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Synthesis and reactions of 4,5-homotropone and 4,5-dimethylenetropone

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Synthesis and reactions of 4,5-homotropone and 4,5-dimethylenetropone

by

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There is no short cut to a new thing. It must be preceded by long and tedious hours of experimentation and scores of disappointment. The only time you cannot afford to fail is the last time you try.

Charles F. Kettering

PART I. SYNTHESIS AND REACTIONS OF 4,5-HOMOTROPONE

INTRODUCTION

The term "aromatic" as applied to organic compounds was first used in the nineteenth century to describe compounds of aromatic odour isolated from natural oils. The terms 'aromatic' and 'benzenoid' were equated during this time when August Kekulé proposed the well-known cyclic structure for benzene and suggested that the peculiar properties of the aromatic compounds are dependent on the properties of this ring system. He later proposed that benzene has a kind of dynamic structure in which each carbon-carbon bond oscillates between a single and double bond.

Nearly sixty years later, Armit and Robinson expanded the concept of aromaticity by formulating the idea of the 'aromatic sextet' of electrons. But present day understanding of the ideas on aromaticity was developed in the mid-1930's by Hückel who formulated what is now known as the 'Hückel's Rule'. It states that, "amongst fully conjugated planar, monocyclic polyolefins only those possessing $(4n+2)$ π-electrons, where n is an integer, will have special aromatic stability".

The concept of aromaticity is still expanding. Reading the current literature, one is apt to see terms such as 'antiaromaticity', 'non-classical aromaticity', 'bicycloaromaticity', 'antibicycloaromaticity', and 'homoaromaticity'.

Of these terms, homoaromaticity is of special interest in this work.

One of the earlier homoaromatic systems studied was that of the homotropylium cation. Since its observation, much research has been devoted to the synthesis of homoaromatic compounds and ions. In fact, the majority of the homotropylium ions and homotropones discussed in the Literature Review section of this manuscript have appeared during its preparation.

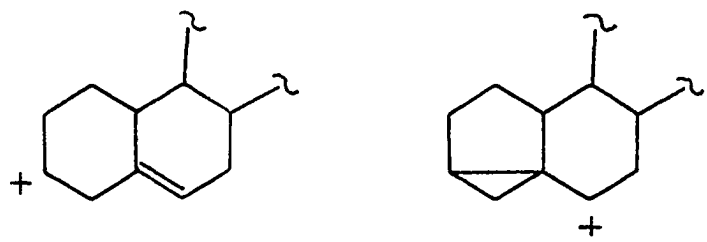
The homotropones are of interest because of their relationship to the parent tropone (cycloheptatrienone) whose unusual properties, specifically its high base strength and unusual chemical reactivity, are attributed to the aromatic tropylium cation. The first homotropone synthesized was the 2,3 isomer prepared in 1963 by Holmes and Pettit (1). 4,5-Homotropone, the other possible homotropone, is of theoretical interest for it contains a homoaromatic system, a cross conjugated ketone, and a cis-divinyl cyclopropane moiety. This latter moiety is known to be subject to Cope rearrangements. In the present case, such a rearrangement would produce a divinyl cyclopropanone.

The approach taken for the synthesis of 4,5-homotropone is based on the observation that base degradation of tropinone methiodide led to a mixture of cycloheptadienones (2). This approach utilizes the plane of symmetry of the

molecule and provides a route to derivatives of scopinone, scopine, and scopolamine in which the oxirane oxygen has been replaced by a methylene group. An added advantage of this procedure is its adaptability for the synthesis of other interesting molecules practically limited only by the dialdehyde precursor and the ingenuity of the investigator.

LITERATURE REVIEW

Homoaromaticity was conceived in the late 1950's and early 1960's as an extrapolation from the terms homoallyl and homoconjugation (3-5). Homoallyl describes a system in which a charge is separated from the site of unsaturation by an intervening carbon atom and homoconjugation is electron delocalization across the intervening carbon atom or atoms. Both these terms were used in conjunction with the cholesteryl-i-cholesteryl cation (6-9). Homoallyl describes the cation

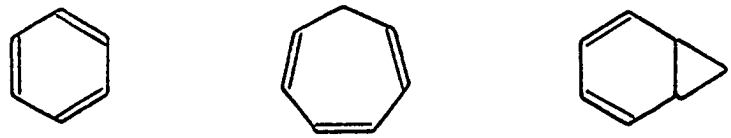


itself and homoconjugation explains the enhanced rates of ionization ascribed to the delocalization of the electron cloud of a neighboring olefinic group in the rate determining step.

Without discussing the merits of various definitions of aromaticity and criteria for detecting and measuring it, suffice it to say that those monocyclic, coplanar, conjugated systems of trigonally hybridized atoms which contain $(4n + 2)$ π-electrons possess relative electronic

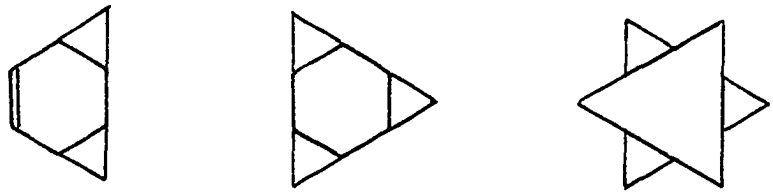
stability. The term aromaticity is thus associated with increased delocalization energy of a substrate relative to an acyclic analogue and with the ability to sustain an induced ring current.

Homoaromaticity is also associated with the ability to sustain an induced ring current. The distinction lies in how the (4n + 2) rule is satisfied as well as how the conjugation is obtained. For homoaromatic compounds a cyclopropane ring can replace an olefinic bond in which case the two electrons in one of the cyclopropane ring bonds are counted as two π-electrons and/or the system is homoconjugated. For example, consider the aromatic system benzene and two possible monohomobenzenes,



cycloheptatriene and norcaradiene. Cycloheptatriene involves homoconjugation or conjugation past an intervening carbon and norcaradiene involves substitution of a cyclopropane ring for an olefinic bond.

As might be anticipated from the prefix mono used above, there are a variety of homoaromatic systems, e.g.,

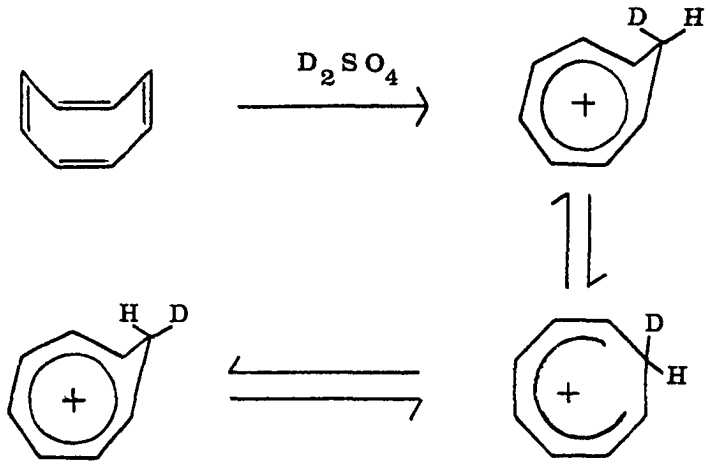


bishomobenzene, trishomobenzene, and even hexahomobenzene.

The terminology, however, is not limited to benzene but is applicable to homocyclopropenylcations (1,3-bishomocyclopropenyl cation), homocyclopentadienide anions

(1,3-bishomocyclopentadienide anion), homocyclooctatetraene, homotropylium cations (1,2-bishomotropylium cation), etc.

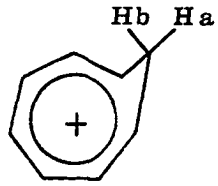
Relatively recent work has established that the $C_8H_8^+$ ion which is generated by protonation of cyclooctatetraene (COT) in concentrated sulfuric acid is a monohomotropylium cation (10). Furthermore, in dideuterio sulfuric acid there was observed considerable stereospecificity in the protonation, the deuterium ion approaching preferentially from inside the fold of the tub conformation, possibly due to the greater electron density on that surface producing the endo deuterio compound. The deuterium equilibration between



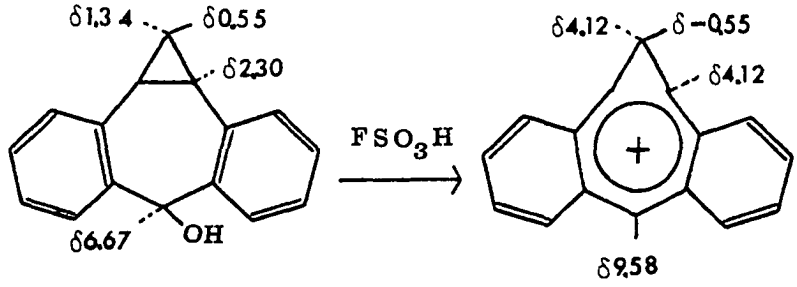
endo and exo position was visualized as proceeding by ring inversion through the planar classical cyclooctatrienyl cation. The free energy of this species was shown to be 22.3 kcal/mole higher than that of the homoaromatic monohomotropylium ion (11).

Several substituted homotropylium cations have been prepared and their nuclear magnetic resonance (nmr) spectra

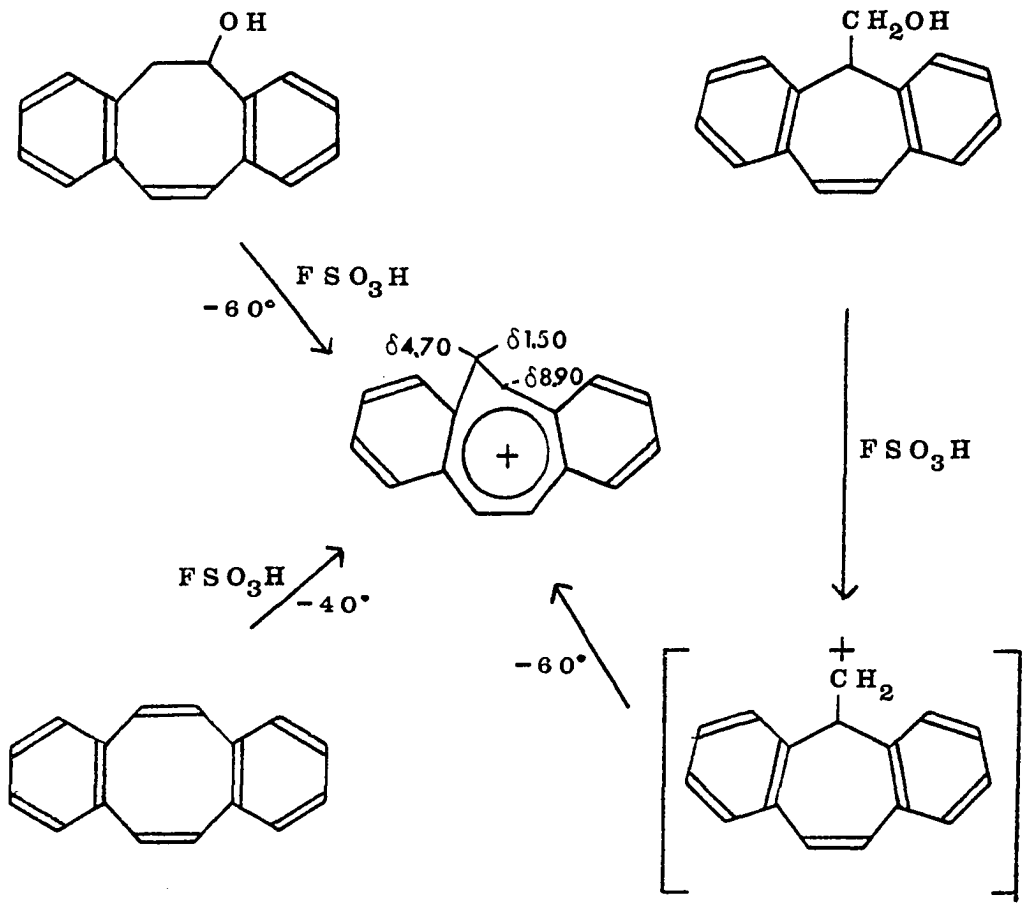
recorded. A striking difference in chemical shift between the exo and endo (Ha and Hb) methylene protons is observed. This shift is due to the marked anistropy of the diamagnetic ring current. For example, if the difference between the exo and endo hydrogens (Ha and Hb) expressed in ppm is equal to Δ, it is observed that protonation of COT produced a



homotropylium cation with Δ = 5.8, methylCOT (12) Δ = 5.0, cyclooctatrienone (10) Δ = 3.1, 2,3-homotropone (1) Δ = 3.1, and benzoCOT (13) Δ = 3.9. In addition, two different dibenzohomotropylium ions have been prepared. Childs and Winstein (14) prepared a dibenzohomocycloheptadienol which when treated with fluorosulfonic acid produced a dibenzohomotropylium cation with a Δ = 4.7. A different

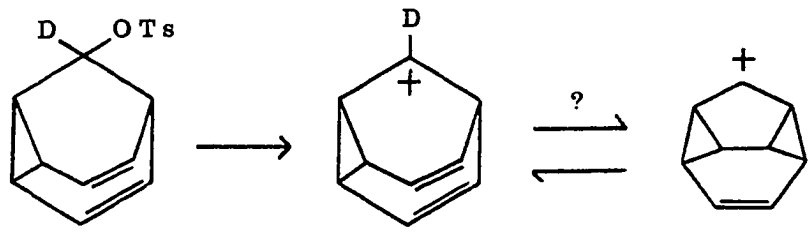


dibenzohomotropylium cation was generated from three different precursors. In each case the same stable homotropylium



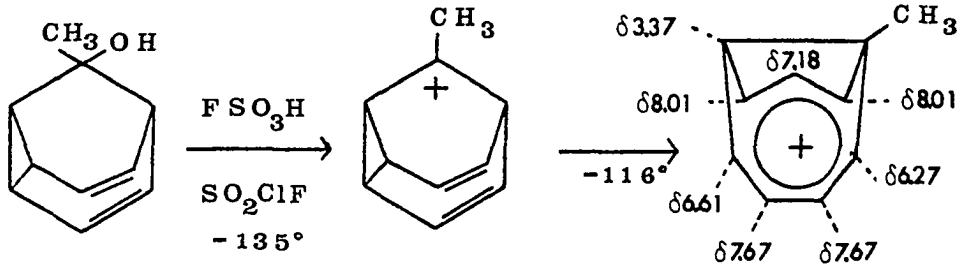
was observed with a $\Delta = 3.2$ (15).

The possible intermediacy of a bishomotropylium cation was suggested in order to explain the extension deuterium



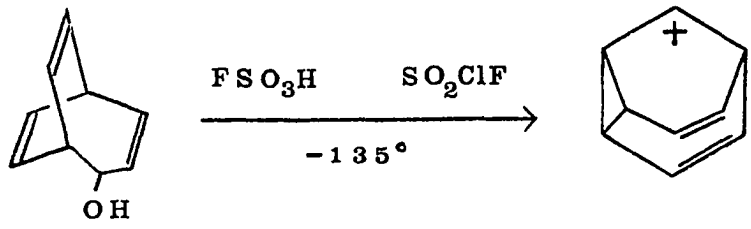
scrambling in the solvolysis products of the 9-D-barbaralyl tosylate (16).

Shortly thereafter, data on the 9-methyl-9-barbaralyl cations was reported (17). When 9-methyltricyclo-[3.3.1.$0^{2,8}$]nona-3,6-dien-9-ol was treated at 135° with a 1:3 mixture of fluorosulfonic acid and fluorosulfinyl-chloride (super acid), the 9-methyl-9-barbaralyl cation was observed. This cation rearranged exclusively at -116° to the 1-methylbicyclo[4.3.0]nonatrienyl cation, a 1,4-bis-

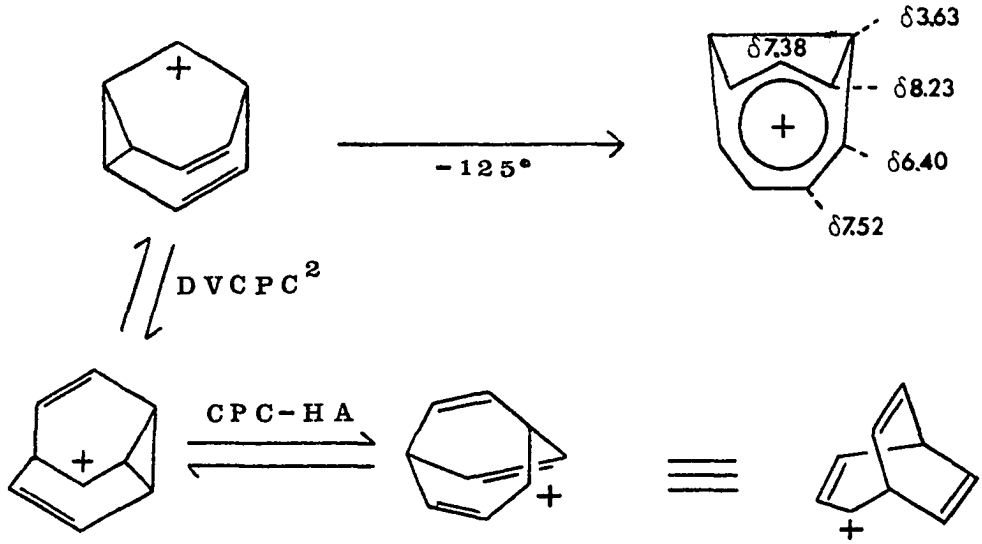


homotropylium cation. The structure was established on the basis of coupling constants obtained by double irradiation experiments and evidence for delocalization of charge as indicated by the deshielding of the seven peripheral protons.

Later the totally degenerate 9-barbaralyl cation and the bicyclo[4.3.0]nona-trienyl cation were reported (18). When bicyclo[3.2.2]nona-3,6,8-trien-2-ol

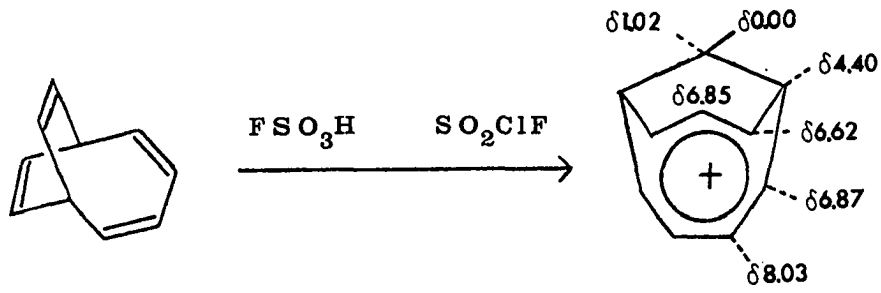


was treated with super acid at -135°, a sharp singlet at δ 6.59 was observed which indicated the cation was undergoing very rapid degenerate rearrangements. In order to explain this total degeneracy, both divinylcyclopropylcarbinyl--divinylcyclopropylcarbinyl (DVCPC^2) rearrangements and cyclopropylcarbinyl-homoallyl (CPC-HA) rearrangements were invoked. The totally degenerate cation underwent ready



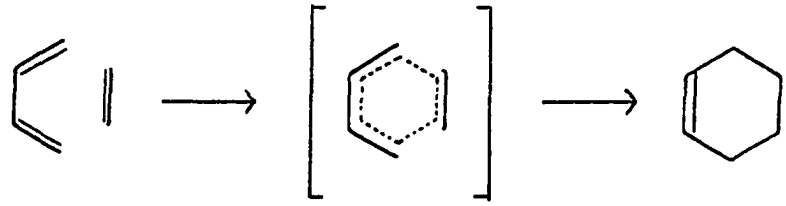
conversion at -125° to the more stable bishomoaromatic cation, the bicyclo[4.3.0]nonatrienyl cation.

Still another 1,4-bishomotropylium cation, the bicyclo[4.3.1]deca-2,4,7-trienyl cation, was observed by

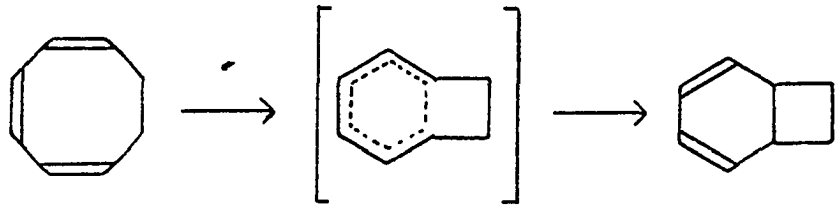


treating bicyclo[4.2.2]deca-2,4,7,9-tetraene with super acid. With this bishomotropylium cation both the deshielding of the peripheral hydrogens as well as the shielding of the methylene hydrogens which are situated directly above the ring were observed (19).

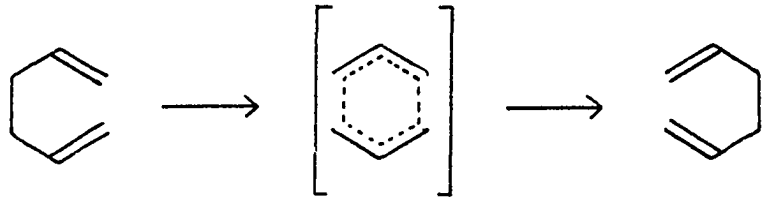
Winstein has once pointed out that the general concepts and terminology of homoaromaticity can be applied to transition states as well as ground states (20). For example, the transition state for the Diels-Alder reaction may be characterized as a 1,3-bishomobenzene type, the valence



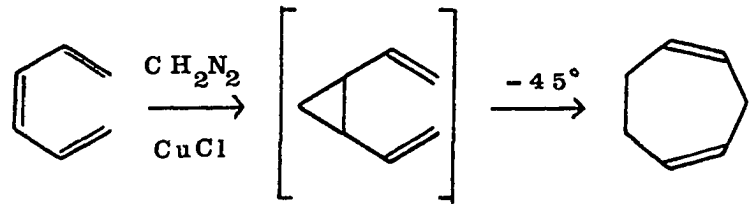
tautomerism between cycloocta-1,3,5-triene and bicyclo-[4.2.0]octa-2,4-diene as a monohomobenzene type, and finally



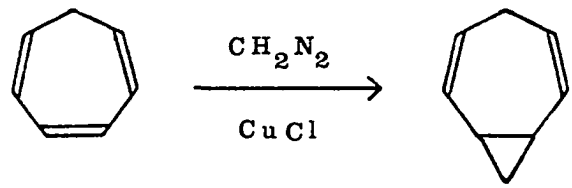
the Cope rearrangement as a 1,4-bishomobenzene type transition state.



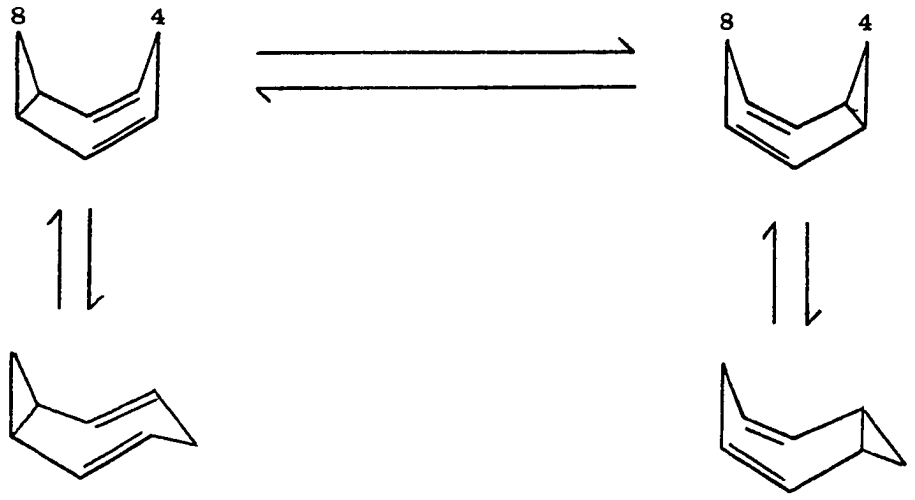
One of the more frequently studied Cope rearrangements is that involving cis-divinylcyclopropanes. The last decade has seen intense investigation of this type of rearrangement. In 1963, Doering and Roth (21) found that the addition of methylene, prepared from diazomethane and cuprous chloride, to cis-1,3,5-hexatriene at -45° yielded only 1,4-cycloheptadiene and its addition products. It



was concluded that the presumed cis-divinylcyclopropane was unstable at this temperature and rearranged to give the observed product. These same authors (22) reacted cycloheptatriene with methylene and one of the isolable products

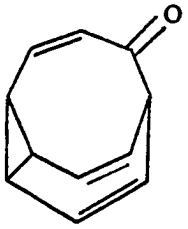


was bicyclo[5.1.0]octa-2,5-diene or homotroplidene. The molecule was unique in that a Cope rearrangement of the cis-divinylcyclopropane would reproduce itself. The temperature dependence of the homotroplidene nmr spectrum demonstrated a fast and reversible valence isomerization. The dynamic equilibrium between the two valence isomeric structures was superimposed on the equilibrium between two

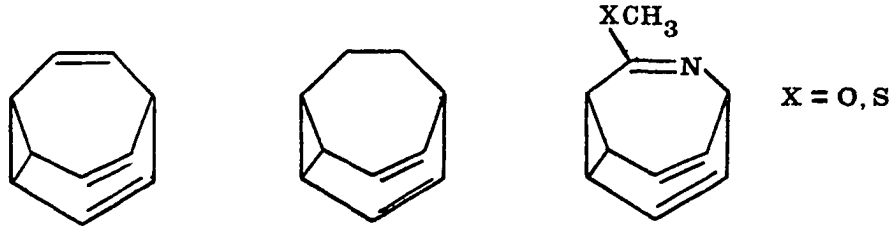


conformations. The authors suggested that a two carbon atom bridge between atoms 4 and 8 would eliminate this complicating factor and would enable thermodynamic data for this degenerate Cope rearrangement to be obtained.

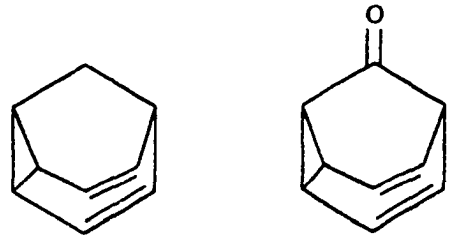
This suggestion catalyzed extensive research and presently several such bridged molecules are known. Compounds with a three carbon atom bridge like homobullvalenone (23),



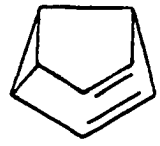
compounds with a two atom bridge as bullvalene (24),



dihydrobullvalene (25), and azabullvalene (26,27), compounds with a one carbon atom bridge such as barbaralane (28,29)



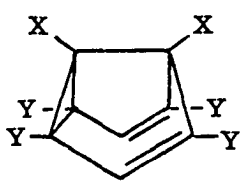
and barbaralone (30), and even a zero atom bridge as semi-bullvalene (31) have been prepared and studied. With the



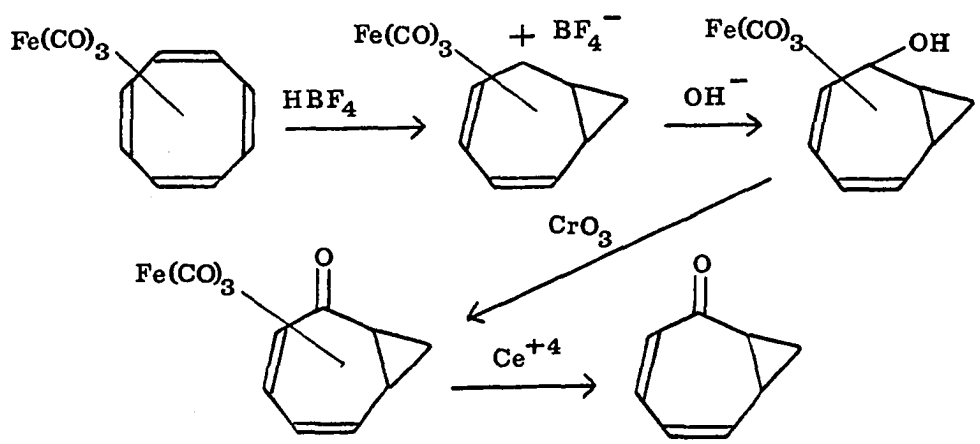
exceptions of azabullvalene and homobullvalenone, which have been shown as the preferred tautomer, all the molecules indicated exhibit degenerate Cope rearrangements. The

energies of activation for these Cope reactions have been measured and are in the range of 6.5 to 14 kcal/mole.

Recently, Hoffmann and Stohrer (32) have investigated the Cope rearrangement using extended Hückel calculations in order to design a molecule substituted in such a manner that its Cope rearrangement cannot be frozen out. The analysis focused on semibullvalene since the activation energy for this degenerage Cope reaction is the lowest recorded. It was concluded that the most likely candidate has the substitution pattern shown where X is a π-electron donor and Y is a π-electron acceptor.



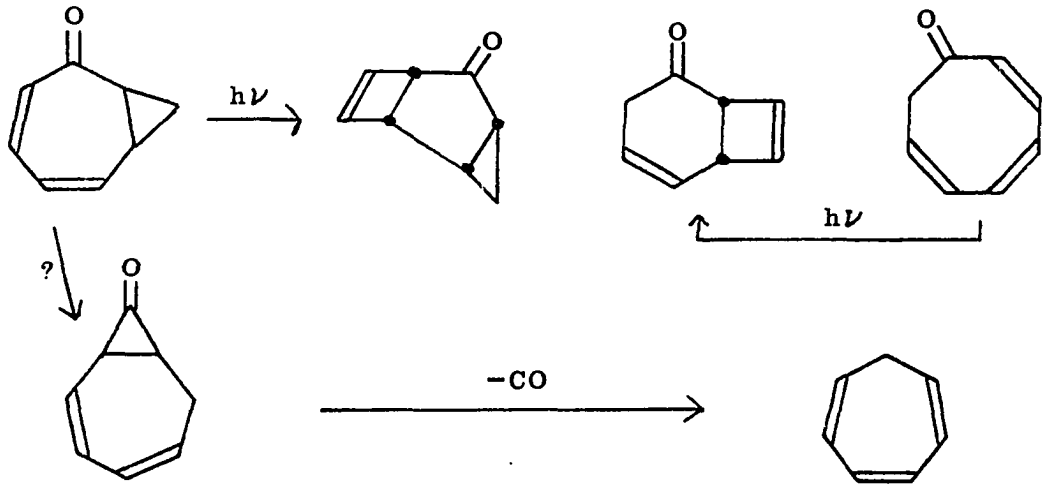
2,3-Homotropone was prepared by Holmes and Pettit (1) in 1963 utilizing an iron tricarbonyl complex of cycloocta-



tetraene. 2,3-Homotropone was found to be a stable pale

yellow liquid. Its basicity was measured using a spectrophotometric method and found to have a $pK_{BH^+} = -2.8$. It formed a stable hexachloroantimonate salt although crystalline hydrogen halide salts could not be isolated. Protonation, vida supra, produced a stable homotropylium cation. It was concluded that the cyclopropane ring did permit delocalization but decidedly less than that of an olefinic bond.

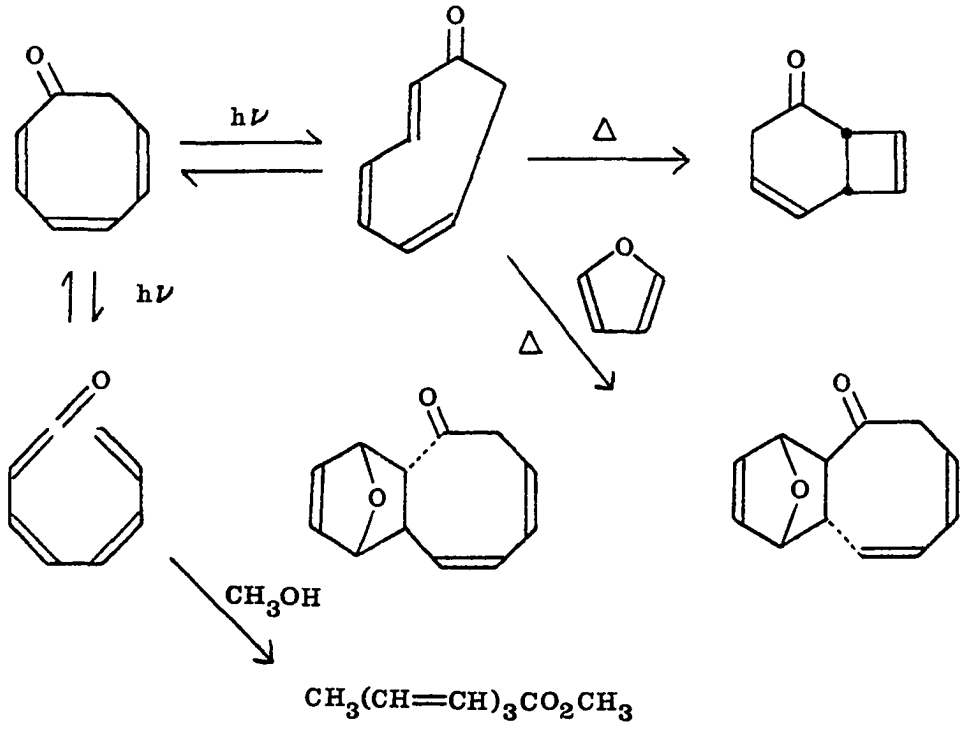
In 1967, Paquette and Cox (33) investigated the photochemical behavior of 2,3-homotropone. Irradition in dilute solution at room temperature led to a variety of products.



The stereospecific formation of a lone tricyclic valence isomer, although two disrotatory modes of cyclization are possible, was rationalized on the basis of secondary steric forces operative during bond reorganization. Bicyclo[4.2.0]-octadienone was shown to be a secondary photoproduct derived

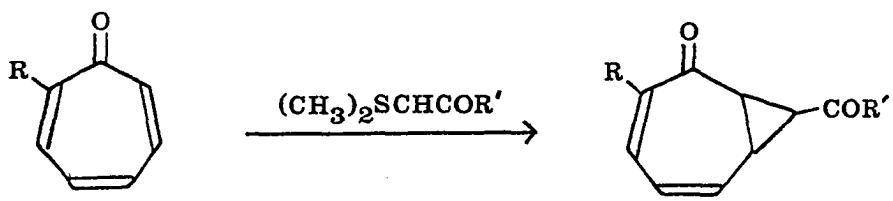
from cyclooctatrienone. One suggested mechanism for the production of tropylidene was a valence bond rearrangement to a cyclopropanone derivative and subsequent loss of carbon monoxide.

In 1962, Büchi and Burgess (34) reported that irradiation of cyclooctatrienone in methanol gave a mixture of methyl octatrienoates whereas irradiation in pentane gave only a bicyclic isomer. It was recently shown, by low temperature infrared studies, that the esters are formed from a ground state ketene intermediate, and the bicyclic isomer is formed from ground state trans,cis,cis-2,4,6-cyclooctatrienone in a thermal cycloaddition (35). The position of the trans olefinic bond was established by trapping the

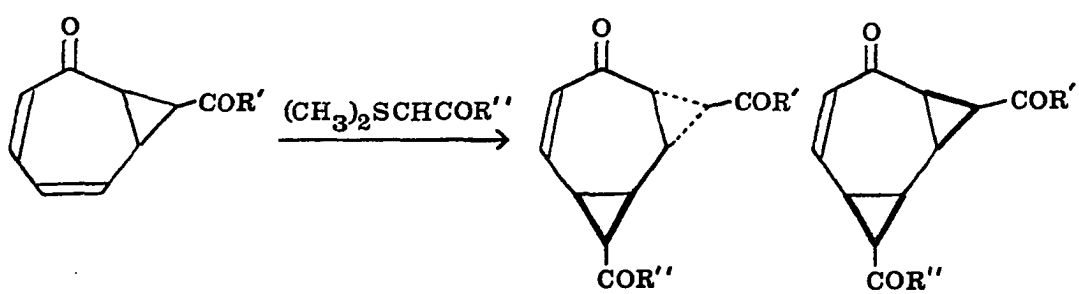


intermediate with furan to give two Diels-Alder adducts with trans ring fusions. Thus, the trans enone is capable not only of an intermolecular 4 + 2 cycloaddition similar to those of trans-cycloheptenone (36,37) and trans-cyclooctenone (38), but also an intramolecular 2 + 2 cycloaddition to give the bicyclic isomer.

