SYNTHETIC APPROACHES TO 1,2-CYCLOOCTATRIENEDIONE

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This is to certify that the

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Synthetic Approaches to 1,2-Cyclooctatrienedione

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Major professor

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ABSTRACT

SYNTHETIC APPROACHES TO 1,2-CYCLOOCTATRIENEDIONE

By

Thomas R. Kowar

Synthetic approaches to 1,2-cyclooctatrienedione 9 and its valence tautomer, bicyclo[4.2.0]-2,4-octadiene-7,8-dione 38, were investigated.[1]

Treatment of 7,8-bis(trimethylsiloxy)-*cis*-bicyclo-[4.2.0]-3,7-octadiene 57 with pyridinium hydrobromide perbromide afforded 3,4-dibromobicyclo[4.2.0]-6-octene-7,8-dione 61 which was converted to benzocyclobutadienoquinone 60 by the action of 1,5-diazabicyclo[4.3.0]-5-nonene. Bromination of 57 with N-bromosuccinimide afforded 60 directly.

The boron trifluoride etherate catalyzed oxidation of 5,6-epoxycyclooctene with dimethylsulfoxide afforded 2-hydroxy-5-cyclooctenone 76 which was subsequently oxidized to 5-cyclooctene-1,2-dione 69. Bromination of 69 with cupric bromide gave *trans*-3,8-dibromo-5-cyclooctene-1,2-dione 85. Attempts to form 9 by the dehydrobromination of 85 were unsuccessful but the use of hexamethylphosphoric triamide as the base provided 3-bromo-2-hydroxy-2,5,7-cyclooctatrienone

93. Bromination of 93 with N-bromosuccinimide afforded 3,7-dibromo-3,5-cyclooctadiene-1,2-dione 125. Treatment of 125 with triethylamine resulted in the formation of 60.

The reaction of 85 with *o*-phenylenediamine afforded 2,7-dibromo-10,11-benzo-9,12-diazabicyclo[6.4.0]-4,8,10,12-dodecatetraene 88 which was subsequently dehydrobrominated with 1,5-diazabicyclo[4.3.0]-5-none to form 10,11-benzo-9,12-diazabicyclo[6.4.0]-2,4,6,8,10,12-dodecahexaene 89. The spectroscopic properties of 89, the quinoxaline derivative of 9, indicated a nonplanar geometry for the eight membered ring.

Attempts to synthesize the bis ethylene ketal of 85 from 85 or from the bis ethylene ketal of 69, 1,2-bis-(spiro-1',3'-dioxolane)-5-cyclooctene 97,[2] were not successful.

The reaction of 69 and *p*-anisaldehyde provided 3,8-di-(*p*-methoxybenzilidene)-5-cyclooctene-1,2-dione 82. An attempt to isomerize 82 to the dibenzyl derivative of 9 using palladium failed. Birch reduction of 82 afforded 3,8-di(*p*-methoxybenzyl)-5-cyclooctene-1,2-dione 109.

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1. P. Yates, E. G. Lewars, and P. H. McCabe, Can. J. Chem., 48, 788 (1970).
2. P. Yates and E. G. Lewars, Chem. Commun., 1537 (1971).

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By

Thomas R. Kowar

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To My Mother and Father

Who Have Given Me So Much

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SYNTHETIC APPROACHES TO

1,2-CYCLOOCTATRIENEDIONE

INTRODUCTION

During the latter half of the nineteenth century the stability of benzene relative to acyclic olefins presented organic chemists with a formidable problem. In 1872 Kekule[1] concluded that benzene had a 1,3,5-cyclohexatriene structure in which the π-electrons are delocalized. Thus electron delocalization became associated with enhanced stability.

This idea was developed quantitatively with the advent of molecular orbital theory by Hückel[2] in 1931. The molecular orbital method places the π-electrons of benzene into molecular orbitals which are common to all of the carbon atoms. Hückel recognized that when the bonding molecular orbitals were completely filled, stability enhancement resulted in a manner analogous to that encountered with the rare gas atomic orbital configurations. Thus Hückel was able to predict that compounds whose bonding molecular orbitals were completely filled would possess the enhanced stability exhibited by benzene.

The conditions for this aromatic stabilization are contained in the Hückel rule[2] which states that "amongst fully conjugated, planar, monocyclic polyolefins only those possessing (4n + 2) π-electrons, where n is an integer, will have special aromatic stability."[1,1]

The prophesy of Hückel's rule has prompted organic chemists to synthesize a wealth of interesting compounds in order to test the validity of the concept of aromaticity. There is, perhaps, no other theory in organic chemistry which has been more critically examined than that of aromaticity. Interestingly, the aromatic theory has also proven to be one of the most durable concepts of organic chemistry. The (4n + 2) rule was originally intended to be valid only for symmetrical, monocyclic systems but has since been successfully applied to many polycyclic and heterocyclic compounds.

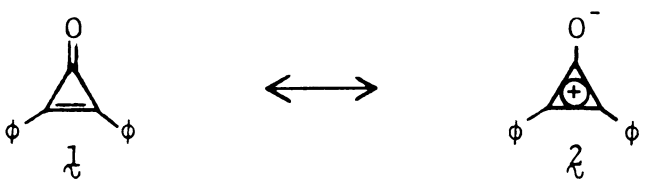
Molecular orbital theory allows for the calculation of the delocalization energy (DE), a measure of the extent to which a particular system is stabilized relative to a model system containing the same number of localized π-electrons. Hückel molecular orbital (HMO) calculations of delocalization energies are based on certain inaccurate assumptions and thus must be interpreted with caution. More sophisticated types of molecular orbital calculations have been developed to circumvent these problems. During the following discussion delocalization energies will be used only in a qualitative sense.

During the past twenty-five years several types of organic ions containing (4n + 2) π-electrons have been synthesized and have been shown to be aromatic.

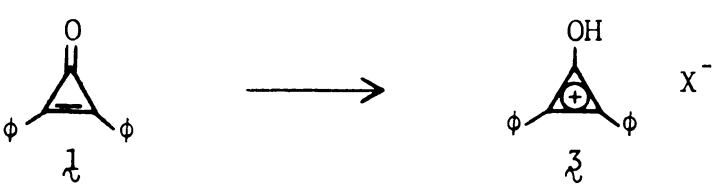
Breslow[3] described the synthesis of triphenylcyclopropenium tetrafluoroborate in 1957. This salt was found to be stable and is considered to be aromatic. Recently the parent ion has been prepared.[4] The aromatic character of the cyclopropenium ion was confirmed by it's nuclear magnetic resonance (nmr) spectrum which exhibits a singlet absorption at δ 11.1 relative to tetramethylsilane (TMS). When this absorption position is corrected[5] for strain, charge, and alteration of ring current, it's value is approximated to occur in the aromatic region of the nmr spectrum. The DE of the cyclopropenium ion is calculated to be 2.00 β.[6]

The first deliberate synthesis of the cycloheptatrienyl (tropylium) cation was reported by Doering and Knox in 1954.[7] Comparison of the infrared and raman spectra of tropylium bromide confirm that the carbonium ion is symmetrical with the positive charge evenly distributed over all seven carbons.[7,8] The nmr spectrum of the tropylium ion consists of a singlet absorption at δ 9.2 relative to TMS.[9] This absorption position is indicative of an aromatic species when it is corrected for charge. HMO calculations indicate that the tropylium ion should have a DE of 2.99 β.[6]

The cyclopropenone system does not meet the conditions for aromaticity as required by Hückel's rule, but nevertheless, is considered to possess aromatic character. Cyclopropenones are expected to be highly strained species due to the incorporation of three sp^2 hybridized carbon atoms into a three-membered ring. Breslow, however, in 1959[10] reported the synthesis of diphenylcyclopropenone 1 as a stable, crystalline material. The less strained cyclopropanone system, first reported by Turro, Hammond, and Leermakers[11] in 1965, is quite unstable and undergoes reactions which result in the relief of ring strain. The difference in stability between these two systems must be attributed to the aromatic character conferred to cyclopropenones by resonance forms such as 2 which contain the aromatic cyclopropenium ion moiety.



Supplementary evidence for this argument is obtained from the fact that cyclopropenones react readily with strong acids to form hydroxycyclopropenium salts 3.[10b,12]

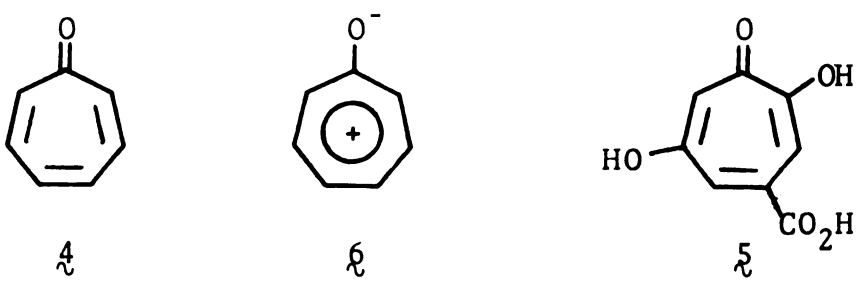


The infrared carbonyl absorption frequency of diphenylcyclopropenone[10a,13] occurs at 1640 cm^{-1} while that of tetramethylcyclopropanone[11] occurs at 1840 cm^{-1} indicating that the carbonyl group of cyclopropenones possesses considerable single bond character.

Dipole moment data also support the importance of the dipolar resonance forms of cyclopropenones. Diphenylcyclopropenone has a dipole moment of 5.08 D[13] while benzophenone has a dipole moment of only 2.97 D indicating appreciable polarization of the cyclopropenone carbonyl double bond. The DE of the parent cyclopropenone is calculated to be 1.36 β.[14]

The first example of a cycloheptatrienone derivative was recognized in 1945 when Dewar[15] proposed the tropone skeleton 4 for the structure of the natural product stepiatic acid 5. Since then many natural products containing the tropone skeleton have been isolated and a large number of synthetic tropones and tropolones have been prepared.

By analogy to cyclopropenone, the tropone system may be considered to be aromatic in nature as a resonance form 6 containing the aromatic tropylium ion can be visualized.

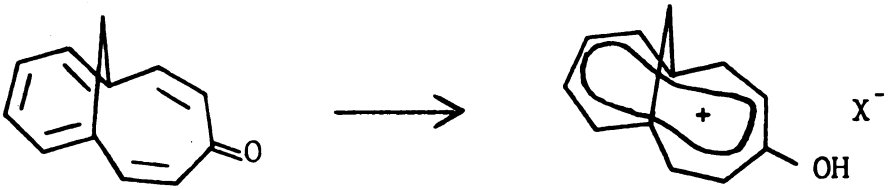


4 6 5

The protons of tropone exhibit absorption in the aromatic region of the nmr spectrum.[16] The infrared carbonyl absorption of tropone occurs at 1590 cm^{-1}[17] which is lower than that of 2,6-cycloheptadienone (1647 cm^{-1})[18] reflecting the single bond character of the carbonyl double bond. Tropone has a dipole moment of 4.3 D[19] which compared to a value of 3.04 D[20] for cycloheptanone indicates a small but significant contribution from the dipolar resonance form. Like the cyclopropenones, tropones react with strong acids to form hydroxytropylium salts. HMO calculations predict tropone to have a DE of 2.55 β.[21]

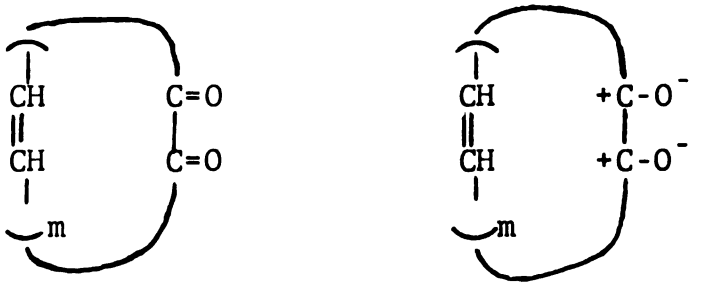
Despite the convincing arguments put forth for the aromatic nature of tropones there have recently appeared several papers which provide evidence which defines these compounds as being more polyenoic than aromatic in nature.[22,23]

Recently 4,9-methano[11]annulenone 7, a 10 π-electron analog of tropone, has been synthesized by Grimme, Reisdorff, Junemann, and Vogel.[24] This compound appears to be a polyenone in the ground state based on an analysis of the 100-MHz nmr spectrum. When 7 was treated with deuteriotrifluoroacetic acid, the aromatic 4-hydroxybicyclo[5.4.1]dodecapentaenylium ion 8 was formed.



7 8

The primary goal of research described in this thesis was the synthesis of 1,2-cyclooctatrienedione 9 which can be considered to be a formal analog of tropone and is a member of a family of cyclic unsaturated α-diketones of type 10.



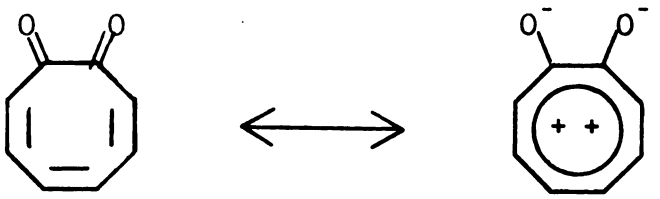
10 11

These compounds are expected to be aromatic when m is an odd integer as resonance forms containing (4n + 2) π-electrons such as 11 can be visualized.

The only known members of this family at the present time are the cyclobutenediones and the cyclohexadiene-1,2-diones.

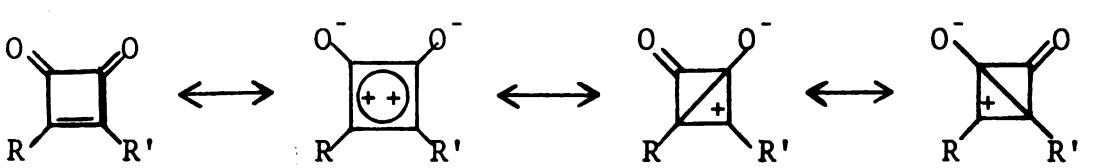
Dione 9 is expected to be aromatic or at least to exhibit some aromatic character by virtue of the contribution of the dipolar resonance form 12 which contains the cyclooctatrienium dication moiety. Although the cyclooctatrienium dication has not been observed

directly, it has been implicated as an intermediate in the anodic oxidation of cyclooctatetraene[25,26] and is expected to be aromatic in accordance with Hückel's rule.



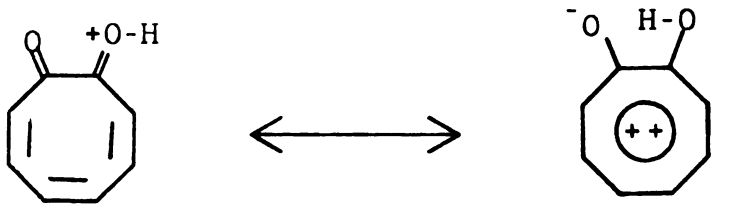
9 12

There are serious objections to dipolar resonance form 12. The charge separation and the electrostatic charge repulsion between the negative charges on the oxygen atoms will increase the energy of 12 and thereby decrease it's importance as a contributor to the overall structure of the molecule. Similar problems are encountered in a consideration of the cyclobutenediones 13[27] whose surprising stability has been attributed to the dipolar resonance form 14 which contains the 2 π-electron aromatic cyclobutenium dication moiety. This case is not completely analogous to cyclooctatriene-1,2-dione, however, as there is no increase in ring strain upon going to the dipolar resonance form and, in addition, cross ring resonance forms 15 and 16 can be visualized.



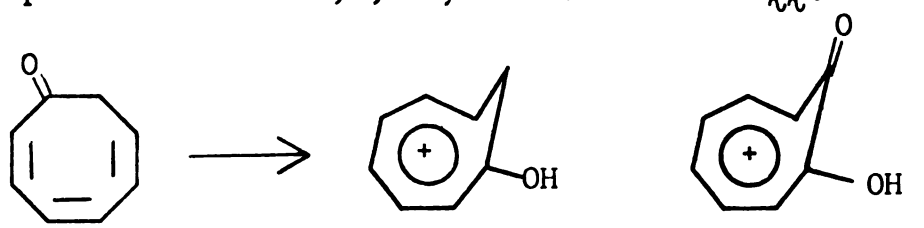
13 14 15 16

Monoprotonation of 1,2-cyclooctatrienedione would reduce the repulsion between the oxygen atoms and would be expected to increase the importance of the aromatic resonance contributor 17.



17

Such a species could also exist as the homotropylium ion 18 analogous to the homotropylium ion 19 formed upon protonation of 2,4,6-cyclooctatrienone 20.[28]



20 19 18

Diprotonation of 1,2-cyclooctatrienedione would further reduce the problem of charge repulsion and, in fact, the resulting dication would be the 1,2-dihydroxycyclooctatrienium dication.

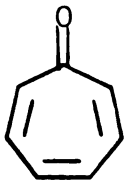
Recent molecular orbital calculations by Gund and Carpino[29] indicate that 1,2-cyclooctatrienedione should possess aromatic stabilization. HMO calculations assign a delocalization energy of 3.07 β to the dione 9 while the more refined Streitwieser-Coulson molecular orbital

(SCMO) calculations predict a DE of 2.76 β for 9.

The SCMO calculations indicate that tropone should have a DE of 2.19 β which is equivalent to a DE to ring atom ratio of 0.31 β when the oxygen atom is neglected. The corresponding ratio for 1,2-cyclooctatrienedione is 0.35 β. The strain resulting from the planar conformation required for aromaticity in 9 is, of course, greater than that required for planarity in the seven-membered ring of tropone. This ring strain should be similar to that resulting from planar cyclooctatetraene which has been estimated[21,30] to be approximately 27 Kcal/mole. The SCMO DE for 1,2-cyclooctatrienedione is 45.6 Kcal/mole and thus the ring strain is not a prohibitive factor in the potential aromaticity of 9.

Chemical evidence also infers that 1,2-cycloocta-trienedione will be a stable, isolable compound. Heptafulvene 21 is the methylene homolog of tropone.[31] While tropone is a distillable liquid, heptafulvene polymerizes at temperatures greater than -80°C. The bis methylene homolog of dione 9, 7,8-dimethylene-1,3,5-cyclooctatriene 22, was reported independently in 1966 by Elix, Sargent, and Sondheimer[32] and by Anet and Gregorovich.[33] This compound was synthesized from it's immediate precursor at 25°C and was shown to be stable in the absence of oxygen and light. The exocyclic methylene groups of this compound constitute an extremely

reactive dienophilic moiety which, in part, accounts for it's high reactivity. The substitution of carbonyl groups for the methylene groups would be expected to decrease such reactivity and by analogy to the difference in stability between heptafulvene and tropone, it would be expected that 1,2-cyclooctatrienedione would be more stable than the corresponding bis methylene cyclooctatriene.



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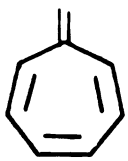

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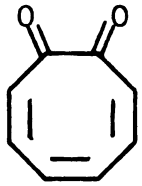

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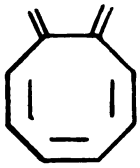


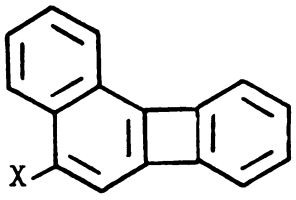
22

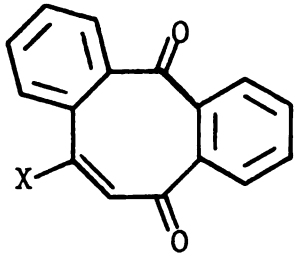
Considering the skepticism concerning the aromaticity of tropones and the demonstration of the polyenoic nature of 7 it might be optimistic to expect that 1,2-cyclo-octatrienedione would be aromatic. It is, however, an interesting molecule and was deemed a worthy synthetic goal. The protonated forms of the target compound would be more likely candidates as aromatic species. The preparation of such ions would bear directly on the problems of the aromatic character of homotropylium ions and cyclooctatrienium dications.

Previous Approaches to 1,2-cyclooctatrienedione.

Although one benzo derivative of 1,2-cyclooctatrienedione is known, the parent system has eluded previous synthetic attempts. The isomeric 1,4-cyclooctatrienedione system has received some attention since the arguments presented for the potential aromaticity of the 1,2-dione apply equally well to the 1,4-dione.

Cava and Ratts, in 1962, reported that the oxidation of the biphenylenes 23 and 24 yields the corresponding halodibenzocyclooctatriene-1,4-diones 25 and 26 respectively.[34] These authors, however, failed to comment on the potential aromaticity of these systems.



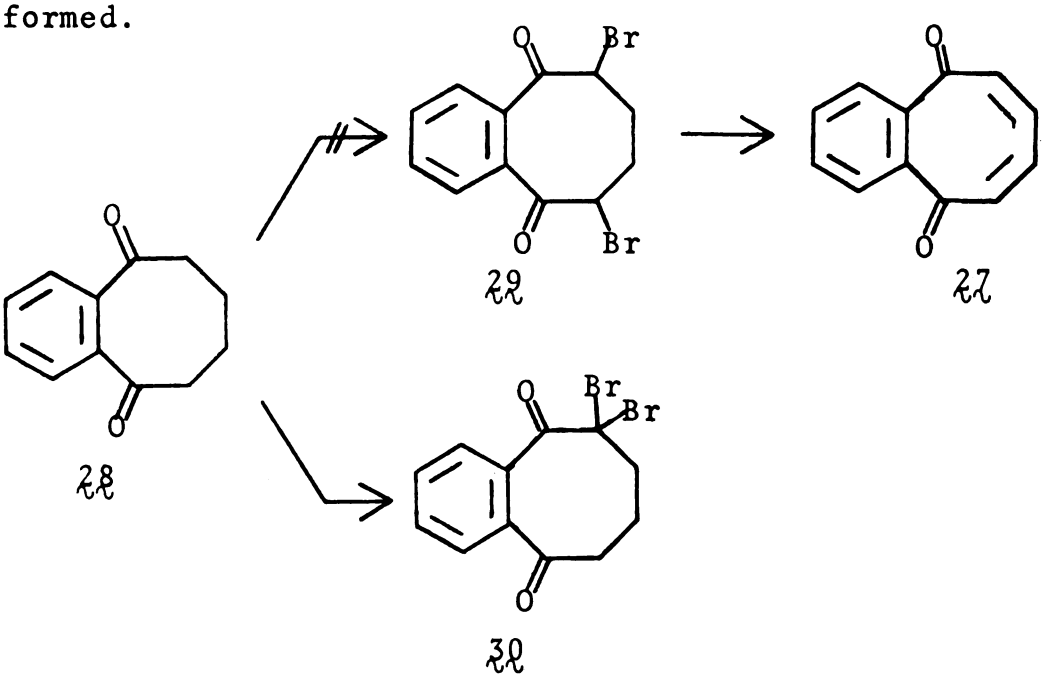


23 X = Br
24 X = Cl

25 X = Br
26 X = Cl

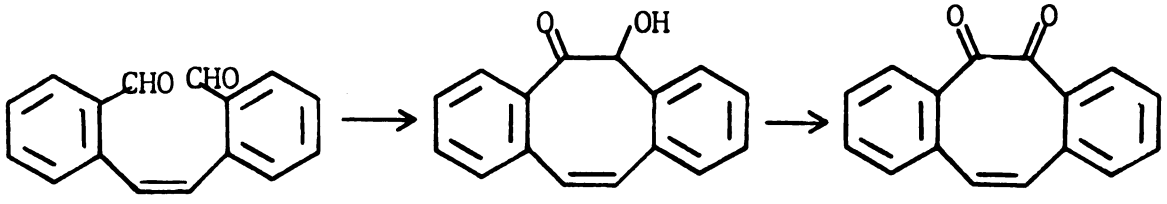
In 1966 McIntyre, Proctor, and Rees[35] attempted the synthesis of benzocycloocta-1,4,6-triene-3,8-dione 27 in order to determine the possibility of electron delocalization in such systems. Bromination of benzocyclooctene-3,8-dione 28 with N-bromosuccinimide (NBS) failed to give the expected 4,7-dibromobenzocyclooctene-3,8-dione 29 which was to be converted to the desired

product by treatment with a suitable base. Instead the isomeric 4,4-dibromobenzocyclooctene-3,8-dione 30 was formed.



