ABSTRACT

PART I

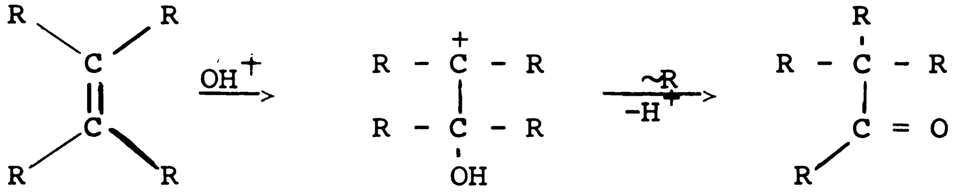
DIRECT OXIDATION OF ALKENES TO KETONES USING PEROXYTRIFLUOROACETIC ACID-BORON FLUORIDE

PART II

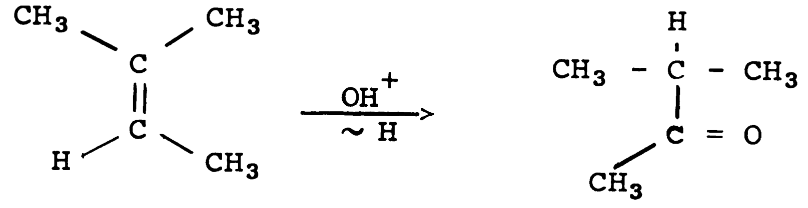
THE ACID-CATALYZED REARRANGEMENT OF OCTAMETHYL-8-OXATETRACYCLO$[4.3.0.0^{2,5}.0^{7,9}]$NON-3-ENE

by Lawrence Robert Lerner

The purpose of the first part of this thesis was to determine the synthetic utility of peroxytrifluoroacetic acid-boron fluoride etherate as an oxidant for effecting a one-step transformation of alkenes to ketones. In a number of cases this transformation was carried out successfully (1). The products can be explained as the result of attack of positive hydroxyl on the double bond, followed by Wagner-Meerwein rearrangement, to yield the corresponding ketone. The products are shown to be the result of hydrogen, methyl, acyl, chlorine or bromine migration, as



well as ring contraction and expansion. The following transformations exemplify these migrations:



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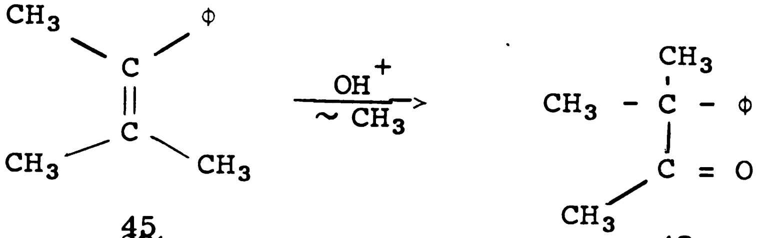
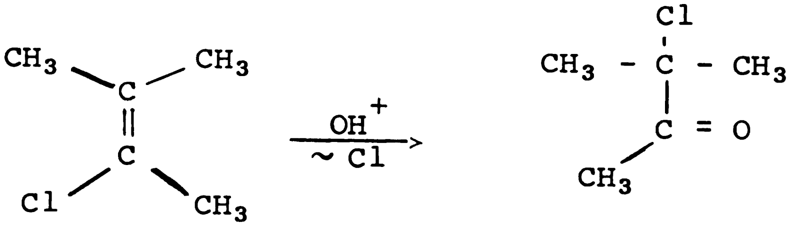


45 48 77%



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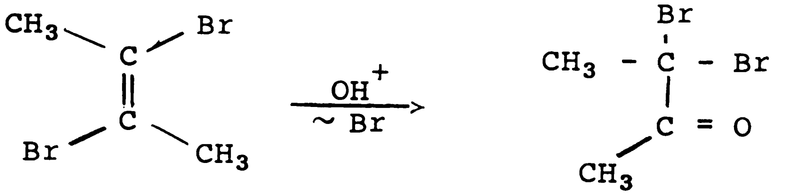

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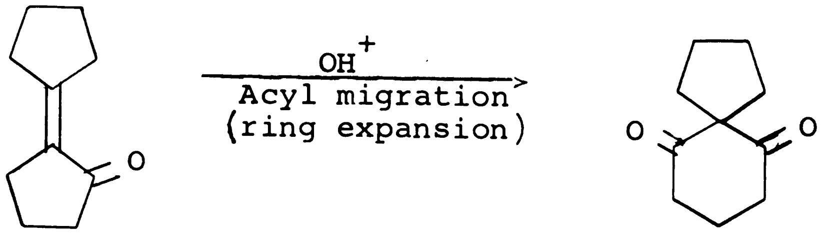

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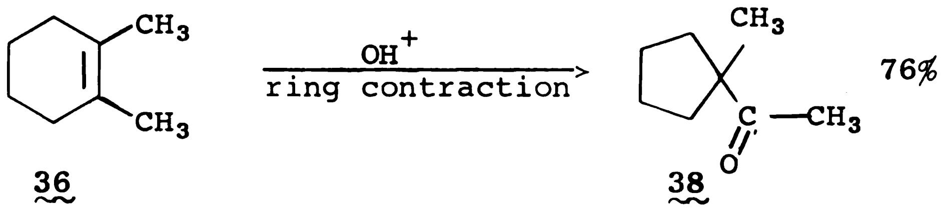
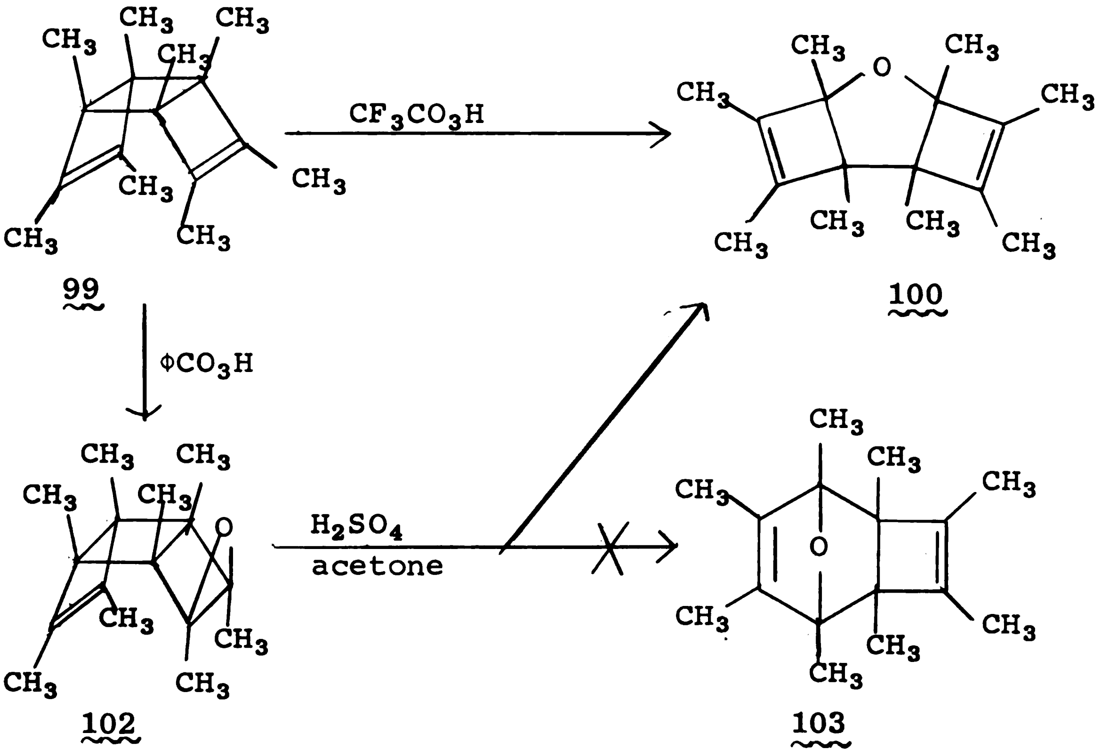
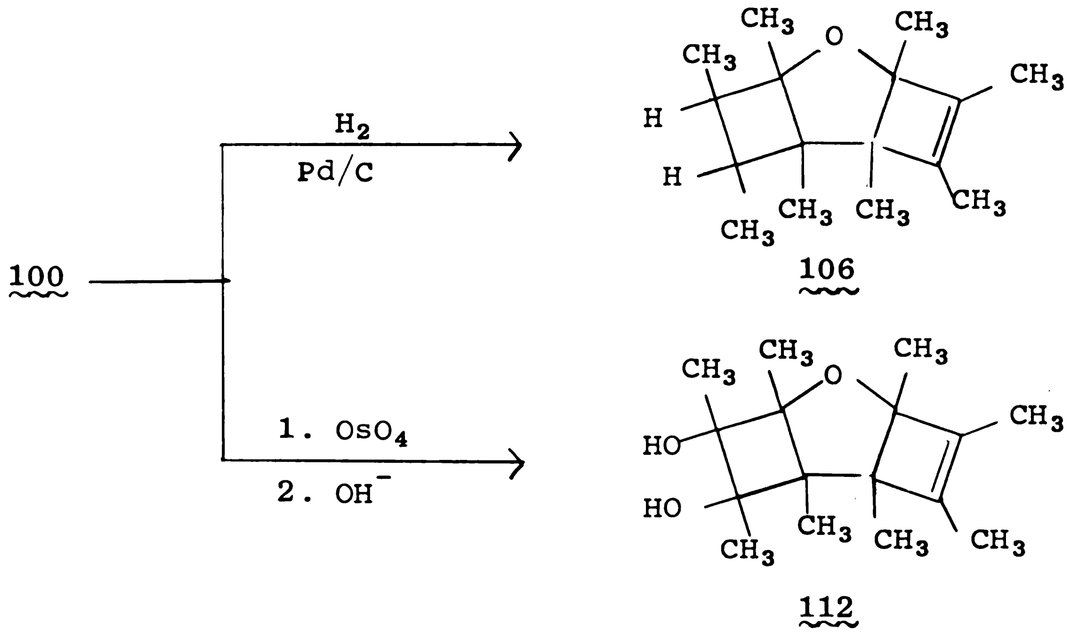


36 38

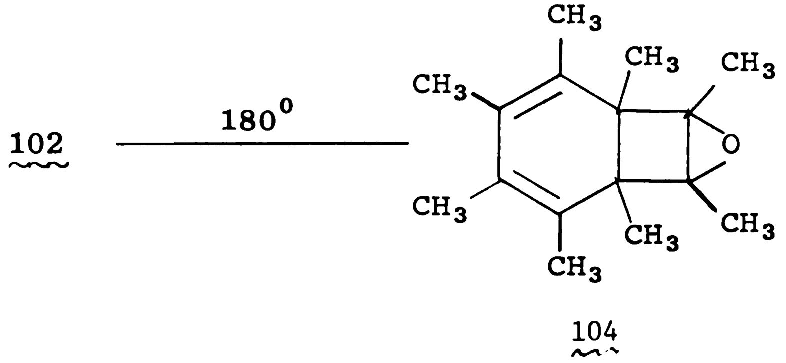
The second part of this thesis deals with the structural determination of a product isolated from the reaction of 99 with peroxytrifluoroacetic acid. The synthesis of this compound, by the acid-catalyzed rearrangement of 102, has been reported by Maier (2), but the previously assigned structure, 103, is shown to be incorrect. The actual structure, 100, is determined by the nmr and ir spectra of 100, and the spectra of its hydrogenation and hydroxylation products (106 and 112, respectively).



99 100 102 103



In addition, it is shown that 102 thermally rearranges to 104 as was reported by Maier in the same article, but some of the previously reported details of the nmr spectrum of 104 are shown to be incorrect.



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1. H. Hart and L. Lerner, J. Org. Chem. 32, 2669 (1967).
2. G. Maier, Chem. Ber. 96, 2238 (1963).

PART I

DIRECT OXIDATION OF ALKENES TO KETONES USING PEROXYTRIFLUOROACETIC ACID-BORON FLUORIDE

PART II

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By

Lawrence Robert Lerner

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To Lenore

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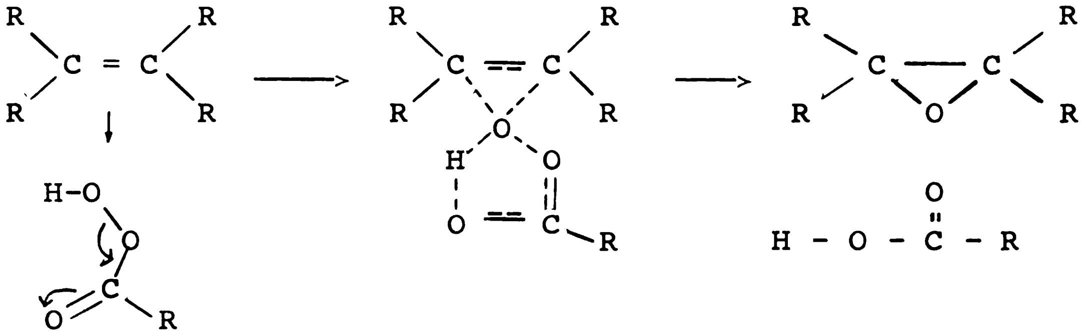
PART I

DIRECT OXIDATION OF ALKENES TO KETONES USING PEROXYTRIFLUOROACETIC ACID-BORON FLUORIDE

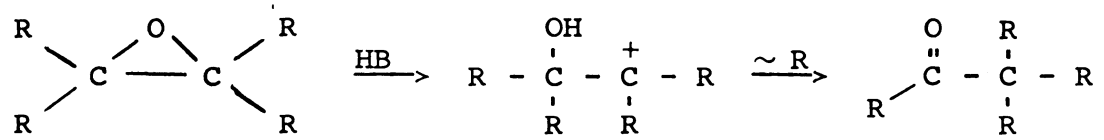
INTRODUCTION

Peracids have long been used to oxidize alkenes to epoxides (1). The reaction is generally believed to involve electrophilic attack of the peracid on the double bond.

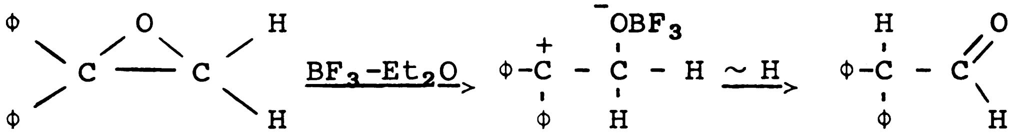


The electrophilic nature of the reaction is borne out by the fact that substituents on the double bond which are electron-donating (e.g. alkyl) increase the reaction rate, whereas those which are electron-withdrawing (e.g. carboxyl) decrease the rate (2). In addition, the stronger the peracid, the faster the rate. Peroxytrifluoroacetic acid is particularly reactive (3). It has a much weaker oxygen-oxygen bond than other peracids and will react readily with negatively substituted double bonds (e.g. ethyl crotonate), whereas other peracids will react only very slowly at best.

Acid-catalyzed ring opening of epoxides, which leads to carbonyl compounds <u>via</u> Wagner-Meerwein rearrangements, is also well known (4).

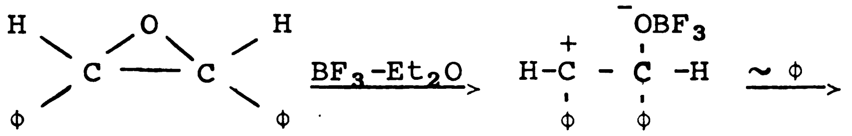


This type of rearrangement is effectively catalyzed by Lewis acids such as boron fluoride. The direction of ring opening is normally such that the more stable carbonium ion is formed. Subsequently or simultaneously, one of the R groups migrates. Migratory aptitudes are generally in the order aryl > acyl > H > t-butyl > ethyl > methyl. A few examples follow:



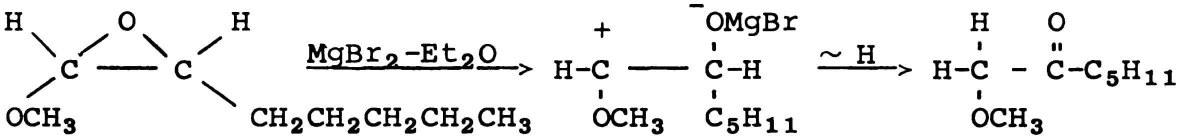
1 2 3

Cope, Trumbull and Trumbull (5) (1958).



4 5

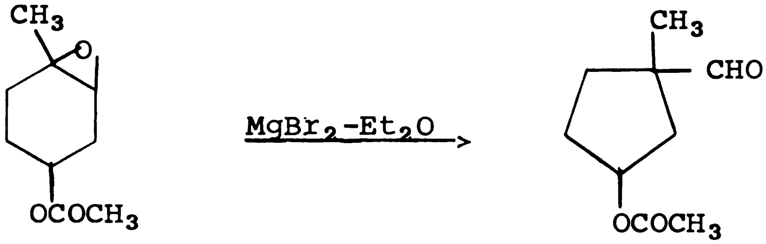
Reif and House (6) (1963).



6 7 8

Stevens and Dykstra (7) (1954).

In some cases ring contraction or expansion may occur as in the following two examples:



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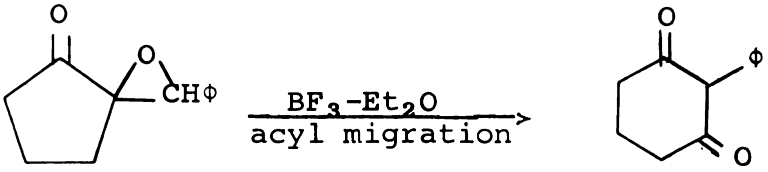
Braude et. al. (8) (1958).

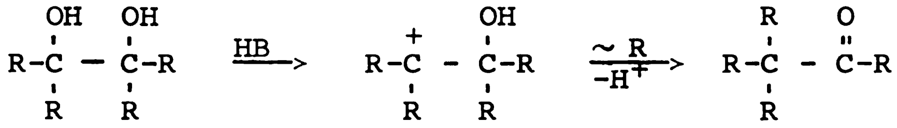


11 12

House and Wasson (9) (1956).

The ring opening and migration may or may not be concerted, though there is evidence for a concerted mechanism in certain cases (10).

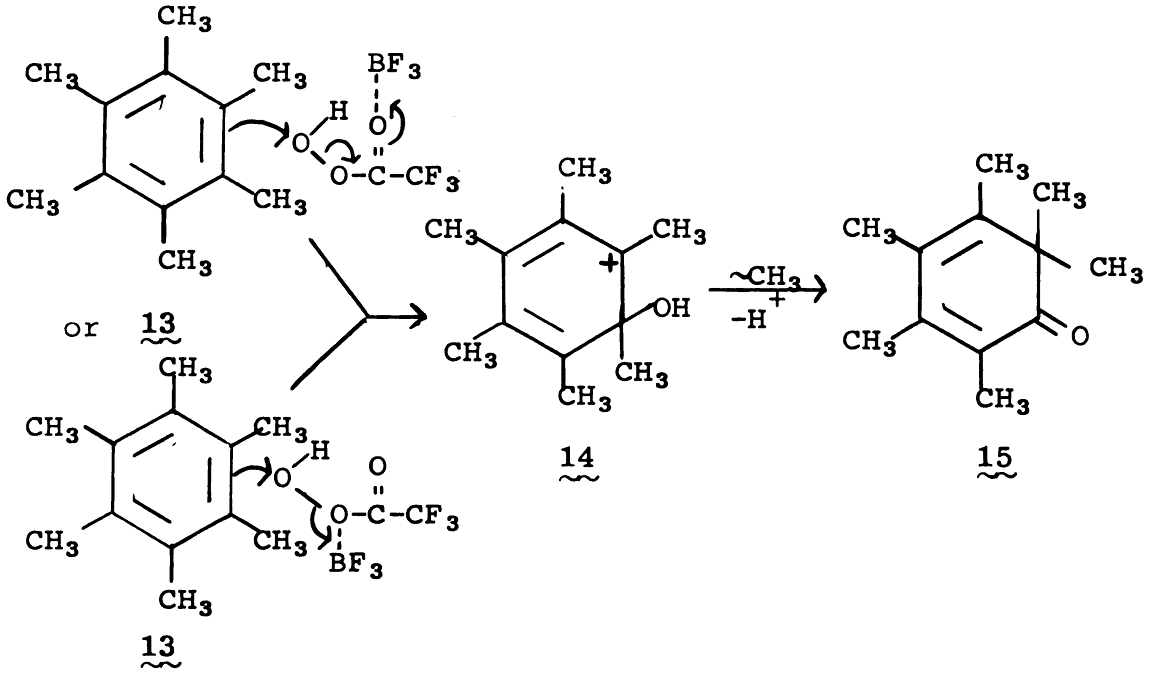
Closely related to the acid-catalyzed epoxide ring opening, is the acid catalyzed pinacol rearrangement (11).



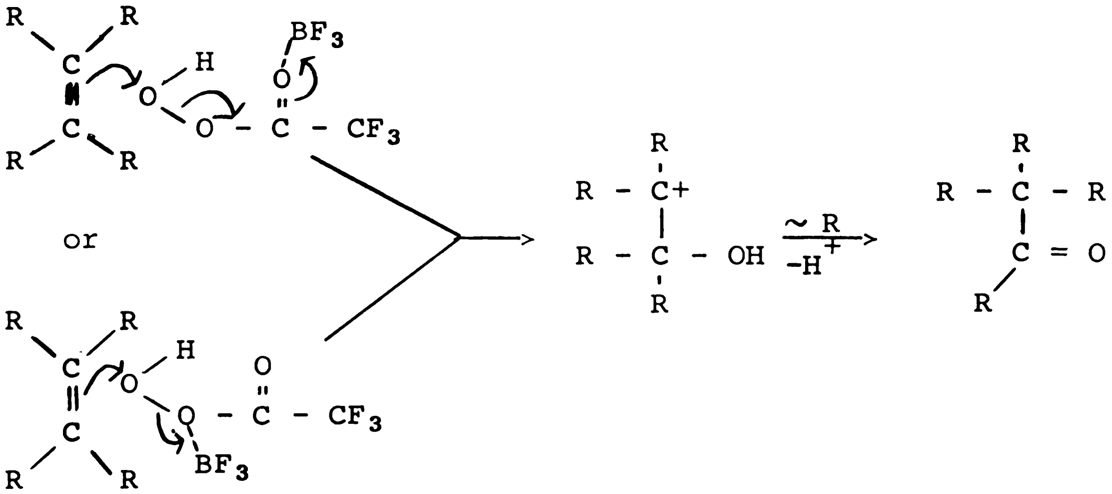
$$\mathrm{R{-}}\underset{\mathrm{R}}{\overset{\mathrm{OH}}{\mathrm{C}}} - \underset{\mathrm{R}}{\overset{\mathrm{OH}}{\mathrm{C}}}\mathrm{{-}R} \xrightarrow{\mathrm{HB}} \mathrm{R{-}}\underset{\mathrm{R}}{\overset{+}{\mathrm{C}}} - \underset{\mathrm{R}}{\overset{\mathrm{OH}}{\mathrm{C}}}\mathrm{{-}R} \xrightarrow[-\mathrm{H}^{+}]{\sim \mathrm{R}} \mathrm{R{-}}\underset{\mathrm{R}}{\overset{\mathrm{R}}{\mathrm{C}}} - \overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}\mathrm{{-}R}$$

In the pinacol rearrangement, as in epoxide ring openings, the more stable carbonium ion is usually formed; this is followed by migration of a group and proton loss. The order of migratory aptitudes, in general, is the same as that for the epoxide ring opening reaction.

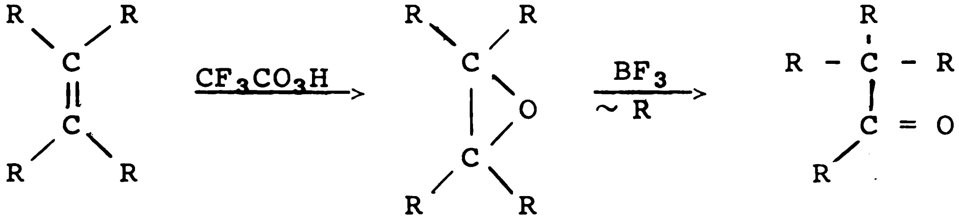
Previous work in this laboratory has demonstrated the usefulness of peroxytrifluoroacetic acid - boron fluoride as an electrophilic oxidant of substituted aromatic compounds (12). With hexaalkylbenzenes, hexaalkylcyclohexadienones were obtained in good yield by electrophilic attack by the oxidant (where boron fluoride aids heterolytic cleavage of the peracid), followed by a Wagner-Meerwein rearrangement and proton loss. For example, hexamethylbenzene (13) was converted into hexamethyl-2,4-cyclohexadienone (15) in 88% yield (13).



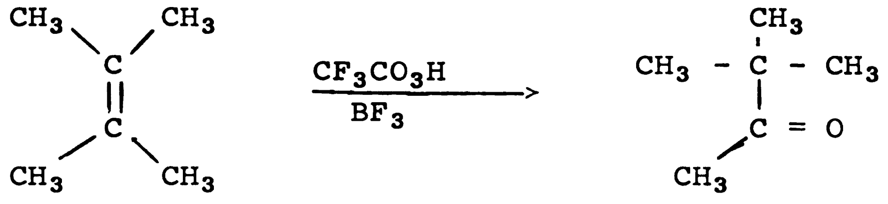
The type of carbonium ion intermediate (14) postulated here could be envisioned in a similar oxidation of an isolated double bond, in which case the intermediate ion would be the same as that suggested in the pinacol rearrangement and should lead to formation of a ketone <u>via</u> migration and proton loss.



A ketone would also result if the initial reaction was epoxidation of the double bond by the peracid, followed by boron fluoride catalyzed rearrangement of the epoxide.

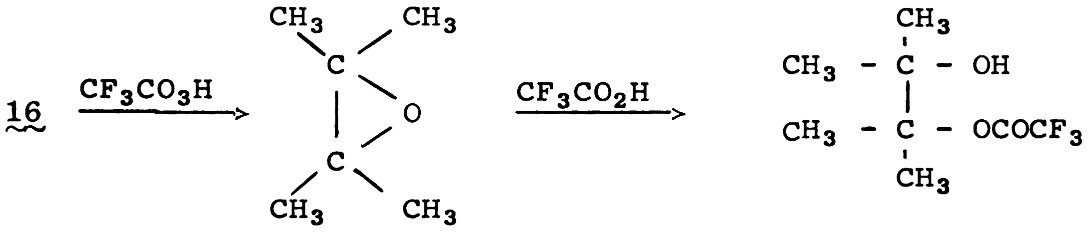


An initial experiment (14) carried out on the oxidation of 2,3-dimethyl-2-butene (16) with peroxytrifluoroacetic acid - boron fluoride resulted in a 75% yield of the anticipated product, pinacolone (17).



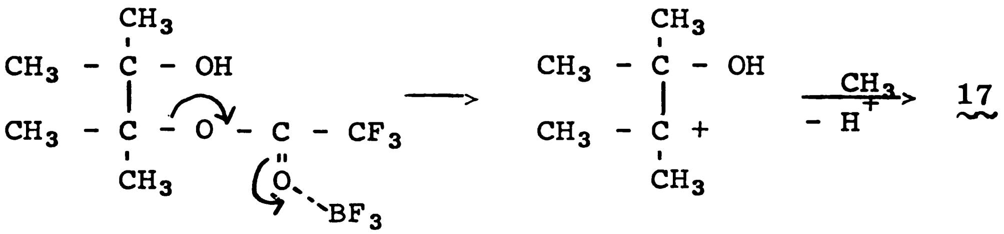
16 17

Without boron fluoride, pinacolone was produced in only 16% yield, and the major product was the hydroxytrifluoroacetate, 19.



18 19

This hydroxytrifluoroacetate was quantitatively converted to pinacolone upon the addition of boron fluoride, possibly <u>via</u> a pinacol rearrangement type intermediate (20) as shown.



19 20

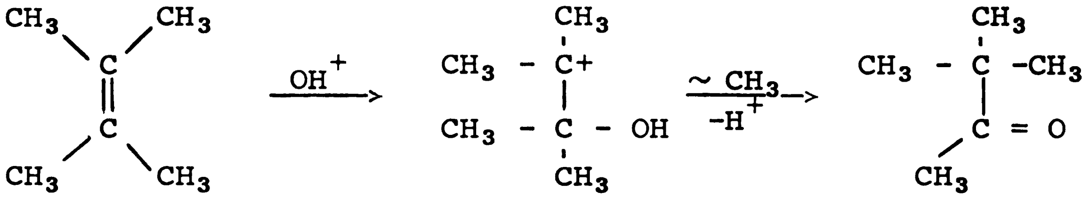
This would be a third possible mechanistic pathway to the ketone, when the oxidation is carried out in the presence of boron fluoride.

Part I of this thesis describes the results of a study on the scope of the oxidation of alkenes to ketones in one step (**15**) and a comparison of migratory aptitudes, reflected in the products obtained, with those found in the acid-catalyzed rearrangement of the corresponding epoxide or glycol.

RESULTS AND DISCUSSION

A. Oxidation of 2,3-Dimethyl-2-butene (16)

It was found to be most convenient to convert 2,3-dimethyl-2-butene (16) to pinacolone (17) by substituting boron fluoride etherate for gaseous boron fluoride which had been used previously (14). Under these conditions the yield of 17 was 72%, as opposed to 75% with gaseous boron fluoride. (For simplicity the attacking oxidant will be represented as OH^+, though any of the mechanisms discussed in the introduction may be operative.)



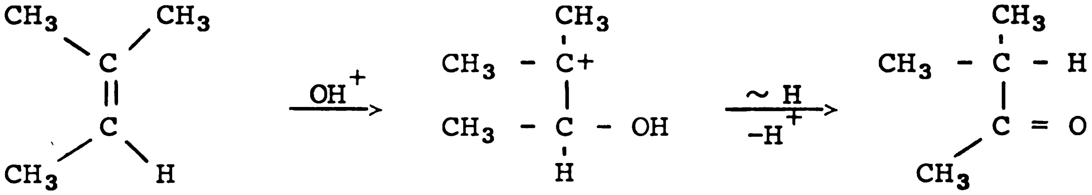
16 20 17

It was also found that if the reaction mixture was not cooled (as was originally done) the yield of 17 increased slightly to 75%. Therefore, by simply adding the peracid in methylene chloride concurrent with the addition of the liquid boron fluoride etherate, at such a rate that the reaction mixture refluxed gently, the entire experiment could be carried out within two hours. Since the total synthesis could be carried out without isolating any intermediate (e.g. epoxide or glycol) and within this short period of time (the peracid was completely consumed within 15 minutes after mixing the reagents), this procedure promised to be an excellent method for effecting the transformation with other alkenes.