Recently, several 2,3-homotropones have been prepared in yields ranging from 30 to 80 per cent by treatment of tropone or tropone derivatives with substituted sulfonium

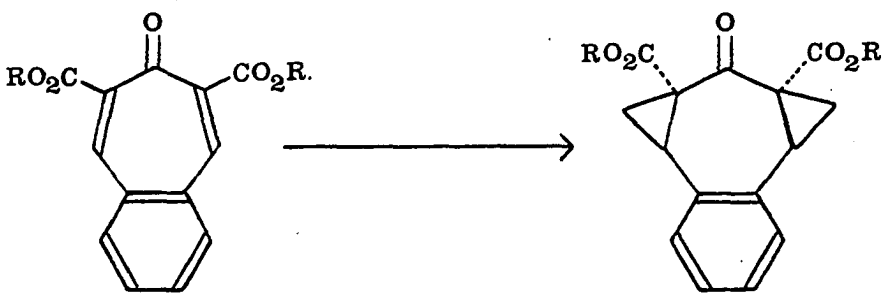


ylides. The substituted 2,3:4,5-bishomotropones were also prepared from either the monohomotropones or directly from the tropones. In most cases the bis adducts have the cyclo-



propane rings anti with respect to each other (39).

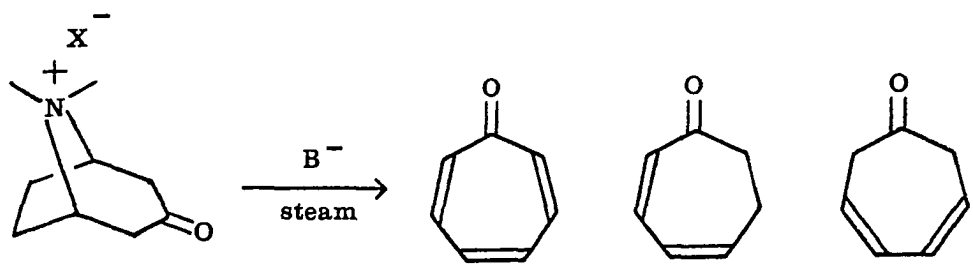
4,5-Benzohomotropone was prepared by treating 4,5-benzotropone with dimethyloxosulfonium methylide. Although attempts to convert the monohomobenzotropone to the bis-homobenzotropone were unsuccessful, conversion of 2,7-diethoxycarbonyl-4,5-benzotropone to the 2,7-diethoxy-carbonyl-4,5-benzo-2,3:6,7-bishomotropone was successful. The two cyclopropane rings were suggested to be <u>syn</u> for base catalyzed hydrolysis of the product followed by treatment with acetic anhydride gave an acid anhydride (40).



RESULTS AND DISCUSSION

Tropone itself was first synthesized simultaneously by three different investigators from three different precursors, namely, anisole (41), cycloheptenone (42) and cycloheptanone (43). Since that time, several additional syntheses have been reported and reviewed (44,45).

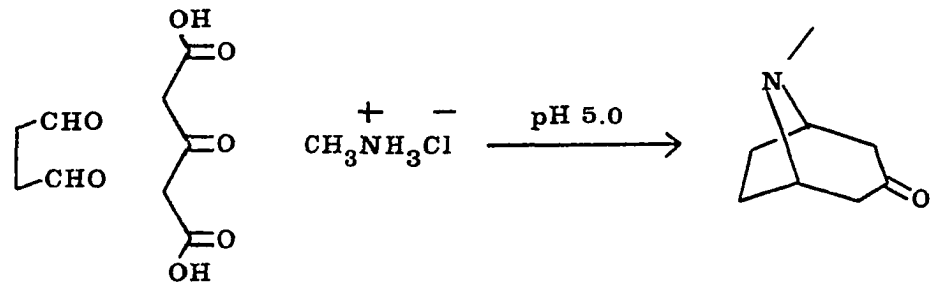
Of all the syntheses of tropone available, the method most amenable to the synthesis of 4,5-homotropone is the



base catalyzed degradation of a tropinone-like derivative. For the preparation of 4,5-homotropone, only the appropriate tropanoid aminoketone need be synthesized.

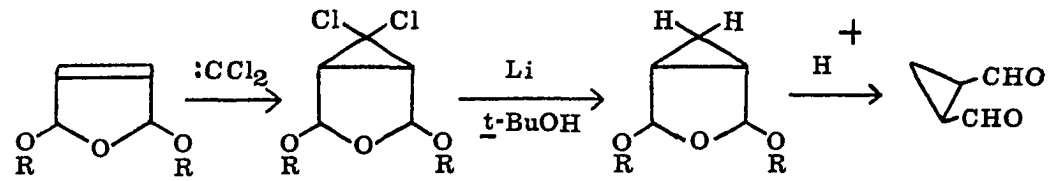
Tropinone itself was first prepared by Willstätter and Ettlinger (46) by a long and laborious method. However, in 1917 Robinson (47) observed that tropinone was formed in small yield when an aqueous solution containing succindialdehyde, acetone, and methylamine was kept at room temperature for thirty minutes. The yield was improved by replacing acetone by the calcium salt of acetonedicarboxylic acid.

Later, Schöpf and Lehmann (48) reinvestigated the reaction in greater detail and found that by using a dilute buffered solution of succindialdehyde, methylamine hydrochloride, and acetonedicarboxylic acid at 25°, a yield of 83% of tropinone was obtained. This elegant synthesis proceeded



under "physiological conditions" and suggested that tropane alkaloids might be formed in plants by some similar process.

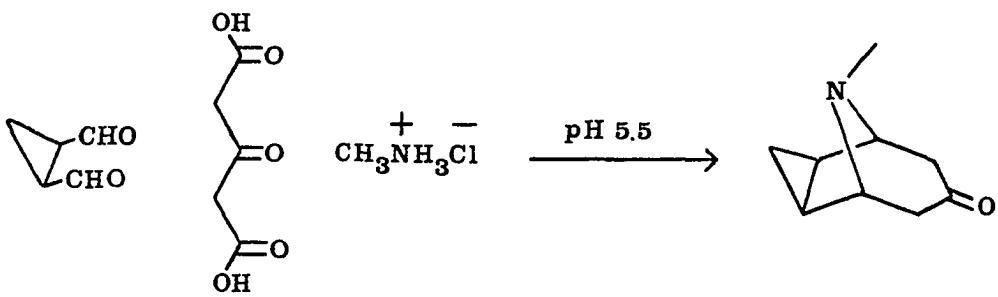
The desired tropanoid aminoketone was prepared by utilization of the Robinson-Schöpf conditions and cis-cyclopropane-1,2-dicarboxaldehyde. The corresponding diacetal was recently prepared by reduction of the dichlorocarbene adduct of 2,5-dimethoxy-2,5-dihydrofuran (49,50).



R = CH_3

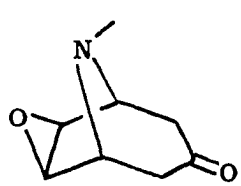
The diacetal was hydrolyzed in dilute sulfuric acid on a

steam bath and allowed to react with methylamine hydrochloride and acetonedicarboxylic acid for three days at room temperature in a solution buffered at pH 5.5. The resulting

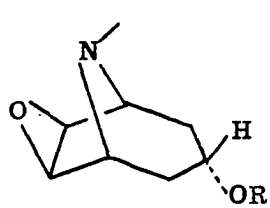


solution was made basic and extracted with ether. The crude material obtained after concentration was sublimed to give the tricyclic aminoketone mp 69-70° in 73% overall yield from the diacetal.

The tricyclic aminoketone is closely related to the biologically important scopinone, scopine and scopolamine in



scopinone



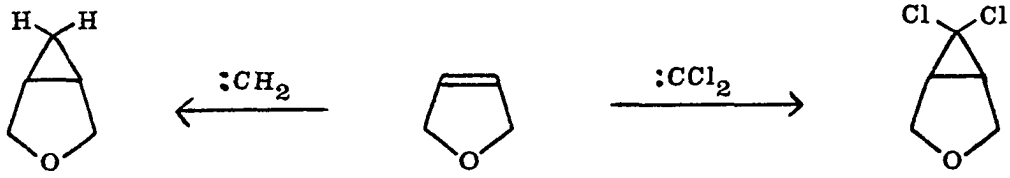
R = H, scopine

$R = COCH(CH_2OH)\phi$, scopolamine

which the oxirane oxygen has been replaced by a methylene. Assuming quantative hydrolysis of the cyclopropane diacetal to the corresponding dialdehyde, a 73% yield in the Robinson-Schöpf condensation was realized. Formation of the diacetal,

however, occurred in overall 6.8% yield from the dimethoxydihydrofuran due to the poor yield in the dichlorocarbene insertion reaction with the overall yield to the aminoketone being only 5%. Accordingly, an alternative synthesis for the dialdehyde was desirable.

The first approach considered was preparation of the diacetal directly *via* a methylene transfer reagent. The reaction of dimethoxydihydrofuran with diazomethane was not attempted for it is known that reaction of 2,5-dihydrofuran with diazomethane yielded only 4% of the cyclopropane product

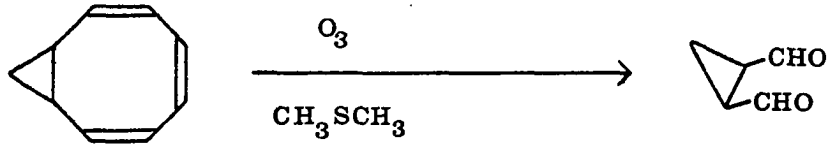


whereas reaction with dichlorocarbene generated from methyl trichloroacetate and sodium methoxide yielded 37% of the dichlorocyclopropane product (51). The reaction of dimethoxydihydrofuran with the Simmons-Smith reagent was attempted. Treatment of dimethoxydihydrofuran with the Simmons-Smith reagent generated by a variety of procedures led only to a dark viscous residue.

A second alternative was another source of the dichloromethylene. Treatment of the dimethoxydihydrofuran with

chloroform and potassium t-butoxide resulted in a 7% yield of the desired adduct. Another source of dichloromethylene is the Seyferth reagent, phenyl(bromodichloromethyl)mercury. In anticipation of the known thermal liability of bicyclic dihalocyclopropanes (52), a mixture of the dichloroadduct was refluxed in benzene with phenylmercuric bromide for one hour. The adduct was quantitatively recovered unchanged. Accordingly, a 1:1 mixture of 2,5-dimethoxy-2,5-dihydrofuran and the Seyferth reagent was refluxed in benzene for one hour. Nearly quantitative yield of phenylmercuric bromide and a yellow-red oil was obtained. The nuclear magnetic resonance spectrum of the crude oil failed to exhibit the three sharp singlets expected for the desired adduct, and the oil was not investigated further.

The third approach entailed ozonolysis of bicyclo[6.1.0]-nona-2,4,6-triene. Ozonolysis of this triene in methanol at



-78°, reductive workup with dimethyl sulfide, followed by the addition of this reaction mixture to an aqueous solution of acetonedicarboxylic acid and methylamine hydrochloride

buffered at pH 5.5 gave a tricyclic aminoketone in 32% yield overall from the triene. The resulting aminoketone was found to be identical by melting point (mp) and both infrared (ir) and nuclear magnetic resonance (nmr) spectra to those of the aminoketone obtained previously. Thus, the overall yield from readily available starting materials was increased from 5% to 14.4%.

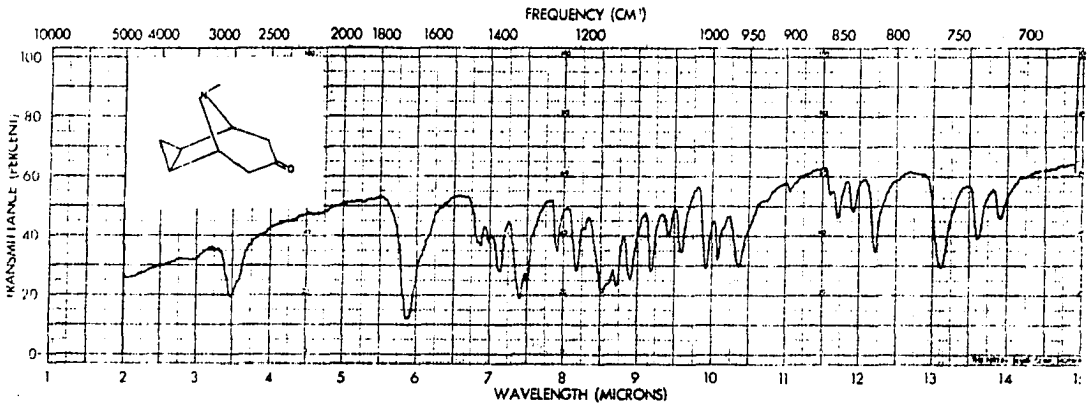
The ir spectrum (Figure 1, page 30) of the tricyclic aminoketone shows significant bands at 3.48 μ (CH) and 5.85 μ (C=O). The nmr spectrum (Figure 2, page 32) reveals signals at δ 3.20 (multiplet, 2H) bridgehead pyrrolidine-piperidone hydrogens, δ 2.78-1.82 (complex multiplet, 7H) methylene hydrogens adjacent to the carbonyl and N-methyl, δ 1.22 (multiplet, 2H) cyclopropyl methine hydrogens, δ 0.95 (multiplet, 1H) exo hydrogen of the cyclopropyl methylene and δ 0.21 (multiplet, 1H) endo hydrogen of the cyclopropyl methylene. The exo hydrogen is tentatively assigned on the basis of a small additional coupling ($J \approx 1$ Hz) observed at δ 0.95 attributed to 'W' coupling with the pyrrolidine-piperidone bridgehead hydrogens. The ultraviolet (uv) spectrum (95% ethanol) exhibits a strong charge-transfer band at 250 nm (log ε 2.97) and no perceptible $n \rightarrow \pi^*$ transition, however, in five per cent hydrochloric acid only the normal $n \rightarrow \pi^*$ transition at 283 nm is observed. This ultraviolet behavior is typical of β carbonyl amines

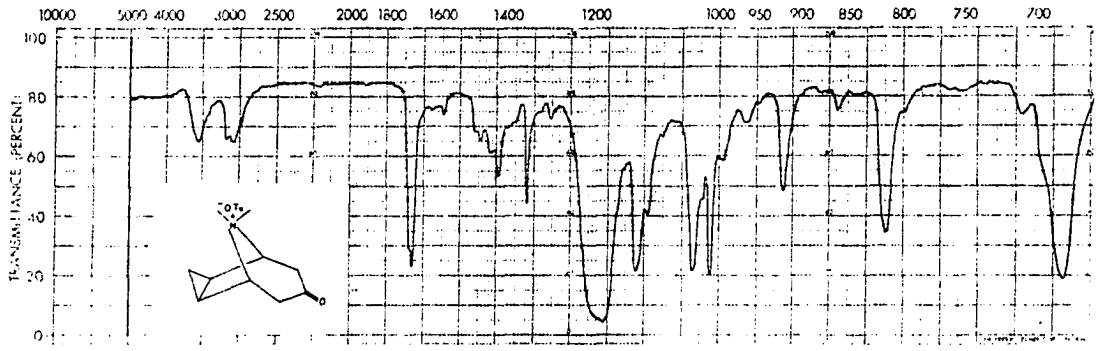
Figure 1. Infrared spectra

Top: Aminoketone (9-methyl-9-azatricyclo-[3.3.1.$0^{6,8}$]nonan-3-one)

Middle: Quaternary tosylate (9,9-dimethyl-3-oxo-9-azoniatricyclo[3.3.1.$0^{6,8}$]-nonane tosylate)

Bottom: 4,5-Homotropone


FREQUENCY (CM⁻¹)
10000 5000 4000 3000 2500 2000 1800 1600 1400 1200 1000 950 900 850 800 750 700
TRANSMITTANCE (PERCENT)
100 80 60 40 20 0
1 2 3 4 5 6 7 8 9 10 11 12 13 14
WAVELENGTH (MICRONS)


10000 5000 4000 3000 2500 2000 1800 1600 1400 1200 1000 950 900 850 800 750 700
TRANSMITTANCE (PERCENT)
100 80 60 40 20 0
OTs

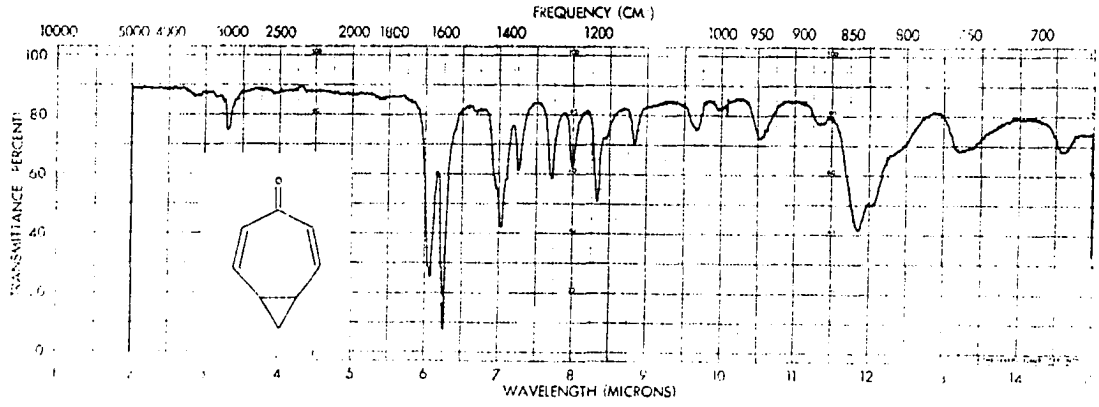
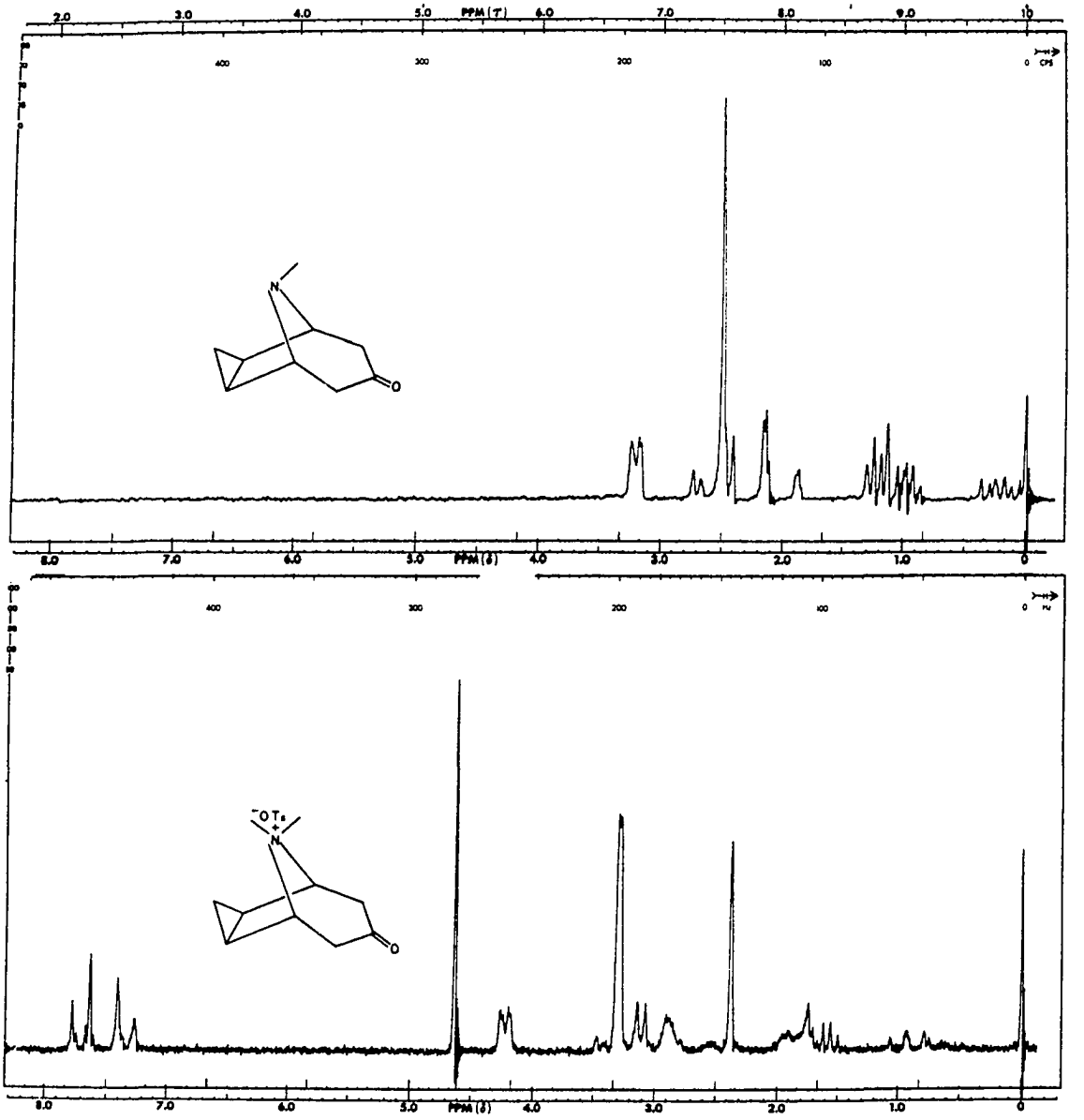

FREQUENCY (CM⁻¹)
10000 5000 4000 3000 2500 2000 1800 1600 1400 1200 1000 950 900 850 800 750 700
TRANSMITTANCE (PERCENT)
100 80 60 40 20 0
O
4 5 6 7 8 9 10 11 12 14
WAVELENGTH (MICRONS)

Figure 2. Nuclear magnetic resonance spectra

Top: Aminoketone (9-methyl-9-azatricyclo-[3.3.1.$0^{6,8}$]nonan-3-one)

Bottom: Quaternary tosylate (9,9-dimethyl-3-oxo-9-azoniatricyclo[3.3.1.$0^{6,8}$]-nonane tosylate)


PPM (δ)
PPM (δ)

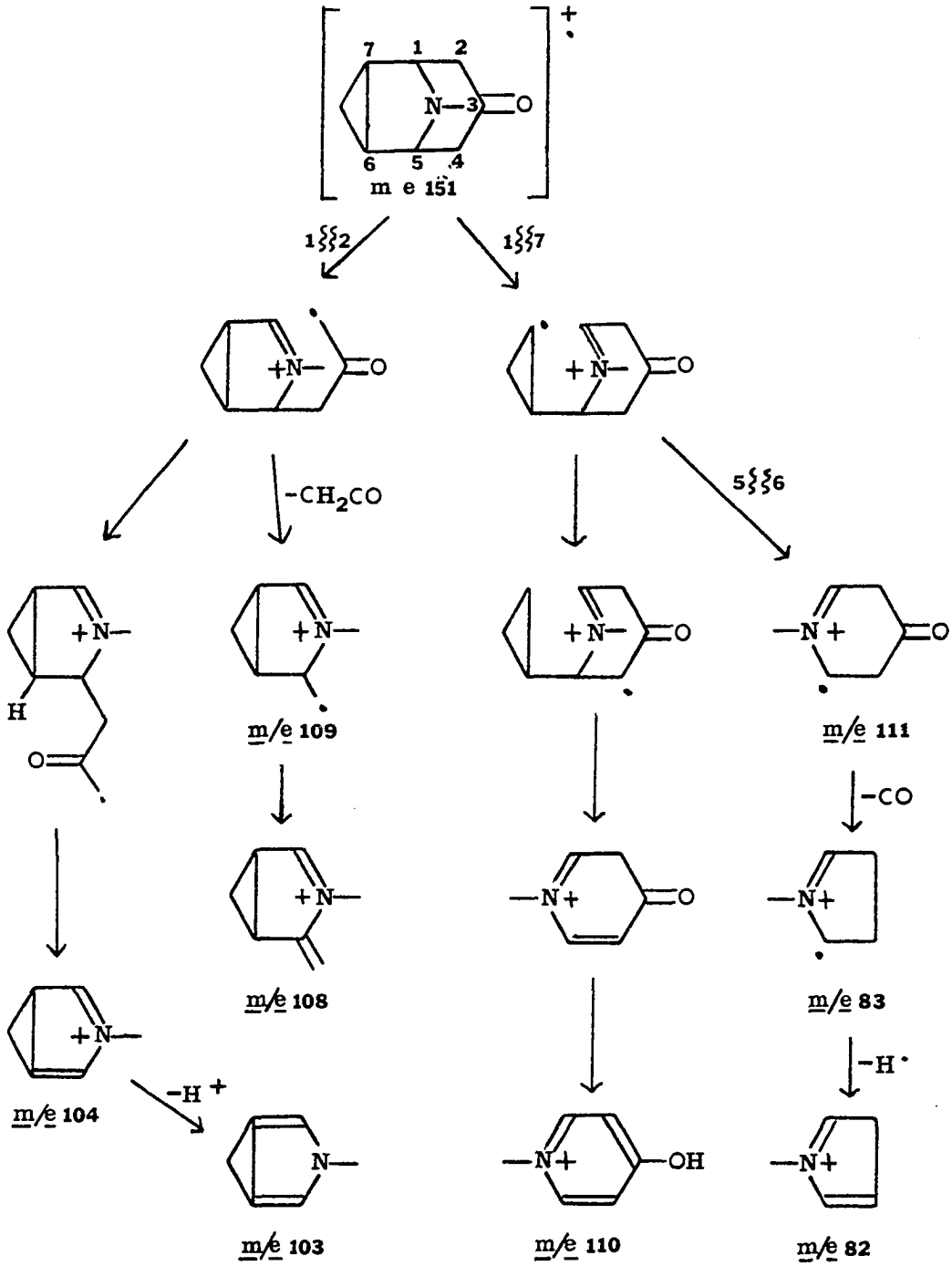
with equitorial electron pairs while β carbonyl amines with axial electron pairs show no such behavior (53).

The mass spectrum of the aminoketone is in complete accord with the tropane alkaloid structure. The main mass spectral fragmentation processes for this alkaloid-type have been thoroughly investigated by deuterium or substituent labelling techniques (54). The mass spectrum (m/e) (relative intensity) exhibits a parent ion at m/e 151 (42). Cleavage of the 1--2 bond gives rise to ions m/e 111 (2), 110 (2), 83 (3) and 82 (18). Cleavage of the 1--7 bond gives fragments with m/e 109 (13) and 108 (100). The McLafferty rearrangement of the species generated by cleavage of the 1--2 bond which would give rise to m/e 104 and 103 appears to be inoperative (Scheme 1, page 35). Two ions of low abundance, but present in the spectra of all tropane alkaloids, namely, the N-methylpyridinium cation, m/e 94 (36), and the species $CH_3--\overset{+}{N}\equiv C--H$, m/e 42 (65), are also present.

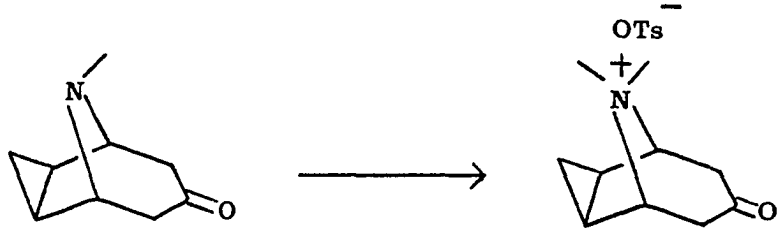
The stereochemistry of the aminoketone, namely, the methylene bridge cis to the nitrogen is assigned by analogy to other products derived from Robinson-Schöpf condensations. All such condensations involving erythro-2,3-disubstituted succindialdehydes for which the stereochemistry has been determined give cis-exo products (55).

Direct evidence for the stereochemical assignment of the tricyclic aminoketone derives from the vigorous conditions

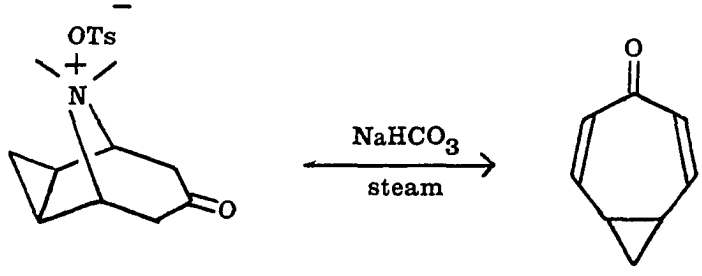
Scheme 1. Mass fragmentation scheme for aminoketone (9-methyl-9-azatricyclo[3.3.1.$0^{6,8}$]nonan-3-one)


m e 151
1§§2
1§§7
-CH2CO
5§§6
m/e 109
m/e 111
-CO
m/e 108
m/e 83
-H+
-H·
m/e 104
m/e 103
m/e 110
m/e 82

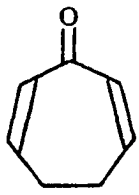
necessary for quaternization. The aminoketone was heated at 96° for eight hours in neat methyl tosylate. The quaternary tosylate was obtained in 90% yield as a white solid mp 172.5-173.5° after recrystallization from ethanol.

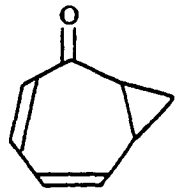


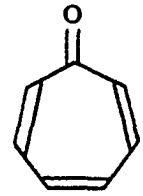
The quaternary tosylate undergoes a double Hofmann elimination upon treatment with sodium bicarbonate followed by rapid steam distillation to give 4,5-homotropone as a clear yellow oil bp 70-72°/0.5 mm in 61% yield based on pure quaternary tosylate.



The ir spectrum (Figure 1, page 30) of 4,5-homotropone shows significant bands at 3.32 μ (CH), 6.06 μ (C=O), 6.24 μ (C=C), 13.3 μ (cis HC=CH) and 14.1 μ (cis HC=CH). The uv spectrum (95% ethanol) exhibits bands at 264 nm (log ε 3.88) and 290 nm (shoulder, 3.66). The uv spectrum (cyclohexane) reveals bands at 248 nm (3.89), 275 nm (shoulder, 3.65), 360 nm (1.52), 390 nm (shoulder, 1.29) and 410 nm (shoulder, 0.80). This suggests that there is relatively little delocalization through the cyclopropane ring. The ultraviolet absorption maxima of 2,6-cycloheptadienone (56), 2,3-homotropone (57), and tropone (58) are shown below for comparison.



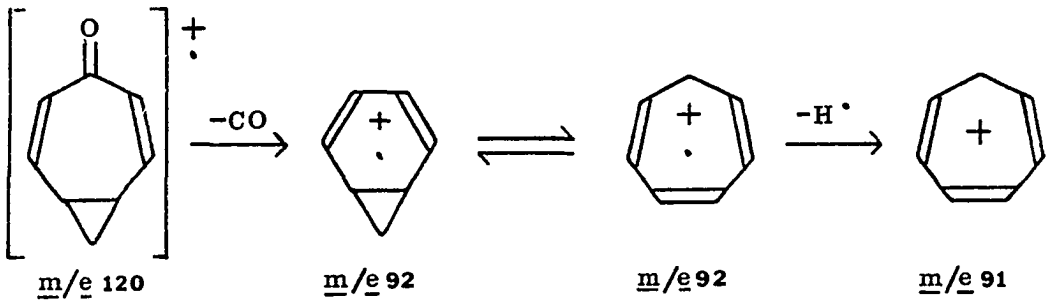




uv max (ethanol)	uv max (ethanol)	uv max (methanol)
235 nm (log ε 4.03)	293 nm (log ε	225 nm (log ε 4.30)
266 nm (shoulder, 3.40)	3.65)	228 nm (4.31)
339 nm (1.52)	340 nm (3.15)	232 nm (4.29)
		303 nm (3.87)

The mass spectrum (m/e) (relative intensity) of 4,5-homotropone exhibits a parent ion at 120 (17), an ion at

92 (100) due to a loss of carbon monoxide, and an ion at 91 (70) due to a further loss of a hydrogen atom. These ions are attributed to the radical cations of 4,5-homotropone,



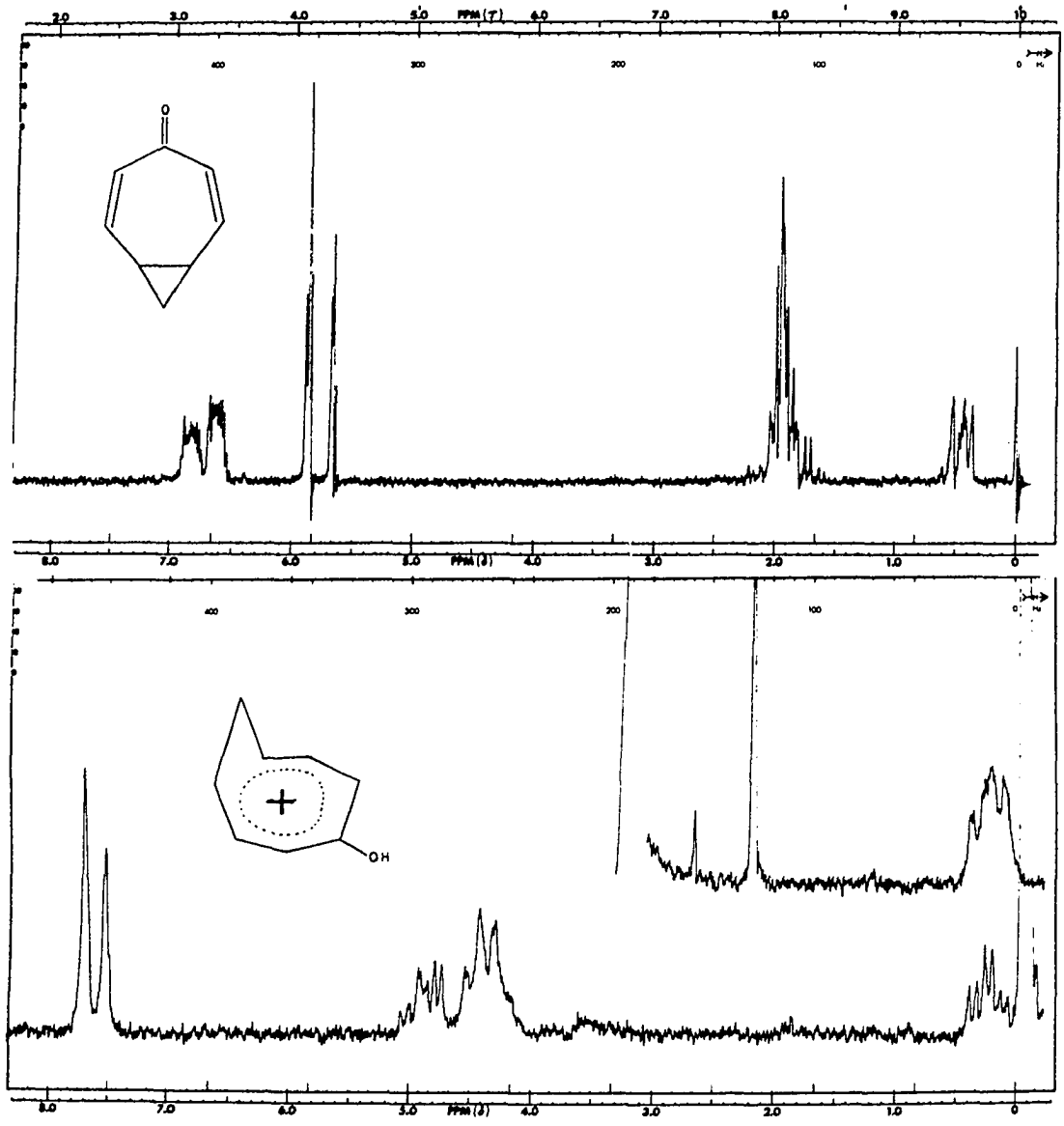
norcaradiene or tropylidene, and the tropylium ion, respectively. Appropriate metastable ions (m/e 70, 90) are also observed for the 120 → 92 and 92 → 91 processes.