28 29 27 30

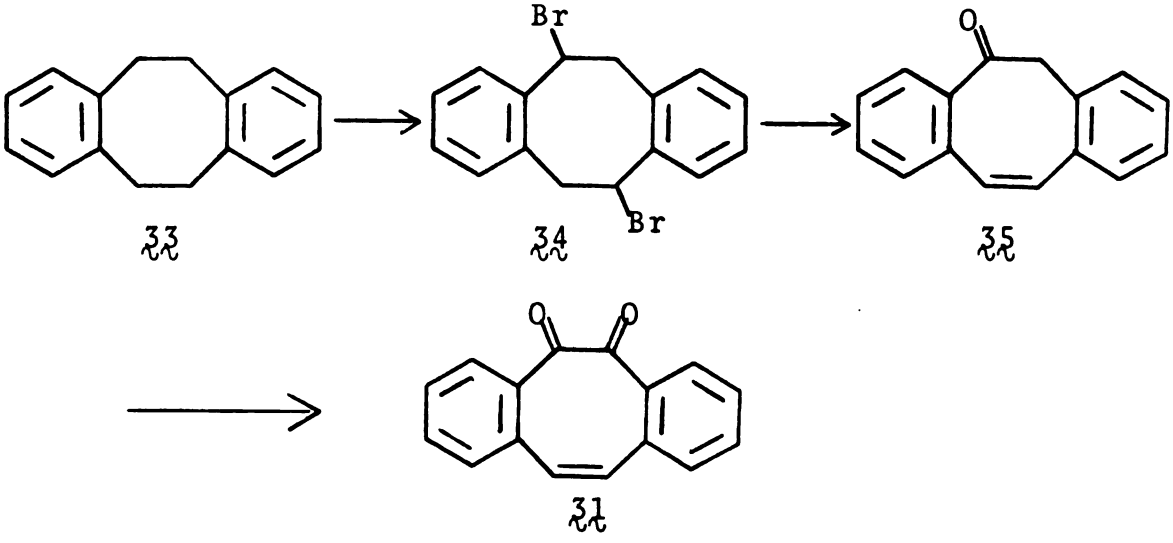
There have been two syntheses of dibenzo[*a*,*e*]cyclooctene-5,6-dione 31. Acyloin condensation of bis aldehyde 32 followed by oxidation afforded Bendall and Neumer[36] the desired 31.



32 31

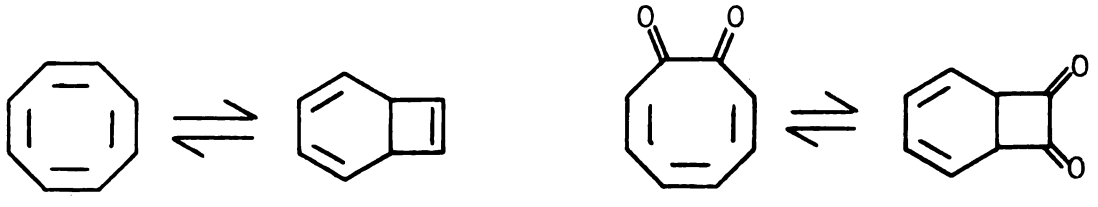
This compound was shown not to be aromatic on the basis of various physical and spectroscopic properties. Such a result is expected due to the annelation effect of the benzene rings. Indeed, dibenzotropones has been shown to to be nonaromatic.

Yates, Lewars, and McCabe[37] synthesized 31 by an alternate route. Bromination of dibenzocycloocta-1,5-diene 33 with N-bromosuccinimide provided 5,11-dibromo-5,6,11,12-tetrahydrodibenzo[*a*,*e*]cyclooctene 34. Treatment of 34 with dimethylsulfoxide and collidine gave dibenzo[*a*,*e*]cyclooctene-5(6H)-one 35 which was subsequently oxidized to 31 by use of selenium dioixde in dioxane.



33 34 35 31

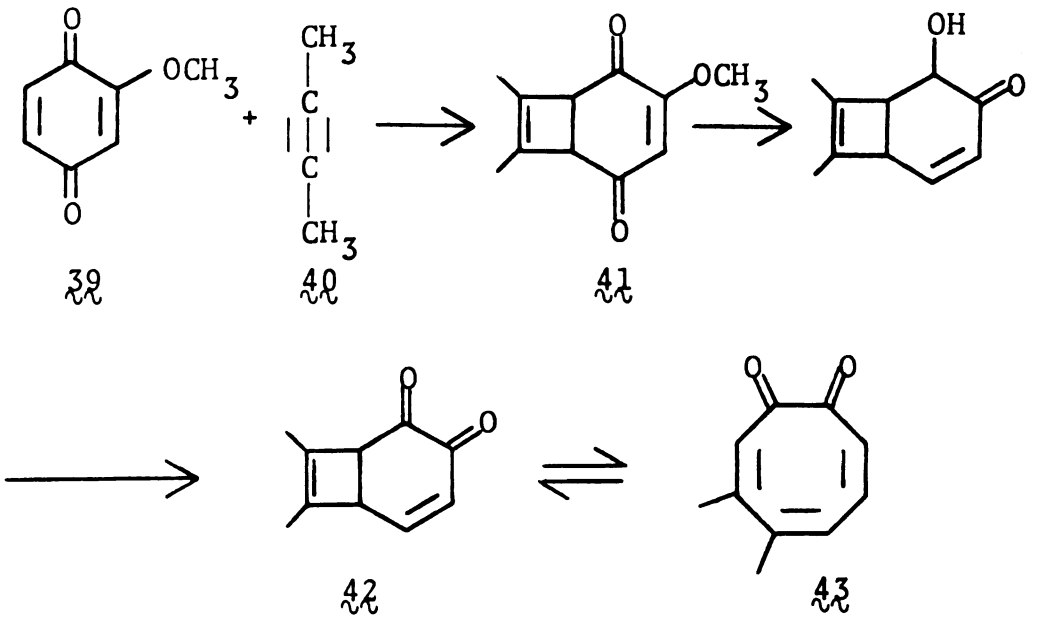
Cyclooctatetraene 36 undergoes a reversible electrocyclic ring closure to bicyclo[4.2.0]octa-2,4,7-triene 37. It is expected that 1,2-cyclooctatrienedione should also be capable of an electrocyclic conversion to bicyclo[4.2.0]octa-2,4-diene-7,8-dione 38.



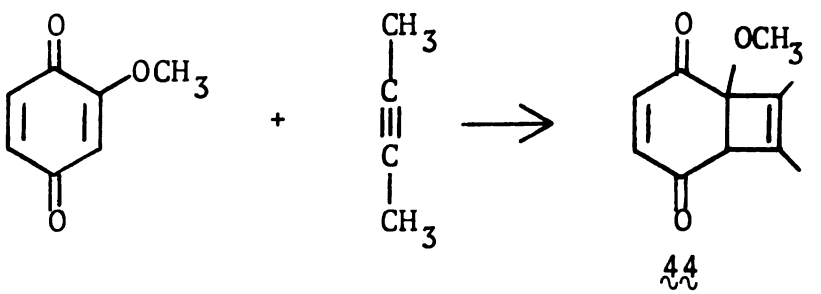
36 37 9 38

There have been two reported synthetic approaches to the bicyclic form of 1,2-cyclooctatrienedione.

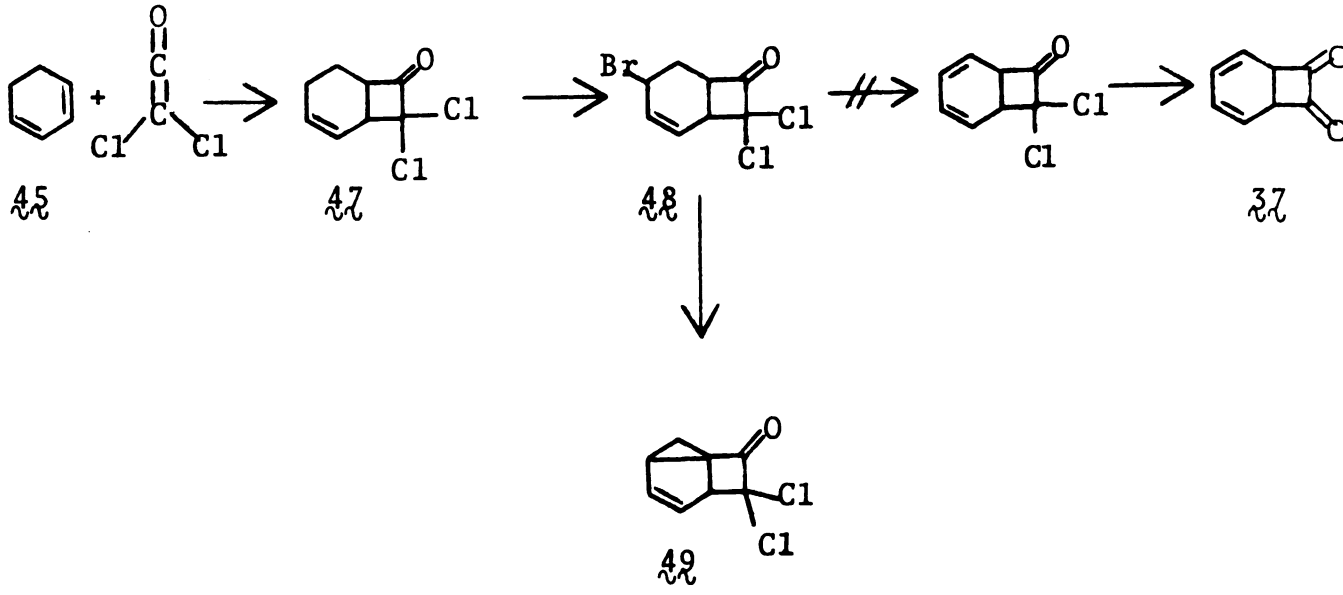
Pappas, Pappas, and Portnoy[38] photolyzed 2-methoxy-1,4-benzoquinone 39 in the presence of dimethylacetylene 40 with the aim of obtaining bicyclic diketone 41. Reduction of 41 followed by hydrolysis and then oxidation was expected to lead to 42 which is a valence tautomer of 4,5-dimethylcyclooctatriene-1,2-dione 43.



These authors, however, were frustrated at the initial step of their synthetic plan as the photolysis product obtained was the isomeric bicyclic diketone 44.



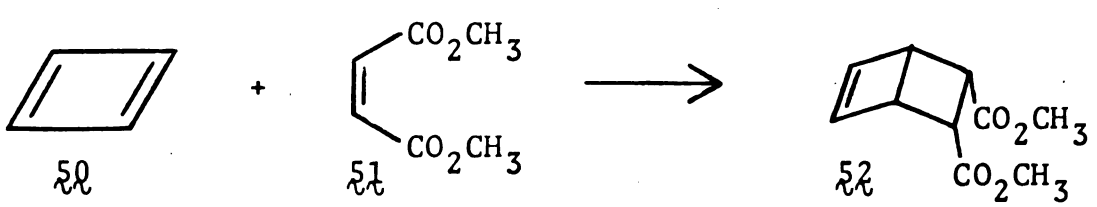
Gund and Carpino[29] developed a clever synthetic scheme for the synthesis of the bicyclic valence tautomer of dione 9. Cycloaddition of 1,3-cyclohexadiene 45 and dichloroketene 46 readily provided bicyclic ketone 47 which was successfully brominated with N-bromosuccinimide. When bicyclic bromoketone 48 was treated with 1,5-diazabicyclo[4.3.0]nona-5-ene (DBN) to effect dehydrohalogenation, the elimination proceeded in an unexpected fashion and gave 3,3-dichlorotricyclo[5.1.0.0]oct-5-ene-2-one 49 as the product.



RESULTS AND DISCUSSION

The primary goal of the research described in this thesis was the synthesis of 1,2-cyclooctatrienedione 9. As mentioned previously 9 should be capable of undergoing an electrocyclic ring closure to bicyclo[4.2.0]-2,4-octadiene-7,8-dione 38. The reverse reaction is also an allowed process and 9 and 38 are therefore expected to exist as an equilibrium mixture. Thus the synthesis of 9 can be approached from either of two directions. A number of different types of synthetic approaches to 9 have been investigated, two of which were directed toward the preparation of bicyclic dione 38.

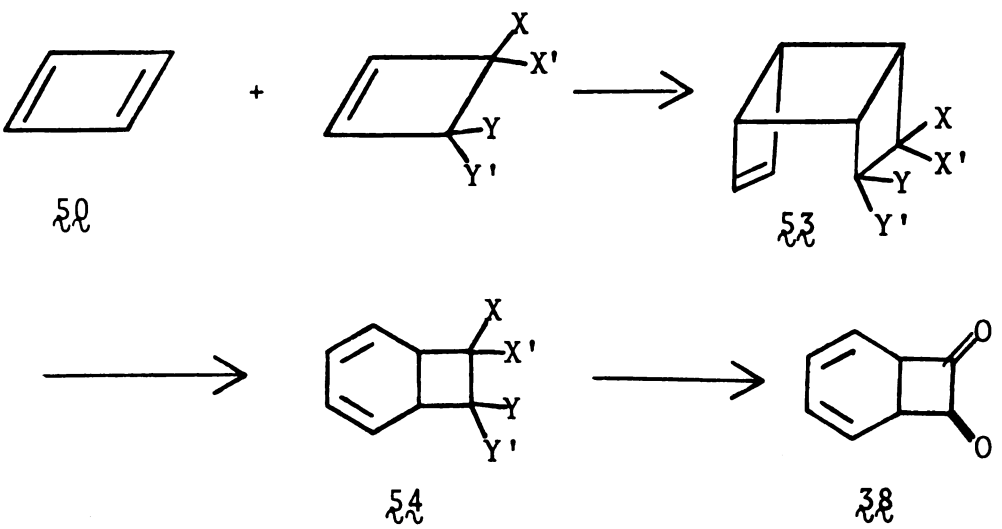
The initial approach to 38 was based on the capability of cyclobutadiene 50 to enter into cycloaddition reactions with olefins. Generation of cyclobutadiene in the presence of dimethylmaleate 51 affords *endo*, *cis*-5,6-dicarbomethoxybicyclo[2.2.0]-2-hexene 52.[39]



50 51 52

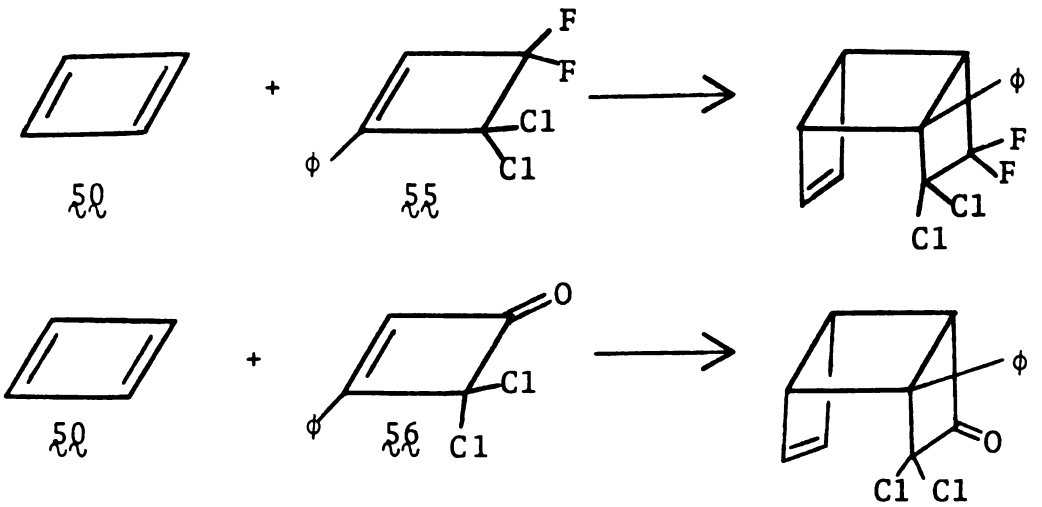
It seemed reasonable therefore that cycloaddition of an appropriately substituted cyclobutene and cyclobutadiene would provide an *endo*-tricyclo[4.2.0.$0^{2,5}$]-3-octene 53 which could then be transformed into 54 by a photochemical orbital symmetry allowed disrotatory[40] cyclobutene ring opening. The cyclobutane functionalities of 54 were then to be converted to the requisite α-diketone moiety of 38 as depicted in Scheme I.

Scheme I



The first cyclobutene investigated was 1,1-difluoro-2,2-dichloro-3-phenylcyclobutene 55[41] whose geminal dihalogen groups were to serve as potential carbonyl groups. Treatment of 55 with cyclobutadiene generated *in situ* from its iron tricarbonyl complex in acetone solution according to the method of Pettit[39,42] afforded only the starting cyclobutene upon workup.

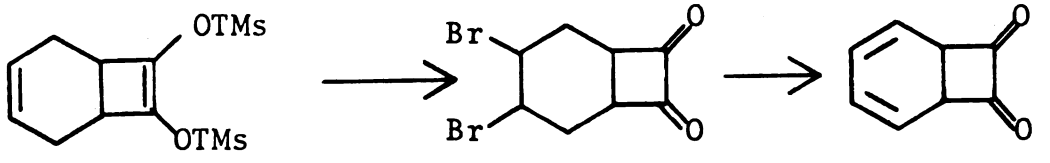
It seemed possible that the electron withdrawing effect of the geminal dihalogen groups was deactivating the double bond of 55 to such an extent that no cycloaddition occurred. In order to partially counter this effect the cycloaddition of cyclobutadiene and 2,2-dichloro-3-phenylcyclobutenone 56[41] was attempted. In this case some reaction had occurred as evidenced by the isolation of a small amount of a brown intractable material in addition to two thirds of the starting material.



Apparently cyclobutadiene dimerization occurs much more rapidly than the cyclobutadiene-cyclobutene 55 cycloaddition reaction. In the case of cyclobutene 56 reaction with cyclobutadiene was somewhat competitive with the dimerization reaction, but the lack of any evidence for the formation of a derivative of 53 suggested that either a cycloaddition was not occurring or that the cycloadduct was unstable under the reaction conditions. Accordingly a different route to 38 was sought.

The second synthetic approach to 38 as outlined in Scheme II utilized 7,8-bis(trimethylsiloxy)bicyclo[4.2.0]-3,7-octadiene 57, a compound which is easily synthesized from *cis*-1,2-dicarbomethoxy-4-cyclohexene 58 by Bloomfield's modified acyloin condensation,[43] as the starting material. The 1,2-bis(trimethylsiloxy)cyclobutene moiety was to serve as a precursor to the cyclobutanedione portion of 34 while the double bond was to be converted to the requisite 1,4-butadiene by a bromination-dehydrobromination sequence.

Scheme II



57 59 38

Wynberg[44] has recently demonstrated that bromine reacts with 1,2-bis(trimethylsiloxy)cycloalkenes by an addition-elimination mechanism to produce 1,2-cycloalkanediones, This method seemed ideal for the conversion of 57 to 38 as the bromination of the double bond could be performed simultaneously to the formation of the dione moiety. There would remain then only the dehydro-

bromination of 3,4-dibromobicyclo[4.2.0]-7,8-octanedione 59. This step suffered potential difficulties as Gund and Carpino[29] have demonstrated that bromoketone 48 undergoes a 1,3-dehydrobromination upon treatment with DBN to form 49. It was expected however that different dehydrobromination conditions would induce 59 to dehydrobrominate in a normal fashion.

Addition of a solution of two equivalents of bromine in chloroform to a solution of 57 in chloroform maintained at 0° followed by removal of the solvent under reduced pressure at room temperature afforded a red-brown oil which yielded a small amount of light yellow crystals upon purification. This same product was obtained in greater yield upon treatment of a solution of 57 in tetrahydrofuran maintained at -78° with a solution of pyridinium hydrobromide perbromide[45] in tetrahydrofuran.

This crystalline material melted at 161-164° with the evolution of a gas which was acidic to moist pH paper and upon cooling a yellow crystalline material of melting point 127-130° was obtained. The ir spectrum of this thermal product exhibited carbonyl absorptions at 1808, 1780, and 1760 cm^{-1} while the nmr spectrum consisted simply of an AA'BB' aromatic multiplet centered at δ 8.0. This data identified the thermal product as benzocyclobutadienoquinone 60[46] and was consistent with the nmr and ir spectra reported[46,47] for an authentic

sample of 60. The formation of 60 from the bromination product of 57 by the thermal elimination of hydrogen bromide suggested that the expected product 53 was not obtained.

The mass spectrum of the bromination product 61 showed parent peaks at m/e 296, 294, and 292 with an intensity ratio of 1:2:1 in accordance with that expected for a molecule containing two bromine atoms. This data together with the elemental analysis indicated a molecular formula of $C_8H_6Br_2O_2$ for 61.

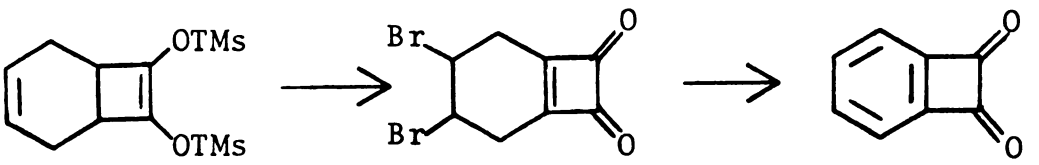
The nmr spectrum of 61 showed a one proton multiplet at δ 4.74 and a two proton multiplet at δ 3.67. The low field nmr multiplet was assigned to a bromomethine hydrogen while the signal at δ 3.67 indicated the presence of allylic hydrogens.

The most distinct features of the ir spectrum of 61 were a cyclobutanone singlet carbonyl absorption at 1795 cm^{-1} and an olefinic absorption at 1615 cm^{-1}. These ir absorption frequencies were very similar to those reported for phenylcyclobutadienoquinone[48].

Dissolution of the bromination product 61 in deuterated dimethylsulfoxide (DMSO), a mild base, resulted in the formation of 60 as evidenced by the nmr spectrum of the solution. Treatment of 61 with DBN[49] resulted in the quantitative formation of benzocyclobutadienoquinone 60. In addition, 61 was not reduced under mild conditions

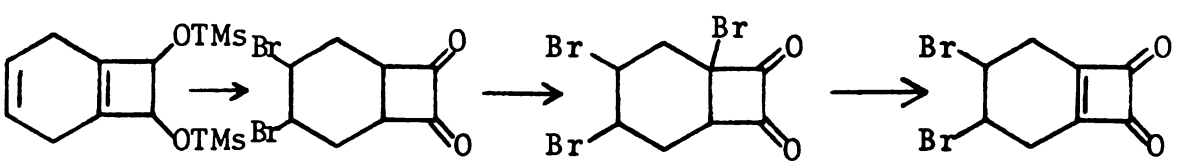
of hydrogenation (10 lb/in^2, Pd/C) and failed to react with bromine paralleling the resistance to such reagents exhibited by phenylcyclobutadienoquinone.

It appeared, therefore, as if 61 contained a cyclobutadienoquinone moiety and accordingly it was concluded that 61 was 3,4-dibromobicyclo[4.2.0]-7,8-octanedione.



57 61 60

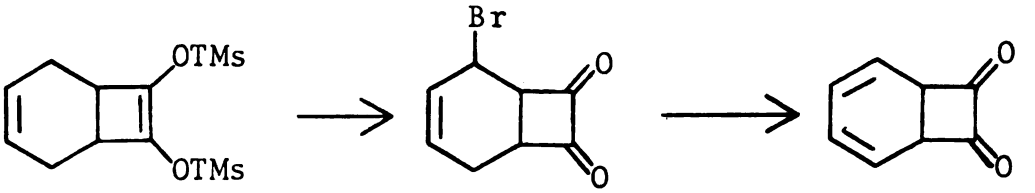
It seems likely that the desired dibromide 59 is an intermediate in the formation of 61. Acid catalyzed bromination of 59 followed by spontaneous loss of hydrogen bromide would lead to the observed product.



