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THE UNIVERSITY OF OKLAHOMA

GRADUATE COLLEGE

9,10-DISUBSTITUTED-9,10-DIHYDRONAPHTHALENE CHEMISTRY

A DISSERTATION

SUBMITTED TO THE GRADUATE FACULTY

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degree of

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BY

JOHN RALPH SMILEY IRELAN

Norman, Oklahoma

1968

9,10-DISUBSTITUTED-9,10-DIHYDRONAPHTHALENE CHEMISTRY

APPROVED BY

John B. Bruce

DISSERTATION COMMITTEE

To

Nancy

and

Our Parents

ACKNOWLEDGMENTS

The author wishes to express his appreciation to Dr. J. J. Bloomfield, who suggested these problems, for his council and assistance during the course of this work. Appreciation is extended to the University of Oklahoma for financial aid in the form of teaching assistantships and for research assistantships on National Science Foundation Grants GP 260 and GP 4439.

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TABLE OF CONTENTS

	Page
LIST OF TABLES	vi
INTRODUCTION	1
Recent Literature	20
RESULTS AND DISCUSSION	26
Part I, Five-Membered Lactones	26
Summary	36
Part II, Five-Membered Bridges	37
Summary	46
Part III, Four-Membered Rings	47
Summary	67
Part IV, 1,2-Cyclobutanediones	69
Summary	76
EXPERIMENTAL	77
Part I	79
Part II	94
Part III	108
Part IV	141
LITERATURE CITED	152
APPENDIX	159
List of Figures	160

LIST OF TABLES

Table		Page
1.	Effect of Metal-Diester Mole Ratio on Yield of Acyloin	52
2.	Kinetic Data for Decomposition of Ether LIII	106
3.	Kinetic Data for Decomposition of Tetraene LX	128

9,10-DISUBSTITUTED-9,10-DIHYDRONAPHTHALENE CHEMISTRY

INTRODUCTION

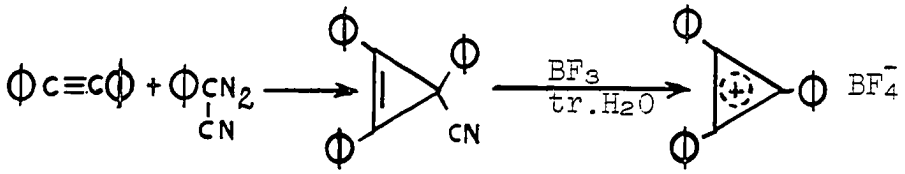
The term "aromatic" at first became synonymous with compounds containing benzene rings, but nothing in the term demands the existence of one. Applications of the term to other systems were amply provided (1-6) as understanding of benzenoid compounds grew and led to what is known as Hückel's rule (7,8), which has become the basis of present day concepts of aromaticity. Hückel's rule states that among "fully conjugated, planar, monocyclic polyolefins only those possessing (4n+2) π-electrons, where n is an integer, will have special aromatic stability." (9) Using this rule, one may term many non-benzenoid molecules "aromatic" such as furan and tropylium salts.

Hückel's rule describes structural requirements for an aromatic system but does not include the chemical reactivity of the molecule. The two interpretations of aromaticity, a) structure and b) chemical reactivity, are not always interchangeable, but the latter is often used to substantiate the former. Thus, a well-established characteristic of aromatic systems, such as electrophilic

substitution, may be safely applied to some of the higher 4n+2 homologs of benzene (as will be seen later).

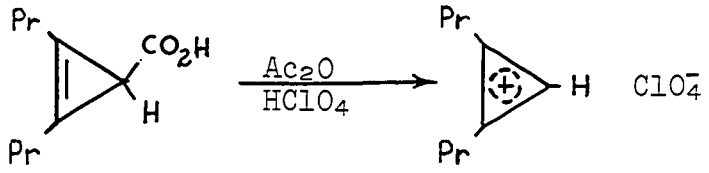
In aromatic compounds a delocalization of π electrons occurs. Perhaps the easiest way to observe the presence of delocalization is by determining the nuclear magnetic resonance spectrum of a molecule. Aromatic compounds set up a diamagnetic ring current in an applied magnetic field, which is responsible for deshielding protons on the periphery of the molecule (10,11). The net effect of the phenomenon is that the peripheral protons of aromatic compounds appear at lower magnetic field than normal vinyl protons. Thus, benzene protons appear with a shift of 7.37 ppm (from tetramethylsilane) while the vinyl protons of cyclohexene appear at 5.60 ppm.

The simplest system conforming to the Hückel rule would contain two-π electrons (n=0). Cyclopropenium salts are good examples of this system. Breslow obtained the first of such compounds by addition of a carbene to an acetylene with subsequent removal of an anion (12).



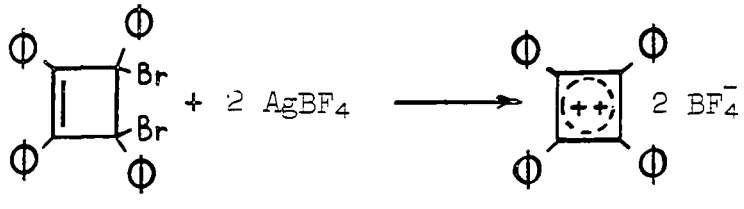
The product had salt-like properties, and its NMR spectrum (13) showed an equivalence of three phenyl groups. Stability of the cation was not dependent on the presence of the phenyl groups, for a dipropylcyclopropenium salt has

been prepared (13)*.



The NMR spectrum of this salt displayed the ring proton at 13.04 ppm and the propyl groups in the range of 3.75 to 5.89 ppm. The low field shift of the ring proton not only demonstrates the influence of the positive charge [tropylium bromide has a shift of 9.38 ppm (16), 2.01 ppm to lower field than benzene] but also the existence of a paramagnetic ring current. (If the spectrum were offset, placing the protons alpha to the ring at 2.0 ppm to compensate for the positive charge, the ring proton would appear at 9.5 ppm or 2.13 ppm downfield from benzene.)

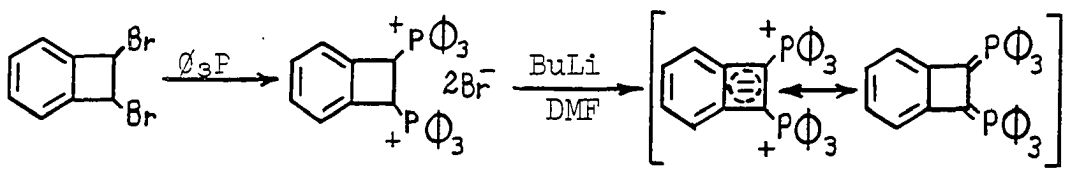
Another example of an aromatic system where n=0 could be obtained by removal of two electrons from a cyclobutadiene molecule, producing a two-π electron system delocalized over four ring carbons. The only successful preparation of such a compound appears to have been performed by Freedman and Young (17).



*See section entitled "Recent Literature" at the end of the Introduction for the preparation of the unsubstituted cyclopropenium salt.

Treatment of 3,4-dibromotetraphenylcyclobutene with silver tetrafluoroborate generated a deep red solution. The F^{19} NMR of this solution displayed a singlet at 70.9 ppm, in the same region as tetrafluoroboric acid and triphenylmethyl tetrafluoroborate. No absorption was observed in the region of fluorine bonded to carbon, and no proton NMR was obtained.

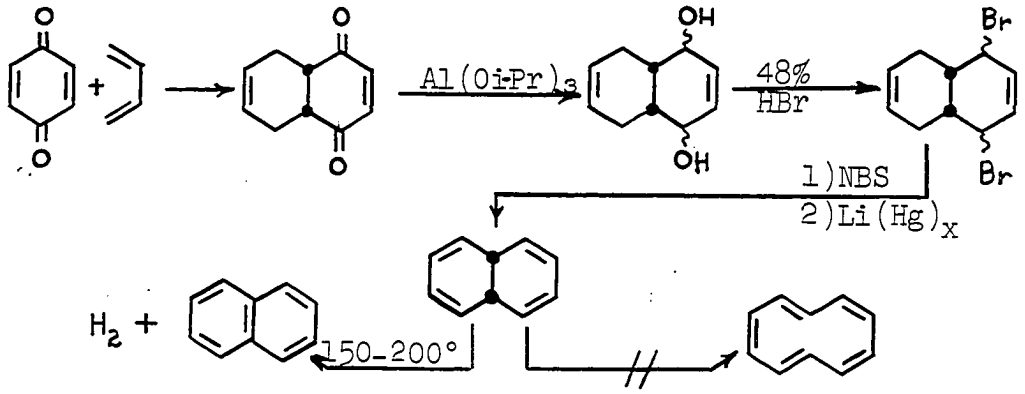
Molecules which fit the Hückel rule where n=1 include, of course, benzene and heterocyclic derivatives. Other well-known systems include cyclopentadienide and tropylium salts, ferrocene, and fulvenes. A less well-known six-π electron system has been prepared by Blomquist and Hruby (18).



Treatment of the bis-phosphonium salt with base in a cold bath gave a dark red solution which was thought to contain the bis-ylide. The NMR spectrum of this compound gave a broad multiplet at 7.55 ppm. Comparing this value to the phosphonium salt (7.80 ppm) it can be seen that an upfield shift has taken place as would be expected from association of a negative charge. [Sodium cyclopentadienide absorbs at 5.33 ppm (16).]

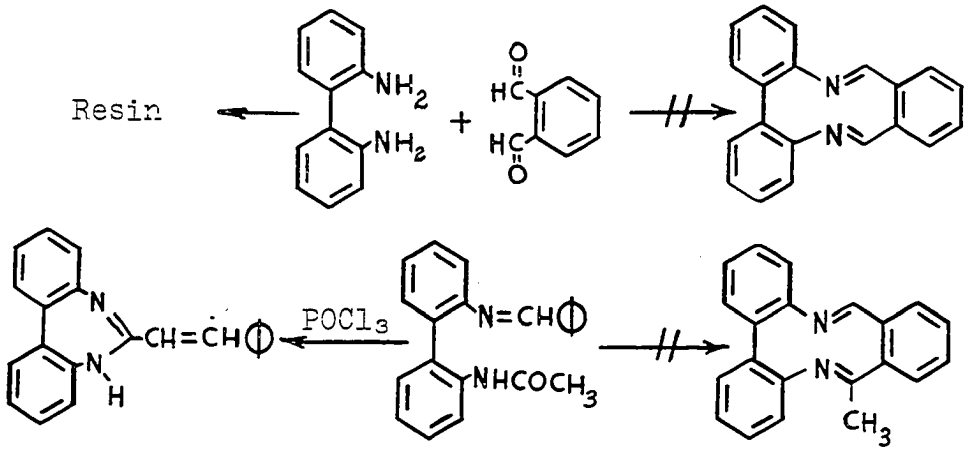
Conjugated monocyclic polyenes which have ten-π electrons or more have been named "annulenes" (19). An

attempt to synthesize the first member of this series, cyclodecapentaene (4n+2=10,n=2), ended in failure (20).



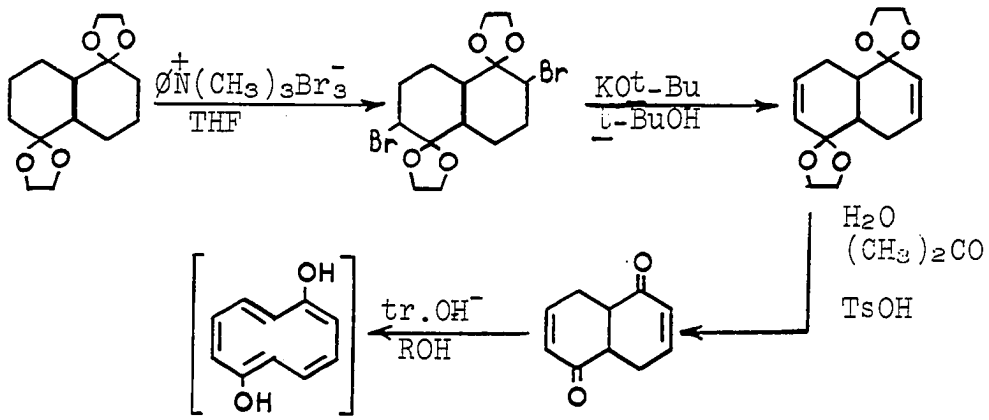
As indicated, cis-9,10-dihydronaphthalene failed to isomerize to cyclodecapentaene. When the compound was heated, no reaction took place until the molecule began to lose hydrogen at about 150° to form naphthalene.*

Other attempts have been made to prepare a monocyclic ten-membered annulene. Blood and Noller (21) tried to prepare heterocyclic cyclodecapentaene by cyclodehydration.



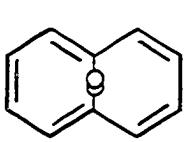
*Cyclodecapentaene has recently been prepared from trans-9,10-dihydronaphthalene. See "Recent Literature" section at the end of the introduction.

As indicated both trials failed to yield the desired ten-π system. Johnson, Bass and Williamson (22,23) prepared $\Delta^{2,6}$-hexalin-1,5-dione for the purpose of isomerizing the molecule to the dienol structure* and thence to a cyclodecapentaene.

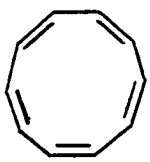


A new band in the ultra violet spectrum at 232 mμ (ϵ =32,000) gave some indication of the possibility, but attempts to convert the molecule to the dienol diacetate ended in formation of mixtures.

A planar model of cyclodecapentaene which would have no ring strain could be realized in structure I if it were not for the overlap of the internal hydrogens. However, an all-cis configuration, as indicated in structure II,



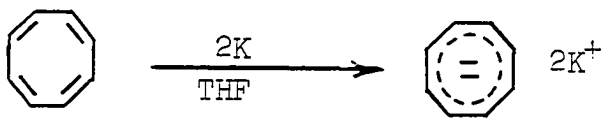
I



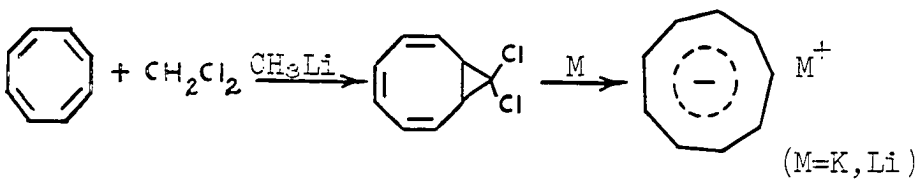
II

*A more recent and similar such attempt has been made. See "Recent Literature" section.

would relieve this situation, and until recently* it has been open to question whether the delocalization energy of the ten-π system could match the ring strain with bond angles of 144°. Two aromatic ten-π electron systems have been synthesized which lend support to the idea that structure II would be stable. A cyclooctatetraenyl dianion was prepared by reducing cyclooctatetraene with potassium metal (24).



Cyclononatetraenyl anion was prepared by adding dichlorocarbene to cyclooctatetraene and reducing the adduct with alkali metal (25,26).



(M=K,Li)

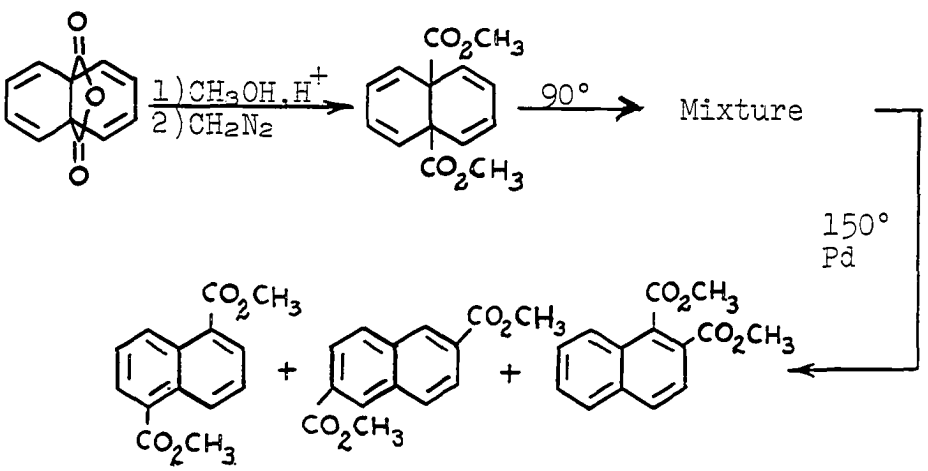
The NMR spectrum of each anion consisted of one singlet, 5.7 ppm for potassium cyclooctatetraenide (dianion) and 7.04 ppm for potassium cyclononatetraenide. (The dianion was located at higher field due to more shielding by the extra negative charge.) These two molecules meet the

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*See preparation of cyclodecapentaene in "Recent Literature" for confirmation of structure II.

requirements of Hückel's rule (n=2) in that they must be planar monocyclic molecules to present a singlet in the NMR.

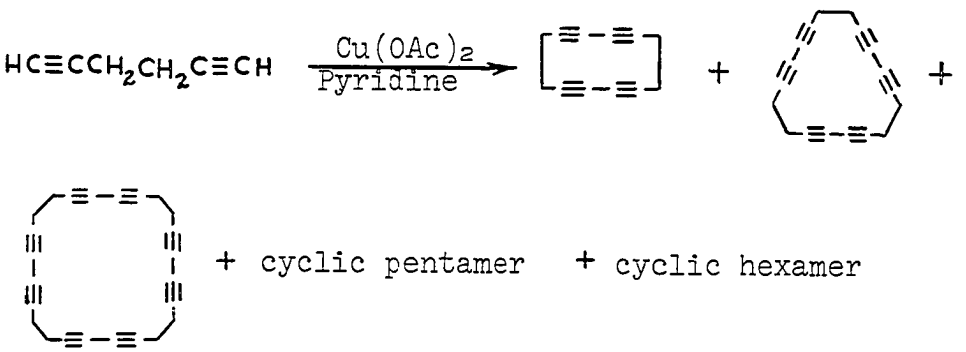
An attempt to synthesize a cyclodecapentaene was performed by Vogel, Meckel, and Grimme (27). They prepared dimethyl cis-9,10-dihydronaphthalene-9,10-dicarboxylate and found that the diester rearranged at 90° to a mixture of esters which was then dehydrogenated to naphthalene diesters.



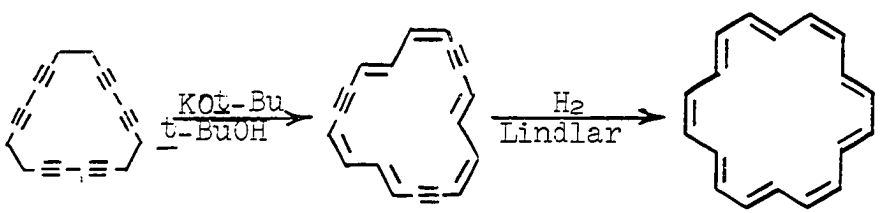
The 2,6 and 1,5 diesters might be indicative of a cyclodecapentaene intermediate if it were not for the presence of the 1,2 diester. Vogel concluded (28) that rearrangement was taking place by several competing routes and therefore the presence of the 1,5 and 2,6 diesters could not be regarded as evidence of a cyclodecapentaene intermediate.

A number of the higher annulenes and dehydroannulenes

have been prepared by Sondheimer and workers (19,29-42).* The method of preparation consisted chiefly of coupling a terminal diacetylene with either cupric acetate in pyridine (19,35,43,44) or with cupric chloride-ammonium chloride in ethanol-water (38,45) to form a mixture of cyclic poly-ynes.



The products were separated by chromatography and rearranged into dehydroannulenes with potassium tert-butoxide in tert-butyl alcohol. The corresponding annulenes were obtained by partial hydrogenation of the dehydroannulenes with a Lindlar catalyst.

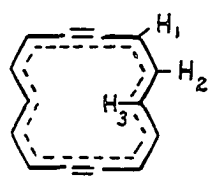


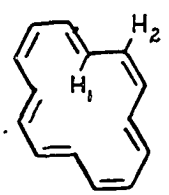
By this method annulenes or dehydroannulenes of 12,14,16, 18,20,24 and 30 members were prepared.

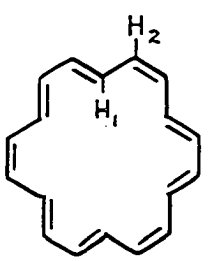
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*See "Recent Literature" for more recent annulenes.

A confirmation of the Hückel rule was obtained from the NMR spectra of these compounds (46-51). As mentioned previously, protons on the outside of an aromatic molecule are deshielded and appear at low magnetic field. In the case of annulenes which possess protons both inside and outside the ring the inner protons would be shielded and thus appear at high magnetic field. This prediction was found to be true of annulenes and dehydroannulenes which fit the Hückel rule. Annulenes and dehydroannulenes of fourteen members displayed outer proton absorptions in the range of 9.6 to 7.4 ppm and inner protons in the range of 0.0 to -5.5 ppm. Eighteen-membered rings displayed outer proton absorptions in the range of 9.3 to 6.6 ppm and inner protons at 2.3 to -3.0 ppm. Notable examples are presented below.



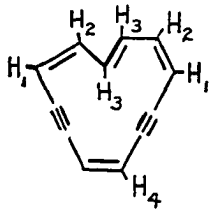




$(C_{14}H_{10})$	$(C_{14}H_{14})$	$(C_{18}H_{18})$
$CDCl_3$,37°	$CDCl_3$,-60°	THF D_6,-60°
H_1: 9.64 ppm (q)	H_1: 0.0 ppm (m)	H_1:-2.99 ppm (m)
H_2: 8.54 ppm (d)	H_2: 7.6 ppm (m)	H_2: 9.28 ppm (q)
H_3: - 5.48 ppm (t)		

In contrast to the 4n+2 annulenes the 4n annulenes displayed the reverse type of spectra. Annulenes and

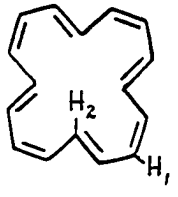
dehydroannulenes of 12,16,20 and 24 members all displayed outer protons in the range of 4.3 to 6.1 ppm and inner protons in the range of 8.4 to 11.6 ppm. Notable examples are given below.



$(C_{12}H_8)$

$(CD_3)_2CO, 37°$

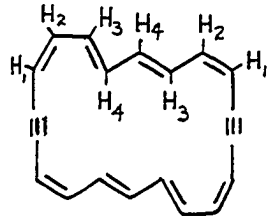
H_1: 4.27 ppm (d,t)
H_2: 5.16 ppm (m)
H_4: 4.68 ppm (t)
H_3:11.18 ppm (m)



$(C_{16}H_{16})$

$CDCl_3, -120°$

H_1: 5.2 ppm (m)
H_2:10.32 ppm (m)



$(C_{20}H_{16})$

THF $D_6, 37°$

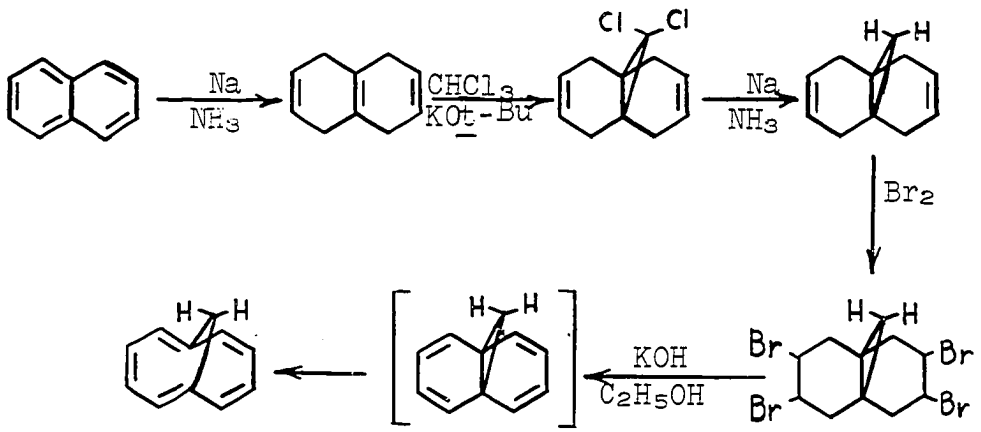
H_1: 5.09 ppm (d)
H_2: 5.68 ppm (t)
H_3: 8.40 ppm (m)
H_4: 7.45 ppm (m)

That these compounds act as though the inner protons are being deshielded would indicate a ring current. Longuet-Higgins (52) has a theoretical interpretation for this behavior and in brief explains that the net ring current may flow in the opposite direction to that of the 4n+2 annulenes. If this were true, the inner protons would appear at lower field than the outer protons.

Sondheimer based his definition of aromaticity on sustained π electron delocalization (48), recognizable with NMR spectra, and attempted few chemical tests for aromaticity. Of those tests he did perform, he found that two [14] dehydroannulenes would undergo substitution reactions to form nitrates, sulfonates, and acylates, but using the same

reagents on [14] annulene destroyed the ring (53). In [18] annulene, sulfonation or acylation attempts destroyed the ring (48),* and the compound was found to add bromine. Also, photolylic stability seems to decrease among the annulenes as ring size increases (37). At best the annulenes synthesized had a short life in daylight.

The closest approach to [10] annulene (cyclodecapentaene)** was achieved by Vogel and Roth (54) when they prepared 1,6-methanocyclodecapentaene.



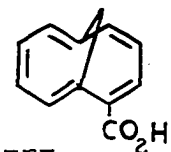
Unlike many of the unbridged annulenes prepared by Sondheimer (19,29-42) this molecule was quite stable to light and insensitive to oxygen. The NMR spectrum of the hydrocarbon displayed an A_2B_2 pattern at 7.3 ppm for the ring

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*Successful substitution has been performed on this molecule. See "Recent Literature" section.

**Except for its recent preparation. See "Recent Literature" section.

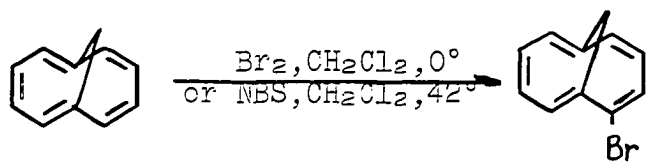
protons and a sharp high field singlet at -0.5 ppm for the two apparently shielded bridge protons.



III

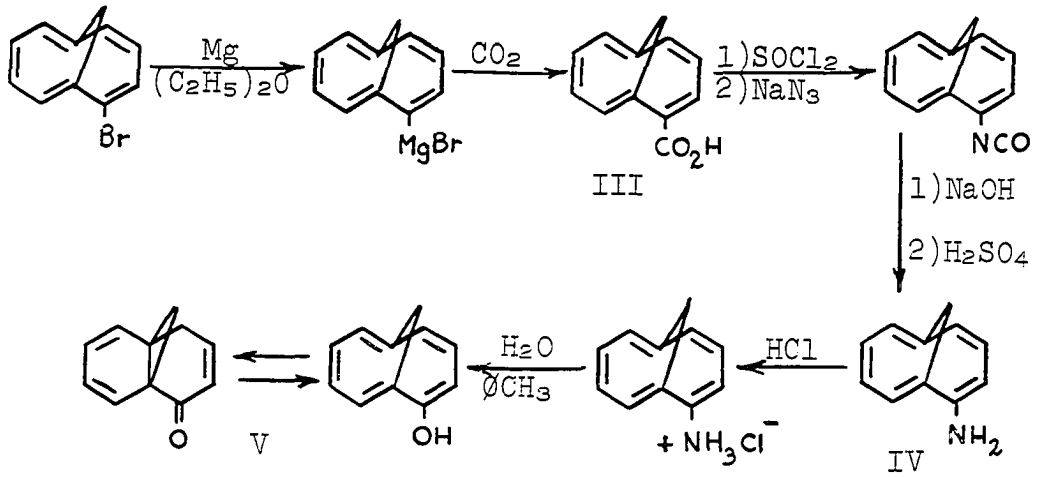
An X-ray crystallographic examination (55) of 1,6-methanocyclodecapentaene-2-carboxylic acid III (56) revealed the bond lengths to be between 1.38 and 1.42Å, and comparing these to those of naphthalene (1.36 to 1.42Å) provides support for aromatic character.

Vogel performed chemical reactions on the substance. He found that maleic anhydride would not react in refluxing benzene, discounting a diene-like structure. A substitution reaction could be performed employing either bromine or N-bromosuccinimide (56,57).



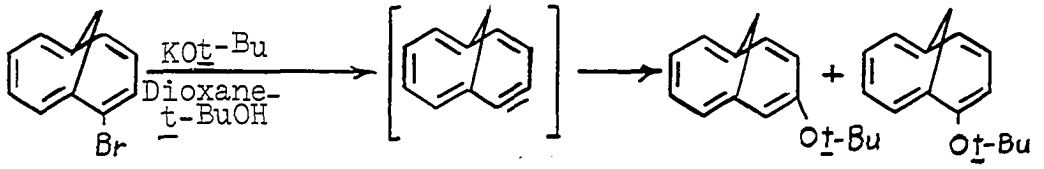
The hydrocarbon could also be acylated with stannic chloride and acetic anhydride to produce the 2-substituted product. Nitration was carried out with cupric nitrate-acetic anhydride (the hydrocarbon was sensitive to strong acid), and a mixture of 2-and 3-nitro substitution products was formed. Thus, the ability of the hydrocarbon to undergo substitution reactions provides a chemical support for aromaticity.

Access to 2-amino and 2-hydroxy cyclodecapentaenes was gained from the 2-bromo compound as outlined below (58).



The 2-carboxylic acid, prepared through a Grignard reaction for X-ray studies (above), was subjected to a Curtius rearrangement and the resulting isocyanate hydrolyzed to the amine (IV). The hydrochloride salt of the air sensitive amine was hydrolyzed with water to form a keto-enol mixture(V). The ketone, in which ring closure to form a cyclopropane ring had occurred, could be separated from the enol form, and the same mixture was obtained when the ketone was placed in a slightly acidic medium. In benzene the keto form was 80% favored, and in DMSO the enol was 97% favored.

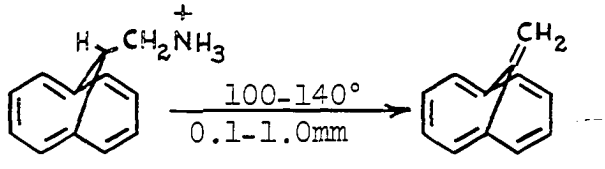
Evidence of an aryne was displayed in the cyclodecapentaene by treating the 2-bromo compound with potassium tert-butoxide forming primarily the 3-substituted product (59).



95 : 5.

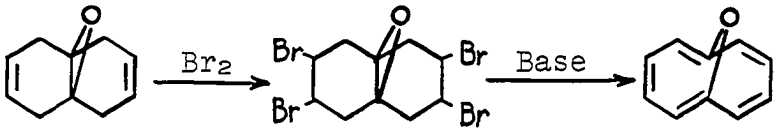
About equal amounts of the 2- and 3-substituted products were obtained using lithium piperidide. To give support to the supposed aryne, tetraphenylcyclopentadienone was used to trap the intermediate and a 2,3-adduct was formed.

Preparation of the 11-methylene compound (60) provided an additional example of shielded protons.

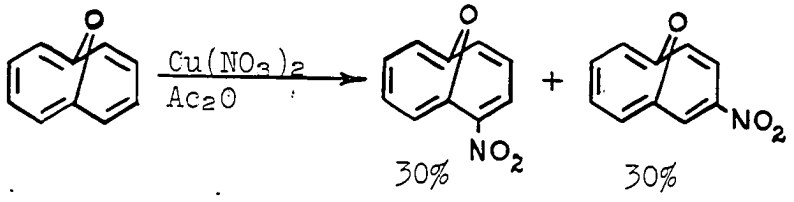


The A_2B_2 pattern of the ring protons appeared at 7.2 ppm, and the 11-exo-methylene protons, being above the π cloud, appeared as a singlet at 3.2 ppm. From the similarity of the ultraviolet spectra of this compound and 1,6-methanocyclodecapentaene, Vogel concluded that the exo-methylene did not electronically react with the ten-π system.

Heterocyclic bridged [10] annulenes have also been prepared. Sondheimer (61) and Vogel (62) independently synthesized 1,6-oxocyclodecapentaene by the same route. The oxo compound had some of the same aromatic characteristics as the 1,6-methano compound.

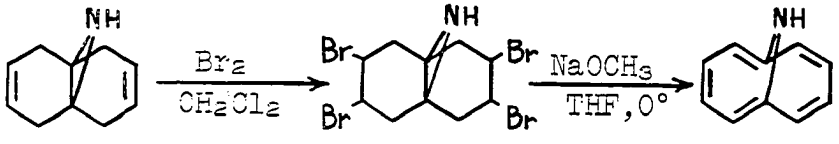


The NMR spectrum displayed only an A_2B_2 pattern centered at 7.48 ppm [7.35 ppm reported by Vogel (62)]. Nitration was possible by treatment with cupric nitrate in acetic anhydride at room temperature.



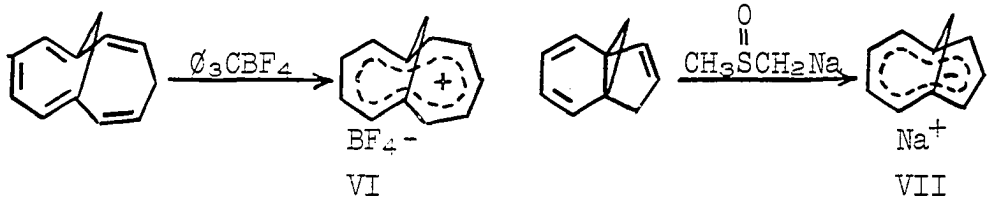
A 1:1 mixture of 2- and 3-nitro products was obtained (same results with the hydrocarbon). Bromination (57) at room temperature gave unclear results but when carried out at -75° followed by treatment with base, it afforded 2-bromo-1,6-oxocyclodecapentaene. Thus, the two compounds might be expected to be somewhat similar, their only difference being the bridge atom.

The 1,6-imido compound was prepared by the same general method as before (63) as was its N-acetyl derivative (62).



The NMR spectrum of the imido compound displayed the expected A_2B_2 pattern at 7.2 ppm for the ring protons and a broad singlet at -1.1 ppm for the shielded proton on nitrogen. The α-protons on the N-acetyl derivative appeared upfield (from normal) at 1.03 ppm.

Since the basic ten-π electron system appeared to be stable when a bridge was employed, corresponding ten-π charged systems were investigated. The eleven-membered cation VI (64) and the nine-membered anion VII (65,66) have both been prepared.

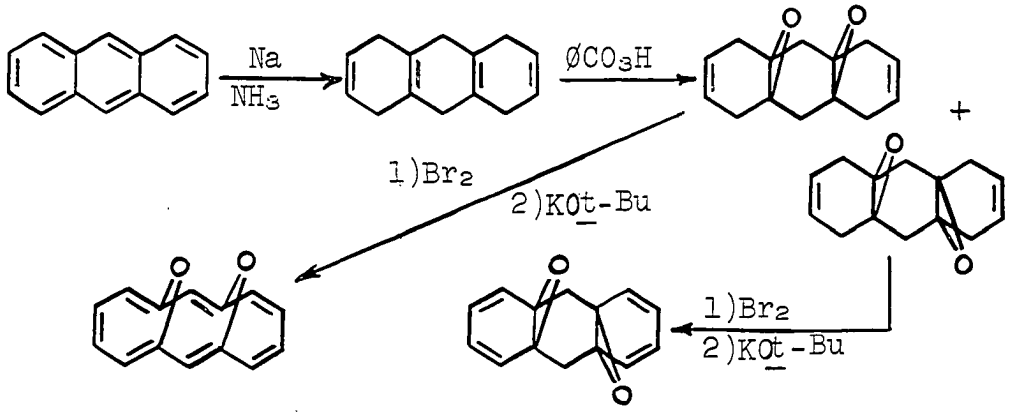


VI VII

The cation displayed an NMR spectrum of a highly split multiplet at 8.3 to 9.6 ppm for the ring protons and the bridge protons as an AX system at -0.3 and -1.8 ppm. The anion showed a multiplet in the range of 6.0 to 5.4 ppm plus an additional small multiplet at 6.8 ppm for the ring protons and an AX system at -0.7 and -1.2 ppm for the bridge protons. Comparison of the ring proton absorptions of these two systems to 1,6-methanocyclodecapentaene (page 13) is rendered difficult since a positive charge will shift peripheral protons to lower field and a negative charge will shift them upfield. A better indication of

aromaticity can be seen by comparing the bridge protons. In both molecules they are at high field and absorb in about the same place, indicating their positions are due primarily to shielding by the π cloud and independent of the respective charges.

Anthracene was the starting material for a larger bridged annulene, employing the same general synthetic sequence (67,68).



As indicated, the isomer containing bridges on both sides of the ring would not lead to an aromatic system, as was found with the corresponding dimethylene bridged compound (69). The annulene showed an AA'BB' NMR pattern centered at 7.94 ppm. Preliminary examination showed the molecule to be amenable to electrophilic aromatic substitution.

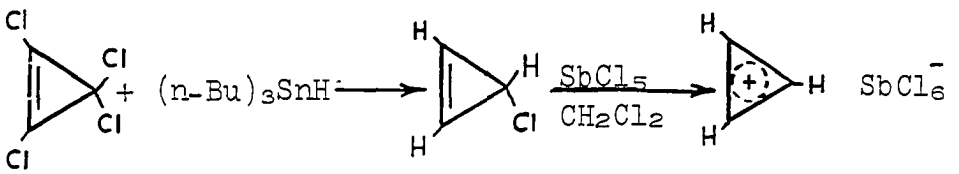
Of all the Hückel aromatic systems presented herein the most stable and the most easily studied were the compounds prepared by Vogel and workers who employed a one-atom bridge in a cyclodecapentaene system. Bridged annulenes containing more than one atom, however, are not known.

Study of larger bridged annulenes would perhaps lend new information concerning the basic ring chemistry, and it was in view of this that the present problem was devised.

Recent Literature

The area of non-benzenoid aromatic chemistry is fairly active with many contributors, and as would be expected, advances have been made during the course of the work presented herein. In the past year a number of publications have appeared which are closely related to the foregoing introduction.

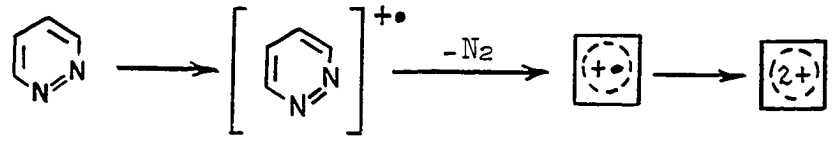
Breslow and coworkers (70) have prepared the simplest homolog of a cyclopropenium ion.



The compound displayed a singlet NMR spectrum at 11.1 ppm, 3.5 ppm downfield from its immediate precursor. Comparison to dipropylcyclopropenium perchlorate (page 3) reveals an upfield shift of 1.9 ppm for the simplest homolog, but comparison is rendered somewhat difficult by the difference in anions. The compound was stable for several hours at room temperature and decomposed upon heating.

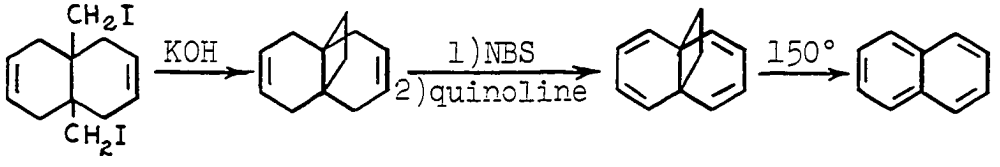
Benn and Sorensen (71) believe the simplest cyclobutadiene dication has been seen in the mass spectrum

of pyrazine.



Peaks of m/e 52(20%), 51(20%), 50(10%), 27(5%), and 26(13%) were observed which correspond to the molecular ions $C_4H_3^+$, $C_4H_2^+$, and either $C_4H_4^{++}$ or $C_2H_2^+$. A weak peak at m/e 26.5, one per cent of the m/e 26 peak and corresponding to $C^{13}C_3H_4^{++}$, gives supporting evidence to the dication ($C^{13}CH_2^+$ would have an m/e 27). Now that a finite existence can be ascribed to this dication, perhaps synthesis of it might in the future be accomplished.