All the oxidations to be discussed were therefore carried out using boron fluoride etherate, but some oxidations were carried out at either 0-8°, at reflux (40°) or at both temperatures, since attempted oxidation without cooling was not tried until this study was well underway.

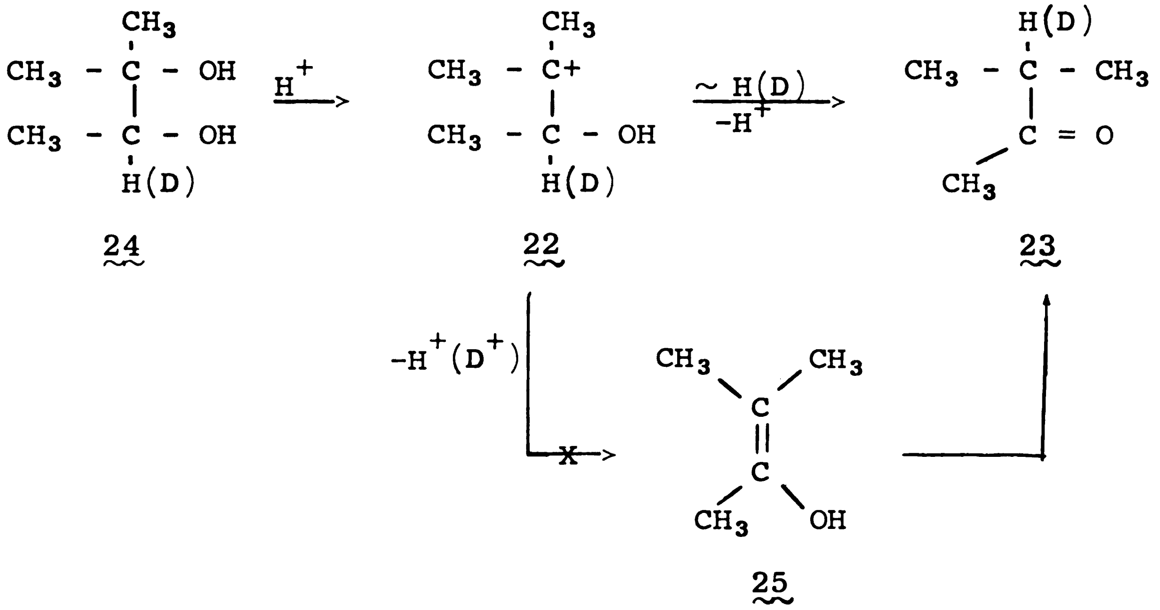
B. Oxidation of 2-Methyl-2-butene (21)

When 2-methyl-2-butene (21) was oxidized at 0°, the exclusive, volatile product was 3-methyl-2-butanone (23) as would be expected by initial attack of the electrophile to form the most stable ion, 22, followed by hydrogen migration and loss of a proton.



21 22 23

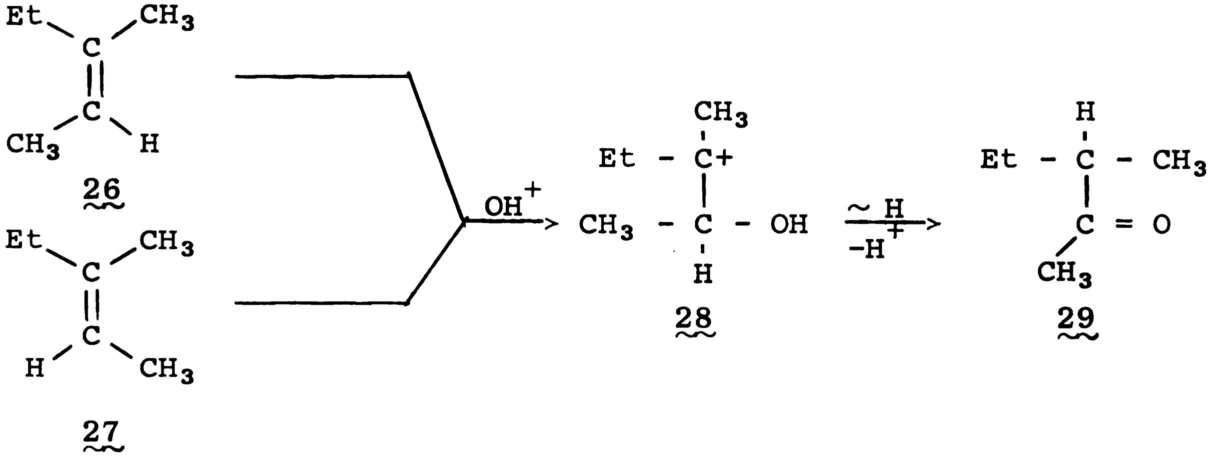
This product (23) was also the major one (> 95%) in the pinacol rearrangement (16) of the corresponding glycol, 24, in aqueous perchloric acid. It was also demonstrated by the same workers, through deuterium labeling, that the hydrogen migration was intramolecular; therefore the reaction did not proceed *via* the enol (25) of 23.



C. Oxidation of cis and trans-3-Methyl-2-pentene (26 and 27)

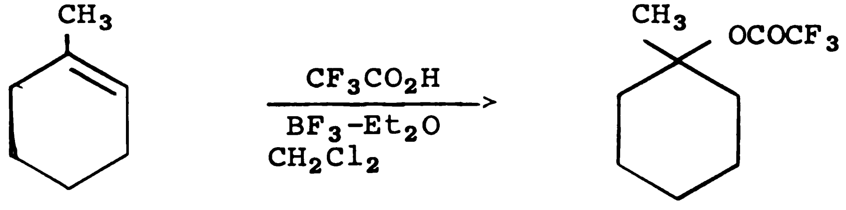
The oxidation of both cis (26) and trans (27)-3-methyl-2-pentene, at 0°, resulted in the formation of 3-methyl-2-pentanone (29) in 63 and 70% yield respectively.

This product, as in the oxidation of 21, is the one expected on the basis of formation of the most stable ion, 28, followed by hydrogen migration and loss of a proton.



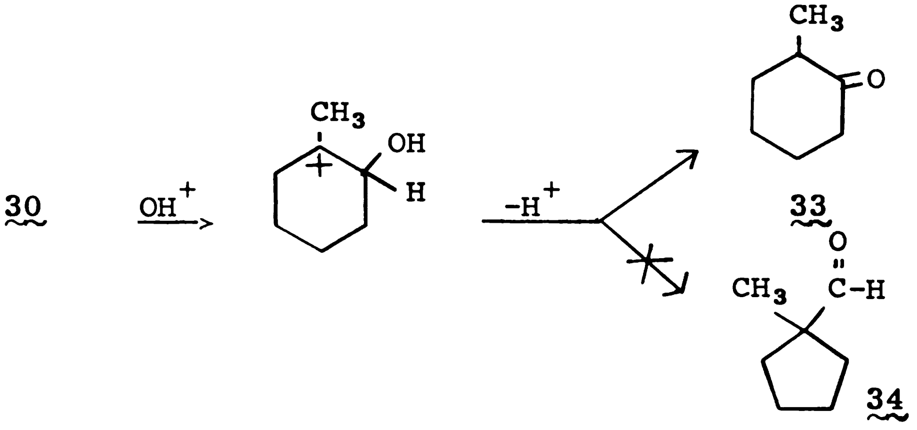
D. Oxidation of 1-Methylcyclohexene (30)

A serious side reaction was found in the oxidation of 1-methylcyclohexene (30). When the oxidation was carried out at 0°, two volatile products were detected. They were identified as 2-methylcyclohexanone (33) and 1-methylcyclohexyl trifluoroacetate (31) obtained in 8 and 15% yield, respectively. When the oxidation was carried out at reflux, the yield of 33 was improved to 41% whereas the yield of 31 dropped to 9%. Compound 31 was undoubtedly formed by the addition of trifluoroacetic acid to 30; 31 was the only product when the peracid was omitted.

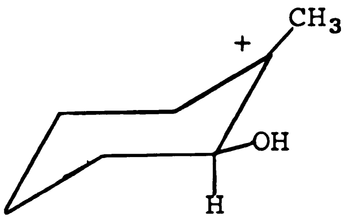


30 31

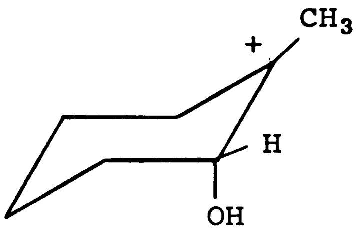
The expected oxidation intermediate 32 might give rise to two products, 33 by hydrogen migration or aldehyde 34 by ring contraction, but only 33 was observed.



The two possible carbonium ion intermediates are 32a and 32b. Either could lead to ring contraction but only 32a (axial hydrogen) leads to hydrogen migration.



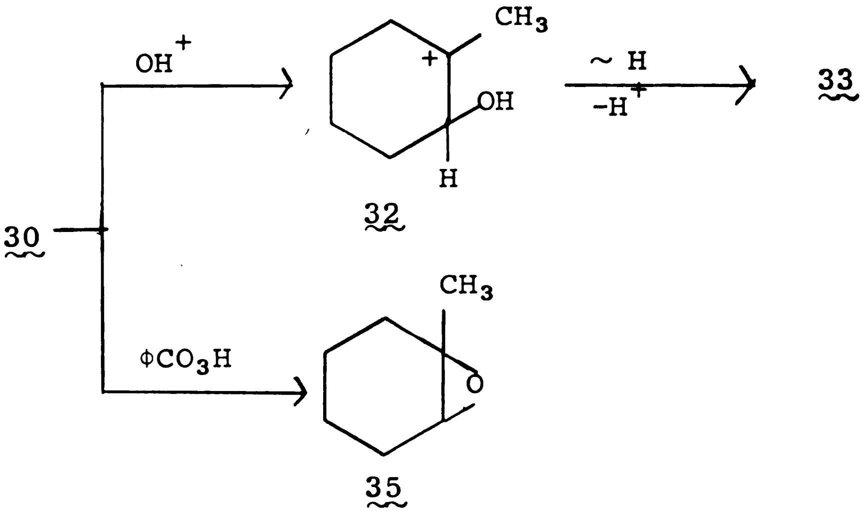
32a



32b

Ion 32a with the equatorial hydroxyl, should be the more stable of the two. From these results 32a is the preferred intermediate and rearranges exclusively by hydrogen migration. This migratory preference might be expected since hydrogen migration is preferred over alkyl migration (ring contraction) in Wagner-Meerwein rearrangements (4).

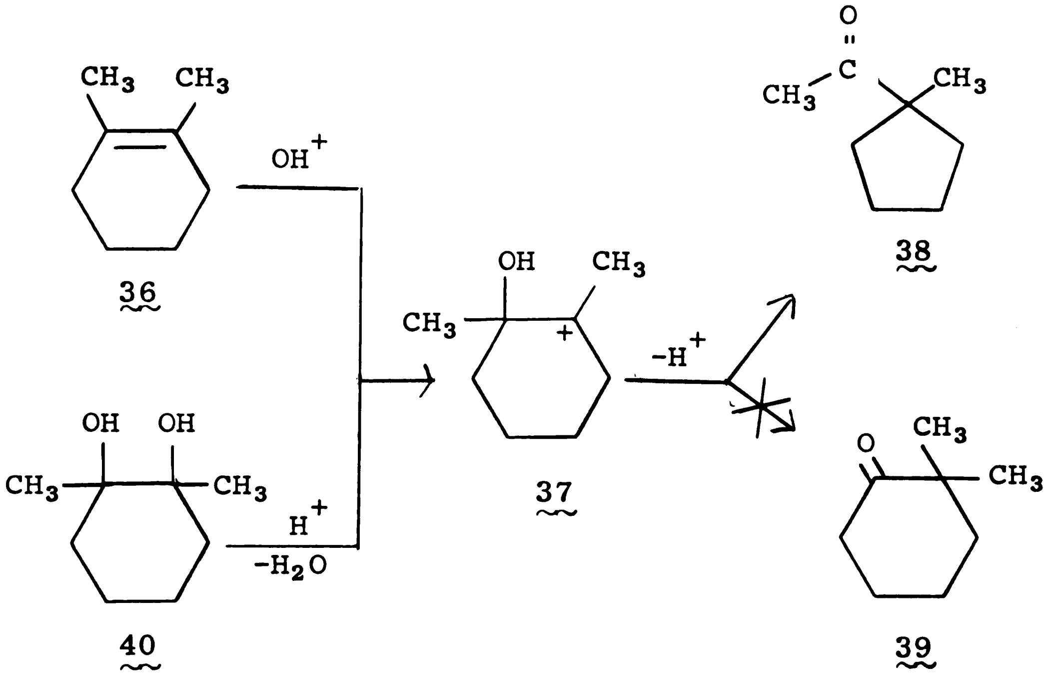
Similar results have been reported (17) in the epoxidation of 30 with perbenzoic acid. Here the expected epoxide 35 was found in 48% yield and the only rearrangement product, formed in 24% yield, was 33. The authors suggested that 33 might have been formed from 32, which, in turn, was formed by direct attack of positive hydroxyl on 30. This, of course, is one of the mechanisms postulated in this thesis for the oxidation with peroxytrifluoroacetic acid - boron fluoride.



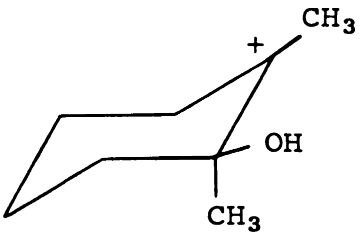
E. Oxidation of 1,2-Dimethylcyclohexene (36)

In contrast to the results on the oxidation of 30, the oxidation of 1,2-dimethylcyclohexene (36) at 0° led exclusively (76% yield) to the ring contraction product, 1-acetyl-1-methylcyclopentane (38), rather than 2,2-dimethylcyclohexanone (39), which would result from methyl migration. In the pinacol rearrangement of the corresponding cis (18) and trans (19) glycols (40) in sulfuric acid, the only product formed was also 38, presumably through the same intermediate, 37.

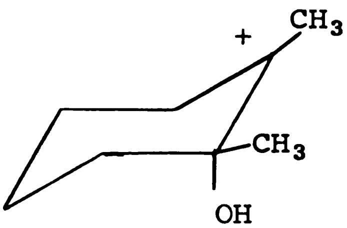
When the glycol rearrangement was carried out in perchloric acid at various temperatures (20), the amount of 38 in the rearranged product was found always to be greater than 90% (the remainder was 39). Bunton and Carr (20) suggested that of the two possible intermediates, 37b



should be more stable than 37a since the carbonium ion center can be stabilized by participation of the hydroxyl group. In addition, 37b would be favored on steric grounds; the methyl group, rather than the smaller hydroxyl group, would



37a



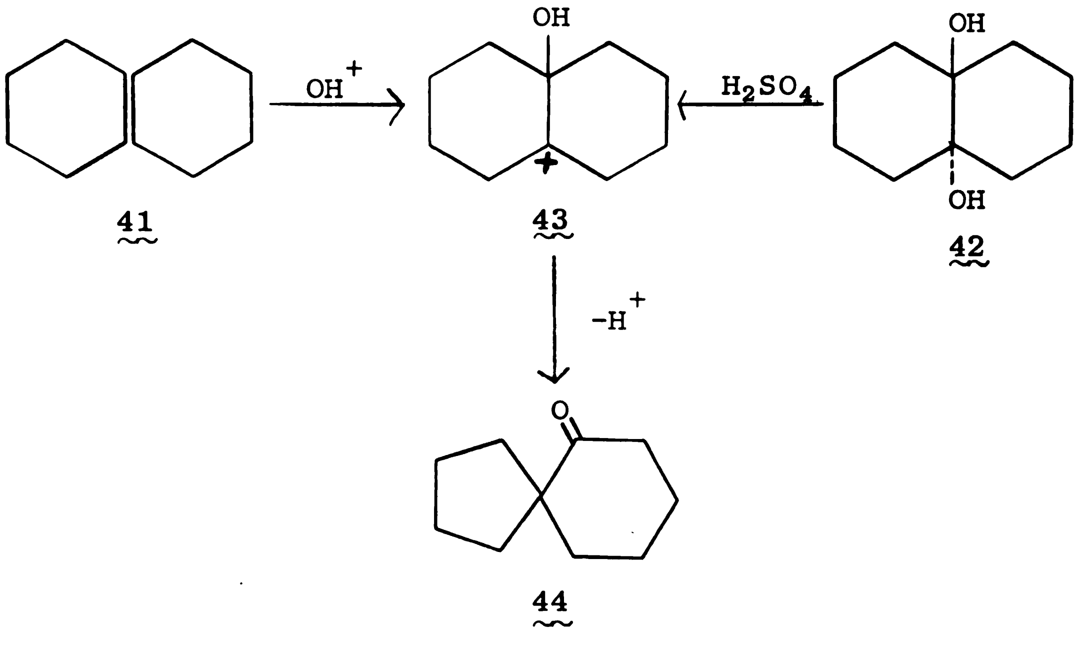
37b

be in the equatorial position (21). Conformation 37b can only lead to ring contraction (methyl group not axial).

Regardless of the intermediate, ring contraction (secondary alkyl migration) would be favored over methyl migration according to migratory aptitudes in Wagner-Meerwein rearrangements (4).

F. Oxidation of $\Delta^{9,10}$-Octalin (**41**)

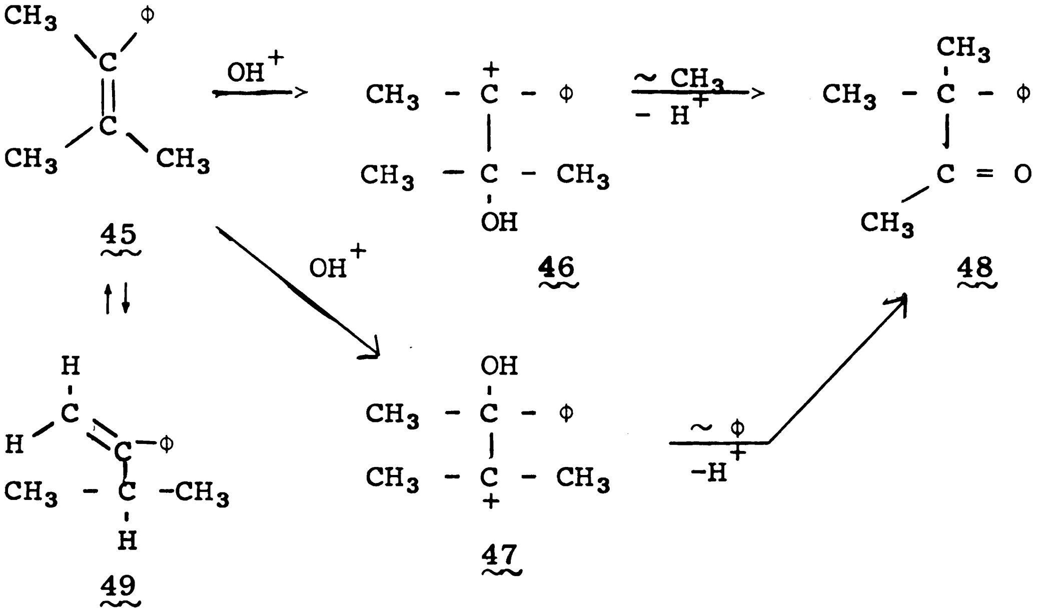
Oxidation of $\Delta^{9,10}$-octalin (**41**) at 0^0 afforded an additional comparison with the pinacol rearrangement of the corresponding trans (**42**) glycol (22). As expected $\Delta^{9,10}$-octalin (**41**) gave the same spiro ketone (**44**) as the glycol, in 86% yield.



G. Oxidation of 2-Methyl-3-phenyl-2-butene (**45**)

The oxidation of 2-methyl-3-phenyl-2-butene (**45**) was of interest because of the possibility of oxidation of the aromatic ring (12) as well as oxidation of the double bond.

Oxidation of 45, at reflux, showed that the only product, 3-methyl-3-phenyl-2-butanone (48), arose from attack on the double bond. The sample of 45 used was contaminated with the isomeric 3-methyl-2-phenyl-1-butene (49), but oxidation of two different mixtures of 45 and 49 indicated that under the reaction conditions the two became equilibrated, with 45 being preferentially oxidized. This assertion is based on the fact that an 80:20 mixture of 45 and 49 resulted in a 96% yield of 48 based on the original amount of 45, or a 77% yield based on the total amount of 45 and 49.

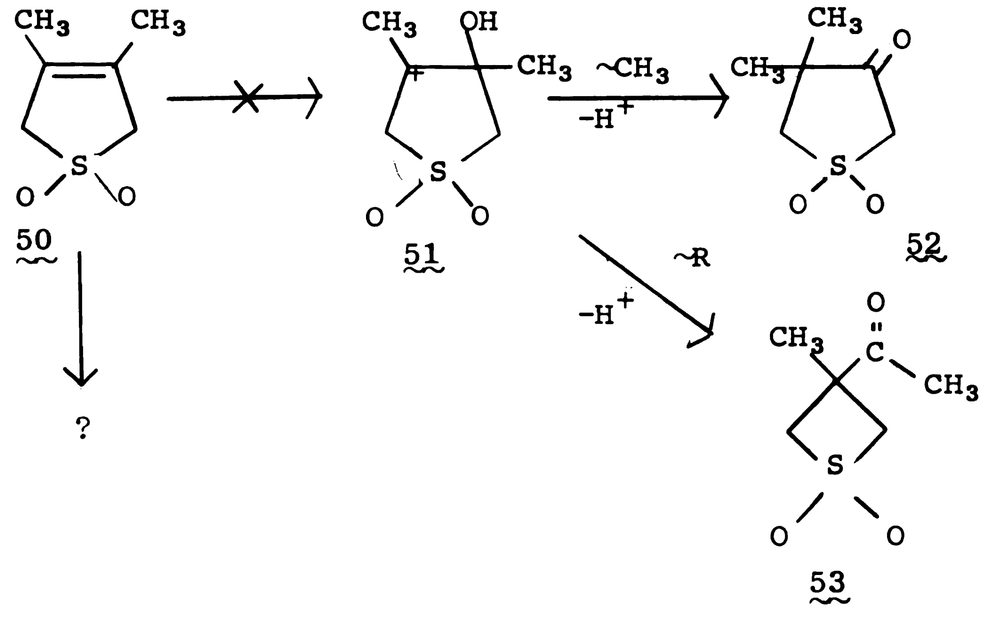


On the other hand, a 46:54 mixture resulted in a 117% yield based on the original amount of 45. Obviously some of 49 must be rearranging to 45 in order to account for the large amount of 48 found. On the basis of the total amount of 45 and 49 used, the yield of 48 was found to be 73%. The presence of 49, therefore, does not detract from the synthetic utility of this oxidation.

The intermediate in the oxidation is probably 46 (the more stable ion), which by methyl migration gives rise to the product. The other intermediate, 47, could be involved, with phenyl migration (preferred over methyl) leading to 48. Whichever is the intermediate, 48 would be the expected product. Unfortunately, there are no reports in the literature on the rearrangement of the corresponding epoxide or glycol for comparison purposes.

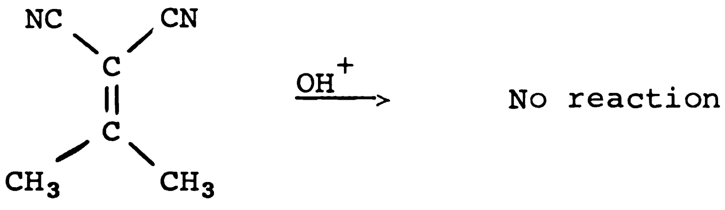
H. Oxidation of 3,4-Dimethyl-2,5-dihydrothiophene-1,1-dioxide (50)

The oxidation of 50 was unsuccessful from a synthetic point of view. The oxidation took place readily at reflux, but only a small amount of material was isolated from the organic layer (30% based on the amount of starting material). These results would indicate that a highly water-soluble product(s) was formed, rather than the expected product 52 or 53. Perhaps this was a sulfonic acid (or degradation product), though there does not appear to be a precedent for this type of a reaction. It is also possible that 52 and 53 are sufficiently water soluble so that any of 52 or 53 formed were lost during the work-up procedure. Since this oxidation was not of synthetic utility, no further investigation was carried out into the exact nature of the products.



I. Oxidation of Isopropylidene Malononitrile (54)

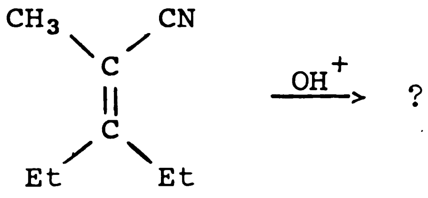
To test the effect of strong electron-withdrawing substituents, the oxidation of isopropylidene malononitrile (54) under refluxing conditions, was attempted. No reaction occurred and apparently the two nitrile groups caused the double bond to be too electron deficient for an electrophilic attack to take place.



54

J. Oxidation of 3-Ethyl-2-methyl-2-pentenenitrile (55)

The oxidation of 55 showed that even one nitrile group was sufficient to deactivate the double bond, so that electrophilic attack did not occur under refluxing conditions. Though a reaction did take place, the only volatile material detected was starting material. A considerable amount of tar was formed indicating polymerization and/or oxidation of the nitrile group had occurred.

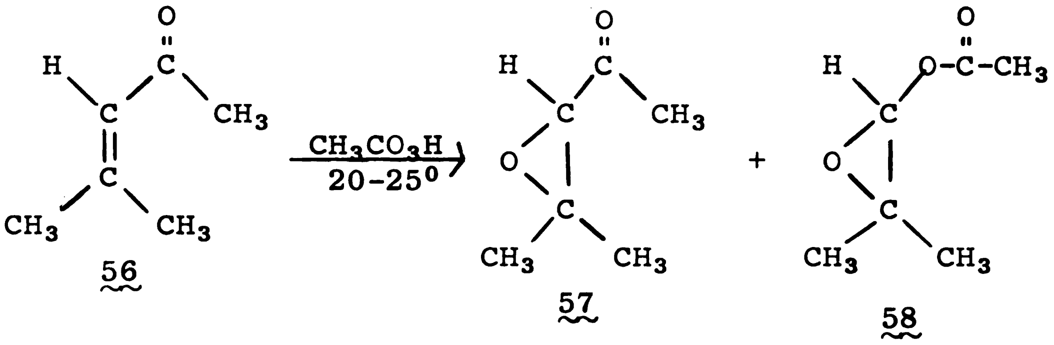


55

K. Oxidation of 2-Methyl-2-butenal [tiglaldehyde (59)]

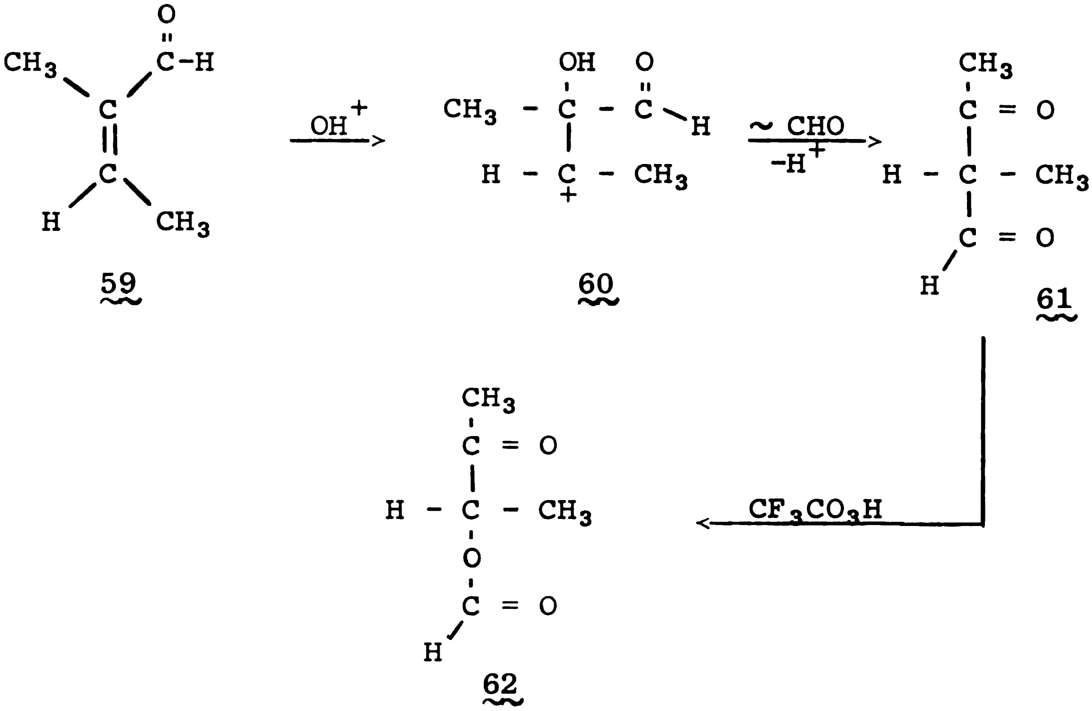
Oxidation of tiglaldehyde (59) was of interest, since products could be formed by either acyl or methyl migration, or by Bayer-Villiger oxidation (23) of the aldehyde to the formate ester.

Both oxidation of the double bond and of the carbonyl group have been noted in the oxidation of other α, β-unsaturated carbonyl compounds, as in the following example (24):

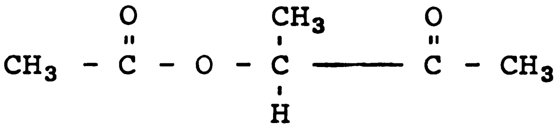


Upon oxidizing tiglaldehyde (59) at reflux, it was found that any initial oxidation product was further oxidized. When a slight excess of peracid was used, it was all rapidly consumed, but out of 25.2 g of 59 used, 14.6 g was recovered and only 3.2 g of volatile product was isolated by distillation. This product appeared to consist of two compounds. They were tentatively assigned the structures 62 and 63. A mixture of 62 and 63 showed strong carbonyl absorption in its ir spectrum at 1722 cm^{-1} and strong absorption between 1150 and 1250 cm^{-1}, which could be associated with an ester group. In its nmr spectrum, 62 showed a singlet at τ 1.96 (1 H) assigned to the formate proton, a quartet at τ 4.89 (1 H) assigned to the proton α to the carbonyl, a singlet at τ 7.87 (3 H) assigned to the methyl attached to the carbonyl, and a doublet at τ 8.62 (3 H) assigned to the remaining methyl group. Compound 63 showed a quartet at τ 5.03 (1 H), assigned to the proton attached to the carbon bearing the methyl group, a singlet at τ 7.90 (6 H) assigned to the methyl protons of the two acetyl groups, and a doublet at τ 8.67 (3 H) assigned to the remaining methyl group.

