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The chemistry and photochemistry of gamma-tropolone methyl ether

Daniel Jerome Pasto
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TROPOLONE METHYL ETHER.

Iowa State University of Science and Technology
Ph.D., 1960
Chemistry, organic

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THE CHEMISTRY AND PHOTOCHEMISTRY OF
GAMMA-TROPOLONE METHYL ETHER

by

Daniel Jerome Pasto

A Dissertation Submitted to the
Graduate Faculty in Partial Fulfillment of
The Requirements for the Degree of
DOCTOR OF PHILOSOPHY

Major Subject: Organic Chemistry

Approved:

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1960

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VITA

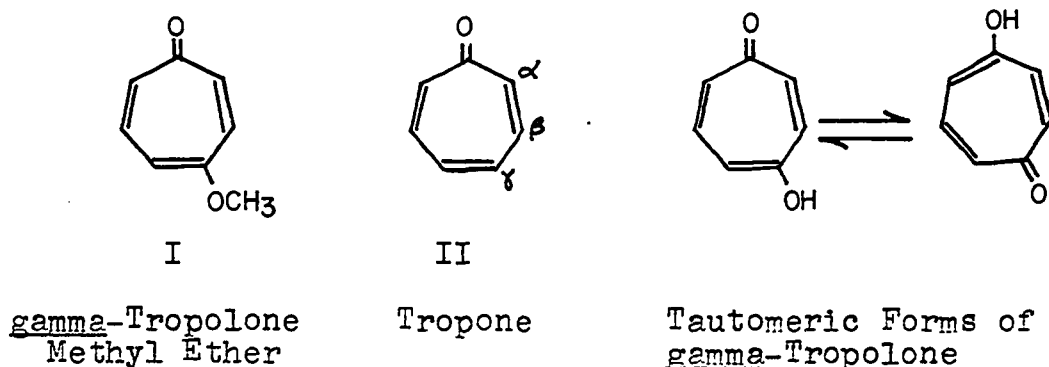
The author was born in Elmira, New York, on January 21, 1936, to Mr. and Mrs. Toivo Pasto. He attended Van Etten Central High School and was graduated in June of 1953. In September of the same year he enrolled at Rochester Institute of Technology. He received the Associate in Applied Science Degree in June of 1956 and continued on for his Bachelor's Degree which he received in November of 1957. During his studies at Rochester Institute of Technology he received scholarships in 1953-4 and 1956-7. The author was employed in the Industrial Laboratory at Eastman Kodak Company, Rochester, New York, as a technician and chemist during his cooperative employment with Rochester Institute of Technology.

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The author has received a National Science Foundation Post-doctoral Fellowship to further his studies under Professor E. J. Corey at Harvard University at Cambridge, Massachusetts.

INTRODUCTION

The troponoid compounds are a family of compounds containing the 2,4,6-cycloheptatrienone nucleus. The parent compound of this family is 2,4,6-cycloheptatrienone or tropone (II) shown below. The main feature of this family is that



they show considerable aromatic character. These compounds undergo substitution reactions rather than undergoing normal addition reactions. This is demonstrated by the ready electrophilic substitution reactions such as halogenation, azo coupling, nitrosation, nitration and sulfonation.^{1,2,3} The troponoid compounds do not undergo Friedel-Crafts alkylations and acylations, or the Gatterman aldehyde and ketone syntheses

¹P. L. Pauson, Chem. Rev., 55, 9 (1955).

²T. Nozoe, Fortschritte der Chemie Organischer Naturstoffe, Wein-Springer, Austria, 1956, pp. 232-301.

³T. Nozoe, Festschrift Prof. Dr. Arthur Stoll, Birkhauser A. G., Basel, Switzerland, 1957, pp. 746-783.

as do benzenoid compounds. In addition troponoid compounds undergo many nucleophilic substitutions such as amination and hydrolysis reactions.

It is easily seen that there can exist three different monosubstituted tropones, the substitution occurring at the α , β or γ carbon atoms. Of particular interest are the hydroxytropones or tropolones designated as alpha-tropolone, beta-tropolone and gamma-tropolone. These tropolones may exist in two tautomeric forms as shown. When these tropolones are further substituted, reactions may occur through both tautomeric forms giving a mixture of products. The nomenclature of polysubstituted tropones uses a numbering system starting from the carbonyl carbon as carbon atom one which gives the lowest set of numbers. In the case of the tropolone methyl ethers, the numbering system starts at the carbonyl carbon and progresses around the ring giving the methoxyl group the lowest possible number.

Alpha-tropolone is unique in that the two oxygen functions are on adjacent carbon atoms and are thus able to form stable chelates with metal ions. The beta- and gamma-isomers cannot form such chelates. The tropolones are acidic in nature due to the presence of the enolic hydroxyl group. The troponoid compounds also form stable salts with mineral acids showing their basic character. The carbonyl function of troponoid compounds, except in the benzotropolones and tro-

pone, does not undergo any of the normal reactions of the carbonyl group.

The chemistry of tropone and alpha-tropolone has been exhaustively studied.^{1,2,3} Beta-tropolone has not been studied extensively due to the unavailability of the compound.⁴ A recent report describing a practical synthesis of gamma-tropolone methyl ether (I), has made it possible to synthesize this compound in the laboratory.⁵ It was therefore of great interest to study the chemistry and photochemistry of gamma-tropolone methyl ether and to compare it with tropone and alpha- and beta-tropolone. The work described in this Thesis is concerned with the chemistry and photochemistry of gamma-tropolone methyl ether and related compounds.

⁴A practical synthesis of beta-tropolone has now been worked out (O. L. Chapman and P. Fitton, Research Journal of P. Fitton (manuscript), Department of Chemistry, Iowa State University of Science and Technology, Ames, Iowa, 1960).

⁵J. Meinwald and O. L. Chapman, J. Am. Chem. Soc., 80, 633 (1958).

HISTORICAL

Colchicine, an alkaloid isolated from the autumn crocus (Colchicum autumnale) in 1820 by Pelletier and Caventou,⁶ for many years defied attempts to elucidate its structure. The compound was of great interest because of its biological activity and peculiar chemical properties. Colchicine was found to contain four methoxyl groups of which one was easily hydrolyzed to give a new compound, colchiceine.⁷ Colchiceine gave an intense green color with ferric chloride and formed a stable copper complex. Colchiceine was acidic and could be reconverted to colchicine by treatment with methanolic hydrochloric acid. Treatment of colchiceine with diazomethane gave colchicine and an isomeric compound isocolchicine.⁸ On treatment with iodine and base one carbon atom was lost giving a phenolic product.⁹ Colchicine gave no reaction with ketonic reagents and on hydrogenation gave a variety of products.^{10,11}

A second natural product, stipitatic acid, isolated from

⁶Pelletier First name not given and Caventou First name not given, Ann. Chim. Phys., 14, 69 (1820).

⁷S. Zeisel and K. R. Stockert, Monatsh. Chem., 34, 1339 (1913).

⁸M. Sorkin, Helv. Chim. Acta, 29, 246 (1946).

⁹A. Windaus, Ann., 439, 59 (1924).

¹⁰H. R. V. Arnstein, J. Am. Chem. Soc., 71, 2448 (1949).

¹¹A. D. Kemp and D. S. Tarbell, ibid., 72, 243 (1950).

Penicillium stipitatum by Birkenshaw¹² and coworkers in 1942 also showed peculiar chemical properties. It was shown to contain three active hydrogens but was titrated as a dibasic acid. Methylation with diazomethane gave two isomeric neutral products which were inert toward carbonyl reagents. Stipitatic acid gave a deep red color with ferric chloride and was decarboxylated by heating to a monobasic acid which displayed properties similar to stipitatic acid. Stipitatic acid when fused with alkali gave 5-hydroxy-isophthalic acid. Stipitatic acid also gave a monobromide when treated with bromine in acetic acid.

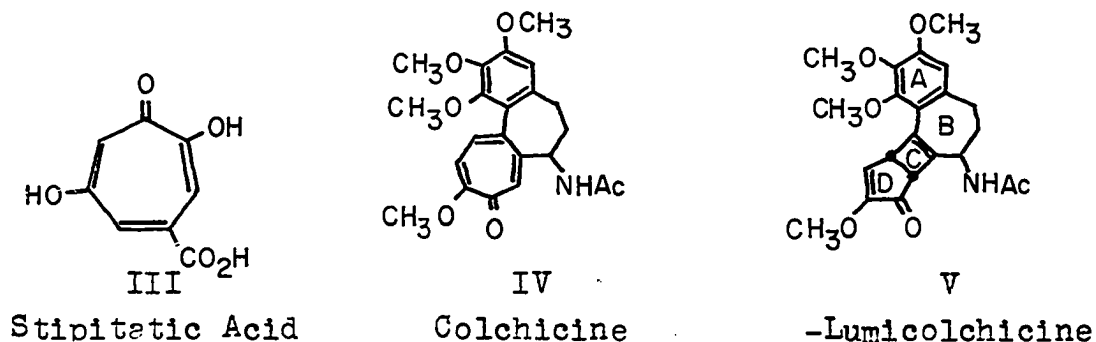
The chemical behavior of both colchicine and stipitatic acid was very confusing and could not be explained by any known type of structure. Dewar,¹³ in 1945, by careful consideration of the experimental evidence and on the basis of theoretical considerations proposed that the structure of stipitatic acid was III. Dewar proposed that this cycloheptatrienolone system be referred to as a tropolone or a tropoid system. A month later, Dewar¹⁴ proposed that colchicine might also contain a tropolone system, and it was later shown that colchicine had the structural formula IV.

¹²J. H. Birkinshaw, A. R. Chambers and H. Raistrick, Biochem. J., 36, 242 (1942).

¹³M. J. S. Dewar, Nature, 155, 50 (1945).

¹⁴M. J. S. Dewar, ibid., 155, 141 (1945).

Also found in the autumn crocus were several alkaloids which differ greatly in chemical properties from colchicine but which were isomeric with colchicine.^{15,16} It was later discovered by Grewe¹⁷ and coworkers that colchicine undergoes photochemical transformations when irradiated with sunlight giving three isomeric compounds. Šantavý¹⁸ compared these lumicolchicines with the unknown alkaloids from autumn crocus and found two of them to be identical to the lumicolchicines. Forbes¹⁹ and Gardner²⁰ and coworkers have proposed the gross structure V for β - and γ -lumicolchicine, the difference between the β - and γ -isomers lies in the stereochemistry of



¹⁵F. Šantavý, H. Hoščálková, R. Podevínský and H. Potěšilová, Chem. Listy, **48**, 886 (1954).

¹⁶F. Šantavý and V. Macak, ibid., **47**, 1214 (1953).

¹⁷R. Grewe and W. Wulf, Ber., **84**, 621 (1951).

¹⁸F. Šantavý, Coll. Czech. Chem. Comm., **16**, 655 (1951).

¹⁹E. J. Forbes, J. Chem. Soc., 1864 (1955).

²⁰P. D. Gardner, R. L. Brandon and G. R. Haynes, J. Am. Chem. Soc., **79**, 6334 (1957).

the C-D ring juncture. The structure of α -lumicolchicine is unknown.

The discovery of the troponoid system opened up a great new area of research. The synthesis of these compounds was difficult and usually gave poor yields. Tropone was first synthesized by Doering and Detert²¹ and Dauben and Ringold²² in 1951 and later by van Tamelin et al.²³ in 1956. Alpha-tropolone has been prepared in many ways including the selenium oxidation of cycloheptanone followed by dehydrogenation, persulfate oxidation of tropone, and by amination of tropone followed by hydrolysis.^{1,2,3} Beta-tropolone has been prepared in small quantities by Johnson and coworkers²⁴ using a diazoacetic ester ring expansion of resorcinol dimethyl ether. Gamma-tropolone had also been prepared in milligram quantities by Nozoe²⁵ and coworkers by hydrolysis of 4-bromotropone obtained as a by-product in the bromination of cyclo-

²¹W. von E. Doering and F. L. Detert, ibid., 73, 876 (1951).

²²H. J. Dauben and H. J. Ringold, ibid., 73, 876 (1951).

²³E. E. van Tamelin, P. Barth and F. Lornitzo, ibid., 78, 5442 (1956).

²⁴R. B. Johns, A. W. Johnson and M. Tišler, J. Chem. Soc., 4605 (1954); A. W. Johnson and M. Tišler, ibid., 1841 (1955).

²⁵T. Nozoe, T. Mukai, Y. Ikegama and T. Toda, Chemistry and Industry, 66 (1955).

heptanone, and by Johnson²⁶ and coworkers by diazoacetic ester ring expansion of hydroquinone dimethyl ether. Finally in 1957, Meinwald and Chapman⁵ reported a procedure capable of synthesizing gamma-tropolone methyl ether in gram quantities by the degradation of 6 β , 7 β -dimethoxytropinone methobromide.

The chemistry of tropone and alpha-tropolone has been exhaustively studied. Certain aspects of the chemistry of these interesting compounds will be discussed later in this Thesis. There has been only one report on the chemistry of beta-tropolone, that being by Johnson and Tišler²⁴ on the halogenation, nitration, azo coupling and formation of a Diels-Alder adduct (the chemical evidence presented leaves the structure of the adduct in doubt).

The chemistry of gamma-tropolone that had been studied includes bromination,^{25,26,27} coupling with diazonium salts,²⁵ methylation,²⁵ benzoylation,²⁵ hydrogenation²⁵ and salt formation.²⁵

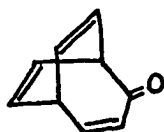
²⁶R. S. Coffey, R. B. Johns and A. W. Johnson, ibid., 658 (1955).

²⁷R. S. Coffey and A. W. Johnson, J. Chem. Soc., 1741 (1958).

DISCUSSION

Diels-Alder Adducts of gamma-Tropolone
Methyl Ether and Tropone

Despite the aromatic character displayed by troponoid compounds, tropones, tropolone and the thujaplicins readily undergo the Diels-Alder reaction with maleic anhydride.^{28,29,30,31} The structures of some of the adducts are still unknown. Due to the interest in highly unsaturated bicyclic systems, it was thought that entry might be gained into the bicyclo [3.2.2] nonatrienone system (VI) via the Diels-Alder



VI

adducts of troponoid compounds. This might be attained by means of bis-decarboxylation reaction with lead tetraacetate.³²

²⁸T. Nozoe, T. Mukai, K. Takase and T. Nagase, Proc. Japan Acad., 28, 477 (1952).

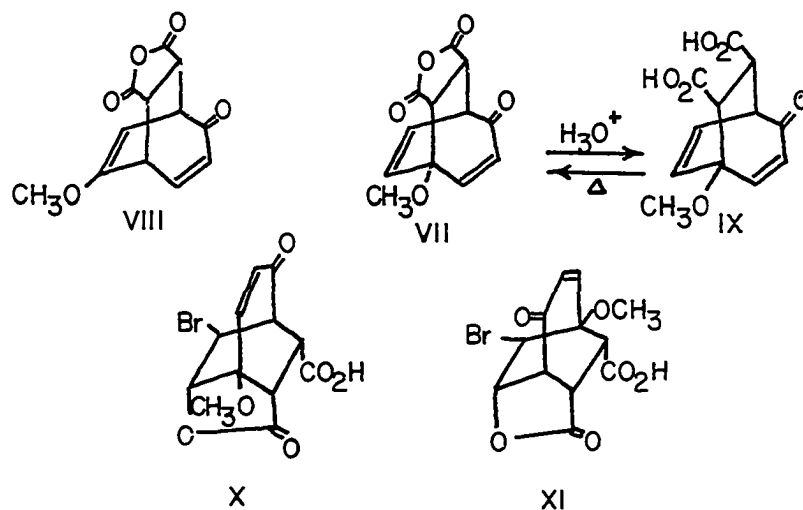
²⁹T. Nozoe, S. Seto and T. Ikemi, ibid., 27, 655 (1951).

³⁰E. Sebe and C. Osaho, ibid., 28, 282 (1952).

³¹E. Sebe and Y. Itaumo, ibid., 29, 107 (1953).

³²W. von E. Doering and M. Finkelstein, J. Org. Chem., 23, 141 (1958); C. A. Grob, M. Okta, E. Renk and A. Weiss, Helv. Chim. Acta, 41, 1191 (1958).

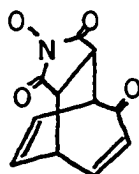
The reaction of gamma-tropolone methyl ether (I) with maleic anhydride in refluxing xylene gave in 64% yield, a single, crystalline adduct. The infrared spectrum of the adduct showed peaks at 5.40, 5.60, and 5.95 μ , and showed a maximum in the ultraviolet at 231 μ (8800). The adduct absorbed two moles of hydrogen giving a non-crystalline material which showed peaks in the infrared at 5.40, 5.60 and 5.85 μ . Treatment of the adduct with dilute acid under mild conditions caused no change. More vigorous hydrolysis in boiling water or hot dilute acid gave a dibasic acid (5.85 and 5.95 μ , $\lambda_{\max}^{95\% \text{ EtOH}}$ 232 μ (5400)) without loss of carbon. The diacid, when subjected to sublimation at 150 $^{\circ}$ and 0.1 mm., gave back pure adduct. Reduction with lithium aluminum hydride followed by acid hydrolysis produced a non-crystalline alcohol which showed no carbonyl absorption in the infrared. This evidence is therefore consistent only with the adduct VII, and not with the alternative adduct (VIII), which contains an enol ether group. The structure of the diacid must be that shown as IX. Treatment of an aqueous solution of the diacid with bromine gave in 71% yield a crystalline bromolactone (5.56, 5.78 and 5.92 μ , $\lambda_{\max}^{95\% \text{ EtOH}}$ 227 μ (5700)), which must have either the structure X or XI. In either case the stereochemistry must be that shown in VII. In an attempt to decarboxylate IX with lead tetraacetate in a refluxing benzene-pyridine mixture, the only materials



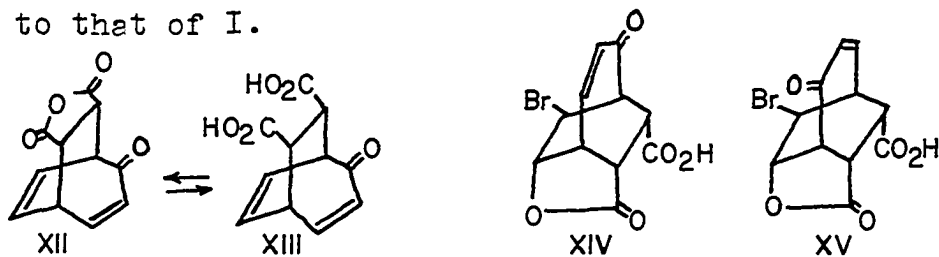
recovered were VII and IX.

In similar fashion a Diels-Alder adduct of troponone (II) and maleic anhydride was prepared in refluxing xylene giving colorless cubes (5.42, 5.64, 6.02, and 6.17 μ , $\lambda_{\text{max}}^{95\% \text{ EtOH}}$ 227 (7000) and 337 μ (120)). (Although this adduct had been prepared previously,²⁸ the structure and stereochemistry were not given³³). Dissolution of the adduct (XII) in boiling water gave on cooling a dibasic acid (XIII) (5.76, 5.87 (weak), 6.09, and 6.17 μ , $\lambda_{\text{max}}^{95\% \text{ EtOH}}$ 228 (7600) and 337 μ (140)). Treatment of an aqueous solution of XIII gave a

³³The N-phenyl maleimide adduct of troponone has been prepared and has been assigned the following structure (see footnote 39).



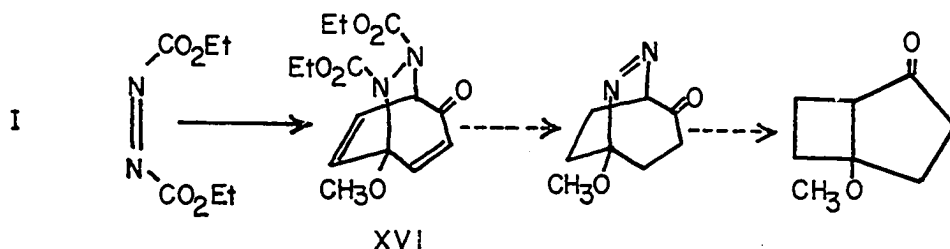
bromolactone (5.63, 5.76, 5.98, and 6.15 μ , $\lambda_{\max}^{95\% \text{ EtOH}}$ 228 (9800) and 275 μ (shoulder) (1300)) which must be either XIV or XV. Again the structure of this adduct must be XII, similar to that of I.



The Diels-Alder reaction of I with diethylazodicarboxylate as the dienophile was also investigated. The Diels-Alder reaction of diethylazodicarboxylate with dienes, gives the 1,2,3,6-tetrahydropyrazine system.³⁴ These adducts readily undergo dehydrogenation with selenium hydroxide to give N,N'-dihydropyrazines.³⁴ Hydrolysis of these adducts in basic media results in immediate decarboxylation and oxidation to the azo compound.³⁴ The azo compounds, derived from the adducts after hydrogenation and hydrolysis, undergo facile pyrolysis with the elimination of nitrogen producing a cyclobutene derivative.³⁵ Knowing this, it was thought that such a procedure might be carried out on the adduct of I with diethylazodicarboxylate leading to the bicyclo[3.2.0]heptane series as shown schematically below.

³⁴O. Diels, J. Blom, and W. Koll, *Ann.*, **443**, 242 (1925); O. Diels and K. Alder, *ibid.*, **450**, 237 (1926); K. Alder and H. Niklas, *ibid.*, **585**, 81 (1954); K. Alder and H. Niklas, *ibid.*, **585**, 97 (1954).

³⁵R. Criegee and A. Rimmelin, *Ber.*, **90**, 414 (1957).



Refluxing I for six hours with diethylazodicarboxylate in xylene produced, after chromatography of the reaction residue, a dark yellow, viscous oil (5.81 μ and $\lambda_{\text{max}}^{95\% \text{ EtOH}} 330 \text{ m}\mu$ (590)) and a colorless crystalline material (2.91 and 5.75 μ) in 21% yield based on diethylazodicarboxylate. The colorless crystals were identified as diethyldicarbamate³⁶ (1,2-dicarbethoxyhydrazine) by analysis, spectral data and melting point.³⁷ The spectral characteristics of the yellow oil are not what one would expect for the adduct XVI.³⁸ The yellow oil partially crystallized but resisted all attempts at purification. Attempted hydrolysis of the yellow

³⁶J. Sanstrom, *Arkiv. Kemi.*, 8, 487 (1955).

³⁷Diethyl dicarbamate has also been isolated from the reaction of cyclohexanone and diethylazodicarboxylate (R. Huisgen and F. Jakob, *Ann.*, 590, 37 (1954)). The appearance of diethyl dicarbamate in the reaction mixture of I and diethylazodicarboxylate is unexplainable.

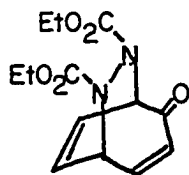
³⁸Tropone gives a normal adduct with diethylazodicarboxylate which shows peaks in the infrared at 5.80 and 5.93 μ although the ultraviolet spectrum is anomalous showing $\lambda_{\text{max}}^{95\% \text{ EtOH}} 209 \text{ m}\mu$. The structure is (continued on next page)

oil in either dilute acid or base lead to the rapid evolution of a gas and unidentifiable tars. A more productive approach might have involved prior hydrogenation with subsequent hydrolysis as shown in the scheme above.

Reactions of gamma-Tropolone Methyl Ether and Tropone
with Grignard and Hydride Reagents

The reaction of I with methyl magnesium iodide, followed by hydrolysis with water, gave a crude reaction product which showed peaks in the infrared at 2.92, 5.85, 6.10, 6.15, and 7.27 μ . Chromatography on an alumina column gave a ketonic fraction in 46% yield (5.85, 6.10, 6.15, and 7.27 μ , Figure 8, page 221; $\lambda_{\max}^{95\% \text{ EtOH}}$ 331 μ (3,600) with end absorption, Figure 19, page 243), and an alcoholic fraction in 19% yield (2.97, 6.08, 6.10, 6.16, 6.22, and 7.25 μ , Figure 8, page 221 $\lambda_{\max}^{95\% \text{ EtOH}}$ 220 (7,300) and 325 μ (4,500), Figure 23, page 251

(Footnote continued from previous page)
shown below and is supported by the nuclear magnetic resonance spectrum (O. L. Chapman, Research Journal, Department of Chemistry, Iowa State University of Science and Technology, Ames, Iowa, 1959).



Analysis of the ketone fraction by gas phase chromatography showed the presence of two compounds, the major component comprising 90% of the mixture. The analysis of the ketone fraction was consistent with the formula $C_9H_{12}O_2$, which indicated the addition of CH_4 to the starting material. The ketone mixture contained an enol ether group as demonstrated by hydrolysis in dilute acid to an enedione (5.85, 5.99, and 6.17, $\lambda_{max}^{95\% EtOH}$ 233 (shoulder) and 388 mu, Figure 19, page 243.

Treatment of the ketone mixture with lithium aluminum hydride gave a mixture of alcohols (2.98, 6.06, 6.13, and 6.21 u, Figure 9, page 223; $\lambda_{max}^{95\% EtOH}$ 256 mu (5,600), Figure 20, page 245). Hydrolysis of the alcohol mixture in dilute acid gave a mixture of a ketoalcohol and 2,4-cycloheptadienone (2.9 and 6.03 u, $\lambda_{max}^{95\% EtOH}$ 228 and 293 mu, Figure 20, page 245). Further treatment in dilute base resulted in dehydration of the ketoalcohol to the 2,4-cycloheptadienone with a maximum in the ultraviolet at 293 mu. The methyl cycloheptadienone was hydrogenated over Adams Catalyst in methanol giving the corresponding methyl-cycloheptanones. Comparison of the methycycloheptanone mixture with authentic methyl-cycloheptanones by gas phase chromatography, showed the presence of 3-methylcycloheptanone and 4-methylcycloheptanone in a ratio of 7:1. The original ketone mixture must therefore have contained 85-90% of a compound resulting from attack

at C₂, 2-methyl-4-methoxy-3,5-cycloheptadienone (XVII), and 10-15% of a compound resulting from attack at C₇, 2-methyl-5-methoxy-3,5-cycloheptadienone (XVIII). The structures are shown on page 19.

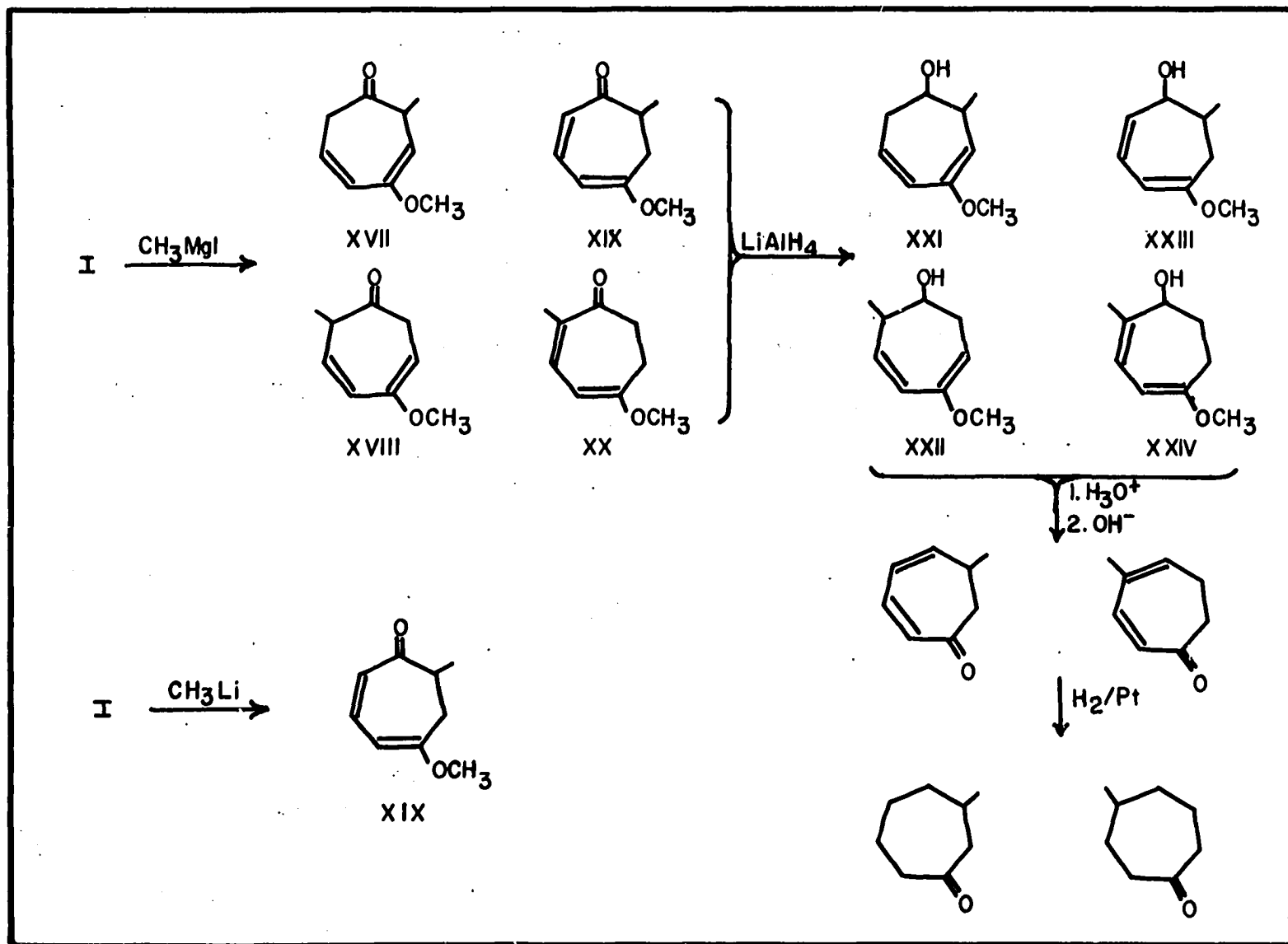
The ketone mixture, when treated with 0.1N base, undergoes double-bond isomerization to a mixture of ketones which shows peaks in the infrared 6.08, 6.14, and 7.27 μ . The ultraviolet spectrum of the new ketone mixture shows an increased intensity at 328 μ with a decrease in the intensity of the end absorption. This ketone mixture when hydrolyzed in dilute acid, gives an enedione with spectral properties identical to those of the enedione obtained by acid hydrolysis of the original ketone mixture.

Treatment of I with methyl lithium, followed by hydrolysis with water, gives a ketone identical in spectral properties with the ketone obtained by base-catalyzed double bond isomerization. The infrared spectrum is shown in Figure 11, page 227. The yield of this ketone by the reaction of I with methyl lithium was very low (12%), although I was recovered in 50% yield. The 328 μ maximum in the ultraviolet spectrum of the ketone obtained by the action of methyl Grignard on I, is probably due to the presence of a small amount of 7-methyl-5-methoxy-2,4-cycloheptadienone, XIX, arising by base-catalyzed double-bond isomerization of the corresponding 3,5-dienone. The isolation of only the 5-methoxy-2,4-

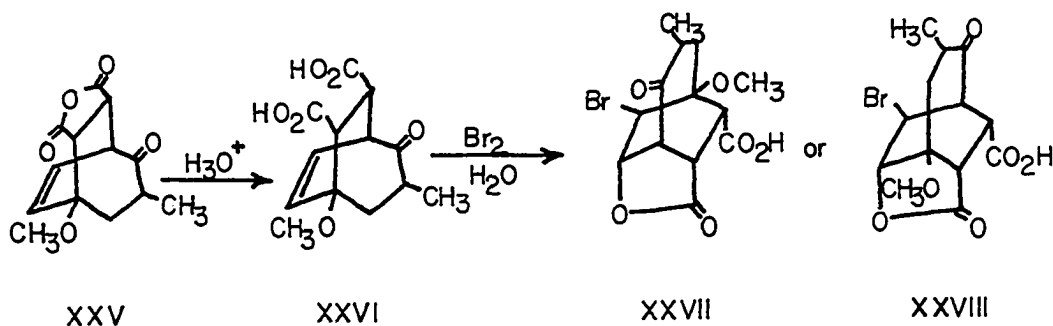
cycloheptadienone, XIX, arising by base-catalyzed double-bond isomerization of the corresponding 3,5-dienone is undoubtedly due to the more basic conditions encountered during the hydrolysis of this reaction mixture. Lithium hydroxide is distinctly more basic than magnesium hydroxide. The original ketone mixture obtained by the action of methyl magnesium iodide on I therefore must contain XVII as the major component, with XVIII, XIX, and 2-methyl-5-methoxy-2,4-cycloheptadienone (XX) as minor components. The alcohol mixture, obtained by hydride reduction of the ketone mixture, must have contained the corresponding alcohols with XXI as the major component and XXII, XXIII, and XXIV as minor components. The conversion of the ketone mixture to the methylcycloheptanones, via the alcohols, is shown in Figure 1, page 19.

Heating the ketone mixture with maleic anhydride in benzene gave in good yield a noncrystalline adduct (XXV); which, when treated with base and benzaldehyde, gave no benzylidene derivative. Hydrolysis of the adduct in boiling water gave a crystalline diacid (XXVI), $C_{13}H_{16}O_6$, which in turn gave an oily bromolactone on treatment with bromine in aqueous solution. The bromolactone did not give a benzylidene derivative on treatment with base and benzaldehyde. The structure and stereochemistry of the bromolactone must be

Figure 1. Structures of compounds derived from gamma-tropolone methyl ether and methyl magnesium iodide



either XXVII or XXVIII with XXV and XXVI as the adduct and diacid. The rearrangement



of 3,5-cycloheptadienone to 2,4-cycloheptadienone during the formation of the adduct has been observed previously.³⁹ This transformation in the above case is facilitated by the presence of the methoxyl which stabilizes the transition state. The failure of the adduct and the bromolactone to give benzylidene derivatives gives additional evidence that the major component in the ketone mixture was formed by attack at C₂.

In an attempt to provide additional evidence as to the position of the methyl group, the conversion of the ketone mixture to a benzoic acid derivative was attempted. The ketone mixture was treated with bromine to form a bromo-compound which was then refluxed in base in an attempt to

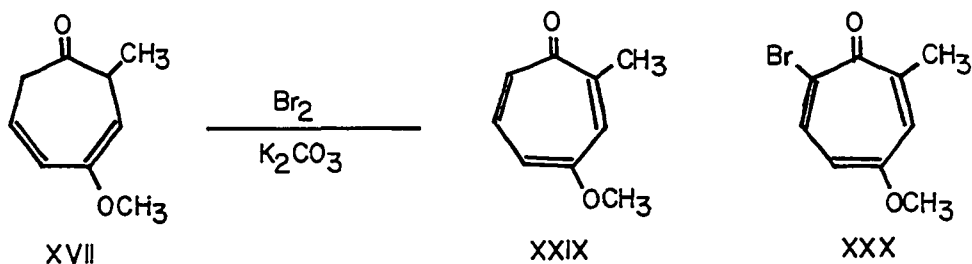
³⁹J. Meinwald, S. L. Emmerman, N. C. Yang and G. Büchi, *J. Am. Chem. Soc.*, **77**, 4401 (1955).

effect ring contraction. Methylation of the crude product gave a small amount of a troponoid compound (identified by its characteristic ultraviolet spectrum: methyl ether $\lambda_{\max}^{95\% \text{ EtOH}}$ 232 (12,000), 254 (shoulder) (6,800) and 343-8 (7,000); anion $\lambda_{\max}^{\text{dil. NaOH}}$ 237 (16,000), 286 (2,000) and 372 mu (11,000); and free tropolone $\lambda_{\max}^{\text{dil. H}_2\text{SO}_4}$ 241 (14,500) and 351 mu (7,500)). The spectral properties would suggest that this compound is substituted in the seven position by a bromine or oxygen function (see the following discussion on the troponoid compounds obtained by bromine oxidation of the ketone mixture, page 22), but any further speculation as to the possible structure would be pure conjecture. No benzenoid derivative was isolated from the reaction.

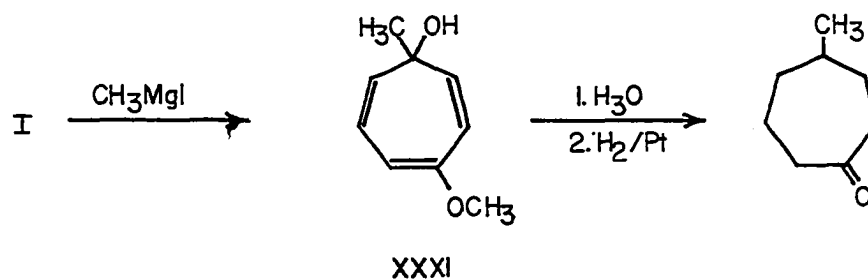
Dehydrogenation of the ketone mixture in carbontetrachloride with bromine produced two new troponoid compounds. The first compound was a pale yellow liquid (6.15, 6.21, 6.38 and 7.30 u, Figure 10, page 225; $\lambda_{\max}^{95\% \text{ EtOH}}$ 228 (24,000) and 328 (12,000), Figure 21, page 247) which undergoes hydrolysis in base at 80° to give the anion ($\lambda_{\max}^{0.1N \text{ NaOH}}$ 231 (21,000) and 357 mu (15,000), Figure 21, page 247). Neutralization of the basic solution produced the ultraviolet spectrum of the free tropolone showing $\lambda_{\max}^{0.1N \text{ H}_2\text{SO}_4}$ 234 (26,000) and 331 mu (13,000), Figure 21, page 247. As the introduction of alkyl groups in the troponoid nucleus causes no shift in ultraviolet maxima from the parent compound,² the structure assigned to

this compound is 2-methyl-gamma-tropolone methyl ether (XXIX).

The second troponoid compound (6.18, 6.27, 6.64, and 7.30 μ , Figure 10, page 225; $\lambda_{\text{max}}^{95\% \text{ EtOH}}$ 232 (14,200), 253 (shoulder) (8,700) and 343 μ (8,300), Figure 22, page 249) was a pale yellow, crystalline material which apparently contained a bromine atom. The anion, produced by basic hydrolysis, showed maxima in the ultraviolet in 0.1N sodium hydroxide at 237-8 (14,400) and 371 μ (12,000), Figure 22, page 249. The free tropolone showed maxima in the ultraviolet in ethanol solution at 241 (14,500) and 349 μ (8,200), see Figure 22, page 249. Comparison of the ultraviolet spectra of 5-bromo-, 5,7-dibromo-, and 2,5,7-tribromo-gamma-tropolone,²⁷ shows that in the case of bromine substitution at positions 2 and 7, a bathochromic shift of 17 μ occurs in the low wavelength band, whereas with bromine substitution only at position 5 no bathochromic shift occurs. The troponoid compound obtained by oxidation of XVII displays a bathochromic shift of 16 μ when compared to gamma-tropolone; consequently the structure assigned to this compound is 2-methyl-7-bromo-gamma-tropolone methyl ether (XXX).



The structure assigned to the alcoholic product, from the reaction of I with methyl magnesium iodide (page 14), is 1-hydroxy-1-methyl-4-methoxy-2,4,6-cycloheptatriene, XXXI. The assignment of this structure is based on spectral evidence (2.97, 6.08, 6.10, 6.16, 6.22 and 7.25 μ ; $\lambda_{\max}^{95\% \text{ EtOH}}$ 220 (7,300) and 325 μ (4,500)) and the fact that acid hydrolysis followed by hydrogenation gives 4-methylcycloheptanone with no evidence for the presence of either the 3- or 2-methyl isomer. The infrared spectrum of XXXI shows hydroxyl absorption and lacks the characteristic troponoid peaks in the 6.0-6.5 μ region (Figure 8, page 221). The 6.0-6.5 μ region is quite similar to the same region in the spectrum of XXI. The ultraviolet spectrum of XXXI is not characteristic of any cycloheptadiene and the intensity is far too weak for a troponoid spectrum (Figure 23, page 251).⁴⁰



⁴⁰4-Methoxycycloheptatrienecarboxylic acid shows maxima in the ultraviolet at 219 (log ϵ 4.21) and 313 μ (log ϵ 4.04) (J. R. Bartels-Keith, A. W. Johnson and A. Langeman, *J. Chem. Soc.*, 4461 (1952)) and the methyl ester showed maxima at 223-225 (log ϵ 4.17) and 314-315 μ (log ϵ 4.05) (R. B. Johns, A. W. Johnson, A. Langeman and J. Murray, *ibid.*, 309 (1955)).

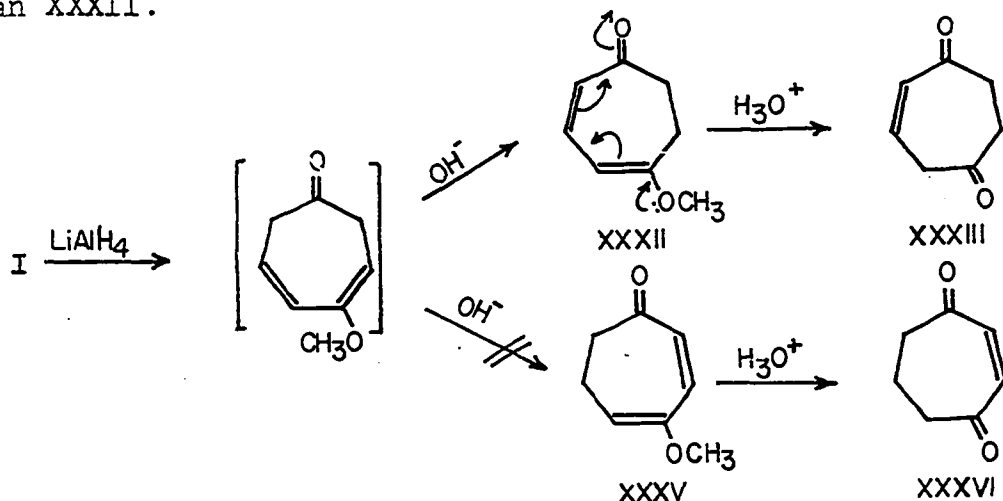
The reaction of I with lithium aluminum hydride, followed by hydrolysis with water, gave two fractions which were easily separated by alumina chromatography. The first fraction was ketonic and showed peaks in the infrared at 6.05, 6.19, and 6.39 μ (Figure 11, page 227) with a maximum in the ultraviolet at 328 $m\mu$ (Figure 24, page 253). Hydrolysis of the ketone in dilute acid at room temperature gave an enedione (5.85, 6.00 and 6.16 μ , Figure 11, page 227; $\lambda_{\text{max}}^{95\% \text{ EtOH}}$ 340 $m\mu$ (6,800) with end absorption). The enedione absorbed 1.0 mole of hydrogen over Adams' Catalyst in methanol giving 1,4-cycloheptanedione, identified as the bis-2,4-dinitrophenylhydrazone.⁴¹ Comparison of the spectral and hydrolysis data for this ketone with ketone XIX, suggests that this ketone has the structure 5-methoxy-2,4-cycloheptadienone,⁴² XXXII, and that the enedione is 2-cyclohepten-1,5-dione, XXXIII.

As in the case of the reaction of I with methyl magnesium iodide, one might envision attack by hydride at either the 2- or 7-position resulting in the formation of 4-methoxy-3,5-cycloheptadienone, XXXIV. The hydrolytic procedure results

⁴¹A. C. Cope, T. A. Liss and G. W. Wood, J. Am. Chem. Soc., 79, 6287 (1957).

⁴²5-Methoxy-2,4-cycloheptadienone and its acid hydrolysis product are apparently quite toxic. Inhalation of small amounts of the vapors caused dizziness and in more concentrated doses caused an intense burning sensation which subsided after 15 minutes. Contact of the material with the skin in extremely small amounts caused a yellowing of the skin.

in the formation of a basic solution which causes the base-catalyzed double-bond isomerization to the observed product. It is important to note that apparently no 4-methoxy-2,4-cycloheptadienone (XXXV) is formed. This isomer could be detected, after acid hydrolysis, by the formation of 2-cycloheptene-1,4-dione, XXXVI, which has only a single intense peak in the infrared at 6.05 μ and a maximum in the ultraviolet at 229 $m\mu$ (see page 187). The exclusive formation of XXXII from XXXIV is undoubtedly due to the interaction of the methoxyl group with the dienone chromophore as illustrated below. In the case of XXXV, no such interaction is possible and XXXV would have a higher ground state energy, *i.e.*, is less stable than XXXII.



5-Methoxy-2,4-cycloheptadienone, XXXII, which is in the same overall state of oxidation as tropone, is converted to tropone in better than 50% yield when heated successively in 1N sulfuric acid and 0.2N sodium hydroxide at 80° . The basic solution was golden-yellow in color and displayed a 414 $m\mu$

(4,200) maximum in the visible region. The intensity of this maximum slowly decreased on heating, while at the same time giving rise to the typical tropone absorption curve.⁴³ From this evidence it appeared that the tropone was arising by some base-catalyzed reaction from the species causing the 414 μ absorption. Such a process in converting the endione, or its enolate anion, to tropone must involve a double-bond isomerization or an internal hydride shift. A process involving reduction-oxidation reactions, first reduction of XXXIII to cycloheptadienone or a molecule in the same oxidation state followed by oxidation to tropone, is unfavorable as the required reduction step would not be expected to occur in aqueous base, although the oxidative step is known to occur in basic solutions (see page 35). A disproportionation mechanism involving the formation of equivalent amounts of gamma-tropolone and cycloheptadienone can not be operative as any gamma-tropolone formed in significant amounts should be easily observed by its anion peak at 360 μ in the ultraviolet. No 360 μ maximum was observed. The possibility that any gamma-tropolone formed has reacted further in some manner must be discounted, as it has been shown that gamma-tropolone is stable in refluxing barium hydroxide solution for

⁴³The tropone ultraviolet spectrum shows $\lambda_{\text{max}}^{95\% \text{ EtOH}}$
 225 (21,200), 228 (22,100), 232 (22,100), 239 (15,500),
 301 (8,050) (inflection), and 312 μ (8,270) (see footnote
 23).

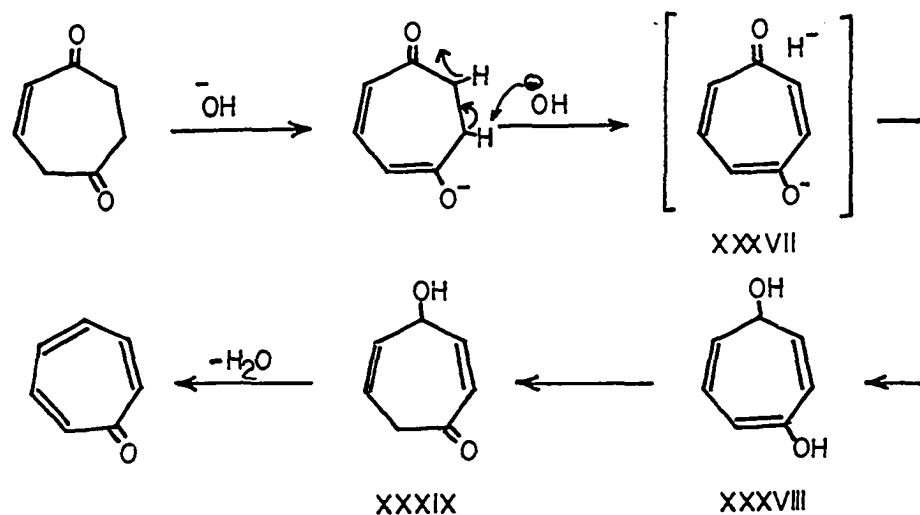
long periods of time.^{25,44}

One possible mechanism for the transformation might involve an internal hydride shift, similar to the Cannizzarro reaction of dialdehydes to give hydroxyacids by intramolecular hydride transfer⁴⁵ in basic solution. Such an internal hydride transfer in the enolate anion of XXXIII leading to reduction of the carbonyl, might go through a transition state XXXVII⁴⁶ which would derive its stability from the incipient gamma-tropolone anion system present. Although attack of hydroxide on an anion leading to the formation of essentially a dianion is unfavorable in this concentration of base, the gain in resonance energy in the transition state XXXVII could be the determining factor. Protonation of the anion XXXVIII would lead to 4-hydroxy-2,5-cycloheptadienone, XXXIX, which being a hydrated aromatic system, would readily eliminate the elements of water in basic solution to give tropone.

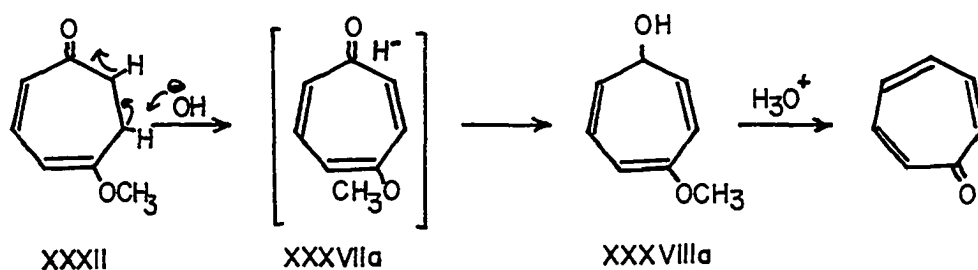
⁴⁴J. Meinwald and O. L. Chapman, Tetrahedron, 3, 311 (1958); J. Meinwald and O. L. Chapman, J. Am. Chem. Soc., 81, 5800 (1959).

⁴⁵T. A. Geissman, Organic Reactions, Vol. 2, John Wiley and Sons, Inc., New York, 1944, pp. 94-113.

⁴⁶The mechanism was suggested by Professor D. Applequist, Department of Chemistry, Illinois University, Urbana, Illinois.



To test for the possible operation of such a mechanism, 5-methoxy-2,4-cycloheptadienone, XXXII, was heated in 0.2N aqueous sodium hydroxide in a similar fashion to see if it would give rise to tropone. If XXXII reacts through the same mechanism as shown above, it was thought that it might be possible to isolate the intermediate alcohol XXXVIIIa from the basic solution by extraction, due to the fact that XXXVIIIa should be much less acidic than XXXVIII. Subsequent acid hydrolysis of the alcohol should then give tropone.

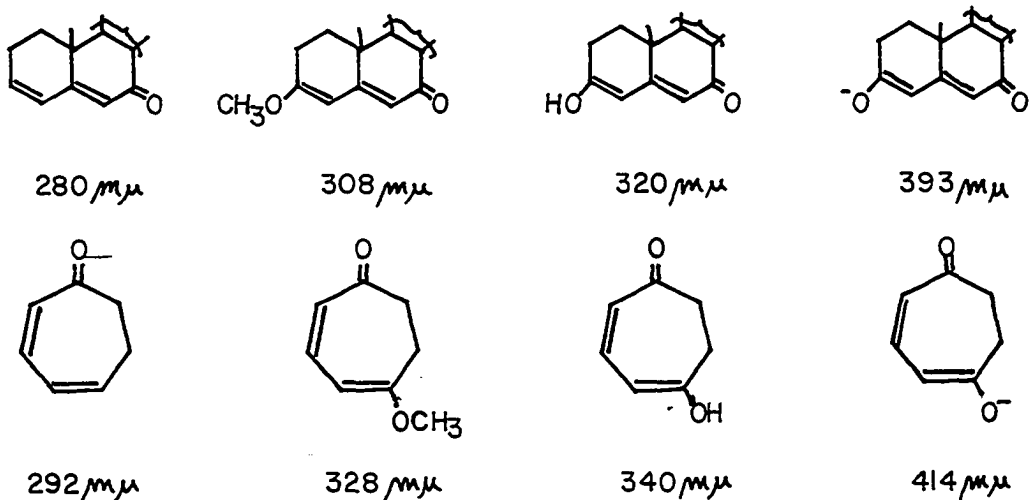


Heating XXXII in 0.2N sodium hydroxide at 90° slowly produced a yellow colored solution. This solution showed a maximum in the visible at 414 mu, as did the basic solution of XXXIII, but in this case the intensity of the maximum slowly increased to an extinction coefficient of 10,800⁴⁷ after 90 minutes of heating. During the same time a 361 mu peak also slowly developed and increased in intensity. Acidification of the basic solution gave an ultraviolet spectrum which showed maxima only at 229 and 331 mu. Again making the solution basic, the 361 and 414 mu maxima were regenerated showing the reversibility of the reactions involved. The 361 mu maximum in base is indicative of the presence of gamma-tropolone anion, which in acid would give the normal spectrum of gamma-tropolone with peaks at 229 and 331 mu. The behavior of the 414 mu maximum also indicated the presence of an enolate anion. As there were no maxima which would indicate that any tropone had formed, the above mechanism for the transformation of XXXIII to tropone via the enolate anion of XXXIII must not be the correct mechanism.

It is important to notice that the 414 mu maximum appears from both the treatment of XXXII and XXXIII with base, and therefore the same species must be present in both solutions,

⁴⁷The extinction coefficient is based on the total concentration of all species present in solution.

but, that this species does not react to give tropone. A comparison of the ultraviolet spectra of 17-hydroxy-3,5-androstadiene-7-one,⁴⁸ 3-hydroxy-3,5-cholestadiene-7-one⁴⁹ and its methyl enol ether⁴⁹ and enolate anion⁴⁹ (part structures are shown below) in the steroid series, with the corresponding cycloheptane analogs, shows a very close parallel in the shifts between the maxima of similar compounds. From the



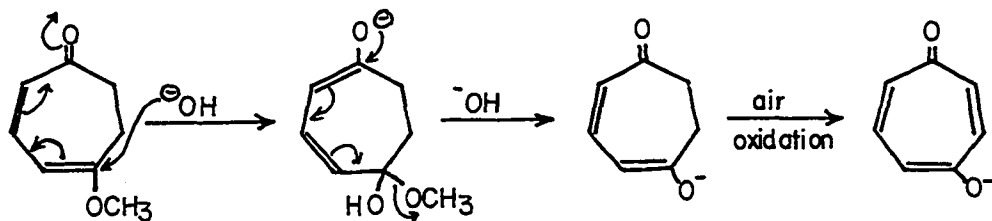
comparison of these spectra and spectra of the basic solutions above, it is reasonable to attribute the absorption at 414 $m\mu$ to the enolate anion of XXXIII.

The mechanism for the conversion of 5-methoxy-2,4-cyclo-

⁴⁸A. Butenandt, E. Hausmann and J. Paland, *Ber.*, **71B**, 1316 (1938); H. Dannenberg, *Abhandl. preuss. Akad. Math. naturw. Kl.*, **21**, 3 (1939).

⁴⁹C. W. Greenhalgh, H. B. Henbest and E. R. H. Jones, *J. Chem. Soc.*, 2375 (1952); J. Barnett, B. E. Ryman and F. Smith, *ibid.*, 526 (1946).

heptadienone to gamma-tropolone anion therefore must be initiated by basic hydrolysis of the doubly vinyligous ester function in XXXII, similar to the basic hydrolysis of I (page 64), directly producing the enolate anion of XXXIII. The anion then undergoes slow air oxidation in the basic solution to give gamma-tropolone anion as evidenced by the presence of the 361 mu absorption maximum in the ultraviolet. The rate of the hydrolysis of XXXII must be faster than the rate of air oxidation of the anion thus causing the intensity of the 414 mu peak to increase toward a maximum value before decreasing. The extinction coefficient for the enolate anion must

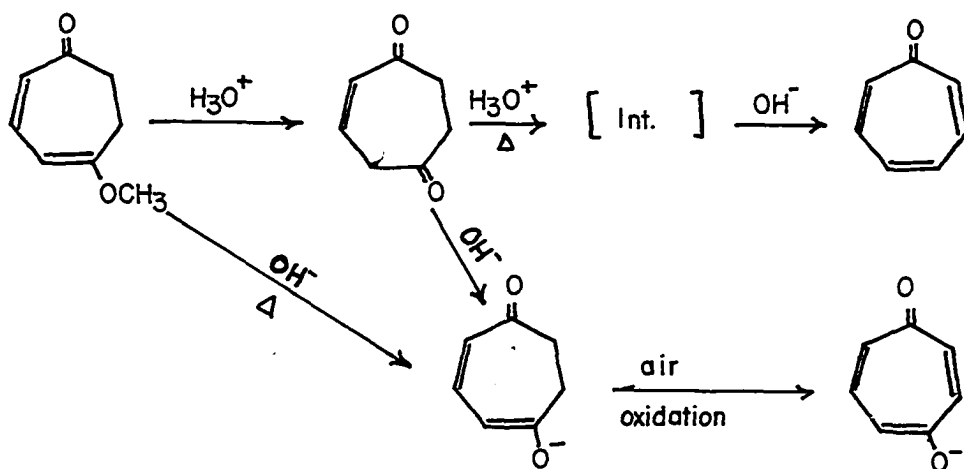


be close to 20,000 based on the observed extinction value when the transformation was 45% complete.

A mechanism which is more consistent with the above observations must be found for the transformation of XXXII to tropone by acid and then basic hydrolysis. Careful inspection of the ultraviolet spectra produced after hydrolyzing XXXII in acid, revealed an interesting fact. The hydrolysis of XXXII in dilute acid at room temperature produced a 340 mu maximum in the ultraviolet whereas hydrolysis in acid

at 50° for 15 minutes produced a spectrum having an intense maximum at 233 mu. It might well be that the species giving rise to this absorption (intermediate Int.) is the one which then reacts with base to give tropone.⁵⁰

The decrease in the intensity of the 414 mu maximum during the subsequent basic treatment is probably due to air oxidation of the enolate anion of XXXIII giving gamma-tropolone. The observed decrease in the intensity of the 414 mu maximum would indicate the formation of only 2-3% of gamma-tropolone anion which would probably not be observable in the ultraviolet due to masking by other absorbing materials in the solution. A mechanism which is more consistent with all of the spectral and chemical data would be as follows:

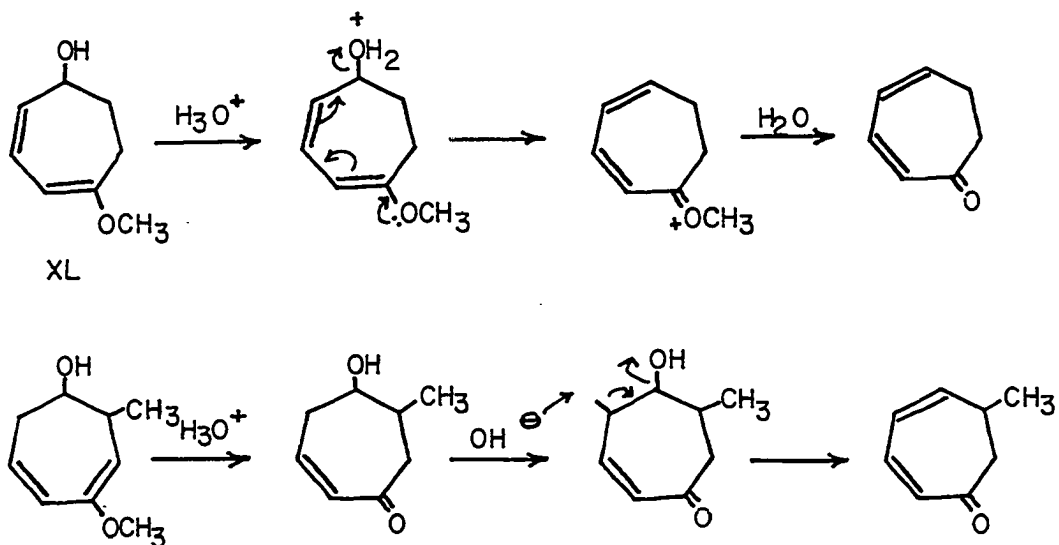


⁵⁰Treatment of a cycloheptadienone mixture with 0.1N acid at 90° also produces a material which absorbs at 230 mu in the ultraviolet (O. L. Chapman and D. J. Pasto, Research Journal of D. J. Pasto, Department of Chemistry, Iowa State University of Science and Technology, Ames, Iowa. 1960).

Hydrogenation of XXXII over Adams' Catalyst in methanol resulted in the absorption of 3.3 moles of hydrogen per mole of compound. Analysis of the products by gas phase chromatography showed the presence of methylcycloheptyl ether, cycloheptanone, 4-methoxycycloheptanone⁵¹ and cycloheptanol in a 3:1:1:1 ratio requiring a total of 3.5 moles of hydrogen per mole of XXXII (see the discussion on the hydrogenation of I on page 64.

