1964

# Studies on the photochemistry of 2-(p-halophenoxy)-4,5-benztropones

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## Recommended Citation

Stoner, Marshall Robert, "Studies on the photochemistry of 2-(p-halophenoxy)-4,5-benztropones " (1964). *Retrospective Theses and Dissertations*. 3890.
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STONER, Marshall Robert, 1938-
STUDIES ON THE PHOTOCHEMISTRY OF
2-(P-HALOPHENOXY)-4,5-BENZTRO-
PONES.

Iowa State University of Science and
Technology, Ph.D., 1964
Chemistry, organic

# STUDIES ON THE PHOTOCHEMISTRY OF 2-(*P*-HALOPHENOXY)-4,5-BENZTROPONES

by

Marshall Robert Stoner

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

1964

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# VITA

Marshall Robert Stoner was born near Kenesaw, Nebraska, on September 24, 1938, to Mr. and Mrs. M. L. Stoner. He attended Kenesaw Public Schools where he graduated from high school in May, 1956. In September, 1956, he enrolled at Hastings College, Hastings, Nebraska. He was granted the Bachelor of Arts degree from Hastings College in May, 1960, with majors in chemistry and mathematics.

In September, 1960, Stoner enrolled at Iowa State University as a graduate student with a teaching assistantship. He carried out research in the area of organic chemistry under Dr. O. L. Chapman. He was awarded a National Science Foundation Cooperative Graduate Fellowship for the 1962-1963 academic year. The following year he received a Texaco Corporation Fellowship. In 1964 he was awarded a Procter and Gamble Summer Fellowship. He was granted the Doctor of Philosophy degree from Iowa State University in November, 1964.

# INTRODUCTION

The photochemistry of unsaturated ketones has been one of the most active and productive areas of organic chemistry. A recent review (1) gives several different types of photochemical reactions observed with these compounds. The reactions include valence tautomerizations, dimerizations, gross structural rearrangements, cleavage reactions, addition reactions and double-bond migrations. The types of compounds showing these reactions vary from simple alkenones to complex steroids and alkaloids.

The troponoid system is one series of unsaturated ketones whose photochemistry has been studied extensively. A variety of interesting photochemical reactions including many of the types mentioned above has been observed with different tropolone compounds. These observations have made it possible to draw some conclusions concerning the electronic and structural features which govern the type of reaction that occurs in a particular tropolone system.

The work described here is a study of photochemical dimerizations of a series of benztropolone ethers. Investigations were made into the structure of the dimers, their interconversions and their cleavage. Attempts were made to learn more about the dimerization process and the structural rearrangements involved.

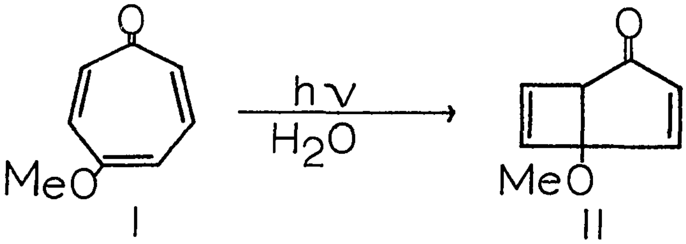
# HISTORICAL

## The Photochemistry of Troponoid Systems

Almost a century ago Struve (2) reported that solutions of the alkaloid colchicine undergo changes in the presence of light. More recently, when workers found that it is the tropolone ring in colchicine which is responsible for its sensitivity to light, they became interested in studying the photochemistry of simpler tropolones and benztropolones. A considerable amount of information has been gained concerning the photochemistry of troponoid compounds.

### Simple troponoid compounds

The first of the simple troponoid compounds reported to undergo photochemical change was γ-tropolone methyl ether (I). Chapman and Pasto (3) found that irradiation of I in aqueous solution with ultraviolet light gives photo-γ-tropolone methyl ether (II). The original seven membered ring undergoes a valence tautomerization to give a bicyclo[3.2.0]heptadienone system.



The irradiation of α-tropolone methyl ether (IIIa) in methanol gives a similar bicyclic product (IVa) initially (4) (see Figure 1, page 4). Continued irradiation of IVa gives the rearranged product Va. Further irradiation after the addition of water to the solution gives the ester VIa. This sequence of photochemical reactions was clarified by studying the products formed from the irradiation of 4- and 6-methyl-tropolone methyl ethers (IIIb, c) (4). The sequence makes it possible to account for the earlier reports (5) that the irradiation of α-tropolone or its methyl ether (VIIa, b) in aqueous solution gives 4-oxo-2-cyclopentenylacetic acid (VIIIa) or its methyl ester (VIIIb). The mechanistic sequence was further confirmed by the prediction of the correct structure for a product obtained from the irradiation of γ-thujaplicin methyl ether (IX). Irradiation of IX gives the rearranged bicyclic photoisomer X, presumably by way of XI (4).

The photochemistry of β-tropolone methyl ether (XII) and tropone (XIII) (1, p. 325) evidently follows quite different paths, giving complex mixtures of products from which no bicyclic products have been isolated. The presence and position of the methoxyl group in the troponoid ring is apparently the determining factor in the type of photoreaction observed (1). The methoxyl group in the α- and γ-tropolone methyl ethers could have a directing influence on

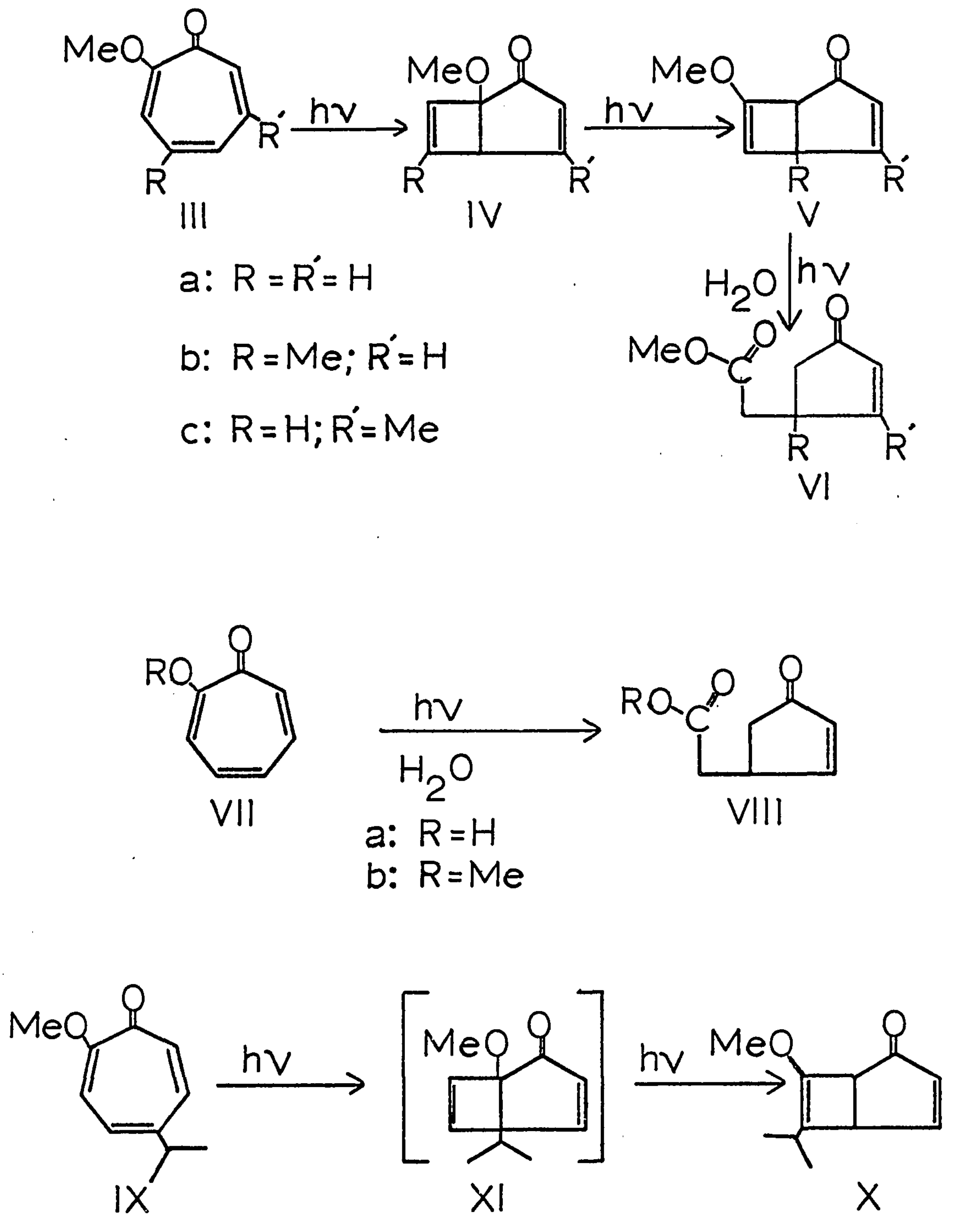
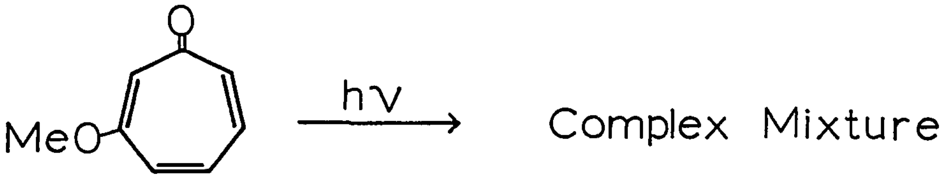
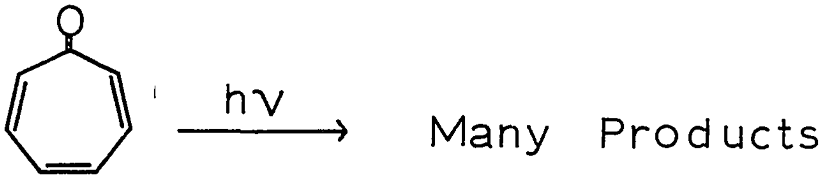


Figure 1. Photochemical transformations in the α-tropolone series

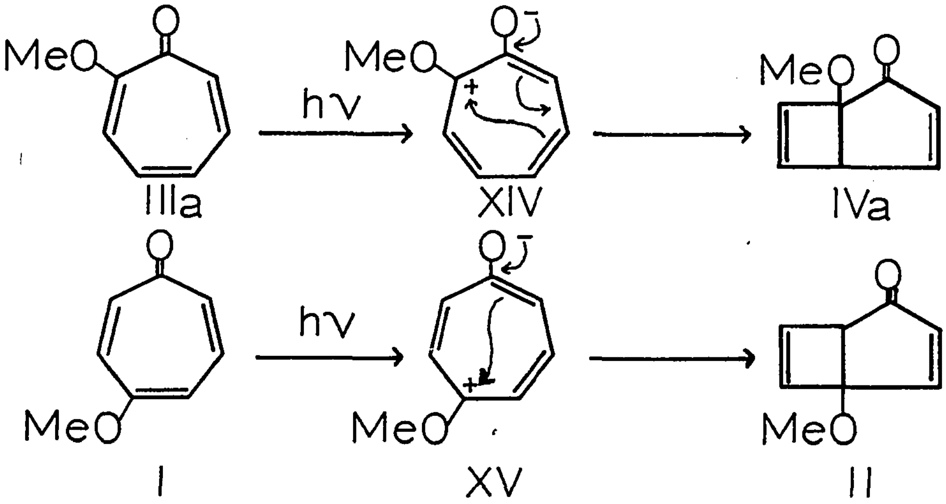


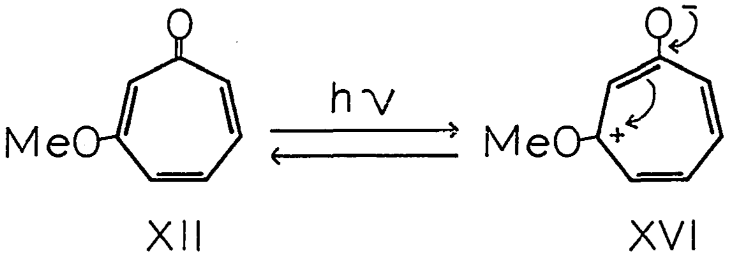
XII



XIII

the distribution of electrons in the intermediates such as XIV and XV leading easily to bicyclic products. The corresponding intermediate XVI from β-tropolone methyl ether can only return to starting material, whereas with tropone there is no methoxyl group to give any directing influence. Therefore it is reasonable that other processes might become important in the irradiation of tropone and β-tropolone methyl ether.





Colchicine and related compounds

The naturally occurring alkaloid colchicine (XVII) (Figure 2, page 7) contains an α-tropolone ether system which, like the simple compound, is isomerized to a bicyclo[3.2.0]heptadienone system under the influence of light. Irradiation of colchicine in aqueous solution in the absence of oxygen gives various amounts of three photoisomers, α-, β-, or γ-lumicolchicine (6-11). Structures XVIII and XIX have been assigned to β- and γ-lumicolchicine, respectively (8, 9, 12). The structure of α-lumicolchicine (XX), a dimer of β-lumicolchicine, was not established until recently (10).

Changing the substituents on colchicine does not influence greatly the ability of its derivatives to form photoproducts of the α-, β-, or γ-lumicolchicine types (7, 11, 13, 14, 15). Several of the compounds related to colchicine and the photoproducts reported are listed in Figure 3, page 8.

It can be noted that in the simple tropolone ethers

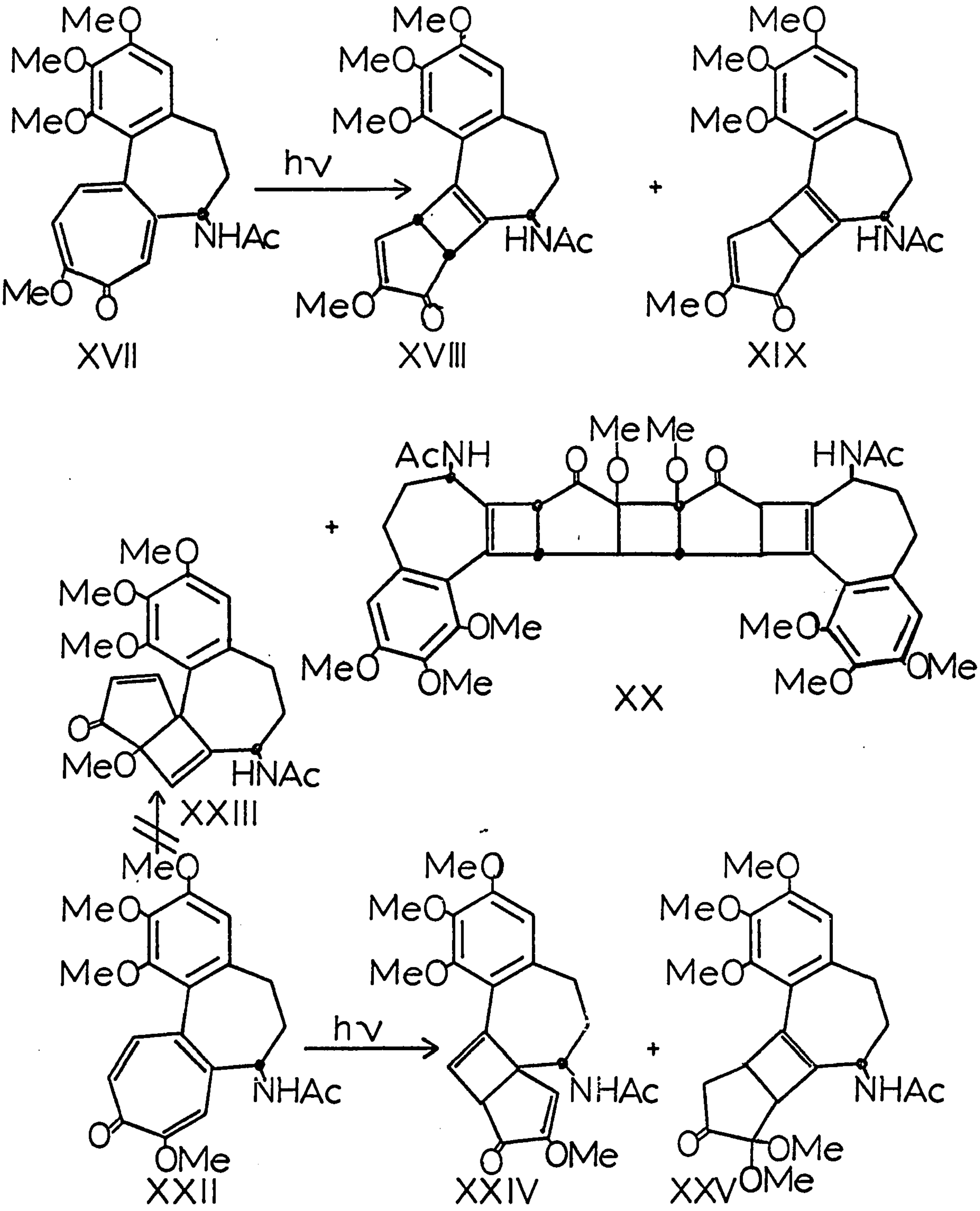
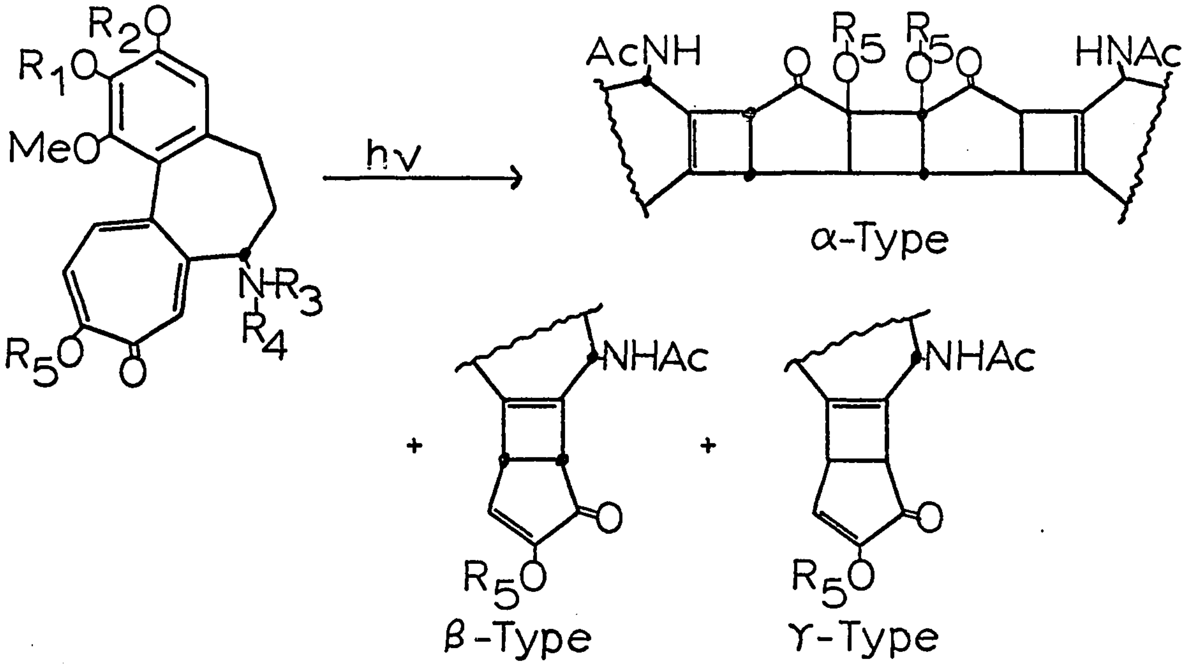


Figure 2. Photochemical transformations of colchicine and isocolchicine

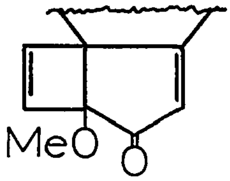


| Compound Irradiated | Substituents | | | | | Products Reported | | | Ref. |
|---|---|---|---|---|---|---|---|---|---|
| | $R_1$ | $R_2$ | $R_3$ | $R_4$ | $R_5$ | α-Type | β-Type | γ-Type | |
| Colchicine | Me | Me | H | Ac | Me | yes | yes | yes | 6-11 |
| 2-Demethyl-colchicine | H | Me | H | Ac | Me | no | yes | no | 7 |
| Colchicoside | Me | Glu[a] | H | Ac | Me | no | yes | yes | 14 |
| 3-Demethyl-colchicine | Me | H | H | Ac | Me | no | yes | yes | 14 |
| Colchiceine | Me | Me | H | Ac | H | yes | yes | yes | 11,13 |
| Demecolcine | Me | Me | Me | H | Me | no | yes | no | 15 |
| N-Methyl-colchicine | Me | Me | Me | Ac | Me | no | yes | no | 15 |

[a] Glu = D-glucose, $C_6H_{11}O_5$

Figure 3. Photochemical transformations of colchicine and related compounds

the photoisomerization initially produces bicyclic products in which the methoxyl group is located at the bridgehead position. Although colchicine and its derivatives contain an α-tropolone system, the isomerization does not go in this way. One possible explanation is that steric factors make the formation of a structure such as XXI unfavorable.

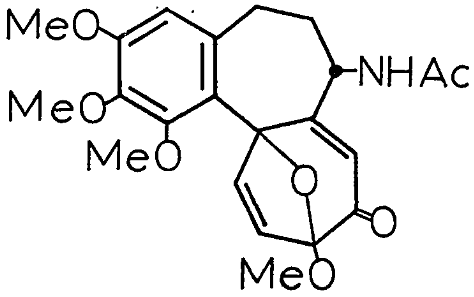


XXI

Another explanation might be that retention of the trimethoxystyryl system is the governing factor in the colchicine photoreactions. A choice between these two possibilities can be made on the basis of the photoproducts formed from isocolchicine (XXII) (Figure 2, page 7). While possible structures XXIII and XXIV contain about equal strain, only XXIV contains the trimethoxystyryl system. On the other hand XXIII possesses the methoxyl group at the bridgehead position. Irradiation of isocolchicine (16, 17) gives primarily the photoisomer XXIV. Irradiation in methanol gives a second product XXV presumably formed after the initial addition of a molecule of methanol to the tropolone system (17). Therefore, retention of the styryl system seems to be the controlling factor in the photochemical transformations of the colchicine series.

When a solution of colchicine is exposed to light in the presence of oxygen a different type of reaction occurs. Jacobi (18) reported that colchicine solutions undergo autoxidation in the presence of light. He was able to separate a brown, resinous oxidation product which he called oxydicolchicine. The analysis corresponded with the formula $(C_{22}H_{25}O_6N)_2O$, in which one atom of oxygen is bound to two molecules of colchicine. This analysis must be taken with reservation in view of the intractable nature of the oxidation product.

Fühner (19) studied the biological activity of oxycolchicine obtained by Zeisel and Friedrich (20) from the chromic acid oxidation of colchicine. He found its activity in frogs to be similar to that reported by Jacobi (18) for oxydicolchicine. Recently Buchanan _et_ _al_. (21) used chemical and spectroscopic evidence to show that the chromic acid oxidation product, oxycolchicine, is a 1:4 oxide (XXVI) of colchicine. This structural assignment was supported by an

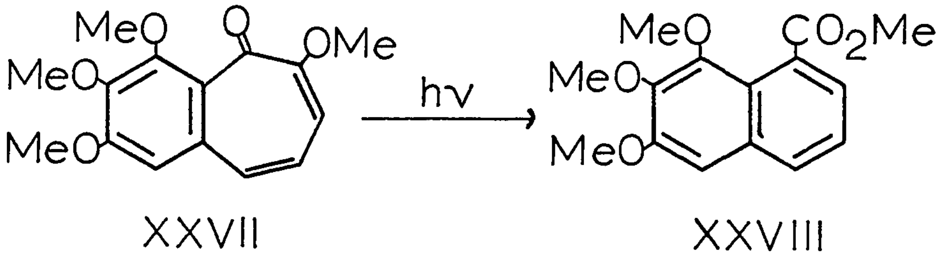


XXVI

independent study by Cross, Šantavý and Trivedi (22). The exact nature of the photooxidation product has not been reported.

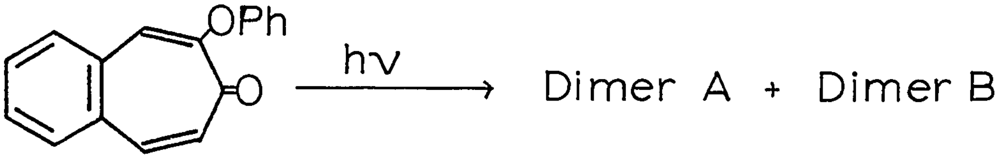
Benztropolones

Compounds in which the tropolone system is fused to a benzene ring have also been the subject of photochemical studies. One such compound is purpurogallin tetramethyl ether (XXVII). Irradiation of XXVII in aqueous ethanol with sunlight gives methyl 6,7,8-trimethoxy-1-naphthoate (XXVIII) among other products (23). It has been suggested that the



reaction proceeds through a norcaradiene intermediate (23).

The 2-phenoxy-4,5-benztropone system (XXIX) is the subject of the work described here. Previous work by Pasto (24) had revealed that the irradiation of the benztropone XXIX in 2-propanol with a mercury arc lamp gives two products. Both products were found to have dimeric molecular weights. The compound which has two carbonyl peaks in the infrared spectrum at 5.83 and 5.96 μ was designated Dimer A; the other compound with a single carbonyl peak at 5.78 μ was designated Dimer B. It was found that Dimer B could be converted to Dimer A by heating the former at its melting point (24).



XXIX

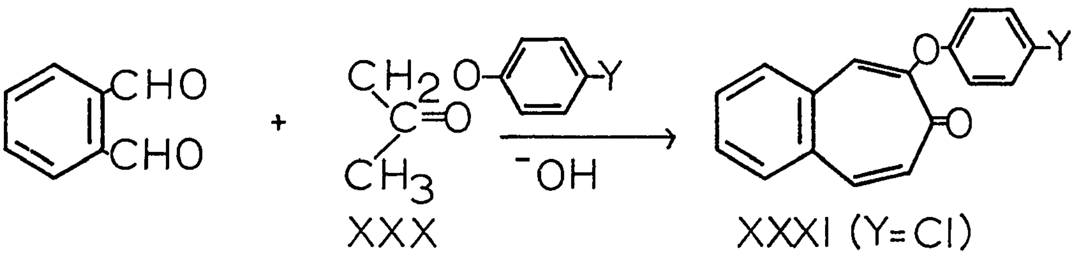
The study on the structures and reactions of Dimer A and Dimer B was continued by Chapman and Smith (25). The work described here is an extension of the study to the 2-(p-halophenoxy)-4,5-benztropone and an investigation of the mechanisms of the thermal and photochemical transformations involved. Some of the experiments carried out by Chapman and Smith which were useful in the structure determinations of the dimers were not repeated for the corresponding halogen-substituted compounds. These results will be discussed where applicable.

# RESULTS AND DISCUSSION

## Synthesis and Irradiation of the 2-(p-Halophenoxy)-4,5-benztropones

At the time this work was begun, the structures of the photoproducts from the irradiation of 2-phenoxy-4,5-benztropone had not been determined. The preparation and irradiation of the 2-(p-halophenoxy)-4,5-benztropones were undertaken so that the halogenated photoproducts could be used for X-ray structure determinations. Although these compounds have not been as useful as expected for this purpose, a study of them has led to many interesting and significant observations.

The 2-(p-halophenoxy)-4,5-benztropones were prepared by the same procedure (26) employed to prepare XXIX. p-Chlorophenoxyacetone (XXX, Y = Cl) was condensed with o-phthalaldehyde in the presence of sodium hydroxide solution to give 2-(p-chlorophenoxy)-4,5-benztropone (XXXI) (m.p. 127-127.5°) in 24% yield. The infrared spectrum (Figure 8,



XXX

XXXI (Y=Cl)
XXXII (Y=Br)

page 33) shows a strong absorption at 6.15 μ, typical for the long wavelength carbonyl absorption of the 4,5-benztropolones (26). The ultraviolet spectrum (Figure 15, page 47) is also typical for the 4,5-benztropolone system (27). The nuclear magnetic resonance spectrum (Figure 11, page 39) shows absorption only in the aromatic region, indicating some aromatic character in the tropolone ring. In a similar manner the use of p-bromophenoxyacetone (XXX, Y = Br) in the condensation reaction yielded 2-(p-bromophenoxy)-4,5-benztropone (XXXII) (m.p. 130-132°, needles). The infrared spectrum (Figure 8, page 33) and ultraviolet spectrum (Figure 15, page 47) are very similar to those of XXXI.

Since the 2-phenoxy-4,5-benztropones contain the α-tropolone ether system, it is interesting to contemplate what product would be formed if they were to follow the same path as the simple compound. An inspection of structure XXXIII (Figure 4, page 15) reveals the improbability of its formation because of steric strain and the destruction of the aromatic system. As will be shown, the photochemistry of the phenoxybenztropones takes another path.

The irradiation of 2-(p-chlorophenoxy)-4,5-benztropone (XXXI) gives a number of products. The irradiations were done with tetrahydrofuran solutions using a mercury arc lamp in a Pyrex immersion well. In the first

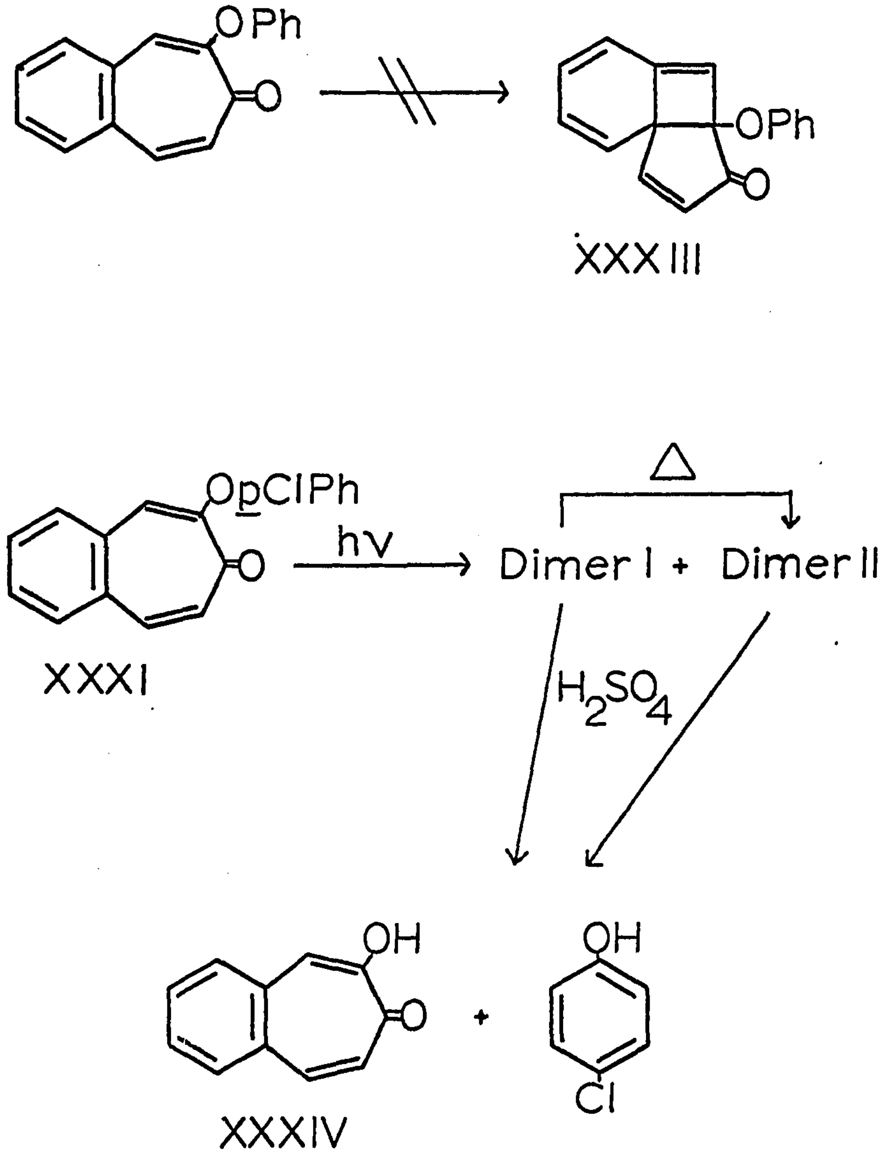


Figure 4. Photochemical transformations of 2-(p-chlorophenoxy)-4,5-benztropone

irradiations the solution was flushed with nitrogen to remove all oxygen from the reaction flask. If the irradiation was stopped before all of the starting material was destroyed, two compounds were isolated which were separated by column chromatography. The compounds will be designated Dimer I (m.p. 225-226°) and Dimer II (m.p. 222-224°) (Figure 4, page 15). The compounds were shown to be dimers of XXXI by analysis and osmometric molecular weight determinations (521 and 569 for Dimer I and Dimer II, respectively; theoretical, 565). Dimer I can be converted to Dimer II by heating it slightly above its melting point. This is probably the reason for the similarity of the melting points. If either dimer is heated to a slightly higher temperature (235-240°) it is converted to the starting material (XXXI).

