1961

# The mechanistic path of the 4-methyl-alpha-tropolone methyl ether to methyl 1-methyl-4-oxo-2-cyclopentenylacetate conversion

Stanford Lee Smith
*Iowa State University*

## Recommended Citation

Smith, Stanford Lee, "The mechanistic path of the 4-methyl-alpha-tropolone methyl ether to methyl 1-methyl-4-oxo-2-cyclopentenylacetate conversion " (1961). *Retrospective Theses and Dissertations*. 1986.
https://lib.dr.iastate.edu/rtd/1986

62–1370

SMITH, Stanford Lee, 1935–
THE MECHANISTIC PATH OF THE 4-METHYL-alpha-TROPOLONE METHYL ETHER TO METHYL 1-METHYL-4-OXO-2-CYCLOPENTENYLACETATE CONVERSION.

Iowa State University of Science and Technology
Ph.D., 1961
Chemistry, organic

University Microfilms, Inc., Ann Arbor, Michigan

# THE MECHANISTIC PATH OF THE 4-METHYL-*alpha*-TROPOLONE METHYL ETHER TO METHYL 1-METHYL-4-OXO-2-CYCLOPENTENYLACETATE CONVERSION

by

Stanford Lee Smith

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:

Signature was redacted for privacy.

In Charge of Major Work

Signature was redacted for privacy.

Head of Major Department

Signature was redacted for privacy.

Dean of Graduate College

Iowa State University
Of Science and Technology
Ames, Iowa

1961

## TABLE OF CONTENTS

# VITA

The author was born in Detroit, Michigan, on June 3, 1935, to Mr. and Mrs. Leland S. Smith. He attended Mumford High School and was graduated in June of 1953. In September of the same year he enrolled at Albion College where he received his Bachelor of Arts degree in chemistry in June of 1957. During his studies at Albion College the author received the Dow Chemical Company scholarship for 1956-57. He was also employed by Albion College as Technical Director of the college theater in 1955-56. The author was employed as a chemist in the research laboratories of Ethyl Corporation, Ferndale, Michigan, in the summer of his senior year.

In September of 1957 the author enrolled at Iowa State College as a graduate student in organic chemistry under Dr. O. L. Chapman. He married Barbara Labick in August of 1958. In November 1959 the author received a two year National Institutes for Health Fellowship. The author was graduated with the Ph.D. degree in organic chemistry from Iowa State University of Science and Technology in November 1961.

# INTRODUCTION

Photochemical reactions have been known and studied for many years and thousands of papers have been published concerning this subject.[1, 2] However, photochemical mechanisms are at best poorly understood.

More than 95% of the mechanistic studies attempted have dealt with photolysis,[3] usually in the vapor phase, of exceedingly simple molecules. For example, there are approximately 500 papers in the literature concerning photolysis of acetone and a similar number dealing with acetaldehyde. Despite such intensive study over a period of forty years this approach has failed to produce results or hypotheses of general applicability to photochemical mechanisms.

One other area of photochemistry, the vitamin D transformations, has been intensively studied.[4] Again, although in this case the structural characteristics of the photochemical transformations occurring are understood, no general mechanistic paths have been defined.

During the past five years a rapidly growing body of knowledge concerning photoisomerizations of complex organic molecules has come into

---

[1] W. A. Noyes, Jr. and P. A. Leighton, The Photochemistry of Gases, Reinhold Publishing Corporation, New York, 1941.

[2] P. deMayo, Ultraviolet Photochemistry. In R. A. Raphael, E. C. Taylor, and H. Wynberg, Eds. Advances in Organic Chemistry, Interscience Publishers Inc., New York, 1960.

[3] Photolysis may be defined as the light induced cleavage of a molecule into two (or more) discrete particles.

[4] L. Fieser and M. Fieser, Steroids, Reinhold Publishing Corporation, New York, 1959, Chapter 4.

existence. Many organic mechanistic problems have been solved by applying the reaction in question to a variety of complex molecules, and present indications are that this general technique will be equally fruitful in the field of photochemical mechanisms.

This investigation constitutes a small part of this new body of knowledge. Hence, the mechanistic studies to be discussed in this thesis are a pioneer effort for which, with two exceptions, there is no historical background. These two exceptions involve troponoid compounds, a class of aromatic compounds which has, itself, been recognized and studied only during the past fifteen years.[5, 6, 7]

---

[5] P. L. Pauson, Chem. Rev., 55, 9 (1955).

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

[7] T. Nozoe, Fortschritte Prof. Dr. Arthur Stoll, Birkenhauser A. G., Basel, Switzerland, 1957, pp. 746-783.

# HISTORICAL

In 1951 Grewe and Wulf[8] reported that exposure of an aqueous colchicine (I) solution to sunlight led to the production of three isomeric products, the *alpha*-, *beta*-, and *gamma*-lumicolchicines. This conversion constituted the first known example of a light induced valence tautomerization[9] in the tropolone system. About the same time Šantavý[10, 11] obtained the *beta*- and *gamma*-isomers by a similar procedure, and noted that these two isomers were identical with two alkaloids previously isolated from *Colchicum autumnale*; the major source of colchicine itself.

Within a few years Forbes[12] and Gardner *et al.*[13] established the gross structure of the *beta*- and *gamma*-lumicolchicines as II. The only difference between the two isomers is in the configuration of the C-D ring juncture.[13] For some time the structure of the *alpha*-isomer remained unknown. Schenk[14] has recently proposed a structure for this

---

[8] R. Grewe and W. Wulf, *Ber.*, *84*, 621 (1951).

[9] A valence tautomerization may be defined as a reaction in which only carbon-carbon bonds are rearranged.

[10] F. Šantavý, *Biol. Listy*, *31*, 246 (1951).

[11] F. Šantavý, *Coll. Czech. Chem. Comm.*, *16*, 665 (1951).

[12] E. J. Forbes, *J. Chem. Soc.*, 1864 (1955).

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

[14] G. O. Schenk, H. J. Kuhn, and O. A. Neumüller, *Tetrahedron Letters*, *No. 1*, 12 (1961).

material, but it remained for Chapman and Smith[15] to conclusively establish that alpha-lumicolchicine is III, a photodimer of beta-lumicolchicine (II).

In 1958 Chapman and Pasto[16] communicated the first example of photoisomerization of a simple tropolone, the isomerization of gamma-tropolone methyl ether (IV) to photo-gamma-tropolone methyl ether (V). These authors showed[17] that the yield of the photoproduct is strongly solvent dependent. Irradiation in polar solvents affords the photoisomer in good yield, but irradiation in nonpolar solvents gives only intractable tars.

It should be noted that beta- and gamma-lumicolchicine (II) and photo-gamma-tropolone methyl ether (V) all have the bicyclo-[3,2,0]-ring structure; although bridging occurs across different carbons in the two cases. The lumicolchicines (II) are bridged in such a manner that the methoxyl group appears on the double bond of the five membered ring. Photo-gamma-tropolone methyl ether (V) is bridged in such a manner that the methoxyl group appears on the bridgehead. These two examples were the only information available concerning photoisomerizations of tropolones or related compounds at the time this investigation was begun.

---

[15] O. L. Chapman and H. G. Smith, J. Am. Chem. Soc., 83, 3914 (1961).

[16] O. L. Chapman and D. J. Pasto, J. Am. Chem. Soc., 80, 6685 (1958).

[17] O. L. Chapman and D. J. Pasto, ibid., 82, 3642 (1960).

During the course of this investigation three more papers concerning tropolone photochemistry have appeared. Two of these are intimately related to this work and will be discussed later. The third, by Forbes and Ripley,[18] reports that irradiation of tetramethylpurpurogallin (VI) gives, among other products, methyl 6,7,8-trimethoxy-alpha-naphthoate (VII).[19] This transformation represents yet a third light catalysed mode of reaction for the tropolone nucleus.

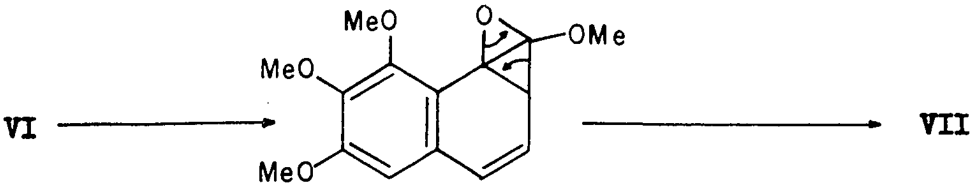
A number of light induced valence tautomerization reactions in related, but non-troponoid, systems have been reported during the course of this investigation.

According to Buchi and Burgess[20] eucarvone (VIII) upon irradiation

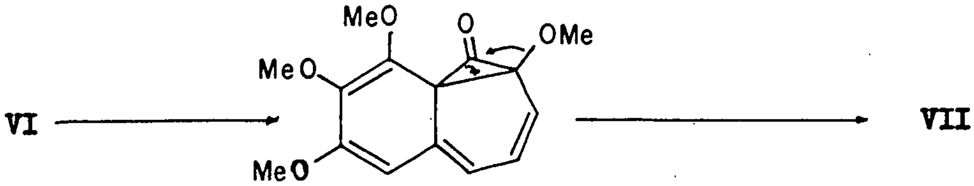
---

[18] E. J. Forbes and R. A. Ripley, J. Chem. Soc., 2770 (1959).

[19] Forbes postulates the high energy intermediate shown below followed by collapse to the photoproduct.



Alternatively, this reaction may proceed via the intermediate shown below (Chapman's path A reaction) (17).



[20] G. Buchi and E. M. Burgess, J. Am. Chem. Soc., 82, 4333 (1960).

gives 1,4,4-trimethylbicyclo-[3,2,0]-hept-6-ene-2-one (IX). Further irradiation of IX leads to an equilibrium mixture containing 75% of 4,4,6-trimethylbicyclo-[3,2,0]-hept-6-ene-2-one (X) and 25% of IX. Identical results are obtained by irradiation of 4,6,6-trimethyl-2,4-cycloheptadieneone (XI). Buchi's rationalization of the interconversion of VIII and XI is shown in Figure 2, page 10.

Hurst and Whitham[21] have also irradiated eucarvone and report that in addition to IX a second product, 1,3,3-trimethylbicyclo-[2,2,1]-hept-5-ene-7-one (XII), is formed. These authors suggest that an excited state having the configuration XIII reacts as shown to give this product. Apparently, the photo equilibrium reaction reported by Buchi was not observed by these workers.

Cycloheptadiene (XIV)[22, 23] and cycloheptatriene (XV)[23] have been photoisomerized to the corresponding bicyclo-[3,2,0]- products (XVI and XVII). The generality of this reaction for the cycloheptadienes has been conclusively established by Chapman and Pasto[22] who have irradiated a number of these compounds. In all cases the corresponding bicyclo-[3,2,0]-valence tautomer was obtained as the only product.[24]

---

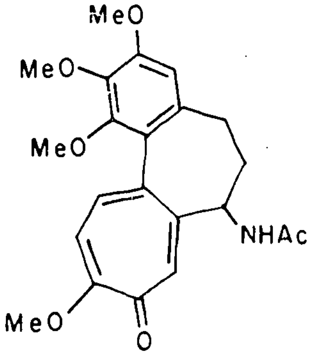
[21] J. J. Hurst and G. H. Whitham, Proc. Chem. Soc., 116 (1961).

[22] O. L. Chapman and D. J. Pasto, Chem. and Ind., 53 (1961).

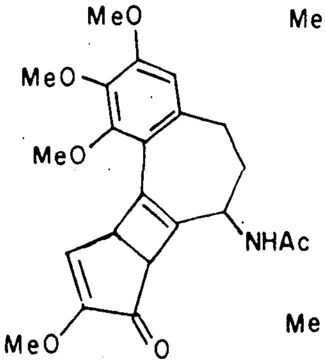
[23] W. G. Dauben and R. L. Cargill, Tetrahedron, 12, 186 (1961).

[24] Two exceptions to this generalization have been found. They are 3,5-cycloheptadieneone and 2-methyl-3,5,cycloheptadienone. (O. L. Chapman, D. J. Pasto, G. W. Borden, and A. A. Griswold, Research Journal of G. W. Borden (manuscript), Department of Chemistry, Iowa State University of Science and Technology, Ames, Iowa.

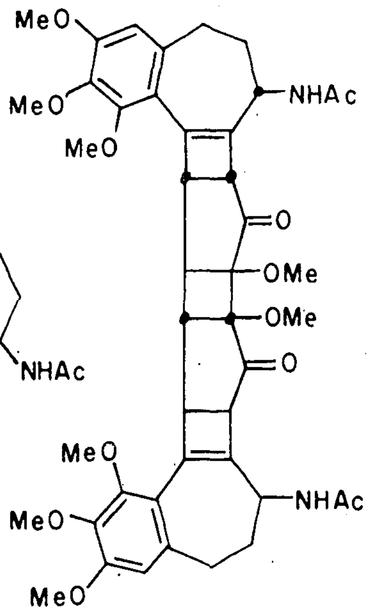
Figure 1. Structures and reactions discussed in the historical section



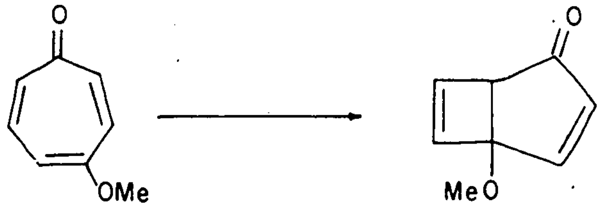
I



II

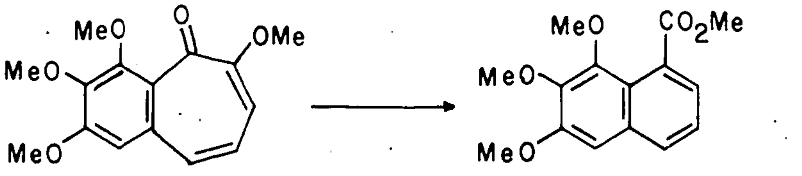


III



IV

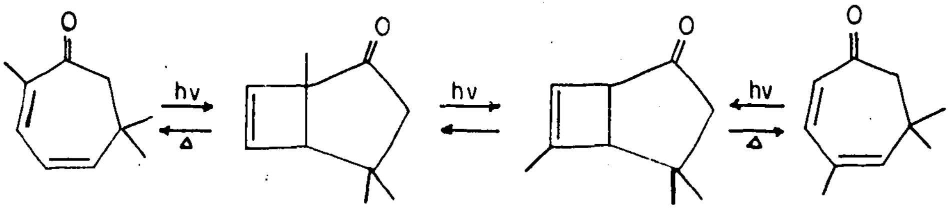
V



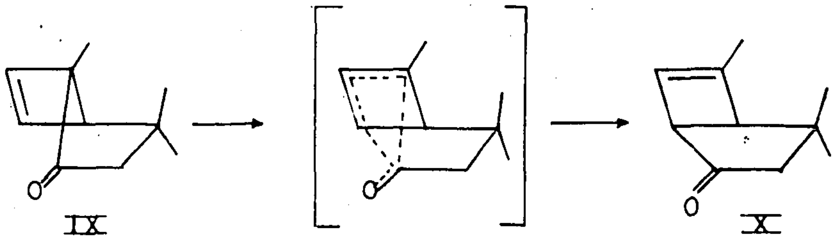
VI

VII

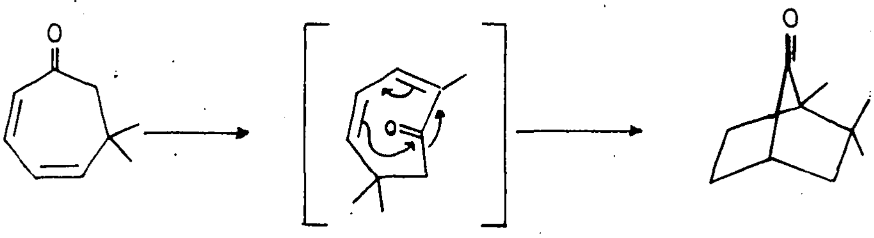
Figure 2. Structures and reactions discussed in the historical section



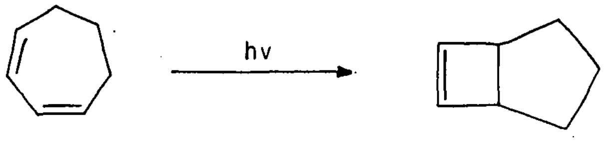
VIII IX X XI



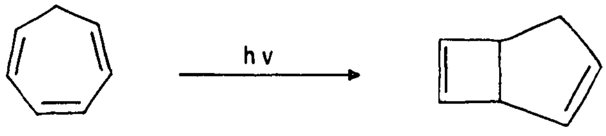
IX X



VIII XIII XII



XIV XVI



XV XVII

## DISCUSSION

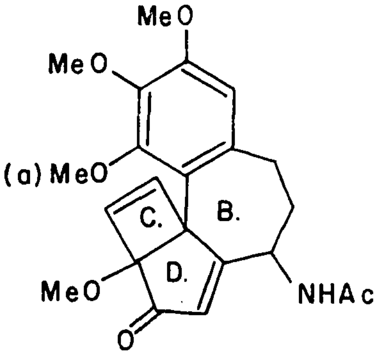
### Photochemistry of 4-Methyltropolone Methyl Ether and 6-Methyltropolone Methyl Ether

Gamma-tropolone methyl ether (IV) has been shown to give a photoproduct (V) in which bridging occurs across the carbon bearing the methoxyl group (Figure 1, page 8). Colchicine (I) while giving a similar bicyclo-[3,2,0]- product (II, Figure 1) bridges so that the methoxyl group occurs as an enol ether in the five membered ring.[25]

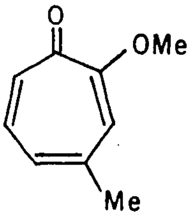
Our interest in determining the mode of reaction of simple alpha-tropolones led us to select the reasonably available methyl ethers of

---

[25] This mode of reaction is undoubtedly governed by steric factors, since reaction bridging across the methoxyl carbon would give a product having a highly strained configuration at the B-C-D ring juncture and strong steric repulsions between the methoxyl group (a) and the olefinic hydrogen of ring C as shown below.

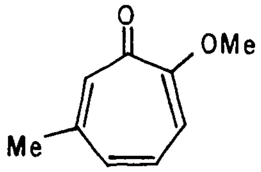


4-methyltropolone (XVIII and XIX) for this study.



XVIII

4-methyltropolone
methyl ether



XIX

6-methyltropolone
methyl ether

Irradiation of an aqueous solution of 4- and 6-methyltropolone methyl ethers (XVIII and XIX) in a pyrex flask gave a bright yellow oil in 80% yield. Vapor phase chromatography[26] showed this material to be a mixture of two products. Upon irradiation under identical conditions pure 4-methyltropolone methyl ether (XVIII) and pure 6-methyltropolone methyl ether (XIX) each gave a single product. The retention times of these products were identical with those of the two products obtained from the irradiation of the mixture of methyl ethers. Separation of the photoproduct mixture by preparative scale vapor phase chromatography gave modest amounts of the pure photoisomers; although considerable losses were encountered due to decomposition in the injection port of the vapor fractometer.

Photo-4-methyltropolone methyl ether showed intense absorption in the infrared at 5.85, 6.14, 6.27, and 6.35 u (Figure 25, page 127) and

---

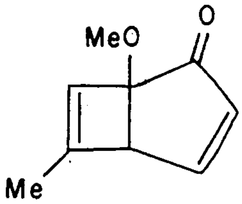
[26] Detailed descriptions of all vapor phase chromatography columns used in this investigation are given on page 125 of the Appendix.

an ultraviolet maximum at 230 mu (Figure 33, page 143). Pyrolysis of the photoisomer at 360° gave a yellow oil identical in infrared absorption to 4-methyltropolone methyl ether (XVIII). Treatment of this material with hot aqueous base gave a solution with an ultraviolet spectrum identical to that of 4-methyltropolone anion (Figure 36, page 149). This solution upon acidification showed an ultraviolet spectrum identical to that of 4-methyltropolone (Figure 37, page 151). Photo-4-methyltropolone methyl ether rapidly absorbed two equivalents of hydrogen giving a tetrahydro derivative which showed an intense peak at 5.75 u in the infrared (Figure 28, page 133) and no high intensity ultraviolet absorption.

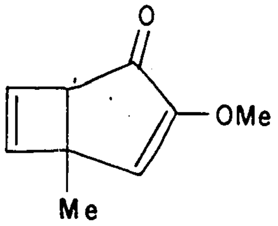
Pure photo-6-methyltropolone methyl ether was obtained as a colorless crystalline solid (m.p. 42.1-44.1°) which showed intense infrared maxima at 5.85 and 6.19 u (Figure 26, page 129) and an ultraviolet maximum at 232 mu (Figure 34, page 145). Pyrolysis of the photoproduct at 395° gave 6-methyltropolone methyl ether; identified by comparison (m.p. and infrared spectrum; Figure 27, page 131) with authentic material. The photoisomer rapidly absorbed one equivalent of hydrogen giving a dihydro derivative which showed infrared maxima at 5.88 and 6.22 u (Figure 28, page 133) and an ultraviolet maximum at 232 mu (Figure 35, page 147). Attempts to prepare a tetrahydro derivative were unsuccessful. Photo-6-methyltropolone methyl ether gave no reaction when treated with either acid or base.

The facile pyrolysis of the photoisomers to their respective starting materials indicated that no gross rearrangement of the carbon skeleton had occurred. The infrared spectral data for the two photoproducts and for the corresponding hydrogenated derivatives as well as analogy with photo-*gamma*-tropolone methyl ether (V) strongly suggested the presence of a cyclopentenone in the photoproducts.[27] However, the ultraviolet maxima of the photoisomers are not consistent with the values predicted for the cyclopentenone chromophore;[28] a fact which, as we shall see, has great significance.

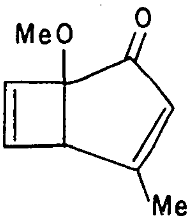
On the basis of the above data it seemed likely that the structure of photo-4-methyltropolone methyl ether was either XX or XXI while that of photo-6-methyltropolone methyl ether was either XXII or XXIII.



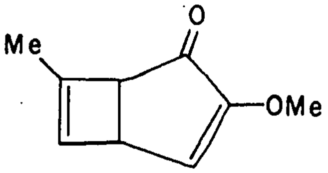
XX



XXI



XXII



XXIII

---

[27] All correlations of infrared absorption maxima with structural groups are taken from Bellamy (L. J. Bellamy, *The Infrared Spectra of Complex Molecules*, 2nd ed., John Wiley and Sons, Inc., New York, 1958.

[28] Fieser and Fieser, *Steroids*, pp. 17-21.

The nuclear magnetic resonance spectrum of photo-4-methyltropolone methyl ether (reproduced in Figure 3, page 17) unambiguously establishes structure XX for this isomer. The signal arising from the methyl group on the cyclobutene double bond appears at 8.12 p.p.m., while that arising from the protons of the methoxyl group appears at 6.58 p.p.m.[29, 30] The two protons on the double bond conjugated with the carbonyl group appear at 2.28 and 3.85 p.p.m. The *alpha* proton ($H_3$) doublet at 3.85 p.p.m. arises from spin-spin coupling of the AX type[31] which gives two lines of equal intensity. The *beta* proton ($H_4$) at 2.28 p.p.m. is a quartet due to further splitting of the AX doublet by the bridgehead proton $H_5$.

---

[29] The positions of the signals observed in a nuclear magnetic resonance spectrum are expressed as parts per million (p.p.m.) on a $\tau$ (Tau) unit scale for which the internal reference compound is tetramethylsilane ($\tau = 10$). The expression for calculating $\tau$ values is

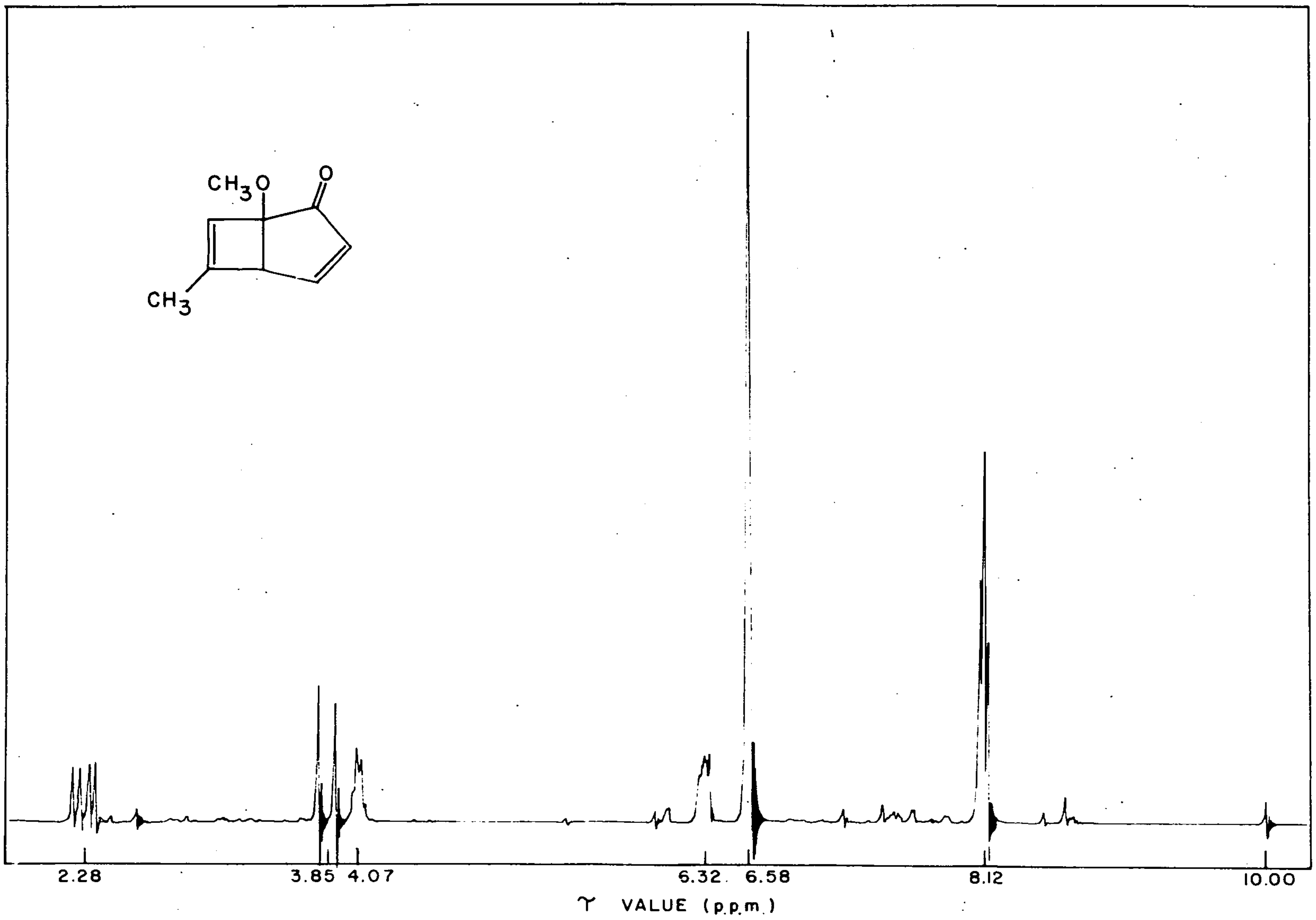
$$\tau\,(\text{p.p.m.}) = \frac{\Delta\,(\text{Me}_4\text{Si}) \times 10^6}{\text{oscillator frequency (cps)}}$$

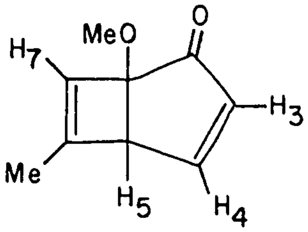
in which $\Delta\,(\text{Me}_4\text{Si})$ is the difference in cycles per second (cps) between the signal from tetramethylsilane and the signal under consideration. (L. M. Jackman, *Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry*, Pergamon Press, New York, 1959, p. 47).

[30] For 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 $\tau$ Values for a Variety of Organic Compounds*, Minnesota Mining and Manufacturing Company, St. Paul, Minnesota, 1958.

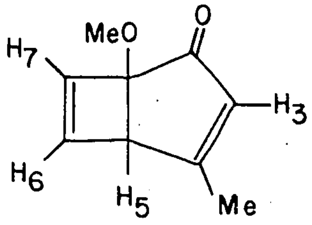
[31] For a brief discussion of spin-spin coupling effects in nuclear magnetic resonance see L. M. Jackman, *op. cit.*, Chapter 6.

Figure 3. Nuclear magnetic resonance spectrum of photo-4-methyltropolone methyl ether (XX)


CH$_3$O
O
CH$_3$
2.28
3.85
4.07
6.32
6.58
8.12
10.00
τ VALUE (p.p.m.)



XX



XXII

Only one cyclobutene proton ($H_7$) is observed. It appears at 4.07 p.p.m. as a quartet arising from coupling with the methyl group on carbon six. The bridgehead proton appears as a multiplet at 6.32 p.p.m. Structure XXI is rigorously excluded from consideration by the presence of signals arising from $H_3$ and $H_5$. The appearance of a single cyclobutene proton, the presence of the methyl group on a double bond, and the $H_3$-$H_4$-$H_5$ coupling pattern conclusively establish structure XX for photo-4-methyltropolone methyl ether.

The nuclear magnetic resonance spectrum of photo-6-methyltropolone methyl ether (Figure 4, page 21) conclusively establishes structure XXII for this material. The signal from the methoxyl protons is observed at 6.57 p.p.m., almost exactly the same value as in XX while the signal arising from the methyl group on the double bond conjugated with carbonyl group appears at 7.88 p.p.m. Significantly, no signal is observed for a <u>beta</u> proton whereas the <u>alpha</u> proton ($H_3$) is seen as a quartet at 4.15 p.p.m. due to coupling with the methyl group on carbon four. Two cyclobutene protons $H_6$ and $H_7$ give signals at 3.21 and 3.62 p.p.m. respectively. The bridgehead proton ($H_5$) appears at 6.32 p.p.m. The signals arising from $H_6$ and $H_7$ are quartets and under high resolution the signal from $H_5$ also appears as a quartet. This twelve line spectrum is typical of an AMX system[32] in which two protons, M ($H_6$) and X ($H_7$), having different chemical shifts are coupled with each other and both are coupled with a third proton A ($H_5$) which has a chemical shift appreciably different from either M or X. The presence of this coupling pattern requires two protons on the cyclobutene double bond and a single bridgehead proton. In conjunction with the quartet from the alpha proton on the double bond conjugated with the carbonyl group, this requirement firmly establishes structure XXII for photo-6-methyltropolone methyl ether.

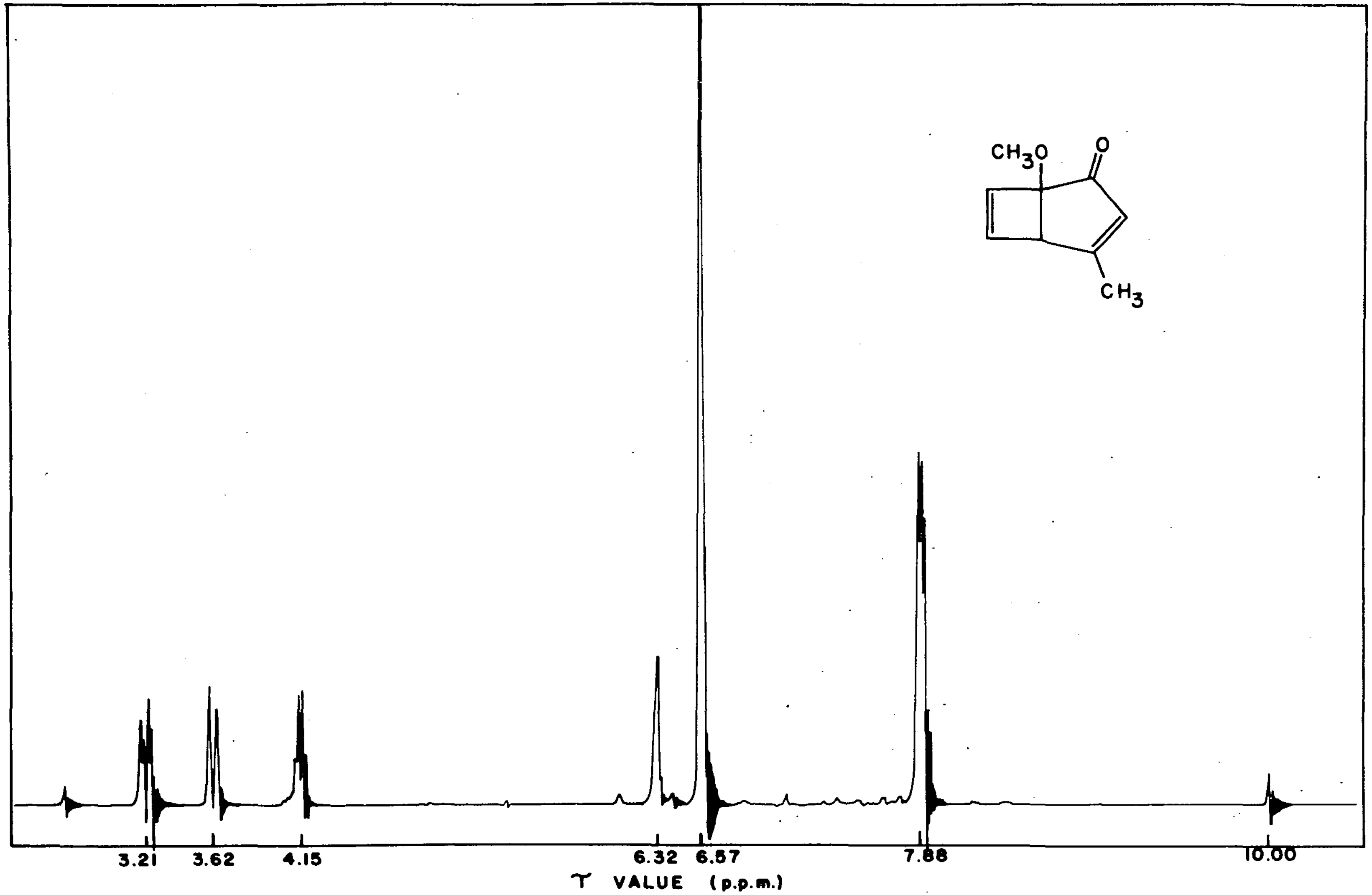
With the assignment of structure XX for photo-4-methyltropolone methyl ether and structure XXII for photo-6-methyltropolone methyl ether, it follows that tetrahydrophoto-4-methyltropolone methyl ether must be XXIV and dihydrophoto-6-methyltropolone methyl ether must be XXV. These structures are in good accord with the spectral data presented above.

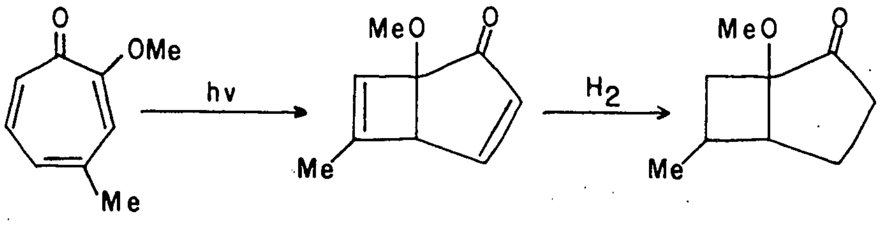
The transformations shown below were thus firmly established. However, the appearance at this stage of the investigation of two reports concerning the photochemistry of alpha-tropolone posed several hitherto unsuspected problems.

---

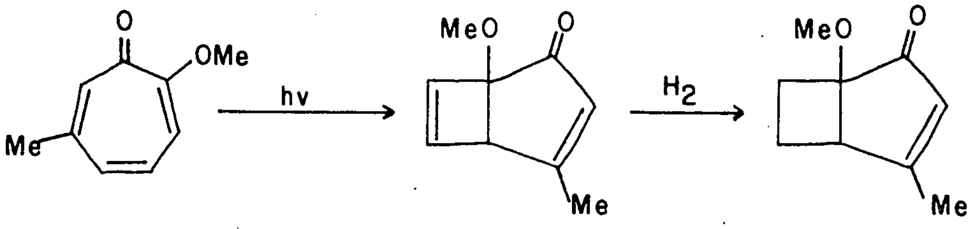
[32] J. D. Roberts, An Introduction to Spin-Spin Splitting in High Resolution Nuclear Magnetic Resonance Spectra, W. A. Benjamin Inc., New York, 1961, p. 61.

Figure 4. Nuclear magnetic resonance spectrum of photo-6-methyltropolone methyl ether (XXII)


CH$_3$O
O
CH$_3$
3.21
3.62
4.15
6.32
6.57
7.88
10.00
τ VALUE (p.p.m.)



XVIII XX XXIV



XIX XXII XXV

Late in 1959 Dauben *et al.*[33] reported that irradiation of an aqueous solution of *alpha*-tropolone (XXVIa) gave 4-oxo-2-cyclopentenylacetic acid (XVIIa) and that irradiation of *alpha*-tropolone in ethanol gave the corresponding ethyl ester (XVIIb). Shortly thereafter, Forbes and Ripley[34] reported that irradiation of an aqueous solution of *alpha*-tropolone methyl ether (XXVIb) gave the corresponding methyl ester (XXVIIc).