Product 62 could be rationalized as the result of electrophilic attack on the double bond followed, or preceeded, by Bayer-Villiger oxidation of the aldehyde.



The presence of 63, if the structure is correctly assigned, cannot as easily be explained, but it is apparently an oxidation product from the reaction.



$$CH_3-\overset{O}{\overset{\|}{C}}-O-\underset{H}{\overset{CH_3}{C}}-\overset{O}{\overset{\|}{C}}-CH_3$$

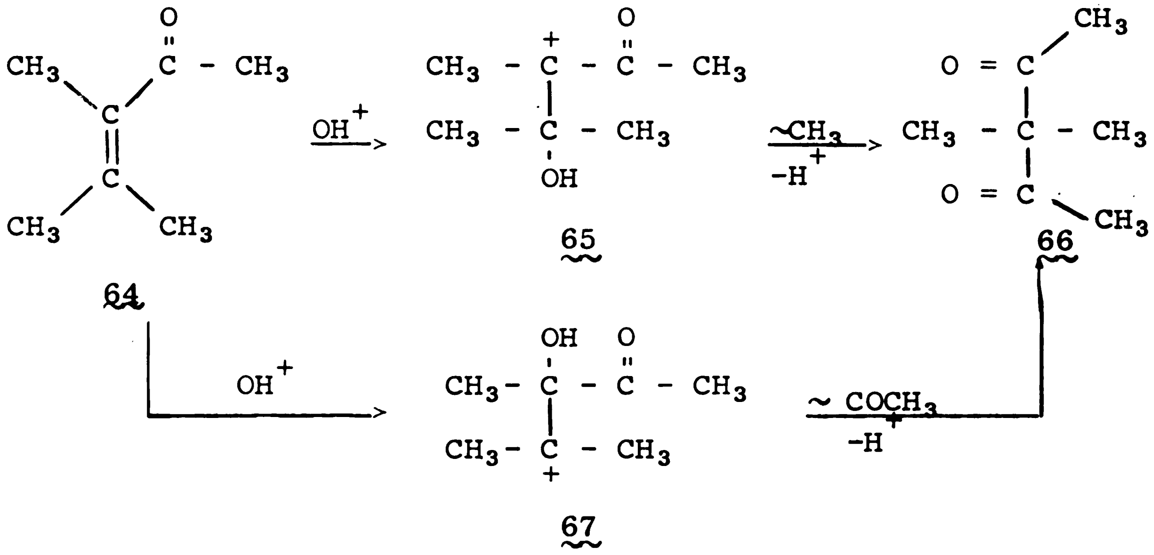
63

House has observed acyl migrations in the rearrangement of a number of α, β-epoxy ketones (25) so that conversion of 60 to 61 in the above scheme is not without precedence.

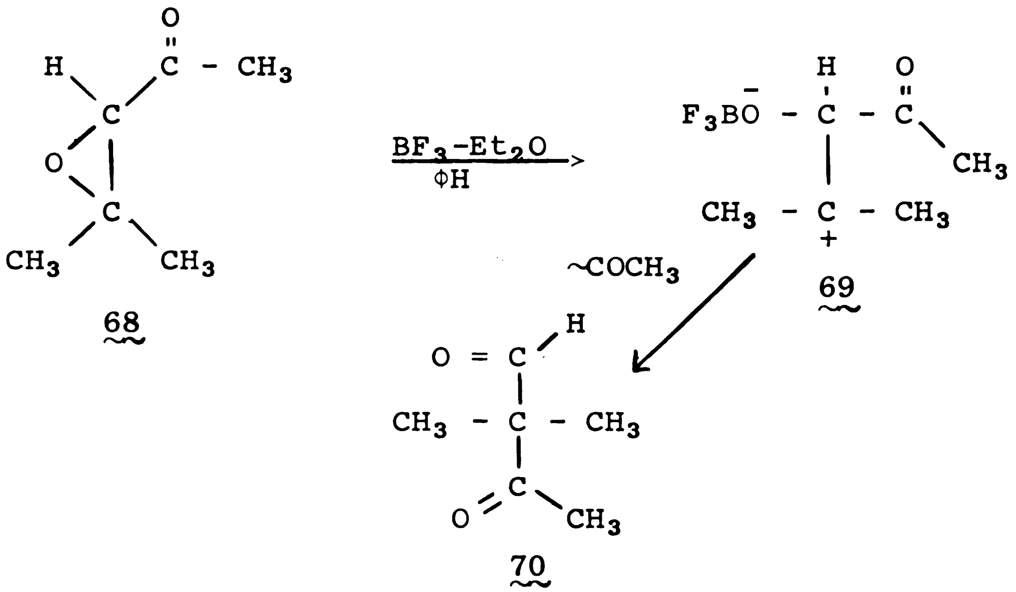
L. Oxidation of 3,4-Dimethyl-3-penten-2-one (64)

In contrast to 59, 3,4-dimethyl-3-penten-2-one (64) was oxidized (reflux) at the double bond, leading to an 81% yield of 66. The fact that some starting material was recovered (conversion of 64 to 66 was 61%) indicates that some further oxidation of the initial product did take place, but apparently the addition of two methyl groups (compare 59 with 64) activated the double bond sufficiently for preferential attack at that position.

Product 66 could have arisen *via* methyl or acyl migration. House and Wasson (26) have observed acyl migration

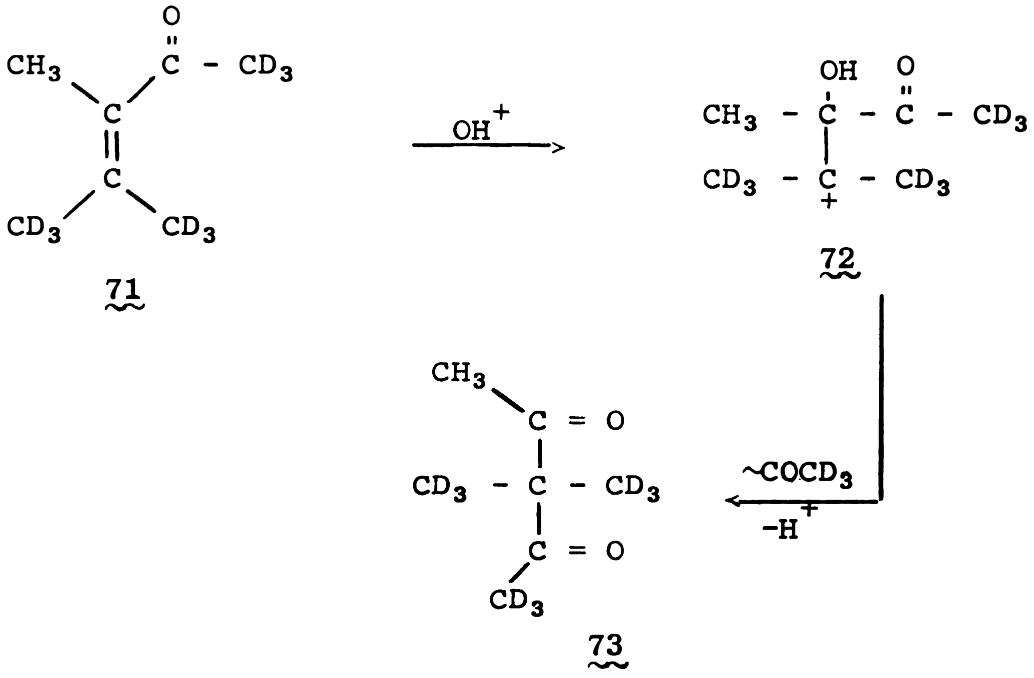


in a related system, where they converted 68 to 70 by boron fluoride etherate catalyzed epoxide ring opening.



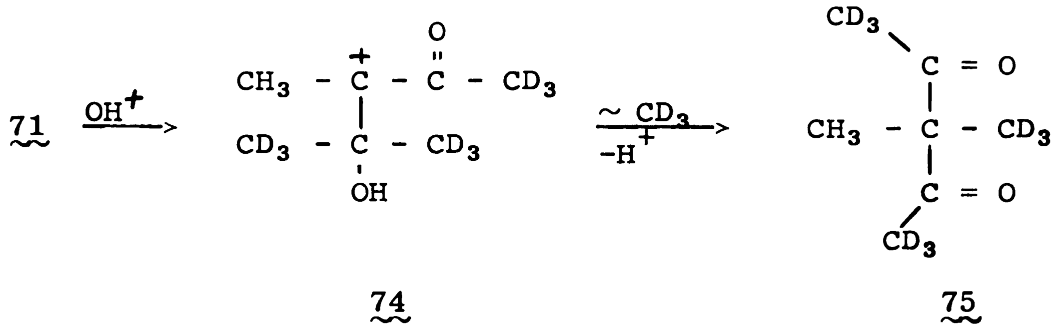
68 69 70

In order to decide between acyl or methyl migration in our system, deuterium labeled starting material 71 was prepared and oxidized. The resulting deuterated diketone 73 showed a single peak in its nmr spectrum at τ 7.93. Acyl migration must have taken place.



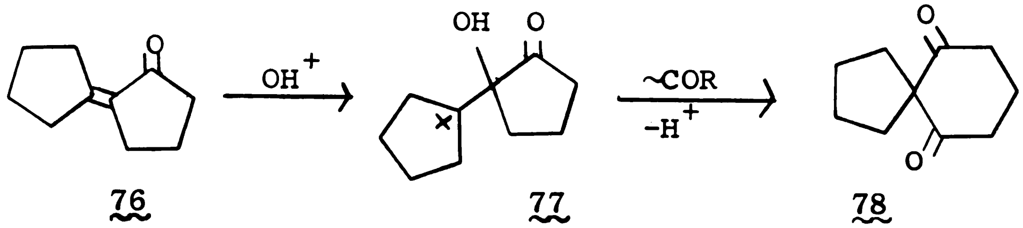
71 72 73

If methyl migration had occurred, the resulting diketone 75 would have had a single nmr absorption at higher field (*ca*. τ 8.7).

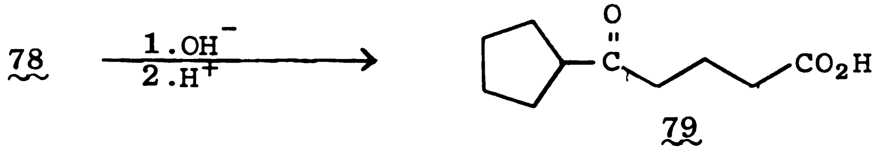


M. Oxidation of 2-Cyclopentylidenecyclopentanone (76)

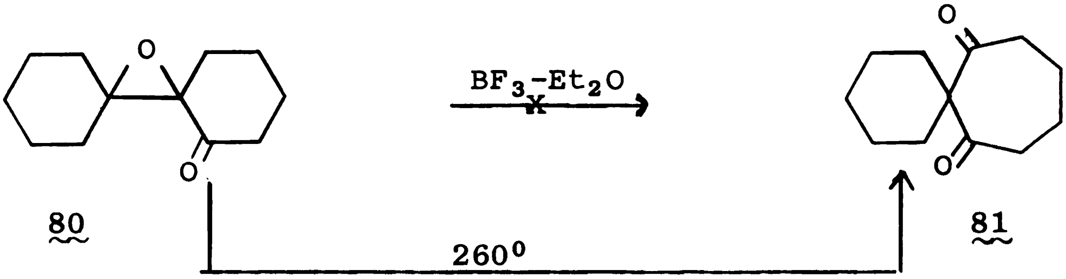
An additional example of acyl migration was found in the oxidation, at reflux, of 2-cyclopentylidenecyclopentanone (76) which gave spiro [4.5]decane-6,10-dione (78) in 43% yield (conversion, 27%).



Surprisingly, 78 does not seem to have been previously prepared. Its structural assignment rests on spectral data and chemical transformations. It had infrared carbonyl bands at 1720 and 1695 cm^{-1}. The nmr spectrum showed a triplet (4H) at τ 7.38 (methylene protons α to the carbonyl) and multiple absorption between τ 7.65 and 8.60 (10H). Compound 78 was converted with base to 5-cyclopentyl-5-oxopentanoic acid 78, whose semicarbazone had a melting point in agreement with the reported value.

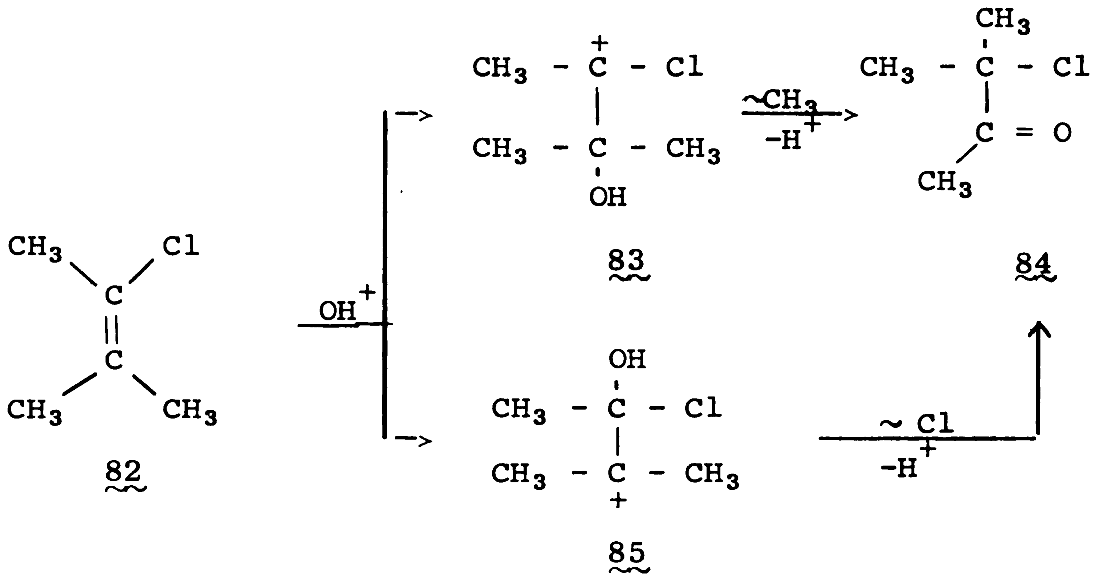


Interestingly House (26) could not affect a similar rearrangement of the epoxide of 2-cyclohexylidenecyclohexanone (80) with boron fluoride etherate, though it could be rearranged thermally to give the expected product 81.

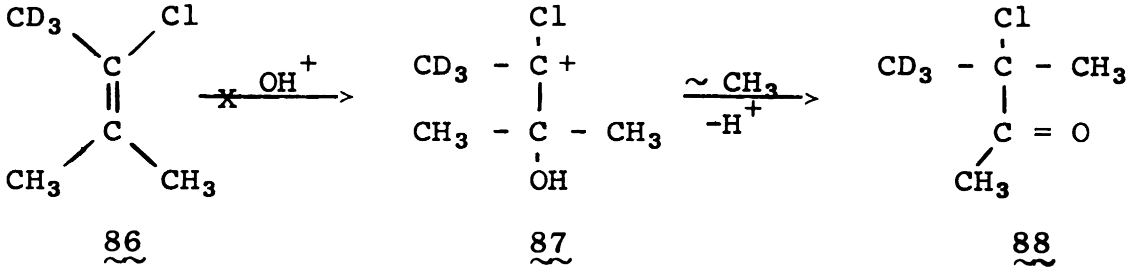


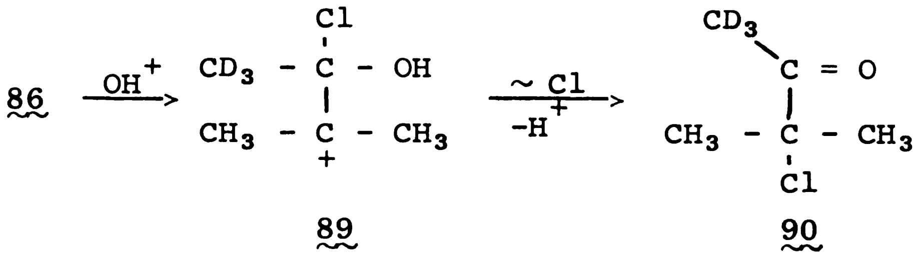
N. Oxidation of 3-Chloro-2-methyl-2-butene (82)

Oxidation of 3-chloro-2-methyl-2-butene (82) offered the interesting possibility for methyl or chlorine migration. The less common chlorine migration has been reported in other olefinic systems (27). The only oxidation product of 82 was 3-chloro-3-methyl-2-butanone (84), obtained in 77% yield. The structure of the product was assigned on the basis of its nmr and infrared spectra (see Experimental Section). This product could arise from two possible intermediates, 83, in which a methyl migrates, and 85, in which chlorine migrates.



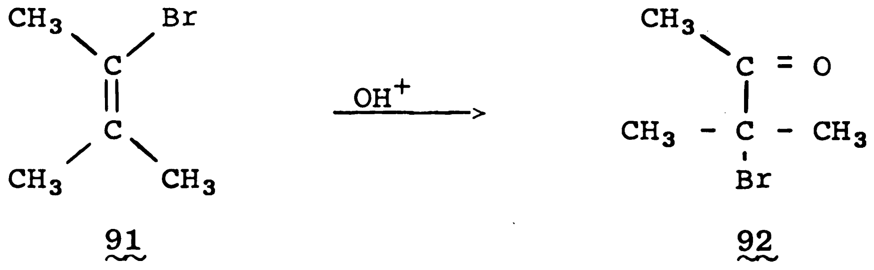
To decide between these alternatives, deuterium labeled starting material 86 was prepared and oxidized. The product isolated had an nmr spectrum consisting of one singlet at τ 8.36. If methyl migration had occurred the product 88 would have had two singlets. The actual product must have arisen, therefore, from chlorine migration where the expected ketone 90 would have only a single peak in its nmr spectrum.





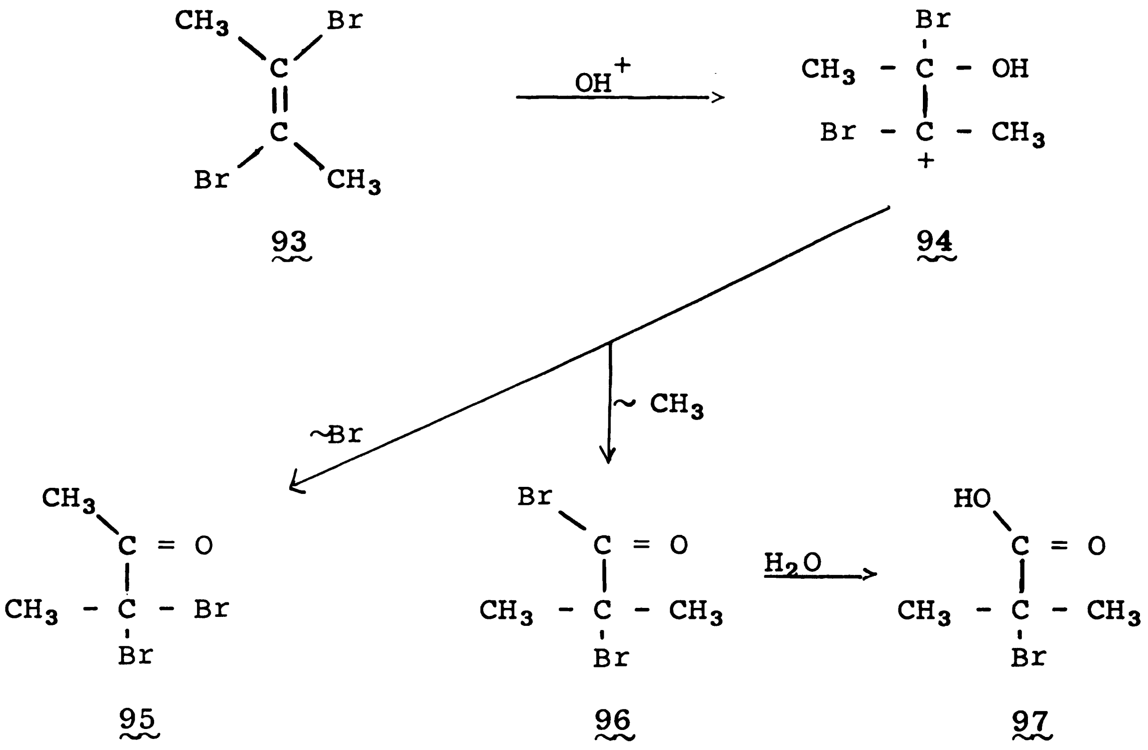
O. Oxidation of 3-Bromo-2-methyl-2-butene (91)

To determine whether halogens, other than chlorine might migrate, 3-bromo-2-methyl-2-butene (91) was oxidized. The major product, obtained in 79% yield, was the expected 3-bromo-3-methyl-2-butanone (92) identified by its infrared and nmr spectra. Since suitably labeled bromobutene could not be synthesized easily to test whether methyl or bromine migration had occurred, attention was turned to the oxidation of the following compound.



P. Oxidation of 2,3-Dibromo-2-butene (93)

In the oxidation of 2,3-dibromo-2-butene (93) two different products 95 and 97, would be obtained from bromine and methyl migration, respectively. Vpc analysis showed only one product from the oxidation of 93, identified as 3,3-dibromo-2-butanone (95), obtained in 69% yield (conversion, 61%). The structural assignment rests on infrared and nmr spectra, elemental analysis, and independent synthesis (see Experimental Section). Since the product was a ketone rather than an acid, bromine migration must have taken place. Although bromine migration in other carbonium ion rearrangements have been reported (28) it appears

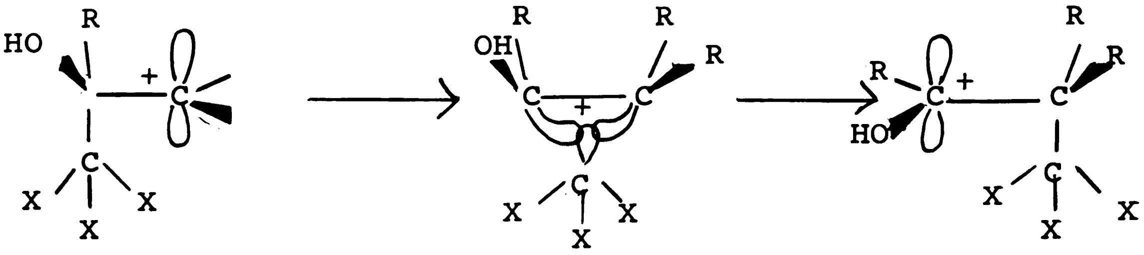


that these are the first examples of a pinacol-type rearrangement with bromine as the migrating group.

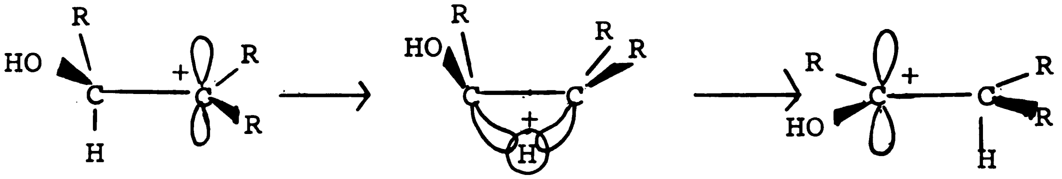
Q. Generalizations about the Oxidation of Alkenes to Ketones Using Peroxytrifluoroacetic Acid - Boron Fluoride

1. Migratory Preferences. As stated earlier, the migratory aptitudes we have observed parallel those found in other Wagner-Meerwein rearrangements. The actual preferences that we have found are H > 2^0 alkyl, or methyl; acyl > 2^0 alkyl > methyl; and chlorine or bromine > methyl.

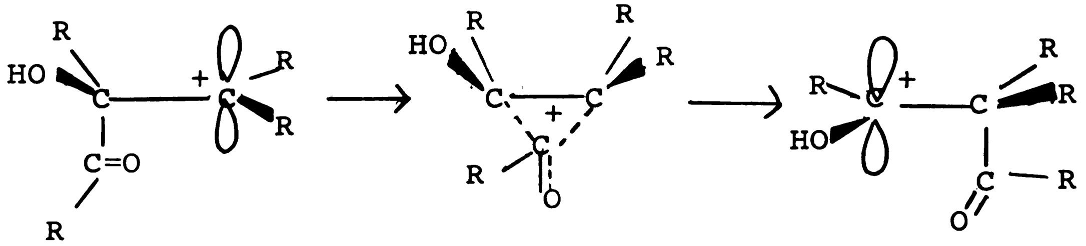
The reasons for various migratory aptitudes are not at all clear since steric hindrance, neighboring group participation (during formation of the carbonium ion), and solvent or temperature effects may play important roles in determining the ability of a group to migrate (4,11,29). In general, the ability to stabilize the positive charge in the transition state is always an important factor. The order of the migratory aptitudes of alkyl groups (3° > 2° > 1°) can be explained in this way. Stabilization of the positive charge is increased with an increase in the number of electron-donating groups attached to the migrating carbon atom. The addition of alkyl groups (which are electron-donating) would then lower the energy of the transition state and thus increase the probability of migration.



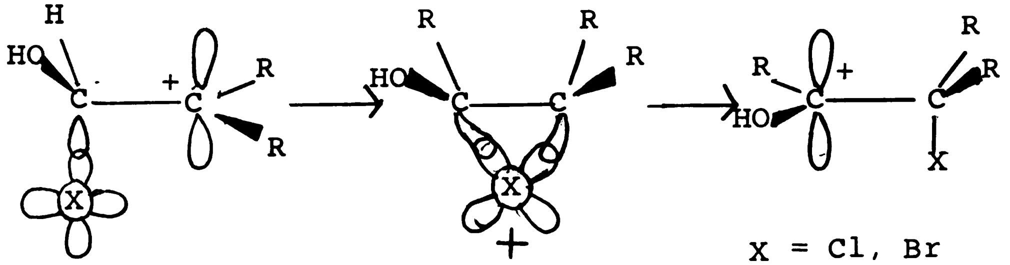
The high migratory aptitude of hydrogen may be due to its small size. It could easily assume the proper position (parallel to the vacant p orbital) for migration to the electron-deficient center. The fact that an s orbital is involved in the migration might be an important factor in the ability of hydrogen to migrate. The spherical s orbital may be capable of better overlap with the other orbitals in the transition state than would the sp^3 orbital of carbon.



The rather high migratory aptitude of acyl groups might be explained by the possibility of additional delocalization of the positive charge to oxygen. This additional delocalization should lower the transition state energy and thereby favor the migration of this group.

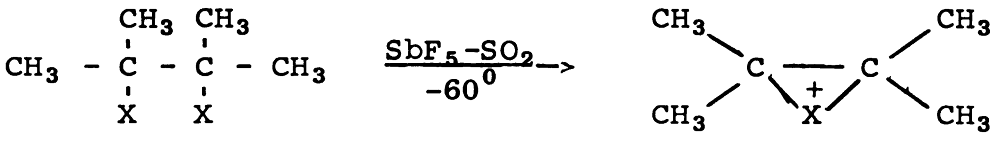


Migration of bromine or chlorine might be favored over methyl migration because of the possibility of overlap of the available p orbitals of these halogens in the transition state. In fact, Olah (30) observed the nmr



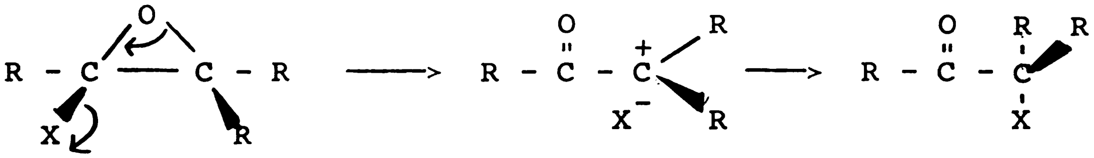
X = Cl, Br

spectra of halonium ions, when 2,3-dihalo-2,3-dimethylbutanes were ionized at -60^0 in antimony pentafluoride-sulfur dioxide.



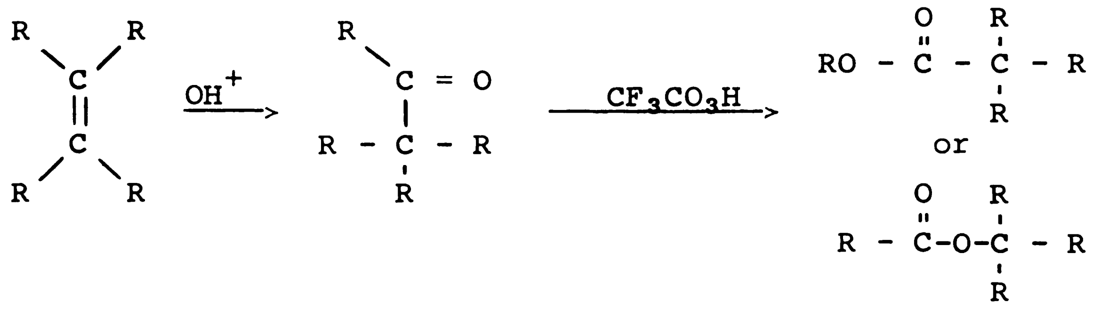
X = I, Br, Cl.

Another possibility is the formation of an ion-pair from the initially formed epoxide (if the peroxytrifluoroacetic acid - boron fluoride oxidation of alkenes involves an epoxide intermediate). Such an intermediate has been

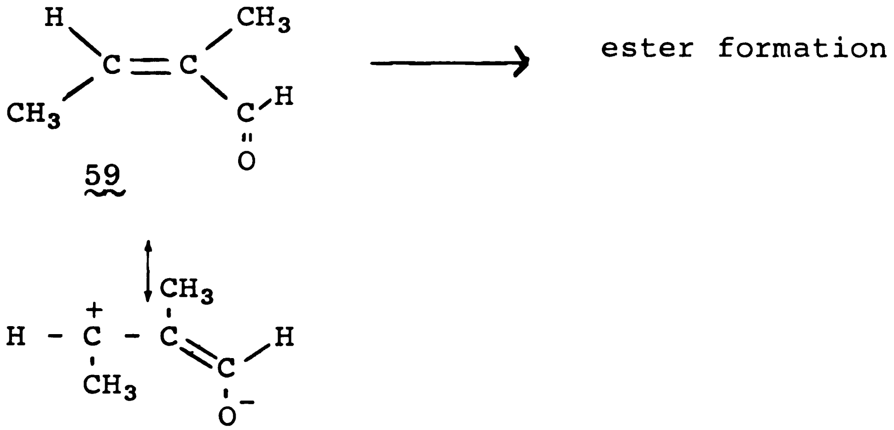


suggested by McDonald and Tabor (27) to explain the products they found in the thermal rearrangement of α-chloroepoxides. Even if such an ion-pair were formed in the rearrangement of the chloroalkenes under our oxidation conditions, it would not necessarily be true for the bromine migrations we have observed. Since bromine is less electronegative than chlorine, ion-pair formation may not be as favored and the formation of a bromonium ion intermediate or transition state may occur instead. In fact, any of the migrations that we have observed could be explained on the basis of a bridged intermediate rather than a transition state. Whatever the factors are which are involved in determining the migratory aptitudes that we have found, they seem in no way different from those observed in related systems.