57 59 61

An alternative method of bromination of 57 which might have circumvented the problems encountered in the direct bromination procedure was the use of NBS. This reagent is known to generate bromine in low concentrations[50]

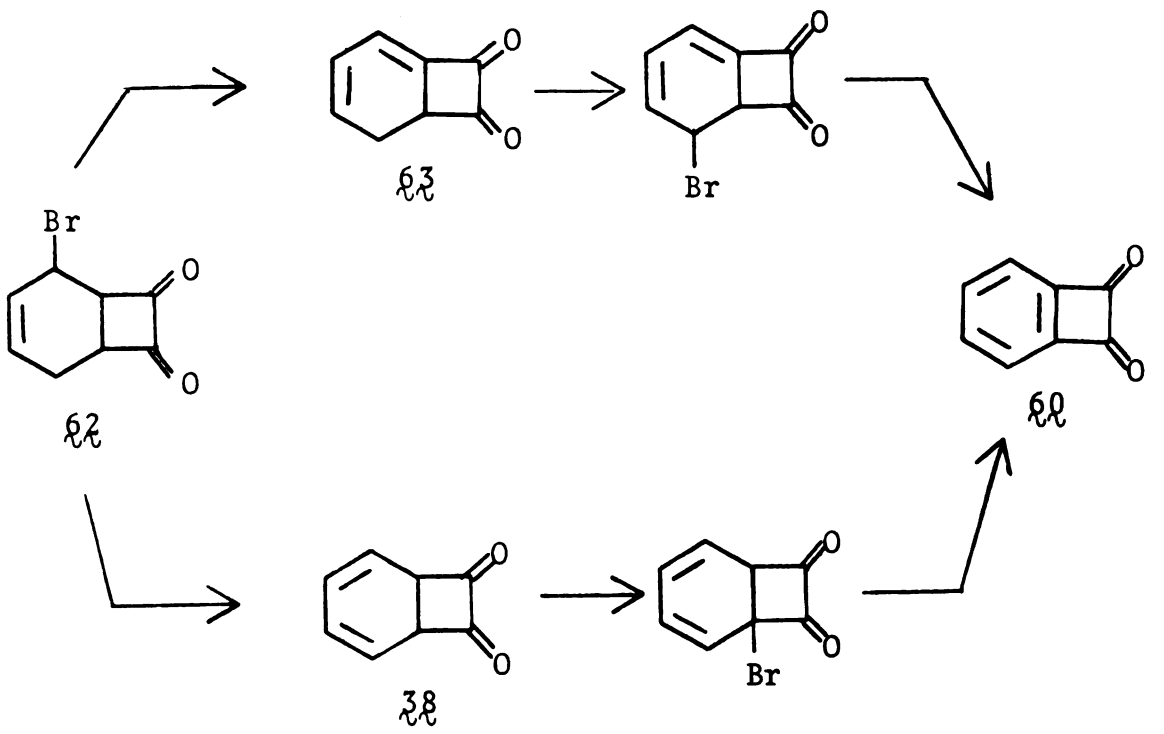
and it was anticipated that the introduction of the bridgehead bromine could possibly be avoided. The expected product from NBS bromination of 57 was bromoketone 62 which could be dehydrobrominated to 38.



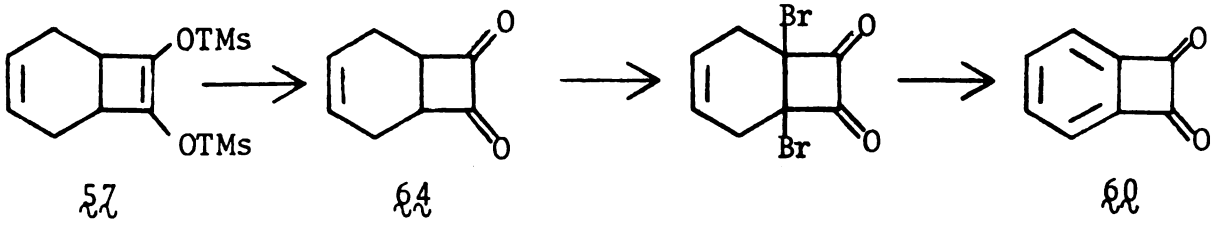
57 62 38

Treatment of 57 with three equivalents of NBS in refluxing carbon tetrachloride under sunlamp irradiation provided a red-brown oil which led to the isolation of a yellow crystalline material, mp 127-130°, upon purification. This product was identified as benzocyclobutadienoquinone 60 by comparison of its nmr and ir spectra to those of an authentic sample.

One can envision a number of plausable mechanisms which account for the formation of 60. Production of 62 followed by loss of hydrogen bromide in either of two ways would result in the formation of 63 or 38. Subsequent bromination and dehydrobromination of these intermediates would provide 60.

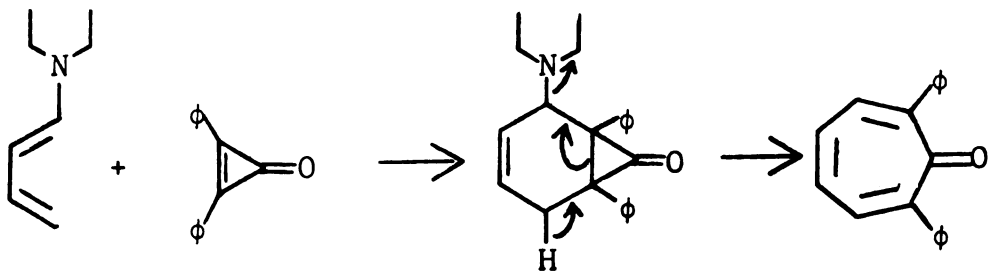


Alternatively intermediate 64 could be brominated at the bridgehead positions followed by dehydrobromination to produce 60.



Diethylamino-1,4-butadiene 65[51] has been shown to undergo Diels-Alder cycloadditions with a number of electrophilic olefins.[51,52] Ciabattoni and Berchtold[53] have shown that this diene reacts with diphenylcyclopropenone 1 to produce 2,7-diphenyltropone 66. The

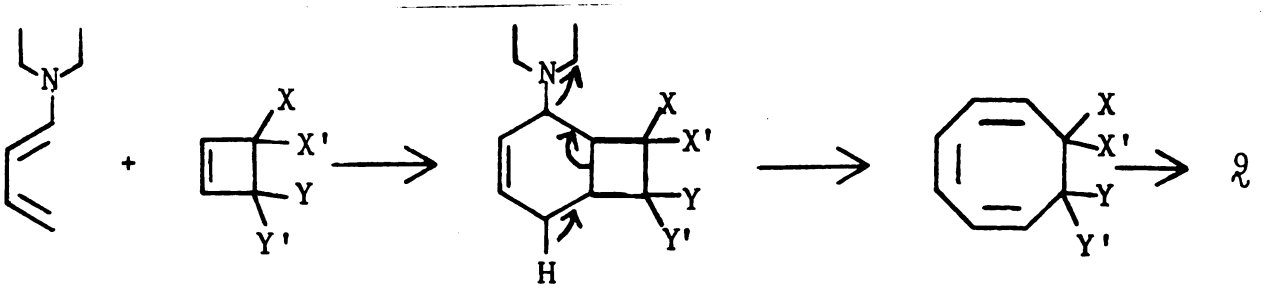
product arises presumably from the Diels-Alder adduct 67 upon elimination of diethylamine.



65 1 67 66

It was expected that cycloaddition of diene 65 with a suitably substituted cyclobutene would produce intermediate 68 which could then eliminate diethylamine with the formation of a potential precursor to dione 9. This synthetic plan is outlined in Scheme III.

Scheme III



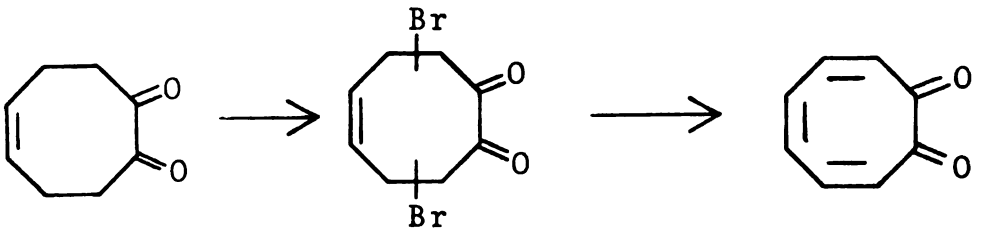
68

With this aim 2,2-dichloro-3-phenylcyclobutenone 56 was treated with 65 in refluxing benzene. The only isolable product from this reaction was the starting cyclobutene 56.

When phenylcyclobutadienoquinone was utilized as the dienophilic component in benzene at room temperature, a red-brown gum was obtained from which an identifiable product could not be isolated. Accordingly this synthetic approach was abandoned.

The synthetic plan directed toward the synthesis of 9 which received the major share of attention was based on the synthesis of the novel diketone 5-cyclooctene-1,2-dione 69[54] and is depicted in Scheme IV.

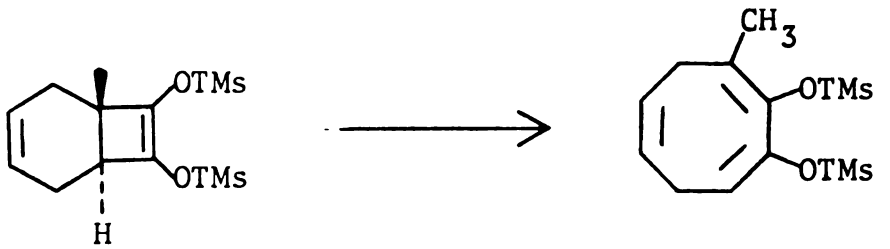
Scheme IV



69 9

Since 69 is functionalized such that theoretically bromine can be introduced into either the allylic or α-carbonyl positions, a bromination-dehydrobromination sequence was envisioned for the introduction of the double bonds.

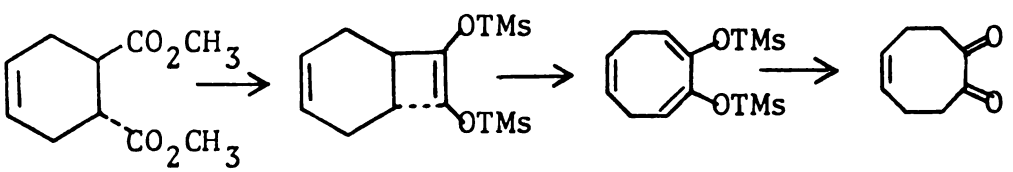
The initial attempt to synthesize 69 was based on the work of Bloomfield[43] who has reported the orbital symmetry allowed thermal conrotatory ring opening of 70 to cyclooctatriene 71.



70 71

It was therefore anticipated that 69 would be available from *trans*-1,2-dicarbomethoxy-4-cyclohexene 72[55] by a modified acyloin condensation followed by thermal ring opening and hydrolysis as shown in Scheme V. Such a sequence has been used by Mori, Nakahara, and Nozaki[56] for the synthesis of large ring α-diketones.

Scheme V



72 73 74 69

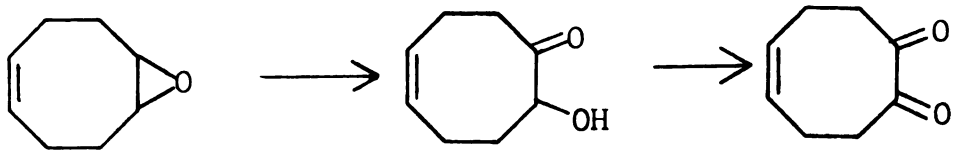
This sequence was successful to a point. *Trans* ester 72 was prepared according to literature methods[57] and successfully cyclized to 73. The thermal ring opening of 73 was initially performed in tetrachloroethylene in order that the reaction could be monitored by nmr spectroscopy. The appearance of additional

olefinic and allylic hydrogen absorptions in the nmr spectrum of a solution of 63 which had been heated at 105° for several hours indicated that the conversion of 73 to 74 was proceeding as expected.

Attempts to force the reaction to completion by heating the sample for longer periods of time were frustrated. The maximum concentration of 74 was attained after nine hours of heating at 105° and thereafter decreased with time. When a sample of the 73-74 equilibrium mixture was hydrolyzed an oily mixture was obtained. The ir spectrum of this mixture showed some evidence of the presence of 69 but the unfavorable equilibrium position rendered this synthetic scheme rather impractical and a new synthesis of 69 was sought.

The boron trifluoride etherate catalyzed conversion of epoxides to acyloins by the use of DMSO[58] proceeds in high yield and has been successfully applied to the oxidation of epoxycyclooctane to 2-hydroxycyclooctanone.[59] It seemed reasonable therefore that the known 5,6-epoxycyclooctene 75[60] could be easily converted to 2-hydroxy-5-cyclooctenone 76 which in turn could be oxidized to diketone 69 as outlined in Scheme VI.

Scheme VI



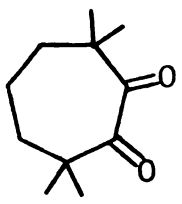
75 76 69

This sequence proved successful as 75 was converted to 76 by DMSO - boron trifluoride etherate in 75% yield. Oxidation of 76 with cupric acetate[61] in acetic acid - water afforded 69 in 51% yield. Attempts to increase the yield of this step by use of ferric chloride,[62] bismuth oxide,[61,63] bismuth acetate,[63] cerium nitrate,[64] and ammonium nitrate-cupric acetate[65] were not successful.

The structure of 69 was confirmed by spectroscopic data. The ir spectrum of 69 exhibits carbonyl absorptions at 1723 and 1708 cm^{-1} with a shoulder at 1693 cm^{-1}. Such multiplet carbonyl absorption is characteristic[66] of α-diketones and arises from coupling of the symmetric and antisymmetric stretching modes of the carbonyl groups. Also present are absorptions at 3530 and 3380 cm^{-1} corresponding, respectively, to the intermolecular and intramolecular hydrogen bonded hydroxyl group of the enol form of 69. These absorptions are weak, however, and 69 exists mainly as a diketone.

Leonard and Mader[67] have studied the ultraviolet spectra of a series of α-diketones and have established that the absorption maximum of these systems undergoes a hypsochromic shift as the geometry of the carbonyl groups changes from a *cis* or *trans* coplanar configuration to a perpendicular configuration.

The intercarbonyl angle of 3,3,7,7-tetramethyl-1,2-cycloheptanedione 77 has been estimated to be 90-110° on the basis of space filling molecular models, while the value for 3,3,8,8-tetramethyl-1,2-cyclooctanedione 78 was approximated to be 100-140°.



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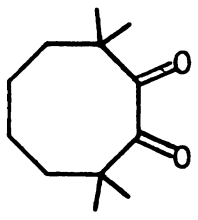
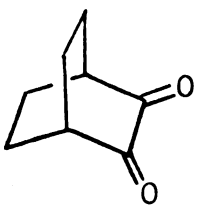


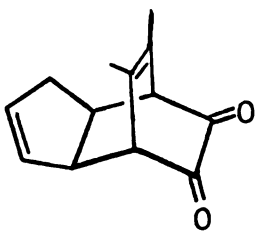
78

Compounds 77 and 78 have ultraviolet absorption maxima of 337 nm and 343 nm respectively in 95% ethanol solution. Using this data the angle between the carbonyl groups of 69 can be estimated. A solution of 69 in 95% ethanol shows an ultraviolet absorption maximum of 335 nm and accordingly its intercarbonyl angle is approximated to be 90-100°.

Birnbaum, Cookson, and Lewin[68] have compared the ultraviolet spectra of diketones 79 and 80.



79



80

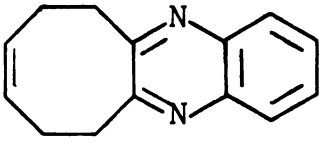
Compound 80 in cyclohexane showed a band at 238 nm (ε 2600) which was absent in the spectrum of 79. This band was interpreted to be a result of an intramolecular charge transfer between the double bond and the diketone moiety of 80.

Dione 69 in cyclohexane exhibits an ultraviolet absorption maximum at 230 nm (ε 99). The spectrum reported for 78 does not include a maximum in the region of 230 nm. This suggests that the 230 nm absorption of 69 may be due to an intramolecular charge transfer effect although a comparison of the extinction coefficients indicates that only a weak interaction is occurring.

The nmr spectrum of 69 consists of an olefinic proton triplet at δ 5.88 and a multiplet at δ 2.53 which corresponds to the α-carbonyl and allylic protons. The multiplet was resolved into two separate multiplets when the spectrum was recorded in the presence of *tris* (dipivalomethano)europium (III).[69]

The mass spectrum of 69 exhibited a parent peak at m/e 138 and prominent peaks at m/e 110 and 82 which arise from the fragments resulting from the loss of one and two molecules of carbon monoxide respectively.

The structure of 69 was further confirmed by the formation of the quinoxaline derivative 81, mp 117-119°, whose spectroscopic properties were in full accord with the assigned structure. In addition, the conversion of 69 to 3,8-di(*p*-methoxybenzilidene)-5-cyclooctene-1,2-dione 82 served to confirm that 69 contained two α-carbonyl methylene groups. The properties of this interesting molecule will be discussed subsequently.



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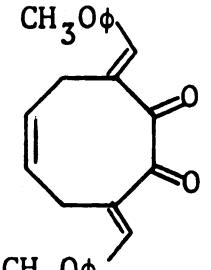
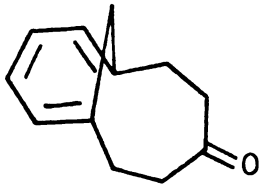


82

The initial attempt to convert 69 to 9 was a simple oxidation by dichlorodicyanoquinone (DDQ). This procedure was used by Vogel to convert ketone 83 to ketone 7.[24]



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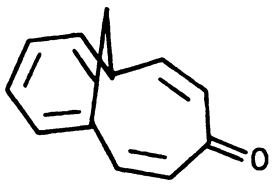
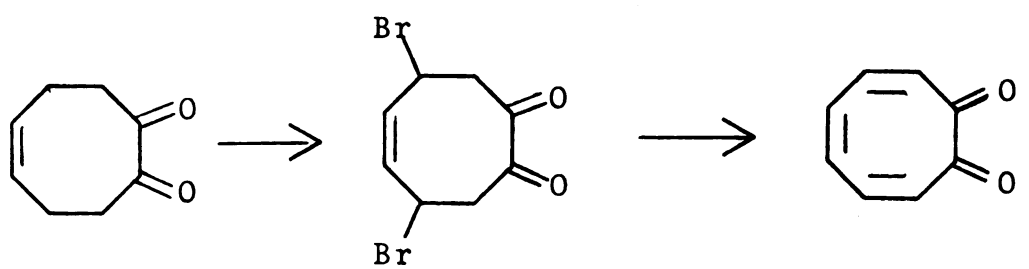


7

As discussed previously, ketone 7 does not exhibit any aromatic properties. The ease of oxidation of 83 is due, apparently, to the formation of a fully conjugated system. It was anticipated that a similar effect would be operative in the oxidation of 69 to 9. Heating a solution of 69 and DDQ in benzene in a sealed tube at 120° for eight hours, however, failed to produce a reaction. The dione 69 was recovered unchanged.

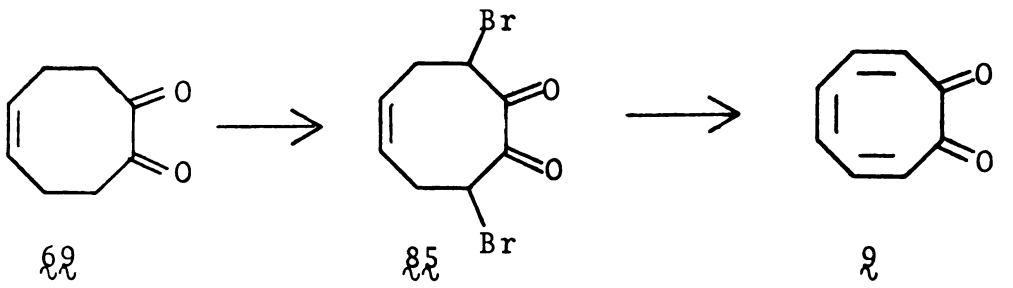
Returning to the synthetic plan outlined in Scheme IV, the bromination of 69 was considered. Allylic bromination of 69 with NBS might be expected to provide dibromodiketone 84 although allylic radical rearrangements[70] would certainly occur and decrease the yield of 84. Dehydrobromination of 84 would then produce 9.



69 84 9

When a solution of 69 and two equivalents of NBS in refluxing carbon tetrachloride containing a catalytic amount of benzoyl peroxide was irradiated with a sunlamp, a black tar was produced. This material failed to provide any identifiable product. An attempt to effect the desired bromination without irradiation or initiator afforded the same intractable material.

The alternative mode of bromination would provide dibromodiketone 85 which was expected to afford 9 upon dehydrobromination.



69 85 9

The initial attempt to synthesize 85 utilized pyrrolidone hydrotribromide (PHT)[71] as the brominating reagent. A solution of 69 and PHT in tetrahydrofuran was stirred at room temperature for twenty hours. Bromination had occurred as evidenced by the precipitation of pyrrolidone hydrobromide from the reaction solution and upon workup several oils were obtained. All of these products showed infrared carbonyl absorptions. The nmr spectra, however, revealed that all of these products were deficient in olefinic proton absorptions due to the bromination of the double bond.

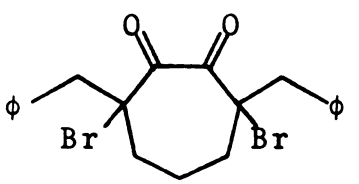
Treatment of 69 with cupric bromide[72] in 1:1 chloroform-ethyl acetate solution at 70° for twelve hours afforded 85 as white crystals, mp 138-141°. The structure proof of 85 was based mainly on spectroscopic evidence.

The elemental analysis and mass spectral parent peaks of m/e 298, 296, and 294 which occurred in a ratio

of 1:2:1 as expected for a dibromide established the correct molecular formula of $C_8H_8Br_2O_2$ for 85.

The position of the infrared carbonyl absorption of α-halogen cycloalkanones has been used as a tool in configurational analysis.[73] When an α-bromine atom occupies an equatorial position of a cycloalkanone and is approximately coplanar with the carbonyl group, the infrared carbonyl absorption is shifted 15-22 cm^{-1} to higher frequency relative to that of the unsubstituted cycloalkanone. There is no change in position when the bromine is in an axial position.

Leonard and Robinson[74] have utilized such an infrared analysis to assign the stereochemistry to the isomeric 3,7-dibromo-3,7-dibenzyl-1,2-cycloheptanediones 86 and 87. The *cis* isomer 86 has one bromine atom in an



86 - *cis*

87 - *trans*

equatorial position and one in an axial position. Accordingly its ir spectrum showed carbonyl absorptions of 1715 and 1698 cm^{-1} corresponding to the carbonyl groups adjacent to the equatorial and axial bromine atoms

respectively. The *trans* isomer 87 is symmetrical with both bromine atoms in equatorial positions and shows the expected single infrared carbonyl absorption at 1720 cm^{-1}.

The stereochemistry assigned to dibromide 85 is *trans*. Molecular models indicate that the *trans* diequatorial configuration should be the most stable. This assignment is confirmed by the infrared carbonyl absorptions of 85 at 1740 and 1727 cm^{-1} which are, respectively, 17 and 19 cm^{-1} higher than the corresponding peaks of diketone 69 at 1723 and 1708 cm^{-1}.

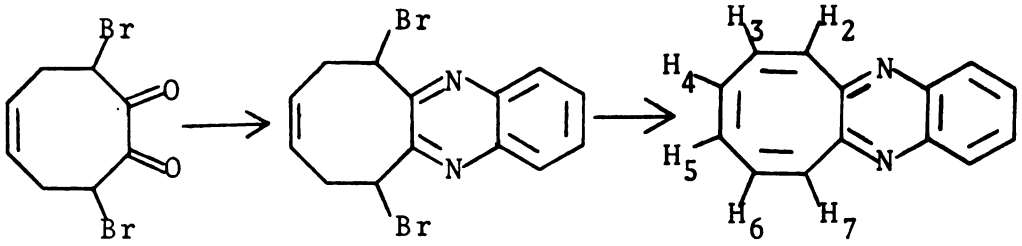
The effect of α-carbonyl halogen atoms on the uv spectrum is opposite that encountered in the infrared spectrum. Axial bromine atoms cause a bathochromic shift of the uv maximum of the carbonyl group of α-bromo cycloalkanones relative to the corresponding unsubstituted cycloalkanones. An equatorial bromine atom, on the other hand, causes little or no change in the uv absorption position of the carbonyl group. The magnitude of the effect of an axial bromine atom is approximately 28 nm with an attendant increase of the extinction coefficient by a factor of 100.[73e,73f,75]

Dibromodiketone 85 does not seem to be amenable to configurational analysis by uv spectroscopy. The positions of the uv absorptions of 77 are essentially unchanged relative to those of 69 although the extinction coefficients are markedly greater.

