PART I
SOLVENT EFFECT IN THE DECOMPOSITION OF CAMPHOR HYDRAZONE

PART II
STUDIES IN THE BICYCLO(3,3,1) NONANE SYSTEM

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Gerald Jerome Papenmeier
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This is to certify that the

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PART I -- SOLVENT EFFECT IN THE DECOMPOSITION OF CAMPHOR HYDRAZONE PART II -- STUDIES IN THE BICYCLO [3,3,1] NONANE SYSTEM

presented by

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has been accepted towards fulfillment of the requirements for

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ABSTRACT

PART I

SOLVENT EFFECT IN THE DECOMPOSITION OF CAMPHOR HYDRAZONE

by Gerald Jerome Papenmeier

Meerwein (1) discovered the mercuric oxidation of camphor hydrazone in 1920. The major products of this oxidation are the isomeric hydrocarbons tricyclene and camphene. The ratio of these two products varied with the solvent. It has been postulated that the diazo intermediate can either lose nitrogen to give the carbene which will lead to tricyclene or become protonated by the solvent to form a diazonium ion which will then lose nitrogen to form the carbonium ion and lead principally to camphene. Thus the product composition would be a function of the acidity of the solvent.

The present investigation of this reaction was initiated to test the above theory and to study the rate of the reaction as a function of the solvent.

The rate of this reaction is remarkably constant for a heterogeneous reaction. An increase in rate was found when the reaction was run in glycolic solvents but there was no correlation between the rate and the ratio of products.

When the acidity of the solvent was increased from ethanol, through 2-methoxyethanol to 2, 2, 2-trifluoroethanol, the amount of camphene increased from 27% to 87%. Essentially pure tricyclene was the product of this reaction in aprotic solvents.

If the solvent protonation theory is correct, a deuterated solvent should give unlabeled tricyclene and monodeuterated camphene. After oxidizing camphor hydrazone in O-deuterated 2-methoxyethanol, the products were separated by vapor phase chromatography and analysed for deuterium by mass spectrometry. It was found that most of the camphene did contain one deuterium atom while very little of the tricyclene incorporated any deuterium. It was demonstrated that neither compound exchanged with the solvent under the conditions of this reaction.

PART II

STUDIES IN THE BICYCLO[3, 3, 1]NONANE SYSTEM

This study was initiated because of the limited amount of work which had been done on the bicyclo[3, 3, 1]nonane system and because the synthesis of clovene, a degradation product of caryophyllene incorporating this system, had not been achieved.

Several preparations of the bicyclo[3, 3, 1]nonane structure have been accomplished but few of these investigators made any further study of the products. Rabe's (2) synthesis of 3-keto-5-methylbicyclo[3, 3, 1]-nonan-1-ol was chosen as the point of departure for this study, because if correct it is a one-step synthesis of a bicyclononane structure which possesses the bridgehead methyl group of clovene and suitable functional groups for a possible attachment of the five-membered ring of clovene.

The structure of this alcohol was established by its nuclear magnetic resonance, infrared and mass spectra. An acetate derivative, prepared using acetic anhydride, acetyl chloride and ketene, was identified by spectral considerations; however, this compound was not identical with a compound which was assigned the formula by Rabe.

The next step in the proposed route to clovene was the esterification of this alcohol with an α, β-unsaturated acid which was to be cyclized. Thus, 3-keto-5-methylbicyclo[3, 3, 1]nonan-1-yl 3-methyl-2-butenoate was prepared and characterized. When the cyclization of the ester was unsuccessful after several attempts, a second ester, ethyl 3-keto-5-methylbicyclo[3, 3, 1]nonan-1-yl isopropylidenemalonate, was prepared and characterized. Apparently the cyclization did succeed with this ester but the product was not fully characterized. The work on this phase of the study was discontinued partly because of the progress of Raphael's group. The synthesis of clovene was accomplished by Raphael (3) and co-workers.

The first solid derivative of Rabe's bicyclic alcohol, 1-bromo-5-methylbicyclo[3, 3, 1]nonan-3-one, was prepared from the alcohol and phosphorus tribromide. The reactivity of this bromide was of interest because of the position of the bromine atom at a bridgehead. Cope (4, 5) studied 1-bromobicyclo[3, 3, 1]nonan-9-one and found that this compound was readily converted to bicyclo[3, 3, 0]octane derivatives when allowed to react with silver nitrate in aqueous alcohol or ammonia. The 3-keto bromide of this study was reacted with silver perchlorate in aqueous dimethyl sulfoxide to yield the parent alcohol and in anhydrous methanol to yield 1-methoxy-5-methylbicyclo[3, 3, 1]nonan-3-one. However, when the solvent was changed to liquid ammonia the principal organic product was not the expected amine but an uncharacterized product which neither possessed the bicyclo[3, 3, 1] structure nor contained an amino group.

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PART I

SOLVENT EFFECT IN THE DECOMPOSITION OF CAMPHOR HYDRAZONE

PART II

STUDIES IN THE BICYCLO[3, 3, 1]NONANE SYSTEM

By

Gerald Jerome Papenmeier

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TABLE OF CONTENTS

TABLE OF CONTENTS - Continued

LIST OF TABLES

TABLE Page

PART I

PART II

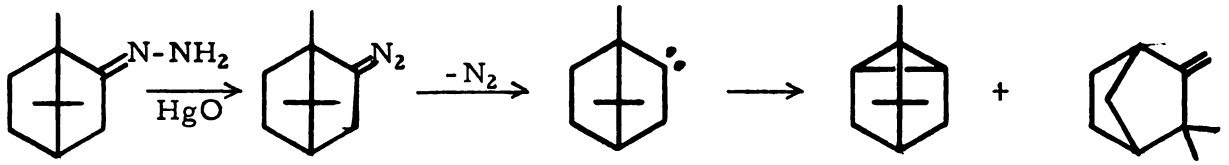
LIST OF FIGURES

PART I

SOLVENT EFFECT IN THE DECOMPOSITION OF CAMPHOR HYDRAZONE

INTRODUCTION

The oxidation of camphor hydrazone (I) with mercuric oxide was reported by Meerwein (1) in 1920. He found the main product to be tricyclene (IV) and proposed a carbene mechanism as shown in equation 1.



I II III IV V

Equation 1.

Since no further check of this hypothesis had been performed, Reusch and co-workers (2) repeated the earlier work using several different solvents and found in each case tricyclene as the major volatile product and a constant rate of nitrogen evolution. Furthermore the tricyclene incorporated less than 1% deuterium based upon one exchangable hydrogen when 0-deuterated ethanol was used as the solvent. This indicates that the carbene intermediate (III) undergoes a 2, 6 hydrogen shift.

The alkaline decomposition of tosylhydrazones near 200° was reported by Shechter (3) and Whiting (4) to give tricyclene in aprotic solvents, but mainly camphene (V) in protonic solvents. These workers favored the mechanism of Meerwein with the further postulation that the protonic solvents could protonate the intermediate diazo compound (II) giving a diazonium ion which could then decompose to several different products, including camphene.

The work of Reusch, using ethanol as the solvent, was inconsistent with the solvent protonation hypothesis but since no common solvents had been used by the Michigan State University and Oxford

University groups, a joint study by these two groups was undertaken. The results of this joint study and a reinvestigation of the incorporation of deuterium in both products are reported here.

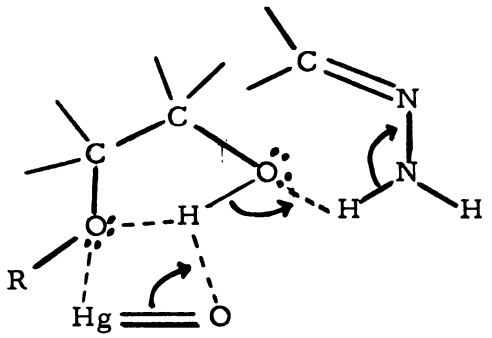
RESULTS AND DISCUSSION

Rate of Decomposition

The rate of reaction was determined by collecting the nitrogen evolved in a gas burette and plotting the volume of gas vs. time. These curves were linear except for an induction period and a period at the termination of the reaction when the rate again decreased. The linear portion of these curves made up at least 50% of the curve except for the very slow rate in the 1, 2-dimethoxyethane where insufficient points were taken.

From the earlier work at Michigan State University on the rate of this reaction, it was found that when an aprotic solvent such as cyclohexane was thoroughly dried, there was a rate decrease. This seemed to indicate the necessity of a protonic molecule such as water at the oxide surface for the reaction to proceed. The very slow rate in the 1, 2-dimethoxyethane found in Table 1 can be explained if this solvent is bound to the mercuric oxide surface through the coordination of the basic oxygen atom to the mercury atom, thus excluding water molecules from the surface.

From Table 1 it will be seen that only when the glycol solvents were used was the rate of the reaction appreciably faster. Assuming that these solvents are bound to the mercuric oxide surface by a hydrogen bond to the oxide oxygen and by the utilization of the second solvent oxygen as a base to coordinate with the mercury atom, the proton which seemed to be necessary in the earlier study would be provided and the coordination of the mercury atom would lower the energy of the transition state. This solvent participation may involve a transition state such as V.



V

The slower rate of O-dueterated 2-methoxyethanol is consistent with transition state V as a deuterium bond to the mercuric oxygen would be weaker and the transition state less stable. A similar effect is noted in 1, 3-propandiol where the geometry is less favorable for this type of transition state.

Products of Decomposition

The volatile products were collected by codistillation with the solvent, dilution with water and extraction with pentane. The only volatile products found were tricyclene and camphene and these could be detected quantitatively by vapor phase chromatography to within 1%.

In earlier studies (3, 4), utilizing the basic decomposition of the tosylhydrazone, the proton donating ability of the solvent seemed important in determining which of the volatile products was isolated. In protonic solvents mostly camphene resulted, while in aprotic solvents tricyclene was formed almost exclusively. However, prior work in this laboratory (2) seemed to indicate that the acidity of the solvent was not important in the mercuric oxide oxidation, even though both reactions were visualized as passing through the same diazo and carbene intermediates. In the oxidation the only protonic solvent used was ethanol while Whiting's group used only glycolic solvents.

In this study, as Table 1 shows, the use of glycolic solvents did increase the amount of camphene found in the oxidation; however, a repeat of the earlier work in ethanol gave only 73% tricyclene instead of 98%. The sample of mercuric oxide used can change the results. To ascertain whether the proton donating ability is important or whether some specific glycol effect, such as that in the rate of the reaction, is operative, the reaction was run in 1, 3-propandiol, and 2, 2, 2-trifluoroethanol. While the acidity of the 1, 3 glycol should be near that of ethanol, it does have the second oxygen atom which could participate if a specific glycol effect was important. Since this solvent does not differ from ethanol and since the trifluoro alcohol, which is much more acidic, gives only 13% tricyclene, the acidity theory seems more likely. Even the slight difference in acidity of a hydrogenated and a deuterated alcohol seems to lower the amount of camphene formed.

The discrepancy between the earlier studies resulted partially from the basic conditions of the tosylhydrazone decomposition. It will be noted in Table 1 that base (3 and 4; 6 and 8; 10 and 11) increases the amount of camphene formed.

Optical Activity in the Decomposition

The oxidation in ethanol gave 98% tricyclene when first attempted but later gave only 73% tricyclene. The only apparent difference in the reaction was the optical activity of the starting material--the earlier workers used d-camphor hydrazone while in the present study d, l-camphor hydrazone was used. According to x-ray and neutron diffraction data (5) the structure of mercuric oxide is composed of left-handed helices. Since hydrazone oxidation occurs at the crystal surface, this dissymmetry could account for the differences in the reactivity of the d- and the l-hydrazones.

Table 1. Results of Mercuric Oxide Oxidation of Camphor Hydrazone

Solvent	Base	Temp.	Rate	Percent Linear	Percent Tricyclene
1. Heptane	--	80	--	--	99
2. 1,2-Dimethoxy-ethane	--	80	1	26	98
3. Ethanol	--	78	28	52	73*
4. Ethanol	x	78	55	71	64
5. 1,3-Propandiol	--	80	65	65	75
6. 2-Methoxyethanol	--	81	127	60	69
7. 2-Methoxyethanol	--	124	185	53	59
8. 2-Methoxyethanol	x	81	250	84	62
9. 2-Methoxyethanol, O-deuterated	--	124	30	57	87
10. 1,2-Ethandiol	--	80	110	--	74
11. 1,2-Ethandiol	x	81	540	55	55
12. 1,2-Ethandiol	--	138	∞	--	57
13. 2,2,2-Trifluoro ethanol	--	74	26	50	13

*Using d,l-hydrazone and yellow mercuric oxide, this value was originally obtained; however, see page 8.

A synthesis of l-camphor from l-borneol gave the l-camphor hydrazone which was compared to both the d-isomer and the racemic mixture. A series of reactions was initiated to determine if the optical properties of the hydrazone could affect the product determination. The d-hydrazone gave 75% tricyclene and the l-hydrazone gave 71% but the racemic hydrazone gave only 69% tricyclene when at least three experiments were carried out on each form and averaged.

When the yellow mercuric oxide was replaced with red oxide, which had been ground till it was orange in color, both d- and l-camphor hydrazones gave 98% tricyclene. Thus these variations in product do seem to originate in the sample of mercuric oxide used for the oxidation but not in a manner which can easily be related to the stereochemistry of the hydrazone.

Isotope Effects in the Decomposition

In the acidity theory advanced by other workers the protonation of the intermediate diazo compound leads to a carbonium ion which can either rearrange to camphene or decompose to tricyclene. When the earlier study of this oxidation was carried out in 0-deuterated ethanol no dueterium was incorporated into the tricyclene molecule, however the small amount of camphene formed was not investigated. As a final check on the protonation theory the oxidation was carried out in 0-deuterated 2-ethoxy ethanol (76% deuterium) and both products analyzed by mass spectroscopy for deuterium. The results of this experiment, shown in Table 2, indicate that the camphene does incorporate deuterium while the tricyclene does not. Unfortunately this reaction proceeds at a faster rate in the undeuterated alcohol so it cannot be shown whether all of the undeuterated camphene arose from a carbene intermediate or from the undeuterated alcohol present. A mixture of

Table 2. Mass Spectroscopy Data[a]

m/e	Products from hydrazone decomposition in ROH[b]		Products from hydrazone decomposition in ROD[b]		Products after reflux in ROD[b] with Hg and HgO	
	Tricyclene	Camphene	Tricyclene	Camphene	Tricyclene	Camphene
134	0.27	0.40	0.26	1.92	6.58	2.38
135	1.15	4.65	1.17	5.33	1.78	0.83
136	100.00	100.00	100.00	100.00	100.00	100.00
137	10.9	11.1	17.9	129.	9.89	9.90
138	0.60	0.75	1.27	14.8	0.50	0.53
139	0.40	0.31	--	1.75	--	--
Percent D_1	--	--	7%	54%	--	--

[a]Mass spectra were taken on a Consolidated Electrodynamics Corporation mass spectrometer, Type 21-103C at an ionizing voltage of 70 volts.

[b]R = $CH_3OCH_2CH_2$-

tricyclene and camphene was refluxed in the deuterated solvent with mercuric oxide and mercury to show that neither exchanged deuterium with the solvent under the conditions of this reaction. Thus the protonation mechanism can account for most if not all of the camphene formed in the oxidation of camphor hydrazone.