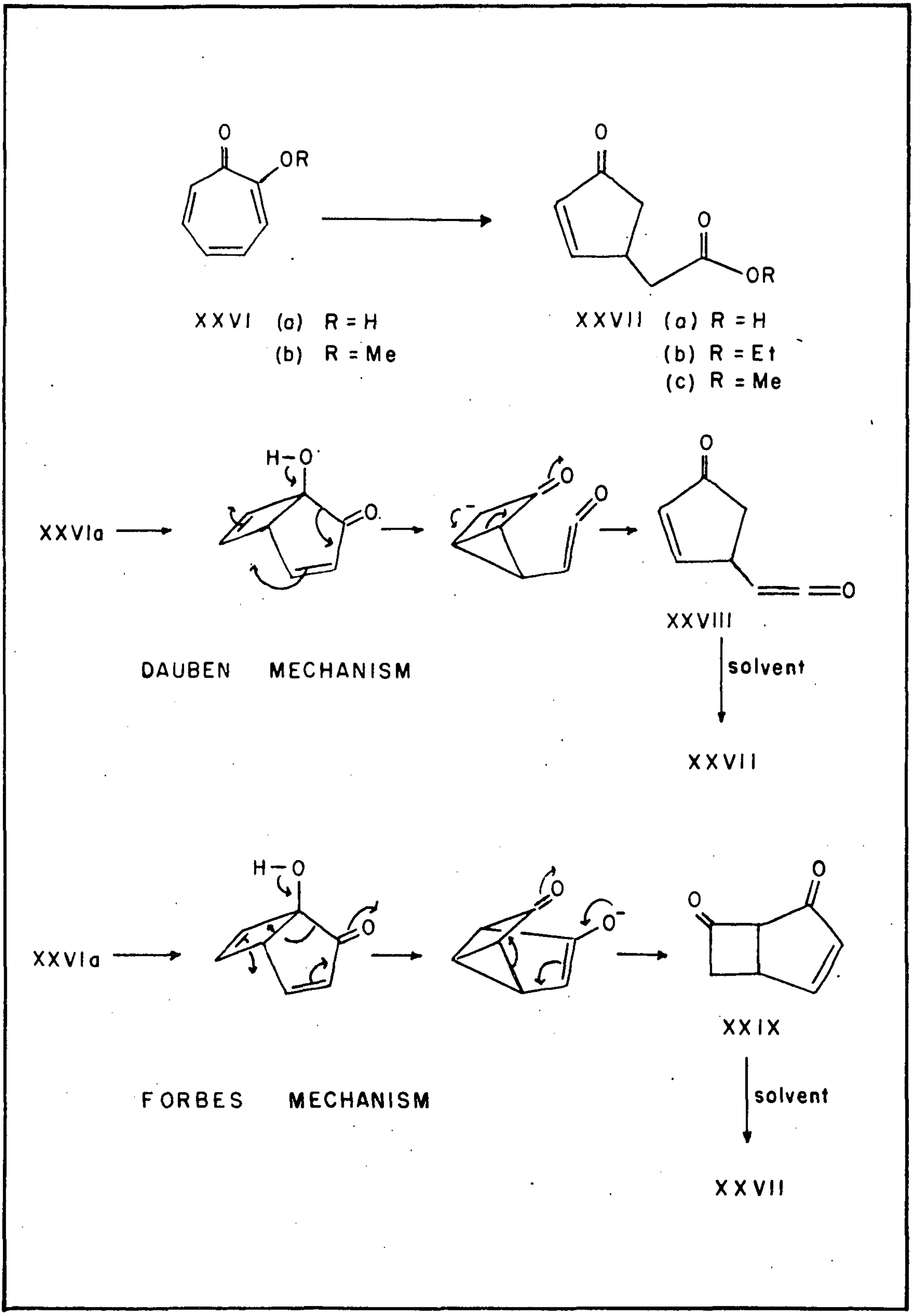
Dauben proposed the mechanism shown in Figure 5, page 24; the first

---

[33] W. G. Dauben, K. Koch, and W. E. Theissen, *J. Am. Chem. Soc.*, *81*, 6087 (1959).

[34] E. J. Forbes and R. A. Ripley, *Chem. and Ind.* 589 (1960).

Figure 5. Reactions reported by Dauben *et al*. and by Forbes and Ripley and the mechanisms proposed by these authors to explain the observed transformations



XXVI (a) R = H
(b) R = Me

XXVII (a) R = H
(b) R = Et
(c) R = Me

XXVIa

XXVIII

solvent

XXVII

DAUBEN MECHANISM

XXVIa

XXIX

solvent

XXVII

FORBES MECHANISM

step of which postulated a bicyclic intermediate on the basis of analogy with photo-gamma-tropolone methyl ether. The ketene intermediate (XXVIII) was required, according to Dauben, to explain the formation of the ethyl ester (XVIIb) upon irradiation in ethanol.

Forbes and Ripley recognized that conversion of alpha-tropolone methyl ether (XXVIb) to the corresponding methyl ester (XVIIc) made the inclusion of a ketene intermediate in the mechanistic rational unlikely. The mechanism favored by these authors is shown in Figure 5; the first step being the same as that proposed by Dauben. Instead of a ketene structure Forbes suggests the intermediacy of a bicyclic diketone (XXIX) which subsequently reacts with solvent to produce the acid or ester.

Several points should be emphasized concerning these proposals. First, in both mechanisms the only step in which light is required is that leading to the initial bicyclic intermediate. Second, both mechanisms require a second intermediate obtained by rearrangement of the initially obtained bicyclic product. Third, neither proposal adequately explains the conversions observed.

The availability of photo-4-methyltropolone methyl ether (XX) and photo-6-methyltropolone methyl ether (XXII), and the fortuitous presence of the methyl substituent in these compounds, offered a unique opportunity to determine the mechanism of the transformations reported by Dauben et al. and by Forbes and Ripley.

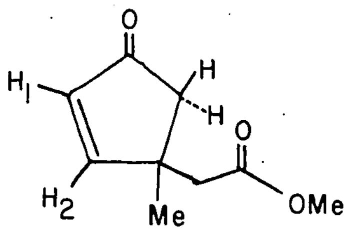
Several questions need to be answered. (1) Are the photoisomers actually intermediates in the transformations, or does the conversion to the acid (or ester) occur via an excited state of the alpha-tropolone nucleus different from that which leads to the photoisomers? (2) If the photoisomers are in fact precursors of the corresponding esters, are there intermediates between the photoproducts and the esters? (3) Is light necessary for the rearrangement of the photoisomers? (4) What are the mechanistic details of the transformations leading to the esters?

The research now to be discussed was instituted in an attempt to answer these questions.

The irradiation of photo-4-methyltropolone methyl ether (XX) as an aqueous solution in a quartz tube was followed by vapor phase chromatography. Reaction times varied with the amount of material irradiated, but never exceeded 24 hours. The product, a pale yellow oil, was isolated in 50% yield. It absorbed strongly in the infrared at 5.77 (shoulder), 5.86, and 6.30 u (Figure 25, page 127), and an ultraviolet maximum appeared at 218 mu (Figure 38, page 153).

The ultraviolet maximum at 218 mu strongly suggested the presence of a cyclopentenone chromophore, in good agreement with the double bond and cyclopentenone absorptions at 6.30 and 5.86 u respectively in the infrared. Absorption at 5.77 u in the infrared indicated the presence of an ester group in the molecule.

The nuclear magnetic resonance spectrum (Figure 6, page 29) of photo-4-ester (XXX) unambiguously establishes this compound as methyl 1-methyl-4-oxo-2-cyclopentenylacetate. The two protons on the cyclopentenone double bond are observed at 2.43 ($H_2$) and 4.00 ($H_1$) p.p.m. Each of these signals is a symmetrical doublet, the spin-spin coupling pattern expected from a simple AX group. The methylene protons adjacent



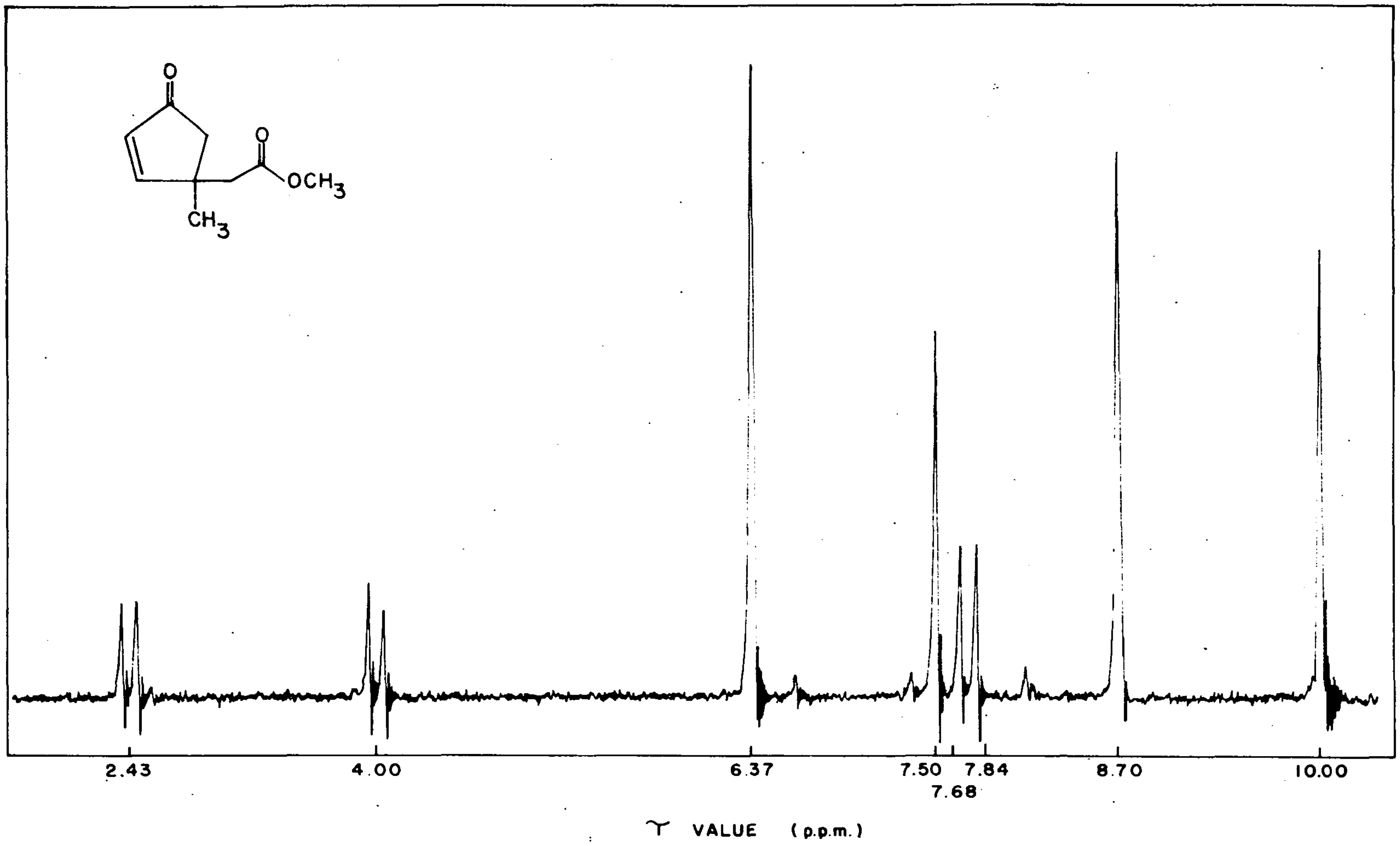
XXX

to the carbonyl group in the cyclopentenone ring are nonequivalent and are found as two unsymmetrical doublets at 7.65 and 7.84 p.p.m. This four line pattern is typical of an AB grouping[35] in which two protons having similar chemical shifts are coupled to each other. The doublets are unsymmetrical because the coupling constant ($J_{AB}$ = 18.5 cps) is of the same magnitude as the difference between the chemical shifts of the two protons. The magnitude of $J_{AB}$ requires that the two protons be on the same carbon. The two-proton singlet at 7.50 p.p.m. is due to the protons of the methylene group adjacent to the ester carbonyl. Since neither the $H_2$ signal (2.43 p.p.m.) nor either of the methylene signals show further splitting, the carbon to which the side chain is attached cannot bear a proton; hence the methyl group must be bonded at this point. Accordingly, the protons of the methyl group give rise to a sharp singlet at 8.70 p.p.m. This singlet requires that the carbon to

---

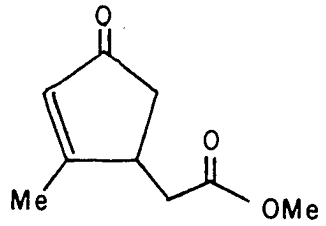
[35] L. M. Jackman, op. cit., p. 89.

Figure 6. Nuclear magnetic resonance spectrum of photo-4-ester (XXX; methyl 1-methyl-4-oxo-2-cyclopentenylacetate)


O
O
OCH3
CH3
2.43
4.00
6.37
7.50
7.84
7.68
8.70
10.00
τ VALUE (p.p.m.)

which the methyl group is attached be bonded only to other carbons. To complete the analysis, the methyl protons of the ester group are observed at 6.32 p.p.m. This nuclear magnetic resonance spectrum rigorously establishes structure XXX without additional evidence.

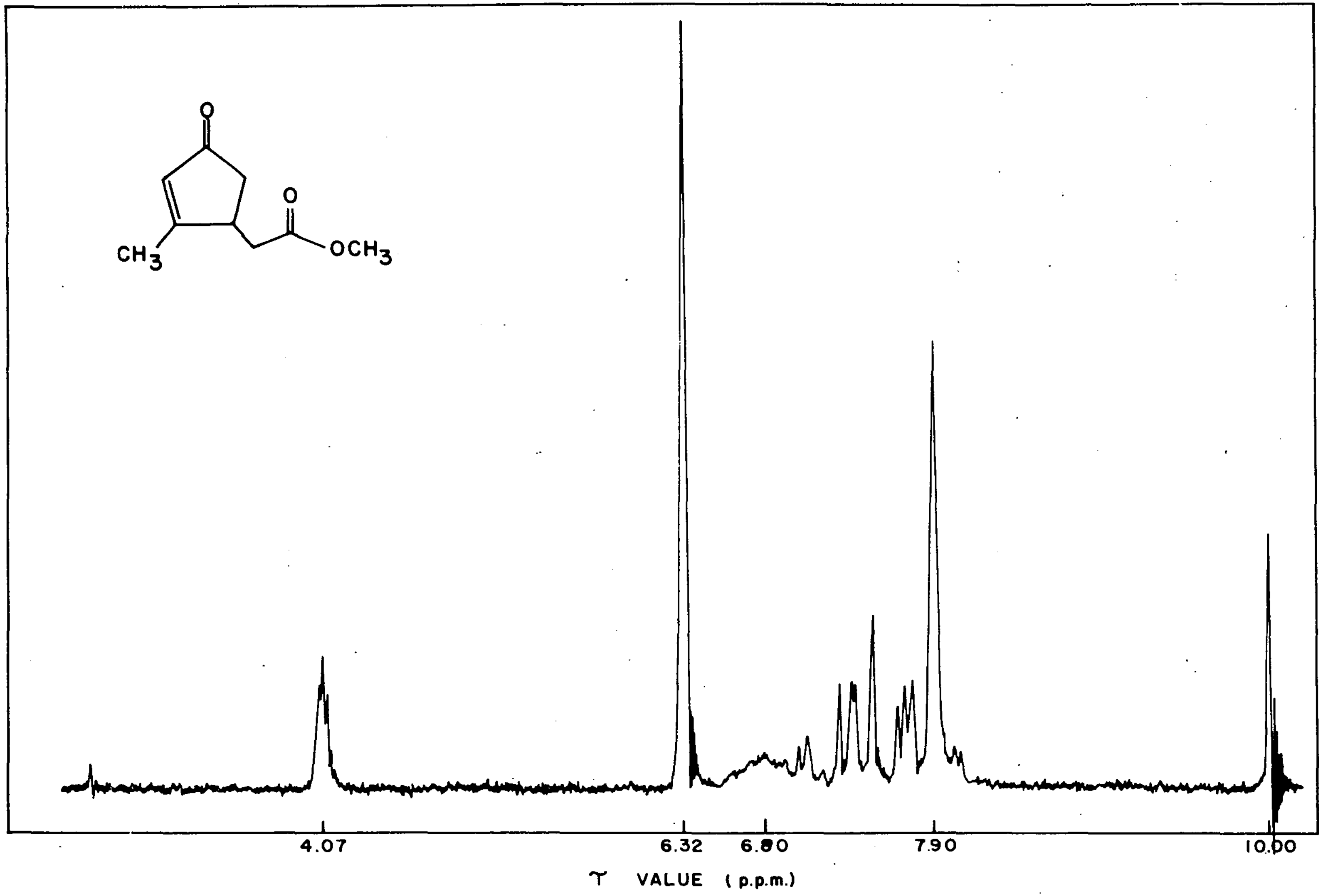
Photo-6-methyltropolone methyl ether was irradiated as an aqueous solution in a quartz tube and the reaction followed by vapor phase chromatography. Again, reaction times varied with the amount of material irradiated, but were always less than one day. The product after purification was a mushy, colorless solid (m.p. 29-30°). Intense absorption in the infrared at 5.76, 5.85, and 6.17 u (Figure 26, page 129) suggested the presence of an ester, a cyclopentenone carbonyl, and a double bond. An ultraviolet maximum was observed at 228 mu (Figure 39, page 155). Structure XXXI for photo-6-ester is consistent with this data, analogous to XXVII and XXX, and strongly supported by the nuclear magnetic resonance spectrum of this compound.



XXXI

The nuclear magnetic resonance spectrum of photo-6-ester (Figure 7, page 32) shows a single olefinic proton signal at 4.07 p.p.m. corresponding to the *alpha* proton of the conjugated double bond. This signal is a

Figure 7. Nuclear magnetic resonance spectrum of photo-6-ester (XXXI)


O
O
CH3
OCH3
4.07
6.32
6.80
7.90
10.00
τ VALUE (p.p.m.)

quartet, establishing the presence of the methyl group on the beta carbon of the chromophore; an assignment further supported by the signal observed for the methyl protons at 7.90 p.p.m. The signal arising from the protons of the ester methyl group appears at 6.32 p.p.m. A complex group of lines appearing between the methyl and methoxyl signals is due to the coupling of the two methylene groups and the tertiary proton. At the present time no such pattern has been analysed.

On the basis of these transformations it seemed probable that the photoisomers obtained from 4-methyltropolone methyl ether (XVIII) and 6-methyltropolone methyl ether (XIX) are actually intermediates in the conversion of the tropolone methyl ethers to the corresponding methyl esters as shown in Figure 8 (page 36). However, reversion to the tropolone followed by photoisomerization to the esters remained a possibility.

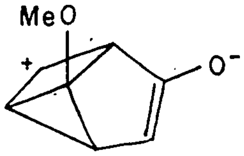
The position of the methyl group in photo-4 ester (XXX) suggested the intermediacy of yet another compound, as does the movement of the methoxyl groups from the bridgehead position in the photoproducts (XX and XXII) to the ester group of the ester products (XXX and XXXI). Participation of a solvent molecule in the reaction must still be explained.

At this stage of the investigation the key mechanistic step became obvious. The ultraviolet spectrum of photo-4-methyltropolone methyl ether (XX; Figure 33, page 143) shows a bathochromic shift of 15 mu.[36]

---

[36] The calculated value is 215 mu (footnote 28). The observed value is 230 mu.

In the analogous case of photo-gamma-tropolone methyl ether[37] (V) this shift results from interaction of the cyclobutene double bond with the cyclopentenone chromophore giving an excited state closely approximated by XXXII. The corresponding excited state for the alpha-tropolone



XXXII

photoisomers must be XXXIII (Figure 8). Simple migration of the $C_1$-$C_2$ bond in XXXIII will give excited state XXXIV in which the carbonium ion is nicely stabilized by the methoxyl group. This presumably is why photo-gamma-tropolone methyl ether shows no analogous reaction. Subsequent collapse of XXXIV would give the suspected intermediate XV. This intermediate could be opened by solvent in several ways giving the required acid or ester. This latter mechanistic problem will be discussed later.

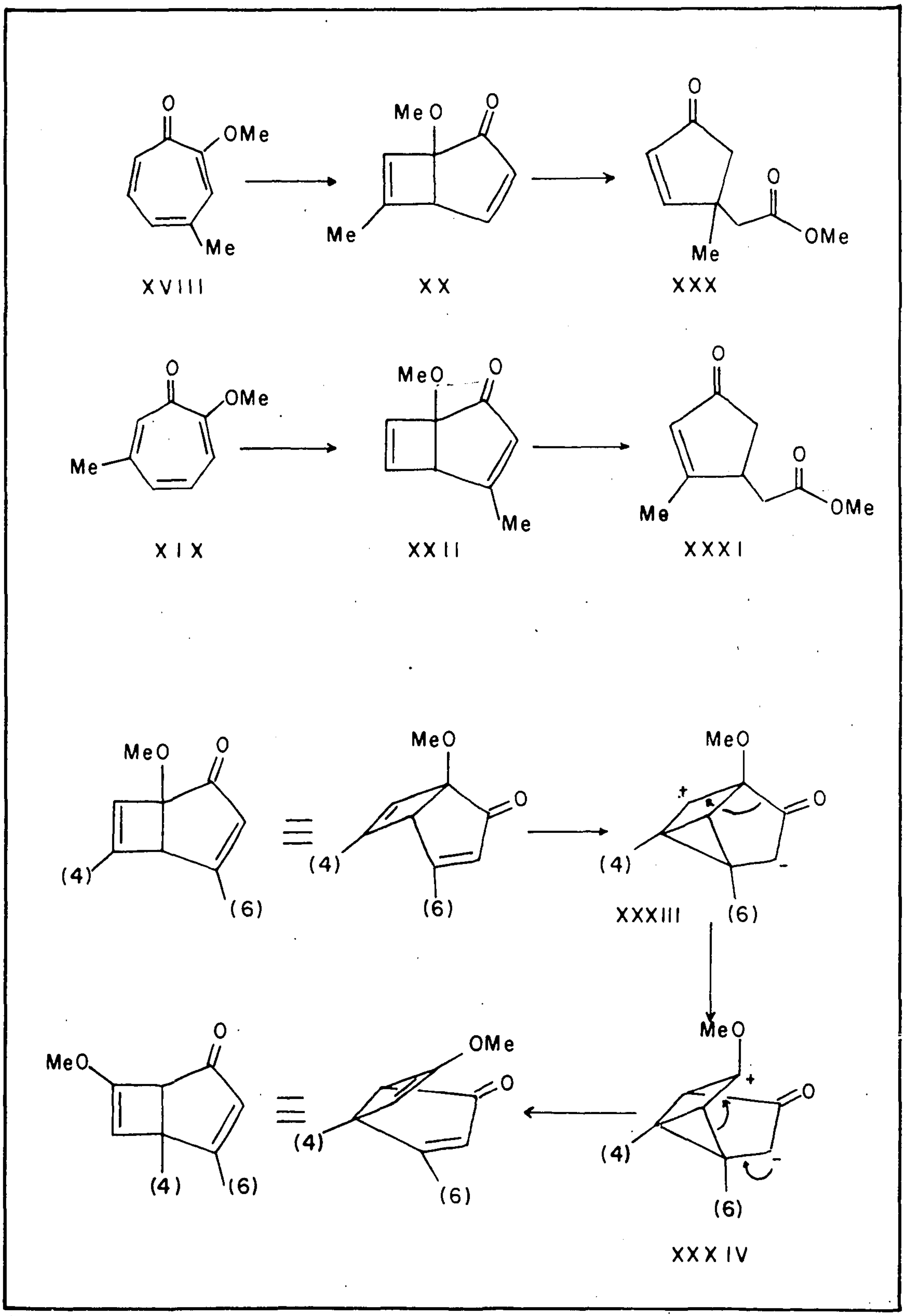
Significant features of this proposal are: (1) the reaction is light catalysed, bond migration occurring in the excited state; (2) the position of the substituents in the final products is readily explained;

---

[37] O. L. Chapman and D. J. Pasto, J. Am. Chem. Soc., 82, 3642 (1960); ibid., 81, 5510 (1959) and references cited therein.

Figure 8. Top: Experimentally established reaction sequence at this stage of the investigation

Bottom: Mechanistic proposal rationalizing the conversion of photoproducts to the predicted intermediates

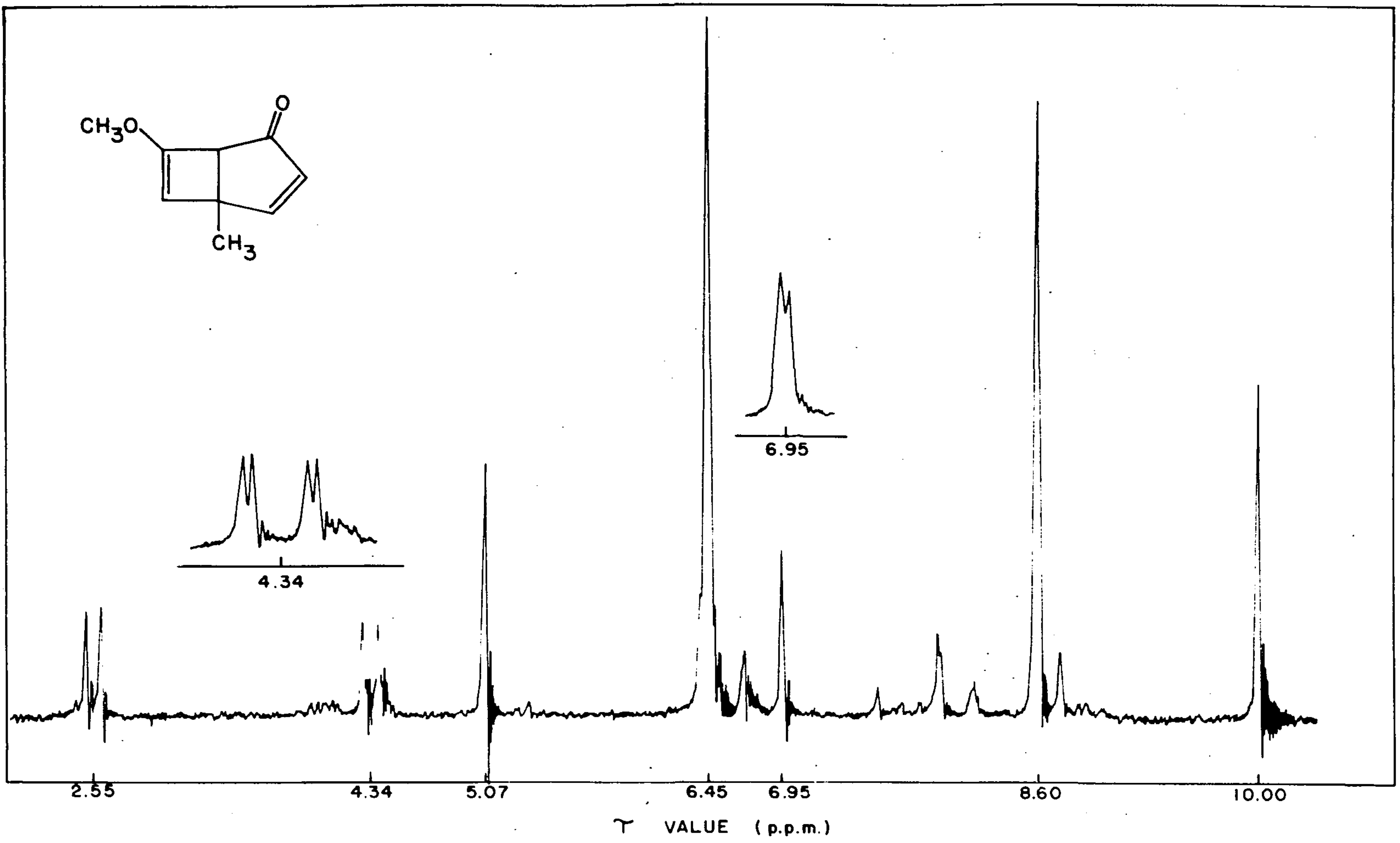

XVIII
XX
XXX
XIX
XXII
XXXI
XXXIII
XXXIV
MeO
OMe
Me
O
(4)
(6)

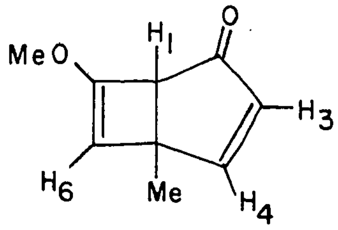
(3) the procedure by which a solvent molecule enters the reaction is implied; and (4) the existence of a potentially isolatable intermediate is predicted. It was therefore decided to attempt the isolation of these intermediates by irradiation of photo-4-methyltropolone methyl ether (XX) and photo-6-methyltropolone methyl ether (XXII) under anhydrous conditions.

When an ethereal solution of XX was irradiated under anhydrous conditions in a quartz tube, conversion to a new product was complete in three hours (1.0 g. of starting material), as shown by vapor phase chromatography. Continued irradiation for a period of 24 hours produced no observable change in the chromatogram. The product, isolated in 40% yield as a colorless liquid, absorbed strongly in the infrared at 5.93, 6.14, and 6.35 u (Figure 25, page 127), indicative of an alpha,beta-unsaturated ketone system (5.93 and 6.14 u) and an unsymmetrical cyclobutene double bond 6.35 u). An ultraviolet maximum was observed at 226 mu (Figure 40, page 157), again, considerably different from the value of 215 mu expected for the predicted intermediate.[28] By analogy with photo-gamma-tropolone methyl ether (V) and with the photoisomers already obtained in this investigation, this bathochromic shift could be explained by the existence of excited state (XXXIV) as postulated on page 34.

The nuclear magnetic resonance spectrum of this compound (Figure 9, page 39) supports the predicted structure XXXVI for lumi-4-methyltropolone methyl ether. The AX type coupling of the protons on the cyclopentenone double bond gives two symmetrical doublets at 2.55 and 4.34 p.p.m. High

Figure 9. Nuclear magnetic resonance spectrum of lumi-4-methyltropolone methyl ether (XXXVI)


CH$_3$O
O
CH$_3$
6.95
4.34
2.55
4.34
5.07
6.45
6.95
8.60
10.00
τ VALUE (p.p.m.)

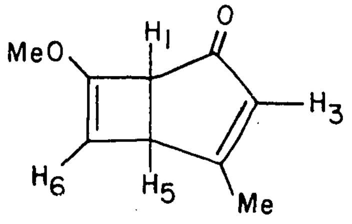


XXXVI

resolution scanning shows the doublet arising from the *alpha* proton ($H_3$) to be split further owing to coupling with the single bridgehead proton ($H_1$) at 6.95 p.p.m. Thus, the methoxyl group must occupy a new position. The presence of the methoxyl group on the cyclobutene double bond is established by observation of a single cyclobutene proton ($H_6$) as a sharp singlet at 5.07 p.p.m. Since neither $H_4$ nor $H_6$ shows further splitting the methyl group must be on the bridgehead as predicted. This assignment is verified by the singlet methyl signal at 8.60 p.p.m. The methoxyl protons of the cyclobutene enol ether appear at 6.45 p.p.m.

In a similar manner, irradiation of an ethereal solution of photo-6-methyltroplone methyl ether (XXII) in quartz under anhydrous conditions afforded, after purification, a 50% yield of a new photoproduct as an extremely hygroscopic colorless solid (m.p. *ca.* 33-35°). This material showed intense infrared absorption at 5.89 and 6.15 u (Figure 26, page 129) and an ultraviolet maximum at 233 mu (Figure 41, page 159). The assumption that this isomer has a structure (XXXVII) similar to XXXVI is supported by the cyclopentenone and double bond absorptions at 5.89 and

6.15 u respectively in the infrared. Structure XXXVII for lumi-6-methyltropolone methyl ether is further supported by examination of the



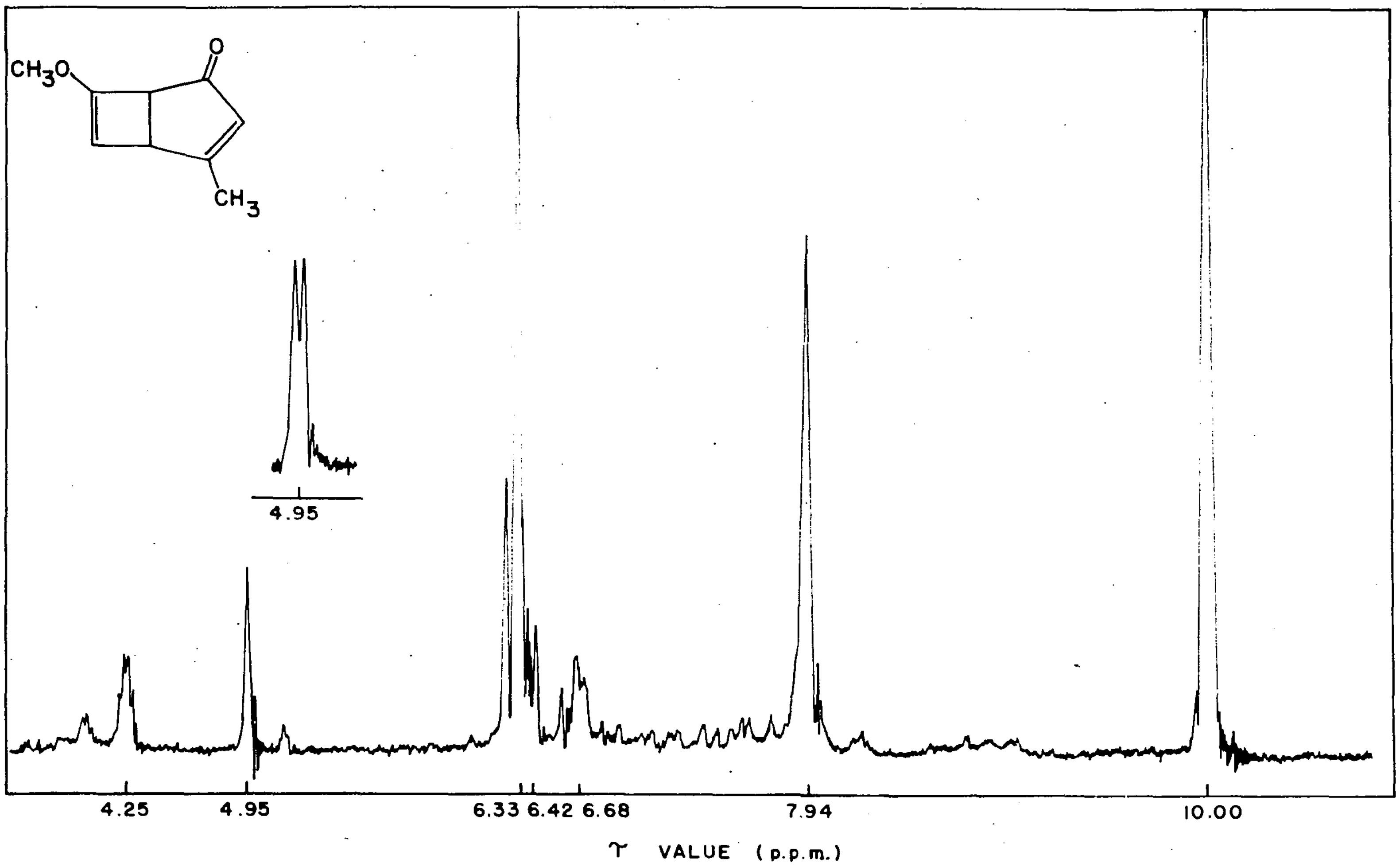
XXXVII

nuclear magnetic resonance spectrum of this material (Figure 10, page 43). Observation of a single cyclopentenone olefinic proton ($H_3$) as a quartet at 4.16 p.p.m. confirmed the placement of the methyl group on the beta carbon of the chromophore. Likewise, the appearance of a single cyclobutene proton ($H_6$) at 4.91 p.p.m. established the position of the methoxyl group. The doublet nature of this signal arises from coupling with the bridgehead proton ($H_5$) which appears as a multiplet at 6.42 p.p.m. The presence of a second bridgehead proton ($H_1$) as a multiplet at 6.68 p.p.m. constitutes further evidence for structure XXXVII. Completing the assignment of spectral lines, the methoxyl and methyl signals are seen at 6.33 and 7.99 p.p.m. respectively.

Conclusive proof of the structures of lumi-4-methyltropolone methyl ether (XXXVI) and lumi-6-methyltropolone methyl ether (XXXVII) was provided by pyrolysis of these compounds to the corresponding methyl substituted beta tropolones.

Pyrolysis of the lumi-4 product (XXXVI) at 415° gave an oil which

Figure 10. Nuclear magnetic resonance spectrum of lumi-6-methyltropolone methyl ether (XXXVII)


CH$_3$O
O
CH$_3$
4.95
4.25
4.95
6.33
6.42
6.68
7.94
10.00
τ VALUE (p.p.m.)

was hydrolysed with hot aqueous base. The ultraviolet spectra of this hydrolysate in acid (Figure 43, page 163) and in base (Figure 42, page 161) were identical with the corresponding spectra for an authentic sample of 5-methyl-beta-tropolone.[38]

Pyrolysis of lumi-6-methyltropolone methyl ether (XXXVII) gave a crude material which could not be readily characterized. However, pyrolysis of a mixture of XXXVI and XXXVII (50:50) at 440° followed by hydrolysis of the pyrolysate with refluxing 20% aqueous HBr gave a single product in good yield which was identical to 5-methyl-beta-tropolone (identified by mixed melting point determination and infrared comparison (Figure 28, page 133) with authentic material). The synthesis of 5-methyl-beta-tropolone is outlined in Figure 11, page 46.

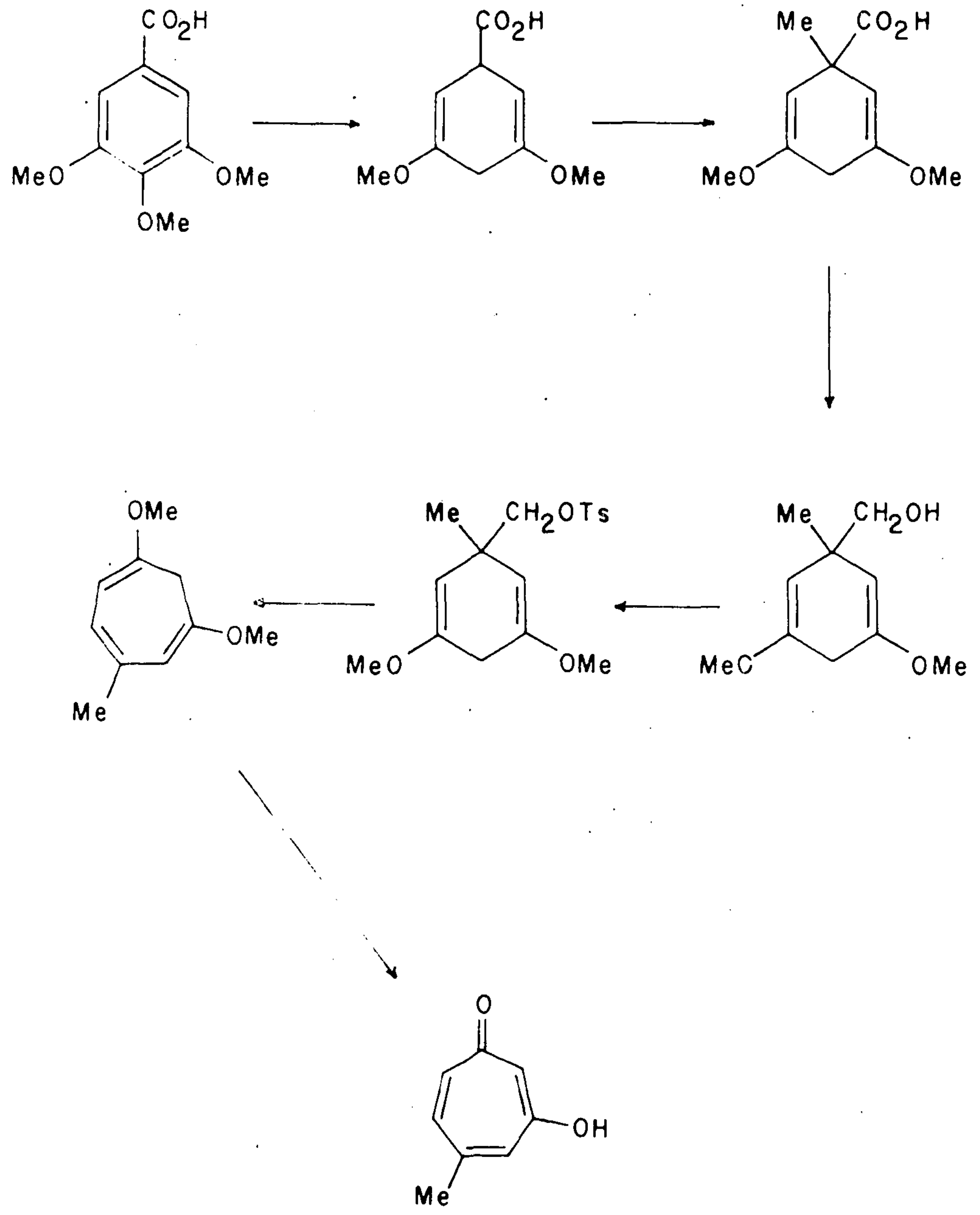
The isolation and characterization of these intermediates strongly supports the mechanism proposed on page 33. Lumi-4-methyltropolone methyl ether (XXXVI) is undoubtedly the predicted precursor of photo-4-ester (XXX) as evidenced by the positions of the methyl and methoxyl groups. Similarly, lumi-6-methyltropolone methyl ether (XXXVII) must be the precursor of photo-6-ester (XXXI).