Dimer I can also be converted to Dimer II by treating it with concentrated sulfuric acid. Heating the dimers with sulfuric acid gives a phenol and 4,5-benztropolone (XXXIV). It should be noted that 2-phenoxy-4,5-benztropone itself does not give XXXIV under similar conditions (25, p. 236). It is assumed that XXXI is also stable to concentrated sulfuric acid under the same conditions and therefore the acid hydrolysis of the dimers cannot proceed through XXXI as is the case for the chlorine-free dimers. The phenol from the hydrolysis of Dimer I was identified as p-chlorophenol by paper chromatography.

All of these observations lead to the conclusion that the basic carbon skeleton of the benztropolone system has not undergone drastic change in the formation of either dimer. The thermal conversions indicate that Dimer I and Dimer II correspond to "Dimer B" and "Dimer A," respectively, in the 2-phenoxy-4,5-benztropone series (24). This conclusion is confirmed by the spectral data to be discussed next.

The spectra of the dimers are very useful in the determination of their structures. The infrared spectrum of Dimer I (Figure 9, page 35) shows a single carbonyl absorption at 5.76 $\mu$. The carbonyl cannot be conjugated with a double bond or phenyl group. If there are two carbonyl groups in the molecule, both must be very similar if not identical.

The nuclear magnetic resonance spectrum of Dimer I (Figure 11, page 39) shows a complex aromatic absorption centered at 2.88 $\tau$ . An AB pattern is apparent with doublets at 3.34 and 4.19 $\tau$ , $J_{AB} = 12.9$ c.p.s. The position and coupling constant are characteristic of a styryl system unperturbed by adjacent hydrogen-bearing carbon atoms. The ratio of the peak areas of the aromatic protons to the two olefinic doublets is 8:1:1. A sharp singlet is located at 5.95 $\tau$ , the area of which bears a 1:1 relationship to each of the olefinic doublets. The position of the singlet is indicative of a hydrogen on a carbon bearing electron withdrawing groups. Since only three kinds of protons other than aromatic protons are observed, the dimer must be made of identical halves.

Assembling all of the information into a tentative structure, one must arrive at structure XXXV for the basic unit of Dimer I. There are four possible dimers which can be written using XXXV (Figure 5, page 19). A choice can be made among these possibilities by examining another photodimer (XXXVI) (Figure 5, page 19) which is formed from XXXI in addition to Dimer I if the irradiation is allowed to proceed until no starting material remains. It can also be formed by the irradiation of Dimer I in a quartz vessel, as was done by Chapman and Smith (25, p. 255) to form the corresponding dimer by the irradiation of Dimer B (from XXIX) in 2-propanol solution in a quartz vessel. This new dimer (m.p. 233-234.5°), which will be designated Dimer III, shows a single carbonyl absorption in the infrared spectrum at 5.86 μ (Figure 10, page 37). The nuclear magnetic resonance spectrum (Figure 13, page 43) shows no olefinic protons. An $A_2B_2$ pattern appears at 5.56 and 6.36 $\tau$ which is ascribed to a cyclobutane ring formed by the cycloaddition of the styryl double bonds of Dimer I. This type of reaction is well known in photochemistry (28, pp. 21-36). The isolated bridgehead proton appears as a singlet at 5.48 $\tau$. The aromatic region of the spectrum shows a remarkable change

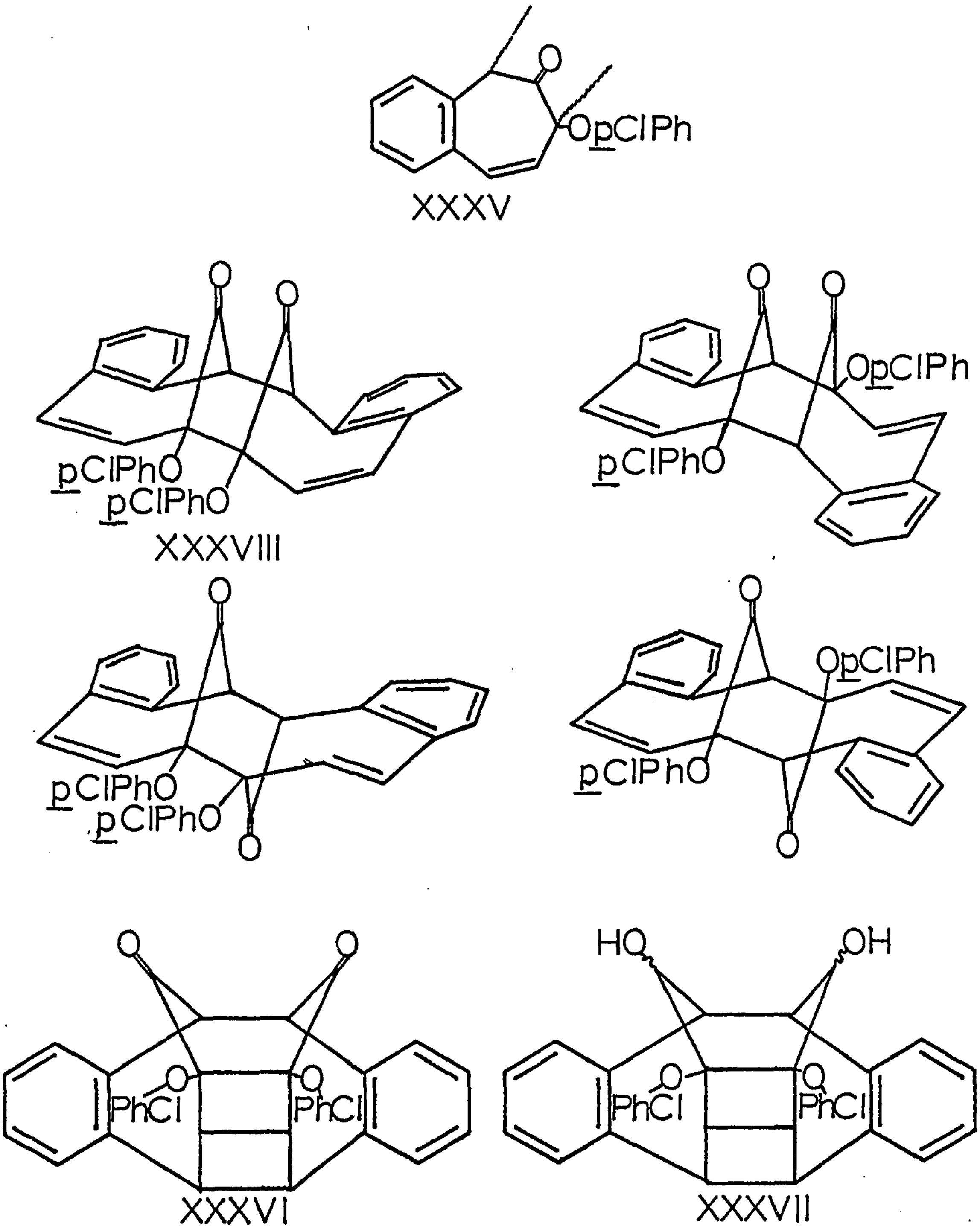
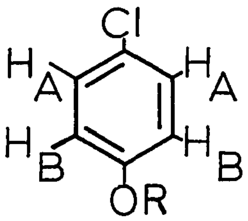


Figure 5. Structures of Dimer I and Dimer III

from that of Dimer I. The $A_2B_2$ pattern arising from the *p*-chlorophenoxy groups is at unexpectedly high position. The normal chemical shifts for the protons on a *p*-chlorophenoxy group, as in *p*-chloroanisole, can be calculated by using the substituent parameters of Martin and Dailey (29). Chemical shifts of 2.74 and 3.15 $\tau$ are obtained for $H_A$ and $H_B$, respectively. This is in good agreement with the values



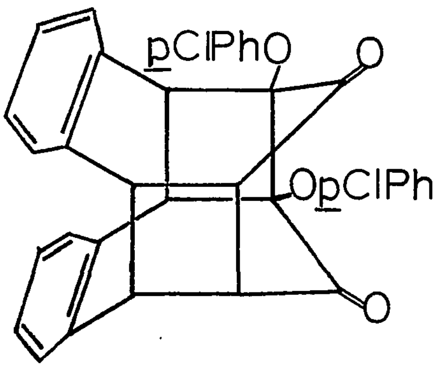
observed for *p*-chlorophenoxyacetic acid (2.73 and 3.12 $\tau$ ) (30). In Dimer III the *p*-chlorophenoxy groups show absorption at 3.00 and 3.76 $\tau$, representing upfield shifts of 0.26 and 0.61 $\tau$-units for $H_A$ and $H_B$, respectively. The aromatic protons of the benzo-groups appear as a relatively sharp singlet at 2.65 $\tau$. The large upfield shift of the *p*-chlorophenoxy protons can best be accounted for by diamagnetic shielding from the carbonyl groups (31) similar to that observed by Chapman *et al*. (10) in α-lumicolchicine. An examination of models shows that the phenyl protons, especially those *ortho* to the ethereal oxygens, can spend an appreciable amount of time in the shielding cone (31) of the carbonyl groups. The suggestion that the shielding arises from the carbonyls is supported by the fact that the absorptions of these protons return to normal positions upon reduction of Dimer III with sodium borohydride to give the corresponding diol (XXXVII) (Figure 5, page 19).

The ultraviolet spectrum of Dimer III (Figure 17, page 51) is consistent with a structure having two o-xylene units and two p-chloroanisole units. Dimer III, like Dimer I and Dimer II, gives 4,5-benztropolone (XXXIV) on treatment with concentrated sulfuric acid. In this case, the benztropolone was not isolated, but was identified by its ultraviolet spectrum. A characteristic shift of the long wavelength peak of XXXIV from 276 mμ to 284 mμ occurs upon the addition of a drop of 1N sodium hydroxide solution to the ultraviolet cells (Figure 20, page 57).

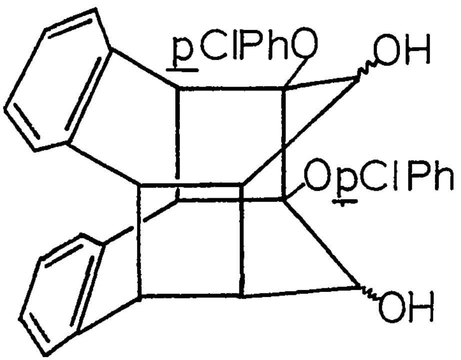
The formation of Dimer III from Dimer I can occur reasonably only if Dimer I has structure XXXVIII. In the other possible structures, either the styryl double bonds are on opposite sides of the molecule or the approach of the styryl double bonds is essentially prohibited by the carbonyl bridges.

Structure XXXIX (or its head-to-tail isomer) is an alternate structure for Dimer III which must be considered. Structure XXXIX also contains a cyclobutane ring which would give an $A_2B_2$ pattern in the nuclear magnetic resonance spectrum. This structure was considered to be unlikely, however, because of the apparent formation of Dimer III from

Dimer I. Structure XXXIX was ruled out definitely on the basis of the nuclear magnetic resonance spectrum of Dimer III diol. Reduction of the carbonyl groups in XXXIX should have little effect on the singlet due to the isolated bridgehead protons. On the other hand, the isolated bridgehead protons of XXXVII would be coupled with the proton on the alcohol carbon, probably showing splitting in the nuclear magnetic resonance spectrum. The nuclear magnetic resonance spectrum of Dimer III diol (Figure 13, page 43) no longer shows a singlet for the bridgehead proton, as expected for XXXVII. Complex multiplets are observed at 5.60, 5.98 and 6.64 $\tau$ . A hydroxyl proton appears at 8.13 $\tau$ which disappears on treatment with deuterium oxide. The upper portion of the $A_2B_2$ pattern arising from the p-chlorophenoxy groups appears at 3.26 $\tau$ with the remainder of the aromatic protons centered at 2.84 $\tau$. The infrared spectrum (Figure 10, page



XXXIX



XXXIX diol

37) shows no absorption in the carbonyl region, but does show peaks at 2.82 and 2.91 μ in the hydroxyl region. An attempt to prepare the diacetate of Dimer III diol by reacting it with acetyl chloride in refluxing benzene was unsuccessful.

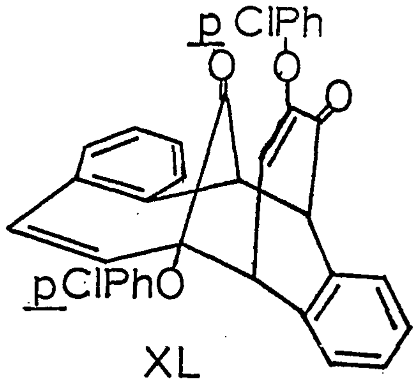
Dimer II can be obtained from the irradiation of XXXI, but since it is usually not produced in good yield, the easiest method of preparation is the thermal isomerization of Dimer I at 230-235°. Dimer II shows two carbonyl absorptions in the infrared spectrum (Figure 9, page 35) at 5.84 and 5.96 μ suggesting the presence of conjugated and nonconjugated carbonyl groups.

The nuclear magnetic resonance spectrum of Dimer II (Figure 12, page 41) shows seventeen protons in the aromatic region centered at 3.00 $\tau$. A styryl double bond is present with doublets at 3.95 and 4.75 $\tau$, J = 13.0 c.p.s. A careful study of the high field peaks (three protons) reveals that it consists of another AB system having doublets at 5.43 and 5.81 $\tau$, J = 4.7 c.p.s. Superimposed upon the AB pattern is the upper half of an AX system at 5.67 $\tau$, J = 10.5 c.p.s. A double resonance experiment carried out with the corresponding Dimer A from XXIX (32) reveals that the other half of the AX system is located in the aromatic region. The nuclear magnetic resonance spectrum, as well as the infrared spectrum, demand an unsymmetrical dimer.

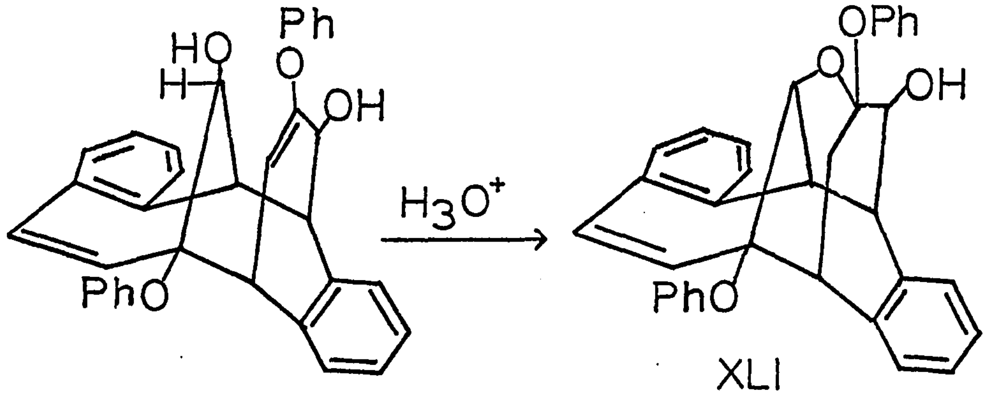
Structure XL (Figure 6, page 25) fits all of the spectral data for Dimer II and can be formed reasonably from Dimer I. The stereochemistry of XL is correct as shown by reactions carried out by Chapman and Smith (25, p. 311) on the corresponding Dimer A. Sodium borohydride reduction of Dimer A gives the expected diol which on reaction with acid forms the internal ether XLI (Figure 6, page 25). The formation of XLI from Dimer A diol requires that the carbonyl bridges of Dimer A be on the same side of the molecule.

Only one irradiation of 2-(p-bromophenoxy)-4,5-benztropone (XXXII) was carried out. The dimer XLII (m.p. 227-229°) (Figure 6, page 25) corresponding to Dimer I was the only product identified although other products were presumably formed. The infrared spectrum (Figure 9, page 35) and the nuclear magnetic resonance spectrum (Figure 12, page 41) are very similar to those of Dimer I. This series of compounds was not further studied.

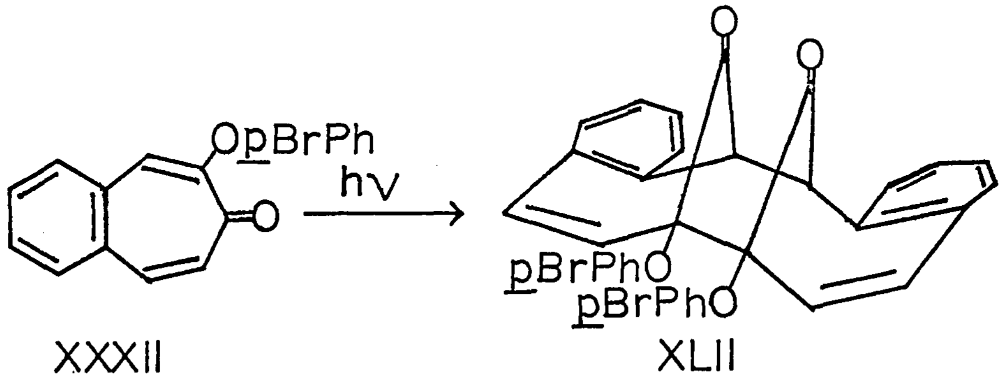
The irradiation of 2-(p-chlorophenoxy)-4,5-benztropone (XXXI) was done in the presence of oxygen to determine whether oxygen would have any effect on the dimerization process. Oxygen was bubbled into a tetrahydrofuran solution of XXXI as it was irradiated. The reaction proceeded remarkably fast with all of the starting material having disappeared after six hours. Chromatography of the reaction mixture gave Dimer I and a considerable



XL



XLI



XXXII

XLII

Figure 6. Structure of Dimer II and photoreaction of 2-(p-bromophenoxy)-4,5-benztropone

amount of a yellow oil. The yellow oil apparently consisted of oxidation products from the tetrahydrofuran. A nuclear magnetic resonance spectrum of the material showed mostly aliphatic protons and only slight absorption in the aromatic region. It has been reported (33) that tetrahydrofuran is oxidized in the presence of oxygen to give a hydroperoxide which decomposes to $\gamma$-butyrolactone (XLIII) or $\gamma$-hydroxybutyryl aldehyde (XLIV) (Figure 7, page 27). The infrared spectrum of the oil indicated that both of these were present in the mixture.

In addition to Dimer I, another irradiation product was isolated from the reaction mixture in low yield. The product was first thought to be a dimer and was designated "Dimer IV" (m.p. 158-160°). The product *may* or *may not* be a dimer. Nevertheless, for historical reasons this designation will be retained for this discussion. The elemental analysis of "Dimer IV" corresponds to a formula of $C_{16}H_{11}ClO_3$. This formula is supported by several analyses on different preparations, one of which included all of the elements present. According to the formula, one carbon atom has been lost and an oxygen atom has been added in going from the starting material (XXXI) to "Dimer IV". An osmometric molecular weight determination in benzene gave a value of 341, which is too low for a dimer but higher than the monomeric molecular weight (287). However, the value may be inaccurate because

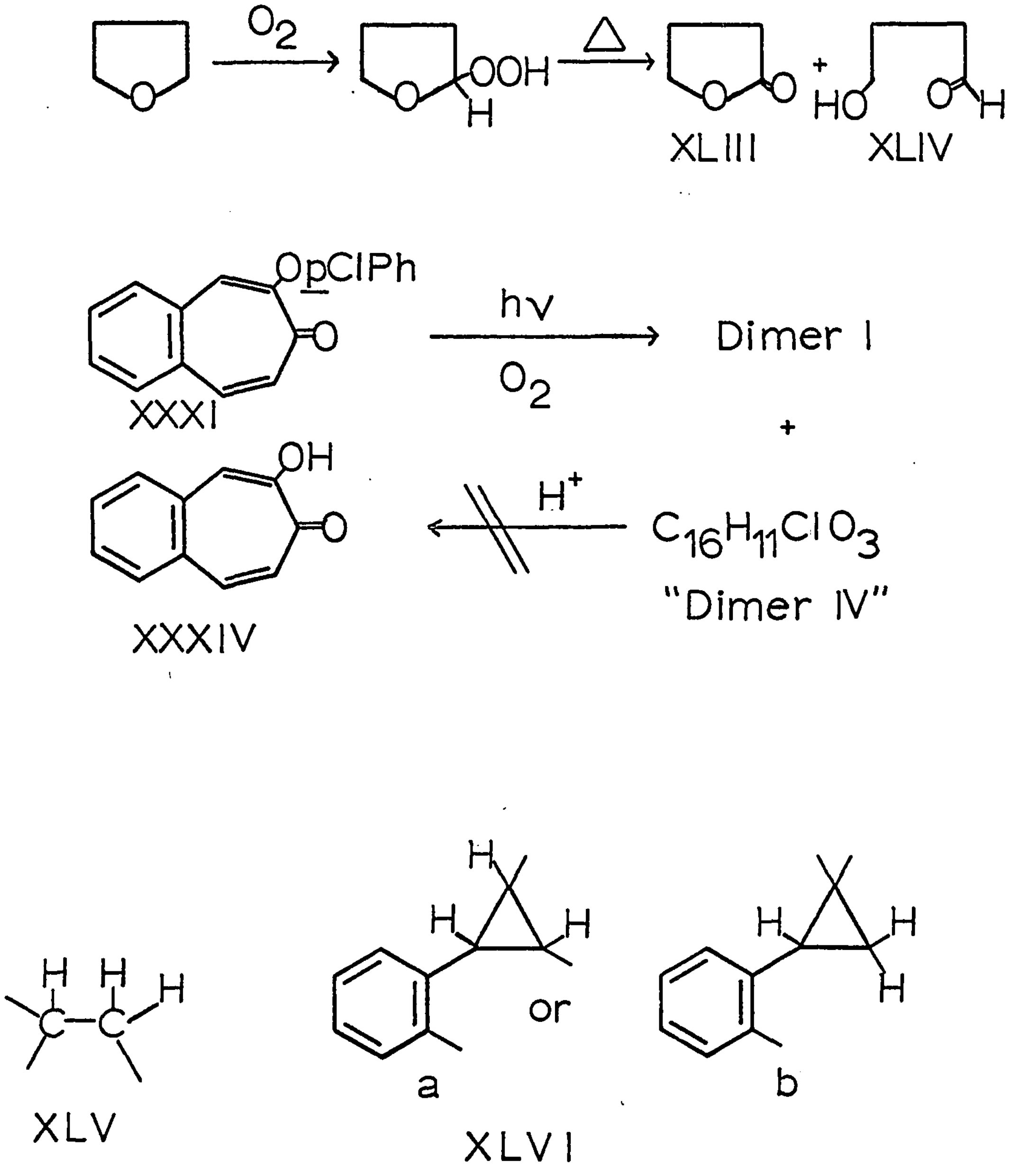


Figure 7. Irradiation of 2-(p-chlorophenoxy)-4,5-benztropone (XXXI) in the presence of oxygen

of the small amount of material available for use in the measurement.

An attempt was made to obtain a mass spectrum of the compound. The spectrum showed a base peak at 280, which is difficult to rationalize on the basis of the empirical formula from the analysis. The peak evidently was due to some volatile impurity in the sample, for it rapidly disappeared after the first scan of the spectrum.

The infrared spectrum of "Dimer IV" (Figure 10, page 37) shows a carbonyl absorption at 5.82 μ. The nuclear magnetic resonance spectrum (Figure 14, page 45) shows three sets of peaks at unexpectedly high field integrating for a ratio of 1:1:1. The pattern can be identified as an AMX system at 7.22, 8.08 and 8.96 $\tau$, $J_{AM}$ = 10.7 c.p.s., $J_{AX} = J_{MX}$ = 6.6 c.p.s. The peaks at 7.22 are broadened somewhat, suggesting a benzilic proton. The aromatic protons appear as a complex multiplet centered at 2.71 $\tau$ with a pair of finely split doublets at 1.76 $\tau$. One aromatic proton is evidently experiencing some abnormal deshielding effect.

To account for the AMX system, one must devise a structure having three hydrogens on saturated carbon atoms, each capable of coupling with the other two rather strongly. The two most obvious possibilities are a methine group adjacent to a methylene group (XLV) and a trisubstituted cyclopropyl ring (XLVI) (Figure 7, page 27). The former is unlikely on the basis of the coupling constants (31) unless it is incorporated in a small, strained ring as in XLVIb. On the other hand the existence of a cyclopropyl ring can explain the high field positions of the absorption. Presumably one of the cyclopropyl carbons is attached to the benzo- ring to give the observed broadening of the lowest peak in the AMX system.

The analysis of "Dimer IV" shows that the _p_-chlorophenoxy group is still present, accounting for one of the oxygen atoms in the molecule. A second oxygen atom is required in a carbonyl group as indicated by the infrared spectrum. The third oxygen atom indicated by the empirical formula must be present as an ethereal function (including an ester or lactone group) in view of the lack of evidence for a hydroxyl group in the infrared or nuclear magnetic resonance spectrum.

In view of the apparent changes in molecular composition occurring in the formation of "Dimer IV," it would not be expected that "Dimer IV" would give 4,5-benztropone (XXXIV) on treatment with sulfuric acid as the other photoproducts of the series do. Treatment of "Dimer IV" with concentrated sulfuric acid gives a compound whose ultraviolet spectrum shows a different long wavelength absorption ($\lambda_{max}^{EtOH}$ 261, 272sh and 280 mμ) than that shown by

XXXIV ($\lambda_{max}^{EtOH}$ 276 mμ). The absorption maxima shifted to 326 mμ upon the addition of a drop of 1N sodium hydroxide to the solution compared with a shift to 284 mμ for XXXIV (Figures 19 and 20, pages 55 and 57). Obviously a very different species is formed from the acid hydrolysis of "Dimer IV."

The number and scale of chemical reactions which could be run on "Dimer IV" was severely limited by the small amount of compound which could be obtained from the irradiations. Unsuccessful attempts were made to isolate and identify the compound formed from the treatment of "Dimer IV" with sulfuric acid. A reduction of Dimer IV with sodium borohydride was attempted. An infrared spectrum of the reduction product showed almost complete lack of carbonyl and strong hydroxyl absorption. A nuclear magnetic resonance spectrum of the crude product was quite complex; absorption from apparent impurities made interpretation difficult. Attempts to purify the sample were unsuccessful. Additional evidence is necessary before a definite structural assignment can be made for "Dimer IV."

In irradiations of XXXI in which all of the starting material was destroyed, no Dimer II could be isolated. This can be explained on the basis of an observation made by Chapman and Smith (25, p. 286) in work with the corresponding Dimer A from 2-phenoxy-4,5-benztropone (XXIX). If Dimer A in tetrahydrofuran solution was stirred under nitrogen in the open light of the room, it would disappear after a number of hours, evidently going to decomposition products. Dimer A did not decompose when the experiment was repeated with tetrahydrofuran solution in the dark or in benzene solution. It was suggested that light and tetrahydrofuran cause a free radical decomposition of Dimer A. It is possible that when irradiations of XXXI are carried out in tetrahydrofuran Dimer II is destroyed under the irradiation conditions. Perhaps only when starting material (XXXI) is present is a large enough concentration of Dimer II built up to isolate it. Other explanations may be that starting material absorbs most of the light necessary for destruction of Dimer II or it may be quenching the reactive excited state of Dimer II.

## Studies of the Dimerization Process

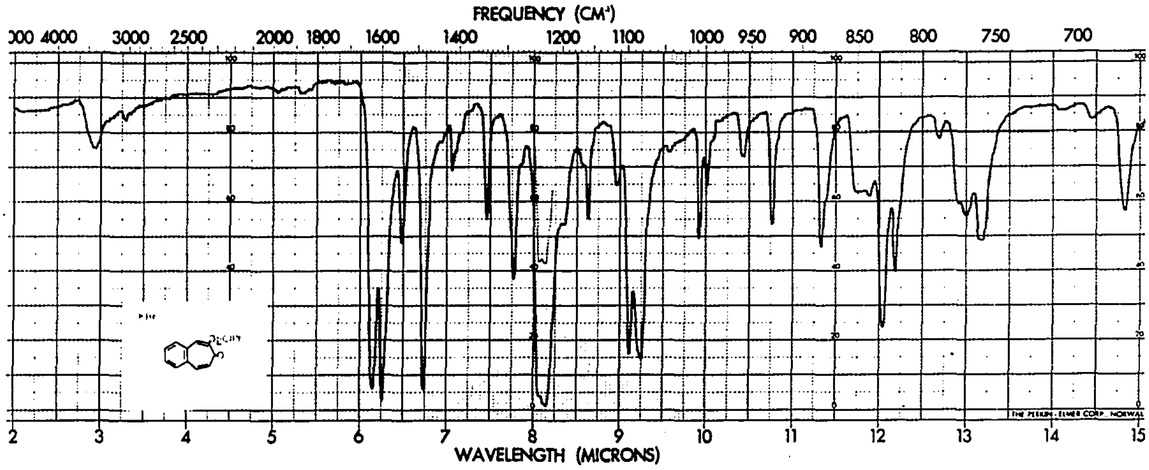
In the study of a photochemical reaction it is of interest to learn something about the excited state which is involved in the formation of products. In most cases the first excited state formed in the irradiation of a compound is an excited singlet state. In this transition the electron which is excited retains its spin-state and remains paired. Since the singlet-singlet transition is spectroscopically allowed, the lifetime of the excited

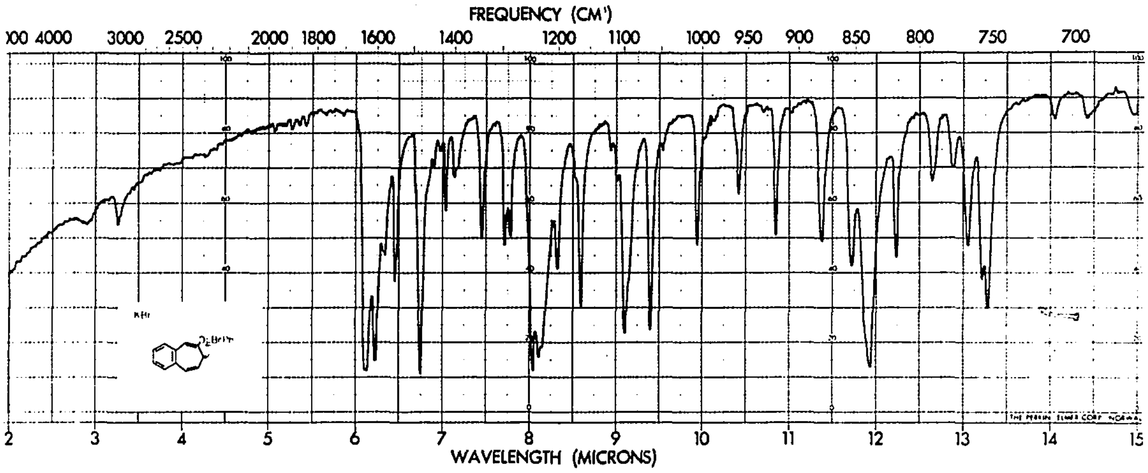
Figure 8. Infrared spectra

Top - 2-(p-Chlorophenoxy)-4,5-benztropone (XXXI)

Middle - 2-(p-Bromophenoxy)-4,5-benztropone (XXXII)

Bottom - 4,5-Benztropolone (XXXIV)


FREQUENCY (CM⁻¹)
4000
3000
2500
2000
1800
1600
1400
1200
1100
1000
950
900
850
800
750
700
KBr
2
3
4
5
6
7
8
9
10
11
12
13
14
15
WAVELENGTH (MICRONS)
THE PERKIN-ELMER CORP. NORWALK


FREQUENCY (CM⁻¹)
4000
3000
2500
2000
1800
1600
1400
1200
1100
1000
950
900
850
800
750
700
KBr
2
3
4
5
6
7
8
9
10
11
12
13
14
15
WAVELENGTH (MICRONS)
THE PERKIN-ELMER CORP. NORWALK