EXPERIMENTAL

Analytical grade mercuric oxide, freshly distilled camphor hydrazones and purified solvents were used in this investigation. Analyses were made by vapor phase chromatography using a 6'x$\frac{1}{4}$" Beckman silicone 550 column or a 6'x$\frac{1}{4}$" column of 20% apieson "L" on chromasorb W. This method of analysis was checked frequently using a mixture of tricyclene and camphene of known proportions.

l-Camphor (6). - A solution of l-borneol (154 g.) in ether (400 ml.) was placed in a three-necked flask equipped with a stirrer, a dropping funnel and a condenser. A solution of sodium dichromate dihydrate (100 g.) and sulfuric acid (75 ml.) in water (500 ml.) was added dropwise with stirring over a 1 hr. period. Stirring was continued for 7 hr. at room temperature. The ether layer was separated and washed twice with 5% sodium bicarbonate solution and dried. The solvent was removed and the camphor used without further purification. There was obtained 113 g. (74%) of l-camphor.

d, l-Camphor hydrazone. - The hydrazone was prepared by refluxing 152 g. d, l-camphor (1 mole) with 236 g. of 85% hydrazine hydrate (4 mole) and 60 g. of glacial acetic acid (1 mole) dissolved in 450 g. of absolute ethanol for 4 hr. After removing the alcohol at aspirator pressure, the reaction mixture was brought to its original volume with ether, the hydrazine layer was removed and the reaction mixture was washed with 10% sodium hydroxide saturated with sodium chloride followed by saturated sodium chloride alone. Removal of the solvent at aspirator pressure followed by distillation at reduced pressure gave 145 g. (87%) of d, l-camphor hydrazone, b.p. 85-7° (1 mm.).

d-Camphor hydrazone. - Using the procedure above 1 mole of d-camphor was converted to d-camphor hydrazone, $[\alpha]_D = -35.3$ (C 10, ether) [lit. value, -40.8 (C. 10, ether)].

l-Camphor hydrazone. - Using the procedure above 61 g. (0.40 mole) of l-camphor was converted in 66% yield to l-camphor hydrazone, $[\alpha]_D = +19.6$ (C 10, ether).

Oxidation procedure. - A solution of 3 g. of camphor hydrazone in 25 ml. of the solvent being investigated was placed in a three-necked flask equipped with a stirrer, a condenser and a solid addition tube. The solution was brought to temperature with stirring and the mercuric oxide (8 g.) was quickly added. The nitrogen evolution was measured by a gas burette attached to the condenser. After the cessation of the nitrogen evolution the stirring was continued for 15 min. at that temperature then cooled to room temperature. The inorganic products were removed by filtration through a medium sinter glass funnel and the volatile products distilled quickly over a short path. The addition of an equal amount of water to the solvent gave a cloudy solution which was extracted three times with pentane. Careful distillation of the solvent from the dried extracts yielded a thick oil containing tricyclene and camphene. Mass spectral analysis was carried out on samples of tricyclene and camphene which had been separated by vapor phase chromatography using the apieson column.

The base used in these experiments consisted of sodium (0.42 g.) dissolved in the alcoholic solvent being studied prior to the addition of the hydrazone.

Possible equilibration. - Since the two products of this reaction are isomers which can readily be interconverted, three experiments were conducted to prove that no isomerization was taking place under the conditions of this reaction.

A mixture of 62% tricyclene and 38% camphene (3.2 g.) was dissolved in absolute ethanol (25 ml.) and the solution brought to reflux. After adding 8 g. of mercuric oxide the mixture was refluxed for 30 min. and the products isolated as usual. The analysis of the products by vapor phase chromatography showed no isomerization.

A sample of approximately 98% tricyclene was refluxed in 2, 2, 2-trifluoroethanol for 30 min. and isolated by a pentane extract after dilution with an equal quantity of water. Analysis gave 96% tricyclene and 4% camphene.

A sample of 66% tricyclene and 34% camphene (1.5 g.) was dissolved in 11 ml. of 2-methoxyethanol which was 76% O-deuterated and refluxed for 5 min. with stirring. A mixture of mercury and mercuric oxide (2.0 g. each) was introduced and reflux continued for 55 min. After standing without stirring at room temperature for 9 hrs. the inorganic material was removed by filtration and the product isolated by a pentane extraction after dilution with an equal quantity of water. Analysis again showed that no isomerization had taken place. The tricyclene and camphene were separated by vapor phase chromatography for mass spectral analysis.

PART II

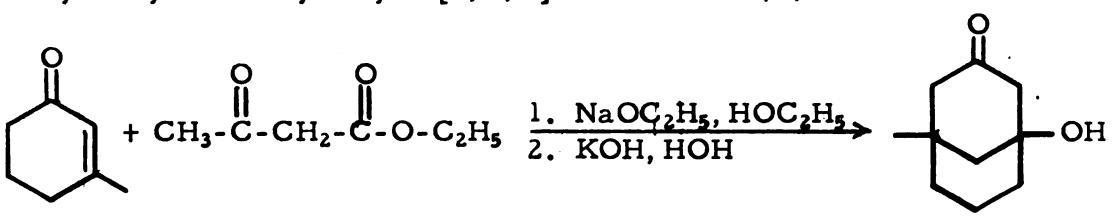
STUDIES IN THE BICYCLO[3,3,1]NONANE SYSTEM

INTRODUCTION

This study was initiated because of the limited amount of work which had been done on the bicyclo[3, 3, 1]nonane system and because the synthesis of clovene, a degradation product of caryophyllene incorporating this system, had not been achieved.

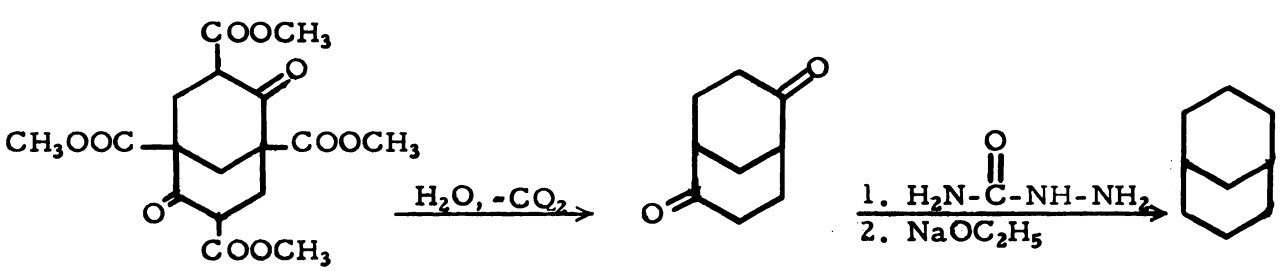
Synthesis of Bicyclo[3, 3, 1]nonane Derivatives

The first synthesis of this ring system is due to Rabe (7) who reported that 3-methylcyclohex-2-ene-1-one (I) and ethyl acetoacetate gave 1-hydroxy-5-methylbicyclo[3, 3, 1]nonan-3-one (II).



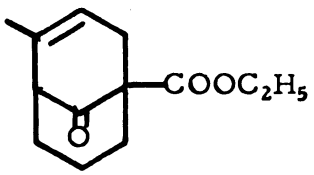
I II

Later, Meerwein (8) synthesized methyl bicyclo[3, 3, 1]nonan-2, 6-dione-1, 3, 5, 7-tetracarboxylate (III) by treating a mixture of methyl malonate and methylene iodide with sodium methoxide; the parent hydrocarbon (IV) was prepared in the manner shown below.

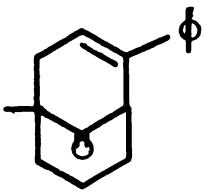


III IV

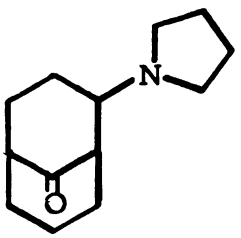
Several years passed before Prelog (9) prepared a 9-keto derivative (V) using an acid catalysed ring closure. Shortly thereafter, Cope (10) prepared several other 9-keto compounds, such as VI, by a similar procedure.



V

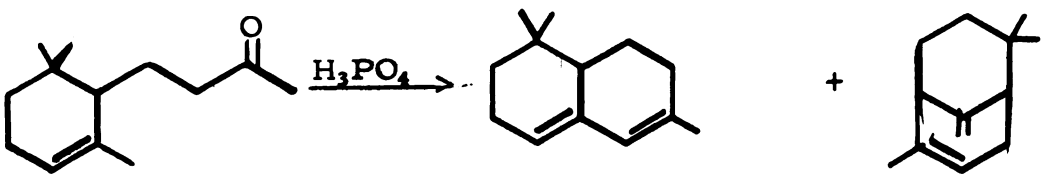


VI



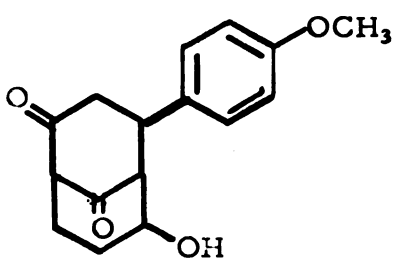
VII

In 1956 Stork (11) used his enamine reaction to prepare VII which he utilized as an entry to the cyclooctane field. In the same year, Buchi (12) reported that the natural product dihydro-α-ionone (VIII) gave the isomeric dienes IX and X when treated with phosphoric acid.

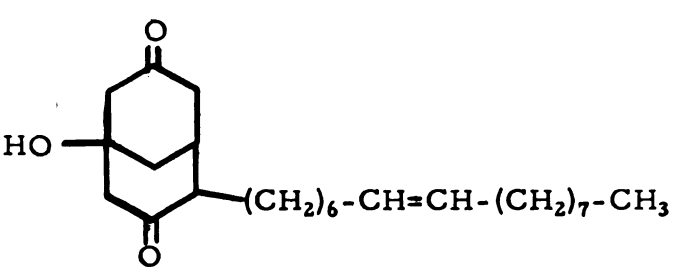


VIII IX X

Papadakis (13) has modified Cope's reaction to give XI, and Dalton (14) converted a product from Tigaso oil into XII by utilizing the Michael reaction to close the second ring.

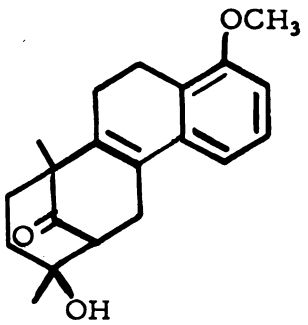


XI

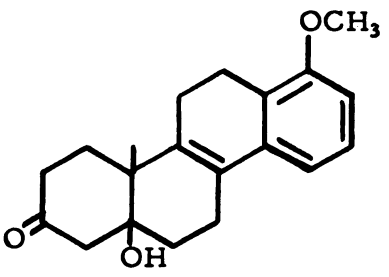


XII

Johnson (15) has shown that some of the intermediate ketols in the Robinson annelation reaction have the bicyclo[3, 3, 1]structure (XIII) rather than structure XIV which had previously been postulated.



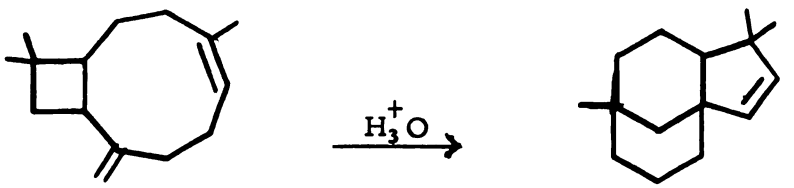
XIII



XIV

Clovene

Clovene (XVI), obtained by treating caryophyllene (XV) with acid, was discovered and named in 1892 by Wallach (16). Although caryophyllene occurs naturally, clovene has never been found in nature,



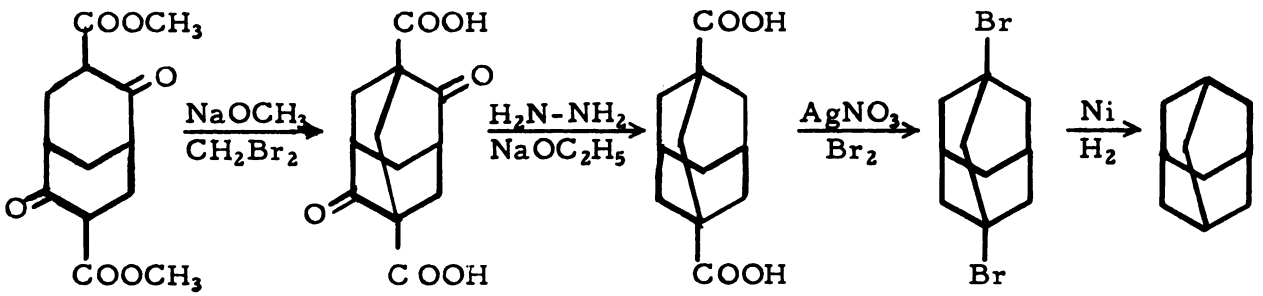
XV XVI

but often arises during the isolation of caryophyllene from natural sources. The structure of both clovene and caryophyllene puzzled investigators for years. Barton (17) and Eschenmoser (18) correctly and independently postulated the structure (XVI) for clovene and further work by Barton (19) led to the proof of this structure.

During the course of this present study, clovene was synthesized by Raphael and co-workers (20).

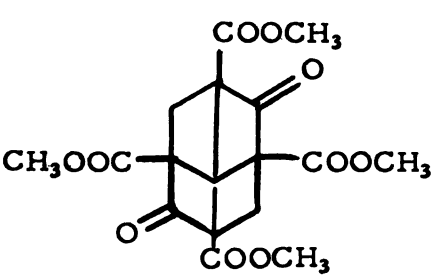
Reactions of Bicyclo[3, 3, 1]nonane Derivatives

The bicyclo[3, 3, 1]nonane skeleton is only one carbon removed from adamantane; this led Prelog (21, 22) to the synthesis of adamantane (XVII) by the following route:

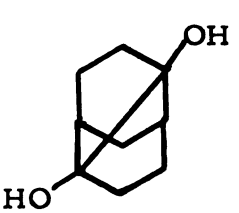


XVII

Meerwein (23) earlier had pointed out the relationship between the bicyclo[3, 3, 1]nonane and adamantane structures; however, he prepared instead a noradamantane derivative-methyl tricyclo[3, 3, 1, $0^{3,7}$]-nonan-2, 6-dione-1, 3, 5, 7-tetracarboxylate (XVIII). In the same paper he also described the first tricyclo[3,3,1,$0^{2,6}$]nonane structure XIX.



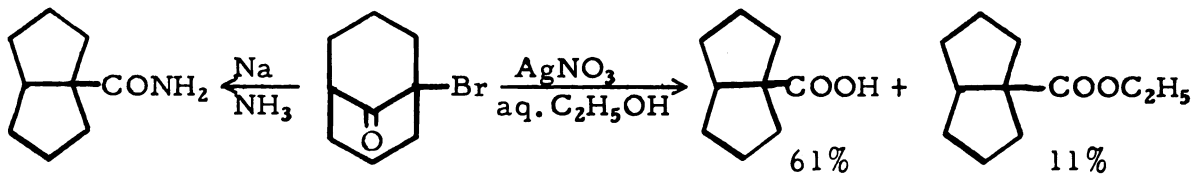
XVIII



XIX

Cope (24, 25) studied 1-bromobicyclo[3, 3, 1]nonan-9-one (XX) and found that this compound was readily converted to 1-derivatives of bicyclo[3, 3, 0]octane. Thus, when the bromide was treated with silver nitrate in 50% ethanol, the acid (XXI) and ethyl ester (XXII) were obtained. The corresponding amide (XXIII) was formed when the bromide was

treated with sodium in liquid ammonia. He was able to reduce this bromide to the parent hydrocarbon.