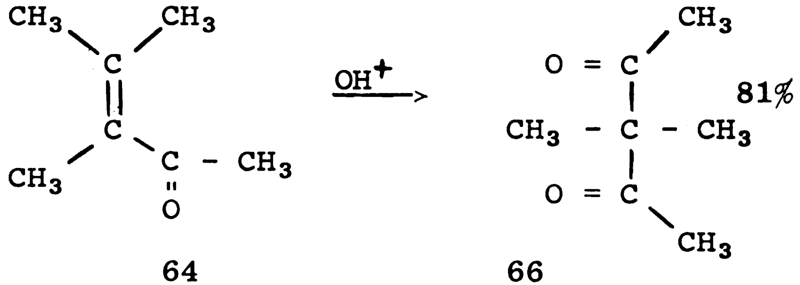
2. The Effect of Substituents on the Double Bond. Since the attack of "positive hydroxyl" on the double bond of alkenes is electrophilic, it would be reasonable to believe that such an attack would be more highly favored when the electron density of the double bond is increased and less favored when the electron density is decreased. The fact that we found that tetra-alkyl substituted alkenes gave better yields of ketones than tri-alkyl substituted alkenes supports this belief. Since alkyl groups are electron-donating, then the more alkyl substituents present, the higher would be the electron density at the double bond. Since the peracid can attack the initially formed ketone to give further oxidation products, there is competition between oxidation of the double bond and the oxidation of the ketone. The more susceptible the alkene is to oxidation, the less likely is the probability of further oxidation of the product.



The over-oxidation of tiglaldehyde (59) is also a reflection of reduced electron density about the double bond. Compound 59 is only tri-substituted and one of the substituents is an electron-withdrawing aldehyde group. Upon replacing the hydrogen and aldehyde substituents with methyl

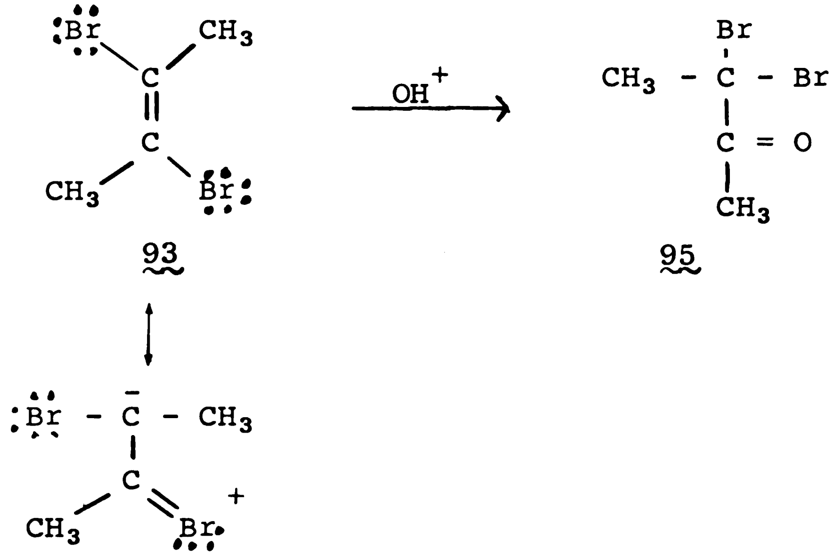


and acetyl groups, the increased electron donation to the double bond is apparently sufficient to cause the oxidation of the double bond of 64 to be preferable to the oxidation of the diketone product 66 (though, some oxidation of the product 66 must also take place since some starting material is recovered; conversion of 64 to 66 was 61%). In the case of both 59 and 64, oxidation of the carbonyl group of the starting material may take place prior to oxidation of the double bond as well as after.

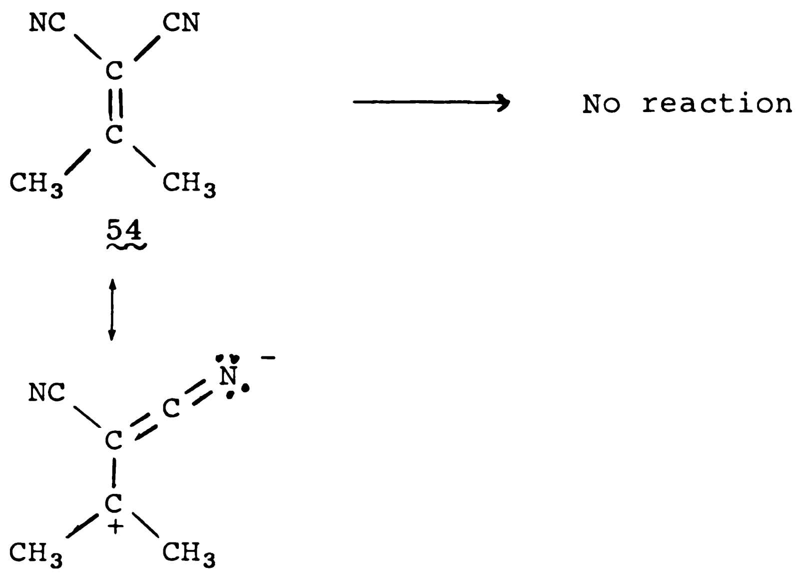


64 66

The presence of halogens about the double bond might also be expected to lower the yield of the anticipated product due to the electronegativity of halogens. But even in the oxidation of 2,3-dibromo-2-butene (93), the yield of ketone 95 was 69%. The relatively high yields of ketones obtained in the oxidation of the haloalkenes that we have studied may be due to the ability of halogens to supply electrons to the double bond through participation of their non-bonding electrons.



The decrease in electron density of the double bond when nitrile substituents are present is apparently great enough to deactivate the double bond toward effective electrophilic attack. In the case of the alkylidenemalononitrile 54, no reaction with peroxytrifluoroacetic acid - boron fluoride took place at all.



54

From our results it is apparent that the conversion of alkenes to ketones is most effective when the alkene being oxidized is highly substituted with electron-donating groups, and least effective when substituted with electron-withdrawing groups.

EXPERIMENTAL

A. General Procedures

1. Melting Points. Melting points were measured on a Gallenkamp melting point apparatus and are uncorrected.

2. Microanalyses. Microanalyses were carried out by Spang Microanalytical Laboratory, Ann Arbor, Michigan.

3. Infrared Spectra. Infrared spectra were obtained on either a Unicam SP 200 or Perkin-Elmer 237B spectrophotometer in CCl_4 solution unless otherwise stated.

4. Mass Spectra. Mass spectra were obtained with a Consolidated Electrodynamics Corporation 21-103C instrument.

5. Nuclear Magnetic Resonance Spectra. These spectra were obtained with either a Varian A-60 or JEOL JNM-C-60H spectrometer, using CCl_4 solutions with tetramethylsilane as an internal standard.

6. Gas Chromatography. All gas chromatographic work was carried out with Varian-Aerograph instruments.

B. General Oxidation Procedures.

1. Using Fisher certified methylene chloride, a methylene chloride solution of peroxytrifluoroacetic acid (31) was prepared by adding in sequence 15.3 g (0.073 mole)

of trifluoroacetic anhydride (City Chemical Corporation) and 1.78 ml (0.066 mole) of 90% hydrogen peroxide (FMC Corporation) to 20 ml of methylene chloride at 0°. The solution was gently swirled at 0° until homogeneous, then allowed to warm to room temperature for several minutes before once again cooling to 0°.

A solution of 0.060 mole of alkene in 100 ml of methylene chloride was prepared in a 500-ml three-necked flask bearing an ice-jacketed addition funnel, thermometer and pressure-equalizing addition funnel. All openings were equipped with drying tubes containing drierite. The solution was cooled to -5° in an ice-ethanol bath and agitated by means of a magnetic stirrer. The cold peroxytrifluoroacetic acid solution was then added dropwise at a constant rate to the alkene solution by means of the ice-jacketed addition funnel over a period of 20 minutes, during which time 8.3 ml (0.066 mole) of 47% boron fluoride etherate (Eastman Organic Chemicals) was added, also dropwise at a constant rate, to the alkene solution by means of the pressure-equalizing funnel. The temperature was kept below 8° during the addition of the reagents.

The mixture was stirred at 0° for 15 minutes after addition was completed, then hydrolyzed with 35 ml of water. The organic layer was washed consecutively with two 35-ml portions of water, three 35-ml portions of saturated aqueous sodium bicarbonate, and two 35-ml portions of water. The solution was then dried over anhydrous magnesium sulfate, filtered, and the solvent partially evaporated by means of a rotary evaporator. The residue was diluted with methylene chloride to exactly 100 ml. A small portion of this solution was set aside for yield determination by vpc comparison with a standard methylene chloride solution of the product. The solvent was removed from the remainder of the solution and vpc analysis carried out on the residue. It should be noted that many alkene solutions turned deep blue or violet during the addition of the reagents and that these solutions faded to yellow or orange during the workup procedure.

2. The above procedure was followed except that the methylene chloride solution of alkene was not cooled, and the rate of adding reagents was adjusted so that the solution refluxed gently. Addition time of the reagents was 10 minutes.

C. Preparation of Alkenes.

1. $\Delta^{9,10}$-Octalin (41). The procedure of Campbell and Harris (32) was followed. To a mechanically stirred solution of 200 g of phosphorus pentoxide in 2000 g of 85% phosphoric acid was added 190 g of mixed β-decalols. The temperature of the mixture was raised to 150° for 10 minutes. While this temperature was maintained, a slight vacuum was applied and the octalin was steam distilled by the dropwise addition of water. The distillation was continued until no more octalin was obtained. The product was

taken up in ether, dried over anhydrous magnesium sulfate and filtered. After the solvent was removed, the product was distilled from sodium (bp 190-194°). The yield was 99.3 g (56%).

This product was heated, with stirring, with 44 g of phosphorus pentoxide at 140° for 1.5 hrs. The flask was cooled and ice added to react with the phosphorus pentoxide. The octalin was taken up in ether, dried over anhydrous magnesium sulfate, filtered, and the solvent removed. Distillation on a stainless steel spinning band column gave 35 ml of product, bp 193-194° (lit. 32, 190-192°) which was 94% pure according to vpa analysis on a 5-ft Carbowax column at 150° (ir spectrum, Figure 18). The major impurity, with a lower vpc retention time and bp, was apparently the isomeric $\Delta^{1,7}$-octalin (lit. 32, bp 189.5-193.5°).

2. 1,2-Dimethylcyclohexene (**36**). Methylmagnesium iodide was prepared from 24.3 g (1.0 mole) of magnesium and 93 ml (1.0 mole) of methyl iodide in a final volume of 300 ml of anhydrous ether using the standard procedure. The Grignard solution was cooled in an ice-ethanol bath. 2-Methylcyclohexanone (100 g, 0.89 mole) was added to the vigorosuly stirred solution by means of a dropping funnel, at such a rate that the temperature of the reaction mixture was kept below 5°. After addition was completed the mixture was allowed to warm to room temperature and hydrolyzed with 40 ml of concentrated sulfuric acid in ice and 200 ml of water. The two layers were separated and the aqueous layer

was extracted with two 100-ml portions of ether. The combined ether layers were then washed consecutively with 100 ml of water, to which had been added 5 ml of saturated aqueous sodium bicarbonate, and twice with 100-ml portions of water. The ether solution was then dried over anhydrous sodium sulfate, filtered and the solvent removed with a rotary evaporator. The resulting oil weighed 88.6 g (78% if all the oil was alcohol).

The alcohol was dehydrated by adding a small crystal of iodine and distilling through a 6-in Vigreaux column. The product which distilled from 88 to 133° was saturated with salt and the organic layer separated. After being dried over anhydrous calcium chloride, the filtered product was redistilled through a stainless steel spinning band column. The fraction boiling at 135° (17 ml, lit. 33, 136°) was 93% pure according to vpc analysis on a 5-ft SE-30 column at 100° (nmr and ir spectra, Figures 1 and 19 respectively).

3. *2-Methyl-3-phenyl-2-butene (45).* In a one-liter three-necked flask equipped with a reflux condenser protected with a drying tube, mechanical stirrer and pressure-equalizing funnel was added 260 ml (0.78 mole) of three molar phenylmagnesium bromide (Arapahoe Chemicals). The stirred solution was cooled with an ice bath and by means of the pressure-equalizing funnel, 70.5 ml (0.67 mole) of 3-methyl-2-butanone in 75 ml of anhydrous ether was added, dropwise.

After addition of the ketone was completed, the reaction mixture was stirred at room temperature for one hr, then poured into a mixture of ice, 200 ml of water and 40 ml of concentrated sulfuric acid. The layers were separated and the aqueous layer extracted with ether. The combined ether layers were washed consecutively with 100 ml of saturated aqueous sodium bisulfite, two 100-ml portions of water and 100 ml of saturated aqueous salt solution. After the product was dried over anhydrous magnesium sulfate, filtered, and the solvent evaporated with a rotary evaporator, 60 g of potassium bisulfate was added to the residue and the material was vacuum distilled. The distillate (65 g, 66%) was a clear colorless liquid, bp_5 68-69^0 (lit. 34, bp_{20} 95-97^0). Vpc analysis on a 5-ft SF-96 column at 170^0 showed one peak but nmr analysis showed that the product was a mixture containing 63% of 2-methyl-3-phenyl-2-butene and 37% 3-methyl-2-phenyl-1-butene. The nmr spectrum (Figure 2) showed a complex absorption, assigned to the phenyl protons of both compounds, centered at τ 2.90. The slightly split doublet (J = 7.0 cps) at τ 4.95 (2 H), multiplet (J = 7.0 cps) centered at τ 7.23 (1 H) and the doublet (J = 7.0 cps) at τ 8.93 (6 H) were assigned to the latter compound while the three broad and slightly split singlets of equal intensity at τ 8.08, τ 8.25 and τ 8.40 were assigned to the former. This material was distilled through a stainless spinning band column to give three fractions; these consisted of 15 ml (bp_5 65-69°) of material which contained 46% of the desired isomer, 20 ml (bp_5 69-69.5°) of material which contained 57% of the desired isomer and 10 ml (bp_5 69.5-69.5°) of material which contained 80% of the desired isomer (nmr spectrum, Figure 3).

4. 3,4-Dimethyl-3-penten-2-one (64). This compound was prepared following the method of Colonge and Mostafari (35). Stannic chloride (4.48 ml) was added, dropwise, to a stirred, ice-cold solution of 150 ml (1.43 moles) of 2-methyl-2-butene and 50 ml (0.66 mole) of acetyl chloride in a 500-ml three-necked flask equipped with a mechanical stirrer, thermometer and pressure-equalizing funnel. The temperature of the reaction mixture was kept between 10 and 22° during the addition. The reaction was very exothermic during the addition of the first two ml of stannic chloride. The reaction mixture was stirred at 0° for 15 min after the addition was completed. After being warmed to room temperature, the reaction mixture was poured onto 400 ml of 15% hydrochloric acid, washed consecutively with water and saturated aqueous sodium bicarbonate, dried over anhydrous magnesium sulfate, filtered, and the solvent removed with a rotary evaporator. The residue was vacuum distilled and the distillation stopped at 31° (45 mm).

The residue was refluxed with 85 g of dimethylaniline for one hr. The upper layer was then washed with water, dried, filtered, and distilled through a 30-cm column packed with glass helices. The product collected (22.2 g, 30%, bp 144-148^0 (lit. 35, 146^0)) was 94% pure according to vpc analysis on a 5-ft FFAP column at 140^0. The nmr spectrum of this compound is shown in Figure 4.

5. 4-Methyl-$\underline{d}_3$-3-methyl-3-penten-2-one-1,1,1,5,5,5-$\underline{d}_6$(71). 3,4-Dimethyl-3-penten-2-one (18 g, 0.16 mole) was stirred for 77 hrs with 238 g (7.2 moles) of MeOD, to which a small piece of sodium had been added. The alcoholic solution was then poured into 250 ml of methylene chloride and washed with 50-ml portions of water until the aqueous layer was clear and neutral to litmus. The methylene chloride layer was then dried, filtered and the solvent removed with a rotary evaporator. The colorless, distilled product, bp 144-148^0, was 90% pure (vpc analysis) and the nmr spectrum (Figure 5) showed that the two olefinic methyl groups were 66% deuterium labeled and the methyl group in the one position at least 98% labeled.

6. 2-Cyclopentylidenecyclopentanone (76). The procedure of Mayer (36) was followed. To a two liter flask cooled with an ice bath and equipped with a dropping funnel, condenser and drying tubes containing drierite, was added 450 ml of absolute ethanol followed by 30 g of sodium. After all the sodium had reacted, 400 g (4.8 mole) of cyclopentanone was added, dropwise, to the chilled solution. The resulting red-brown reaction mixture was kept at 0^0 for one

day and the solution then decanted from the solid which had formed. Most of the ethanol was removed with a rotary evaporator. Water was then added to the residue and the two resulting layers were separated. The organic layer, after being dried over anhydrous magnesium sulfate and filtered, was vacuum distilled. The resulting pale green liquid (85 g, 24%) $bp_{0.7}$ 83-85° (lit. 36, bp_2 88.5-90.0°), was greater than 99% pure according to vpc analysis on a 10-ft FFAP column at 235° (ir spectrum, Figure 20).

7. 3-Chloro-2-methyl-2-butene (82). This alkene was prepared following the procedure of Behal (37). 3-Methyl-2-butanone (68 g, 0.8 mole) was added dropwise, with stirring, to 166 g of phosphorus pentachloride cooled with an ice bath. After addition was completed, the reaction mixture was allowed to warm slowly and refluxed 3.5 hrs (HCl was evolved). The resulting solution was poured onto ice and the layers were separated. The organic layer was washed with saturated aqueous sodium bisulfite followed by water. After being dried over anhydrous magnesium sulfate and filtered, the crude product was distilled through a Teflon spinning band column. The colorless liquid, bp 93-98° (lit. 37, 97-98°) was collected (7.9 g, 9.3%) and by vpc analysis on a 5-ft XF-96 column at 70° was 90% pure (nmr spectrum Figure 6). The major impurities appear to be the starting ketone and the other dehydrochlorination isomer, 2-chloro-3-methyl-1-butene (ir bands at 1710 and 1635 cm^{-1} respectively).

8. 2-Chloro-3-methyl-2-butene-1,1,1-$\underline{d}_3$ (86). This compound was prepared as above except that 3-methyl-2-butanone-1,1,1,4-$\underline{d}_4$ was used. This ketone was prepared by refluxing, for two days, 90 ml (0.85 mole) of unlabeled ketone with 125 ml (6.9 moles) of D_2O, to which had been added a spatula of anhydrous potassium carbonate. The two layers were then separated and the aqueous layer was extracted with methylene chloride. The organic layers were combined, washed with water, dried over anhydrous magnesium sulfate, filtered and the solvent distilled (the distillation was stopped at a head temperature of 48^0). The nmr spectrum showed that the one position was about 80% deuterium labeled. The alkene prepared from this ketone also showed, in its nmr spectrum (Figure 7), about 80% deuterium label in the one position.

D. Results of Alkene Oxidations

1. 2,3-Dimethyl-2-butene (17). This alkene (7.09 ml, 0.060 mole, Aldrich Chemical Co.) was oxidized by procedures B1 and B2. Vpc analysis on a 20-ft SE-30 column at 80^0 showed one major product peak. This product was identified as 3,3-dimethyl-2-butanone (pinacolone) by comparison of its vpc retention time, and ir and nmr spectra with those of an authentic sample. The yield of pinacolone was 72 and 75% by procedures B1 and B2 respectively.

2. *2-Methyl-2-butene (**21**).* The oxidation of 6.3 ml (0.060 mole) of 2-methyl-2-butene (Aldrich Chemical Co.) by procedure B1 resulted in a 53% yield of 3-methyl-2-butanone. Vpc analysis was carried out on a 5-ft FFAP column at 80°. The product was identified by comparison of its vpc retention time and ir and nmr spectra with those of an authentic sample.

3. *cis-3-Methyl-2-pentene (**26**).* The oxidation of 7.3 ml (0.060 mole) of this alkene (Aldrich Chemical Co.) by procedure B1 resulted in a 63% yield of 3-methyl-2-pentanone according to vpc analysis on a 5-ft SE-30 column at 120°. The product was identified by its nmr spectrum (triplet at τ 9.15 (3 H), doublet at τ 8.97 (3 H), multiplet at τ 8.57 (2 H), singlet at τ 7.97 (3 H) and multiplet at τ 7.63 (1 H)) and the identity of its ir spectrum with the published spectrum (38).

4. *trans-3-Methyl-2-pentene (**27**).* This alkene (7.3 ml, 0.060 mole, Aldrich Chemical Co.) was oxidized in the same manner as the *cis* isomer. The yield of 3-methyl-2-pentanone was 70%.

If the boron fluoride etherate is excluded from the oxidation, vpc analysis of the residue shows only small amounts of ketone, the major volatile products being three compounds with longer retention times which have the following ir bands in common: 3600, 1780 and multiple bands between 1250 and 1050 cm^{-1}. These products appear to be hydroxytrifluoroacetates similar to the ones Emmons (3) has obtained in his studies on peroxytrifluoroacetic acid oxidations of alkenes. This residue was then dissolved in 100 ml of methylene chloride, cooled to 0° and 17 ml of boron fluoride ethereate was added dropwise, with stirring. After standing at 0° for 1 hr after addition was completed the solution was worked up as described in procedure B1. Vpc analysis of the residue now showed only one peak which was identified as 3-methyl-2-pentanone.

5. 1-Methylcyclohexene (30). This alkene (7.0 ml, 0.060 mole) was oxidized by both procedure B1 and B2. Using procedure B1 the yield of the only detectable oxidation product, 2-methylcyclohexanone, was 8%. Vpc analysis was carried out on a 10-ft Apiezon L column at 115° and this product was identified by comparison of its ir and nmr spectra and vpc retention time with those of an authentic sample. The only other major volatile product detected was 1-methylcyclohexyl trifluoroacetate (15%). This product was identified by its nmr and ir spectra (Figures 8 and 21 respectively). It was also prepared as the exclusive product by mixing at 0°, 0.0041 mole each of 1-methylcyclohexene in 70 ml of methylene chloride, boron fluoride etherate and trifluoroacetic acid. This solution was kept at 0° for 3 hrs, hydrolyzed with 10 ml of water and washed with 10 ml of 5% aqueous sodium hydroxide followed by 10 ml

of water. After the product was dried over anhydrous magnesium sulfate, filtered and the solvent evaporated, vpc analysis showed one peak with the same retention time and ir spectrum as the trifluoroacetate found in the oxidation.

Following procedure B2, the yield of 2-methylcyclohexanone was 41%, whereas the yield of trifluoroacetate was 9%.

6. 1,2-Dimethylcyclohexene (**36**). Procedure B1 was followed using 7.1 g (0.060 mole) of 93% pure 1,2-dimethylcyclohexene. One major product was detected by vpc analysis on a 5-ft SE-30 column at 150° and it was assigned the structure 1-acetyl-1-methylcyclopentane on the following evidence. The compound had a carbonyl band in the ir at 1700 cm^{-1}; the nmr spectrum consisted of two singlets at τ 7.87 and τ 8.77 (3 H each) and a broad band at τ 7.93-8.85 (8 H). The distilled material, bp$_7$ 50 (lit. 18, bp$_{11}$ 50.2-50.9) gave a semicarbazone, recrystallized from 20% ethanol, with a mp 139.5-141.0° (lit. 18, 141°). The yield of ketone was 76%.

7. $\Delta^{9,10}$-Octalin (**41**). Procedure B1 was followed, 8.7 g (0.060 mole) of 94% pure octalin gave a 79% yield (vpc analysis on a 5-ft SE-30 column at 180°) of spiro[4.5]decan-6-one (86% yield based on consumed starting material). The structure assignment was based on the following evidence

The compound had a carbonyl band in the ir at 1700 cm^{-1} and the distilled product, bp_1 45-55 (lit. 39, bp_{20} 105-110), gave a semicarbazone which, recrystallized from ethanol, had a mp of 187-190° (lit. 40, 188-190°).

8. *2-Methyl-3-phenyl-2-butene (45)*. A mixture (8.8 g, 0.060 mole) containing 80% 2-methyl-3-phenyl-2-butene and 20% 3-methyl-2-phenyl-1-butene was oxidized by procedure B2. The single product (vpc analysis on a 5-ft SF-96 column at 170°) was 3-methyl-3-phenyl-2-butanone in 77% yield based on the total amount of both alkenes and 96% based on the tetra-substituted alkene. When the oxidation was repeated using a mixture containing 46% 2-methyl-3-phenyl-2-butene and 54% of the other isomer, the yield of 3-methyl-3-phenyl-2-butanone was 73% based on both alkenes and 117% based on the tetra-substituted alkene.

The product was assigned its structure on the following evidence. It had a carbonyl band in the ir (liquid film) at 1701 cm^{-1} (lit. 41, ν^{KBr} at 1701 cm^{-1}) and an nmr spectrum consisting of three singlets at τ 2.79 (5 H), τ 8.08 (3 H) and τ 8.58 (6 H). The semicarbazone, obtained from vpc purified material, after recrystallization from ethanol, had a mp of 185-187° (lit. 42, 185-187°).

9. *3,4-Dimethyl-2,5-dihydrothiophene-1,1-dioxide (50)*. This alkene [(43), 7.9 g, 0.054 mole] was oxidized by procedure B2 but worked up as follows. The reaction mixture was hydrolyzed with 35 ml of water, 20 min after the addition

of the reagents was completed. The organic layer was then washed with two 35-ml portions of water followed by 35-ml portions of 10% aqueous sodium hydroxide until the aqueous layer was no longer yellow. The combined alkaline washes were acidified with concentrated hydrochloric acid, saturated with salt and extracted with four 50-ml portions of methylene chloride. After the product was dried over anhydrous magnesium sulfate and filtered the solvent was evaporated leaving a residue (2.0 g) of viscous yellow oil. The original methylene chloride layer, after drying, filtering and evaporating the solvent, yielded 0.4 g of off white solid which decomposed at 158°. These products were not further investigated due to the small amount of material recovered.

10. *Isopropylidene Malononitrile (**54**).* This compound did not react under the reaction conditions of procedure B2. The reaction mixture did not warm nor darken in color during the addition of the reagents. After workup, the colorless residue showed only one peak on the vpc (10-ft FFAP column at 225°) with the same retention time as the starting material.

11. *3-Ethyl-2-methyl-2-pentenenitrile (**55**).* This alkene [(44), 7.8 g, 0.060 mole] was oxidized by procedure B2. This oxidation differed from most of the other alkene oxidations studied in that the solution did not warm to reflux during the addition of the reagents until the addition

was almost complete and then continued to reflux, without external heating, for about 10 min. After workup, the residue showed only one major peak in the vpc (5-ft SE-30 column at 150-240°) which had the same retention time and ir spectrum as the starting material. Vacuum distillation, bp_2 40-133°, gave mostly starting material with considerable amounts of tar as the residue. Investigation of this oxidation was stopped at this point.

12. <u>2-Methyl-2-butenal [(59), tiglaldehyde]</u>. This compound (25.2 g, 0.30 mole) was oxidized using a variation of procedure B2 and five times the quantity of reagents and solvent. The addition time of the reagents was 55 min. The reaction mixture was then refluxed for 3 hrs, hydrolyzed with 125 ml of saturated aqueous sodium chloride and washed consecutively with three 100-ml portions of the salt solution, three 100-ml portions of saturated aqueous sodium bicarbonate and one 100-ml portion of salt solution. The sodium bicarbonate washings were combined and extracted with 100 ml of methylene chloride. After the combined organic layers were dried and filtered, the solution was distilled until a head temperature of 43° was reached. The residue was diluted to 100 ml with methylene chloride and vpc analysis on a 5-ft Carbowax column at 145° showed that 14.6 g of starting material remained. The only other peaks on the vpc trace were from two oxidation products with almost identical retention times, which amounted to about 3.2 g.

These products were not fully characterized but showed the following spectral characteristics. A mixture of the two compounds (vpc collected) showed strong carbonyl absorption in the ir at 1722 cm^{-1} and strong absorption between 1150 and 1250 cm^{-1}, which could be associated with an ester group. The peak with longest retention time was collected and showed in its nmr spectrum a quartet (J = 7 cps) at τ 5.03 (1 H), a singlet at τ 7.90 (6 H) and a doublet (J = 7 cps) at τ 8.67 (3 H) which could possibly be assigned to the structure shown on page 22 (63). The other product showed in its nmr spectrum a singlet at τ 1.96 (1 H), a quartet (J = 7 cps) at τ 4.89 (1 H), singlet at τ 7.87 (3 H) and a doublet (J = 7 cps) at τ 8.62 (3 H). This spectrum fits well for the formate ester of 3-hydroxy-2-butanone (62). This compound could not be obtained pure enough for a reliable mass spectrum but the former compound could and showed a parent peak at mass 130, base peak at 43 and one prominent peak at 87. These peaks can be readily explained with the assigned structure.

13. <u>3,4-Dimethyl-3-penten-2-one (64)</u>. Procedure B2 was followed in oxidizing this alkene (3.4 g, 0.028 mole) using one half the amount of reagents and solvent. Only starting material and one product were detected by vpc analysis on a 10-ft FFAP column at 160°. The product had a carbonyl band in its ir spectrum at 1700 cm^{-1} and an nmr spectrum consisting of two singlets of equal intensity at

τ 7.93 and τ 8.70, which was consistent with the structure 3,3-dimethyl-2,4-pentanedione (nmr spectrum, Figure 9). In addition, the mp (21-22°) was the same as the reported value (45) for this compound. The yield of diketone was 61% (81% based on consumed starting material).

14. <u>4-Methyl-$\underline{d}_3$-3-methyl-3-penten-2-one-1,1,1,5,5,5-$\underline{d}_6$</u> (**71**). This compound was oxidized in the same manner as the non-deuterated compound described above. The vpc-collected product showed one singlet in its nmr spectrum at τ 7.93 and a much smaller peak at τ 8.70 (Figure 10) and was therefore assigned the structure 3,3-dimethyl-$\underline{d}_6$-2,4-pentanedione-1,1,1-$\underline{d}_3$ with 66% deuterium in the 3-position.