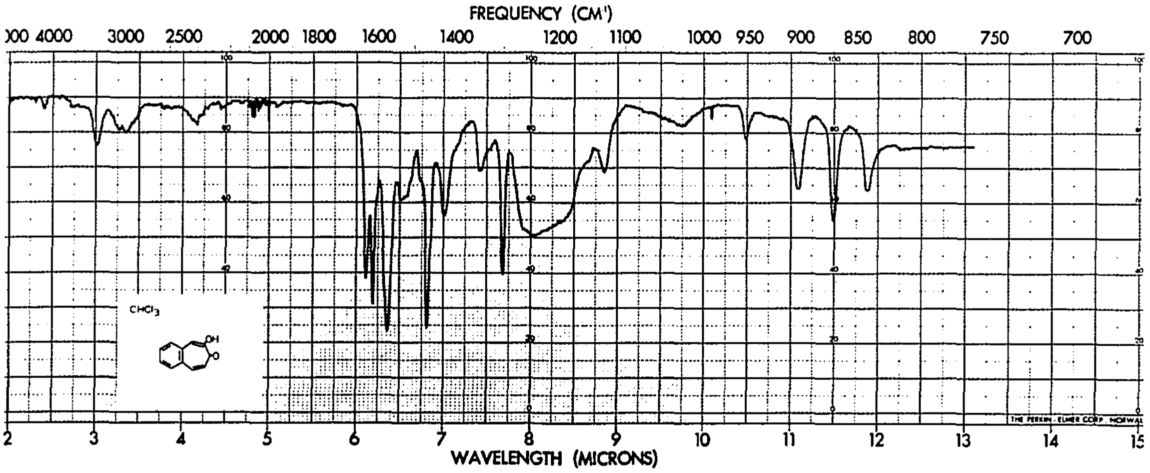
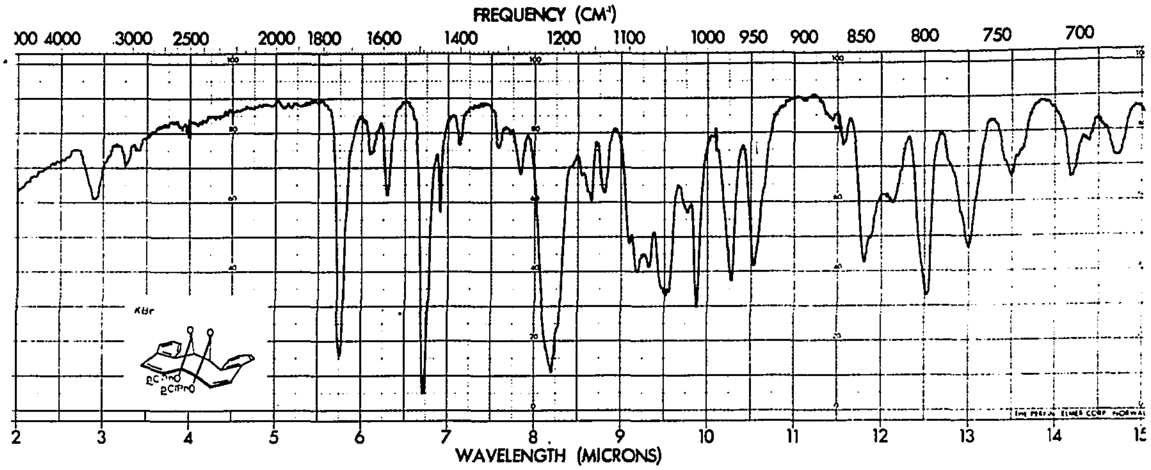

FREQUENCY (CM⁻¹)
4000
3000
2500
2000
1800
1600
1400
1200
1100
1000
950
900
850
800
750
700
CHCl₃
OH
2
3
4
5
6
7
8
9
10
11
12
13
14
15
WAVELENGTH (MICRONS)
THE PERKIN-ELMER CORP. NORWALK

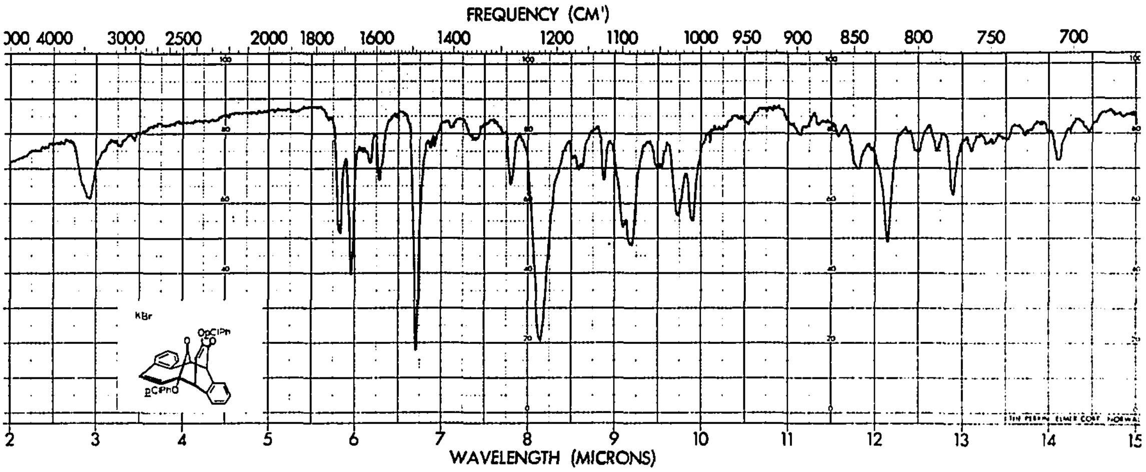
Figure 9. Infrared spectra

Top - Dimer I (XXXVIII)

Middle - Dimer II (XL)

Bottom - Bromo-dimer (XLII)


FREQUENCY (CM⁻¹)
000 4000 3000 2500 2000 1800 1600 1400 1200 1100 1000 950 900 850 800 750 700
KBr
pClPhO
pClPhO
THE PERKIN-ELMER CORP. NORWALK
2 3 4 5 6 7 8 9 10 11 12 13 14 15
WAVELENGTH (MICRONS)


FREQUENCY (CM⁻¹)
000 4000 3000 2500 2000 1800 1600 1400 1200 1100 1000 950 900 850 800 750 700
KBr
OpClPh
pClPhO
THE PERKIN-ELMER CORP. NORWALK
2 3 4 5 6 7 8 9 10 11 12 13 14 15
WAVELENGTH (MICRONS)

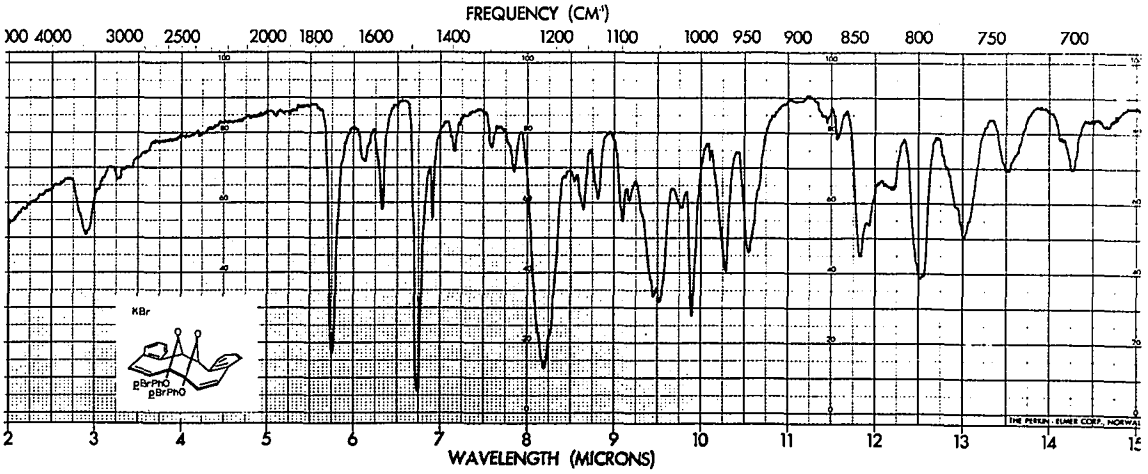
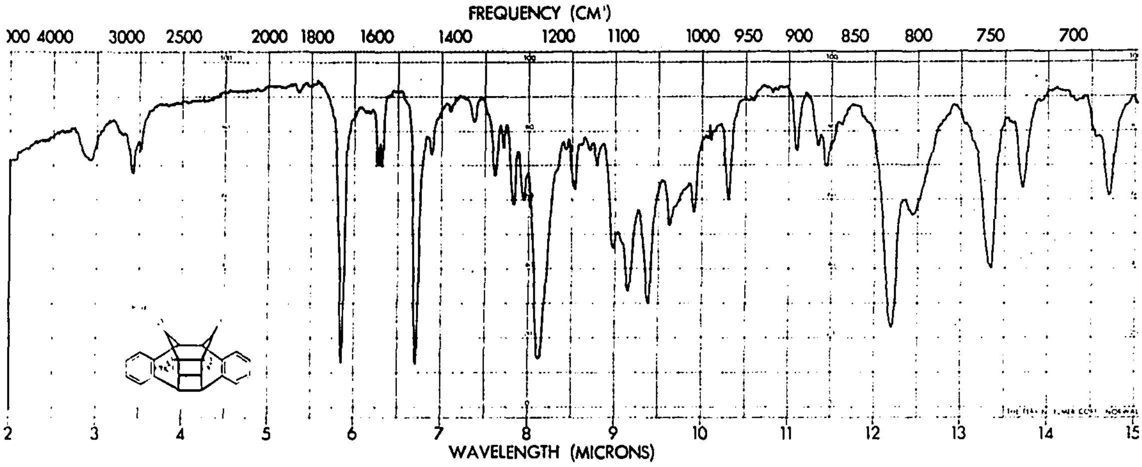

FREQUENCY (CM⁻¹)
000 4000 3000 2500 2000 1800 1600 1400 1200 1100 1000 950 900 850 800 750 700
KBr
pBrPhO
pBrPhO
THE PERKIN-ELMER CORP. NORWALK
2 3 4 5 6 7 8 9 10 11 12 13 14 15
WAVELENGTH (MICRONS)

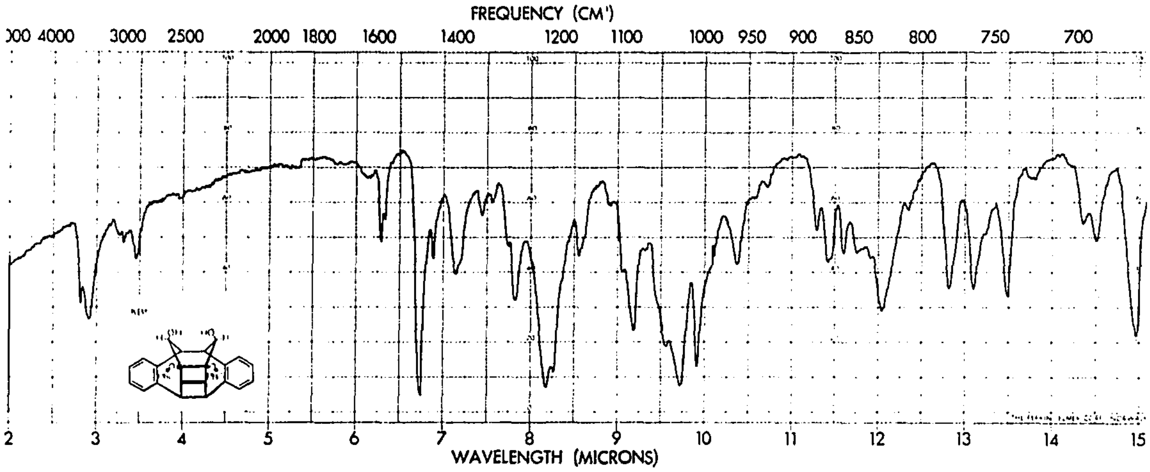
Figure 10. Infrared spectra

Top- Dimer III (XXXVI)

Middle- Dimer III diol (XXXVII)

Bottom- "Dimer IV"


FREQUENCY (CM')
)00 4000 3000 2500 2000 1800 1600 1400 1200 1100 1000 950 900 850 800 750 700
2 3 4 5 6 7 8 9 10 11 12 13 14 15
WAVELENGTH (MICRONS)


FREQUENCY (CM')
)00 4000 3000 2500 2000 1800 1600 1400 1200 1100 1000 950 900 850 800 750 700
KBr
2 3 4 5 6 7 8 9 10 11 12 13 14 15
WAVELENGTH (MICRONS)

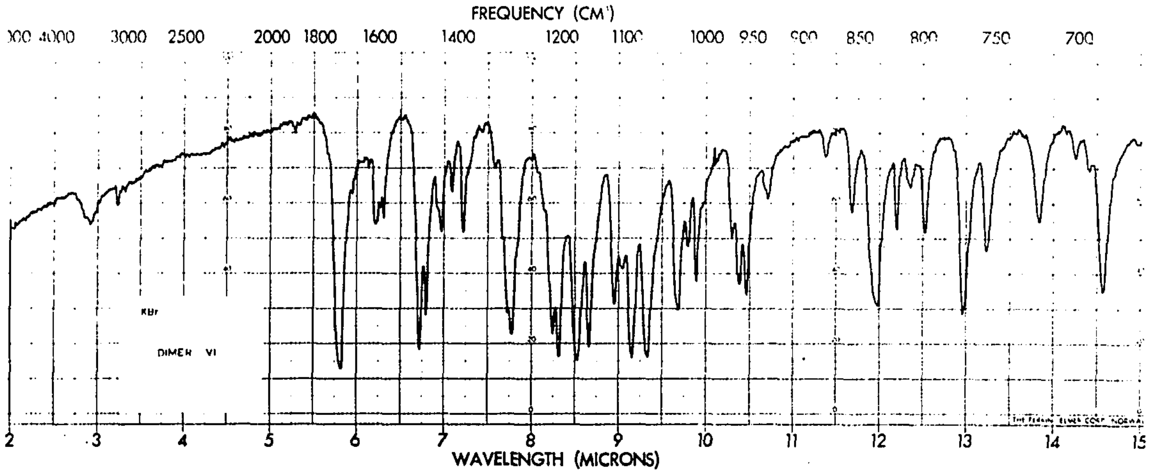
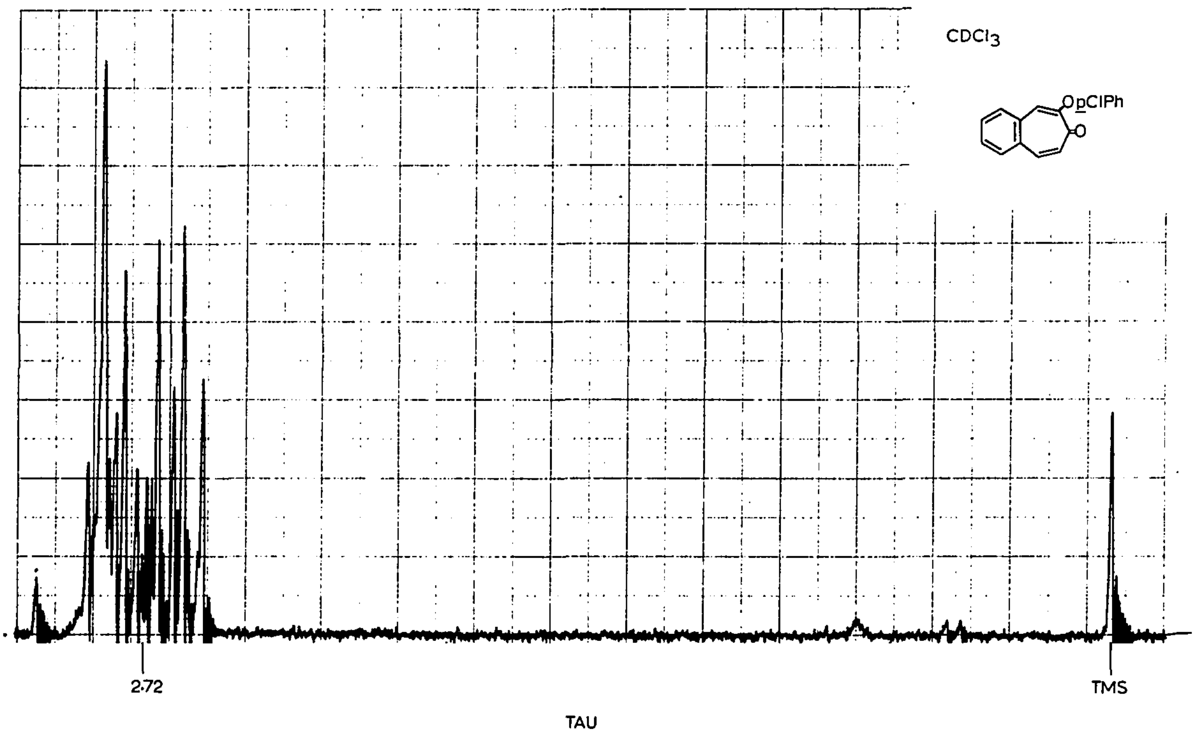

FREQUENCY (CM')
)00 4000 3000 2500 2000 1800 1600 1400 1200 1100 1000 950 900 850 800 750 700
KBr
DIMER VI
2 3 4 5 6 7 8 9 10 11 12 13 14 15
WAVELENGTH (MICRONS)

Figure 11. Nuclear magnetic resonance spectra

Top - 2-(p-Chlorophenoxy)-4,5-benztropone (XXXI)

Bottom - Dimer I (XXXVIII)


CDCl$_3$
OpClPh
O
2·72
TMS
TAU

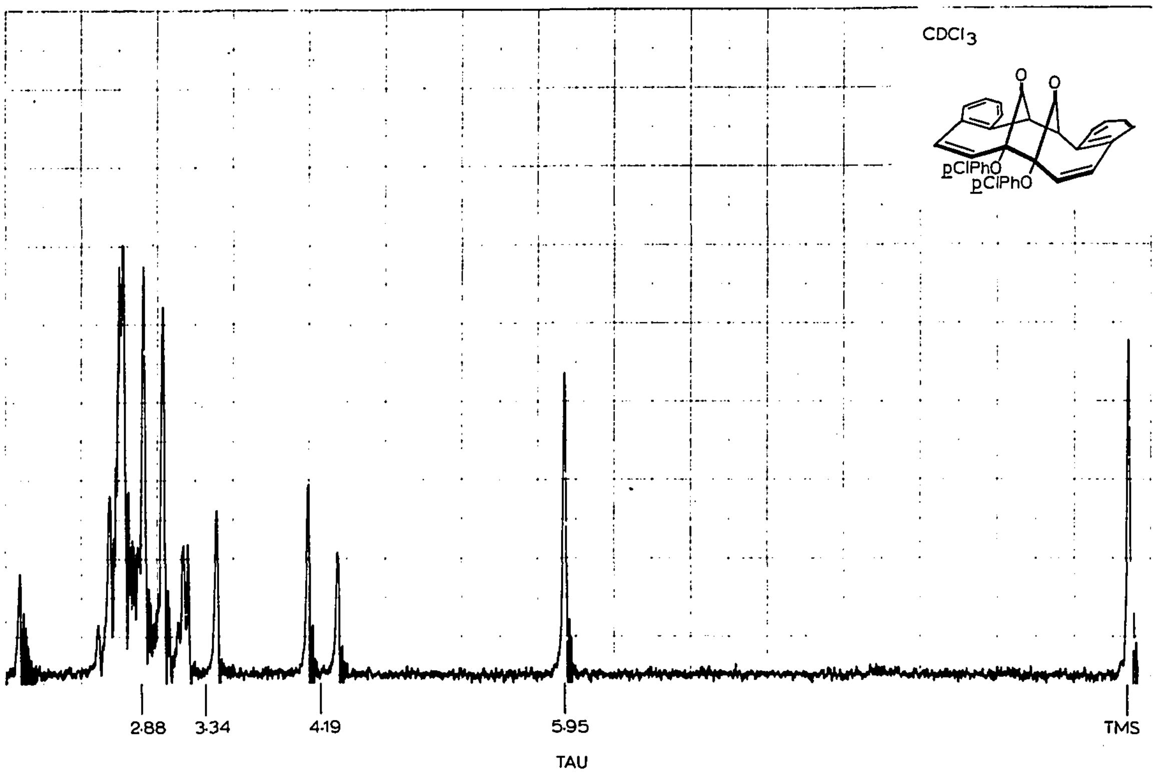
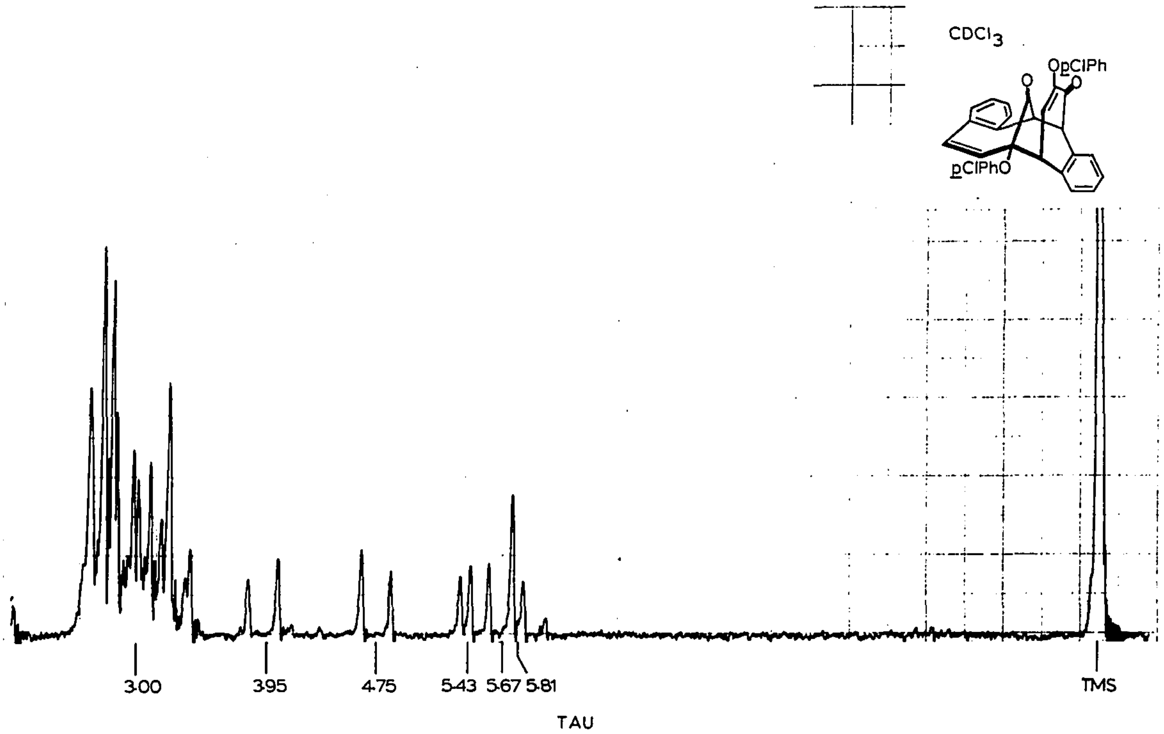

CDCl$_3$
O
O
pClPhO
pClPhO
2·88
3·34
4·19
5·95
TMS
TAU

Figure 12. Nuclear magnetic resonance spectra

Top - Dimer II (XL)

Bottom - Bromo-dimer (XLII)


CDCl3
OpClPh
pClPhO
3.00
3.95
4.75
5.43
5.67
5.81
TMS
TAU

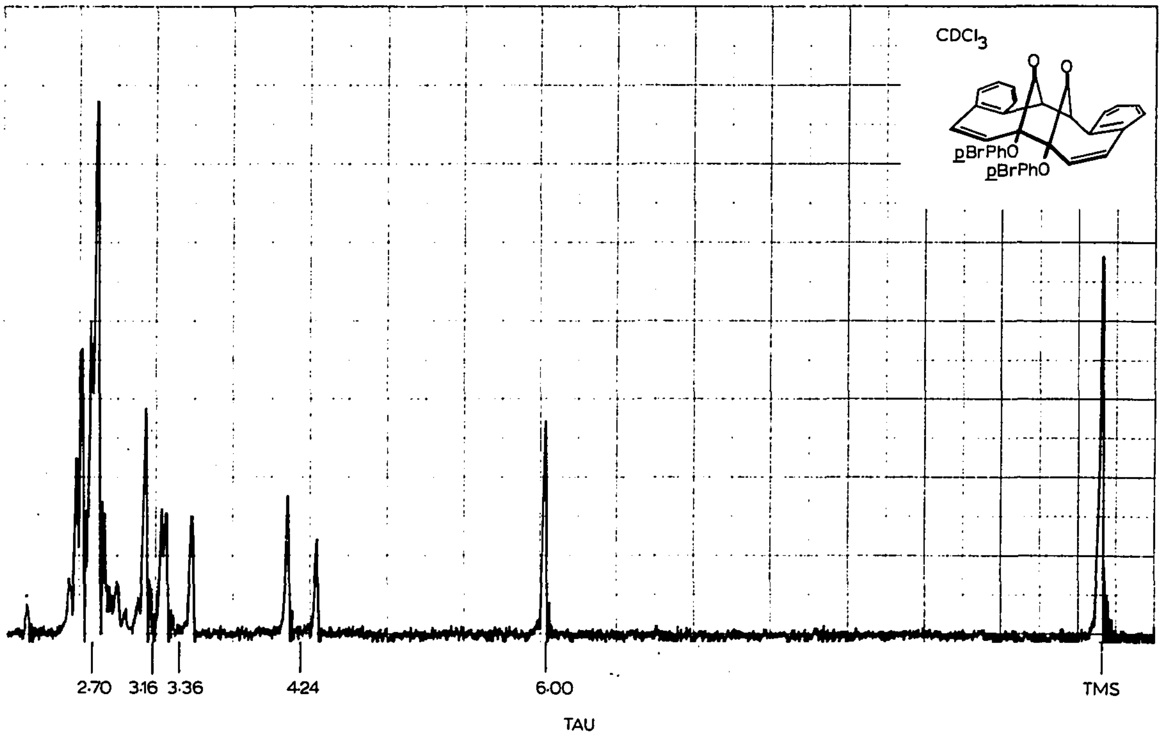
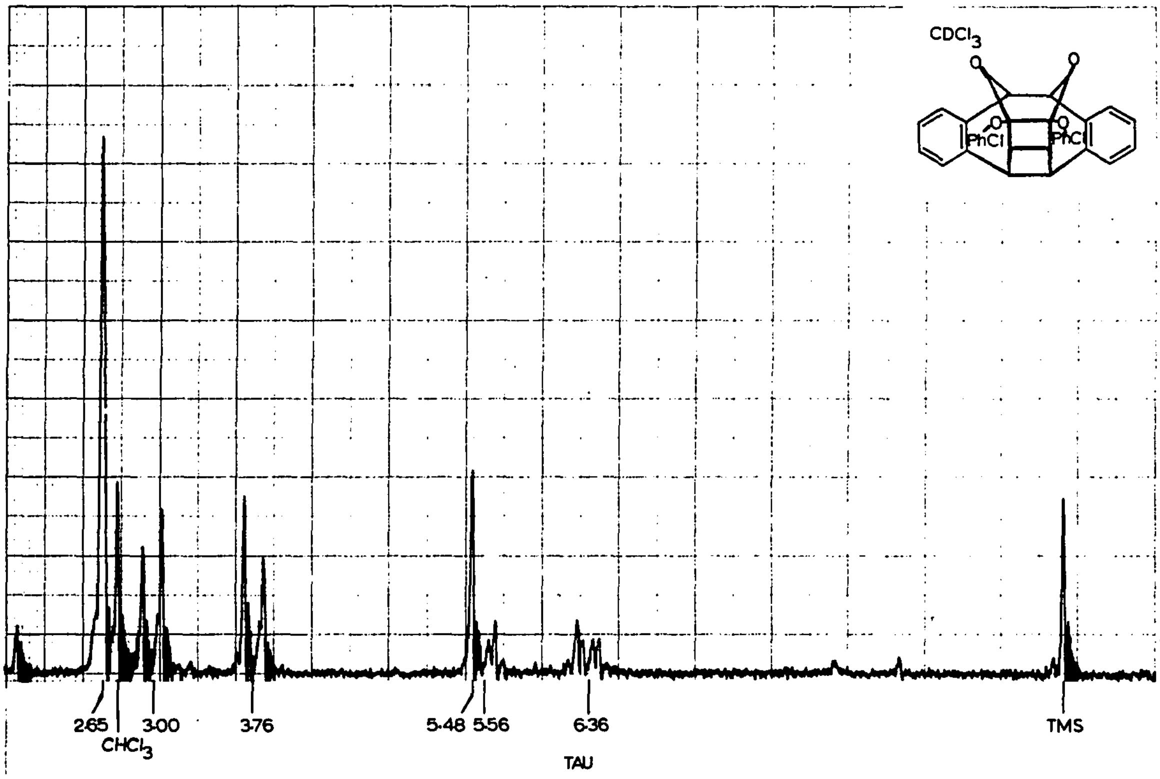

CDCl3
pBrPhO
pBrPhO
2.70
3.16
3.36
4.24
6.00
TMS
TAU

Figure 13. Nuclear magnetic resonance spectra

Top - Dimer III (XXXVI)

Bottom - Dimer III diol (XXXVII)


CDCl$_3$
O
O
O
O
PhCl
PhCl
2·65
CHCl$_3$
3·00
3·76
5·48
5·56
6·36
TMS
TAU

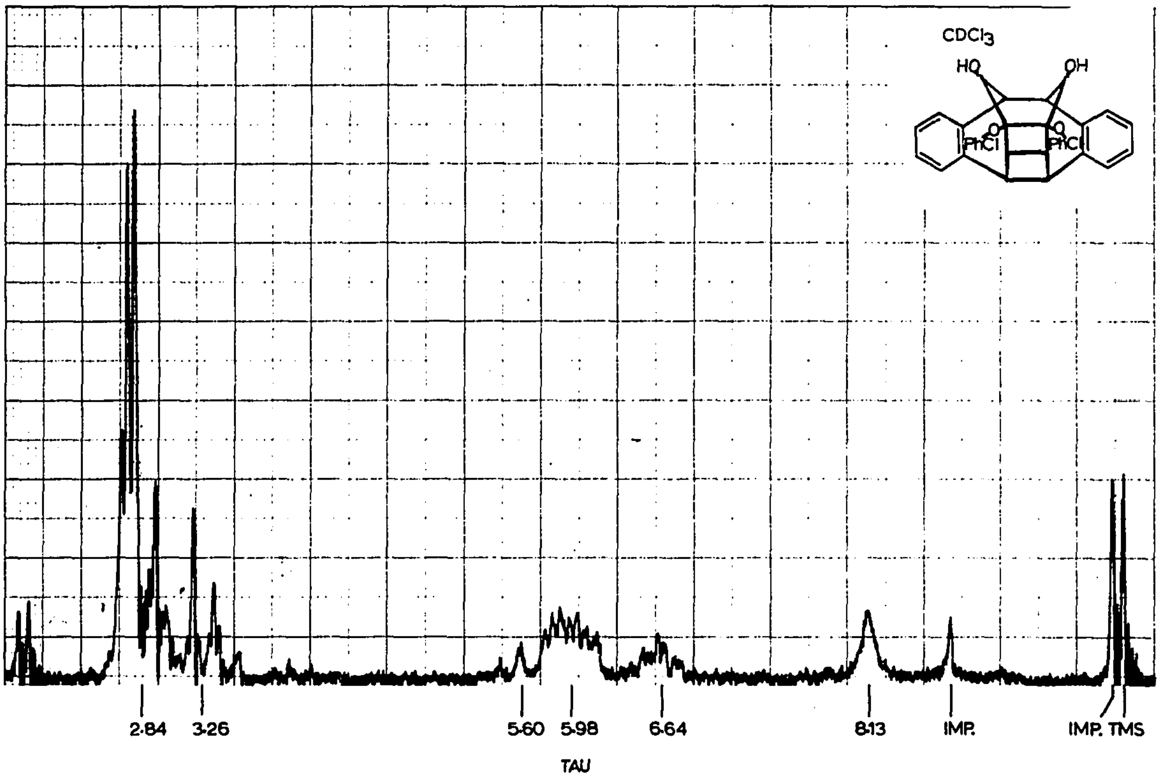

CDCl$_3$
HO
OH
O
O
PhCl
PhCl
2·84
3·26
5·60
5·98
6·64
8·13
IMP.
IMP.
TMS
TAU

Figure 14. Nuclear magnetic resonance spectrum of "Dimer IV"

