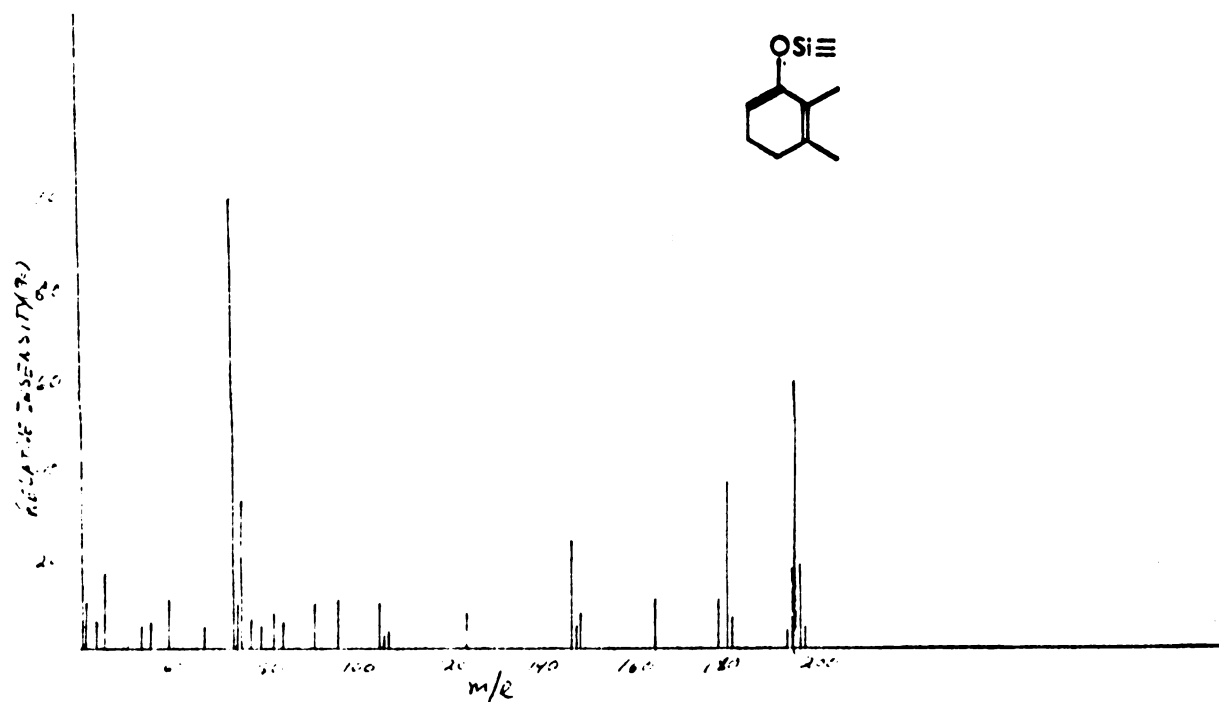


Figure 108. Mass spectrum of 56.

