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CHEMICAL AND PHOTOCHEMICAL STUDIES OF
UNSATURATED CYCLOOCTANE DERIVATIVES.

Iowa State University of Science and Technology
Ph.D., 1965
Chemistry, organic

University Microfilms, Inc., Ann Arbor, Michigan

CHEMICAL AND PHOTOCHEMICAL STUDIES OF
UNSATURATED CYCLOOCTANE DERIVATIVES

by

Thomas Kenneth Hall

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

Major Subject: Organic Chemistry

Approved:

Signature was redacted for privacy.

In Charge of Major Work

Signature was redacted for privacy.

Head of Major Department

Signature was redacted for privacy.

Dean of Graduate College

Iowa State University
of Science and Technology
Ames, Iowa

1965

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VITA

The author was born September 28, 1936, in Minneapolis, Minnesota. When he was 12, his family moved to California. In June, 1954, he graduated from Bellarmine College Preparatory in San Jose, California. Having been awarded a Walterstein Achievement Scholarship he entered the University of Santa Clara in September, 1954, majoring in engineering. Dissatisfied with engineering, he changed his major to biology in September, 1955. He entered St. Louis University Medical School in September, 1957, where he decided that medicine was not for him. In October, 1958, having decided that he wanted to teach, he dropped out of medical school, with the intention of re-entering the University of Santa Clara the following fall. During the intervening period he worked as an encyclopedia salesman, and then as a chemical laboratory technician at Aerojet-General Corp. in Sacramento, California. While in Sacramento, he met, wooed, and wed Sandra Jean Pullan, without whom the rest of this tale would not be possible. In September, 1959, he returned to the University of Santa Clara with a major in chemistry and a minor in philosophy. In June, 1961, two years and one and a half boys later, he finally received his B.S. degree.

In September, 1961, the author began his graduate studies in organic chemistry at Iowa State University under Dr. O. L. Chapman. After two and a half years as a teaching assistant,

he was awarded a NASA Traineeship. In August, 1965, now with three boys, he completed the requirements for his degree, with a major in organic chemistry and minors in biochemistry and inorganic chemistry, and was granted the degree, Doctor of Philosophy, from Iowa State University.

INTRODUCTION

The work described in this thesis is concerned primarily with two areas of the chemistry of cyclooctene derivatives: first, with an attempt to prepare an aromatic system containing six π -electrons in an eight-membered ring; and second, with the photochemistry of cyclooctene-3-one.

The first area of investigation involved the attempted synthesis of $\Delta^{1,4,6}$ -cyclooctatriene-3,8-dione and its precursors, as well as the attempted preparation of cyclooctatetraene dication.

The second area was concerned with an exploration of the properties of cyclooctenone when irradiated with ultraviolet light in protic solvents. Some effort was expended in an attempt to determine whether the reaction observed for cyclooctenone was generally applicable in other unsaturated ketone systems. Experiments were performed in order to try to obtain information about the reaction mechanism.

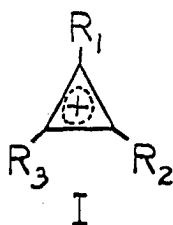
HISTORICAL

Cyclic Aromatic Cations and
their Corresponding Ketones

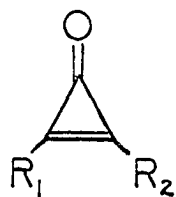
Carbonium ions have long interested organic chemists because of their role as reaction intermediates. Recently, a number of monocyclic aromatic carbonium ions have been prepared; these are of interest primarily because they have electronic configurations which fit the "Huckel ($4n+2$) rule" and exhibit aromatic properties. The inherent stability associated with such systems has been cited in rationalizing the stability and properties of the corresponding ketones (1, Chapter 10).

Many of the known examples of such aromatic ions and their corresponding ketones are discussed in Streitweiser's book (1). Consequently, no attempt will be made here to describe completely the work in this field prior to 1961. As far as possible all reported examples from the literature of 1961 through June, 1965, will be mentioned.

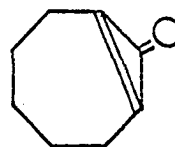
Breslow prepared several cyclopropenium fluoborates, as well as several cyclopropenones (2,3,4,5,6). Volpin (7) also prepared diphenylcyclopropenone.



	R_1	R_2	R_3
a.	ϕ	ϕ	ϕ
b.	H	ϕ	ϕ
c.	H	Et	Et

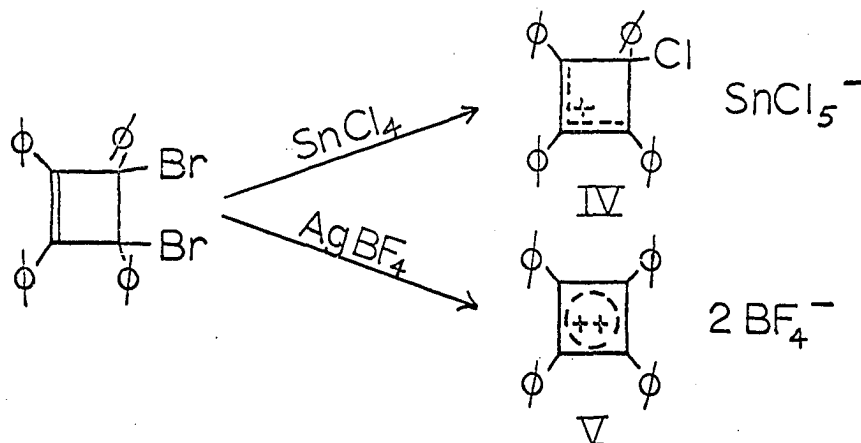


II



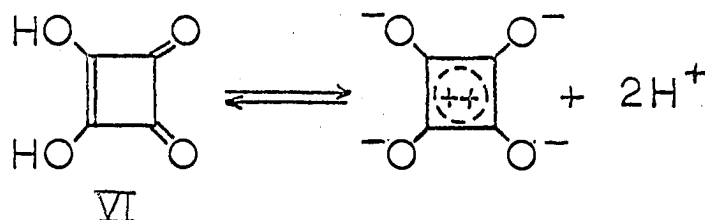
III

In 1962 Katz (8) reported his unsuccessful attempt to prepare the cyclobutenium dication system and Freedman (9) reported its successful preparation. Subsequent X-ray work by Bryan (10) showed Freedman's compound to be an allylic monocation (IV). A further effort by Freedman (11) resulted in the successful preparation of this system (V) in solution. This is the first example of an aromatic cyclic dication ever

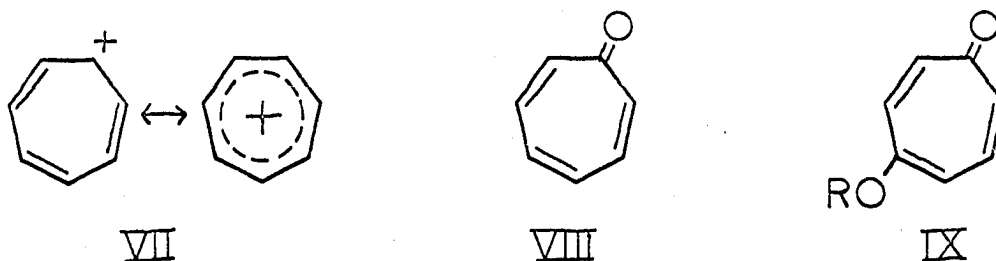


reported. Several of the corresponding diketones have been prepared (1, Chapter 10; 12). The most striking of these (13) is "squaric acid" (VI), which exhibits a very high acidity,

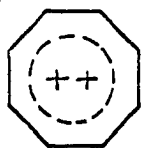
presumably due to the high stability of the resonance-stabilized aromatic dianion.



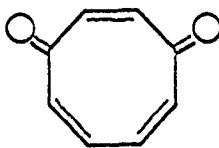
The first reported cyclic aromatic carbonium ion, the tropylium ion (VII), was prepared in 1891 by Merling (14) but not characterized. In 1954 Doering (15) reopened the question and proved the structure of Merling's compound. This is the most extensively investigated of the known aromatic carbonium ions. An excellent review is available (16) which includes a discussion of the corresponding tropones (VIII) and tropolones (IX). Several instances have been reported in which the tropylium ion functions as a charge-transfer acceptor (17, 18, 19).



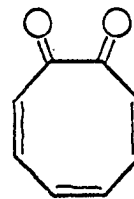
There are no known reports of the preparation of cyclo-octatetraene dicarbonium ion (X) or its corresponding ketones (XI, XII).



X



XI



XII

Simple Hückel molecular orbital calculations (20) predict a delocalization energy (D.E.) for the cyclopropyl cation of 2.00β and for tropylium ion of 2.99β . Similar calculations give a 2β D.E. for the cyclobutenium dication. The D.E. for benzene by the same HMO method is 2β . We have done simple HMO calculations for a few cyclooctatetraene systems; the results are presented in the Results and Discussion section of this dissertation.

Nuclear magnetic resonance spectroscopy has provided a powerful tool for the investigation of aromatic systems. The diamagnetic shielding (21, p. 18) of ring protons caused by "ring currents" is an important diagnostic method for detecting aromatic character. The relation between ring currents and aromaticity is a subject for active current research (22, 23, 24).

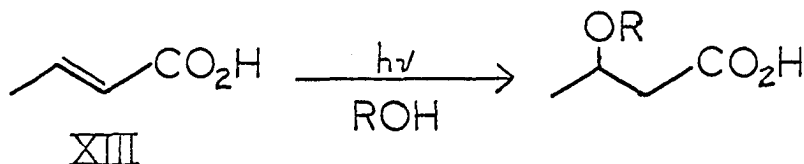
Fraenkel et al. (25) have studied the relation between π -electron density and chemical shift in the n.m.r. spectrum for tropylium cation, benzene, and cyclopentadienyl anion. They arrive at a simple expression for this relationship: $\delta = aq$, where δ is the chemical shift relative to benzene,

q is the charge per carbon atom, and a is an empirical constant (~ 10 ppm).

Solvent Photoaddition to Conjugated Double Bonds

A few examples of solvent photoaddition to a double bond conjugated to a carbonyl group or another unsaturated group are scattered throughout the literature. Some of these are gathered together in Schönberg's book (26, p. 73) on preparative organic photochemistry.

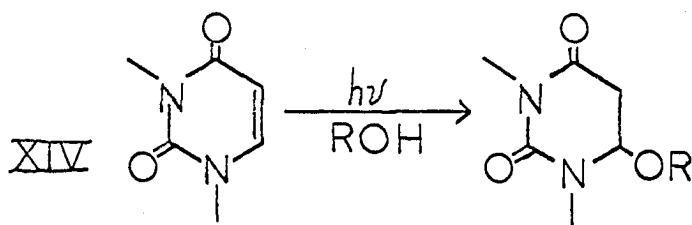
Stoermer and Stockmann (27) observed the photoaddition of water, methanol, and ethanol to the double bond of crotonic acid (XIII), the sodium salt of crotonic acid, and mesaconic acid (2-methylfumaric acid). The corresponding amides



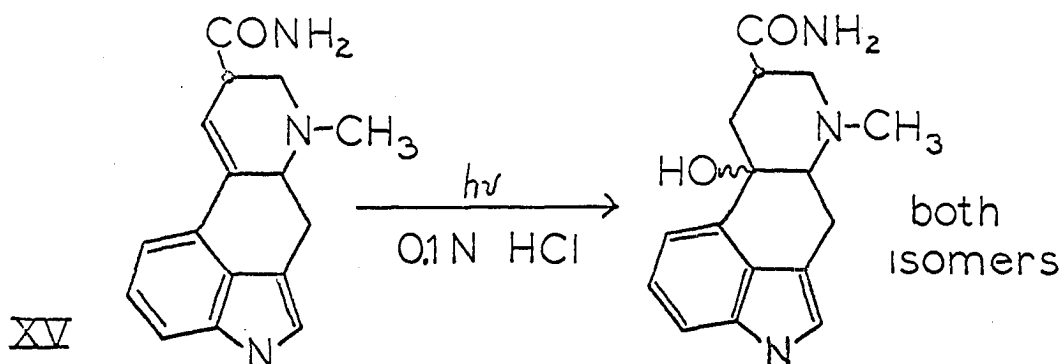
and all other unsaturated acids irradiated simply isomerized or allomerized. In an earlier paper, Stoermer (28) claims, without substantiation, that *o*-chlorocinnamic acid isomerizes via the addition and elimination of acetic acid when irradiated in acetic acid.

Wang has studied extensively the photochemistry of nucleic acids (29,30,31,32). Thymine and 1,3-dimethyluracil (XIV) add methanol across the double bond when irradiated in ice containing 2% methanol. In pure ice the only products are dimeric

for all uracil and thymine derivatives investigated. An apparently contradictory previous report by Wang (33) claims the addition of water across the double bond of 1,3-dimethyluracil when it was irradiated in water.

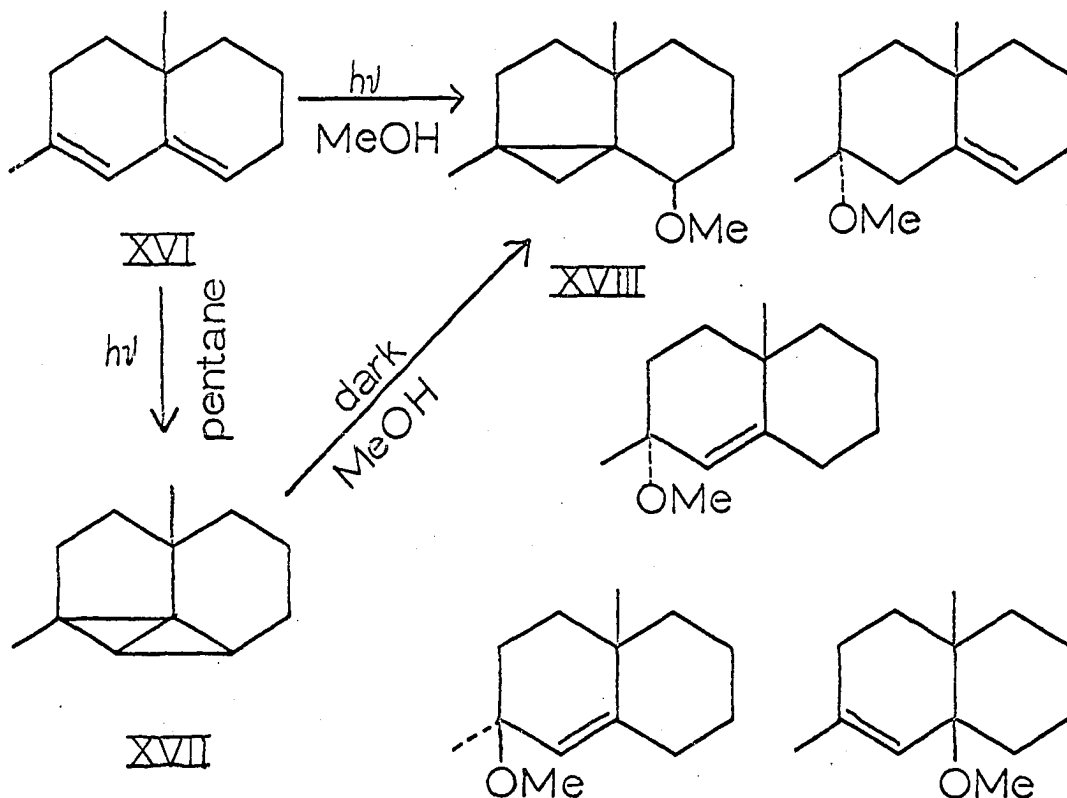


Bernardi et al. (34) and Stoll and Schientz (35) have investigated the photoaddition of water to ergotamine (XV) in weakly acidic solution.



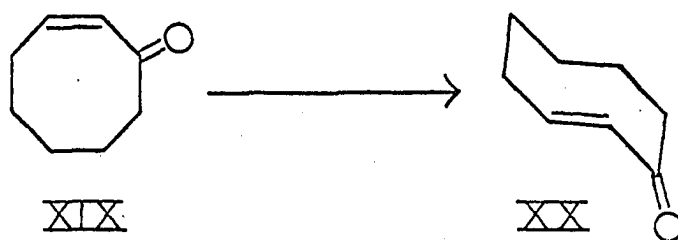
W. G. Dauben (36) has investigated the photoaddition of methanol to ergostadiene and substituted hexalin derivatives. The irradiation of 3,10-dimethyl- $\Delta^{3,5}$ -hexalin (XVI) in methanol gives a variety of methanol addition products whose relative amounts vary with methanol concentration. When this irradiation is performed in pentane, the bicyclobutane intermediate (XVII) is isolated. This bicyclobutane intermediate

reacts in the dark with methanol to form only one ether (XVIII), in direct contrast to the irradiation in methanol, where a number of other ethers are formed. Dauben feels that there is a competition between the solvent reaction and the formation of the bicyclobutane.



Medium ring unsaturated ketones have been little investigated as such with regard to their photochemical properties. Very recently Eaton (37) reported the photochemical conversion of cis-cyclooctene-3-one (XIX) to the highly strained trans-compound (XX). Eaton (38) and Corey (39) independently reported the analogous reaction for cis-cycloheptene-3-one (XV) at low temperatures. In both the 7 and 8-membered rings the

trans-compound is apparently very reactive. Eaton obtained Diels-Alder adducts of XX at room temperature, and also reported that XX dimerized at room temperature. Corey (40) was able to obtain cycloaddition products of XX with olefins in good yield.

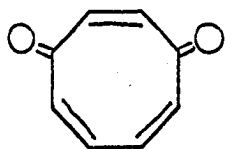


There is no report in the literature of the photoaddition of solvent to the double bond in simple unsaturated ketones. An observation by Dr. H. Juneja (41) in this laboratory that $\Delta^{2,6}$ -cyclooctanone might be incorporating acetic acid when irradiated prompted a more detailed investigation.

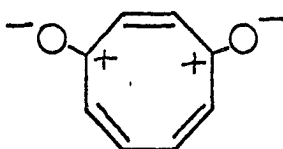
RESULTS AND DISCUSSION

Attempted Preparation of Cyclooctatriene-1,4-dione

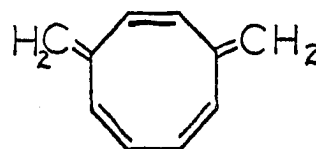
This investigation was initiated in order to prepare cyclooctatriene-1,4-dione (XXI). This compound fits the Hückel ($4n + 2$) rule, having six π -electrons; thus it was anticipated that it might provide a unique example of an aromatic six π -electron system in an eight-membered ring. It should be noted however that a necessary condition must be fulfilled before XXI could exhibit aromaticity; i.e., resonance structure XXI-a must contribute significantly to the resonance hybrid so that the p-orbitals on the carbonyl carbon will be sufficiently available for efficient delocalization of the six π -electrons around the ring. The most efficient delocalization of π -electrons will occur when the ring is planar, since all p-orbitals will then be parallel. Thus there will be two opposing energy factors; the strain energy or energy required to flatten the ring must be provided from the energy gained through delocalization of π -electrons. The difference between these will be the stabilization energy.



XXI



XXI-a



XXII

Simple Huckel molecular orbital calculations (1, p.33) were performed for several related systems in order to determine delocalization energies. The resonance integral for the carbonyl groups was assumed to be 1.414β , a value which may be slightly high, but which should nevertheless yield qualitatively correct results (1, p. 120).

The systems for which calculations were carried out were XXI, XXI-a, and XXII.

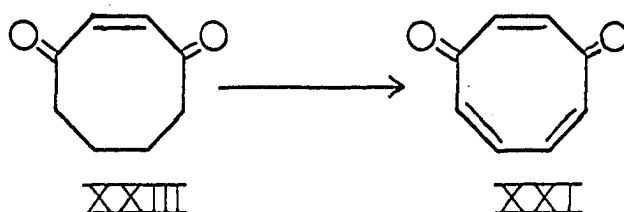
The calculated* delocalization energies were as follows: XXI, 2.495β ; XXI-a, 3.657β ; XXII, 2.354β . If β is assumed to have the value 18 kcal/mole, these energies then become: XXI, 44.9 kcal/mole; XXI-a, 65.8 kcal/mole; XXII, 42.3 kcal/mole.

All of these structures have considerably more delocalization energy than the 21-23 kcal/mole which has been estimated (1, 42) as the strain energy of a flattened cyclooctatetraene ring.