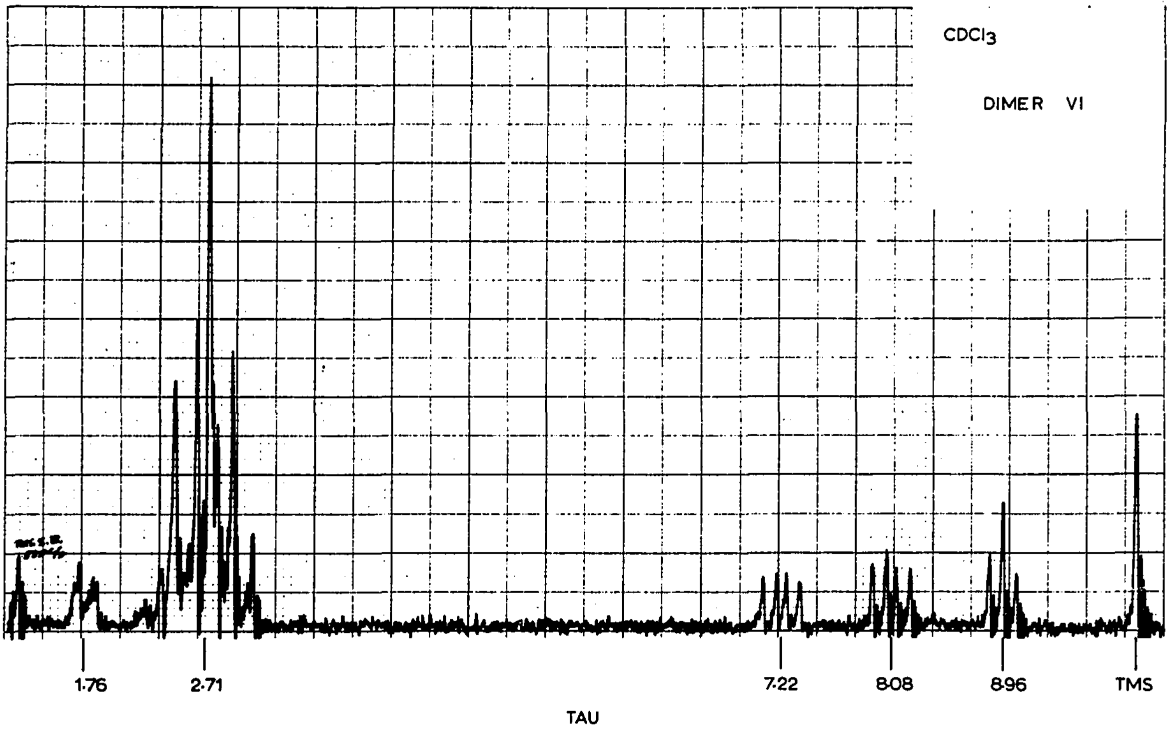

CDCl3
DIMER VI
1·76
2·71
7·22
8·08
8·96
TMS
TAU

Figure 15. Ultraviolet spectra

A. 2-(p-Chlorophenoxy)-4,5-benztropone (XXXI)

B. 2-(p-Bromophenoxy)-4,5-benztropone (XXXII)

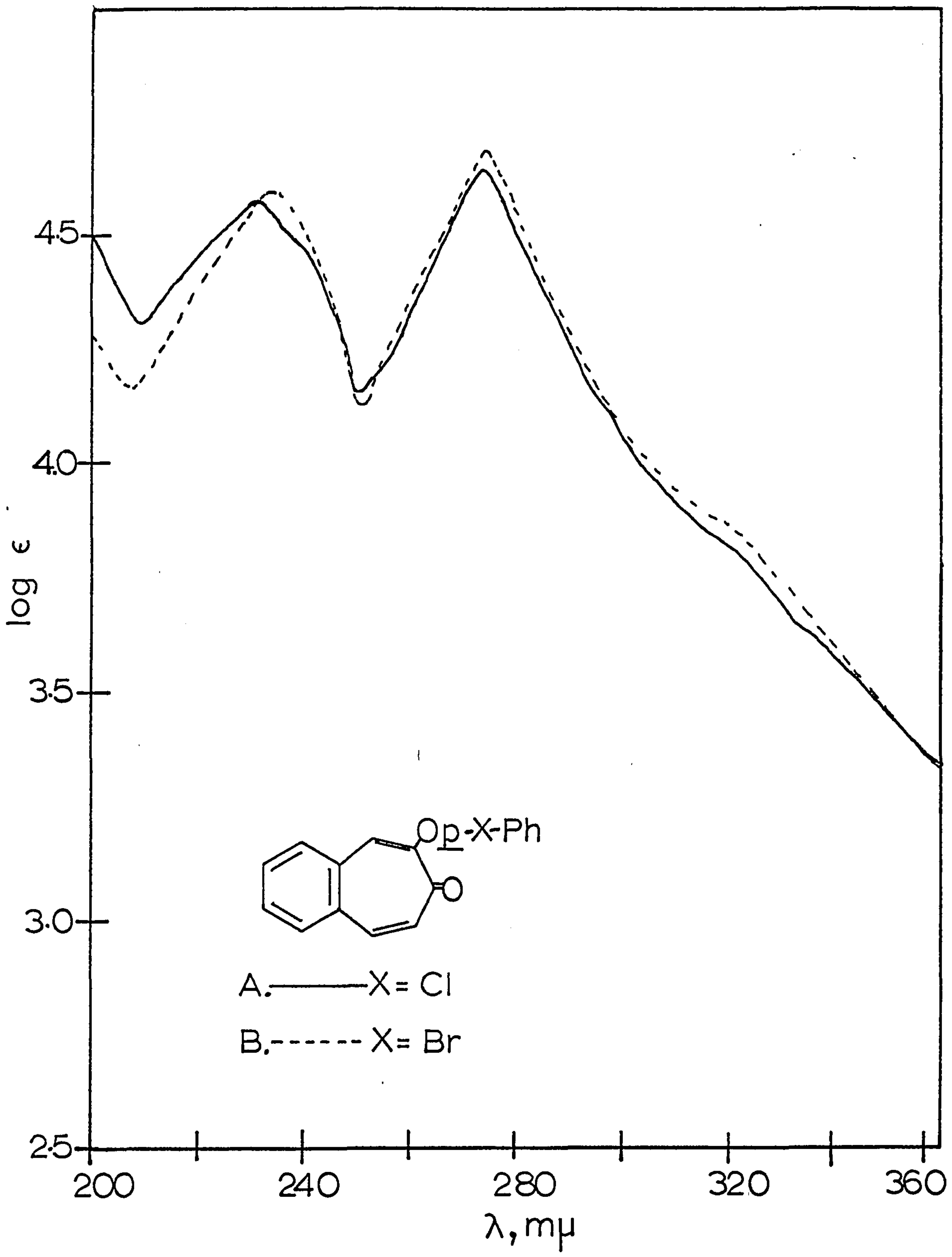

4.5
4.0
3.5
3.0
2.5
log ε
200
240
280
320
360
λ, mμ
Op-X-Ph
O
A. ——— X= Cl
B. - - - - - X= Br

Figure 16. Ultraviolet spectra

A. Dimer I (XXXVIII)

B. Dimer II (XL)

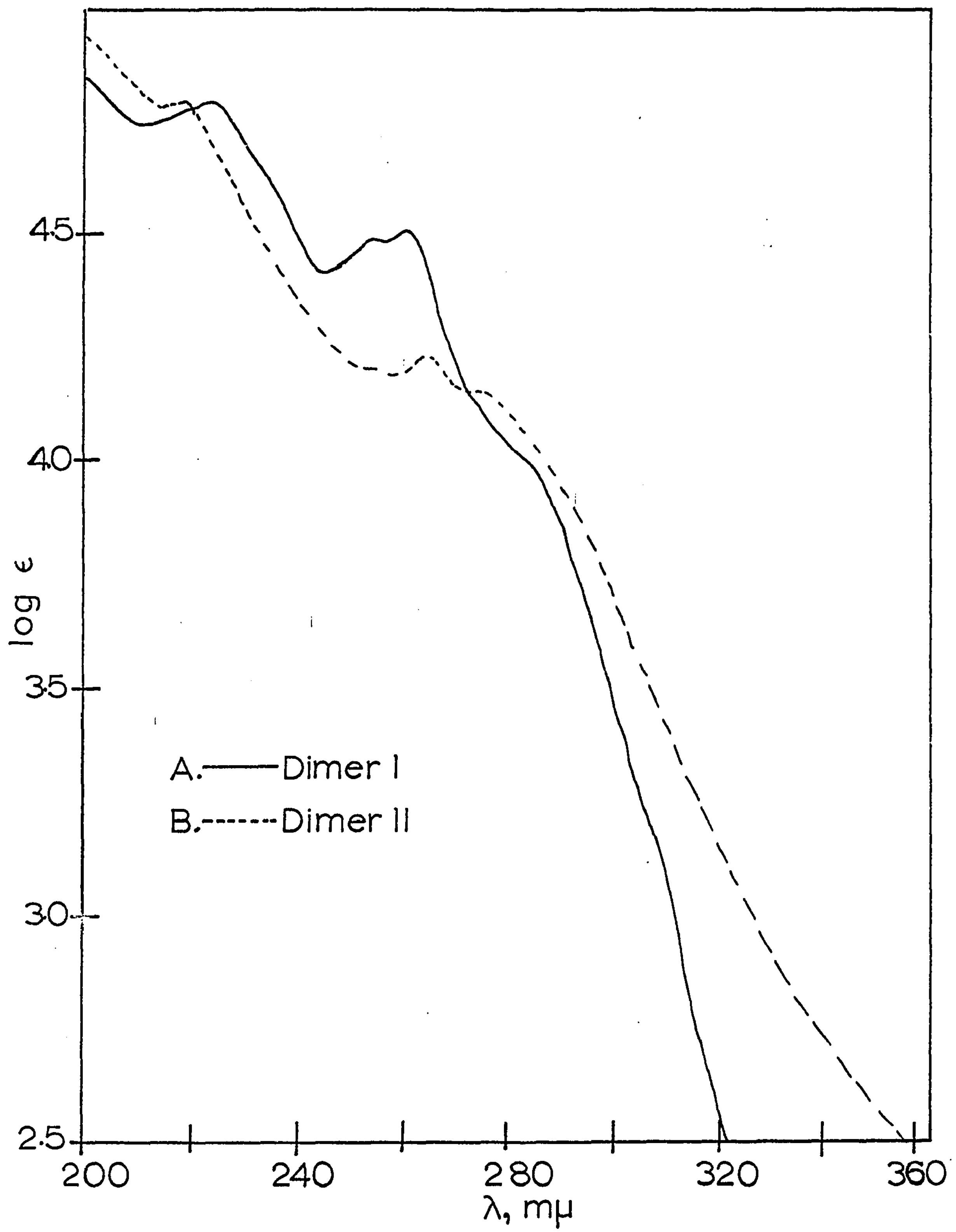

log ε
4.5
4.0
3.5
3.0
2.5
200
240
280
320
360
λ, mμ
A. —— Dimer I
B. - - - - - - Dimer II

Figure 17. Ultraviolet spectra

A. Dimer III (XXXVI)

B. Dimer III diol (XXXVII)

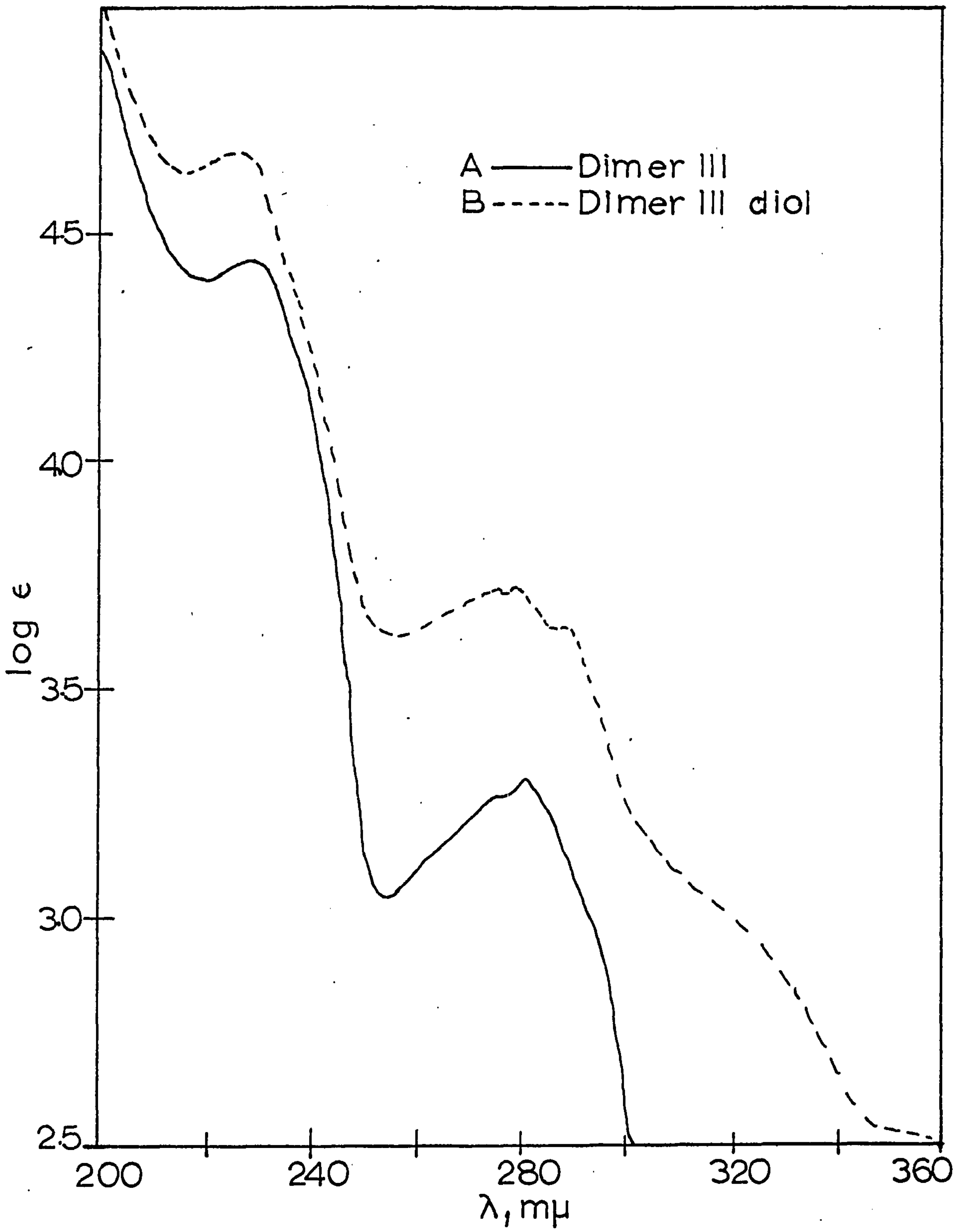

A ——— Dimer III
B ----- Dimer III diol
log ε
4.5
4.0
3.5
3.0
2.5
200
240
280
320
360
λ, mμ

Figure 18. Ultraviolet spectrum of "Dimer IV"

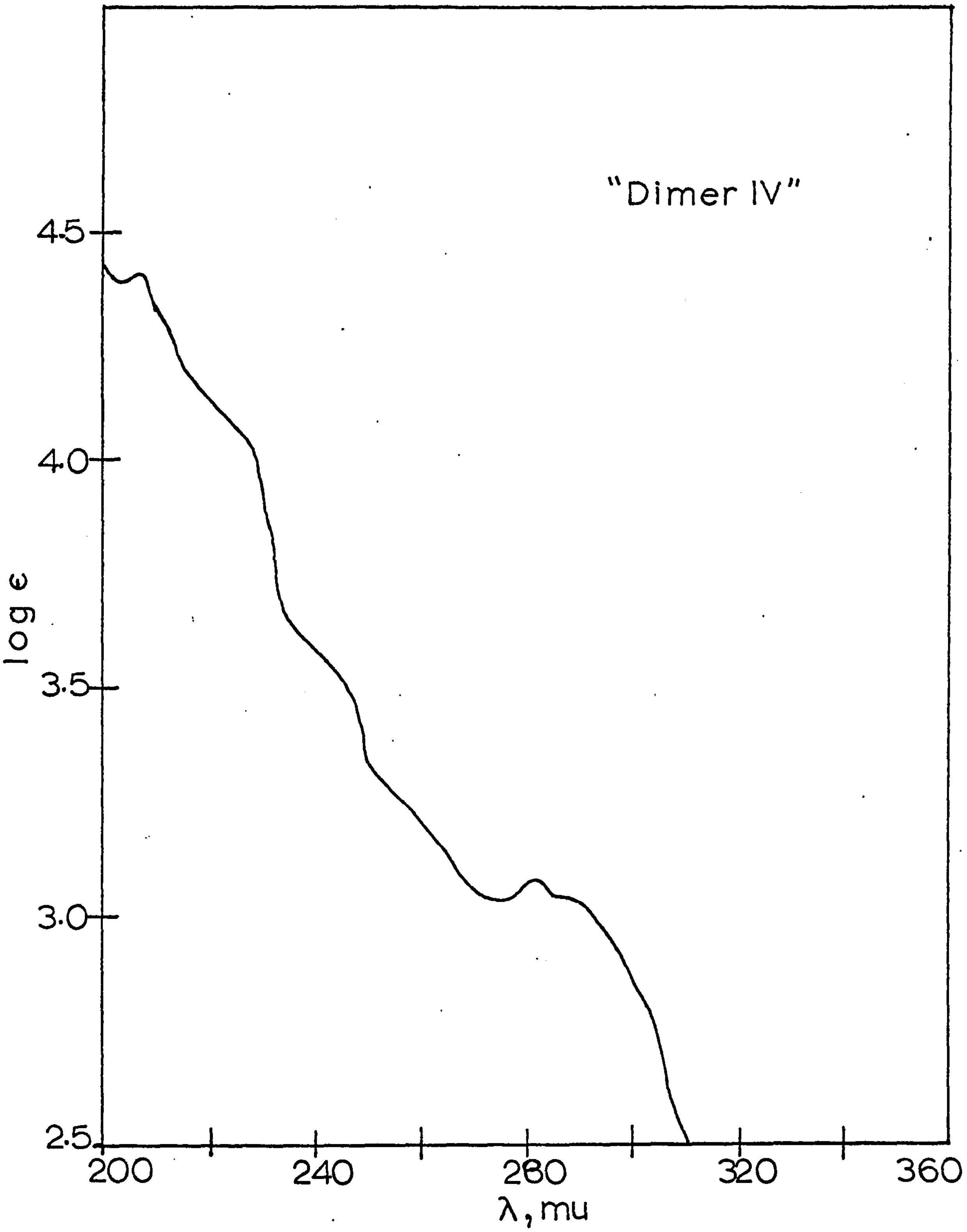

"Dimer IV"
4.5
4.0
3.5
3.0
2.5
log ε
200
240
280
320
360
λ, mu

Figure 19. Ultraviolet spectra of 4,5-benztropolone (XXXIV)

A. 95% Ethanol solution

B. 1N Sodium hydroxide added

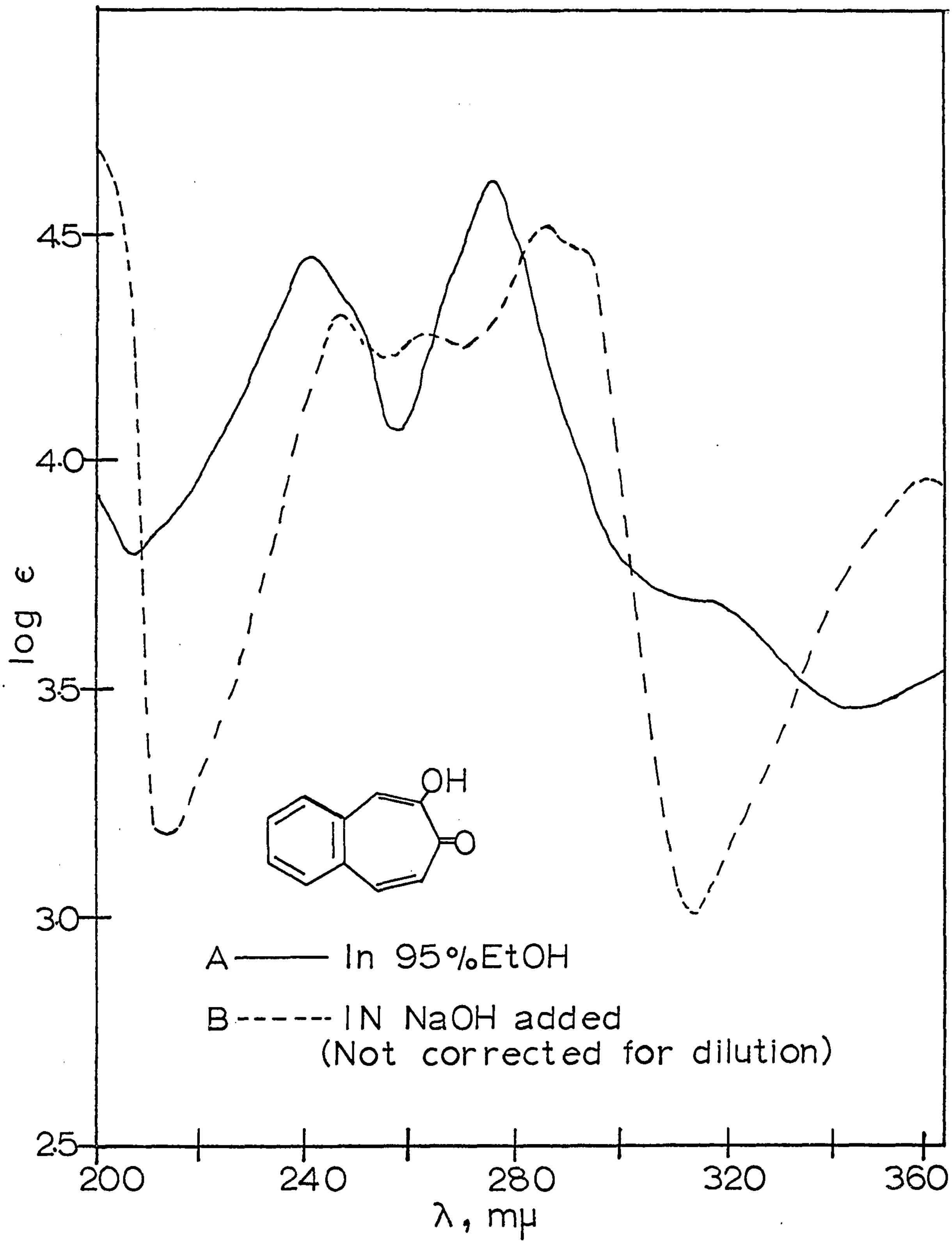

log ε
4.5
4.0
3.5
3.0
2.5
200
240
280
320
360
λ, mμ
OH
O
A —— In 95%EtOH
B ------ IN NaOH added
(Not corrected for dilution)

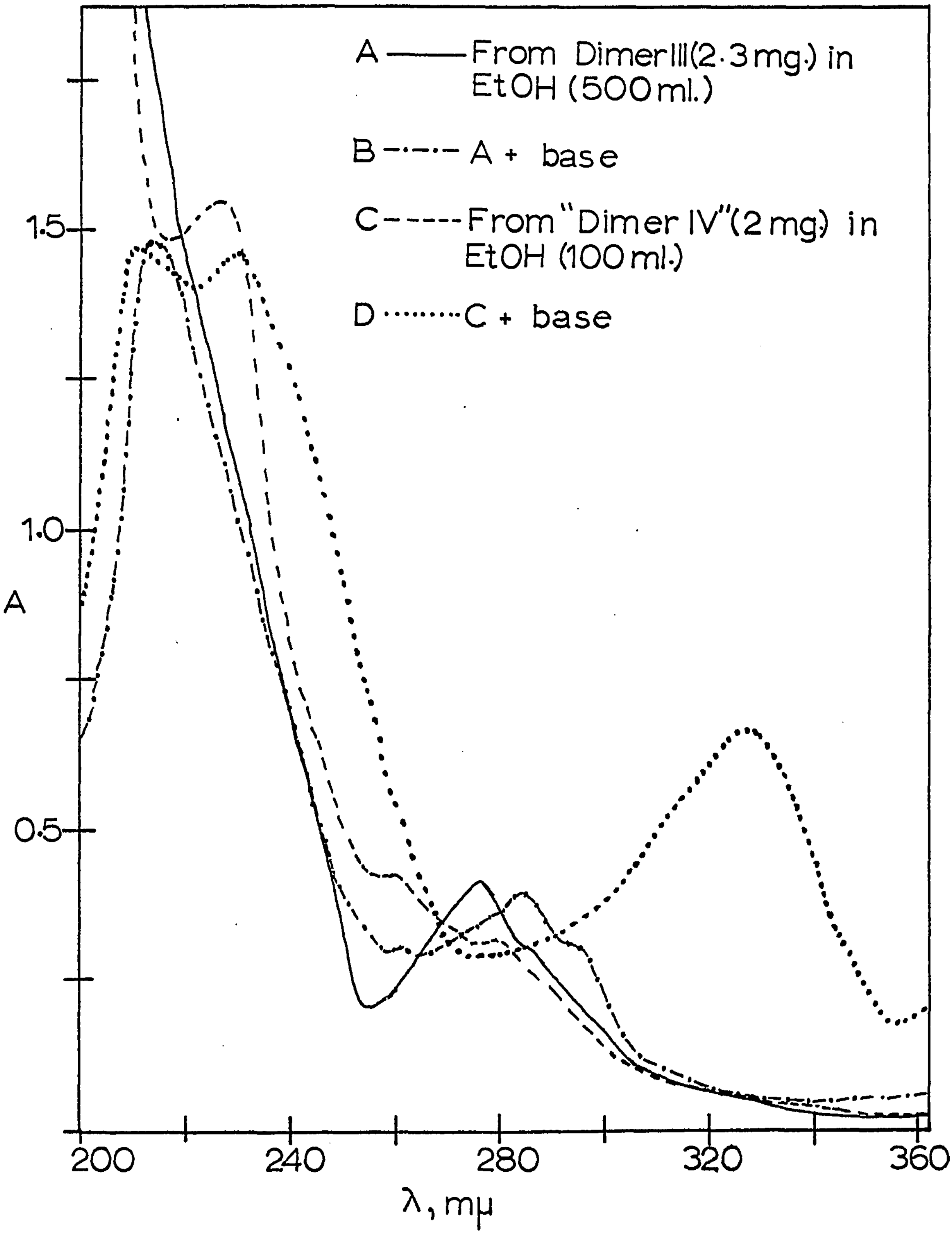
Figure 20. Ultraviolet spectra of acid hydrolysis products

A. From Dimer III (XXXVI) in 95% ethanol

B. From Dimer III (XXXVI) with 1N sodium hydroxide added

C. From "Dimer IV" in 95% ethanol

D. From "Dimer IV" with 1N sodium hydroxide added


A ——— From DimerIII(2·3mg.) in EtOH (500ml.)
B —·—·— A + base
C ------ From "Dimer IV"(2mg.) in EtOH (100ml.)
D ········ C + base
1.5
1.0
0.5
A
200
240
280
320
360
λ, mμ

singlet state is relatively short.

In some cases the excited-singlet intermediate can undergo intersystem crossing to the triplet state, in which one electron inverts its spin and is no longer paired. The triplet-state intermediate has a relatively longer lifetime than the excited-singlet state. Therefore, the triplet state has been considered the most likely species to be involved in an intermolecular reaction (34, 35). Triplet-state intermediates often can be quenched by oxygen and certain other molecules which can deactivate the intermediate by energy transfer (34, 36). Quenching of the triple-state intermediate inhibits reactions in which that intermediate is an active participant.

The triplet state may be attained also by a photosensitization process rather than as a result of direct irradiation. In this process energy absorbed by the sensitizer is transferred to the molecule involved in the photochemical reaction. Sensitizers which undergo intersystem crossing efficiently to the triplet state will produce the triplet state in the acceptor molecule when energy is transferred. Energy transfer is most efficient when the triple energy of the sensitizer is near or slightly above the triplet energy of the acceptor molecule (37).

Irradiations of 2-(p-chlorophenoxy)-4,5-benztropone (XXXI) in the presence of oxygen were done for the purpose of learning something about the excited state involved in the formation of the dimers. If the important intermediate in the dimerization process were a triplet state, oxygen might be expected to inhibit the reaction. As was noted above, formation of Dimer I and Dimer III proceeds even in the presence of oxygen. No Dimer II was isolated from the irradiations; it is probably destroyed under the conditions of the irradiation. The most notable effect of the oxygen is to provide an alternate reaction which competes for the starting material (XXXI) as evidenced by the formation of "Dimer IV."

The effect of sensitizers on the dimerization of XXXI was also studied. It was thought that if the triplet state were the important intermediate in dimer formation, some change in the reaction would be noted. A sensitizer might increase the rate of the reaction if energy were transferred to the phenoxybenztropone or the sensitizer might quench the reaction if the energy transfer were to go in the opposite direction. Benzophenone, benzil and naphthalene were chosen as sensitizers to cover a range of triplet-energy values. The triplet-energy values ($S_0 \longrightarrow T_1$) are reported (38) as follows: benzophenone, 68 kcal./mole; naphthalene, 61 kcal./mole; benzil, 54 kcal./mole. Benzophenone and benzil undergo intersystem crossing efficiently and are good triplet state sensitizers (39). Naphthalene has been found to be a less efficient sensitizer (40, p. 743).

Solutions of XXXI containing one of each of the sensitizers as well as control solutions containing only XXXI were irradiated simultaneously on a rotating wheel. Infrared analysis of the solutions indicated that the formation of Dimer I and Dimer II occurred to about the same extent regardless of the presence or absence of sensitizers. Calculations were not made to determine what fraction of the light was absorbed by the sensitizers in the region where the benztropone absorbs.

The fact that the formation of dimers is unaffected by the presence of oxygen or sensitizers would seem to suggest, but not require, that the dimerization does not proceed through the triplet state. Proposing that the dimerization proceeds by way of an excited singlet would not be unprecedented. Anthracene (41) and methyl β-naphthyl ether (42) are examples of compounds believed to dimerize through excited-singlet states. A more definite determination of the excited state involved in the dimerization process would require more careful studies with sensitizers and quenchers as well as a detailed spectral study of the phenoxybenztropones.

The involvement of a short-lived excited-singlet state in an intermolecular reaction would be more credible if evidence could be found for the existence of a ground state complex between two or more molecules of the phenoxybenztropones. Such a complex could be excited by the irradiating light and react to form dimer, offering an alternative to the process in which an excited molecule collides with another molecule. Experiments were carried out, to determine whether a ground state complex might exist in solutions of the phenoxybenztropones.

Aggregation of solute molecules in solution can sometimes be detected by measuring the absorbance of light as a function of concentration. According to Beer's law, the absorbance at a given wavelength is directly dependent upon the concentration. A deviation from Beer's law with increasing concentration may be an indication of aggregation or complex formation (43, p. 3).

The absorbance of XXXI was measured as a function of concentration at its two maxima between 200 and 360 mμ. Both tetrahydrofuran and isooctane were used as solvents. A plot of the absorbance against concentration of XXXI in tetrahydrofuran solution is shown in Figure 21, page 62. A broader range of concentration was covered by using both 0.1 cm. and 1 cm. cells. Within experimental error no deviation from Beer's law could be noted. An apparent upward trend in the curve at the upper limit of measurement in the 1 cm. cells did not continue as higher concentrations were measured in the 0.1 cm. cells. This deviation was attributed

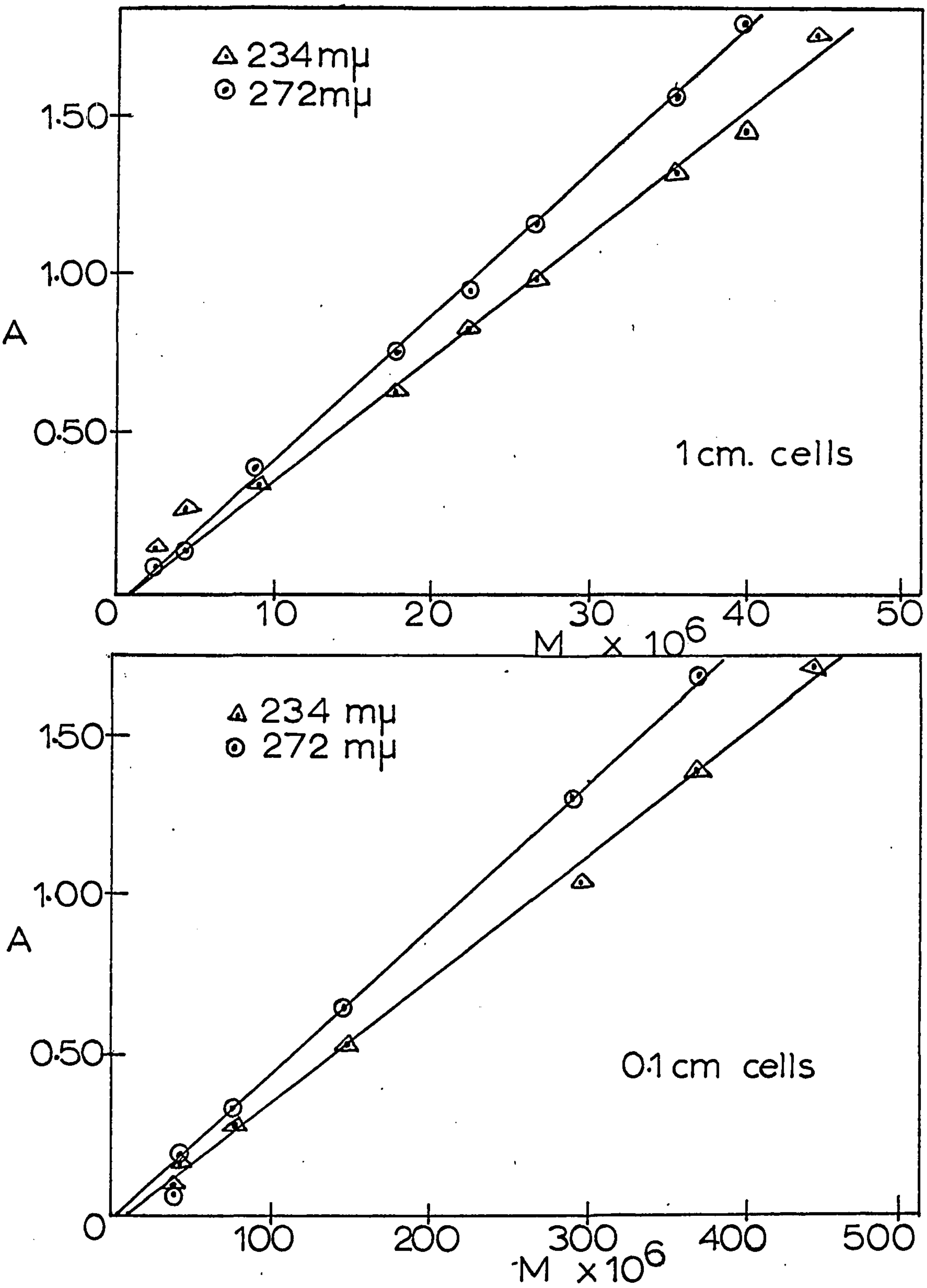


Figure 21. Beer's law plot of 2-(p-chlorophenoxy)-4,5-benztropone (XXXI) in tetrahydrofuran

to the measuring instrument. Measurements of the absorbance of XXXI in isooctane gave similar results.