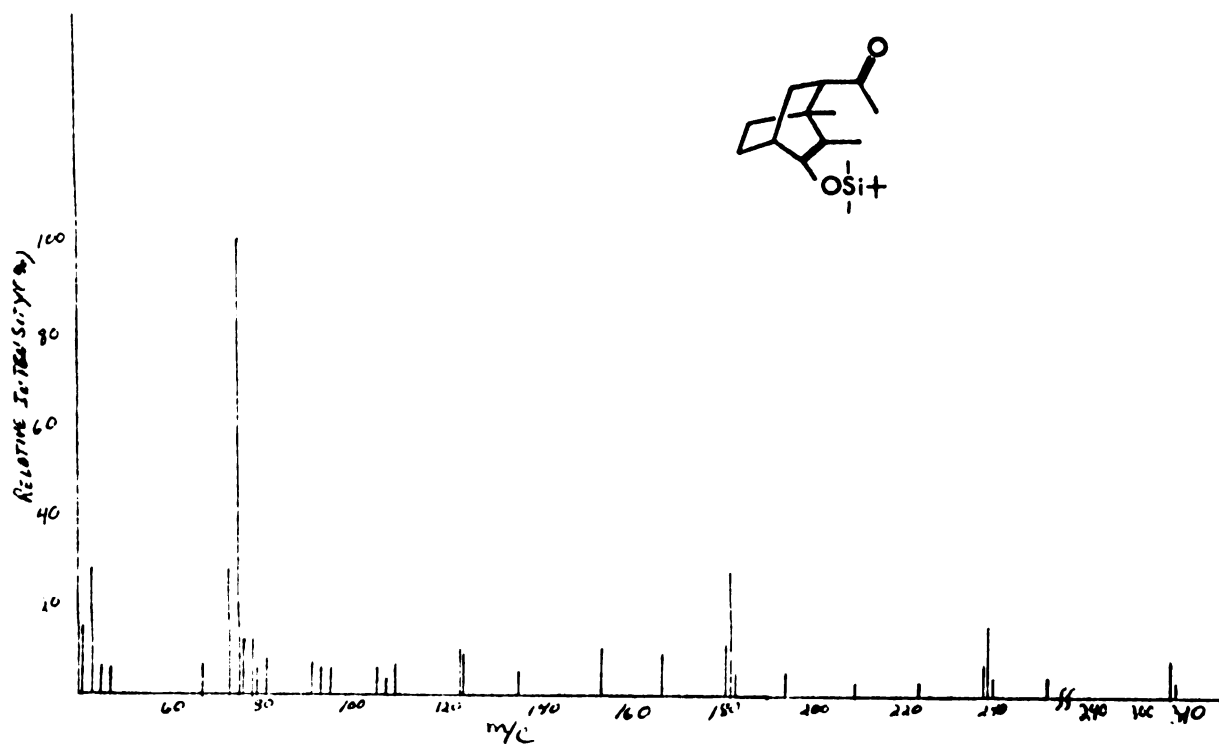


Figure 109. Mass spectrum of 57.

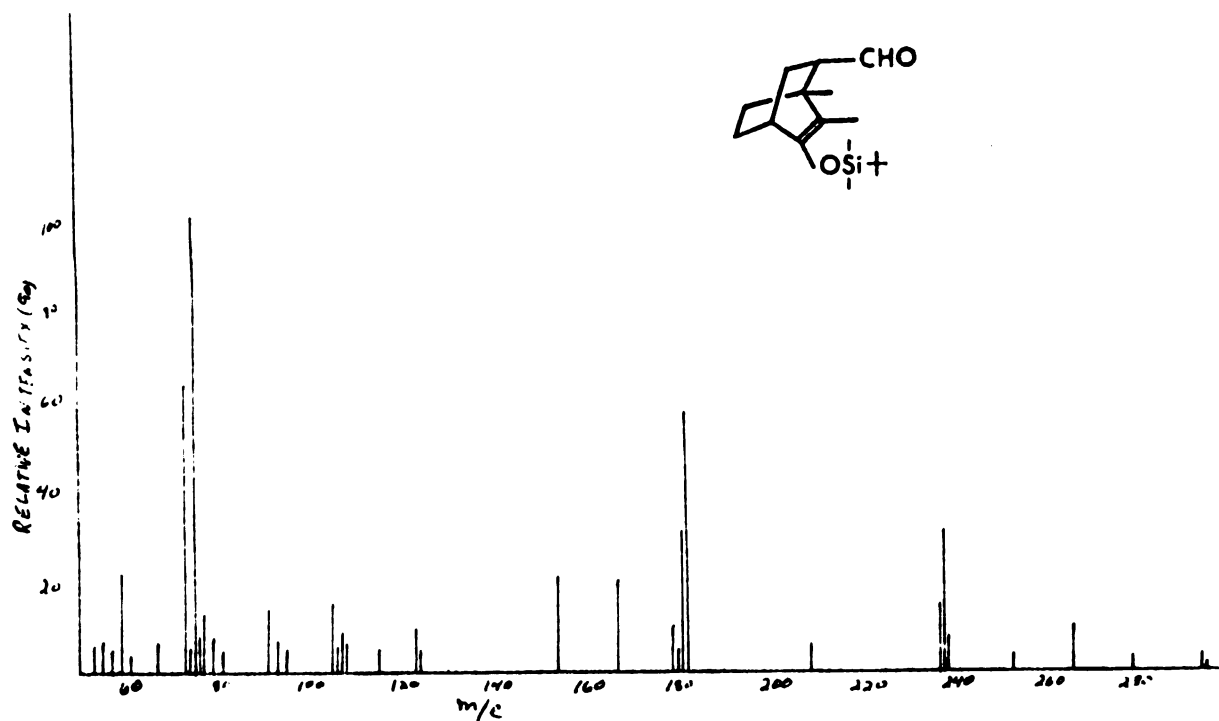


Figure 110. Mass spectrum of 58.