Lithium aluminum hydride reduction of XXXII gave an alcohol XL which showed peaks in the infrared at 2.78, 6.10 and 6.22 μ (Figure 9, page 223) and showed a maximum in the ultraviolet in ethanol solution at 256 $m\mu$ (7,800) (Figure 26, page 257). The structure of XL must be 5-methoxy-2,4-cycloheptadienol. Treatment of XL with dilute acid at room temperature instantaneously gave 2,4-cycloheptadienone. The rapid hydrolysis of XL is presumably due to the favorable position of the protonated hydroxyl for expulsion with the help of the unshared electrons of the methoxy group as shown below. The hydroxyl group in alcohol XXI is not favorably disposed and requires the further action of base on the ketoalcohol for the formation of the cycloheptadienone.

⁵¹The structure of this compound was assigned from spectral data. Attempted analysis of the semicarbazone met with failure. The 2,4-dinitrophenylhydrazone resisted attempts at purification and could not be analyzed.



The presence of the 293 μ peak in the hydrolysis of the alcohol mixture containing XXI may arise from XXIII and XXIV, but one cannot exclude the possibility that acid hydrolysis of XXI does not give the cycloheptadienone directly in a slow reaction.

The second product isolated from the reaction of I with lithium aluminum hydride (page 24) was an alcohol (2.77, 6.06, 6.14, and 6.22 μ , Figure 9, page 223; $\lambda_{\text{max}}^{95\% \text{ EtOH}}$ 255 μ (5,520), Figure 27, page 259). Hydrolysis of the alcohol in dilute acid produced a compound which showed an ultra-violet spectrum with maxima at 227 (5,600) and 292 μ (1,400) (Figure 27, page 259), apparently corresponding to a mixture of a ketoalcohol and 2,4-cycloheptadienone. Treatment of the ketoalcohol:2,4-cycloheptadienone mixture with base to effect total conversion to 2,4-cycloheptadienone gave a deep lavender-colored solution. This solution showed a maximum

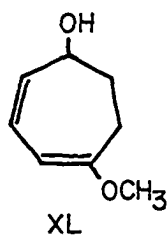
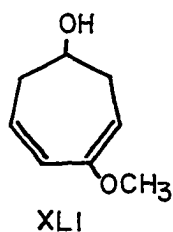
in the visible region at 557 μ , the intensity of which decreased with time, not giving rise to the expected cycloheptadienone, but instead giving tropone in 35% yield. This reaction was completely unexpected. The alcohol when hydrogenated over Adams' Catalyst in methanol absorbed 1.93 moles of hydrogen per mole of compound. The resulting hydrogenation product was homogeneous (as determined by gas phase chromatography) and showed peaks at 2.9 and 9.1 μ in the infrared indicative of a hydroxy ether. The hydrogenation data demonstrated that the alcohol was in a lower state of oxidation than tropone, leaving the mechanism of the transformation to tropone to be determined.

Van Tamelin⁵² has shown that 2,4-cycloheptadienone undergoes air oxidation in dilute base (pH 11-12) at room temperature to give tropone in 38% yield. It was demonstrated that heating a cycloheptadienone mixture under the same conditions used to effect the conversion of XLI to tropone, gave tropone in 62% yield. Therefore the ketoalcohol, derived from the alcohol, undergoes dehydration in the basic solution and then undergoes air oxidation to tropone.

Although the infrared spectrum of the alcohol, obtained from I by hydride reduction, was very similar in the 6.0-6.5 μ region to that of XXI, and dissimilar to that of XL (see

⁵²E. E. van Tamelin and G. T. Hildahl, J. Am. Chem. Soc., 78, 4405 (1956).

Figure 9, page 223), the hydrolysis and ultraviolet data did not rigorously discriminate between XLI and XL as the structure of the alcohol. In an attempt to distinguish between



the three alcohols, XXI, XL and the unknown alcohol (XLI), the alcohols were subjected to oxidation by manganese dioxide in chloroform. It was thought that alcohols XXI and XLI should be unaffected by manganese dioxide whereas XL, being an allylic alcohol, should be readily oxidized to the corresponding dienone XXXII. The expected result was not observed. Treatment of all three alcohols with manganese dioxide resulted in the formation of a 328 mu maximum in the ultraviolet indicative of the formation of the 5-methoxy-2,4-cycloheptadienone system. Therefore the alcohols XXI and XLI either undergo prior double bond isomerization on the surface of the manganese dioxide with subsequent oxidation, or undergo oxidation directly without rearrangement to give the 4-methoxy-3,5-cycloheptadienone system, which then undergoes double-bond isomerization to the 5-methoxy-2,4-dienone system. The action of manganese dioxide on XXI (and XLI as this was later shown to be the correct structure) is in direct

contrast to the action of manganese dioxide on 3,5-cycloheptadienol, which is reported to be inert to this type of oxidation.³⁹ It was also noted that the relative rates of the oxidations differed by a factor of about ten. The relative rates of oxidation of XXI, XL, and XLI were approximately 9, 1 and 10.5. If double-bond migration occurred prior to oxidation, the relative rate of oxidation of XXI and XLI would be similar to, or slower than, that of XL. This type of reasoning suggests a transannular interaction between the hydroxyl function and the diene system which is responsible for the oxidation.⁵³ If this is true, the reaction must depend entirely on the presence of the methoxy group on the diene. Further careful studies are required with this system in order to determine the true mechanism of the reaction. Due to the unexpected oxidation results, the structure of the unknown alcohol still remained in doubt.

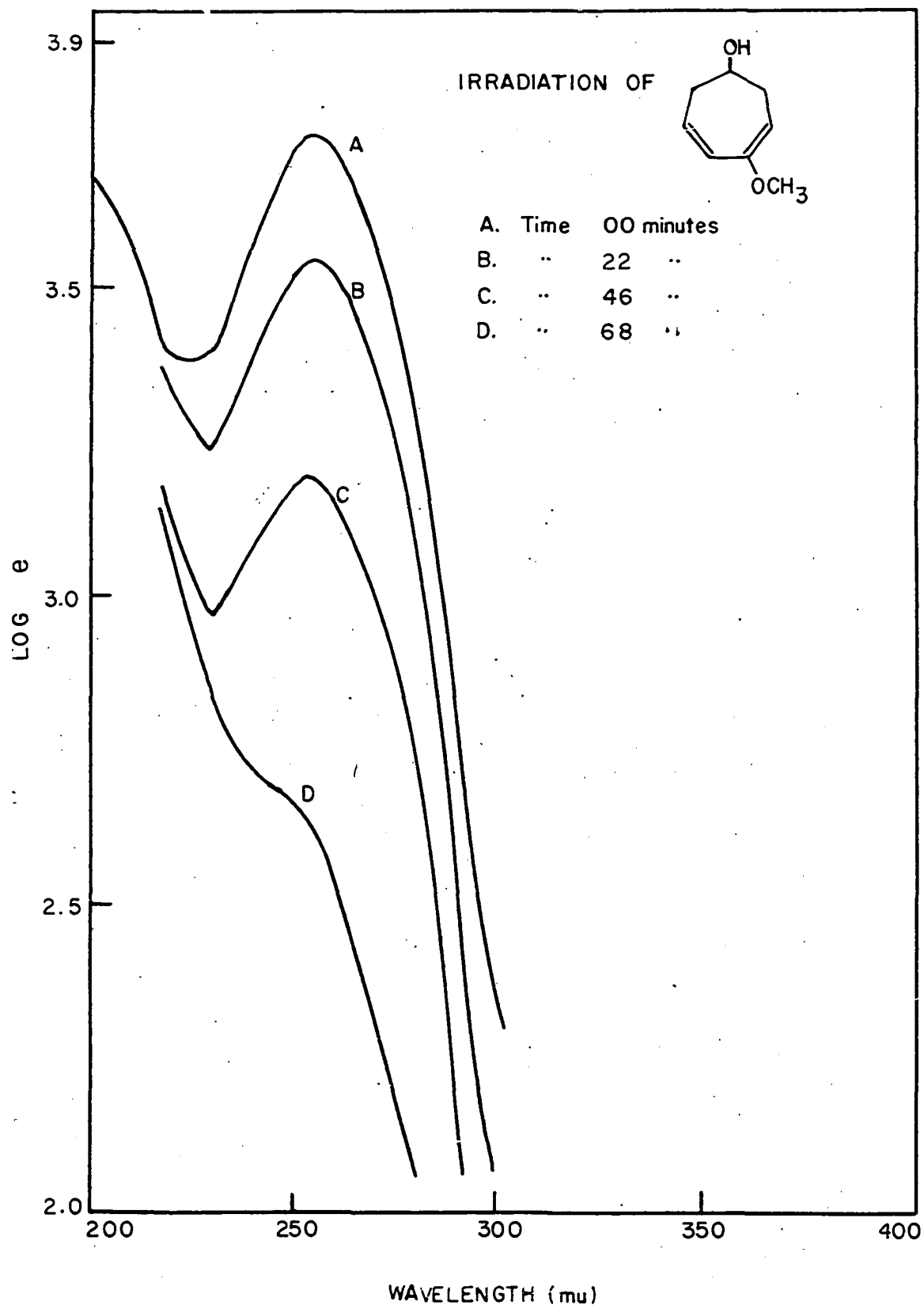
The structure of the unknown alcohol was finally clarified by a photochemical transformation followed by acid hydrolysis of the photoproduct. Previous experience with the irradiation of 1,3-cycloheptadiene (see page 99) led us to believe that irradiation of the dienols might give the

⁵³Evidence for such a transannular interaction in the cycloheptadiene series is provided by 3,5-cycloheptadienone which shows an anomalous ultraviolet spectrum with a maximum at 213-214 μ (see footnote 39) whereas cycloheptadiene shows a maximum at 241 μ (see footnote 117).

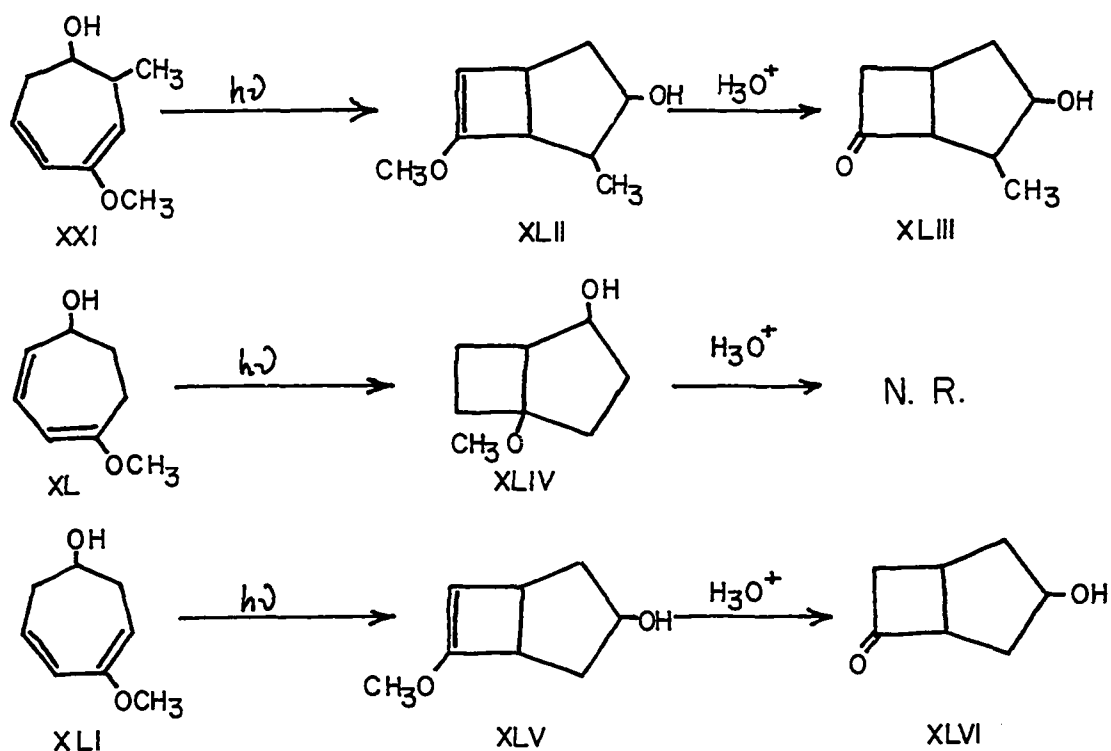
correspondingly substituted bicyclo $\overline{3.2.0}$ hept-6-ene compounds. Acid hydrolysis of the enol ethers, obtainable from XXI and possibly XLI, would give cyclobutanone derivatives, whereas the photoproduct from XL would not. Irradiation of the three alcohols in ethereal solution in quartz vessels with a General Electric UA3 mercury arc lamp, revealed a rapid disappearance of the diene ultraviolet absorption, see Figure 2, page 39.

Irradiation of XXI gave a photoproduct XLII, which was soluble in 0.1 normal sulfuric acid. The chloroform extract of the acid solution showed a peak in the infrared at 5.65 μ indicating the formation of 2-methyl-3-hydroxy-7-ketobicyclo- $\overline{3.2.0}$ heptane, XLIII. The irradiation of XL gave a photoproduct XLIV (see Figure 12, page 233, for the infrared spectrum) which was insoluble in sulfuric acid and did not undergo hydrolysis to a cyclobutanone derivative, as shown by the infrared of the product recovered from the attempted acid hydrolysis. The unknown alcohol XLI, from the hydride reduction of I, gave a photoproduct XLV, which was soluble in sulfuric acid and underwent acid hydrolysis to a cyclobutanone derivative (5.63 μ , Figure 12, page 229), 3-hydroxy-6-ketobicyclo $\overline{3.2.0}$ heptane, XLVI. The above results show that the unknown alcohol has the structure 4-methoxy-3,5-cycloheptadienol, XLI. The above evidence gives no indication of the purity of XLI, that is whether or not any XL is

Figure 2. Irradiation of 4-methoxy-3,5-cycloheptadienol (XLI)



present as might be indicated by the hydrolysis data. The following scheme shows the chemistry involved in the irradiation and hydrolysis reactions.



To determine the homogeneity of the alcohol fraction containing **XLI**, the sample was analyzed by gas phase chromatography on an LB 550X column. The sample showed two peaks, of which the first peak (35%) was shown to be identical with **XL** by comparison of retention times. Therefore the alcohol fraction contained both **XL** and **XLI** and during the acid hydrolysis **XL**, and not **XLI**, was giving rise to the cycloheptadienone peak (292 μ).⁵⁴ It was also shown that **XLI**

⁵⁴The ultraviolet spectrum of the alcohol after acid hydrolysis showed the presence of 27% 2,4-cycloheptadienone.

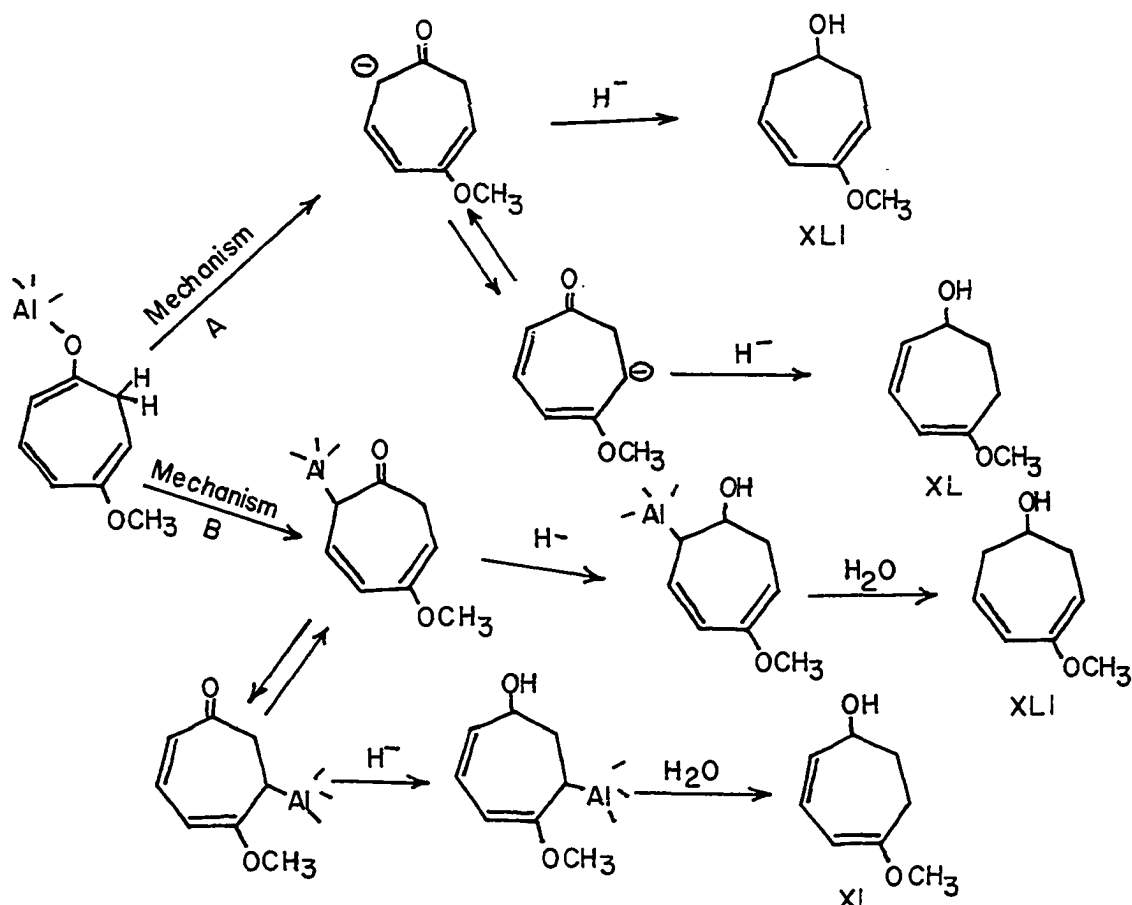
does not rearrange to XL by base-catalyzed double bond isomerization or during the chromatography procedure (by gas phase analysis both before and after chromatography). Therefore XL must arise during the reduction reaction or possibly during the hydrolysis step.

The isolation of XLI from the reaction of I with lithium aluminum hydride supports the earlier suggestion that the hydride attack must occur at C₂ or C₇ (page 24) giving 1:8 addition and the formation of the enolate salt of 4-methoxy-3,5-cycloheptadienone. On hydrolysis, XXXIV would readily rearrange to give XXXII.

The mechanism for the formation of XL and XLI is somewhat more obscure. The alcohol XL is not formed from XLI, or vice versa, after the hydrolysis or during the chromatography.

It is possible that the aluminum enolate salt of 4-methoxy-3,5-cycloheptadienone may dissociate to give the enolate anion which immediately reacts, via the keto-form, with hydride before much double-bond isomerization occurs (mechanism A). Another possibility is that the aluminum may transfer from the oxygen atom to the alpha-carbon giving a ketone which would undergo further reduction (mechanism B). The aluminum complex may then undergo hydrolysis to give XLI

or undergo allylic shift⁵⁵ with the aluminum ending up on C₃ which on hydrolysis would give XL as shown in the following scheme.



An additional possibility is that localized hydrolysis of the aluminum enolate salt, during the addition of water, would produce 4-methoxy-3,5-cycloheptadienone which would undergo further reduction in another part of the reaction mixture accompanied by some prior double-bond isomerization.

⁵⁵Allylic Grignard reagents are known to undergo rearrangement to give a mixture of the two possible allylic reagents (E. E. Royals, Advanced Organic Chemistry, Prentice-Hall, Inc., New York, 1954, pp. 696-697).

As a study of the reaction of tropone (II) with Grignard reagents or lithium aluminum hydride had not been reported in the literature,⁵⁶ these reactions were run in conjunction with the gamma-tropolone methyl ether work for comparison. Addition of an ethereal solution of methyl magnesium iodide to tropone caused the formation of a flocculent yellow precipitate which redissolved on further addition of the Grignard reagent. The reaction mixture was hydrolyzed with water. The ether layer was decanted, and the water layer was saved for later extraction. The ether layer, after evaporation, gave a 50% yield of a ketone (5.85 and 6.03 u (weak), Figure 13, page 231; $\lambda_{\text{max}}^{95\% \text{ EtOH}}$ 217 and 298 mu (weak), Figure 28, page 261). This ketone absorbed two moles of hydrogen over Adams' Catalyst in methanol giving 2-methylcycloheptanone. Reduction with lithium aluminum hydride gave a mixture of alcohols as indicated by the ultraviolet spectrum (241 and 247 mu, Figure 29, page 263). 3,5-Cycloheptadienol is reported to have a maximum at 241 mu³⁹ and 2-methyl-2,4-cycloheptadienol would be expected to show a maximum at 246

⁵⁶Tropone has been reported to react with methyl lithium to give the corresponding 2-methyl-3,5-cycloheptadienone (G. Closs and L. Closs, Abstracts of Papers Presented at the 137th Meeting of the American Chemical Society, April 1960, p. 83-o) which can be oxidized with bromine to the corresponding 2-methyltropone. 2-Methyltropone in turn reacts with methyl lithium to give 2,7-dimethyl-3,5-cycloheptadienone.

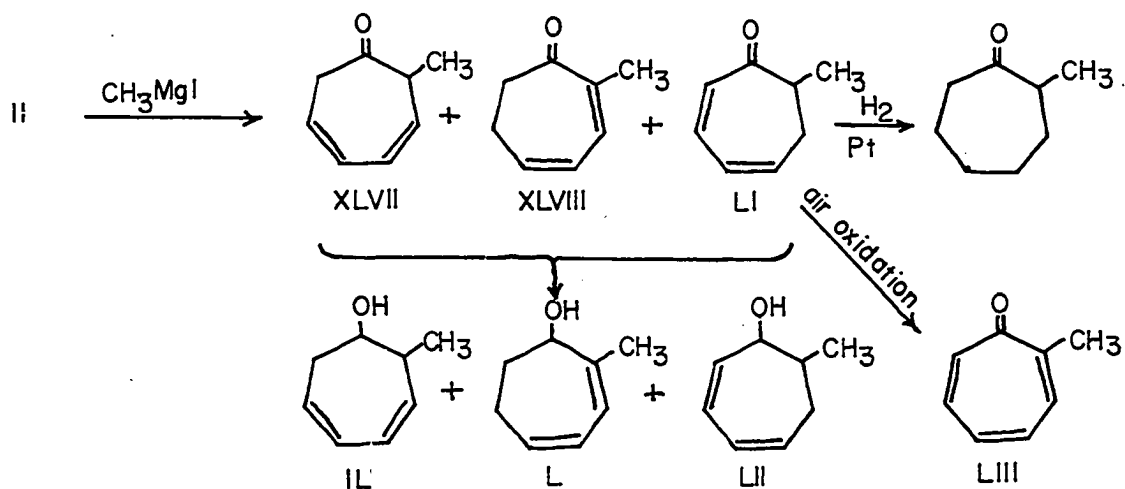
mu.⁵⁷ The ketone mixture probably contained predominantly 2-methyl-3,5-cycloheptadienone, XLVII, with some 2-methyl-2,4-cycloheptadienone, XLVIII, both of which on hydrogenation would give 2-methylcycloheptanone. The alcohol mixture therefore contained 2-methyl-3,5-cycloheptadienol, XLIX, and 2-methyl-2,4-cycloheptadienol, L. The possibility of the presence of 2-methyl-4,6-cycloheptadienone (LI) and 2-methyl-4,6-cycloheptadienol (LII) in the ketone and alcohol fractions cannot be ignored. The 298 mu peak in the ketone fraction is less than what would be expected for XLVIII (302 mu)⁵⁸ and might be a result of the summation of the spectra of XLVIII and LI (292 mu) giving a maximum at 298 mu. In this case there is no strongly directing group to dictate the final product during double bond isomerization as there is in the case of XVII and all possible ketones may be present. A diagram of the above chemistry is shown on page 25.

The water layer from the Grignard reaction with II (page 44) was extracted with methylene chloride. The methylene chloride extract was separated by gas phase chromatographic techniques giving an additional 3% yield of the ketone mix-

⁵⁷An alkyl substituent on a diene chromophore causes a bathochromic shift of 5 mu (L. Fieser and M. Fieser, Steroids, Reinhold Publishing Corporation, New York, 1959, p. 17).

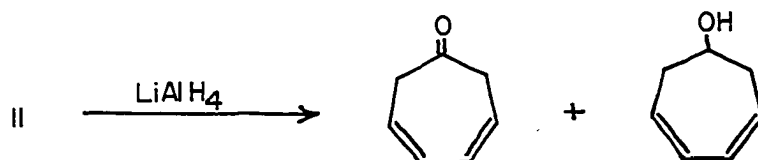
⁵⁸An alpha substituent on a dienone chromophore causes a bathochromic shift of 10 mu (L. Fieser and M. Fieser, ibid., p. 19).

ture, a 10% recovery of II, and another compound, LIII, in 4% yield. Compound LIII displayed the typical tropone ultra-violet (see Figure 28, page 261) and infrared spectra with the exception of a 7.30 μ peak in the infrared (see Figure 10, page 225) not found in the tropone spectrum. The fact that alkyl substituents on a troponoid nucleus cause no shift in the ultraviolet maximum, along with the presence of the 7.30 μ peak in the infrared, suggests that LIII is 2-methyltropone. The 2-methyltropone probably arose by air oxidation of the ketone mixture during the basic hydrolysis.



The reaction of II with lithium aluminum hydride gave in 67% yield a pale yellow liquid (2.76, 2.80 and 5.83 μ). Chromatographic separation on alumina gave a ketone (5.83 and 6.27 μ , $\lambda_{\text{max}}^{95\% \text{ EtOH}}$ (shoulder) 220 $\text{m}\mu$) and an alcohol (2.76, 2.80 and 6.20 μ , $\lambda_{\text{max}}^{95\% \text{ EtOH}}$ 241 $\text{m}\mu$) in a ratio of 2:3.

Hydrogenation of the mixture resulted in the absorption of two moles of hydrogen and gave, as one product, cycloheptanone identified as its 2,4-dinitrophenylhydrazone. A portion of the crude product was refluxed with N-phenyl maleimide in benzene giving the adducts of 2,4-cycloheptadienone and 3,5-cycloheptadienol.⁵⁹ This identifies the ketone as 3,5-cycloheptadienone and the alcohol as 3,5-cycloheptadienol.⁵⁹ The same comments on the mechanism can be made concerning the



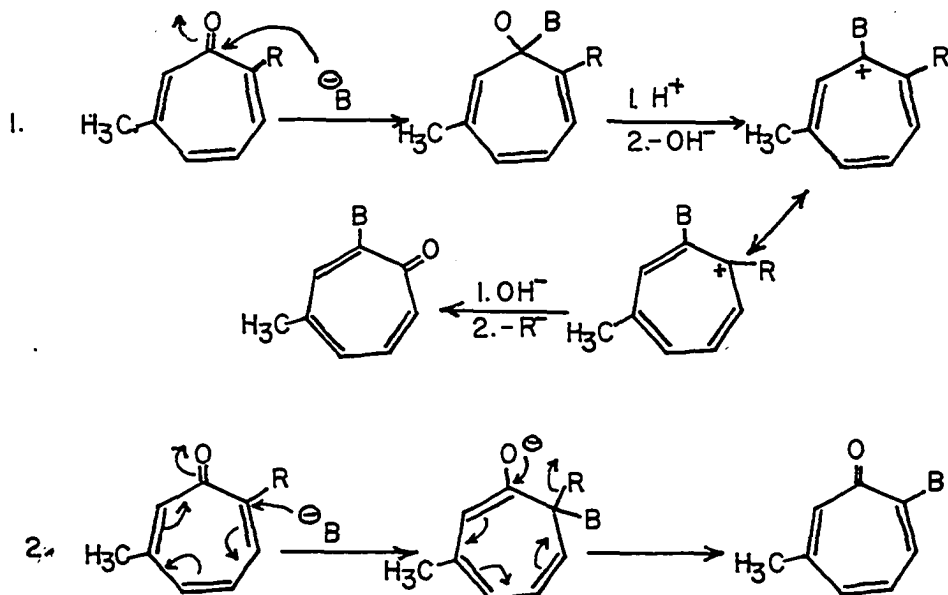
reaction of II with hydride as for the reaction of I with hydride (page 42), except that no double bond isomerization apparently occurs.

The foregoing work lends full support to the proposed mechanism for the reactions of troponoid compounds with Grignard and hydride reagents. Haworth *et al.*⁶⁰ in 1954, first proposed that anion attack on a troponoid compound may occur in either of two ways; attack at the carbonyl carbon, C₁, or

⁵⁹3,5-Cycloheptadienone and 2,4-cycloheptadienone give identical adducts in the Diels-Alder reaction corresponding to the adduct of 2,4-cycloheptadienone (see footnote 39).

⁶⁰P. Akroyd, R. D. Haworth and P. R. Jeffries, *J. Chem. Soc.*, 286 (1954).

by attack at C₂ in the α -tropolone series leading to the direct displacement of the R group as shown below:



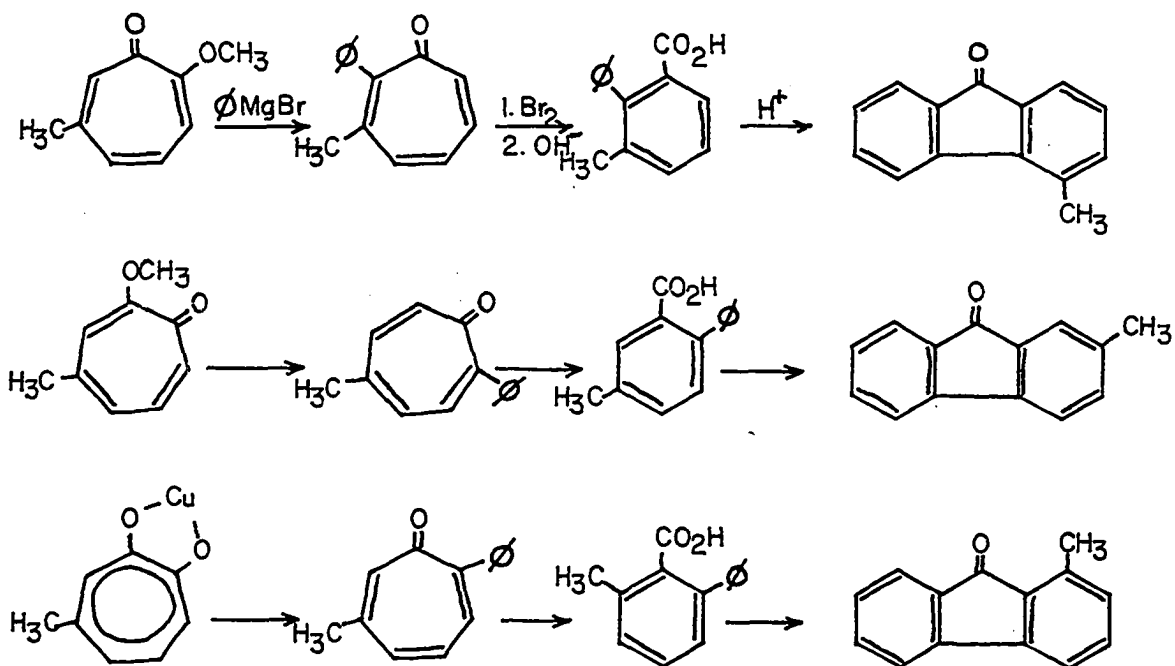
Mechanism 2, whereby attack occurs at C₂, was favored by many chemists⁶¹ for the substitution reaction with various anionoid reagents, although there was no clear-cut evidence for the operation of this mechanism in the Grignard and hydride reactions. The reaction of tropolone methyl ether with Grignard reagents to give 2-substituted tropones was

⁶¹T. Nozoe, T. Mukai, and J. Minegishi, Proc. Japan Acad., 27, 419 (1951); T. Nozoe, Y. Kitahara, and S. Masamune, ibid., 27, 649 (1951); T. Nozoe, Y. Kitahara, S. Masamune, and S. Yamaguchi, ibid., 28, 85 (1952); T. Nozoe, T. Mukai, and I. Murata, ibid., 28, 142 (1952); T. Nozoe, S. Seto, and S. Matsumura, ibid., 28, 483 (1952); W. von E. Doering and L. H. Knox, J. Am. Chem. Soc., 74, 5683 (1952); W. von E. Doering and C. F. Hiskey, ibid., 74, 5688 (1952).

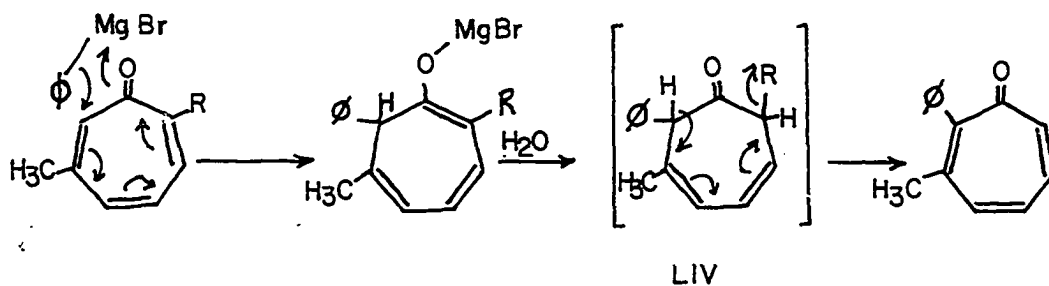
thought to occur by attack at C₂ and displacement of the methoxyl group. With this line of reasoning, Haworth⁶⁰ assigned the structures 2-phenyl-6-methyltropone and 2-phenyl-4-methyltropone as the products from the action of phenyl Grignard on 6-methyltropolone methyl ether and 4-methyltropolone methyl ether, respectively.

In a report published in 1955, Haworth and Tinker⁶² described the isolation of a third methylphenyltropone from the action of phenyl Grignard on the copper chelate of 4-methyltropolone. This indicated that the mechanism of attack at C₂ in the tropolone methyl ethers was not valid, as only two methylphenyltropones would be predicted possible. Then in an elegant piece of work, Haworth⁶² demonstrated in the following manner that attack by the Grignard reagent must have occurred at C₇ in the tropolone methyl ethers. The methylphenyltropones were brominated and treated with base to effect rearrangement to the methyl-phenyl-substituted benzoic acids. The benzoic acids were cyclized in acid to the corresponding methyl fluorenones as shown in the following scheme:

⁶²R. D. Haworth and P. B. Tinker, J. Chem. Soc., 911 (1951).



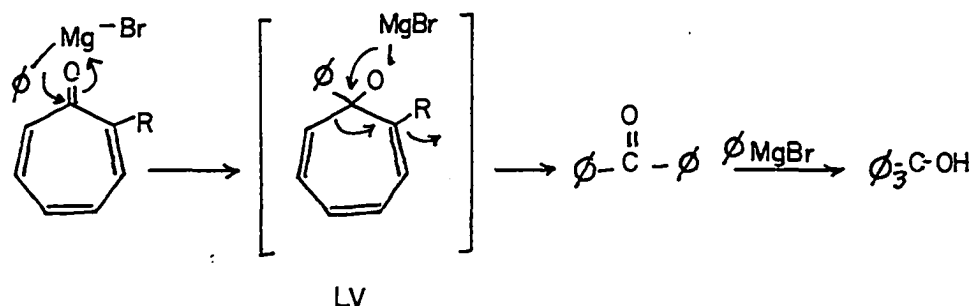
With this conclusive evidence Haworth proposed the following mechanism for the reaction with the Grignard reaction:



The intermediate LIV ($\text{R} = \text{OCH}_3$), being a methanol addition compound of an aromatic system, undergoes immediate elimination of methanol to give back the aromatic system.

In addition to forming 2-substituted tropones, the

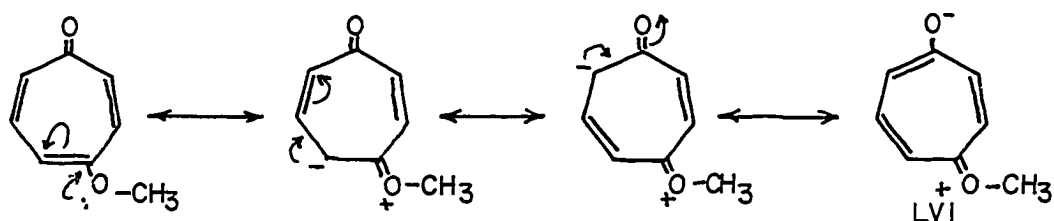
reaction of Grignard reagents with alpha-tropolone methyl ether or the methyl substituted alpha-tropolone methyl ethers gives in about 20% yield triphenyl carbinol and diphenyl tolyl carbinol, respectively. In the case of alpha-tropolone methyl ether, the reaction must be initiated by attack at the carbonyl carbon giving the intermediate LV which undergoes ring contraction to give benzophenone. The benzophenone then reacts with a second mole of Grignard reagent to give the triphenylcarbinol.



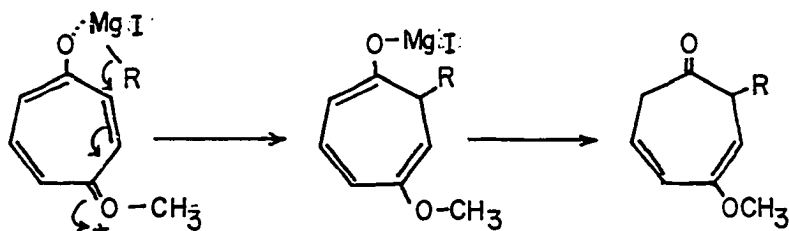
Intermediates of the type LIV and LV had not been isolated prior to this work. In the case of gamma-tropolone methyl ether and of tropone, R is hydrogen and does not eliminate to give the troponoid compound or the ring contraction product. This enables the isolation of the intermediate dienone (XVII and XLVII) and the cycloheptatrienol (XXXI) corresponding to the intermediates LIV and LV, respectively.

The predominance of attack at C₂ in the reaction of I

with methyl Grignard reagent is undoubtedly caused by electronic effects due to the methoxyl group. The resonance effect of the methoxyl group makes carbon atoms 5 and 7 more negative than 2 as is illustrated in the following scheme.



The Grignard reagent may then coordinate with the carbonyl oxygen in LVI followed by attack of R^- on C_2 feeding the electrons back to the methoxyl oxygen giving the enolate salt of the 3,5-dienone.



In the reaction of Grignard reagents with the alpha-troponone methyl ethers, the predominant attack is at the least favorable position electronically and is undoubtedly forced to go at this position because of the steric hindrance to attack at C_2 .

Therefore the mode of attack in the reaction of troponoid compounds with Grignard reagents is controlled by steric and electronic interactions, the former exerting a stronger influence than the latter. It appears that the carbonyl attack

occurs only when there is steric and electronic hindrance and it would appear that in the absence of these two effects, as in the tropone case, no carbonyl attack will occur.

The Acid- and Base-Catalyzed Hydrolysis
of gamma-Tropolone Methyl Ether

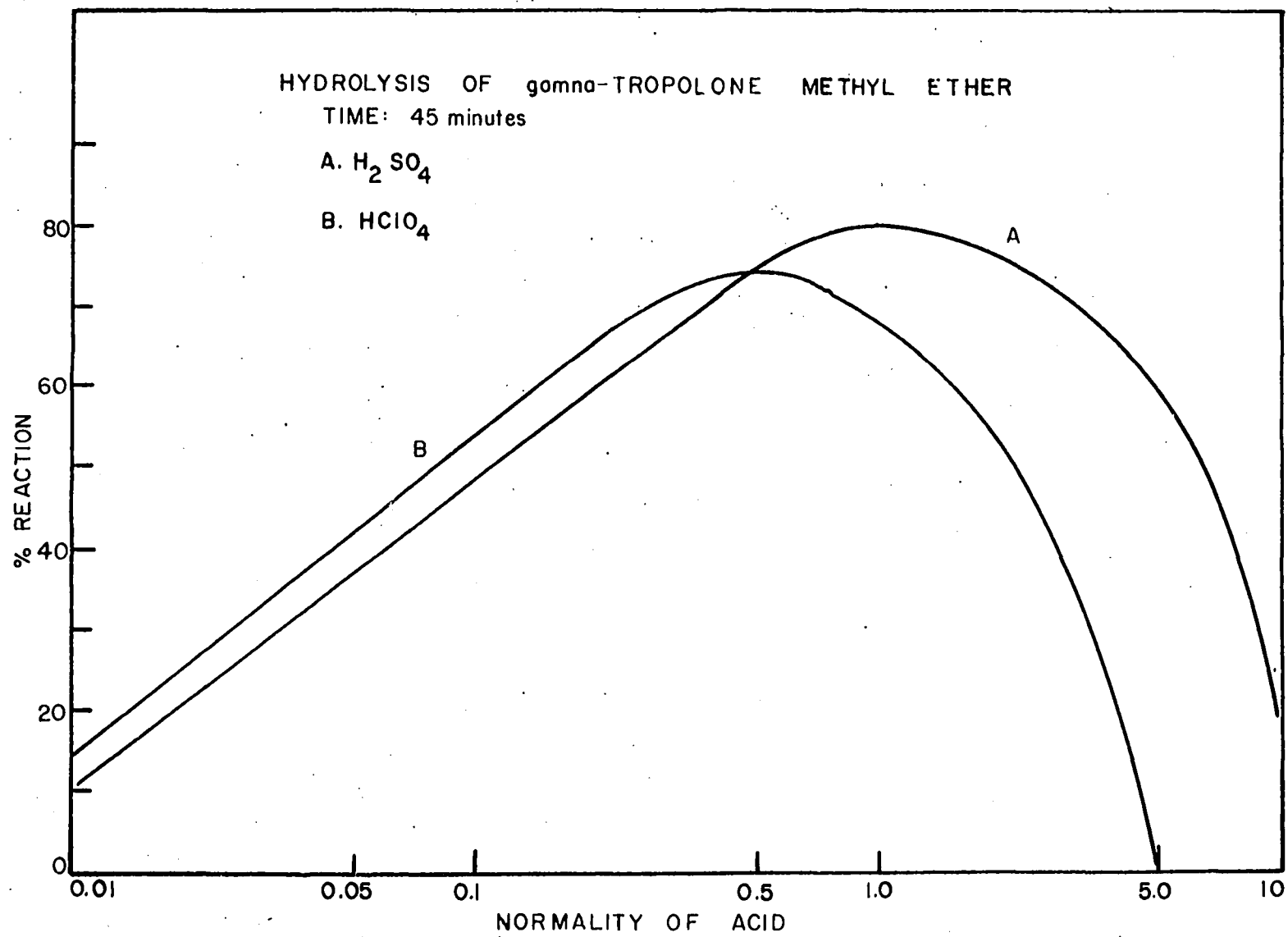
The rate of acid-catalyzed hydrolysis of I was measured for comparison with the rates of acid-catalyzed ring opening reactions of bicyclic compounds derived from I (to be discussed in a later section of this Thesis). The hydrolysis of I was run in several concentrations of perchloric and sulfuric acid. It was noted that the rate of hydrolysis increased with acid concentration up to 0.5 and 1.0N in perchloric and sulfuric acids, respectively, and then rapidly decreased with further increase in the acid concentration (see Figure 3, page 55).

A first order plot of the logarithm of the total reacted I versus time gave a linear plot, while a second order plot of the reciprocal of total reacted I versus time gave a non-linear plot indicating a first order dependence on I.

The phenomenon of a rate maximum in an acid-catalyzed reaction has been observed in the decarbonylation reaction of substituted benzaldehydes,⁶³ in the decarboxylation of sub-

⁶³H. Burkett, W. M. Shubert, F. Schultz, R. B. Murphy, and R. Talbot, J. Am. Chem. Soc., 81, 3923 (1959).

Figure 3. Hydrolysis rate curve of gamma-tropolone methyl ether



stituted benzoic acids and their methyl esters,⁶⁴ and in the hydrolysis of N,N'-diarylformamidines.⁶⁵

In the decarbonylation of the substituted benzaldehydes, the rate decrease is attributed to the increased protonation of the carbonyl oxygen, which species is not involved in the decarbonylation.⁶³ The rate determining step is the proton abstraction (of the aldehydic proton) in which water is the base (specific oxonium ion catalysis⁶⁶). The rate decrease in the decarboxylation of the substituted benzoic acids and their methyl esters is due to the formation of an acyloxonium ion in the more concentrated acid which does not undergo decarboxylation.⁶⁴

The hydrolysis of the formamidines is more closely related to the hydrolysis of I. The rate of hydrolysis of the formamidines is independent of acid concentration in dilute acid but decreases in more concentrated acid where Hammett's $\log k$ ⁶⁷ diverges from the hydrogen ion concentration. The rate of hydrolysis is proportional to hydronium ion concentration and water activity and inversely proportional to a_{H_2O} .

⁶⁴W. M. Shubert, R. E. Zahler and J. Robins, *ibid.*, 77, 2293 (1955).

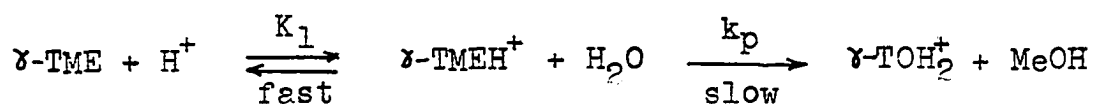
⁶⁵R. H. DeWolfe, *ibid.*, 82, 1585 (1960).

⁶⁶R. P. Bell, Acid-Base Catalysis, Oxford Press, New York, 1941, Chap. VII.

⁶⁷L. P. Hammett, Physical Organic Chemistry, McGraw-Hill Book Co., Inc., New York, 1940, p. 267.

The rate of hydrolysis of I is proportional to the acid concentration in dilute acid and appears to be inversely proportional in higher acid concentration. This effect may be due to the decreased activity of water, which may appear in the rate determining step, or to a second acid-base equilibrium giving a species which does not undergo hydrolysis.

A mechanism involving a molecule of water in the rate determining step is shown as follows where γ -TME is I and γ -TOH is free gamma-tropolone:



This mechanism gives the following kinetic expression. The dependence of the rate on the activity of water in high acid

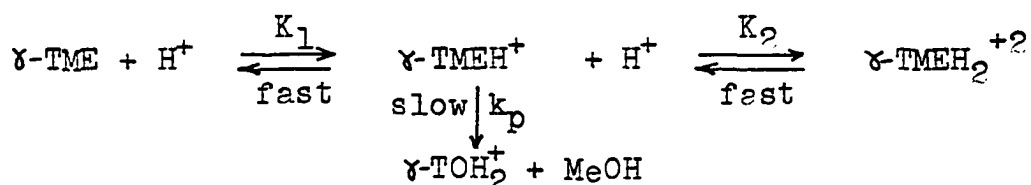
$$\text{Eq. (1)} \quad \frac{-d[\gamma\text{-TME}]_{\text{total}}}{dt} = \frac{k_p a_{\text{H}_2\text{O}} [\gamma\text{-TME}]_{\text{total}} K_1 [\text{H}^+]}{1 + K_1 [\text{H}^+]}$$

concentration is apparent in equation 1, as the denominator $1 + K[\text{H}^+]$ approaches $K_1[\text{H}^+]$ and cancels out leaving only the dependence on the water activity. Solving for K_1 and k_p from the rate curves at low acid concentration gives values of 24.8 and $1.44 \times 10^{-4} \text{ sec.}^{-1}$, respectively. Using these values and the values for the activity of water at 25^{068} (the hydrolysis reactions were run at 80° and the use of the values for

68J. N. Pearce and A. F. Nelson, J. Am. Chem. Soc., 55, 3075 (1933).

the activity of water 25° will undoubtedly introduce error) in equation 1 gives excellent correlation up to 0.2N acid and shows a rate maximum around 1.0N (see Figure 4, page 60).

The second possible mechanism involving a second acid-base equilibrium to give a diprotonated species is shown as follows where product is produced only via the mono-protonated species. Equation 2 gives the kinetic expression for this



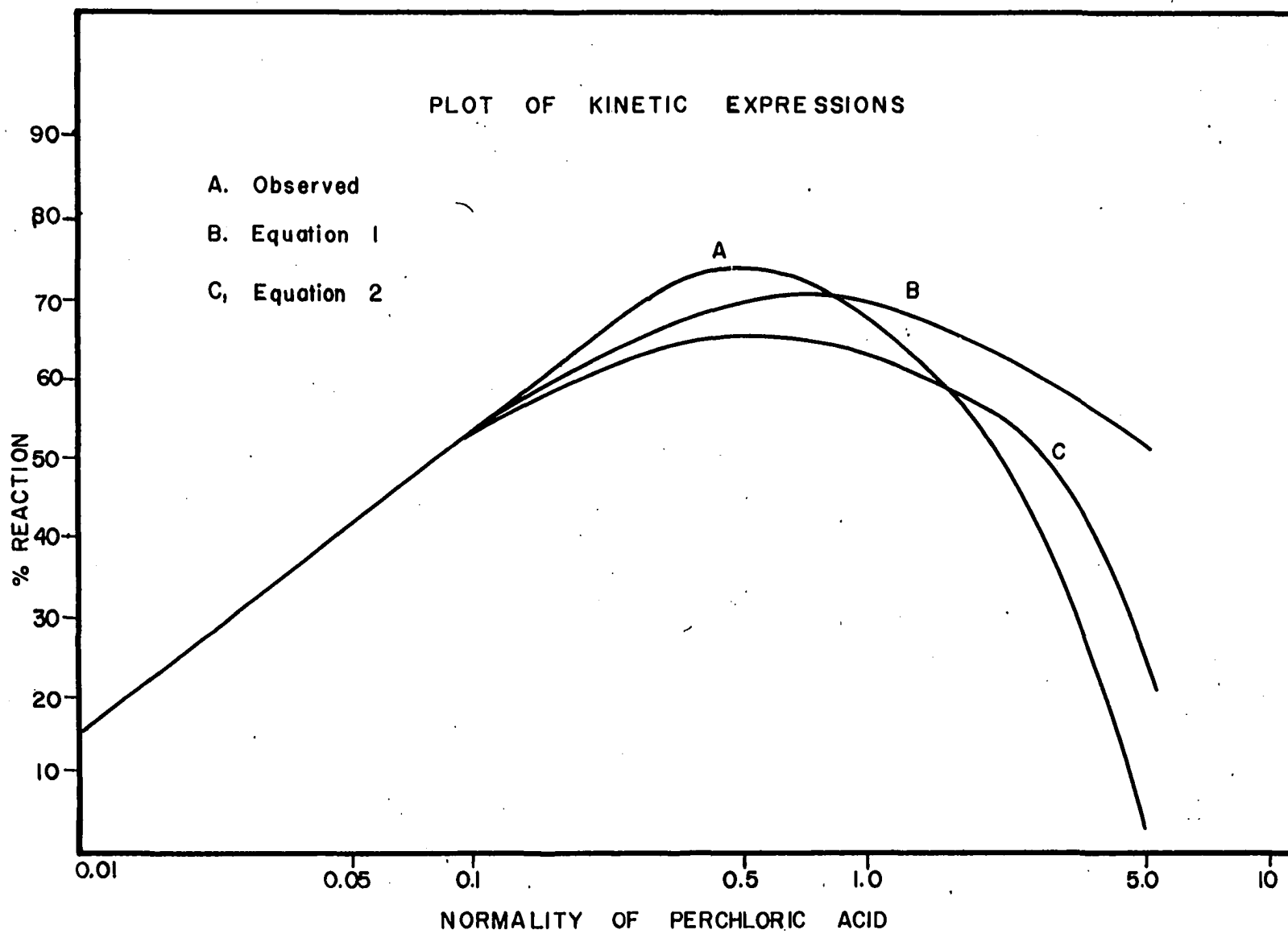
$$\text{Eq. (2)} \quad \frac{-d[\gamma\text{-TME}]_{\text{total}}}{dt} = \frac{k_p a_{\text{H}_2\text{O}}[\gamma\text{-TME}]_{\text{total}} K_1 [\text{H}^+]}{1 + K_1[\text{H}^+] + K_2 K_1 [\text{H}^+]^2}$$

mechanism. In low acid concentrations this equation reverts to equation 1 having the same values for K_1 and k_p . Using a value of 0.1 for K_2 , equation 2 gives a rate maximum at the correct acid concentration (see Figure 4, page 60) but still deviates quite badly.

With the available information, mathematically distinguishing between the two mechanisms is impossible. Chemically the first mechanism is most plausible, and is favored as the operative mechanism, as the diprotonated species should undergo more rapid hydrolysis than the monoprotated species. The possibility that a diprotonated species can exist is entirely conceivable, as two basic sites are present in the

Figure 4. Plot of kinetic expressions

- A. Observed
- B. Equation 1
- C. Equation 2



molecule (the carbonyl oxygen and the methoxyl oxygen with the former being more basic).

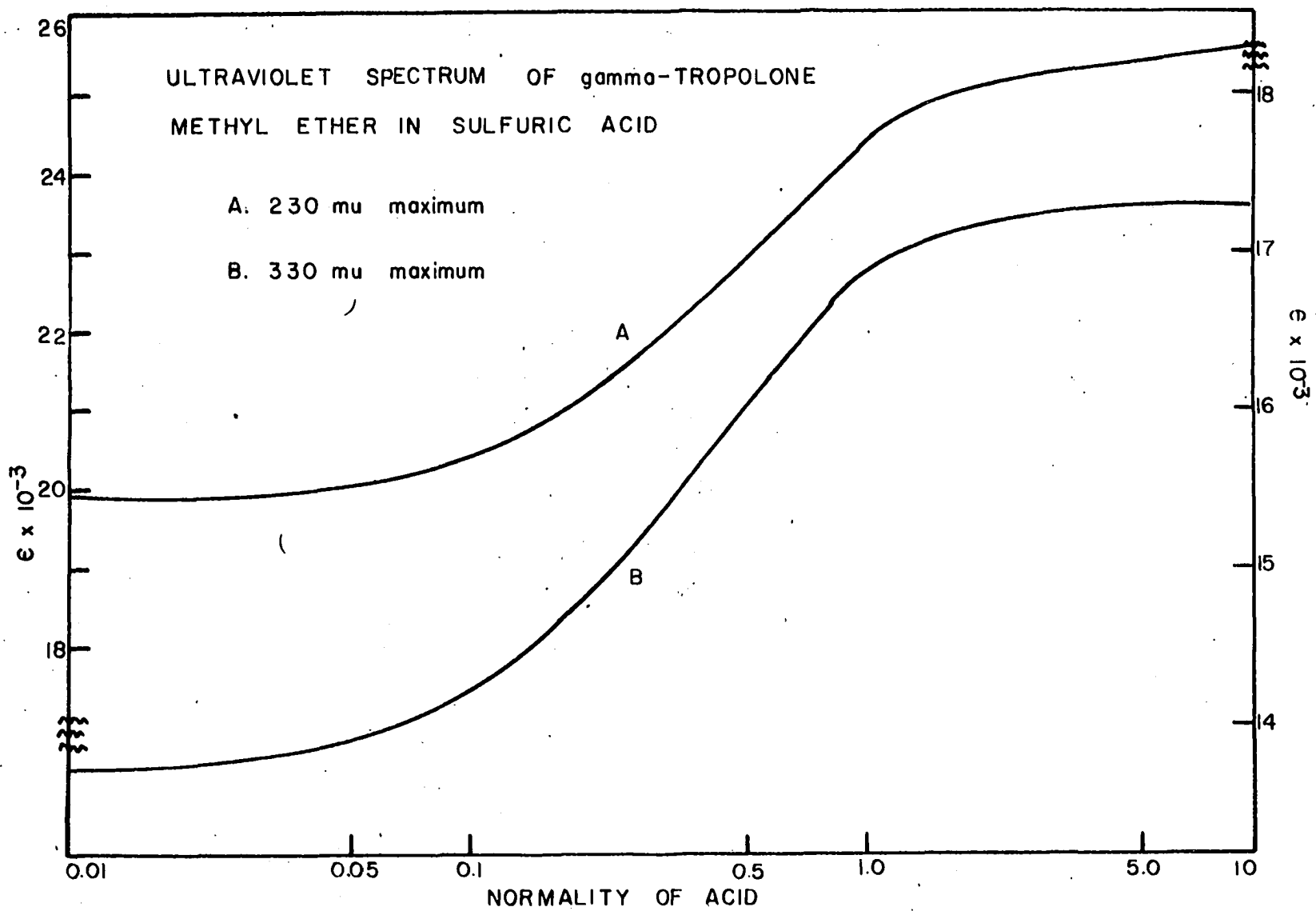
The ultraviolet spectrum of I in acid solutions of varying strength, was recorded to see if the existence of a mono-protonated and diprotonated species could be detected spectrally. Figure 5, page 63, shows the plot of extinction coefficient versus the logarithm of acid concentration for the 230 and 330 μ bands of I in sulfuric acid solution. These curves resemble typical titration curves and have equivalence points at 0.44 and 0.35 normal acid for the 230 and 330 μ bands, respectively. A similar determination of the spectrum of I in perchloric acid of constant ionic strength gave an equivalence point at 0.11 normal perchloric acid. The difference between the results of the sulfuric and perchloric acid systems is undoubtedly due to the fact that sulfuric acid is diprotic and the normality is not representative of the activity of hydrogen ion. Attempts at calculating K_1 from these curves gave values which average close to 6. This value for K_1 , when used in the above kinetic expressions leads to impossible results (i.e., per cent reactions of over 100%).

The hydrolysis data for I in 0.0896 normal sodium hydroxide gave a linear plot for the logarithm of unreacted I versus time. The pseudo-first order constant as calculated from the slope of the line is 2.5×10^{-4} sec.^{-1} . Attempted reaction of I with sodium methoxide in absolute methanol gave

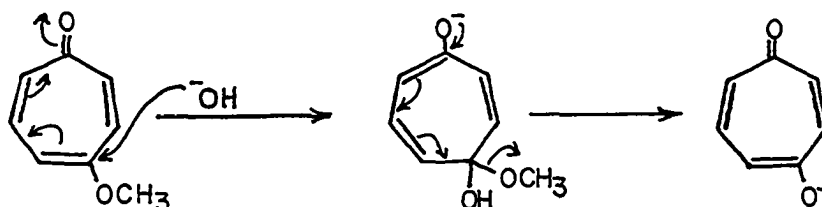
Figure 5. Change of extinction coefficient of gamma-tropolone methyl ether in sulfuric acid

A. 230 mu maximum

B. 330 mu maximum



no gamma-tropolone anion. The base-catalyzed hydrolysis of I must then occur by hydroxide attack at C₄ followed by elimination of the methoxyl group. Hydroxide attack on the methyl group with expulsion of the gamma-tropolone anion does not occur as demonstrated by the experiment using sodium methoxide.



The base catalyzed hydrolysis of I is similar to the hydrolysis of an ester, I being a doubly vinyligous ester.

The Hydrogenation of gamma-Tropolone Methyl Ether

With the earlier observation that hydrogenation of XXXII resulted in the abnormal absorption of 3.3 moles of hydrogen per mole of compound giving a mixture of products (page 33) it was decided to investigate the hydrogenation of I.