The sequence leading from the tropolone methyl ethers (XVIII and XIX) to the corresponding esters (XXX and XXXI) now appeared to be as shown in Figure 14, page 55; although reversion to the tropolones

---

[38] This compound was prepared by Dr. P. Fitton according to the procedure of Chapman and Fitton (O. L. Chapman and P. Fitton, *J. Am. Chem. Soc.*, *83*, 1005 (1961)). The synthesis is shown in detail in Figure 11, page 46.

Figure 11. Synthesis of 5-methyl-*beta*-tropolone



5 – METHYL – beta – TROPOLONE

followed by isomerization to the lumiproducts remained an unlikely possibility. It remained necessary to elucidate the nature of the transformation of the lumiproducts (XXXVI and XXXVII) to the corresponding esters (XXX and XXXI), and to rigorously establish the sequential nature of the conversion.

An $8.8X10^{-5}M$ solution of lumi-4-methyltropolone methyl ether (XXXVI) in 95% ethanol was treated with two drops of ca. one normal hydrochloric acid and the ultraviolet spectrum of the resulting solution (ca. 0.02 N in HCl) measured at intervals over a period of six hours. The resulting spectra are reproduced in Figure 12, page 49. A smooth transition from the lumi-4- product (XXXVI) to photo-4-ester (XXX) is observed. Two isobestic points appear indicating that only two absorbing species are present in the solution.

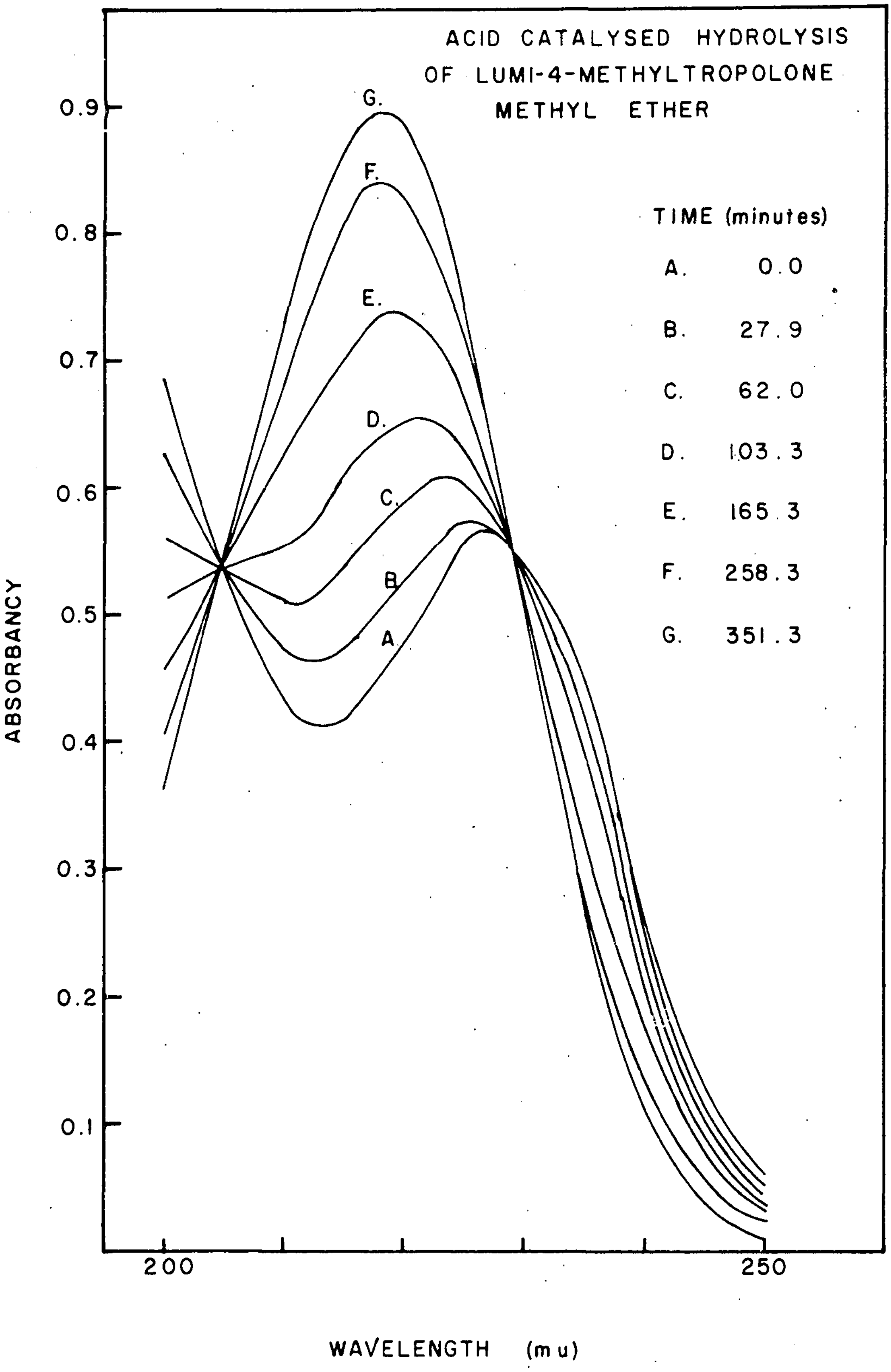
A similar experiment was attempted with lumi-6-methyltropolone methyl ether (XXXVII), but the reaction was so rapid that the first spectrum obtained was that of photo-6-ester (XXXI).[39] The incorporation of a molecule of water in the reaction sequence was thus established, but it was necessary to determine whether, in neutral media, this reaction was light catalysed.

An aqueous solution of lumi-4-methyltropolone methyl ether (XXXVI) was divided into two equal portions, and each portion was placed in a quartz irradiation tube. One was irradiated while the other was

---

[39] Less than two minutes had elapsed between addition of the acid and completion of the first spectral determination.

Figure 12. Ultraviolet spectra taken at intervals during the acid catalysed conversion of lumi-4-methyltropolone methyl ether (XXXVI) to photo-4-ester (XXX)


ACID CATALYSED HYDROLYSIS
OF LUMI-4-METHYLTROPOLONE
METHYL ETHER
ABSORBANCY
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
200
250
WAVELENGTH (mu)
G.
F.
E.
D.
C.
B.
A.
TIME (minutes)
A. 0.0
B. 27.9
C. 62.0
D. 103.3
E. 165.3
F. 258.3
G. 351.3

subjected to identical treatment except that all light was excluded. Vapor phase chromatography proved that even after the sample exposed to light had been completely converted to the ester (XXX) the dark sample contained only unchanged starting material. Thus, the hydrolysis of the lumi-products (XXXVI and XXXVII) to the esters (XXX and XXXI) is light catalysed.

The sequential nature of the reactions discussed above in the transformation of the alpha-tropolone methyl ethers (XVIII and XIX) to the corresponding photo esters (XXX and XXXI) was established by irradiating an ethereal solution of 6-methyltropolone methyl ether (XIX) in a quartz tube and analysing the reaction solution periodically by vapor phase chromatography. By assuming the total area under all peaks in any given chromatogram to be one, the relative percentage of each product present at a given time could be determined.[40] The data thus obtained are tabulated in Table 2, page 113 and are plotted in Figure 13, page 52.

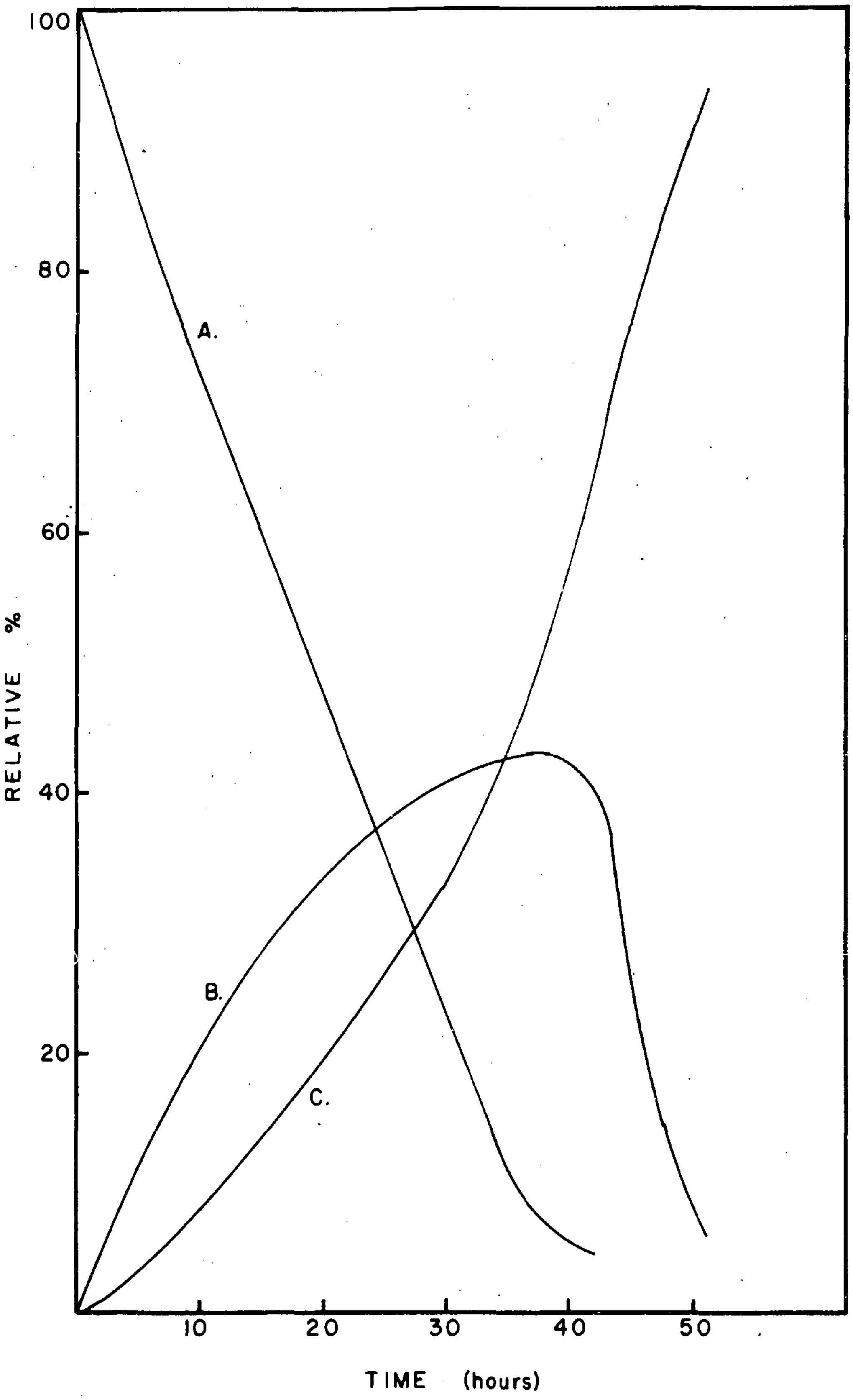
The continuous disappearance of 6-methyltropolone methyl ether (XIX); the concommitant increase in the concentration of photo-6-methyltropolone methyl ether (XXII) which reaches a maximum and then

---

[40] This treatment is not rigorously quantitative, since strictly speaking the individual peak areas should be corrected for differences in the thermal conductivities of the various components. Further, since no standard was included in the reaction mixture, the absolute amounts of the various materials present cannot be determined; hence no allowance is made for decomposition of any compounds.

Figure 13. Relative percent distribution versus time analysis illustrating the sequential conversion of 6-methyltropolone methyl ether (XVIII) to lumi-6-methyltropolone methyl ether

A. 6-methyltropolone methyl ether (XVIII)
B. photo-6-methyltropolone methyl ether (XXII)
C. lumi-6-methyltropolone methyl ether (XXXVII)


100
80
60
40
20
RELATIVE %
A.
B.
C.
10
20
30
40
50
TIME (hours)

decreases; and the initially slow, but continuous production of lumi-6-methyltropolone methyl ether (XXXVII) demand that the reaction be sequential. A similar result was obtained upon irradiation of an aqueous solution of 6-methyltropolone methyl ether (XIX) in quartz except that the final product was photo-6-ester. Unfortunately, the number of measurements obtained was insufficient to permit treatment in the above manner.

The detailed mechanistic path of the light catalysed conversion of alpha-tropolones to 4-oxo-2-cyclopentenylacetic acids (Figure 14, page 55) is clearly defined by the movements of the methyl and methoxyl substituents in the 4-methyltropolone methyl ether (XVIII) sequence. Additional confirmation of the mechanism is provided by the transformations of 6-methyltropolone methyl ether (XIX) and its valence tautomers (XXII and XXXVII).

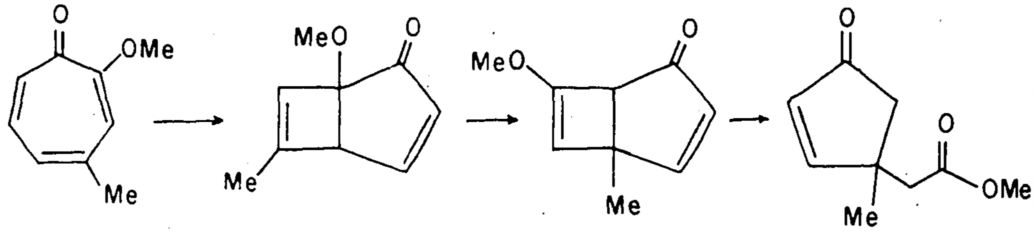
A priori, formation of two valence tautomers might be expected upon irradiation of 4-methyltropolone methyl ether (see XX and XXI, page 14. The exclusive (or nearly exclusive) formation of one isomer (XX) suggests that the excited state leading to XX has a very specific structure of a highly polar nature which is stabilized by the methoxyl group. This excited state might be visualized as XXXIX (Figure 14, page 55). A similar structure (XL) has been proposed by Pasto[41] to explain the

---

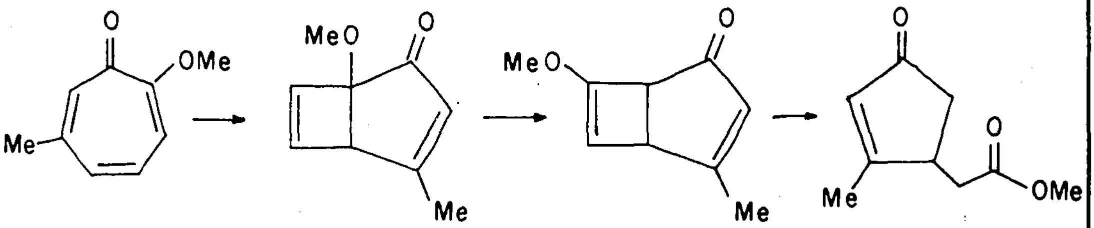
[41] D. J. Pasto, The Chemistry and Photochemistry of gamma-Tropolone Methyl Ether, Unpublished Ph.D. Thesis, Ames, Iowa, Library, Iowa State University of Science and Technology, 1960, p. 97.

Figure 14. Top: Established sequence of reactions in the conversion of _alpha_-tropolone methyl ethers (XVIII and XIX) to the corresponding methyl esters (XXX and XXXI)

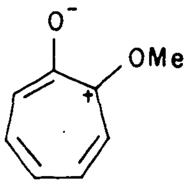
Bottom: Excited state of the tropolone nucleus for 4-methyltropolone methyl ether (XXXIX) and _gamma_-tropolone methyl ether (XXXX)



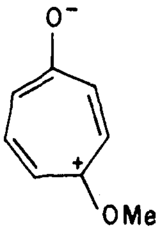
XVIII XX XXXVI XXX



XIX XXII XXXVII XXXI



XXXIX



XL

formation of a single valence tautomer (V) upon irradiation of gamma-tropolone methyl ether (IV). The observation[17, 40] that polar solvents are required in order for this reaction to occur supports the proposed polar nature of the tropolone excited state which leads to valence tautomerization.

The mechanistic steps in the conversion of photo-4-methyltropolone methyl ether (XX) to lumi-4-methyltropolone methyl ether (XXXVI) have been discussed on page 33 and need not be mentioned further.

The existence of excited state XXXIV for lumi-4-methyltropolone methyl ether (XXXVI) and lumi-6-methyltropolone methyl ether (XXXVII) also explains the facile light catalysed hydrolysis of these compounds. Reversible addition of water to XXXIV gives XLI. It should be emphasized that XLI is still an excited molecule. Three mechanistic paths now present themselves (Figure 15, page 60).

Irreversible rearrangement of XLI via path A would give XLII which may subsequently collapse to the corresponding ester (XLIII).

Alternatively, XLI might collapse immediately to XLIV (path B). Subsequent rearrangement via a retroaldol type reaction would also give the ester XLIII.

Path C indicates yet a third choice. Collapse of XLI could give the unstable intermediate XLV. A retroaldol type reaction followed by rearrangement of the resulting anion also gives an ester product (XLVI). Fortunately, the presence of the methyl substituents in photo-4-ester (XXX) and photo-6-ester (XXXI) permits us to discard this proposal since it predicts the wrong products.

A fourth possibility, light catalysed addition of water to the enol ether leading directly to XLIV might be considered. This path is extremely unlikely, since the light sources used provide no radiant energy in the regions where simple olefinic chromophores absorb (ca. 150-190 mu). Further, the transparency of the irradiation vessels and solvents used decreases sharply below ca. 200 mu.

Thus, light induced hydrolysis of lumi-4-methyltropolone methyl ether (XXXVI) and lumi-6-methyltropolone methyl ether (XXXVII) to the corresponding esters (XXX and XXXI) must occur via excited state XLI and subsequently via either path A or path B.

The questions raised on page 25 may now be answered. (1) Photo-4-methyltropolone methyl ether (XX) and photo-6-methyltropolone methyl ether (XXII) are intermediates in the conversion of 4-methyl- and 6-methyltropolone methyl ether (XVIII and XIX) to the corresponding esters (XXX and XXXI). (2) There is one other intermediate (XXXVI and XXXVII) between the photo products and the esters. (3) All steps in the sequence of reactions require light. (4) Finally, the mechanistic details of all the transformations have been elucidated.

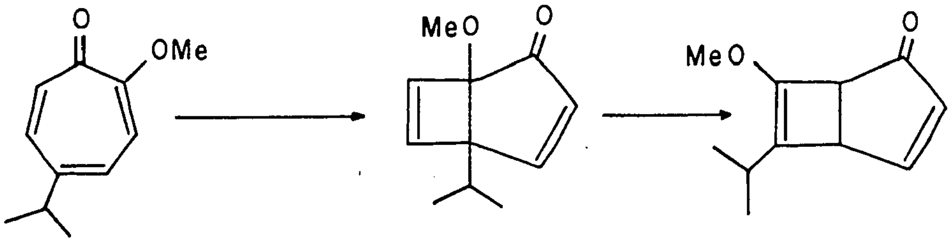
Dauben and Koch[42] have provided additional support for these mechanistic proposals by isolating the intermediates (XLVII and XLVIII) in the alpha-tropolone methyl ether (XXVIb) series and by verifying the sequential nature of the transformation of XVIb to XVIIc as shown below.

---

[42] W. G. Dauben, K. Koch, O. L. Chapman, and S. L. Smith, J. Am. Chem. Soc., 83, 1768 (1961).

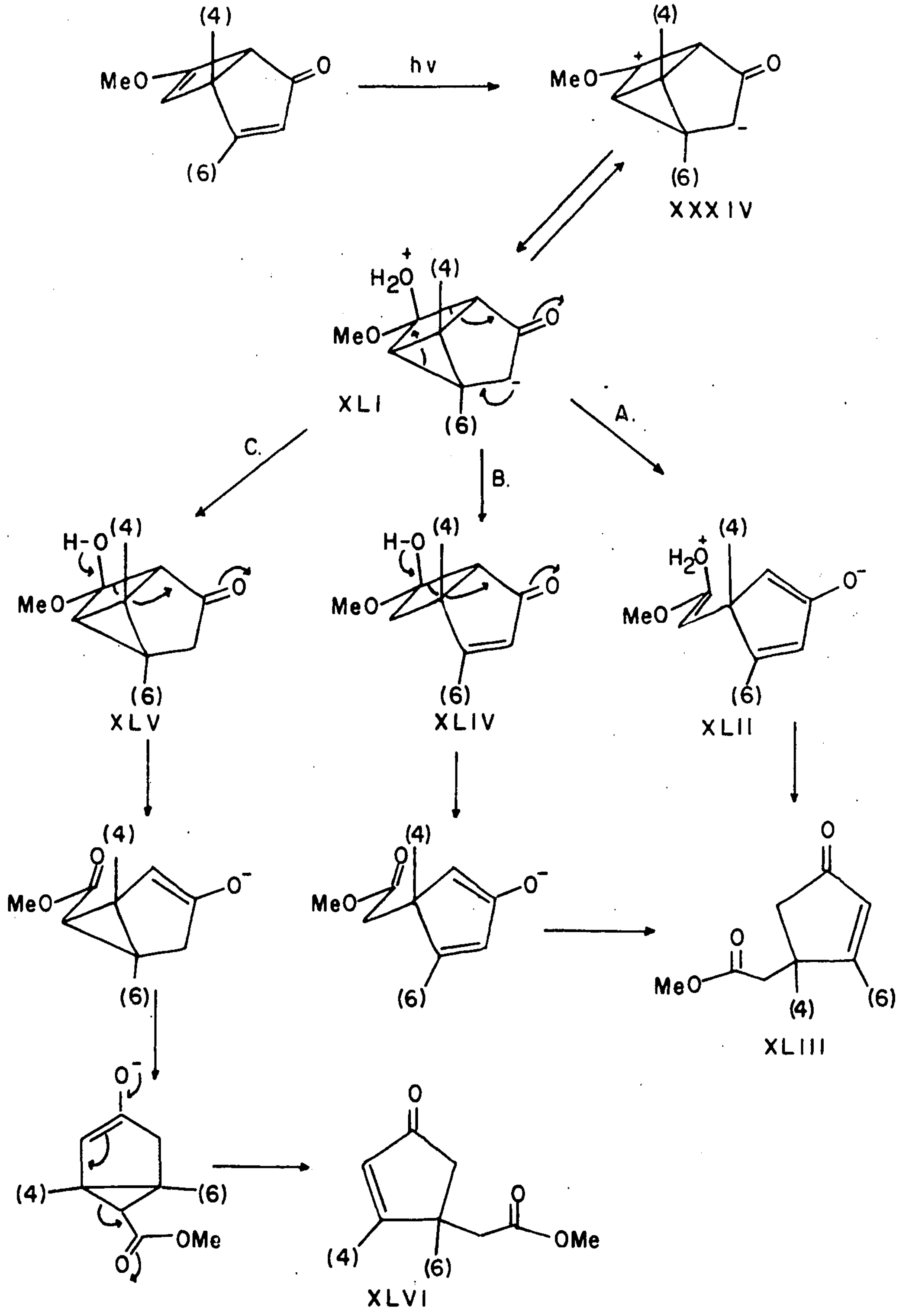
XLVII XLVIII

In the same paper Dauben and Koch report that irradiation of *gamma*-thujaplicin methyl ether (XLIX) gave photoisomer (L). Undoubtedly L arises from photoisomerization of LI. The mechanistic explanation of the photo-4-methyltropolone methyl ether (XX) to lumi-4-methyltropolone methyl ether (XXXVI; Figure 8) isomerization must now be considered as rigorously established.



XLIX LI L

Figure 15. Mechanistic proposals for the light catalysed hydrolysis of lumi-4- and lumi-6-methyltropolone methyl ether (XXXVI) and (XXXVII) to the corresponding photo esters (XXX and XXXI)


hν
XXXIV
XLI
A.
B.
C.
XLV
XLIV
XLII
XLIII
XLVI
MeO
OMe
$H_2\overset{+}{O}$
H-O
(4)
(6)

## Diels-Alder Reaction of 4-Methyltropolone and Maleic Anhydride

Chapman and Pasto[17, 43] have commented on the fact that bridging occurs across the same two carbon atoms in both the Diels-Alder adduct[43] and the photoisomer[17] of gamma-tropolone methyl ether (IV). These authors suggest that the tropolone excited states leading to these products may be similar or even identical. Diels-Alder adducts of several other tropolones have been prepared,[44, 45, 46, 47] but the results are somewhat ambiguous and offer no opportunity to test this hypothesis. In light of the specificity displayed in the photoisomerizations of 4-methyltropolone methyl ether (XVIII) and 6-methyltropolone methyl ether (XIX) it was decided to study the Diels-Alder reaction of 4-methyltropolone (LII) to determine whether the same specificity would be manifest.

Reaction of an equimolar mixture of LII and maleic anhydride in refluxing xylene gave a single crystalline product (m.p. 177.1-177.9°) in 58% yield. This material showed infrared maxima at 2.90, 5.34, 5.58, and 6.00 u (Figure 29, page 135) and an ultraviolet maximum at 227 mu

---

[43] O. L. Chapman and D. J. Pasto, J. Am. Chem. Soc., 81, 3696 (1959).

[44] T. Nozoe, S. Seto, and T. Ikemi, Proc. Japan Acad., 27, 655 (1951).

[45] T. Nozoe, T. Mokai, K. Yakase, and T. Nagase, ibid., 31, 777 (1955).

[46] E. Sebe and C. Osaho, ibid., 28, 282 (1952).

[47] E. Sebe and Y. Itaimo, ibid., 29, 107 (1953).

(Figure 44, page 165). The 5.34 and 5.58 u (Figure 29, page 135) absorption maxima in the infrared indicate the presence of the five membered anhydride, while the peak at 2.90 u suggests the presence of an alcohol. Ultraviolet absorption at 227 (Figure 44, page 165) mu establishes the presence of an alpha,beta-unsaturated ketone; an assignment supported by the 6.00 u absorption in the infrared.

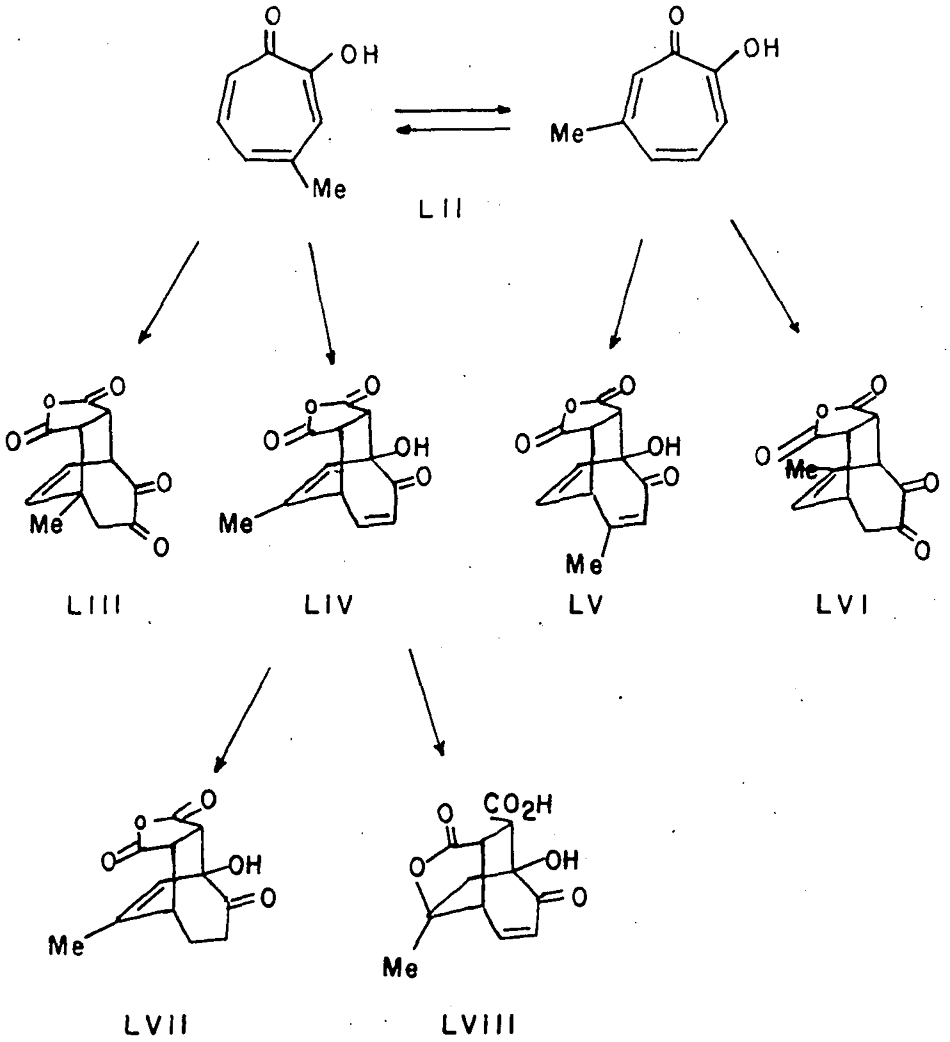
Treatment of a warm aqueous slurry of the adduct with a few drops of concentrated hydrochloric acid afforded a single crystalline material (m.p. 190.6-191.3°) in 66% yield. Infrared absorption (Figure 29, page 135) at 5.70 u indicated a gamma lactone, and absorption at 2.90, 3.06, and 5.85 u suggested the presence of an alcohol and a carboxylic acid. The ultraviolet spectrum (Figure 45, page 167) of this material showed a maximum at 229 mu which in conjunction with an infrared absorption at 6.05 u established the presence of an alpha,beta-unsaturated ketone. Sublimation of this material gave the adduct quantitatively indicating that no gross rearrangement of the carbon skeleton had occurred.

Catalytic hydrogenation of the adduct gave a crystalline dihydro derivative which absorbed in the infrared at 5.37, 5.58, and 5.82 u (anhydride and saturated ketone).

Attempts to acetylate the hydroxyl group with acetic anhydride in pyridine were unsuccessful.

Since 4-methyltropolone (III) exists as a tautomeric mixture one might expect four possible Diels-Alder adducts (two from each tautomer as shown in Figure 16a, page 64). The isolation of only one adduct,

Figure 16a. Possible Diels-Alder adducts from 4-methyltropolone (LII) and maleic anhydride


O
OH
Me
LII
LIII
LIV
LV
LVI
LVII
LVIII
CO2H

and that in 58% yield is, to say the least, surprising.

Structures LIII and LVI are inconsistent with the observed ultraviolet maximum at 227 mu. This fact, in conjunction with the absence of any infrared absorption attributable to an alpha diketone system, excludes them from further consideration. Conversely, both LIV and LV are in excellent accord with the observed infrared data; however, the ultraviolet maximum of the material in hand is consistent only with structure LIV.[48]

Since the lactone formed upon acid treatment of the adduct shows an ultraviolet maximum at 229 mu the lactone must be LVII, and the stereochemistry of the anhydride bridge must be as shown in LIV.

The position of the methyl group in LIV is supported by the formation of a dihydro derivative, since the sterically hindered trisubstituted double bond of LIV would be extremely resistant to catalytic hydrogenation. The dihydro derivative must be LVIII.

Failure of acetylation attempts is in accord with a tertiary hydroxyl group in LIV.

In accord with the prediction of Chapman and Pasto[17] bridging in the Diels-Alder reaction of 4-methyltropolone (LII) occurs across the carbon bearing the oxygen function. Isolation of only one such product (LIV) when two such products might be expected (LIV and LV) was perplexing. Both of these phenomena are, however, explicable in

---

[48] The calculated maximum for LIV is 227 mu; that calculated for LV is 239 mu (see ref. 17).

mechanistic terms.

For many years workers studying the Diels-Alder reaction have proposed mechanisms which fall in one of two categories. In one, known as the two bond mechanism, it is proposed that formation of the adduct occurs in two steps; formation of the first bond being rate controlling. The alternate mechanism proposes that both bonds are formed simultaneously. Both of these mechanistic proposals are discussed by Woodward and Katz[49] in a very significant paper. These authors[49] proposed a new mechanism containing the best features of the two mentioned above.

More recently, Roberts and Lutz[50] and Berson et al.[51] have presented evidence in support of the Woodward mechanism. Berson further suggests that the Diels-Alder mechanism may actually be a continuum varying smoothly from virtually simultaneous bond formation in cases involving non-polar addends to quite distinctly separate bond formation in cases involving polar compounds.

Walling and Peisach[52] have proposed a two step diradical mechanism to explain their data from the dimerization of isoprene, but it is doubtful whether this postulate is generally applicable. Most proponents

---

[49] R. B. Woodward and T. B. Katz, Tetrahedron, 5, 70 (1959).

[50] J. D. Roberts and R. P. Lutz, J. Am. Chem. Soc., 83, 2191 (1961).

[51] J. A. Berson, A. Remanick, and W. A. Mueller, J. Am. Chem. Soc., 82, 5501 (1960).

[52] C. Walling and J. Peisach, J. Am. Chem. Soc., 80, 5819 (1959).

(including Walling) of the two step mechanism or more recently the Woodward mechanism have favored polar contributions of some sort. The data of Roberts[50] and of Berson,[51] while not conclusive, cast considerable doubt on the general applicability of any diradical mechanism while tending to support the Woodward intermediate.

Applying the Woodward mechanism to the reaction of 4-methyltropolone (LII) with maleic anhydride provides the following explanation (Figure 16b, page 69).

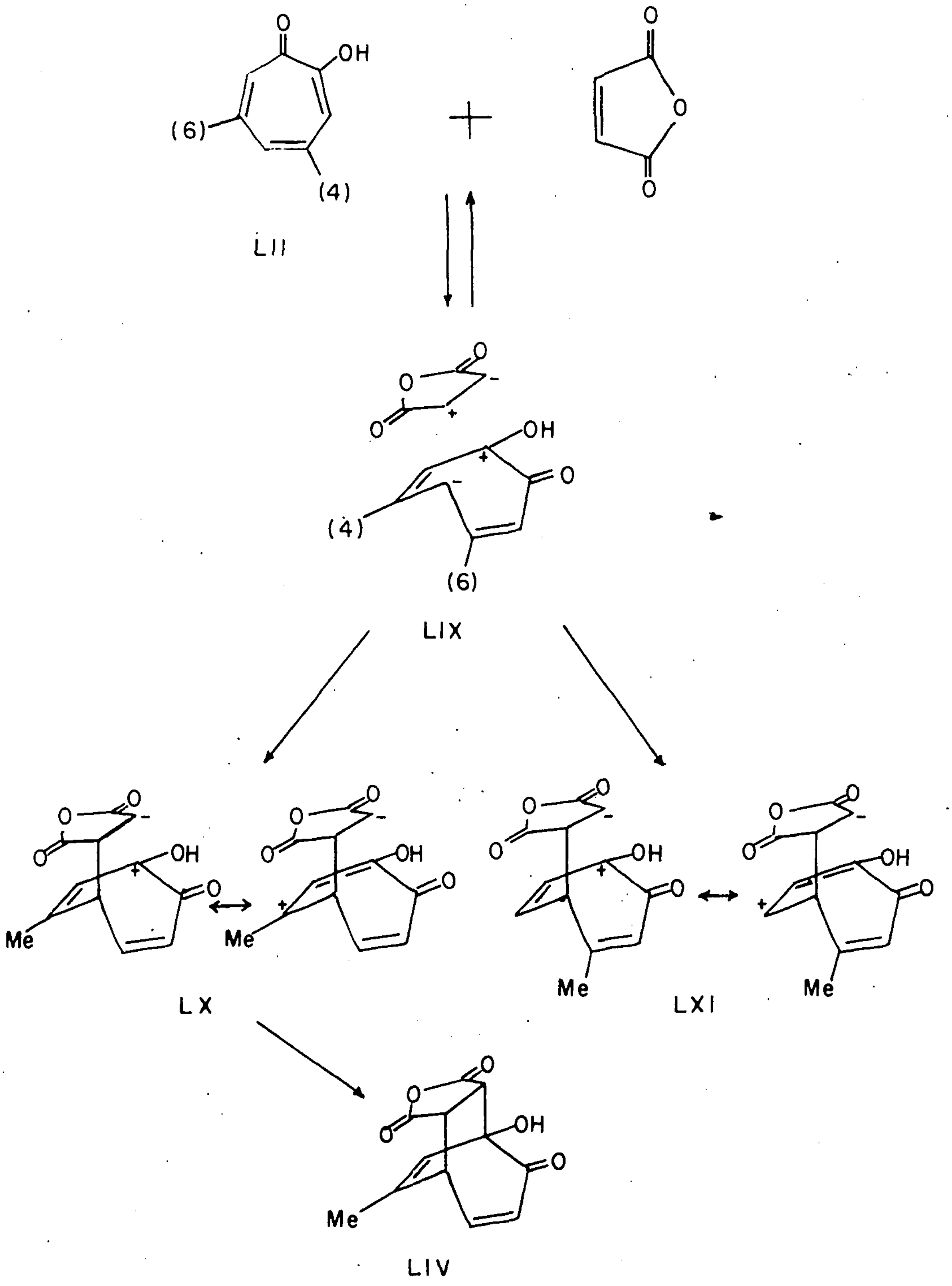
Association of a maleic anhydride molecule with a molecule of 4-methyltropolone (LII) gives a polarized complex, an extreme example of which would be LIX. Obviously, orientation in such a manner that the incipient carbonium ion is stabilized by the hydroxyl group is preferred. At this stage no significant difference may be observed which might favor either the 4-methyl or the 6-methyl tautomer.