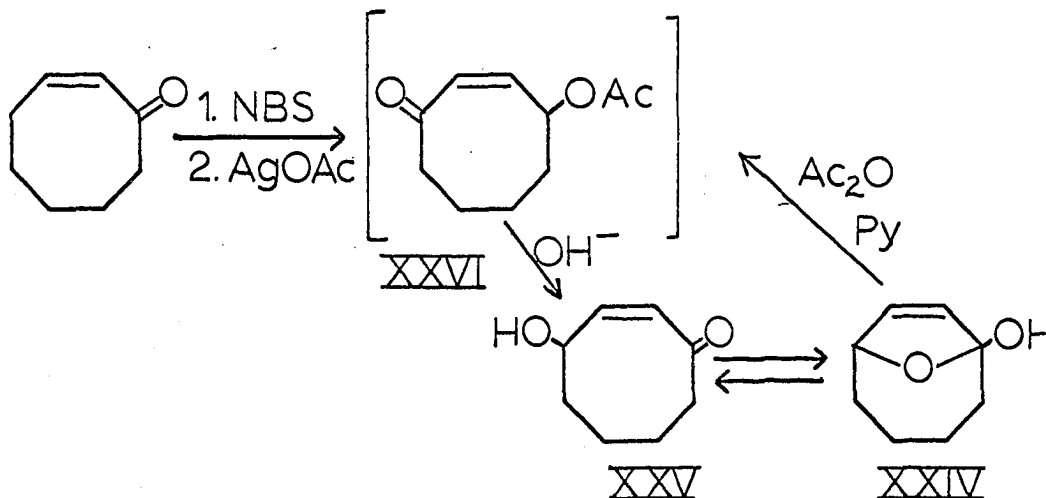
It should be noted that XXI is only slightly more stable than XXII, whereas XXI-a is 23.5 kcal/mole more stable than XXI. Thus it seemed plausible that XXI might be stable if it could be synthesized, and several synthetic routes were examined.

*We are indebted to Prof. C. H. DePuy and Lynn Rodewald for the use of their MOCAL computer program for these calculations.

The most direct approach appeared to be preparation of cyclooctene-3,8-dione (XXIII), followed by introduction of two double bonds. Many approaches to the synthesis of XXIII were investigated.



Bromination of cyclooctene-3-one (XIX) with N-bromo-succinimide, followed by acetolysis with silver acetate in acetic acid, basic hydrolysis, and chromatography on alumina yielded 9-oxabicyclo-(4.2.1)-2-nonenol (XXIV) in 12.8% overall yield. Treatment of XXIV with acetic anhydride in pyridine



gave a crude acetate (XXVI) whose infrared spectrum (maxima at 5.77 and 6.03 μ), ultraviolet spectrum (λ_{max}^{EtOH} 223 $m\mu$), and n.m.r. spectrum were consistent with structure XXVI. Attempted chromatography gave only XXIV, and no acetate products.

The infrared spectra of XXIV were very informative. The spectrum when run on a potassium bromide pellet (Figure 1) showed no carbonyl absorption, but very strong hydroxyl group absorption at 3.02μ , and a weak band at 6.16μ due to a double bond. However, when the spectrum was recorded in chloroform solution (Figure 1), alcohol bands were observed at 2.78 and 2.97μ , in addition to a low intensity band at 6.03μ , which is the characteristic wavelength for carbonyl group stretching in cyclooctene-3-one, and a weak band at 6.16μ due to a double bond.

The n.m.r. spectrum of XXIV (Figure 2) showed a quartet centered at 4.26τ ($J_{\text{vinyl}} = 6$ c.p.s.), a crude doublet at 5.01τ , a sharp singlet at 6.32τ , and two poorly resolved multiplets centered at 8.13 and 8.45τ . The relative peak areas were 2:1:1:8.

Thus it appears that XXIV should be represented in both its hemiketal form and in an open keto-alcohol form XXV, with the infrared spectra indicating an equilibrium between the two forms favoring XXIV.

Chapman (43) has reported a trend in vinyl coupling constants for olefinic protons in cis-cyclic olefins which further substantiates the structure assignment. For a five-membered ring, the expected value for the vinyl coupling constant is 6 c.p.s., and for an eight-membered ring it is 12-13 c.p.s. The value found here (6 c.p.s.) thus indicates the presence of the smaller five-membered ring in XXIV.

Figure 1. Infrared spectra

Top - cycloocten-3-one (XIX)

Middle - 9-oxabicyclo-(4.2.1)-2-nonenol (XXIV)
in potassium bromide pellet

Bottom - 9-oxabicyclo-(4.2.1)-2-nonenol (XXIV)
in chloroform

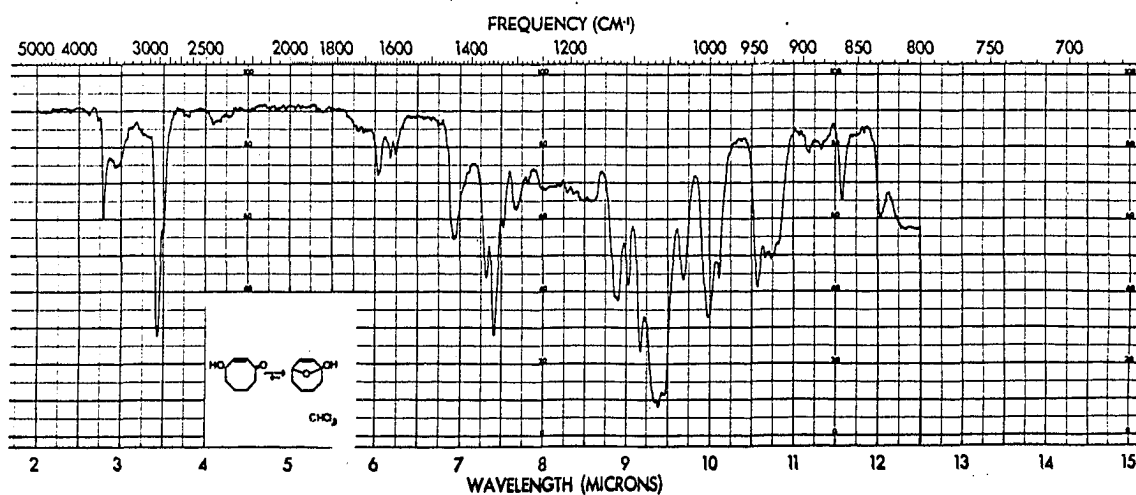
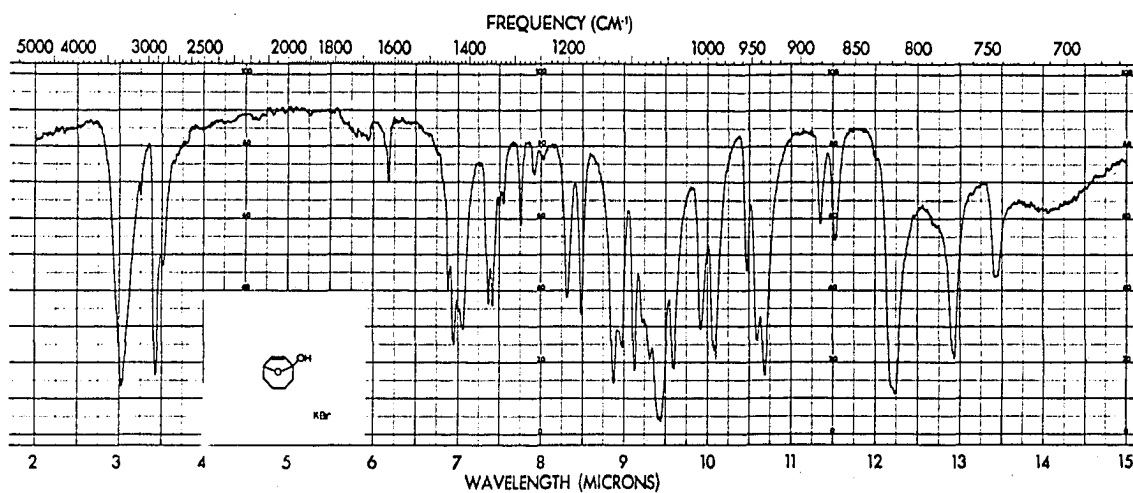
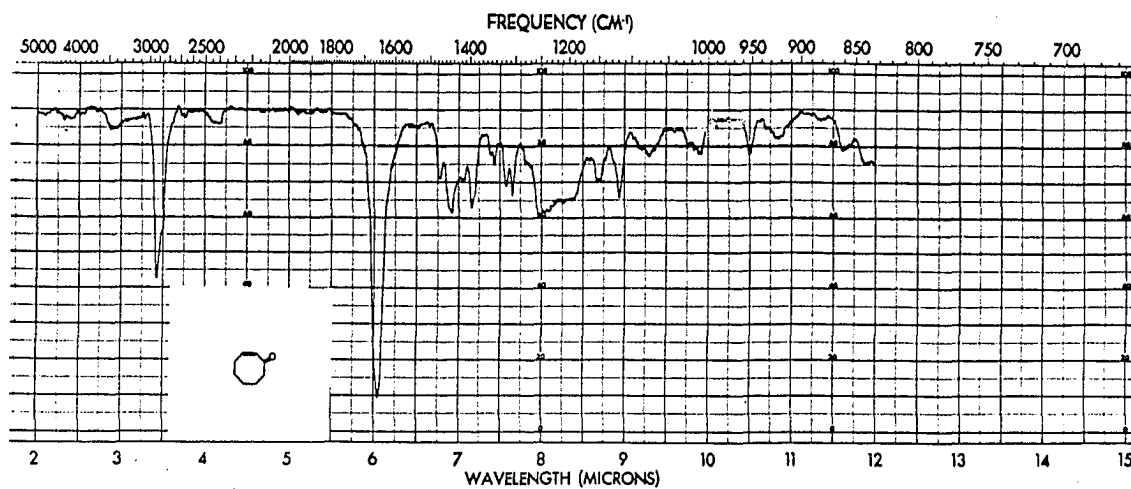
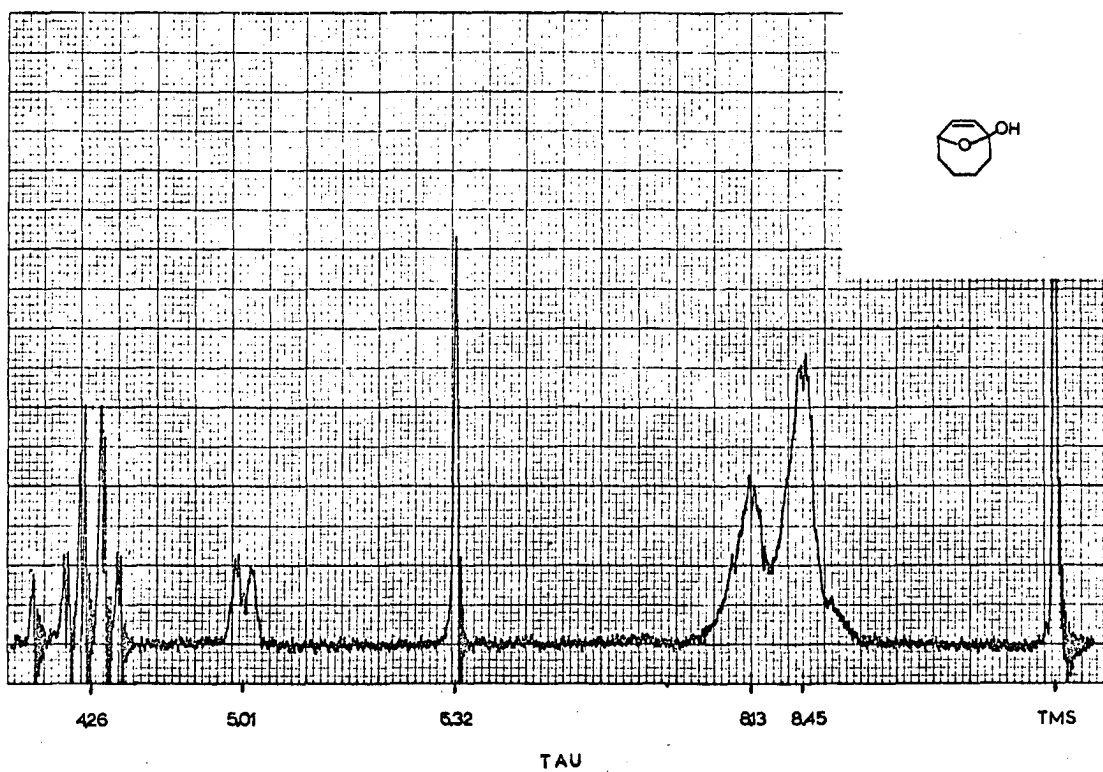
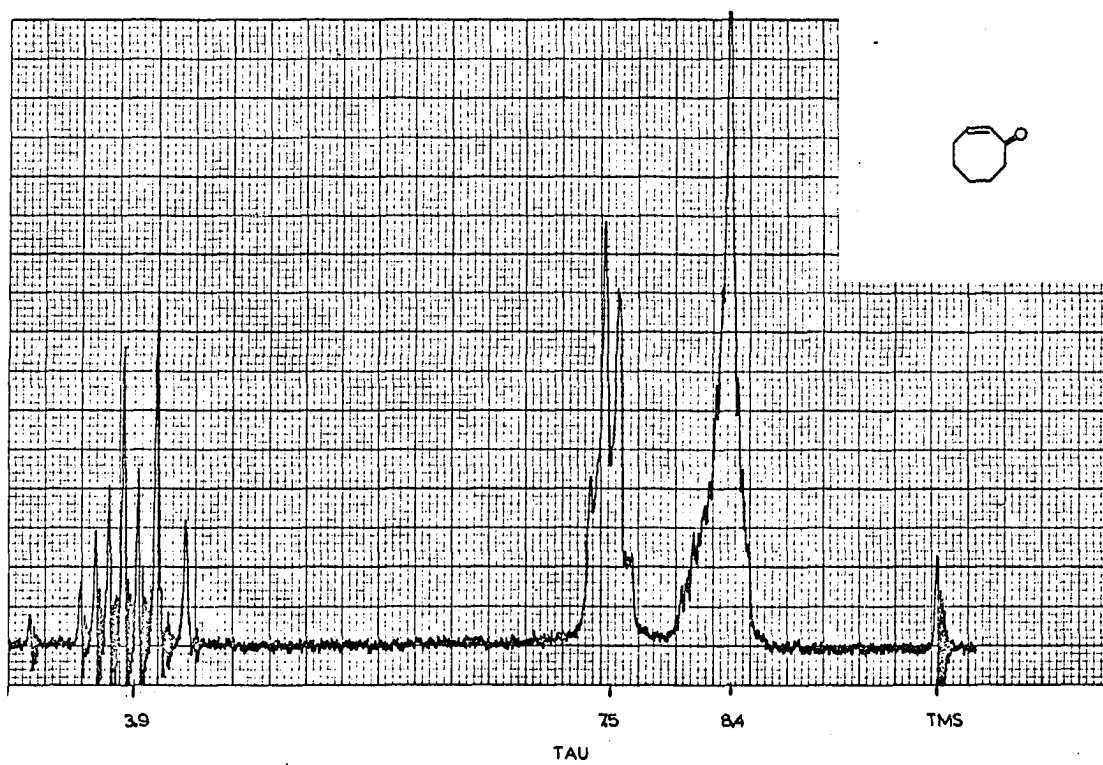


Figure 2. Nuclear magnetic resonance spectra

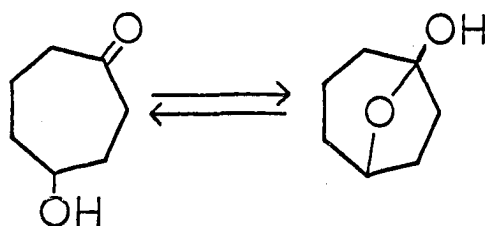
Top - cycloocten-3-one (XIX)

Bottom - 9-oxabicyclo-(4.2.1)-2-nonenol (XXIV)



In addition, Chapman and King (44) have correlated alcohol type with the multiplicity observed for alcohol proton resonances in dimethyl sulfoxide solution, finding triplet, doublet, and singlet multiplicity for primary, secondary, and tertiary alcohols respectively. The n.m.r. spectrum of XXIV in dimethyl sulfoxide shows a sharp singlet for the alcohol proton, thus showing it to be tertiary.

Infrared evidence for a similar equilibrium was presented by Doering and Sayigh (45) and by Yates and Anderson (46) in a seven-membered ring system.

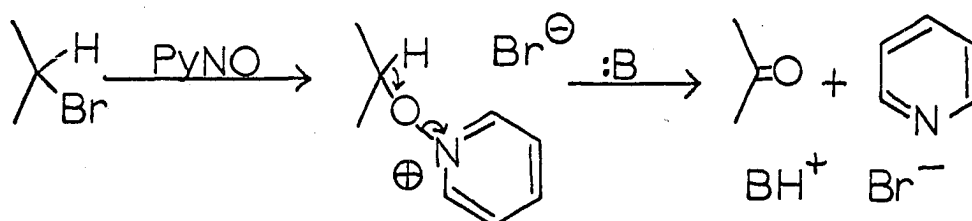


Another method for the preparation of XXIV involves oxidation of cyclooctene-3,8-diol (XXVII) with manganese dioxide in chloroform at room temperature. XXVII was prepared from the corresponding diacetate (XXVIII), which was a minor product in the selenious acid oxidation of cyclooctene in acetic acid-acetic anhydride. The manganese dioxide oxidation proceeded smoothly to a 75% (v.p.c.) yield of XXIV. Prolonged exposure of XXIV to these oxidizing conditions did not cause any observable oxidation of XXIV to the dione (XXIII).

Chromic acid oxidation of XXIV resulted only in the recovery of starting material in low yield.

It thus appeared that no approach to the synthesis of XXIII which proceeded via the keto-alcohol XXV would be successful, and other approaches were examined.

DePuy and Zaweski (47) utilized pyridine-N-oxide for the oxidation of an organic bromide. Since this method of oxidation avoids the intermediacy of a hydroxy-ketone intermediate, it was examined for use in the preparation of XXIII.

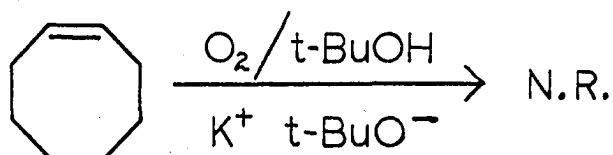


Cyclooctene-3-bromide (XXIX) was oxidized by this method, and did yield cyclooctene-3-one, although the yield (< 15%) was low. An attempt to perform the same oxidation on cyclooctene-3,8-dibromide (XXX) was unsuccessful.

A similar reaction, utilizing dimethyl sulfoxide as oxidizing agent has been reported by several investigators (48, 49, 50, 51, 52). Attempts to oxidize XXX with dimethyl sulfoxide at temperatures ranging from 30-160°, both with and without the presence of base as a catalyst, were totally unsuccessful. Infrared spectra on the crude reaction mixtures showed very little, if any, ketonic absorption. A variation of this method (49) in which XXX was converted to the ditosylate with silver tosylate, and then heated in dimethyl sulfoxide

containing sodium bicarbonate was mildly encouraging in that some oxidation did occur, but the yield was so low and the product mixture so complex that no isolable materials were obtained.

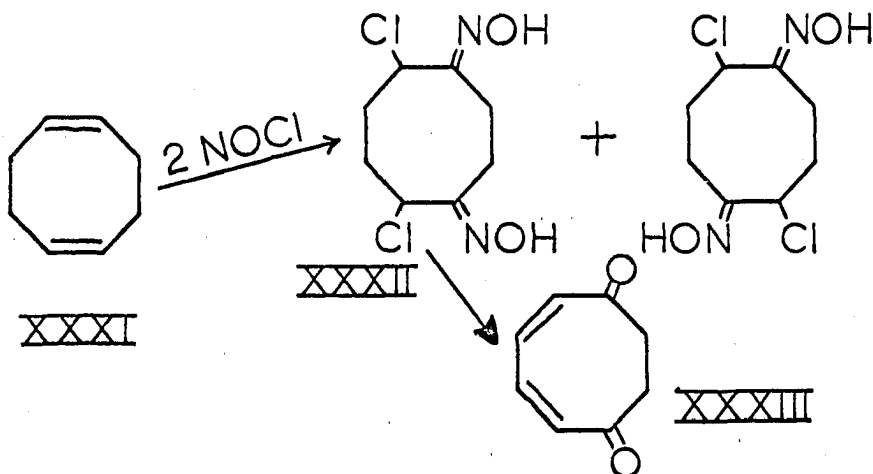
Another approach to the preparation of XXIII involved air oxidation of cyclooctene in basic solution. A 4:1 excess of



base to olefin was employed. After 24 hours, no reaction was observed.