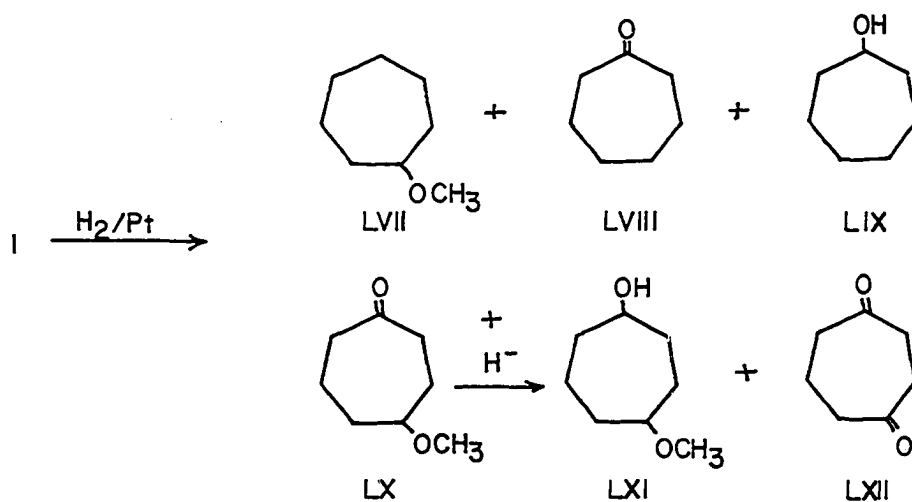
The hydrogenation of I in neutral aqueous solution over Adams' Catalyst resulted in the absorption of 3.58 moles of hydrogen per mole of I. The hydrogenation solution was extracted with chloroform, and the chloroform extract was fractionated by preparative scale gas phase chromatography. The compounds isolated were methylcycloheptyl ether (LVII), cycloheptanone (LVIII), cycloheptanol (LIX), 4-methoxycyclo-

heptanone (LX)⁵¹ and 4-methoxycycloheptanol (LXI). The structure of LVII was identified by comparison of its infrared spectrum and gas phase chromatographic retention time with authentic material prepared by treating the sodium salt of cycloheptanol with methyl iodide. LVIII was identified by its infrared spectrum and preparation of the 2,4-dinitrophenylhydrazone. LIX was identified as cycloheptanol by infrared absorption and retention time comparison with cycloheptanol. The structure of compound LX was assigned from spectral data and LXI was related to LX by hydride reduction of LX to give an alcohol (2.9 and 9.16 u in chloroform). An additional compound was isolated as its bis-2,4-dinitrophenylhydrazone from a crude derivative mixture from a large scale hydrogenation. A small amount of a derivative insoluble in boiling ethanol was shown to be the bis-2,4-dinitrophenylhydrazone of 1,4-cycloheptandione (LXII) by melting point and mixed melting point with authentic derivative.⁴¹ The yield of the 1,4-cycloheptandione was 1.5% as calculated from the amount of the derivative obtained.

The rate of hydrogenation of I in acid solutions showed a similar rate phenomenon to that observed in the acid-catalyzed hydrolysis of I. The rate maximum occurred at 0.5N in hydrochloric acid.

Not only did the rate of hydrogenation vary with acid concentration, but the yields of the various products also

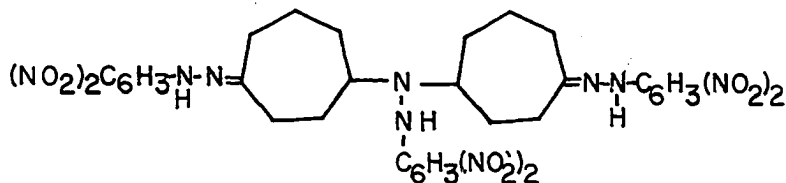
changed (see the table on page 166). The yields of LVII and LXII remained essentially constant in all acid concentrations, whereas the yields of LIX and LXI rapidly increased, in solutions up to 0.5N hydrochloric acid, at the expense of LVIII and LX. It was independently shown that cycloheptanone rapidly undergoes reduction in 0.1N hydrochloric acid over Adams' Catalyst; it is therefore more instructive to look at the sums of LVIII and LIX relative to LX and LXI. From this it is seen that there is more C-O bond cleavage² as the concentration of the acid increases up to 0.5N, whereafter the sums of LVIII and LIX relative to LX and LXI remain constant.



It seems reasonable to postulate that the complete hydrogenation of a molecule of I, except perhaps the carbonyl reduction to the corresponding alcohol, occurs during one absorption of the molecule on the catalyst. If this were not true, a greater yield of 1,4-cycloheptandione should be formed. The small amount of LXII that is formed, probably

arises from the hydrolysis of the enol ether on the surface of the catalyst, the catalyst acting as a Lewis acid catalyzes the hydrolysis. The extent of hydrogenation is probably partially dependent on the activity and adsorptive power of the catalyst. This may be supported by the fact that using an apparently inferior grade of platinum oxide⁶⁹ as catalyst, I absorbed only 2.5 moles of hydrogen per mole of compound in 0.1N hydrochloric acid and gave predominantly 1,4-cycloheptan-dione, isolated as the bis-2,4-dinitrophenylhydrazone.

The hydrogenation of gamma-tropolone in neutral solution was also run in order to compare the results with those reported by T. Nozoe.²⁵ Nozoe reports that gamma-tropolone absorbs 3 moles of hydrogen and gives a product which in turn gives a 2,4-dinitrophenylhydrazone, melting point 241°, for which he gives the following structure based on analytical data.



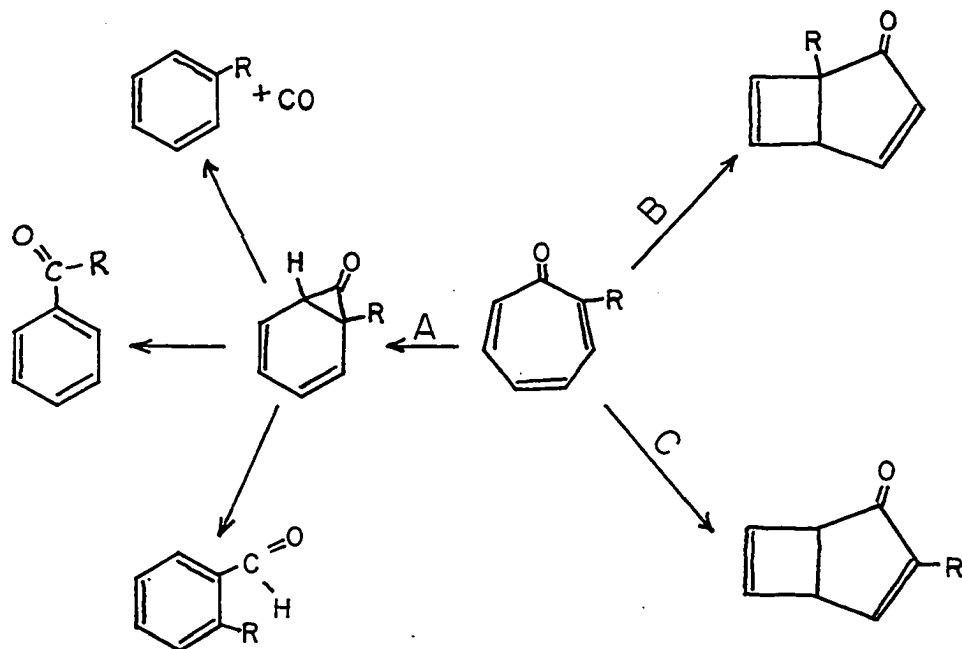
⁶⁹A platinum catalyst was obtained from Englehard Industries, 113 Astor Street, Newark 2, New Jersey, which was specified as 84.23% platinum dioxide. This catalyst was quite different from the catalyst normally used for the work contained in this Thesis. The catalyst used for the work contained in the Thesis was obtained from the American Platinum Works of Newark, New Jersey.

Hydrogenation of gamma-tropolone in neutral aqueous solution resulted in the absorption of 2.5 moles of hydrogen and gave a residue which in turn gave a derivative with melting point, and mixed melting point with authentic bis-2,4-dinitrophenylhydrazone of 1,4-cycloheptandione, 242.5-245°. The derivative isolated by Nozoe must therefore be the bis-2,4-dinitrophenylhydrazone of 1,4-cycloheptandione. The principle product of the hydrogenation in neutral solution is 1,4-cycloheptandione (XLII).

The Photochemistry of gamma-Tropolone Methyl Ether

The interest in and the study of photochemical transformations of unsaturated molecules has gained great momentum in the past few years. Our interest in this field, particularly in the lumicolchicines, led us to investigate the photochemistry of I. I was chosen for this study due to our interest in the chemistry of I and the desirability to work with a simple, readily available compound where effects from other parts of the molecule would be absent.

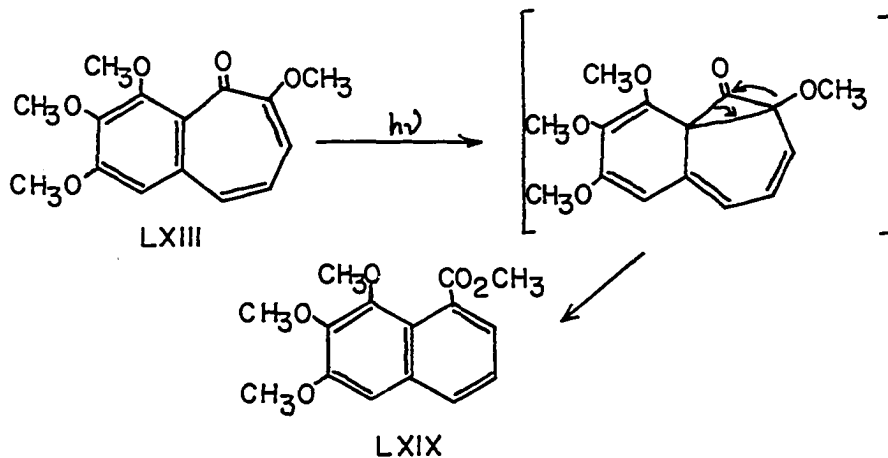
There are three types of photoisomerization reactions potentially available for simple troponoid compounds. These reactions are illustrated in the following scheme utilizing a 2-substituted tropone as an example. The valence tautomerization via path A leads to a norcaradiene-type structure



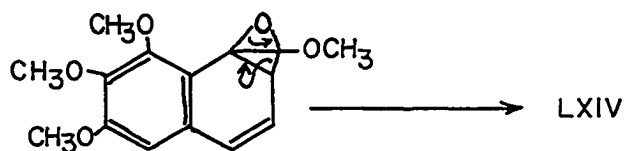
which is well known in cycloheptatriene chemistry.⁷⁰ The intermediate cyclopropanone would probably undergo further reaction for which three possibilities are shown. Loss of carbon monoxide would lead to a substituted benzene whereas migration of hydride or the R group would give the substituted benzaldehyde or the benzoyl derivative, respectively. An example of valence tautomerization via path A, followed by migration of the R group, is the photoisomerization of tetramethyl purpurogallin, LXIII, to methyl-6,7,8-trimethoxy-

⁷⁰See for example K. Alder and G. Jacobs, *Ber.*, **26**, 1528 (1953).

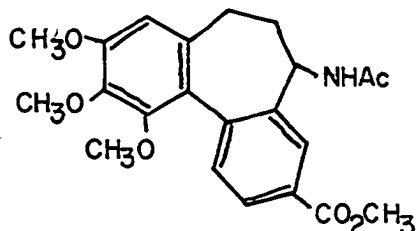
naphthoate, LXIV.⁷¹ It may also be that α -lumicolchicine is a methyl benzoate derivative formed in like manner.⁷²



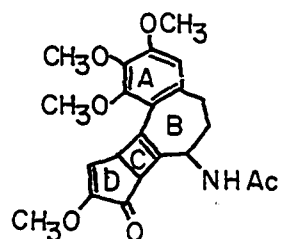
⁷¹E. J. Forbes and R. A. Ripley, J. Chem. Soc., 2770 (1959). The mechanism shown by Forbes for this photoisomerization involves the formation of the high energy intermediate shown below followed by collapse to the photoisomer.



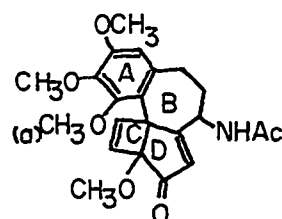
⁷²It was previously suggested that α -lumicolchicine is a substituted benzaldehyde (O. L. Chapman and D. J. Pasto, J. Am. Chem. Soc., 82, 3642 (1960)) formed via path A with hydride migration. α -lumicolchicine shows a peak in the infrared at 5.78 μ which would be more consistent with a methyl benzoate than with a substituted benzaldehyde. With this reasoning it is thought that the structure of α -lumicolchicine may be that shown below.



Reactions via path B had not been recognized prior to the investigation of the photochemistry of I. Subsequent to the completion of this work, it was found that alpha-tropolone⁷³ and its methyl ether,⁷⁴ and the 4- and 6-methyl-alpha-tropolone methyl ethers,^{75,76} undergo light-catalyzed valence tautomerization via path B. Reaction via path C is known only by the formation of the beta- and gamma-lumicolchicines and is probably due to steric requirements as shown below. Reaction via path B would give a product with a highly



β -Lumicolchicine
via Path C



Product via Path B

strained arrangement at the B-C-D juncture, and with considerable steric repulsion between the methoxyl group (a) and the

⁷³W. G. Dauben, K. Koch and W. E. Thiessen, *ibid.*, **81**, 6087 (1959).

⁷⁴E. J. Forbes and R. A. Ripley, *Chemistry and Industry*, 589 (1960).

⁷⁵W. G. Dauben, Department of Chemistry, University of California, Berkeley, The photochemistry of troponoid compounds, private communication, 1960.

⁷⁶L. Chapman and S. L. Smith, The Photochemistry of Troponoid Compounds, Research Journal of S. L. Smith, Department of Chemistry, Iowa State University of Science and Technology, Ames, Iowa, 1960.

hydrogen on the cyclobutene double bond. Reaction via path C, or path A, would be expected in the beta-tropolone series as it would be impossible to form a product in which the oxygen function is at the bridgehead.

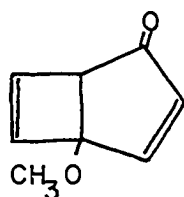
The irradiation of an aqueous solution of gamma-tropolone methyl ether (I) in a pyrex vessel with a mercury arc lamp or with direct sunlight, gave in 50-60% yield a single photoisomer, photo-gamma-tropolone methyl ether, and varying amounts of a red polymer. It was shown that irradiation of an aqueous solution of the photoisomer in a pyrex vessel led to the formation of the red polymer. The optimum condition for obtaining the photoisomer was irradiation of a 0.03-0.06 molar solution for 18-24 hours with a General Electric UA3 mercury arc lamp and recycling the recovered starting material.

The red polymer showed peaks in the infrared at 5.75, 5.86 and 5.95 μ and had only very low intensity absorption in the ultraviolet. The material absorbed 0.67 mole of hydrogen per mole (based on monomer molecular weight) giving a red material which showed only 5.75 and 5.86 μ peaks in the infrared region. The red polymer gave several fractions on chromatography (see Experimental, page 170) which all showed similar absorption in the infrared. No further work was carried out on the polymer.

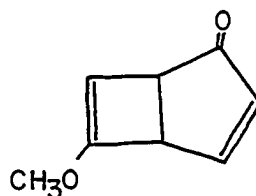
Photo-gamma-tropolone methyl ether showed a single

intense peak in the infrared at 5.86 μ (Figure 14, page 233) with maxima in the ultraviolet at 243 and 328 $m\mu$ (Figure 30, page 265). Pyrolysis of photo-gamma-tropolone methyl ether at 360° gave I in quantitative yield indicating that no gross rearrangement of the carbon skeleton had occurred.⁷⁷ The photoisomer rapidly absorbed one mole of hydrogen giving a dihydro-derivative (5.85 μ (Figure 14, page 233); 215 $m\mu$ (Figure 30, page 265)) and more slowly absorbed a second mole of hydrogen giving a tetra-hydroderivative (5.76 μ (Figure 14, page 233); no high intensity absorption in the ultraviolet). The spectral data for the dihydro- and tetrahydro-derivatives strongly suggested the presence of a cyclopentenone and a cyclopentanone chromophore, respectively. The ultraviolet spectrum for photo-gamma-tropolone methyl ether, however, is not consistent with what one would expect for a simple cyclopentenone. The reaction of I via path A must be excluded from consideration due to the pyrolytic reversibility of the reaction. Reaction of I via path B or C, which is suggested by the spectral data, would lead to either LXV or LXVI, respectively.

⁷⁷The dihydroderivative, LXVII, undergoes pyrolysis at 360° but the products were not identified. The tetrahydro-derivative, LXVIII, does not undergo pyrolysis at this temperature.



LXV



LXVI

In order to distinguish between the two possible structures for the photoisomer, the compound was subjected to mild acid treatment. If the photo-isomer were LXVI, a diketone should be formed. The treatment of the photoisomer with dilute acid at room temperature produced no reaction. More vigorous acid treatment gave gamma-tropolone. This evidence favors structure LXV for the structure of the photoisomer.

The nuclear magnetic resonance spectrum of the photoisomer left no doubt as to which was the correct structure. The nuclear magnetic resonance spectrum is reproduced in Figure 34, page 273. The protons on the double bond conjugated with the carbonyl group appear as doublets at 4.13 and 2.57 p.p.m.⁷⁸ The doublet arises from spin-spin coupling of the AX type^{79a} which produces a pair of doublets in which the

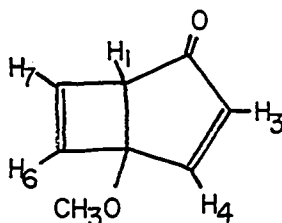
⁷⁸The positions of the signals observed in a nuclear magnetic resonance spectrum is reported on a τ (tau) unit scale in parts per million (p.p.m.). (L. M. Jackman, Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry, Pergamon Press, New York, 1959, p. 47).

^{79a}L. M. Jackman, ibid., p. 89.

^bL. M. Jackman, ibid., pp. 89-91.

^cL. M. Jackman, ibid., p. 85.

lines of are equal intensity. The alpha-proton at 4.13

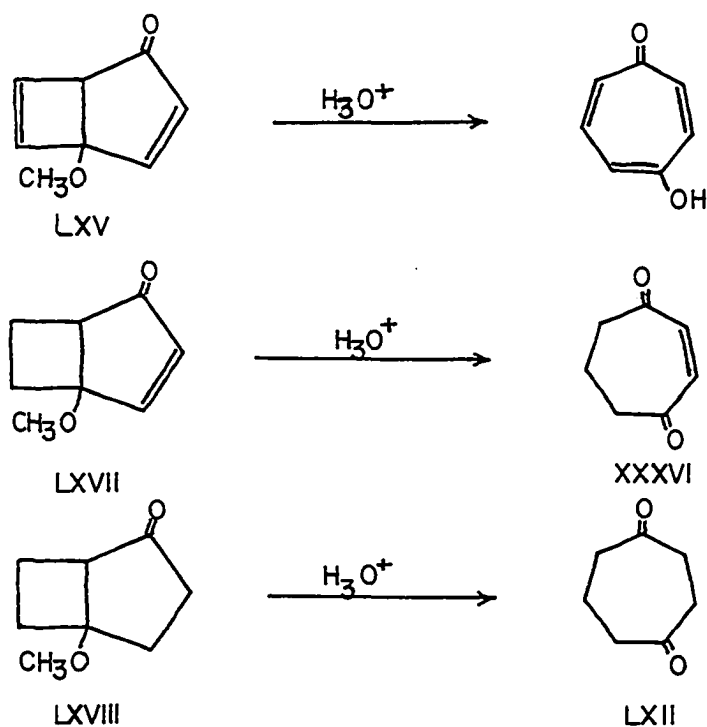


p.p.m.,⁸⁰ H₃, is further split due to coupling of H₃ with the bridgehead proton, H₁. The beta-proton, H₄, at 2.57 p.p.m., is split by coupling only with H₃. The multiplet centered at 3.60 p.p.m. is of the ABX type requiring two adjacent, quite similar protons A and B (H₆ and H₇) of which one or both are coupled to a third proton X (H₁) of greatly different chemical shift.^{79b} The presence of this multiplet in the spectrum of the photoisomer demands two adjacent protons on the cyclobutene double bond and rigorously excludes LXVI from consideration. The proton H₁ is partly obscured at the base of the methoxyl proton peak at 6.65 p.p.m.

From the assignment of LXV as the structure of photo-gamma-tropolone methyl ether, it follows that the dihydro-

⁸⁰For the assignment of proton signals see G. Van Dyke Tiers, Characteristic Nuclear Magnetic Resonance (NMR) "Shielding Values" (Spectral Positions) for Hydrogen in Organic Structures, Part I: Tables of γ Values for a Variety of Organic Compounds, Minnesota Mining and Manufacturing Company, St. Paul, Minnesota, 1958.

and tetrahydro-derivatives have the structures LXVII and LXVIII, respectively. The assignment of these structures is supported by the acid-catalyzed ring opening reactions of LXVII to 2-cycloheptene-1,4-dione (XXXVI) and LXVIII to 1,4-cycloheptanedione (LXII). An authentic sample of



2-cycloheptene-1,4-dione (characterized as the bis-2,4-dinitrophenylhydrazone) was prepared by oxidation of 2-cycloheptene-1,4-diol obtained by reductive hydrolysis of the corresponding diacetate.⁴¹

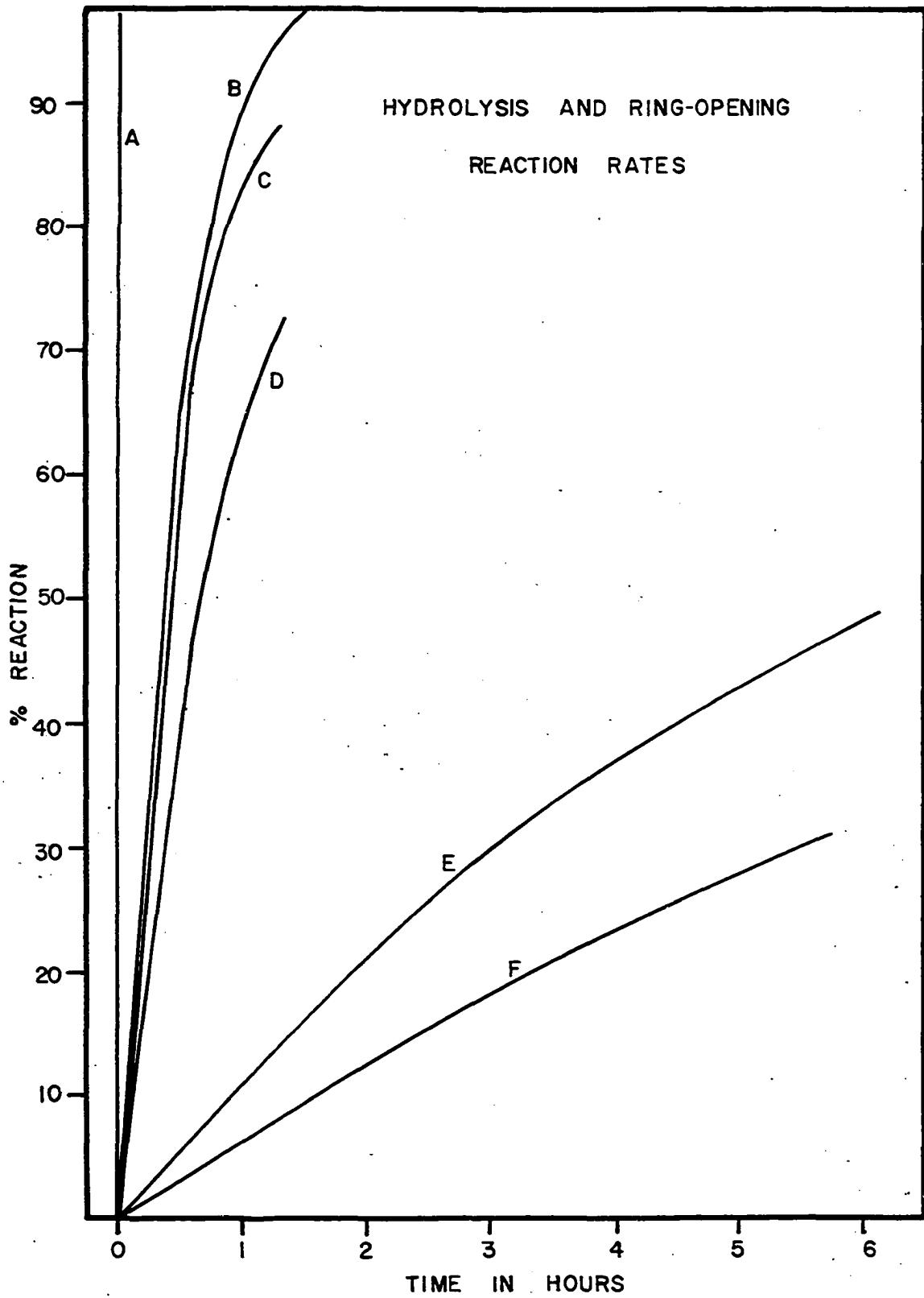
The rate of acid-catalyzed ring opening of LXVIII was exceedingly rapid compared to the rate of ring opening of LXV and LXVII. The ketones LXV and LXVII gave normal

derivatives when treated with acidic 2,4-dinitrophenylhydrazine reagent, whereas LXVIII gave only the bis-2,4-dinitrophenylhydrazone of 1,4-cycloheptenedione. The conversion of LXVIII to LXII is complete in 0.1N acid at room temperature in less than one minute, while the conversion of LXV to gamma-tropolone is only 55% complete after 18 hours in 0.1N acid at 80°. The rapid ring opening of LXVIII was entirely unexpected, as one would have expected that LXV would have opened more rapidly than LXVII and LXVIII because of the greater gain in resonance energy in going to the final product. Dihydrophoto-gamma-tropolone methyl ether (LXVII) undergoes ring-opening only slightly faster than LXV. Figure 6, page 79, shows the rates of ring opening of LXV, LXVII and LXVIII and the rates of hydrolysis of I in acid and base for comparison.

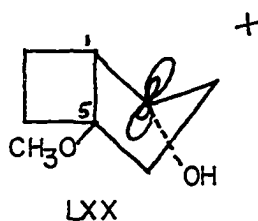
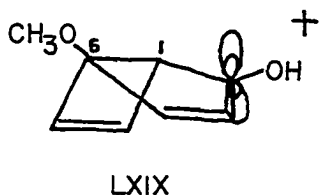
A reasonable explanation for the observed phenomena is based on the carbonium ions obtained by protonation of the carbonyl functions. During the C₁-C₅ bond breaking process, the electrons of the C₁-C₅ bond must interact with the vacant p-orbital of the carbonium ion. For maximum interaction the C₁-C₅ bond and the vacant orbital of the carbonium ion must lie in the same plane. Protonation of the carbonyl function of LXV leads to a carbonium ion contained in a rigid, planar, five-membered ring. The vacant p-orbital of the carbonium ion is perpendicular to the plane of this ring, and the C₁-C₅

Figure 6. Hydrolysis and ring-opening reaction rates

- A. Ring opening of 5-methoxybicyclo[3.2.0]heptane-2-one in 0.1N HCl at 22°C
- B. Ring opening of photo-gamma-tropolone methyl ether in 0.1N NaOH at 22°C
- C. Hydrolysis of gamma-tropolone methyl ether in 0.0896N NaOH at 80°C
- D. Hydrolysis of gamma-tropolone methyl ether in 0.10N HClO₄ at 80°C
- E. Ring opening of 5-methoxybicyclo[3.2.0]hept-3-ene-2-one in 0.1N H₂SO₄ at 80°C
- F. Ring opening of photo-gamma-tropolone methyl ether in 0.1N H₂SO₄ at 80°C

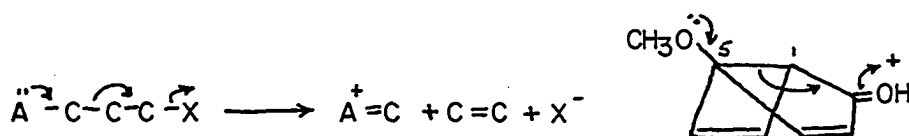


bond and is in the worst possible orientation for the required interaction with the vacant orbital (shown as LXIX). The carbonium ion derived from LXVIII is in a flexible, five-membered ring, and the vacant orbital can achieve the correct orientation for interaction with C₁-C₅ bond as shown in LXX. On the basis of this reasoning one would predict that



LXVII should undergo acid-catalyzed ring opening at a rate comparable with that of LXV rather than LXVIII. It is also very probable that the bridgehead methoxyl plays an important role in these ring opening reactions due to its electron donating ability during the C₁-C₅ bond breaking process.

The ring opening reactions observed with LXV, LXVII and LXVIII are identical to the fragmentation reactions of Grob.⁸¹ The fragmentation process involves an electron transfer as shown in the following scheme



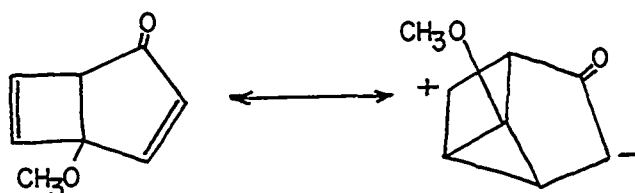
⁸¹C. A. Grob, Experimentia, 13, 126 (1957).

where A is an electron donor (-OR, -NR₂, -OH, etc.) and X is an electronegative group which may accept the negative charge (halogen, -OH₂⁺, tosylate, keto groups, etc.). In the ring opening reactions of LXV, LXVII, and LXVIII the methoxyl group acts as the electron donor and the protonated carbonyl as the electron acceptor.

With the structure of photo-gamma-tropolone methyl ether now resolved, it is necessary to comment on the anomalous ultraviolet spectrum of LXV. Such bathochromic shifts have been previously observed in the ultraviolet spectra of certain cyclopentenone derivatives.⁸² The anomalous behavior of LXV in the ultraviolet may be due to the interaction of the non-conjugated cyclobutene double bond with the cyclopentenone system, an electronic effect due to the methoxyl group, or steric destabilization of the ground state relative to the excited state. As the dihydrophoto-gamma-tropolone methyl ether (LXVII) displays normal cyclopentenone absorption in the ultraviolet, one may exclude the electronic interaction of the methoxyl group and the strain of the molecule as reasons for the anomalous absorption spectrum of LXV. There-

⁸²H. Conroy, *J. Am. Chem. Soc.*, 74, 491 (1952); J. Fajkos, *Coll. Czech. Chem. Comm.*, 23, 1559 (1958); K. Wiesner, F. Bickelhaupt and D. R. Babin, *Experientia*, 15, 93 (1959); K. Wiesner, F. Bickelhaupt, and Z. Valenta, *Tetrahedron*, 4, 418 (1959); K. Wiesner, M. Götz, D. L. Simmons, L. R. Fowler, F. W. Bachelor, R. F. C. Brown, and G. Büchi, *Tetrahedron Letters*, No. 2, 15 (1959).

fore the anomalous absorption must be due to an interaction of the non-conjugated cyclobutene double bond with the cyclopentenone chromophore. The electronic interaction of non-conjugated double bonds with alpha, beta-unsaturated carbonyl systems has been recognized previously.⁸³ This interaction might be illustrated as follows:



This is the first recorded instance of an electronic interaction between a cyclopentenone system and a non-conjugated double bond. The observed shift, 28 μ relative to LXVII, is also the largest shift yet observed for any interaction of this type. In view of the above observation, it is somewhat surprising that the Diels-Alder adducts of gamma-tropolone methyl ether (I) and tropone (II) with maleic anhydride showed normal ultraviolet absorption although they have the same general configuration. This may be due to the greater overlap of the π -electron clouds in LXV due to the forcing together of the cyclobutene and cyclopentenone rings by formation of the C₁-C₅ bond.

⁸³See S. L. Emmerman and J. Meinwald, J. Org. Chem., 21, 375 (1956) and the references cited therein.

Chemical evidence for the interaction of the cyclobutene double bond and the cyclopentenone system has been provided by the facile base-catalyzed ring opening of photo-gamma-tropolone methyl ether to gamma-tropolone methyl ether (see Figure 7, page 85), and by some novel light-catalyzed transformations in the alpha-tropolone methyl ether series.^{73,74,75,76} Treatment of photo-gamma-tropolone methyl ether with 0.1N sodium hydroxide at room temperature caused a rapid conversion of LXV to gamma-tropolone methyl ether. Similar treatment of the dihydro- and tetrahydroderivatives, LXVII and LXVIII, gave no reaction. Therefore the reaction must be dependent on the presence of the cyclobutene double bond. The mechanism of the base-catalyzed transformation of LXV to I may be visualized as follows.

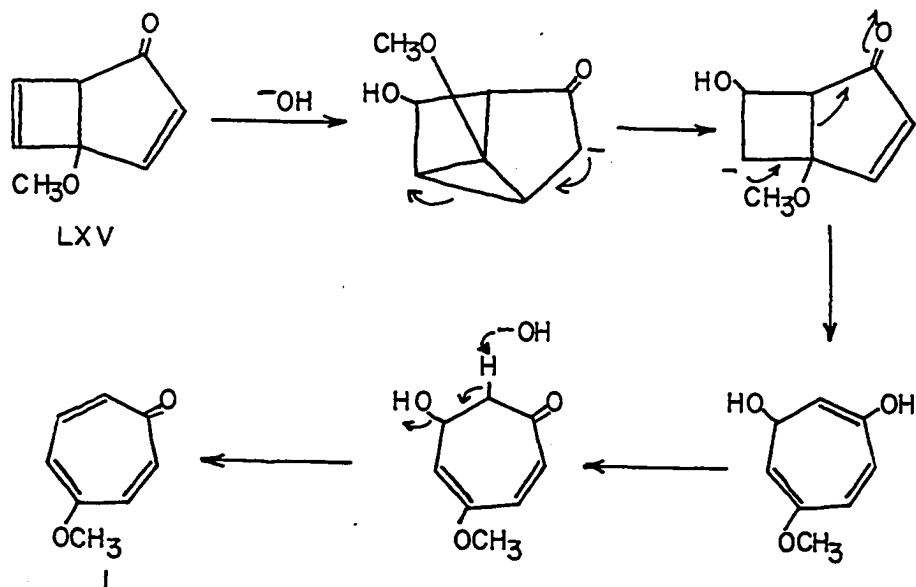
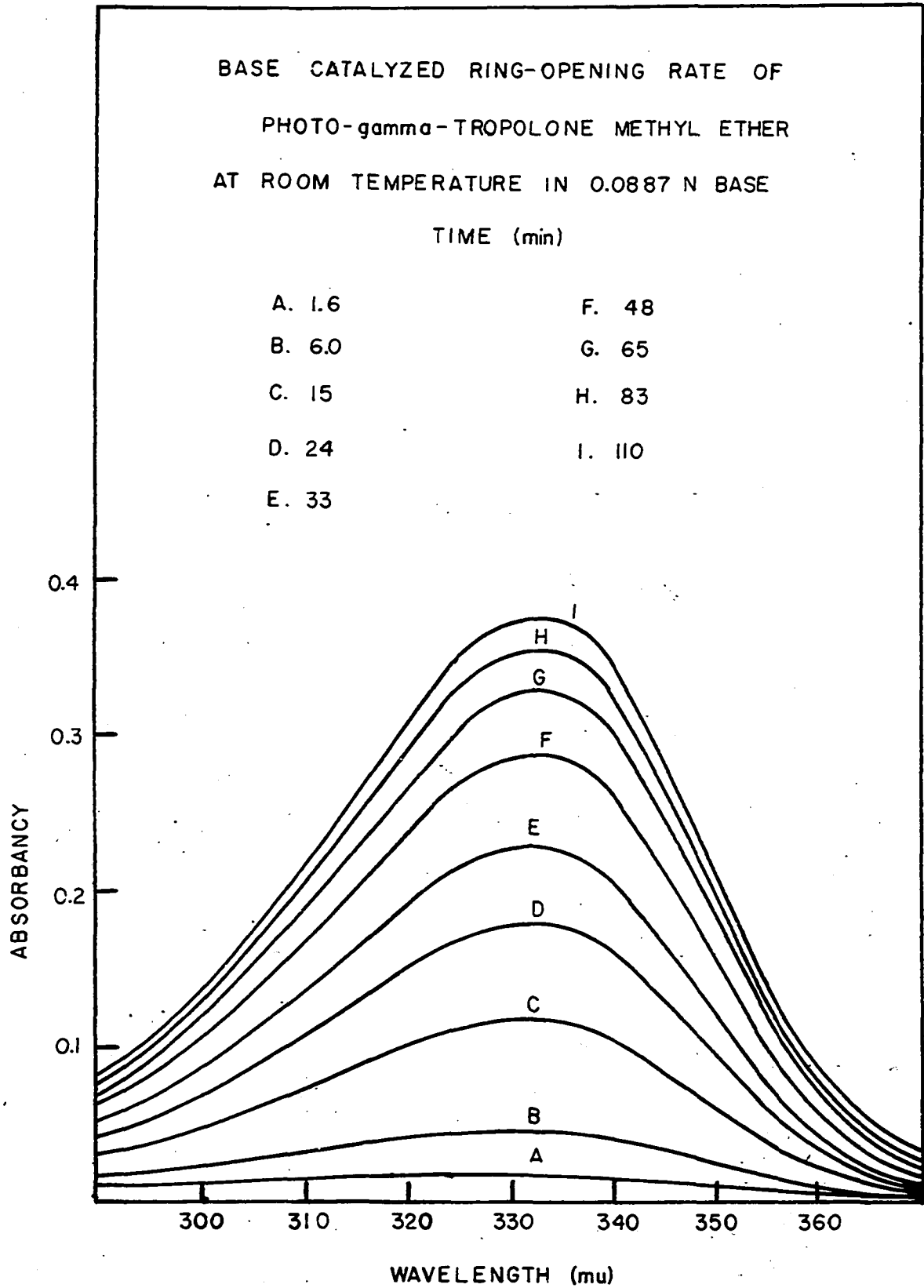
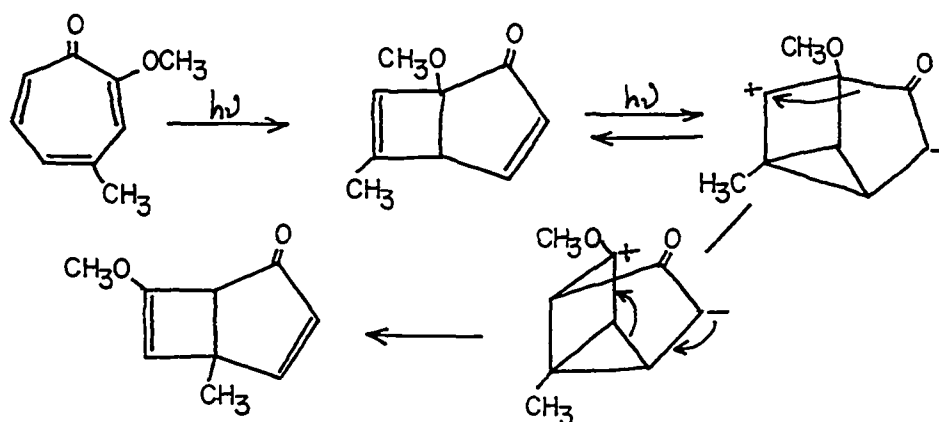


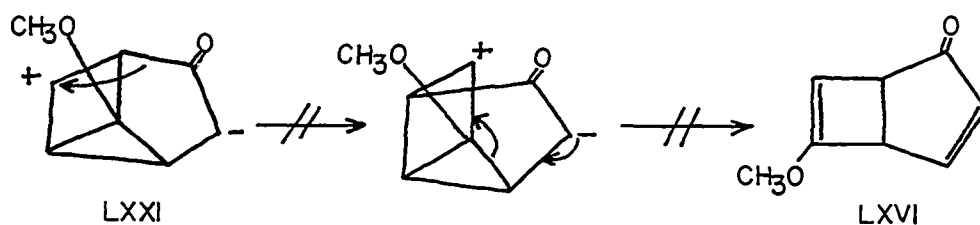
Figure 7. Base catalyzed ring-opening rate of photo-gamma-
tropolone methyl ether at room temperature



Evidence for similar double bond interaction has been observed in the photoproducts of 4- and 6-methyl-alpha-tropolone methyl ethers.⁷⁶ The primary photoproduct undergoes rearrangement to a secondary product which may be visualized to occur as shown in the following scheme (shown for 4-methyl-alpha-tropolone methyl ether). Photo-gamma-tropolone methyl ether would not be expected to undergo



further rearrangement,⁸⁴ as the intermediate carbonium ion would not be stabilized by the bridgehead methoxyl as it

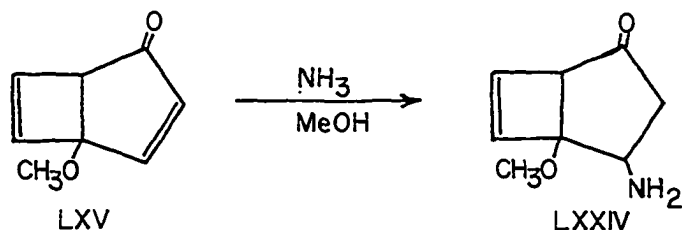


⁸⁴Preliminary experiments on the irradiation of photo-gamma-tropolone methyl ether in ethereal solution in quartz shows that gamma-tropolone methyl ether is formed and may be in equilibrium with the photoisomer (O. L. Chapman and A. Griswold, Research Journal of A. Griswold (manuscript), Department of Chemistry, Iowa State University of Science and Technology, Ames, Iowa, 1960).

is in the above transformation. The preceding chemical evidence strongly suggests the existence of transition states, in other bicyclo[3.2.0]hepta-3,6-diene-2-one systems, similar to LXXI by the interaction of the non-conjugated cyclobutene double bond with the cyclopentenone system.

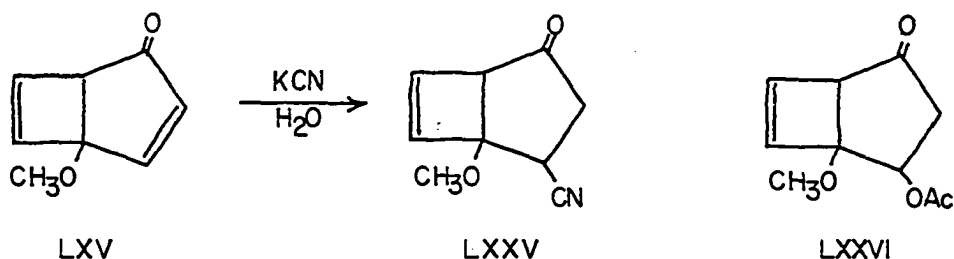
In a series of experiments to determine whether the base-catalyzed ring opening of photo-gamma-tropolone methyl ether to I was a general base-catalyzed reaction or a specific base-catalyzed reaction, catalyzed only by hydroxide ion, some surprising results were obtained. The rates of transformation of LXV to I in solutions of sodium acetate in water at 90° and sodium acetate in absolute methanol at reflux temperature (64°) are comparable to the observed rate of ring opening of LXV in refluxing ethanol. The residue recovered from the methanolic sodium acetate solution showed a peak in the infrared at 5.75 μ , along with the characteristic peaks of LXV and I, indicating the possible presence of a cyclopentanone or acetate derivative. The reaction of LXV with a methanolic solution of anhydrous ammonia or aqueous potassium cyanide produced a very rapid reaction at room temperature but gave essentially no ring opening reaction to I. The residue recovered after treatment of LXV with anhydrous ammonia in methanol showed peaks in the infrared at 2.75, 5.75, and 5.99 μ with low intensity absorption in the ultraviolet at 253, 270, and 325 $m\mu$. The species giving rise to

the 5.75 u peak may be a cyclopentanone derivative formed by Micheal addition of ammonia to the cyclopentenone⁸⁵ system giving LXXIV. The species giving rise to the 5.99 u peak is unknown, but is probably a cycloheptyl derivative. The



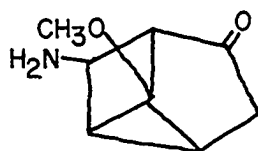
structure of LXXIV was assigned from spectral evidence only.

The reaction of LXV with an aqueous solution of potassium cyanide gave a single product with peaks in the infrared at 4.55 and 5.72 u (see Figure 15, page 235). The structure of the ketone may be that shown as LXXV formed by Micheal addition of cyanide ion to the cyclopentenone system.⁸⁵ There was no evidence for the presence of any products that would be produced by ring opening. (Some doubt has been cast as to

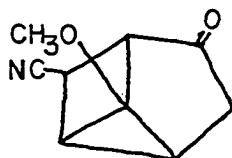


⁸⁵Ammonia and cyanide ion readily add to cyclopentenone to form the corresponding 3-amino- and 3-cyanocyclopentanone (O. L. Chapman and D. J. Pasto, Research Journal of D. J. Pasto (manuscript), Department of Chemistry, Iowa State University of Science and Technology, Ames, Iowa, 1960).

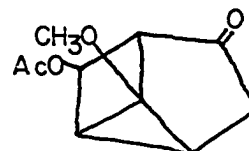
whether the structures of the ammonia and cyanide addition products are correct. The chemical properties of 2-keto-5-methoxybicyclo[3.2.0]hept-6-ene (page 102) would indicate that structures such as LXXIV, LXXV and LXXVI would be very susceptible to ring opening under the conditions of the experiment. It may be that the products are tricyclic compounds derived from LXXI by addition of the reagents used. Such structures may be shown as LXXIVa, LXXVa, and LXXVIa. The nuclear magnetic resonance spectrum of these compounds would



LXXIVa



LXXVa



LXXVIa

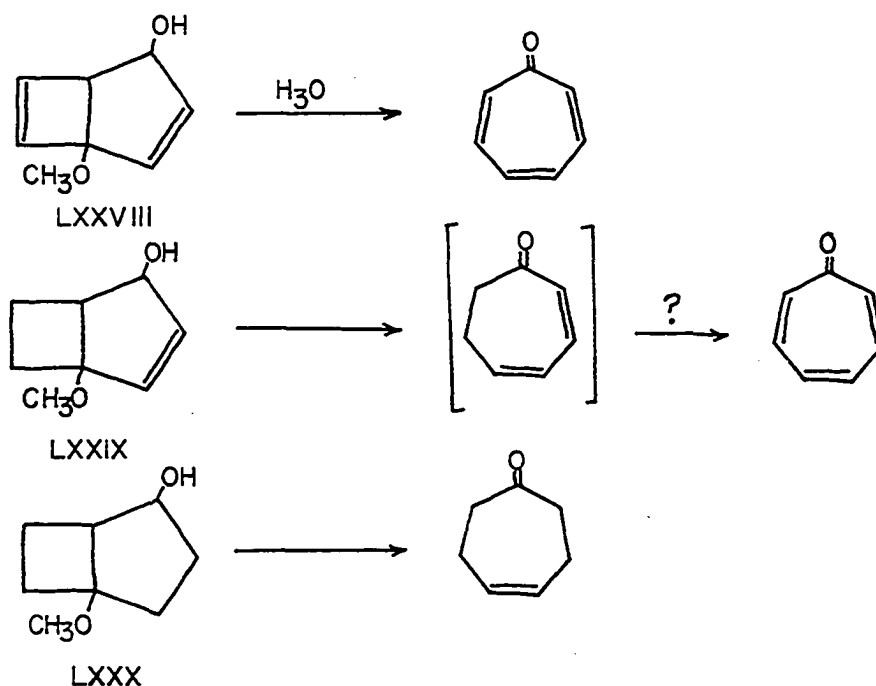
help to confirm either the bicyclic or the tricyclic system if present.) The product from the treatment of LXV with sodium acetate in absolute methanol displaying the 5.75 μ peak in the infrared by comparison may be the acetoxy-cyclopentenone derivative (LXXVI) formed by addition of acetate to the cyclopentenone system. As ammonia and cyanide ion are both good nucleophilic reagents, and both are distinctly basic, it was of interest to treat LXV with iodide ion which is a good nucleophilic reagent but is not basic. Treatment of LXV with an aqueous solution of potassium iodide at 74° did not accelerate the rate of ring opening of LXV, and did not undergo addition or give any addition product. The fore-

going evidence indicates that the ring opening reaction is catalyzed by strong bases and that the product ratio depends on the relative rates of addition and ring opening reactions.

The preceding discussion not only revealed some interesting chemistry involving LXV, but also opened up possible new synthetic approaches to the formation of different troponoid compounds. The pyrolysis and acid- or base-catalyzed ring opening reactions of substituted bicyclo[3.2.0]hepta-3,6-diene-2-ones offer a potential synthetic route to new troponoid compounds. Such a process would involve the formation of a primary photoproduct followed by either a light-catalyzed isomerization or chemical transformation to a new photoisomer with subsequent ring opening.

In an attempt to test the feasibility of such a sequence, the transformation of photo-gamma-tropolone methyl ether to tropone was attempted. Lithium aluminum hydride reduction of LXV gave an alcohol (LXXVIII) (2.96, 6.20, and 6.41 μ) (Figure 15, page 235); low intensity absorption in the ultraviolet), but attempted acid-catalyzed ring opening gave only a 29% yield of tropone after refluxing in 1.0N hydrochloric acid for 11 hours. Reduction of the dihydro- and tetrahydro-photo-gamma-tropolone methyl ether with lithium aluminum hydride gave alcohols LXXIX and LXXX, respectively. Attempted acid-catalyzed ring opening of LXXIX gave tropone in very poor yield (10%) after heating in 1.0N

hydrochloric acid for 32 hours. The tropone may have arisen from some LXXVIII present in the alcohol LXXIX or by air oxidation of the 2,4-cycloheptadieneone formed. The ring opening reaction of LXXX in acid was apparently more rapid, but the products could not be isolated. The expected product from LXXX would be 4-cycloheptenone.



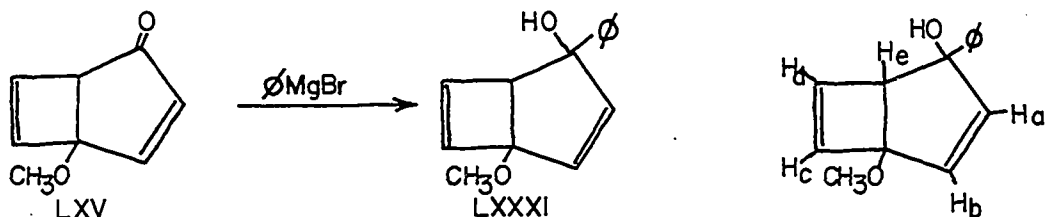
The correspondingly slower rates of acid-catalyzed ring opening reactions of these alcohols compared to the parent ketones must be due to the poorer stabilization of the incipient carbonium ion in addition to the inability for interaction of the C₁-C₅ bond with the incipient carbonium ion. Although the carbonium ions formed in the case of LXXVIII and LXXIX are stabilized by being in an allylic position, the stereochemistry of the molecule inhibits interaction of the

C₁-C₅ bond with the carbonium ion. The carbonium ion formed from LXXX is not stabilized in any manner, and, even though interaction with the C₁-C₅ bond is possible, a greater decrease in the ring opening rate as compared with the parent ketone LXVIII is observed.

It was then thought that if a system similar to LXXVIII could be prepared in which the incipient carbonium is stabilized to a greater degree, the ring opening reaction should proceed at a faster rate. The placement of a phenyl-group at the C₂ position would provide the needed stability for the incipient carbonium ion. Photo-gamma-tropolone methyl ether was treated with phenyl magnesium bromide giving the corresponding 2-hydroxy-2-phenyl-5-methoxy-bicyclo[3.2.0]hepta-3,6-diene, LXXXI. The infrared spectrum of LXXXI, Figure 15, page , showed hydroxyl absorption at 2.90 u. The ultra-violet spectrum, Figure 31, page 235, showed a low intensity shoulder at 247 mu with a weak maximum at 332 mu. The nuclear magnetic resonance spectrum of LXXXI is shown in Figure 35, page 267. The cyclopentene double bond now appears as an AB type system^{79b} consisting of a pair of doublets at 3.88 and 4.30 p.p.m. (J_{ab} 5.4 c.p.s.⁸⁶). The H_b proton appears as the 3.88 p.p.m. doublet being split by spin-spin coupling with only H_a. The doublet at 4.30 p.p.m. is assigned to the proton

⁸⁶J_{AB} is the spin-spin coupling constant, in cycles per second (c.p.s.), between protons A and B.

H_a and is further split by weak coupling with H_e . This type of transannular coupling is also observed in the nuclear mag-

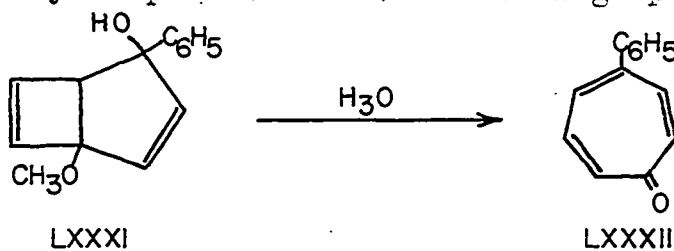


netic resonance spectrum of photo-gamma-tropolone methyl ether.

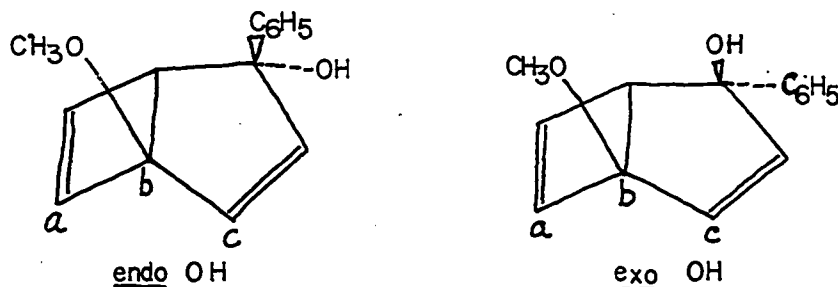
The protons of the cyclobutene double bond now form an AB type system with doublets at 3.30 and 3.58 p.p.m. (J_{cd} 2.9 c.p.s.). The proton H_c appears at 3.30 p.p.m. and is coupled only with H_d . The proton H_d appears at 3.58 p.p.m. and is further split by coupling with the bridgehead proton H_e . The methoxyl protons are shown as a singlet at 6.73 p.p.m. and the phenyl protons appear as a multiplet at 2.65 p.p.m. Assignment of the hydroxyl-proton and H_e is ambiguous. Either the peak at 7.25 p.p.m. or the combined peaks at 7.93 and 8.75 p.p.m. may represent the hydroxyl-proton. Consideration of the peak areas is very instructive. The 7.24 p.p.m. peak area represents 1.5 protons whereas the sum of the areas of the 7.93 and 8.75 p.p.m. peaks corresponds to exactly one proton. Therefore the 7.93 and 8.75 p.p.m. peaks are assigned to the hydroxyl proton. These peaks apparently consist of two doublets, the 7.93 p.p.m. peak and the central peak of the 8.75 p.p.m. multiplet comprising one doublet and the two outermost peaks forming the second doublet. Cause for splitting of the hydroxyl proton as such may be explained by the possible presence of two isomers from the Grignard reaction, one with the hydroxyl group endo

and one with the hydroxyl *exo*.⁸⁷ The chemical environment of the hydroxyl proton is distinctly different in the two cases and may be the reason for splitting into the two doublets. If there is interaction between H_e and the hydroxyl proton in the *exo* conformation, it is reasonable to expect that H_e would also be split. There are several peaks at the base of the methoxyl protons centered at 6.57 ppm and these may represent proton H_e .

Treatment of LXXXI with 0.5N hydrochloric acid and gentle heating resulted in a rapid reaction producing maxima in the ultraviolet at 258 and 334 μ . The residue obtained by extraction showed peaks in the infrared at 5.85, 5.99, 6.16 μ and aromatic peaks. It was not possible to unambiguously identify the hydrolysis product, but one would expect to obtain 4-phenyltropone (LXXXII). The ring opening reaction of

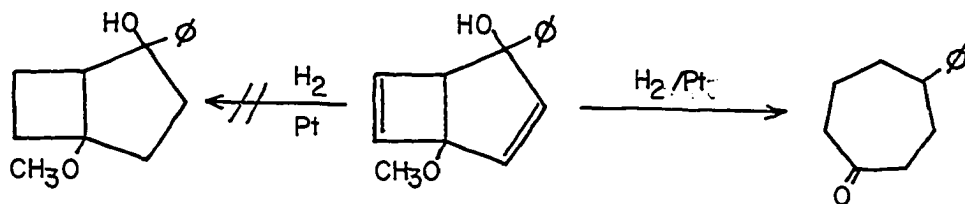


⁸⁷Exo is defined as being outside the angle formed by atoms a, b, and c while endo is within this angle.



LXXXI to LXXXII is complete in 15 minutes. This is in marked contrast to the rate of ring opening of LXXVIII. This rate enhancement is probably due to the release of steric crowding on ring opening.

From the rapid rate of ring opening of LXXXI, it was expected that the tetrahydroderivative (LXXXIII) would undergo acid-catalyzed ring opening extremely rapidly. In support of this statement, it was found that it was impossible to hydrogenate LXXXI to the desired tetrahydroderivative, as ring opening apparently occurred on the surface of the catalyst resulting in the absorption of 3.08 moles of hydrogen per mole of compound. The product showed a peak in the infrared at 5.88 μ in carbontetrachloride. Although the product was not



LXXXIII

LXXXI

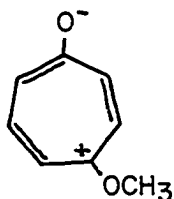
not positively identified, the infrared spectrum and hydrogenation data suggested 4-phenylcycloheptanone as a good possibility.

Inspection of models of the system LXXXI indicates that the most stable isomer produced in the Grignard reaction is the one with the hydroxyl group endo. The model of the isomer with the hydroxyl group exo indicates that there must be considerable steric interaction between the ortho hydrogens of

the phenyl group and the cyclobutene hydrogen restricting free rotation of the phenyl group. The hydrogenation of LXXXI might possibly occur from the underside of the molecule due to the presence of the methoxyl group and phenyl groups on the upper side. If this were true, the hydroxyl group would be on the side of the catalyst. The catalyst, being a Lewis acid, would catalyze the loss of water to form the carbonium ion which would immediately undergo ring opening and subsequent hydrogenation.

The failure to form LXXXIII suggested that the use of a methyl group at position 2 might be more desirable. Treatment of photo-gamma-tropolone methyl ether with methyl magnesium iodide gave an alcohol (2.93, 6.13, and 6.38 u; no high intensity absorption in the ultraviolet) which on hydrogenation undergoes ring opening to give some methylcycloheptanone (5.88 u in carbontetrachloride), as indicated by comparison of gas phase chromatographic retention times with authentic 4-methylcycloheptanone. At this point all attempts to make a derivative of this type were abandoned. It is interesting to note the differences observed between LXXVIII, LXXXI and LXXXIV on hydrogenation. The alcohol LXXVIII undergoes normal hydrogenation with no ring opening whereas LXXI and LXXXIV undergo ring opening. This effect, as indicated above, is probably due to steric crowding in the molecule and stabilization of the intermediate carbonium ion.

The isolation of only one photoisomer from the irradiation of I is significant. It appears that the excited state of I must have considerable polar character and is highly stabilized by the methoxyl group. Such an excited state may be visualized as LVI. Irradiation of tropone would lead to



LVI

an excited state which would not be stabilized as is LVI. This may be the reason why tropone has not given a simple photoisomer on irradiation, but apparently gives a red polymeric material similar to that obtained from the irradiation of I. It may also be that a photoproduct is formed, but is very reactive and undergoes further light-catalyzed or thermal reactions.

It should also be noted that bridging occurs across the same two carbon atoms of I in both the Diels-Alder and the photochemical reactions. It very well may be that the excited state of I in both reactions is similar. If this were true, it was visualized that a light-catalyzed Diels-Alder reaction might be realized. The irradiation of aqueous and benzene solutions of gamma-tropolone methyl ether and maleic anhydride gave only red polymeric material with no adduct being formed. The excitation of I may occur within a solvent cage followed

by a fast ring closure while still within the cage. Under these conditions excited I would not encounter a maleic anhydride molecule. If the reaction could be run with no solvent, *i.e.*, using excess molten maleic anhydride as the solvent, the light-catalyzed reaction might be realized.

The Photochemistry of 1,3-Cycloheptadienes

Several reports have appeared on the photochemistry of conjugated cyclic dienes in the six-membered ring series.^{88,89} 1,3-Cyclohexadiene and substituted 1,3-cyclohexadienes normally undergo ring fission to give the corresponding hexatrienes. Only in the case of irradiation of pyro- and isopyrocalfiferol has a bicyclo[2.2.0]hexene system been formed.⁹⁰ Barton, in reviewing the photochemistry of unsaturated compounds, has given the following generalization concerning the photochemistry of cyclic dienes.⁸⁹

If one considers any ring of $2n$ members containing $(n-1)$ conjugated double bonds, then, in principle, irradiation with ultraviolet light of the appropriate wavelength should furnish an open chain compound containing $(n-1+1) = n$ conjugated double bonds. Quite different considerations apply to rings that contain $(2n+1)$ members and n conjugated

⁸⁸See the references cited in O. L. Chapman and D. J. Pasto, *J. Am. Chem. Soc.*, **82**, 3642 (1960).