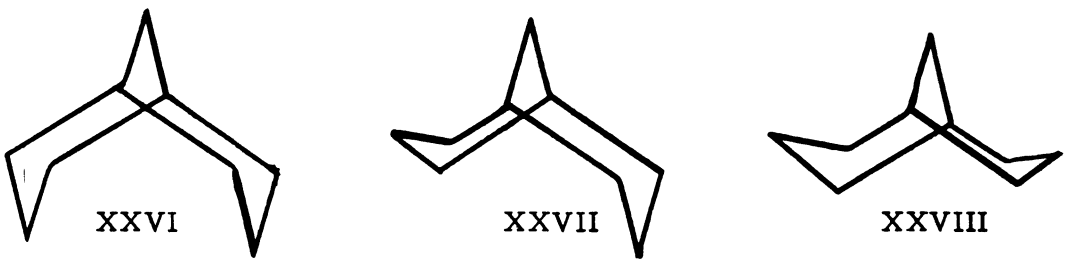
XXIII XX XXI XXII

In a recent study of the solvolyses of the epimeric mesylates of XXIV and XXV, Parker and Martin (26) have found no assistance in XXIV.

XXIV XXV

Conformation of Bicyclo[3, 3, 1]nonane

Bicyclo[3, 3, 1]nonane is limited to three forms (XXVI, XXVII, XXVIII), since the rigidity of the molecule makes the "twist" form of either ring impossible. It is unlikely that XXVIII is very important since this form has hydrogen interactions at C_3-C_9 and C_7-C_9 as well as the eclipsed arrangement along the sides of both boats. Recent studies by Parker (26) and Pumphrey (27) indicate that in the hydrocarbon, form XXVI predominates. Even in the 9-keto derivative, where the C_3-C_9 hydrogen interaction of XXVII is removed, the evidence still leads Parker to choose XXVI over XXVII.



XXVI XXVII XXVIII

DISCUSSION

3-Keto-5-methylbicyclo[3, 3, 1]nonan-1-ol (II) and Its Acetate (XXIX)

The point of departure for this study is Rabe's (7) synthesis of 3-keto-5-methylbicyclo[3, 3, 1]nonan-1-ol (II). This reaction was chosen because if correct it is a one-step synthesis of a bicyclononane structure which possesses the bridgehead methyl group of clovene and suitable functional groups for a possible attachment of the five-membered ring of clovene.

After several unsuccessful attempts to improve the yield of this reaction (see Table 2) by changing the solvent, the method of forming the ethyl acetoacetate anion and the temperature of the reaction, the original procedure of Rabe was utilized as the preparation of II for the balance of this study.

Rabe's structural proof of II was less than conclusive. It consisted largely in the preparation of an acetate derivative (XXIX) and reduction of the alcohol, through a diol (XXX), to a hydrocarbon, presumably 1-methylbicyclo[3, 3, 1]nonane. We found the product of Rabe's reaction to be an approximately equal mixture of II and an unidentified unsaturated keto alcohol which could be separated from II only by a redistillation of the original distillate or by passing this mixture through a vapor phase chromatography column. The solid acetate which Rabe had prepared apparently was the acetate of this impurity, as in our hands the acetate (XXIX) remained liquid below 0°. Since the original conditions for acetate formation were quite severe--i.e., II was refluxed 20 hrs. with acetic anhydride--the acetate was also prepared by reaction of II with acetyl chloride and ketene. All three methods gave a product having

the same vapor phase chromatography retention time and infrared spectrum. Furthermore, the lack of any rearrangements of the bicyclo structure during the preparation of the acetate derivative, such as Cope (24, 25) had observed in the 9-keto series, was demonstrated by the lithium aluminum hydride reduction of the acetate to a diol (XXX) and its oxidation back to II.

The nuclear magnetic resonance spectra of the alcohol and its acetate are shown in Figures 1 and 2 (pages 22 and 23). The peak at highest field occurring at 8.94 τ in the alcohol and 8.93 τ in the acetate is due to the methyl at C-5. The hydrogens on carbons 6, 7, 8 and 9 form an unresolved multiplet extending from about 7.7 τ to 8.9 τ in both spectra with the largest peak occurring at 8.6 τ. In the alcohol this portion of the spectrum integrates for 10 hydrogens and includes the singlet assigned to the pair of hydrogens on C-4 which is found at 7.92 τ in the alcohol and 7.84 τ in the acetate. The pair of hydrogens on C-2 should occur down field from those at C-4 due to the effect of the oxygen atom at C-1. The singlets at 7.62 τ in the alcohol and 7.20 τ in the acetate are assigned to these C-2 hydrogens and both peaks integrate for two hydrogens. The broad band at 6.35 τ in the alcohol is assigned to the alcoholic hydrogen and integrates for 0.95 proton. The sharp singlet at 8.04 τ in the acetate spectrum is assigned to the methyl of the acetate group due to its position in the spectrum; however, because of its position, it could not be integrated accurately.

The infrared spectrum of the alcohol (Figure 3, page 24) has bands at 2.96μ, 8.85μ and 7.51μ which can be assigned to the O-H stretch, tertiary O-H deformation and tertiary C-O stretch respectively. The absorption at 5.90μ is assigned to the carbonyl group and the absorption at 3.45μ to the C-H stretch. A strong band at 6.87μ is assigned to the methyl group at C-5. The infrared spectrum of the acetate (Figure 4, page 25) exhibited a C-H stretch at 3.45μ and the methyl deformation at

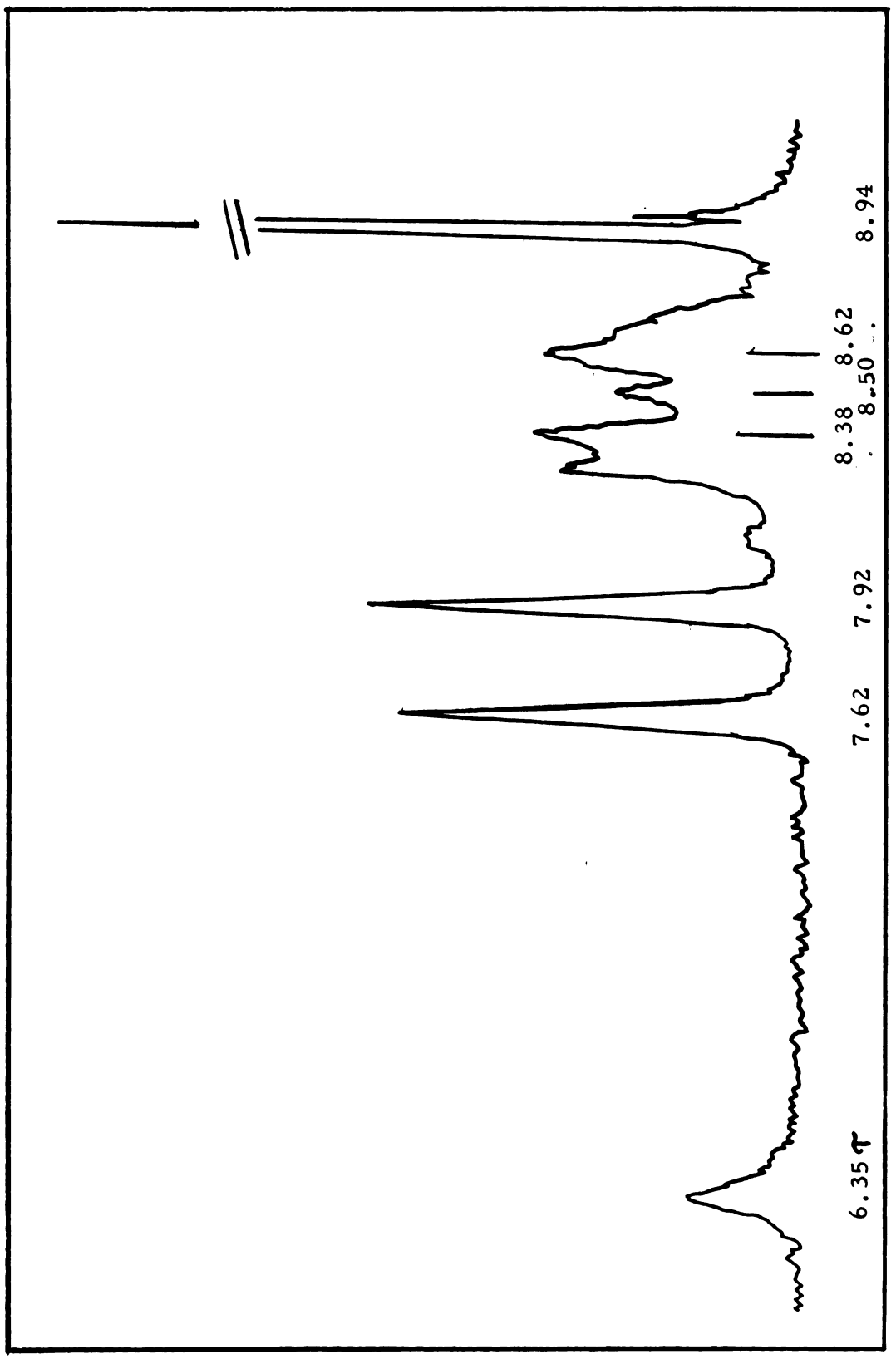


Figure 1. Nuclear magnetic resonance spectrum of 3-keto-5-methylbicyclo[3, 3, 1]nonan-1-ol (II).

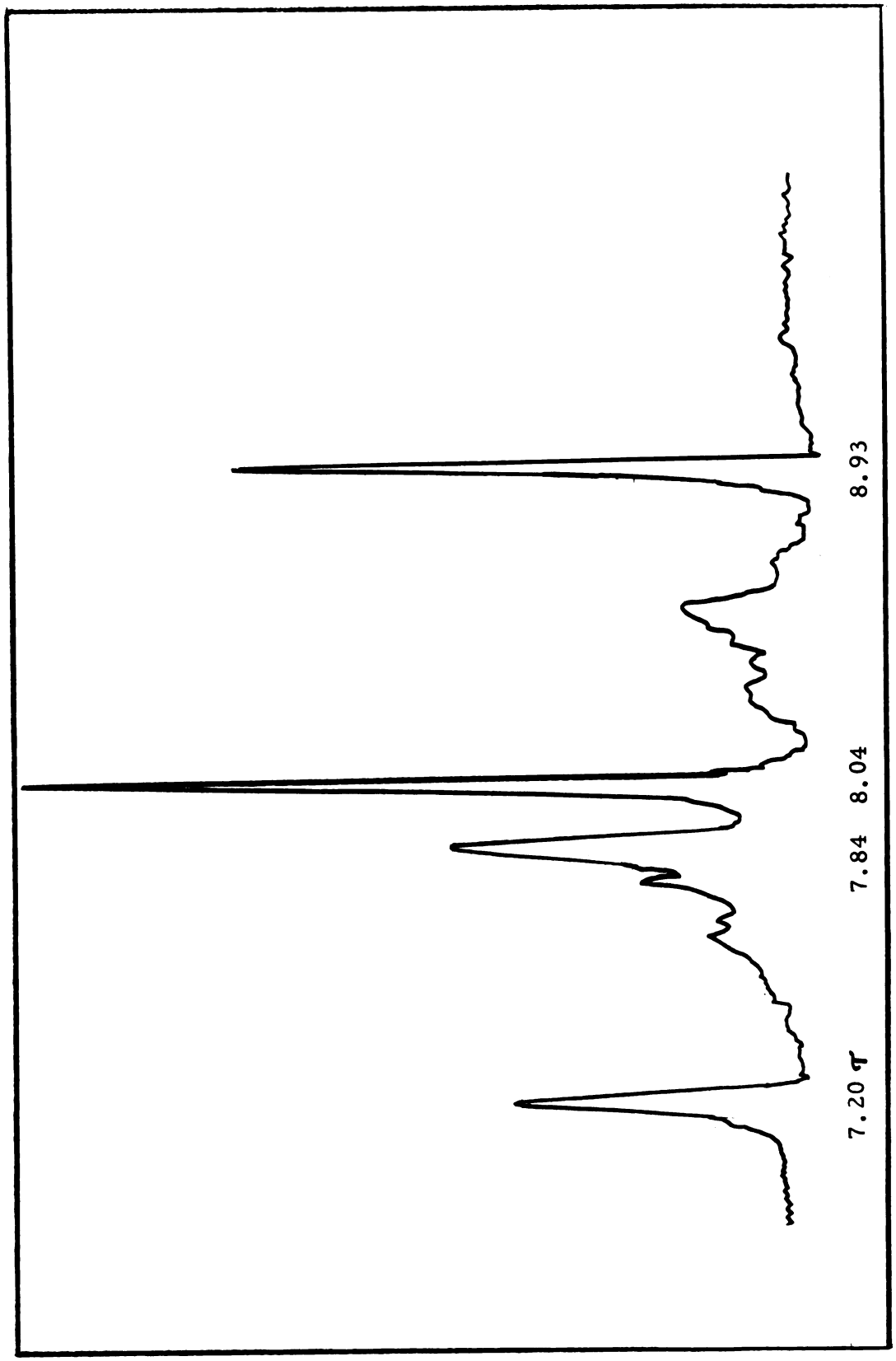


Figure 2. Nuclear magnetic resonance spectrum of 3-keto-5-methylbicyclo[3, 3, 1]nonan-1-yl acetate (XXIX).