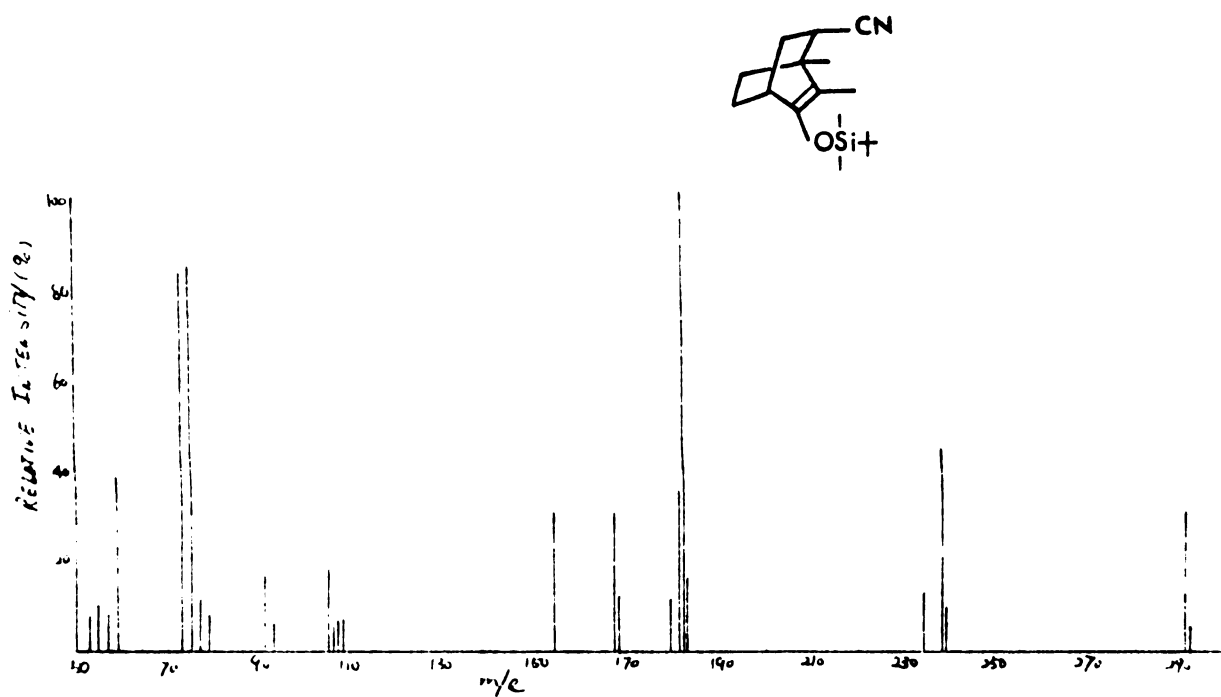


Figure 111. Mass spectrum of 59.