The assigned *trans* diequatorial configuration of **85** is further substantiated by its nmr spectrum. It has been determined that α-bromo carbonyl methine protons which have axial configurations are deshielded and therefore have chemical shifts further downfield than their equatorial counter parts.[76] For example, the methine proton of *cis*-4-phenyl-2-bromocyclohexanone occupies an axial position and gives rise to an nmr signal at δ 4.87. The methine proton of the corresponding *trans* isomer is equatorial and exhibits an nmr signal at δ 4.38.

Thus the single methine proton nmr absorption of **85** at δ 5.15 is consistent with a *trans* diequatorial configuration. This nmr absorption consists of a four line pattern which was expected for an X portion of an ABX system. Further features of the nmr spectrum of **85** include an olefinic multiplet at δ 6.05 and a multiplet at δ 2.90 representing the AB part of the ABX system. These assignments were verified by decoupling experiments.

Chemical evidence confirming the structure of **85** was obtained by the formation of the quinoxaline derivative **88**. Compound **88** was also of interest as it served as the precursor to the quinoxaline derivative of the target compound 1,2-cyclooctatrienedione.



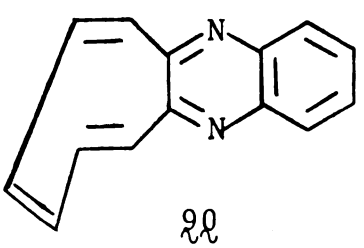
85 88 89

Treatment of 88 with DBN in DMSO led to the formation of 89, the quinoxaline derivative of 9. The structure of 89 was confirmed by its spectroscopic properties.

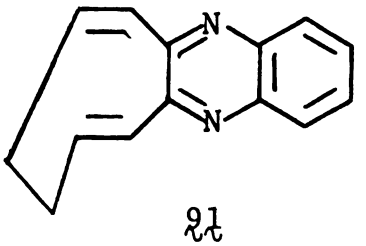
The mass spectral parent peak of m/e 206 together with the elemental analysis established the correct molecular formula of $C_{14}H_{10}N_2$ for 89.

The nmr spectrum of 89 shows an aromatic AA'BB' pattern at δ 7.92 corresponding to the hydrogens of the benzene ring. The α-imino hydrogens, H_2 and H_7, appear as a doublet of an AB quartet, J = 11.5 Hz, at δ 6.88. The other half of the AB quartet at δ 6.43 arises from H_3 and H_6 and appears as a doublet of doublets, J = 1.5 Hz, due to the coupling to hydrogens H_4 and H_5 which appear as a doublet at δ 6.15.

The coupling constant for the coupling of H_3 and H_4 (H_5 and H_6) is expected to be 9-13 Hz[77] if a planar triene moiety is present in 89. The observed value of 1.5 Hz demonstrates that only a weak interaction is occurring and therefore it was concluded that 89 exists in a nonplanar conformation such as 90.



90



91

This idea is further substantiated by the electronic spectuum of 89 which exhibits an absorption maximum at 354 nm. The quinoxaline derivative of dione 77 shows an absorption maximum at 323 nm.[67] On the basis of this value the absorption maximum of 91 is predicted to be 353 nm. Since the uv spectrum of 89 agrees almost exactly with that expected for 91, it must be concluded that the C_4-C_5 double bond does not possess a geometry which allows for π-orbital interaction as expected for conformation 90.

It is expected that 89 should be more planar than 9 because the imino carbon atoms are maintained in a fully unsaturated six-membered ring. The carbonyl groups of 9, on the other hand, are expected to repel each other due to electrostatic interaction and thereby cause a deviation from a planar geometry. The nonplanity of 89 clearly suggests that 9 will not be a planar molecule and therefore any aromatic character which it might possess will be obscured.

The conversion of 85 to 9 appeared to be a simple task as a variety of dehydrohalogenation reagents are known. This, however, was not the case. Dibromide 85 reacted easily with a number of different dehydro-

halogenating reagents under a variety of conditions but the products of the reaction were generally intractable materials. Table I summarizes the unsuccessful attempts to dehydrobrominate 85.

It was clear from these experiments that the dehydrohalogenation was complicated by side reactions and possibly that the desired product 9, if formed, was undergoing further transformations under the reaction conditions. In several experiments the starting dibromide 85 was the only product which could be isolated although the quantity obtained was usually less than the original amount. Another interesting observation was the fact that material balance was not maintained in all cases indicating that some of the product material was water soluble. This was verified by the colored aqueous washes in the workups of the various reactions. Attempts to isolate products from the aqueous phases, however, were fruitless.

Particularly interesting is the fact that the ir spectra of the oils obtained in experiments 1 and 13 were nearly identical. The carbonyl infrared absorption at 1800 cm^{-1} suggested that the product might be the bicyclic tautomer 38. The nmr spectrum of these oils did not bear out this contention and suggested that a mixture of materials was present. The small amount of material obtained precluded a further purification and

Table I. Summary of attempts to dehydrobrominate 85.

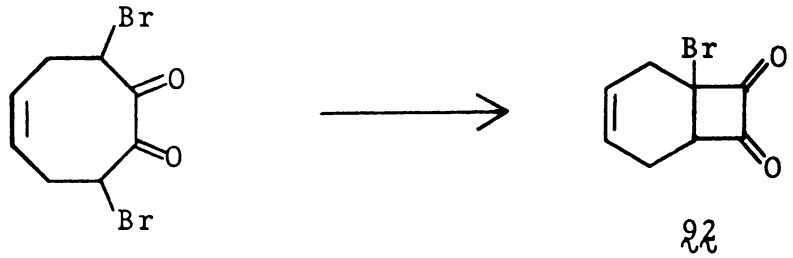
Exp.	Dehydrohalogenating reagent	Conditions	Results*	Ref.
1	DBU	DMSO, 25°, 12 hr	intractable material and yellow-red oil with ir carbonyl absorption at 1800 cm^{-1}	78
2	DBU	$CHCl_3$, 25°, 4 hr	intractable material	78
3	Et_3N	C_6H_6, 25°, 4 hr	brown oil which yielded 50% s.m.	79
4	LiCl	DMF, 140°, 1 hr	brown oil exhibiting broad ir carbonyl absorptions	80
5	$NaHCO_3$	DMSO, 100°, 4 hr	brown oil consisting of four components none of which showed ir carbonyl absorptions	81
6	DBU	Et_2O, 0°, 2 hr	50% s.m. recovered	78
7	$AgNO_3$	EtOH, 60°, 1 hr	60% s.m. recovered	82
8	HMPA	130°, 1/2 hr	yellow oil consisting of three components; ir carbonyl absorptions at 1775 and 1650 cm^{-1}	83

Table I. (Continued)

Exp.	Dehydrohalogenating reagent	Conditions	Result*	Ref.
9	$Et_4N^+Cl^-$	CH_3CN, 82°, 18 hr	60% s.m. recovered	84
10	DBN	CH_2Cl_2, 0°, 2 hr	brown oil	49
11	Proton Sponge	DMSO, 60°, 4 hr	s.m. recovered	85
12	LiCl	HMPA, 54°, 10 hr	red-brown oil	86
13	LiBr, Li_2CO_3	HMPA, 55°, 4 hr	yellow oil exhibiting ir carbonyl absorption at 1800 cm^{-1}	86
14	LiCl	DMF, 85°, 21 hr	33% s.m. recovered	80
15	$CaCO_3$	DMF, 80°, 3 hr	s.m. recovered	87
16	DBN	THF, -76°, 1 hr	s.m. recovered	49
17	DBN	THF, -33°, 1 hr	s.m. recovered	49
18	DBU	2:1 DMSO-THF, 0°, 1/2 hr	s.m. and brown gum	78
19	DBU/TCNE	CH_2Cl_2, 0°, 1 hr	intractable material	78

*s.m. = starting material

structure elucidation. One can visualize a Favorski type elimination product 92 which would explain the presence of a cyclobutanone moiety. Compound 92 could



92

then undergo further reaction to product a number of additional products.

Experiment 19 describes an attempt to trap any dehydrohalogenation products of 85 by the use of tetracyanoethylene as a dienophile. Unfortunately only intractable material was obtained from this experiment.

Hexamethylphosphoramide (HMPA) has been used successfully in the past to effect dehydrohalogenation.[83] The yellow oil obtained in experiment 8 was interesting as it exhibited a carbonyl ir absorption at 1650 cm^{-1} indicating the presence of an α,β-unsaturated carbonyl group. The small quantities of product which were being obtained prompted a reduction in the temperature at which the reaction was being performed. When a solution of 85 in HMPA was heated to 75° for four hours only one product, in addition to unreacted starting material, was obtained.

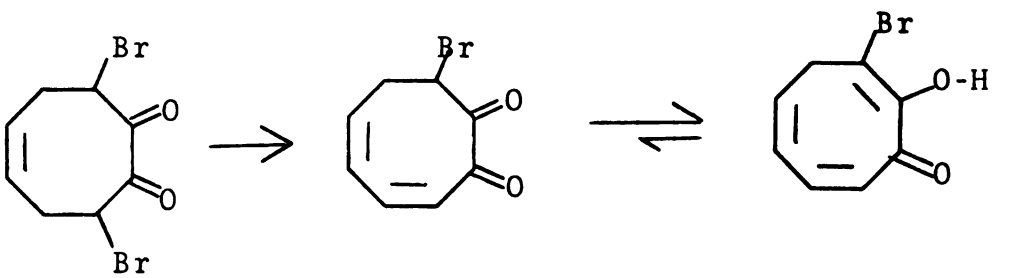
This crystalline compound, mp 101-103°, was shown to have an elemental composition of $C_8H_7BrO_2$ on the basis of its mass spectral parent peaks of m/e 216 and 214 whose intensity ratio was 1:1 and the elemental analysis.

The ir spectrum of this material showed carbonyl and olefinic absorptions at 1662, 1622, and 1600 cm^{-1} respectively as well a hydroxylic absorption at 3365 cm^{-1} indicating the presence of an intramolecular hydrogen bonded hydroxyl group. One sample of this material showed, in addition to these absorptions, a carbonyl absorption at 1714 cm^{-1} in conjunction with a reduced hydroxylic absorption. This suggested that an enol-keto tautomerization was occurring at a position substituted with an equatorial bromine atom. The peak at 1662 cm^{-1} is characteristic of α,β-unsaturated ketones and, in fact, is identical to that reported for 2,4-cycloocta-dienone.[88]

The nmr spectrum of this material in deuterated chloroform showed a one proton singlet corresponding to an intramolecularly hydrogen bonded hydroxylic hydrogen at δ 7.86, a three proton olefinic hydrogen multiplet at δ 6.64, a one proton olefinic hydrogen at δ 5.73, and a broad two proton allylic hydrogen singlet at δ 3.16. When the nmr spectrum was taken on the sample in deuterated DMSO the hydroxyl proton was observed as a broad singlet at δ 10.5-8.5. In addition, the broad

singlet at δ 3.16 was resolved into a sharp two proton doublet, J = 8.0 Hz. The magnitude of this coupling constant is characteristic of the coupling observed between allylic hydrogens and the adjacent olefinic hydrogen.

On the basis of this spectroscopic data it was concluded that this material was 3-bromo-2-hydroxy-2,5,7-cyclooctatrienone 93. This novel ketone results from a single dehydrobromination of 85 to form 3-bromo-5,7-cyclooctadiene-1,2-dione 94 followed by enolization.



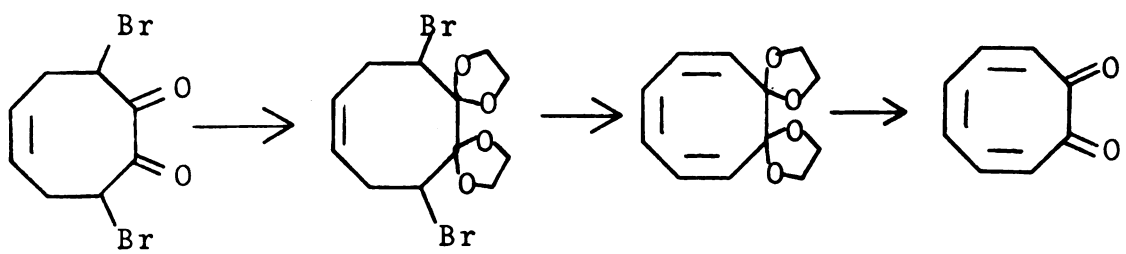
85 94 93

The uv spectrum of 93 further confirms its structural assignment. There are two chromophores in 93. The absorption position of the 1-hydroxy-2-bromoenone chromophore is calculated to be 303 nm by use of the Woodward rules.[89] The value calculated for the dienone chromophore is 314 nm and therefore the absorption maximum of longest wavelength of 93 should occur at 314 nm. The experimental value of 297 nm is in close agreement with the lower wavelength maximum. The experimental maximum is quite broad, however, and contains an inflection point at 315 nm suggesting that

the dienone chromophore is buried beneath the substituted enone chromophore. Compound 93 was also obtained by dehydrohalogenation of 85 with lithium bromide and lithium carbonate in DMF[90] at 105° for one hour although isolation was complicated by other products and the yield was lower.

The lack of success in the direct dehydrobromination of 85 prompted some modification in the synthetic approach to 9 as outlined in Scheme VII. It was believed that ketalization of the carbonyl groups of 85 would allow the dehydrobromination to be effected without the attendant side reactions which the product was apparently undergoing. The diketone moiety would be protected from base induced reactions and could be regenerated from 96 under acidic conditions to which the product 9 would be stable.

Scheme VII



85 95 96 9

Several attempts to prepare bis ketal 95 were unsuccessful as summarized in Table II.

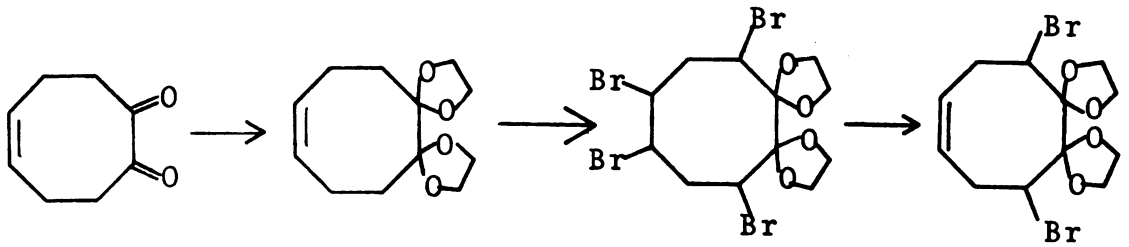
Table II. Synthetic approaches to bis ketal 95.

Exp.	Ketalization reagents	Conditions	Result	Ref.
1	Ethylene glycol, tosic acid	C_6H_6, 81°, 12 hr	s.m.	--
2	Ethylene glycol, tosic acid	C_7H_8, 111°, 22 hr	s.m.	91
3	Ethylene glycol, boron trifluoride etherate	CH_2Cl_2, 25°, 24 hr	s.m.	92
4	Ethylene glycol, oxalic acid	C_6H_6, 81°,	s.m.	94
5	Triethylortho-formate, ammonium nitrate	C_2H_6O, 79°, 20 hr	s.m.	93

The complete lack of reactivity of 77 under the various ketalization conditions must be attributed to the steric interaction which would result from the introduction of the ketal groups. The bromine atoms are not sterically hindering the carbonyl groups from reacting as evidenced by the formation of the quinoxaline derivative 89. The ketalization process would begin with the formation of the ethylene glycol hemiketal of 85. Apparently the steric hindrance in this initially formed product causes the equilibrium position of the ketalization reaction to lie heavily in favor of 85 and thereby prevents the formation of 95.

It was anticipated that bis ketal 95 could be synthesized by bromination of the bis ketal 97 derived from diketone 69. Pyridinium hydrobromide perbromide has been shown to effect bromination α to ketal groups.[95] This reagent suffered from the disadvantage that it would also brominate the double bond of 97 but it was assumed that debromination could be effected at a latter stage to reintroduce the olefinic moiety. This sequence is shown in Scheme VIII.

Scheme VIII



69 97 95

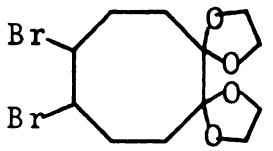
Bis ketal 97 was synthesized in 60% yield from 63 by the use of tosic acid and ethylene glycol in refluxing benzene. The spectroscopic properties of 97 were in full accord with the assigned structure.[54]

Treatment of 97 with three equivalents of pyridinium hydrobromide tribromide in THF provided, upon workup, a light yellow oil. When one equivalent of pyridinium hydrobromide tribromide was used this same yellow oil was obtained. Upon cooling this oil crystallized and

upon further purification white crystals, mp 77-79°, were obtained.

The elemental analysis of this material established the molecular formula of $C_{12}H_{18}Br_2O_4$ which is that expected for simple bromine addition to the double bond.

The nmr spectrum of this material however exhibited four multiplets at δ 4.8-4.4, δ 4.4-3.6, δ 3.6-3.3, and δ 2.6-1.7 which integrated for one, seven, two, and eight protons respectively. This data is not consistent with that expected for the bromine adduct 98 but did seem to fit the transannular adducts 99 or 100.



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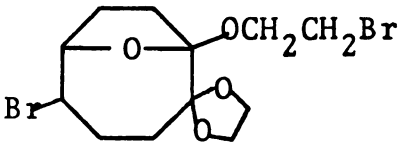

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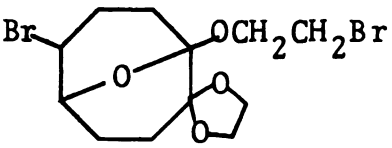
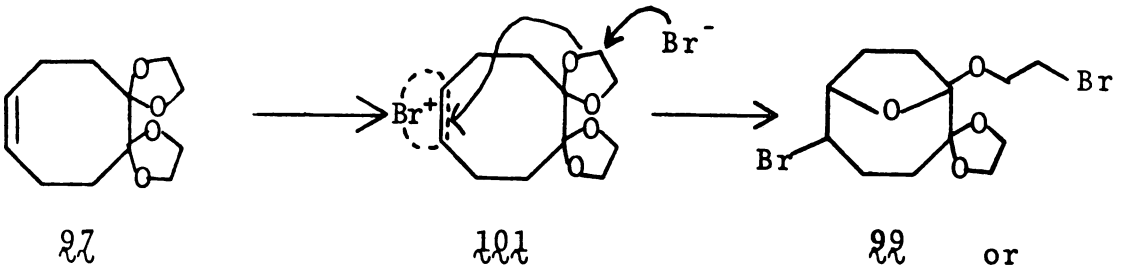


100

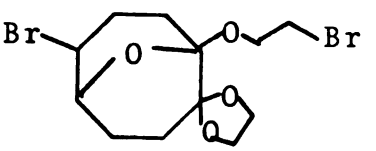
The eight proton multiplet was assigned to the eight-membered ring aliphatic hydrogens. The seven proton multiplet corresponded to the ketal hydrogens, the methylene hydrogens adjacent to the oxygen of the bromoethylether moiety, and the bromomethine hydrogen. The two proton multiplet was assigned to the methylene hydrogens adjacent to the bromine of the bromoethylether while the remaining signal was seen to arise from the ether bridge methine hydrogen.

During the course of this work it was learned that Yates[96] had performed the same experiment and had also assigned structure 99 or 100 to this product.

Mechanistically 99 or 100 can be seen to result from the initially formed bromonium ion intermediate 101 by attack of the ketal by a bromide ion with concommitant formation of the ether bridge.



97 101 99 or



100

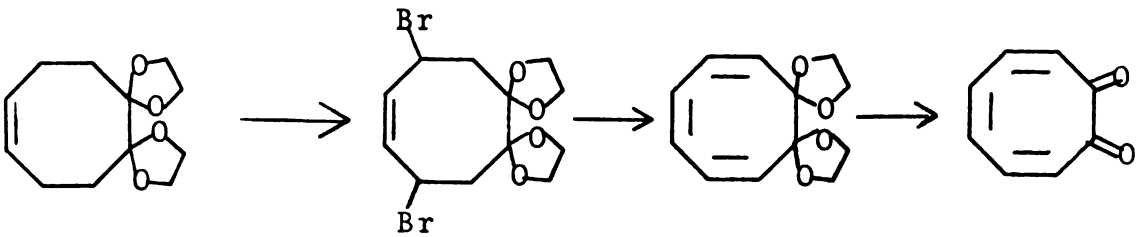
Two other brominating reagents which allow for bromination α to carbonyl groups in the presence of a double bond are cupric bromide[72] and pyrrolidone hydrotribromide.[71]

An attempt to form 95 by bromination of 97 with PHT in tetrahydrofuran solution failed to produce any identifiable products.

The use of cupric bromide as the brominating reagent transformed 97 into a brown oil whose nmr showed a very low ratio of olefinic protons. In addition, the hydrogen bromide generated during the course of the reaction caused a partial cleavage of the ketal moieties as evidenced by the carbonyl absorption observed in the infrared spectrum of this material.

Another approach to 9 from 97 involved a double allylic bromination of 97 followed by dehydrohalogenation and hydrolysis as outlined in Scheme IX.

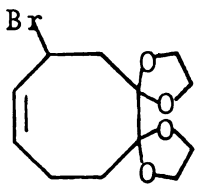
Scheme IX



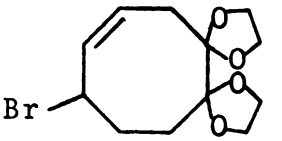
97 96 9

The reaction of ketal 97 and NBS proved to be a classic example of nature's control over man. When 97 was treated with two equivalents of NBS in refluxing carbon tetrachloride in the presence of benzoyl peroxide under sunlamp irradiation a yellow oil was obtained. This material had spectral data which was identical to that of 99 or 100.

Treatment of 97 with one equivalent of NBS under the same conditions produced a white crystalline material, mp 95-100°, whose nmr spectrum was consistent with either compound 102 or 103. The ir spectrum of this



102

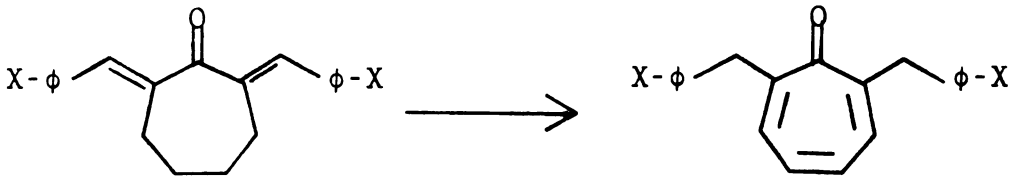


103

product lacked a carbonyl absorption thereby confirming the intactness of the ketal moieties. The mass spectrum of this material, however, exhibited a parent peak at m/e 198 indicating that 102 or 103 was not obtained.

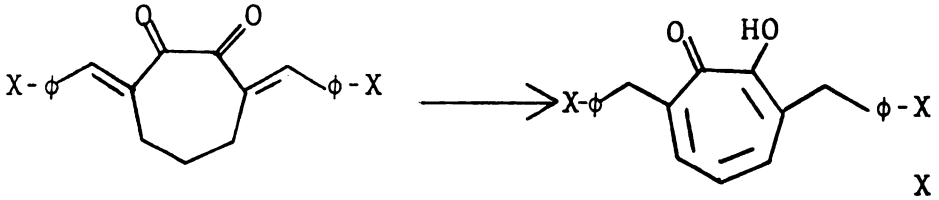
As this material melted over a range, an attempt to sublime it was made. This resulted in the formation of oily crystals. The bromination was then repeated, once but the third and subsequent ten attempts failed, producing only an oily mixture whose composition appeared to be variable. As the reaction could not be repeated the identification of this material was not completed.

Substituted tropones 104 and tropolones 105 have been synthesized by the palladium catalyzed dehydrogenation - rearrangement of 2,7-di(benzilidene)cycloheptanones 106[97] and 3,7-di(benzilidene)-1,2-cycloheptanediones 107[98] respectively.