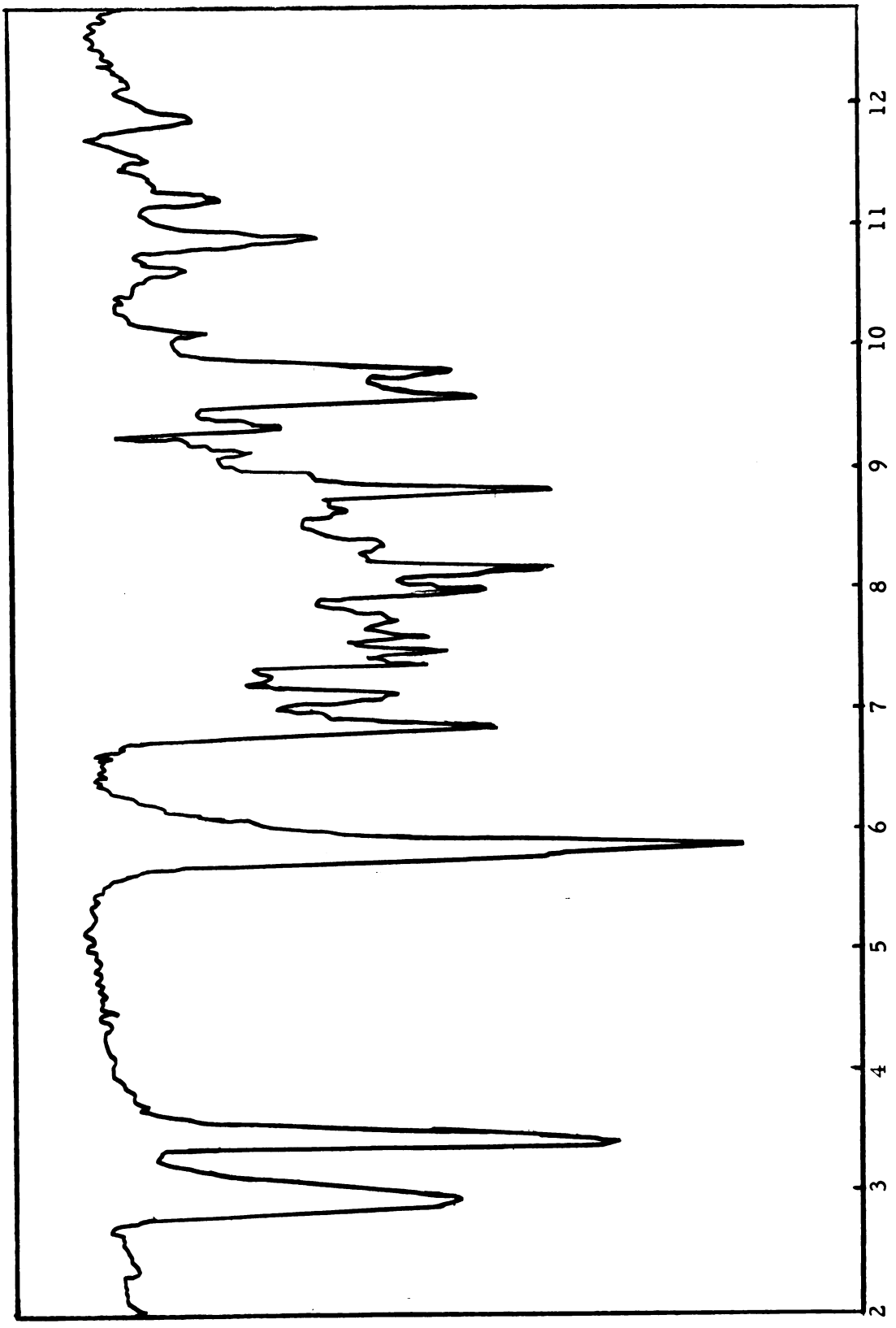


Figure 3. Infrared spectrum of 3-keto-5-methylbicyclo[3, 3, 1]nonan-1-ol(II) (neat).

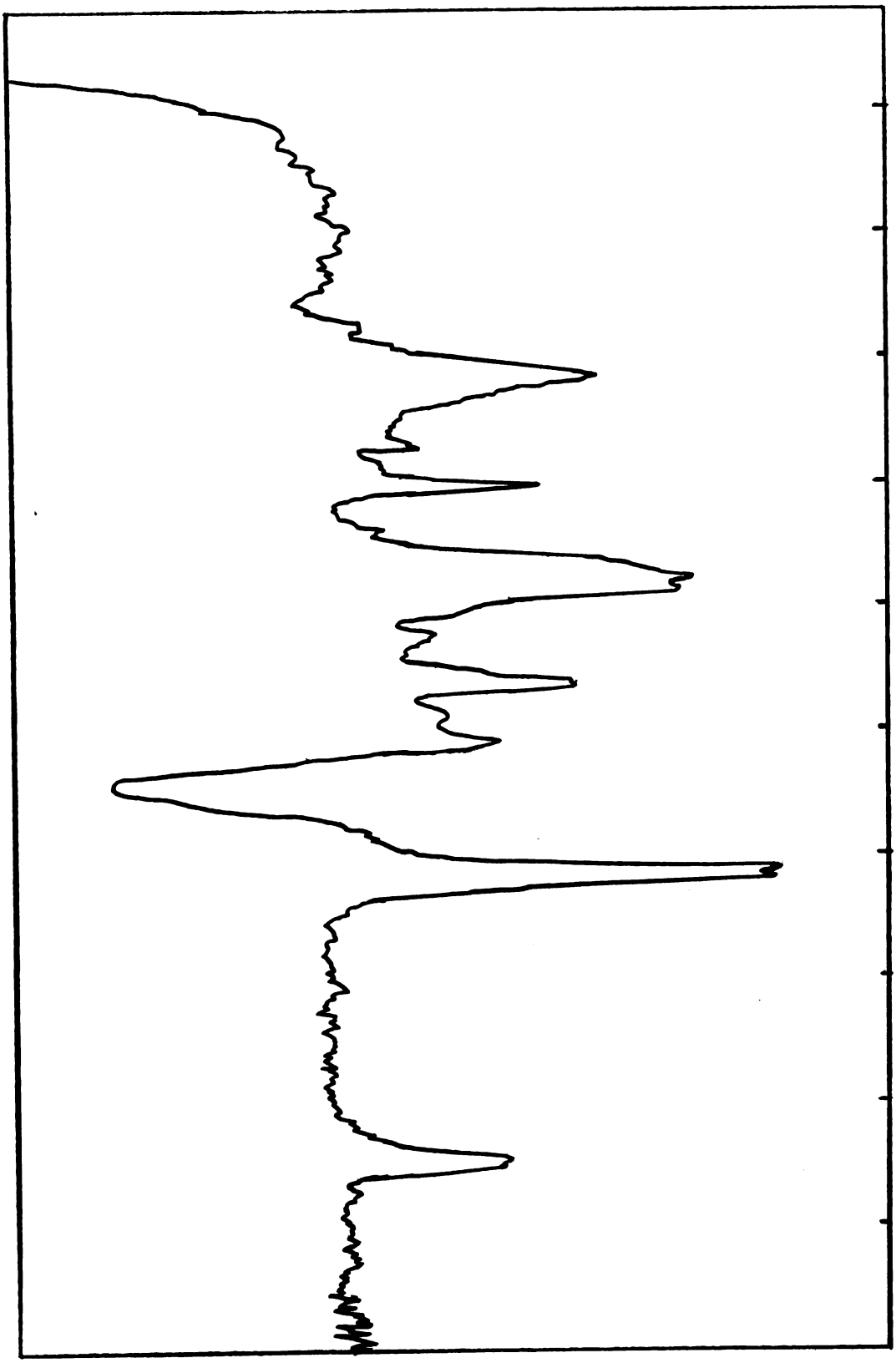


Figure 4. Infrared spectrum of 3-keto-5-methylbicyclo[3, 3, 1]nonan-1-yl acetate (XXIX) (CCl_4).

6.91μ. It differed from the alcohol in that the carbonyl region contained a doublet at 5.84μ and 5.89μ which is assigned to the ester and ketone. Another band at 8.15μ is assigned to the C-O stretch of the ester group.

To complete the spectroscopic data a mass spectrum of the keto-alcohol was taken. The values of all of the large peaks down to mass 80, where the solvent benzene masks the spectrum, are recorded in Table 1 on page 27. A plausible mode of decomposition of this compound in the mass spectrometer follows in Figure 5 (page 27).

The structure of Rabe's alcohol rests upon a firmer foundation after the reaction sequence and spectral data presented above. However, we are forced to the conclusion that the acetate derivative which he prepared was not the acetate XXIX.

Synthetic Approach to Clovene (XVI).

The bicyclic keto-alcohol II contains two of the three rings of clovene. A synthetic approach to clovene is given in Figure 6 (page 28). Esterification of this alcohol with 3-methyl-2-butenoyl chloride to give XXXI was to have been followed by a cyclization reaction. Although this was attempted several times (see experimental), it was never successful. The carbanion of the product would have been less stable than the carbanion of the starting ester and this may be the underlying reason for the failure of the reactions catalyzed by base. The steric hinderance of the gem-dimethyl group undoubtedly helped to account for these failures.

The synthesis of the diester XXXII resulted in a compound which would give rise to a product, XXXIII, possessing a more acidic proton than the starting compound. When this reaction was run using sodium hydride, a small amount of this material was isolated by distillation. The nuclear magnetic resonance spectrum indicated that this was the expected product. In the ultraviolet spectrum the extinction coefficient of the unsaturated ester absorption was much lower; however, this could

Table 1. Partial Mass Spectrum of 3-Keto-5-methylbicyclo[3, 3, 1] nonan-1-ol (II)[a]

Mass Number	Intensity	Percent Isotope Peak	Theoretical Percent Isotope Peak	Formula
111	1,164	--	--	$C_7H_{11}O$
112	90.7	7.8 of 111	7.78	--
125	355	--	--	$C_8H_{13}O$
126	31.6	8.9 of 125	8.89	--
153	24.7	--	--	$C_9H_{13}O_2$
168	42.3	--	--	$C_{10}H_{16}O_2$
169	4.9	11.6 of 168	11.14	--

[a]Mass spectrum was taken on a Consolidated Electrodynamics Corporation spectrometer, Type 21-103C at an ionizing voltage of 70 volts.

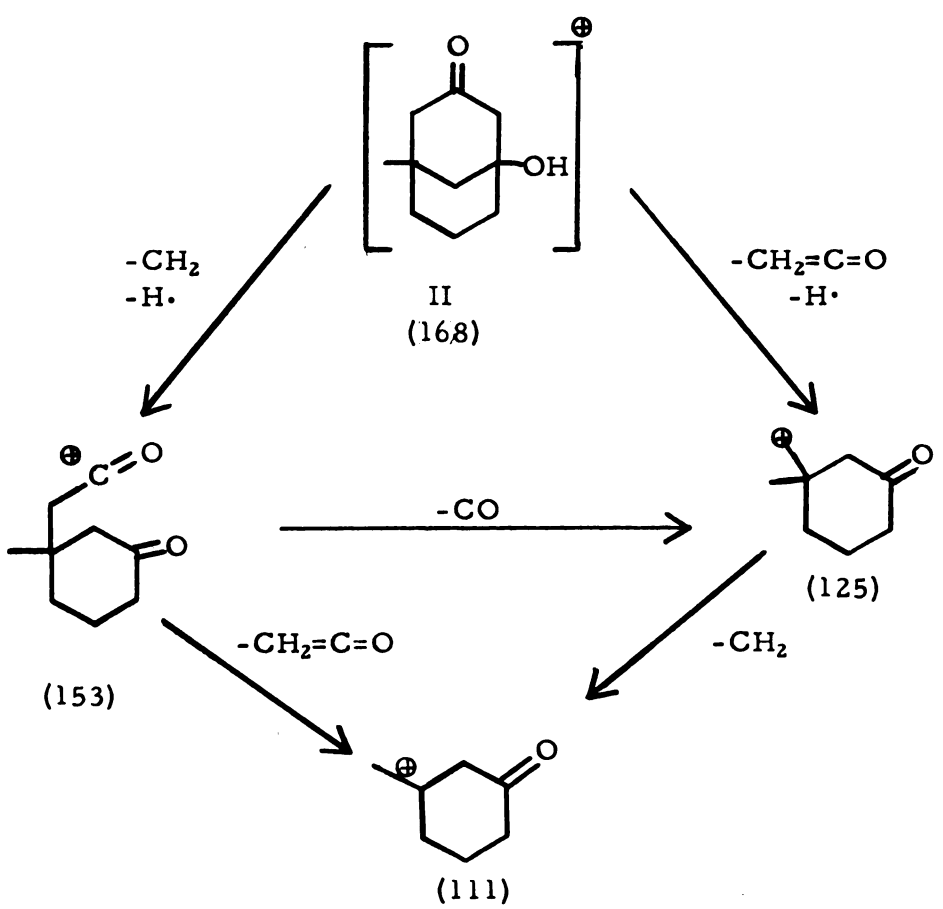


Figure 5. Possible mode of decomposition of II.

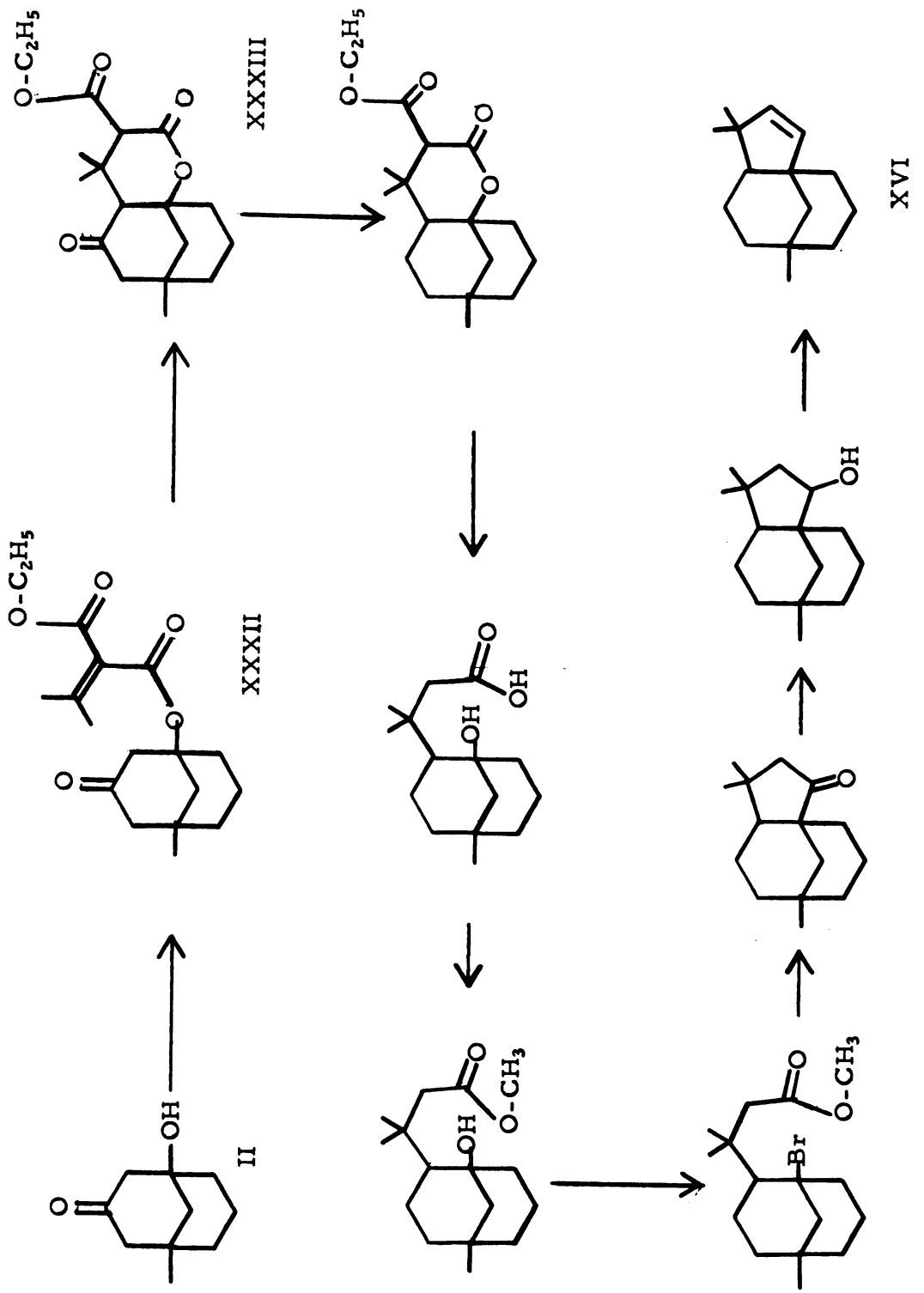


Figure 6. Synthetic approach to clovene (XVI).

arise from the hydrolysis of the ester as well as cyclization. The infrared spectrum of this solid did not show the C=C stretch which was visible in the starting ester. Although the cyclized compound, XXXIII was not adequately characterized, it seems quite likely that the compound was indeed prepared. Work on this phase of the study was discontinued at this point, partly as a consequence of the progress reported by Raphael's group in Glasgow.