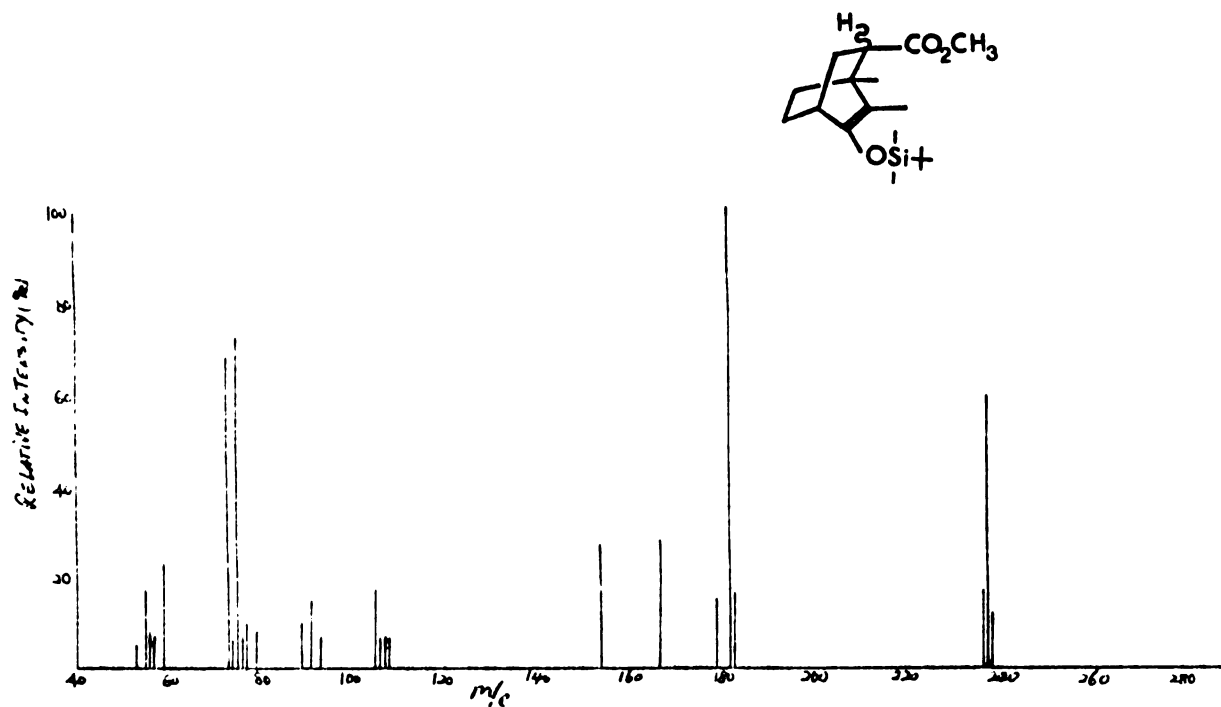


Figure 112. Mass spectrum of 60.

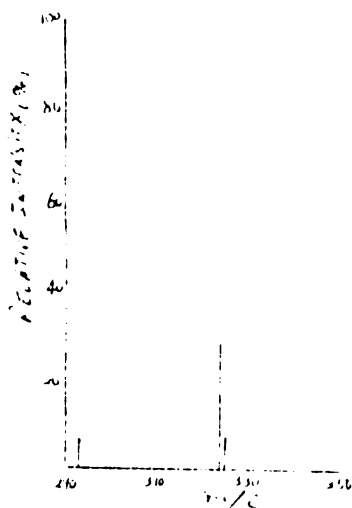
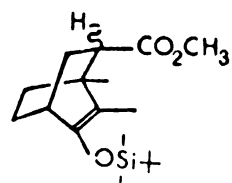


Figure 113. Mass spectrum of 60.