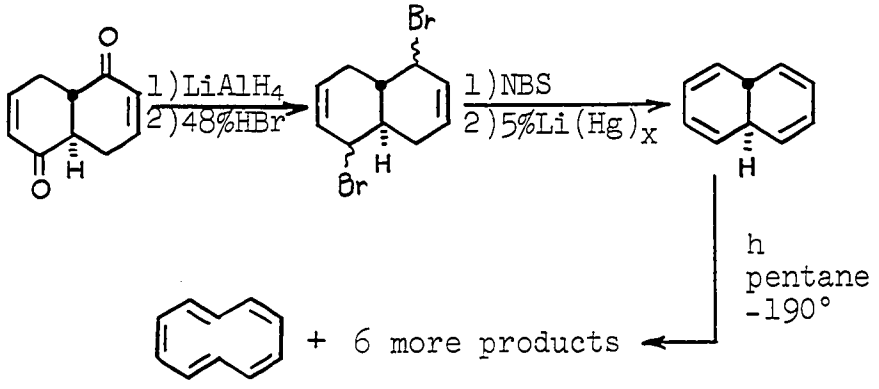
In 1966 Vogel and workers published the preparation of 9,10-ethano-9,10-dihydronaphthalene (72).



The route followed was different than that presented in this work (see Results and Discussion, Part III), the latter being published later the same year (73). The German workers confirmed the results obtained in this laboratory. The compound displayed an NMR spectrum inconsistent with the desired cyclodecapentaene. The vinyl protons appeared upfield from 1,6-methanocyclodecapentaene, and the bridge

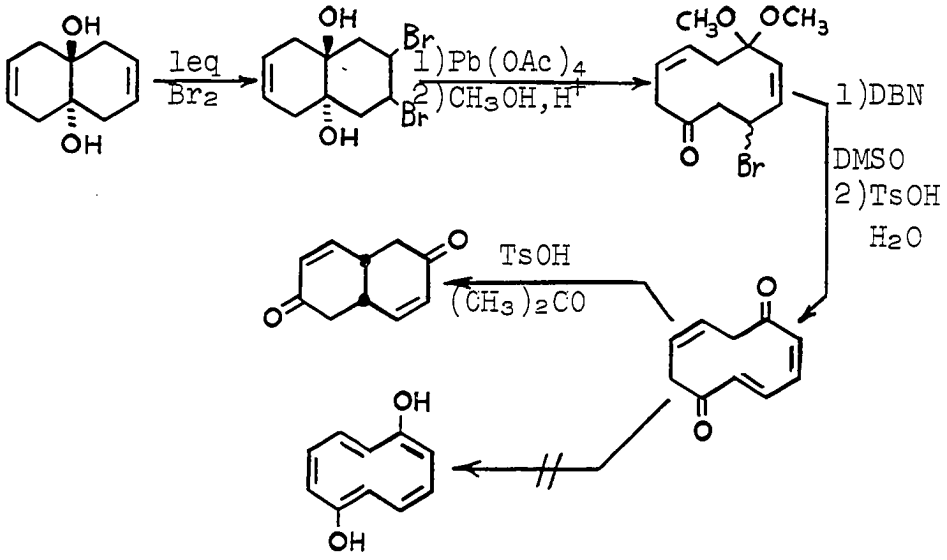
protons showed no upfield shift from an expected ten-π electron cloud. Attempts to isomerize the molecule into aromaticity by heating led to decomposition, producing naphthalene and ethylene.

The long-awaited cyclodecapentaene ([10] annulene) was synthesized in 1967 by Van Tamelen and Burkoth (74).



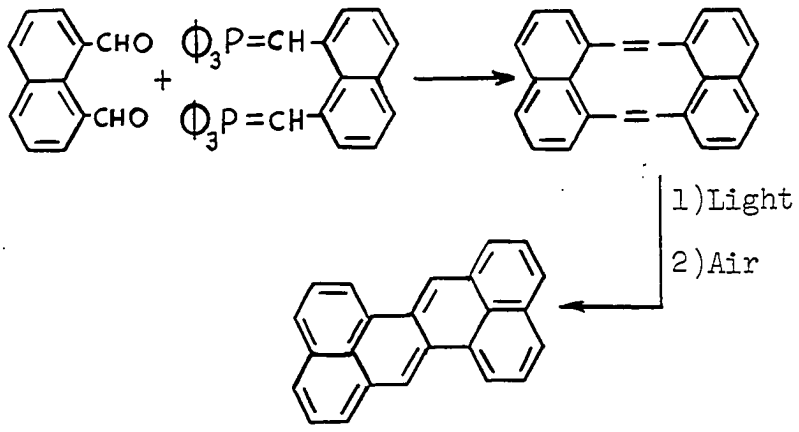
Due to the earlier failure with cis-9,10-dihydronaphthalene (20) they investigated photolytic isomerization of trans-9,10-dihydronaphthalene at -190°C. A 40% yield was estimated from the amount of cyclodecane obtained from a cold reduction with diimide. When the photolyzed mixture (at-190°) was warmed to room temperature and cooled again to -190°, the cyclodecapentaene could not be detected (by UV). It had rearranged to cis-9,10-dihydronaphthalene. In order to effect this transition the molecule must exist in the strained planar decagon structure (page 6) and not as shown above with two trans-double bonds.

Mulligan and Sondheimer (75) prepared a diketone which is the keto form of a cyclodecapentaene diol.



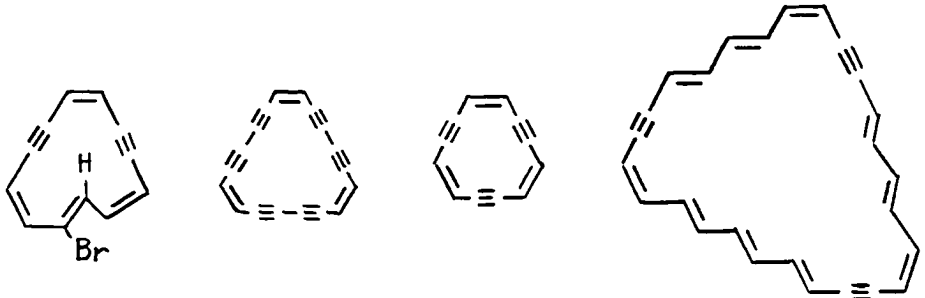
Efforts to isomerize to the aromatic system with either acid or base or to convert the diketone to the diol diacetate all failed. When refluxed with acid in acetone, the system rearranged to the cis-fused diketone shown. Perhaps the desired diol cannot be obtained due to interaction of internal hydrogens (page 6), and with this observation the above results are not unexpected.

Another ten-π electron system was synthesized by Mitchell and Sondheimer (76) by a Wittig reaction on naphthalene-1,8-dialdehyde. The dinaphthyl system does not behave as an aromatic system, and the authors feel that the substance is not planar but in a boat configuration with two cis-double bonds.



One of the criteria of Hückel's rule is therefore not met. The material slowly rearranged in light, and air oxidized it to zethrene. Attempts to brominate the molecule in an effort to insert triple bonds led only to derivatives of zethrene.

New annulenes of greater than ten members have been reported in the past year.



VIII IX X XI

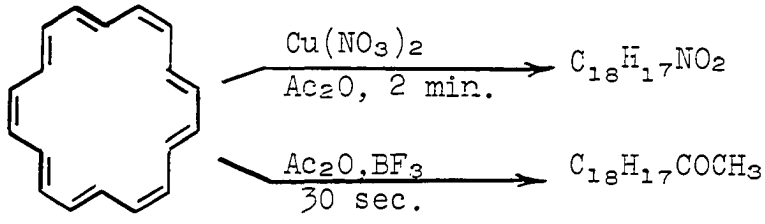
Annulene VIII, prepared from a cyclic hexabromide (77), is a brominated species of one prepared by Sondheimer (page 11) and displays the internal proton at 16.31 ppm. The signal is far downfield and thus indicates it is locked inside the ring more so than the non-brominated compound.

As noted previously (page 11), other non-aromatic 4n-π systems display downfield internal protons.

Annulene IX of eighteen-π electrons (78) demonstrates another example of an aromatic system. Its NMR spectrum displays a singlet at 7.02 ppm which is 2.90 ppm down field from non-aromatic annulene X of twelve-π electrons.

The C_{26} annulene XI (79) displayed an NMR spectrum of a broad multiplet in the range of 5.5 to 8.0 ppm. Although the compound is Hückel aromatic (by definition), its NMR spectrum shows no difference in inner and outer protons and thus no definite ring current, as was also found for [30] annulene (48).

Contrary to an earlier report (48), [18] annulene can be acylated and nitrated using the same reagents as previously tried (page 12) but for a shorter time (80).



Yields of 60 and 30% respectively were obtained. The compound can thus be classified as aromatic by chemical methods.

RESULTS AND DISCUSSION

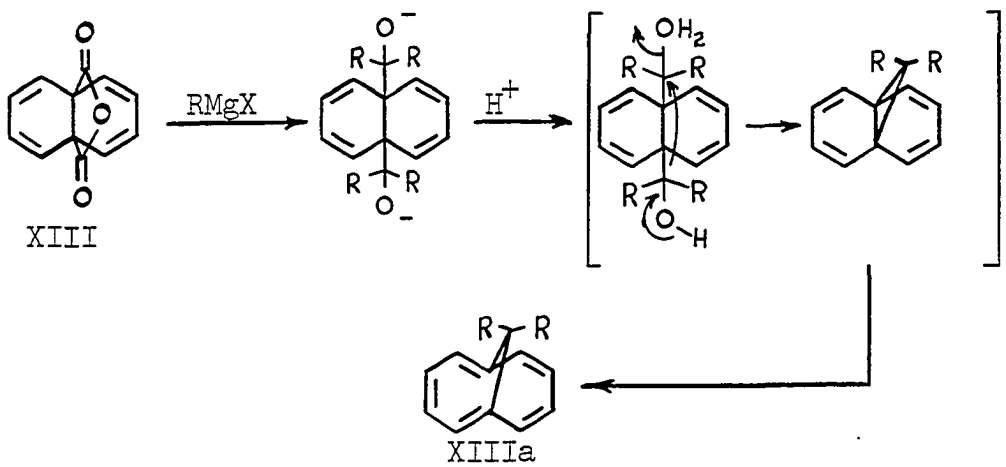
Part I

Five Membered Lactones

In searching for methods to prepare bridged cyclodecapentaenes the idea of treating 9,10-dihydronaphthalene-9,10-dicarboxylic acid anhydride (27) with a Grignard reagent was envisioned. The literature seems to give little information on this type reaction past the preparation of desired ketones, aldehydes, or alcohols. Grignard and Tissier (81) found that anhydrides reacted with three equivalents of reagent to form tertiary alcohols and the magnesium salt of the corresponding acid. Using equimolar quantities of Grignard reagent and acetic-formic anhydride, Edwards and Kammann (82) were able to prepare 35% yields of aldehydes at -70°. Ketones are also available using a 1:1 ratio (83,84). Berlingozzi (85) was successful in preparing a lactone from 4,5-dihydrophthalic anhydride using two equivalents of Grignard reagent.

It seemed possible that if the anhydride XIII were treated with excess Grignard reagent, rearrangement might

occur (perhaps in workup) by the route indicated below to produce a methylene bridged cyclodecapentaene XIIIa.

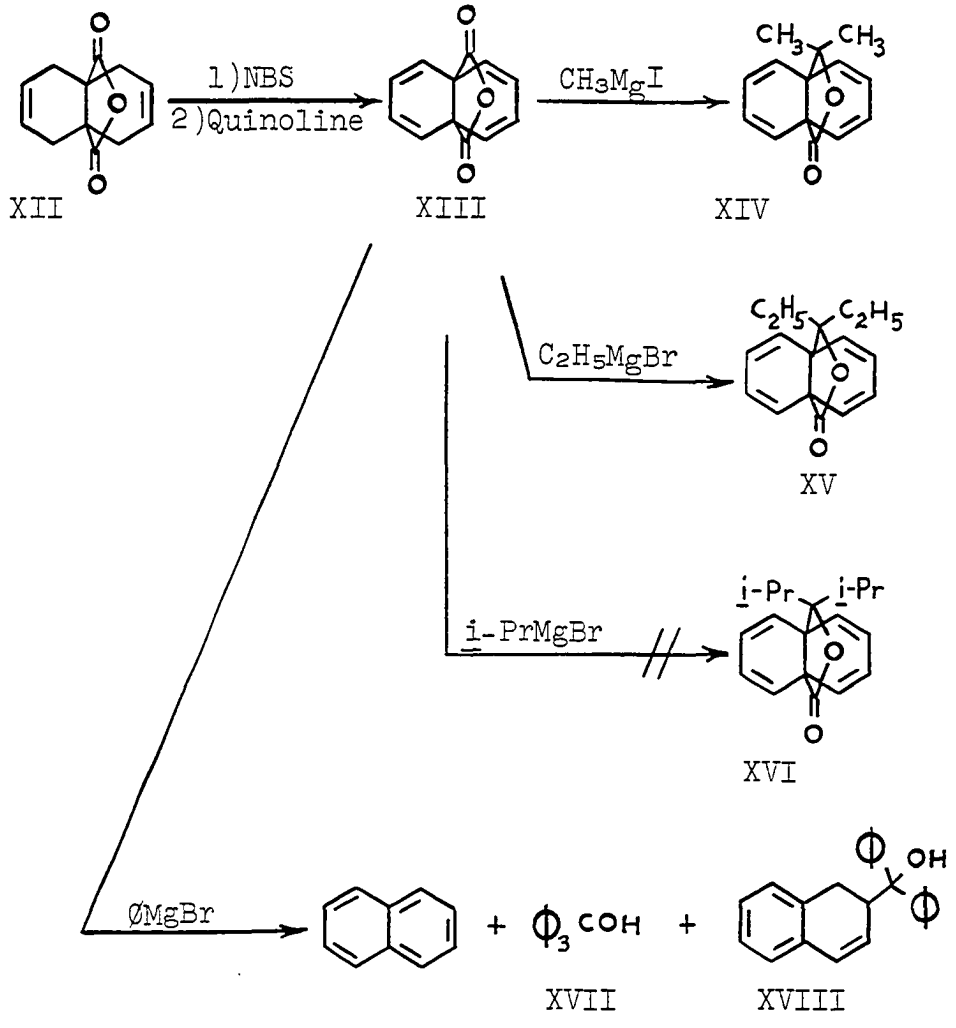


With the proposed scheme in mind, anhydride XIII was treated with seven equivalents of methyl magnesium iodide. The only products obtained were a large amount of polymer, an undetermined amount of naphthalene, and the dimethyl lactone XIV (Scheme I, page 28) in 26% yield. The lactone was also the only isolable product when the mixture was refluxed overnight in an effort to force further reaction. When the lactone was treated with excess methyl magnesium iodide a dark, gummy multicomponent mixture was obtained which had no aromatic protons (other than naphthalene), a carbonyl stretch like the starting material, and no visible hydroxyl protons in the NMR. No attempt was made to separate the mixture.

Attention was then directed to synthesis of other lactones using this method. The diethyl lactone XV was

prepared in only 9.6% yield using excess ethyl magnesium bromide or XIII. Preparation of the more hindered isopropyl lactone XVI was attempted also. Excess isopropyl magnesium bromide on XIII yielded, after chromatography, only a small amount of material (ca. 5% of starting material) whose NMR spectrum gave promise of containing the desired product. However, it appeared to be a mixture.

Treatment of XIII with excess phenyl magnesium bromide

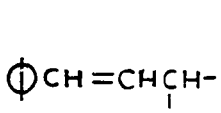


Scheme I

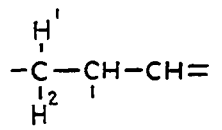
did not yield a lactone but gave a mixture of naphthalene, triphenyl carbinol XVII in 10.3% yield, and a second alcohol which subsequently was proved to be XVIII in 15.5% yield.

Proof of the structure of XVIII was obtained by a systematic approach followed by synthesis of two derivatives. Microanalysis of XVIII agreed with a formula of $C_{23}H_{20}O$, which is equivalent to the addition of two phenyl groups to XIII and the loss of carbon dioxide. The infrared spectrum yielded little information past a hydroxyl absorption. The NMR spectrum (CCl_4) displayed a complex aromatic region of fourteen protons, an AX pattern in the vinyl region (J=10cps) with each peak split into a doublet (J=3cps) of two protons, a one proton multiplet of ten peaks at 3.5 to 3.9 ppm appearing roughly like a triplet and in groups of 3,4, and 3 peaks, a six-line pattern at 2.3 to 3.2 ppm representing two protons (7 to 8 peaks in $CDCl_3$), and the alcohol proton at 1.96 ppm.

The facts that the major product contained aliphatic protons, as seen in the NMR spectrum, and that triphenyl carbinol also was isolated were indicative of a rearrangement. Interpretation of the vinyl pattern led to partial structure A.



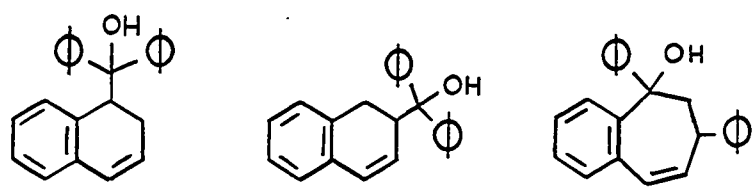
A



B

The two aliphatic protons at 2.3-3.2 ppm displayed a wide pattern, indicating non-equivalent protons of about the same shift, perhaps on the same carbon. Although the multiplet at 3.5-3.9 ppm seemed to be a triplet and thus coupled with a methylene, the complexity of the pattern indicated more than two different protons were coupled with it, and perhaps it was connected to the vinyl pattern. To account for all the protons, structure B was assumed for the aliphatic portion of the molecule.

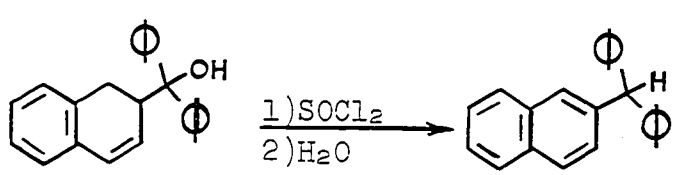
Three possible structures were visualized that could fit the data.



C D E

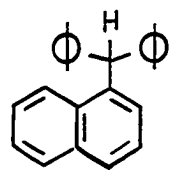
In structure C the methylene protons would be expected to appear as a double doublet split into an eight-line spectrum. The NMR spectrum was not well defined, however, so structure C could not be discounted.

Dehydration of XVIII with thionyl chloride in carbon tetrachloride and subsequent boiling with water produced a mixture which was placed on Florisil and washed with hexane.



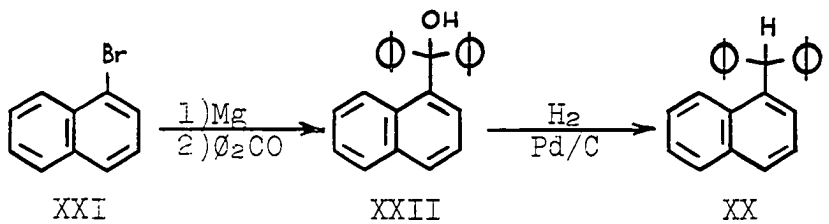
XVIII XIX

A single component was thus obtained whose NMR spectrum displayed a complex aromatic region and a singlet at 5.61 ppm with an integral ratio of 17:1. Since dehydration of compound E should lead to a compound with vinyl protons, it could be ruled out, leaving XIX or XX as the possible dehydration product.

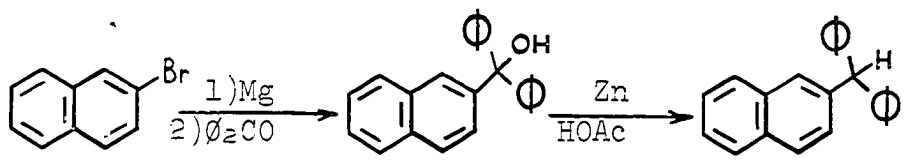


XX

These two hydrocarbons were synthesized by treatment of the corresponding naphthyl Grignard reagent with benzophenone and subsequent reduction of the alcohol.



XXI XXII XX

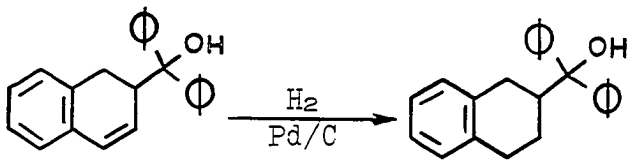


XXIII XXIV XIX (86)

The NMR spectrum of XX was unlike that of the dehydration product, possessing a singlet at 6.20 ppm for the benzyl

proton, whereas the NMR spectrum of XIX superimposed on that of the dehydration product of XVIII.

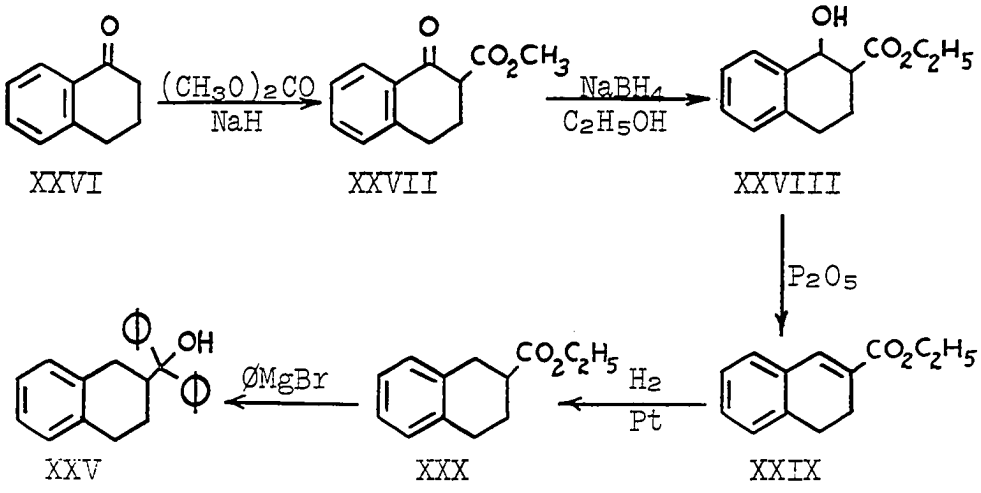
Alcohol XVIII was hydrogenated over palladium on carbon producing an alcohol XXV which had absorbed one equivalent of hydrogen, confirming the presence of one double bond in XVIII.



XVIII XXV

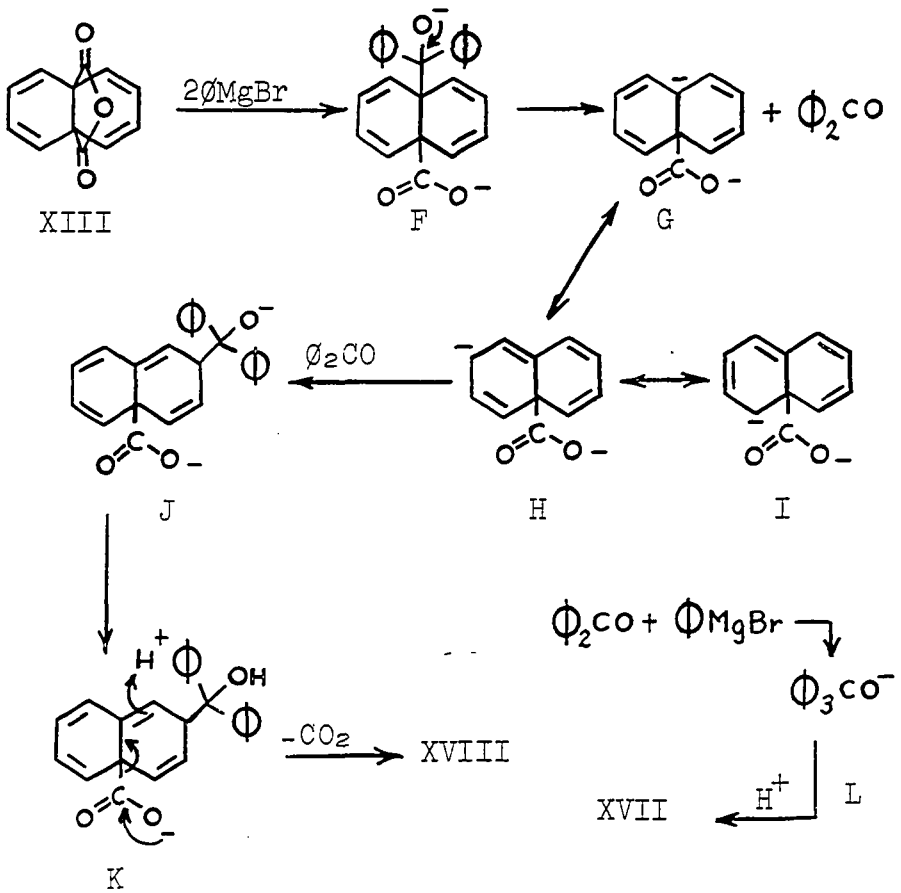
Because an analytical sample of the dehydration product XIX was not obtained, and since it was felt that the dehydration conditions might have caused rearrangement leading to XIX, a synthesis of the hydrogenation product XXV was devised. The original method employed reduction of α- or β- tetralone to the corresponding alcohol, conversion to the halide, and preparation of the α- or β-Grignard followed by treatment with benzophenone. In each case formation of the Grignard reagent failed, and the scheme was substituted with another synthesis but only for the β-isomer.

The synthesis began with α-tetralone XXVI as shown on page 33. It was alkylated to the β-keto ester XXVII followed by reduction to XXVIII and dehydration to the α,β-unsaturated ester XXIX.



Ester XXIX was hydrogenated to XXX, which was treated with phenyl magnesium bromide to produce alcohol XXV. The first step produced unreacted starting material and the desired keto ester XXVII, which were not well separated. Reduction of XXVII with sodium borohydride in absolute ethanol was allowed to become too warm, and transesterification took place. Dehydration of XXVIII with phosphorous pentoxide allowed easy chromatographic separation of XXIX from the hydrocarbon resulting from the small amount of starting ketone in the mixture. Hydrogenation of XXIX went smoothly using Adams catalyst, and the Grignard reaction in the last step produced a mixture which was chromatographed to yield alcohol XXV. The NMR and IR spectra of this product superimposed on those of the hydrogenated product from XVIII, and a mixed melting point showed no depression. The second alcohol obtained in the reaction of phenyl magnesium bromide with anhydride XIII thus proved to be structure XVIII or D.

A possible mechanism by which the two alcohols from the Grignard reaction might be formed is suggested below.



Initial attack of the Grignard reagent at one of the carbonyls to produce 9,10-dihydronaphtho-9-phenone-10-carboxylate followed by attack of a second Grignard at the ketone yielded dianon F which was probably quite hindered. Loss of benzophenone, probably due to steric hindrance, produced anions G, H and I, I being the least likely due to proximity of the carboxylate. Intermediate G would regenerate F by reaction with benzophenone but probably could not, for no lactone was found in the product mixture. Anion H, in

competition with excess Grignard reagent for the ejected benzophenone, would give alcoholate J. At this point alcoholates J and L were produced. Acidification of the mixture with ammonium chloride solution would then give triphenyl carbinol XVII and, with loss of carbon dioxide in K, yield XVII. It is interesting to note that no products corresponding to these two alcohols were observed in preparation of lactones XIV and XV.

Naphthalene was produced in all the Grignard reactions. A possible source of this product could come from decarboxylation of anions G, H and I upon acidification followed by air oxidation of the resulting dihydronaphthalenes. However, this possibility assumes formation of alcohols from the dimethyl and diethyl lactone preparations corresponding to XVIII and XVII, but none were isolated. Another source is formation of the lactone upon acidification of the mixture followed by loss of the bridge to form naphthalene, carbon monoxide and the dialkyl (aryl) ketone. This source is less likely, for no benzophenone was isolated in the phenyl Grignard reaction. Thus, naphthalene probably comes about by another mechanism.

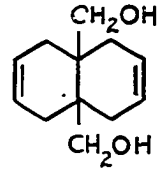
Summary

The method of preparing a methylene bridged cyclodecapentaene by reaction of excess Grignard reagent with 9,10-dihydronaphthalene-9,10-dicarboxylic acid anhydride did not work under the conditions tried. However, the reaction yielded a lactone at the nine and ten positions of 9,10-dihydronaphthalene in low yields. As the group in the Grignard reagent became larger, lower yields of lactones were produced. In the case of the phenyl Grignard reaction no lactone was obtained, but an alcohol was produced which was a rearrangement product. The structure of this product was determined by spectra and synthesis of two derivatives. A mechanism for the rearrangement is suggested.

Part II

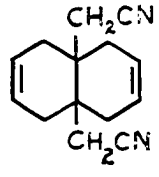
Five-Membered Bridges

Bridged cyclodecapentaenes containing five- and six-membered bridges across the one and six positions are not known, and it was thought that bis-homologation of the reduced starting material XXXI followed by cyclization could lead to such systems.

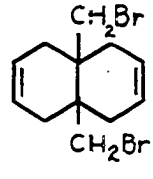


XXXI

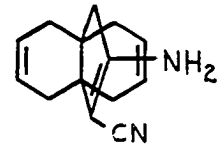
Success at homologation and cyclization has been reported recently (87-91).



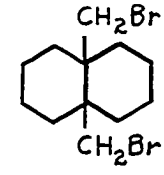
XXXII



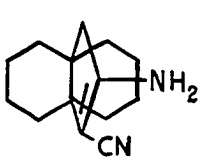
XXXIII



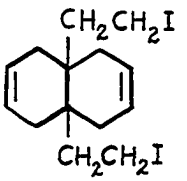
XXXIV



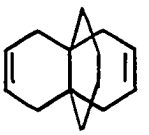
XXXV



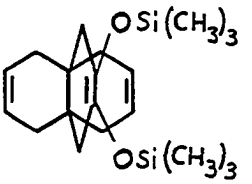
XXXVI



XXXVII



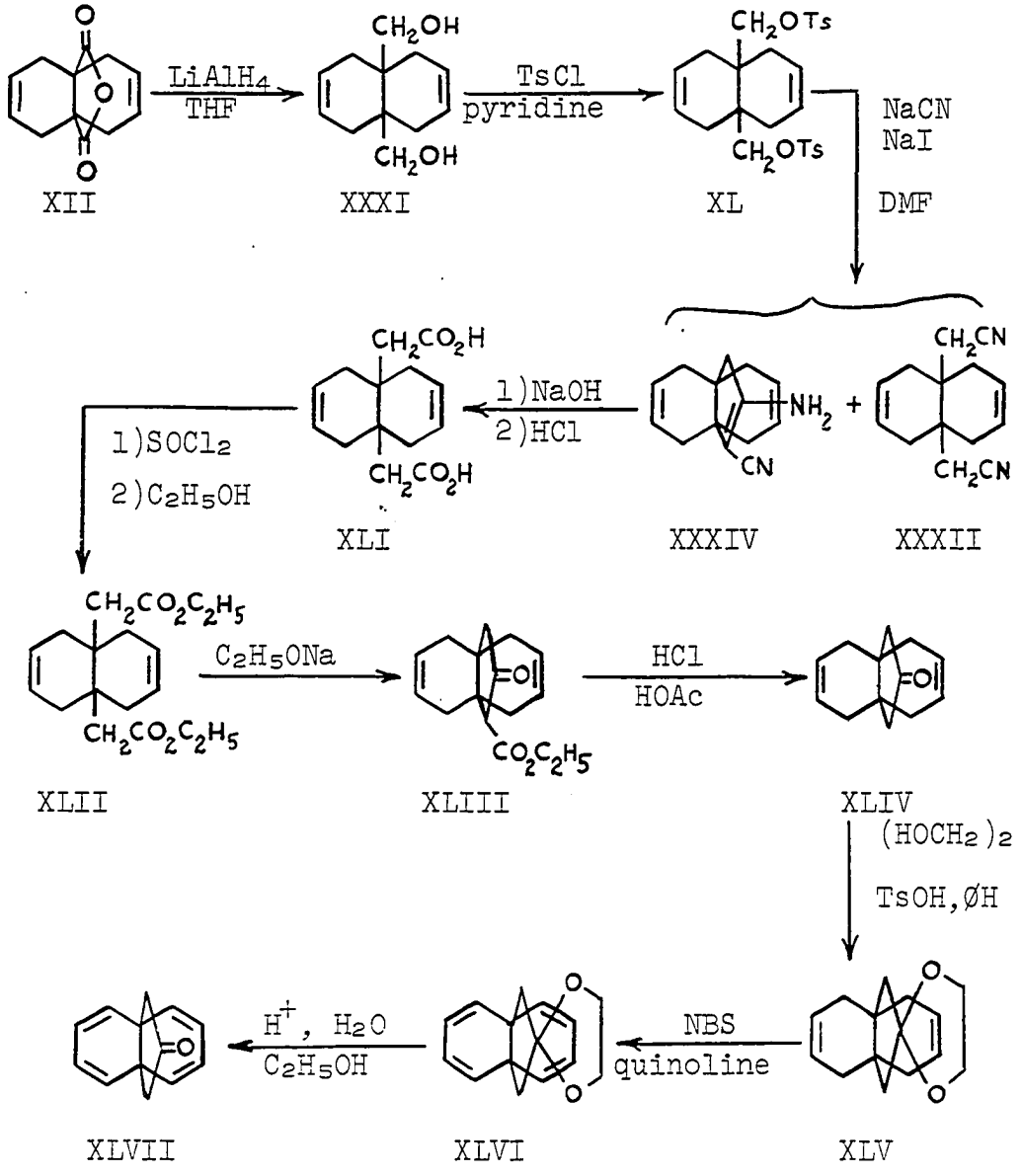
XXXVIII



XXXIX

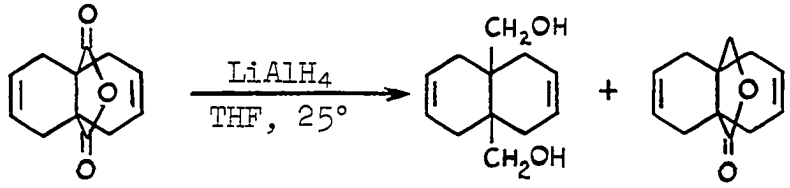
Preparation of dinitrile XXXII and cyclization to the Thorpe product XXXIV has been accomplished by three different groups. The procedure consists of teatment of the ditosylate (87) or dimesylate (90) of diol XXXI and dibromide XXXIII with sodium cyanide in dimethyl sulfoxide or dimethyl formamide. The same procedure was successful on the saturated dibromide XXXV to produce XXXVI. Diiodide XXXVII was prepared from dinitrile XXXII by hydrolysis, reduction, and then treatment with sodium iodide. Cyclization to XXXVIII was accomplished with n-butyllithium (90). Disiloxane XXXIX was prepared in good yield by a modification of the acyloin condensation from the dimethyl ester derived from XXXII (91).

When the problem was begun according to Scheme II, page 39, use was made of the one publication available at that time (87) concerning these systems. The bis-homologation was performed using a modification of the procedure (92) and the remainder of the synthesis carried out as presented. When partially complete, the synthesis of ketone XLIV appeared (89), and materials isolated in the scheme up to XLIV were not characterized.



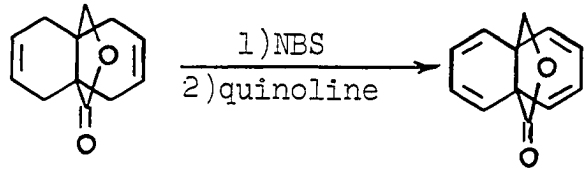
Scheme II

In the first step of the sequence an unexpected mixture was obtained. The reaction mixture in the lithium aluminum hydride reduction of XII was not refluxed, and a mixture of diol XXXI and lactone XLVIII was obtained (93).



XII XXXI 60% XLVIII 33%

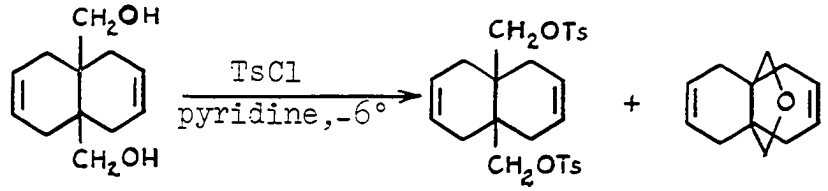
Bloomfield and Lee (94) have been successful in performing this reduction to lactone XLVIII only, using 0.5 mole lithium aluminum hydride in tetrahydrofuran at -55° with an 83% yield. Since XLVIII was available, it was converted to the tetraene lactone XLIX in 10.4% yield by allylic bromination followed by dehydrobromination.



XLVIII XLIX

Subsequent reductions of XIII were carried out at reflux and diol XXXI was obtained in high yields, as has been reported (95).

The simple conversion of diol XXXI in scheme II to ditosylate XL was performed at -6° using pyridine as solvent. Unless some anhydrous ether was added, the side product ether L was formed in significant amounts.



XXXI XL L

The ditosylate XL has been prepared without difficulty (92)*, but under these conditions a little ether was used.

The dinitrile-Thorpe product mixture (XXXII and XXXIV) was then obtained in 40% yield using a 1:2:6 mole ratio of XL, sodium iodide, and sodium cyanide in boiling dimethyl formamide, which is a slight modification of the procedure described (87,92). The crude mixture was directly hydrolyzed to diacid XLI with sodium hydroxide in ethylene glycol-water. Esterification of XLI with thionyl chloride in benzene followed by treatment with absolute ethanol gave diester XLII in high yield. Dieckmann condensation of the crude diester with sodium ethoxide in benzene gave β-keto ester XLIII in high yield. Hydrolysis of XLIII and decarboxylation to a 68% yield of ketone XLIV was carried out in acetic acid-hydrochloric acid.

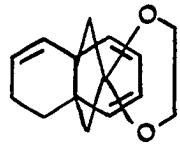
Up to this point the crude product of each reaction had been used directly in the next step with little characterization. Ketone XLIV was characterized and found to be a solid, contrary to the report of Altman and coworkers (88), who claim the substance to be a liquid. The product obtained in this laboratory gave a cleaner NMR spectrum than they described. They prepared XLIV by acidic hydrolysis of Thorpe product XXXIV in a sealed tube at 175°, and it is

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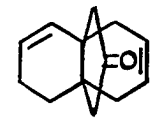
*Tetrahydrofuran was used in that case to dissolve the diol.

probable that their more severe conditions yielded a mixture of double bond isomers. Indeed, significant amounts of liquid product were obtained in this laboratory when prolonged reflux periods (XLIII to XLIV) were employed. Double bond isomerization must occur, for an unexpected product appeared two steps later when unrecrystallized XLIV was used. The yields of the two methods from XXXIV are comparable (45% by their method and 46% by this method), but a cleaner product is obtained by the longer route.

Ketone XLIV was converted to its glycol ketal XLV to prevent α-bromination in the next step. Ketal XLV was brominated with N-bromosuccinimide and dehydrobrominated with quinoline to yield XLVI. Hydrolysis of the crude mixture and separation by preparative gas chromatography using a 20% carbowax on ABS Anachrom column at 190° provided a mixture of XLVII and another ketone eluting as a single peak. The ketone mixture also gave a single peak on an analytical column of 15% diethylphthalate. In another run, column chromatography of the reaction mixture on silicic acid hydrolyzed the ketals to the same ketone mixture. The ketone mixture was reketalized, and separation was effected by preparative gas chromatography using the same carbowax column (at 198°) into ketal XLVI (8.2%) and what is thought to be ketal LI as determined from the NMR spectrum.



LI



LII

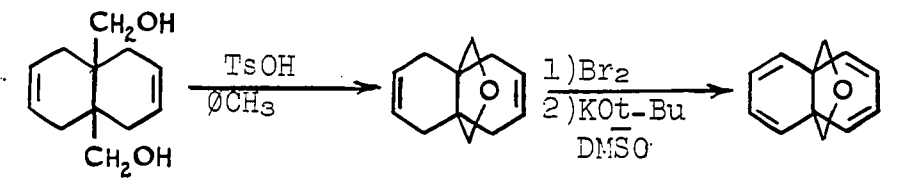
The spectrum of LI(CCl_4) showed a vinyl multiplet at 5.2-6.0 ppm in what appeared to be a close A_2B_2 pattern with a multiplet in the center, a singlet at 3.72 ppm, and a group of multiplets in the methylene region at 1.7-2.5 ppm having major peaks at 1.95, 2.20, and 2.43 ppm and with a singlet at 2.00 ppm. It is suspected that ketal LI is the product derived from ketone LII, a double-bond isomer of XLIV obtained during the hydrolysis of XLIII mentioned earlier.