⁸⁹D. H. R. Barton, *Helv. Chim. Acta*, **42**, 2604 (1959) and the references cited therein.

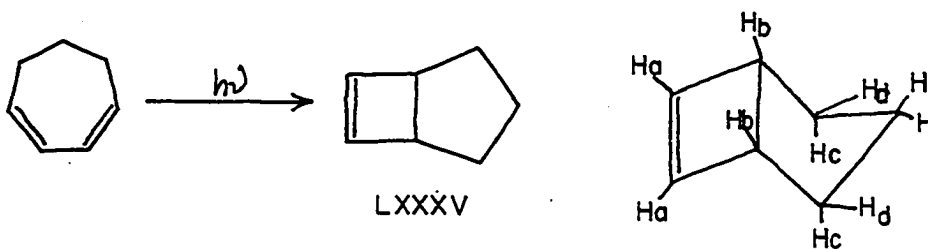
⁹⁰W. G. Dauben and G. F. Fonken, *J. Am. Chem. Soc.*, **79**, 2971 (1957).

double bonds. Here it can be predicted that cleavage reactions should not be observed, only bridging reactions.

The postulate is based in part on the photochemical transformations of colchicine and gamma-tropolone methyl ether. Since Barton first proposed this generalization, additional support has been provided by the photochemical transformations of members of the alpha-tropolone series.^{73,74,75,76} There has been no report on the photoisomerization of cycloheptatriene or of cyclopentadiene, or of their derivatives.

Although 1,3-cycloheptadiene does not specifically fit under the $(2n+1)$ membered ring: n double bond classification, one might expect only bridging reactions to occur. The irradiation of 1,3-cycloheptadiene was undertaken to test this idea.

The irradiation of a 2-3% solution of 1,3-cycloheptadiene in anhydrous ether was carried out in a quartz vessel with a mercury arc lamp for 2-3 days. Fractional distillation of the irradiated solution gave a very volatile, liquid olefin (6.40 u) which was identified as bicyclo[3.2.0]hept-6-ene (LXXXV). The nuclear magnetic resonance spectrum of LXXXV

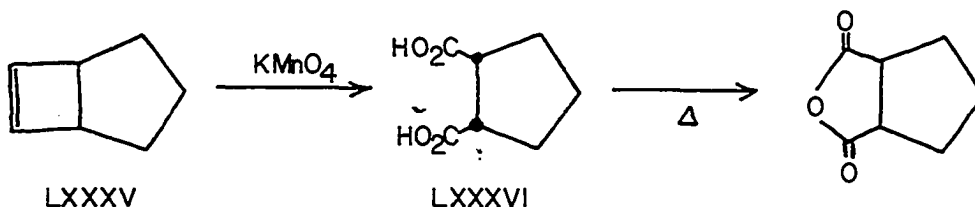


is shown in Figure 37, page 279. The cyclobutene protons, H_a , appear as a single peak at 4.19 p.p.m. This singlet is due to an unexpectedly small or completely absent spin-spin coupling of these protons with the neighboring protons. This same type of phenomena is also encountered with cyclobutene.⁹¹ The appearance of these protons as a singlet is in direct contrast with the cyclobutene protons of LXV and LXXXI which appear as ABX and AB patterns, respectively. The doublet occurring at 6.89 p.p.m. must be due to the bridgehead protons, H_b , although one would normally expect either a singlet or a triplet on applying spin-spin coupling rules when there is apparently no coupling between the two bridgehead protons. The cause for the appearance of these protons as a doublet must be due to a nonequivalence of the protons H_c and H_d , otherwise a triplet would result. Spin-spin coupling with H_a does not occur as is indicated by the singlet for the protons H_a . The non-equivalence of protons H_c and H_d with H_b is undoubtedly due to their trans and gauche relationship with H_b , respectively. This is due to the rigidity of the carbon atoms bearing the proton H_c and H_d imposed by the cyclobutene ring. The coupling between H_b and H_c should be greater than the coupling between H_b and H_d , as in cases

⁹¹J. D. Roberts, Nuclear Magnetic Resonance, McGraw-Hill Book Co., Inc., New York, 1959, p. 54.

where the dihedral angle between $H_aC_1C_2$ and $C_1C_2H_b$ is 90° the coupling constant is nearly zero.⁹² In this case the coupling constant between H_b and H_d must be very small or non-existent. The multiplets at 7.85 and 8.48 p.p.m. represent the methylene hydrogens. The appearance of two bands in this region may be due to the non-equivalence of two of the protons of the methylene groups as discussed above.

Pyrolysis of LXXXV at temperatures above 468° gave 1,3-cycloheptadiene in quantitative yield indicating no gross rearrangement of the carbon skeleton. The olefin, LXXXV, absorbed one mole of hydrogen over Adams' Catalyst giving the saturated hydrocarbon bicyclo[3.2.0]heptane. Oxidation of LXXXV with permanganate gave in good yield cis-1,2-cyclopentanedicarboxylic acid (LXXXVI) which in turn readily gave the corresponding anhydride.



In an attempt to prepare the diacid LXXXVI by ozonolysis of LXXXV, LXXXV absorbed two moles of ozone instead of the expected one mole. The ozonide was hydrolyzed with aqueous hydrogen peroxide giving a volatile acid and apparently a

⁹²L. M. Jackman, Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry, Pergamon Press, New York, 1959, p. 87.

ketoacid. The volatile acid was identified as formic acid by paper chromatography. The ketoacid (5.58 (weak), 5.72 (shoulder) and 5.83 u) forms a 2,4-dinitrophenylhydrazone which retains the 5.83 u peak in the infrared. The structure of the ketoacid is unknown.

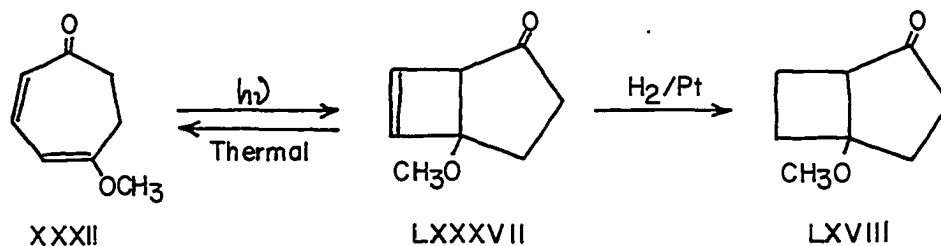
The irradiation of 5-methoxy-2,4-cycloheptadienol (XL), 4-methoxy-3,5-cycloheptadienol (XLI) and 2-methyl-4-methoxy-3,5-cycloheptadienol (XXI) which gives respectively 2-hydroxy-5-methoxybicyclo[3.2.0]hept-6-ene (XLIV), 3-hydroxy-6-methoxybicyclo[3.2.0]hept-6-ene (XLV) and 2-methyl-3-hydroxy-7-methoxybicyclo[3.2.0]hept-6-ene (XLII) has already been discussed in connection with the proof of structure of the three alcohols (page 38).

The irradiation of the crude reaction product mixture of I with lithium aluminum hydride in ether in a quartz vessel caused the rapid disappearance of the 328 mu maximum (5-methoxy-2,4-cycloheptadienone, XXXII) in the ultraviolet. The residue obtained after removing the solvent showed an intense carbonyl peak in the infrared at 5.78 u. The gas phase chromatogram on LB550X and TCEP columns showed no peak which would correspond to anisole.⁹³ Alumina chromatography gave

⁹³Irradiation of a mixture of cycloheptadienone in ethereal solution in quartz produces benzene (O. L. Chapman and G. W. Borden, Research Journal of G. W. Borden (manuscript), Department of Chemistry, Iowa State University of Science and Technology, Ames, Iowa, 1960) and it was thought that anisole might be formed in the irradiation of the 5-methoxy-2,4-cycloheptadienone.

a ketonic fraction which showed peaks in the infrared at 5.78, 6.13 and 6.38 μ and showed intense end absorption with a weak maximum at 328 μ in the ultraviolet. Hydrogenation of a portion of the ketone in methanol over Adams' Catalyst gave 5-methoxybicyclo[3.2.0]heptane-2-one (LXVIII) identified by comparison with authentic LXVIII, obtained by hydrogenation of photo-gamma-tropolone methyl ether (LXV). The structure of the photoisomer of XXXII must be 5-methoxybicyclo[3.2.0]hept-6-ene-2-one (LXXXVII).

The ketone LXXXVII proved to be an extremely unstable compound. The compound undergoes slow ring opening to XXXII on standing at room temperature. An ethanol solution of LXXXVII undergoes 52% ring opening in two hours at room temperature.

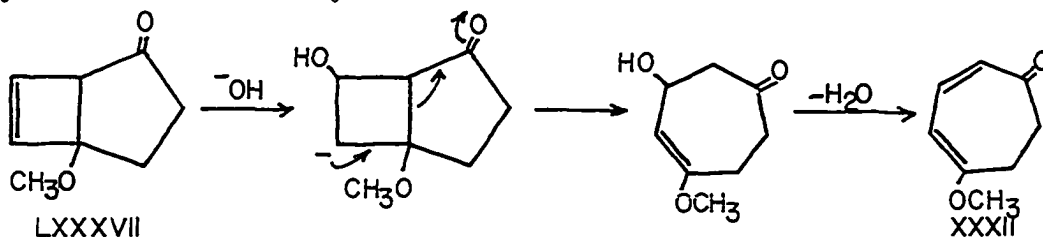


One would expect that LXXXVII would undergo rapid acid-catalyzed ring opening due to the flexibility of the cyclopentanone ring (see the discussion of the mechanism for the acid-catalyzed ring opening reactions of photo-gamma-tropolone methyl ether (LXV) and the dihydro (LXVII) and tetrahydro (LXVIII) derivatives, page 77). Treatment of LXXXVII with 0.1N sulfuric acid caused a rapid generation of 2-cyclo-

heptene-1,5-dione, as its enol, as seen by the rapid formation of a 340 m μ peak in the ultraviolet. The intensity of the 340 m μ maximum increased up to 15 minutes and then decreased giving rise to a 233 m μ peak. Heating the acid solution of LXXXVII produced a solution which showed only 233 m μ maximum (the same phenomena was observed by heating XXXII and a cycloheptadienone mixture in dilute acid). The acid-catalyzed ring opening rate of LXXXVI is appreciably slower than the rate of ring opening of LXVIII in acid, but rate measurements are complicated by the concurrent thermal ring opening of LXXXVI.

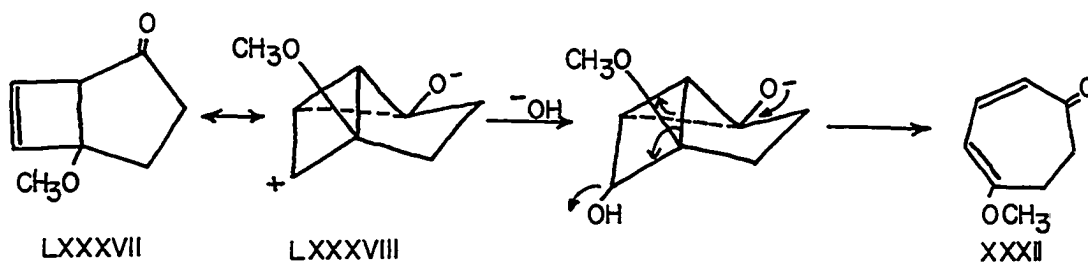
Treatment of LXXXVII with 0.1N sodium hydroxide also produced a rapid ring opening reaction to XXXII as observed in the ultraviolet. The rate of ring opening of LXXXVII is apparently greater than the rate of base-catalyzed ring opening of photo-gamma-tropolone methyl ether LXV (the absolute rate was not determined for LXXXVII as impure material was used and the reaction was further complicated by the thermal reaction). From the discussion on page 83 concerning the mechanism for the base-catalyzed ring opening of photo-gamma-tropolone methyl ether which is dependent on the presence of the cyclobutene double bond and its interaction with the cyclopentenone system, one would not have expected LXXXVII to undergo a base-catalyzed ring opening reaction by this mechanism. Hydration of the cyclobutene double bond, as

in LXV, would give an intermediate carbanion, which in some respects resembles an intermediate carbanion in the mechanism on page 83, which might undergo ring opening. The required hydration of the cyclobutene double bond as shown in this



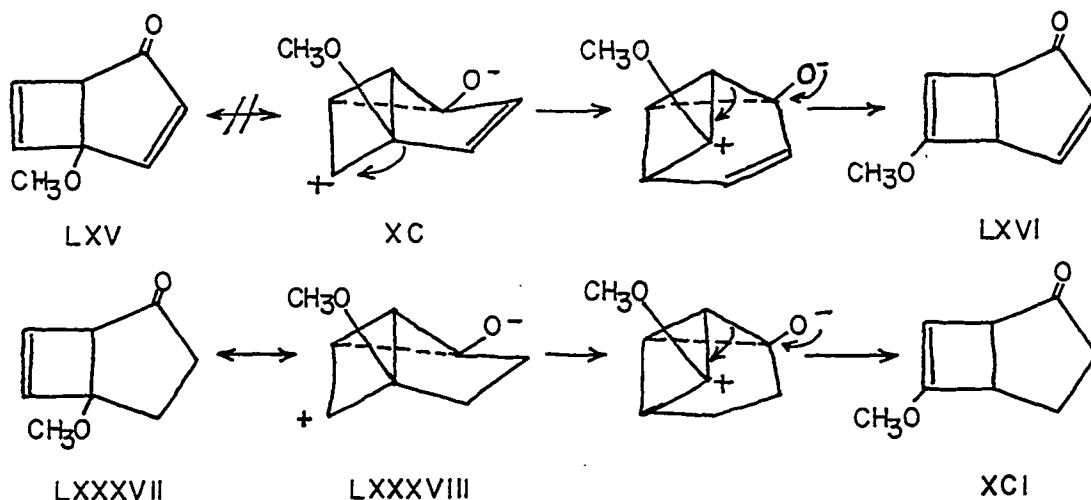
case, would not be expected to occur as isolated double bonds do not undergo addition of base under these conditions. The ease of hydration of the cyclobutene double bond in photo-gamma-tropolone methyl ether (LXV) is due to the double bond interaction producing the resonance form LXXI which has a lowered electron density on C₇ enabling base to attack.

One might visualize an interaction between the cyclobutene double bond and the carbonyl function (resonance form LXXXVIII). Attack of base would then occur at C₆ and would then undergo ring opening to give XXXII. It is important to

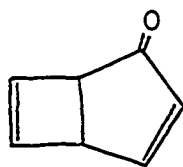


note that there is probably interaction of the cyclobutene double bond with both C₂ and C₄ which are equidistant. The interaction shown in LXXXVIII may also occur in LXV, but it is doubtful if such an interaction as is shown in XC, does

occur as LXV is apparently not transformed to LXVI on irradiation.⁸⁴ This type of transformation might be realized with LXXXVII and the resulting product XCI may be the species giving rise to the strong peak in the infrared at 6.13 μ . Insufficient material prevented further work in this system and this should be investigated in the future.



The preceding photochemical isomerizations have not only provided some very interesting chemistry, but have opened a novel synthetic route to bicyclo[3.2.0]heptyl systems already containing functional groups in either or both rings. The introduction of functional groups into a preformed bicyclo[3.2.0]heptyl system is very difficult by classical methods. By judicious choice of the starting diene, any substituent can be placed at any position in the final bicyclo[3.2.0]heptyl system. Such a procedure might lead to bicyclo[3.2.0]hepta-3,6-diene-2-one (LXXXIX), which has not been obtained

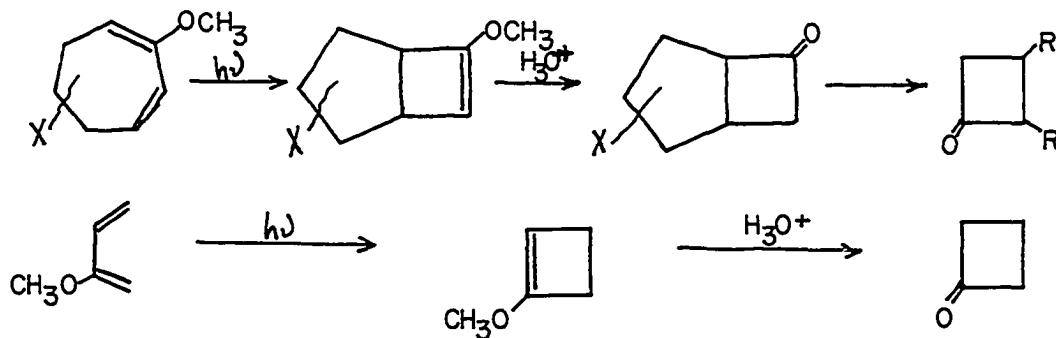


LXXXIX

thus far by the irradiation of tropone.

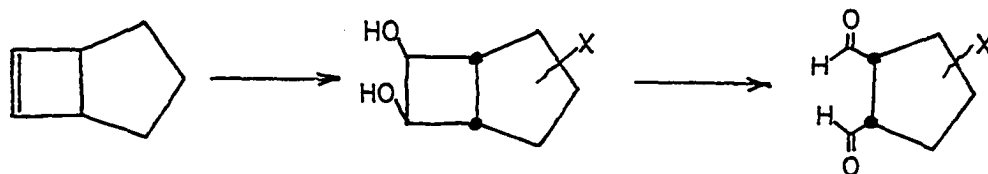
The solvolysis of the various alcohols containing the cyclobutene double bond is also of interest. The solvolysis of the isomers of 2-hydroxybicyclo[3.2.0]heptane has been carried out by Winstein.⁹⁴ It would be interesting to compare the effects of the cyclobutene double bond on the solvolysis reaction with the saturated isomer.

The synthesis of substituted cyclobutanones is made relatively simply by the light-catalyzed ring closure of a methoxydiene followed by hydrolysis of the cyclobutenyl enol ether (see page 38). The cyclopentane ring may then be degraded to give various substituted cyclobutanones. It is also possible that acyclic methoxydienes may undergo light-catalyzed ring closure to give cyclobutanones also.



⁹⁴S. Winstein, F. Gadiant, E. T. Stafford, and P. E. Klinedinst, Jr., *J. Am. Chem. Soc.*, **80**, 5895 (1958).

Hydroxylation of the cyclobutene double bond and oxidation with periodic acid would provide the dialdehyde which may also be useful as an intermediate.



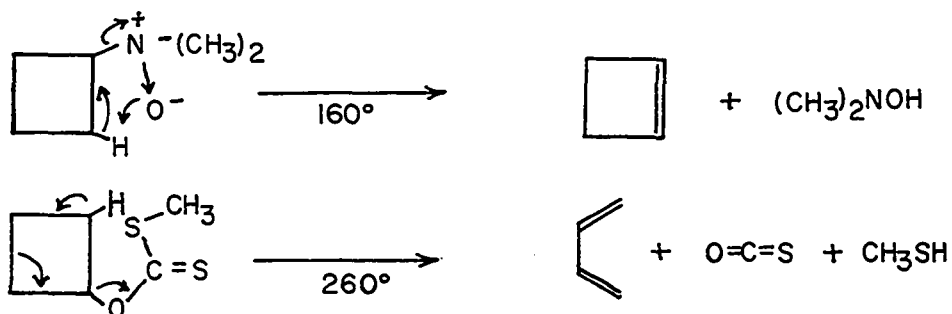
These are only a few of the potential uses for the bicyclo[$\bar{3}$.2.0]heptyl systems that may be formed by photoisomerization of the corresponding diene.

The photochemical isomerization of 1,3-cycloheptadienes to bicyclo[$\bar{3}$.2.0]hept-6-ene by bridging across the ring is in accord with expectation. The Barton generalization should therefore be extended to include conjugated cyclic dienes of $(2n+1)$ members as compounds that normally undergo bridging reactions.

The ease of pyrolysis of the cyclobutene compounds LXV, LXXXV and LXXXVII prompted an investigation into the pyrolysis of the cyclobutene derivatives. The pyrolysis of LXV was quantitative at 360° , the pyrolysis of LXXXV was rapid above 360° and LXXXVII was unstable at room temperature. The pyrolytic reaction is apparently very temperature dependent as indicated by the table on page 195 for the pyrolysis of LXXXV.

A literature search revealed that the pyrolysis of

cyclobutene compounds is well known^{95,96} and that cyclobutene itself undergoes pyrolysis at 150°. ⁹⁶ A careful study of the pyrolysis of cyclobutene has been carried out by Cooper and Walters⁹⁶ showing cyclobutene undergoes pyrolysis to 1,3-cyclobutene at 150°. Roberts has reported the synthesis of cyclobutene by pyrolysis of N,N-dimethylcyclobutyl amine oxide (XCIII) at 160°, but that pyrolysis of cyclobutyl xanthate (XCIV) at 260° gave butadiene.⁹⁷ Roberts has given the following mechanism for the reaction.



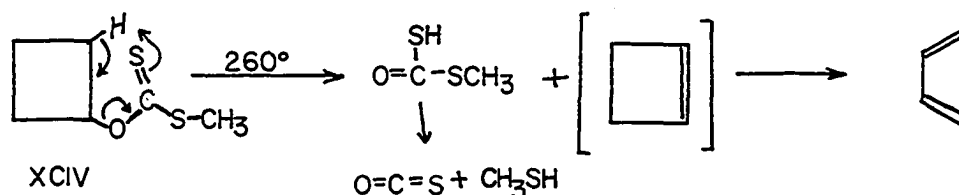
Cyclobutene was prepared (in poor yield) by pyrolysis of the amine oxide XCIII at 160°. Gas phase chromatographic analysis showed the presence of 1% of 1,3-butadiene in the cyclobutene. Samples of the cyclobutene were pyrolyzed in a closed glass container at varying temperatures. Analysis of these samples by gas phase chromatography showed

⁹⁵E. Vogel, Angew. Chem., 66, 640 (1954); E. Vogel, ibid., 72, 21 (1960).

⁹⁶W. Cooper and W. D. Walters, J. Am. Chem. Soc., 80, 4220 (1958).

⁹⁷J. D. Roberts and C. W. Sauer, ibid., 71, 3925 (1949).

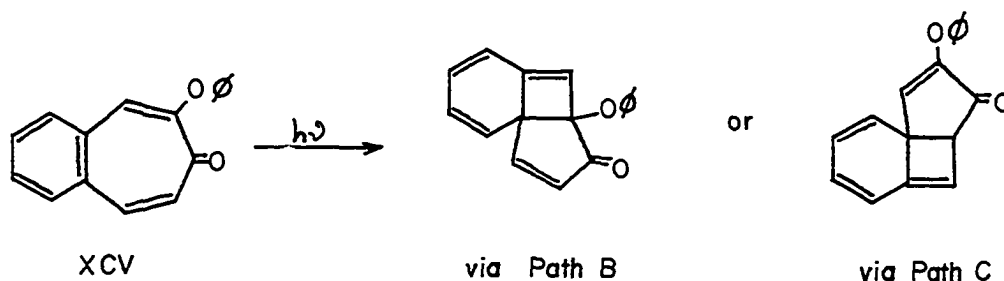
the presence of 16% of 1,3-butadiene at 182°, 51% at 200° and 100% at 252°. Therefore, a more reasonable mechanism for the pyrolysis of the cyclobutyl xanthate (XCIV) would involve a normal cis-1,2-elimination⁹⁸ forming cyclobutene which, being unstable at 260°, would immediately undergo ring opening to 1,3-butadiene. The substitution on a cyclobutene undoubtedly



influences the stability of the compound toward pyrolytic ring opening.

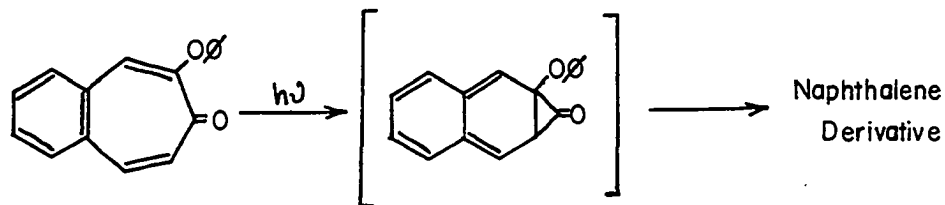
The Photochemistry of 4,5-Benzo-2-phenoxytropone

The irradiation of 4,5-benzo-2-phenoxytropone (XCV) would not be expected to give a product via paths B or C, as the resulting products would be sterically unfavorable. Therefore it was thought that 4,5-benzo-2-phenoxytropone might be



⁹⁸See discussion and references cited in C. H. DePuy and R. W. King, to be published in Chem. Rev., (ca. 1960).

forced to react via a path A type mechanism, possibly leading to a naphthalene derivative.



The irradiation of XCV in isopropanol in a pyrex vessel gave two products easily separated by alumina chromatography. Molecular weight determination by cryoscopic methods in benzene, or by the Rast method in camphor, indicated dimeric compounds. The two compounds will simply be referred to as dimer A and dimer B in the following discussion.

Dimer A, formed in up to 50% yield, showed peaks in the infrared at 5.83, 5.96, 6.06, and 6.12 μ (Figure 16, page 237). The ultraviolet spectrum showed strong end absorption with a shoulder at 215 $m\mu$ (50,300) with a maximum at 263 $m\mu$ (17,200) (Figure 32, page 269). The nuclear magnetic resonance spectrum of dimer A is shown in Figure 36, page 277. The doublets at 3.97 and 4.66 p.p.m. represents two olefinic protons (J 12 c.p.s.). This set of doublets is characteristic of protons on a cis-disubstituted double bond.^{79c} The presence of this double bond is also supported by the presence of a 14.5 μ ⁹⁹ peak in the infrared. The multiplet centered

⁹⁹L. J. Bellamy, The Infrared Spectra of Complex Molecules, John Wiley and Sons, Inc., New York, 1958, p. 34.

at 5.52 p.p.m. corresponds to three protons and apparently consists of a single doublet overlapping a pair of doublets. The single doublet, with peaks at 5.52 and 5.68 p.p.m. (J 9.5 c.p.s.), must represent a single proton which may be coupled to another proton which may be hidden under the aromatic protons at 2.96 p.p.m. as there is no other proton signal present with a coupling constant J of 9.5 c.p.s. There is the possibility that this proton is coupled in some way with the aromatic protons which show a J of 9.5 c.p.s. In the same region with this doublet is a pair of doublets with centers at 5.34 and 5.71 p.p.m. (J 4.9 c.p.s.). The character of the protons giving rise to these signals is ambiguous. The signals of terminal methylene protons and protons on carbon bearing electronegative substituents appear in this region. This region is apparently too far up field to represent protons on an ordinary double bond and no definite assignment can be made. The peak area of the aromatic protons at 2.96 p.p.m. corresponds to 22 protons and is indicative of a dimeric compound.

Dimer A absorbs two moles of hydrogen over Adams' Catalyst and gives a tetrahydroderivative (melting point $219.5-221^{\circ}$) which shows peaks in the infrared at 2.85, 5.68, and 6.02 μ (Figure 16, page 237). The ultraviolet spectrum, shown in Figure 32, page 269, shows little change from that of dimer A. Refluxing the tetrahydroderivative in hydro-

chloric acid apparently gives a different compound (melting point 252-258°) which shows a carbonyl peak in the infrared at 5.70 u. This compound was not further characterized. A similar hydrogenation of dimer A over an inferior grade of platinum oxide⁶⁹ resulted in the absorption of two moles of hydrogen, but gave a product with peaks in the infrared at 5.73 and 5.83 u. This compound was not further characterized.

Ozonolysis of dimer A with one mole of ozone¹⁰⁰ gave a single product which shows peaks in the infrared at 5.64 and 5.83 u (Figure 18, page 241). The compound apparently undergoes decarboxylation or decarbonylation on melting.

Treatment of dimer A with lithium aluminum hydride gave a non-crystalline alcohol which showed double bond absorption at 6.02 u in the infrared. The ultraviolet spectrum showed little change from that of the dimer A. In addition to the isolation of the alcohol, one molar equivalent of phenol was also isolated. This would indicate that a phenyl ester was present which undergoes reductive hydrolysis to phenol and the alcohol. The presence of the phenyl ester was also indicated by the carbonyl absorption at 5.68 u in the tetrahydro-derivative. The alcohol readily forms an acetate in acetic anhydride-pyridine solution. Manganese dioxide oxidation of

¹⁰⁰Dimer A has been shown to absorb two moles of ozone (O. L. Chapman and P. Fitton, Research Journal of P. Fitton (manuscript), Department of Chemistry, Iowa State University of Science and Technology, Ames, Iowa, 1960).

the alcohol caused the generation of 5.83 and 5.97 μ peaks in the infrared. Dimer A was unaffected by treatment with sodium borohydride, but on treatment with zinc in acetic acid gave a material which showed a 5.73 μ shoulder and a 5.87 μ peak in the infrared.

Evidence for the presence of an alpha-beta-unsaturated ketone was provided by the preparation of a 2,4-dinitro-phenylhydrazone (5.84 and 6.18 μ , $\lambda_{\text{max}}^{\text{CHCl}_3}$ 387 μ (25,400)) and an oxime (5.84 and 6.09 μ (see Figure 18, page 241), $\lambda_{\text{max}}^{95\% \text{ EtOH}}$ 260 (33,600) with a shoulder at 215 μ (108,000)). In the preparation of the oxime, a second derivative was also isolated. This material showed poorly defined hydroxyl absorption and no carbonyl absorption in the infrared and may be a hydroxamic acid oxime. Treatment of the oxime with polyphosphoric acid gave a neutral compound (2.83, 2.94, 6.19, 6.27, 6.33, and 6.51 μ , $\lambda_{\text{max}}^{95\% \text{ EtOH}}$ 249, 287, and 390 μ) and an acidic compound (2.86, 5.70, and 5.86 μ , $\lambda_{\text{max}}^{95\% \text{ EtOH}}$ 242, 288, and 298 μ). The spectral data for the neutral compound suggests an aromatic compound. The acidic fraction apparently contained the phenyl ester moiety. Similar treatment of the possible hydroxamic acid gave the neutral compound as the only isolatable product. This Beckman rearrangement reaction is significant as it is the only instance in which dimer A is cleaved into two fragments.

Pyrolysis of dimer A at 280^o produced phenol. There was

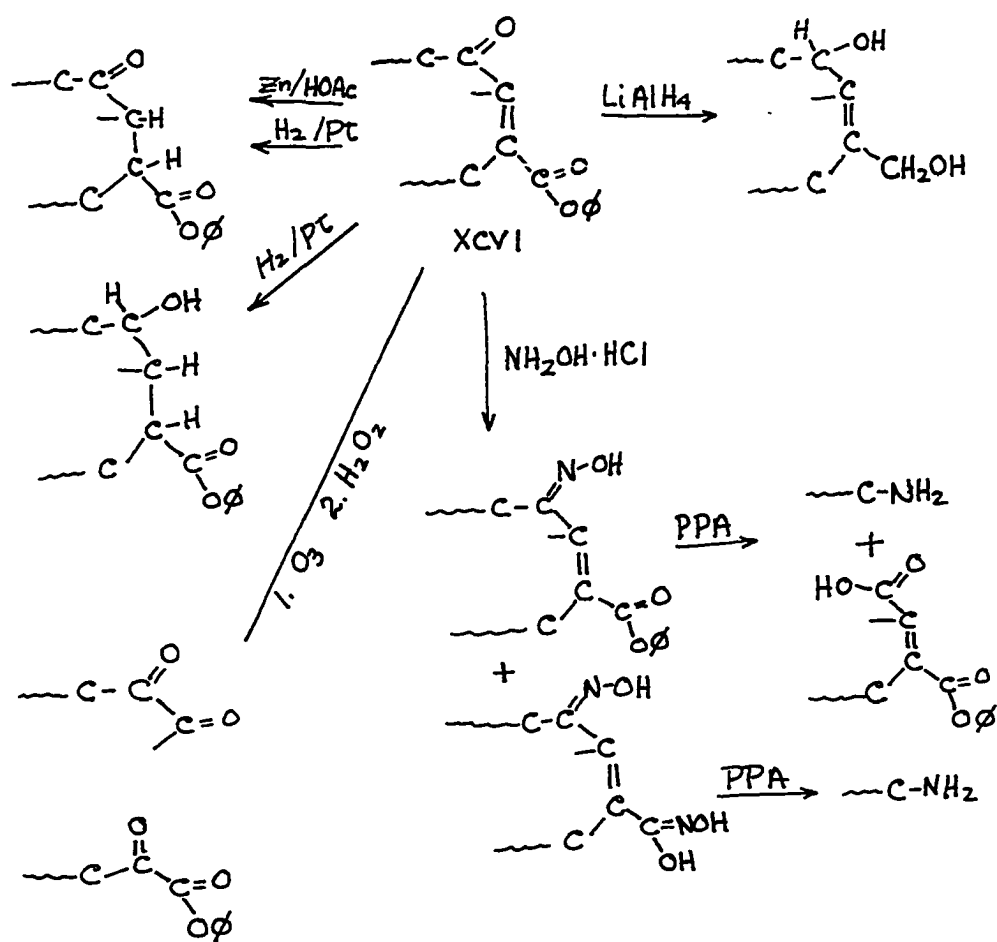
no other characterizable product obtained from the pyrolysis.

The presence of the phenyl ester group in the tetrahydro-derivative was indicated by the recovery of phenol after lithium aluminum hydride reduction. Attempted hydrolysis of the ester in refluxing base and in acid proved unsuccessful. This would indicate that the ester, if present, is sterically hindered. Similar results were obtained by Forbes and Ripley in trying to hydrolyze the ester formed in the irradiation of purpurogallin.⁷¹

Dimer A on treatment with ethylene glycol in acid or with ethyl orthoformate gave no ketal. It was hoped to effect hydrogenation and then regenerate the ketone so as to investigate its environment.

The foregoing chemical evidence might suggest the partial structure shown below (XCVI). The apparent non-contribution of the chromophore to the ultraviolet absorption is not clear, although the chromophore may be distorted so as not to add significantly to the ultraviolet absorption. It is also not apparent why the ketone function (if present as such) is not reduced by sodium borohydride.

The second fraction isolated in 1-3% yield from the irradiation of 4,5-benzo-2-phenoxytropone, designated as dimer B, showed a single carbonyl peak in the infrared at 5.78 μ with double bond absorption at 6.13 μ (Figure 16, page 237). The ultraviolet spectrum, shown in Figure 33, page 271,



showed maxima at 217 (43,400) as 261 μ (25,700). The nuclear magnetic resonance spectrum, shown in Figure 36, page 277, showed a pair of doublets at 3.35 and 4.12 p.p.m. (J 12.9 c.p.s.) corresponding to the two protons of a cis-disubstituted double bond. The single peak at 5.95 p.p.m. corresponds to one proton which is apparently a bridgehead proton or a proton on a carbon having electronegative substituents. This

proton is apparently not coupled to any other proton. The peak area of the aromatic protons at 2.71 p.p.m. corresponds to only 10 protons which would indicate a monomeric material contrary to the molecular weight data. An alternative, but not a very likely explanation, would be that dimer B is a completely symmetrical molecule. Perhaps the most important fact concerning dimer B is, that on heating at its melting point, it is transformed into dimer A.

Dimer B did not absorb hydrogen over Adams' Catalyst, did not absorb ozone, did not react with 2,4-dinitrophenylhydrazine, sodium borohydride, or zinc in acetic acid, and did not undergo hydrolysis in refluxing acid or base. Dimer B undergoes reduction with lithium aluminum hydride giving a crystalline alcohol and one molar equivalent of phenol. The infrared spectrum of the alcohol showed hydroxyl absorption at 2.82 and double bond absorption at 6.13 μ (Figure 17, page 239). The ultraviolet spectrum was dramatically different from dimer B, and showed maxima at 237.5, 248, 257, and 299 μ with shoulders at 233, 277, and 288 μ (Figure 33, page 271). The nuclear magnetic resonance spectrum, shown in Figure 37, page 279, showed a pair of doublets at 3.57 and 3.85 p.p.m. corresponding to two olefinic protons (J 13 c.p.s.). The chemical shift between these doublets is greatly reduced upon reduction of the dimer B to the alcohol indicating a closer similarity of the protons. The signals appearing

at 5.00, 6.08, and 6.93 p.p.m. all correspond to one proton each, but the assignment of the protons is ambiguous. The aromatic protons appear as an unusual, intense single peak at 2.78 p.p.m. and corresponds to 12 protons.

Acetylation of dimer B alcohol was very difficult. Allowing the alcohol to stand overnight in acetic anhydride-pyridine solution produced no acetate. Treatment with ketene also failed to produce the acetate. The acetate was finally formed by refluxing the alcohol in acetyl chloridebenzene solution. The acetate had an intense peak in the infrared at 5.82 μ (Figure 17, page 239), and the ultraviolet showed no change from the alcohol in peak positions (Figure 33, page 271). The nuclear magnetic resonance spectrum, shown in Figure 37, page 279, showed a single peak at 3.49 p.p.m. which appears to be finely split. Apparently the two olefinic protons seen in this region in the alcohol and dimer B have coalesced into a single peak indicating an even greater similarity of the two protons. Signals corresponding to one proton each are observed at 3.88 and 6.28 p.p.m., but the assignment of these protons is ambiguous. The protons of the methyl group of the acetoxy group apparently appear at 8.58 p.p.m. The signal for these protons appears at an abnormally high field position, displaying a diamagnetic shift of 0.7 p.p.m. from the normal position.^{92a} The location of the methyl group is too far out for any $-\overset{\text{O}}{\text{C}}-\text{CH}_3$ and is more

in the region of the $\overset{\text{OH}}{\text{-C-CH}_3}$ group. This factor, along with the abnormal absorption for the acetate group in the infrared, suggested acetylation had not occurred but that acetyl chloride had added to the molecule in a different fashion. Reduction of the acetate back to the alcohol with lithium aluminum hydride excluded any such reaction. Therefore, the abnormal infrared and nuclear magnetic resonance spectra must be a consequence of the stereochemistry or strain in the molecule. The aromatic proton peak now appears as a sharp doublet at 2.76 and 2.84 p.p.m. and corresponds to 12 protons.

It is important to notice that the ratio of the peak areas of the aromatic protons to the olefinic and aliphatic protons in dimer A indicates a dimeric compound, whereas the ratio in the case of dimer B, alcohol and acetate indicates monomeric compounds. It is entirely possible that the molecular weight data is in error for dimer B and its alcohol. This problem could easily be resolved by mass spectrometry as the alcohol readily sublimes at 270° .

The striking difference between the chemistry of the dimer A series of compounds and the dimer B series compounds is noteworthy. The difference in the general reactivities of the dimers toward various reagents is very dramatic. The rate of acetylation of the two alcohols also shows great contrast. In the transformation of dimer B to dimer A on heating, apparently some bond is being ruptured to give rise to

the dicarbonyl compound dimer A. The stability of the transition state must be due to the presence of the carbonyl function present in dimer B, as the alcohol derived from dimer B is stable toward heat. This might indicate the cleavage of a bond alpha-beta to a carbonyl function. With our previous experience in the formation of cyclobutene compounds in the irradiations of troponoid compounds, and in their ease of pyrolytic ring opening, it would suggest the possible presence of a cyclobutene or benzocyclobutene moiety in dimer B.

There are several important degradative experiments which should be carried out in both series. In dimer A only three of the possible four oxygen atoms have been identified. It is doubtful if the remaining oxygen atom belongs to an enol ether due to the stability of the Dimer A in acid. A pertinent experiment would be a limited Birch reduction to give the cyclohexadienyl enol ethers from the phenoxy groups. Acid hydrolysis would result in the liberation of cyclohexenone and an alcohol and an acid function. The products obtained from the Beckman rearrangement of the dimer A oxime would give important information, as this was the only reaction giving cleavage of the molecule. Further oxidative studies should also be carried out to determine the nature of the double bonds.

In the dimer B series the important compound to start degradative experiments on is the alcohol or its acetate.

Oxidative experiments on the alcohol might lead to useful information. Dimer B should also be subjected to a limited Birch reduction to determine the number of phenoxy groups present in the molecule and their location.

The prediction of any structures for any of the compounds at this time is not justified because of the limited amount of information available and the apparent complexity of the problem.

EXPERIMENTAL

Experimental for Diels-Alder Adducts of gamma-Tropolone
Methyl Ether and Tropone

Diels-Alder adduct of gamma-tropolone methyl ether and maleic anhydride A solution of 1.00 g. (0.00735) of gamma-tropolone methyl ether and 0.80 g. (0.00815 mole) of maleic anhydride in 10 ml. of xylene was refluxed for six hours under nitrogen. On cooling crystals formed which were collected by filtration. Removal of the solvent from the filtrate in a stream of dry nitrogen gave a second crop of crystals. Two sublimations at 150° and 0.1 mm. gave a pale yellow, tacky material which gave after recrystallization from benzene-Skelly B 1.10 g. (65% of the theoretical) of pale yellow cubes (VII), melting point 184.5-185.0°. The infrared spectrum in potassium bromide included peaks at 5.40, 5.62, 6.01 and 6.13 μ (weak). In the ultraviolet the adduct showed $\lambda_{\text{max}}^{95\% \text{ EtOH}}$ 231 (6,300) and 337 μ (160).

Anal. Calcd. for $\text{C}_{12}\text{H}_{10}\text{O}_5$: C, 61.54; H, 4.27. Found: C, 61.78; H, 4.51.

Attempted acid hydrolysis of the adduct VII with dilute acid A solution of 0.1 g. of the adduct VII in 40% acetone-methanol was acidified with six drops of 1.0 N hydrochloric acid and heated gently for a few minutes. The solvent was removed, and the residue was sublimed giving a pale yellow sublimate which was identical in the infrared with that of

pure adduct.

Hydride reduction of VII A slurry of 2.0 g. of the adduct VII and 3 g. of lithium aluminum hydride in 200 ml. of ether was stirred for 12 days. The excess hydride was decomposed by careful addition of a saturated ammonium chloride solution. The ether layer was decanted and dried over sodium sulfate. The ether when removed under reduced pressure left no residue. The aqueous layer was filtered and concentrated under reduced pressure with gentle heating. The concentrated aqueous layer was then extracted with butanol giving a yellow viscous residue. The infrared spectrum of the residue showed strong hydroxyl absorption and no absorption in the 5.0-6.0 μ region.

Hydrogenation of the adduct VII A solution of 0.30 g. of the adduct VII in 30 ml. of tetrahydrofuran was hydrogenated over Adams' catalyst absorbing 61 ml. of hydrogen (23° and 745 mm.) corresponding to 1.9 moles of hydrogen per mole of adduct. The catalyst was removed by filtration, and the tetrahydrofuran was removed under reduced pressure leaving a viscous residue. The residue was sublimed at 150° and 0.1 mm. giving a sticky, amorphous material which showed no high intensity absorption in the ultraviolet. The infrared spectrum showed peaks at 5.37, 5.60 and 5.86 μ in chloroform.

Hydrolysis of the adduct VII to the diacid IX Dissolution of 0.95 g. of the adduct VII in 20 ml. of hot dis-

tilled water gave white crystals on cooling. The material was recrystallized from water and dried under vacuum at 30° giving crystals which lost water above 146°, sintered at 173° and immediately resolidified and finally melted at 185°. The infrared spectrum in potassium bromide showed peaks at 5.85, 6.03 and 6.13 μ (weak) and the ultraviolet spectrum showed $\lambda_{\text{max}}^{95\% \text{ EtOH}}$ 231 (6,000) and 340 μ (140).

Anal. Calcd. for $\text{C}_{12}\text{H}_{12}\text{O}_6 \cdot 1/2\text{H}_2\text{O}$: C, 55.17; H, 5.02. Found: C, 55.17; H, 5.16.

Drying at 170° for 30 seconds gave a 5.75% loss in weight; the product thus obtained was analyzed immediately.¹⁰¹

Anal. Calcd. for $\text{C}_{12}\text{H}_{12}\text{O}_6$: C, 57.15; H, 4.80. Found: C, 57.19; H, 4.62.

Sublimation of a portion of the diacid IX at 150° and 0.1 mm. gave a tacky, pale yellow material. Recrystallization of this material from benzene-Skelly B gave a product identical in melting point, infrared and ultraviolet spectrum to the adduct.

Preparation of the bromolactone (X or XI) via the diacid IX
 A solution of 0.40 g. (0.0017 mole) of adduct VII in 20 ml. of hot distilled water was cooled to 40° and 0.09 ml. of bromine (0.0015 mole) was added dropwise with stirring.

¹⁰¹The drying procedure was carried out by Midwest Micro-lab, Inc., 7838 Forest Lane, Indianapolis, Indiana.

The solution, when allowed to cool, precipitated 0.40 g. of the bromolactone (71%). Two recrystallizations from ethyl acetate gave colorless crystals, melting point 100.5-103.0°. The infrared spectrum in potassium bromide showed peaks at 5.61, 5.84, 6.01 and a shoulder at 6.13 μ . The ultraviolet spectrum showed $\lambda_{\text{max}}^{95\% \text{ EtOH}}$ 228 (6,400) and 328 μ (44).

Anal. Calcd. for $\text{C}_{12}\text{H}_{11}\text{O}_6\text{Br}$: C, 43.52; H, 3.35. Found: C, 43.62; H, 3.44.¹⁰²

Reaction of gamma-tropolone with diethylazodicarboxylate A solution 2.0 g. (0.0147 mole) of I and 2.70 g. (0.0154 mole) of diethylazodicarboxylate in 10 ml. of xylene was heated at reflux for six hours under nitrogen. The solvent was removed in a stream of dry nitrogen with gentle heating leaving a viscous red residue which could not be induced to crystallize. The residue was chromatographed on alumina giving the following fractions: Fraction I eluted with Skelly B-benzene (1:1) was a viscous yellow oil which showed a 5.81 μ peak (broad) in the infrared and an ultraviolet spectrum showing $\lambda_{\text{max}}^{95\% \text{ EtOH}}$ 330 μ (590) and end absorption at 210 μ (17,000); Fraction II eluted with Skelly B-benzene (1:9) which was identical in properties to fraction I; fraction III eluted with benzene which had an identical spectrum with fractions I and II but crystallized slowly on standing;

¹⁰²Additional drying was required at 100° to remove solvent from the compound prior to analysis (see reference 101).

and Fraction IV, eluted with chloroform, which crystallized readily and showed a single sharp peak in the carbonyl region of the infrared at 5.75 μ and only very low intensity absorption in the ultraviolet. Fractions I, II and III resisted all attempts at further purification. Fraction IV was recrystallized from Skelly B-benzene giving 0.56 g. of colorless needles, melting point 129-130° with sublimation, reported for diethyl dicarbamate 133-134°³⁷. The infrared spectrum showed peaks at 2.91 and 5.75 μ .

Anal. Calcd. for $C_3H_6NO_2$: C, 40.90; H, 6.85; N, 15.91.
Found: C, 41.00; H, 6.74; N, 15.95.

Attempts to hydrolyze fractions I and II with acid or base led only to decomposition products.

Diels-Alder adduct of tropone with maleic anhydride²⁸

A solution of 5.1 g. (0.047 mole) of tropone and 4.7 g. (0.048 mole) of maleic anhydride in 15 ml. of xylene was heated at reflux under nitrogen for two hours. The solution was cooled, and the precipitated crystals were collected by filtration. The mother liquor was heated overnight giving a second crop of crystals (total yield 4.90 g., 50% of the theoretical). The product was recrystallized from chloroform-Skelly B giving colorless cubes, melting point 178.8-179.4°, reported 180°.²⁸ The infrared spectrum in potassium bromide showed peaks at 5.42, 5.64, 6.02 and 6.17 μ . The ultraviolet spectrum showed $\lambda_{\max}^{95\% \text{ EtOH}}$ 227 (7,000) and 337 μ (120).

Anal. Calcd. for $C_{11}H_8O_4$: C, 64.71; H, 3.95. Found: C, 64.49; H, 4.10.

Hydrolysis of adduct XII to the diacid XIII Dissolu-
tion of 2.0 g. of adduct XII in 20 ml. of boiling water gave, on cooling, tan flakes which lost water above 148° and melted sharply at $178.2-179.2^\circ$. The infrared spectrum in potassium bromide showed peaks at 5.76, 5.87 (weak), 6.09 and 6.17 μ with intense, broad hydroxyl absorption. The ultraviolet spectrum showed $\lambda_{\max}^{95\% \text{ EtOH}}$ 228 (7,600) and 337 μ (140).

Anal. Calcd. for $C_{11}H_{10}O_5$: C, 59.46; H, 4.53. Found: C, 59.54; H, 4.68.

Preparation of the bromolactone (XIV or XV) from the diacid XIII A solution of 0.3 g. of the diacid XIII in 10 ml. of distilled water at 40° was treated with 0.07 ml. of bromine. The solution was allowed to cool, and the crystals that formed were collected. Two recrystallizations from ethyl acetate gave colorless crystals, melting point $201.2-203.7^\circ$. The infrared spectrum in potassium bromide showed peaks at 3.02, 5.63, 5.76, 5.98 and 6.15 μ . The ultraviolet spectrum showed $\lambda_{\max}^{95\% \text{ EtOH}}$ 228 (9,800) with a shoulder at 275 μ (1,300).

Anal. Calcd. for $C_{11}H_9O_5Br$: C, 43.88; H, 3.01. Found: C, 43.80; H, 2.99.

Experimental for Reactions of gamma-Tropolone Methyl Ether
and Tropone with Grignard and Hydride Reagents

Reaction of gamma-tropolone methyl ether with methyl magnesium iodide A solution of 2.0 g. (0.0147 mole) of I in 20 ml. of ether was added slowly with vigorous stirring to an ethereal solution of 0.022 mole (50% molar excess) of methyl magnesium iodide prepared from 3.12 g. of methyl iodide and 2 g. of magnesium in 25 ml. of ether. Upon addition of the ethereal solution of I to the Grignard solution, a dense yellow precipitate formed immediately. The reaction mixture was stirred at room temperature for one hour and then decomposed by the careful addition of distilled water. The ether layer was decanted, and the aqueous phase was extracted with two portions of ether. The ether fractions were combined and dried over sodium sulfate. The ether was removed under reduced pressure leaving 1.45 g. of a dark yellow residue which showed peaks in the infrared spectrum at 2.92, 5.85, 6.10, 6.15 and 7.27 μ . The aqueous layer was then extracted twice with methylene chloride. The extract was dried over sodium sulfate, and the solvent was removed under reduced pressure leaving 0.1 g. of a yellow liquid which was identical in the infrared with I.

The ether extract residue was chromatographed on a 20 x 1 cm. alumina column giving the following fractions:

<u>Fraction</u>	<u>Solvent system</u>	<u>Weight of material recovered</u>
I	benzene-Skelly B	0.90 g.
II	benzene	70 mg.
III	benzene-ether	70 mg.
IV	ether	60 mg.
V	ether-chloroform	90 mg.
VI	chloroform	90 mg.
VII	chloroform-methanol	25 mg.

Fraction I (45% of the theoretical) showed carbonyl absorption in the infrared at 5.85 u. Fractions II through VI (19% of the theoretical) showed hydroxyl but no carbonyl absorption in the infrared. Fraction VII showed absorption at 5.74 and 5.85 u in the infrared but was not further identified.

2-Methyl-4-methoxy-3,5-cycloheptadienone (XVII) Fraction I from the chromatographic separation above was distilled through a micro head giving a pale yellow liquid, boiling point 58-60° at 0.2 mm., n_D^{22} 1.5188. The infrared spectrum showed peaks at 5.85, 6.09, 6.15 and 7.27 u, see Figure 8, page 221. The ultraviolet spectrum showed end absorption at 210 mu (7,300) and $\lambda_{\max}^{95\% \text{ EtOH}}$ 331 mu (3,600), see Figure 19, page 243.

Anal. Calcd. for $C_9H_{12}O_2$: C, 71.02; H, 7.95. Found: C, 71.28; H, 8.28.

Analysis of the ketone by gas phase chromatography on

1 meter columns of varying polarity showed the presence of predominantly one ketonic product.

<u>Column stationary phase</u> ^{102a}	<u>% area major peak</u>	<u>% area minor peaks</u>
Theed	90	10
Ucon Polar LB550X grease	95	5
Apieazon Non-polar grease	90	10

Acid hydrolysis of 50 mg. of the ketone in one ml. of methanol containing five drops of 3 N hydrochloric acid gave a viscous, dark yellow oil after removal of the solvent under reduced pressure. The hydrolysis product showed peaks in the infrared at 5.85, 5.99 and 6.16 μ (weak), see Figure 8, page 221. The ultraviolet spectrum showed $\lambda_{\text{max}}^{95\% \text{ EtOH}}$ 233 (shoulder) and 338 μ , see Figure 19, page 243.

Base catalyzed transformation of 2-methyl-4-methoxy-3,5-cycloheptadienone (XVII) to 2-methyl-4-methoxy-4,6-cycloheptadienone (XIX) To a solution of 20 mg. of the ketone XVII in 0.5 ml. of ethanol was added 1 ml. 1.0 N sodium hydroxide producing a red solution. The solution was shaken for two minutes and was extracted with two one ml. portions of ether. The ether extract was dried over sodium sulfate, and the solvent was removed by evaporation. The ultraviolet spectrum of the residue showed a decrease in end absorption and an increase in the 328 μ maximum; the ratio A_{328}/A_{210} at the

^{102a}For specifications of the columns used see Appendix.

beginning was 0.67 and was 1.05 at the end.¹⁰³ The infrared spectrum showed weak absorption at 5.85 μ and strong absorption at 6.05 and 6.16 μ .

Maleic anhydride adduct of 2-methyl-4-methoxy-3,5-cycloheptadienone (XXV) A solution of 0.35 g. of the ketone and 0.25 g. of maleic anhydride in 2 ml. of benzene was refluxed for six days. The benzene was removed by a stream of air leaving a dark viscous residue. Sublimation of this residue at 130° at 0.1 mm. gave a pale yellow, glassy material which could not be induced to crystallize. The infrared spectrum in chloroform showed peaks at 5.36, 5.60 and 5.85 μ .

A 100 mg. portion was dissolved in boiling water and one drop of 10 N sulfuric acid was added. The solution was filtered and cooled giving a mass of tan crystals (XXVI). The material was recrystallized twice from water giving colorless needles, melting point 153.0-153.5°.

Anal. Calcd. for $C_{13}H_{16}O_6$: C, 58.20; H, 6.01. Found: C, 58.25; H, 6.11.

Treatment of 55 mg. of the adduct in 0.5 ml. of ethanol with an excess of benzaldehyde and one drop 30% sodium hydroxide produced a yellow solution but no precipitate. The solution was acidified, diluted with three ml. of water and extracted with chloroform. The infrared of this chloro-

¹⁰³The ratio of the absorbancy at 331 μ to the absorbancy at 210 μ (A_{331}/A_{210}) for 5-methoxy-2,4-cycloheptadienone was 1.03.

form solution showed no change in the carbonyl region.

Preparation of the bromolactone (XXVII or XXVIII) from the adduct XXV Dissolution of 40 mg. of the adduct in boiling water followed by the addition of bromine until a slight excess of bromine remained, gave an oily bromolactone which was extracted with chloroform. The chloroform solution, after drying over sodium sulfate, showed peaks in the infrared at 5.58, 5.79 and 5.82 μ .

The chloroform was evaporated and the bromolactone was treated with benzaldehyde and sodium methoxide in one ml. of methanol but gave no precipitate. The solution was diluted with water and extracted with chloroform. The solvent was removed in a stream of dry air. The infrared spectrum of the residue showed maxima at 5.76 and 5.85 μ indicating that no benzylidene derivative had formed.

2-Methyl-4-methoxy-3,5-cycloheptadienol (XXI) An ethereal solution of 750 mg. of 2-methyl-4-methoxy-3,5-cycloheptadienone (XVII) was added to a suspension of lithium aluminum hydride (100% excess) in ether, and the mixture was stirred at room temperature for one hour. The reaction mixture was hydrolyzed with moist sodium sulfate, and the solid present was removed by filtration. The ethereal solution was dried over sodium sulfate, and the ether was removed under reduced pressure leaving a viscous, pale yellow liquid, 2-methyl-4-methoxy-3,5-cycloheptadienol (XXI). The infrared spectrum

of the product showed peaks at 2.98, 6.06, 6.13 and 6.21 μ , see Figure 9, page 223. The ultraviolet spectrum of the crude alcohol showed $\lambda_{\max}^{95\% \text{ EtOH}}$ 256 μ (5,600), see Figure 20, page 245.

Conversion of XXI to 3-methylcycloheptanone Acid

hydrolysis of 500 mg. of 2-methyl-4-methoxy-3,5-cycloheptadienol (XXI) in 0.5 ml. of methanol, 0.2 ml. of water and 0.01 ml. of concentrated hydrochloric acid at room temperature for ten minutes gave, after removal of the solvent under reduced pressure, a mixture of ketones which showed peaks in the infrared at 2.9 and 6.03 μ . The ultraviolet spectrum of the ketone mixture showed $\lambda_{\max}^{95\% \text{ EtOH}}$ 228 and 293 μ , see Figure 20, page 245. Subsequent base treatment of a portion of the ketone mixture produced no further change in either the infrared or the ultraviolet spectrum.

The ketone mixture was dissolved in 20 ml. of methanol and hydrogenated over Adams' Catalyst. The catalyst was removed by filtration, and the methanol was removed under reduced pressure leaving a colorless, sweet smelling liquid which showed in the infrared an intense maximum at 5.88 μ in carbontetrachloride.

The resulting ketonic product was analyzed by gas phase chromatography on a one meter Theed column^{102a} showing peaks at 9.2 and 11.0 minutes (6:1 ratio). Comparison with authen-

tic samples of 3- and 4-methylcycloheptanone¹⁰⁴ showed the 9.2 minute peak to be 3-methylcycloheptanone and the 11.0 minute peak to be 4-methylcycloheptanone. Treatment of the ketonic product with ethanolic 2,4-dinitrophenylhydrazine reagent gave a poorly defined derivative. The ethanolic solution was diluted with water and extracted with chloroform. The chloroform extract was dried over sodium sulfate, and the chloroform was removed under reduced pressure. The residue was dissolved in benzene and chromatographed on 10 x 1 cm. Bentonite-Celite (3:1 by weight) column. Elution with benzene gave a major fraction, melting point 124-126°, which when recrystallized twice from ethanol gave fine yellow plates, melting point 128°.

Manganese dioxide oxidation of 2-methyl-4-methoxy-3,5-cycloheptadienol (XXI) A solution of 20 ul. of 2-methyl-4-methoxy-3,5-cycloheptadienol (XXI) in 10 ml. of chloroform was

¹⁰⁴D. W. Adamson and J. Kenner, J. Chem. Soc., 181 (1939). The methylcycloheptanones were obtained in only very low yields by diazomethane ring expansion of the corresponding methylcyclohexanones. The 3-methyl- and the 4-methylcycloheptanones (from the ring expansion of 3-methylcyclohexanone) could not be satisfactorily separated by preparative scale gas phase chromatography and so the isomers were identified by comparison with 4-methylcycloheptanone (obtained by ring expansion of 4-methylcyclohexanone); 4-methylcycloheptanone semicarbazone, melting point 157.5-158.5°, reported 158-160°. A 2,4-dinitrophenyl hydrazone was prepared in the usual manner and was recrystallized from ethanol giving fine orange plates, melting point 142.5-144.0°. Anal. Calcd. for C₁₄H₁₈N₄O₄: C, 54.93; H, 5.92; N, 18.04. Found: C, 54.87; H, 5.86; N, 18.04.

stirred at room temperature with 0.3 g. of active manganese dioxide. Aliquots were periodically removed and diluted in ethanol for ultraviolet analysis. At time zero the solution showed a maximum in the ultraviolet at 256 μ . After ten hours the spectrum showed maxima at 256 and 329 μ with an A_{257}/A_{329} of 0.75. After 34 hours only a 329 μ maximum and end absorption were observed.