15. <u>2-Cyclopentylidenecyclopentanone</u> (**76**). This alkene (9.0 g, 0.060 mole) was oxidized by procedure B2. Only starting material and one product were detected by vpc analysis on a 10-ft FFAP column at 250°. The ir and nmr spectra (Figures 22 and 11, respectively) of the product were consistent with the structure spiro[4.5]decane-6,10-dione. The yield of diketone was 27% (43% based on consumed starting material).

<u>Anal</u>. Calcd for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49.

Found: C, 72.12; H, 8.60.

Further structure proof was obtained by converting 2 g of distilled product ($bp_{0.9}$ 100-103°, mp 11.5-12.5°) to 5-cyclopentyl-5-oxopentanoic acid by reflux for 30 min with 12 ml of 6N sodium hydroxide in 50 ml of ethanol. The product, after dilution with 60 ml of water and acidification with concentrated hydrochloric acid, was extracted with two 30-ml portions of ether, dried over anhydrous magnesium sulfate, filtered, and the solvent removed with a rotary evaporator. The semicarbazone was then prepared directly from the residue as follows. The residue was taken up in 20 ml of ethanol. Water was then added until the solution became cloudy, followed by clarification with a few drops of ethanol. Semicarbazide hydrochloride (2 g) and sodium acetate (3 g) was then added, dissolved, and the solution heated for a few seconds in a boiling water bath. After being cooled to room temperature, the solution was placed in an ice bath and the sides of the flask were scratched with a glass rod until white crystals formed (1.3 g, 45% overall, mp 176-178°). Repeated crystallization from ethanol gave a constant mp of 180-182° (lit. 46, 181-182°).

Anal. Calcd for $C_{11}H_{19}N_3O_3$: C, 54.76; H, 7.94; N, 17.41. Found: C, 54.62; H, 7.96; N, 17.34.

16. 3-Chloro-2-methyl-2-butene (**82**). Oxidation of 7.04 g (0.060 mole) of 90% pure alkene by procedure B2 gave one major product (vpc analysis on a 10-ft FFAP column at 130°) assigned the structure 3-chloro-3-methyl-2-butanone on the following evidence. The ir spectrum showed a carbonyl band at 1712 cm^{-1} and the nmr spectrum (Figure 12) consisted of two singlets at τ 7.68 (3 H) and τ 8.33 (6 H). The nmr spectrum compared favorably with the published spectrum (lit. 47, singlets at τ 7.65 and τ 8.31).

17. 2-Chloro-3-methyl-2-butene-1,1,1-d_3 (**86**). Procedure B2 was followed, as for the non-deuterated compound. The vpc-collected product had an nmr spectrum (Figure 13) consisting of a singlet at τ 8.36 and a small absorption at τ 7.68. The product was therefore assigned the structure 3-chloro-3-methyl-2-butanone-1,1,1-d_3 with the one position about 80% labeled with deuterium.

18. 3-Bromo-2-methyl-2-butene (**91**). 3-Bromo-2-methyl-2-butene [(48), 8.9 g, 0.060 mole] was oxidized by procedure B2. One major product was detected by vpc analysis on a 10-ft FFAP column at 110^0 and was assigned the structure 3-bromo-3-methyl-2-butanone on the following evidence. The nmr spectrum consisted of two singlets at τ 7.63 (3 H) and τ 8.18 (6 H) and the ir spectrum showed a carbonyl band at 1710 cm^{-1}. Both spectra were, therefore, very similar to the analogous 3-chloro-3-methyl-2-butanone. The yield of ketone was 79%.

19. 2,3-Dibromo-2-butene (**93**). This alkene (6.4 g, 0.030 mole, K & K Laboratories) was oxidized by procedure B2 using half the amount of reagents and solvent. After workup the residue was distilled through a short path distillation apparatus (bp $60\text{-}130^0$, 5.3 g; pot residue 0.5 g). Vpc analysis on a 10-ft SE-30 column at 125^0 showed one major product, comprising 80% of the total peak areas and starting material comprising 14%. This product (61% yield; 69% based on unrecovered starting material) was assigned

the structure 3,3-dibromo-2-butanone on the following evidence. The ir spectrum (liquid film) showed a carbonyl band at 1715 cm^{-1} and the nmr spectrum consisted of two singlets of equal intensity at τ 7.33 and τ 7.50 (lit. 49, τ 7.04 and τ 7.22). This product was also independently synthesized by brominating 2-butanone in the presence of phosphorus following the procedure which Schotte (50) used to brominate 3-pentanone. Vpc analysis showed three products. The first product to appear on the vpc showed, in its nmr spectrum, a quartet (J = 7 cps) at τ 5.65 (1 H), a singlet at τ 7.70 (3 H) and a doublet (J = 7 cps) at τ 8.32 (3 H). This compound was assigned the structure 3-bromo-2-butanone (lit. 51, τ 5.40, τ 7.74, and τ 8.40).

The second product had a vpc retention time, and nmr and ir spectra identical with those of the oxidation product.

<u>Anal.</u> Calcd for $C_4H_6Br_2O$: C, 20.90; H, 2.64; Br, 69.51.

Found: C, 21.01; H, 2.76; Br, 69.66.

The third product showed in its nmr spectrum a quartet (J = 7 cps) at τ 5.10 (1 H), a singlet at τ 5.65 (2 H) and a doublet (J = 7 cps) at τ 8.22 (3 H) (lit. 51, τ 4.88, τ 5.40 and τ 8.00). The difference in chemical shifts between these compounds and the reported values is probably due to the fact that my nmr spectra were obtained from samples dissolved in carbon tetrachloride, containing TMS, whereas the reported spectra were of neat samples, using an external sample of TMS in carbon tetrachloride as the reference.

SUMMARY

1. A number of alkenes were oxidized to ketones in one step by peroxytrifluoroacetic acid - boron fluoride.

2. Electron-withdrawing substituents or the absence of electron-donating groups about the double bond tended to lower the yield of ketone or stop the oxidation altogether.

3. Migratory aptitudes were found to parallel those observed in other Wagner-Meerwein rearrangments.

4. The products were shown to be the result of hydrogen, methyl, acyl, chlorine, or bromine migration, as well as ring contraction and expansion.

5. The products 3-bromo-3-methyl-2-butanone (92) and 3,3-dibromo-2-butanone (95) from the oxidation of 3-bromo-2-methyl-2-butene (91) and 2,3-dibromo-2-butene (93), respectively, are believed to be the result of the first reported examples of bromine migration in a pinacol-type rearrangement.

6. The oxidation of 2-cyclopentylidenecyclopentanone (76) resulted in the first reported synthesis (43% yield) of spiro[4.5]decane-6,10-dione (78).

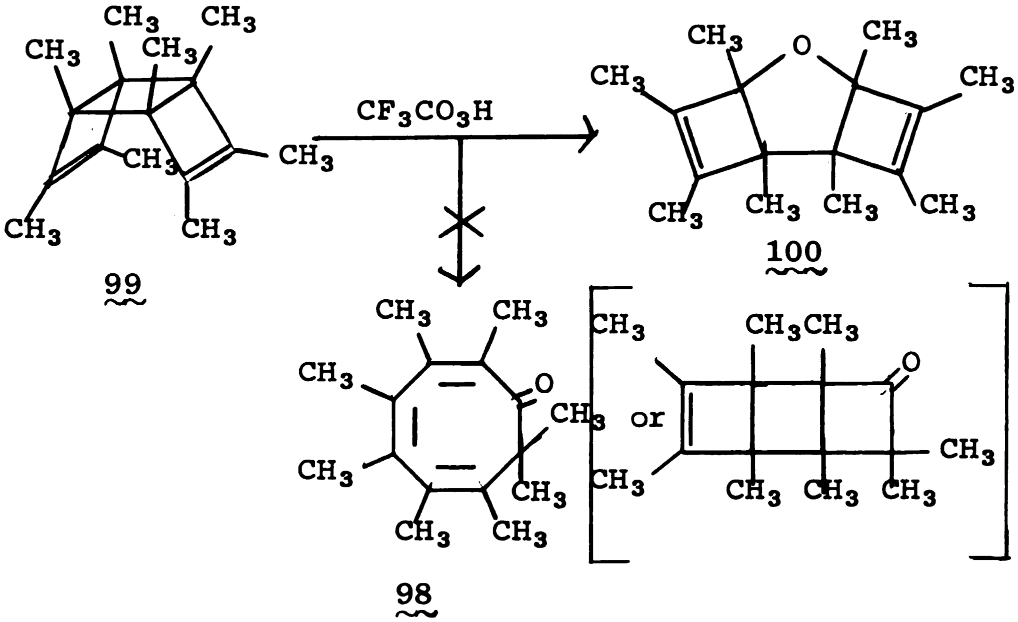
PART II

THE ACID-CATALYZED REARRANGEMENT OF OCTAMETHYL-8-OXATETRACYCLO[$4.3.0.0^{2,5}.0^{7,9}$]NON-3-ENE

INTRODUCTION

The chemistry and photochemistry of hexaalkyl-2,4-cyclohexadienones has been extensively investigated in this laboratory (13,52). We believed that a similar study of the next higher, fully methylated, homolog, octamethyl-2,4,6-cyclooctatrienone (**98**) might be of interest.

An attempted synthesis of this compound, or one of its valence tautomers, by the oxidation of octamethyl-*syn*-tricyclo[4.2.0.$0^{2,5}$]octa-3,7-diene **99** with peroxytrifluoroacetic acid proved unsuccessful. A number of products were obtained, however. One of these, isolated in 6% yield, was assigned the structure **100**.



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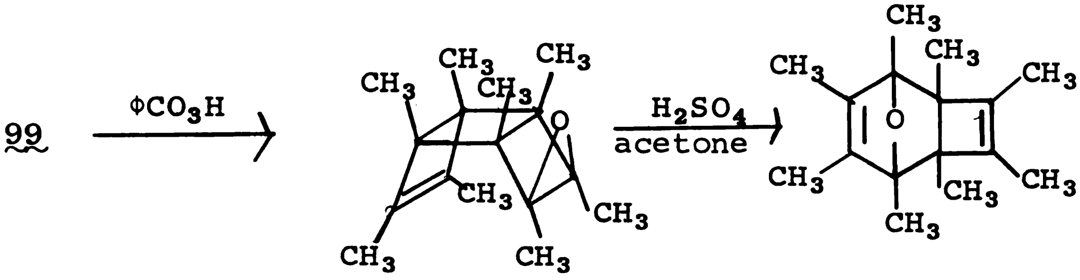
On searching the literature, it was discovered that Maier (53) had prepared what was undoubtedly the same compound by the epoxidation of **99**, followed by acid catalyzed rearrangement, but his structure assignment, 103, was different from ours.



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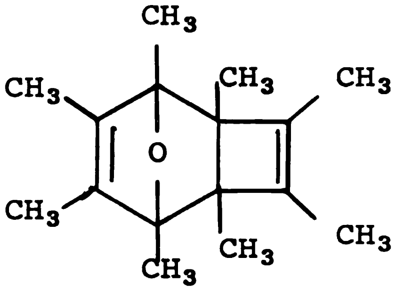
Part II of this thesis is concerned with the structure determination and chemistry of the oxidation product of 99.

RESULTS AND DISCUSSION

A. The Acid-catalyzed Rearrangement of Octamethyl-8-oxa-tetracyclo[$4.3.0.0^{2,5}.0^{7,9}$]non-3-ene (102)

1. Nuclear Magnetic Resonance and Infrared Spectra.

The nmr and ir spectra of the product from the peroxytrifluoroacetic acid oxidation of 99 and the acid-catalyzed rearrangement of 102 were identical in every respect. Maier's assignment (53) of structure 103 was based on the following evidence. The ir spectrum showed a sharp band at 1695 cm^{-1} assigned to the disubstituted double bond of the four-membered ring. The nmr spectrum showed four equally intense peaks; quartets (J = 1 cps) at τ 8.46 and τ 8.54 assigned to the methyl groups at the double bonds, and two sharp singlets at τ 8.93 and τ 8.98 assigned to the remaining methyl groups. Since the molecule has a plane of symmetry (from the center of the double bonds through oxygen), all that should be seen in the nmr are four equally intense singlets. To explain the splitting between the



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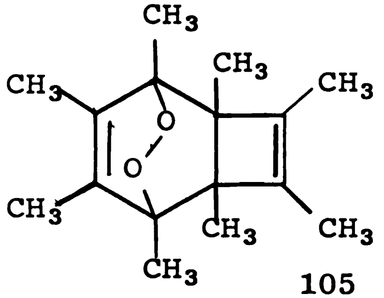
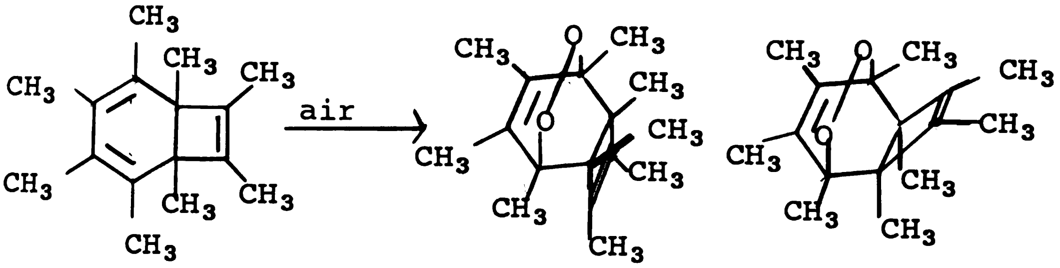
olefinic methyl groups, Maier claims that this is due to the special geometry of the system with a strained 1,4-bridged six-membered ring. To support this claim, Maier points out that Criegee (54) found similar results with the endo peroxide 105. But, upon examination of Criegee's



105

article, we found that he states that the nmr spectrum consisted of four slightly split signals of equal intensity. This could be explained by twisting of the molecule, due to strain (causing all the expected equivalent methyls to be in slightly different environments), or by the possibility that the peroxide bridge may not be linear, which would also make the environment of each methyl slightly different. In addition, it is possible that Criegee obtained a mixture of peroxides (105a and 105b). These isomers might have almost identical nmr spectra and the similarity of their chemical shifts would also account for the slight splitting of the singlets observed by Criegee. It should also be noted that the peroxide has a different number of atoms in its ring system from the number in 103.

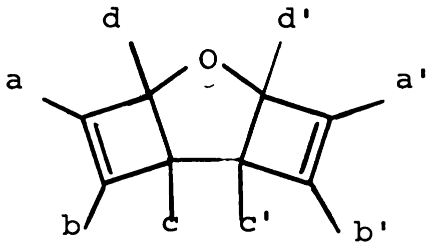


105a 105b

In any case, if the non-equivalence of the olefinic methyls in 103 was caused by strain, then the other methyls would be expected to have different environments also, and appear as two slightly split singlets. In fact, these signals are sharp.

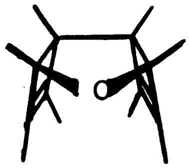
The structural assignment, 100, made in this thesis does not require any such dubious rationalization of the spectral evidence. (This structure was apparently not considered by Maier.) The ir band at 1695 cm^{-1} would arise from the two disubstituted double bonds in the four-membered rings (Figure 23). The olefinic methyls would not be equivalent, and therefore would be expected to couple, thus appearing as two quartets in the nmr spectrum. Each pair of aliphatic methyls (cc'; dd') should appear as a sharp singlet (Figure 15).

The actual geometry, *syn* (100a) or *anti* (100b) could not be deduced from these data.

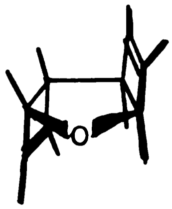


100

(a = a', b = b', c = c', d = d', but a ≠ b ≠ c ≠ d)



100a



100b

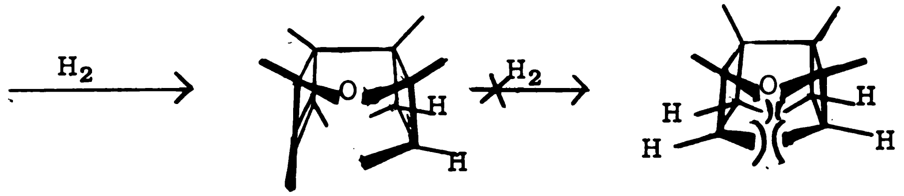
(For clarity, the methyl groups will, from now on, be represented by lines.)

Further reactions were carried out on **100** to test the validity of the structural assignment and to more clearly determine its geometry.

2. *Hydrogenation*. Compound **100** smoothly took up one mole of hydrogen after being shaken overnight in a Parr hydrogenator at 4 atm using 5% Pd/C in ethanol with slight heating. The compound would not take up an additional mole of hydrogen even after 72 hours. This fact would tend to support assignment of the *syn* structure **100a**, where addition

of a second mole of hydrogen from the least hindered side would be extremely unfavorable, due to the interaction of the *endo* methyls. This problem would be less serious in

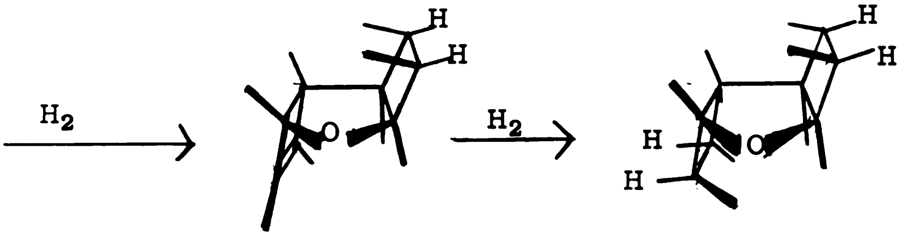
100a



106a 107a

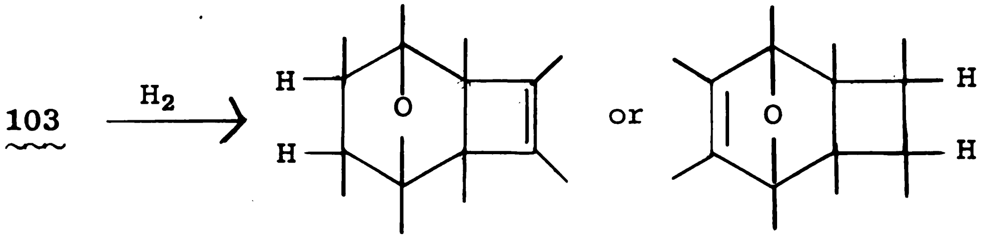
the case of the anti isomer, 100b, going to 106b, and finally to 108 with an additional mole of hydrogen.

100b



106b 108

Examination of the nmr spectrum of 106 (Figure 16) showed a multiplet for the methine protons (τ 7.6 - 8.4), two doublets for the methyl groups adjacent to the protons (τ 8.91 and 9.21, J = 7 cps), two quartets for the olefinic methyls (τ 8.45 and 8.57, J = 1 cps) and four singlets for the remaining methyl groups, (τ 8.80, 8.92, 9.00 and 9.02). This spectrum is readily rationalized by structure 106a or 106b. On the other hand, according to Maier's structure, 103, the expected hydrogenation product 109 or 110 should show only two singlets and a doublet for the methyl groups other than the olefinic ones, and a quartet for the methine protons. Once again, a special rationalization would be required to explain the two quartets, rather than one singlet for the vinyl methyls.

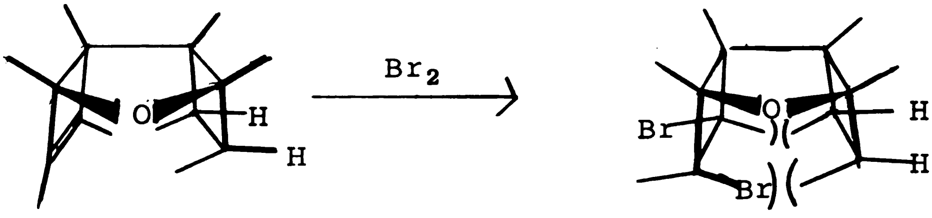


109 110

The infrared spectrum of the hydrogenation product is, perhaps, even more revealing. The band at 1695 cm^{-1} (Figure 24) is still present, though qualitatively diminished in size relative to the other bands. If 109 were the product, then the 1695 cm^{-1} band would be expected, but of approximately the same intensity as in 103, the starting material. On the other hand, if 110 were the product, then this band should be completely absent. For our postulated product, 106, one cyclobutene ring would remain and a diminished band at 1695 cm^{-1} would be expected.

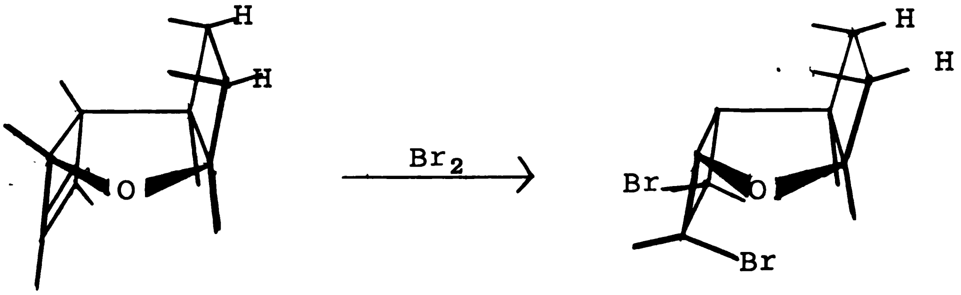
3. *Bromination*. Compound 100 readily took up two moles of bromine in carbon tetrachloride, but the complex mixture of products obtained indicated that rearrangement was taking place. This assertion is further supported by the fact that the hydrogenation product, 106, was inert under the same conditions. This would also favor the *syn*

structure 106a (and thus 100a), since addition of bromine to 106a would result in the formation of the highly strained molecule 111a. Such strain would not be present were bromine



106a 111a

to add to the *anti* isomer (106b ——> 111b).

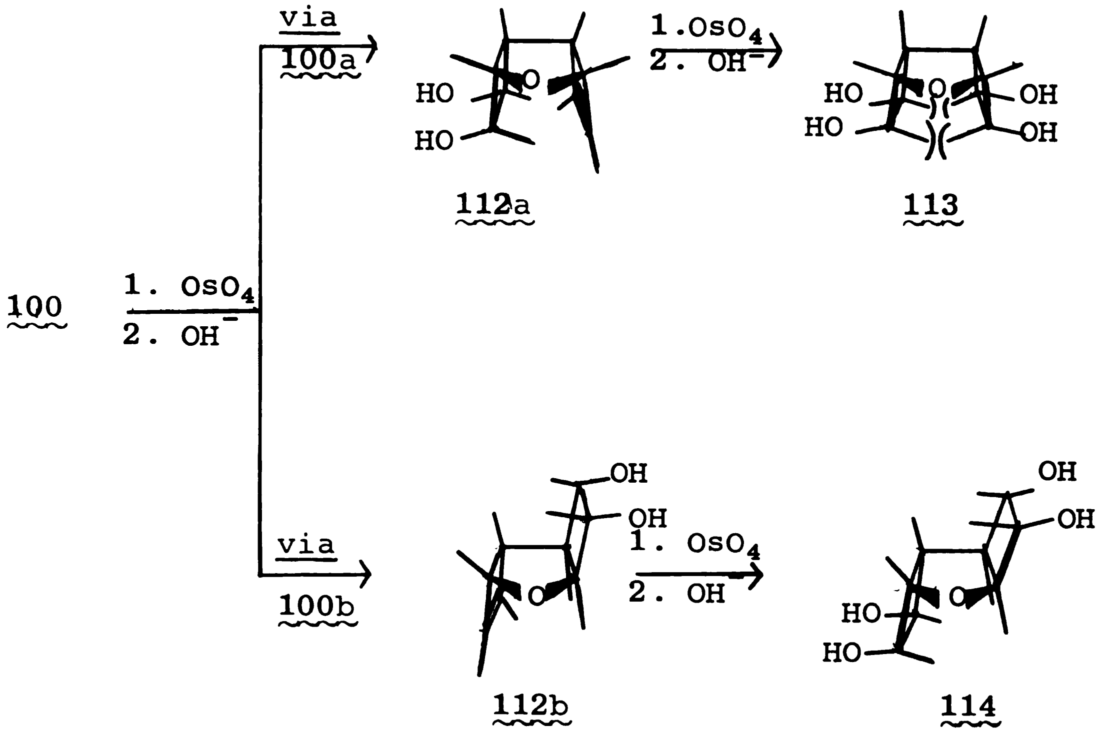


106b 111b

Because of the complexity of the bromination reaction, no data could be obtained to further clarify the structure of 100.

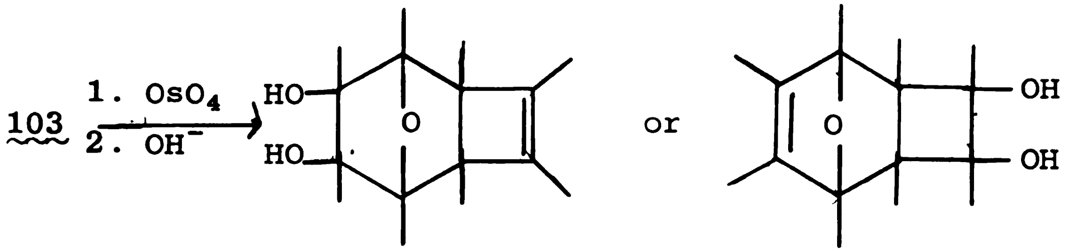
4. *Hydroxylation*. Maier (53) had reported that 103 (or 100) reacted with one mole of osmium tetraoxide upon remaining overnight in an ether solution containing pyridine, and with two moles (after isolation of the initial glycol) after four weeks. The fact that two moles were taken up might speak in favor of the *anti* structure 100b, but the

slowness of the addition of the second mole might indicate rearrangment prior to addition; alternatively, very slow addition without rearrangement may have occurred to produce the highly strained molecule 113.



Since Maier did not report any spectral data for either compound, it was decided to repeat his work, at least to the diol stage. Following his procedure (53), one mole of osmium tetraoxide was added to 100. The nmr and ir spectra of the product were compatible with structure 112a or 112b but not with structures 115 or 116, if Maier's compound had the structure (103) which he assigned to it.

The ir spectrum (Figure 25) showed strong hydroxyl bands at 3405, 3560 and 3720 cm^{-1}, as well as a weak band

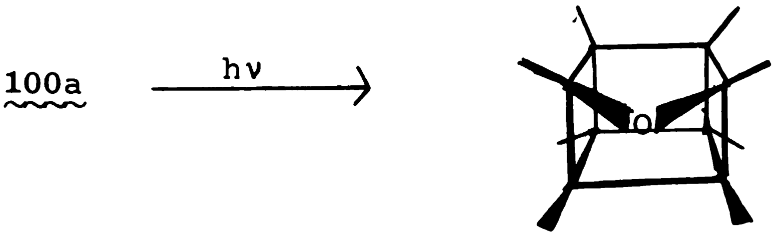


115

116

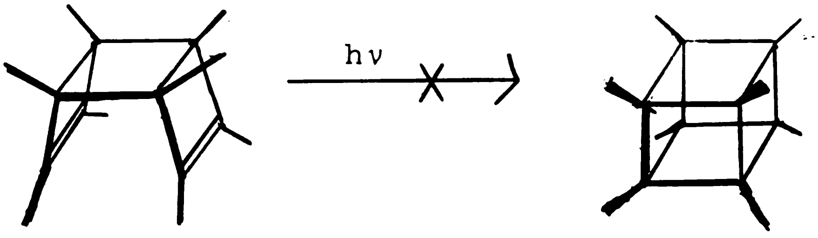
at 1695 cm^{-1}. The nmr spectrum (Figure 17) showed two broad singlets (τ 6.86 and τ 7.40) for the hydroxyl protons (these signals disappeared upon adding a few drops of deuterium oxide), two quartets (τ 8.43 and τ 8.53, J = 1 cps) for the olefinic methyl groups and five singlets [τ 8.63, 8.77, 8.97, 9.00 (3 H each) and τ 8.98 (6 H)] for the remaining methyls. If Maier's structure 103 had been correct, then the glycol 115 or 116 would be expected to show, in its nmr spectrum, three singlets for the quarternary methyls and a singlet for the hydroxyl protons (as well as for the olefinic methyls). Therefore, the spectra of both the hydroxylation and hydrogenation products provide further evidence in support of structure 100 and against structure 103.

5. Attempted Photolysis. If 100 had the syn configuration (100a), then it was thought that it might possibly undergo photolytic intramolecular cyclization to 117.



117

Under a variety of conditions (see Experimental Section), either no reaction occurred or the solutions turned yellow with no volatile products being obtained. These results do not necessarily rule out structure 100a. Criegee has reported (55) that he could not prepare octamethylcubane (118) by the photolysis of 99 (these compounds are closely related to 100a and 117, respectively).