Acidic hydrolysis of XLVI to tetraene ketone XLVII was effected at room temperature in ethanol-water in 89% yield. The NMR spectrum of this compound (see Appendix, figure 6) displayed an A_2B_2 pattern centered at 5.62 ppm for the vinyl protons and a singlet at 3.40 ppm for the α-protons. By comparing this spectrum with that of 1,6-methanocyclodecapentaene prepared by Vogel (54) (see page 13), it can be seen that ketone XLVII is not aromatic. If it were, the vinyl protons would be expected at lower field and the α-protons at higher field.

It was felt that a thermal experiment on XLVII would be of little value due to the results from heating other compounds, as explained later. In view of these other

experiments, it is possible that heating the ketone might yield naphthalene and cyclopropanone, probably requiring a temperature above 200° (XLVII was isolated by gas chromatography at 198°). Cyclopropanone has been synthesized (96) and found to polymerize at room temperature.

The availability of diol XXXI prompted the synthesis of another tetraene already described (95) for thermal study as shown in Scheme III.

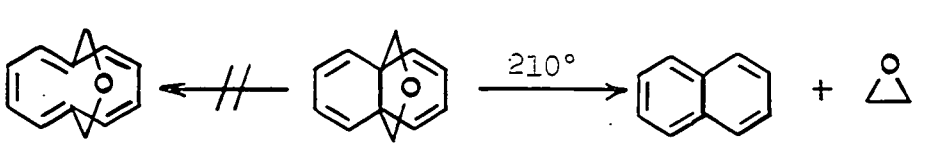


XXXI L LIII

Scheme III

The last step of the scheme was performed in dimethyl sulfoxide rather than in tert-butyl alcohol (as reported), but a poorer yield was obtained (4.3% compared to 7-10% in ref. 95). The remainder of the scheme was unchanged.

Ether LIII was heated in a sealed NMR tube using cyclododecane as solvent with the hope that the compound would isomerize to the corresponding cyclodecapentaene LIV.



LIV LIII

However, the compound began losing a molecule of ethylene oxide at 210-212° to form naphthalene. Ethylene oxide was isolated from the reaction by breaking the NMR tube in a partially evacuated system containing another NMR tube with carbon tetrachloride in it. The new NMR tube was cooled (while inside) in an ice-salt bath for four hours and when removed, produced a spectrum of one singlet at 2.53 ppm, identical to that of an authentic sample of ethylene oxide.

The decomposition at 210° was followed by NMR, and by the ratio of integrals of vinyl protons in LIII to naphthalene protons a kinetic plot was obtained (see Appendix, figure 29). The data was taken in this manner because too many variables in the spectrometer were not accounted for, and comparison of the integrals at various times with the integral at time zero was rendered useless. As seen in figure 29, the kinetic plot closely approaches a straight line, and thus a first order reaction might be assumed. The half life is estimated at 12.6 hours from the data and 12.4 hours from the straight line approximation. As the reaction progressed, other products were being formed in increasing quantities as seen in the NMR spectra and made reading of the integral difficult toward the latter part of the reaction. Perhaps if the clean integrals could be taken, the plot would more closely follow first order kinetics.

Summary

The tetraene ketone, tricyclo-[4.4.3.$0^{1,6}$]-12-one-2,4,7,9-tridecatetraene, was prepared by a ten-step synthesis using $\Delta^{2,6}$-hexalin-9,10-dicarboxylic acid anhydride as starting material. Lithium aluminum hydride reduction of this anhydride yielded an unexpected mixture of a diol and a lactone, and the lactone was converted to the corresponding tetraene lactone. Formation of the ditosylate of the diol also produced a mixture. Products of the synthesis from this point were not analyzed until tricyclo-[4.4.3.$0^{1,6}$]-12-one-3,8-tridecadiene was obtained, which was found to have different characteristics than those reported (88). This ketone was converted to its ketal, which was converted to the ketal of the final product in low yield. The final product was obtained by simple hydrolysis in high yield.

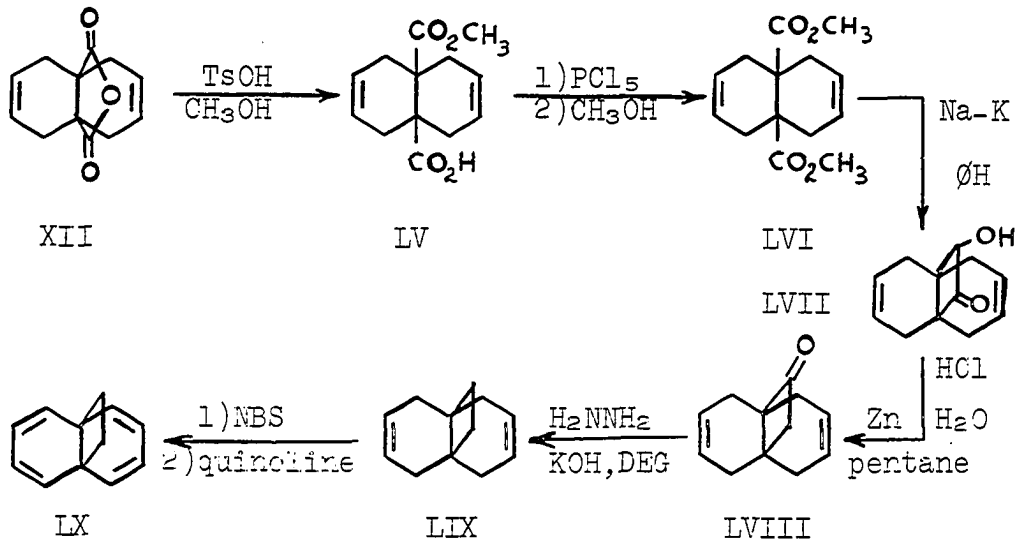
The tetraene ether, 12-oxatricyclo-[4.4.3.$0^{1,6}$]-2,4,7,9-tridecatetraene, was prepared by a known scheme (95) and found to decompose slowly at 210° to yield naphthalene and ethylene oxide.

Part III

Four-Membered Rings

The successful synthesis of the first bridged [10] annulene by Vogel and Roth (54) and the remarkable stability of the molecule compared to unbridged annulenes (see page 13) prompted an attempt to synthesize the next higher bridged homolog, 1,6-ethanocyclodecapentaene. The prospect of obtaining the ethano-compound by isomerization of 9,10-ethano-9,10-dihydronaphthalene seemed promising since the methano-compound had essentially been prepared by that method (page 12). Synthesis of 9,10-ethano-9,10-dihydronaphthalene was then carried out in six steps according to Scheme IV, page 48. This synthesis, different than one carried out by Vogel and coworkers (72), described on page 21, was published later the same year (73).

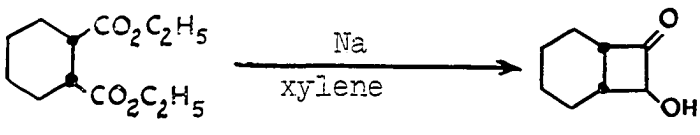
The scheme presented on page 48 represents a method by which clean products may be obtained and does not reflect the difficulties encountered en route to the final product, LX. These difficulties will be described in turn in the ensuing discussion. As in Parts I and II, the starting material was anhydride XII.



Scheme IV

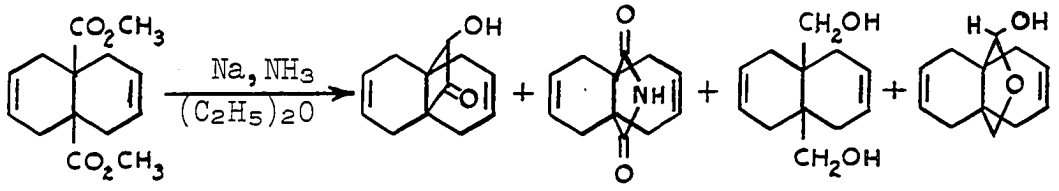
Esterification of XII with p-toluene sulfonic acid in methanol for three days yielded ester-acid LV. This product could be separated easily from other products in the preparation of XII and thus allowed use of crude XII. Diester LVI was prepared by phosphorous pentachloride treatment of LV followed by esterification with methanol.

At this point it was thought that an acyloin condensation of LVI might yield α-ketol LVII. At that time only one successful cyclization to a four-membered ring had been reported. The α-ketol LXII was isolated in 12% yield (97).



LXI LXII

With this scant background, the condensation of LVI was attempted using four equivalents of sodium in liquid ammonia, and the following mixture was obtained (98).



LVI	LVII	LXIII	XXXI	LXIV
	10.1%	35.6%	21.1%	6.4%

After chromatographic separation on silicic acid, the desired acyloin LVII was isolated in 10% yield. Imide LXIII could come about by aminolysis of diester LVI, but XXXI and LXIV are more difficult to explain. Evidently they were obtained in a Bouveault-Blanc-type reduction, using ammonia as proton source. Hemiacetal LXIV is a logical intermediate in this reduction to diol XXXI.

Since a large quantity of LVII was needed, the cyclization was attempted in an inert solvent, i.e., refluxing toluene using four equivalents of sodium, in an attempt to increase the yield, but only unreacted starting material was obtained. A publication by Goldfarb and coworkers (99), suggested the efficacy of sodium-potassium alloy (1:1 weight ratio), and the cyclization was attempted in refluxing xylene with this alloy. A 77% yield of a mixture of LVI and LVII was obtained which, after recrystallization, gave a 26% yield

of LVII. Ultimately, the reaction was performed in refluxing benzene using a high speed stirrer, and high yields, free of diester LVI, were obtained. The results of several runs are tabulated in Table 1.

TABLE 1

EFFECT OF METAL-DIESTER MOLE RATIO ON YIELD OF ACYLOIN

Mole Ratio				Yield, %	
LVI	Na	K	Solvent	Crude	Recryst.
1	4.00	-	toluene	0	-
1	6.1	3.6	xylene	77	26[a]
1	7.65	4.46	xylene	87	32[a]
1	3.07	1.84	benzene	110	39[a]
1	3.84	2.32	benzene	89	-[a,b]
1	3.95	2.30	benzene	-	61[a,c]
1	4.42	2.54	benzene	99	57[a]
1	5.05	2.97	benzene	94	70[d]
1	5.60	3.15	benzene	91	76[d]
1	5.97	3.32	benzene	91	70[d]
1	6.69	4.11	benzene	92	71[d]
1	5.57	3.23	benzene	91	80[d]
1	5.61	2.85	benzene	93	78[d]
1	5.71	3.17	benzene	93	81[d]
1	5.71	3.24	benzene	92	79[d]

[a]The crude product was a mixture of diester LVI and acyloin LVII. The recrystallized yield is that obtained free of diester.

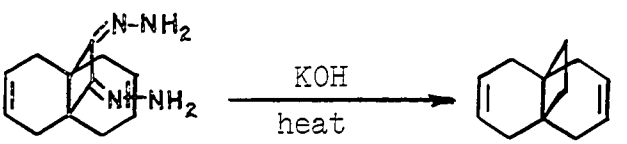
[b]The crude product was used in another reaction, and a considerable quantity of diester was recovered.

[c]The reaction was worked up immediately after addition of diester was completed and contained starting material.

[d]The crude yield was free of starting material, and the recrystallized yield is that obtained after one recrystallization. In the last four runs an additional amount was obtained from the recrystallization liquids.

When the reaction was first performed in benzene, the total metal content was above the required four equivalents, and starting material was found in the product. It was eventually found that the ratio of sodium to diester LVI was critical and needed to be above a ratio of 5:1; otherwise the cyclization was incomplete. A factor not reflected in the data above was the period of reflux after completion of addition of diester LVI. Long reflux times were necessary, especially for large (0.4 mole) scale reactions. The best yields of acyloin LVII were thus obtained when the mole ratio of sodium to diester LVI was above 5:1 and overnight reflux was employed before workup.

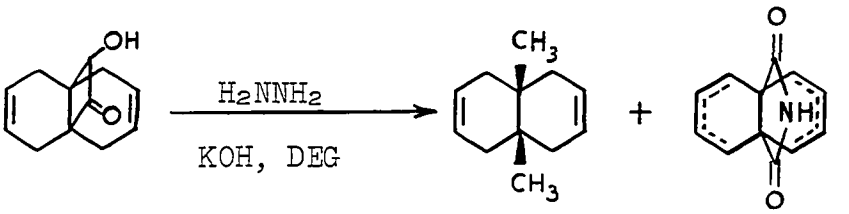
The next part of the synthesis called for reduction of the α-ketol to a hydrocarbon, and it was thought this might be accomplished in one step with a Wolff-Kishner reduction. Using the analogy of osazone formation of sugars, it was hoped an oxidation step would occur leading to dihydrazone LXV, which would then reduce in the normal manner to hydrocarbon LIX.



LXV LIX

Using the Huang-Minlon modification (100) of the Wolff-Kishner reduction, the reaction was performed in diethylene glycol. An oxidation step did seem to be involved but in

the manner of ring rupture rather than desired at the alcohol only. The following mixture was obtained.



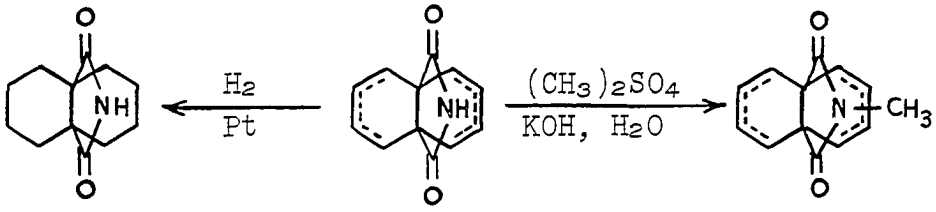
LVII LXVI LXVII

30.9% 21.8%

The hydrocarbon cis-9,10-dimethyl-$\Delta^{2,6}$-hexalin was obtained in 30.9% yield and the imide mixture LXVII in 21.8%. Compound LXVI was identified by analysis and by its NMR and IR spectra. Recent publication of its preparation (90) confirms the above structure. Identification of imide mixture LXVII was more involved.

The NMR spectrum of LXVII in $CDCl_3$ displayed a broad peak in the range of 8.3 to 9.2 ppm for the labile proton, and two multiplets, one in the vinyl region and one in the allyl proton area, with an integral ratio of 1:4:8. The IR spectrum was almost identical to that of imide LXIII, indicating a closely related system for LXVII. A Rast molecular weight determination revealed a weight of 388, or the possibility of a dimer, but repetition gave a weight of 521. Comparison of these values to the Rast value of 473 obtained from imide LXIII indicates that these molecules may be associating and that a true molecular weight cannot be derived from the Rast. Compounds LXVII could be alkylated with

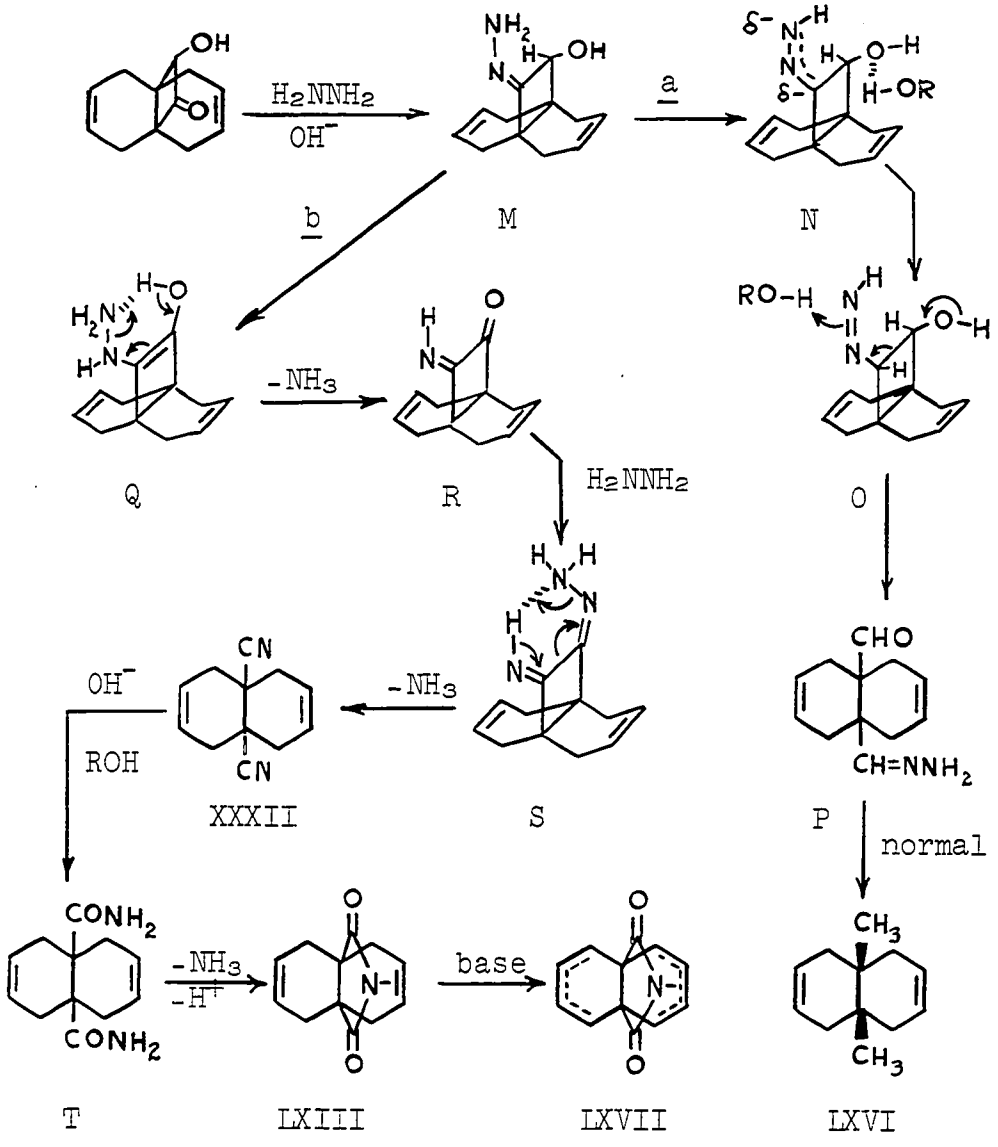
dimethyl sulfate to LXVIII, confirming the presence of a labile proton.



LXIX LXVII LXVIII

It was difficult to obtain a sharp melting range for LXVII, but upon hydrogenation of the material the sharp-melting saturated imide LXIX was produced. Hydrogenation of the known imide LXIII yielded the same product. Altman and co-workers (88) have reported the synthesis of LXIX, and their compound has a lower melting point (c.a. 35°) than found in this laboratory. It is suggested by the poor analysis they obtained that their compound was impure.

A mechanism for the products LXVI and LXVII is suggested in Scheme V on page 54. Formation of hydrazone M is a logical first step, and as the heat of the reaction was increased, decomposition of M might proceed by the two paths a and b. In path a, leading to LXVI, the trans hydrazide anion N is assumed as postulated by Szmant (101). The proton needed for reduction of the hydrazide ion could be supplied from a solvent molecule hydrogen-bonded to the alcohol function, leading to trans structure O. Trans ring cleavage might then occur leading to aldehyde-hydrazone P. Formation of the dihydrazone followed by a normal Wolff-Kishner reduction would produce cis-9,10-dimethyl-$\Delta^{2,6}$-hexalin LXVI.

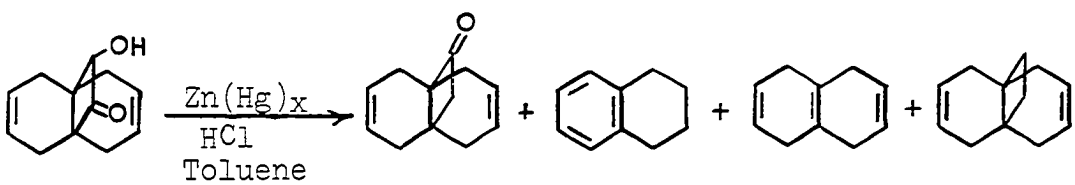


Scheme V

In path b, leading to imide mixture LXVII, removal of the proton under the alcohol function by base leads to enol structure Q. Loss of ammonia, perhaps via a six-membered intermediate, would result in keto-imine R. Formation of hydrazone-imine S could easily occur with excess hydrazine present. Ring opening with loss of ammonia, perhaps via a

six-membered intermediate, would yield dinitrile XXXII. This step is analogous to the formation of nitriles by basic treatment of aldehyde phenyl hydrazones (102) or other related eliminations (103-106) and the six-atom intermediate to that suggested by Leonard and Gelfand (107) in a Wolff-Kishner elimination having α-leaving groups. Partial hydrolysis of XXXII with base would lead to diamide T. Loss of ammonia in the hot basic mixture would leave imide LXII as the anion. Allylic rearrangement of the double bonds would produce anion mixture LXVII. It is interesting to note that LXVII could not be hydrolyzed under basic conditions (2:1 ethylene glycol-water, 6N sodium hydroxide).

Since the Wolff-Kishner reaction produced ring-opened products, a different approach was necessary. The Clemmenson reduction was performed on ketol LVII in a two-phase system of toluene-6N hydrochloric acid over zinc amalgam and gently refluxed for 22 hours. The reduction produced ketone LVIII in 36% yield, a mixture of hydrocarbons LXX, LXXI, and LIX, and unreacted starting material.

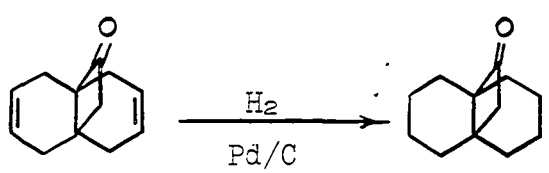


LVII LVIII LXX LXXI LIX

From later runs it was determined that the product ratio of LVIII to hydrocarbon mixture increased with shorter reflux

times. A reflux time of 9 hours gave ketone LVIII in 44.5% yield, and the hydrocarbon mixture from this run was identified by comparison of NMR spectra to consist of tetralin LXX in 6.6% yield, diene LIX in 7.1% yield, and isotetralin LXXI in a trace quantity.

Reduction in benzene at 60° for 72 hours produced ketone LVIII in 50.5% yield and the hydrocarbon mixture in 4.2% yield. The hydrocarbon mixture was shown by retention times on gas chromatography to contain 44.2% diene LIX, 21.9% tetralin LXX, 7.3% isotetralin LXXI, and 20.5% ketone LXX. The acyloin LVII was recovered in 19.9% yield. Thus, temperature was also found to be an important factor.* By trial and error it was eventually discovered that ketone LVIII could be produced as the sole product in 63% yield if the reaction was carried out at 27-35° using pentane as the organic solvent and if the reaction was stirred at the liquid-liquid interface for 11 hours. Saturated ketone LXXII was prepared from LVIII by hydrogenation with absorption of two equivalents of hydrogen.

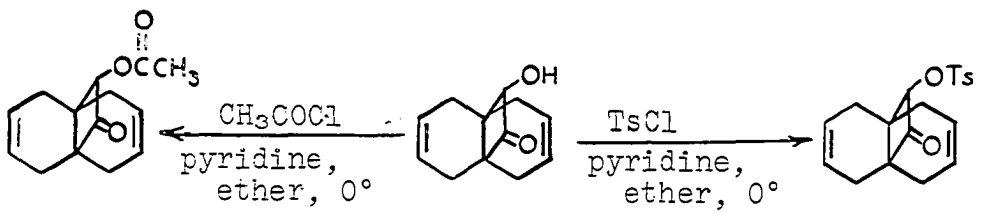


LVIII LXXII

*Part of the work on the Clemmenson reduction of LVII and identification of resulting mixtures was done with the aid of Mr. Kenneth Krajca, June-August, 1966, University of Oklahoma.

Production of ketone LVIII could easily follow a dissolving metal reduction mechanism (108), with diene LIX as the normal Clemmenson reduction product of LVIII. Tetralin LXX is probably the acidic rearrangement product of isotetralin LXXI. Treatment of diene LIX with acid was not investigated, but it is thought that isotetralin was produced by loss of the bridge in LIX in the acidic medium. Some support for this suspicion is obtained from the product ratio of LIX to tetralin-isotetralin, which seemed to increase with decreasing temperature (1.08:1 using toluene at reflux to 1.5:1 in benzene at 60°).

Before the reaction in pentane was attempted, attention was devoted to other efforts for obtaining ketone LVIII in better yields than described in the toluene reaction. To this end, keto-acetate LXXIII and keto-tosylate LXXIV were prepared for calcium in liquid ammonia reductions (109,110).

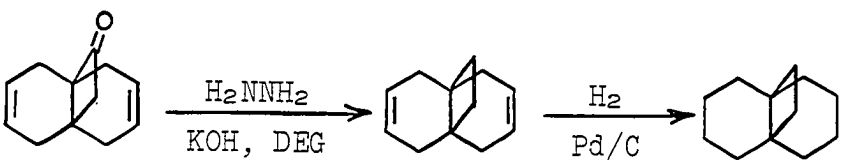


LXXIII LVII LXXIV

It was reasoned that either of these α- substituents would be better leaving groups than the hydroxyl group in acyloin LVII and thus give better yields of LVIII. Both reactions yielded mixtures, and after chromatographic separations only

7.1% ketone LVIII was realized from LXXIII and 1.9% LVIII from tosylate LXXIV.

Ketone LVIII being obtained, a Wolff-Kishner reduction of it gave diene LIX as the sole product in 66% yield.



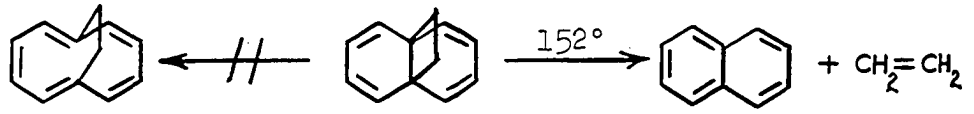
LVIII LIX LXXV

Diene LIX readily absorbed two equivalents of hydrogen to yield hydrocarbon LXXV. The desired end product of the synthesis, tetraene LX, was obtained by either bromination in carbon tetrachloride followed with dehydrobromination using potassium tert-butoxide in dimethyl sulfoxide or allylic bromination with N-bromosuccinimide followed by treatment with quinoline at 140° for 15 minutes. A 16% crude yield was obtained after column chromatography from the butoxide reaction, and a clean product of 13.5% yield was obtained after gas chromatographic separation of the quinoline reaction mixture. Hydrogenation of LX yielded LXXV with absorption of four equivalents of hydrogen.

The tetraene LX displayed an NMR spectrum (see Appendix, figure 7) of an A_2B_2 pattern in the range of 5.1-5.9 ppm (centered at 5.49 ppm) for the vinyl protons and a singlet at 2.53 ppm for the bridge protons. Comparison of this spectrum with that of LIII (Part II) shows that the vinyl protons are

roughly in the same position, and thus by analogy, LX is not aromatic just as LIII is not. A thermal experiment was then tried in an effort to drive LX into aromaticity with the hope that one less atom than in LIII might yield a cyclodecapentaene.

A sample of LX dissolved in hexachlorobutadiene was sealed in an NMR tube under nitrogen and heated for thirty-minute periods at increasing temperatures until changes began taking place at 152°, as displayed in the NMR spectrum.



LXXVI LX

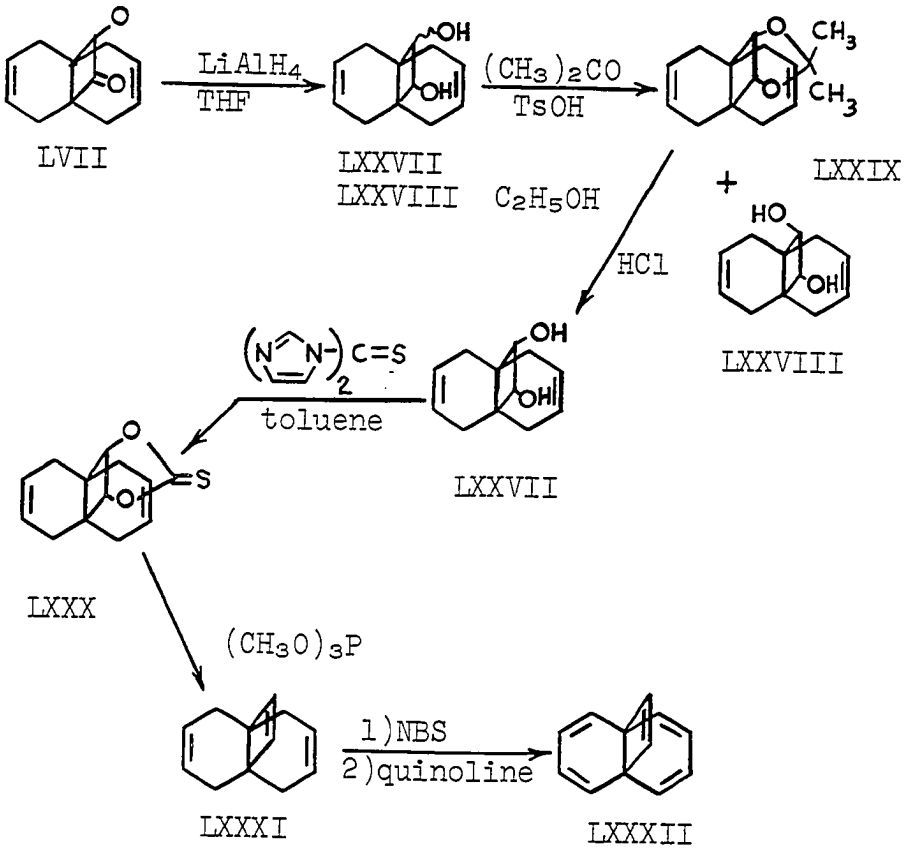
The compound did not rearrange to the desired cyclodecapentaene LXXVI but decomposed to naphthalene and ethylene (72, 73). The NMR tube was sealed into a partially evacuated apparatus containing another NMR tube which held bromine in carbon tetrachloride. The sealed NMR tube was then broken and the bromine color in the companion tube slowly disappeared. The NMR spectrum of the carbon tetrachloride solution displayed a singlet at 3.62 ppm, the same chemical shift as 1,2-dibromoethane. Thus, the reaction had generated ethylene, which was brominated to 1,2-dibromoethane.

A kinetic plot of the decomposition is shown in the Appendix, figure 30. Up to about 35% reacted (0.43, 8 hours), the plot closely approaches a straight line, and deviation is

noted as the concentration of tetraene LX decreases from that point. The decomposition was followed by taking NMR spectra at intervals and comparing the integral of naphthalene with that of part of the tetraene. Other products were being formed and interfered with reading of the integrals. The margin of error is not known but undoubtedly became greater as the reaction progressed. In the initial stage, little contamination was present, and past the point mentioned above, contamination was increasingly noticeable. The half-life of the reaction was plotted from the data at 15 hours (point at 0.69), and from the straight line approximation the value becomes 12.5 hours.

The presence of substituents in the four-membered ring made possible the investigation of substituted 9,10-ethano-bridged-9,10-dihydronaphthalenes. One example, involving the synthesis of 9,10-etheno-9,10-dihydronaphthalene LXXXII, was visualized with the hope it would isomerize to an ethylene bridged cyclodecapentaene and not decompose to naphthalene and acetylene. The synthesis was carried out in part according to Scheme VI from the readily available acyloin LVII.

Reduction of acyloin LVII with lithium aluminum hydride produced diol mixture LXXVII and LXXVIII in 97% yield. It was found that the amount of <u>cis</u> diol could be increased at the expense of the <u>trans</u> diol by slow addition of a dilute solution of LVII to the reducing agent. These

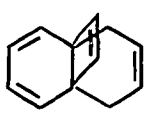


Scheme VI

diols were first separated by column chromatography, but the most effective and simplest separation, particularly with large quantities, was effected by first converting the cis-diol to its cyclic acetonide LXXIX. The diol mixture was dissolved in acetone containing a small amount of p-toluene-sulfonic acid and allowed to stand for one day. Removal of the acid and acetone left liquid acetonide LXXIX and solid diol LXXVIII. A hexane wash separated LXXIX from the insoluble LXXVIII and after distillation, provided LXXIX in 65% yield. The cis diol LXXVII was easily regenerated in 97%

yield by treatment with ethanol-hydrochloric acid. Cyclic thiocarbonate LXXX was then prepared using N,N'-thiocarbonyldimidazole (111,112) in toluene and used crude in the next reaction. The thiocarbonate was converted in six days to triene LXXXI in 50% yield by treatment with refluxing trimethyl phosphite (112). This compound (LXXXI) was prepared by Paquette and Philips (113) by the same route used here except for separation of the diol mixture and appeared long after this work was complete.

The last step of the synthesis failed. Treatment of LXXXI with N-bromosuccinimide followed by quinoline at 145° for 15 minutes provided an eight-component mixture. Separation of the mixture by gas chromatography on a 20% carbowax column (on ABS Anachrom) yielded a small amount of starting triene LXXXI, β-methyl naphthalene, and a component whose NMR spectrum described the tetraene LXXXIII (or an isomer) in about 2.3% yield.



LXXXIII

The outside peaks of an A_2B_2 pattern at 5.4-5.9 ppm could be seen with what appeared to be the pattern for the vinyl protons of LXXXI superimposed upon it. Methylene protons appeared at 1.90-2.02 ppm, in the same location as those of LXXXI and in a slightly different pattern. The integral

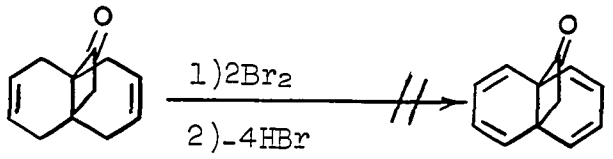
ratio was 2:1.

Treatment of LXXXI with N-bromosuccinimide followed by 1,5-diazabicyclo-[4·3·0]-5-nonene (114) in tert-butyl alcohol produced a ten-component mixture which was separated on the same chromatographic column above. Small quantities of triene LXXXI and tetraene LXXXIII were isolated. Attempted separation using a 1% cupric chloride on 15% carbowax column yielded only LXXXI.

It appeared as though LXXXI would not yield the desired pentaene, and it was thought that synthesis of it might be achieved by converting one of the compounds in the scheme to the corresponding tetraene followed by introduction of the double bond into the bridge. This procedure was attempted with LXXVII, LVII, and keto-acetate LXXIII but mostly with acetonide LXXIX. A variety of conditions for halogenation-dehydrohalogenation were tried, but no product recognizable (by NMR) as a tetraene was obtained. In most cases N-bromosuccinimide or bromine in carbon tetrachloride were used as halogenating reagents. Dehydrohalogenation was attempted primarily with quinoline or potassium tert-butoxide and to a lesser extent with 1,5-diazabicyclo-[4·3·0]-5-nonene, 5% lithium amalgam, or triethyl amine.

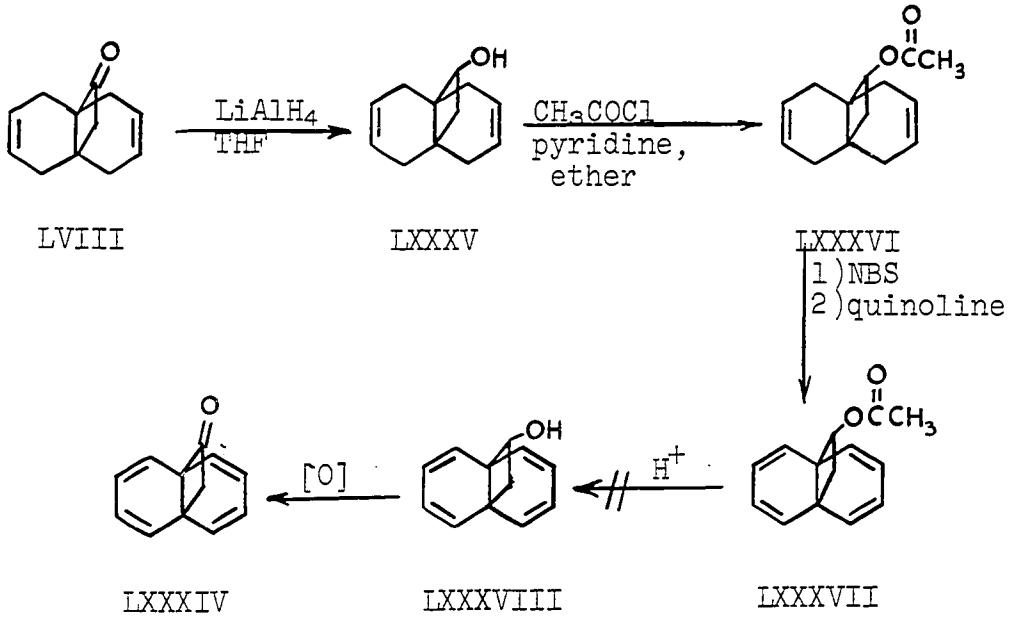
The Clemmenson reduction of ketol LVII in pentane made ketone LVIII readily available without purification. Interest in the corresponding tetraene ketone LXXXIV was developed to find out if it would eliminate ketene when heated, i.e.

analogous to the decomposition of tetraene LX.



LVIII LXXXIV

Direct conversion by halogenation-dehydrohalogenation using the same methods as above failed to produce the desired product. It was thought that the product might be too unstable to the dehydrohalogenation conditions, and another route was devised. Ketone LVIII was thus reduced to alcohol LXXXV with the intention of reoxidizing it after conversion to a tetraene according to Scheme VII.



LVIII LXXXV LXXXVI

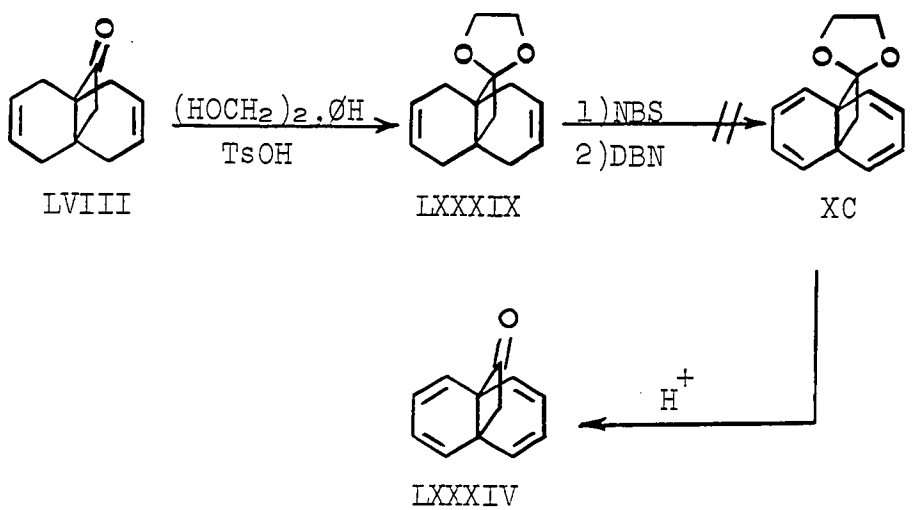
LXXXIV LXXXVIII LXXXVII

Scheme VII

It was thought that basic conditions on alcohol LXXXV might eliminate the bridge as acetaldehyde, and therefore a

dehydrohalogenation step could not be performed at that point. The alcohol was converted to acetate LXXXVI in high yield, and it in turn converted to tetraene acetate LXXXVII in 36% yield. Hydrolysis of this compound failed to produce alcohol LXXXVIII either by treatment with acid in ethanol-water or lithium aluminum hydride at 0°. Both reactions yielded naphthalene, and thus the scheme ended at this point.

In another scheme (Scheme VIII) an attempt was made to obtain ketone LXXXIV through its ethylene ketal XC.