The nmr spectrum (Figure 3, page 40) of 4,5-homotropone is virtually unchanged from +40° to -55° and exhibits signals at δ 6.65 (multiplet, 2H) hydrogens β to the carbonyl, δ 5.75 (multiplet, 2H) hydrogens α to the carbonyl, δ 1.90 (broad complex multiplet, 3H) cyclopropyl methine hydrogens and exo hydrogen of the cyclopropyl methylene, and δ 0.45 (multiplet, 1H) endo hydrogen of the cyclopropyl methylene. The endo and exo hydrogens of the cyclopropyl methylene are tentatively assigned on the basis of diamagnetic shielding of the endo hydrogen by the carbonyl function. The coupling constant for the olefinic protons ($J \approx 12.5$ Hz) is in accord with expectation (59,60). The fact that the nmr spectrum is unchanged over a 95° temperature range demonstrates

Figure 3. Nuclear magnetic resonance spectra

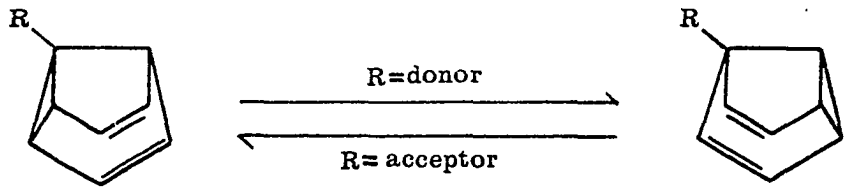
Top: 4,5-Homotropone

Bottom: 4-Hydroxyhomotropylium cation


2.0
3.0
4.0
5.0
PPM(τ)
6.0
7.0
8.0
9.0
10
O
8.0
7.0
6.0
5.0
PPM(δ)
4.0
3.0
2.0
1.0
0
OH

that 4,5-homotropone does not exhibit the facile Cope rearrangement common to most cis-1,2-divinyl cyclopropanes.

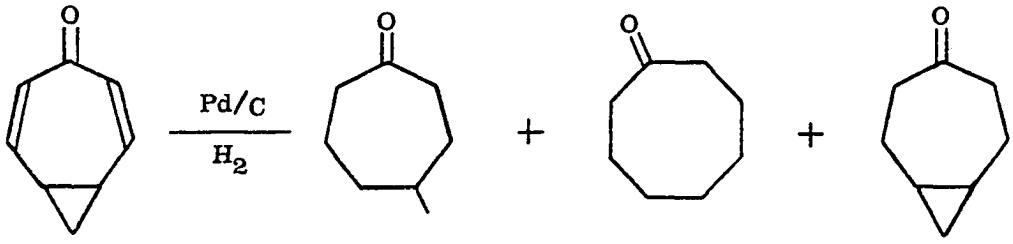
The fact that equilibrium lies strongly away from the cyclopropanone has been explained by Hoffmann and Stohrer (32) based on extended Hückel calculations on the equilibrium position of certain substituted semibullvalenes. The Cope



equilibrium was shifted markedly to the right with π-electron donors while π-electron acceptors shift the equilibrium in the opposite direction. In the present case the ketone oxygen lone pair is the lone-pair donor and thus equilibrium would be strongly favored away from the cyclopropanone.

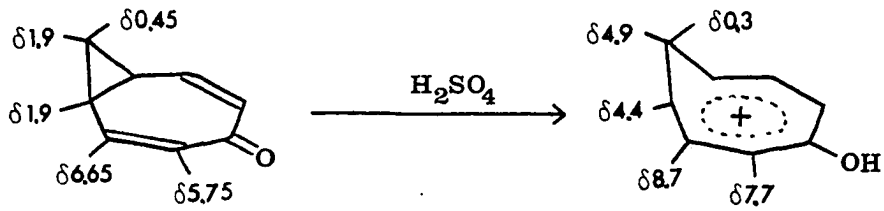
Atmospheric pressure hydrogenation of 4,5-homotropone with 5% palladium on charcoal gave three compounds in the

approximate ratio of 1:7:2 which were separated by preparative gas chromatography. The components were identified as



4-methyl-cycloheptanone, cyclooctanone and bicyclo[5.1.0]-octan-4-one by comparison of their ir spectra as well as mixed melting points with known derivatives of authentic samples. Hydrogenolysis of cyclopropanes is known and documented. With vinyl cyclopropanes, that bond which is adjacent to the vinyl substituent is usually opened (61). Thus, hydrogenation of 4,5-homotropone with two vinyl substituents adjacent to the cyclopropane ring would be expected to yield predominately cyclooctanone.

The nmr spectrum (Figure 3, page 40) of 4,5-homotropone in concentrated sulfuric acid shows dramatic shifts in accord with expectation for the 4-hydroxyhomotropylium cation. The peripheral hydrogens are deshielded nearly uniformly 2 ppm downfield. The exo hydrogen is deshielded 3 ppm while the endo hydrogen is shielded 0.15 ppm upfield. The large chemical shift difference, 4.6 ppm, between the endo and exo protons of the methylene group demonstrates a high



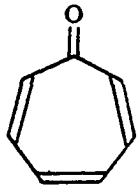
degree of delocalization in the 4-hydroxyhomotropylium cation.

Quenching the solution of the 4-hydroxyhomotropylium cation by addition to cold saturated sodium bicarbonate followed by extraction with ether resulted in regeneration of 4,5-homotropone in 30% yield as the only distillable product.

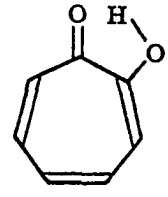
Having demonstrated the reversible formation of the 4-hydroxyhomotropylium cation from 4,5-homotropone, the basicity of 4,5-homotropone was investigated. The spectrophotometric method chosen was that of David and Geissman (62) for it is least subject to errors in measurement of solution volumes as well as the effects of medium changes upon absorption, and does not in principle differ from the classical method (63). The procedure involves locating the absorption wavelengths, λ_i and λ_u, close to the points of maximal difference between the extinction coefficients, ε_i and ε_u, of the essentially completely ionized and nearly unionized species, respectively. The difference, $\Delta\bar{\varepsilon} = \bar{\varepsilon}_i - \bar{\varepsilon}_u$, where $\bar{\varepsilon}_i$ and $\bar{\varepsilon}_u$ are the apparent molar extinction coefficients at

λ_i and λ_u, is plotted as a function of H_o. At the inflection point of the resulting sigmoidal curve, it can be shown that the substrate is half-ionized and therefore $H_o = pK_{BH^+}$.

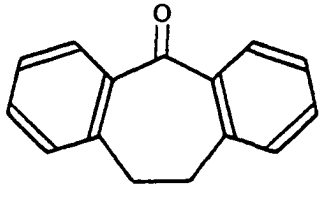
Figure 4a, page 46a, shows the sigmoidal curve that is obtained when the $\Delta\bar{\varepsilon}$s of 4,5-homotropone in various sulfuric acid solutions are plotted against the H_o values of these solutions. A similar curve (Figure 4b, page 46c) is obtained when only $\bar{\varepsilon}_i$s are plotted as a function of H_o. The inflection points were taken as the mid-point of the 'straight-line' portions of the curves. The $pK_{BH^+} = -4.20$ of 4,5-homotropone thus obtains. The pK_{BH^+} of tropone, tropolone (64), 2,3:6,7-dibenzocycloheptanone, 2,3:6,7-dibenzotropone (65), 2,3-homotropone and 2,6,6-trimethylcyclohepta-2,4-dienone (1) are shown below for comparison.



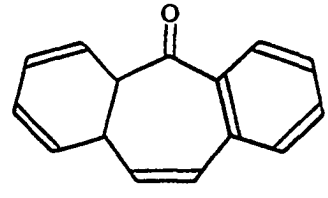
pK_{BH^+} -1.02



pK_{BH^+} -0.89



pK_{BH^+} -5.69



pK_{BH^+} -5.25

Figure 4a. A plot of $\Delta\bar{\varepsilon}$ versus H_o of 4,5-homotropone

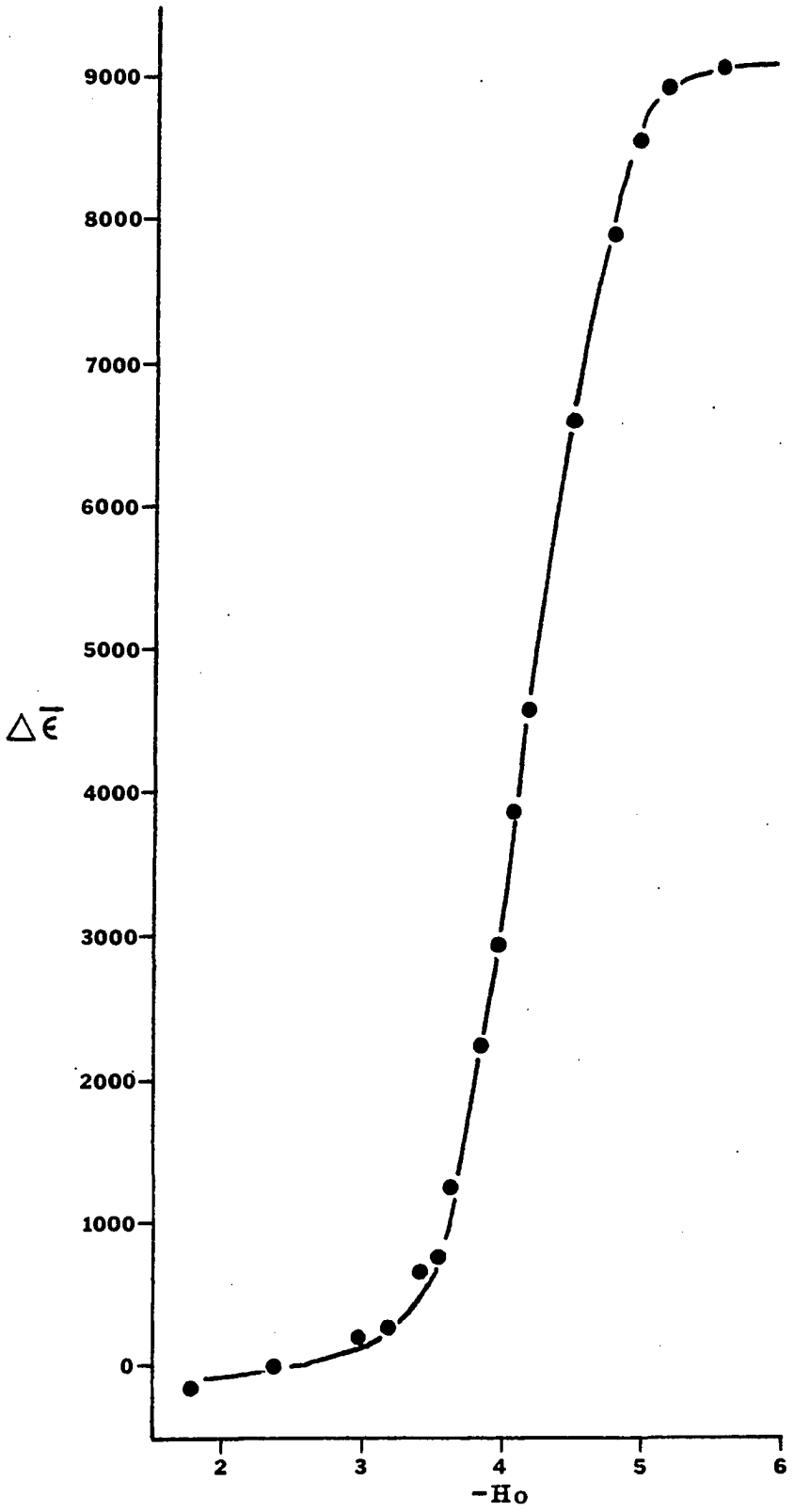
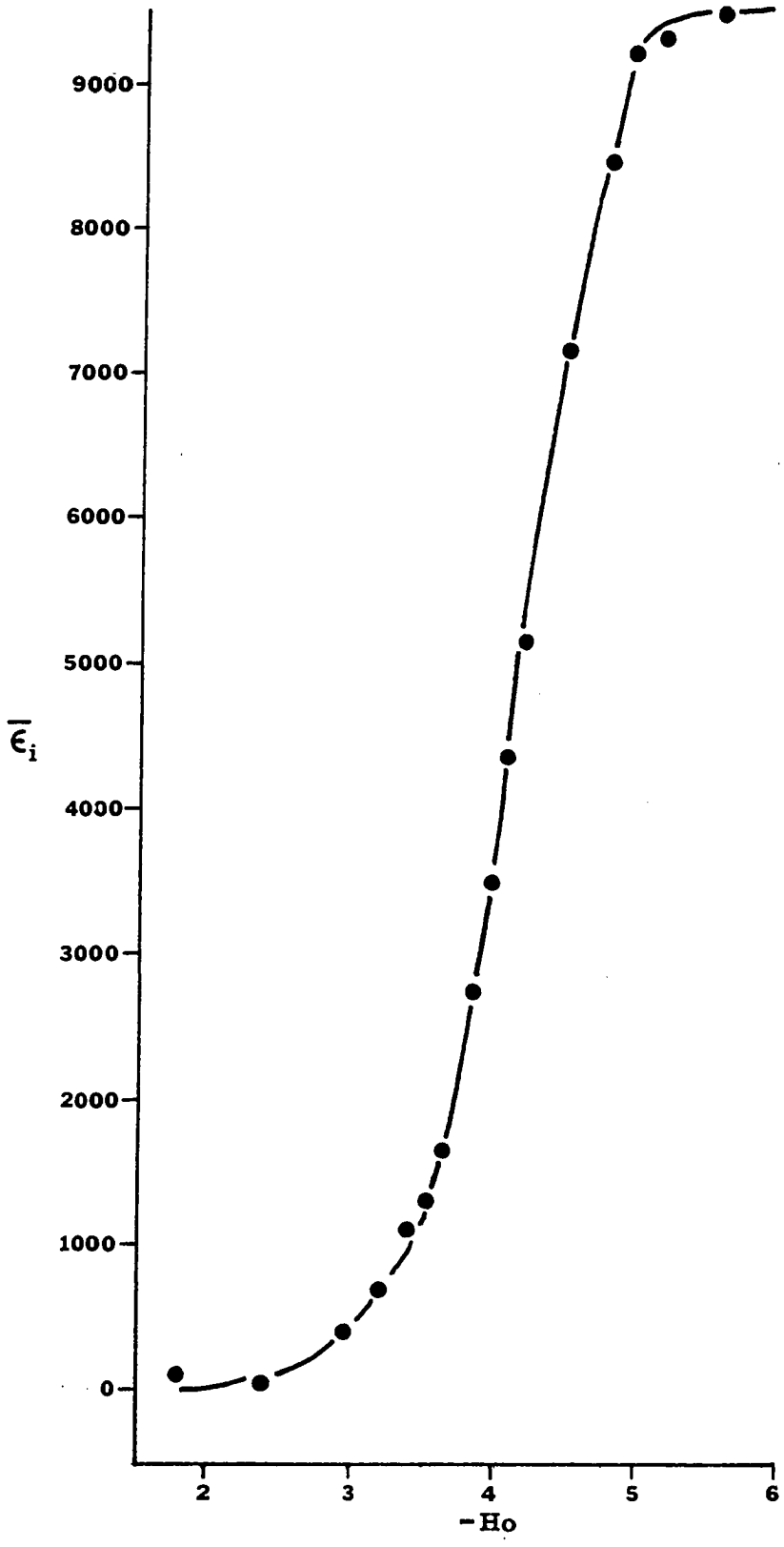
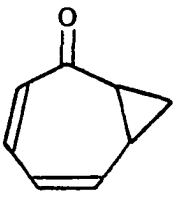
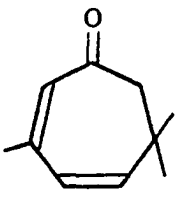

9000
8000
7000
6000
5000
4000
3000
2000
1000
0
$\Delta\bar{\epsilon}$
2
3
4
5
6
-Ho

Figure 4b. A plot of $\bar{\varepsilon}_i$ versus H_o of 4,5-homotropone


9000
8000
7000
6000
5000
4000
3000
2000
1000
0
$\overline{\epsilon}_i$
2
3
4
5
6
-Ho



pK_{BH^+} = -2.8



pK_{BH^+} = -4.9

It is most desirable to compare the basicity of 4,5-homotropone to that of a planar heptatrienone, but, unfortunately, such a system is not readily available. In 1963, Culbertson and Pettit (66) were able to show the existence of a linear-correlation between the pK_{BH^+} and the a_{or}^2, the coefficient of the atomic orbital of the carbonyl carbon atom in the lowest lying non-bonding molecular orbital. Using this relationship, the predicted basicity for a planar heptatrienone ($a_{or}^2 = 0.25$) is $pK_{BH^+} = -4.7$. Justification for the use of this relationship in the present case is seen in the reasonable agreement of the observed basicity of eucarvone, (2,6,6-trimethylcyclohepta-2,4-dienone, $pK_{BH^+} = -4.9$) and that predicted for heptadienone ($pK_{BH^+} = -5.3$; $a_{or}^2 = 0.33$). The value $pK_{BH^+} = -4.2$ for 4,5-homotropone is indeed higher than that predicted but not as high as that observed for 2,3-homotropone $pK_{BH^+} = -2.8$. Since both homotropones have the same heptatrienone model, the result indicates that there is a greater protonation π energy, the gain in π energy of the protonated

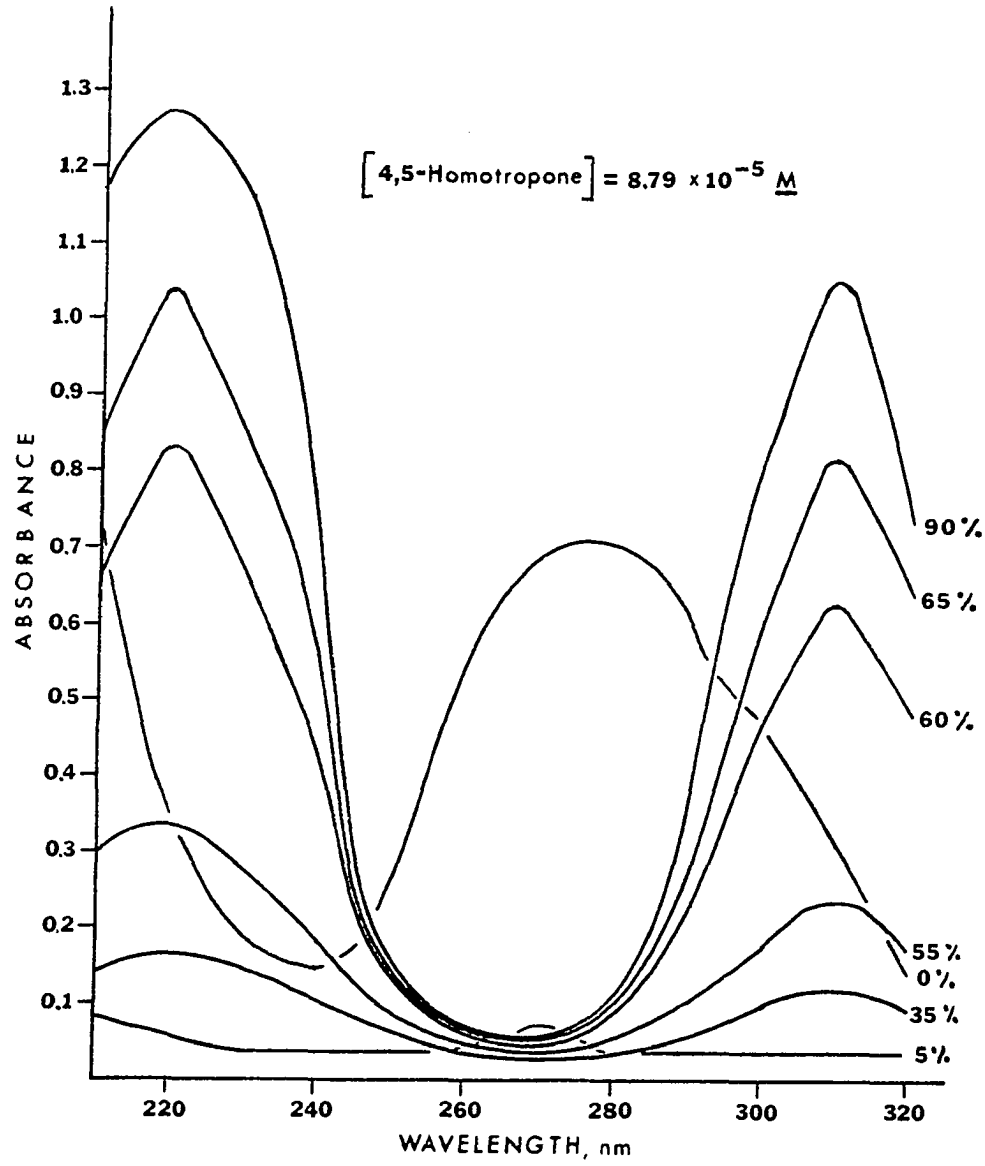
over the neutral compound, in 2,3-homotropone than in 4,5-homotropone.

A curious phenomenon, however, is apparent on examination of the individual spectra of the various solutions. In pure water, the ultraviolet spectrum of 4,5-homotropone is obtained, in concentrated sulfuric acid that of the 4-hydroxytropylium cation is obtained, while in dilute acid only weak absorptions ascribed to the cation are observed. (See Figure 5, page 50).

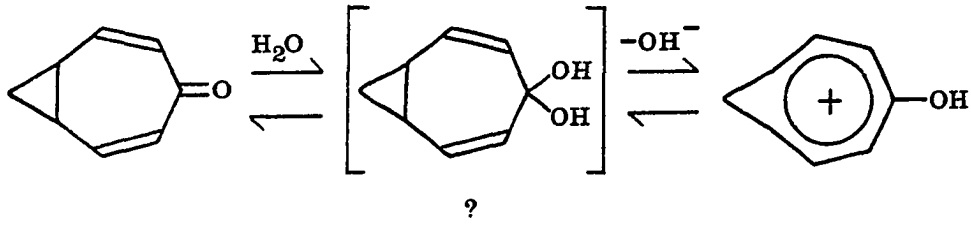
This phenomenon can be explained by an intermediate species which lacks ultraviolet absorption and is in equilibrium with both 4,5-homotropone and the 4-hydroxy-homotropylium cation. In pure water all of the substrate exists as 4,5-homotropone, at very low acid concentrations nearly all the substrate is converted to the intermediate and at higher acid concentrations the concentration of the 4-hydroxyhomotropylium cation increases.

The intermediate species probably arises by destruction of the carbonyl moiety for destruction of the cyclopropane ring leaves a cycloheptadienone, destruction of a double bond leaves at least a cycloheptenone, both of which would have considerable ultraviolet absorption. However, destruction of the carbonyl group, for example the formation of a carbonyl hydrate, would give rise to little or no ultraviolet absorption as exemplified by bicyclo[5.1.0]octa-2,5-diene (homotroplidene) which has been reported to have

Figure 5. Ultraviolet absorption spectra of 4,5-homotropone in various sulfuric acid solutions


[4,5-Homotropone] = 8.79 x10⁻⁵ M
ABSORBANCE
1.3
1.2
1.1
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
220
240
260
280
300
320
WAVELENGTH, nm
90%
65%
60%
55%
0%
35%
5%

no ultraviolet absorption above 215 nm (22). Unfortunately,



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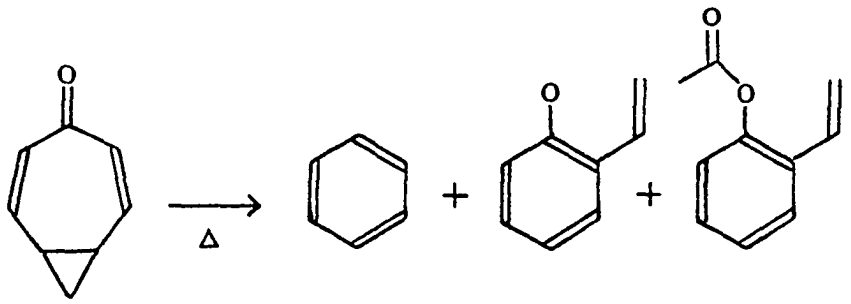
attempts to observe the nmr spectrum of the intermediate species in water at room temperature in the presence of sulfuric acid were unsuccessful.

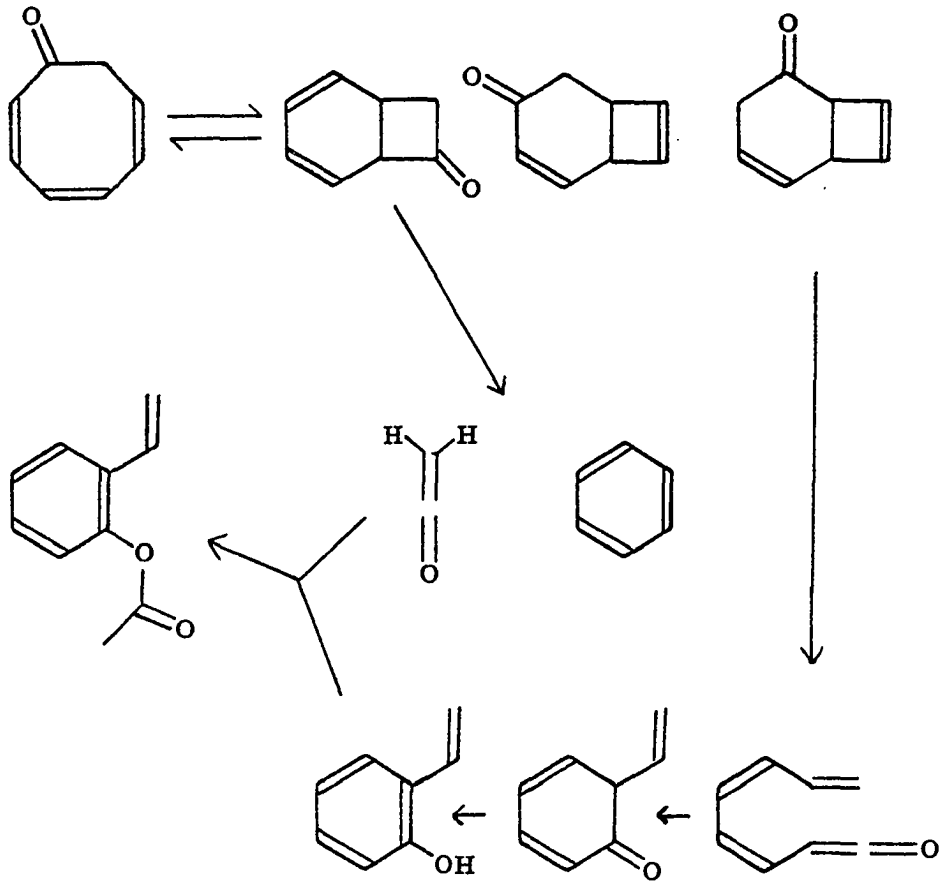
The accuracy of the basicity measurement might be questioned in light of the foregoing observations. However, the equilibrium nature of the overall process was established by regeneration of 4,5-homotropone in 30% yield by neutralization of a solution of the cation. The catalyzed hydration equilibrium of carbonyls is known to be rapid (67). In addition, there was no change in absorbance of the samples over a 24 hour period. This suggests that a true, rapid equilibrium is observed and gives credence to the basicity value obtained.

Thermolysis of 4,5-homotropone by slow vaporization (590°, 2μ pressure) through a quartz tube packed with quartz chips and subsequently analyzed by gas chromatography produced three compounds in approximately a 1:1:1 ratio. The individual components were isolated by preparative gas

chromatography and identified as benzene, o-vinyl phenol, and o-vinyl phenyl acetate by comparison of their ir and *nmr* spectra with those of authentic samples.



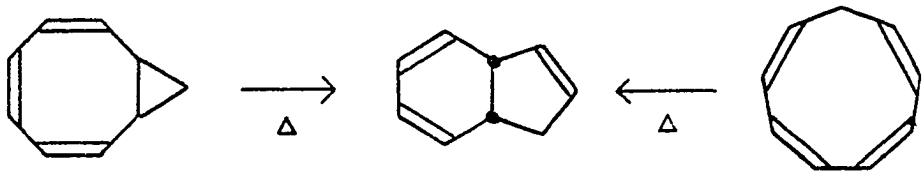
The three compounds formed in this thermolysis are the identical products formed in the pyrolysis of cycloocta-trienone. Büchi and Burgess (34) reported a 1:1:1 mixture of benzene, o-vinyl phenol, and o-vinyl phenyl acetate. To account for the observed products they envisioned thermal equilibration of all four valence isomers, fragmentation of the cyclobutanone isomer to benzene and ketene, isomerization of the bicyclic photoisomer to the cis,cis-ketene, and cyclization of this ketene to a cyclohexadienone followed by irreversible tautomerization to the more stable phenol. The phenol was then partly acetylated to the phenyl acetate by the ketene liberated in the degradation.



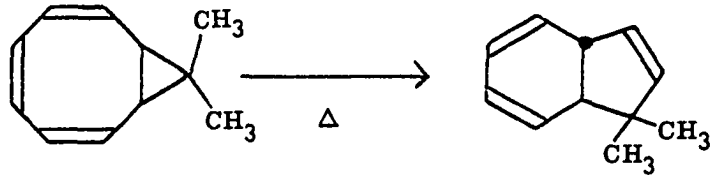
Attention is drawn to the fact that a temperature of 590° under the reaction conditions is necessary for the complete conversion of 4,5-homotropone to products whereas only 400° was needed under identical conditions for the complete conversion of cyclooctatrienone to the same products. Under the specified reaction conditions, it is reasonable to assume that once cyclooctatrienone is formed, it would undergo further reaction to the observed products. Thermolysis of 4,5-homotropone at 400° resulted in approximately 7% conversion to products with no detectable amount of cyclooctatrienone.

The identical products from the thermolysis of 4,5-homotropone and cyclooctatrienone as well as the much lower temperature needed for the conversion of the latter to products is consistent with the possibility that cyclooctatrienone is an intermediate. Before discussion of a possible mechanism for the formation of cyclooctatrienone, a digression to a related system is necessary.

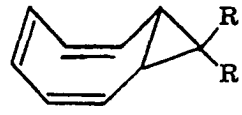
Vogel and coworkers (68-70) prepared bicyclo[6.1.0]nona-2,4,6-triene and discovered its thermal rearrangement to cis-



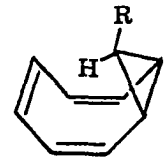
3a,7a-dihydroindene. The suggested intermediate was the all cis cyclononatetraene and indeed it has been prepared and shown to undergo the expected cyclization (71). The importance of conformation was suggested by Staley and Henry (72) who reported that the 9,9-dimethyl derivative rearranged to the trans-dihydroindene in contrast to the parent system and



the 9-monoalkyl derivatives. In the former case the favored conformation for thermal rearrangement was considered to be the exo conformation which is adopted because of severe steric



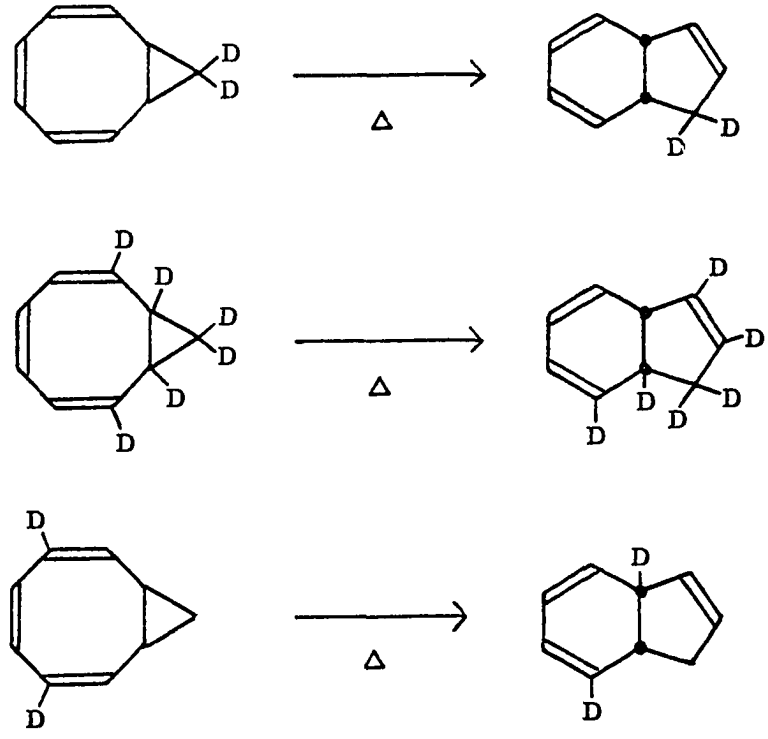
exo



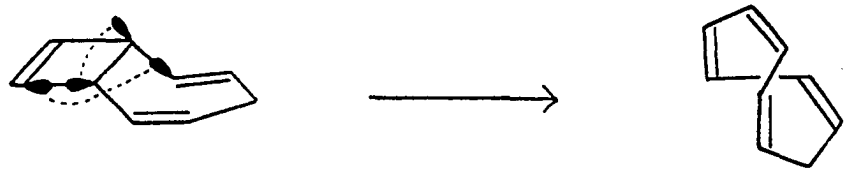
endo

interactions in the endo conformation.

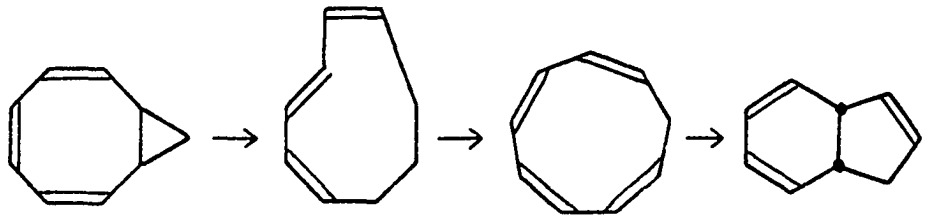
Three different specifically deuterated bicyclo[6.1.0]-nonatrienes have been prepared and their thermal rearrangement products identified (73). These are shown below.



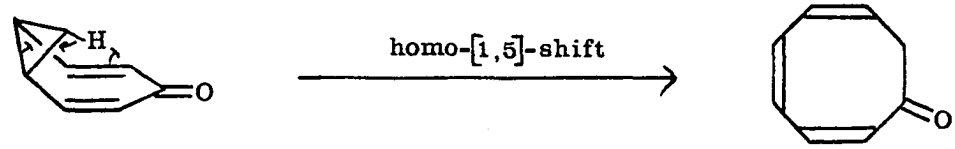
The results from the preceding labeled compounds demonstrated that three [$_{\sigma}2_{s}$ + $_{\sigma}2_{a}$] plausible mechanistic formulations "allowed" in terms of orbital symmetry were not operative. These are also depicted below.

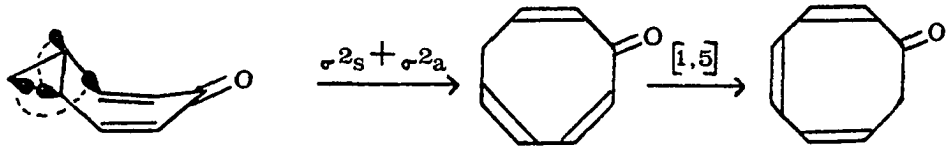


Presently, the mechanism is believed to proceed via three state-conservative isomerizations (73).

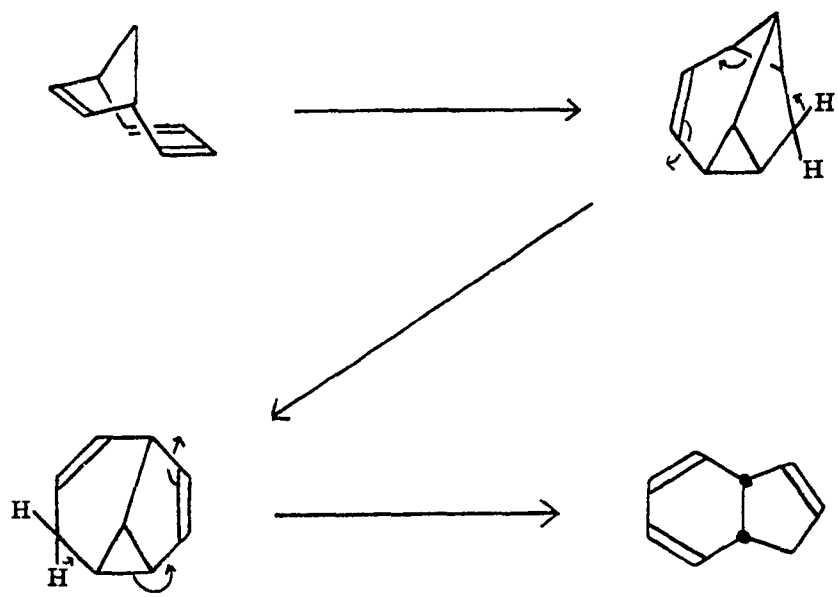


Returning to the discussion of cyclooctatrienone formation from 4,5-homotropone, there are at least two possible orbital symmetry allowed processes for this conversion: a homo-[1,5]-sigmatropic shift and a $[_{\sigma}2_{s} + {}_{\sigma}2_{a}]$ cycloaddition followed by a suprafacial-[1,5]-sigmatropic shift. A discussion of each follows.