Molecular weight measurements using a vapor pressure osmometer have also been used to detect aggregation in solution (44). Aggregation is indicated by a lower observed value for the concentration than that calculated. The concentrations of XXIX and XXXI in benzene and tetrahydrofuran solutions were calculated from measurements obtained with the osmometer using benzil as a standard. The results from the tetrahydrofuran solutions were too erratic to be used. A plot of the resistance values obtained from the osmometer versus the concentration in molar fraction of solute in benzene is shown in Figure 22, page 64. Within experimental error no deviation from ideal behavior can be detected.

No evidence for complex formation in the ground state of the phenoxybenztropones could be detected with the methods used. It is possible that a smaller concentration of complex than detectable by the methods used is responsible for the photodimerization process. At this point it would be premature to draw further conclusions concerning the species involved in the dimerization process without more evidence.

Examination of the structures of Dimer I and Dimer II shows that they are derived, in a formal sense at least, from XLVII rather than from XXXI. The possibility of XLVII being an intermediate in the dimerization process was investi-

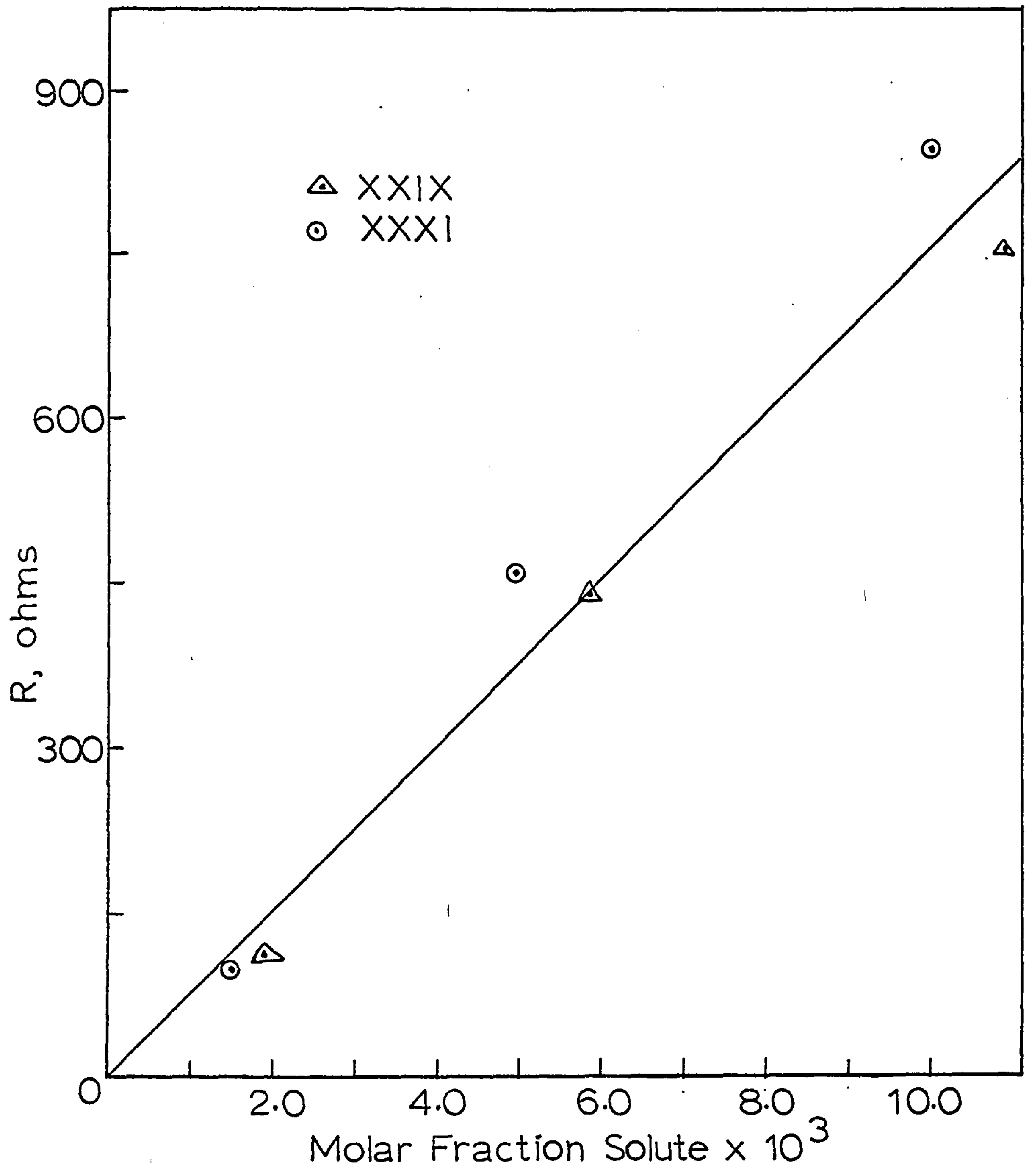
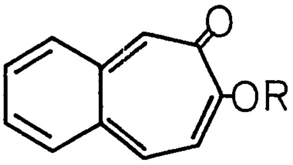


Figure 22. Vapor pressure osmometer measurements on 2-phenoxy-4,5-benztropone (XXIX) and 2-(p-chlorophenoxy)-4,5-benztropone (XXXI) in benzene

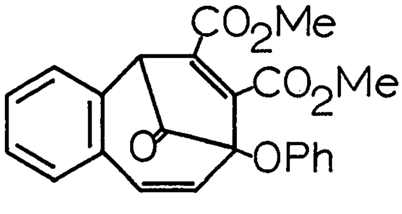
gated. An attempt was made to trap XLVII by irradiating 2-phenoxy-4,5-benztropone (XXIX) in the presence of dimethyl



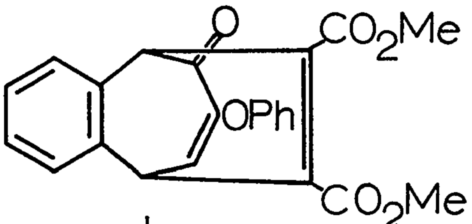
XLVII
R = Ph or pClPh

$MeO_2CC{\equiv}CCO_2Me$

XLVIII



XLIX



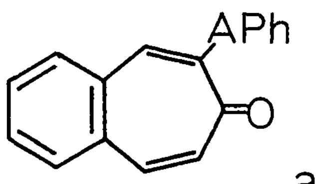
L

acetylenedicarboxylate (XLVIII) as a dienophile. If XLVII were formed, it was thought that adducts such as XLIX or L might be obtained. When the irradiation was carried out, dimer formation occurred but no compounds such as XLIX or L were found. Similar experiments by Chapman and Smith (25, pp. 254, 278) using maleic anhydride and tetracyanoethylene as dienophiles were unsuccessful. These results suggest that XLVII is not an intermediate in the dimerization process.

## Studies of the Phenyl Shift

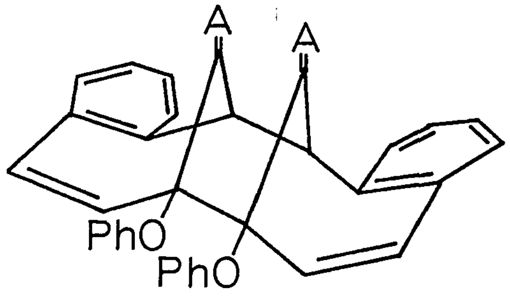
One of the interesting aspects of the dimerization process is an apparent oxygen-to-oxygen phenyl shift in going from the starting material to the dimers. Examples of phenyl shifts from carbon to oxygen are known in the photoreactions of tetrabenzoylethylene (LI) (45) and the *cis*-1,2-dibenzoylethylenes (LII) (46) (Figure 23, page 67). A diradical intermediate (LIII) was proposed for the latter (46). Examples of phenyl shifts from oxygen to oxygen are known in cases where the *o*-phenoxybenzoyloxy radical (LIV) is produced (47).

In spite of the analogies for phenyl shifts, past experience with rearrangements in the α-tropolone ethers (4) made it seem advisable to attempt to confirm the phenyl shift. It was decided to replace the phenoxy oxygen atom of 2-phenoxy-4,5-benztropone with a different heteroatom (A) as in LV. If dimerization of LV were to occur with the accompanying phenyl shift, the heteroatom (A) should be located in the carbonyl position as in LVI. Sulfur and amino-



LV

a: A = S
b: A = NH



LVI

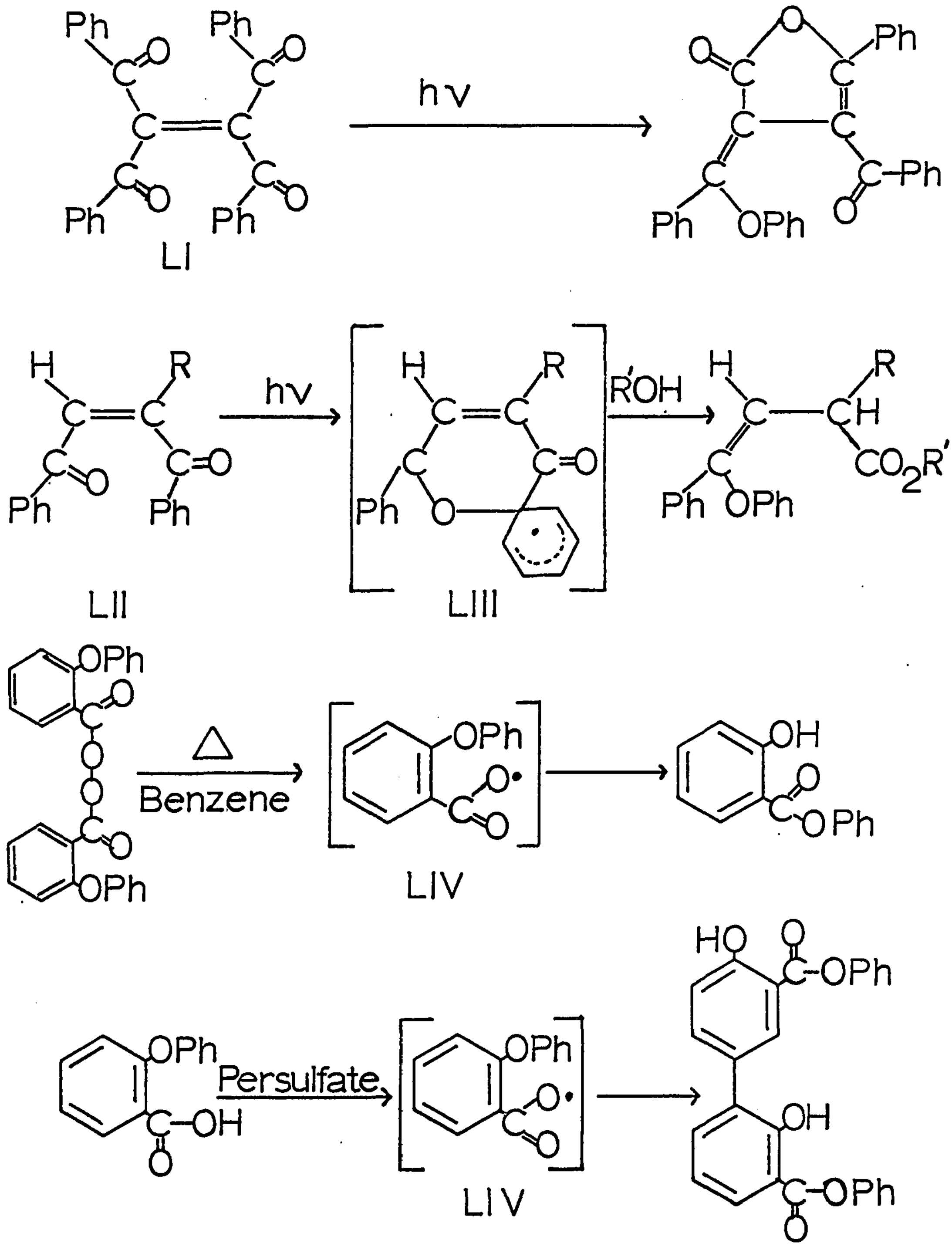


Figure 23. Examples of phenyl migrations

nitrogen were chosen as the best candidates for heteroatom substitution.

2-Thiophenoxy-4,5-benztropone (LVa) was prepared by the same method (26) used for the preparation of the phenoxy compounds with the exception that thiophenoxyacetone was used in the place of phenoxyacetone. The infrared spectrum (Figure 26, page 76) and nuclear magnetic resonance spectrum (Figure 27, page 78) of the condensation product (m.p. 108.5-109.5°) were consistent with those expected for LVa. The irradiation of LVa progressed very slowly. Only starting material and tars were obtained. No dimer could be found. An irradiation of LVa in quartz for 200 hours also gave nothing but decomposition products and starting material. Another irradiation in tetrahydrofuran containing 5% water was carried out in the hope that, if LVIa were formed, the thioketone would be hydrolized to give sulfide ion in solution. No sulfide ion could be detected by testing with lead acetate solution.

Although the results were not as hoped, they do indicate that the atom attached to the phenyl group plays an important role in the dimerization. Substitution of the oxygen by sulfur prevents dimer formation.

Attempts were made to prepare the anilinobenztropone LVb by condensing anilinoacetone with *o*-phthalaldehyde. A small amount of material was obtained which appeared to be

LVb from the infrared spectrum, but not enough of it could be isolated and purified for characterization and irradiation. The major product from the condensation was a high-melting, yellow, fluorescent material which was not further characterized.

Other efforts in the study of the phenyl shift were directed toward finding a closer analogy for the oxygen-oxygen migration. One might envisage that the phenyl shift is initiated by an $n \longrightarrow \pi^*$ excitation of the carbonyl to form an intermediate (LVII) (Figure 24, page 70) in which the carbonyl oxygen possesses radical character as proposed in the case of the dibenzoylethylenes (LII) (46). This could lead to a bridged intermediate (LVIII). An apparently very similar situation would exist if one could form the o-phenoxyphenoxyl radical (LIX) which might give the bridged intermediate (LX) and proceed with a shift of the phenyl group. A method to produce such a radical was suggested by recent work (48) on the photochemical analog of the Fries rearrangement with phenyl esters (LXI). One of the suggested intermediates is a phenoxyl radical (LXII). This appeared to be a good system in which to test the possibility of a phenyl shift.

For this purpose 2-phenoxy-4-methylphenyl acetate (LXIII) (Figure 24, page 70) was prepared from the corresponding phenol which had been synthesized by Ungnade (49).

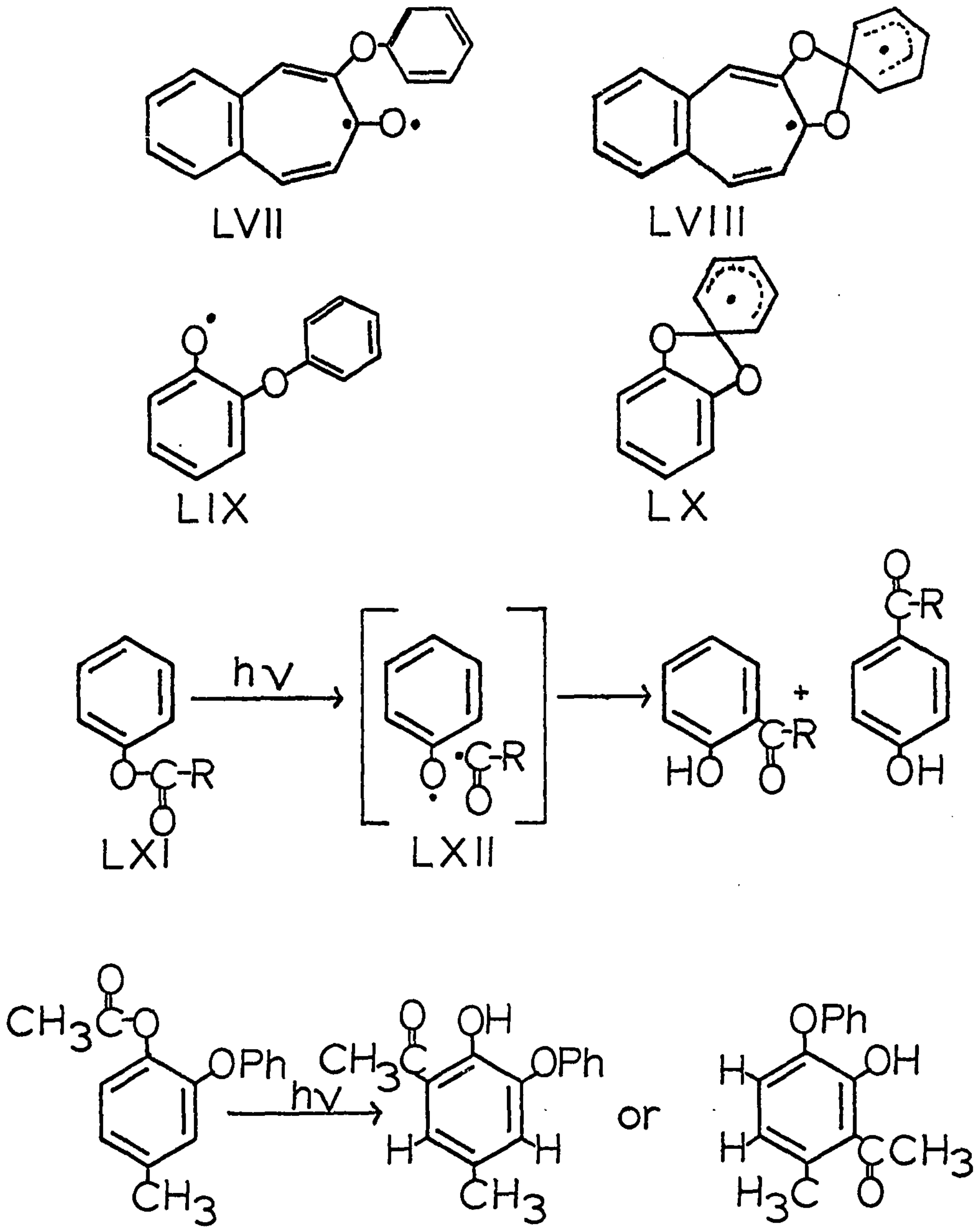


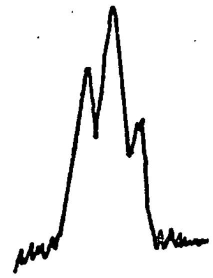
Figure 24. Study of a photochemical Fries rearrangement

The methyl group in the 4-position was intended to serve two purposes: (a) to label the benzene ring so a phenyl shift could be detected, and (b) to block one of the positions to which the acetyl group could return, increasing the probability of a phenyl shift.

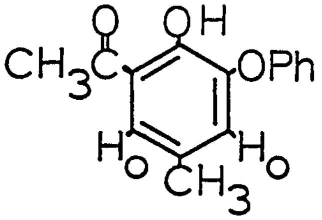
The phenoxyphenyl acetate LXIII was irradiated in ethanol solution with an immersion lamp in a quartz well. The product obtained was characterized as an o-hydroxyacetophenone on the basis of a positive ferric chloride test, a carbonyl absorption in the infrared spectrum (Figure 26, page 76) at 6.08 μ and a peak in the nuclear magnetic resonance spectrum (Figure 27, page 78) at -1.98 $\tau$. All of these observations indicate the presence of a hydroxyl hydrogen intramolecularly hydrogen-bonded to a carbonyl oxygen. Assuming that only the acetyl group and possibly the phenyl group undergo rearrangement, two possibilities for the structure of the photoproduct exist: LXIV, in which no phenyl shift has occurred, or LXV, in which the phenyl group has shifted from one oxygen to the other.

It was difficult to devise chemical methods to distinguish between these two possibilities with only a limited amount of material. Nuclear magnetic resonance offered the most attractive solution to the problem. The absorption of the phenoxy groups is superimposed on that of the other aromatic ring making it impossible to determine the substitution pattern of the ring in question by a simple examination of the spectrum. However, it has been reported (50) that the *ortho* protons in a substituted toluene will couple with the protons of the methyl group to give observable splitting of the methyl absorption. In this particular case structure LXIV possesses two hydrogens *ortho* to the methyl group, whereas structure LXV possesses only one hydrogen in an *ortho* position. The two structures should show different multiplicity in the methyl absorption.

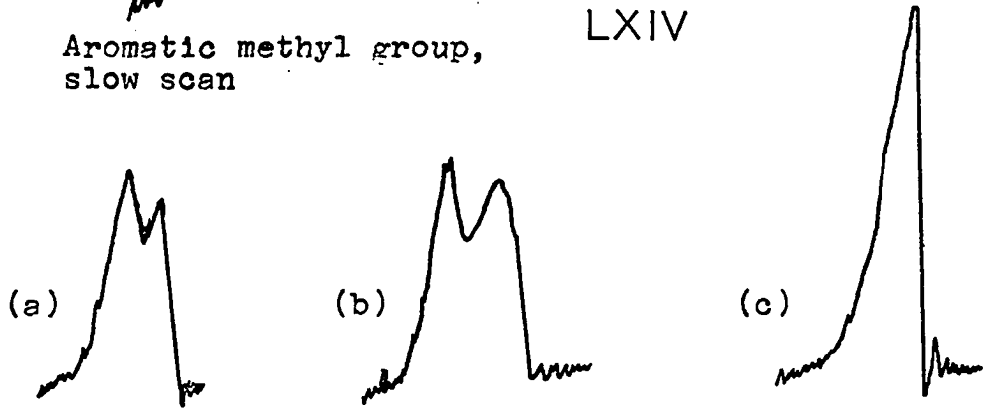
A slow scan of the high field methyl group (7.76 $\tau$) in the irradiation product revealed it to be a finely split triplet with lines spaced 0.66 ± .02 c.p.s. apart (Figure 25, page 73), indicating the presence of two hydrogens *ortho* to the methyl group. The source of the splitting was confirmed by a double resonance experiment. Saturation of a proton in the aromatic region 284 c.p.s. down field from the methyl group collapsed the triplet to a double (Figure 25, page 73). Saturation of another proton 299 c.p.s. down field from the methyl group also collapsed the triplet to a doublet. Saturation of both protons collapsed it to a singlet. A scan of the aromatic region while the methyl group was saturated revealed the two *ortho* protons as an AB pattern at 2.77 and 3.04 $\tau$ with a coupling constant, J = 2.2 c.p.s., in the range expected for coupling between *meta* protons (31). This evidence proves that the photo-



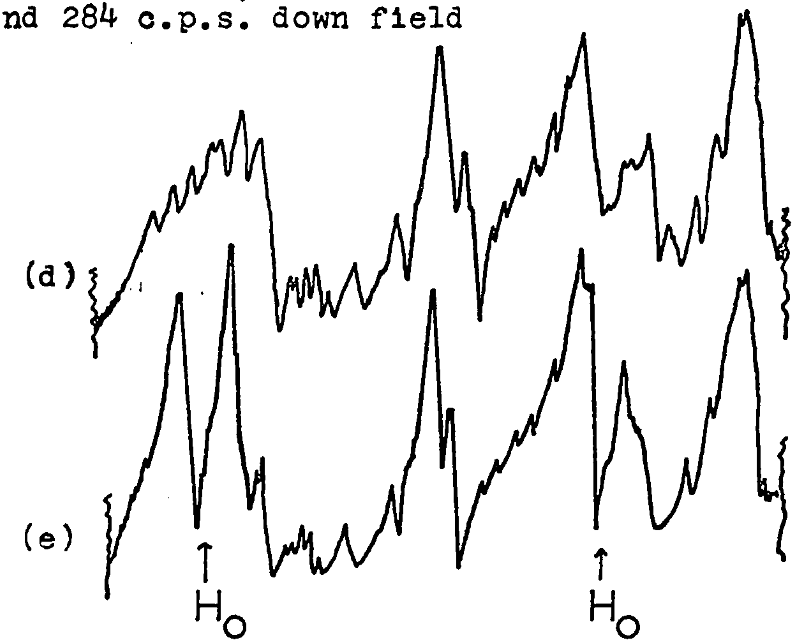
Aromatic methyl group, slow scan



LXIV



Aromatic methyl group (a) with irradiating signal 299 c.p.s. down field, (b) 284 c.p.s. down field and (c) 299 and 284 c.p.s. down field



A portion of the aromatic region (d) without and (e) with saturation of the aromatic methyl group, revealing the positions of the *ortho* protons ($H_o$)

Figure 25. Double resonance experiment with 2-hydroxy-3-phenoxy-5-methylacetophenone (LXIV)

product is 2-hydroxy-3-phenoxy-5-methylacetophenone (LXIV). The fact that the phenyl shift was not observed may be because the suggested free radical intermediate does not exist; or such a shift in this particular system may not be thermodynamically favored.

Although the phenyl shift was not observed, the problem provided an interesting exercise in structure elucidation. The method has great potential in the determination of substitution patterns on a wide variety of aromatic compounds which contain benzylic methyl, methylene or methine groups. However, initial studies indicate that the splitting observed is dependent upon the nature of the substituents on the aromatic ring (50, 51). More investigation is necessary to ascertain the limitations of the method.

## Rearrangement and Cleavage of the Dimers

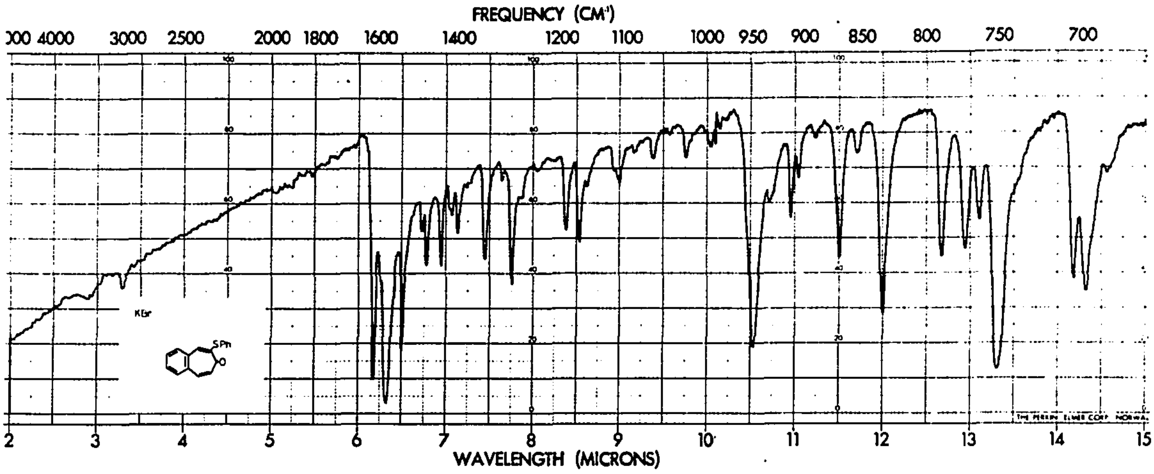
The thermal reactions of the dimers are worthy of special comment. As mentioned previously, Dimer I can be converted to Dimer II by heating it slightly above its melting point (230-235°). The rearrangement can be visualized as starting by homolytic cleavage of the bond between the two phenoxy-bearing carbons to give diradical LXVI (Figure 30, page 83). Rebonding of the two unpaired electrons of LXVI can give either Dimer I or Dimer II. The

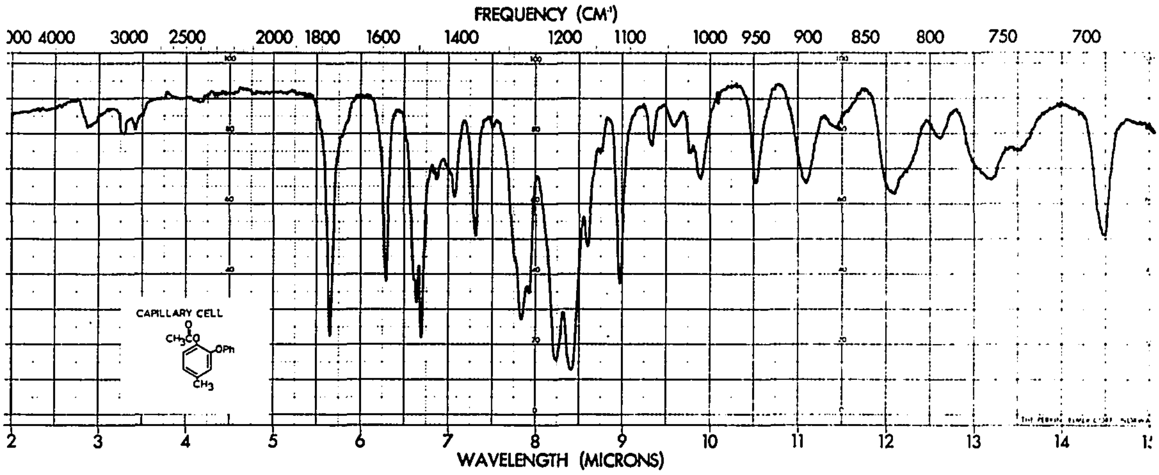
Figure 26. Infrared spectra

Top - 2-Thiophenoxy-4,5-benztropone (LVa)

Middle - 2-Phenoxy-4-methylphenyl acetate (LXIII)

Bottom - 2-Hydroxy-3-phenoxy-5-methylacetophenone (LXIV)


FREQUENCY (CM⁻¹)
00 4000
3000
2500
2000
1800
1600
1400
1200
1100
1000
950
900
850
800
750
700
KBr
SPh
O
THE PERKIN-ELMER CORP., NORWALK
2
3
4
5
6
7
8
9
10
11
12
13
14
15
WAVELENGTH (MICRONS)


FREQUENCY (CM⁻¹)
00 4000
3000
2500
2000
1800
1600
1400
1200
1100
1000
950
900
850
800
750
700
CAPILLARY CELL
CH₃CO
OPh
CH₃
THE PERKIN-ELMER CORP., NORWALK
2
3
4
5
6
7
8
9
10
11
12
13
14
1
WAVELENGTH (MICRONS)