The next step is the formation of one bond leading to transition states which, in the extreme, may be represented by LX and LXI.[53] Here a crucial difference is observed. In the transition state arising from the 4-methyl tautomer (LX) the developing carbonium on the seven membered ring is stabilized by both a hydroxyl group <u>and a methyl group</u>. The latter stabilization is completely lacking in the transition state

---

[53] Actually, formation of the second bond probably begins before the first bond is completed; hence LX or LXI would not be the precise structure of the transition state. The argument used is, however, completely applicable; structures LX and LXI being used for purposes of clarity.

Figure 16b. Mechanistic explanation of the Diels-Alder reaction between 4-methyltropolone (LII) and maleic anhydride


O
OH
(6)
(4)
LII
O
O
O
O
O
O
OH
O
(4)
(6)
LIX
O
O
O
OH
O
Me
Me
OH
O
LX
O
O
O
OH
O
Me
Me
LXI
O
O
O
OH
O
Me
LIV

for the 6-methyl tautomer (LXI). Such stabilization will be especially significant in the non-polar solvent xylene. This transition state energy difference coupled with the tautomeric equilibrium between the 4-methyl and 6-methyl isomers fully explains the formation of only one product. Collapse of LX gives the adduct completing the mechanistic explanation.[54]

The results discussed above support the postulate of Chapman and Pasto that the excited state of the tropolone nucleus which leads to photoisomerization, and the transition state of the tropolone nucleus in the Diels-Alder reaction have the same structure. At the present time, however, the data available do not permit any further generalizations along this line.

## The Photochemistry of Thujic Acid and Methylthujate

The mechanism postulated to explain the conversion of 4-methyltropolone methyl ether (XVIII) and 6-methyltropolone methyl ether (XIX) to photo-4-methyltropolone methyl ether (XX) and photo-6-methyltropolone methyl ether (XXII) respectively, and the support of this proposal by the Diels-Alder reaction of 4-methyltropolone (LII), prompted a search for other systems in which this postulate could be tested. Ready availability of a sample of thujic acid (LXIIa) led to its selection for this purpose.

Irradiation of LXIIa could give products analogous to the

---

[54] The author is indebted to Dr. E. Wenkert for a stimulating discussion of this mechanistic problem.

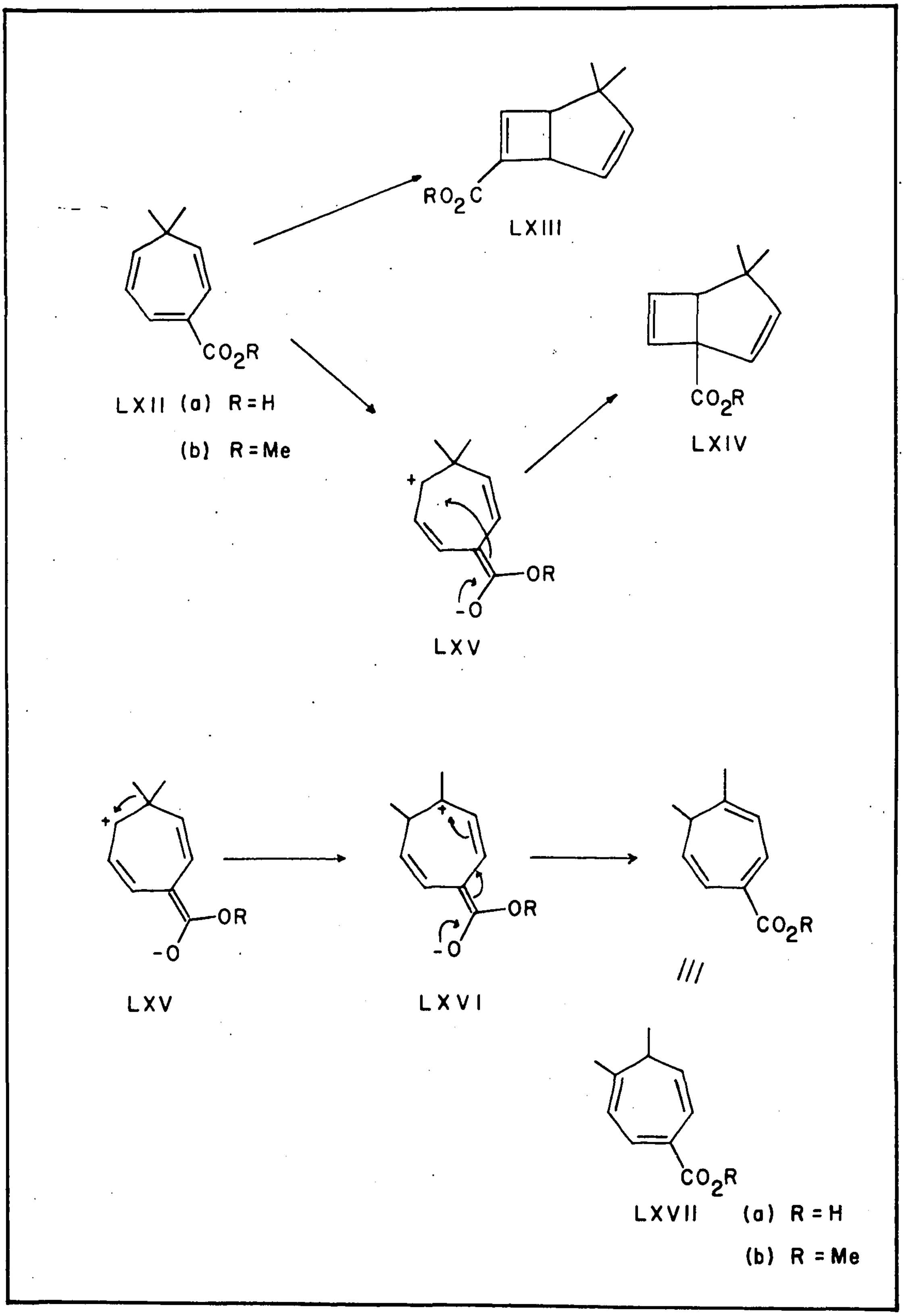
photoisomer XVII obtained by Dauben and Cargill[23] upon irradiation of cycloheptatriene (XV) in ether. If such a reaction did occur, two products (LXIII and LXIV) might be expected as shown in Figure 17, page 73. However, if polar excited states such as LXV do in fact contribute significantly to these valence tautomerization reactions, LXIV should be the predominant if not the only bicyclic product obtained.

The hypothetical existence of excited state LXV offers a much more intriguing possibility; a simple light induced Wagner-Meerwein rearrangement. Migration of a methyl group in LXV would give a more stable excited state LXVIa which could then collapse to the rearranged product LXVIIa. Considering the relative energies of the species involved, the rearrangement reaction seemed at least as likely as the valence tautomerization.

A yellow oil was obtained by irradiating an ethereal solution of thujic acid (LXIIa) in a quartz tube for seven hours. Chromatography of this material on silicic acid gave one discrete fraction as a white, crystalline solid (m.p. 114.5-115.3°), in 56% yield. The infrared spectrum of this material (Figure 30, page 137) was almost identical to that of thujic acid (Figure 29, page 135). The ultraviolet spectrum (Figure 46, page 169) showed maxima at 216 mu and 292 mu; a shift of 2 mu and 10 mu respectively from the ultraviolet maxima of thujic acid.

Neither bicyclic product (LXIII or LXIV) would be expected to show infrared absorption similar to that of thujic acid, and the ultraviolet spectrum of the crystalline photoproduct is completely inconsistent with these structures. Conversely, a compound such as LXVIIa should give an

Figure 17. Proposed mechanism and products for the irradiation of thujic acid and methylthujate (LXIIa and LXIIb)



LXII (a) R = H

(b) R = Me

LXIII

LXIV

LXV

LXV

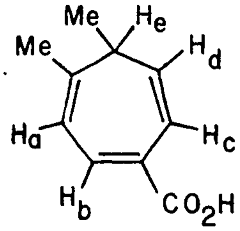
LXVI

LXVII (a) R = H

(b) R = Me

infrared spectrum similar to that of thujic acid. The bathochromic shifts observed in the ultraviolet spectrum of the photoisomer, which is otherwise quite similar to that of thujic acid, support a structure such as LXVIIa differing from the starting material only in the presence of a methyl group on the chromophore.

Photothujic acid is shown conclusively to be LXVIIa by the nuclear magnetic resonance spectrum of this material[55] (Figure 18, page 76). Two methyl signals appear at 7.97 and 8.75 p.p.m. The former is a singlet arising from the methyl group on the double bond. The latter is a doublet ($J = 7.35$ cps) owing to coupling with the tertiary proton $H_e$, which is hidden beneath the methyl signal at 7.97 p.p.m. (shown by integration). Four one proton signals are observed in the olefinic region. The AX pattern arising from coupling of $H_a$ and $H_b$ is seen as two symmetrical doublets at 2.31 and 3.80 p.p.m. respectively. Coupling of $H_c$ and $H_d$ gives rise to two doublets at 3.30 and 4.00 p.p.m. The $H_d$ signal



LXVIIa

---

[55] For comparison the nuclear magnetic resonance spectrum of thujic acid is reproduced in Figure 19, page 78.

Figure 18. Nuclear magnetic resonance spectrum of photothujic acid (LXVIIa)

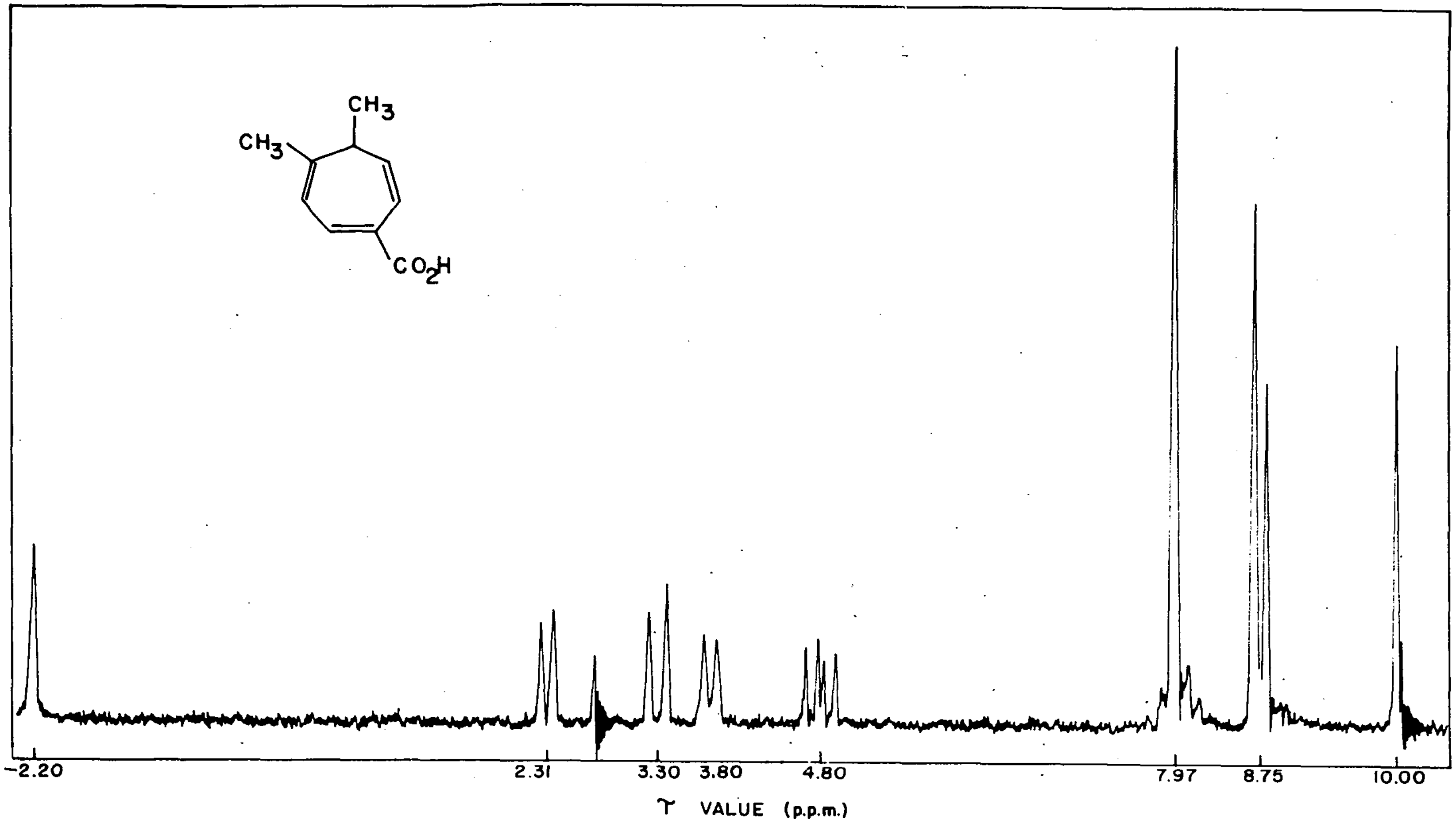
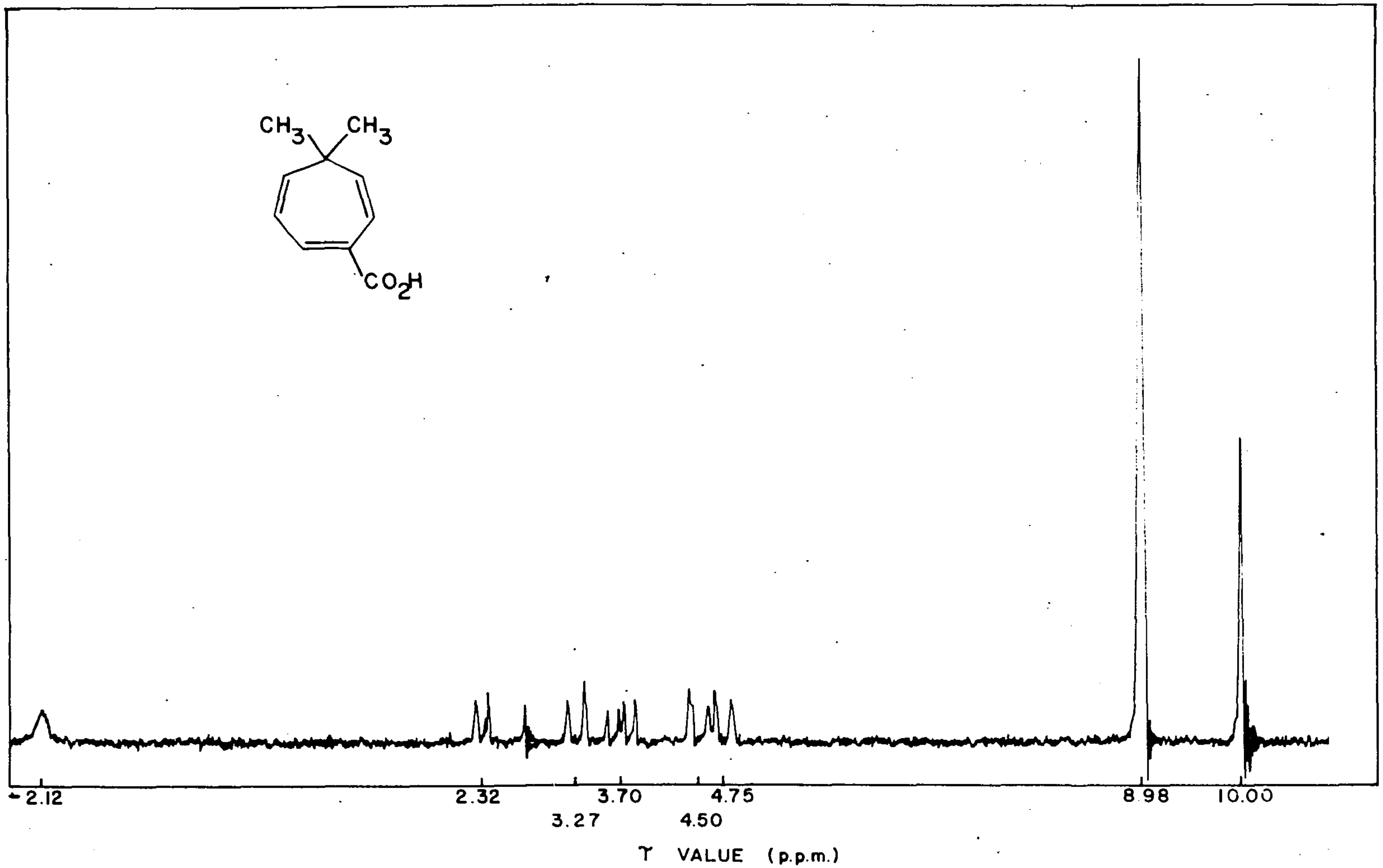
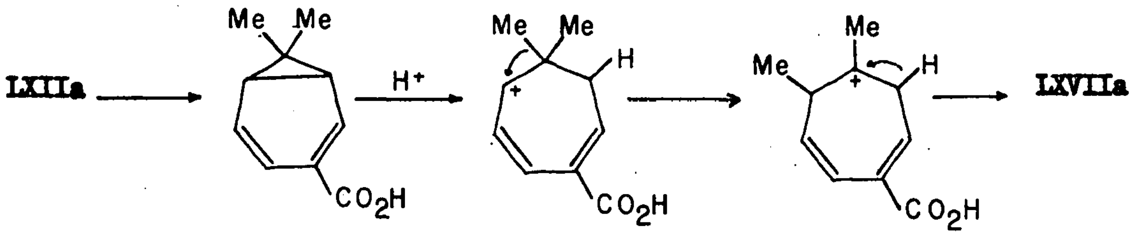

CH3
CH3
CO2H
-2.20
2.31
3.30
3.80
4.80
7.97
8.75
10.00
τ VALUE (p.p.m.)

Figure 19. Nuclear magnetic resonance spectrum of thujic acid (LXIIa)


CH3
CH3
CO2H
2.12
2.32
3.27
3.70
4.50
4.75
8.98
10.00
τ VALUE (p.p.m.)

at 4.80 p.p.m. is split again due to coupling with $H_e$. Finally, the hydroxyl proton of the acid is observed at -2.20 p.p.m.

While the conversion of thujic acid (LXIIa) to photothujic acid (LXVIIa) seemed to offer dramatic confirmation of the mechanistic proposals made above, it was necessary to establish conclusively that the reaction was in fact light induced. After refluxing an ethereal solution of LXIIa in the dark for seven hours pure thujic acid (LXIIa) was quantitatively recovered; indicating that the reaction under investigation was not an acid-catalysed reaction. However, it remained possible that photothujic acid (LXVIIa) arose from acid-catalysed rearrangement of some meta-stable photoisomer (LXVIII) as shown below. This possibility was rigorously excluded from consideration by irradiation of methylthujate (LXIIb).

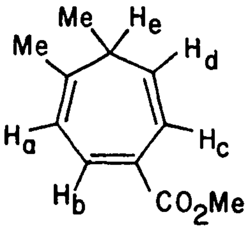


LXVIII

The irradiation of methyl thujate (LXIIb) was followed by vapor phase chromatography which showed that two major products were formed in <u>ca</u>. 75:25 ratio. This mixture was isolated in 70% yield.

The major product, separated as a colorless oil by either vapor phase or column chromatography, showed an infrared spectrum (Figure 30, page 137) quite similar to that of methyl thujate (LXIIb; Figure 30, page 137). The ultraviolet spectrum (Figure 47, page 171) of the photoproduct showed maxima at 216.5 and 293 mu; again a bathochromic shift of 2 mu and 10 mu respectively from the maxima observed for methylthujate.

Structure LXVIIb which is suggested by these data is firmly established by examination of the nuclear magnetic resonance spectrum (Figure 20, page 82) of photomethylthujate (LXVIIb).[56] The two



LXVIIb

symmetrical doublets at 2.55 and 3.93 p.p.m. arise from AX type coupling of $H_a$ and $H_b$ respectively. $H_c$ and $H_d$ give two doublets at 3.46 and 4.92 p.p.m. respectively, the latter being split again by coupling with the tertiary proton ($H_e$) which is buried under the olefinic methyl signal at 8.02 p.p.m. The saturated methyl group appears as a doublet at 8.79 p.p.m. due to coupling with $H_e$. Finally, the methoxyl protons of the

---

[56] For comparison the nuclear magnetic resonance spectrum of methylthujate (LXIIb) is reproduced in Figure 21, page 84. This spectrum has been published previously by J. Grippenberg, Acta Chem. Scand., 10, 487 (1956).

Figure 20. Nuclear magnetic resonance spectrum of photomethylthujate (LXVIIb)

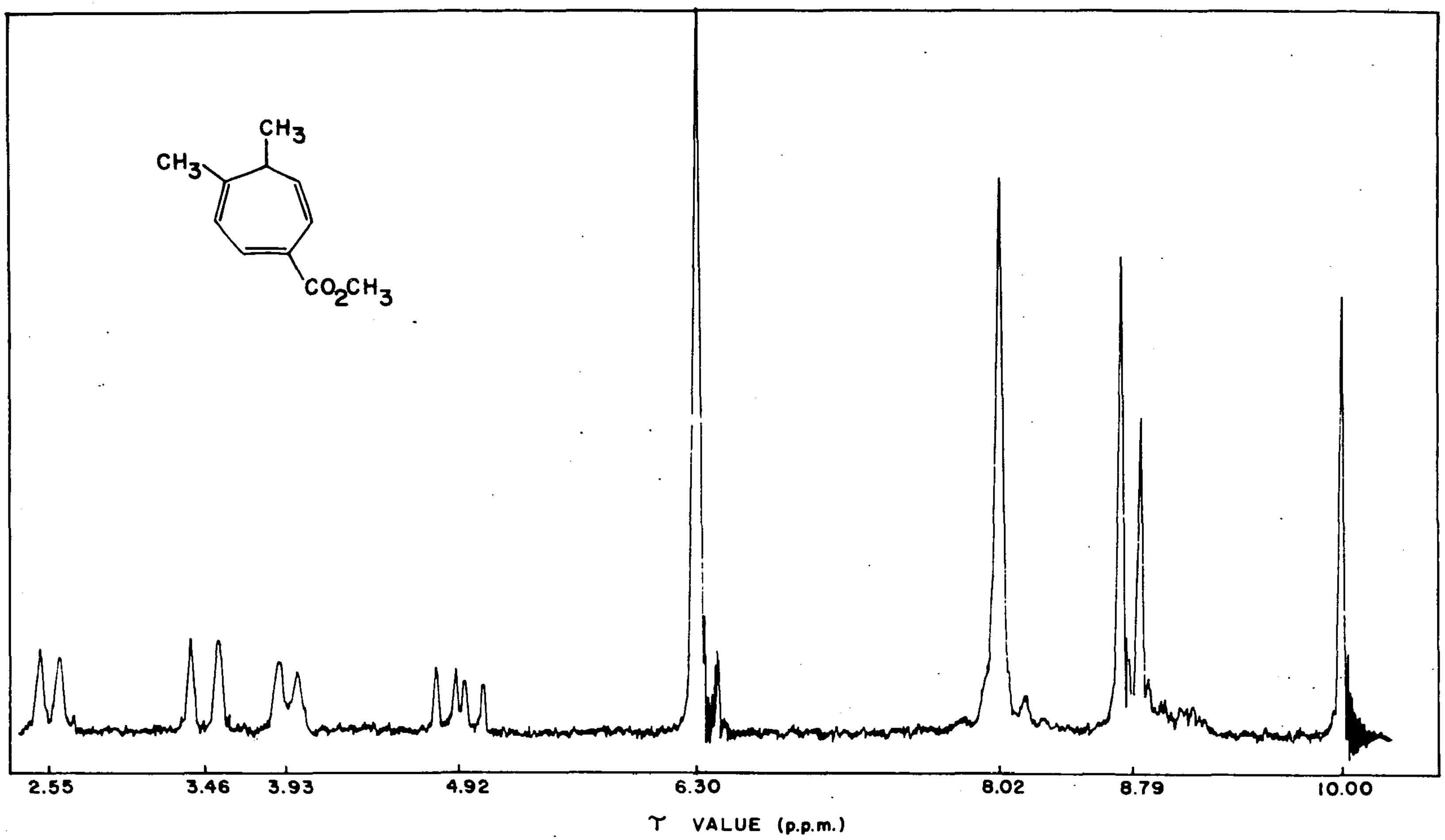
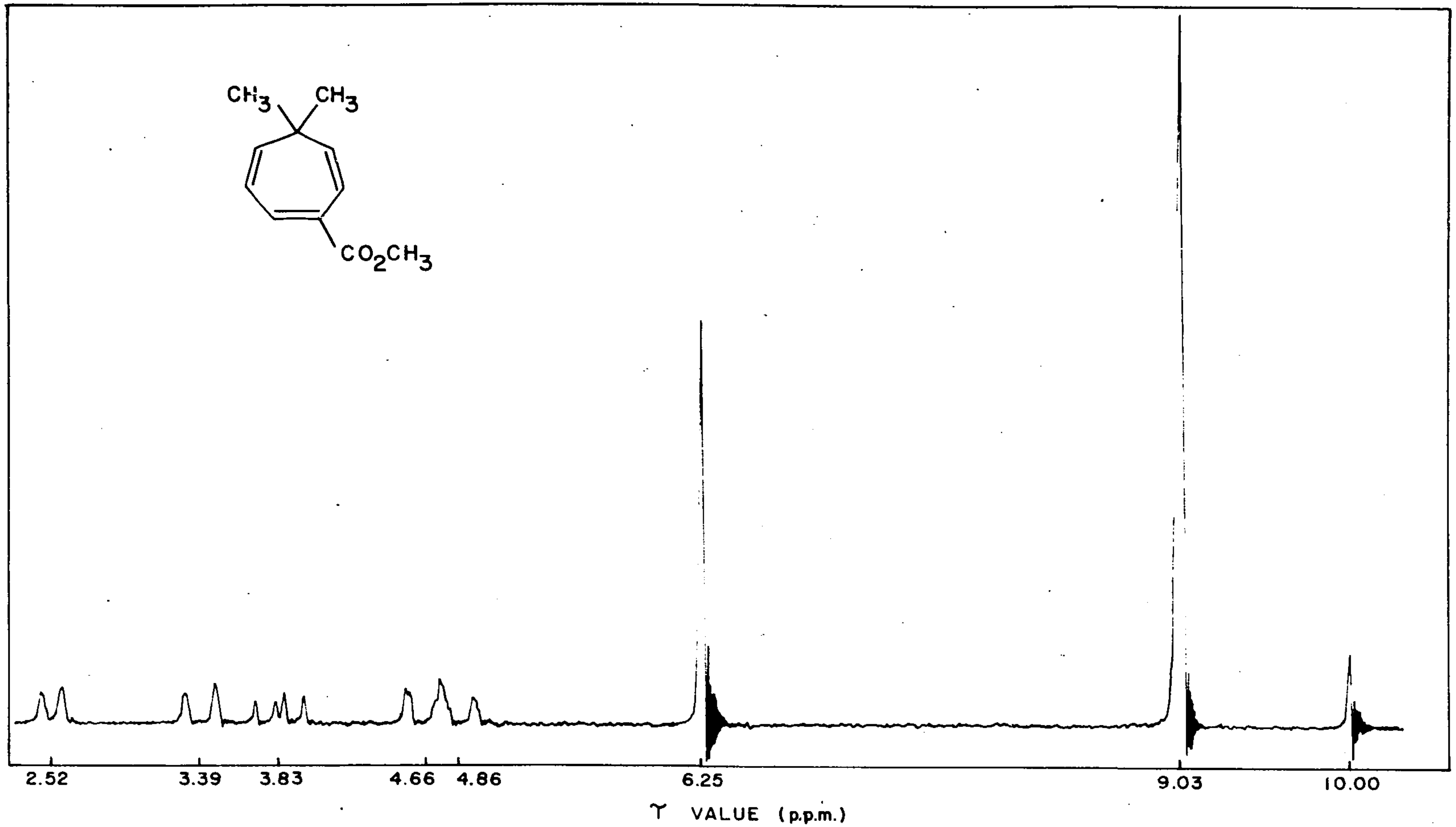

CH3
CH3
CO2CH3
2.55
3.46
3.93
4.92
6.30
8.02
8.79
10.00
τ VALUE (p.p.m.)

Figure 21. Nuclear magnetic resonance spectrum of methyl thujate (LXIIb)

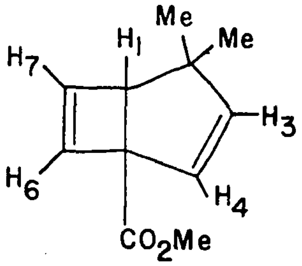

CH3
CH3
CO2CH3
2.52
3.39
3.83
4.66
4.86
6.25
9.03
10.00
τ VALUE (p.p.m.)

ester appear at 6.30 p.p.m.

The rearrangement of thujic acid (LXIIa) and its methyl ester (LXIIb) to photothujic acid (LXVIIa) and photomethylthujate (LXVIIb) respectively is thus rigorously established as a light catalysed reaction. To the author's knowledge this is the only known example of a simple light catalysed methyl migration.

The minor product, present in the reaction mixture to the extent of 25%, was isolated as a colorless liquid by vapor phase chromatography. Strong infrared absorption at 5.79 u (Figure 31, page 139) indicated the presence of an ester group attached to a saturated carbon. Weak infrared absorptions at 6.21 and 6.40 u suggested cyclopentene and cyclobutene double bonds.

Structure LXIVb for alpha-lumimethylthujate was conclusively established by examination of its nuclear magnetic resonance spectrum (Figure 22, page 88).

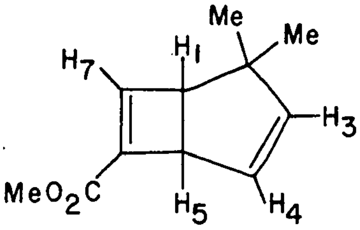


LXIVb

The two methyl groups appear as sharp singlets at 8.92 and 8.97 p.p.m. The singlet nature of these signals proves that both methyl groups are still attached to the same carbon. Two symmetrical doublets arising from AX type coupling of the cyclobutene protons are seen at 3.55 ($H_6$) and 3.88 ($H_7$) p.p.m. A second set of doublets at 4.31 and 4.62 p.p.m. are due to AX type coupling of $H_2$ and $H_3$ respectively. The signal from $H_3$ is split again due to coupling with the bridgehead proton $H_5$ which appears at 6.80 p.p.m. The methoxyl group of the ester appears at 6.36 p.p.m. This spectrum rigorously establishes structure LXIVb without additional evidence.

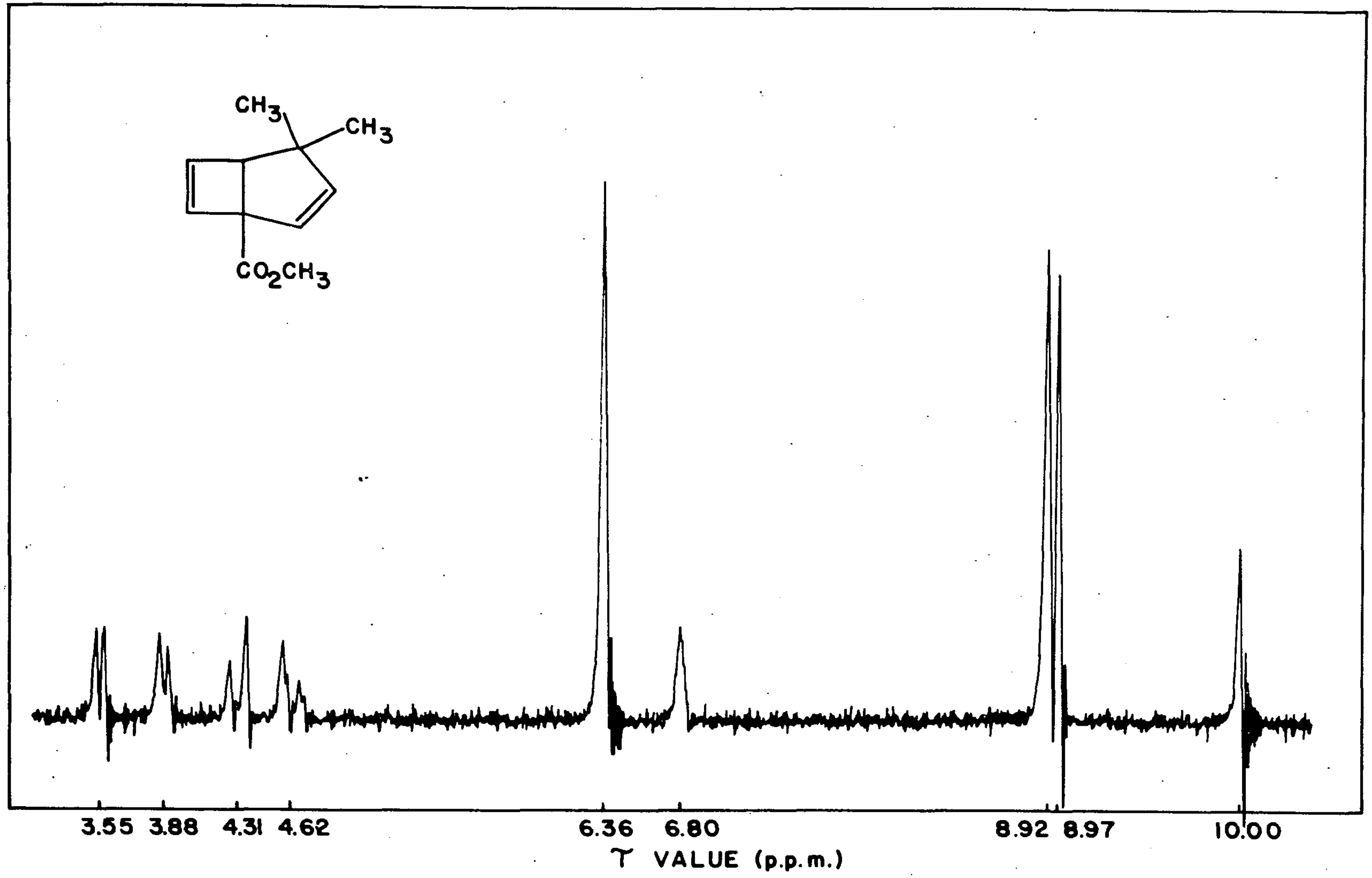
A third product, constituting less than 2% of the reaction mixture, was also isolated by vapor phase chromatography. The infrared spectrum of this material (Figure 31, page 139) showed strong absorption at 5.82 and 6.24 u (alpha,beta-unsaturated ester and cyclopentene double bond).

Structure LXIIIb was firmly established by examining the nuclear magnetic resonance spectrum (Figure 23, page 91) of beta-lumimethylthujate. Significantly, only one cyclobutene proton is observed (3.34 p.p.m.) while two bridgehead protons appear as multiplets at 6.22 ($H_5$) and 7.10 ($H_1$) p.p.m. The position of the ester group on the cyclobutene double bond is thus rigorously established. The protons on the cyclopentene double bond appear as doublets at 4.22 and 4.67 p.p.m.



LXIIIb

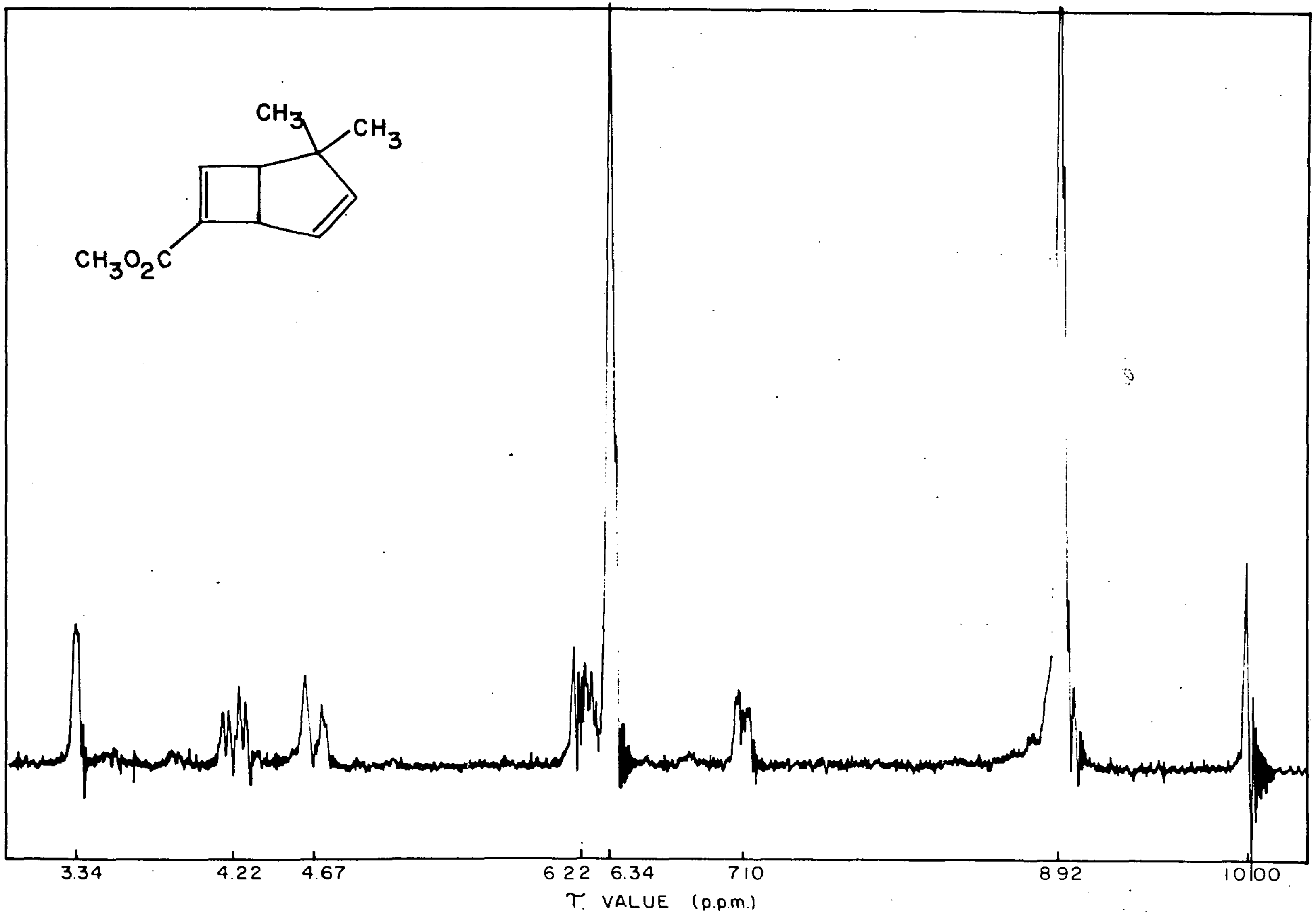
Figure 22. Nuclear magnetic resonance spectrum of *alpha*-lumimethylthujate (LXIVb)


CH3
CH3
CO2CH3
3.55
3.88
4.31
4.62
6.36
6.80
8.92
8.97
10.00
τ VALUE (p.p.m.)