The characterization of esters XXXI and XXXII was entirely spectroscopic in nature. The nuclear magnetic resonance spectra of both esters (Figures 7 and 8, page 30 and 31) had the same absorption for the C-5 methyl, C-2 and C-4 hydrogens and the multiplet for the protons on carbons 6, 7, 8 and 9 as the parent alcohol and its acetate. In addition ester XXXI had absorptions at 4.46 τ (1 hydrogen), 7.90 τ and 8.15 τ. The first absorption is in the range of vinyl protons while the latter two absorptions were assigned to the two vinyl methyl groups. The vinyl proton was split into a multiplet with a splitting of 1.25 c.p.s. and each methyl peak was split into a doublet, also with a 1.25 c.p.s. splitting. The integration of the methyls was impossible as the first coincided with the C-4 hydrogens and the second fell in the range of the hydrogens on carbons 6, 7, 8 and 9. Ester XXXII showed a quartet at 5.90 τ and a triplet at 8.75 τ which were each split by 7.5 c.p.s. These signals undoubtedly arise from the ethyl group. A doublet at 8.00 τ and 8.01 τ was assigned to the two vinyl methyls which lie in slightly different orientations and thus show resonance at different fields.

The infrared spectrum of ester XXXI (Figure 9, page 32) had absorptions at 3.47μ (C-H stretch), 5.90μ (C=O stretch), 6.10μ (C=C stretch), 6.95μ (CH_3 deformation), a doublet at 7.50μ and 7.44μ (gem-dimethyl), 8.23μ (C-O ester stretch) and 11.80μ (vinyl C-H deformation). The carbonyl absorption was not resolved into a doublet as in the spectrum

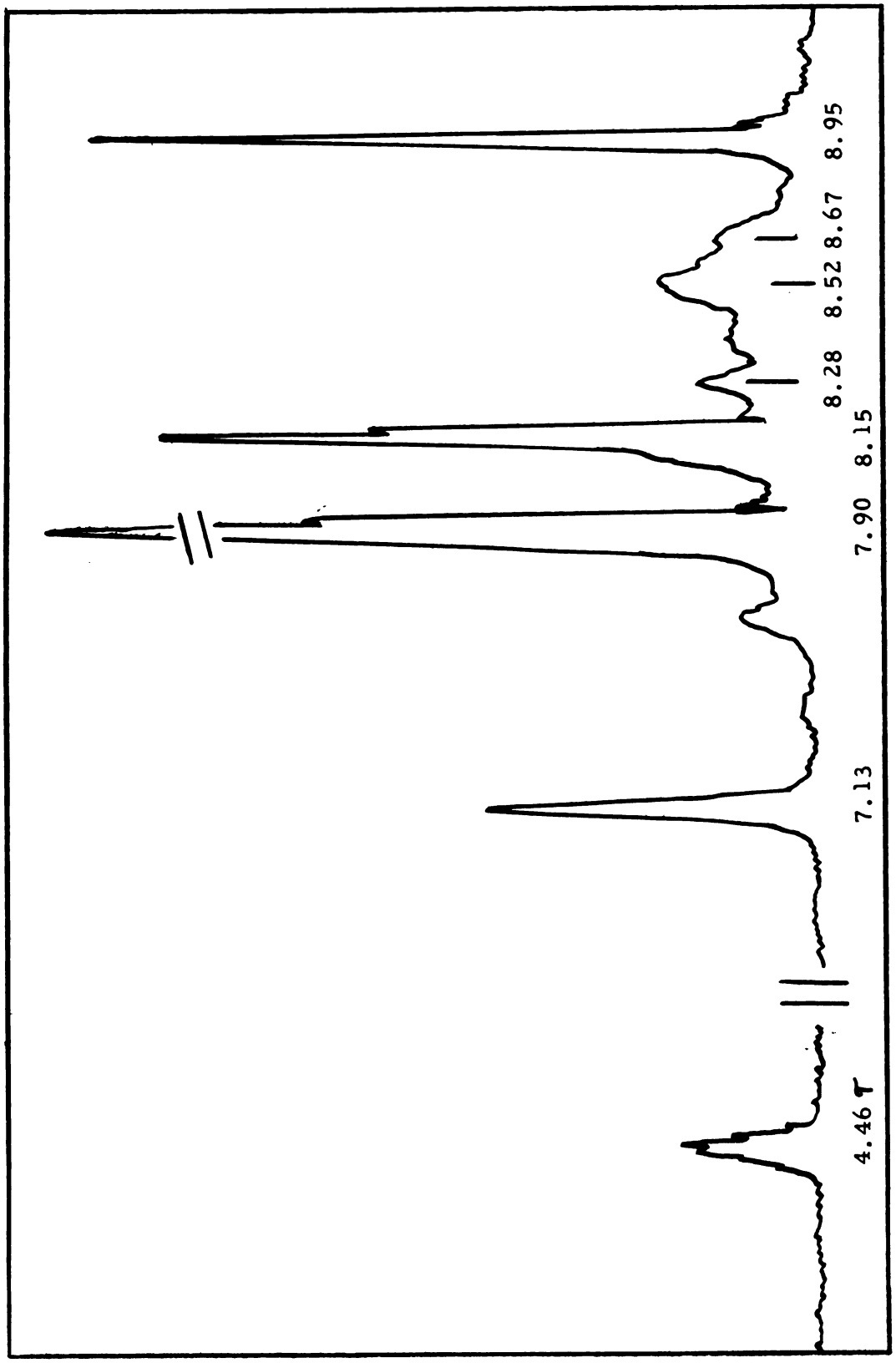


Figure 7. Nuclear magnetic resonance spectrum of 3-keto-5-methylbicyclo[3, 3, 1]nonan-1-yl 3-methyl-2-butenoate (XXXI).

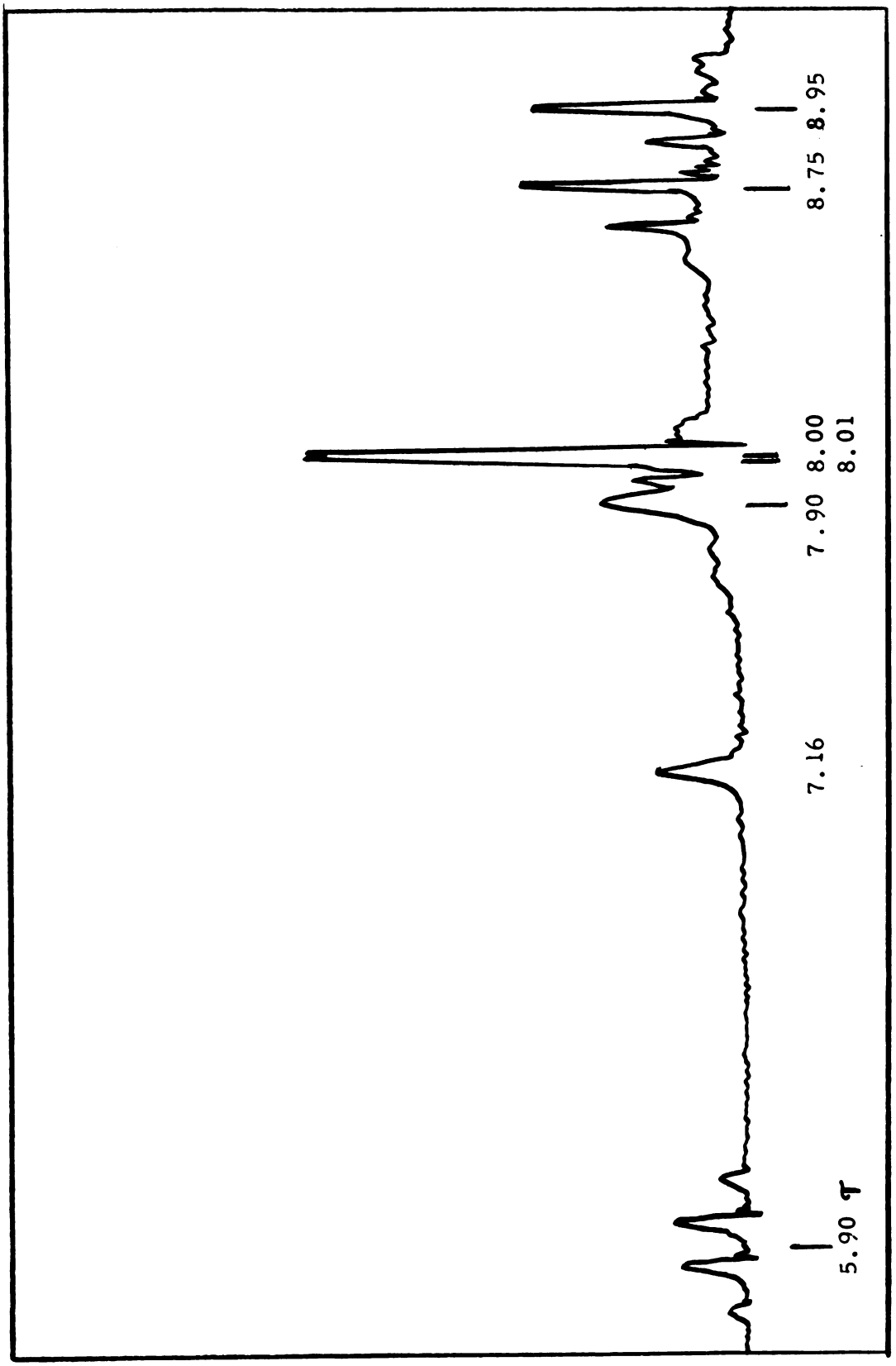


Figure 8. Nuclear magnetic resonance spectrum of ethyl 3-keto-5-methylbicyclo[3,3,1]nonan-1-yl isopropylidenemalonate (XXXII).

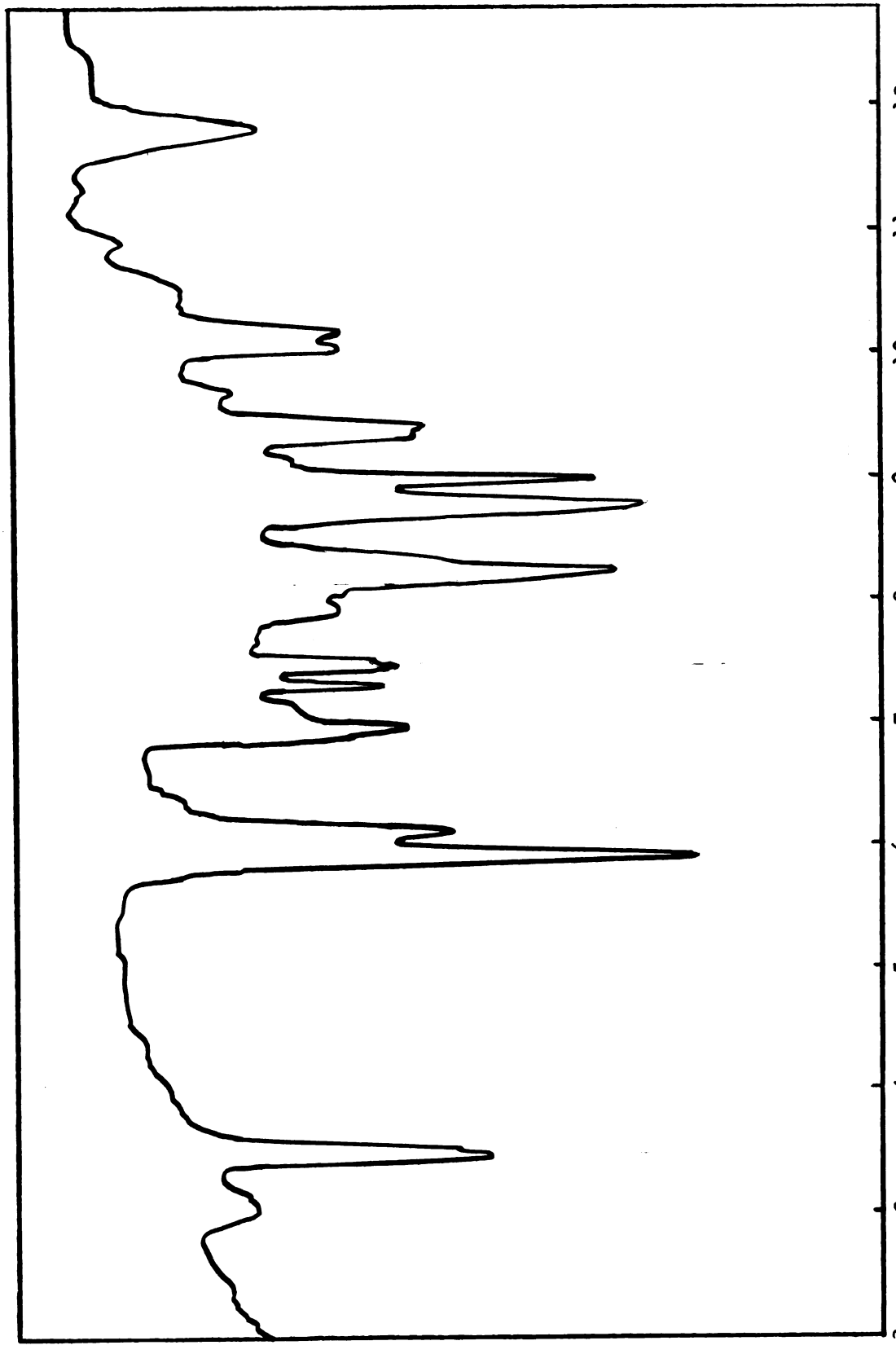


Figure 9. Infrared spectrum of 3-keto-5-methylbicyclo[3, 3, 1]nonan-1-yl 3-methyl-2-butenoate (XXXI) (neat).

of the acetate; however, this is consistent with the shift of the ester carbonyl to longer wavelengths as a result of its unsaturated character. The infrared spectrum of the second ester, XXXII (Figure 10, page 34), had absorptions at 3.45μ (C-H stretch), 5.87μ (C=O stretch), 6.13μ (C=C stretch), 6.93μ (CH_3 deformation), 7.32μ (gem-dimethyl--unresolved in this spectrum) and 8.06μ (C-O ester stretch). The weakness of the 6.13μ band and the absence of a vinyl C-H deformation are consistent with a tetrasubstituted carbon-carbon double bond.

Characterization and Reactions of 1-Bromo-5-methylbicyclo[3, 3, 1]nonan-3-one (XXXIV)

The bromide, XXXIV, was easily prepared from the corresponding alcohol using phosphorus tribromide. This compound was characterized by its elemental analysis (page 51), nuclear magnetic resonance spectrum (Figure 11, page 35) and infrared spectrum (Figure 12, page 36). The nuclear magnetic resonance spectrum of XXXIV is quite similar to the spectrum of the alcohol except for the shift of some of the bands to lower fields. The C-5 methyl occurs at 8.85 τ as compared to 8.94 τ in the alcohol. The pair of hydrogens on C-2 and C-4 are found at 7.08 τ and 7.86 τ (7.62 τ and 7.92 τ in the alcohol). The C-2 hydrogens underwent the greatest shift, as expected, since they are in closer promixity to the bromide. The effect of the bromine atom, relative to an oxygen, is also noticed in the pattern of hydrogens on carbons 6, 7, 8 and 9. In this spectrum this group is split into two parts of four protons each. The group at higher fields has peaks at 8.50 τ and 8.63 τ exactly the same as in the spectrum of the alcohol; however, the other four protons have moved down field to the pair of hydrogens on C-4 and interfer with the integration of this peak. The integration of this spectrum shows two protons at 7.08 τ , six in the 7.73 τ and 7.86 τ region, four in the region around 8.50 τ and three at 8.85 τ. .