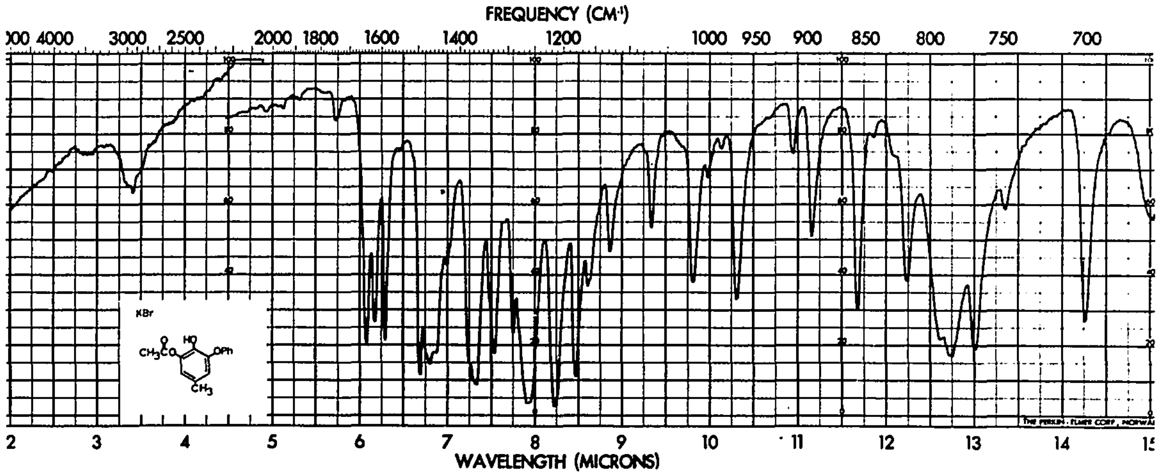
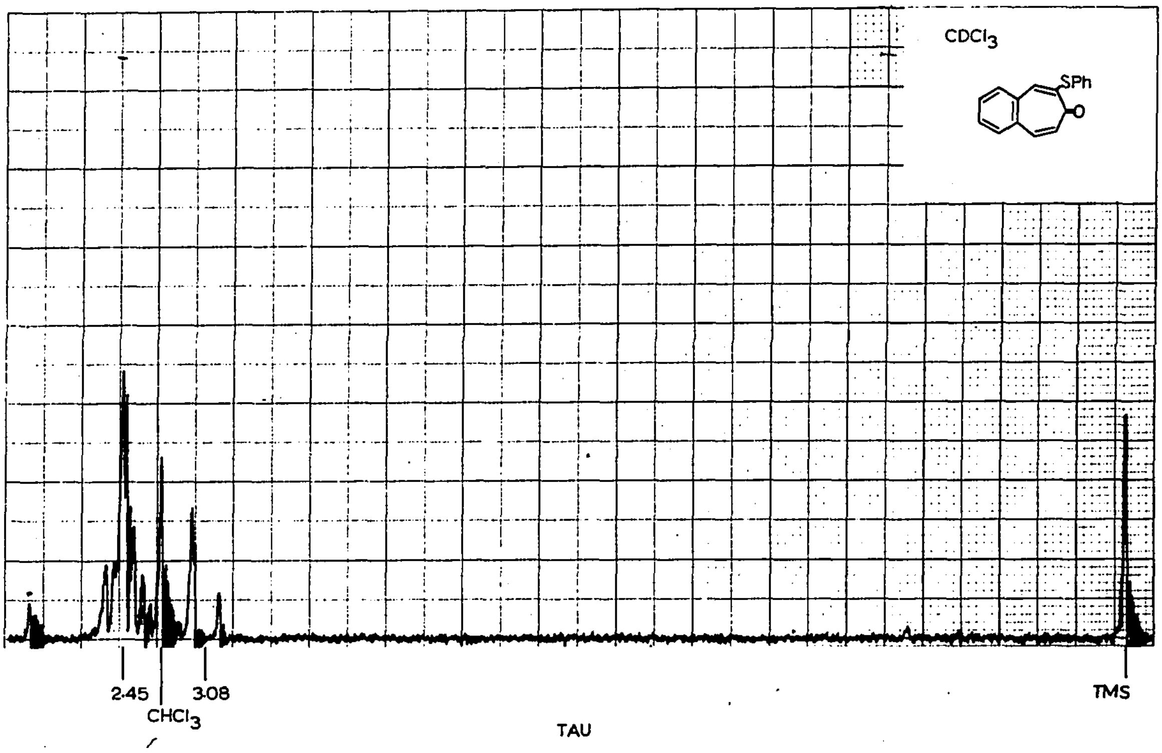

FREQUENCY (CM⁻¹)
00 4000
3000
2500
2000
1800
1600
1400
1200
1000
950
900
850
800
750
700
KBr
CH₃CO
HO
OPh
CH₃
THE PERKIN-ELMER CORP., NORWALK
2
3
4
5
6
7
8
9
10
11
12
13
14
1
WAVELENGTH (MICRONS)

Figure 27. Nuclear magnetic resonance spectra

Top - 2-Thiophenoxy-4,5-benztropone (LVa)

Bottom - 2-Hydroxy-3-phenoxy-5-methylacetophenone (LXIV)


CDCl$_3$
SPh
O
2.45
CHCl$_3$
3.08
TMS
TAU

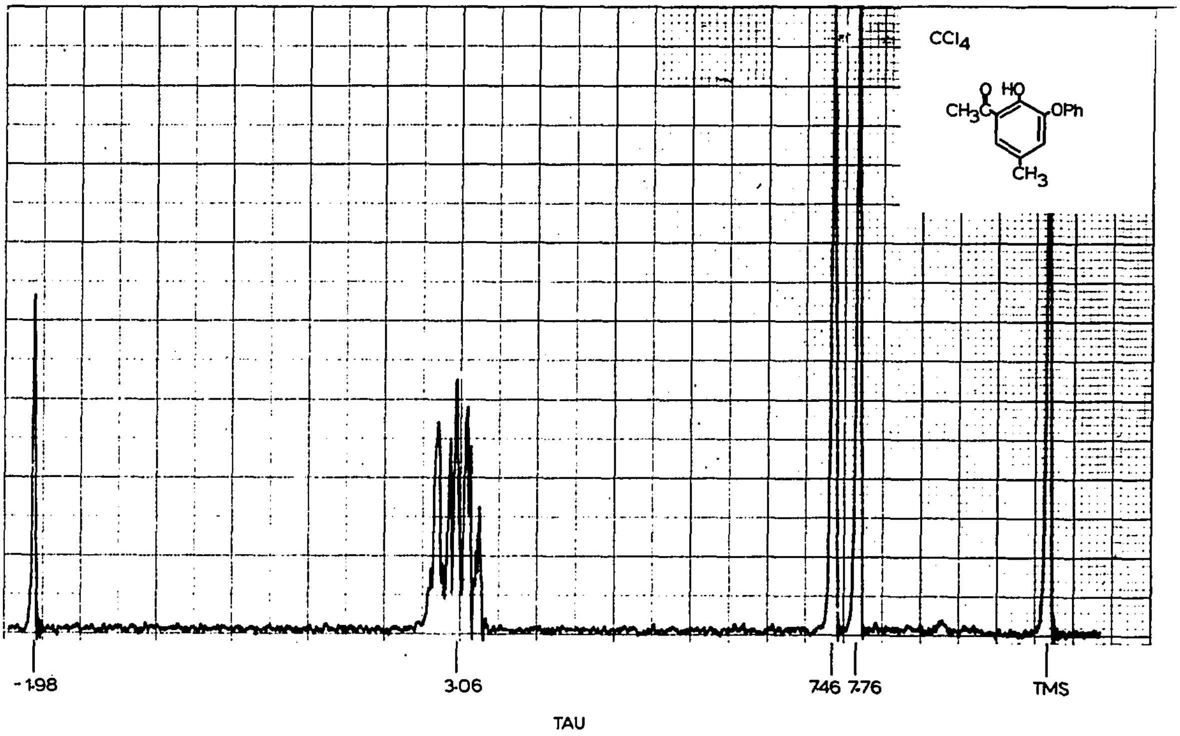
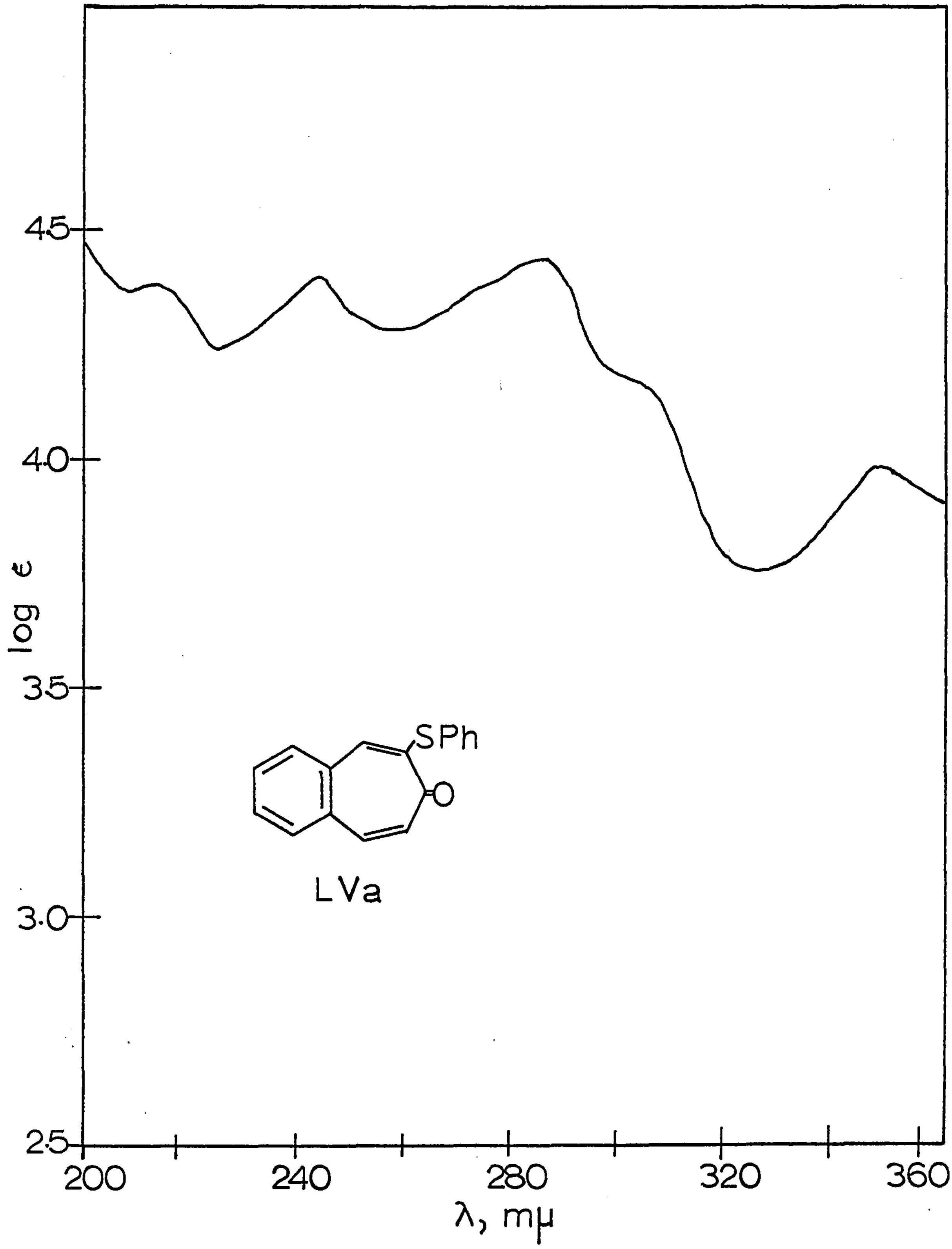
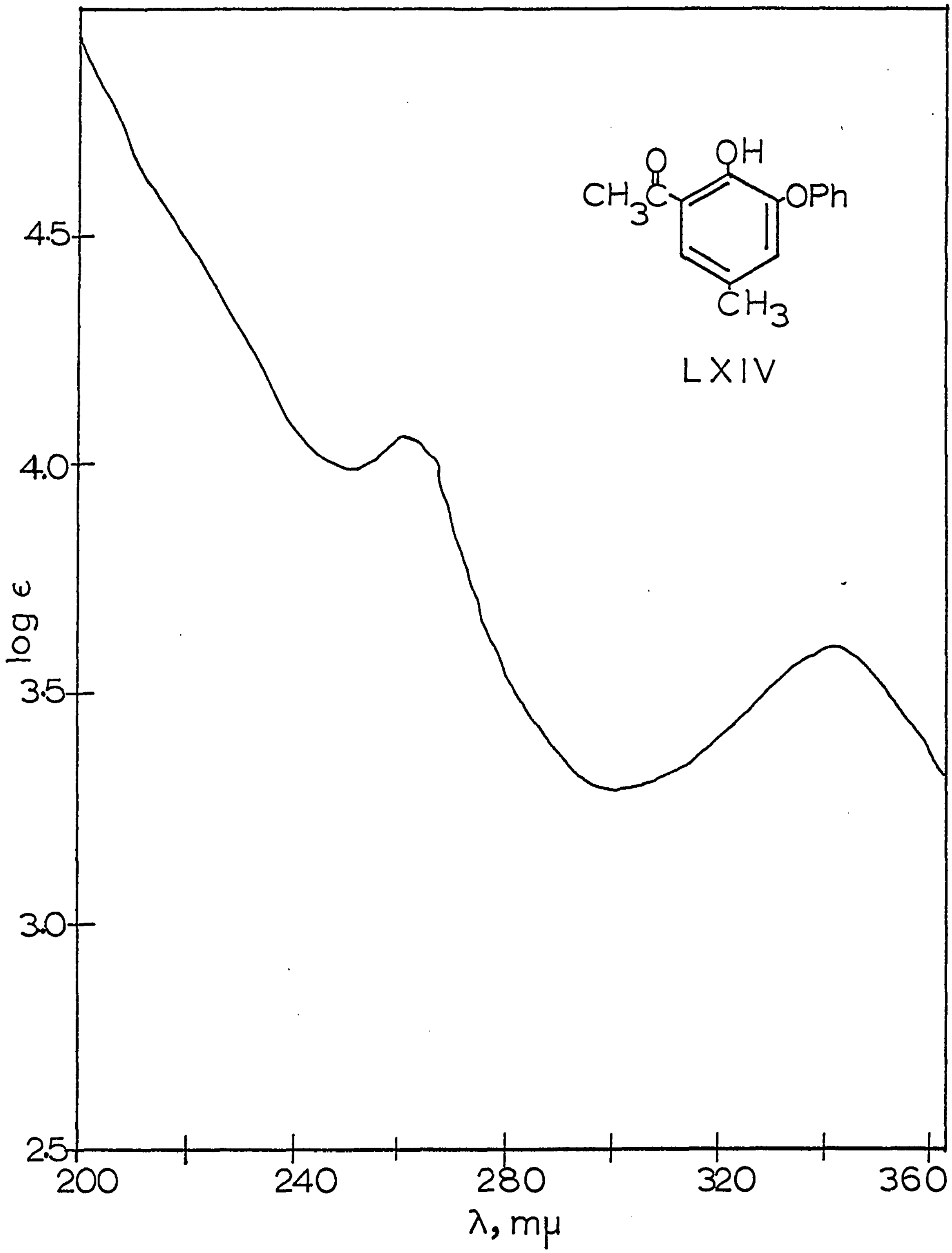

CCl$_4$
O
HO
CH$_3$C
OPh
CH$_3$
-1.98
3.06
7.46
7.76
TMS
TAU

Figure 28. Ultraviolet spectrum of 2-thiophenoxy-4,5-benztropone (LVa)



LVa

Figure 29. Ultraviolet spectrum of 2-hydroxy-3-phenoxy-5-methylacetophenone (LXIV)


log ε
4.5
4.0
3.5
3.0
2.5
200
240
280
320
360
λ, mμ
OH
$CH_3C$
O
OPh
$CH_3$
LXIV

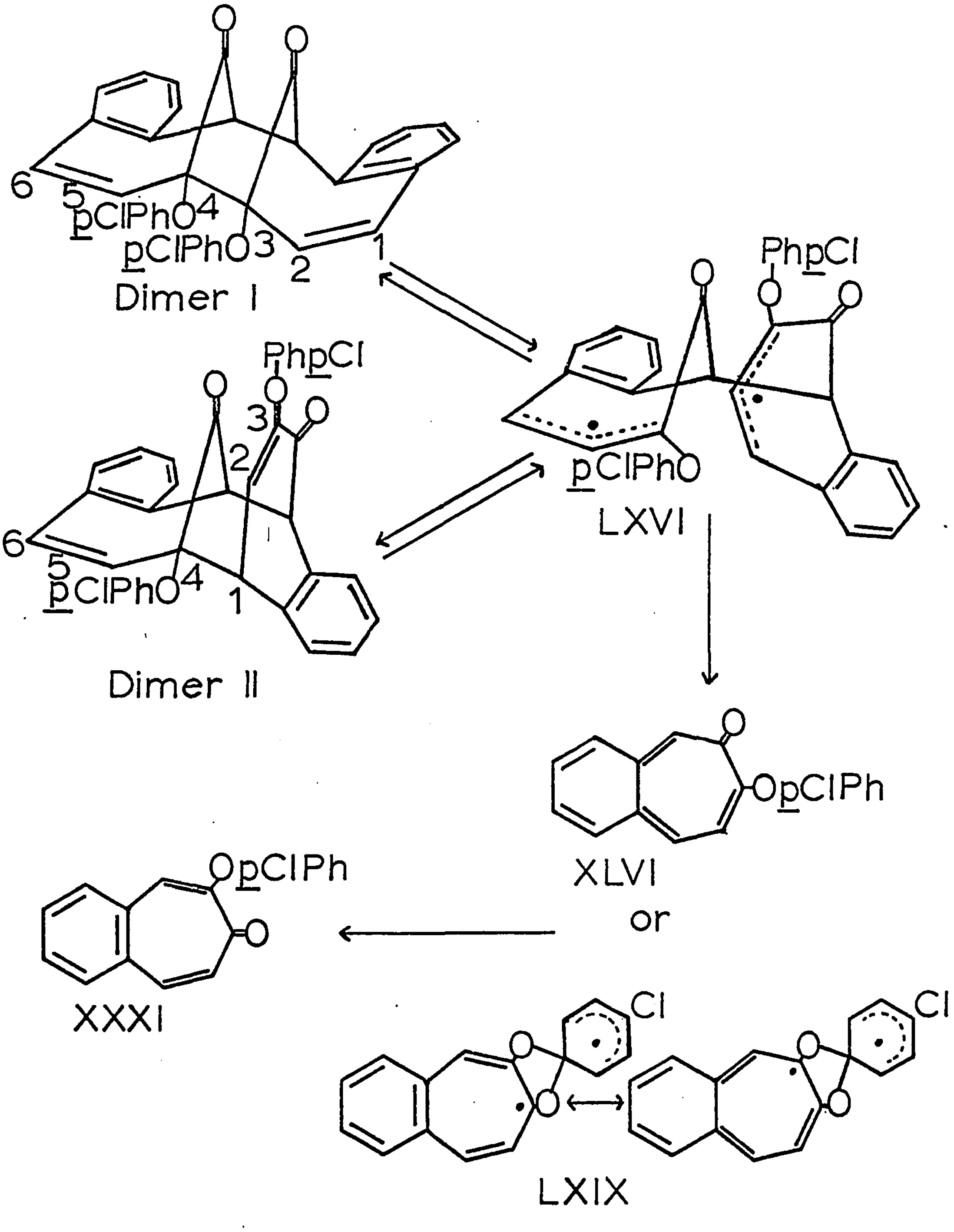
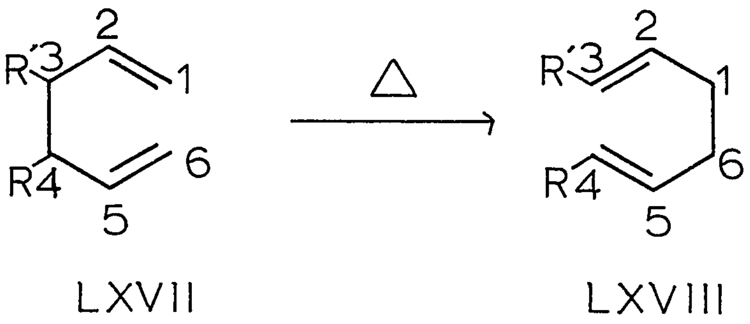


Figure 30. Thermal reactions of Dimer I and Dimer II.

rearrangement of Dimer I to Dimer II would be expected to be favored thermodynamically because of the decrease in angle strain and electronic and steric repulsions. Evidence was found indicating that an equilibrium actually exists between the dimers at the temperature of the rearrangement. After Dimer II was heated at 231-233° for a short period, Dimer I was detected in the mixture by the observation of a pair of peaks in the infrared spectrum at 10.25 and 10.55 μ, a characteristic pattern for Dimer I. Not enough Dimer I was present to attempt to isolate it, as the equilibrium does favor Dimer II.

A formal analogy can be drawn between this rearrangement and the well-known Cope rearrangement (52). The Cope rearrangement is a thermal reaction observed in substituted 1,6-dienes (LXVII) in which a new carbon-carbon bond is formed between carbons 1 and 6 as the original bond between carbons 3 and 4 is broken; at the same time a migration of the double bonds occurs to give the new diene LXVIII. In Dimer I a 1,6-diene is present, but the normal Cope rearrange-



LXVII LXVIII

ment is not observed. The rearrangement of Dimer I to Dimer II involves only half of the diene system; bond breakage occurs between carbons 3 and 4 and bond formation occurs between carbons 1 and 4 with the migration of one double bond (Figure 30, page 83).

The thermal cleavage of the dimers to monomer poses more difficult mechanistic problems. The phenyl shift which occurred in the formation of the dimers must occur again to give XXXI. The possibility of XLVII being an intermediate in the thermal cleavage was tested by cleaving both Dimer I and Dimer II in the presence of maleic anhydride. No adduct of XLVII could be detected in either case. According to the law of microscopic reversibility, it should be possible to reach the same intermediate involved in the cleavage by starting with XXXI. Heating XXXI with maleic anhydride to the same temperature at which cleavage occurs gave no adduct which could be isolated. All of the peaks in the infrared spectrum of the reaction mixture could be accounted for as originating from either XXXI or maleic anhydride. The pyrolysis could involve a bridged intermediate such as LXIX which is not trapped by maleic anhydride.

The thermal reactions of the phenoxybenztropone dimers have some similarities to the reactions of the dicyclopentadiene system studied by Woodward and Katz (53). It is known that cyclopentadiene (LXX) dimerizes readily by a Diels-Alder reaction to give dicyclopentadiene (LXXI) (Figure 31, page 87). The reaction can be reversed by heating LXXI at 200° to give two molecules of cyclopentadiene. To learn more of the detailed mechanism of the Diels-Alder reaction, Woodward and Katz investigated the thermal reactions of a set of hydroxy-substituted dicyclopentadienes. They found that by heating 1-α-hydroxydicyclopentadiene (LXXII) at 140°, *syn*-8-hydroxydicyclopentadiene (LXXIII) is formed. Heating 1-β-hydroxydicyclopentadiene (LXXIV) at 140° gives *anti*-8-hydroxydicyclopentadiene (LXXV). Both reactions were found to involve an equilibrium between the two isomers, although in the latter case the equilibrium lies far to the side of LXXV because of steric effects. In both reactions the stereochemical integrity is maintained. No LXXV is formed from LXXII and no LXXIII is formed from LXXIV. Additional experiments in which the optically active alcohols underwent the isomerization with complete retention of optical integrity demonstrated beyond doubt that the reaction involves the cleavage of only one bond (between *a* and *b*) joining the two halves of the dimer. At the same time a new bond (between *c* and *f*) is formed while the other bond (between *e* and *d*) remains intact. On the basis of this fact and the additional knowledge that the cleavage of the other bond (between *e* and *d*) will occur at a higher temperature, Woodward and Katz argued that the

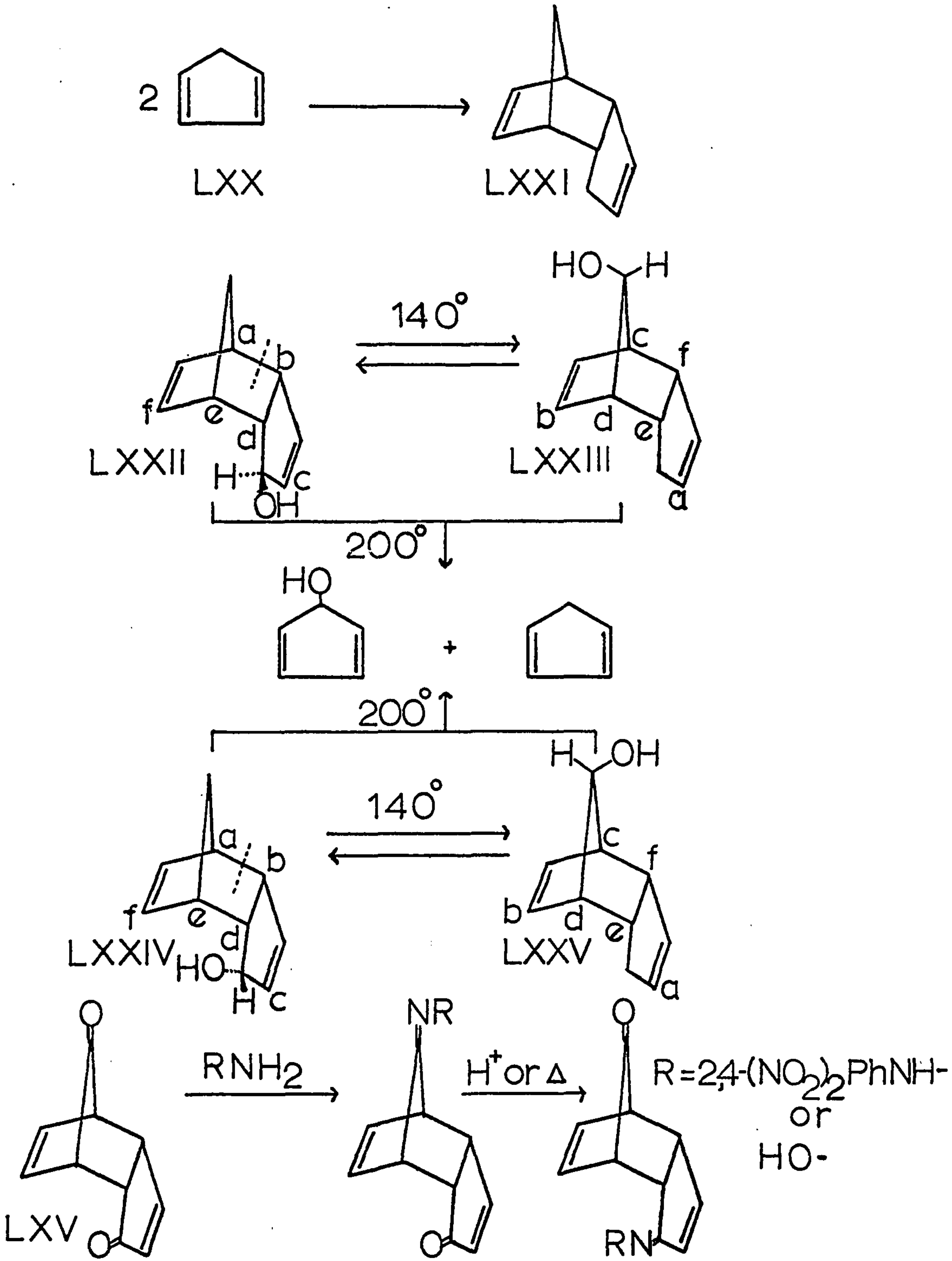


Figure 31. Thermal rearrangements of the dicyclopentadiene series

dimerization reaction must also be a two-stage process. Other dicyclopentadiene derivatives have been found to undergo similar reactions. An example is the recent report by Baldwin (54) of the rearrangement of mono-Schiff bases derived from dicyclopentadienone (LXXVI).

The similarity of the reactions just described to those of the phenoxybenztropone dimers is obvious. That one of the bonds between the two halves of Dimer I can be severed while maintaining the integrity of the other is demonstrated by its rearrangement to Dimer II. That both bonds can be cleaved at a higher temperature has also been demonstrated. The dimerization of the phenoxybenztropones is, at least formally, a four-centered reaction analogous to the Diels-Alder reaction, although the former is a photochemical reaction. Probably the most important difference between the two reactions is that the rearrangement of the cyclopentadiene dimers is actually a Cope rearrangement; the rearrangement of Dimer I to Dimer II is not.

## Mechanisms for Dimerization

Any mechanism for the formation of the phenoxybenztropone photodimers must meet certain requirements. In the 2-phenoxy-4,5-benztropone (XXIX) series it has been established that Dimer B (corresponding to Dimer I) is not derived photochemically from Dimer A (corresponding to Dimer II). But it has not been established that Dimer A is derived from Dimer B, since Dimer A is destroyed faster than Dimer B. Observation of the products isolated from irradiation of 2-(p-chlorophenoxy)-4,5-benztropone (XXXI) indicate that the same conclusions can be made for Dimer I and Dimer II. It is known that Dimer I is converted to Dimer III on irradiation and to Dimer II on thermal rearrangement. It would seem reasonable that the primary mechanistic problem is to account for the formation of Dimer I. Any mechanism must account for an exchange in relative positions of the phenoxy groups and carbonyl groups in going from XXXI to the dimers. The mechanism must also account for the stereochemistry of dimers in which the phenoxy groups and carbonyl bridges are eclipsed.

A study of the isomerizations and rearrangements of other tropolone systems (1-17) suggests that consideration of a mechanism envisaged as involving polar intermediates would not be out of order in the case of the phenoxybenztropones. The propensity of the tropolones to form bicyclic ring systems on irradiation leads one to a consideration of Mechanism A shown in Figure 32, page 90. Polarization of the carbonyl and a rearrangement of the double bonds gives the intermediate LXVII. Return of the electron pair on the carbonyl oxygen and migration of the phenyl group gives a

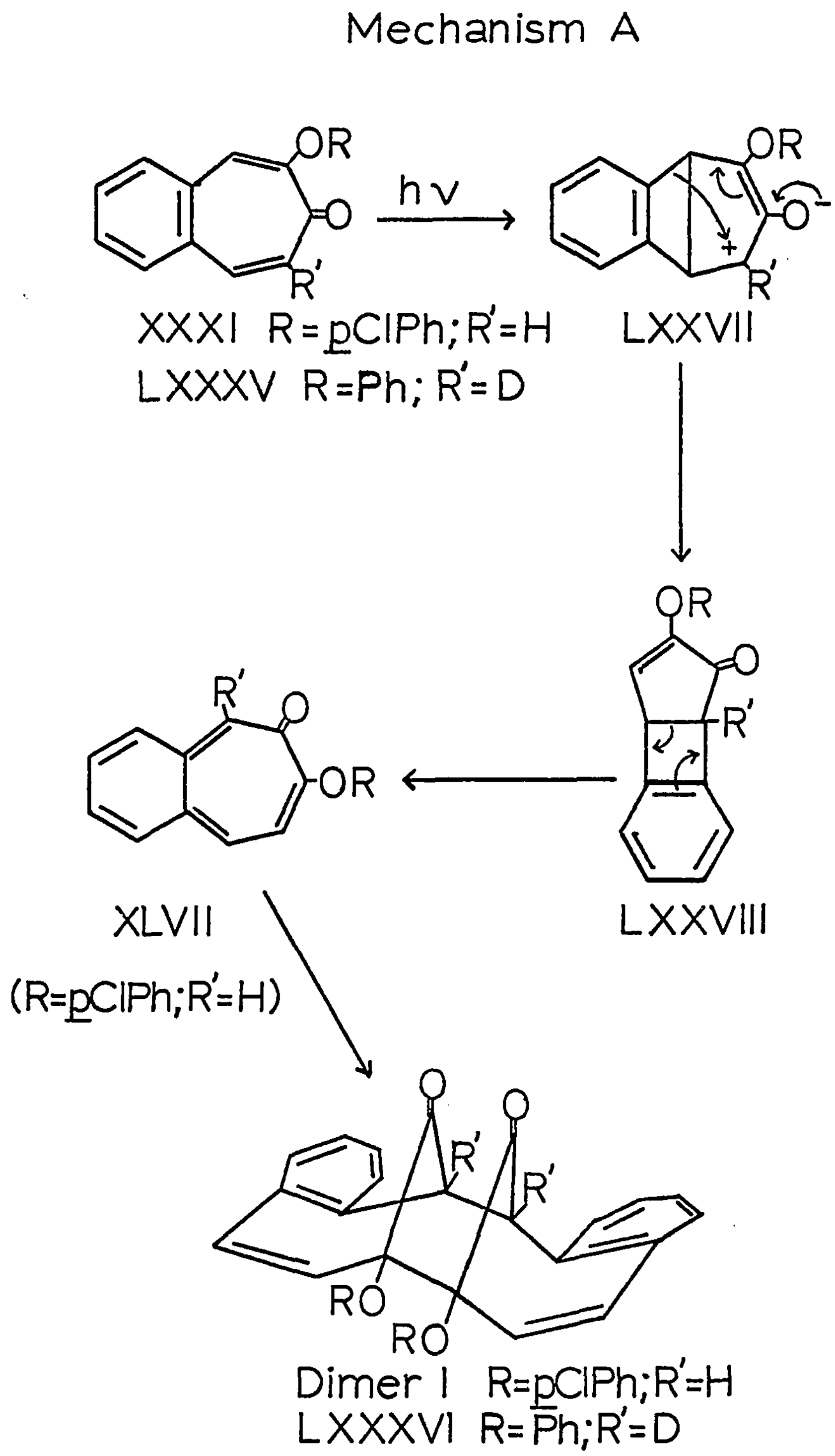


Figure 32. Mechanism A for the formation of Dimer I

benzobicyclo[3.2.0]heptadienone (LXXVIII). Opening of the bicyclic system to a seven-membered ring gives the previously discussed intermediate XLVII which can dimerize to give Dimer I. The fact that all attempts to trap the intermediate XLVII have failed casts some doubt on the validity of Mechanism A. Nor is it obvious why the intermediate XLVII should dimerize to give the observed stereochemistry.