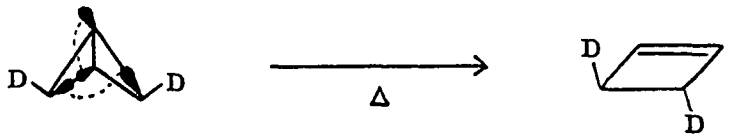


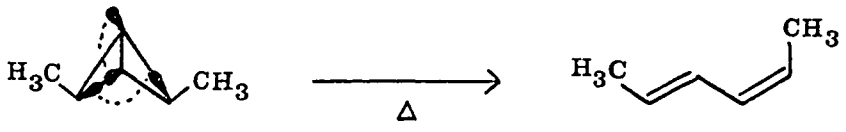
A recent example of a homo-[1,5]-sigmatropic shift is the conversion of bicyclo[4.2.1]nona-2,4,8-triene to cis-dihydroindene via an intramolecular Diels-Alder adduct followed by two consecutive homo-[1,5]-hydrogen shifts (74). In this case as well as those previously observed (75), the hydrogen



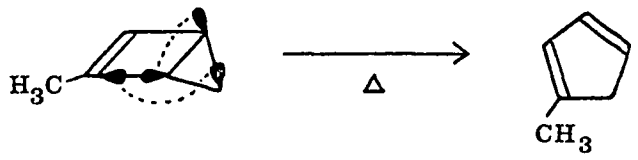
that migrates is on an atom adjacent to the cyclopropane ring and not a hydrogen in the cyclopropyl methylene. Furthermore, in the structurally similar bicyclo[6.1.0]nona-2,4,6-triene, a homo-[1,5]-hydrogen shift would produce the all cis-nonatetraene directly. However, the 9,9-dideuterio derivative produced the 1,1-dideuterio-cis-dihydroindene and not that predicted by a homo-[1,5]-shift of the type described. These data suggest another pathway may be operative.

A second possibility is the $[_{\sigma}2_s + {}_{\sigma}2_a]$ cycloaddition followed by a sigmatropic-[1,5]-hydrogen shift. The thermal isomerization of deuterium (76) and methyl (77) labeled bicyclo[1.1.0]butanes, and the thermal conversion of



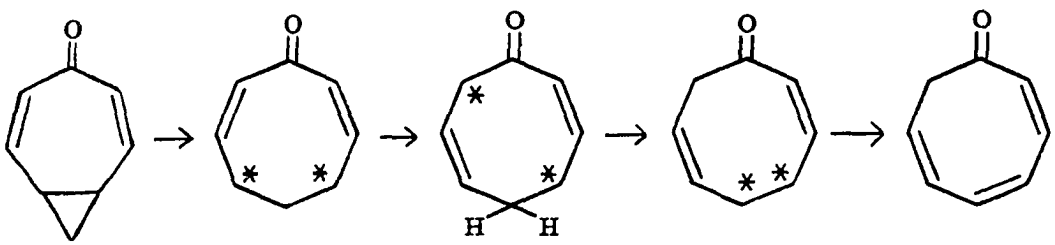


2-methylbicyclo[2.1.0]pent-2-ene to 1-methylcyclopentadiene (77) are examples of the $[_{\sigma}2_s + {}_{\sigma}2_a]$ cycloaddition. The



sigmatropic-[1,5]-shift is also known and documented (78). In contrast to the previously discussed allowed pathway, both steps of the present mechanistic formulation have precedence.

A third possibility, a nonconcerted pathway, can be considered in light of the high activation energy needed for the conversion. With a high activation energy, the energy surface for a concerted reaction cannot be far removed from that for alternative stepwise processes. One such process is the thermally allowed electrocyclic ring opening of 4,5-homotropone followed by a hydrogen shift and collapse to cyclooctatrienone.



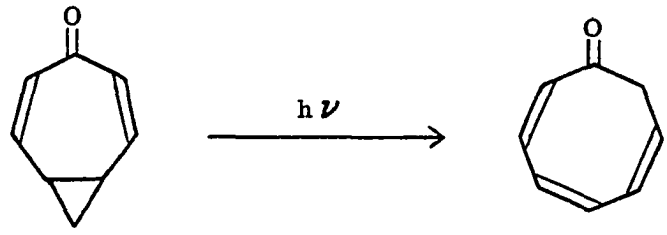
A definitive statement as to the mechanism cannot be made. A nonconcerted pathway is reasonable because the homo-[1,5]-sigmatropic shift as depicted is unprecedented and $[{}_{\sigma}2_{s} + {}_{\sigma}2_{a}]$ cycloadditions have only been observed in highly strained bicyclic systems.

The photochemical behavior of 4,5-homotropone was also investigated. A 0.03 molar solution of 4,5-homotropone in diethyl ether was irradiated with 3500 Å light. Aliquots analyzed at one hour intervals indicated the slow disappearance of starting material while a pale yellow solid precipitated out of solution. After twenty-four hours, thin

layer chromatography indicated the total disappearance of starting material. Evaporation of the solvent yielded a pale yellow solid in nearly quantitative yield. This material was insoluble in both polar and nonpolar solvents, did not melt below 300°, and its ir spectrum consisted mainly of a broad band between 6.2 μ and 13.5 μ. This material was not investigated further.

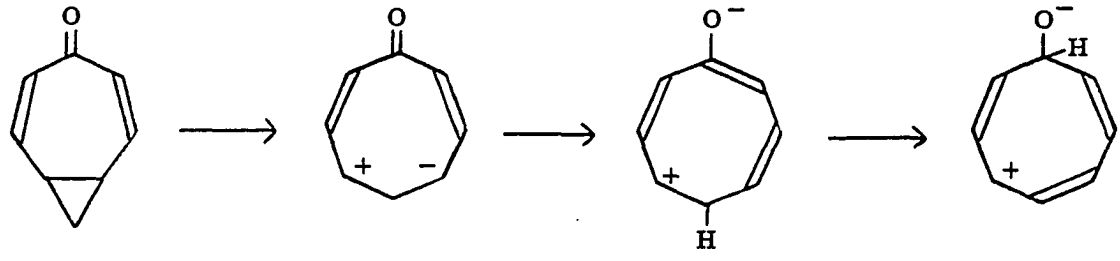
Small scale irradiation of a 0.042 molar solution of 4,5-homotropone in methanol with 3500 Å light was conducted. Aliquots at one hour intervals analyzed by gas chromatography indicated the steady increase of a single photoproduct for the initial seven hours. After this time, a steady state was apparently reached and secondary photoproducts appeared. Continued irradiation, twenty-four hours total, caused complete disappearance of both starting material and initial photoproduct.

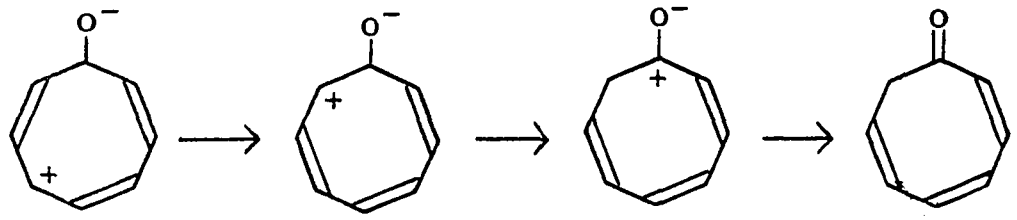
Preparative scale irradiation of a 0.042 molar methanolic solution of 4,5-homotropone with 3500 Å light was conducted for seven hours. The resulting solution was concentrated and the remaining oil chromatographed on a silica gel column using 5% ethyl acetate/hexane as eluent. After an initial forerun, a 19.7% yield of a clear yellow oil was obtained. This oil was identified as 2,4,6-cyclo-octatrienone by comparison of its ir and nmr spectra to those of an authentic sample.



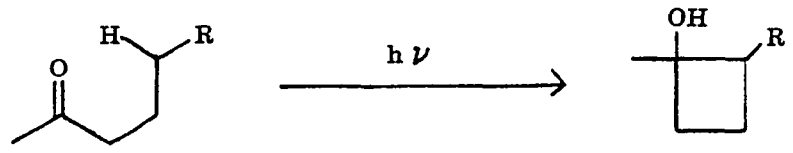
Simultaneous irradiation of 0.05 molar methanolic solutions of cyclooctatrienone and 4,5-homotropone, followed by gas chromatography, produced nearly identical gas chromatographic traces except for the absence of 4,5-homotropone in the former.

In the electrocyclic ring opening of 4,5-homotropone, the thermal process is clearly allowed while the photochemical process is ambiguous because of oddities in the correlation diagram and the uncertainty in n--π* <u>versus</u> π--π* character of the low lying excited states. Assuming the electrocyclic ring opening to a zwitterion, this zwitterion can then undergo a sigmatropic-[1,5]-shift followed by a hydride shift to give cyclooctatrienone.

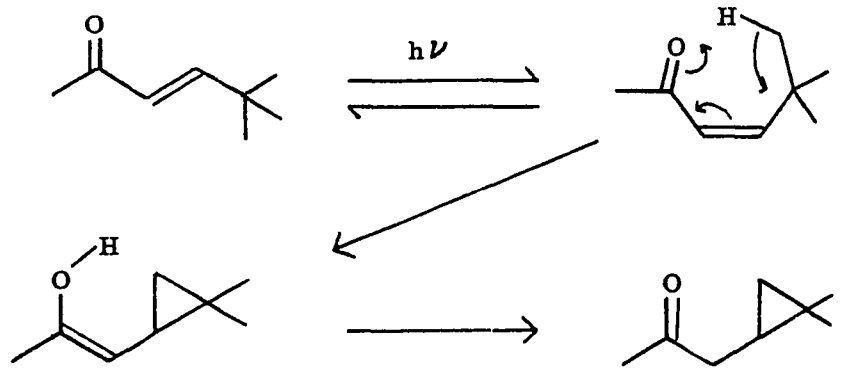




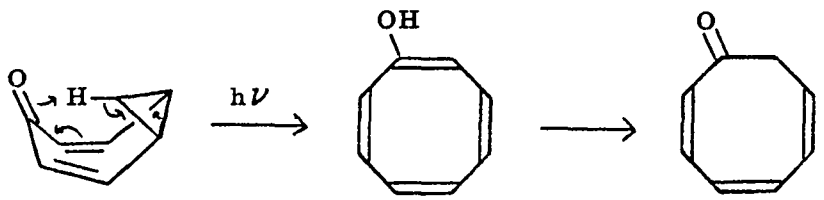
Another mechanistic possibility is a hydrogen abstraction reaction. An intramolecular hydrogen abstraction process is observed with aliphatic and alicyclic ketones. Yang and Yang (79) reported that long chain aliphatic ketones led to formation of cyclobutanols upon irradiation. This hydrogen



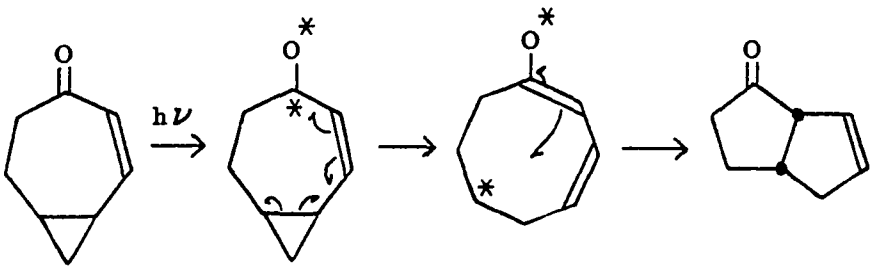
abstraction was also observed in unsaturated ketones, e.g., β-t-butyl methylvinyl ketone (80). This substrate upon irradiation underwent cis-trans isomerization followed by



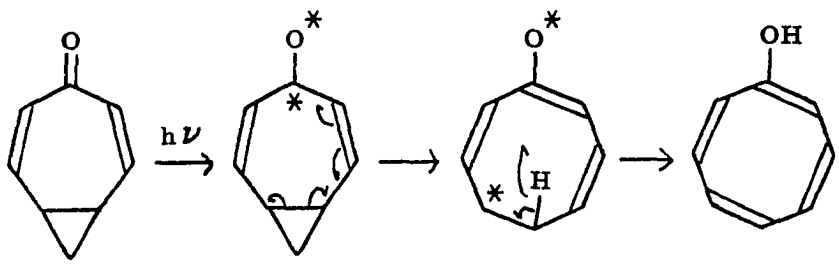
δ hydrogen abstraction and resulted in a β,γ cyclopropyl ketone. A similar hydrogen abstraction in 4,5-homotropone would lead directly to the enol of cyclooctatrienone. However, this type of abstraction reaction is more difficult in the present case because of the orthogonality of the carbonyl π* orbital to the δ C--H sigma bond.



A third mechanistic possibility is analogous to that proposed for the formation of a bicyclic ketone by irradiation of dihydro-4,5-homotropone (81). Since this reaction could be sensitized and undergo the same reaction with the performed triplet, the process was thought to proceed <u>via</u> the process depicted below. A similar process with 4,5-homotropone,



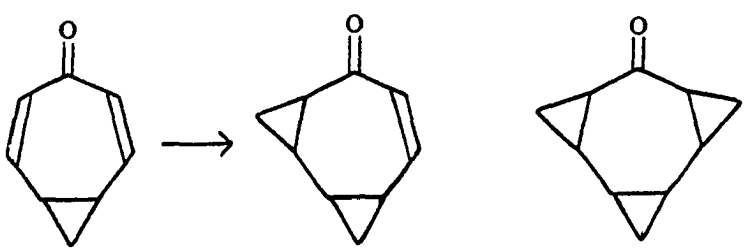
but followed by hydrogen abstraction would lead to the enol of cyclooctatrienone. Both this and the previous pathway are



closely related. They differ in that the former takes place in one step whereas the latter is a stepwise formulation.

Three different possible pathways for the formation of cyclooctatrienone from 4,5-homotropone have been described. The latter two pathways have precedents in nonpolar solvents. The formation of cyclooctatrienone in a polar solvent, methanol, suggests a polar intermediate may be involved. Furthermore, the fact that no other products not accounted for by cyclooctatrienone photolysis were observed, suggests that the intramolecular deactivation of the presumed zwitterion is faster than intermolecular reaction with solvent.

Preparation of bis and tris homotropones was also



investigated. Treatment of 4,5-homotropone with trimethylsulfoxonium methylide was unsuccessful. During the addition, a dark red viscous material began to adhere on the sides of the reaction vessel. The crude mixture was diluted with ether, poured into water, and the organic layer separated. Molecular distillation of the resulting viscous material gave 0.6% of a yellow oil identified as 4,5-homotropone by comparison of the ir spectrum with that of an authentic sample.

In order to obtain crystallographic data on 4,5-homotropone a crystalline derivative was sought. 2,3-Homotropone readily forms a hexachloroantimonate salt (1). Treatment of 4,5-homotropone at -78° under nitrogen with an equimolar mixture of antimony pentachloride and hydrogen chloride in methylene chloride followed by addition of benzene failed to yield a crystalline derivative.

EXPERIMENTAL

General

All melting points were taken on a Fisher-Johns melting point apparatus and are uncorrected. Microanalyses were performed by Spang Microanalytical Laboratory, Ann Arbor, Michigan. Infrared (ir) spectra were recorded on a Beckman IR 9, IR 12 or a Perkin Elmer 21 spectrometer. Ultraviolet (uv) spectra were obtained on a Cary 14 spectrophotometer. Nuclear magnetic resonance (nmr) spectra were obtained on a Varian A-60 spectrophotometer in carbon tetrachloride using tetramethylsilane (TMS) as internal standard unless otherwise indicated. Mass spectra were obtained on an Atlas CH-4 mass spectrometer. Analytical gas chromatography was performed on an Aerograph Model 1520 utilizing a flame ionization detector. Preparative gas chromatography was performed on an Aerograph Model A-90-P. All reaction solvents were Baker reagent grade. Anhydrous magnesium sulfate was used for all drying operations unless otherwise indicated. All concentration of solutions was done at aspirator pressure with a water bath at 50°. All photolyses were done in Pyrex vessels and degassed prior to irradiation by bubbling nitrogen through the solution for 45 minutes.

Preparation of 2,5-dimethoxy-2,5-dihydrofuran

Into a water jacketed electrolysis cylinder (14 in x 2 1/2 in) containing a carbon rod (16 in x 1/2 in) anode and

a thin-walled brass tubing (12 in x 2 in) cathode, was placed a solution composed of 5.0 g ammonium bromide, 240 ml methanol and 68 g furan. The current was supplied by a battery charger (Montgomery Ward Model #16402 with a DC output of 6/12 volts and 4/4 amperes) set at an output of 12 volts. The reaction proceeded at 16±2° for approximately 24 hr or until nmr analysis indicated 95% conversion. This mixture was poured into 100 ml methanol in which 4 g sodium had been dissolved. The reaction mixture was concentrated, the sodium bromide filtered off and the remaining oil distilled through a six inch Vigreux column to give 90.2 g (69.5%) 2,5-dimethoxy-2,5-dihydrofuran, bp 45-48°/10 mm (lit. (82) bp 50-51°/13 mm).

Preparation of 6,6-dichloro-2,4-dimethoxy-3-oxabicyclo-[3.1.0]hexane

A slightly modified version of Maier and Sayrac (49,50) was used. To an ice cold solution of 150 g (2.78 mole) sodium methoxide, 300 g (2.31 mole) of 2,5-dimethoxy-2,5-dihydrofuran, and 1600 ml of olefin-free pentane contained in a Morton flask equipped with a high-speed stirrer and reflux condenser was added slowly 483 g (2.55 mole) of ethyl trichloroacetate. The reaction was stirred at 0° for 5 hr and the suspension was allowed to settle overnight at room temperature. The clear yellow solution was decanted from the finely divided sodium chloride, concentrated and fractionally distilled through a six inch Vigreux column. The first

fraction, 155 g, (bp 25-55°/14 mm) was discarded, the second fraction, 205 g, (bp 55-60°/14 mm) was 2,5-dimethoxy-2,5-dihydrofuran (lit. (82) bp 50-51°/13 mm), and the final fraction, 50.1 g (10.2%), (bp 50-55°/0.2 mm) was 6,6-dichloro-2,4-dimethoxy-3-oxabicyclo[3.1.0]hexane (lit. (49) bp 55-57°/0.5 mm).

Preparation of 2,4-dimethoxy-3-oxabicyclo[3.1.0]hexane

To a solution of 60.1 g (.284 mole) of 6,6-dichloro-2,4-dimethoxy-3-oxabicyclo[3.1.0]hexane, 88 g t-butanol, and 500 ml of anhydrous ether contained in a Morton flask equipped with a Herschberg stirrer, condenser and nitrogen inlet tube was added slowly 16.5 g (2.39 mole) of clean lithium in small pieces over a period of 3 hr. The resulting vigorous reaction was controlled by the judicious application of an ice bath. After the reaction subsided, the mixture was refluxed for 2 hr, cooled, filtered through glass wool to remove excess lithium and poured slowly into 300 ml of ice water. The ether layer was separated and the aqueous layer was extracted twice with ether. The combined ether fractions were washed twice with saturated sodium chloride solution and dried over anhydrous sodium sulfate. The solution was concentrated and vacuum distilled to give 27.3 g (67%) of 2,4-dimethoxy-3-oxabicyclo[3.1.0]hexane bp 64-66°/14 mm (lit. (49) bp 65-66°/14 mm).

Preparation of 9-methyl-9-azatricyclo[3.3.1.$0^{6,8}$]nonan-3-one

A solution of cis-cyclopropane-1,2-dicarboxaldehyde was prepared by heating on a steam bath 27.0 g (0.19 mole) of 2,4-dimethoxy-3-oxabicyclo[3.1.0]hexane with 270 ml 0.1 N sulfuric acid for ten minutes. This aqueous solution of dialdehyde was then added to a solution of 50.0 g (0.34 mole) recrystallized commercial acetonedicarboxylic acid, 23.5 g (0.35 mole) methylamine hydrochloride, and 43.0 g sodium dihydrogen phosphate in 4.5 l. water. The solution was adjusted to pH 5.5 with saturated sodium carbonate solution and stirred 72 hr at room temperature. The solution was then made basic to pH 10 with solid sodium carbonate, saturated with sodium chloride and continually extracted with ether for 48 hr. The ether was dried and concentrated to give a crude crystalline solid. Sublimation at 30°/0.20 mm gave 20.8 g (73%) of 9-methyl-9-azatricyclo[3.3.1.$0^{6,8}$]nonan-3-one, mp 69-70°.

The 9-methyl-9-azatricyclo[3.3.1.$0^{6,8}$]nonan-3-one was characterized by the following data: ir (KBr) (Figure 1, page 30) 3.48, 5.85, 7.40, 8.50, 9.90, 12.32 and 13.10 μ; nmr (CCl_4) (Figure 2, page 32) δ 3.20 (multiplet, 2H), 2.78-1.82 (complex multiplet, 7H), 1.22 (multiplet, 2H), 0.95 (multiplet, 1H), 0.21 (multiplet, 1H); uv max (95% ethanol) 250 nm (log ε 2.97), uv max (5% hydrochloric acid) 283 nm (log ε 1.28); mass spectrum (70 eV) m/e (relative

intensity) 151 (parent, 42), 150 (15), 111 (2), 110 (2), 109 (13), 108 (100), 107 (7), 95 (4), 94 (36), 83 (3), 82 (18), 81 (11), 80 (5), 68 (11), 57 (5) and 42 (65).

Anal. Calcd. for $C_9H_{13}NO$: C, 71.49; H, 8.67; N, 9.26. Found: C, 71.31; H, 8.66; N, 9.17.

Attempted reactions of 2,5-dimethoxy-2,5-dihydrofuran with the Simmons-Smith reagent

The zinc/copper couple was prepared by three different published procedures: washing zinc dust successively with 5% hydrochloric acid and 2% aqueous copper sulfate (83), adding zinc dust to hot glacial acetic acid containing cupric acetate (84), and by refluxing a suspension of zinc dust with cuprous chloride in diethyl ether (85). The resulting couple was treated with methylene iodide or with ethyl iodide and then methylene iodide in dry diethyl ether. To this solution was added 2,5-dimethoxy-2,5-dihydrofuran in ether or the couple was filtered through glass wool and then added to the 2,5-dimethoxy-2,5-dihydrofuran.

In all cases the reagent was reacted with a 50% excess of 2,5-dimethoxy-2,5-dihydrofuran and the mixture refluxed in ether for at least 72 hr. The reaction mixture was then poured into water. The ether layer was separated, dried over anhydrous sodium sulfate and concentrated to leave a nondistillable residue which was not investigated.

Preparation of 6,6-dichloro-2,4-dimethoxy-3-oxabicyclo[3.1.0]-hexane via chloroform and potassium t-butoxide

Dichlorocarbene was generated by the usual procedure (86) from 11.8 g (0.10 mole) chloroform and 11.2 g (0.10 mole) potassium t-butoxide in an ether solution of 28.8 g (0.20 mole) 2,5-dimethoxy-2,5-dihydrofuran. The reaction mixture was then treated with aqueous phosphoric acid and extracted with ether. The ether extract was dried, concentrated and fractionally distilled through a six inch Vigreux column. The initial fraction, 18.7 g (bp 48-52°/12 mm) was 2,5-dimethoxy-2,5-dihydrofuran (lit. (82) bp 50-51°/13 mm), and the final fraction, 1.50 g (7%) (bp 50-55°/0.5 mm) was 6,6-dichloro-2,4-dimethoxy-3-oxabicyclo[3.1.0]hexane (lit. (49) bp 55-57°/0.5 mm).

Attempted reaction of 2,5-dimethoxy-2,5-dihydrofuran with phenyl(bromodichloromethyl)mercury

Phenyl(bromodichloromethyl)mercury was prepared from phenylmercuric chloride, potassium t-butoxide and bromodichloromethane (87). The bromodichloromethane was prepared from bromoform, chloroform and aluminum chloride (88).

Into a flame dried flask was placed 42.1 g (0.096 mole) of phenyl(bromodichloromethyl)mercury, 37.2 g (0.29 mole) of 2,5-dimethoxy-2,5-dihydrofuran and 50 ml dry benzene. This reaction mixture was refluxed under nitrogen 1 hr during which time a flaky solid precipitated and the solution

darkened considerably. The reaction mixture was cooled, filtered and concentrated. (The precipitate, phenylmercuric bromide, was collected, dried and weighed, 30.1 g (94%), mp 284-285° (lit. (87) mp 286°)). Fractional vacuum distillation of the resulting oil gave 20.6 g (bp 47-53°/12 mm) 2,5-dimethoxy-2,5-dihydrofuran (lit. (82) bp 50-51°/13 mm) and 11.4 g (bp 40-54°/0.2 mm) of a red-yellow oil. The nmr spectrum of this oil indicated the total absence of the desired product and the oil was not investigated further. (The desired 6,6-dichloro-2,4-dimethoxy-3-oxabicyclo[3.1.0]-hexane was found to be stable under the reaction conditions in the presence of phenylmercuric bromide as evidenced by nmr spectroscopy).

Preparation of bicyclo[6.1.0]nona-2,4,6-triene

Cyclooctatetraene dianion was prepared by the method of LaLancette and Benson (89). It was then treated with methylene chloride as *per* Katz and Garratt (90). Typically, 10.4 g (0.10 mole) cyclooctatetraene gave 5.28 g (44.7%) of bicyclo[6.1.0]nona-2,4,6-triene, bp 45-48°/5.0 mm (lit. (90) bp 51°/7.0 mm).

Preparation of 9-methyl-9-azatricyclo[3.3.1.$0^{6,8}$]nonan-3-one via bicyclo[6.1.0]nona-2,4,6-triene

A solution of 1.18 g (0.10 mole) of bicyclo[6.1.0]nona-2,4,6-triene in methanol was ozonized with a Welsback

Ozonizer at -78° until the initially pale yellow solution turned a pale blue indicating an excess of ozone. Nitrogen was then bubbled through the solution to remove the excess ozone. The resulting clear solution was treated with 5 ml dimethyl sulfide at -60° for 1 hr, an additional 5 ml dimethyl sulfide was added and the solution allowed to warm to 0° and stirred for 1 hr, and finally allowed to warm to room temperature (91). The resulting solution was added to 4.00 g (0.027 mole) acetonedicarboxylic acid, 2.00 g (0.03 mole) methylamine hydrochloride and 4 g sodium dihydrogen phosphate in 1000 ml of water. The solution was adjusted to pH 5.5 with sodium carbonate and stirred 72 hr at ambient temperature. Workup as previously described yielded a red oil. This crude oil was extracted with hot hexane. Concentration of the extract gave 0.48 g (32%) of 9-methyl-9-azatricyclo[3.3.1.$0^{6,8}$]nonan-3-one identical by melting point and superimposability of the ir and nmr spectra to that previously described.

Preparation of 9,9-dimethyl-3-oxo-9-azoniatricyclo-[3.3.1.$0^{6,8}$]nonane tosylate

A 5.00 g (0.03 mole) sample of 9-methyl-9-azatricyclo-[3.3.1.$0^{6,8}$]nonan-3-one was heated at 96°±5° for 8 hr in 25 ml neat methyl tosylate. The resulting suspension was diluted with 50 ml dry ether and filtered under vacuum. The

solid was washed with ether and recrystallized from absolute ethanol to give 10.0 g (90.2%) 9,9-dimethyl-3-oxo-9-azoniatricyclo[3.3.1.$0^{6,8}$]nonane tosylate, mp 172.5-173.5°.

The 9,9-dimethyl-3-oxo-9-azoniatricyclo[3.3.1.$0^{6,8}$]-nonane tosylate was characterized by the following data: ir (KBr) (Figure 1, page 30) 3.45, 5.85, 8.45, 8.90, 9.65, 9.90, 10.87, 12.27 and 14.65 μ; nmr (D_2O, sodium 2,2-dimethyl-2-silapentane-5-sulfonate as internal reference) (Figure 2, page 32) δ 7.52 (AA'BB' multiplet, 4H), 4.22 (broad doublet, 2H), 3.50-2.75 (complex multiplet, 4H), 3.29 (broad singlet, 6H), 2.36 (singlet, 3H), 1.85 (broad multiplet, 2H), 1.58 (multiplet, 1H), and 0.85 (multiplet, 1H).

Anal. Calcd. for $C_{17}H_{23}NO_4S$: C, 60.51; H, 6.87; N, 4.15; S, 9.50. Found: C, 60.29; H, 6.89; N, 4.13; S, 9.54.

Preparation of 4,5-homotropone

A solution of 10.0 g (0.30 mole) of 9,9-dimethyl-3-oxo-9-azoniatricyclo[3.3.1.$0^{6,8}$]nonane tosylate and 20.0 g sodium bicarbonate in 40 ml water was rapidly steam distilled until 1000 ml of distillate was collected. The distillate was saturated with sodium chloride and continually extracted with ether for 24 hr. The resulting extract was washed twice with 50 ml portions of cold 5% hydrochloric acid, twice with cold 50 ml portions of saturated sodium

bicarbonate, and finally with 50 ml brine. The solution was dried, concentrated and the residual oil vacuum distilled to give 2.10 g (61%) of 4,5-homotropone as a pale yellow oil bp 70-72°/0.5 mm.

The 4,5-homotropone was characterized by the following data: ir (neat) (Figure 1, page 30) 3.32, 6.06, 6.24, 7.02, 7.72, 8.37, 13.3 and 14.1 μ; nmr (CS_2) (Figure 3, page 40) δ 6.65 (multiplets, 2H), 5.75 (doublet of multiplets, 2H, J ≈ 12.5 Hz), 1.90 (broad multiplet, 3H), and 0.45 (multiplet, 1H) (the nmr spectrum was unchanged over the range of +40° to -55°); uv max (95% ethanol) 264 nm (log ε 3.88) 290 nm (shoulder, 3.66) uv max (cyclohexane) 248 nm (3.89), 275 nm (shoulder, 3.65), 360 nm (1.52), 390 nm (shoulder, 1.29), 410 nm (shoulder, 0.80); mass spectrum (70 eV) m/e (relative intensity) 120 (parent, 17), 92 (100), 91 (70), 66 (18), 65 (38), 63 (16).

Anal. Calcd. for C_8H_8O: C, 79.97; H, 6.71. Found: C, 79.87; H, 6.80.

Hydrogenation of 4,5-homotropone

With an atmospheric-pressure hydrogenator, a suspension of 10 mg of 5% palladium/calcium carbonate in hexane was prereduced with hydrogen. To this was added a solution of 180 mg 4,5-homotropone in 15 ml hexane. After the uptake of hydrogen ceased (2.79 equivalents), the solution was filtered

through Celite and concentrated. Analytical gas chromatography indicated three components in the ratio of 1:7:2. Pure samples were obtained by preparative gas chromatography on a 10 ft x 3/8 in column with 15% Carbowax 20 M on 60-80 Chromosorb W. The first component was identified as 4-methylcycloheptanone on the basis of the following data: ir (neat) 3.43, 5.81, 6.84, 8.05, 8.64 μ. (The ir spectrum was identical to an authentic sample prepared by a known procedure (92).); semicarbazone derivative mp 157-158° (lit. (92) mp 159°) mixed melting point with an authentic sample mp 157-159°. The second component was identified as cyclooctanone on the basis of the following data: ir (neat) 3.42, 5.78, 6.80, 6.90, 7.51, 8.31, 8.90, 11.85 μ. (The ir spectrum was identical to a commercial (Aldrich) sample.); semicarbazone derivative mp 164-165° (lit. (93) mp 164-165°) mixed melting point with an authentic sample mp 164-165°. The third component was identified as bicyclo[5.1.0]octan-4-one on the basis of the following data: ir (neat) 3.42, 5.80, 6.82, 7.55, 8.78, 9.73 μ. (The ir spectrum was identical to that of an authentic sample prepared by a known procedure (94).); 2,4-dinitrophenylhydrazone mp 137-138° (lit. (94) mp 137.0-137.6°) mixed melting point with an authentic sample 136-138°.

Preparation of the 4-hydroxyhomotropylium cation

To 1/2 ml of cold concentrated sulfuric acid contained in a nmr tube was added 30 mg of 4,5-homotropone. The dark solution was shaken, a capillary tube containing tetramethylsilane was placed inside the nmr tube, and the spectrum recorded. The resulting nmr spectrum (Figure 3, page 40) exhibited signals at δ 8.7 (multiplet), 7.7 (multiplet), 4.9 (multiplet), 4.4 (multiplet), and 0.3 (multiplet).

The acid solution of the cation was carefully neutralized by addition to a cold saturated solution of sodium bicarbonate. The resulting solution was extracted with ether, dried, concentrated and distilled to give 9.0 mg (30%) of 4,5-homotropone as evidenced by the superimposability of the ir spectrum with that of an untreated sample.

Basicity of 4,5-homotropone

The spectrophotometric method used was that of Davis and Geissman (62). The absorption wavelengths, λ_i and λ_u, close to the points of maximal difference between the extinction coefficients, ε_i and ε_u, of the essentially completely ionized and nearly unionized species were selected at 310 nm and 270 nm, respectively, by comparison of the ultraviolet spectra of 4,5-homotropone in concentrated sulfuric acid and distilled water.

Aqueous sulfuric acid solutions ranging from 30% to 70% were prepared by dilution of Baker reagent grade sulfuric

acid. Exact concentrations were determined by titration with standard base. The H_o values of these solutions were obtained by interpolation from a standard curve constructed using the values of Paul and Long (95).

A 8.79×10^{-4} M aqueous stock solution of 4,5-homotropone was prepared in a 100 ml volumetric flask. One ml aliquotes of the stock solution were placed into 10 ml volumetric flasks and diluted with the appropriate acid solution. Five ml aliquotes of distilled water were placed into 50 ml volumetric flasks and also diluted with the appropriate acid solution. (These latter solutions were used as the reference solvent and titrated with standard base.) The ultraviolet absorption spectra of the diluted stock solutions with the appropriate reference solvents were recorded with a Cary 14 spectrophotometer.

The difference, $\Delta\bar{\varepsilon} = \bar{\varepsilon}_i - \bar{\varepsilon}_u$, was plotted against H_o and gave the sigmoidal curve shown in Figure 4a, page 46a. The $\bar{\varepsilon}_i$s were also plotted against H_o and gave the sigmoidal curve shown in Figure 4b, page 46c. The inflection points (where $H_o = pK_{BH^+}$) were taken at the mid-points of the 'straight-line' portions of the curves. The $pK_{BH^+} = -4.20$ of 4,5-homotropone was thus obtained.

Thermolysis of 4,5-homotropone in the vapor phase

A 1.076 g sample of 4,5-homotropone was pyrolyzed (590°, 2 μ pressure) on a vacuum pyrolysis apparatus (96). The crude pyrolyslate was analyzed by gas chromatography and

found to contain three components in the approximate ratio of 1:1:1. Pure samples of the three components were obtained by preparative gas chromatography using a 10 ft x 3/8 in column with 15% SE 30 on 60/80 Chromosorb W. The first component was identified as benzene by comparison of its ir and nmr spectra to those of an authentic sample. The second component was identified as o-vinyl phenol by the following data: ir (neat) 3.01, 3.41, 6.18, 6.25, 6.92, 8.18, 8.45, 8.95, 10.05, 10.70, 11.00, 11.90, 12.08, 13.15, 13.35 μ; nmr (CCl_4) δ 7.5-6.7 (complex multiplet, 6H (5H after treatment with deuterium oxide)), 5.67 (doublet of doublets, 1H, J = 17.5 Hz and J = 1.5 Hz), 5.18 (doublet of doublets, 1H, J = 10.5 Hz and J = 1.5 Hz). (The above spectra were identical to those of an authentic sample prepared by a known procedure (97).) The third component was identified as o-vinyl phenyl acetate by the following data: ir (neat) 3.40, 5.73, 6.20, 6.30, 6.81, 6.98, 7.39, 8.35, 8.56, 9.19, 9.96, 11.00, 12.12, 12.75, 13.13, 13.65 μ; nmr (CCl_4) δ 7.6-6.8 (complex multiplet, 4H), 6.72 (doublet of doublets, 1H, J = 17.5 Hz and J = 11.0 Hz), 5.64 (doublet of doublets, 1H, J = 17.5 Hz and J = 1.5 Hz), 5.22 (doublet of doublets, 1H, J = 11.0 Hz and J = 1.5 Hz), 2.16 (singlet, 3H). (The above spectra were identical to those of an authentic sample prepared by a known procedure (34).)