Coupling of $H_3$ with the bridgehead proton $H_5$ causes further splitting of the doublet at 4.22 p.p.m. The methoxyl protons of the ester appear at 6.34 p.p.m. Interestingly, both methyl groups are observed as a six proton signal at 8.92 p.p.m. This suggests that the 8.97 p.p.m. signal in the nuclear magnetic resonance spectrum of alpha-lumimethylthujate (LXIVb) must be due to the exo methyl group which is shifted by diamagnetic shielding of the ester carbonyl on the bridgehead of that compound. The nuclear magnetic resonance spectrum conclusively establishes structure LXIIIb for beta-lumimethylthujate.

Formation of photothujic acid (LXVIIa) and photomethylthujate (LXVIIb) seems to offer dramatic support for the mechanism proposed in Figure 17. However, it is still possible that these products arise via photoisomerization to a bicyclic intermediate such as LXVIII followed by either thermal or photochemical rearrangement. The postulated existence of excited state LXV is certainly supported by the formation of alpha-lumimethylthujate (LXIIIb), and equally strong support is provided by analogy with the photochemical reactions of alpha- and gamma-tropolones. Conversely, some isopropylbenzoic acids (or the corresponding esters) ought to be formed if LXVIII or its methyl ester were important species in the mechanistic scheme. No such products could be isolated from the product mixture. On the basis of these facts the mechanism proposed in Figure 17 constitutes the most reasonable path for the reactions discussed above, although it cannot be considered rigorously established at the present time.

Figure 23. Nuclear magnetic resonance spectrum of *beta*-lumimethylthujate (LXIII)


CH3
CH3
CH3O2C
3.34
4.22
4.67
6.22
6.34
7.10
8.92
10.00
τ VALUE (p.p.m.)

## METHODS AND MATERIALS

Irradiation Vessels  The pyrex vessels used were flat bottomed bottles (Figure 24, page 96) equipped with internal cooling coils and a 24/40 standard taper joint on top. Agitation was provided by a magnetic stirrer. Vessels having volumes of 100 ml., 250 ml., 500 ml., and 1000 ml. were available.

The quartz vessels used were round bottomed tubes (Figure 24, page 96) ca. eight inches long by either 10 mm. or 20 mm. in diameter surmounted by a 24/40 standard taper joint. No provisions were made for either stirring or cooling. Vessels having volumes of ca. 100 ml. and 200 ml. were available.

Irradiation Lamps  The ultraviolet light sources used were General Electric UA-3 360 watt mercury arc lamps with quartz bulbs. The radiant energy distribution for these lamps is shown in Table 1, page 93. Further data concerning these lamps may be obtained from General Electric Lamp Division.[57]

Irradiation Enclosure  A General Electric UA-3 lamp supported by a vertical rod was positioned in the center of an aluminum foil lined, 2½ X 2 ft., rectangular transite box (Figure 24) which was built inside a walk-in hood. The lower front of the box was enclosed by a 16 in. high foil lined sheet of transite. The whole box could be closed off

---

[57] Ultraviolet Lamps, General Electric Co., Lamp Division, Cleveland, Ohio, Technical Information Bulletin LS-104 (June, 1957).

Table 1. Spectral energy distribution of the UA-3 lamp[a]

| Wavelength band millimicrons | Principal lines | Radiant energy watts |
|---|---|---|
| 220-230 | - | 0.72 |
| 230-240 | - | 0.91 |
| 240-250 | - | 1.51 |
| 250-260 | 2537 | 3.95 |
| 260-270 | 2652 | 2.94 |
| 270-280 | - | 0.33 |
| 280-290 | 2804 | 1.84 |
| 290-300 | 2967 | 1.76 |
| 300-310 | 3022 | 3.26 |
| 310-320 | 3131 | 6.86 |
| 320-330 | - | 0.32 |
| 330-340 | - | 0.65 |
| 340-350 | - | 0.17 |
| 350-360 | - | 0.30 |
| 360-370 | 3654 | 9.74 |
| 370-380 | - | 0.30 |
| 380-400 | - | 0.75 |
| 400-410 | 4047 | 3.50 |
| 410-430 | - | 0.31 |
| 430-440 | 4358 | 6.09 |
| 440-540 | - | 0.82 |
| 540-550 | 5461 | 6.45 |
| 550-570 | - | 0.34 |
| 580-760 | - | 1.36 |

[a] These data were taken from the source given in footnote 57.

by a sheet metal lined sliding door on the hood. The walls of the box were equipped with racks, water outlets, and electrical outlets. All controls and electrical equipment were outside the hood, connections being made through a sealed copper tube.

Irradiation Procedure Solutions to be irradiated were placed in the appropriate vessel, but were usually not flushed with nitrogen unless the solvent used was ether. The vessel was then positioned in the box at the same height as the lamp bulb at a distance of four to eight inches. Depending on the boiling point of the solvent being used, the vessel was equipped with either a stopper or a condenser.

Instrumentation All infrared spectra were obtained using a Perkin Elmer model 21 infrared spectrophotometer. Ultraviolet spectra shown in Figures 44 and 45 were obtained using a Beckman model DU spectrophotometer; those shown in Figures 46 and 47 using a Beckman model DK-2A spectrophotometer. All other ultraviolet spectra were measured on a Cary model 14 spectrophotometer.

Nuclear magnetic resonance spectra were measured in either deuterochloroform or carbontetrachloride with 1% tetramethylsilane as internal reference.

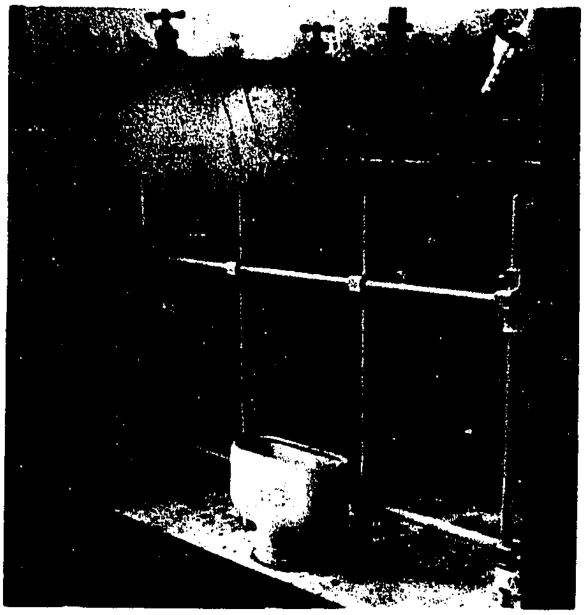
Vapor phase chromatographic analyses were made on either a Perkin Elmer model 154 Vaporfractometer or an F&M Scientific Co. model 500 Gas Phase Chromatograph. Columns used for vapor phase chromatographic analysis are listed in the Appendix.

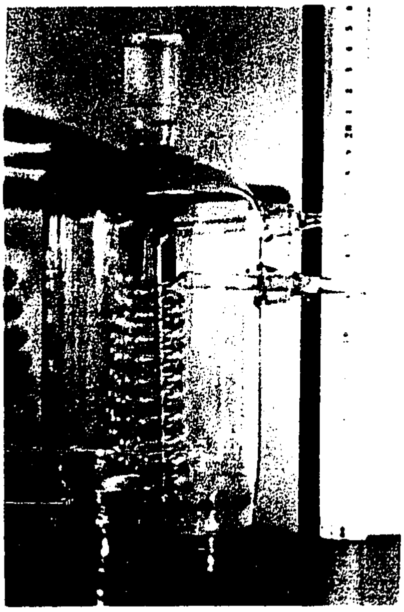
Melting points were obtained on Fisher-Johns melting point apparatus and are uncorrected.

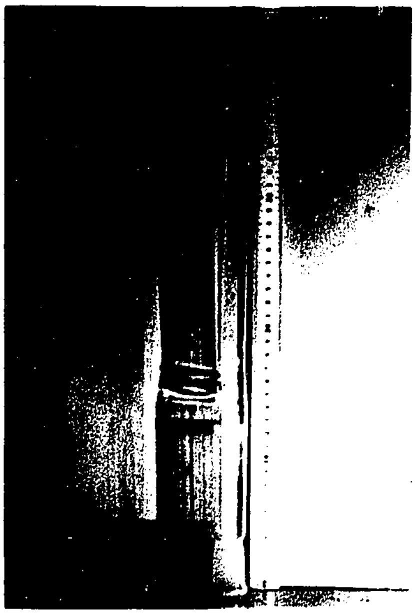
Figure 24. Top: Irradiation enclosure

Bottom left: Pyrex irradiation vessel

Bottom right: Quartz irradiation vessel







Preparation of 4-Methyltropolone (LII) 4-Methyltropolone (LII) was prepared according to the procedure given by Haworth and Hobson.[58] The yield was increased slightly by making the following changes in their procedure: (1) The aqueous solution of 3-carboxy-4-carboxymethyltropolone obtained from oxidation of purpurogallin was acidified to pH 1 rather than just neutralized. (2) The subsequent continuous extraction with ether was extended from 40 hours to approximately one week.

Preparation of Mixed 4- and 6-Methyltropolone Methyl Ethers (XVIII and XIX) 4-Methyl- and 6-methyltropolone methyl ethers were obtained and separated by the procedure of Haworth and Hobson.[58] Alternatively, small amounts of pure 6-methyltropolone methyl ether (XIX) were obtained by the following procedure.

Crude oily methyltropolone methyl ether mixture was heated with five successive portions of petroleum ether (b.p. 60-70°). Decantation and concentration of the hot solutions afforded a gummy solid which gave, after several recrystallizations, 654 mg. of crystalline 6-methyltropolone methyl ether; m.p. 96.8-98° (reported 96-97°);[58] $\lambda_{\max}^{H_2O}$ 240 mu (35,300) and 330 mu (8,800) (Figure 32, page 141); Infrared maxima (Figure 27, page 131): 3.38, 3.54, 6.14, 6.26, 6.37, 6.80, 7.78, 7.88, 8.49, 8.75, 9.66, 10.10, 10.80, and 11.05 u.

The residues from the recrystallization mother liquors were combined with the remaining crude 4-methyltropolone methyl ether mixture and distilled (98-99°/0.05 mm.) giving 3.451 g. of mixed methyl ethers

---

[58] R. D. Haworth and J. D. Hobson, J. Chem. Soc., 561 (1951).

as a slushy hygroscopic solid; m.p. room temperature to 65°; $\lambda_{\max}^{H_2O}$ 241 mu (33,300) and 347 mu (8,250).

Purification of Thujic Acid (LXIIa) Crude thujic acid donated by Crown Zellerbach Corp. was placed in a Soxhlet apparatus and extracted for twelve hours with petroleum ether (b.p. 60-70°). The solution thus obtained was concentrated to ca. 50 ml. Precipitated thujic acid was collected by suction filtration. One recrystallization from pet. ether gave 9.3 g. of thujic acid (LXIIa) as shiny yellow plates; m.p. 90-91.8° (reported 88°);[59] Infrared maxima (Figure 29, page 135): 2.84, 3.25, 3.40, 3.48, 3.78, 3.95, 5.92, 6.16, 6.46, 6.80, 7.10, 7.25, 7.34, 7.49, 7.81, 9.17, 9.68, and 10.32 u; $\lambda_{\max}^{\text{isooct.}}$ 214 mu (18,600) and 282.5 mu (5,690) (Figure 46, page 169).

---

[59] Technical Information on Properties of Thujaplicin, Crown Zellerbach Corp., Chemical Products Division, Camas, Washington (1960).

## EXPERIMENTAL

### Experimental for Photochemistry of 4-Methyltropolone Methyl Ether and 6-Methyltropolone Methyl Ether

Photoisomerization of Mixed 4-Methyltropolone Methyl Ethers (XVIII and XIX) to Photo-4- and Photo-6-methyltropolone Methyl Ethers (XX and XXII) A solution of mixed methyl ethers (7.30 g.) in 2 l. of water was placed in two one l. pyrex irradiation flasks, and irradiated in the usual manner. The extent of reaction was determined by ultraviolet analysis of aliquots withdrawn at intervals during the irradiation. Reaction was stopped after 16 hrs. at which time the extinction value of the irradiation solution at 345 mu was 9% of its original value. Extraction of the reaction mixture with methylene chloride (1 X 100 ml., 4 X 60 ml., 3 X 50 ml.), drying over anhydrous sodium sulfate, and concentration under aspirator vacuum gave 5.90 g. of red oil. Molecular distillation (100°/0.5 mm.) of this oil gave a bright yellow oil.

The pure photoproducts were isolated by vapor phase chromatography at 140° using a 2 m. by 15 mm. column containing 20% Union Carbide UCON-1b550x on 40-60 mesh celite. Two major peaks were observed corresponding to the two photoproducts. Two minor peaks were observed; one closely adjacent to each of the major peaks. These minor constituents constituted approximately 5% of the total material. ((At a later date these minor products were shown to have retention times identical with those of the corresponding photo esters (XXX and XXXI).)) The major peaks were identified by comparison of retention times with an authentic sample of photo-6-methyltropolone methyl ether (XXII).

Photo-4-methyltropolone methyl ether (XX), fraction 1, was molecularily distilled at 85° and 0.04 mm.[60] and again at 63° and 0.02 mm. giving 1.176 g. of pale yellow oil; $\lambda_{max}^{H_2O}$ 230 mu (6,310) and 345 mu (370; Figure 33, page 143); Infrared maxima: 3.41, 3.54, 5.85, 6.14, 6.27, 6.35, 6.69, 6.86, 6.97, 7.29, 7.45, 7.85, 8.75, 8.96, 9.31, 9.95, 10.23, 10.32, 10.42, 11.10, and 11.99 u (Figure 25, page 127).

Anal. Calcd. for $C_9H_{10}O_2$: C, 71.31; H, 6.71. Found: C, 71.30; H, 6.71.

Photo-6-methyltropolone methyl ether (XIX), fraction 2, was molecularily distilled twice at 55° and 0.04 mm.[60] giving 1.000 g. of a pale yellow oil which upon standing gave colorless crystals; m.p. 42.1-44.1°; $\lambda_{max}^{H_2O}$ 229 mu (6,190) and 340 mu (170; Figure 34, page 145); Infrared maxima: 3.41, 3.54, 5.85, 6.19, 6.96, 7.25, 7.59, 7.84, 7.91, 8.42, 8.60, 9.06, 9.20, 9.40, 9.82, 9.91, 10.35, 11.20, 11.65, and 11.80 u (Figure 26, page 129).

Anal. Calcd. for $C_9H_{10}O_2$: C, 71.31; H, 6.71. Found: C, 71.54; H, 6.74.

Photoisomerization of 4-Methyltropolone Methyl Ether (XVIII) to Photo-4-methyltropolone Methyl Ether (XX) A solution of 2.85 g. of 4-methyltropolone methyl ether (XVIII) in 1 l. of water was irradiated in a pyrex flask for 26 hrs. The reaction was followed by ultraviolet analysis of aliquots until the extinction value at 345 mu was less than

---

[60] Temperatures listed for molecular distillations are bath temperatures, not true boiling points.

10% of its original value. Extraction with methylene chloride, drying over anhydrous sodium sulfate, and concentration of the extract gave a reddish oil. This material when molecularily distilled (85°/0.08 mm.)[60] gave 2.0 g. (71% yield) of pale yellow oil which was identical in all respects with photo-4-methyltropolone methyl ether (XX) obtained by irradiating the mixed methyl ethers.

Photoisomerization of 6-Methyltropolone Methyl Ether (XIX) to Photo-6-methyltropolone Methyl Ether (XXII) A solution of 2.5 g. of 6-methyltropolone methyl ether (XIX) in 1 l. of water was irradiated in a pyrex flask in the usual manner. The reaction was followed by vapor phase chromatography using a 4 ft. by ¼ in. column packed with 20% silicone gum rubber on Chromosorb-P, programed at 15°/min. between 50 and 225°. Extraction with methylene chloride (5 X 25 ml.) gave, after drying over anhydrous sodium sulfate and concentration of the extract, a crude crystalline mixture. This material was dissolved in ether and purified by streaming the ethereal solution through an alumina column. The resulting mixture of yellow oil and crystals from concentration of the eluent ethereal solution was recrystallized several times from ether giving 866 mg. (34.6% yield) of photo-6-methyltropolone methyl ether (XXII); m.p. 43.5-45.5°. The infrared, ultraviolet, and nuclear magnetic resonance spectrum of this material was identical with that of photo-6-methyltropolone methyl ether obtained by irradiating the mixture of methyl ethers.

Pyrolysis of Photo-4-methyltropolone Methyl Ether (XX) Photo-4-methyltropolone methyl ether (XX; approximately 25 mg.) was dropped into a vertical, 6 in. by 3/4 in., pyrex helicies packed pyrolysis column at 360°.[61] The column was swept with a stream of oxygen free nitrogen. Pyrosylate was collected in a tube immersed in a Dry Ice/acetone bath. After cooling, the column and collection tube were washed with chloroform which upon concentration gave a yellow oil which showed infrared maxima at 3.36, 5.85, 6.26, 6.35, 6.68, 6.81, 7.10, 7.81, 7.96, 8.71, 10.15, and 10.55 u (Figure 27, page 131). This material was heated at 60-70° for six minutes with 10 ml. of 10 N aqueous sodium hydroxide. The resulting dark yellow solution was diluted to 100 ml. and a one ml. aliquot of this latter solution again diluted to 100 ml. The ultraviolet spectrum of this final solution (Figure 36, page 149) was identical with that of 4-methyltropolone in base. Acidification (pH 5-6) gave a solution with an ultraviolet spectrum identical with that of 4-methyltropolone (Figure 37, page 151).

Pyrolysis of Photo-6-methyltropolone Methyl Ether (XXII) A solution of 50 mg. of photo-6-methyltropolone methyl ether (XXII) in 12 ml. of pentane was pyrolysed at 395° using the apparatus described above. The cooled pyrolysis column was washed with chloroform, and the combined chloroform and pentane solutions concentrated to give a white crystalline solid with an infrared spectrum (Figure 27, page 131) identical to that of 6-methyltropolone methyl ether (XIX; Figure 27, page 131). One recrystallization from hexane gave fine needles; m.p.

---

[61] This 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))).

95-96° (reported for 6-methyltropolone methyl ether 96-97°[57]).

Hydrogenation of Photo-4-methyltropolone Methyl Ether (XX) A solution of 106.4 mg. of photo-4-methyltropolone methyl ether (XX) in 65 ml. of methanol was allowed to absorb two equivalents of hydrogen over Adams' catalyst at 27.5° and 760 mm. No change was observed in the rate of hydrogen absorption until two equivalents had been absorbed. At this point hydrogen absorption ceased.

Filtration of the reaction mixture and concentration under a stream of dry air gave a pleasant smelling, yellow-brown oil. Molecular distillation (room temperature/0.05 mm.)[60] gave 99 mg. of tetrahydro-photo-4-methyltropolone methyl ether (XXIV) as a colorless liquid which showed no high intensity ultraviolet absorption. The compound showed infrared maxima at 2.75, 2.90, 3.54, 5.76, 6.26, 6.85, 7.13, 7.26, 7.55, 9.32, and 9.88 u (Figure 28, page 133).

A semicarbazone was prepared in the usual manner.[62] Five recrystallizations from water gave fine white crystals; m.p. 183-185°.

Anal. Calcd. for $C_{10}H_{18}N_3O_2$: C, 56.85; H, 8.11; N, 19.89. Found: C, 57.16; H, 8.07; N, 19.67.

Hydrogenation of Photo-6-methyltropolone Methyl Ether (XXII) A solution of 80 mg. of photo-6-methyltropolone methyl ether (XXII) in 30 ml. of methanol was allowed to absorb one molar equivalent of hydrogen over Adams' catalyst at 28° and 760 mm. Filtration followed by

---

[62] R. 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. 218.

concentration under a stream of dry air gave a colorless liquid. Two molecular distillations at room temperature and 0.04 mm.[60] using a Dry Ice/acetone bath on the collection vessel gave 57.6 mg. of colorless crystalline dihydrophoto-6-methyltropolone methyl ether (XXV) which melted upon warming to room temperature. The ultraviolet spectrum of this material (Figure 35, page 147) showed $\lambda_{max}^{95\% EtOH}$ 232 mu (12,450) and a shoulder at 280 mu (1,286). The infrared spectrum (Figure 28, page 133) showed maxima at 3.39, 3.53, 5.88, 6.22, 6.98, 7.25, 7.55, 7.66, 8.06, 8.43, 8.69, 9.02, 9.39, 9.69, 9.90, 11.11, and 11.66 u.

A 2,4-dinitrophenylhydrazone was prepared in the usual manner.[63] This derivative decomposed during attempted recrystallization. It was purified by streaming it through a column of Bentonite-Celite (1:3 by weight) in benzene. The benzene was removed in a stream of dry air, and the residue recrystallized rapidly from ethanol-water giving red-orange crystals; m.p. 117.2-119.5°.

Anal. Calcd. for $C_{15}H_{16}N_4O_5$: C, 54.21; H, 4.85; N, 16.86. Found: C, 54.31; H, 4.87; N, 16.64.

Photochemical Conversion of Photo-4-methyltropolone Methyl Ether (XX) to Photo-4-Ester (XXX) Photo-4-methyltropolone methyl ether (XXX; 710 mg.) was dissolved in 10 ml. of 95% ethanol, and the resulting solution was diluted to 560 ml. with water. This latter solution was divided equally among three quartz tubes and irradiated in the usual

---

[63] N. D. Cheronis and J. B. Entrikin, Semimicro Qualitative Organic Analysis, Thomas Y. Crowell Company, New York, 1957. p. 247.

manner. After five hours, vapor phase chromatographic analysis (4 ft. by $\frac{1}{4}$ in. silicone gum rubber column at 150°) indicated complete conversion to a new product. Extraction with methylene chloride (1 X 50 ml.; 4 X 25 ml.), concentration, and molecular distillation (bath brought from room temperature to 100°/0.1 mm.)$^{60}$ gave 374 mg. of pale yellow oil. An ethereal solution of this material was passed through an alumina column. Molecular distillation (60°/0.1 mm.)$^{60}$ of the residue obtained by evaporation of the ether gave 103 mg. of colorless liquid photo-4-ester (XXX); $\lambda_{max}^{95\%\ EtOH}$ 218 mu (7,680) (Figure 38, page 153); Infrared maxima: 3.43, 5.77 (shoulder), 5.86, 6.30, 6.98, 7.45, 8.75, 8.97, 9.36, and 9.93 u (Figure 25, page 127).

*Anal.* Calcd. for $C_9H_{12}O_3$: C, 64.21; H, 7.19. Found: C, 64.55; H, 7.14.

*Photochemical Conversion of Photo-6-methyltropolone Methyl Ether (XXII) to Photo-6-ester (XXXI)* Crude photo-6-methyltropolone methyl ether (XXXI; *ca.* 0.5 g.) was dissolved in 200 ml. of water and irradiated in a quartz tube. The reaction was followed by periodicly withdrawing aliquots, extracting the aliquots with methylene chloride, concentrating the extract and analysing the residue by vapor phase chromatography (4 ft. by $\frac{1}{4}$ in. silicone gum rubber column at 150°). Conversion to a new product was complete in six and a half hours.

Extraction of the reaction solution with methylene chloride, drying over anhydrous sodium sulfate, and concentration gave a yellow oil. This material was dissolved in ether and streamed through an alumina column. Concentration of the eluent and molecular distillation

($85^\circ$/0.05 mm.)$^{60}$ of the residue gave 85.7 mg. of colorless liquid which crystallized upon cooling giving photo-6-ester as a mushy solid; m.p. *ca.* 29-30°; $\lambda^{H_2O}_{max}$ 228 mu (14,110) (Figure 39, page 155); Infrared maxima: 3.41, 3.54, 5.76, 7.85, 6.17, 6.97, 7.10, 7.27, 7.37, 7.69, 8.05, 8.55, 10.10, and 11.61 u (Figure 26, page 129).

*Anal.* Calcd. for $C_9H_{12}O_3$: C, 64.21; H, 7.19. Found: C, 64.35; H, 7.40.

*Photoisomerization of Photo-4-methyltropolone Methyl Ether (XX) to Lumi-4-methyltropolone Methyl Ether (XXXVI)* A solution of 1.0017 g. of photo-4-methyltropolone methyl ether (XX) in 180 ml. of anhydrous ether was placed in a brush flamed quartz tube, flushed with nitrogen and irradiated in the usual manner. The reaction was followed by periodic vapor phase chromatographic analysis of aliquots (2 ft. by ¼ in. silicone gum rubber column at 150°). Conversion was complete in three hours. Continued irradiation for a period of 24 hours produced no noticeable change in the composition of the reaction mixture. Concentration of the reaction solution gave a red-orange oil which was molecularily distilled twice (120°/0.1 mm. and 85°/0.08 mm.). This material was dissolved in ether and passed through an alumina column. Concentration of the ether solution followed by molecular distillation ($35^\circ$/0.08 mm.)$^{60}$ gave 0.4 g. of lumi-4-methyltropolone methyl ether (XXXVI) as a colorless liquid; $\lambda^{95\%\ EtOH}_{max}$ 226 mu (6,420) and 275 mu (523) (Figure 40, page 157); Infrared maxima: 3.45, 3.56, 5.93, 6.14, 6.35, 6.90, 7.00, 7.29, 7.45, 7.79, 8.55, 8.84, 8.95, 9.32, 9.47, 9.89, 10.30, 10.58, and 11.26 u (Figure 25, page 127).

**Anal.** Calcd. for $C_9H_{10}O_2$: C, 71.31; H, 6.71. Found: C, 71.67; H, 6.71.

Photoisomerization of Photo-6-methyltropolone Methyl Ether (XXII) to Lumi-6-methyltropolone Methyl Ether (XXXVII) A solution of 855 mg. of photo-6-methyltropolone methyl ether (XXII) in 225 ml. of nitrogen flushed anhydrous ether was irradiated in a quartz tube in the usual manner. Vapor phase chromatographic analysis of aliquots (4 ft. by ¼ in. silicone gum rubber column at 185°) showed the reaction to be complete after eleven hours. (The reaction was 50% complete in one hour, but deposition of decomposition products on the walls of the vessel caused a continual decrease in the rate of reaction.)

Concentration of the reaction solution and molecular distillation of the resulting red oil (room temperature to 170°/0.1 mm.) gave a pale yellow oil which formed a glass upon cooling in Dry Ice/acetone and partially crystallized upon warming to room temperature.

This material was dissolved in ether and passed through an alumina column. Concentration of the eluent followed by molecular distillation (room temperature to 50°/0.1 mm.)[60] of the residue gave, after cooling and warming as before, 417 mg. of crystalline material contaminated with a small amount of yellow oil.

Repetition of the above procedure gave lumi-6-methyltropolone methyl ether (XXXVII) as a colorless, hygroscopic, oily-crystalline solid; m.p. ca. 33-35°; $\lambda_{max}^{H_2O}$ 233 mu (9,730) and 320 mu (563) (Figure 41, page 159); Infrared maxima: 3.43, 3.55, 5.60, 5.76, 5.89, 6.15, 6.99, 7.28, 7.60, 7.75, 8.05, 8.30, 8.56, 9.05, 9.77, 10.38, 10.55, 11.10, and 11.64 u (Figure 26, page 129).

Anal. Calcd. for $C_9H_{10}O_2$: C, 71.31; H, 6.71. Found: C, 71.48; H, 6.68.

Pyrolysis of Lumi-4-methyltropolone Methyl Ether (XXXVI) A solution of 35 mg. of lumi-4-methyltropolone methyl ether (XXXVI) in 10 ml. of cyclohexane was pyrolysed at 415° in the manner previously described (page 102). The cooled column and collection tube were washed with cyclohexane, and the combined solutions were concentrated to 10 ml. A one ml. aliquot of this solution was diluted to give a solution ca. 2.3 X $10^{-5}$ M in pyrolysis product (assuming no loss of material) which showed; $\lambda_{max}^{cyclohexane}$ 290 mu (2,170), 238 mu (5,480), and 217 mu (11,300).

The remaining 9 ml. of pyrolysis solution was evaporated to dryness, and the residue was heated for 5 minutes with approximately 2 ml. of 10 N aqueous sodium hydroxide. The resulting pale yellow solution was diluted to 100 ml. giving a solution which showed; $_{max}^{Aq. NaOH}$ 257.5 mu (8,000), 304 mu (1,500) and intense end absorption (Figure 42, page 161).

Acidification (15 small drops of concentrated hydrochloric acid) of the solutions in the sample and reference cells gave a solution which showed; $\lambda_{max}^{Aq. HCl}$ 246 mu (9,500), 295 mu (1,200), and no end absorption (Figure 43, page 163).

Attempted Pyrolysis of Lumi-6-methyltropolone Methyl Ether (XXXVII)

Lumi-6-methyltropolone methyl ether (XXXVII; 285 mg.) was pyrolysed neat at 450° on the column previously described (page 102). Washing the cooled column and collection trap with chloroform gave a brownish-black solution which yielded a red-brown oil after concentration. Heating this material for 10 minutes with 5 N aqueous sodium hydroxide gave only intractable tars from which no pure compound could be isolated.

Pyrolysis of Mixed Lumi-4- and Lumi-6-methyltropolone Methyl Ethers (XXXVI and XXXVII)[64] A mixture of lumi-4- and lumi-6-methyltropolone methyl ethers (XXXVI and XXXVII; 723 mg.) was dropped neat into the pyrolysis column previously described (page 102) at 440°. After cooling, the column and collection trap were washed with chloroform, and the resulting solution was concentrated giving a red-black oil. Two molecular distillations (room temperature to 180°/0.1 mm.) of this material gave 373 mg. of pale yellow oil.

Approximately one half of this material was dissolved in 20% aqueous hydrogen bromide and the resulting solution heated at 105-115° for three and one half hours. The solid tropolone hydrobromide obtained by evaporating the reaction mixture to dryness was dissolved in 3 ml. of water and neutralized with dilute sodium hydroxide solution. Slight acidification, cooling, and scratching produced a large quantity of white crystalline 3-hydroxy-5-methyltropolone (5-methyl-beta-tropolone) which after one recrystallization from water showed; m.p. 134.5-136°; Infrared maxima: 2.94, 3.45, 3.94, 5.25, 6.07, 6.30, 6.45, 6.73, 6.99, 7.26, 7.46, 7.70, 7.95, 8.29, 8.68, 9.62, 10.48, 11.35, 11.54, 12.03, and 13.50 u (Figure

---

[64] This mixture was obtained by irradiating an ethereal solution of photo-4- and photo-6-methyltropolone methyl ethers (XX and XXII) with a Hanovia immersion lamp. Vapor phase chromatographic analysis indicated that only lumi-4- and lumi-6-methyltropolone methyl ether (XXXVI and XXXVII) were formed in ca. 50:50 ratio. Concentration of the reaction solution gave the material used in this experiment.

28, page 133).

The infrared spectrum of this material was superimposable on that of an authentic sample of 3-hydroxy-5-methyltropolone (see below); m.p. 137-139°; mixed m.p. 135-139.5°.

Synthesis of 3-Hydroxy-5-methyltropolone[65] 1,4-Dihydrodimethoxybenzoic acid (crude, 30 g.) was added to a suspension of potassium amide (from 15 g. of potassium) in liquid ammonia (500 ml.). Methyl iodide (75 g.) was added. The mixture was stirred for one half hour, and then ammonium chloride (50 g.) was added.

After the ammonia had evaporated, the product was dissolved in water and made acidic by the addition of hydrochloric acid at 0°. Extraction with methylene chloride and evaporation of the solvent gave crude 1,4-dihydro-3,5-dimethoxy-1-methylbenzoic acid (16.1 g.).

This product was immediately reduced by adding it as an ether suspension to a slurry of lithium aluminum hydride (4.68 g.) in ether (100 ml.) under nitrogen. Work up in the usual manner gave an oil (13.2 g.) which on distillation (110°/0.75 mm.) gave 1,4-dihydro-3,5-dimethoxy-1-methylbenzyl alcohol (8.25 g.).

Anal. Calcd. for $C_{10}H_{15}O_3$: C, 65.63; H, 8.2. Found: C, 65.19; H, 8.75.

The alcohol (8.25 g.) was dissolved in pyridine (95 ml.) and p-toluenesulfonyl chloride (9.5 g.) was added. After standing for two days at 0°, the product was poured into ice water and the crude tosylate

---

[65] This synthesis was carried out by Dr. Peter Fitton. The whole scheme is shown in Figure 11, page 46. It is an adaptation of the general method developed by Chapman and Fitton (see footnote 38).

(14.4 g.) was filtered off.

The tosylate (14.4 g.) was immediately added to pyridine (25 ml.) and the mixture refluxed for 15 minutes. The cooled reaction solution was diluted with chloroform, and was washed with excess hydrochloric acid. Removal of the solvent gave a yellow oil (4.93 g.).

The crude oil (4.73 g.) was oxidized by the method of Johns _et al._[66] to crude 5-methyl-_beta_-tropolone. Recrystallization from water gave pure 5-methyl-_beta_-tropolone; m.p. 138-139°; $\lambda_{max}^{95\% \text{ EtOH}}$ 247, 255, 272, 297, and 312 mu; $\lambda_{max}^{0.1N \text{ NaOH}}$ 257, 267, 295, and 305 mu.

_Anal_. Calcd. for $C_8H_8O_2$: C, 70.60; H, 5.88. Found: C, 70.54; H, 5.92.

_Acid Catalysed Conversion of Lumi-4-methyltropolone Methyl Ether (XXXVI) to Photo-4-ester (XXX)_ An 8.8 X $10^{-5}$ molar solution of lumi-4-methyltropolone methyl ether (XXXVI) in 95% ethanol was placed in a 1 cm. quartz ultraviolet cell. A matched cell was filled with pure 95% ethanol and used as a reference. After obtaining the ultraviolet spectrum of lumi-4-methyltropolone methyl ether, two drops of approximately 1 N hydrochloric acid were added to each cell (_ca_. 0.02 N solutions in the cells), and the ultraviolet spectrum of the reaction solution was measured at intervals. The resulting spectra (Figure 12, page 49) changed from that of lumi-4-methyltropolone methyl ether (XXXVI) to that of photo-4-ester (XXX). Two isobestic points were clearly visible. The data obtained were not sufficiently accurate to permit kinetic analysis.

_Acid Catalysed Conversion of Lumi-6-methyltropolone Methyl Ether (XXXVII) to Photo-6-ester (XXXI)_ A 6.93 X $10^{-4}$ molar solution of

---

[66] R. B. Johns, A. W. Johnson, and M. Tisler, _J. Chem. Soc._, 4605 (1954).

lumi-6-methyltropolone methyl ether (XXXVII) in water was prepared. A 1 ml. aliquot of this solution was diluted 1:10 with 0.0211 N hydrochloric acid giving a solution $6.93 \times 10^{-5}$ molar in 0.0190 N hydrochloric acid. This solution was immediately placed in a quartz sample cell and its ultraviolet spectrum measured. The reference cell contained a previously prepared 0.0190 N hydrochloric acid solution. Less than two minutes had elapsed since mixing of the reagents, but the spectrum obtained was that of photo-6-ester (XXXI).

Comparison of Photochemical and Dark Reactions of Lumi-4-methyltropolone Methyl Ether (XXXVI) Lumi-4-methyltropolone methyl ether (XXXVI; 141 mg.) was dissolved in 200 ml. of 25% (by volume) ethanol-water. This solution was divided into two portions each of which was placed in a quartz irradiation tube. One tube was irradiated in the usual manner. The other tube was wrapped in aluminum foil and placed in a bath at the same temperature as the vessel in the irradiation box (45°). Aliquots were withdrawn from both tubes at intervals and extracted with methylene chloride. The extract was dried over anhydrous sodium sulfate, concentrated, and the residue analysed by vapor phase chromatography (4 ft. by $\frac{1}{4}$ in. silicone gum rubber column at 135°).

No change was observed in the dark solution after five hours at which time all the material exposed to light had been converted to photo-4-ester (XXX).

Photoisomerization of 6-Methyltropolone Methyl Ether (XIX) to Lumi-6-methyltropolone Methyl Ether (XXXVII) A solution of approximately 470 mg. of 6-methyltropolone methyl ether (XIX) in 100 ml. of anhydrous ether was placed in a quartz tube and irradiated in the usual manner for 50 hours. The sequential nature of the reaction was shown by periodically withdrawing aliquots and analysing their concentrates by vapor phase chromatography using a 2 ft. silicone gum rubber column programmed at 15°/minute between 50 and 310°. The data thus obtained are contained in Table 2 and are plotted in Figure 13, page 52.

It was necessary to change vessels after 40 hours because light absorbing decomposition products were deposited on the walls of the original vessel.

Concentration of the reaction solution under a stream of dry nitrogen gave 417 mg. of a dark red oil. Two molecular distillations

Table 2. Relative distribution of products versus time for the irradiation of an ethereal solution of 6-methyltropolone methyl ether (XIX) in quartz

| | Relative percent present | | |
|---|---|---|---|
| Time in hours | 6-Methyltropolone methyl ether | Photo-6-methyltropolone methyl ether | Lumi-6-methyltropolone methyl ether |
| 0 | 100 | - | - |
| 4 | 87.8 | 9.91 | 2.36 |
| 8 | 76.1 | 16.95 | 7.03 |
| 12 | 65.8 | 23.5 | 10.7 |
| 28½ | 31.0 | 41.9 | 27.1 |
| 32½ | 17.65 | 40.0 | 42.4 |
| 35 | 10.78 | 41.4 | 48.0 |
| 40½ | 5.4 | 43.1 | 51.5 |
| 44 | - | 27.5 | 72.5 |
| 46 | - | 19.5 | 80.5 |
| 48 | - | 13.6 | 86.4 |
| 50 | - | 8.19 | 91.9 |

(room temperature to 170°/0.1 mm.)[60] gave 64.4 mg. of a pale yellow oil which had the same retention time on the 2 ft. silicone gum rubber column as authentic lumi-6-methyltropolone methyl ether (XXXVII), and which gave infrared, ultraviolet, and nuclear magnetic resonance spectra identical to authentic material.