Irradiation of 2-methyl-4-methoxy-3,5-cycloheptadienol (XXI) and conversion to 2-methyl-3-hydroxy-7-ketobicyclo- $\overline{[3.2.0]}$ heptane (XLIII) A solution of 25 ul. of 2-methyl-4-methoxy-3,5-cycloheptadienol (XXI) in 60 ml. of nitrogen-flushed ether was irradiated with a General Electric UA-3 lamp in a quartz vessel at reflux temperature (reflux was maintained by heat from the lamp). The intensity of the 256 μ maximum in the ultraviolet rapidly decreased to 20% in 20 minutes and to 1% in 36 minutes. The ether was removed under reduced pressure leaving a sharp smelling, liquid residue which showed absorption at 5.83 and 6.16 μ in the infrared.

The chloroform was evaporated from the infrared sample and one ml. of 0.1 N sulfuric acid was added giving a homogeneous solution. The mixture was shaken for five minutes and then extracted with chloroform. The chloroform extract was dried over sodium sulfate. The infrared of this chloroform solution showed peaks at 3.0, 5.66, 5.83 and 6.03 μ .

Bromine oxidation of 2-methyl-4-methoxy-3,5-cycloheptadienone (XVII) A solution of 0.31 g. of bromine (0.0017 mole) in 10 ml. of chloroform was added slowly to a solution of 0.26 g. of XVII (0.0017 mole) in 20 ml. of chloroform over 0.5 g. of potassium carbonate. The mixture was stirred at room temperature for three hours and then filtered. The chloroform was removed under reduced pressure leaving a dark yellow residue. The infrared spectrum of this residue showed peaks at 5.86 (weak), 6.04 and 6.21 μ . The ultraviolet spectrum showed maxima at 230 and 334 μ in ethanol. The residue was chromatographed on a 20 x 1 cm. alumina column giving fraction I with benzene-chloroform (5:1 through 1:2) and fraction II with benzene chloroform (1:4 through 1:9).

Fraction I, 16 mg., was recrystallized from Skelly B giving pale yellow needles, melting point 120.5-122° with prior sublimation. The infrared spectrum showed peaks at 6.18, 6.27, 6.64 and 7.30 μ , see Figure 10, page 225. The ultraviolet showed $\lambda_{\max}^{95\% \text{ EtOH}}$ 232 (14,300), 253 (shoulder) (8,700) and 343 μ (8,300), see Figure 22, page 249.

Hydrolysis of fraction I in 0.1 N sodium hydroxide was complete in 45 minutes at 75°, giving in the ultraviolet $\lambda_{\max}^{0.1N \text{ NaOH}}$ 237-238 (14,400) and 371 μ (12,000), see Figure 22, page 249. Neutralization of the basic solution with dilute sulfuric acid shifted the ultraviolet absorption to $\lambda_{\max}^{\text{dil. H}_2\text{SO}_4}$ 241 (14,500) and 349 μ (8,200), see Figure 22,

page 249.

Fraction II (50 mg.) was a pale yellow liquid which was molecularly distilled at 110° and 0.07 mm. The infrared spectrum showed maxima at 6.15, 6.21, 6.38, 6.56, 7.20 and 7.30 μ , see Figure 10, page 225. The ultraviolet spectrum showed $\lambda_{\text{max}}^{95\% \text{ EtOH}}$ 228 (24,000) and 328 μ (12,000), see Figure 21, page 247. Hydrolysis in 0.1N sodium hydroxide at 75° was complete in 150 minutes giving an ultraviolet spectrum which showed $\lambda_{\text{max}}^{0.1N \text{ NaOH}}$ 231 (21,000) and 357 μ (15,000), see Figure 21, page 247. Neutralization of the basic solution with dilute sulfuric gave an ultraviolet spectrum showing $\lambda_{\text{max}}^{\text{dil. H}_2\text{SO}_4}$ 234 (26,000) and 311 μ (13,000), see Figure 21, page 247.

Attempted conversion of 2-methyl-4-methoxy-3,5-cycloheptadienone (XVII) to a benzoic acid derivative A solution of 0.25 g. (0.00167 mole) of 2-methyl-4-methoxy-3,5-cycloheptadienone (XVII) in 20 ml. of carbontetrachloride was treated with 0.44 g. (0.00275 mole) of bromine over 1 g. of sodium carbonate. The reaction mixture was stirred at room temperature for five hours and 0.5 ml. of pyridine was added. The mixture was filtered, and the filtrate, after washing with 15 ml. of 1 N sulfuric acid and 10 ml. of water, was dried over sodium sulfate. The solvent was removed under reduced pressure leaving a dark semi-crystalline material which showed peaks in the infrared at 5.83, 6.16, 6.23, 6.28

and 6.60 μ . The ultraviolet spectrum showed $\lambda_{\text{max}}^{95\% \text{ EtOH}}$ 229 and 339 μ .

The residue was dissolved in 7 ml. of ethanol and 0.5 g. of potassium hydroxide was added. The mixture was refluxed seven hours. The solution turned dark red. Acidification with hydrochloric acid and dilution with water gave a brown precipitate which was extracted with two 10 ml. portions of chloroform. The extract was dried over sodium sulfate, and the chloroform was removed under reduced pressure leaving a dark red, non-crystalline residue. The residue was dissolved in ether and methylated with a solution of diazomethane in ether prepared by basic decomposition of N-methylnitrosourea. The ether was removed and the crystalline residue was chromatographed on a 10 x 1 cm. alumina column. The only characterizable product obtained was 16 mg. of pale yellow needles which after recrystallization from Skelly B melted at 136-138 $^{\circ}$. The infrared spectrum of this product showed peaks at 6.18, 6.28, 6.37 and 6.61 μ . The ultraviolet spectrum showed $\lambda_{\text{max}}^{95\% \text{ EtOH}}$ 232 (12,000), 254 (shoulder) (6,800) and 343-348 μ (7,000). A solution of 10 μ g. in 8 ml. of water and two drops of 30% sodium hydroxide was heated at 90 $^{\circ}$. Ultraviolet analysis showed that the hydrolysis was complete after 45 minutes. The final ultraviolet spectrum showed maxima at 237 (16,000), 286 (2,000) and 372 μ (11,000). The solution was acidified with two drops of 10 N sulfuric acid,

and the ultraviolet spectrum shifted to μ 41 (14,500) and 351 μ (7,500). No benzenoid product was isolated.

1-Hydroxy-1-methyl-4-methoxy-2,4,6-cycloheptatriene

(XXXI) Fractions II through VI (page 129) from the chromatography of the gamma-tropolone methyl ether-methyl magnesium iodide reaction mixture showed maxima in the infrared at 2.97, 6.08, 6.10, 6.16, 6.22 and 7.25 μ , see Figure 8, page 221. The ultraviolet spectrum showed $\lambda_{\text{max}}^{95\% \text{ EtOH}}$ 220 (7,300) and 325 μ (4,500), see Figure 23, page 251.

N-phenyl maleimide adduct of 1-hydroxy-1-methyl-4-methoxy-2,4,6-cycloheptatriene (XXXI) A solution of 90 mg. of 1-hydroxy-1-methyl-4-methoxy-2,4,6-cycloheptatriene (XXXI) in one ml. of benzene was refluxed for eight days with 100 mg. of N-phenyl maleimide. The benzene was removed by a stream of air leaving a dark viscous residue. The residue was chromatographed on a 15 x 1 cm. alumina column giving 0.11 g. of an amorphous material on elution with benzene. Recrystallization of this material from benzene gave colorless crystals, m.p. 198-199 $^{\circ}$.

Anal. Calcd. for $\text{C}_{19}\text{H}_{19}\text{NO}_4$: C, 70.16; H, 5.83; N, 4.31.
Found: C, 70.41; H, 5.12; N, 4.36.

Conversion of 1-hydroxy-1-methyl-4-methoxy-2,4,6-cycloheptatriene (XXXI) to 4-methylcycloheptanone A solution of 30 mg. of 1-hydroxy-1-methyl-4-methoxy-2,4,6-cycloheptatriene (XXXI) in 0.5 ml. of methanol and three drops of 6 N hydro-

chloric acid was heated at 50° for one minute. The methanol was removed by a stream of air, and the residue was dissolved in chloroform. The chloroform solution was dried over sodium sulfate, and the chloroform was then removed under reduced pressure. The residue was dissolved in methanol and hydrogenated over Adams' Catalyst. The catalyst was removed by filtration, and the methanol was removed under reduced pressure. Analysis of the residue by gas phase chromatography on a Theed column^{102a} showed peaks at 5.8 (61%) and 7.6 (39%) minutes. A mixture of authentic 4-methylcycloheptanone and sample showed peaks at 5.8 (33%) and 7.6 (67%) minutes.

Reaction of gamma-tropolone methyl ether with methyl lithium A solution of 2.00 g. (0.0147 mole) of I in 20 ml. of ether was slowly added to an ethereal solution of methyl lithium (100% excess) prepared from 5.08 g. of methyl iodide and excess lithium in ether. A heavy yellow precipitate formed on addition of the methyl lithium.

A. Hydrolysis of the above reaction mixture with water gave a yellow ether layer and red aqueous layer. The ether layer was dried over sodium sulfate, and the ether was removed under reduced pressure leaving 0.21 g. of a liquid identified as I by its infrared spectrum. The aqueous layer was extracted with chloroform, and after drying and removal of the solvent 1.07 g. of I was recovered. No product was isolated.

B. In an attempt to detect any metallation reaction,

the reaction mixture (above) was poured over crushed Dry Ice and allowed to warm to room temperature. The solution was carefully neutralized with methanolic hydrochloric acid, and the solvent was removed under reduced pressure leaving a viscous, dark red residue. The material was chromatographed on alumina giving the following three fractions: Fraction I (0.15 g., 7.5%) eluted with a benzene-chloroform mixture showed peaks in the infrared at 6.08, 6.14 and 6.38 μ , see Figure 11, page 227. The ultraviolet spectrum showed end absorption and $\lambda_{\text{max}}^{95\% \text{ EtOH}}$ 328 μ (3,200). Fraction I on dilute acid hydrolysis gave an ultraviolet spectrum showing $\lambda_{\text{max}}^{0.1N \text{ H}_2\text{SO}_4}$ 233 and 309 μ and showed peaks in the infrared at 5.85, 6.00 and 6.16 μ in chloroform. Fraction II, 1.0 g., eluted with a chloroform-methanol mixture was identical to I (infrared spectra comparison). Fraction III, 0.05 g., was a dark red compound eluted with chloroform-methanol-acetic acid mixtures which showed an intense peak in the infrared at 5.85 μ . This compound resisted attempts at purification and was not further investigated.

Reduction of gamma-tropolone methyl ether with lithium aluminum hydride A solution of 2.0 g. (0.0147 mole) of I in 25 ml. of ether was added to a suspension of 0.0294 moles of lithium aluminum hydride in 25 ml. of ether. The solution was stirred at room temperature for 10 minutes, and the excess hydride was cautiously decomposed by the addition of distilled

water. The ether layer was decanted and the aqueous solution was twice extracted with 15 ml. of ether. The ether fractions were combined and were dried over sodium sulfate. The ether was removed under reduced pressure leaving a pale yellow liquid which showed peaks in the infrared at 2.77, 6.05, 6.16 and 6.39 μ . Analysis by gas phase chromatography on a LB 550X column^{102a} at 150° showed peaks with 3.0, 4.0 and 6.0 minute retention times. The residue was chromatographed on a 35 x 1 cm. alumina column giving the following fractions:

<u>Fraction</u>	<u>Eluting solvent system</u>	<u>Weight of material</u>	<u>Functional identity</u>
I	Skelly B-benzene (3:2)	0.64 g.	ketonic
II	Skelly B-benzene (4:1)	0.24 g.	ketonic
III	benzene	0.12 g.	alcoholic
IV	benzene-chloroform(1:1)	0.08 g.	alcoholic
V	benzene-chloroform (19:1)	0.13 g.	alcoholic
VI	chloroform	0.18 g.	alcoholic
VII	chloroform	0.10 g.	alcoholic

5-Methoxy-2,4-cycloheptadienone (XXXII)

Fractions I

and II from the chromatography above were combined and molecularly distilled at 70-80°, 1.5 mm., giving a pale yellow liquid which rapidly darkened even in sealed ampules. The infrared spectrum showed peaks at 6.05, 6.16 and 6.39 μ , see Figure 11, page 227. The ultraviolet spectrum showed $\lambda_{\max}^{95\% \text{ EtOH}}$ 328 μ (8,500) with end absorption at 210 μ

(8,200), see Figure 24, page 253.

A solution of 38.6 mg. of the ketone (XXXII) in 15 ml. of methanol was hydrogenated over Adams' Catalyst absorbing 21.1 ml. of hydrogen at 28° and 745 mm. corresponding to 3.3 mole of hydrogen absorbed per mole of ketone. The catalyst was removed by filtration and the methanol was removed under reduced pressure. The residue was analyzed by gas phase chromatography on a one meter LB 550X column^{102a} showing the presence of methyl cycloheptyl ether, cycloheptanone, 4-methoxycycloheptanone and cycloheptanol in a ratio of 3:1:1:1. The compounds were identified by comparison with compounds isolated from the hydrogenation of I (see page 164).

A solution of 30 mg. of the ketone (XXXII) in 1 ml. of water was hydrolyzed by the addition of four drops of 10 N sulfuric acid. The solution was twice extracted with two one ml. portions of chloroform. The chloroform extract was dried over magnesium sulfate, and the solvent was removed by a stream of air. The infrared spectrum of the residue in chloroform showed peaks at 5.85, 6.00 and 6.16 μ , see Figure 11, page 227. The ultraviolet spectrum showed $\lambda_{\text{max}}^{95\% \text{ EtOH}}$ 233 (5,400) and 297 μ (1,000), see Figure 24, page 253. The residue when hydrogenated in 10 ml. of methanol over Adams' Catalyst absorbed 1.0 mole of hydrogen. The catalyst was removed by filtration and the methanol was removed under reduced pressure. The residue was treated with ethanolic

2,4-dinitrophenylhydrazine reagent and the resulting derivative was twice recrystallized from ethanol-nitrobenzene giving melting point and mixed melting point with authentic bis-2,4-dinitrophenylhydrazone of 1,4-cycloheptandione of 241-245°. ⁴¹

5-Methoxy-2,4-cycloheptadienol (XL) A solution of 100 mg. of 5-methoxy-2,4-cycloheptadienone (XXXII) in 10 ml. of ether was added to 0.2 g. of lithium aluminum hydride in 10 ml. of ether. The reaction mixture was stirred at room temperature for 10 minutes. The excess hydride was decomposed by the careful addition of distilled water. The solids were removed by filtration and the ether filtrate was dried over sodium sulfate. The ether was removed under reduced pressure leaving a colorless viscous liquid which showed peaks in the infrared at 2.78, 6.10 and 6.22 μ , see Figure 9, page 223. The ultraviolet spectrum showed $\lambda_{\max}^{95\% \text{ EtOH}}$ 256 μ (7,800), see Figure 26, page 255. Analysis by gas phase chromatography on a LB 550X column^{102a} at 150° showed a single peak with a retention time of 3.0 minutes.

Acid hydrolysis of 5-methoxy-2,4-cycloheptadienol (XL)

An aliquot of an ultraviolet stock solution of 5-methoxy-2,4-cycloheptadienol (XL) in ethanol was diluted with 0.1N sulfuric acid. The ultraviolet spectrum immediately showed the presence of a single maximum at 296 μ (5,000), see Figure 26, page 257. The reported ultraviolet spectrum of 2,4-

cycloheptadienone shows $\lambda_{\text{max}}^{95\% \text{ EtOH}}$ 292 mu (5,900).⁵²

Manganese dioxide oxidation of 5-methoxy-2,4-cycloheptadienol (XL) A solution of 50 mg. of 5-methoxy-2,4-cycloheptadienol (XL) in 10 ml. of chloroform was stirred at room temperature with 0.50 g. of active manganese dioxide. Aliquots were removed periodically, and the chloroform was evaporated. The residue was dissolved in 95% ethanol and the ultraviolet spectrum recorded. A peak at 330 mu slowly developed giving a ratio of $A_{330\text{mu}}/A_{256\text{mu}}$ of 0.60 after 84 hours.

Irradiation of 5-methoxy-2,4-cycloheptadienol (XL) and attempted hydrolysis of the photoproduct A solution of 70 mg. of 5-methoxy-2,4-cycloheptadienol (XL) in 50 ml. of anhydrous ether in a quartz vessel was irradiated with a mercury arc lamp. Ultraviolet analysis showed rapid disappearance of the starting material. The irradiation was stopped after 50 minutes with 5% of starting material remaining. The ether was removed under reduced pressure. The infrared spectrum of the residue showed peaks at 2.94 and 6.18 u in chloroform, see Figure 12, page 229.

The residue was treated with one ml. of 0.1 N sulfuric acid at 40° for five minutes. The photoproduct remained insoluble in the sulfuric acid. The mixture was extracted with ether and the extract was dried over sodium sulfate. The ether was removed under reduced pressure. The infrared

spectrum of the extracted residue showed only a very weak 5.63 μ peak and was otherwise identical to the spectrum of the photoproduct before treatment with acid, see Figure 12, page 229.

Conversion of 5-methoxy-2,4-cycloheptadienone (XXXII) to tropone A one ml. aliquot of a solution of 10.5 mg. of 5-methoxy-2,4-cycloheptadienone (XXXII) in 25 ml. of 95% ethenol was treated at 80° for five minutes with four drops of 10 N sulfuric acid in 5 ml. of water. The solution was neutralized with 30% sodium hydroxide and two drops excess of 30% sodium hydroxide was added producing a golden-yellow solution. The ultraviolet of this solution showed $\lambda_{\text{max}}^{\text{dil. NaOH}}$ 414 μ , the intensity of which slowly decreased with time at room temperature (4,200 at five minutes and 3,700 after 1.5 hours). The basic solution was heated at 80° for 30 minutes. The yellow color slowly faded with generation of the typical tropone ultraviolet spectrum. The basic solution was made slightly acidic with 10 N sulfuric acid and diluted to 10.0 ml. with distilled water. The ultraviolet spectrum of this solution showed the typical tropone spectrum⁴³ with maxima at 225, 228, 231.5, 239 and 312 μ . The yield of tropone was 51% based on the extinction coefficient of the 228 μ peak.

Treatment of 5-methoxy-2,4-cycloheptadienone (XXXII) with base A solution of 32.4 mg. of 5-methoxy-2,4-cycloheptadienone (XXXII) was dissolved in 20 ml. of distilled

water and five drops of 30% sodium hydroxide were added. The solution was diluted to 25.0 ml. with water. The solution was heated at 90°. One ml. aliquots were removed periodically and diluted to 10.0 ml. with 0.1 N sodium hydroxide and the ultraviolet spectrum recorded. A 414 m μ peak appeared immediately and increased in intensity on further heating (ϵ value of 10,600 after 90 minutes). A 361 m μ peak appeared after 15 minutes and increased in intensity also (this peak appeared as a shoulder on the 414 m μ peak making the calculation of the ϵ value meaningless).

Simultaneously, one ml. aliquots were removed and diluted to 25.0 ml. with 0.1 N sulfuric acid. The ultraviolet spectra of these solutions were recorded showing peaks at 229 and 331 m μ having ϵ values of 12,000 and 5,600, respectively, corresponding to 45% gamma-tropolone and 55% 2-cyclohepten-1,5-dione (XXXIII).

4-Methoxy-3,5-cycloheptadienol (XLI) Fractions V, VI and VII from the chromatographic separation of the lithium aluminum hydride-gamma-tropolone methyl ether reaction mixture (page 141) were combined and analyzed by gas phase chromatography on a LB 550X column^{102a} at 150° showing two peaks with 3.0 and 4.0 minute retention times (35% and 65%, respectively). Molecular distillation at 90° and 0.08 mm. gave a colorless, viscous liquid. The infrared spectrum showed peaks at 2.77, 6.06, 6.14 and 6.22 μ , see Figure 9, page 223. The ultra-

violet spectrum showed $\lambda_{\max}^{95\% \text{ EtOH}}$ 255 m μ (5,520), see Figure 27, page 259.

A solution of 37.0 mg. of 4-methoxy-3,5-cycloheptadienol (XLI) in 12 ml. of methanol hydrogenated over Adams' Catalyst absorbed 1.93 moles of hydrogen per mole of compound. The catalyst was removed by filtration, and the solvent was removed under reduced pressure. The infrared spectrum of the residue showed peaks at 2.78, 2.80 and 9.21 μ . Analysis by gas phase chromatography showed only two very closely overlapping peaks.

Attempted base-catalyzed transformation of 4-methoxy-3,5-cycloheptadienol (XLI) to 5-methoxy-2,4-cycloheptadienol (XL) A 40 mg. portion of 4-methoxy-3,5-cycloheptadienol (XLI) was heated at 50° for five minutes with two ml. of 1 N sodium hydroxide. The solution was extracted with one three ml. portion of ether. The ether extract was dried over sodium sulfate. The ether was evaporated and the residue was analyzed by gas phase chromatography on a LB 550X column^{102a} at 150° showing two peaks with 3.0 and 4.0 minute retention times (35% and 65%, respectively).

Manganese dioxide oxidation of 4-methoxy-3,5-cycloheptadienol (XLI) A solution of 20 mg. of 4-methoxy-3,5-cycloheptadienol (XLI) in 10 ml. of chloroform was stirred at room temperature with 400 mg. of active manganese dioxide. Aliquots were removed periodically and the ultraviolet spectra

were recorded. A 330 mu peak appeared and rapidly increased in intensity with respect to the 255 mu peak. The absorbancy ratio of 330 mu/255 mu was 0.58 after nine hours.

Conversion of 4-methoxy-3,5-cycloheptadienol (XLI) to 3-hydroxy-6-ketobicyclo[3.2.0]heptane (XLVI) A solution of 133 mg. of 4-methoxy-3,5-cycloheptadienol in 50 ml. of ether, from a can freshly opened, when irradiated in a quartz vessel for 68 minutes showed a 95% reduction in the extinction coefficient of the 255 mu peak of the dienol XLI, see Figure 12, page 229. The ether was removed under reduced pressure. The residue was treated with one ml. of 0.1 N sulfuric acid at room temperature for five minutes giving a homogeneous solution. This solution was extracted with ether, and the extract was dried over sodium sulfate. The ether was removed under reduced pressure. The residue was molecularly distilled at 70° and 0.2 mm. giving a colorless, viscous liquid which showed an intense peak in the infrared at 5.63 u, see Figure 12, page 229.

Conversion of 4-methoxy-3,5-cycloheptadienol (XLI) to tropone A solution of 6.9 mg. of 4-methoxy-3,5-cycloheptadienol in 25 ml. of 95% ethanol was prepared as a stock solution. A one ml. aliquot of this solution was acidified with four drops of 10 N sulfuric acid and was heated at 80° for five minutes. The solution was neutralized with 30% sodium hydroxide and two drops excess base was added producing a

lavender colored solution. The visible spectrum of this solution showed $\lambda_{\text{max}}^{\text{dil. NaOH}}$ 557 μ for which the extinction coefficient decreased with time at room temperature (3,900 after one minute and 3,000 after 60 minutes). The basic solution was heated at 80° for 10 minutes. The solution was then acidified with 10 N sulfuric acid and diluted to 10.0 ml. with distilled water. The ultraviolet spectrum of this solution showed the typical tropone absorption⁴³ with $\lambda_{\text{max}}^{\text{dil. H}_2\text{SO}_4}$ 225, 227.5, 231, 239 (shoulder) and 312 μ . The yield of tropone based on the extinction coefficient of the 227.5 μ peak was 35%.

Conversion of cycloheptadienones to tropone A one ml. aliquot of a solution of 17.7 mg. of a freshly distilled cycloheptadienone mixture in 25 ml. of ethanol was diluted to 8 ml. with distilled water containing two drops of 30% sodium hydroxide. The solution was heated at 90° for 15 minutes. The solution became pale yellow but the visible spectrum showed no maximum. The solution was cooled and diluted to 10.0 ml. with distilled water. A one ml. aliquot was diluted to 10.0 ml. with 0.1 N sulfuric acid, and the ultraviolet spectrum was recorded showing the characteristic tropone spectrum with extinction coefficients of 13,300 at 231 μ , and 5.130 at 311 μ , corresponding to yields of 61 and 62% respectively.

Reaction of tropone with methyl magnesium iodide A

solution of 1.5 g. (0.014 mole) of tropone¹⁰⁵ in 35 ml. of ether was added to an ethereal solution of methyl magnesium iodide prepared from 3.2 g. (0.022 mole) of methyl iodide and excess magnesium in ether. A fluffy yellow precipitate immediately formed which on further addition of the Grignard reagent dissolved giving a pale yellow solution. This solution was allowed to stir at room temperature for 10 minutes. The reaction mixture was then carefully hydrolyzed by the addition of water. The ether layer was decanted and dried over sodium sulfate. The solvent was removed under reduced pressure leaving 0.75 g. of a dark red residue. Analysis by gas phase chromatography showed only one peak with a retention time of 4.7 minutes on a Perkin-Elmer R Column^{102a} at 150°. The residue showed a peak at 5.88 μ in the infrared in chloroform, and the ultraviolet spectrum showed $\lambda_{\max}^{95\% \text{ EtOH}}$ 217 and 298 μ .

The aqueous phase from the hydrolysis was diluted with water to dissolve the inorganic salts and then extracted twice with methylene chloride. The extract was dried over sodium

^{105A} A convenient isolation procedure was devised for the isolation of tropone from the degradation solutions of 6, β -hydroxy-tropinone methiodide which alleviates the necessity of forming the picrate with subsequent decomposition of the picrate (see reference 23). The hot degradation solution was saturated with sodium chloride and was allowed to cool. The solution was extracted with three portions of methylene chloride. The extract was dried over sodium sulfate and the solvent was removed under reduced pressure. The residue was vacuum distilled at 75° at 3.0 mm. giving a 43% yield of tropone.

sulfate, and the solvent was removed under reduced pressure leaving 0.35 g. of a dark orange mobile liquid. Gas phase chromatographic analysis showed the presence of peaks at 4.8 (15%), 12.8 (60%) and 14.2 (25%) minutes on the R column as described above. The three fractions were separated and collected in a preparative scale run. The fraction at 4.8 minutes (XLVII) showed peaks at 6.03 and 5.85 μ in the infrared, see Figure 13, page 231, and a maximum at 298 μ in the ultraviolet with end absorption. The fraction at 12.8 minutes was identified as tropone by its characteristic ultraviolet and infrared spectra. The fraction at 14.2 minutes showed a typical tropone infrared spectrum except for the addition of a 7.30 μ peak, see Figure 10, page 225. The ultraviolet spectrum showed 228, 231 and 310 μ maxima in ethanol, see Figure 28, page 261.

Reduction of the ketone mixture containing XLVII with lithium aluminum hydride A 20 mg. portion of this ketonic fraction was reduced with lithium aluminum hydride in ether giving an alcohol whose infrared spectrum showed peaks at 2.76, 2.80 and 6.21 μ and whose ultraviolet spectrum showed $\lambda_{\text{max}}^{95\% \text{ EtOH}}$ 241 and 247 μ , see Figure 29, page 263.

Conversion of 2-methyl-3,5-cycloheptadienone (XLVII) to 2-methylcycloheptanone A solution of 35.5 mg. of the crude extract residue from above in 15 ml. of methanol was hydrogenated over Adams' Catalyst. The catalyst was removed by

filtration, and the methanol was removed under reduced pressure. Analysis by gas phase chromatography on a Theed column^{102a} at 75° showed a single peak at 5.0 minutes which increased in size on addition of authentic 2-methyl-cycloheptanone.

Preparation of 2-methylcycloheptanone¹⁰⁶ A solution of 2.0 g. of sodium in 150 ml. of liquid ammonia was concentrated to about 15 ml. and 80 ml. of anhydrous ether was added. This solution was allowed to stand at room temperature for one hour. A solution of 10 g. of cycloheptanone in 50 ml. of ether was added producing a dark colored solution. After allowing to stand three minutes, a solution of 14.2 g. of methyl iodide in 15 ml. of ether was rapidly added producing a white precipitate. The reaction mixture was refluxed for 1.5 hours and then 100 ml. of water was added. The ether layer was decanted, washed with water and dried over magnesium sulfate. The ether was removed under reduced pressure and the residue was fractionally distilled giving 8.0 g. of starting material and 2.0 g. of a liquid, boiling point 75-78° at 16 mm. This fraction was separated into three fractions by preparative scale gas phase chromatography on a Perkin-Elmer R column^{102a} at 100°. Fraction I, at 9.6 minutes, was prob-

¹⁰⁶M. Godchot and Mlle. Cauquil, Compt. Rend., 188, 794 (1929); M. Mousseron, R. Jacquier, and H. Christol, Bull. Soc. Chim. France, 346 (1957).

ably 2,2-dimethylcycloheptanone but was not characterized. Fraction II, at 13.1 minutes, gave a 2,4-dinitrophenylhydrazone which after recrystallization from ethanol melted at 120-121°, reported for 2-methylcycloheptanone 2,4-dinitrophenylhydrazone 121-122°. ¹⁰⁶ Fraction III gave a 2,4-dinitrophenylhydrazone which, when recrystallized from ethanol, gave a melting point and mixed melting point with authentic cycloheptanone 2,4-dinitrophenylhydrazone of 144.5-145.5°.

Lithium aluminum hydride reduction of tropone A solution of 1.50 g. (0.0142 mole) of tropone in 10 ml. of ether was added slowly to a stirred suspension of 0.5 g. of lithium aluminum hydride in 20 ml. of ether. The reaction mixture was stirred at room temperature for 10 minutes and was carefully decomposed by the addition of moist sodium sulfate. The solid present was removed by filtration, and the filtrate was dried over sodium sulfate. The ether was removed under reduced pressure giving 1.00 g. (67% crude yield) of a dark yellow liquid which showed peaks in the infrared at 2.78, 2.82, 5.84 and 6.27 μ peaks. Analysis by gas phase chromatography on a Theed column^{102a} showed two peaks with retention times of 8.3 (60%) and 4.2 (40%) minutes. The 8.3 minute peak showed peaks in the infrared at 2.76, 2.80 and 6.20 μ , see Figure 13, page 231, and an ultraviolet maximum at 241 $m\mu$. The 4.2 minute peak showed peaks in the infrared at 5.83 and 6.27 μ , see Figure 13, page 231, and the ultraviolet showed

end absorption with a shoulder at 220 μ in ethanol.

Hydrogenation of 40.5 mg. of the crude reaction mixture in 15 ml. of methanol over Adams' Catalyst resulted in the adsorption of 2.00 moles of hydrogen per mole of compound. The catalyst was removed, and the methanol was evaporated under reduced pressure. The residue was treated with 2,4-dinitrophenylhydrazine reagent giving a derivative which gave melting point and mixed melting point with authentic cycloheptanone 2,4-dinitrophenylhydrazone of 143.5-144.5°.

A solution of 0.40 g. of crude product was refluxed for six days with 0.64 g. of N-phenyl maleimide in 3 ml. of benzene. The reaction mixture was chromatographed directly on a 30 x 1 cm. alumina column giving the following fractions:

<u>Fraction</u>	<u>Solvent system (20 ml.)</u>	<u>Weight of material</u>	<u>Melting point</u>
1	benzene	--	--
2	benzene	--	--
3	benzene-chloroform (6:1)	0.05 g.	193-195°
4	benzene-chloroform (3:1)	0.03 g.	200.0-200.5° ¹⁰⁷
5	benzene-chloroform (1:1)	0.02 g.	145-175°
6	benzene-chloroform (1:3)	0.02 g.	120-160°
7	chloroform	0.05 g.	170-175°
8	chloroform	0.11 g.	185.5-187.0° ¹⁰⁷
9	chloroform-acetone (6:1)	0.06 g.	183-184°
10	chloroform-acetone (3:1)	--	--

¹⁰⁷The melting points of the N-phenyl maleimide adducts of 2,4-cycloheptadienone and 3,5-cycloheptadienol are respectively 199-202° and 185-188° (see footnote 39).

Reduction of tropone in refluxing ether for 24 hours increased the yield of alcohol formed as shown by the decreased intensity of the carbonyl absorption in the infrared and the increased hydroxyl absorption.

Preparation of N-phenyl maleimide¹⁰⁸ In a one l. three-necked flask equipped with a stirrer, condenser and addition funnel, 24.5 g. (0.25 mole) of maleic anhydride was dissolved in 300 ml. of benzene. With vigorous stirring 23.2 g. (0.25 mole) of aniline was added over a five minute period. The resulting mixture was stirred under reflux for 0.5 hour. Thionyl chloride, 32.7 g. (0.275 mole), was added dropwise and the resulting mixture was refluxed until the precipitate dissolved giving a yellow-brown solution (11-12 hours). The benzene was removed under aspirator pressure. The residue was dissolved in 100 ml. of benzene and placed on a 16 x 1.5 inch alumina column and was eluted with benzene giving 41 g. (95%) of a yellow-brown crystalline mass. The material was sublimed at 110° and 0.1 mm. giving 30.6 g. (71%) of yellow needles with melting point 86-88°, reported 88-89°. ¹⁰⁸

Irradiation of 3,5-cycloheptadienol A solution of 0.20 g. of the crude ketone-alcohol mixture in 5 ml. of ether was slowly added to 0.1 g. of lithium aluminum hydride in 10 ml. of ether. The reaction mixture was decomposed with water

¹⁰⁸A. E. Kretov and N. E. Kul'chitskaya, Zhur. Obschei Khim., 26, 208 (1956); J. Gen. Chem. U.S.S.R., 26, 221 (1956) (English translation).

after being stirred for 10 minutes. The solid was removed by filtration, and the filtrate was dried over sodium sulfate. The ether was removed under reduced pressure. The residue was dissolved in 40 ml. of methanol and irradiated in a quartz vessel with a mercury arc lamp. The irradiation was followed in the ultraviolet. After two hours the extinction coefficient of the λ_{41} maximum indicated that the reaction was 95% complete. The methanol was removed under reduced pressure. The residue thus obtained showed peaks in the infrared at 2.75, 3.30, 3.42, and 3.51 μ . A solution of 15.5 mg. in 10 ml. of methanol was hydrogenated over Adams' Catalyst absorbing 1.05 moles of hydrogen per mole of compound.

Experimental for Acid- and Base-Catalyzed Hydrolysis
of gamma-Tropolone Methyl Ether

Acid-catalyzed hydrolysis of gamma-tropolone methyl ether

A stock solution of I was prepared containing 310.1 mg. of I in 250 ml. of distilled water with subsequent dilution 1:1 with distilled water. Aliquots of this stock solution were diluted 1:1 with standardized acid solutions giving a reactant concentration of I of 4.56×10^{-3} molar, except where noted in the following tabulations. These solutions were maintained at $80 \pm 0.5^\circ$ and were analyzed by periodically removing 0.1 ml. aliquots and diluting these to 10.0 ml. with 0.1N sodium hydroxide. The ultraviolet spectra of these solutions were

recorded and the amount of gamma-tropolone formed was determined from a graph of the following equation:

$$([\bar{\gamma}\text{-TME}] - [\bar{\gamma}\text{-T}^-])2160 + [\bar{\gamma}\text{-T}^-](21,400) = \text{Absorbancy}^{109}$$

and where

$$[\bar{\gamma}\text{-TME}] + [\bar{\gamma}\text{-T}^-] = 4.56 \times 10^{-5}$$

<u>Time (min.)</u>	<u>Absorbancy</u>	<u>$[\bar{\gamma}\text{-T}^-] \times 10^5$</u>	<u>% completion</u>
<u>0.0100 N sulfuric acid</u>			
10	0.153	0.296	6.5
20	0.160	0.328	7.2
30	0.169	0.378	8.3
40	0.183	0.442	9.7
50	0.191	0.483	10.6
60	0.209	0.583	12.8
<u>0.0500 N sulfuric acid</u>			
10	0.164	0.355	7.8
20	0.213	0.606	13.3
30	0.277	0.966	20.6
40	0.330	1.21	26.6
50	0.380	1.47	32.2
60	0.439	1.78	39.1
<u>0.100 N sulfuric acid</u>			
10	0.241	0.752	16.5
20	0.321	1.16	25.5
30	0.408	1.62	35.5
40	0.481	1.99	43.7
50	0.534	2.27	49.8
60	0.582	2.52	55.2

¹⁰⁹The absorbancy was determined at 360 mu where the extinction coefficient in 0.1 N sodium hydroxide of gamma-tropolone methyl ether is 2,160 and of gamma-tropolone anion is 21,400. Gamma-tropolone methyl ether is abbreviated as $\bar{\gamma}\text{-TME}$ and gamma-tropolone anion as $\bar{\gamma}\text{-T}^-$.

<u>Time (min.)</u>	<u>Absorbancy</u>	<u>$[\alpha - T] \times 10^5$</u>	<u>% completion</u>
<u>0.500 N sulfuric acid</u>			
10	0.330	1.16	26.5
20	0.502	2.10	46.1
30	0.627	2.75	60.2
40	0.712	3.18	69.8
50	0.766	3.46	76.0
60	0.800	3.64	79.9
<u>0.750 N sulfuric acid</u>			
10	0.311	1.11	24.4
20	0.491	2.05	44.9
30	0.639	2.81	61.6
40	0.733	3.31	72.4
50	0.794	3.61	79.2
60	0.834	3.82	83.8
<u>1.00 N sulfuric acid</u>			
10	0.281	0.957	21.0
20	0.481	1.99	43.6
30	0.651	2.87	63.0
40	0.744	3.35	73.5
50	0.802	3.65	80.1
60	0.836	3.83	84.0
<u>1.50 N sulfuric acid</u>			
10	0.263	0.866	19.0
20	0.465	1.91	41.9
30	0.629	2.76	60.6
40	0.732	3.28	72.1
50	0.788	3.58	78.6
60	0.819	3.74	82.0
<u>2.00 N sulfuric acid</u>			
10	0.281	0.961	21.1
20	0.466	1.92	42.1
30	0.620	2.71	59.5
40	0.728	3.27	71.8
50	0.775	3.51	77.1
60	0.818	3.73	81.9

Time (min.) Absorbancy $\overline{[\chi - T^-]}$ x 10⁵ % completion

5.0 N sulfuric acid

$$\overline{[\chi - TME]} + \overline{[\chi - T^-]} = 4.31 \times 10^{-3}$$

$$\text{Reactant concentration: } 4.31 \times 10^{-4}$$

10	0.227	0.647	15.0
20	0.346	1.25	28.9
30	0.458	1.81	42.0
40	0.537	2.20	51.1
50	0.616	2.59	60.0
60	0.659	2.81	65.1

10.0 N sulfuric acid

$$\overline{[\chi - TME]} + \overline{[\chi - T^-]} = 4.31 \times 10^{-5}$$

$$\text{Reactant concentration: } 4.31 \times 10^{-4}$$

10	0.126	0.10	2.4
15	0.158	0.33	7.6
34	0.227	0.71	16.5
45	0.262	0.89	20.7
85	0.306	1.12	26.0
120	0.334	1.25	29.1

0.0100 perchloric acid

10	0.151	0.282	6.2
20	0.164	0.351	7.7
30	0.185	0.457	10.0
40	0.200	0.538	11.8
50	0.215	0.607	13.3
60	0.230	0.693	15.2

0.0500 N perchloric acid

10	0.188	0.483	10.6
20	0.262	0.853	18.7
30	0.324	1.18	25.9
40	0.392	1.53	33.6
50	0.455	1.86	40.8
60	0.507	2.12	46.6

0.100 N perchloric acid

10	0.212	0.597	13.1
20	0.338	1.25	27.5
30	0.451	1.84	40.4
40	0.537	2.28	50.0
50	0.618	2.71	59.3
60	0.662	2.93	64.2

<u>Time (min.)</u>	<u>Absorbancy</u>	<u>$[\bar{\epsilon} - T] \times 10^5$</u>	<u>% completion</u>
<u>0.500 N perchloric acid</u>			
10	0.261	0.852	18.7
20	0.438	1.77	38.8
30	0.587	2.53	55.7
40	0.692	3.08	67.7
50	0.757	3.42	75.0
60	0.781	3.54	77.7
<u>0.750 N perchloric acid</u>			
10	0.267	0.88	19.3
20	0.421	1.68	36.9
30	0.544	2.32	50.8
40	0.647	2.85	62.5
50	0.723	3.23	71.0
60	0.773	3.50	76.8
<u>1.00 N perchloric acid</u>			
10	0.232	0.703	15.4
20	0.380	1.47	32.3
30	0.509	2.14	47.0
40	0.611	2.67	58.5
50	0.688	3.06	67.2
60	0.751	3.39	74.4
<u>1.50 N perchloric acid</u>			
10	0.210	0.583	12.8
20	0.317	1.14	25.1
30	0.435	1.75	38.5
40	0.528	2.24	49.1
50	0.608	2.65	58.2
60	0.665	2.95	64.6
<u>2.00 N perchloric acid</u>			
10	0.238	0.738	16.2
20	0.327	1.19	26.2
30	0.422	1.68	36.8
40	0.508	2.14	46.9
50	0.578	2.50	54.8
60	0.629	2.75	60.4

<u>Time (min.)</u>	<u>Absorbancy</u>	<u>$[\bar{\gamma}-T^-] \times 10^5$</u>	<u>% completion</u>
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5.9 N perchloric acid

$$\frac{[\bar{\gamma}-TME]}{[\bar{\gamma}-T^-]} + [\bar{\gamma}-T^-] = 4.50 \times 10^{-3}$$
 Reactant concentration: 4.50×10^{-3}

1 hr.	0.097	--	--
6 hr.	0.196	0.51	11.4
20 hr.	0.432	1.74	38.7

Base-catalyzed hydrolysis of γ -tropolone methyl ether

A stock solution of 58.6 mg. of I in 50.0 ml. of distilled water was prepared and was diluted 1:1 with distilled water. A 2.5 ml. aliquot of this solution was diluted to 25.0 ml. with 0.0995 N sodium hydroxide giving a reactant concentration of 4.31×10^{-4} molar. This solution was heated at $80 \pm 0.5^\circ$. One ml. aliquots were removed periodically and diluted to 10.0 ml. with 0.1 N sodium hydroxide, and the ultraviolet spectra were recorded. The γ -tropolone anion concentration was determined by use of the equations on page 158.

<u>Time (min.)</u>	<u>Absorbancy</u>	<u>$[\bar{\gamma}-T^-] \times 10^5$</u>	<u>% completion</u>
7	0.150	0.290	6.7
13	0.333	1.25	29.0
21	0.453	1.86	43.0
30	0.595	2.61	60.7
40	0.688	3.11	72.3
50	0.748	3.41	79.2
60	0.786	3.61	83.8
90	0.821	3.72	86.3

Reaction of γ -tropolone methyl ether with sodium methoxide in methanol

A solution of 50.0 mg. of I in 50.0 ml. of 0.100 N sodium methoxide in anhydrous methanol was

prepared. Sealed tubes containing 6 ml. of this solution were heated at $80 \pm 0.5^\circ$. Periodically tubes were removed and 1 ml. aliquots were diluted 1:10, 1:2 and 1:10 in aqueous 0.1 N sodium hydroxide, and the ultraviolet spectra were recorded. There was no change observable over the course of 45 minutes.

Ultraviolet spectra of gamma-tropolone methyl ether in sulfuric acid solutions A series of solutions of I were prepared by diluting 0.1 ml. aliquots of a stock solution of I to 10.0 ml. in standard acids. The ultraviolet spectra were recorded immediately, see Figure 5, page 63.

<u>Normality of H₂SO₄</u>	<u>λ(μ)</u>	<u>ϵ</u>	<u>λ(μ)</u>	<u>ϵ</u>
0.000	223.6	20,000	331.7	13,600
0.00975	225.3	19,900	332.2	13,700
0.0488	225.7	20,000	332.7	13,800
0.0728	226.7	20,300	332.9	14,100
0.0979	226.7	20,300	333.2	14,100
0.242	228.0	21,600	333.5	15,100
0.493	229.5	22,700	333.7	15,900
0.724	230.3	23,600	333.8	16,500
0.982	231.1	24,600	333.9	17,000
1.96	231.5	25,200	333.9	17,200
2.95	231.6	25,200	334.0	17,200
4.92	232.3	25,500	333.7	17,300
9.82	233.1	25,600	333.4	17,300

Ultraviolet spectra of gamma-tropolone methyl ether in perchloric acid solutions of constant ionic strength Solutions of lithium perchlorate in perchloric acid were prepared with a total perchlorate concentration of 2.00 molar. Aliquots (0.100 ml.) of a stock solution of I were diluted to 10.0 ml. with the acid solutions, and the ultraviolet spectra were recorded immediately.

<u>Normality of acid</u>	<u>λ (μ)</u>	<u>ϵ</u>	<u>λ (μ)</u>	<u>ϵ</u>
0.000 ^{110a}	225.4	19,100	332.9	12,600
0.00832	226.5	18,700	333.7	12,900
0.0440	229.3	20,300	333.4	14,000
0.0916	230.6	21,200	333.5	14,400
0.228	232.2	23,400	333.7	15,600
0.459	232.2	24,100	333.6	16,100
0.689	232.3	24,600	333.6	16,400
0.919	232.8	24,400	333.6	16,400
1.44	232.3	24,600	333.7	16,500
1.96	232.9	24,800	333.4	16,600
4.42 ^{110b}	233.0	25,600	333.0	16,800

Experimental of Hydrogenation of gamma-Tropolone Methyl Ether

Hydrogenation of gamma-tropolone methyl ether in hydrochloric acid solutions A. The hydrogenation of I in acid solutions was carried out on 50 mg. quantities of I in 10 ml. of the hydrochloric solutions over 7.5 mg. of prereduced platinum oxide. All hydrogenations were carried out at a constant stirring rate at room temperature and at atmospheric pressure. The volume of hydrogen adsorbed versus time was measured and recorded.

The solutions were extracted with three 2 ml. portions of methylene chloride. The extracts were combined and dried over sodium sulfate. The solvent was carefully removed by distillation through an 8 inch Vigreux column leaving in each case a colorless, liquid residue. The infrared spectra of the residue showed peaks at 2.9, 5.86 and 9.16 μ . Analysis

^{110a}Run in 2.000 molar lithium perchlorate.

^bNo lithium perchlorate was present in this solution.

Acid concentration time (min.)	0.0N	0.01N	0.1N	0.5N	1.0N	5.0N	10N
	(Moles of H ₂ adsorbed/mole of TIME)						
20	0.31	0.75	0.94	1.01	0.70	0.70	0.09
40	0.78	1.41	1.80	2.02	1.45	1.39	--
60	1.22	2.06	2.43	2.59	2.13	2.07	1.08
80	1.77	2.58	3.20	3.22	2.80	2.64	1.60
100	2.29	2.97	3.65	--	--	--	2.04
120	2.79	3.38	3.90	3.68	3.76	3.90	2.32
150	3.38	3.80	--	3.86	4.00	4.41	3.04
Total moles H ₂ adsorbed	3.58	4.05	3.94	4.17	4.00	4.41	4.06

by gas phase chromatography on a one meter LB 550X column^{102a} at 175° showed the presence of six peaks with 2.0, 3.2, 4.4, 9.7, 14.0 and 19.8 minute retention times. The peaks were separated by preparative scale gas phase chromatography.

Peak A, at 2.0 minutes, showed no hydroxyl or carbonyl absorption in the infrared and showed only an intense 9.12 μ peak. Comparison by gas phase chromatography on a LB 550X column^{102a} at 150° and infrared spectra showed the compound to be identical with authentic methyl cycloheptyl ether (LVII).

Peak B, at 3.2 minutes, showed only a 5.90 μ peak in the infrared in chloroform solution. Comparison by gas phase chromatography on a LB 550X column^{102a} at 150°, showed B to be cycloheptanone (LVIII). Fraction B gave a 2,4-dinitrophenylhydrazone which was identical in melting point and mixed melting point with authentic cycloheptanone 2,4-dinitrophenylhydrazone, melting point 144-146°.

Peak C, at 4.4 minutes, showed only hydroxyl absorption in the infrared and was shown to be cycloheptanol (LIX) by comparison of infrared spectra and gas phase chromatographic retention time on a LB 550X column^{102a} at 150°.

Peak D, at 9.7 minutes, showed no hydroxyl in the infrared but displayed strong peaks at 5.90 and 9.16 μ in chloroform solution. The structure tentatively assigned to C is 4-methoxycycloheptanone (LX).

Peak E, at 14.0 minutes, showed peaks in the infrared at 2.9 and 9.16 μ and was identical in retention time with a compound obtained from fraction D by lithium aluminum hydride reduction of 10 mg. in ether followed by hydrolysis with water. The structure of E is tentatively assigned as 4-methoxycycloheptanol (LXI).

Peak F, at 19.8 minutes, did not appear in large enough quantities to identify (see part B).

The following tabulation shows the per cent yield of compounds A through F as determined from gas phase chromatography chromatograms.

<u>Normality of HCl</u>	<u>A</u>	<u>B</u>	<u>C</u>	<u>B+C</u>	<u>D</u>	<u>E</u>	<u>D+E</u>	<u>F</u>
	(per cent yield of products)							
0.0	2	8	1	9	76	12	88	1
0.01	6	12	29	41	44	6	50	3
0.1	7	22	33	55	22	11	33	5
0.5	4	4	61	65	3	23	26	5
1.0	6	1	63	64	0.3	25	25	5
5.0	6	4	59	63	1	25	26	5
10	5	18	43	62	4	25	29	5

B. A solution of 0.20 g. of I was hydrogenated as described above in 0.1N hydrochloric acid. The residue from the extraction was dissolved in ethanol, and acidic 2,4-dinitrophenylhydrazine reagent was added. The precipitate was filtered and washed with ethanol. The derivative was leached with boiling ethanol and filtered while hot giving 40 mg. of a derivative which, when recrystallized from an ethanol-nitrobenzene mixture, gave a melting point and mixed melting point with authentic bis-2,4-dinitrophenylhydrazone of 1,4-cycloheptanedione of 242.5-244.0°. ⁴¹ This corresponds to a yield of 5% of 1,4-cycloheptanedione (LXII).

A hydrogenation of 0.8 g. of gamma-tropolone methyl ether in neutral aqueous solution, followed by extraction and preparation of the bis-2,4-dinitrophenylhydrazone as described above, gave 40 mg. (1.5%) of the bis-2,4-dinitrophenylhydrazone of 1,4-cycloheptanedione, melting point and mixed melting point 242-245°.

C. A solution of 0.50 g. of I was hydrogenated as above in 0.1N hydrochloric acid, but using a catalyst obtained from Englehard, ⁶⁹ absorbing 2.2 moles of hydrogen. The hydrogenation solution was extracted with chloroform and the extract was dried over sodium sulfate. The residue, after removal of the solvent, gave a derivative with 2,4-dinitrophenylhydrazine which was totally insoluble in boiling ethanol. Recrystallization from an ethanol-nitrobenzene mixture gave

melting point and mixed melting point with authentic bis-2,4-dinitrophenylhydrazone of 1,4-cycloheptanedione of 242.5-243.5°. ⁴¹

Hydrogenation of gamma-tropolone in neutral aqueous solution A solution of 1.0 g. of gamma-tropolone methyl ether (I) in 10 ml. of 1 N sodium hydroxide was heated at reflux for 45 minutes. The solution was cooled, neutralized with hydrochloric acid and diluted to 25.0 ml. A 5.0 ml. aliquot of this solution was diluted to 25 ml. with distilled water, and was hydrogenated over Adams' Catalyst absorbing 2.5 moles of hydrogen per mole of compound. The hydrogenation solution was extracted with chloroform, and the chloroform extract was dried over sodium sulfate. The chloroform was evaporated, and the residue was dissolved in ethanol and treated with acidic 2,4-dinitrophenylhydrazine reagent. The derivative (70% yield) was recrystallized from nitrobenzene-ethanol giving melting point and mixed melting point with authentic bis-2,4-dinitrophenylhydrazone of 1,4-cycloheptanedione, 242.5-245°. ⁴¹

Preparation of methyl cycloheptyl ether (LVII) ¹¹¹ A solution of 5.0 g. of cycloheptanone in 25 ml. of ether was

¹¹¹Methyl cycloheptyl ether is reported to have been prepared by hydrogenation of a product obtained by reacting anisole with diazomethane (H. Meerwein, H. Disselnkötter, F. Rappen, H. v. Rintelen and H. van de Vloed, Ann., **604**, 151 (1957)). The boiling point was given as 163-165° with n_D^{18} 1.4813. The only analysis given was for methoxyl which was 10% in error.

added dropwise to 1 g. of lithium aluminum hydride in 50 ml. of ether. The excess hydride was decomposed with water. The solids were removed by filtration, and the filtrate was dried over sodium sulfate. The solution was concentrated, and 1.0 g. of sodium was added and the mixture was heated at 120° for four hours giving a solid salt. The solid was cooled to room temperature, and 12 g. of methyl iodide was carefully added and the mixture was refluxed overnight. The reaction mixture was filtered and fractionally distilled through an 8 inch Vigreux column giving 1.45 g. (25%) of a colorless liquid, boiling point 147-148^olll at atmospheric pressure and with n_D^{25} 1.4463.

Anal. Calcd. for $C_8H_{16}O_2$: C, 74.91; H, 12.58. Found: C, 75.14; H, 12.39.

Experimental of Photochemistry of gamma-Tropolone Methyl Ether

Irradiation of gamma-tropolone methyl ether A. A solution of 5.00 g. of I in 2.5 l. of distilled water was flushed with nitrogen and sealed in a pyrex flask under reduced pressure. The flask was placed on the laboratory roof in direct sunlight for 14 days (eight days actual sunshine). The solution became turbid, and a red powder precipitated. Centrifugation of the solution gave 1.45 g. of a dark red amorphous powder, melting point 50-200° with decomposition. The red powder showed peaks in the infrared at 5.72, 5.84 and

5.98 u. The ultraviolet spectrum showed $\lambda_{\text{max}}^{95\% \text{ EtOH}}$ 325 mu of low intensity and end absorption. The powder was partially soluble in dilute alkali and was insoluble in dilute acid. Hydrogenation of 174 mg. (0.00128 mole based on monomer) of the red powder in 30 ml. of tetrahydrofuran over Adams' Catalyst resulted in the adsorption of 6.77×10^{-4} mole of hydrogen in 1.5 hours. The resulting amorphous red powder showed carbonyl absorption in the infrared at 5.75 and 5.89 u.

Chromatography of the original red powder on a 30 x 1 cm. alumina column gave the following fractions:

<u>Fraction</u>	<u>Eluent solvent system</u>	<u>Material found</u>
1	Skelly B	nothing
2	Skelly B-benzene	viscous red liquid
3	chloroform-ether	viscous dark red liquid
4	chloroform	red semisolid
5	chloroform	dark red solid, m.p. 48-52°
6	chloroform	dark red solid, m.p. 52-55°
7	methylene chloride	dark red solid, m.p. 77-82°
8	acetone	nothing
9	acetone-methanol	nothing
10	methanol	major fraction of a dark red solid with melting point of decomposition above 250°

The infrared and ultraviolet spectra of all fractions were identical except the carbonyl region in the infrared became more diffuse in the later fractions.

The original solution, after centrifugation, was extracted with three portions of methylene chloride. The extracts were combined and dried over sodium sulfate. The solvent was removed under reduced pressure leaving a red, liquid residue. Fractional distillation through a short head gave 1.19 g. of a colorless liquid, 5-methoxybicyclo[3.2.0]hepta-3,6-diene-2-one (photo-gamma-tropolone methyl ether, LXV), boiling point 34° at 0.1 mm., n_D^{25} 1.4952, and 1.22 g. of a pale yellow liquid, boiling point 97° at 0.07 mm., which was identified as I by its characteristic infrared and ultraviolet spectra.

B. A solution of 5.0 g. of I in one l. of distilled water in a pyrex vessel with internal cooling (temperature maintained at $15-20^{\circ}$) was irradiated with a General Electric UA-3 mercury arc lamp for 24 hours at a distance of 15 cm. The solution became turbid, and a red solid precipitated which was identical to that found in A above. The solution was extracted with three portions of methylene chloride. The extracts were combined and dried over sodium sulfate. The solvent was removed under reduced pressure, and the residue was fractionally distilled giving 1.2 g. of photo-gamma-tropolone methyl ether and 3.0 g. of I. The yield of the photoproduct

based on unrecovered starting material was in the range 50-60% in all runs. The infrared spectrum showed peaks at 5.86, 6.31 and 6.42 μ , see Figure 14, page 233. The ultraviolet spectrum showed $\lambda_{\text{max}}^{95\% \text{ EtOH}}$ 243 (1,600) and 328 μ (380) with strong end absorption for freshly distilled material. Characteristic extinction coefficients were difficult to obtain. The value for the 243 μ maximum diminishes on standing alone or in ethanol solution, and disappears completely when heated in ethanol. Figure 30, page 265, shows the ultraviolet spectrum of freshly distilled material.

Anal. Calcd. for $\text{C}_8\text{H}_8\text{O}_2$: C, 70.57; H, 5.92. Found: C, 70.34; H, 6.05.

The 2,4-dinitrophenylhydrazone was prepared in the usual manner and recrystallized from ethanol giving orange-red needles, melting point 171-172 $^{\circ}$. The ultraviolet spectrum showed $\lambda_{\text{max}}^{\text{CHCl}_3}$ 262 (11,600) and 375 μ (25,400).

Anal. Calcd. for $\text{C}_{14}\text{H}_{12}\text{N}_4\text{O}_5$: C, 53.17; H, 3.83. Found: C, 53.29; H, 4.09.

Hydrogenation of photo-gamma-tropolone methyl ether over Adam's Catalyst in methanol resulted in rapid absorption of one mole of hydrogen and a much slower absorption of the second mole of hydrogen.

Irradiation of photo-gamma-tropolone methyl ether (LXV)

A solution of 121 mg. of photo-gamma-tropolone methyl ether (LXV) in 50 ml. of distilled water was flushed with nitrogen

and irradiated in a pyrex vessel with internal cooling coils as in Method B above. After 10 hours the solution, which had become turbid, was extracted with methylene chloride. The extract was dried over sodium sulfate, and the solvent was removed under reduced pressure. The infrared spectrum of the residue was identical in the carbonyl region to that of the amorphous red powder described above.

Pyrolysis of photo- γ -tropolone methyl ether (LXV)

Photo- γ -tropolone methyl ether (LXV, 50 mg.) was dropped into a neutral pyrex helices-packed, vertical column six inches in length preheated to 360°. ¹¹² A stream of nitrogen was passed through the column to sweep the product gases through with an estimated contact time of about 10 seconds. After the pyrolysis the column was cooled to room temperature and washed with chloroform. This chloroform wash was combined with the chloroform solution of the collected pyrolysis product. The infrared and ultraviolet spectra of this chloroform solution were identical in every respect to that of authentic γ -tropolone methyl ether. There was no visible charring or decomposition during the pyrolysis.

Attempted hydrolysis of photo- γ -tropolone methyl ether (LXV) in dilute acid Treatment of a small amount of

¹¹²This is the same column used by Professor C. H. DePuy for acetate pyrolysis (D. H. Froemsdorf, C. H. Collins, G. S. Hammond and C. H. DePuy, J. Am. Chem. Soc., 81, 643 (1959)).

photo-gamma-tropolone methyl ether (LXV) with 0.1 N sulfuric acid showed no change in the ultraviolet spectrum after one hour at 22°. Extraction of the acid solution with methylene chloride gave a residue, after removal of the solvent, which was identical in infrared absorption to the starting material.

Acid-catalyzed ring opening of photo-gamma-tropolone methyl ether (LXV) A solution of 19.6 mg. of photo-gamma-tropolone methyl ether (LXV) in 24 ml. of water was diluted 1:2 in water and then 1:10 in 0.1 N sulfuric acid. This solution was heated at 80±1°. Aliquots (1 ml.) were periodically removed and diluted to 10.0 ml. with 0.1 N sulfuric acid and 0.1 N sodium hydroxide, and the ultraviolet spectra were recorded.

Time (hours)	Absorbancy (333 mu maximum in 0.1 N H ₂ SO ₄)	% reaction ^{113a}	Absorbancy (360 mu maximum in 0.1 N NaOH)	% reaction ^{113b}
1	0.021	5.6	0.033	5.3
2	0.059	16	0.073	12
3	0.090	24	0.105	17
4	0.110	30	0.138	23
5	0.132	36	0.164	28
7 1/4	0.168	45	0.216	35
18 1/4	0.210	73	0.340	55

^{113a}These values are based on the value of the extinction coefficient for gamma-tropolone in 0.1 N sulfuric acid as being 12,900, the same as in neutral aqueous solution.