Qualitative thermolysis of 4,5-homotropone and 2,4,6-cyclooctatrienone at 400° in the vapor phase

A sample of 120 mg (1.0 mmole) 4,5-homotropone was pyrolyzed (400°, 2 μ pressure) on a vacuum pyrolysis apparatus. An nmr analysis of the crude pyrolyslate indicated approximately 7% conversion to products with no detectable amount of 2,4,6-cyclooctatrienone.

A sample of 120 mg (1.0 mmole) 2,4,6-cyclooctatrienone was pyrolyzed as described above. An nmr analysis of the crude pyrolyslate indicated complete conversion to products.

Photolysis of 4,5-homotropone in diethyl ether

A solution of 120 mg (1.0 mmole) 4,5-homotropone in 30 ml of ether contained in a large Pyrex test tube was irradiated in a Rayonette reactor using the 3500 Å lamps. Samples were withdrawn at one hour intervals and analyzed by thin layer chromatography on silica gel with 10% ethyl acetate/hexane as eluent. This analysis indicated a steady decrease of starting material while a pale yellow solid precipitated from the reaction. After 24 hr, the starting material was nearly totally destroyed. Concentration of the resulting solution gave 112 mg of a yellow solid. This material was insoluble in common solvents (carbon tetrachloride, chloroform, methylene chloride, acetone and water), did not melt below 300°, and its ir spectrum consisted of

a broad band between 6.2 and 13.5 μ. This material was not investigated further.

Qualitative irradiation of 4,5-homotropone in methanol

A solution of 150 mg 4,5-homotropone in 30 ml methanol contained in a large Pyrex test tube was irradiated in a Rayonette reactor using the 3500 Å lamps. The progress of the photolysis was monitored by periodically removing a small aliquot and analyzing the solution by gas chromatography with a 8 ft x 1/4 in column with 10% SF 96 on 60-80 Chromosorb W. The analysis indicated the slow formation of an initial photoproduct which reached a maximum concentration after approximately 7 hr. Further irradiation resulted in additional photoproducts.

Preparative photolysis of 4,5-homotropone in methanol

A solution of 760 mg (6.33 mmole) of 4,5-homotropone in 150 ml methanol was irradiated in a Pyrex vessel with the 3500 Å lamps of a Rayonette reactor. After 7 hr of irradiation, the reaction mixture was concentrated and chromatographed on 40 gm silica gel using 5% ethyl acetate/ hexane as eluent. After an initial forerun, 150 mg of a pale yellow oil was obtained. This oil was identified as 2,4,6-cyclooctatrienone by the following data: ir (neat) 3.38, 5.93, 6.07, 12.02 μ; nmr (CCl_4) δ 6.9-5.5 (complex multiplet, 6H), 3.05 (broad doublet, 2H, $J \approx 8.0$ Hz).

(The above spectra were superimposable with those of an authentic sample.) Continued elution produced 600 mg of 4,5-homotropone.

Qualitative irradiation of 4,5-homotropone and 2,4,6-cyclooctatrienone in methanol

Simultaneous irradiation of 0.05 M methanolic solutions of 4,5-homotropone and 2,4,6-cyclooctatrienone in separate Pyrex test tubes was conducted in a Rayonette reactor using the 3500 Å lamps. The progress of the photolysis was followed by removing aliquotes at one hour intervals and analyzing these aliquotes by analytical gas chromatography on a 8 ft x 1/4 in column with 10% SF 96 on 60-80 Chromosorb W. The analysis indicated the complete destruction of 4,5-homotropone after approximately 24 hours while 2,4,6-cyclooctatrienone was totally converted to products after approximately 4 hr. Furthermore, gas chromatographic traces of the two photolyses indicated no additional products were formed in the irradiation of 4,5-homotropone that were not present in the photolysis of 2,4,6-cyclooctatrienone.

Attempted reaction of 4,5-homotropone with dimethyl oxasulfonium methylide

A suspension of 6.4 g (0.05 mole) trimethyloxasulfonium chloride (80) and 2.25 g (0.053 mole) sodium hydride in

100 ml tetrahydrofuran was refluxed under nitrogen overnight. The resulting suspension was cooled, filtered, and stored under nitrogen at -15°. An aliquot of this solution was treated with water and titrated with standard acid and found to be 0.350 N with respect to ylide.

To 1.0 g (0.0084 mole) 4,5-homotropone in 12 ml dry tetrahydrofuran cooled under nitrogen in an ice bath was added 29.0 ml of 0.350 N ylide (0.01 mole) over 1/2 hr. The reaction mixture was stirred for 3 hr during which time a dark red, tarry material collected on the sides of the reaction flask. The reaction mixture was poured into water, extracted with ether, and dried. After concentration, a viscous red oil remained. Attempted molecular distillation yielded 6 mg of a material whose ir spectrum was identical to that of 4,5-homotropone.

Attempted reaction of 4,5-homotropone with hydrogen chloride and antimony pentachloride

A solution of 120 mg (1.0 mmole) of 4,5-homotropone in dry chloroform was added to a -78° solution of 178 mg (1.0 mmole) of antimony pentachloride and 36 mg (1.0 mmole) of dry hydrogen chloride in chloroform. After 1 hr at this temperature, the solution was allowed to warm to room temperature and 25 ml of dry benzene was added. A dark red oil separated which resisted all attempts at recrystallization.

PART II. SYNTHESIS AND REACTIONS OF 4,5-DIMETHYLENETROPONE

INTRODUCTION

Characterization of reactive molecules is an active area of investigation in organic chemistry. The development of low temperature spectroscopic techniques have enabled chemists to observe these reactive species and obtain insight to their structure and chemistry. Some molecules characterized by these techniques include trans-cycloheptenone, trans-cyclooctenone, trans,cis,cis-cyclooctatrienone, o-xylylene, cyclopentadienone, α-lactones, and a variety of ketenes. These reactive species were characterized utilizing the liquid nitrogen technique at 77°K. Some highly reactive molecules cannot be characterized at that temperature but require a more complex and sophisticated technique which utilizes matrix isolation and/or liquid helium temperatures. This latter technique has permitted the characterization of the long sought cyclobutadiene and benzyne.

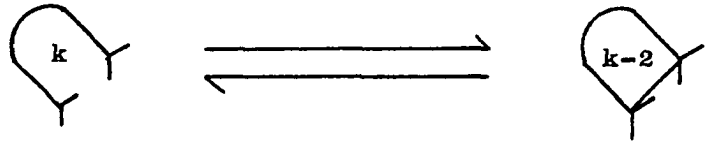
Although these techniques may appear as a panacea for the investigation of reactive molecules, they are presently limited to thermal or photochemical generation of the reactive species. However, this is not necessarily a severe restriction. The elucidation of the many cheletropic, electrocyclic, and sigmatropic reactions will permit further investigations of reactive species provided the appropriate precursor can be synthesized.

This portion of the present manuscript is concerned with the preparation of 4,5-dimethylenetropone as well as attempts to generate and trap tropoquino-4,5-dimethide. The synthesis of the former utilizes the tropane alkaloid degradation found useful for the preparation of 4,5-homotropone, while the generation of the latter utilizes the electrocyclic ring opening of cyclobutenes to generate a butadiene moiety. Electrocyclic ring opening of 4,5-dimethylenetropone would lead to tropoquino-4,5-dimethide, anticipated to be a highly reactive molecule. Successful Diels-Alder addition to the dimethide would lead to a variety of bicyclic tropones, while nucleophilic addition would provide a synthetic entry to a series of azulene derivatives.

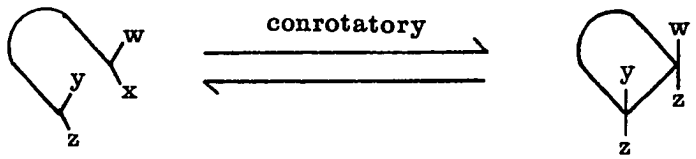
LITERATURE REVIEW

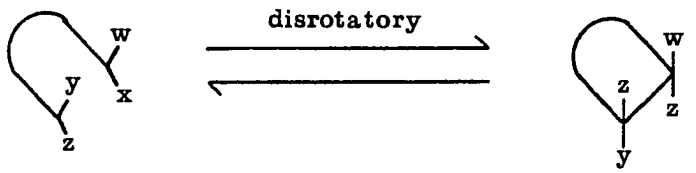
Olefins and polyolefins undergo many and varied concerted reactions which frequently proceed in a highly stereospecific manner. The synthetic utility of these reactions is unquestionable for they include the well-known Diels-Alder and Cope reactions and the Claisen rearrangement. A characteristic of these reactions is a negative entropy of activation, indicative of a high degree of order in the transition state.

Woodward and Hoffmann (75) interpreted these concerted reactions in terms of the symmetry properties of the reactant and product. The definitive rules which were developed are important for they not only explain the large majority of these reactions presently known, but also permit predictions to be made on reactions hitherto not investigated. Most germane to the present work is the electrocyclic reaction of the cyclobutene-butadiene interconversion. An electrocyclic reaction is defined as the formation of a single bond between the termini of a linear, conjugated system containing k π-electrons or the converse process. Two modes of closure are possible, conrotatory and disrotatory. The

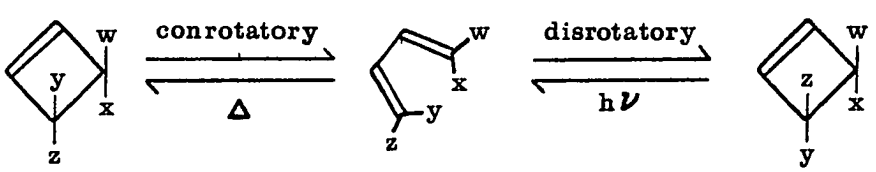


transition state of the former is characterized by a two-fold axis of symmetry while the latter is characterized by a plane of symmetry.

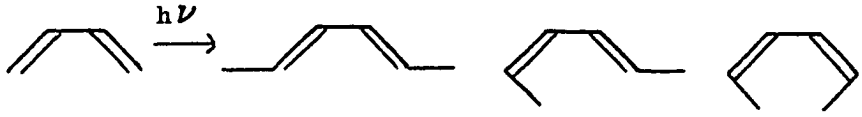




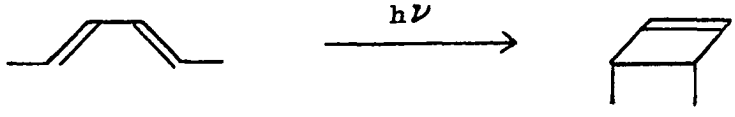
The stereochemical pathway is predominately determined by the symmetry properties of the highest occupied molecular orbital. Butadiene, with 4 π-electrons, has four molecular orbitals, X_1, X_2, X_3, and X_4. Thus, the thermal ground state reaction will be determined by X_2 while the photochemical excited state reaction will be determined by X_3. The development of a bonding interaction between the termini of X_2 can only occur <u>via</u> conrotatory motion and disrotatory motion for X_3. Thus for butadiene, thermal closure proceeds conrotatory and photochemical closure proceeds disrotatory.



Srinivasan (98) has demonstrated that irradiation with 2537 Å light of 2,4-hexadiene in ether rapidly led to a photostationary state. Furthermore, rate studies which were



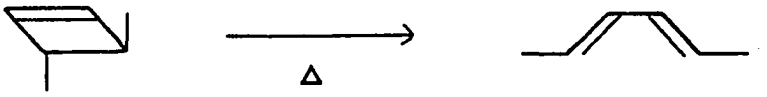
carried out separately on each of the three 2,4-hexadiene isomers at conversions (to all other isomers) of less than 10% showed that the rate of formation of cis-3,4-dimethylcyclobutene was detectable only when pure trans-trans-2,4-hexadiene



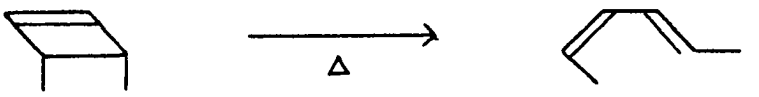
had accumulated. This is the first clear example that the photochemical closure of a 1,3-diene occurs by a disrotatory process in which the stereochemistry of reactant is known and the diene is linear without any constraints on the mode of closure.

Winter (99) investigated the thermal behavior of both cis and trans-3,4-dimethylcyclobutene and found that each isomer at 175° clearly furnished a single different

2,4-hexadiene derived from a conrotatory process. Thus, trans-3,4-dimethylcyclobutene produced trans,trans-2,4-hexa-

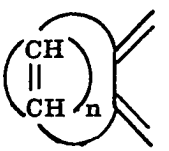


diene while cis-3,4-dimethylcyclobutene gave cis-trans-2,4-

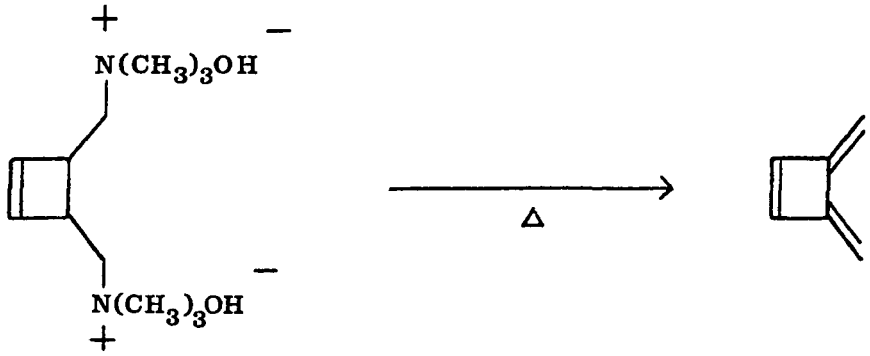


hexadiene.

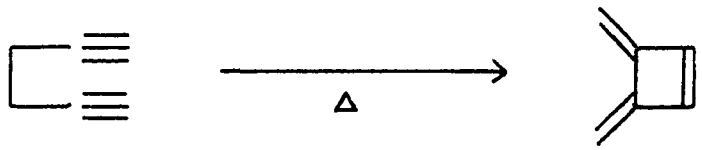
It is interesting to compare the reactivities of a series of cyclic vinylogues which include the butadiene moiety as 1,2 bis exo methylenes.



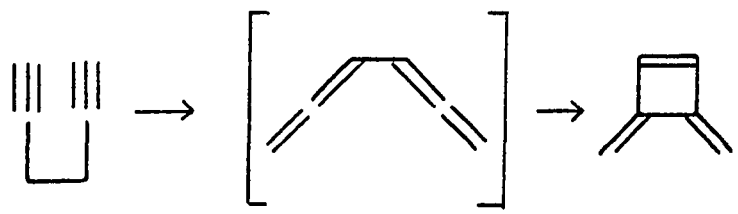
3,4-Dimethylenecyclobutene was initially synthesized in low yield via a thermal degradation of a bis quaternary hydroxide (100). Subsequently, the vapor phase thermal



rearrangement of hexa-1,5-diyne at 350° gave dimethylene-cyclobutene in 85% yield. It was demonstrated that the

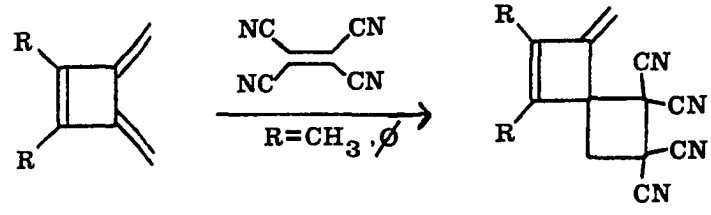


reaction follows a first order rate law and suggested that the large entropy of activation (-9.4 e. u. at 232°) places the rearrangement in the same category as the Cope and other rearrangements which are believed to possess cyclic transition states. The overall process for the formation of dimethylene-cyclobutene was suggested to consist of a Cope-type

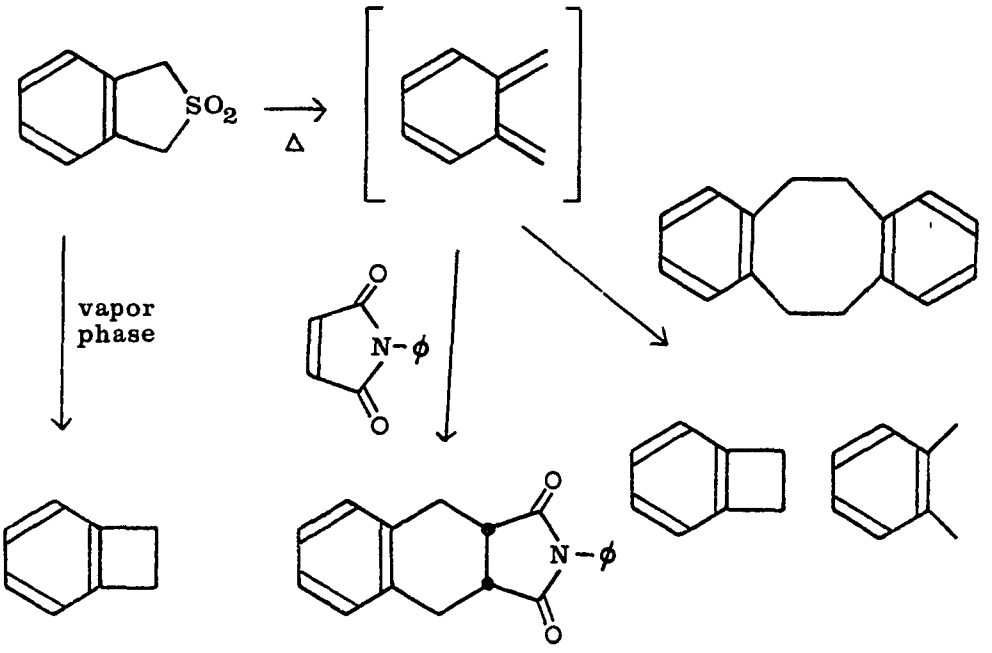


rearrangement followed by an electrocyclization of the resulting diallene with conrotation of the terminal methylene groups (101).

Attempted Diels-Alder reactions of dimethylenecyclobutene yielded only a copolymer with maleic anhydride and no reaction with N-phenylmaliemide and tetracyanoethylene under a variety of reaction conditions (102). The lack of reaction with tetracyanoethylene contrasts the results observed with 1,2-diphenyl-3,4-dimethylenecyclobutene (103) and 1,2-dimethyl-3,4-dimethylenecyclobutene (104). They failed to yield Diels-Alder adducts and gave instead 2 + 2 adducts.

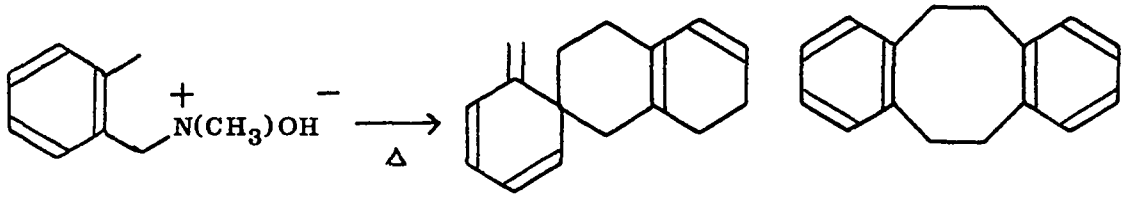


Heating 1,3-dihydroisothianaphthene-2,2-dioxide in a molten state at 280° resulted in the evolution of sulfur dioxide and a volatile liquid (16%) which was analyzed as a 4:2 mixture of benzocyclobutene and o-xylene. In addition, a 4% yield of 1,2,5,6-dibenzocyclooctadiene was obtained from the residue. Vapor phase pyrolysis led to a 67% yield of benzocyclobutene. The isolated products were rationalized on the basis of o-xylylene as an intermediate. Support for the



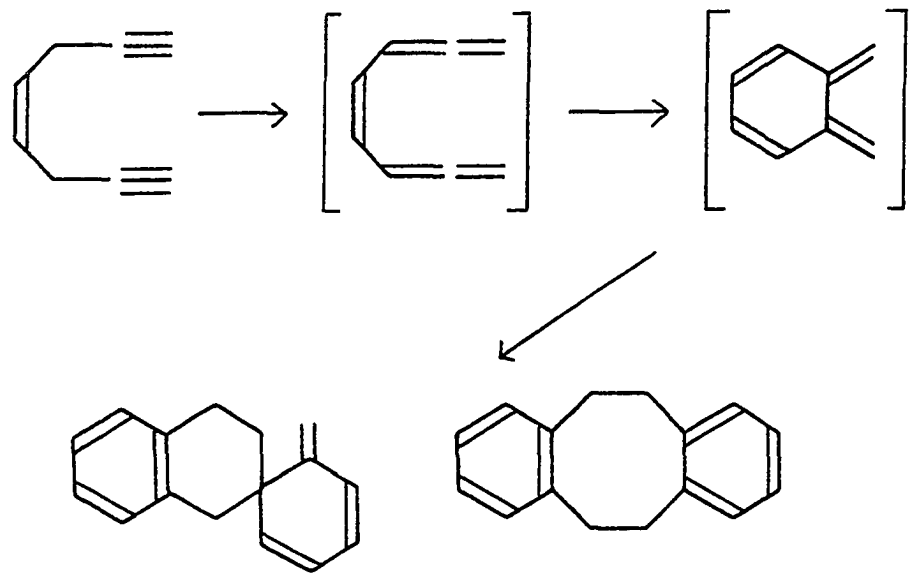
proposed intermediate was obtained by heating an intimate mixture of the dioxide with N-phenylmaliemide which yielded the Diels-Alder adduct of the o-xylylene (105).

Errede (106) observed that the Hofmann degradation of o-methylbenzyltrimethylammonium hydroxide at low pressure in a modified flow system generated o-xylylene. The condensate was collected in a cold trap and warmed to ambient temperature. Under these conditions two dimers were isolated, a spiro-o-xylylene (61%) and 1,2,5,6-dibenzocyclooctadiene (20%).



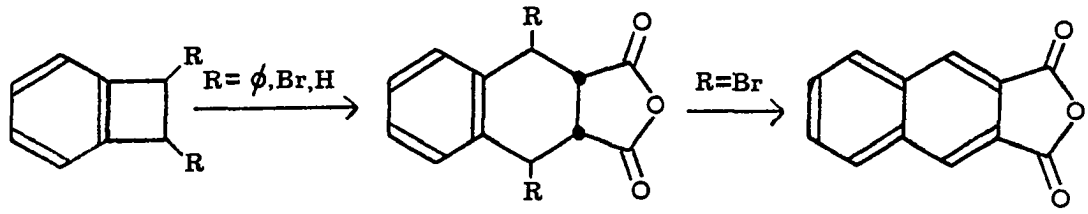
Since the ultimate fate of o-xylylene was greatly dependent on the reaction conditions prevailing after its presumed generation, it was suggested that low temperature dimerization produced the spiro-o-xylylene, medium temperature produced the dibenzocyclooctadiene and high temperatures yielded benzocyclobutene.

Efraim and Sondheimer (107) found that isomerization of cis-4-octen-1,7-diyne with potassium t-butoxide in t-butanol at 50-65° for 15 minutes gave rise to two aromatic dimers

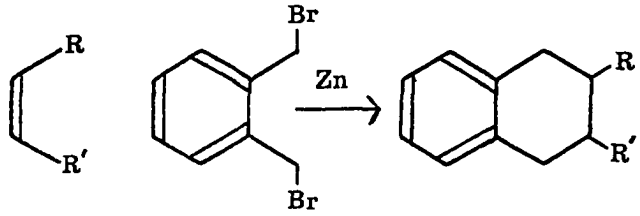


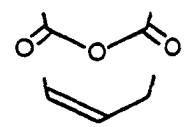
besides conjugated linear monomeric products. These dimers were the same dimers isolated in previous experiments which generated o-xylylene. The reaction was believed to be analogous to the thermal isomerization of hexa-1,5-diyne, vida supra. In the present case the reaction was believed to proceed to the diallene which underwent thermal cyclization to o-xylylene followed by dimerization.

Jensen and coworkers (108) reported that substituted benzocyclobutenes readily gave apparent Diels-Alder adducts upon heating with maleic anhydride. Similar adducts were

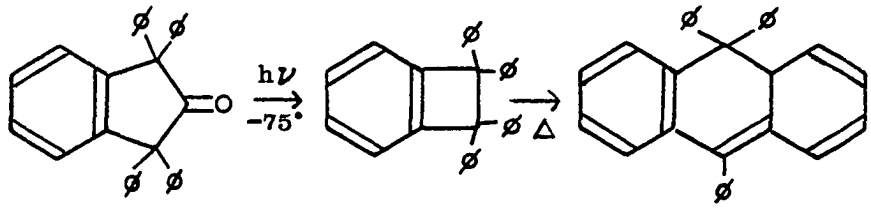


observed in the reduction of o-xylene dibromide with zinc in the presence of a variety of dienophiles (109).

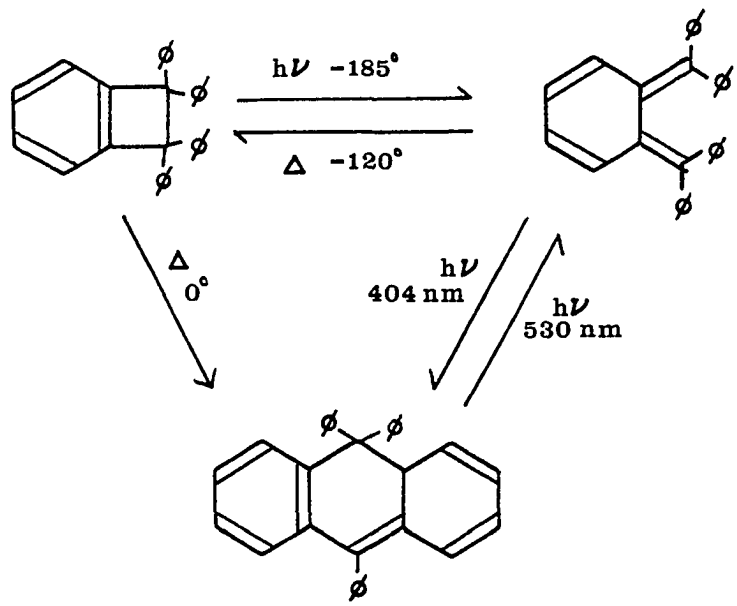


R	R'	Yield
CN	H	80%
CO_2Et	H	60%
CHO	H	40%
		93%
		40%

Photodecarbonylation at -75° of tetraphenyl-2-indanone gave rise to tetraphenylbenzocyclobutene which thermally

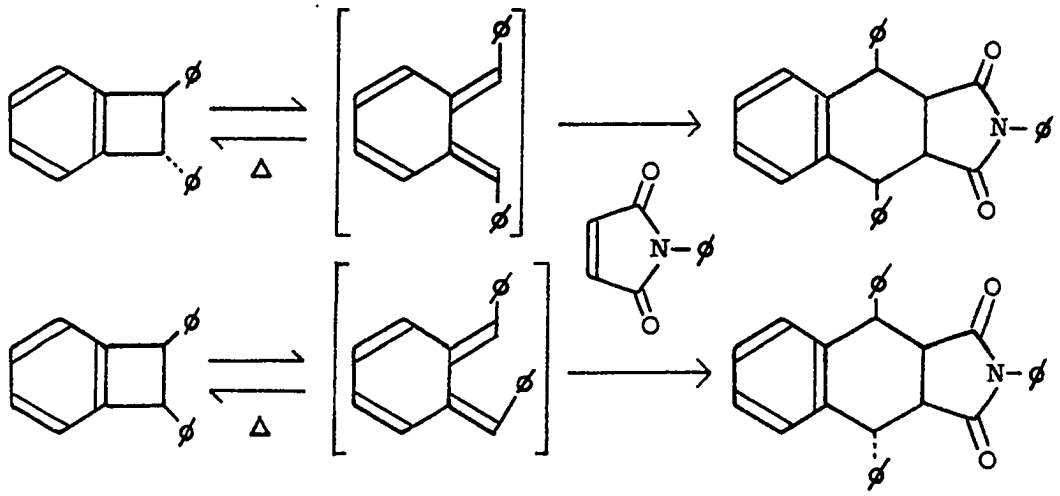


rearranged to 9,9-diphenyl-8a,9-dihydroanthracene. Continued irradiation of tetraphenylbenzocyclobutene at -185° produced 7,7,8,8-tetraphenyl-o-quinodimethane as evidenced by low temperature absorption spectroscopy. Thermal cyclization of this intermediate afforded, depending on the temperature used, the cyclo isomers, benzocyclobutene or a dihydroanthracene. These were interpreted as being the kinetically or thermodynamically determined products, respectively (110).



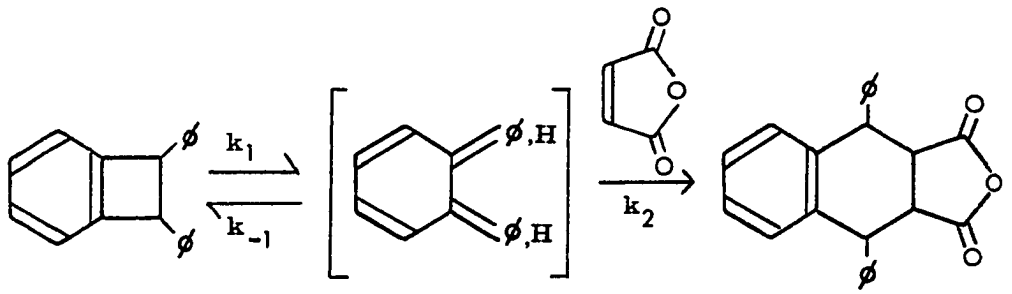
Furthermore, flash photolysis of these cyclo isomers revealed the presence of the common o-xylylene intermediate which rapidly cyclized to the benzocyclobutene [τ = 3.6 x 10^{-5} sec at 23°; Arrhenius activation parameters: E = 15.3 kcal/mole, A = 3.2 x 10^{15} sec^{-1} (measured between -53° and +23°)] while the formation of the dihydroanthracene from the benzocyclobutene was relatively slow (111).

The stereochemistry of the Diels-Alder reaction of the isomeric cis and trans diphenylcyclobutenes indicated that the thermal electrocyclic ring opening is stereospecific. Thus, the trans diphenylcyclobutene gave one diasteromeric adduct



while the cis isomer gave a different diasteromer. The structures of the adducts were determined by chemical and spectroscopic data (112).

The kinetics of the Diels-Alder reaction of the isomeric diphenylcyclobutenes with excess maleic anhydride in toluene at 50° were followed dilatometrically and the pseudo-first-

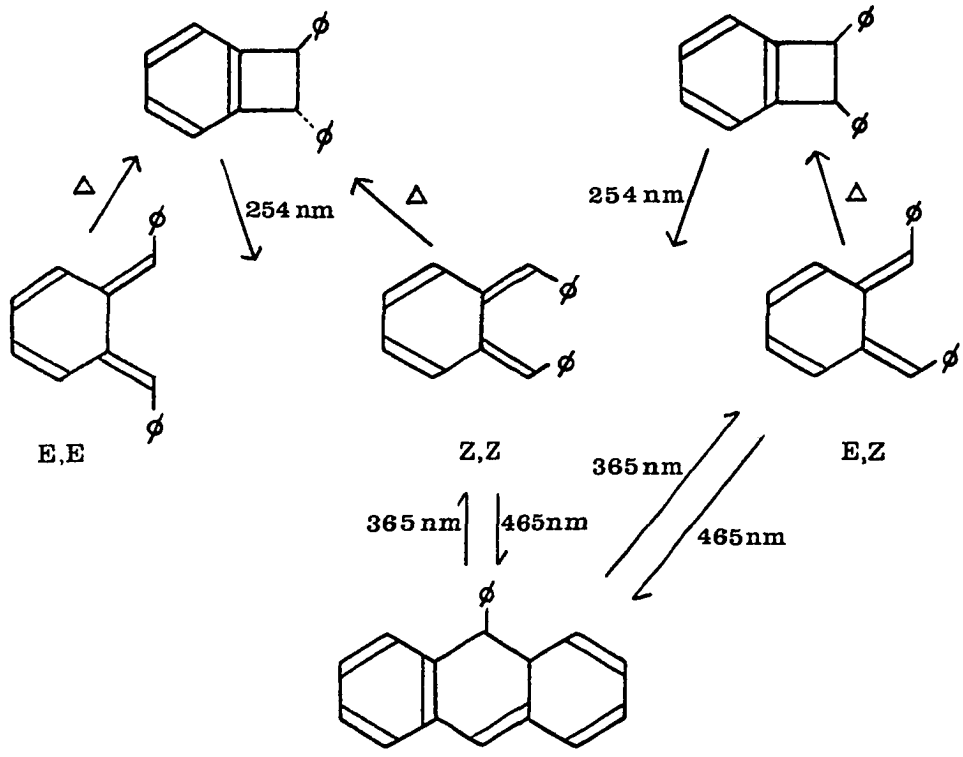


order rate constant k_D measured. A plot of k_D against maleic anhydride concentration [D] gave a curve tending to plateau

at high values of [D] indicating that not only the bimolecular Diels-Alder reaction k_2 but also the proposed valence tautomerization k_1 codetermined the k_D value. Use of the Bodenstein theorem showed k_D as a linear function of $k_D/[D]$. The ring opening of the cis isomer was found to be 70 times slower than for the trans isomer at various temperatures. It was also observed that the cis isomer in refluxing carbon tetrachloride was isomerized to the trans isomer. However, the diastereomeric adducts isolated in 95-100% yield indicated that the Diels-Alder reaction of the isomeric o-xylylenes is much faster than stereoisomerization (113).

Irradiation of the isomeric diphenylcyclobutene derivatives at -189° consecutively with 254 and 365 nm light produced o-quinodimethanes. The photoproducts obtained from the two isomers were not identical but contained different proportions of photocycloizable and nonphotocyclizable fractions as evidenced by irradiation with 465 nm light which caused seco-cyclo isomerization to the isodihydroanthracene. The fraction able to photocyclize was attributed to the E,Z and/or Z,Z configuration while the E,E configuration was attributed to the photostable fraction. A cis-trans isomerization of the reactants was eliminated for the exact composition of the photoproducts was a function of reactant configuration. Moreover, the composition was controlled by the viscosity of the medium but was independent of the

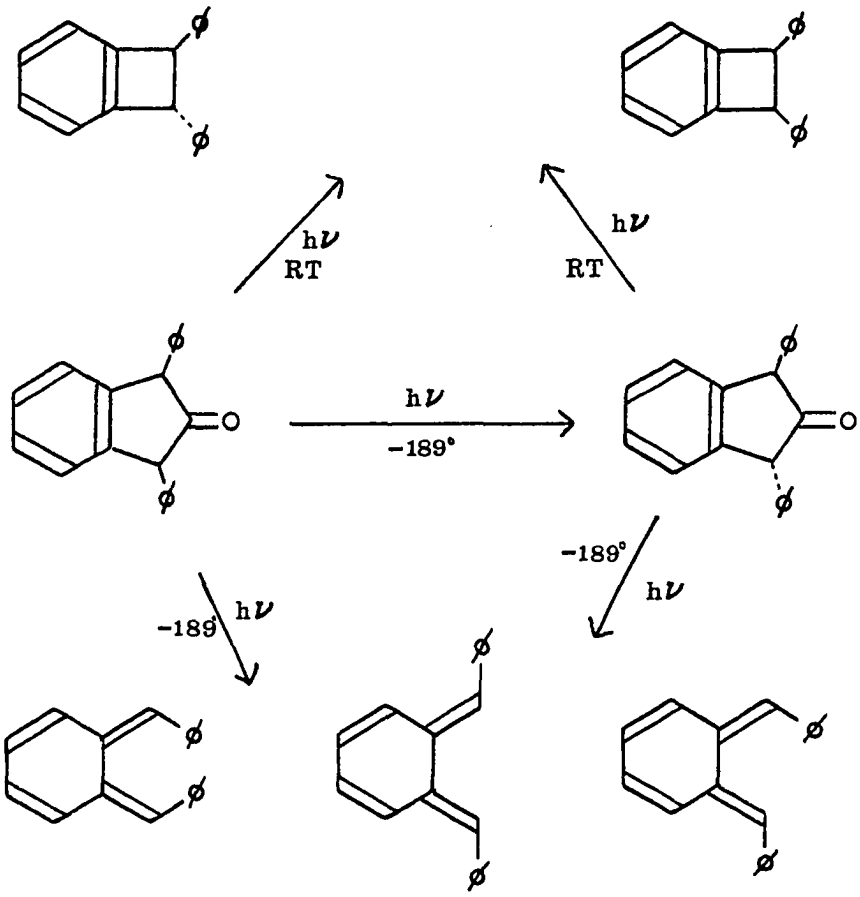
progress of the reaction. A photostereomutation of the E,E configuration to the E,Z and/or Z,Z configuration and vice



versa was also eliminated for the isodihydroanthracene products were not changed whether or not the irradiation with 465 nm light was preceded by treatment with 485, 475, 365, 313, or 254 nm light. Since the E,E fraction was obtained from both isomers, the light induced ring opening is nonstereospecific (114).