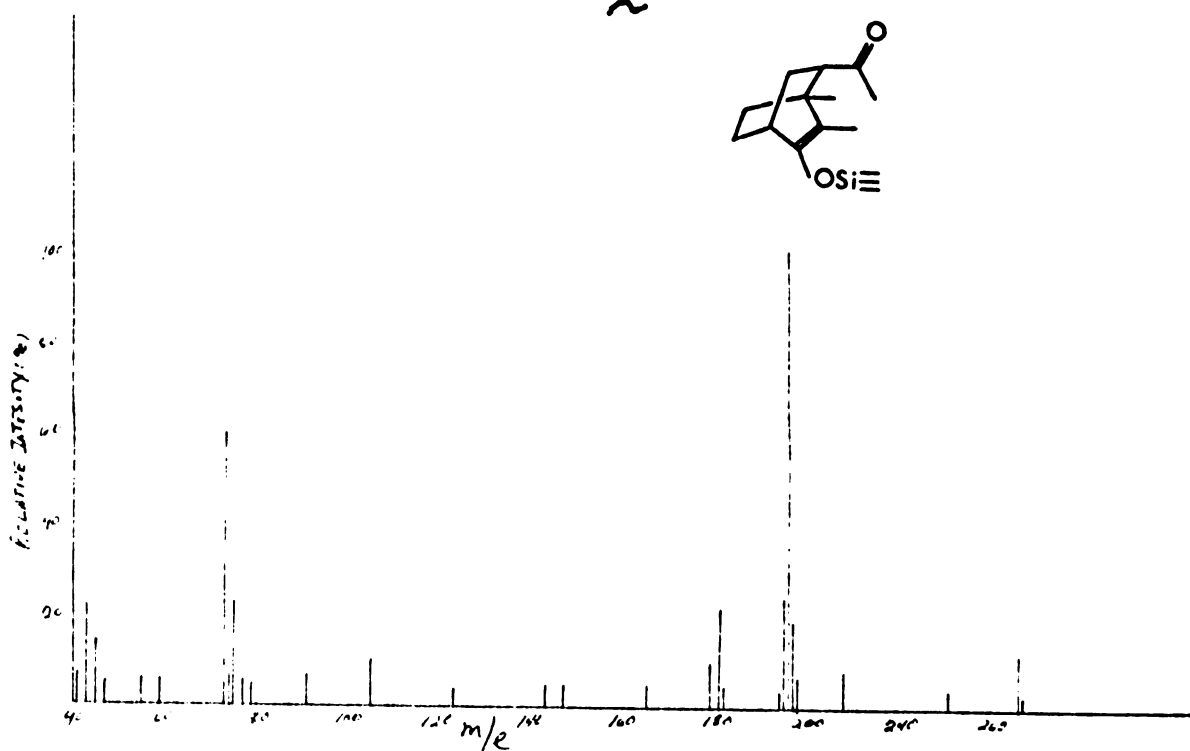
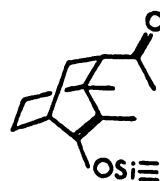
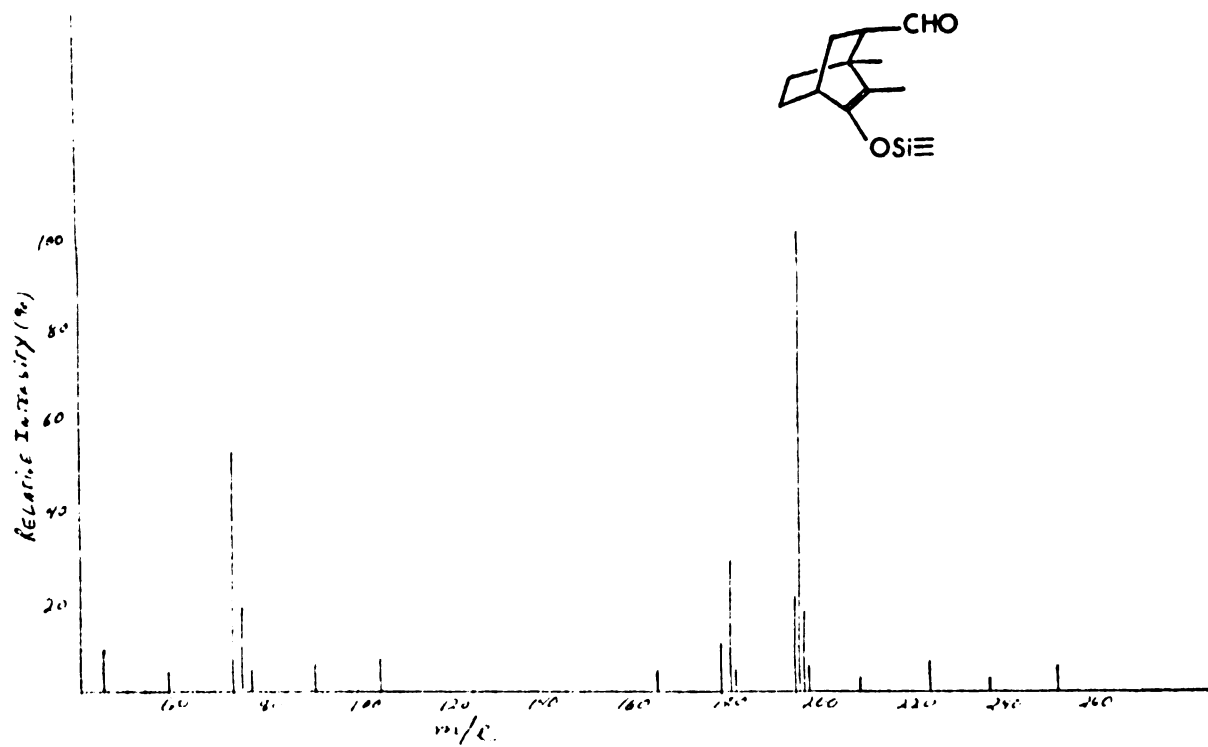


Figure 114. Mass spectrum of 61.