Photochemical Conversion of 6-Methyltropolone Methyl Ether (XIX) to Photo-6-ester (XXXI) Approximately 425 mg. of 6-methyltropolone methyl ether (XIX) was dissolved in 140 ml. of water and irradiated in a quartz tube. The composition of the reaction mixture was determined periodically by withdrawing aliquots, extracting the aliquots with chloroform, and examining the concentrated extracts by vapor phase chromatography (2 ft. by $\frac{1}{4}$ in. silicone gum rubber column provided by the F & M Scientific Company, programmed at 15°/minute from 50 to 310°). After 28$\frac{1}{4}$ hours more than 90% of the material present had a retention time identical to that of photo-6-ester (XXXI). Minor peaks corresponding to photo-6-methyltropolone methyl ether (XXII) and lumi-6-methyltropolone methyl ether (XXXVII) were also observed.

The aqueous reaction mixture was extracted with chloroform (4 X 20 ml.). The extract was dried over anhydrous sodium sulfate and concentrated giving 536 mg. of oily orange liquid. Two molecular distillations (room temperature to 150°/0.1 mm.)[60] gave 107 mg. of photo-6-ester as a pale yellow oil. The infrared and ultraviolet spectra of this material were identical with those of authentic photo-6-ester.

Attempted Acid and Base Catalysed Isomerizations of Photo-6-methyltropolone Methyl Ether (XIX) Two solutions 1.2 X $10^{-4}$ molar in photo-6-methyltropolone methyl ether (XIX) were prepared. One solution was 8.8 X $10^{-2}$ N in sulfuric acid. The other solution was 8.8 X $10^{-2}$ N in sodium hydroxide. Both solutions were held at 22.5°, and were analysed periodicly by withdrawing aliquots and examining their ultraviolet spectra. No change could be detected in either solution after 2½ hours.

Two solutions identical to the above were prepared and placed in an oil bath at 80°. No change was detected in the ultraviolet spectrum of the acid solution over a period of two days. The spectrum of the basic solution varied erratically and uninterpretably, probably indicating decomposition of the starting material.

## Experimental for Diels-Alder Reaction of 4-Methyltropolone with Maleic Anhydride

Diels-Alder Adduct of 4-Methyltropolone (LII) and Maleic Anhydride A solution of 2.72 g. of 4-methyltropolone (LII) and 1.96 g. of maleic anhydride in 65 ml. of xylene was refluxed for eight hours under anhydrous conditions. The reaction apparatus was wrapped with aluminum foil to prevent any light reaching the reaction. Experience on previous runs had indicated that this procedure would increase the yield of adduct and decrease the formation of tarry by-products.

Cooling the reaction mixture gave 2.61 g. of a tan crystalline material. Concentration of the filtrate to ca. 7 ml. afforded an additional 0.1 g. of the same material (total yield 58%). Further concentration of the reaction mixture gave only intractable tars from which no pure compounds could be isolated.

Recrystallization from xylene or sublimation at 100° under aspirator vacuum gave white crystals; m.p. 177.1-177.9°; $\lambda_{\text{max}}^{95\%\ \text{EtOH}}$ 227 mu (7,550) and a shoulder at 254 mu (4,190; Figure 44, page 165). Infrared maxima: 2.90, 5.34, 5.58, 6.00, 7.00, 7.27, 7.40, 8.79, 8.91, 9.26, 9.80, 10.21, 10.35, 10.88. and 11.15 u (Figure 29, page 135).

Anal. Calcd. for $C_{12}H_{10}O_5$: C, 61.54; H, 4.30. Found: C, 61.60; H, 4.58.

Preparation of Lactone (LVIII) from Adduct (LIV) A slurry of 1.5 g. of adduct in 60 ml. of water was treated with 18 drops of concentrated hydrochloric acid and heated until a clear solution resulted (ca. 20 minutes). Concentration of the reaction mixture under a stream of dry air gave 0.96 g. of crystalline material. Three recrystallizations from water gave fine white crystals; m.p. 190.6-191.3°; $\lambda_{\text{max}}^{95\%\ \text{EtOH}}$ 229 mu (9,830) and a shoulder at 256 mu (4,030; Figure 45, page 167). Infrared maxima: 2.90, 3.09, 3.26, 5.70, 5.86, 6.05, 6.96, 7.04, 7.23, 7.28, 7.40, 7.55, 7.69, 7.83, 7.96, 8.11, 8.29, 8.49, 8.59, 8.77, 8.88, 9.15, 9.66, 10.00, 10.33, 10.49, 10.78, 11.29, 11.89, 12.44, 13.13, 13.50, and 14.45 u (Figure 29, page 135).

Anal. Calcd. for $C_{12}H_{12}O_6$: C, 57.14; H, 4.76. Found: C, 56.78; H, 4.76.

Sublimation of the lactone (LVIII) gave quantitatively a material whose infrared spectrum and melting point were identical with that of the adduct (LIV).

Catalytic Hydrogenation of the Adduct (LIV) Adduct (136 mg.) in 40 ml. of tetrahydrofuran was hydrogenated over Adams' catalyst at atmospheric pressure and 28°. The reaction was stopped after 1.5 equivalents of hydrogen had been absorbed. Filtration through a celite pad and removal of the solvent by distillation gave a white crystalline solid which showed infrared maxima at 5.37 and 5.58 u (five-membered anhydride) and 5.82 u (saturated ketone). This material was not further characterized.

## Experimental for Photochemistry of Thujic Acid and Methylthujate

Irradiation of Thujic Acid (LXIIa) Thujic acid (1.0 g.) dissolved in *ca*. 175 ml. of nitrogen flushed anhydrous ether was placed in a quartz tube and irradiated in the usual manner. The reaction was followed by ultraviolet analysis of aliquots withdrawn periodically. After five hours the spectrum showed a shift of 2 mu and 10 mu respectively in the two peaks of the thujic acid spectrum (Figure 46, page 169). The extinction values of these peaks were about 50% of their initial value. Irradiation for an additional two hours produced no change in the spectrum of the reaction mixture, and the reaction was stopped. Concentration of the reaction solution under aspirator vacuum gave 0.93 g. of yellow oil which could not be crystallized.

Chromatography on silicic acid (20 cm. by 2 cm.) gave the following results:

| Fraction | Volume | Eluent | Residue |
|---|---|---|---|
| 1 | 25 ml. | benzene | - |
| 2 | " | " | 0.48 g. of yellow-white solid |
| 3 | " | " | 0.08 g. " |
| 4 | " | " | 0.02 g. of yellow oil |
| 5 | " | " | trace of yellow oil |
| 6-9 | 25 ml. ea. | 50:50 benzene-chloroform | " |
| 10-13 | 25 ml. ea. | chloroform | " |
| 14 | 25 ml. | 75:25 chloroform methanol | " |

A small amount of colored material remained at the top of the column.

Recrystallization from petroleum ether (b.p. 60-70°) of the combined residues from fractions 2 and 3 gave photothujic acid (LXVa) as fine creamy-white crystals; m.p. 114.5-115.3°; $\lambda^{\text{isooct.}}_{\text{max}}$ 216 mu (15,900) and 292 mu (7,090; Figure 46, page 169). Infrared maxima: 2.85, 3.20, 3.55, 3.80, 3.95, 5.97, 6.23, 6.47, 6.90, 7.28, 7.59, 7.82, 8.85, 9.23, 10.25, 10.62, and 11.10 u (Figure 30, page 137).

Anal. Calcd. for $C_{10}H_{12}O_2$: C, 73.75; H, 7.36. Found: C, 73.85; H, 7.43.

The yellow oils from the remaining fractions were combined and molecularly distilled (room temperature to 180°/0.1 mm.) giving ca. 100 mg. of pale yellow oil. Vapor phase chromatography (4 ft. by $\frac{1}{4}$ in. silicone gum rubber column at 300°) showed this material to be a mixture of two products in a ration of about 10:1.

Preparation of Silver Thujate A slurry of 3.5 g. of impure thujic acid in 25 ml. of water was treated with 2 ml. of concentrated ammonium hydroxide (ca. 30% excess). A clear yellow-orange solution resulted. Addition of a solution of 3.70 g. of silver nitrate in 10 ml. of water gave an immediate precipitate which was permitted to stand for four hours. Filtration of the reaction mixture gave a brown powder. Treatment of the filtrate with silver nitrate solution afforded a small amount of precipitate which was combined with the above material. After drying on a vacuum desiccator over anhydrous calcium sulfate, 4.23 g. (75%) of silver thujate was obtained.

Preparation of Methylthujate (LXIIb) A. A mixture of 4.23 g. of silver thujate, 15 ml. of methyliodide (34 g., ca. 10 fold excess) and 60 ml. of anhydrous ether was refluxed in the dark for 14 hours. Anhydrous conditions were maintained at all times. An oily residue was obtained upon concentration of the reaction mixture. This material was dissolved in 50 ml. of ether, washed with 10 ml. of concentrated sodium thiosulfite, 10 ml. of water, and dried over anhydrous sodium sulfate. Concentration and subsequent molecular distillation (55°/0.08 mm.)[60] gave 2.1 g. (82%) of methylthujate (LXIIb) as a pale yellow oil which crystallized on cooling.

B. An ethereal solution of thujic acid (LXIIa) was treated with ethereal diazomethane (20% excess) and allowed to stand overnight. Concentration of the reaction mixture under aspirator vacuum gave 3 g. of a yellow oil. After molecular distillation (55°/0.08 mm.),[60] passage through an alumina column (eluent benzene), and a second molecular distillation, 1.9 g. of colorless solid methylthujate (LXIIb) was obtained; m.p. 30-34.5° (reported 34.5°);[67] $\lambda_{max}^{95\% \, EtOH}$ 212 mu (20,000) and 282.5 mu (5,460; Figure 47, page 171). Infrared maxima: 3.39, 5.84, 6.20, 6.49, 6.84, 6.96, 7.27, 7.35, 7.51, 7.88, 8. 1, 8.40, 9.22, 9.55, 10.31, 12.65, 13.50, and 13.90 u (Figure 30, page 137).

Vapor phase chromatographic analysis of this material (4 ft. by $\frac{1}{4}$ in. IAC-446 column at 180°) gave a single peak under conditions known to show the presence of impurities.

*Irradiation of Methylthujate (LXIIb)* A solution of methylthujate (LXIIb; 2.0 g.) in 200 ml. of anhydrous ether was placed in a quartz tube, flushed with dry nitrogen, and irradiated in the usual manner. Aliquots were withdrawn at approximately 20 minute intervals and analysed by vapor phase chromatography (4 ft. by $\frac{1}{4}$ in. IAC-446 column at 185°). The reaction was stopped after five hours and fifty minutes at which time *ca*. 80% of the methylthujate had reacted. Two new photoproducts were observed in a ratio of 75:25.

Concentration of the reaction mixture gave 1.8 g. of a light yellow oil which was chromatographed on an alumina column (13 in. by 2 in.). Fractions were analysed by vapor phase chromatography (IAC-446 column, 185°), and the following results were obtained:

---

[67] E. F. Kurth, *J. Am. Chem. Soc.*, *72*, 5778 (1950).

| Fraction | Volume | Eluent | Residue |
|---|---|---|---|
| 1-69 | 25 ml. ea. | benzene and 20:80 pet. ether-benzene | none |
| 70-77 | 25 ml. ea. | 20:80 pet. ether-benzene | 50 mg. of methylthujate |
| 78-81 | 25 ml. ea. | 50:50 pet. ether-benzene | 0.15 g. of methylthujate plus lumimethylthujate |
| 82-86 | " | " | 0.24 g. all compounds |
| 87-95 | " | " | 0.33 g. " |
| 96-105 | " | " | 0.22 g. photomethylthujate |
| 106 | 400 ml. | benzene | 0.05 g. photomethylthujate |
| 107 | 300 ml. | chloroform | nothing |

Two molecular distillations (55°/0.15 mm.)[60] of the combined residues from fractions 96-105 and 106 gave photomethylthujate (178 mg.; LXVIIb) as a pale yellow oil; $\lambda_{max}^{95\%\ EtOH}$ 216.5 mu (15,350) and 293 mu (6,950; Figure 47, page 171). Infrared maxima: 3.38, 5.84, 6.24, 6.52, 6.85, 6.97, 7.24, 7.37, 7.59, 7.96, 8.25, 8.40, 8.82, 9.21, 9.30, 9.85, 10.19, 12.16, 12.44, 12.76, 13.40, 13.89, and 14.89 u (Figure 30, page 137).

Anal. Calcd. for $C_{11}H_{14}O_2$: C, 74.13; H, 7.92. Found: C, 74.45; H, 7.96.

The remaining fractions were combined and the minor product isolated by vapor phase chromatography (4 ft. by ¼ in. LAC-728 column at 180°). This material was purified by vapor phase chromatography (LAC-446 column at 140°) giving alpha-lumimethylthujate (LXIVb) as a colorless liquid and beta-lumimethylthujate (LXIIIb), present in less than 2%, as a colorless liquid.

Alpha-lumimethylthujate (LXIVb) showed infrared maxima at 3.29, 3.38, 3.48, 5.78, 6.81, 6.97, 7.35, 7.84, 7.97, 8.13, 8.41, 8.65, 9.09, 9.54, 10.05, 10.74, 12.01, 12.52, 13.08, 13.80, and 14.33 u (Figure 31, page 139).

Beta-lumimethylthujate (LXIIIb) showed infrared maxima at 3.39, 5.82, 6.25, 6.85, 6.97, 7.35, 7.45, 7.65, 7.84, 7.98, 8.21, 8.41, 8.59, 8.82, 9.09, 9.25, 9.92, 10.75, 10.97, and 11.44 u (Figure 31, page 139).

## ACKNOWLEDGEMENTS

The author wishes to acknowledge and thank the many people whose help has enabled him to carry out this work. In particular he wishes to thank his parents, Mr. and Mrs. Leland S. Smith, and his wife, Barbara, for guidance, support and patience.

The author wishes to thank Dr. O. L. Chapman for suggesting the research problem and for guidance during the work, both as a supervisor and as a close friend.

The author wishes to thank Dr. C. H. Depuy for helpful discussions and for permitting liberal use of his groups' vapor phase chromatography apparatus. Dr. Peter Fitton graciously prepared an authentic sample of 5-methyl-beta-tropolone, and Dr. Roy King has given invaluable advice concerning vapor phase chromatography and pyrolysis work. The author wishes to thank Dr. E. Wenkert for many helpful discussions concerning portions of this work.

Crown Zellerbach Corporation, Camas, Washington, provided samples of thujic acid and of thujaplicins. Dr. J. A. F. Gardner provided a sample of pure gamma-thujaplicin.

The author wishes to acknowledge the financial support provided by a Research Corporation Grant. The National Institutes of Health provided his salary and tuition from March 1960 through November 1961 (Grant #10,708), and the Iowa State Research Fund provided support for research during his tenure as a National Institutes of Health Research Fellow.

A portion of this work has been published:

Photoisomerizations in the alpha-Tropolone Series: The Mechanistic Path of the alpha-Tropolone to 4-Oxo-2-cyclopentenylacetic Acid Conversion. W. G. Dauben, K. Koch, O. L. Chapman, and S. L. Smith, *J. Am. Chem. Soc.*, **83**, 1768 (1961).

# APPENDIX

Vapor phase chromatography columns used in this investigation.

Preparative scale UCON-1b550x: 1 m. by 15 mm. pyrex tube packed with UCON-1b550x[68] (1:4 by weight) on 30/60 mesh Celite; Maximum temperature 200°.

4 ft. Silicone Gum Rubber: 4 ft. by $\frac{1}{4}$ in. stainless steel tube packed with Silicone Gum Rubber (1:4 by weight) on 60/80 mesh Chromosorb-P; Maximum temperature 350°.

2 ft. Silicone Gum Rubber: 2 ft. by $\frac{1}{4}$ in. stainless steel tube packed with Silicone Gum Rubber (1:5 by weight) on Chromosorb-P; Maximum temperature 350°.

IAC-446: Polyester; crosslinked diethylene glycol adipate (1:4 by weight) on 60/80 mesh Chromosorb-P; Maximum temperature 225°.

IAC-728: Polyester; crosslinked diethylene glycol succinate (1:4 by weight) on 60/80 mesh chromosorb-P; Maximum temperature 225°.

---

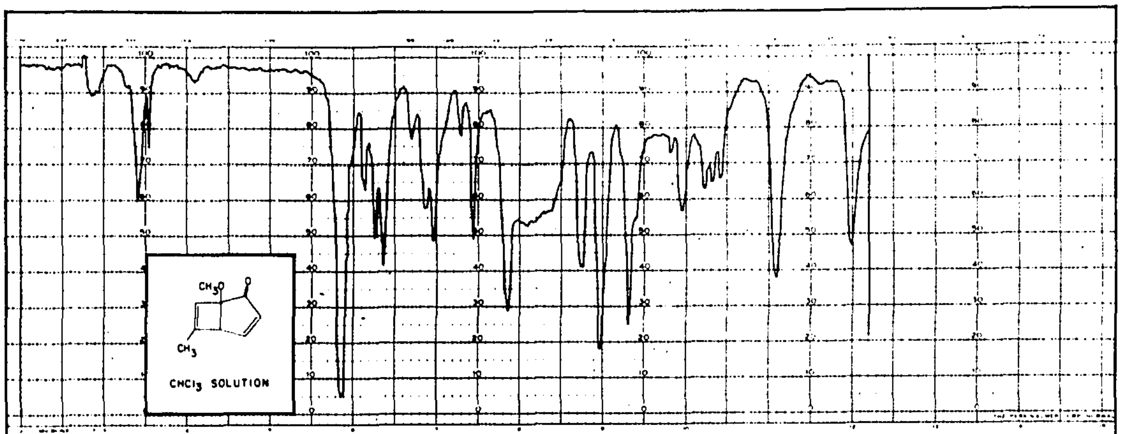
[68] The UKON oils and greases are poly alkyl ethers manufactured by Union Carbide Corporation.

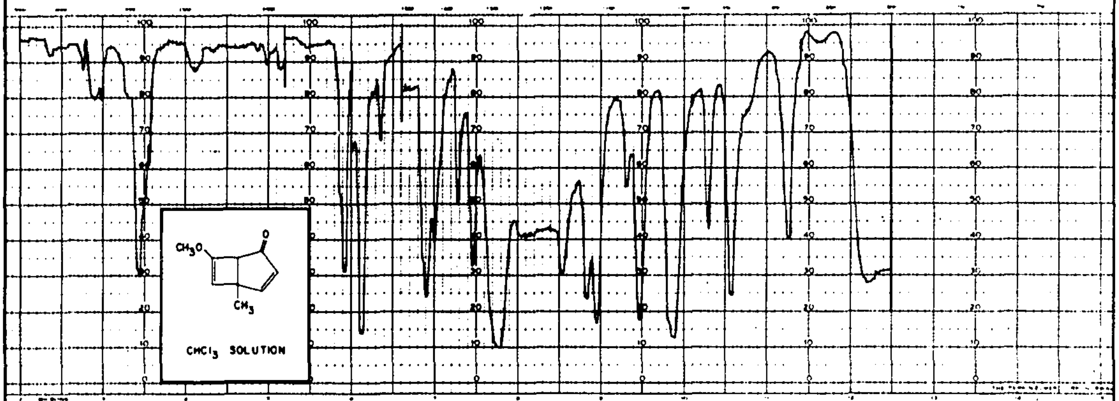
Figure 25. Infrared spectra

Top: Photo-4-methyltropolone methyl ether (XX)

Middle: Lumi-4-methyltropolone methyl ether (XXXVI)

Bottom: Photo-4-ester (XXX)


CH$_3$O
O
CH$_3$
CHCl$_3$ SOLUTION


CH$_3$O
O
CH$_3$
CHCl$_3$ SOLUTION

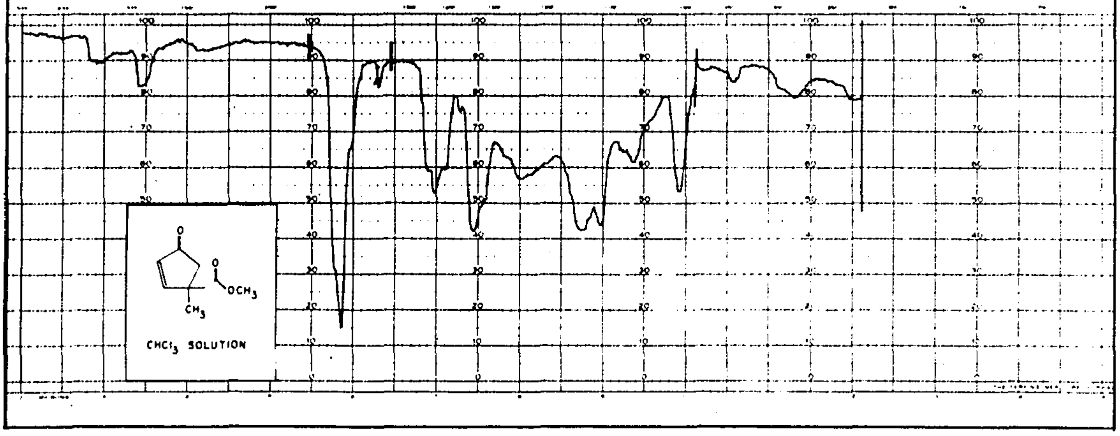
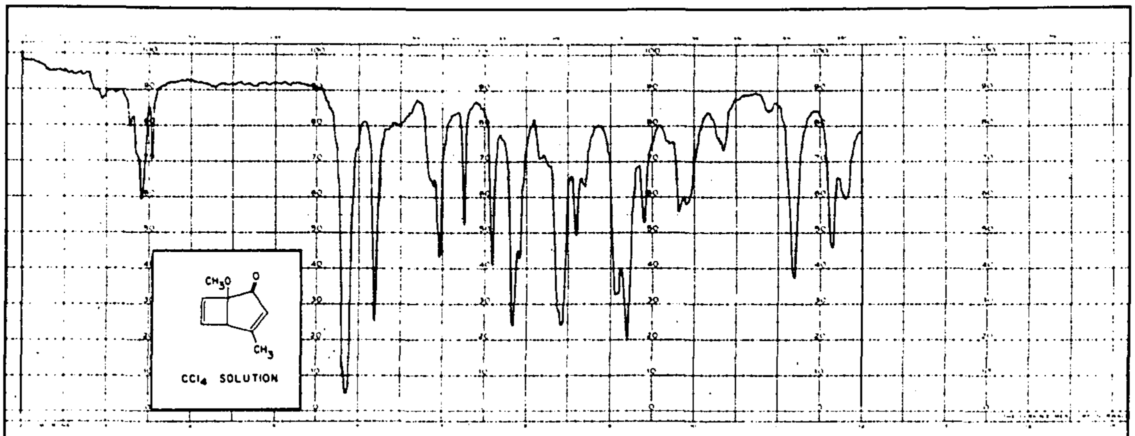

O
O
OCH$_3$
CH$_3$
CHCl$_3$ SOLUTION

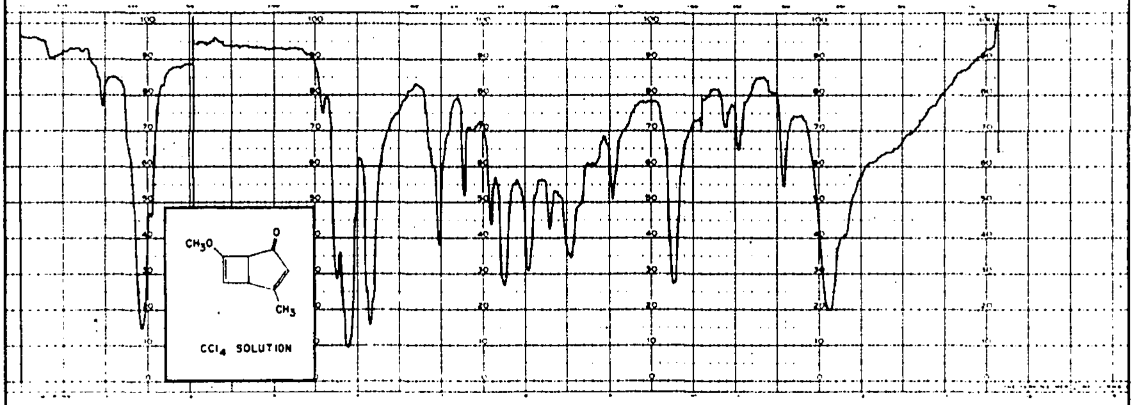
Figure 26. Infrared spectra

Top: Photo-6-methyltropolone methyl ether (XXII)

Middle: Lumi-6-methyltropolone methyl ether (XXXVII)

Bottom: Photo-6-ester (XXXI)


CH₃O
O
CH₃
CCl₄ SOLUTION


CH₃O
O
CH₃
CCl₄ SOLUTION

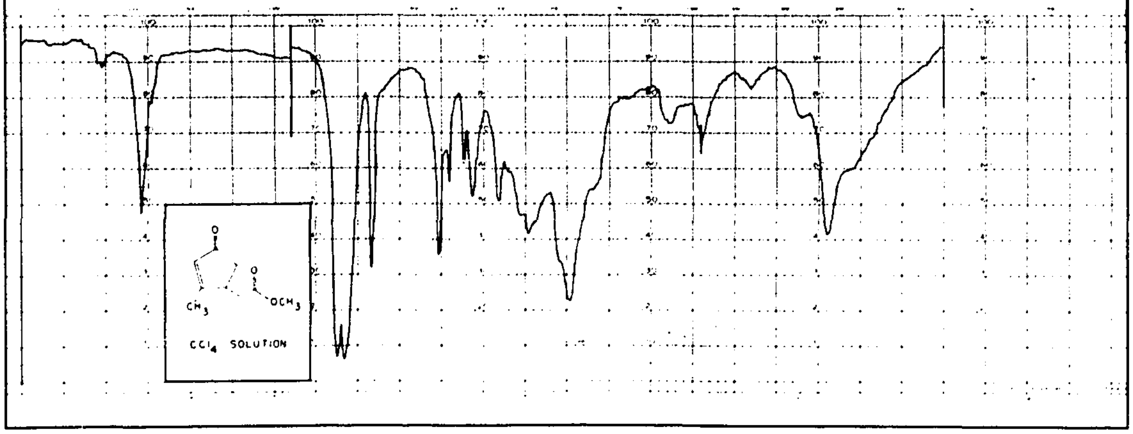
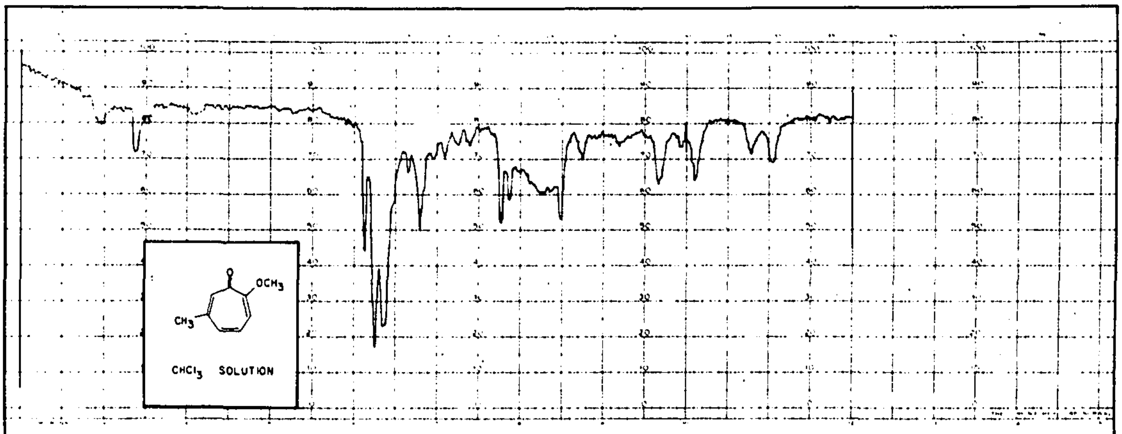

O
O
CH₃
OCH₃
CCl₄ SOLUTION

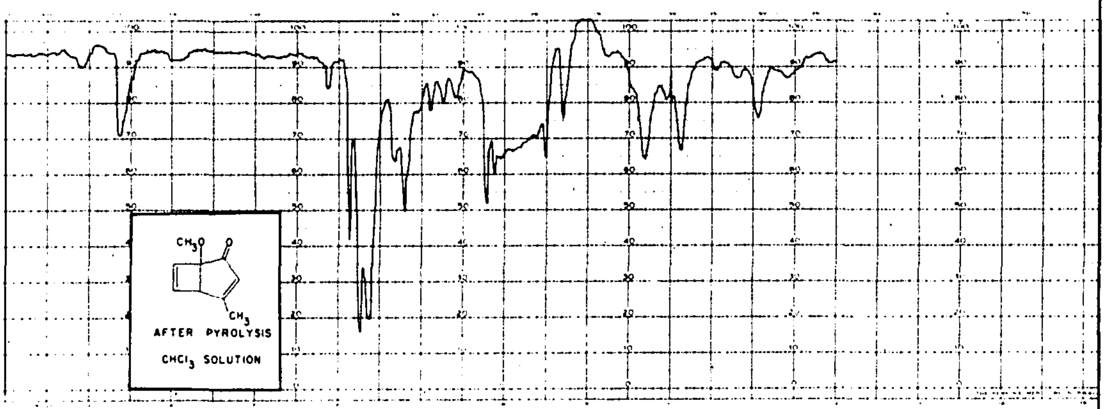
Figure 27. Infrared spectra

Top: 6-Methyltropolone methyl ether (XIX)

Middle: Pyrolysis product from photo-6-methyltropolone methyl ether (XXII)

Bottom: Pyrolysis product from photo-4-methyltropolone methyl ether (XX)


OCH₃
CH₃
CHCl₃ SOLUTION


CH₃O
CH₃
AFTER PYROLYSIS
CHCl₃ SOLUTION

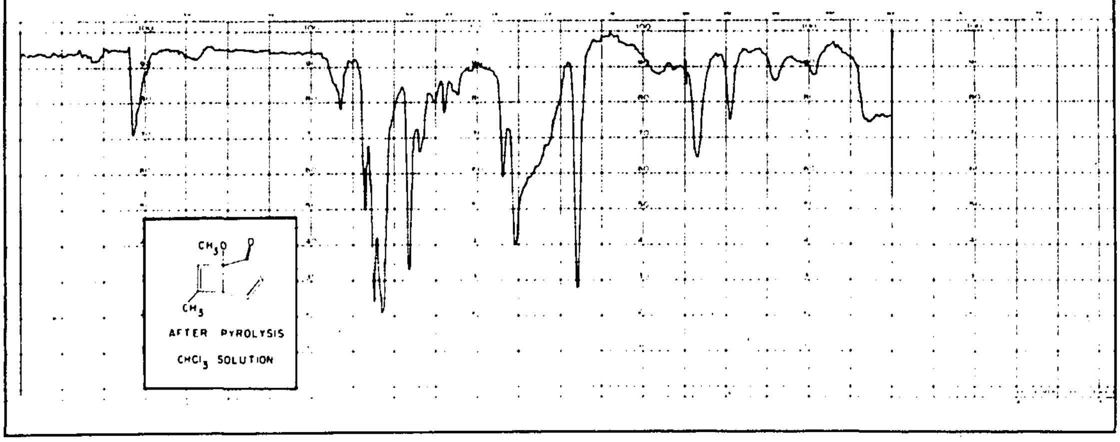

CH₃O
CH₃
AFTER PYROLYSIS
CHCl₃ SOLUTION

Figure 28. Infrared spectra

Top: Tetrahydrophoto-4-methyltropolone methyl ether (XXIV)

Middle: Dihydrophoto-6-methyltropolone methyl ether (XXV)

Bottom: Comparison of pyrolysis mixture from lumi-4- and lumi-6-methyltropolone methyl ethers (XXXVI and XXXVII) with 5-methyl-beta-tropolone

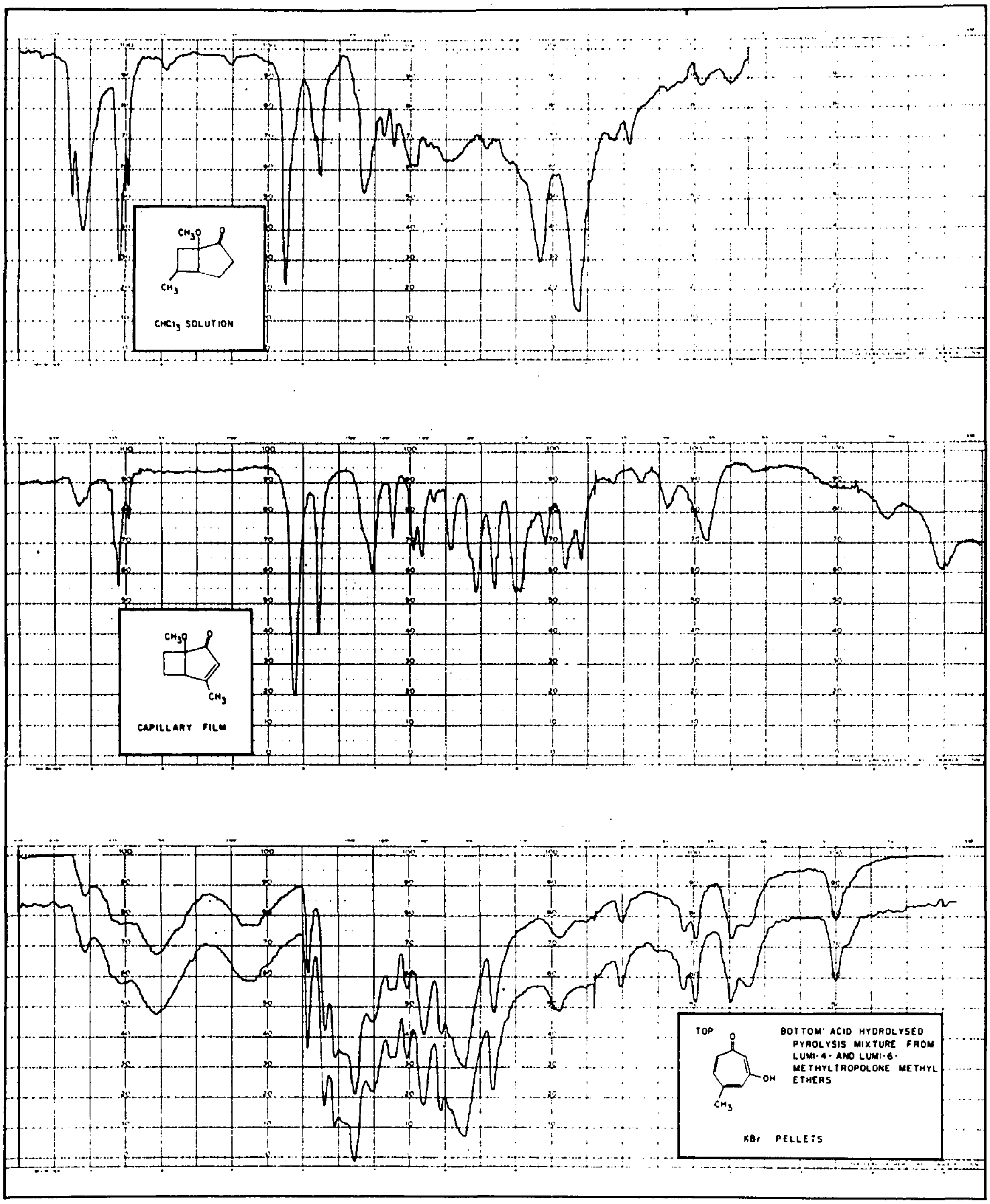
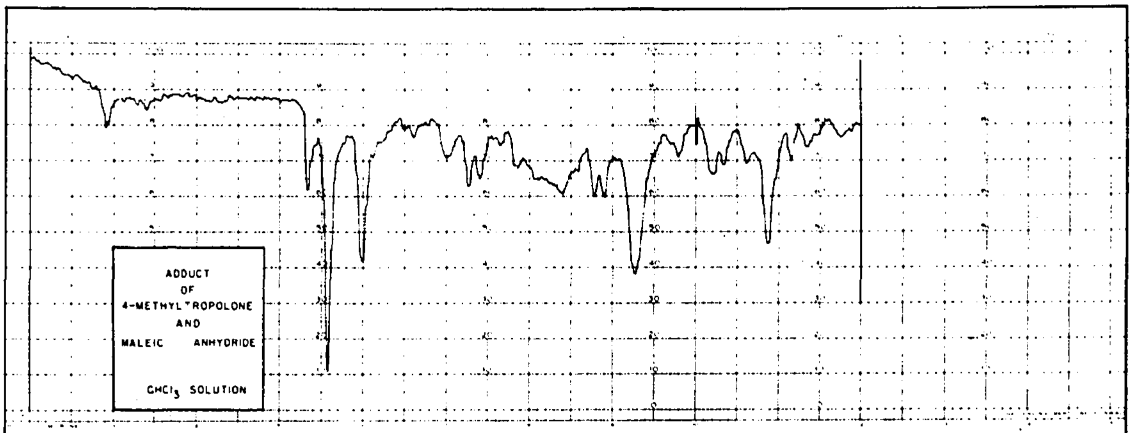

CH3O
O
CH3
CHCl3 SOLUTION
CH3O
O
CH3
CAPILLARY FILM
TOP
O
OH
CH3
BOTTOM: ACID HYDROLYSED PYROLYSIS MIXTURE FROM LUMI-4- AND LUMI-6-METHYLTROPOLONE METHYL ETHERS
KBr PELLETS