Since none of these approaches involving allylic oxidation had proved successful, several entirely different approaches were tested.

It was thought that the well-known (53) addition of nitrosyl chloride to olefins might be utilized to obtain a bis-adduct (XXXII) of 1,5-cyclooctadiene (XXXI) which could be converted to XXXIII.



In a preliminary experiment cyclooctene was treated with isoamyl nitrite and hydrochloric acid. Two crystalline solids were obtained, XXXIV (m.p. 92-93°) and XXXV (m.p. 101-101.5°) in a total yield of 31%. These two compounds had the same elemental composition. XXXIV was converted to XXXV on refluxing with isopropanol-urea (54). XXXIV had $\lambda_{\text{max}}^{\text{EtOH}}$ 293 $m\mu$ (53), while XXXV had no intense absorption above 210 $m\mu$.

The infrared spectrum of XXXV (Figure 3) showed an intense hydroxyl absorption at 3.10 μ and a weak band (-C=N-stretch) at 6.07 μ . These bands were both absent in the infrared spectrum of XXXIV (Figure 3).

The n.m.r. spectrum of XXXIV (Figure 4) shows a broad multiplet (1H) at 4.45 τ for the proton on carbon bearing chlorine, a similar multiplet (1H) at 5.28 τ on the carbon bearing nitrogen, a broad multiplet at 7.87 τ (\sim 4H) for the methylene protons adjacent to the substituted carbons, and a broad multiplet at 8.36 τ (\sim 8H) for the remaining methylene protons.

The n.m.r. spectrum of XXXV (Figure 4) shows a broad singlet (1H) at 0.54 τ for the oxime hydroxyl proton, a poorly resolved quartet (1H) at 5.45 τ for the proton on carbon bearing chlorine, a poorly resolved multiplet (1H) centered at 7.14 τ for one of the methylene protons adjacent to the oxime group, and two poorly resolved multiplets (11H) centered at 7.87 and 8.44 τ .

The above data, coupled with the general nature (53) of

Figure 3. Infrared spectra

Top - 2-chlorocyclooctanone oxime (XXXV)

Bottom - nitroso dimer (XXXIV)

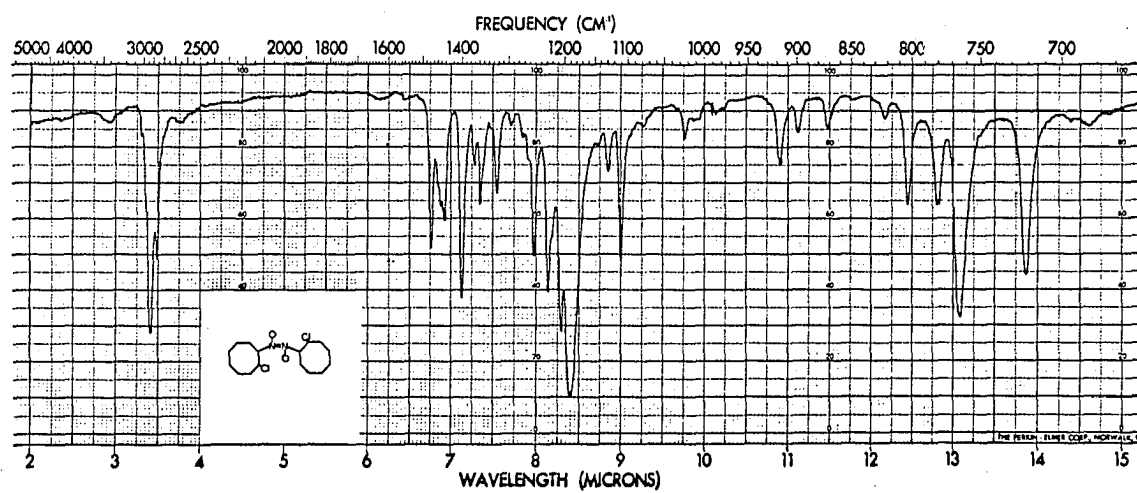
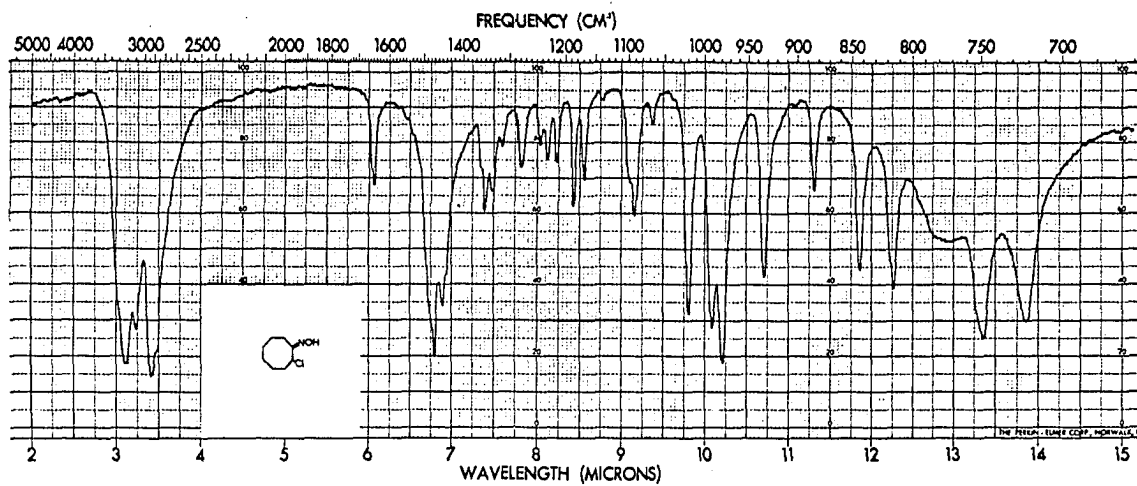
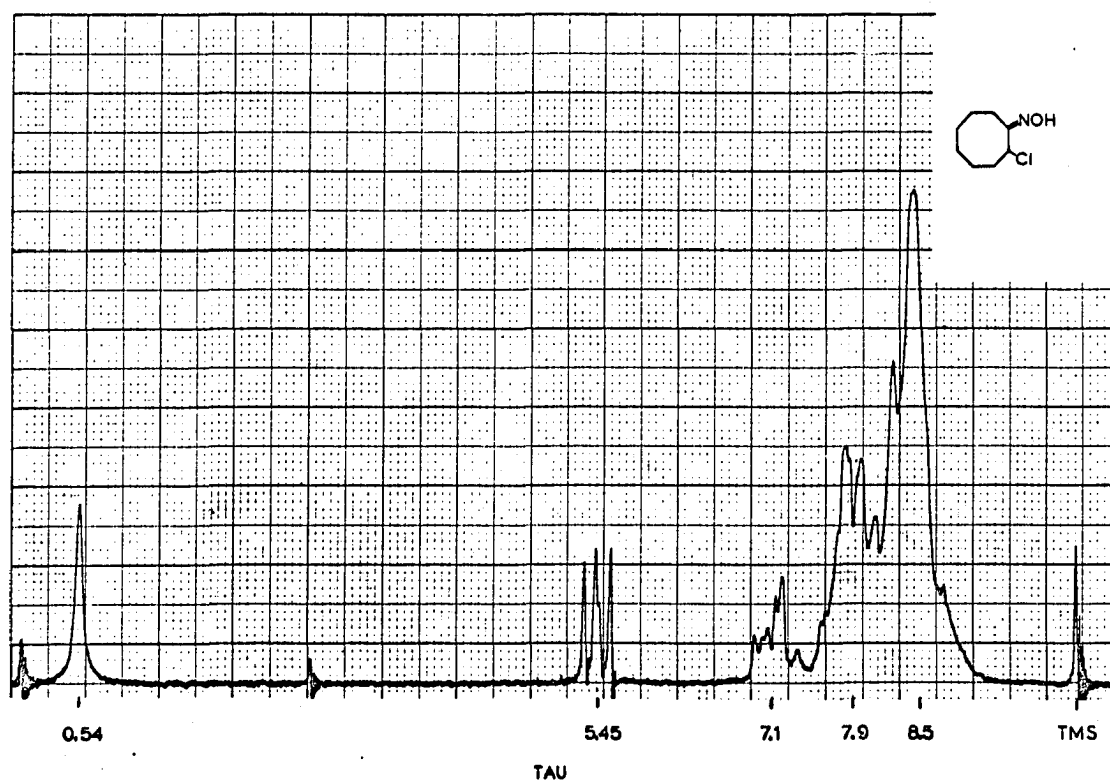
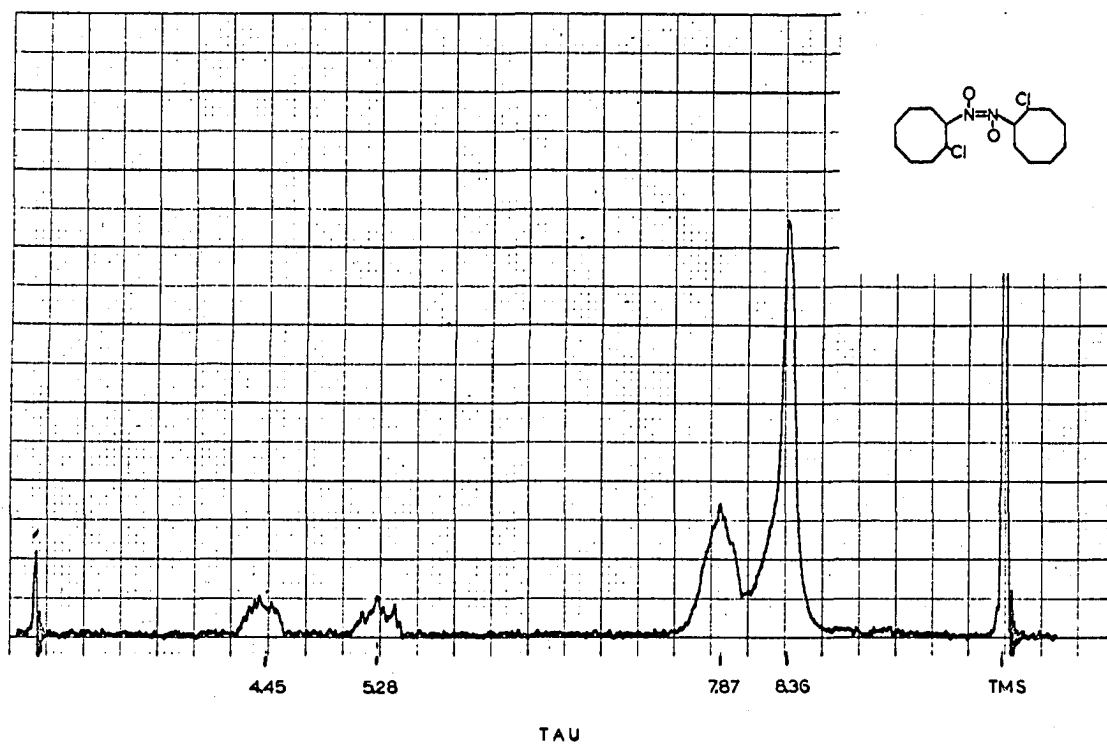


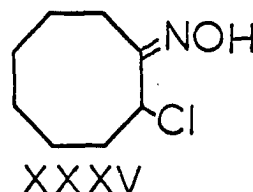
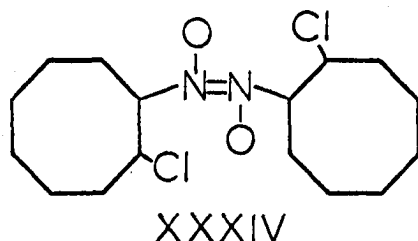
Figure 4. Nuclear magnetic resonance spectra

Top - nitroso dimer (XXXIV)

Bottom - 2-chlorocyclooctanone oxime (XXXV)



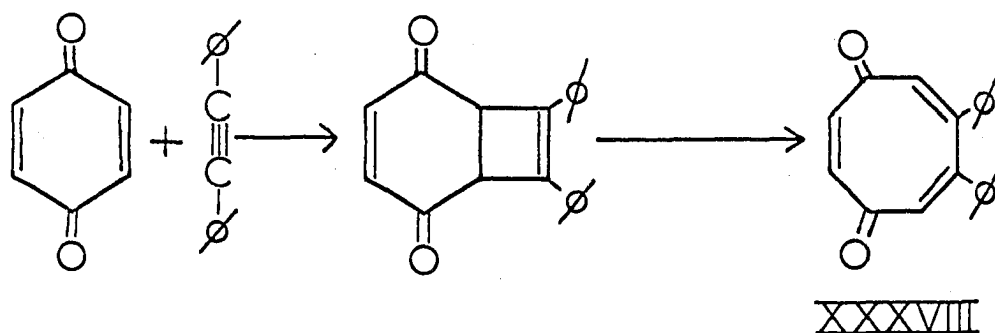
the nitrosyl chloride reaction with olefins strongly suggest the following structures for XXXIV and XXXV.



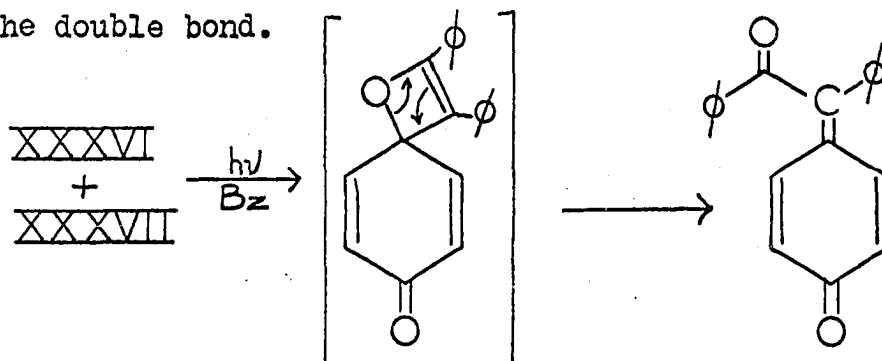
An attempt to convert XXXV to cyclooctenone according to the procedure of Wallach (55) by treatment with dimethyl aniline and aqueous sulfuric acid was unsuccessful, giving a reaction product with carbonyl absorption at 5.90μ and no absorption at 6.03μ . The use of aniline as base gave the same results.

Since this work appeared to be without application for the preparation of cyclooctenone, and since Metzger (56) at the same time published his results on the reaction of 1,5-cyclooctadiene (XXXI) with nitrosyl chloride indicating that it would add only one mole, this line of investigation was not continued.

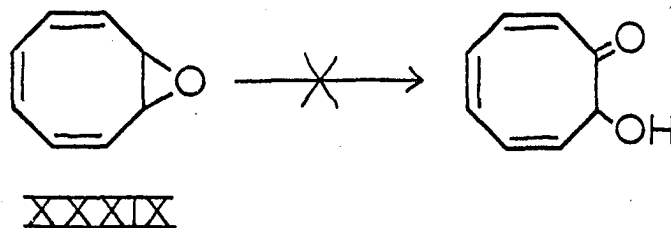
One of the more direct approaches to the synthesis of a system like XXI involved an attempt to cyclo-add diphenylacetylene (XXXVI) to the double bond of *p*-benzoquinone (XXXVII). It was hoped that the adduct could be tautomerized to XXXVIII. A 1:1 molar mixture of XXXVI and XXXVII was heated for 24 hours in a sealed tube at 105-130°. No reaction was observed. A 1:1 mixture dissolved in *o*-dichlorobenzene was heated at



temperatures up to 210° in an n.m.r. tube and no reaction was observed. The same sample was irradiated and no reaction was observed. Shortly after this experiment was performed, it was reported by Bryce-Smith (57) and Zimmerman (58) that on irradiation XXXVI reacts with XXXVII to give a product derived from cycloaddition to the carbonyl group of XXXVII rather than the double bond.



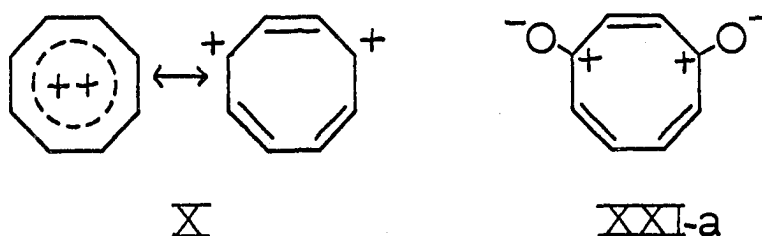
Cohen and Tsuji (59) reported the boron trifluoride catalyzed rearrangement of epoxides to α -hydroxyketones in dimethyl sulfoxide. It was decided to try this reaction on cyclooctatetraene monoepoxide (XXXIX) in an attempt to prepare the α -hydroxyketone precursor to XXI.



Cyclooctatetraene monoepoxide in dimethyl sulfoxide, when heated on the steam bath with a catalytic amount of boron trifluoride etherate, gave a crude reaction mixture having strong infrared absorption maxima at 3.54, 3.67, 5.83, 5.93, and 6.22 μ . Buchi and Burgess (60) have reported the thermal isomerization of XXXIX to β -cycloheptatriene carboxaldehyde, which has bands in its infrared spectrum at 3.55, 3.68, 5.92, and 6.22 μ . β -cycloheptatriene carboxaldehyde was converted to β -phenylacetaldehyde (5.82 μ) on heating. A comparison of this data to that of Buchi and Burgess suggests that XXXIX undergoes an acid-catalyzed rearrangement corresponding to its thermal rearrangement. Since the desired conversion of XXXIX to an α -hydroxyketone did not occur, the reaction was not further investigated. The same reaction appeared to occur, but more slowly, when XXXIX was heated in dimethyl sulfoxide without acid catalysis.

Attempted Preparation of Cyclooctatetraene Dication (X)

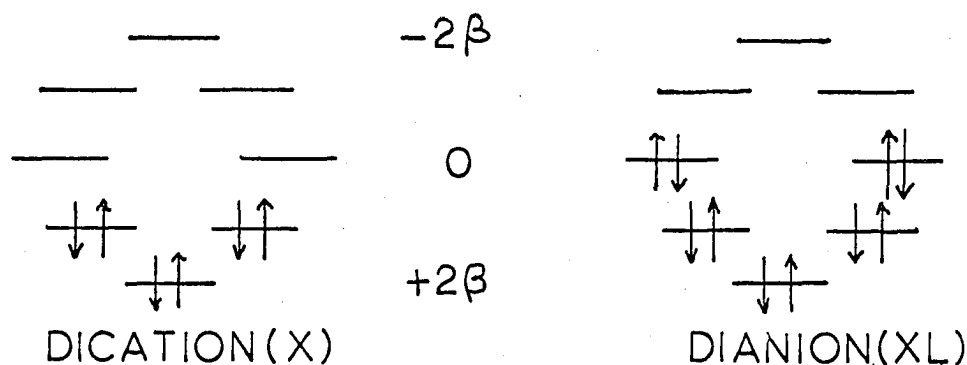
X corresponds to XXI-a for purposes of simple HMO calculations, and thus has about 65 kcal/mole delocalization energy in such calculations. This is considerably more than the D.E. calculated for XXI (44.9 kcal/mole). If X could be prepared, further efforts toward the preparation of XXI could be under-



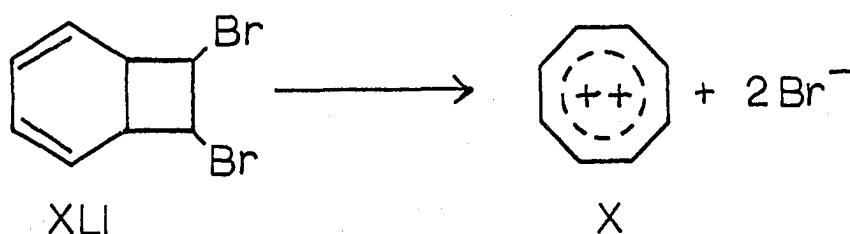
taken with a greater confidence in the possibility that it could be a stable species. On the other hand, if X could not be prepared, one might question the wisdom of further pursuing the synthetic attack on XXI.