Scheme VIII

Ketone LVIII was converted to ketal LXXXIX using a trace of p-toluenesulfonic acid in benzene with a water separator. Conversion to ketal XC was attempted using N-bromosuccinimide followed by 1,5 diazabicyclo-[4·3·0]-5-nonene in tert-butyl alcohol. A preliminary NMR revealed possible presence of XC, and an analytical gas chromatography showed a five-

component mixture. Attempted column chromatographic separation on either silicic acid or Florisil hydrolyzed any ketals present and yielded only small amounts of starting ketone LVIII. It is thought that LXXXIV is very sensitive to acid and perhaps loses the bridge under very mild conditions. No further attempt was made to obtain the compound.

Summary

Preparation of 9,10-ethano-9,10-dihydronaphthalene was accomplished by way of a very successful acyloin condensation of dimethyl-$\Delta^{2,6}$-hexalin-9,10-dicarboxylate to a four-membered ring. First attempted in liquid ammonia, the condensation yielded an unusual mixture which included reduction products. Wolff-Kishner reduction of the acyloin yielded ring-opened products for which a mechanism is suggested. Clemmenson reduction of the acyloin using toluene produced a mixture of hydrocarbons and a four-membered ketone. Attempts to improve the yield of the ketone by dissolving metal reductions gave poor results. The tetraene was finally obtained and purified by a gas chromatographic separation. It was found that the tetraene decomposed slowly at 152° to naphthalene and ethylene. The kinetics of this reaction is discussed.

Preparation of 9,10-etheno-9,10-dihydronaphthalene was attempted by way of reduction of the acyloin to a diol and converting the cyclic carbonate of the diol to the corresponding four-membered etheno-compound. Conversion of the resulting triene to the desired product failed. Conversion

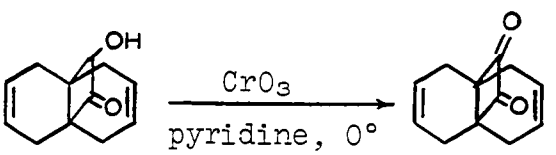
of any of the compounds in the sequence to its corresponding tetraene also failed.

Preparation of tricyclo-[4.4.2.$0^{1,6}$]-11-one-2,4,7,9-dodecatetraene by either of two routes failed. Tricyclo-[4.4.2.$0^{1,6}$]-11-acetoxy-2,4,7,9-dodecatetraene was successfully prepared.

Part IV

1,2-Cyclobutanediones

The ready availability of acyloin LVII prompted numerous synthetic schemes (Part III), all of which involved reduction of the functional groups in the four-membered ring. Interest was then turned to its oxidation product, the strained four-membered diketone XCI and its reactivity. Preparation of XCI was first attempted with an Oppenauer oxidation using aluminum isopropoxide and cyclohexanone in toluene (115), but the only isolated product appeared to be the Claisen condensation product of cyclohexanone. Oxidation of LVII with chromium trioxide in pyridine yielded a mixture of XCI and unreacted LVII.

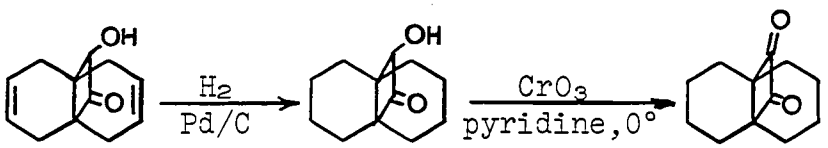


LVII XCI

A high yield of XCI was obtained from oxidation with acetic anhydride-dimethyl sulfoxide (116). Surprisingly, diketone XCI is red in color, a little unusual for a neutral compound containing only carbon, hydrogen, and oxygen. Some nonbonding

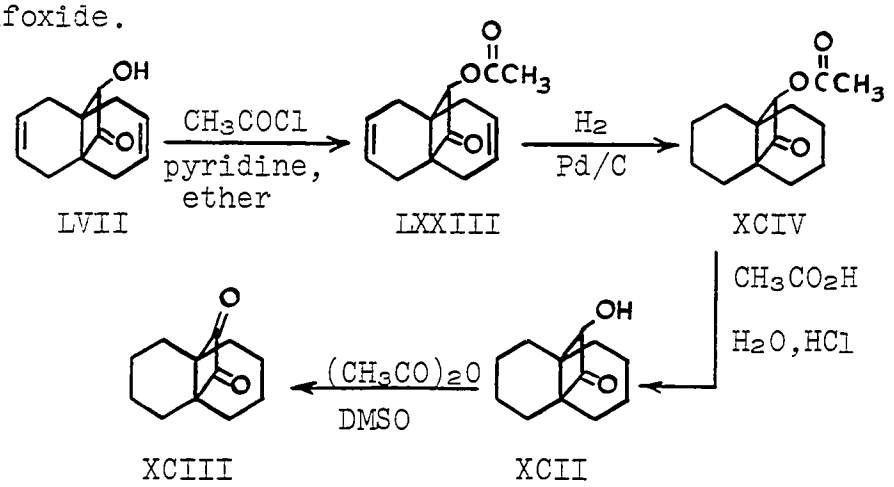
interaction with the double bonds evidently exists for the saturated analog is yellow-orange. Photochemical studies have been performed on XCI (117).

For comparative purposes the saturated analog of XCI was desired. Its preparation was first accomplished by hydrogenation of LVII to XCII and oxidation of XCII to diketone XCIII with chromium trioxide in pyridine.



LVII XCII XCIII

An unusual amount of catalyst was needed in the first step, and a low yield was obtained. The catalyst was being poisoned and needed replacing after about 0.5 equivalents of hydrogen had been absorbed. A better procedure proved to come from hydrogenation of keto-acetate LXXIII followed by hydrolysis and oxidation with acetic anhydride-dimethyl sulfoxide.



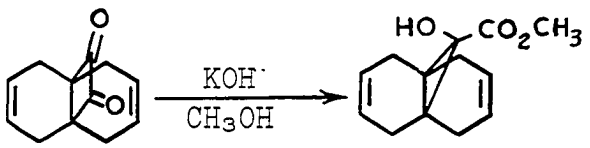
LVII LXXIII XCIV

XCIII XCII

Scheme IX

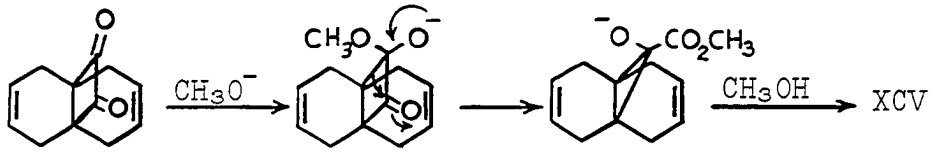
By this process, as shown in Scheme IX, no purification was necessary for keto-acetates LXXIII and XCIV, and they could be used crude in the next step. An overall yield of 96% was obtained in the sequence LVII to XCII, and the oxidation step yielded 89.5% XCIII.

When solid potassium hydroxide was added to a methanolic solution of diketone XCI, the red color disappeared in about five seconds, before the base dissolved completely. After workup the hydroxycyclopropyl ester XCV was obtained in quantitative yield.



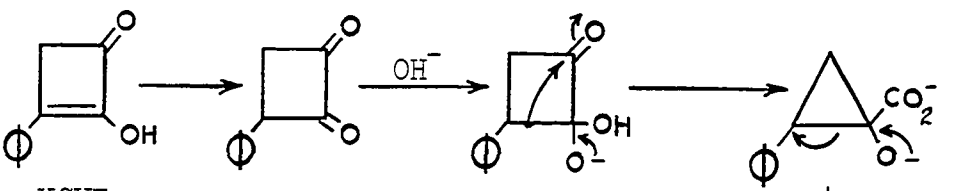
XCI XCV

It is thought that the reaction follows the familiar benzilic acid rearrangement.

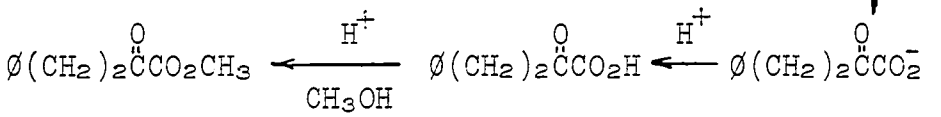


XCI

In an analogous system by Skattebøl and Roberts (118) cyclobutane dione XCVI was treated with base for three hours, and after esterification, pyruvate XCVII was obtained. The mechanism was thought to follow the path indicated and includes a benzilic acid rearrangement.

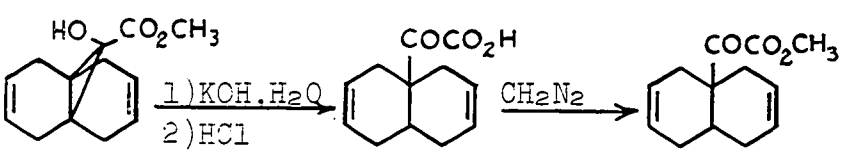


XCVI



XCVII

Because of the very rapid reaction, there was some doubt as to the validity of the structure proposed for XCV. The compound was therefore saponified for nine hours with the thought that a ring-opened product would result as with the Skattebøl and Roberts experiment (118). The acidified product was esterified with diazomethane, and the expected product, pyruvate XCVII, was obtained in 60% yield.

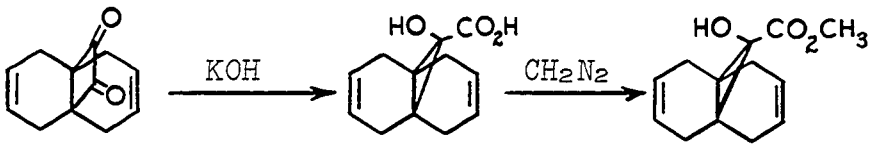


XCV XCVIII

Ring-opening is thought to be the slow step for a sample was removed from the saponification and esterified after one hour reflux, and a considerable amount of XCV was present.

Since XCV was easily obtained, its corresponding acid should not be difficult to synthesize. The acid XCIX was thus prepared in 89% yield using potassium hydroxide in water

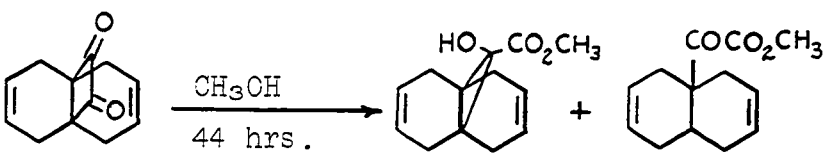
at room temperature. The suspended red solid disappeared in about 10 min. into the basic solution.



XCI XCIX XCV

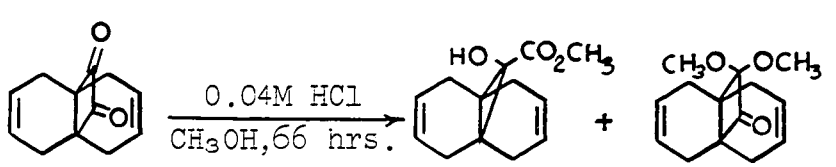
Diazomethane esterification of this acid yielded hydroxy-ester XCV.

A neutral methanol solution of diketone XCI was refluxed for 44 hrs. in the dark [to retard photochemical reactions (117)], and a two component mixture of 7.6% pyruvate XCVIII and 58.1% hydroxy-ester XCV was obtained.



XCI XCV XCVIII

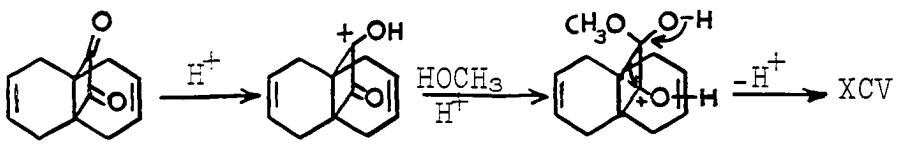
Thus, the cyclopropane system can be obtained without the use of base. This conclusion is supported by the results obtained from performing the same experiment but employing a small amount of acid (c.a. 0.04M). Diketone XCI was thus treated in methanol at reflux for 66 hrs. in the dark.



XCI XCV C

Hydroxy-ester XCV was produced in 59.8% yield. No pyruvate XCVIII was present, but a 7.7% yield of what is suspected to be dimethyl ketal C was obtained. The NMR spectrum (CCl_4) of the second substance displayed a vinyl multiplet at 5.57 ppm (4H) a singlet O-methyl at 3.43 ppm (6H) and a broad methylene region of many peaks at 1.5-2.8 ppm (8H). The IR spectrum (KBr) showed a carbonyl stretch at 1780 cm^{-1}. This substance was not investigated further.

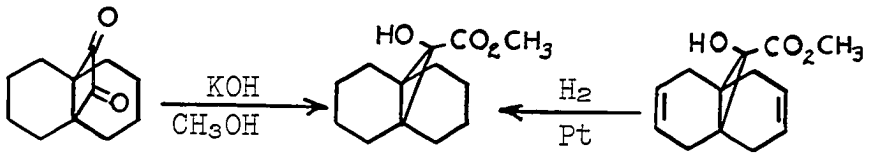
Since the hydroxy-ester XCV is formed in neutral and acidic media, the same general path might be expected in these two media as with the basic reaction but much more slowly. Thus, a benzilic acid type rearrangement under acid conditions might be assumed for the neutral and acidic media.



XCI

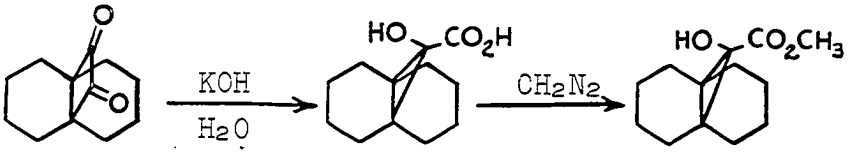
As noted, when an acidic medium was used no pyruvate XCVIII was obtained. The formation of this product therefore must depend on removal of the hydroxyl proton in hydroxy-ester XCV, which is retarded in neutral medium and quite suppressed in an acidic medium.

Treatment of saturated diketone XCIII with basic methanol produced hydroxy-ester CI in 20 sec. at room temperature.



XCIII CI XCV

The same product could be obtained by hydrogenation of hydroxy-ester XCV. Unfortunately CI could not be purified. Distillation of the resulting oil from either reaction produced a mixture, and the substance would not solidify to allow recrystallization. Saturated hydroxy-acid CII could be prepared in 20 min. from XCIII and could be purified.



XCIII CII CI

Diazomethane esterification yielded the ester CI. Thus by the same methods as with XCI, the saturated hydroxy-ester CI can be prepared from the diketone XCIII.

Summary

Tricyclo-[4·4·2·$0^{1,6}$]-11,12-dione-3,8-dodecadiene and the saturated analog were prepared from the corresponding acyloins. The unsaturated diketone was treated with basic methanol and rapidly produced a hydroxycyclopropyl ester via a benzilic acid rearrangement. Saponification of the ester followed by esterification yielded a methyl-$\Delta^{2,6}$-hexalin-9-pyruvate, analogous to a known system. The same hydroxycyclopropyl ester was prepared, but much more slowly, in neutral and acidic methanol as well as a small amount of pyruvate in neutral methanol and a small amount of dimethyl ketal of the starting dione in acidic methanol. Treatment of the dione with aqueous base yielded the hydroxycyclopropyl carboxylic acid, which was esterified to yield the same hydroxycyclopropyl ester as before. The corresponding cyclopropyl compounds were also prepared from the saturated diketone.

EXPERIMENTAL

All melting points and boiling points are uncorrected. All chromatographic solvents and most other solvents were distilled before use. Thin layer chromatography was performed on 5 x 20 cm glass plates coated with silica gel H. The silica gel H plates were immersed in iodine vapor for visualization.

Gas chromatographic separations were performed on an Aerograph Autoprep Model A-700 gas chromatograph. Infrared spectra (IR) were recorded on a Beckman IR-8 spectrophotometer and run in solution in 0.1 mm cells, as a thin film between two salt discs, or in potassium bromide pellets. Nuclear magnetic resonance (NMR) spectra were recorded on a Varian A-60 spectrophotometer using tetramethylsilane as internal reference. Chemical shifts are reported in parts per million (ppm) downfield from tetramethylsilane. Ultraviolet spectra (UV) were recorded on a Beckman Model DK-1 and performed in 95% ethanol or isooctane as solvents.

Microanalyses were carried out by the Alfred Bernhardt Laboratories, Mülheim, West Germany.

The starting material used for all $\Delta^{2,6}$-hexalin-9,10-

disubstituted compounds and the corresponding 9,10-disubstituted-9,10-dihydronaphthalene compounds was $\Delta^{2,6}$-hexalin-9,10-dicarboxylic acid anhydride XII prepared from acetylene dicarboxylic acid and butadiene as described by Alder and Backendorf (119).

Part I

Five-Membered Lactones

Preparation of 9,10-dihydronaphthalene-9,10-dicarboxylic acid anhydride XIII. The method used has been described by Vogel (120). To 20.4g (0.10 mole) anhydride XII dissolved in 150 ml carbon tetrachloride was added 35.6g (0.20 mole) powdered N-bromosuccinimide and 0.10g azobisisobutyronitrile and the mixture heated to boiling on a steam bath. After the exothermic reaction had subsided, the mixture was refluxed with stirring for 30 min., cooled, and the succinimide filtered out. The solvent was stripped from the filtrate, 65 ml distilled quinoline (distilled from zinc dust) was added to the light yellow oil, and the mixture was immersed in an oil bath at 145°. The mixture was heated for 15 min. at 140-145° with stirring, and, while still hot, poured into 300 ml ice-hydrochloric acid containing 50 ml concentrated hydrochloric acid. The mixture was extracted twice with ether, and the ethereal solution was washed with water, 1:10 hydrochloric acid, and sodium bicarbonate solutions. The ether was dried and evaporated and the resulting oil distilled through a short head at 0.40 mm collecting two

fractions: No. 1, bp 55-100°, 3.06g yellow oil; No. 2, bp 100-109°, 6.13g yellow solid. Fraction No. 2 was treated with charcoal in hexane and recrystallized from it, leaving 4.44g white solid XIII (22.2%), mp 73.5-75.5° [lit. (120), 75-76°]. The IR spectrum (KBr) indicated vinyl C-H stretch at 3070 cm^{-1} and anhydride stretch at 1790 cm^{-1} (strong) and 1860 cm^{-1} (weak).

Preparation of 9-(9,10-dihydronaphthalene)-dimethyl carbinol-10-carboxylic acid lactone XIV. To a Grignard reagent prepared from 5.10g magnesium turnings and 29.8g methyl iodide (0.212 mole) in 200 ml dry ether was added, dropwise with stirring (mechanical), a 50 ml solution of 6.00g (0.03 mole) anhydride XIII in dry ether over a two-hour period. The mixture was stirred for 22.5 hrs. Then 45 ml of a solution of 11.2g ammonium chloride in water was added, dropwise with stirring, over a 1.5 hr. period. The ethereal solution was decanted from the thin paste, dried, and evaporated leaving 2.22g yellow solid. (Naphthalene was present, identified by comparison of samples on thin layer chromatography.) The yellow solid was boiled with hexane, decanted from the 0.42g yellow gum, treated with charcoal, and recrystallized from 70 ml hexane leaving 1.07g white solid XIV, mp 89.5-91.5°. The paste left in the flask was stirred for 20 min. with a 250 ml ice-cold solution containing 40 ml concentrated hydrochloric acid and filtered.

The residue was washed with ether and the ether washed three times with water, dried, and evaporated leaving 3.57g yellow oil. This oil was boiled with hexane, treated with charcoal, and cooled leaving 0.60g white solid XIV (1.67g total, 26% yield). The IR spectrum (KBr) presented a weak band at 3050 cm^{-1} (vinyl C-H), a strong band at 1760 cm^{-1} (carbonyl), and a weak band at 1455 cm^{-1} (C=C stretch). The NMR spectrum (CCl_4) displayed a complex vinyl pattern at 5.2-6.0 ppm with the downfield portion appearing as half of an A_2B_2 pattern (8H), and a singlet for the two methyl groups at 1.43 ppm (6H) (see Appendix, figure 2). The UV spectrum (95% ethanol) showed maxima at 243 mμ (ϵ = 8800) and 249 mμ (ϵ = 8600) (see Appendix, figure 9). The analytical sample was obtained after recrystallizing three times from hexane, mp 90.8-91.6°. Anal. Calcd for $C_{14}H_{14}O_2$: C, 78.48; H, 6.59. Found: C, 78.45; H, 6.77.

Preparation of 9-(9,10-dihydronaphthalene)-diethylcarbinol-10-carboxylic acid lactone XV. To a Grignard reagent prepared from 3.00g magnesium turnings and 9.0g ethyl bromide (0.125 mole) in 30 ml dry ether was added dropwise with stirring, a 45 ml dry ether solution of 4.46g XIII (0.0223 mole) over a one-hour period. The mixture was stirred at room temperature for six hours and then saturated ammonium chloride solution (70 ml) was added dropwise in 1.5 hrs. The ether was decanted, washed with sodium bicarbonate

solution (the latter yielded 0.02g yellow tar upon acid work-up), and water, dried, and evaporated leaving 2.59g yellow oil. The oil (four components by thin layer chromatography) was placed on 80g Florisil (2.8 x 25 cm column) and eluted with benzene-hexane mixtures, collecting 50 ml fractions. Naphthalene was washed off rapidly using 20% benzene in hexane followed by a two-component mixture beginning in fraction 15 and continuing through 3000 ml 20% benzene wash and most of a 1500 ml 50% benzene wash. Evaporation of the solvent left 1.15g yellow solid, which was recrystallized from hexane leaving 0.35g white solid XV. More XV was obtained from concentration of the recrystallization liquid (0.17g, 0.52 total, 9.6% yield), mp (combined solids) 95-104°. The IR spectrum (KBr) displayed a 1755 cm^{-1} carbonyl. The NMR spectrum (CCl_4) showed a complex vinyl region in the range of 5.15-6.00 ppm with the downfield portion appearing as half of an A_2B_2 pattern (8H), the $O-CH_2$ protons at 1.90 ppm as a quartet (J=7cps) with the downfield half finely split (4H), and the methyl groups at 0.95 ppm as a triplet (J=7cps) with the upfield peak finely split (6H). The NMR spectrum of the analytical sample (see Appendix, figure 3) displayed a slightly cleaner spectrum, but the ethyl groups were still marred by fine splitting. The UV spectrum (95% ethanol, see Appendix, figure 10) showed absorption at 245 mμ (ϵ =7350) and 251 (7170). The analytical sample was obtained after recrystallization four times from hexane, mp 109.2-110.5°.

Anal. Calcd for $C_{16}H_{18}O_2$: C, 79.31; H, 7.49. Found: C, 79.44; H, 7.58.

Reaction of phenyl magnesium bromide with XIII, Preparation of 2-(1,2-dihydronaphthyl)-diphenyl carbinol XVIII. To a Grignard reagent prepared under dry purified nitrogen from 2.20g magnesium turnings and 14.0g bromobenzene in 200 ml dry ether (0.092 mole) was added, dropwise with stirring, a 55 ml dry ether solution of 4.00g anhydride XIII (0.02 mole) during a 90 min. period. The reaction was stirred for four hours at room temperature. To the mixture was then added, dropwise with stirring, a 22 ml aqueous solution of 5.89 ammonium chloride during a 30 min. period. Stirring was continued for 1.5 hrs. after addition. The mixture was filtered, and the residue was washed with ether. The ether solution was washed with sodium bicarbonate solution, dried, and evaporated leaving 5.29g yellow gum containing six components by thin layer chromatography. Sublimation of the naphthalene and biphenyl was carried out at 0.10 mm (condensor at -6°) for two days collecting 0.237g white solid. The remaining 5.05g material was placed on 150g silicic acid (3.6 x 32 cm column) and eluted with hexane and hexane-benzene mixtures, collecting 50 ml fractions.

Fraction 2-25 (hexane) contained 0.339g white solid after sublimation (a two-component mixture by thin layer chromatography with the same R_f values of naphthalene and biphenyl). Fractions 26-70 (30% benzene in hexane) contained

0.075g of a two-component mixture.

Fractions 71-93 (50% benzene) contained 0.567g of a single component, mp 108-120°, which was later proved to be 2-(1,2-dihydronaphthyl)-diphenyl carbinol XVIII. Recrystallization four times from hexane provided the analytical sample, mp 118.7-120.0°. The IR spectrum (CCl_4) showed bands at 3600 cm^{-1} (OH), 3070, 3040 (vinyl and aromatic), and 2860-2960 cm^{-1} (aliphatic CH) but no carbonyl stretch. The NMR spectrum (CCl_4) displayed a complex aromatic pattern at 6.7 to 7.6 ppm (14H), and eight-line pattern in the vinyl region which appeared as an AX system (J=10cps) at 6.44 and 5.69 ppm with each peak split into a doublet (J=3cps) (2H), a multiplet of ten peaks at 3.5 to 3.9 ppm appearing in three groups of 3, 4, and 3 peaks (1H), a group of six peaks at 2.62, 2.81, 2.50, 3.07, and 2.05 ppm in order of decreasing intensity (2H, this section shows up as 7-8 peaks in $CDCl_3$), and a singlet at 1.96 ppm (1H). Introduction of D_2O into the sample erased the peak at 1.96 ppm. The UV spectrum (95% ethanol) showed absorption at 261 mμ (ϵ=16,200) (see Appendix, figure 11).

Anal. Calcd for $C_{23}H_{20}O$: C, 88.34; H, 6.45. Found: C, 88.17; H, 6.33.

Further elution with 50% benzene washed off 0.408g of a two-component mixture (fractions 94-103) which was mostly (85-90%) the alcohol isolated in the previous fractions (adding the two crude quantities yields 0.975g, 15.5%). Further

elution with 50% benzene washed off 0.383g of a two-component mixture in fractions 104-120 followed by one component of 0.075g in fractions 121-128 and two components of 0.080g in fractions 129-143. Fractions 104-143 were combined and found to be predominately tripenyl carbinol XVII (0.538g, 10.3%). Recrystallization twice from 1:2 benzene-hexane gave the melting point at 160-161.2° [lit. (123), 162.5°], mixed mp 160-162°. The IR spectrum ($CHCl_3$) showed absorptions at 3000 cm^{-1} (OH), 3070 and 3010 cm^{-1} (aromatic CH). The NMR spectrum ($CDCl_3$) displayed a singlet at 7.15 ppm (15H) and a singlet at 2.81 ppm (1H).

Further elution with benzene-hexane mixtures (up to 75% benzene) washed off 0.207g of a four-component mixture (60 fractions). Elution with 7% ethyl acetate in benzene washed off 0.994g of a six-component mixture (20 fractions). Attempted recrystallization of the larger quantity from benzene-hexane gave a dark yellow oil. The liquid from recrystallization yielded a small amount of yellow solid upon dilution with hexane whose IR spectrum (CCl_4) showed broad weak absorptions at 1785, 1705, and 1690 cm^{-1} (no-OH absorption). The solid was a six-component mixture by thin layer chromatography. These fractions were not investigated further.

Dehydration of XVIII with thionyl chloride. Alcohol XVIII, 87 mg, was mixed with 0.5 ml thionyl chloride, and

the mixture was allowed to react with heating on a steam bath until nothing distilled out. Carbon tetrachloride (one ml) was added, boiled out, and the process repeated three times. Water (one ml) was added, and the mixture was heated on a steam bath 30 min. Carbon tetrachloride (one ml) was added, boiled out, and the process repeated three times until the residue was dry. The dark mixture was placed on 3.0g silicic acid (1.7 x 2.9 cm column) and washed with hexane producing 30 mg XIX, whose NMR spectrum (CCl_4) displayed a complex aromatic region at 7.0 to 7.8 ppm (17H) with a singlet at 7.11 ppm and a singlet at 5.61 ppm (1H).

Preparation of 1-naphthyldiphenyl carbinol XXII. To the Grignard reagent prepared from 0.58g magnesium turnings and 5.00g 1-bromonaphthalene in 80 ml dry ether (0.024 mole), was added, dropwise with stirring, a 20 ml dry ether solution of 4.40g benzophenone (0.024 mole) over a 1.5 hr. period (at room temperature). After stirring for one hour, a 10 ml solution of 3.2g ammonium chloride was added during a 20 min. period followed by 20 ml 3N hydrochloric acid. The ethereal layer was washed three times with water, dried, and evaporated to leave 7.44g solid + oil. Recrystallization from benzene-hexane (1:2) gave 4.09g yellow solid, mp 130-133.5°. More solid was obtained from concentration of the liquor, and the combined solids were treated with charcoal and recrystallized from 1:2 benzene-hexane three times yielding 2.82g slightly green solid XXII (37.6%) mp 134.0-135.1°

[lit. (121), 134-135°].

Preparation of 1-naphthyldiphenylmethane XX. To 1.00g carbinol XXII in 50 ml 95% ethanol were added 20 ml ethyl acetate, 0.10g 5% Pd/C, and three drops concentrated hydrochloric acid, and the mixture was hydrogenated at atmospheric pressure. The mixture was filtered, and the residue was washed with ethanol. The residue remaining was washed with benzene, and both filtrates were allowed to evaporate for one month. The solids obtained were recrystallized from hexane, mp 149.2-150.5°, producing 0.25g XX as white needles (26.3%). The NMR spectrum (CCl_4) showed a complex aromatic region at 6.8-8.0 ppm (17H) with a sharp peak at 7.13 ppm and a singlet at 6.20 ppm (1H). The analytical sample was obtained after recrystallization three times from hexane, mp 149-2-150.3° [lit. (121), 148-149°].

Anal. Calcd for $C_{23}H_{18}$: C, 93.84; H, 6.16. Found: C, 93.91; H, 6.35.

Preparation of 2-naphthyldiphenylcarbinol XXIV. To the Grignard reagent prepared from 1.16g magnesium turnings and 10.00g 2-bromonaphthalene in 80 ml dry ether (0.048 mole) was added, dropwise with stirring, a 40 ml dry ether solution of 8.75g benzophenone over a one-hour period. The mixture was stirred 30 min., and 20 ml water was slowly added with stirring. The ethereal layer was washed with water, dried, and evaporated leaving 15.92g yellow oil. Recrystallization three

times from benzene-hexane (1:2) provided 5.36g light yellow solid XXIV (35.8%). Gomberg and Sullivan (86) prepared this compound from ethyl-2-naphthylcarboxylate.

Preparation of 2-naphthyldiphenylmethane XIX. The method used was described by Gomberg and Sullivan (86). To 2.50g carbinol XXIV (8.1 mmoles) in 50 ml glacial acetic acid was added 2.0g zinc dust, and the mixture was refluxed 43 hrs. The solution was decanted from the zinc, poured into 200 ml water, and 35g sodium bicarbonate was slowly added with stirring. The mixture was extracted with ether and the ethereal solution was washed with water, sodium bicarbonate solution, and water. The ether was dried and evaporated, and the resulting solid was placed on 50g Florisil (3.4 x 11 cm column). The column was washed with hexane yielding 2.02g XIX as a clear oil which slowly crystallized (88.3%). Recrystallization three times from hexane provided the analytical sample, mp 70.1-71.5° [lit. (86), 77-8°]. The NMR spectrum (CCl_4) displayed a complex aromatic region at 7.0-7.8 ppm (17H) with a sharp peak at 7.11 ppm and a singlet at 5.61 ppm (1H). The spectrum superimposed on that of hydrocarbon XIX obtained by dehydration of alcohol XVIII.

Anal. Calcd for $C_{23}H_{18}$: C, 93.84; H, 6.16. Found: C, 93.78; H, 6.19.

Hydrogenation of alcohol XVIII, Preparation of 2-tetralyldiphenylcarbinol XXV. Alcohol XVIII (51 mg, 0.16 mmole) was

reduced at atmospheric pressure absorbing one equivalent of hydrogen in 40 ml 95% ethanol containing 5 mg 5% Pd/C. The catalyst was filtered off, the solvent evaporated, and the resultant solid was then recrystallized three times from hexane, mp 106-107.5°. The IR spectrum (CCl_4) showed absorptions at 3620 cm^{-1} (OH), 3070, 3030 (aromatic CH), 2850, and 2940 (aliphatic CH). The NMR spectrum (CCl_4) showed a complex aromatic region at 6.8-7.6 ppm (14H) with a singlet at 6.91 ppm, a group of peaks at 2.25-3.0 ppm, and a broad region at 1.2-2.0 ppm with a sharp peak at 1.90 ppm (8H). The peak at 1.90 ppm disappeared upon introduction of D_2O. The UV spectrum (95% ethanol, see Appendix, figure 12) showed maxima at 273 mμ (ϵ =1300), 266 mμ (ϵ =1670), 259 mμ (ϵ =1500), 261 mμ sh (ϵ =1440), and 253 mμ sh (ϵ =1100).

Anal. Calcd for $C_{23}H_{22}O$: C, 87.86; H, 7.05. Found: C, 88.11; H, 7.16.

Preparation of 2-carbomethoxy-1-tetralone XXVII. A quantity of 4.14g sodium hydride in oil (50.6% dispersion, 0.087 mole) was washed three times with dry benzene and covered with 500 ml benzene. Dimethyl carbonate (8.47g, 0.094 mole) and one ml of methanol were added, and the mixture was brought to reflux with stirring. The reaction was protected from moisture by a calcium chloride drying tube. Dropwise addition of a 100 ml dry benzene solution of 11.60g 1-tetralone XXVI (0.08 mole) was carried out with stirring, during

a seven-hour period. The mixture was stirred at reflux for 37 hrs., cooled, and a 50 ml water solution of 4.0g acetic acid was added (rapidly) followed by 150 ml water. The organic layer was washed with water and sodium bicarbonate solution, dried, and the solvent stripped to leave 14.9g of dark oil. This product was distilled through a 4 in. Vigreaux column at 0.60 mm, bp 97-105°, to give 3.45g colorless liquid. The IR spectrum (film) displayed a carbonyl stretch at 1685 cm^{-1}, which identified the distillate as the starting material. The residue from distillation, 10.02 dark liquid XXVII (62.0%), which showed two carbonyl stretch frequencies in the IR spectrum (film) at 1745 and 1685 cm^{-1}, was used directly in the next step.

Preparation of 2-carboethoxy-1-tetralol XXVIII. To a 50 ml absolute ethanol solution of 2.0g sodium borohydride (0.053 mole) was added (rapidly) a 20 ml absolute ethanol solution of 10.02g crude XXVII with stirring. The mixture became warm and probably transesterified at this point. The mixture was stirred for 3.5 hrs. at room temperature, was then cooled in ice, and 13.0g acetic acid were added slowly with stirring. The solution was concentrated to 25% of the volume and poured into a water-ether mixture. The ethereal layer was washed three times with water and twice with sodium bicarbonate solution, dried, and evaporated leaving 6.37g XXVIII (63%), which was used directly in the next step. An

accurate yield cannot be given because some spillage had occurred.

Preparation of 3-carboethoxy-1,2-dihydronaphthalene XXIX. To a 100 ml dry benzene solution of 6.37g β-hydroxy ester XXVIII (0.03 mole) was added 2.5g phosphorous pentoxide (0.0175 mole, rapidly), and the mixture was stirred for 20 min., and then refluxed for 30 min. (calcium chloride tube attached), and finally cooled and allowed to stand overnight. The benzene was decanted from the gum and stripped to leave 6.20g dark oil. The oil was placed on 120g Florisil (4.8 x 12.0 cm column) and washed with one liter of hexane to give 1.41g liquid. Washing with 1.5 liters benzene yielded 3.04g yellow oil which was distilled at 0.35 mm, bp 100-104°, to produce 1.66g light yellow liquid XXIX (28.4%). The IR spectrum (film) showed absorptions at 1705 cm^{-1} (carbonyl) and 1630 cm^{-1} (C=C stretch). The NMR spectrum (CCl_4) displayed the benzyl-vinyl proton at 7.42 ppm split into a fine triplet (J=1cps, 1H), the aromatic protons at 7.08 ppm, s, (4H), the OCH_2 protons at 4.19 ppm, q, (J=7cps, 2H), the remaining ring protons in a broad region of eight lines at 2.3-3.0 ppm with fine splitting on the upfield side (4H), and the methyl group at 1.29 ppm, t, (J=7cps, 3H). A weak singlet at 3.70 ppm indicated the presence of the methyl ester.

Preparation of 2-carboethoxytetralin, XXX. To 1.66g

unsaturated ester XXIX (0.082 mole) dissolved in 40 ml 95% ethanol was added a spatula tip (c.a. 0.05g) Adams catalyst and three drops concentrated hydrochloric acid. The compound was hydrogenated at atmospheric pressure and absorbed an equivalent of hydrogen. The mixture was filtered, the filtrate concentrated to 25% of the volume and poured into water. The mixture was extracted with ether and the ether washed with sodium bicarbonate solution and water, dried, and evaporated to leave 1.59g almost colorless XXX (95%). The IR spectrum (film) showed an ester carbonyl stretch at 1730 cm^{-1} and no absorption for C=C stretch. The NMR spectrum (CCl_4) displayed an aromatic singlet at 6.95 ppm (4H), the OCH_2 protons at 4.10 ppm, q, (J=7cps, 2H), the benzyl protons at 2.55-3.05 ppm, m, (4H), the remaining ring protons at 1.1-2.2 ppm, and the methyl group at 1.21 ppm, t, (J=7cps, 3H). The product was used directly in the next step.

Preparation of 2-tetralyldiphenylcarbinol XXV. To the Grignard reagent prepared from 0.92 magnesium turnings and 6.00g bromobenzene in 100 ml dry ether (0.038 mole) was added, dropwise with stirring, a 35 ml dry ether solution of 1.59g ester XXX (0.0078 mole) over a 10 min. period, and the mixture was refluxed for one hour. After the mixture cooled, a 30 ml solution of 6.5g ammonium chloride was slowly added. The ethereal solution was washed twice with water, dried, and evaporated leaving 3.30g yellow oil which was treated with

charcoal in hexane and placed on 100g Florisil (3.1 x 25.5 cm column). The column was eluted with 25% benzene in hexane, collecting 50 ml fractions, and followed by thin layer chromatography. Fractions 6 and 7 contained 0.20g of one component; fractions 8-10, 0.51g of two components; 11-14, 0.88g of two components (predominately carbinol XXV); and 15-30, 1.13g of carbinol XXV (46%) which slowly crystallized. The 1.13g XXV was recrystallized twice from hexane, mp 107.0-108.3°. The IR spectrum (CCl_4) showed absorption at 3620 cm^{-1} (OH), 3070, 3030 (aromatic C-H), 2850, and 2940 (aliphatic CH). The NMR spectrum (CCl_4) showed a complex aromatic region at 6.8-7.6 ppm (14H), with a singlet at 6.91 ppm, a multiplet at 2.25-3.0 ppm and a broad region at 1.2-2.0 ppm with a singlet at 1.92 ppm (8H). The peak at 1.92 ppm was shifted upfield with increased temperature. The NMR superimposed on the NMR of the hydrogenated product of XVIII. The UV spectrum was like that of hydrogenated XVIII (see Appendix, figure 12). The analytical sample was obtained after two more recrystallizations from hexane, mp 107.2-108.3°, mixed mp with hydrogenated XVIII, 107.0-108.2°.

Anal. Calcd for $C_{23}H_{22}O$: C, 87.86; H, 7.05. Found: C, 88.06; H, 7.08.

Part II

Five-Membered Bridges

Preparation of 9,10-dihydronaphthalene-9-hydroxymethyl-10-carboxylic acid lactone XLIX. To 5.00g lactone XLVIII (94) (0.0263 mole) dissolved in 50 ml carbon tetrachloride were added 9.37g N-bromosuccinimide (0.0526 mole) and a spatula tip of azobisisobutyronitrile (c.a. 0.10g). The mixture was refluxed on a steam bath for 2 hrs., cooled, filtered, and the solvent stripped from the filtrate. To the resulting light yellow oil was added 20 ml distilled quinoline (from zinc dust). The mixture was immersed in an oil bath at 140° and heated with stirring at 140-145° for 15 min. The hot, dark mixture was poured with stirring into 100 ml of ice-hydrochloric acid mixture containing 16 ml concentrated hydrochloric acid. The acidic mixture was extracted twice with ether and the ether washed with water, 1:10 hydrochloric acid, sodium bicarbonate solution, and dried. Evaporation of the ether left 2.97g yellow liquid which was boiled with 80 ml hexane. The hexane was decanted from the tar, treated with charcoal, and then evaporated. The residue was placed on 30g of Florisil, washed with

benzene, and the benzene evaporated. The resulting material was heated to solution in hexane, allowed to cool, and the hexane decanted from the yellow oil that first formed. The hexane was cooled to -18° and 0.51g XLIX (10.4%) crystallized, mp 46-50.5°. The analytical sample was obtained after four recrystallizations from hexane, mp 57.5-58.5°. The IR spectrum (KBr) showed vinyl CH at 3050 and 3020 cm^{-1}, aliphatic CH at 2970 and 2910 cm^{-1}, and lactone carbonyl stretch at 1770 cm^{-1}. The NMR spectrum (CCl_4) displayed an A_2B_2 vinyl pattern at 5.3-6.1 ppm (centered ca 5.72 ppm, 8H), and a singlet at 4.16 ppm (2H) (see Appendix, figure 1). The UV spectrum (see Appendix, figure 15) showed maxima at 241 mμ (ϵ=9000) and 247 (8900).