^{113b}No account has been made in the calculations of these values for the additional gamma-tropolone methyl ether formed by the action of base on photo-gamma-tropolone methyl ether during the final dilution in base.

Base-catalyzed ring opening of photo- γ -tropolone methyl ether (LXV) A solution of 19.0 mg. of photo- γ -tropolone-methyl ether (LXV) in 50 ml. of distilled water was prepared. This solution was diluted 1:100 with standardized sodium hydroxide giving a reactant concentration of 2.79×10^{-5} molar. The ultraviolet spectrum was recorded immediately showing the generation of maxima at 222 and 324 mu. The following tabulations show the rate of generation of γ -tropolone methyl ether:

<u>Time (min.)</u>	<u>Absorbancy (324 mu)</u>	<u>% reaction</u>
<u>Final concentration of base: 0.00945 N</u>		
6	0.012	3.3
15	0.020	5.4
24	0.029	8.0
36	0.046	12.5
48	0.062	16.9
65	0.090	24.8
83	0.116	32.0
110	0.151	41.6
185	0.232	64.2
<u>Final concentration of base: 0.0445 N</u>		
6	0.031	8.5
15	0.076	21.0
24	0.119	32.8
36	0.174	48.0
48	0.218	60.3
65	0.265	73.2
83	0.300	82.8
110	0.337	92.8
<u>Final concentration of base: 0.0887 N</u>		
6	0.044	12.2
15	0.117	32.3
24	0.178	49.1
33	0.228	63.3
48	0.287	79.2
65	0.329	90.6
83	0.352	97.1
110	0.373	103

Base-catalyzed ring opening of photo- γ -tropolone methyl ether (LXV) in the presence of trivalent iron A solution of 50 mg. of photo- γ -tropolone methyl ether (LXV) in 5 ml. of 0.1 N sodium hydroxide was heated for one hour at 80°. The reaction mixture was allowed to cool and neutralized with 1.5 N hydrochloric acid. A solution of 50 mg. of ferric chloride was added, and the solution was made neutral by the addition of 0.1 N base. The solution was then extracted with chloroform, but no red color was extracted by the chloroform indicating no α -tropolone had been formed during the ring opening reaction.

Reaction of photo- γ -tropolone methyl ether (LXV) with ammonia in methanol A solution of 29.7 mg. of photo- γ -tropolone methyl ether (LXV) in 3 ml. of absolute methanol was cooled in an ice bath. Anhydrous ammonia was slowly bubbled through the solution which rapidly turned yellow. The ultraviolet spectrum of the solution showed peaks at 253, 270 and 325 m μ . The solvent was removed under reduced pressure, and the residue was dissolved in methylene chloride. The methylene chloride solution was dried over sodium sulfate. The infrared spectrum of this solution showed peaks at 2.75, 5.76 and 5.99 μ .¹¹⁴ The ultraviolet spectrum showed that less than 1% γ -tropolone methyl ether was present.

¹¹⁴Treatment of γ -tropolone methyl ether with anhydrous ammonia in refluxing benzene for 10 hours gave recovery of starting material.

Reaction of photo- γ -tropolone methyl ether (LXV) with sodium acetate in water A solution of 23.5 mg. of photo- γ -tropolone methyl ether (LXV) in 10 ml. of 0.1 N sodium acetate in water was heated at 90°. Aliquots were periodically removed and analyzed for the formation of γ -tropolone methyl ether. The ultraviolet spectra showed the following increase in the 333 μ maximum: after 20 minutes an ϵ value of 605, after 50 minutes an ϵ value of 1,090, and after 75 minutes an ϵ value of 1,700. The solution was cooled and extracted twice with methylene chloride. The infrared spectrum of this solution, after drying over sodium sulfate, showed a peak at 5.87 and weak peaks corresponding to γ -tropolone methyl ether.

Reaction of photo- γ -tropolone methyl ether (LXV) with sodium acetate in absolute methanol A solution of 23.8 mg. of photo- γ -tropolone methyl ether (LXV) in 5.0 ml. of 0.1 N sodium acetate in absolute methanol was refluxed, and aliquots were periodically removed and analyzed by their ultraviolet spectra. A 327 μ maximum formed with ϵ value of 710 after 20 minutes, 1,800 after 45 minutes, and 3,660 after 75 minutes. The solvent was then removed under reduced pressure leaving a residue which showed peaks in the infrared at 5.75 (medium), 5.87 (strong) and weak peaks characteristic of γ -tropolone methyl ether.

Reaction of photo- γ -tropolone methyl ether (LXV) with potassium cyanide in aqueous solution. A solution of 0.40 g. of photo- γ -tropolone methyl ether (LXV) and 0.35 g. of potassium cyanide in 15 ml. of distilled water was allowed to stand at room temperature for 1.5 hours. Analysis by ultraviolet spectra showed the generation of a 36% yield of γ -tropolone methyl ether. The solution was extracted with methylene chloride, and the extract was dried over sodium sulfate. The solvent was removed leaving a pale yellow liquid (LXXV) which showed peaks in the infrared at 4.55 and 5.72 μ , see Figure 15, page 235. The ultraviolet spectrum showed only a low intensity maximum at 300 μ with low intensity end absorption.

The basic solution was then carefully acidified with dilute sulfuric acid. The solution was then extracted with methylene chloride. The extract was dried over sodium sulfate and the solvent was evaporated. The residue showed peaks in the infrared at 5.73 (shoulder) and 5.86 μ .

The ketone (LXXV) gave a 2,4-dinitrophenylhydrazone from diglyme which was recrystallized from an nitrobenzene-ethanol mixture three times giving a melting point of 206.5-208.0°. The infrared spectrum of the derivative showed peaks at 2.92, 3.01 and 4.46 μ along with the usual aromatic peaks. The ultraviolet spectrum showed $\lambda_{\text{max}}^{\text{CHCl}_3}$ 251 (15,200) and 353 μ (23,900).

Reaction of photo- γ -tropolone methyl ether (LXV) with iodide ion in aqueous solution A solution of 15.7 mg. of photo- γ -tropolone methyl ether (LXV) in 10 ml. of 0.1 N potassium iodide was heated at 74°. Aliquots were periodically removed, and the ultraviolet spectra were recorded giving the following results:

<u>Time (hours)</u>	<u>ϵ (325 mu peak)</u>	<u>% reaction</u>
1	350	2.7
8	840	6.5
21	1580	12
49	2500	19
96	2860	22
140	3000	23

The methylene chloride extract showed only a 5.87 u peak and the characteristic γ -tropolone methyl ether peaks.

Ring opening of photo- γ -tropolone methyl ether (LXV) in refluxing ethanol A solution of 21.2 mg. of photo- γ -tropolone methyl ether (LXV) in 10.0 ml. of 95% ethanol was heated at reflux. Aliquots (0.10 ml.) were periodically removed and diluted to 10.0 ml. with 95% ethanol, and the ultraviolet spectra were recorded.

<u>Time (hours)</u>	<u>ϵ (325 mu peak)</u>	<u>% reaction</u>
1	370	1
3.5	620	2
19	1100	6
25	1670	11
45	2570	17
78	4160	30
115	6150	45

2-Hydroxy-5-methoxybicyclo[3.2.0]hepta-3,6-diene

(LXXVIII) A solution of 0.5 g. of photo-gamma-tropolone methyl ethyl (LXV) in 15 ml. of ether was added slowly to a suspension of 0.5 g. of lithium aluminum hydride in 20 ml. of ether. The reaction mixture was stirred at room temperature for 4 hours. The excess hydride was decomposed by the addition of moist sodium sulfate. The ether was removed under reduced pressure leaving 0.42 g. (84%) of a pale yellow, viscous liquid. The liquid was molecularly distilled at 90° and 1.0 mm. giving a viscous, colorless liquid. The infrared spectrum showed peaks at 2.96, 6.20 and 6.41 μ , see Figure 15, page 235.

Conversion of 2-hydroxy-5-methoxybicyclo[3.2.0]hepta-3,6-diene (LXXVIII) to tropone A solution of 24.7 mg. of 2-hydroxy-5-methoxybicyclo[3.2.0]hepta-3,6-diene (LXXVIII) in 5.0 ml. of 1.0 N hydrochloric acid was heated at reflux, and aliquots were removed periodically to be analyzed by ultraviolet spectroscopy. The ultraviolet spectra developed the typical tropone absorption with maxime at 225, 228, 231.5, 239 (shoulder) and 312 μ .⁴³ The yield of tropone based on the extinction coefficient of the 228 μ maximum was 29%.

Hydrogenation of 2-hydroxy-5-methoxybicyclo[3.2.0]-hepta-3,6-diene (LXXVIII) A solution of 400 mg. of 2-hydroxy-5-methoxybicyclo[3.2.0]hepta-3,6-diene (LXXVIII) in 20 ml. of methanol was hydrogenated over Adams' Catalyst

absorbing 2.02 moles of hydrogen per mole of compound. The catalyst was removed by filtration, and the solvent was removed under reduced pressure. The residue showed peaks in the infrared at 2.9 and 9.2 μ . The gas phase chromatogram on a Ucon Polar column^{102a} at 175° showed two peaks with retention times of 64.0 (39%) and 70.6 (61%) minutes.

Acid-catalyzed ring opening of 2-hydroxy-5-methoxy-bicyclo[3.2.0]heptane (LXXX) A solution of 167 mg. of 2-hydroxy-5-methoxybicyclo[3.2.0]heptane (LXXX) in 10.0 ml. of 1.0 N hydrochloric acid in methanol was heated at reflux temperature. Aliquots were removed periodically and the solvents were removed under reduced pressure. The residue was dissolved in chloroform and the infrared spectrum of the solution was taken. After 1.5 hours the infrared spectrum showed hydroxyl absorption with only weak 5.87 and 6.06 μ peaks.

Reaction of photo- γ -tropolone methyl ether (LXV) with phenyl magnesium bromide A solution of 1.00 g. (0.00735 mole) of photo- γ -tropolone methyl ether (LXV) in 20 ml. of ether was slowly added to 0.0147 mole of phenyl magnesium bromide in ether. The solution turned deep yellow. The reaction was hydrolyzed with an equivalent amount of hydrochloric acid. The ether layer was decanted and washed with water, 5% sodium bicarbonate, and finally with water. The solution was then dried over sodium sulfate, and the ether was removed under reduced pressure giving 1.6 g. (101%) of a

viscous, yellow liquid (LXXXI). Molecular distillation at 135° and 0.4 mm. gave a yellow, viscous material which crystallized on standing in the refrigerator. The melting point was very near or below room temperature and could not be determined. The infrared spectrum showed peaks at 2.90, 6.06, 6.14 μ along with characteristic aromatic absorption peaks, see Figure 15, page 235. The ultraviolet spectrum showed end absorption with a shoulder at 248 μ (2,420) and $\lambda_{\max}^{95\% \text{ EtOH}}$ 332 μ (1,110), see Figure 31, page 267. The nuclear magnetic resonance spectrum is shown in Figure 35, page 275.

Anal. Calcd. for $\text{C}_{14}\text{H}_{14}\text{O}_2$: C, 78.48; H, 6.59. Found: C, 78.14; H, 6.76.

Acid-catalyzed ring opening of 2-hydroxy-2-phenyl-5-methoxybicyclo[3.2.0]hepta-3,6-diene (LXXXI) A solution of 49.7 mg. of LXXXI in 5.0 ml. of methanol and 5.0 ml. of 1.0 N hydrochloric acid was heated gently, and aliquots were periodically removed for ultraviolet analysis. A 258 μ peak appeared instantly in the ultraviolet and after 15 minutes of gentle heating showed $\lambda_{\max}^{95\% \text{ EtOH}}$ 258 μ (11,000) and a low intensity maximum at 334 μ . The solvent was partially removed, and the remainder was extracted with ether. The extract was dried over sodium sulfate, and the solvent was removed under reduced pressure. The infrared spectrum of the residue showed peaks at 5.84, 5.99 and 6.16 μ .

Hydrogenation of 2-hydroxy-2-phenyl-5-methoxybicyclo-
/3.2.0/hepta-3,6-diene (LXXXI) A solution of 56.6 mg. of
2-hydroxy-2-phenyl-5-methoxybicyclo/3.2.0/hepta-3,6-diene
(LXXXI) in 20 ml. of methanol absorbed 3.09 mole of hydrogen
per mole of starting material over Adams' Catalyst. The
catalyst was removed by filtration, and the solvent was re-
moved under reduced pressure. The infrared spectrum of the
residue showed a weak hydroxyl peak with an intense peak at
5.88 μ . A 2,4-dinitrophenylhydrazone was prepared in the
usual manner but gave a wide melting range (135-145 $^{\circ}$) even
after recrystallization.

2-Hydroxy-2-methyl-5-methoxybicyclo/3.2.0/hepta-3,6-
diene (LXXXIV) and hydrogenation A solution of 0.30 g.
(0.0022 mole) of photo-gamma-tropolone methyl ether (LXV) in
10 ml. of ether was added to 0.0044 mole of methyl magnesium
iodide in 10 ml. of ether prepared from 0.0044 mole of methyl
iodide with excess magnesium. The reaction was hydrolyzed
with an equivalent amount of 0.1 N sulfuric acid. The ether
layer was decanted and washed with water, 5% sodium bicar-
bonate, and finally with water. The ether solution was dried
over sodium sulfate, and the ether was removed under reduced
pressure. The residue molecularly distilled with considerable
decomposition at 100 $^{\circ}$ and 0.02 mm. giving 0.12 g. (36%).
The infrared spectrum of the distillate showed peaks at 2.93,
6.07, 6.16 and 6.38 μ . The material was dissolved in methanol

and hydrogenated over Adams' Catalyst. The catalyst was removed by filtration, and the solvent was removed under reduced pressure. The infrared spectrum of the residue showed a 5.98 μ peak in carbontetrachloride. The gas phase chromatogram showed three peaks on a Theed column^{102a} at 72° with retention times of 8.4, 11.4 and 13.9 minutes. 4-Methylcycloheptanone showed a peak with a retention time of 13.7 minutes on the same column. Addition of 4-methylcycloheptanone to the hydrogenation residue gave a symmetrical peak, of increased intensity, with a retention time of 13.7 minutes.

5-Methoxybicyclo[3.2.0]hept-3-ene-2-one (LXVII) A solution of 1.00 g. of photo-gamma-tropolone methyl ether (LXV) in 25 ml. of methanol was hydrogenated with 1.0 mole of hydrogen over Adams' Catalyst. The catalyst was removed by filtration, and the methanol was removed under reduced pressure. The residue was twice distilled at 61° at 0.90 mm., and 57° at 0.75 mm. The infrared spectrum showed peaks at 5.85 and 6.14 μ , see Figure 14, page 233. The ultraviolet spectrum showed $\lambda_{\max}^{95\% \text{ EtOH}}$ 215 (6,470) and 331 μ (195), see Figure 30, page 265.

A 2,4-dinitrophenylhydrazone was prepared in the usual manner and recrystallized from ethanol giving orange-red needles, melting point 174.5-175.5°, and $\lambda_{\max}^{\text{CHCl}_3}$ 258 (15,500) and 377 (29,800).

Anal. Calcd. for $\text{C}_{14}\text{H}_{14}\text{N}_4\text{O}_5$: C, 52.82; H, 4.44. Found:

C, 52.99; H, 4.51.

Attempted base-catalyzed ring opening of 5-methoxybicyclo[3.2.0]hept-3-ene-2-one (LXVII) A solution of 5-methoxybicyclo[3.2.0]hept-3-ene-2-one (LXVII) in 0.1 N sodium hydroxide was allowed to stand at room temperature. Aliquots were removed and analyzed by ultraviolet measurements. A 332 mu peak appeared indicating the presence of 15% of photo-gamma-tropolone methyl ether (LXV) after 2 hours. The solution was heated at 80° for 2.5 hours producing no new peaks except the development of a 360 mu peak and the disappearance of the 332 mu peak.

Acid-catalyzed ring opening of 5-methoxybicyclo[3.2.0]hept-3-ene-2-one (LXVII) A solution of 13.3 mg. of 5-methoxybicyclo[3.2.0]hept-3-ene-2-one (LXVII) in 25 ml. of water was diluted 1:2 in acid, the total acidity being 1.20 N sulfuric acid. The acid solution was heated at 80° and 1 ml. aliquots were periodically removed and the ultraviolet spectra were recorded.

<u>Time (hours)</u>	<u>Absorbancy at 229 mu</u>	<u>% reaction</u> ¹¹⁵
1	0.373	15.0
2	0.393	27.3
3	0.409	29.8
5	0.497	43.8
15	0.592	59.3

¹¹⁵The molar extinction coefficients used at 229 mu were 10,900 for 2-cycloheptene-1,4-dione and 2,910 for 5-methoxybicyclo[3.2.0]hept-6-ene-2-one.

Hydrolysis of 92 mg. of 5-methoxybicyclo[3.2.0]hept-3-ene-2-one (LXVII) in 5.0 ml. of 1 N hydrochloric acid gave a 90% yield of 2-cyclohepten-1,4-dione after refluxing for 10 hours. The solution was extracted with ether, and the ether was evaporated leaving a yellow, pasty residue. The residue was treated with ethanolic 2,4-dinitrophenylhydrazine reagent giving a dark red derivative, melting point 235-260° (insufficient material prevented further purification). The bis-2,4-dinitrophenylhydrazone showed maxima in the ultraviolet at 271 and 397 m μ in chloroform solution. The ultraviolet spectrum of this derivative was superimposable with the spectrum of authentic bis-2,4-dinitrophenylhydrazone of 2-cyclohepten-1,4-dione.

Preparation of 2-cyclohepten-1,4-dione bis-2,4-dinitrophenylhydrazone¹¹⁶ A solution of 4.2 g. (0.0198 mole) of 2-cyclohepten-1,4-diol diacetate⁴¹ in 25 ml. of anhydrous ether was added dropwise to 0.95 g. (0.025 mole) of lithium aluminum hydride in 50 ml. of ether. The mixture was allowed to stir overnight at room temperature. The excess hydride was decomposed by the addition of saturated ammonium chloride solution. The ether layer was decanted, and the aqueous layer was continuously extracted with ether for 60 hours. The

¹¹⁶A previous report on the preparation of the bis-2,4-dinitrophenylhydrazone of 2-cyclohepten-1,4-dione gave the melting point as 259-260 with decomposition (I. Ernest and J. Hofman, Chem. Listy, 45, 261 (1951)).

ethereal solutions were combined and dried over sodium sulfate. The solvent was removed under reduced pressure leaving 2.55 g. of a colorless viscous liquid. The infrared spectrum showed peaks at 2.98 and 6.10 μ .

A solution of 1.3 g. (0.010 mole) of crude 2-cyclohepten-1,4-diol in 30 ml. of acetone was cooled to -10° in an ice-salt bath. A solution of 1.40 g. (0.0140 mole) of chromic anhydride in 6 ml. of distilled water and 2.5 ml. of concentrated sulfuric acid was added dropwise during the course of 1/2 hour with vigorous stirring. The reaction mixture was allowed to stir at room temperature for three hours. The reaction mixture was then diluted with 100 ml. of distilled water and extracted with three portions of ether. The yellow ether extracts were combined, washed with 5% sodium bicarbonate and water, and dried over sodium sulfate. The ether was removed under reduced pressure giving 0.44 g. (35%) of a pale yellow paste. The infrared spectrum showed peaks at 6.02 and 6.16 μ , see Figure 18, page 241. The ultraviolet spectrum showed $\lambda_{\max}^{95\% \text{ EtOH}}$ 229 μ (10,000), see Figure 25, page 255.

The bis-2,4-dinitrophenylhydrazone was prepared in the usual manner and recrystallized twice from nitrobenzene-ethanol giving scarlet cubes, melting point $294-295^{\circ}$.¹¹⁶ The ultraviolet spectrum showed $\lambda_{\max}^{\text{CHCl}_3}$ 271 (51,900) and 397 μ (72,400).

Anal. Calcd. for $C_{19}H_{16}N_2O_8$: C, 47.11; H, 3.33. Found: C, 47.40; H, 3.52.

Pyrolysis of 5-methoxybicyclo[3.2.0]hept-3-ene-2-one (LXVII) A 25 mg. sample of 5-methoxybicyclo[3.2.0]hept-3-ene-2-one (LXVII) was dropped into a six inch vertical, pyrex-helices packed pyrolysis column,¹¹² preheated to 360°, in a stream of nitrogen with an estimated residence time of about 10 seconds. The pyrosylate was a colorless liquid with a strong, sharp odor. The infrared spectrum showed peaks at 5.88 and 6.06 μ . The ultraviolet spectrum showed $\lambda_{\max}^{95\% \text{ EtOH}}$ 220, 272 (weak) and 328 μ . The gas phase chromatogram on a Ucon Polar column^{102a} at 186° showed the presence of three peaks. Peak I, at 20.2 minutes, comprised 60% of the product and showed peaks in the infrared at 6.00 and 6.28 μ . The ultraviolet spectrum showed $\lambda_{\max}^{95\% \text{ EtOH}}$ 222 μ . Peak II (14%), at 42.9 minutes, was an unidentified impurity peak also appearing in the starting material. Peak III (26%), at 46.7 minutes, was identified as unpyrolyzed starting material by its infrared spectrum.

Hydride reduction of 5-methoxybicyclo[3.2.0]hept-3-ene-2-one (LXVII) and conversion to 2,4-cycloheptadienone A solution of 100 mg. of 5-methoxybicyclo[3.2.0]hept-3-ene-2-one (LXVII) in 20 ml. of ether was added to a suspension of 0.5 g. of lithium aluminum hydride in 30 ml. of ether. The excess hydride was carefully decomposed by addition of distilled

water. The solid was removed by filtration, and the ether filtrate was dried over sodium sulfate. The ether was removed under reduced pressure. The infrared spectrum of the residue showed peaks at 2.9, 6.25 and 9.25 μ . The ultraviolet spectrum showed only low intensity end absorption.

A solution of 13.5 mg. of the 2-hydroxy-5-methoxybicyclo/3.2.0/hept-3-ene (LXXIX) in 5.0 ml. of 1.0 N hydrochloric acid was refluxed, and aliquots were periodically removed for ultraviolet analysis. A low intensity 292 μ maximum appeared but slowly transformed into a typical tropone spectrum with maxima at 225, 228, and 231.5 μ . The yield of tropone based on the extinction coefficient at 228 μ was 10%.

5-Methoxybicyclo/3.2.0/heptane-2-one (LXVIII) Hydrogenation of photo-gamma-tropone methyl ether (LXVIII) in methanol over Adams' Catalyst with 2.00 moles of hydrogen gave, after filtration and removal of the solvent under reduced pressure, a colorless, sweet-smelling liquid, boiling point of 61° at 0.9 mm. and n_D^{25} 1.4677. The infrared spectrum showed a single intense peak at 5.75 μ , see Figure 14, page 233.

Anal. Calcd. for $C_8H_{12}O_2$: C, 68.53; H, 8.65. Found: C, 68.32; H, 8.82.

Treatment of 5-methoxybicyclo/3.2.0/heptane-2-one (LXVIII) with acidic 2,4-dinitrophenylhydrazine reagent gave the bis-2,4-dinitrophenylhydrazone of cycloheptan-1,4-dione,

melting point 246-247° after recrystallization from nitrobenzene-ethanol, reported melting point 242.0-242.4°. ⁴¹

The ultraviolet spectrum showed $\lambda_{\text{max}}^{\text{CHCl}_3}$ 256 (19,800) and 363 μ (40,200).

Anal. Calcd. for $\text{C}_{19}\text{H}_{18}\text{N}_2\text{O}_8$: C, 46.92; H, 3.73. Found: C, 47.26; H, 3.76.

All attempts to form a mono-2,4-dinitrophenylhydrazone failed.

Acid-catalyzed ring opening of 5-methoxybicyclo[3.2.0]heptane-2-one (LXVIII) Treatment of 5-methoxybicyclo[3.2.0]heptane-2-one (LXVIII) with 0.1 N methanolic hydrochloric acid for one minute gave cycloheptane-1,4-dione as identified by its bis-2,4-dinitrophenylhydrazone. A solution 15.2 mg. of 5-methoxybicyclo[3.2.0]heptane-2-one (LXVIII) in 10.0 ml. of 0.001 N methanolic hydrochloric acid was heated at reflux. Aliquots were periodically removed and immediately evaporated to dryness. The residue was dissolved in chloroform, and the infrared spectra were recorded from 5.0 to 6.5 μ . The relative amounts of 5-methoxybicyclo[3.2.0]heptane-2-one (LXVIII) and 1,4-cycloheptandione were estimated from the intensities of the 5.75 and 5.87 μ peaks respectively.

<u>Time (minutes)</u>	Relative % to <u>5.75 μ</u>	and	<u>5.87 μ</u> peaks
5	100		--
10	90		10
20	50		50
30	35		65
42	10		90
60	5		95

Attempted base-catalyzed ring opening of 5-methoxybicyclo[3.2.0]heptane-2-one (LXVIII) A solution of 38.3 mg. of 5-methoxybicyclo[3.2.0]heptane-2-one (LXVIII) in 25 ml. of 0.1 N sodium hydroxide was let stand at room temperature. Aliquots (2 ml.) were periodically removed and extracted with 0.5 ml. of chloroform. The chloroform solution was dried over sodium sulfate, and the infrared spectra of the chloroform solutions were recorded. After one hour at room temperature there was no observable change in the infrared. The solution was then heated at 80° for 105 minutes but still no change was observed.

Pyrolysis of 5-methoxybicyclo[3.2.0]heptane-2-one (LXVIII) Pyrolysis of 20 mg. of 5-methoxybicyclo[3.2.0]heptane-2-one (LXVIII) at 360° in a six inch vertical, pyrex-helices packed column¹¹² gave, after washing the column with chloroform, a product which had an infrared spectrum identical to pure starting material (LXVIII).

Attempted light-catalyzed Diels-Alder reaction of γ -tropolone methyl ether with maleic anhydride A. A solution of 0.5 g. of I and 0.4 g. of maleic anhydride in 5.0 ml. of benzene was irradiated in a pyrex vessel with internal cooling. A control solution was also prepared and placed in a dark place. Aliquots were periodically removed from the irradiation, and the solvent was evaporated. Infrared spectra of the residues showed no 5.95 μ peak. The characteristic

peaks of I had greatly diminished after 24 hours, and a tarry precipitate formed on the side of the vessel which showed only 5.8 μ absorption in the infrared.

B. A solution of 0.5 g. of I and 0.4 g. of maleic anhydride was dissolved in 5 ml. of water and irradiated in a pyrex vessel. After 30 hours a tarry precipitate formed which showed peaks in the infrared at 2.96, 5.88 and 6.13 μ . The aqueous solution was extracted with chloroform and the extract was dried over sodium sulfate. The ether was evaporated leaving a residue which showed 5.88 μ carbonyl absorption. The aqueous control solution after five days precipitated a tan precipitate, melting point 212° , which was identified as gamma-tropolone.

Irradiation of tropone A solution of 0.100 g. of 6 β -hydroxytropinone methobromide (0.40 mmole) and 33.6 mg. of sodium bicarbonate (0.40 mmole) in 25 ml. of water was heated at 85° for 1.5 hours giving a 57% yield of tropone as determined by the extinction coefficient of the 228 μ peak in the ultraviolet. The solution was diluted to 50 ml. and irradiated in a pyrex vessel with a mercury arc lamp. After three hours there remained only a low intensity shoulder at 225 μ in the ultraviolet. The solution was extracted with methylene chloride, and the extract was dried over sodium sulfate. The solvent was removed under reduced pressure; the infrared spectrum of the yellow residue showed peaks at

5.71, 5.85, 6.03 and 6.26 μ . Hydrogenation of the residue in methanol over Adams' Catalyst gave a product which showed peaks in the infrared at 5.81, 5.95 and 6.30 μ .

Irradiation of freshly distilled tropone¹⁰⁵ in distilled water gave similar results giving no characterizable product.

Experimental of Photochemistry of 1,3-Cycloheptadienes

Irradiation of 1,3-cycloheptadiene A solution of 4.0 g. of freshly distilled 1,3-cycloheptadiene in 200 ml. of ether was flushed with nitrogen for one hour under full aspirator vacuum while immersed in a Dry Ice trap. The solution was irradiated in a quartz vessel with a mercury arc lamp. The rate of decay of 1,3-cycloheptadiene was observed by periodically removing aliquots and analyzing by ultraviolet spectroscopy. After irradiation for 42 hours in refluxing ether, 90% of the 1,3-cycloheptadiene had disappeared. The solvent was slowly removed by distillation through a six inch micro-Vigreux column. The residue was then fractionally distilled giving 1.90 g. (48%) of bicyclo[3.2.0]hept-6-ene (LXXXV), boiling point 96.0° at 745 mm., density 0.863 g./ml. at 25°, n_D^{25} 1.4660 and molar refractive index of 30.22, calculated 30.34. The infrared spectrum showed peaks at 3.18, 3.28, 3.39, 3.50 and 6.40 μ . The nuclear magnetic resonance spectrum is shown in Figure 37, page 279.

Hydrogenation of bicyclo[3.2.0]hept-6-ene (LXXXV) A

solution of 46.8 mg. of bicyclo[3.2.0]hept-6-ene (LXXXV) in 15 ml. of methanol when hydrogenated over Adams' Catalyst absorbed 12.5 ml. of hydrogen at 28° and 743 mm. corresponding to 0.99 mole of hydrogen per mole of compound.

Similar hydrogenation of bicyclo[3.2.0]hept-6-ene (LXXXV) in 3 ml. of methylene chloride over 15 mg. of platinum oxide also resulted in adsorption of one mole of hydrogen. The methylene chloride solution was then separated by preparative scale gas phase chromatography, the bicyclo[3.2.0]heptane appearing first on a 1 meter oxydipropionitrile column.^{102a} The hydrocarbon was collected in a Dry Ice trap and transferred to a 10 cm. gas cell, and the infrared spectrum was recorded showing peaks at 3.355 and 3.49 μ with no absorption in the double bond region.

The product from the hydrogenation was inert to dilute bromine in carbontetrachloride and dilute aqueous permanganate.

Pyrolysis of bicyclo[3.2.0]hept-6-ene (LXXXV) to 1,3-cycloheptadiene Pyrolysis of 20 μ l. samples (17.2 mg.) of bicyclo[3.2.0]hept-6-ene (LXXXV) in a vertical 10 cm. pyrex-helices packed pyrolysis column¹¹² at varying temperatures in a stream of nitrogen with an estimated contact time of 30 seconds gave the results shown in the tabulation below. The pyrolysis column was connected to a vacuum line, and the

pyrolysis product was transferred to a 25 ml. volumetric flask immersed in a liquid nitrogen trap. The sample was dissolved in 95% ethanol and diluted to 25.0 ml. Aliquots (0.20 ml.) were then diluted to 10.0 ml. with 95% ethanol, and the amount of 1,3-cycloheptadiene was determined by ultraviolet analysis.

<u>Temperature °C</u>	<u>Extinction coefficient at 243 mμ¹¹⁷</u>	<u>% reaction</u>
200	--	0.0
222	--	0.0
263	--	0.0
316	360	6.8
360	4000	75
411	4700	89
468	5200	98
529	5300	100
598	1900	(decomposition occurred)

Permanganate oxidation of bicyclo[3.2.0]hept-6-ene

(LXXXV) A solution of 0.55 g. of bicyclo[3.2.0]hept-6-ene (LXXXV) in 20 ml. of distilled water and 10 ml. of acetone and 2.00 gm. of potassium permanganate was added. The solution was made basic by addition of 1 ml. of 30% sodium hydroxide and filtered through a Celite pad. The solution was then acidified with sulfuric acid and extracted with ether. The extract was dried over magnesium sulfate, and the ether was then evaporated leaving 0.44 g. of an acidic residue (47%). Two recrystallizations from ether gave large, colorless

¹¹⁷The ultraviolet spectrum of 1,3-cycloheptadiene was found to show $\lambda_{\text{max}}^{95\% \text{ EtOH}}$ 241 m μ (5,300). The reported ultraviolet spectrum shows $\lambda_{\text{max}}^{\text{isooctane}}$ 248 m μ (7,400) (E. Pesch and S. L. Friess, J. Am. Chem. Soc., 72, 5757 (1950)).

crystals, melting point 138.0-138.8°, reported for cis-1,2-cyclopentane-dicarboxylic acid 134-135°¹¹⁸ and 139-140°.¹¹⁹ The infrared spectrum showed peaks at 3.05 and 5.85 u (broad). Anal. Calcd. for C₇H₁₀O₄: C, 53.16; H, 6.32. Found: C, 52.99; H, 6.22.

Sublimation of the diacid at 100° and 0.1 mm. readily gave an anhydride. Attempted recrystallization from Skelly B gave poorly defined crystals, melting point 57-61°, reported for the anhydride 73.5-74.0°.¹¹⁹ The infrared spectrum showed peaks at 5.42 and 5.63 u.

Ozonolysis of bicyclo[3.2.0]hept-6-ene (LXXXV) A solution of 234 mg. of bicyclo[3.2.0]hept-6-ene (LXXXV) in 55 ml. of methylene chloride was cooled in a Dry Ice-ethanol bath. A stream of ozone and air was passed through the solution; 2.09 mole of ozone was adsorbed per mole of compound. The methylene chloride solution was warmed to room temperature and stirred with 20 ml. of 3% hydrogen peroxide solution. The methylene chloride was allowed to evaporate leaving a sticky material insoluble in the aqueous layer. The mixture was extracted with ether, and the extract was dried over magnesium sulfate. The ether was evaporated leaving 400 mg. of a sharp smelling, viscous residue which showed peaks in the

¹¹⁸L. N. Owen and A. G. Peto, J. Chem. Soc., 2383 (1955).

¹¹⁹S. F. Birch, R. A. Dean, N. J. Hunter, and E. V. Whitehead, J. Org. Chem., 20, 1178 (1955).

infrared at 2.97, 5.58, 5.72 (shoulder) and 5.83 μ in chloroform.

Treatment of a portion of the acid residue with 2,4-dinitrophenylhydrazine reagent gave a poorly defined derivative, melting point 110-125° which still showed the presence of a 5.83 μ peak in the infrared.

Volatile acid determination by paper chromatography¹²⁰

A 5 mg. portion of the acid residue was neutralized with ammonium hydroxide in ethanol. Approximately a 1 mg. equivalent of the neutralized acid fraction was placed on a 4.25 x 7.75 inch piece of Watman #1 filter paper. A standard was prepared from one drop of formic acid, neutralized by ammonium hydroxide in ethanol, and placed on the strip of filter paper. The bottom of the paper chromatogram was immersed in a solvent system composed of 99 ml. of 95% ethanol and 1 ml. of concentrated ammonium hydroxide and allowed to stand for 5 hours. The paper chromatogram was removed and allowed to thoroughly dry. The chromatogram was then developed by spraying with an indicator solution composed of 50 mg. of bromophenol blue and 0.2 g. of citric acid dissolved in 100 ml. of distilled water. The unknown acid mixture showed two spots; the first with an R_f value of 0.32 and the second with a very low R_f value. The formic acid chromatogram gave a single spot, R_f value

¹²⁰E. P. Kennedy and H. A. Barker, Anal. Chem., **23**, 1033 (1951).

0.32, literature value 0.31.¹²⁰ A second chromatogram showed similar spots with R_f values of 0.34.

Non-volatile acid determination by paper chromatography¹²¹ A small drop of the unknown acid mixture was placed on a 4.25 x 7.75 inch strip of Watman #1 filter paper. A drop of a solution of glutaric acid in distilled water was similarly applied and allowed to dry. The bottom edge of the paper was immersed in a solvent system of 74% phenol, 24% water and 2% formic acid and allowed to stand for 6 hours. The paper was removed and allowed to dry thoroughly. The chromatogram was developed by spraying with an indicator solution composed of 400 mg. of bromophenol blue per liter of 95% ethanol. The unknown acid mixture showed a single spot with R_f value 0.64. The glutaric acid showed R_f values of 0.79 and 0.82, literature value of 0.86.¹¹²

Irradiation of 5-methoxy-2,4-cycloheptadienone (XXXII)

A solution of 1.4 g. (0.0103 mole) of I in 10 ml. of ether was added to a suspension of 0.2 g. of lithium aluminum hydride in 20 ml. of ether. The reaction mixture was stirred for 30 minutes and was hydrolyzed with distilled water. The solid was removed by filtration, and the solution was dried over sodium sulfate. The ether solution was diluted to 100 ml. with ether, and the solution was irradiated in a quartz vessel

¹²¹J. B. Stark, A. E. Goodban, and H. S. Owens, ibid., 23, 413 (1951).

with a mercury arc lamp. Analysis by ultraviolet spectroscopy showed the rapid disappearance of the 328 μ peak of XXXII. The 256 μ peak, representative of alcohols XL and XLI, slowly decreased in intensity and developed a shoulder at 263 μ . The ether was removed and the residue was analyzed by gas phase chromatography on LB 550X and TCEP columns^{102a} for the presence of anisole.⁹³ The chromatograms showed no peak that corresponded to anisole by retention time comparison. The residue, after removal of the ether, showed an intense peak in the infrared at 5.78 μ in addition to peaks corresponding to alcohols XL and XLI and the ketone XXXII.

The residue was chromatographed on a 10 x 0.5 cm. alumina column. The first fraction (\sim 150 mg.), 2-keto-5-methoxybicyclo[3.2.0]hept-6-ene (LXXXVII), was eluted with benzene-Skelly B (3:1) and showed peaks in the infrared at 5.78, 6.13 and 6.38 μ . The ultraviolet showed a weak maximum at 328 μ with intense end absorption at 210 μ .

Base-catalyzed ring opening of 2-keto-5-methoxybicyclo[3.2.0]hept-6-ene (LXXXVII) The ultraviolet spectra of LXXXVII in 0.1 N sodium hydroxide showed the rapid increase of a 340 μ maximum with time at 22^o (5-methoxy-2,4-cycloheptadienone (XXXII) shows a peak at 340 μ in 0.1 N sodium hydroxide). The following tabulation shows the per cent of reaction at various times:

<u>Time (minutes)</u>	<u>% reaction</u> ¹²³
0	12
1.5	24
4.5	40
6.5	48
10.5	60
16	71
20	77
30	87
40	91
60	94

Acid-catalyzed ring opening of 2-keto-5-methoxybicyclo-
/3.2.0/hept-6-ene (LXXXVII) The ultraviolet spectrum of LXXXVII in 0.09 N sulfuric acid gave an immediate increase in the intensity of the 340 mu maximum at 22° (2-cyclohepten-1,5-dione shows a 340 mu maximum in the ultraviolet in dilute acid). After 15 minutes, the intensity of the 340 mu peak decreased and a shoulder at 233 mu developed. Heating the acid solution at 60° for 10 minutes produced a spectrum which showed only a distinct 233 maximum with end absorption.

Ring opening of 2-keto-5-methoxybicyclo/3.2.0/hept-6-ene (LXXXVII) in ethanol solution at room temperature Allow-
ing an ethanol solution of LXXXVII to stand at 22° caused an increase in the intensity of the 328 mu peak in the ultra-

¹²³The ultraviolet spectrum of 2-keto-5-methoxybicyclo/3.2.0/hept-6-ene showed a 328 mu maximum indicative of the presence of 5-methoxy-2,4-cycloheptadienone. 2-Keto-5-methoxybicyclo/3.2.0/hept-6-ene was found to undergo ring opening to the starting ketone at room temperature with no solvent present and the measurement of the reaction rate takes into account the amount of 5-methoxy-2,4-cycloheptadienone present at the beginning (12%).

violet. The following tabulation shows the per cent ring opening reaction at various times:

<u>Time (hours)</u>	<u>% reaction</u> ¹²³
0	12
1.25	37
2	52

Hydrogenation of 2-keto-5-methoxybicyclo[3.2.0]hept-6-ene (LXXXVII) Approximately 100 mg. of the photoproduct was dissolved in 10 ml. of methanol and was hydrogenated over Adams' Catalyst. The catalyst was removed by filtration, and the methanol was removed under reduced pressure. The residue was analyzed by gas phase chromatography on a LB 550X column^{102a} at 150°. The chromatogram showed an intense peak with a retention time of 8.05 minutes in addition to peaks due to hydrogenation products of XXXII. 5-Methoxybicyclo[3.2.0]heptane-2-one (LXVIII) showed a peak with a retention time of 8.1 minutes. Admixture of LXVIII to the hydrogenation product produced a single symmetrical peak with a retention time of 8.05 minutes.

Pyrolysis of cyclobutene Cyclobutene was prepared in poor yield by pyrolysis of N,N-dimethylcyclobutyl amine oxide (LXXXVIII) at 160°. ¹²² Analysis by gas phase chromatography on a 2 meter silver nitrate column^{102a} at room temperature showed the presence of 1% of 1,3-butadiene.

¹²²J. D. Roberts and C. W. Sauer, J. Am. Chem. Soc., 71, 3925 (1949).

Small samples of cyclobutene (approximately 10 mg.) were transferred from a vacuum line to a 10 ml. pyrolysis vessel which was subsequently immersed for 60 seconds in a Woods' Metal bath at various temperatures. The pyrolysis product was then transferred to a small sample vial, and samples were removed by a syringe and injected into the gas phase chromatography column and analyzed.

<u>Temperature °C</u>	<u>% 1,3-butadiene</u>	<u>% cyclobutene</u>
182	16	84
200	51	49
252	100	--

Experimental of Photochemistry of
4,5-Benzo-2-phenoxytropone

Irradiation of 4,5-benzo-2-phenoxytropone (XCV) A solution of 5.0 g. of 4,5-benzo-2-phenoxytropone (XCV) was dissolved in one l. of isopropanol and irradiated in a pyrex vessel with a mercury arc lamp for three days (temperature 20-45°). The isopropanol was removed under reduced pressure, and the residue was dissolved in 75% Skelly B-benzene and placed on a 24 x 1 inch alumina column. The following fractions were obtained:

<u>Fraction</u>	<u>Solvent system</u>	<u>Identity</u>
I	Skelly B-benzene	"Dimer A"
II	benzene and benzene- chloroform (4:1)	"Dimer B"
III	chloroform	starting material

Fraction I, designated as "Dimer A", was recrystallized three times from 95% ethanol giving colorless needles with melting point of 200.5-201.0°. The infrared spectrum showed peaks at 5.85, 5.96, 6.06 and 6.12 μ , see Figure 16, page 237. The ultraviolet spectrum showed end absorption with a shoulder at 215 μ (50,300) and $\lambda_{\text{max}}^{95\% \text{ EtOH}}$ 263 μ (17,200), see Figure 32, page 269. The nuclear magnetic resonance spectrum is shown in Figure 36, page 277. The molecular weight was determined as 448 and 468 by melting point depression in camphor¹²⁴ and as 438 and 468 by freezing point depression in benzene, calculated as 496 for the dimer molecular weight.

Anal. Calcd. for $\text{C}_{34}\text{H}_{24}\text{O}_4$: C, 82.24; H, 4.88. Found: C, 82.18; H, 4.87.¹²⁵

"Dimer A" on treatment with 2,4-dinitrophenylhydrazine reagent slowly gave a derivative which, when recrystallized from ethanol-chloroform, gave orange needles, melting point 241-242.5°. The infrared spectrum of the derivative in chloroform showed 5.84 and 6.18 μ peaks, and the ultraviolet spectrum showed $\lambda_{\text{max}}^{\text{CHCl}_3}$ 387 μ (25,400).

Fraction II, designated as "Dimer B", was recrystallized

¹²⁴The analysis was carried out by Geller Microanalytical Laboratories at Bardonia, New York.

¹²⁵The analysis was performed after additional drying at 160° for one minute. Analysis before drying gave: C, 81.27; H, 4.95.

as colorless rhombs from ethanol, melting point 208.5-209.5°, or as fine needles from chloroform-ethanol, melting point 212.4-212.7°. The infrared spectrum showed peaks at 5.78 and 6.13 μ (weak), see Figure 16, page 237. The ultraviolet spectrum showed $\lambda_{\text{max}}^{95\% \text{ EtOH}}$ 217 (43,400), 255 (shoulder) (24,500) and 261 μ (25,700), see Figure 33, page 271. The nuclear magnetic resonance spectrum is shown in Figure 36, page 277. Molecular weight determination by the freezing point lowering method in benzene gave 500, calculated for dimeric molecular weight 496.

Anal. Calcd. for $\text{C}_{34}\text{H}_{24}\text{O}_4$: C, 82.24; H, 4.88. Found: C, 82.14; H, 5.07.¹²⁶

Treatment of dimer B with hot ethanolic 2,4-dinitrophenylhydrazine reagent gave no derivative. Refluxing dimer B in acetylchloride and benzene led to recovery of starting material.

Attempted base-catalyzed hydrolysis of dimer A A solution of 80 mg. of dimer A in 5 ml. of ethanol and 5 ml. of 6.0 N sodium hydroxide was refluxed for 72 hours. The solution was cooled, and the crystals that formed on cooling were removed by filtration. The infrared absorption of these crystals, melting point 193-198°, was identical to that of the starting material.

¹²⁶This analysis was performed after drying at 160° for 30 seconds.

Attempted acid-catalyzed hydrolysis of dimer A A

solution of 0.50 g. of dimer A in 5 ml. of ethanol and 10 ml. of concentrated hydrochloric acid was refluxed for four days. The solution became light yellow in color. The solution was diluted with water and allowed to cool. The crystals that formed on cooling were removed by filtration giving 0.45 g. of material, melting point 194-196°. The infrared spectrum of the recovered material was identical to that of the starting material.

Hydrogenation of dimer A A. A solution of 0.527 g.

of dimer A in 30 ml. of tetrahydrofuran was hydrogenated over Adams' Catalyst adsorbing 57 ml. of hydrogen at 28.5° and 736 mm. corresponding to 2.1 mole of hydrogen per mole compound. The catalyst was removed by filtration, and the solvent was removed under reduced pressure. The residue was recrystallized from ethanol giving colorless crystals, melting point 219.5-221°. The infrared spectrum showed hydroxyl absorption at 2.86 μ , a single carbonyl peak at 5.69 and double bond absorption at 6.02 μ , see Figure 16, page 237. The ultraviolet spectrum showed end absorption with a shoulder at 215 (51,900) and $\lambda_{\text{max}}^{95\% \text{ EtOH}}$ 263 μ (14,000), see Figure 32, page 269.

Anal. Calcd. for $\text{C}_{34}\text{H}_{28}\text{O}_4$: C, 81.58; H, 5.60. Found: C, 81.29; H, 5.40.

Treatment of the tetrahydroderivative with acetic

anhydride in pyridine gave a material which showed peaks in the infrared at 5.69 and 5.76 μ .

A similar hydrogenation was halted after the adsorption of 0.92 moles of hydrogen. The material that was recovered showed 5.69, 5.77 (shoulder) and 5.97 μ (weak) peaks.

B. A similar hydrogenation employing a platinum oxide catalyst obtained from Englehard⁶⁹ gave a material which showed peaks in the infrared at 5.73 and 5.83 μ . This product has not been further characterized.

Treatment of tetrahydro-dimer A with refluxing acid A solution of 37.6 mg. of tetrahydro-dimer A in 15 ml. of ethanol and 4 ml. of 6 N hydrochloric acid was refluxed for 48 hours. There was no observable change in the ultraviolet spectrum. The solvent was partially removed and a solid precipitated. The crystals were removed by filtration and recrystallized from chloroform-ethanol; melting point 252-258° with decomposition. The infrared spectrum showed a peak at 5.70 in the carbonyl region. This material was not further characterized.

Zinc and acetic acid reduction of dimer A A solution of 0.20 g. of dimer A in 20 ml. of glacial acetic acid was heated and 0.5 g. of powdered zinc was added slowly. The solution was diluted with 50 ml. of water, and the resulting solution was extracted with chloroform. The extract was washed with dilute sodium hydroxide and water, and dried over

sodium sulfate. The solvent was removed leaving a yellow-orange, semicrystalline material which showed a peak in the infrared at 5.87 with a shoulder at 5.73 μ .

A solution of 75 mg. of the crude material was hydrogenated in methanol over Adams' Catalyst adsorbing approximately 1.6 mole of hydrogen per mole of compound. The material obtained after removing the catalyst and solvent showed only a broad peak in the infrared at 5.81 μ . This material was not further characterized.

Reduction of dimer A with lithium aluminum hydride A solution of 0.56 g. (0.00113 mole) of dimer A in 20 ml. of ether was added to 0.5 g. of lithium aluminum hydride in 30 ml. of ether. The reaction mixture was stirred for 18 hours. The excess hydride was decomposed by the addition of water, and 10 N sulfuric acid was added until the water layer was acidic. The ether layer was decanted, and the aqueous layer was extracted with three portions of chloroform. The chloroform extract was combined with the ether solution and extracted with three 20 ml. portions of 0.1 N sodium hydroxide. The sodium hydroxide extract was acidified with 10 N sulfuric acid. The acidified solution was extracted with three 20 ml. portions of ether. The ether extract was combined and diluted to 100 ml. An aliquot (3.00 ml.) was diluted to 10.0 ml. in 95% ethanol, and the ultraviolet spectrum was recorded showing maxima at 217 and 272 μ indicating the presence of 86 mg.

(0.000915 mole) of phenol¹²⁷ or 0.81 mole of phenol recovered per mole of starting material. The ether was removed, and the residue was dissolved in water and a solution of bromine in aqueous potassium bromide was added until the bromine color remained. The precipitate was collected and sublimed giving a melting point of 90.5-91.5°, reported value for 2,4,6-tri-bromophenol 95°. ¹²⁸

The original chloroform-ether solution was dried over sodium sulfate, and the solvent was evaporated leaving a colorless viscous material which failed to crystallize. The infrared spectrum showed peaks at 2.81, 2.90 and 6.02 u (weak), see Figure 17, page 239. The ultraviolet spectrum showed maxima at 215 (shoulder) and 258 mu, see Figure 32, page 269. The alcohol residue readily formed a non-crystalline acetate on standing overnight in 2 ml. of acetic anhydride and 1 ml. of pyridine. Treatment of a portion of the alcohol with manganese dioxide in chloroform produced a substance with peaks in the infrared at 5.83 and 5.97 u.

Attempted reduction of dimer A with sodium borohydride

A solution of 0.56 g. of dimer A in 30 ml. of ether was re-

¹²⁷The reported maxima for phenol are 217 and 273 mu (2,050) (A. E. Gillam and E. S. Stern, An Introduction to Electronic Absorption Spectroscopy in Organic Chemistry, Edward Arnold, Ltd., London, 1955, pp. 10, 119, and 163; J. M. Vandenberg, C. Henrich and S. Bash, Science, 114, 576 (1951)).

¹²⁸R. L. Shriner, R. C. Fuson and D. Y. Curtin, The Systematic Identification of Organic Compounds, 4th ed., John Wiley and Sons, Inc., New York, 1956, p. 325.

fluxed for one hour with 0.5 g. of sodium borohydride. The excess hydride was decomposed by the addition of dilute hydrochloric acid. The ether was decanted and dried over sodium sulfate. Evaporation of the ether gave a residue identical in infrared absorption to that of starting material (dimer A).

Ozonolysis of dimer A A solution of 0.55 g. (0.0011 mole) in 50 ml. of methylene chloride was treated with 0.0012 mole of ozone at -30° .¹⁰⁰ The methylene chloride solution was added to 100 ml. of 5% hydrogen peroxide and stirred on a magnetic stirrer until the methylene chloride had evaporated leaving a material insoluble in the aqueous phase. The material was recovered by filtration and air dried. Recrystallization from chloroform-hexane gave white, microplates, melting point $145-146.5^{\circ}$ with apparent loss of a gas. The infrared spectrum showed peaks at 5.64 and 5.83 μ , see Figure 18, page 241.

Anal. Found: C, 74.19; H, 6.83.

Heating the compound above its melting point caused bubbling and gave an amorphous material with decreased absorption at 5.83 μ but retaining the intense 5.64 μ peak.

Pyrolysis of dimer A Pyrolysis of 0.50 g. of dimer A in a sealed tube at 280° for one hour gave 90-100 mg. of phenol, identified by its infrared and ultraviolet spectra and the melting point of the 2,4,6-tribromo-derivative. No other characterizable product was obtained.

Attempted ketal formation with dimer A

A. A solution of 0.35 g. of dimer A, 2.5 g. of ethylene glycol and 0.01 g. of p-toluene sulfonic acid in 20 ml. of benzene was refluxed for 3 hours with an azeotrope collector. The benzene was removed by distillation, and 3 ml. of 30% sodium hydroxide was immediately added. The solution was diluted with 50 ml. of water and extracted with three portions of chloroform. The extract was dried over sodium sulfate, and the solvent was evaporated. The crude residue had a melting point of 192-195° and an infrared spectrum identical to that of starting material.

B. A solution of 0.30 ml. of ethyl orthoformate, 2 ml. of dry benzene, 1 drop of absolute ethanol, 1 drop of concentrated sulfuric acid and 0.25 g. of dimer A was heated at 80° for three hours. The acid was quenched with 2 ml. of pyridine, and the mixture was diluted to 30 ml. with ether. The solution was washed with 5% sodium bicarbonate solution and dried over magnesium sulfate. The solvent was removed under reduced pressure leaving a residue that was identical in the infrared with that of starting material.

Beckman rearrangement of dimer A oxime

A solution of 0.5 g. of dimer A and 0.75 g. of hydroxylamine hydrochloride in 2.5 ml. of pyridine and 2.5 ml. of ethanol was refluxed one hour. The solvent was removed by a stream of air, and the residue was triturated with water. The insoluble material

was filtered and fractionally recrystallized from ethanol-chloroform giving two fractions. The first fraction, colorless prisms from chloroform-ethanol, melting point $240-242^{\circ}$, showed peaks in the infrared at 2.92, 3.09, 5.84 and 6.09 μ , see Figure 18, page 241. The ultraviolet spectrum showed end absorption with shoulders at 215 (108,000) and 260 μ (33,600).

Anal. Found: C, 79.80; H, 5.17; N, 3.60.

The second fraction was insoluble in chloroform, ethanol and benzene and melted at $283-285^{\circ}$ with decomposition. The infrared spectrum showed sloppy hydroxyl absorption but no absorption in the carbonyl region.

Anal. Found: C, 76.35; H, 5.19; N, 5.28.

A 40 mg. portion of the first oxime fraction was treated with 1.0 g. of polyphosphoric acid at 100° for 15 minutes. The mixture was cooled and diluted to 20 ml. with crushed ice. The mixture was extracted with methylene chloride. The extract was dried over magnesium sulfate, and the solvent was evaporated. The residue was chromatographed on a 10 x 0.5 cm. alumina column. A neutral fraction was eluted with Skelly B-benzene mixtures which recrystallized from Skelly B giving pale yellow needles, melting point $113-117.5^{\circ}$ C. The ultraviolet spectrum showed maxima in ethanol at 249, 287 and 390 μ . The infrared spectrum showed peaks at 2.83, 2.94, 6.19, 6.27, 6.33 and 6.51 μ .

Anal. Found: C, 76.64; H, 5.68.

An acidic fraction was eluted with methanol-acetic acid mixtures which showed peaks in the infrared at 2.86, 5.70 and 5.86 μ . The ultraviolet spectrum showed maxima in ethanol at 242, 288 and 298 $m\mu$.

Treatment of the second oxime fraction with polyphosphoric acid in a similar manner gave the neutral fraction as the only characterizable product. Recrystallization from methanol gave pale yellow needles, melting point 119-120°.

Thermal conversion of dimer B to dimer A Heating dimer B at its melting point for one minute gave dimer A, identical in all respects in the infrared to that of pure dimer A.

Hydrogenation of dimer B Attempted hydrogenation of dimer B in methanol over Adams' Catalyst at atmospheric pressure or at 53.6 lb/in² resulted in no adsorption of hydrogen and gave back material identical in melting point and infrared absorption with pure dimer B.

Reduction of dimer B with lithium aluminum hydride
A slurry of 0.40 g. (0.00081 mole) of dimer B in 10 ml. of ether was added to 0.3 g. of lithium aluminum hydride in 10 ml. of ether. The mixture was stirred at room temperature for 10 hours. The excess hydride was decomposed by the addition of distilled water. The mixture was acidified by adding 10 N sulfuric acid. The ether was decanted, and the aqueous

layer was twice extracted with ether. The ether extract was extracted with three 20 ml. portions of 0.1 N sodium hydroxide. The sodium hydroxide extract was acidified by addition of 10 N sulfuric acid. The acidified solution was extracted with three 20 ml. portions of ether. The ether extract was diluted to 100 ml. with ether. A 3 ml. aliquot was diluted to 10.0 ml. and the ultraviolet spectrum was recorded showing maxima at 217 and 272 μ indicative for the presence of 78 mg. of phenol (0.00083 mole)¹²⁷ corresponding to 1.03 moles of phenol per mole starting material. A second identical run gave 0.86 mole of phenol per mole of starting material.

The original ether solution was dried over sodium sulfate, and the solvent was removed by evaporation leaving a colorless crystalline material. Recrystallization from chloroform-ether gave clusters of colorless needles, melting point 267-268°. The infrared spectrum showed peaks at 2.82 and 6.13 μ , see Figure 17, page 239. The ultraviolet spectrum¹²⁹ showed end absorption with a shoulder at 233 (27,600) and maxima at 237.5 (28,800), 248 (33,500), 257 (40,100), 277 (shoulder) (7,800), 288 (shoulder) (5,500) and 299 μ (3,100), see Figure 33, page 271. The nuclear magnetic resonance spectrum is shown in Figure 37, page 279. Molecular

¹²⁹The extinction coefficient was calculated on the basis of a molecular weight of 406 (reduction of a phenyl ester to a primary alcohol).

weight determination by the freezing point method in benzene gave the value 401, calculated for reduction of a phenyl ester to an alcohol 406.

Heating a few milligrams of the alcohol at 275° for one minute or sublimation at 270° led to recovery of unchanged alcohol.

Acetylation of dimer B alcohol Acetylations employing acetic anhydride in pyridine or ketene in chloroform failed. Acetylation was accomplished by refluxing 0.40 g. of the alcohol, obtained by hydride reduction of dimer B, in 20 ml. of benzene-acetyl chloride (1:1) for one hour giving 0.46 g. of a colorless, crystalline compound. Four recrystallizations from chloroform-ether gave clusters of colorless needles, melting point $239.0-239.6^{\circ}$. The infrared spectrum showed a single intense peak at 5.81 μ , see Figure 17, page 239. The ultraviolet spectrum¹³⁰ showed $\lambda_{\text{max}}^{95\% \text{ EtOH}}$ 218 (shoulder) (27,800), 230 (25,600), 237 (27,400), 247.5 (31,000), 257 (39,000), 270 (inflection) (12,500), 288 (shoulder) (8,500), and 298 μ (shoulder) (4,400), see Figure 33, page 271. The nuclear magnetic resonance spectrum is shown in Figure 37, page 279.

Reduction of dimer B alcohol acetate with lithium aluminum hydride A slurry of 40 mg. of the acetate (ob-

¹³⁰The extinction coefficient was calculated on the basis of a molecular weight of 464.

tained above) was added to a suspension of 0.2 g. of lithium aluminum hydride in 20 ml. of ether and allowed to stir overnight at room temperature. The excess hydride was decomposed by careful addition of water. The solid was removed by filtration, and the ether filtrate was dried over sodium sulfate. Evaporation of the solution gave a crystalline material which was recrystallized from chloroform-ether, melting point and mixed melting point with pure dimer B alcohol of 265-267°. The infrared spectrum of this material was identical in every respect with that of pure alcohol obtained by hydride reduction of dimer B.

Attempted manganese dioxide oxidation of dimer B alcohol

A solution of 17.7 mg. of alcohol, obtained by hydride reduction of dimer B, in 15 ml. of chloroform was stirred for three days with 0.70 g. of active manganese dioxide at room temperature. The manganese dioxide was removed by filtration, and the infrared spectrum of the chloroform solution was identical to that of the starting alcohol.