It should be noted that there was good reason to believe that X would be a stable, flat, aromatic ion. Katz (61, 62) has prepared cyclooctatetraene dianion (XL), a 10 π -electron system, and characterized it as a stable aromatic ion. Simple HMO theory predicts the same delocalization energy for the dianion and the dication in an eight-membered ring, since each has just six π -electrons in bonding orbitals; the "extra" four electrons for the dianion are in non-bonding orbitals, not in anti-bonding orbitals. The dianion and the dication should have about the same strain problems with respect to

attaining a planar configuration. Thus it is not unreasonable to attempt a direct synthesis of the dication.



Cyclooctatetraene dibromide (XLI) was chosen as the starting material. One must remove two halide ions from XLI and the bicyclic ring system must open up to an eight-membered ring. Attempts to remove bromide by treatment with strong Lewis acids such as antimony pentachloride were unsuccessful because polymerization occurred immediately; apparently the preferred reaction here is at the diene system where a cationic chain polymerization is possible.



Consequently the mode of reaction was altered. Silver-ion assisted solvolyses in polar solvents such as acetonitrile were used in all other trials. Silver fluoborate, hexafluoro-

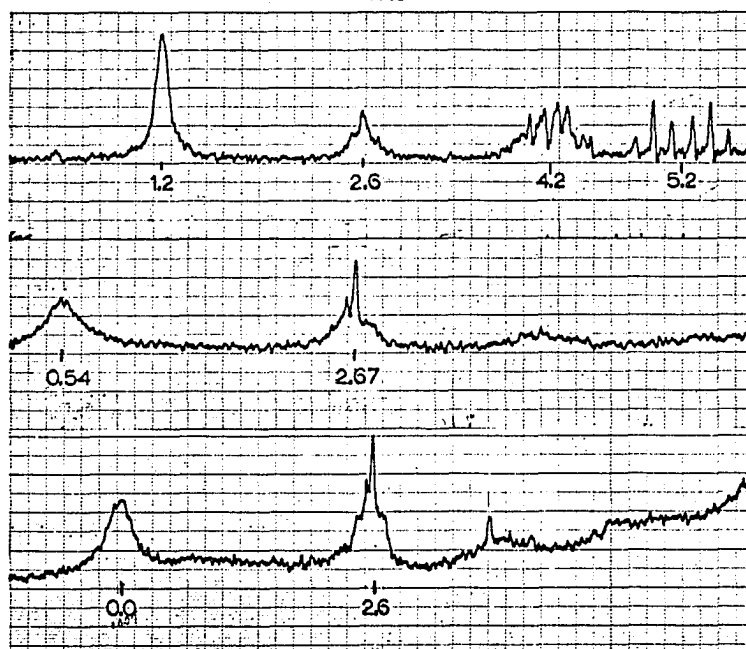
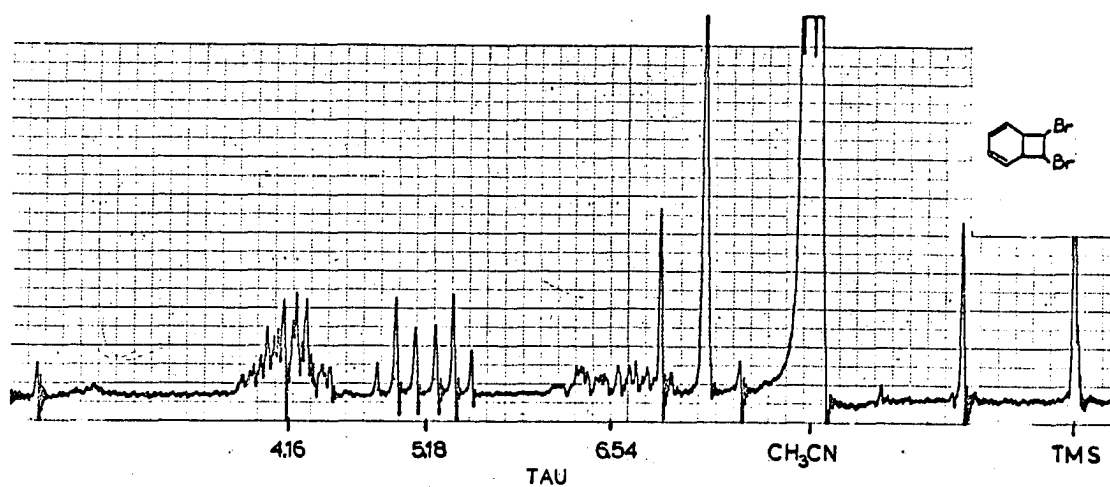
antimonate, and perchlorate were used because the anions are poor complexing agents. The solvolyses were performed under a wide variety of conditions and followed by n.m.r.

In a typical reaction, equimolar amounts of XLI and silver fluoborate were dissolved in acetonitrile and then combined. The n.m.r. spectrum of the solution was recorded at intervals after the reaction began (Figure 5). For reference purposes the n.m.r. spectrum of XLI is also shown (Figure 5) in acetonitrile. After 30 minutes reaction time, two new peaks appeared, a broad singlet at 1.2τ and a multiplet centered at 2.6τ . After 24 hours, XLI is essentially gone, the 1.2τ peak has broadened and moved downfield to 0.5τ , and the 2.6τ peak has increased somewhat in intensity. The spectrum is essentially the same after 4 days except for a slight downfield shift from 0.5τ to 0.0τ for the broad low field peak.

Thus an initial formation of a peak is seen around 1τ , and this shifts downfield as time elapses, while at the same time a peak forms around 2.6τ . In many cases the downfield peak is so broad as to be barely discernible from the baseline, and in some cases it is seen as low as -3τ (very broad). No method could be devised to make line positions and widths reproducible, and all attempts to recover and characterize components of the reaction mixture were unsuccessful. However, a low field peak always forms and moves downfield, and a peak always forms around 2.6τ .

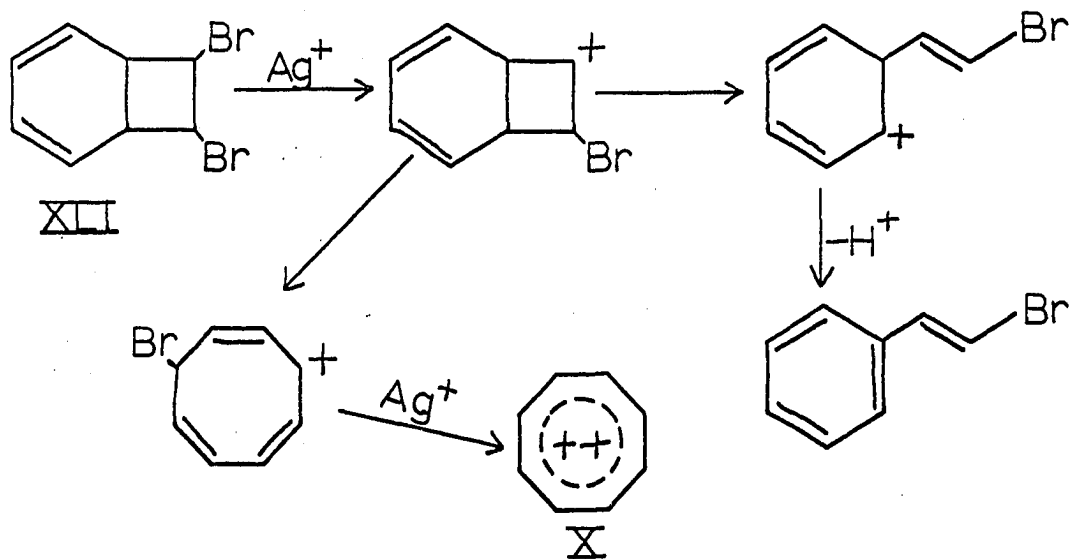
Figure 5. Nuclear magnetic resonance spectra

- Top - cyclooctatetraene dibromide (XLI)
in acetonitrile
- Bottom - reaction of XLI with silver fluoborate
in acetonitrile
- top - 30 minutes
- middle - 24 hours
- bottom - 4 days
- note: Each of these spectra is on
a different scale expansion.



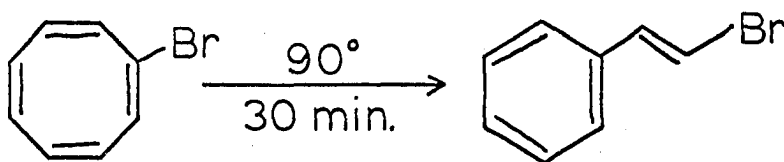
If it is truly aromatic, X should have all identical protons; and their n.m.r. line position should be considerably downfield from the position of normal olefinic protons, due to deshielding by the double positive charge. The relationship derived by Fraenkel *et al.* (cf. *supra*, p. 5) predicts a line position for X of 0.1τ . Whether or not this relationship is truly applicable to a doubly charged species is debatable, since it is a first-order approximation based on singly charged ions. In any event, the observed line position agrees rather well with the calculated value, and it is most tempting to assign this low field peak to X. The multiplet at 2.6τ is obviously benzenoid. In several runs this multiplet shows a sharp singlet at 2.5τ and a doublet at slightly higher field. This is very similar to the β -bromostyrene spectrum (63, Figure 497).

The following mechanism can account for these two product types:



This mechanism is consistent with the data, but obviously neither it nor the product structures have been rigorously established. The data only suggests this explanation.

An indication that the assignment of a styrene as the structure of the compound causing the multiplet in the 2.6 region is correct may be found in a reaction reported by Cope and Burg (64).



Assuming the low field peak to be caused by X, two of the more puzzling aspects of this investigation are 1) the reason for the downfield protons to shift as the reaction proceeds and 2) the reason for line broadening of this peak.

A possible, but not entirely attractive, explanation for the line broadening would invoke a rather pronounced effect due to exchange of fluoborate anions in tight ion groups around the dication and accompanying changes in the net effective positive ring charge, so that there would be a spectrum of net effective ring charges in solution, and thus a broad absorption.

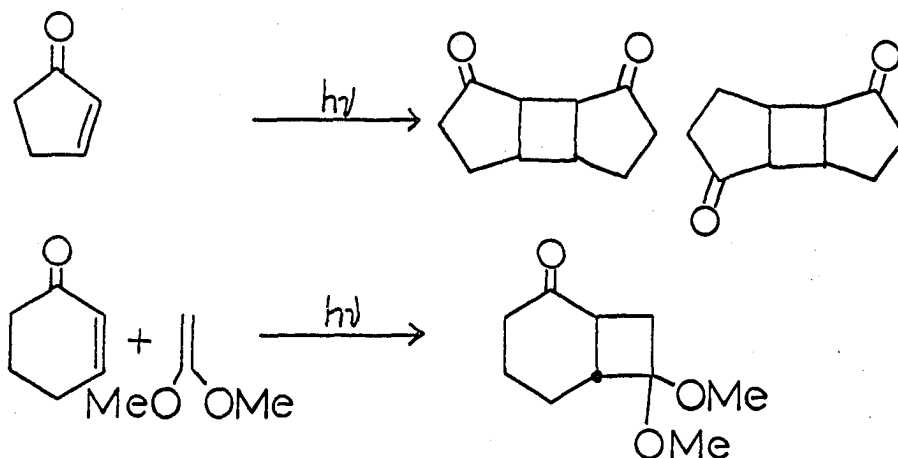
Changing relative concentrations of dication and fluoborate anion may be responsible for the downfield shift. The

ratio of dication/fluoborate increases as the reaction proceeds. This may result in less effective dication charge neutralization by fluoborate, and thus a higher effective positive charge in the dication.

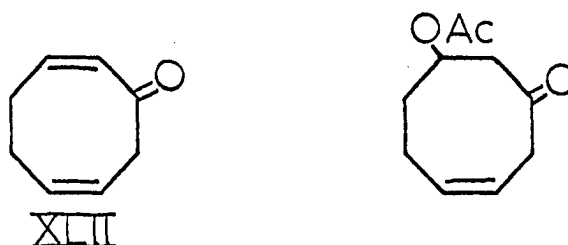
Both of these explanations suffer from the rather obvious fault that they require marked electrical interaction between non-bonded species. However, no dication of this type has ever been investigated, and it may well have abnormal solvation properties due to the dispersal of two positive charges over such a large framework. This interpretation should be viewed with caution however, in view of the results of a control experiment using a singly charged species, the tropylium ion. The n.m.r. line position of tropylium fluoborate in acetonitrile was found to be almost invariant when fluoboric acid or water was added to the n.m.r. sample (< 0.2 ppm variation), and the absorption was always a sharp singlet.

Solvent Photoaddition to Cyclooctene-3-one

The behavior of cyclooctene-3-one (XIX) on irradiation in protic solvents has proved to be most unusual. The majority of similar ketones simply dimerize on irradiation (65, 66), although the irradiation of cyclohexene-3-one or cyclopentene-3-one in olefins results in cycloaddition of the olefin to the double bond of the unsaturated ketone (40, 67, 68).



Thus the observation of Juneja (41) that $\Delta^{2,6}$ -cyclo-octanone (XLII) might incorporate the elements of acetic acid on irradiation in that solvent seemed to indicate that further investigation would be informative.

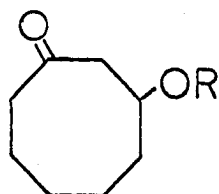


Inasmuch as the preparation of $\Delta^{2,6}$ -cyclooctenone in a pure state involves separation from the $\Delta^{2,5}$ -isomer, it was decided to use cyclooctene-3-one (XIX) for this study.

Irradiation of a 0.01 M solution of XIX in glacial acetic acid gave a crude product which v.p.c. analysis showed to be a 90:10 mixture of a product (XLI) and XIX. The crude product was estimated to be 84% volatile by v.p.c. area comparison. Distillation showed it to be 91% volatile.

The infrared spectrum of XLIII (Figure 6) indicated the presence of acetate ($5.77, 8.13\mu$) and saturated ketone group (5.88μ).

The n.m.r. spectrum of XLIII (Figure 7) provided evidence which allowed complete structure assignment. A broad multiplet (1H) at 4.66τ for a proton on a carbon bearing acetate, a sharp doublet at 7.29τ and a rough doublet at 7.53τ (4H) for methylene protons adjacent to a carbonyl group, a sharp singlet (3H) at 7.92τ for the acetate methyl group, and a broad multiplet (8H) centered at 8.35τ for the remainder of the methylene protons allowed assignment of 3-acetoxycyclo-octanone as the structure of XLIII.



R=	Ac	XLIII
	Me	XLIV
	Et	XLV
	OH	XLVI
	t-Bu	XLVII

The structural assignment was further confirmed by a double resonance experiment. Irradiation of the methine proton



Figure 6. Infrared spectra

Top - 3-acetoxycyclooctanone (XLIII)

Bottom - 3-methoxycyclooctanone (XLIV)

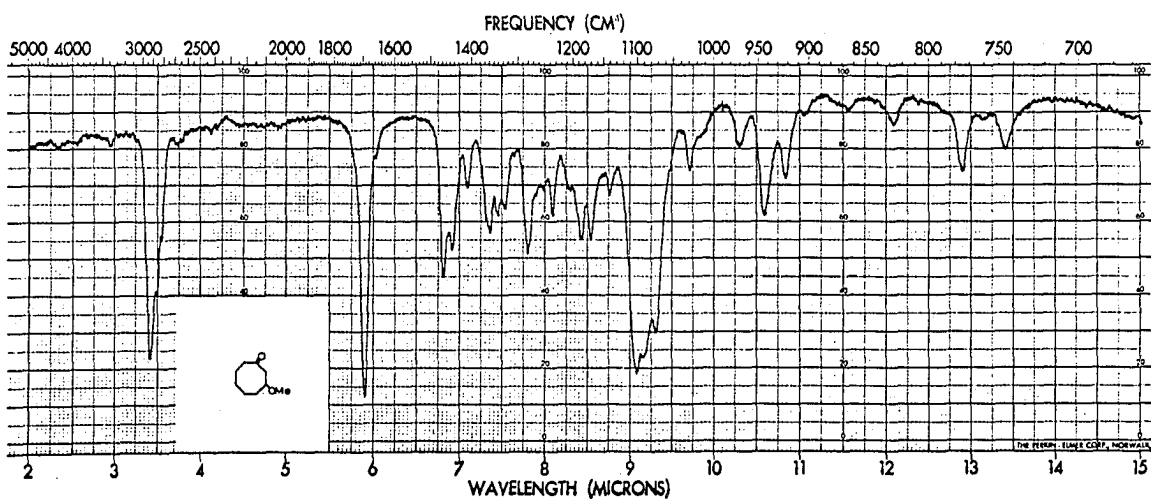
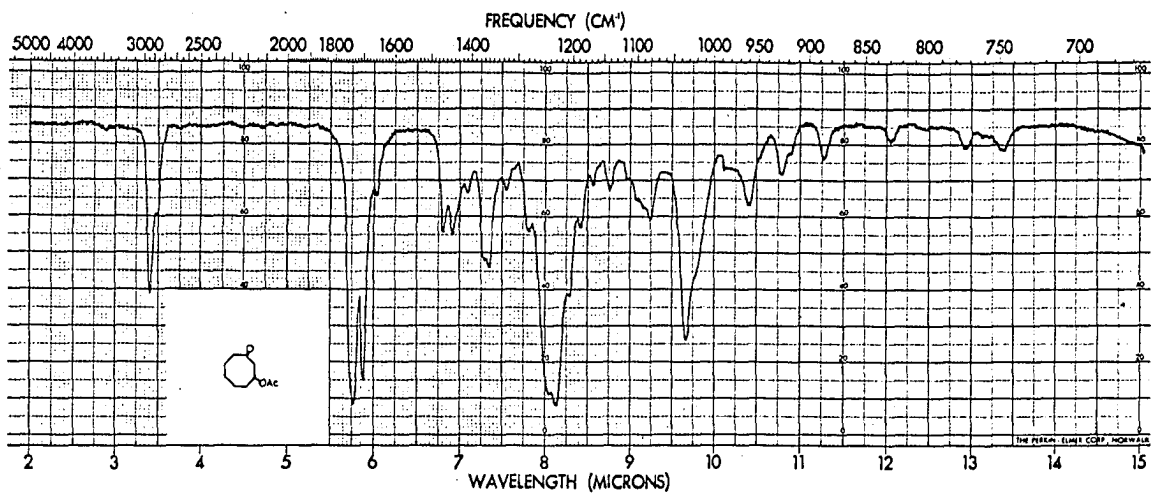
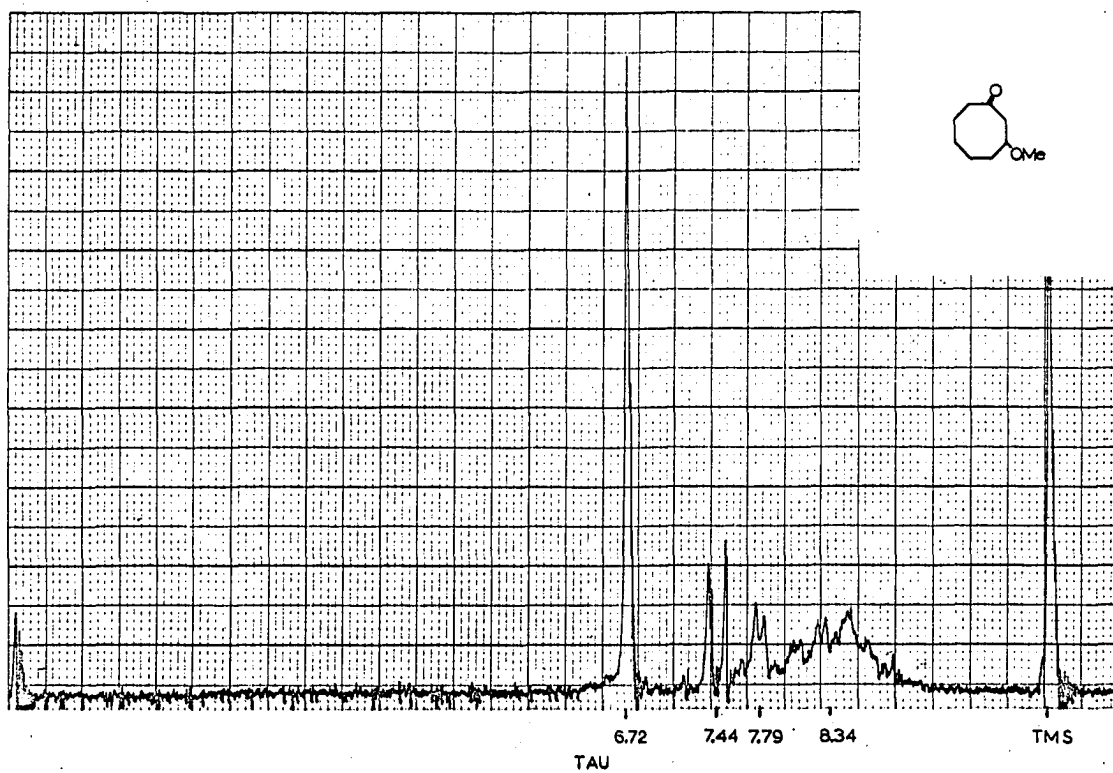
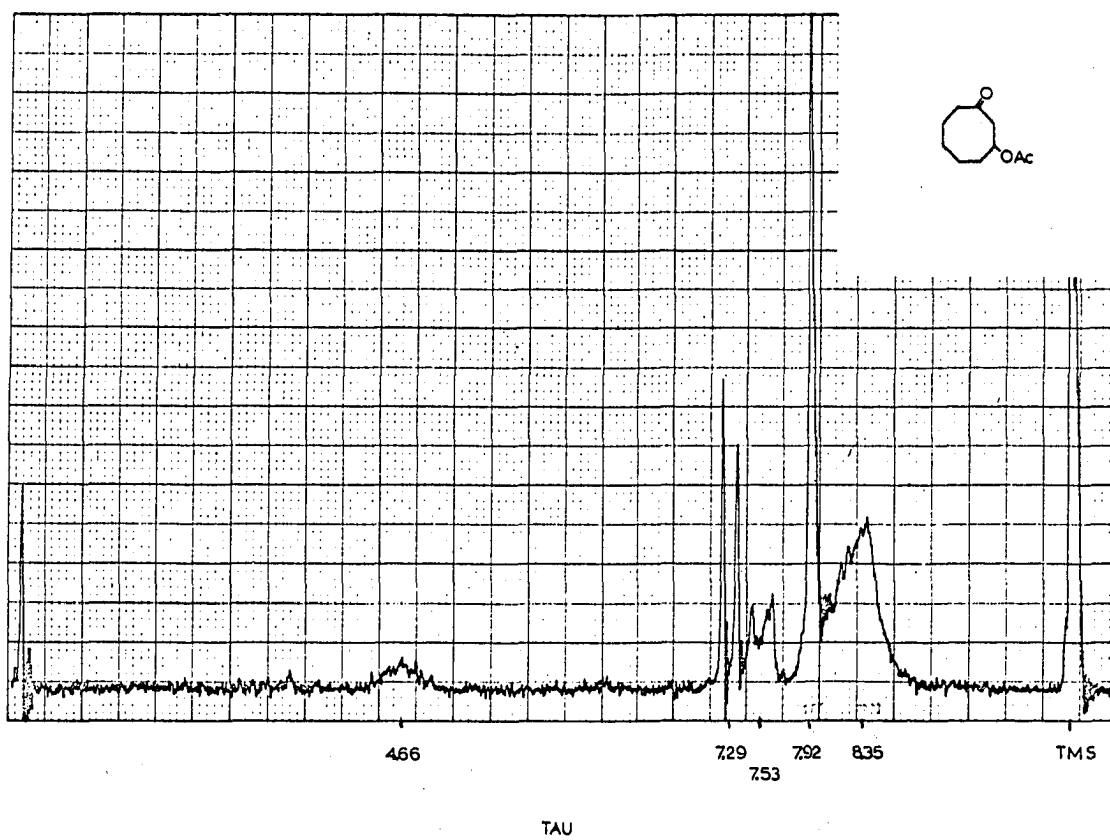