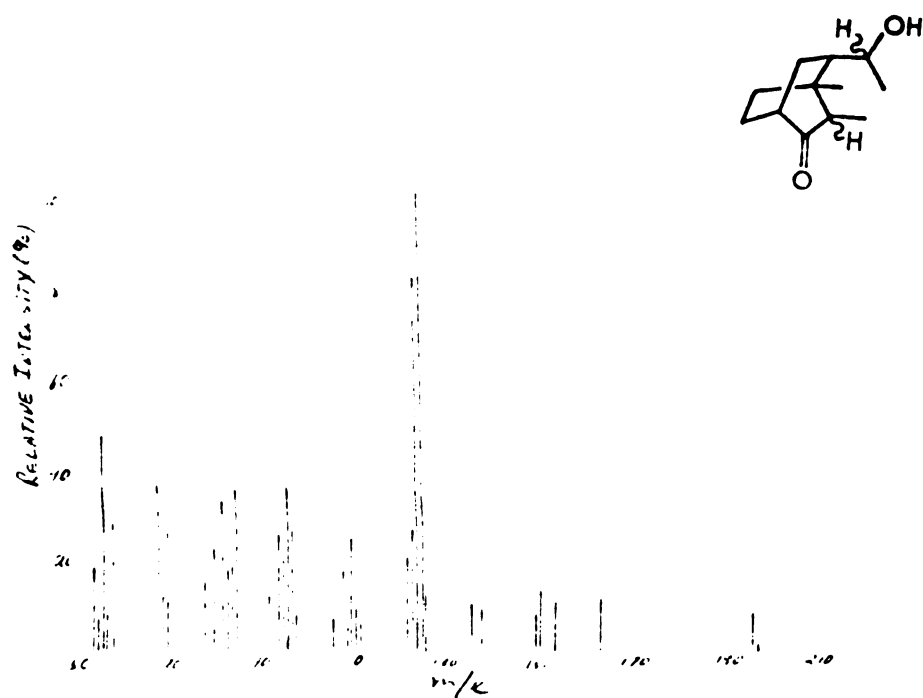


Figure 117. Mass spectrum of 64.