Attempted zinc and acetic acid reduction of dimer B

A solution of 0.20 g. of dimer B in 10 ml. of glacial acetic acid was heated on a hot plate and 0.5 g. of powdered zinc was slowly added. The mixture was heated for 30 minutes and was then diluted to 50 ml. with distilled water. The solution was extracted with chloroform, and the chloroform solution was washed with dilute sodium hydroxide and water. The chloroform

solution was dried over sodium sulfate, and the solvent was evaporated leaving a material, melting point 211-213^o, whose infrared spectrum was identical to that of dimer B.

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The following publications have been published from the work contained in this Thesis:

1. 2,5-Dibenzylidene-3-cyclopentenone, O. L. Chapman and D. J. Pasto, J. Org. Chem., 24, 120 (1959).
2. A Diels-Alder Adduct from gamma-Tropolone Methyl Ether, O. L. Chapman and D. J. Pasto, J. Am. Chem. Soc., 81, 3696 (1959).
3. Photo-gamma-Tropolone Methyl Ether, O. L. Chapman and D. J. Pasto, ibid., 80, 6685 (1958).
4. A Novel Base-Catalyzed Isomerization of a Bicyclic System to a Troponoid System, O. L. Chapman and D. J. Pasto, ibid., 81, 5510 (1959).
5. Photochemical Transformation of Simple Troponoid Systems. I. Photo-gamma-Tropolone Methyl Ether, O. L. Chapman and D. J. Pasto, ibid., 82, 3642 (1960).

APPENDIX

Gas Phase Chromatographic Columns Used in Experimental

- Perkin-Elmer R: Two meters, Ucon LB-550-X Grease.¹³¹
- Ucon LB-550-X: One meter, Ucon LB-550-X Grease on 60/80 mesh firebrick (30:100).
- THEED: One meter of tetrakis(beta-hydroxyethyl)ethylene diamine on Celite (10:100).
- Apiezon: One meter of Apiezon L Grease on 40/60 mesh firebrick (33:100).
- Oxydipropionitrile: One meter of oxydipropionitrile on Celite (25:100).
- Silver Nitrate: One meter of silver nitrate:ethylene glycol on Celite.
- T.C.E.P.: One meter of tris(cyanoethoxy)propane on 60/80 mesh firebrick (33:100).

¹³¹The Ucon LB-550-X Greases are polyalkylene glycols obtainable from Union Carbide Chemicals Company, New York 17, New York.

Figure 8. Infrared spectra

Top. 1-Hydroxy-1-methyl-4-methoxy-2,4,6-cyclohepta-
triene (XXXI)

Middle. 2-Methyl-4-methoxy-3,5-cycloheptadienone:
2-methyl-4-methoxy-4,6-cycloheptadienone
mixture (XVII)

Bottom. 2-Methyl-5-cyclohepten-1,4-dione:2-methyl-6-
cyclohepten-1,4-dione mixture

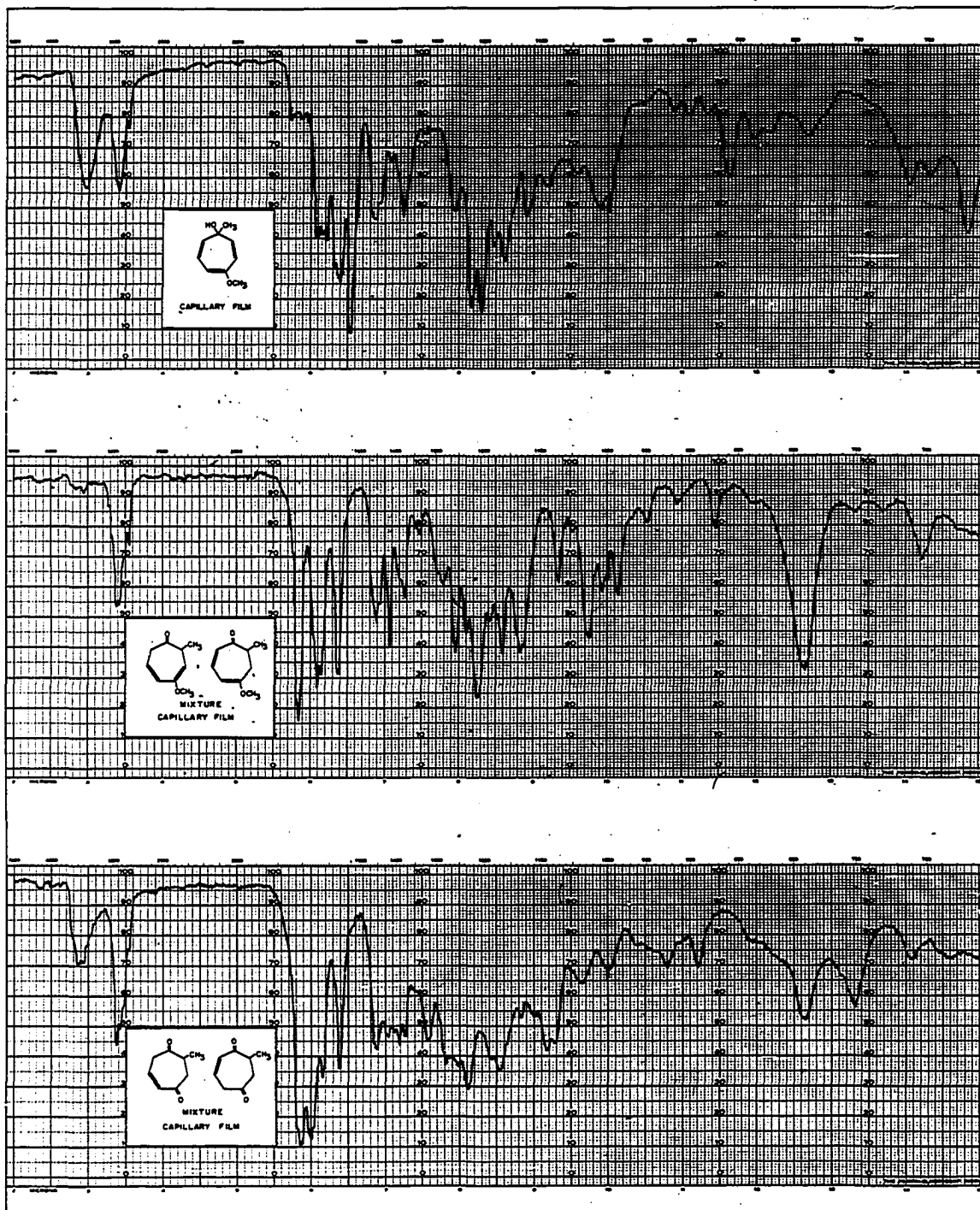


Figure 9. Infrared spectra

Top. 2-Methyl-4-methoxy-3,5-cycloheptadienol (XXI)

Middle. 5-Methoxy-2,4-cycloheptadienol (XL)

Bottom. 4-Methoxy-3,5-cycloheptadienol (XLI)

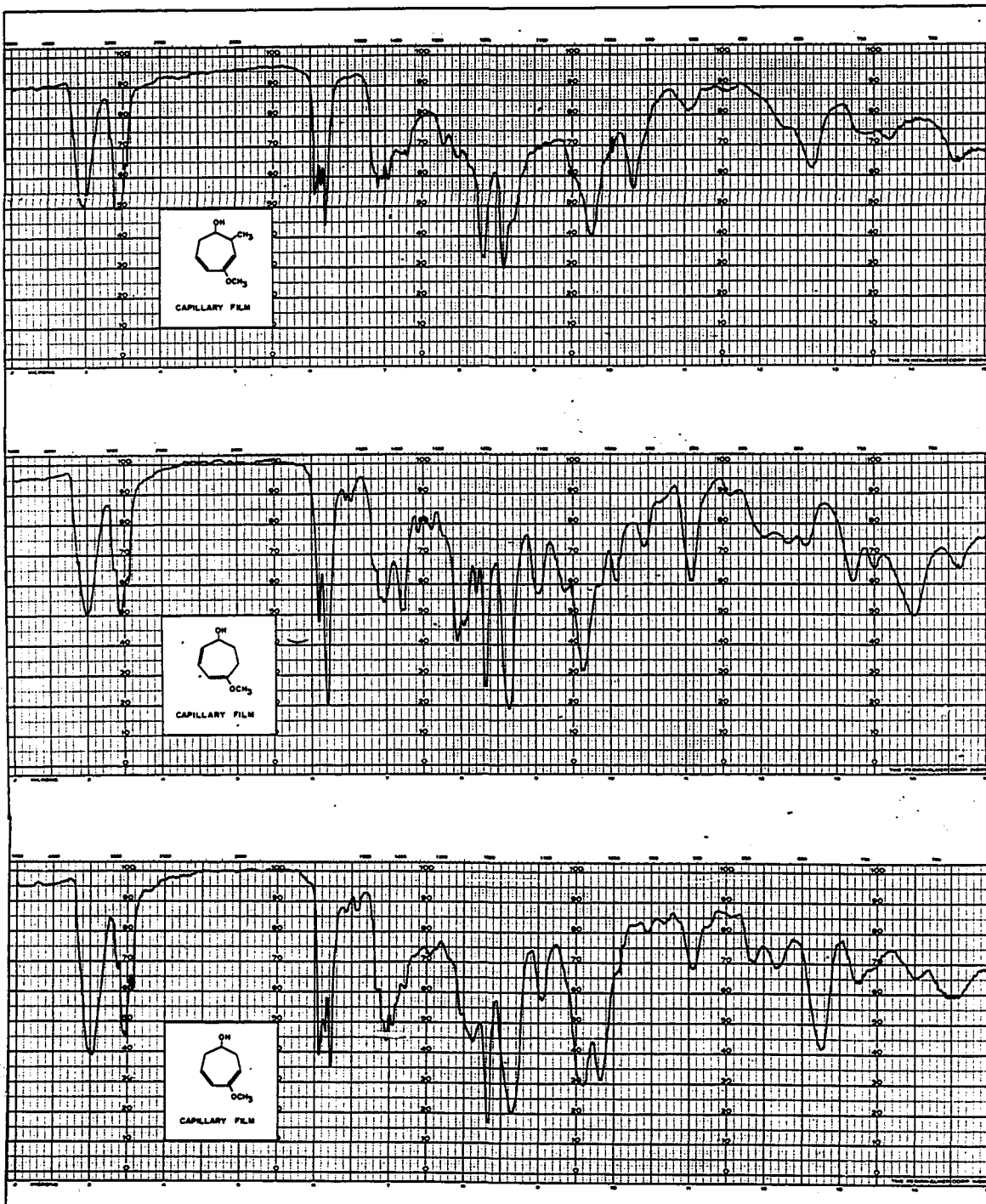


Figure 10. Infrared spectra

Top. 2-Methyl-gamma-tropolone methyl ether (XXIX)

Middle. 2-Methyl-7-bromo-gamma-tropolone methyl ether
(XXX)

Bottom. 2-Methyltropone (LIII)

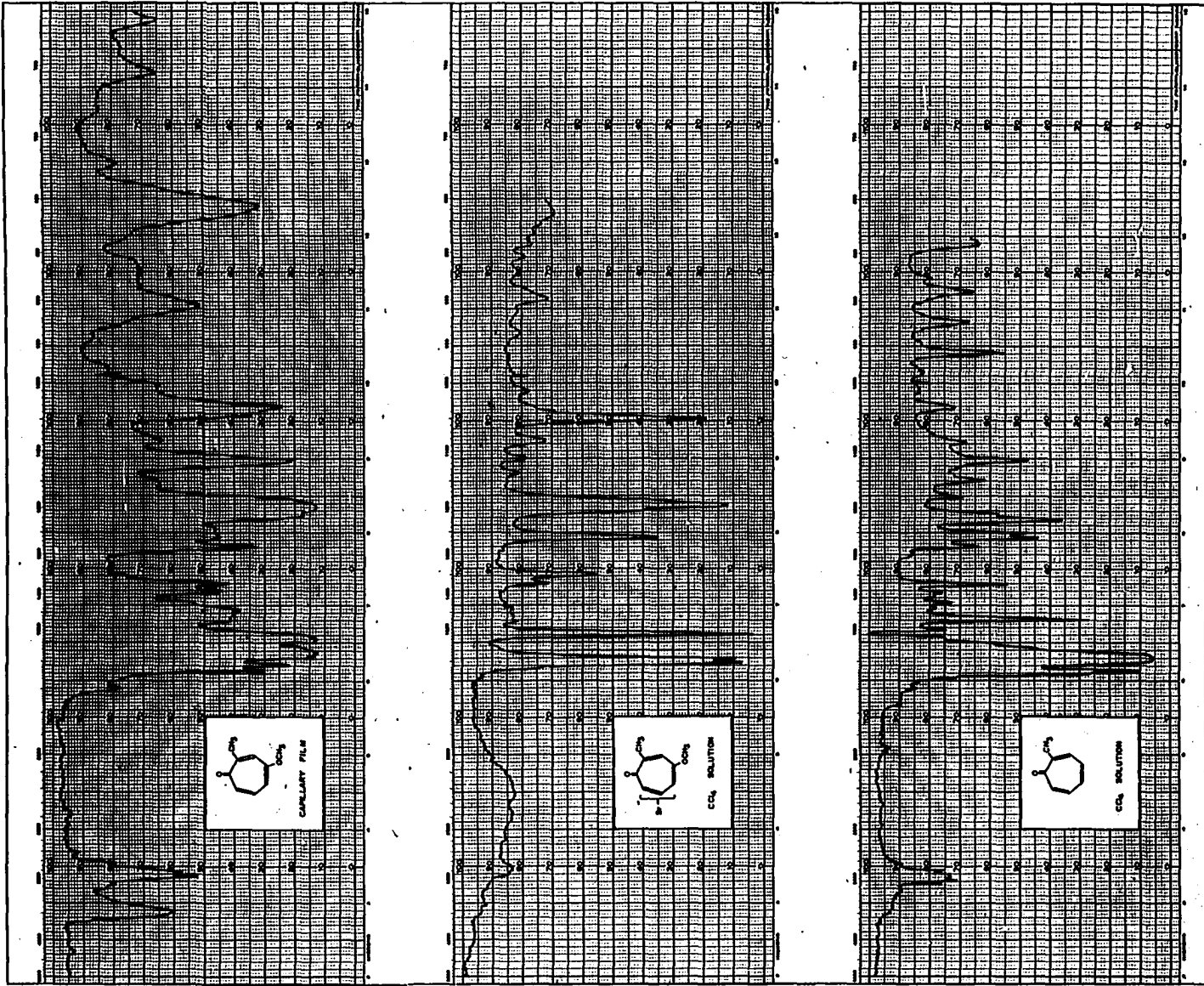


Figure 11. Infrared spectra

Top. 2-Methyl-4-methoxy-4,6-cycloheptadienone (XIX)

Middle. 5-Methoxy-2,4-cycloheptadienone (XXXII)

Bottom. 2-Cyclohepten-1,5-dione (XXXIII)

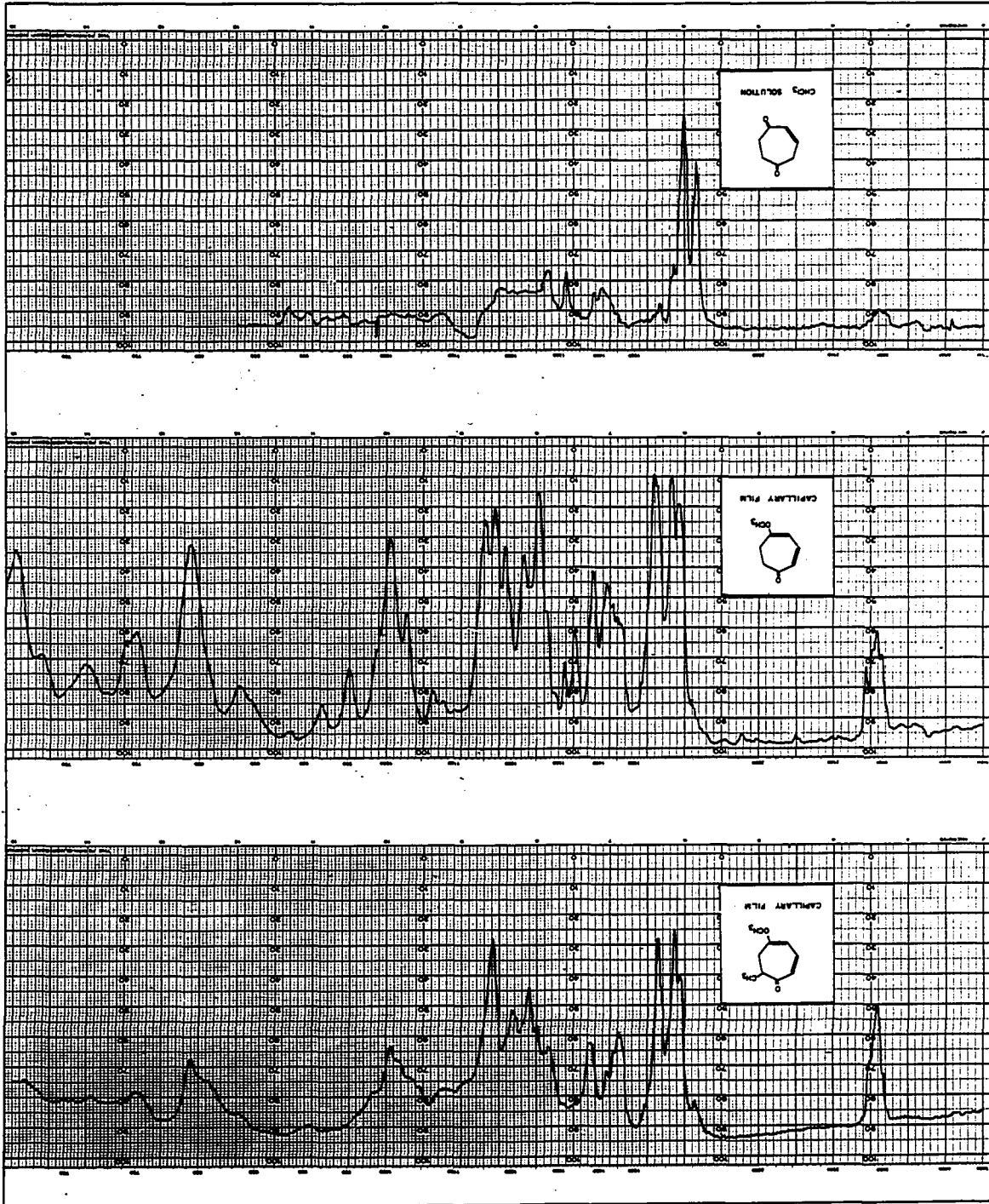


Figure 12. Infrared spectra

Top. 3-Hydroxy-6-ketobicyclo[3.2.0]heptane (XLVI)

Middle. 2-Hydroxy-5-methoxybicyclo[3.2.0]hept-6-ene
(XLIV)

Bottom. 2-Hydroxy-5-methoxybicyclo[3.2.0]hept-6-ene
after attempted acid hydrolysis

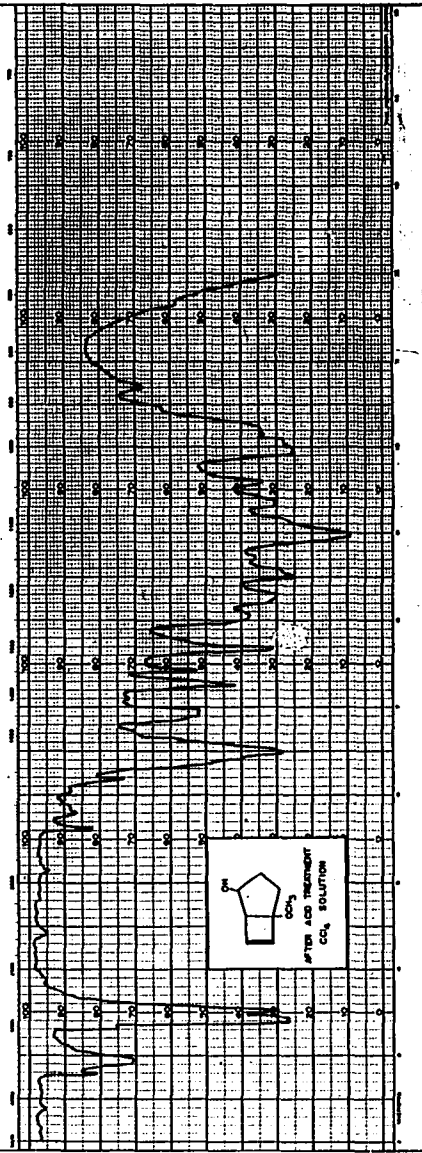
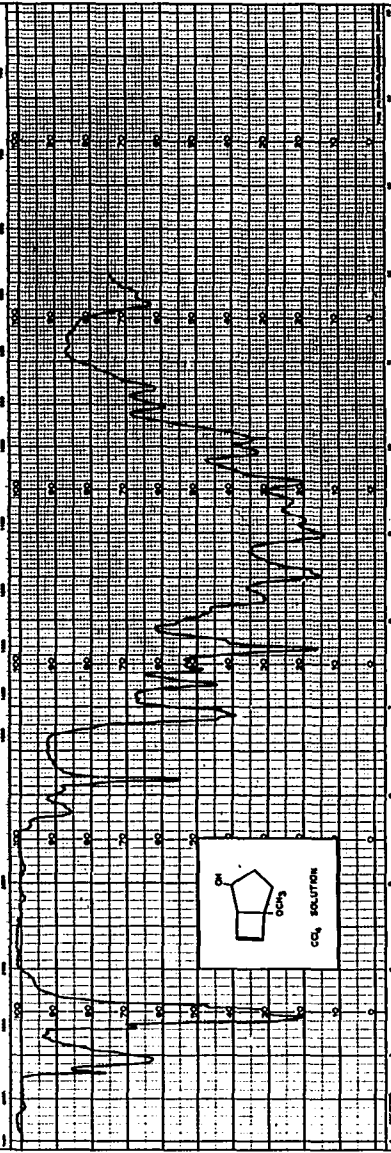
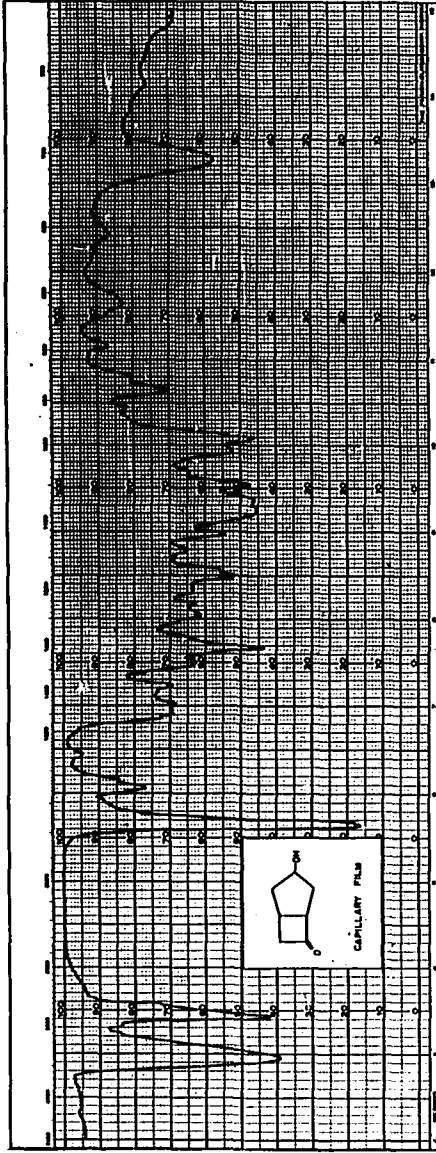


Figure 13. Infrared spectra

Top. 2-Methyl-3,5-cycloheptadienone (XLVII)

Middle. 3,5-Cycloheptadienone

Bottom. 3,5-Cycloheptadienol

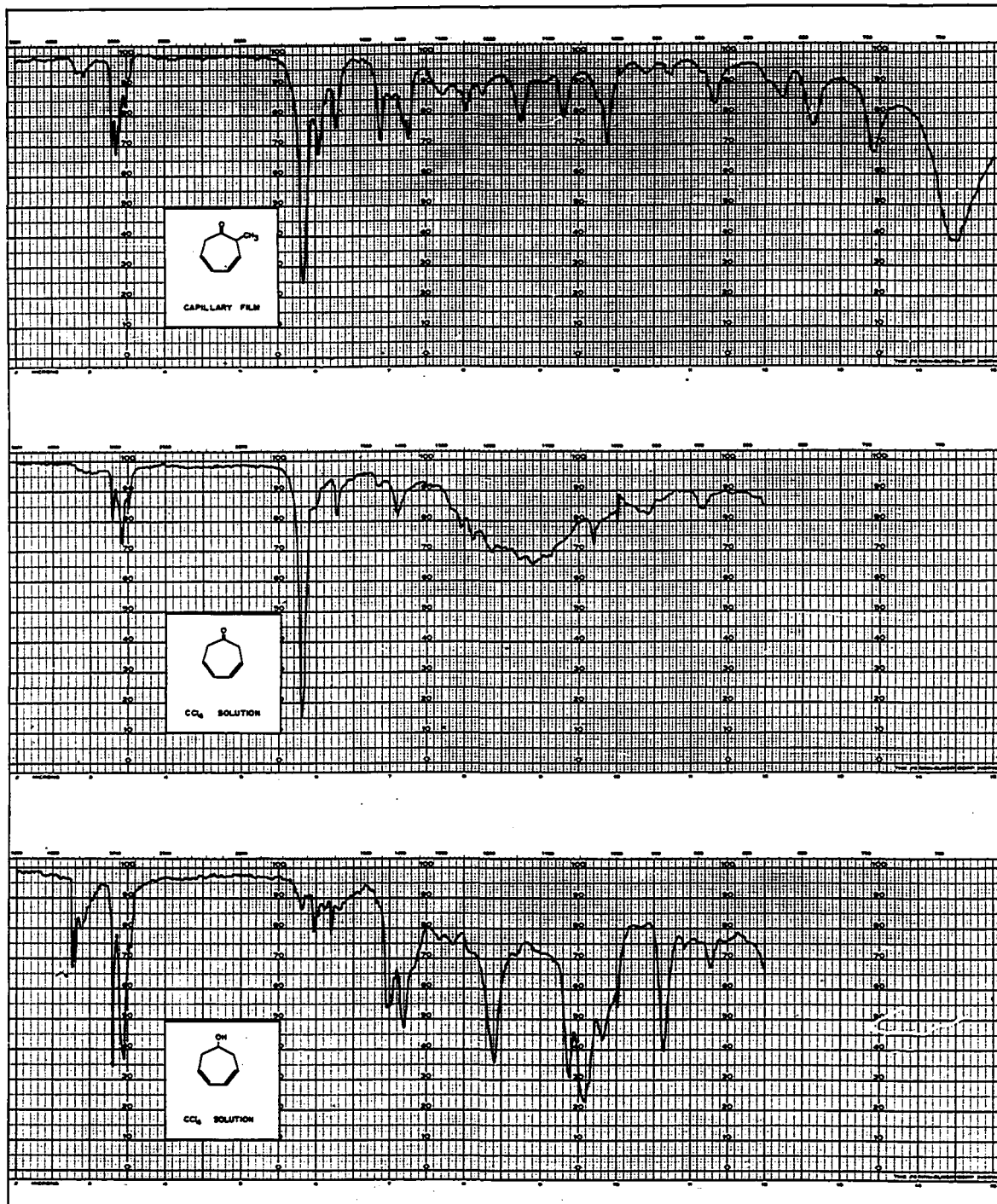


Figure 14. Infrared spectra

Top. Photo-gamma-tropolone methyl ether (LXV)

Middle. 5-Methoxybicyclo[3.2.0]-3-hepten-2-one (LXVII)

Bottom. 5-Methoxybicyclo[3.2.0]/heptan-2-one (LXVIII)

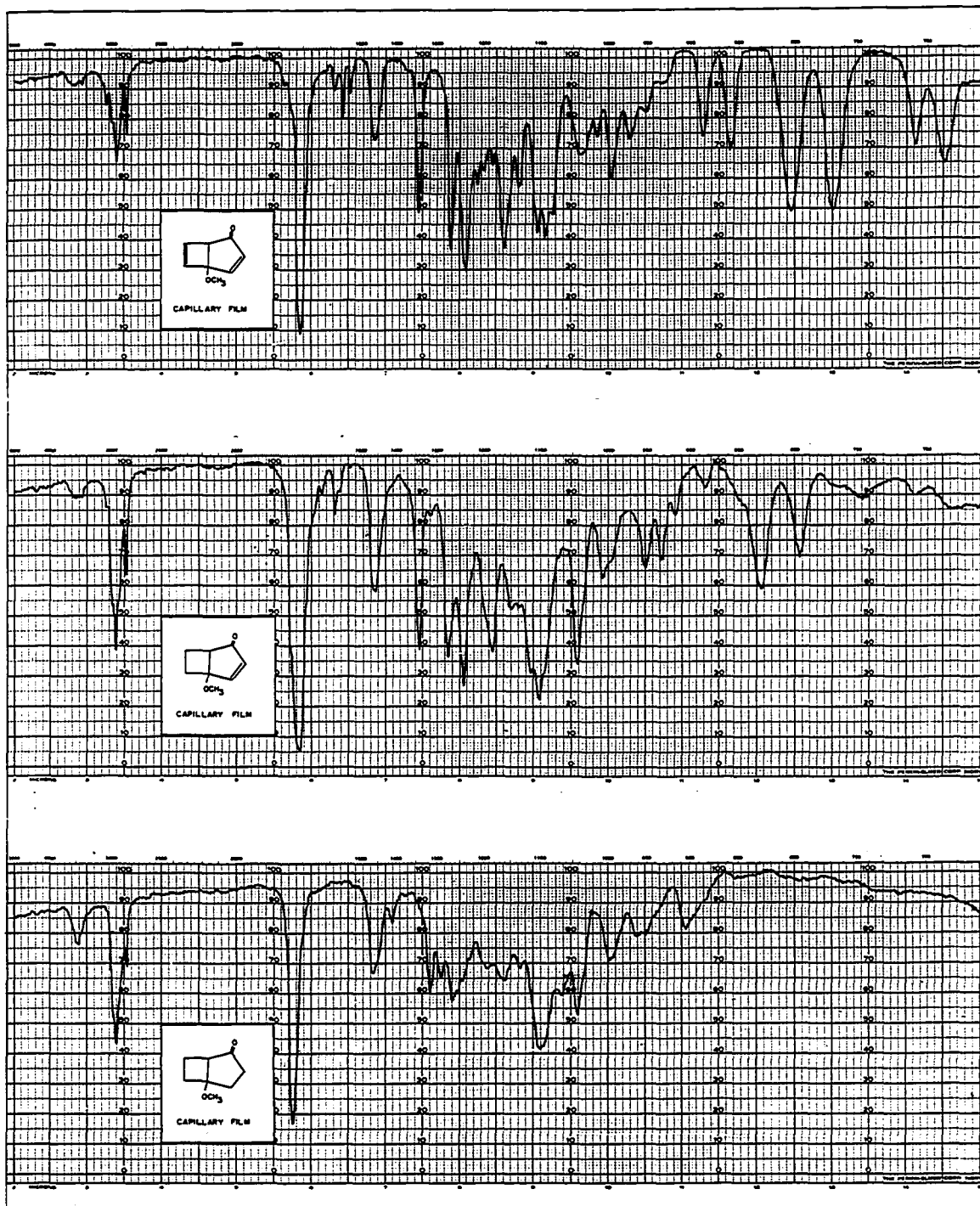


Figure 15. Infrared spectra

Top. 2-Hydroxy-5-methoxybicyclo[3.2.0]hepta-3,6-diene
(LXXVIII)

Middle. 2-Hydroxy-2-phenyl-5-methoxy[3.2.0]hepta-
3,6-diene (LXXXI)

Bottom. 4-Cyano-5-methoxybicyclo[3.2.0]hept-6-ene-2-one
(LXXV)

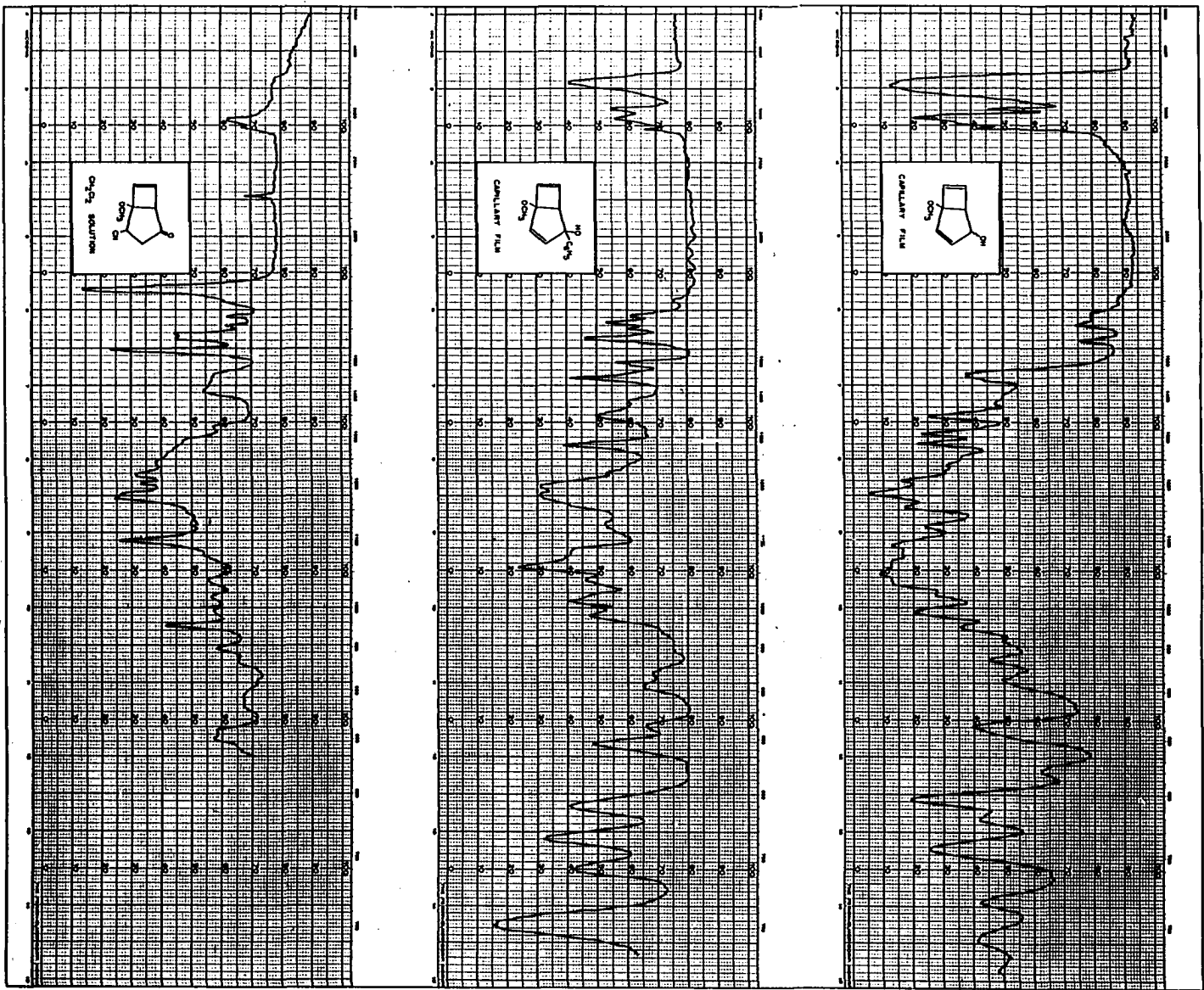


Figure 16. Infrared spectra

Top. Dimer A

Middle. Dimer B

Bottom. Tetrahydro-dimer A

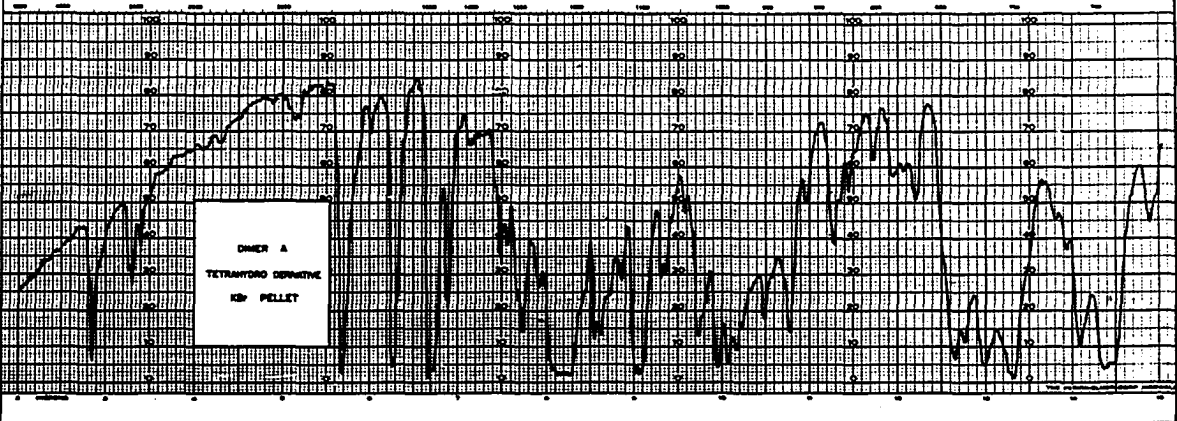
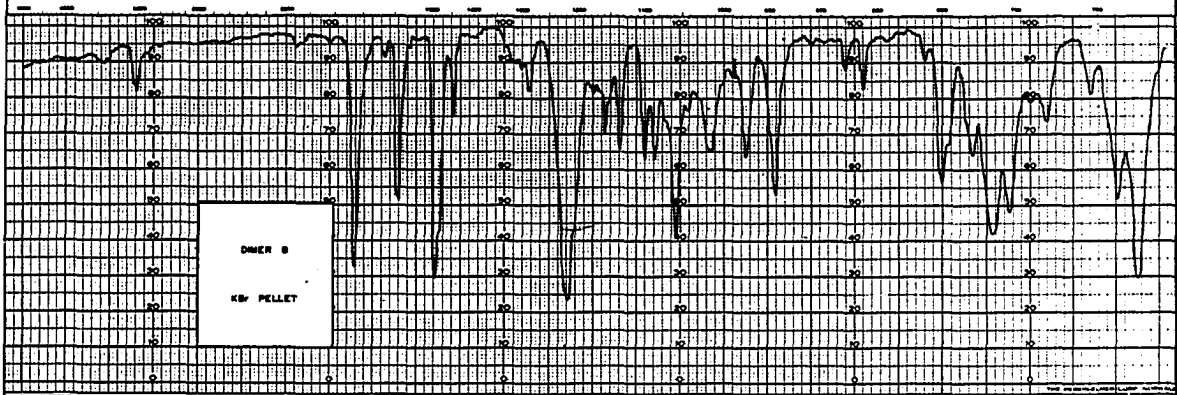
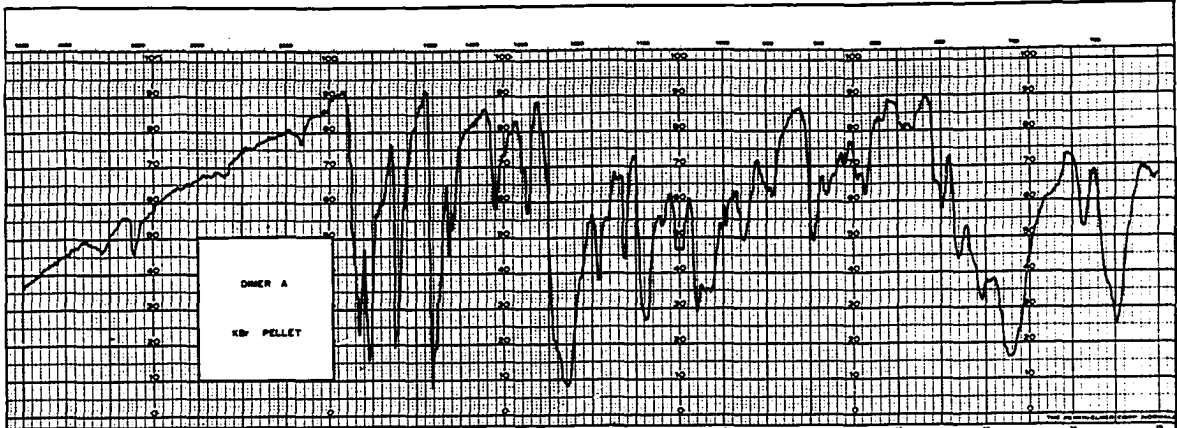


Figure 17. Infrared spectra.

Top. Dimer A hydride alcohol

Middle. Dimer B hydride alcohol

Bottom. Dimer B hydride alcohol acetate

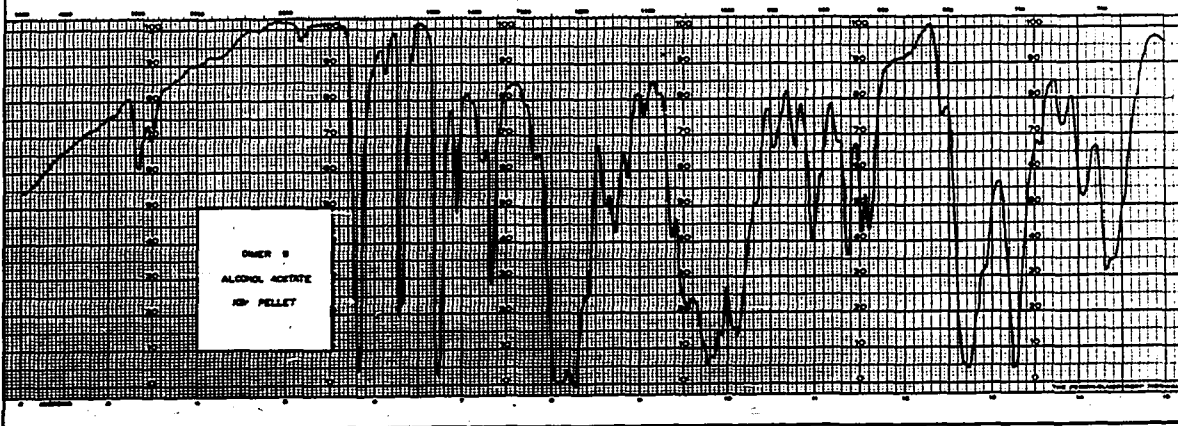
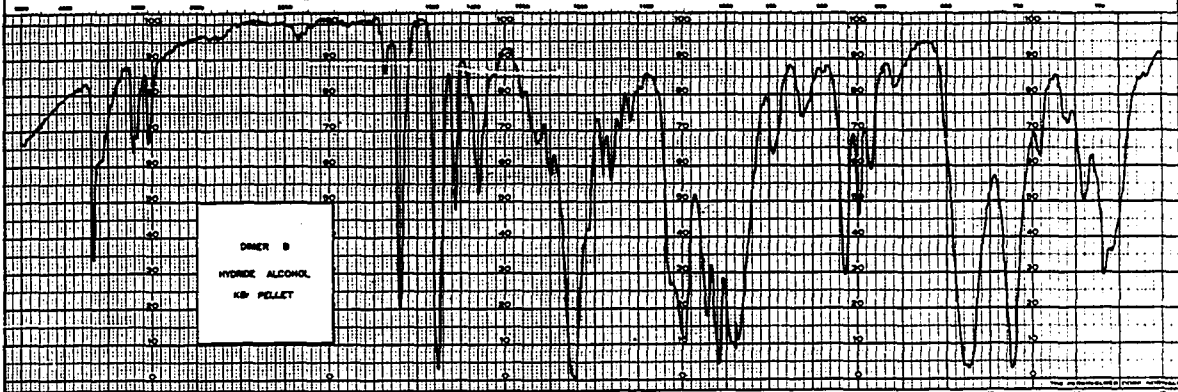
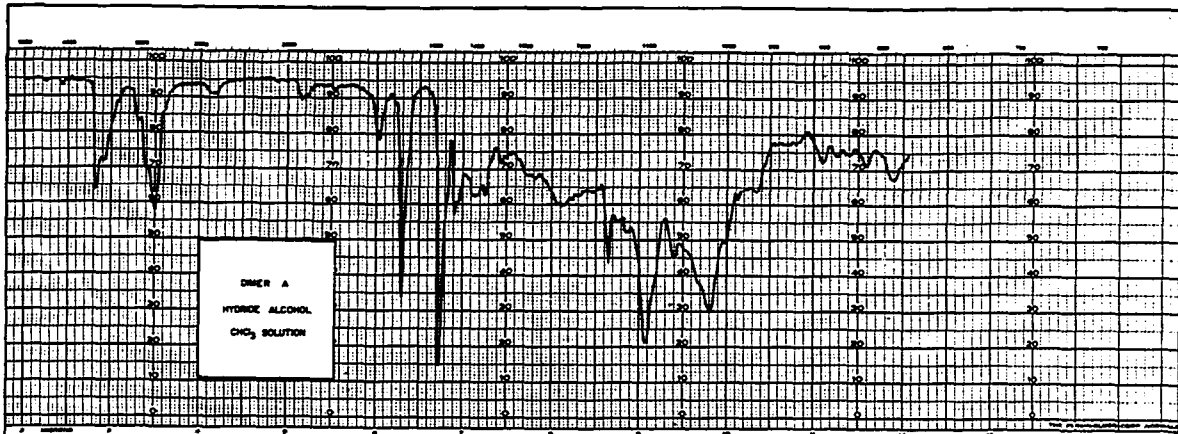


Figure 18. Infrared spectra

Top. Dimer A oxime

Middle. Dimer A ozonolysis product

Bottom. 2-Cycloheptene-1,4-dione (XXXVI)

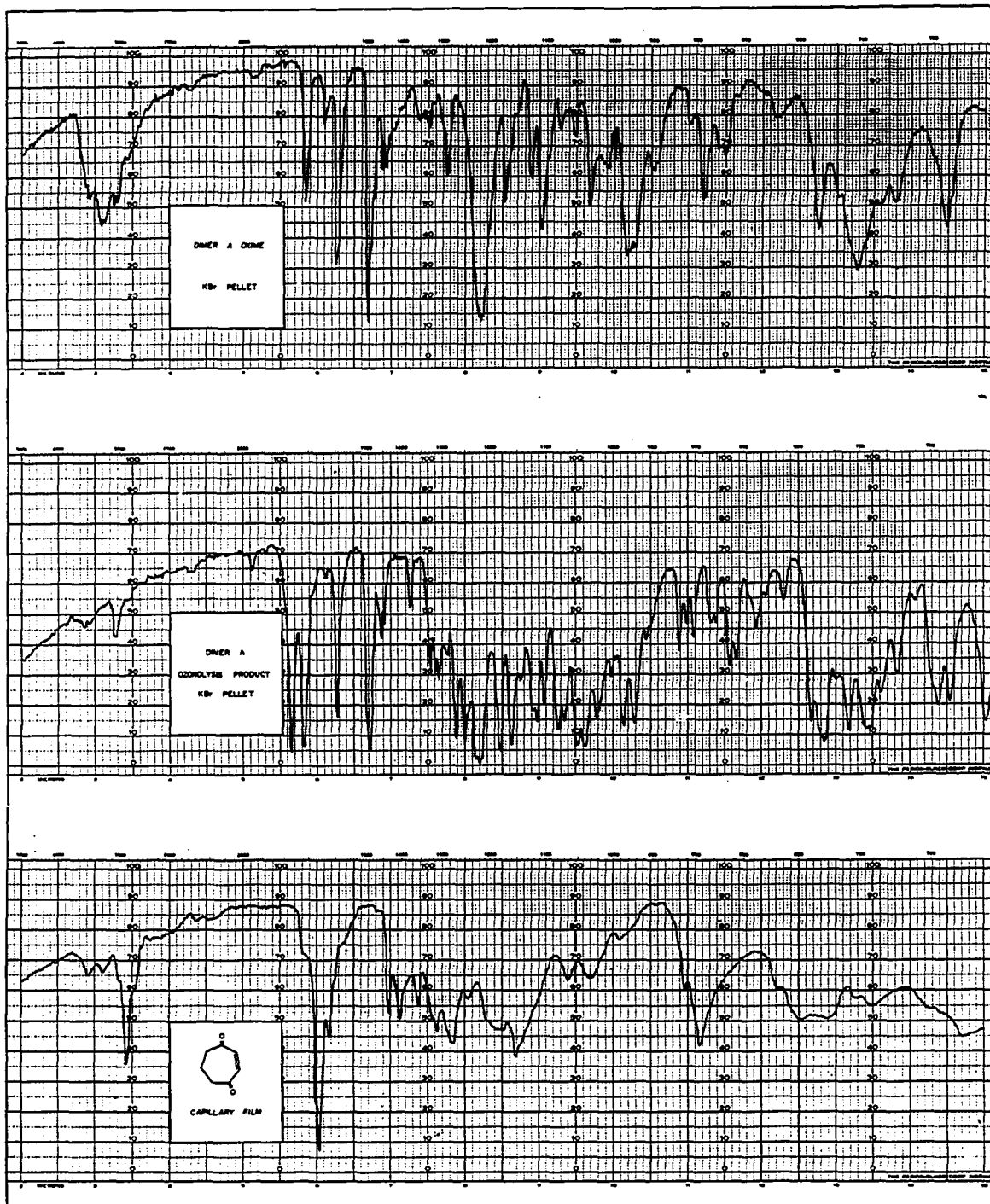


Figure 19. Ultraviolet spectra.

- A. 2-Methyl-4-methoxy-3,5-cycloheptadienone:
2-methyl-4-methoxy-4,6-cycloheptadienone
mixture (XVII and XIX)
- B. 2-Methyl-5-cyclohepten-1,4-dione:2-methyl-6-
cyclohepten-1,4-dione mixture

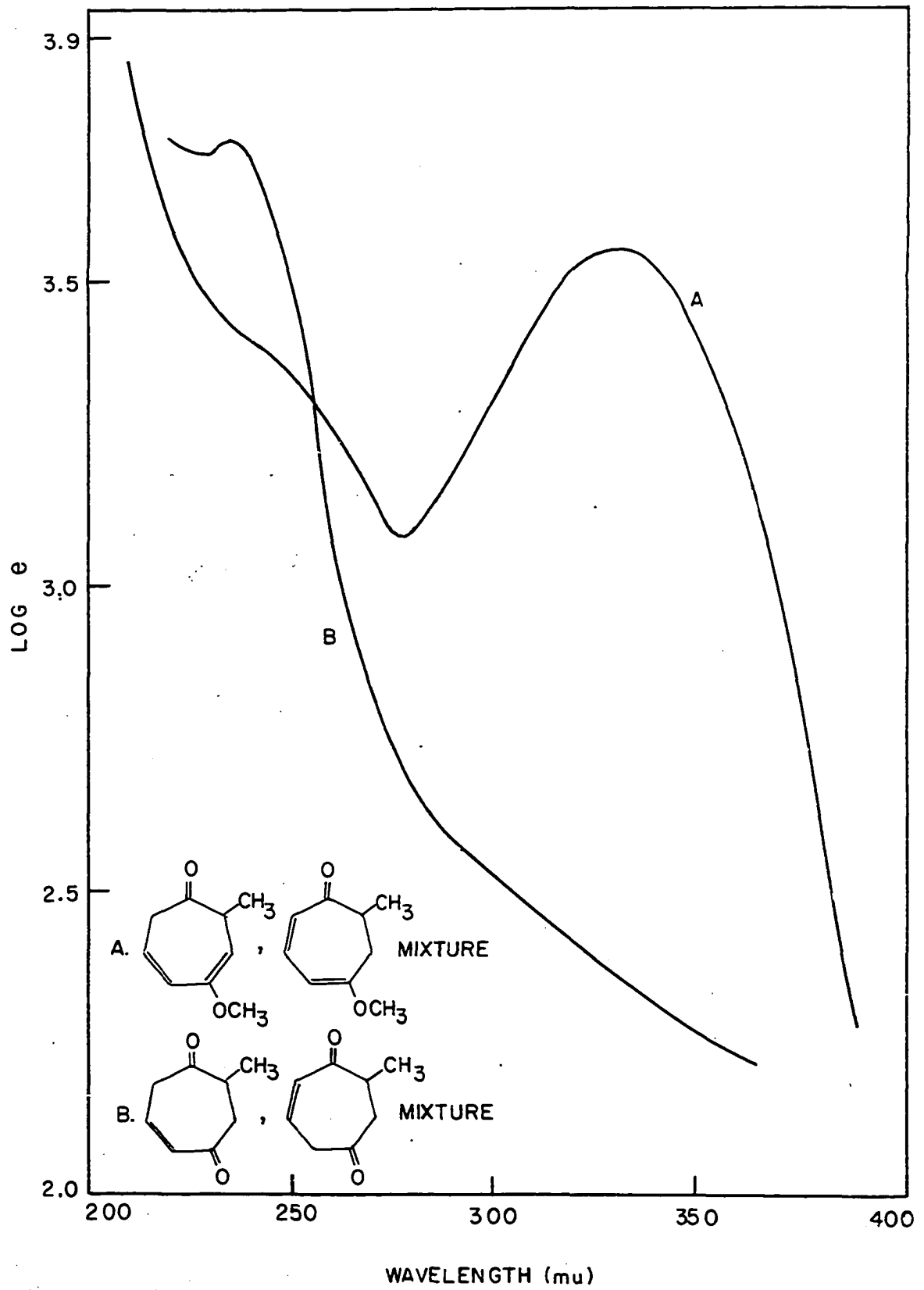


Figure 20. Ultraviolet spectra

- A. 2-Methyl-4-methoxy-3,5-cycloheptadienol mixture (XXI)
- B. Hydrolysis product of 2-methyl-4-methoxy-3,5-cycloheptadienol mixture

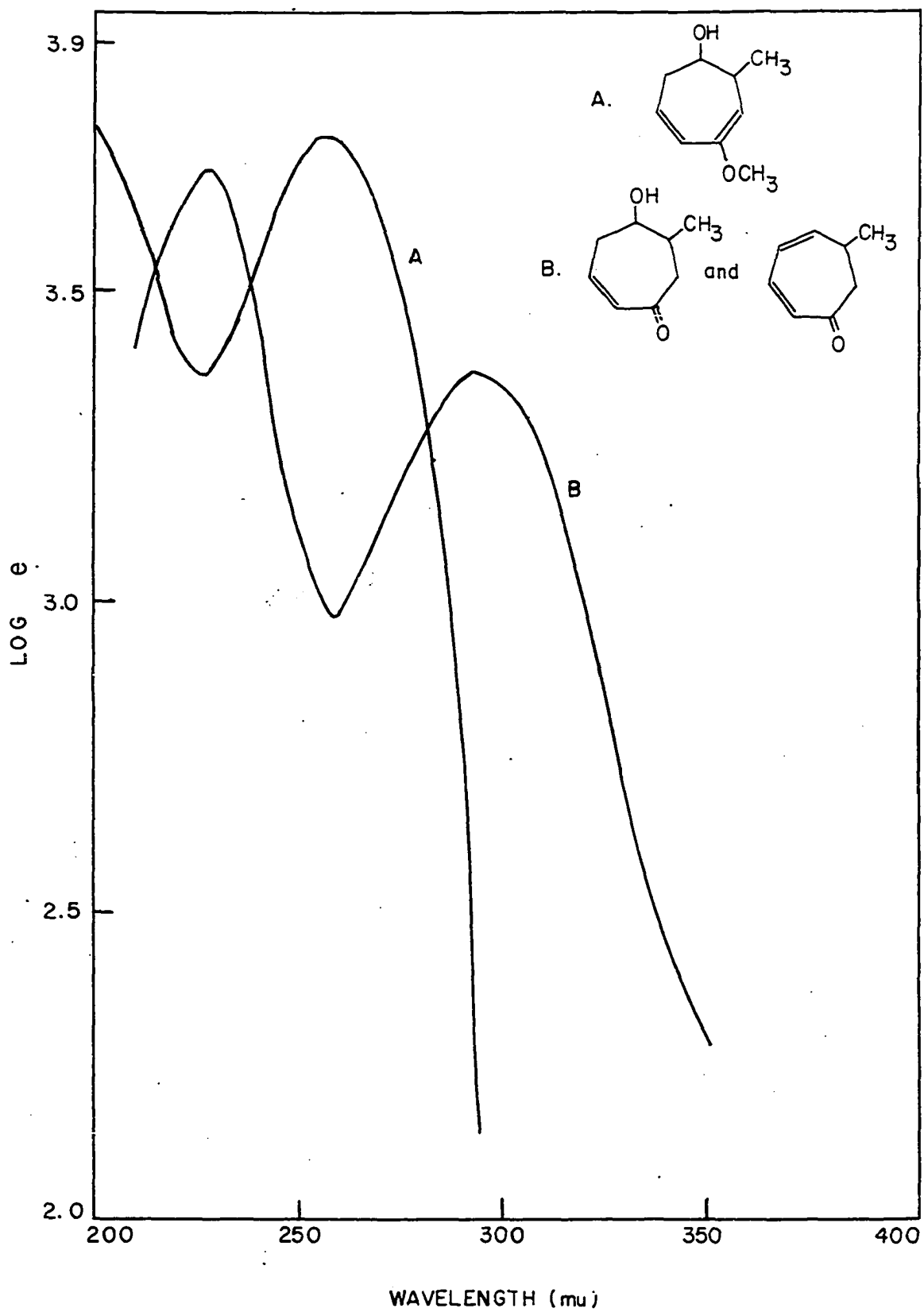


Figure 21. Ultraviolet spectra

- 2-Methyl-gamma-tropolone methyl ether (XXIX)
- Anion in 0.1 N sodium hydroxide
- Free tropolone in 0.1 N sulfuric acid

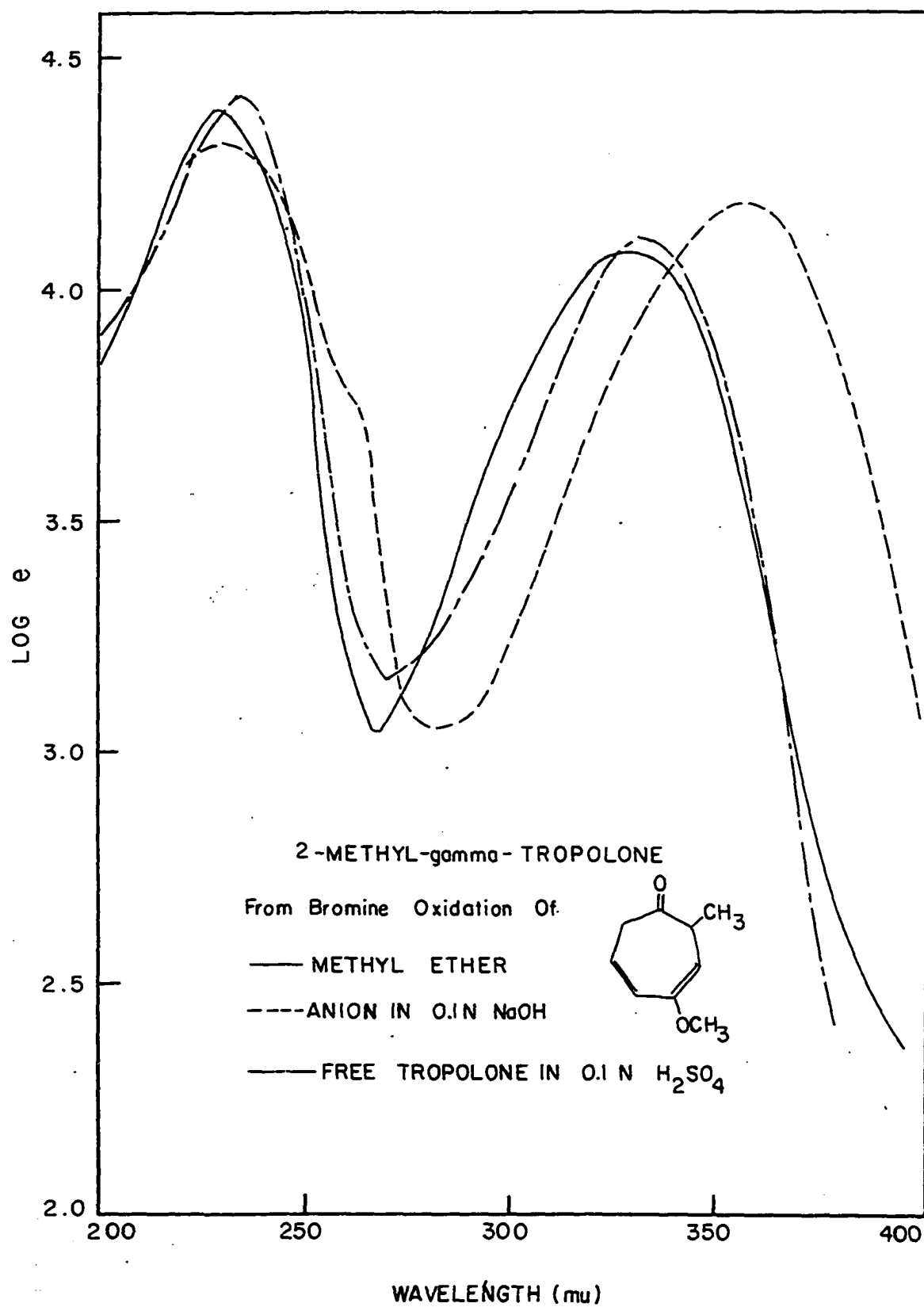


Figure 22. Ultraviolet spectra

- 2-Methyl-7-bromo-gamma-tropolone methyl ether (XXX)
- Anion in 0.1 N sodium hydroxide
- Free tropolone in 0.1 N sulfuric acid