Figure 7. Nuclear magnetic resonance spectra

Top - 3-acetoxycyclooctanone (XLIII)

Bottom - 3-methoxycyclooctanone (XLIV)



at 4.66τ caused the collapse of the doublet at 7.29τ to a singlet, thus showing that two protons adjacent to the carbonyl group were coupled to a proton on carbon bearing acetate. This firmly establishes the position of acetate in the β -position.

Irradiation of a 0.01 M solution of XIX in methanol gave a crude product which was shown to be an 85:15 mixture of a product (XLIV) and XIX. It was estimated that the crude product was 67% volatile by v.p.c. area comparison. Distillation of the crude product indicated 65% volatile product.

The infrared spectrum of XLIV (Figure 6) showed a saturated carbonyl group (5.91μ) and the presence of ether bonds (9.07 , 9.16 , and 9.31μ).

The n.m.r. spectrum of XLIV (Figure 7) showed: a sharp singlet (4H) at 6.72τ which can be assigned to the methoxymethyl group and to the methine proton on carbon bearing the methoxyl group; a sharp, partially split doublet (2H) at 7.44τ and a crude doublet (\sim 2H) at 7.79τ for four methylene protons adjacent to a carbonyl group; and a broad multiplet (\sim 8H) centered at 8.34τ for the remaining methylene protons. This allows assignment of 3-methoxycyclooctanone as the structure of XLIV.

Irradiation of a 0.01 M solution of XIX in 95% ethanol gave a crude product which was 69% volatile by v.p.c. area comparison. Analysis by v.p.c. showed one product (XLV) and

XIX in the ratio 83:17.

The infrared spectrum of XLV (Figure 8) showed a saturated carbonyl group (5.90μ), and a broad ether band ($9.08-9.30\mu$).

The n.m.r. spectrum of XLV (Figure 9) is somewhat complicated due to overlap of the ethyl absorption on the remainder of the spectrum (triplet centered at 8.88τ , and quartet at 6.54τ). The quartet at 6.54τ integrated for three protons (undoubtedly including the methine proton on carbon bearing the ethoxyl group), and the remainder of the spectrum for 15 protons, including approximately two protons each in the multiplets at 7.41 and 7.71τ , for the methylene protons adjacent to the carbonyl group. Thus XLV is 3-ethoxycyclooctanone.

The irradiation of a 0.01 M solution of XIX in water gave a crude product which had absorption maxima in the infrared at 2.92 (broad), 5.89 , and 5.92μ . Vapor phase chromatography on a Perkin-Elmer R column showed one product (XLVI) and starting material in the ratio 88:12. Area comparisons indicated 72% of the crude product was volatile.

An attempt to collect samples of XLVI for identification purposes from a preparative scale Carbowax 20M column apparently resulted in a reverse-aldol reaction on the column. The infrared spectrum of crude collected material indicated the presence of aldehyde hydrogen (3.70μ), two carbonyl groups (5.83 , 5.88μ), and bands at 7.10 and 7.37μ which are char-

Figure 8. Infrared spectra

Top - 3-ethoxycyclooctanone (XLV)

Bottom - 3-t-butoxycyclooctanone (XLVII)

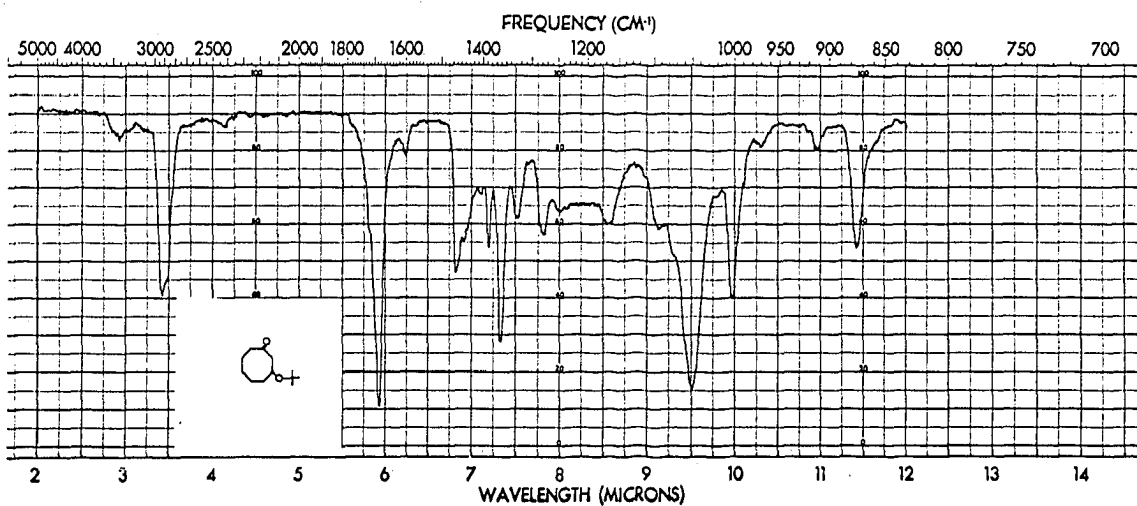
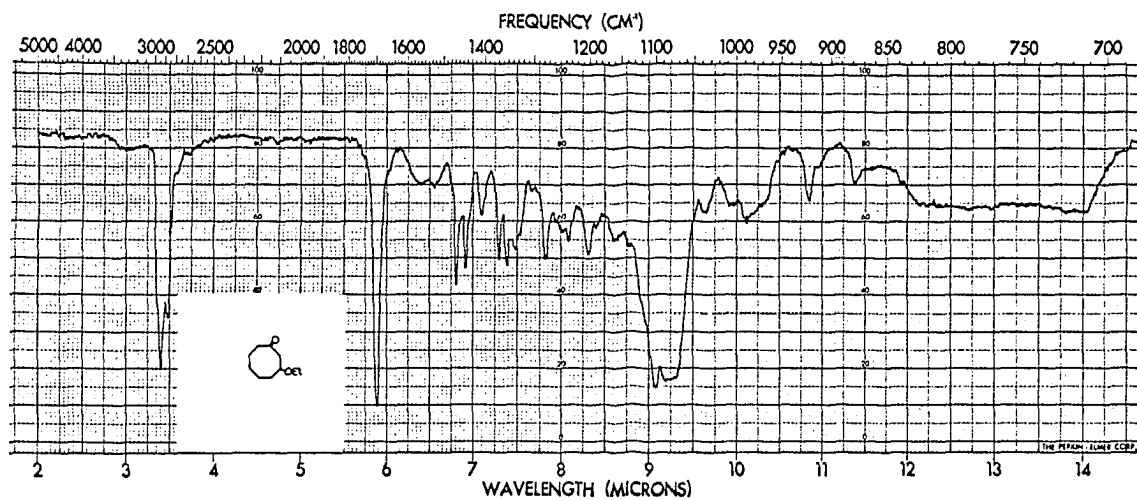
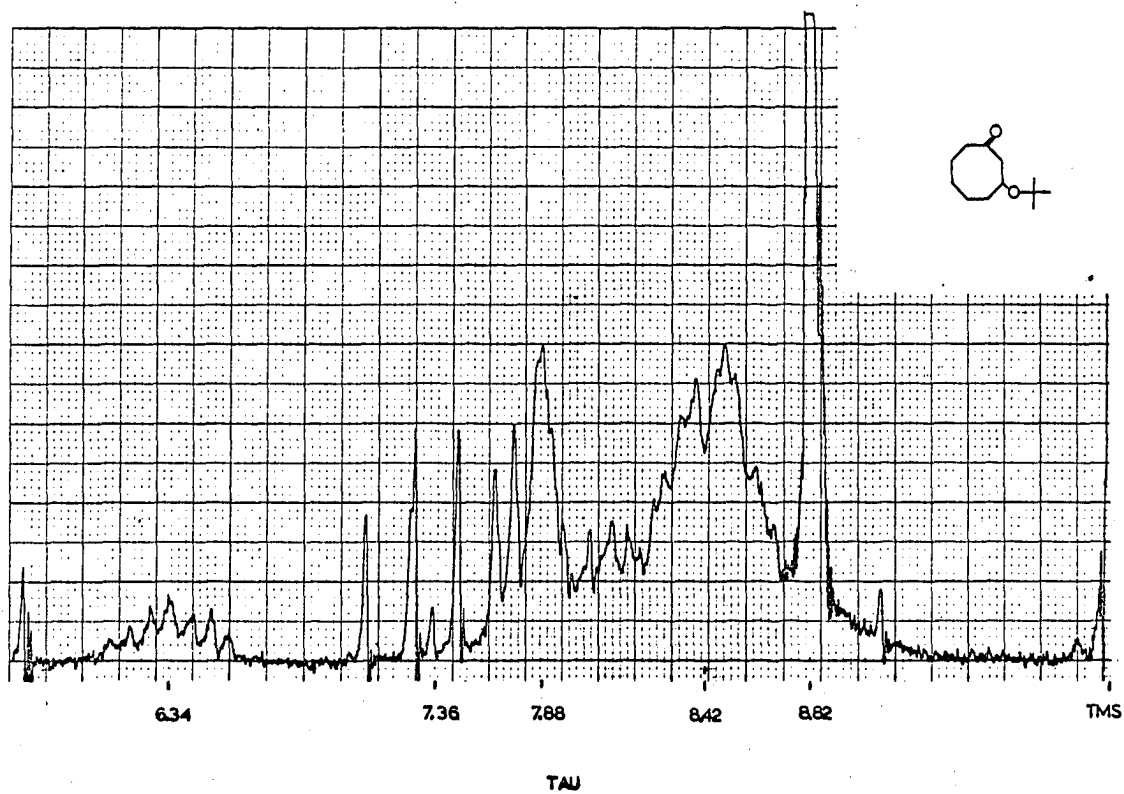
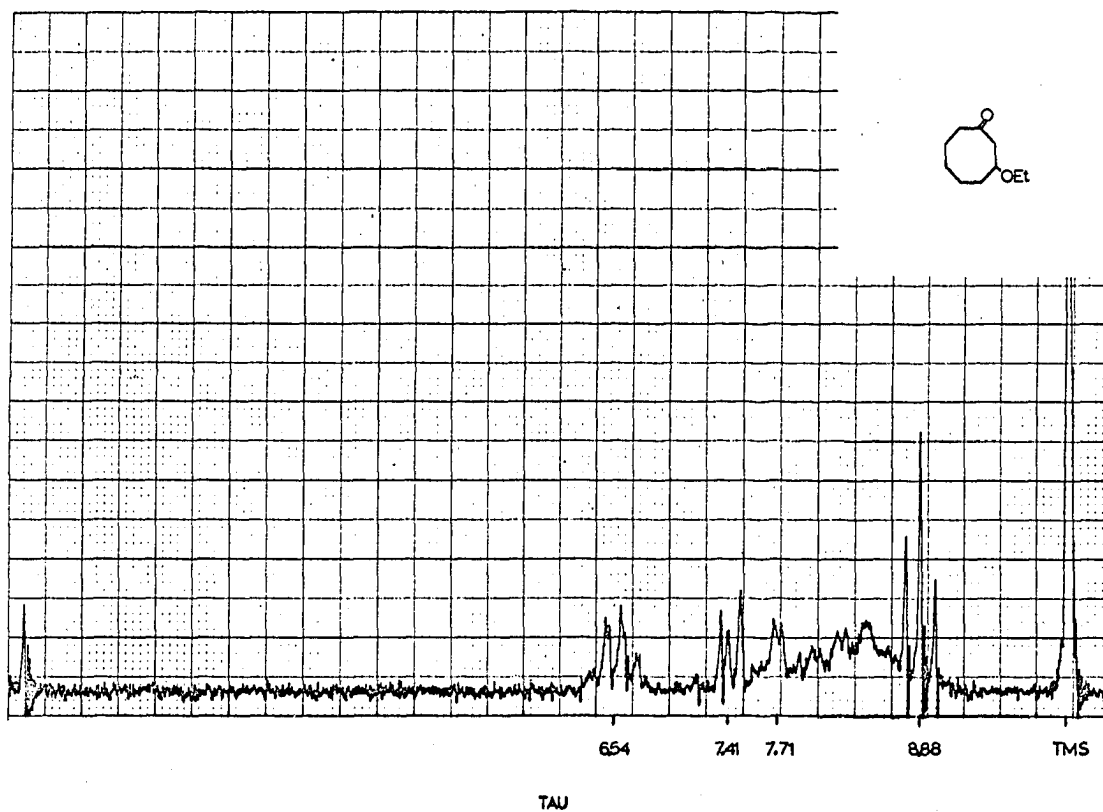


Figure 9. Nuclear magnetic resonance spectra

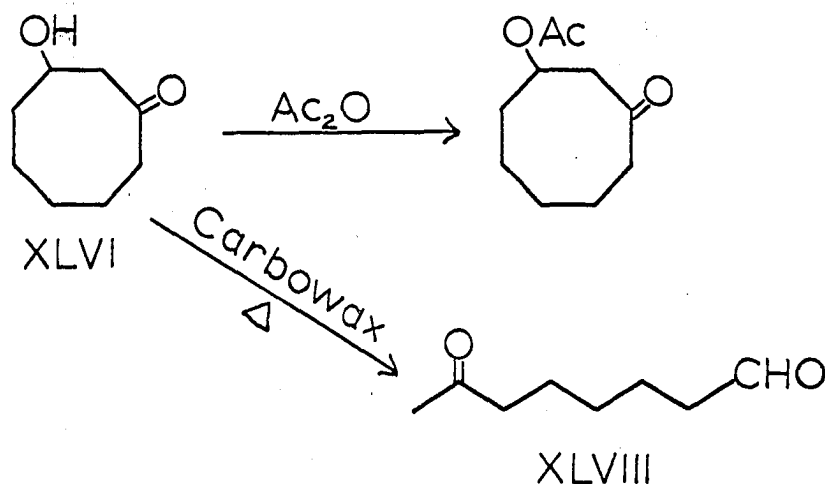
Top - 3-ethoxycyclooctanone (XLV)

Bottom - 3-t-butoxycyclooctanone (XLVII)



acteristic of methyl ketones. The n.m.r. spectrum indicated the presence of an aldehyde proton (0.28τ), and a methyl ketone (7.94τ). Thus the rearrangement product is probably 7-keto-octanal (XLVIII).

Thus it was reasonably certain that XLVI was 3-hydroxycyclooctanone. In order to prove this beyond doubt the crude



photoproduct was acetylated to give a product which had the same v.p.c. retention time as XLIII and an identical infrared spectrum.

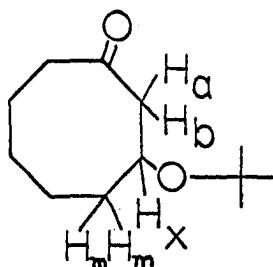
The irradiation of XIX in *t*-butanol is a very sensitive reaction, and no way has been found to obtain quantitatively reproducible results. An adduct (XLVII) is always formed, in yields varying from 5-22%, most often in the 10% range. The reaction is slow relative to the rate in the other solvents, and the amount of non-volatile product is always high.

The infrared spectrum (Figure 8) of XLVII shows an intense

carbonyl band at 5.92μ , suggesting a saturated 8-membered ring, and an ether band at 9.51μ .

The n.m.r. spectrum (Figure 9) of XLVII shows multiplets centered at 6.34 (methine proton on carbon bearing oxygen), 7.36 and 7.88 (methylene protons adjacent to a carbonyl group), 8.42 (other methylene protons), and a sharp singlet at 8.82τ (t-butyl group) in the ratio 1:4:8:9.

In a double resonance experiment, irradiation at 1.56τ caused the methine multiplet to collapse to a crude quartet.



This is best interpreted as evidence that the methine proton is coupled to only H_a and H_b when H_m is irradiated, and therefore as evidence that the t-butoxyl group is in the β -position.

Thus it can be seen that in each protic solvent investigated an adduct is formed resulting from solvent addition across the double bond of XIX. The nature of the non-volatile material has not been investigated, but it is presumed to be

dimeric. Eaton and Lin (37) have reported that trans-cyclo-octenone dimerizes rapidly, even in the dark, and α , β - unsaturated ketones in general are known (26, 64, 65) to dimerize on irradiation.

The precise nature of this solvent addition is unknown, although we have obtained information which suggests a general mechanism. The main problem stems from the fact that irradiation of cis-cyclooctenone in cyclohexane (37) in Pyrex results in a photostationary state in which cis- and trans-cyclooctenone are present in a 1:4 ratio. The trans isomer (XX) is apparently highly reactive in thermal dimerization and Diels-Alder processes (37), as well as in thermal cycloaddition to olefins (67). Thus the first question is whether the solvent addition is a true photoreaction at all, or whether it is simply a thermal addition to the trans isomer or some other reactive intermediate. In order to examine this question, several experiments were performed.