An alternate Mechanism B is shown in Figures 33 and 34, pages 92 and 93. The initial step can be either (a) the formation of a ground state complex (probably with the molecules aligned with dipoles opposed as in LXXIX) which is excited by irradiation, or (b) the collision of a photochemically excited molecule (LXXX) with a ground state molecule. In either event the species formed is LXXXI in which the two molecules are joined by a bond between the two carbonyl carbons. An oxygen-oxygen phenyl shift analogous to the phenyl migrations previously mentioned (45-47) gives LXXXII via the bridged intermediate LXXXIII. Rotation about the bond between the two parts of the molecule gives LXXXIV which can form Dimer I by coupling between the two radicals.

Mechanism B accounts for the phenyl migration without any rearrangement of the carbon atoms in the tropolone ring. It does not involve the rearranged monomer unit XLVII. It also accounts for the observed stereochemistry of Dimer I.

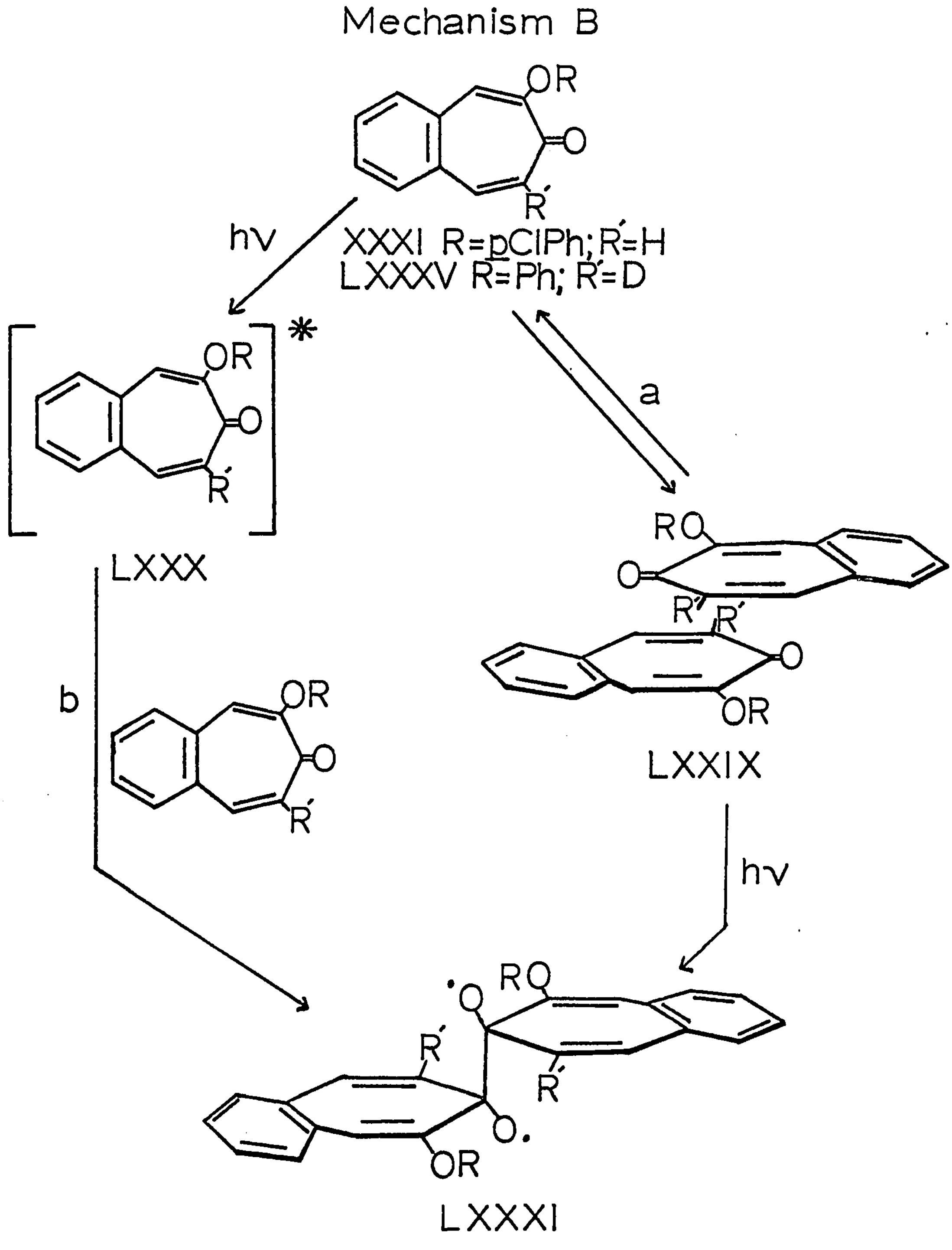


Figure 33. Mechanism B for the formation of Dimer I - Part 1

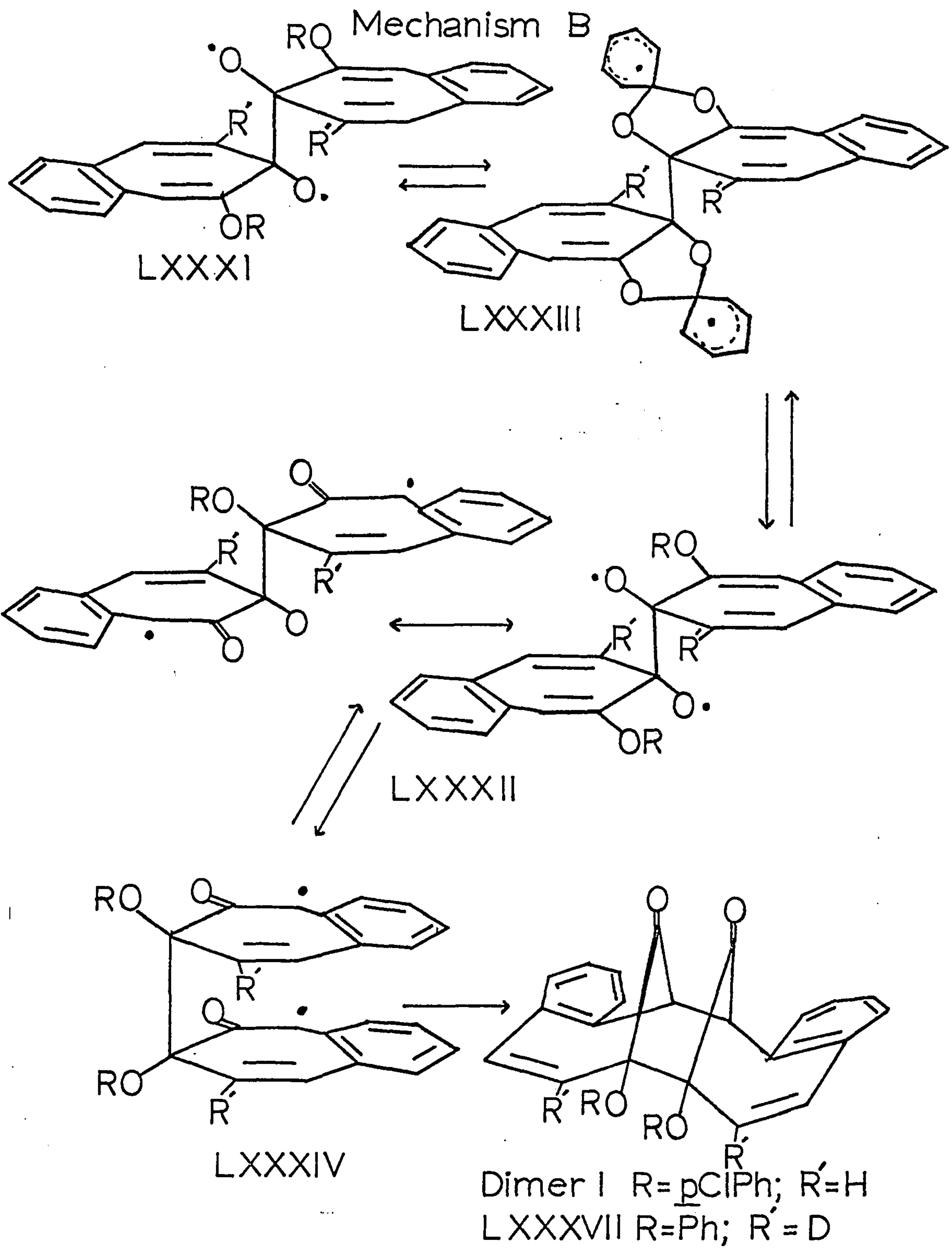


Figure 34. Mechanism B for the formation of Dimer I - Part 2

A choice between Mechanisms A and B can be made on the basis of a deuterium labeling experiment. 2-Phenoxy-4,5-benztropone-7-d (LXXXV) was synthesized by condensing o-phthalaldehyde with phenoxy-2-propanone-$d_5$. The deuterated phenoxybenztropone was irradiated to give the dimer corresponding to Dimer I as shown by its infrared spectrum (Figure 35, page 97). It will be noted that Mechanism A would give dimer LXXXVI with the deuterium at the bridgehead position. Mechanism B would give dimer LXXXVII with the deuterium at the β-carbon of the styryl double bond. The nuclear magnetic resonance spectrum (Figure 36, page 99) of the deuterated dimer indicates clearly the position of the deuterium. The bridgehead proton is apparent at 5.95 $\tau$. The olefinic region is very different from that of the undeuterated dimer. The higher field absorption from the β-proton of the styryl double bond at 4.12 $\tau$ is absent while the lower field absorption of the α-proton at 3.38 $\tau$ appears as a singlet. The deuterated dimer definitely has structure LXXXVII.

Mechanism A can be eliminated from consideration, as can any other mechanism altering the relative position of carbon-7 in the tropolone ring. Mechanism B is favored for the formation of Dimer I by best accounting for all of the experimental observations.

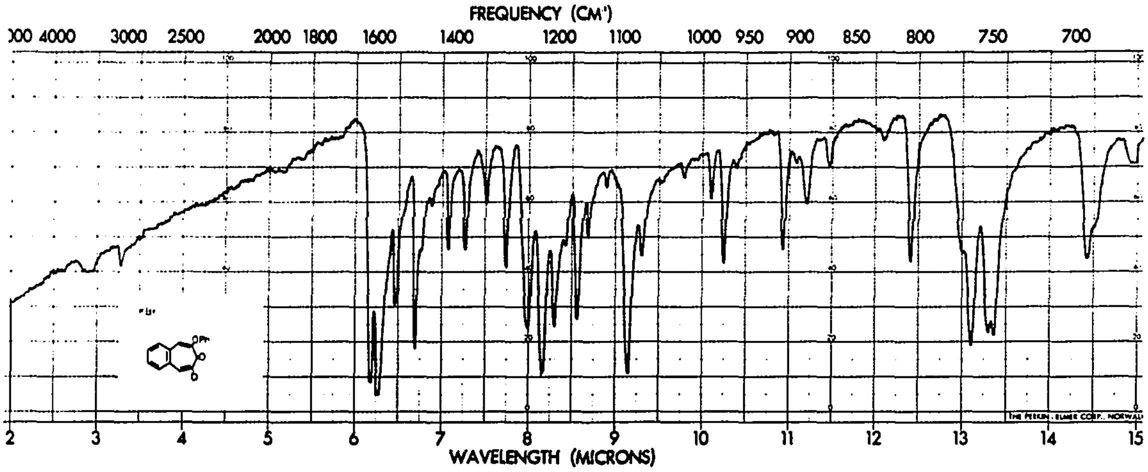
Dimer II may be formed from Dimer I by a photochemical process, or it may be formed from a vibrationally excited state of Dimer I. Dimer III can be accounted for by an intramolecular photochemical addition of the styryl double bonds of Dimer I.

Little can be said about the mode of formation of the new photoproduct obtained from the irradiations in the presence of oxygen until the structure of the so called "Dimer IV" is determined. From what is known to this point the process must be drastically different from that involved in the formation of the other photoproducts. Oxygen evidently plays some role in the reaction to bring about the replacement of one of the carbon atoms from the original molecule with an oxygen atom. For the chemist with an unsatisfied curiosity, the perpetual parade of unanswered questions provides the only incentive necessary to drive him to greater and deeper investigation.

Figure 35. Infrared spectra

Top - 2-phenoxy-4,5-benztropone-7-d (LXXXV)

Bottom - Dimer B-$\underline{d}_2$ (LXXXVII)


FREQUENCY (CM⁻¹)
)00 4000 3000 2500 2000 1800 1600 1400 1200 1100 1000 950 900 850 800 750 700
WAVELENGTH (MICRONS)
2 3 4 5 6 7 8 9 10 11 12 13 14 15
OPh
O
O
THE PERKIN-ELMER CORP., NORWALK

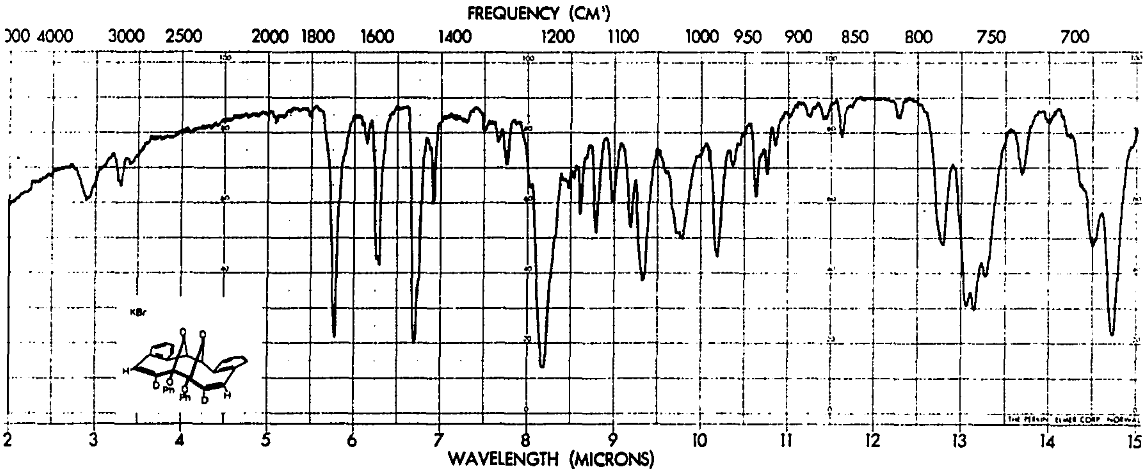
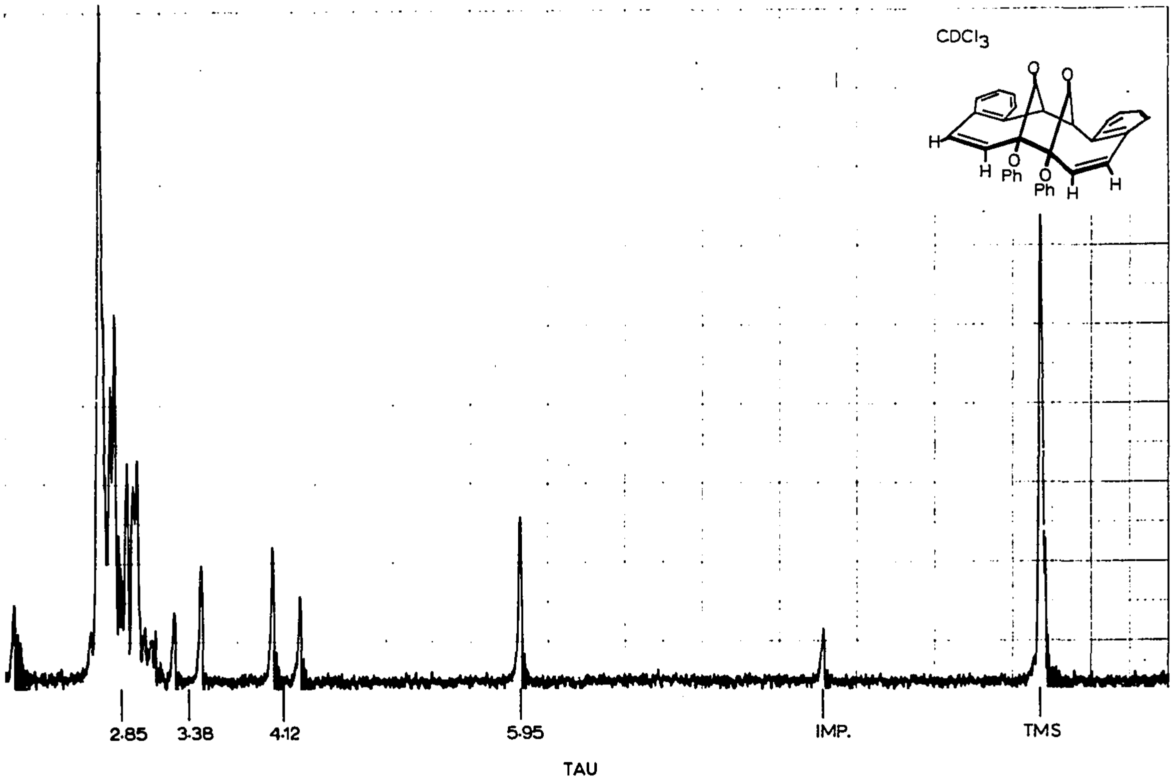
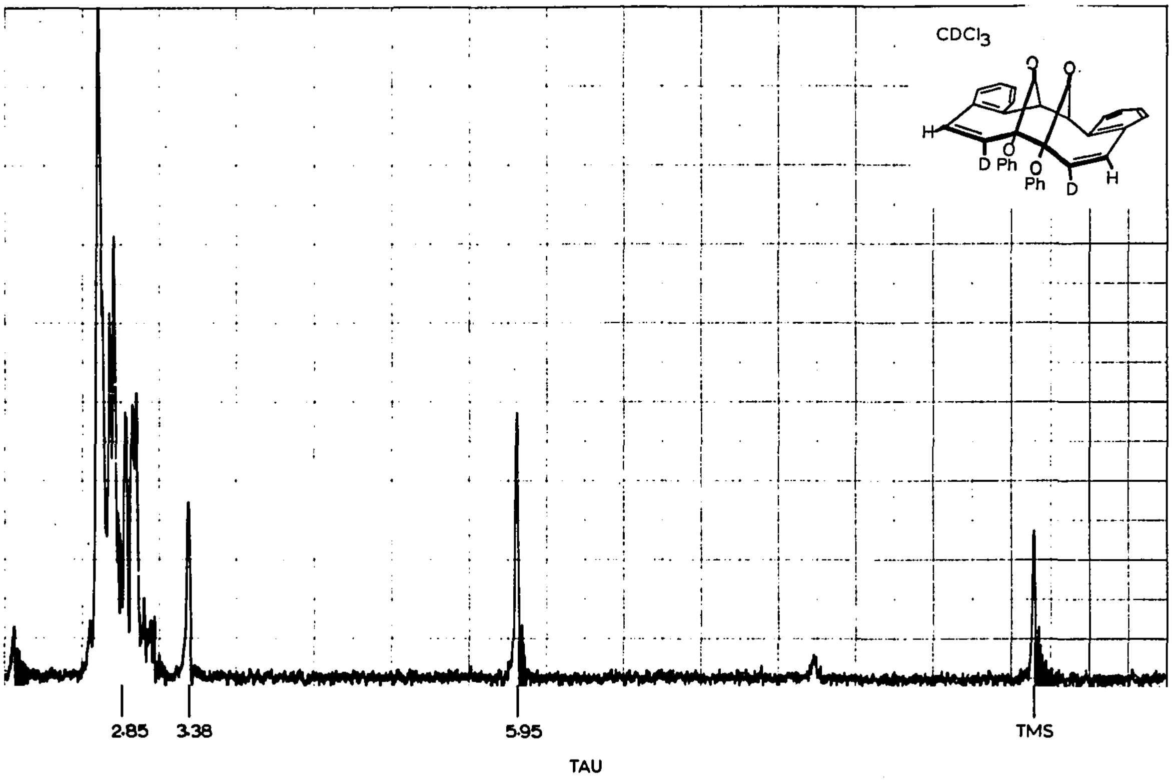

FREQUENCY (CM⁻¹)
)00 4000 3000 2500 2000 1800 1600 1400 1200 1100 1000 950 900 850 800 750 700
WAVELENGTH (MICRONS)
2 3 4 5 6 7 8 9 10 11 12 13 14 15
KBr
H
Ph
Ph
H
THE PERKIN-ELMER CORP., NORWALK

Figure 36. Nuclear magnetic resonance spectra

Top - Dimer B

Bottom - Dimer B-$\underline{d}_2$ (LXXXVII)


CDCl3
O
O
H
H
Ph
O
Ph
H
H
2·85
3·38
4·12
5·95
IMP.
TMS
TAU


CDCl3
O
O
H
D
Ph
O
Ph
D
H
2·85
3·38
5·95
TMS
TAU

# EXPERIMENTAL

## Instruments and Methods

All melting points are uncorrected and were measured on a Kofler microscope hot stage equipped with a polarizer.

The ultraviolet spectra were obtained in 95% ethanol solution unless otherwise noted. The spectra and absorbance measurements were recorded on a Beckman Model DK-2A spectrophotometer made available by a grant (NSF-G14916) from the National Science Foundation.

The infrared spectra of all solids were obtained in potassium bromide pellets unless otherwise indicated; the spectra of liquids were obtained with capillary film cells. The spectra were recorded on a Perkin-Elmer Model 21 spectrometer.

The nuclear magnetic resonance spectra were run in deuteriochloroform unless otherwise indicated. The spectra were measured on a Varian Associates Model HR-60 spectrometer operating at 60 Mc. Spectra were calibrated by the side band technique using tetramethylsilane as internal standard. Chemical shifts are reported as $\tau$-values (55).

Molecular weights were measured with a vapor pressure osmometer assembled by Mr. T. A. Rettig.

The analyses were performed by Schwarzkopf Microanalytical Laboratory, Woodside, New York, unless otherwise noted.

Ethyl acetate-washed alumina was prepared by soaking chromatography grade alumina (Chicago Apparatus Co., 80-200 mesh) in ethyl acetate for 5-6 days. The alumina was filtered with suction, washed a few times with distilled water, and dried at 110-125° for 45 hours.

## Experimental for the Synthesis and Irradiation of the 2-(*p*-Halophenoxy)-4,5-benztropones

### Preparation of 2-(*p*-chlorophenoxy)-4,5-benztropone (XXXI)

The method of Tarbell *et al*. (26) was used to prepare the substituted phenoxybenztropones. *p*-Chlorophenoxyacetone (XXX, Y = Cl) (36.7 g.) prepared by the method of Hurd and Perletz (56) and *o*-phthalaldehyde (25 g.) were dissolved in methanol (1400 ml.) and water (2000 ml.). A solution of sodium hydroxide (5 g.) in 50% methanol (150 ml.) was added with stirring. The solution soon turned from yellow to cloudy-cream in color, then to brown. The mixture was allowed to sit at room temperature for 5 days. The mixture was then filtered to give light brown crystals. Recrystallization from 2-propanol gave XXXI (12.4 g., 23.5%) as tan crystals, m.p. 124-126°. A sample was recrystallized twice from 2-propanol and then from benzene for analysis, m.p. 127-127.5. The ultraviolet spectrum (Figure 15, page 47) and infrared spectrum (Figure 8, page 33) are typical for the 4,5-benztropolone system (26, 27). The nuclear magnetic resonance spectrum is shown in Figure 11, page 39.

Anal. Calcd. for $C_{17}H_{11}ClO_2$: C, 72.22; H, 3.92; Cl, 12.54. Found: C, 72.43; H, 3.91; Cl, 12.60.

## Preparation of 2-(p-bromophenoxy)-4,5-benztropone (XXXII)

The same procedure was used to prepare XXXII from p-bromophenoxyacetone (XXX, Y = Br) (44.7 g.) and o-phthalaldehyde (25 g.). Recrystallization from 2-propanol gave light brown needles (9.9 g., 18%), m.p. 130-132°. A sample was recrystallized from 2-propanol to give almost colorless plates, m.p. 123-124°. (The compound has two different crystalline forms, with different melting points. The colorless plates were formed when a hot solution was filtered into a cold flask.)

Anal. Calcd. for $C_{17}H_{11}BrO_2$: C, 62.40; H, 3.39; Br, 24.43. Found: C, 62.40; H, 3.42; Br, 24.13.

## Irradiation of 2-(p-chlorophenoxy)-4,5-benztropone (XXXI)

A. A solution of XXXI (6.8 g.) in tetrahydrofuran (251 ml.), freshly distilled from lithium aluminum hydride, was placed in an immersion irradiation apparatus. The solution was flushed with nitrogen for 20 minutes. The irradiation was done with a Hanovia Type A 550-watt high-pressure mercury arc lamp in a Pyrex well. The solution was stirred with a magnetic stirrer and cooled with tap water running through the well. The progress of the reaction was followed by removing aliquots and measuring the ultraviolet spectra. After 19 hours the ultraviolet spectrum showed that the absorbance of the peak at 274 mμ was 47% of its original value. A brown polymer layer had formed on the well which made the last few hours of irradiation inefficient. The solvent was removed under reduced pressure on a rotary evaporator to give a brown resin. (In some irradiations the mixture was dissolved in a small amount of benzene at this point and most of the Dimer I crystallized on sitting). The irradiation mixture was dissolved in 1:4 Skelly B-benzene. The solution was poured onto a 1-1/2" x 14" column prepared with 400 g. of ethyl acetate-washed alumina. Elution of the column with 800 ml. of 1:4 Skelly B-benzene gave Dimer I (XXXVIII). Recrystallization from benzene containing a few drops of Skelly B gave 930 mg. of colorless crystals, m.p. 225-226°. The yield was 16% based on unrecovered starting material. An inspection of the infrared spectrum (Figure 9, page 35) and the nuclear magnetic resonance spectrum (Figure 11, page 39) showed Dimer I to be analogous to the Dimer B obtained by Pasto (24) from the irradiation of 2-phenoxy-4,5-benztropone (XXIX). The molecular weight of Dimer I was determined by the vapor pressure osmometric method to be 521 (calcd., 565). The ultraviolet spectrum is shown in Figure 16, page 49.

Anal. Calcd. for $C_{34}H_{22}Cl_2O_4$: C, 72.22; H, 3.92; Cl, 12.54. Found: C, 72.47; H, 4.10; Cl, 12.50.

Elution with 600 ml. of 1:3 Skelly B-benzene yielded Dimer II (XL) (180 mg., 3.2%) as colorless hexagonal plates after recrystallization from ethanol-chloroform, m.p. 222-224°. Inspection of the infrared spectrum (Figure 9, page 35) and nuclear magnetic resonance spectrum (Figure 12, page 41) showed Dimer II to be analogous to Dimer A obtained from XXIX (24). The ultraviolet spectrum is shown in Figure 16, page 49. The molecular weight of Dimer II measured by the osmometric method was found to be 569 (calcd., 565).

Anal. Calcd. for $C_{34}H_{22}Cl_2O_4$: C, 72.22; H, 3.92; Cl, 12.54. Found: C, 72.43; H, 3.72; Cl, 12.56.

Elution of the column with 600 ml. of benzene gave starting material (XXXI) (1.1 g.), identified by its melting point and infrared spectrum. Elution with mixtures of benzene, ether, chloroform and methanol gave brown tars (about 2 g.) which were not further characterized.

B. An irradiation of 2-(p-chlorophenoxy)-4,5-benztropone (XXXI) (4.0 g.) in freshly distilled tetrahydrofuran (290 ml.) was allowed to proceed until the absorbance at 274 mμ decreased to 15% of its original value (17 hours; no brown polymer formed on the immersion well). A Hanovia Type A lamp in a Pyrex well was used as before. The solvent was removed from the mixture which was chromatographed on a 1-1/2" x 14" column prepared with 350 g. of ethyl acetate-washed alumina. Elution with 1.2 l. of 2:3 Skelly B-benzene gave nothing. Elution with 2.4 l. of 1:3 Skelly B-benzene gave Dimer I (710 mg., 18%), identified by its melting point and infrared spectrum.

Elution of the column with 1.6 l. of 1:9 Skelly B-benzene gave Dimer III (XXXVI) (100 mg., 2.5%). Recrystallization from ethanol-chloroform gave colorless needles, m.p. 233-234.5°. By a comparison of the infrared spectrum (Figure 10, page 37) and the nuclear magnetic resonance spectrum (Figure 13, page 43), it was found that Dimer III corresponds to the dimer obtained by Chapman and Smith (25, p. 255) on the irradiation of Dimer B. The ultraviolet spectrum is shown in Figure 17, page 51.

_Anal_. Calcd. for $C_{34}H_{22}Cl_2O_4$: C, 72.22; H, 3.92; Cl, 12.54. Found: C, 72.10; H, 4.00; Cl, 12.69.

Elution of the column with 1:3 ether-benzene (2.4 l.), ether (1 l.), chloroform (0.5 l.), and 1:9 methanol-chloroform (1 l.) gave brown tars (1.8 g.) which were not characterized. Some material did not elute from the column.

### Irradiation of 2-(p-bromophenoxy)-4,5-benztropone (XXXII)

A solution of XXXII (5.0 g.) in freshly distilled tetrahydrofuran (200 ml.) was flushed with nitrogen for about 20 minutes. The solution was irradiated with a Hanovia Type A lamp using a Pyrex well. After 9 hours the absorbance at 275 mμ had decreased to 10% of its original value. The mixture remaining after removal of the solvent was dissolved in 2:3 Skelly B-benzene. The mixture was eluted through a column prepared with 375 g. of ethyl acetate-washed alumina. The first 6 fractions eluted with 600 ml. of 2:3 Skelly B-benzene gave the bromo-dimer XLII (300 mg., 6%), m.p. 227-229°. Dimer XLII was shown to be the bromo-analogue of Dimer I by the similarity of the infrared spectrum (Figure 9, page 35) and nuclear magnetic resonance spectrum (Figure 12, page 41).

Anal. Calcd. for $C_{34}H_{22}Br_2O_4$: C, 62.40; H, 3.39; Br, 24.43. Found: C, 62.75; H, 3.06; Br, 24.42.

Other fractions from the chromatography column consisted of tars and solids which were not further characterized.

### Irradiation of 2-(p-chlorophenoxy)-4,5-benztropone (XXXI) in presence of oxygen

A solution of XXXI (3.85 g.) in freshly distilled tetrahydrofuran (265 ml.) was irradiated with a Hanovia Type

A lamp in a Pyrex well. Oxygen was bubbled into the solution during the irradiation. After five hours the absorbance at 274 mμ had decreased to 8% of its original value. The solvent was removed on a rotary evaporator to give a yellow viscous oil (8 g.). The material was dissolved in 1:3 Skelly B-benzene and chromatographed on a 1-1/2" x 20" column prepared with 300 g. of silica gel. Elution with 600 ml. of 1:3 Skelly B-benzene gave nothing. Elution with 800 ml. of 1:9 Skelly B-benzene gave Dimer I. Recrystallization from benzene-Skelly B yielded colorless crystals (86.1 mg., 2.2%), m.p. 228-229°.

Elution of the column with an additional 800 ml. of 1:9 Skelly B-benzene gave a compound which was recrystallized from 95% ethanol to yield slightly yellow rhombic crystals (35.3 mg., 0.92%), m.p. 158-160°. The compound was designated "Dimer IV." The infrared spectrum and nuclear magnetic resonance spectrum are shown in Figure 10, page 37, and Figure 14, page 45. The ultraviolet spectrum is represented in Figure 18, page 53. An osmometric molecular weight determination gave a value of 341; calculated, 575. An attempted mass spectrum showed an intense peak at 280 which disappeared rapidly after the first scan, evidently from an impurity.

<u>Anal</u>. Calcd. for $(C_{16}H_{11}ClO_3)_n$: C, 67.02; H, 3.87; Cl, 12.38; O, 16.74. Found: C, 66.97; H, 3.88;

Cl, 12.55; O, 16.66.

Elution of the column with 1800 ml. of benzene gave brown tars with the odor of phenol. Elution with 800 ml. of chloroform and 1500 ml. of 1:3 methylene chloride-chloroform gave yellow oils which showed strong peaks at 5.65 and 5.82 μ in the infrared spectrum. The nuclear magnetic resonance spectrum showed complex multiplets at 7.47, 5.77, 6.17, 7.70 and 8.17 $\tau$ and a singlet at 2.00 $\tau$. These products were assumed to be oxidation products from tetrahydrofuran (33).

One sample of XXXI (2.5 g.) was irradiated in the presence of oxygen for 10 hours. Chromatography of the mixture on Woelm neutral alumina, activity II, gave Dimer I (75 mg., m.p. 224-226°) and Dimer III (11.5 mg., m.p. 230-233°). No "Dimer IV" was isolated from this irradiation.