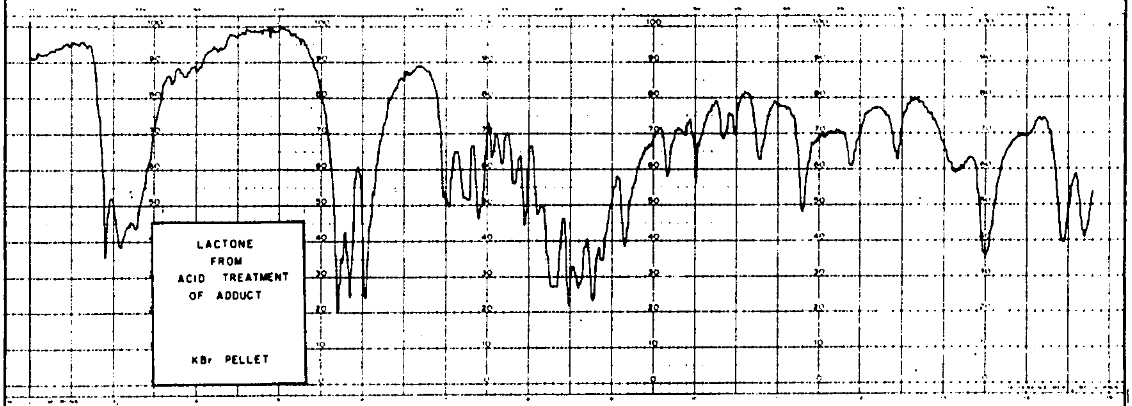
Figure 29. Infrared spectra

Top: Diels-Alder adduct of 4-methyltropolone and maleic anhydride (LIV)

Middle: Lactone from acid treatment of the adduct (LVIII)

Bottom: Thujic acid (LXIIa)


ADDUCT
OF
4-METHYLTROPOLONE
AND
MALEIC ANHYDRIDE
CHCl3 SOLUTION


LACTONE
FROM
ACID TREATMENT
OF ADDUCT
KBr PELLET

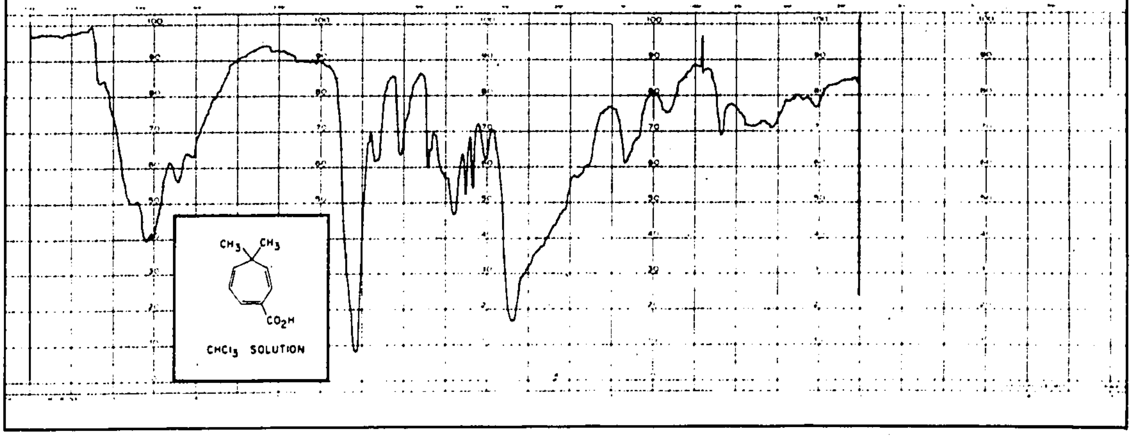
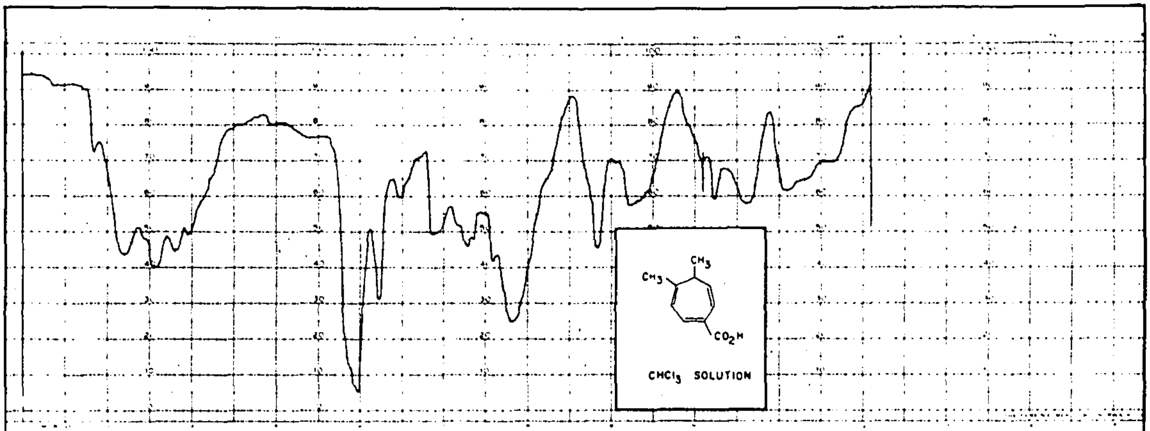

CH3
CH3
CO2H
CHCl3 SOLUTION

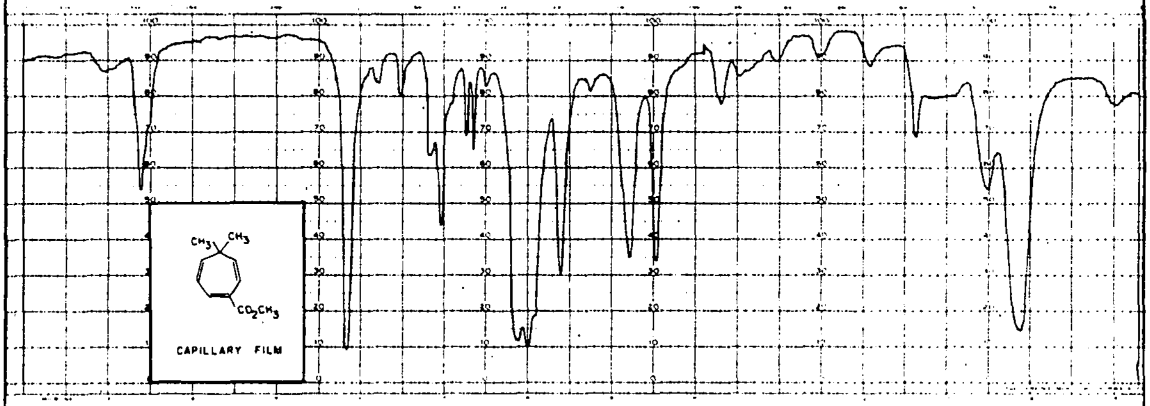
Figure 30. Infrared spectra

Top: Photothujic acid (LXVIIa)

Middle: Methylthujate (LXIIb)

Bottom: Photomethylthujate (LXVIIb)


CH₃
CH₃
CO₂H
CHCl₃ SOLUTION


CH₃
CH₃
CO₂CH₃
CAPILLARY FILM

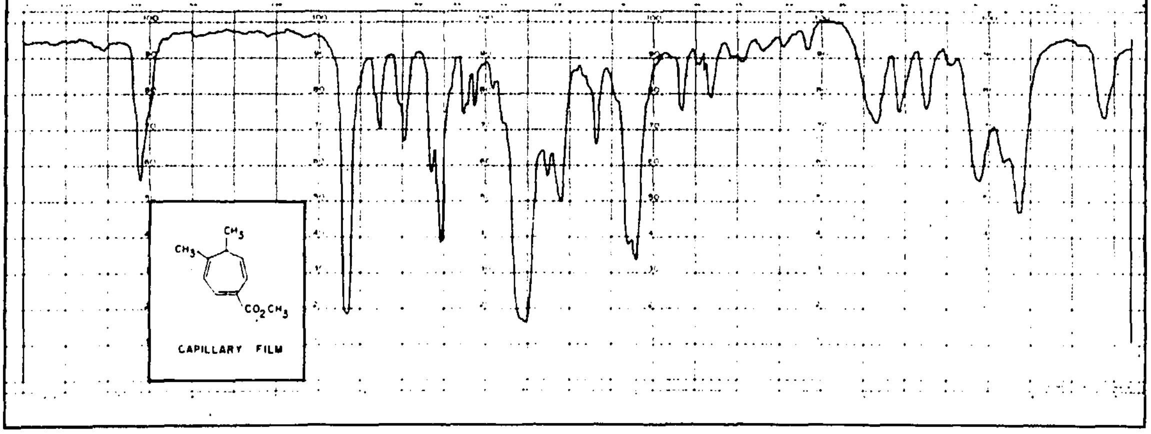

CH₃
CH₃
CO₂CH₃
CAPILLARY FILM

Figure 31. Infrared spectra

Top: alpha-Lumimethylthujate (LXIVb)

Bottom: beta-Lumimethylthujate (LXIII)

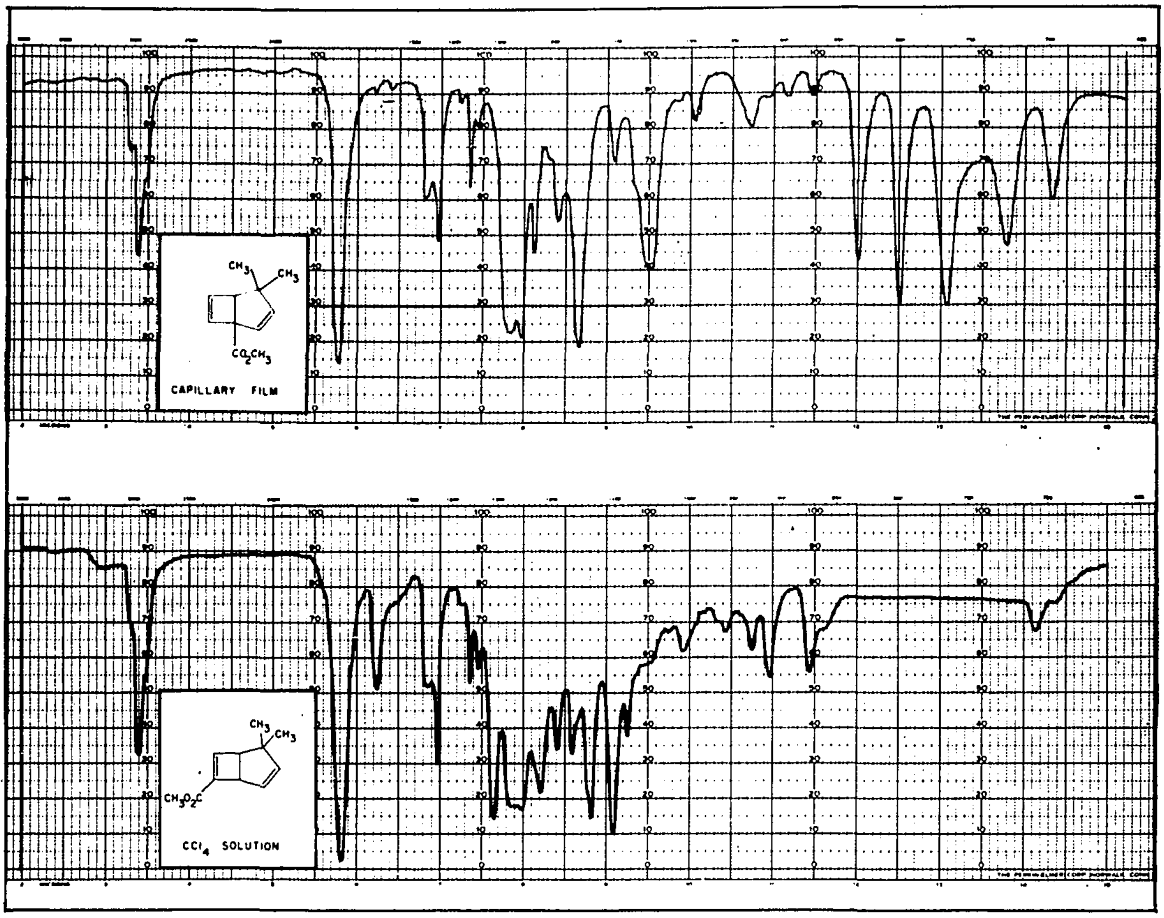

CH$_3$
CH$_3$
CO$_2$CH$_3$
CAPILLARY FILM
CH$_3$
CH$_3$
CH$_3$O$_2$C
CCl$_4$ SOLUTION

Figure 32. Ultraviolet spectrum of 6-methyltropolone methyl ether (XIX)

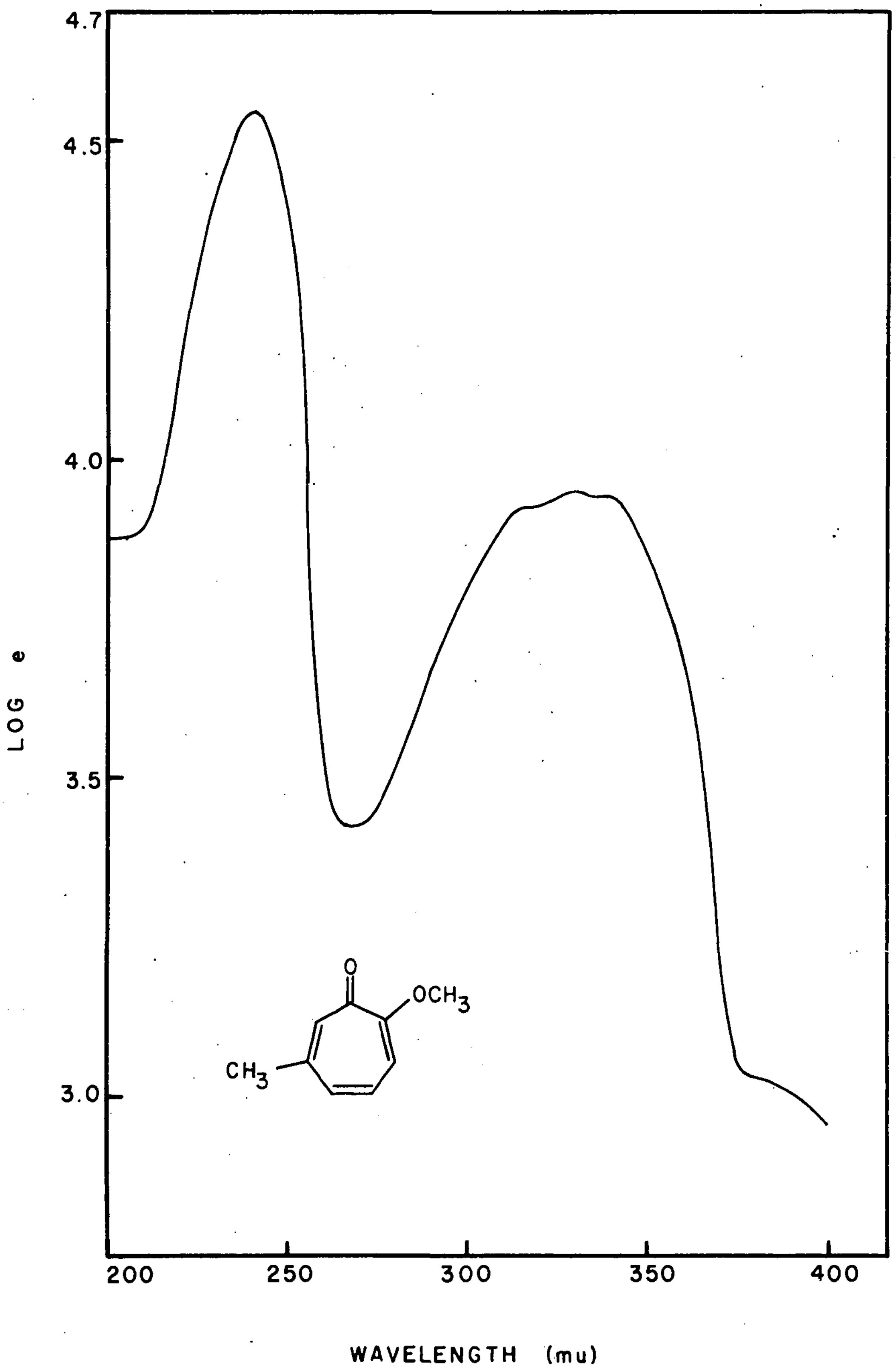

4.7
4.5
4.0
3.5
3.0
LOG e
200
250
300
350
400
WAVELENGTH (mu)
O
OCH3
CH3

Figure 33. Ultraviolet spectrum of photo-4-methyltropolone methyl ether (XX)

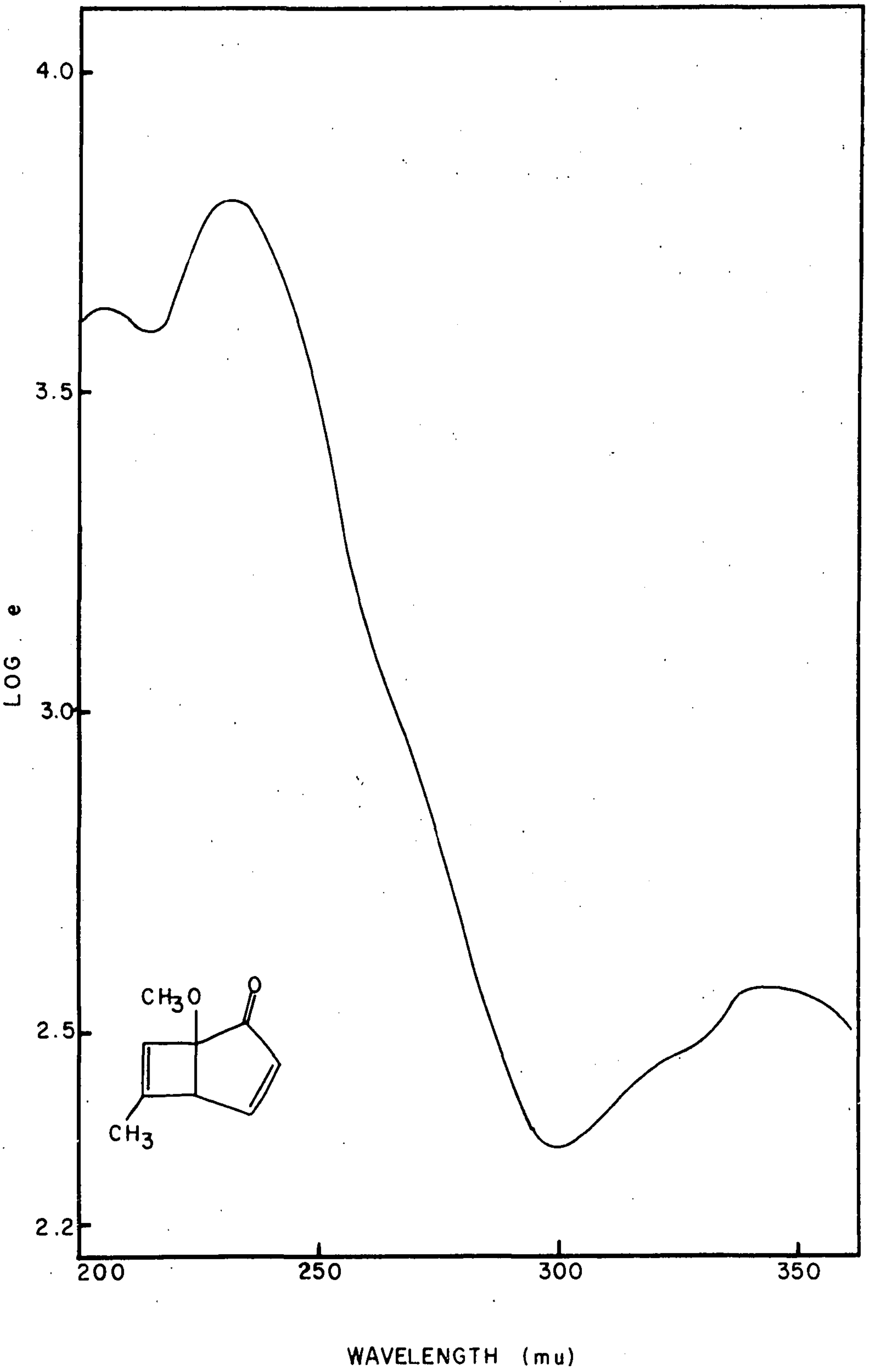

4.0
3.5
3.0
2.5
2.2
LOG e
200
250
300
350
WAVELENGTH (mu)
CH3O
O
CH3

Figure 34. Ultraviolet spectrum of photo-6-methyltropolone methyl ether (XXII)

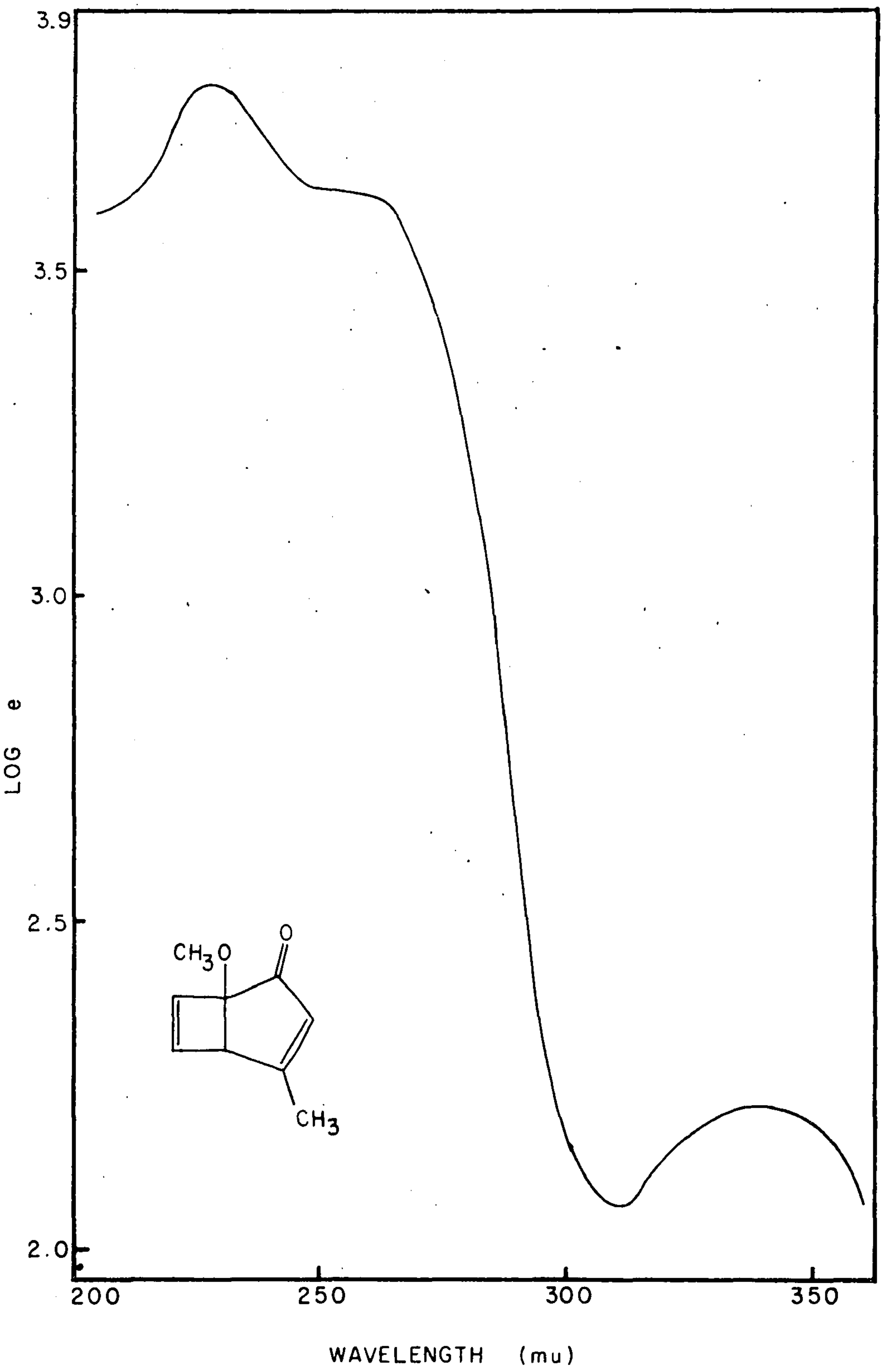

3.9
3.5
3.0
2.5
2.0
LOG e
200
250
300
350
WAVELENGTH (mu)
CH$_3$O
O
CH$_3$

Figure 35. Ultraviolet spectrum of dihydrophoto-6-methyltropolone methyl ether (XXV)

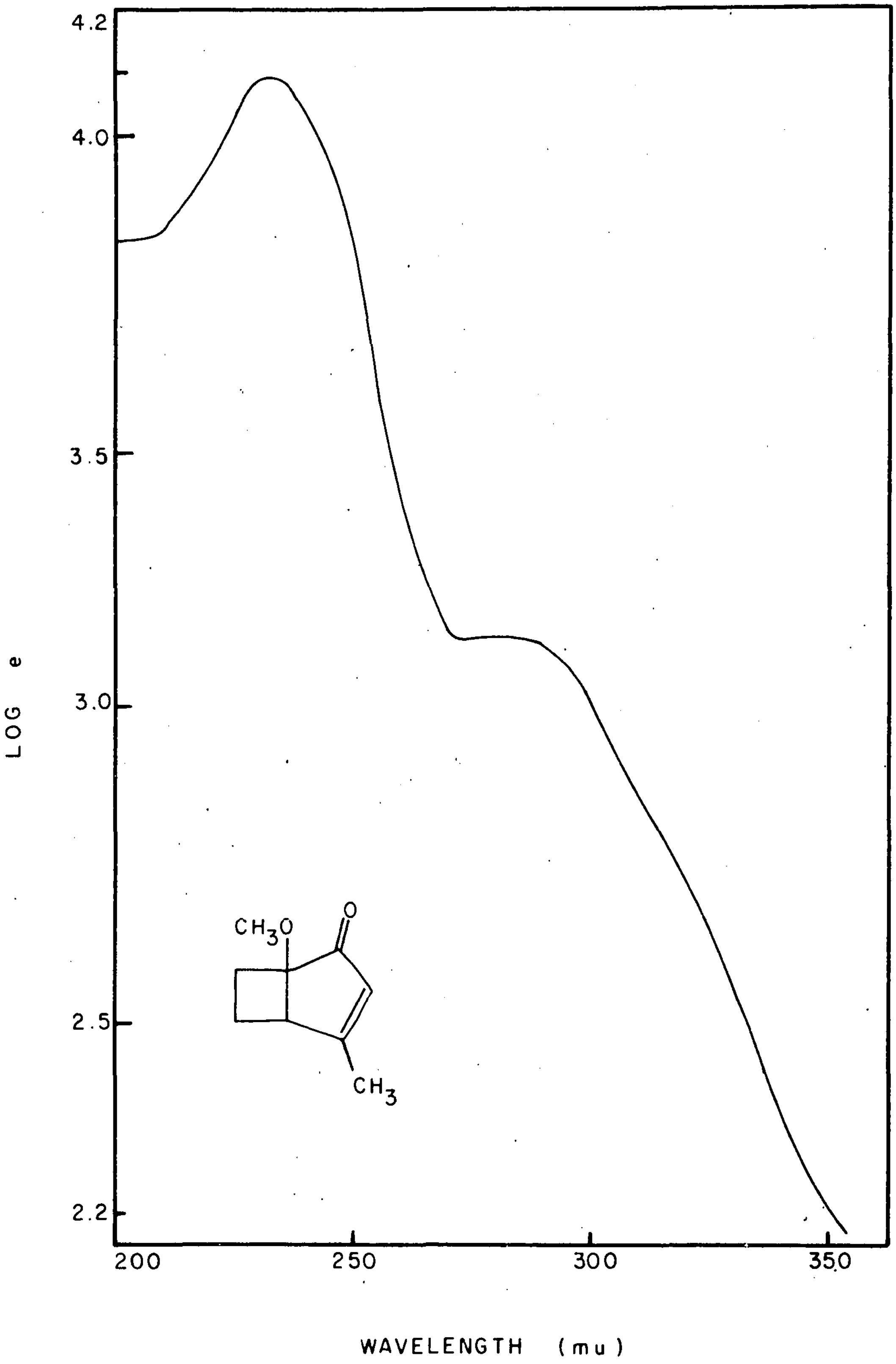

4.2
4.0
3.5
3.0
2.5
2.2
LOG e
200
250
300
350
WAVELENGTH (mu)
CH3O
O
CH3

Figure 36. Ultraviolet spectra

A. Basic hydrolysate from pyrolysed photo-4-methyltropolone methyl ether (XX)

B. 4-Methyltropolone (XVIII) in base

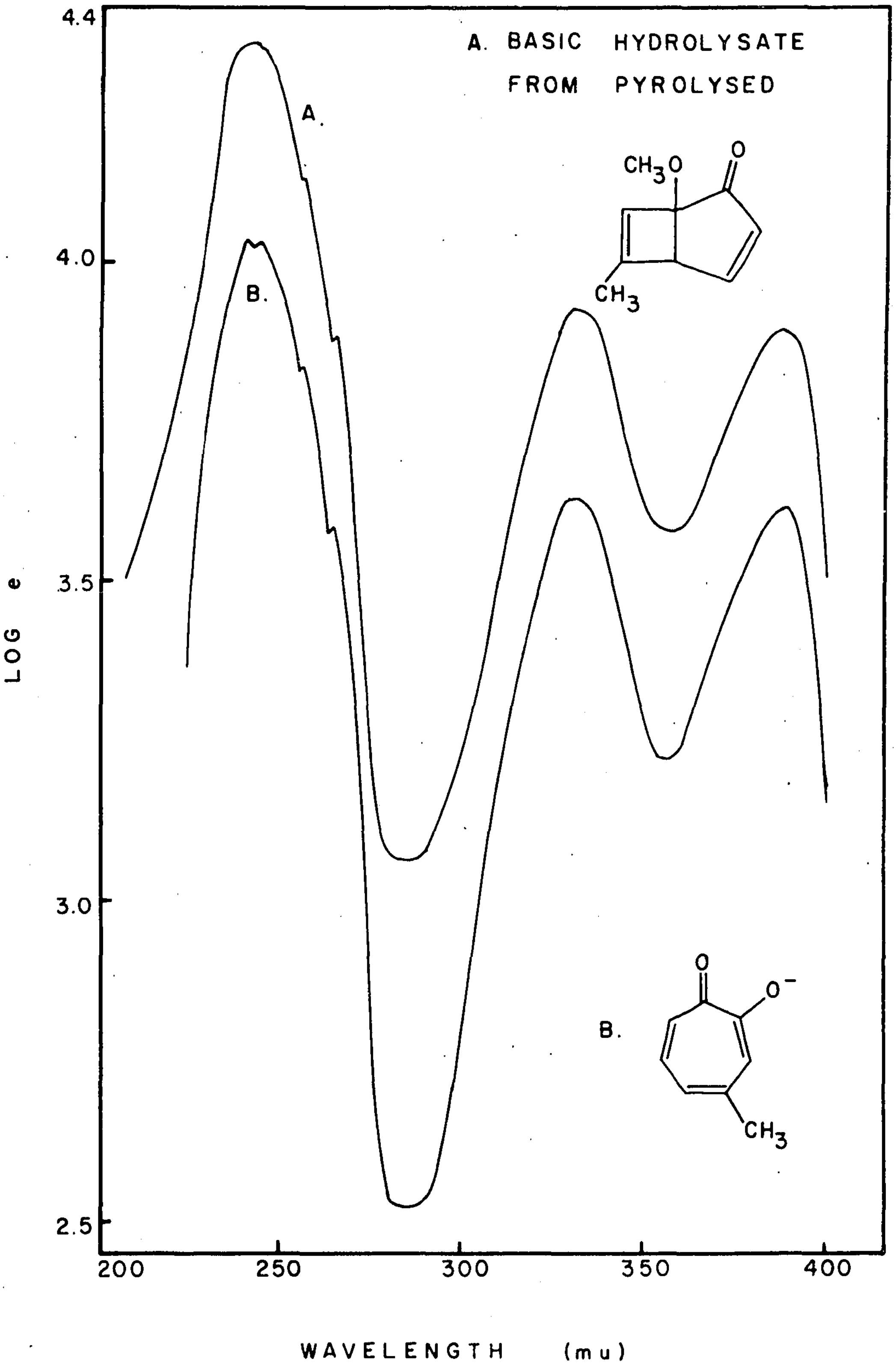

A. BASIC HYDROLYSATE
FROM PYROLYSED
A.
B.
$CH_3O$
O
$CH_3$
B.
O
$O^-$
$CH_3$
4.4
4.0
3.5
3.0
2.5
LOG e
200
250
300
350
400
WAVELENGTH (mu)

Figure 37. Ultraviolet spectra

A. 4-Methyltropolone (XVIII)

B. Acidified basic hydrolysate from pyrolysed photo-4-methyltropolone methyl ether (XX)

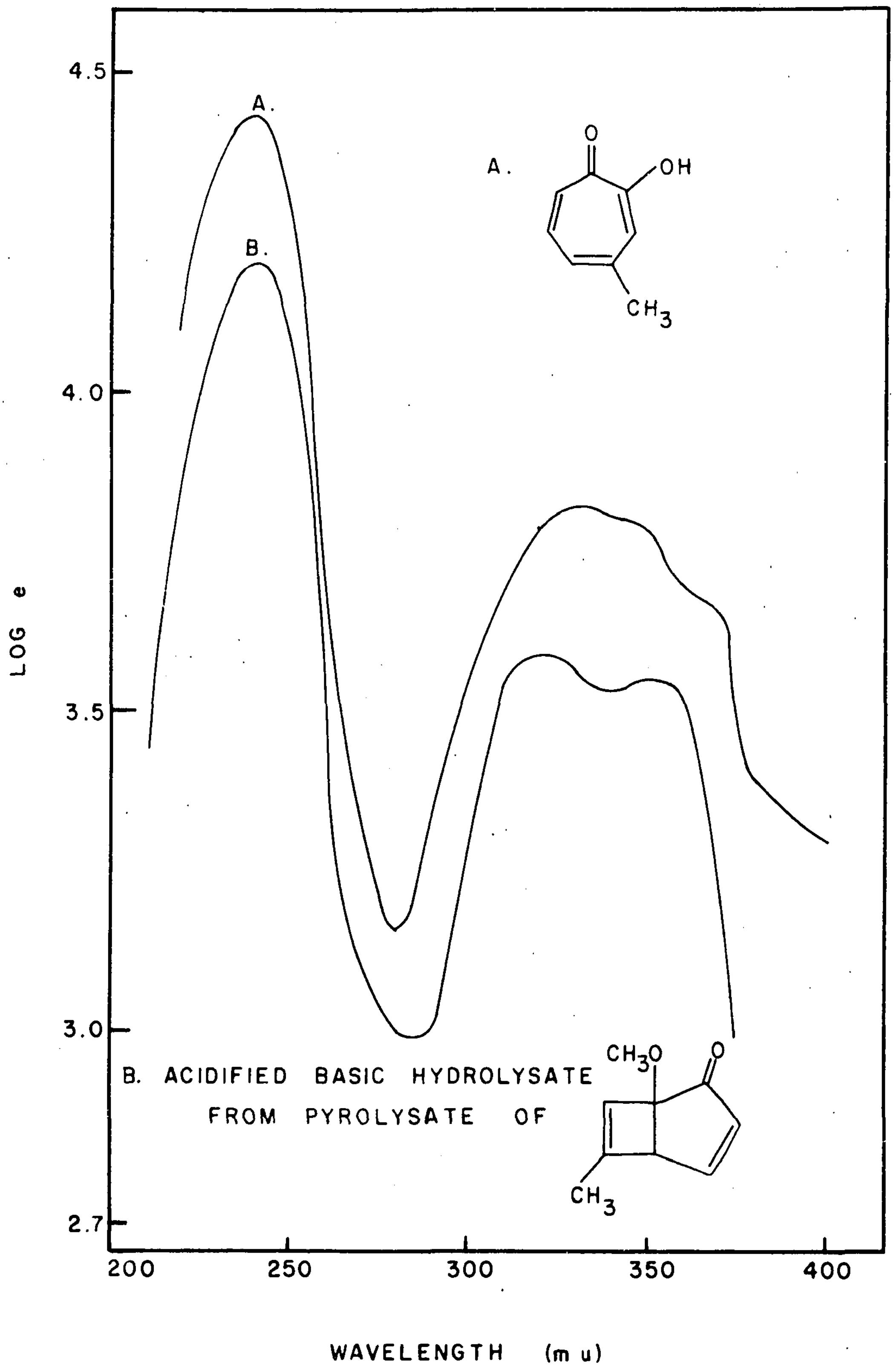

A.
B.
A.
O
OH
CH3
4.5
4.0
LOG e
3.5
3.0
2.7
B. ACIDIFIED BASIC HYDROLYSATE
FROM PYROLYSATE OF
CH3O
O
CH3
200
250
300
350
400
WAVELENGTH (m u)

Figure 38. Ultraviolet spectrum of photo-4-ester (XXX)

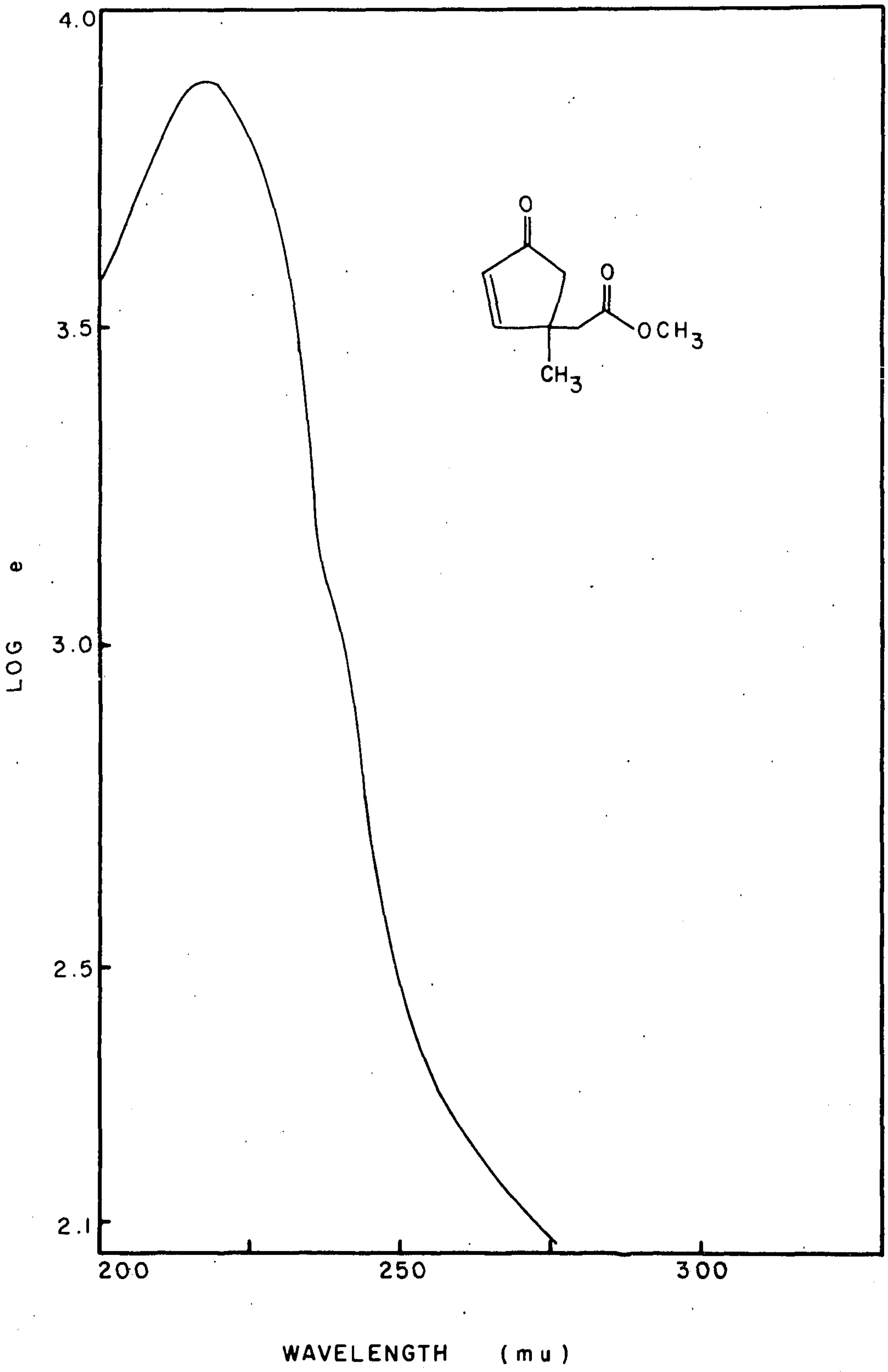

4.0
3.5
3.0
2.5
2.1
LOG e
200
250
300
WAVELENGTH (mu)
O
O
OCH3
CH3

Figure 39. Ultraviolet spectrum of photo-6-ester (XXXI)