Irradiation of the symmetric diphenyl-2-indanones at room temperature produced a mixture of the diphenyl

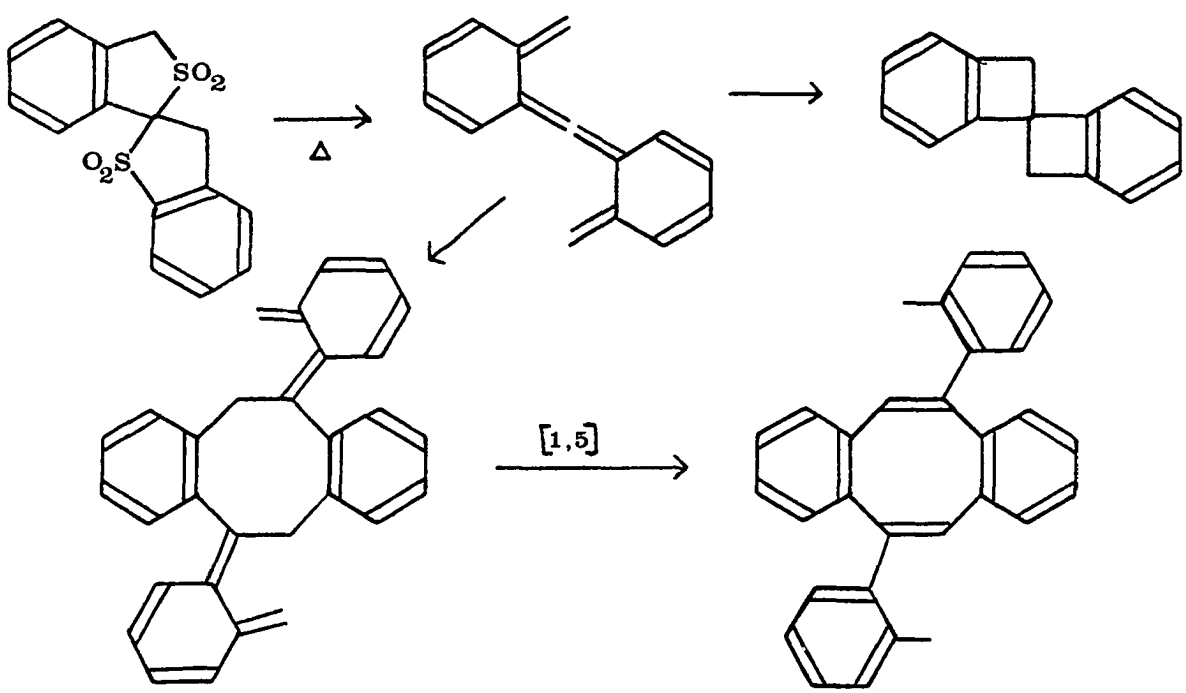
benzocyclobutenes. Photodecarbonylation in hydrocarbon mixtures at -189° with 313 nm light afforded a mixture of the isomeric o-quinodimethanes. The E,E configuration was formed from the cis isomer in 61.5% yield and in 95% yield from the trans isomer. A stepwise monitoring of the reaction showed



that the ratio of the two configurational types formed from the trans isomer was independent of the progress of the reaction. However, the product composition of the cis isomer was a function of the irradiation time since a photostereomutation of the starting material took place. In this latter

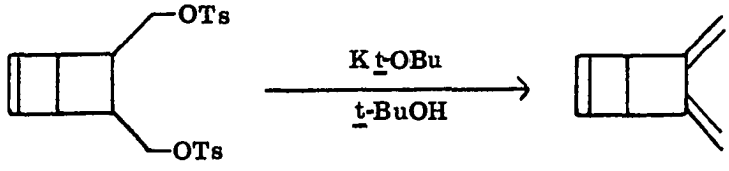
case, extrapolation to zero time demonstrated that the initially formed products are almost exclusively o-quinodimethanes having the photocyclizable configuration. It was further demonstrated that in the case of the cis isomer, photostereomutation and photodecarbonylation resulted from the same electronically excited singlet state. This verified a stepwise noncheletropic light induced carbon monoxide elimination (115,116).

Cava and Kuczkowski (117) reported the isolation of two hydrocarbon products generated in the gas phase pyrolysis of the spirobisulfone depicted below. Thermal extrusion of sulfur dioxide produced the allenic o-xylylene which underwent

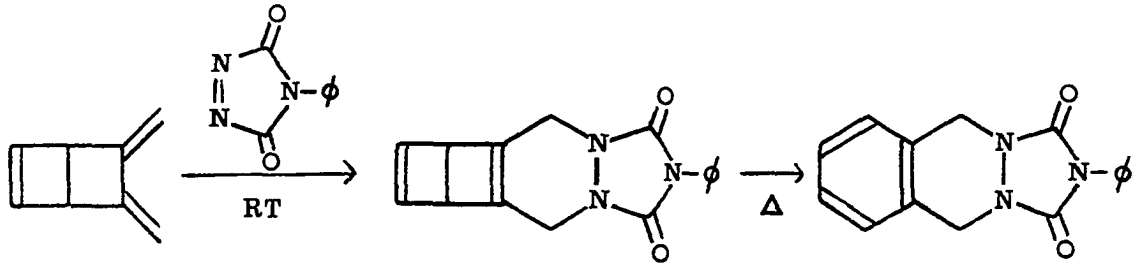


intramolecular cyclization to give the spirobibenzocyclobutene and an intermolecular nonconcerted [4 + 4] addition product. This 4 + 4 adduct then underwent two sigmatropic-[1,5]-hydrogen shifts to give the observed dimer.

Dewar o-xylylene has recently been prepared and characterized. Unlike o-xylylene itself, the Dewar isomer is

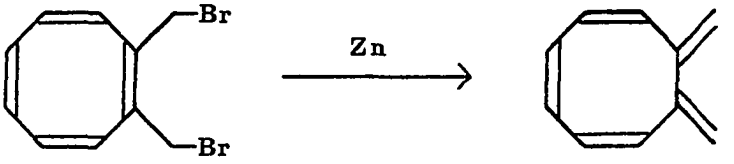


thermally stable at room temperature but with decomposition perceptible at 60°. Treatment with 2-phenyl-2,4,5-triazoline-

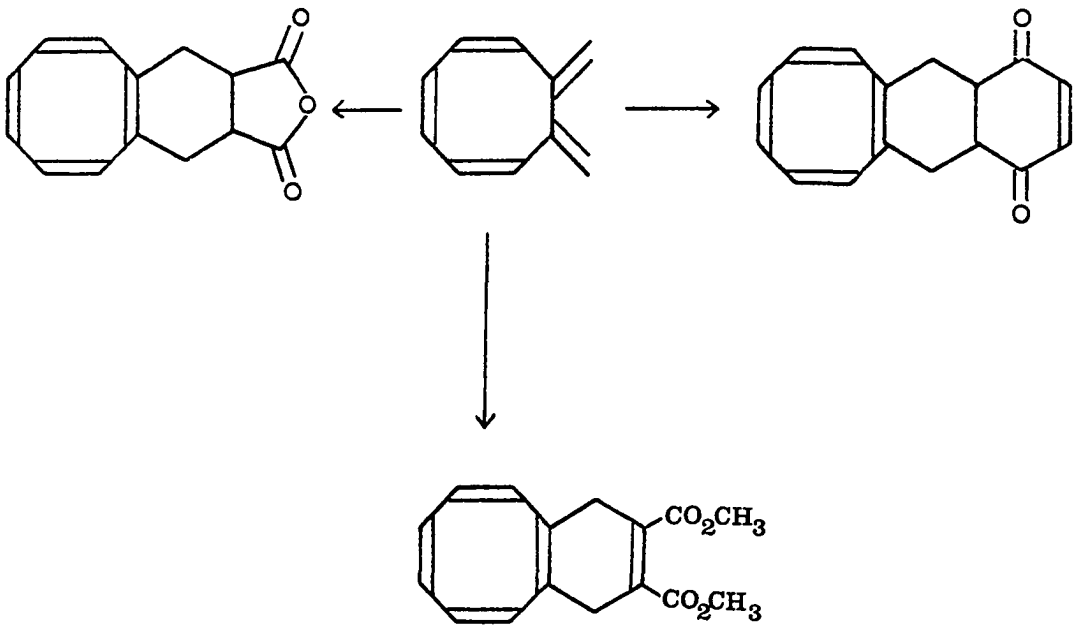


1,3-dione yielded the Diels-Alder adduct which upon brief warming gave the benzenoid adduct (118).

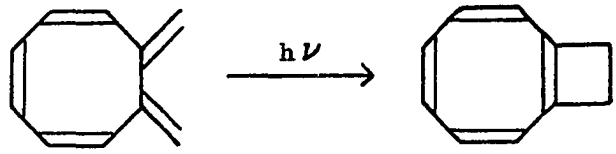
The synthesis of 7,8-dimethylene-1,3,5-cyclooctatriene was reported via treatment of 1,2-bis(bromomethyl)cyclo-octatetraene with zinc in dimethylformamide at room temperature (119). The exocyclic double bonds were the most



reactive diene system in thermal 1,4 cycloadditions and added readily to a variety of dienophiles. Thus, in refluxing cyclohexane, adducts were obtained with maleic anhydride (37%), p-benzoquinone (34%), and dimethylacetylene-dicarboxylate (52%).

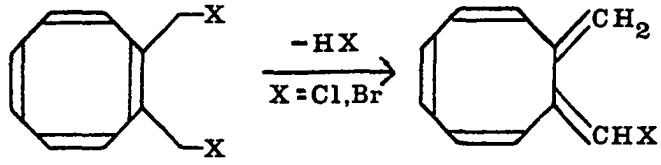


Irradiation of a solution of the dimethylenecyclo-octatriene in methanol at ambient temperature led to



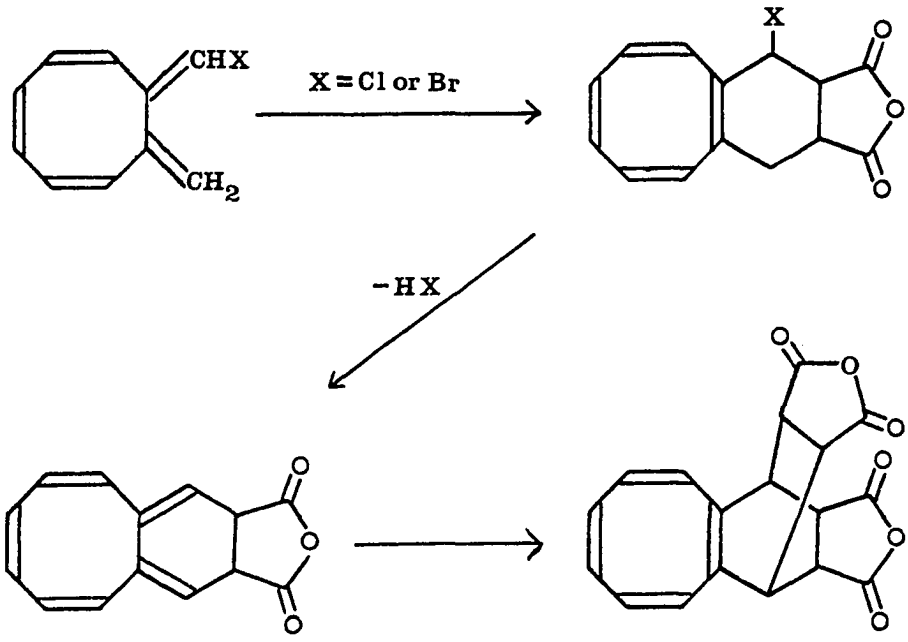
bicyclo[6.2.0]deca-1,3,5,7-tetraene in 10% yield as the only nonpolymeric product isolated. The material was a yellow oil which was stable in dilute carbon tetrachloride solution but rapidly decomposed in the neat at room temperature. The structural assignment was based on spectroscopic data and the results of catalytic hydrogenation.

The 7-methylene-8-halomethylene-1,3,5-cyclooctatrienes were prepared by dehydrohalogenation of the bis(halomethyl)-cyclooctatetraene. The bromopentaene consisted of a single



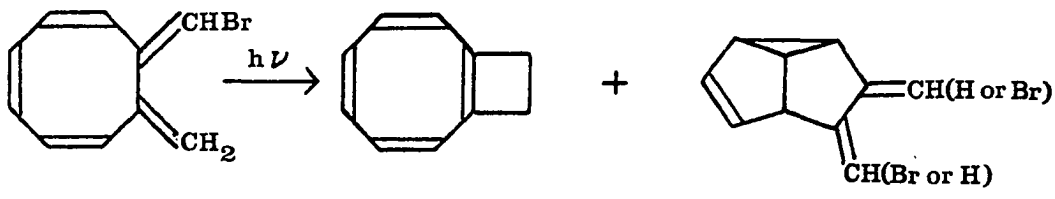
stereoisomer whereas the chloropentaene was a 1:1 mixture of the two stereoisomers.

The Diels-Alder reaction of the methylene halomethylene cyclooctatrienes with excess maleic anhydride in refluxing cyclohexane did not lead to the simple 1:1 adducts but gave



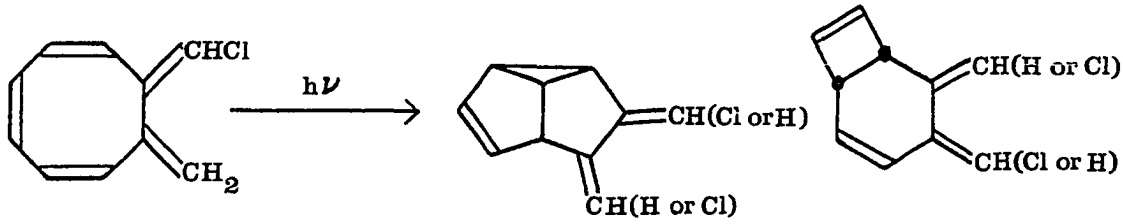
bis adducts. Presumably the initially formed mono-adduct suffered dehydrohalogenation under the reaction conditions to give a dimethylenecyclooctatriene which then reacted with a second molecule of maleic anhydride (120).

Irradiation of the methylene bromomethylene cycloocta-triene led to bicyclo[6.2.0]tetraene (7%) and a tricyclic



isomer (1%) for which it was not possible to determine which of the two exocyclic carbon atoms was bonded to a bromine.

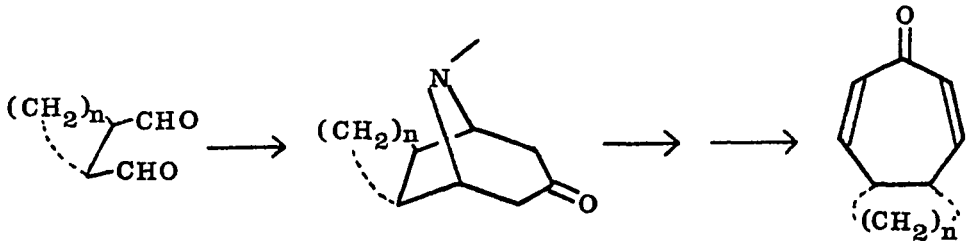
Similar irradiation of the chloromethylene derivative resulted in no appreciable carbon-chlorine bond cleavage. The endocyclic triene system was now more photolabile than the exocyclic chlorodiene system and gave a 10.9% yield of a tricyclic isomer as well as a 2.8% yield of a bicyclic isomer. The structures of the products were based on spectroscopic properties and Diels-Alder reactions but again



in neither case was it possible to determine which of the two exocyclic methylene carbons was bonded to chlorine (121).

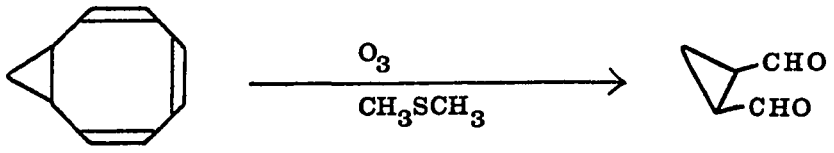
RESULTS AND DISCUSSION

The synthesis of 4,5-dimethylenetropone was based on the initial observation that base-catalyzed degradation of tropinone methiodide gave a mixture of isomeric cycloheptadienones (2). Furthermore, the successful preparation of 4,5-homotropone, as discussed in Part I, as well as the synthesis of 4,5-trimethylenetropone (122) suggested that

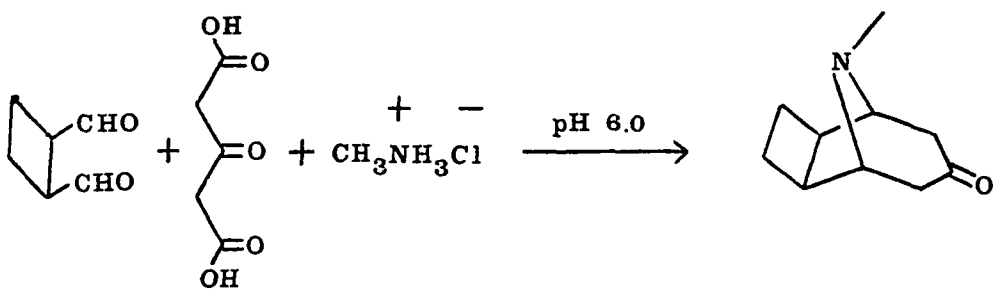


the tropane alkaloid degradation procedure provided a workable synthetic scheme.

The required dialdehyde precursor appeared accessible in light of the generation of cis-1,2-cyclopropane dicarboxyaldehyde via ozonolysis of bicyclo[6.1.0]nona-2,4,6-triene



and the reported synthesis (123) of bicyclo[6.2.0]deca-2,4,6-triene. This latter triene was ozonized and reacted with dimethyl sulfide. The resulting solution was treated with methylamine hydrochloride and acetonedicarboxylic acid in an aqueous solution buffered at pH 6.0 to give an aminoketone,



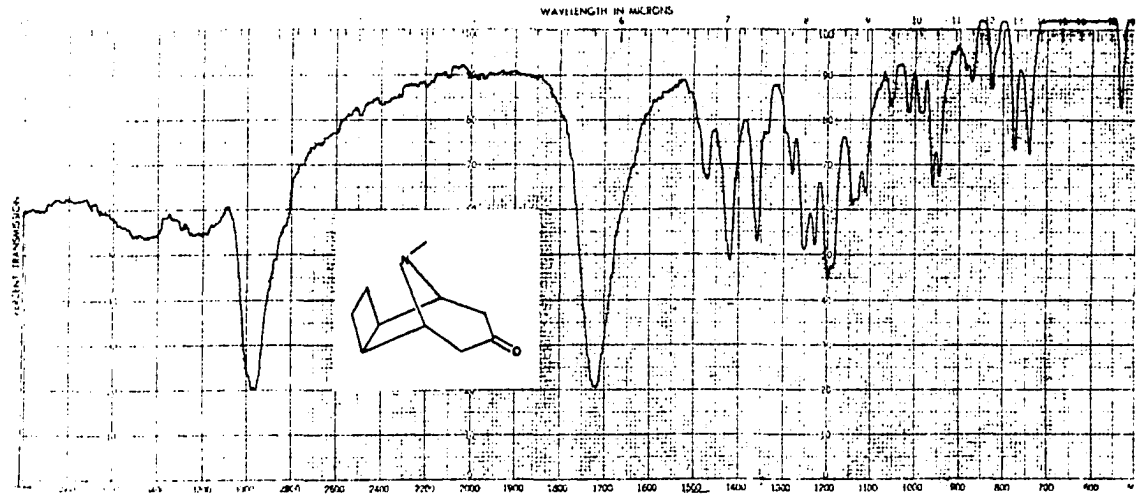
mp 89-90°, in 73.4% overall yield from the bicyclic triene. The stereochemistry of the aminoketone (dimethylene bridge cis to the nitrogen bridge) is assigned by analogy to other products derived from Robinson Schöpf condensations (55). The ir spectrum (Figure 6, page 111) of the aminoketone shows significant bands at 3.36 μ (C-H) and 5.80 μ (C=O). The nmr spectrum (Figure 7, page 113) has signals at δ 3.12 (multiplet, 2H) pyrrolidine-piperidone bridgehead hydrogens, and δ 2.8-1.5 (complex multiplet, 13H) N-methyl, methylene hydrogens adjacent to the carbonyl and cyclobutane hydrogens. The ultraviolet spectrum (95% ethanol) shows a strong charge-transfer band at 248 nm (log ε 3.09) and no perceptible $n \rightarrow \pi^*$ transition.

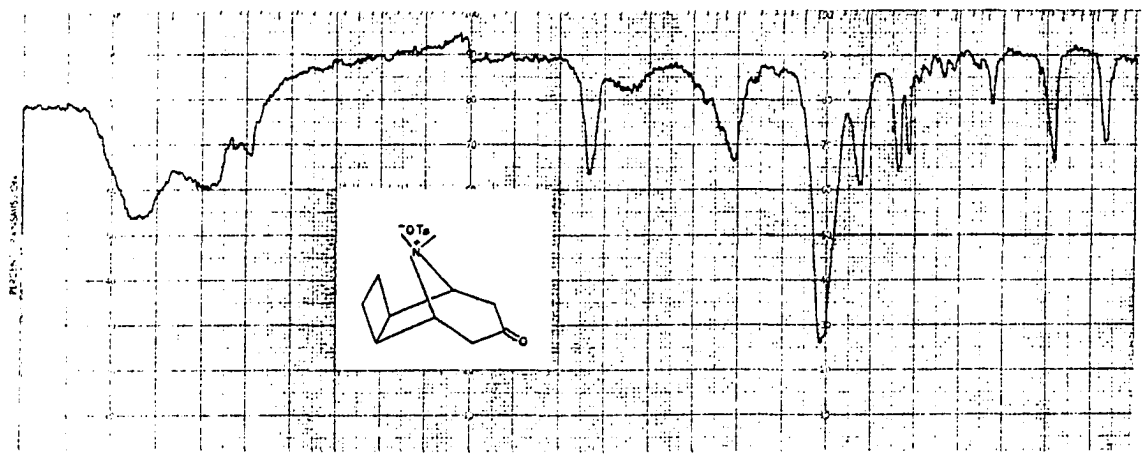
Figure 6. Infrared spectra

Top: Aminoketone (10-methyl-10-azatricyclo[4.3.1.$0^{2,5}$]decan-8-one)

Middle: Quaternary tosylate (10,10-dimethyl-8-oxo-10-azoniatricyclo[4.3.1.$0^{2,5}$]-decane tosylate)

Bottom: Bicyclo[5.2.0]nona-2,5-dien-4-one


WAVELENGTH IN MICRONS


OTs

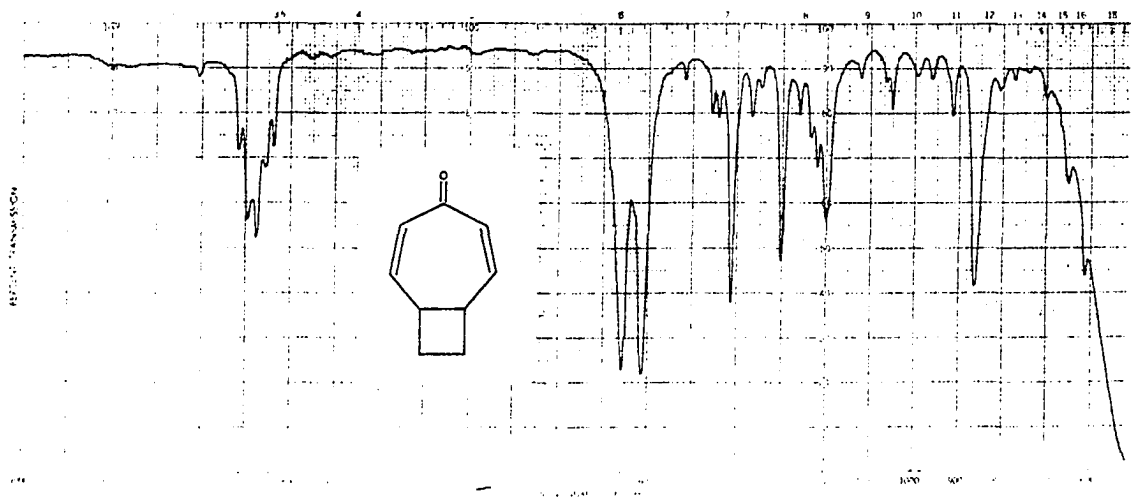
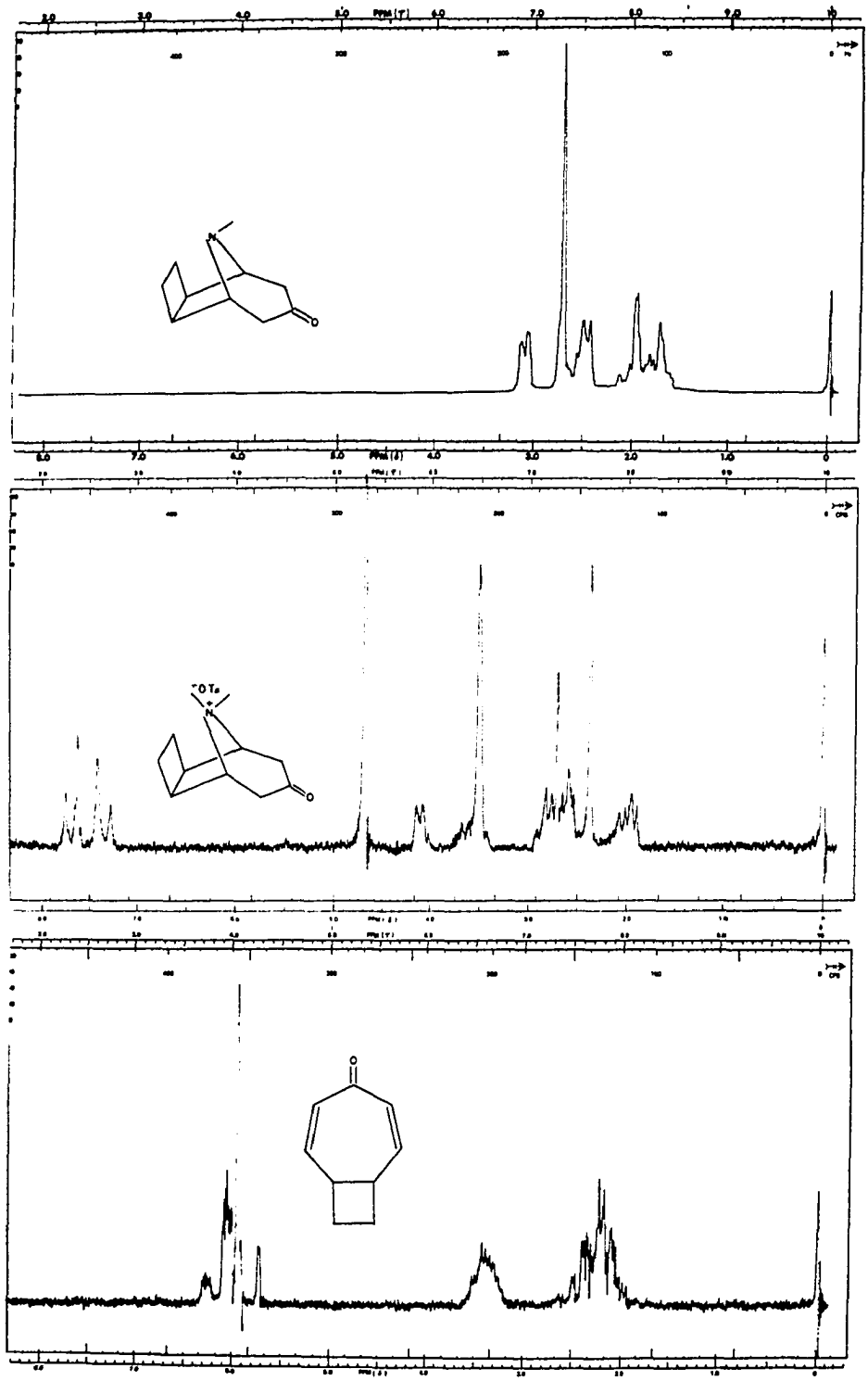


Figure 7. Nuclear magnetic resonance spectra

Top: Aminoketone (10-methyl-10-azatricyclo-[4.3.1.$0^{2,5}$]decan-8-one)

Middle: Quaternary tosylate (10,10-dimethyl-8-oxo-10-azoniatricyclo[4.3.1.$0^{2,5}$]-decane tosylate)

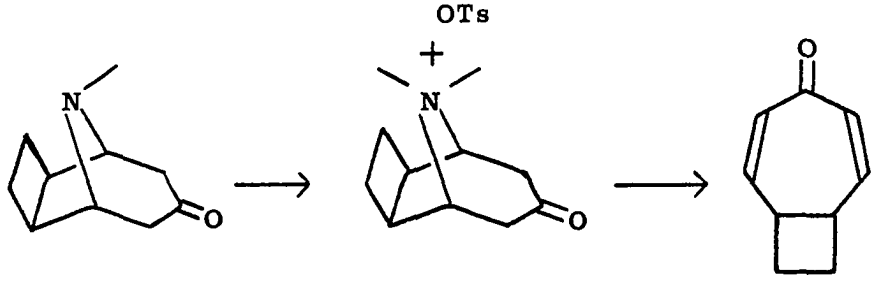
Bottom: Bicyclo[5.2.0]nona-2,5-dien-4-one



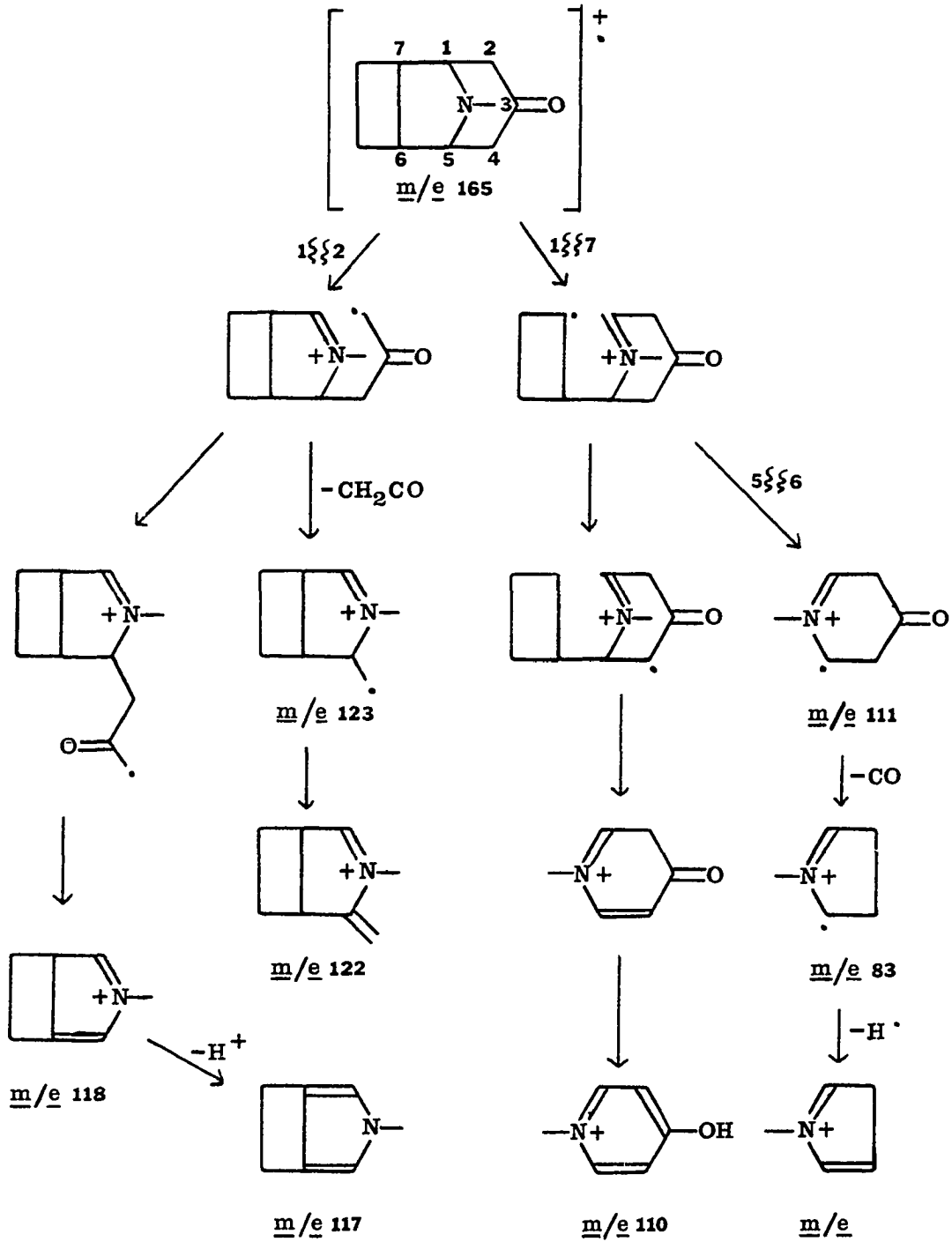
The mass spectrum m/e (relative intensity) of the aminoketone is in complete accord with the tropane alkaloid structure (54). The aminoketone shows a parent ion at 165 (85). Cleavage of the 1,2-bond produces ions 111 (3), 110 (59), 83 (11), and 82 (16). Cleavage of the 1,7-bond with subsequent transformations as depicted (Scheme 2, page 116) produces ions 123 (3), 122 (76), 108 (39), and 107 (3). Two ions present in the spectra of all tropane alkaloids, namely the N-methyl pyridinium cation, 94 (100), and the species $CH_3-\overset{+}{N}\equiv C-H$, 42 (22), are also present.

Quaternization of the aminoketone was achieved by heating a sample at 60° for six hours in neat methyl tosylate. The quaternary tosylate was obtained in 89% yield as white plates, mp 186-187°, after two recrystallizations from absolute ethanol.

The quaternary tosylate was degraded by rapidly stirring a mixture of the quaternary tosylate, sodium bicarbonate, ether, and water for 36 hours. The ether layer was separated, washed, dried, concentrated and vacuum distilled to give bicyclo[5.2.0]nona-2,5-dien-4-one, bp 78-79°/0.7 mm in 33% yield.