Anal. Calcd for $C_{12}H_{10}O_2$: C, 77.40; H, 5.41. Found: C, 77.29; H, 5.45.

Preparation of 9,10-bishydroxymethyl-$\Delta^{2,6}$-hexalin XXXI. To 49.0g lithium aluminum hydride (1.29 moles) was rapidly added 600 ml dry tetrahydrofuran (distilled from calcium hydride-lithium aluminum hydride). To this mixture was added, dropwise with stirring, a 400 ml dry tetrahydrofuran solution of 150.0g anhydride XII (0.735 mole) over a 3 hr. period. The mixture was refluxed 6 hrs. on a steam bath, cooled in ice, and 196 ml water was added, dropwise with stirring. The resulting slurry was poured into one liter of 6N hydrochloric acid in an ice bath. The organic layer was separated,

concentrated to 25% of its volume, and ether was added. The aqueous phase was washed with ether. The organic solutions were combined, washed with water and sodium bicarbonate solution, dried, and evaporated leaving 140.9g XXXI (98.8%), mp 147-160° [a sharp melting range for this compound is difficult to obtain (74) and may lie anywhere within 130-172°C]. The IR spectrum (KBr) showed strong OH absorption at 3300 cm^{-1} and vinyl CH at 3020 cm^{-1}. The NMR spectrum ($CDCl_3$) displayed the vinyl protons at 5.55 ppm split into a fine triplet (J=1cps, 4H), the OH protons as a broad peak at 3.81 ppm (shifted upfield by an increase in temperature), the OCH_2 protons as a sharp singlet at 3.60 ppm (6H for both), and the allyl protons as a broadened singlet (c.a. 8 cps at base) at 2.03 ppm (8H).

Preparation of $\Delta^{2,6}$-hexalin-9,10-bishydroxymethyltosylate XL. To a 600 ml distilled pyridine solution of 276.0g p-toluenesulfonyl chloride (1.45 moles) at -6° was added, dropwise with stirring, a 500 ml distilled pyridine solution of 140.9g diol XXXI (0.725 mole) during a 4 hr. period. When approximately 1/6 of diol XXXI had been added, 100 ml anhydrous ether was added, and the expected salt, pyridine hydrochloride, began to form. The mixture was stirred for 13.5 hrs. at -6° under a calcium chloride tube and then poured into three liters of ice-hydrochloric acid containing one liter of concentrated hydrochloric acid. The mixture was extracted

twice with benzene and the benzene washed with water and sodium bicarbonate solution. The dried benzene solution was stripped to give 321.8g light yellow solid. The solid was ground in a mortar and washed with 500 ml hexane leaving 286.8g light cream solid XL (78.7%), mp 126-129° [lit. (73), 128-130°].

The hexane was evaporated and the residue distilled (short head) at 0.40 mm, bp 54-61°, to give 24.02g colorless ether L (18.8%). The NMR spectrum (CCl_4) of L displayed a triplet in the vinyl region at 5.49 ppm (J=1.5cps, 4H), a singlet at 3.56 ppm for the OCH_2 protons (4H), and a quartet at 2.01 ppm for the allyl protons (J=1.5cps, 8H). The UV spectrum (95% ethanol, see Appendix, figure 13) showed λ max. at 243 mμ (ϵ=259).

Preparation of $\Delta^{2,6}$-hexalin-9,10-diacetonitrile XXXII and its Thorpe product XXXIV. The procedure was adapted from one used by Bloomfield and Mitra (87). To 450 ml distilled dimethylformamide (from calcium hydride) was added 100.0g ditosylate XL (0.200 mole), 60g sodium iodide (0.400 mole), and 60g sodium cyanide (1.22 moles), and the mixture was refluxed for 16 hrs. The mixture was cooled some and the solvent distilled under reduced pressure. The residue was heated with two successive 500 ml portions of benzene, filtered, and the benzene stripped. The resultant oil was dissolved in 200 ml benzene, 300 ml hexane was added, and the mixture filtered

leaving 3.86g tan solid. The filtrate was stripped, the residue dissolved in benzene, and the benzene washed three times with water. All liquids were filtered, leaving 2.03g solid. The benzene layer was dried and evaporated leaving 21.22g black paste. The paste was washed with ether (100 ml) leaving 7.90g brown solid. The salts insoluble in the first benzene wash were stirred in one liter of water, the mixture filtered through Celite, and the black gum remaining was boiled twice with 300 ml portions of benzene, the benzene yielding 3.22g blackish solid. The combined solids of 17.01g (40.2%) XXXII and XXXIV gave an IR spectrum (KBr) with absorptions at 3520, 3410 (NH), 3020 (vinyl CH), 2180 (nitrile of XXXIV), 2250 (nitrile of XXXII), and 1640 cm^{-1} (C=C stretch). The mixture was used directly in the next step.

Preparation of tricyclo-[4.4.3.$0^{1,6}$]-12-one-3,8-tridecadiene XLIV. To 100 ml water was added 80 ml ethylene glycol, 40g sodium hydroxide (1.0 mole), and 17.01g nitrile mixture XXXII and XXXIV (0.080 mole), and the mixture refluxed 27 hrs. The mixture was cooled, diluted to 500 ml with water, washed with 100 ml benzene, and the basic solution poured into 200 ml 6 N hydrochloric acid with stirring. The mixture was cooled in an ice bath, the solid filtered out, washed with water, and dried in air to leave 13.64g XLI (68%). The IR spectrum (KBr) indicated absorptions for acid OH (2400-3700 cm^{-1}, broad) and carbonyl (1710 cm^{-1}).

To the 13.64g crude XLI (0.055 mole) was added 100 ml dry benzene (distilled from calcium hydride) and 15 ml thionyl chloride (ca. 0.208 mole), and the mixture refluxed 45 min. The mixture was cooled, filtered (to remove silicon dioxide from previous step), and the solvent stripped from the filtrate. To the acid chloride were then added 20 ml absolute ethanol (slowly with stirring). The mixture was stirred at room temperature for five hours and poured into water. The water was washed with benzene and the benzene layer washed with sodium bicarbonate solution, dried, and stripped to leave 17.76g crude diester XLII (quantitative from XLI). The IR spectrum (film) displayed a carbonyl absorption at 1730 cm^{-1} and no OH absorption.

To the 17.76g crude diester XLII (0.058 mole) dissolved in 130 ml dry benzene was added 2.55g sodium metal (0.111 mole) and 8.0 ml absolute ethanol (c.a. 0.16 mole) and the mixture refluxed 16.5 hrs. with a calcium chloride tube attached. Solvent was slowly distilled from the mixture until a constant temperature was reached (78°). Benzene was added to the cooled mixture, and the solution was washed with water, 1:10 hydrochloric acid, and sodium bicarbonate solution. The solution was dried over anhydrous magnesium sulfate and evaporated to leave 14.39g liquid XLIII (95%). The IR spectrum (film) displayed carbonyl absorptions at 1765 and 1730 cm^{-1}.

To a 70 ml glacial acetic acid solution of 14.39g

keto ester XLIII (0.055 mole) was added 10 ml water and 10 ml concentrated hydrochloric acid (0.12 mole) and the mixture refluxed 11 hrs. The mixture was cooled, diluted to 400 ml with water, and washed twice with ether. The ethereal solution was washed with water and sodium bicarbonate solution, dried, and evaporated to leave 10.95g liquid. The liquid was distilled through a 4 in. Virgreaux column at 0.12 mm, bp 69-73°, producing 7.03g white solid XLIV (67.6%) mp 38.5-40.5°. The IR spectrum (CCl_4) showed a carbonyl frequency at 1745 cm^{-1}. The NMR spectrum (CCl_4) displayed the vinyl protons as a finely split triplet at 5.57 ppm (J=1cps, 4H), a sharp singlet at 2.08 ppm (α-protons), and a broadened singlet at 2.02 ppm for the allyl protons (12H). The UV spectrum (95% ethanol, see Appendix, figure 14) had λ max. at 291 mμ (ϵ =38.2).

Anal. Calcd for $C_{13}H_{16}O$: C, 82.94; H, 8.57. Found: C, 82.75; H, 8.56.

Preparation of tricyclo-[4·4·3·0.^{1,6}]-12,12-dioxyethylene-3,8-tridecadiene XLV. To 8.40g ketone XLIV (0.045 mole) dissolved in 150 ml benzene was added 0.1g p-toluenesulfonic acid monohydrate and 5 ml ethylene glycol and the mixture refluxed for 23 hrs. with a water separator containing calcium chloride covered with glass wool. The mixture was cooled, washed with sodium bicarbonate solution and water, dried, and evaporated. The resulting liquid was distilled at

0.07 mm, bp 84-88°, collecting 9.82g colorless liquid XLV (94.6%). The IR spectrum (film) showed C=C stretch at 1660 cm^{-1}, many bands from 1000 to 1350 cm^{-1}, and no carbonyl frequency. The product was distilled again at 0.07 mm, bp 87-88°, $n_D^{27.0}$ 1.5232. The NMR spectrum (CCl_4) displayed the vinyl protons as a fine triplet at 5.45 ppm (J=1cps, 4H), the OCH_2 protons as a singlet at 3.73 ppm (4H), and the methylene region in the range of 1.5-2.4 ppm including weak bands at 1.63 and 2.30 ppm, a wide multiplet at 1.86-2.13 ppm, and a sharp singlet for the five-membered ring protons at 1.80 ppm (12H). Anal. Calcd for $C_{15}H_{20}O_2$: C, 77.55; H, 8.68. Found: C, 77.80; H, 8.73.

Preparation of tricyclo-[4.4.3.0.^{1,6}]-12,12-dioxyethylene-2,4,7,9-tridecatetraene XLVI. To 7.44 crude ketal XLV (0.032 mole) dissolved in 100 ml carbon tetrachloride were added 11.40g N-bromosuccinimide (0.064 mole) and a spatula tip of azobisisobutyronitrile, and the mixture was refluxed with stirring for 30 min. The mixture was cooled, filtered, and the solvent stripped from the filtrate. To the resulting oil was added 30 ml quinoline, the mixture immersed in an oil bath at 145°, and heated with stirring at 140-145° for 15 min. The hot mixture was poured with stirring into 150 ml ice-hydrochloric acid containing 30 ml concentrated hydrochloric acid. The dark mixture was then washed three times with ether, the ether washed with 1:10 hydrochloric acid and

sodium bicarbonate solutions, dried over anhydrous magnesium sulfate, and evaporated to leave 3.84g yellow liquid. The product was distilled (short path) at 0.25 mm, bp 60-110°, to give 2.90g yellow liquid. The liquid mixture was placed on 88g silicic acid (3.1 x 25 cm column) and washed with hexane-benzene mixtures, collecting 60 ml fractions. Fractions 1-19 (hexane), 20-28 (20% benzene in hexane), 29-31 (50% benzene), and 32-36 (75% benzene) contained small amounts of material of little interest, but fractions 38-50 (75% benzene) contained a mixture of ketones (by NMR). The combined fractions 38-50 (1.61g) were converted back to ketal XLVI by the same procedure used to prepare ketal XLV (page 100) producing 1.98g liquid plus solid mixture. It was determined in another run that ketone XLVII could not be separated from its contaminant but that the ketals of these two ketones were separable by gas chromatography.

The mixture was separated on 20% carbowax on ABS Anachrom (3/8 in. x 10 ft. column) at 198° with 150 ml/min. helium flow. Fraction No. 1 eluted at 41 min. and 0.54g yellow oil was collected. The NMR spectrum (CCl_4) displayed a complex vinyl region at 5.3-6.0 ppm in what appeared to be a close A_2B_2 pattern with a closer vinyl pattern in the center, a singlet at 3.72 ppm for the OCH_2 protons and a methylene region at 1.7-2.5 ppm with low sharp multiplets at 2.43, 2.31,and 2.20 ppm, a more intense sharp multiplet at 1.95 ppm, a strong singlet at 2.00 ppm, and a weak singlet at 1.70

ppm. The spectrum seemed to describe ketal LI.

Fraction No. 2 eluted at 53 min. and 0.65g white solid XLVI was collected, mp 53-57°. The substance was sublimed at 0.025 mm, 45°, collecting 0.597g XLVI, mp 58-60° (8.2% yield). The IR spectrum (CCl_4) indicated a vinyl CH band at 3030 cm^{-1}. The NMR spectrum (CCl_4) showed a vinyl A_2B_2 pattern at 5.2-5.9 ppm (centered at 5.51 ppm, 8H), the OCH_2 protons as a singlet at 3.73 ppm (4H), and the bridge protons as a singlet at 2.16 ppm (4H). (See Appendix, figure 5). The UV spectrum (95% ethanol, see Appendix, figure 17) showed maxima at 245 mμ (ϵ=7700) and 251 sh(7380). The analytical sample was obtained by recrystallization four times from hexane, mp 60.1-61.5°.

Anal. Calcd for $C_{15}H_{16}O_2$: C, 78.92; H, 7.06. Found: C, 78.79; H, 7.23.

Preparation of tricyclo-[4·4·3.$0^{1,6}$]-2,4,7,9-trideca-tetraene-12-one XLVII. To 0.32g ketal XLVI (1.40 mmoles) dissolved in 30 ml ethanol water (3:1) were added a few crystals of p-toluenesulfonic acid monohydrate and the solution stirred at room temperature for 17.5 hrs. The solution was poured into sodium bicarbonate solution and extracted with ether. The ethereal solution was washed four times with water, dried, and evaporated to leave 0.23g white solid XLVII (89%), mp 65-75°. The analytical sample was obtained by sublimation at 0.05 mm and 44° and two recrystallizations from

hexane, mp 73.8-75.3°. The IR spectrum (KBr) showed absorptions at 3040 cm^{-1} (vinyl CH) and 1740 cm^{-1} (carbonyl). The NMR spectrum (CCl_4) displayed a vinyl A_2B_2 pattern at 5.25-6.05 ppm (centered at 5.62 ppm, 8H) and the α-protons as a singlet at 3.40 ppm (4H). (See Appendix, figure 6). The UV spectrum (95% ethanol, see Appendix, figure 18) showed maxima at 253 mμ (ϵ=5800) and 258 (5800).

Anal. Calcd for $C_{13}H_{12}O$: C, 84.75; H, 6.57. Found: C, 84.69; H, 6.59.

Preparation of 12-oxatricyclo-[4.4.3·$0^{1,6}$]-2,4,7,9-tridecatetraene LIII. The procedure was adapted from that used by Bloomfield and Quinlin (95). To 50 ml dry dimethylsulfoxide (distilled from calcium hydride and passed through three feet of 4A molecular sieve) under dry purified nitrogen was added 6.0g potassium tert-butoxide (53.5 mmoles) and the mixture stirred at room temperature until the base dissolved. To the mixture was then added, slowly with stirring, a 100 ml suspension of 5.16g 12-oxatricyclo-[4·4·3·$0^{1,6}$]-tridecane-3,4,8,9-tetrabromide in dry dimethylsulfoxide over a 30 min. period. The mixture was stirred under nitrogen for 20 hrs. and then heated for two hours at 80°. The mixture was poured into water and extracted with ether. The ether was washed four times with water, dried, and evaporated to leave 1.49g yellow oil which was placed on 45g silicic acid (2.1 x 25 cm column) and eluted with benzene, collecting 35 ml fractions.

Fractions 5-7 contained 77 mg LIII (4.3%) and 8-15 contained 173 mg of a two-component mixture (by thin layer chromatography). Fractions 5-7 were combined, recrystallized from pentane in Dry Ice-acetone and sublimed at 45 mm and 55° (condensor at -5°C), mp 73-75° [lit. (95), 74-75°]. The IR spectrum (CCl_4) showed absorptions at 3030 cm^{-1} (vinyl CH), 2860, and 2920 cm^{-1} (aliphatic CH). The NMR spectrum (CCl_4) see (Appendix, figure 4) displayed a vinyl A_2B_2 pattern at 5.25-5.90 ppm (centered at 5.56 ppm, 8H) and the OCH_2 protons as a singlet at 3.92 ppm (4H). The UV spectrum (95% ethanol, see Appendix, figure 16) showed maxima at 242 mμ (ϵ =3380) and 247 sh(3220).

Thermal decomposition of 12-oxatricyclo-[4·4·3·$0^{1,6}$]-2,4,7,9-tridecatetraene LIII. An NMR tube containing 42 mg ether LIII in cyclododecane under dry purified nitrogen was sealed and heated for 30 min. intervals at various increasing temperatures until decomposition started at 210-212° (as seen in the NMR spectrum). The reaction was followed at that temperature by recording the NMR spectrum at intervals. The naphthalene resonance slowly increased in magnitude with time as did a singlet appearing at 2.45 ppm. The data in Table 2 was taken by comparison of the integral of naphthalene formed with twice the integral of the upfield half of the vinyl A_2B_2 pattern of LIII (see Appendix, figure 4 for spectrum).

TABLE 2

KINETIC DATA FOR DECOMPOSITION OF ETHER LIII

Time, hrs. (at 210-212°)	% LIII left	ln $LIII_o/LIII$
0.5	96.9	0.0295
1.0	92.2	0.0769
2	89.3	0.113
4	77.0	0.262
6	72.3	0.322
8	63.6	0.451
11	55.8	0.581
15	45.2	0.797
19	41.2	0.888

The half-life of the reaction ($t_{1/2}$) was estimated at 12.6 hrs. from the data (see Appendix, figure 29 for kinetic plot). The NMR tube was sealed under pressure in one leg of an H-shaped arrangement of 8 mm glass tubing. In the other leg was an NMR tube containing carbon tetrachloride. A sharpened nail was sealed in the same leg as the sealed NMR tube. When the arrangement was sealed the reaction NMR tube was broken with the nail and the other leg immersed in an ice-salt bath for 4 hrs. The apparatus was opened, and the NMR tube containing carbon tetrachloride displayed a spectrum of one singlet at 2.53 ppm, identical to an authentic sample of

ethylene oxide. The peak at 2.45 ppm in the other tube had disappeared.

Part III

Four-Membered Rings

Preparation of $\Delta^{2,6}$-hexalin-9-carbomethoxy-10-carboxylic acid LV. To 258.6g crude anhydride XII (1.27 moles) dissolved in 1400 ml methanol was added 5.0g p-toluenesulfonic acid monohydrate, and the mixture was refluxed 2.5 days. The solvent was stripped and the remaining solid dissolved in 1000 ml water containing 80g sodium carbonate (0.755 mole, some warming was needed to effect solution). The basic solution was washed with 500 ml hexane and 500 ml ether and then poured, slowly with stirring, into 500 ml 7N hydrochloric acid (3.50 eq.). The mixture was filtered, the solid washed with water, then ground in a mortar, and washed again with water. The solid was dried under vacuum overnight to leave 281.1g white solid LV (94.0%), mp 139-147°. A sample was recrystallized for analysis from 1:1 benzene-hexane, mp 146.6-147.4° [lit. (122), 143-144°]. The NMR spectrum (CCl_4) displayed the acid proton at 12.13 ppm as a singlet (1H), the vinyl protons as a broadened singlet at 5.53 ppm (4H), the ester methyl as a singlet at 3.65 ppm (3H), and the allyl protons as a broadened and rounded quartet at

1.9-3.0 ppm (centered at 2.45 ppm, 8H).

Preparation of dimethyl-$\Delta^{2,6}$-hexalin-9,10-dicarboxylate LVI. To a 1500 ml dry benzene solution of 292.3g acid-ester LV (1.24 moles) was added, slowly with stirring, 262.3g solid phosphorous pentachloride (1.26 moles) and the solution refluxed for two hours. The solvent (and phosphorous oxychloride) was stripped, 200 ml dry benzene was added and stripped (to remove last of phosphorous oxychloride). The acid chloride was cooled and 100 ml methanol was added with rapid stirring. The solid (slurry) was heated with 600 ml more methanol until solution was effected, and then the methanol was stripped. The solid was heated with 200 ml methanol, and the solvent was stripped. The solid was then treated with charcoal in methanol and recrystallized from methanol to leave 192.1g white solid LVI. More product (70.0g) was obtained from concentration of the liquid (84.6% total), mp 98-100°. The IR spectrum (KBr) showed a vinyl CH stretch at 3030 cm^{-1} and an ester carbonyl at 1735 cm^{-1}. The NMR spectrum (CCl_4) displayed the vinyl protons as a fine triplet at 5.48 ppm (J=1cps, 4H), the ester methyl groups as a singlet at 3.60 ppm (6H), and the allyl protons as a broad, round quartet at 1.9-2.9 ppm (centered at 2.38 ppm, 8H).

Preparation of tricyclo-[4.4.2.$0^{1,6}$]-11-ol-12-one-3,8-dodecadiene LVII, Reaction in liquid ammonia. To 800 ml

liquid ammonia (filtered through glass wool before condensation) under dry purified nitrogen was added 400 ml dry ether (passed through four feet of 4A molecular sieve before use) and 4.60g sodium metal (freshly cut and trimmed under dry benzene) in small pieces with stirring. To the blue mixture was then added, dropwise with stirring, a 250 ml dry ether solution of 12.5g diester LVI (0.05 mole) over a 2 hr. period. The ammonia was then evaporated during a 36 hr. period with the aid of a little heat (heating mantle) with ether being added periodically to maintain a liquid level (c.a. 1.2 l). The red mixture was cooled in an ice bath, and a mixture of 18 ml concentrated hydrochloric acid in 200 ml water was added over a 2 hr. period. The ethereal solution was washed with sodium bicarbonate solution, water, 190 ml 5% sodium hydroxide solution, and water, dried, and evaporated to leave 4.50g solid.

The sodium bicarbonate and sodium hydroxide washes were separately acidified with dilute hydrochloric acid, extracted with ether, the ethereal solution washed with water, dried, and evaporated to yield 1.89g solid LXIII from bicarbonate and 1.97g LXIII from sodium hydroxide. The combined solids (3.86g, 35.6%) were recrystallized from cyclohexane-chloroform, mp 205-218° [lit. (122), 215°]. The IR spectrum (KBr) showed NH bands at 3440 and 3180 cm^{-1} and carbonyl bands at 1775 (weak) and 1710 cm^{-1} (strong). The NMR spectrum ($CHCl_3$) displayed the imide proton as a very broad peak

at 8.5-9.5 ppm (1H), the vinyl protons as a multiplet at 5.8-6.05 ppm (4H), and the allyl protons as a group of four multiplets at 1.8-2.9 ppm with a sharp peak in one of them at 2.17 ppm (8H).

Anal. Calcd for $C_{12}H_{13}NO_2$: C, 70.92; H, 6.45; N, 6.89. Found: C, 70.83; H, 6.58; N, 7.01. Calcd mol. wt.: 203. Found (Rast): 473.

The 4.50g neutral material (after basic wash) was recrystallized from ethyl acetate to leave 1.48g diol XXXI, whose IR and NMR spectra were like those of the compound prepared as described in Part II of the experimental (page 95). The remaining 3.02g material was placed on 140g silicic acid (3.7 x 27 cm column) and eluted with 5% ethyl acetate in benzene, collecting 100 ml fractions. Fractions 14-22 contained 0.958g acyloin LVII (10.1%). The IR spectrum ($CHCl_3$) showed weak OH absorption at 3600 cm^{-1} and a carbonyl frequency at 1780 cm^{-1}. The NMR spectrum ($CHCl_3$) showed a vinyl multiplet at 5.55-6.10 ppm (4H), the OCH proton as a broad singlet at 4.53 ppm (1H), the OH proton at 3.72 ppm as a broad peak which moved upfield with increased temperature (1H), and the allyl protons as a group of four multiplets at 1.7-2.8 ppm (8H). The analytical sample was obtained after four recrystallizations from benzene-hexane (1:6), mp 81.5-82.5°.

Anal. Calcd for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42. Found: C, 75.64; H, 7.43.

Fractions 23 and 24 contained a mixture of two components. Fractions 25-38 contained 0.613g hemiacetal LXIV

(6.4%) and was recrystallized five times from benzene-hexane (1:6) to obtain the analytical sample, mp 97.0-98.0°. The IR spectrum ($CHCl_3$) showed an OH absorption at 3600 cm^{-1} and C=C stretch at 1670 cm^{-1}. The NMR spectrum ($CHCl_3$) displayed the vinyl protons as a slightly broadened doublet at 5.56 ppm (J=2cps, 4H), the proton under two oxygens as a poor doublet at 5.30 ppm (J≅5cps, 1H), the OH proton as a broad peak at 4.75 ppm and moved upfield by increased temperature (1H), the OCH_2 protons in an AB pattern at 3.55 and 3.90 (J=7.6cps, 2H), and the allylic protons as a group of multiplets at 1.5-2.7 ppm with the major peak at 2.05 ppm (8H).

Anal. Calcd for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 75.09; H, 8.29.

The eluant was changed to 20% ethyl acetate in benzene, and in fractions 76-87 was eluted 0.546g diol XXXI (2.03g total, 20.9%), whose NMR spectrum was like the sample prepared in Part II (page 95).

Preparation of tricyclo-[4·4·2·$0^{1,6}$]-11-ol-12-one-3,8-dodecadiene LVII, Reaction in benzene. The glass equipment for this reaction was dried in the oven overnight. Benzene was dried by refluxing overnight over calcium hydride. The reaction was run under dry, purified nitrogen at 0.5 cm from introduction of benzene until after addition of ethanol.

To 600 ml dry distilled benzene was added with stirring at reflux, 11.6g potassium metal (0.298 eq.), followed by

11.6g sodium metal (0.504 eq.), both added in small chunks and both freshly cut and trimmed under dry benzene. The mixture was stirred at high speed for five minutes using a "Stir-O-Vac" high speed stirrer to finely disperse the metals. Stirring was reduced to a moderate speed and a 160 ml dry benzene solution of 25.0g diester LVI (0.10 mole) was added during a 100 min. period from a Hershberg funnel. The mixture was refluxed for one hour,* cooled in a water bath, and 18.4g absolute alcohol (0.40 mole) was added dropwise with stirring, followed by 50g acetic acid (0.834 mole) and 200 ml water. The benzene layer was washed with saturated sodium bicarbonate and saturated sodium chloride solutions and the aqueous solutions backwashed with 200 ml benzene. The combined benzene solutions were dried and evaporated under vacuum overnight to leave 17.8g light pink LVII (93.7%), mp 77.6-80.4°. Recrystallization from cyclohexane yielded 13.3g fluffy white LVII, mp 79.6-80.3°. The IR spectrum ($CHCl_3$) showed bands at 3600 cm^{-1} (-OH, weak) and 1780 cm^{-1} (carbonyl). The NMR spectrum ($CHCl_3$) showed a highly split vinyl multiplet at 5.55-6.10 ppm (4H), the proton under oxygen as a singlet at 4.53 ppm (1H), the hydroxyl proton as a broad singlet at 3.59 ppm (1H, moved upfield with increased temperature), and a complex methylene region at 1.7-2.8 ppm with major peaks at

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*It was determined that for larger scale reactions of 0.40 mole diester the reflux period needed to be lengthened to 6-12 hrs. to complete the reaction.

1.93, 2.18, and 2.50 ppm, and a sharp singlet at 2.02 ppm (8H). The UV spectrum (95% ethanol, see Appendix, figure 20) showed λ max. at 312 mμ (ϵ =51.9) and 300 sh(46.8). The analytical sample was obtained by recrystallization once from ethanol-water and five times from cyclohexane, mp 81.5-82.5°. Anal. Calcd for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42. Found: C, 75.64; H, 7.43.

This compound formed a semicarbazone, mp 187.5-189.5° from ethanol-water and then chloroform-cyclohexane. Anal. Calcd for $C_{13}H_{17}N_3O_2$: C, 63.14; H, 6.93; N, 16.99. Found: C, 63.28; H, 6.80; N, 16.95.

Reaction of hydrazine with acyloin LVII. Preparation of cis-9,10-dimethyl-$\Delta^{2,6}$-hexalin LXVI and imide mixture LXVII. To 30.00g acyloin LVII (0.158 mole) in 180 ml diethylene glycol was added 15 ml water, 54 ml 95% hydrazine hydrate, and 76.2g potassium hydroxide pellets and the mixture refluxed with stirring for 1.5 hrs. After cooling slightly, a six-inch straight tube was mounted in the reaction flask and the condensor arranged for distillation. Distillation was carried out until the temperature of the reaction liquid reached 200° (about 8 hrs. required). The system was allowed to cool to about 130°, and pentane was added to wash out the condensor. Water was added to the distillation flask to dilute the mixture before it solidified.

The distillate was diluted with pentane, washed with

water, 1:10 hydrochloric acid and sodium bicarbonate solution, dried, and evaporated to leave 8.24g colorless liquid LXVI (32.2%, double bond isomers). A quantity of 2.06g of this liquid was placed on 70g silicic acid (2.8 x 23 cm column) and eluted with hexane, collecting 20 ml fractions. Fractions 6 and 7 contained 0.876g white waxy solid LXVI, mp 68-70°. The solid was sublimed twice at atmospheric pressure and room temperature to produce the analytical sample, mp 73.0-74.7° [lit. (90), 69-71]. The IR spectrum (KBr) showed vinyl stretch at 3030 cm^{-1}, aliphatic stretch at 2830-2980 cm^{-1}, and C=C stretch at 1655 cm^{-1}. The NMR spectrum (CCl_4) displayed the vinyl protons as a triplet at 5.56 ppm (J=1.5cps, 4H), the allyl protons as a broad multiplet at 1.86 ppm with minor peaks at 1.3-2.3 ppm (8H), and a singlet for the methyl groups at 0.90 ppm (6H).

Anal. Calcd for $C_{12}H_{18}$: C, 88.82; H, 11.18. Found: C, 88.66; H, 11.24.

Fractions 8-11 contained 0.503g of a two-component mixture and 0.30g of primarily the second component (liquid) was recovered from the rotary evaporator. The IR spectrum (film) of this liquid was identical to the solid obtained above except for four minor peaks. The NMR spectrum (CCl_4) was superimposable upon that of the solid above except the allyl protons displayed a slightly different multiplet. This component is probably a double bond isomer of the solid above for only the solid (one component by gas chromatography) was

obtained in 30.6% yield from another run on 10.00g acyloin LVII with shorter reaction time (5.5 hrs.).

The basic aqueous mixture was washed with ether (to remove stopcock grease) and poured into 360 ml 4N hydrochloric acid with stirring. The mixture was washed twice with ether and the ether washed with water, sodium bicarbonate solution, and water, dried, and evaporated leaving 10.12g yellow solid. The solid was recrystallized from benzene-hexane leaving 7.00g light yellow solid LXVII (21.8%) as one component by thin layer chromatography. The analytical sample was obtained by recrystallizing from benzene-hexane four times and ethanol-water three times, mp 138.0-139.8°. The IR spectrum (KBr) displayed NH bands at 3440 and 3180 cm^{-1} and carbonyls at 1710 (strong) and 1775 cm^{-1} (weak). The spectrum was superimposable upon that of LXIII except for a few minor peaks in the fingerprint region. The NMR spectrum ($CDCl_3$) showed a very broad peak for the imide proton at 8.3-9.2 ppm (1H, erased by addition of D_2O), the vinyl protons as many peaks at 5.4-6.1 ppm (4H), and the allyl protons as a multiplet at 1.2-2.9 with the major peaks at 2.2 ppm (8H).

Anal. Calcd for $C_{12}H_{13}NO_2$: C, 70.92; H, 6.45; N, 6.98. Found: C, 70.32; H, 6.26; N, 7.07. Calcd mol. wt.: 203. Found (Rast): 388, 521.

Preparation of N-methyl-$\Delta^{1,5*}$-hexalin-9,10-dicarboximide LXVIII. A solution was made from 0.70g imide mixture LXVII (3.45 mmoles) and 1.5g potassium hydroxide pellets in 50 ml water and the mixture heated on a steam bath for 5 min. To the mixture was then added, dropwise with stirring, 1.0 ml dimethyl sulfate, and the mixture was heated for 10 min. The mixture was cooled, filtered, the residue washed three times with water, and dried in air to leave 0.35g white solid LXVIII (47%). The analytical sample was obtained after recrystallization three times from benzene-hexane and twice from hexane, mp 147.8-150.0°. The IR spectrum (KBr) showed carbonyl bands at 1695 cm^{-1} (strong) and 1770 cm^{-1} (weak). The NMR spectrum ($CDCl_3$) showed the vinyl protons as a multiplet at 5.7-6.0 ppm (4H) and the allyl protons as a group of multiplets at 1.8-3.0 ppm with the N-methyl group as a singlet at 2.90 ppm (11H).

Anal. Calcd for $C_{13}H_{15}NO_2$: C, 71.86; H, 6.97; N, 6.45. Found: C, 71.70; H, 6.75; N, 6.55.

Preparation of decalin-9,10-dicarboximide LXIX. To 0.56g imide mixture LXVII (2.76 mmoles) in 50 ml 95% ethanol was added a spatula tip (c.a. 0.05g) Adams catalyst and the mixture hydrogenated at atmospheric pressure, two equivalents of hydrogen being absorbed. The catalyst was filtered out and

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*Probably a mixture of $\Delta^{1,5}$, $\Delta^{2,6}$, $\Delta^{1,6}$ and $\Delta^{1,7}$ hexalins.

the solvent evaporated to leave 0.56g solid LXIX (98%), which was recrystallized from benzene-hexane, mp 186-188°. Two more recrystallizations from benzene-hexane produced the analytical sample, mp 186.8-188.1°[lit. (88), 150-151°]. The IR spectrum (KBr) showed NH bands at 3190 and 3450 cm^{-1} and carbonyl bands at 1710 (strong) and 1780 cm^{-1} (weak). The NMR spectrum ($CDCl_3$) showed the NH proton as a broad flat peak at 8.2-8.7 ppm (1H, erased by addition of D_2O) and the remainder of the protons as a broad multiplet at 1.1-2.1 ppm (16H).

Anal. Calcd for $C_{12}H_{17}NO_2$: C, 69.53; H, 8.27; N, 6.76. Found: C, 69.56; H, 8.21; N, 6.76.

Clemmenson reduction of acyloin LVII, Reaction using toluene. Preparation of ketone LVIII. Zinc amalgam was prepared from 270g granulated zinc (technical), 240 ml water, 24 ml hydrochloric acid (conc.), and 18g mercuric chloride. The mixture was swirled and shaken for five minutes and the liquid decanted. To the amalgam was added 700 ml distilled toluene, 55.1g acyloin LVII (0.29 mole), 400 ml water, and 400 ml concentrated hydrochloric acid. The mixture was refluxed 9 hrs., cooled, and the organic layer washed with water and sodium bicarbonate solution. The toluene was dried and stripped. The resulting mixture was distilled through a 4 in. Vigreaux collecting four fractions: fraction No. 1, bp 69-102°, 4.7 mm, 11.2lg liquid + solid (LVIII, LIX, LXX, and

LXXI); fraction No. 2, bp 100-115°, 4.7 mm, 10.23g solid LVIII; fraction No. 3, bp 85-145°, 1.7 mm, 2.48g pink liquid; and fraction No. 4, bp 127-164°, 0.7 mm, 2.45 dark oil. The liquid in fraction No. 1 was separated from the solid to give 8.01g liquid and 3.20g solid. The NMR spectrum of the liquid (neat) showed distinct patterns for tetralin LXX (6.6% yield), diene LIX (7.1% yield), and isotetralin LXXI (trace). The solid was added to fraction No. 2 giving 22.43g ketone LVIII (44.5%, spectra described in the next experiment). Fractions Nos. 3 and 4 consisted of mixtures and were not investigated.

Preparation of tricyclo-[4.4.2.$0^{1,6}$]-11-one-3,8-dodecadiene LVIII, Clemmenson reduction of LVII using pentane. Zinc amalgam was prepared from 150g technical zinc, 130 ml water, 10g mercuric chloride, and 13 ml concentrated hydrochloric acid. The mixture was shaken 5 min. and the liquid discarded. To the amalgam was added 300 ml 6 N hydrochloric acid, 350 ml pentane, and 30.00g acyloin LVII, and the mixture stirred at the liquid-liquid interface at 27° for 6 hrs. and at 35° for 11 hrs. (about 4 hrs. after solid LVII had disappeared from pentane layer). The pentane solution was washed with water and sodium bicarbonate solution, dried, and evaporated to leave 17.33g light yellow solid LVIII, (63.0%), mp 67-80°. Recrystallization from hexane-pentane yielded 14.04g with an additional 1.48g from concentration of the liquid, mp 79-81.5°.

The IR spectrum (CCl_4) showed a vinyl stretch at 3050 cm^{-1} and carbonyl at 1775 cm^{-1}. The NMR spectrum ($CHCl_3$) displayed a vinyl multiplet at 5.8-6.1 ppm (4H), the bridge protons as a singlet at 2.63 ppm (2H), and the allyl protons as a group of four multiplets at 1.7-2.6 ppm (8H). The UV spectrum (isooctane, see Appendix, figure 22) showed maxima at 276 mμ sh(ϵ =13.6), 286 (19.6), 296 (24.6), 310 (24.0), and 322 (16.8). The analytical sample was obtained by recrystallizing four times from benzene-hexane, mp 80.8-82.0°.

Anal. Calcd for $C_{12}H_{14}O$: C, 82.72; H, 8.10. Found: C, 82.78; H, 8.28.

This compound formed a semicarbazone, mp 235.0-235.5(dec.) from methanol.

Anal. Calcd for $C_{13}H_{17}N_3O$: C, 76.51; H, 7.41; N, 18.17. Found: C, 67.54; H, 7.39; N, 18.04.

Ketone LVIII was also prepared from keto-acetate LXXIII. Keto-acetate LXXIII was prepared from 2.80g acyloin LVII (14.7 mmoles), 2.0g acetyl chloride (25.7 mmoles), and 15 ml pyridine (procedure to be described later). The crude product was dissolved in 40 ml dry dioxane and added, dropwise with stirring, to a solution of 4.10g calcium turnings (102 mmoles) dissolved in 500 ml liquid ammonia over a 30 min. period. The mixture was stirred 20 min., and 50 ml methanol was added over a 30 min. period followed by 5.0g solid ammonium chloride. The ammonia was evaporated with a water bath and warmed with a steam bath at the end. Water (200 ml) was

added and the mixture neutralized with acetic acid. The mixture was extracted with ether and the ether washed with water, sodium bicarbonate solution, and water, dried, and evaporated to leave 1.86g yellow oil of four components by thin layer chromatography. The mixture was placed on 65g silicic acid (2.8 x 21.5 cm column) and eluted with benzene, collecting 60 ml fractions. Ketone LVIII washed off in fractions 4-7 to give 0.182g LVIII (7.1% from LVII) with the same spectra as previously prepared material.

Ketone LVIII was also prepared from keto-tosylate LXXIV. The procedure used was as described above for keto-acetate LXXIII employing 4.10g calcium metal (102 mmoles) and 3.41g keto-tosylate LXXIV (9.3 mmoles). The same workup afforded 1.73g yellow liquid of eight components. The oil was placed on 40g silicic acid (2.1 x 23 cm column) and eluted with benzene collecting 35 ml fractions. Ketone LVIII washed off in fractions 4-7 and weighed 0.031g (1.9%) and had the same spectra as previously described.