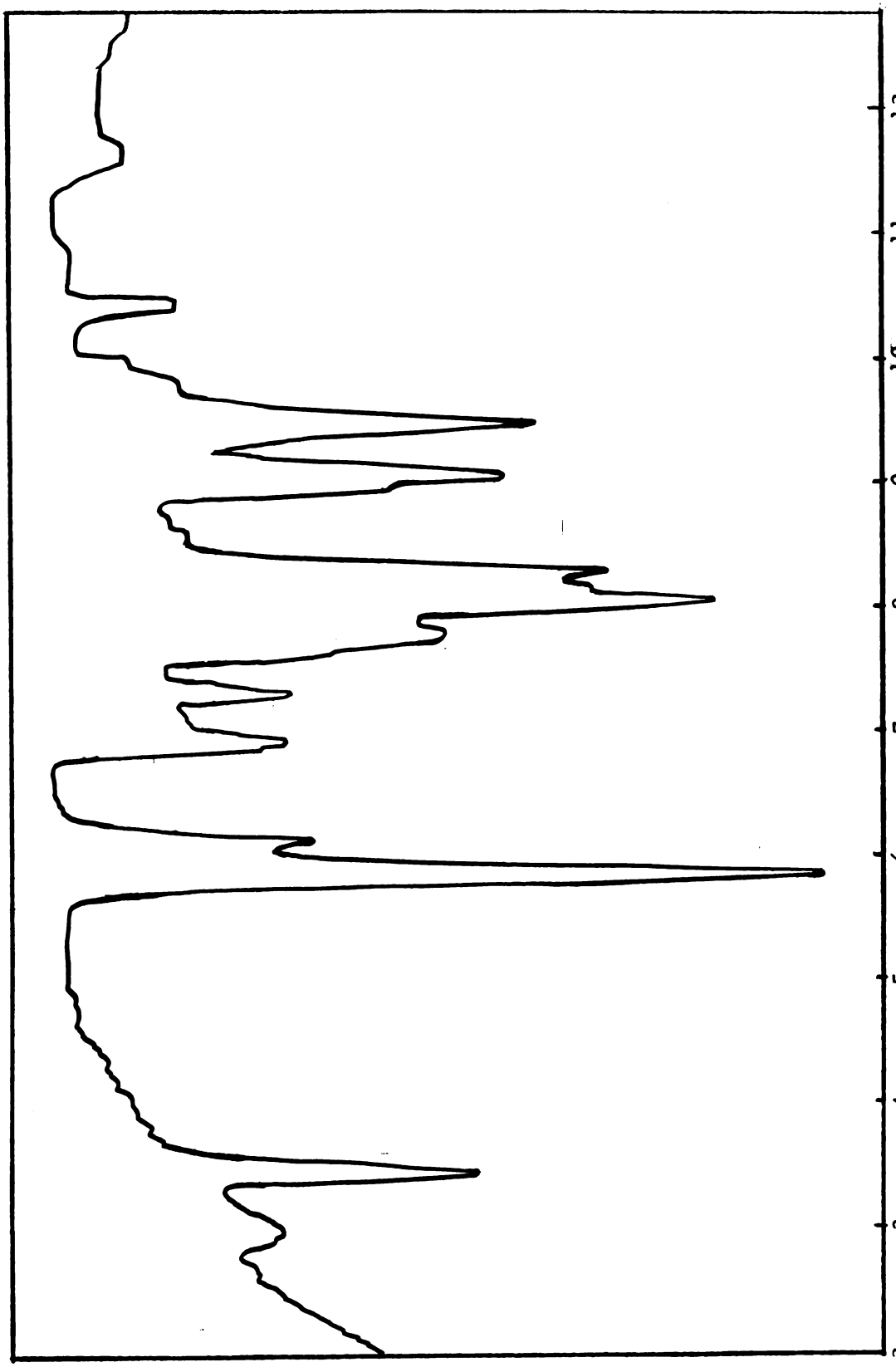


Figure 10. Infrared spectrum of ethyl 3-keto-5-methylbicyclo[3, 3, 1]nonan-1-yl isopropylidene-malonate (XXXII) (neat).

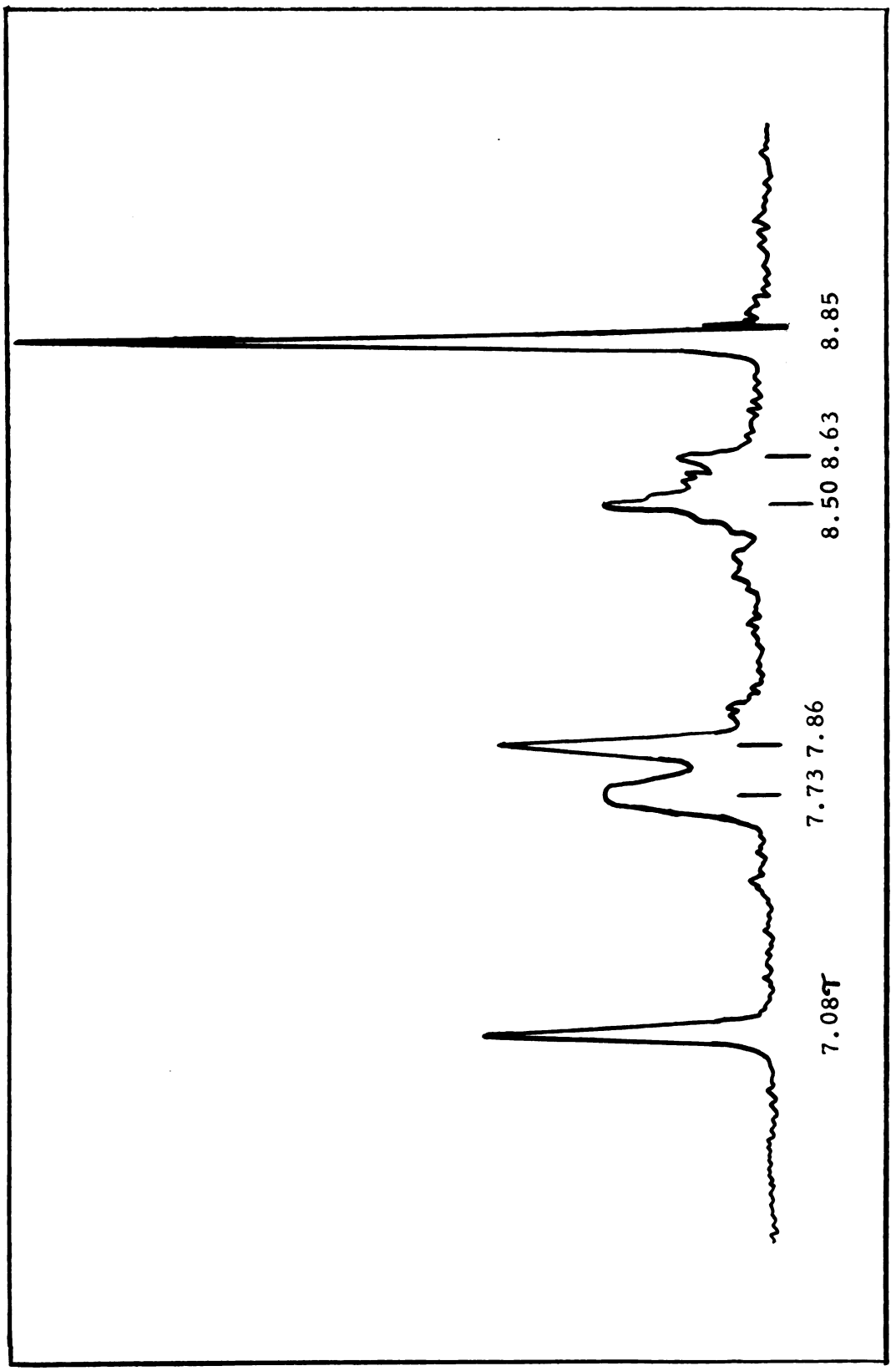


Figure 11. Nuclear magnetic resonance spectrum of 1-bromo-5-methylbicyclo[3, 3, 1]nonan-3-one (XXXIV).

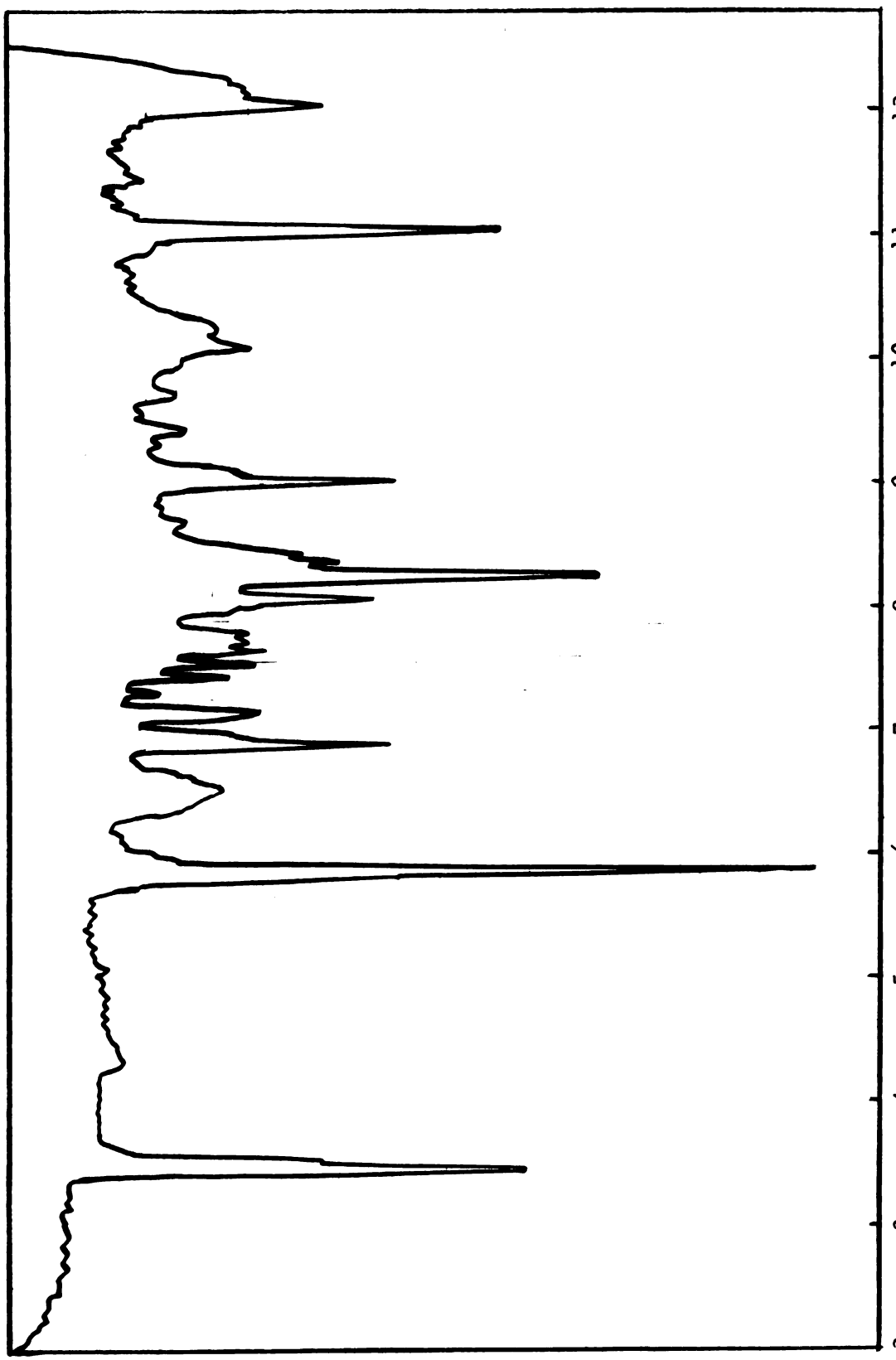


Figure 12. Infrared spectrum of 1-bromo-5-methylbicyclo[3, 3, 1]nonan-3-one (XXXIV). (CCl_4).

The infrared spectrum of this bromide has the usual C-H stretch band at 3.44μ and the carbonyl stretch at 5.87μ. A weaker band at 6.87μ may be assigned to the CH_3 deformation. Other prominent bands occurring at 8.24μ, 9.00μ and 11.00μ find counterparts in the spectrum of the alcohol.

This bromide was of interest because of the location of the bromine at a bridgehead. Many earlier studies of the reactivity of bridgehead halides have been summarized by Applequist and Roberts (27) and Schöllkopf (28). The difficulty in causing displacement reactions to occur at bridgeheads has been attributed to the fact that inversion mechanisms are impossible and carbonium ions prefer a planar configuration which is difficult or impossible to achieve at many commonly encountered bridgeheads. Few studies, however, have been made of systems which have as much flexibility as the 3, 3, 1-system. The reactions of 9-keto derivatives of this system which Cope (24, 25) has studied occurred by rearrangement.

The bromine was removed in a dimethyl sulfoxide-water mixture by silver perchlorate only after refluxing. The product was demonstrated to be the unrearranged alcohol by vapor phase chromotography retention time and infrared spectrum. When the solvent mixture was replaced by anhydrous methanol, an immediate precipitate of silver bromide was observed although several hours at room temperature or above was necessary to complete the reaction. When the reaction was allowed to proceed to completion almost quantitative yields of silver bromide were realized.

Tertiary halides in general are quite easily solvolyzed; however, silver ion and 1-bromonorbornane is unreactive even when treated with silver ion under forcing conditions for extended periods of time. Carbonium ions may be formed at this position only through the diazotizations of the 1-amino compound. In the 2, 2, 2-system the results are

almost the same. By contrast the immediate precipitate from XXXIV and silver perchlorate in methanol seems somewhat surprising. However, the 3, 3, 1-bicyclononane system is essentially a strainless system in contrast to the smaller bicyclic compounds which are quite strained. While the strain involved in forming a bridgehead carbonium ion is prohibitive in the 2, 2, 1- and 2, 2, 2-systems, this strain can be accepted in the 3, 3, 1-system. 1-Adamantyl bromide, which incorporates the 3, 3, 1-nonane structure, is even more reactive although it still is less reactive than t-butyl bromide.

When the solvent was changed to liquid ammonia in an unsuccessful attempt to prepare the 1-amino derivative the reaction with silver perchlorate did not proceed as well. This could be due to the lower temperature but also may be attributed to solubility problems and the possibility that the amine, like the alcohol, is unstable to base. Two acid insoluble products, as well as recovered starting material, were formed in this reaction.

Characterization of 1-Methoxy-5-methylbicyclo-[3, 3, 1]nonan-3-one (XXXV)

The methyl ether, XXXV, was characterized by an elemental analysis (page 52), nuclear magnetic resonance spectrum (Figure 13, page 39) and infrared spectrum (Figure 14, page 40).