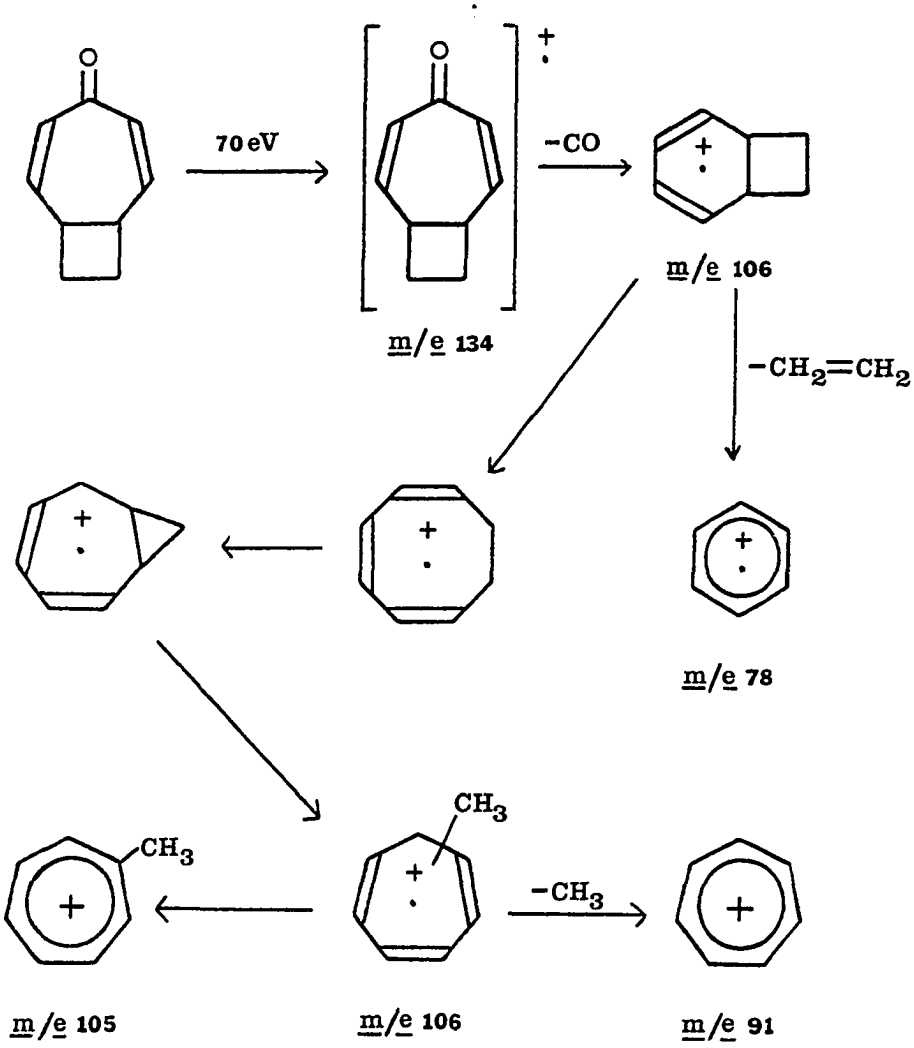


Scheme 2. Mass fragmentation scheme for aminoketone (10-methyl-10-azatricyclo[4.3.1.$0^{2,5}$]decan-8-one)

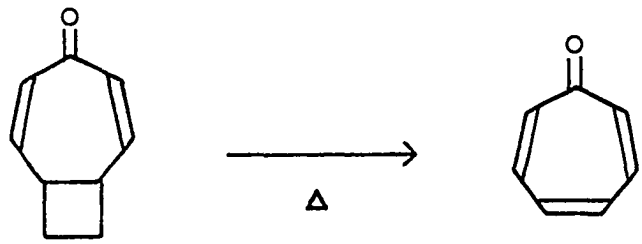

m/e 165
1§§2
1§§7
-CH2CO
5§§6
m/e 123
m/e 111
-CO
m/e 122
m/e 83
-H+
m/e 118
-H·
m/e 117
m/e 110
m/e

The ir spectrum (Figure 6, page 111) of the bicyclic dienone exhibits bands at 3.38 μ (C-H), 6.02 μ (C=O), 6.19 μ (C=C) and 11.60 μ (-CH=CH-). The nmr spectrum (Figure 7, page 113) possesses signals at δ 6.16 (multiplet, 2H) hydrogens β to the carbonyl, 5.83 (multiplet, 2H) hydrogens α to the carbonyl, 3.38 (multiplet, 2H) bridgehead hydrogens and 2.20 (multiplet, 4H) cyclobutane methylenes. The uv spectrum (cyclohexane) exhibits absorptions at 228 nm (log ε 4.08), 238 nm (shoulder, 3.95), 263 nm (3.28), and 367 nm (1.48). The uv spectrum (95% ethanol) exhibits absorptions at 235 nm (log ε 4.09), 276 nm (3.32), and 340 nm (shoulder, 1.79). The ultraviolet absorption behavior is nearly identical to that of 2,6-cycloheptadienone and suggests that unlike 4,5-homotropone which exhibits some conjugation through the cyclopropane ring, the cyclobutane ring offers no conjugative effect.

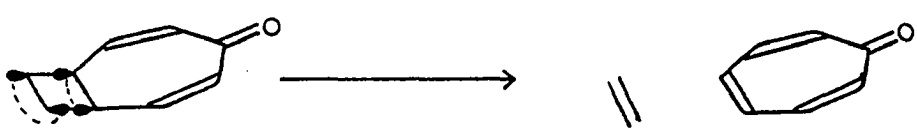
The mass spectrum m/e (relative intensity) of bicyclo-[5.2.0]nona-2,5-dien-4-one shows a parent ion at 134 (12). The initial loss of 28 yielding 106 (15) is probably due to the loss of carbon monoxide rather than ethylene for it is difficult to explain the ion 91 (49) in the latter case. The ion 106 (15) either loses ethylene to give 78 (100) or by a series of rearrangements produces a methyl tropylium species. This species either loses a hydrogen or methyl radical to give the methyl tropylium ion 105 (24) or the tropylium ion 91 (49), respectively.

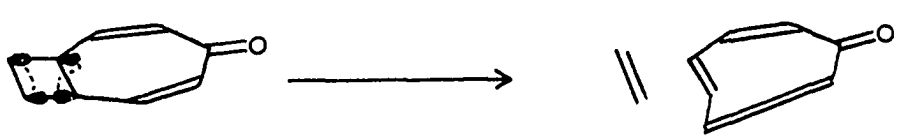


It was of interest to compare the thermal behavior of bicyclo[5.2.0]nona-2,5-dien-4-one with that of 4,5-homotropone or bicyclo[5.1.0]octa-2,5-dien-4-one which upon thermal degradation yielded 2,4,6-cyclooctatrienone. Thermolysis (500°, 4 μ pressure) on a vacuum pyrolysis apparatus yielded a single product in 78% yield identified as tropone by the superimposability of its ir and nmr spectra with those on an authentic sample.

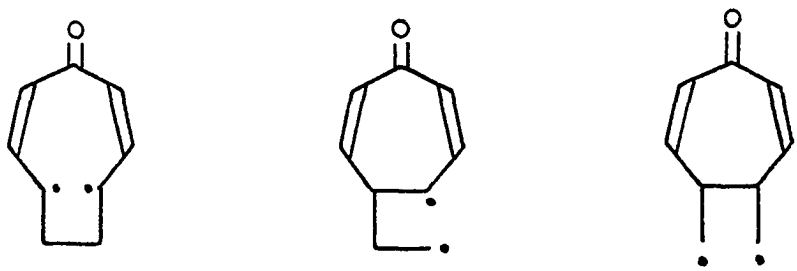


The mechanism of this reaction can be considered as a concerted thermally allowed $[_{\sigma}2_s + {}_{\sigma}2_a]$ process. The reaction can proceed either supra with the tropone moiety and antara with the ethylene or antara with the tropone and supra with





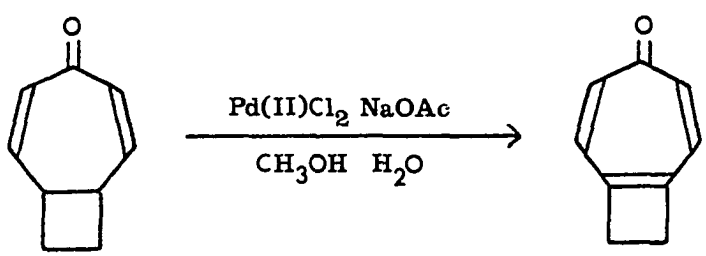
the ethylene. The majority of evidence for cyclobutane thermolysis, however, suggests that a diradical species may be involved (124). Three different diradical species can be considered, namely, a diallyl, primary-allyl, and a diprimary species. The observed product is most easily envisioned as



proceeding from the primary-allyl species. Presumably, the geometric constraints on the diallyl and diprimary species favor recombination to the starting dienone rather than further reaction to products. The primary-allyl species, lacking severe geometric constraints, can attain the status of a twixtyl (125) and have a range of molecular conformations suitable for decomposition to the observed product.

Dehydrogenation of bicyclo[5.2.0]nona-2,5-dien-4-one was first attempted by heating a suspension of the dienone, p-benzoquinone and 10% palladium on charcoal in decalin at 150° for 36 hours. Upon workup, the only material isolated was p-benzoquinone and hydroquinone. Similar results were obtained after only 18 hours reaction time. Presumably, the starting dienone and/or the desired product are unstable

to the reaction conditions. Attention was turned to milder dehydrogenation conditions. Treatment of the dienone with dichlorodicyanoquinone in refluxing benzene failed to precipitate the hydroquinone which is quantitatively insoluble in the reaction solvent. An nmr analysis of the crude reaction mixture indicated only the presence of the starting dienone. Finally, reaction of bicyclo[5.2.0]nona-2,5-dien-4-one with palladium(II) chloride and sodium acetate in aqueous methanol resulted in the slow precipitation of palladium metal. After 12 hours, the solution was filtered and extracted with ether. Concentration of the ether followed by chromatography on Florisil yielded 4,5-dimethylenetropone as a cream colored solid, mp 122-123°, in 2% isolated yield.



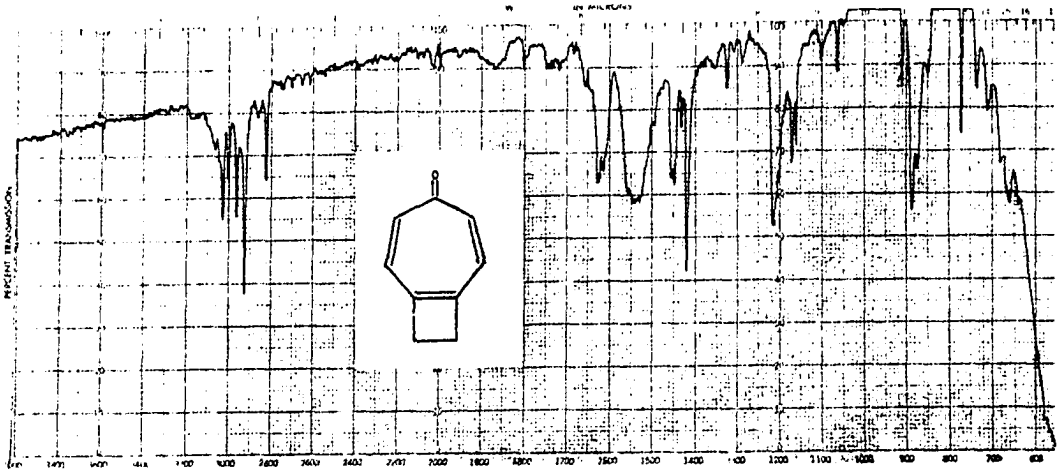
The ir spectrum (Figure 8, page 123) of 4,5-dimethylene-tropone shows significant bands at 3.42 μ (C-H), 6.19 μ (C=O), 6.50 μ (C=C) and 11.45 μ (CH=CH). The most unusual feature of the ir spectrum is the intensity and position of the carbonyl and olefinic stretching vibrations. Tropone, itself, has the carbonyl and olefinic stretching vibrations

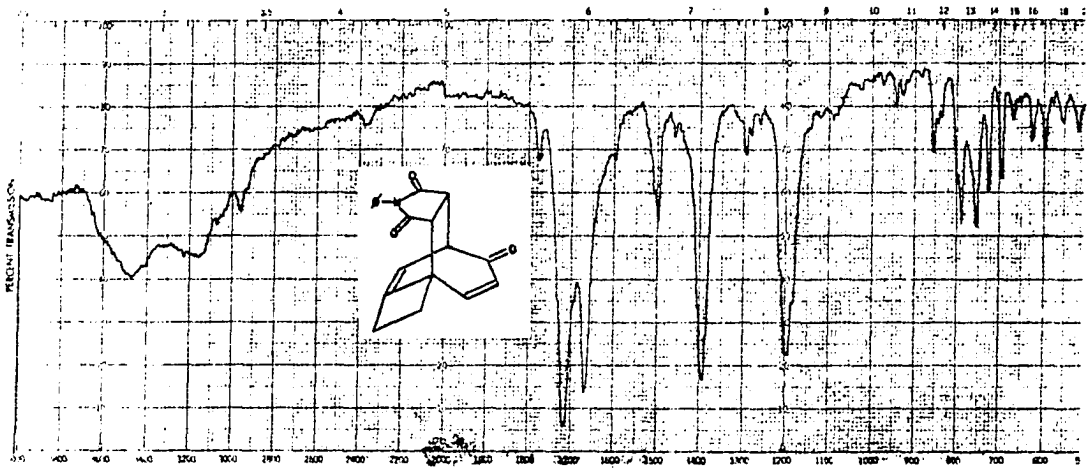
Figure 8. Infrared spectra

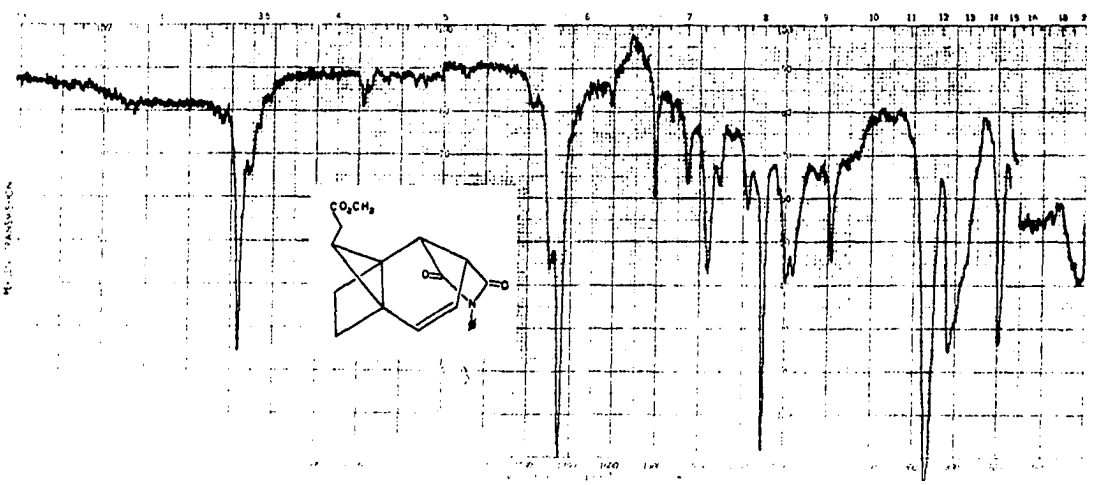
Top: 4,5-Dimethylenetropone

Middle: Diels-Alder adduct (4-phenyl-4-azatetracyclo[5.4.3.$0^{2,6}$ $0^{7,10}$]-trideca-3,5,12-trioxo-10,13-diene)

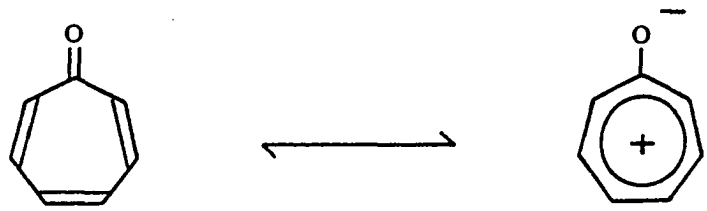
Bottom: Propellane (methyl-4-phenyl-4-azatetracyclo[7.2.1.$0^{2,6}$ $0^{1,9}$]-dodeca-3,5-dioxo-7-en-12-yl acetate)



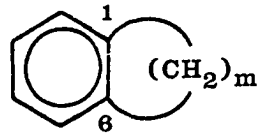



CO2CH3

at 6.12 and 6.33 μ, respectively, whereas 4,5-dimethylene-tropone has these same vibrations at 6.19 and 6.50 μ. This implies a decrease in the double bond character of the respective groups relative to tropone. The high wavelength absorptions for the tropone molecule is attributed to the increase in the contribution of the delocalized species depicted below. Presumably, inclusion of a 4,5-dimethylene



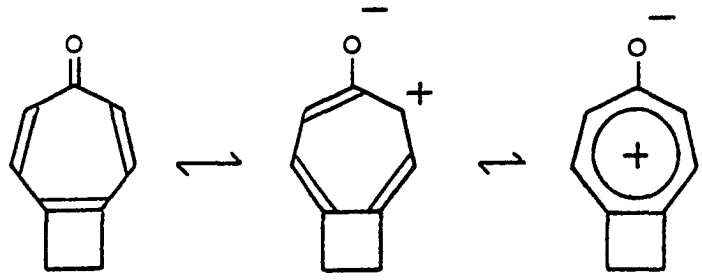
bridge further enhances this contribution. Supporting theoretical evidence for this effect is the CNDO/2 calculated bond localization in a series of benzocycloalkenes. Increase in the size of the cycloalkene resulted in a decrease of the 1--6 bond length (126). Extrapolating the results of the



m	1,6-Bond Length Å
1	1.420
2	1.421
3	1.412
4	1.403
Benzene	1.390

benzocycloalkenes to tropocycloalkenes, specifically tropocyclobutene, a dimethylene cyclobutane would be favored over

a cyclobutene with the consequent enhancement of the delocalized species of 4,5-dimethylenetropone.



The nmr spectrum (Figure 9, page 127) of 4,5-dimethylenetropone consists of two equally intense singlets at δ 6.77 and δ 2.90 for the olefinic and cyclobutane hydrogens, respectively. The uv spectrum (95% ethanol) exhibits bands at 228 nm (log ε 4.28), 310 nm (3.96) and 321 nm (shoulder, 3.89).

The mass spectrum m/e (relative intensity) of 4,5-dimethylenetropone consists of a parent ion at 132 (58). Loss of carbon monoxide gives 104 (100). This ion loses either a hydrogen or acetylene to give 103 (50) or 78 (59), respectively.

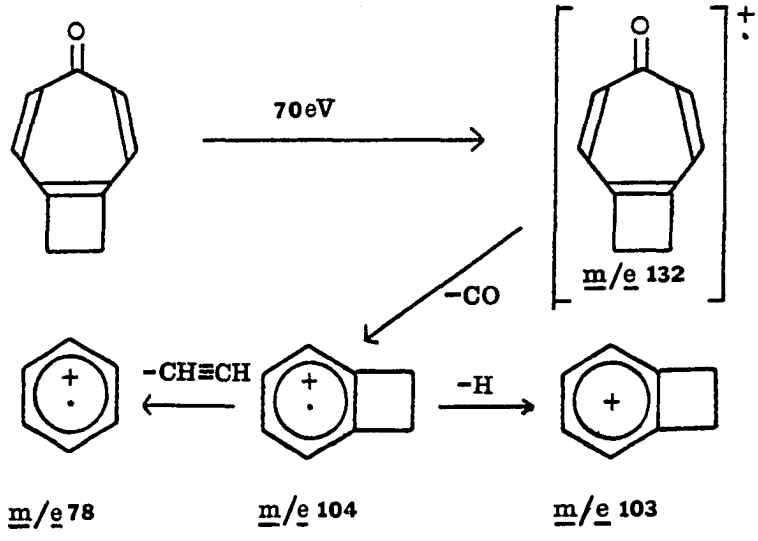
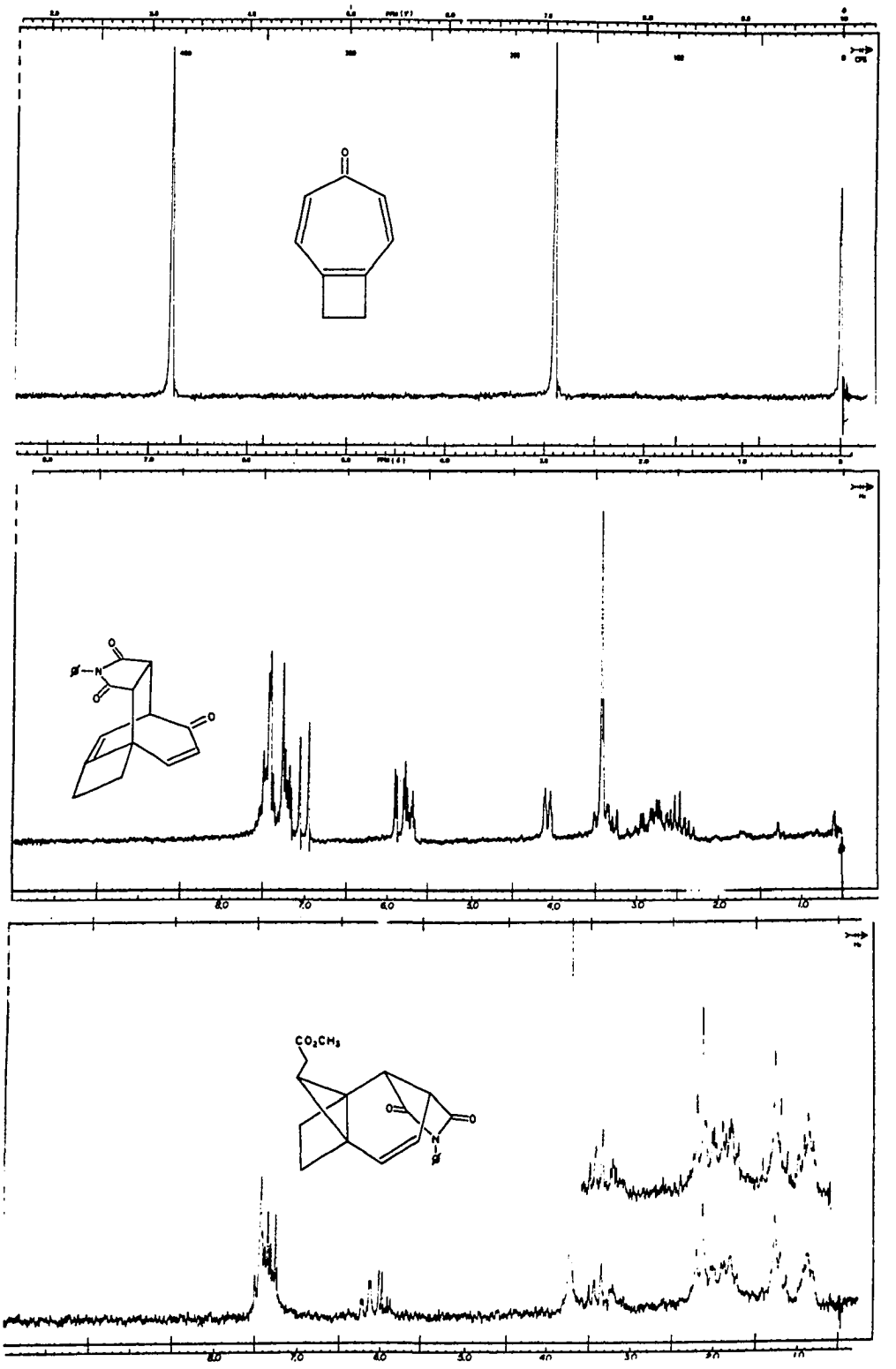


Figure 9. Nuclear magnetic resonance spectra

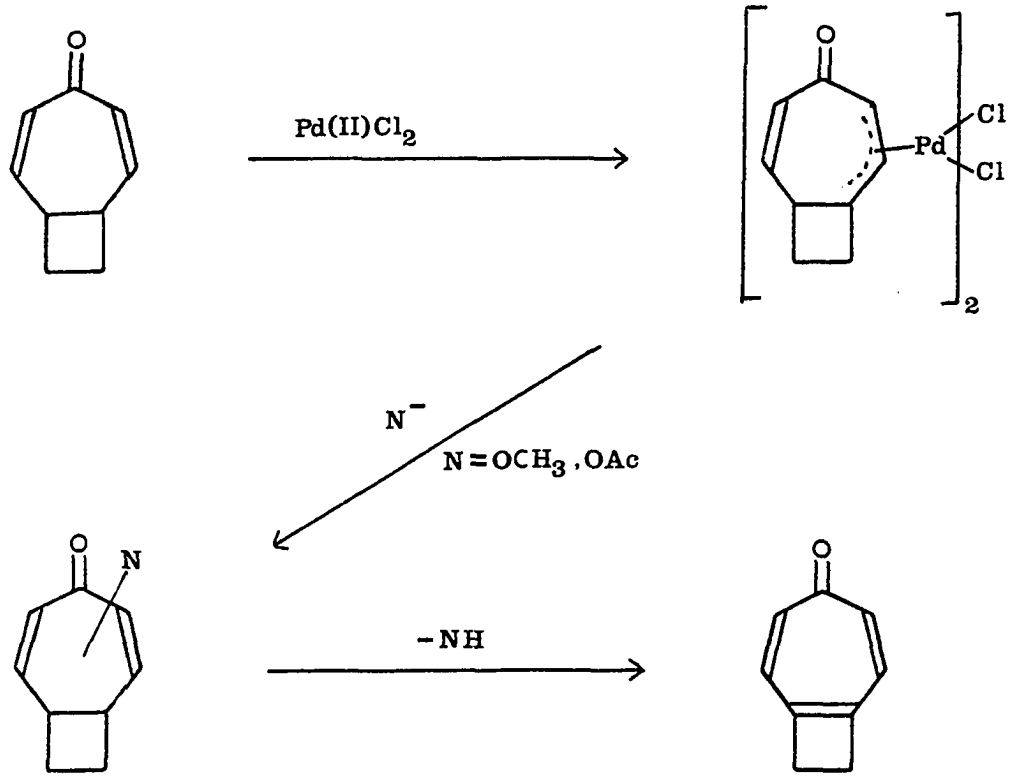
Top: 4,5-Dimethylenetropone

Middle: Diels-Alder adduct (4-phenyl-4-azatetracyclo[5.4.3.$0^{2,6}$ $0^{7,10}$]-trideca-3,5,12-trioxo-10,13-diene)

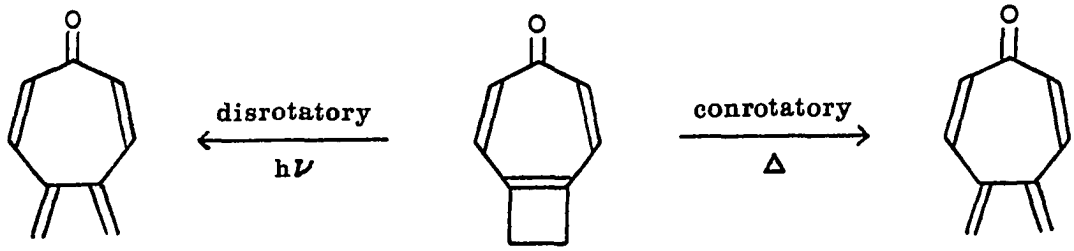
Bottom: Propellane (methyl-4-phenyl-4-azatetracyclo[7.2.1.$0^{2,6}$ $0^{1,9}$]-dodeca-3,5-dioxo-7-en-12-yl acetate)


CO2CH3

A plausible mechanism for the conversion of bicyclo-[5.2.0]nona-2,5-dien-4-one to 4,5-dimethylenetropone consists in the initial formation of a π-allyl palladium complex. This complex may then undergo nucleophilic attack by methanol or acetate ion to give allyl methyl ethers or allyl acetates. These ethers or acetates lose methanol or acetic acid to give 4,5-dimethylenetropone.

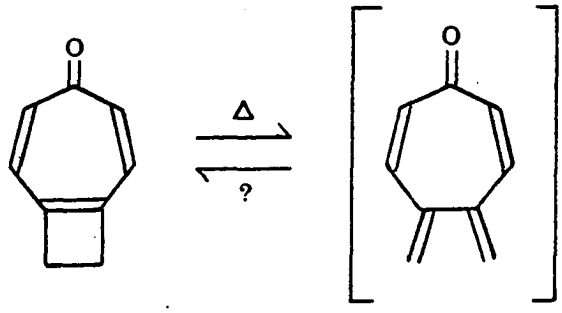


A priori, the electrocyclic ring opening of the cyclobutene moiety in 4,5-dimethylenetropone could occur either thermally or photochemically as exemplified by similar cyclobutene ring openings of benzocyclobutenes (See Literature



Review section). Either the thermally allowed conrotatory or the photochemically allowed disrotatory opening would generate the butadiene. The photochemical reaction was investigated first. Irradiation through Pyrex of a thin film of 4,5-dimethylenetropone in a low temperature infrared cell at 77° K with a 500 Watt Hanovia lamp for 1/2 hour resulted in no observable change in the infrared spectrum. Continued irradiation for one hour without the Pyrex filter also resulted in no observable change in the infrared spectrum as compared to the initial cold sample. The unsuccessful photochemical ring opening prompted investigation of the thermal electrocyclic reaction. Flash thermolysis of 4,5-dimethylenetropone (500°, 1 μ pressure) onto a liquid nitrogen cooled sodium chloride plate in a low temperature ir cell produced a species with significant intense infrared absorptions at 6.10 μ and 6.26 μ attributed to carbonyl and olefin, respectively. In addition, a moderately intense band at 10.87 μ attributed to terminal methylene was also present. After warming the sample to room temperature and recooling

to 77°K, these bands decreased markedly in intensity and broadened. (See Figure 10, page 132). This species is tentatively identified as tropoquino-4,5-dimethide on the basis of its thermal instability and the observed infrared spectrum.



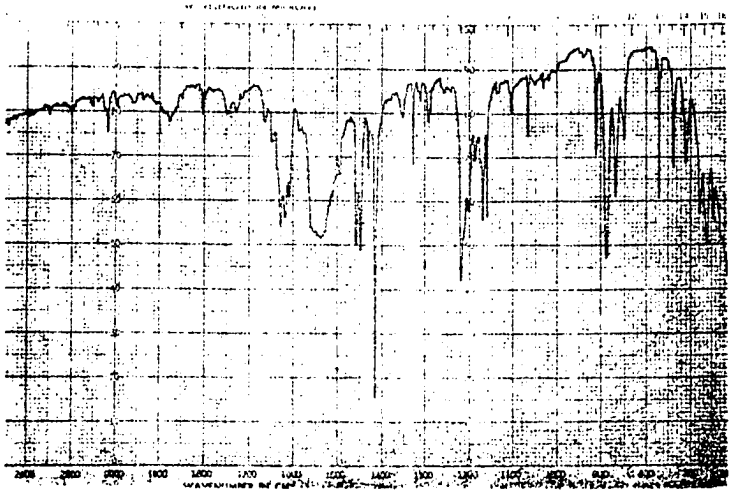
Attempts were made to trap the labile product with dienophiles on the same apparatus used for the observation of its infrared spectrum. Flash thermolysis of 4,5-dimethylenetropone onto a sodium chloride plate between sublimed samples of N-phenyl maleimide formed a 'sandwich' of pyrosylate between samples of dienophile. This sandwich was warmed to Dry Ice acetone temperatures and maintained for four hours. The 'sandwich' was warmed to room temperature and the sodium chloride plate washed with methylene chloride. Concentration of the resulting solution followed by chromatography yielded N-phenyl maleimide and trace quantities of additional materials which were not characterized.

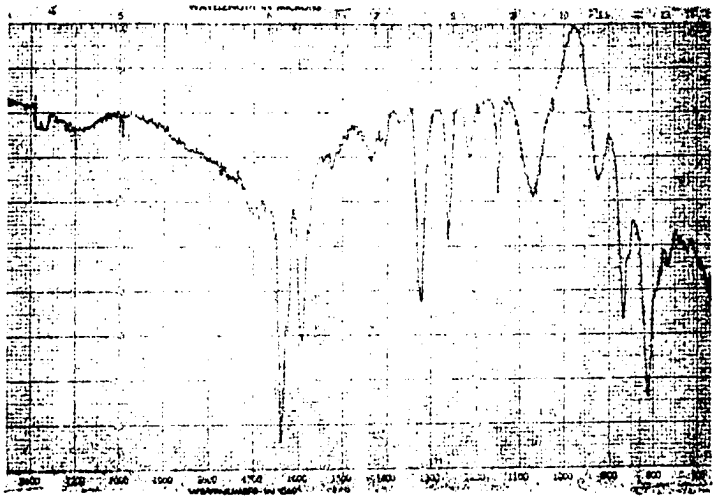
Figure 10. Infrared spectra

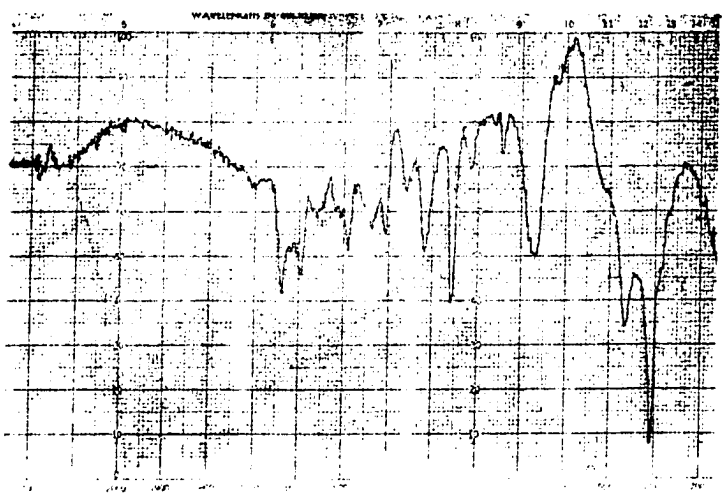
Top: 4,5-Dimethylenetropone at 190°

Middle: Pyrolysis product of 4,5-dimethylenetropone at -190°

Bottom: Pyrolysis product of 4,5-dimethylenetropone after warming to 0° and recooling to -190°

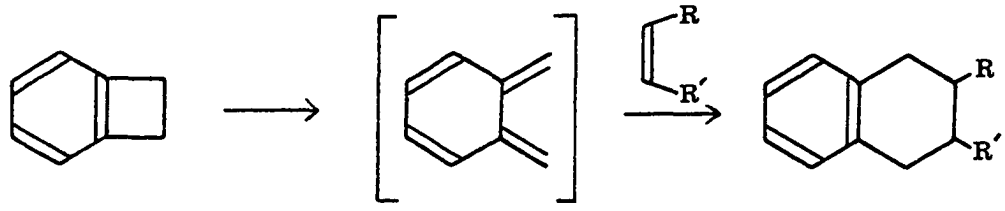






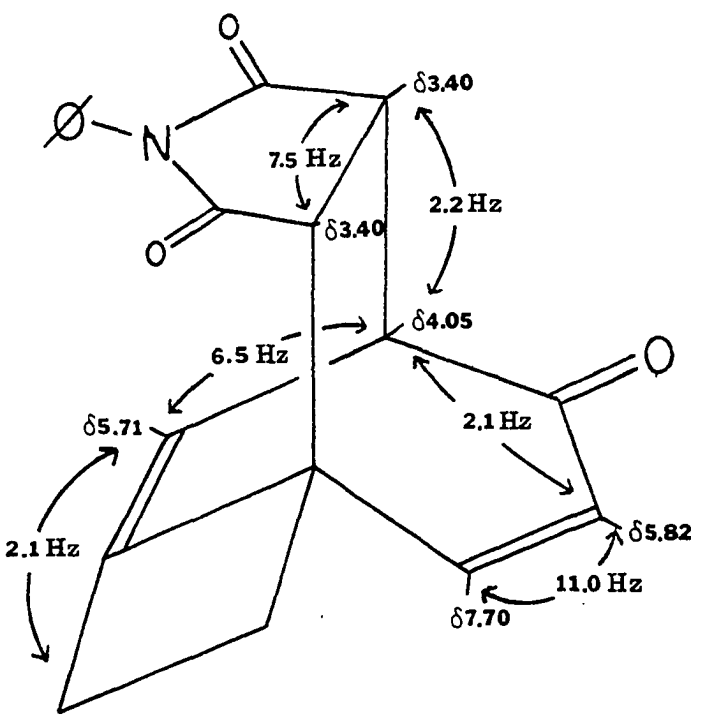
It is well known that Diels-Alder reactions are accelerated by electron donating substituents in the diene (electron rich) and electron withdrawing substituents in the dienophile (electron poor). However, some reactions are known in which the converse applies, namely, an electron poor diene reacts preferentially with an electron rich dienophile. This type of cycloaddition is called the Diels-Alder reaction with "inverse electron demand" (127). On the supposition that 4,5-tropoquinodimethide is an electron poor diene requiring an electron rich dienophile, a similar trapping experiment was attempted with 1,1-dimethoxyethylene, an electron rich dienophile. A 'sandwich' of the pyrosylate of 4,5-diemthylenetropone and 1,1-dimethoxyethylene was allowed to react at Dry Ice acetone temperature for four hours. Similar workup as previously described resulted in trace quantities of materials which were not characterized. The failure of these trapping experiments is probably due to the small surface area of the sodium chloride plate as well as the desired reaction can only occur at the interface of solid reactants.