### Irradiation of Dimer I

Dimer I (530 mg.) was dissolved in ether (170 ml.) and enough tetrahydrofuran (25 ml.) to dissolve the material. The solution was flushed with nitrogen for 30 minutes, then irradiated with a Hanovia Type A immersion lamp in a quartz well. After 90 minutes the irradiation was stopped. The tetrahydrofuran was removed on a rotary evaporator. The brown residue was dissolved in 1:3 Skelly B-benzene and eluted through a 3/4" x 8" column prepared with 50 g. of ethyl acetate washed alumina. Elution with 125 ml. of 1:3 Skelly B-benzene gave Dimer I (100 mg.). Further elution with 100 ml. of the same solvent mixture gave Dimer III (175 mg.) which was identified by its infrared spectrum and melting point. Elution with additional Skelly B-benzene and benzene gave unidentified tars.

### Treatment of Dimer I with sulfuric acid

A sample of Dimer I (305 mg.) was placed in a small Erlenmeyer flask. To the flask was added concentrated sulfuric acid (2.3 ml.). The mixture was heated over a steam bath for ten minutes after which time most of the solid had dissolved to give an amber solution. The solution was cooled and diluted with distilled water (20 ml.) producing a flocculent yellow precipitate. The precipitate was filtered and washed with water. An infrared spectrum ($CHCl_3$) of the precipitate showed peaks at 5.84, 5.96 and 6.11 μ in the carbonyl region. The precipitate was dissolved in 5% potassium hydroxide solution (25 ml.) giving a yellow solution. The solution was extracted with chloroform. The extract was dried with sodium sulfate, filtered, and evaporated to dryness on a rotary evaporator to give a dirty-yellow solid. Recrystallization from ethanol-chloroform gave colorless plates (160 mg.), m.p. 218-223°. The infrared spectrum showed peaks at 5.84 and 5.97 μ. Both the melting point and infrared spectrum were identical with those of Dimer II (XL).

The basic aqueous layer remaining from the extraction was acidified with 6N hydrochloric acid solution causing the disappearance of the yellow color. The acidic solution was extracted with chloroform. The extracts were dried, filtered and evaporated to dryness on a rotary evaporator to give yellow plates. Recrystallization from ethanol gave brown plates (34.7 mg.). When a melting point was taken, the irregular plates sublimed to form hexagonal plates at about 145° and melted at 157-159°. Concentration of the mother liquors gave an additional crop of darker brown crystals (12 mg.), m.p. 154-157°. The melting point, infrared spectrum (Figure 8, page 33) and ultraviolet spectrum (Figure 19, page 55) were the same as those reported by Tarbell *et al*. (26, 57) for 4,5-benztropolone (XXXIV).

### Treatment of Dimer II with sulfuric acid

A small sample of Dimer II (30 mg.) was placed in a small flask. Concentrated sulfuric acid (1 ml.) was added to dissolve the material. The solution was heated on a steam bath for five minutes during which it turned to a dark brown color. The solution was cooled and diluted with water (5 ml.) to give a yellow precipitate. The precipitate was filtered and dried. An infrared spectrum ($CHCl_3$) of the crude product still showed peaks at 5.83 and 5.96 μ from unreacted Dimer II. The hydrolysis product was separated from unreacted Dimer II by its greater solubility in ethanol. An infrared spectrum of the material showed it to be 4,5-benztropolone (XXXIV), m.p. 158-160°.

## Treatment of Dimer III with sulfuric acid

A sample of Dimer III (2.3 mg.) was treated with 3 drops of concentrated sulfuric acid to give an amber solution. The solution was diluted with water (2 ml.) and allowed to cool. The solution was extracted with chloroform which was then removed by evaporation. The brown residue was dissolved in 95% ethanol (5 ml.) and diluted 100 times. An ultraviolet spectrum of the product showed a maximum at 276 mμ. Upon addition of a drop of 1N sodium hydroxide to both cells, the spectrum changed to show maxima at 215, 284 and 294sh mμ (Figure 20, page 57). The position and shift of the long wavelength portion of the spectrum were the same as those observed for 4,5-benztropolone (XXXIV) (Figure 19, page 55).

## Treatment of "Dimer IV" with sulfuric acid

A sample of "Dimer IV" (2 mg.) was treated with a few drops of concentrated sulfuric acid and heated on a steam bath for about five minutes. The solution was then cooled, diluted with water and extracted with chloroform. The chloroform was removed by evaporation. The residue was dissolved in 95% ethanol (10 ml.) and diluted 10 times. An ultraviolet spectrum of the solution showed maxima at 229, 261, 272sh and 280 mμ (Figure 20, page 57). Addition of a drop of 1N sodium hydroxide solution to each cell shifted the long wavelength maxima to a single maximum at 326 mμ. The maximum at 225 mμ shifted slightly to 229 mμ.

### Identification of the hydrolyzed phenol

Paper chromatography was used to identify the phenol liberated from the acid hydrolysis of Dimer I. A sheet of Whatman No. 1 paper (8" x 11") was formed into a cylinder by stapling the two edges together. The materials to be chromatographed were dissolved in benzene. A drop or two of each solution was placed on the base line 3/4" from the bottom. The paper was lowered into a glass cylinder containing an isoamyl alcohol-concentrated ammonium hydroxide-water (30:15:5) solvent system like that used by Siegel and Schlögl (58). After about 24 hours the paper was removed, dried, and sprayed with a diazotized sulfanilic acid solution prepared by the procedure of Mann and Leone (59).

Dimer I was treated with sulfuric acid as before. After the solution was diluted with water, the precipitate was filtered with little washing and dissolved in benzene.

Chromatograms of the hydrolysis mixture were run simultaneously with p-chlorophenol, m-chlorophenol, and 4,5-benztropolone. The results with the average Rf values from four runs are shown in Table 1.

Table 1. Paper chromatography of acid hydrolysis products from Dimer I

| Sample | Color | Rf value |
|---|---|---|
| p-Chlorophenol | reddish-brown | 0.81 ± .02 |
| m-Chlorophenol | yellow | .75 ± .04 |
| 4,5-Benztropolone | tan | .90 ± .02 |
| Unknown phenol | reddish-brown | .77 ± .03 |

The color of the hydrolized phenol on spraying with diazotized sulfanilic acid clearly identifies it as p-chlorophenol. The Rf values for the unknown phenol were usually lower than p-chlorophenol, probably because of residual sulfuric acid in the hydrolized product.

### Reduction of Dimer III with sodium borohydride

Dimer III (XXXVI) (80 mg.) dissolved in freshly distilled tetrahydrofuran (3 ml.). To the solution was added sodium borohydride (52 mg.) dissolved in water (1.5 ml.). The solution was stirred with a magnetic stirrer at room temperature for 10 hours. Additional sodium borohydride (13 mg.) in water (1 ml.) and tetrahydrofuran (1 ml.) was added. After an additional 6-1/2 hours the solution was diluted with water (1.5 ml.). The tetrahydrofuran was removed on a rotary evaporator.

The aqueous mixture was extracted with ether. The extract was dried with anhydrous magnesium sulfate evaporated to give a white resinous solid (80 mg.). Recrystallization from benzene-Skelly B and chloroform-Skelly B gave colorless crystals of Dimer III diol (XXXVII) (77 mg.), m.p. 223-225.5°.

Anal. Calcd. for $C_{34}H_{26}Cl_2O_4$: C, 71.71; H, 4.60; Cl, 12.45. Found: C, 71.90; H, 4.86; Cl, 12.39.

An attempt was made to prepare the diacetate of Dimer III diol (65 mg.) by refluxing with acetyl chloride (2 ml.) in benzene (2 ml.) for three hours. The mixture was poured onto ice, extracted with benzene, and washed with 5% sodium hydroxide solution and water. Evaporation of the benzene gave a white resin (40 mg.). A nuclear magnetic resonance of the crude material showed more than one type of methyl group.

## Attempted reduction of "Dimer IV"

A sample of "Dimer IV" (30 mg.) was dissolved in freshly distilled tetrahydrofuran. Sodium borohydride

(25 mg., an excess) was dissolved in water (1 ml.) and added to the solution. The solution was stirred with a magnetic stirrer for 24 hours. It was then diluted with water (4 ml.). The tetrahydrofuran was removed on a rotary evaporator. The remaining aqueous solution was extracted with ether. The ether was dried and evaporated to give a colorless oil. An infrared spectrum of the oil showed a strong hydroxyl absorption (3.03 $\mu$) and only slight carbonyl absorption. A nuclear magnetic resonance spectrum of the product was quite complex, evidently further complicated by impurities. An attempt to purify the material by chromatography through silica gel gave a dark oil with quite different spectra. The reaction was not repeated.

## Experimental for
## Studies of the Dimerization Process

### Irradiation of 2-(p-chlorophenoxy)-4,5-benztropone (XXXI) in the presence of sensitizers

Samples of XXXI (570 mg., 0.2 mole) were placed in eight 18 x 150 mm. Kimax test tubes. In each of the first three pairs of tubes was placed 0.04 mole of one of the following sensitizers with triplet energies ($E_t$) (38) as shown: benzophenone, $E_t$ = 68 kcal./mole; naphthalene, $E_t$ = 61 kcal./mole; benzil, $E_t$ = 54 kcal./mole. No sensitizer was placed in the fourth pair of test tubes. The material in each test tube was dissolved in freshly distilled tetrahydrofuran (20 ml.) and flushed with nitrogen for 20 minutes. The tubes were sealed with rubber septums. They were then placed evenly around a rotating wheel (33 r.p.m.) and irradiated with a Hanovia Type A mercury arc lamp held in a Pyrex water-cooled immersion well about 16 cm. from the nearest tube. The progress of the reaction was followed by removing aliquots periodically and measuring the infrared spectra in the carbonyl region. After 80 hours of irradiation the benztropone peaks at 6.14 and 6.25 μ had decreased in intensity. In all of the samples, peaks appeared at 5.84 and 5.95 μ with a shoulder at 5.76 μ indicating that Dimer I and Dimer II had been formed. The relatively intensities of the peaks of the unsensitized samples were not significantly different from those in the sensitized samples.

### Beer's law plot of 2-(*p*-chlorophenoxy)-4,5-benztropone (XXXI)

The absorbance of XXXI in the ultraviolet region (200-360 mμ) was measured as a function of concentration in tetrahydrofuran and isooctane solutions. Both 1 cm. and 0.1 cm. cells were used for the tetrahydrofuran solutions to cover a broader concentration range. Only the 1 cm. cells were used for isooctane solutions. The absorbance was plotted against concentration at the two maxima (Figure 21, page 62). The calculated ε-values are shown in Table 2 and Table 3. Within experimental error, no deviation from Beer's law was observed. The apparent deviation at the upper and lower limits of measurement can be reasonably attributed to the measuring instrument.

Table 2. Absorbance of 2-(p-chlorophenoxy)-4,5-benztropone (XXXI) in tetrahydrofuran

| Concentration | 235 mμ | | 272 mμ | |
|---|---|---|---|---|
| M x $10^6$ | A | ε x $10^{-4}$ | A | ε x $10^{-4}$ |
| | | 1 centimeter cells | | |
| 2.65 | 0.145 | 5.47 | 0.136 | 5.13 |
| 4.42 | 0.227 | 5.14 | 0.208 | 4.71 |
| 8.83 | 0.332 | 3.76 | 0.381 | 4.31 |
| 17.66 | 0.635 | 3.60 | 0.744 | 4.21 |
| 22.08 | 0.830 | 3.75 | 0.950 | 4.30 |
| 26.49 | 0.992 | 3.74 | 1.160 | 4.38 |
| 35.32 | 1.335 | 3.78 | 1.570 | 4.44 |
| 39.74 | 1.466 | 3.69 | 1.790 | 4.50 |
| 44.15 | 1.784 | 4.04 | - | - |
| | | 0.1 centimeter cells | | |
| 39.7 | 0.090 | 2.26 | 0.070 | 1.76 |
| 44.2 | 0.159 | 3.60 | 0.193 | 4.37 |
| 73.6 | 0.256 | 3.48 | 0.308 | 4.19 |
| 147.2 | 0.538 | 3.65 | 0.641 | 4.35 |
| 294.3 | 1.091 | 3.70 | 1.307 | 4.41 |
| 367.9 | 1.391 | 3.78 | 1.669 | 4.54 |
| 441.5 | 1.715 | 3.88 | - | - |

Table 3. Absorbance of 2-(p-chlorophenoxy)-4,5-benztropone (XXXI) in isooctane

| Concentration $M \times 10^6$ | 234 mμ A | 234 mμ $\epsilon \times 10^{-4}$ | 270 mμ A | 270 mμ $\epsilon \times 10^{-4}$ |
|---|---|---|---|---|
| 6.6 | 0.302 | 4.54 | 0.290 | 4.36 |
| 13.3 | 0.593 | 4.46 | 0.565 | 4.25 |
| 26.6 | 1.172 | 4.41 | 1.121 | 4.21 |
| 39.9 | 1.826 | 4.58 | 1.738 | 4.36 |

## Molecular weight measurements of 2-(p-chlorophenoxy)-4,5-benztropone (XXXI) and 2-phenoxy-4,5-benztropone (XXIX)

Molecular weight measurements of XXXI and XXIX were made with a vapor pressure osmometer in benzene and tetrahydrofuran solutions. Benzil was used as a standard to prepare calibration curves. The molecular weights were not actually calculated but only the observed molar fraction of solute. These values were compared with the actual calculated values of concentration as shown in Table 4. A plot of the resistance values obtained from the osmometer for the benzene solutions is shown in Figure 22, page 64. No indication of aggregation of solute could be noted from these measurements.

Table 4. Osmometric molecular weight data for phenoxybenztropones in benzene and tetrahydrofuran

| Solvent, temp. | 2-Phenoxy-4,5-benztropone<br>Molar fraction x $10^2$ | | | 2-(p-Chlorophenoxy)-4,5-benztropone<br>Molar fraction x $10^2$ | | |
|---|---|---|---|---|---|---|
| | Calcd. | Obsd. | R[a] | Calcd. | Obsd. | R[a] |
| Benzene, 29° | 0.188 | 0.144 | 1.31 | 0.157 | 0.136 | 1.15 |
| | 0.585 | 0.593 | 0.99 | 0.498 | 0.623 | 0.80 |
| | 1.090 | 1.021 | 1.07 | 1.007 | 1.156 | 0.87 |
| Tetrahydrofuran, 25.5° | 0.217 | 0.162 | 1.34 | 0.246 | 0.125 | 1.97 |
| | 0.547 | 0.500 | 1.09 | 0.510 | 0.537 | 0.95 |
| | 1.052 | 1.312 | 0.80 | 0.958 | 1.078 | 0.89 |

[a] Ratio of calculated value to observed value.

Irradiation of 2-phenoxy-4,5-benztropone (XXIX) with dimethyl acetylenedicarboxylate

A solution of 2-phenoxy-4,5-benztropone (XXIX) (9.8 g.) and dimethyl acetylenedicarboxylate (XLVIII (11.7 g.) in tetrahydrofuran (250 ml.) was flushed with nitrogen for 30 minutes. The solutions was irradiated with a Hanovia Type A immersion lamp. After 8 hours an ultraviolet spectrum showed the peak at 274 mμ to be 28% of its original height. The solvent was removed on a rotary evaporator. The tarry residue was dissolved in 1:1 Skelly B-benzene and poured onto a 1-1/2" x 16" column prepared with 470 g. ethyl acetate-washed alumina. Elution with 800 ml. of 1:1 Skelly

B-benzene gave a small amount of oily material. Elution with 1300 ml. of 3:1 Skelly B-benzene and then with 1500 ml. benzene gave Dimer B (2.0 g.) (24), m.p. 209-210°. Elution with 1400 ml. benzene-ether mixtures (3:1 and 1:1) gave 2-phenoxy-4,5-benztropone (1.1 g.). Further elution with benzene-ether, ether, chloroform and methanol gave brown tars and amorphous solids which were not further characterized. No adduct with dimethyl acetylenedicarboxylate was found.

## Experimental for Studies of the Phenyl Shift

### Preparation of 2-thiophenoxy-4,5-benztropone (LVa)

Thiophenoxyacetone (31 g.) prepared by the method of Werner (60) was condensed with o-phthalaldehyde (25 g.) as in the preparation of the phenoxybenztropones (26). The materials were dissolved in methanol (2000 ml.) and water (1750 ml.). Addition of sodium hydroxide (5 g.) in 50% methanol solution (150 ml.) to the solution caused a change in color to cloudy yellow. The mixture was allowed to stand at room temperature for 4 days.

The reaction mixture was filtered to give dirty yellow crystals (1.46 g.). A large amount of tarry material was scraped from the bottom of the reaction beaker. Additional material was obtained by concentrating the reaction mixture and extracting with ether. The product could not be separated easily from the tar by recrystallization from 2-propanol or benzene. Elution of the materials through ethyl acetate-washed alumina with benzene proved to be the most satisfactory method of purification. A total of 13.6 g. (5%) of 2-thiophenoxy-4,5-benztropone (LVa), m.p. 108-109°, was obtained. Recrystallization from 2-propanol gave yellow rods, m.p. 108.5-109.5°. The ultraviolet spectrum (Figure 28, page 80) and infrared spectrum (Figure 26, page 76) are typical for the 4,5-benztropone system. The nuclear magnetic resonance spectrum (Figure 27, page 78) shows peaks only in the aromatic region.

Anal. Calcd. for $C_{17}H_{11}OS$: C, 77.24; H, 4.58; S, 12.13. Found: C, 77.53; H, 4.78; S, 12.41

### Irradiation of 2-thiophenoxy-4,5-benztropone (LVa)

2-Thiophenoxy-4,5-benztropone (1.32 g.) was dissolved in freshly distilled tetrahydrofuran (240 ml.) and flushed with nitrogen for 30 minutes. The solution was irradiated with a Hanovia Type A immersion lamp in a Pyrex well. After 19 hours the ultraviolet spectrum showed the peak at 286 mμ at 60% of its original height. The solvent was removed and an infrared spectrum taken of the residue. The spectrum showed that the mixture contained mostly starting material. Recrystallization from benzene gave 2-thiophenoxy-4,5-

benztropone (LVa).

The irradiation was repeated using tetrahydrofuran containing 5% water. A lead acetate test of the irradiation solution for sulfide ion was negative. After 127 hours of irradiation, only starting material and tars were obtained by eluting the mixture of an alumina column.

Similar results were obtained by irradiating for 200 hours in tetrahydrofuran using a quartz immersion well. No dimer could be isolated.

### Attempted preparation of 2-anilino-4,5-benztropone (LVb)

Anilinoacetone (5.85 g.) prepared by the procedure of Wolf (61) was dissolved in methanol (450 ml.) and water (300 ml.) with o-phthalaldehyde (5.26 g.). The solution was cooled with ice as sodium hydroxide (1.0 g.) in 50% methanol (30 ml.) was added with stirring. The solution was allowed to sit at room temperature for 7 days.

A few crystals which had formed on the bottom of the flask were removed and recrystallized from 2-propanol to give a yellow-brown solid (250 mg.), m.p. 180-190°. An infrared spectrum ($CHCl_3$) showed strong absorption at 5.96, 6.26, 6.40, 6.70, and 6.87 µ. An ultraviolet spectrum in ethanol (c = 10.3 g./l.) showed maxima at 247 mµ (A = 0.46) and 283 mµ (A = 0.34). The material was difficult to recrystallize and would turn to brown tar easily. Not enough material could be obtained in good purity to further characterize it.

An attempt to obtain more product from the tar produced in the condensation by chromatography on alumina gave a yellow fluorescent solid which did not melt below 350°. The ultraviolet and infrared spectra were similar to those of the previous product. A nuclear magnetic resonance spectrum showed peaks in the aromatic region (2.86 $\tau$), olefinic region (4.60, 4.82 $\tau$) and aliphatic region (6.88, 8.02, 8.20, 8.44 $\tau$), not the absorption expected for 2-anilino-4,5-benztropone (LVb). Another condensation of anilinoacetone with o-phthalaldehyde gave primarily the yellow fluorescent solid with a very high melting point. The material was not further characterized.

## Preparation of 2-phenoxy-4-methylphenyl acetate (LXIII)

The method of Ungnade (49) was used to prepare 2-phenoxy-4-methylphenol. The phenol (12.6 g.) was placed in a 100 ml. three-necked flask fitted with an addition funnel and a reflux condenser. A drying tube and hydrogen chloride trap were placed in the top of the condenser. Acetyl chloride (7.7 g., 0.5 mole excess) was added through the dropping funnel while the mixture was stirred. After being stirred for 30 minutes, the mixture was heated over a steam bath for 90 minutes. The excess acetyl chloride was then removed under reduced pressure. The residue was distilled to give starting material (2 g.) and crude LXII (9.7 g., 64%), b.p. 110-116°/0.13 mm. A portion of the product was redistilled for an analytical sample, b.p. 100°/0.15 mm., $n_D^{20}$ = 1.6666. The infrared spectrum (capillary film) is shown in Figure 26, page 76.

Anal. Calcd. for $C_{15}H_{14}O_3$: C, 74.36; H, 5.82. Found: C, 74.37; H, 5.98.

### Irradiation of 2-phenoxy-4-methylphenyl acetate (LXIII)

A solution of 2-phenoxy-4-methylphenyl acetate (3.65 g.) in absolute ethanol (335 ml.) was flushed with nitrogen for 30 minutes. The solution was irradiated with a Hanovia Type A mercury arc lamp in a quartz immersion well. After 85 hours the irradiation was stopped. An infrared spectrum of the irradiation mixture showed that the peak at 5.66 μ (phenyl acetate carbonyl) had decreased in intensity and a new peak had appeared at 6.09 μ. (The well of the immersion apparatus was coated with a brown film which probably reduced the efficiency of the irradiation for the last several hours). The ethanol was removed under reduced pressure on a rotary evaporator. The residue was chromatographed in two portions on a 1" x 16" column prepared with 100 g. of silica gel. The fractions eluted with 1:9 ether-benzene were recrystallized from Skelly B-ethanol to give yellow needles (570 mg., 15.6%), m.p. 84.5-86.5°. A solution of the substance in ethanol gave a dark green color with the ferric chloride test. The infrared and nuclear magnetic resonance spectra (Figure 26, page 76 and Figure 27, page 78) show that the product is an o-hydroxyacetophenone. The ultra-violet spectrum is shown in Figure 29, page 82. A double resonance experiment showed the product to possess two hydrogens ortho to the methyl group. The compound was identified as 2-hydroxy-3-phenoxy-5-methylacetophenone (LXIV).

Anal. Calcd. for $C_{15}H_{14}O_3$: C, 74.36; H, 5.82. Found: C, 74.64; H, 6.01

## Experimental for
## Rearrangement and Cleavage of the Dimers

### Thermal conversion of Dimer I (XXXVIII) to Dimer II (XL)

Dimer I (XXXVIII) (828 mg.) was placed in a small Erlenmeyer flask. The flask was immersed in a silicone oil bath which had previously been heated to a temperature of 237°. A stream of nitrogen was blown into the flask. The temperature of the bath dropped to 232-234°. After about five minutes the Dimer I had melted. The heating was continued for an additional three minutes. The flask was then removed from the oil bath and allowed to cool. The

The material was dissolved in a small amount of benzene and eluted through a 3/4" x 10" column prepared with 50 g. of activated alumina (Chicago Apparatus Company, 80-100 mesh). Elution with 375 ml. of benzene gave colorless crystals (273 mg.), m.p. 218-223°, identified as Dimer II (XL) by infrared and nuclear magnetic resonance spectra. The mother liquors were concentrated and combined with the next 90 ml. benzene fraction to give additional Dimer II (72 mg.), m.p. 214-221°, contaminated with unchanged Dimer I. Further elution with 300 ml. of benzene gave mostly 2-(p-chlorophenoxy)-4,5-benztropone (42.7 mg.), m.p. 122-125°. Elution with 400 ml. of 1:4 ether-benzene gave tars.

### Thermal conversion of Dimer I (XXXVIII) to 2-(p-chlorophenoxy)-4,5-benztropone (XXXI)

Dimer I (XXXVIII) (460 mg.) was placed in a small flask. The flask was placed in a silicone oil bath at 100° which was then heated to 240°, requiring a period of about 25 minutes. The flask was removed and allowed to cool. The material was dissolved in benzene and chromatographed on a 1" x 6" column prepared with 50 g. of activated alumina (Chicago Apparatus Company, 80-200 mesh) in benzene. Elution with 350 ml. of benzene gave nothing. Elution with 110 ml. of 1:4 ether-benzene gave 2-(p-chlorophenoxy)-4,5-benztropone (XXXI) (152 mg.), identified by melting point (m.p. 123-125°)

and infrared spectrum. An additional 30 mg. of XXXI was obtained by concentration of the mother liquors. Elution with more benzene-ether mixtures (500 ml.), ether (150 ml.) and chloroform (350 ml.) gave unidentified tars.

Thermal reactions of Dimer II (XL)

A. Dimer II (78 mg.) was placed in a small flask and immersed in a silicone oil bath which had been heated to 240°. The temperature dropped to 236°, at which temperature the material had melted after one minute. The flask was removed after five minutes with the temperature of the bath at 237°. A brown tar with the odor of phenol remained in the flask. An infrared spectrum ($CHCl_3$) of the crude material showed absorption at 5.83 and 5.95 μ from unchanged Dimer II. More intense peaks appeared at 6.14 and 6.23 μ, characteristic for 2-(p-chlorophenoxy)-4,5-benztropone (XXXI).

B. In an attempt to determine whether the conversion of Dimer I to Dimer II is reversible, Dimer II (81 mg.) was heated in a silicone oil bath at the temperature of the isomerization (231-232°). After four minutes of heating, the material was removed from the oil bath and allowed to cool. An infrared spectrum ($CHCl_3$) of the crude material showed a shoulder at 5.76 μ suggesting the presence of Dimer I, peaks at 5.83 and 5.96 μ attributed to Dimer II and a peak at 6.14 μ attributed to 2-(p-chlorophenoxy)-4,5-

benztropone (XXXI). Strong evidence for the presence of Dimer I was the appearance of a pair of peaks at 10.25 and 10.55 μ, a characteristic absorption pattern for Dimer I. A few milliliters of ethanol were added to dissolve XXXI and part of the Dimer II. An infrared spectrum of the undissolved material showed more intense bands at 10.25 and 10.55 μ, strongly supporting the presence of Dimer I. No attempt was made to isolate Dimer I because of the small amount present in the mixture.

### Thermal trapping experiments with maleic anhydride

A. 2-Phenoxy-4,5-benztropone (XXIX) (465 mg.) was mixed with maleic anhydride (370 mg., 1 mole excess). The mixture was placed in a 10 mm. tube. The tube was evacuated at 0.25 mm. and sealed. The sealed tube was dropped into an oil bath at 220°. The material in the tube melted and boiled. The mixture was removed after five minutes of heating. An infrared spectrum of the mixture showed only absorption attributable to XXIX or maleic anhydride. Recrystallization of the mixture from 2-propanol gave XXIX (400 mg.).

B. Dimer I (162 mg.) was mixed with maleic anhydride (112 mg.) and sealed in a 10 x 120 mm. tube evacuated at 0.25 mm. The sealed tube was dropped into a silicone oil bath which had been heated to 255°. The bath temperature dropped to 243-244°. After 7 minutes the tube was removed and allowed to cool. An infrared spectrum of the mixture showed absorption indicating the presence of maleic anhydride, XXXI, Dimer I and Dimer II. An attempt to isolate a maleic anhydride adduct by recrystallization from chloroform-Skelly B was unsuccessful.

## Experimental for Mechanisms of Dimerization

### Preparation of 2-phenoxy-4,5-benztropone-7-d (LXXV)

Phenoxyacetone (5.0 g.) was placed in a 50 ml. flask sealed with a rubber septum. Deuterium oxide (10 ml.) and sodium carbonate (10 mg.) were added to the flask. The mixture was stirred with a magnetic stirrer and heated slightly with the heat given off by the stirrer motor. The deuterium oxide was removed with a syringe after a period of 8 to 12 hours and fresh deuterium oxide and sodium carbonate were added. The process was repeated until a total of 160 ml. of deuterium oxide was used over a period of seven days. A nuclear magnetic resonance analysis of the phenoxyacetone showed a 95% deuterium exchange in the methyl group and essentially complete exchange in the methylene group.

The condensation of the phenoxyacetone-$\underline{d}_5$ was carried out in the same deuterium oxide (160 ml.) used for the exchange, to which was added o-phthalaldehyde (4.0 g.)

in methanol-$\underline{d}_1$ (62) (150 ml.). Sodium methoxide (1.3 g.) in deuterium oxide (20 ml.) was added to the solution. After stirring for five days, the mixture was filtered. The product was eluted through an alumina column with benzene to purify it. Recrystallization from 2-propanol gave 2-phenoxy-4,5-benztropone-7-$\underline{d}$ (LXXXV) (2.1 g., 24%), m.p. 135-136.5°, as slightly yellow needles. The infrared spectrum of LXXXV is shown in Figure 35, page 97.

### Irradiation of 2-phenoxy-4,5-benztropone-7-$\underline{d}$ (LXXXV)

The irradiation of LXXXV (1.9 g.) was done in tetrahydrofuran (165 ml.) with a Hanovia Type A lamp in a Pyrex well. After 17 hours the absorbance of the solution at 274 mμ was 21% of its original value. The solvent was evaporated and the residue chromatographed on a 1" x 18" column prepared with 200 g. of Woelm neutral alumina, activity I. Elution with Skelly B-benzene mixtures and benzene gave nothing. Elution with 1:5 ether-benzene gave Dimer B-$\underline{d}_2$ (LXXXVII) (45 mg.), m.p. 214-215.5°. The infrared spectrum (Figure 35, page 97) is very similar to that of Dimer B. The nuclear magnetic resonance spectrum (Figure 36, page 99) shows that the deuterium atoms are located at the β-carbons of the styryl double bonds as in structure LXXXVII.

# SUMMARY

Irradiation of 2-(p-chlorophenoxy)-4,5-benztropone (I) in tetrahydrofuran solution gives dimeric products, Dimer I, Dimer II and Dimer III. All of the dimers give 4,5-benztropolone on treatment with sulfuric acid. Chemical and spectroscopic evidence is given for the structures of the dimers. Dimer I is isolated from irradiations of I under a variety of conditions. Dimer II is obtained from irradiations of I or from thermal rearrangements of Dimer I. Dimer I and Dimer II can be converted to I by heating at 235-240°. Dimer II is obtained by irradiating I for a longer period of time or by irradiating Dimer I in quartz.

Dimerization proceeds in the presence of sensitizers and oxygen. The possible implications of this observation are discussed. An additional product with an empirical formula $C_{16}H_{11}ClO_3$ is isolated from the irradiation of I in the presence of oxygen. The structure of the new product has not been determined. No evidence for a ground state complex between the phenoxybenztropones in solution could be obtained from Beer's law or osmometric molecular weight studies.

The dimers appear to be derived formally from a rearranged intermediate in which the p-chlorophenoxy and carbonyl groups are exchanged in position. Attempts to trap

such an intermediate in the photochemical and thermal reactions with dienophiles were unsuccessful. 2-Thiophenoxy-4,5-benztropone (II) was prepared and irradiated in an attempt to confirm an apparent phenyl migration in the dimerization. No dimer of II could be isolated. No phenyl shift was observed in the irradiation of 2-phenoxy-4-methylphenyl acetate, which gave the normal product of a photochemical Fries rearrangement.

The thermal rearrangement and cleavage of the dimers are of interest because of their similarity to the Cope rearrangement and the Diels-Alder reaction. A mechanism for these reactions is presented. Mechanisms for the photochemical dimerization are proposed. A mechanism involving rearrangement of the seven-membered tropolone ring was eliminated. The irradiation of 2-phenoxy-4,5-benztropone-7-d gave a dimer analogous to Dimer I. The nuclear magnetic resonance spectrum showed that the deuterium atom had not changed its relative position in the seven membered ring during the dimerization.

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# ACKNOWLEDGMENT

The author wishes to acknowledge and thank Dr. O. L. Chapman for his patient guidance, counsel and inspiration throughout this research work. The author wishes to thank Dr. R. W. King and Dr. T. H. Kinstel for helpful discussions concerning the nuclear magnetic resonance and mass spectroscopy work.

The author expresses his gratitude to his parents, Mr. and Mrs. M. L. Stoner, for their interest and moral support during his years of graduate study.

The author wishes to thank his colleagues in the laboratory for their many helpful suggestions, discussions and favors which assisted with the completion of this work.

The author acknowledges the assistance of Miss Alice K. Peterson in the work with 2-(*p*-bromophenoxy)-4,5-benztropone and of Mr. Mike Fung in the work with 2-phenoxy-4,5-benztropone-7-*d*.

The author gratefully acknowledges the financial support provided by a National Science Foundation Cooperative Graduate Fellowship from September, 1962 through August, 1963, by a Texaco, Inc. Fellowship from September, 1963 through May, 1964 and by a Procter and Gamble Summer Fellowship for the summer, 1964. A publication which originated in part from the work in this thesis is:

O. L. Chapman, H. G. Smith, R. W. King, D. J. Pasto and M. R. Stoner, Journal of the American Chemical Society, 85, 2031 (1963).