The nuclear magnetic resonance spectrum had the same three singlets that all of the bicyclononane derivatives exhibited--the C-5 methyl at 9.03 τ , C-4 protons at 8.48 τ and the C-2 protons at 7.86 τ. In addition to theses, there was a sharp singlet at 8.68 τ which was assigned to the ether methyl. The integration of the C-4 hydrogens, methoxy methyl and the hydrogens on carbons 6, 7, 8 and 9 gave 13 hydrogens relative to either the C-5 methyl or the pair of hydrogens on C-2.

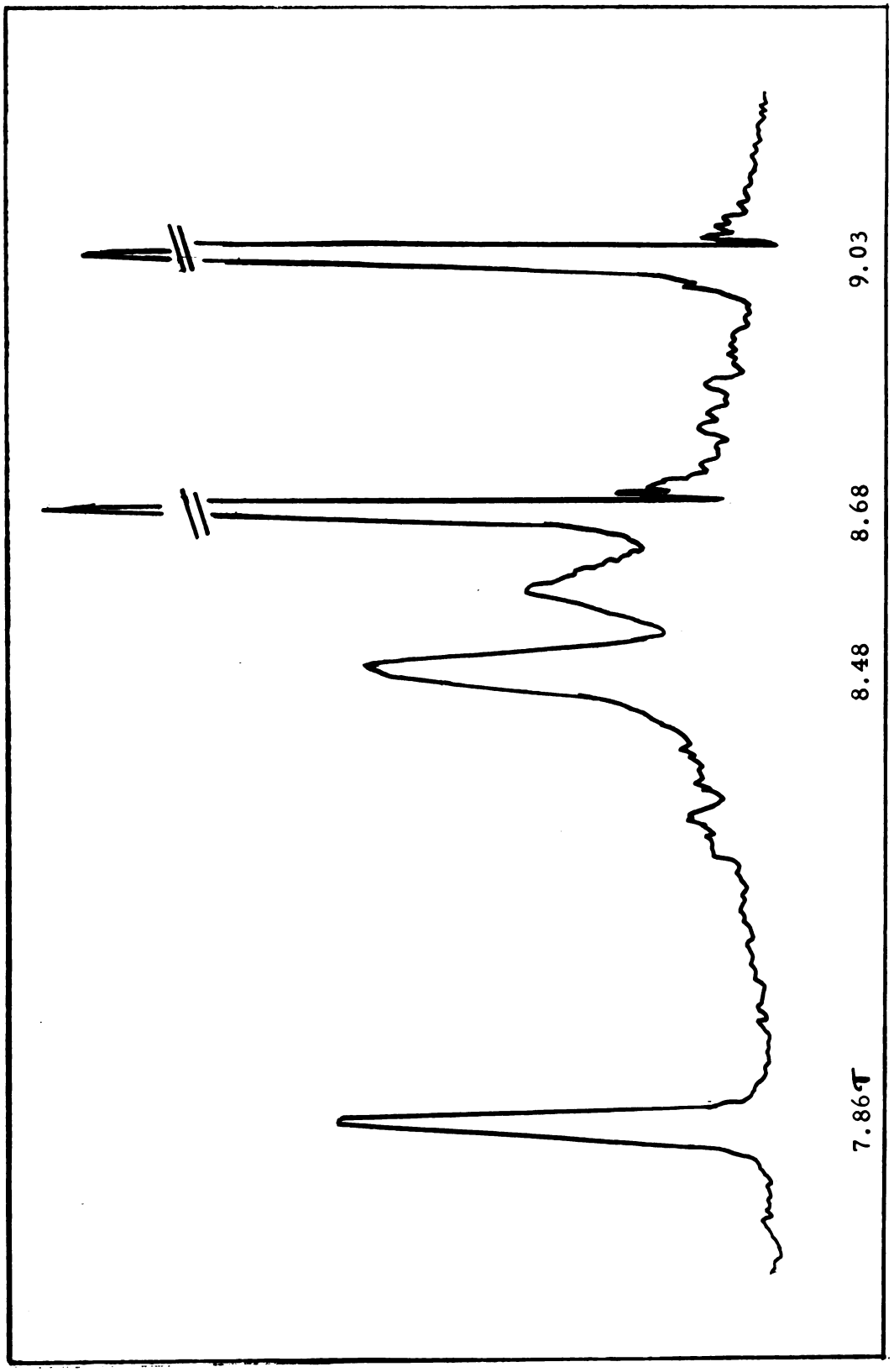


Figure 13. Nuclear magnetic resonance spectrum of 1-methoxy-5-methylbicyclo[3, 3, 1]nonan-3-one (XXXV).

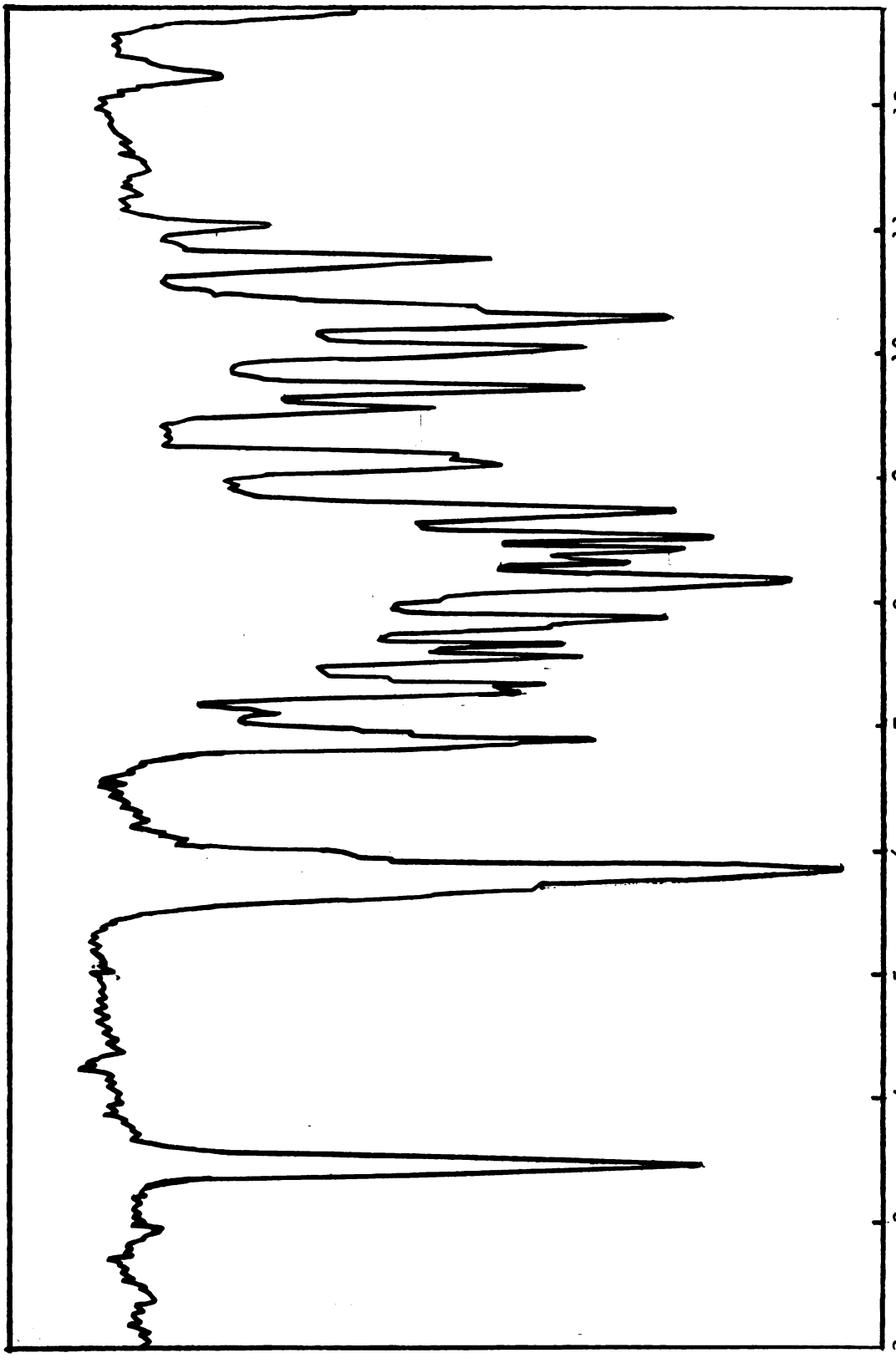


Figure 14. Infrared spectrum of 1-methoxy-5-methylbicyclo[3, 3, 1]nonan-3-one (XXXV)(neat).

The infrared spectrum of this compound showed a large number of sharp bands. The C-H stretch at 3.46μ, the carbonyl stretch at 5.85μ and the CH_3 deformation at 6.84μ are common to all of the compounds in this series. A very strong band at 8.15μ probably is due to the C-O stretch of the ether.

An attempt to cleave this ether with aluminum tribromide and hydrogen bromide in glacial acetic acid gave a 72% recovery of the starting ether after distillation.

The reactions of the bicyclo-nonane systems are summarized in Figure 15 (page 42).

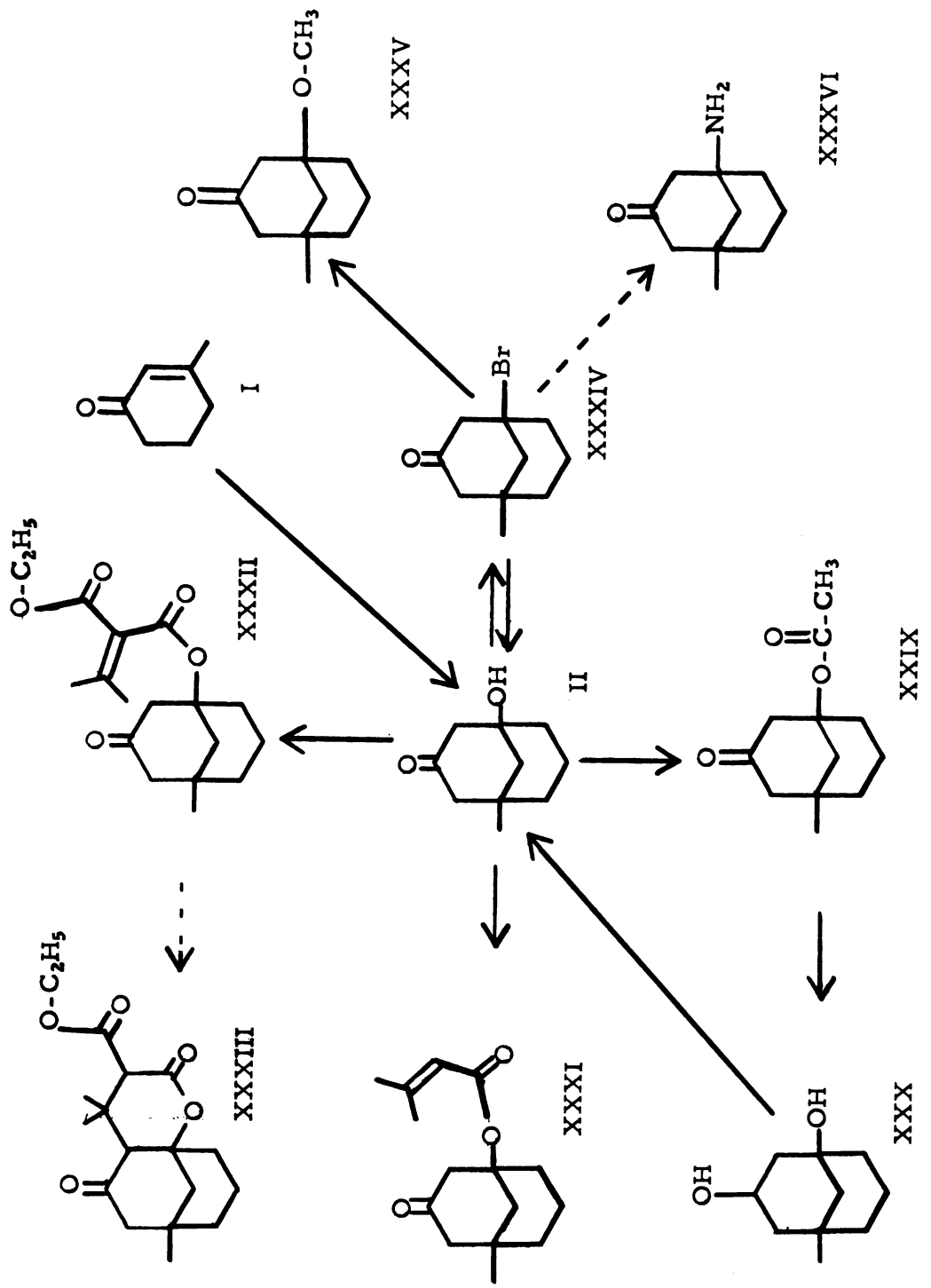


Figure 15. Reactions of the bicyclo[3, 3, 1]nonane system.

EXPERIMENTAL

Melting points were determined on a Kofler hot stage. The infrared spectra were recorded on a Perken-Elmer, Model 21, spectrophotometer, and the ultraviolet spectra were taken with a Cary, Model 11, spectrophotometer. The nuclear magnetic resonance spectra were determined in carbon tetrachloride solution using a Varian Associates, A-60, high resolution spectrometer. Vapor phase chromatography analyses were made using an Aerograph, A-90-P, gas chromatograph with a 0.25-in., 5-ft. column of S.E. 30 on chromosorb W. Microanalyses were performed by Spang Microanalytical Laboratory, Ann Arbor, Michigan, and Clark Microanalytical Laboratory, Urbana, Illinois.

3-Keto-5-methylbicyclo[3,3,1]nonan-1-ol (II)

To a solution of 23 g. (1.0 mole) of sodium in 1 l. of absolute ethanol, 260 g. (2.0 moles) of ethyl acetoacetate was added. To this refluxing mixture 110 g. (1.0 mole) of 3-methylcyclohex-2-en-1-one was added dropwise. After 48 hr. a solution of 56 g. (1.0 mole) of potassium hydroxide in 270 ml. of water was added and reflux continued for an additional 18 hr. After the ethanol was removed by distillation, the product was taken up in ether, dried and distilled, b.p. 123-138^{o} at 2 mm. A second distillation was usually necessary to secure a pure product. Table 2 (page 44) gives a summary of the reaction yields under different conditions. N.m.r. spectrum is shown in Figure 1 (page 22) and the infrared spectrum in Figure 3 (page 24).

Table 2. Preparation of 3-Keto-5-methylbicyclo[3, 3, 1]nonan-1-ol (II)

	I Mole	Ethyl Acetoacetate Mole	Base (Mole)	Solvent (Ml.)	Reaction Time	Reaction Temp.	Yield[a] Percent
1.	1.00	2.00	Sodium (1.00)	Ethanol (1000)	48 hr.	78°	26
2.	0.20	0.30	Sodium (0.30)	Ethanol (100)[b] Benzene (300)	48 hr.	80°	--
3.	0.20	0.40	Potassium Hydroxide (0.25)	95% Ethanol (280)[c]	48 hr.	78°	--
4.	0.20	0.30	Sodium (0.30)	Ethanol-Benzene (300)[b] Dimethylformamide (200)	48 hr.	95°	10
5.	0.20	0.40	Piperidine (0.040)	--	48 hr.	95°	2.4
6.	0.15	0.40	Sodium (0.20)	n-Butanol (200)	48 hr.	100°	11
7.	0.15	0.40	Sodium (0.20)	n-Butanol (200)	72 hr.	27°	--
8.	1.00	5.00	Sodium (5.00)	Ethanol (1500)	48 hr.	78°	--

[a]Yield based upon I consumed.