106 104

X = H
p-CH_3
p-$CH(CH_3)_2$
p-OCH_3
p-$N(CH_3)_2$

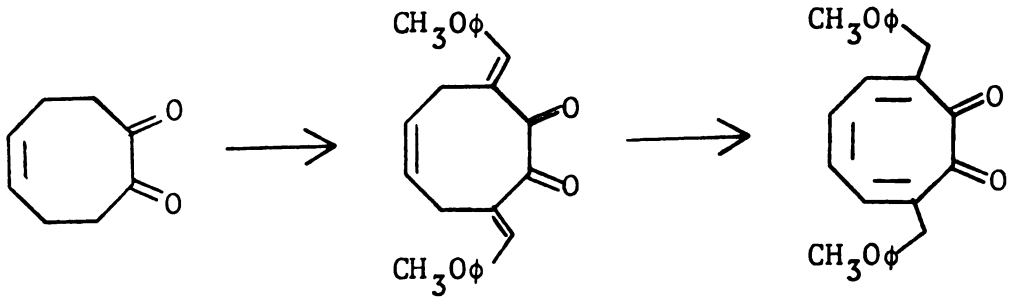


107 105

X = H
p-CH_3
p-OCH_3
p-Cl
p-NO_2

As previously discussed, benzilidene derivative 82 is available from diketone 69. By analogy to the above tropone synthesis it was expected that 82 could be isomerized with palladium to 3,8-di(p-methoxybenzyl)-1,2-cyclooctatrienedione 108 as illustrated in Scheme X.

Scheme X



69 82 108

p-Methoxybenzaldehyde was selected as the condensating agent for the conversion of 69 to 82 because its aromatic hydrogens would appear as a well defined AB quartet in the nmr spectrum and thereby be easily distinguished from any aromatic absorptions which might arise from the parent ring of 108.

The piperidine catalyzed condensation of 63 and *p*-methoxybenzaldehyde proceeded readily with the production of beautiful yellow crystals, mp 162.5-165°, of 82 in 39% yield. The structural assignment of 82 was confirmed by spectroscopic data. The molecular formula of $C_{24}H_{22}O_4$ was established by elemental analysis and the mass spectral parent peak at m/e 374. The ir spectrum of 82 showed a conjugated carbonyl absorption at 1675 cm^{-1}.

The most interesting aspect of the nmr spectrum of 82 was the position of the absorption of the olefinic benzilidene hydrogens which appears as a singlet at δ 7.9. The ring olefinic protons show resonance at δ 6.25. The difference between these two absorption positions is due to the benzilidene olefinic hydrogen being in the deshielding region of the carbonyl group.[99] This serves to confirm that the phenyl groups are *trans* to the diketone moiety in agreement with the stereochemistry expected on the basis of a consideration of the mechanistic aspects of the condensation reaction.[100]

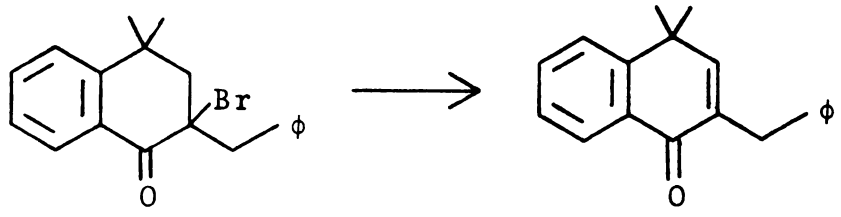
The isomerization of 82 to 108 was conducted in refluxing triethylene glycol with 10% palladium on charcoal as the catalyst. The resulting brown oil consisted of six components for which a chromatographic separation did not seem feasable. The spectrum of the crude mixture contained a hydroxylic absorption at 3500 cm^{-1} suggesting the presence of an alcohol as one of the components of the mixture. Also present was a broad carbonyl absorption from 1685 to 1725 cm^{-1}.

The nmr spectrum of the crude mixture did not exhibit the expected AB aromatic quartet but rather an adulterated triplet aromatic absorption. The integration ratio of aromatic to methoxy protons, however, remained 4:3. There was no olefinic proton absorption present. This indicates that the desired 108 was not present in the crude reaction mixture.

Compound 82 was useful for other purposes however. Lithium in ammonia[101] reduction of 82 provided 3,8-di(*p*-methoxybenzyl)-5-cyclooctene-1,2-dione 109 in 85% yield. The structure of 109 was in full accord with its spectroscopic properties and elemental analysis.

It was expected that 109 could be brominated at the α-carbonyl positions to form 110 as the 3,7-dibromo-3,7-dibenzyl-1,2-cycloheptanediones 86 and 87 are known. Dehydrobromination of 110 was to then be

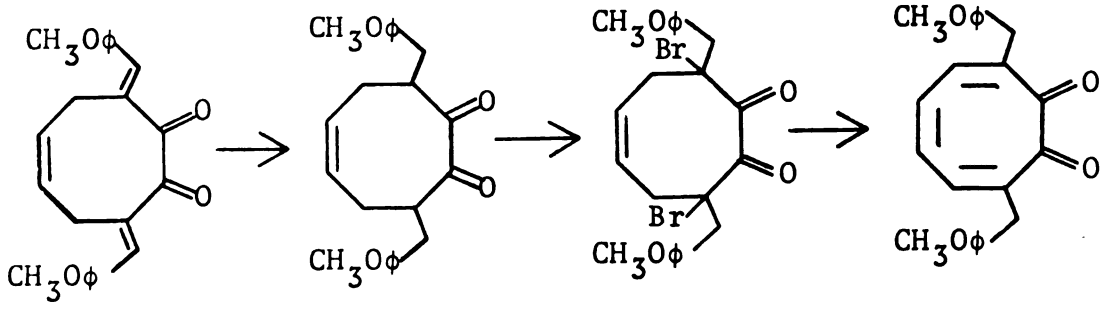
effected by the use of tetraethylammonium chloride[84] a reagent which has been shown to dehydrobrominate 2-benzyl-2-bromoketone 111 exclusively to the corresponding endocyclic α,β-unsaturated ketone 112.



111 112

This synthetic sequence is shown in Scheme XI.

Scheme XI



82 109 110 108

Attempts to brominate 109 with cupric bromide or pyrrolidone hydrotribromide resulted only in the recovery of starting material.

A light yellow oil was obtained upon treatment of 109 with pyridinium hydrobromide tribromide in acetic acid solution. This oil showed an ir carbonyl absorption

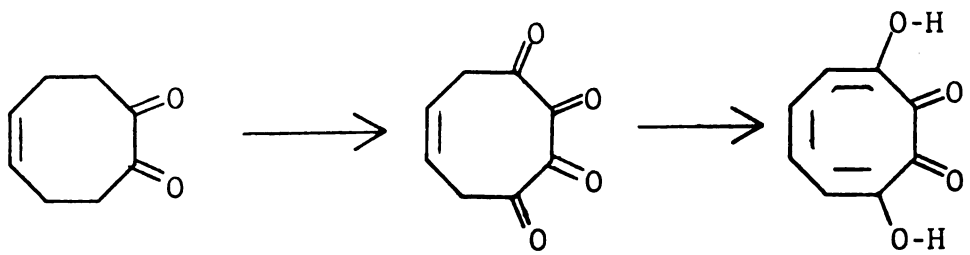
at 1735 cm^{-1} indicating that α bromination had occurred. The nmr spectrum of this oil, however, exhibited a very low ratio of phenyl protons to methoxy protons indicating that extensive bromination of the phenyl rings had occurred.

One attempt to chlorinate the three and eight positions of 109 with sulfuryl chloride[102] in carbon tetrachloride led only to the recovery of starting material.

An interesting derivative of 9 is 3,8-dihydroxy-1,2-cyclooctatrienedione 113. An attractive feature of this compound is that the hydrogen bonding between the hydroxyl and carbonyl groups was expected to confer a measured degree of planarity to the molecule and thereby enhance any aromatic character which might be present.

Several brief attempts to synthesize 103 from diketone 69 were made. Synthetically the plan was a simple one as shown in Scheme XII. There are a number of conceivable methods available for the conversion of 69 to 5-cyclooctene-1,2,3,4-tetraone 114. The tetraketone was then expected to tautomerize to 113 as a fully conjugated system would result.

Scheme XII

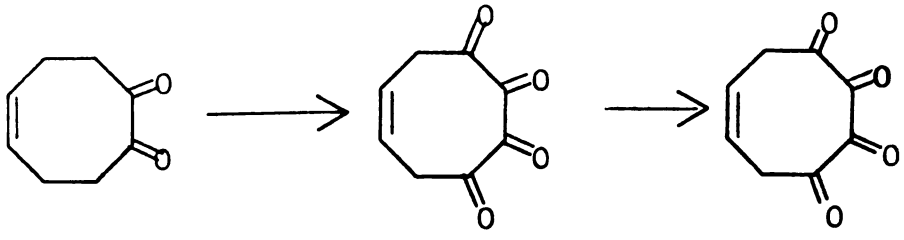


69 114 113

Selenium dioxide[103] is a reagent which has been shown to oxidize α-carbonyl methylene groups to carbonyl functions. Upon treatment of 69 with selenium dioxide in either acetic anhydride or in aqueous dioxane solution only asphalt like material was obtained.

There are available a number of indirect methods of converting ketones into α-diketones. α-Oximino ketones, which are prepared by the action of alkyl nitrites on ketones, have been hydrolyzed to diketones by a number of different types of reagents such as iron pentacarbonyl in the presence of a catalytic amount of boron trifluoride etherate,[104] pyruvic acid,[105] and levulinic acid.[106] It was therefore anticipated that the bis α-oximino diketone 115 could be prepared from diketone 69 and then hydrolyzed to tetraketone 114 as depicted in Scheme XIII.

Scheme XIII



69 115 114

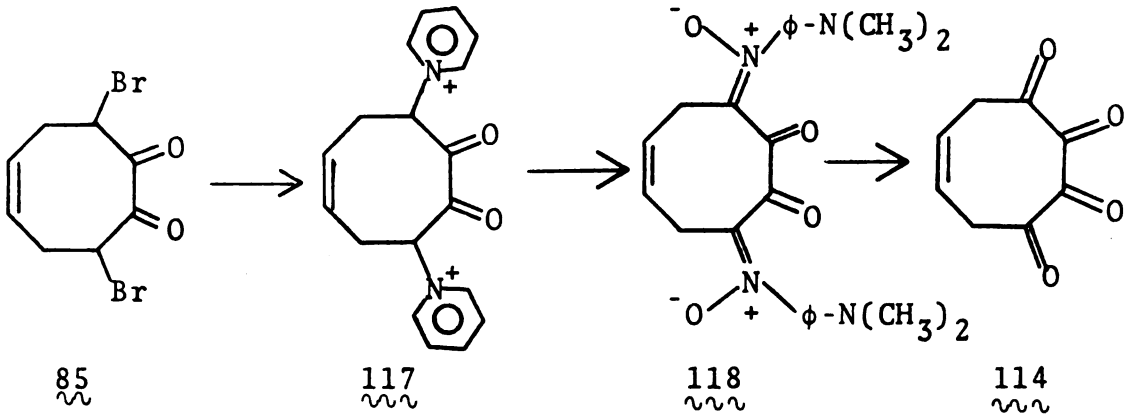
Treatment of 69 with isoamyl nitrite[107] in methanol in the presence of anhydrous hydrogen chloride at -10° failed to produce any reaction and the starting material was recovered unchanged. The use of methyl nitrite[108] in the place of isoamyl nitrite produced the same result.

As discussed previously geminal dihalides can be hydrolyzed to carbonyl groups. It was conceivable that bromination of 85 might result in the formation of 3,3,8,8-tetrabromo-5-cyclooctene-1,2-dione 116. This tetrabromide could then be hydrolyzed to 114 by a reagent such as silver trifluoroacetate.[46] Interestingly when 85 was treated with cupric bromide the starting material was recovered quantitatively. Apparently 85 is not susceptable to further bromination presumably due to the steric hindrance which would result.

Another promising method for the conversion of 85 to 114 involves the Krönke reactions.[109] In this sequence an α-bromoketone is converted to the corresponding pyridinium bromide which is then reacted with *p*-nitroso-

N,N-dimethylaniline to form a nitrone. Upon hydrolysis the nitrone yields an α-diketone. Accordingly 85 was to be converted to its bis pyridinium salt 117 which in turn was to be reacted with p-nitroso-N,N-dimethylaniline to form nitrone 118 which could be hydrolyzed to tetraketone 114 as shown in Scheme XIV.

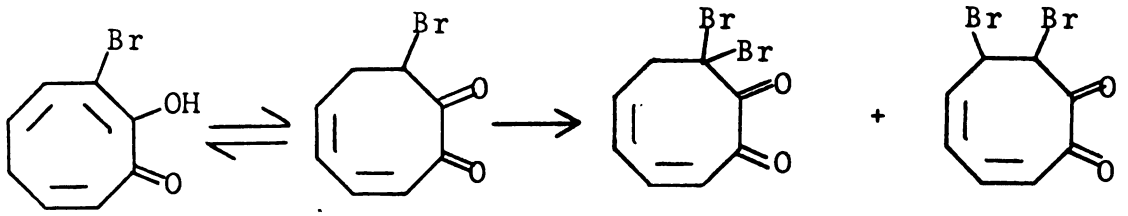
Scheme XIV



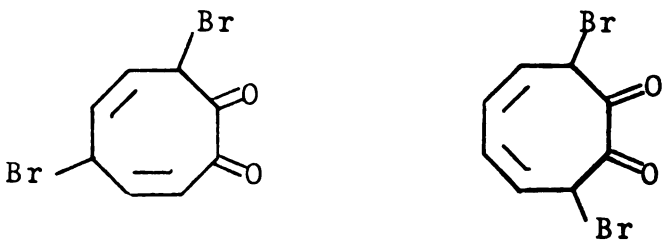
85 117 118 114

Unfortunately treatment of 85 with pyridine in refluxing toluene failed to produce any 117, rather a black intractable material was obtained.

Another derivative of 9 whose synthesis seemed plausible was 3-bromo-1,2-cyclooctatrienedione 119. The reaction of 93 with NBS was expected to lead to four possible bromination products, 120, 121, 122, and 123. It was interesting though that each of these conceivable products would lead to the same product, 119 upon treatment with base.

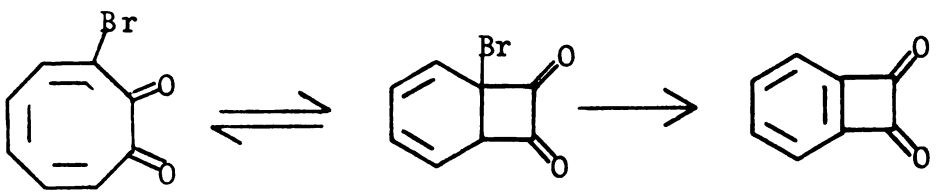


93 94 120 121



122 123

The synthesis of 119 suffered one major disadvantage. Its bicyclic tautomer 124 would be capable of forming benzocyclobutadienoquinone by elimination of hydrogen bromide.



119 124 60

Surprisingly NBS bromination of 93 produced a single yellow crystalline product, mp 106-109°, in 85% yield. The composition of this material was $C_8H_6O_2Br_2$ as determined by elemental analysis and the mass spectral parent peaks of m/e 296, 294, and 292 whose relative intensities were 1:2:1 respectively.

The infrared spectrum of this material lacked the hydroxyl absorption exhibited by the starting material indicating that the molecule was existing as a diketone. The two distinct ir carbonyl frequencies at 1677 and 1724 cm^{-1} confirmed this idea. The carbonyl absorption at 1677 cm^{-1} suggested the presence of an α,β-unsaturated ketone while that at 1724 cm^{-1} could be interpreted as either an α-bromoketone or simply as an α-methylene ketone.

The nmr spectrum of the bromination product exhibited a doublet at δ 7.68 (H_A), an overlapping pair of doublets at δ 6.55 (H_B), a pair of doublets at δ 5.95 (H_C), a heptet at δ 5.23 (H_D), a pair of doublets at δ 3.84 (H_E), and a pair of doublets converged to a triplet at δ 3.22 (H_F). Each signal integrated for one proton.

A consideration of the observed coupling constants in conjunction with decoupling experiments established the couplings and coupling constants reported in Table III.

The absorptions at δ 3.84 and δ 3.22 suggested the presence of either two allylic hydrogens or two α-carbonyl hydrogens. Another possibility is the presence of an allylic and an α-carbonyl hydrogen.

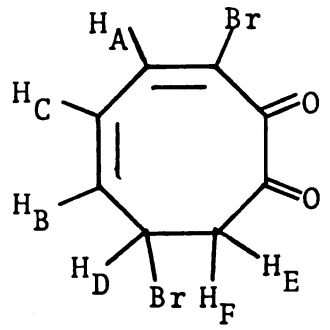
The chemical shift of the absorption due to H_A together with the observation that H_A is coupled only to H_C indicated that H_A might be a β-hydrogen of an α-bromo-α,β-unsaturated ketone moiety.

Table III. Summary of couplings and coupling constants of the bromination product of 93.

Coupling	Coupling Constant (Hz)
H_A - H_C	6.0
H_B - H_C	12.0
H_B - H_D	8.5
H_D - H_E	5.5
H_D - H_F	13.5
H_E - H_F	13.5

The most critical requirement which any structural formulation for the bromination product must meet is the presence of a hydrogen (H_D) which is coupled to three other hydrogens (H_B, H_E, and H_F). Three of the expected bromination products 121, 122, and 123 fail to meet this requirement. Compound 120 possesses a hydrogen atom which fulfills the coupling constraints of H_D. This structural formulation fails, however, as 120 possesses a plane of symmetry which requires that the allylic hydrogens be equivalent.

A structure for the unknown which is consistent with all of the constraints imposed by the nmr data is 125.



125

The coupling constants observed for the bromination product are reasonably close to those expected for 125. The coupling between H_A and H_C, however, is lower than the expected 9-13 Hz.[77] The observed value of 6 Hz is consistent with a conformation in which the angle between H_A and H_C is approximately 45°.

The uv spectrum of the unknown is also consistent with a conformation in which the double bonds of 125 are not coplanar. The calculated absorption maximum of 125 is 339 nm. The experimental value of 299 nm reflects the lack of complete conjugation between the double bonds.

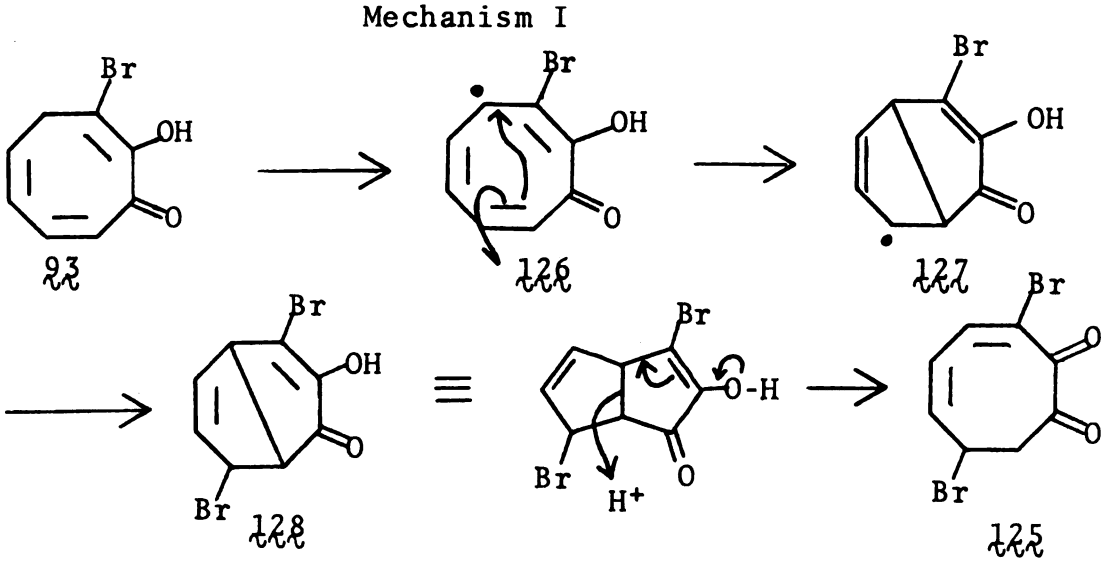
A molecular model of the conformation of 125 in which the angle between the double bonds is approximately 45° shows that the angles between H_D and H_E and H_F are approximately 80° and 170° respectively. The H_D - H_E and H_D - H_F coupling constants of 5.5 and 13.5 Hz, respectively, are consistent with the general relationship between the dihedral angle and coupling constant of vicinal hydrogens as deduced by Karplus.[110]

The carbonyl absorptions of diketone 69 occur at 1723 and 1708 cm^{-1} due to coupling of the symmetric and antisymmetric stretching modes of the individual carbonyl groups. It has been suggested that the absorption position of the individual carbonyl groups can be approximated by the mean of the coupled frequencies.[111] Accordingly the unperturbed frequency of the carbonyl groups of 69 is estimated to be 1716 cm^{-1}.

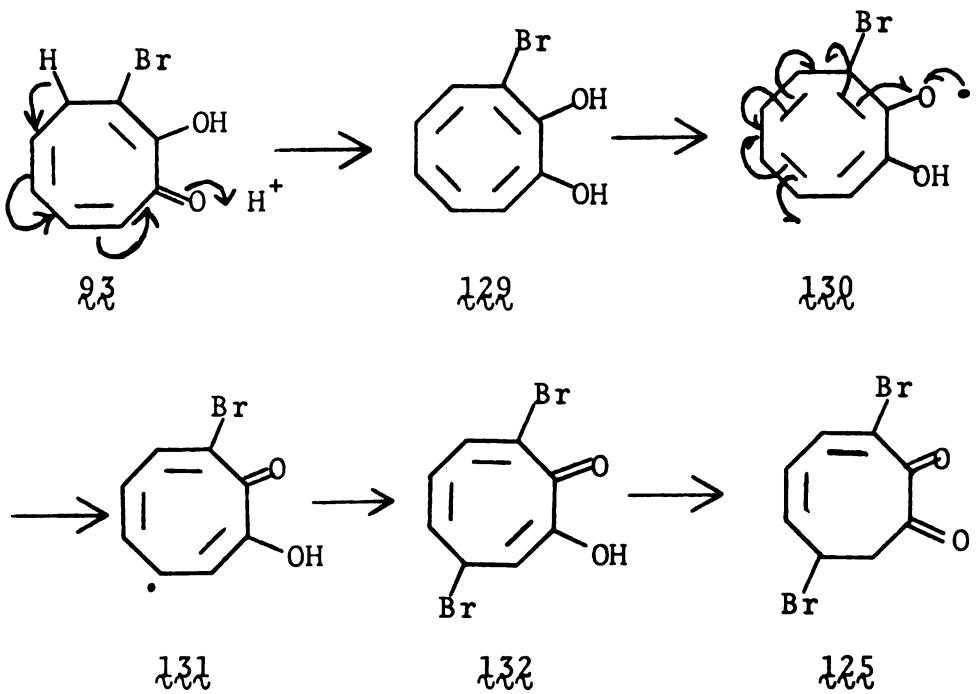
The carbonyl absorption of 125 at 1724 cm^{-1} is slightly high when compared to that of 69. The bent conformation of 125, however, provides a plausible explanation. In this conformation the nonconjugated carbonyl group of 125 has a configuration which very roughly approximates that of a cyclopentanone. It seems reasonable that this slight compression of the carbonyl bond angle should be sufficient to cause the increase in the carbonyl frequency relative to that expected.

Two plausible mechanisms can be envisioned for the formation of 125 as outlined below.

Mechanism I



Mechanism II



93 129 130

131 132 125

In mechanism I rearrangement of the initially formed radical 126 would lead to the bicyclic radical 127 which could be brominated to form bicyclic dibromide 128. The acid catalyzed rearrangement of 128 would then afford 125.

Alternatively enolization of 93 would provide 3-bromo-1,2-dihydroxycyclooctatetraene 129 which could be oxidized to form radical 130. Rearrangement of 130 to radical 131 followed by bromination would lead to the formation of the enol 132 of 125.

Neither of these mechanisms is completely satisfactory. Mechanism I suffers from the fact that intermediate 128 is expected to be a reasonably stable compound. Molecular models do not reveal an inordinate

amount of ring strain in 128 thereby eliminating the relief of strain as a driving force for the ring opening.

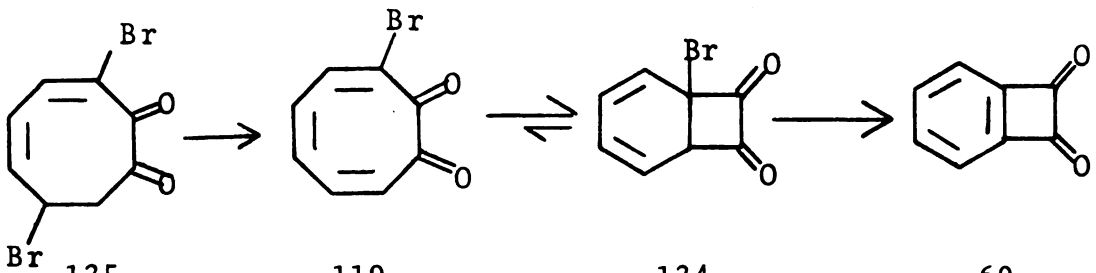
Mechanism II is deficient as the cyclooctatetraene derivative 129 seems to be more strained than 93 on the basis of a comparison of the molecular models of these compounds. Furthermore, there was no evidence of the presence of 129 in the samples of 93.