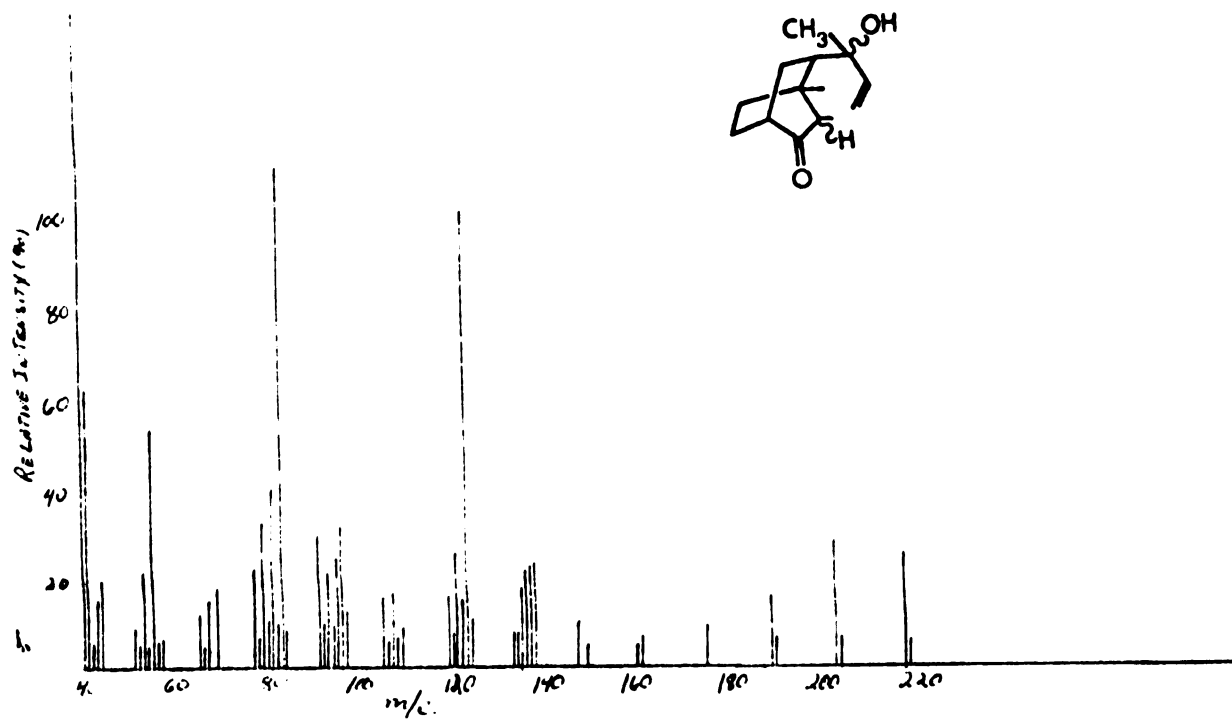


Figure 118. Mass spectrum of 67.

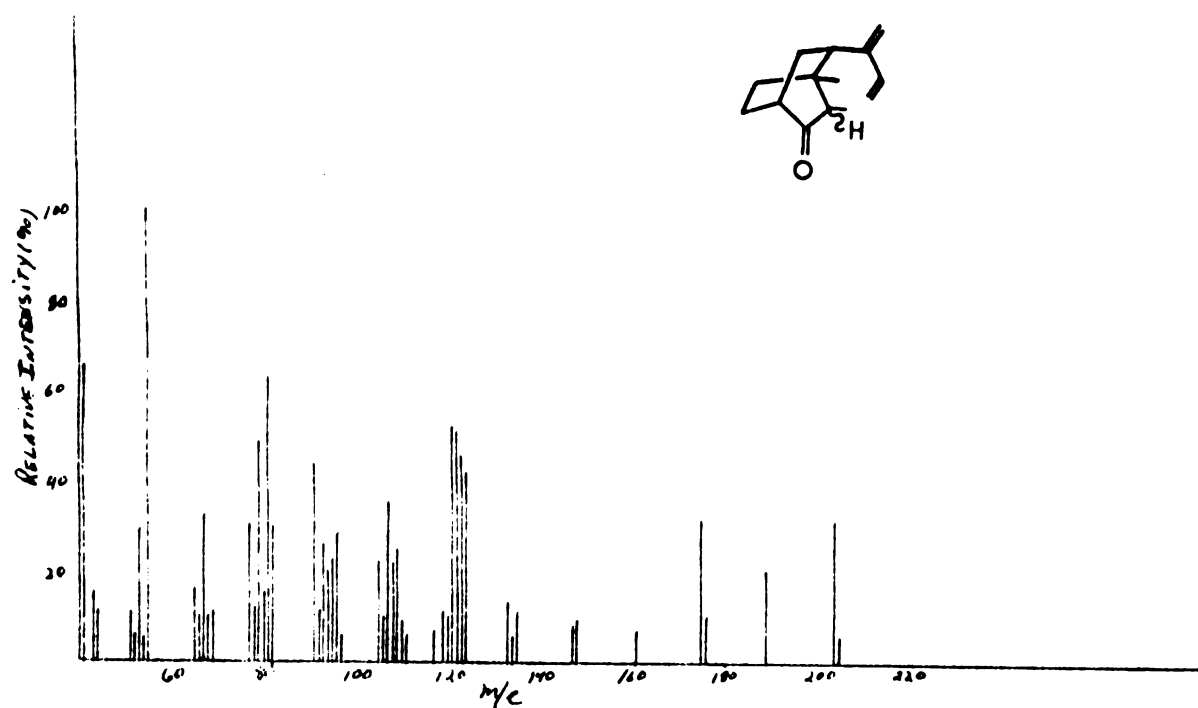


Figure 119. Mass spectrum of 68.