Preparation of tricyclo-[4·4·2·$0^{1,6}$]-11-acetoxy-12-one-3,8-dodecadiene LXXIII. To 3.00g acyloin LVII (15.8 mmoles) in 20 ml distilled pyridine and 50 ml dry ether in an ice bath was added, dropwise with stirring, a 40 ml solution of 3.0 ml acetyl chloride in 40 ml dry ether over a 15 min. period. The mixture was stirred for one hour in ice and four hours at room temperature. The mixture was poured

into water and the ethereal solution washed with 2 N hydrochloric acid and four times with water, dried, and evaporated to leave 3.63g yellowish solid LXXIII (99%). Recrystallization from hexane gave 2.74g cream solid LXXIII (75%), mp 71.0-73.5°. The analytical sample was obtained after recrystallization from chloroform-cyclohexane and then ethanol-water, mp 73.0-73.7°. The IR spectrum ($CHCl_3$) showed carbonyl absorptions at 1790 and 1740 cm^{-1}. The NMR spectrum ($CHCl_3$) displayed a vinyl multiplet at 5.75-6.1 ppm (4H), the bridge proton under oxygen as a singlet at 5.45 ppm (1H), and the remainder of the protons as a group of multiplets at 1.6-2.9 ppm with the acetate methyl as a singlet at 2.1 ppm (11H). Anal. Calcd for $C_{14}H_{16}O_3$: C, 72.39; H, 6.94. Found: C, 72.19; H, 6.88.

Preparation of tricyclo-[4.4.2.$0^{1,6}$]-11-one-3,8-dodecadiene-12-p-toluenesulfonate LXXIV. To 20 ml dry distilled pyridine was added, slowly with stirring, 3.36g p-toluenesulfonyl chloride (15.7 mmoles) followed by dropwise addition of 3.80g acyloin LVII (20 mmoles) in 10 ml pyridine. A calcium chloride drying tube was attached and the mixture stirred for 20 hrs. at room temperature. The mixture was poured with stirring into 200 ml ice-hydrochloric acid containing 35 ml concentrated hydrochloric acid and extracted with ether. The ethereal solution was washed with sodium bicarbonate solution, dried, and evaporated leaving 5.59g light orange solid. Recrystallization from benzene-hexane yielded 4.09g white solid

LXXIV (69%), mp 121.8-123.7°. The analytical sample was obtained after five recrystallizations from benzene-hexane, mp 123.8-124.6°.

Anal. Calcd for $C_{19}H_{20}O_4S$: C, 66.26; H, 5.85, S, 9.31. Found: C, 66.46; H, 5.85; S, 9.44.

Preparation of tricyclo-[4.4.2.$0^{1,6}$]-dodecane-11-one LXXII. To 0.78g ketone LVIII (4.48 mmoles) in 50 ml 95% ethanol was added a spatula tip of 5% Pd/C, and the compound was hydrogenated at atmospheric pressure, absorbing two equivalents of hydrogen. The ethanol was evaporated, the mixture taken up in ether, filtered through Celite, and the ether evaporated to leave 0.70g slightly colored liquid. The product was distilled at 0.15 mm, bp 54.5°, to give 0.66g white solid LXXII (83%) melting slightly above room temperature (27-30°), $n_D^{26.5}$1.5000. The IR spectrum (film) displayed a carbonyl stretch at 1775 cm^{-1}. The UV spectrum (isooctane, see Appendix, figure 21) showed λ max. at 294 mμ (ϵ=31.6). Anal. Calcd for $C_{12}H_{18}O$: C, 80.85; H, 10.18. Found: C, 80.72; H, 10.00.

Preparation of tricyclo-[4.4.2.$0^{1,6}$]-3,8-dodecadiene LIX. To 5.70g ketone LVIII (0.327 mole) in 45 ml diethylene glycol and 7.5 ml 85% hydrazine hydrate was added 10.3g potassium hydroxide pellets and the mixture refluxed one hour under nitrogen. The mixture was cooled, the apparatus

arranged for distillation, and distillation was carried out under nitrogen until the temperature of the distillation liquid reached 220° (required 4 hrs.). The apparatus was cooled and washed with pentane. The basic mixture was dissolved in water and washed with pentane. The combined pentane solutions (and distillate) were washed with water, 1:10 hydrochloric acid, sodium bicarbonate solution, and water, dried, and evaporated to leave 5.00g slightly colored liquid. The product was distilled through a 4 in. Vigreaux column at 6.1 mm, bp 72-74°, leaving 3.46g colorless liquid LIX (66%). The IR spectrum (film) showed vinyl stretch at 3030 cm^{-1} and C=C stretch at 1640 cm^{-1}. The NMR spectrum (neat) displayed the vinyl protons as a multiplet at 5.9-6.1 ppm (4H), the allyl protons as a crude doublet at 1.76 ppm (J=4cps, 8H), and the bridge protons as a singlet at 1.48 ppm (4H). The UV spectrum (95% ethanol, see Appendix, figure 23) showed absorptions at 220 mμ sh(ϵ =1410), 232 low (204), 240 sh(246), 258 max. (453), 265 sh(438), and 295 sh(29.4). The analytical sample was obtained by distillation at atmospheric pressure under nitrogen through a 4 in. Vigreaux column, bp 209°, n_D^{25}1.5116.

Anal. Calcd for $C_{12}H_{16}$: C, 89.94; H, 10.06. Found: C, 89.84; H, 10.18.

Preparation of tricyclo-[4·4·2·$0^{1,6}$]-2,4,7,9-dodecatetraene LX. A mixture of 22.15g N-bromosuccinimide (0.124

mole), 0.10g azobisisobutyronitrile, 9.95g diene LIX (0.062 mole), and 180 ml carbon tetrachloride was refluxed for 30 min. The mixture was cooled, filtered, and the solvent stripped from the filtrate. To the resulting yellow liquid was added 50 ml distilled quinoline (from zinc dust), the mixture immersed in an oil bath at 140°, and heated with stirring at 140-145° for 20 min. The hot dark liquid was then poured with stirring into 200 ml ice-hydrochloric acid containing 45 ml concentrated hydrochloric acid. The mixture was washed three times with pentane and the combined pentane solution washed with 1:10 hydrochloric acid and sodium bicarbonate solution. After drying, the pentane was evaporated to leave 8.04g dark yellow liquid. The liquid was placed on 360g silicic acid (5.0 x 40 cm column) and eluted with hexane, collecting four approximately 1000 ml fractions. Fractions 1,3 and 4 did not contain the desired product (by thin layer chromatography and comparison to previous runs), and fraction No. 2 of 5.41g liquid was distilled through a stainless steel spinning band column. Seven fractions of 2.48g total (each a mixture) were collected at 4.2-4.6 mm, bp 46-66° and were separated by preparative gas chromatography on 20% carbowax on ABS Anachrom (3/8 in. x 20 ft. column) at 150° collecting 1.308g LX (13.5%) which eluted at 68 min., n_D^{25}1.5441. In another run of 4.64g diene LIX, tetraene LX was isolated in an impure state after two chromatographic separations on silicic acid and yielded 729 mg crude LX (16.1%).

The NMR spectrum (CCl_4, see Appendix, figure 7) exhibited a vinyl A_2B_2 pattern at 5.1-5.9 ppm centered at 5.49 ppm (8H) and the bridge protons as a singlet at 2.53 ppm (4H). The UV spectrum (95% ethanol, see Appendix, figure 25) showed maxima at 233 mμ (ϵ =4340), 283 (2320), and 226 sh(4070). Anal. Calcd for $C_{12}H_{12}$: C, 92.26; H, 7.74. Found: C, 92.07; H, 7.50.

Preparation of tricyclo-[4.4.2.$0^{1,6}$]-dodecane LXXV. To 269mg diene LIX (1.67 mmoles) in 40 ml 95% ethanol was added 26mg 5% Pd/C and the compound hydrogenated at atmospheric pressure, absorbing two equivalents of hydrogen. The mixture was diluted with pentane, and the pentane was washed four times with water, dried, and evaporated. The residue was distilled four times bulb to bulb at 2.1 mm, approx. bp 82-83° to give 250 mg clear liquid LXXV (91%), n_D^{25}1.4954. The IR spectrum (film) showed no vinyl nor C=C stretches. The NMR spectrum (CCl_4) displayed the bridge protons as a sharp singlet at 1.63 ppm (4H) and the remainder of the protons as a broad singlet at 1.38 ppm (16H).
Anal. Calcd for $C_{12}H_{20}$: C, 87.73; H, 12.27. Found: C, 87.67; H, 12.08.

Hydrocarbon LXXV was also obtained from tetraene LX by hydrogenation. Four equivalents of hydrogen were absorbed, and the same NMR spectrum was observed.

Thermal decomposition of tricyclo-[4·4·2·$0^{1,6}$]-2,4,7,9-dodecatetraene LX. An NMR tube containing 87 mg tetraene LX in hexachlorobutadiene as solvent was sealed under nitrogen and heated for short periods (c.a. 30 min.) at increasing temperatures until new peaks began to appear in the NMR spectrum at 150-152°. The reaction was followed at that temperature by recording the NMR spectrum at intervals. The naphthalene resonance and a singlet at 5.32 ppm slowly increased with time. The data in Table 3 was obtained by comparison of the integrals of naphthalene with twice the downfield half of the vinyl A_2B_2 pattern (spectrum of tetraene in Appendix, figure 7).

The half-life of the reaction from the data comes to 15 hrs. while with a straight line approximation (see Appendix, figure 30) the figure is 12.5 hrs. The NMR tube was placed in an H-shaped arrangement of 8 mm glass tubing containing a sharpened nail in the same leg as the reaction tube and another NMR tube in the other leg containing one drop of bromine in carbon tetrachloride. The arrangement was sealed under a reduced pressure of nitrogen. The sealed NMR tube was broken by dropping the nail on it and the leg containing the other NMR tube cooled in an ice-salt bath for 4 hrs. The arrangement was then opened. The NMR spectrum of the reaction tube showed the peak at 5.32 ppm to be missing. The NMR spectrum of the other tube (now colorless) displayed one sharp singlet at 3.62 ppm, the same shift as an authentic sample of

1,2-dibromoethane and a weak singlet at 5.32 ppm (probably ethylene).

TABLE 3

KINETIC DATA FOR DECOMPOSITION OF TETRAENE LX

Time, hrs.	% LX left	ln LX_o/LX
0.5	97.4	0.0247
1	94.5	0.0563
2	89.9	0.125
3	85.2	0.160
4	79.8	0.226
6	72.3	0.323
9	62.0	0.478
12	56.7	0.566
15	50.0	0.683
27.5	24.3	1.415

Preparation of cis- and trans-tricyclo-[4.4.2.$0^{1,6}$]-11,12-diol-3,8-dodecadiene, LXXVII and LXXVIII. To 6.0g lithium aluminum hydride (0.157 mole, 0.632 eq.) was added 100 ml dry distilled tetrahydrofuran (distilled from calcium hydride-lithium aluminum hydride). The mixture was brought to reflux with stirring, and a 65 ml dry tetrahydrofuran solution of 20.00g acyloin LVII (0.105 mole) was added dropwise over a 3.5 hrs. period under dry nitrogen. The mixture

was refluxed for two hours, cooled, and 24 ml water were added, dropwise with stirring. To the mixture was added 75 ml 6N hydrochloric acid, and the organic layer was washed with sodium bicarbonate solution. The solvent was evaporated leaving two phases which were added to ether. The resulting ethereal solution was washed with water, sodium bicarbonate solution, and water, dried, and evaporated to leave 19.67g white solid LXXVII and LXXVIII (97.2%). Separation was usually effected in the next step of the synthesis, but initial separation was performed by chromatography on a 2.0g sample from another run.

A quantity of 2.0g diol mixture was placed on 62.5g silicic acid (2.8 x 23 cm column) and eluted with ethyl acetate (solvent too polar). Both components eluted within four fractions. Fraction No. 2 contained the first component, fraction No. 3 was a mixture, and fraction No. 4 contained predominately the second component. Fraction No. 2 was sublimed at 0.05 mm, 75° and recrystallized from benzene-hexane five times to give the analytical sample of cis-diol LXXVIII, mp 78.0-79.0°. The NMR spectrum ($CHCl_3$) displayed a vinyl multiplet at 5.9-6.1 ppm (4H), the protons under oxygen as a singlet at 3.58 ppm (2H), the hydroxyl proton as a broad peak at 2.90 ppm (shifted upfield with increased temperature, 2H), and the allyl protons appearing as a group of four multiplets at 1.5-2.6 ppm with the strongest peak at 1.9 ppm (8H). Anal. Calcd for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 74.83; H, 8.60.

Fraction No. 4 was boiled twice with ether and the remaining solid (mp 152.0-154.1°) recrystallized twice from ethyl acetate, twice from ethanol-water, and twice from chloroform to yield the analytical sample of trans-diol LXXVIII, mp 154.6-155.8°.

Anal. Calcd for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 74.96; H, 8.25.

Preparation of tricyclo-[4.4.2.$0^{1,6}$]-11, 12-dioxyisopropylene-3,8-dodecadiene LXXIX. A quantity of 19.67g diol mixture LXXVII and LXXVIII (0.102 mole) was dissolved in 200 ml acetone, 0.5g p-toluenesulfonic acid was added, and the mixture allowed to stand 24 hrs. The mixture was concentrated to 25% of the volume and poured into sodium bicarbonate solution. The mixture was extracted with ether, the ether washed three times with water, then dried and evaporated to leave 21.85g liquid plus solid. Hexane was added. The mixture was filtered and the remaining solid washed with more hexane to leave 3.75g trans-diol LXXVIII (18.6% from acyloin LVII). The hexane was evaporated and the residue distilled at 0.35 mm, bp 88-94°, to give 15.67g clear liquid LXXIX (64.9% from acyloin (LVII). The analytical sample was obtained by distillation through a 4 in. Vigreaux column at 0.15 mm, bp 69-70.5°, n_D^{25}1.5048. The IR spectrum (film) displayed a band at 1635 cm^{-1} (C=C stretch) and several bands at 1040-1220 cm^{-1}. The NMR spectrum (neat) showed the vinyl proton as a

multiplet at 5.65-6.00 ppm (4H), the protons under oxygen as a singlet at 3.89 ppm (2H), the allyl protons as a group of broad doublets at 2.54, 2.30, 1.91 (strongest), and 1.70 ppm (J=3-4cps), and another hidden beneath one of the singlet methyl groups at 1.42 ppm (11H), and the other methyl group as a singlet at 1.12 ppm (3H).

Anal. Calcd for $C_{15}H_{20}O_2$: C, 77.55; H, 8.68. Found: C, 77.54; H, 8.41.

The cis-diol LXXVII was regenerated from acetonide LXXIX by dissolving 14.31g LXXIX (61.7 mmoles) in 200 ml 95% ethanol containing 4 ml concentrated hydrochloric acid and let stand for two days. The mixture was concentrated to 25% of the volume, poured into water, and extracted with ether. The ether was washed three times with water, dried, and evaporated to leave 11.45g white solid LXXVII (96.8%).

Preparation of tricyclo-[4·4·2·$0^{1,6}$]-11,12-dioxythiocarbonyl-3,8-dodecadiene LXXX. The procedure used for preparing this compound and the following triene LXXXI was developed by Corey and Winter (112). To 50 ml dry toluene was added 2.59g N,N'-thiocarbonyldimidazole [14.5 mmoles, prepared as described by Staab and Walter (111)] and 2.10g cis-diol LXXVII (10.9 mmoles) and the mixture refluxed 40 min. (calcium chloride drying tube attached). The mixture was cooled and after ether was added was washed four times with water, dried over anhydrous magnesium sulfate, and the

solvent evaporated to leave 2.47g yellow solid LXXX (96.5%). Recrystallization from benzene-hexane afforded yellow solid LXXX, mp 118-121.5° [lit. (113), 122.5-123°]. The IR spectrum ($CHCl_3$) showed only two strong bands at 1325 and 1295 cm^{-1}. This compound was normally used in the next step without purification.

Preparation of tricyclo-[4·4·2·$0^{1,6}$]-3,8,11-dodecatriene LXXXI. To 11.71g crude thiocarbonate LXXX(50.1 mmoles) was added 180 ml trimethyl phosphite and the mixture refluxed under dry nitrogen for 5.5 days. The mixture was cooled and hexane was added, causing two layers to form. The lower, hexane-insoluble layer, was washed three times with hexane and the combined hexane solutions evaporated leaving 16.1g liquid. The liquid was placed on 300g silicic acid (5.0 x 32.5 cm column) and washed with hexane yielding a colorless liquid which was distilled through a 4 in. Vigreaux column at 8.5 mm, bp 71-72°, to give 3.97g colorless liquid LXXXI (50.1%), n_D^{25}1.5158. The IR spectrum (film) displayed a vinyl stretch at 3030 cm^{-1}. The NMR spectrum (neat) displayed a vinyl multiplet at 5.52-5.78 ppm with a sharp singlet at 5.52 ppm (6H) and the allyl protons as a broad doublet at 1.94 ppm (J=4cps, 8H). The UV spectrum (95% ethanol, see Appendix, figure 24) indicated absorptions at 220 mμ sh(ϵ =1890), 238 low (66.6), 247 sh (92.7), 255 sh (121), 265 max. (137), and 275 sh (109). The analytical sample was obtained by a second

distillation through a 4 in. Vigreaux column at 8.5 mm, bp 71.5-72°.

Anal. Calcd for $C_{12}H_{14}$: C, 91.08; H, 8.92. Found: C, 91.05; H, 9.00.

Preparation of tricyclo-[4·4·2·$0^{1,6}$]-2,4,8,11-dodecatetraene LXXXIII (or double bond isomer), attempted preparation of tricyclo-[4·4·2·$0^{1,6}$]-2,4,7,9,11-dodecapentaene LXXXII. To 3.92g triene LXXXI (24.8 mmoles) in 125 ml carbon tetrachloride was added 8.83g N-bromosuccinimide and the mixture brought to reflux with stirring. To the boiling mixture was added c.a. 0.10g azobisisobutryonitrile and the mixture refluxed 1.5 hrs. (with no effect). One drop of bromine was added to the boiling mixture and the mixture refluxed 25 min. The mixture was cooled, filtered, and the solvent evaporated from the filtrate. To the resulting dark oil was added 20 ml distilled quinoline (from zinc dust), the mixture immersed in an oil bath at 140°, and heated at 140-145° for 15 min. under dry purified nitrogen. The hot solution was poured with stirring into 100 ml ice-hydrochloric acid containing 15 ml concentrated hydrochloric acid. Water (100 ml) was added and the mixture extracted four times with pentane and three times with ether. The combined organic solutions were washed with 1:20 hydrochloric acid and sodium bicarbonate solutions, dried, and evaporated. The resulting oil was placed on 66g silicic acid (4.5 x 10 cm column) and washed with hexane to yield

1.39g liquid. The liquid was separated into five major components by gas chromatography on 20% carbowax on ABS Anachrom (3/8 in. x 20 ft. column) at 165°. Fraction No. 1 eluted at 18 min. and proved to be starting triene LXXXI (by NMR spectrum) in almost immeasurable quantity. Fraction No. 2 eluted in 23 min. weighed 87 mg and had an NMR spectrum (CCl_4) that fit for tetraene LXXXIII (2.3%). The vinyl protons appeared as a close A_2B_2 pattern at 5.4-5.9 ppm with a multiplet in the center and a sharp singlet at 5.52 ppm (8H) and the methylene protons as a multiplet at 1.90-2.02 ppm (4H). The substance was not investigated further. Fraction No. 3, 84 mg, eluted in 35 min. and displayed an NMR spectrum (CCl_4) having an aromatic multiplet at 7.2-7.8 ppm, many vinyl peaks at 5.0-6.0 ppm (but no sharp singlet for the bridge protons), and many peaks in the region 2.1-3.1 ppm. Fraction No. 4, 141 mg, eluted in 75 min. and displayed an NMR spectrum (CCl_4) of β-methylnaphthalene. An aromatic multiplet at 7.0-7.8 ppm could be seen and a sharp singlet at 2.42 ppm (the spectrum was superimposed on an authentic sample of β-methylnaphthalene). Fraction No. 5, 138 mg, eluted in 205 min. and showed an NMR spectrum (CCl_4) of an aromatic multiplet at 7.1-7.6 ppm having three sharp peaks and a singlet at 3.37 ppm.

Other attempts to prepare LXXXII ended in similar results. Using N-bromosuccinimide as the halogenating reagent and 1,5-diazabicyclo-[4.3.0]-5-nonene as dehydrohalogenating reagent afforded only small amounts of starting triene LXXXI

and tetraene LXXXIII after gas chromatographic separation (same column as before). In another run, separation was attempted on a 20% carbowax column containing 1% cupric chloride and only a small amount of starting triene LXXXI was isolated.

Preparation of tricyclo-[4.4.2.$0^{1,6}$]-11-ol-3,8-dodecadiene LXXXV. To 1.0g lithium aluminum hydride (0.025 mole) was added 50 ml dry tetrahydrofuran (distilled from calcium hydride-lithium aluminum hydride) followed by a 25 ml dry tetrahydrofuran solution of 3.17g ketone LVIII (0.0182 mole) with stirring over a 30 min. period. The mixture was refluxed 30 min., cooled in a water bath, and 6 ml water slowly added. After 4 hrs. stirring the solid was filtered out and the solvent evaporated from the filtrate to leave 3.24g light yellow liquid. The liquid was distilled (short head) at 0.5 mm, bp 61.5-63°, yielding 2.81g white solid LXXXV (87.5%), mp 46-49.5°. Treatment with charcoal and recrystallization from hexane three times produced the analytical sample, mp 48-49.5°. The IR spectrum (CCl_4) showed absorptions at 3600 cm^{-1} (OH) and 3040 cm^{-1} (vinyl CH). The NMR spectrum (CCl_4) displayed a vinyl multiplet at 5.7-6.2 ppm (4H), a double doublet for the proton under oxygen at 3.57 and 3.72 ppm (J=6cps, 1H), and the remainder of the protons as a series of sharp peaks at 1.3-2.5 ppm with a major peak at 1.92 ppm (11H).
Anal. Calcd for $C_{12}H_{16}O$: C, 81.77; H, 9.15. Found: C,

81.63; H, 9.04.

Preparation of tricyclo-[4·4·2·$0^{1,6}$]-11-acetoxy-3,8-dodecadiene LXXXVI. To 1.00g alcohol LXXXV (5.68 mmoles) dissolved 40 ml dry ether and 4 ml distilled pyridine in an ice bath was added, dropwise with stirring, a 20 ml dry ether solution of 2.0g acetyl chloride (25.8 mmoles) over a 15 min. period. The mixture was stirred at room temperature for 15 hrs. and water was added. The ethereal solution was washed with 1:10 hydrochloric acid and sodium bicarbonate solution, dried, and evaporated to yield 1.27g light yellow liquid. The product was distilled at 0.12 mm, bp 63.5-64°, to yield 1.11g colorless liquid LXXXVI (89.5%). The analytical sample was obtained after a second distillation at 0.11 mm, bp 63.5-64.0°, n_D^{25}1.5015. The IR spectrum (film) showed a 1740 cm^{-1} carbonyl. The NMR spectrum (CCl_4) displayed a vinyl multiplet at 5.7-6.05 ppm (4H), the proton under oxygen as a triplet at 4.57 ppm (J=8cps, 1H), and the remainder of the protons as a group of multiplets at 1.5-2.5 ppm with a sharp singlet at 1.93 ppm for the acetate methyl and what appears to be a doublet for the bridge methylene at 1.84 ppm (J=8cps, 11H total). The UV spectrum (95% ethanol, see Appendix, figure 19) showed maxima at 210 mμ (ϵ=382), 263 (12.0), 276 (12.4), and 283 (8.8).

Anal. Calcd for $C_{14}H_{18}O_2$: C, 77.03; H, 8.31. Found: C, 76.88; H, 8.52.

Preparation of tricyclo-[4·4.2.$0^{1,6}$]-11-acetoxy-2,4,7,9-dodecatetraene LXXXVII. To 9.30g acetate LXXXVI (42.7 mmoles) in 150 ml carbon tetrachloride was added 15.2g N-bromosuccinimide (85.4 mmoles) and a spatula tip of azobis-isobutyronitrile and the mixture refluxed with stirring for 30 min. The mixture was cooled, filtered, and the solvent stripped from the filtrate. To the resulting oil was added 30 ml distilled quinoline (from zinc dust), the mixture was immersed in an oil bath at 145°, and heated at 140-145° for 15 min. The hot mixture was poured with stirring into 150 ml ice-hydrochloric acid containing 30 ml concentrated hydrochloric acid and extracted twice with ether. The ether solution was washed with 1:10 hydrochloric acid and sodium bicarbonate solutions, dried, and evaporated to leave 7.52g dark liquid. The liquid was distilled (short head) at 0.35 mm, bp 67-106°, yielding 5.58g yellow liquid. The distillate was placed on 180g silicic acid (4.5 x 24 cm column) and eluted with hexane-benzene mixtures, collecting 75 ml fractions. Fractions 1-39 (hexane) contained 0.41g light colored oil. Fractions 40-68 (20% benzene) and 69-71 (50% benzene) yielded nothing. The rest of the chromatography (50% benzene, fractions 75-125) was combined in groups according to the purity displayed by thin layer chromatography as follows: 83-97 (1.90g) one component; 80-82 and 98-109 (1.41g) one component and a trace impurity; 77-99 (0.47g) a small amount of a second component; 72-73 (0.04g), 74-76 (0.22g) and 110-125

(0.30g) all showed two components. Adding the weights of fractions 80-109 gave a yield of 3.31g acetate LXXXVII (36.2%). The analytical sample was obtained by distillation of fractions 83-97 (short path) at 0.10 mm, bp 66.0-66.5°, yielding 1.36g colorless liquid LXXXVII, n_D^{25} 1.5315. The IR spectrum (film) showed a vinyl stretch at 3040 cm^{-1} and carbonyl stretch at 1740 cm^{-1}. The NMR spectrum (CCl_4, see Appendix, figure 8) displayed a complex vinyl region with the proton under oxygen mixed in with what appears to be an A_2B_2 pattern at 5.0-6.1 ppm (9H), a doublet for the remaining bridge protons at 2.75 ppm (J=7cps, 2H), and the acetate methyl as a singlet at 1.98 ppm (3H). The UV spectrum (95% ethanol, see Appendix, figure 26) showed maxima at 276 mμ (ϵ=2730) and 232 (4280).

Anal. Calcd for $C_{14}H_{14}O_2$: C, 78.48; H, 6.59. Found: C, 78.33; H, 6.64.

Preparation of tricyclo-[4·4·2·$0^{1,6}$]-11,11-dioxyethylene-3,8-dodecadiene LXXXIX. To 7.96g ketone LVIII (45.6 mmoles) and 4 ml ethylene glycol in 100 ml benzene was added a spatula tip of p-toluenesulfonic acid, and the mixture was refluxed with a water separator containing calcium chloride in the trap for 12.5 hrs. The mixture was cooled, washed with water and sodium bicarbonate solution, dried, and benzene evaporated to leave 10.99g yellow oil. The product was distilled at 0.25 mm, bp 85-89°, to give 8.88g colorless

liquid LXXXIX (89.4%). The analytical sample was obtained by redistillation through a 4 in. Vigreaux column at 0.30 mm, bp 82-83°, n_D^{25} 1.5247. The IR spectrum (film) showed two strong bands at 1035 and 1082 cm^{-1}. The NMR spectrum (CCl_4) displayed the vinyl protons as a multiplet at 5.55-6.10 ppm with two strong peaks at 5.77 and 5.83 ppm (4H), the ketal protons as a close multiplet at 3.6-3.9 ppm (4H), and the remainder of the protons as a group of five multiplets at 1.45-2.55 ppm with a singlet at 1.93 ppm for the bridge protons (10H).

Anal. Calcd for $C_{14}H_{18}O_2$: C, 77.03; H, 8.31. Found: C, 76.80; H, 8.36.

Attempted preparation of tricyclo-[4·4·2·$0^{1,6}$]-11,11-dioxyethylene-2,4,7,9-dodecatetraene XC. To 2.00g ketal LXXXIX (9.17 mmoles) dissolved in 40 ml carbon tetrachloride was added 3.27g N-bromosuccinimide (18.3 mmoles) and a spatula tip of azobisisobutyronitrile and the mixture refluxed 20 min. The mixture was cooled, filtered, and the solvent stripped from the filtrate to give 3.75g oil. The oil was dissolved in 40 ml tert-butyl alcohol, 2.50g 1,5-diazabicyclo-[4·3·0]-5-nonene added, and the mixture stirred at room temperature for 21 hrs. The mixture was stripped down to a few ml and placed on 100g Florisil (4.8 x 9.5 cm column). The column was washed with benzene rapidly, yielding 1.45g yellow oil whose NMR spectrum (CCl_4) showed an aromatic pattern for

naphthalene, a complex vinyl region at 5.0-6.1 ppm, multiplets at 4.0-4.5 and 3.3-3.8 ppm, and a complex methylene region at 1.5-2.7 ppm with the bridge protons as a singlet at 2.36 ppm. Two additional singlets appeared at 1.60 and 1.18 ppm. The product was placed on 42g silicic acid (2.1 x 24 cm column) and washed with benzene-hexane mixtures. Very little was obtained from the column. Fractions 5-30 (20% benzene) yielded a small quantity of material showing an NMR spectrum (CCl_4) which displayed a vinyl multiplet at 5.1-6.2 ppm and a continuous series of peaks from 1.2 ppm to 4.6 ppm. A weak singlet at 3.57 ppm could be seen which corresponded to ketone LVIII but no peaks resembled a ketal. Fractions 31-45 yielded a small amount of ketone LVIII. Nothing more came off the column (up to 75% benzene).

Part IV

1,2-Cyclobutanediones

Preparation of tricyclo-[4·4·2·$0^{1,6}$]-11,12-dione-3,8-dodecadiene XCI. To 5.00g acyloin LVII (26.3 mmoles) in 79 ml distilled dimethyl sulfoxide (from calcium hydride) was added 56 ml acetic anhydride (116), and the mixture was allowed to stand in the dark for 9 days. The mixture was poured into water, extracted with ether, and the ether washed twice with water, twice with sodium bicarbonate solution, and twice with water, dried, and evaporated. The resulting red oil was heated on a steam bath and pulled on the vacuum pump alternately until no liquid would distill leaving 4.92g red solid XCI. Recrystallization from 80 ml hexane (filtered hot) afforded 4.16g red solid XCI (84%), mp 110-115°. The analytical sample was obtained by sublimation (twice) at 0.10 mm, 60°, mp 111-115°. The IR spectrum (KBr) showed vinyl stretch at 3050 cm^{-1} and double carbonyl stretches at 1760 and 1790 cm^{-1}. The NMR spectrum (CCl_4) displayed a vinyl multiplet of three sharp peaks at 5.68-5.86 with a group of weaker peaks on each side at 5.4-5.6 and 5.9-6.15 ppm (4H) and the allyl protons as a group of four multiplets at 1.85-

3.0 ppm including two sharp peaks at 2.03 ppm and 2.28 ppm (8H). The UV spectrum (isooctane, see Appendix, figure 28) showed λ max. at 260 mμ (ϵ =450) and in the visible at 545 mμ (ϵ =46.4).

Anal. Calcd for $C_{12}H_{12}O_2$: C, 76.57; H, 6.43. Found: C, 76.25; H, 6.47.

Preparation of tricyclo-[4.4.2.$0^{1,6}$]-dodecane-11-ol-12-one XCII. To 4.00g acyloin LVII (21.0 mmoles) in 60 ml 95% ethanol was added 0.10g Pd/C and the compound hydrogenated at atmospheric pressure. Incomplete hydrogenation was observed (by IR spectrum), and hydrogenation was repeated three times more, each with fresh catalyst (1.2g total used), before no double bonds were present in the IR spectrum. After each hydrogenation the solution was concentrated to 25% volume, poured into water, and extracted with ether. The ether solution was washed four times with water, dried, and evaporated to leave 2.45g colorless oil in the last step which slowly crystallized. Recrystallization from hexane afforded 1.40g white fluffy solid XCII (39.3%), mp 89.5-91.0°. The analytical sample was obtained after two more recrystallizations from hexane, mp 93.8-95.3°. The IR spectrum (CCl_4) showed a hydroxyl absorption at 3450 cm^{-1} and a carbonyl stretch at 1770 cm^{-1}. The NMR spectrum (CCl_4) showed a poorly resolved singlet for the proton under oxygen at 5.14 ppm (1H), a broad peak at 4.10 ppm for the hydroxyl proton (moved

upfield with increased temperature, 1H), and the remainder of the protons as a broad multiplet at 0.80-2.20 ppm (16H). Anal. Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 74.35; H, 9.36.

The saturated acyloin XCII was also obtained by hydrogenation of the unsaturated keto-acetate LXXIII. To 2.46g keto acetate LXXIII (10.6 mmoles) in 50 ml 2:1 95% ethanol-ethyl acetate was added a spatula tip of 5% Pd/C, and the compound was hydrogenated at atmospheric pressure, absorbing two equivalents of hydrogen. The catalyst was filtered out and the solvent evaporated to leave 2.46g colorless liquid XCIV which was dissolved in 35 ml acetic acid. Water (10 ml) and 4 ml concentrated hydrochloric acid were added and the mixture stirred 18 hrs. at room temperature. The mixture was poured into water, and 25g sodium bicarbonate were added slowly with stirring. The aqueous mixture was extracted with ether and the ether washed with sodium bicarbonate solution and water. After drying, the ether was evaporated leaving 2.22g cream solid with two carbonyl absorptions at 1790 and 1740 cm^{-1}. The solid was dissolved in 40 ml of 95% ethanol, 13 ml water and 2 ml concentrated hydrochloric acid were added, and the mixture was stirred at room temperature for 23 hrs. The solution was poured into water and worked up as before to yield 2.01g light yellow solid XCII (97% from LXXIII). The IR spectrum (CCl_4) was identical to that obtained from hydrogenation of LVII.

Preparation of tricyclo-[4.4.2.$0^{1,6}$]-dodecane-11,12-dione XCIII. To 6.94g saturated acyloin XCII (35.8 mmoles) in 105 ml distilled dimethyl sulfoxide was added 70 ml acetic anhydride (116) and the mixture allowed to stand in the dark 4 days. The solution was poured into water and extracted with ether. The ether was washed four times with water, twice with sodium bicarbonate solution, dried, and evaporated. The liquid remaining was distilled down to 10 mm, bp 85°, and the distillate discarded. The remaining orange oil was distilled (short path) at 0.20 mm, bp 72-74°, to yield 6.41g orange liquid. The product was distilled a second time (short head) at 0.10 mm collecting the fraction boiling at 67-70°, yielding 5.98g orange solid XCII (89.5%). The analytical sample was obtained by sublimation twice at 0.07 mm, 40°, mp 37-38°. The IR spectrum (CCl_4) displayed two carbonyl frequencies at 1775 and 1785 cm^{-1} with a shoulder at 1820 cm^{-1}. The NMR spectrum (CCl_4) showed a broad peak at 1.2-2.0 ppm centered at 1.49 ppm on what appears to be a doublet (J=3cps). The UV spectrum (isooctane, see Appendix, figure 27) showed λ max. at 225 mμ (ϵ=560) and in the visible at 468 mμ (ϵ=76.3).

Anal. Calcd for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 75.05; H. 8.49.

Preparation of tricyclo-[4.4.1.$0^{1,6}$]-3,8-undecadiene-11-ol-11-carboxylic acid XCIX. To 0.40g diketone XCI (2.1

mmoles) suspended in 30 ml water were added 1.0g potassium hydroxide pellets, one at a time with stirring, until no solid remained (about 5 min.). The solution was stirred 20 min., diluted with water, and poured into 50 ml water containing 3 ml concentrated hydrochloric acid. The mixture was extracted three times with ether and the ether washed three times with water, dried, and evaporated to leave 0.39g light yellow solid XCIX (89%), mp 140-145°. Recrystallization four times from benzene-hexane provided the analytical sample as a white solid, mp 145.5-147.5° (dec.). The IR spectrum (KBr) showed an acid hydroxyl (broad range) and a carbonyl stretch at 1690 cm^{-1}. The NMR spectrum ($CDCl_3$) showed the alcohol and acid protons together as a broad peak at 6.4-7.0 ppm (2H, erased by addition of D_2O), the vinyl protons as two close triplets at 5.55 and 5.68 ppm (J≅1cps, 4H), and the allyl protons as a group of multiplets at 1.95-2.9 ppm with the largest peak at 2.30 ppm (8H).

Anal. Calcd for $C_{12}H_{14}O_3$: C, 69.88; H, 6.84. Found: C, 69.88; H, 6.82.

Preparation of methyl tricyclo-[4·4·1·$0^{1,6}$]-3,8-undecadiene-11-ol-11-carboxylate XCV. To 1.00g diketone XCI (5.23 mmoles) dissolved in 50 ml methanol was added 0.5g potassium hydroxide pellets with stirring (the color changed from red to light yellow in about 5 sec.), and the mixture was stirred at room temperature 20 hrs. The solution was poured into 250

ml water containing 3 ml concentrated hydrochloric acid and extracted three times with ether. The ether was washed four times with water, dried, and evaporated to leave 1.17g light yellow solid XCV (100%). Recrystallization three times from hexane gave the analytical sample, mp 74.4-75.7°. The IR spectrum (KBr) showed absorptions at 3480 cm^{-1} (OH) and 1720 cm^{-1} (carbonyl). The NMR spectrum (CCl_4) displayed the vinyl protons as two multiplets at 5.38-5.46 and 5.51-5.64 ppm (4H), the methoxyl protons as a singlet at 3.56 ppm (3H), the hydroxyl proton as a broadened singlet (erased by addition of D_2O) at 3.12 ppm (1H), and the allyl protons as a group of four multiplets at 1.85-2.90 ppm with the major peak at 2.22 ppm (8H).

Anal. Calcd for $C_{13}H_{16}O_3$: C, 70.89; H, 7.32. Found: C, 71.07; H, 7.28.

This compound could also be prepared from hydroxy-acid XCIX. To 0.10g acid XCIX (0.485 mmole) was added 40 ml 0.1M diazomethane in ether and the resulting solution stirred for 20 min. at room temperature. Evaporation of the ether left 0.12g light yellow oil XCV (100%) which slowly crystallized. The IR and NMR spectra of this product were superimposable on those of the material prepared with base in methanol.

Preparation of 9-methoxalyl-$\Delta^{2,6}$-hexalin XCVIII. To 0.50g hydroxy-ester XCV (2.3 mmole) suspended in 40 ml water was added 1.0g potassium hydroxide and the mixture refluxed

9 hrs. The solution was cooled and poured into 30 ml water containing 2 ml concentrated hydrochloric acid. The mixture was extracted with ether twice and the ether washed three times with water, dried, and evaporated to leave 0.39g dark yellow oil which slowly crystallized. The acid was dissolved in ether and esterified using 0.1M diazomethane in ether (excess used). Evaporation of the ether left 0.46g dark yellow oil which was placed on 20g Florisil (2.6 x 6.8 cm column) and washed with benzene to yield 0.30g slightly yellow liquid XCVIII (60%). The analytical sample was obtained after bulb to bulb distillation twice at 0.08 mm, 89-95°, leaving 270 mg colorless liquid XCVIII (54%), n_D^{25}1.5026. The IR spectrum (film) displayed two carbonyl frequencies at 1735 and 1715 cm^{-1}. The NMR spectrum (CCl_4) showed the vinyl protons as a multiplet at 5.35-5.85 ppm with two major peaks at 5.53 and 5.59 ppm (4H), the methoxyl protons as a singlet at 3.70 ppm (3H), and the allyl protons as four multiplets at 1.8-3.0 with the major one appearing as a broad singlet at 2.15 ppm (9H).

Anal. Calcd for $C_{13}H_{16}O_3$: C, 70.89; H, 7.32. Found: C, 70.60; H, 7.32.

Reaction of unsaturated diketone XCI in neutral methanol. A solution of 4.05g dione XCI (21.5 mmoles) in 170 ml methanol was refluxed in the dark under dry purified nitrogen for 44 hrs. The solution was concentrated to one-fourth of

its original volume, poured into water, and extracted with ether. The ethereal solution was washed three times with water, dried, and evaporated to leave a mixture of two components. The mixture was placed on 100g silicic acid (4.8 x 11.5 cm column) and washed with hexane (nothing eluted) followed by 500 ml benzene which yielded 0.36g colorless oil XCVIII (7.6%) which showed an NMR spectrum (CCl_4) like the one described above in the preparation of methoxalate XCVIII. The column was washed with 500 ml 10% ethyl acetate in benzene, and 2.75g light yellow solid XCV (58.1%) washed off whose NMR spectrum (CCl_4) was like that described above for hydroxy-ester XCV. Further washing with ethyl acetate mixtures yielded no material. A methanol wash yielded a small amount of dark gum.