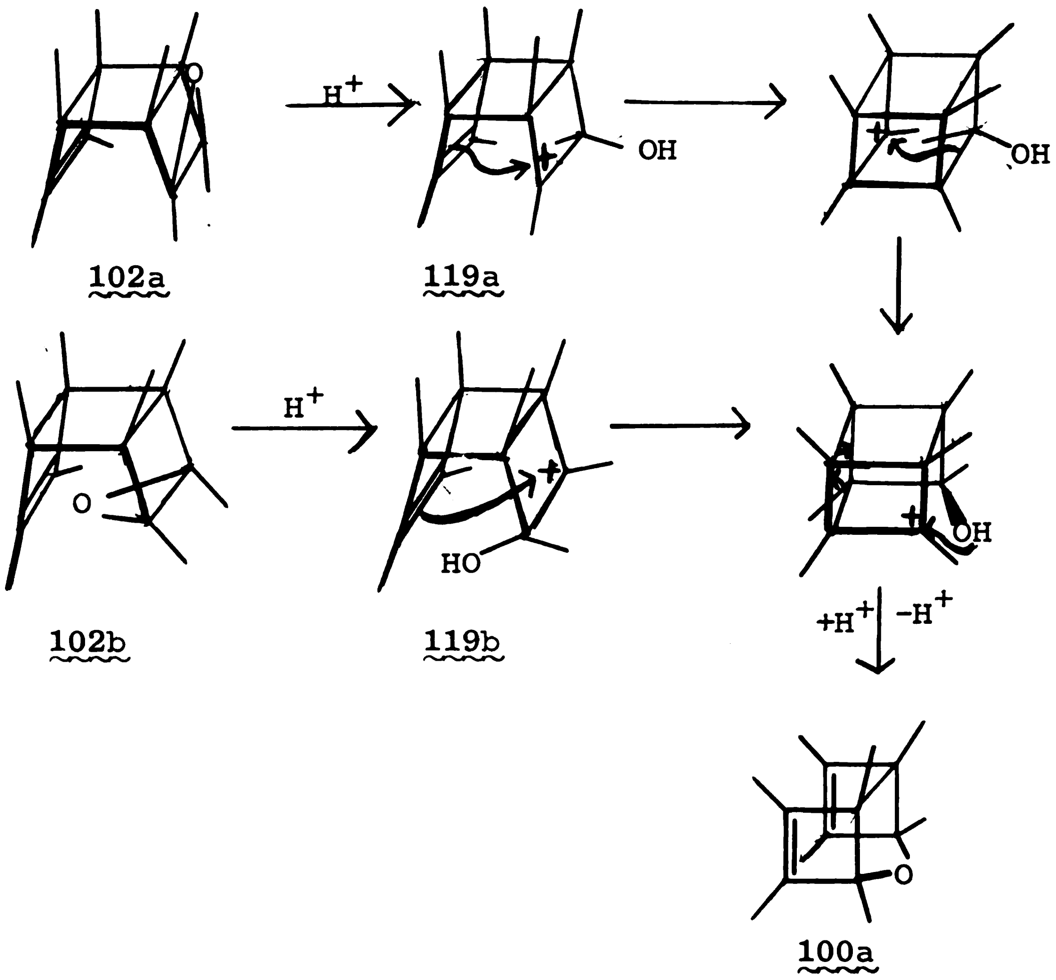


99 118

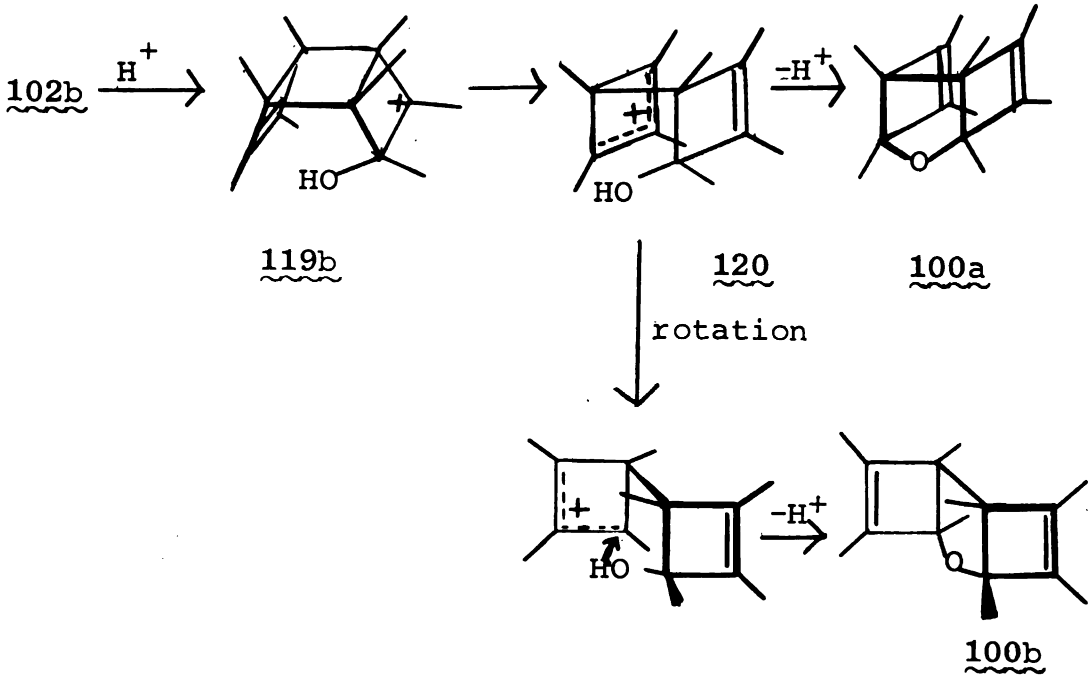
Criegee (55) (1962).

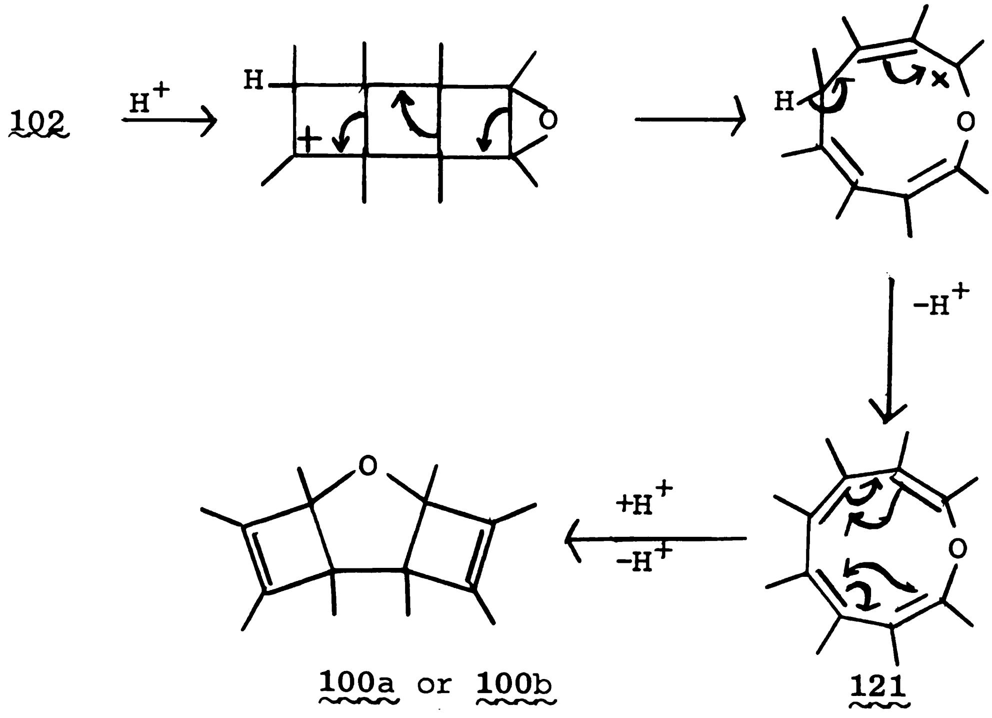
6. Mechanism. A discussion of the possible mechanisms which may account for the transformation of 102 to 100 must be only speculative at this time, since the exact geometries of 102 and 100 are not known with certainty. A number of mechanisms for converting either possible epoxide (102a or 102b) to either the *syn* (100a) or *anti* (100b) product can be postulated, depending upon the role of the acid in the rearrangement. Only a few possibilities are shown here.

It might be reasonable to assume that the epoxide ring is first broken to give a stable tertiary carbonium ion 119a or 119b, which could rearrange by a number of bond shifts to the *syn* product 100a. In addition, the *endo*

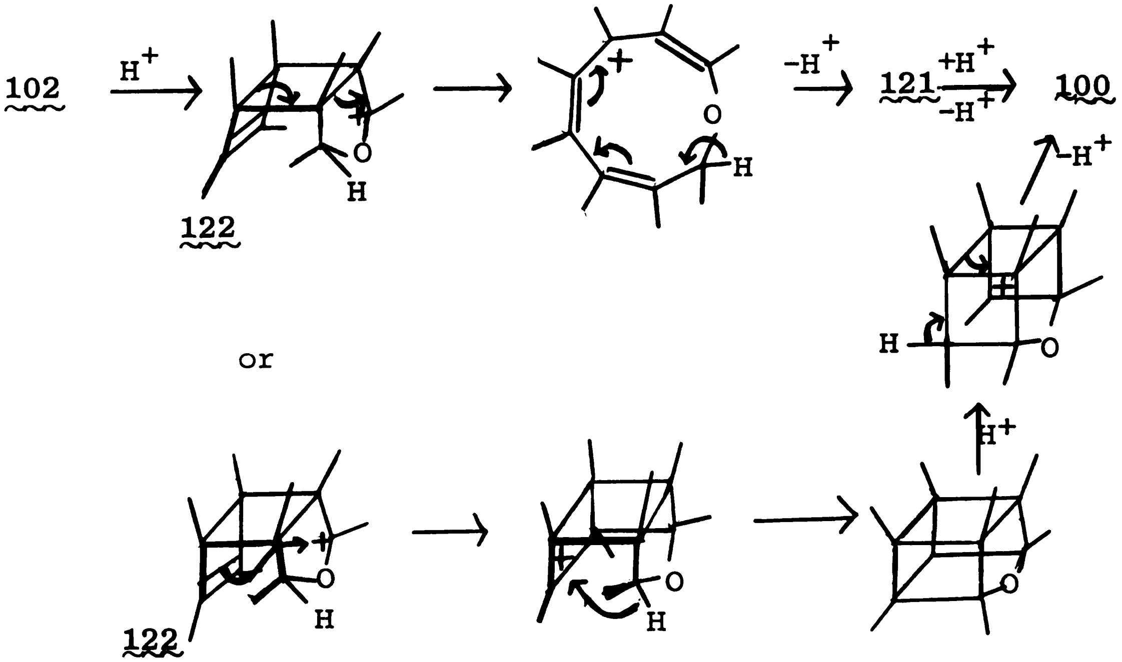


epoxide **102b** could rearrange *via* and allylic cation (**120**) to either the *syn* (**100a**) or *anti* (**100b**) product. This type of rearrangement is not possible for the *exo* epoxide (**102a**). The OH group would always be on the side away from the positive charge and could not close to the tetrahydrofuran ring. The possibility also exists that the proton could add to the double bond of **102** and cause rearrangement through a 10π oxacyclononatetraene structure **121** (**121** would probably not be aromatic since it cannot assume a planar conformation) to either **100a** or **100b**.


102b
H+
+
HO
119b
+
HO
120
-H+
O
100a
rotation
+
HO
-H+
O
100b


102
H+
H
+
O
H
x
O
-H+
+H+
-H+
O
O
121
100a or 100b

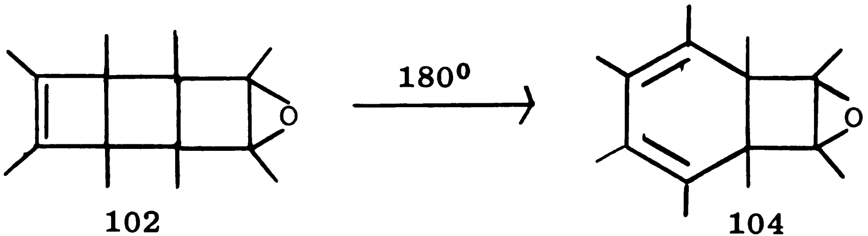
Structure 121 might also be formed by attack of the proton on the carbon-carbon bond of the epoxide ring. This type of ring opening might occur due to the relief of strain, which would result, in going from the tetracyclic structure 102 to the tricyclic intermediate 122.



More work will have to be done in order to determine which, if any, of these mechanisms is correct.

B. Thermal Rearrangement of Octamethyl-8-oxatetracyclo-[4.3.0.0^{2,5}.0^{7,9}]non-3-ene (102).

Maier (53) reported that upon melting, 102 rearranged to a new isomer, 104. Maier stated that the nmr spectrum of 104 consisted of four equally intense signals at τ 8.28, τ 8.43, τ 8.49 and τ 8.91. Later in the same article, (in reference to compound 103) he stated that in all the previously mentioned compounds the methyl groups gave very



102 104

Maier (53) (1963).

sharp signals in their nmr spectra. From this, we assume that the four signals in the nmr spectrum of 104 were singlets. If this is so, then it would appear that the structural assignment was incorrect. The methyl groups attached to the double bonds would not be equivalent and the nmr spectrum should consist of two quartets for these methyls and two sharp singlets for the remaining methyls (there is a plane of symmetry going through the oxygen and between the double bonds).

This thermal rearrangement was repeated. The nmr spectrum of the crude material showed that it was a mixture containing 43% starting material and 57% of a product having four equally intense peaks at τ 8.28, τ 8.42, τ 8.48 and τ 8.91. These values correspond well with Maier's values, but the peaks at τ 8.42 and τ 8.48 were quartets (J *ca.* = 0.8 cps). It is concluded that Maier's structural assignment, 104, was correct, but the splitting that we found was either missed or incorrectly reported by Maier.

EXPERIMENTAL

A. Preparation of Octamethyl-*syn*-tricyclo[4.2.0.0$^{2\ 5}$]octa-3,7-diene (**99**)

This compound was most conveniently prepared by following a slight modification of the procedure of Rosenburg and Eimutis (56). A cold solution of 2-butyne (12 g, 0.22 mole) in 20 ml of cyclohexane was added, by means of an ice-jacketed addition funnel equipped with a drying tube containing drierite, to a magnetically stirred suspension of 14.8 g (0.11 mole) of anhydrous aluminum chloride in 30 ml of cyclohexane prepared in an erlenmeyer flask cooled by means of an ice bath. The addition was started when the aluminum chloride suspension started to become viscous (cyclohexane melts at 6.5°). The 2-butyne solution was added dropwise over a period of 40 min during which time the reaction mixture slowly turned red-brown. After addition was completed, the reaction mixture was allowed to warm to room temperature, at which time magnetic stirring became difficult. The solution was then stirred intermittantly for 3 hrs. The reaction mixture was poured onto crushed ice and the gummy material in the reaction flask was scraped onto the ice. This mixture was stirred for about 0.5 hr until all the red-brown complex was destroyed (white solid formed in the upper layer). The layers were separated and the organic layer was washed with water. The aqueous layer was extracted with cyclohexane and the combined cyclohexane layers were dried over anhydrous sodium sulfate, filtered, and the solvent removed with a rotary evaporator. The residue was suspended in a small amount of acetone at 0° and filtered to give 5.0 g (42% yield) of white solid mp 188-192° (lit. 57, 198°). The nmr spectrum showed two singlets of equal intensity at τ 8.60 and τ 9.08 (lit. 56, τ 8.58 and τ 9.07).

B. Preparation of 1,2,3,4,5,6,7,9-Octamethyl-8-oxatetracyclo[4.3.0.$0^{2,5}$.$0^{7,9}$]non-3-ene (**102**)

Octamethyl-*syn*-tricyclo[4.2.0.$0^{2,5}$]octa-3,7-diene (7.1 g, 0.033 mole) was dissolved in 100 ml of benzene in a 300 ml erlenmeyer flask cooled by means of an ice bath. The solution was magnetically stirred and 6.5 g (0.033 mole) of 87% *meta*-chlorobenzoic acid (Research Organic/Inorganic Chemical Co.) dissolved in 130 ml of benzene was added dropwise. The temperature of the reaction mixture was kept below 12°. A white solid (*meta*-chlorobenzoic acid) formed during the addition. After addition was completed, the solution was stirred at room temperature for 1.5 hrs and then washed with three 50-ml portions of 5% aqueous sodium hydroxide and two 50-ml portions of water. After the product was dried over anhydrous magnesium sulfate and filtered, the solvent was removed with a rotary evaporator. The residue (7.3 g, 96% yield) was a white solid, mp 180-183° (lit. 53, 180°).

This product had an nmr spectrum consisting of four singlets of equal intensity at τ 8.38, τ 8.78, τ 9.13 and τ 9.22 (lit. 53, τ 8.38, τ 8.79, τ 9.11 and τ 9.21).

C. Preparation of 1,2,3,4,5,6,7,9-Octamethyl-8-oxatricyclo[$4.3.0.0^{7,9}$]nona-2,4-diene (104)

The previously prepared epoxide (55 mg) was sealed in a vial and placed in an oil bath maintained at 185^0. When the compound had just melted, the vial was removed from the bath and allowed to cool. The vial was then opened and the crude product taken up in carbon tetrachloride. The nmr spectrum of this solution (Figure 14) showed it to be a mixture of starting material (43%) and the reported product [(53), 57%].

D. Preparation of 1,3,4,5,6,7,8,9-Octamethyl-2-oxatricyclo[$5.2.0.0^{3,6}$]nona-4,8-diene (100)

1. Octamethyl-*syn*-tricyclo[$4.2.0.0^{2,5}$]octa-3,7-diene (3.4 g, 0.015 mole) was oxidized following procedure B1 in the first part of this thesis except that 98% hydrogen peroxide (0.4 ml, 0.017 mole) was substituted for 90% hydrogen peroxide, no boron fluoride was used and cooling was carried out with an acetone-carbon tetrachloride-dry ice bath adjusted so that the temperature of the alkene solution (200 ml of methylene chloride) was at -25^0. After workup, vpc analysis on a 5-ft SE-30 column at 170^0 showed a 6%

yield of the desired product (mp 67-68.5°, vpc collected) which showed the peak of shortest retention time. A complicated set of other peaks was also observed at longer retention times. The nmr and ir spectra of the product are shown in Figures 15 and 23.

2. This procedure, which is the method of choice, is a modification of the procedure of Maier (53). The epoxide (7.3 g) prepared by procedure B was dissolved in 200 ml of acetone to which was then added 10 ml of 2N sulfuric acid. The solution was stirred for 10 hrs, then diluted with 1 liter of water. The solution was extracted with four 75-ml portions of pentane, and the combined pentane extracts were washed with two 60-ml portions of saturated aqueous sodium bicarbonate and one 50-ml portion of water. After the product was dried over anhydrous magnesium sulfate and filtered, the solvent was removed with a rotary evaporator. The residue was chromatographed through 180 g of alumina using hexane as the eluant. The solid collected (3.9 g, 53%, mp 56-61°) was off-white (the solid formed upon standing or scratching from a yellow oil) but showed an nmr spectrum identical to the vpc-collected material prepared by procedure D1.

E. Reactions of 1,3,4,5,6,7,8,9-Octamethyl-2-oxatricyclo[5.2.0.0^{3,6}]nona-4,8-diene (**100**)

1. *Hydrogenation*. To 200 mg of 5% Pd/C in a pressure

bottle, was added 2.0 g of alkene dissolved in 25 ml of absolute ethanol, followed by four drops of concentrated hydrochloric acid. The bottle was then attached to a Paar hydrogenator and shaken overnight under 4 atm of hydrogen, with heating (external temperature 35^0). Vpc analysis of the crude product (after filtering and evaporating off the solvent) on a 5-ft SE-30 column at 174^0 showed a single peak with a longer retention time than that of the starting material. The nmr spectrum (Figure 16) of the crude and vpc collected product were essentially the same; the product was assigned the structure 1,3,4,5,6,7,8,9-octamethyl-2-oxatricyclo[5.2.0.$0^{3,6}$]non-4-ene (ir spectrum, Figure 24).

<u>Anal</u>. Calcd for $C_{16}H_{26}O$: C, 81.99; H, 6.83.

Found: C, 81.97; H, 6.82.

Hydrogenation for an additional 48 hrs showed no further change. In addition, this product would not react with bromine following procedure E4 for the unhydrogenated compound.

2. <u>Hydroxylation</u>. Following the procedure of Maier (53), 1.0 g (0.0043 mole) of the alkene dissolved in 10 ml of anhydrous ether was added to a solution of osmium tetraoxide (1 g, 0.0039 mole) and pyridine (0.63 ml, 0.0079 mole) in 10 ml of anhydrous ether. The solution was allowed to stand overnight and then filtered to isolate the brown solid (2.0 g, 80%).

The solid brown osmate-pyridine complex was dissolved in 40 ml of methylene chloride and placed in a 200-ml flask.

To the solution was added 2 g of mannitol and 0.6 g of potassium hydroxide, dissolved in 50 ml of water. The mixture was shaken for 2 days, then filtered through Celite to break up the resulting emulsion. The layers were separated and the aqueous layer was extracted with four 25-ml portions of methylene chloride. The combined organic layers were dried over anhydrous magnesium sulfate, filtered and the solvent removed with a rotary evaporator. The resulting yellow oil was sublimed (100°, 2 mm) and the slightly brown solid which resulted (0.3 g, 27%) was recrystallized from pentane (mp 116-120°, lit. 53, 128°), resublimed and recrystallized once again from pentane (mp 119-122°, white solid). The nmr and ir spectra are shown in Figures 17 and 25 respectively and the glycol was assigned the structure 1,3,4,5,6,7,8,9-octamethyl-2-oxatricyclo[5.2.0.$0^{3,6}$]non-8-ene-4,5-diol.

<u>Anal</u>. Calcd for $C_{16}H_{26}O_3$: C, 72.14; H, 9.84.
Found: C, 72.03; H, 9.75.

3. <u>Attempted Photolysis</u>. No reaction was observed when 34 mg of alkene dissolved in 6 ml of acetone was irradiated using a 450W Hanovia lamp through Pyrex for 2.5 hrs, or when the alkene dissolved in 3 ml of benzene containing <u>ca</u>. 35 mg of acetophenone was irradiated for 4.5 hrs.

When 85 mg of alkene dissolved in 2 ml of acetone in an all quartz apparatus was irradiated for 9.5 hrs, the solution turned yellow. Vpc analysis on a 5-ft SE-30 column at 220° showed a decrease in peak area of the starting material, but no volatile products were detected. When 6 ml of benzene was substituted for the acetone, the same results were found except that a yellow polymeric material collected on the walls of the quartz tube.

4. Bromination. The alkene (0.1 g, 4.3×10^{-4} mole) was dissolved in 1 ml of carbon tetrachloride. The solution was cooled in an ice bath and a 5% bromine solution in carbon tetrachloride was added dropwise. The solution immediately turned pale yellow and remained so until 0.9 ml of bromine solution (8.3×10^{-4} mole) had been added. At this point the solution turned orange. An additional 0.3 ml of bromine solution was added and the solvent was removed with a rotary evaporator. Vpc analysis on a 5-ft SE-30 column at 175° showed no starting material but instead a very broad complex of poorly resolved peaks of longer retention time. This crude material was refluxed with 3 ml of methanol and 75 mg of potassium hydroxide for 10 min (white solid formed). Vpc analysis of the product at 105° showed at least four peaks. No further analysis was carried out.

SUMMARY

1. The product of the acid-catalyzed rearrangement of octamethyl-8-oxatetracyclo[4.3.0.$0^{2,5}$.$0^{7,9}$]non-3-ene (102) was shown to be octamethyl-2-oxatricyclo[5.2.0.$0^{3,6}$]nona-4,8-diene (100) and not the previously reported structure, 103.

2. The assignment of structure 100 was based on its nmr and ir spectra, and the spectra of its hydrogenation product 106 and its hydroxylation product 112.

3. The rearrangement product probably has the *syn* configuration (100a). This assignment was based on the high reactivity of only one of its two double bonds.

4. The thermal rearrangement product of 102 was shown to be octamethyl-8-oxatricyclo[4.3.0.$0^{7,9}$]nona-2,4-diene (104) based on its nmr spectrum. The structural assignment previously reported in the literature was correct, but the reported nmr spectrum was incorrect in some details.

SPECTRA

NUCLEAR MAGNETIC RESONANCE SPECTRA

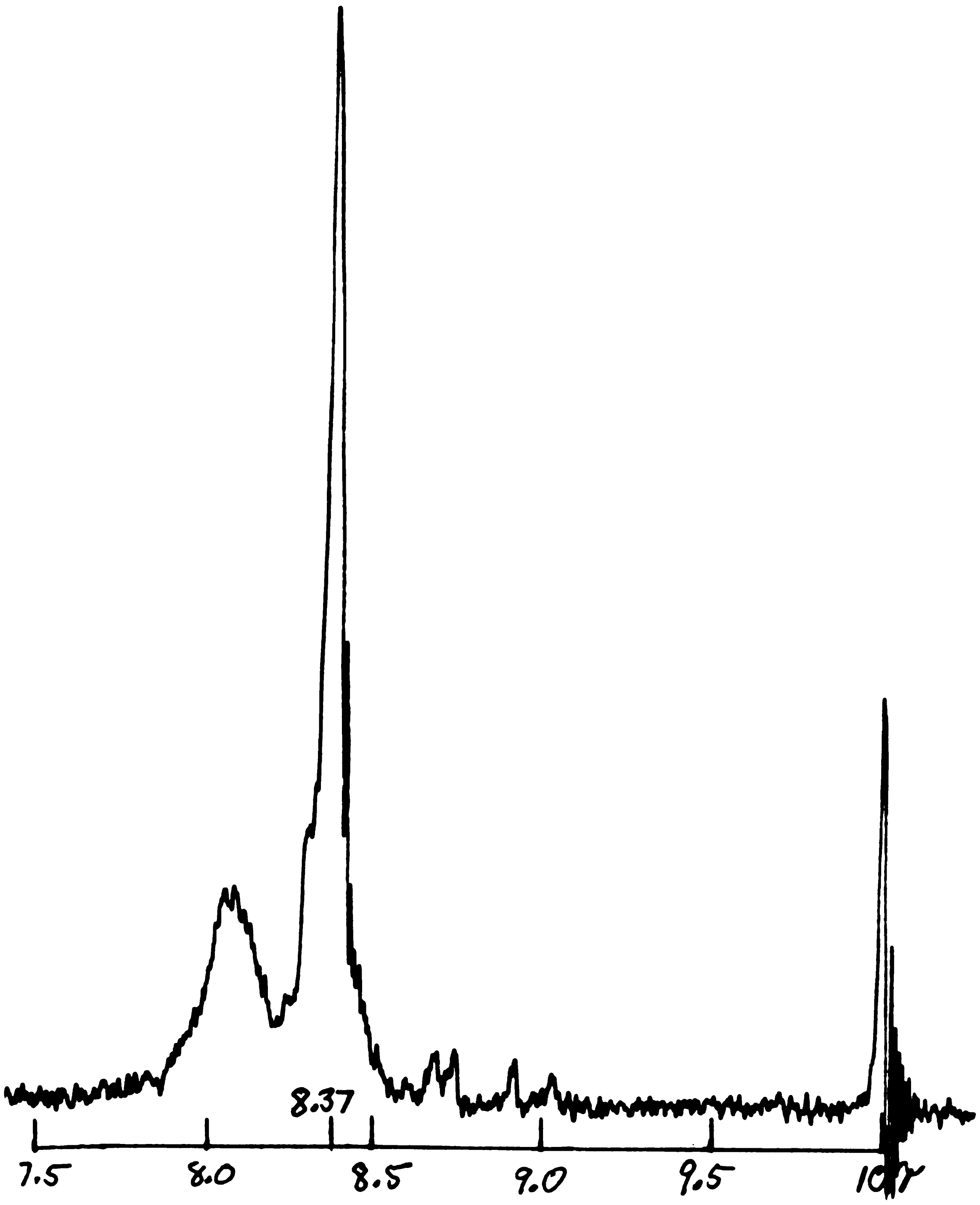


Figure 1. Nmr spectrum of 1,2-dimethylcyclohexene (36).

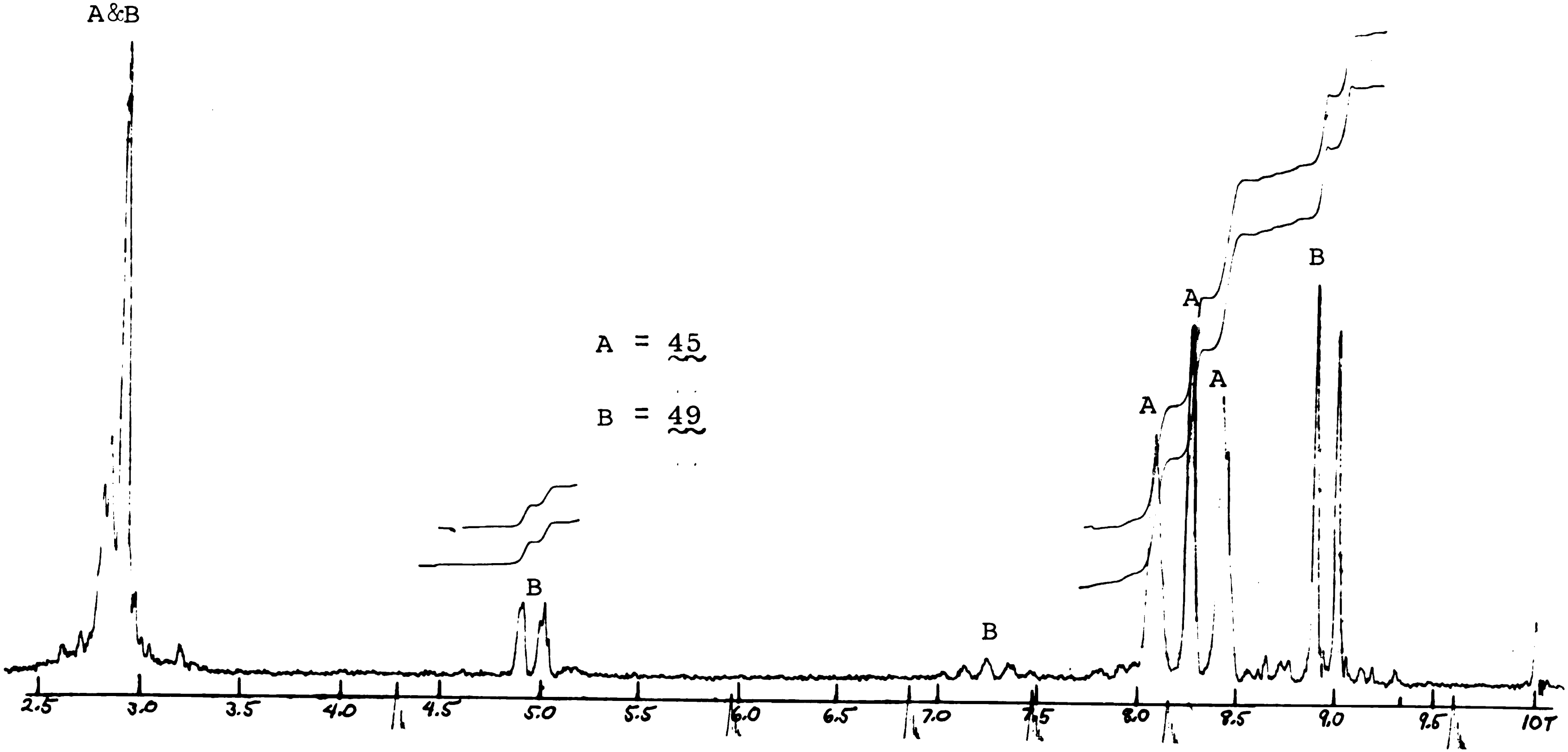


Figure 2. Nmr spectrum of a 63:37 mixture of 2-methyl-3-phenyl-2-butene (45) and 3-methyl-2-phenyl-1-butene (49).