The in situ generation of o-xylylene and the successful trapping of this reactive species by dienophiles (108, 109) prompted a similar in situ generation of tropoquino-4,5-dimethide. A sample of 4,5-dimethylenetropone and



N-phenyl maleimide was heated with benzene in a sealed tube for 48 hours at 208°. Evaporation of the benzene followed by chromatography on Florisil yielded a white solid, mp 177-179°, in 62% yield. This product was identified as a 1:1 adduct by a molecular ion at m/e 305. Additional spectral evidence eliminated a Diels-Alder addition to tropoquino-4,5-dimethide and indicated a [4 + 2] cycloaddition of N-phenyl maleimide to a diene portion of the tropone. The ir spectrum (Figure 8, page 123) exhibits significant bands at 3.38 μ (C-H), 5.63, 5.82 and 6.00 μ (C=O), and 13.28, 13.80 and 14.42 μ (CH=CH). The 100 MHz nmr spectrum (Figure 9, page 127) reveals signals at δ 7.33 (multiplet, 5H), 7.00 (doublet, 1H, J = 11.0 Hz), 5.82 (doublet of doublets, 1H, J = 11.0 Hz and J = 2.1 Hz), 5.71 (doublet of triplets, 1H, J = 6.5 Hz and J = 2.1 Hz), 4.05 (doublet of multiplets, 1H, J = 6.5 Hz), 3.40 (multiplet, 3H) and 3.10-2.20 (complex multiplet, 3H). A sample of the adduct was treated with the

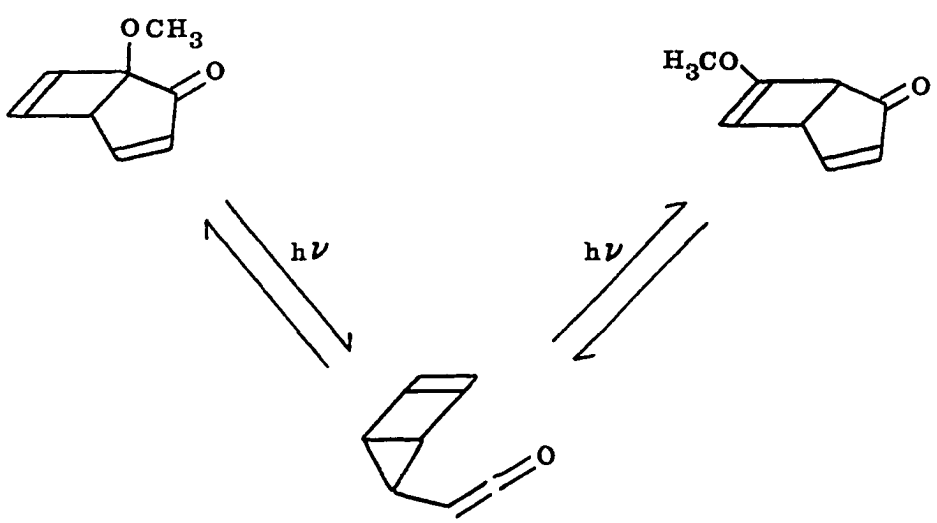
lanthanide shift reagent tris-(1,1,1,2,2,3,3-heptafluoro-7,7-dimethyloctadionato)europium, $Eu(fod)_3$. The resulting 100 MHz spectrum showed increasing downfield shift of the hydrogen resonances with increasing concentration of the shift reagent. The nmr spectrum of the adduct in a deuteriochloroform solution saturated with $Eu(fod)_3$ resolved the multiplet at δ 3.40 into three signals, a doublet of doublets (J ≈ 7.5 Hz and J ≈ 2.2 Hz), and a doublet (J ≈ 7.5 Hz) slightly overlapped by a complex multiplet. The tentative nmr assignments are summarized in the diagram below. The uv



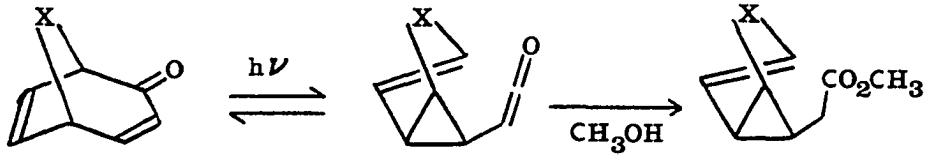
spectrum (cyclohexane) exhibited bands at 210 nm (log ε 4.17) and 340 nm (2.11). The mass spectrum m/e (relative intensity)

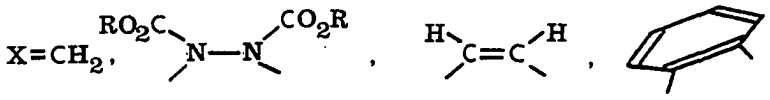
exhibits a parent ion at 305 (90). The most intense ions are 277 (27), 158 (16), 131 (14), 130 (100), 129 (69), 128 (36), 119 (44), 115 (59), 91 (24). The ion m/e 277 is related to the parent m/e 305 by a metastable ion at 251. The successive losses of carbon monoxide, phenyl isocyanate, and an additional molecule of carbon monoxide account for the m/e 277, 158 and 130 ions, respectively.

The Diels-Alder adduct bears a structural similarity to bicyclo[3.2.0]hepta-3,6-dien-2-one. Low temperature irradiation of a derivative of this bicyclic system was shown to generate an infrared observable ketene (128). Furthermore, a study of derivatives in which the zero-atom bridge was

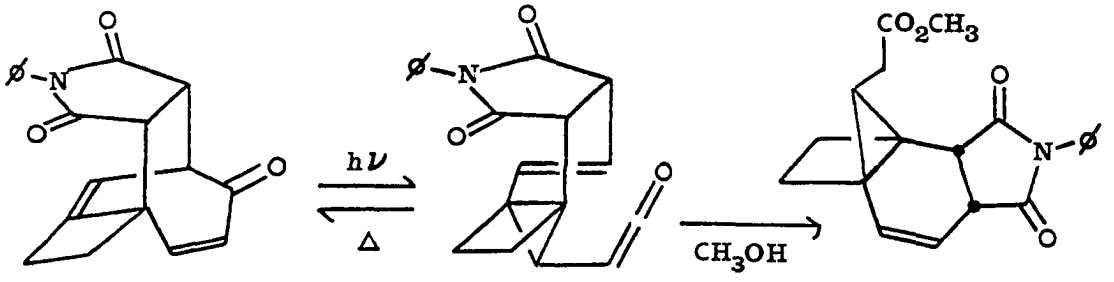


replaced by one- and two-atom bridges was shown to be a general reaction viewed as a homoelectrocyclic reaction (129).

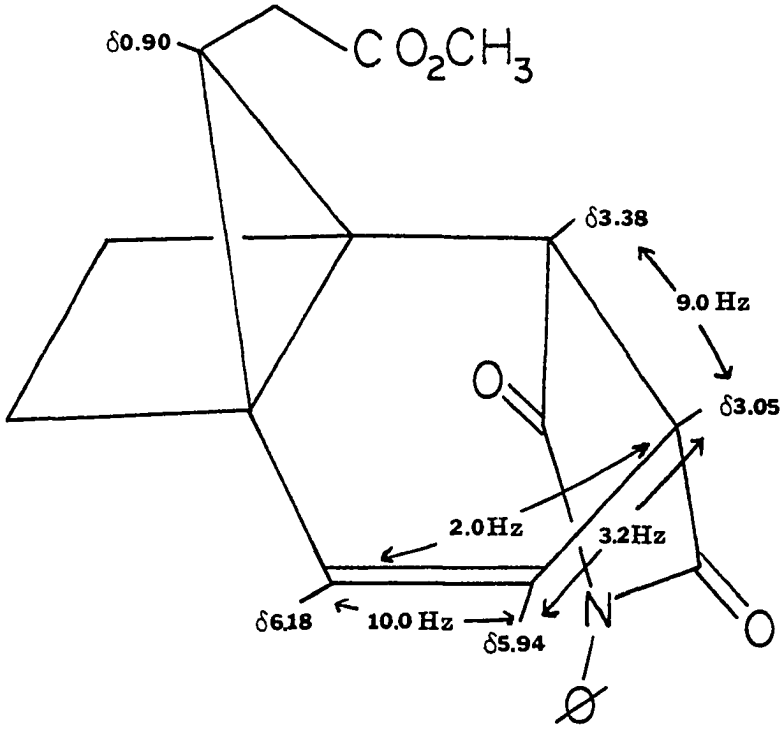




A similar reaction in the Diels-Alder adduct would generate a ketene in a propellane molecule. This prompted irradiation of the adduct. Low temperature irradiation through Pyrex of the Diels-Alder adduct dispersed in nujol produced a medium intensity ketene band at 4.74 μ. The ketene was stable at low temperature in the dark but warming to -60° caused the rapid disappearance of the ketene and apparent regeneration of the adduct. Preparative scale irradiation of the Diels-Alder adduct in methanol at -40° followed by evaporation of the solvent and chromatography on Florisil yielded a glassy material which resisted attempts at crystallization. The



structure of the methanol addition product is tentatively assigned the propellane structure on the basis of its spectral characteristics and method of synthesis. The ir spectrum (Figure 8, page 123) exhibits significant bands at 3.37 μ (C-H), 5.60, 5.71 and 5.80 μ (C=O). The nmr spectrum (Figure 9, page 127) exhibits signals at δ 7.35 (multiplet, 5H), 6.18 (doublet of doublets, 1H, J = 10.0 Hz and J = 2.0 Hz), 5.94 (doublet of doublets, 1H, J = 10.0 Hz and J = 3.2 Hz), 3.72 (singlet, 3H), 3.38 (doublet, 1H, J = 9.0 Hz), 3.05 (doublet of multiplets, 1H, J = 9.0 Hz), 2.30-1.70 (complex multiplet, 6H), and 0.90 (multiplet, 1H). The tentative nmr assignments are summarized in the diagram below. The mass spectrum m/e



(relative intensity) shows a parent ion at 337 (16). The most intense ions are 309 (13), 305 (23), 278 (14), 277 (36), 218 (10), 191 (10), 159 (10), 158 (30), 157 (16), 149 (19), 131 (34), 130 (100), 117 (32), 116 (31), 115 (26). The loss of carbon monoxide from the parent ion gives the m/e 309 ion. The consecutive losses from the parent ion of methanol, carbon monoxide, phenyl isocyanate, and another molecule of carbon monoxide account for the m/e 305, 277, 158, and 130 ions, respectively.

EXPERIMENTAL

General

All melting points were taken on a Fisher-Johns melting point apparatus and are uncorrected. Microanalyses were performed by Spang Microanalytical Laboratory, Ann Arbor, Michigan. Infrared (ir) spectra were recorded on a Beckman IR 9 or IR 12 spectrophotometer. Ultraviolet (uv) spectra were obtained on either a Cary 14 or a Beckman DK 2A spectrophotometer. Nuclear magnetic resonance (nmr) spectra were obtained on a Varian A-60 or a Varian HA 100 spectrophotometer in carbon tetrachloride using tetramethylsilane as internal standard unless otherwise indicated. Mass spectra were obtained on an Atlas CH-4 instrument. High resolution mass spectra were obtained on an MS 902 spectrophotometer. Analytical gas chromatography was performed on an Aerograph Model 1520 utilizing a flame ionization detector. Preparative gas chromatography was performed on an Aerograph Model A-90-P. Anhydrous magnesium sulfate was used for all drying operations unless otherwise indicated. All concentration of solutions was done at aspirator pressure with a water bath at 50°.

Preparation of bicyclo[6.2.0]deca-2,4,6-triene

The procedure outlined by Staley and Henry was used (123). In 600 ml liquid ammonia was dissolved 2.78 g (0.40

mole) clean lithium wire and then 20.8 g (0.20 mole) cyclooctatetraene was added dropwise. To the resulting tan suspension was slowly added 37.8 g (0.20 mole) 1,2-dibromoethane over 1/2 hour. The ammonia was allowed to evaporate overnight. The resulting residue was extracted with ether. The combined ether extracts were washed with saturated sodium chloride, dried and concentrated to leave a yellow oil which was fractionally distilled to give 6.40 g (bp 25-37°/4.5 mm) cyclooctatetraene (lit. (130) bp 42-42.5°/17 mm) and 9.40 g (54.5% based on unrecovered cyclooctatetraene) (bp 52-54°/4.5 mm) of bicyclo[6.2.0]deca-2,4,6-triene (lit. (123) bp 55°/4.6 mm).

Preparation of 10-methyl-10-azatricyclo[4.3.1.$0^{2,5}$]decan-8-one

A solution of 7.0 g (0.053 mole) bicyclo[6.2.0]deca-2,4,6-triene in 100 ml methanol was ozonized with a Welsbach Ozonizer at -50° until the solution turned a pale blue. The resulting solution was treated with nitrogen to remove the excess ozone, 20 ml dimethyl sulfide was added, and the mixture was stirred 1 hr at -50°. The cooling bath was removed, an additional 10 ml dimethyl sulfide was added, and the solution was warmed to room temperature over 1 hr. The resulting clear solution was added to 12.5 g (0.085 mole) acetonedicarboxylic acid, 6.0 g (0.089 mole) methylamine

hydrochloride, and 15.0 g sodium dihydrogen phosphate in 1200 ml water. The pH was adjusted to pH 6.0 with saturated sodium carbonate and stirred 5 days at ambient temperature. The nearly black solution was made basic to pH 10 with solid sodium carbonate, saturated with sodium chloride and continually extracted with ether for 36 hr. The ethereal solution was dried and concentrated to give a dark red oil which was extracted with hot hexane. Evaporation of the hexane gave 6.50 g (73.4%) 10-methyl-10-azatricyclo-[4.3.1.$0^{2,5}$]decan-8-one, mp 89-90°.

The 10-methyl-10-azatricyclo[4.3.1.$0^{2,5}$]decan-8-one was characterized by the following data: ir (KBr) (Figure 6, page 111) 3.36, 5.80, 6.80, 7.04, 7.36, 8.00, 8.13, 8.33, 8.40, and 10.50 μ; nmr (CCl_4) (Figure 7, page 113) δ 3.12 (multiplet, 2H), 2.8-1.5 (complex multiplet, 13H); uv max (95% ethanol) 248 nm (log ε 3.09); mass spectrum (70 eV) m/e (relative intensity) 165 (parent, 85), 123 (3), 122 (76), 111 (3), 110 (59), 108 (39), 107 (3), 95 (77), 94 (100), 83 (11), 82 (16), 42 (22).

Anal. Calcd. for $C_{10}H_{15}NO$: C, 72.69; H, 9.15; N, 8.48. Found: C, 72.80; H, 9.18; N, 8.53.

Preparation of 10,10-dimethyl-8-oxo-10-azoniatricyclo-[4.3.1.$0^{2,5}$]decane tosylate

A mixture of 3.00 g of 10-methyl-10-azatricyclo-[4.3.1.$0^{2,5}$]decan-8-one in 20 ml methyl tosylate was heated

at 60° for 6 hr. The resulting suspension was diluted with 50 ml of dry ether and filtered. The solid was washed with ether and recrystallized from absolute ethanol to give 5.70 g (89%) 10,10-dimethyl-8-oxo-10-azoniatricyclo-[4.3.1.$0^{2,5}$]decane tosylate, mp 186-187°.

The 10,10-dimethyl-8-oxo-10-azoniatricyclo[4.3.1.$0^{2,5}$]-decane tosylate was characterized by the following data: ir (KBr) (Figure 6, page 111) 3.35, 5.80, 7.09, 8.27, 8.89, 9.65, 9.88, 14.66 μ; nmr (D_2O, sodium 2,2-dimethyl-2-silapentane-5-sulfonate as internal reference) (Figure 7, page 113) δ 7.50 (AA'BB' multiplet, 4H), 4.10 (multiplet 2H), 3.48 (broad singlet, 6H), 2.9-1.9 (unresolved multiplet, 13H).

Anal. Calcd for $C_{18}H_{25}NO_4S$: C, 61.50; H, 7.18; N, 3.99; S, 9.11. Found: C, 61.34; H, 7.13; N, 3.98; S, 9.06.

Preparation of bicyclo[5.2.0]nona-2,5-dien-4-one

A heterogeneous solution of 7.50 g (0.022 mole) 10,10-dimethyl-8-oxo-10-azoniatricyclo[4.3.1.$0^{2,5}$]decane tosylate, 16.0 g sodium bicarbonate, 200 ml water and 200 ml ether was rapidly stirred for 36 hr at room temperature. The ether layer was separated, washed with 5% hydrochloric acid, 5% sodium bicarbonate, and saturated sodium chloride, dried, and concentrated to give a yellow oil. Vacuum distillation of the crude oil gave 1.16 g (33%) bicyclo[5.2.0]nona-2,5-dien-4-one bp 78-79°/0.7 mm.

The bicyclo[5.2.0]nona-2,5-dien-4-one was characterized by the following data: ir (neat) (Figure 6, page 111) 3.38, 6.02, 6.19, 7.08, 7.68, 8.33, and 11.60 μ; nmr (CCl_4) (Figure 7, page 113) δ 6.16 (multiplet, 2H), 5.83 (multiplet, 2H), 3.38 (multiplet, 2H), 2.20 (multiplet, 4H); uv max (cyclohexane) 228 nm (log ε 4.08), 238 nm (shoulder, 3.95), 2.63 nm (3.28) and 367 nm (1.48); uv max (95% ethanol) 235 nm (log ε 4.09), 276 nm (3.32) and 340 nm (shoulder, 1.79); mass spectrum (70 eV) m/e (relative intensity) 134 (parent, 12), 133 (23), 106 (15), 105 (24), 92 (42), 91 (49), 79 (26), 78 (100), 77 (18), 53 (19), 52 (18), 51 (24), 50 (12), 39 (6), 28 (46).

Anal. Calcd for $C_9H_{10}O$: C, 80.56; H, 7.51. Found: C, 80.55; H, 7.34.

Thermolysis of bicyclo[5.2.0]nona-2,5-dien-8-one

Degradation of 402 mg (3.0 mmole) bicyclo[5.2.0]nona-2,5-dien-8-one on a vacuum pyrolysis apparatus (96) (500°, 4 pressure) yielded 249 mg (78%) of a single product. A sample was collected by preparative gas chromatography utilizing a 10 ft x 3/8 in column with 15% SE 30 on 60/80 Chromosorb W and identified as cycloheptatrienone by the following data: ir (neat) 3.30, 6.12, 6.33, 6.57, 6.79, 7.97, 8.21, 11.14, 12.02, 12.76 μ; nmr (CCl_4) δ 6.90 (broad singlet). The above spectra were superimposable with those of an authentic sample.

Attempted dehydrogenation of bicyclo[5.2.0]nona-2,5-dien-8-one with palladium on charcoal

A suspension of 250 mg (1.87 mmole) bicyclo[5.2.0]nona-2,5-dien-8-one, 250 mg 10% palladium/charcoal, and 500 mg (4.63 mmole) p-benzoquinone in 100 ml decalin was heated at 150° for 36 hr. After cooling, the mixture was filtered to remove the palladium on charcoal. The decalin was removed by chromatography on silica gel eluting with hexane. Elution with 10% ethyl acetate hexane gave unreacted p-benzoquinone mp 113-115° (lit. (131) mp 111-113°). Further elution with 50% ethyl acetate/hexane gave hydroquinone mp 169-170° (lit. (132) mp 170.3°). No additional material was eluted.

Attempted dehydrogenation of bicyclo[5.2.0]nona-2,5-dien-8-one with dichlorodicyanoquinone

A solution of 134 mg (1.0 mmole) bicyclo[5.2.0]nona-2,5-dien-8-one and 226 mg (1.0 mmole) dichlorodicyanoquinone was refluxed in benzene for 72 hr. (No precipitate was formed.) The benzene was removed under vacuum and an nmr analysis of the crude material indicated only the presence of bicyclo[5.2.0]nona-2,5-dien-8-one.

Preparation of 4,5-dimethylenetropone

A solution of 1.00 g (0.075 mole) bicyclo[5.2.0]nona-2,5-dien-4-one, 6.50 g sodium acetate, and 1.33 g (0.076 mole)

palladium(II) chloride in a mixture of 30 ml methanol and 300 ml water was vigorously stirred at ambient temperature overnight. The resulting solution was filtered to remove precipitated palladium metal, saturated with solid sodium chloride and extracted with ether. The ether was dried and concentrated to give a dark red oil. This material was chromatographed on 20 ml Florisil prepared and eluted with 3% ethyl acetate/hexane. The bulk of the material (730 mg) eluted with the first 100 ml. (Analysis of this material by nmr indicated the presence of the starting dienone and possible methanol addition products which were not further investigated). Continued elution yielded a cream colored solid 22 mg (2.0%). Low temperature recrystallization from hexane followed by sublimation a 0.10 mm and room temperature yielded 4,5-dimethylenetropone, mp 122-123°.

The 4,5-dimethylenetropone was characterized by the following data: ir (KBr) (Figure 8, page 123) 3.42, 6.19, 6.50, 6.90, 7.04, 8.23, 11.30, 11.45 μ; nmr (CCl_4) (Figure 9, page 127) δ 6.77 (singlet, 4H) and 2.90 (singlet, 4H); uv max (95% ethanol) 228 nm (log ε 4.28), 310 nm (3.96) and 321 nm (shoulder, 3.89); mass spectrum (70 eV) m/e (relative intensity) 132 (parent, 58), 105 (10), 104 (100), 103 (50), 78 (59) and 77 (34).

Anal. Calcd for C_9H_8O: C, 81.79; H, 6.10. Found: C, 81.91; H, 6.14.

Photolysis of 4,5-dimethylenetropone at 77°K

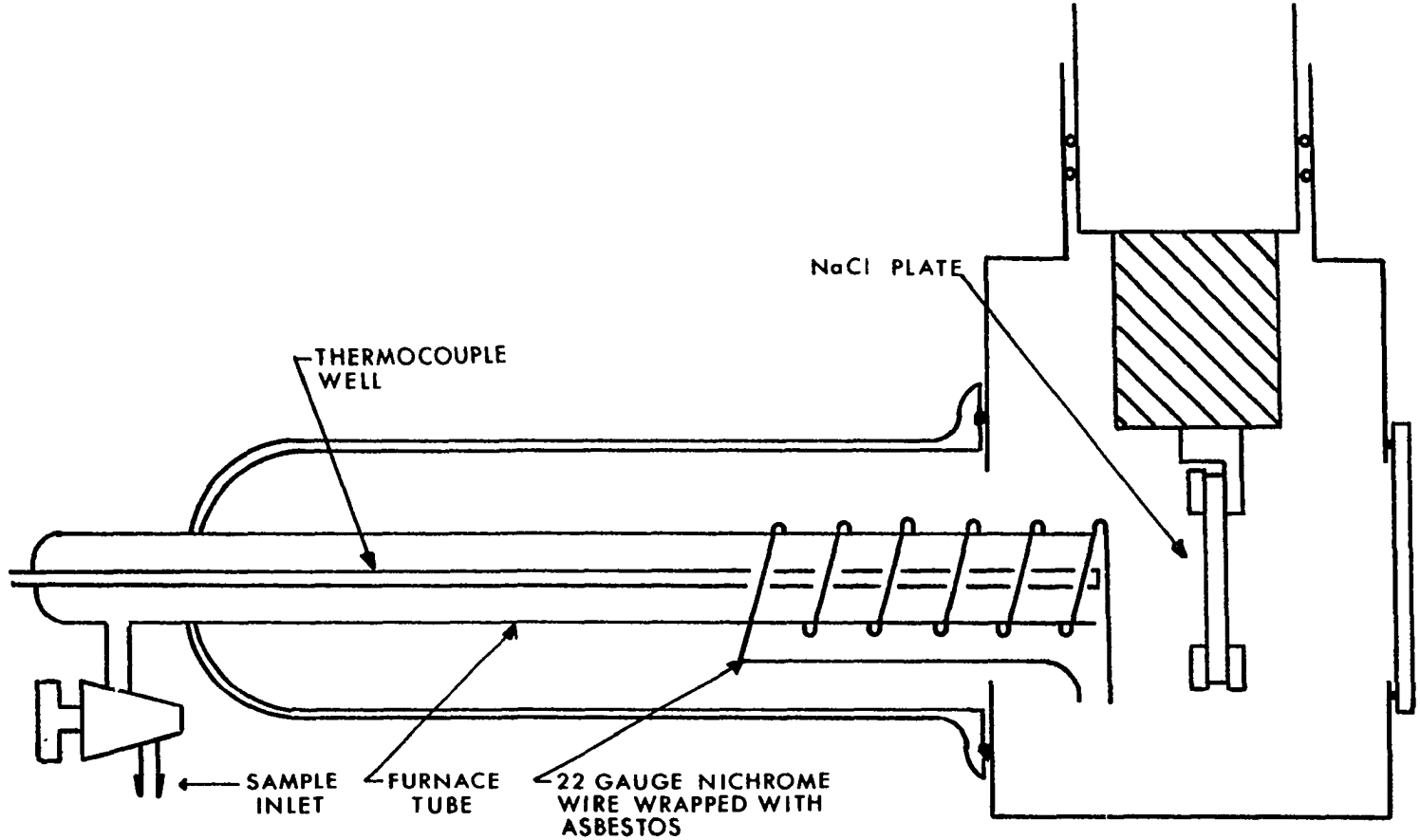
A *ca.* 5 mg sample of 4,5-dimethylenetropone was sublimed onto a sodium chloride plate in a low temperature irradiation ir cell (133). Irradiation through a Pyrex filter utilizing a 550 Watt Hanovia lamp focused onto the sodium chloride plate was initiated, and the ir spectrum recorded at frequent intervals. After 1/2 hr total irradiation, no observable change in the spectrum was recorded. The Pyrex filter was removed and irradiation was continued for an additional hour. The resulting ir spectrum was completely superimposable with that of the initial cold sample.

Thermolysis ir cell

The apparatus consists of a low temperature ir cell in which one side has been replaced by a small electrically heated furnace assembly. The furnace has an outer jacket attached to the ir cell *via* a metal flange and an O-ring connector. The furnace itself is a Pyrex tube with 22 gauge nichrome wire wrapped with asbestos. This type extends beyond the outer jacket *via* a glass ring seal and has a vacuum stopcock with a 14/20 joint used as sample inlet. Concentric with the furnace tube is a Pyrex thermocouple well. (See Figures 11 and 12, pages 149 and 151).

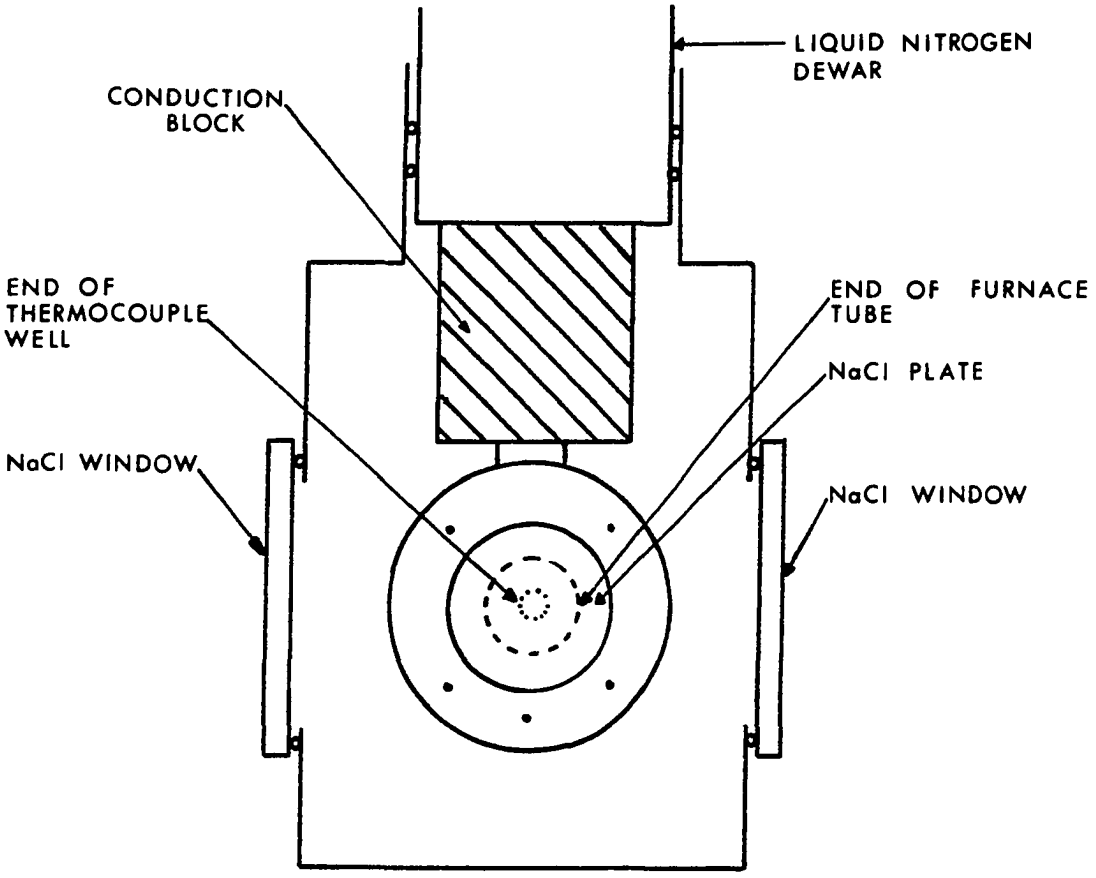
In normal operation the cell is evacuated and the furnace heated slightly above the desired thermolysis temperature. Liquid nitrogen is added to the Dewar and final

Figure 11. Side view of thermolysis infrared cell


NaCl PLATE
THERMOCOUPLE WELL
SAMPLE INLET
FURNACE TUBE
22 GAUGE NICHROME WIRE WRAPPED WITH ASBESTOS

SIDE VIEW

Figure 12. Front view of thermolysis infrared cell


LIQUID NITROGEN DEWAR
CONDUCTION BLOCK
END OF THERMOCOUPLE WELL
END OF FURNACE TUBE
NaCl PLATE
NaCl WINDOW
NaCl WINDOW

FRONT VIEW

temperature adjustments are made. The entire apparatus is equilibrated for 1 hr and the substrate introduced *via* the sample inlet. After deposition is complete, the furnace is cooled, the sodium chloride plate rotated 90°, and the ir spectrum recorded.

In trapping experiments a slightly different procedure is used. The cell is evacuated, cooled with liquid nitrogen, and a sample of trapping reagent is deposited on the sodium chloride plate by sublimation. The furnace is now heated to the desired temperature and the substrate is deposited. The furnace is cooled and an additional sample of trapping reagent is deposited. Thus a sandwich of pyrosylate between layers of trapping reagent is formed.

Flash thermolysis of 4,5-dimethylenetropone

A 5 mg sample of 4,5-dimethylenetropone was sublimed at 1 μ pressure through the thermolysis tube heated at 500° onto a liquid nitrogen cooled sodium chloride plate in the thermolysis ir cell. After deposition was complete, the ir spectrum was recorded. The resulting ir spectrum (Figure 10, page 132) exhibited significant bands at 6.10, 6.26 and 10.87 μ. Upon warming to -110°, these bands rapidly decreased in intensity. After warming to room temperature and recooling the sample to liquid nitrogen temperature, the resulting ir spectrum (Figure 10, page 132) indicated the marked decrease in intensity of these bands.

Attempted trapping of the liable product with N-phenyl maleimide

A 10 mg sample of 4,5-dimethylenetropone was thermolized at 500° onto a liquid nitrogen cooled sodium chloride plate between two 10 mg samples of N-phenyl maleimide. The cell was slowly warmed to -75° and maintained at this temperature for 4 hr. The sodium chloride plate was then warmed to room temperature and washed with methylene chloride. Evaporation of the solvent gave 21 mg of a brown viscous oil which was chromatographed on 7 ml of Florisil using 10% ethyl acetate/hexane as eluent. The first fraction eluted contained 12 mg N-phenyl maleimide, mp 89-91° (lit. (134) mp 90-91°). Continued elution with ethyl acetate yielded 5 mg of a brown residue which by thin layer chromatography on silica gel eluting with chloroform consisted of several components and was not investigated.

Attempted trapping of the liable product with 1,1-dimethoxyethylene

The procedure is that described above but with 1,1-dimethoxyethylene as trapping reagent. From 10 mg 4,5-dimethylenetropone and 20 mg total of 1,1-dimethoxyethylene was obtained 6 mg of a dark brown residue. Thin layer chromatography on alumina of this residue and eluting with chloroform indicated several components and was not investigated further.

Reaction of 4,5-dimethylenetropone and N-phenyl maleimide

A mixture of 14.7 mg (1.12 mmole) of 4,5-dimethylenetropone and 39.9 mg (1.58 mmole) of N-phenyl maleimide in 2 ml of benzene was placed in a heavy-walled tube, cooled with liquid nitrogen, evacuated, and sealed. The tube was heated for 48 hr at 208° ± 5°. The tube was opened, washed with benzene and concentrated. The resulting solid was chromatographed on Florisil with 10% ethyl acetate/hexane. The first component eluted was 12.5 mg of N-phenyl maleimide mp 89-90° (lit. (134) mp 90-91°). Continued elution gave 21 mg (62%) of a Diels-Alder adduct mp 177-179°.

The Diels-Alder adduct was characterized by the following data: ir (KBr) (Figure 8, page 123) 3.38, 5.63, 5.82, 6.00, 12.50, 12.71, 13.28, 13.80, 14.42 μ; nmr ($CDCl_3$) (100 MHz) (Figure 9, page 127) δ 7.33 (multiplet, 5H), 7.00 (doublet, 1H, J = 11.0 Hz), 5.82 (doublet of doublets, 1H, J = 11.0 Hz and J = 2.1 Hz), 5.71 (doublet of triplets, 1H, J = 6.5 Hz and J = 2.1 Hz), 4.05 (doublet of multiplets, 1H, J = 6.5 Hz), 3.40 (multiplet, 3H), and 3.10-2.20 (complex multiplet, 3H); nmr ($CDCl_3$, saturated with tris-(1,1,1,2,2,3,3-heptafluoro-7,7-dimethyloctadionato)europium) (100 MHz) δ 7.80-7.00 (complex multiplet), 6.37 (broad doublet), 5.90 (broad doublet), 4.48 (doublet of doublets, J ≈ 7.5 Hz and J ≈ 2.2 Hz), 3.60-3.40 (multiplet), 2.80-2.00 (multiplet); uv max (cyclohexane) 210 nm (log ε 4.17) and 340 nm (2.11); mass

spectrum (70 eV) m/e (relative intensity) 305 (90), 277 (27), 158 (16), 131 (14), 130 (100), 129 (69), 128 (36), 119 (44), 115 (59), 91 (24).

High resolution of the molecular ion M^+ in lieu of microanalysis; calcd for $C_{19}H_{15}NO_3$: 305.1052, found 305.1047.

Irradiation of the Diels-Alder adduct at 77°K

A 5 mg sample of the Diels-Alder adduct dispersed in nujol was placed on a sodium chloride plate in a low temperature irradiation ir cell (133) and cooled to 77°K. The sample was irradiated through Pyrex and the ir spectrum monitored at frequent intervals. The ir spectrum exhibited a ketene band at 4.74 μ. The ketene was stable at low temperature in the dark but warming to -60° caused the rapid disappearance of the ketene and apparent regeneration of the adduct.

Irradiation of the Diels-Alder adduct in methanol at -40°

A solution of 7 mg of the Diels-Alder adduct in 10 ml of methanol contained in a small Pyrex test tube was cooled to -40° and irradiated for 1 hr with a 550 watt Hanovia lamp. The solution was concentrated at room temperature under vacuum to give a viscous oil which was chromatographed on Florisil with 10% benzene/hexane to give 6 mg of a methanol addition product as a glass which resisted crystallization.

The methanol addition product was characterized by the following data: ir (CCl_4) (Figure 8, page 123) 3.37, 5.60, 5.71, 5.80, 7.24, 8.00, 8.37, 8.47, 9.17 μ; nmr (CCl_4) (100 MHz) (Figure 9, page 127) δ 7.35 (multiplet, 5H), 6.18 (doublet of doublets, 1H, J = 10.0 Hz and J = 2.0 Hz), 5.94 (doublet of doublets, 1H, J = 10.0 Hz and J = 3.2 Hz), 3.72 (singlet, 3H), 3.38 (doublet, 1H, J = 9.0 Hz), 3.05 (doublet of multiplets, 1H, J = 9.0 Hz), 2.30-1.70 (complex multiplet, 6H), 0.90 (multiplet, 1H); mass spectrum (70 eV) m/e (relative intensity) 337 (parent, 16), 309 (13), 305 (23), 278 (14), 277 (36), 218 (10), 191 (10), 159 (10), 158 (30), 157 (16), 149 (19), 131 (34), 130 (100), 117 (32), 116 (31), 115 (26).

High resolution of the molecular ion M^+ in lieu of microanalysis, calcd for $C_{20}H_{19}NO_4$: 337.1339, found 337.1325.

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