Although 125 was not one of the expected products from the bromination of 93, it was a suitable precursor to 119. Treatment of 125 with triethylamine in chloroform solution produced an immediate reaction. The ir spectrum of the reaction mixture showed a carbonyl absorption which is characteristic of benzocyclobutadienoquine 60 and lacked the carbonyl absorptions of 125.

When a sample of 125 in deuterated chloroform was treated with a limited amount of triethylamine, the nmr spectrum of the reaction mixture showed the aromatic proton AA'BB' pattern of 60 along with the signals due to the starting material. There as no indication of the presence of the expected products 119 and 124.

Thin layer chromatographic analysis of the reaction mixture revealed the presence of 60 as the only product in addition to nonmoving brown material.

From these experiments it was concluded that 119 had been formed. The production of 60 from 125 requires



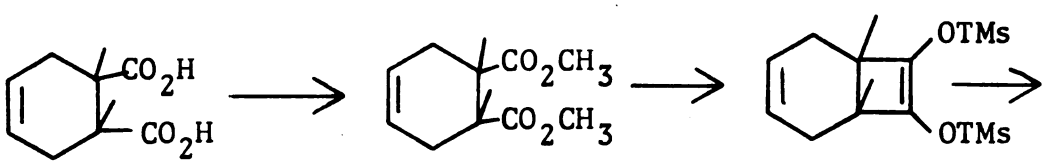
125 119 124 60

the intermediacy of the 119-124 equilibrium mixture. The fact that neither of these intermediates could be observed in the nmr spectrum of the reaction mixture was surprising as 1,3,5-cyclooctatriene and its bicyclic valence tautomer exist as a 85%-15% equilibrium mixture at 100°.[112] The energy of activation for the interconversion of 119 and 124 must be small since 60 is formed immediately from 125 at room temperature. The dehydrobromination of 124 was expected to proceed readily with the formation of an aromatic system as the driving force.

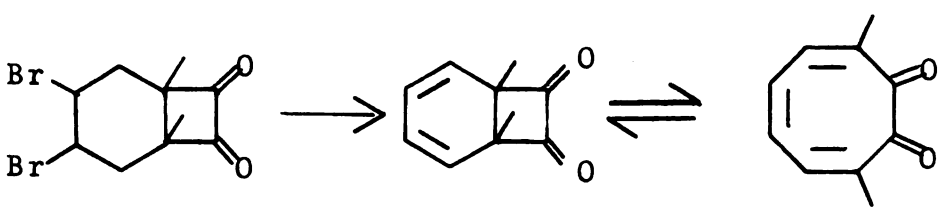
Although 1,2-cyclooctatrienedione was not isolated, some interesting organic chemistry has been generated. The failure of 85 to produce 9 upon treatment with base suggests that 9 may not be a stable compound. The demonstration of the nonplanarity of 89 implies that 9 will not be planar and therefore not aromatic.

Suggestions for Future Study

The synthetic plan outlined in Scheme II should be successful when a slight modification is incorporated. *cis*-1,2-Dimethyl-4-cyclohexene-1,2-dicarboxylic acid 133 is available from the cycloaddition of 2,3-dimethylmaleic anhydride and butadiene.[113] Esterification of 133 followed by the modified acyloin condensation would be expected to lead to the formation of 134. Treatment of 134 with pyridinium hydrobromide perbromide would then provide 135. The presence of the bridgehead methyl groups in 134 would prevent the bromination - dehydrobromination which had occurred in the formation of 61 from 57. Dehydrobromination of 135 would result in the formation of 136, the bicyclic tautomer of 3,8-dimethyl-1,2-cyclo-octatrienedione 137.



133 134



135 136 137

EXPERIMENTAL

General Procedures

The infrared spectra were recorded on a Perkin-Elmer Model 237B spectrophotomer. The nmr spectra were obtained using a Varian T-60 spectrometer with chemical shifts reported as δ values measured from an internal standard of tetramethylsilane. The uv spectra were recorded on a Unicam Model SP-800 spectrophotometer using 1 cm quartz cells. Mass spectra were obtained with a Hitachi Perkin-Elmer RMU-6 mass spectrometer.

Melting points were determined on a Thomas Hoover melting point apparatus and are uncorrected.

Microanalyses were performed by Spang Microanalytical Laboratory, Ann Arbor, Michigan or Galbraith Laboratories, Inc., Knoxville, Tennessee.

Molecular models were constructed from Framework Molecular Models by Prentice-Hall, Inc., Englewood Cliffs, New Jersey.

3,4-Dibromobicyclo[4.2.0]-6-octene-7,8-dione (Dione 61).

To a solution of 2.82 g (1 x 10^{-2} mol) of 7,8-bis (trimethylsiloxy)-*cis*-bicyclo[4.2.0]-3,7-octadiene[43] in 50 ml of anhydrous tetrahydrofuran maintain at -78° was added dropwise a solution of 6.4 g (2 x 10^{-2} mol) of pyridinium hydrobromide perbromide in 50 ml of anhydrous tetrahydrofuran over a period of an hour. The solution was stirred for an additional hour. Upon warming to room temperature the solid pyridinium hydrobromide was filtered and the solvent removed under reduced pressure at room temperature. The resulting red-brown oily crystals were triturated with ether and filtered. Recrystallization of the crude product from methylene chloride-cyclohexane produced 0.8 g (27%) of dione 61 as very light yellow crystals: mp 161-164°; ir ($CHCl_3$) 3000 (C-H), 1795 (C=O), and 1615 cm^{-1} (C=C); nmr ($CDCl_3$) δ 4.74 (m, 2, CHBr) and δ 3.67 (m, 4, allylic); mass spectrum (70eV) 134 (parent).

Anal. Calcd for $C_8H_6Br_2O_2$: C, 32.65; H, 2.04.
Found: C, 32.63; H, 2.04.

Reaction of 3,4-dibromobicyclo[4.2.0]-6-octene-7,8-dione 61 and 1,5-diazabicyclo[4.3.0]-5-nonene (Benzocyclobutadienoquinone 60).

To a solution of 0.6 g (2.04×10^{-3} mol) of 3,4-dibromobicyclo[4.2.0]-6-octene-7,8-dione in 30 ml of methylene chloride was added dropwise, over a period of an hour, a solution of 0.5 g (4×10^{-3} mol) of 1,5-diazabicyclo[4.3.0]-5-nonene in 15 ml of methylene chloride. The solution was then stirred at room temperature for 20 hr. The solution was then washed well with water and saturated sodium chloride solution and then dried over anhydrous magnesium sulfate. Removal of the solvent afforded 250 mg (92.5%) of benzocyclobutadienoquinone 60: mp 129-132°; ir ($CHCl_3$) 1808, 1777, and 1760 cm^{-1} (C=O); nmr ($CDCl_3$) δ 8.00 (AA'BB' pattern, aromatic); mass spectrum (70eV) m/e 132 (parent).

Reaction of 7,8-bis(trimethylsiloxy)-*cis*-bicyclo[4.2.0]-3,7-octadiene and N-bromosuccinimide (Benzocyclobutadienquinone 60).

A solution of 2.82 g (1×10^{-2} mol) of 7,8-bis(trimethylsiloxy)-*cis*-bicyclo[4.2.0]-3,7-octadiene and a catalytic amount of benzoyl peroxide in 60 ml of carbon tetrachlordde and 5.4 g (3×10^{-2} mol) of N-bromosuccinimide was heated to reflux with simultaneous irradiation with a sunlamp for 15 min. Upon cooling the succinimide was filtered and the solvent removed under reduced pressure at room temperature. The orange oily residue was chromatographed on silicic acid with chloroform as the elutant. The first component eluted gave yellow crystals upon removal of the solvent. Recrystallization of this material from methylene chloride - petroleum ether (bp 40-60°) (1:1) gave 58 mg (4.4%) of benzocyclobutadienoquinone: mp 129-132°; ir ($CHCl_3$) 1808, 1777, and 1760 cm^{-1} (C=O); nmr ($CDCl_3$) δ 8.00 (AA'BB' pattern, aromatic); mass spectrum (70eV) m/e 132 (parent).

7,8-Bis(trimethylsiloxy)-*trans*-bicyclo[4.2.0]-3,7-octadiene (Bis ether 73).

Through a column containing 35 g of basic alumina was passed 150 ml of toluene directly into a 500 ml three neck round bottom flask equipped with a nitrogen inlet tube, a reflux condensor, and a magnetic stirrer. To the flask was then added 3.0 g (1.32×10^{-1} mol) of small, cleanly cut pieces of sodium followed by the addition of a solution of 16.0 g (1.5×10^{-1} mol) of chlorotrimethylsilane and 6.0 g (3×10^{-2} mol) of *trans*-dimethyl-4-cyclohexene-1,2-dicarboxylate in 25 ml of toluene. The mixture was then refluxed with stirring under nitrogen for 48 hr. Upon cooling the solid material was filtered and the solvent removed under reduced pressure. The yellow residue was distilled under reduced pressure giving 5.9 g (70%) of bis ether 73 as a colorless oil: bp 71-72° (0.025 mm); ir (film) 3000, 2950, 2900, 2840 (C-H) and 1685 cm^{-1} (TMS-O-C=C-OTMS); nmr (CCl_4, $CHCl_3$ internal standard) δ 5.67 (s, 2, olefinic), δ 2.16 (s, 6, allylic and cyclobutenyl), and δ 0.15 (s, 18, TMS).

2-Hydroxy-5-cyclooctenone (Ketone 76).

A solution of 62 g (0.5 mol) of 5,6-epoxycyclooctene in 200 ml of dimethylsulfoxide was stirred at 95° for 90 hr. Boron trifluoride etherate was added in one ml portions at 0, 24, 48, and 72 hr. After cooling the solution was poured into 400 ml of water and extracted with three 100 ml portions of chloroform. The combined extracts were washed with 50 ml of water and then dried over anhydrous magnesium sulfate. Removal of the solvent provided a yellow oil which was distilled under reduced pressure. A forerun of 4.4 g of a mixture of starting epoxide and product was collected followed by 52.7 g (75%) of 2-hydroxy-5-cyclooctenone: bp 78-79° (0.5 mm); ir (neat) 3400 (C-OH), 3000, 2912 (C-H), 1700 (C=O), and 1685 cm^{-1} (C=C); nmr (CCl_4) δ 5.72 (m, 2, olefinic), δ 4.30 (m, 2, HC-OH), δ 2.0-3.0 (m, 6, allylic and α-carbonyl), and δ 1.70 (m, 2, $-CH_2-CHOH$).

5-Cyclooctene-1,2-dione (Diketone 69).

A three neck one liter round bottom flask equipped with a mechanical stirrer and a reflux condensor was charged with 52.7 g (0.375 mol) of 2-hydroxy-5-cyclooctenone, 168 g (0.84 mol) of cupric acetate monohydrate, 35 ml of methanol, and 420 ml of 50% aqueous acetic acid. The mixture was heated with an open flame to reflux with stirring for two hr. After cooling the solid material was filtered and washed with water and ether. The combined filtrate and washes were poured into 500 ml of saturated sodium chloride solution. The aqueous solution was then extracted with six 100 ml portions of ether. The combined extracts were washed with saturated sodium bicarbonate solution until neutral and then with saturated sodium chloride solution. After drying over anhydrous magnesium sulfate the ether was removed. The resulting yellow oil was distilled under reduced pressure yielding 26.4 g (51%) of 5-cyclooctene-1,2-dione: bp 56-57° (0.5 mm); mp 35-36.5° ir ($CHCl_3$) 3050 (C-H), 1723, 1708, and 1692 cm^{-1} (C=O); nmr ($CDCl_3$) δ 5.88 (m, 2, olefinic) and δ 2.53 (m, 8, allylic and α-carbonyl); uv max (cyclohexane) 230 (ε 99), 281 (ε 35.6), 288 (ε 33.3), and 345 nm (ε 17.2); mass spectrum (70eV) m/e 138 (parent), 110 (-CO), and 82 (-2CO).

Anal. Calcd for $C_8H_{10}O_2$: C, 69.62; H, 7.30.
Found: C, 69.40: H, 7.16.

10,11-Benzo-9,12-diazabicyclo[6.4.0]-4,8,10,12-dodecatetraene (Quinoxaline 81).

To a solution of 0.69 g (5×10^{-3} mol) of 5-cyclooctene-1,2-dione in 50 ml of glacial acetic acid was added a solution of 0.54 g (5×10^{-3} mol) of technical *o*-phenylenediamine in 20 ml of glacial acetic acid. The resulting solution was stirred at 60° for 12 hr. The solution was then poured into water and the resulting precipitate was filtered. This solid was recrystallized from water-methanol and then chromatographed on silicic acid eluting with chloroform. Removal of the solvent from the main chromatographic fraction provided 0.6 g (57%) of the quinoxaline as white crystals: mp 117-119°; ir ($CHCl_3$) 2975 cm^{-1} (C-H); nmr ($CDCl_3$) δ 7.9 (AA'BB' pattern, 4, aromatic), δ 5.56 (t, J = 4 Hz, 2, olefinic), δ 3.42 (t, J = 7Hz, 4, α-imino), and δ 2.74 (m, 4, allylic); mass spectrum (70eV) m/e 210 (parent).

Anal. Calcd for $C_{14}H_{14}N_2$: C, 80.07; H, 6.72.
Found: C, 79.93; H, 6.77.

3,8-Di(*p*-methoxybenzilidene)-5-cyclooctene-1,2-dione (Dione 82).

A solution of 3.5 g (2.54×10^{-2} mol) of 5-cyclooctene-1,2-dione, 14.2 g (1×10^{-1} mol) of *p*-anisladehyde, and 25 drops of piperidine in 30 ml of absolute ethanol was refluxed with stirring for nine hr. Upon cooling a yellow crystalline material was obtained. This material was recrystallized from acetone giving 3.7 g (39%) of dione 82 as beautiful yellow crystals: mp 162.5-165°; ir ($CHCl_3$) 3000, 2950 (C-H) and 1675 cm^{-1} (C=O); nmr ($CDCl_3$) δ 7.9 (s, 2, olefinic), δ 7.3 (AB quartet, J_{AB} = 8 Hz, 8, aromatic), δ 6.25 (t, 2, olefinic), δ 3.9 (s, 6, methoxy), and δ 3.38 (d, 4, allylic); uv max (cyclohexane) 208 (ε 2.8×10^{-3}), 233 (ε 2.08×10^{3}), and 327 nm (ε 2.18×10^{3}); mass spectrum (70eV) m/e 374 (parent).

Anal. Calcd for $C_{24}H_{22}O_4$: C, 77.07; H, 5.93.

Found: C, 76.96; H, 5.96.

trans-3,8-Dibromo-5-cyclooctene-1,2-dione (Dibromide 85).

A three neck 500 ml round bottom flask equipped with a magnetic stirrer, a gas inlet tube, and a reflux condensor was charged with 6.9 g (5×10^{-2} mol) of 5-cyclooctene-1,2-dione, 44.6 g (0.2 mol) of cupric bromide, and 200 ml of a 1:1 ethyl acetate-chloroform solution. The mixture was stirred under nitrogen for 15 min at room temperature and then at 75° for 12 hr. Upon cooling the cuprous bromide was filtered and washed with chloroform. The combined filtrate and wash was washed with water until neutral followed by a wash with saturated sodium chloride solution. After drying over anhydrous magnesium sulfate, the solvents were removed giving a brown solid material. Trituration with cyclohexane removed the brown material affording white crystals. Recrystallization of the crude product from methylene chloride-cyclohexane provided 5.0 g (34%) of dibromide 85, mp 136-139°. An analytical sample was obtained by sublimation: mp 138-141°; ir ($CHCl_3$) 3000, 2925 (C-H) and 1740, 1727 cm^{-1} (C=O); nmr ($CDCl_3$) δ 6.07 (m, 2, olefinic), δ 5.15 (ABX quartet, 2, CHBr), and δ 2.90 (m, 4, allylic); uv max (cyclohexane) 288 (ε 244), 280 (ε 302) and 224 (ε 742); mass spectrum (70eV) m/e 298, 296, 294 (parent).

Anal. Calcd for $C_8H_8Br_2O_2$: C, 32.46; H, 2.73.
Found: C, 32.71; H, 2.82.

2,7-Dibromo-10,11-benzo-9,12-diazabicyclo[6.4.0]-4,8,10,12-dodecatetraene (Quinoxaline 88).

To a solution of 3.4 g (0.15×10^{-2} mol) of 3,8-dibromo-5-cyclooctene-1,2-dione in 140 ml of glacial acetic acid was added a solution of 1.24 g (0.15×10^{-2} mol) of freshly distilled *o*-phenylenediamine in 40 ml of glacial acetic acid. The resulting solution was stirred at room temperature for 24 hr. The solution was poured into 500 ml of water and extracted with four 100 ml portions of ether. The extracts were washed with water, saturated sodium bicarbonate solution, water, and saturated sodium chloride solution and then dried over anhyrous sodium sulfate. Removal of the solvent gave 3.9 g (72%) of quinoxaline 88 as a white powder, mp 177-182°. An analytical sample was prepared by sublimation: mp 180-182°; ir ($CHCl_3$) 2975 cm^{-1} (C-H); nmr ($CDCl_3$) δ 8.00 (AA'BB' pattern, 4, aromatic), δ 5.93 (t, J = 9 Hz, 2, CHBr), δ 5.54 (t, J = 4 Hz, 2, olefinic), and δ 3.30 (m, 4, allylic); mass spectrum (70eV) m/e 370, 368, 366 (parent)

Anal. Calcd for $C_{14}H_{12}Br_2N_2$: C, 45.69; H, 3.29.
Found: C, 45.72; H, 3.28.

10,11-Benzo-9,12-diazabicyclo[6.4.0]-2,4,6,8,10,12-dodeahexaene (Quinoxaline 89).

To a solution of 3.68 g (1 x 10^{-2} mol) of quinoxaline 88 in 85 ml of dimethylsulfoxide was added a solution of 2.5 g (2 x 10^{-2} mol) of 1,5-diazabicyclo[4.3.0]nona-5-ene in 25 ml of dimethyl-sulfoxide and the resulting solution was stirred at room temperature for 18 hr. The reaction mixture was poured into 500 ml of water and extracted with five 100 ml portions of methylene chloride. The extracts were washed well with water and saturated sodium chloride solution and then dried over anhydrous sodium sulfate. Removal of the solvent gave 1.6 g of a red powder which was chromatographed on neutral alumina eluting with benzene. The first three 20 ml fractions which were collected consisted of a mixture of starting material and product. Subsequent fractions upon removal of the solvent provided 1.0 g (48.5%) of quinoxaline 89 as a very light yellow powder. An analytical sample was prepared by recrystallization from pentane: mp 143-145°; ir ($CHCl_3$) δ 7.94 (AA'BB' pattern, 4, aromatic), δ 6.88 (d of AB quartet, J_{AB} = 11.5 Hz, 2, H_2, H_7), δ 6.43 (coupled d of AB quartet, J_{BC} = 1.5 Hz, 2, H_3, H_6), and 6.15 (d, 2, H_4, H_5); uv max (cyclohexane) 354 (ε 3.09 x 10^4), 334 (ε 5.15 x 10^3), 284 (ε 4.12 x 10^3), 245 (ε 227 x 10^4), and 205 nm (ε 2.78 x 10^4); mass spectrum (70eV) m/e 206 (parent).

Anal. Calcd for $C_{14}H_{10}N_2$: C, 81.62; H, 4.89;
Found: C, 81.54; H, 4.84.

3-Bromo-2-hydroxy-2,5,7-cyclooctatrienone (Ketone 93).

A solution of 3.0 g (1 x 10^{-2} mol) of 3,8-dibromo-5-cyclooctene-1,2-dione in 70 ml of dry hexamethylphosphoric triamide was maintained at 80° with stirring for 18 hr. The yellow-red solution was poured into 500 ml of saturated sodium chloride solution and extracted with four 100 ml portions of cyclohexane. The extracts were washed with two 150 ml portions of water and then saturated sodium chloride solution and dried over anhydrous sodium sulfate. Removal of the solvent under reduced pressure provided 0.8 g of a red-brown semisolid which was chromatographed on silicic acid eluting with carbon tetrachloride-benzene (10:2). Fractions 6-18 (20 ml) afforded 0.325 g (15.0%) of ketone 93. Sublimation of the crude product afforded 93 as white crystals: mp 101-103°; ir ($CHCl_3$) 3365 (O-H), 1662 (C=O), 1622 and 1600 cm^{-1} (C=C); nmr ($CDCl_3$) δ 7.86 (s, 1, hydroxyl), δ 6.64 (m, 3, H_6, H_7, H_8), δ 6.73 (q, J = 8 Hz, 1, H_5), and δ 3.16 (bd. m, 2, allylic); uv max (cyclohexane) 297 (ε 5 x 10^3), 254 (ε 1.27 x 10^4), 246 (ε 1.23 x 10^4), 239 (ε 1.04 x 10^4) and 198 nm (ε 6.55 x 10^3); mass spectrum (70eV) 216, 214 (parent).

Anal. Calcd for $C_8H_7BrO_2$: C, 44.69; H, 3.28.
Found: C, 44.65; H, 3.27.

1,2-Bis(spiro-1',3'-dioxolane)-5-cyclooctene (Bis ethylene ketal 27).

A 100 ml round bottom flask equipped with a Dean-Stark trap and a reflux condensor was charged with 2.7 g (2 x 10^{-2} mol) of 5-cyclooctene-1,2-dione, 2.48 g (4 x 10^{-2} mol) of ethylene glycol, 45 ml of benzene, and a catalytic amount of tosic acid. The mixture was refluxed with the separation of water for 20 hr. Upon cooling the solution was washed with two 10 ml portions of 10% sodium hydroxide solution followed by several washes with water and then saturated sodium chloride solution. After drying over potassium carbonate, the solvent was removed under reduced pressure. The resulting yellow oil was distilled at reduced pressure giving 2.7 g (60%) of ketal 27 as a colorless oil which crystallized upon standing; bp 80° (0.1 mm); mp 66-67°; ir ($CHCl_3$) 2940 and 2870 cm^{-1} (C-H); nmr ($CDCl_3$) δ 5.78 (t, 2, olefinic), δ 4.02 (s, 4, ketal methylene), δ 3.98 (s, 4, ketal methylene), δ 2.22 (m, 4, allylic), and δ 1.90 (m, 4, α-ketal methylene); mass spectrum (70eV) m/e 226 (parent).

Anal. Calcd for $C_{12}H_{18}O_4$: C, 63.77; H, 8.03.
Found: C, 63.77; H, 7.96.

1-(2'-bromoethoxy)-2-(spiro-1',3'-dioxolane)-5-bromo-9-oxabicyclo[4.2.1]nonane (Ketal 99 or 100):

To a solution of 1.13 g (5×10^{-3} mol) of 1,2-bis-(spiro-1',3'-dioxolane)-5-cyclooctene in 10 ml of tetrahydrofuran was added a solution of 1.6 g (5×10^{-3} mol) of pyridinium hydrobromide perbromide in 10 ml of tetrahydrofuran with stirring over a period of 30 min. The pyridinium hydrobromide was filtered and the solvent removed under reduced pressure at room temperature. The resultant yellow oil crystallized upon cooling. Recrystallization of this material from hexane afforded 0.8 g (42%) of ketal 89 or 90 as feathery white crystals: mp 77-79°; ir ($CHCl_3$) 2900 and 2950 cm^{-1} (C-H); nmr ($CDCl_3$) δ 4.8-4.4 (m, 1, ether bridge methine), δ 4.4-3.6 (m, 7, ketal methylene, bromomethine, and -O-CH_2-CH_2Br), δ 3.6-3.3 (m, 2, -O-CH_2CH_2Br), and δ 2.6-1.7 (m, 8, eight membered ring aliphatic).

Anal. Calcd for $C_{12}H_{18}Br_2O_4$: C, 37.34; H, 4.70.
Found: C, 37.45; H, 4.65.