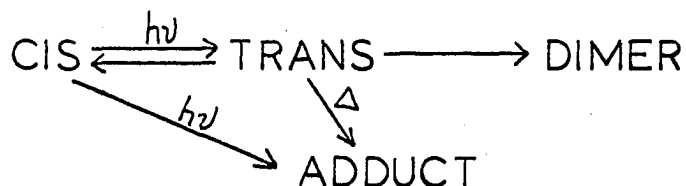
The irradiation of cis-cyclooctenone (XIX) in cyclohexane resulted in a photostationary state (80% trans/20% cis) in 45-60 minutes. Addition of a small amount of methanol (\sim 5:1 molar excess) and stirring for 1 hour resulted in a mixture of adduct (XLIV) and XIX in the ratio 1:2. Prior to methanol addition, it is possible to regenerate XIX with a small amount of sulfuric acid. Methanol does not cause this regeneration.

Irradiation of a similar solution, but containing the

same amount of methanol from the start, for 1 hour resulted in a mixture of adduct (XLIV) and XIX in the ratio 3:2. The actual yield (v.p.c.) of adduct was double that in the previous experiment.

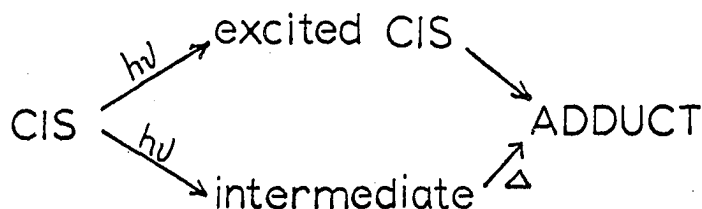
The formation of a photostationary equilibrium mixture of cis- and trans-cyclooctenone, as well as the facile dimerization of the trans isomer, has been reported by Eaton (37). The fact that the relative amount and the absolute amount of adduct formed increase when methanol is present during irradiation strongly suggests that a photoaddition to cis-XIX is occurring in addition to the thermal addition of solvent to trans-XIX.

Thus these two experiments suggest the following general scheme, which depicts both thermal and photochemical routes to the adduct.



The precise nature of the photochemical mode of adduct formation can not be stated, for we have no data which allows a choice between mechanisms which can be postulated. There are basically two mechanisms, although several variations of the second are possible. First, the addition could be a simple attack of solvent on excited cis-XIX. Second, cis-XIX could

be converted to some reactive intermediate other than trans-XIX, and this could be attacked by solvent.



Another experiment which may have importance in a consideration of the reaction mechanism is the irradiation of cis-XIX in quartz. In methanol within 10 minutes there is nearly complete ($> 95\%$) disappearance of cis-XIX in the ultraviolet spectrum. On standing in the dark this irradiated solution slowly (1-2 hours) regenerates cis-XIX until there is a net loss of 60% cis-XIX (ultraviolet analysis). Removal of solvent (either before or after regeneration of cis-XIX), followed by v.p.c. analysis shows the product to be 90% volatile and a 45:55 mixture of adduct (XLIV) and cis-XIX. Irradiation for 90 minutes results in a crude product which is essentially non-volatile. If 5% of XLIV is added prior to the 90 minute irradiation, v.p.c. analysis after irradiation shows less than 1% present.

This data suggests initial rapid adduct formation, followed by destruction of the adduct. Examination of the results of irradiation of XIX in t-butanol in quartz tends to confirm this interpretation.

Irradiation in t-butanol for 10 minutes results in loss

of 80% of cis-XIX; on standing for 11 hours, cis-XIX was slowly regenerated to 55% of its original concentration. Analysis by v.p.c. showed 5% adduct (XLVII) and 55% XIX. Irradiation for 30 minutes caused the loss of 84% cis-XIX; after standing 3 hours, 25% of the original cis-XIX was present (u.v. analysis). Analysis by v.p.c. after solvent removal showed 2% adduct and 24% XIX. Irradiation for 90 minutes gave essentially no volatile products.

These experiments indicate that cis-XIX is being converted to some species, presumably trans-XIX, which is capable of reconversion to cis-XIX. The initial rapidity of adduct formation in methanol, the relative slowness of regeneration of cis-XIX, and the decrease in adduct yield on slightly prolonged irradiation in t-butanol suggest that a process is occurring whereby adduct is formed from a species derived from cis-XIX during the first stages of irradiation, prior to the formation of trans-XIX. This is consistent with the experiments in cyclohexane which were discussed above, in which more adduct was formed when methanol was present from the beginning of the irradiation than was formed if methanol was added in the dark to a solution highly enriched in trans-XIX.

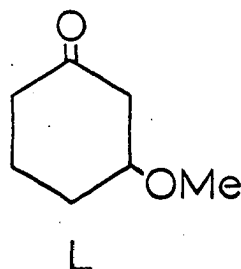
It seems clear that adduct formation can occur thermally via trans-XIX, and also from cis-XIX in some sort of photochemical process (which may involve a reactive intermediate derived from cis-XIX). In addition cis-XIX can be regenerated

in solution from the photomixture, presumably by alcohol catalysis. It is not possible to say what the primary process in Pyrex is, although in quartz the formation of adduct from trans-XIX in a thermal process seems to be relatively unimportant, since adduct formation in quartz is very fast and the yield of adduct is not increased by allowing an irradiated solution, enriched in trans-XIX, to stand for some time in the dark prior to workup.

Attempted Solvent Photoaddition in Other Systems

Solvent addition to α , β -unsaturated ketones would be very useful if it were a general reaction. Several systems were investigated in order to find out whether the reaction observed for cyclooctenone (XIX) would occur in other molecules.

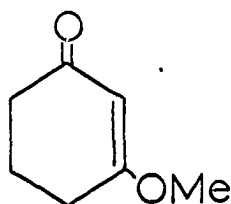
Cyclohexenone (XLIX), when irradiated in methanol, appears to give a small amount ($\sim 5\%$) of adduct (L). The infrared spectrum on a sample of L collected from the v.p.c. showed a strong band at 5.85μ , indicating a saturated 6-membered ring ketone, and a strong band at 9.15μ which suggests the presence of an ether linkage. Cyclohexenone in ethanol however



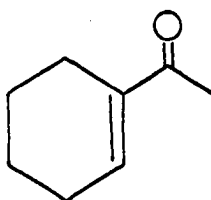
gives only a trace of a compound with a retention time similar to L.

A solution of β -methoxycyclohexenone (LI) in methanol is totally unreactive when irradiated, as is 1-acetylcyclohexene (LII) in acetic acid.

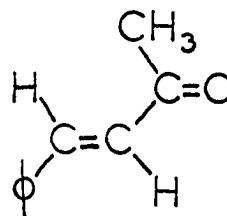
A solution of trans-benzalacetone (LIII) in methanol simply undergoes cis-trans isomerization on irradiation.



LI



LII



LIII

Therefore solvent photoaddition to cyclooctenone is a rather isolated example of this sort of reaction having little general application. This sort of addition apparently occurs to a small extent with cyclohexenone, but not with the other systems investigated. This is not too surprising, for in the Historical section we noted that examples of solvent photoaddition to any kind of unsaturated carbonyl system are few. The addition to cyclooctenone (XIX) provides the first example, however, of this reaction in a simple unsaturated ketone.

EXPERIMENTAL

Experimental for Attempted Preparation of
Cyclooctatriene-1,4-dionePreparation of cycloocten-3-one (XIX) by Cope's method

Cycloocten-3-one was initially prepared by the method of Cope et al. (69). Bromination of cyclooctene with N-bromosuccinimide, followed by treatment with silver acetate gave cyclooctene-3-acetate. Basic hydrolysis, followed by chromic acid oxidation in acetic acid, and distillation, gave cyclooctenone. $\lambda_{\text{max}}^{95\% \text{ EtOH}}$ 228 $m\mu$ (8050); the infrared and the n.m.r. spectra are shown in Figures 1 and 2.

Preparation of cyclooctene-3-ol from cyclooctene

Cyclooctene (110 g.; 1.0 mole), mercuric acetate (350.6 g.; 1.1 mole), and acetic acid (500 ml.) were placed in a 1 liter 3-neck flask fitted with a mechanical stirrer and reflux condenser. The mixture was stirred 45 minutes at room temperature while a canary yellow precipitate formed, and then refluxed for 10 hours. The dark solution was cooled to room temperature and filtered to remove metallic mercury (190 g.; 95%). The solution was concentrated by removing acetic acid (\sim 400 ml.) on the Rotovac. The residue was poured into water (1 l.) and extracted with three portions (250 ml.) of ether. The combined ether extracts were washed with 5% sodium carbonate solution, then with water, and dried over magnesium sulfate.

Filtration and removal of the solvent left crude product (117.3 g.). This was distilled to obtain the pure monoacetate (84.5 g.; 50.3%), b.p. 102-110°/12 mm.

The monoacetate was added dropwise, with ice-water cooling to a solution of potassium hydroxide (59.5 g.; 1.06 mole) in water (70 ml.) and ethanol (150 ml.). The solution turned pale orange, and was stirred for 3 hours at room temperature. An aliquot showed no acetate carbonyl absorption in its infrared spectrum. After dilution with water (250 ml.) the mixture was extracted with two portions (250 ml.) of ether. The combined ether extracts were washed with 5% hydrochloric acid and with water, dried over magnesium sulfate, and concentrated on the Rotovac to give crude product (68.6 g.). Distillation gave pure alcohol (50.2 g.; 39.8% overall yield), b.p. 106-109°/12 mm., reported (68) b.p. 74°/2 mm. Vapor phase chromatography on a Perkin-Elmer R column showed a single peak.

Oxidation of cyclooctene-3-ol to cyclooctene-3-one (XIX)

In a modified Jones oxidation (70), a solution of chromium trioxide (15.9 g.; 0.159 mole), water (80 ml.), and concentrated sulfuric acid (12.8 ml.) was slowly added to a solution of cyclooctene-3-ol (30.0 g.; 0.238 mole) in acetone (80 ml.). The solution was cooled in ice-water and very slowly stirred with a magnetic stirrer. The addition time was 65 minutes, after which the mixture was allowed to stir 45 minutes more. The acetone layer was separated. The aqueous layer was diluted

with water (400 ml.) and extracted with three portions (100 ml.) of ether. The combined ether and acetone fractions were washed twice with water (100 ml.) and dried over magnesium sulfate. Removal of solvent on the Rotovac yielded crude product (27.5 g.). Vapor phase chromatography on a Perkin-Elmer R column at 150° showed the oxidation was about 85% complete. The crude product (27.5 g.) was dissolved in acetone (75 ml.) and titrated with the same concentration chromic acid solution as used above (30 ml.) until the orange chromic acid color remained. Work up as before, followed by distillation gave cyclooctenone (20.0 g.; 67.7% yield), b.p. 66-68°/2.5 mm., reported (69) b.p. 89°/14 mm. Vapor phase chromatography on the R column showed > 98% purity with only a trace (< 1%) of cyclooctenol present. The retention time was identical with that of an authentic sample of cyclooctenone, as was the infrared spectrum.

Pyridine-chromic acid oxidation (71) or pyridine-lead tetraacetate oxidation (72) always left an intolerable amount of starting material, even after several oxidations. Separation of cyclooctenol from cyclooctenone by distillation is difficult, and for this reason, as well as the relative ease of workup and greater yield, the Jones oxidation is preferable.

Attempted base-catalyzed air oxidation of cyclooctene

Potassium (15.6 g.; 0.4 mole) is added to *t*-butanol (500 ml.) in small portions with continuous stirring. When the

potassium had dissolved cyclooctene (11.0 g.; 0.1 mole) was added. Air was passed continuously through the solution through a fritted-glass bubbler. After 13 hours 100 ml. of solution was removed. This portion was diluted with water (500 ml.) and 6 N hydrochloric acid (70 ml.), and extracted with two portions (250 ml.) of ether. The combined ether extracts were treated with anhydrous sodium carbonate and then magnesium sulfate. Filtration followed by solvent removal on the Rotovac gave an oil which showed very little carbonyl absorption in the infrared. After 24 hours the remainder of the reaction mixture was worked up as above; again there was very little carbonyl absorption in the infrared spectrum of the crude product.

Selenious acid oxidation of cyclooctene

In a modification of a known procedure (73) cyclooctene (28.0 g.), acetic acid (56.0 g.), and acetic anhydride (56.0 g.) were placed in a 250 ml. flask with a magnetic stirrer, condenser, and thermometer. This was heated on an oil bath at 119° while selenious acid (11.0 g.) was added in small portions (1 hour). This temperature was maintained for 10 hours after addition was complete. After cooling and filtering to remove metallic selenium, the mixture was poured into ice-water (1000 ml.) and extracted with ether (3 x 250 ml.). The combined ether extracts were washed with water, dried over

magnesium sulfate, and concentrated to give crude product (40.6 g.). Distillation gave cyclooctene-3-acetate (14.5 g.; 34%), b.p. 57°/0.6 mm., reported (69) b.p. 57°/1 mm. No diacetate could be distilled.

Preparation of 9-oxabicyclo-(4.2.1)-2-nonenol
XXIV from cyclooctenone

A solution of cycloocten-3-one (12.4 g.; 0.1 mole), carbon tetrachloride (75 ml.), N-bromosuccinimide (17.8 g.; 0.1 mole) and benzoyl peroxide (1 g.) was purged with nitrogen, and then heated on an oil bath (90°) under nitrogen. In 10 minutes the reaction began to reflux very vigorously; the heat was removed and the reaction proceeded spontaneously for 15 minutes. The mixture was then heated 15 minutes more, cooled, and filtered. The filtrate was washed with 5% sodium carbonate (3 x 50 ml.), and water. After drying over magnesium sulfate, the solvent was removed on the Rotovac to give crude bromide (21 g.). This was diluted with acetic acid (25 ml.) and slowly added, with cooling, to a stirred slurry of silver acetate (16.7 g.) and acetic acid (30 ml.). After standing overnight the mixture was filtered and then concentrated on the Rotovac. The residue was diluted with water, neutralized with solid sodium carbonate, and extracted with ether. After drying the ethereal solution over magnesium sulfate, removal of solvent gave crude product (16.7 g.) whose infrared spectrum showed intense peaks at 5.76, 6.02, and 8.12 μ . Some of this

crude product (14.0 g.) was placed in a round-bottom flask and cooled in ice. A solution of potassium hydroxide (5.3 g.) in ethanol (14 ml.) and water (8.5 ml.) was slowly added over 15 minutes with stirring. After 24 hours water (400 ml.) was added, and the solution was extracted with ether. The combined ether extracts were washed with water, dried over magnesium sulfate, and concentrated to give crude product (7.2 g.). The crude product was chromatographed on neutral alumina (400 g.) with 40/60 benzene/ether to give pure crystalline XXIV (1.8 g.; 12.8% yield), m.p. 94-95° (sublimes). The ultraviolet spectrum of XXIV showed a low intensity ($\epsilon < 1000$) absorption at 228 $m\mu$. The infrared spectrum was run in both potassium bromide pellets (Figure 1) and in chloroform (Figure 1). The n.m.r. spectrum is shown in Figure 2.

Anal. Calc. for $C_8H_{12}O_2$: C, 68.54; H, 8.63. Found: C, 68.25; H, 8.95

Preparation of 9-oxabicyclo-(4.2.1)-2-nonenol (XXIV)
from cyclooctene-3,8-diacetate (XXVIII)

A solution of XXVIII (1.8 g.) in ether (10 ml.) was slowly dropped into a slurry of lithium aluminum hydride (2.1 g.) in ether (160 ml.). After 6 hours the excess hydride was destroyed with saturated sodium sulfate. The solution was filtered, dried over magnesium sulfate, and concentrated to give crude diol (1.0 g.). The crude diol (0.9 g.) was dissolved in chloroform, manganese dioxide was added (10 g.), and the slurry

was stirred at 30-33° for 46 hours. Filtration, followed by concentration, gave a crude product. Vapor phase chromatography on a Carbowax 1500 (15% on Gaspak) column at 150° showed one major product (75%) and several minor products. An infrared spectrum on a collected sample of the major product was identical to that of authentic XXIV. Addition of a small amount of Skelly B to the crude material caused it to cloud up; the further addition of benzene (2 drops) caused crystallization. Filtration gave a white solid (550 mg.) whose infrared and n.m.r. spectra were identical with those for authentic XXIV.

Acetolysis of 9-oxabicyclo-(4.2.1)-nonenol (XXIV)

A solution of XXIV in pyridine (10 ml.) and acetic anhydride (6 ml.) was stirred for 12 hours at room temperature, then poured into ice-water (250 ml.), allowed to stand 45 minutes, and then extracted with ether. The combined ether extracts were washed with 0.1 N hydrochloric acid, 5% sodium bicarbonate, water, and then dried over magnesium sulfate. Removal of solvent on the Rotovac gave crude product (217 mg.). The infrared absorption of the crude material showed intense absorption at 5.77μ (acetate) and 6.03μ (cyclooctene-3-one); the ultraviolet spectrum showed an intense $\lambda_{\text{max}}^{95\% \text{ EtOH}}$ 223 $m\mu$. The n.m.r. spectrum of the crude material showed multiplets at 3.88 τ (3H), 7.41 τ (2H), 8.33 τ (\sim 6H), and a sharp singlet at 7.92 τ (\sim 4H). Chromatography of the crude material on

Woelm neutral (grade III) alumina (25 g.) gave only XXIV (120 mg.), m.p. 92-94°. Repetition of the same reaction followed by chromatography on silica gel again gave only XXIV. Vapor phase chromatography on a preparative scale R column gave no products with acetate carbonyl absorption in the infrared spectrum.

Attempted oxidation of XXIV with chromic acid

A solution of XXIV (1.8 g.) in ether (15 ml.) was placed in a 50 ml. 3-neck flask equipped with condenser, addition funnel and magnetic stirrer. A solution was prepared by adding concentrated sulfuric acid (1 ml.) to sodium dichromate (1.6 g.) and diluting to 6 ml. This solution was slowly dropped into the ether solution over 20 minutes. After stirring an additional 25 minutes, ether (20 ml.) was added and the solution stirred 10 minutes more. Then the aqueous layer was separated and washed with ether (2 x 10 ml.). These extracts were combined with the ether layer from the reaction, washed with 5% sodium carbonate and water, dried over sodium sulfate, and concentrated to give crude product (750 mg.). Chromatography on a silica gel column gave pure XXIV (260 mg.) on elution with 80/20 benzene/ethyl acetate. No products were eluted prior to XXIV, and only tars were eluted later.

Pyridine-N-oxide oxidation of cyclooctene-3-bromide (XXIX)

A solution of freshly distilled pyridine-N-oxide (4.41 g.; .0464 mole) in benzene (25 ml.) was slowly dropped into cyclooctene-3-bromide (8.76 g.; .0469 mole) with stirring at room temperature (47). After $3\frac{1}{2}$ hours a heavy viscous oil, insoluble in benzene, had formed. After further reaction (12 hours) a white precipitate had formed and the oil had vanished. The precipitate (A) was filtered off (5.63 g.; 43%). The solid was very hygroscopic and rapidly became sticky.

A solution of A (5.63 g.; .027 mole) in water (10 ml.) was prepared and cooled in an ice-bath. To this cold solution was added a mixture of potassium hydroxide (1.5 g.; .027 mole) in water (10 ml.) over a period of 30 minutes. After 15 minutes further stirring, water (10 ml.) was added, and the solution was stirred 30 minutes more. After dilution with water (25 ml.), the reaction mixture was extracted with four portions (25 ml.) of ether. The combined ether extracts were washed with water, dried over magnesium sulfate, and concentrated to give crude product (1.06 g.). The crude product had a sharp strong band at 6.04μ (characteristic of cyclooctene-3-one) in its infrared spectrum. This was not purified or further characterized.

An attempt to perform the same reaction on cyclooctene-3,8-dibromide (XXX) was unsuccessful.

Attempted oxidation of cyclooctene-3,8-dibromide (XXX)
with dimethyl sulfoxide

A solution of dimethyl sulfoxide (250 ml.) containing XXX (12.0 g.; .045 mole) was stirred at 30° for 22 hours. The solution was poured onto ice (400 g.) and extracted with three portions (250 ml.) of ether. The combined ether extracts were washed with water, dried over magnesium sulfate, and concentrated to give an oily product (11.1 g.) whose infrared spectrum was almost identical with that of XXX.