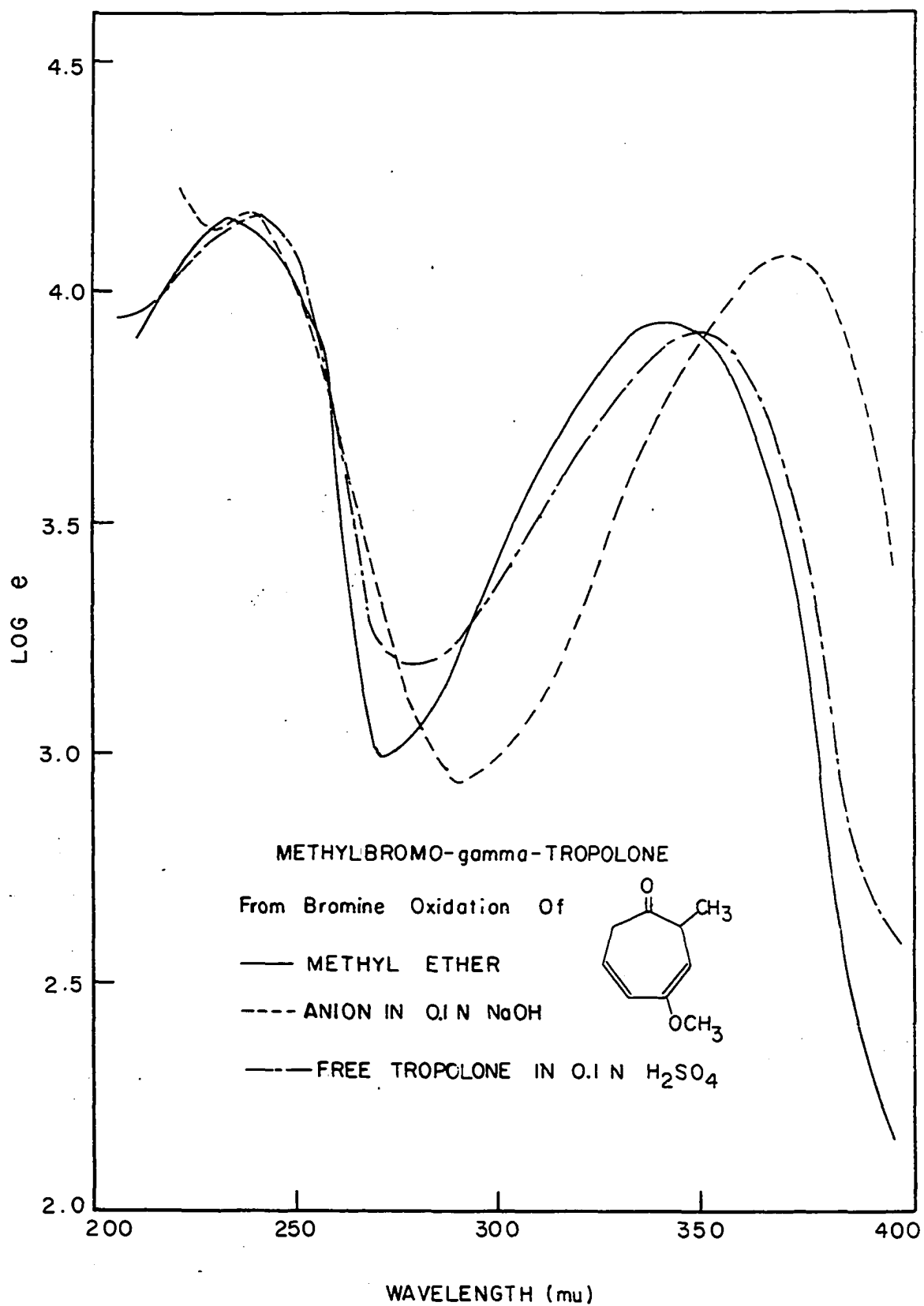


Figure 23. Ultraviolet spectrum of 1-hydroxy-1-methyl-4-methoxy-2,4,6-cycloheptatriene (XXXI)

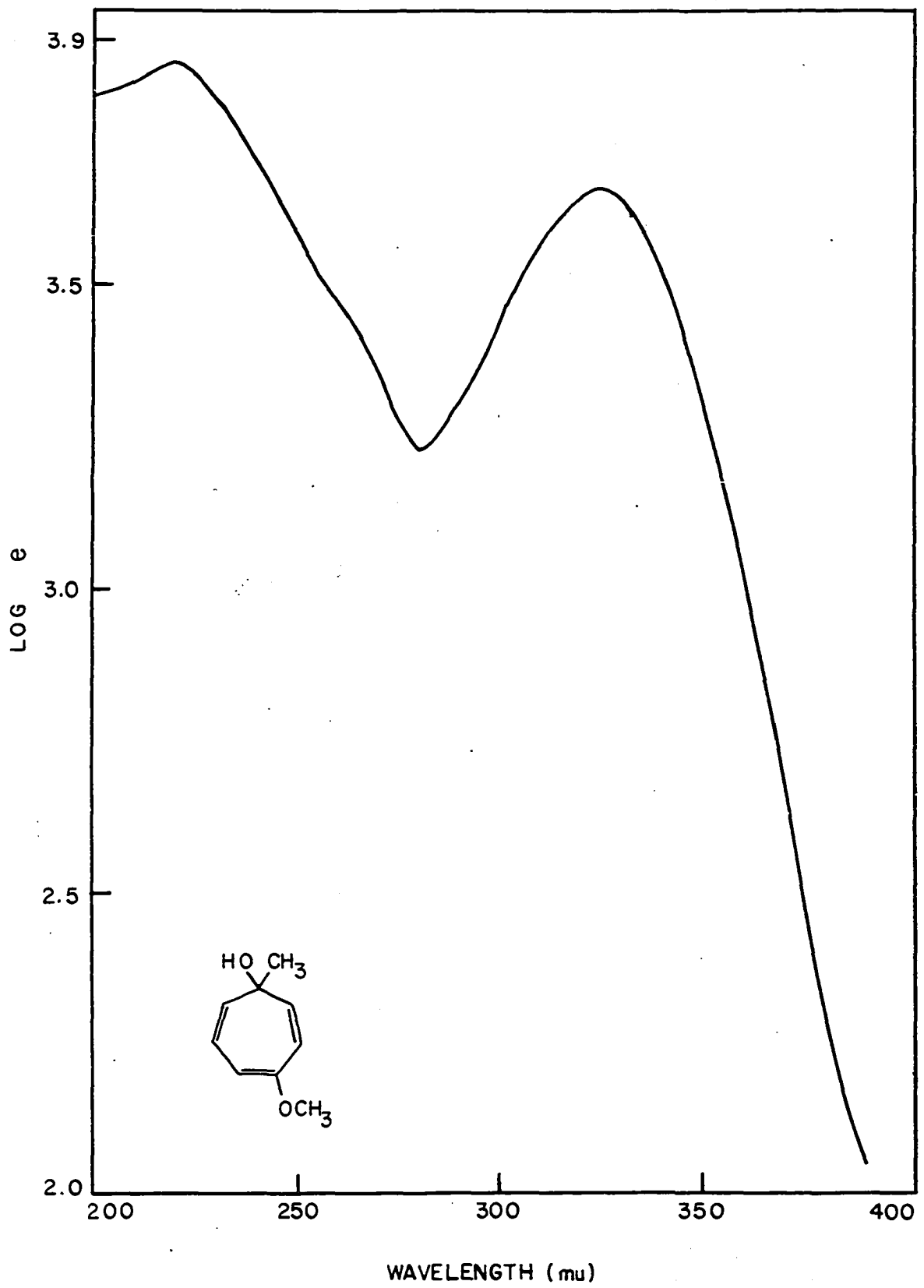


Figure 24. Ultraviolet spectra

A. 5-Methoxy-2,4-cycloheptadienone (XXXII)

B. 2-Cyclohepten-1,5-dione (XXXIII)

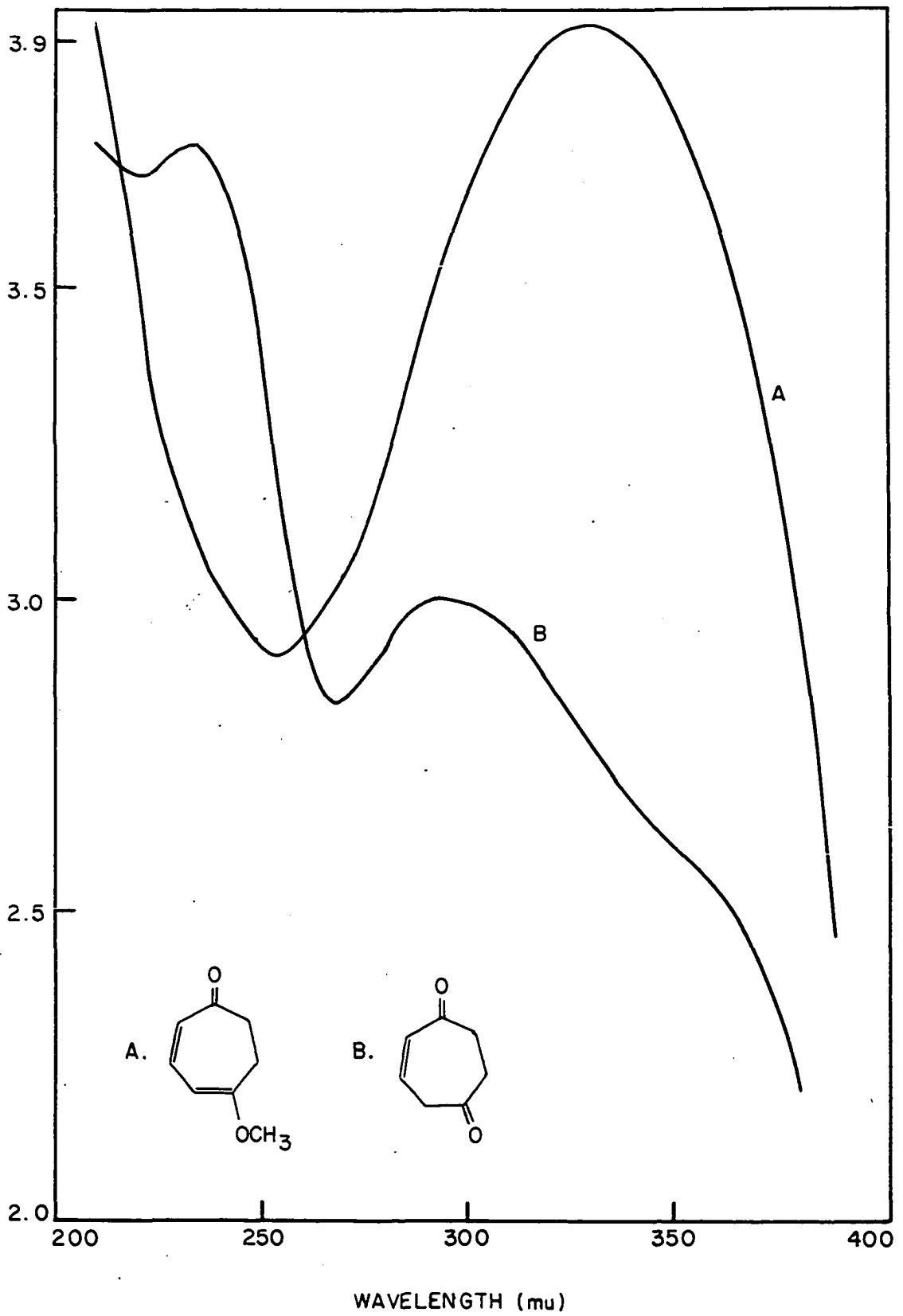


Figure 25. Ultraviolet spectrum of 2-cycloheptene-1,4-dione
(XXXVI)

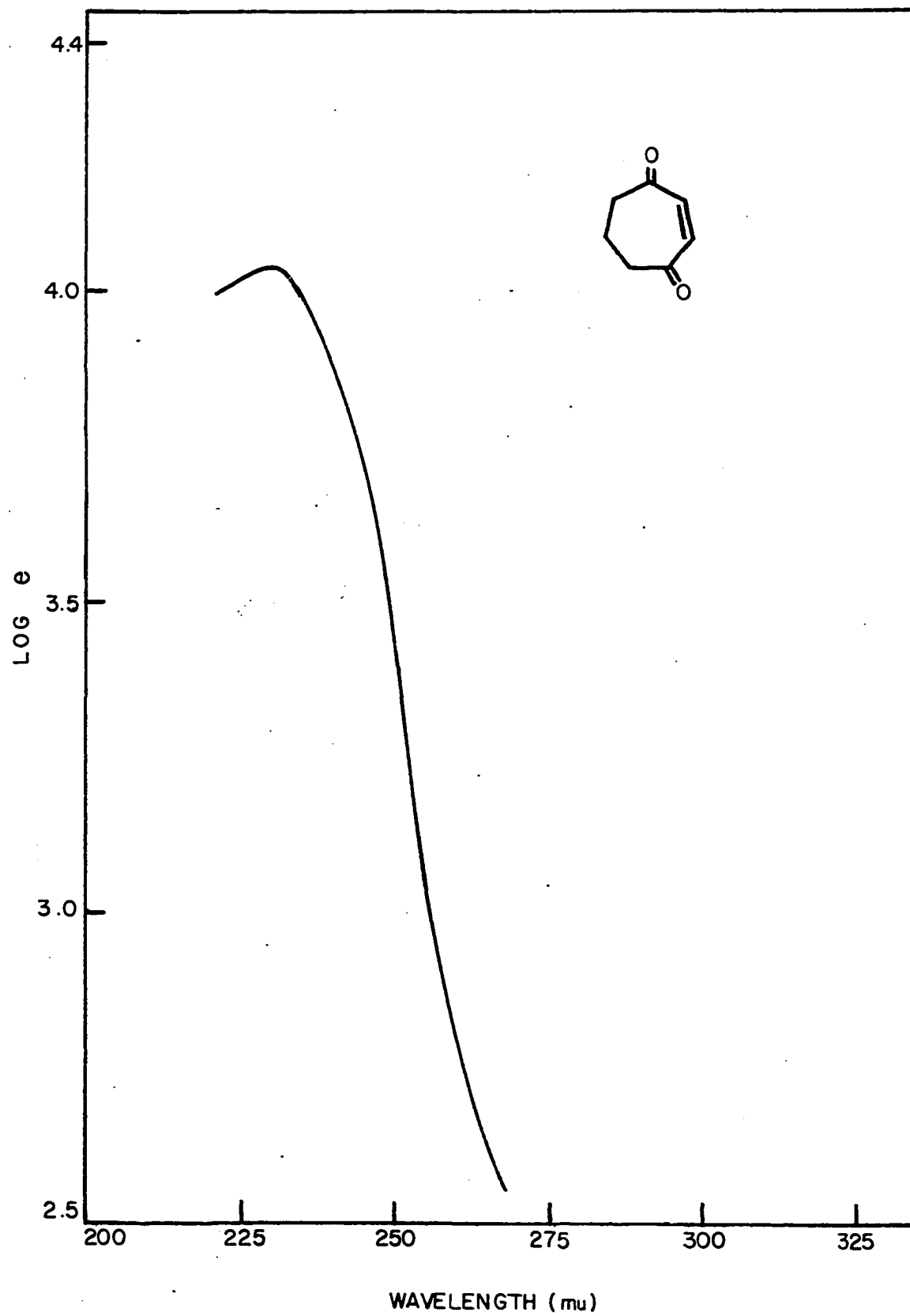


Figure 26. Ultraviolet spectra

- A. 5-Methoxy-2,4-cycloheptadienol (XL)
- B. 2,4-Cycloheptadienone from acid hydrolysis of
5-methoxy-2,4-cycloheptadienol (XL)

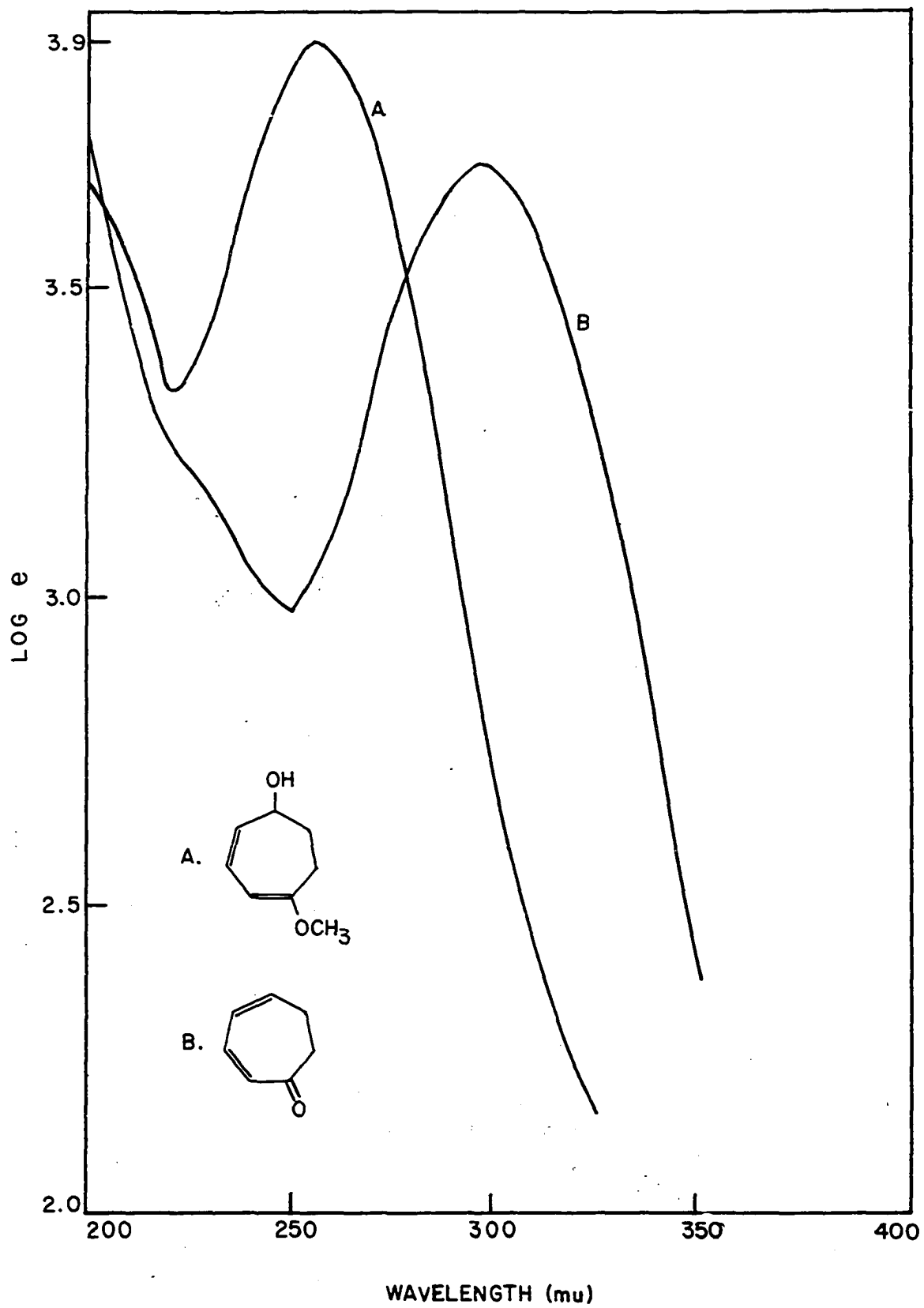


Figure 27. Ultraviolet spectra

- A. 4-Methoxy-3,5-cycloheptadienol (XII)
- B. Acid hydrolysis product of 4-methoxy-3,5-cycloheptadienol

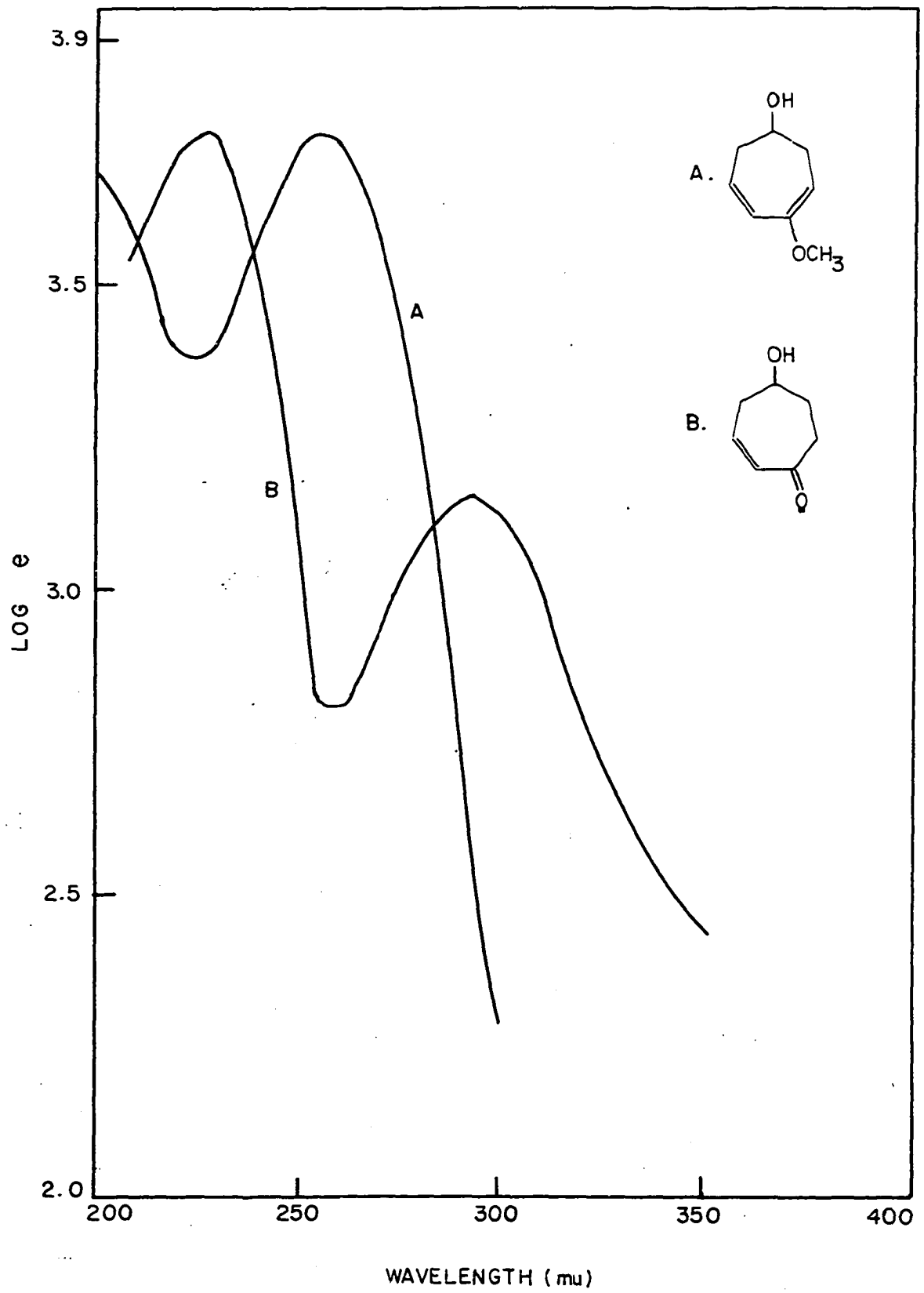


Figure 28. Ultraviolet spectra

A. 2-Methyltropone (LIII)

B. 2-Methyl-3,5-cycloheptadienone (XLVII)

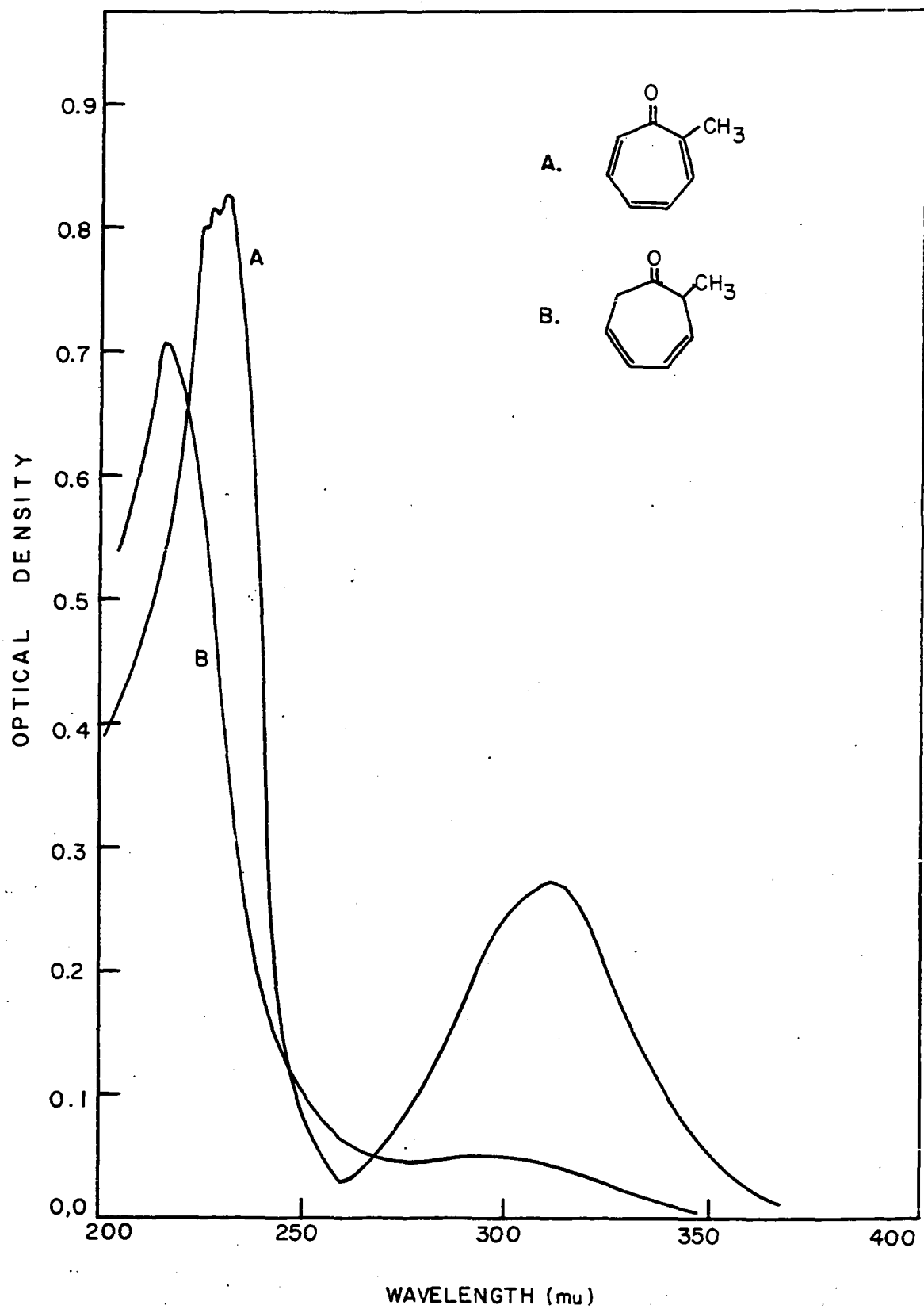


Figure 29. Ultraviolet spectrum of alcohol from hydride reduction of 2-methyl-3,5-cycloheptadienone

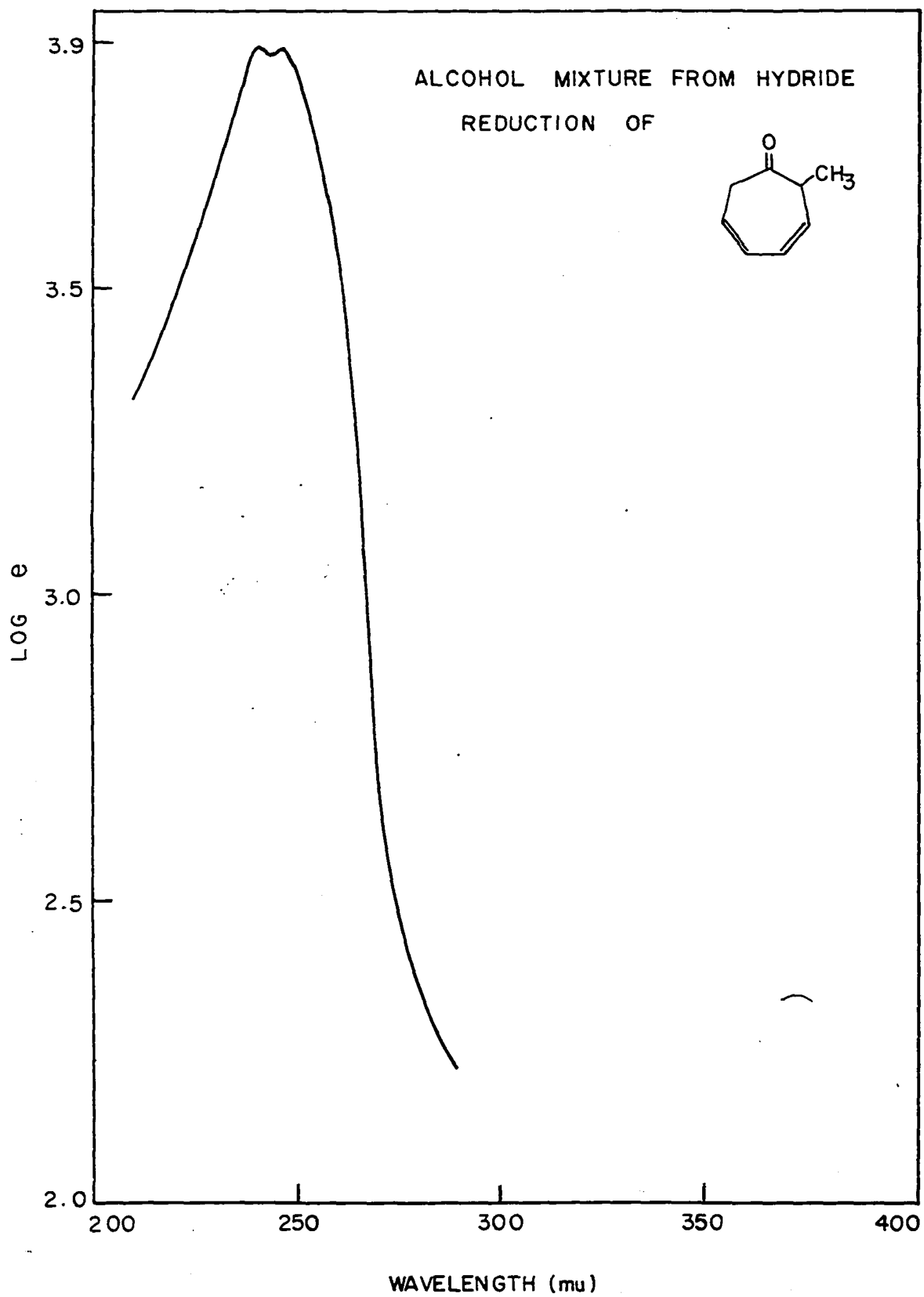


Figure 30. Ultraviolet spectra

- A. Photo-gamma-tropolone methyl ether (LXV)
- B. 5-Methoxybicyclo[3.2.0]hept-3-ene-2-one (LXVII)

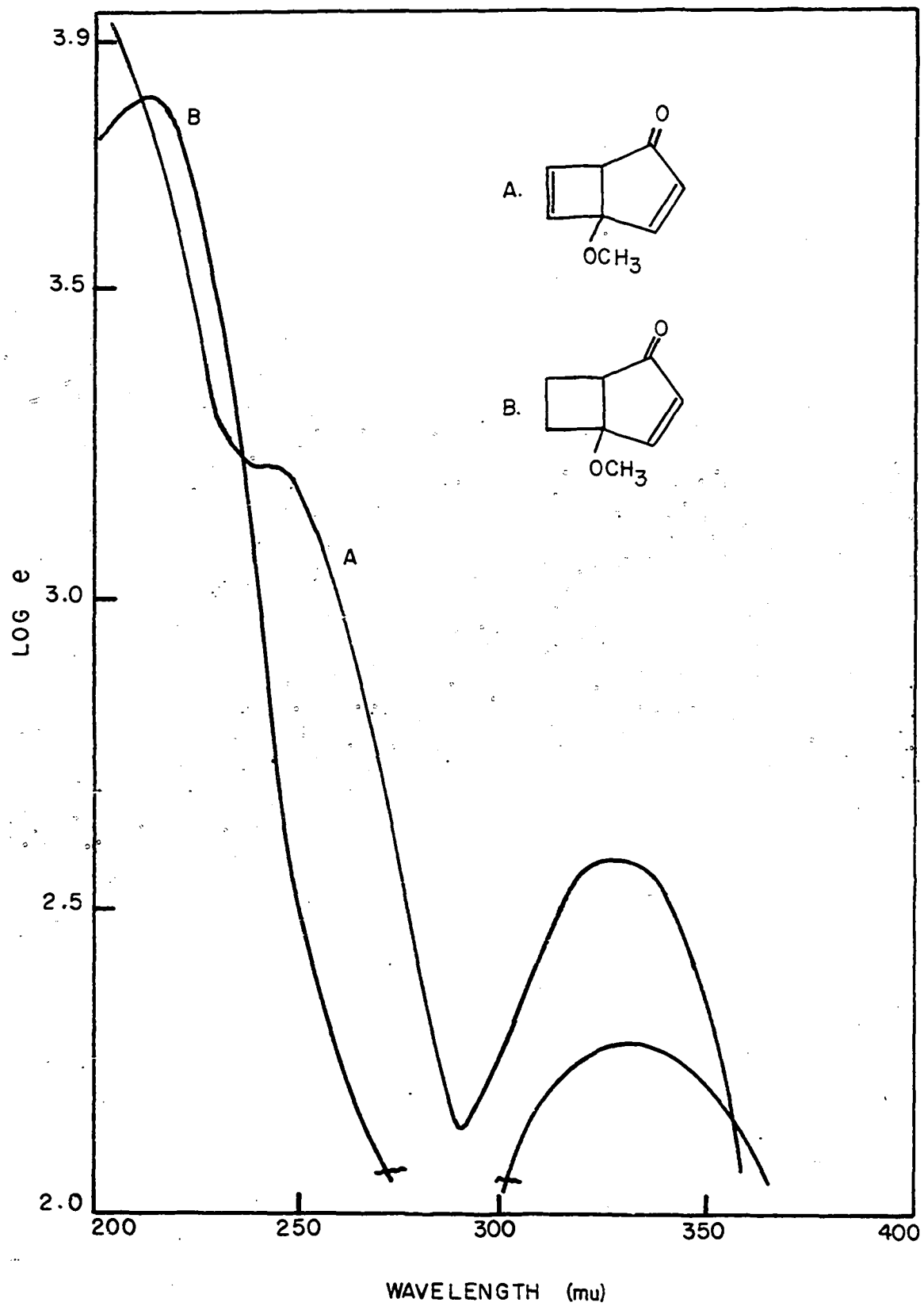


Figure 31. Ultraviolet spectra

- A. 2-Hydroxy-2-phenyl-5-methoxybicyclo[3.2.0]hepta-3,6-diene (LXXXI)
- B. 2-Hydroxy-5-methoxybicyclo[3.2.0]hepta-3,6-diene (LXXVIII)

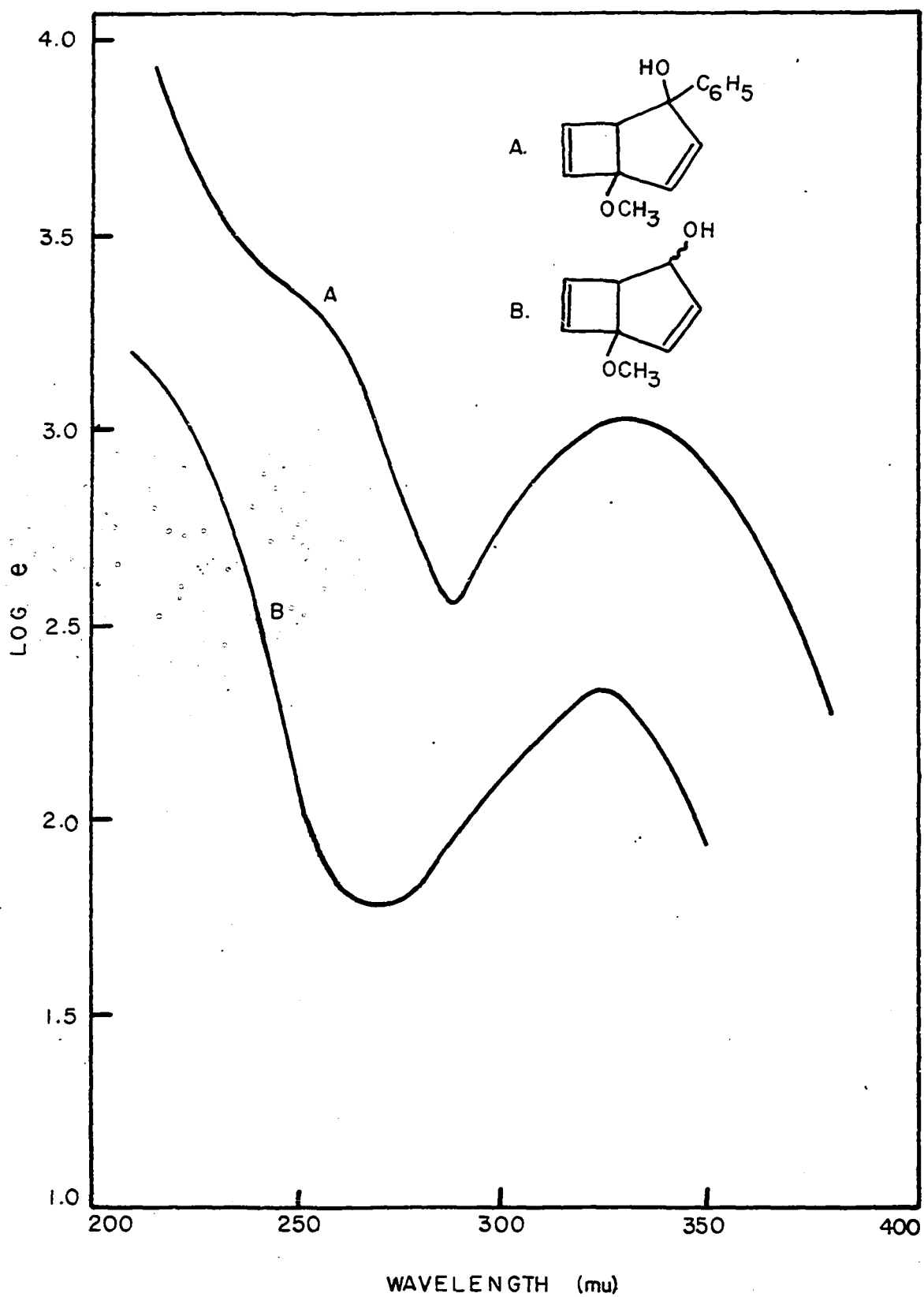


Figure 32. Ultraviolet spectra

- Dimer A
- Tetrahydro-dimer A
- Dimer A hydride alcohol

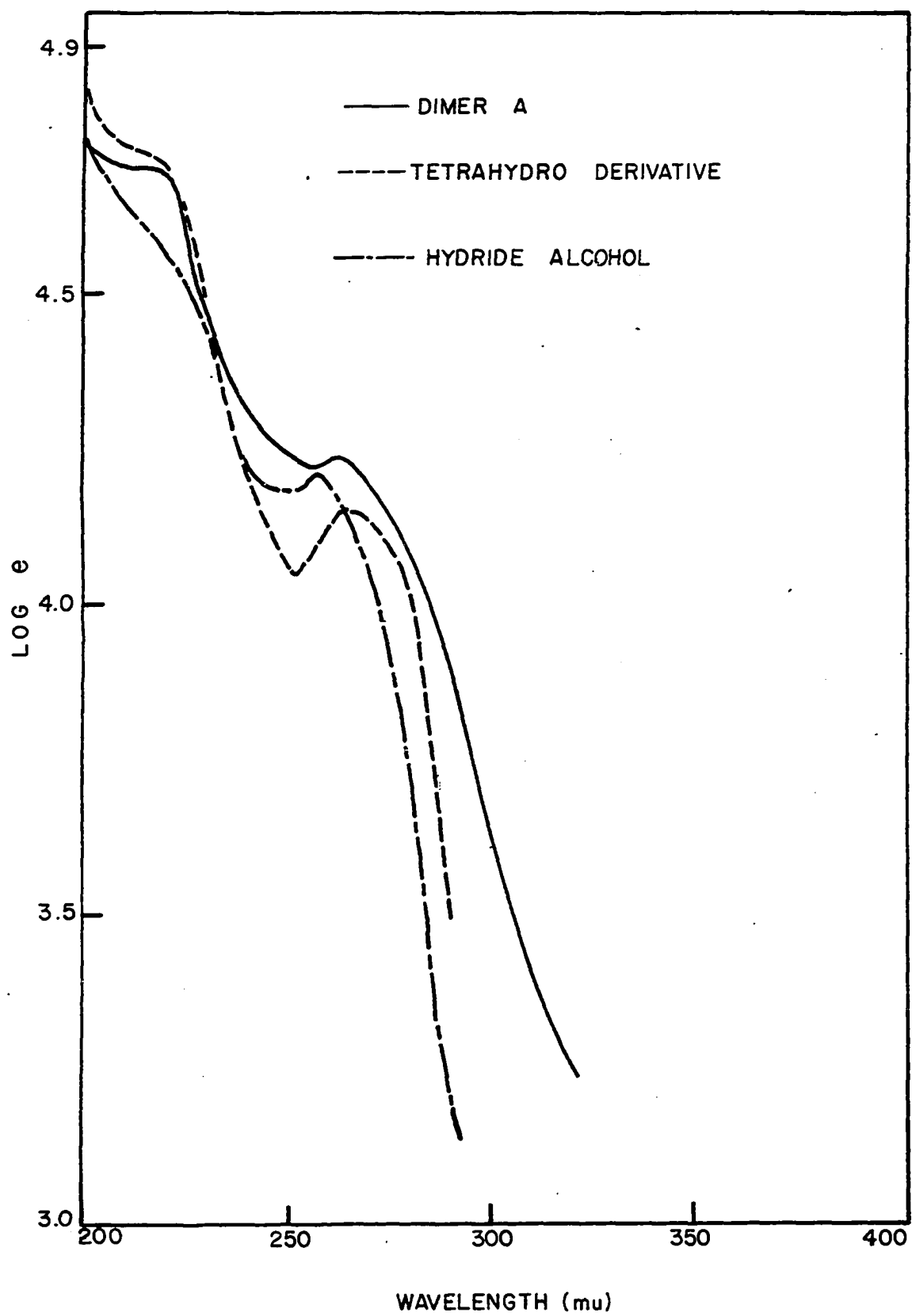


Figure 33. Ultraviolet spectra

_____ Dimer B

----- Dimer B hydride alcohol

----- Dimer B hydride alcohol acetate

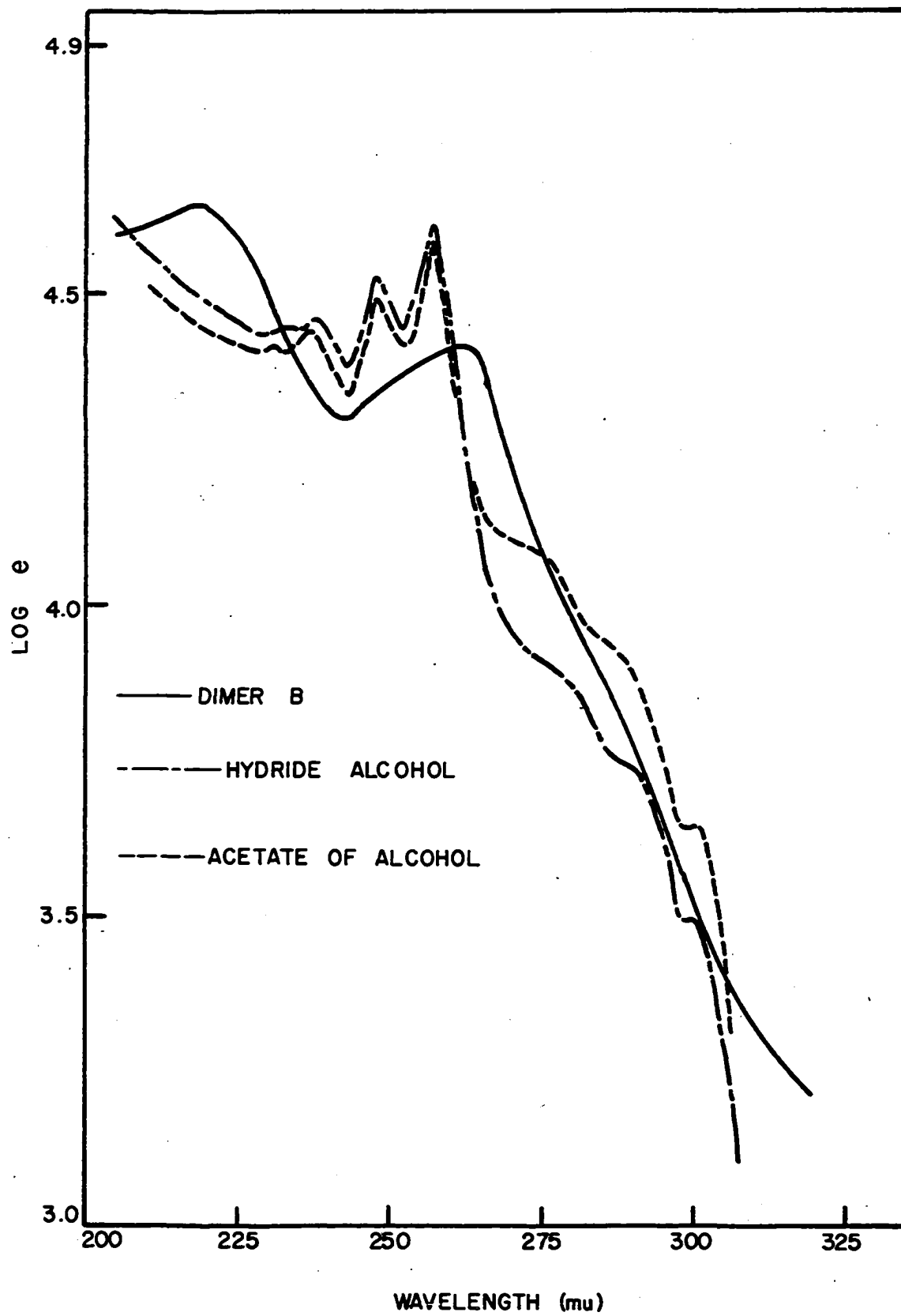


Figure 34. Nuclear magnetic resonance spectrum of photo-
gamma-tropolone methyl ether (LXV)

NMR SPECTRUM OF PHOTO- γ -TROPOLONE METHYL ETHER

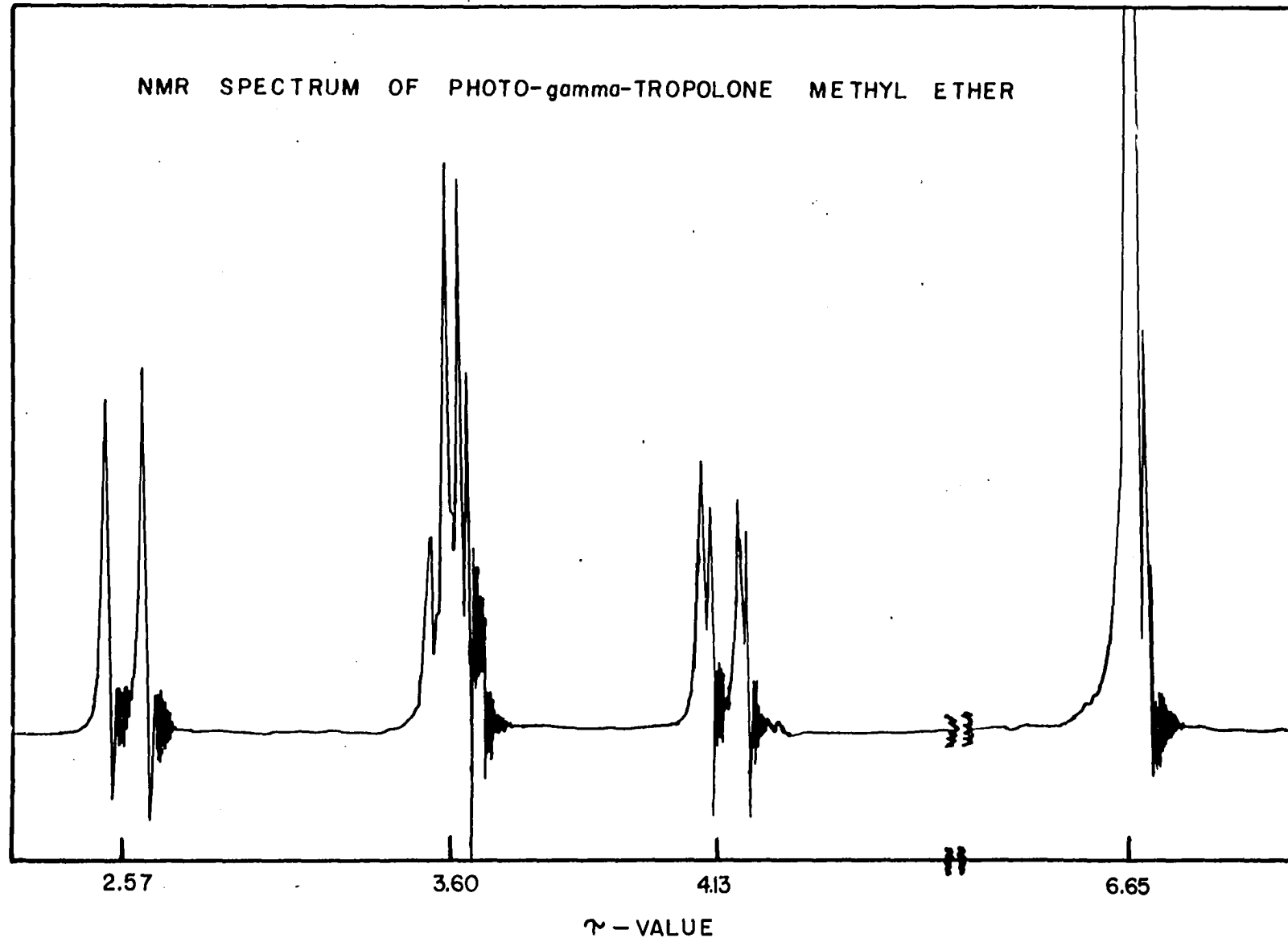


Figure 35. Nuclear magnetic resonance spectrum of 2-hydroxy-
2-phenyl-5-methoxybicyclo[3.2.0]hepta-3,6-diene
(LXXXI)

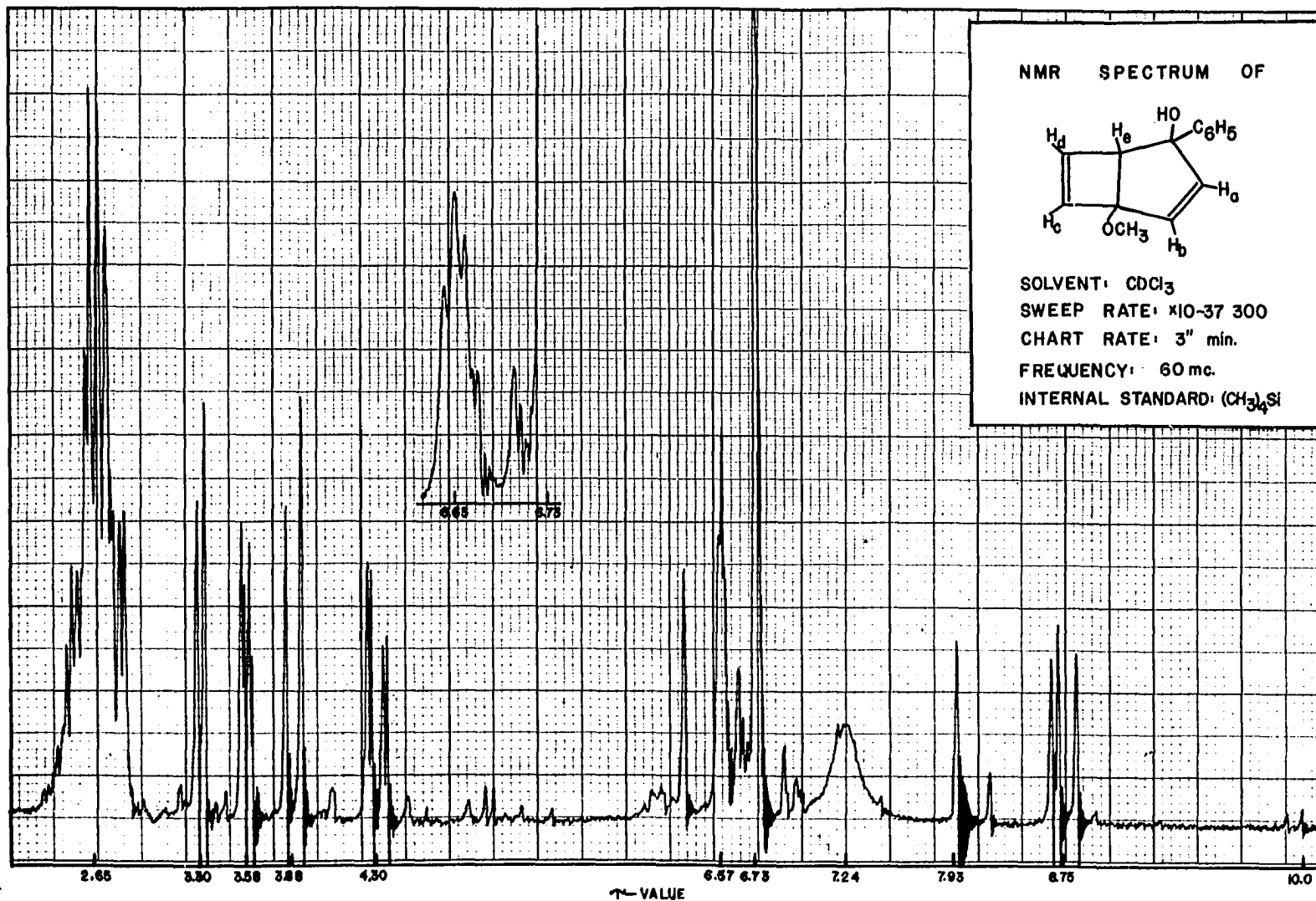
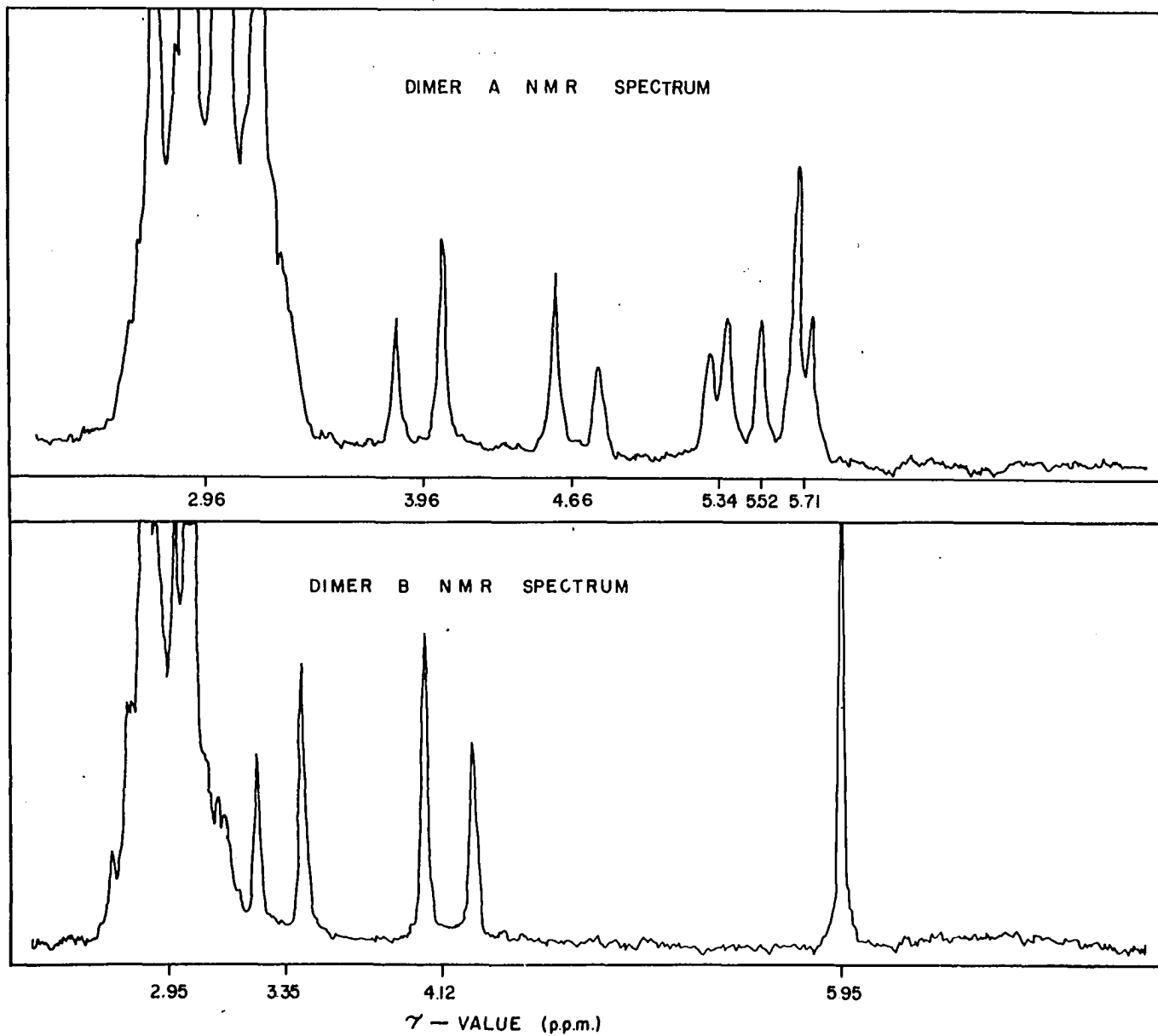


Figure 36. Nuclear magnetic resonance spectra

Top. Dimer A

Bottom. Dimer B



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Figure 37. Nuclear magnetic resonance spectra

Top. Bicyclo[3.2.0]hept-6-ene

Middle. Dimer B hydride alcohol

Bottom. Dimer B alcohol acetate