3,8-Di(*p*-methoxybenzyl)-5-cyclooctene-1,2-dione (Dione 109).

To a solution of 2.0 g (2.9×10^{-1} g -atoms) of lithium in one liter of liquid ammonia was added dropwise, with stirring, a solution of 15.0 g (4×10^{-2} mol) of 3,8-di(*p*-methoxybenzilidene)-5-cycloctene-1,2-dione in 400 ml of tetrahydrofuran over a period of 15 min. When the addition was complete 60.0 g of ammonium chloride was added in portions and the ammonia was allowed to evaporate. The residue was poured into water and extracted with four 100 ml portions of ether. The extracts were washed with water until neutral and then dried over anhydorus magnesium sulfate. Removal of the solvent gave a light yellow oil which crystallized upon standing overnight. Recrystallization of this material from petroleum ether (bp 40-60°)-methylene chloride (5:1) afforded 12.8 g (85%) of dione 109: mp 91.5-94°; ir ($CHCl_3$) 2930 (C-H) and 1705 cm^{-1} (C=O); nmr ($CDCl_3$) δ 7.03 (AB quartet, J_{AB} = 8 Hz, 8, aromatic), δ 5.85 (t, 2, olefinic), δ 3.80 (s, 6, methoxy), and δ 2.0-3.4 (m, 10, allylic, benzylic, and α-carbonyl); mass spectrum (70eV) m/e 378 (parent).

Anal. Calcd for $C_{24}H_{26}O_4$: C, 76.25; H, 6.93.

Found: C, 76.06; H, 6.85.

3,7-Dibromo-3,5-cyclooctadiene-1,2-dione (Dione *ttt*).

A solution of 108.7 mg (5.0×10^{-4} mol) of 3-bromo-2-hydroxy-2,5,7-cycloctatrienone and a catalytic amount of benzoyl peroxide in 15 ml of carbon tetrachloride and 89.0 mg (5.0×10^{-4} mol) of N-bromosuccinimide were heated to reflux with simultaneous irradiation with a sunlamp for 30 min. The succinimide was filtered upon cooling and the solvent removed under reduced pressure. The residue was purified by preparative thin layer chromatography on silicic acid eluting with benzene-methylene chloride (10:12). There was obtained 125 mg (85%) of dione *ttt* as a yellow crystalline material. An analytical sample was obtained by sublimation: mp 106-109°; ir ($CHCl_3$) 1724, 1677 (C=O) and 1575 cm^{-1} (C=C); nmr ($CDCl_3$) δ 7.68 (d, 1, olefinic, H_A), δ 6.55 (d of d, 1, olefinic, H_B), δ 5.95 (d of d, 1, olefinic, HC), δ 5.23 (heptet, 1, bromo methine, H_D), δ 3.84 (d of d, 1, α-carbon carbonyl, H_E), and δ 3.22 (t, 1, α-carbonyl, H_F); uv max (cyclohexane) 299 (ε 7.5×10^3), 235 (ε 3.83×10^3), and 212 (ε 6.47×10^3); mass spectrum (70eV) m/e 296, 294, 292 (parent).

Anal. Calcd for $C_8H_6Br_2O_2$: C, 32.65; H, 2.04.
Found: C, 32.68; H, 2.11.

Reaction of 3,7-dibromo-3,5-cyclooctadiene-1,2-dione 125 and triethylamine (Benzocyclobutadienoquinone 60).

To a solution of 100 mg (4.65×10^{-4} mol) of 3,7-dibromo-3,5-cyclooctadiene-1,2-dione in 0.4 ml of deuterated chloroform was added one drop of triethylamine. The solution immediately turned light brown. The nmr spectrum of the reaction mixture showed absorptions corresponding to the starting material and benzocyclobutadienoquinone. The ir spectrum of the reaction mixture exhibited the carbonyl absorptions characteristic of 60. Thin layer chromatographic analysis of the reaction mixture on silicic acid eluting with chloroform demonstrated the presence of 60 as the only identifiable product.

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Table IV. Mass Spectrum of 3,4-Dibromobicyclo-[4.2.0]-6-octene-7,8-dione

m/e	Rel. Intensity	m/e	Rel. Intensity
296	1.4	82	1.3
294	2.8	81	1.7
292	1.4	80	1.3
		79	15.5
268	2.5	78	100.0
266	4.8	77	17.5
264	2.5	76	62.5
		75	5.5
188	0.5	74	37.8
187	4.1	73	3.3
186	0.5		
185	4.1	66	2.5
		65	0.9
160	0.3	64	0.8
159	2.0	63	6.3
158	0.2	62	3.3
157	2.2	61	3.3
		60	2.5
134	0.3		
133	0.3	54	0.6
132	0.6	53	4.4
131	0.3	52	15.6
130	0.2	51	35.9
		50	38.0
121	0.6	49	8.4
119	0.8	48	10.3
117	0.5		
		41	0.6
107	0.6	40	1.1
106	5.2	39	17.5
105	2.7	38	13.9
104	3.0	37	10.6
		36	1.4
95	0.6		
93	0.6		

Table V. Mass Spectrum of 5-Cyclooctene-1,2-dione

m/e	Rel. Intensity	m/e	Rel. Intensity
139	7.0	69	13.9
138	69.6	68	57.4
		67	56.5
110	15.7	66	16.5
109	8.7	65	13.0
		63	5.2
96	3.5	62	3.5
95	13.9	61	2.6
94	29.6		
93	2.6	56	3.5
92	5.2	55	22.6
91	3.5	54	100.0
		53	85.2
83	7.0	52	10.4
82	50.4	51	15.7
81	52.2	50	10.4
80	2.6		
79	10.4	44	2.6
78	2.6	43	7.8
77	5.2	42	30.4
		41	76.5
		40	36.5
		39	99.1
		38	11.3
		37	4.4
		32	4.4

Table VI. Mass Spectrum of *trans*-3,8-dibromo-5-cyclooctene-1,2-dione

m/e	Rel. Intensity	m/e	Rel. Intensity	m/e	Rel. Intensity
298	1.2	127	3.1	69	5.4
296	2.3	123	1.2	68	20.4
294	1.2	122	2.3	67	62.3
		121	3.5	66	62.3
218	1.5	120	3.9	65	28.1
217	8.5	119	3.9	64	2.7
216	1.9	118	3.9	63	8.5
215	8.5			62	4.2
		110	4.2	61	2.3
190	1.5	109	21.2		
189	11.2	107	21.9	57	5.4
188	1.9	107	30.4	56	5.0
187	11.5	106	1.9	55	36.5
		105	5.4	54	17.7
162	2.3	104	2.3	53	41.5
161	5.4			52	20.8
160	2.3	96	3.1	51	26.2
159	5.4	95	8.1	50	17.3
		94	32.3	49	3.1
148	1.2	93	3.1		
147	3.1	92	2.7	44	2.7
146	1.2	91	5.4	43	7.7
145	3.1	90	2.3	42	7.3
		89	1.9	41	36.5
138	8.9			40	20.4
137	15.8	85	3.5	39	21.2
136	14.2	84	2.3	38	11.5
135	14.6	83	3.1	37	4.6
		82	18.9	36	7.3
134	3.1	81	45.0	35	1.5
133	1.5	80	42.3		
132	2.7	79	100.0		
		78	13.9		
		77	44.2		
		76	3.1		
		75	1.9		
		74	3.1		
		73	1.2		

Table VII. Mass Spectrum of 10,11-benzo-9,12-diaza-bicyclo[6.4.0]-2,4,6,8,10,12-dodecahexaene.

m/e	Rel. Intensity	m/e	Rel. Intensity
207	4.2	91	2.1
206	27.5	90	7.3
205	39.4	89	9.8
		88	6.2
180	7.3	87	4.7
179	8.3	86	1.6
178	4.2		
177	3.1	79	3.1
		78	31.1
154	2.1	77	39.9
153	3.1	76	60.1
152	4.7	75	44.6
140	2.1	74	23.8
		73	2.1
130	1.6		
129	5.7	66	2.1
128	3.1	65	5.7
127	4.2	64	19.7
126	2.1	63	37.8
		62	17.6
116	2.1	61	6.7
115	2.6		
114	2.6	53	6.2
113	1.6	52	43.0
		51	71.5
104	4.2	50	100.0
103	13.5	49	3.7
102	22.8		
101	7.3	43	11.4
100	4.2	42	4.2
99	3.7	41	12.9
98	2.6	40	7.8
		39	61.2
		38	31.1
		37	16.1
		32	12.9

Table VIII. Mass Spectrum of 3-bromo-2-hydroxy-2,5,7-cyclooctatrienone

m/e	Rel. Intensity	m/e	Rel. Intensity
217	1.7	67	2.6
216	13.0	66	6.1
215	1.7	65	18.3
214	13.9	64	7.8
		63	13.9
188	2.6	62	7.0
187	0.9	61	4.4
186	2.6		
185	0.9	57	3.5
		56	3.5
174	93.0	55	12.2
172	100.0	54	2.6
		53	24.4
136	4.4	52	20.0
135	16.5	51	40.0
134	2.6	50	21.7
		49	3.5
108	4.4	44	18.3
107	37.4	43	7.8
106	6.1	42	8.7
105	14.8	41	6.1
		40	4.4
95	2.6	39	43.5
94	4.4	38	19.1
93	6.1	37	8.7
92	7.8	36	8.7
91	32.2	32	27.8
90	2.6	30	0.9
89	5.2		
82	7.8		
81	4.4		
80	12.2		
79	29.5		
78	33.9		
77	73.0		
76	3.5		
75	3.5		
74	4.4		

Table IX. Mass Spectrum of 3,7-dibromo-3,5-cyclooctadiene-1,2-dione.

m/e	Rel. Intensity	m/e	Rel. Intensity	m/e	Rel. Intensity
296	0.06	147	1.3	85	0.6
294	0.12	146	0.9	84	0.3
292	0.06	145	7.6	83	0.4
		144	0.8	82	35.6
266	0.1	143	6.9	81	15.5
254	0.2	141	0.5	80	36.5
252	0.3	136	1.3	79	2.3
250	0.2	135	7.0	78	86.3
		134	25.0	77	100.0
220	0.3	133	4.5	76	16.3
217	0.5	132	0.9	75	6.0
216	4.8	131	0.6	74	8.5
215	8.4	130	0.4	73	3.0
214	5.9	129	0.3		
213	8.3	128	0.5	66	3.0
212	1.1	127	0.3	65	11.3
		122	0.5	64	9.0
198	0.6	119	2.5	63	17.5
196	0.5	118	0.7	62	7.8
194	0.4	117	2.4	61	4.8
189	0.3	116	0.4	56	4.0
188	2.8	115	0.4	55	6.8
187	14.1			54	1.8
186	8.1	109	1.0	53	16.9
185	5.3	108	1.5	52	25.3
		107	13.1	50	36.3
175	2.1	106	9.9	49	12.5
174	22.6	105	15.6	44	6.2
173	5.4	104	0.5	43	0.9
172	21.7	103	0.5	42	7.5
171	3.8	102	0.3	41	3.0
170	0.3	101	0.2	40	9.8
169	0.3			39	36.2
168	0.3	95	9.4	38	25.0
167	0.3	94	1.7	37	12.5
166	0.5	93	3.6	36	1.7
165	0.9	92	5.0	32	75.0
160	0.8	91	1.3		
159	8.5	90	1.4		
158	5.0	89	3.1		
157	8.8	88	0.4		
156	4.5	87	0.6		
155	6.3	86	0.7		

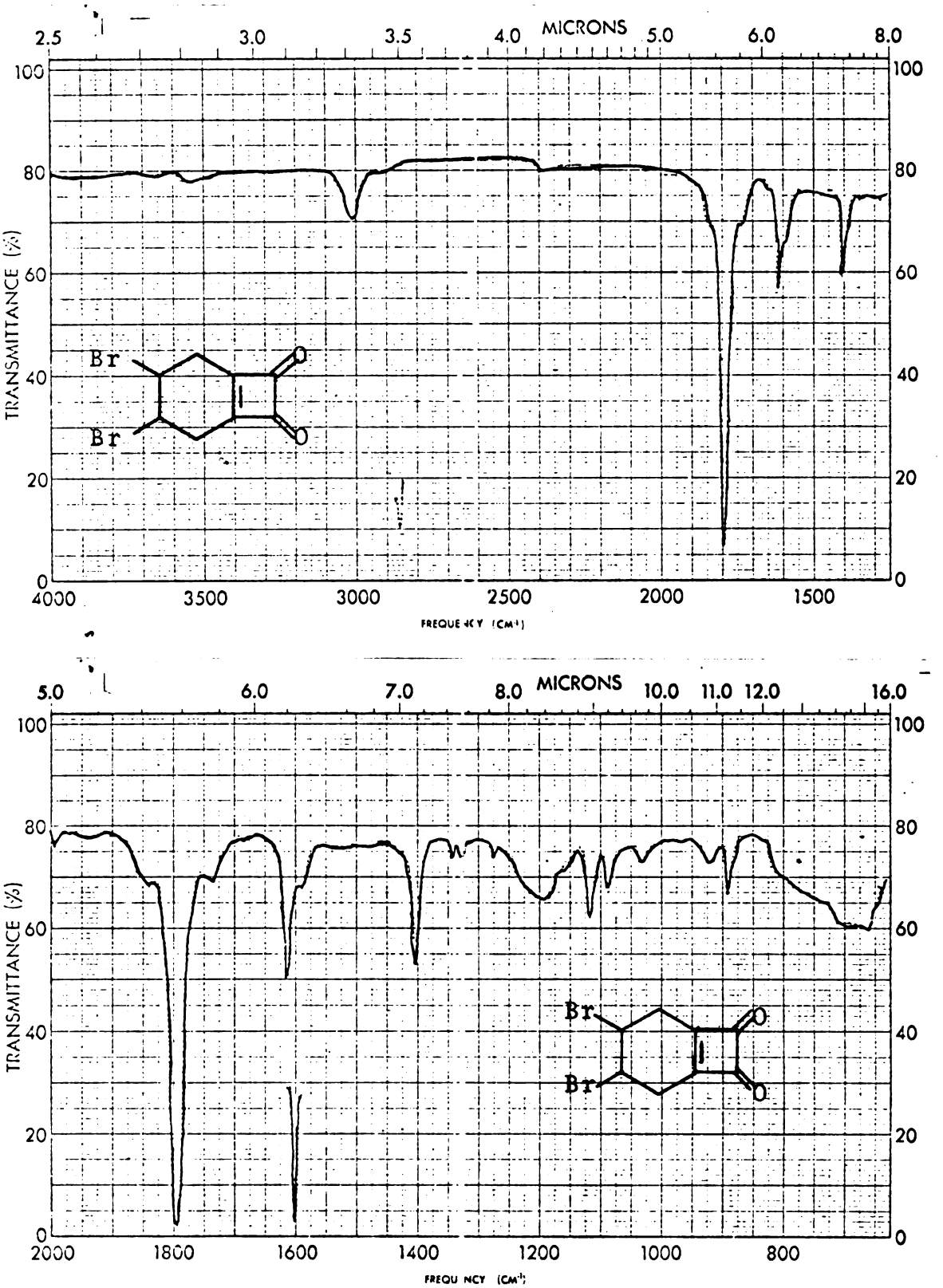

Figure 1. Infrared spectrum of 3,4-dibromobicyclo-[4.2.0]-6-octene-7,8-dione 61 ($CHCl_3$)

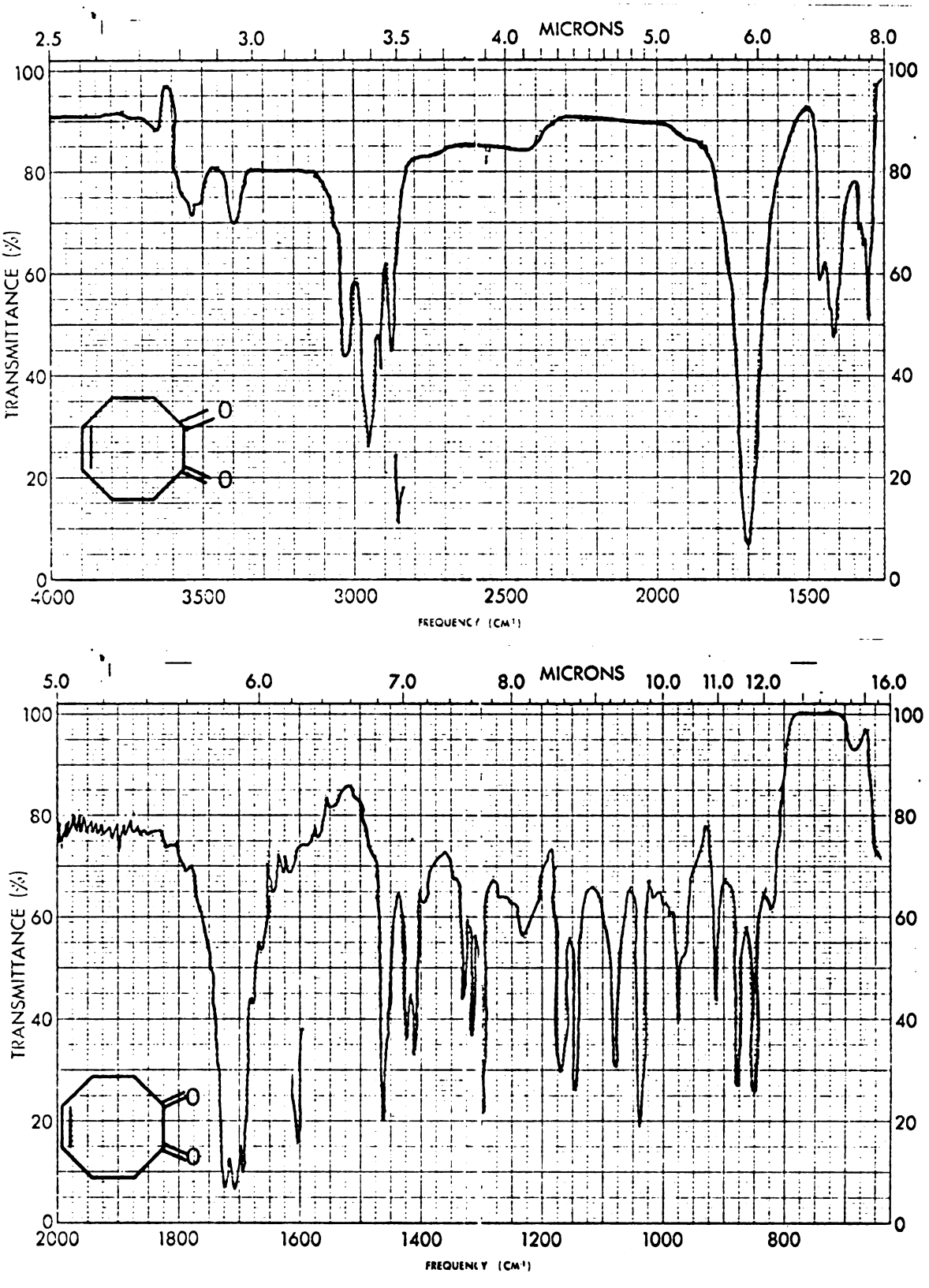

Figure 2. Infrared spectrum of 5-cyclooctene-1,2-dione 69 ($CHCl_3$)

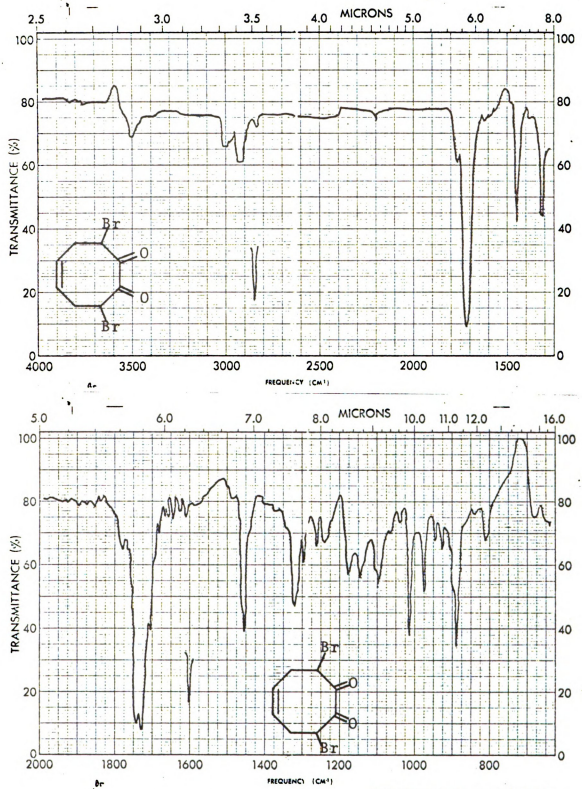

Figure 3. Infrared spectrum of *trans*-3,8-dibromo-5-cyclooctene-1,2-dione **85** ($CHCl_3$)

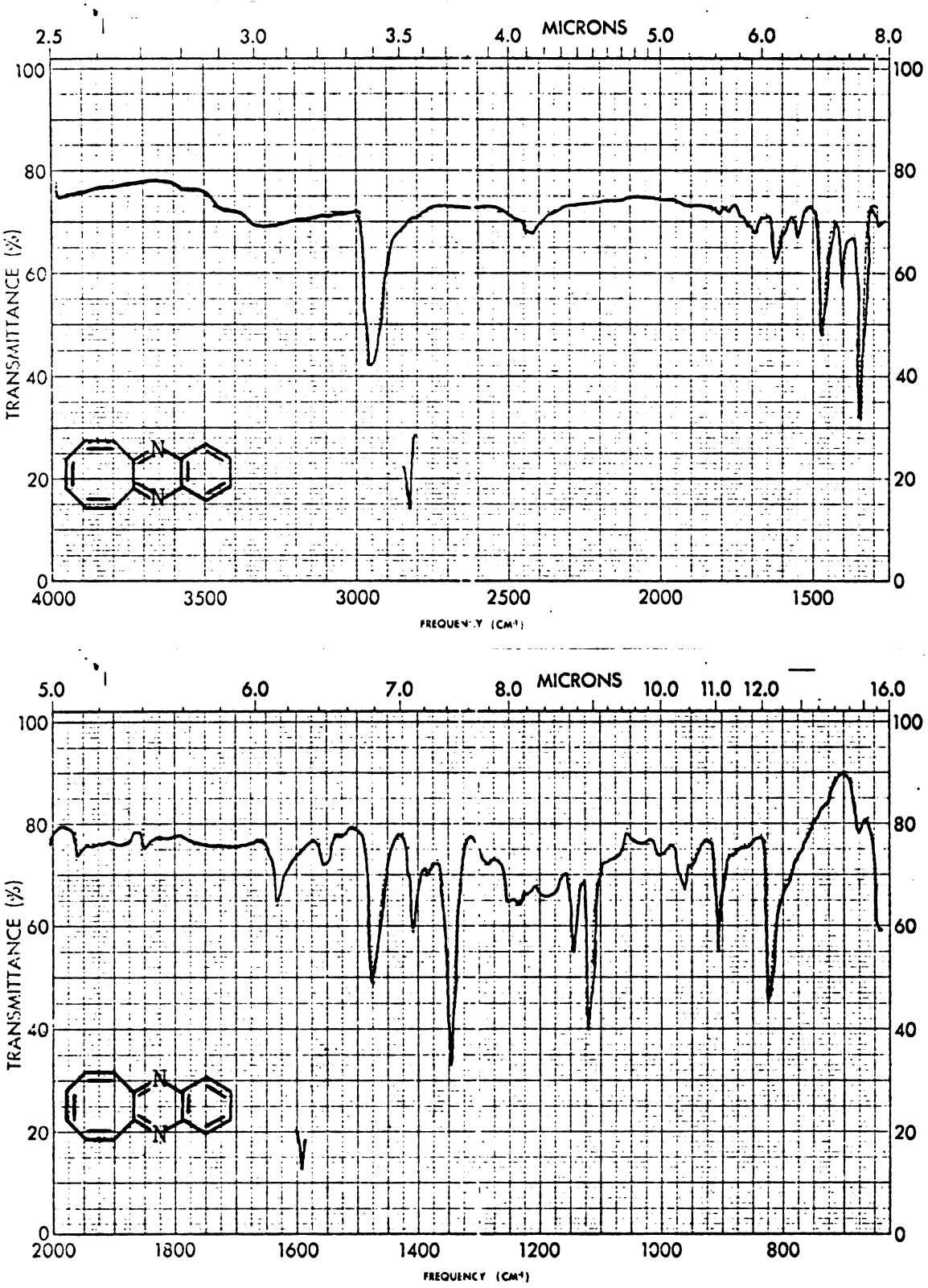

Figure 4. Infrared spectrum of 10,11-benzo-9,12-diazabicyclo[6.4.0]-2,4,6,8,10,12-dodecahexaene 89 ($CHCl_3$)