The same residue was dissolved in dimethyl sulfoxide (100 ml.), heated to 58-65° and stirred for 18 hours. The mixture was worked up as before to give an oily product (10.3 g.) whose infrared spectrum was little changed from that of XXX.

The same residue was dissolved in dimethyl sulfoxide (100 ml.) containing sodium bicarbonate (10 g.). The mixture was stirred (8 hours) at room temperature and worked up as above. Again there was little apparent reaction.

The residue was slowly added (5 minutes) to a solution of dimethyl sulfoxide (100 ml.) containing sodium bicarbonate (10 g.) at 150-160°. The mixture was stirred 5 minutes, cooled, and worked up as before to give an oily product (8.8 g.). Again there was little apparent reaction.

In each of these crude reaction mixtures a very small amount of absorption occurred between 5.8 - 6.1 μ in the infrared spectrum.

The reaction of cyclooctene with nitrosyl chloride

To a cold (0-5°) stirred mixture of cyclooctene (11 g.; 0.1 mole), isoamyl nitrite (17.5 g.; 0.15 mole), and acetic acid (15 ml.), concentrated hydrochloric acid (10.3 ml.; 12 mole) was added over a period of 15 minutes. The green solution was allowed to stand for 30 minutes at 0°. A white crystalline solid (XXXIV) was filtered off (1.3 g., m.p. 92-93°). The filtrate was poured into 3 times its volume of water, and solid sodium carbonate was added until no more carbon dioxide was evolved. This solution was immediately extracted with ether. The ether extract was washed with water, dried over magnesium sulfate, concentrated on the Rotovac. Repeated cooling and filtration gave 4.2 g. of another white solid (XXXV). One recrystallization from Skelly B gave a melting point 101-101.5°. The total yield of XXXIV and XXXV was 5.5 g. (31%).

XXXIV had $\lambda_{\text{max}}^{\text{EtOH}}$ 293 $m\mu$; its n.m.r. and infrared spectra are shown in Figures 4 and 3.

Anal. Calc. for $\text{C}_{16}\text{H}_{28}\text{N}_2\text{O}_2\text{Cl}_2$: C, 54.70; H, 8.034.
Found: C, 54.50; H, 8.10.

XXXV had no ultraviolet absorption above 210 $m\mu$; its n.m.r. and infrared spectra are shown in Figures 4 and 3.

XXXIV can be converted to XXXV by refluxing in an isopropanol/urea solution (54).

The above data, coupled with the general nature of the nitrosyl chloride reaction with olefins, suggests XXXIV as the

dimer of the nitrosyl chloride addition product, and XXXV as the corresponding monomeric oxime.

The attempted conversion of 2-chlorocyclooctanone oxime (XXXV) to cycloocten-3-one

A solution (55) of 2-chlorocyclooctanone oxime (3.9 g.) in dimethyl aniline (10 ml.) was warmed in an oil bath to 115° for 45 minutes, then cooled in ice. After adding 20 ml. of aqueous sulfuric acid (2 parts water to 1 part concentrated sulfuric acid), the solution was refluxed for 2 minutes and then cooled. Steam distillation followed by ether extraction of the distillate gave a black oily liquid with infrared absorption at 5.90 μ and none at 6.03 μ . The use of aniline as the base gave the same results.

Attempted reaction of p-benzoquinone (XXXVI) with diphenylacetylene (XXXVII) without solvent

Diphenylacetylene (0.890 g.; .005 mole) and p-benzoquinone (0.54 g.; .005 mole) were placed in a 10 x 120 mm. Pyrex tube. The tube was evacuated to 0.05 mm., sealed off, and heated in an oil bath for 18 hours at 105° and then for 6½ hours at 125-130°. After cooling, the tube was opened and the contents removed and chromatographed on neutral alumina. Elution with 50/50 Skelly B-benzene gave pure diphenylacetylene (0.852 g.), m.p. 58-59°.

Attempted reaction of p-benzoquinone (XXXVI) with diphenylacetylene (XXXVII) (in solution)

Diphenylacetylene (17.8 mg.; 10 mmole) and p-benzoquinone (21.6 mg.; 20 mmole) were dissolved in o-dichlorobenzene (1 ml.); the solution was placed in an n.m.r. tube, evacuated, and sealed off. The mixture was allowed to stand at room temperature (18 hours), then heated in a 165-170° oil bath (4 hours), and then in a 200-210° bath (8 hours). There was no change evident in the n.m.r. spectrum. Then the tube was irradiated (6 hours) with a General Electric UA-3, 360 watt mercury arc lamp, and then with a 550 watt mercury arc lamp (4 hours). Again there was no change in the n.m.r. spectrum.

Preparation of cyclooctatetraene monoepoxide (XXXIX)

XXXIX was prepared according to the method of Cope and Tiffany (74). A solution of 40% peracetic acid (60 ml.) containing sodium acetate was slowly added to cyclooctatetraene (31.2 g.) in a 500 ml. flask equipped with a stirrer, addition funnel and a thermometer which reached into the solution. The rate of addition and an ice-water bath were regulated very carefully so that the reaction temperature was always 29-31° (addition time was about 40 minutes). This temperature was maintained for 90 minutes after addition was complete. Then the mixture was poured into water (300 ml.) and extracted with pentane. The combined pentane extracts were washed with 5%

sodium hydroxide and water. After drying over magnesium sulfate, the pentane was removed on the Rotovac, leaving crude product (21.5 g.). Distillation gave the monoepoxide (XXXIX) (8.0 g.), b.p. 80-82°/13 mm., reported (74) b.p. 74-75°/12 mm.

Attempted acid-catalyzed oxidation of cyclooctatetraene monoepoxide (XXXIX) with dimethyl sulfoxide

A solution of XXXIX (2.55 g.) in dimethyl sulfoxide containing boron trifluoride etherate (24 ml.) was heated on the steam bath for 8 hours, then poured into water (200 ml.) and extracted with ether. The combined ether extracts were washed with water, dried over magnesium sulfate, and concentrated to give crude product (1.0 g.). A large amount of high melting polymer was discarded during the workup. The crude material had an infrared spectrum with strong absorption at 3.54, 3.67, 5.83, 5.93, and 6.22 μ . Silica gel chromatography gave very poor separation. In view of the fact that Buchi had reported (60) the thermal isomerization of XXXIX to β -cycloheptatriene carboxaldehyde, having infrared absorption maxima at 3.55, 3.68, 5.82, 5.92, and 6.22 μ , it was assumed that a similar, acid-catalyzed, rearrangement had occurred here. Thus the reaction had no utility for the preparation of 8-hydroxy-cyclooctatrienone (XII).

Attempted oxidation of cyclooctatetraene monoepoxide (XXXIX) with dimethyl sulfoxide

A solution of XXXIX (1.1 g.) in dimethyl sulfoxide (2.0 ml.) was allowed to stand in a stoppered flask at room temperature under nitrogen for 21 hours. The solution was then diluted with water (100 ml.), and extracted with ether. The combined ether extracts were washed with water, dried over magnesium sulfate, and concentrated to give a crude product (0.95 g.) whose infrared spectrum revealed no sign of a reaction.

The crude product in dimethyl sulfoxide (2 ml.) above was then heated on the steam bath for 7 hours and allowed to stand overnight at room temperature. The mixture was worked up as before. The crude product showed weak carbonyl absorption at 5.82 and 5.93μ , in a spectrum very similar to that of the crude product obtained from the boron trifluoride etherate-catalyzed reaction.

Experimental for Attempted Preparation of
Cyclooctatetraene Dication

Silver ion-assisted solvolysis of 7,8-dibromobicyclo-(4.2.0)-octa-2,4-diene (XLI)

A number of these experiments were conducted under somewhat varied conditions of solvent, temperature and atmosphere, and using both silver fluoborate and hexafluoroantimonate. Inasmuch as no procedure was developed which was truly satis-

factory, no attempt will be made to describe each experiment. One procedure will be given, and the n.m.r. spectra from one run will be shown (Figure 5) to illustrate the sort of results obtained.

A solution of XLI (0.30 g.), freshly recrystallized from pentane, in acetonitrile (2.5 ml.) was added to a solution of silver fluoborate (0.714 g.) in acetonitrile (2.5 ml.) at room temperature in an open beaker. Silver bromide began to precipitate immediately. After 15 minutes a sample was filtered into an n.m.r. tube and the spectrum was run immediately (Figure 5). Silver bromide precipitated continually in the n.m.r. tube. The n.m.r. spectrum was again determined on the same sample after 24 hours (Figure 5), and again after 4 days (Figure 5). After 6 hours, the silver bromide (21%) was filtered off.

Similar experiments were carried out under carefully controlled conditions using liquid sulfur dioxide, very pure, dry acetonitrile, and nitromethane as solvents. Precautions were taken to exclude oxygen and moisture. Low temperature experiments were conducted. Several attempts to induce crystallization were futile. An attempt to trap the dication by a reaction with aqueous sodium carbonate was unsuccessful.

Preparation of 7,8-dibromobicyclo-(4.2.0)-
octa-2,4-diene (XLI)

XLI was prepared according to the method of Cope (75) by treating cyclooctatetraene with bromine in methylene chloride. XLI is a low-melting solid (m.p. 34-35° from pentane). It slowly decomposes on standing at room temperature; consequently it must be kept under refrigeration and recrystallized immediately before use. The n.m.r. spectrum is given in Figure 5.

Studies on the n.m.r. spectrum of tropylium fluoborate

Tropylium fluoborate was prepared according to the procedure of Fraenkel (25).

A solution containing tropylium fluoborate (100 mg.) in acetonitrile (1.75 ml.) was prepared, and its n.m.r. spectrum was determined. The tropylium ion showed a sharp singlet at 0.74 τ . Dilution of this solution to twice its original volume moved the peak to 0.83 τ . The addition of aqueous fluoboric acid (50%; 5 drops) moved the peak to 0.71 τ .

Another solution was prepared with tropylium fluoborate (100 mg.) in acetonitrile (1.75 ml.), and water (3 drops) was added. The peak was at 0.68 τ .

The effect of silver ion on the n.m.r. spectrum
of cyclooctatetraene

A solution was prepared containing cyclooctatetraene (0.50 ml.) in acetonitrile (2.0 ml.) which had been distilled

twice from phosphorus pentoxide. The n.m.r. spectrum was determined on a Varian HR-60 n.m.r. spectrometer. With no silver ion present a sharp singlet at 4.26τ was observed. Three drops of a saturated silver nitrate solution (in acetonitrile) was added, and the sharp singlet moved to 4.15τ . Three more drops were added, and the peak moved to 3.91τ . Apparently the presence of silver ion produces no gross shifts due to complexing.

Experimental for Solvent Photoaddition to
Cyclooctene-3-one

Irradiation of cyclooctene-3-one (XIX) in acetic acid

A solution of XIX (1.00 g.; .008 mole) in acetic acid (500 ml.) was purged with nitrogen for 30 minutes, capped with rubber septa, and irradiated with a 550 watt Hanovia type A mercury arc lamp in a water-cooled Pyrex immersion well. After $2\frac{1}{2}$ hours the solution was concentrated to 150 ml. on a rotary evaporator, diluted with water (2 l.) and extracted with ether. The combined ether extracts were washed with water, 5% sodium carbonate, and water. Removal of the ether on a rotary evaporator after drying over magnesium sulfate left crude product (1.10 g.). Vapor phase chromatography on a Carbowax 1500 (15% on Gaspak) column showed XIX (11%) and one other product (89%), 3-acetoxycyclooctene-3-one (XLIII). Distillation of crude XLIII showed the product to be 91% volatile.

Comparison of the total v.p.c. area of crude XLIII with the total area of XIX indicated 84% volatile products in crude XLIII. Analytical and spectral samples of XLIII were collected from both the Carbowax column and from a preparative scale SE-30 column (20% on Chromasorb P). The ultraviolet spectrum showed no high intensity maximum above $210\text{ m}\mu$. The infrared and n.m.r. spectra are shown in Figures 6 and 7.

Anal. Calc. for $\text{C}_{10}\text{H}_{16}\text{O}_3$: C, 65.24; H, 8.69. Found: C, 65.13; H, 8.70.

Irradiation of cyclooctene-3-one (XIX) in methanol

A solution of XIX (0.62 g.; 0.005 mole) in absolute methanol (500 ml.) was purged 30 minutes with nitrogen, capped with rubber septa, and irradiated with a 550 watt Hanovia type A mercury arc lamp in a water-cooled Pyrex immersion well for 110 minutes (91% decay of $226\text{ m}\mu$ band in the ultraviolet spectrum). Removal of solvent on the Rotovac gave crude product (0.75 g.). Vapor phase chromatography on a Perkin-Elmer R column at 177° showed 85% 3-methoxycyclooctanone (XLIV) and 15% XIX and no other products. The total area under this curve was 67% of the area under the curve of an identical size sample of XIX, thus indicating that about 33% of the crude photoproduct was non-volatile. A trap-to-trap distillation of the crude adduct (0.556 g.) separated the volatile components (0.360 g.; 65%). Analytical and spectral samples of XLIV were

collected from a preparative scale Carbowax 20M (2% on Chromasorb P) column. There was no intense absorption above 210 in the ultraviolet spectrum. The infrared and n.m.r. spectra are shown in Figures 6 and 7.

Anal. Calc. for $C_9H_{16}O_2$: C, 69.24; H, 10.25. Found: C, 69.34; H, 10.40.

Irradiation of cyclooctenone (XIX) in water

A solution of XIX (0.60 g.; 4.8 mmole) in water (500 ml.) was purged with nitrogen for 30 minutes, capped with rubber septa, and irradiated for 100 minutes in a water-cooled Pyrex immersion well using a 550 watt Hanovia type A mercury arc lamp (> 95% disappearance by ultraviolet analysis). Ammonium sulfate (200 g.) was dissolved in the reaction mixture, which was then extracted with ether. Drying of the combined ether extracts over magnesium sulfate, followed by removal of solvent on the Rotovac gave crude product (0.55 g.). Vapor phase chromatography on a Perkin-Elmer R column at 177° showed starting material and one product (XLVI) in the ratio 12:88. Comparison of v.p.c. areas indicated 72% volatile products in the crude mixture. An attempt to collect samples from a preparative scale Carbowax 20M column at 178° resulted in near quantitative rearrangement of XLVI to a compound which appeared to be 7-keto-octanal (XLVIII); the infrared spectrum on the crude collected product was grossly different from that of the crude

photoproduct, having absorption maxima at 3.70, 5.83, 5.88, 6.03, 7.10, and 7.37 μ . The crude photoproduct had maxima at 2.92 (broad), 5.89, and 5.92 μ . The n.m.r. on the crude collected product showed an aldehyde triplet at 0.28 τ and a singlet at 7.94 τ , probably due to a CH₃-CO- group.

The crude photoproduct was dissolved in acetic anhydride (4 ml.) containing sodium acetate (50 mg.) and allowed to stand 24 hours with occasional swirling. The solution was diluted with water and extracted with ether. The combined ether extracts were washed with 5% hydrochloric acid and water. Drying over magnesium sulfate, followed by solvent removal gave crude product (0.52 g.). Vapor phase chromatography on the R column (175°) showed two peaks in the ratio 1:2. These were identified by retention times as 3-acetoxycyclooctanone (XLIII) and cyclooctene-3-one (XIX). The infrared spectrum of a collected sample of the compound here identified as XLIII was identical to that of an authentic sample. Thus XLVI was 3-hydroxycyclooctanone.

Irradiation of cyclooctene-3-one (XIX) in ethanol

A solution of XIX (0.60 g.; 4.8 mmole) in 95% ethanol (500 ml.) was purged with nitrogen for 30 minutes, capped with rubber septa, and irradiated with a 550 watt Hanovia type A mercury arc lamp in a water-cooled Pyrex immersion well. The reaction, followed by observing the decay of the 228 $m\mu$ band

in the ultraviolet spectrum, was stopped after 90 minutes. Removal of solvent on the Rotovac gave crude product (0.71 g.). Vapor phase chromatography on a Perkin-Elmer R column (177°) showed one product, 3-ethoxycyclooctanone (XLV), in addition to XIX, in the ratio 83:17. Using cyclooctenone as a standard for area comparisons, 69% of the crude product was volatile. Analytical and spectral samples of XLV were collected from a preparative scale Carbowax 20M column (20% on Chromasorb P). The ultraviolet spectrum of XLV showed no intense absorption above 210 $m\mu$. The infrared and n.m.r. spectra are shown in Figures 7 and 8.

Anal. Calc. for $C_{10}H_{18}O_2$: C, 70.61; H, 10.58. Found: C, 70.24; H, 10.45.

Irradiation of cyclooctene-3-one (XIX) in t-butanol

A solution of XIX (0.62 g.; 5.0 mmole) in t-butanol (500 ml.) was purged with nitrogen for 30 minutes, capped with rubber septa, and irradiated with a 550 watt Hanovia type A mercury arc lamp in a Pyrex immersion well for 3 hours. Removal of solvent on the Rotovac gave crude product (0.72 g.). Vapor phase chromatography on the R column (177°) showed one product, 3-t-butoxycyclooctanone (XLVII), and XIX in the ratio 22:78. The product was found to be 40% volatile by v.p.c. area comparisons. Analytical and spectral samples were collected from a preparative scale R column. The infrared and n.m.r. spectra

are shown in Figures 7 and 8. The molecular weight of XLVII from the mass spectrometer was 198.

Anal. Calc. for $C_{12}H_{22}O_2$: C, 72.73; H, 11.11. Found: C, 72.70; H, 11.24.

The results of this irradiation varied considerably as conditions were changed, and were not quantitatively reproducible. A sample of the sort of variations encountered is found in the following tabulation:

<u>concentration</u>	<u>irradiation time</u>	<u>% XLVII</u>	<u>% XIX</u>	<u>% volatile</u>
1.0 g./1200 ml.	9 hr.	5	6	11
0.60/500	1	8	78	86
0.71/1300	8.5	22	11	33

The dark reaction of trans-cyclooctenone (XX) with methanol

A solution of XIX (0.155 g.; 1.25 mmole) in cyclohexane (250 ml.) was purged 30 minutes with nitrogen, capped with rubber septa and irradiated with a 550 watt Hanovia type A mercury arc lamp in a Pyrex immersion well. The reaction was followed by observing the decay of the $223m\mu$ band of cis-cyclooctenone in the ultraviolet spectrum. After one hour a steady state was reached with about 20% cis-cyclooctenone present. The lamp was turned off and methanol (2 ml.) was added. After one hour stirring in the dark, the ultraviolet spectrum was essentially unchanged. A 1 ml. control aliquot, removed before methanol addition, showed only a very slight

change in its ultraviolet spectrum after one hour. The solvent was removed on the Rotovac (water bath temperature $< 40^{\circ}$). Vapor phase chromatography on a Perkin-Elmer R column (177°) indicated the presence of only the methanol adduct (XLIV) and cyclooctenone (identified by retention times) in the ratio of about 1:2. Comparison of the total area in the chromatograph with the area under the peak for a pure cyclooctenone sample indicated 60% volatiles present.

If 1:3 sulfuric acid was added instead of methanol, the ultraviolet spectrum showed slow regeneration of cis-XIX.

Irradiation of cis-cyclooctenone (XIX)
in cyclohexane containing methanol

A solution of cis-XIX (0.155 g.; 1.25 mmole) in cyclohexane (250 ml.) containing methanol (2 ml.) was purged with nitrogen for 30 minutes, capped, and irradiated with a 550 watt Hanovia type A mercury arc lamp in a Pyrex immersion well. The reaction was followed by observing the ultraviolet spectrum. After one hour, cis-XIX was 65% destroyed. Then the solvent was removed on the Rotovac. Vapor phase chromatography on a Perkin-Elmer R column (177°) indicated the presence of the methanol adduct and cyclooctenone in the ratio of about 3:2 (identified by retention times). The crude photoproduct was 80% volatile (v.p.c.).

Irradiation of cis-cyclooctenone (XIX)
in methanol in quartz

A solution of XIX (0.36 g.; 2.9 mmole) in methanol (300 ml.) was purged for 30 minutes with nitrogen, capped with rubber septa, and irradiated with a 550 watt Hanovia type A mercury arc lamp in a quartz immersion well (water-cooled). After 10 minutes the lamp was turned off. The ultraviolet spectrum showed > 95% loss of cis-XIX. On standing in the dark this solution gradually regenerated cis-XIX. After 3 hours, the ultraviolet spectrum indicated 40% cis-XIX was present. After 13 hours, 42% cis-XIX was present. Removal of solvent and vapor phase chromatography on a Perkin-Elmer R column (177°) showed 3-methoxycyclooctanone (XLIV) and XIX present in a ratio 45:55. The same ratio was obtained when the reaction mixture was worked up immediately after lamp extinction.