Reaction of unsaturated diketone XCI with acidic methanol. To 1.00g diketone XCI dissolved in 50 ml methanol were added 3 drops concentrated hydrochloric acid, and the mixture was refluxed in the dark under purified nitrogen for 66 hours. The solution was poured into water and extracted with ether. The ether was washed three times with water, dried, and evaporated leaving 1.18g light yellow oil of two components. The mixture was placed on 30g silicic acid (2.1 x 17.7 cm column) and eluted with 5% ethyl acetate in benzene, collecting 30 ml fractions. Fractions 11-22 contained 0.09g of one component which was thought to be ketal C (7.7%). The

IR spectrum (KBr) showed a 1780 cm^{-1} carbonyl. The NMR spectrum (CCl_4) displayed a vinyl multiplet at 5.5-5.68 ppm (4H), a singlet at 3.43 ppm for the methoxyl protons (6H), and a broad methylene region of many peaks at 1.5-2.8 ppm (8H).

Fraction 23 contained a trace quantity of a two component mixture. Fractions 24-28 contained 0.72g of XCV (59.8%) whose NMR spectrum (CCl_4) was like that of hydroxy ester XCV. Further elution yielded nothing.

Preparation of tricyclo-[4·4·1·$0^{1,6}$]-undecane-11-ol-11-carboxylic acid CII. To 0.46g saturated dione XCIII (2.4 mmoles) suspended in 10 ml water was added 1.0g potassium hydroxide pellets, one at a time with stirring (5 min.), and the mixture stirred 1.5 hrs. (solid disappeared in 20 min.). The solution was diluted with water, poured into 20 ml 2N hydrochloric acid, and extracted twice with ether. The ether was washed three times with water, dried, and evaporated to leave 0.45g light yellow solid CII (89%), mp 104-115° (dec.). The analytical sample was obtained after four recrystallizations from benzene-hexane, mp 113.1-115.0° (dec.). The IR spectrum (KBr) showed an acid hydroxyl (broad range) and a carbonyl at 1710 cm^{-1}. The NMR spectrum ($CDCl_3$) displayed the hydroxyl and acid protons together as a broad singlet at 7.41 ppm (erased by addition of D_2O, 2H) and the remainder of the protons as a broad region of multiplets at 1.1-2.2 ppm with the major peak at 1.4 ppm (16H).

Anal. Calcd for $C_{12}H_{18}O_3$: C, 68.54; H, 8.63. Found: C, 68.36; H, 8.59.

Preparation of methyl tricyclo-[4.4.1.$0^{1,6}$]-dodecane-11-ol-11-carboxylate CI. To 1.00g saturated diketone XCIII (5.2 mmoles) dissolved in 30 ml methanol was added one pellet of potassium hydroxide (color changed from orange to light yellow in 20 sec.) and the solution stirred at room temperature for 1.5 hrs. The solution was poured into water and extracted twice with ether. After washing the ether three times with water, the ether was dried and evaporated to leave 0.98g light yellow oil CI (84%). Attempts to purify this material failed, and spectra were run on the crude sample from another run. Recrystallization attempts only yielded oils and distillation yielded mixtures. The IR spectrum (film) showed absorptions at 3460 cm^{-1} (OH) and 1730 cm^{-1} (carbonyl). The NMR spectrum (CCl_4) displayed the hydroxyl proton at 4.37 ppm as a broad singlet (moved upfield with increase in temperature, 1H), the methoxyl protons as a singlet at 3.69 ppm (3H), and the remainder of the protons in a broad region of multiplets at 0.90-2.2 ppm with the major peak at 1.37 ppm (16H).

This compound was also prepared from hydroxy-acid CII. To 0.10g CII (0.476 mmole) was added 40 ml of 0.1M diazomethane in ether and the resulting solution stirred at room temperature for 20 min. Evaporation of the ether left 0.10g

light yellow oil CI (94%) whose IR and NMR spectra were like those obtained from a sample prepared in basic methanol.

The compound was also prepared from hydroxy-ester XCV. Hydrogenation of 0.50g XCV (2.27 mmoles) in 30 ml 95% ethanol containing a spatula tip of Adams catalyst was conducted at atmospheric pressure with absorption of two equivalents of hydrogen. The catalyst was filtered out, the filtrate diluted with ether, and the ether washed four times with water. Evaporation of the dried ether solution yielded 0.51g light yellow oil CI (100%) whose NMR spectrum (CCl_4) was like that described for the product obtained from basic methanol.

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APPENDIX

List of Figures

Figure	Description
1	NMR spectrum of 9,10-dihydronaphthalene-9-hydroxymethyl-10-carboxylic acid lactone
2	NMR spectrum of 9-(9,10-dihydronaphthalene)-dimethyl carbinol-10-carboxylic acid lactone
3	NMR spectrum of 9-(9,10-dihydronaphthalene)-diethylcarbinol-10-carboxylic acid lactone
4	NMR spectrum of 12-oxatricyclo-[4·4·3·$0^{1,6}$]-2,4,7,9-tridecatetraene
5	NMR spectrum of tricyclo-[4·4·3·$0^{1,6}$]-12,12-dioxyethylene-2,4,7,9-tridecatetraene
6	NMR spectrum of tricyclo-[4·4·3·$0^{1,6}$]-2,4,7,9-tridecatetraene-12-one
7	NMR spectrum of tricyclo-[4·4·2·$0^{1,6}$]-2.4,7,9-dodecatetraene
8	NMR spectrum of tricyclo-[4·4·2.$0^{1,6}$]-11-acetoxy-2,4,7,9-dodecatetraene
9	UV spectrum of 9-(9,10-dihydronaphthalene)-dimethyl carbinol-10-carboxylic acid lactone
10	UV spectrum of 9-(9,10-dihydronaphthalene)-diethylcarbinol-10-carboxylic acid lactone
11	UV spectrum of 2-(1,2-dihydronaphthyl)-diphenyl carbinol
12	UV spectrum of 2-tetralyldiphenylcarbinol
13	UV spectrum of 12-oxatricyclo-[4·4·2.$0^{1,6}$]-3,8-tridecadiene
14	UV spectrum of tricyclo-[4·4·3·$0^{1,6}$]-12-one-3,8-tridecadiene

15 UV spectrum of 9,10-dihydronaphthalene-9-hydroxymethyl-10-carboxylic acid lactone

16 UV spectrum of 12-oxatricyclo-[4·4.3·$0^{1,6}$]-2,4,7,9-tridecatetraene

17 UV spectrum of tricyclo-[4·4·3·$0^{1,6}$]-12,12-dioxyethylene 2,4,7,9-tridecatetraene

18 UV spectrum of tricyclo-[4·4·3·$0^{1,6}$]-2,4,7,9-tridecatetraene-12-one

19 UV spectrum of tricyclo-[4·4·2·$0^{1,6}$]-11-acetoxy-3,8-dodecadiene

20 UV spectrum of tricyclo-[4·4·2·$0^{1,6}$[-11-ol-12-one-3,8-dodecadiene

21 UV spectrum of tricyclo-[4·4·2·$0^{1,6}$]-dodecane-11-one

22 UV spectrum of tricyclo-[4·4·2·$0^{1,6}$]-11-one-3,8-dodecadiene

23 UV spectrum of tricyclo-[4·4·2·$0^{1,6}$]-3,8-dodecadiene

24 UV spectrum of tricyclo-[4·4·2·$0^{1,6}$]-3,8,11-dodecatriene

25 UV spectrum of tricyclo-[4.4·2·$0^{1,6}$]-2,4,7,9-dodecatetraene

26 UV spectrum of tricyclo-[4·4·2·$0^{1,6}$]-11-acetoxy-2,4,7,9-dodecatetraene

27 UV spectrum of tricyclo-[4·4·2·$0^{1,6}$]-dodecane-11,12-dione

28 UV spectrum of tricyclo-[4·4·2·$0^{1,6}$]-11,12-dione-3,8-dodecadiene

29 Kinetic Plot of the decomposition of 12-oxatricyclo-[4·4·3.$0^{1,6}$]-2,4,7,9-tridecatetraene

30 Kinetic Plot of the decomposition of tricyclo-[4·4·2.$0^{1,6}$]-2,4,7,9-dodecatetraene

Figure 1

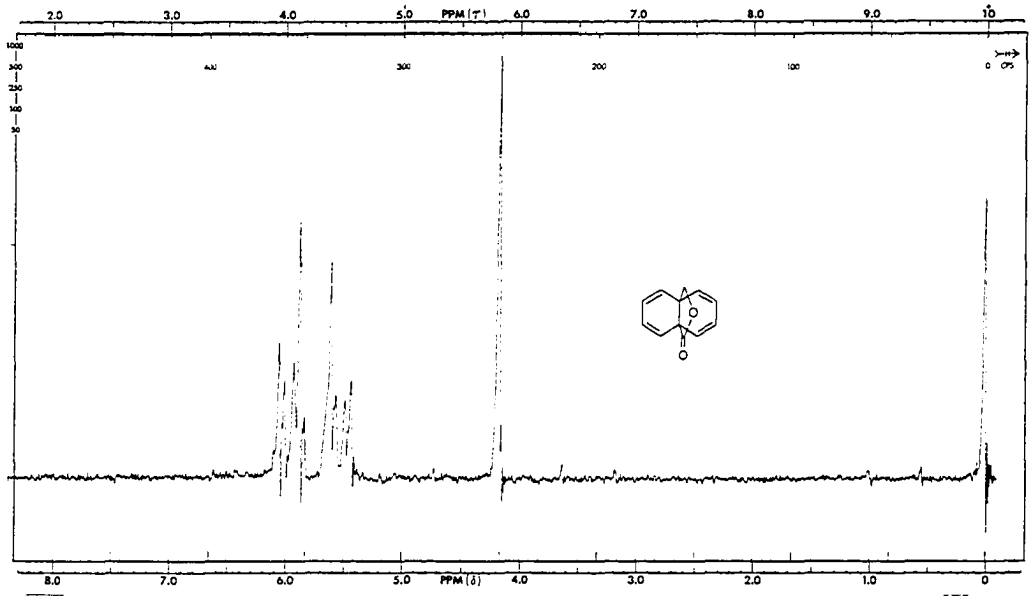


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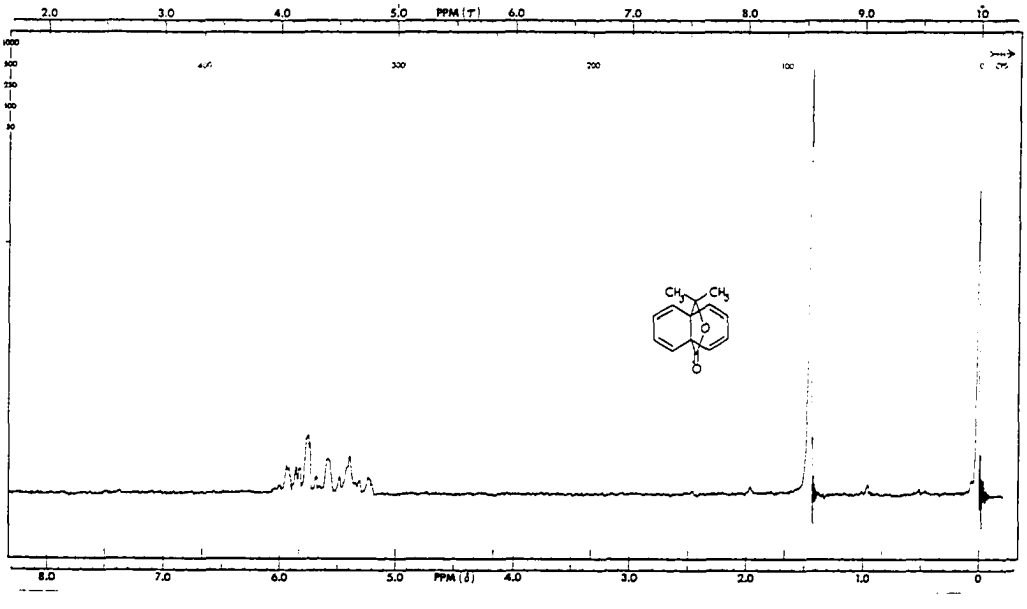


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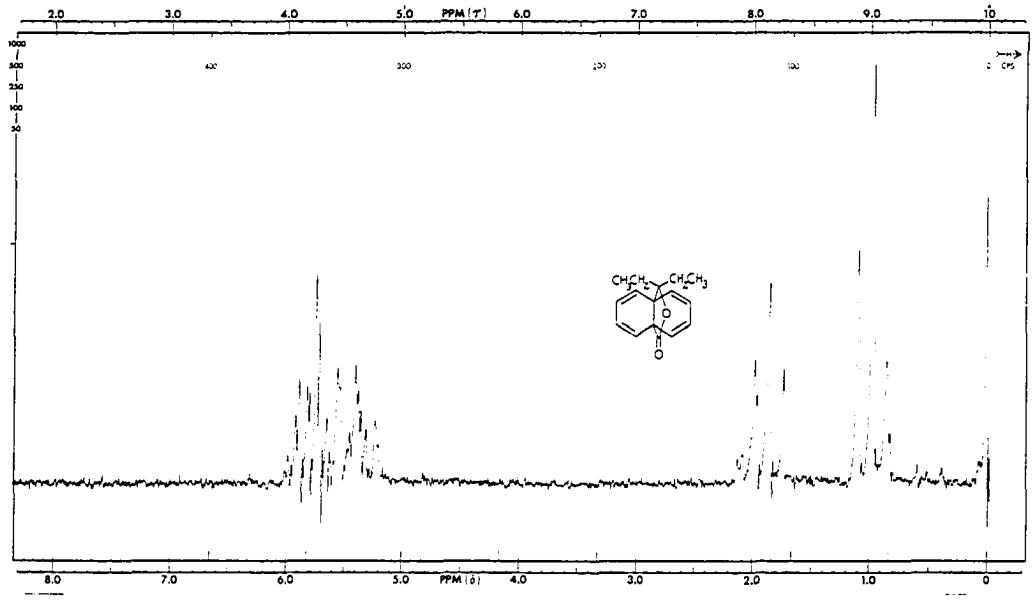


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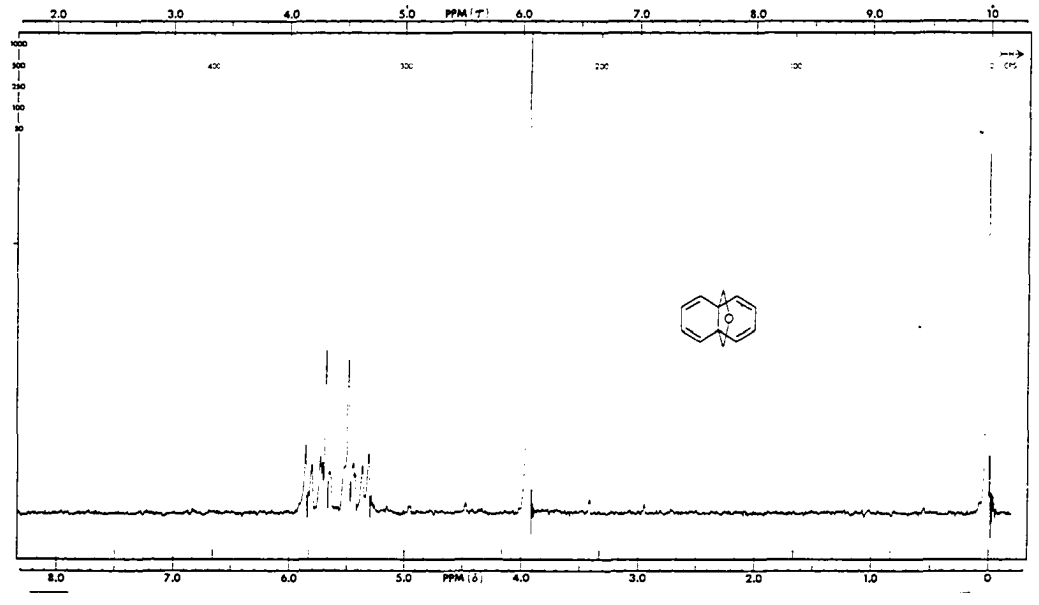


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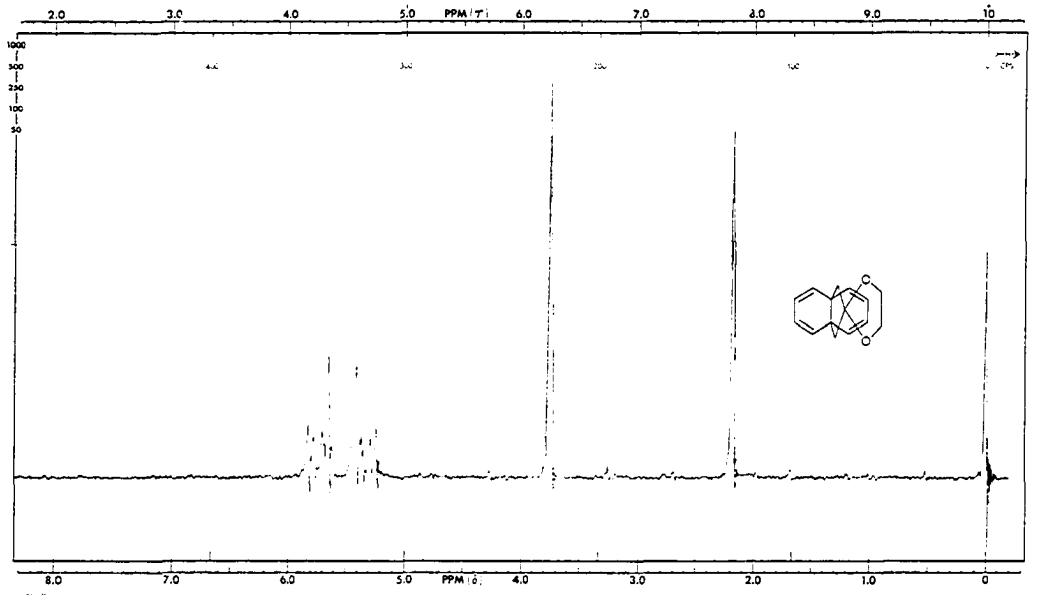


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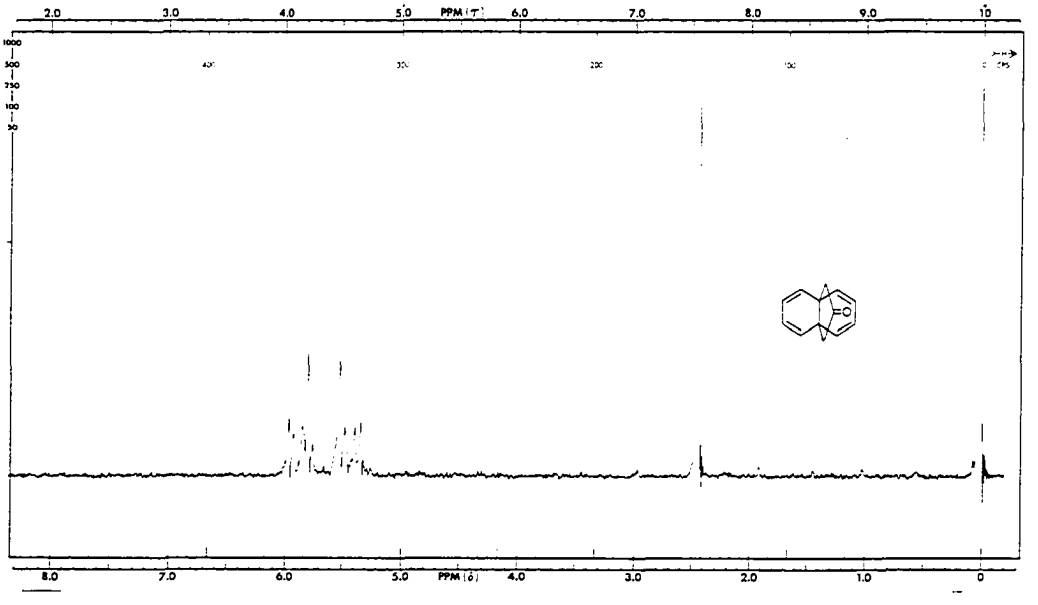


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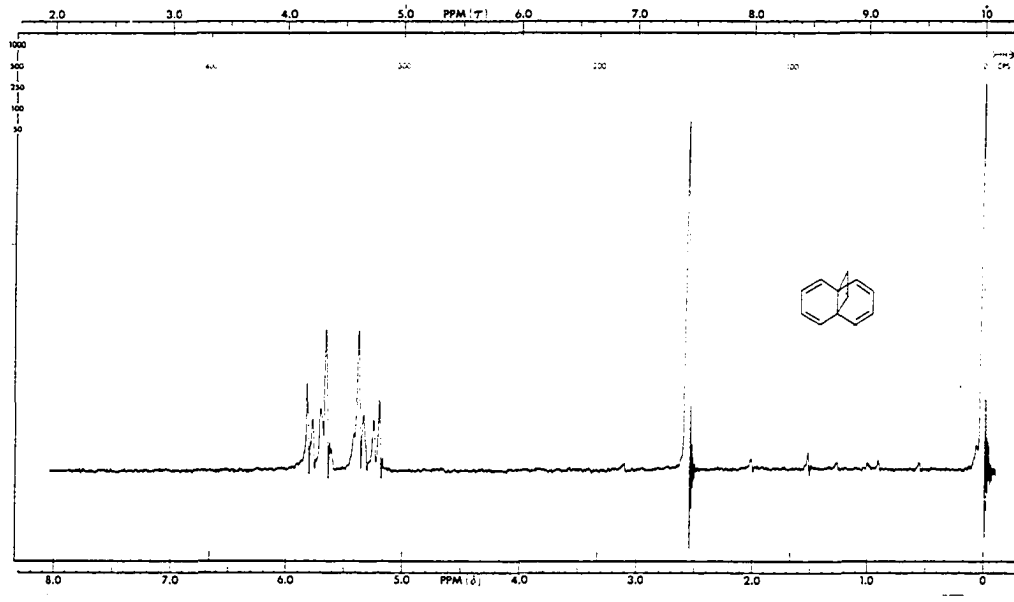
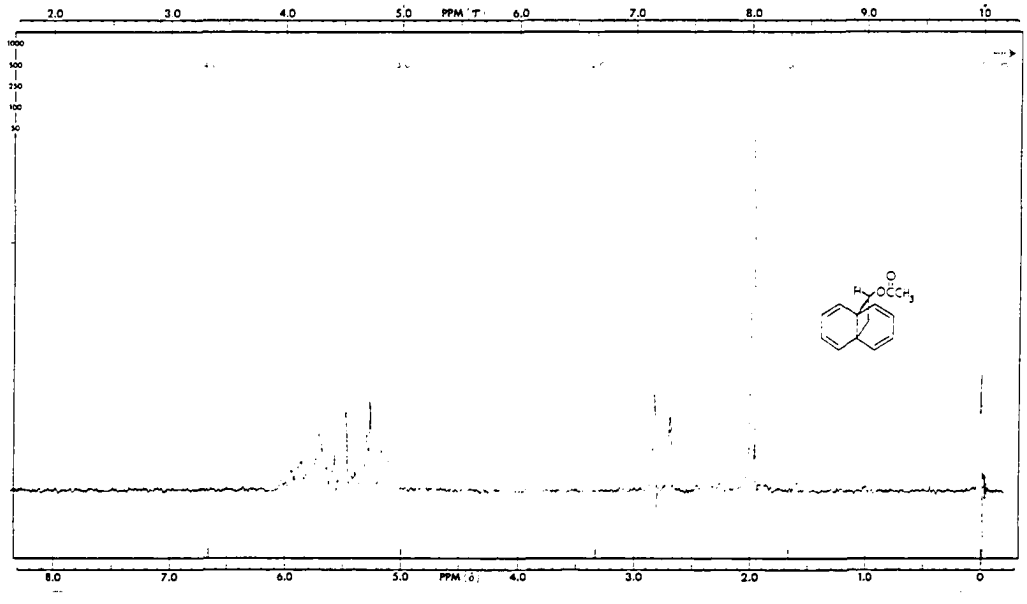


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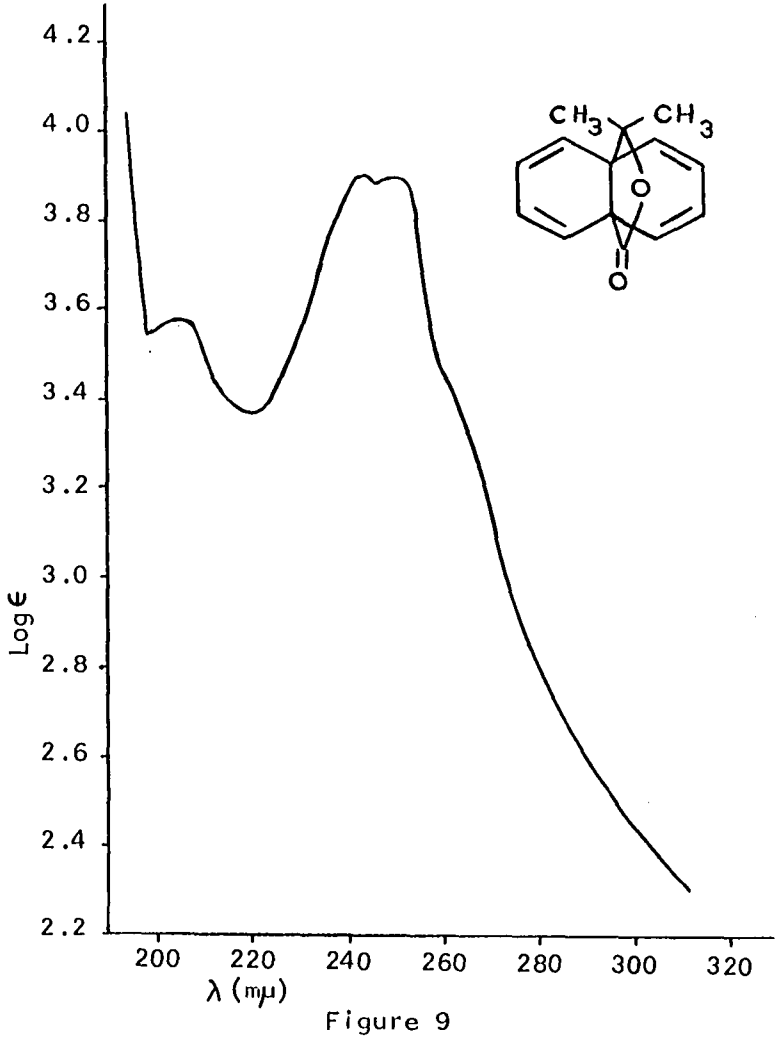


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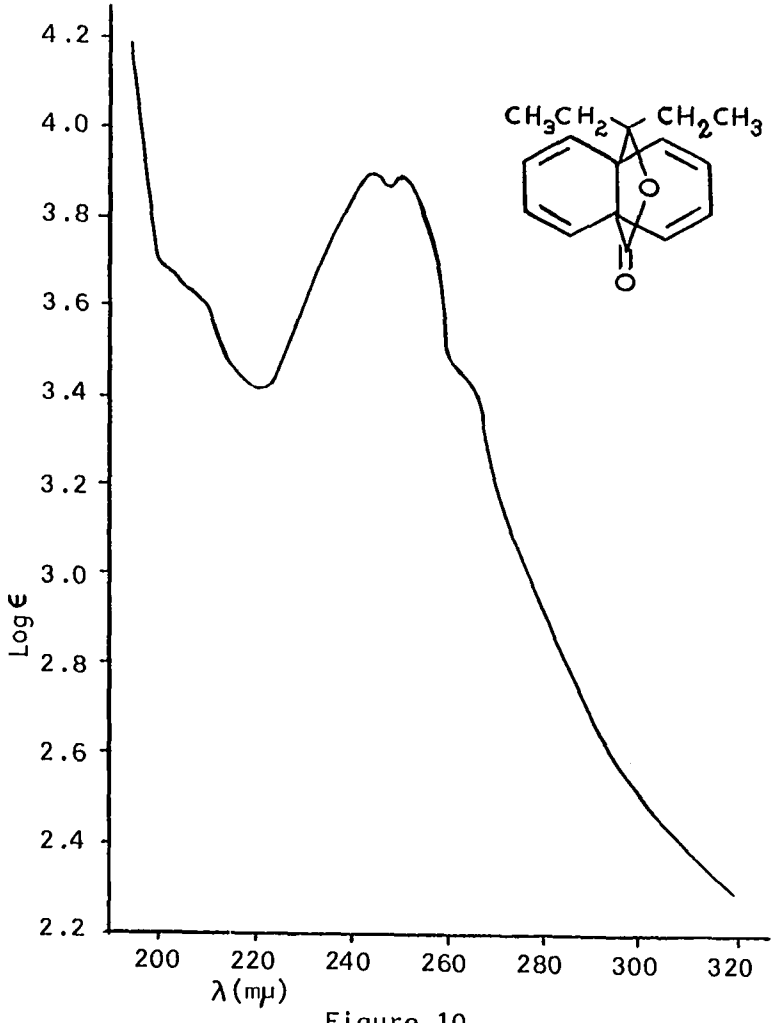


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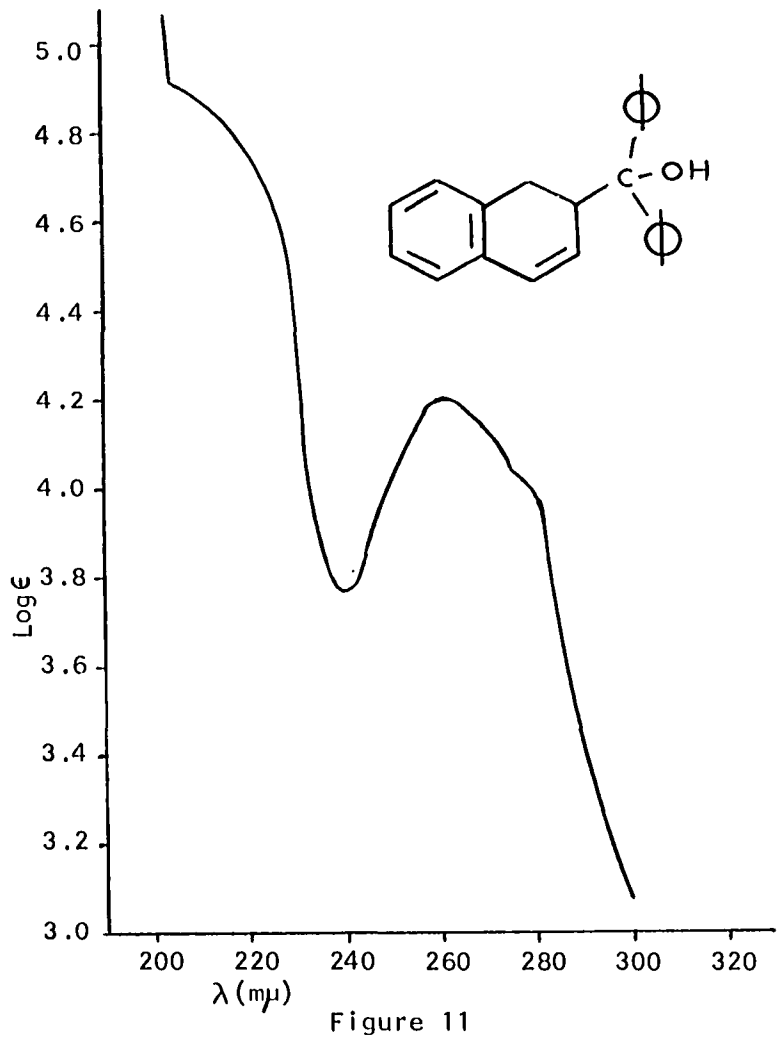


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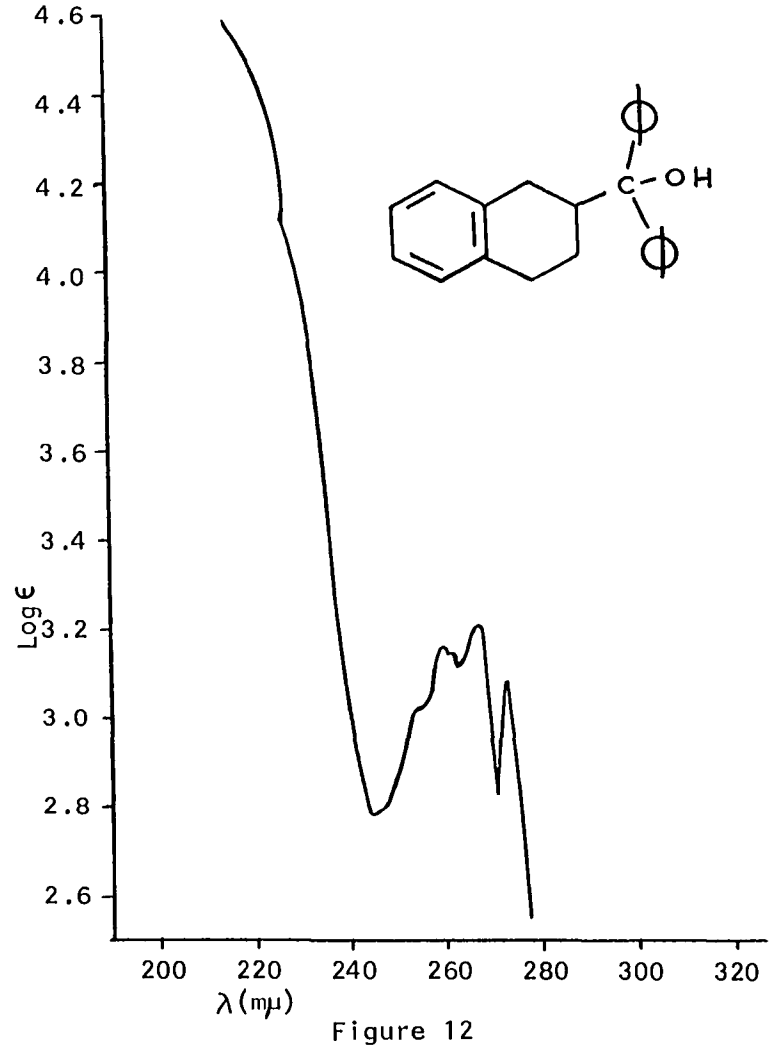


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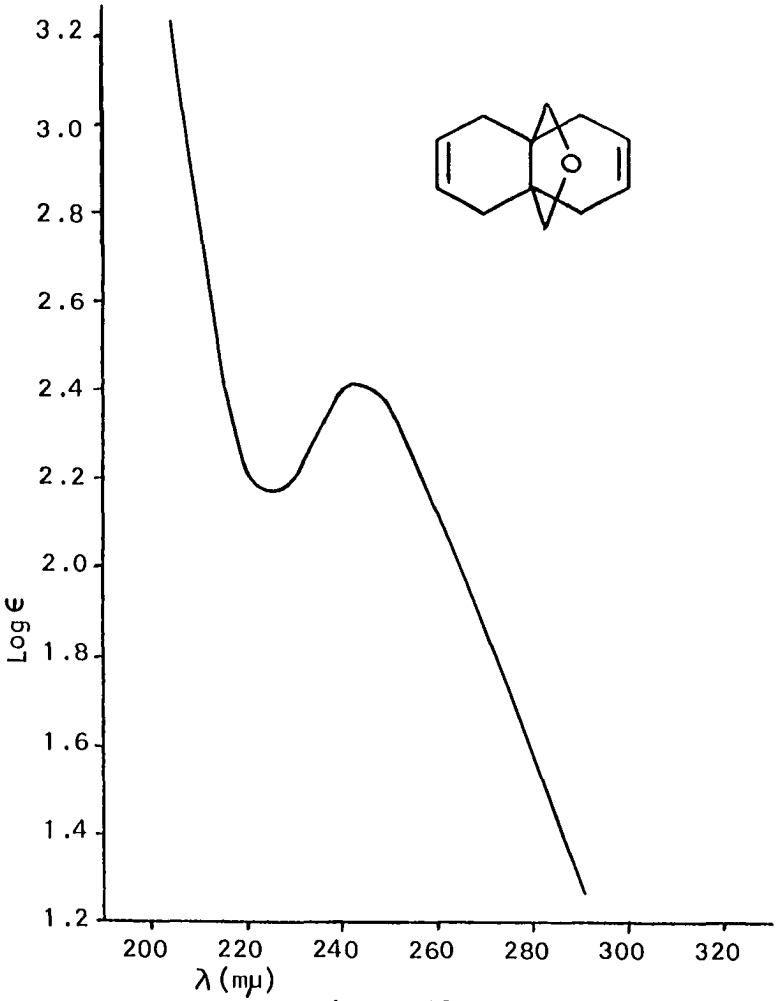


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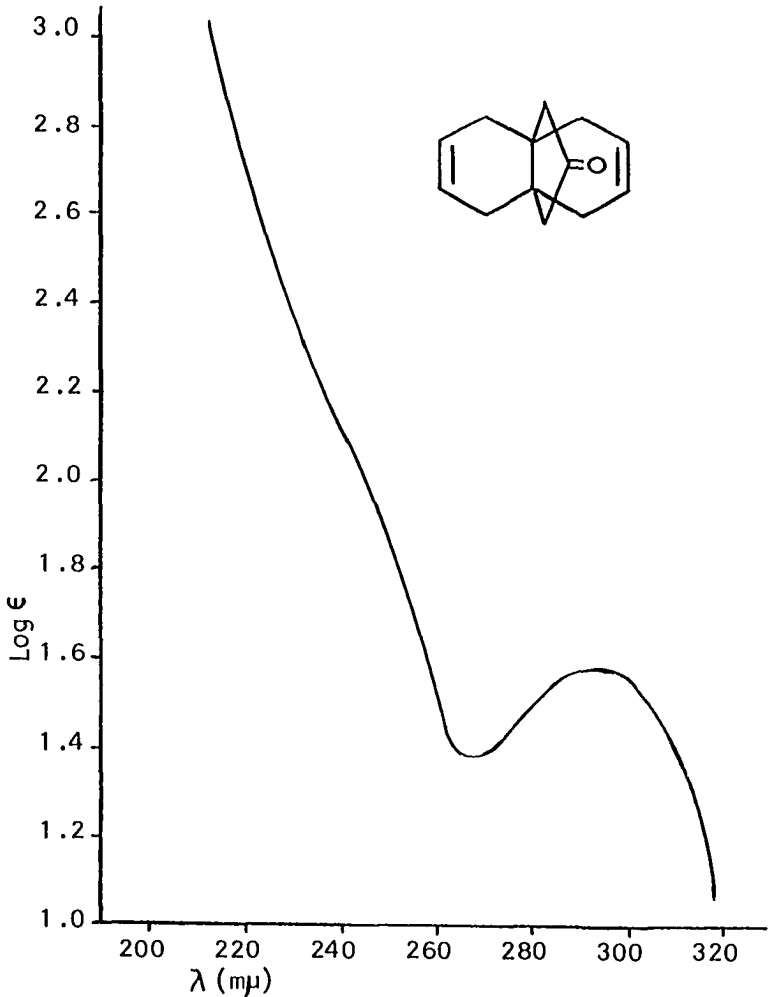