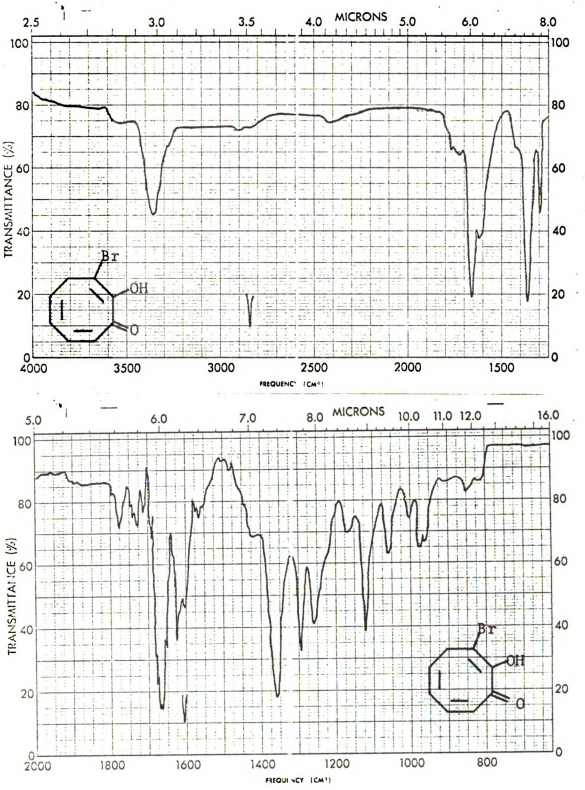

Figure 5. Infrared spectrum of 3-bromo-2-hydroxy-2,5,7-cyclooctatrienone $\underset{\sim}{\nu}$ ($CHCl_3$)

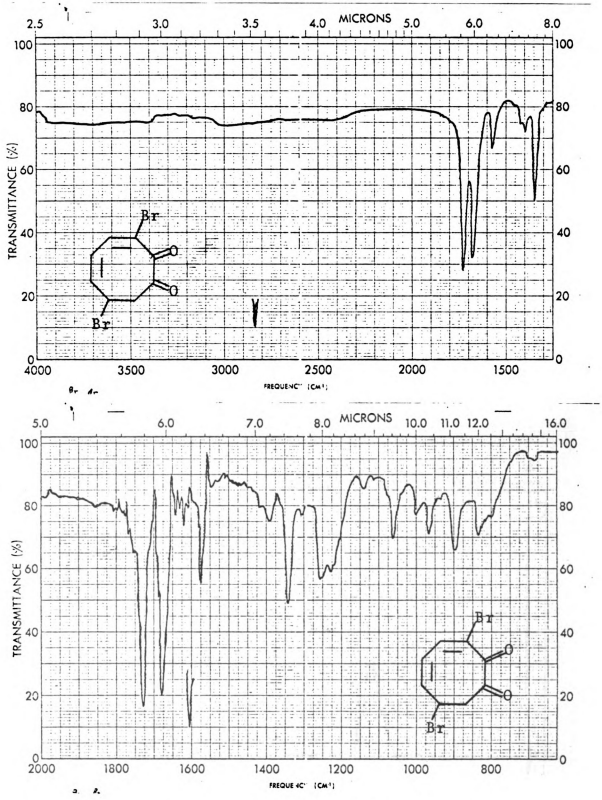

Figure 6. Infrared spectrum of 3,7-dibromo-3,5-cyclooctadiene-1,2-dione 125 ($CHCl_3$)

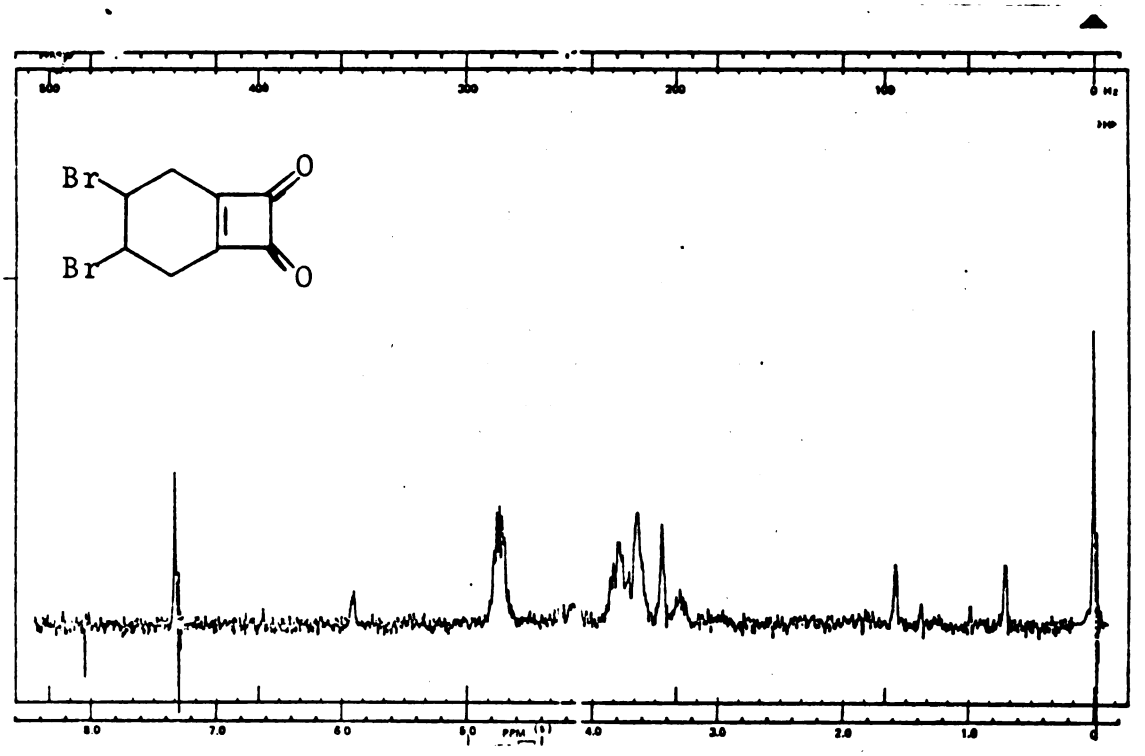

Figure 7. Nmr spectrum of 3,4-dibromobicyclo[4.2.0]-6-octene-7,8-dione 61 ($CDCl_3$)

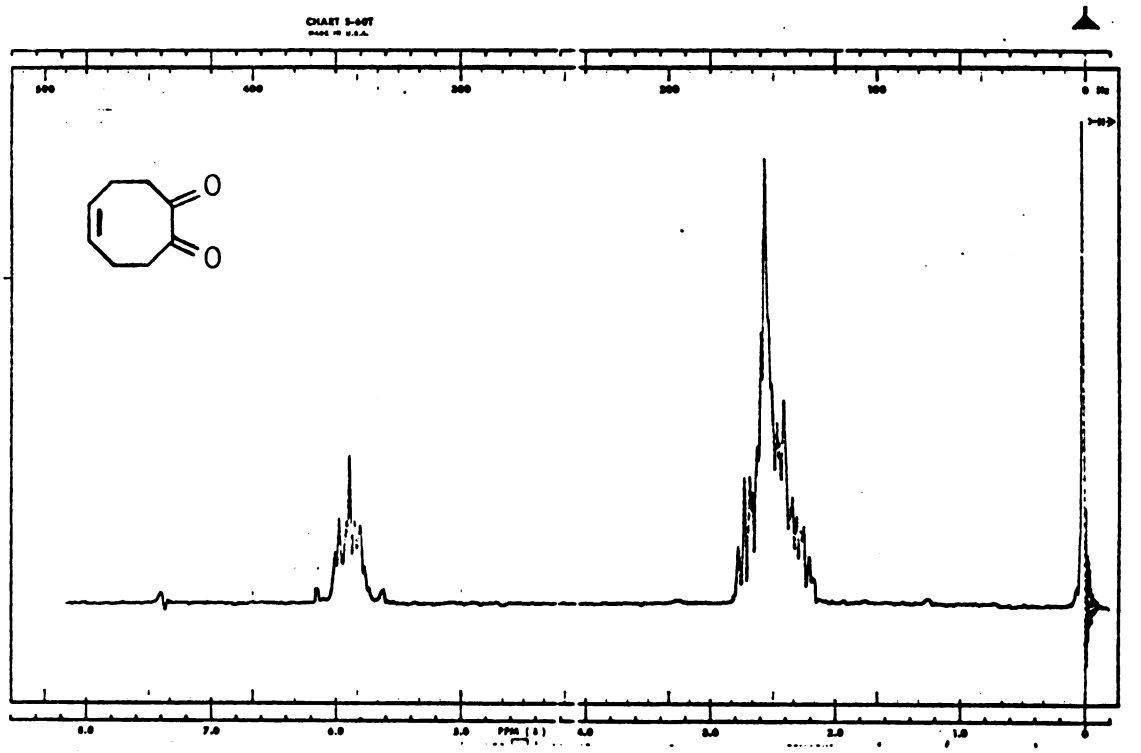

Figure 8. Nmr spectrum of 5-cyclooctene-1,2-dione 69 ($CDCl_3$)

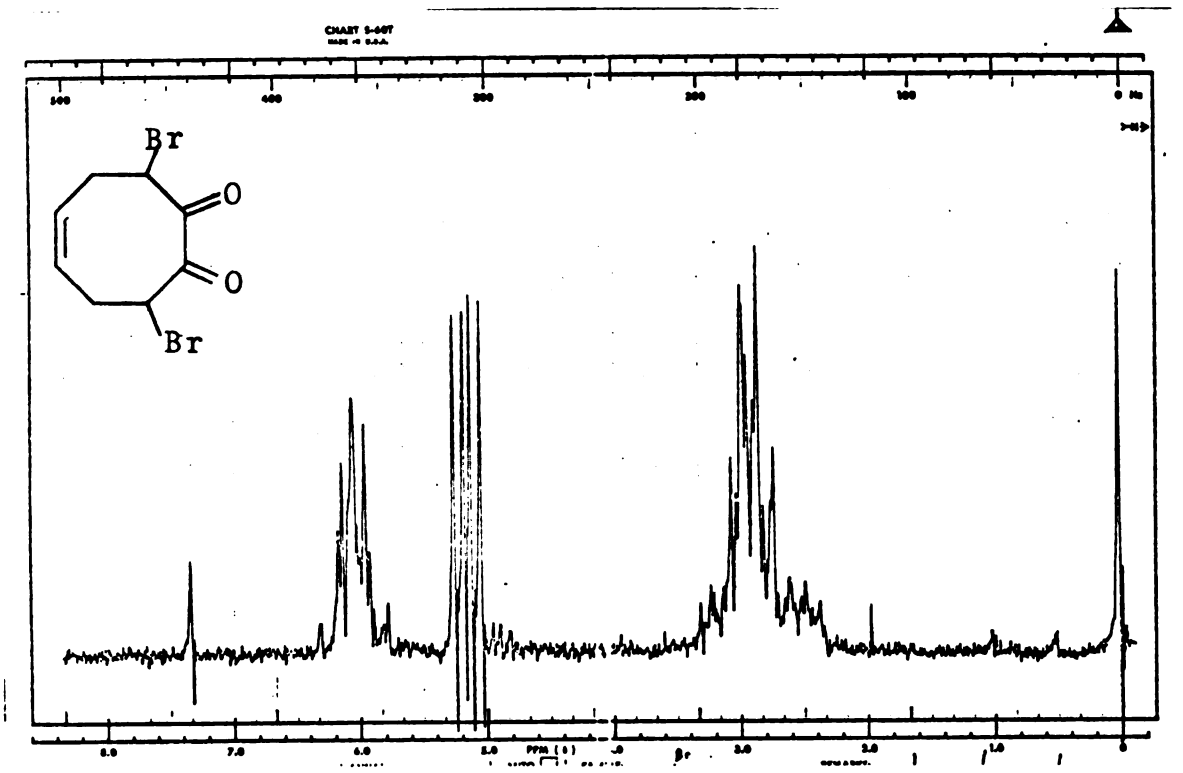

Figure 9. Nmr spectrum of *trans*-3,8-dibromo-5-cyclooctene-1,2-dione 85 ($CDCl_3$)

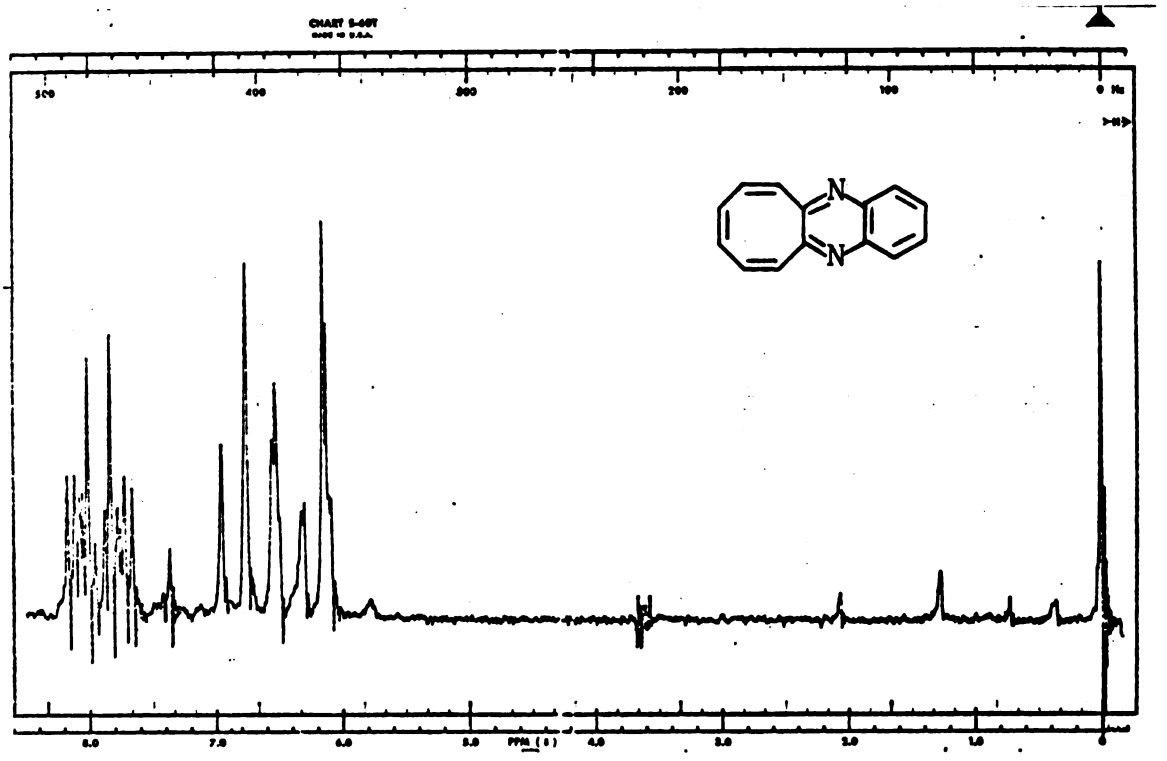

Figure 10. Nmr spectrum of 10,11-benzo-9,12-diazabicyclo [6.4.0]-2,4,6,8,10,12-dodecahexaene 89 ($CDCl_3$)

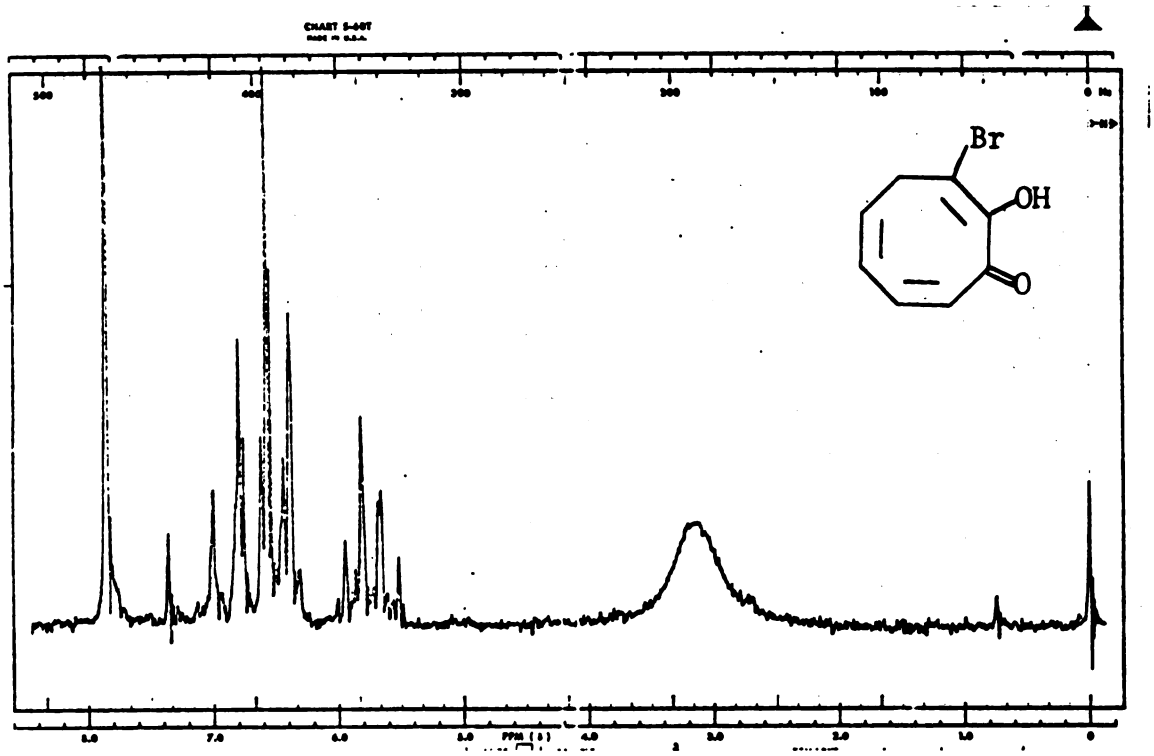

Figure 11. Nmr spectrum of 3-bromo-2-hydroxy-2,5,7-cyclooctatrienone 93 ($CDCl_3$)

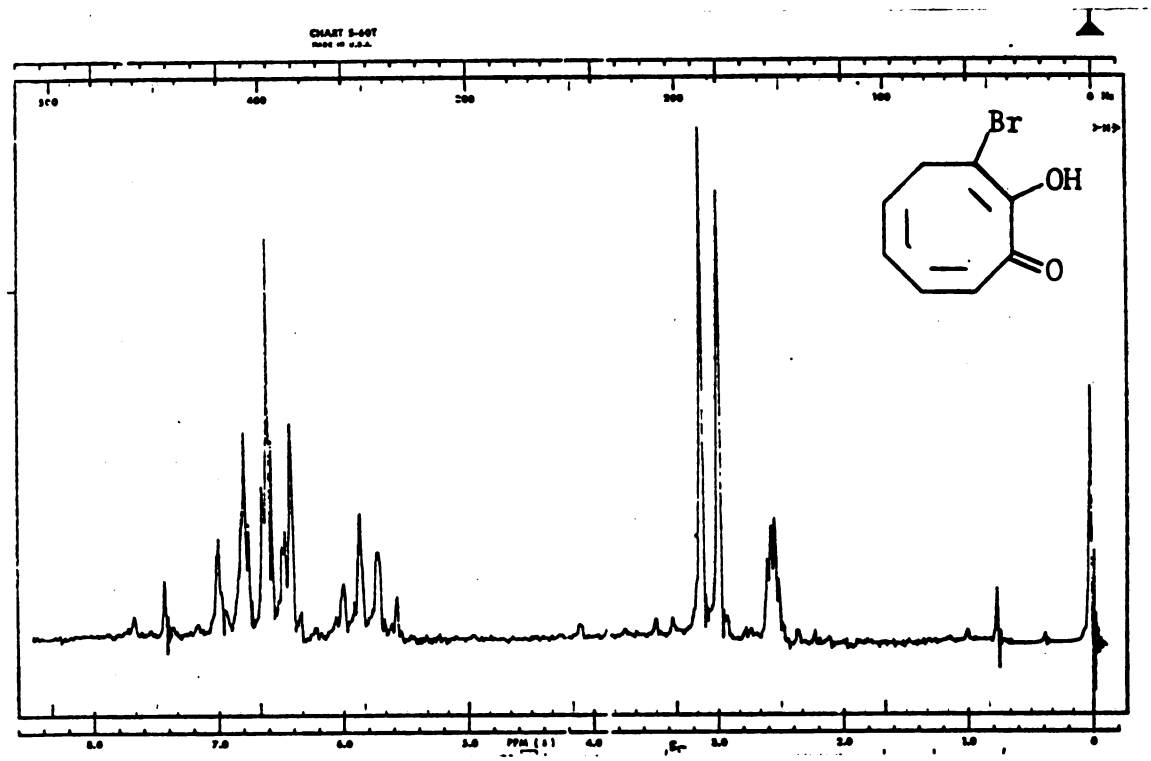

Figure 12. Nmr spectrum of 3-bromo-2-hydroxy-2,5,7-cyclooctatrienone 93 (DMSO-d_6)

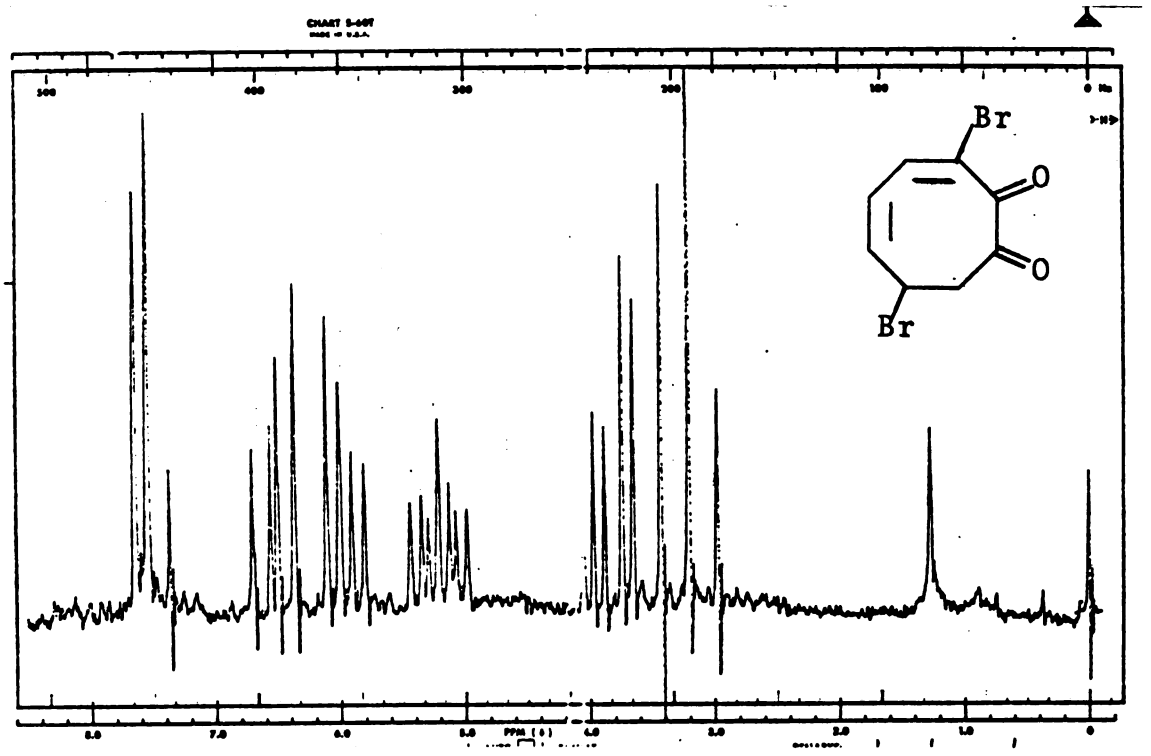

Figure 13. Nmr spectrum of 3,7-dibromo-3,5-cyclooctadiene-1,2-dione 125 ($CDCl_3$)