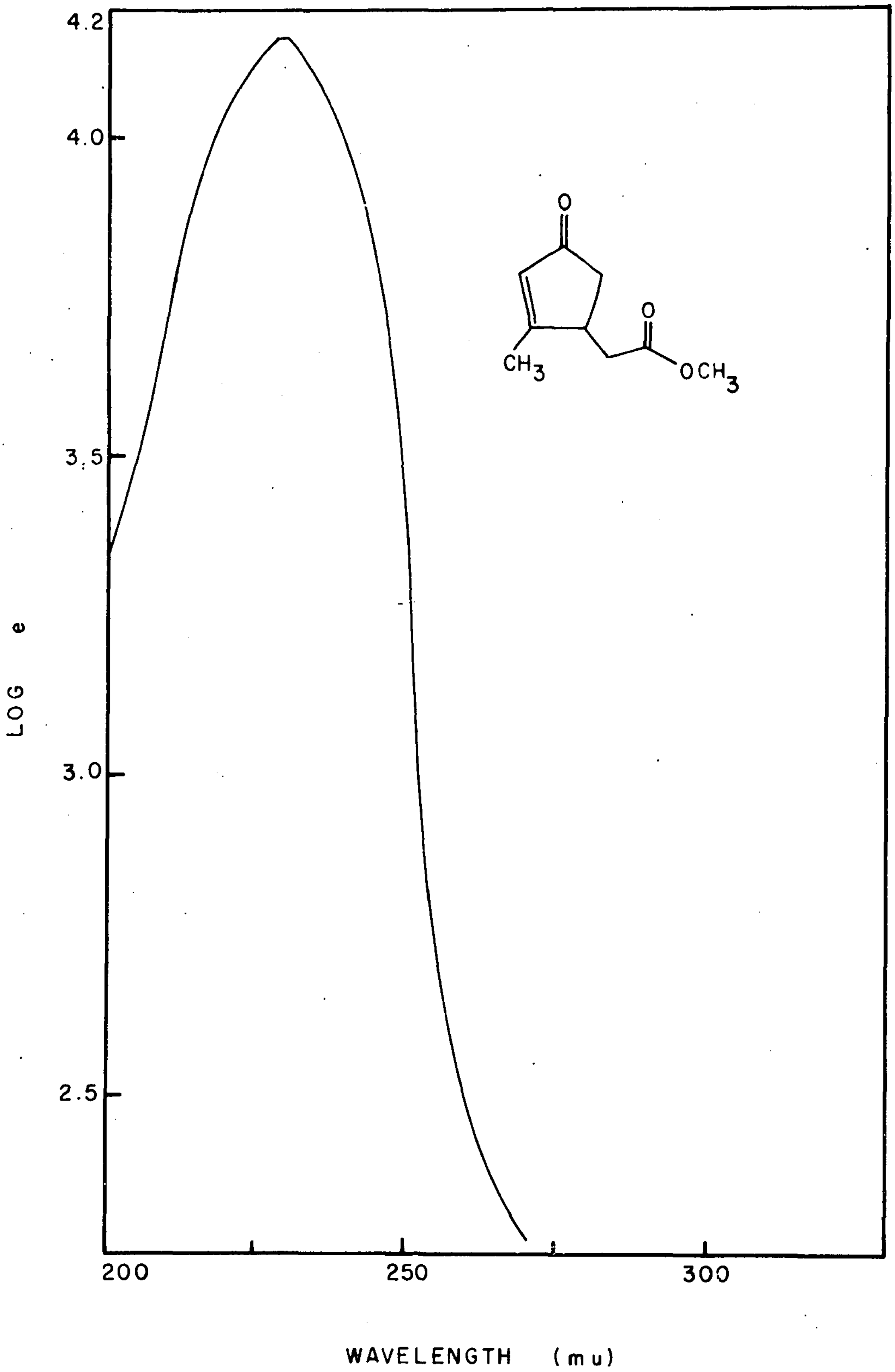

4.2
4.0
3.5
3.0
2.5
LOG e
200
250
300
WAVELENGTH (mu)
O
O
CH3
OCH3

Figure 40. Ultraviolet spectrum of lumi-4-methyltropolone methyl ether (XXXVI)

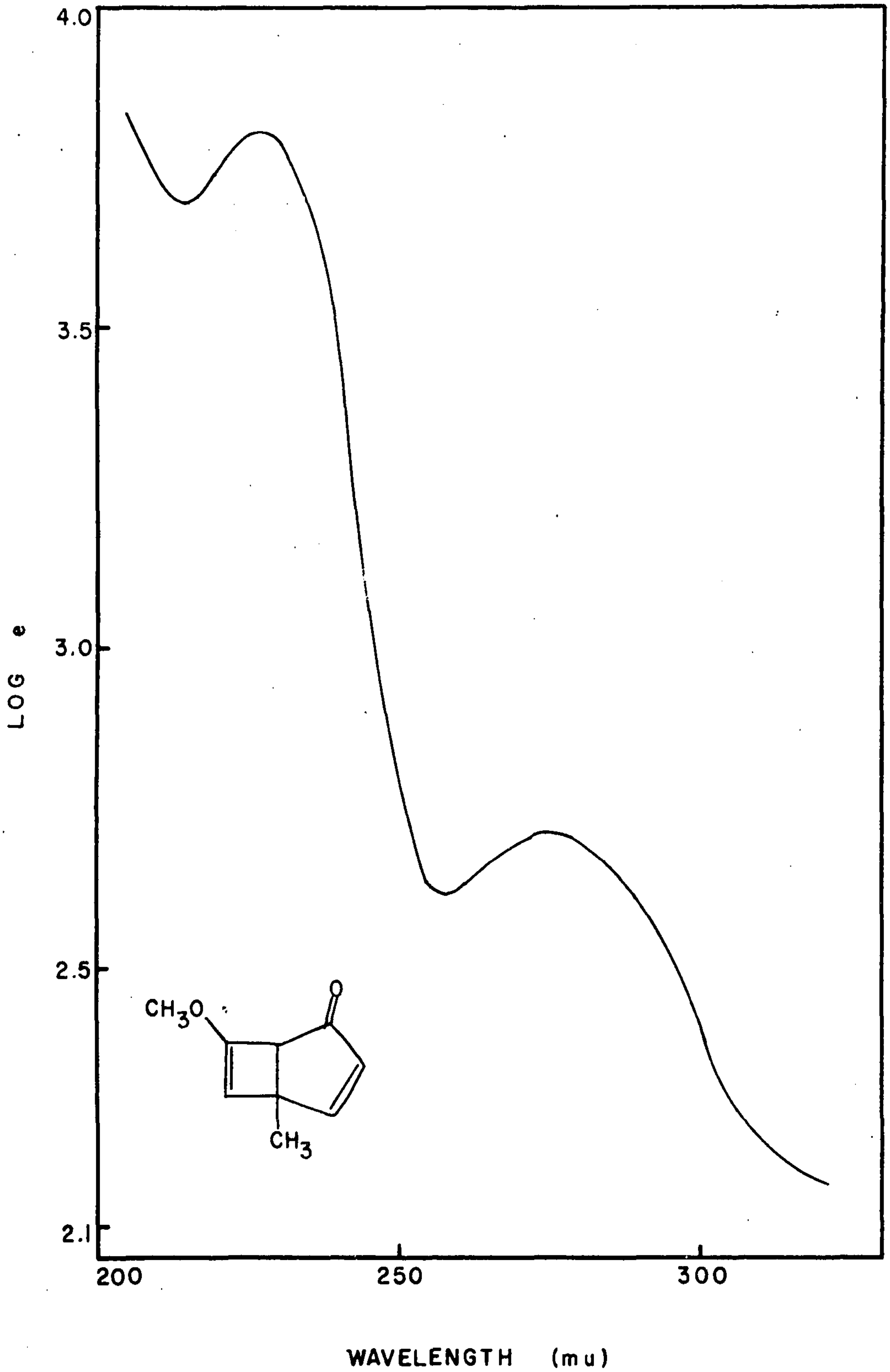

4.0
3.5
3.0
2.5
2.1
LOG e
200
250
300
WAVELENGTH (mu)
CH$_3$O
O
CH$_3$

Figure 41. Ultraviolet spectrum of lumi-6-methyltropolone methyl ether (XXXVII)

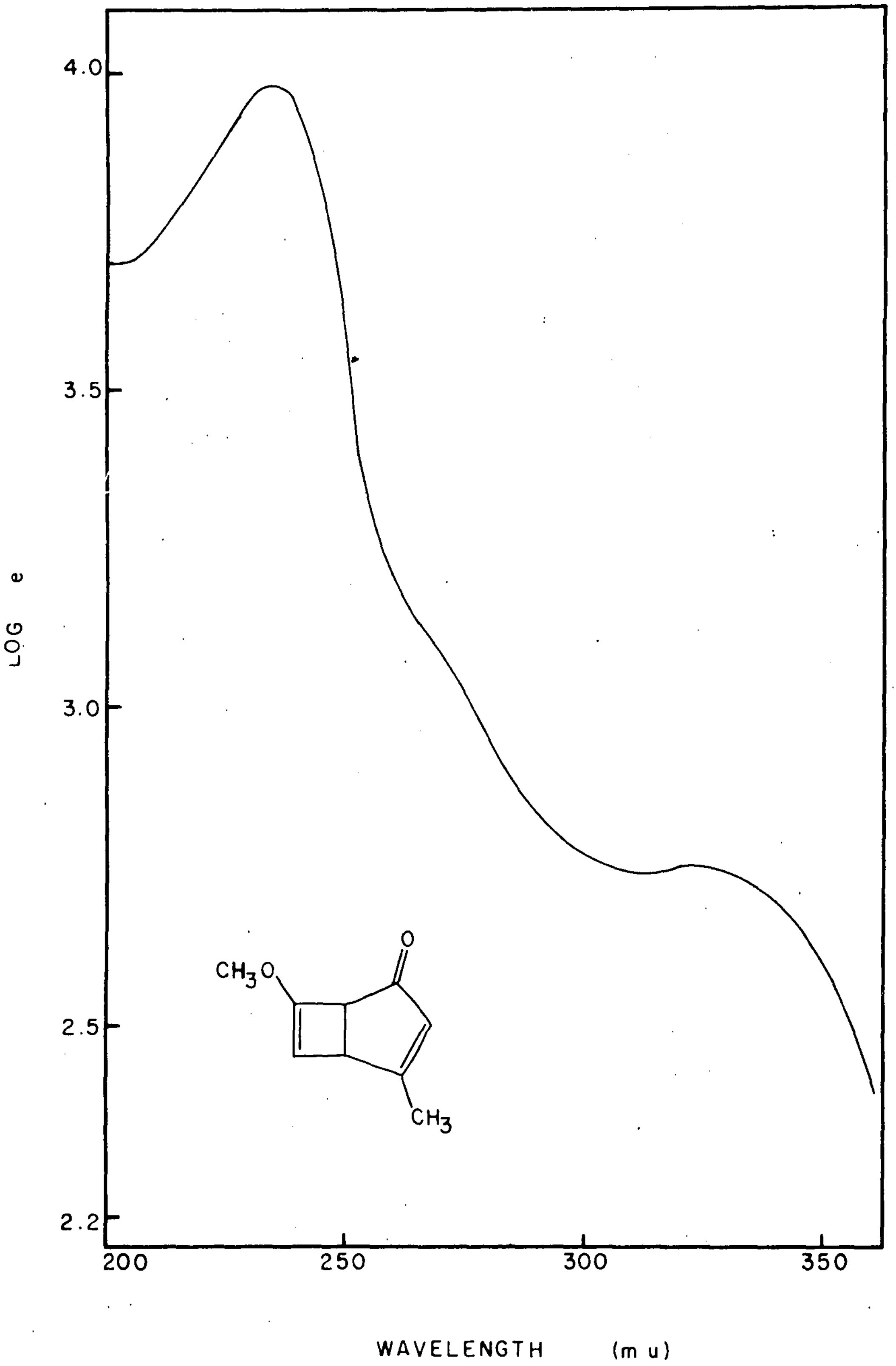

4.0
3.5
3.0
2.5
2.2
LOG e
200
250
300
350
WAVELENGTH (m u)
CH3O
O
CH3

Figure 42. Ultraviolet spectra

A. 2-Hydroxy-5-methyltropolone in base

B. Basic hydrosylate from pyrolyzed lumi-4-methyltropolone methyl ether (XXXVI)

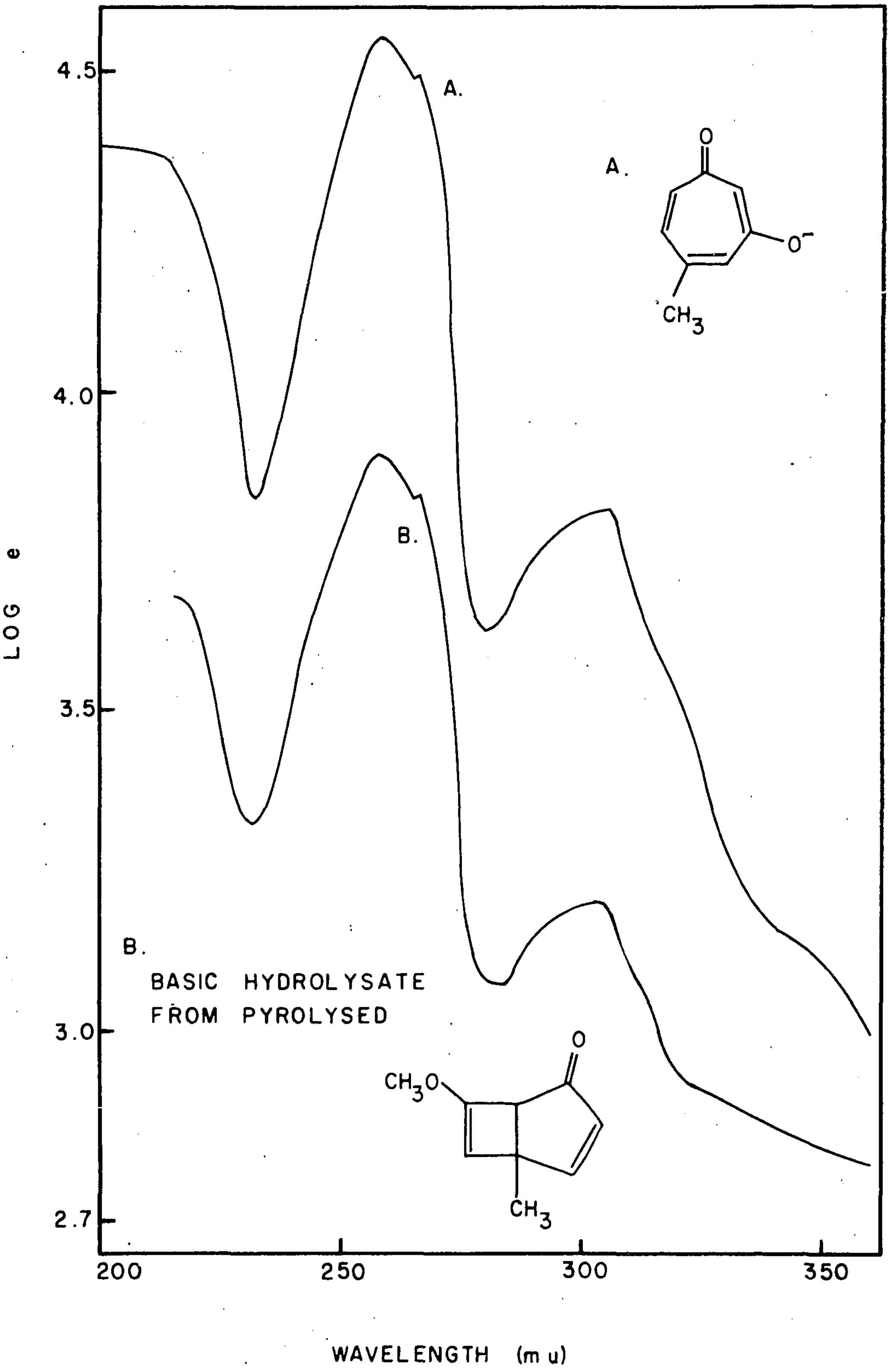

4.5
4.0
3.5
3.0
2.7
LOG e
200
250
300
350
WAVELENGTH (m u)
A.
A.
O
O⁻
CH3
B.
B.
BASIC HYDROLYSATE
FROM PYROLYSED
O
CH3O
CH3

Figure 43. Ultraviolet spectra

A. 2-Hydroxy-5-methyltropolone

B. Acidified based hydrosylate from pyrolysed lumi-4-methyltropolone methyl ether (XXXVII)

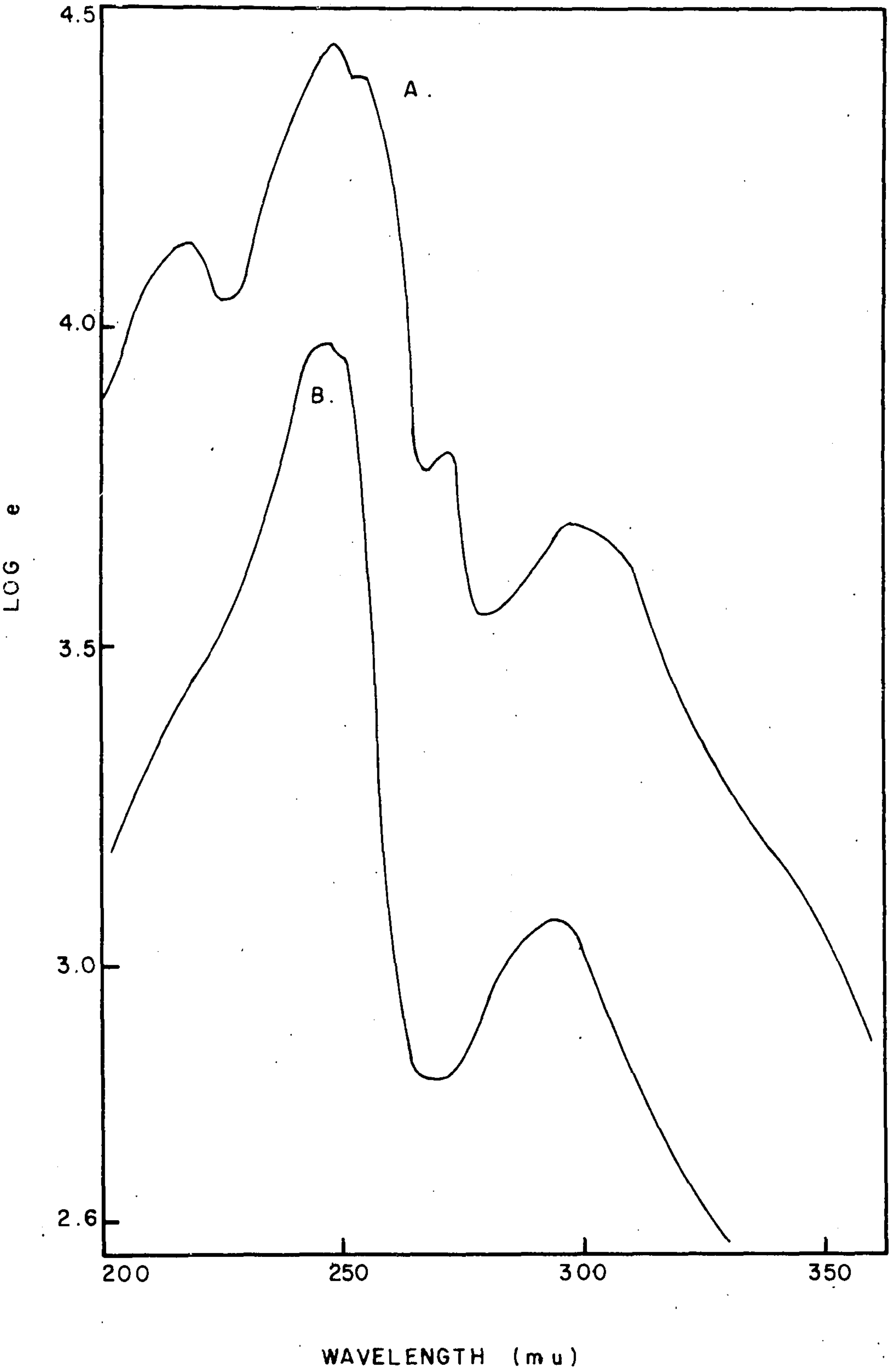

4.5
4.0
3.5
3.0
2.6
LOG e
A.
B.
200
250
300
350
WAVELENGTH (mu)

Figure 44. Ultraviolet spectrum of the Diels-Alder adduct of 4-methyltropolone and maleic anhydride (LIV)

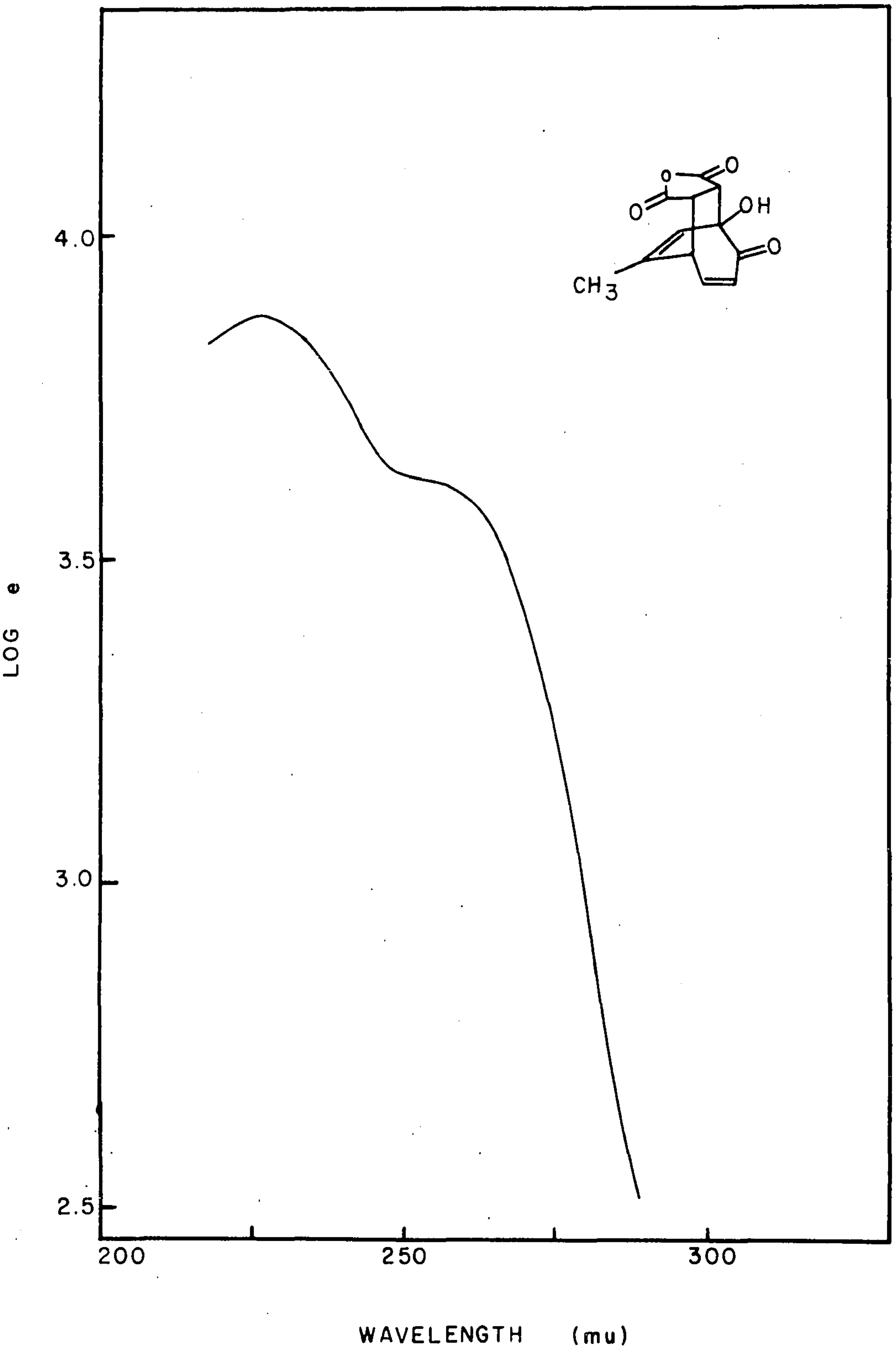

O
O
O
OH
O
CH3
4.0
3.5
3.0
2.5
LOG e
200
250
300
WAVELENGTH (mu)

Figure 45. Ultraviolet spectrum of the lactone (LVIII) formed by acid treatment of the Diels-Alder adduct of 4-methyltropolone and maleic anhydride

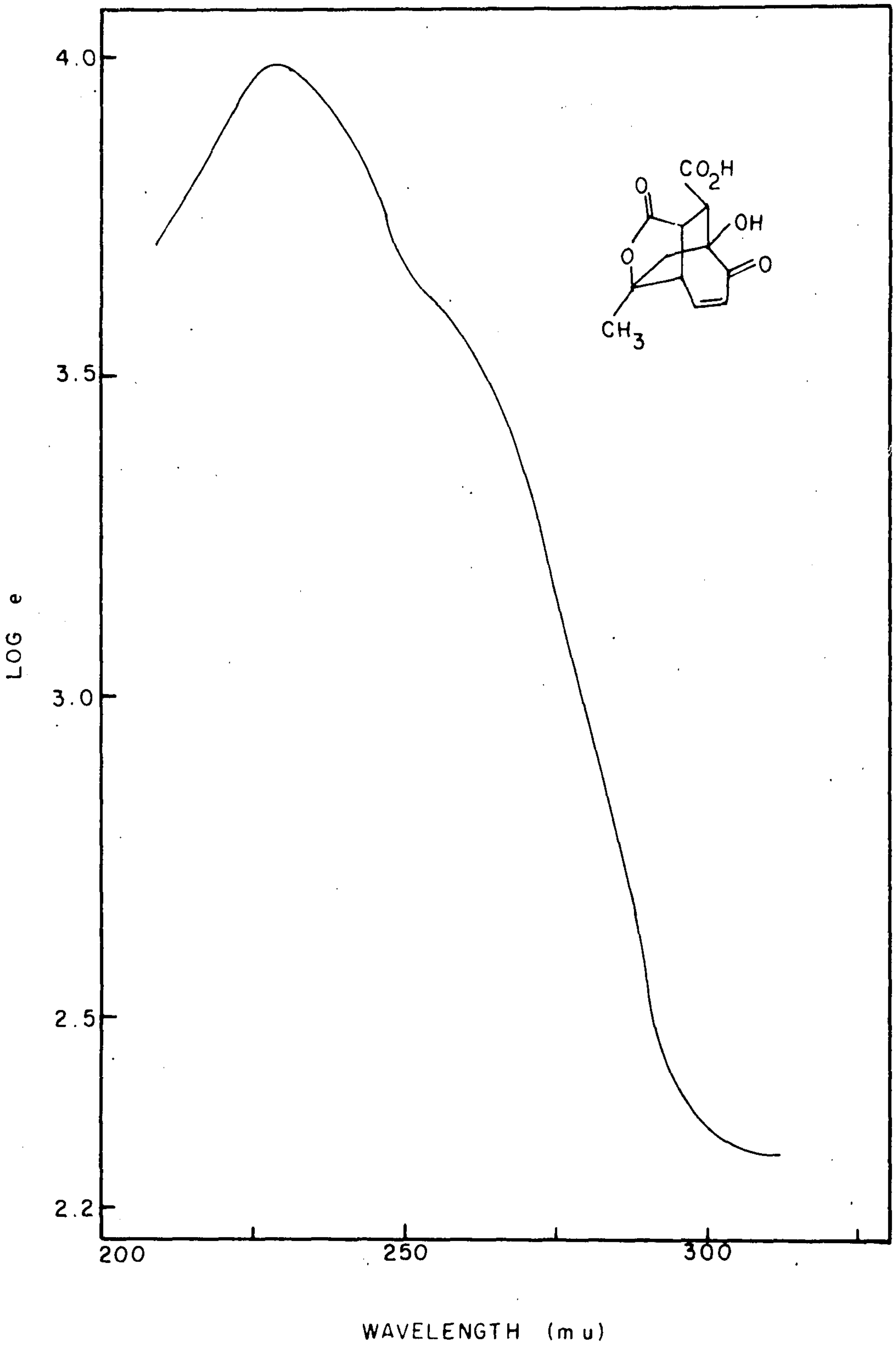

4.0
3.5
3.0
2.5
2.2
LOG e
200
250
300
WAVELENGTH (mu)
CO2H
OH
O
O
O
CH3

Figure 46. Ultraviolet spectra

—— Thujic acid (LXIIa)

----- Photo thujic acid (LXVIIa)

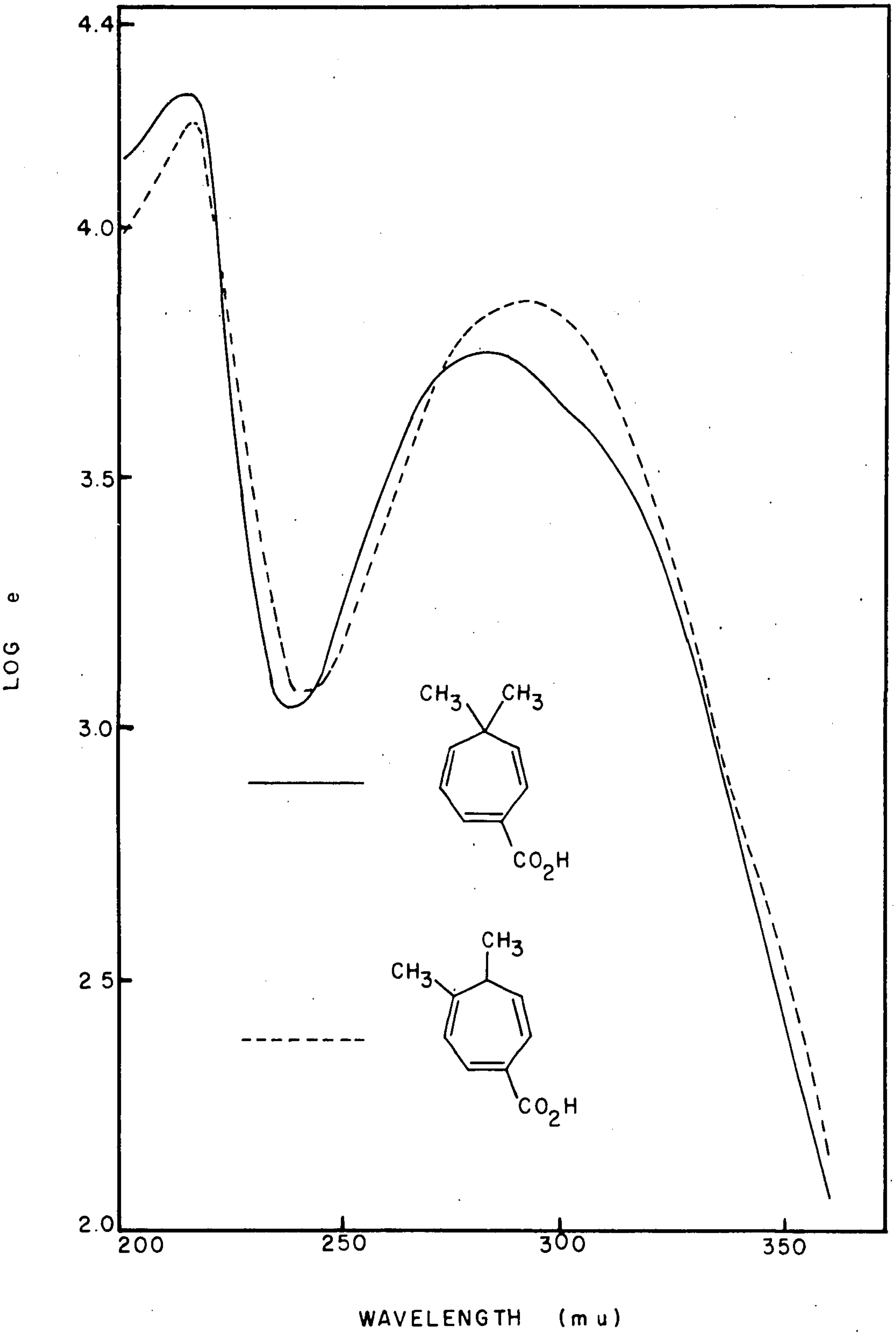
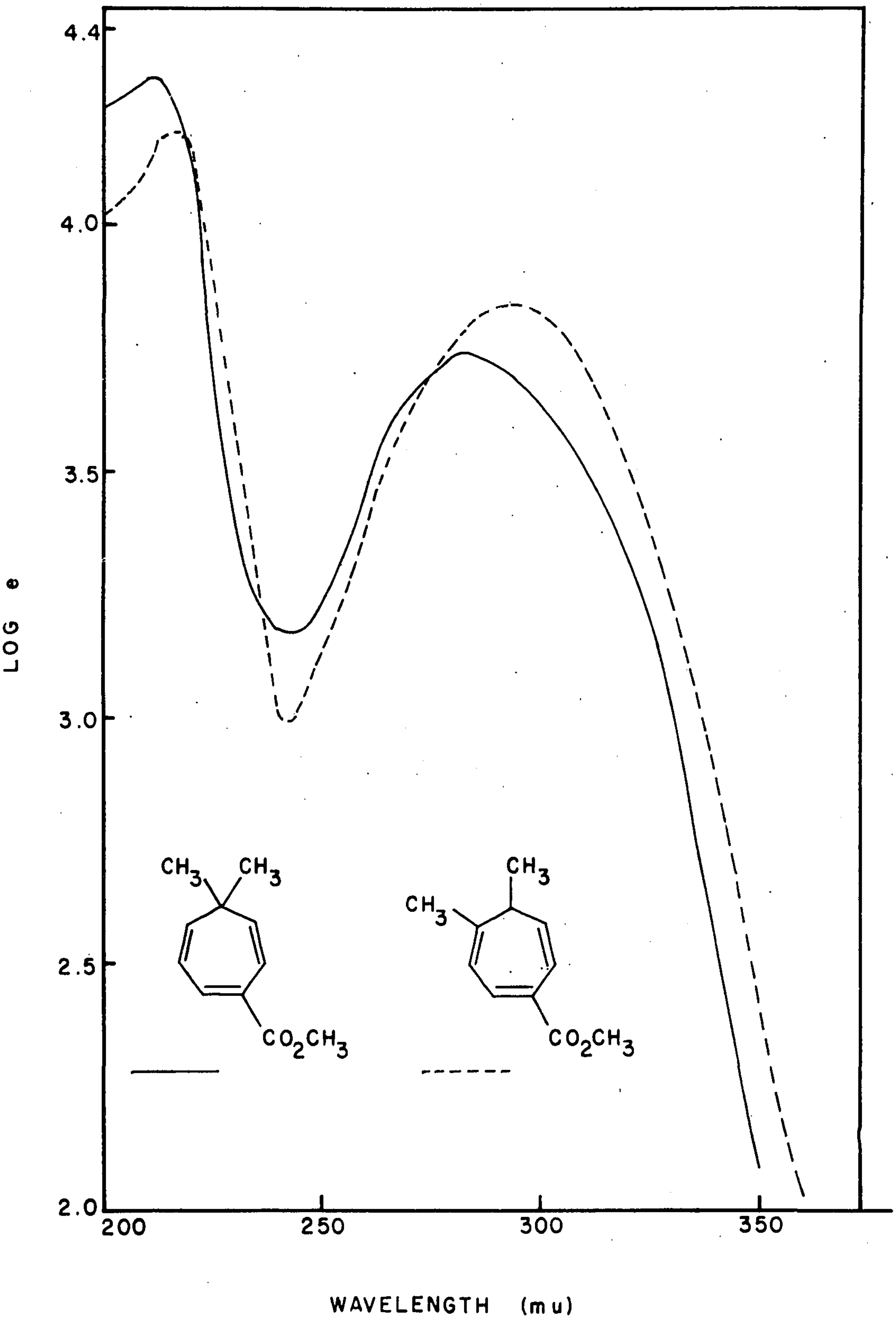

4.4
4.0
3.5
3.0
2.5
2.0
LOG e
200
250
300
350
WAVELENGTH (mu)
CH3
CH3
CO2H
CH3
CH3
CO2H

Figure 47. Ultraviolet spectra

——— Methyl thujate (LXIIIb)

----- Photomethyl thujate (LXVIIb)


4.4
4.0
3.5
3.0
2.5
2.0
LOG e
200
250
300
350
WAVELENGTH (mu)
CH3
CH3
CO2CH3
CH3
CH3
CO2CH3