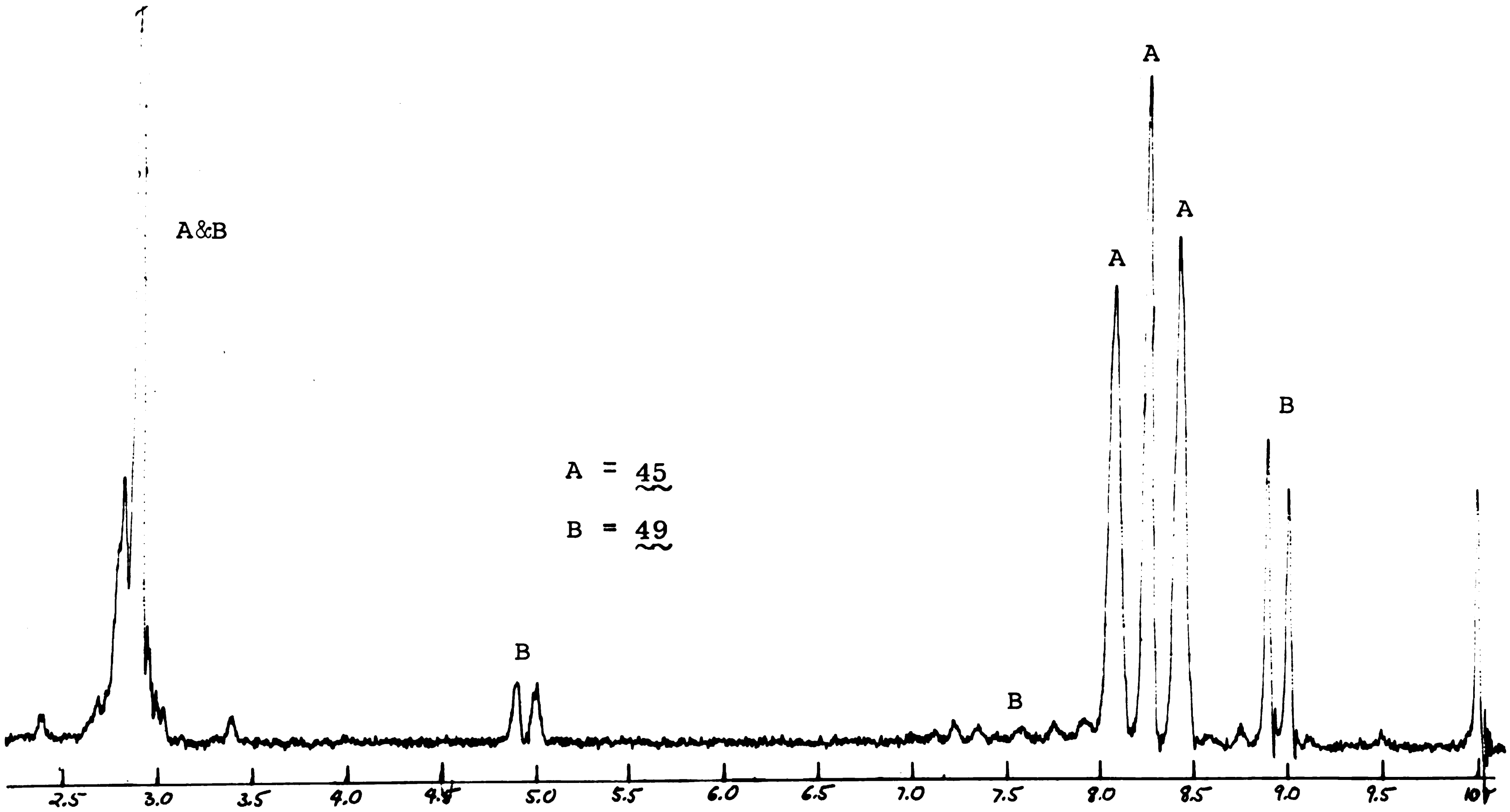


Figure 3. Nmr spectrum of an 80:20 mixture of 45 and 49.

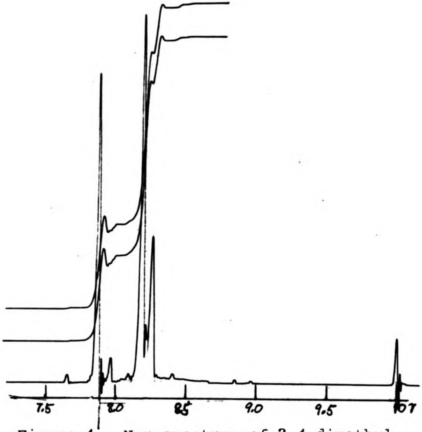


Figure 4. Nmr spectrum of 3,4-dimethyl -3-penten-2-one (64).

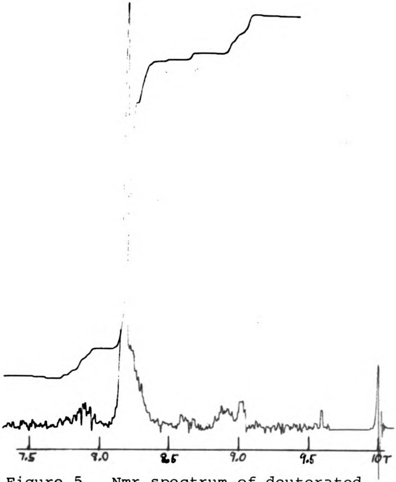


Figure 5. Nmr spectrum of deuterated 3,4-dimethyl-3-penten-2-one (71).

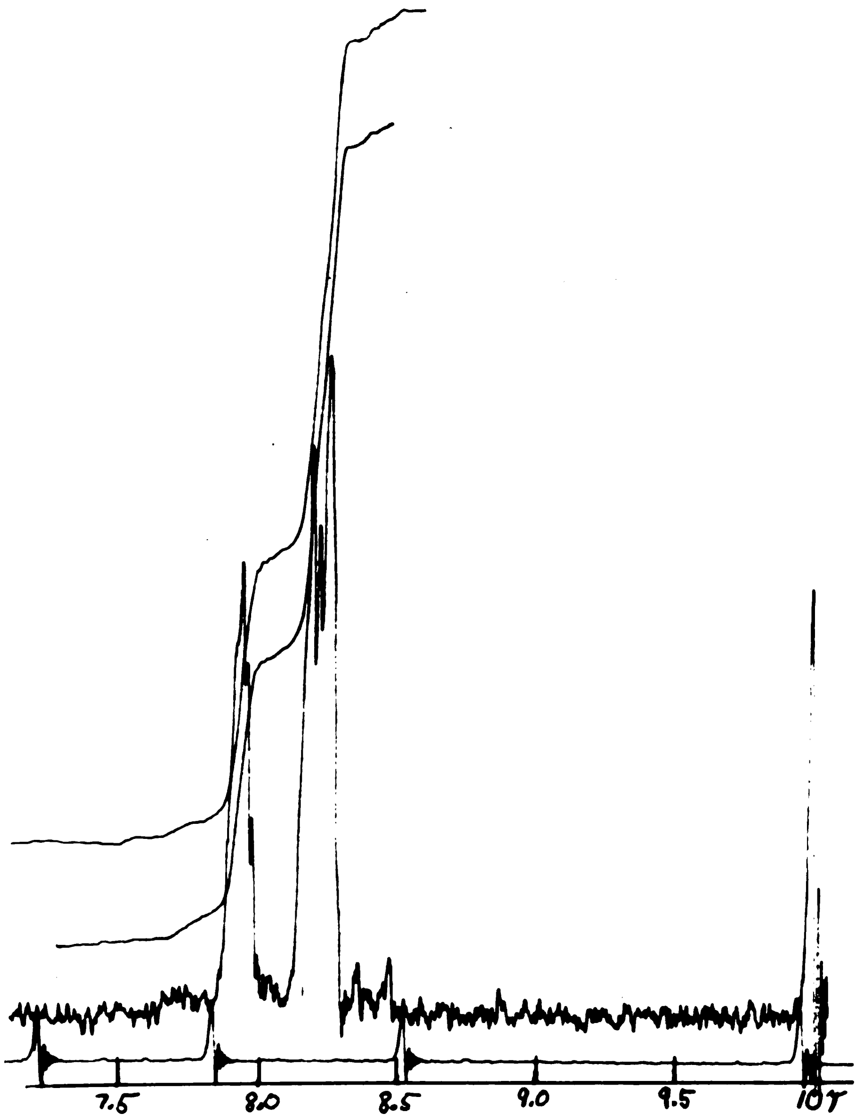


Figure 6. Nmr spectrum of 3-chloro-2-methyl-2-butene (82).

Figure 7. Nmr spectrum of deuterated 3-chloro-2-methyl-2-butene (86).

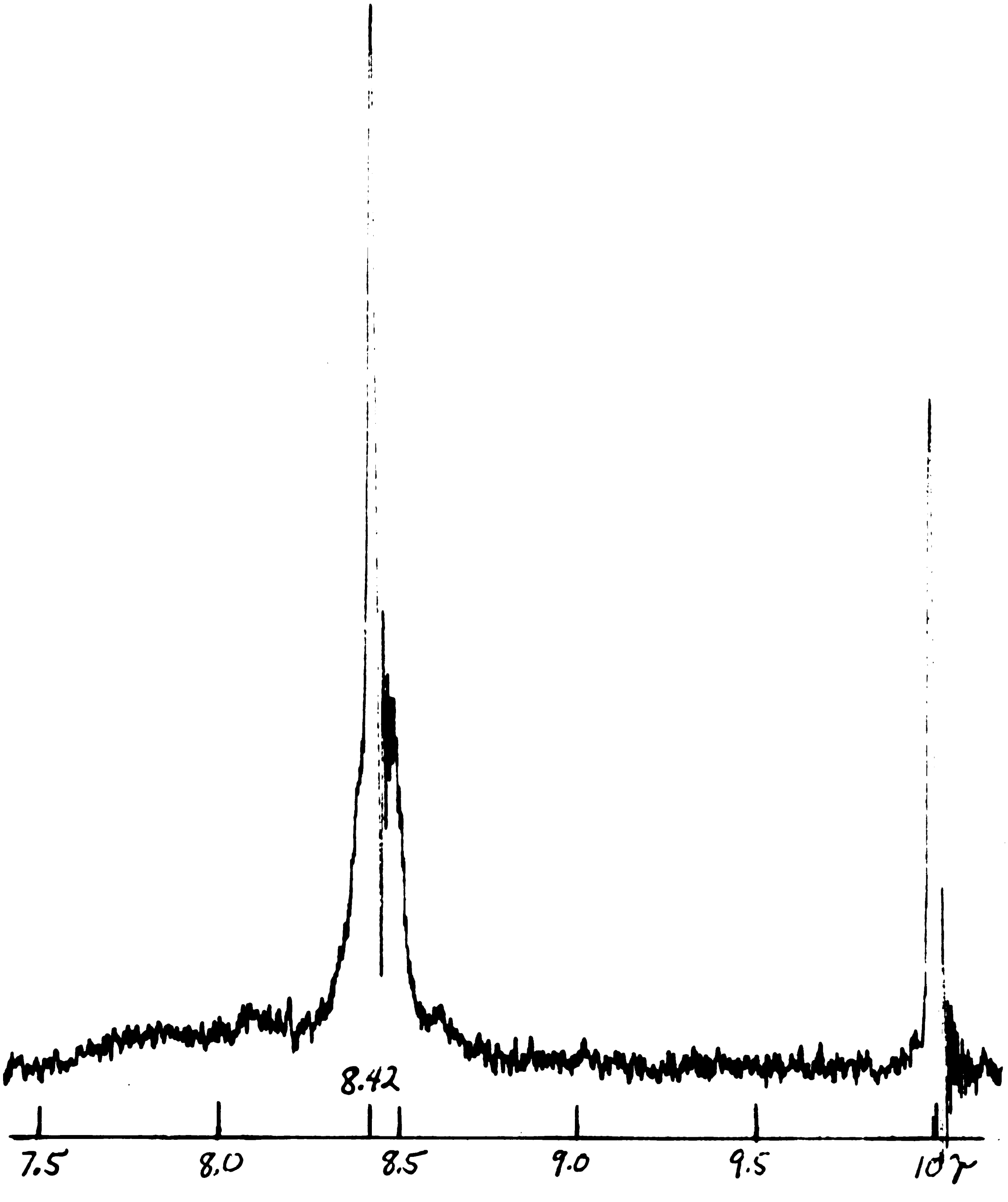


Figure 8. Nmr spectrum of 1-methylcyclohexyl trifluoroacetate (31).

Figure 9. Nmr spectrum of 3,3-dimethyl -2,4-pentanedione (66).

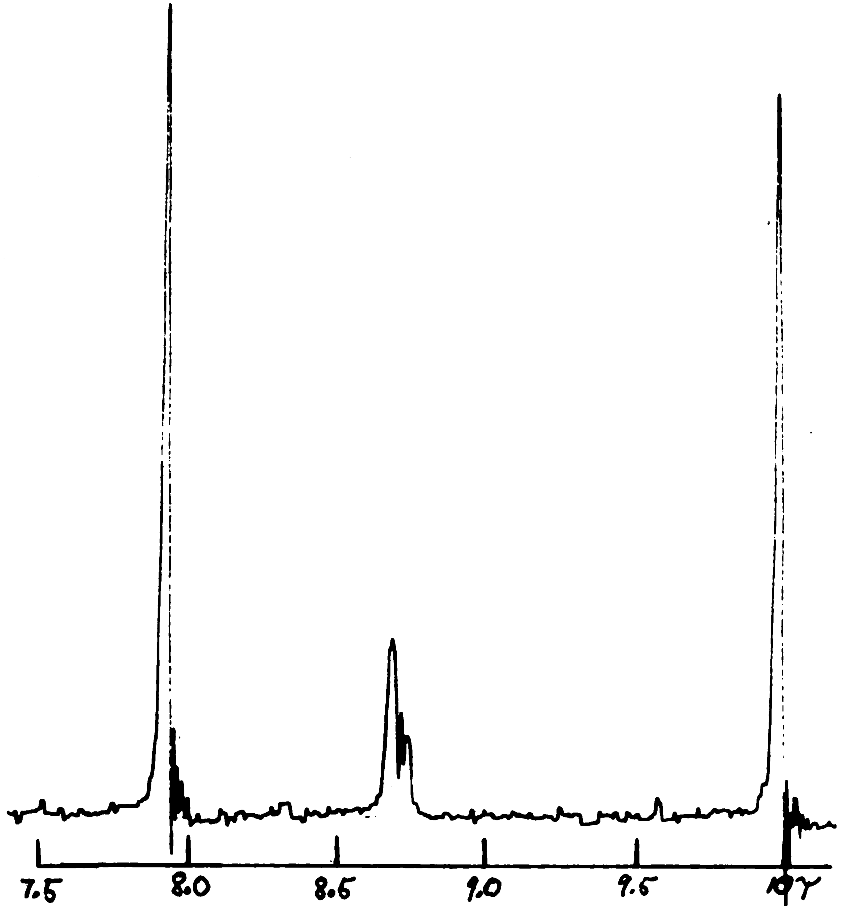


Figure 10. Nmr spectrum of deuterated 3,3-dimethyl-2,4-pentanedione (71).

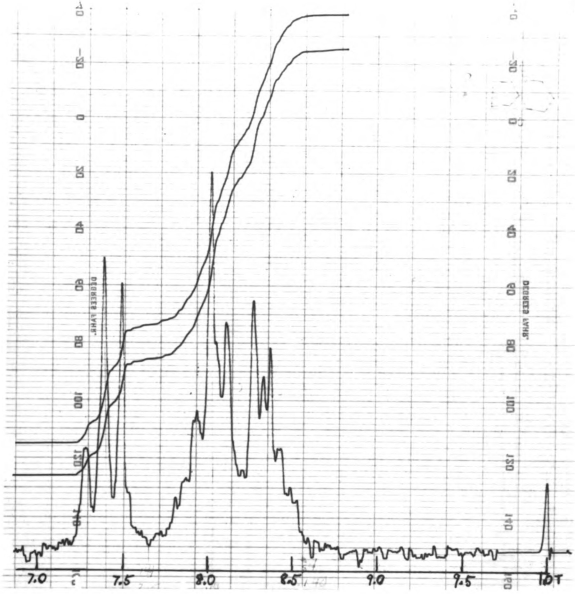


Figure 11. Nmr spectrum of spiro[4.5]decane-6,10-dione (78).

Figure 12. Nmr spectrum of 3-chloro-3-methyl-2-butanone (84).

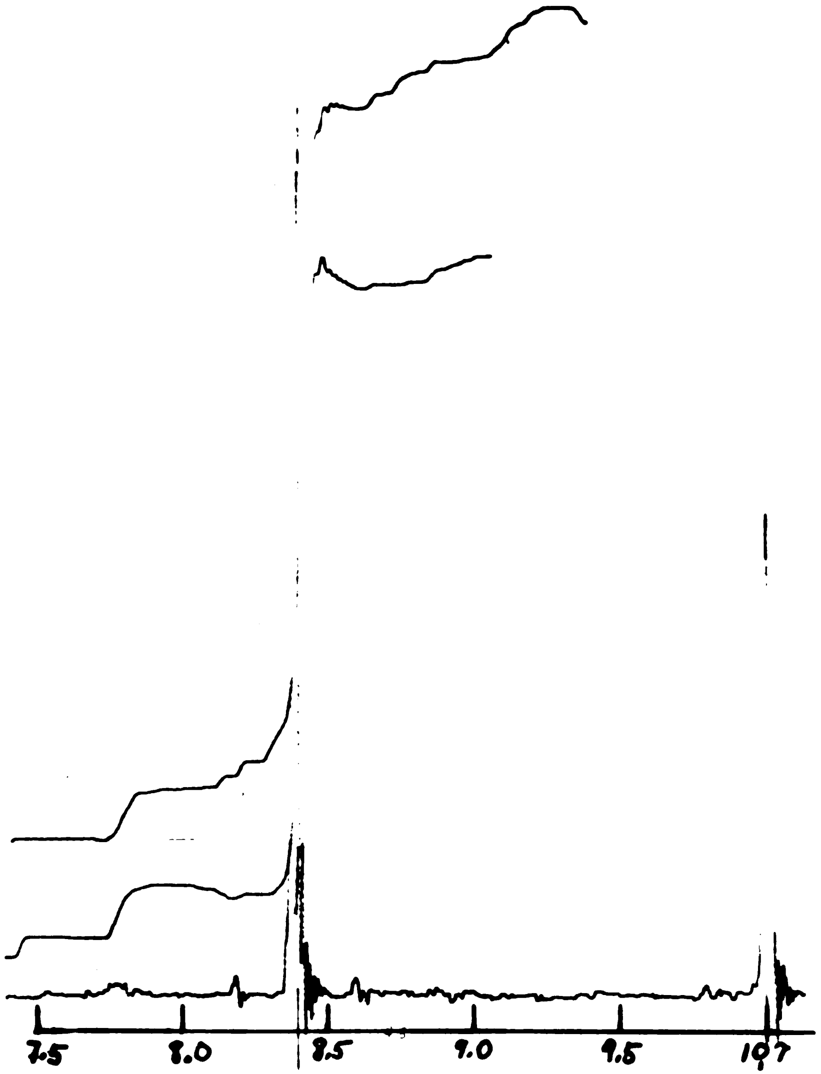


Figure 13. Nmr spectrum of deuterated 3-chloro-3-methyl-2-butanone (90).

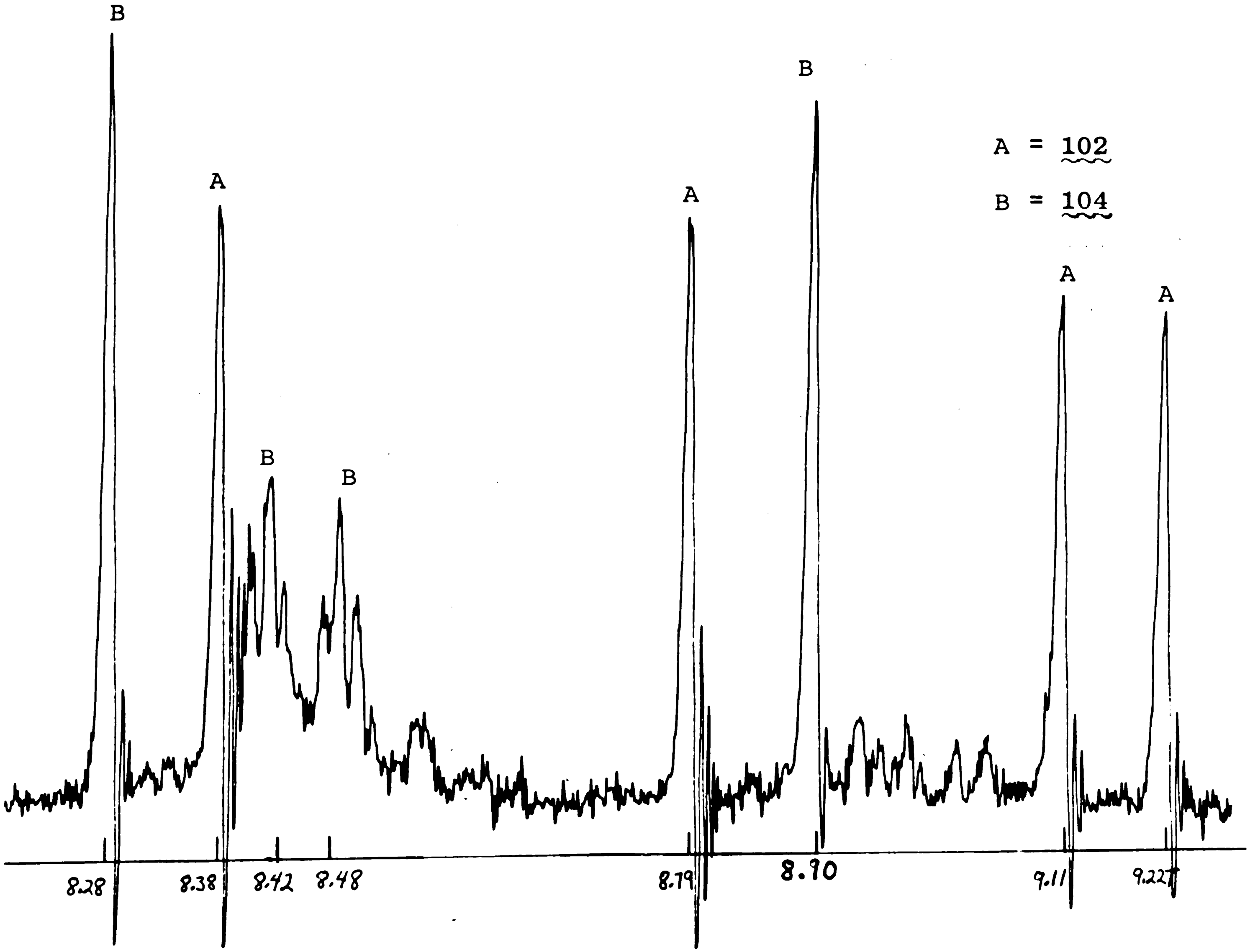


Figure 14. Nmr spectrum of a 43:57 mixture of octamethyl-8-oxatetracyclo-[4.3.0.0^{2,5}.0^{7,9}]non-3-ene (102) and octamethyl-8-oxatricyclo-[4.3.0.0^{7,9}]nona-2,4-diene (104).

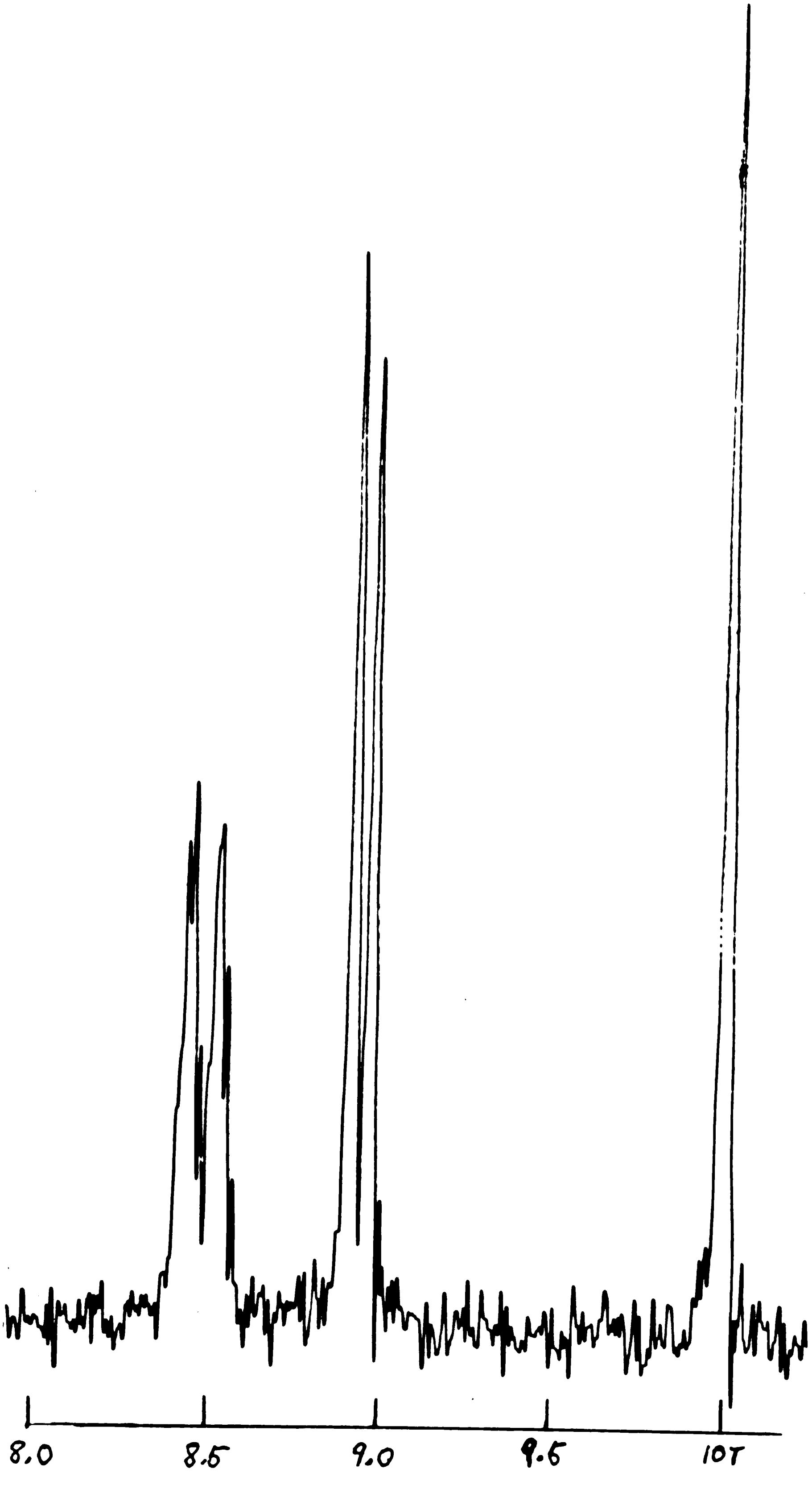


Figure 15. Nmr spectrum of octamethyl-2-oxatricyclo-[5.2.0.0^{3,6}]nona-4,8-diene (100).

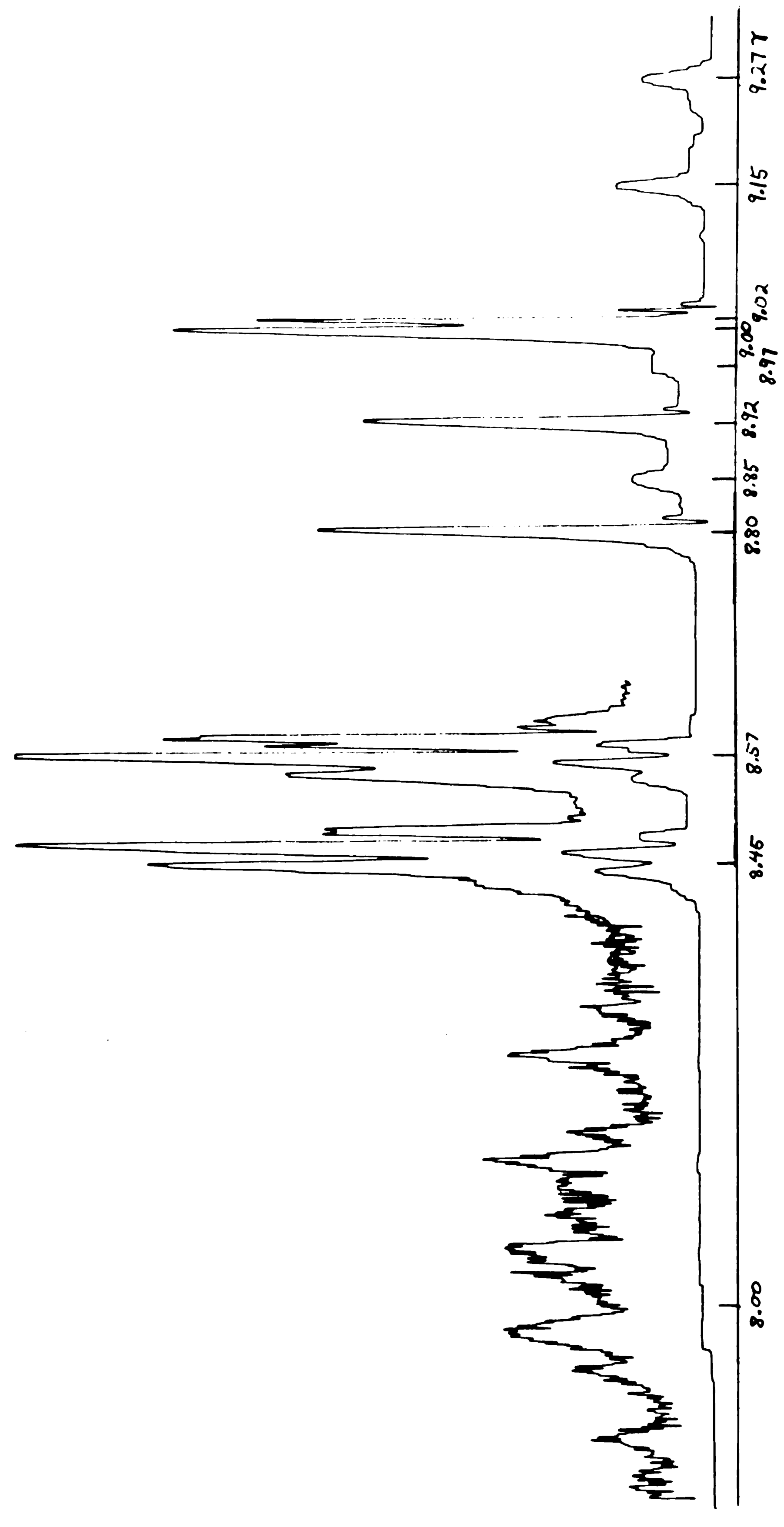


Figure 16. Nmr spectrum of the hydrogenation product (106) of 100.