[b]Anion of ethyl acetoacetate preformed by removal of ethanol-benzene azetrope.

[c]Second part of this synthesis omitted.

3-Keto-5-methylbicyclo[3, 3, 1]nonan-1-yl Acetate (XXIX)

Procedure I. A mixture of 5.0 g. (0.030 mole) of 3-keto-5-methylbicyclo[3, 3, 1]nonan-1-ol and 10 ml. (10 g., 0.10 mole) of acetic anhydride was refluxed for 20 hr. After removal of the volatile products by distillation, the product was distilled under reduced pressure to give 4.0 g. (73%) of product, b.p. 106° at 0.23 mm.

Procedure II. Acetyl chloride (2.4 g., 0.030 mole) was added slowly to 5.0 g. (0.030 mole) of 3-keto-5-methylbicyclo[3, 3, 1]nonan-1-ol and the mixture warmed on a steam bath for 1 hr. After standing overnight at room temperature it was poured onto ice and extracted with ether. After washing with a 10% solution of sodium bicarbonate and drying over anhydrous magnesium sulfate the ether extract was distilled under reduced pressure to yield 3.5 g. (63%) of product, b.p. 131-174° at ~ 25 mm.

Procedure III. A solution of 1.52 g. (0.010 mole) of 3-keto-5-methylbicyclo[3, 3, 1]nonan-1-ol and 1 drop of concentrated sulfuric acid in 10 ml. of pure dry carbon tetrachloride was treated for 2 hr. with ketene generated by the pyrolysis of acetone. After washing with a 5% sodium bicarbonate solution and drying, the carbon tetrachloride solution was distilled to yield 1.1 g. (59%) of product, b.p. 93-110° at 0.11-0.18 mm. The n.m.r. spectrum is shown in Figure 2 (page 23) and the infrared spectrum in Figure 4 (page 25).

5-Methylbicyclo[3, 3, 1]nonan-1, 3-diol (XXX)

A solution of 2.1 g. (0.020 mole) of 3-keto-5-methylbicyclo [3, 3, 1]nonan-1-yl acetate in 10 ml. of dry ether was added dropwise to a stirred suspension of 0.80 g. (0.022 mole) of lithium aluminum hydride in 15 ml. of dry ether. After standing at room temperature for 45 min.,

this mixture was refluxed for 3 hr. and then hydrolyzed with water and filtered. The ether solution was distilled, giving a mixture of product (70%) and 3-keto-5-methylbicyclo[3,3,1]nonan-1-ol (30%).

Oxidation of XXX

A small amount of XXX (0.04 g.) which had been collected from the v.p.c. was oxidized by the method of Jones (30) to II. The yield of 0.03 g. (75%) of II was identified by its v.p.c. retention time and its infrared spectrum.

3-Methyl-2-butenoyl Chloride

A mixture of 20 g. (0.200 mole) of 3-methyl-2-butenoic acid and 28 g. (0.235 mole) of thionyl chloride was refluxed until the evolution of hydrogen chloride ceased, and distilled to give 19.8 g. (77%) of product.

3-Keto-5-methylbicyclo[3,3,1]nonan-1-yl 3-Methyl-2-butenoate (XXXI)

To a solution of 14.4 g. (0.0086 mole) of 3-keto-5-methylbicyclo [3,3,1]nonan-1-ol in 100 ml. of dry chloroform was added 13.0 g. (0.0091 mole) of 3-methyl-2-butenoyl chloride, and the mixture was refluxed for 9 hr. The mixture was cooled and poured into ice water, and the product washed with a 5% solution of sodium bicarbonate and dried. Distillation yielded 18.0 g. (88%) of a viscous oil, b.p. 123-7° at 0.42-0.45 mm. The n.m.r. spectrum is shown in Figure 7 (page 30) and the infrared spectrum in Figure 9 (page 32).

Unsuccessful Attempts to Cyclize XXXI

Procedure I. A solution of 2.40 g. (0.010 mole) of XXXI in 30 ml. of benzene was added to a solution of 0.25 g. (0.011 mole) of sodium

in 1 ml. of absolute ethanol and distilled to remove the benzene-ethanol azetrope. Dry dimethyl formamide (15 ml.) was added to the reaction mixture which was then refluxed for 3 hr. This mixture was cooled, poured into water, the layers separated and the aqueous phase then extracted with benzene. The benzene solution was dried and distilled to give only the starting ester (~70%).

Procedure II. A solution of 2.40 g. (0.010 mole) of XXXI in 30 ml. of benzene, to which 0.17 g. (0.010 mole) of p-toluenesulfonic acid had been added, was refluxed for 20 hr. The benzene was extracted with a 5% solution of sodium bicarbonate, dried and distilled to yield only the starting ester.

Procedure III. To a solution of 2.40 g. (0.010 mole) of XXXI in 30 ml. of toluene 0.024 g. (0.010 mole) of sodium hydride was added and the mixture refluxed for 2 hr. After the addition of 20 ml. of dimethyl formamide the mixture was refluxed for 30 min., cooled and poured into water. The toluene layer was separated and washed with water, dried and distilled to give only unchanged ester.

Procedure IV. To a solution of 2.40 g. (0.010 mole) of XXXI in 20 ml. of benzene and 20 ml. of dimethyl formamide a catalytic amount of sodium hydride was added and the mixture refluxed for 48 hr. After extraction with water the dried benzene layer was distilled. Only unchanged starting ester was collected.

Procedure V. Approximately 0.5 g. of XXXI was dissolved in an ether and dimethyl formamide mixture containing three drops of concentrated sulfuric acid. After standing overnight this solution was extracted with water and a 5% solution of sodium bicarbonate, dried and the organic solvent removed by distillation. The yield of starting material was approximately 80%.

Procedure VI. XXXI (2.40 g., 0.010 mole) was treated with 5 drops of concentrated sulfuric acid and warmed on a steam bath. After 5 min. the color had changed from yellow to dark brown. This mixture was allowed to stand at room temperature for 27 hr. After washing with a 5% solution of sodium bicarbonate the oil was distilled to give recovered starting material.

Procedure VII. A solution of 2.40 g. (0.010 mole) of XXXI in 50 ml. of dimethyl sulfoxide containing a catalytic amount of sodium hydride was allowed to stand for 3 days without any apparent change occurring. This solution was then warmed on a steam bath for 6 hr. After addition of water the organic material was extracted with ether and the ether layer distilled to recover unchanged starting material.

Procedure VIII. A solution of 2.40 g. (0.010 mole) of XXXI and 1 ml. of triethyl amine in 25 ml. of ethylene glycol was sealed in a combustion tube which was heated to 290° and kept at 275° for 24 hr. The mixture was poured into water and extracted with ether. After the ether layer was washed with a 5% solution of hydrochloric acid and dried, it was distilled in an oil-jacketed flask and gave ethylene glycol and almost a quantitative yield of the starting ester.

Reaction of XXXI with Ozone

A solution of 0.50 g. (0.0021 mole) of XXXI in 15 ml. of methylene chloride was treated with an ozone-oxygen mixture. Zinc dust and 25 ml. of water was added and the mixture distilled into a cooled solution of 2,4-dinitrophenylhydrazine and phosphoric acid in ethanol. The 2,4-dinitrophenyl hydrazone of acetone was isolated from this mixture. After recrystallization the m.p. was 125°; mixture m.p. was 124.5-126°.

Monoethyl Isopropylidenemalonoyl Chloride

A mixture of 20.2 g. (0.10 mole) of diethyl isopropylidenemalonate, 5.6 g. (0.10 mole) of potassium hydroxide and 60 ml. of absolute ethanol was allowed to react for 20 hr. at room temperature. After the ethanol was evaporated under vacuum the mixture was acidified with 20% hydrochloric acid and the product extracted with ether. The ether was removed at room temperature and the crude product was dissolved in 25 ml. of carbon tetrachloride. To this solution 50 g. (0.40 mole) of thionyl chloride was added and the mixture warmed on a steam bath for 8 hr. Distillation of this mixture yielded 8.90 g. (47%) of the product, b.p. 60-61° at 0.17 mm.

Monoethyl Isopropylidenemalonanilide

A mixture of 1.0 g. (0.005 mole) of monoethyl isopropylidenemalonoyl chloride, 5 ml. of aniline and 25 ml. of benzene was allowed to react at room temperature for 1 hr. The benzene solution was washed with 5% hydrochloric acid and 10% sodium hydroxide. Evaporation of the benzene and recrystallization from an alcohol-water mixture gave white crystals, m.p. 97.5-97.7°. Calc. for $C_{14}H_{17}NO_3$: C, 68.00%; H, 6.93%; Found: C, 67.96%; H, 7.00%.

Ethyl 3-Keto-5-methylbicyclo[3,3,1]nonan-1-yl Isopropylidenemalonate (XXXII)

A mixture of 2.1 g. (0.011 mole) of monoethyl isopropylidenemalonoyl chloride and 1.6 g. (0.010 mole) of II in 10 ml. of carbon tetrachloride was allowed to stand for 36 hr., then refluxed for 5 hr. This mixture was poured into water and the organic layer was separated, dried and distilled to yield 1.07 g. (46%) of product, b.p. 159-162° at 0.03 mm. $\lambda_{max.}$ 220 mμ (ϵ = 11,800). Diethyl isopropylidenemalonate - $\lambda_{max.}$ 219 mμ (ϵ = 11,030). The n.m.r. spectrum is shown in Figure 8 (page 31) and the infrared spectrum in Figure 10 (page 33).

Attempted Cyclization of XXXII

Procedure I. To a solution of 0.40 g. (0.0012 mole) of XXXII in 20 ml. of benzene, 0.072 g. (0.0015 mole) of 52% sodium hydride in mineral oil was added and the mixture refluxed for 1 hr. After standing overnight the mixture was again refluxed for 1 hr. and water was added. After removal of the benzene by evaporation, approximately 0.25 g. of a yellow semi-solid mass was obtained but not identified. $\lambda_{max.}$ 220 mμ (ϵ = 4,400); 288 mμ (ϵ = 460). Acidification of the aqueous phase yielded a trace of an acid, probably due to hydrolysis of XXXII.

Procedure II. To a solution of 0.053 g. (0.0023 mole) of sodium in 10 ml. absolute ethanol, 0.67 g. (0.0021 mole) of XXXII was added and the solution refluxed for 1 hr. After cooling, water was added and the product extracted with ether. $\lambda_{max.}$ 218 mμ (ϵ = 7,520); 291 mμ (ϵ = 60). Acidification of the aqueous phase again yielded a trace of an acid.

Procedure III. Hydrogen chloride gas was bubbled through a refluxing solution of 0.40 g. (0.0012 mole) of XXXII in 25 ml. of carbon tetrachloride for 1.5 hr. and the reflux continued overnight. The crude product gave the following ultraviolet spectrum: $\lambda_{max.}$ 218 mμ (ϵ = 8,500); 295 mμ (ϵ = 1,090).

Procedure IV. To a solution of 1.30 g. (0.0040 mole) of XXXII in 50 ml. of benzene, 0.20 g. (0.0044 mole) of 52% sodium hydride in mineral oil was added and the resulting mixture refluxed for 18 hr. After addition of water and ether extraction of the aqueous phase, the combined organic solution was evaporated to yield 0.90 g. (69%) of product. This crude product was distilled giving a liquid fraction (~90%), b.p. 96-98° at 0.04 mm. and a higher boiling solid fraction (~ 10%). The liquid material [$\lambda_{max.}$ 218 mμ (ϵ = 4,520); 290 mμ (ϵ = 2,150)] is tentatively given structure XXXIII on the basis of its n.m.r, and infra-red spectra.

1-Bromo-5-methylbicyclo[3, 3, 1]nonan-3-one (XXXIV)

A mixture of 1.68 g. (0.010 mole) of II and 1.1 ml. (3.0 g., 0.011 mole) of phosphorus tribromide was allowed to stand at room temperature for 6 hr. during which time a solid appeared. After addition of water to the cooled mixture it was filtered to give a crude yield of 1.86 g. (80%) of XXXIV. After several recrystallizations from an ether-petroleum ether mixture the resulting white crystals melted at 52.4-53.0°. Calc. for $C_{10}H_{15}BrO$: C, 51.97%; H, 6.54%; Found: C, 52.09%; H, 6.41%. The n.m.r. spectrum is shown in Figure 11 (page 35) and the infrared spectrum in Figure 12 (page 36).

Reaction of XXXIV with Aqueous Silver Perchlorate

A solution of 0.200 g. (0.87 mmole) of XXXIV in 10 ml. of dimethyl sulfoxide was slowly added to a cooled solution of 0.207 g. (1.00 mmole) of silver perchlorate in 10 ml. of water. After allowing this mixture to warm to room temperature it stood for 21 hr. No precipitate appeared so the mixture was warmed on a steam bath for 3.5 hr. The precipitated silver bromide was removed by filtration and the organic material removed by extraction with ether. Both the infrared spectra and v.p.c. retention times of the resulting oil and II were the same.

1-Methoxy-5-methylbicyclo[3, 3, 1]nonan-3-one (XXXV)

To a solution of 23 g. (0.10 mole) of XXXIV in 75 ml. of dry methanol, 23 g. (0.11 mole) of silver perchlorate was added. An immediate precipitate resulted. After standing in darkness overnight 17.7 g. (94%) of silver bromide was collected by filtration. Distillation of the organic material yielded 6.0 g. (30%) of XXXV, b.p. 110° at 0.06 mm. A sample collected from the v.p.c. was analyzed: Calc.:

C, 72.49%; H, 9.95%; Found: C, 71.78%; H, 9.84%. N.m.r. spectrum is shown in Figure 13 (page 39) and the infrared spectrum in Figure 14 (page 40).

Attempted Reaction of XXXV with Hydrogen Bromide

A solution of 2.5 g. (0.014 mole) in 10 ml. of glacial acetic acid was added to 5 ml. (3.5 g., 0.043 mole) of constant boiling hydrobromic acid containing a catalytic amount of aluminum tribromide. After refluxing for 4 hr., the mixture was allowed to stand overnight. Water was added and the mixture extracted with ether. Distillation yielded 1.80 g. (72%) of an oil which was identified as XXXV by its infrared spectrum.

Attempted Preparation of 1-Amino-5-methylbicyclo-[3,3,1]nonan-3-one (XXXVI)

A solution of 2.31 g. (0.010 mole) of XXXIV in 50 ml. of dry benzene was cooled and added to ~ 75 ml. of liquid ammonia which had been freshly distilled from sodium. Silver perchlorate (2.10 g., 0.011 mole) was added and the mixture stirred for 2 hr. The ammonia was distilled and the benzene layer filtered to remove the silver salts and extracted with a 2% solution of hydrochloric acid. The aqueous layer was neutralized with sodium bicarbonate and extracted with ether. Distillation of the ether gave no product. The benzene was removed from the original solution yielding 1.10 g. of organic material. This material was analysed by v.p.c. which indicated three major components. The first (56%) was a solid material which was not characterized but was a rearrangement product, the second (38%) was recovered XXXIV and the third (6%) was II.

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