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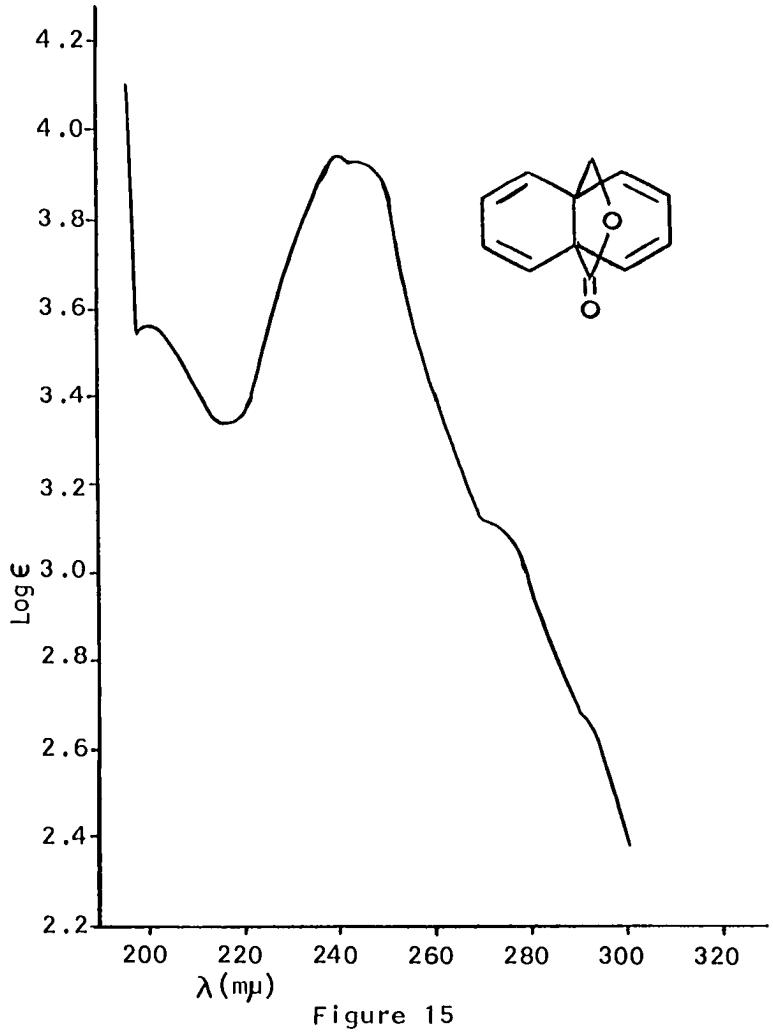


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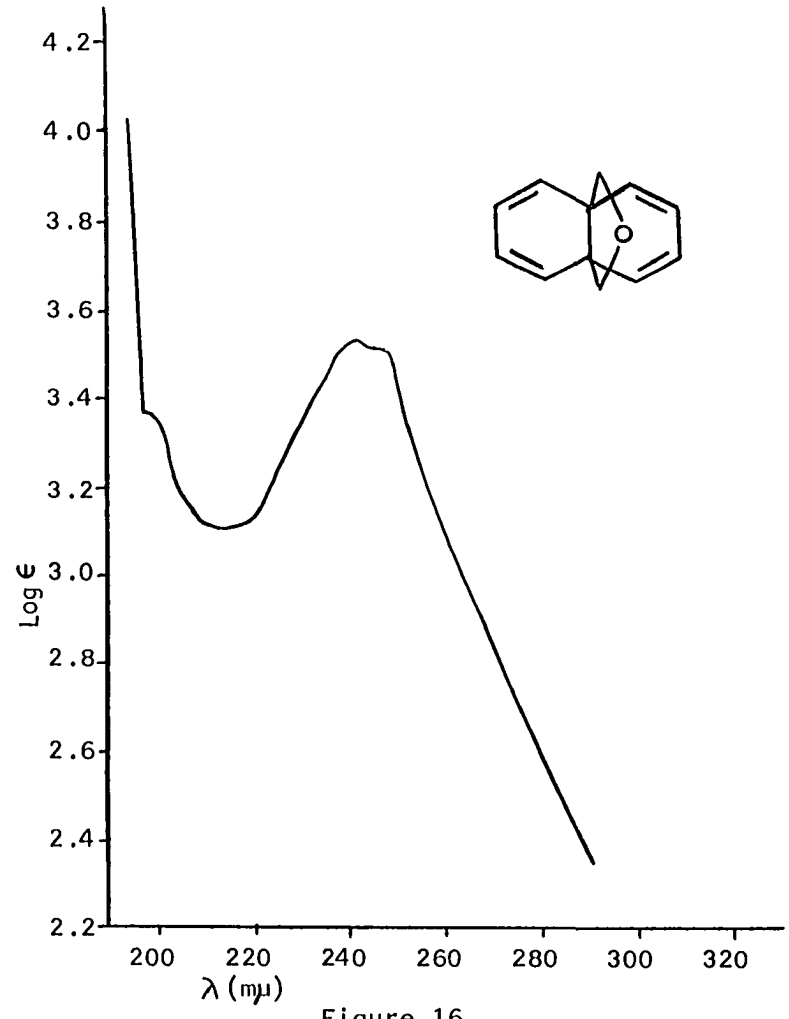


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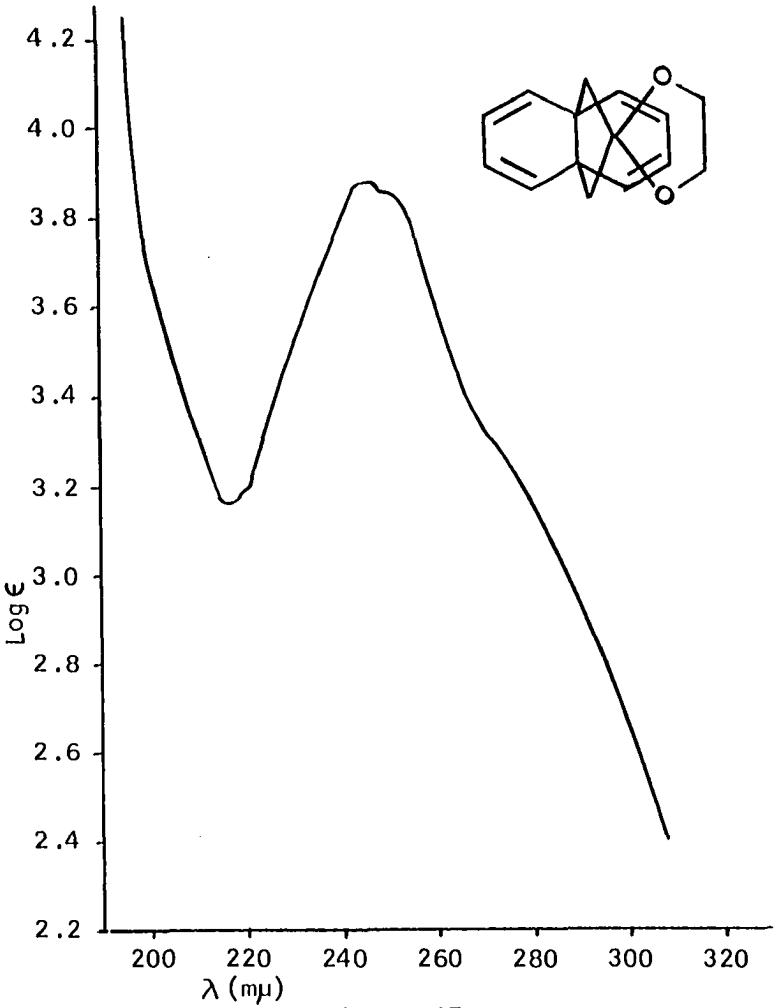


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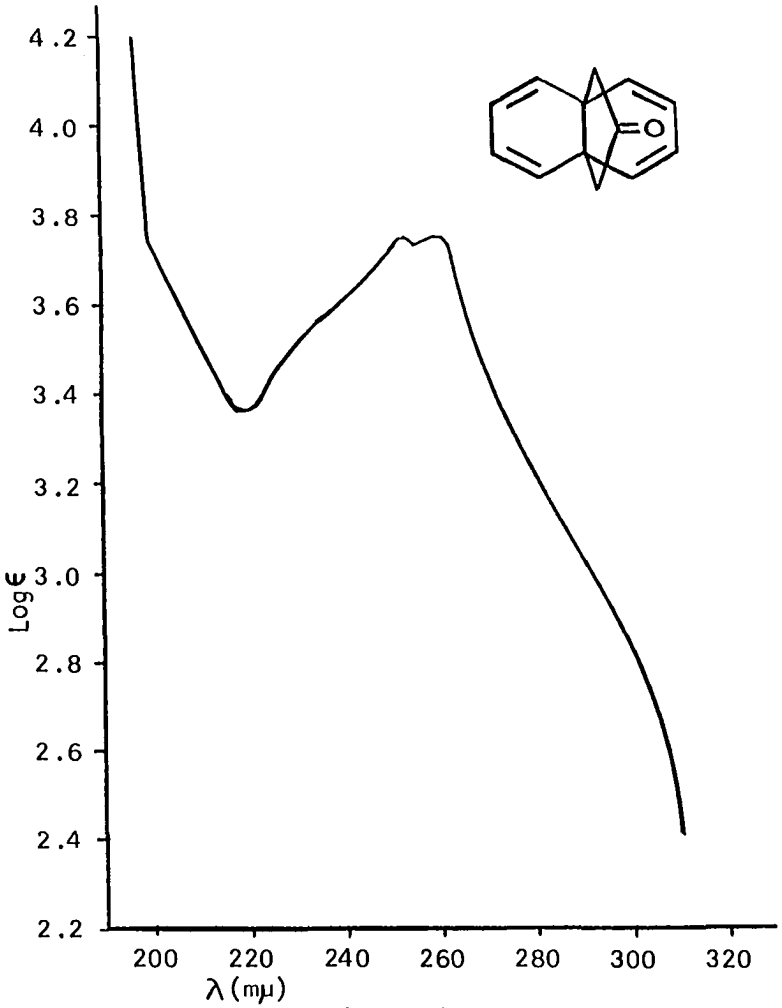


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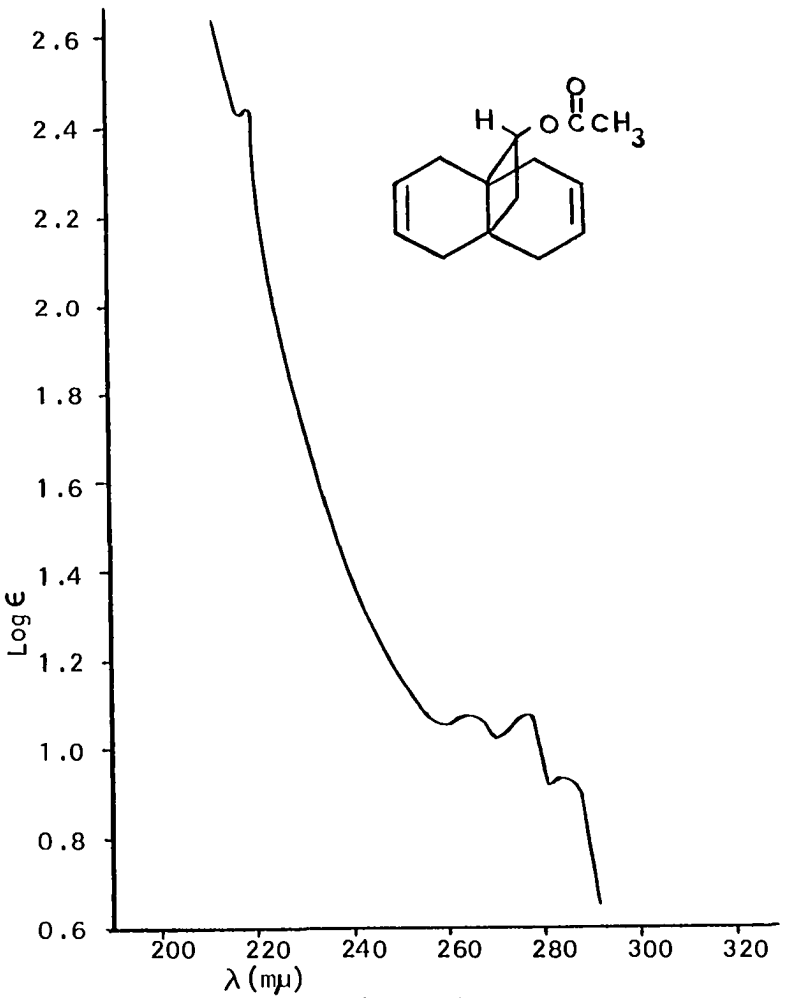


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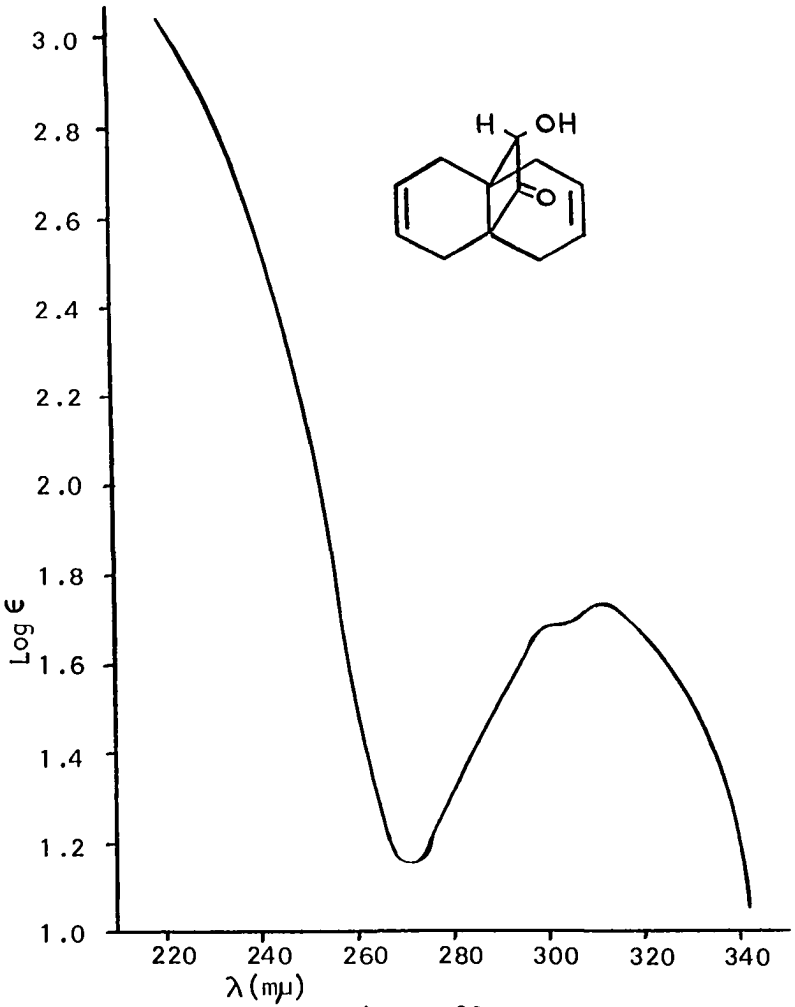


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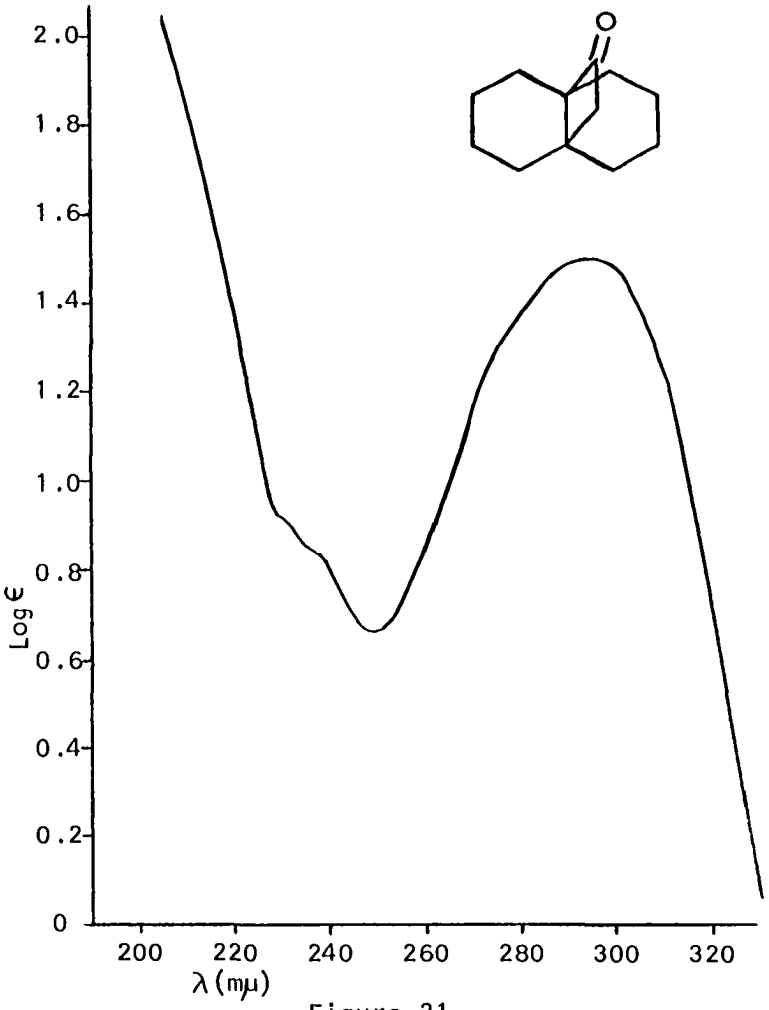


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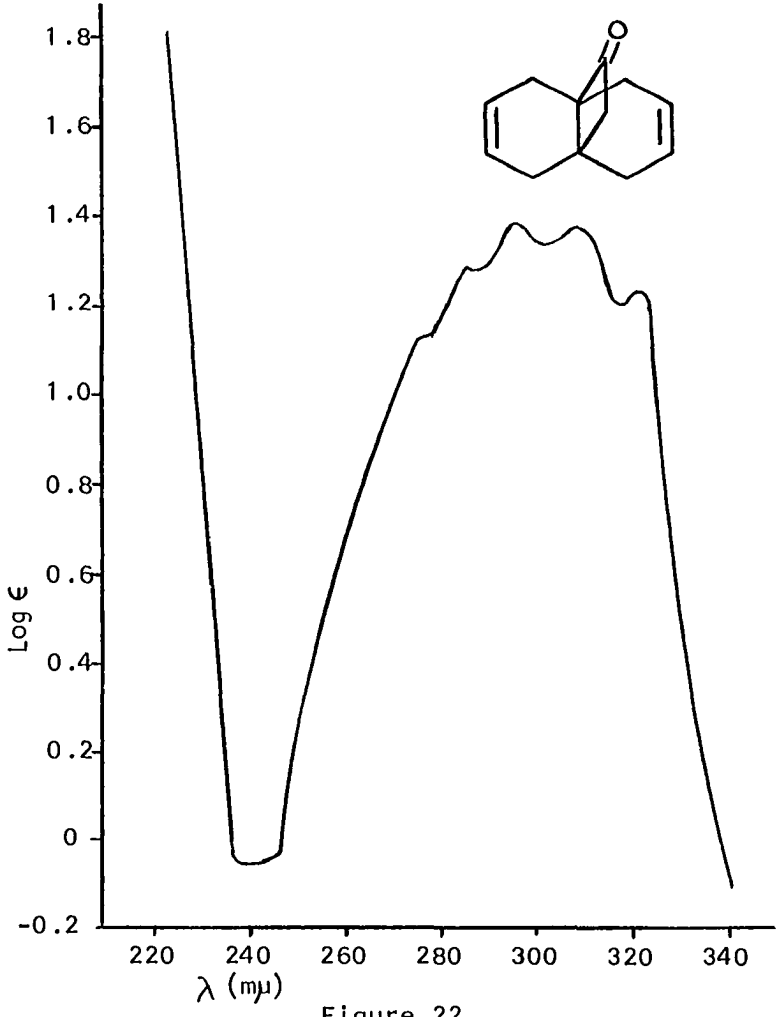


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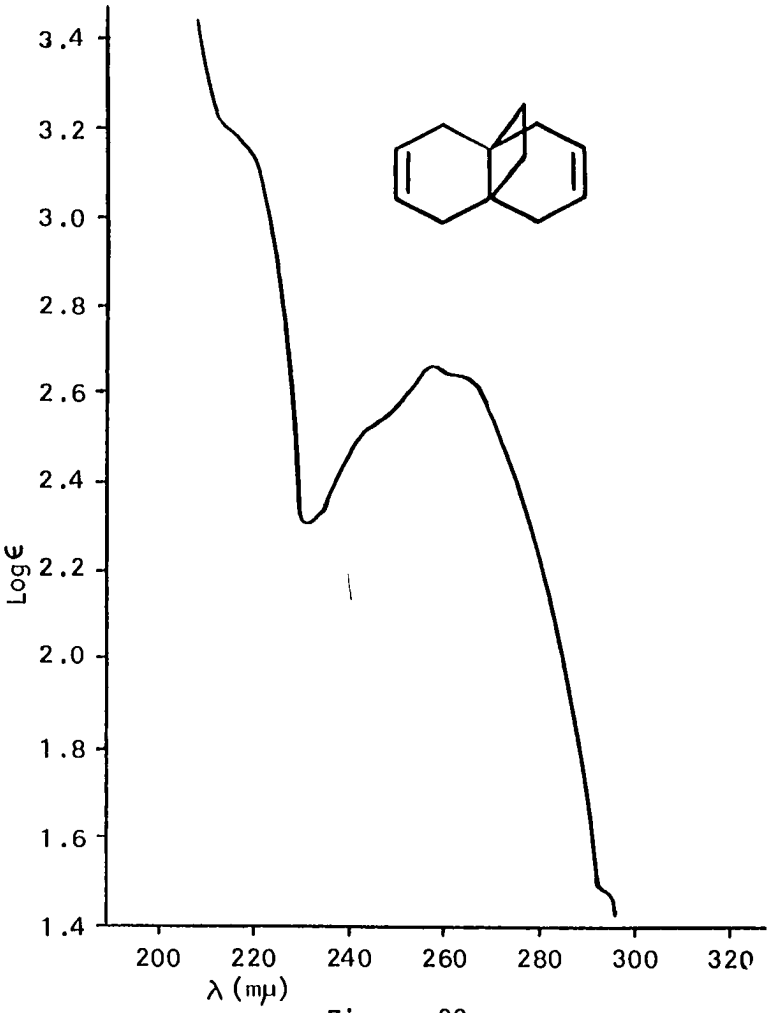


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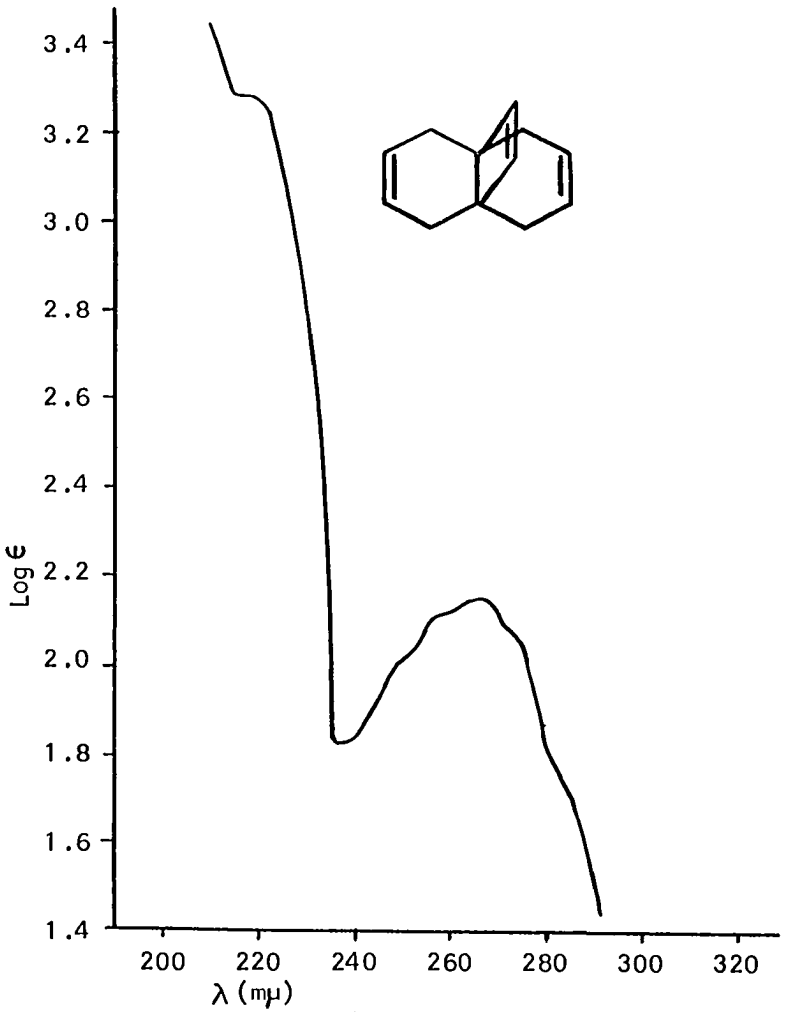


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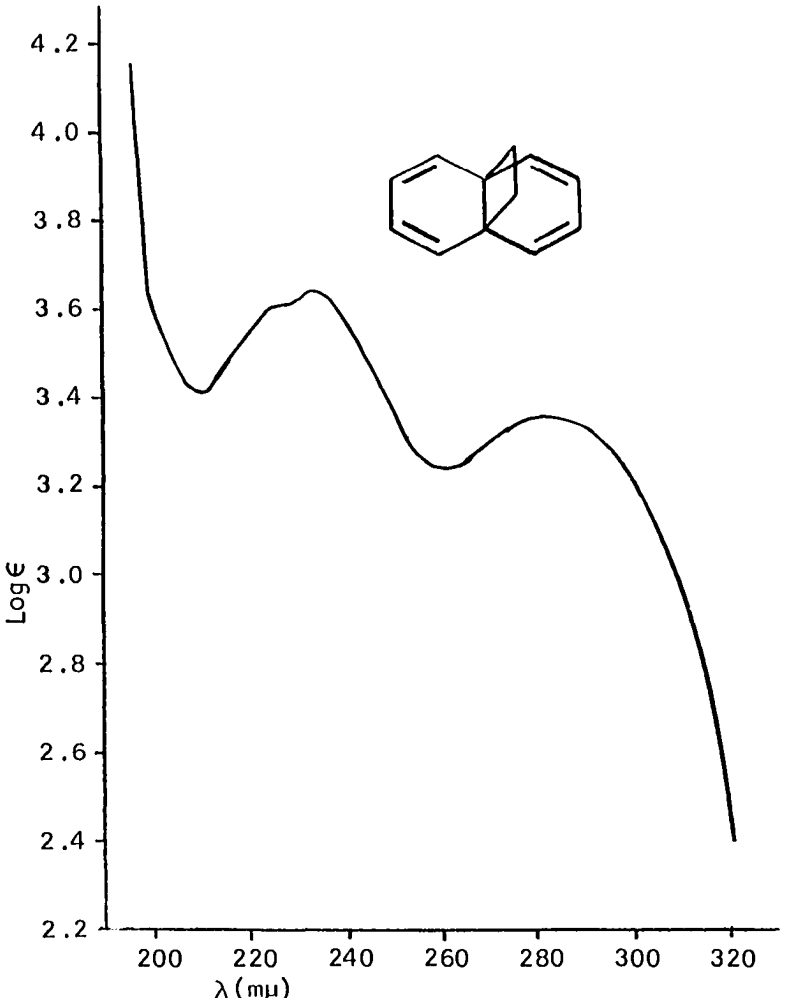


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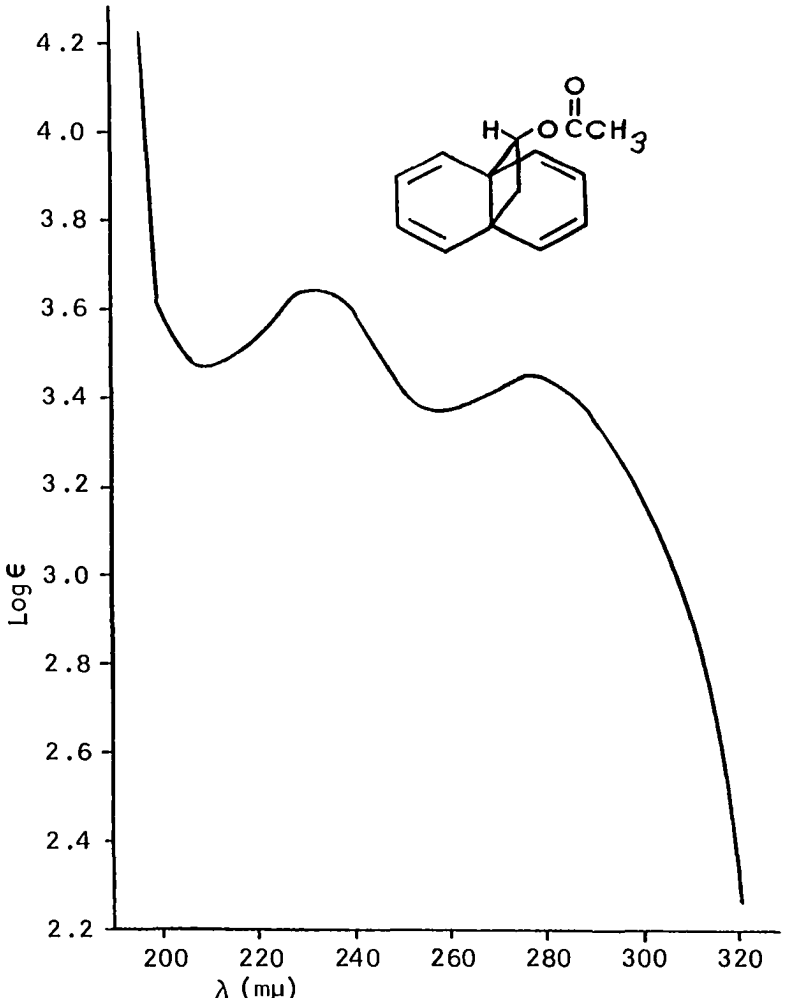


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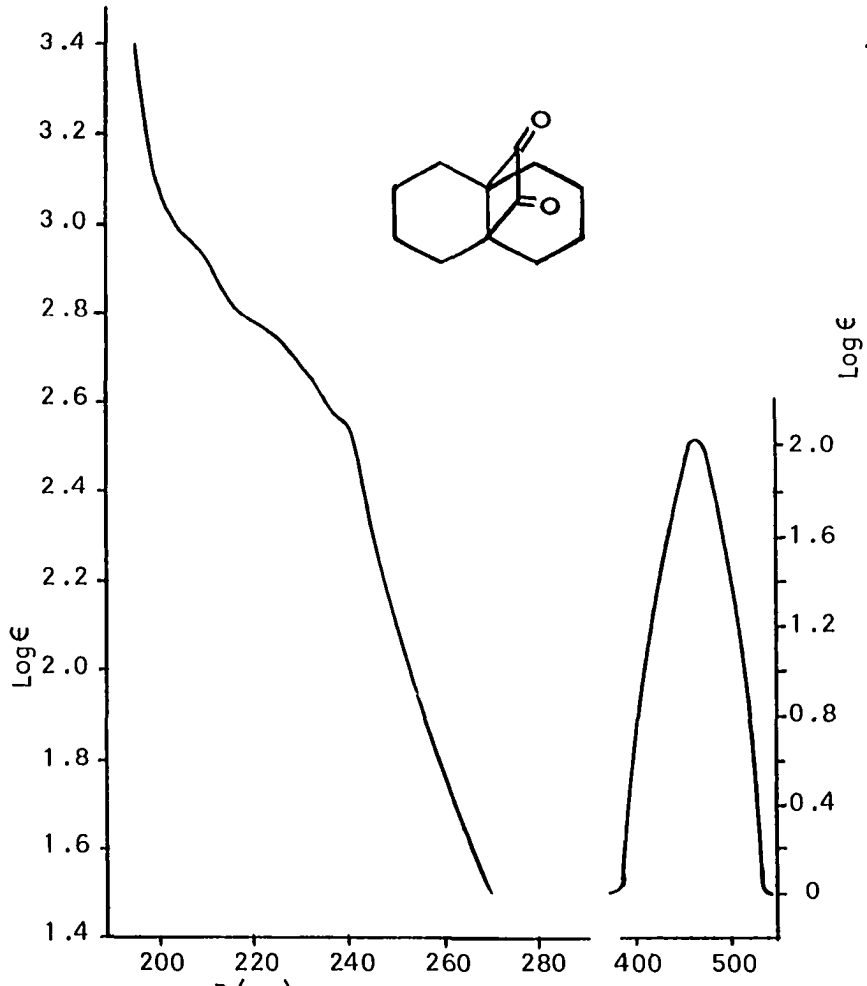


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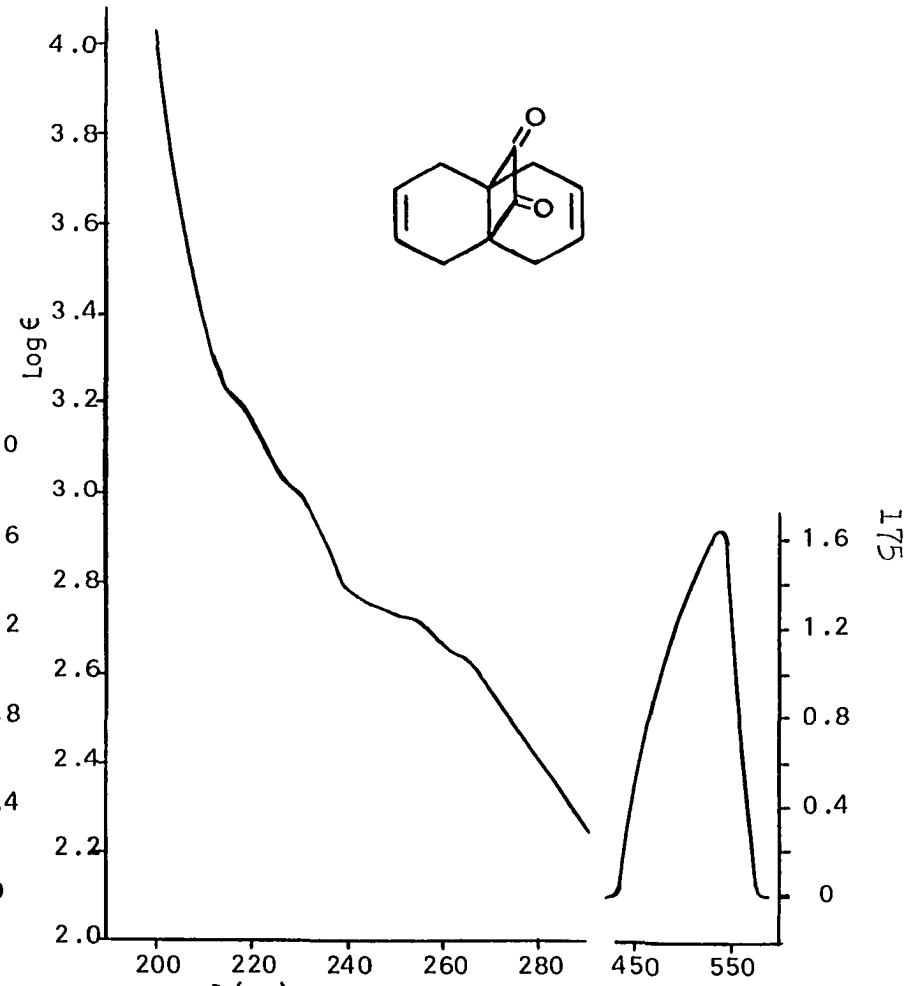


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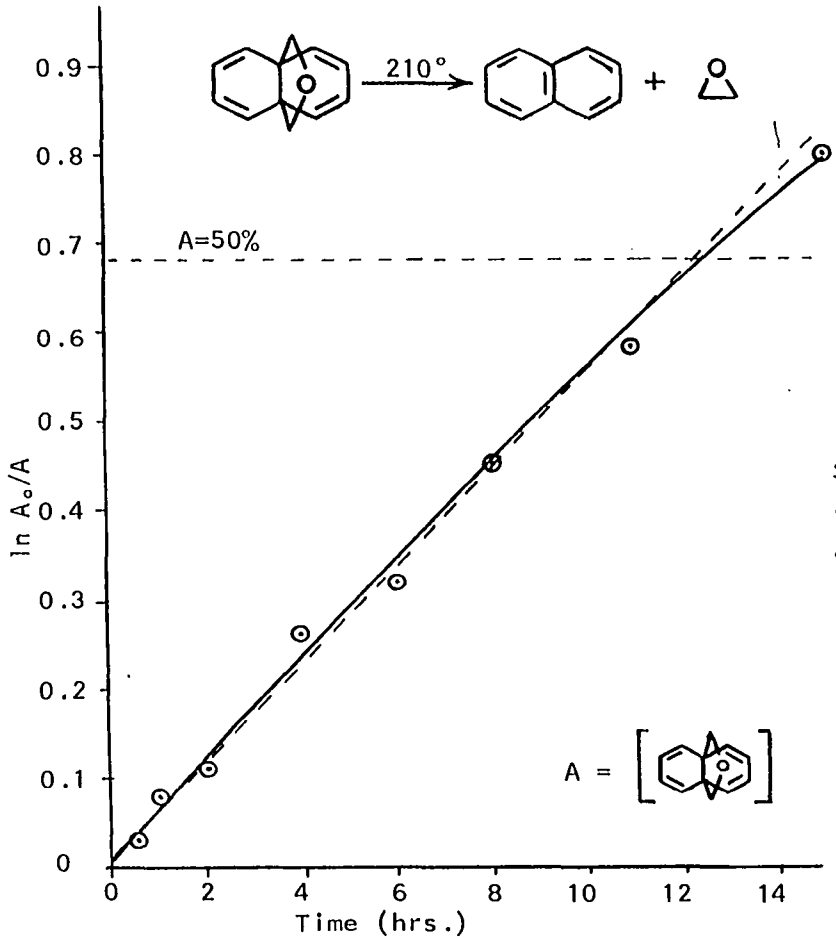


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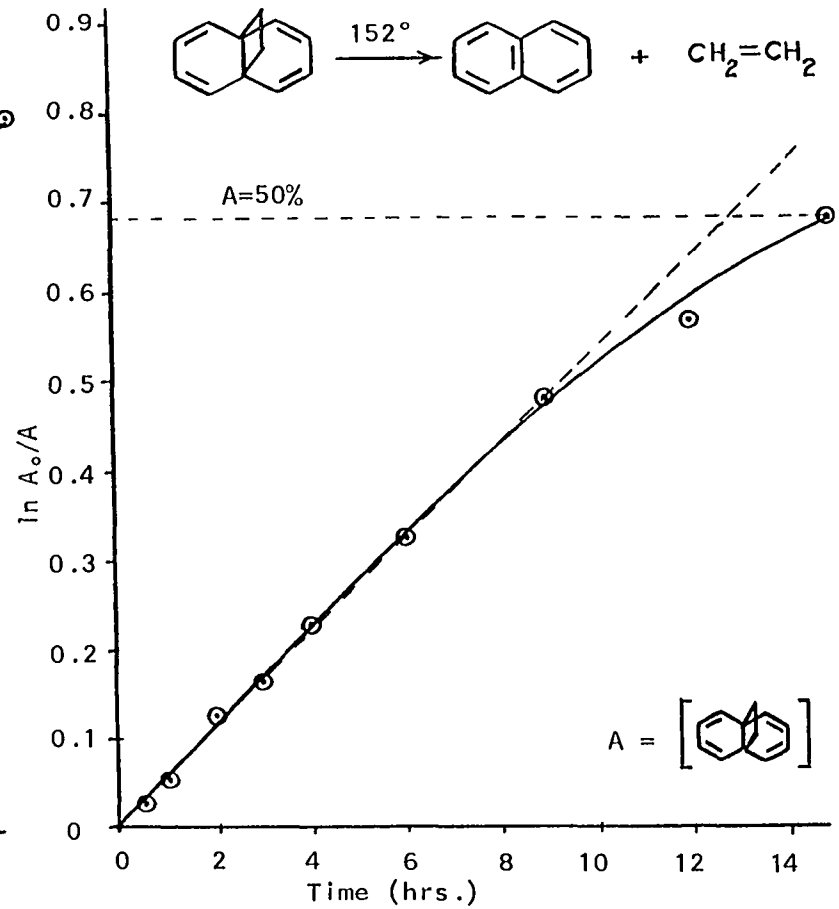


Figure 30