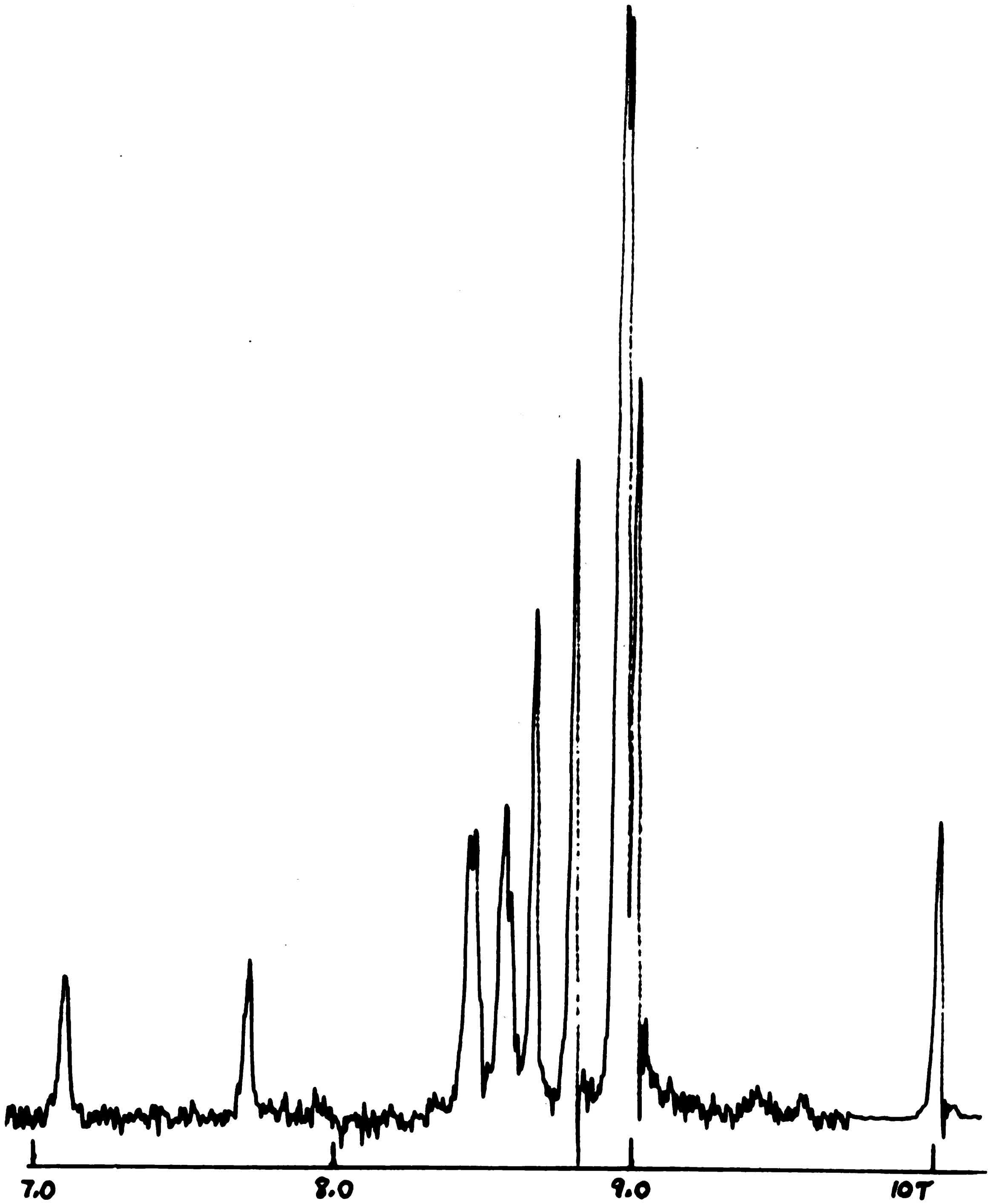


Figure 17. Nmr spectrum of the hydroxylation product (112) of 100.

INFRARED SPECTRA

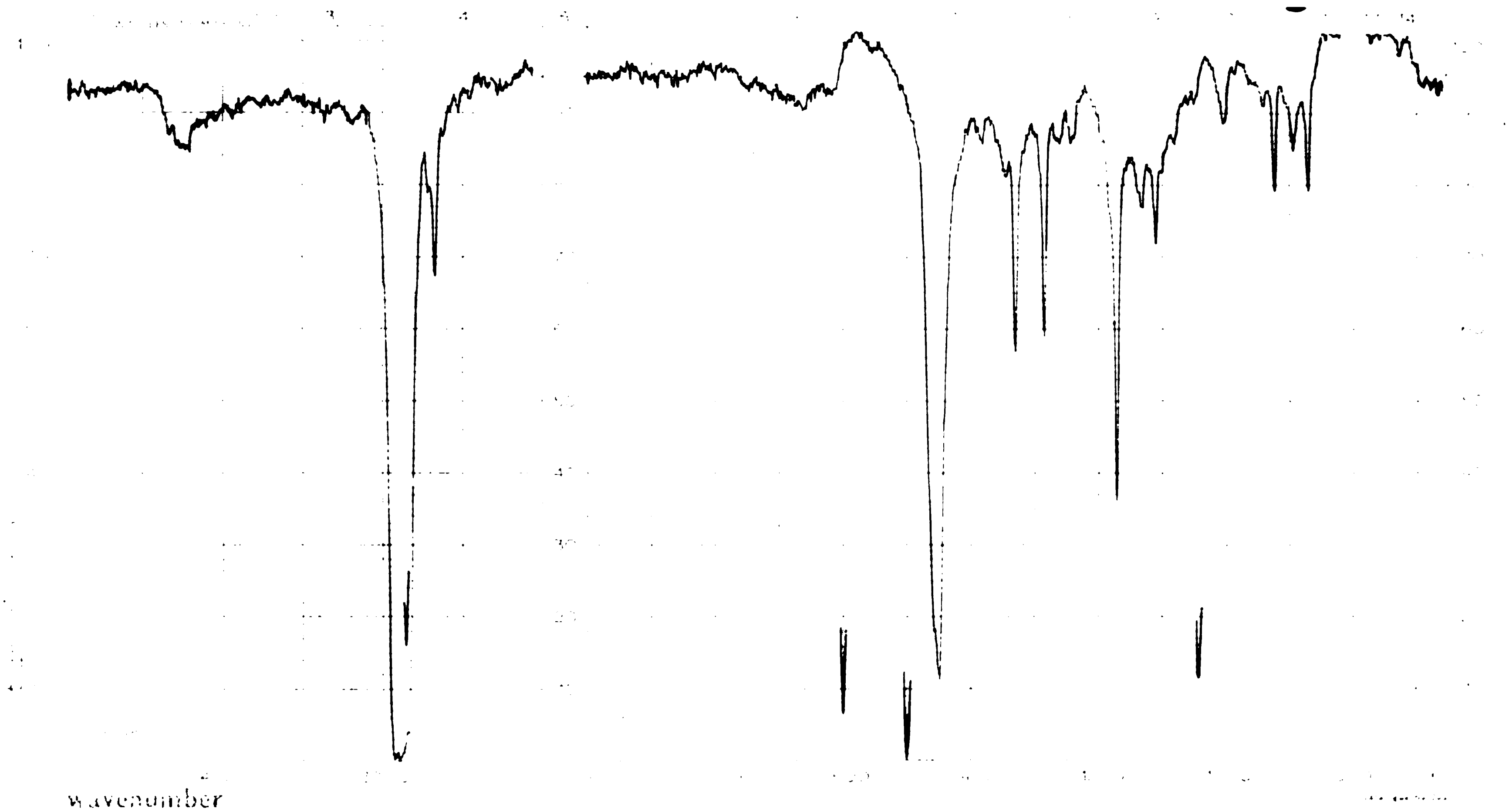


Figure 18. Infrared spectrum (CCl_4) of $\Delta^{9,10}$-octalin (41).

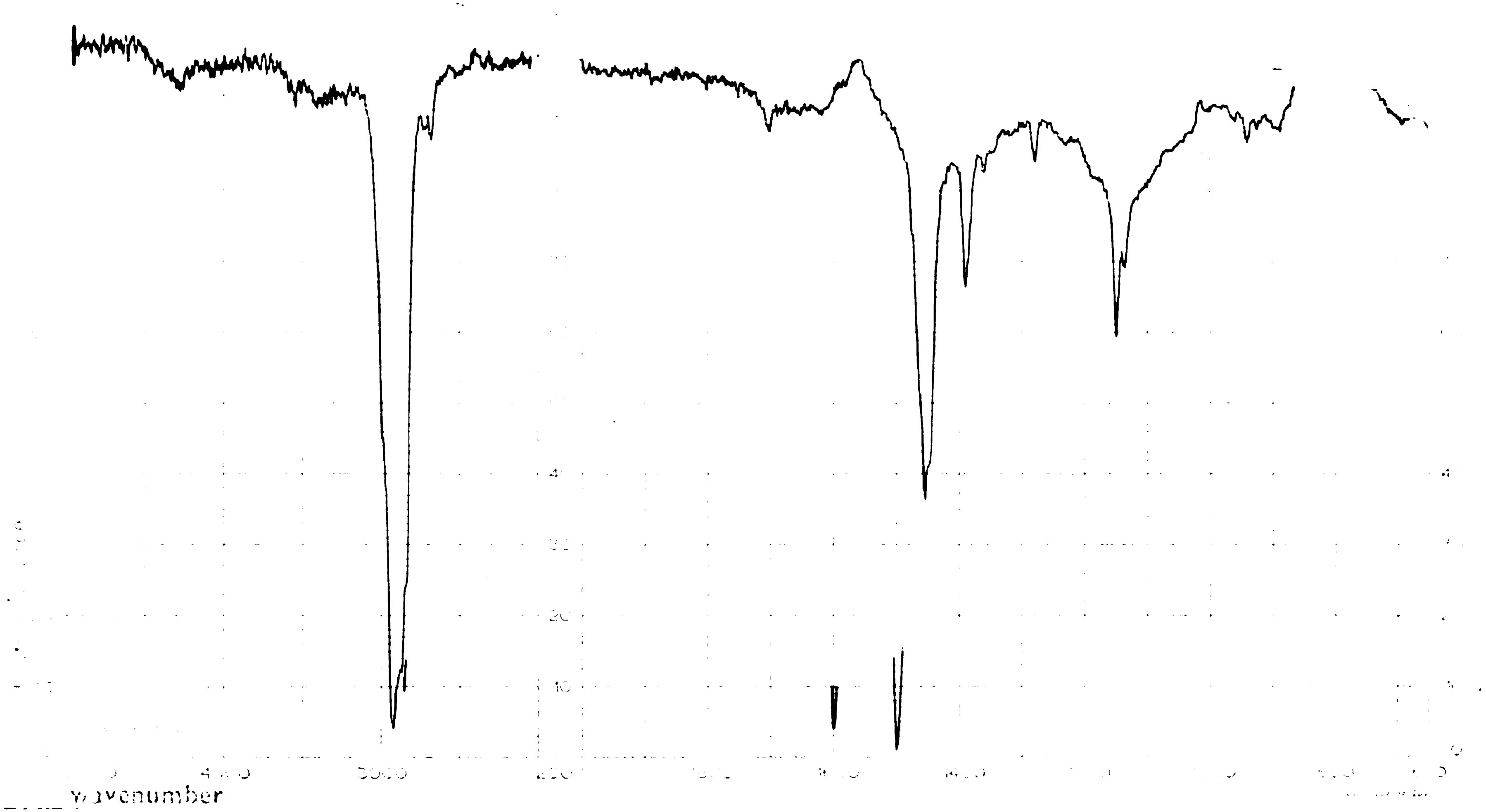


Figure 19. Infrared spectrum (CCl_4) of 1,2-dimethylcyclohexene (36).

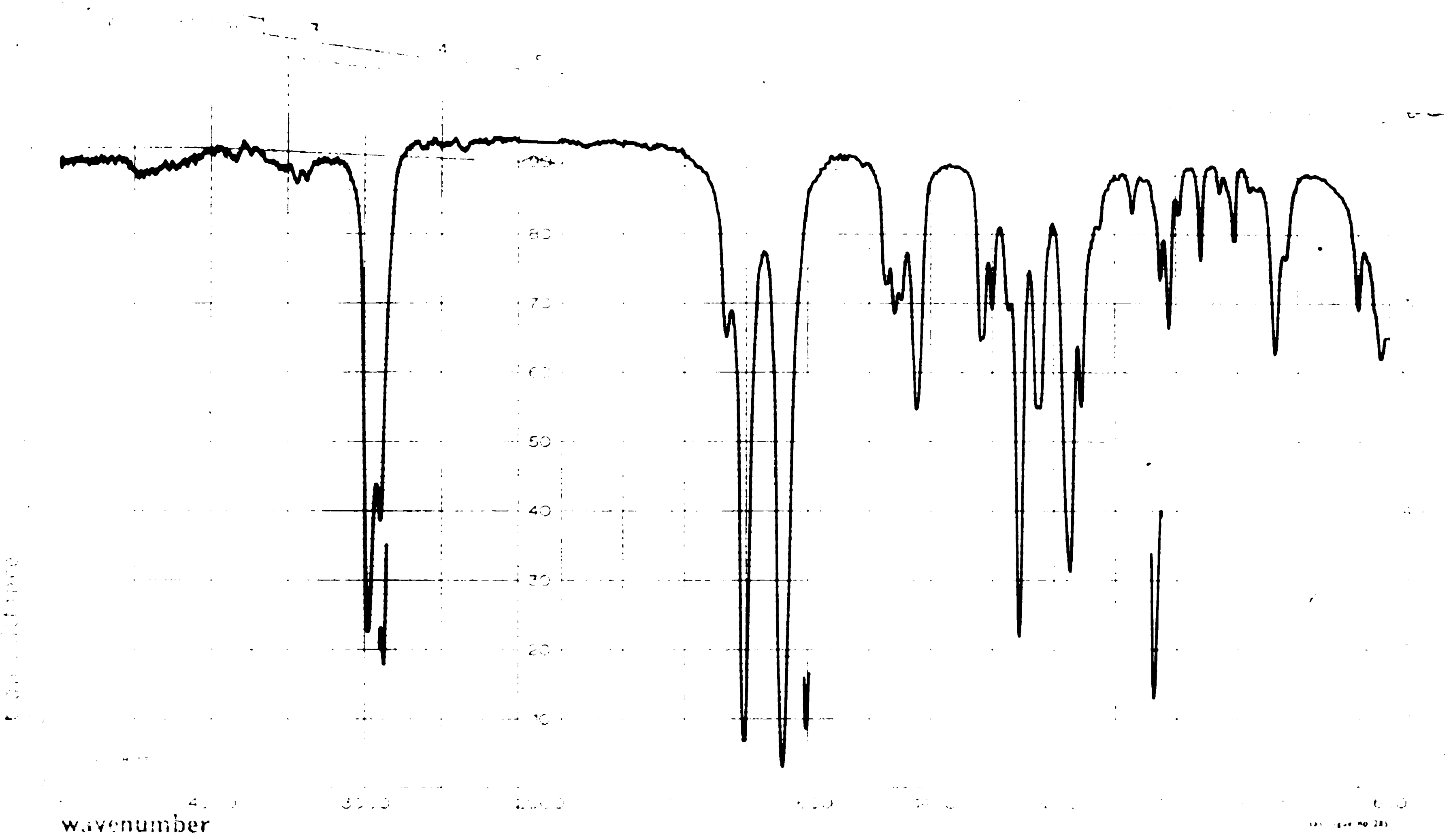


Figure 20. Infrared spectrum (liquid film) of 2-cyclopentylidenecyclopentanone (76).

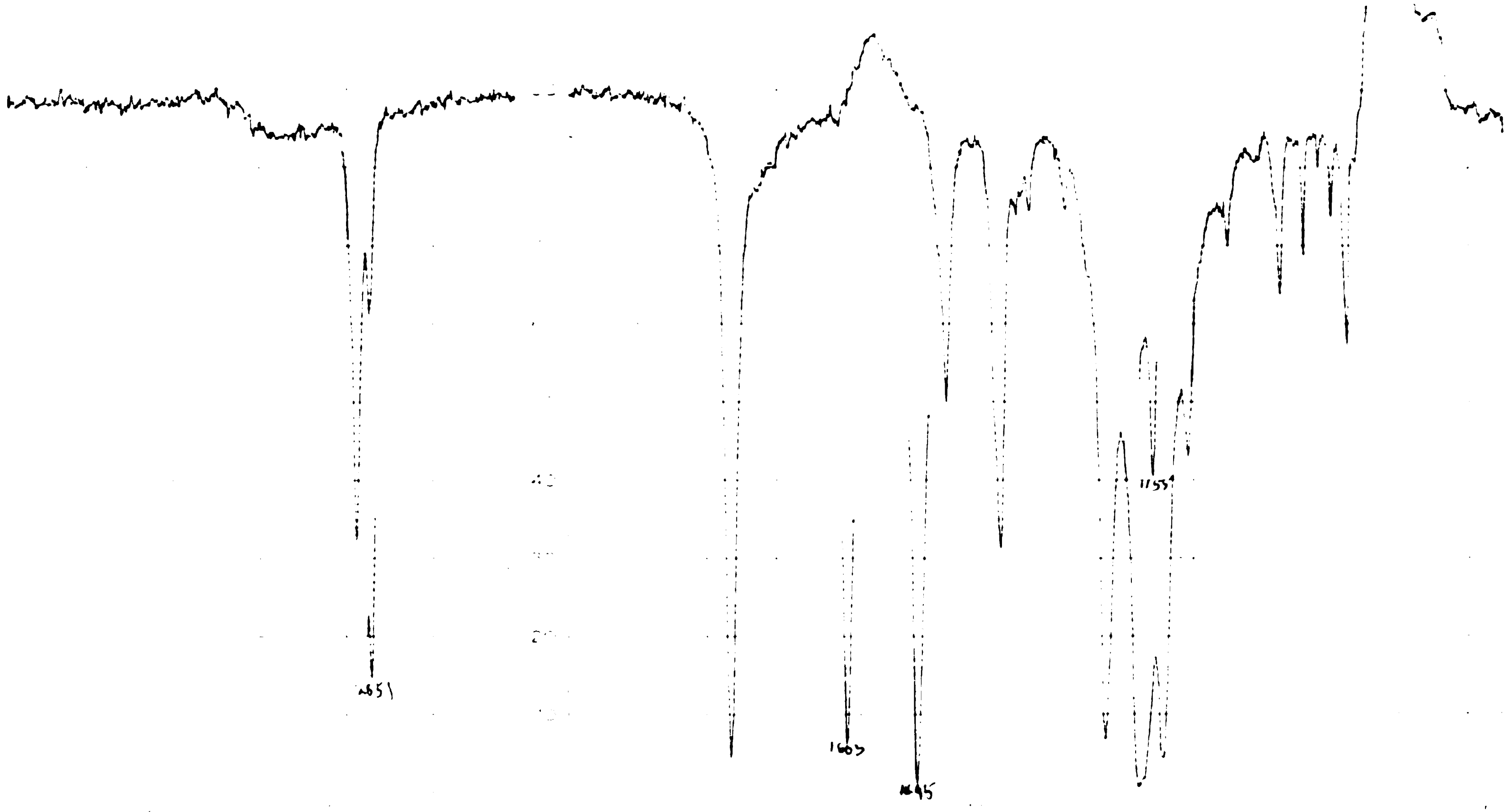


Figure 21. Infrared spectrum (CCl_4) of 1-methylcyclohexyl trifluoroacetate (31).

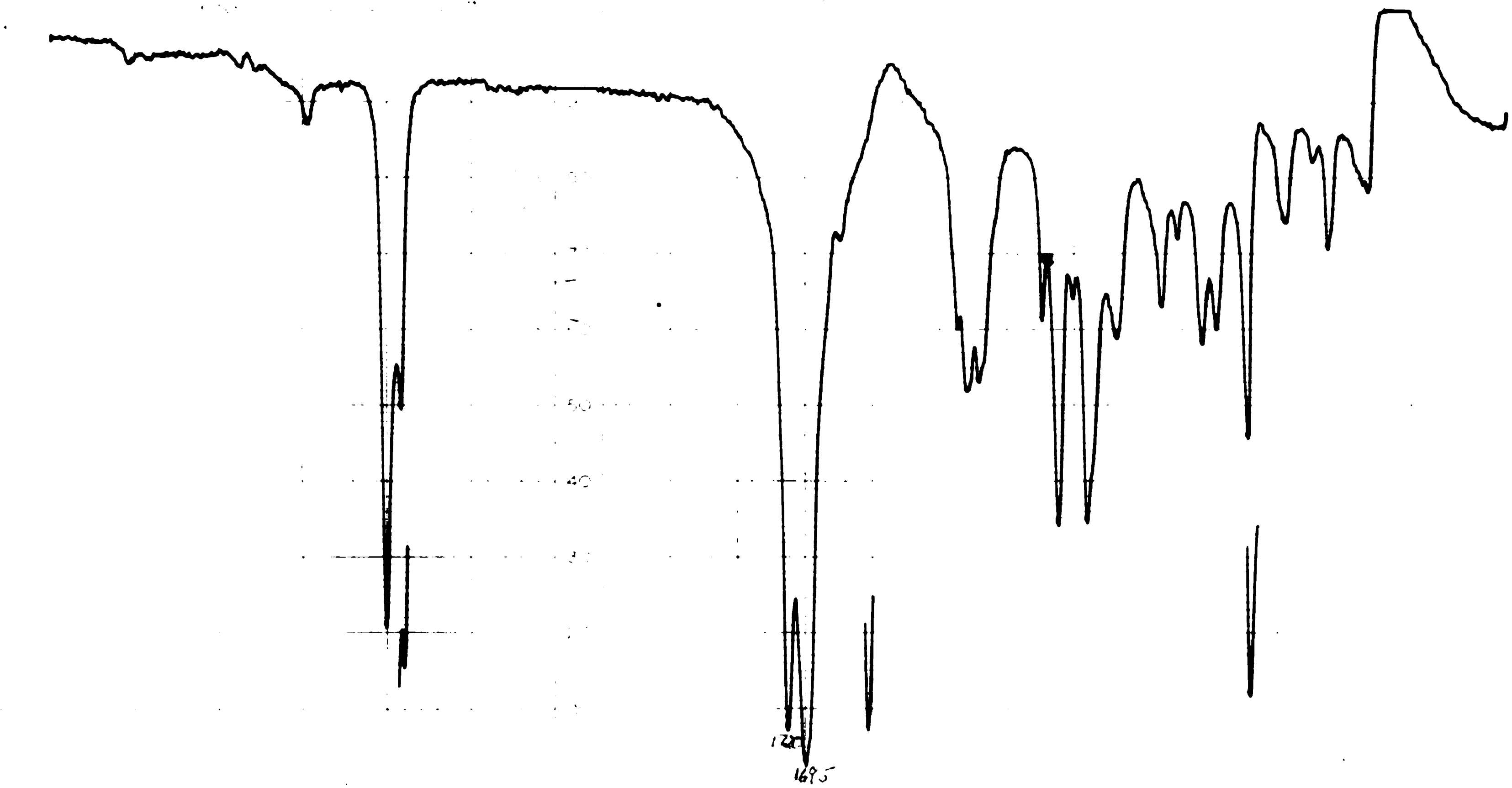


Figure 22. Infrared spectrum (CCl_4) of spiro[4.5]decane-6,10-dione (78).

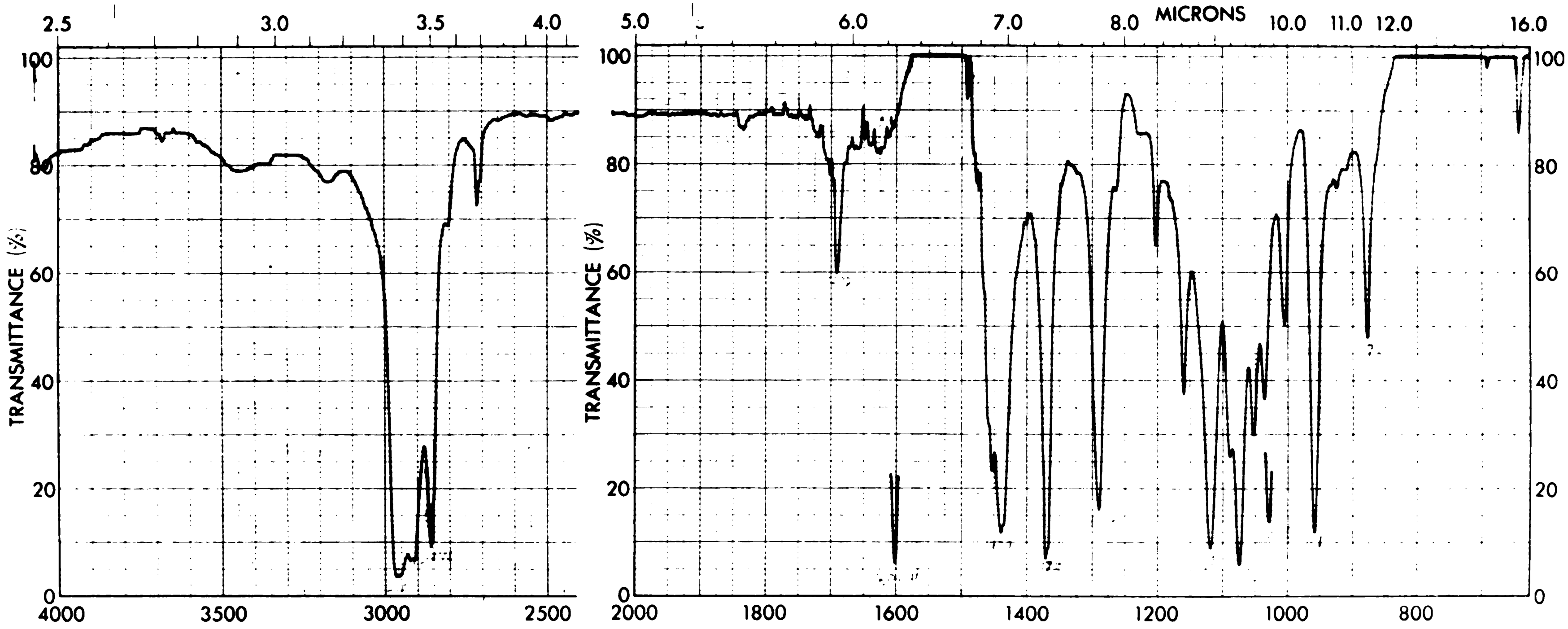


Figure 23. Infrared spectrum (CCl_4) of octamethyl-2-oxatricyclo[5.2.0.$0^{3,6}$]nona-4,8-diene (100).

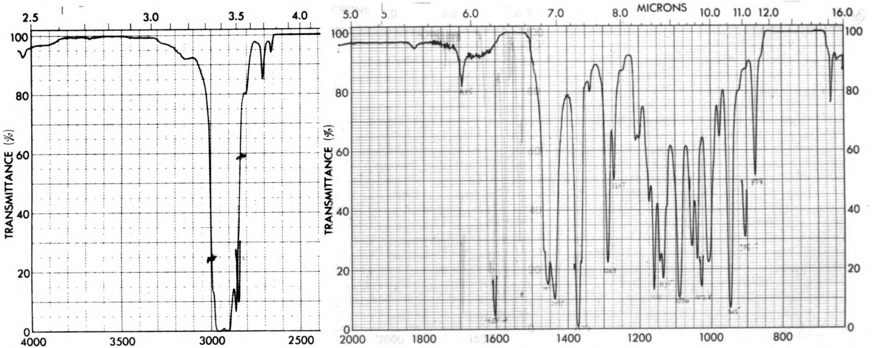


Figure 24. Infrared spectrum (CCl_4) of the hydrogenation product (**106**) of **100**.

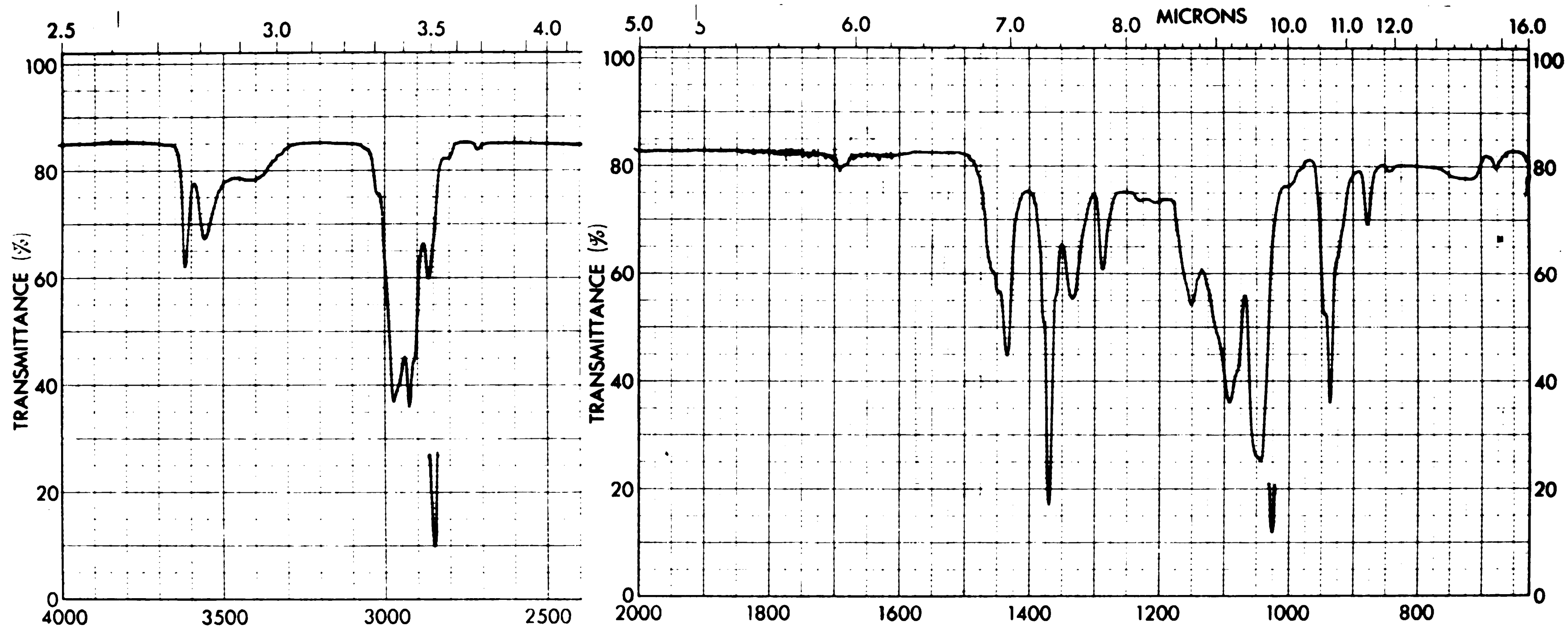


Figure 25. Infrared spectrum (CCl_4) of the hydroxylation product (112) of 100.

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