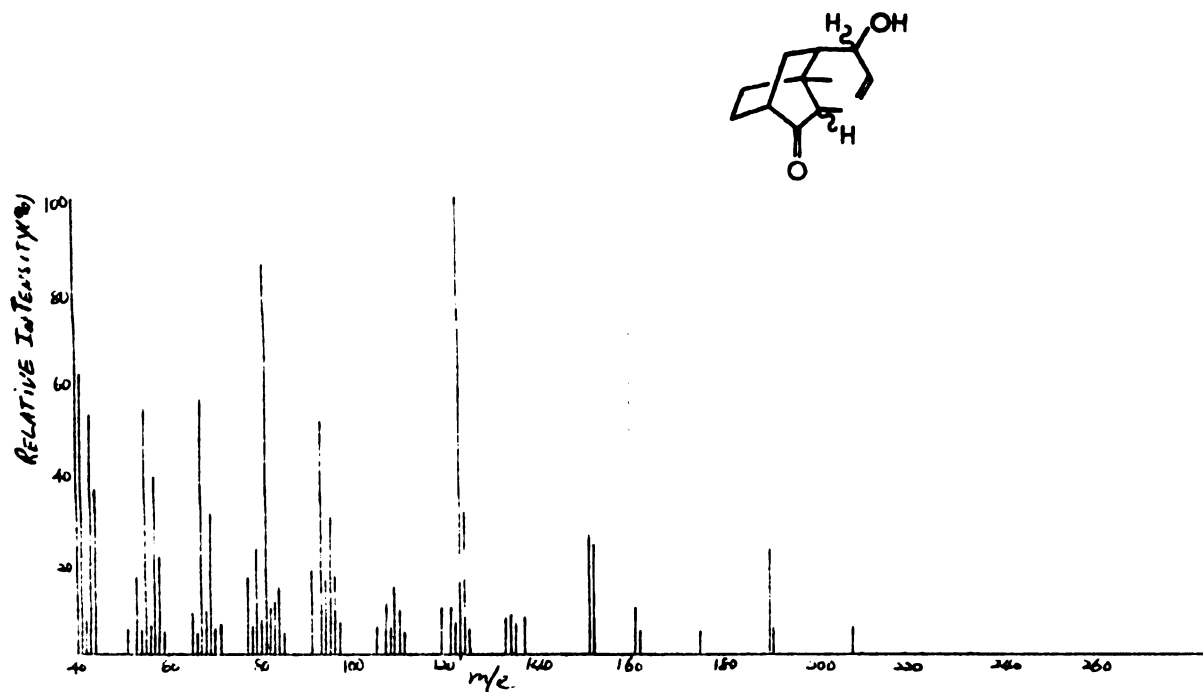


Figure 120. Mass spectrum of 69.

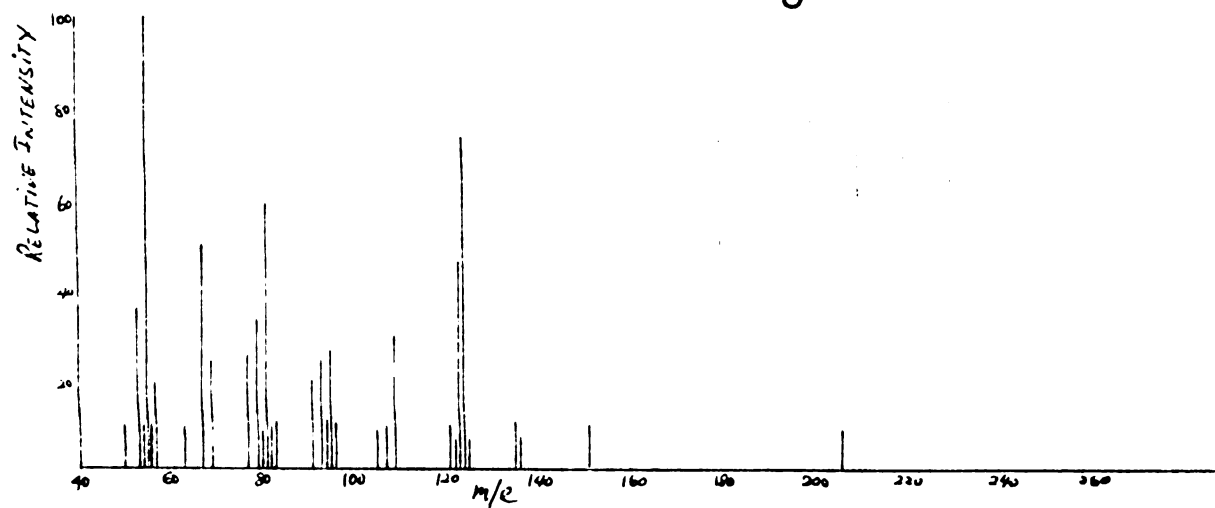
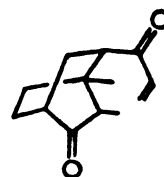


Figure 121. Mass spectrum of 45.

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