Ultraviolet spectra which were recorded very soon (5 minutes) after lamp extinction showed a small but distinct absorption at $205 m\mu$, which disappeared completely within 15 minutes, without any observable increase in the $229 m\mu$ band. (A similar band at about $207 m\mu$ occurs in irradiations in 95% ethanol or t-butanol in Pyrex.)

Prolonged irradiation (90 minutes) results in a crude product which is essentially non-volatile in the v.p.c.

If 5% XLIV was added prior to irradiation for 90 minutes,

less than 1% XLIV was present after the irradiation.

Irradiation of cyclooctenone (XIX)
in quartz in t-butanol

A solution of XIX (0.36 g.; 2.9 mmole) in t-butanol (300 ml.) was purged for 30 minutes with nitrogen, and irradiated with a 550 watt Hanovia type A mercury arc lamp in a quartz immersion well. The reaction was followed by observing decay of the 229 $m\mu$ band for cis-XIX. When the reaction was finished, the solvent was removed on the Rotovac and the crude mixture was analyzed by v.p.c. on a Perkin-Elmer R column (177°).

Irradiation for 10 minutes reduced absorption of cis-XIX to 20% of its original value. On standing in the dark for 11 hours the cis-XIX concentration rose to 55% of its original value. Analysis by v.p.c. showed 5% adduct (XLVII) and 55% starting material (XIX).

Irradiation for 30 minutes caused the cis-XIX absorbance to decrease to 16% of its original value. On standing 3 hours in the dark, the cis-XIX absorption rose to 25% of its original value. Analysis showed 2% adduct (XLVII) and 24% XIX.

Irradiation for 90 minutes resulted in a crude product which was non-volatile in the v.p.c.

Preparation of 1,5-cyclooctadiene-3-one (XLII)

A solution of 1,5-cyclooctadiene (54 g.; 0.5 mole), N-bromosuccinimide (72 g.; 0.4 mole), carbon tetrachloride (400 ml.) and benzoyl peroxide (1.0 g.) was purged with nitrogen for one hour, and then heated at reflux under nitrogen with mechanical stirring. After 20 minutes an exothermic reaction began and refluxing became very vigorous. After one hour the reaction was allowed to cool. The mixture was filtered to remove succinimide, washed with 5% sodium carbonate and water, and then dried over magnesium sulfate. Removal of solvent on the Rotovac gave crude product (97.5 g.).

This crude bromide was dissolved in acetic acid (300 ml.) and slowly dropped into a stirred, cooled slurry of silver acetate (83.5 g.) in acetic acid (300 ml.). The reaction mixture was allowed to stand in the dark for 36 hours, diluted with water (5 l.) and extracted with ether after separating the oily layer. The oily layer and ether extracts were combined, washed with water, and dried over magnesium sulfate. Removal of solvent on the Rotovac gave crude product (63 g.). The mixture was distilled to obtain the monoacetate, b.p. 60-65°/0.13 mm. Vapor phase chromatography on a Perkin-Elmer W column (Carbowax 1500) at 134° showed a poorly resolved mixture (~70:30). The infrared spectrum showed an intense band at 5.76 μ .

This mixture (28.9 g.) was dissolved in ether (250 ml.)

and slowly added over one hour to a stirred slurry of lithium aluminum hydride (27 g.) in ether (500 ml.). After addition was complete the reaction was stirred 45 minutes, after which the excess hydride was destroyed with aqueous sodium sulfate. After filtration the ether layer was separated, and the aqueous layer was extracted with ether. The combined ether fractions were dried with magnesium sulfate and anhydrous potassium carbonate. Removal of solvent, followed by distillation gave a mixture of two alcohols (17.3 g.), b.p. 65-67°/0.90 mm.

This mixture was oxidized according to the method of Holum (71). A slurry of pyridine-chromic acid complex was prepared by adding chromic oxide (43.4 g.) in portions over one hour to chilled pyridine (500 ml.) with vigorous stirring. A solution of cyclooctadienol (17.3 g.) in pyridine (70 ml.) was added in one portion with cooling to the above slurry. The mixture was stirred 45 minutes, then allowed to stand 22 hours at room temperature. The mixture was then diluted with water (2400 ml.) and extracted with ether. The combined ether extracts were washed with 3 M hydrochloric acid, 5% sodium bicarbonate, water, and then dried over magnesium sulfate. Removal of solvent on the Rotovac provided crude ketone (12.5 g.). Vapor phase chromatography on a Perkin-Elmer R column showed a mixture (~ 70/30) of two compounds. The infrared spectrum of the crude mixture showed no hydroxyl absorption, and maxima at 5.99, 6.07, and 13.25 μ .

Experimental for Attempted Solvent
Photoaddition in Other Systems

The irradiation of 1-acetylcyclohexene (LII)

A solution of 1-acetylcyclohexene (0.627 g.; 5 mmole) in acetic acid (750 ml.) was purged with nitrogen for 40 minutes, capped with rubber septa, and then irradiated with a 550 watt Hanovia type A mercury arc lamp in a Pyrex immersion well for 5 hours. The mixture was concentrated to 50 ml. on the Rotovac, poured into water (2 l.), and extracted with ether (3 x 200 ml.). The combined ether extracts were washed with sodium carbonate solution, then with water, and dried over magnesium sulfate. After filtration and removal of ether on the Rotovac an oil (0.83 g.) was recovered. Vapor phase chromatography on a Carbowax 1500 column (150°) showed only solvent and starting material.

Preparation of 3-methoxycyclohexenone (LI)

Into a 1 liter 2-necked flask connected with 10 mm. glass tubing to a condenser was placed ether (400 ml.), 95% ethanol (160 ml.) and 40% sodium hydroxide (40 ml.) solution. The flask was cooled in ice-water and stirred with a magnetic stirrer. Then DuPont EXR-101 (14.4 g.) was added; the water bath was allowed to come to room temperature and then slowly heated to 50°. Soon after, yellow diazomethane was evolved and distilled (along with ether) into an iced flask containing ether

(50 ml.). After about 250 ml. of ethereal diazomethane had been collected the heat was removed. 1,3-cyclohexanedione (6.68 g.; 0.06 mole), freshly recrystallized from benzene, was dissolved in a minimum amount of chloroform and added dropwise to the diazomethane solution (20 minutes). The excess diazomethane was destroyed by allowing the reaction mixture to stand several hours at room temperature. Then the solvent was removed on the Rotovac, giving crude product (8.0 g.). Distillation gave pure 3-methoxycyclohexenone (4.0 g.); b.p. 50-51°/0.1 mm.; n_D^{26} 1.5123, reported (75) n_D^{25} 1.5118-1.5120.

Irradiation of 3-methoxycyclohexenone (LI) in methanol, and in methanol-water

A solution of 3-methoxycyclohexenone (0.605 g.; 4.8 mmole) in methanol (750 ml.) was purged with nitrogen for 1 hour, and then irradiated with a 550 watt Hanovia type A mercury arc lamp in a Pyrex immersion well. The reaction was followed by observing the ultraviolet spectrum. After 22 hours irradiation, no change was observed in the ultraviolet spectrum. Then water (10 ml.; .625 mole) was added to the mixture. After 75 minutes in the dark there was no change in the ultraviolet spectrum. Then this solution was irradiated for 14 hours, and no change in the ultraviolet spectrum was seen.

Irradiation of trans-benzalacetone (LIII) in methanol

A solution of trans-LIII (1.0 g.; 6.8 mmole) in methanol (1300 ml.) was purged for 30 minutes with nitrogen, capped, and irradiated with a 550 watt Hanovia type A mercury arc lamp in a Pyrex immersion well. After 48 hours, trans-LIII was 60% consumed (u.v. analysis). Removal of solvent on the Rotovac gave a viscous oil (1.05 g.). Analysis by v.p.c. on a Carbowax 1500 column (150°) showed the presence of only the cis and trans isomers (identified by retention time), although the infrared spectrum of the crude material showed trace amounts of carbonyl-containing components (5.15, 5.85 μ) in addition to cis- and trans-LIII (5.92, 6.02 μ).

Irradiation of cyclohexenone (XLIX) in methanol

A solution of cyclohexenone (0.326 g.; 3.8 mmole) in methanol (500 ml.) was purged with nitrogen for 30 minutes, capped with rubber septa, and irradiated with a 550 watt Hanovia type A mercury arc lamp in a Pyrex immersion well until 60% destruction of XLIX was indicated by the ultraviolet spectrum (42 hours). Removal of solvent on the Rotovac gave crude product (0.25 g.). Vapor phase chromatography on a Carbowax 1500 column (150°) showed XLIX and one other peak (L) in the ratio 1.3:1. A sample of L was collected; its infrared spectrum showed absorption maxima at 5.85 and 9.15 μ . The infrared data, and analogy with the cyclooctenone irradiation, suggests

that L is 3-methoxycyclohexanone. This was not further characterized. Later attempts to repeat this experiment always gave L, but only in trace amounts (identified by retention time).

All attempts to perform this irradiation in 95% ethanol gave only trace amounts of a compound whose retention time was similar to that of L, but which was not characterized.

SUMMARY

There has been no report of the preparation of a compound containing six π -electrons in an eight-membered ring. Hückel molecular orbital calculations suggested that cyclooctatriene-1,4-dione (XXI) and cyclooctatetraene dication (X) might be stable aromatic species if they were prepared.

A variety of approaches to the synthesis of XXI were unsuccessful. During the course of this investigation 9-oxabicyclo-(4.2.1)-2-nonenol (XXIV) was prepared, fully characterized, and shown to be in equilibrium with a small amount of 8-hydroxycyclooctene-3-one (XXV) in solution. The nitroso dimer (XXXIV) and the oxime (XXXV) resulting from the addition of nitrosyl chloride to cyclooctene were prepared and characterized.

An attempt was made to prepare X from cyclooctatetraene dibromide by silver-ion assisted solvolysis. Evidence was obtained (n.m.r.) which suggested the presence of X in solution, but X could not be isolated.

Very few instances are known in which a solvent adds to the double bond of an unsaturated compound on irradiation with ultraviolet light; no example of such an addition to a simple unsaturated ketone has been reported. Irradiation of cyclooctenone (XIX) in methanol, ethanol, *t*-butanol, water and acetic acid resulted in formation of an adduct in which RO- is attached in the 3-position of cyclooctanone. Evidence was

obtained which strongly suggests that this reaction involves a photochemical addition of solvent to cis-XIX, in addition to a thermal addition of solvent to trans-XIX.

Irradiation of cyclohexenone (XLIX), 1-acetylcyclohexene (LII), benzalacetone (LIII), and 3-methoxycyclohexene (LI) resulted in essentially no solvent addition. However, XLIX when irradiated in methanol did give trace amounts of an adduct which may be 3-methoxycyclohexanone.

LITERATURE CITED

1. Streitweiser, Andrew, Jr., Molecular Orbital Theory for Organic Chemists. New York, New York, John Wiley and Sons, Inc. 1961.
2. Breslow, R. and Chin Yuan, J. Am. Chem. Soc., 80, 5991 (1958).
3. Breslow, R. and H. Hover, J. Am. Chem. Soc., 82, 2644 (1960).
4. Breslow, R., R. Haynie and J. Mirra, J. Am. Chem. Soc., 81, 247 (1959).
5. Breslow, R. and R. Peterson, J. Am. Chem. Soc., 82, 4426 (1960).
6. Breslow, R., J. Posner and A. Krebs, J. Am. Chem. Soc., 85, 234 (1963).
7. Volpin, M. E., Y. D. Koreschkov and D. N. Kursanov, Izvest. Akad. Nauk S.S.S.R., Otdel. Khim. Nauk, 560 (1959); not translated, abstracted in Chemical Abstracts, 53, 21799 (1959).
8. Katz, T. J., J. R. Hall and W. C. Neikam, J. Am. Chem. Soc., 84, 3199 (1962).
9. Freedman, H. H. and A. M. Frantz, Jr., J. Am. Chem. Soc., 84, 4165 (1962).
10. Bryan, R. F., J. Am. Chem. Soc., 86, 733 (1964).
11. Freedman, H. H. and A. A. Young, J. Am. Chem. Soc., 86, 735 (1964).
12. Wasserman, H. H. and E. V. Dehmlow, J. Am. Chem. Soc., 84, 3787 (1962).
13. Park, J. D., S. Cohen and J. R. Lacher, J. Am. Chem. Soc., 84, 2919 (1962).
14. Merling, G., Ber., 3108 (1891).
15. Doering, W. von E. and L. H. Knox, J. Am. Chem. Soc., 76, 3203 (1954).

16. Nozoe, T., in J. W. Cook and W. Carruthers, eds. Progress in Organic Chemistry, 5, 132. Washington, D. C., Butterworths. 1961.
17. Feldman, M. and S. Winstein, Tet. Letters, 853 (1962).
18. Feldman, M. and S. Winstein, J. Am. Chem. Soc., 83, 3338 (1961).
19. LeGoff, E. and R. B. LaCount, J. Am. Chem. Soc., 85, 1354 (1963).
20. Roberts, J. D., A. Streitweiser and C. M. Ragan, J. Am. Chem. Soc., 74, 4579 (1952).
21. Jackman, L. M., Nuclear Magnetic Resonance Spectroscopy. New York, New York, The MacMillan Co. 1959.
22. Elvidge, J. A. and L. M. Jackman, J. Am. Chem. Soc., 83, 859 (1961).
23. Abraham, R. J., R. C. Sheppard, W. A. Thomas and S. Turner, Chem. Comm., 43 (1965).
24. Elvidge, J. A., Chem. Comm., 160 (1965).
25. Fraenkel, G., R. E. Carter, A. McLachlan and J. H. Richards, J. Am. Chem. Soc., 82, 5846 (1960).
26. Schönberg, Alexander, Preparative Organische Photochemie. Berlin, Springer-Verlog. 1958.
27. Stoermer, R. and H. Stockmann, Ber., 1786 (1914).
28. Stoermer, R., Ber., 658 (1911).
29. Wang, S. Y., Nature, 190, 690 (1961).
30. Wang, S. Y., Fed. Proc., 24, No. 2, part III, 71 (1965).
31. Wang, S. Y., Photochem. and Photobiol., 1, 37 (1962).
32. Wang, S. Y., Photochem. and Photobiol., 1, 135 (1962).
33. Wang, S. Y., M. Apicella and B. R. Stone, J. Am. Chem. Soc., 78, 4180 (1956).
34. Bernardi, L., G. Bosisio, O. Goffredo and B. Patelli, Gazz. Chim. Ital., 95, 384 (1965).

35. Stoll, A. and W. Schientz, *Helv. Chim. Acta*, 38, 585 (1955).
36. Dauben, W. G., in *Organic Photochemistry*, p. 547. London, Butterworths. 1965. Reprinted in *Pure and Applied Chemistry*, 9, 547 (1964).
37. Eaton, P. E. and Kang Lin, *J. Am. Chem. Soc.*, 86, 2087 (1964).
38. Eaton, P. E. and Kang Lin, *J. Am. Chem. Soc.*, 87, 2052 (1965).
39. Corey, E. J., M. Tada, R. LeMahieu and L. Libit, *J. Am. Chem. Soc.*, 87, 2051 (1965).
40. Corey, E. J., J. D. Bass, R. LeMahieu and R. B. Mitra, *J. Am. Chem. Soc.*, 86, 5570 (1964).
41. Juneja, H., unpublished research notes. Ames, Iowa, Iowa State University of Science and Technology. (1964).
42. Allendoerfer, R. D. and P. H. Rieger, *J. Am. Chem. Soc.*, 87, 2336 (1965).
43. Chapman, O. L., *J. Am. Chem. Soc.*, 85, 2014 (1963).
44. Chapman, O. L. and R. W. King, *J. Am. Chem. Soc.*, 86, 1256 (1964).
45. Doering, W. von E. and A. A.-R. Sayigh, *J. Org. Chem.*, 26, 1365 (1961).
46. Yates, P. and C. D. Anderson, *Can. J. Chem.*, 41, 1033 (1963).
47. DePuy, C. H. and E. F. Zaweski, *J. Am. Chem. Soc.*, 81, 4920 (1959).
48. Kornblum, N., J. W. Powers, G. J. Anderson, W. J. Jones, H. O. Larson, O. Levand and W. M. Weaver, *J. Am. Chem. Soc.*, 79, 6562 (1957).
49. Kornblum, N., W. J. Jones and G. J. Anderson, *J. Am. Chem. Soc.*, 81, 4113 (1959).
50. Baizer, M. M., *J. Org. Chem.*, 25, 670 (1960).
51. Hunsberger, I. M. and J. M. Tien, *Chem. and Ind. (London)*, 88 (1959).

52. Nace, H. R. and J. J. Monagle, J. Org. Chem., 24, 1792 (1959).
53. Beckham, L. J., W. A. Fessler and M. A. Kise, Chem. Rev., 48, 319 (1951).
54. Miller, J. B., J. Org. Chem., 26, 4905 (1961).
55. Wallach, O., Ann., 345, 127 (1906).
56. Metzger, H., Angew. Chem., Int'l. Ed., 2, 688 (1963).
57. Bryce-Smith, D., G. I. Fray and A. Gilbert, Tet. Letters, 2137 (1964).
58. Zimmerman, H. E. and L. Craft, Tet. Letters, 2131 (1964).
59. Cohen, T. and T. Tsuji, J. Org. Chem., 26, 1681 (1961).
60. Buchi, G. and E. M. Burgess, J. Am. Chem. Soc., 84, 3106 (1962).
61. Katz, T. J., J. Am. Chem. Soc., 82, 3784 (1960).
62. Katz, T. J., J. Am. Chem. Soc., 82, 3785 (1960).
63. NMR Spectra Catalog, Varian Associates, Palo Alto, California. 1962.
64. Cope, A. C. and M. Burg, J. Am. Chem. Soc., 74, 168 (1952).
65. Eaton, P. E., J. Am. Chem. Soc., 84, 2344 (1962).
66. DeMayo, P., in R. A. Raphael, E. C. Taylor and H. Wynberg, eds., Advances in Organic Chemistry, Volume 2, p. 387. New York, New York, Interscience Publishers, Inc. 1960.
67. Hammond, G. and N. Turro, Science, 142, 1541 (1963).
68. Eaton, P. E., J. Am. Chem. Soc., 84, 2454 (1962).
69. Cope, A. C., M. R. Kinter and R. T. Keller, J. Am. Chem. Soc., 76, 2757 (1954).
70. Bowden, K., I. M. Heilbron, E. R. H. Jones and B. C. L. Weedon, J. Chem. Soc., 39 (1946).
71. Holum, J. R., J. Org. Chem., 26, 4814 (1961).

72. Partch, R. E., Tet. Letters, 41, 3071 (1964).
73. Azatyan, V. D. and R. S. Gyuli-Kevkhyan, Doklady Akad. Nauk Armyan S.S.S.R., 21, 209 (1955); not translated, abstracted in Chemical Abstracts, 50, 11257 (1956).
74. Cope, A. C. and B. D. Tiffany, J. Am. Chem. Soc., 73, 4158 (1951).
75. Ralls, J. W., W. C. Wildman, K. E. McCaleb and A. L. Wilds. U. S. Patent 2,674,627. April 6, 1954. Abstracted in Chemical Abstracts, 49, P1814 (1955).

ACKNOWLEDGMENT

The author wishes to thank Professor O. L. Chapman for his patient guidance of this research and for his encouragement.

The author wishes to recognize the helpfulness of the many discussions with his colleagues which greatly stimulated the performance of this research. The author is particularly grateful for a discussion with Mr. Leo F. Englert which resulted in the work on cyclooctatetraene dication.

The author is indebted to the National Aeronautics and Space Administration for a NASA Traineeship which was in effect from March, 1964 to August 1965.

The author wishes to thank Dr. R. W. King and R. L. Thrift for their valuable assistance with the nuclear magnetic resonance spectroscopy which was so necessary to this research.

The author is deeply grateful to his wife, Sandra, for immeasurable patience, encouragement, and help, and for her meticulous typing of this thesis.